European Urology Today

EAU23 Congress News

38th Annual Congress of the European Association of Urology

Vol. 35 No. 1 - 10-13 March 2023

Springtime in Milan: Host to Europe's largest urology event

38th Annual Congress marks 50th Anniversary and change of Secretary General

By Chris Chapple
EAU Secretary General, 2015-2023

Welcome to Milan! We are returning to Italy's fashion capital almost exactly ten years to the day that we held our 28th Annual Congress here. Much has changed in the meantime, so much so that we are also glad to be back to a springtime congress for the first time in four years.

EAU23 is notable too in that it marks the end of our Anniversary Year, during which we have celebrated our fifty years as a urological society for all of Europe. Every participant in Milan will receive a copy of *EAU:50*, a special commemorative publication that looks at the past, present and future of the EAU at fifty.

In conjunction with EAU23, the EAU History Office is holding the 7th International Congress on the History of Urology. The day-long programme will examine some highlights in urology that coincide with the EAU's five decades of excellence. The congress marks the conclusion of the EAU's 50th Anniversary celebrations that started in Amsterdam at EAU22.

Be sure to drop by on the first day of the congress if you are interested in insights on fifty years of the EAU but more importantly, fifty years of urology from the people who shaped the field. Admission is free for all EAU23 delegates.

Scientific highlights
For EAU23 we received a very healthy number of abstracts, allowing us to select the 1500 highest-quality submissions for a range of interesting poster and video sessions that will take place throughout the congress.

Every congress day starts with two plenary sessions that cover the biggest topics in current-day urology. These sessions feature ground-breaking research, and state-of-the-art lectures by the undoubted experts in the field. The plenary sessions are followed by related game-changing sessions that offer the very latest, up-to-the-minute developments and trial results.

On the first day of the congress, apart from the aforementioned History Congress, we are organising the EAU23 Patient Day. Our Patient Office is holding its second in-person Patient Day after a successful debut in Amsterdam. Patient Day offers a platform where healthcare professionals and patient advocates can meet to share perspectives and experiences. Patient voices will also be represented throughout in the EAU23 Scientific Programme.

The recently-renovated Allianz MiCo, the largest congress venue in Europe, will host EAU23.

"The congress marks the conclusion of the EAU's 50th Anniversary celebrations that started in Amsterdam at EAU22."

Friday also features the Urology Beyond Europe sessions, where we pair up for joint sessions with other urological societies. Look forward to a range of unique topics and speakers at these sessions!

On Saturday, our focus turns to our younger colleagues. YUORday is a full-day programme by the Young Urologists Office and the European Society of Residents in Urology designed to meet the needs of urologists who are just starting out: information about scholarships and educational programmes, surgical techniques, getting into research and much more. We also have a redesigned live surgery programme with longer, simultaneous procedures and more opportunities for moderated interaction. The live surgery will come from four Milanese hospitals with expert surgeons from all over the world.
Following the plenary session on early detection, Sunday is "prostate cancer day" at EAU23 with four related thematic sessions. As on every congress day, there will be a range of courses on offer from the European School of Urology. We end EAU23 on Monday with two final plenary sessions, thematic and abstract sessions, and the "Best of EAU23" souvenir session.

Change in leadership
EAU23 will also be notable for me and for the future of our Association as at the General Assembly I will be formally stepping down as Secretary General after eight wonderful years. Our Secretary General-Elect since EAU22, Arnulf Stenzl (DE) will succeed me and lead the EAU in the coming years.

Arnulf and I have worked together closely in the past years when he joined the EAU Executive and before, when he led the Scientific Congress Office. He is a great colleague with a well-deserved international reputation as a superb clinician, a scientist and a surgeon. He has the expertise, experience, and knowledge, having previously run our SCO, to be an excellent person to lead this organisation as it enters its sixth decade. I certainly know he will do this extremely successfully.

I first attended the EAU Congress in Amsterdam in 1990. Almost exactly thirty years ago, I started getting involved in the EAU/EBU East West Programme, which would evolve into the European School of Urology. I became the ESU's chair in 1999 and joined the EAU Executive in 2004 as Adjunct Secretary General for Education.

I am very proud of the initiatives and Offices that we started during my tenure as Secretary General and I am pleased to leave behind a very robust organisation. We have a well-organised Central Office in the Netherlands, with a fantastic and dedicated crowd of people working for all the Offices and Sections. The Central Office means there is continuity across different periods of leadership. The strength of the EAU lies in the dedicated team of people working there.

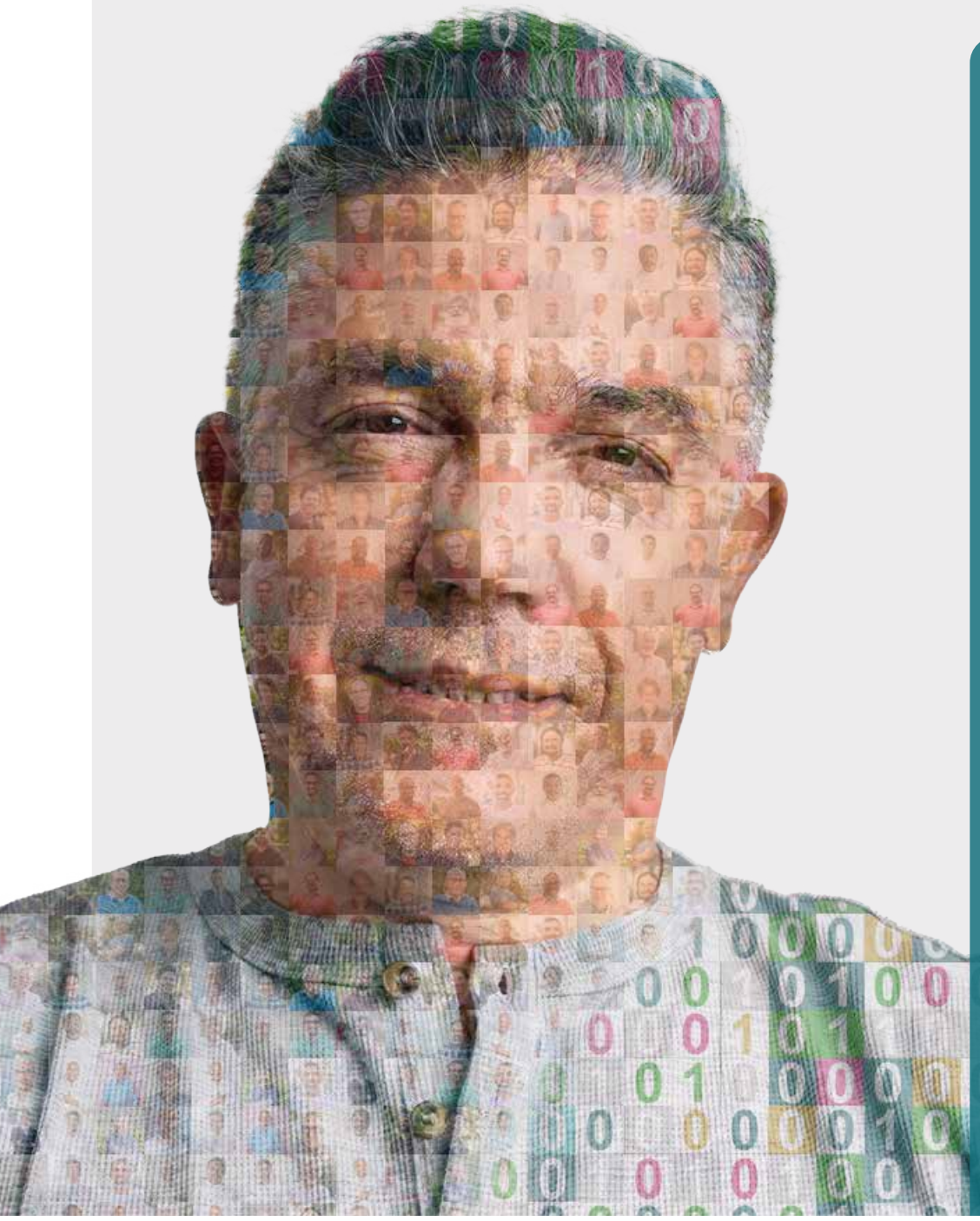
As urologists, we have a role as working doctors and surgeons; therefore, we work for the EAU part-time. But we obviously know we have a very professional, experienced, hard-working team of people who facilitate everything we do. The EAU is now one of the top, truly international societies. It's a pan-European association but with affiliations across the world.

Opening Ceremony
All in all, I think you can agree that we have a great programme to look forward to, with special thanks to the wonderful Scientific Congress Office under the leadership of Peter Albers.

I look forward to seeing you all in person and hereby invite you to join us in celebrating our colleagues who made a great contribution to our field during the EAU23 Opening Ceremony. See who will be honoured this year on pages 4 and 5 of this special Congress Edition of European Urology Today. Afterward the ceremony you are very welcome for a drink at the networking reception.
I hope you have a great congress!

Prof. Chapple and his successor as Secretary General, Prof. Arnulf Stenzl. Read more about the transition in EAU:50, which features in-depth interviews with both.

BPH Outcomes Study Educational Visualisation Tool



Discover more about how risk factors for disease progression interact and affect treatment response in individual profiles with moderate to severe LUTS/ BPH at the risk of progression.

Scan the QR codes to access the **BPH Outcomes Study** and associated **Educational Visualisation Tool** to understand the outcomes in different individual profiles

BPH Outcomes Study - Educational Visualisation Tool is intended for educational purposes and not for clinical use. The BPH tool is solely intended to inform healthcare professionals to help visualise and understand the results of the statistical modelling published by Gravas S *et al* 2022.
The BPH Tool has not been validated for and is not intended for clinical use with individual patients. It is not intended to substitute for medical advice or intended to drive or inform to take decisions with diagnosis or therapeutic purposes of any condition for any individual patients.

References: 1. Gravas S, *et al.* EAU Guidelines on the Management of Non-Neurogenic Male Lower Urinary Tract Symptoms (LUTS), incl. Benign Prostatic Obstruction (BPO), 2021. Available at: http://uroweb.org/guideline/treatment-of-non-neurogenic-maleluts/ Accessed January 2023. **2.** Avodart Italy SmPC Summary of Product Characteristics (SmPC) effective 22 October 2020. **3.** Combodart Italy SmPC Summary of Product Characteristics (SmPC) effective 22 October 2020.

Abbreviations: BPH, benign prostatic hyperplasia; LUTS/BPH, lower urinary tract symptoms secondary to benign prostatic hyperplasia.

In Italy the registered trade name for dutasteride is Avodart and for dutasteride-tamsulosin is Combodart.

Abbreviated Product Information – Avodart

Soft Capsules 0,5 mg
Prescription SSN
Class A*
Price € 11,78**

*Providing system: medicinal product subject to medical prescription (RR) ** Without prejudice to any reductions and/or modifications imposed authoritatively by the competent Health Authority.

Therapeutic Indications

Avodart is indicated for the treatment of moderate to severe symptoms of benign prostatic hyperplasia (BPH). Reduction of the risk of acute urinary retention and surgery with moderate to severe symptoms of benign prostatic hyperplasia

Posology and method of administration

Avodart can be administrated alone or in combination with the alpha blocker tamsulosin (0,4 mg). Adults (including the elderly): The recommended dose is one capsule (0.5 mg) taken orally per day. The capsules must be swallowed whole and must not be chewed or opened as contact with the contents of the capsule may cause irritation of the oropharyngeal mucosa. The capsules can be taken with or without food. Although early improvement can be seen, it may take up to 6 months before a response to treatment is achieved. No dose adjustment is required in the elderly. The most commonly observed adverse reactions include impotence, altered (decreased) libido, ejaculation disorder, breast disorder.

Full SmPC of AVODART (23 November 2017) for EU is available at - https://mri.cts-mrp.eu/portal/details?productnumber=SE/H/0304/001

Scan the QR code to access the Italian SmPC of Avodart

Abbreviated Product Information – Combodart

Hard capsules 0,5 mg
No prescription SSN
Class C*
Price € 32,70**

*Providing system: medicinal product subject to medical prescription (RR) ** Without prejudice to any reductions and/or modifications imposed authoritatively by the competent Health Authority.

Therapeutic Indications

Combodart is indicated for the treatment of moderate to severe symptoms of benign prostatic hyperplasia (BPH). Reduction of the risk of acute urinary retention and surgery with moderate to severe symptoms of benign prostatic hyperplasia

Posology and method of administration

The recommended dose of Combodart is one capsule (0.5 mg/0.4 mg) once a day.

When appropriate, Combodart can be used to replace dutasteride and tamsulosin hydrochloride used together in current dual therapy to simplify treatment.

When clinically appropriate, a direct switch from dutasteride or tamsulosin hydrochloride monotherapy to Combodart may be considered. The most commonly observed adverse reactions include dizziness, impotence, altered (decreased) libido, ejaculation disorder, breast disorder.

Full SmPC of COMBODART (23 November 2017) for EU is available at - https://mri.cts-mrp.eu/portal/details?productnumber=DE/H/2251/001

Scan the QR code to access the Italian SmPC of Combodart

For the use of registered medical practitioner or a Hospital or a Laboratory only. Avodart/Duodart is for use in men only. Avodart/Duodart trade marks are owned by or licensed to the GSK group of companies.

Adverse events should be reported. Reporting forms and information can be found at https://yellowcard.mhra.gov.uk/ or search for MHRA Yellowcard in the Google Play or Apple App Store.
Adverse events should also be reported to GlaxoSmithKline on 0800 221 441.

Submitted to AIFA on 23/01/2023
GlaxoSmithKline S.p.A. Viale dell'Agricoltura, 7 37135 Verona Italy

PM-GBL-DUT-ADVT-230001 | Date of preparation: January 2023.

Presenting the 2023 Congress Gift

In new book, History Office Chair explores cultural norms on modesty

Prof. Philip Van Kerrebroeck (Antwerp, BE) is the proud author of this year's Congress Gift book. We spoke to him about his newest publication.

Could you tell us, broadly speaking what your new book is about?

The 2023 Congress Gift *Cache-sexe: Covered, uncovered, discovered* delves into the heart of what are still controversial and emotionally charged issues in contemporary life: our genitals and the way we cover them.

Although taboos around nudity and sex were largely eradicated in the second half of the 20th century, the genital area retains enigmatic aspects that make it a subject that is not often publicly discussed, let alone shown without reluctance. Therefore we can ask the question whether these are amongst the last elements of the human body to be uncovered and scrutinised? As an extension of these inhibitions, the cache-sexe is likewise a topic that is still approached with some hesitation.

This book aims to discuss the following questions: how do humans perceive their genitals? How are our genitals perceived by others? And why do humans need, and use, a cache-sexe to cover their genitals? I will discuss the various forms of genital coverings, from the apron to the tanga, but also their absence

Figure 1: A lonka-lonka, shell and natural pigments (ca. 1970), Western Australia, private collection.

Figure 2: Female cache-sexe (ca. 1960), Kirdi people, Cameroon, private collection.

in some situations and societies. Controversial types of cache-sexe will be addressed, as well as more subtle forms. The aim is to present a broad view of the topic, including medical, geographical, historical and anthropological perspectives. I elaborate on the meanings of the different forms of cache-sexe and refer to typical real-life examples, but also representations in various artworks and ritual objects, based on unique and sometimes hitherto unpublished documentation. (Fig.1) The daily use of the cache-sexe is illustrated with rare and even historic photographs. I also take a look at the present day and how we deal with the cache-sexe in the 21st century.

Is this a topic you have been interested in for a while or was there recent inspiration?

Indeed I have been interested in this topic for more than 40 years, and collected information, documentation and even examples of cache-sexe. (Fig.2) I have discovered that women and men of all times, ages, worldwide have been using some form of cache-sexe, but sometimes documentation and certainly examples are difficult to find. First of all these were utensils and hence once worn out, they were abandoned or thrown away. Secondly some types of cache-sexe were considered 'taboo' or indecent by early colonisers and hence destroyed.

Already for a long time I wanted to bring together the information I had accumulated all these years, and hence I am very grateful to the Executive of the EAU and the EAU History Office that they accepted my proposal for this book. I reviewed extensively the existing literature and interviewed several anthropologists that did field research, and curators of museums and collections worldwide with an interest in this topic. Furthermore I used the documentation I have accumulated on objects from my own collection. As a result this book presents information and several images that have never been published before.

In what ways can the urologist relate to the topic at hand?

The EAU's Secretary General Prof. Chris Chapple answers this question very well in his foreword to the book. He indicates "Cultural norms and sensitivities have always differed greatly, not just in terms of geography but also across time, and this book reminds us of how differently we experience nudity, shame and the covering of genitalia in different periods of human history and still do to this day. Many relevant aspects are addressed in this book: art, expression, shame, freedom, restriction and even religion."

He continues as follows with his personal appreciation of the book: "Short and long chapters have something to offer every reader, and make this a publication of general interest but also sometimes quite surprising and intriguing."

I hope that the EAU members attending the Annual Congress in Milan can appreciate the text and illustrations of *Cache-Sexe: Covered, uncovered, discovered!*

EAU Members with the right entitlements can collect their copy of *Cache-Sexe* at the EAU Booth, K36 in the Exhibition Hall (Blue Area).

Table of Contents

EAU23 Award Gallery

EAU Willy Gregoir Medal

L. Martínez-Piñeiro
Madrid, Spain

For a significant contribution to the development of the urological specialty in Europe

Previous Winners

2022	K-E. Andersson, Lund, Sweden
2020/21	M. Wirth, Dresden, Germany
2019	F. Hamdy, Oxford, United Kingdom
2018	V. Mirone, Naples, Italy
2017	P. Abrams, Bristol, United Kingdom
2016	W. Artibani, Verona, Italy
2015	L. Boccon-Gibod, Paris, France
2014	M. Pavone-Macaluso, Palermo, Italy
2013	C. Abbou, Creteil, France
2012	M. Marberger, Vienna, Austria
2011	U. Studer, Berne, Switzerland
2010	F. Debruyne, Nijmegen, The Netherlands
2009	P. Van Cangh, Brussels, Belgium †
2008	F. Pagano, Padua, Italy
2007	H. Frohmüller, Würzburg, Germany †
2006	A. Borkowski, Warsaw, Poland
2005	R. Turner Warwick, Exeter, United Kingdom †
2004	F. Schröder, Rotterdam, The Netherlands
2003	A. Le Duc, Paris, France
2002	R. Küss, Paris, France †
2001	J. Blandy, London, United Kingdom †
2000	H. Marberger, Innsbruck, Austria †
1999	T. Hald, Copenhagen, Denmark †
1998	F. Solé-Balcells, Barcelona, Spain †
1996	A. Steg, Paris, France †
1994	L. Giuliani, Genoa, Italy †
1994	G. Chisholm, Edinburgh, United Kingdom †
1992	J. Martínez-Piñeiro, Madrid, Spain
1990	R. Hohenfellner, Mainz, Germany
1988	H. Hopkins, Reading, United Kingdom †

EAU Frans Debruyne Life Time Achievement Award

J. Catto
Sheffield, United Kingdom

For a longstanding and important contribution to the activities and development of the EAU

Previous Winners

2022	J. Palou, Barcelona, Spain
2020/21	H. Van Poppel, Leuven, Belgium
2019	F. Montorsi, Milan, Italy
2018	D. Jacqmin, Strasbourg, France
2017	P-A. Abrahamsson, Malmö, Sweden
2016	P. Teillac, Toulouse, France
2015	H. Villavicencio, Barcelona, Spain
2014	L. Denis, Antwerp, Belgium †
2013	J. Breza, Bratislava, Slovakia
2012	R. Hautmann, Neu-Ulm, Germany
2011	A. Le Duc, Paris, France
2010	R. Vela Navarrete, Madrid, Spain
2009	J. Mattelaer, Kortrijk, Belgium
2008	R. Ackermann, Düsseldorf, Germany †
2007	L. Boccon-Gibod, Paris, France
2006	C. Schulman, Brussels, Belgium

EAU Crystal Matula Award

J. Gómez Rivas
Madrid, Spain

For a young promising European urologist

Previous Winners

2022	V. Kasivisvanathan London, United Kingdom
2021	V. Phé, Paris, France
2020	D. Tilki, Hamburg, Germany
2019	M. Albersen, Leuven, Belgium
2018	S. Silay, Istanbul, Turkey
2017	C. Gratzke, Munich, Germany
2016	A. Briganti, Milan, Italy
2015	M. Rouprêt, Paris, France
2014	S. Shariat, Vienna, Austria
2013	P. Boström, Turku, Finland
2012	P. Bastian, Düsseldorf, Germany
2011	S. Joniau, Leuven, Belgium
2010	J. Catto, Sheffield, United Kingdom
2009	M. Ribal Caparros, Barcelona, Spain
2008	V. Ficarra, Padua, Italy
2007	M. Michel, Mannheim, Germany
2006	A. De La Taille, Creteil, France
2005	M. Matikainen, Tampere, Finland
2004	P. Mulders, Nijmegen, The Netherlands
2003	B. Malavaud, Toulouse, France
2002	M. Kuczyk, Hanover, Germany
2001	B. Djavan, Vienna, Austria
2000	A. Zlotta, Toronto, Canada
1999	G. Thalmann, Berne, Switzerland
1998	F. Montorsi, Milan, Italy
1996	F. Hamdy, Oxford, United Kingdom

Supported by LABORIE

EAU Innovators in Urology Award

P. Wiklund
Stockholm, Sweden

For inventions and clinical contributions which have had a major impact on influencing the treatment and/or diagnosis of a urological disease

Previous Winners

2022	Y. Fradet, Quebec, Canada
2020/21	J. Barentsz, Nijmegen, The Netherlands
2019	P. Alken, Mannheim, Germany
2017	R. Turner-Warwick, Exeter, United Kingdom †
2016	J. Gil-Vernet Vila, Barcelona, Spain †
2015	S. Horenblas, Amsterdam, The Netherlands
2014	R. Gaston, Bordeaux, France
2013	U. Studer, Berne, Switzerland
2012	J. Wickham, Dorking, United Kingdom †
2011	C. Chaussy, Munich, Germany

Best Papers published in Urological Literature Awards

Best Paper on Fundamental Research

Determinants of anti-PD-1 response and resistance in clear cell renal cell carcinoma
Cancer Cell 39 (2021); https://doi.org/10.1016/j.ccell.2021.10.001

L. Au, E. Hatipoglu, M. Robert de Massy, K. Litchfield, G. Beattie, A. Rowan, D. Schnidrig, R. Thompson, F. Byrne, S. Horswell, N. Fotiadis, S. Hazell, D. Nicol, S. Shepherd, A. Fendler, R. Mason, L. Del Rosario, K. Edmonds, K. Lingard, S. Sarker, M. Mangwende, E. Carlyle, J. Attig, K. Joshi, I. Uddin, P. Becker, M. Werner Sunderland, A. Akarca, I. Puccio, W. Yang, T. Lund, K. Dhillon, M. Vasquez, E. Ghorani, H. Xu, C. Spencer, J. López, A. Green, U. Mahadeva, E. Borg, M. Mitchison, D. Moore, I. Proctor, M. Falzon, L. Pickering, A. Furness, J. Reading, R. Salgado, T. Marafioti, M. Jamal-Hanjani, on behalf of the PEACE Consortium, G. Kassiotis, B. Chain, J. Larkin, C. Swanton, S. Quezada, S. Turajlic (London, Sutton, United Kingdom; Bizkaia, Spain; Melbourne, Australia; Antwerp, Belgium)

Best Paper on Clinical Research

Neoadjuvant Pembrolizumab and Radical Cystectomy in Patients with Muscle-Invasive Urothelial Bladder Cancer: 3-Year Median Follow-Up Update of PURE-01 Trial
Clin Cancer Res (2022); https://doi.org/10.1158/1078-0432.CCR-22-2158

G. Basile, M. Bandini, E. Gibb, J. Ross, D. Raggi, L. Marandino, T. Costa de Padua, E. Crupi, R. Colombo, M. Colecchia, R. Lucianò, L. Nocera, M. Moschini, A. Briganti, F. Montorsi, A. Necchi (Milan, Italy; Vancouver, Canada; Massachusetts, New York, United States of America)

European Urology® Awards

Best Scientific Paper

Stereotactic Radiotherapy and Short-course Pembrolizumab for Oligometastatic Renal Cell Carcinoma—The RAPPORT Trial
European Urology; Volume 81, Issue 4, P364-372, April 1, 2022

S. Siva, M. Bressel, S. Wood, M. Shaw, S. Loi, S. Sandhu, B. Tran, A. Azad, J. Lewin, K. Cuff, H. Liu, D. Moon, J. Goad, L-M. Wong, M. LimJoon, J. Mooi, S. Chander, D. Murphy, N. Lawrentschuk, D. Pryor (Melbourne, Brisbane, Australia)

Supported by ELSEVIER

Best Scientific Paper on Fundamental Research

A Phase 2 Trial of the Effect of Antiandrogen Therapy on COVID-19 Outcome: No Evidence of Benefit, Supported by Epidemiology and In Vitro Data
European Urology; Volume 81, Issue 3, P285-293, March 1, 2022

K. Welén, E. Rosendal, M. Gisslén, A. Lenman, E. Freyhult, O. Fonseca-Rodríguez, D. Bremell, J. Stranne, Å. Balkhed, K. Niward, J. Repo, D. Robinsson, A. Henningsson, J. Styrke, M. Angelin, E. Lindquist, A. Allard, M. Becker, S. Rudolfsson, R. Buckland, C. Carlsson, A. Bjartell, A. Nilsson, C. Ahlm, A-M. Connolly, A. Överby, A. Josefsson (Gothenburg, Umea, Uppsala, Lingkoping, Jonkoping, Malmo, Sweden)

Supported by ELSEVIER

Best Scientific Paper on Clinical Research

Circumcision and Risk of Febrile Urinary Tract Infection in Boys with Posterior Urethral Valves: Result of the CIRCUP Randomized Trial
European Urology; Volume 81, Issue 1, P64-72, January 1, 2022

L. Harper, T. Blanc, M. Peycelon, J. Michel, M. Leclair, S. Garnier, V. Flaum, A. Arnaud, T. Merrot, E. Dobremez, A. Faure, L. Fourcade, M. Poli-Merol, Y. Chaussy, O. Dunand, F. Collin, L. Huiart, C. Ferdynus, F. Sauvat (Saint Denis de La Réunion, Bordeaux, Paris, Nantes, Montpellier, Rennes, Marseille, Limoges, Reims, Besançon, Saint-Pierre, France)

Supported by ELSEVIER

European Urology® Awards

Best Scientific Paper on Robotic Surgery

Robot-assisted Prostate-specific Membrane Antigen–radioguided Salvage Surgery in Recurrent Prostate Cancer Using a DROP-IN Gamma Probe: The First Prospective Feasibility Study
European Urology; Volume 82, Issue 1, P97-105, July 1, 2022

H. de Barros, M. van Oosterom, M. Donswijk, J. Hendrikx, A. Vis, T. Maurer, F. van Leeuwen, H. van der Poel, P. van Leeuwen (Amsterdam, Leiden, The Netherlands; Hamburg, Germany)

Supported by the VATTIKUTI FOUNDATION

Resident's Corner Award (2) for the Best Scientific Paper by a Resident

First-in-human Intravesical Delivery of Pembrolizumab Identifies Immune Activation in Bladder Cancer Unresponsive to Bacillus Calmette-Guérin
European Urology; Volume 82, Issue 6, P602-610, Dec. 1, 2022

K. Meghani, L. Cooley, B. Choy, M. Kocherginsky, S. Swaminathan, S. Munir, R. Svatek, T. Kuzel, J. Meeks (Chicago, San Antonio, United States of America)

Updating and Integrating Core Outcome Sets for Localised, Locally Advanced, Metastatic, and Nonmetastatic Castration-resistant Prostate Cancer: An Update from the PIONEER Consortium
European Urology; Volume 81, Issue 5, P503-514, May 01, 2022

K. Beyer, L. Moris, M. Lardas, M. Omar, J. Healey, S. Tripathee, G. Gandaglia, L. Venderbos, E. Vradi, T. van den Broeck, P-P. Willemse, T. Antunes-Lopes, L. Pacheco-Figueiredo, S. Monagas, F. Esperto, S. Flaherty, Z. Devecseri, T. Lam, P. Williamson, R. Heer, E. Smith, A. Asiimwe, J. Huber, M. Roobol, J. Zong, M. Mason, P. Cornford, N. Mottet, S. MacLennan, J. N'Dow, A. Briganti, S. MacLennan, M. Van Hemelrijck , on behalf of the PIONEER Consortium (London, Aberdeen, Liverpool, Newcastle-upon-Tyne, Cardiff, United Kingdom; Leuven, Belgium; Athens, Greece; Milan, Rome, Italy; Rotterdam, Utrecht, Arnhem, The Netherlands; Berlin, Dresden, Germany; Porto, Braga, Portugal; Leon, Spain; Paris, St. Etienne, France; Massachusetts, New Jersey, United States of America)

Platinum Awards

M. Albersen, Leuven, Belgium
J-N. Cornu, Rouen, France
T. Morgan, Ann Arbor, United States of America
A. Mottrie, Melle, Belgium
G. Novara, Padova, Italy
A. Vickers, New York, United States of America

Best Abstract Awards Oncology

First Prize

Proteomic profiling of muscle invasive bladder cancer treated with neoadjuvant chemotherapy
Abstract Nr. AM23-2797

A. Contreras-Sanz, M. Reike, G. Negri, Z. Htoo, S. Spencer Miko, K. Nielsen, M. Roberts, J. Scurll, K. Ikeda, G. Wang, R. Seiler, G. Morin, P. Black (Vancouver, Canada)

Second Prize

The Stockholm3 prostate cancer screening trial (STHLM3): An interim analysis of mortality results after 6.5 years of follow-up
Abstract Nr. AM23-3772

C. Micoli, A. Crippa, A. Discacciati, H. Vigneswaran, T. Palsdottir, M. Clements, M. Aly, J. Adolfsson, W. Fredrik, P. Wiklund, T. James, J. Lindberg, H. Grönberg, L. Egevad, T. Nordström, M. Eklund (Solna, Sweden)

EAU23 Award Gallery

EAU Hans Marberger Award

R. Campi
Florence, Italy

For the best European paper published on Minimally Invasive Surgery in Urology

Robotic Versus Open Kidney Transplantation from Deceased Donors: A Prospective Observational Study. *European Urology 39 (2022) 36–46; https://doi.org/10.1016/j.eururo.2022.03.007*

Previous Winners

2022	A. Martini, Milan Italy
2021	A. Gallioli, Barcelona, Spain
2020	A. Larcher, Milan, Italy
2019	G. Simone, Rome, Italy
2018	D. Dalela, Detroit, United States of America
2017	R. Autorino, Cleveland, United States of America
2016	M. Gundeti, Chicago, IL, United States of America
2015	S. Tyritzis, Athens, Greece
2014	C. Netsch, Hamburg, Germany
2013	J. Rassweiler, Heilbronn, Germany
2012	A. Alcaraz, Barcelona, Spain
2011	M. Rouprêt, Paris, France
2010	M. Marszalek, Vienna, Austria
2009	H. Jung, Fredericia, Denmark
2006	J. Grosse, Aachen, Germany
2004	E. Pieras Ayala, Barcelona, Spain

Supported by KARL STORZ SE & CO.KG

EAU Prostate Cancer Research Award

E. Ventimiglia
Milan, Italy

For the best paper published on clinical or experimental studies in prostate cancer

Long-term Outcomes Among Men Undergoing Active Surveillance for Prostate Cancer in Sweden. *JAMA Network Open (2022); https://doi:10.1001/jamanetworkopen.2022.31015*

Previous Winners

2022	T. Nordström, Stockholm, Sweden
2021	W. Fendler, Essen, Germany
2020	D. Osses, Rotterdam, The Netherlands
2019	V. Kasivisvanathan, London, United Kingdom
2018	H. Ahmed, London, United Kingdom
2017	M. Shiota, Fukuoka, Japan
2016	J. Pencik, Vienna, Austria
2015	M. Spahn, Berne, Switzerland
2014	Z. Culig, Innsbruck, Austria
2013	I. Ahmed, Glasgow, United Kingdom

Supported by the FRITZ H. SCHRÖDER FOUNDATION

New EAU Honorary Members

For an important influence on European urology

A. Chiu
Taipei, Taiwan

C. Evans
Sacramento, United States of America

H. Haas
Heppenheim, Germany

A. Rodríguez
Winston Salem, United States of America

M. Roobol
Rotterdam, The Netherlands

A. de la Taille
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Best Abstract Awards Non-Oncology

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Similar artefact susceptibility for water- and air-filled urodynamic systems: Results from a randomized controlled non-inferiority trial
Abstract Nr. AM23-4013

M. Kasten, O. Gross, M. Wettstein, C. Anderson, V. Birkhäuser, J. Borer, M. Koschorke, S. Mccallin, U. Mehnert, H. Sadri, L. Stächele, T. Kessler, L. Leitner (Zürich, Switzerland)

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Multi-center, prospective, single arm, pivotal study to evaluate the efficacy and safety of robotic-assisted surgery easyuretero-100 in patients in need of retrograde intrarenal surgery
V040

S. Cho, J. Kim, B. Cheon, J. Han, D-S. Kwon, J. Lee (Seoul, South Korea)

Second Prize

Robotic augmentation cystoplasty: 1-year outcome of the anterior and posterior approaches
V083

C. Yee, P. Lam, Y. Hong, P. Lai, Y. Tam, T. Ng, S. Yuen, M. Tam, C. Chan, K. Lo, J. Teoh, P. Chiu, C. Ng (Hong Kong, China)

Third Prize

Technique and outcomes from prostate capsule-sparing during robotic male cystectomy
V016

A. Ta, J. Olphert, W. Tan, M. Alkhamees, G. Shaw, A. Sridhar, J. Kelly (London, United Kingdom)

Best Abstracts by Residents-in-Urology Awards

First Prize

Global variation in the quality of multiparametric magnetic resonance imaging of the prostate from the PRIME Trial (the GLIMPSE Study)
Abstract Nr. AM3-3336

A. Ng, F. Giganti, A. Asif, V. Chan, M. Rossiter, A. Nathan, P. Khetrapal, L. Dickinson, S. Punwani, C. Brew-Graves, A. Freeman, M. Emberton, C. Moore, C. Allen, V. Kasivisvanathan, Q. Prime (London, United Kingdom)

Second Prize

Proximal urethrostomy (PU) versus urethroplasty (U) for complex urethral strictures (CUS)
Abstract Nr. AM23-0748

N. Rahav, M. Udah, S. Cohen, B. Chertin, O. Shenfeld (Jerusalem, Israel)

Third Prize

Prostate cancers detected in the PSA interval 1.8-3 ng/mL - results from the Göteborg 2 prostate cancer screening trial
Abstract Nr. AM23-1041

F. Möller, M. Månsson, J. Wallström, M. Hellström, J. Hugusson, R. Arnsrud Godtman (Skövde, Gothenburg, Sweden)

Young Academic Urologists Awards

Best Paper by YAU

Three-dimensional Model-assisted Minimally Invasive Partial Nephrectomy: A Systematic Review with Meta-analysis of Comparative Studies

F. Piramide, K. Kowalewski, G. Cacciamani, I. Rivero Belenchon, M. Taratkin, U. Carbonara, M. Marchioni, R. De Groote, S. Knipper, A. Pecoraro, F. Turri, P. Dell'Oglio, S. Puliatti, D. Amparore, G. Volpi, R. Campi, A. Larcher, A. Mottrie, A. Breda, A. Minervini, A. Ghazi, P. Dasgupta, A. Gozen, R. Autorino, C. Fiori, M. Di Dio, J. Gomez Rivas, F. Porpiglia, E. Checcucci (Turin, Bari, Chieti, Peschiera del Garda, Modena, Milan, Florence, Cosenza, Italy; Arnhem, The Netherlands; Mannheim, Hamburg, Germany; Seville, Barcelona, Madrid, Spain; Moscow, Russia; Aalst, Melle, Belgium; New York, Virginia, United States of America; London, United Kingdom; Edirne, Turkey)

Best Abstract by YAU

Can we rely on available models to identify candidates for extended Pelvic Lymph Node Dissection (ePLND) in men staged with PSMA-PET? External validation of the Briganti nomograms and development of a novel tool to identify optimal candidates for ePLND

G. Gandaglia, D. Robesti, L. Bianchi, R. Schiavina, E. Brunocilla, L. Afferi, A. Mattei, F. Zattoni, P. Rajwa, S. Shariat, C. Kesch, J. Sierra, P. Gontero, G. Marra, H. Guo, J. Gomez Rivas, J. Zhuang, D. Amparore, F. Dal Moro, F. Porpiglia, C. Darr, W. Fendler, M. Picchio, F. Montorsi, A. Briganti (Milan, Bologna, Padua, Orbassano, Turin, Italy; Lucerne, Switzerland; Vienna, Austria; Essen, Germany; Madrid, Spain; Nanjing, China)

Best reviewer YAU

Riccardo Bertolo, Rome, Italy

European Urological Scholarship Programme Awards

EUSP Best Scholar

Analysis of gene expression signatures and immune cell infiltrates in tumour tissue and microenvironment after neoadjuvant treatment with axitinib and avelumab in patients with localized high-risk RCC to assess mechanisms and predictors of response

Y. Abu Ghanem, Ramat Gan, Israel

Best Patient Poster Awards

First Prize

Global Patient Survey: Reported Experience of Diagnosis, Management, and Burden of Renal Cell Carcinomas in >2,200 Patients from 39 Countries
Abstract Nr. AP23-0022

R. Giles, L. Marconi, D. Maskens, R. Martinez, K. Kastrati, C. Castro, J. Julian Mauro, R. Bick, M. Hickey, J. Björkqvist, D. Heng, J. Larkin, A. Bex, E. Joasch, S. Maclennan, M. Jewett (Duivendrecht, The Netherlands; Coimbra, Portugal; Toronto, Calgary, Canada; Mountain View, Houston, USA; Weikersheim, Germany; Mexico City, Mexico; Madrid, Spain; London, Aberdeen, United Kingdom)

Second Prize

A comprehensive summary of patient and caregiver experiences with bladder cancer: Results of a survey from 49 countries
Abstract Nr. AP23-0027

L. Makaroff, A. Filicevas, S. Boldon P. Hensley, A. Kamat (Cambridge, United Kingdom; Brussels, Belgium; Toronto, Canada; Lexington, Houston, USA)

Third Prize

How can we improve patient-clinician communication in men diagnosed with prostate cancer?
Abstract Nr. AP23-0021

K. Beyer, A. Lawlor, S. Remmers, L. Venderbos, P-P. Willemse, M. Omar, E. Smith, C. Bezuidenhout, L. Collette, S. Maclennan, S. Evans-Axelsson, J. N'Dow, M. Roobol, M. Van Hemelrijck (London, Aberdeen, United Kingdom; Rotterdam, Utrecht, Arnhem, The Netherlands; Stockholm, Sweden; Leuven, Louvain-la-Neuve, Belgium)

Helmut Haas Award

H. Heers
Marburg, Germany

For a significant scientific contribution to the development of the Outpatient and Office Urology

End of life care - Preferences of patients with advanced urologic malignancies

H. Heers, F. Urhahn, A. Pedrosa Carrasco, A. Morin, M. Gschnell, J. Huber, L. Flegar, C. Volberg (Marburg, Germany)

Why is advanced tumour visualisation useful?

A constructive review of imaging (PDD, NBI, IMAGE1 S)

Prof. Marko Babjuk
Dept. of Urology, Hospital Motol and 2nd Faculty of Medicine, Charles University, Praha (CZ)

marek.babjuk@fnmotol.cz

The success of treatment in Non-muscle-invasive bladder cancer (NMIBC) is dependent upon the biological characteristics of the tumour and on correctly selected and performed treatments. The strategy is based on transurethral resection, followed by individually tailored adjuvant treatment according to individual risk of tumour recurrence and progression.

Transurethral resection of bladder cancer (TURBT) is the initial and critical step in the management of NMIBC. This procedure has a diagnostic and therapeutic role and its quality can be measured according to the early recurrence rate after completed procedures. In some studies, the 3-months recurrence rate varies between 0-61.3%, showing a huge heterogeneity in the quality of transurethral resection. It is well known, that up to 50% of patients develop a tumour recurrence within 12 months from primary treatment, most likely the result of missed lesions.

There are more options for improving the outcomes of TURBT, one of them is getting a higher quality of tumour visualisation. When using the modern equipment (cameras and light source), white light cystoscopy (WLC) remains the gold standard in the diagnosis of bladder cancer. It may be today supplemented with enhanced optical technologies, which improve tumour detection, particularly of small papillary and flat lesions such as carcinoma in situ (CIS) and reduce the risk of undetected tumours.

Fluorescence diagnosis (PDD)

Principle of the method

Fluorescence-guided photodynamic diagnosis (PDD) is a technique of tumour visualisation based on the intravesical instillation of 5-aminolevulinic acid (5-ALA) or its hexyl ester (HAL). These prodrugs are metabolised into protoporphyrin IX, whereby, accumulation in cancer cells produces an intensive red fluorescence when excited by blue light.

Clinical efficacy and available evidence

It has been confirmed that fluorescence-guided biopsy is more sensitive than WLC for the detection of malignant lesions. This benefit was particularly evident in patients with CIS. In a systematic review and meta-analysis, PDD had higher sensitivity than WLC in the pooled estimates for analyses. It improved sensitivity at the patient-level from 71% to 92% and the biopsy-level from 65% to 93%. On the other hand, the specificity of PDD was 63%, which was lower than 81% of WLC [1].

Most often PDD-guided TURBT is connected with reduced recurrence rates compared to standard white-light TURB. In a recent systematic review and network meta-analysis that included 22 studies with 4519 patients, they compared the recurrence rates of NMIBC depending on the type of tumour visualiation during TURBT (WLC vs PDD vs NBI) combined with single immediate intravesical chemotherapy (SIIC) administration. In total, 6 subgroups were established, including a control group 'WLC without SIIC'. In these settings, PDD alone without SIIC was associated with a lower probability of a 12-months recurrence rate and the addition of SIIC further lowered recurrence rates. Results for NBI were comparable to those of PDD according to the surface under the cumulative ranking (SUCRA) curve. There were only a small number of randomised controlled clinical trials with NBI, which the authors noted as a limitation [2].

In another recent systematic review and meta-analysis of 12 randomised controlled trials (RCT) with 2,288 patients, authors compared TURBT using WLC to PDD. The primary outcomes were recurrence rates at 12 and 24 months. The secondary outcome was to evaluate reported adverse effects. Authors focused on the medium- and long-term effects of PDD and studies reporting results from shorter periods were excluded. Use of PDD led to a reduction of recurrence rates at both 12 months and 24 months. Use of WLC only was clearly associated with increased risk of recurrence after 12 and 24 months, respectively. According to GRADE analysis, the certainty of evidence was considered moderate for recurrence rate outcomes. Two included studies reported lower recurrence rates even after 60 months of follow up. Only two out of twelve studies reported all encountered adverse events, including haematuria and bladder irritation symptomatology (spasms, frequency and urgency). In one case, the frequency of adverse events was similar between PDD and WLC, while the other reported higher rates of symptoms in the PDD group (28% vs 17.5%) [3].

Partially opposed to these encouraging results, isa recent Cochrane systematic review that encompassed 16 randomised controlled trials up until March 2021. Although authors suggested that PDD may reduce the risk of tumour recurrence depending on the risk group, the certainty of evidence was low [4].

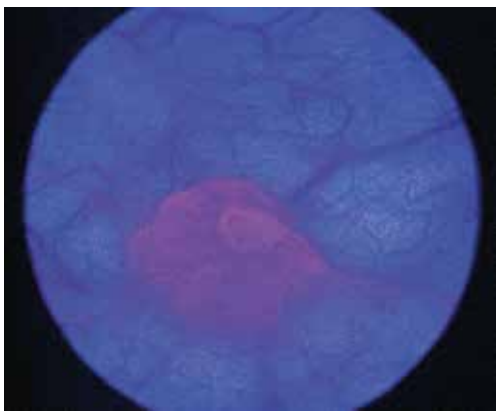
Some level of scepticism is supported by recently published results of the prospective randomised multicentre "PHOTO" trial. This research not only contradicted benefit in terms of mid-term recurrence rates but failed to find any cost-effectiveness of PDD compared to standard visualisation. Authors analysed results of 426 patients that underwent TURBT for primary NMIBC (209 with PDD and 217 with WLC). Median follow-up was 44 months. Baseline structure of tumour risk groups was comparable, as were the rates of postoperative single instillations and adjuvant intravesical treatments between the two arms. Three-year recurrence-free survival rates were also comparable at 57.8% and 61.6% for PDD and WLC, respectively. However, the number of recurrences in the WLC control group was higher during the first 12 months. The difference was the most pronounced in the course of the first 6 months (23 WLC group vs 12 PDD group). Proportion of recurrences reversed after one year of follow-up [5].

In real life we need to remember some practical limitations of PDD. This method expects special equipment (light source, telescope, camera) which must be mutually compatible. Together with the instilled substance, it significantly increases the cost of the procedure. Additionally, PDD is dependent on exogenous administration of the precursor that must be metabolised to photoactive form. This process requires a certain time. Usual recommendations for HAL are 1-2 hours before the procedure. Moreover, the photodynamic effect can be observed for a limited time only (photo-bleaching).

Narrow-band imaging (NBI)

Principle of the method

In NBI technology white light is filtered into 2 bandwidths of 415nm (blue) and 540nm (green). These wavelengths are strongly absorbed by haemoglobin, thus enhancing surface capillary visualisation and contrast between normal urothelium and hypervascular tumour areas.



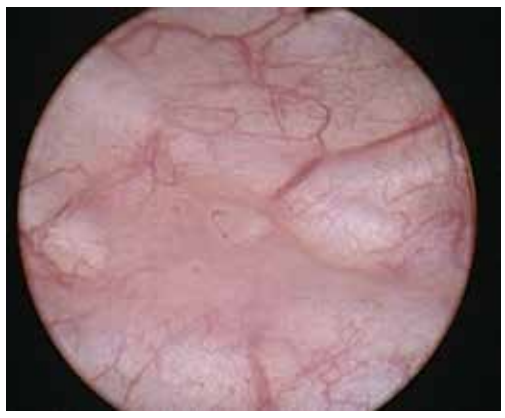
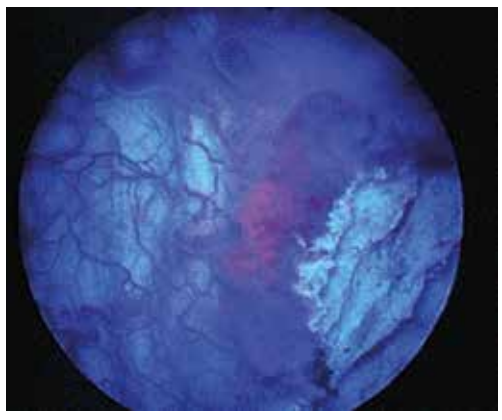


Figure 1: TaLG bladder cancer with PDD and WLC



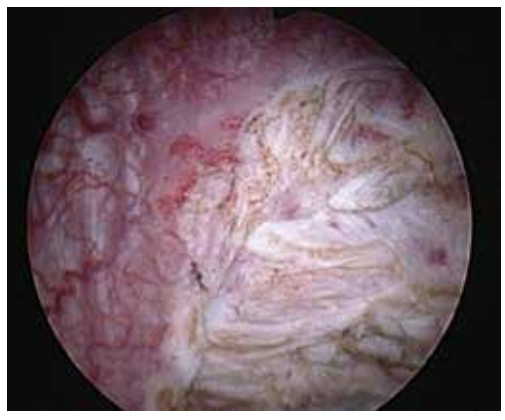
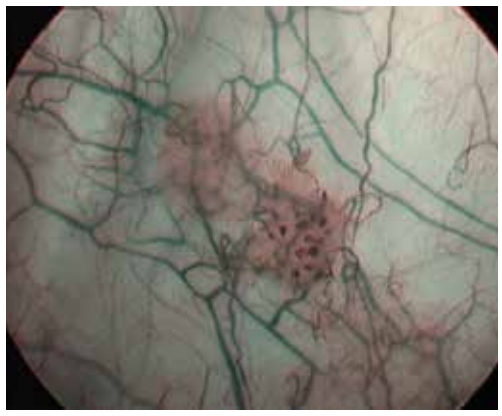


Figure 2: Residual high-grade lesion after resection with PDD and WLC



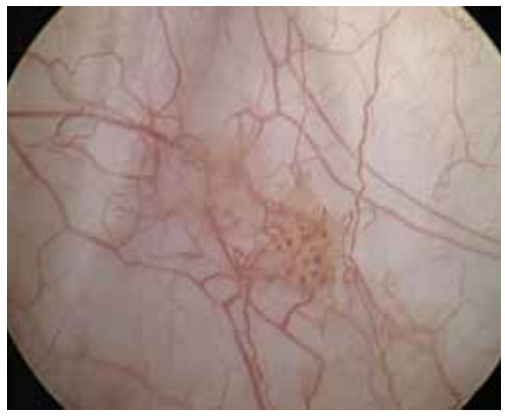


Figure 3: TaLG papillary tumour with NBI and WLC

The utilisation of NBI is simple and devoid of a learning curve, with no need for patient preparation, no contraindications and no adverse effects. The surgeon is able to toggle between WL and NBI mode, taking on average an additional 3 minutes to complete the procedure. It can be used an endless number of times and the cost is likened to WLC TURBT.

Clinical efficacy and available evidence

The use of NBI in urology was first described in a study by Bryan et al in 2008 using a flexible cystoscope in a group of patients with recurrent NMIBC [6]. This was the first report of an increased tumour detection rate versus WLC.

The improved detection rate of NBI comparing to WLC was demonstrated by more authors [7]. A prospective comparative study between WLC, NBI and PDD included 175 high-risk patients demonstrated that both NBI and PDD had a higher diagnostic sensitivity for CIS and flat dysplasia (95,7% vs WL 65,2%) with similar specificities (NBI 52%, PDD 48%, WL 56,8%) [8]. The research concluded that for this purpose, NBI is a reliable alternative to PDD. Similarly, a recently published retrospective single centre evaluation suggested non-inferiority of NBI compared to PDD in the detection of CIS [9].

The role of NBI-assisted resection on recurrence rates has been studied in a large randomised multicentre trial by the Clinical Research Office of the Endourological Society (CROES). This study included only primary tumours and revealed no differences in the tumour recurrence rate at 12 months, with the exception of the low-risk patient group [10]. However, the value was burdened with some methodological limitations.

In 2022, the Cochrane group published results of their comprehensive literature search, which evaluated the potential benefit of NBI guided TURBT compared to WLC guided TURBT. Based on limited confidence in the time-to-event data, authors found that participants who underwent NBI + WLC TURBT had a lower risk of disease recurrence over time compared to participants who underwent WLC TURBT (6 studies, 1244 participants; low certainty of evidence). No studies examined disease progression as a time-to-event outcome or a dichotomous outcome. There was no effect on the risks of major or minor adverse events. [11].

Professional Image Enhancement System (IMAGE1 S)

Principle of the method

The concept is based on several image enhancement modalities containing a white light, spectra A, spectra B, chroma and clara mode. Spectra A and B increases image contrasts by colour tone shift algorithms, chroma enhances the sharpness of the displayed image, and clara uses a local brightness adaptation in the image to achieve greater visibility of darker regions within the image. Additionally, the system is able to provide a standard WLC with the IMAGE1 S image simultaneously.

Clinical efficacy and available evidence

IMAGE1 S was recently investigated in a large prospective international trial organised by CROES. The results showed no difference in the overall recurrence rates between IMAGE1S and WL assistance 18-mo after TURBT in patients with NMIBC. However, IMAGE1S-assisted TURBT considerably reduced the likelihood of disease recurrence in primary, low/intermediate risk patients [12]. There is no doubt that the data needs further validation.

Summary and conclusion

Tumour visualisation using modern equipment and advanced imaging is essential for high quality TURBT. During procedures, it improves the visibility and detection of CIS and small papillary lesions (Figure 1) and improves the evaluation of tumour areas before, during and after resection (Figure 2,3). Most of the research data supports the opinion that these benefits are translated into a reduced number of recurrences in patients' after TURBT. For this reason, the EAU guidelines recommend the application of advanced imaging during TURBT if these methods are available. The optimal method of advanced visualisation however remains to be specified.

References

1. Mowatt, G. Int J Technol Assess Health Care 2011; 27: 3-10.
2. Sari Motlagh, R. BJU Int 2021; 128: 280-9.
3. Veeratterapillay, R. Eur Urol Open Sci 2021; 31: 17-27.
4. Maisch, P. Cochrane Database Syst Rev. 2021.
5. Heer, R. NEJM Evidence 2022.
6. Bryan, RT. BJU Int 2008; 101: 702-6.
7. Kim, SB. Investig Clin Urol 2018; 59: 98-105.
8. Drejer, D. Urology 2017; 102: 138-42.
9. Kumarasegaram, V, Urology, 2022; 61: 83–6.
10. Naito, S. Eur Urol 2016; 70: 506-15.
11. Lai, LY, Cohrane Database Syst Rev 2022.
12. De la Rosette, J. WJU 2022; 40: 727-38.

Saturday, 11 March 15:18 - 15:37
Thematic Session: Rapid-fire debates: Common problems and controversies in bladder cancer
Yellow Area, eURO Auditorium 2

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MRI-guided active surveillance strategy

Patient risk stratification: Diagnostic, prognostic and monitoring

Dr. Lars Boesen
Dept. Of Urology, Herlev and Gentofte Hospital (DK)

lars.ploug.boesen@regionh.dk

Active surveillance (AS) for early-stage prostate cancer (PCa) should be offered to men with low- or favourable intermediate-risk cancer, who are expected to have slow-growing and non-aggressive disease. AS traditionally involves close monitoring through regular PSA measurements, digital rectal examinations (DRE) and protocol-based biopsies. Active curative treatment can be initiated if the cancer shows signs of progression. Disease progression is defined clinically by rising PSA and/or DRE-upstaging, or pathologically by the Gleason score/grade group (GG) upgrading or tumour-volume upscaling at biopsy.

However, PSA, DRE and systematic biopsies contribute to poor risk assessment with high misclassification rates at diagnosis. This results in high 'AS-failures' over time, due to clinical progression, histological reclassification, or patient intolerance to stringent AS protocols that often include multiple repeat biopsy sessions. AS is designed to retain oncological safety while avoiding side effects of active treatment, but there is a risk of missing significant tumours at diagnosis and/or during surveillance. The optimal AS selection criteria and monitoring strategies are currently not agreed on across different institutions and centres.

More precise tools are needed to help identify which patients have an indolent disease and can safely be monitored with AS, and which patients may require more aggressive treatment. There is a need for improved patient risk stratification using *diagnostic, prognostic/predictive, and monitoring* biomarkers. Growing scientific evidence supports the use of MRI as a biomarker in AS to meet this demand (Fig. 1).

Prostate MRI as a biomarker in AS

The use of prostate MRI in PCa management has shown several advantages over standard systematic biopsies for significant PCa detection, localisation, and staging [1]. Because MRI provides detailed images of the prostate gland, allowing for the precise location and size of suspicious lesions to be identified with high sensitivity, it can be used as a diagnostic biomarker for guiding MRI-targeted biopsies for improving detection of significant disease. Conversely, several studies have shown that MRI has a high negative predictive value >90% for ruling out significant GG ≥2 PCa, avoiding the need for invasive biopsies [2]. In men considered eligible for AS, MRI improved detection of GG ≥2 PCa at initial assessment and identified men with more aggressive disease potentially qualifying for active treatment [3]. The MRI-improved detection of higher-grade cancers at inclusion match well with the up to 30% protocol-based discontinuation of AS due to upgrading within the first years of AS enrolment. This is probably caused by undergrading and misclassification at inclusion [4]. Equally, a normal MRI can rule out significant disease with a high negative predictive value confirming AS eligibility.

The use of an MRI-first diagnostic pathway in biopsy-naïve men with suspicion of PCa has been shown to reduce detection of men with GG 1 PCa by up to 50%, slightly increase detection of men with higher-grade cancer (GG ≥2) potentially needing active treatment, and improve tumour-grade determination compared with radical prostatectomy specimen. This could potentially reduce the overall number of men needing AS because fewer men are diagnosed with GG1 PCa initially, while less men with unfavourable disease would be enrolled in AS. Furthermore, a normal MRI could confirm AS eligibility in men with 'grey-zone' PCa risk-features such as multiple positive biopsy cores, PSA between 10-20 ng/mL and/or low volume GG2 disease.

Several MRI features such as the visibility of the lesions, high PI-RADS scores, and low ADC-values on diffusion-weighted imaging have all been associated with adverse pathology and unfavourable outcomes. Men on AS with visible PI-RADS 4-5 lesions are significantly more likely to progress to active treatment, and the absence of a focal lesion has a very good PCa specific survival of 15+ years. Thus, MRI appearance on multiparametric sequences could be used as a prognostic biomarker to better distinguish between aggressive and non-aggressive PCa, where especially MRI-visibility seems one of the strongest predictors for adverse outcomes. Furthermore, the Assist trial [5] showed that an MRI performed before confirmatory biopsy in AS resulted in 50% fewer AS failures and less grade progression compared with systematic biopsies over 2-years of follow-up.

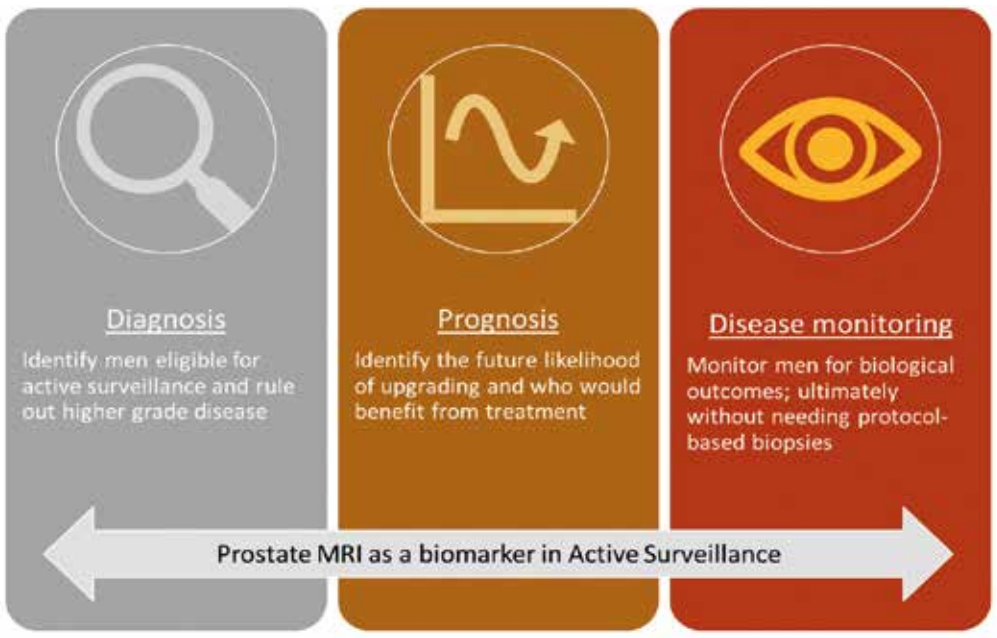

Figure 1: Prostate MRI as a biomarker in active surveillance.

Serial MRI-monitoring

Optimally, repeated MRIs during the monitoring of AS could non-invasively track changes in disease aggression providing information on stability or progression. An MRI guided AS strategy where only progression on MRI (such as growth of lesions or appearance of new lesions) trigger either direct reclassification or repeat biopsies appears attractive for both the physician and the patient (Fig. 2). For this purpose, specific recommendations for using MRI for serial monitoring of men in AS have been published as the PRECISE criteria [6]. Like the PI-RADS score, which is designed to objectively assess the likelihood of significant cancer from a score of 1-5 in a detection-setting, PRECISE grades change on MRI from a score of 1-5 on the likelihood of tumour aggression in men on AS. The clinical purpose is to identify men who progress in a timely manner, promoting repeat biopsy and/or treatment, and to avoid standardised protocol-based biopsies in men with regression or stable MRI findings.

Findings from the PRECISE task force showed that only 5% of men on AS with stability in PRECISE score (1-3) experienced clinical progression over a median follow-up of ~75 months [7]. Thus, regression or stability on MRI may be used non-invasively to avoid protocol-based AS-biopsies, which could reduce the intensity and burden of surveillance for both the individual and the healthcare system. Although the PRECISE score seems to be reproduceable and robust across centres and interobservers, it has not yet been validated in larger cohorts. There is no consensus regarding the threshold for tumour growth or change in conspicuity to define radiological progression. Furthermore, the timing of serial MRIs during follow-up has not been specified. The pooled sensitivity and specificity for serial MRIs to detect progression have been reported to be ~60% and ~75% in a recent meta-analysis [8]. Although there is heterogeneity between included studies, the negative and positive predictive values range from 81-88% and 37-50%, Thus MRI is better at ruling-out than ruling-in progression and still cannot be recommended as a stand-alone test for prompting therapy or replacing surveillance biopsies.

