European Urology Today

EAU22 Congress News

37th Annual Congress of the European Association of Urology

Vol. 34 No. 2 - June/July 2022

EAU22 in Amsterdam: Special in so many ways

Our Secretary General looks ahead to this year's Annual Congress

By Chris Chapple
EAU Secretary General

It is a great pleasure to welcome you to the 37th Annual EAU congress, held in Amsterdam from 1-4 July. It seems so long since we last had the opportunity of meeting face-to-face, and we very much look forward to welcoming you to Amsterdam. This is the first regular congress since EAU19 in Barcelona, over three years ago.

Clearly, the covid crisis has had a significant impact on everybody, and we are sure that you, like us, are looking forward to meeting face-to-face. We realise that several of our friends and colleagues will still not be able to attend due to current restrictions and we will miss them.

"We can now offer a congress experience to those who are unable to join us while still creating a live and interactive in-person event for those who travel to Amsterdam."

Aside from a pleasurable reunion with all of our members, colleagues and friends, a congress in Amsterdam marks a return to a city that has played an important part in the EAU's foundation and development. Not only was Amsterdam the site where the association's founding statutes were signed in 1973: it was also the site of the 1990 congress that opened the door to new visitors and members after the fall of the iron curtain and the opening up of Europe.

EAU22 is our first so-called 'hybrid' annual congress that we have offered our delegates. We are welcoming visitors and faculty in-person in Amsterdam, while also using lessons learned from the past two virtual congresses to reach new audiences. We can now offer a congress experience to those who are unable to join us while still creating a live and interactive in-person event for those who travel to Amsterdam.

The EAU is adapting with the times and amending its services to continue meeting the needs of its members. Beyond our Annual Congress, we will continue to offer a combination of online and in-person events to address the needs of all of our members in accessing educational resources and developing their careers.

Congress highlights
The most notable change for our annual congress this year is that it takes place on four, rather than five days. The congress will now start with Plenary Sessions on the first day and end after a full day of scientific sessions on Monday. This more concentrated congress structure was introduced for EAU21 and is now used as a template for the in-person congress as well.

At the congress, there will be 2,580 presentations by 900 speakers, 56 courses and hands-on training programmes by the European School of Urology, numerous industry sessions and workshops. Each of the eight Plenary Sessions will end with an opportunity to 'meet the experts' in the post-plenary session and ask some further questions you might have after their talks. Several of the plenary sessions are preceded by a game changer session with the very latest developments and trial results so keep an eye on the scientific programme for those last-minute additions.

The EAU22 Exhibition will feature over 150 booths. As ever, you will be able to pick up a hard copy of the latest EAU Guidelines, this year's congress gift and a variety of other publications at the EAU Booth, so be sure to visit booth D60 for any questions you might have.

Prof. Chapple speaking at the 34th Annual EAU Congress in Barcelona, in March 2019. EAU22 in Amsterdam will be the first regular, in-person Annual Congress in over three years

EAU22 is a rare summer congress: a chance to enjoy Amsterdam in the sun

We also like to cater for specific parts of our membership (and beyond!). Parallel to EAU22 we have EAUN22, the 22nd International Meeting of the European Association of Urology Nurses. We have a day-long programme dedicated to young urologists, YUORDay22 on the Saturday. This brings together the Young Urologists Office (YUO) and the European Society of Residents in Urology (ESRU) for a session that addresses the career and educational needs of younger urologists. YUORDay22 also features the hotly contested Guidelines Cup, a competition which will determine which EAU junior members know the EAU Guidelines the best.

For the first time we have an in-person edition of the Patient Day, a special programme devised by the recently formed EAU Patient Office. On Monday the 4th, there will be a series of patient information sessions, roundtable discussions with patient representatives and other activities designed to bring further awareness to the patient's perspective.

Since it would be impossible to attend every session, the daily highlights will be summarised every day in the EAU TV news shows. Key opinion leaders will discuss the presented developments in the on-site TV studio. These will be broadcasted online that same day.

"Several of the plenary sessions are preceded by a game changer session with the very latest developments and trial results so keep an eye on the scientific programme for those last-minute additions."

Anniversary
We are using this return to Amsterdam after 32 years to mark the beginning of an anniversary year for our association. With important founding events taking place in both 1972 and 1973, we felt that starting an anniversary year in Amsterdam and ending it in Milan for EAU23 was a suitable way to commemorate this 50-year golden jubilee.

Don't miss this year's Opening Ceremony. Of course, this is where the best and brightest are honoured with the EAU's prestigious awards, but this year it will also mark the start of this anniversary year with special talks and the unveiling of our anniversary logo. You can read all about the 50th anniversary activities at EAU22 and how the association was founded in 1972-73 on page 3.

So, I once again welcome you, on behalf of the entire EAU, to our Annual Congress, whether you are joining us in Amsterdam or following from across the world. Look forward to four days of essential and up-to-the-minute latest urological science, but also a chance to meet like-minded colleagues and exchange experiences in a truly international forum.

European Urology Today

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European Association of Urology

Colophon

Patient Day at EAU22

Collaborations to optimise care and treatment

After the success of the inaugural *Patient Day* last year, the EAU Patient Office is pleased to welcome delegates to this year's edition at EAU22. *Patient Day* will take place on Monday, 4 July 2022 in historic Amsterdam, the Netherlands. Expect no less than vital insights into the patients' perspective and contemporary updates on their urological care and treatment.

With the core aim of stimulating innovations and promoting positive impact, Patient Day is made possible through the collaboration with the European Cancer Leagues (ECL), eUROGEN, Europa Uomo, the International Kidney Cancer Coalition (IKCC), the World Bladder Cancer Patient Coalition (WBCPC) and the World Federation for Incontinence and Pelvic Problems (WFIPP) Patient Day encourages open dialogue, underscores the needs of patients and their care support system, and incorporates the crucial role of health care professionals into patient-centred care.

Consisting of themed sessions led and co-created by patients and patient advocates we encourage you to come along and hear from those at the sharp end of surgery. Learn how to best meet patients needs.

Explore what the Patient Day has to offer you via **www.eau22.org/patients**.

Check out the Patient Information Award winners in the Awards spread found on pages 4 and 5.

EAU Patient Day is supported by an unrestricted grant from Pfizer Oncology.

Monday, 4 July, 07:45 - 17:30
Patient Day
Grey Area, Room Emerald

EAU22 | AMSTERDAM 1-4 July 2022

Patient Day

Monday, 4 July
Grey Area, Room Emerald

07.45 - 08.45	Patient poster presentations
09.00 - 10.30	Roundtable: Sustainable continence care
10.45 - 11.45	Roundtable: Fatigue in prostate cancer patients
12.00 - 13.00	Functional urology
13.15 - 14.15	Kidney cancer session
14.30 - 15.30	Bladder cancer session
15.45 - 16.45	Prostate cancer session
17.00 - 17.30	Life after cancer

Visit **eau2022.org** for more information.

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@EAUPatientInformation @EauPatient

eauPI Patient Information

The EAU is celebrating its 50th Year

Amsterdam Congress marks the start of anniversary year for the Association

By Loek Keizer

Delegates in Amsterdam won't be able to miss the fact that the European Association of Urology is entering its fiftieth year. From the opening ceremony onward, special attention will be drawn to this golden jubilee. The EAU is celebrating this milestone in the period between its two Annual Congresses EAU22 (Amsterdam) and EAU23 (Milan).

The first steps to create the EAU were taken in 1972, with the final constituent assembly taking place in Amsterdam in 1973. Another major milestone for the EAU's history is its first congress, which took place in 1974. As a result, the EAU decided to celebrate its golden jubilee in the period between EAU22 in Amsterdam and EAU23 in Milan, rather than selecting a single date to mark the occasion.

Activities in Amsterdam
During the opening ceremony of EAU22 **(Friday, 1 July, 18:00-19:45)** the anniversary will be officially kicked off. The anniversary logo will be unveiled, and the ceremony will conclude with special attention to the occasion and some of the people who made it possible.

During the congress, delegates can visit the Congress History Area, in the Green Area, for a video presentation on the five decades of the EAU. Not only will it feature highlights from the EAU's history but also place those events in the context of contemporary events and developments. In addition, the EAU History Office's special session will feature guest speaker and former Secretary-General of the EAU, Prof. Frans Debruyne for his personal take on the EAU's 50 years of excellence in urology. **(Saturday, 2 July 11:00-13:30).**

After EAU22 winds down, the EAU will continue to fly its anniversary logos until the end of EAU23. In addition, regular updates on social media will offer highlights from each of the fifty years as we approach EAU23. In every edition of EUT between congresses we will examine another episode of the EAU's long history.

See you in Milan!
The end of the anniversary celebrations will be marked at EAU23 with a special Congress on the History of Urology and the presentation of a special book, tentatively called *EAU:50*. The book will present an overview of the EAU's history so far, but also act as a "State of the Association" and reflect on how far the association has come and where it is going.

The 7th International Congress on the History of Urology marks the first such event since its sixth iteration held in Munich in 2016 (also in conjunction with that year's Annual EAU Congress). It will be held on the first day of EAU23 and free to attend for all EAU23 delegates. More details to be announced on **www.eau23.org** and future editions of *European Urology Today*!

50 years of the EAU (1972-202... 3?)

Selecting a single date to commemorate the founding of a complex international association like the EAU can be a challenge. The process of establishing the association took place over two years, and the first congress took place later still.

Already in 1970, prominent European urologists discussed the need for establishing a European society, a continent-wide counterweight to the American Urological Association, a much older (1902) and established society at the time. The first concrete steps in the foundation of the EAU took place in the wings of the 66th Congress of the Association Française d'Urologie (AFU) in September 1972. Prof. Giorgio Ravasini (1905-1992), chair of urology in Padua assembled ten urologists from across Europe for a lunch at the urology department of Hôpital Necker in Paris.

It was at this lunch that the ambitions for what would become the EAU were discussed and put on paper: the society would be headquartered in Switzerland, there would be no presidency but a committee and it would be up to Prof. Willy Gregoir (1920-2000) of Brussels to draw up the statutes. Plans were also made to establish a journal, *European Urology*.

The next major step in the foundation of the society was in November 1972, at the 'Nouvel Hôtel' in Zurich. **(NB: If any reader knows exactly which hotel this could be, please let us know! eut@uroweb.org)** Attending the meeting were Profs. Alken, Atanassov-Sophia, Badenoch, Balogh, Couvelaire, Gregoir, Marberger, Mayor, Mebel, Petkovic, Puigvert, Ravasini, Wesolowski and Zvara, representing departments from both sides of the iron curtain. Indeed, the make-up and character of the future society was debated: membership based on merit, "democratic" principles or as a representation of the continent. In the end, scientific merit would be considered the most important and the EAU would start as a small, select club of several hundred members. Prof. Gregoir was elected as Secretary General.

The Schiller hotel in Amsterdam in 1970. Here the EAU's statutes were accepted in 1973 by the association's "founding fathers".

On 3 and 4 July, 1973 the Hotel Schiller in Amsterdam was the site of the final constituent assembly. This took place during the 16th congress of the Société Internationale d'Urologie (SIU). The statutes were accepted and the first list of 259 members was submitted for approval. The first European congress was scheduled to take place in Padua, Italy in September 1974. The EAU was off to a flying start in its first decade!

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EAU22 Award Gallery

EAU Willy Gregoir Medal

K-E. Andersson
Lund, Sweden

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

Previous Winners

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-C. Abbou, Creteil, France
2012	M. Marberger, Vienna, Austria
2011	U. Studer, Bern, 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. Palou
Barcelona, Spain

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

Previous Winners

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

V. Kasivisvanathan
London, United Kingdom

For a young promising European urologist

Previous Winners

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 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, Bern, Switzerland
1998	F. Montorsi, Milan, Italy
1996	F. Hamdy, Oxford, United Kingdom

Supported by LABORIE

EAU Innovators in Urology Award

Y. Fradet
Quebec, Canada

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

Previous Winners

2020/21	J. Barentsz, Nijmegen, The Netherlands
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, Bern, Switzerland
2012	J. Wickham, Dorking, United Kingdom †
2011	C. Chaussy, Munich, Germany

Best Papers published in Urological Literature Awards

Best Paper on Fundamental Research

Extensive heterogeneity in somatic mutation and selection in the human bladder
Science 370, 75082 (2020) https://www.science.org/doi/10.1126/science.aba8347

A. Lawson, F. Abascal, T. Coorens , Y. Hooks, L. O'Neill, C. Latimer, K. Raine, M. Sanders, A. Warren, K. Mahbubani, B. Bareham, T. Butler, L. Harvey, A. Cagan, A. Menzies, L. Moore, A. Colquhoun, W. Turner, B. Thomas, V. Gnanapragasam, N. Williams, D. Rassl, H. Vöhringer, S. Zumalave, J. Nangalia, J. Tubío, M. Gerstung, K. Saeb-Parsy, M. Stratton, P. Campbell, T. Mitchell, I. Martincorena (Hinxton, Cambridge, United Kingdom; Rotterdam, The Netherlands; Victoria, Australia; Santiago de Compostela, Vigo, Spain)

Best Paper on Clinical Research

Extended Versus Limited Pelvic Lymph Node Dissection During Radical Prostatectomy for Intermediate- and High-risk Prostate Cancer: Early Oncological Outcomes from a Randomized Phase 3 Trial
European Urology 79 (2021); https://doi.org/10.1016/j.eururo.2020.11.040

J. Lestingi, G. Guglielmetti, Q-D. Trinh, R. Coelho, J. Pontes Jr., D. Bastos, M. Cordeiro, A. Sarkis, S. Faraj, A. Mitre, M. Srougi, W. Nahas (Sao Paulo, Brazil; Boston, USA)

European Urology® Awards

Best Scientific Paper

The Additive Diagnostic Value of Prostate-specific Membrane Antigen Positron Emission Tomography Computed Tomography to Multiparametric Magnetic Resonance Imaging Triage in the Diagnosis of Prostate Cancer (PRIMARY): A Prospective Multicentre Study
European Urology; Volume 80, Issue 6, Pages 682-689

L. Emmett, J. Buteau, N. Papa, D. Moon, J. Thompson, M. Roberts, K. Rasiah, D. Pattison, J. Yaxley, P. Thomas, A. Hutton, S. Agrawal, A. Amin, A. Blazevski, V. Chalasani, B. Ho, A. Nguyen, V. Liu, J. Lee, G. Sheehan-Dare, R. Kooner, G. Coughlin, L. Chan, T. Cusick, B. Namdarian, J. Kapoor, O. Alghazo, H. Woo, N. Lawrentschuk, D. Murphy, M. Hofman, P. Stricker (Sydney, Victoria, Queensland, Australia)

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Best Scientific Paper on Fundamental Research

Integrated Expression of Circulating miR375 and miR371 to Identify Teratoma and Active Germ Cell Malignancy Components in Malignant Germ Cell Tumors
European Urology; Volume 79, Issue 1, Pages 16-19

L. Nappi, M. Thi, N. Adra, R. Hamilton, R. Leao, J-M. Lavoie, M. Soleimani, B. Eigl, K. Chi, M. Gleave, A. So, P. Black, R. Bell, S. Daneshmand, C. Cary, T. Masterson, L. Einhorn, C. Nichols, C. Kollmannsberger (Vancouver, Toronto, Surrey, Beaverton, Canada; Indianapolis, Los Angeles, Portland, USA; Coimbra, Portugal)

Supported by ELSEVIER

Best Scientific Paper on Clinical Research

Shockwave Lithotripsy Versus Ureteroscopic Treatment as Therapeutic Interventions for Stones of the Ureter (TISU): A Multicentre Randomised Controlled Non-Inferiority Trial
European Urology; Volume 80, Issue 1, Pages 46-54

R. Dasgupta, S. Cameron, L. Aucott, G. MacLennan, R. Thomas, M. Kilonzo, T. Lam, J. N'Dow, J. Norrie, K. Anson, N. Burgess, C. Clark, F. Keeley, S. MacLennan, K. Starr, S. McClinton (London, Aberdeen, Edinburgh, Norwich, Bristol, Nottingham, United Kingdom)

Supported by ELSEVIER

European Urology® Awards

Best Scientific Paper on Robotic Surgery

A DROP-IN Gamma Probe for Robot-assisted Radioguided Surgery of Lymph Nodes During Radical Prostatectomy
European Urology; Volume 79, Issue 1, Pages 124-132

P. Dell'Oglio, P. Meershoek, T. Maurer, E. Wit, P. van Leeuwen, H. van der Poel, F. van Leeuwen, M. van Oosterom(Leiden, Amsterdam, The Netherlands; Melle, Belgium; Milan, Italy; Hamburg, Germany)

Supported by the VATTIKUTI FOUNDATION

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

Is There a Detrimental Effect of Antibiotic Therapy in Patients with Muscle-invasive Bladder Cancer Treated with Neoadjuvant Pembrolizumab?
European Urology, Volume 80, Issue 3, Pages 319-322

F. Pederzoli, M. Bandini, D. Raggi, L. Marandino, G. Basile, M. Alfano, R. Colombo, A. Salonia, A. Briganti, A. Gallina, F. Montorsi, A. Necchi (Milan, Italy)

Effect of Simulation-based Training on Surgical Proficiency and Patient Outcomes: A Randomised Controlled Clinical and Educational Trial
European Urology, Volume 81, Issue 4, Pages 385-393

A. Aydin, K. Ahmed, T. Abe, N. Raison, M. Van Hemelrijck, H. Garmo, H. Ahmed, F. Mukhtar, A. Al-Jabir, O. Brunckhorst, N. Shinohara, W. Zhu, G. Zeng, J. Sfakianos, M. Gupta, A. Tewari, A. Gozen, J. Rassweiler, A. Skolarikos, T. Kunit, T. Knoll, F. Moltzahn, G. Thalmann, A. Lantz Powers, B. Chew, K. Sarica, M. Shamim Khan, P. Dasgupta (London, United Kingdom; Sapporo, Japan; Guangzhou, China; New York, USA; Heilbronn, Sindelfingen, Germany; Athens, Greece; Salzburg, Austria; Bern, Switzerland; NS, Vancouver, Canada; Istanbul, Turkey)

Platinum Awards

M. Rouprêt, Paris, France
S. Loeb, New York, United States of America
M. De Santis, Berlin, Germany
F. Witjes, Nijmegen, The Netherlands
B. Ljungberg, Umeå, Sweden

Best Abstract Awards Oncology

First Prize

Robot assisted radical cystectomy with intracorporeal urinary diversion versus open radical cystectomy: Results from the iROC prospective randomised controlled trial
Abstract Nr. A0759

J. Catto, J. Kelly, P. Khetrapal, G. Ambler, F. Ricciardi, S. Khan, A. Feber, S. Dixon, N. Williams, I. Ahmed, P. Charlesworth, M. Cumberbatch, S. Hussain, A. Noon, S. Kotwal, A. Koupparis, E. Rowe, J. Mcgrath, N. Vasdev, C. Brew-Graves, D. Hagan, iROC Trial study Group (Sheffield, London, Glasgow, Reading, Leeds, Bristol, Exeter, Stevenage, United Kingdom)

Supported by IPSEN

Second Prize

Target vs. target plus standard biopsy in naïve patients: Results of a prospective randomized controlled trial
Abstract Nr. A0455

E. Checcucci, M. Manfredi, S. De Cillis, D. Amparore, F. Piramide, A. Piana, G. Volpi, M. Sica, P. Verri, S. Granato, M. Burgio, L. Ola, B. Carbonaro, D. Zamengo, A. Quarà, M. Della Corte, G. Busacca, P. Alessio, A. Pecoraro, I. Stura, G. Migliaretti, C. Fiori, S. De Luca, F. Porpiglia (Turin, Orbassano, Italy)

EAU22 Award Gallery

EAU Ernest Desnos Prize

A. Jardin
On behalf of the Cercle Félix Guyon
Paris, France

For extraordinary contributions to the History of Urology

Previous Winners

2020/21 M. Moran, Tucson, United States of America
2019 Karl Storz SE & CO.KG
2018 S. Musitelli, Zibido San Giocomo, Italy

EAU Hans Marberger Award

A. Martini
Milan, Italy

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

Salvage Robot-assisted Renal Surgery for Local Recurrence After Surgical Resection or Renal Mass Ablation: Classification, Techniques, and Clinical Outcomes. European Urology; https://doi.org/10.1016/j.eururo.2021.04.003

Previous Winners

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, 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

T. Nordström
Stockholm, Sweden

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

Prostate cancer screening using a combination of risk-prediction, MRI, and targeted prostate biopsies (STHLM3-MRI): a prospective, population-based, randomised, open-label, non-inferiority trial. Lancet Oncology ; https://doi.org/10.1016/S1470-2045(21)00348-X

Previous Winners

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, Bern, 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

J. Denstedt
London, Canada

R. Nijman
Groningen, The Netherlands

M. Wirth
Dresden, Germany

Best Abstract Awards Non-Oncology

First Prize

Trans-ethnic genome-wide association study reveals new therapeutic targets for benign prostatic hyperplasia
Abstract Nr. A0590

M. Ng, K. Matsuda, C. Tanikawa, C. Terao, Y. Kamatani, W. Wei, A. Auton, 23andme Research Team, B. Turney, R. Bryant, D. Furniss (Oxford, United Kingdom; Tokyo, Yokohama, Japan; Sunnyvale, USA)

Supported by IBSA

Best Video Awards

First Prize

Eight-yr experience of robotic IVC thrombectomy: surgical technique, perioperative and oncologic outcomes
V74

L. Misuraca, U. Anceschi, G. Tuderti, R. Mastroianni, M. Ferriero, A. Brassetti, A. Bove, S. Guaglianone, M. Desai, I. Gill, M. Gallucci, G. Simone (Rome, Italy, Los Angeles, USA)

Second Prize

A video demonstration and case series of a modified split thickness skin graft technique using Artiss Sealant® performed with penile cancer procedures
V73

J. Churchill, C. Fankhauser, M. Lau, V. Sangar, A. Parnham (Manchester, United Kingdom)

Third Prize

Colored perfusion areas-based 3D virtual models: The Rainbow Kidney as a new tool to optimize the clamping strategy during robot-assisted partial nephrectomy
V72

D. Amparore, F. Piramide, A. Pecoraro, E. Checcucci, S. De Cillis, A. Piana, P. Verri, S. Granato, M. Sica, M. Burgio, B. Carbonaro, M. Manfredi, C. Fiori, F. Porpiglia (Orbassano, Italy)

Best Abstracts by Residents-in-Urology Awards

First Prize

Update from the PEDAL trial: A prospective single arm paired comparison of ability to diagnose and locate prostate cancer between multiparametric MRI and 18F-PSMA-PET/CT
Abstract Nr. A0743

V. Tran, T. Sutherland, K. Taubman, S. Lee, D. Lenaghan, K. Sethi, N. Corcoran, N. Lawrentschuk, H. Woo, L. Tarlinton, T. Spelman, L. Thomas, R. Booth, J. Hegarty, E. Perry, L. Wong (Melbourne, Sydney, Australia; Christchurch, New Zealand)

Second Prize

Non-muscle invasive bladder cancer subtypes with differential response to intravesical bacillus Calmette-Guerin treatment

Abstract Nr. A0068

F. De Jong, T. Laajala, R. Hoedemaeker, S. Rinaldetti, K. Jordan, A. Van Der Made, B. Nieuwkamer, E. Boevé, E. Janssen, T. Mahmoudi, J. Boormans, D. Theodorescu, J. Costello, T. Zuiverloon (Rotterdam, Delft, The Netherlands; Turku, Finland; Luxembourg, Luxembourg; Aurora, Los Angeles, USA; Stavanger, Norway)

European Urological Scholarship Programme Awards

EUSP Best Scholar Clinical

Prostate cancer risk stratification using micro-RNAs, Ki-67 and topoisomerase II: a multicenter study in a high-risk radical prostatectomy cohort

G. Marra, Turin, Italy

EUSP Best Scholar Lab

Histone methyltransferases KMT2C and KMT2D in urothelial carcinoma of the lower and upper urinary tract

E. Laukhtina, Vienna, Austria

Young Academic Urologists Awards

Best Paper by YAU

Upper tract urothelial carcinoma in the lynch syndrome tumour spectrum: A comprehensive overview from the European Association of Urology - Young Academic Urologists and the Global Society of Rare Genitourinary Tumors

C. Lonati, A. Necchi, J. Gómez Rivas, L. Afferi, E. Laukhtina, A. Martini, E. Ventimiglia, R. Colombo, G. Gandaglia, A. Salonia, A. Briganti, F. Montorsi, A. Mattei, C. Simeone, M.I. Carlo, S. Shariat, P. Spiess, M. Moschini, EAU-YAU: Urothelial Carcinoma Working Group, the Global Society of Rare Genitourinary Tumors GSRGT (Brescia, Milan, Italy; Lucerne, Switzerland; Madrid, Spain; Vienna, Austria; Moscow, Russia; New York, Dallas, Tampa, USA; Prague, Czech Republic)

Best Poster by YAU

Pathways and perceived barriers to paediatric urology subspecialisation: A study of incumbent attitudes and opinions

F. O'Kelly, L. t'Hoen, B. Banuelos, R. Lammers, A. Radford, S. Sforza, M. Hiess, E. Bindi, A. Spinoit, S. Silay, B. Haid (Dublin, Ireland; Rotterdam, Groningen, The Netherlands; Berlin, Munich, Germany; Leeds, United Kingdom; Florence, Sienna, Italy; Vienna, Austria; Ghent, Belgium; Istanbul, Turkey)

Best Reviewer YAU

D. D'Andrea, Vienna, Austria

Best Patient Poster Awards

First Prize

The EAU Policy Office - working with and for patients
Abstract Nr. AP22-0005

S. Collen, H. Van Poppel, P. Van Kerrebroeck (Brussels, Belgium)

Second Prize

RelMAGINE: a prostate cancer research consortium with impact due to its patient and public involvement and engagement
Abstract Nr. AP22-0022

S. Green, S. Tuck, J. Long, T. Green, A. Greene, P. Ellis, A. Haire, C. Moss, F. Cahill, N. Mccartan, L. Brown, A. Santaolalla, T. Marsden, J. Rodriquez, J. Hadley, S. Punwani, G. Attard, H. Ahmed, C. Moore, M. Emberton, M. Van Hemelrijck (London, United Kingdom)

Third Prize

Solutions for supporting deprived populations of patients and carers
Abstract Nr. AP22-0014

M. Costin, L. Makaroff (Chinnor, United Kingdom)

How COVID-19 has changed the world of urology

An EAU perspective

Prof. Chris Chapple
EAU Secretary General
Sheffield (GB)

c.chapple@uroweb.org

Prior to 2019 few urologists (myself included) would have known much detail about coronaviruses and indeed cared far less about the subject. Coronaviruses are enveloped, single-stranded RNA viruses that can be subdivided into 4 different classes, i.e., α, β, γ, and δ. COVID-19 belongs to the β-coronavirus family, and it has been noted that there is a similarity between the genomic sequence of human COVID-19 and a virus seen in bats; however, the intermediate host between bats and humans has yet to be identified. (Fig 1)

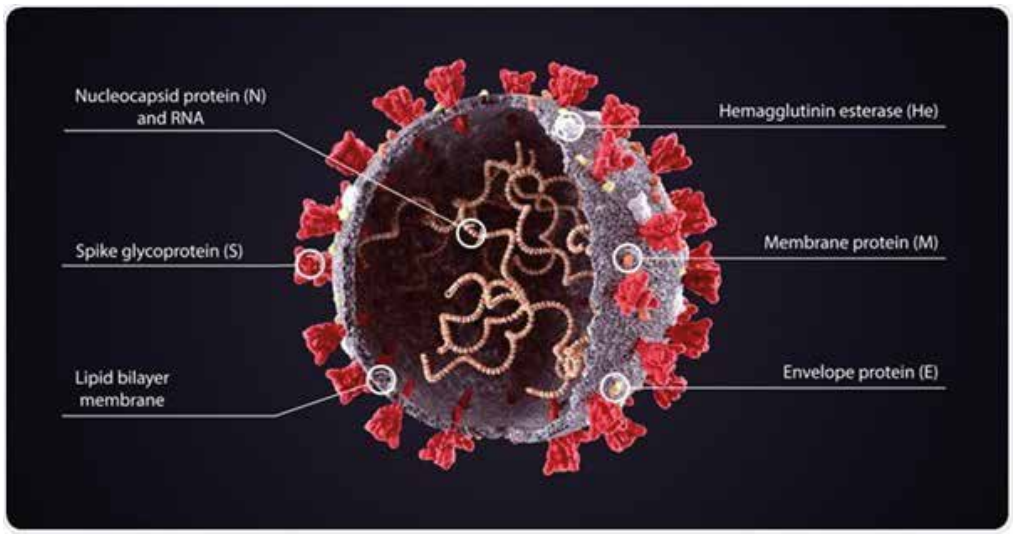

Figure 1: The structure of the SARS-CoV-2 coronavirus, the virus that causes COVID-19

In recent years, several coronaviruses have caused epidemics. In 2002–2003 there was the SARS-CoV epidemic in China and in 2012 there was the MERS-CoV epidemic in Saudi Arabia. The appearance of the new viral SARS-CoV-2 (COVID-19) strain in 2019 is thought to have originated in the Wuhan region of China and has resulted in a global pandemic which, as we all know, is ongoing.