However, despite differences in AS-protocols and MRI reporting across institutions, emerging data show that men with both stable MRIs and PSA-kinetics should avoid routine surveillance biopsies. Interestingly, it seems that men with GG 1 PCa upgraded during monitoring on confirmatory biopsy tend to have less aggressive disease outcomes compared with men initially diagnosed with the same (up)-graded cancer [9]. More studies are needed to confirm whether it is safe to apply a more conservative treatment-strategy for men upgraded during surveillance.

AS for everybody with low-risk PCa?

While AS should be offered for most men with low-risk PCa, opinions differ on whether it is safe to include young men (≤60 yrs.) and men with a familiar history of PCa and/or known germline mutations. Various studies reporting age-ranges show that many clinical practice AS programs apply a lower age threshold for AS-recommendations. However, emerging data from a world-wide GAP3-database show that young men on AS may have a lower or at least an equal risk of disease progression and potentially even a lower risk of upgrading at radical prostatectomy compared with older men (>60 years) [10]. These results indicate that young men should not automatically be excluded from initial AS.

A familiar history of PCa does not seem to predispose to progression on AS, but germline mutations have been found to be associated with more aggressive disease and prognosis. It has been reported that BRCA-mutation carriers with low-risk PCa in AS are associated with more aggressive cancer and potentially a higher risk of grade-reclassification compared with non-carriers [11]. However, most current data often include only small numbers of mutation carriers, short follow-up or pathology solely based on systematic biopsy with its inherent limitations.

Larger studies using contemporary MRI-guided surveillance are needed to confirm these findings before making definite clinical recommendations. Assessment of mutation status may aid in decisions when balancing AS over immediate active curative treatment. Although, the prevalence of such mutations is very low in low risk PCa AS cohorts, and genetic testing and counselling of all men on surveillance seem very circumstantial and costly. Thus, until larger scale studies with long-term follow-up become available, AS may still be considered a feasible option for well-informed men with low risk PCa if they are carefully monitored at specialised clinics, preferably using MRI-guided surveillance and biopsies with shorter surveillance intervals.

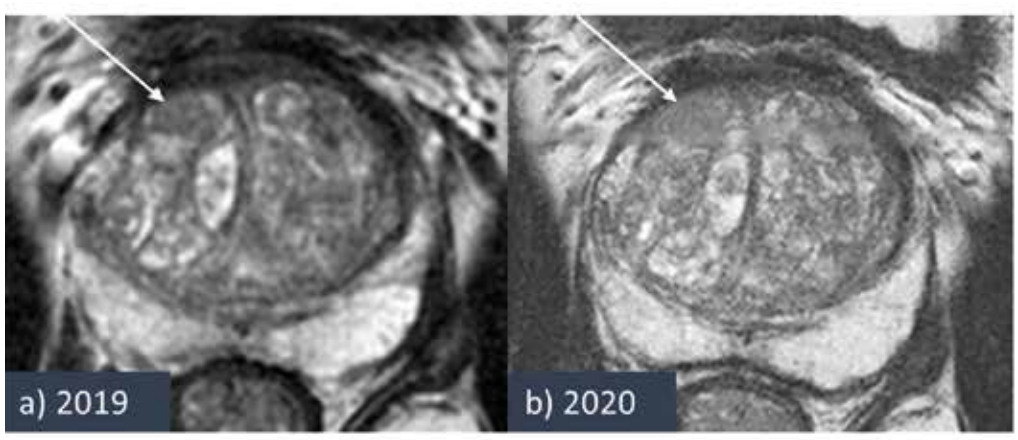

Figure 2: Tumour-suspicious lesion on MRI (a) at diagnosis in 2019 (white arrow) where targeted biopsies showed GG1 PCa with 6 mm maximum cancer core length (MCCL). The patient went on AS and confirmatory MRI after one year (b) showed revealed tumour-growth (larger lesion) with a more homogenous appearance and lower ADC-value. Repeated targeted biopsy showed upgrading to GG 2 with MCCL 9 mm.

Conclusion

The advantages of an MRI-guided AS strategy is its high sensitivity and negative predictive value for aggressive cancer, which in turn, confirms a patients eligibility for AS. It also provides detailed images of the prostate to detect any changes in tumour conspicuity such as shape, size, and location, during the monitoring phase. At present, abandoning protocol-based confirmatory biopsies in all men with stable MRI-findings cannot be recommended in routine practice, but emerging data suggest that if the MRI is performed accordingly with high image quality in expert-centres, surveillance-biopsies may be avoided if PSA-kinetics and/or PSA-density and clinical impression (DRE) is concordant. Several tools for standardised MRI reporting at diagnosis (PI-RADS), MRI quality control assurance (PI-QUAL) and MRI criteria for radiological progression during AS (PRECISE) are now available, which further encourages the use of MRI as an additional biomarker both at diagnoses to confirm eligibility for AS, and during follow-up in an MRI-guided AS management strategy. However, MRI findings should always be used in conjunction with familiar/genetic risk and clinical parameters for individualised patient-tailored AS-risk management.

References

1. Drost F-JH, Osses DF, Nieboer D, et al: Prostate MRI, with or without MRI-targeted biopsy, and systematic biopsy for detecting prostate cancer. Cochrane Database Syst. Rev. 2019. DOI: 10.1002/14651858.cd012663.pub2.
2. Sathianathen NJ, Omer A, Harriss E, et al: Negative Predictive Value of Multiparametric Magnetic Resonance Imaging in the Detection of Clinically Significant Prostate Cancer in the Prostate Imaging Reporting and Data System Era: A Systematic Review and Meta-analysis. Eur. Urol. 2020; 78: 402-414
3. Schoots IG, Petrides N, Giganti F, et al: Magnetic resonance imaging in active surveillance of prostate cancer: A systematic review. Eur. Urol. 2015; 67: 627–636.
4. Bokhorst LP, Valdagni R, Rannikko A, et al: A Decade of Active Surveillance in the PRIAS Study: An Update and Evaluation of the Criteria Used to Recommend a Switch to Active Treatment. Eur. Urol. 2016; 70: 954–960.
5. Klotz L, Pond G, Loblaw A, et al: Randomized Study of Systematic Biopsy Versus Magnetic Resonance Imaging and Targeted and Systematic Biopsy in Men on Active Surveillance (ASIST): 2-year Postbiopsy Follow-up. Eur. Urol. 2020; 77.
6. Moore CM, Giganti F, Albertsen P, et al: Reporting Magnetic Resonance Imaging in Men on Active Surveillance for Prostate Cancer: The PRECISE Recommendations—A Report of a European School of Oncology Task Force. Eur. Urol. 2017; 71: 648–655.
7. Giganti F, Stabile A, Stavrinides V, et al: Natural history of prostate cancer on active surveillance: stratification by MRI using the PRECISE recommendations in a UK cohort. Eur. Radiol. 2021; 31.
8. Rajwa P, Pradere B, Quhal F, et al: Reliability of Serial Prostate Magnetic Resonance Imaging to Detect Prostate Cancer Progression During Active Surveillance: A Systematic Review and Meta-analysis. Eur. Urol. 2021; 80.
9. Perera M, Jibara G, Tin AL, et al: Outcomes of Grade Group 2 and 3 Prostate Cancer on Initial Versus Confirmatory Biopsy: Implications for Active Surveillance. Eur. Urol. Focus 2022. DOI: 10.1016/j.euf.2022.12.008.
10. Remmers S, Helleman J, Nieboer D, et al: Active Surveillance for Men Younger than 60 Years or with Intermediate-risk Localized Prostate Cancer. Descriptive Analyses of Clinical Practice in the Movember GAP3 Initiative. Eur. Urol. Open Sci. 2022; 41: 126–133.
11. Carter HB, Helfand B, Mamawala M, et al: Germline Mutations in ATM and BRCA1/2 Are Associated with Grade Reclassification in Men on Active Surveillance for Prostate Cancer. Eur. Urol. 2019; 75: 743–749.

Monday, 13 March 13:35 - 13:45
Thematic Session: How to assess men with familial prostate cancer
Yellow Area, eURO Auditorium 2

Population-based organised prostate cancer testing

Swedish experience can help future European programmes

Prof. Ola Bratt
Chairman of the Swedish Working Group for Organized Prostate Cancer Testing, University of Gothenburg; Consultant Urologist, Sahlgrenska University Hospital.

Prostate cancer is one of the most common cancer related causes of death in all European countries. A long, asymptomatic, organ confined stage in combination with the fact that the disease usually is incurable when symptomatic makes screening attractive. The European randomised screening trial showed that screening for prostate cancer may reduce cancer-specific mortality at least as much as screening for breast cancer and colorectal cancer do, but the diagnostic methods used in that trial led to unacceptably high rates of overdiagnosis and overtreatment.

In agreement with almost all other national healthcare authorities, the Swedish National Board of Health and Welfare in 2018 recommended against a national screening programme for prostate cancer. But they also acknowledged that unorganised PSA testing was widespread, ineffective and resource demanding. This led the Swedish Ministry of Health and Social Affairs to commission the Confederation of Regional Cancer Centres in Sweden to standardise prostate cancer testing and make it more efficient. The Confederation assigned a national, multidisciplinary expert group, which later the same year outlined the concept of population-based, regional organised prostate cancer testing (OPT) programmes.

The first two OPT programmes were launched in 2020 in two of the most populated Swedish regions, Region Västra Götaland (including Gothenburg) and Region Skåne (including Malmö and Lund). Both started in 2020 with inviting all 12,000 plus 9,000 men, aged 50 years [1]. In March 2023, 6 of the 21 Swedish regions have an OPT programme operating. A further 11 regions are planning to start later in 2023.

What is "organised prostate cancer testing" (OPT)?
The regional OPT programmes report results to a national working group. The working group publishes updated recommendations annually for OPT, which are available online in Swedish and English [2]. The recommendations cover testing, organisation, coordination and quality control.

In summary:

- OPT programmes are organised within the public, tax-financed, healthcare system.
- The target population is men aged 50 to 74
- All men in the target population should actively be informed about the potential pros and cons and offered structured, repeated testing if they opt for testing.
- All regional OPT programmes should use the same, nationally agreed, brief information about pros and cons.
- The programme should initially invite a few birth cohorts to evaluate the functionality of the regional infrastructure.
- The programme should include all steps from invitation through the diagnostic pathway to biopsy result notification.
- A regional OPT office should organise the programme.
- A nationally available online administrative system automatically generates invitation letters and letters for notifying test results.
- PSA testing intervals, use of MRI, indication for and extent of prostate biopsies, and follow-up should adhere to an algorithm (Figure 1). Individualised management should be minimised to allow for evaluation of the algorithm's performance.
- After a benign biopsy men should be re-invited according to the algorithm, not be followed up in routine healthcare (with a few, specified exceptions).
- All results should be registered in the national OPT register for internal quality control, national analysis and research.

What makes OPT different from a national screening programme?
The Swedish OPT programmes are in most aspects identical to a screening programme, but there are some important differences:

- The OPT programmes are regional; a Swedish screening programme would be national.
- Men invited to OPT receive a letter with a brief, neutral description of the potential advantages and disadvantages that includes a statement that the National Board of Health and Welfare recommends against screening but supports individual, informed decisions about PSA testing; an invitation to national screening programme would inform that the Board considers the advantages to outweigh the disadvantages.
- The primary aims of OPT are to organise the widespread unorganised PSA testing, make testing for prostate cancer more efficient and socioeconomically equal, and to fill diagnostic and organisational knowledge gaps. Registration and reporting of diagnostic outcomes are therefore obligatory. The OPT concept is based on the view that *learning by doing is better than doing without learning*; a national screening programme would require a more solid evidence base.
- The regional OPT programmes may be adapted to regional circumstances. Some regions may use a test algorithm that reduces the need for MRI scanning, others may refrain from starting OPT because of lack of resources; a national screening programme would be uniform and mandatory for all regions.
- The OPT programmes are small pilot boats, navigating the waters of an archipelago to gain needed knowledge to safely guide a national screening programme through the fairways of the sea, avoiding shallows and rocky islands.

Early experiences
Some important learning points from the first three years of regional OPT are:

- OPT involves an unimaginable amount of detailed planning. But however well you plan, you will encounter unexpected pitfalls.
- Most medical decisions are simple – many organisational matters are difficult.
- It's wise to test the infrastructure by inviting a few birth cohorts in a few pilot projects (small unexpected pitfalls are better than big ones).
- Communication with all stakeholders is essential. Stakeholders include the invited men, the public, media, directly involved healthcare professionals (primary care, clinical chemistry, radiology, pathology, urology, oncology), patients organisations, professional societies and related authorities.
- Active follow-up is required to make involved urologists manage men in OPT according to the algorithm, or else the algorithm's performance will be difficult to evaluate (urologists tend to individualise).
- Proportions of positive tests and diagnostic outcomes are age-dependent and differ from those in a clinical setting.
- Register, report and analyse all outcomes for quality control and research.

Some practical considerations
Before launching an OPT project, sufficient resources must be secured for all parts of the diagnostic pathway and for the management of the men who are diagnosed with cancer. When we actively invite healthy men, we take upon ourselves a particular responsibility not to cause any unnecessary harm, such as anxiety during prolonged waiting times.

The mental frame-shift from personalised clinical care to population-based testing may be difficult. We must recognise that we initially deal with men, not patients, and that most men who participate in OPT never become urological patients. Even among men who are investigated for a raised PSA, a minority are diagnosed with cancer. The Swedish "OPT philosophy" is letting men remain men as long as possible to avoid making them patients. Participants are notified of MRI results by an automated standard letter, which means that those with an unsuspicious scan and a low PSA density do not meet a urologist. We believe this routine prevents turning men into patients.

Men with a biopsy indication are referred to a contracted urology unit that has agreed to manage OPT patients according to the algorithm. Their instruction is to focus on the biopsy only; men who wish to discuss other urological matters should be kindly requested to make an appointment with their general practitioner or urologist. Nonetheless, the OPT offices spend considerable efforts to follow-up the outcome of urology appointments to make sure that no OPT patient receives unwarranted individualised urology follow-up. This may seem unduly bureaucratic, but if men with a raised PSA in the setting of a full-scale OPT/screening programme are "absorbed" into routine urological care, urology services may quickly become congested. This would also make the test algorithm difficult to evaluate.

The future
The European Union Council's new recommendation to evaluate the feasibility and effectiveness of organised prostate cancer screening programmes directs the light to the Swedish OPT programmes, as they are specifically designed for this purpose and have been up and running for some years now. We are looking forward to sharing our experiences with others who are in the early phases of planning or launching similar programmes. One forum for exchanging experiences is the EAU initiated PRAISE-U programme, which received a substantial grant from the EU5Health programme for implementing OPT. The three largest Swedish OPT programmes are associated with PRAISE-U.

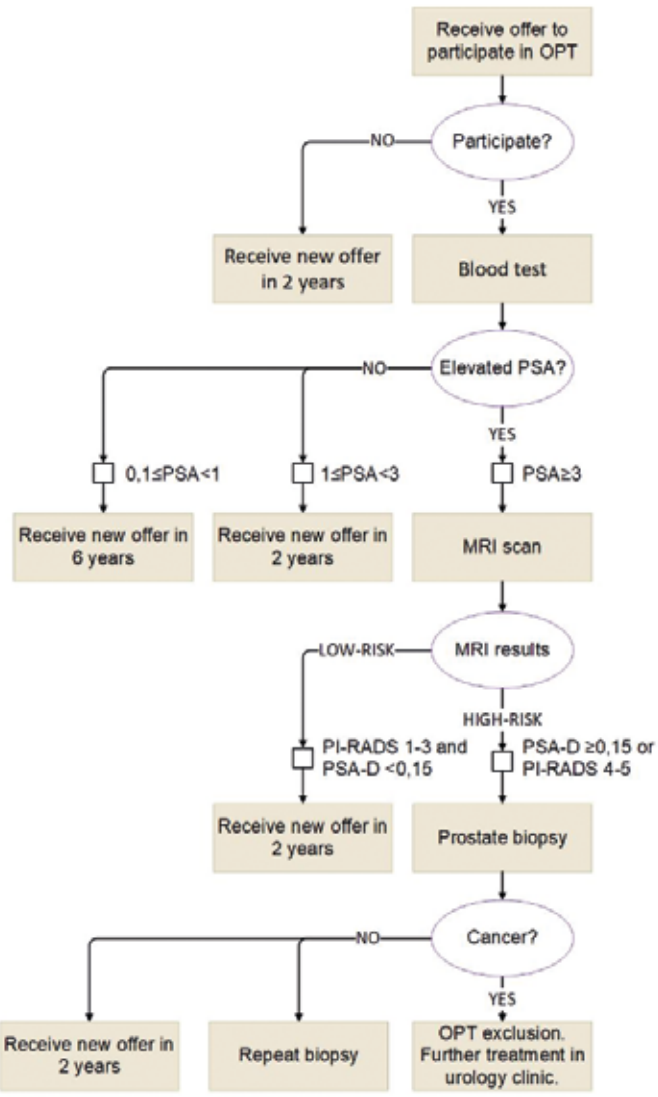

Figure 1: Standard testing algorithm for the Swedish regional organised prostate cancer testing (OPT) programmes [2].

Although PRAISE-U and the experiences from the Swedish OPT programmes will facilitate the implementation of formal, population-based screening programmes för prostate cancer, it will be many years of hard work before a majority of European men can be offered organised screening. The conditions are very different across the Union's member states. Some are well prepared, others are not. There also remain some crucial knowledge gaps: some scientific, others organisational. For example:

- How do we best use complimentary tests (biomarkers, risk calculators, TRUS with volume measurement to calculate PSA density) to select men with a raised PSA for an MRI? MRI resources are a limiting factor in many countries, so this may be pivotal for the decision whether or not to launch a national screening programme.
- What is the optimal use of MRI for men with persistently raised PSA? In the previous screening trials men with a persistently raised PSA had a systematic biopsy every screening round, but there is probably no need to repeat as frequently the MRI in men with a stable PSA and a low PSA density (MRI resources again).
- What proportion of invited men will obtain a PSA test and how many of those who do will have an indication for an MRI or a prostate biopsy? These proportions are different in a screening compared with a clinical setting, and they differ between countries, age groups and screening rounds. Reliable data is essential for resource allocation.
- Will men comply with the long follow-up intervals in a screening algorithm, or will they obtain parallel PSA testing in general practice or urology? Parallel testing would probably not be cost-effective.
- How are adequate MRI reading and biopsy skills secured? Studies have revealed great variations of MRI assessment and targeted biopsy results. Managers of screening programmes should consider applying quality measures such as structured training, audits, and feedback of biopsy results to reporting radiologists.

Some of these knowledge gaps will be filled over the next few years by the ongoing screening trials in Finland [3], Sweden [4] and Germany [5], others by the PRAISE-U programme and other population-based OPT programmes (we learn as we go!).

Conclusions
We are experiencing a momentous step forward for European prostate cancer care, but the journey to the new EU recommendation has been long and tough. The early pioneers struggled up a rocky slope in heavy mist with rain in their faces. The past decade the mist and clouds have begun to disperse; we have seen glimpses of the mountain top. Now we are standing there on the top, with a magnificent view of the landscape in front of us. The sunshine glitters in the sea at the horizon. We still have many miles ahead of us, but we are walking downhill and see a path that windles in lush valleys towards an evidence-based, unequivocally beneficial, cost-effective prostate cancer screening programme. I'm convinced that we will get there before sunset and that there´s a snug pub with cold drinks waiting for us. The first pint is on me!

References

[1]. Alterbeck M, Järbur E, Thimansson E, et al. Designing and implementing a population-based organised prostate cancer testing programme. Eur Urol Focus 2022; 8:1568-74.
[2]. Confederation of Regional Cancer Centres in Sweden. Recommendations on organised prostate cancer testing (OPT) 2023. [Available at https://cancercentrum.se/samverkan/vara-uppdrag/prevention-och-tidig-upptackt/prostatacancertestning/organised-prostate-cancer-testing/.]
[3] Auvinen A, Rannikko A, Taari K, et al. A randomised trial of early detection of clinically significant prostate cancer (ProScreen): study design and rationale. Eur J Epidemiol 2017; 32:521-7.
[4] Kohestani K, Månsson M, Arnsrud Godtman R, et al. The GÖTEBORG prostate cancer screening 2 trial: a prospective, randomised, population-based prostate cancer screening trial with prostate-specific antigen testing followed by magnetic resonance imaging of the prostate. Scand J Urol 2021; 55:116-24.
[5] Arsov C, Becker N, Hadaschik BA, et al. Prospective randomised evaluation of risk-adapted prostate-specific antigen screening in young men: the PROBASE trial. Eur Urol 2013; 64:873-5.

Sunday, 12 March 14:20 – 14:30
Thematic Session: The road to evidence-based European policy on early detection of prostate cancer
Yellow Area, eURO Auditorium 1

Pathophysiology of persistent LUTS after BPH surgery

An investigation on causes and factors involved

Prof. Giorgio Ivan Russo
University of Catania, Catania (IT)

giorgioivan1987@gmail.com

The prevalence of lower urinary tract symptoms (LUTS) associated with benign prostatic enlargement (BPE) increases with age. The impact of LUTS on patients relates directly to their quality of life (QOL), and, therefore, avoiding such symptoms should be a primary consideration when choosing a therapy. Although many options have been introduced as BPE treatment modalities in the surgical area, transurethral resection of the prostate (TURP) is still considered the benchmark of surgical therapy for BPE [1,2]. However, previous studies have reported that 25% to 30% of patients who undergo prostatectomy have an unfavorable outcome.

"LUTS persistence after surgery is a common health issue and urologists should continue to address and resolve it."

Reasons for LUTS persistence after surgery are now under investigation and they can be related to several factors. At first, it is important to understand that the pathophysiology of LUTS secondary to BPE occurs in a very long period and it influences many aspects. The induced mechanical stretches of bladder secondary to BPE (Figure 1) determines a modification of different pathways that influence genomic expression of proteins, including, NGF (nerve growth factor), EGF (epidermal growth factor), BMP (Bone morphogenetic protein), PAR-2 (Protease-activated receptor 2) and MMP (matrix metalloproteinase) [3].

Among these, NGF plays a significant role (Figure 2). This molecule is involved in the activation of many other pathways that determines neuronal differentiation and growth, and promotion of proliferation. As of consequence of its major release, NGS increase is able to induce overactive bladder (OAB), modify bladder sensitivity and neuroplasticity.

A study published by Hu, et al. in 2018 demonstrated that the urinary NGF levels were different between moderate and severe LUTS (10.513 vs. 12.334 pg/µmol, P=0.002) and in patients with non-OAB, mild, moderate, and severe OAB (8.132 vs. 10.128 vs. 13.232 vs. 14.029 pg/µmol, P<0.001). A year after TURP, compared with the good outcome group, the LUTS persistent group had higher one-year NGF (10.847 vs. 7.850 pg/µmol, P<0.001), and smaller NGF postsurgical change (1.472 vs. 3.165 pg/µmol, P=0.031) [4].

In conclusion, LUTS persistence after surgery is a common health issue and urologists should continue to address and resolve it. Identifying patients who could benefit from surgery to avoid complaints is crucial. In those patients with LUTS persistence after surgery, a good medical history of the past and a correct diagnosis framework are key to resolve symptoms and avoid further complications.

"Reasons for LUTS persistence after surgery are now under investigation and they can be related to several factors."

To know more, join the state-of-the-art lecture "Reasons/pathophysiology of persistent LUTS after BPH surgery" during the Thematic Session "Male LUTS/BPO surgery: Where do we stand?".

References

1. Emberton M, Neal DE, Black N, Fordham M, Harrison M, McBrien MP, et al. The effect of prostatectomy on symptom severity and quality of life. Br J Urol 1996;77:233–47.
2. Neal DE, Ramsden PD, Sharples L, Smith A, Powell PH, Styles RA, et al. Outcome of elective prostatectomy. BMJ 1989;299:762–7.
3. Mirone V, Imbimbo C, Longo N, Fusco F. The Detrusor Muscle: An Innocent Victim of Bladder Outlet Obstruction. Eur Urol 2007;51:57–66.
4. Hu H, Zhang W, Liu X, Wang H, Fang Z, Liang C, et al. Nerve Growth Factor Levels are Associated with Overactive Bladder Symptoms and Long-Term Treatment Outcome after Transurethral Resection of the Prostate in Patients with Benign Prostatic Hyperplasia. Journal of Urology 2018;200:620–5.

Sunday, 12 March 11:24-11:40
Thematic Session: Male LUTS/BPO surgery: Where do we stand?
eURO Auditorium 2, Yellow Area

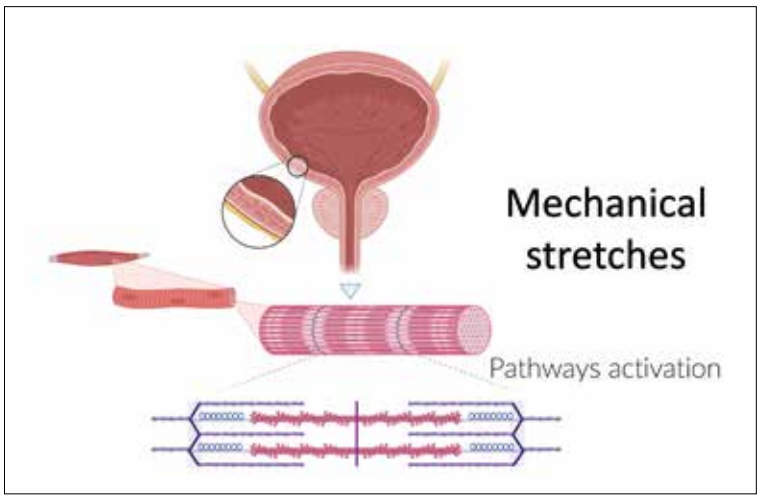

Figure 1. Mechanical stretches induced by benign prostatic hyperplasia (BPH)

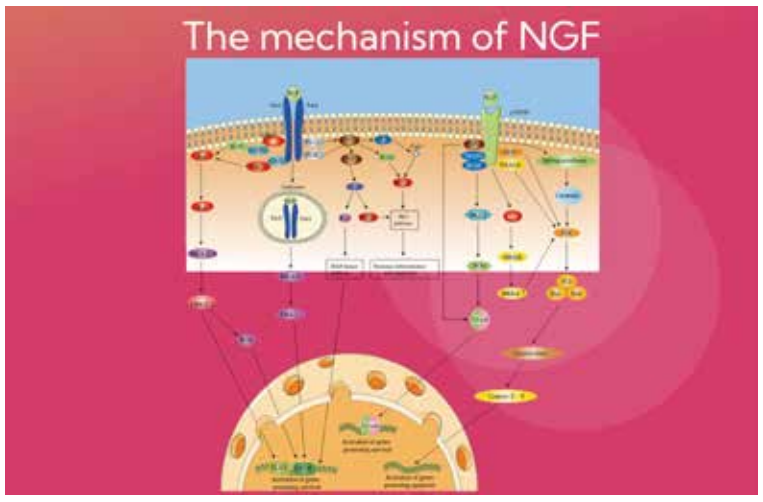

Figure 2. Pathways involved in the NGF mechanism of action

Wound healing and PROs in Fournier's gangrene

Study findings, major challenges and potential solutions

Dr. Laila Schneidewind
University Hospital Rostock
Dept. of Urology, Rostock (DE)

laila.schneidewind@med.uni-rostock.de

Fournier's gangrene (FG) is a sporadic, life-threatening, necrotizing, bacterial infection affecting the perineum, perineal region, and genitals. Hence, the incidence is very low (1.6 cases per 100,000 male patients in the United States). Most of the limited knowledge about FG arises from retrospective single-institutional studies with very small patient cohorts. Furthermore, the prognosis, survival and outcome of FG have not improved in recent years, despite more intensive critical-care therapy for those patients.

Our own multicentre retrospective study of 154 cases showed that survival time did not improve in recent years (p=0.268) with up to 15.4% of the patients dying during inpatient treatment. The key points for successful treatment of FG are immediate surgical debridement, accompanied by intensified antibiotic therapy and intensive care medical management. However, further research to improve the outcome of FG is desperately needed. Unfortunately, due to the rareness of the disease, it is challenging to perform robust prospective clinical studies.

We completed a survey about the practice patterns in diagnostics and treatment of FG in German academic medicine to describe the situation and identify implications for planning a prospective clinical registry. Overall, we concluded that the contemporary practice patterns in FG are very heterogenous, but the outcome is still problematic and the disease is difficult to predict.

We also identified some essential points for a registry study such as histological confirmation of the disease. Additionally, we performed a comparable survey in European hospitals where the practice in FG is very heterogenic and mostly case-based in Europe, e.g. vacuum-assisted wound closure (VAC) is mostly used (n=50; 42.7%) as adjunct wound therapy, 41 (35.0%) do not use an additional therapy for the wound, and in 17 (14.5%) of the cases, hyperbaric oxygenation (HBO) is used.

The major challenges in FG are the short time from diagnosis to treatment, standardisation, establishment of guidelines and disease awareness. Consequently, we concluded that there is no standard of care in the diagnosis, treatment and long-term care of FG in Europe. As already mentioned, the disease is very difficult to predict. Further research could be conducted with a prospective registry supplemented by online predictive and educational tools. Therefore, improving the outcome is the first major challenge in FG, but improving survival is only one aspect of this severe disease.

What about the long-term situation of FG patients, such as wound situation, quality of life or general health status? To our knowledge, there is only very sparse data reflecting these issues. Suijker et al. performed a retrospective cohort study on the quality of life in patients surviving necrotizing soft tissue infection. They found statistically significant decreased scores in Short Health Form 36 questionnaire for the domains of physical functioning, role physical functioning, and general health in comparison to the Dutch reference population. They concluded that necrotizing soft tissue infections negatively affect the quality of life, especially in physical domains. Naturally, if the outcome is improved, research about long-term aspects such as the wound situation or quality of life is absolutely warranted.

In our opinion, improving health-related quality of life (HRQoL) and the wound situation of FG patients are the second major challenges in FG. Consequently, we performed a multicentric retrospective study in male long-term survivors of FG with the primary aim to describe patient-reported outcomes (PROs) and HRQoL, especially concerning the wound.

In the study, we included 39 patients with a median age of 65 years (IQR 53– 74). Twenty patients were already deceased (51.3%), nine patients were lost to follow up (23.1%), and 10 patients participated in the survey (25.6%). The median survival time was 27 months (IQR 9 – 60). The median IPSS (International Prostate Symptom Score) was 13.5 (IQR 4.3 – 22.3), five patients (50%) had severe erectile dysfunction. Three patients (30%) reported problems with the wound, two (20%) complained about wound pain and one (10%) about the wound healing situation. The mean global health score in WOUND-QoL was 1.83 (SD 1.1), which is significantly less than in the German reference population (p<0.001). In the FLQA-w the mean subscales were for physical aliment 1.8 (SD 1.1), everyday life 1.5 (SD 0.5), social life 1.6 (SD 0.8) and psychological well-being 1.8 (SD 1.2). The mean general health score in SF-36 was 64.0 (SD 10.5).

In summary the wound situation of long-term FG survivors has a deeply negative impact on HRQoL especially in physical domains. Further research is essential to ensure the quality of care. One first approach could be the development of a disease-specific validated QoL questionnaire for FG patients, specifically addressing the wound situation and physical impairment.

Looking to the literature, adjunct wound therapy is discussed especially with VAC, HBO, and the therapy with larvae (Lucilla sericata larvae), but it remains unclear if these adjunct therapies could improve outcome, wound situation or even HRQoL. Furthermore, it remains unclear which patients will benefit from these specific therapies.

As a whole, there are two major challenges in the treatment and care of FG patients: improving the outcome and the establishment of long-term survival, and bettering the wound situation as well as HRQoL. Unfortunately, there is no standard of care in the diagnosis, treatment and long-term care of FG all over Europe. Additionally, the disease is very difficult to predict and there are more challenges in FG such as awareness of FG and time to treatment and the standardisation of care. For these reasons, further robust research on a rare disease is essential. This can be done with a prospective international online registry.

Due to modern data integration solutions, the registry could be accompanied by online predictive tools and educational information which, could be the steps for the solution of the first two major challenges in FG. Therefore, our approach is the establishment of a prospective FG registry study and data base for improvement of patient care.

We would also like to underscore that the development of antimicrobial resistance (AMR) all over Europe is alarming, even in rare infectious disease such as FG. Antimicrobial stewardship (ABS) as well as improving disease management are absolutely necessary.

Additionally, we as urologists should bear therapy of infectious disease in mind because it is an essential part of our specialisation. We need to be precise and cautious about prescription of antibiotic therapy.

References can be requested from the corresponding author.

Saturday, 11 March 16:15 - 16:25
ESIU Meeting: Urogenital infections in urology
Yellow Area, Amber 3

Opinion: Are you prepared to be naked?

The societal and feministic perspective of urology

Kristien Hemmerechts (BE)
Author

k.hemmerechts@skynet.be

The 7th International Congress on the History of Urology takes place on Friday 10 March, during EAU23. A number of speakers will cover a diverse range of topics, including the political and sociological drivers of the history of urology and the developments over the 50 years since the EAU was established. In this article, well-known author Kristien Hemmerechts shares her perspective on diversity, which she will present on Friday, 10 March.

Hemmerechts: I have a problem with gynaecologists and also with hairdressers. I know I'm supposed to talk about urologists, but I don't have any experience with them yet, in spite of having suffered multiple bladder infections, but it never crossed my mind to consult a urologist. Maybe I should have done, maybe my life would have taken an entirely different direction had I done so.

I like a hairdresser to focus on my hair, to get on with it, and to definitely not expect small talk – or even any talk – from me. For years now I've had my hair trimmed by my daughter, she's no professional but she has a professional attitude. Likewise I want my gynaecologist to be professional: to know what he or she is up to, to get on with it, to be business-like and to know their business. And again, no small talk, please.

"So if you ask me what the world needs right now, I would say we need efficient and professional practitioners of medicine with lots of experience and expertise."

For a long time I changed gynaecologists every couple of years and then at one point I stopped making appointments, I just couldn't take it anymore. Then one day I felt a lump in my breast, and I realised at once it was no good. My stepdaughter recommended the nephew of her mum's boyfriend. She had his mobile number sitting in her phone, so I could see him the next day. Was I impressed with this man! He managed to examine my breasts and my private parts with me barely noticing. I love that expression: 'private parts'. We don't say it that way in my mother tongue, which is Dutch, but it's an ace expression, for those parts are private and should be treated as such. I doubt whether there is one single woman on this planet who doesn't hate that device to open you up, the duckbill speculum. With him it was over and done before I had time to even think how I disliked it.

So if you ask me what the world needs right now, I would say we need efficient and professional practitioners of medicine with lots of experience and expertise. That is the first and foremost requirement, also of hairdressers by the way. It doesn't matter what gender or race they are, of how they define their sexuality, as long as they are efficient.

Having said that I would find it odd if the person handling the mammography machine were a man. They have to take hold of your breasts and push them between those plates. It's unpleasant enough when a woman does it. I guess I'm a bit old-fashioned in this respect. I must confess e.g. to preferring gendered toilets. I know I will have to get used to gender neutral ones – the world has decided that it is the way forward, and who am I to argue with the world.

A young woman writer recently told me she did not want to have her picture taken for professional purposes by a man. She felt it would be wrong for a newspaper to send a male photographer to her house. I was stunned. I've had my picture taken by many male photographers. Once by an Italian, he kept shouting: Bella! Bella! I was wondering whether all Italian photographers were like that.

I've also had my picture taken by women, but never by a black photographer. Recently the paper has sent a photographer who had been born in China and had been adopted by Belgian people. Her pictures were very good. You'd be surprised what difference a photographer can make. Same is true of urologists, of course. Not to forget the hairdressers. My guess is that the photographer with Chinese roots was sent as part of a drive to have a more diverse team. For the arts I'm all in favour of diversity. The more diversity, the more ideas, the more perspectives, the more wealth. To what extent does this also hold for the world of medicine?

The western – scientific – way of practising medicine has been dominant and has yielded tremendous successes. It has also led to the sense of it being the right, the enlightened way, and all other ways being considered backward and primitive, though occasionally their benefits are acknowledged as in the case of acupuncture.

There are a number of very good reasons to strive for diversity in your team. For a start, a lot of talent goes untapped if you exclude certain groups. Intelligence, ability and talent are not the privilege of a specific category. Moreover a diverse team may inspire people to seek professions or careers that otherwise they might feel excluded from. I can remember the first time I was treated by a doctor who was not white. He was a dentist, and without me asking for it, he whitened my teeth. And another slightly related memory: I had given birth to my son, and I was wheeled on a bed to a room. Before entering I was asked whether I objected to sharing with a black woman. I was shocked, not because of her, but because of the question. You don't have to tell me the colour of your skin doesn't matter, because it does. And exactly for that reason it is crucial to demonstrate the opposite. And how can you demonstrate the opposite? By having as diverse a team as possible.

But then there is the final hurdle: to what extent do you expect everybody on your team to conform to the established code of conduct? To what extent will they only be professionally successful, to what extent will they only come up for promotion if they play it by the written and especially the unwritten rules? How much space is there for members of the team to be different?

"The more diversity, the more ideas, the more perspectives, the more wealth. To what extent does this also hold for the world of medicine?"

It's extremely nice and energising to work in an environment where you feel you fit in, where you feel you can be yourself. Everybody benefits, including the patients who are treated by happy and relaxed doctors. Unfortunately such work environments are rare. Many organisations – hospitals, universities, companies, banks – will claim they invite discussion, that they are open to disagreement, that they encourage the debate, that they strive for transparency. In most cases this is nothing but window dressing. The power is usually in the hands of a very limited group of people. This group has only one aim: to keep this power, by whatever means. They don't have the well-being of the organisation at heart, they are concerned with their own wellbeing, and often – though not always – they are male. I think men are better at lobbying and networking. I'm definitely no good at it. At the University where I was teaching I stopped attending meetings for it was a total waste of time. Everything had already been settled and decided. We had to attend to uphold the pretence of democracy and transparency. I didn't know how to fight this, to resist it.

"A diverse team may inspire people to seek professions or careers that otherwise they might feel excluded from."

So if you ask me what organisations and institutions should do, I would say: start by being honest. Don't fool yourself and don't fool others. When you use the word 'diversity', have you stopped to think what it means? Do you realise that it may entail a code of practice that is unfamiliar to you, and therefore potentially scary? To what extent are you willing to have your way of doing things challenged? To what extent are you willing to relinquish some of your power? Of your status? Of your privileges? To what extent are you willing to admit that you have power, status, privileges?

I once attended open heart surgery for the purpose of writing about it. It started early in the morning and went on for quite a while. At a certain moment the surgeon, who had made a name for himself by fixing the heart of our then king, suggested we take a break for coffee. As I remember there were some five people in attendance; they had to watch as part of their training.

'What about them?' I asked pointing to the people who stood there motionless and stiff, like guards of a royal coffin. 'Won't they have coffee?' For a second he seemed puzzled, almost as if he was not aware of the presence of these underlings. As far as he was concerned they did not exist, and they certainly had no need for coffee. It was clear that in that hospital you had to submit to this surgeon, you had to pay him respect as if he were some tribal leader. It was take it or leave it.

I have no way of assessing whether this is typical of hospitals, whether such hierarchies are established everywhere, but I'm sure it is fairly general, and I'm equally sure it will be vehemently denied. It takes a lot of courage to look critically at your own behaviour, and to allow junior people to express criticism. In my experience the criticism will inevitably lead to retaliation. And thus so many people shut up and feel quietly miserable at work. And possibly they take it out on their inferiors and patients.

There are two options: you play the game according to the rules or you quit. And a third option: you have a burn-out. A Dutch poet once wrote: to be naked and to begin. So my question to you is: are you prepared to be naked? Are you prepared to lay off the signs of your status and achievements, and to listen, to really listen, even when what you hear will not be to your liking?

Friday, 10 March, 09:05 - 09:20
7th International Congress on the History of Urology
Yellow Area, Amber 7

Precision medicine for patients with mCRPC

What are the best predictive factors for successful treatment with Lu-PSMA?

Dr. Francesca Serani
DIMES, Alma Mater Studiorum University of Bologna Nuclear Medicine department, IRCCS Azienda Ospedaliero-Universitaria di Bologna (IT)

Dr. Stefano Fanti
DIMES, Alma Mater Studiorum University of Bologna Nuclear Medicine department, IRCCS Azienda Ospedaliero-Universitaria di Bologna (IT)

177Lutetium Prostate-Specific Membrane Antigen (Lu-PSMA) is a radiolabelled small molecule inhibitor that binds with high affinity to PSMA delivering β particle radiation. It has been shown to have a high level of antitumour activity and a favourable safety profile for the treatment of patients with metastatic castration-resistant prostate cancer (mCRPC) [1].

Although evaluating the same radiopharmaceutical in essentially the same population, these two successful trials differed in their predefined end-points and inclusion criteria.The TheraP trial was a randomised phase II trial comparing Lu PSMA with cabazitaxel. The primary endpoint was PSA response rate, defined by reduction of at least 50% from baseline, and the secondary endpoint was progression free survival (PFS) and radiographic progression, assessed with CT or bone scan [2]. Lu PSMA showed to be superior for PSA response and PFS compared to cabazitaxel.

The VISION trial was a randomized phase III trial comparing Lu PSMA with standard care therapy to standard care therapy alone. The primary outcome was the evaluation of overall survival (OS) and image based PFS while the secondary endpoints were objective response, disease control and time to symptomatic skeletal events [3]. In this trial Lu PSMA improved OS and image based PFS.

In addition, in the TheraP trial prostate cancer with known significant sarcomatoid, spindle cell or neuroendocrine small cell components were excluded from the trial, while there is no mention of it in the VISION trial.

They both included a progressive mCRPC patient population, previously treated with one taxane, with adequate renal, bone and liver function with ECOG 0 to 2. All patients had to be selected for trial enrolment by a 68Ga-PSMA PET/CT (PSMA PET). That is where we started noticing the major differences in the selected populations: when we start talking “Nuclearese”, or for the newbies, the Nuclear Medicine language.

The TheraP trial included patients who at PSMA PET showed a significant PSMA avidity, defined as a minimum uptake of maximum standardized uptake value (SUVmax) of 20 at a site of disease, and SUVmax greater than 10 at sites of measurable disease (≥10mm). Patients were excluded if they showed sites of disease positive in the 18Fluorine-fluorodeoxyglucose PET/CT (FDG PET), with minimal PSMA expression defined as FDG intensity greater than 68Ga-PSMA activity or 68Ga-PSMA SUVmax less than 10 [2].

The VISION trial included patients who were PSMA-positive at the PSMA PET, defined as lesion uptake greater than that of liver parenchyma. Patients with PSMA-negative metastatic lesion (lymph node with a short axis of at least 2.5 cm, solid-organ lesions with a short axis of at least 1.0 cm and bone lesion with a soft-tissue component of at least 1.0 cm in the short axis), defined as PSMA uptake equal to or lower than that of liver parenchyma, were excluded [3]. In this trial no FDG PET was performed.

Given the high and numerous direct and indirect costs of Lu PSMA (and the low but not negligible toxicity of this therapy) the questions of how to correctly select patients, if there are predictive factors for successful treatment and which population can actually benefit from this treatment [5] should be answered in the future.

Discussion

Gafita et al [1] validated a nomogram predictive of outcomes after Lu-PSMA in patients with mCRPC. This nomogram is a multi-centre retrospective evaluation developed and validated using international data, where the primary endpoints were OS and PSA PFS. The secondary endpoint was PSA decline of 50% or more (PSA50). The model includes patients representative of the VISION trial patient cohort [1].

In this analysis they evaluated 18 pretherapeutic parameters as putative predictors for outcome after Lu PSMA. Out of all 18, the selected predictors for OS, PFS and PSA50 are showed in table 1 [1].

Outcome	Predictors
Overall Survival (OS)	Time since diagnosis Chemotherapy status Baseline haemoglobin Number of metastases Tumour SUVmean at PSMA PET Bone involvement Liver involvement
PSA Progression Free Survival	Time since diagnosis Chemotherapy status Tumour SUVmean at PSMA PET Pelvic nodal involvment Bone involvement Liver involvement
PSA decline ≥ 50% (PSA50)	Chemotherapy status Tumour SUVmean at PSMA PET Pelvic nodal involvment Liver involvement

Table 1: Predictors of Lu PSMA therapy response divided per end-point. Modified from (1)

The nomograms for OS, PSA PFS and PSA50 combine traditional clinical prognostic variables and incorporate novel prognostic variables that are relevant for the patient population taken in consideration [1].

A higher tumour SUVmean at PSMA PET is associated with a higher probability of response to LuPSMA treatment for OS, PSA PFS and PSA50. Previous treatment with chemotherapy has shown to have a negative impact on all the outcomes considered: OS, PSA PFS and PSA50, together with liver involvement [1]. This may be explained by the fact that this kind of patient has a more advanced disease that is more difficult to control.

The presence of pelvic lymph node metastases correlated with a longer time to PSA progression and a decline ≥ 50% of PSA [1].

A longer time since first diagnosis is associated with better OS and PSA PFS, together with the absence of bone involvement. Several factors might be responsible for the resistance mechanism of bone metastases from prostate cancer, for instance tumour microenvironment and lower target expression [1].

It has been observed that higher levels of haemoglobin and less than 20 metastases are associated with better prognosis [1].

Eventually, the patient population was stratified into two risk groups (high risk vs low risk) using the calculated optimal cut-off for their risk scores (197 points for OS nomogram and 178 points for PSA PFS nomogram). The median OS for low-risk patients versus high-risk patients was 19,9 months versus 8,2 months in the complete set, and the median PSA PFS during Lu PSMA for low-risk patients versus high-risk patients was 8,8 months versus 3,3 months in the complete set [1].

In Gafita et al., the nomogram FDG PET was not evaluated because it was available only for a limited number of patients. Previous use of androgen receptor signalling inhibitors was not associated with an outcome in their models, which may be related to low statistical power [1].

A TheraP tertiary end-point was to investigate an association between total tumour quantitative parameters on PSMA PET, FDG PET and baseline characteristics with clinical outcomes [5].

In the analysis, conventional biomarkers (ECOG, alkaline phosphatase, haemoglobin, bone and liver metastases) were not found to be significant for determining PSA response rate, the primary endpoint of the TheraP trial [5]. However, two PET parameters were found to be statistically significant for therapy response in mCRPC patients: PSMA PET mean standardised uptake value (SUVmean) and FDG PET metabolic tumour volume (MTV) [5].

A mean standardised uptake value (SUVmean) of 10 at PSMA PET was predictive of a higher likelihood of favourable response to LU PSMA than cabazitaxel. No other PSMA PET parameters were found to be significant in predicting treatment response [5]. This result is concordant with the one from Gafita et al. [1]; even though PSMA expression correlates with the aggressiveness of prostate cancer, the higher the PSMA expression the greater the delivery of Lu PSMA to the tumour target [1].

The explanation of this result may reside in the intrinsic difference between SUVmax and SUVmean: while the first measures the highest concentration of the radiotracer in metastasis, SUVmean measures the average concentration of the radiotracer within the entire tumour volume. The higher this value, the greater the delivered radiation to tumour sites from Lu PSMA [5].

Even if today there is not a univocal PSMA PET parameter to select patients, a refinement of patient selection for Lu PSMA is needed to optimise outcome [6].

FDG PET shows tumour deposits with high glucose metabolism, which can be seen as dedifferentiation for prostate cancer and, therefore, a high proliferation rate. A metabolic tumour volume (MTV) greater than 207 mL was associated with lower responses regardless of the randomly assigned treatment. This means that these patients, regardless of the therapy received, may benefit from an intensification of treatments [5].

In the TheraP trial the “a priori” selection excluded patients with discordant results from FDG PET and PSMA PET.This was a consistent decision made upon previous results that FDG+/PSMA– lesions are a negative predictor of overall survival in patients with mCRPC undergoing RLT [7].

One of the things that was not taken into account in any the aforementioned studies is the evaluation of the homologous recombination repair gene mutation status of the patients. This is possibly due to the fact that the trials and studies evaluating Lu PSMA started before the results of the PARP inhibitor therapy came out [8]. In the future, adding this parameter can lead to a better understanding of the response to Lu PSMA therapy As of now, few clinical trials have started patient enrolment going into this direction [9.

Conclusion

In summary, we want to highlight the best predictive factors currently known for successful treatment with Lu PSMA of mCRPC patients. It is now widely accepted that the selection of the patient has to be done carefully and attentively. To offer such a high-cost and specialised treatment, we must assess if the patient will benefit from it, and it may be possible that offering a better therapy for the current stage will lead to an optimisation of resources.

References:

1. Gafita A, Calais J, Grogan TR, et al. Nomograms to predict outcomes after 177Lu-PSMA therapy in men with metastatic castration-resistant prostate cancer: an international, multicentre, retrospective study. Lancet Oncol. 2021;22:1115-1125.
2. Hofman MS, Emmett L, Sandhu S, et al. [177Lu] Lu-PSMA-617 versus cabazitaxel in patients with metastatic castration-resistant prostate cancer (TheraP): a randomised, open-label, phase 2 trial. Lancet. 2021;397:797-804.
3. Sartor O, de Bono J, Chi KN, et al. Lutetium-177-PSMA-617 for Metastatic Castration-Resistant Prostate Cancer. N Engl J Med. 2021;385:1091-1103.
4. Fallah J, Agrawal S, Gittleman H, et al. FDA Approval Summary: lutetium Lu 177 vipivotide tetraxetan for patients with metastatic castration-resistant prostate cancer. Clin Cancer Res. December 2022:CCR-22-2875.
5. Buteau JP, Martin AJ, Emmett L, et al. PSMA and FDG-PET as predictive and prognostic biomarkers in patients given [177Lu]Lu-PSMA-617 versus cabazitaxel for metastatic castration-resistant prostate cancer (TheraP): a biomarker analysis from a randomised, open-label, phase 2 trial. Lancet Oncol. 2022;23:1389-1397.
6. Hotta M, Gafita A, Czernin J, Calais J. Outcome of Patients with PSMA PET/CT Screen Failure by VISION Criteria and Treated with 177Lu-PSMA Therapy: A Multicenter Retrospective Analysis. J Nucl Med. 2022;63:1484-1488.
7. Michalski K, Ruf J, Goetz C, et al. Prognostic implications of dual tracer PET/CT: PSMA ligand and [18F]FDG PET/CT in patients undergoing [177Lu]PSMA radioligand therapy. Eur J Nucl Med Mol Imaging. 2021;48:2024-2030.
8. Keisner SV. Rucaparib and olaparib for the treatment of prostate cancer: A clinician’s guide to choice of therapy. J Oncol Pharm Pract. 2022;28:1624-1633.
9. Gafita A, Marcus C, Kostos L, Schuster DM, Calais J, Hofman MS. Predictors and Real-World Use of Prostate-Specific Radioligand Therapy: PSMA and Beyond. Am Soc Clin Oncol Educ Book. 2022;42:1-17.

Sunday 12 March 17:50 - 18:00
Thematic Session: Is precision medicine possible in patients with mCRPC?
Yellow Area, eURO Auditorium 1

Genetic testing in renal stone disease

15% of stone formers have a molecular genetic cause

Prof. John Sayer
Professor of Renal Medicine Translational and Clinical Research Institute, Newcastle University (GB)

Urology is an attractive surgical specialty and has moved rapidly with innovation and precision therapies. Sub-specialisation into endourology and kidney stones provides the urologist opportunities to become adept at preventative therapies and personalised approaches for improved patient outcomes. The consideration of the urine's colour, odour and composition was an ancient art [1, 2] which now has been taken forward into modern day urology, especially kidney stone disease. The application of modern-day genetics and genomics to kidney stone disease provides a robust assessment tool for the diagnosis of genetic diseases and genetic risk factors underlying kidney stone disease.

The benefits of a molecular genetic diagnosis
There are numerous benefits of undertaking a molecular genetic approach to kidney stones. A precision medicine diagnosis can be made, which allows a tailored plan for patient management, focussing on prevention of recurrent stones [3]. A molecular genetic diagnosis provides insights into disease pathogenesis and allows novel medical therapies to be designed. It also allows targeted screening of at-risk relatives and family members who may also be predisposed to kidney stone disease.

When and why perform genetic investigations?
Kidney stones are common, with 1 in 11 people having a stone within their lifetime, and over 50% recurrence risk within 5-10 years. Kidney stones predominantly affect working age adults, 10% require hospital admission and 5% require urological surgical intervention. Stone incidence is also increasing, and rates in females are catching up with males [4], pointing to the fact that both environmental and genetic factors are interacting to increase risk. It is well known that kidney stones cluster within families, there is a family history of stones in up to 37% of kidney stone formers and the heritability has been estimated to be up to 60% [5]. 80% of kidney stones are calcium oxalate containing or calcium phosphate containing [6] and up to 70% of people with hypercalciuria who form kidney stones have a relative with kidney stones disease [7].

Clearly, we are not at a stage where blanket genetic testing can provide all the answers but a reasonable approach to a recurrent kidney stone formed would be to consider the chemical composition of the stone, whether there is a relevant family history of kidney stone disease, the age of onset of stone disease and the biochemical features of serum and urine. These considerations and tests often then point towards an underlying genetic condition. Monogenic disorders such as cystinuria, primary hyperoxaluria, and APRT deficiency, all may lead to frequent and recurrent stones, chronic kidney disease and a risk of kidney failure. Sometimes there may be relevant extra renal manifestations such as deafness (e.g. distal renal tubular acidosis), oxalosis of tissues (e.g. primary hyperoxaluria), and bone disease (e.g. hypophosphatemia rickets with hypercalciuria). Biochemical abnormalities detected on 24-hour urine testing such as hypercalciuria, hyperoxaluria, and hypocitraturia may all have underlying monogenic causes and genetic testing is an effective means of identifying these disorders.

Is genetic testing worthwhile and how do I do it?
There is a growing list of monogenic causes of stone disease which includes over 35 rare inherited disorders. A previous study identified a molecular generic cause in 15% of stone formers when applying a next generation sequencing panel to a cohort of 268 patients with stones or nephrocalcinosis [8]. This study pointed to the immediate and practical implications of a genetic diagnosis, confirming the clinical diagnosis in 60% of cases but in 40% provided new diagnostic and practical implications which allowed targeted medical therapies and approaches to be used for stone treatment and prevention. The findings were replicated in other studies showing 17% solve rate in paediatric cohorts of stone formers [9] and 30% solve rate in a cohort of young stone forms who manifested phenotypes before 25 years of age [10].

"There is a family history of stones in up to 37% of kidney stone formers and the heritability has been estimated to be up to 60%."

The typical approach when genetically investigating a recurrent stone former would be to use next generation sequencing (NGS) to perform a targeted gene panel for known causes of inherited kidney stones. This method is obviously resource dependent, but the cost of such assays are rapidly decreasing to less than 500 Euro. Alternative approaches of whole exome and whole genome sequencing with the application of virtual gene panels are also rapidly entering clinical practice. The nuances of the underlying NGS technologies are not essential knowledge as both provide excellent and comparable diagnostic yields. The clear advantage of genome wide approaches allows the reanalysis of data over time and the ability to incorporate new knowledge regarding gene variants into its interpretation [11, 12].

My personal approach is to, following informed consent, take a single EDTA blood sample for DNA storage from every recurrent kidney stone former to allow genetic investigations to proceed if there are features suggesting a monogenic cause. The yield of a NGS panel approach will be 10-20% but the use of exome or genome sequencing will allow alternative predictive genetic data to be generated and will provide valuable data to allow future understanding of this important disease. Recruiting kidney stone forming patients to research registries (such as ERKNet), databases and biobanks remains an important priority if we are to gain the benefits of the genomic revolution.

"Recruiting kidney stone forming patients to research registries, databases and biobanks remains an important priority."

Genetic versus environmental factors in kidney stone disease
It is clear that there is interplay of both genetic and environmental factors in kidney stone formation. These interact with both urinary inhibitors of stone formation (such as citrate, magnesium, pyrophosphate, and others) as well as urinary promoters of stone formation (such as calcium, phosphate, urate, cystine) [13] which will tip the balance towards calculus formation. A good example of this interplay would be 1,25 dihydroxy Vitamin D levels. These are influenced by diet, lifestyle, ethnicity, exposure to sunlight as well as metabolic processes withing the liver and kidney, which are undertaken by key enzymes, the expression of which are genetically determined. Vitamin D overdose leading to kidney stone disease is unusual, but in the context of a mutation in CYP24A1 encoding CYP24A1, the enzyme which inactivates 1,25 dihydroxy Vitamin D, a phenotype of hypercalcaemia, hypercalciuria and kidney stones is seen [14]. Aside from full blown pathogenic variant in CYP24A1, more subtle variants, known as polymorphisms, (or risk alleles) may play a role in risk of calcium stone formers [15].

We have therefore become good at detecting and defining rare disease variants that account for monogenic kidney stone disease. The variants are defined as causal and have, in most cases, have a defined pathophysiology. At the alternate end of the spectrum, we have also become adept at genome wide association studies (GWAS) that are able to examine large populations and identify common genetic variants that have tiny but accumulative effects on risk of kidney stone disease. These genetic variants can be gathered and used to form polygenic risk scores. What remains fascinating, is that many of these common genetic risk alleles are in or nearby genes implicated in the rare monogenic stone diseases. Finally, there is the middle ground between monogenic and GWAS identified variants where genetic sequencing of carefully phenotyped populations, such as those in the UKBiobank, allows genetic variants that are intermediate (i.e. not common or rare) to be examined and this approach has successfully identified coding gene variants with moderate to large effects sizes [16]. A good example of this are variants in SLC34A1 which can be causal for rare monogenic kidney stone disease as well as acting as moderate and minor risk alleles for calcium stone formation. These variants may therefore explain the missing heritability of kidney stones (Figure 1).

In conclusion, analogous to sending kidney stones for biochemical analysis, performing a genetic screen for kidney stone formers provides valuable information. A monogenic disorder will be identifiable in over 15% of cases. In cases where a monogenic disorder is excluded, risk alleles may be identified and going forward will contribute enormously to our understanding of the pathogenicity of kidney stone disease. Genetic studies allow a more precise and personalised approach to stone formers. I urge urologists to interact with nephrologists and clinical geneticists interested in kidney stone disease to maximise the gains from these very affordable and increasingly powerful genetic testing approaches.

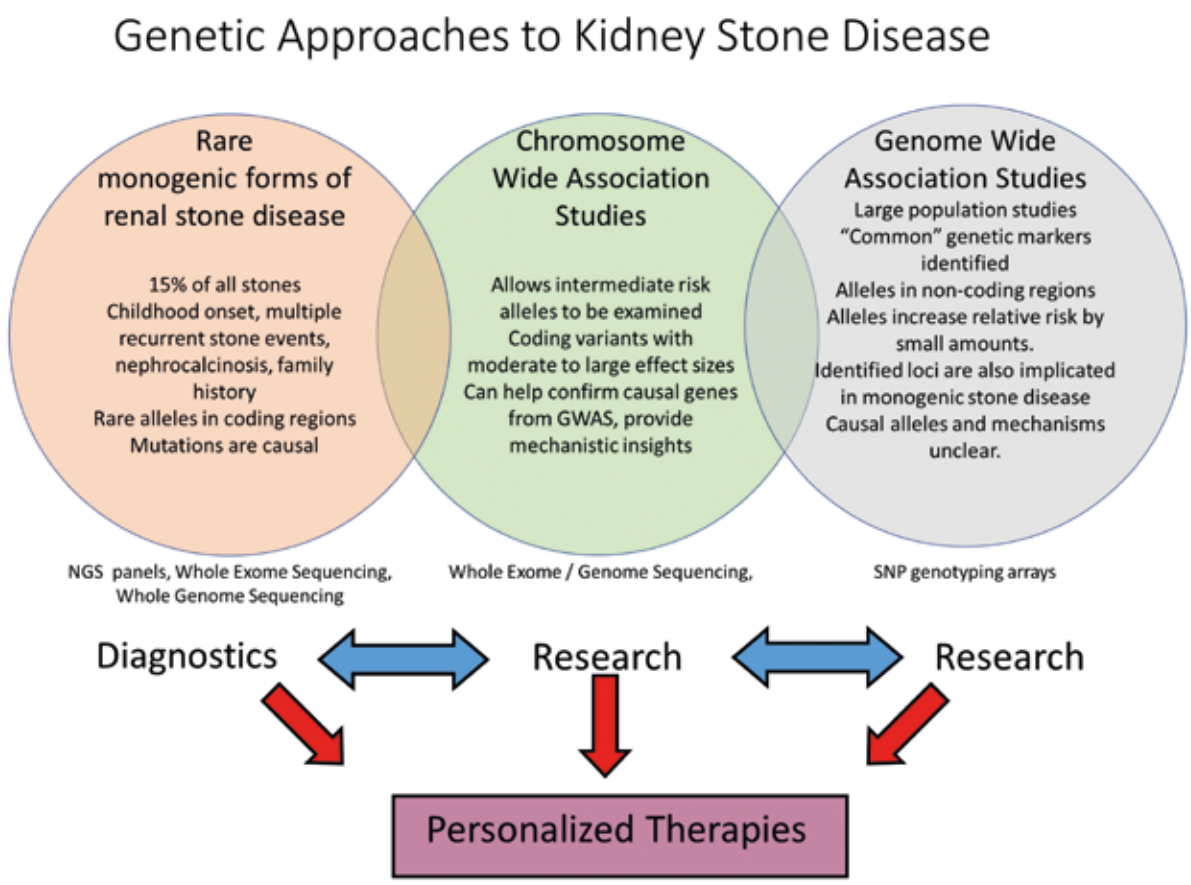

Figure 1: Genetic studies in kidney stone formers
The combination of identifying rare monogenic stone disease variants as well as intermediate and common risk alleles allows a diagnostic and research pathway to lead towards precision medicine and personalised therapies for patients.