The latest worldwide statistics at the time of writing this article in early January 2022 are: 325,059,702 cases (Deaths: 5,550,316, Recovered: 265,862,733). (www.worldometers.info/coronavirus/)

It goes without saying that COVID-19, and particularly the latest Omicron variant, is highly contagious. It has 3 main routes for transmission: person-to-person contact, aerosol, and touch. In addition to infecting the respiratory system, the virus also infects the blood, digestive, and urinary systems. As a result, the presence of the virus has been detected in faecal, blood, and urine samples. The incubation period for COVID-19 ranges between 2 and 14 days.

At an early stage, the EAU, realising the catastrophic potential for this pandemic and the huge responsibility towards each and every urologist globally in particular its family of more than 19,000 members, set up a working party through its Guidelines Office led by Profs. Ribal and N'Dow. In this landmark initiative, key opinion leaders within our membership came together to produce an EAU guideline on COVID-19 to assist urological surgeons across the globe as they do their very best to deal with the crisis of our generation. (Fig. 2)

It was clear early in the pandemic that the mortality rate of asymptomatic patients who tested positive for COVID-19 after surgery was significantly increased. Therefore, when making treatment decisions urologists should choose the appropriate treatment plan according to a priority level. This publication recommended that urological work should be triaged as follows:

- **Low priority:** clinical harm very unlikely if postponed for 6 months
- **Intermediate priority:** clinical harm possible, but unlikely, if postponed for 3–4 months
- **High priority:** clinical harm very likely if postponed for >6 weeks
- **Emergency:** life-threatening situation – cannot be postponed for >24 h.

Even prior to the Covid-19 pandemic there were significant pressures on modern clinical practice, which varied between different countries, which included:

a) An ageing population and an increasing proportion of patients with long-term conditions and multiple comorbidities
b) Advances in technology and science and democratisation of knowledge and increased accountability with changing patient and societal expectations
c) Staffing levels and practical expertise
d) Availability of technology and economic issues
e) Morale among health care professionals

Against this backdrop, the COVID-19 pandemic has placed substantial demands on existing healthcare resources which may already have been overstretched, understaffed, and under-resourced. This has tested urologists and continues to have a major impact on the way in which we work, who we can treat, and our ability to provide as effective a service for all of our patients as we would hope.

Covid has caused a lack of available beds and concerns over whether a patient is Covid positive or not: as doctors we are forced to make decisions about cancelling and restricting access to surgery. This produces stress on our professional and moral commitments; the challenge of knowing what care patients need but being unable to provide it due to constraints beyond our control.

"The covid-19 crisis has produced major challenges in the delivery of healthcare. The EAU has been able to adjust to this with the innovative use of technology."

In addition, the drastic reduction in face-to-face meetings and social interaction due to a combination of travel restrictions and the consequences of lockdowns has taken a considerable toll on feelings of wellbeing not only in the population at large but in clinicians of all disciplines. We are all now resigned to wearing masks at work, social distancing, conducting a large proportion of clinical consultations virtually by phone or video link, and having to prioritise our clinical activity.

Management decisions are now being made based on institutional guidelines, albeit with consensus regarding the prioritisation of most urological procedures, including those in the outpatient setting, urological emergencies, and many inpatient surgeries for both oncological and non-oncological conditions. This has certainly been in keeping with the prioritisation guidelines provided by the EAU consensus document. Certainly, if one reviews the different areas of urological practice it is clear that patient safety is the critical factor in all decision making and it is worthwhile considering the underlying evidence. During the pandemic, triage decisions have required even more interspecialist coordination and communication than usual, in particular, emphasising the importance of ensuring that patients are free of Covid prior to elective procedures.

1. Uro-oncology: Oncological patients appear to have an estimated two-fold increased risk of contracting Covid-19 than the general population. Whilst the diagnosis and timely treatment of cancer patients should not be compromised, during this pandemic, there has been severely impaired access to hospitalisation and many surgical interventions have been deferred or postponed. Certainly, in appropriate instances, administering neoadjuvant therapy as a way of deferring surgery can decrease risk to the patient and preserve health care resources.

2. Minimally-Invasive Surgery (MIS): Concern over the use of minimally-invasive techniques has been raised due to a potential risk of viral transmission via the creation of a pneumoperitoneum. Conversely, the use of laparoscopy during the pandemic can reduce the length of stay and blood loss as compared to open surgery, and thus increase the availability of beds. Overall, MIS appears to have proven beneficial, as long as adequate precautions are taken to reduce aerosol production through trocars and to wear of full personal protective equipment (PPE).

3. Endourology: In the case of an obstructed/infected kidney, urgent decompression of the system is suggested, which can be achieved safely via either stenting or percutaneous nephrostomy. Obviously emergency department upper tract stone presentations are usually characterised by severe pain. Whenever possible, the ureteral stent or nephrostomy tube should be placed under local anaesthesia, sparing a general anaesthetic.

4. Reconstructive and Functional Urology: Most cases cannot be considered to have clinical priority, except where renal deterioration is a concern, and this is an area of urological practice which has been severely affected.

5. Kidney Transplantation: Concern can clearly be expressed about the safety of kidney transplantation during the COVID-19 pandemic, particularly related to immuno-suppressive therapy. Decisions should be made on a case-by-case basis according to the patient's situation. Managing immunosuppression in these patients is challenging. Suspending kidney transplantation during the COVID-19 pandemic has been recommended, especially for high-risk older recipients with comorbidities.

A very important additional factor is the massive impact that the pandemic has had on all aspects of medical training, particularly surgical training, not only in the operating room but also in outpatient clinics. At the EAU we have attempted to address urological education by providing educational activities online. The EAU's 2020 annual congress had to be held in a virtual format as an abbreviated meeting. Based on our experience, in 2021 we held a full congress designed as a virtual programme broadcast from Amsterdam. We used the modern tools of webinar technology, with all the scientific content of the meeting transmitted online via real-time or on-demand streaming. This proved to be a very effective meeting as evidenced by the following statistics. (Fig. 3)

We have also used these technologies to maintain an active and effective series of educational programmes provided by the education office of the EAU, the European School of Urology (ESU).

In addition, our family of *European Urology* journals led by Profs. Catto, Gratzke, Briganti and Waltz have identified and prioritised a large number of pertinent articles of particular importance to our management of patients on **www.europeanurology.com/covid-19-resource**

In conclusion, the current COVID-19 pandemic has forced urologists across the world to react to the unforeseen crisis situation and has shown the importance of updating many aspects of urology practice, from patient consultation to the triage of urologic surgeries in order to ensure the safety of their patients and staff. The EAU has led the urological world with new COVID-19 focussed treatment guidelines. In addition, the association has embraced teleconferencing and online education, and shown how effective this can be as an alternative to face-to-face meetings in delivering ongoing education and personal support.

Due to space constraints, the entire reference list can be made available to interested readers upon request by sending an email to: communications@uroweb.org.

EUROPEAN UROLOGY 78 (2020) 21–28

available at www.sciencedirect.com
journal homepage: www.europeanurology.com

European Association of Urology

Brief Correspondence – Editor's Choice

European Association of Urology Guidelines Office Rapid Reaction Group: An Organisation-wide Collaborative Effort to Adapt the European Association of Urology Guidelines Recommendations to the Coronavirus Disease 2019 Era

Maria J. Ribal[a,], Philip Cornford[b], Alberto Briganti[c], Thomas Knoll[d], Stavros Gravas[e], Marek Babjuk[f,g], Christopher Harding[h], Alberto Breda[i], Axel Bex[j,k], on behalf of the GORRG Group, Jens J. Rassweiler[l], Ali S. Gözen[l], Giovannalberto Pini[m], Evangelos Liatsikos[n], Gianluca Giannarini[o], Alex Mottrie[p,q], Ramnath Subramaniam[r], Nikolaos Sofikitis[s], Bernardo M.C. Rocco[t], Li-Ping Xie[u], J. Alfred Witjes[v], Nicolas Mottet[w], Börje Ljungberg[x], Morgan Rouprêt[y], Maria P. Laguna[z,aa], Andrea Salonia[c], Gernot Bonkat[bb], Bertil F.M. Blok[cc], Christian Türk[dd,ee], Christian Radmayr[ff], Noam D. Kitrey[gg], Daniel S. Engeler[hh], Nicolaas Lumen[ii], Oliver W. Hakenberg[jj], Nick Watkin[kk], Rizwan Hamid[ll], Jonathon Olsburgh[mm], Julie Darraugh[nn], Robert Shepherd[nn], Emma-Jane Smith[nn], Christopher R. Chapple[oo], Arnulf Stenzl[pp], Hendrik Van Poppel[qq], Manfred Wirth[rr], Jens Sønksen[ss,tt], James N'Dow[uu], on behalf of the EAU Section Offices and the EAU Guidelines Panels*

Figure 2: The EAU Guideline Office's Rapid Reaction Group

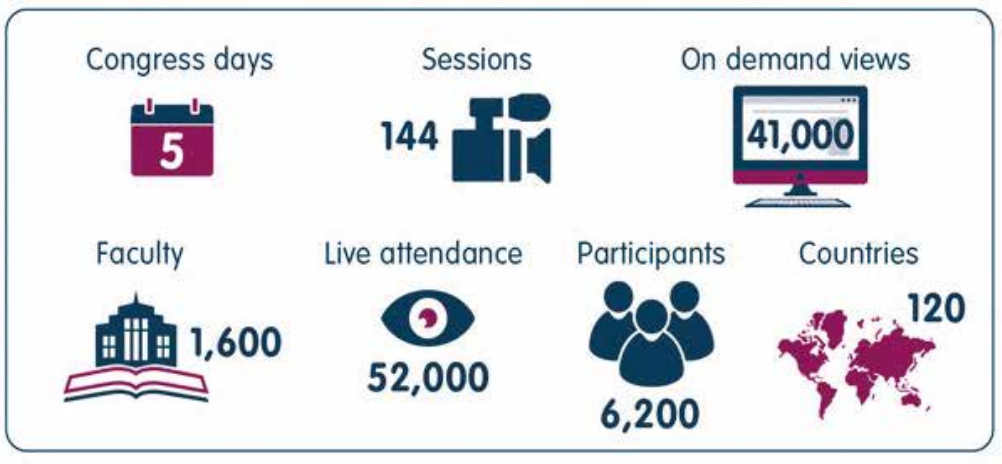

Figure 3: Some statistics from the successful EAU21 Virtual Congress, held on 8-12 July 2021

Use of access sheaths in children

While boundaries are pushed, care must be taken to ensure safe placement

Prof. Bhaskar Somani
Professor of Urology and a Consultant Endourologist
University Hospital Southampton NHS Trust
Southampton (GB)

Ureteral access sheaths are increasingly used while treating kidney stones via ureteroscopy (URS). There are several advantages to it especially avoiding multiple passes in the ureter to remove stones, maintaining a low intrarenal pressure and temperature while having a good vision. It also decreases the risk of urinary tract infections (UTIs) and sepsis. Their sizes range from 9.5F-16F in outer diameter. Care must be taken while inserting it as ureteral perforations and rarely avulsions are known to happen with their improper use. [1,2]

There is an increasing trend of kidney stone disease (KSD) related intervention in the paediatric age group. [3] Ureteroscopy is becoming increasingly popular with excellent results for kids. [4] While it has become safer, large stones and stones in the lower pole are also being treated with good outcomes. Some of these relate to the use of a ureteral access sheath (UAS) which has allowed a widening of indications for ureteroscopy in kids.

There are several published papers on the use of UAS in paediatric patients. While the risk of ureteral trauma still remains, major injury or avulsions are now rare due to the use of small size UAS, better training and increased sub-specialisation. [5] The size of UAS should be adapted to prevent ureteric injuries. We have looked at the safety and outcomes of using UAS for treatment of paediatric renal stones. [6] Data was collected from two European endourology centres (Southampton and Barcelona) for 48 patients. Patients had 9.5/11.5F UAS used and apart from a minor ureteral injury and UTI, no other intra-operative and post-operative complications were noted over a follow-up period of 17 months.

One of the reasons for a lack of widespread use and apprehension in using UAS for paediatric patients is the long-term effect it has on the ureter. There is a lack of long-term data in the use of paediatric UAS. Retrospective data on 21 children who underwent flexible ureteroscopy and laser fragmentation (FURSL) for a stone size of 15.4mm, showed a stone-free rate of 95% with no intra or post-operative complications. [7] Over a mean follow-up of 26 months, there were no ureteric strictures, or any other long-term complications related to the use of UAS.

"While the risk of ureteral trauma still remains, major injury or avulsions are now rare due to the use of small size UAS, better training and increased sub-specialisation."

The use of UAS has also allowed for treatment of large and lower pole stones (LPS) in children. [8] In a recent paper on FURSL for LPS in 57 paediatric patients, UAS was used in 42%, with a final SFR of 98.2% and minor Clavien I complications related to UTI in 4 patients. This is despite 54.4% having multiple stones and a post-operative stent rate of only 54% which is much lower than what is cited for adult literature.

While ureteroscopy has proven its safety in paediatric patients, the risk of failure to access and complications are higher in patients <6 years of age. The risk of failure to access was found to be 4.4% and complication rate of 24% in <6 years compared to 1.7% and 7.1% in the older age group. [9] Care must therefore be taken with the use of UAS in younger age group.

"UAS has allowed endourologists to push the boundaries for ureteroscopic stone treatment in the paediatric setup."

Recently with the advent of smaller 7.5Fr ureteroscopes, it might be possible to decrease the size of UAS further and still have the advantages it offers especially in the paediatric setting. This would minimise the ureteral trauma or the need for pre-stenting in certain situations. It would also allow for reduced need to post-operative stenting. While the role of alpha blockers has shown to increase the success rate of UAS placement in the adult setting, safety and efficacy of this is still lacking in the paediatric setting.

UAS has allowed endourologists to push the boundaries for ureteroscopic stone treatment in the paediatric setup. However, care must be taken to ensure their safe placement and avoid ureteral injuries. Perhaps, more studies of access sheaths in pediatric patients will encourage modification of equipment, to further optimize its use in this population.

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Monday, 4 July 08:00 - 10:00
Plenary Session 08
Grey Area, eURO Auditorium 2

Advertorial

Advancements in laser technology

Bringing opportunities to endourology

Dr. Armin Secker, Head of Section Endourology and Stone-Center, University Clinic of Münster (DE)

What advances over the last 10 years have you seen in your endourology practice that have influenced the way that you treat your patients, and what advances do you think you will see in the next 10 years?

"I am excited to see the development of smart lasers and artificial intelligence, from which we can receive live feedback about stone composition and the device can automatically adjust itself..."

Personally, I have seen a tremendous change in the treatment for prostate hyperplasia. For instance, in 2013 we had 40 procedures per year and in 2021 we had almost 500. The number of laser treatments for prostate is still not very high in Germany, with only about 13 to 15% of procedures being done with a laser. However, when it comes to obstructive therapy in our department, laser therapy accounts for about 90% of procedures, which has also driven our ability to treat even older people.

In the future, I am excited to see the development of smart lasers and artificial intelligence, from which we can receive live feedback about stone composition and the device can automatically adjust itself to help avoid causing damage to surrounding tissue.

"This new laser technology has given us different treatment options, especially for ureteroscopy."

How has laser technology given you treatment options for your patients?
The new laser systems give us the opportunity to treat even bigger or more complex stones. So, with cases of obesity and patients taking anticoagulants increasing, in combination with a ureteroscope, lasers give us an option of both treating stones and a chance to treat those complicated cases in complicated situations. For example, we can easily treat high-volume stones in a kidney with one session of flexible ureteroscopy, normally without any problems like time in the OR or postoperative complications. We don't need more than 60 minutes for a big stone and if we stay under the 60-minute period, the percentage of urosepsis after surgery is still quite low.

So, *"This new laser technology has given us different treatment options, especially for ureteroscopy"*.

What is your driver to decide on the approach?
For me it starts with the ALARA [as low as reasonably achievable] principle: I usually start with a low energy setting which allows dusting, so I can shrink the stone, just gently, to have an idea of how the stone reacts to the laser and to decrease the whole volume. Then, I increase the energy and decrease the pulse width and start fragmenting. This combination of starting with dusting then fragmenting can give you an idea of how the stone will react and can provide samples for analysis.

What are your key learnings about these advances and how important are the outcomes for you and your patients?
One key learning is that while, on the one hand, we have had high stone-free rates, we have also had to think more about the avoidance of complications. For instance, high power might also mean high rates of complications. So, with the power of our lasers, let's say a holmium or thulium laser, this high power might have an impact on the tissue surrounding the stone in the ureter or in the kidney. For me, for instance, I say 10 to 15 watts within the ureter and 20 to 25 watts within the kidney might be the very limit that I would use. Another key learning is considering the impact on pressure within the kidney. I'm hoping we will have new technology to measure pressure to inform when to adapt the procedure for different patients, like using an access sheath. I think this is quite promising and hopefully we will have those tools in the very near future.

"...lasers give us an option of both treating stones and a chance to treat those complicated cases in complicated situations."

Eponyms and Dutch urological innovations in perspective

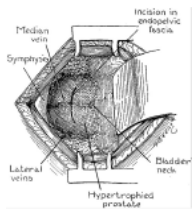
Origins of terminologies and procedures involved

Dr. Pieter Dik
Retired paediatric urologist
Utrecht (NL)

An eponym is a person, place, or thing named after (or believed to be named after) someone or something. Discoveries and innovations are often named after the discoverer or an influential person. Examples of these include Alzheimer's disease and the Apgar score.

All urologists know famous names such as Bricker and Millin, which are indeed typical examples of eponymes. Bricker and Millon did not invent nor describe uretero-ileal stoma and retropubic prostatectomy, respectively. How come their names are associated with these procedures? Who were the urological surgeons who pioneered these procedures many years before?

The Dutch urologist, Dr. Willem J. van Stockum (1860-1913) started to do prostatectomy operations in the early years of the 20th century. On November 3, 1908 he performed the first "Prostatectomia Suprapubica Extravesicalis" and published this method in the Zentralblatt für Chirurgie journal in January 1909.



Dr. Willem J. van Stockum

The Irish urologist Dr. Terence Millin (1903-1980) performed a similar operation, the "Retropubic Prostatectomy" and published this "new extravesical technique" as a report on 20 cases in The Lancet, Dec.1;2(6380):693-6,1945. He was aware that this operation was performed some decades before and correctly referred in his paper to the case reports of van Stockum.

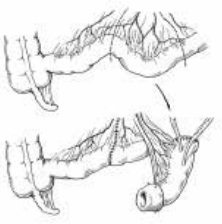
Dr. Terence Millin

The Dutch urological surgeon Dr. Hendrikus J. Zaaijer (1876-1932) was working in the University Hospital of Leiden when he performed the first uretero-ileal-cutaneo-stomy in 1911 on a patient with total incontinence because of a vesico-vaginal fistula. Unfortunately, she died 11 days later due to extensive malignancy of the cervix. The second case was a patient with carcinoma of the bladder. This patient died six days postoperatively from peritonitis.

"Eponyms for surgical procedures or tools are handy but sometimes inappropriate"

Dr. Eugene M. Bricker employed urinary diversion by an uretero-ileal stoma method in hundreds of patients since 1950. Bricker was probably not aware of the two aforementioned patient cases of Zaaijer. This may be explained by the fact that Zaaijer did not publish his cases in literature. Nonetheless, Zaaijer

Dr. Hendrikus J. Zaaijer



Dr. Eugene M. Bricker

was quite famous in the Netherlands because of his surgical innovations. In 1908, he was also the first to perform a successful long-term autotransplant of the kidney in a dog. This dog lived another eight years. It may have been possible that Zaaijer's stoma operation was discussed during European congresses.

Later, Dr L. Seiffert from Neunkirchen made a conduit with the use of jejunum. He performed this operation on two patients. The first patient survived for three years, while the second one died of renal failure. In 1950, Dr. Heinz Haffner from the St. Louis City Hospital in the United States created an ileal conduit when he was "unable to use coecum as a reservoir and was forced to use an isolated segment of the ileum alone" during an operation. Perhaps he was inspired by Zaaijer or Seiffert? One will never know for sure.

Why was the eponym for the retropubic prostatectomy operation "Millin" instead of "van Stockum"? It is because Millin popularised this operation and published many cases.

In the case of the uretero-ileal cutaneo-stoma operation, the eponym became "Bricker" and the name Zaaijer is totally unknown to most urologists. This is mainly because Zaaijer did not publish his first two cases, probably because he was disappointed about the complications and outcome which is an outstanding example of "publish or perish".

I must confess, I am not a true advocate for the use of eponyms. It seems odd to me that a name of a person should live on as a kind of trademark or glorification. On the other hand, it is easier to refer to and discuss about scheduled operations e.g "Mr. Johnson will undergo a Bricker" is shorter than "Mr. Johnson will undergo a uretero-ileal-cutaneo-stomy".

However, *my personal* concern against the use of eponyms is that my family name would be unsuitable for an eponym.

Saturday, 2 July 11.00 - 13.30
EAU History office
Grey Area, Room G107

Urologist asks for medical instrument that was invented by Dr Dik

Sexual function after augmentation surgery in childhood

Towards a better understanding of the transition of our patients to adulthood

eauyau
Young Academic Urologists

Dr. Beatriz Bañuelos Marco
Urology Department
Charité Medical University
Berlin (DE)

Spina Bifida (SB), the incomplete closure of the neural tube occurs in 3.5 per 1000 live births worldwide nowadays and >80-95% of children with SB live into adulthood. This improvement in overall survival is likely to be secondary to advances in health care. Up to 48% of SB patients with untreated urological problems had evidence of kidney damage, which increases to 100% in patients with an overactive pelvic floor (detrusor/sphincter dyssynergia; DSD) when not properly treated. The early management with Clean Intermittent Catheterisation (CIC) is the Gold Standard to achieve a low-pressure reservoir that is safe for the upper urinary tracts of the SB patients.

It has been shown that high leak point pressure (>40cmH20), decreased functional bladder capacity as well as detrusor overactivity are associated with kidney damage. Bladder and bowel management are important to preserve renal and bladder function but also key points in a better quality of life (QoL) in this group of patients regarding urinary continence, infection-free rates, independency and a better self-esteem.

Augmentation Cystoplasty (AC) offers a solution to achieve a better continence and preserve the renal function by decreasing the bladder pressure. Generally, the SB patients who undergo this surgery have high bladder pressure, upper tract deterioration and urinary incontinence, not responding to intermittent catheterisation, oral or intravesical anticholinergic medication and/or intra-detrusor injection therapy with BOTOX.

One of the main problems these patients face is when they transition from paediatric to adult care. This, on the other hand is also a difficult process for the urologist given that is not clearly standardised. Sexual function and fertility remain challenges for the physicians, the SB patients and their caretakers highlighting the importance of the concept of life-long congenital urology. It seems that the systems currently in place do not facilitate enough discussing such issues with adolescents, this falls as responsibility onto the caregiver. The Young Academic Urologists (YAU) Paediatric Urology Group found it important to assess the care that adolescent SB patients are receiving with the aim to address the needs of these patients when transitioning into adulthood. We aimed to achieve a better understanding and to provide adult urologists some insight to guide these patients towards a healthy, complete and happy sex life.

We gathered four experts in the field as well as an experienced leader of a patient group and mother of a girl with SB and asked questions relevant to the following areas of care:

a) Diversion, urinary incontinence and sexual life
b) Impact of a stoma on body image perception and self-esteem
c) Specific female concerns with regard to fertility and recurrent urinary infections
d) Specific male concerns on anejaculation and erectile dysfunction

Their answers are discussed in view of the available literature.

The experts were identified by performing a literature review and a group discussion within the paediatric urology expert group of the European Association of Urology's YAU. The patient group representative was invited to join a telephone interview by one of the authors. We interviewed: Dr. Raimund Stein, Head of Paediatric Urology Department, Universitätsmedizin Mannheim; Dr. Dan Wood, Consultant Urologist specialist in Adolescent Reconstruction University College Hospital United Kingdom; Prof. Ricardo Gonzalez, Consultant Paediatric Urologist Auf der Bult-Zentrum für Kinder und Jugendliche, Hannover; Dr. Anja Lingnau, Head of Paediatric Urology Department, Charité Universitätsmedizin Berlin; and Silvia Hintringer, Chair of the Austrian Patients Group "Spina Bifida" since over 20 years and mother of a girl with a neurogenic bladder.

Diversion, urinary incontinence and sexual life
Many SB patients have difficulties developing sexual activity, self-esteem being one of the most prominent concerns. There is a consensus between the literature, the clinicians consulted and the patient group representative that incontinence is an important limitation for the sexual life of the SB patient.

An interesting point, yet not addressed in literature or brought up by the experts is a potential difference in perception concerning the burden caused by incontinence between women and men. This should be addressed in future studies looking into gender diverse aspects of treatment. From the clinical experience of the experts, which is supported by the literature, we infer that urinary diversion improves sex life by offering a solution to urinary incontinence that leads to improvement of body image, self-esteem and the better ability to cope.

The patient group representative pointed out that female patients placed greater importance on a stable partner for a fulfilling sexual relationship than the severity of the procedures they underwent or urinary incontinence. Unlike men, who place more emphasis on the negative impact of feeling ashamed.

Impact of the stoma on perception of body image and self esteem
Negative self-perception it is frequently cited as an obstacle for a satisfying sex life. It is logical to think that the cosmesis of the stoma may influence the self-esteem and therefore the sexual activity of the patients, this is an important issue to address when discussing concerns regarding sex life. Lack of self-confidence is one the most frequent obstacles to starting a relationship. Based on the experience of the consulted experts and the patient representative, it appears to be a less common concern in males than in females. However, this must not be an impediment to address this matter with our patients, as self-esteem and the idea of their own sex lives and sexual satisfaction are based on individual expectations and variations between them.

Specific female concerns on fertility and recurrent urinary infections
Fertility might be impaired in women with SB, and antenatal complications, foetal loss as well as neural tube defect in their offspring are more frequent, requiring close obstetric and urological surveillance as well as awareness of the importance of folic acid prophylaxis before conception. Patients need counselling about these risks before pregnancy, and when pregnant, they should be managed in a unit, which can provide high- risk obstetric, and urology cover.

"Augmentation Cystoplasty (AC) offers a solution to achieve better continence and preserve the renal function by decreasing the bladder pressure."

There is a general misconception that paediatric urologists should cover fertility related issues, and the patients' representative in this way expressed it. This is due to the patients and the patients' families' experience with gynaecologists unfamiliar with congenital malformations. The lack of availability of high-quality sex education for patients with SB stresses the need of "transitional gynaecology" in order to address these girls needs properly. Recurrent UTIs are a topic frequently addressed in the regular consultation of SB patients and even more important after urinary diversion and augmentation cystoplasty due to the anatomical characteristics. UTIs related to intercourse in women are a common presenting complaint. The lack of evidence and literature relating to treating intercourse-related UTIs in SB patients leads to the assumption that these should be managed as inpatients with non-neurogenic bladder emptying disorders.

Specific male concerns on anejaculation and/or erectile dysfunction
Men with SB may also demonstrate orgasm and ejaculatory dysfunction, which has been reported in 75% of affected patients. Quality of ejaculation also appears to be impaired. It has been reported that 78% of men with SB were able to ejaculate, but only 17% reported it to be forceful. Like erectile quality, ejaculatory function also correlates with the level of the lesion. Men with SB also ejaculate less frequently than the general population, and ejaculation can occur differently, often being described as more of a dribble than propulsive. In view of this data we aimed at looking into an experts and patient representatives perspective of these specific problems.

Over 91% of patients indicate that physicians should talk to patients with SB about their sexual health. However, more than half of those patients with SB have no recollection of such a conversation with their providers. The patient group representative in the interview addresses this, whereas the experts consulted referred the patients mostly to a specialist (andrologist). Both patient representative and experts agreed that they bring the topic up with the patients once in puberty.

"An innovative method of enhancing sensation with regards to sexuality is the TOMAX procedure, involving a microsurgical connection between the ilioinguinal nerve and the dorsal penile nerve."

The treatment of ED in SB patients is possible and effective. It is highly important for a healthy and happy sex life, self-confidence, and maintaining long-term relationships. Men with ED often respond to established therapies, including oral medications.

People with SB experience sensation differently, with "normal" sensation reported in only 20% of cases. In men, only 41% have normal erections, with ambulant men more likely to report normal erections than those in a wheelchair. Additionally, those with SB are less likely to have feelings of sexual excitement consistent with orgasm compared to the general population.

An innovative method of enhancing sensation with regards to sexuality is the TOMAX procedure, involving a microsurgical connection between the ilioinguinal nerve and the dorsal penile nerve. While it clearly requires a special set of expertise it has been shown to be effective in a relevant proportion of patients.

Regarding fertility, subfertility is common concern, despite the fact that testosterone levels have been reported to be normal, there seems to be a failure on the level of Sertoli cells or germinal cells.

Conclusions
We do not intend to conclude evidence-based recommendations but to raise awareness to a very important topic that currently is scarcely documented in the literature. Therefore, our conclusions are based on the opinion of experts respected in their field and should be not standardised in the clinical practice, but considered for further study.

Patients with SB find impediments to develop normal sexual relationships for a variety of reasons, including impaired self-esteem and dependence on caregivers. From the work that our group performed regarding this topic we can highlight the challenges that our SB patients have to face when they start sexual activity.

Self-esteem and urinary incontinence are very important concerns. Urinary diversion seems to improve sexual life by offering a solution to urinary incontinence. Female patients found it important to have a stable partner for a fulfilling sexual relationship, while men stress feeling ashamed or pressured by urinary incontinence. Recurrent UTIs and those related to intercourse in women are a common urological consultation. Patients and their representatives express their concern on the lack of sexual education.

Physicians should be encouraged to ask all post-pubertal patients if they have any urinary, faecal, or sexual concerns at every visit to both establish a solid physician- patient relationship.

Acknowledgements:
We would like to thank Mrs. Hintringer, chairwomen of the Austrian Spina Bifida Patients Group, as well as the experts we consulted for their support and willingness to answer our questions. Furthermore we would like to acknowledge the contribution of Mesrur Selçuk Silay, Anne Françoise Spinoit as members of the Pediatric Urology Group of the EAU Young Academic Urologists, as well as Tom Marcelissen for their help with conceiving the questions and performing the literature search.

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Research:
Sexual function in adult patients who have undergone augmentation surgery in childhood: what is really important? Bañuelos Marco B, Hiess M, Stein R, Gonzalez R, Lingnau A, Wood D, Radford A, Haid B; Pediatric Urology Group of the EAU Young Academic Urologists. *Int J Impot Res*. 2021 Mar;33(2):170-177. doi: 10.1038/s41443-020-00355-x. Epub 2020 Oct 10. Erratum in: Int J Impot Res. 2021 Dec 1

On behalf of the YAU Paediatric Urology Group
Manuela Hiess, Raimund Stein,
Ricardo Gonzalez, Anja Lingnau, Dan Wood,
Anna Radford, Bernhard Haid

Sunday, 3 July 14:00 - 15:30
Thematic Session 08
Green Area, Room 1

Key updates on mOCRPC treatment

Balancing benefits, patient individual factors, and risks

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Prostate cancer progression is a continuous process and can occur in different stages. A sole prostate-specific antigen (PSA)-progression following androgen deprivation therapy (ADT) can occur upon different patient histories such as local recurrence in the prostate after prostatectomy or persistent local disease after radical radiation therapy with absence of metastatic disease or with no detectable recurrent disease in the primary site and no detected involved lymph nodes, bone or visceral organs. Overall, absence of distant metastases (M1a-M1c) defines the non-metastatic disease state, lymph below aortic bifurcation (N1) are not considered, whereas all studies leading to an approval of systemic therapy for this disease state used conventional imaging modalities: MRI or CT in combination with bone scans.

One definition of progression during ADT is based on PSA increases and follows the PCWG3 consensus: a 25% increase from nadir with a starting value of 1.0 ng/ml, with a minimum rise of 2 ng/ml, while maintaining castrate testosterone values (<50 ng/dl) [1].

The European Association of Urology (EAU) defines castration-resistant prostate cancer (CRPC) as either biochemical progression (three consecutive rises in PSA one week apart and a PSA > 2 ng/mL) or radiologic progression (at least two new bone scan lesions or a soft tissue lesion using Response Evaluation Criteria in Solid Tumors [RECIST]) in the presence of serum testosterone < 50 ng/dl or 1.7 mol/l [2].

Patients with CRPC but no distant metastasis (non-metastatic CRPC [nmCRPC/m0CRPC]) are especially at high risk of developing metastases if the PSA-doubling time is shorter than 10 months. Thus, a careful monitoring of patients treated with ADT with a regular calculation of PSA-DT is recommended. Since PSA-DT is based on a rather complex algorithm, web-based calculators should be used. [3]

Approved systemic treatment options for m0CRPC
Apalutamide, darolutamide, and enzalutamide are second generation non-steroidal anti-androgens with a higher affinity for the androgen receptor (AR) than bicalutamide. While first generation non-steroidal anti-androgens still allow transfer of ARs to the nucleus, apalutamide, enzalutamide and darolutamide also block AR translocation in the nucleus and therefore suppress transcriptional activity. [4-6] Darolutamide has structurally unique properties with a more flexible and polar structure, thus leading to different pharmacokinetic properties. [7] In particular, preclinical studies and a Phase I study with healthy volunteers showed darolutamide did not cross the blood-brain barrier. [8-9] Furthermore due to increased polarity, the interactions and metabolism via CYP P 450 system differed and resulted to less potential drug-drug interaction of darolutamide [10] (Figure 1). The key substance characteristics of all three agents are summarised in table 1.

Clinical data of apalutamide, enzalutamide, and darolutamide in nmCRPC patients
Three large randomised-controlled phase III trials, PROSPER [4], SPARTAN [5] and ARAMIS [6], evaluated metastasis-free survival (MFS) as the primary endpoint in patients with nmCRPC (m0CRPC) treated with enzalutamide vs. placebo (PROSPER) or apalutamide vs. placebo (SPARTAN) or darolutamide vs. placebo (ARAMIS), respectively. The non-metastatic (M0) status was determined by MRI, CT and bone scans. Only patients at high risk for the development of metastasis with a short PSA-DT of ≤ 10 months were included in all three trials. Patient characteristics in both trials revealed that about two-thirds of participants had a PSA-DT of six months.

All three trials showed a significant MFS benefit, as well as, significant overall survival benefit (OS) [14-16], as summarised in Table 2.

In addition, for the benefit of delaying progression to metastatic disease or death in patients with nmCRPC, the risk of treatment-emergent adverse events (AEs) and Quality of Life (QoL) should be considered in this mainly asymptomatic patient population. In the primary analysis of the SPARTAN trial, 96.5% and 93.2% of patients experienced an AE of any grade in the apalutamide and placebo group, respectively [5]. The incidence of Grade 3–4, the AEs was 45.1% for apalutamide and 34.2% in the placebo arm. The incidences of fatigue, rash, falls, fractures, mental impairment, and hypothyroidism were higher compared to placebo [5]. The final analysis of the SPARTAN trial reported a safety profile of apalutamide similar to that in the primary analysis (Fig. 2A) [14]. Grade 3–4 hypertension and falls occurred more frequently in the apalutamide arm compared to placebo arm [14].

In the primary analysis, AEs associated with death occurred in 10 patients treated with apalutamide wherein in some of the cases, the causes of death wereacute myocardial infarction, cardiorespiratory arrest, cerebral haemorrhage, myocardial infarction, multiple organ dysfunction, and pneumonia. In two patients, the causes of death were prostate cancer and sepsis. One patient in the placebo arm died due to cardiorespiratory arrest [5].

In the primary analysis, treatment discontinuation due to AEs were 10.6% in the apalutamide arm compared with 7.0% in the placebo arm; the most common AEs leading to treatment discontinuation were rash, fatigue, sepsis, and dizziness [5]. In the final analysis, discontinuation rates in apalutamide and placebo groups due to progressive disease were 43% and 74%, and discontinuation rates due to AEs increased to 15% and 8.4%, respectively [14].

In the PROSPER trial, treatment-related AEs were mostly consistent with the established safety profile of enzalutamide. In the primary analysis, the incidence of any-grade AEs was 87% and 77% in the enzalutamide and placebo arm, respectively. Grade 3–4 AEs were experienced by 31% in the enzalutamide arm and 23% of patients in placebo arm. Compared with the placebo arm, fatigue, hypertension, mental impairment disorders, major cardiovascular AEs, as well as, fall and fracture occurred with a higher incidence in the enzalutamide arm (Fig. 2B) [4].

The final analysis of PROSPER reported a safety profile of enzalutamide comparable to that at the time of primary analysis. AEs of Grade 3 or higher were experienced by 48% of patients receiving enzalutamide compared with 27% receiving placebo. [15].

Treatment discontinuation due to an AE occurred in 9% of patients in the enzalutamide arm compared with 6% in the placebo arm in the primary analysis of PROSPER, increasing to 17% and 9%, respectively, in the final analysis [4, 15]. A total of 32 patients who received enzalutamide and four patients in the placebo arm died without evidence of radiographic progression [4].

The primary analysis of ARAMIS reported 83.2% and 76.9% of patients with an AE of any grade in the darolutamide and placebo arms, with Grade 3–4 AEs occurring in 24.7% and 19.5% patients, respectively [6]. In terms of tolerability, darolutamide was well tolerated with no clinically relevant difference compared to the placebo arm was observed for the incidence of AEs typically associated with ARIs, including falls, hypertension, and mental impairment [6]. The most common adverse reactions frequently reported in the active treatment versus placebo arm of ARAMIS were fatigue, extremity pain, and rash. Only fatigue had an incidence higher than 10% with darolutamide [6].

With longer follow-up time and duration of treatment in the final analysis of ARAMIS, the incidence of AEs with darolutamide remained low. The minimal or no difference for darolutamide compared with placebo was confirmed for most ARI-associated AEs, such as fatigue, falls, fractures, rash, mental impairment disorders, and hypertension. (Fig. 2C), [16, 17]. Moreover, drug discontinuation rates due to AEs in the final analysis of ARAMIS were similar in the darolutamide and placebo arms (8.9% vs. 8.7%) and remained unchanged from those at the primary analysis [6, 16, 17]. On a related note, the incidence of Grade 5 AEs was similar in both treatment arms (4.0% vs. 3.4% in the darolutamide and placebo arms, respectively). In ARAMIS, 37 deaths were reported in the darolutamide arm with one death considered related to treatment (perforation of the small intestine), 18 deaths in the placebo arm two deaths considered treatment-related (myocardial infarction and intracranial haemorrhage) [6].

Current treatment guidelines
Following the approval the FDA and the EMA, international guidelines such as from the National Comprehensive Cancer Network (NCCN) and the EAU, as well as, national guidelines (e.g. German S3 guideline prostate cancer) now recommend that patients with nmCRPC/m0CRPC and a PSADT ≤ 10 months should be treated with enzalutamide, apalutamide, or darolutamide in addition to continuing ADT, to delay metastasis and prolong OS [2, 18, 19]. Guideline recommendations are based on high-level evidence of efficacy, which all three ARIs demonstrated in their respective phase 3 clinical trials with MFS being the primary efficacy endpoint. Final analysis of all three trials revealed significant OS, suggesting that MFS can be considered a sufficiently strong surrogate of OS [20, 21]. Taking the general high QoL in a rather asymptomatic patient population into account, it is important to take possible treament-emergent AEs and maintenance of QoL in consideration.

Conclusions
High-risk nonmetastatic CRPC or m0CRPC is a heterogeneous state defined by rising PSA, as short PSA-DT ≤ 10 months and absence of distant metastasis in conventional imaging. In the past two years, treatment options for high-risk-nmCRPC-patients evolved rapidly with the FDA and EMA approval of the second-generation ARIs apalutamide, enzalutamide, and darolutamide. All three agents have demonstrated significant prolongation of MFS and a significant OS benefit in patients with high-risk nmCRPC, resulting in international and national guideline recommendation for treatment of castration resistant disease [4-6, 14-17].

Second-generation ARIs have overall acceptable tolerability in general and maintain QoL in patients with non-metastatic disease. Their distinct safety profiles and potential for drug–drug interactions with frequent co-medications in this patient population should be considered for treatment decision, whereas therapeutic options that do not escalate ADT-related AEs or contribute to additional therapeutic burden due to drug–drug interactions may be preferred. In conclusion, recently 3 efficacious second-generation ARIS became available and are recommended for the treatment of nmCRPC. Balancing benefits, patient individual factors, and risks is important for the appropriate treatment decisions for these patients [22].

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Due to space constraints, the entire reference list can be made available to interested readers upon request by sending an email to: communications@uroweb.org.

Monday, 4 July 14:00 - 15:30
Thematic Session 16
Orange Area, eURO Auditorium 1

Table 2: Cross-trial efficacy comparison in mOCRPC

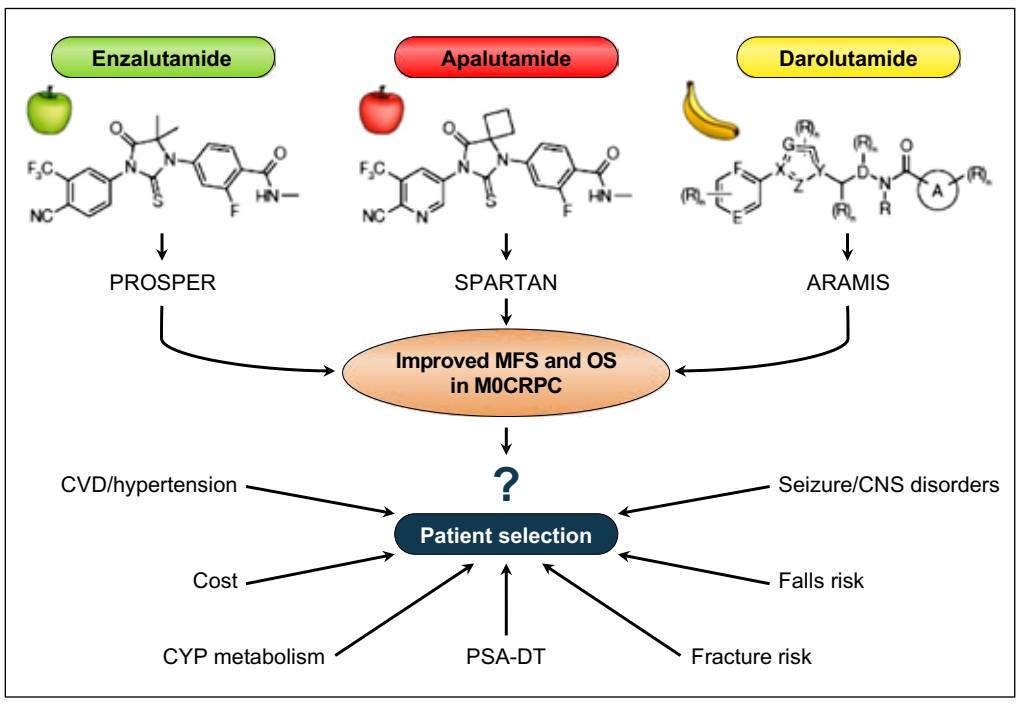
Drug	Study	Median MFS (months)	Median TTPP (months)	median OS (months)
Enzalutamide	PROSPER	36.6 vs. 14.7 (HR=0.29; p<0.001)	37.2 vs. 3.9 (HR=0.07; p<0.001)	NR vs. NR (HR=0.73; p=0.001)
Apalutamide	SPARTAN	40.5 vs. 16.2 (HR=0.28; p<0.001)	NR vs. 3.7 (HR=0.06; p N/A)	NR vs. 39.0 (HR=0.78; p=0.016)
Darolutamide	ARAMIS	40.4 vs. 18.4 (HR=0.41; p<0.001)	33.2 vs. 7.3 (HR=0.13; p<0.001)	NR vs. NR (HR=0.69; p=0.003)

MFS metastasis-free survival, *TTPP* time to PSA progression, *OS* overall survival

Table 1: Comparison of the second-generation androgen receptor antagonists for nmCRPC

	APALUTAMIDE	ENZALUTAMIDE	DAROLUTAMIDE
Half-life	3-4 days	5.8 days	20 hours
Status	FDA & EMA approved	FDA & EMA approved	FDA & EMA approved
Dosage	240 mg po once daily	160 mg po once daily	600 mg po twice daily
Blood-Brain Barrier penetration	Yes	Yes	no
CYP Induction	Strong: CYP3A4 & CYP2C19 Moderate: - Weak: CYP2C9	Strong: CYP3A4 Moderate: CYP2C9 & CYP2C19 Weak:-	Strong: - Moderate: - Weak: CYP3A4
Increase of serum testosterone level	Yes	Yes	no
Key phase III trial	SPARTAN	PROSPER	ARAMIS
N (patients)	1207	1401	1502

Abbreviations: EMA: European medicines agency; FDA, Food and Drug Administration; nmCRPC, non-metastatic castration-resistant prostate cancer.



Overview on structure and factors that are important in selecting the right substance for the right patient

Systemic treatment options for mCRPC

Is there a single one-size-fits-all sequence approach?

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Prostate cancer (PCa) is the second most frequently diagnosed cancer worldwide and the second leading cause of cancer deaths in men. PCa that progresses despite castrate concentrations of testosterone and failure of androgen-deprivation with or without additional agents approved in the hormone-sensitive setting of the disease is termed castration-resistant prostate cancer (CRPC).

Offering life-prolonging agents in the stage of metastatic CRPC (mCRPC) is crucial since we have a variety of drugs available with different modes of actions and side effect profiles. Thus, the benefit of intensifying treatment in the earlier stage of disease, has proven benefit for overall survival (OS) in the metastatic hormone-sensitive prostate cancer (mHSPC) setting for docetaxel [1,2], enzalutamide [3,4], apalutamide [5] abiraterone/prednisone [6,7], as well as, in the non-metastatic CRPC setting (nmCRPC) with three androgen-receptor (AR) targeting agents (ARTA) (enzalutamide, apalutamide and darolutamide [8-10]) complicates and reduces the armamentarium of agents remaining for the mCRPC setting. Recent data from the phase III PEACE-1 and ARASENS trials underlined that even a "triplet" approach of adding abiraterone plus prednisone or darolutamide to androgen deprivation therapy (ADT) and six cycles of docetaxel is of OS benefit. [11,12] Hence also positive OS data for the use of abiraterone/prednisone for two years in addition to three years of ADT +/- radiotherapy as reported from the STAMPEDE investigators for high-risk localised disease anticipates intensified treatments in the earlier stage of the disease. [13] The main goal is a potential cure or a long metastasis-free interval with an optimal quality of life when intensifying treatment in the initial stage of PCa, but most patients will arrive during their course of disease also at the stage of metastatic castration resistance.

Particularly at this stage of disease, an approach as personalised as possible should be the treating physician's goal, and this mission starts with the optimal sequencing of available treatments. But does sequence really matter? This article and the presentation "Systemic treatment options for mCRPC and how to sequence them" during the Thematic Session 16: All you need to know about castration-resistant prostate cancer (CRPC) at EAU22 will shed some light on this complex topic.

"Given the OS benefit seen with cabazitaxel or olaparib versus hormone switch, the best strategy for the vast majority of patients seems to be to change to a drug with a different mechanism of action and to step away from back-to-back sequencing of these novel hormonal agents."

General considerations
There are no prospective trial data or head-to-head comparisons that identify the ideal sequencing and guide our treatment choice in mCRPC. Some treating physicians might think that for the ease and presumably lower side effect profile of ARTA in an asymptomatic patient, one would want to just go to another hormonal agent. However, there is growing data that shows that that strategy is not leading to great success. Given the OS benefit seen with cabazitaxel or olaparib versus hormone switch, the best strategy for the vast majority of patients seems to be to change to a drug with a different mechanism of action and to step away from back-to-back sequencing of these novel hormonal agents. Moreover, the current guidelines clearly state not to use the sequence of two AR-targeting agents.

1. Sequencing two consecutive lines of AR-targeted agents in the mCRPC setting
Multiple approaches have been made to answer the question of using abiraterone/prednisone or enzalutamide in first-line mCRPC mainly when mHSPC treatment with the addition of one of the novel hormonal agents was not the standard.
Most data that tried to answer that important question were of retrospective nature [14] and only one phase II trial addressing this specific sequence question gave some hints that abiraterone followed by enzalutamide would have a higher rate of PSA > 50% response, but overall the PFS was short sequencing one or the other way round. [15] This might be since after enzalutamide treatment a high rate of AR amplification has been reported and AR amplification is linked to potential abiraterone resistance. [16] There are prospective data from the PLATO trial that shows abiraterone after enzalutamide is a 2.5% PSA response rate. [17] Two other large trials gave us evidence that sequencing two ARTAs is not giving benefit to mCRPC patients. Both the PROfound study [18], investigating olaparib in patients with homologous repair deficiency (HRD) versus a second ARTA and the CARD study [19], randomising cabazitaxel versus a second ARTA underlined that efficacy is low when sequencing two ARTAs. The question remains if these mechanisms of resistance of two ARTAs can be extrapolated in the mHSPC – mCRPC sequence setting. When we look at the subsequent treatments presented from the ARASENS trial, 50% of patients received a second ARTA in the mCRPC setting after progression on docetaxel and darolutamide in mHSPC. One should be curious how these patients performed when using the second ARTA after darolutamide failure.