References

1. Connor, H., Medieval uroscopy and its representation on misericords – Part 1: uroscopy. Clinical Medicine, 2001. 1(6): p. 507-509.
2. Nöske, H.D., [The "Pisse-Prophet" or the "English fortune-teller from urine". A critical book on uroscopy bei Thomas Brian]. Urologe A, 2005. 44(9): p. 1062-3.
3. Hill, F. and J.A. Sayer, Precision medicine in renal stone-formers. Urolithiasis, 2019. 47(1): p. 99-105.
4. Scales, C.D., Jr., et al., Prevalence of kidney stones in the United States. Eur Urol, 2012. 62(1): p. 160-5.
5. Goldfarb, D.S., et al., A twin study of genetic and dietary influences on nephrolithiasis: a report from the Vietnam Era Twin (VET) Registry. Kidney Int, 2005. 67(3): p. 1053-61.
6. Sayer, J.A., Progress in Understanding the Genetics of Calcium-Containing Nephrolithiasis. J Am Soc Nephrol, 2017. 28(3): p. 748-759.
7. Stechman, M.J., N.Y. Loh, and R.V. Thakker, Genetics of hypercalciuric nephrolithiasis: renal stone disease. Ann N Y Acad Sci, 2007. 1116: p. 461-84.
8. Halbritter, J., et al., Fourteen monogenic genes account for 15% of nephrolithiasis/nephrocalcinosis. J Am Soc Nephrol, 2015. 26(3): p. 543-51.
9. Braun, D.A., et al., Prevalence of Monogenic Causes in Pediatric Patients with Nephrolithiasis or Nephrocalcinosis. Clin J Am Soc Nephrol, 2016. 11(4): p. 664-72.
10. Daga, A., et al., Whole exome sequencing frequently detects a monogenic cause in early onset nephrolithiasis and nephrocalcinosis. Kidney Int, 2018. 93(1): p. 204-213.
11. Cirino, A.L., et al., A Comparison of Whole Genome Sequencing to Multigene Panel Testing in Hypertrophic Cardiomyopathy Patients. Circ Cardiovasc Genet, 2017. 10(5).
12. Hocking, L.J., et al., Genome sequencing with gene panel-based analysis for rare inherited conditions in a publicly funded healthcare system: implications for future testing. Eur J Hum Genet, 2022.
13. Halbritter, J., Genetics of kidney stone disease-Polygenic meets monogenic. Nephrol Ther, 2021. 17s: p. S88-s94.
14. Willows, J. and J.A. Sayer, CYP24A1 mutations and hypervitaminosis D. Clin Med (Lond), 2019. 19(1): p. 92-93.
15. Howles, S.A., et al., Genetic variants of calcium and vitamin D metabolism in kidney stone disease. Nat Commun, 2019. 10(1): p. 5175.
16. Sun, B.B., et al., Genetic associations of protein-coding variants in human disease. Nature, 2022. 603(7899): p. 95-102.

Sunday 12 March 14:33 - 14:43
Personalised stone approach through innovation
Pink Area, Coral 6

What is the best method of risk stratification before biopsy?

Algorithm for further risk stratification ready to be tested in pilots across Europe

***Renée Hogenhout**, MD/PhD candidate Dept. of Urology, Erasmus MC Cancer Institute, Rotterdam (NL)*

Co-author: Prof. Dr. Monique J. Roobol, Professor Decision Making in Urology.

On the 20th of September 2022, after three decades of research, the European Commission added prostate, lung and gastric cancer to the list to be addressed by the cancer screening recommendations, on top of cervical, colorectal and breast cancer. This gives the green light to implement good quality prostate cancer screening programmes throughout Europe. But what is a good quality programme?

Rapid technological developments in the detection of prostate cancer, a generally slow-growing disease

The strict answer is that we do not know, and in a world of exponentially increasing technological advancements, we will probably never know. Especially with prostate cancer being a slow-growing process, we are constantly overtaken by time. This conundrum makes it difficult, or even nearly impossible, to translate the long-term outcomes of new tools to current practice in time. By the time the long-term outcomes of a certain newly developed tool or screening strategy become available, it might be replaced by the next. A prime example is the traditional PSA-based screening strategy that was used by the European Randomized Study of Screening for Prostate Cancer (ERSPC) [1] and the Prostate, Lung, Colorectal and Ovarian (PLCO) Cancer Screening trial [2]. Elevated PSA levels were followed by systematic sextant prostate biopsy (a one-size-fits-all strategy). We had to wait for almost two decades before the data of these trials became mature enough to publish the first results. Those results showed us that screening indeed could avoid suffering and dying from prostate cancer, which opened the way for further research. However, sextant biopsy was replaced by laterally-directed biopsy, and later on by MRI-targeted biopsy to improve cancer detection, causing a stage shift and making long-term outcomes from the ERSPC and PLCO not fully translatable to the present time [3]. Also, the reported overdiagnosis resulting from this strategy (~50% [1]) is no longer current with the rise of risk calculators and MRI as a stratification tool.

But this doesn't mean that the knowledge gained so far is useless and that we should wash our hands of the matter. On the contrary, letting prostate cancer run its course leads to a high disease-specific mortality rate. To illustrate this, in the seventies, before the PSA discovery, two out of three prostate cancer patients died of their disease [4]. More recently, after the recommendation against prostate cancer screening a stage migration to advanced prostate cancer stages was observed in, amongst others, the USA and Germany [5, 6], requiring expensive and invasive treatments with a negative impact on quality of life [7]. To combat what is by now the second leading cause of male cancer death [8], we need to make a start with a risk-based screening strategy for prostate cancer that is the best way to go according to current available knowledge. We can build on the important lessons learned from the past and focus on the favourable short-term outcomes from ongoing state-of-the-art screening trials, as long as we remain aware of the pitfalls and keep validating and updating the implemented tools and strategies.

"In the seventies, before the PSA discovery, two out of three prostate cancer patients died of their disease."

Pilot testing by the PRAISE-U consortium

Next month, the EAU-led Prostate cancer Awareness and Initiative for Screening in the European Union (PRAISE-U) initiative will start. The main aims of the PRAISE-U consortium are to gain insight into the state-of-play of and need for population-based prostate cancer screening in the 27 EU member states, and to initiate several nationally tailored pilot testing sites throughout Europe. Analyses arising from these pilot studies will focus on aspects like acceptance, logistical capacity, quality control, avoiding unnecessary prostate biopsy, overdiagnosis, and cost effectiveness.

Risk-based screening strategy

The European Association of Urology (EAU) position paper published a flexible algorithm to conduct a risk-based prostate cancer screening strategy, which is used by the PRAISE-U consortium as a starting point [9, 10]. This strategy aims to leverage the proven benefit of PSA testing while reducing unnecessary diagnostic procedures and combatting overdiagnosis by using new risk stratification tools. Some steps in the algorithm have already been validated, while others are still being investigated.

The flexible algorithm for further risk stratification can be easily adapted according to local resource availability. Although many variations are therefore possible, the essence of a risk-based prostate cancer screening programme is to break the link between elevated PSA and immediate biopsy to reduce unnecessary biopsy procedures and overdiagnosis. Table 1 shows that PSA density alone as a simple biomarker already provides a huge improvement in discriminative ability in significant prostate cancer detection compared to PSA only. Depending on availability, risk stratification can be further extended with risk calculators whether or not they are enhanced with MRI data or advanced (genetic) blood biomarkers further increasing the discriminative ability.

Tool	AUC
PSA	0.64 (95% CI 0.59-0.69) [11]
PSA density	0.78 (95% CI 0.74-0.82) [11]
Traditional RCs	0.76-0.80 [12]
MRI-informed RCs	0.81-0.87 [12]
Blood-based RC*	0.86 (95% CI 0.83-0.89) [12]
*Stockholm3.	

Table 1 – Discriminative ability for csPCa detection of several stratification tools

Several variations of the algorithm (variation 5) are presented in figure 1. Every variation has its own pros and cons compared to the one-size-fits-all strategy (variation 0). In general, with any strategy, some clinically significant prostate cancers will be missed simply because men are excluded from biopsy based on probabilities. No prediction comes with 100% certainty. On the other hand, overdiagnosis can never be ruled out completely against an acceptable percentage of missed significant cancers. A safety net for those false negatives is, therefore, mandatory (i.e. re-entering the algorithm) and active surveillance should be offered to overdiagnosed men.

"The essence of a risk-based prostate cancer screening programme is to break the link between elevated PSA and immediate biopsy to reduce unnecessary biopsy procedures and overdiagnosis."

The simplest pathway is to apply risk stratification with clinical variables, for example by using a risk calculator (variation 1). Most risk calculators are accessible to every clinician (e.g. online, mobile application), easy to use, inexpensive and noninvasive. The general condition is that the risk calculator's performance must be evaluated within the target population and recalibrated if necessary. Several risk calculators, the so-called traditional RCs (i.e. not MRI-informed), have been developed. Of these, the Rotterdam Prostate Cancer Risk Calculator (RPCRC) and the Prostataclass showed the highest discriminative ability (AUC=0.79) [11]. To illustrate clinical implication, using the RPCRC avoids one-third of the biopsy procedures (cut-off 12.5%) [12]. Other well-known tools with good performance representing variation 1 are the STHLM3 model [13] and the 4Kscore [14], which combine clinical variables with other blood biomarkers. A comment should be made, however, on the price of these last two scores, especially if they were to be applied on a population-based level.

"In the light of the present and future financial pressure on the European healthcare system, avoiding unnecessary MRIs by pre-risk stratification is an essential step."

Meanwhile, MRI has taken an important role in the diagnostic process of prostate cancer. Performing MRI before biopsy is highly recommended as it improves the detection of clinically significant prostate cancer and reduces overdiagnosis (variation 2-5) [15]. However, the availability of high-quality MRI and expert readers can sometimes be limited. Fortunately, attractive alternatives have been developed. The Göteborg trial compared multiparametric MRI, as today's golden standard for prostate cancer imaging, with the less expensive bi-parametric MRI [16]. Their promising results regarding cancer detection encourage research in prospective, multicenter and multiobserver settings to work towards large-scale implementation [17, 18]. However, another important lesson that we have learned from this trial is that performing MRI in all men with elevated PSA levels (variation 2) result in many negative MRI outcomes (75-77%). In the light of the present and future financial pressure on the European healthcare system [19], avoiding unnecessary MRIs by pre-risk stratification is an essential step. In 2018, Mannaerts et al. found that with a risk-based patient selection strategy using the RPCRC in a clinical cohort, one-third of MRI scans can be avoided [20]. Such a strategy (variation 3) is currently being applied in a screening cohort by the ProScreen trial using the 4Kscore and the STHLM3-MRI study with favourable (preliminary) results [21, 22].

"The PRAISE-U consortium will assess national needs among the EU member states and coordinate pilot testing sites to gain insight into the feasibility and effectiveness of different risk-based prostate cancer screening strategies."

Since, on the one hand, not all significant cancers are visible on MRI, and on the other, the detection rate of significant cancer is relatively low in equivocal lesions (PIRADS 3), risk-stratification after MRI is also preferred. Several MRI informed risk calculators have been developed (Table 1) and compared, of which one appears to be clinical useful according to decision curve analysis [23, 24]. Application of the model in a clinical cohort could reduce 28% of biopsy procedures at the cost of missing only 2.6% of clinically significant cancers. The Organised PCa Testing (OPT) project in Sweden is currently investigating such an approach in a screening setting, with PSA-density as a stratification tool (variation 4) [25].

Conclusion

The European Commission has given the green light to implement good quality prostate cancer screening programmes across Europe. The PRAISE-U consortium will assess national needs among the EU member states and coordinate pilot testing sites to gain insight into the feasibility and effectiveness of different risk-based prostate cancer screening strategies. Many stratification tools have been developed and proven their usefulness, however mainly in a clinical setting and in the short term. Validation studies of these tools in a screening setting are ongoing with promising preliminary results. Some pieces of the puzzle have been slotted into place while others are yet to be laid. But at the same time that knowledge gaps are being filled, new ones will always arise due to the rapid technical developments in the detection of prostate cancer which is a generally slow-growing disease. It is a continuous, dynamic process that started three decades ago and will never end. However, an important step is now being taken with the implementation of these pilot testing sites that build on the valuable knowledge gained so far, fulfilling a crucial monitoring role and strive for continuous improvement.

References can be requested from the corresponding authors.

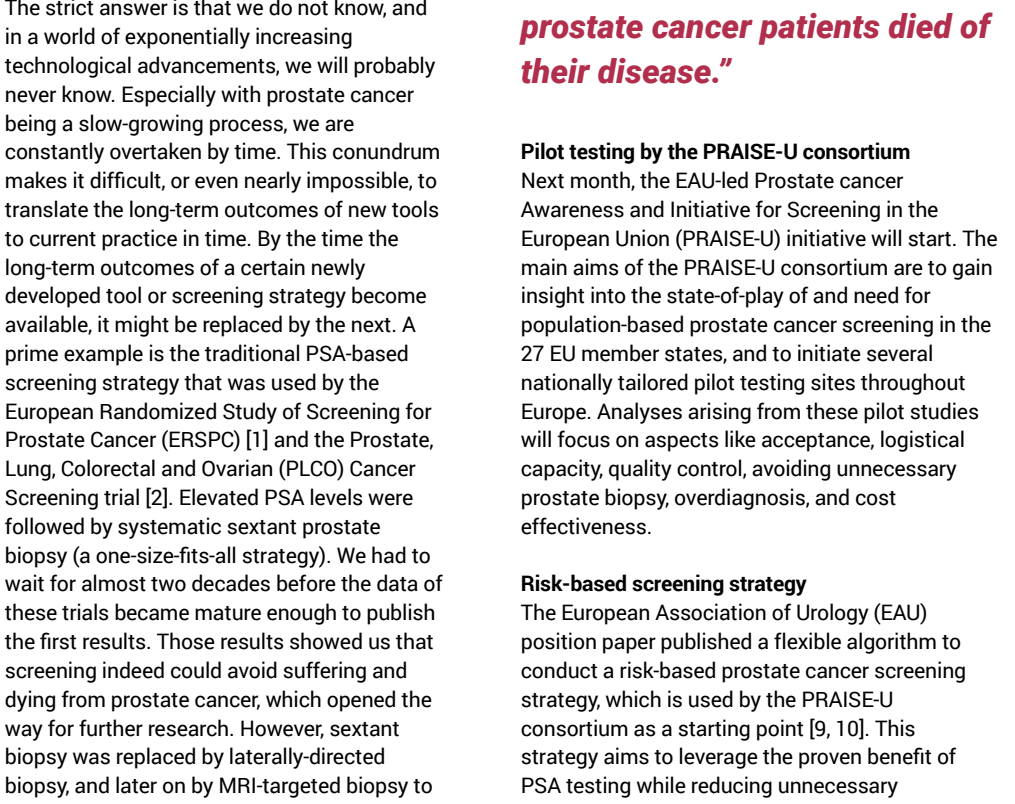

Figure 1 – Variations on the EAU's risk-adapted early prostate cancer detection strategy (variation 5) aiming to improve the one-size-fits-all strategy (variation 0).

Sunday 12 March 08:33 - 08:41
Plenary Session: The right management of prostate cancer: Early detection and active surveillance
Yellow Area, eURO Auditorium 1

Sexuality in metastatic prostate cancer

What can we do to improve patients' quality of life during ADT treatment?

Prof. Andrea Salonia
Experimental Oncology/Unit of Urology, IRCCS Ospedale San Raffaele; Vita-Salute San Raffaele University (IT)

salonia.andrea@hsr.it

Dr. Edoardo Pozzi
Experimental Oncology/Unit of Urology, IRCCS Ospedale San Raffaele;Vita-Salute San Raffaele University (IT)

Prostate cancer (PCa) is the most common urological cancer and accounts for nearly a quarter of all new cancers in men [1]. Since the widespread use of prostate-specific antigen (PSA) testing in the 1990s, the incidence of PCa has risen sharply [1,2]. All areas of PCa from diagnosis through to surgical and medical treatments are rapidly advancing. Besides ongoing evaluation of novel biomarkers and genetic profiling, ground-breaking advances in MRI imaging, biopsy techniques, prostatectomy techniques (thus including every type of robot-assisted radical prostatectomy), imaging-guided radiotherapy, and multiple large-scale clinical trials of new drugs within the last decades have made PCa a more and more approachable disease, with better prognosis even at metastatic (+m) stages [1,3,4].

In this context, the median survival of patients with newly diagnosed metastatic PCa is approximately 42 months with ADT alone, being highly variable as +m population is highly heterogeneous [5]. As this holds true, the quality of life (QoL) of +m PCa patients remains pivotal [6]. As such, sexual dysfunction (e.g., lower sexual desire (LSD), erectile dysfunction (ED), anejaculation and ejaculatory disorders, lack of orgasmic function, etc.) are listed among the most distressful and bothersome dysfunctions in men treated for +m PCa [6]. The early institution of ADT (any type) in men with +m PCa should be well balanced against the sex-related side effects and long-term morbidity. Equally relevant, the impact of ADT on bone events, cognitive function, and QoL have been appreciated and reported.

Published evidence: clinical and pre-clinical
Compelling evidence has accumulated over the years with nine currently published studies, specifically evaluating the impact of ADT and sexual function impairment among men with PCa [7–16]. In a recently published study by Corona et al, when combing these studies, it has been demonstrated that ADT resulted in a five to six-fold increased risk of reduced libido and in a three-fold increased risk of developing ED [17]. Reported data on ED were confirmed even when those studies using healthy subjects as a control group were excluded from the analysis (risk for ED = 3.08 [1.96; 4.82]; $p < 0.0001$) or when only case–control studies were considered (risk for ED = 2.57 [1.71; 3.85]; $p < 0.0001$). Finally, the risk was higher when studies lasting less than 52 weeks were compared to longer trials (ED risk 3.36 [2.56; 7.40] vs. 2.22 [1.68; 2.92]; $Q = 4.90$, $p = 0.03$) [17].

In line with these data, the European Male Aging Study (EMAS), a population-based survey performed on more than 3,400 men recruited from eight European centres, clearly demonstrated that LSD along with ED and reduced morning erections, were the most sensitive and specific symptoms in identifying hypogonadal aging men [18]. Similar results were reported in other large cohorts (n = 4890) of subjects seeking first medical help for ED or in the Testosterone Trials, a survey performed in up to 800 community-dwelling men recruited from 12 sites in the USA [19,20]. The increased risk of ED after ADT confirms the available pre-clinical data regarding the interconnection between circulating testosterone levels and ED pathophysiology. In this context, the androgen receptor signalling is a pivotal step for penile erections.

"Educational and sex-oriented approaches are essential steps for guaranteeing the best outcomes in almost every sexual problem."

Accordingly, data has documented that androgens modulate nearly every pathway involved in regulating penile erection at a local level [21]. In particular, androgens are critical for maintaining the right balance between trabecular smooth muscle and connective tissue [22,23]. Moreover, the interconnection between testosterone per se and nitric oxide (NO) pathway is well-established. Likewise, testosterone is involved in the negative control of Ras homolog gene which contains its intrinsic kinase pathway; this strictly regulates the phenomenon of penile detumescence [22,23]. Lastly, androgens are also involved in the regulation of α1-adrenergic responsiveness of smooth muscle cells resulting in increased sympathetic cavernosal smooth muscle tone [22].

Patient counselling
Educational and sex-oriented approaches are essential steps for guaranteeing the best outcomes in almost every sexual problem [24–26]. This is particularly true in men with PCa undergoing ADT, where multiple problems can influence couple fitness [6]. Body feminisation including gynecomastia, hot flushes, loss of muscle mass, and genital shrinkage, along with sexual dysfunction and mood disturbances, can profoundly affect patient and partner self-esteem and psychological well-being [27]. This is even more relevant in +m PCa, with an incredible number of psychologic rebounds. Therefore, correct patient management can be achieved through collaboration with GPs, psychologists, sexologists, uro-andrologists and medical oncologists. In this context, patients and partners need to be counselled and informed. Open and correct communication is pivotal for the management of couples' expectations along with patient's personal experience. Couples should be exhaustively informed that the orgasm sensation could be still experienced, even in the absence of firm erections, so that penetrative intercourse is not considered essential to remaining sexually active. In the presence or not of firm erections, patients and their partners should be informed that ADT increases the threshold for triggering the orgasm experience, so a more intense sexual stimulation over a longer period is required [17]. An adequate educational program and intervention is beneficial to mitigate the decline in sexual intimacy in men undergoing ADT and may allow couples to maintain more successful and satisfactory intimate and emotional relationships, thus including sexual activity. Finally, the inclusion and empowerment of a partner – whenever actually present – throughout the educational process could enhance outcomes and continuation of sexual activity, even in +m PCa individuals.

References can be requested from the corresponding authors.

Friday, 10 March 08:00 – 10:00
Plenary Session: Challenges in supportive care in GU cancers
Yellow Area, eURO Auditorium 1

Classification of mesh complications

It's time for a new patient-centred classification system, practical for clinical use

Dr. Carolina Ochoa Vargas
Consultant Urological Surgeon, Bristol Urological Institute, Bristol (GB)

carolina.ochoavargas@gmail.com

Prof. Hashim Hashim
Consultant Urological Surgeon & Director of the Urodynamics Unit, Bristol Urological Institute, Bristol (GB)

h.hashim@gmail.com

The use of synthetic material in female pelvic floor surgery over the last 30 years has been significant. In the 1990's, tension-free retropubic sub-urethral synthetic tapes/slings for stress urinary incontinence (SUI) were introduced [1]. Following that, the transobturator tapes (TOT) and single-incision slings were introduced [2]. The use of mesh for vaginal prolapse surgery has also spread as it achieved anatomical efficacy with a 29% risk reduction of recurrence [3]. However, most of these trials did not report long-term complications. In a retrospective study of over 92,000 women in England, complications have been reported in 9.8% of cases at 5 years [4]. Complications can either be mesh related, such as infection and healing abnormalities [5] and/or procedural-related, such as during insertion. A wide range of complications have been reported, such as mesh exposure (2.7–4.4%), voiding dysfunction requiring surgery in 3%, urinary tract infections (UTIs) in 10.7–17.1%, neurological symptoms in 5.4–9.7% [6] chronic pain in 4.5% up to 9% [7], bowel related problems and even systemic complications [8].

"The classification system translates complex clinical findings into organised descriptions, standardising communication."

In 2011, due to the uniqueness of the complications, the International Continence Society (ICS) and the International Urogynecological Association (IUGA), jointly established a classification system based on the category, time and site (CTS) [9]. The purpose was to standardise the language and increase awareness of complications following female pelvic floor procedures using prostheses and grafts in pelvic surgery. The secondary aim was to support the creation of a registry of complications to inform and guide surgeons, patients, and the industry. This registry, known as CTS Classification, incorporates a vast range of clinical scenarios into a numerical and ordinal code so that no additional descriptors are necessary.

How CTS Classification works

The CTS system describes a complication according to its anatomical site and severity involving three (or four) letters and three numerals. C stands for category [1 to 7]. The first three are vaginal complications from no exposure to more than 1 cm. Categories 4 and 5 include perforation into the urinary tract, rectal or bowel accordingly. Category 6 includes musculoskeletal complications (fistula); the last one, 7, includes systemic complications. Next to the number will be a capital letter (A-D). A: Asymptomatic, B: Symptomatic, C: Infection, D: Abscess. A subclassification for pain is also included in the system, with a lowercase letter 'a' being no pain to 'e' being spontaneous pain. The time (T) is when the complication is clinically diagnosed, starting from T1 (48 h) to T4 (over a year). S (site) establishes that the least severe complication involves the anatomical site into which it was inserted (vaginal complications S1, S2). Surrounding anatomical structures involved will be S3 (trocar passage related), S4 (not associated with trocar skin or musculoskeletal complications) and S5 (intraabdominal complications). S0 (Systemic complications with no specific site) (Figure 1).

The classification system replaced the term "erosion" with more specific terms for clarity. The new proposed terms are Contraction (shrinkage), Prominence (protrusion, with no epithelial separation), Separation, Exposure (mesh visualisation), Extrusion (gradual exposure), Perforation (opening into a hollow organ), Dehiscence (open along sutured lines), and Sinus tract formation (fistulous tract). It also determines that all complications should be listed and reported separately, and if there is a progression over time, the highest category should be used.

"However, the classification system has also been criticised for being cumbersome for clinical use and more suitable for research."

The system translates complex clinical findings into organised descriptions, including essential details for treatment planning. It also gives surgeons a well-characterised understanding of potential complications, which is advantageous in preoperative counselling. In addition, the CTS standardises communication, making it suitable for surgical audits, complication registries, and publications.

Usability in the real world?

After its publication, several groups assessed the usability of the ICS/IUGA CTS system in academic and clinical practice. The applicability and reliability of the system have been proven [10, 11]. However, the system has also been criticised for being cumbersome for clinical use and more suitable for research [12]. A large number of variables makes it difficult to compare subgroups, and interobserver variability has also been demonstrated [13]. Batalden et al. [12] argue that 30% of their cases could not be retrospectively coded in an academic tertiary care referral hospital with Female Pelvic Medicine and Reconstructive Surgery board-certified surgeons. In the same study, the authors concluded that the CTS classification did not predict treatment or outcome, while patient symptoms predicted both.

Several publications recommend altering the system to include common functional disorders such as voiding dysfunction and, de novo overactive bladder [11, 12]. Petri et al. [14] also suggested that rare complications like dyspareunia of the partner, urine loss during intercourse, and foreign body sensation may be placed in the miscellaneous category. The CTS system is also considered doctor-centred since patient satisfaction is not included in the classification [12].

"Over 92,000 women in England, complications have been reported in 9.8% of cases at 5 years [4]."

Another problem with the classification system is that it does not specify the type of mesh. Some patients may have more than one mesh with multiple complications, for example, more than one extrusion or exposure.

In 2013 Gutman et al. [15] published a pelvic floor complication scale (PFCS). They aimed to develop a tool for assessing peri and postoperative complications specific to pelvic reconstructive surgery (prolapse and urinary incontinence). The investigators rated specific intraoperative plus immediate and delayed postoperative complications on a scale from 0 to 10 based on severity, patient bothers, and duration of the disability. They compared their system with the Clavien-Dindo classification system. They concluded that PFCS could reflect complications specific to pelvic floor surgery. However, despite being specific for pelvic floor surgery, this scale includes non-mesh procedures. Moreover, it still needs to be validated.

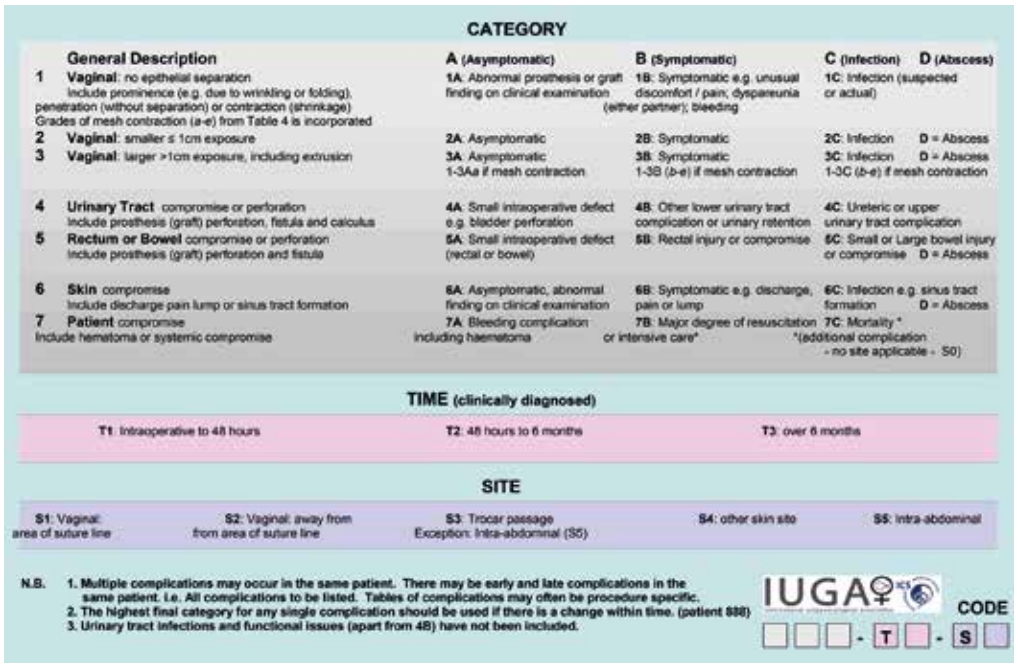

Figure 1. International Continence Society/International Urogynecological Association classification system, see www.ics.org.

Conclusion

In summary, the CTS is the most currently available specific mesh-related complications classification system. However, there is a need for a new classification system, which ideally would be patient-centred, adequately describe the complication, and be agile enough to use in clinical practice. In addition, it needs to include associated symptoms, e.g. bowel and bladder, and functional disorders may enhance the ability to use it in counselling and management.

References are available on request from the authors.

Sunday, 12 March 14:12 - 14:17
EAU Guidelines Session: Non-neurogenic female LUTS
Yellow Area, eURO Auditorium 2

Application of AI to overcome scientific information overload

Novel uses of natural language processing for more meaningful science

Jenny Ghith
Pfizer Inc.
Collegeville, PA

On behalf of the INSIDE-PC Working Group*

INSIDE-PC (artificial **INtelligence to **S**upport **I**nformed **DE**cision making in Prostate Cancer) Working Group: Arnulf Stenzl, Cora Sternberg, Andrew Armstrong, Andrea Sboner, James N'Dow, Lucile Serfass, Christopher Bland and Bob Schijvenaars*

The scale of data and scientific literature available today is surpassing metrics predicted only a few years back. Over 3,200 clinical trials in urologic cancers are ongoing as of January 2023. [1] Approximately 20,000 cancer-related articles were accepted in 10 high impact urology journals in 2022 (Figure 1). The COVID-19 pandemic only accelerated data availability, as researchers set new standards and operated within a short time frame to produce findings, vaccines, and treatments [2], with articles being published at a rate of up to 14,000 each month. [3] In addition to surges in scientific data, digital advances are enabling substantive increases in patient-level data through electronic health records, wearables, and mobile apps.

What is information overload?
These increases in knowledge are cause for celebration but are also a double-edged sword. In a 2021 internal survey of 150 US and EU physicians, 60% of oncologists and 80% of urologists treating patients reported they were not able to easily find answers in the literature to complex questions on treatment of prostate cancer (Figure 2). Amongst physicians, information overload can lead to practice inconsistency, scepticism, uncertainty, distrust of medical evidence, and lack of awareness or adherence to recommendations from Societies and Committees. Moreover, access to an excess of complex and conflicting cancer-related information can cause worry and confusion among patients, who are increasingly turning to search engines like Google and social media for their health information.[4,5]

How can artificial intelligence (AI) and language models help? What are the challenges?
AI is being used in oncology for tasks such as diagnostics, imaging, drug discovery, and cancer prognostics, but has been more of a nascent field in literature mining and writing academic papers. AI can help clinicians search and analyse literature, extract useful information, identify knowledge gaps, and stay updated on new developments in the field. Machine learning development speed is staggering in multiple areas, including text analysis, speech, images, and combinations of these. Interest in this area is only increasing. For example, in late 2022 ChatGPT was released by OpenAI and gained over one million users within 5 days. ChatGPT is a state-of-the-art language model that uses neural network architecture to generate human-like text in response to a prompt. As of January 22, 2023, ChatGPT has also been listed on PubMed as an author on 2 publications and 2 pre-print articles. [6,7]

A major limitation of language models like ChatGPT that provide text answers to queries, is *hallucination*; answers generated may be mostly correct but are not always so, which can result in inaccuracies and the creation of misinformation. The models are often not able to explain their answer as the computations performed to generate the answer are different from human reasoning (this can be described as a "black box" where there is no transparency in how AI algorithms process information). [8] Hence, there is emerging research in *Explainable AI*, which is a set of processes or methods that allow human users to comprehend and trust the results and output created by AI systems.[9] There is a lot of cause for excitement given the progress in this subfield of AI, but also a need for prudence and general education. Regardless of the platform or use case, clinicians should understand the data used to train these AI models and be aware that language and even data itself can contain biases (e.g., in race, ethnicity, and gender). Frequency and social bias towards popularity can also occur. Feeding biased data into AI algorithms can produce systemically biased outputs. [8]

Project INSIDE-PC
AI is the catalyst to disrupt information overload and lead towards more meaningful science. The INSIDE-PC (*artificial **IN**telligence to Support **I**nformed **DE**cision making in **P**rostate **C**ancer*) project explores novel uses of natural language processing and AI to derive insights and answer queries from the complex universe of scientific literature and clinical trial databases. With this technology, content and meaning are extracted from searches *inside* publications and clinical trial databases to identify not just the presence of key terms but the context in which these terms are being used (called "semantics"). The semantic analysis and AI framework used to help experts delve INSIDE publications for information related to a specific query can also be repurposed to address other future questions of scientific interest (Figure 4).

INSIDE-PC tackles one of the most complex issues within the literature for oncologists and urologists who treat genitourinary cancers – specifically the issue of therapeutic sequencing. This includes consideration of how to sequence classes of drugs such as NHTs, PARP inhibitors and emerging agents like radioligand therapies. Building from work previously published in *BJUI* by Stenzl et al. [8], AI algorithms are used to emulate how human clinicians extract sequences for advanced prostate cancer treatment from scientific publications in order to answer the question: *what are the outcomes when using drug X (or drug class X) followed by drug Y (or drug class Y)*? A sequence (A->B) is a temporal relationship (e.g., patients who were initially treated with treatment A and subsequently treated with B) that can be challenging to extract and interpret from the literature.

Ultimately, INSIDE-PC helps to address this challenge as users can filter their searches for a specific treatment sequence and extract the associated scientific publications that reported its use. The full text of scientific documents are searched for the sequence, and each document is analysed for sentences that are relevant based on the context, and users are provided with the ability to sort on parameters including the level of evidence and type of outcome. The dashboard is under development and will be presented with its validation during the EAU Congress on March 13, 2023, during the thematic session *"Is Artificial Intelligence (AI) in Urology Ready for Prime Time?"*.

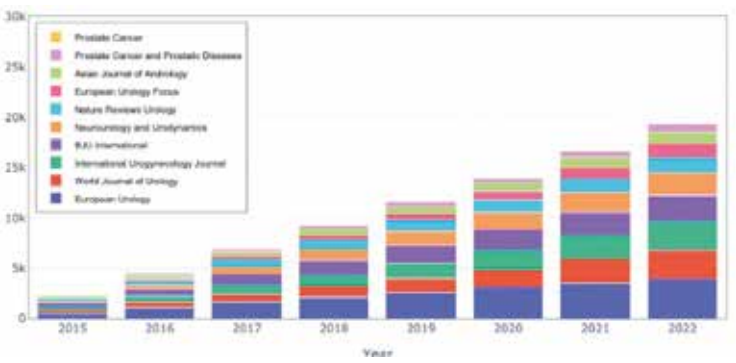

Figure 1: Growth in urology journal publications

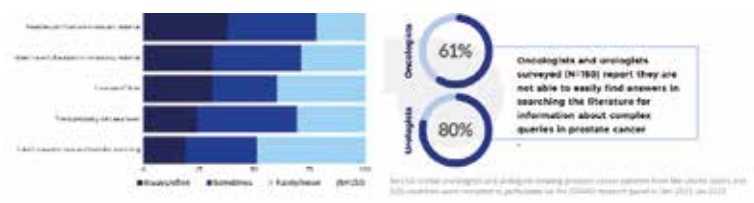

Figure 2: Information overload amongst urologists and oncologists

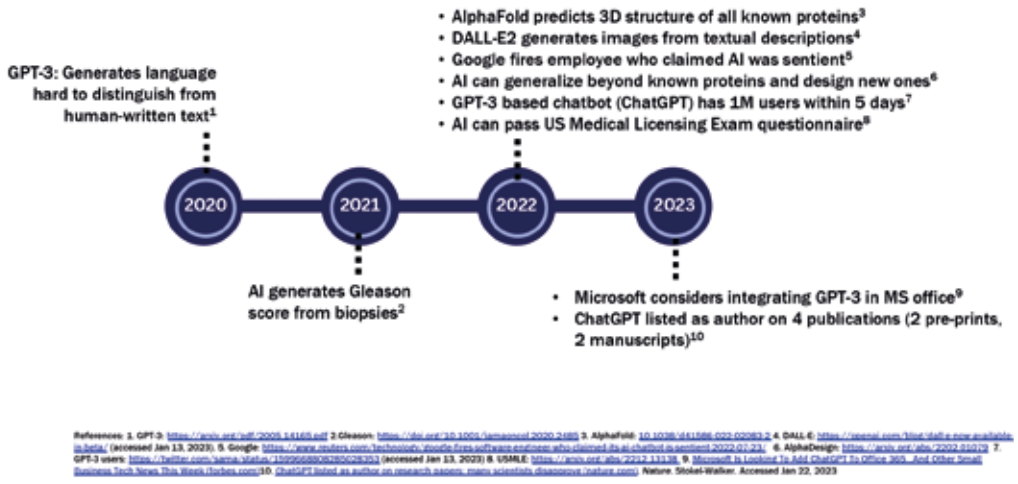

Figure 3: Progress in AI language models and image generation

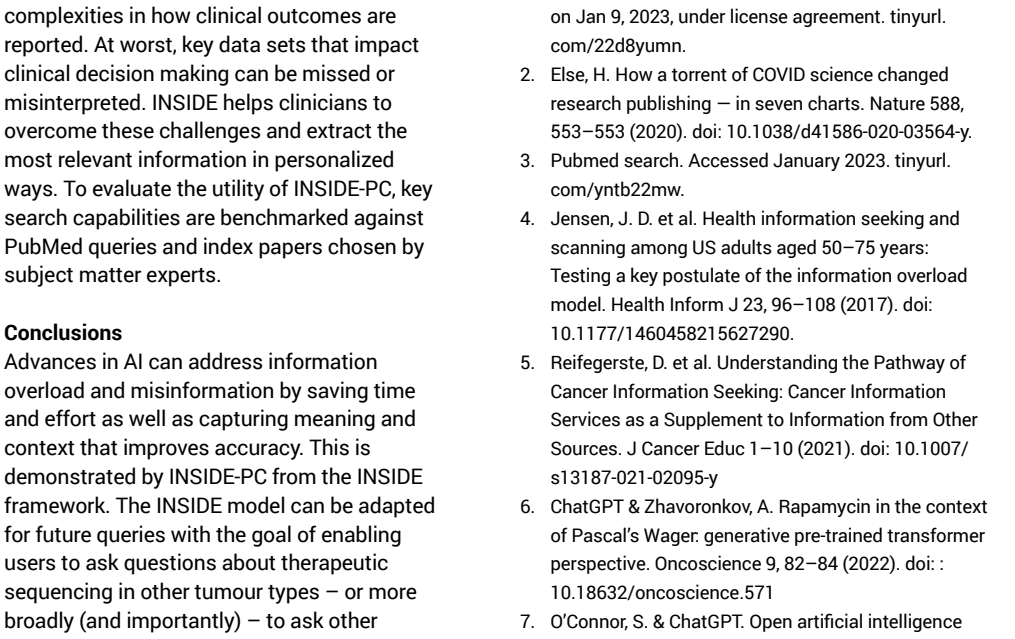

*Figure 4: The premise of INSIDE-PC**

Searching the scientific literature and clinical guidelines for specific therapeutic sequences of key interest in traditional ways (e.g., via searches on PubMed) is difficult because of the heterogeneity in how sequences are described, the time-consuming and complex nature of searching, the similarity of terms related to "genetic sequencing", and the complexities in how clinical outcomes are reported. At worst, key data sets that impact clinical decision making can be missed or misinterpreted. INSIDE helps clinicians to overcome these challenges and extract the most relevant information in personalized ways. To evaluate the utility of INSIDE-PC, key search capabilities are benchmarked against PubMed queries and index papers chosen by subject matter experts.

Conclusions
Advances in AI can address information overload and misinformation by saving time and effort as well as capturing meaning and context that improves accuracy. This is demonstrated by INSIDE-PC from the INSIDE framework. The INSIDE model can be adapted for future queries with the goal of enabling users to ask questions about therapeutic sequencing in other tumour types – or more broadly (and importantly) – to ask other questions of relevance for prostate cancer itself or different cancers entirely.

Ultimately the technology can be used to

1. **Extract additional information and relationships between terms** (e.g., identifying adverse events or subgroups and how they are impacted by treatments)
2. **Develop direct question & answering systems** that deliver precise answers to queries and can handle simple requests and tasks (vs. traditional search engines, where users must extract answers themselves)
3. **Advance more targeted data extraction** (e.g., ingest trial and real-world evidence data for further analysis or hypothesis generation)
4. **Develop "living SLRs" and Guidelines** (that allow Committees to surface the most relevant information more quickly and accurately)
5. **Develop tools to automatically summarize text and write** short articles

For these reasons, it is incumbent upon clinicians to stay informed and understand the strengths and limitations of emerging AI technologies. It will help the healthcare community to obtain more personalized information and achieve better outcomes for patients. In fact, in many ways AI is no longer emerging—it is already here today.

References

1. Digital Science. (2018) Dimensions [Software] available from https://app.dimensions.ai. Accessed on Jan 9, 2023, under license agreement. tinyurl.com/22d8yumn.
2. Else, H. How a torrent of COVID science changed research publishing — in seven charts. Nature 588, 553–553 (2020). doi: 10.1038/d41586-020-03564-y.
3. Pubmed search. Accessed January 2023. tinyurl.com/yntb22mw.
4. Jensen, J. D. et al. Health information seeking and scanning among US adults aged 50–75 years: Testing a key postulate of the information overload model. Health Inform J 23, 96–108 (2017). doi: 10.1177/1460458215627290.
5. Reifegerste, D. et al. Understanding the Pathway of Cancer Information Seeking: Cancer Information Services as a Supplement to Information from Other Sources. J Cancer Educ 1–10 (2021). doi: 10.1007/s13187-021-02095-y
6. ChatGPT & Zhavoronkov, A. Rapamycin in the context of Pascal's Wager: generative pre-trained transformer perspective. Oncoscience 9, 82–84 (2022). doi: : 10.18632/oncoscience.571
7. O'Connor, S. & ChatGPT. Open artificial intelligence platforms in nursing education: Tools for academic progress or abuse? Nurse Educ Pract 66, 103537 (2023). doi: 10.1016/j.nepr.2022.103537
8. Stenzl, A. et al. Application of Artificial Intelligence to Overcome Clinical Information Overload in Urologic Cancer. BJU Int, 130: 291-300 (2021). doi: 10.1111/bju.15662
9. Khan, M. S. et al. Explainable AI: A Neurally-Inspired Decision Stack Framework. Biomimetics 7, 127 (2022). doi: 10.3390/biomimetics7030127.

Monday 13 March, 10:50 - 11:00
Thematic Session: Is artificial intelligence (AI) in urology ready for prime time?
Pink Area, Coral 4

Sleep-related painful erections

Pathophysiology and management of a rare disease

Mr. Mark Johnson
Urology trainee, Yorkshire and Humber deanery (GB)

Co-author: Prof. David Ralph FRCS (Urol), University College London Hospital (GB)

Sleep-related painful erections (SPRE) is a parasomnia typified by painful erections occurring during rapid-eye-movement (REM) sleep that differ from painless erotic erections. Parasomnias are defined as undesirable experiences or physical phenomena whilst during sleep, falling asleep or waking up [1]. Men with SRPE can experience pain with each REM cycle causing them to wake and leading to sleep fragmentation and daytime fatigue. Other causes of penile pain, such as phimosis or Peyronie's disease, can co-exist with SRPE. However, these clearly have different pathology and do not explain SRPE [2].

SRPE is a rare condition not currently recognised in international urological guidelines. This can lead to an incorrect or a delay in diagnosis. The literature for SRPE is limited to retrospective case series and case reports, leading to a high-level bias, and contradiction. The aim of this review is to discuss the pathophysiology, diagnostic tests, and treatment options currently available.

Pathophysiology
The pathophysiology of SRPE is undefined. The available evidence is summarised below.

Penile compartment syndrome
Normal/physiological penile erections are an ischemic event resulting from veno-occlusion of the corpus cavernosa of the penis, which resolves with detumescence [3].

Persistence (> 4 hours in duration) of a penile erection results in a compartment syndrome of the corpus cavernosum and is defined as ischemic priapism. This results in time-dependent histological changes in the tissue from ischemia, to infarction and fibrosis. Stuttering priapism is a sub-type of ischemic priapism typified by recurrent minor episodes of painful priapism often at night or in the early morning. This condition most commonly affects men with sickle cell disease, however can be idiopathic.

There are obvious similarities in the clinical features between stuttering priapism and SRPE. However, men with SRPE often have significantly more episodes of painful erection each night and detumescence usually occurs very shortly after waking [4]. A comparison of penile blood gas analysis would be helpful in defining the similarities and differences between these two conditions.

Hypertonicity of the pelvic floor
Contraction of the pelvic floor muscles occurs normally during the rigid phase of penile erection [3]. Hypertrophy and contraction of these muscles could result in pain that radiates to the penis during sleep-related erections. This may explain why men with SRPE report pain in different locations (e.g. penis, perineum, scrotum, and lower abdomen) [5]. Hypertrophy of the pelvic floor has been noted in two patients on Doppler ultrasound [6] and increased muscle tone has been noted on electromyography [5]. However, the pelvic floor would contract during erotic erections which are pain-free in men with SRPE.

Obstructive sleep apnoea (OSA)
OSA is known to alter autonomic and hormonal pathways and is already implicated in other urological conditions such as nocturnal polyuria [7]. There are two cases in the literature of successful treatment of SRPE with continuous positive airway pressure [8]. In contrast, there are only five cases in the literature of men with SRPE and OSA [2] and in a larger series, the Apnoea-hyponea index was normal in all eight patients that underwent polysomnography [4], making the association between OSA and SRPE less likely.

Increased androgens
Physiological sleep-related erections are androgen dependent [9]. It is therefore postulated that increased androgens may be responsible for increased SRPE. However, the three largest case series have failed to show an association with increased testosterone levels and SRPE. Furthermore, the use of anti-androgens as a treatment has been found to be ineffective [3,6,7].

Alterations in autonomic function
Penile erection is regulated autonomic control. Acetylcholine under parasympathetic control initiates a cascade that results in vasodilation, veno-occlusion, and penile erection. Contraction of the smooth muscle (and therefore, detumescence) occurs under sympathetic control [3]. There is no direct test for measuring penile autonomic function. A reduction in cardiac vagal activity and increased accelerations of the heart rate was found in men with SRPE when compared to controls [5]. These findings may suggest an alteration in autonomic function in men with SRPE. Despite this, β-adrenergic blockers do not appear to be helpful in the management of SRPE [2].

Compression of the Lateral Preoptic area (LPOA)
Bilateral lesions in the LPOA eliminate sleep-related erections, whilst awake erections remain intact [10]. Szucs et al, found compression at the lateral hypothalamic border (area corresponding to the LPOA) in a patient with SRPE. Of those patients that also underwent a brain MRI, no others were found to have an abnormality in this area [11].

Psychological factors
There is some evidence that SRPE fully resolved with improvement in marital issues and anxiety. However, it is impossible to draw firm conclusions regarding cause or effect. Poor sleep is a risk factor for mental illness and marital issues. It would therefore seem reasonable that an improvement in symptoms could increase sleep quality, thus improve mental wellbeing and strengthen a marriage [2, 12]. Interestingly, sleep fragmentation as seen in men with SRPE has been found to increase the sensitivity to pain. This could create a vicious circle of increased sleep fragmentation leading to increased pain [13].

Investigations
Multiple investigations have been used to better understand the cause of SRPE. As demonstrated above, it is unclear which investigations are helpful. At present, there is no structured approach to the diagnostics. SRPE is a clinical diagnosis based predominantly on the history provided from the patient. A good history is often enough to start the patient on oral medications as described later in this article.

The following investigations have previously been used and can be considered, based on the history and examination findings at the time of presentation: serum hormonal profile, polysomnography/overnight oximetry, nocturnal penile tumescence, brain MRI, and pelvic floor electromyography. However, many of these tests are expensive and may not alter the management.

Management
Oral medications that aim to [1] abolish nocturnal erections through hormonal manipulation, [2] reduce sleep fragmentation or [3] suppress REM sleep, and/or [4] relax the muscles of the pelvic floor have all been used to treat men with SRPE. The available evidence is summarised below.

Baclofen
Baclofen relaxes skeletal muscles by inhibiting the release of aspartate and glutamate. Baclofen is a GABA-b receptor agonist with actions in the spinal cord and brain. Based on animal data, Baclofen has been found to have inhibitory effect on penile erection [14]. It has also been used to treat pelvic floor hypertonicity (more commonly in women) as a pelvic floor muscle relaxant [15]. The combination of these two factors may explain its beneficial effect in men with SRPE.

In the literature, Baclofen has been used in 27 patients [5, 16 - 18] across four case series and a case report. Seven of these patients have reported full remission of symptoms, 17 have reported partial improvement in symptoms, and 3 patients have reported no improvement. Follow-up protocol was variable across the studies and ranged from weeks to more than 5 years. In these 27 patients, three discontinued the medication due to side effects. A symptom relapse often occurred upon cessation of the medication.

Anti-androgens
Anti-androgens block androgen receptors thus inhibiting the effect of testosterone. These medications have been used successfully to manage patients with stuttering priapism by causing a hypogonadal state and inhibiting penile erection (erotic and sleep-related). Side effects of these medications are often intolerable and include erectile dysfunction, loss of libido, reduction in muscle mass, cognitive impairment, and cardiovascular disease [19].

Cyproterone acetate [5, 18, 20] has been used in 26 patients, 17 reported no improvement in their symptoms. Four patients have reported a partial response and four patients reported full remission of their symptoms. The final patient reported an improvement when using cyproterone acetate and baclofen in combination. Sixteen of these 26 patients reported significant side effects including erectile dysfunction, tiredness, and hot flushes. Bicalutamide has also been used in one patient unsuccessfully.

"Oral baclofen appears to be the most effective treatment currently available."

Adrenergic receptor agonists and antagonists
Adrenergic receptor agonists and antagonists have been used in the treatment of SRPE. α-adrenergic agonists have an inhibitory effect on cavernosal smooth muscles and inhibit penile erection [21]. The α-agonist, etilefrine has been used successfully in the context of stuttering priapism in men with sickle cell disease [22].

Based on the aforementioned, β-adrenergic hyperactivity that was seen in men with SRPE, β-blockers have also been used [23]. β-blockers also have a direct effect on testicular Leydig cells and can lower serum testosterone, which can affect penile erection [24].

The α-agonist, pseudoephedrine has been used in 19 men, resulting in an improvement in symptoms in six patients and having no effect in the remaining 13 patients [18]. Four of the men reported side effects in the form of palpitations and hypertension. β-blockers have been used in five patients with SRPE and have been found to have a temporary positive effect in one of these patients [8, 17, 23]. One of the patients did report an improvement when used alongside bromazepam.

Phosphodiesterase-5 inhibitors (PDE5i)
PDE5i are commonly used for the treatment of erectile dysfunction [25]. PDE5 is an enzyme that is responsible for the inhibition of cyclic guanosine monophosphate (cGMP). Therefore, inhibition of PDE5 increases intracavernosal cyclic GMP preventing detumescence of the penis. PDE5i also appear to have a paradoxical effect in reducing prolonged erections in men with stuttering priapism when used in low doses [26]. Based on this, PDE5i have been used in the management of SRPE. Overall, PDE5i are well tolerated with mostly mild and short lived side effects, including headache, flushing, nasal congestion, and gastroesophageal reflux symptoms.

PDE5i have been used in eight patients with SRPE. One patient reported full remission of symptoms, two patients have reported a partial improvement in symptoms, and the remaining men reported no response [5, 18].

Antidepressants, antipsychotics, antiepileptics and benzodiazepines
Antidepressants, antipsychotics, antiepileptics and benzodiazepines have also been used in men with SRPE in variable success. Notably, clonazepam is a REM-sleep suppressant and has been used successfully to treat other REM-sleep parasomnias. It was found to be effective in five patients. Amitriptyline is the most commonly used antidepressant medication in this context and has been helpful in four men and had no improvement in four other men. Unfortunately, these psychotropic medications are often poorly tolerated and should be avoided in the long term [2, 27, 28].

Surgical management
Surgical management with implantation of a penile prosthesis has also been used in two patients. This results in destruction of the tissue of the corpus cavernosa which prevents any subsequent spontaneous erections. Unfortunately, the two patients that underwent surgery continued to have symptoms [18]. This suggests that the pain does not originate from the penis and is likely to be a referred pain from elsewhere.

Conclusion
SRPE is a rare parasomnia the results in penile pain that wakes the patient up following each REM sleep cycle. Poor sleep is often the primary complaint and can have a significant physical and psychological toll on the patient. It is a clinical diagnosis and the pathophysiology is currently undefined. Investigations that are deemed appropriate are based on the patient history and examination findings. Oral baclofen appears to be the most effective treatment currently available. However, the symptoms often return upon cessation of baclofen. Given the rarity of this condition, collaborative research between multiple institutions is likely to be required to gain a better understanding of SRPE.

References can be requested from the corresponding authors.

Monday 13 March 12:30 - 12:40
Thematic Session: Immediate and delayed management of priapism
Yellow Area, Amber 3

Today's European Urology Events

Best Paper &
Resident Corner Awards
2023

Saturday 11th March 2023

14:00- 14:15 Yellow Area, Level +2
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RESIDENTS CORNER

First-in-human Intravesical Delivery of Pembrolizumab Identifies Immune Activation in Bladder Cancer Unresponsive to Bacillus Calmette-Guérin

Meghani K., Cooley L.F., Choy B., Kocherginsky M., Swaminathan S., Munir S.S., Svatek R.S., Kuzel T., Meeks J.J.

Volume 82, Issue 6 - Pages 602 - 610

RESIDENTS CORNER

Updating and Integrating Core Outcome Sets for Localised, Locally Advanced, Metastatic, and Nonmetastatic Castration-resistant Prostate Cancer: An Update frrom the PIONEER Consortium

Beyer K., Moris L., Lardas M., Omar M.I., Healey J., Tripathee S., Gandaglia G., Venderbos L.D.F., Vradi E., van den Broeck T., Willemse P.-P., Antunes-Lopes T., Pacheco-Figueiredo L., Monagas S., Esperto F., Flaherty S., Devecseri Z., Lam T.B.L., Williamson P.R., Heer R., Smith E.J., Asiimwe A., Huber J., Roobol M.J., Zong J., Mason M., Cornford P., Mottet N., MacLennan S.J., N'Dow J., Briganti A., MacLennan S., Van Hemelrijck M., PIONEER Consortium

Volume 81, Issue 5 - Pages 503 - 514

BEST SCIENTIFIC PAPER

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Siva S., Bressel M., Wood S.T., Shaw M.G., Loi S., Sandhu S.K., Tran B., A. Azad A., Lewin J.H., Cuff K.E., Liu H.Y., Moon D., Goad J., Wong L.-M., LimJoon M., Mooi J., Chander S., Murphy D.G., Lawrentschuk N., Pryor D.

Volume 81, Issue 4 - Pages 364 - 372

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Volume 82, Issue 6 - Pages 639 - 645

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A Phase 2 Trial of the Effect of Antiandrogen Therapy on COVID-19 Outcome: No Evidence of Benefit, Supported by Epidemiology and In Vitro Data

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Volume 81, Issue 3 - Pages 285 - 293

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Circumcision and Risk of Febrile Urinary Tract Infection in Boys with Posterior Urethral Valves: Result of the CIRCUP Randomized Trial

Harper L., Blanc T., Peycelon M., Michel J.L., Leclair M.D., Garnier S., Flaum V., Arnaud A.P., Merrot T., Dobremez E., Faure A., Fourcade L., Poli-Merol M.L., Chaussy Y., Dunand O., Collin F., Huiart L., Ferdynus C., Sauvat F.

Volume 81, Issue 1 - Pages 64 - 72

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Today's European Urology Events

ESU
Course 26

Saturday
11 March 2023

16.00 – 18.00
Pink area, ESU room 5

EAU Writing Course

Welcome – 5 min.
J.W.F. Catto (GB), A. Briganti (Italy) , R. Siemens (CA)

How to write the Introduction and Methods Sections across study types
S. Psutka, (USA)

Statistical slip-ups (and how to avoid them)
A. Vickers, (USA)

How to write the results/discussion section - 25 mins
K. Ghani, (USA)

What the editor looks for when reviewing the results and discussion - 25 mins
R. Siemens (CA)

Wrap up/discussion - 10 mins
J.W.F. Catto (GB), A. Briganti (Italy) , R. Siemens (CA)

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Are bacteriophages replacing antibiotics?

In pursuit of an engineered phage alternative for the treatment of UTIs

Dr. Lorenz Leitner
Department of Neuro-Urology, Balgrist University Hospital, University of Zürich (CH)

lorenz.leitner@gmail.com

Bacteriophages, also known as phages, are viruses that infect, replicate within, and lyse bacteria. They were discovered in 1917 by the French-Canadian microbiologist Dr. Félix d'Hérelle, who observed their ability to kill bacterial pathogens in a laboratory setting. Since then, phage therapy has been explored as a treatment for bacterial infections, however, with the discovery of antibiotics, there was a decline in interest. The use of phages in medicine has also been hindered by a lack of understanding and regulation, as well as the difficulty of mass producing and standardising them. Despite these challenges, recent advances in the understanding of phages and their potential applications have renewed interest in phage therapy as a viable alternative to antibiotics.

History of phage therapy and biology
Phage therapy is a form of treatment for bacterial infections that utilises phages to target and kill specific pathogens (Figure 1). [1] In 1917, Dr. d'Hérelle observed an agent able to kill bacteria in a petri dish and he later named it "bacteriophage," derived from the Greek words βακτήριον (baktérion) and φαγεῖν (phageín), meaning “to devour rods” or “bacteria eater”. He hypothesised that phages specifically targeted and infected bacteria and then applied this principle to develop a treatment for bacterial infections. In 1919, Dr. d'Hérelle used phage for the first time to successfully treat a patient with dysentery. The discovery of phages came at a crucial time in medical history when bacterial infections were a significant cause of morbidity and mortality. Phage therapy gained popularity as a treatment option in the 1920s and 1930s, particularly in Eastern Europe to treat a variety of bacterial infections. It is still used today in some parts of the former Soviet Union as an integral part of their healthcare system. However, the development of antibiotics in the 1940s led to a decline in phage therapy research and usage.