2. What has to change then? Chemotherapy (CHT) and other strategies
Docetaxel has proven efficacy in mCRPC as the first drug approved in 2004 showing an OS benefit in two phase III trials. [1,2] The recommended dose and schedule is 75 mg/m2 every three weeks according to the reported trials. Since 2011, a number of agents have been approved adding the armamentarium of agents to be offered to mCRPC agents with a varying approval according to local authorities (Figure 1). Cabazitaxel 25 mg/m2 improved survival compared to mitoxantrone (15.1 vs 12.7 mo, HR 0.7; p < 0.001) in the TROPIC study evaluating patients with mCRPC who had progressed on docetaxel leading to approval in 2010 for post-docetaxel mCRPC. [20] Therefore, the sequence of docetaxel followed by cabazitaxel is a valid option with high evidence. Though cabazitaxel did not succeed to be superior to docetaxel in first-line mCRPC. [21] The dose of cabazitaxel was amended to 20 mg/m2 in the guidelines following the results of the PROSELICA trial. [22]

Radionuclide therapy with Radium-223 – still "in" in times of 177Lutetium-PSMA-617 or is it the outdated nuclear medicine physician's treatment?
With the latest data on 177Lutetium (Lu)-Prostate-specific-membrane-antigen-(PSMA)-617 reported in the phase III VISION trial, a new attractive treatment has entered the treatment landscape of mCRPC. [23] Though the objective is to get as many life-prolonging agents as possible in and if a patient qualifies for radium-223 as per definition in label, physicians should include and consider this important treatment that has shown an OS benefit in the ALSYMPCA trial. [24] By inclusion criteria of the ALSYMPCA trial [24] the patient must be symptomatic for bone pain, but clearly should not have critical bone lesions requiring surgical stabilization or soft tissue involvement. Approval of radium-223 is different from region to region. In the ALSYMPCA trial, when enrolling at a time where novel hormonal agents have not entered the market yet, 43% were docetaxel naïve and therefore received radium-223 early; hence in first-line mCRPC.

The warning and change of label resulting from the results of the ERA-223 trial which reported a higher incidence of bone fractures in the radium-223 plus abiraterone/prednisone arm stopped the approach of adding systemic oral hormonal treatment to the radionuclide treatment. [25] Thus, the EORTC phase III PEACE-3 trial is giving radium-223 plus enzalutamide a new chance in first-line mCRPC versus enzalutamide alone. [26] The inclusion criteria have been amended to have the patient under established bone-protecting agents and the results presented at ASCO 2021 by Gillessen et al. underlined that this strategy almost annulated the risk for bone fractures. [27]

Is 177Lu-PSMA-617 the new game changer in mCRPC? When to consider treatment (pre- or post-Cabazitaxel)
PSMA-PET-CT imaging with different tracers, mostly 66Ga-PSMA or 18F-PSMA, is widely available nowadays, but with regional variations. Therefore, it has been implemented, approved, and reimbursed for the staging of high-risk localised PCa, biochemical recurrence after definitive local treatment, and for the evaluation of eligibility for treatment with 177Lu-PSMA.

With the positive phase III trial data of 177Lu-PSMA-617 in the VISION trial, another treatment option has arrived in mCRPC pre-treated patients. [23] The trial enrolled 831 mCRPC patients with PSMA-PET positive lesions pre-treated with at least one novel hormonal agent and one line of taxane-based CHT. Patients were randomised to receive up to six cycles with the 177Lu-PSMA-617 as a six-weekly infusion with protocol-permitted systemic agents, which were mostly glococorticosteroids or a second novel hormonal agent since cabazitaxel or investigational drugs were not permitted, versus protocol-permitted systemic agents alone. The trial met its primary endpoint OS with a median OS of 15.3 versus 11.3 months (HR 0.62, 95%CI: 0.52 to 0.74; p<0.001). Adverse events of grade 3 or higher were reported in 52.7 % of patients, mainly consisting of thrombocytopenia and anaemia, but generally well manageable and quality of life was not adversely affected.

The earlier reported phase II trial TheraP with PSA response as primary endpoint was randomised against cabazitaxel 20 mg/m2 after pre-treatment with an ARTA and docetaxel. [28] Thus, the selection criteria were more rigid, since in addition to a 66Ga-PSMA-PET, an FDG-PET was mandatory to exclude patients with FDG-PET-positive metastases who are not benefiting from treatment. The trial met its primary endpoint with a more favourable side-effect profile than cabazitaxel, and gave us a clue that the radionuclide therapy should be discussed in a line prior to cabazitaxel. This was also to guarantee that bone marrow function is maintained. On the contrary, cabazitaxel has high evidence of activity and OS benefit when given after docetaxel and remains standard until the approval of 177Lu-PSMA. Certainly, 177Lu-PSMA will only be available in high-volume centres associated with waiting time for treatment until it is more widely available.

PARP inhibitors in a specified subgroup of mCRPC patients, in what line best to use?
The PROfound study was the first phase III randomised trial showing an improvement in OS for mCRPC with an alteration in BRCA1/2 or ATM genes, treated with olaparib after at least one ARTA versus hormone switch, even if a substantial crossover was observed. [29] In addition, olaparib significantly improved time to pain progression, a key secondary endpoint and was associated with better health-related quality of life (HRQoL) over time, compared with hormone switch to NHT. [30,31] The CARD trial, a large randomised phase III trial, showed that not delaying chemotherapy for eligible patients improves survival. [19] However, the PROfound trial was designed prior to the CARD data. Therefore, according to the results from PROfound and the current guidelines, olaparib should be used after one ARTA and prior to a taxane if a BRCA1,2 mutation has been identified (depending on local regulatory approval) by somatic or germline testing. Therefore, a next-generation sequencing (NGS) testing is crucial and the latest in the mCRPC setting in identifying patients eligible for a PARP-inhibitor.

Recently, two phase III trails in first-line mCRPC have been presented at ASCO GU 2022 combining a PARP-inhibitor with abiraterone/prednisone. The PROpel study [32] enrolled patients independent of the homologous recombinant repair (HRR) status to receive either abiraterone/prednisone plus olaparib or abiraterone/prednisone plus placebo and reached its primary endpoint rPFS for this "all comer population" with an impressive rPFS of the combination of two years. In contrast, the MAGNITUDE trial [33] prospectively enrolled by the HRR status and the preplanned futility analysis in the HRR- arm revealed no benefit of adding niraparib to abiraterone/prednisone regarding the primary endpoint rPFS. Thus, the trial reached its primary endpoint rPFS in the HRR+ group and an encouraging rPFS was seen especially in the BRCA1/2 positive patient cohort. The OS of both trials is still pending and therefore combining a PARP inhibitor to abiraterone/prednisone is not yet standard of care.

Immunotherapy – first approach with Sipoleucel-T – failure to be integrated as routine standard of care
Sipuleucel-T is an autologous active cellular immunotherapy that was approved in 2010 based on results of the IMPACT trial, which reported a 4.1-mo survival benefit over placebo (25.8 versus 21.7 mo, HR 0.77; p = 0.03) in asymptomatic mCRPC patients without visceral metastases .[34] After initial approval by the EMA the company restrained approval because of logistics with production.

Other approaches to bring immunotherapy forward in metastatic prostate cancer (mPCa) have failed so far, at least with checkpoint inhibitors in monotherapy in unselected patients, as well as, enzalutamide with and without atezolizumab. [35] For a very small proportion of mCRPC patients (about 3% as reported by Abeda et al. [36]) with microsatellite instability-high (MSI high) or mismatch repair deficiency (dMMR), pembrolizumab is authorized by the U.S. Food and Drug Administration (FDA) after progression on prior treatments. Thus, combination trials are ongoing mostly with ARTAs in mCRPC and results must be awaited.

3. Finding the optimal sequence
Despite the FIRSTANA trial [21] showing non-superiority of cabazitaxel to docetaxel in first-line mCRPC, no prospective phase III trial in mCRPC has addressed a sequencing question.

The physician's choice of docetaxel or an ARTA (enzalutamide or abiraterone) in treatment-naïve mCRPC during ADT monotherapy in the mHSPC setting was mainly based on the more favourable side-effect profile and more convenient oral administration of the ARTAs, as well as, of patient's grade of symptomatology from his PCa since formally COU-AA-302 [37] and PREVAIL [38] included only asymptomatic or mildly symptomatic patients.

Since 2014, we have high-level evidence that adding docetaxel or an ARTA or even the triplet (ADT plus docetaxel plus abiraterone/prednisone or plus darolutamide) in some patients, prolong OS when added to ADT in mHSPC. Therefore, most patients with mCRPC receive one or is some cases two of the approved agents in mCRPC already in mHSPC. This situation limits treatment choices in the mCRPC setting to the drug classed not being used in mHSPC or even nmCRPC. Cabazitaxel and radium-223 remain exclusive options in mCRPC not having evidence in the mHSPC setting. Thus, progress has been made and other types of agents have shown benefit in later lines of mCRPC treatment such as 177Lu-PSMA in PSMA-PET positive tumours and PARP-inhibitors in patients with homologous recombination deficiency (HRD) (most benefit for BRCA1,2 mutations). The sequence for the latter is clearly defined as by trial inclusion criteria: 177Lu-PSMA in PSMA-PET positive mCRPC after one line of AR-targeted agent and one taxane and olaparib after one AR-targeted agent in the specified subgroup according to local approval status.

In summary, no single one-size-fits-all sequence approach will make its way in the future. It is up to us clinicians to re-assess the current biological and clinical rationale for each treatment line to get as many approved treatments to our patients as possible, and offer them the possibility of a long life with mPCa with the most optimal quality of life. This will require assessments of chemofitness, as well as, disease characteristics which now includes PSMA positivity and presence of DNA repair (DDR) defects to determine the next treatment to deploy for a given patient.

Future outlook for mCRPC
Numerous trials continue to investigate the future role of approved, novel agents, and combined strategies in mCRPC. The OS data of the PROpel and MAGNITUDE trials will tell us if PARP inhibitors should be offered in the future (independent of the HRR status) in combination with abiraterone/prednisone in first-line mCRPC. Thus, a significant proportion of patients will have received abiraterone or another ARTA already in mHSPC and will therefore not qualify.

Due to space constraints, figure 1 and the entire reference list can be made available to interested readers upon request by sending an email to: communications@uroweb.org.

Monday, 4 July 14:00 - 15:30
Thematic Session 16
Orange Area, eURO Auditorium 1

How to build successful prospective trials

A BURST-inspired model

Ms. Nikita R. Bhatt
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Co-Chair BURST, United Kingdom

Collaborative research is being undertaken at a pace never before seen as its strengths and benefits are realised, resulting in good quality practice-changing research. With several surgical initiatives being developed, urology has seen the rise of collaborative research over the last few years. Our lecture "How to build collaborative prospective trials" during the EAU22 congress session "YUORDay22: EAU Young Urologists Office (YUO) & European Society of Residents in Urology (ESRU)", will focus on how to utilise this collaborative model to build successful prospective trials. In order to build such a trial, the foundation of strong collaboration is key.

The British Urology Researchers in Surgical Training (BURST) [1], is an international research group comprising of urological trainees, medical students, core surgical trainees, consultants, methodologists and basic scientists. The aim of the BURST Research Collaborative is to produce high impact multi-centre audit and research which can improve patient care.

Although it retains its British core, the BURST Research Collaborative has become an international organisation with a broad reach with over 500 collaborators from around the world since its official launch at the British Association of Urological Surgeons in 2015. The first large international cohort study launched by BURST was MIMIC (a Multi-centre Cohort Study: Evaluating the role of inflammatory markers in patient's presenting with acute ureteric colic) [2] (Figure 1), led by Mr. Taimur Shah. This established the BURST network and led to the formation of a number of national and international collaborations. It has developed into a prize-winning collaborative that has presented work around the world and impacted urological research and practice.

We have continued to build trials with the strength of this cooperation and our relationship with our collaborators. Since MIMIC, we have successfully completed and published IDENTIFY (The Investigation and DEtection of urological Neoplasia in paTIents reFerred with suspected urinary tract cancer: A multicentre analysis) another prospective multicentre international collaborative trial (Figure 2) [3]. The high-quality data collected by these trials will also lend itself to calculators that can be used in practice: a spontaneous stone passage prediction tool and a urinary tract cancer prediction tool.

We are currently recruiting for our prospective international trial on improving quality in transurethral resection of bladder tumour (TURBT) surgery with randomised feedback to sites: Transurethral REsection and Single instillation intra-vesical chemotherapy Evaluation in bladder Cancer Treatment (RESECT). This is the largest ever study on TURBT ever performed, with over 6000 TURBT cases already entered in our database.

Recruitment for RESECT is still open, **www.bursturology.com/Studies/Resect/Overview/** for more information or email us at **resect@bursturology.com**. You will receive PubMed indexed collaborative authorship, with the opportunity for mainline authorship for our highest recruiters. In addition, you get access to a free data collection and reporting tool to audit your own practice, and you can use your own data as you wish. The success of our previous trials is testament to our high-quality work and research output. Participation in this trial will help you understand the workings of a collaborative research model closely and allow you to reap its benefits first hand. We are conducting a collaborator engagement meeting during the conference to discuss the progress of RESECT and future plan. This would be a good opportunity to meet the team face to face.
Please join us at EAU22 to understand how BURST produces prospective international trials that change practice. For more information, please visit our website **www.bursturology.com/about/about-burst** and join us in our currently recruiting trial RESECT.

Due to space constraints, the entire reference list can be made available to interested readers upon request by sending an email to: communications@uroweb.org.

Saturday, 2 July 10:00 - 17:00
YUORDay22
Green Area, Room 1

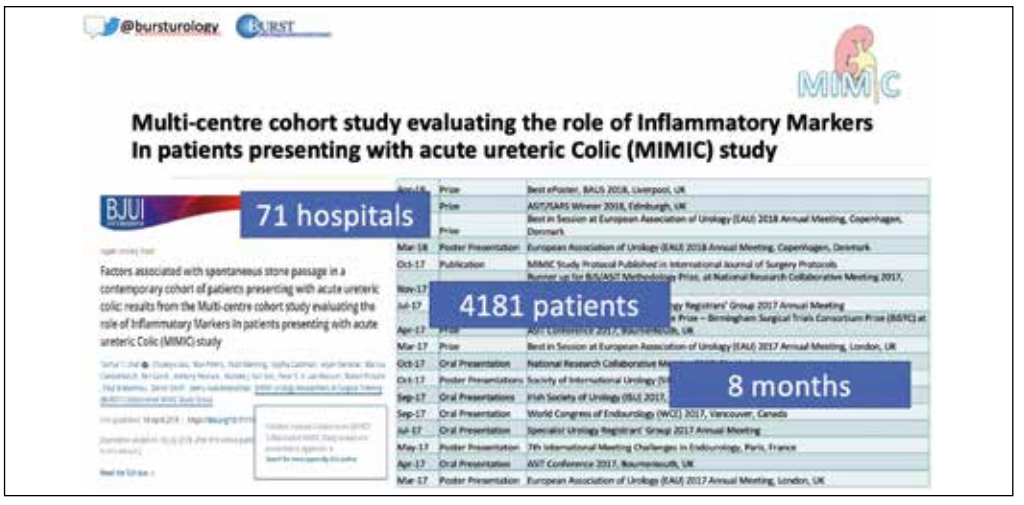

Figure 1: MIMIC was our first prize winning prospective international trial

Figure 2: With over 11,000 patients IDENTIFY was the largest ever study of its kind

How to become a good consultant

Tips on how to cope

By Dr. Esteban Emiliani
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Let us start with the fundamentals. The first (and most obvious) step in coping with residency and becoming a good consultant is to study hard. During residency, you should get to know the basics by heart and learn the craft. Try to find a residency in a hospital with a large volume of patients, as this will enhance learning and is more likely to deliver a rewarding experience.

I would strongly suggest that, after completing the residency, you undertake a fellowship to master one subspecialty and give yourself a good opportunity to fulfil a specific role within a team. Nowadays such training is highly valued as the trend is towards working in subspecialties. Read and get to know all the literature of your subspecialty, including grey areas and likely future trends as a basis for starting research lines. Go abroad and open your mind to new ways of thinking. Enrol in as many studies as you can. These steps will also give you the chance to increase your network, which will be valuable in launching your career.

As you go through each stage in the process, be as fully engaged as you can. Once you become a consultant, this comprehensive preparation will help as you start to think about how to become a good one. From an academic point of view, this pathway will open up excellent career opportunities, but you have to be vigilant and cautious with regard to your physical and mental health. The incidence of burnout is rising sharply among residents and urologists worldwide. It is a reality that has affected many of us.

I experienced burnout myself during my residency and learned that coping with residency and becoming a good consultant both require adherence to the same principle: take care of yourself! We know that this job involves long hours of work, but do not pass the threshold where you lose sight of your personal life or your physical and especially, mental health.

Found below are my suggestions as to what you can do to avoid becoming embroiled in such a terrible scenario. These can help improve your performance and efficiency, and enable you to become a good team player. Most of these activities can all be done during a busy day and will give you a better overall quality of life.

First of all, sleep! This is a must. Try to make it eight hours per night, and avoid screen time for at least one and a half hours before sleeping. I know this is hard as we spend many hours in the hospital but you will rapidly see how you become more lucid, active and creative – qualities crucial in enhancing your performance in the operative room. In this same line, make sure you give yourself breaks from social media and set "virtual boundaries". Avoid the hoax of "FOMO" (fear of missing out), set limits on your phone or put it down and out of reach on occasion.

"...after completing the residency, you undertake a fellowship to master one subspecialty and give yourself a good opportunity to fulfil a specific role within a team."

Start practicing meditation. In my case, this was a game changer. Studies have shown that 80% of thought processes are repetitive and mostly negative. You can start with just 10 minutes of meditation per day, or perhaps download an app (I recommend *Headspace* or *Calm*) to guide you in how to stop ruminative thoughts. I have found that many ideas for studies and the enthusiasm to perform them are products of having a "quiet mind".

In addition, a couple of weeks of meditation have been shown to reduce stress, aggression and irritability [1]; the result will be that you are far more able to cope with patients, huge workloads, and burnt-out co-workers who need your reliability and empathy. Further proven benefits are enhanced focus on work tasks, reduction in job-related stress and increased job satisfaction. [2]

Try to get some sun (or bright light) exposure daily, and not simply through a window. Take a walk during lunchtime or coffee break. Hundreds of good quality papers have shown the beneficial impact of this practice on metabolism and well-being (through its effects on neurotransmitters and hormones). [3] If meditation is not for you, you can always go to the gym or perform some outdoor activities. Exercising is always recommended.

"Learn from your mistakes, do not judge or be too hard on yourself."

Avoid the vending machine at the hospital. Let me put it another way: eat healthy and avoid processed foods (which are sometimes the only products offered by vending machines). A cup of coffee per day is enough (better drink it in the mornings). Try to opt for freshly-brewed coffee and avoid coffee from the vending machine. Also, remember to drink water throughout the day.

From an academic point of view, be up to date. Look for opportunities to engage in continuous medical education, go to meetings, talk to colleagues about your and their practice. Be engaged in your subspecialty community so that you can collaborate in studies. The sense of community and social connection among urologists is wonderful.

Some of my colleagues enjoy reading about medical errors and ethics (I would recommend any book by Atul Gawande, such as "Complications" or "The Checklist"). I also encourage listening to some podcasts focused on well-being during your commute, and comic relief is healthy, too.

Finally, and especially at the beginning of your surgical learning curve, **learn from your mistakes but do not judge yourself and do not be too hard on yourself.** Be gentle and compassionate when complications occur (because they will). You have to learn to work in a team, and this will make you less judgmental of others and more compassionate and supportive of colleagues when they make mistakes. It will also enhance your connection with patients and your appreciation of their needs, particularly when things go wrong.

In conclusion, I would emphasise that taking care of yourself should be your top priority. This will make you a good consultant. You can then focus on your practice, your patients and your team.

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Saturday, 2 July 10:00 - 17:00
YUORDay22
Green Area, Room 1

What we know about outpatient surgery in Europe

Survey results and foreseeable trends

Prof. Dr. Helmut Haas
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The EAU Section of Outpatient and Office Urology (ESUO), previously known as the EAU Section of Urologists in Office, sees one of its tasks in the exploration of the field of outpatient urology in Europe. We found that the designated terminology "office" was not comprehensive enough to describe the different forms of outpatient treatment sufficiently, so we renamed our section accordingly.

An outpatient urologist (OU), in our definition, treats outpatients in more than half of his/her working time in an established professional profile and not only temporarily. Outpatients are treated in urological offices, medical centres, and outpatient departments of hospitals. The respective urologists are either self-employed or employed or work in a combination of both, depending on their countries' rules and traditions.

At present, there is a remarkable number of 16,532 outpatient urologists (out of 30,299 urologists in total) who are working in 26 European countries.

Survey

Outpatient surgery is assumed to be an important section in the professional field of OUs; to what extent, we did not know yet. Therefore, we conducted a survey in 16 countries that has been processed by the section members. Unfortunately, the results can only be rough estimates, as the structures of the databases in the countries are either missing or not comparable with each other. Therefore, our aim could only be recording to what extent OUs perform outpatient surgery in which country; whether there are possibly characteristic structures and patterns in which institutions; and in which form of employment interventions are performed by OUs. To avoid the impression of scientific exactness, we present the results in a rough grid only.

The results show that in two-thirds of the responding countries, outpatient surgery is performed by OUs on a large scale (>50% of the countries' OUs), and in one third of them to a smaller extent (<50% of the countries' OUs). In Greece and the Netherlands, all of OUs perform outpatient surgery (fig. 1).

In four countries (Albania, Greece, the Netherlands, and Poland) more than half of the OUs also treat inpatients, in the other countries in a minor extent (fig. 2).

We asked the status of employment (i.e. self-employed, employed, and combination) and the place of work of OU performing outpatient surgery. However, we did not find a correlation between these criteria and the score of outpatient surgery. It is performed as well in offices, medical centres, and outpatient departments of hospitals and in all forms of employment. Obviously, this depends on the country's medical infrastructure and traditions. Outpatient surgery is an integral part of urology. In recent years, we have seen a trend to perform more and more procedures on an outpatient basis, including day surgery. Moreover, novel minimal invasive methods of prostate treatment are on their way to the outpatient institutions, supplementing the traditional interventions (fig. 3).

To support this development, the ESUO will deal with this subject in its meeting during the EAU22 congress.

See you at EAU22

The ESUO meeting "Urological surgery and interventions in an office and outpatient setting" at EAU22 will start with special measures in preparing surgery in an outpatient setting, including the support of nurses and the whole staff. Sedation, local and general anaesthesia will play an important role.

Fig. 1: Outpatient surgery by outpatient urologists (dark green: > 50 %, light green: < 50 %)

Fig. 2: Inpatient treatment by outpatient urologists (dark green: > 50 %, light green: < 50 %)

Usual outpatient procedures		
Open surgery	**Transurethral interventions**	**Prostate diagnostics**
meatotomy	Bladder biopsy	Transrectal biopsy
circumcision	Bladder coagulation	Transperineal biopsy
excision of atheroma	Botox injection	
vasectomy	DJ stent extraction	
resection of hydrocele	Urethral dilatation	
testicular biopsy		

Fig. 3: Usual outpatient procedures

The various open operations (penile and testicular surgeries), transurethral interventions (e.g. treatment of urethral strictures, Botox injections, and management of ureteral stents), and prostate biopsy will be presented using instructive videos and discussed with the audience.

The emerging role of novel methods in treating benign prostate hyperplasia (e.g. Urolift, Rezum, iTind, and embolization) in outpatient and day-case surgery will be a hot topic. Prevention and management of complications and legal aspects will complement the meeting.

In this meeting, our section aims to encourage European OUs to widen their therapeutic spectrum.

We encourage you to join us at the ESUO meeting at EAU22 on Saturday, 22 March 2022, from 10:30 to 14:00 CET at Room 4 located in the Green Area.

If you would like to join ESUO, please send us an email to ESUO@uroweb.org.

Saturday, 2 July 10:30 - 14:00
Meeting of the EAU Section of Urologists in Office (ESUO)
Green Area, Room 4

Simulation: How do we train in the future?

The importance of metrics and standardisation

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"The art of progress is to preserve order amid change and to preserve change amid order."–Alfred North Whitehead (1861–1947). From the series *Great Ideas of Western Man*.

The acquisition, maintenance and application of skill in surgery and procedure-based medicine are matters of great importance. There is now continued debate and public interest on methods that may be used for quality assurance of surgical performance.

Agents of change:
Traditionally, procedural skills have been acquired in a formal, structured apprenticeship training system. This was based on a model developed by William Stewart Halsted at Johns Hopkins at the end of the 19th and beginning of the 20th century. The apprenticeship phase in surgery and procedural-based medicine is unlike others because the trainees are being prepared to carry out interventional procedures on sick patients which are frequently life-threatening and almost always pose some risk of morbidity and mortality.

There is now an accumulating body of evidence which suggests that the safety of the procedure is directly correlated to the skill of the operator. [1,2] Furthermore, reduced work hours and changing work practices, e.g., image guided interventional procedures (laparoscopic, robotic, endovascular, endoscopic, etc) make the flaws in this approach to training very apparent.

Simulation training:
The Halstedian apprenticeship approach to training is no longer fit for purpose. It is inefficient, lacks transparency and assessment is subjective, which can be (unfairly) used against the trainee to constrain training progression or indeed completion. There also seems to be unanimous agreement amongst the different procedural-based disciplines that simulation-based training is a better way to train. However, there is disagreement on how best to use simulation. There is even more disagreement amongst the different professional groups as to what constitutes an adequate level of simulation fidelity for it to be useful and usable.

Effectiveness of simulation training:
Quantitative evidence already exists which demonstrates that simulation is a better way to train. [3] The optimal application of this approach (i.e., proficiency based progression or PBP) has demonstrated the power of simulation to dramatically improve suturing skills, laparoscopic surgical skills, interventional cardiology skills, orthopaedic surgery skills, and anaesthetist skills for childbirth.

In the next 12-24 months ORSI Academy and ERUS will report compelling simulation training data for robot-assisted procedure skills. A recent systematic review and meta-analysis of published, peer-reviewed, prospective, randomised and blinded clinical studies showed that a PBP simulation-based approach to training resulted in a 60% reduction in objectively assessed performance errors in comparison to a quality assured traditional approach. [4] However, publications on simulation to date have only demonstrated how superficially simulation is understood with scant attention paid to the underlying science of what makes for effective simulation training.

A revolution in computer technology has led to the problems faced by surgeons. This same technology offers a very powerful training solution. Aviation has used computer generated virtual reality (VR) simulations to train pilots for decades. However, unlike aeroplanes and airports with standardised features, real patients are all different. Furthermore, the aviation industry has over decades worked out precise protocols for dealing with different aeroplanes, airport terrains and flight scenarios.

Surgery in comparison was very much a craft with individual surgeons applying their own art to procedure performance. To utilise simulations for training, surgeons had first to develop surgical procedure templates (for a reference approach), including for example; the individual steps of the procedure, and the choice of instruments.

They also had to identify optimal and deviations from optimal performance (i.e., errors, critical/sentinel errors) so that engineers and computer scientists could build the simulation and accurately characterise the operation so that performance was quantifiable.

The science of simulation training:
PBP simulation training is a scientific approach to surgical skills training that is objective, transparent and fair to the trainee as well as the trainer. The performance metrics (i.e., procedure steps, errors and critical/sentinel errors) are the cornerstone of PBP training. These are derived from, validated by, and benchmarked on experienced surgeons who are actually good at performing the procedure in question. The metrics are developed initially during a detailed procedure characterisation with three to five experienced surgeons. [5,6]

The metrics explicitly identify observable performance before, during, and after the surgical procedure. They are then validated initially at a Delphi consensus meeting and then construct validity. The latter requires that the metrics can be scored reliably by independent raters (i.e., with an interrater reliability (IRR) >0.8) and the performance assessments reliably discriminate between the objectively assessed performance of experienced and less experienced surgeons. Only when all of these validation criteria are met, a proficiency benchmark can be quantitatively defined, based on the mean performance of the experienced practitioners.

In addition, the performance metrics should be explicit and binary scores, and not Likert scale assessments. Despite the voluminous reports on Likert scale assessments, they have been demonstrated to be unreliable, [7] and thus, by default not valid. PBP validated metrics are then used to give the trainee explicit formative performance feedback during training, thus accelerating their learning using deliberate practice [8] training rather than simply requiring the trainee to engage in repeated practice.

Furthermore, PBP training is delivered by faculty who know and can score the metrics with an IRR > 0.8 and have been taught (in a train-the-trainers course) how to use the metrics for deliberate rather than repeated practice.

Deliberate practice and standardisation:
VR computer and other types of simulation means that surgeons can now learn how to perform specific skills or procedures using the exact same devices, in the same way on simulations. In the past they learned these skills (and made mistakes) on real patients but on a virtual patient or a simulation they can perform the exact same procedure repeatedly and learn what not to do, as well as what to do.

This type of learning with performance feedback (i.e., deliberate practice) constitutes a very powerful approach to training that contrasts with the traditional apprenticeship model where performance feedback and learning was much more hit-and-miss. This scientific and metric-based approach means that simulation training and proficiency benchmarking can be standardised and implemented across training centres, the EU and wider afield. Furthermore, the metrics, curriculum and proficiency benchmarks are not based on the opinions of a few key opinion leaders but consensus between practicing clinicians at formal modified-Delphi meetings. Likewise, proficiency benchmarks are based on the actual measured performance levels of practicing clinicians. This approach to training necessitates a standardised curriculum and systematic and agreed approach to delivering it. Such an approach has the potential to considerably reduce performance heterogeneity by 'trainees'.

Order amid change:
Agents of change have forced surgery and medicine to consider how future doctors are optimally prepared for safe and effective clinical practice. This will unavoidably mean a change to the way doctors are trained. The 'Scientific Method' has as stated by Whitehead, the capacity to preserve order amid change. Proposals and ideas about training can be quantitively evaluated in a scientific way with robust empirical evidence underpinning decisions.

Figure 1a-d: 1a The sculpture at the front of ORSI Academy representing the ambition to scientifically measure performance to augment and enhance robotic surgical skills learning; 1b-d three different ORSI faculty surgeons training robotic surgical skills using the exact same metric-based, deliberate practice curriculum for all trainees.

The leadership of ERUS, the EAU and ORSI Academy are well advanced in this scientific 'conversation' and are very aware of the stakes involved. They also know that the scientific method and the data derived from studies in robotics, endourology, train-the-trainers etc. will guide and underpin their decision-making, thus preserving change amid order. Good quality scientific data can also mitigate the risk that change gets bogged down in endless deliberations.

Training must be more than an interesting educational experience:
This scientific and evidence-based approach to the acquisition of skills for the operating room relies on systematic, simulation-based, skills curriculum for training and education. [6] It means that surgeons (and other health care workers) can be optimally prepared for the operating room with their performance benchmarked against other surgeons before performing it in vivo. Research has now shown that surgeons trained using this approach perform significantly better and make fewer errors than traditionally trained surgeons. [3,9-12]

Conclusions:
Training with metric-based simulation ensures learning to a quantitatively defined performance level and greater homogeneity in trainee skill-sets. [6] Evidence from prospective, randomised studies shows that a PBP approach to education and training produces trainees with skill-sets that are 40-60% better than trainees using a traditional approach to training. These studies also show that trainees who receive the exact same curriculum but without the quantitatively defined performance benchmark perform only marginally better than those receiving traditionally training. [11]

These results clearly demonstrate that simulation training is effective for skills acquisition but the simulation training must be more than an interesting educational experience. A PBP approach to training may be conceptually and intellectually appealing but it represents a paradigm shift in how surgeons and doctors are educated and trained. [13-17]

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Saturday, 2 July 14:15 - 18:00
Meeting of the EAU Robotic Urology Section (ERUS)
Purple Area, Room Elicium 1

A new early detection strategy for prostate cancer

High time to implement our knowledge of 30 years of research

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For almost two decades, we had to wait for the first results of the two leading randomised trials for prostate cancer screening to be published. In 2009, the first results of the Prostate, Lung, Colorectal and Ovarian (PLCO) trial in the United States (US) and the European Randomised study of Screening for Prostate Cancer (ERSPC) did not end the debate on whether prostate cancer screening affects disease-specific mortality: in fact, it was fuelled by their contradictory results [1,2]. The debate in question ended in 2016 when reevaluation of the PSA testing rates in the PLCO trial showed significant contamination [3]. Shortly after, microsimulation models that accounted for such conditions, found compatible evidence among the ERSPC and PLCO trials that screening reduces prostate cancer-specific mortality [4]. Hence, from this moment on, we have level 1a evidence that PSA-based screening reduces prostate cancer-specific mortality. Updates on the ERSPC show an even larger benefit with longer follow-up in terms of absolute reduction in prostate cancer mortality and thus a decreasing number needed to invite (see fig. 1) [5].

However, the remaining issue is the harmful overdiagnosis that comes with screening. The rate of overdiagnosis estimated by the ERSPC was 50%, which is the price that was paid for the reduced rate of death from prostate cancer [2]. Therefore, the benefit of traditional PSA-based screening for prostate cancer does not outweigh its harms.

"The traditional PSA-based screening strategy from 1993 has become outdated with the rise of new stratification tools like MRI and risk calculators."

What happens if we do not screen?
To date, this imbalance in harms and benefits still forms one of the leading arguments against prostate cancer screening. However, the disrecommendation by the US Preventive Services Task Force in 2012 taught us what happens if we let prostate cancer run its course. Namely, in subsequent years, a stage migration was observed to more advanced cancers at the time of diagnosis [6]. Furthermore, to date, prostate cancer has become the most frequently diagnosed cancer among men in 112 countries and after lung cancer, the second leading cause of male cancer death [7]. The increasing burden of prostate cancer on society sparked public awareness on this matter. This expanding awareness in the absence of an organised early detection program paved a way for opportunistic screening. Compared to organised PSA-based screening, opportunistic screening does not go with reduced mortality as the benefit of screening but does go with even more overdiagnosis. To illustrate, the number of men needed to be diagnosed to prevent one prostate cancer death with this unstructured way of screening is expected to be almost twice as high [8].

The way out
In view of the foregoing, traditional PSA-based screening, opportunistic screening, and no screening programme at all do not appear to be desirable scenarios. Besides, a lot has happened since the first screening trials were established. The PSA-based screening strategy from 1993 has become outdated with the rise of new stratification tools like MRI and risk calculators. Against this background, an algorithm was recently developed for an organised prostate cancer screening strategy that uses the proven benefit of PSA testing and tackles overdiagnosis at the same time by applying further risk stratification using these new tools (see fig. 2) [9].

The algorithm
The algorithm starts with offering PSA testing to well-informed men in certain age groups (fig. 2A). Optimal testing intervals are dependent on previous PSA level, age, and comorbidity. The principle behind this is that the risk of developing clinically significant prostate cancer in the given time intervals (or remaining life expectancy) is not increased and therefore, more frequent testing is redundant. Further risk stratification is indicated for men with an elevated PSA level (fig. 2B). For those men, an individualised risk assessment of biopsy-detectable prostate cancer can be made by using risk calculators and MRI. The presented steps all aim to detect clinically significant prostate cancer at an early stage and reduce the number of unnecessary diagnostic procedures that will lead to less negative screening outcomes and insignificant cancer diagnoses. Important to realize is that for every step, a small number of diagnoses of clinically significant cancers will be missed. Therefore, the algorithm contains a safety net after every "negative screen" in terms of clinical follow-up. On the other hand, overdiagnosis of insignificant cancers will always remain to some degree. To prevent subsequent overtreatment, these men can be offered active surveillance to postpone or avoid active treatment.

Aspects to keep in mind and future challenges
Not all steps presented in the algorithm are based on studies in a screening setting or with the highest level of evidence. Also, the consensus is lacking on which diagnostic pathway and risk stratification tools are best. Fortunately, several screening trials are currently running that include the new stratification tools in different ways. Although these trials require, like the ERSPC and PLCO, a long follow-up to assess the effect on prostate cancer mortality, their preliminary results are promising when it comes to adequately detecting clinically significant prostate cancer and limiting overdiagnosis [10]. Another aspect to take into account is that some risk stratification tools will not, or not yet, be fully available in every region (e.g. high-quality MRI, expert readers, biomarker(panel)s, or calibrated risk calculators). However, starting with applying the easily obtainable biomarker PSA density, as a simple, inexpensive, but strong predictor yields a huge gain compared to the purely PSA-based strategy.

Europe's Beating Cancer Plan
The rise of prostate cancer in the list of cancer incidence and mortality rates reflects the necessity of implementing an organised early detection programme in the very near future. With this increasing burden of prostate cancer, we cannot wait another decade or longer for the long-term outcomes of the new screening trials to be published. Besides, as discussed above, the public awareness in combination with no organised screening at all paves the way for opportunistic screening, the situation right now, and does not go with any benefit and is related with even greater harm in terms of overdiagnosis. Thirty years of research has provided us level 1 evidence on the positive effect of PSA-based screening on prostate cancer-specific mortality, and indirect evidence that points towards a solid early detection strategy, with much improvement compared to the PSA-only strategy. This sound is heard by the Europe's Beating Cancer Plan committee who now encourages the Council to consider including prostate cancer screening in the update of the Council recommendations in 2022.

Summary
Traditional PSA-based screening reduces prostate cancer-specific mortality but goes with significant overdiagnosis. However, no organised screening at all paves the way for opportunistic screening which is an undesirable alternative due to the lack of benefit and the even greater harm in terms of overdiagnosis. Besides, prostate cancer incidence and related mortality continue to rise. New risk stratification tools such as risk calculators and MRI are the cornerstones in a new, balanced early detection strategy for prostate cancer. Although the optimal pathway for using these tools is not yet known, awaiting for the long-term outcomes of the new screening trials to answer, most important is to stop the increasing burden of prostate cancer in the very near future by disconnecting the link between PSA and immediate biopsy. This necessity and our current knowledge gained from thirty years of research on early detection of prostate cancer are recognised by the Europe's Beating Cancer Plan committee and now encourages the Council to consider including prostate cancer screening in the update of the Council recommendations in 2022.

Due to space constraints, the entire reference list can be made available to interested readers upon request by sending an email to: communications@uroweb.org.

Friday, 1 July 10:30 - 13:30
Special Session Prostate Cancer
Orange Area, eURO Auditorium 1

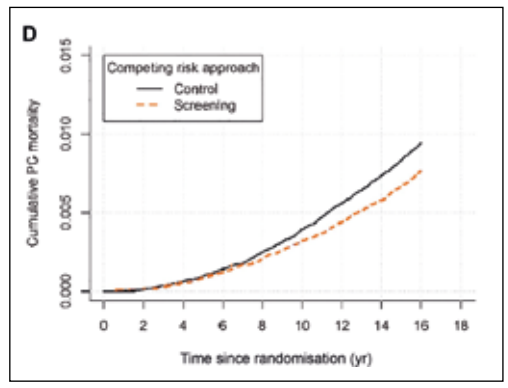

Figure 1: Prostate cancer-specific mortality estimated by the competing risk approach [5]. Note: Reprinted from Eur Urol, 2019; Vol 76/issue 1. Hugosson J et al, A 16-yr Follow-up of the European Randomized study of Screening for Prostate Cancer, pp. 43-51, Copyright 2022, with permission from Elsevier.

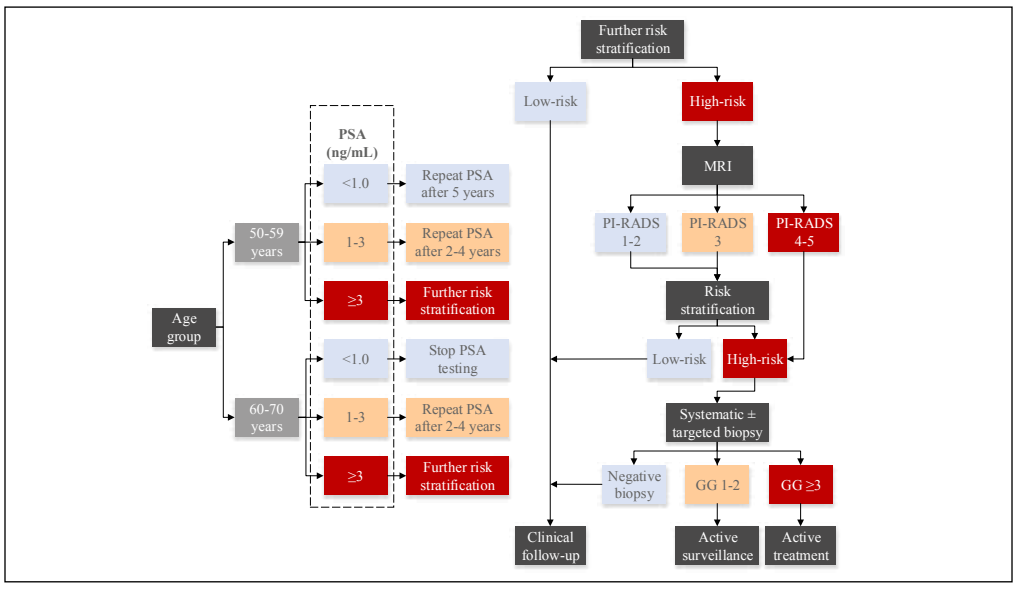

Figure 2: (A) Flow chart for PSA interval testing in different age groups. (B) Algorithm for a risk-stratified early detection strategy for prostate cancer in men with elevated PSA [9]. Note: Reprinted from Eur Urol, 2021;Vol 79/issue 3, Van Poppel H et al, Early Detection of Prostate Cancer in 2020 and Beyond: Facts and Recommendations for the European Union and the European Commission, pp. 327-329, Copyright 2021, with permission from Elsevier.

SUO Lecture 2022: Data gaps in HPV-driven penile cancer?

Classification, vaccination, testing, treatment and screening

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Firstly, I would like to thank the European Association of Urology (EAU) and the Society of Urologic Oncology (SUO) for the distinguished honour of delivering the SUO lecture at the EAU annual meeting 2022.

The topic which I will be speaking about at the meeting pertains to "What are the data gaps in HPV-driven penile cancer?" Prior to embarking on this topic, I would like to highlight that I do not have any financial disclosures relevant to the subject matter and only leadership disclosures as the vice chair of the NCCN bladder and penile cancer panel, the president of the Global Society of Rare Genitourinary Tumors, and a member of the ASCO/EAU panel on penile cancer.

The outline of my talk will be to review the biological pathways of relevance in penile cancer as well as pathological classification, discuss if there is a role of human papillomavirus (HPV) vaccination in prevention, highlight some of the challenges in standardised HPV testing, assess if there are any therapeutic implications of HPV status in treatment, and determine if there is any prognostic value of HPV testing in screening and surveillance.

Biology and classification
Prior to discussing the diagnostic and therapeutic implications of HPV in penile cancer, I would like to conduct a brief review of the important cancer biologic concepts central in understanding this malignancy. The concept of a cancer immunogram was proposed and popularised by Blank et al. and has great relevance in understanding cancer biology. [1] In this model of carcinogenesis and progression, a number of important host and tumour characteristics, and biological parameters, predict if and how cancer will ensue. This includes tumour foreignness (i.e. tumour mutational load) and sensitivity to immune effectors, as well as innate host immune environment characteristics: lymphocyte count, intra-tumoural T cell, PD-L1 status, absence of soluble inhibitors, and the absence of inhibitory tumour metabolism.

"It is critical to appreciate that penile squamous cell carcinomas are not one group of homogenous tumours, but are classified as HPV dependent or HPV independent tumours."

As has been deciphered, there is significant interplay between the tumour and host environment that drive the likelihood and pattern of progression of penile neoplasms. This includes their propensity to metastasise which in part is determined by PD-L1 status and loss of human leukocyte antigen expression. In terms of the interaction of penile tumours and the host tumour immune environment, this can be dichotomised into immune inflamed or immune excluded tumours.

It is critical to appreciate that penile squamous cell carcinomas are not one group of homogenous tumours, but are classified as HPV dependent or HPV independent tumours; both having very distinguished biological pathways. The HPV dependent pathway of penile carcinogenesis is much better characterised with HPV serotypes 16 and 18 being the predominant ones associated with cancer progression. This is through its viral integration and downstream effects on p53, hTERT, and the retinoblastoma proto-oncogene with these mediated through E6 and E7 whereby inducing genomic instability and the loss of tumour suppressor genes.

It is equally important to understand that HPV contributes to a host of other malignancies including cervical, head and neck, anal, vulvar, and vaginal cancer. Recent estimates indicated that roughly 13,000 penile cancer cases were attributable to penile cancer in 2017, with 70.2% suspected to be resulting from HPV 16/18 infection. When this is looked at on a global scale, we see that HPV attributable anogenital cancers have a much higher reported prevalence in many parts of North and South America as well as northern portions of Europe. Although, such data does suffer from significant under-reporting in many parts of the world, such as Africa.

We will now discuss important concepts related to the pathological classification of penile malignancies. In a prior analysis by Eich et al., a multi-institutional study was conducted to determine the impact of morphology, p16, and HPV status on the outcomes in squamous cell carcinoma of the penis. [2] On Cox multivariate logistic regression analysis, the strongest predictor of recurrence was perineural invasion. For metastatic progression it was lymphovascular invasion and the presence of HPV related tumours based on histology (favourable predictor). And lastly, for overall mortality, it was lymphovascular invasion and urethral involvement.

"HPV contributes to a host of other malignancies including cervical, head and neck, anal, vulvar, and vaginal cancer."

As we explore and discuss the data gaps in evolving to an HPV driven diagnostic and therapeutic paradigm, we can take reflection of some important work re-defining the care of head and neck squamous cell carcinoma. In a prior study by Dahlstrom et al., the authors proposed a staging system for patients with HPV related oropharyngeal cancer which was personalised to the biology and pattern of progression of these tumours. [3] This work was critical in popularising the concept that a subclassification of HPV head and neck tumour staging by HPV status had scientific merit and this work was subsequently validated by the International Collaboration on Oropharyngeal cancer Network for Staging. Unfortunately, no such scientifically rigorous HPV driven staging system is developed in penile cancer, with only a subclassification of penile cancer intraepithelial neoplasia developed, again missing the scientific rigor and prognostic robustness that has been so elegantly developed in oropharyngeal carcinoma.

HPV vaccination
One of the greatest areas of enthusiasm as it relates to penile cancer and many HPV related cancers, is that they are believed to be in large part preventable through the vaccination of high-risk men and women within the population. The efficacy of HPV quadrivalent vaccines in preventing many HPV related cancers are well established, like head and neck, as well as cervical cancer. Although the rates of HPV vaccination remain disappointingly low worldwide including North America and Europe, with the limited access and education on the merits of HPV vaccination in many parts of South America and Africa being of significant concern. The landmark HIMS study by Giuliano et al. established the safety of a quadrivalent HPV vaccine in 4,065 healthy boys and men in preventing HPV infection and the subsequent development of external genital lesions. [4] It is of note however, that although this study was impactful, it did not show a decreased prevalence in the incidence of penile cancer attributable to HPV vaccination among high-risk males. This most likely is a direct consequence on the rarity of this cancer and ultimately underpowering of the study constituting a limitation and clear gap in our knowledge on the subject matter.

HPV testing
Over recent years, many assays have been developed and commercialised for HPV testing. Only a certain subset of these tests are approved by North American or European governing bodies, and they also vary significantly in their diagnostic performance and level of peer reviewed literature supporting their clinical value. In this regard, the lack of standardisation in approved HPV testing assays and inconsistencies across studies make this an area of concern and a knowledge gap in global diagnostic standards.

Treatment
The therapeutic implications of HPV status have been eluded to in the prior section, but will be touched on in greater detail here. A number of studies have convincingly demonstrated that HPV status portends a favourable prognosis for penile cancer and may in fact predict a more significant treatment response to radiotherapy among HPV positive tumours. Due to the paucity of penile malignancies evaluated and treated at any given tertiary care referral centre, clinical trials specifically focused on HPV positive squamous cell carcinomas have in large part been conducted as basket trials. Although there is clinical merit in this type of accrual approach, most notably for rare malignancies, one must be cognisant that the genomic profiles of such diverse anatomically situated tumours can be heterogeneous and unique to a certain extent, whereby the findings of such baskets trials must be interpreted with caution and warrant subsequent clinical real world validation for the individual subset of HPV specific tumour sites. Once again, highlighting an unmet need and gap in our knowledge base in HPV driven penile cancer therapeutic approaches at this time.

Screening
An emerging area of active research and enthusiasm relates to the role of circulating DNA (cDNA) in the screening and surveillance of many malignancies with HPV related cancers being an ideal example where this has great promise. In a recent systematic review and meta-analysis by Balachandra et al., the performance of blood-based biomarkers of HPV associated cancers was critically assessed. [5] This well conducted review nicely detailed the great potential value of cDNA based biomarkers for HPV associated cancers most notably for oropharyngeal and cervical cancer. Although these studies seem to have an emerging role in refining our diagnostic, prognostic, and surveillance acumen, they remain with a relatively low sensitivity so refinements will be needed and relevant to the area of penile cancer, they have not been studied in a meaningful way as to their clinical value. Hence, we are left at this time with current rudimentary clinical tools, with the hopes that this will emerge as a novel tool in our therapeutic armamentarium in the near future.

Conclusion
There have been exciting advances in our understanding of the biological pathways in penile cancer. Although HPV plays a critical role in penile carcinogenesis and we have made promising advances in our HPV directed strategies, there remains a plethora of unmet needs and knowledge gaps which must be overcome in making the next leap in our diagnostic and therapeutic strategies in penile cancer.

"...the lack of standardisation in approved HPV testing assays and inconsistencies across studies make this an area of concern..."

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Friday, 1 July 08:00 - 10:15
Plenary Session 02
Grey Area, eURO Auditorium 2

Antibiotic prophylaxis in female pelvic surgery

Selection, timing, dosing and redosing are four rules for effective result

Prof. Elisabetta Costantini
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The primary rationale for antimicrobial prophylaxis is to decrease the incidence of surgical site infection and other preventable periprocedural infections, with the secondary goal of reducing antibiotic overuse. [1]

The choice of a correct pre-operative antibiotic prophylaxis is of primary importance in female pelvic surgery, especially when meshes are implanted and this is even more if the mesh is positioned by the vaginal route.

Postoperative infectious complications related to the prosthesis have been recorded, [2] wound infection (3-6%), urinary tract infection (UTI) (3.5-31%) mesh infections (1%), vaginal infections (0-18.4%), and pelvic abscess (1-2%). On these bases and taking into consideration that approximately one third of urogynecological surgical procedures for pelvic organ prolapse (POP) or stress urinary incontinence are performed using a mesh material, antibiotic prophylaxis is recommended [3] and the choice of a correct regimen is of paramount interest.

Effective prophylaxis

Shapiro in 2017 [4] demonstrated that gynecologic surgeons overuse antibiotics for surgical prophylaxis without adhering to the American College of Obstetricians and Gynecologists (ACOG) and many surgeons indiscriminately use antibiotic prophylaxis for all surgeries even when evidence-based medicine indicates otherwise. Indiscriminate antibiotic prophylaxis can lead to multidrug resistant (MDR) pathogens, higher medical expenses and unnecessary exposure to adverse reactions or toxicities. [5-6]

There are four major rules to obtain an effective prophylaxis: (1) correct antibiotic selection, (2) timing of administration, (3) dosing, and (4) redosing. *Goede* reported that 75% of cases were missing correct application of at least one of these four components. [7]

Antibiotic selection should consider the most likely infectious organisms associated with the site(s) of surgery (the lower urinary tract, skin, vagina, and intestine) and with the local antibiotic resistance patterns.

The optimal duration of antibiotics prophylaxis in female pelvic surgery is not known. Studies comparing single dose to multi-dose antibiotic prophylaxis regimens in patient undergoing prolapse surgery with mesh are lacking [8] and it is unclear if these women have any additional benefit. The correct timing is the administration within two hours prior to the incision.

To make the best choice also in accordance with Antibiotic Stewardship it is useful to create multi-disciplinary round tables and make a joint decision between surgeons, infectious disease specialists, and pharmacists.

The American Urological Association (AUA) and The American College of Obstetrics and Gynecology (ACOG) published their guidelines on the use of antibiotic prophylaxis in POP surgery taking into consideration some differences between abdominal and vaginal surgery. Female pelvic surgery is considered clean-contaminated procedure and we should consider that vagina could favour the spread of germs with the need of additional anaerobic coverage. (Table 1)

Both in abdominal sacrocolpopexy and vaginal approach the most common infectious complication is UTI (9.2% in abdominal approach; 6-34.7% in vaginal approach) [9-10] while the rates of superficial surgical site infections are quite low (1.8%-3.9% in abdominal approach and 0.4-5% in vaginal approach). [9-11] In abdominal approach, mesh infection is uncommon, especially if the procedure is performed with laparoscopic or robotic approach, possibly due to the lack of contact of the prosthesis with the vagina (except in the case of total hysterectomy) and the extreme biocompatibility of the most-used monofilament macroporous polypropylene materials. [12-13]

Also in vaginal anti-incontinence procedures which involve the use of mesh the rate of UTI is high (5.9-10.4%) while the rates of superficial surgical site infections are rare (1%). [14-18]

Swartz [19] showed that after anti-incontinence surgery there are non-significant differences in UTI rate between women undergoing pre-treatment antibiotic prophylaxis (in according to the AUA and ACOG recommendation), and patients who additionally received 3 days of postoperative antibiotics. Nevertheless in the second group there was increased risk of adverse events (7.8% vs. 0.9%). Therefore it was advisable to carry out only prophylaxis.