Phages are the most abundant replicating units on earth, they coexist and coevolve with bacteria, and they modify and shape bacterial communities and evolution. They can be classified into two main types based on their life cycle: lytic and temperate phages (Figure 2). Lytic phages enter a bacterial cell and immediately begin replicating, eventually causing the host cell to burst and release new phages. Temperate phages, on the other hand, integrate their genetic material into the host cell's genome and remain dormant until triggered to enter the lytic cycle. As temperate phages can serve as vectors for horizontal gene exchange between

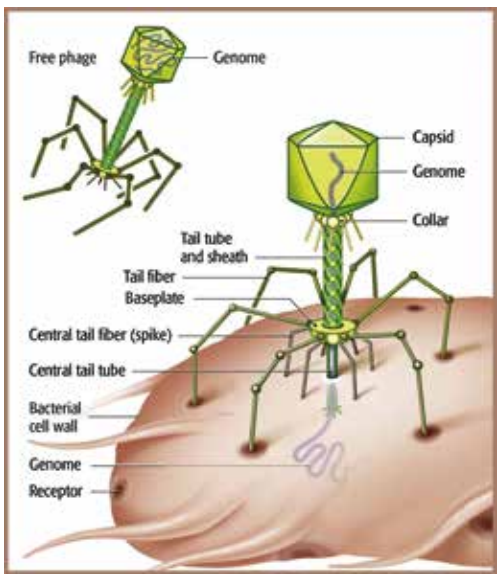

Figure 1: Illustrates the morphology and action of phages. A free-floating phage seeks out a susceptible bacterial host and attaches to the cell wall using its tail fibres to bind with surface receptors. Once attached, the phage infects the bacteria by injecting its genetic material through a central tail tube. It's worth noting that phage tail fibres are usually highly specific for the surface receptors on a bacterium, which means that a particular phage can only infect a narrow range of bacteria. [2]

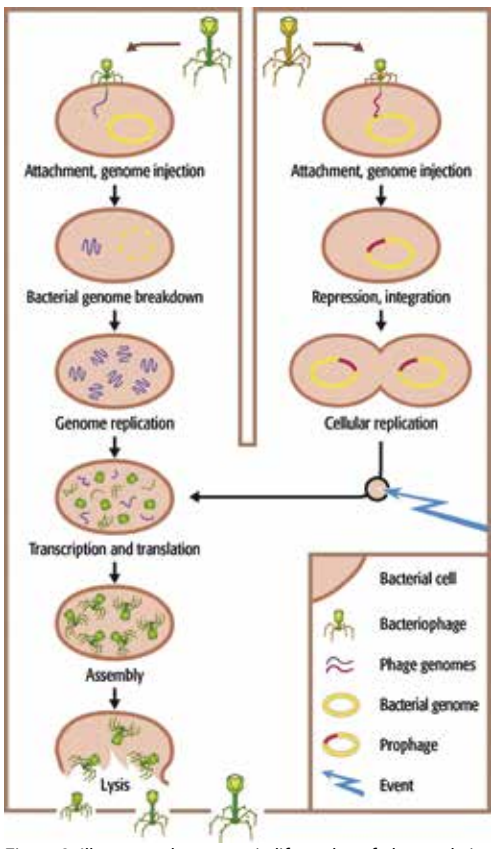

Figure 2: Illustrates the two main life cycles of phages: lytic and temperate. When a phage infects a susceptible bacteria, it injects its genetic material into the host. In the lytic pathway (left), the bacterial genome breaks down and the phage genome replicates, resulting in mature new phage clones that burst the host bacteria, which then diffuse through the surrounding environment and can infect new susceptible bacteria. In contrast, temperate phages (right) have a different strategy. After injection of the genome, it can be integrated into a specific section of the bacterial genome and will be passively replicated every time the bacterial cell divides. The phage genome that is integrated in the bacterial genome or existing as an extrachromosomal plasmid is called a prophage. Environmental factors (such as starvation or other unfavourable growth conditions) can induce a temperate phage to enter the lytic cycle (left). Phage therapy mainly uses lytic phages to treat pathogenic bacterial infections. [1]

bacteria, including antibiotic resistance genes, mainly lytic phages are selected for therapeutic purposes. [1]

Phages vs. common antibiotic therapy
The main advantages and disadvantages of phage therapy, as well as the distinctions from conventional antibiotics, are closely connected to and stem from their biology. Phages are not only specific for certain bacterial species but even possess strain level specificity. The ability to target definite bacterial strains makes them a useful tool to treat infection-causing pathogens without the risk of collateral damage to the patient's beneficial microbiome, which is a common side effect of antibiotics. At the same time, this high level of specificity requires sensitivity testing of the patient’s bacterial isolate prior to starting treatment, similar to what is done for antibiotic sensitivity testing.

A concern for any antibacterial therapy – old or new – is the development of resistance. The close coexistence and coevolution of phages with their host bacteria has led to the development of several bacterial defence strategies against phage that can allow bacteria to become resistant. However, the high abundance of phages in nature usually allows for the identification of new candidate phages for therapy, even in cases where the target bacteria are resistant or develop resistance. This contrasts to the difficulty of finding effective antibiotics in cases of multidrug-resistant bacteria. Interestingly, resistance to phage may result in changes to the host bacteria that make it less pathogenic or even revert antibiotic sensitivity due to survival pressure. [3] Phages that use different mechanisms of bacterial infection can be combined together or combined with antibiotics to result in highly synergistic effects for the inactivation of bacteria and reduction of antibiotic resistance.

The logical trade-off of an antimicrobial strategy with such high specificity is the requirement to have rather large phage banks at one’s disposition and to perform extensive sensitivity testing against the infection-causing pathogens. Furthermore, subsequent production of the right phages for a target infection can be difficult, expensive, labour intensive and time-consuming. The production process for phages is complex, making it difficult to produce many different phages. This makes phage therapy a highly personalised treatment option to select patients.

Furthermore, the regulatory environment surrounding phage therapy is a complicated issue, as phages are classified as biological products and their use as therapeutic agents is not well-regulated in many countries. This lack of regulation is hindering the ability to conduct clinical studies and administer phage therapy to patients, slowing the development of this option and the creation of standardised treatment protocols. While there have been several case reports, case series, and a few randomised controlled trials (RCT) that did not reveal safety concerns, there is still a lack of high-quality efficacy data. More research is needed to get phage therapy widely adopted as a mainstream treatment option.

Phage therapy in the context of urology
Urinary tract infections (UTIs) represent an important model disease to optimise the evidence base for phage therapy. As a closed compartment, the urinary bladder allows for a longer interaction with existing bacteria after instillation of a phage preparation. Since many patients, especially those with neurogenic lower urinary tract dysfunction, rely on intermittent catheterisation or an indwelling catheter in their daily lives, phage therapy could become an important treatment option for acute or recurrent UTIs in this population.

Several successful urological applications of phages have already been published. *In vitro* coating of permanent catheters with specific phages against *Pseudomonas aeruginosa, Escherichia coli*, and *Proteus mirabilis* resulted in a reduction of biofilm formation. Khawaldeh et al. succeeded in eradicating *P. aeruginosa* and achieving clinical improvement in a patient with recurrent foreign-body-associated (double-J-stent) UTIs, using a combination of phages and antibiotics after repeated antibiotic therapy failed.

In 2018, our research group was able to show a reduction in the bacterial load in 67% of all patients with asymptomatic bacteriuria in a clinical application of a phage cocktail licensed in Georgia. The world's first RCT on the use of phages for UTIs found a comparable success rate for phages and antibiotics, but no superiority of phages over placebo in patients with UTIs undergoing transurethral resection of the prostate. [4] Important note, the overall success rate in all three groups in this trial was unusually low. Locus Biosciences, a clinical-stage biotechnology company, posted preliminary results in 2021 from their multi-centre phase 1b RCT (LBx-1001 Study, CT.gov NCT04191148.) using engineered phages, with the main finding of a 2-3 log reduction of urine *E. coli* concentration (colonies forming units (CFU)/mL) compared to placebo across the duration of the treatment.

Overcoming limitations with engineered phages
Genetic engineering can be a useful strategy to increase the speed of testing the sensitivity of pathogens to phages, and to increase the host range or antimicrobial activity. This would allow the use of phages to be expanded beyond highly personalised treatment and applied to a broader range of patients. With natural phages, the use of multiple phage "cocktail" that can target many strains of bacteria at once, is necessary to be active against different strains. However, it remains challenging to determine the optimal number and type of phages in such a "cocktail", and to evaluate in each case, how many phages would have therapeutic value for a specific infection. Additionally, combining phages in “cocktail” solutions can result in stability issues that cause low concentrations of individual phages and can compromise their therapeutic value.

Research projects
In collaboration with a national and international network of leading phage experts, as well as basic and clinical scientists, we are pursuing an engineered phage alternative strategic approach for the treatment of UTIs. To achieve this, two important research projects are ongoing - CAUTIphage: Engineered bacteriophages as antibiotic alternatives for treating catheter associated urinary tract infections (http://p3.snf.ch/project-189957); and ImmnoPhage: (https://www.hochschulmedizin.uzh.ch/de/projekte/immunophage.html). After identifying phages with a broad host spectrum, these phages are genetically modified and engineered into so-called reporter phages and phages with enhanced homologous and heterologous therapeutic effects (Figure 3).

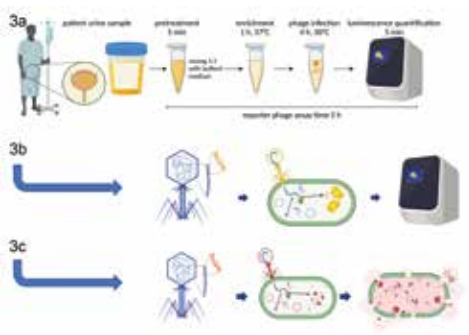

Figure 3: Illustrates a strategy for diagnosing and treating urinary tract infections (UTIs) using engineered phages. 3a) Urine samples are collected from patients with a UTI and incubated with reporter phages. If bioluminescence is detected within 5 hours, treatment with a specific phage can be started. 3b) The genome of a wild-type phage (shown in blue) is equipped with a gene for bioluminescence (shown in yellow). If the engineered reporter phage (shown in yellow) infects the bacteria, bioluminescence can be detected after the engineered protein is expressed . 3c) The same wild-type phage (shown in blue) can be equipped with both homologous and heterologous antimicrobial effector genes (shown in red). These payload proteins allow for enhanced killing of the uropathogen and additional killing of polymicrobial communities after bacterial lysis.

By engineering a nanoluciferase reporter gene into the phage genome, we developed a rapid phage-based diagnostic assay to detect the most prevalent pathogens causing UTIs. Upon host infection and expression of the nanoluciferase protein, bioluminescence can be detected. Overall, *E. coli, Klebsiella* spp., and *Enterococcus* spp. were each detected with high sensitivity (68%, 78%, 85%) and specificity (99%, 99%, 99%) at a resolution of 10^3 CFU/mL within 5 hours directly in patient urine. [5] This technique can be used to identify phages that should be effective for therapy. The very same phages were additionally engineered for target-specific effector gene delivery and host-dependent production of colicin-like bacteriocins and cell wall hydrolases. Testing these engineered phages *ex vivo* in patient urine, superior dual phage- and effector-mediated enhanced killing and suppression of resistance of uropathogen growth could be demonstrated compared to wild-type phages. [6]

Conclusions
Phage therapy has the potential to be an effective alternative to traditional antibiotic treatment for bacterial infections. However, there are still several challenges that need to be overcome before it can be widely adopted. These include the lack of standardised protocols and regulation, the difficulty of producing phages on a large scale, and the need for more research to identify the best suited patients for phage therapy. Despite these challenges, the potential of engineered phages, together with the growing need for new treatments for antibiotic-resistant bacterial infections, make phage therapy an area of research worth exploring further.

References

1 Salmond, G. P. & Fineran, P. C. A century of the phage: past, present and future. *Nat Rev Microbiol* 13, 777-786, doi:10.1038/nrmicro3564 (2015).
2 Leitner, L., Kessler, T. M. & Klumpp, J. Bacteriophages: a Panacea in Neuro-Urology? *Eur Urol Focus* 6, 518-521, doi:10.1016/j.euf.2019.10.018 (2020).
3 Valerio, N. *et al.* Effects of single and combined use of bacteriophages and antibiotics to inactivate Escherichia coli. *Virus Res* 240, 8-17, doi:10.1016/j.virusres.2017.07.015 (2017).
4 Leitner, L. *et al.* Intravesical bacteriophages for treating urinary tract infections in patients undergoing transurethral resection of the prostate: a randomised, placebo-controlled, double-blind clinical trial. *Lancet Infect Dis* 21, 427-436, doi:10.1016/S1473-3099(20)30330-3 (2021).
5 Meile, S. *et al.* Engineered reporter phages for rapid detection of Escherichia coli, Klebsiella spp., and Enterococcus spp. in urine. b*ioRxiv,* 2022.2011.2023.517494, doi:10.1101/2022.11.23.517494 (2022).
6 Du, J. *et al.* Enhancing bacteriophage therapeutics through in situ production and release of heterologous antimicrobial effectors. *bioRxiv*, 2022.2003.2009.483629, doi:10.1101/2022.03.09.483629 (2022).

Sunday 12 March, 09:13 - 09:21
Plenary Session: Challenges in urogenital infections
Yellow Area, eURO Auditorium 2

Treatment of stress incontinence after BPO surgery

Persistent SUI after BPO surgery is one of the biggest challenges in urological clinical practice

Prof. Mauro Gacci
Associate Professor Unit of Urological Robotic Surgery and Renal Transplantation, at University of Florence (IT)

Male LUTS/BPO, a common condition in patients above 50 years, is initially treated through lifestyle modifications and/or medications. For more severe symptoms, surgery for BPO is usually performed by resection, vaporization or enucleation of the prostate.

The main postoperative complications include bleeding, sexual dysfunction, persistent or de novo LUTS, recurrent BPO, urethral stenosis, bladder neck stricture and stress urinary incontinence (SUI). The frequency of these adverse events depends on patient characteristics (age, comorbidities, prostate size, evolution of the disease, etc.), surgical technique and peri-operative parameters, learning curve and postoperative interval [1].

The concept of stress urinary incontinence (SUI) after BPO surgery covers various situations. First is 'short term' SUI, which covers the issue of SUI in the months following surgery for BPO relief. These symptoms are also named 'transient' SUI because of their spontaneous improvement with time. The rate of short-term SUI varies according to the technique used. Historical cohorts with transurethral resection of the prostate (TURP) have shown rates of 0–40% of short-term incontinence [2]. Modern endoscopic enucleation of the prostate (EEP) techniques have shown to lead to a 3-43% rate of SUI in the postoperative period [3]. Most cases of transient incontinence lead to conservative management, including physiotherapy. Medium and long-term SUI are defined as persistent SUI. An overall rate of 0–8.4% has been reported for persistent SUI [1].

Persistent SUI after BPO surgery is one of the most challenging situations for urologist's daily clinical activity, due to the severe impact on patients' quality of life, which can jeopardise the improvement of preoperative male LUTS [1].

Pathophysiology
The pathophysiology of transient and persistent SUI after BPO surgery is not precisely understood, but some hypotheses have been raised. Hypoxic insult, changes in neuroplasticity and/or progressive detrusor hypertrophy from chronic outlet obstruction over time are the main investigated etiological factors for postoperative SUI [4].

Mechanical distension of the bladder from BOO may cause epithelial and smooth muscle cells in the bladder wall to undergo modifications of gene expression and protein synthesis via several transduction mechanisms. The result is smooth muscle hypertrophy and collagenous deposition, which eventually creates a thickened bladder wall with poor contractility, small capacity and low compliance. Following sudden relief of BOO, however, these hyperactive neuronal pathways may persist and be the source of irritative storage symptoms and DO. BOO can exist either with or without symptoms characteristic of the overactive bladder (OAB) complex, including urgency, frequency and nocturia [4].

"Permanent SUI is a severe complication after surgery for LUTS/BPO that can be caused by several pathophysiological mechanisms."

Correct pre-operative diagnosis and characterisation of LUTS is crucial before offering surgical intervention to relieve BOO. Machino et al. noted that post-operative persistent DO was more frequently reported in patients without clear obstruction at the pre-operative Abrams-Griffiths nomogram (60%) than in those who were obstructed (27%).

Multiple studies suggest that recurrent or persistent obstruction accounts for only a minority of LUTS cases after TURP, as suggested by Nitti et al. Cases of direct surgery failure (persistent obstruction), prostatic regrowth (recurrent obstruction) or other strictures (bladder neck contracture, urethral stricture, meatal stenosis) can nonetheless occur and require repeat intervention.

Transient SUI might be due to anatomical changes once enucleation has been done, and dependent of the healing of the prostatic fossa, once the surgery is done. Persistent SUI may be more related to definitive sphincter injury (purely iatrogenic), but also to a very low sphincter function already existing before the intervention, or because of a severe bladder dysfunction or a neurogenic background that further worsens the situation. Before any treatment, an accurate evaluation of detrusor activity is mandatory; if a bladder dysfunction is present, it can lead to the persistence or worsening of storage symptoms and/or voiding symptoms after BPO relief [5]

Diagnostic evaluation
The first evaluation is of the medical history to evaluate the type, timing and severity of UI, define the surgical procedure technique used and to record associated voiding dysfunction and/or other urinary symptoms. The physical examination includes an abdominal examination (to detect an enlarged bladder), a genital exam, a perineal and digital rectal exam. This phase assists in better defining incontinence (pure SUI or mixed) and identifying other medical conditions that need rapid referral to an appropriate specialist [6]

A voiding diary and pad test should be used to quantify symptom severity, including urinary frequency, number of incontinence episodes, voided volume, and diurnal or nocturnal micturition. Validated symptom score questionnaires, like International Prostate Symptom Score (IPSS) or AUA symptom index (AUA-SI), can help to measure UI severity and evaluate clinical outcomes [7]. The International Index of Erectile Function (IIEF) can be used to investigate the coexistence of erectile dysfunction.

Laboratory testing can also provide clues to alternative aetiologies of LUTS, such as infection (urinalysis with microscopy, culture) or malignancy (urinary cytology, prostate-specific antigen). The fundamental examination to be carried out in patients with LUTS after surgery is the urodynamic examination (UDS), as it serves to elucidate the nature of LUTS and guide appropriate subsequent therapy. Pressure-flow studies are required to evaluate detrusor function and exclude obstruction [8]. Endoscopic evaluation (urethro-cystoscopy) is also suggested to assess the absence of concomitant bladder disease and rule out any urethral stenosis or bladder neck sclerosis [1].

Options	Mechanism of Action	Cure rate *(Dry Rate)*
PERI-URETHRAL INJECTION OF BULKING AGENTS	Increase passive urethral resistance	-
SLING	Relocation and compression of the bulbar urethra with the chance to adjust or not the level of compression on the urethra (adjustable and fixed respectively)	
Fixed		
AdVance XP™		47%
The Virtue™		50%
IStop TOMS™		-
Adjustable		
ATOMS™		80%
Remeex™		-
Argus™ and ArgusT™		-
PERI URETHRAL BALLOONS	Adjustable peri-urethral compression	
Pro-ACT™		45%
ARTIFICICAL URINARY SPHINCTER	Circumferential compression of the urethra by a cuff filled with liquid.	
AMS800™		58%

Table 1. Surgical treatment of male SUI after BPH surgery.

Treatments
Conservative treatment for SUI post-BPO surgery includes: lifestyle advice, containment, bladder training and pelvic floor muscle training (PFMT). Modifications of lifestyle factors include: diet, physical activity, and reduction of fluid intake based on 24-h urine output measurement [9]. This option could be proposed for patients with minimal incontinence during the first months after surgery. Containment devices, such as absorbent pads, external collection devices or penile clamps, should be considered as palliative options for patients with massive incontinence. Bladder training allows patients to increase the amount of urine they can hold and to control the urgency, with concomitant improvement of the stress component of urinary incontinence [10]. PFMT, such as Kegel exercises, have been shown to significantly improve SUI after EEP without any significant adverse events [11]. in particular, PFMT significantly reduces the time needed to reach continence recovery, though at 12 months the continence rate for SIU after TURP could be similar in patients with vs. without treatment [12].

"Before any treatment, an accurate evaluation of detrusor activity is mandatory."

In the case of failure of conservative management, no specific medication has been proven to be effective in treating pure SUI after BPO surgery [1], though muscarinic receptors antagonists and beta-3 agonists can be used for persistent or de novo urge incontinence/ OAB [3]. Duloxetine has been extensively tested for SUI after prostate surgery, but mainly after RP. In particular, as reported in a systematic review of 8 studies, duloxetine resulted in a mean dry rate of 58%, mean improvement in pad number of 61% and mean improvement in 1-h pad weight of 68% in a short (<12 months) follow up [3].

Surgical options are considered after a minimum of 12 months of follow-up after surgery, given the high recovery rate in the short-term. Periurethral injections of bulking agents have been proposed for the management of male SUI after BPH surgery, but available evidence remain scarce. In particular, a systematic review based on data from 5 trials did not reach a significant level of evidence to define any recommendation [13].

Fixed or adjustable male slings have been introduced as alternatives to artificial urinary sphincter (AUS) in patients with mild to moderate UI, while those with more severe UI (>250 grams of urine loss per day) seemed to be more satisfied after AUS than after a sling [1].

Urinary retention, chronic pain, wound infection, urethral erosion and risk of explantation are the main complications. The retro-urethral transobturator fixed male sling (AdVance XP) has demonstrated encouraging results, with a dry rate close to 50% at a follow up of more than 5 years [14]. Encouraging results also appear to be related to implantation of a Virtue male sling (satisfaction rate 50%) [1]. Angulo et al. reported a clinically meaningful efficacy of the ATOMS device - an adjustable male sling - for the management of SUI after TURP (satisfaction rate 80% at 3 years) [1]. This result is confirmed by a retrospective trial, but with a lower safety profile (10% explantation rate, 5% of urinary retention, 7% of hematoma) [15].

The Pro-ACT system is a non-circumferential compression device based on two balloon devices introduced under fluoroscopic control transperineally. In a retrospective cohort study, 45% of patients were dry and 31% improved UI 20 months after implantation [16]. Migration, infections, erosion, multiple subsequent adjustments and need of reinterventions are the most frequently reported complications.

AUS has been the principal treatment of male SUI, whatever the underlying etiology. However, very few articles make the actual distinction between patients with a history of RP and a history of BPO surgery. Overall, the literature seems to be in accordance with the fact that AUS results in RP patients are comparable to those with SUI after BPO surgery (dry rate 58%) [17]. In particular, in a systematic review of 87 UI after BPO surgery, AUS showed good results in terms of dry rate, improvement of quality of life and patient satisfaction [18].

Conclusions
Permanent SUI is a severe complication after surgery for LUTS/BPO that can be caused by several pathophysiological mechanisms involving bladder, bladder neck, prostate, urinary sphincter and urethra. An adequate evaluation to measure the severity of incontinence, understand the aetiology and plan a tailored treatment is mandatory. Conservative and invasive intervention options to improve both symptoms and QoL are mainly derived from the literature on post-PR, with a very low level of evidence.

The list of references are available upon request.

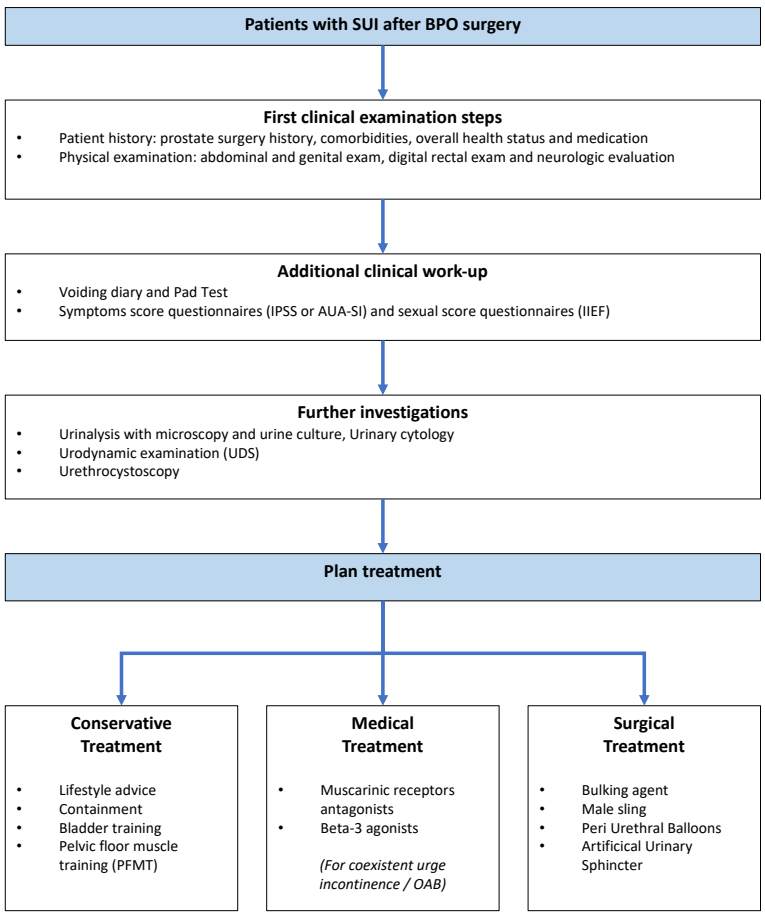

Figure 1. LUTS' treatment after BPH surgery.

Sunday 12 March 12:05 - 12:15
State-of-the-art lecture Evaluation and treatment of stress incontinence after BPO surgery
Yellow Area, eURO Auditorium 2

Patient Day at EAU23 puts patients first

Patients and advocates get a hands-on role at the congress

Patient advocates, healthcare providers, patients and medical experts will come together during Patient Day at EAU23 in Milan in the interest of sharing knowledge and bettering the patient experience. EAU23 Patient Day aims to improve patient outcomes through education, shared decision-making and offering patient a platform to voice their perspectives and experiences. On the first day of the 38th Annual EAU Congress, the EAU Patient Office presents a dynamic programme with several roundtables and workshops to help advocates hone their skills, build their network and empower patients.

The day kicks off with a special abstract session dedicated to a selected number of posters submitted by patients and patient advocates. The session seeks to highlight the needs of patients with urological disease; identify innovations in patient centred care, and to listen to patients' voices as they report the outcomes and experiences of their treatment.

Survivorship and chronic disability
Surviving cancer treatment often comes with a cost. Many cancer survivors suffer from chronic health disability, and/or live with the consequences. Chronic urological diseases are among the most prevalent causes of chronic health disability and often co-exist with other chronic medical and psychiatric illnesses. During a special roundtable we will address the needs of patients suffering from chronic urological illness and strategies that empower them to manage their disability in partnership with healthcare professionals.

Back to the basics
An informed patient is an empowered patient. It is essential that patients and their advocates are well oriented with both the conditions and the jargon. The Roundtable "What is Cystitis" will feature Dr. J. Meijlink (NL), Chair of the International Painful Bladder Foundation (IPBF), Mrs Lynne Van Poelgeest, President of the World Federation of Incontinence and Pelvic Problems (WFIPP), and urologist Prof. G. Bonkat (CH), discussing the basics like taxonomy and nomenclature, management plans, and the patient's experienced pathway, to give patients confidence in navigating what can be a confusing and traumatic process. Giving patients the tools to understand their condition, as well as the associated nomenclature and processes, helps them to more effectively communicate with their physicians.

Empowerment is the bedrock of the patient process
Patient-physician communication is the bedrock of shared decision-making. It fosters an open dialogue between patients and physicians on the true status of the patient through every stage of their disease, from diagnosis to treatment to rehabilitation, which is essential to improving patient outcomes. At the Patient Day Roundtable on Patient-Physician Communication, experts like Dr. Rachel Giles (NL), CEO at the International Kidney Cancer Coalition (IKCC) and Ms Jacqueline Daly (IE), co-founder of East Galway & Midlands Cancer Support, will discuss the importance of patient engagement and best practice strategies to support a healthy dialogue.

Building skills through hands-on workshops
Patient Day at EAU23 further offers interactive and hands-on sessions for delegates to actively build their skillsets. We encourage patient advocates and nurses to join the Presentation Skills Workshops available throughout the Annual Congress. These workshops are led by Vivienne Parry (GB) of BBC Radio 4. Parry is a scientist and broadcaster who understands the importance of presentation skills in the medical field like no other.

Patient Day's Clinical Leadership Development Workshop aims to flip the classroom on the experts and have patients lead the discussion.
Dr. M. Jewett (CA) leads the discussion to define patient engagement and how it can help clinical practice and patient outcomes. To register for the Presentation Skills Workshop and the Clinical Leadership Development Workshop, send an email to: info.patientinformation@uroweb.org

Meeting place for Patient Advocates
Advocates can use the skills developed in these workshops and roundtables to build their network at the Patient Lounge, a premier networking area where Patient Day attendees can relax, regroup and discuss with their peers between sessions. The Patient Lounge is located in the exhibition area, Booth K36

This year at EAU23, Patient Day takes a priority position on the first day of the Congress, highlighting the importance of patient engagement and their role in shared decision-making. Furthermore, patients will have representation throughout the full EAU23 scientific programme to highlight the patient's role in improving outcomes. Therefore, we encourage delegates from all specialities to attend these patient-related sessions and expand their knowledge of the patient experience to better help their own practice.

We would like to thank our principal supporter, Pfizer Oncology, and Astellas, for making Patient Day possible. Thanks to their unrestricted educational grant we are able to host this day at no cost to Patient Advocates.

EAU23 Patient Day Friday 10 March	
09:00	Urological Patient Presentations
10:15	Roundtable discussion: Patient-Physician Communication
11:30	Roundtable discussion: Surviving Urological Cancer and Chronic disability from Urological Disease
13:30	Roundtable discussion: What is Cystitis?

Additional Sessions with Patient Representation

Friday, 10 March	Saturday, 11 March	Sunday, 12 March	Monday, 13 March
08:00 Plenary Session: Challenges in Supportive Care in GU Cancers	**08:00** Thematic Session: Locally advanced BCa: Misconception of informed consent	**10:15** Clinical Leadership Development Workshop	**10:15** Clinical Leadership Development Workshop
10.45 Special Session: Meeting of the Young Academic Urologists (YAU)		**13:45** Plenary Session: Controversies on EAU Guidelines II: Testicular and bladder cancer and stones	
		13:45 Thematic Session: EAU Guideline session: Non-neurogenic female LUTS	

New 2023 EAU Guidelines to be presented in Milan

As the world emerges from the disruption caused by the COVID 19 pandemic, this year has seen something of a return to normality for the European Association of Urology (EAU) Guidelines Office (GO). Following a successful EAU22 Congress in Amsterdam, Guidelines Panels tentatively began resuming physical meetings in order to update their texts and recommendations for 2023.

The GO are delighted to announce that the 2023 edition of the EAU Guidelines (extended USB and Pocket) will be available for collection by all full EAU members at EAU23 from the EAU Booth in the exhibition hall. For the 2023 edition of the Guidelines, the majority of Panels have completed broad and comprehensive literature searches covering the full scope of their Guidelines. Additionally, a number of Guidelines have seen significant revision with the addition of new sections, or the completion of comprehensive updates of specific sections, resulting in new and updated recommendations. Highlights include:

- a new section on management of genitourinary tuberculosis in the Urological Infections Guidelines;
- a new section on penile size, abnormalities and dysmorphia in the Sexual and Reproductive Health Guidelines;
- the Testicular Cancer Guidelines have seen a major revision and restructuring of the entire text;
- the Muscle-invasive and Metastatic Bladder Cancer Guidelines have seen a major revision and restructuring of the section on Disease Management; and
- the Non-neurogenic Male LUTS Guidelines have undergone a major revision in the section on Surgical Treatment.

Last but definitely not least, we are also proud to announce the launch of the **new joint EAU ASCO Penile Cancer Guidelines at EAU23**.

The IMAGINE project, aimed at measuring baseline adherence to EAU Guidelines recommendations across Europe, published its first set of results in European Urology which would not have been possible without the support of the European National Urological Societies.

The PIONEER project entered its fifth year, publishing core outcome sets for prostate cancer patients and launching an online search tool for prostate cancer diagnostic and prognostic biomarkers. As well as hosting another successful studyathon. More institutions have been recruited to the cause, adding additional data sets to the project and joining that of the more than 3.5 million prostate cancer patients already available in the PIONEER platform.

Similarly, the OPTIMA project, aimed at building a state-of-the-art Big Data analytic platform for the development of dynamic computer-interpretable guidelines for breast, lung & prostate cancer, continued to develop, establishing its governance, legal and ethical structures. Most importantly, OPTIMA has already secured access to electronic health records and registries covering over 200 million people across Europe, with a strategy to expand this number further.

More information on ordering your copy of the EAU Guidelines can be found on the EAU website.

The yearly publication of the EAU Guidelines would not be possible without the unwavering support of the EAU Executive Committee and Management team, our highly valued Guidelines Panels and Associates, our Guidelines Committees, EAU membership and every user of the Guidelines globally. So, on behalf of the EAU Guidelines Office Board, thank you for your support and inspiration.

We look forward to seeing you all in Milan!

Phalloplasty for Penile cancer

Specific considerations following penectomy

Mr. Wai Gin (Don) Lee
Department of Urology
University College London Hospitals NHS Foundation Trust
London (GB)

Penile reconstruction, or phalloplasty, refers to the construction of a neophallus through the use of local or distant tissue flaps. Phalloplasty is typically offered when all other options for reconstruction have failed or are inappropriate due to the complex techniques required. In penile cancer, these conditions would arise following a total penectomy or organ-sparing surgery resulting in a functional penile length too short for sexual intercourse or to void while standing.

Phalloplasty was first pioneered by N. Bogoraz in 1936 using a tube pedicled abdominal graft and transplanted cartilage as a phallic stiffener [1]. The first patient had suffered traumatic penile amputation, but several men following penectomy for penile cancer were reported in a subsequent case series of 16 men published in 1939.

In recent years, many technical innovations for phalloplasty have been driven by the increasing numbers of individuals requesting transmasculine gender affirmation surgery. Reconstruction post-penectomy is more complex, and in this case men should be referred to a tertiary centre with the necessary expertise. Even then, experience can be limited. Only one out of 316 men in a large study reporting the outcomes of phalloplasty had penile cancer [2]. This article will briefly summarise the technical concepts and surgical considerations for phalloplasty in this cohort of patients.

Goals of surgery
The ideal goal of reconstruction is to create a neophallus that is aesthetically pleasing and sensate (to both erogenous and tactile stimulus) while allowing voiding while standing and sexual intercourse. Ideally, this should be achieved in a single operation with minimal donor site morbidity. Disappointingly, no current technique satisfies all of the above requirements [3[.

Contemporary phalloplasty techniques usually employ a distant flap that is transferred as a free flap using microsurgical techniques, or as a pedicled flap while maintaining its own blood supply. The most common flap used by far is the radial artery forearm free (RFF) flap. Other alternatives include the anterolateral thigh (ALT) flap, musculocutaneous latissimus dorsi (MLD) flap and local abdominal flap [3].

Surgical technique
Briefly, penile reconstruction is generally performed over 2 to 3 stages depending on local practices. The first stage involves the creation of a neophallus with or without an integrated urethra, followed by microvascular transfer or rotation to the recipient site. There are several alternatives to an integrated (or tube-in-tube) urethra. A glans is also fashioned either at the same time or at a later stage (glansplasty). An erectile device can be inserted after an interval of at least 3 months.

"In recent years, many technical innovations for phalloplasty have been driven by the increasing numbers of individuals requesting transmasculine gender affirmation surgery."

Two surgical teams are usually required for a phalloplasty – one team raises the flap while the other prepares the recipient site. The RFF flap is supplied by the radial artery while venous outflow is via the cephalic and basilic veins [4]. If possible, the radial artery is anastomosed to the inferior epigastric artery via a groin incision while the veins are anastomosed to branches of the ipsilateral saphenous vein. A “tube within a tube” urethra is integrated in the flap design and an anastomotic urethroplasty to the native urethra is typically performed with a covering suprapubic catheter and urethral stent. In almost 90% of patients, tactile and erogenous sensation is achieved by neurorrhaphy between the lateral and medial branches of the lateral cutaneous nerve of the forearm with the dorsal penile nerves, if present [4].

Alternatively, an ALT flap may be preferred given the more easily hidden donor site. The flap is supplied by perforations originating from the lateral circumflex femoral artery, with sensation from the lateral femoral cutaneous nerve [5]. The MLD flap has limited sensation (~20%) because it is supplied by the thoracodorsal neurovascular bundle.

Figure 1. Single cylinder device prepared with Dacron cap in place

Figure 2: The neophallus deflated

Figure 3: The neophallus inflated

Author	n	Age	Primary surgery	Inguinal lymph node dissection	Flap used	Integrated urethra
Garaffa (4)	15	43.6 (39-54)*	Total penectomy	n = 12	RFF	Yes
Akino (7)	1	16	Total penectomy	No	RFF	Yes
Hoebeke (8)	1	16	Total penectomy	No	RFF	Yes
Lee (5)	1	63	Total penectomy	No	ALT	Yes
Sasaki (9)	1	51	Partial penectomy	No	RFF	Yes
Di Summa (10)	1	48	Total penectomy	Yes	ALT	No

Abbreviations: RFF, radial free forearm; ALT, anterolateral thigh.

*Median (range)

Table 1: Summary of papers reporting phalloplasty following penile cancer treatment

Inserting an erectile device requires special consideration, given the lack or loss of typical anatomical landmarks. A rear tip extender or malleable penile prosthesis can be placed in the crus of the penis (if preserved) at the time of phalloplasty to help identify the structures for subsequent penile prosthesis insertion. A penoscrotal incision is typically used, and dilatation of the cylinder space within the neophallus is performed to size 18 Hegar [6]. The device is prepared as routine, but a polyethylene terephthalate (Dacron) cap is sutured to the cylinder tip to prevent migration within the neophallus (Fig. 1). The device is kept partially inflated for a week to allow a capsule to form.

Specific considerations following penectomy
Penile reconstruction in men following either partial or total penectomy can be complicated by surgical scarring and the loss of structures that would normally be present at the recipient site. Thorough and precise surgical planning is therefore required when considering penile reconstruction in this population. Ideally, the urologist who performed the penectomy should be consulted or their operation report reviewed. This is not always possible, so it is essential that the reconstructive urologist has the experience to manage unexpected intraoperative findings.

Anastomotic variations may be required when structures like the long saphenous vein and dorsal penile nerves are sacrificed in the primary surgery. Alternative venous anastomoses can be performed to the femoral vein, the venae comitantes of the inferior epigastric artery or the dorsal penile vein, if present. Similarly, neurorrhaphy to the ilioinguinal nerves or genital branch of the genitofemoral nerve may be required instead.

When present, a perineal urethrostomy will need to be reversed and re-routed to the orthotopic position while maximising native urethral length. Our experience suggests that it is rare for a man to decline reversal of his perineal urethrostomy, although this would minimise the risk of future urethral complications.

Timing of surgery
The timing of the surgery is essential. Our centre recommends a minimum of one year of recurrence-free survival before we consider penile reconstruction. Phalloplasty involves complex reconstruction and it is not advisable to offer the surgery without an adequate period of follow-up. A single stage total penectomy followed by immediate RFF phalloplasty has been described, but the patient subsequently developed nodules suspicious of distant tumour recurrence in the lungs at the time the manuscript was published [8]. Delaying reconstruction by a year was successful in another 16-year-old male with no tumour recurrence after 7 years of follow-up [7]. This patient did not suffer any persistent adverse psychological impact due to the delayed approach.

Surgical and functional outcomes
There is little published data on phalloplasty following surgical treatment for penile cancer, given the rarity of the condition and complexity of reconstruction. Only one cross-sectional retrospective study reported the outcomes of penile reconstruction following penile cancer (n=15) [4] in addition to a handful of case reports (Table 1).

Functional and cosmetic outcomes following RFF phalloplasty were excellent after a median (range) follow-up of 20 (1-68) months [4]. All were satisfied with the cosmesis and size of the neophallus (Fig 2 and 3), and 90% of men reported sensation. Five out of seven men with an erectile device could engage in sexual intercourse. Urethral complications (strictures and fistulae) were the most common complication, occurring in 47% of men, and one man required explant of his erectile device due to infection (14%).

Conclusion
Phalloplasty following penectomy for penile cancer is a challenging endeavour that requires several surgical stages. Both microsurgical free flaps or pedicled flaps should be offered for penile reconstruction, but it is important to individualise the choice depending on the requirements of the patient. An erectile device is usually required for sexual intercourse. Men report good satisfaction and quality of life following phalloplasty despite the significant risk of complications.

References

1. Schulteiss D, Gabouev AI, Jonas U. Nikolaj A. Bogoraz (1874- 1952): Pioneer of phallosplasty and penile implant surgery. *J Sex Med*. 2005;2(1):139-146.
2. Doornaert M, Hoebeke P, Ceulemans P, Tsjoen G, Heylens G, Monstrey S. Penile reconstruction with the radial forearm flap: An update. *Handchirurgie Mikrochirurgie Plastische Chirurgie*. 2011;43(4):208-214.
3. Lee WG, Christopher N, Ralph DJ. Penile Reconstruction and the Role of Surgery in Gender Dysphoria. *Eur Urol Focus*. 2019;5(3):337-339.
4. Garaffa G, Raheem AA, Christopher NA, Ralph DJ. Total phallic reconstruction after penile amputation for carcinoma. *BJU Int*. 2009;104(6):852-856.
5. Lee GK, Lim AF, Bird ET. A novel single-flap technique for total penile reconstruction: the pedicled anterolateral thigh flap. *Plast Reconstr Surg*. 2009;124(1):163-166.
6. Lee WG, Christopher AN, Ralph DJ (2020). IPP in Neophallus. In Mulcahy J, Moncada I, Garcia E and Salamanca J (editors) T*extbook of Urogenital Prosthetic Surgery*. Editorial Medica Panamericana SA. 213-31.
7. Akino T, Shinohara N, Hatanaka K, Kobayashi N, Yamamoto Y, Nonomura K. Successful penile reconstruction after multimodal therapy in patients with primitive neuroectodermal tumor originating from the penis. *Int J Urol.* 2014;21:619-21.
8. Hoebeke PB, Rottey S, Van Heddeghem N, Villeirs G, Pauwels P, Schrauwen W, et al. One-stage penectomy and phalloplasty for epithelioid sarcoma of the penis in an adolescent. *Eur Urol* 2007;51:1429-32.
9. Sasaki K, Nozaki M, Morioka K, Huang TT. Penile reconstruction: combined use of an innervated forearm osteocutaneous flap and big toe pulp. *Plast Reconstr Surg.* 1999;104:1054-8.
10. di Summa P, Sapino G, Bauquis O. Total urethra and penile shaft reconstruction with combined pedicled anterolateral thigh flap and radial forearm free flap after total penectomy. *Arch Plast Surg* 2022;49:448-52.

Saturday 11 March 15:42 - 15:52
ESGURS Meeting: Complex genitourethral reconstruction in benign and malignant disease
Pink Area, Coral 4

EAU23 Scientific Programme

Friday, 10 March

Plenary Sessions
08:00 - 10:00 Challenges in supportive care in GU cancers
08:00 - 10:00 Functional aspects of kidney transplantation

Game Changing Sessions
10:00 - 10:30 to be confirmed
10:00 - 10:30 to be confirmed

Thematic Sessions
10:45 - 12:15 Joint session of the EAU, EANM, ESMO and ESTRO: Multidisciplinary management of urothelial cancer 2.0
10:45 - 12:15 European Urology Surgery-in- Motion: Solving difficult situations in endourology
10:45 - 12:15 Value-based alternatives for typical urological procedures
12:30 - 14:00 Emergencies in urology
12:30 - 14:30 9th ESO Prostate Cancer Observatory: Innovation and care in the next 12 months
13:30 - 15:00 Curiosities in pediatric urology
14:15 - 15:45 Controversies in reconstruction: When to use the robot and when to use the knife
15:15 - 16:15 Semi-live surgery: BPH
15:15 - 16:15 Semi-live surgery: Surgical treatment

Special Sessions
08:30 - 16:30 7th International Congress on the history of urology in conjunction with EAU23 and the EAU's 50th anniversary: Paradigm shifts in urology: 50 years of major developments
10:45 - 15:15 Meeting of the Young Academic Urologists (YAU)
18:00 - 19:30 EAU Opening Ceremony

Patient Information Sessions
09:00 - 10:00 Urological Patient Presentations
10:15 - 11:15 Roundtable: Patient-Physician Communication
11:30 - 12:30 Roundtable discussion: Surviving Urological Cancer and Chronic disability from Urological Disease
13:30 - 14:30 Roundtable discussion: What is Cystitis?

Urology beyond Europe Sessions
10:45 - 12:45 Joint Session of the European Association of Urology (EAU) and the Urological Society of India (USI)
10:45 - 12:45 Joint Session of the European Association of Urology (EAU) and the Urological Society of Australia and New Zealand (USANZ)
10:45 - 12:45 Joint Session of the European Association of Urology (EAU) and the Maghreb Union countries
10:45 - 12:45 Joint Session of the European Association of Urology (EAU) and the World Chinese Urologists
10:45 - 12:45 Joint Session of the European Association of Urology (EAU) and the Federation of ASEAN Urological Associations (FAUA)
10:45 - 12:45 Joint Session of the European Association of Urology (EAU) and the Société Internationale d'Urologie (SIU)
10:45 - 12:45 Joint Session of the European Association of Urology (EAU) and the Pakistan Association of Urological Surgeons (PAUS)
10:45 - 12:45 Joint Session of the European Association of Urology (EAU) and the Canadian Urological Association (CUA)
13:00 - 15:00 Joint Session of the European Association of Urology (EAU) and the Arab Association of Urology (AAU)
13:00 - 15:00 Joint Session of the European Association of Urology (EAU) and the Iranian Urological Association (IUA)
13:00 - 15:30 Joint Session of the European Association of Urology (EAU) and the Japanese Urological Association (JUA)
13:00 - 15:00 Joint Session of the European Association of Urology (EAU) and the Korean Urological Association (KUA)
13:00 - 15:00 Joint Session of the European Association of Urology (EAU) and the Confederación Americana de Urología (CAU)
13:00 - 15:00 Joint Session of the European Association of Urology (EAU) and the Pan-African Urological Surgeons Association (PAUSA)
13:00 - 15:00 Joint Session of the European Association of Urology (EAU) and the Caucasus/Central Asian countries

Video Sessions
10:45 - 12:15 Challenging cases in robotic renal transplantation
12:30 - 14:00 Reconstruction: Pick and mix
14:15 - 15:45 How to improve robotic cystectomy

Abstract Sessions
10:45 - 12:15 Preventing complications of male LUTS/BPO surgical management: The male health challenge
12:30 - 14:00 Male voiding LUTS: Clinical issues, diagnosis, and medical treatment
14:15 - 15:45 Understanding mechanisms and pathologies behind lower urinary tract symptoms
15:15 - 16:45 Prostate cancer biopsy indication: Added value of PET or Micro-US and markers

Saturday, 11 March

Plenary Sessions
08:00 - 10:00 Locally advanced BCa: Misconception of informed consent
08:00 - 10:00 Incontinence nightmares

Game Changing Session
10:00 - 10:30 to be confirmed

Thematic Sessions
10:45 - 12:15 Small renal masses in hereditary syndromes
12:30 - 14:00 EAU Guideline session: Effective treatment in upper tract urothelial tumours
15:15 - 17:15 Rapid-fire debates: Common problems and controversies in bladder cancer
17:30 - 19:00 Hot debates in penile and testis cancer

Special Sessions
10:15 - 18:00 YUORDay23 - EAU Young Urologists Office (YUO) & European Society of Residents in Urology (ESRU)
10:30 - 19:00 EAU23 Live Surgery Session: Technology developments never end!

Section Meetings
10:15 - 13:45 Meeting of the EAU Section of Oncological Urology (ESOU)
10:15 - 13:45 Meeting of the EAU Section of Urologists in Office (ESUO)
10:15 - 13:45 Joint meeting of the EAU Section of Transplantation Urology (ESTU), EAU Section of Urological Research (ESUR), US Renal Transplant Society (USTRS), and YAU
10:15 - 13:45 Joint meeting of the EAU Section of Uropathology (ESUP), EAU Section of Urological Research (ESUR) and the EAU Section of Urological Imaging (ESUI)
10:15 - 13:45 Meeting of the EAU Section of Andrological Urology (ESAU)
10:15 - 13:45 Meeting of the EAU Section of Female and Functional Urology (ESFFU)
15:30 - 19:00 Meeting of the EAU Section of Genitourinary Reconstructive Surgeons (ESGURS)
15:30 - 19:00 Meeting of the EAU Section of Infections in Urology (ESIU)

Video Sessions
10:15 - 11:45 Tips and tricks in genito-urethral surgery
12:00 - 13:30 Minimising side effects and optimising outcomes in prostate cancer
15:30 - 17:00 Impacting stone management
17:15 - 18:45 Refining BPH enucleation

Abstract Sessions
10:15 - 11:45 Urological trauma and complications
10:15 - 11:45 Prostate cancer: Role of imaging and PSA density for biopsy indication, and tumour staging
12:00 - 13:30 History of urology
12:00 - 13:15 Treatment of urogenital infections
15:30 - 17:00 Short- and long-term outcomes after local treatment for muscle-invasive bladder cancer
15:30 - 17:00 Basic research, screenign and transition in paediatric urology
15:30 - 17:00 Long term cancer control of prostate cancer
15:30 - 17:00 Prostate cancer Biopsies: Protocols, peri-lesionnal, methods of targeting, routes and complications
15:30 - 17:00 Andrology: Androgens, comorbidities and fertility
15:30 - 17:00 Minimally Invasive Surgical Therapy (MIST) for male LUTS management
17:15 - 18:45 Markers for improved diagnosis and outcome of non-muscle invasive bladder cancer
17:15 - 18:45 Education and training in urology
17:15 - 18:45 Novel biomarkers in prostate cancer
17:15 - 18:45 Prostate cancer: Biopsy protocols, role of imaging to risk stratify biopsy indication, pathological issues
17:15 - 18:45 Update on mRCC - surgery and medical therapy. Miscellaneous on localised RCC
17:15 - 18:45 Stones: Diagnosis and conservative management
17:30 - 19:00 Debatable surgical approaches

Sunday, 12 march

Plenary Sessions
08:00 - 10:00 Challenges in urogenital infections
08:00 - 10:30 The right management of prostate cancer: Early detection and active surveillance

Game Changing Sessions
10:00 - 10:30 to be confirmed
10:00 - 10:30 to be confirmed

Thematic Sessions
10:45 - 12:15 Clinically meaningful questions in the management of advanced, hormone sensitive prostate cancer
10:45 - 12:15 Male LUTS/BPO surgery: Where do we stand?
13:45 - 15:15 EAU Guideline session: Nonneurogenic female LUTS
13:45 - 15:15 The road to evidence-based European policy on early detection of prostate cancer
15:30 - 17:00 Joint session of the EAU and the Advanced Prostate Cancer Consensus (APCCC)
15:30 - 17:00 Controversies on EAU Guidelines: Prostate, bladder cancer and men's health
17:15 - 18:45 Next steps in immunotherapy for GU malignancies
17:15 - 18:45 Is precision medicine possible in patients with mCRPC?

Section Meetings
13:45 - 17:15 Meeting of the EAU Section of Urolithiasis (EULIS)
13:45 - 17:15 Meeting of the EAU Robotic Urology Section (ERUS)
13:45 - 17:15 Meeting of the EAU Section of Uro-Technology (ESUT)
17:30 - 19.00 Out of the box session: Pushing the limits in urological surgery

Video Sessions
10:45 - 12:15 Modifications in partial nephrectomy
14:00 - 15:30 Complex retroperitoneal surgery
15:45 - 17:15 Multi modal penile cancer management
17:30 - 19:00 Repair of complex fistulae & Award session
17:30 - 19:00 Robotic (r)evolution

Abstract Sessions
10:45 - 12:15 Functional outcome after prostatectomy: Challenges and solutions
10:45 - 12:15 Stones: Basic research and metabolics
10:45 - 12:15 Transplantation in urology
10:45 - 12:15 Urethral strictures: Research, diagnosis and treatment
10:45 - 12:15 Locally advanced kidney cancer
10:45 - 12:15 Metastatic urothelial cancer: News in immunotherapy and more
10:45 - 12:15 Cell biology, novel biomarkers and trials in non-muscle invasive bladder cancer
10:45 - 12:15 How can we improve diagnosis, staging and treatment of upper tract urothelial cancer?
10:45 - 12:15 Clinical trials in progress
14:00 - 15:30 Lymph node management during prostatectomy: Modern staging and outcome
14:00 - 15:30 Andrology: Risk factors, comorbidities and sexological aspects of male sexual functioning
14:00 - 15:30 Minimally invasive treatments in children
14:00 - 15:30 Most common diseases in paediatric urology
14:00 - 15:30 Penile Cancer: data-driven innovation in rare cancer management
14:00 - 15:30 Non-muscle invasive bladder cancer: From diagnosis to follow-up
15:45 - 17:15 Pathophysiological and clinical aspects of chronic pelvic pain and of male stress incontinence
15:45 - 17:15 Andrology: Male factor infertility: Novel concepts in conception
15:45 - 17:15 Storage LUTS/OAB and neurogenic LUTS disorders
15:45 - 17:15 Basic research and diagnostic tools for urogenital infections
15:45 - 17:15 Testicular Cancer: Biomarkers and the evolving role for retroperitoneal dissection
15:45 - 17:15 Treatment of Non-muscle Invasive Bladder Cancer (NMIBC)
17:30 - 19:00 Female stress urinary incontinence: More than slings
17:30 - 19:00 Stones: Safety of endourological intervention
17:30 - 19:00 E-Health, instruments and disposables in urology and affordable medicine
17:30 - 19:00 Urogenital reconstruction apart from the urethra
17:30 - 19:00 Localised kidney cancer: Preoperative surgical planning, surgical & functional outcome predictors
17:30 - 19:00 Sequelae of surgically treated upper tract urothelial carcinoma
17:30 - 19:00 Prostate cancer - prime time for smart screening

Monday, 13 March

Plenary Sessions
08:00 - 10:00 Stones 2023: Progress and challenges
08:00 - 10:00 Men's health as a catchphrase: Evidence vs. marketing in the ageing male

Game Changing Sessions
10:00 - 10:30 to be confirmed
10:00 - 10:30 to be confirmed

Thematic Sessions
10:45 - 12:15 ERN eUROGEN: Update on rare & complex urology
10:45 - 12:15 Is artificial intelligence (AI) in urology ready for prime time?
10:45 - 12:15 Latest scientific developments in male post prostatectomy incontinence (PPI)
12:30 - 14:00 Controversies on EAU Guidelines: Testicular and renal cancer and stones
12:30 - 14:00 Immediate and delayed management of priapism
12:30 - 14:00 How to assess men with familial prostate cancer
12:30 - 14:00 EAU Data initiatives

Special Sessions
10:45 - 12:15 Best of EAU23 Abstracts:An expert discussion
14:15 - 16:15 Best of EAU23: Take Home Messages

Video Sessions
10:45 - 12:15 Extending the boundaries in high risk prostate cancer
12:30 - 14:00 Advancing robotic reconstructive surgery
12:30 - 14:00 To the upper tract and beyond
14:15 - 15:45 Expanding horizons in endourology
14:15 - 15:45 Better safe than sorry preventing and treating bladder neck issues

Abstract Sessions
10:45 - 12:15 Guidelines and evidence-based medicine
10:45 - 12:15 Stones: Percutaneous nephrolithotomy
10:45 - 12:15 Active surveillance and focal therapy: Standard of care?
10:45 - 12:15 Prostate cancer diagnosis by imaging: which role for MRI, PET and Micro-US
10:45 - 12:15 How can we improve staging and outcomes of muscle-invasive bladder cancer patients?
10:45 - 12:15 Partial nephrectomy: Surgical advancements & technique comparison
10:45 - 12:15 Cell biology and novel biomarkers in kidney cancer
12:30 - 14:00 Ablative therapy for BPO relief: EEP vs robotics vs aquablation
12:30 - 14:00 Stones: New technology and shock wave lithotripsy
12:30 - 14:00 Rare and complex urology
12:30 - 14:00 Improving local treatment of prostate cancer
12:30 - 14:00 Cell biology and novel biomarkers in muscle invasive- and upper tract urothelial cancer
12:30 - 14:00 Cell biology and novel therapies in prostate cancer
14:15 - 15:45 Novel prognostic factors and optimal treatment for patients with metastatic prostate cancer
14:15 - 15:45 Andrology: Medical and surgical therapy of male sexual dysfunction
14:15 - 15:45 Stones: Ureteroscopy and stents
14:15 - 15:45 Prostate cancer imaging and biopsy prediction: Stage, pathology results, outcomes, local recurrence post RT
14:15 - 15:45 Interventions to improve outcomes of local treatment of muscle-invasive bladder cancer
14:15 - 15:45 Localised renal cell carcinoma: Not only surgery!

Schedule of ESU and HOT Courses

Friday, 10 March

ESU Course

08:00 - 11:00 **ESU Course 1**
Theranostics in prostate cancer

08:00 - 11:00 **ESU Course 2**
Chronic pelvic pain in men and women

08:00 - 11:00 **ESU Course 3**
Advanced vaginal reconstruction

08:00 - 11:00 **ESU Course 4**
Lower urinary tract dysfunction and urodynamics

08:00 - 11:00 **ESU Course 5**
Adrenals for urologists

11:30 - 13:30 **ESU Course 6**
Prostate cancer screening and active surveillance - Where are we now?

11:30 - 13:30 **ESU Course 7**
Updates and controversies: Urolithiasis, female and male LUTS guidelines 2023: What has changed?

11:30 - 13:30 **ESU Course 8**
Robot-assisted laparoscopic radical cystectomy

11:30 - 13:30 **ESU Course 9**
How we manage upper tract tumours

11:30 - 13:30 **ESU Course 10**
Practical tips for pelvic laparoscopic surgery: Cystectomy, radical prostatectomy adenomectomy and sacrocolpopexy

13:45 - 16:45 **ESU Course 11**
Prostate cancer challenges and controversies from guidelines to real-world

13:45 - 16:45 **ESU Course 12**
Male genital diseases

13:45 - 16:45 **ESU Course 13**
Percutaneous nephrolithotripsy (PCNL)

13:45 - 16:45 **ESU Course 14**
Robotic renal surgery

13:45 - 16:45 **ESU Course 15**
Advanced endourology in the non-standard patients with urolithiasis

Hands-on-Training

13:00 - 13:50 **HOT 1.01**
ESU/ESUT Hands-on Training Course in Basic Laparoscopy

13:00 - 13:50 **HOT 1.02**
ESU/ESUT/EULIS Hands-on Training Course in Endoscopic Stone Treatment, Step 1

13:00 - 13:50 **HOT 1.03**
ESU/ESUT Hands-on Training Course in Transurethral Treatment, Step 1

14:00 - 14:50 **HOT 1.04**
ESU/ESUT Hands-on Training Course in Basic Laparoscopy

14:00 - 14:50 **HOT 1.05**
ESU/ESUT/EULIS Hands-on Training Course in Endoscopic Stone Treatment, Step 1

14:00 - 14:50 **HOT 1.06**
ESU/ESUT Hands-on Training Course in Transurethral Treatment, Step 1

15:00 - 15:50 **HOT 1.07**
ESU/ESUT Hands-on Training Course in Basic Laparoscopy

15:00 - 15:50 **HOT 1.08**
ESU/ESUT/EULIS Hands-on Training Course in Endoscopic Stone Treatment, Step 1

15:00 - 15:50 **HOT 1.09**
ESU/ESUT Hands-on Training Course in Transurethral Treatment, Step 1

16:00 - 16:50 **HOT 1.10**
ESU/ESUT Hands-on Training Course in Basic Laparoscopy

16:00 - 16:50 **HOT 1.11**
ESU/ESUT/EULIS Hands-on Training Course in Endoscopic Stone Treatment, Step 1

16:00 - 16:50 **HOT 1.12**
ESU/ESUT Hands-on Training Course in Transurethral Treatment, Step 1

13:30 - 15:00 **HOT 1.13**
ESU/ESFFU Hands-on Training in Sacral Neuromodulation Procedure Standardisation

15:15 - 16:45 **HOT 1.14**
ESU/ESFFU Hands-on Training in Sacral Neuromodulation Procedure Standardisation

Saturday, 11 March

ESU Course

08:00 - 11:00 **ESU Course 16**
The infertile couple: Urological aspects

08:00 - 11:00 **ESU Course 17**
Urinary tract and genital trauma

08:00 - 11:00 **ESU Course 18**
Updated renal, bladder and prostate cancer guidelines 2023: What has changed?