Illiano [20] demonstrated that perioperative prophylaxis using a single dose of antibiotic, clindamycin and gentamycin, is sufficient in women who underwent prolapse surgery using mesh, regardless of the surgical approach used (laparoscopic or transvaginal). (Fig. 1)

Besides infections, another problem of vaginal prosthetic surgery is vaginal mesh exposure. No correlation was found between the type or duration of antibiotic prophylaxis and mesh exposure [19]. *Svenningsen* emphasized that the antibiotic prophylaxis prevented the developing postoperative infections or prolonged postoperative pain after anti incontinence surgery, but did not offer protection against tape exposure. [21]

Illiano confirmed that the vaginal mesh exposure may not be related to the type of antibiotic therapy, but rather to technical problems. [20] When a polypropylene mesh is implanted, a complex series of foreign body reactions occurs, until it is covered with fibrous tissue. Its presence may further induce local immunosuppression and improve the survival of any bacteria near the mesh. Bacteria form a biofilm on the surface of the mesh, difficult to eradicate. [22-23] The characteristics of the mesh are therefore important to reduce biofilm formation. Meshes with pore size diameter greater than 75 mm, which permit fibroblasts, macrophages, polymorphonuclear leukocytes to penetrate the mesh, are associated with reduced incidence of mesh infections compared with the use of mesh with small pores (<10 mm).

Conclusion

In conclusion, the practice of correct antibiotic prophylaxis, the choice of the right material and the expertise of the surgeon are the fundamental elements for a surgical procedure with few complications.

The principles to be considered are the patient's susceptibility to the infection, the surgical procedure with the different likelihood of bacterial invasion at the operative site, i.e for vaginal procedures consider additional anaerobic coverage especially when hysterectomy is performed, the potential morbidity of any subsequent infection, the morbidity and adverse events due to the use of antimicrobials other than the risk of multidrug resistance. Patient-specific factors and local antimicrobial susceptibilities, as reflected in local antibiograms, should also influence the choice of the agent.

Data	Protocol A			Protocol B			Protocol C		
	VA (*N* = 11)	AA (*N* = 19)	*p* value	VA (*N* = 10)	AA (*N* = 20)	*p* value	VA (*N* = 9)	AA (*N* = 18)	*p* value
Urinary tract infection, *n* (%)	6 (54.5)	1 (5.3)	0.002	3 (30)	5 (25)	0.77	0 (0)	3 (16.7)	0.19
Fever, *n* (%)	0 (0)	2 (10)	0.27	1 (10)	2 (10)	0.09	0 (0)	3 (16.7)	0.19
Surgical site infection, *n* (%)	0	0	nc	0	0	nc	0	0	nc
Superficial surgical site infection, *n* (%)	0	0	nc	0	0	nc	0	0	nc
Deep surgical site infection, *n* (%)	0	0	nc	0	0	nc	0	0	nc
Prosthetic infection, *n* (%)	0	0	nc	0	0	nc	0	0	nc
Vaginal infection, *n* (%)	0	0	nc	0	0	nc	0	0	nc
Vaginal mesh exposure, *n* (%)	0	1 (5)	0.45	2 (20)	1 (5)	0.09	0	0	nc

Figure 1 : Post-operative complications (vaginal vs abdominal approach). Protocol A: multidose group pre and post-surgery; Protocol B: double dose group pre and post-surgery; Protocol C: single-dose group [20]

Due to emerging MDR, all the recommendations remain in flux; clinicians are urged to consult their local antibiograms and local infectious disease experts where needed. We all know the tremendous variability of bacteria susceptibility in clinical practice, with variation from hospital to hospital and provider to provider. The absence of strong evidence to support such variations, lead to rapid changing paradigms in periprocedural prophylaxis in different setting.

Finally, high-level evidence in the choice of the right prophylaxis and regimen is still lacking and the recommendations are subject to changes.

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Saturday, 2 July 14:15 - 17:50
Meeting of the EAU Section of Infections in Urology (ESIU)
Grey Area, Room Emerald

Table 1: American Urological Association (AUA) and American College of Obstetrics and Gynaecology (ACOG) recommendations

	AUA RECOMMENDATIONS	ACOG RECOMMENDATIONS
Abdominal or vaginal pelvic organ prolapse surgery Anti-incontinence surgery	Cefazolin or 2nd generation Cephalosporins (Cefoxitin/Cefotetan)	Cefazolin
	ALTERNATIVES	**ALTERNATIVES**
	Ampicillin-Sulbactam Aminoglycoside + Metronidazole, Clindamycin	Metronidazole + Gentamicin or Aztreonam Clindamycin + Gentamicin or Aztreonam

Treating recurrent stress urinary incontinence

PURSUIT results to greatly benefit healthcare professionals and patients

Dr. Caroline Pope
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There is great uncertainty regarding the best treatment for women with recurrent, or persistent, stress urinary incontinence (SUI) following a primary treatment. PURSUIT is a UK National Institute of Health Research (NIHR)-funded randomised controlled trial (RCT) which has been designed to provide the necessary high-quality scientific and clinical evidence to inform practice and guide decision-making for patients and healthcare professionals.

Women are often reluctant to seek further treatment after experiencing a failed primary continence procedure. In addition, inconsistent classification by researchers means that exact rates of recurrent and persistent SUI are unclear. Many women with this condition have lived with symptoms, which severely affect their quality of life, for a significant period of time. Experience of having an unsuccessful treatment can cause considerable distress and there are substantial cost-implications associated with ongoing symptoms.

Added to this, women are understandably concerned and reticent about treatment because of the (now well-publicised) potential complications of vaginal mesh surgery, which up until recently was the most common surgical treatment for primary SUI. Patients express desire to return to normal life, but this is often balanced with a strong wish to minimise the severity of surgery or complications.

Current evidence is lacking

The James Lind Alliance, a group of healthcare professionals and patients, identified recurrent SUI treatment as a top 10 research priority. Over a decade later the issue remains unaddressed. Current NICE guidelines (NG123) on the management of urinary incontinence in women [1] suggest that women whose primary surgical procedure for SUI has failed (including women whose symptoms have returned) should be referred to a regional multidisciplinary team for management, but the evidence to support their onward treatment pathway is lacking.

A systematic review and meta-analysis of previous RCTs comparing surgical procedures for treatment of recurrent SUI showed no significant difference in their effectiveness. However, the analysis was potentially underpowered due to a lack of published evidence in the field. [2] Tincello et al. surveyed patients and clinicians to explore opinion on preferred treatment options for women with recurrent SUI. [3] Patient views were highly individual, and the clinician surveys demonstrated that there was no consensus on which treatment is best. Furthermore, survey responses highlighted that there was lack of equipoise among surgeons.

Current treatment options

Treatment practice across the UK is highly variable. [3] Decisions are partly dependent on the mechanism of the recurrent SUI (hypermobility or intrinsic sphincter deficiency), the surgeon's expertise and personal opinion, and the patient's preference, which is often strongly influenced by (a wish to avoid) the previously failed procedure.

The use of midurethral tape for the treatment of recurrent SUI is currently (2022) suspended within the National Health Service (NHS). Thus available treatments are: 1) endoscopic bulking injections; 2) autologous urethral sling; 3) colposuspension and 4) artificial urinary sphincter (AUS).

Colposuspension and autologous sling are preferred by some surgeons for treating hypermobility SUI, as they restore support for the urethra. Autologous sling or AUS are believed to be more appropriate for women with sphincter deficiency, as they compress the urethra, thereby restoring some resistance. For both mechanisms, endoscopy is a less invasive procedure than surgery and is thought to carry less risk of side effects. There are different marketed bulking agents available for endoscopic treatment, but a Cochrane review of trials comparing agents found no clear-cut conclusions regarding efficacy and there was insufficient evidence to guide practice. The review also compared injections with surgical treatment. It suggested greater symptomatic improvement was observed with surgical treatments, but this advantage needed to be weighed against the higher complication rate. [4]

Study rationale

This NIHR-funded study (Health Technology Assessment, reference 17/95/03) 'Proper Understanding of Recurrent Stress Urinary Incontinence Treatment in women (PURSUIT) is a randomised controlled trial (RCT) of endoscopic and surgical treatment. It has been designed to address the dearth of scientific evidence and answer the question "what is the best treatment for women with recurrent SUI after failed primary surgery?".

Study design

PURSUIT is a two-arm RCT set in urology and urogynaecology units in 24 NHS hospitals across the United Kingdom. Women aged ≥18 years with bothersome recurrent or persistent SUI following a primary SUI intervention who are seeking further treatment are randomised to receive either endoscopic urethral bulking injection(s) or a surgical operation. (Figure 1)

Women randomised to the surgical arm decide which operation to have through a preference-based shared decision-making process with their surgeon. Surgical treatment options include all those available under usual NHS care (as described above). All women receive their allocated treatment and aftercare in hospital in accordance with routine NHS clinical care. A total of 250 women will be recruited over a 2-year period and followed up for 3-years, with equal numbers joining each treatment arm. The trial includes an integrated QuinteT Recruitment Intervention (QRI) [5] aimed at evaluating and optimising recruitment and informed consent and implementing recruitment intervention strategies, if needed. A nested qualitative interview study is also being conducted to explore clinicians' and patients' views on the treatment options and to understand patients' experiences of their intervention.

The primary objective is to identify whether surgical treatment achieves a superior symptomatic outcome compared to endoscopic bulking injection(s) treatment at 1-year post randomisation using the validated patient reported outcome measure (PROM) of continence (International Consultation on Incontinence Questionnaire - Urinary Incontinence - Short Form (ICIQ-UI-SF)). The secondary objectives of the study are to assess: the longer-term (2- and 3-years post randomisation) clinical impact of the interventions on continence (ICIQ-UI-SF); the improvement of symptoms post-intervention (Patient Global Impression of improvement (PGI-I)); operative measures; sexual function (Pelvic Organ Prolapse (POP)/Urinary Incontinence Sexual Questionnaire, IUGA-Revised (PISQ-IR)); the safety of each intervention (adverse events) and the likelihood of re-treatment; the cost-effectiveness from an NHS and societal perspective at 1-year post randomisation and from a secondary care NHS perspective at 3-years post randomisation; women's experiences of interventions and associated quality of life (QoL, EuroQol Group's 5-dimension health status questionnaire (EQ-5D-5L)) and clinicians' views of interventions.

Progress and challenges

PURSUIT opened to recruitment in January 2020 but was paused only 10 weeks later with the emergence of the COVID-19 pandemic. At the end of September 2020, the study received the go ahead to re-start recruitment, but the impact of the pandemic on clinical and research teams at open and planned hospital sites is long-lasting and their capacity to conduct the study has still not returned to pre-pandemic levels even now, nearly 2-years on.

In addition to the direct impact of the pandemic, the Royal College of Surgeons' (RCS) prioritisation classification (used in hospitals by waiting list co-ordinators to determine the order in which operations should be undertaken) has further hindered study progress. Classification ranges from P1 (priority 1 – immediate treatment) to P4 (priority 4 – procedures to be performed in >3 months). All incontinence procedures, including those for recurrent SUI, have been classified as P4, since the condition is not life-threatening. In practice, with the substantial backlog of operations which has built up during the pandemic, this currently means "delayed indefinitely".

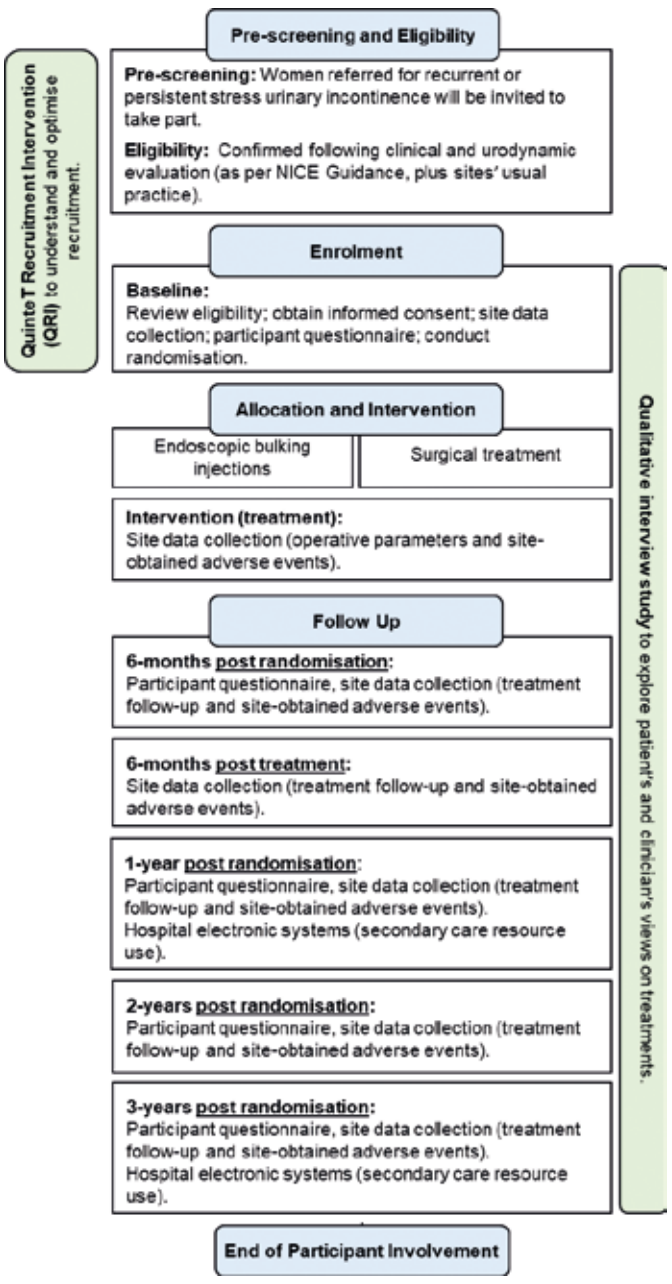

Figure 1: Trial flowchart

We have questioned the ongoing appropriateness of the RCS classification for women with recurrent SUI. Their symptoms often started after childbirth, they have already had a treatment which has failed, and some of these women have also undergone removal of vaginal mesh which may have caused their symptoms to deteriorate to a level worse than when they first presented. The women eligible for PURSUIT have had chronic problems, affecting them for years or even decades. Despite multiple medical interventions, they continue to experience embarrassing leakage, which profoundly affects their self-esteem, relationships, and their occupation. These severe symptoms are marginalised by placement in the P4 category; a backwards step, considering that it took years for incontinence to receive due recognition for its true impact on women.

Given these challenges, only added to by the ongoing strain on healthcare delivery, PURSUIT is considerably behind original projected timelines for delivery. Only in the last few months have hospital teams begun to regain some capacity to conduct minimal study activity, recruitment has been slow to progress and waiting lists for study interventions are, in many hospitals, >12 months. Despite these testing circumstances, it is evident that there is enormous ongoing support for PURSUIT from the funder, the clinical and research communities, our patient and public involvement contributors and, importantly, from the women whose quality of life is so adversely affected by living with this condition.

Conclusion/impact on healthcare

The results from PURSUIT will be of great benefit to healthcare professionals and patients seeking further treatment by providing the high-quality, scientific evidence which is currently lacking on endoscopic bulking injections and surgical treatments. The findings will give a solid basis for guiding treatment and improving symptoms and quality of life for women presenting with recurrent SUI in the future.

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Saturday, 2 July 10:30 - 14:00
Meeting of the EAU Section of Female and Functional Urology (ESFFU)
Purple Area, Room Elicium 2

Email: pursuit-trial@bristol.ac.uk
Study website: https://pursuit.blogs.bristol.ac.uk/
Twitter: @PursuitTrial

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Potentiating immunotherapy with improved oncolytic viruses

Unleashing full potential of OVs in combination with other treatments

Dr. Geertje Van Der Horst
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Clinical problem
Prostate cancer is the most common cancer in males and the third cause of cancer-related death in men in Europe. [1,2] Current treatments of primary prostate cancer with androgen deprivation therapy are initially very effective. However beneficial responses are followed by tumour recurrence at distant sites leading to incurable, metastatic castration-resistant disease.

Urothelial carcinoma of the bladder is the sixth most common cancer in Europe. [2] Despite the prevalence and high economic costs, bladder cancer is still relatively understudied. [3] For patients with metastatic UCB, systemic cisplatin-based chemotherapy is the standard-of-care. [4] This treatment has considerable side-effects and approximately 30% of patients either fail to respond or suffer recurrent disease within five years.

Immunotherapy has emerged as a viable and attractive strategy for the treatment of solid tumours, including those of the human bladder and prostate. Despite the success of immu-notherapeutic approaches in several tumour types, prostate cancer has remained largely unresponsive. Moreover, only about 30% of patients with metastatic bladder cancer will respond to immune checkpoint inhibition and the development of novel therapy for these urological malignancies is, therefore, needed.

Oncolytic virotherapy
Currently, several immunotherapy approaches and combinations are under investigation in numerous clinical trials and various clinical scenarios, including immune checkpoint inhibi-tors (ICIs), cell-based therapy and cancer vaccines. [5-9] ICIs encompass antibodies blocking the PD-1/PD-L1 pathway. These compounds have shown impressive and durable responses in several clinical studies. [10-21] Prostate and bladder cancers frequently escape from im-mune surveillance by creating an immune-suppressive tumour microenvironment. As a re-sult, tumours from these patients remained largely unresponsive to treatment. [22-24] Tak-en together, more effective therapies for high-risk, advanced or metastatic patients are warranted.

Oncolytic viro-immunotherapy is a promising cancer treatment in which replication-competent oncolytic viruses are used that specifically infect, replicate in and lyse malignant tumour cells, while minimising harm to normal cells. [25-26] Infection of tumour cells by oncolytic viruses (OVs) is now also recognised for their immunotherapeutic potential by promoting strong antiviral and antitumour immune responses. Genetically engineered or naturally-occurring OVs can be exploited to kickstart the immune system either alone or combined with current immunotherapies for the treatment of bladder and prostate cancer patients. Worldwide, multiple OVs are under investigation and various clinical trials are ongoing with a.o. Adenovirus (AD), Newcastle Disease virus (NDV), Reovirus (RV) and Her-pes simplex virus (HSV). Although OVs were originally designed to function as tumour-lysing therapeutics, they have now been shown to initiate systemic anti-tumour immune responses (immunogenic cell death or ICD).

Upon oncolysis, tumour cells release damage-associated molecular patterns (DAMPs) [27-28] and pathogen-associated molecular patterns (PAMPs).[27-30] DAMPs and PAMPs are recognised by antigen presenting cells and presented to T-cells thereby initiating a system-ic, adaptive immune response. [31]

It is no longer considered critical for viruses to directly infect and kill every tumour cell. [32, 33] Successful virotherapy results in inducing more effective anti-tumour immune respons-es and/or reduction of immune suppression that shield tumour cells from the immune sys-tem. [25, 34-40] OVs may, therefore, enhance anti-tumour responses in patients that fail to respond to current immune checkpoint blockade.

The outcomes of clinical trials highlight that the efficacy of oncolytic viro-immunotherapy varies between patients, depending on the tumour type and the applied oncolytic virus. [7,8] The observed heterogeneous anti-tumour responses to oncolytic viruses emphasise the clin-ical need for better stratification of cancer patients for viro-immunotherapy by selecting the most promising candidate OV in future clinical trials.

Developing oncolytic viruses for clinical use: a consortium approach
To rapidly develop and implement viro-immunotherapy as a treatment modality for cancer, multiple academic institutions collaborate in the Dutch Oncolytic Viro-Immuno Therapy consortium (OVIT). The OVIT consortium consists of multidisciplinary team of researchers and clinicians of three Dutch universities that are experts in virology, cancer immunology, (uro) oncology and surgery. [41] The major aim of the OVIT consortium is to develop an effi-cacious, safe and affordable viro-immunotherapy for patients with pancreatic, urothelial or glioblastoma tumours using promising oncolytic viruses from the participating groups, i.e., optimised Adenovirus, mammalian Reovirus and Newcastle disease virus strains.

Our data show that the variable responses to OV therapy is related to the susceptibility of the tumour cells to virus-induced oncolysis and the efficiency with which the immune sys-tem is activated upon OV infection of the tumour. Considering the variety of OVs, the multi-tude of genomic modifications in tumours and the diversity of tumour microenvironment immune landscapes, there is a clear need for platforms with predictive potential.

Oncolytic viro-immunotherapy in urological cancers
At the Leiden University Medical Center (LUMC), we have found that oncolytic potency of reoviruses in (urological) cancers can be enhanced by selection and genetic modification leading to the identification of a promising, spontaneous jin-3 mutant Reovirus. [42,43]

Furthermore, we recently isolated and identified a novel, promising candidate non-human primate Adenovirus (NHP-AdV007) with strong oncolytic properties across multiple human tumour cell lines.[44,45] Non-human primate-derived adenoviruses form a valuable alter-native for the use of human adenoviruses in vaccine development and gene therapy strate-gies by virtue of the low seroprevalence of neutralising immunity in the human popula-tion.[44,45]

Selected Adenovirus and Reovirus strains display oncolytic properties in human PCa and BCa cell lines and ex vivo-cultured, patient-derived tumour tissues.[43] Moreover, the tested viruses induce multiple mediators of immunogenic cell death and immunostimulatory genes, but responses vary among the used OV and tumour combinations.[43] The latter observations highlight the importance of OV-tumour matching, hence a more personalised approach.

Combination therapy with oncolytic viruses
Various clinical trials have demonstrated that oncolytic, replication-competent mammalian reoviruses and human adenoviruses are safe for patients and can display antitumour effica-cy in a variety of malignancies. Full responses of these monotherapeutic approaches, how-ever, were found in only a minority of patients. It is, therefore, crucial to understand how OVs can be exploited in combination with existing treatment modalities, i.e., chemotherapy and immunotherapy, to unleash their full potential.

Due to space constraints, the entire reference list can be made available to interested readers upon request by sending an email to: communications@uroweb.org.

Friday, 1 July 08:00 - 10:15
Plenary Session 02
Grey Area, eURO Auditorium 2

ctDNA dynamics in advanced bladder cancer

Use of circulating tumour DNA could be used for "live" monitoring of treatment response

Prof. Jørgen Bjerggaard Jensen
Chairman of the Nordic Urothelial Research Group (NORTH-REG) Department of Urology, Aarhus University Hospital, Aarhus (DK)

At the time of diagnoses, approximately one quarter of the patients with muscle invasive bladder cancer (MIBC) presents with metastasis or fixed tumour and are thereby not candidates for local curative intended treatment with cystectomy or radiotherapy. Of the remaining approximately 75% of MIBC patients with supposedly localized disease, between one third to two thirds will experience a metastatic relapse despite intended radical local treatment.

The main reason for this is the presence of occult metastatic disease at the time of diagnoses. These micro deposits of metastasis is not visible despite modern FDG-PET/CT or other currently available imaging modalities. This will inevitably lead to a recurrence visible on imaging if left untreated which ultimately can lead to a fatal outcome.

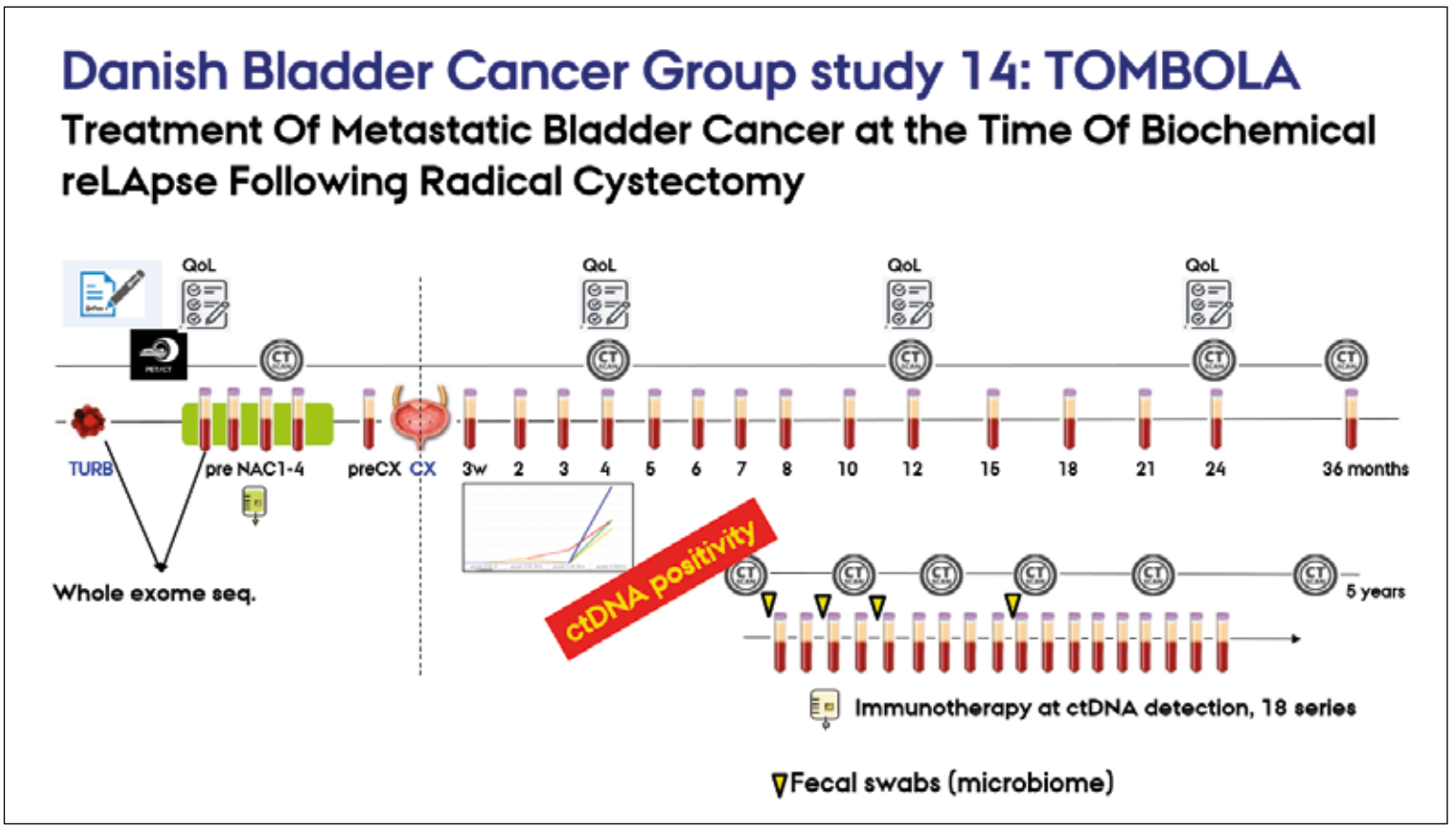


Figure 1: Design of Danish Bladder Cancer Study no. 14 – TOMBOLA. All patients are diagnosed with localized MIBC and undergo standard neoadjuvant chemotherapy followed by radical cystectomy. During a close follow-up regimen, immunotherapy with Atezoluzimab is started if ctDNA is detected. During neoadjuvant chemotherapy and immunotherapy, ctDNA is measured in additional observational plasma samples to estimate the potential use of ctDNA in treatment monitoring.

Selection of patients for adjuvant treatment
In order to reduce the high treatment failure rate in MIBC patients, neoadjuvant chemotherapy has been recommended to high-risk patients prior to local radical treatment. Another strategy is to offer adjuvant systemic treatment after surgery in patients with a high risk of recurrence based on conventional risk parameters (e.g. non-organ confined disease or remnant MIBC following neoadjuvant chemotherapy).

However, both strategies will inevitably lead to both overtreatment in classical high-risk patients as well as undertreatment in a fraction of the classical low-risk patients. This is based on the fact that not all apparently high-risk patients experience recurrence why these patients could do without a potentially harmful and expensive treatment if better selection was possible. Moreover, some supposedly low-risk patients will develop a recurrence. Nevertheless, because the risk is low per se, adjuvant treatment is typically not given to these patients, neither as standard in clinical trials. Instead, low-risk patients, which despite this may develop recurrence, are treated at the time of recurrence.

At this time point, the metastatic burden is higher, the disease is more molecularly heterogeneous, and therefore theoretically more treatment refractory compared to treatment close to the radical local treatment. If all patients with remnant metastatic disease, and only these, instead could be treated at a very early time point this will reduce the number of patients undergoing superfluous and potentially harmful treatment alongside with a reduction in cost as the non-recurrent high risk patients will be omitted from additional treatment. Methods to identify these patients have been lacking but the future looks bright regarding this with the development of new molecular methods for detection of circulating tumour DNA (ctDNA).

"Live" monitoring of treatment response in metastatic disease
Another current challenge in advanced urothelial cancer is whether patients undergoing systemic oncological treatment have a response justifying the continuation of a systemic treatment; or whether they should be undergoing another potentially more effective treatment or maybe abandon treatment all together. Thus, patients without tumour reduction effect of the given treatment but suffering from severe side effects could be spared the latter. Current standard regarding oncological response to systemic treatment is response estimated by e.g. RESIST criteria from imaging. This is, however, associated with a certain lead time before true tumour reduction can be seen and a certain interval between imaging is required in order to see any changes.

Circulating tumour DNA
One very promising biomarker in modern molecular medicine is circulating tumour DNA (ctDNA). Small fragments of DNA from tumour cells is released into circulation. The tumour DNA contains tumour-specific mutations and other genomic alterations, which can be used as highly specific biomarkers. Typically, ctDNA from plasma samples is used as a marker of metastatic disease whereas urine-based ctDNA is more useful to estimate local tumour presence in the urothelium.

Regarding the concept of ctDNA as a biomarker, it is important to recognize that the techniques for identifying ctDNA in its current use is based on a highly specialized individual design of assays designed individually to each patient or expensive sequencing approaches. This is time consuming and requires advanced laboratory and bioinformatic methods. However, the techniques and facilities are constantly evolving, leading to a more and more easily available technique in studies and hopefully in a near future daily practice.

"Another current challenge in advanced urothelial cancer is whether patients undergoing systemic oncological treatment have a response justifying the continuation of a systemic treatment."

While identification of the highly tumour-specific and patient-specific mutations in blood samples is associated with an extreme high positive predictive value (and a positive quantity related correlation with tumour burden) the negative predictive value is not perfect. Thus, selection of new tumour clones during ongoing systemic treatment can result in false negative findings or at least a nonlinear correlation between ctDNA dynamics and tumour burden. It is therefore important to continue to use conventional imaging in parallel to the introduction of this promising diagnostic technique, at least until more prospective studies and clinical trials have been conducted.

ctDNA in selection of patients for additional treatment following radical cystectomy
ctDNA represents the mutational spectrum of the tumour and is thus highly tumour-specific. Detection of ctDNA following local radical treatment has proved to be associated with certainty of remnant carcinoma cells and thus leading to recurrence following a variable lead time. In a previous study, this lead time was proven to be variable between few months to years, but very important, all positive findings in patients lead to later or simultaneous clinical recurrence. [1]

With this in mind, the Danish Bladder Cancer Group has established an ongoing intervention study – the TOMBOLA trial – , a national, interdisciplinary collaboration between five clinical centres (Aarhus, Aalborg, Odense, Herlev, Rifshosp.) and the Dept. of Molecular Medicine (MOMA), Aarhus. In the TOMBOLA trial, plasma ctDNA positivity following neoadjuvant chemotherapy and cystectomy in MIBC patient as indication to administer Atezolizumab as early postoperative additional treatment. [2] (Fig. 1)

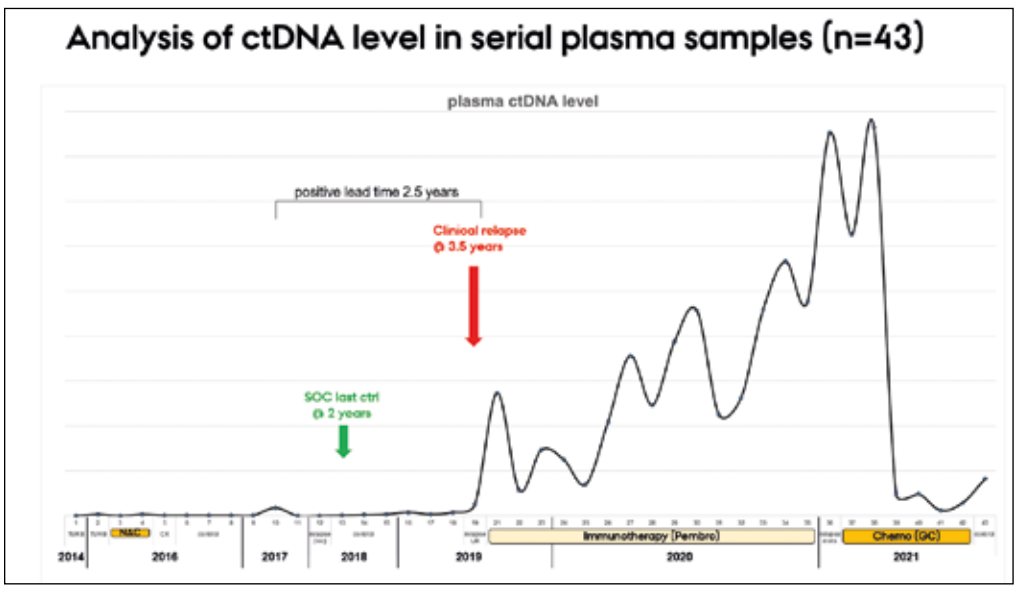


Figure 2: Patient example with multiple time point measurement of ctDNA following diagnosis of MIBC and standard treatment with neoadjuvant chemotherapy and radical cystectomy. Noticeably, there is a 2.5 year lead time from postoperative positive ctDNA until metastasis is visible on imaging and immunotherapy is initiated. Concordant with an increase in ctDNA during immunotherapy, there was progression on imaging and the patient underwent re-induction with conventional Gemcitabin-Cisplatin resulting in apparently complete response on imaging but still detectable dissemination on ctDNA despite a much lower level. Unfortunately, this indicates that the patients will have an identificable recurrence within the near future. (Courtesy of Associate Prof. Karin Birkenkamp-Demtröder).

In the TOMBOLA setup, multiple time points for ctDNA measurement are used over the whole standard-of-care follow-up period after cystectomy, but the long-term hope is that we will be able to identify the majority of high-risk patients by positive ctDNA very early, a short time after CX in order to have the longest possible lead time to the time where a recurrence would have been visible on the first or second (4m/8m) conventional imaging. This will in theory lead to prolonged relapse-free survival, better long-term outcome and will reduce the current logistic challenges in the postoperative setting. Furthermore, a "continuous" monitoring surveillance scheme may be associated with a better quality of life.

A somewhat similar study is the ongoing IMvigor011 that is also using positive ctDNA to trigger early immunotherapy. [3] In the IMvigor011, the patients are restricted to the classical high-risk patients that otherwise typically all would undergo adjuvant treatment. Introduction of widespread standard use of adjuvant immunotherapy can actually hamper the field of ctDNA as studies will be forced to show non-inferiority of selected use of immunotherapy compared to a very liberal use. Introduction of new diagnostic methods like ctDNA therefore calls for an intellectual reset of knowledge learned from studies without the use of these techniques. In the IMvigor011 study, randomization is fortunately made against no adjuvant treatment, thus making it a superiority study.

ctDNA in "live" monitoring of treatment response
Whereas ctDNA in identification of residual tumour is a more or less binary outcome, the quantity of ctDNA in blood samples can be used as a surrogate marker of metastatic burden and thus as an indicator of treatment response. In patients treated with immunotherapy, a pseudo-progression on imaging can be seen in otherwise highly responsive patients and irrespectively of this, there is need for a certain interval between imaging to estimate response. Contrary to this, ctDNA has a very short half-time of about two hours. Therefore, more or less "live" monitoring is possible very early in different active treatments and intervals between these where the patient is undergoing follow-up only. (Fig. 2)

For the moment, this is not considered as decisive for shift in treatment but should at least lead to shorter intervals between imaging and assessments if a rising level is identified in a patient, or may be used to spare patients for some CT scans. Hopefully, ongoing research will shed more light into this field in the near future and bring ctDNA into the future standard treatment monitoring.

Due to space constraints, the entire reference list can be made available to interested readers upon request by sending an email to: communications@uroweb.org.

Monday, 4 July 08:00 - 10:15
Plenary Session 07
Orange Area, eURO Auditorium 1

When and how to de-escalate surveillance in LR-NMIBC

Alternative approaches and their benefits

Mr. Hugh Mostafid, FRCS (Urol) FEBU
Consultant Urologist, Royal Surrey Hospital, Guildford
Senior Lecturer, Imperial College, London (GB)

Clear guideline recommendations exist regarding follow-up surveillance for low-risk non-muscle-invasive bladder cancer (LR-NMIBC), including the EAU Guidelines for NMIBC [1]. Nevertheless, there is evidence to suggest that such patients have more frequent cystoscopies than recommended by the Guidelines which in turn not only leads to more transurethral resection of bladder tumour (TURBT) but also an increased number of pathological specimens with no cancer [2]. Studies of active surveillance in LR-NMIBC have confirmed the rate of progression to muscle-invasive bladder cancer (MIBC) in LR-NMIBC under observation is extremely low [3]. This supports the notion that de-escalating surveillance in LR-NMIBC would not lead to "missing" patients who might progress to MIBC.

Options for de-escalating surveillance in LR-NMIBC

Less frequent cystoscopy

The current EAU Guidelines for NMIBC recommend that LR-NMIBC patients should undergo cystoscopy at three months post TURBT and if clear, again at nine months later and then annually for five years.

However, this is a weak recommendation as only one randomised trial of cystoscopic surveillance for NMIBC was carried out with a sample size of only 97 patients.

LR-NMIBC has a low overall recurrence rate of 20% and the majority of these recurrences occur in the first year of follow-up. Partly based on this observation and the need to control costs in a national health system, the UK National Institute for Health and Care Excellence (NICE) published their bladder cancer guidelines for the UK in 2015. Following the development of a health economic model, NICE recommended that patients with LR-NMIBC who had a clear cystoscopy at three and 12 months should be discharged back to the general practitioner with no further urological follow-up [4].

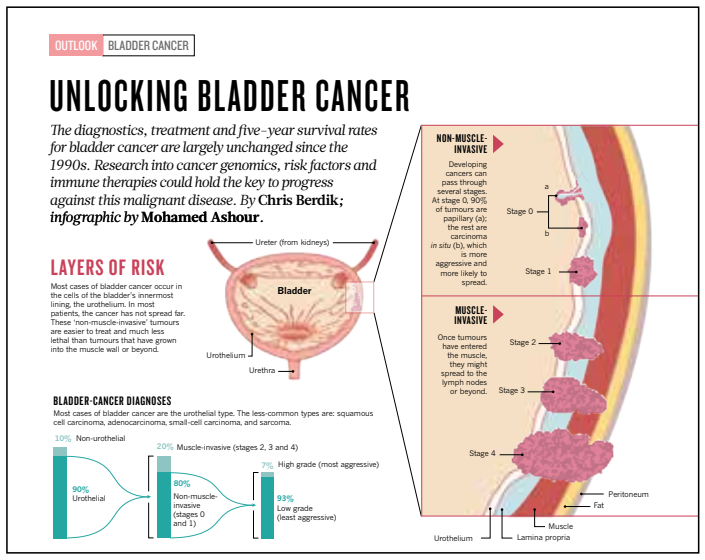
The effects of this policy were presented at the EAU Annual Congress in Copenhagen in 2018. A questionnaire was sent out to every urology department in the UK regarding the policy of discharging LR-NMIBC at 12 months. Under half of the 237 departments in the UK replied and from these, only three patients had re-presented with a recurrence. There was no progression to a higher stage or grade [5]. Interestingly, patient dissatisfaction at being discharged was reported as being the only significant issue but only in patients who were already expecting to be followed up in five years. Conversely, new patients who were told from the outset that they would be discharged after 12 months were happy with this policy. Anecdotally many of these patients were pleased to be "cured" and freed from the burden of cystoscopic surveillance.

Ultrasound

A different approach has been advocated by Prof. Joan Palou (ES) and others: replacing cystoscopy with ultrasound. In a 2015 study by Niwa et al., 166 patients with LR-NMIBC were divided into two groups: one for cystoscopy and one for ultrasound surveillance [6]. Both groups had a similar five- and 10-year recurrence-free survival although as expected. The time to first recurrence was shorter in the cystoscopy group. Such an approach has in fact been adopted by the EAU Guidelines for NMIBC as an option for elderly frail patients who may find regular cystoscopic surveillance challenging [1].

Urine-based biomarkers

Recently, there has been considerable commercial interest in urine-based biomarkers for bladder cancer, with the ultimate aim that these tests could entirely replace the cystoscope. For such tests to be successful, they require a high sensitivity and acceptable specificity. However, such tests suffer from what can be referred to as "low-risk paradox". These tests may be suitable to a group of patients, but these tests also have the lowest sensitivity (~40% overall) which makes them unsuitable as a replacement for cystoscopy, especially in LR-NMIBC. Nonetheless, it has been advocated to alternate urine-based biomarkers with cystoscopy for five years of surveillance as recommended by the EAU Guidelines to reduce the burden of cystoscopic surveillance [7].



Future developments

The recent development of low-cost, single-use flexible cystoscopy has introduced an intriguing paradigm in terms of de-escalating surveillance for LR-NMIBC, at least from the perspective of the urologist and health economics. Single-use scopes are simple and require minimal investment. This raises the possibility of "re-inventing" flexible cystoscopy as a true office procedure which could be carried out during a traditional outpatient consultation rather than in a dedicated endoscopic suite with its associated costs and staffing requirements. The potential benefits of such a "de-escalation" warrant further investigation.

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Saturday, 2 July 10:30 - 14:35
Joint meeting of the ESOU, ERUS, and ESUT
Orange Area, Room 2

PSMA PET for recurring prostate cancer

PSMA PET may lead to an earlier detection of metastasis compared with CI

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Prostate-specific membrane antigen (PSMA) is highly expressed on most prostate cancer (PCa) cells, and several PSMA ligands for PET imaging are now available worldwide. The use of PSMA PET is currently suggested by several international guidelines for investigating PCa in different clinical settings [1], and in particular for recurrent PCa. There is an amount of published data suggesting that PSMA-based radioligands carry the highest diagnostic value in the imaging of PCa. [2]

The nuclear medicine community has come a long way since the first in-human applications of 68Ga-PSMA-11, which date back to 2012. Prospective, randomised clinical trials incorporating PSMA imaging will probably soon be published; their results are needed to provide even more robust evidence of its role in improving patient outcome.

Imaging of recurring PCa after radical treatment aims at treatment changes and thus possibly a better clinical outcome. PSMA PET demonstrated higher sensitivity than 11C-choline or 18F-fluciclovine PET in this setting [3,4], and scan positivity increases with higher PSA values. A common limitation of PSMA PET for this purpose is the lack of robust validation of PSMA PET positive findings, and lack of accurate evaluation of its impact on outcome, since most of the data are retrospective or with a short median follow-up time. Nonetheless, it is evident that among all available imaging methods, PSMA PET is clearly superior, both for the higher accuracy and for the possibility to study with a single examination the local recurrence (prostatic bed), the lymph nodes, the bone and the other metastases.

A number of publications confirm a significant impact of PSMA PET at least on clinical management. A meta-analysis investigating the impact of PSMA PET on management of biochemical recurrent patients (11 studies, 908 patients) reported changes in 54% of patients, although substantial heterogeneity among the included studies was noted. [5] According to the EAU Guidelines, PSMA PET is the most sensitive imaging modality to detect metastasis in this patient setting and should be offered to patients with a PSA higher than 0.2 ng/mL after RP [1]; another setting where PSMA PET is actually recommended by EAU Guidelines is persistence of PSA after radical prostatectomy. (Figure 1)

In a large single-arm, multicentre prospective study, 635 patients with biochemical recurrence after radical prostatectomy (41%), radiation therapy (27%), or both (32%) were enrolled, with the main aim of evaluating the positive predictive value and the detection rate of PSMA PET. [6] PSMA PET showed recurrent PCa in 75% of patients; the positive predictive value was 0.84 in the 87 patients validated by histopathology and 0.92 in the 217 patients validated by the composite reference standard. As expected, the PSMA PET detection rate was associated with increased PSA values, ranging from 38% in patients with a PSA lower than 0.5 ng/mL to 97% in those with a PSA higher than 5.0 ng/mL.

In castration-resistant PCa (CRPC), the number of available treatments is steadily rising over ADT, but in this setting, conventional imaging (CI) is still recommended despite PSMA PET's emergence as a more accurate imaging modality. A multicentre retrospective study including 200 patients with PSA >2.0 ng/mL, negative conventional imaging and high risk for metastasis, reported PSMA PET positive in 196/200 (98%) of patients. Overall PSMA PET showed pelvic diseases in 44%, including 24% with local prostate bed recurrence and distant metastasis in 55% despite negative CI. The overall accuracy of PSMA PET was 95% for osseous lesions and 60% for soft-tissue lesions.

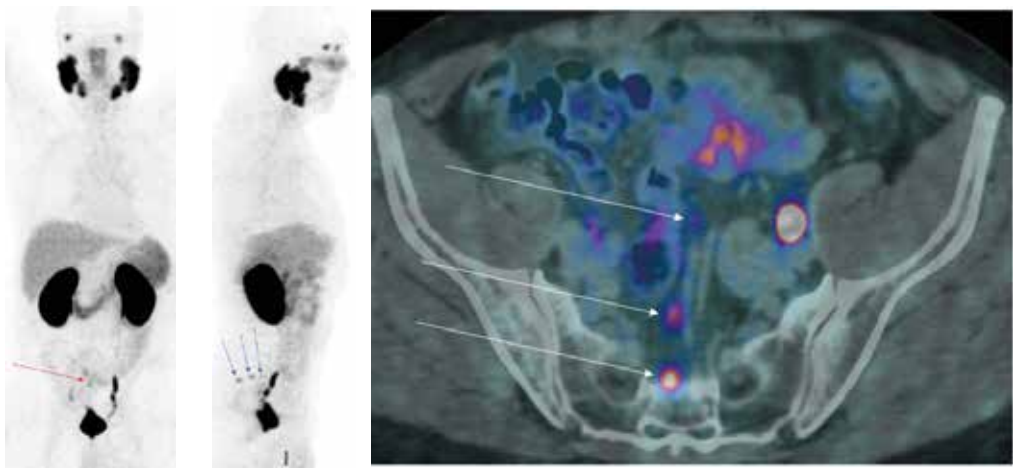

Figure 1: 67 yo patient, PSA persistence (0,18) after RARP (pGS: 4+4; iPSA 8,5; pT3aN1R1 with 19 lns removed) PSMA PET: small focal areas of pathologic uptake (left image, coronal view, red arrow), attributable to three small lymph nodes (centre image, sagittal view, blue arrows). The focal nodal uptake is better seen in PET/CT transaxial image (right, white arrows)

According to these results, it may be suggested that PSMA PET leads to an earlier detection of metastasis compared with CI and a change of clinical subtype, which may trigger earlier or different treatments. However, if and how this could impact on patient outcome in terms of overall survival and quality of life has yet to be determined and further studies are warranted.

References

1. EAU Prostate Cancer Guidelines 2021: https://uroweb.org/guideline/prostate-cancer/
2. Perera M, Papa N, Roberts M, et al. Gallium-68 prostate-specific membrane antigen positron emission tomography in advanced prostate cancer: updated diagnostic utility, sensitivity, specificity, and distribution of prostate-specific membrane antigen-avid lesions: a systematic review and meta-analysis. Eur Urol. 2020; 77:403-417.
3. Morigi JJ, Stricker PD, van Leeuwen PJ, et al. Prospective comparison of 18F-fluoromethylcholine versus 68Ga-PSMA PET/CT in prostate cancer patients who have rising PSA after curative treatment and are being considered for targeted therapy. J Nucl Med. 2015; 56:1185-1190.
4. Calais J, Ceci F, Eiber M, et al.18F-fluciclovine PET-CT and 68Ga-PSMA-11 PET-CT in patients with early biochemical recurrence after prostatectomy: a prospective, single-centre, single-arm, comparative imaging trial. Lancet Oncol. 2019; 20:1286-1294.
5. Han S, Woo S, Kim YJ, Suh CH. Impact of 68Ga-PSMA PET on the management of patients with prostate cancer: a systematic review and meta-analysis. Eur Urol. 2018; 74:179-190.
6. Fendler WP, Calais J, Eiber M, et al. Assessment of 68Ga-PSMA-11 PET accuracy in localizing recurrent prostate cancer: a prospective single-arm clinical trial. JAMA Oncol. 2019; 5:856-863.
7. Fendler WP, Weber M, Iravani A, et al. Prostate-Specific Membrane Antigen Ligand Positron Emission Tomography in Men with Nonmetastatic Castration-Resistant Prostate Cancer. Clin Cancer Res. 2019 Dec 15; 25(24):7448-7454.

Saturday, 2 July 14:00 - 15:30
Special Session EAU, EANM, ESMO and ESTRO
Grey Area, eURO Auditorium 2

PSMA PET/CT for advanced prostate cancer

Staging and monitoring techniques and guidelines

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Accurate staging and identification of metastatic sites have never been more important as new treatment options emerge for managing high-risk prostate cancer. EAU Guidelines still recommend cross-sectional imaging and bone scan (BS) as primary staging modalities.

PSMA PET/CT for primary staging
Conventional imaging with computerized tomography (CT) and whole-body technetium bone scans (BS) are limited by their suboptimal diagnostic performance. [1] Abdominal CT indirectly assesses nodal invasion by using lymph node (LN) diameter and morphology. Usually, LNs with a short axis > 8 mm in the pelvis and > 10 mm outside the pelvis are considered malignant. A meta-analysis reported overall sensitivity and specificity of CT for LN detection as 42% and 82%, respectively. [2] The accuracy of bone scan in 23 different series was reported to be PSA dependent as low as 2.3% in patients with PSA levels < 10 ng/mL, and 16.2% in patients with PSA levels of 20.0-49.9 ng/mL. [3]

Positron emission tomography (PET/CT) using prostate-specific membrane antigen (PSMA) ligand tracers (^{68}Ga and ^{18}F) on the contrary has been shown to provide superior detectability of nodal and distant metastatic sites. The proPSMA study randomized 302 patients with high-risk prostate cancer into conventional imaging or ^{68}Ga PSMA PET/CT before curative-intent surgery or radiotherapy. [4] PSMA PET/CT had 27% absolute greater area under curve (AUC) for accuracy than conventional imaging (92% vs 65%). Subgroup analysis revealed superior results for PSMA PET/CT in patients with metastatic pelvic lymph nodes and distant metastasis. [4] Other prospective studies reported high specificity (90.9 and 94.4%) but limited sensitivity (41.5 and 41.2%) for LN detection rates depending on the size of metastatic lesions. [5,6] We recently reported on 96 patients who had ^{68}Ga-PSMA PET/CT for primary staging prior to radical prostatectomy with extended pelvic lymph node dissection (PLND). The per-patient sensitivity and specificity of PSMA PET/CT for nodal staging were 53.3% and 98.8%, respectively. [7]

Limited number of studies reported improved results to detect bone metastases for PSMA PET/CT compared to conventional BS. In a prospective study with 113 patients with biopsy-proven prostate cancer, higher sensitivity and specificity were reported for PSMA PET/CT than conventional BS (96.2% vs. 73.1%, and 99.1% vs. 84.1%). [8] A recent comparative study evaluated 112 patients with intermediate-high risk prostate cancer where PSMA PET/CT confirmed the presence of bone metastasis in all patients with M1 disease and in 8 of 81 patients with M0 disease according to BS. [9] A meta-analysis comparing PSMA PET/CT, choline-PET/CT, NaF-PET/CT, magnetic resonance imaging (MRI), and BS in the diagnosis of bone metastases found that PSMA PET/CT showed the highest per-patient sensitivity and specificity (97% and 100%), respectively. [10]

Finally, a prospective multicentre study with 108 intermediate to high-risk prostate cancer referred for primary staging reported a management plan change in 21% of cases due to additional lymph node and/or distant metastases detected by PSMA PET/CT. [11]

PSMA for staging at biochemical recurrence or persistent PSA following definitive treatment
In a meta-analysis and systematic review, high ^{68}Ga PSMA-PET positivity rates were found in patients with biochemical recurrence (BCR) even at low prescan PSA levels (33% for PSA <0.2 ng/dL, 45% for PSA 0.2-0.49 ng/dL). [12] The pooled sensitivity and specificity on a per-lymph node and per-patient basis, PSMA PET/CT has shown better diagnostic accuracy than conventional imaging modalities as well as than choline and fluciclovine PET/CT [13,14] establishing its role as the standard imaging modality for patients with persistent PSA and with BCR leading to an alteration of the planned management in 53% of the patients. [15]

"PSMA PET/CT is currently the standard imaging modality in patients with BCR and PSA persistence following definitive treatment."