08:00 - 11:00 **ESU Course 19**
Male prosthetic urology

08:00 - 11:00 **ESU Course 20**
Robotic-assisted laparoscopic prostatectomy

08:00 - 11:00 **ESU Course 21**
Treatment of localised renal masses

15.30 - 17.30 **ESU Course 25**
Modern treatment in testicular cancer

16:00 - 18:00 **ESU Course 22**
Oligometastatic prostate cancer

16:00 - 18:00 **ESU Course 23**
Practical tips for paediatric stone surgery

16:00 - 18:00 **ESU Course 24**
Laparoscopy for beginners

16.00 - 18.00 **ESU Course 26**
EAU Writing course

16:00 - 18:00 **ESU Course 27**
Practical neuro-urology

Hands-on-Training

09:00 - 09:50 **HOT 2.01**
ESU/ESUT Hands-on Training Course in Basic Laparoscopy

09:00 - 09:50 **HOT 2.02**
ESU/ESUT/EULIS Hands-on Training Course in Endoscopic Stone Treatment, Step 1

09:00 - 09:50 **HOT 2.03**
ESU/ESUT Hands-on Training Course in Transurethral Treatment, Step 1

10:00 - 10:50 **HOT 2.04**
ESU/ESUT Hands-on Training Course in Basic Laparoscopy

10:00 - 10:50 **HOT 2.05**
ESU/ESUT/EULIS Hands-on Training Course in Endoscopic Stone Treatment, Step 1

10:00 - 10:50 **HOT 2.06**
ESU/ESUT Hands-on Training Course in Transurethral Treatment, Step 1

11:00 - 11:50 **HOT 2.07**
ESU/ESUT Hands-on Training Course in Basic Laparoscopy

11:00 - 11:50 **HOT 2.08**
ESU/ESUT/EULIS Hands-on Training Course in Endoscopic Stone Treatment, Step 1

11:00 - 11:50 **HOT 2.09**
ESU/ESUT Hands-on Training Course in Transurethral Treatment, Step 1

12:00 - 12:50 **HOT 2.10**
ESU/ESUT Hands-on Training Course in Basic Laparoscopy

12:00 - 12:50 **HOT 2.11**
ESU/ESUT/EULIS Hands-on Training Course in Endoscopic Stone Treatment, Step 1

12:00 - 12:50 **HOT 2.12**
ESU/ESUT Hands-on Training Course in Transurethral Treatment, Step 1

10:00 - 13:00 **HOT 2.13**
ESU/ESFFU Hands-on Training in Urodynamics

09:30 - 13:00 **HOT 2.15**
ESU/ESUI Hands-on Training Course in Prostate MRI reading for urologists

15:30 - 16:20 **HOT 2.16**
ESU/ESUT Hands-on Training Course in Basic Laparoscopy

15:30 - 16:20 **HOT 2.17**
ESU/ESUT/EULIS Hands-on Training Course in Endoscopic Stone Treatment, Step 1

15:30 - 16:20 **HOT 2.18**
ESU/ESUT Hands-on Training Course in Transurethral Treatment, Step 1

16:30 - 17:20 **HOT 2.19**
ESU/ESUT Hands-on Training Course in Basic Laparoscopy

16:30 - 17:20 **HOT 2.20**
ESU/ESUT/EULIS Hands-on Training Course in Endoscopic Stone Treatment, Step 1

16:30 - 17:20 **HOT 2.21**
ESU/ESUT Hands-on Training Course in Transurethral Treatment, Step 1

15:15 - 18:15 **HOT 2.22**
ESU/ESFFU Hands-on Training in Urodynamics

15:00 - 18:35 **HOT 2.23**
ESU/ESUI PSMA/PET CT image reading for urologists

15:15 - 18:45 **HOT 2.24**
ESU/ESUI Hands-on Training Course in Prostate MRI reading for urologists

Sunday, 12 March

ESU Course

08:00 - 11:00 **ESU Course 28**
Prostate cancer update: 2022-2023

08:00 - 11:00 **ESU Course 29**
Focal therapy in prostate cancer

08:00 - 11:00 **ESU Course 30**
Nerve-sparing cystectomy and orthotopic bladder substitution: Surgical tricks and management of complications

08:00 - 11:00 **ESU Course 32**
Advanced indications in robotic surgery

08:00 - 11:00 **ESU Course 33**
Metabolic workup and non-surgical management of urinary stone disease

08:00 - 11:00 **ESU Course 34**
Practical approach to paediatric urology

14:30 - 17:30 **ESU Course 35**
Retropubic radical prostatectomy: Tips, tricks and pitfalls

14:30 - 17:30 **ESU Course 36**
All about the current BPO surgical therapy

14:30 - 17:30 **ESU Course 37**
Lymphadenectomy in urological malignancies

14:30 - 17:30 **ESU Course 38**
Renal transplantation: Technical aspects, diagnosis and management of early and late urological complications

14:30 - 17:30 **ESU Course 39**
Office management of male sexual dysfunction

14:30 - 17:30 **ESU Course 40**
Practical management of non-muscle-invasive bladder cancer (NMIBC)

14:30 - 17:30 **ESU Course 41**
Advanced course on upper tract laparoscopy: Kidney, ureteropelvic junction (UPJ), ureter and stones

Hands-on-Training

09:00 - 09:50 **HOT 3.01**
ESU/ESUT Hands-on Training Course in Transurethral Treatment, Step 1

09:00 - 09:50 **HOT 3.02**
ESTs1 Exam

09:00 - 09:50 **HOT 3.03**
E-BLUS Exam

10:00 - 10:50 **HOT 3.04**
ESU/ESUT Hands-on Training Course in Transurethral Treatment, Step 1

10:00 - 10:50 **HOT 3.05**
ESTs1 Exam

10:00 - 10:50 **HOT 3.06**
E-BLUS Exam

11:00 - 11:50 **HOT 3.07**
ESU/ESUT Hands-on Training Course in Transurethral Treatment, Step 1

11:00 - 11:50 **HOT 3.08**
ESTs1 Exam

11:00 - 11:50 **HOT 3.09**
E-BLUS Exam

09:30 - 12:30 **HOT 3.10**
ESU/ESUT/ESUI Hands-on Training in MRI Fusion Biopsy

09:00 - 12:30 **HOT 3.11**
ESU/ESUI Hands-on Training Course in Prostate MRI reading for urologists

14:00 - 14:50 **HOT 3.12**
ESU/ESUT Hands-on Training Course in Transurethral Treatment, Step 1

14:00 - 14:50 **HOT 3.13**
ESTs1 Exam

14:00 - 14:50 **HOT 3.14**
E-BLUS Exam

15:00 - 15:50 **HOT 3.15**
ESU/ESUT Hands-on Training Course in Transurethral Treatment, Step 1

15:00 - 15:50 **HOT 3.16**
ESTs1 Exam

15:00 - 15:50 **HOT 3.17**
E-BLUS Exam

16:00 - 16:50 **HOT 3.18**
ESU/ESUT Hands-on Training Course in Transurethral Treatment, Step 1

16:00 - 16:50 **HOT 3.19**
ESTs1 Exam

16:00 - 16:50 **HOT 3.20**
E-BLUS Exam

14:00 - 17:00 **HOT 3.21**
ESU/ESUT/ESUI Hands-on Training in MRI Fusion Biopsy

14:00 - 17:30 **HOT 3.22**
ESU/ESUI Hands-on Training Course in Prostate MRI reading for urologists

Monday, 13 March

ESU Course

08:00 - 11:00 **ESU Course 31**
Dealing with the challenge of infection in urology

08:00 - 11:00 **ESU Course 42**
Flexible ureterorenoscopy and retrograde intrarenal surgery: Instrumentation, technique, tips, tricks and indications

08:00 - 11:00 **ESU Course 43**
Advanced course on laparoscopic renal surgery

08:00 - 11:00 **ESU Course 44**
Prolapse management and female pelvic floor problems

08:00 - 11:00 **ESU Course 45**
Prostate cancer imaging: When and how to use it

08:00 - 11:00 **ESU Course 46**
Surgical complications during laparoscopic/robotic urological procedures: Prevention, diagnosis, management, complications

08:00 - 11:00 **ESU Course 47**
Advanced course on urethral stricture surgery

Hands-on-Training

09:00 - 12:00 **HOT 4.01**
ESU/EWPU Hands-on Training course in laparoscopic pediatric urology

09:30 - 12:30 **HOT 4.02**
ESU/ESUI Hands-on Training course in urological ultrasound

EAU23 Industry Sessions & Workshops

Friday, 10 March, 16:45 - 17:45

Pfizer
High-risk NMIBC: Current treatment journey, pathophysiology, and unmet medical need - what´s next for urologists?

AstraZeneca
Lighting the way in mCRPC

Astellas Pharma
Overcoming myths in the management of OAB

Ferring
Multi-disciplinary Management of Cardiovascular Disease in Prostate Cancer: How and How Much?

Janssen
Evolution and revolution in prostate cancer: what does the future hold?

PROCEPT BioRobotics
The Evolution of Heat-Free Robotic BPH Therapy with Aquablation

Saturday, 11 March, 14:15 - 15:15

Astellas Pharma
Navigating the evolving treatment landscape: The next steps to advancing care in urothelial carcinoma

Medscape
Organized by Medscape Oncology Global, supported by an independent educational grant from Bayer Harnessing the Potential of Advanced Prostate Cancer Therapies: Maximizing Clinical Benefits for Patients

Teleflex
Dedication to the Data: The UroLift System for the treatment of lower urinary tract symptoms in men with benign prostatic hyperplasia.

IBSA
Management of urinary tract infections in the era of antimicrobial resistance

MSD
Evolving treatment landscape in localised RCC after nephrectomy

Accord Healthcare
ADT in current clinical practice: Challenges and future perspective

Recordati
Hormonal therapy in prostate cancer: Sharing experience for advanced nursing practice

Coloplast
TFL in Endourology : A new and easy concept to drive efficacy and safety

Sunday, 12 March, 12:45 - 13:45

Astellas Pharma
Optimising current clinical practice for mHSPC throughout the patient journey

Pierre Fabre
Unveiling prostatic inflammation to optimize LUTS management

Recordati
Physician and Patient perspectives to frame prostate cancer management

Janssen
Debates in early stage bladder cancer: How would you treat this patient?

Intuitive
Robotic surgery: how does digitalization impact patient outcomes?

Pfizer
Bridging the Gap: Better Outcomes through Patient Partnered Research

What is the best urodynamic test to diagnose DU?

A comparison and investigation of various methods

Dr. Vincenzo Li Marzi
Department of Urological Robotic Surgery and Renal Transplantation, Careggi University Hospital, Florence (IT)
President of the Italian Society of Urodynamics (SIUD)

Co-authors: Dr. Enrico Ammirati, Dr. Alessandro Giammò. *Department of Neuro-Urology, CTO/Unipolar Spinal Cord Unit, AOU Città della Salute e della Scienza di Torino, Turin, Italy.* **On behalf of the Italian Society of Urodynamics (SIUD).**

The International Continence Society defines the condition of underactive bladder (UAB) as a syndrome characterised by slow urinary stream, hesitancy and straining to void, with or without a feeling of incomplete bladder emptying sometimes with storage symptoms [1]. The definition refers to a syndromic condition, i.e. a set of signs and symptoms, without a reference to urodynamic parameters.

The concept of detrusor underactivity (DU), which refers to a urodynamic measurement, is different. DU refers to a low detrusor pressure or short detrusor contraction time, usually in combination with a low urine flow rate resulting in prolonged bladder emptying and/or a failure to achieve complete bladder emptying within a normal time span measured by urodynamics [2]. This definition is clear and correctly identifies a urodynamic parameter, but open to different interpretations. No reference is made to the minimum force that the detrusor contraction should have or what its ideal duration is. No reference is made to the relationship with urethral resistance, which modulates the bladder force necessary for emptying especially in males. Lastly and importantly, a voiding phase is needed for a urodynamic diagnosis. Furthermore, DU does not refer to a single pathophysiological condition but can be related to obstruction, neurogenic bladder, urinary retention, etc.

Similar to the relationship between overactive bladder (OAB) and detrusor overactivity (DO), not all cases of UAB correspond to the urodynamic finding of DU. Given the lack of shared cutoffs that can determine with certainty the presence of DU on urodynamic investigation, it is difficult to establish its real prevalence. According to urodynamic assessments including a pressure-flow study, the prevalence in male population is 9 – 28% < 50 years, increasing up to 48% for males older than 70 years. On the other hand, there seems to be a clear prevalence in the older age in the female population (> 65 years), with values between 12% and 45%; it seems that female patients admitted to nursing facilities have a high prevalence of mixed storage and voiding dysfunction (urodynamic DO on filling cystometry in combination with urodynamic DU on pressure-flow studies, according to the old definition: detrusor hyperactivity with impaired contractility-DHIC), the cause of both incontinence and voiding difficulties [2, 3].

DU can originate from an alteration of any of the mechanisms of the normal functioning of the micturition cycle. In some cases, the pathology is due to an alteration of the bladder innervation, afferent or efferent, as in diabetic neuropathy, Parkinson's disease, multiple sclerosis, Guillain-Barré syndrome. It is also possible that DU is linked to myogenic factors such as, decompensated obstruction, for example. Other causes may be related to the use of drugs (e.g. antimuscarinics, antihistamines, antipsychotics), pelvic surgery, functional phenomena (e.g. Fowler's syndrome, dysfunctional voiding), or even idiopathic such as a "normal" consequence of ageing [4].

The definition of DU and the diagnostic criteria are based on urodynamic measurements. The parameters taken into consideration are a reduced detrusor contraction strength and a poor flow, responsible for an incomplete bladder emptying. As already mentioned above, there is a lack of shared cutoffs to define the DU condition. Furthermore, there is no universally shared definition of incomplete bladder emptying, as there is no post-voiding residual value that is significantly pathological. Most of the definitions of DU are based on male populations.

The following cutoffs are applied to define DU in men:

- BCI (bladder contractility index, pDetQmax +5xQmax) < 100; Abrams (1999) [5]
- BOOI (pDetQmax – 2xQmax)<20 and Qmax<12 mL/s; Nitti et al. (2002) [6]
- BCI<100 and BOOI <20 and BVE%<90 (bladder voiding efficiency = volume voided/[volume voided + post void residual volume] × 100%) Gammie et al. (2016) [7]

Jeong et al. compared the concordance of different measurements of DU in the men and found a considerable variation (5.4% - 55.8%) in the diagnosis of this condition. In particular, BCI criteria tended to overestimate DU compared with other criteria [8].

The following cutoffs are applied to define DU in women:

- Pdet@Qmax ≤10 cm H2O and Qmax ≤12 mL/s; Jeong et al (2012) [9]
- Pdet@Qmax<30 cm H2O and Qmax<10 mL/s; Abarbanel and Marcus (2007) [10]
- Pdet@Qmax<20 cm H2O and Qmax<15 mL/s and BVE < 90%; Griffiths (2004) [11]
- Pdet@Qmax<20 cm H2O + Qmax; Gammie (2016) [12]

Defining the quality of female bladder emptying is very complicated. The anatomical peculiarity of the female urinary tract, a very short urethra and the absence of urethral resistance linked to the presence of the prostate, allows women to urinate even by simply relaxing the muscles of the perineal plane. Furthermore, bad micturition habits are frequent in the female population: women may use abdominal straining or postpone micturitions for many hours, with possible episodes of bladder overdistention. The absence of urethral resistances, unlike in males, makes the female bladder much more prone to decompensation in obstructive situations (eg. pelvic organ prolapse) with consequent rapid loss of contractility and risk of retentive episodes.

Some non-invasive urodynamic methods have been applied for the definition of DU. A simple flowmetry may help in suspecting a condition of hypocontractility. Rubilotta et al. identified post-void residual (PVR) ratio of 40% (percentage of PVR to bladder volume) to differentiate simple obstructive conditions to obstructive conditions associated with DU [13]. Lee et al. emphasised the role of maximum flow rate (Qmax) assessment in addition to PVR: the DeltaQ parameter (Qmax – Qave) may help clinicians in differentiating between bladder outlet obstruction (BOO) and DU [14]. The ultrasound assessment of detrusor muscle thickness (DWT) was also considered as a predictive parameter of DU. Rademakers et al. identified DWT and bladder capacity as possible predictors of DU. In their study, all patients with DWT ≤ 1.23 mm and bladder capacity >445 ml had DU; the single parameter of BWT < 1.23mm was related in 78% of cases to a condition of DU [15].

Over time, several studies have been conducted on the application of the stop-test during uroflowmetry. It is possible to ask the patient to voluntarily interrupt voiding with a perineal contraction, to exercise a simple urethral compression with the fingers or with the use of cuff systems (non-invasive urodynamics). After a brief obstruction in healthy individuals, an isovolumetric intravesical contraction is expected which causes a temporary increase in flow. In males with DU, the reduced ability to increase bladder contraction power should result in a lower flow after a temporary obstruction. The perineal contraction stop test method is not recommended, as it tends to underestimate bladder contractility and can cause somatic inhibition; the use of penile cuffs can be perceived by the patient as unpleasant and make it difficult to generate a physiological flow. Therefore, these methods have not found wide application in clinical practice.

One of the main limitations related to the various definitions of DU is the choice of urodynamic parameters. Most definitions take into account the Qmax and the detrusorial contraction at maximum flow (pDetQmax). The bladder performs its function by maintaining a functional reserve, so that it can be emptied even in conditions of increased resistance. Therefore, what we measure is the minimum detrusor pressure sufficient to guarantee bladder emptying. As such, the definitions of DU do not take into account bladder functional reserve. The only parameter that could correlate with the maximum detrusor contraction force would be the isovolumetric pressure, which can be obtained by voiding while keeping the bladder neck closed with the balloon of a closed catheter. The complexity of the test and the discomfort perceived by the patient make this evaluation difficult to perform in daily clinical practice. To date, we still have not found a single and shared definition of DU. The differences between gender, the multiplicity of pathophysiological causes, and the invasiveness of the urodynamic investigation make it difficult to diagnose a DU condition with accuracy.

References

1. Chapple CR, Osman NI, Birder L, et al. Terminology report from the International Continence Society (ICS) Working Group on Underactive Bladder (UAB). NeurourolUrodyn.2018;37(8):2928-2931.
2. D'Ancona C, Haylen B, Oelke M, Abranches-Monteiro L, Arnold E, Goldman H, Hamid R, Homma Y, Marcelissen T, Rademakers K, Schizas A, Singla A, Soto I, TseV, de Wachter S, Herschorn S; Standardisation Steering Committee ICS and the ICSWorking Group on Terminology for Male Lower Urinary Tract & Pelvic Floor Symptoms and Dysfunction. The International Continence Society (ICS) report on the terminology for adult male lower urinary tract and pelvic floor symptoms and dysfunction. NeurourolUrodyn.2019;38(2):433-477.
3. Nadir I. Osman, Christopher R. Chapple, Paul Abrams, Roger Dmochowski, Francois Haab, Victor Nitti, Heinz Koelbl, Philip van Kerrebroeck, Alan J. Wein. Detrusor Underactivity and the Underactive Bladder: A New Clinical Entity? A Review of Current Terminology, Definitions, Epidemiology, Aetiology, and Diagnosis, EurUrol2014; 65: 389 – 398.
4. Yu YD, Jeong SJ. Epidemiology of underactive bladder. Common but under researched. Investig Clin Urol. 2017;58 (Suppl 2):S68-S74.
5. Abrams P. Bladder outlet obstruction index, bladder contractility index and bladder voiding efficiency: three simple indices to define bladder voiding function. BJU Int 1999;84(1):14-5.
6. Nitti VW, Lefkowitz G, Ficazzola M, Dixon CM. Lower urinary tract symptoms in young men: videourodynamic findings and correlation with noninvasive measures. J Urol 2002;168:135-8.
7. Gammie A, Kaper M, Dorrepaal C, Kos T, Abrams P. Signs and symptoms of detrusor underactivity: an analysis of clinical presentation and urodynamic tests from a large group of patients undergoing pressure flow studies. EurUrol 2016;69:361-9.
8. Seong Jin Jeong, Jung Keun Lee,Kwang Mo Kim, et al. How do we diagnose detrusor underactivity? Comparison of diagnostic criteria based on an urodynamic measure, Investig Clin Urol 2017;58(4):247-254.
9. Jeong SJ, Kim HJ, Lee YJ, et al. Prevalence and clinical features of detrusor underactivity among elderly with lower urinary tract symptoms: a comparison between men and women. Korean J Urol.2012;53(5):342-348.
10. Abarbanel J,Marcus EL. Impaired detrusor contractility in community-dwelling elderly presenting with lower urinary tract symptoms. Urology. 2007;69:436-440.
11. Griffiths D. Detrusor contractility–order out of chaos. Scand J Urol Nephrol Suppl. 2004;215:93-100.
12. Gammie A, Kaper M, Dorrepaal C, Kos T, Abrams P. Signs and symptoms of detrusor underactivity: an analysis of clinical presentation and urodynamic tests from a large group of patients undergoing pressure flow studies. Eur Urol. 2016;69:361-369.
13. Rubilotta E, Balzarro M, Trabacchin N, Righettii R, D'Amico A, Blaivas JG, Antonelli A. Post-void residual urine ratio: A novel clinical approach to the post-void residual urine in the assessment of males with lower urinary tract symptoms. Investig Clin Urol. 2021; 62(4):470-476.
14. Lee KS, Song PH, Ko YH. Does uroflowmetry parameter facilitate discrimination between detrusor underactivity and bladder outlet obstruction? Investig Clin Urol. 2016;57(6):437-441.
15. Rademakers KL, van Koeveringe GA, Oelke M; FORCE Research Group, Maastricht and Hannover. Ultrasound detrusor wall thickness measurement in combination with bladder capacity can safely detect detrusor underactivity in adult men. World J Urol. 2017; 35(1):153-159.

Saturday 11 March 12:00 - 12:15
ESFFU Meeting: The complex world of treatment of non-neurogenic and neurogenic bladder dysfunctions
Blue Area, Room 1

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Young urologists: A career in kidney transplantation?

An opportunity to combine research activity with surgical training

Dr. Angelo Territo
Fundació Puigvert, Dept. of Urology, Autonoma University of Barcelona (ES)

The development of surgical skills for young urologists (i.e., < 40 years old) is a collective goal for the European Association of Urology (EAU) and the European School of Urology (ESU). In this regard, EAU and ESU offer many learning resources aimed at preparing the frontrunners in urology. These include scholarship programs, clinical visits, international exchange programs, online education courses, as well as hands-on training courses. In addition, the Young Academic Urologists (YAU) have various working groups which allow young urologists to enhance their academic careers according to their personal interests and future objectives, while also improving their scientific skills, academic network, cooperation, and exploring new ideas and projects.

YAU Kidney Transplant Working Group

More than 20,000 kidney transplantations (KT) are currently performed each year in Europe. KT remains a challenging task, and it cannot be carried out optimally without the involvement of urologists who have the primary responsibility to take care of the kidney. Given the epidemiological and clinical relevance as well as the important role of urologists in KT, a dedicated YAU working team was designed and created by Dr. Angelo Territo in June 2021, under the umbrella of the EAU and YAU Office.

Picture 1. YAU Kidney Transplant Working Group (Dr. Romain Boissier, Dr. Alessio Pecoraro, Dr. Angelo Territo, Dr. Thomas Prudhomme, Dr. Riccardo Campi) and Dr. Irfan Donmez (member of the YAU Paediatric Working Group) at EMUC 2022 in Budapest.

Opportunities for young urologists

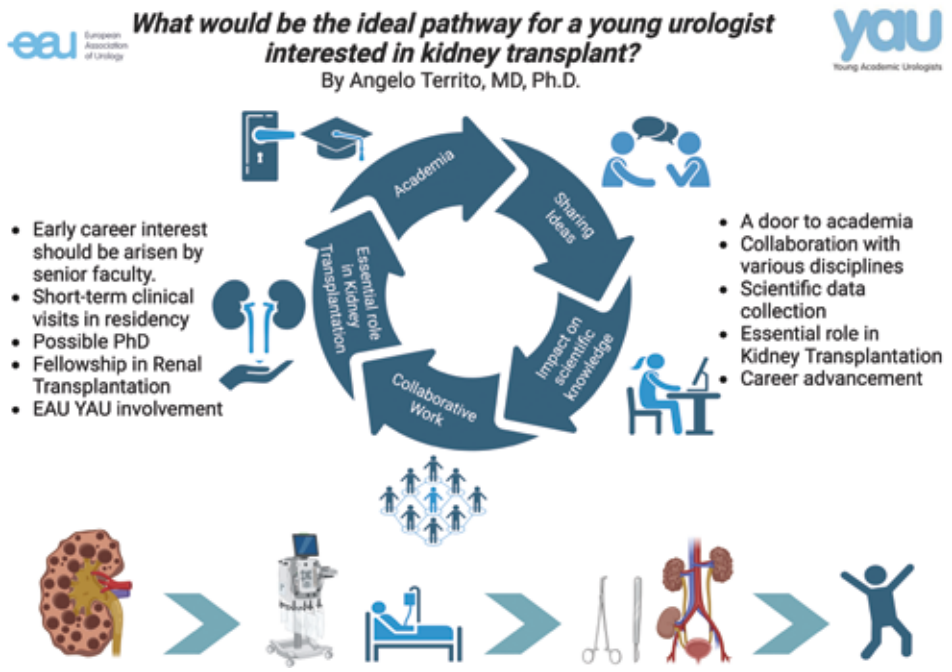
The YAU KT Working Group aims to support young and promising urologists in the field of KT, in which urologists play crucial roles, and expertise is a fundamental issue. Accordingly, one of the main missions of the YAU KT Working Group is to emphasise the role of urologists in KT among different medical and surgical specialists (general and vascular surgeons, nephrologists, and transplant coordinators). Furthermore, the collaboration with other YAU groups, EAU offices and sections (e.g. ESTU, ERUS, RAKT), and guidelines panel members is carried out in order to potentiate any initiatives on clinical, basic, and translational research in all fields of KT.

The YAU KT Working Group promotes research activities and educational projects:

- The **research activities** address several subjects in both conventional open KT and emerging robotic surgery. In particular, studies are conducted on topics such as the urological malignancies in KT recipients, the polycystic renal disease and KT, the learning curve in KT, the use of graft from elderly donors, the urological complication in KT, as well as the use of innovative devices to ensure better graft preservation during KT. Moreover, KT in children represents a more delicate situation due to challenging anatomical aspects. Therefore, the working groups YAU KT and Paediatric Urology (led by Dr. Beatriz Bañuelos Marco (ES)) have joined forces to (Picture 1) present reliable data on various subsets of paediatric KT, such as preoperative assessment, early graft dysfunction, bladder dysfunction & RT etc.
- The **educational projects** are currently focusing on the development of a structured curriculum for open KT and surgical training in high-volume centres, by means of clinical visits or fellowships at the highest volume European centres for KT.

Proposal for a curriculum in KT and future perspectives

According to the available evidence, open and robotic KT seem to have a similar learning curve, with approximately 30 cases needed to achieve optimal results in terms of operative time, re-warming/ischemia time, complication rate, and functional outcomes (1). Therefore, the development of a **standardised curriculum** represents a primary endpoint for the transplant community. In this regard, EAU Sections (ESTU, YAU, ERUS, ESU) are currently working together to propose a standardised training surgical curriculum on KT, considering the available data and the experiences of the main clinical leaders in this field. In our view, this should represent a preliminary step for a structured research pathway. A subsequent validation is needed in real clinical practice, potentially including available dedicated courses that are becoming landmarks for surgeons' training worldwide (i.e., ORSI Academy, in collaboration with the ERUS RAKT Working Group, headed by Dr. Alberto Breda).



Picture 2: The ideal pathway for a young urologist interested in KT

In this regard, promotion of involvement in KT among residents and young urologists should be highly supported by our urological communities since trees grow out of seeds. Early career interest in KT should be promoted, which will probably bring short-term clinical visits to various centres around Europe during residency - supported by national and international associations - that end up with fellowship training afterwards. Then, young urologists who have scientific interest in KT, can become a member of the YAU KT working group and help us to shape the KT society. Picture 2 shows the ideal pathway for a young urologist interested in KT.

Conclusion

In summary, KT demands specific training that should include theoretical lessons, non-technical skills development, dry-lab simulation, wet-lab simulation (or animal models), and active exposure to all main steps of the procedure in order to gain enough confidence and expertise before starting KT as the first surgeon. However, combining research activity with a surgical training curriculum is a more exciting way of promoting interest in KT. For these reasons, we strongly believe that the world of KT can be inspiring for urologists. There is the unique opportunity to grow up as a surgeon and a researcher at the same time, being exposed to challenging clinical/surgical scenarios and stimulating unexplored issues and/or still open debates. Last but not least, the kidney is urologists' specialty, thus, kidney transplantation too!

Acknowledgment: a thanksgiving to Dr. Irfan Donmez to contribute in this article.

Saturday, 11 March 12:45 - 13:00
Joint meeting of ESTU, ESUR, USTRS and YAU: Technological and research matters in kidney transplantation
Yellow Area, Amber 3

Experience with a new bladder voiding management system

A new indwelling transurethral catheter design may improve tolerability and safety

Dr. Nicolás Urday
Department of Urology, Hospital de Alta Complejidad, Juan Domingo Perón, Formosa (AR)

Co-authors: Naber Kurt*, Yardy George**, Apóstolo Claudio, Wirz Walter, Luco Montero Rogelio, Copes Guillermina; Rainero Federico, Corbetta, Juan Pablo. *Department of Urology, Technical University of Munich, Munich, Germany. **Department of Urology, Ipswich Hospital, Ipswich, United Kingdom.

Since 1972, when Lapides and colleagues introduced the clean intermittent catheterisation, there have been a few changes in the way that voiding dysfunction was treated. Urinary tract infections are the most common urological complication with indwelling patients [1]. Bacteria can enter the bladder during insertion of the catheter, through the catheter lumen, or from around the outside of the catheter. "Even with thoroughly aseptic catheter insertion and care, the chance of developing significant bacteriuria is 3 to 10% every day the catheter is indwelling" (Imam) [2]. We tested a new device that could improve the quality of life in patients with urinary voiding problems.

We determined the initial results, safety, and efficacy of a new Bladder Voiding Management System (CymActive™) which consists of a self-retaining intraurethral catheter, with a patient-controlled magnetic valve that allows cyclical bladder voiding without external appliances.

We selected patients with indwelling Foley catheter, and with acute urinary retention due to prostatic obstructive pathology (BPH). They were catheterised with the CymActive™ system. None of whom presented with evidence of neurogenic bladder. We performed uroculture prior to placement of the device, and after its removal. Data was collected from patient's daily questionnaires, and weekly visits during catheterisation for 30 days. The variables evaluated were: insertions, tolerability, effectivity, and device-associated infections.

Figure 1: Introduction: history of catheterisation.

Ten patients were included in the study. Seven were Foley carriers awaiting prostate surgery, and the remaining three were catheterised for the first time. Of 10/10 successful insertions; 8/10 showed good tolerance to the device. In 2/10 the protocol was discontinued due to discomfort. 10/10 showed average PVR of 25 ml at the first control; successful valve openings and closings in ≥ 95% of more than 1,500 voids. 1/10 urinary infections during the trial.

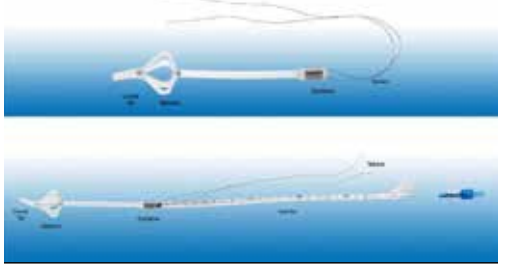


Figure 2: Methods: general characteristics of the catheter

"Even with thoroughly aseptic catheter insertion and care, the chance of developing significant bacteriuria is 3 to 10% every day the catheter is indwelling."

In conclusions, this pilot experience, demonstrated that CymActive™ is potentially useful and safe for these patients. A major sample will be needed to define better outcomes and characteristics of patients who benefit from this device.

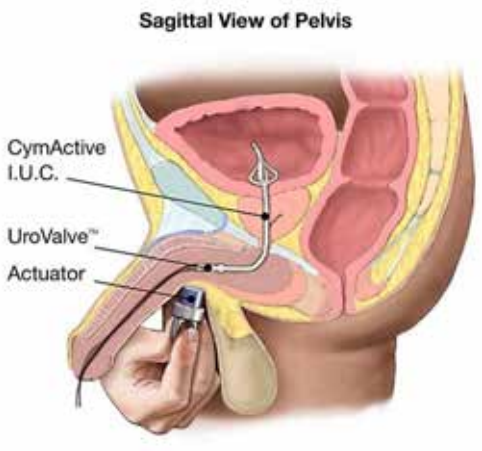


Figure 3: Methods: general characteristics of the catheter

References

1. Lapides J, Diokno AC, Silber SM, et al. Clean, intermittent self-catheterization in the treatment of urinary tract disease. J Urol. 1972;167 (4): 1584–1586, 2002.
2. Catheter-Associated Urinary Tract Infections. Talha H. Imam , MD, University of Riverside School of Medicine.

Last review/revision Jul 2021 | Modified Sep 2022

Saturday 11 March 18:30 - 18:40
ESIU Meeting: Urogenital infections in urology
Yellow Area, Amber 3

Imaging standards for testicular cancer

Role in diagnosis and local staging

Prof. Pasquale Martino
MD, FEBU, President of the Italian Society of Integrated Diagnostics in Urology, Andrology, and Nephrology (SIEUN)
University of Bari (IT)

Testicular cancer is a relatively rare disease, accounting for about 1 to 1.5% of male malignancies and 5% of all urological malignancies. In Western society, the incidence is around 10 new cases per 100,000 individuals per year. Testicular cancer affects young adults with greater incidence, and represents the most common cancer between 15 and 35 years of age.

Infections complications in kidney transplant The overwhelming majority of tumours are germ cell in origin. Most cases of testicular cancer are organ confined at diagnosis and have a good overall prognosis [1]. The survival rate has grown to 90% in the last 30 years.

The anatomical-pathological classification of the WHO distinguishes testicular neoplasms into two large groups: germline and non-germline neoplasms. Germline neoplasms, derived from germline cells, represent about 95% of all testicular neoplasms which are divided into subgroups. Non-germline neoplasms are rarer.

Seminoma is the most common single cell type in adult, yolk sac tumour, and mature teratoma in prepuberal boys. Lymphoma and metastases (10% of cases) are prevalent in the elderly. Non-seminomatous germ cell tumours may present with a single cell type, or have multiple histologic patterns in 40% to 60% of cases. More than 10% of testicular germ cell tumours are seen in patients with cryptorchidism. Sex cord and stromal tumours are typically small, usually discovered incidentally, and benign in about 90% of cases. Mesenchymal tumours of the testis, both benign and malignant, are rare [2].

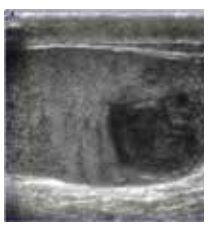
Along with clinical examination, diagnostic imaging plays an important role in the assessment of testicular and extratesticular lesions (in diagnosis and initial staging); specifically in examining the primary tumour prior to orchiectomy and evaluating for regional and/or distant metastasis.

Scrotal ultrasound (US) is increasingly popular as a complement to the urological examination. This resulted in an incidental finding in asymptomatic patients of an increasing number of small non-palpable lesions, which only 30% are malignant.

This review focuses on the role of imaging in the diagnosis and local staging of testicular cancer.

Testicular cancer usually presents as a palpable and painless mass. In most cases, the tumour manifests itself with the appearance of a hard and indolent lump on a testicle In 10% of cases, it is associated with testicular pain or disorders already ascribable to its metastatic localization.

The imaging techniques that are generally used in the diagnosis, staging and follow-up of testicular tumour are:



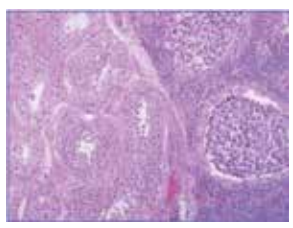
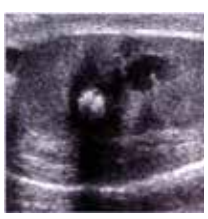


Fig. 1a seminoma, 1b histology



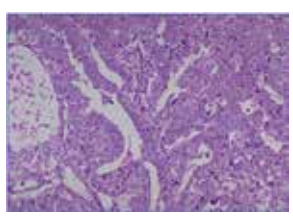


Fig. 2a embryonal carcinoma, 2b histology

- Ultrasound (US): for baseline investigation
- Magnetic Resonance Imaging (MRI): rarely used; inconclusive, or nondiagnostic US findings
- Computerized tomography (CT) scan: for staging
- Fluorodeoxyglucose (FDG)-positron emission tomography (PET): for disease recurrence and follow-up of residual masses

Scrotal US with grayscale, colour Doppler, and contrast-enhanced ultrasound (CEUS) elastography, while using a high-frequency linear transducer, remains the modality of choice for the evaluation of scrotal pathology. Scrotal US represents the first-line imaging modality for the evaluation of lesions testicular and extratesticular due to its low cost, wide availability, and high diagnostic accuracy.

Ultrasonography has greater than 90% sensitivity and specificity for detecting testicular neoplasia in the appropriate clinical setting [3,4]. It can distinguish between intratesticular or extratesticular mass, and differentiate cystic lesions from solid masses with sensitivity close to 100% [5].

US examination should always evaluate the contralateral testis to rule out bilateral, synchronous, albeit rare, tumours that occur in 2% of seminomas [6]. Even in patients with suspicion of metastatic cancer, a scrotal US should be used to identify an active primary tumour or a "burned out" testicular mass, which is typically a small, impalpable scar or calcification.

"Multiparametric US improves the characterization of testicular masses and can reduce the number of unnecessary orchidectomies."

Assessment of vascularity is of limited help. In general, it is not correlated with histology and varies with size. In an early study of 28 patients with surgically proven testicular tumours, 95% of lesions greater than 1.5 cm demonstrated increased vascularity, while 86% of lesions less than 1.5 cm were hypovascular [7]. The increased sensitivity of modern ultrasonographic equipment allows nowadays detecting vessels within both benign and malignant nodules of very small size. Some truly avascular lesions do exist, however, and this finding can be useful to lower the probability of malignancy [2].

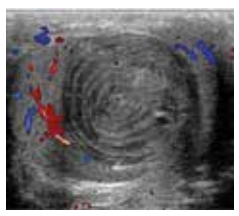
On US, seminomas generally appear as hypoechoic, homogeneous, well-defined, mono- or multifocal lesions, with rare anechoic areas (fig.1a-1b). Non-seminomatous neoplasms appear as inhomogeneous lesions with mixed structure, calcifications, indefinite limits, and very often with invasion of adjacent structures (fig.2a-2b). Tumours are almost always vascularized (or hypervascularised), although the absence of blood flow does not rule out testicular cancer.

Unfortunately, only a limited number of focal testicular lesions present an appearance suggestive enough for a benign histology at grey-scale US, such as in cases of epidermoid cysts with onion-ring appearance, of with intralesional macrocalcifications, or with shell calcifications, all lacking vascularization at colour Doppler interrogation (fig.3a- 3b).

Indeed, a high sensitivity of the US corresponds to a limited specificity of the same. Therefore, it is important to try to improve the specificity of the method by:

1. Integrating imaging at the clinic: Take patient characteristics (e.g. age, ethnicity, medical history) into account. Germ cell tumours are prevalent in the young. Lymphomas, metastases, or other relatively rare lesions are more likely in the elderly. Germ cell tumours are rare in African Americans; in these patients, the possibility of uncommon lesions should also be considered (Fig.4).

The presence of pain makes acute situations more probable (focal orchitis, segmental infarction, and hematoma after trauma). In case of bilaterality, consider non-neoplastic lesions (only 1 to 2% of tumours are bilateral).



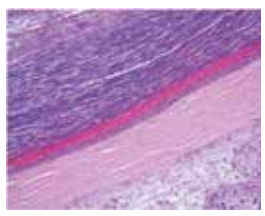


Fig. 3a Epidermoid cyst, 3b histology

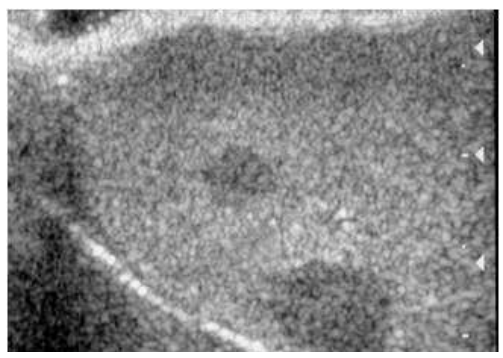
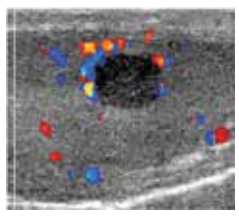


Fig. 4 sarcoidosis

2. Evaluating the vascularity of the lesions: Tumours are almost always vascularized on colour Doppler (with modern US); to consider the possibility of non-neoplastic lesions if the vascularization is absent (fig.5a-5b)

3. Integrate different techniques: colour Doppler is sensitive enough, but not to exclude hypovascular tumour in all cases. The absence of flows must be confirmed with the CEUS (8) (fig. 5a-5b).
For many years, magnetic resonance imaging (MRI) has been proposed as an alternative or integrative method for the study of solid scrotal lesions and for their characterization.



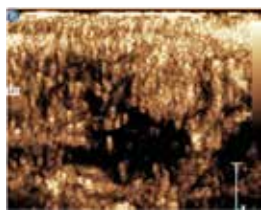


Fig. 5a hypovascular seminoma, 5b hypovascular seminoma-CEUS

There are few studies and few case series reporting the results and diagnostic possibilities of MRI compared to US, especially with the use of new methods. In view of the high sensitivity of US in studying the testicles, MRI is rarely necessary. It is suggested in the presence of a discrepancy between US findings and physical examination, inconclusive US findings, in case of diffuse neoplastic infiltration of the testis [9] (fig.6).

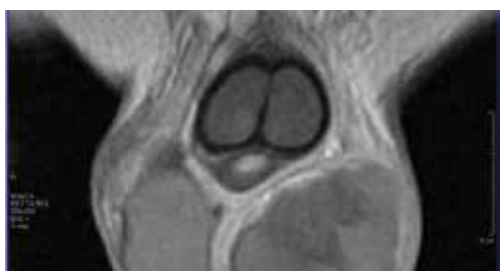


Fig. 6 choriocarcinoma-MRI

4. Evaluating the consistency of the lesion: Although not all soft nodules are benign, and not all hard nodules are malignant, testicular elastography can help us in the characterization of small testicular nodules (< 1cm). If soft, they are generally benign, having limited role in larger nodules (10). More than the consistency, its variation over time is important (fig.7).

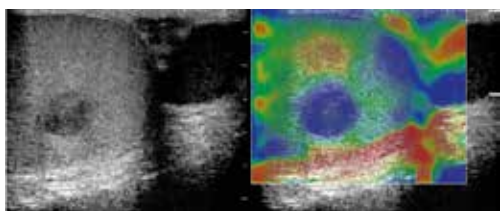


Fig. 7 seminoma elastography

5. Considering unusual pathologies: An example is hyperplasia of adrenal remnants, burned-out tumour. Among the secondary lesions of the testicle we consider lymphoma in the elderly (fig.8), leukaemia (clinically manifest in 10% of patients), and metastasis (i.e. in the prostate, lung, gastrointestinal tumours, melanoma, or kidney).

It can be deduced that imaging has a central role in the assessment of scrotal masses. Although US represents the examination of choice, it does not always provide an accurate characterization of the nature of scrotal mass lesions. A pre-treatment diagnosis of their benign nature based on imaging findings may obviate unnecessary radical orchiectomy [11]. Sometimes scrotal MRI may be validly recommended afterwards if there are inconclusive US findings or if these are inconsistent with the clinical examination in terms of differentiation and characterization between intratesticular and paratesticular lesions (in rare cases of uncertain or indeterminate US findings) and in local staging of testicular malignancies (in-patients planned for testis-sparing surgery) [12-13].

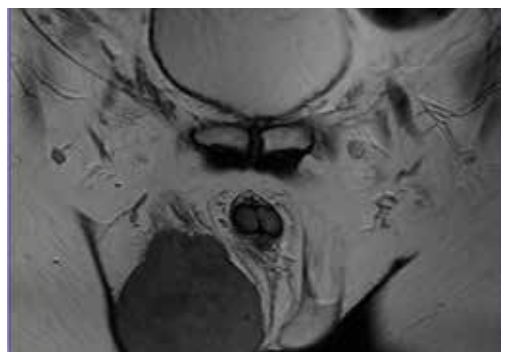


Fig. 8 lymphoma - MRI

In conclusion, we can state that multiparametric US (in some cases associated with MRI) improves the characterization of testicular masses and can reduce the number of unnecessary orchidectomies.

I would like to express my appreciation for my friends Prof. Michele Bertolotto, Dr. Libero Barozzi, Prof. Pietro Pavlica, and Dr. Massimo Valentino who provided some of the images and most importantly, for their support in the realization of this report.

References

1. Thomas KL, Jeong D, Montilla-Soler J, Feuerlein S. The role of diagnostic imaging in the primary testicular cancer: initial staging, response assessment and surveillance. Transl Androl Urol 2020;9 (Suppl 1):S3-S13. doi: 10.21037/tau.2019.07.01
2. Atlas of ultrasonography in Urology, Andrology, and Nephrology (P. Martino, A.B. Galosi editors) M. Bertolotto et all. Springer 2017; 40:483-492
3. Marko J, Wolfman DJ, Aubin AL, et al. Testicular Seminoma and Its Mimics: From the Radiologic Pathology Archives. Radiographics 2017;37:1085-98
4. Wilson SR, Greenbaum LD, Goldberg BB. Contrast-enhanced ultrasound: what is the evidence and what are the obstacles? AJR Am J Roentgenol 2009;193:55-60.
5. Coursey Moreno C, Small WC, Camacho JC, et al. Testicular Tumors: What Radiologists Need to Know—Differential Diagnosis, Staging, and Management. RadioGraphics 2017;37:400-15.
6. Sohaib SA, Koh DM, Husband JE. The role of imaging in the diagnosis, staging, and management of testicular cancer. AJR Am J Roentgenol 2008;191:387-95
7. Horstman WG, Middleton WD, Melson GL, Siegel BA (1991) Color Doppler US of the scrotum. Radiographics : a review publication of the Radiological Society of North America, Inc 11 (6):941-957; discussion 958. doi:10.1148/radiographics.11.6.1749858
8. Atlas of ultrasonography in Urology, Andrology, and Nephrology (P. Martino, A.B. Galosi editors) L.Barozzi et all. Springer 2017; 38:461-469
9. Spectrum of Extratesticular and Testicular Pathologic Conditions at Scrotal MR ImagingPardeep K. Mittal, MD Ahmed S. Abdalla, MD Argha Chatterjee, MD Deborah A. Baumgarten, MD, MPH Peter A. Harri, MD Jay Patel, MD Courtney C. Moreno, MD Helena Gabriel, MD Frank H. Miller, M RadioGraphics 2018; 38:806–83
10. Real-time tissue elastography for testicular lesion assessment, 1 Andrea Sacchi, Giovanni Magistretti,1 Joan Almolla, and Maurizio Salvadore3, Eur Radiol. 2012; 22(4): 721–730
11. Tsili AC, Bertolotto M, Rocher L, et al. Sonographically indeterminate scrotal masses: how MRI helps in characterization. Diagn Interv Radiol 2018; 24:225–236
12. Tsili AC, Argyropoulou MI, Dolciami M, Ercolani G, Catalano C, Manganaro L: When to ask for an MRI of the scrotum. Andrology. 2021;9: 1395-1409. https://doi.org/10.1111/andr.13032
13. Incidentally detection of non-palpable testicular nodules at scrotal ultrasound: What is new? M. Valentino, M. Bertolotto , P.Martino, L. Barozzi, P. Pavlica. Archivio Italiano di Urologia e Andrologia 2014; 86, 4

Saturday 11 March, 12:32 - 12:46
Joint meeting of ESUP, ESUR and ESUI: From conventional to molecular diagnostics
Pink Area, Coral 4

Management & prevention of UTI after kidney transplantation

A focus on the association with possible neurogenic bladder

Dr. José Medina-Polo
Hospital Universitario 12 de Octubre, HM Hospitals & ROC Clinic, Madrid (ES)

Urinary tract infections (UTIs) are more common in patients with end-stage renal disease and those who have undergone kidney transplantation. Moreover, there is a higher incidence of isolation-resistant microorganisms.

Infections complications in kidney transplant recipients are associated with higher morbidity and mortality. It is estimated that half of kidney transplant patients will develop UTIs within three years of transplantation. Therefore, urologists have an important role in diagnosing, preventing, and managing urinary infections in patients on the waiting list for kidney transplantation and those with transplanted grafts.

A higher risk of UTIs in patients with chronic kidney disease includes anatomical and functional disorders of the urinary tract, loss of antibacterial properties of the urine, mild immunosuppression in uraemia, and inhibition of protective mucosa production in the urothelium. Moreover, patients with ADPKD (autosomal dominant polycystic kidney disease) and chronic kidney disease associated with stone disease entail a higher risk for UTIs. Among risk factors for UTIs after kidney transplant include age, female, longer pretransplantation dialysis time, and urinary tract obstruction [5].

The first point of interest is the diagnosis study required before kidney transplantation in patients with end-stage renal disease. Recurrent urinary infections require further studies, including flow study, and evaluation of postvoid-residual urine. According to previous data, urodynamics or voiding cystourethrogram may be indicated as well.

The study is mandatory in case of bladder dysfunction as the incidence of neurogenic bladder is higher. The reason for neurogenic bladder may be the cause of end-stage renal disease or may be related to comorbidities such as neurogenic bladder due to diabetes mellitus. A normal bladder is defined as one that stores urine at low pressure, does not leak, and empties nearly completely by natural voiding [1].

Not only do UTIs need to be managed correctly, but asymptomatic bacteriuria is also highly prevalent. Reportedly, it is estimated that up to 50% of recipients need treatment in specific situations. International guidelines such as the guidelines of the European Association of Urology (EAU) and IDSA (Infectious Diseases Society of America) state that asymptomatic bacteriuria should not be treated in kidney transplant patients after the short-term post-transplant period [4].

Other indications for evaluation and treatment of asymptomatic bacteriuria involve recipients with a risk for developing pyelonephritis such as patients with indwelling devices, neurogenic bladder, or combined transplant. Hospitalization for UTIs occurred more frequently in patients treated due to asymptomatic bacteriuria, with up to 36% risk of infections due to resistant microorganisms.

A survey about the current practice among urologists reported that 29.5% of the responders screen routinely asymptomatic bacteriuria after kidney transplantation, 27.3% and 27.3% during the first two and six months after kidney transplant, respectively. Around 20.4% treat asymptomatic bacteriuria with antibiotics in the first two months after kidney transplant, 29.5% in the first six months, and 38.6% if a urological procedure or biopsy is expected (Figures 1 and 2).

The revision by Coussement et al. demonstrated that the treatment of asymptomatic bacteriuria is not indicated two months after kidney transplantation as it can be associated with a higher incidence of hospitalizations and no differences in terms of incidence of symptomatic UTIs [2]. However, repeated isolation of asymptomatic bacteriuria and recurrent UTIs is associated with a higher incidence of pyelonephritis. This involves the group of patients in which preventive measures are required, with a focus on non-antibiotic management.

In the early postoperative periods, the use of urinary catheters is one of the main risk factors for infections. Both urethral catheters and ureteral stents are used during kidney transplant surgery. It is recommended that urethral catheters be removed in the first week after the kidney transplant unless any other patient characteristic requiring prolonged bladder drainage exists. The routine use of ureteral stents may prevent urological complications such as urinary fistula. However, it should be removed as soon as possible.

"When prescribing antimicrobial treatment for UTI, we should bear in mind that the choice, dosage and interval may require adjustment."

Worrisome findings of a survey among urologists reported long periods before catheter removal: less than one week by 38.6% of responders, one to two weeks by 34.1%, and two to three weeks by 25% for the urethral catheter. Ureteral double J stent was removed between one to two weeks by 14.3%, two to three weeks by 28.6% and three to four weeks by 57.1% (Figures 3 and 4).

The evidence on preventing UTIs in patients with kidney transplantation and neurogenic bladder is limited; in many revisions, both are considered exclusion criteria. According to the EAU Guidelines on Urological Infections, alternatives such as local or oral probiotics containing strains for vaginal flora regeneration, cranberry products, D-mannose, and endovesical installations with hyaluronic acid and chondroitin sulphate have a weak recommendation [3]. The study by Pagonas et al., a revision of the effect of cranberry juice and L-methionine in 82 kidney transplant recipients with recurrent urinary tract infections, reported that cranberry juice might reduce the number of UTI episodes [3].

The strategies with strong evidence recommendation in the prevention of recurrent urinary infections include vaginal oestrogen replacement in post-menopausal women and immunoactive prophylaxis. Regarding immunoactive prophylaxis, many studies are based on the formula OM-89, which contains 18 serotypes of *Escherichia coli* lysed bacteria. OM-89 consists of one tablet per day for three months, and a booster course can be added every 10 days for six to nine months. The proposed treatment strategy is the stimulation of dendritic cells, neutrophils and phagocytosis by macrophages. There are other alternatives, such as the sublingual formula MV140 or an intramuscular/vaginal tablet.

The studies published with a focus on kidney transplant recipients are also scarce. Zgoura et al. included 14 controls and cases with three subcutaneous injections of inactivated bacteria, reporting a reduced incidence of UTIs with higher isolation of non-E. coli bacteria in the control group. The sublingual vaccination with the formula MV-140 for six months in 43 kidney transplant recipients reported a reduction in the incidence of UTIs from 4.2 to 2.7 episodes per year. However, it should be advised that patients have a higher risk of infections. Although 46.5% had fewer infections, only 16.3% were free of UTIs after one year. Another important point to mention is that 39.5% of patients included in the study have urinary tract structural or functional abnormalities.

When prescribing antimicrobial treatment for UTI, we should bear in mind that the choice, dosage and interval may require adjustment. Aminoglycosides have a nephrotoxic potential. The combination of loop diuretics and cephalosporins is nephrotoxic. Nitrofurantoin is contraindicated in patients with an estimated glomerular filtration rate of less than 30mL/min [1].

Finally, it should be mentioned that antimicrobial prophylaxis following kidney transplantation needs to be optimised in terms of antibiotic selection and duration. Although antimicrobial prophylaxis reduces bacteriuria and the incidence of early urinary infections after kidney transplantation, a longer duration of prophylaxis has not proved to have a beneficial effect.

The main conclusions of the management of UTIs in immunocompromised patients with chronic kidney disease and kidney transplant are the following:

- Treat any infection before transplantation
- Perioperative antibiotic prophylaxis on a short-prescription basis is required
- Perioperative low-dose trimethoprim-sulfamethoxazole is indicated
- Urinary catheters require prompt removal.

The topic will be reviewed with practical recommendations in the EAU23 presentation "Management of UTI in patients after kidney transplantation with neurogenic bladder" during the Meeting of the EAU Section of Infections in Urology (ESIU) "Urogenital infections in urology".

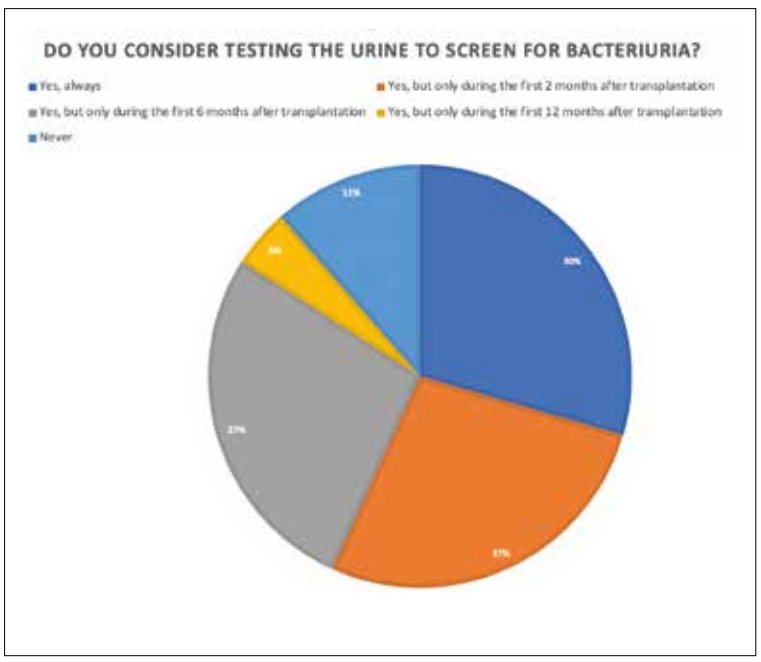


Figure 1

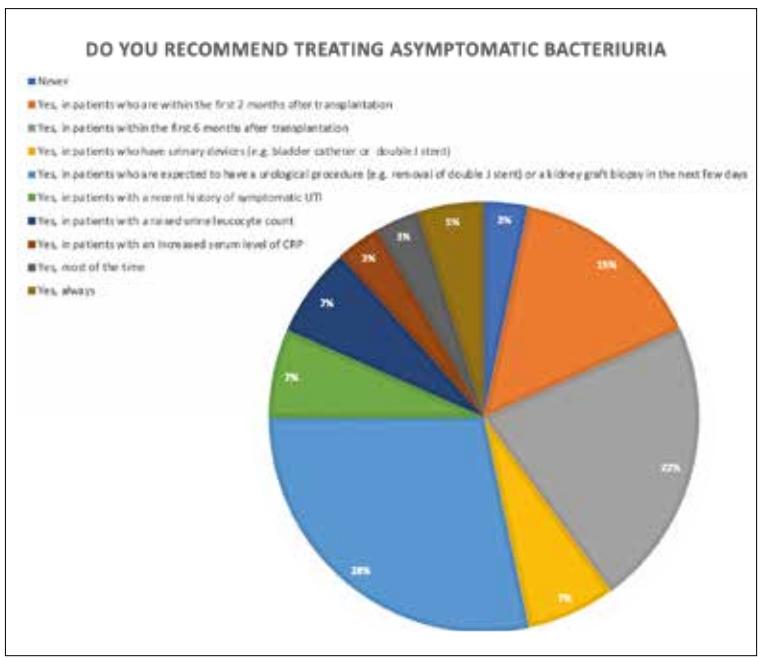


Figure 2

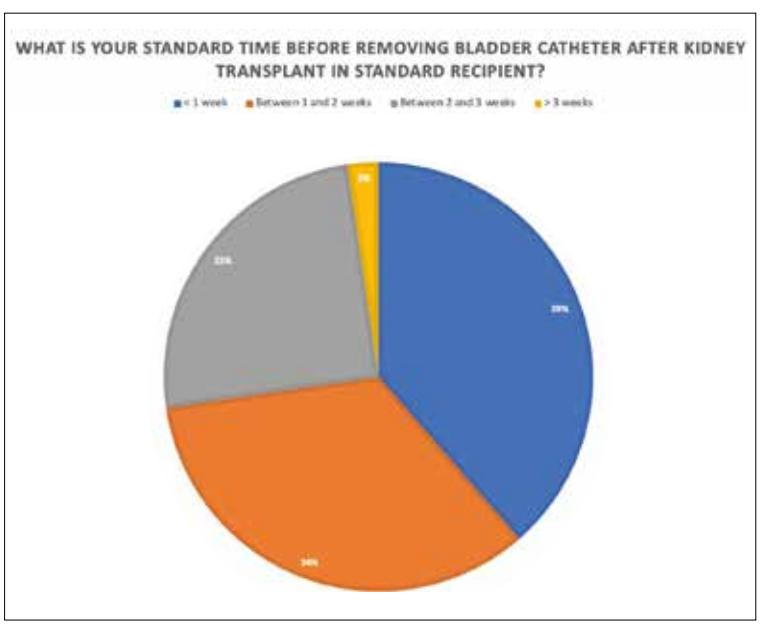


Figure 3

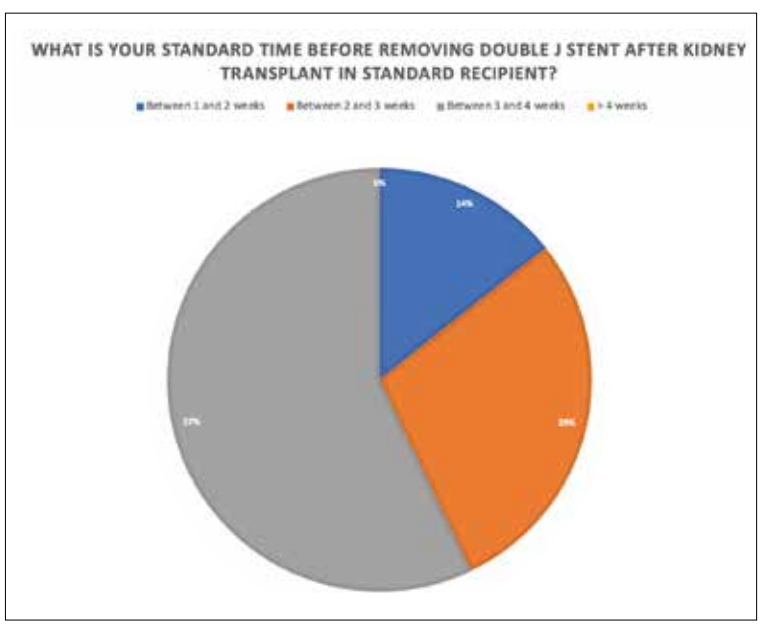


Figure 4

References:

1. Tandogdu Z, Cai T, Koves B, Wagenlehner F, Bjerklund-Johansen TE. Urinary Tract Infections in Immunocompromised Patients with Diabetes, Chronic Kidney Disease, and Kidney Transplant. Eur Urol Focus. 2016;2(4):394-9.
2. Barry JM. Kidney transplantation into patients with abnormal bladders. Transplantation. 2004;77(7):1120-3.
3. Bonkat G, Bartoletti R, Bruyère F, Cai T, Geerlings SE, Köves B, Schubert S, Wagenlehner F, Devlies W, Horváth J, Mantica G, Mezei T, Pilatz A, Pradere B, Veeratterapillay R. EAU Guidelines on Urological Infections. ISBN 978-94-92671-16-5. 2022.
4. Coussement J, Kamar N, Matignon M, Weekers L, Scemla A, Giral M, et al. Antibiotics versus no therapy in kidney transplant recipients with asymptomatic bacteriuria (BiRT): a pragmatic, multicentre, randomized, controlled trial. Clin Microbiol Infect Off Publ Eur Soc Clin Microbiol Infect Dis. 2021;27(3):398-405.
5. Pagonas N, Hörstrup J, Schmidt D, Benz P, Schindler R, Reinke P, et al. Prophylaxis of recurrent urinary tract infection after renal transplantation by cranberry juice and L-methionine. Transplant Proc. 2012;44(10):3017-21.

Saturday, 11 March 16:05 - 16:15
ESIU Meeting: Urogenital infections in urology
Amber 3, Yellow Area

Sexual dysfunction after a radical cystectomy

Is there an ideal sexual preserving technique for radical cystectomy?

Dr. Géraldine Pignot
Institut Paoli-Calmettes
Marseille (FR)

Radical cystectomy (RC) is a major intervention with morbidity rates that should not be disregarded. In addition to the usual post-operative complications, RC also impacts long term functional outcomes, with serious psychological and social drawbacks. Although improvements in perioperative care have decreased complication rates, the side effects during long-term treatment still compromise patients' quality of life (QOL). As survivorship from bladder cancer improves, appropriate assessment and treatment of these QOL conditions is needed. While standard questionnaires may be offered (IIEF-5 for men, FSFI for women), there is inconsistent use of patient-reported outcome measures (PROMs) after cystectomy. Yet, they are important tools available to understand patient-focused outcomes from care and to accurately assess health-related QOL. Various PROMs have been developed for patients with bladder cancer, although the disease's heterogeneity makes selection difficult [1]. Regarding sexual heath, it is found that up to 75% of both male and female patients reported sexual dysfunction after RC. Research on the treatment's impact on sexual health has been widely identified as an unmet need in bladder cancer patients [2]. It is clear that assessment of sexual health needs is largely overlooked for patients undergoing cystectomy compared to those undergoing other cancer treatments [3,4].

Over the past decade, surgical pioneers have adopted minimally invasive RC techniques in an effort to reduce surgical morbidity [5]. Additionally, improvement of imaging modalities, increased knowledge of pelvic structure anatomy and function, the advancement of surgical techniques and emerging technologies have facilitated the development of less destructive methods for treating bladder cancer. In a new era of functional optimisation, evaluating postoperative sexual outcomes has become a new surgical endpoint. Sex-sparing techniques are gaining popularity, with the aim of achieving definitive oncological control while attempting to preserve sexual function [6,7]. Here we summarise the role of pre-operative counseling regarding sexual health needs and the place of organ and nerve-sparing techniques for cystectomy in male and female patients.

Importance of pre-operative counseling

Preoperative counseling is a major component of the surgical management of bladder cancer, including providing comprehensive information on urinary diversion, nutritional evaluation, and adequate sexual function assessment, in order to identify educational needs and to propose prehabilitation if necessary. Patients reported that in survivorship, unmet informational needs revolved around changes in body image, stomal appliances, incontinence and sexual function, with a significant impact on depression and worries [8]. Indeed, pre-operative sexual health counseling for patients undergoing cystectomy is routine for neither male nor female patients. Between 50 and 80% of patients report having received little or no information on sexual life after RC [9].

Additionally, a well-documented gender bias exists in the assessment of sexual outcomes for women undergoing cystectomy. Recently, gender differences in oncological and functional outcomes after RC have received increased attention [10]. Many women report receiving inadequate preoperative counseling regarding risks of sexual dysfunction, nerve-sparing techniques and post-operative sexual health, regardless of disease stage or receipt of chemotherapy [9]. The main reasons for this gender disparity have been documented to include advanced patient age, inadequate time and uncertainty of baseline function [11,12].

Regarding patients' preferences for pre-operative counseling modality, the majority of them preferred a discussion led by healthcare professionals, but also requested written material to refer to later. Preoperative sexual health assessments should include measurements of erection quality, firmness and desire for men, and dryness, desire, orgasm and dyspareunia for women, ideally using validated questionnaires. However, in a recent survey including 140 urologists, the majority of them did not routinely counsel patients about sexual dysfunction. Moreover, 41.2% of them did not routinely discuss the potential for pelvic organ-sparing RC with sexually active patients [11,13]. While patients varied in the importance they placed on sexual function, with factors such as age, relationship status and oncological concerns affecting prioritisation, both younger and older patients expressed the desire for an option to retain sexual function [14]. In the end, as with the choice of urinary diversion, nerve sparing techniques and postoperative sexual health must be based on comprehensive counseling.

Nerve-sparing radical cystectomy for the male: time to optimise techniques

Selection of patients

According to the guidelines, in a radical cystoprostatectomy, including excision of the prostate and seminal vesicles is recommended [15]. Of course, the preservation of sexuality should in no way compromise the oncological quality of the surgery. However, for selected patients, the surgical technique may be adapted. Sexually active patients with localised disease (cT2) away from the bladder neck, prostate or prostatic urethrawho are properly informed could discuss sexual-sparing techniques.

Technical Aspects

Several techniques have been proposed to preserve sexual function during cystecomy: preservation of the prostate, seminal vesicles and nerve preservation.

- Prostate-sparing procedure:
  The first iteration of preservation of sexual function in RC proposed the preservation of the prostate through distal transection of the bladder specimen at the level of the bladder neck. This technique carried the risk of violating the bladder tumor and producing positive margins with an increased risk of metastatic recurrence [16]. This risk was reduced by performing prior endoscopic resection of the bladder neck and prostate [17,18]. Another option is en bloc removal of the prostatic parenchyma, bladder neck and bladder, as a "cysto-adenomectomy", by incising the prostatic capsule transversally until reaching the prostatic parenchyma, and then separating the parenchyma from the prostatic capsule in a maneuver similar to that performed during the enucleation of an adenoma [19]. The urethra is sectioned distally and an anastomosis between the neobladder and the remaining distal prostatic capsule is performed. However, all of these prostate-sparing techniques require that there is no secondary prostatic involvement from urothelial neoplasia and that the presence of a primary prostate cancer has been previously ruled out. Considering that incidental prostate cancer is a relatively common finding during histopathological evaluation of RC specimens [20], these prostate-sparing procedures require appropriate monitoring of the residual prostatic capsule in postoperative follow-up.
- Nerve-sparing procedure:
  Extensive knowledge of pelvic anatomy and nerve-sparing surgical techniques in men is well understood from studies about prostate anatomy and nerve-sparing prostatectomy. In well-selected patients, the preservation of neurovascular bundles has been shown to be oncologically safe, especially for patients with incidental prostate cancer [21], while leading to improved sexual function outcomes and urinary continence in those undergoing orthotopic neobladder [22]. Nerve-sparing procedures have been more widely adopted since the development of the robotic approach, with excellent functional results:up to 75% daytime continence at 1 month postoperatively and recovery of preoperative erectile function up to 77.5% at 12 months [23-25]. The degree of nerve sparing was graded intraoperatively by the surgeon independently on each side and depending on the location of the tumour.

Sex-sparing radical cystectomy in females: time to change our point of view

Selection of patients

Although bladder cancer is more common in men than in women, it is often more aggressive in female patients, and the proportion of women requiring radical treatment is higher [26]. In female patients, the standard surgical procedure is represented by anterior pelvic exenteration involving en bloc resection of the bladder and adjacent pelvic organs, including the uterus, ovaries, anterior vaginal wall and, in many cases, urethra [15]. However, sexual dysfunction being derived from such a highly demolitive surgery is a key concern [27]. Functional outcomes among women undergoing RC are understudied, with limitations stemming from the use of validated questionnaires, heterogeneous patient populations and small sample sizes [28, 29]. Despite the high risk for sexual dysfunction after cystectomy, there is little data on and attention given to these issues in women, which contrasts with the level of attention paid to the sexual function of men undergoing similar urologic procedures.

The consequences of anterior exenteration are numerous. Patients may experience:

- Neurovascular bundle damage, since the pelvic sensory fibers of the inferior hypogastric plexus are mainly concentrated in the posterior fornix along lateral sides of the cervix and rectum, and are therefore destroyed by exenteration.
  Autonomic and nociceptive nerve injuries are often associated with pain disorders, such as dyspareunia, vulvodynia, and vaginismus [30]
- Shortening or narrowing of the vagina
- Frequent devascularisation and denervation of the clitoris in the case of urethra removal
- Voiding issues when performing with an orthotopic neobladder [31,32]

According to current guidelines, sexual-sparing cystectomy is an option to consider for women highly motivated to preserve sexual function as soon as strict oncological inclusion criteria are met: localised tumour (cT2) detected on preoperative imaging (ideally MRI) away from the bladder neck, trigone or dorsolateral bladder walls. In these well-selected women, organ-sparing approaches can be performed safely without negatively impacting oncological outcomes [33].

Technical Aspects

Various types of pelvic-organ-sparing techniques, usually called "sex-sparing", have been proposed, aiming at the preservation of neurovascular bundles, vagina, uterus and ovaries.

- Vagina:
  According to a recent survey, vaginal preservation is important, and dyspareunia is the most common post-operative change in sexual function after RC [9, 34]. MRI is the best imaging to confirm the absence of involvement of the trigone or the dorsolateral bladder walls, allowing for full preservation of the anterior vaginal wall. Using a vaginal valve and following the vesico-vaginal dissection plane, as for promontofixation, the midline dissection is anatomical. Then, the neurovascular bundles located on the lateral wall of the vagina can be kept to preserve clitoral function [35]. The endopelvic fascia can be incised very close to the bladder neck to reduce the risk of damage to neurovascular paraurethral structures, which is crucial for both sexual and continence functionality.
- Uterus:
  The risks of uterine invasion have been investigated in preliminary studies to determine which group of patients is suitable for organ-sparing cystectomy. Before the era of MRI, it was proven that uterine involvement in bladder cancer was only 0.3%–12.5% [36,37]. Hydronephrosis on CT, tumor size ≥4.8 cm, positive lymph node status and tumor location at the bladder neck or trigone have been reported as risk factors for sexual organ invasion [38,39]. Now, a patient who shows no uterine invasion on preoperative pelvic MRI meets the necessary criteria and can be considered suitable for preserving the uterus, regardless of clinical stage, tumor location or size [40].
  Uterus-sparing surgery would leave the reproductive organs and nerves intact and bring noticeable progression in sexual outcomes. Moreover, in the case of orthotopic bladder substitution, the continence rate was shown to be significantly higher and the clean intermittent catheterisation significantly lower compared to standard radical cystectomy [41,42]. Uterus preservation should therefore be offered to women receiving a neobladder whenever justifiable.
  Moreover, the meticulous anatomical preservation of utero-vaginal neurovascular hypogastric plexus represents the cornerstone of a rapid and effective recovery of physiological functions in terms of urinary continence and sexual activity. The robotic approach could be of interest for this nerve preservation [43,44]. Additionally, pregnancy after organ-sparing cystectomy with urinary diversion in highly motivated young patients is possible [45].
- Ovaries:
  According to a recent survey of urologists, reasons for oophorectomy at the time of RC included concern for urothelial carcinoma involvement (54%), development of subsequent ovarian disease (50%) and surgical ease of pelvic node dissection (36%) [46, 47]. Many urologists remain unaware of the risks associated with oophorectomy, believing that there is no effect on health or QOL associated with this procedure.
  The current understanding of ovarian cancer pathogenesis and the effect of premature oophorectomy has led to a shift in practice within gynecology. Indeed, oophorectomy-induced surgical menopause has been shown to increase the risk of osteoporosis, cognitive impairment, cardiovascular disease and all-cause mortality, and is associated with poorer QOL scores compared to natural menopause [48–50]. This paradigm is now supported by the gynecologic community, but has been slow to translate to other disciplines.
  Regarding the risk of developing subsequent ovarian disease during the observation period, data on the lifetime risk of ovarian cancer stratified by germline mutations in BRCA1/BRCA2 and mismatch repair genes are emerging. In the absence of strong evidence, being aware of the low incidence of ovarian cancer, which accounts for only 1.3% of all new cancer cases, and the fact that most ovarian cancer cases are sporadic, it does not seem logical to perform systematic concomitant oophorectomy during RC in a patient with no history of hereditary breast or ovarian cancer [47,51]. Finally, the surgical ease of removing the ovarian pedicles, rather than sparing the ovaries, during pelvic node dissection is not an understandable argument. For a skilled surgeon, successful lymph node dissection with organ sparing is feasible by clipping the utero-ovarian pedicle, instead of the lombo-ovarian pedicle, and flipping the ovary out of the pelvis, without compromising oncological outcomes [52]. Thus, with the growing focus on cancer survivorship, preservation of the ovaries at the time of RC has become an increasingly important consideration in urologic oncology. A preoperative agreement must be concluded between the operating surgeon and the patient in all cases in order to avoid the systematic extirpation of the ovaries in not only premenopausal patients, but possibly also in selected postmenopausal patients after a careful evaluation of preoperative sexual function and assessment of putative history of breast and ovarian cancer.

Conclusions

With a growing focus on QOL in cancer survivorship, further efforts should be directed at reducing the barriers to sexual health pre-operative counseling. Much more work is needed preoperatively, including not only counseling/rehabilitation, improved measurement and consistency of PROMs to assess sexual function in male and female patients, but also specific information about the sexual consequences of surgery and possible options for sex-sparing procedures.

In female patients, anterior exenteration "d'office" is no longer acceptable. For well-selected sexually active patients, sex-sparing cystectomy is oncologically safe and may offer functional benefits in preserving pelvic reproductive organs and their nerve structures, with a significant impact on QOL both in terms of sexual health and urinary continence.

Sexual health after cystectomy is best co-managed with a multidisciplinary treatment approach, including preoperative counseling, neoadjuvant chemotherapy that may help expand selection criteria and indications, intraoperative nerve and organ preservation, and postoperative interventions to mitigate sexual side effects.

References can be requested from the corresponding authors.

Saturday 11 March 08:45 - 08:55
Plenary Session: Locally advanced BCa: Misconception of informed consent
Yellow Area, eURO Auditorium 1

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What's new in neurogenic bladder dysfunction treatment?

Storage and voiding phases; invasiveness vs effectiveness

Dr. Charalampos Konstantinidis
Dept. of Urology, Neuro-Urology Unit National Rehabilitation Center, Athens (GR)

The treatment strategy for Neurogenic Lower Urinary Tract Dysfunction (NLUTD) is based on the individual pathophysiology of the dysfunction as it is documented by urodynamics. Additional aggravating factors such as lithiasis or reflux have to be considered., as well as some specific conditions related to the nature of the neurogenic disease impairing cognitive function or resulting in severe disability. Understanding each patient's needs and dexterities is essential for offering realistic management options [1].

In cases where the restoration of the Lower Urinary Tract (LUT) function is impossible, the management of NLUTD contains two main goals. The first one is the protection of the upper urinary tract. This is a matter of life for these patients. We can achieve this goal by establishing sufficient bladder capacity and compliance accompanied by storage under low pressure and complete voiding under acceptable pressure [2]. The second goal, with equal importance, is the achievement of urinary continence or at least contained continence. This is a matter of Quality of Life.

Although there are no clear data regarding the exact secure pressure for the Upper Urinary Tract (UUT) we accept 40cm/H2O as a safe cut pressure in the storage phase [3] and during the voiding phase up to 80cm/H2O. Special consideration has to be taken for impaired compliance. The storage phase takes place during 99.8% of the daytime, so in the case of a low compliance bladder, the upper urinary tract is exposed to higher pressures over a prolonged period, increasing the potential danger for reflux and renal dilatation [4, 5].

Assisted bladder emptying by bladder expression or triggered voiding is not recommended as the LUT is exposed to a high-pressure condition putting the UUT in danger. In exceptional conditions, where relatively low pressures have been documented by urodynamics, assisted bladder emptying can be allowed, under close patient follow-up. Antimuscarinics are the first-line treatment for Neurogenic Detrusor Overactivity (NDO). Their action, in the filling phase, is not only limited to the inhibition of the detrusor contraction but also mediated to the inhibition of afferent stimuli (the sensory part), resulting in the inhibition or delay of the release of the reflexes of the detrusor contraction [6, 7]. Antimuscarinics increase bladder capacity, improve compliance and reduce the amplitude of detrusor contractions resulting in decreased intravesical pressure [1]. A higher dose or drug combination may be needed for better clinical outcomes, increasing, on the other hand, the complication rate and severity [8-14].

Although it is not established, a clear algorithm for drug selection and high-level evidence in neurogenic patients is missing [15 - 17], a lot of studies support the effectiveness of almost all antimuscarinic agents [18 - 21]. Beta 3 agonists, although they show promising signs of improving the symptoms of NLUTD, they did not have a proven urodynamic effect on capacity and detrusor pressure [22, 23]. Alpha-blockers are effective for bladder outlet resistance reduction, while parasympathomimetics are not recommended for improving detrusor contraction [1, 24]. Intermittent catheterisation using an aseptic technique, if it is possible, is the standard option for bladder emptying when spontaneous voiding is impossible or unsafe for the UUT [1, 24]. Indwelling catheters should be kept in case there is no other realistic option available. In this case the suprapubic route is preferable [24]. Intradetrusor botulinum toxin injection (using OnabotulinumtoxinA) is an effective minimally invasive treatment option for NDO [1, 2, 24].

Recently, AbobotulinumtoxinA has received a positive opinion in Europe for the management of urinary incontinence (UI) in adults with NDO due to spinal cord injury (SCI) (traumatic or non-traumatic) or multiple sclerosis (MS), who are regularly performing clean intermittent catheterisation (CIC) [25, 26]. The use of electrostimulation and neuromodulation has been applied in NLUTD. Sacral anterior root stimulation (SARS) accompanied by sacral deafferentation is not favourable nowadays despite the proven long-term good results due to the need for rhizotomies in the era of "regenerative medicine". Additionally, the abandonment of the method did not allow the evolution of the relative equipment. On the other hand, Sacral Neuromodulation which is widespread for refractory Overactive bladder Syndrome (OAB) is not established as an officially approved treatment option for neurogenic patients. During the last years, SNS on neurogenic patients with incomplete lesions has been studied in several trials and results are very promising [27]. Tibial nerve stimulation has also been tested in NLUTD, but evidence for its effectiveness is still limited [1, 24].

In case minimally invasive treatment is not effective, a surgical approach is recommended [1, 24]. Bladder augmentation is an established procedure that guarantees a low-pressure reservoir with efficient capacity and normal compliance. In female patients where neurogenic Stress Urinary Incontinence (nSUI) is the case, placement of an autologous sling is recommended. In males with nSUI, an artificial sphincter placement is a valuable option when there is an increased complication rate, compared to non-neurogenic individuals.

A summary of all treatment options for the establishment of low pressure in the LUT is demonstrated in Table I. During the Storage Phase, the administration of antimuscarinics, beta3 agonists and/or botulinum toxin is usually an effective treatment option. If conservative or minimally invasive treatment fails, surgical intervention, mainly by bladder augmentation, is an available and very efficient management option. During the Voiding Phase, low pressure is obtained by the use of intermittent catheterisation, administration of alpha-blockers or sphincterotomy of the external sphincter. In some cases, the patient's comorbidities force less favourable solutions, such as continuous bladder drainage through indwelling catheters or incontinent stomas.

Similar to a lot of things in medicine, the effectiveness of a treatment is increasing as the invasiveness is increasing as well (Figure 1). This means that the most effective treatment options are the most invasive ones. Intermittent catheterisations and antimuscarinics are the mainstream in the treatment of NLUTD. This management combination is less invasive and has relatively high effectiveness.

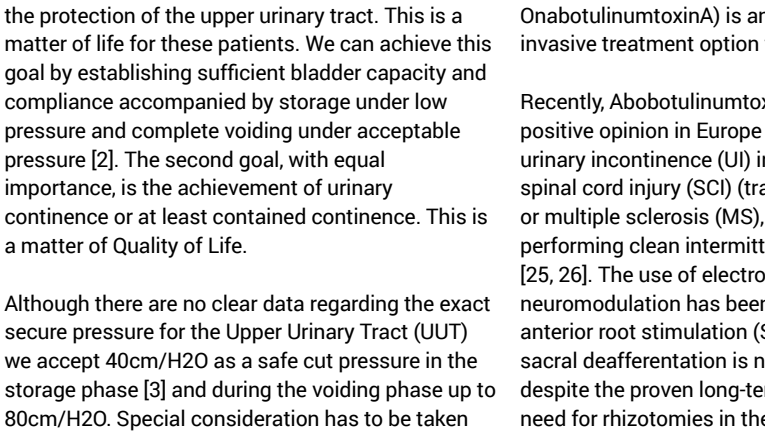

Figure 1. Treatment options for NLUTD. Invasiveness and effectiveness correlation

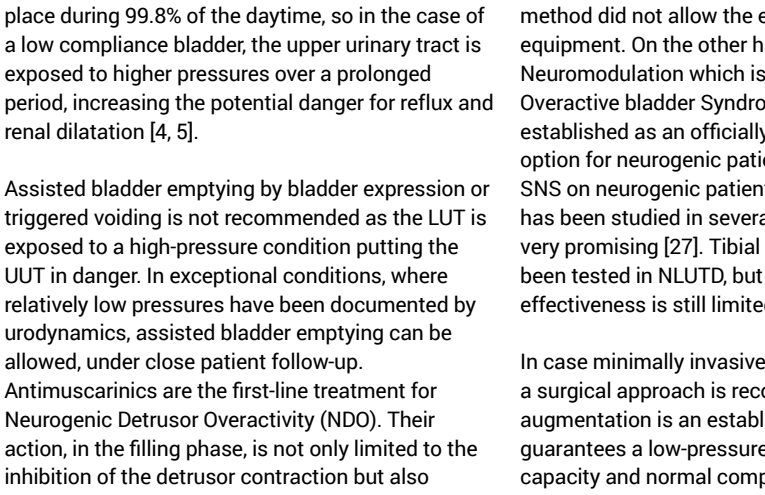

Table I. Treatment options for NLUTD

References

1. Blok B, Castro-Diaz D, Del Popolo J, Groen J, Hamid R, Karsenty G, et al. EAU Guidelines on Neuro-Urology 2022. EAU Guidelines Office, Arnhem. The Netherlands. https://uroweb.org/guidelines/neuro-urology
2. Apostolidis A, Drake MJ, Emmanuel A, Gajewski J, Hamid R, Heesakkers J, et al.: Neurologic Urinary and Fecal Incontinence (Committee 10), In: Incontinence: 6th edition 2017, 6th International Consultation on Incontinence, Tokyo, September 2016. Editors Abrams P, Cardozo L, Wagg A, Wein A.
3. McGuire EJ, Woodside JR, Borden TA, Weiss RM. Prognostic value of urodynamic testing in myelodysplastic patients. J Urol. 1981 Aug; 126 (2):205-9. doi: 10.1016/s0022-5347(17)54449-3. PMID: 7196460.
4. Tarcan T, Sekerci CA, Akbal C, Tinay I, Tanidir Y, Sahan A, Sahin B, Top T, Simsek F. Is 40 cm H2O detrusor leak point pressure cut-off reliable for upper urinary tract protection in children with myelodysplasia? Neurourol Urodyn. 2017 Mar; 36(3):759-763. doi: 10.1002/nau.23017. Epub 2016 Apr 15. PMID: 27080436.
5. Tarcan T, Demirkesen O, Plata M, Castro-Diaz D. ICS teaching module: Detrusor leak point pressures in patients with relevant neurological abnormalities. Neurourol Urodyn. 2017 Feb; 36(2):259-262. doi: 10.1002/nau.22947. Epub 2015 Dec 23. PMID: 26693834.
6. Andersson KE. Antimuscarinic mechanisms and the overactive detrusor: an update. Eur Urol. 2011 Mar; 59(3):377-86. doi: 10.1016/j.eururo.2010.11.040. Epub 2010 Dec 8. PMID: 21168951.
7. Yamaguchi O. Antimuscarinics and overactive bladder: other mechanism of action. Neurourol Urodyn. 2010; 29(1):112-5. doi: 10.1002/nau.20796. PMID: 19693952.
8. Horstmann M, Schaefer T, Aguilar Y, Stenzl A, Sievert KD. Neurogenic bladder treatment by doubling the recommended antimuscarinic dosage. Neurourol Urodyn. 2006; 25(5):441-5. doi: 10.1002/nau.20289. PMID: 16847942.
9. Appell RA. Overactive bladder in special patient populations. Rev Urol. 2003; 5 Suppl 8 (Suppl 8): S37-41. PMID: 16985989; PMCID: PMC1502390.
10. Cameron AP, Clemens JQ, Latini JM, McGuire EJ. Combination drug therapy improves compliance of the neurogenic bladder. J Urol. 2009 Sep; 182(3):1062-7. doi: 10.1016/j.juro.2009.05.038. Epub 2009 Jul 18. PMID: 19616807.
11. Amend B, Hennenlotter J, Schäfer T, Horstmann M, Stenzl A, Sievert KD. Effective treatment of neurogenic detrusor dysfunction by combined high-dosed antimuscarinics without increased side-effects. Eur Urol. 2008 May; 53(5):1021-8. doi: 10.1016/j.eururo.2008.01.007. Epub 2008 Jan 17. PMID: 18243516.
12. Nardulli R, Losavio E, Ranieri M, Fiore P, Megna G, Bellomo RG, Cristella G, Megna M. Combined antimuscarinics for treatment of neurogenic overactive bladder. Int J Immunopathol Pharmacol. 2012 Jan-Mar; 25(1 Suppl): 35S-41S. doi: 10.1177/03946320120250s106. PMID: 22652160.
13. Bennett N, O'Leary M, Patel AS, Xavier M, Erickson JR, Chancellor MB. Can higher doses of oxybutynin improve efficacy in neurogenic bladder? J Urol. 2004 Feb; 171(2 Pt 1):749-51. doi: 10.1097/01.ju.0000103274.38694.b1. PMID: 14713802.
14. Menarini M, Del Popolo G, Di Benedetto P, Haselmann J, Bödeker RH, Schwantes U, Madersbacher H; TcP128-Study Group. Trospium chloride in patients with neurogenic detrusor overactivity: is dose titration of benefit to the patients? Int J Clin Pharmacol Ther. 2006 Dec; 44(12):623-32. doi: 10.5414/cpp44623. PMID: 17190372.
15. Madersbacher H, Mürtz G, Stöhrer M. Neurogenic detrusor overactivity in adults: a review on efficacy, tolerability and safety of oral antimuscarinics. Spinal Cord. 2013 Jun; 51(6):432-41. doi: 10.1038/sc.2013.19. PMID: 23743498.
16. Madhuvrata P, Singh M, Hasafa Z, Abdel-Fattah M. Anticholinergic drugs for adult neurogenic detrusor overactivity: a systematic review and meta-analysis. Eur Urol. 2012 Nov; 62(5):816-30. doi: 10.1016/j.eururo.2012.02.036. Epub 2012 Feb 25. PMID: 22397851.
17. Nicholas RS, Friede T, Hollis S, Young CA. Anticholinergics for urinary symptoms in multiple sclerosis. Cochrane Database Syst Rev. 2009 Jan 21; (1):CD004193. doi: 10.1002/14651858.CD004193.pub2. Update in: Cochrane Database Syst Rev. 2015; 6: CD004193. PMID: 19160231
18. van Rey F, Heesakkers J. Solifenacin in multiple sclerosis patients with overactive bladder: a prospective study. Adv Urol. 2011;2011:834753. doi: 10.1155/2011/834753. Epub 2011 May 5. PMID: 21687581; PMCID: PMC3114086.
19. Amarenco G, Sutory M, Zachoval R, Agarwal M, Del Popolo G, Tretter R, Compion G, De Ridder D. Solifenacin is effective and well tolerated in patients with neurogenic detrusor overactivity: Results from the double-blind, randomized, active- and placebo-controlled SONIC urodynamic study. Neurourol Urodyn. 2017 Feb;36(2):414-421. doi: 10.1002/nau.22945. Epub 2015 Dec 29. PMID: 26714009.
20. Kaga K, Yamanishi T, Kaga M, Fuse M, Kamasako T, Ishizuka M. Urodynamic efficacy of fesoterodine for the treatment of neurogenic detrusor overactivity and/or low compliance bladder. Int J Urol. 2020 Oct;27(10):899-904. doi: 10.1111/iju.14319. Epub 2020 Aug 7. PMID: 32767525; PMCID: PMC7589380.
21. Konstantinidis C, Samarinas M, Tzitzika M, Kratiras Z, Panagiotakopoulos G, Giannitsas K, Athanasopoulos A. Efficacy of fesoterodine fumarate (8 mg) in neurogenic detrusor overactivity due to spinal cord lesion or multiple sclerosis: A prospective study. Neurourol Urodyn. 2021 Nov;40(8):2026-2033. doi: 10.1002/nau.24790. Epub 2021 Sep 9. PMID: 34498773.
22. Krhut J, Borovička V, Bílková K, Sýkora R, Míka D, Mokriš J, Zachoval R. Efficacy and safety of mirabegron for the treatment of neurogenic detrusor overactivity-Prospective, randomized, double-blind, placebo-controlled study. Neurourol Urodyn. 2018 Sep; 37(7):2226-2233. doi: 10.1002/nau.23566. Epub 2018 Mar 31. PMID: 29603781.
23. Welk B, Hickling D, McKibbon M, Radomski S, Ethans K. A pilot randomized-controlled trial of the urodynamic efficacy of mirabegron for patients with neurogenic lower urinary tract dysfunction. Neurourol Urodyn. 2018 Nov; 37(8):2810-2817. doi: 10.1002/nau.23774. Epub 2018 Aug 31. PMID: 30168626.
24. Ginsberg DA, Boone TB, Cameron AP, Gousse A, Kaufman MR, Keays E, Kennelly MJ, Lemack GE, Rovner ES, Souter LH, Yang CC, Kraus SR. The AUA/SUFU Guideline on Adult Neurogenic Lower Urinary Tract Dysfunction: Treatment and Follow-up. J Urol. 2021 Nov;206(5):1106-1113. doi: 10.1097/JU.0000000000002239. Epub 2021 Sep 8. PMID: 34495688.
25. Kennelly M, Cruz F, Herschorn S, Abrams P, Onem K, Solomonov VK, Del Rosario Figueroa Coz E, Manu-Marin A, Giannantoni A, Thompson C, Vilain C, Volteau M, Denys P; Dysport CONTENT Program Group. Efficacy and Safety of AbobotulinumtoxinA in Patients with Neurogenic Detrusor Overactivity Incontinence Performing Regular Clean Intermittent Catheterization: Pooled Results from Two Phase 3 Randomized Studies (CONTENT1 and CONTENT2). Eur Urol. 2022 Aug;82(2):223-232. doi: 10.1016/j.eururo.2022.03.010. Epub 2022 Apr 7. PMID: 35400537.
26. Denys P, Castaño Botero JC, Vita Nunes RL, Wachs B, Mendes Gomes C, Krivoborodov G, Tu LM, Del-Popolo G, Thompson C, Vilain C, Volteau M, Kennelly M; Dysport CONTENT program group. AbobotulinumtoxinA is effective in patients with urinary incontinence due to neurogenic detrusor overactivity regardless of spinal cord injury or multiple sclerosis etiology: Pooled analysis of two phase III randomized studies (CONTENT1 and CONTENT2). Neurourol Urodyn. 2023 Jan;42(1):153-167. doi: 10.1002/nau.25062. Epub 2022 Nov 2. PMID: 36321799.
27. van Ophoven A, Engelberg S, Lilley H, Sievert KD. Systematic Literature Review and Meta-Analysis of Sacral Neuromodulation (SNM) in Patients with Neurogenic Lower Urinary Tract Dysfunction (nLUTD): Over 20 Years' Experience and Future Directions. Adv Ther. 2021 Apr;38(4):1987-2006. doi: 10.1007/s12325-021-01650-9. Epub 2021 Mar 13. PMID: 33713279; PMCID: PMC8004509.

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Which supportive care intervention is best?

Endourology management: Patient needs, expectations and QoL

Dr. Silvia Proietti
Department of Urology, IRCCS San Raffaele Hospital, Milan (IT)

'Supportive care' is a typically used term in oncology and harbours different definitions for different groups of clinicians and patients. Despite the fact that broad variations of supportive care exist, all definitions involve factors addressing symptom management and quality of life (QoL) improvement, for oncologic patients having treatment, and those with advanced diseases [1].

A clear definition of supportive care is essential for good communication between clinicians, patients and their families. Hui et al. developed a conceptual framework in which 'supportive care' lies under its umbrella, 'palliative care'. This includes the full range of issues for patients throughout the disease trajectory, from survivorship to bereavement [2]. Hence, it is a general misconception that supportive care is related only to end-of-life care.

The decision-making process for supportive care includes several diverse factors, such as cancer stage, performance-status, prognosis, comorbidities, patient preferences, and social background. When making a 'supportive care' intervention, it is important to identify the specific supportive care needs of the individual, balancing the pros and cons of each treatment choice, taking into consideration the patient's life expectancy and their QoL.

There is ample evidence showing the importance of supportive care in urological malignancies, with consistent improvements in physical and psychological well-being [3,4]. Despite these valuable advantages, there is still no consensus on the indications and timing of intervention for supportive care in urologic oncology [3].

Urologists are part and parcel of the supportive care in urological cancer management, since they usually diagnose the disease, follow-up the patients and advise them over time [5]. The most common situations that require endourological management in the field of supportive care in patients with urological cancers are addressed below.

Supportive care: Endourological management of ureteral obstruction

Ureteral malignant obstruction represents a common urologic scenario, but often the best method of urinary diversion poses a challenging dilemma for clinicians. The aetiology of obstruction is important for estimating a patient's prognosis (i.e. primary tumour, lymphadenopathy or metastasis). It is often an extrinsic compression, with non-urological malignancies more commonly implicated than urological cancers.

An obstruction may be diagnosed during staging of the disease or during an investigation for impaired renal function or incidental hydronephrosis. On the other hand, some patients may be symptomatic from the obstruction with acute flank pain or chronic lumbar discomfort, or present with renal failure, urinary tract infections and sepsis [6].

The management of ureteral obstruction with decompression strives to relieve pain, to prevent urosepsis and deterioration in renal function, and consequently, to allow systemic anticancer therapies. One of the aims of urinary diversion may also be to prolong life expectancy, but unfortunately the prognosis of patients with malignant ureteral obstruction is generally poor, even if the urinary decompression is performed [7].

There is no consensus on the superiority of ureteral stent vs percutaneous nephrostomy in the management of ureteral obstruction in terms of efficacy, complications and QoL implications. This is due to the lack of homogenous, comparative and prospective data on this issue [6]. Therefore, treatment decisions must be tailored case by case with a multidisciplinary approach, involving patients, their family and members of their supportive care team.

Retrograde placement of ureteral stents sometimes may be technically challenging and associated with a high failure rate due to extrinsic pelvic/retroperitoneal obstruction or trigone invasion [8,9]. Also, patients with ureteral stents may experience bothersome irritative urinary tract symptoms, pain and mild haematuria.

While polymer ureteral stents may be effective in relieving obstructions in the short term, unfortunately, the stents require regular substitution, are prone to obstruction, tumour ingrowth, encrustation, migration and are a source of infections [10]. When a single polymer stent has failed, the use of tandem polymer stents can be considered. However, they still need regular replacement, exposing an already high-comorbid patient group to further multiple hospital admissions and interventions [11].

Metallic ureteric stents may be used more effectively than polymeric stents in maintaining lumen patency, reducing stent related lower urinary tract symptoms and the frequency of replacement (mean indwelling-time 1-3 years) [10]. Nevertheless, available evidence on the exact indication for metallic ureteral stents is small due to low quality and heterogenous data. Randomised controlled studies are needed to evaluate cost-effectiveness. Patients need to be selected according to aetiology, site of obstruction, and prognosis. This will help to improve outcomes and patient satisfaction.

An alternative to urinary decompression with retrograde stent insertion is the placement of a nephrostomy tube. However, the associated external urine bag is often seen as a disability by some patients, for which they may initially reject this option [6]. When disease-factors allow, antegrade stenting can be considered in patients who desire to be free of external tubes.

Patients with nephrostomies may also have complications related to tube occlusion, leakage and inadvertent displacement requiring multiple hospital admissions. Rare intra-postoperative complications can be from adjacent organ injury or bleeding. Although there are case reports and small retrospective studies on tumour seeding and invasion through the percutaneous nephrostomy tract, percutaneous nephrostomy on upper-tract urothelial cancer can be considered as part of a treatment strategy if renal function preservation is needed [12].

As reported by Hsu et al., patient preference is strongly conditioned by a clinician's opinion. Yet, as there are no strong clinical guidelines on the use of nephrostomy vs ureteral stenting, clinicians often rely on their personal experience, logistical factors and preference in counselling their patients [6]. The preference on different urinary decompression methods also vary between different clinical specialties (i.e. radiologists vs urologists) and institutions. Lastly, there is also a sort of Hamlet dilemma "to drain or not to drain" still present among urologists for this subset of patients.

Endourological management of upper urinary tract carcinoma in 'imperative' cases

There is a general misperception that surgery is the antithesis of supportive care, but it is not. The argument for conservative measures rather than nephroureterectomy in the setting of a solitary kidney, bilateral UTUC, and pre-existing severe chronic kidney disease are predicated on the morbidity and mortality associated with dialysis. This would be a potential consequence of extirpative surgery in patients with imperative indications for endoscopic management.

In our study on 29 patients with UTUC who underwent imperative conservative endourological treatment, we recorded overall survival (OS) rates of 96.4% with a median follow-up of 23 months (IQR 14-35) [13]. Although renal function declined in our series, only one patient (3.4%) showed a clinically significant impairment. When reviewing the 2010 United States Renal Data System (USRDS) Annual Data Report, their results showed that 5-year overall survival for end-stage renal disease was only 39%, but our data suggests that in carefully-selected patients, endoscopic management of UTUC should be considered. The authors of the USRDS report argued that conservative treatment should be considered for high-grade tumours in imperative conditions due to the significant morbidity and mortality associated with end-stage renal disease [14]. Similarly, Go et al. showed that mortality rates remain above 20 percent per year with the use of dialysis, with more than half of the deaths related to cardiovascular disease [15].

A meta-analysis showed that older aged patients with a medium and high Charlson Comorbidity Index (CCI) at the initiation of dialysis were associated with increased risk of death [16]. In our cohort, most of the patients were of advanced age (median 69 years; IQR 63-79) with a median CCI of 6 (IQR 4-8) and a median estimated 10-year survival of 2% (IQR 0-53%) [13]. Despite their advanced age and associated comorbidities, the patients in our study achieved approximately 95% of OS rates after their UTUC diagnosis. Our rationale for performing endoscopic management in 'imperative cases' was corroborated by Krambeck et al. who in their series of patients with UTUC imperative conditions (average age 74 years; 35-month follow-up) reported the cancer-specific and overall survival of 49.3% and 35%; in contrast OS rates on chronic haemodialysis for a 70-year-old patient are 70.6%, 38.8%, and 19.2%, respectively, at 1, 3, and 5 years [17].

Endoscopic management of UTUC has important positive implications on a patient's QoL. As a matter of facts, QoL evaluations in haemodialysis patients have revealed that patients would give up one-quarter to one-half of their remaining life expectancy in current health if the sacrifice would allow them to have perfect health for a shorter time [18]. Additionally, Verberne et al. reported that patients with chronic renal disease managed conservatively had 352.7 hospital-free days per year, versus 282.7days in patients on dialysis, contributing to worse QoL in the dialysis group [19].

In our study, 61.1% of the patients had at least one recurrence and the 24-month RFS was 31.7% [13]. This is in line with the outcomes reported by Krambeck et al. who found a 5-year local recurrence-free survival of 27.1% [17]. Our results had also corroborated the safety of endoscopic management of UTUC patients, even those with serious comorbidities. Despite high CCI, the complication rate was low with Clavien-Dindo complication grade III and IV in only 3 (2.2%) and 1 (0.7%) cases respectively, in a total of 137 endoscopic procedures performed [13].

At this point, the question arises, why should endoscopic management in 'imperative' cases be considered a supportive care? Surely, because the end-point of the decision of performing conservative treatment in patients (otherwise candidate to nephroureterectomy and consequently to dialysis), is based on the concept that the life-expectancy in this subset of patients is associated with a better QoL. Certainly, endourologists should perform accurate preoperative patient counselling explaining all the personalised pros and cons associated with the UTUC conservative treatment.

Endourological management of urinary stones in patients with urological malignancies

Urinary tract stones are one of the most common urinary tract pathologies. The prevalence of kidneys stones increased from 3.2% in 1980 to 10.1% in 2016 [20], affecting nearly 11% of men and 7% of women [21]. This risk increases with age. Stone disease in patients with urological malignancies could be related to recurrent burden for stone-former patients, extraosseous calcification (i.e. calcium salt precipitation outside of the skeletal system) secondary to paraneoplastic syndromes or side effects of anticancer therapy with bone resorption, tumour lysis after chemotherapy (i.e. risk of uric acid stones) or urinary stasis due to malignant ureteral compression.

The decision for treatment of asymptomatic renal stones is arguable in the field of supportive care, whereas an endourological surgery for a symptomatic renal/ureteral stone is justified to prevent complications. This decision has to be based on each patient-specific situation.

Conclusion

In the field of supportive care in patients with urological malignancies and endourological problems, clinicians should tailor the care to a patient's needs at the time, expectations and QoL. Although, in this complex clinical scenario, the choice is never black and white, but it should be an informed decision between patients and clinicians, by balancing out the pros and cons of the different approaches.

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References

1. Hui D. Definition of supportive care: does the semantic matter? Curr Opin Oncol 2014;26(4):372-9
2. Hui D, De la Cruz M, Mori M et al. Concepts and definitions for "supportive care," "best supportive care," "palliative care," and "hospice care" in the published literature, dictionaries, and textbooks. Support Care Cancer 2013; 21: 659-85
3. Hugar LA, Wulff-Burchfield EM, Winzelberg GS et al. Incorporating palliative care principles to improve patient care and quality of life in urologic oncology. Nat Rev Urol. 2021; 18: 623-25
4. Wu JN, Meyers FJ, Evans CP. Palliative care in urology. Surg Clin North Am 2011; 91: 429-444
5. Umbher MH, Wagg A, Hamza M et al. Top ten Palliative care clinicians should know about urological care. J Palliat Med 2022; online ahead of print
6. Hsu L, Li H, Pucheril D et al. Use of percutaneous nephrostomy and ureteral stenting in management of ureteral obstruction. World J Nephrol 2016; 5: 172-81
7. Chung PH, Krabbe LM, Darwish OM et al. Degree of hydronephrosis predicts adverse pathological features and worse oncological outcomes in patients with high grade urothelial carcinoma of the upper urinary tract. Urol Oncol 2014; 32: 981-88
8. Chitale SV, Scott-Barrett S, Ho ET et al. The management of ureteric obstruction secondary to obstruction secondary to malignant pelvic disease. Clin Radiol 2022; 57: 1118-21
9. Docimo SG, Dewolf WC. High failure rate of indwelling ureteral stents in patients with extrinsic obstruction: experience at 2 institutions. J Urol 1989; 142: 277-79
10. Khoo CC, Abboudi H, Cartwright R et al. Metallic Ureteric Stents in Malignant Ureteric Obstruction: A Systematic Review. Urology 2018; 118:12-20
11. Elsamra SE, Leavitt DA, Motato HA et al. Stenting for malignant ureteral obstruction: Tandem, metal or metal-mesh stents. Int J Urol. 2015; 22:629-36.
12. Huang GL, Luo HL, Chiang PH. Does preoperative percutaneous nephrostomy insertion worsen upper-tract urothelial cancer oncological outcome? A retrospective single centre study. BMC Urol 2019; 19: 50
13. Proietti S, Marchioni M, Eisner B et al. Conservative treatment of upper urinary tract carcinoma in patients with imperative indications. Minerva Urol Nephrol 2021; 73: 245-52
14. USRDS (2010) United States renal data system 2010 annual data report. Atlas of chronic kidney disease and end-stage renal disease in the United States, Bethesda, MA (2010). National institutes of health, national institute of diabetes and digestive and kidney diseases)
15. Go AS, Chertow GM, Fan D et al: Chronic kidney disease and the risks of death, cardiovascular events, and hospitalization. N Engl J Med 2004, 351: 1296-305
16. Pan Y, Xu XD, Guo LL et al: Association of early versus late initiation of dialysis with mortality: systematic review and meta-analysis. Nephron Clin Pract 2012; 120: 121-31
17. Krambeck AE, Thompson RH, Lohse CM et al: Imperative indications for conservative management of upper tract transitional cell carcinoma. J Urol 2007; 178: 792-6
18. Churchill DN, Torrance GW, Taylor DW et al: Measurement of quality of life in end-stage renal disease: The time trade-off approach. Clin Invest Med 1987; 10:14-20
19. Verberne WR, Dijkers J, Kelder JC et al: Value-based evaluation of dialysis versus conservative care in older patients with advanced chronic kidney disease: a cohort study. BMC Nephrol 2018; 19: 205
20. Chewcharat A and Curhan G. Trends in the prevalence of kidney stones in the United States from 2007 to 2016. Urolithiasis 2021; 49: 27-39.
21. Scales CD Jr, Smith AC, Hanley JM and Saigal CS. Prevalence of kidney stones in the United States. Eur Urol 2012; 62: 160-165.

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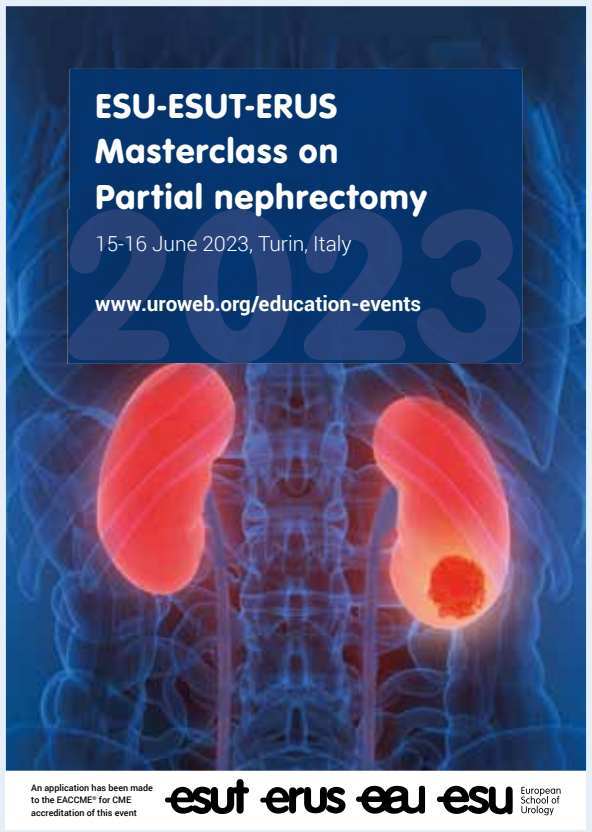

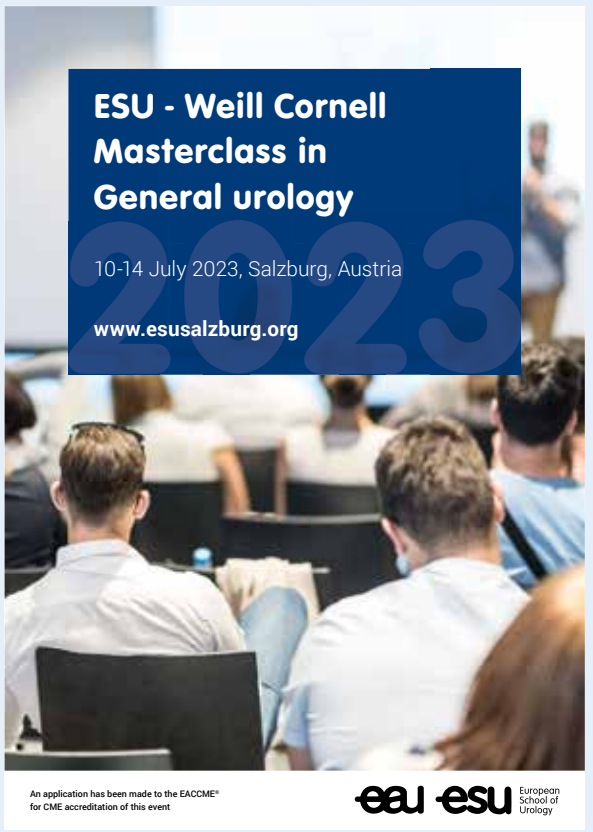

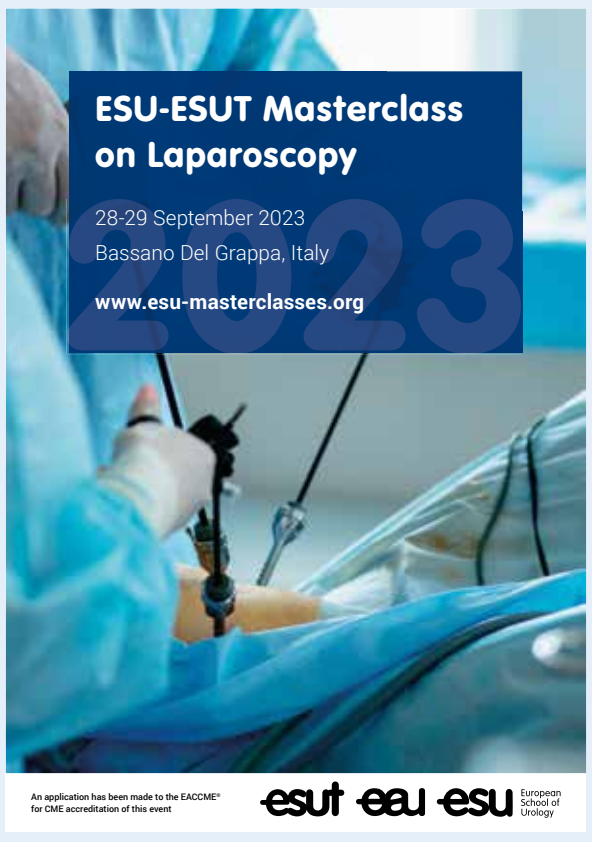

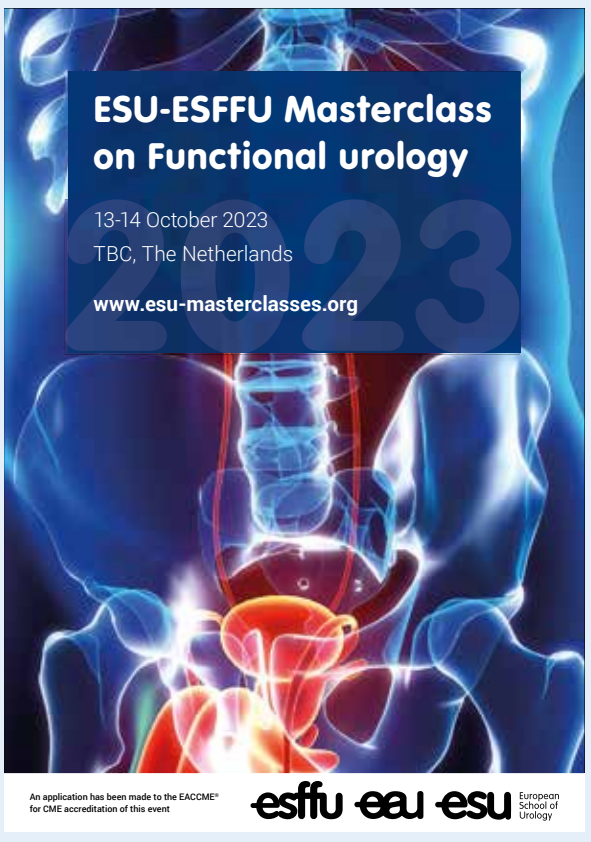

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EAU leads innovative data initiatives

Provides support to evidence-based policy making

Prof. Dr. Monique Roobol
Dept. of Urology, Erasmus MC Rotterdam (NL)

m.roobol@erasmusmc.nl

In the past decade, there has been an explosion of healthcare-related data. With the digitalisation of medical records, increasing affordability of molecular testing, advent of medical informatics and widespread use of wearables, the sheer volume of data available for analysis is staggering [1].

Big data in healthcare
"Big data" refers to large and complex datasets generated by a wide range of sources. These datasets are typically characterised by their large volume, high velocity, and extensive variety. They can be difficult to store, process, and analyse using traditional data management and analysis tools.

Big data can be structured, unstructured, or semi-structured. Structured data refers to data that is organised in a specific format such as tables, spreadsheets, and databases. Examples of structured data include clinical and financial data. Unstructured data refers to data that does not have a specific format such as text, images, and videos. Semi-structured data is a form of data that has some kind of structure but it is not as rigid as structured data.

There is a discussion that "big" is no longer the correct parameter, but rather how "smart" the data are, focusing on the insights that the volume of data can reasonably provide. This aspect is fundamental in the health sector. The potential of big data in improving health is enormous. However, its potential value is unlocked only when leveraged to drive decision making and enable such evidence-based decision making, it is necessary to have efficient processes to analyse and turn high volumes of data into meaningful insights [2].

Due to the complexity and diversity of the data, as well as, the computational power and storage required to handle it, the analysis of big data often requires specialised software, infrastructure, and expertise. How can we bridge the gap between the collected data, and our understanding and knowledge of human health? This is covered by "data science".

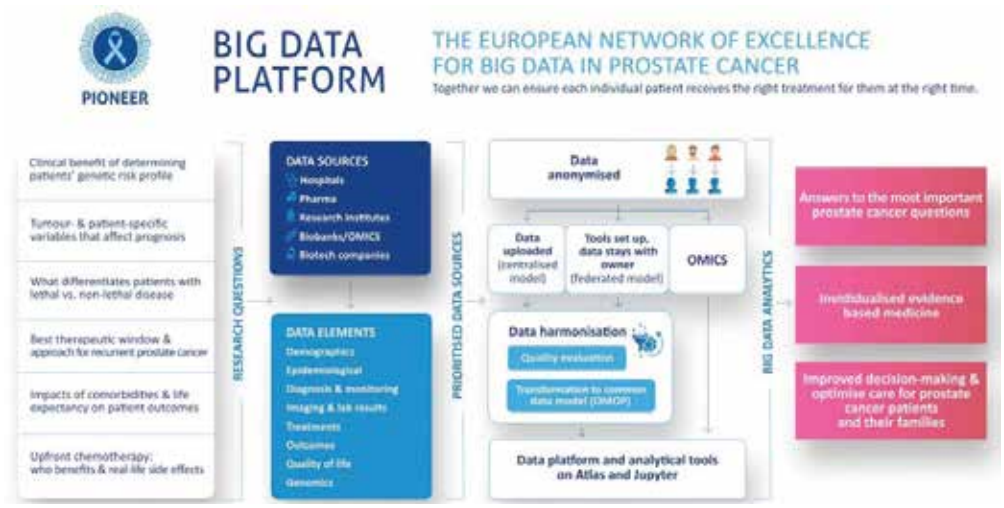
Data science has been defined by three distinct forms of analysis tasks: description, prediction, and counterfactual prediction [3]. Descriptives are useful for exploring and finding patterns in the data which may lead to testable hypotheses. Prediction analysis can improve diagnostics and prognostics, while counterfactual prediction constructs models to address flaws inherent to observational data for inferring causality [4].

In summary, big data refers to large and complex datasets generated by a wide range of sources. Although big data can provide valuable insights, it is often difficult to process and analyse using traditional methods.

Big data and artificial intelligence
Since the capacity of the human brain to process information is limited, there is an urgent need to develop and implement alternative strategies to process big data. In addition to the increased availability of data, the augmentation of storage and computing power has boosted the development of data-processing techniques such as machine learning (ML) and artificial intelligence (AI), which are becoming increasingly important tools to tackle complex issues e.g. cancer care. A growing body of studies highlight AI as an emerging tool to help personalise cancer-care strategies by analysing available data. A recent study identified 97 registered clinical trials for AI in cancer diagnosis, most of them started after 2017 [5,6].

Big data and AI are both powerful tools that are being used to advance cancer research. A few examples are:

- Genomic data: The Cancer Genome Atlas (TCGA) and the International Cancer Genome Consortium (ICGC) have generated large amounts of genomic data that can be used to identify genetic mutations associated with different types of cancer.
- Drug discovery: AI can be used to analyse large amounts of data from preclinical and clinical studies to identify potential new therapies and inform drug development. For example, machine learning algorithms can be used to analyse data from electronic health records, genomic data, and clinical trials to identify new drug candidates and drug interactions.
- Radiology and pathology: Big data and AI can be used to analyse medical images such as CT (computerized tomography) scans, MRI (magnetic resonance imaging) scans, and pathology slides to identify patterns and biomarkers associated with cancer.
- Clinical decision support: AI can also be used to analyse large amounts of clinical data, such as electronic health records, to identify patterns and predict outcomes. For example, machine learning algorithms can be used to predict which patients are at high risk of progression, or to predict which patients are likely to respond well to a certain treatment.



Figures 1 and 2. Examples of data innovation projects supported by the European Union. For more info: www.prostate-pioneer.eu and www.optima-oncology.eu

Although these technologies are promising, more research is needed to fully realise their potential in cancer research. There is also a need for more data and big data infrastructure to handle and analyse the large amount of data. Additionally, ML models are only as good as the data they are trained on; data diversity and data governance are necessary in ensuring that the models are unbiased and generalizable to different patient populations.

Big data and policy makers
Big data analyses have the potential to provide valuable insights that can inform and guide policy decisions, but it is not a given that policy makers will automatically accept these insights. The use of big data in policy making is still a relatively new field. For it to be adopted more widely, there are a number of challenges that need to be addressed.

One challenge is the quality of the data. Policy makers need to have confidence that the data being used is accurate, reliable, and unbiased. This can be difficult to achieve, particularly with large and complex datasets, and requires a significant investment in data cleaning, integration, and quality control. Another challenge is the lack of understanding of the data science techniques used to analyse big data, which can make it difficult for them to assess the credibility and usefulness of the results. Lastly, the ethical and legal issues associated with the use of big data are still being resolved. This could be an obstacle for policy makers, who might be concerned about issues such as data privacy and data security.

Despite these challenges, there is considerable progress in healthcare. The use of big data analytics has been used to improve patient outcomes, reduce healthcare costs, and improve the efficiency of healthcare delivery systems.

Big data projects in urology
With the vision of establishing a connected data infrastructure and an ecosystem for big data analysis, the EAU already started aggregating data regarding urological conditions (primarily urology cancers) in 2016. This is essential as urology faces many barriers to potential improvements in better patient outcomes.

The Innovative Health Initiative (IHI) is a public-private partnership between the European Union and the European life science industries. IHI's goals are to translate health research and innovation into tangible benefits for patients and society to ensure that Europe remains at the cutting edge of interdisciplinary, sustainable, patient-centric health research.

IHI funded the projects PIONEER and OPTIMA. PIONEER focuses on predictions regarding patient outcomes concerning particular interventions. OPTIMA broadens the spectrum of prostate, breast and lung cancer research to explore commonalities across cancer patients.

PIONEER, the European network of excellence for big data in prostate cancer (PCa), is led by the EAU and Bayer (figure 1). PIONEER consists of 38 partners across nine countries and aims to unlock the potential of big data and big data analytics. Currently, 95 PCa data sources have been identified and 23 datasets are ready for analyses. A total of 56 research questions have been identified among all relevant stake holders (i.e. clinicians, industry and patients). Data have been analysed, also in the form of a so-called study-a-thon, and 11 manuscripts have been published (see https://prostate-pioneer.eu/outcomes/newsletters) [7]. PIONEER will continue to collect PCa data and address knowledge gaps in care to improve PCa-related outcomes, health system efficiency and quality of health and social care across Europe. Please visit https://prostate-pioneer.eu/ or contact pioneer.info@uroweb.org for more information.

OPTIMA, tackling cancer through real world data and AI, is led by the EAU and Pfizer. OPTIMA aims to implement a vast federated and centralized network of European data providers to help answer the highest priority research questions in prostate, breast, and lung cancer.

OPTIMA brings together 38 partners from across 13 countries. It consists of private and public stakeholders in the clinical, academic, patient, regulatory, data sciences, legal and ethical and pharmaceutical fields. A special focus is on research questions where the existing evidence underpinning clinical practice guidelines is weak or lacking. In parallel, the consortium will develop an application in clinical settings of comprehensive dynamic computer-interpretable guidelines (potentially refined with AI) to better support shared decision making. Please visit https://www.optima-oncology.eu/ or contact communication@optima-oncology.eu for more information.

EAU UroEvidenceHub
The challenge in medicine is that clinical trials – the mainstay of clinical guidelines – are often conducted in small groups; information on long-term (adverse) effects and safety are missing, and key subgroups are frequently not represented. These imply that evidence gaps are there and cannot be filled fast enough with high-quality randomised clinical trials. Therefore, the EAU has started an ambitious new data innovation programme, UroEvidenceHub, which is parallel to and following up the current data innovation initiatives PIONEER and OPTIMA.

To kickstart this programme, the EAU is developing a new state-of-the-art technology platform called the Data Haven. The Data Haven aims to become the largest urology database by collecting large volumes of Real World Data and generating reliable Real World Evidence. The Data Haven will be interoperable with current/future data hubs and other relevant urology data initiatives. Aside from data providers and users, stakeholders from academia, data science and IT companies, patient organisations, regulatory bodies and industry will be invited as well to become involved leading to a tight-knit ecosystem of excellence.

The EAU UroEvidenceHub will elevate the current urological guidelines and will offer a new way of interaction between clinicians and patients, to make shared treatment decisions on a truly personalised basis in the most optimal way possible. Please contact datainnovation@uroweb.org for more information.

Time is against us if we do not progress. Urology has always been at the forefront of innovation, embracing new technology and data. Together, we are able to shift in how medicine will be done in the future and how care will be provided. However, a new approach to knowledge exchange within the medical community is required to succeed.

With more effort to improve data collection, sharing and quality, data governance, education and training of policy makers, we are likely to see big data analyses increasingly accepted and used in healthcare policy making in the future. These data innovations will help urologists improve and individualize the EAU Guidelines and ultimately will provide more personalized care for all urology patients.

The list of references are available upon request.

Sunday 12 March 14:30 - 14:40
Thematic Session: The road to evidence-based European policy on early detection of prostate cancer
Yellow Area, eURO Auditorium 1

Paradigm shifts in urology

Five decades of advances in uro-technology

Prof. Javier Angulo
Clinical Department, Faculty of Medical Sciences, Universidad Europea, Madrid (ES)

javier.angulo@universidadeuropea.es

Historically speaking, a 50-year span does not seem that long in terms of years. However, a span can also be a period of time separating two momentous dates or events during which something exists, functions, or happens. In this case, we look at the span between the first constituent assembly of the European Association of Urology (EAU) which took place from 3 to 4 July 1973 and the 38th Annual EAU Congress in Milan which will be held from10 to 13 March 2023. We are celebrating a half century of the EAU and how it has witnessed and influenced the development of urology across the globe. One clear indicator of this is the increase in membership from 259 to over 18,000 medical professionals.

From cavern to metaverse

Progress is moving extremely fast and undoubtedly, the engine of that change is technology. Considering that the year 2000 saw a rise in mobile phone technology, the increasing sophistication seen in computers and the Internet is also evident in Artificial Intelligence (AI). We are experiencing a high velocity in AI advancement; it can be found in practically all the technological elements that we use today.

Current development of AI is led by four main factors:

1. Large amount of data available
2. Development of computing and information technology
3. Progress in the production of software
4. Knowledge and use of different strategies to solve problems such as random forest, neural networks, and deep learning.

However the real question is, is AI the art of making programmes and machines that mimic and surpass the performance of biological beings in areas that require operations, specific skills, and simulate complex cognitive operations? If the answer is yes, we are probably still far from the limits of that metaverse. Of course, neither are we in the cavern of urology.

On the shoulders of giants

Before the EAU was established, urology was already more than surgery of the urinary tract. The very early steps for a modern medical discipline such as urology were possible, standing on the shoulders of giants. Henry Thompson (1820-1904), Felix Guyon (1831-1920), Maximilian Nitze (1848-1906), Joaquín Albarrán (1860-1912), James Israel (1848-1926), Georges Marion (1869-1960), Leopold Casper (1859-1959), Alexander von Lichtenberg (1880-1949) and Antonio Puigvert (1905-1990) were some of the most outstanding giants in early European urology. They established the basis both for anatomic surgery, endoscopy, and the art of urologic consultation, understanding renal function, urinary infection, stone disease, and neoplasia. However, the world changed after the Great War and became more technology-focused rather than knowledge-based.

Hugh Hampton Young (1870-1945) established the fundamentals of oncologic prostate surgery at the John Hopkins Hospital in Maryland and was the pioneer of urology in the United States. Reed Miller Nesbit (1898-1979) developed modern transurethral resection of the prostate in the 1950s through his brilliant improvement of the mechanism of the Stern-McCarthy resectoscope, a spring-loaded modification that allowed the surgeon to manipulate the instrument with one hand alone. Later, José Iglesias de la Torre (1904-1979) improved the resectoscope with simultaneous irrigation, suction and low intravesical pressure, as we use it today. The foundations for modern transurethral surgery had been lain.

Most medical advances with direct application on modern urology came from social change and other health-related disciplines. The World Health Organization was created in 1948 to internationally coordinate epidemic response although its role appears to have declined in our modern, globalized world as we recently saw with the COVID-19 pandemic.

In 1953, the structure of deoxyribonucleic acid (DNA), with its two entwined helices and paired organic bases was determined by Francis Crick (1916-2004) and James D. Watson (1928-) in Cambridge using X-ray diffraction and the mathematics of a helix transform. The discovery had a major impact on biology, particularly in the field of genetics, enabling later researchers to understand the genetic code and also the molecular basis of disease.

The plastic surgeon Joseph Murray (1919-2012) performed in Harvard the first long-term successful kidney transplantation between monozygotic twins in 1954. The organ survived for eight years. The first successful kidney transplanted from a deceased donor using the immunosuppressive drug azathioprine was performed in 1962. For his efforts in the field, Murray was honoured with the Nobel Prize in medicine in 1990.

"We are experiencing a high velocity in AI advancement; it can be found practically in all the technological elements that we use today."

The first laser (light amplification by stimulated emission of radiation) was built in 1960 by the engineer and physicist Theodore H. Maiman (1927-2007) at the Hughes Research Laboratories in California. The pivotal landmark upon which the solid bioethical foundations on which clinical research is based was the Declaration of Helsinki in 1964. Charles Huggins (1901-1997), surgeon and researcher from Ann Arbor was Nobel Prize laureated in 1966 for the discovery that hormones can be used to control prostate cancer (PCa). This was in fact the first proof that cancer could by controlled by drugs, and for that Huggins is often referred as the father of modern-era chemotherapy.

Major developments after 1973

The significant paradigm shifts in urology within the last five decades can be summarised in several principles for genitourinary (GU) health improvement which will be discussed later. Some of these advances are anonymous and often depend on multidisciplinary collaboration; however, others are mainly based on titanic personalities that, after standing on the shoulders of giants, have been able to foresee and take the next steps of development. Serendipity, evolving techniques and improvements in equipment are the tools they used to build innovation.

It is impossible to mention all the names involved in this race for excellence, but I will at least try to mention the milestones reached.

Infectious diseases kept in check

During the last decades, urinary tuberculosis has disappeared, and novel antibiotics have kept bacterial infections in check. However, new GU infectious diseases have emerged such as the human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS) epidemic in 1981 with the producing agent identified two years later. On the other hand, retroviral treatments have become a safe and effective tool to live with HIV infection.

Bacterial resistance to antibiotics became a first-line sanitary problem, with the advent and spread of extended spectrum beta-lactamase and carbapenemase producing pathogenic enterobacteria. Vaccination for viral diseases has evolved, but there is still some need to improve immune control of common urinary pathogens and develop novel and better antiviral agents. In this regard, messenger ribonucleic acid (mRNA) vaccines first used to control the COVID-19 pandemic are a promising option for cancer immunotherapy. Technological advances have optimised mRNA-based vaccine stability, structure, and delivery methods. Multiple clinical trials are now enrolling patients with various cancer diagnoses. Encouraging results with mRNA-based cancer treatment vaccines as monotherapy and in combination with checkpoint inhibitors have been obtained.

Techn revolution in diagnostic imaging

In the early 1970s, the use of ultrasound (US) as a means of creating images of the abdomen, small parts, and pelvis was introduced at radiology practice and medical literature. In 1972, computed tomography (CT) scan was established and only a decade later in 1982, magnetic resonance imaging (MRI) was on the stage. These diagnostic imaging modalities became so popular and necessary that nobody would understand current hospital practice and particularly urologic practice without them. In fact, even more than urine and blood testing, US has been incorporated in all urologic departments worldwide since the 1990s as the first clinical approach to diagnosis.

Significant progress in computer equipment throughout the acquisition of a picture archiving and communication system (PACS) freed the technologists from film development, greatly enhanced productivity, and dramatically increased its use. This has also caused a stage shift in several malignancies including kidney cancer to low-stages, thus improving the therapeutic efficacy and ultimately, prognosis. In addition, PCa diagnosis was improved by both the advent of Prostate Specific Antigen (PSA) and the widespread use of US-guided prostate biopsy.

The retaining of US technology in urology departments has enabled the integration of medical and surgical knowledge within urology, with office endoscopy and urodynamics as complementary diagnostic tools.

Multiparametric MRI (mpMRI) has managed to change the paradigms on PCa detection and risk classification. Investigations to integrate morphologic and functional evaluation of the tissue were initiated in the 1980s, but again, more technological development was needed. It was not until 2012 that a common terminology for evaluating prostate MRI was established with the first version of Prostate Imaging Reporting and Data System (PI-RADS). Afterwards, image-guided targeted prostate biopsy improved diagnosis of PCa and consolidated alternative therapeutic approaches such as active surveillance and focal therapies.

Although initially investigated for diagnosis of brain tumours, the clinical applications of positron emission tomography/computed tomography (PET/CT) with radiolabeled choline in patients with prostate cancer was established in 2003. PET/MRI hybrid devices and new tracers such as [68Ga]-PSMA are under investigation in the diagnostic imaging of PCa.

Organ transplantation achieved excellent results

Solid organ transplantation is one of the most remarkable and dramatic therapeutic advances in medicine in the past 60 years. The field has progressed from what was a clinical experiment to a routine and reliable practice; it was not only clinically effective and cost-effective, but also life-saving. Some of the major milestones of this remarkable multidisciplinary clinical science evolution stems from the serial confluence of cultural acceptance, legislation that facilitates organ donation, technical advances in organ preservation, surgery, immunology, immunosuppression and the effective management of complications.

The role of urologists involved in kidney transplantation has allowed the increase of living donor kidney transplants with minimal skin incision and the advent of laparoscopic-guided donor nephrectomy (Rosales 2010) has accelerated such practice.

There is no doubt that minimally invasive technique in kidney transplant is helpful, and the robotic-assisted kidney transplant (RAKT) has been incorporated. Longer ischemia time is still controversial and the outcomes remain very dependent on individual surgeon expertise. However, it is anticipated that in the next decade, the integration of further digitization, ergonomic instrumentation, and AI within robotics will exponentially improve RAKT outcomes with an increase in costs.

Urologic surgery: Less invasive and more precise

Progressive minimalization and technological improvement of flexible elements and laser technology have allowed the endoscopic access to the entire urinary tract. Cystoscopy (Nitze, 1877), ureteral catheterization (Albarrán, 1897), open nephroscopy (Rupel and Brown, 1941) and antegrade nephrostomy (Goodwin, 1955) were the first steps in endourology. However, it was not until the 1970s that innovation allowed full access to the upper urinary tract with the fundamental milestones of Teflon tubing (Takayasu, 1974), percutaneous nephrostomy for renal calculi extraction under radiological control (Fernström and Johansson, 1976), transurethral ureteroscopy (Pérez-Castro, 1979), extracorporeal shockwave lithotripsy (Chaussy, 1980) and flexible ureterorenoscope (Bagley, 1983) achieving full upper urinary tract access for stone clearance.

A number of technological advances in equipment design with reduced calibre and wide-working channel allowed the simultaneous use of instruments and active deflection at the distal end. These were followed by high-definition digital imaging leading us to current standards.

Pioneer applications of the laser in urology in the 1980s included the use of a CO2 laser for condylomata, photodynamic therapy for bladder carcinoma, pulsed-dye laser for urolithiasis and the Nd:YAG lasers for prostatic vaporization.

The modern era of lasers in urology in the 1990s began with the use of side-firing fibres and their application in the treatment of benign prostatic hyperplasia (BPH). Thulium and Holmium lasers both for BPH surgery and lithotripsy have increased in popularity despite their cost.

"In the years to come, we should be aware if we are applying critical thinking or paying too much attention to algorithms that make the clinical decisions for us."

The British urologist John Wickham (1927-2017) was the first to use the term "minimally invasive surgery" and attracted attention and criticism in 1987 when he predicted the paradigm shift in practical surgery. He stated, "Surgeons applaud large incisions and denigrate keyhole surgery. Patients, in contrast, want the smallest wound possible, and we at Britain's first department of minimally invasive surgery are convinced that patients are right".

Doctors and patients alike became fascinated with laparoscopic surgery and the first laparoscopic nephrectomy (Clayman, 1991), cystectomy (Parra, 1992), prostatectomy (Schuessler, 1992), and partial nephrectomy (Winfeld, 1993) were performed. However, after these first successful reports, laparoscopic surgery remained unrealistic due to its difficulty and duration.

Development of urologic laparoscopy was made technically feasible in several centres of excellence in France and Germany when large series were accumulated, and learning-curves were lowered at the end of the 1990s. Results of well-trained teams were comparable in terms of oncologic outcomes and sometimes better for improved functional outcomes. Single-port access, mini-laparoscopy, natural orifice transendoscopic surgery (NOTES) and hybrid techniques were the natural evolution of laparoscopy.

Adoption of laparoscopic prostatectomy was hindered by the technical and ergonomic challenges over the vast open retropubic radical prostatectomy experience developed after Patrick Walsh (1938-), who popularized the technique of anatomic nerve-sparing radical prostatectomy for organ-confined PCa all over the world.

The experience and outcomes achieved by a group of distinguished oncological surgeons in academic centres was another drawback for the generalization of the laparoscopic approach in the United States. However, this tendency changed with the introduction of da Vinci robotic surgical

system, and the technical shift from open to laparoscopic robotic radical prostatectomy became a reality worldwide.

Early studies indicated that robotic prostatectomy had promising outcomes in short-term oncological control, potency and continence. However, the results of experienced surgeons with radical prostatectomy, following any approach, set high standards in oncologic and functional outcomes. Robotic surgery has helped generalize excellent results in other challenging techniques such as partial nephrectomy and radical cystectomy.

To determine the true place of robotics in the surgical podium, validated questionnaires, and analogue assessment scales are essential to determine true functional results and need to be combined with careful long-term oncologic outcomes.

Reconstructive urology remains the most classical and one of the most precise surgical fields continually being developed. It is also unique as it serves to restore both structure and function to the GU tract. Multidisciplinary experience, refined surgical technique, use of grafts, flaps, tissue engineering and scaffolds, meshes and prosthesis make it one of the most interesting fields of current urology for academic surgeons worldwide.

Targeted therapy with tailored prediction
Until the late 1990s, cancer treatment drugs - with the exception of hormone treatments - worked by killing cells that were in the process of replicating their DNA and cell division. As such, chemotherapy had a greater effect on cancer cells but also killed normal cells. Targeted therapies developed in the 21st century work by influencing the processes that control growth, division, and spread of cancer cells, as well as, the signals that cause cancer cells to die naturally. Targeted therapies work by inhibiting growth signal (hormone-like substances that instruct cells when to grow and divide), inhibiting angiogenesis, and inducing apoptosis (the natural process through which cells with DNA are too damaged to repair and forced to die).

As more is learned about the molecular biology of cancer, researchers continue to accumulate targets that will benefit the development of new drugs. Very recently cancer immunotherapy has revolutionized the field of oncology by prolonging survival. Along with monoclonal antibodies and small signalling pathway inhibitors, new classes of molecules such as antisense oligodeoxynucleotides and small interfering RNA (siRNA) are being developed The search for gene mutations that cause some patients to respond better to certain drugs is another field of development along with targeted drugs aimed at proteins produced by specific gene mutations in cancer cells.

Benefitting from lessons learned in two decades of clinical trials, functional urology has progressed with a more precise use of pharmacology in controlling prevalent disorders such as lower urinary tract symptoms, urinary incontinence and erectile dysfunction. Evidence-based medicine is increasingly used and patient-reported outcomes are now considered more important than physician reported outcomes.

Teaching and practice for the new generation
New generations will probably benefit from AI instructors using virtual reality to create immersive learning experiences in an augmented reality scenario, and make productive curriculum materials more individualised for professionals. Educators will need to define to which extent they will be introduced into teaching and learning AI. An enriched metaverse learning environment would blend both physical and virtual worlds. This is to provide the best learning opportunities for students and young professionals in a collaborative setting wherein learning will become decentralized.

In the years to come, we should be aware if we are applying critical thinking or paying too much attention to algorithms that make the clinical decisions for us. AI is going to direct us to a world where we will receive information that our profiles predict we deserve to receive, and that is a world that is dangerously self-absorbed and limiting. In my opinion, these are the paradigms that changed urology in the last 50 years and will continue to change it in the near future.

Friday 10 March, 15:30 - 15:45
7th International Congress on the history of urology
Yellow Area, Amber 7

Management of floppy glans after penile prosthesis surgery

From diagnosis to treatment strategy

Dr. Marta Skrodzka
St. George's University Hospital, London (GB)

drmartaskrodzka@gmail.com

Prof. David Ralph
University College Hospital & St Peter's Andrology Centre, London (GB)

david.ralph@nhs.net

Penile implant insertion by large volume surgeons is associated with low risk of complications and the patients' satisfaction rates, which exceed 95% in most published series. Although penile prosthesis implantation provides excellent axial rigidity of the shaft, patients need to be aware that the erection with penile implant may differ in certain aspects compared to natural erection. In particular, patients may notice a lack of engorgement, hypermobility, or floppiness of the glans penis. The classification of glans disorders is presented in Table 1.

Diagnosis	Characteristics
Soft glans syndrome	Compromised glans engorgement in patients with erectile dysfunction
Real glans hypermobility	Instability of the glans after penile implant insertion despite good position and size of the cylinders
Floppy glans syndrome	Instability of the glans after penile prosthesis insertion due to: - Poor position of the cylinders (cross-over, tunical perforation, other) - Implant undersized or oversized

Table 1. Classification of glans disorders following penile prosthesis insertion

Glans issues may cause patient dissatisfaction due to difficulties during penetrative sex, painful intercourse, and a poor cosmetic result. These may prevent the patient from using an otherwise fully functional implant.

Soft glans is defined as lack of appropriate engorgement of the glans spongiosum. Patients may complain about cold glans, compromised sensitivity, and penile length as it may be perceived as shorter. This may cause partner complaints and dissatisfaction. Glans deflection is not observed, but soft glans may contribute to a floppy glans phenomenon.

Floppy glans syndrome (FGS) and real glans hypermobility have similar clinical presentation. They are observed when the cylinders are fully inflated and the glans of the penis does not stay in the same axis with penile shaft, but droops ventrally, dorsally, or laterally. Two main factors that may be responsible for lack of glans stability are incorrect position of the implant tips and the anatomy of the glans.

Real glans hypermobility means the glans droops despite the implant's cylinders being correctly sited in the tips of the cavernosal bodies (Fig. 1). This may be related to structural anomaly of the corporoglans ligament or tips of the cavernosal bodies being disproportionally narrow in comparison to the glans. Men with erectile dysfunction are described to have thinner corporoglans ligaments in comparison to men with good erectile function. Impairment of corporoglans ligament structure and function can be also related to previous implant surgeries or it's complications e.g. erosion.

FGS results from improper glans support. Etiologically it may be caused by wrong size of the cylinders (too short/long) or malposition of the cylinders (cylinders localized off-centre, distal tunical erosion, proximal perforation, cross-over). It is more common in patients with fibrotic cavernosal bodies e.g. in Peyronie's disease, post priapism, or re-do surgeries. In these cases dilatation of cavernosal bodies may be difficult and is associated with increased risk of incomplete dilatation, crossover and tunical perforation.

Supersonic transporter deformity (SST), named after the silhouette of a Concorde aircraft, is a classic example of FGS presenting as ventral droop caused by undersized cylinders (Fig. 2). Reverse SST deformity is a variant of FGS syndrome, where oversized cylinders press against the ventral tip of the cavernosal bodies and push the glans dorsally causing droop. In most cases, lateral droop should be treated surgically as it is usually a sign of serious complications such as distal perforation, proximal perforation, or cylinders crossover.

Diagnosis
The first step in diagnostic process is a physical examination with a fully inflated implant. The direction of the droop indicates possible cause of the abnormality. Imaging modalities such as magnetic resonance (MRI) or penile ultrasound (USS) with the inflated device can be helpful. An experienced uro-radiologist is invaluable.

Treatment
A. Conservative management
Conservative management includes PDE-5 (5-Phosphodiestherase type 5) inhibitors, intraurethral alprostadil, and vacuum erectile device. It aims to support glans engorgement. Non-surgical treatment may be helpful in cases of soft glans, real glans hypermobility, and floppy glans syndrome, as long as there is no risk of damage to tunica albuginea and urethra or of an implant's function impairment. It may increase satisfaction from penile prosthesis and in some cases, improve sensation of the patients who complain of cold glans. In mild cases, some authors advise pulling the foreskin

Figure 1. 1a) Real glans hypermobility – ventral glans droop despite correct position of the implant. 1b) MRI image – adequate length of the cylinders seating at the tips of cavernosal bodies.

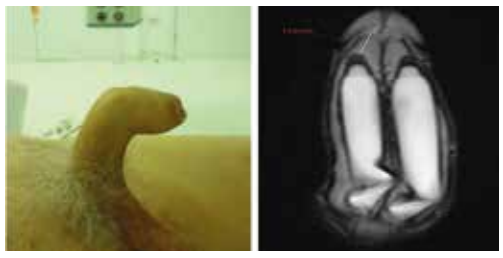


Figure 2. 2a) Floppy glans syndrome – SST deformity caused by undersized cylinders. 2b) MRI image of disproportionally short cylinders demonstrating a gap between cylinders and cavernosal tips.

Figure 3 . Floppy glans syndrome with lateral droop. 3a) Distal perforation; 3b) Proximal perforation; 3c) Cross-over.

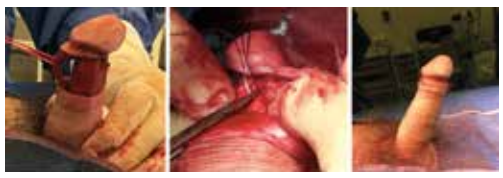


Figure 4. Glanspexy procedure. 4a) Exposure of plane between cavernosal tips and glans. 4b) Careful placement of the sutures. 4c) The final effect.

proximally during attempted penetrative intercourse or use of a condom to overcome glans hypermobility by stabilising the glans on the tips of the inflated cylinders. If satisfactory for the patient, medical management can help avoid extra surgery and additional complications.

B. Surgical correction
Surgical intervention should be offered when the device malposition endangers the function of the implant, integrity of tunica albuginea, or creates risk of a urethral injury. It should always be considered in patients whose cylinders are misplaced or not properly sized.

For FGS: Revision surgery and correction of the position or size of the cylinders usually resolves the problem. In case of undersized cylinders, revision and supplementation with rear tip extenders or exchange of cylinders into appropriate size is advised. It is very important to incise the old pseudocapsule and re-dilate corporal tips to secure adequate position of distal cylinders.

An oversized implant increases risk of erosion. During revision surgery it should be replaced with the correct size cylinders. Usually additional manoeuvres are not necessary and the old pseudo-capsule can be used as long as cylinder tips are not positioned off-centre. In case of cylinder tips being placed too superficially (off-centre), the same strategy is used as in undersized cylinders. It includes incision of the old pseudocapsule and re-dilatation of corporal tips to provide central cavernosal space for cylinders. The same rules apply to cross-over or cylinder perforation. In extreme cases additional strengthening to tunical integrity may be necessary.

In cases of minimal cylinder over/undersizing, glanspexy can be offered (details are described in section below). This is a less invasive option which minimizes the risk of infection in comparison with implant revision.

For real glans hypermobility: The glanspexy is typically used in real glans hypermobility. Several approaches have been described, all based on one principle of glans realignment on the penile shaft. Glans is surgically fixed on the side opposite to the tilt e.g. dorsal anchoring for ventral deflection. (Figure 3) In selected cases, sutures in multiple quadrants can be necessary. Usually (hemi) circumferential incision is used to expose the plane between the glans and the corporal tips. Sutures to fix the glans are inserted with ultimate attention to protect the neurovascular bundle, the urethra and implant cylinders.

Penoplasty is an alternative technique for patients preferring less invasive surgery and accepting circumcision. Its principle is based on a Nesbit technique and involves removal of an ellipse of penile skin and dartos from an aspect opposite to the glans deflection to stabilize the glans. The technique does not require exposure of the corpora and minimises operative risks. It can be applied in dorsal and ventral deflections, but it is particularly effective in dorsal and reverse SST deformities. Both techniques have a high success rate.

Summary
In case of glans engorgement or stability issues, the accuracy of the position and size of the implant should always be assessed before the final diagnosis. Imaging might be helpful, especially with support of an experienced uro-radiologist Conservative therapy can always be attempted before a revision surgery as long as it is safe for the penile structures and the function of the implant. The surgical treatment should be tailored to a clinical scenario.

Saturday 11 March 11:31 - 11:41
ESAU Meeting: Disorders in reproductive and sexual health
Pink Area, Coral 6

VI-RADS: The new PI-RADS for bladder cancer?

Bladder MRI has the potential to affect the entire management of patients with bladder cancer

Prof. Valeria Panebianco
Radiological Sciences
Sapienza University of Rome (IT)

Bladder cancer diagnostic is evolving, as benefits for patients have demonstrated during the last decade [1]. Evidence on the applicability of bladder Magnetic Resonance Imaging (MRI) for bladder cancer staging in clinical practice has been shown since the in the late 1980s [2].

Since then, the technological advancement have allowed to improve MR acquisition in terms of contrast resolution and tissue characterization, which has now become the imaging gold-standard for different pathologies in urology, particularly prostate cancer [3].

MRI and the development of a standardised system for its reporting, the Prostate Imaging-Reporting and Data System (PI-RADS) [3–5] -, has revolutionised prostate cancer diagnostic pathway, switching from a conventional to a personalised way of diagnosing this disease in 2019 [6]. Indeed, the PI-RADS scoring system was the game-changer in this setting [7], as MRI is currently the first line exam for patients experiencing PSA elevation [6].

The question is are we experiencing what happen with prostate cancer, today for bladder cancer? Do we have, or will we soon have the means, to sustain as a community a new bladder cancer MRI pathway? Let's now examine the data.

In 2018, the Vesical Imaging-Reporting and Data System (VI-RADS) was developed by a group of international experts [8]. Most likely as a solution to determine evidence of mini-invasive surgical advancement. Indeed, the procedure of trans-urethral resection of bladder tumour (TURBT), although being the foundation of bladder cancer surgical management, "*remains an anachronism in modern surgical oncology*" [9].

The VI-RADS score is a 5-point assessment scale, in this case defining the likelihood of staging a bladder tumour as muscle-invasive. The five categories, represent in increasing order respectively, a very low- and low- likelihood of muscle invasiveness (Figure 1-2), an indeterminate likelihood (Figure 3), and a high- and very high- likelihood of muscle invasiveness (Figure 4-5).

The VI-RADS score has been validated by research groups worldwide; such as one of the first retrospective investigating its role on a cohort of

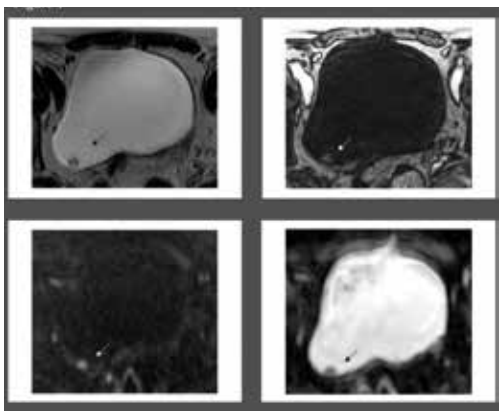


Figure 1

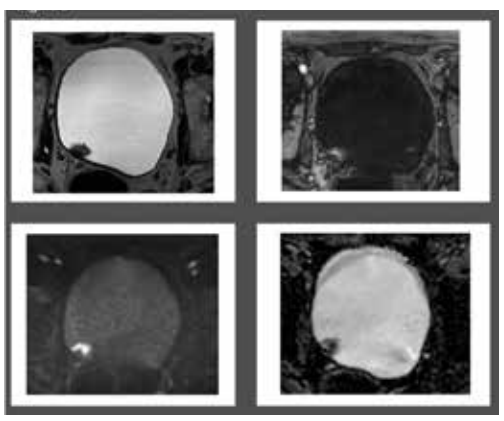


Figure 2

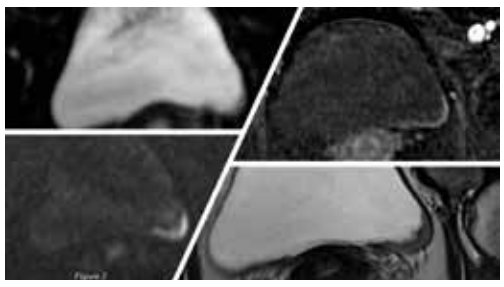


Figure 3

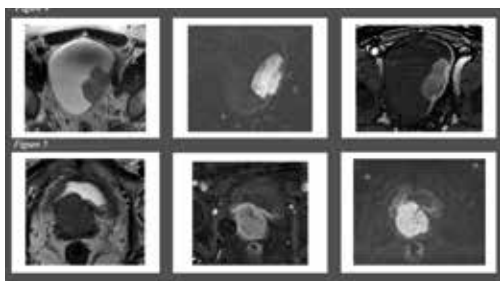


Figure 4-5

330 consecutive patients by Wang et al. from China [10] and the prospective multi-centre study by the Egyptian group led by Metwally et al. [11]. Up to date, seven meta-analyses published on its accuracy and reproducibility among different readers.

From results of the latest published multi-centre meta-analysis by Del Giudice et al. [12], we can infer that MRI and VI-RADS scoring provide high sensitivity and specificity when using both a VI-RADS cut-off of 3 and 4 for the definition of muscle-invasive bladder cancer, with an area under the curve > 0.9. From this meta-analysis no influence of clinical characteristics, nor of cumulative reader's experience, were found, differing from study design and radiological characteristics which appeared to influence the estimated outcome [12]. Looking at these data we can conclude that, "on-paper" at least, the VI-RADS score does what it was developed for.

Three basic questions exists that we need to answer, in order to understand whether MRI will be used in the daily clinical practice as first line pre-operative imaging, as it is done for prostate cancer:

1. *What are the benefits for patients?*
2. *What are the barriers for its widespread diffusion?*
3. *what are the future developments that we need to expect?*

Benefits for patients

- *Non-invasive staging tool:* VI-RADS scoring currently is best suited in the pre-resection setting and before intravesical bacille Calmette-Guerin administration. Pre-operative MRI and VI-RADS scoring allow to non-invasively and accurately stage tumours, and predict therapy response, identifying tumours that need a more radical approach from the start. Among patients with high-risk Non-muscle-invasive bladder cancer (NMIBC), VI-RADS scoring might be of use for disease risk stratification, and as an indication to undergo secondary resection of the tumour in cases of VI-RADS 4 and 5, or to avoid it in cases of VI-RADS 1 and 2.
- *non-invasive surveillance too:* MRI and VI-RADS scoring may be a viable alternative to cystoscopy in NMIBC surveillance, after tumour resection, reducing costs associated with the disease. The bladder wall's structural changes must be considered in this setting, and expert "hands" should be sought by Urologists.
- *non-invasive surgical timing and planning*: MRI and VI-RADS scoring might be useful in patients diagnosed with muscle-invasive bladder cancer (MIBC) to define appropriate timing for radical treatments, and to identify those likely to benefit from neoadjuvant therapy or trimodal therapy, those suitable for bladder-sparing surgery and chemoradiation, or to plan a therapeutic trans-urethral tumour resection that is surgically feasible.
- *support Patient and Advocacy groups*, who are keen to improve the bladder cancer diagnostic paradigm, likely due to long waiting times for diagnostic trans urethral resection of bladder tumour (TURBT), resulting in significant delays to definitive management and potential harm for patients with MIBC [13,14].

Barriers

- *Understanding the clinical utility:* Studies investigating the long-term impact of applying MRI and VI-RADS in the pre-operative setting are needed to acknowledge to which extent their use improves health outcomes relative to the current best alternative. For this, results from comparative randomised clinical trials are warranted. The preliminary data of the "BladderPath: Image Directed Redesign of Bladder Cancer Treatment Pathway" trial [15], led by Professor Nicholas James from the University of Birmingham, which aims at assessing whether some bladder tumour surgery can be replaced by MRI scans to determine the stage of the cancer, suggest that this approach is feasible [16].
- *Mutual trust and certification:* The relationship between physicians, as well as those between academic and non-academic centres must improve. We must also create validation and certification processes to strengthen such connections. New pathways towards certification for bladder MRI acquisition and VI-RADS reporting will be needed. Another potential barrier pertains to the public acceptance of imaging for surgical decision-making.

Future developments

- *non-invasive prediction tool:* The VI-RADS score has the potential to become a clinical predictor of perioperative outcomes, as well as a tool for predicting tumour aggressiveness and response to therapy. Multiple studies have demonstrated the validity of MRI functional sequences and quantitative parameters for predicting tumour grade [17–21]. Also, assessment of tumour response can be evaluated in different clinical setting: before, interim and after therapy [22–24].
- *radiomics and machine learning*: Radiomics analysis and machine learning applications of medical images has developed exponentially over the past decade, in the field of oncological imaging, including for bladder cancer. In spite of early promises, larger, multi-centre datasets are needed before radiomics, and machine learning algorithms can be used in routine clinical practice to support and improve local staging of bladder cancer and assist in optimising therapeutic management.

The standard diagnostic pathway for bladder cancer has not changed in 30 years. Bladder MRI has the potential to affect the entire management of patients with bladder cancer, from staging and prediction to assessment of response to treatment. Is VI-RADS the new PI-RADS for bladder cancer? It will likely be so, with further evidence and efforts shedding light on clinical utility, mutual trust between practitioners and institutions, and new pathways towards certification.

References

1. Lenis AT, Lec PM, Chamie K, Mshs M. Bladder Cancer: A Review. JAMA 2020;324:1980. https://doi.org/10.1001/jama.2020.17598.
2. Fisher MR, Hricak H, Tanagho EA. Urinary bladder MR imaging. Part II. Neoplasm. Radiology 1985;157:471–7. https://doi.org/10.1148/radiology.157.2.4048458.
3. Barentsz JO, Richenberg J, Clements R, Choyke P, Verma S, Villeirs G, et al. ESUR prostate MR guidelines 2012. Eur Radiol 2012;22:746–57. https://doi.org/10.1007/s00330-011-2377-y.
4. Weinreb JC, Barentsz JO, Choyke PL, Cornud F, Haider MA, Macura KJ, et al. PI-RADS Prostate Imaging – Reporting and Data System: 2015, Version 2. European Urology 2016;69:16–40. https://doi.org/10.1016/j.eururo.2015.08.052.
5. Turkbey B, Rosenkrantz AB, Haider MA, Padhani AR, Villeirs G, Macura KJ, et al. Prostate Imaging Reporting and Data System Version 2.1: 2019 Update of Prostate Imaging Reporting and Data System Version 2. European Urology 2019;76:340–51. https://doi.org/10.1016/j.eururo.2019.02.033.
6. Mottet, R.C.N. van den Bergh N., E. Brier, P. Cornford, M. De Santis, S. Fanti, et al. EAU Guidelines: Prostate Cancer. EAU Guidelines 2019.
7. Engels RRM, Israël B, Padhani AR, Barentsz JO. Multiparametric Magnetic Resonance Imaging for the Detection of Clinically Significant Prostate Cancer: What Urologists Need to Know. Part 1: Acquisition. European Urology 2019:S0302283819307419. https://doi.org/10.1016/j.eururo.2019.09.021.
8. Panebianco V, Narumi Y, Altun E, Bochner BH, Efstathiou JA, Hafeez S, et al. Multiparametric Magnetic Resonance Imaging for Bladder Cancer: Development of VI-RADS (Vesical Imaging-Reporting And Data System). European Urology 2018;74:294–306. https://doi.org/10.1016/j.eururo.2018.04.029.
9. Mostafid H, Babjuk M, Bochner B, Lerner SP, Witjes F, Palou J, et al. Transurethral Resection of Bladder Tumour: The Neglected Procedure in the Technology Race in Bladder Cancer. European Urology 2020;77:669–70. https://doi.org/10.1016/j.eururo.2020.03.005.
10. Wang H, Luo C, Zhang F, Guan J, Li S, Yao H, et al. Multiparametric MRI for Bladder Cancer: Validation of VI-RADS for the Detection of Detrusor Muscle Invasion. Radiology 2019;291:668–74. https://doi.org/10.1148/radiol.2019182506.
11. Metwally MI, Zeed NA, Hamed EM, Elshetry ASF, Elfwakhry RM, Alaa Eldin AM, et al. The validity, reliability, and reviewer acceptance of VI-RADS in assessing muscle invasion by bladder cancer: a multicenter prospective study. Eur Radiol 2021. https://doi.org/10.1007/s00330-021-07765-5.
12. Del Giudice F, Flammia RS, Pecoraro M, Moschini M, D'Andrea D, Messina E, et al. The accuracy of Vesical Imaging-Reporting and Data System (VI-RADS): an updated comprehensive multi-institutional, multi-readers systematic review and meta-analysis from diagnostic evidence into future clinical recommendations. World J Urol 2022;40:1617–28. https://doi.org/10.1007/s00345-022-03969-6.
13. Bryan RT, Catto JWF, Jefferson KP, Patel P, James ND, on behalf of the BladderPath Trial Management Group. Reply to Trey Durdin, Alvin Goh, and Eugene Pietzak. Can an Imaging-guided Pathway Replace the Current Paradigm for Muscle-invasive Bladder Cancer? European Urology 2021;80:18–9. https://doi.org/10.1016/j.eururo.2021.04.034.
14. Del Giudice F, Leonardo C, Simone G, Pecoraro M, De Berardinis E, Cipollari S, et al. Preoperative detection of VI-RADS (Vesical Imaging-Reporting and Data System) score 5 reliably identifies extravesical extension of urothelial carcinoma of the urinary bladder and predicts significant delayed time-to-cystectomy: time to reconsider the nee. BJU Int 2020. https://doi.org/10.1111/bju.15188.
15. https://www.birmingham.ac.uk/research/crctu/trials/bladder-path/index.aspx n.d.
16. Bryan RT, Liu W, Pirrie SJ, Amir R, Gallagher J, Hughes AI, et al. Comparing an Imaging-guided Pathway with the Standard Pathway for Staging Muscle-invasive Bladder Cancer: Preliminary Data from the BladderPath Study. European Urology 2021;80:12–5. https://doi.org/10.1016/j.eururo.2021.02.021.
17. Li Q, Cao B, Liu K, Sun H, Ding Y, Yan C, et al. Detecting the muscle invasiveness of bladder cancer: An application of diffusion kurtosis imaging and tumor contact length. European Journal of Radiology 2022;151:110329. https://doi.org/10.1016/j.ejrad.2022.110329.
18. Rosenkrantz AB, Mussi TC, Spieler B, Melamed J, Taneja SS, Huang WC. High-grade bladder cancer: Association of the apparent diffusion coefficient with metastatic disease: Preliminary results. J Magn Reson Imaging 2012;35:1478–83. https://doi.org/10.1002/jmri.23590.
19. Sevcenco S, Ponhold L, Heinz-Peer G, Fajkovic H, Haitel A, Susani M, et al. Prospective evaluation of diffusion-weighted MRI of the bladder as a biomarker for prediction of bladder cancer aggressiveness. Urologic Oncology: Seminars and Original Investigations 2014;32:1166–71. https://doi.org/10.1016/j.urolonc.2014.04.019.
20. Zhang M, Chen Y, Cong X, Zhao X. Utility of intravoxel incoherent motion MRI derived parameters for prediction of aggressiveness in urothelial bladder carcinoma. J Magn Reson Imaging 2018;48:1648–56. https://doi.org/10.1002/jmri.26165.
21. Zhou G, Chen X, Zhang J, Zhu J, Zong G, Wang Z. Contrast-enhanced dynamic and diffusion-weighted MR imaging at 3.0T to assess aggressiveness of bladder cancer. European Journal of Radiology 2014;83:2013–8. https://doi.org/10.1016/j.ejrad.2014.08.012.
22. Bandini M, Calareso G, Raggi D, Marandino L, Colecchia M, Gallina A, et al. The Value of Multiparametric Magnetic Resonance Imaging Sequences to Assist in the Decision Making of Muscle-invasive Bladder Cancer. European Urology Oncology 2020:S2588931120300821. https://doi.org/10.1016/j.euo.2020.06.004.
23. Ahmed SA, Taher MGA, Ali WA, Ebrahem MAES. Diagnostic performance of contrast-enhanced dynamic and diffusion-weighted MR imaging in the assessment of tumor response to neoadjuvant therapy in muscle-invasive bladder cancer. Abdom Radiol 2021;46:2712–21. https://doi.org/10.1007/s00261-021-02963-7.
24. Pecoraro M, Del Giudice F, Magliocca F, Simone G, Flammia S, Leonardo C, et al. Vesical Imaging-Reporting and Data System (VI-RADS) for assessment of response to systemic therapy for bladder cancer: preliminary report. Abdom Radiol 2022;47:763–70. https://doi.org/10.1007/s00261-021-03365-5.

Saturday 11 March 10:39 - 10:53
Joint meeting of ESUP, ESUR and ESUI: From conventional to molecular diagnostics
Pink Area, Coral 4

Fournier's gangrene primary and secondary management

Wound-healing techniques and treatment strategies

Prof. Jens Rassweiler
Chair of Urology and Andrology
Danube Private University, Krems (AT)

jens.rassweiler@gmail.com

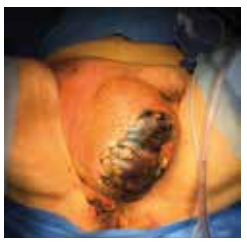
Co-authors: Scheitlin, W[2], Hatiboglu G[2], Agatep J[3], Condendo C[3], Goezen AS[4],
[2]Department of Urology, SLK Kliniken Heilbronn, Germany, [3]Department of Urology, East Avenue Medical Center, Manila, Phillipines, [4]Department of Urology, Medius-Klinik, Ostfildern-Ruit

Fournier's gangrene is an aggressive and frequently fatal polymicrobial soft tissue infection of the perineum, peri-anal region, and external genitalia (Fig. 1a). It is an anatomical sub-category of necrotising fasciitis with which it shares a common etiology and management pathway [1, 2]. Typically, there is painful swelling of the scrotum or perineum with sepsis. Examination shows small necrotic areas of skin with surrounding erythema and oedema. Crepitus on palpation and a foul-smelling exudate occurs during the advanced stage of the disease [3].

Risk factors include diabetes mellitus, malnutrition, immunotherapy, alcohol abuse, recent urethral or perineal surgery, and high body mass index. The degree of internal necrosis is usually vastly greater than suggested by external signs. It requires immediate radical surgery with complete removal of affected tissue (Fig. 1b). Once the patient is stabilized and the wounds are clean, postoperative management includes mesh-graft and skin-flaps (1-3).

Options for secondary management
Both can be associated with secondary wound healing problems mostly requiring secondary surgical procedure (Fig. 2a). Moreover, the cosmetic results of mesh-grafts are not convincing. Other alternatives have been tested, such as hyperbaric oxygen therapy, application of honey, and vacuum-techniques (3-5).

Based on the promising results with the use of low-intensity extracorporeal shock wave therapy (Li-ESWT) in the management of chronic ulcers (6-8), we initially used Li-ESWT in three cases with secondary healing of skin-flaps (Fig. 2b) (9). Subsequently, we were able to close an open wound completely by Li-ESWT only in three more patients (Fig. 3a, 3b, 4). In another two cases, we used ESWT prior to plastic surgery.



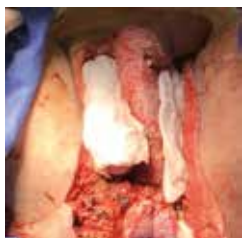


Figure 1a, 1b

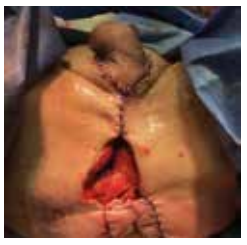


Figure 2a, 2b

Figure 3a, 3b

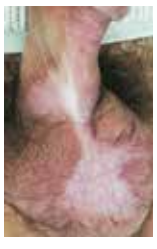


Figure 4a, 4b, 4c

Patients and technique of ESWT
This is a two-institutional study (Heilbronn, Manila): Eight men (aged 27 to 68 years) were admitted with severe Fournier's gangrene requiring complete excision of the scrotal and perineal skin (Fig. 1a, 1b, 3a, 4a). They were all treated in our intensive care unit (ICU) for 10 to 14 days. Wound dressing was applied every other day. Once granulation of the wound started, we closed the wound by using the skin flap from the surrounding area in three patients. Unfortunately, they showed dehiscence of the wound during the follow-up (Fig. 2a).

"The positive effect of Li-ESWT on wound healing can be also very interesting for urologists dealing with secondary wound healing such as in the postoperative management of Fournier's gangrene."

We treated all three patients with Li-ESWT by using the electromagnetic device Duolith SD1 ultra (Storz-Medical, Taegerwilen, Switzerland) applying three times weekly (Mondays, Wednesdays, and Fridays) with 2000 shock waves at 3 Hz with an energy density of 0.25 mJ/mm2 distributed equally on the rims of the wound (Fig. 3a). The treatment was well tolerated with no need of anaesthesia or analgesia. The wounds of all three patients showed a dramatic progress in the healing process (Fig. 2b) with almost complete healing after 12 weeks. No further surgical procedure was required.

Based on this, we treated three patients with complete necrosis of the scrotal and penile skin requiring radical excision (Fig. 4a, 4b, 4c) following ICU for 7 to 10 days. Since there was not much tissue available for adequate plastic surgery of penile and scrotal skin, we started to treat the patients with the Li-ESWT-protocol.

Interestingly, all three patients responded very well on the treatment starting with intensive granulation tissue covering the wound after six weeks (Fig. 4b). Even more impressive, we were able to close the entire wound after 12 weeks (Fig 2d) without any surgical procedure. This was not due closure by just fibrotic tissue. Instead, the locally present scrotal skin was restored as well as the penile skin with an optimal cosmetic result after three months (Fig. 4c)

Discussion
There have been several attempts to improve the wound healing after complete surgical excision in case of Fournier's gangrene. A more recent comparative case series suggested the benefit of using hyperbaric oxygen therapy in 16 patients compared to 12 cases without the use of said therapy in terms of reduced mortality and fewer debridements (4).

A low-quality randomised controlled trial (RCT) with 30 patients found that use of honey-soaked dressings resulted in a shorter hospital stay (28 vs. 32 days) compared to dressing soaked with Edinburgh solution of lime (5). No evidence of benefit in the use of negative-pressure (vacuum) wound therapy in Fournier's gangrene was found (3).

Already in 1990, Haupt et al. examined the effect of shock waves on wound healing in an in-vivo porcine model using the Dornier XL1-experimental lithotripter and concluded that low energy levels (14 kV) coincided with an increased vascularization (10). In 2007, Schaden et al. initiated the first trials on Li-ESWT for wound healing (6). In the meantime, several experimental and clinical studies documented an accelerated tissue repair and regeneration in various wounds following ESWT (7, 8). However, the biomolecular mechanism by which this treatment modality exerts its therapeutic effects still remains unclear. Potential mechanisms include initial neovascularization with ensuing durable and functional angiogenesis. Furthermore, recruitment of stem cells, stimulated cell proliferation and differentiation, anti-inflammatory and antimicrobial effects, and suppression of nociception are considered important facets of biological responses to therapeutic shock waves (7).

One advantage of ESWT for wound healing represents the fact that the effect can be seen directly unlike in other urological indication such as Peyronie's disease, erectile dysfunction, and lower urinary tract symptoms (LUTS) (11,12). The last case of complete restoration of the local skin distinguishing between scrotal and penile skin might indicate that stem cell activation might be the underlying mechanism (7). In this context, the recent studies of Tom Lue's group are very interesting showing experimentally the proliferation of stem cells of the pelvic floor muscles in an birth injury simulation model (13).

In conclusion, the positive effect of Li-ESWT on wound healing can be also very interesting for urologists dealing with secondary wound healing such as in the postoperative management of Fournier's gangrene.

References

1. Eke, N. Fournier's gangrene: a review of 1726 cases. Br J Surg, 2000. 87: 718.
2. Mopurgo E, Galandiuk S. Fournier's gangrene. Surg Clin North Am. 2002;1213-24.
3. G. Bonkat, R. Bartoletti, F. Bruyère, T. Cai, S.E. Geerlings, B. Köves, S. Schubert, A. Pilatz, R. Veeratterapillay, F. Wagenlehner. EAU-Guidlines on Urological Infections. European Association of Urology 2022
4. Mladenov A, Diehl K, Müller O, von Heymann C, Kopp S, Peitsch WK. Outcome of necrotizing fasciitis and Fournier's gangrene with and without hyperbaric oxygen therapy: a retrospective analysis over 10 years. World J Emerg Surg. 2022 Aug 5;17(1):43.
5. Subrahmanyam, U., Ugane SP. Honey dressing beneficial in treatment of fournier's gangrene. Indian J Surg, 2004. 66: 75.
6. Schaden W, Thiele R, Kölpl C, Pusch M, Nissan A, Attinger CE, Maniscalco-Theberge ME, Peoples GE, Elster EA, Stojadinovic A. Shock wave therapy for acute and chronic soft tissue wounds: a feasibility study. J Surg Res. 2007;143(1):1-12
7. Mittermayr R, Antonic V, Hartinger J, Kaufmann H, Redl H, Téot L, Stojadinovic A, Schaden W. Extracorporeal shock wave therapy (ESWT) for wound healing: technology, mechanisms, and clinical efficacy. Wound Repair Regen. 2012;20(4):456-65.
8. Taheri P, Shahbandari M, Parvaresh M, Vahdatpour B. Extracorporeal Shockwave Therapy for Chronic Venous Ulcers: A Randomized Controlled Trial. Galen Med J. 2021 Apr 25;10:e1931. doi: 10.31661/gmj.v10i0.1931. eCollection 2021.
9. Rassweiler JJ, Scheitlin W, Goezen AS, Rassweiler-Seyfried MC. Low-energy Shockwave Therapy in the Management of Wound Healing Following Fournier's Gangrene. Eur Urol Open Sci. 2022 Sep 13;45:8-11.
10. Haupt G, Haupt A, Ekkernkamp A, Gerety B, Chvapil M. Influence of shock wave healing. Urology 1992; 39: 529-532
11. Rassweiler J: Re: Extracorporeal shock wave therapy (ESWT) in Urology: A systematic review of outcome in Peyronie`s disease, erectile dysfunction, and chronic pain. (Words of Wisdom) Eur Urol 2018; 74: 115-117
12. Sokolakis I, Pyrgidis N, Neisius A, Gierth M, Knoll T, Rassweiler J, Hatzichristodoulou G, on behalf of the German Society for Shock Wave Lithotripsy. The effect of low-intensity shock wave therapy on non-neurogenic lower urinary tract symptoms. A systematic review and meta-analysis of pre-clincal and clinical studies. Eur Urol Focus 2022 May;8(3):840-850
13. Lin G, Van Kuiken M, Wang G, Banie L, Tan Y, Zhou F, Wang Z, Chen Y, Zhang Y, Lue TF. Microenergy acoustic pulse therapy restores function and structure of pelvic floor muscles after simulated birth injury. Transl Androl Urol. 2022 May;11(5):595-606. doi: 10.21037/tau-22-30.

Friday 10 March 13:03 - 13:13
Thematic Session: Emergencies in urology
Yellow Area, eURO Auditorium 2

Is precision medicine possible in patients with mCRPC?

Optimal treatment sequencing in the area of triplet therapies for hormone-sensitive disease

Prof. Thomas Steuber
Martini-Clinic, Prostate Cancer Center
University Hospital Hamburg-Eppendorf (DE)

steuber@uke.de

During the last decade, treatment of metastatic hormone sensitive prostate cancer (mHSPC) has evolved from Androgen deprivation therapy (ADT) alone to combined treatment concepts. Numerous prospective randomised controlled trails (RCT), testing ADT in combination with new hormonal agents (NHA) or Docetaxel chemotherapy upfront have demonstrated a substantial overall survival (OS) benefit vs. ADT alone, is meanwhile defined as standard of care for men suffering from mHSPC [1-6]. Given the various drugs approved for mHSPC treatment, consideration of patients´ disease extent (volume and risk categories) and comorbidity are crucial to select the optimal therapy.

Despite these significant advances, most patients, especially those with high volume/risk tumours, ultimately will progress to metastatic castration resistant prostate cancer (mCRPC). Due to the lack of data from prospective trials, several rules have been established to guide physicians to individually select the optimal treatment sequence: 1. expose to as many drugs as possible during mCRPC 2. find the optimal timing for therapy switch by using regular imaging, biomarker, pain and quality of life assessment 3. response to drug and drug class of previous therapy largely influences the choice of the next treatment line. E.g. due to various mechanisms of cross resistance, sequencing NHA such as Abiraterone followed by Enzalutamide or vice versa, has been shown to be inferior to PARP-Inhibitor treatment for men with homologous recombination repair (HRR) gene alterations or to second line chemotherapy with Cabacitaxel [7, 8]. 4. LU177-PSMA-Ligand therapy may offer some advantages over Cabacitaxel for some patients previously treated with NHA and Docetaxel [9].

"LU177- PSMA-Ligand therapy may offer some advantages over Cabacitaxel for some patients previously treated with NHA and Docetaxel."

More recently, triple therapy combining ADT with Docetaxel plus NHA have been tested against ADT/Docetaxel in mHSPC patients. The multi-institutional investigator-initiated PEACE-1 trial concurrently added Abiraterone to ADT/Docetaxel and could establish an overall survival benefit in favour of the triple approach for all studied men (10). However, subgroup analysis revealed only a value for men with synchronous high volume mHSPC according to the CHAARTED criteria (HR 0.72, 95% CI 0.55–0.95) while the point estimate for the HR for was less pronounced for the subgroup of patients with low-volume mHSPC (HR 0.83, 95% CI 0.5–1.38).

The ARASENSE RCT again defined ADT/Docetaxel (plus placebo) as standard of care (SOC) and added Darolutamide in the experimental arm in mHSPC all-comer patients [11]. Darolutamide is so far approved only for men with nonmetastatic CRPC [12]. Again, the trial was in favour of the triple according to OS analysis and to all secondary endpoints. Subgroup analysis was positive for many predefined clinical categories, however, a stratification between high vs. low volume was not reported. In conclusion, both large prospectively randomised trials managed to establish a substantial benefit in favour of the triple vs. ADT/Docetaxel and the authors concluded that the triple approach may be considered the new SOC. Several limitations, however, deserve to be mentioned: 1. the exact patient population benefiting from the triple therapy needs to be defined. 2. the triple therapy has never been tested against ADT/NHA, which is currently considered SOC. In their summary from the 2021 APCCC meeting, the expert panel concluded that the triple therapy should focus on synchronous high volume mHSPC patients that are fit for chemotherapy. The lack of data with respect to the ADT/NHA comparison and the increased toxicity related to cytotoxic therapy need to be discussed with the patient [13].

"While sequencing Enzalutamide after Darolutamide may not be considered due to the congruent mode of action, adding Abiraterone might nevertheless be an option."

The concurrent application of three mHSPC drugs upfront raises the important question about the optimal sequence for progressing mCRPC. Little if anything is known about the efficacy of subsequent therapies. For the ARASENSE trial [11], 45.9% (n=299) of patients in the Darolutamide group and 19.1% (n=125) of patients in the placebo group were receiving ongoing study treatment. Subsequent life-prolonging systemic antineoplastic therapy is reported in the supplementary appendix. Accordingly, in the experimental arm, 56.8% vs. 75.6% in the control arm received life prolonging drugs beyond progression. Among these therapies, more than 50% received another NHA (predominantly Abiraterone) and roughly 40% were treated with another line of chemotherapy, with half of them getting re-exposed to Docetaxel. Unfortunately, the detailed response rates by drug class or progression free survival 2 (PFS2) as a surrogate for response to the next treatment line were not reported.

What can we learn from other trials? By simply looking at the inclusion criteria for current mCRPC drugs, most of the trials predominantly included men treated with ADT only for mHSPC, and only the latest trials e.g., the PROPEL trial, leading to the approval of Abiraterone in combination with Olaparip in an all-comer population accepted pre-treatment with an NHA (except of Abiraterone) or Docetaxel for mHSPC [14], but none of those patients received concurrent Docetaxel plus a NHA upfront. Recommendation of subsequent treatment strategies, therefore, need to be extrapolated from previous metastatic prostate cancer trials.

Sequencing NHA as first line mCRPC treatment after triple therapy

The concept of using Abiraterone within the triple therapy as suggested by the PEACE-1 consortium means that Abiraterone is continued beyond concurrent Docetaxel chemotherapy until progression [10]. Since Enzalutamide is the only approved hormonal drug beside Abiraterone in mCRPC, adding Enzalutamide would be "in label". However, data from sequencing studies revealed poor response rates due to several mechanisms of cross resistance between both drugs. Expected PFS rates range between 2-3 months and no survival benefit could be established [15]. Darolutamide as suggested in ARASENSE has not yet been tested in other mHSPC trials and is not approved for mCRPC. Therefore, limited data is reported with respect to sequential therapy.

The ARAMIS study evaluated the efficacy and safety of Darolutamide in nonmetastatic CRPC [12]. Among Darolutamide patients who entered active or long-term follow-up for survival (n=315), 112 (35.6%) patients subsequently received Abiraterone as a life-prolonging therapy. However, no efficacy or safety outcomes are available for these patients. While sequencing Enzalutamide after Darolutamide may not be considered due to the congruent mode of action, adding Abiraterone might nevertheless be an option.

Data from the TITAN study, where mHSPC patients were treated with ADT in combination with Apalutamide until progression, suggested, that the rate of AR mutations is limited under Apalutamide exposition (4). Accordingly, NHA treatment (predominantely Abirateron) provided a similar PFS2 compared to chemotherapy as first-line mCRPC treatment. Whether these data may be extrapolated to the use of Darolutamide in the context of triple therapy remains questioned.

Sequencing chemotherapy as first line mCRPC treatment after triple therapy

The concept of early Docetaxel chemotherapy for mHSPC has been established already in 2014 after reporting compelling data from the CHAARTED, GETUG-AFU15 and the STAMPEDE trials [1,2]. Subgroup analysis of GETUG suggested that Docetaxel re-exposition after early Docetaxel is inferior to sequencing with Abiraterone or Enzalutamide. Therefore, Cabacitaxel would be the preferred chemotherapy line beyond progression after early Docetaxel. Cabacitaxel is approved for mCRPC patients pre-treated with Docetaxel in mCRPC patients with a significant OS benefit compared to Mitoxantrone or a second line of NHA. However, the efficacy of Cabacitaxel has not yet been reported in the context of men progressing after triple therapy.

"The efficacy of Cabacitaxel has not yet been reported in the context of men progressing after triple therapy."

Sequencing PARP-inhibitors as first line mCRPC treatment after triple therapy

Olaparib is the first PARP-I that is approved for mCRPC patients with a BRCA1/2 mutation progressing after Abiraterone and/or Enzalutamide [7]. Since two third of patients included in the pivotal PROFOUND trial were also exposed to sequential Docetaxel chemotherapy, Olaparib is considered as a second or third line mCRPC treatment. These data have been extrapolated to the current treatment landscape and prior NHA +/- chemotherapy may have been given also for mHSPC patients. Progression after triple therapy would therefore be "in label" for the prescription of Olaparib, when somatic or germline BRCA mutations are detected. However, again no data is available indicating the efficacy of Olaparib for patients pre-treated with triple therapy. More recently, Olaparib in combination with Abiraterone is approved for mCRPC all-comer populations regardless of their HRR status [14]. However, the very current label recommends the combinational treatment for "mCRPC patients in whom chemotherapy is not yet clinically indicated". This would exclude patients pre-treated with Abiraterone (with concurrent chemotherapy) or any other prior chemotherapy.

Sequencing LU177-PSMA-Ligand first line mCRPC treatment after triple therapy

For many years LU177-PSMA-Ligand therapy has been considered as an individual mCRPC treatment concept for intensively pre-treated patients with multiple PSMA positive lesions on PSMA-PET scan. Most recently, with positive results from the RC Vision trial, this concept is approved for mCRPC patients, pre-treated with at least one line of NHA and one line of chemotherapy [17]. With this label in mind, a patient progressing after any of the two triple concepts would already fulfil criteria for reimbursement and thus LU177-PSMA-Ligand could be considered as first line mCRPC therapy.

In conclusion, the optimal treatment sequence for men progressing after one of the triple therapy concepts needs to be defined. According the rationale derived from the discussed trials, Abiraterone (after Darolutamide), Olaparib in BRCA1 or 2 positive men, second line chemotherapy with Cabacitaxel and LU177-PSMA-Ligand therapy are valid mCRPC options. The optimal order, however, needs to be determined on upcoming prospective trials.

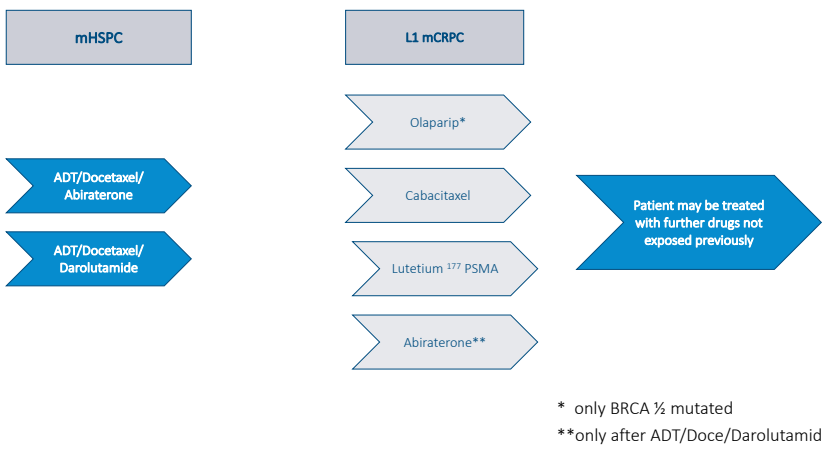


Figure 1. Plausible mCRPC sequences after triple therapy for mHSPC

References

1. Kyriakopoulos CE et al, Chemohormonal Therapy in Metastatic Hormone-Sensitive Prostate Cancer: Long-Term Survival Analysis of the Randomized Phase III E3805 CHAARTED Trial. J Clin Oncol. 2018 Apr 10;36(11):1080-1087
2. James ND, et al. Addition of docetaxel, zoledronic acid, or both to first-line long-term hormone therapy in prostate cancer (STAMPEDE): survival results from an adaptive, multiarm, multistage, platform randomised controlled trial Lancet. 2016; 387:1163-77.
3. Fizazi K, et al. Abiraterone plus Prednisone in Metastatic, Castration-Sensitive Prostate Cancer N Engl J Med. 2017; 377:352-60,
4. Chi K. et al, Apalutamide in Patients With Metastatic Castration-Sensitive Prostate Cancer: Final Survival Analysis of the Randomized, Double-Blind, Phase III TITAN Study J Clin Oncol 2021 Jul 10;39(20)
5. Armstrong AJ et al. ARCHES: A Randomized, Phase III Study of Androgen Deprivation Therapy With Enzalutamide or Placebo in Men With Metastatic Hormone-Sensitive Prostate CancerJ Clin Oncol. 2019 Nov 10;37(32)
6. Davis ID et al, Enzalutamide with Standard First-Line Therapy in Metastatic Prostate CancerN Engl J Med. 2019 Jul 11;381(2)
7. de Bono JS, et al. Olaparib for Metastatic Castration-Resistant Prostate Cancer N Engl J Med. 2020;382(22):2091–2102
8. de Witt R, Cabazitaxel versus Abiraterone or Enzalutamide in Metastatic Prostate Cancer N Engl J Med. 2019 Dec 26;381(26):2506-2518
9. Hofman MS, [177Lu]Lu-PSMA-617 versus cabazitaxel in patients with metastatic castration-resistant prostate cancer (TheraP): a randomised, open-label, phase 2 trial. Lancet. 2021 Feb 27;397(10276):797-804.
10. Fizazi K et al. Abiraterone plus prednisone added to androgen deprivation therapy and docetaxel in de novo metastatic castration-sensitive prostate cancer (PEACE-1): a multicentre, open-label, randomised, phase 3 study with a 2 × 2 factorial design. Lancet 2022; 399:1695-07
11. Smith M et al. Darolutamide and Survival in Metastatic, Hormone-Sensitive Prostate Cancer New Engl J Med 2022;386(12):1132-42.
12. Fizazi K, Darolutamide in Nonmetastatic, Castration-Resistant Prostate Cancer, N Engl J Med. 2019 Mar 28;380(13):1235-1246
13. Gillesen S, Management of Patients with Advanced Prostate Cancer: Report from the Advanced Prostate Cancer Consensus Conference 2021 Eur Urol. 2022 Jul;82(1):115-141.
14. Clarke NW, Abiraterone and Olaparib for Metastatic Castration-Resistant Prostate Cancer NEJM Evid 2022; 1 (9)
15. Khalaf D et al. Optimal sequencing of enzalutamide and abiraterone acetate plus prednisone in metastatic castration-resistant prostate cancer: a multicentre, randomised, open-label, phase 2, crossover trial Lancet Oncol 2019;20(12);1730-39
16. Lavaud P et al. Anticancer Activity and Tolerance of Treatments Received Beyond Progression in Men Treated Upfront with Androgen Deprivation Therapy With or Without Docetaxel for Metastatic Castration-naïve Prostate Cancer in the GETUG-AFU 15 Phase 3 Trial. Eur Urol. 2018 May;73(5):696-703
17. Sartor O et al, Lutetium-177-PSMA-617 for Metastatic Castration-Resistant Prostate Cancer. J Med. 2021 Sep 16;385(12):1091-1103.

Sunday 12 March 18:00 - 18:10
Thematic Session: Is precision medicine possible in patients with mCRPC?
Yellow Area, eURO Auditorium 1

Management of paediatric kidney trauma

When can children safely participate in sporting activities again?

Dr. Lisette 't Hoen
Paediatric Urology Department, Sophia Children's Hospital, Erasmus Medical Centre, Rotterdam (NL)

Renal trauma is the most common urogenital trauma in children. In the case of blunt abdominal trauma, renal injury is found in 10-20% of instances. There is a higher risk for more severe injuries in children compared to adults because of their anatomical differences. The kidney is surrounded by less perirenal fat, a more elastic rib cage due to less ossification, weaker abdominal muscles and foetal kidney lobulations are still present.

Blunt trauma is the main mechanism of injury to the kidney. The American Association for the Surgery of Trauma (AAST) scale is most commonly used to stratify severity of injury, ranging from grades I – V. In 2019 the World Society of Emergency Surgery (WSES) kidney trauma classification was introduced. This grading system specifies four grades and is based on the AAST scale, but also includes the hemodynamic status of the patient [1].

Clinical guidelines are provided by the American Urological Association (AUA) and European Association for Urology (EAU), including a separate guideline for paediatric renal trauma, from the perspective of the urologist [2-4]. The WSES-AAST have also developed guidelines for urogenital trauma from the surgical trauma perspective[1]. In these guidelines, detailed flowcharts are presented for diagnosis and acute management using the AAST and WSES grading systems. A shift from surgical to conservative management for most renal trauma cases has been seen in children and adults. While minimally invasive management through embolisation is used for the most severe or high-risk cases.

Lack of guidelines for recovery

The next stage of renal trauma, specifically recovery after renal trauma, has not been highlighted in literature. It remains unclear when it is safe to mobilise or even return to sporting activities after renal trauma. The answer to this question is not straightforward and will depend on the degree of renal trauma and what type of activity is being considered. However, it is an important clinical issue, especially for children. Children are typically more physically active than adults and also their return to school could be hindered due to lack of proper instructions.

The urological guidelines provide no guidance regarding mobility and sporting activities after renal trauma. The surgical trauma guidelines state that mobility can be resumed when gross haematuria has ceased. Sporting activities may be recommenced when microscopic haematuria has stopped and within 2 – 6 weeks after renal trauma for the lower grades. For the more severe renal injuries, up to 12 months of no sports could be necessary. There is no mention of relevant factors that will influence the duration of immobility requirement.

Evaluation

As part of a Young Academic Urologists Working Group Paediatric Urology project, a survey was constructed to evaluate the clinical management of renal trauma. In regard to mobility and sporting activities, the survey responders reported a large variation in clinical management. For the low grade renal injuries almost all responders stated that it was safe to return to sporting activity, however, with variable time to return to sporting activity ranging from 2 – >12 weeks. In the case of higher grade injuries and conservatively managed penetrating trauma, the majority of respondents indicated that sporting activities could resume after >12 weeks, conversely, part of the respondents stated that no return to sports was possible. This is of significant importance for children, given that in some parts of Europe children will be prohibited from participating in sport ever again after renal injury.

We can gain new insights by exploring the views on management of mobility and sports after trauma to other solid abdominal organs. For paediatric patients, the American Paediatric Surgical Association (APSA) have developed guidelines for blunt liver and spleen injury. According to the APSA guidelines, no bedrest is required after the injury and physical activity can be resumed after injury grade + 2 weeks [5]. These guidelines have been validated in a large cohort of 366 patients and were found to be safe [6]. The Arizona, Texas, Oklahoma, Memphis, Arkansas Consortium (ATOMAC) guidelines, also for blunt liver and spleen injury, specifically state that it is safe for children to return to school when comfortable and able [7].

Conclusion

In order to determine the optimal management of mobility and sporting activity after renal trauma, further research is needed. The current guidelines for blunt liver and spleen trauma could be tested in the renal trauma setting. A prospective multi-centre study could be conducted to compare outcomes, such as return to mobility, time to return to sports, and complications between patients managed conservatively and those managed surgically. Additionally, the study should assess the impact of different factors, such as the grade of the injury and age on the outcomes.

Given the great variation that is presented in the management of mobility and sporting activity after renal trauma in paediatric patients, we want to highlight the importance of more clarity and evidence-based guidance for this group of patients.

On behalf of the YAU Pediatric Urology Working Group: Fardod O'Kelly, Rianne Lammers, Anne-Françoise Spinoit, Bernhard Haid, Simone Sforza, Selçuk Silay, Numan Baydilli, Muhammet Irfan Donmez, Eduardo Bindi, Beatrix Bañuelos Marco

References

1. Coccolini F, et al. WSES-AAST Expert Panel. Kidney and uro-trauma: WSES-AAST guidelines. World J Emerg Surg. 2019 Dec 2;14:54. doi: 10.1186/s13017-019-0274-x.
2. Morey AF, et al. Urotrauma: AUA guideline. J Urol 2014, 192: 327
3. Kitrey NC, et al. EAU Guidelines on Urological Trauma 2022. Edn. Presented at the EAU Annual Congress Amsterdam 2022. ISBN 978-94-92671-16-5.
4. Radmayr C, et al. EAU Guidelines on Paediatric Urology 2022. Edn. Presented at the EAU Annual Congress Amsterdam 2022. ISBN 978-94-92671-16-5.
5. Stylianos S. Evidence-based guidelines for resource utilization in children with isolated spleen or liver injury. The APSA Trauma Committee. J Pediatr Surg. 2000 Feb;35(2):164-7; discussion 167-9. doi: 10.1016/s0022-3468(00)90003-4.
6. Notrica DM, et al. Adherence to APSA activity restriction guidelines and 60-day clinical outcomes for paediatric blunt liver and splenic injuries (BLSI). J Paediatric Surg. 2019 Feb;54(2):335-339. doi: 10.1016/j.jpedsurg.2018.08.061.
7. Notrica DM, et al. Nonoperative management of blunt liver and spleen injury in children: Evaluation of the ATOMAC guideline using GRADE. J Trauma Acute Care Surg. 2015 Oct;79(4):683-93. doi: 10.1097/TA.0000000000000808.

Friday, 10 March 13:35 - 13:40
Thematic Session: Curiosities in paediatric urology
Pink Area, Coral 7

New transrectal prostate biopsy approach:

May improve tolerability and safety

Dr. Marcin Sieczkowski
Gdansk (PL)

sieczkowski@gmail.com

Histopathological examination is the essential basis in the diagnosis of prostate cancer. Most likely, it will be a long time before prostate biopsy will be replaced by the new biochemical tests or imaging-based solutions. That is why it is highly important to determine what is the best approach concerning this procedure. The Guidelines of the European Association of Urology (EAU) clarify much on the matter, but there are still many issues that remain uncertain [1].

For years, transrectal prostate biopsy with antimicrobial prophylaxis, usually based on fluoroquinolones, remained the standard. Due to the increasing bacterial resistance to fluoroquinolones, their side effects and rising rate of infectious complications, changes in approach to prostate biopsy have been necessary. In line with the European Commission's final decision (EMEA/H/A-31/1452), fluoroquinolones have been banned to be used for all perioperative prophylaxis [2]. This recommendation has been also confirmed by the EAU Guidelines panel as in regards to prostate biopsy [1]. This decision is just one of many strategies that can contribute to patient safety during prostate biopsy.

Non-antibiotic strategies

Among different non-antibiotic strategies tested for this purpose, the beneficial effect has been achieved by use of a rectal povidone-iodine preparation. Meta-analysis by Pradere et al. showed the reduction of infectious complications rate (RR 0.50, 95% CI 0.38-0.65, p <0.000001, I2=27%, 1,686 participants, 8 eight studies) as well as re-hospitalisation (RR 0.38, 95% CI 0.21-0.69, p=0.002, I2=0%, 620 participants, 4 four studies) following the application of this method [3]. However, this proved to be an insufficient measure.

Up until now, the best results so far in reducing infectious complications related to prostate biopsy have been obtained by changing from transrectal to transperineal route. The same meta-analysis demonstrated that transperineal biopsy was associated with significantly reduced infectious complications as compared to transrectal one (RR 0.55, 95% CI 0.33-0.92, p=0.02, I2=0%, 1,330 participants, 7 seven studies) [3]. This insight is also supported by the large population-based study from England where patients undergoing transperineal biopsy were less likely to be readmitted because of sepsis (1.0% vs 1.4%; aRD -0.4%, CI -0.6 to -0.2) [4].

The above results seem to fully justify the EAU Guidelines stating that transperineal biopsy should be a primary choice and transrectal approach should be abandoned despite any possible logistical challenges [1]. Unfortunately, these challenges are not the only problems associated with transperineal route.

The previously mentioned population study from England demonstrated that patients undergoing transperineal biopsy were more likely to have an overnight hospital stay (12.3% vs 2.4%; aRD 9.7%, 95% confidence interval [CI] 7.1-12.3) and were more likely to be readmitted with urinary retention (1.9% vs 1.0%; aRD 1.1%, CI 0.7-1.4) than those undergoing a transrectal procedure [4]. The authors concluded that this means that use of the transperineal route would prevent one readmission for sepsis in 278 patients at the cost of three additional patients readmitted for urinary retention [4].

Despite advances in performing transperineal prostate biopsy under local anaesthesia, it may also be associated with more discomfort. The systematic review by Xiang et al. revealed that the transperineal approach significantly increased patient pain (RR = 1.83, 95% CI 1.27–2.65) [5]. Furthermore, the issue of an increased risk of erectile dysfunction after transperineal biopsy remains unclear. It is known that up to 25% of males undergoing this procedure have been reported to experience deficits in sexual function [6]. Tan et al. have postulated that transperineal access may induce erectile dysfunction through neuropraxia at a higher rate than the transrectal approach given passage of multiple punctures through the prostatic apex where the neurovascular bundles are converging [6].

Systemic antibiotic strategies

Finding a simple antibiotic strategy to reduce infectious complications after transrectal prostate biopsy in the post-quinolones era is difficult. Targeted prophylaxis based on the rectal swab may reduce infective complications and prove to be more cost-effective in the long term. However, it is unclear whether there is sufficient evidence to recommend its use in pre-biopsy screening programmes as no randomised controlled trials (RCTs) are available on non-fluoroquinolones. An additional limitation of rectal swab cultures is that they must be taken preferably one week prior to the biopsy which complicates practicalities [7, 8].

Another option is an augmented prophylaxis with two (or more) antibiotics of different classes. Meta-analysis of 10 RCTs by Pilatz et al. confirmed the benefit of this strategy. However, no established standard combination exists to date. Most importantly, the systemic use of two antibiotics for antimicrobial prophylaxis contradicts the principles of antibiotic stewardship [9].

New approach

Facing the above problems mentioned above, Drug-Eluting Biopsy Needle (DEBN) may be another alternative for reducing post-biopsy infectious complications rate. DEBN may limit the systemic prophylaxis to only one systemic antibiotic supported by local release of another antibiotic of different class; therefore, reducing the risks of side effects as well as changes of the microbiome.

"Up until now, the best results in reducing infectious complications related to prostate biopsy have been obtained by changing from transrectal to transperineal route."

DEBN is a patented (PCT/PL2016/000006) medical device which is a novel approach to the problem of transrectal ultrasound prostate biopsy (TRUS-Bx) related infectious complications. It consists of a polymer coated biopsy needle and anaesthesia needle containing an antibiotic that is released directly to the prostate during the biopsy procedure. This solution may allow the co-administration of various antibiotics, thereby broadening their spectrum of activity and potentially reducing the number of infectious complications.

DEBN is the first medical device to enable simultaneous organ-targeted delivery of antibiotics during prostate biopsy procedure. The presented model of DEBN contains poly(vinyl alcohol) and amikacin sulphate.

DEBN clinical trial

After numerous preclinical tests including studies on different formulations, microbiological and animal models, validation of production, packaging, sterilisation, biocompatibility, and ageing tests, the clinical trial was planned to assess the suitability of DEBN. This clinical investigation will be performed as a multicentre, double-blind, and non-inferiority trial in the eight clinical sites in Poland and Hungary specialised in the prostate biopsy procedure. The aim of this study is to assess whether safety and efficacy of transrectal biopsy performed with DEBN are non-inferior to standard transrectal biopsy combined with augmented prophylaxis. The main observation will focus on the rate of infectious complications in the study arms. Primary hypothesis of the investigation states that transrectal prostate biopsy performed with DEBN is non-inferior to standard transrectal prostate biopsy combined with augmented prophylaxis (fosfomycin trometamol 3 g p.o. + amikacin 15 mg/kg i.m.).

This clinical investigation aims to enrol approximately 123 subjects, including a potential 20% drop-out. The patient population of this study will be male aged ≥45 and < 80 years with an indication to transrectal prostate biopsy. Patient participation will last up to 44 days and will require five visits [Fig. 1]. The first four visits are on-site visits, and the last visit (visit 5) will be performed as a telephone visit, unless any safety concerns or any other reasons occur that in the investigators opinion require the visit to be performed on-site. Additionally, in case of any safety concerns, an unscheduled visit may be performed (telephone or on-site) at any time between Visit 3 and Visit 5, at the discretion of the investigator.

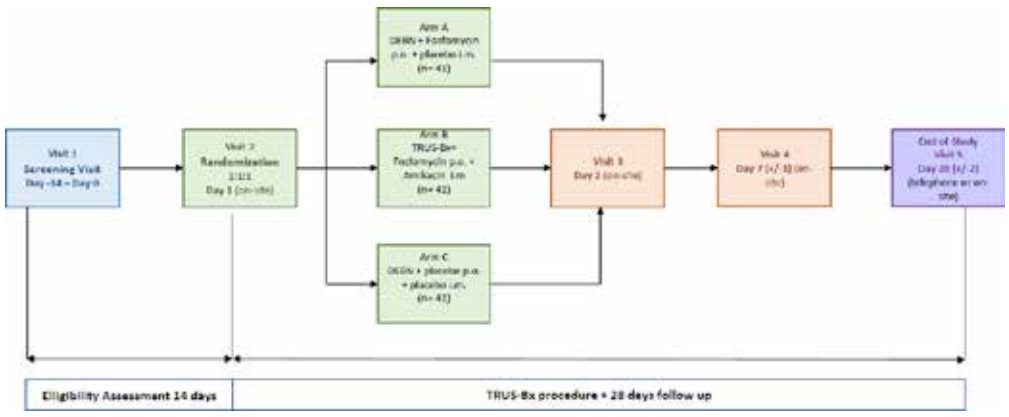


Fig. 1 DEBN trial investigation design scheme

The screening phase begins when written informed consent is obtained from the subject and ends at randomisation. The duration of the screening phase should not exceed 2 two weeks and all examinations must be performed ≤ 14 days prior to planned randomiszation. A patient's eligibility for the study will be finally confirmed during the Baseline Visit (Visit 2) at Study Day, which is the day of randomisation and transrectal prostate biopsy.

Subjects fulfilling the inclusion criteria and not meeting the exclusion criteria will be randomised in a 1:1:1 ratio to one of the three treatment arms:

- Arm A: DEBN transrectal prostate biopsy + fosfomycin 3 g p.o. + placebo i.m.
- Arm B: standard transrectal prostate biopsy + augmented prophylaxis (fosfomycin 3 g p.o. + amikacin 15 mg/kg i.m.)
- Arm C: DEBN transrectal prostate biopsy + placebo p.o. + placebo i.m.
- After the biopsy, the patient will be observed for post-biopsy infectious complications during the follow-up period until day 28. All follow-up visits will be scheduled to occur from the date of transrectal prostate biopsy:
- Visit 3 will be an on-site visit on day 2. Safety assessments will be performed during this visit. At the end of this visit, the second dose of fosfomycin (3 g p.o.) or placebo will be administered.
- Visit 4 on day 7 (+/- 1 day) will be an on-site visit. Safety assessments and success of the biopsy (procedure-related complications) will be performed during this visit.
- Visit 5 on day 28 (+/- 2 days) after the transrectal prostate biopsy will be a telephone visit. This visit will be an End of Study Visit. Safety assessments will be performed.

Patient safety will be monitored by through medical interview and physical examination. Vital signs will be measured, while as well as monitoring the haematology, biochemistry, inflammatory blood parameters, urinalysis, urine culture, and rectal swab will be monitored. Additionally, scales and questionnaires such as I-PSS (International Prostate Symptom Score), IIEF-15 (International Index of Erectile Function), EQ-5D (i.e. EuroQol instrument, a five-dimensional three-level generic measure) will be performed.

The monitoring of adverse events will be performed throughout the study period since the randomisation. Antibiotic prophylaxis will be administered with instructions of not taking any additional systemic antimicrobial treatment. Clinical investigation will be blinded. Placebo will be used for masking amikacin in study arm A and fosfomycin and amikacin in study arm C.

Due to technical reasons, blinding will be executed by introducing blinded and unblinded site teams. The blind team will be responsible for patient recruitment and all study assessments, while the unblinded team will be responsible for transrectal prostate biopsy and antibiotic prophylaxis administration, as well as, medical device and antibiotic prophylaxis management and documentation. These two teams will not contact each other to share the randomisation results.

Non-inferiority study design was chosen as an optimal one, taking into account that superiority of local anti-infectious prophylaxis is not expected to be superior to the systemic one. Non-inferiority design is commonly used to show that there is no difference between the new device or treatment. Active control to supports the conclusion that the new device is not materially worse than the control, which means it is also effective. This design was also chosen also for ethical reasons, as it would not be ethical to use only placebo, or a no-prophylaxis control only.

Non-inferiority margin was chosen as 15% is based on statistical considerations. Primary efficacy criteria is defined as the success rate understood. The rate of biopsies non-complicated by infection (absence of urosepsis or urinary tract infection resulting in the need of systemic antibiotic administration) was chosen as the main area of interest for DEBN, as well as, and to provide the answer for scientific questions on safety and efficacy of transrectal prostate biopsy performed with DEBN.

References

1. EAU Guidelines. Edn. presented at the EAU Annual Congress Amsterdam, the Netherlands 2022. ISBN 978-94-92671-16-5
2. EMA. Quinolone- and fluoroquinolone-containing medicinal products - European Medicines Agency. European Medicines Agency. Published September 17, 2018. https://www.ema.europa.eu/en/medicines/human/referrals/quinolone-fluoroquinolone-containing-medicinal-products
3. Pradere B, Veeratterapillay R, Dimitropoulos K, et al. Nonantibiotic Strategies for the Prevention of Infectious Complications following Prostate Biopsy: A Systematic Review and Meta-Analysis. *Journal of Urology*. 2021;205(3):653-663. doi:10.1097/ju.0000000000001399
4. Berry B, Parry MG, Sujenthiran A, et al. Comparison of complications after transrectal and transperineal prostate biopsy: a national population-based study. BJU *International*. 2020;126(1):97-103. doi:10.1111/bju.15039
5. Xiang J, Yan H, Li J, Wang X, Chen H, Zheng X. Transperineal versus transrectal prostate biopsy in the diagnosis of prostate cancer: a systematic review and meta-analysis. *World Journal of Surgical Oncology*. 2019;17(1). doi:10.1186/s12957-019-1573-0
6. Tan JL, Papa N, Hanegbi U, et al. Predictors of erectile dysfunction after transperineal template prostate biopsy. *Investigative and Clinical Urology*. 2021;62(2):159. doi:10.4111/icu.20200236
7. Taylor AK, Zembower TR, Nadler RB, et al. Targeted Antimicrobial Prophylaxis Using Rectal Swab Cultures in Men Undergoing Transrectal Ultrasound Guided Prostate Biopsy is Associated With Reduced Incidence of Postoperative Infectious Complications and Cost of Care. *Journal of Urology*. 2012;187(4):1275-1279. doi:10.1016/j.juro.2011.11.115
8. Singh P, Kumar A, Yadav S, et al. "Targeted" prophylaxis: Impact of rectal swab culture-directed prophylaxis on infectious complications after transrectal ultrasound-guided prostate biopsy. *Investigative and Clinical Urology*. 2017;58(5):365. doi:10.4111/icu.2017.58.5.365
9. Pilatz A, Dimitropoulos K, Veeratterapillay R, et al. Antibiotic Prophylaxis for the Prevention of Infectious Complications following Prostate Biopsy: A Systematic Review and Meta-Analysis. *Journal of Urology*. 2020;204(2):224-230. doi:10.1097/ju.0000000000000814

Saturday 11 March 18:40 - 18:50
Urogenital infections in urology
Yellow Area, Amber 3

The (hidden) role of the nurse and the stoma therapist

Measuring stoma self-care skills by using the Urostomy Education Scale (UES)

Dr. Bente Thoft Jensen
Asst professor -FAAN
Dept. of Urology,
Aarhus University Hospital & Aarhus University (DK)
Chairman of the EAUN Bladder Cancer Group

Uro-oncology nurses are at the forefront in every Enhanced Recovery after Surgery (ERAS) programme and are vital in screening, preparing and educating patients ahead of surgery to adjust for common risk factors, current impairments and limitations that can compromise functional recovery after surgery [1].

The role of stoma care in the ERAS pathway
Stoma care is an integrated component of the multi-professional cancer care continuum in radical cystectomy pathways [2] and affects both the pre- and postoperative setting. ERAS has successfully reduced length of hospital stay (LOS) across surgical specialties and significantly changed the surgical paradigm of care in major cancer surgery now in both the pre- and post-operative setting [3]. Historically, stoma care was provided in the post-operative setting, but due to changes in the patient pathway and the reduced time to teach and adapt to the stoma postoperatively, stoma care should now be introduced already in prehabilitation setting. This change will maximise the individual's ability to obtain stoma competencies and manage the stoma independently, thus regaining self-care as soon as possible.

Key Skills for stoma care
Stoma care includes skill-building and counselling about living with an ostomy, stomal and peristomal skin care, and the skills needed to change an ostomy pouch [4]. The ability to manage an ostomy appliance independently is the single most important factor for predicting a positive psychological adjustment to life with a stoma after cancer surgery [5-7]. Practicing the skills related to a full change of an ostomy pouch is a first step towards independence and acceptance following stoma surgery [4, 5, 8].

Key skills include; emptying the pouch, removing the pouching system, cleaning and observing the stoma and the peristomal skin, and preparing and applying the new appliance [8]. The patient's ability to collectively perform these skills is defined as stoma self-care [9]. Stoma self-care education requires cognitive, affective, and psychomotor learning [10]. Cognitive learning refers to the individual's ability to understand the information conveyed, and affective learning refers to their attitudes and feelings toward the stoma. Affective learning begins with willingness to view the urostomy, leading to participation in stoma care and the recognition of the advantages of independence linked in self-care. Psychomotor learning refers to the ability to perform the practical skills necessary to change the appliance and obtain a mental image of how the skills are performed.

Everyday life and hidden aspects
The creation of a urostomy impacts multiple aspects of daily life. These changes influence urine elimination, body image, personal care, sexual and psycho-social health and health-related quality of life. Several studies have demonstrated that new stoma patients have many physical and psychological needs that remain unmet at the time of discharge from their initial hospitalisation [11]. Concerns regarding body image and sexual function, pain/rashes around the stoma and challenges regarding the appliance are prevalent [12-14]. These factors can lead to additional clinic visits or phone service requirements, stoma-related complications and impaired health-related quality of life [15-17]. The stoma nurse or therapist may be available in small class sessions or one-on-one consultations before and after surgery. In these sessions, other perspectives of living beyond stoma surgery are often put forward by the patient or family members. The aspects discussed here describe the *hidden role* of the stoma nurse and involve individual needs, mostly about the fear of recurrence, loneliness, lack of self-esteem due to sexual aspects, lack of confidence with the stoma and a change in their social position. Both women and men report a significant amount of unmet needs [18]. Women especially request information regarding sexual aspects, and the preferred staff member to approach is the clinical nurse specialist [16]. However, surprisingly few ask for counselling or resources outside the hospital service despite indicating an unmet need [19].

Pre-operative psychological support
Special attention should be paid to patients with a history of mental illness or other cognitive impairments, as they are at higher risk of psychological problems or delirium post-operatively [20]. Pre-operative psychological support can allow patients to express and work through any emotional concerns, feelings and anxiety about their surgery and the urostomy [21]. After surgery, counselling can provide information to help the patient understand and gain control of the new lifestyle situation. Thus, it is important to create an environment in which the patient and their relatives feel free to express themselves and ask any questions on their own terms. This helps to reduce stress and anxiety and increases trust and cooperation between the patient, the stoma nurse and other staff members [6].

A new emerging multi-modal, multi-disciplinary, and goal-oriented (instead of the traditional disease-oriented) approach is ideal when deciding whether to surgically intervene in elderly patients with multiple comorbidities and impairments. Thus, it is pivotal to establish patients' goals and priorities as well as a shared decision-making process involving the prehabilitation team (e.g. stoma nurse, dietician, physiotherapist, anaesthesiologist and surgeon). Here, the nurse supports the patient and their family in discussing the benefits and risks of the proposed stoma surgery, as well as potential alternative definitive treatments. Identification of the patient's goals, hopes and their surgical expectations ensure adequate informed consent and a tailored and appropriate treatment [22].

After the shared clinical decision process, patients should be informed about and motivated to take on the important role they have in maximising their early post-operative recovery and regaining physical function and confidence in stoma care. Giving patients information both before and after surgery will help them to gain control of their situation and cope better physically and mentally.

Stoma care education
It is well known that coping strategies following urostomy surgery are improved when patients receive relevant information and education on stoma care and a care plan based on a shared decision process [23-25]. Patients report that education should be provided by a nurse with expertise in ostomy care or a stoma therapist, and stoma supportive care (pre- and post-operatively) is highly requested [21]. Unfortunately, there is little published evidence on the value of pre- and post-operative educational sessions, although exiting evidence indicates that the positive effect of pre-operative stoma education on post-operative stoma self-care is sustainable up to one year [26].

The literature demonstrates a discussion as to whether stoma care should be managed by well-informed and experienced ward nurses or specialised stoma care nurses in practice. Across Europe, there are different approaches depending on the local pathway and the investigated aspect of stoma care [27]. To decide the best path to assure quality of care, standardised supportive care plans should be available to guide the process and allow for key areas where further interventions can be identified, and the Urostomy Education Scale (UES) can facilitate this process [17]. However, the use of standardised care plans is not intended to offer a 'one size fits all' approach to care and patients' individual needs must be considered and used to individualise care plans to the patient's capacity [6]. So far, there are no available evidence-based standard care plans, although international societies in the field of stoma care have provided practice guidelines and recommendations that could encourage their construction. However, there is an urgent need for international consensus on uro-stoma education plans to support patients and spouses, and the UES can facilitate and guide the development of evidence-based care plans.

The Urostomy Education Scale
The UES is a highly validated and reliable scale developed with support from the EAUN. It is cross-culturally validated and translated to several languages (Figure 1). The scale is based on internationally recognized minimum standards in stoma care categorised into **seven skills** considered necessary for changing a uro-stoma appliance [17, 27, 28]. This tool documents the progress of a patient's level of stoma self-care during the teaching process and has the ability to involve the patient already in the prehabilitation setting by introducing the scale as an instrument to communicate with the patient and guide the practical teaching process based on the patients physical and mental capacity. Moreover, the scale can help identify specific skills which need increased awareness in a day-to-day care plan.

The seven skills are reaction to the stoma, removing the stoma appliance, measuring the stoma diameter, adjusting the size of the urostomy diameter in a new stoma appliance, skin care, fitting a new stoma appliance and the procedure for emptying stoma collection devices.

Each skill is rated on a four-point scale ranging from 0 to 3 points depending on the patient's need for support. The total score ranges from 0 to 21 points, with higher scores indicating a higher level of independence to perform stoma self-care (Figure 1). Detailed information of the UES has been published previously [17, 27, 28].

To improve stoma self-care skills, continuously daily education and adjustment is recommended by the stoma therapist societies. This often puts stoma therapists under tremendous pressure, as hands on teaching and practical training is time consuming and there is no quick fix.

Therefore, practical (hands-on) training with a stoma appliance and testing different appliances in the prehab setting is of high importance for familiarising a patient with the upcoming change of bodily functions, at least on a contractual level. It may be an abstract situation for both the patient, family or nurse to begin with, but those motivated will become quite competent with self-care skills [26].

Tips and tricks
To improve the level of self-efficacy, it is important to consider:

- Goal-setting in a shared decision process with relevant clinicians
- Focus on interventions to enhance the specific stoma self-care skills needed to change a stoma appliance
- Provide continuous individualised goal-directed stoma education pre- and post-operatively
- Continuous access to supportive care pre- and post-operatively as well as in the rehab setting is needed by the patients and spouses, who rate it as highest importance for ultimately performing an independent change of a stoma appliance

Conclusion
The role of the nurse and the stoma therapist has significantly changed over the past decade, perhaps due to the "hidden role during hospitalization", to becoming a key player in preparation for surgery! Measuring stoma self-care skills is possible and the UES can promote a common language between patients, ward nurses, stoma-nurses in both the primary care setting and rehab setting, and secure adequate support and follow-up. Moreover, the UES can initiate early involvement of the patient, inform practice and improve targeted and tailored stoma care. Stoma prehabilitation is effective and can sustainably improve stoma care self-efficacy. Thus, the Stoma Therapist has become a key player and a highly recognised contributor in the pre-operative setting, and pivotal to the patient's health-related quality of life.

References can be requested from the corresponding author.

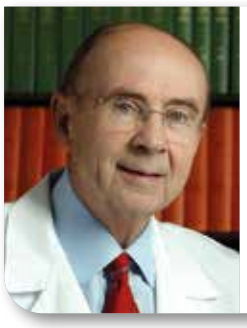
Skill	0 points	1 points	2 points	3 points	Score
1. Reaction to the stoma	The patient shows no interest in/has difficulty coping with the stoma.	The patient has seen and touched the stoma on the initiative of the nurse	The patient has seen and touched the stoma on his/her own initiative	The patient copes with the stoma and is pre-paring for the future	
2. Removing the stoma appliance	The nurse removes the stoma appliance	The patient needs assistance to remove the stoma appliance	The patient needs verbal guidance to remove the stoma appliance	The patient can remove the stoma appliance independently	
3. Measuring the stoma diameter	The nurse measures the stoma diameter	The patient needs assistance to measure the stoma diameter correctly	The patient needs verbal guidance to measure the stoma diameter correctly	The patient can meas-ure the stoma diameter correctly independently	
4. Adjusting the size of the urostomy diameter in a new stoma appliance	The nurse cuts the size of the urostomy diameter	The patient needs assistance to cut the size of the urostomy diameter	The patient needs verbal guidance to cut the size of the urostomy diameter	The patient can cut the size of the urostomy diameter inde-pendently	
5. Skin care	The nurse cleans and dries the skin	The patient needs assistance to clean and dry the skin	The patient needs verbal guidance to clean and dry the skin	The patient can clean and dry the skin independently	
6. Fitting a new stoma appliance	The nurse fits a new stoma appliance	The patient needs assistance to fit a new stoma appliance	The patient needs verbal guidance to fit a new stoma appliance	The patient can fit a new stoma appliance independently	
7. Emptying procedure (Emptying bag and attaching/detaching night bag)	The nurse performs the emptying procedure	The patient needs assistance to perform the emptying procedure	The patient needs verbal guidance to perform the emptying procedure	The patient can perform the emptying pro-cedure independently	
Total points					

Figure 1. The Urostomy Education Scale

Saturday, 11 March 09:25 - 09:35
Plenary Session: Locally advanced BCa: Misconception of informed consent
eURO Auditorium 1, Yellow Area

Nerve-sparing radical prostatectomy: A European discovery?

Let's take a look back in time



Prof. Patrick Walsh
James Buchannan Urological Institute Johns Hopkins Hospital (US)

pwalsh@jhmi.edu

The first operation for the cure of prostate cancer was performed via the perineal approach by Hugh Hampton Young at Johns Hopkins Hospital in 1904. In 1947, Terence Millin, an Irish urologist who worked in London, pioneered the retropubic approach. [1,2)] Although surgery proved effective in controlling cancer, it had substantial morbidity: impotence (90-100%), total incontinence (10-25%), and major bleeding, which was often life threatening when performed retropubically. For this reason, when treatment with external beam radiation began in the 1960s, surgery rapidly fell into disuse.

In 1974, I arrived at Johns Hopkins Hospital to assume the position as the third director of the James Buchannan Urological Institute. When I arrived, I was surprised to learn that radical prostatectomies were rarely performed, even at the centre where it had been pioneered. Over the prior decade, I had trained at outstanding centres on the east and west coast but had never heard anyone suggest that these complications might be preventable. They were considered the price a patient paid for a chance at cure. At this time, I wondered what caused them and if it was possible to prevent them. As a successor of Hugh Young, I felt the personal responsibility to solve this problem.

I began by looking into the anatomy of the dorsal vein complex and Santorini's plexus and was surprised that had never been charted. Also, although the location of the cavernous nerves was not known, because all men were impotent, it was universally assumed that the nerves must run through the prostate. And only later did it become clear that men were incontinent because the location of the sphincter responsible for passive urinary control was not known. Why were we so ignorant? Because of limitations in using the adult cadaver. In the post mortem state, the abdominal contents compress the bladder and prostate into a thick pancake of tissue and formalin preservatives dissolve the fatty tissue planes making dissections impossible. So, I decided to use the operating room as an anatomy laboratory.

Urologists were reluctant to operate because of the life threatening bleeding. So, this was the first problem I tackled. While performing radical cystectomies and the rare radical retropubic prostatectomy, I identified a common trunk of vessels over the urethra. This led to a technique that reduced blood loss dramatically, providing a safer and more thorough cancer operation. [3] Soon thereafter a patient came back to see me and told me that he was fully potent. How could that be? At that time everyone believed that because the nerves must run through the prostate, it would be impossible to preserve potency. But from this one patient I knew that was not true, but where were the nerves? The answer was not available in any textbook. In March 1977, my wife and I attended an important international conference and the night before the meeting we went downtown to a restaurant. As we were about to sit down, I noticed an older man standing behind the maître d' who looked very lonely. For the first and only time in my life, I went up to a total stranger and asked him if you would like to join us for dinner and why he was in town? It turned out that he was attending the same meeting and had been advised by the concierge, like us, to go to this same restaurant. His name was Pieter Donker, the Professor and Chairman of Urology at the University of Leiden in the Netherlands, whose specialty was neurourology. (Figure 1) After a wonderful dinner and conversation, I thought that was the end of it.

Professor Pieter J. Donker 1914-1999

But four years later, 4000 miles away we met again. He was now retired and I was invited by Udo Jonas, Donker's successor, and my good friend Fritz Schroder to spend five days at the Boerhaave Surgical Congress in Leiden, operating, lecturing, and visiting laboratories. Finally, on my last day, Friday February 13, 1981, my 43rd birthday, my host told me that Dr. Donker appreciated my kindness a few years earlier and wanted to return the favour by taking me to see the windmill museum in Leiden. When I met Donker, I asked him what he was doing now that he was retired and learned that he was working in an anatomy laboratory. Without any premonition of what I was going to see, I asked to go there instead.

In the laboratory, he took out a stillborn infant, a dissecting microscope, and his drawings. When I asked what he was doing, he said that he was dissecting out the nerves to the bladder. When I asked why, he said this it had never been done before, for the reasons I've given previously. When I asked about the location of the cavernous nerves, he said he had never looked. Three hours later, we located them outside the prostate. [4] Figure 2. From this observation, we knew where these microscopic nerves were located in a foetus. The trick was how to identify them in the adult male pelvis. It was like having the schematic to your television set and trying to find some tiny filamentous wires inside.

I returned to Hopkins and once again used the operating room as an anatomy laboratory. While performing a radical prostatectomy in October1981, I noticed that the capsular arteries and veins of the prostate were located in the exact site where the nerves were present in our foetal dissections. I speculated that these vessels might provide the scaffolding for these microscopic nerves and that this neurovascular bundle could be used as the macroscopic landmark to identify them in the operating room. (Figure 3.) This observation fulfils the advice of Dr. Merrill Sosman, the Peter Bent Brigham radiologist "You only see what you look for and you recognise only what you know".

In March, 1982, Donker and I met again. He had performed more foetal dissections and microscopic step-section reconstructions that confirmed our original anatomical observation. I told him about my idea of the neurovascular bundle and he agreed with the suggestion. When I returned home, I performed a radical cystectomy on a 60-year-old man. I had never seen or heard of a patient who was potent after a cystectomy but on his 10th postoperative day he awoke with an erection! I now knew that we were on the right track.

Using that technique, on April 26, 1982, I performed the first nerve-sparing radical prostatectomy on a 52-year-old man. He died 35 years following surgery, cancer free, having lived a normal life. To confirm our findings, we conducted further anatomical studies by removing en bloc the pelvic organs from a male cadaver that had been perfused with Bouin's shortly after death, prepared 10,000 whole mount step sections, and performed a 3D reconstruction. This confirmed the constant association of the cavernous nerves with the capsular vessels to the prostate. [5]

The final piece of the puzzle that remained was the fascia surrounding the prostate. Although everyone who performed prostatectomies was familiar with Denonvilliers' fascia, little or nothing had been written about the layers of the lateral pelvic fashion. However, based upon a whole mount step-sectioned prostate that was harvested by Dr. Herbert Lepor (US) when he was a resident, it became clear that the lateral pelvic fascia was divided into two layers, the prostatic fascia and levator fascia with the neurovascular bundle positioned between them and that if nerve sparing is properly performed, the prostatic fascia must remain on the prostate. Armed with this information, it also became possible to excise the neurovascular bundle thus providing wider margins of excision than ever before. This is why I called it an anatomic radical prostatectomy: nerve-sparing when possible; wide excision when necessary. Dr. Joseph Eggleston (US)., the director of surgical pathology, studied surgical specimens removed by the perineal, standard retropubic, and nerve-sparing approaches and concluded that nerve-preservation did not compromise the adequacy of the surgical margins. [6]

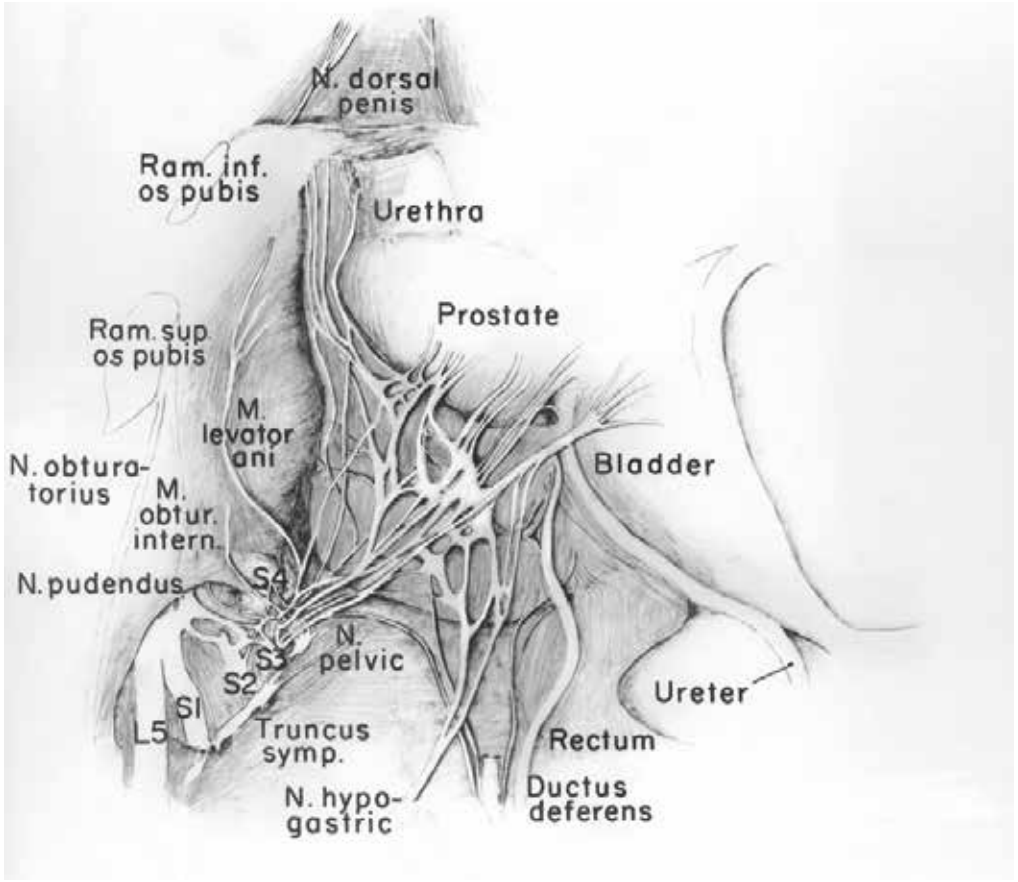


Figure 2. Optional: Dissection of left pelvic plexus in stillborn male. Bladder has been retracted to right. Peritoneum, pelvic vessels, pelvic fascia and pubic symphysis have been removed.

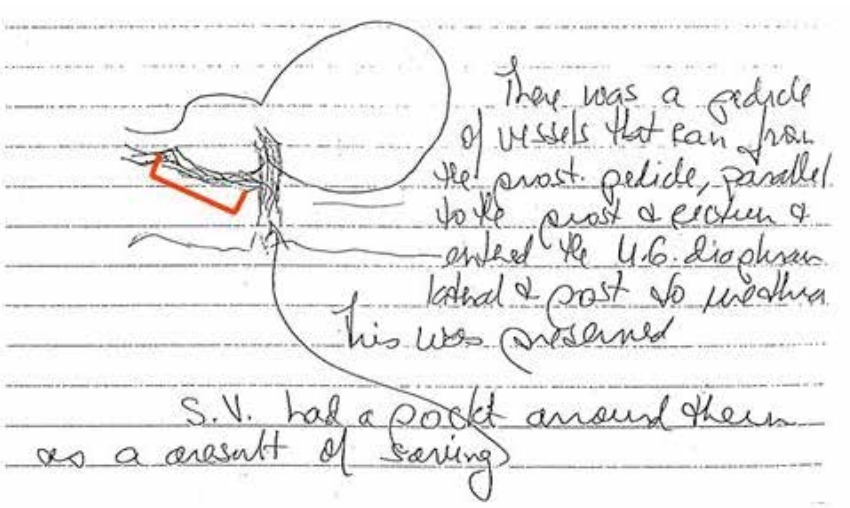


Figure 3. October,1981: author's intraoperative drawing of the capsular vessels of the prostate that travelled in the same location as the cavernous nerves in the foetus.

Based on these discoveries, over the next decade radical prostatectomy became the most common form of treatment for localised prostate cancer in the U.S. In 1982, only 7% of men with prostate cancer underwent surgery. However, by 1992, with the availability of a safer procedure that had fewer side effects, and PSA screening to identify more men with curable disease, 70% of men ages 50-59 and 55% ages 60-69 underwent surgery and that year 100,000 operations were performed. A decade later, deaths from prostate cancer had declined by 33%, greater than for any other cancer in men or women over the same time. What would have happened without Pieter Donker's contribution?

In closing, this discovery would not have happened if: a patient had told me that he was potent following surgery and I had not listened and wondered why; and I had not invited an older, lonely man who was a total stranger to dinner; and I had not met him four years later 4000 miles away; and I had gone to the windmill museum and not asked to see what he was doing in retirement. If you asked Yogi Berra to explain how all this happened he would say that "it's too much of a coincidence to be coincidental". If you asked Albert Einstein, he would say, "coincidence is God's way of remaining anonymous". And if you asked St. John Paul II, he would say that "in divine providence nothing is a coincidence". That is what I believe.

References:

1. Young HH: The early diagnosis and radical cure of carcinoma of the prostate: being a study of 40 cases and presentations of a radical operation which was carried out in 4 cases. Bull Johns Hopkins Hosp 1905; 16: 315.
2. Millin T: Retropubic Urinary Surgery. London: Livingston 1947.
3. Reiner WG and Walsh PC: An anatomical approach to the surgical management of the dorsal vein and Santorini's plexus during radical retropubic surgery. J Urol 1979; 121: 198.
4. Walsh PC and Donker PJ: Impotence following radical prostatectomy: insight into etiology and prevention. J Urol 1982; 128: 492.
5. Lepor H, Gregerman M, Crosby R, Mostofi FK and Walsh PC: Precise localization of the autonomic nerves from the pelvic plexus to the corpora cavernosa: a detailed anatomical study of the adult male pelvis. J Urol 1985; 133: 207.
6. Walsh PC, Lepor H and Eggleston JC: Radical prostatectomy with preservation of sexual function: anatomical and pathological considerations. Prostate 1983; 4: 473.

Friday, 10 March 11:00 – 11:15
7th International Congress on the History of Urology
Yellow Area, Amber 7

EAU journey on advocacy on prostate cancer

Building alliances and preparing for the future

Prof. Hein Van Poppel
EAU Policy Office Chairman
Urology – KULeuven (BE)

hendrik.vanpoppel@kuleuven.be

In 2021 the creation of the EAU Policy Office was approved at the EAU General Assembly during the EAU22 Virtual Congress in Amsterdam. This was a significant milestone in ensuring that the field of urology is included in political discourse across Europe. The role of the EAU Policy Office is to advocate, that is, to influence policy and legislation on behalf of urologists on issues that have an impact on urological care, to the benefit of and in partnership with patients.

A key advocacy priority for the Policy Office has been the inclusion of Prostate Cancer into Europe's Beating Cancer Plan. On World Cancer Day, 4 February 2020, the President of the European Commission, Ursula von der Leyen, and Health Commissioner, Stella Kyriakides, jointly announced Europe's Beating Cancer Plan. The plan would cover the whole pathway of cancer, from prevention and early detection to treatment and care to survivorship and quality of life, but it would have a key focus on prevention and early detection.

President of the European Commission, Ursula von der Leyen, on World Cancer Day.

The previous European cancer plan dated back to the early 1990s, resulting in the EU Council 2003 Recommendation on Screening, but Prostate Cancer received very little attention.

Why did the EAU decide to act?

1. Prostate Cancer is an important health problem
Prostate cancer is the most prevalent male cancer in the European Union, with approximately 450,000 men being diagnosed each year. Currently one in seven men are diagnosed with prostate cancer by the time they are 74 years old.

2. Prostate Cancer is killing more men than before
The 27 EU member states are estimated to experience a 55% rise in relative mortality rates from prostate cancer by 2040 due to demographic change. [1] Currently in Germany it is now the number two male cancer killer behind lung cancer. In the Baltics and Scandinavian countries it is the number one male cancer killer.

3. Quality of life and health system expenses
An important benefit for European publicly funded healthcare systems is that the early detection of prostate cancer saves costs compared to later stage prostate cancer. Even though they need to be repeated, PSA tests and a good quality mpMRI scans are cheaper than treating advanced and metastatic disease, which only marginally improves survival but greatly impacts quality of life. While the cost of robot-assisted radical prostatectomy, which is one of the most used treatments for early prostate cancer, does not exceed €15,000 per patient, the cost of managing patients with castration-resistant, non-curable prostate cancer can be estimated at approximately €140,000 per patient per year, sometimes reaching €300,000 during a patient's lifetime in Western countries. [2,3,4]

4. Screening decreases mortality
The European Randomised Study of Screening for Prostate Cancer (ERSPC) demonstrates that PSA screening reduces disease-specific mortality at 11 years by 21%, which is equivalent to one death prevented per 781 men invited for screening, or one per 27 instances of prostate cancer detected. The evidence shows that after 20 years of follow-up the number of patients needed to screen and diagnose Prostate Cancer decreased to 101 and 13 respectively to prevent one prostate cancer death. [5,6] This decrease in death becomes more and more significant with longer follow-up (A 44% decrease is seen after 14 years of follow-up in the Gothenburg cohort (Hugosson), and 52% after 19 years in the Rotterdam cohort of the ERSPC) . [5,7]

Progress has also been made in reducing over-diagnosis through better use of PSA: age-related PSA, PSA density, PSA velocity, availability of free risk calculators (PCPT and ERSPC) +/- molecular biomarkers [8] and the use of MRI before biopsy, which decreases the number of biopsies and detects more significant and fewer insignificant cancers. [8,9]

We can reduce overtreatment through active surveillance in 65% of low and intermediate risk, and the use of Nomograms MAP (age, PSA, GG, MRI volume, PIRADS, MRI ECE). [10]

5. Opportunistic Screening does not work
The PSA test has been available for over 30 years and is now widely available on the European market. With virtually no organised PSA early detection programmes, the test is currently used in most countries in an opportunistic manner. The evidence demonstrates that opportunistic testing does not have an impact on decreased mortality, is costly, and can be associated with the harms of overdiagnosis and treatment. [11]

What are the EAU's advocacy goals?
The aims of the EAU's advocacy are to encourage a more rational and organised use of PSA testing using risk stratified approaches to decrease prostate cancer deaths, stop increasing rate of too-late diagnosis, stop costly and inefficient opportunistic testing and to improve the quality of life of prostate cancer patients.

The first step to achieve this was to update the White Paper on Prostate Cancer in June 2020 to influence the EU's Beating Cancer Plan. The White Paper built on previous publications from 2019 and 2017. In November 2020, we organised a virtual

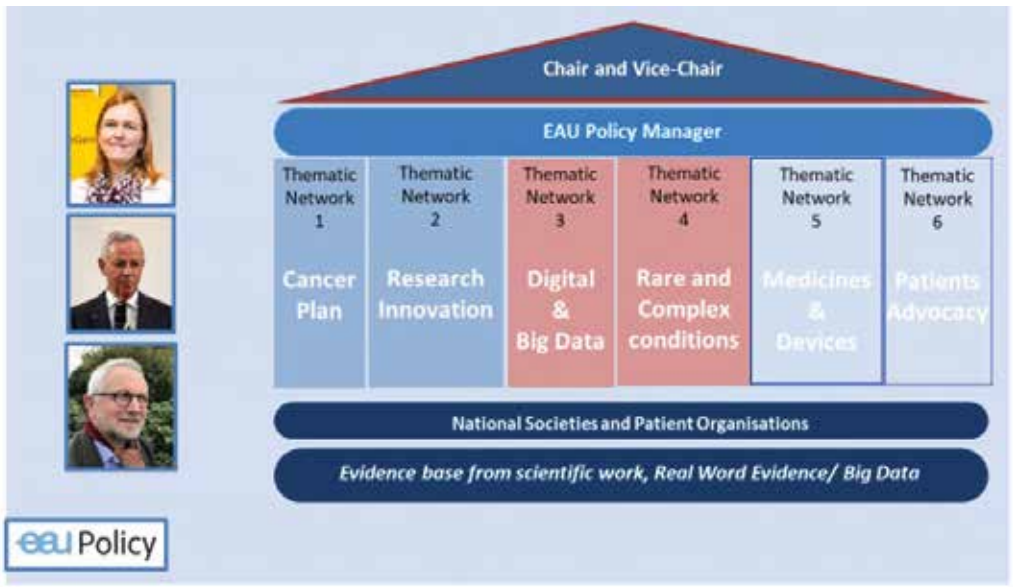


Fig. 1 Structure of the EAU Policy Office

The Czech minister of health, Mr. Vlastimil Valek, signing the Prague Declaration on Prostate Cancer at the Prostaforum during the Czech EU Presidency,

European Prostate Cancer Awareness Day (EPAD) which focused on the early detection recommendations in the White Paper. The following year, the EAU published recommendations: PSA Testing as Part of a Risk-Adapted Early Detection Strategy for Prostate Cancer, which included a risk adapted algorithm. [12]

We worked closely with members of the EAU Patient Advocacy Group (EPAG), such as EuropaUomo and the European Cancer Organisation (ECO), ensuring a joint approach to advocacy and fostering awareness on this shared concern. We met in person with a number of Members of the European Parliament (MEPs) to discuss our recommendations as they compiled their report on the Beating Cancer Plan.

The EAU collaborated with other stakeholders and with ERSPC to provide information to scientists and academics involved in the evidence review on Prostate Cancer screening commissioned by the Chief Scientific Advisors of the European Commission. We also collaborated with industry funded advocacy campaigns such as the Let's Talk Prostate Cancer campaign to raise awareness.

The support and engagement of National Urological Societies was critical for the success of the advocacy campaign, many of whom contacted their national MEPs and Department of Health or screening committee or public health agency. The National Societies collaboration has been most helpful during the Presidencies of the EU Council. Most recently, the Czech Urological Society collaborated with their national agencies to organise the Prostaforum in Prague in the auspices of the Czech EU Presidency, resulting in the Prague Declaration on Prostate Cancer. Their minister of health, Mr. Vlastimil Valek, also chaired a meeting in December 2022 where the EU Council Screening Recommendations were updated to include Prostate Cancer.

What did Europe approve in December 2022?
When the new screening recommendations were published, prostate cancer was included on the list of new cancers to be addressed. Specifically, the EU Council recommended that countries should "consider a stepwise approach, including piloting and further research, to evaluate the feasibility and effectiveness of the implementation of organised programmes aimed at ensuring appropriate management and quality on the basis of prostate-specific antigen (PSA) testing for men, in combination with additional magnetic resonance imaging (MRI) scanning as a follow up test."

The future? PRAISE-U
What does this mean in practice? The EAU is now leading a consortium that has been funded by the European Commission in EU4Health to support the implementation of the EU Council Recommendations. This project will perform a needs assessment, develop guidelines and quality assurance mechanisms, and support 5 pilots across the EU. More news on this will follow the start of the project on 1 April 2023.

References:

1. European Cancer Information System, Prostate Cancer Incidence and Mortality Estimates, 2022, Found at : https://ecis.jrc.ec.europa.eu
2. Cornford, P., et al., EAU-ESTRO-SIOG Guidelines on Prostate Cancer. Part II: Treatment of Relapsing, Metastatic, and Castration-Resistant Prostate Cancer. Eur Urol, 2017. 71(4): p.630-642. 47
3. Forsmark, A., et al., Health Economic Analysis of Open and Robot-assisted Laparoscopic Surgery for Prostate Cancer Within the Prospective Multicentre LAPPRO Trial. Eur Urology 2018. 74(6): p. 816-824. 48
4. Wu B, et al., Cost of care for patients with metastatic castration-resistant prostate cancer initiating on docetaxel versus oral targeted therapies in the United States. Journal of Clinical Oncology, 2018. 36(30, suppl.): p. 88
5. Osses, D.F., et al., Results of Prostate Cancer Screening in a Unique Cohort at 19yr of Follow-up. Eur Urol, 2018
6. Minozzi S, et al. European Code against Cancer 4th Edition: Process of reviewing the scientific evidence and revising the recommendations. Cancer Epidemiol 39 Suppl 1:S11-9, 2015
7. Hugosson J, Månsson M, Wallström J, Axcrona U, Carlsson S, et al., for the GÖTEBORG-2 Trial Investigators, Prostate Cancer Screening with PSA and MRI Followed by Targeted Biopsy Only. N Engl J Med 2022; 387:2126-2137 DOI: 10.1056/NEJMoa2209454
8. Mannaerts CK, et al. Eur Urol Oncol 2018;1:109–17
9. Amin A, et al. J Urol 2020;203:910–7
10. Lantz A, et al. Eur Urol Oncol 2022;5:187–94
11. Arnsrud Godtman R, et al. Eur Urol. 2015;68(3):354-60
12. Van Poppel H, et al. Prostate-specific Antigen Testing as Part of a Risk-Adapted Early Detection Strategy for Prostate Cancer: European Association of Urology Position and Recommendations for 2021. Eur Urol (2021), https:// doi.org/10.1016/j.eururo.2021.07.024

Sunday 12 March, 13:50 - 14:00
Thematic Session: The road to evidence-based European policy on early detection of prostate cancer
Yellow Area, eURO Auditorium 1

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