PSMA PET/CT for treatment monitoring
The level of evidence for the role of PSMA PET/CT to evaluate treatment response is scarce as the data about the changes of PSMA uptake characteristics under systemic treatment are limited and equivocal. Preclinical and clinical studies indicate that the initial response to ADT is a PSMA upregulation. [16] Few studies reported increased PSMA expression [17,18] or no increased PSMA expression at all after a median of 3 months under enzalutamide or abiraterone. [19] Patients with metastatic castration-resistant prostate cancer (mCRPC) who received 3 cycles of docetaxel showed reasonable correlation between PSMA expression and RECIST criteria. [20] PSMA flares in the absence of disease progression and discordant results with PSA levels have been reported in patients with mCRPC as well. [21] Recently, consensus statements on PSMA PET/CT response assessment criteria noted that PSMA PET/CT should only be used for assessing treatment response if the treatment plan is expected to change. PSMA PET/CT scan is recommended to be performed not earlier than 3 months after the start of ADT and other hormonal interventions to avoid a potential flare phenomenon. [22] PSMA PET/CT response should categorize patients as responders (stable disease, partial response, or complete response) and non-responders (progression). Semi-quantitative evaluation with SUV parameters and volumetric PET measurements are recommended to optimize reproducibility. [22]

PSMA based radioligand therapy (RLT)
Radioligand therapy (RLT) offers a new approach for personalized and targeted treatment of patients in mCRPC with encouraging antitumour activity and a favourable toxicity profile. The phase-3 VISION trial showed that Lutetium-177 (^{177}Lu)-PSMA-617 radioligand therapy prolonged imaging-based progression-free survival and overall survival (OS) when added to standard of care in patients with PSMA-positive mCRPC. [23] Another phase-2 trial (TheraP) reported higher PSA response for ^{177}Lu-PSMA RLT compared to cabazitaxel in patients with mCRPC who had progressed after docetaxel treatment. [24] Recently, Gafita et. al. developed nomograms to predict outcomes after ^{177}Lu-PSMA therapy in men with mCRPC. Tumor SUV_{max} was found as an independent predictor in all 3 nomograms to predict OS, PSA-progression-free survival, and PSA decline of ≥ 50%. [25]

Conclusion
PSMA PET/CT provides higher accuracy to detect lymph node and distant metastases in primary and secondary setting during the course of prostate cancer. Owing to its superiority over conventional imaging techniques, PSMA PET/CT is currently the standard imaging modality in patients with BCR and PSA persistence following definitive treatment. It also seems to be a promising tool to monitor patients receiving systemic treatment and RLT, however further evidence needs to be produced here to establish its definitive role and to answer whether this will translate to better treatment outcomes.

Due to space constraints, the entire reference list can be made available to interested readers upon request by sending an email to: communications@uroweb.org.

Sunday, 3 July 10:30 - 12:00
Thematic Session 02
Grey Area, eURO Auditorium 2

EAU22 | AMSTERDAM 1-4 July 2022

EAU22 Scientific Programme

Friday, 1 July

Plenary Sessions

7:30 - 8:00	Game changing session 1
7:30 - 8:00	Game changing session 2
8:00 - 10:15	Challenges in renal cancer
8:00 - 10:15	Going viral in urology
10:15 - 10:45	Post plenary discussion 'Challenges in renal cancer': Meet the experts
10:45 - 11:15	Post plenary discussion 'Going viral in urology': Meet the experts

Special Sessions

10:30 - 13:30	Prostate cancer early detection: What men need to know
10:30 - 12:00	Controversies on EAU Guidelines I
12:15 - 13:45	New technologies and urological applications
12:30 - 15:00	Meeting of the Young Academic Urologists (YAU)
14:00 - 16:00	Active surveillance for intermediate risk prostate cancer: What urologist and patients should know
18:00 - 19:30	EAU Opening Ceremony

Urology Beyond Europe

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

Video Sessions

10:45 - 12:15	Challenging situations in kidney surgery
12:30 - 14:00	Shining a laser on endourology
14:15 - 15:45	New techniques in penile cancer and urethral surgery

Abstract Sessions

10:45 - 12:15	Affordable techniques in urology - High quality at low costs
10:45 - 12:15	Modern education and resident´s surgical training in 2022
10:45 - 12:15	Infections - Bench to bedside
10:45 - 12:15	Localised kidney cancer: Histology, diagnosis and prognosis
10:45 - 12:15	NMIBC - BCG, urinary markers, therapeutic pathways and mechanisms of action
12:30 - 14:00	Virtual platforms and the future of urology
12:30 - 14:00	Infections - Prophylaxis, treatment and complications
12:30 - 14:00	Localised kidney cancer: Treatment outcomes and complications
12:30 - 14:00	NMIBC early diagnosis and improvement of endoscopic management
14:15 - 15:45	Searching the evidence in urology: Systematic reviews and meta-analysis
14:15 - 15:45	Risk stratification and treatment for recurrent disease
14:15 - 15:45	Localised kidney cancer: Alternative treatments in special situations
14:15 - 15:45	NMIBC - Advancements in diagnostics, follow-up and treatment

Saturday, 2 July

Plenary Sessions

8:15 - 10:30	Nightmares in surgery of retroperitoneal disease
8:15 - 10:30	Perioperative treatment of urothelial cancer in 2022
10:45 - 11:15	Post plenary discussion 'Nightmares in surgery of retroperitoneal disease': Meet the experts
11:15 - 11:45	Post plenary discussion 'Perioperative treatment of urothelial cancer in 2022': Meet the experts

Special Sessions

10:00 - 17:00	YUORDay22: EAU Young Urologists Office (YUO) & European Society of Residents in Urology (ESRU)
10:45 - 13:45	Rapid-fire debates: Common problems in bladder cancer
11:00 - 13:30	EAU History office: Dutch and anniversary contributions to urology
14:00 - 15:30	Joint session of the EAU, EANM, ESMO and ESTRO: Modern diagnostic and therapeutic approaches in PCa
15:45 - 17:45	8th ESO Prostate Cancer Observatory: Innovations and care in the next 12 months

Video Sessions

10:45 - 12:15	Evolving surgical technologies in prostate cancer
12:30 - 14:00	Functional urology: The full Monty
14:15 - 15:45	Training models and complication management
16:00 - 17:30	Different approaches to RARP

EAU Section Meetings

10:30 - 14:00	Answering clinically important questions in reproductive and sexual medicine and surgery **(ESAU)**
10:30 - 14:35	Controversies in onco-urology **(ESOU, ERUS, ESUT)**
10:30 - 14:00	Surgical matters in kidney transplant **(ESTU, ESOU, ESGURS)**
10:30 - 13:50	Biomarkers in uro-oncology: From bench to bedside **(ESUP, ESUR)**
10:30 - 14:00	Urinary incontinence: Are doctors, guidelines and patients all in agreement? **(ESFFU)**
10:30 - 14:00	Urological surgery and interventions in an office and outpatient setting **(ESUO)**
11:00 - 18:30	Technology developments never end! **(ESUT, ERUS, EULIS)**
14:15 - 18:00	Meet the experts in robotic surgery **(ERUS)**
14:15 - 17:45	New perspectives in the management of stones **(EULIS)**
14:15 - 18:00	Contemporary urogenital reconstruction and continence restoration in male, female and transgender patients **(ESGURS)**
14:15 - 18:00	Ongoing studies and upcoming changes in imaging **(ESUI)**
14:15 - 17:50	The role of infections in urology and difficult to treat situations **(ESIU)**

Abstract Sessions

10:45 - 12:15	Stones - Decision-making, imaging and shock wave lithotripsy
10:45 - 12:15	Active surveillance and modern diagnostics
12:30 - 14:00	New insights in the management of upper tract urothelial cancer
12:30 - 14:00	Focal therapy in prostate cancer
14:15 - 15:15	Trials in Progress
14:15 - 15:45	Minimally-invasive partial nephrectomy in localised kidney cancer
15:00 - 16:30	Prostate cancer screening and early detection - Reloaded!
16:00 - 17:30	Metastasectomy and systemic treatment in mRCC - What can we achieve?

Sunday, 3 July

Plenary Sessions

7:30 - 8:00	Game changing session 3
7:30 - 8:00	Game changing session 4
8:00 - 10:15	PCa high-risk local treatment
8:00 - 10:00	Personalised surgical management of LUTS/BPO
10:30 - 11:00	Post plenary discussion 'PCa high risk local treatment': Meet the experts
11:00 - 11:30	Post plenary discussion 'Personalised surgical management of LUTS/BPO': Meet the experts

Thematic Sessions

10:30 - 11:30	Semi-live surgery: Robotic reconstructive surgery
10:30 - 12:00	Management of mHSPC
10:30 - 12:00	Testis cancer: Pushing boundaries in diagnosis and treatment
10:30 - 11:30	Semi-live surgery: Transition of urological conditions - From childhood to adulthood
10:30 - 12:00	Prosthetics in reconstructive urology: Business as usual or still experimental
13:30 - 15:00	Genetic profiling in prostate cancer: Already prime time?
14:00 - 15:30	Female stress urinary incontinence: Practical surgical management
14:00 - 15:30	Controversies in paediatric urology
14:00 - 15:30	Men's health: An update on hypogonadism management
15:45 - 17:15	AI in urology

Special Sessions

8:30 - 11:00	Leadership and the EAU
11:45 - 13:15	Controversies on EAU Guidelines II
12:15 - 13:45	European Urology: Surgery-in-Motion: Technical innovations in the evolving world of robotic surgery
12:15 - 13:45	European public-private research network funding through the IMI: PIONEER real-world evidence, big data and prostate cancer
15:15 - 17:15	Joint session of the EAU and the Advanced Prostate Cancer Consensus (APCCC)
15:45 - 17:15	ERN eUROGEN: Update on rare and complex urology

Video Sessions

10:30 - 12:00	Technically challenging partial nephrectomies
12:15 - 13:45	Ureteric adventures
14:00 - 15:30	Current status in radical cystectomy
15:45 - 17:15	Awards ceremony and focal therapies
15:45 - 17:15	Urological curiosities

Abstract Sessions

10:30 - 12:00	Andrology - Male hypogonadism and penile curvature
10:30 - 12:00	Cell biology and novel therapies in prostate cancer
10:30 - 12:00	Insight in the overactive bladder and the bladder pain syndrome
10:30 - 12:00	Prostate cancer biopsy protocols and methods of targeting
10:30 - 12:00	PCa localised imaging grade prediction, reporting and markers
10:30 - 12:00	History of urology pearls
12:15 - 13:45	Improvements in metastatic prostate cancer: Focus on imaging and treament
12:15 - 13:45	Andrology - Male sexual dysfunction, diagnosis and therapy
12:15 - 13:45	Testicular cancer - Tailoring treatments to reduce toxicities
12:15 - 13:45	Surgical management of male and female SUI: Tapes, balloons, sphincters and more
12:15 - 13:45	LUTS/BPH - Basic research and medical therapy
12:15 - 13:45	Prostate biopsies: Which route, which complications, which pathological results?
12:15 - 13:45	Complex surgery in urology
12:15 - 13:45	Basic research and new drugs in paediatric urology
14:00 - 15:30	Lymph nodes in prostate cancer
14:00 - 15:30	Penile cancer - Novel models and nodal disease
14:00 - 15:30	Laboratory research on urethral strictures and preclinical and clinical aspects of neurourology
14:00 - 15:30	Minimally invasive therapies for male lower urinary tract symptoms
14:00 - 15:30	Prostate biopsy indication and strategy: Which role for which imaging by MRI, PET, US
14:00 - 15:30	Bladder cancer radical therapy, surgery and QOL impact
14:00 - 15:30	Stones - Epidemiology, basic research and metabolics
15:45 - 17:15	Recent advances in surgical treatment options for paediatric urology
15:45 - 17:15	Reproductive health - Male infertility and andrological effects of COVID-19
15:45 - 17:15	Postoperative risk estimation and multimodal treatment of prostate cancer
15:45 - 17:15	Males LUTS, nocturia and NOUR: From evaluation to treatment
15:45 - 17:15	Clinical assessment of urethral strictures
15:45 - 17:15	Ablative surgery for BPO relief: Laser, robot and aquablation
15:45 - 17:15	Advanced bladder cancer: Staging, predicting factors and systemic therapy

Monday, 4 July

Plenary Sessions

7:30 - 8:00	Game changing session 5
7:30 - 8:00	Game changing session 6
8:00 - 10:15	Liquid biomarkers in 2022 and beyond: Ready for prime time?
8:00 - 10:00	Stones: The sky is the limit
10:30 - 11:00	Post plenary discussion 'Liquid biomarkers in 2022 and beyond: Ready for prime time?': Meet the experts
11:00 - 11:30	Post plenary discussion 'Stones: The sky is the limit': Meet the experts

Thematic Sessions

10:30 - 12:00	Guidelines session: Urolithiasis
10:30 - 12:00	Difficult cases in renal transplantation
10:30 - 12:00	Guidelines session: Complications of prostate cancer treatment and their management
12:15 - 13:45	Key questions in adjuvant treatment of renal cell carcinoma
12:15 - 13:45	Semi-live surgery: Robotic cystectomy
14:00 - 15:30	All you need to know about castration-resistant prostate cancer (CRPC)
14:00 - 15:30	Complications in stone treatment
14:00 - 15:30	Management of defects in genetic and epigenetic factors influencing the male reproductive potential
14:00 - 15:30	Androgen receptor and cellular plasticity in prostate cancer: How to improve therapies

Patient Information Sessions

7:45 - 8:45	Patient poster presentations
9:00 - 10:30	Roundtable WFIPP/EAU: Sustainable continence care
10:45 - 11:45	Roundtable: Fatigue in prostate cancer patients
12:00 - 13:00	Functional urology
13:15 - 14:15	Kidney cancer
14:30 - 15:30	Bladder cancer
15:45 - 16:45	Prostate cancer
17:00 - 17:30	Life after cancer

Video Sessions

10:30 - 12:00	Partial nephrectomy road maps
12:15 - 13:45	Novel approaches in retroperitoneal and transplant surgery

Abstract Sessions

10:30 - 12:00	Best EAU22 abstracts selected by the Scientific Committee
10:30 - 12:00	Liquid- and tumour biomarkers in prostate cancer
10:30 - 12:00	The patient's choice of how to treat prostate cancer?
10:30 - 12:00	Trauma and urogenital reconstruction
10:30 - 12:00	Optimising treatment in locally advanced disease
10:30 - 12:00	Stones and endourology - Percutaneous and ureteroscopic management
12:15 - 13:45	Guidelines, evidence-based medicine and education
12:15 - 13:45	Advanced urothelial cancer - Organoids, response mechanisms and biomarkers
12:15 - 13:45	Modern renal transplantation
12:15 - 13:15	Rare diseases with special focus on von Hippel-Lindau
12:15 - 13:45	Novel therapies and biomarkers in renal cancer
12:15 - 13:45	Improving functional outcome of prostatectomy
12:15 - 13:45	Stones and endourology - URS and stenting
14:00 - 15:30	Surgical management and quality outcome in prostate cancer treatment
14:00 - 15:30	Stones and endourology - Lasers, heat and pressure

Special Sessions

15:45 - 17:45	Best of EAU22 session

Schedule of ESU and HOT Courses at EAU22

Friday, 1 July

9:00 - 12:00 **HOT Course 50**
ESU/ESFFU Hands-on Training Course in Urodynamics

10:00 - 13:00 **ESU Course 24**
Flexible ureterorenoscopy and retrograde intrarenal surgery: Instrumentation, technique, tips, tricks and indications

11:00 - 14:00 **ESU Course 01**
Theranostics in prostate cancer

11:00 - 14:00 **ESU Course 02**
Chronic pelvic pain in men and women

12:30 - 15:30 **ESU Course 05**
Robot renal surgery

14:30 - 17:30 **ESU Course 03**
Advanced vaginal reconstruction

14:30 - 17:30 **ESU Course 04**
Lower urinary tract dysfunction and urodynamics

14:30 - 17:30 **ESU Course 06**
Advanced endourology in the non-standard patients with urolithiasis

14:30 - 17:30 **ESU Course 14**
Adrenals for urologists

Saturday, 2 July

8:30 - 10:30 **ESU Course 07**
How to write the introduction and methods

8:30 - 10:30 **ESU Course 09**
Treatment of small renal masses

8:30 - 10:30 **ESU Course 10**
Oligometastatic prostate cancer

8:30 - 10:30 **ESU Course 11**
Prosthetic surgery in urology

9:00 - 12:30 **HOT Course 01**
ESU/ESUT/ESUI Hands-on Training Course in Prostate MRI reading for urologists

9:00 - 12:00 **HOT Course 04**
ESU/ESFFU Hands-on Training Course in Urodynamics

11:00 - 14:00 **ESU Course 12**
Robotic-assisted laparoscopic prostatectomy

11:00 - 14:00 **ESU Course 15**
Practical approach to paediatric urology

11:00 - 14:00 **ESU Course 16**
Urinary tract and genital trauma

12:00 - 14:00 **ESU Course 13**
How to write results and discussion

14:15 - 15:45 **HOT Course 06**
ESU/ESFFU Hands-on Training Course in Sacral Neuromodulation

14:30 - 17:30 **ESU Course 17**
Prostate cancer screening and active surveillance – Where are we now?

14:30 - 16:30 **ESU Course 18**
Practical aspects of cancer pathology for urologists. The 2022 WHO novelties

14:30 - 16:30 **ESU Course 19**
Updates and controversies: Urolithiasis, Non-neurogenic Female and Male LUTS guidelines 2022: What has changed?

14:30 - 17:30 **ESU Course 20**
Lymphadenectomy in urological malignancies

14:30 - 17:30 **ESU Course 21**
Retropubic radical prostatectomy: Tips, tricks and pitfalls

14:30 - 16:30 **ESU Course 22**
Practical neuro-urology

14:30 - 17:30 **ESU Course 23**
Perioperative immunotherapy and multidisciplinary management of localized genitourinary cancers

16:00 - 17:30 **HOT Course 07**
ESU/ESFFU Hands-on Training Course in Sacral Neuromodulation

Sunday, 3 July

8:30 - 11:30 **ESU Course 08**
Metabolic workup and non-surgical management of urinary stone disease

8:30 - 11:30 **ESU Course 25**
Male genital diseases

8:30 - 11:30 **ESU Course 26**
Metastatic prostate cancer

8:30 - 11:30 **ESU Course 27**
Focal therapy in prostate cancer

8:30 - 11:30 **ESU Course 28**
Nerve-sparing cystectomy and orthotopic bladder substitution. Surgical tricks and management of complications

8:30 - 11:30 **ESU Course 29**
Dealing with the challenge of infection in urology

8:30 - 11:30 **HOT Course 05**
ESU/ESFFU Hands-on Training Course in Urodynamics

9:00 - 9:50 **HOT Course 11**
ESU/ESUT Hands-on Training Course in Basic laparoscopy

9:00 - 9:50 **HOT Course 18**
ESU/ESUT/EULIS Hands-on Training Course in Endoscopic stone treatment - step 1

10:00 - 10:50 **HOT Course 12**
ESU/ESUT Hands-on Training Course in Basic laparoscopy

10:00 - 10:50 HOT Course 19
ESU/ESUT/EULIS Hands-on Training Course in Endoscopic stone treatment - step 1

11:00 - 11:50 **HOT Course 13**
ESU/ESUT Hands-on Training Course in Basic laparoscopy

11:00 - 11:50 **HOT Course 20**
ESU/ESUT/EULIS Hands-on Training Course in Endoscopic stone treatment - step 1

12:00 - 14:00 **ESU Course 30**
Robot-assisted laparoscopic radical cystectomy

12:00 - 14:00 **ESU Course 31**
How we manage upper tract tumours

12:00 - 14:00 **ESU Course 32**
How to proceed with hematuria

12:00 - 14:00 **ESU Course 33**
Renal transplantation: Technical aspects, diagnosis and management of early and late urological complications

12:00 - 14:00 **ESU Course 34**
Management and outcome in invasive and locally advanced bladder cancer

12:00 - 14:00 **ESU Course 35**
Prostate cancer update: 2021-2022

13:00 - 13:50 **HOT Course 14**
ESU/ESUT Hands-on Training Course in Basic laparoscopy

13:00 - 13:50 **HOT Course 21**
ESU/ESUT/EULIS Hands-on Training Course in Endoscopic stone treatment - step 1

13:45 - 15:45 **HOT Course 08**
ESU/ESUT/ESUI Hands-on Training Course in Fusion Biopsy, Introduction

14:00 - 17:30 **HOT Course 02**
ESU/ESUT/ESUI Hands-on Training Course in Prostate MRI reading for urologists

14:00 - 14:50 **HOT Course 15**
ESU/ESUT Hands-on Training Course in Basic laparoscopy

14:00 - 14:50 **HOT Course 22**
ESU/ESUT/EULIS Hands-on Training Course in Endoscopic stone treatment - step 1

14:30 - 17:30 **ESU Course 36**
Practical management of non-muscle-invasive bladder cancer (NMIBC)

14:30 - 17:30 **ESU Course 37**
Advanced course on upper tract laparoscopy: Kidney, ureteropelvic junction (UPJ), ureter and stones

14:30 - 17:30 **ESU Course 38**
Percutaneous nephrolithotripsy (PCNL)

14:30 - 17:30 **ESU Course 39**
Management of BPO: From medical to surgical treatment, including setbacks and operative solutions (SOS)

14:30 - 17:30 **ESU Course 40**
Surgery or radiotherapy for localised and locally advanced prostate cancer

14:30v17:30 **ESU Course 41**
Office management of male sexual dysfunction

15:00 - 15:50 **HOT Course 16**
ESU/ESUT Hands-on Training Course in Basic laparoscopy

15:00 - 15:50 **HOT Course 23**
ESU/ESUT/EULIS Hands-on Training Course in Endoscopic stone treatment - step 1

15:30 - 17:30 **ESU Course 42**
Practical tips for pelvic laparoscopic surgery: Cystectomy, radical prostatectomy adenomectomy and sacrocolpopexy

16:00 - 18:00 **HOT Course 09**
ESU/ESUT/ESUI Hands-on Training Course in Fusion Biopsy, Introduction

16:00 - 16:50 **HOT Course 17**
ESU/ESUT Hands-on Training Course in Basic laparoscopy

16:00 - 16:50 **HOT Course 24**
ESU/ESUT/EULIS Hands-on Training Course in Endoscopic stone treatment - step 1

Monday, 4 July

8:30 - 11:30 **ESU Course 43**
Ultrasound in urology

8:30 - 11:30 **ESU Course 44**
Prolapse management and female pelvic floor problems

8:30 - 11:30 **ESU Course 45**
The infertile couple: Urological aspects

8:30 - 11:30 **ESU Course 46**
Advanced course on urethral stricture surgery

8:30v11:30 **ESU Course 47**
Updated renal, bladder and prostate cancer guidelines 2022: What has changed?

8:30 - 11:30 **ESU Course 48**
Prostate cancer imaging: When and how to use it

8:30 - 11:30 **ESU Course 49**
Improving your communication and presentation skills

9:00 - 12:30 **HOT Course 03**
ESU/ESUT/ESUI Hands-on Training Course in Prostate MRI reading for urologists

9:30 - 11:00 **HOT Course 10**
ESU/ESUI Hands-on Training Course in Urological ultrasound

12:00 - 14:00 **ESU Course 50**
Peno-scrotology and basic lower urinary tract endoscopy – Questions you are scared to ask

12:00 - 14:00 **ESU Course 52**
Laparoscopy for beginners

12:00 - 14:00 **ESU Course 53**
Prostate biopsy: Tips and tricks

12:00 - 14:00 **ESU Course 55**
Testicular cancer

12:00 - 15:00 **ESU Course 56**
Prostate cancer challenges and controversies from guidelines to real-world

12:15 - 15:15 **ESU Course 51**
Advanced course on laparoscopic renal surgery

12:15 - 15:15 **ESU Course 54**
Update on stone disease

For the complete list of Hands on Training ESTs1 and E-BLUS exams on Monday 4 July, check the scientific programme at www.eau22.org/scientific programme

EAU22 Industry Sessions

Friday, 1 July

16.15 - 17.45 **Janssen**
Looking towards the future: considerations for treatment strategies across the spectrum of advanced prostate cancer

16.15 - 17.45 **GlaxoSmithKline**
Challenges in diagnosis and management of resistent pathogens causing UTI and recurrent UTIs

16.15 - 17.45 **Advanced Accelerator Applications Novartis (by Medscape)**
Perspectives on the management of metastatic castration resistant prostate cancer

16.15 - 17.45 **Astellas**
Pioneering the management of OAB: Building on a decade of treatment

16.15 - 17.15 **Eisai**
A CLEAR way forward in first-line management of advanced RCC: Focus on the role of KISPLYX® (lenvatinib) + pembrolizumab combination treatment

16.45 - 17.45 **Coloplast (industry workshop)**
"Coloplast TFL Drive: a new way to drive settings Because Energy and Total Power are essential"

19.30 - 20.30 **Pfizer**
Evolving Concepts in Metastatic Prostate Cancer

Saturday, 2 July

13.15 - 14.15 **Ferring (EAUN)**
Optimal management of prostate cancer patients with side-effects from GnRH agonists and GnRH antagonists

18.30 - 20.00 **Astellas**
Focusing on the management of LA/mUC: Advancing care to improve patient outcomes

18.30 - 20.00 **AstraZeneca**
Navigating the real-world use of PARP inhibitors in BRCAm mCRPC: a practical discussion

18.30 - 20.00 **Bristol Myers Squibb**
Immuno-Oncology for Muscle-Invasive Urothelial Carcinoma: Exploring Opportunities for Perioperative Use

18.30 - 20.00 **Pierre Fabre**
Male LUTS and sex life: What do patients want from treatments?

18.30 - 20.00 **Janssen**
Practical considerations for early-stage bladder cancer: case-based discussions for managing patients with NMIBC and MIBC

19.00 - 20.00 **Guangzhou Red Pine Medical Instrument Co., Ltd. (Industry workshop)**
The future of single-use FURS

Sunday, 3 July

17.45 - 19.15 **Astellas**
Evidence-based approaches for optimising metastatic hormone-sensitive prostate cancer (mHSPC) patient care: treatment intensification to improve survival

17.45 - 19.15 **Telix**
Improvements in metastatic prostate cancer: Focus on imaging and treament

17.45 - 19.15 **Bayer**
Advancing patient care in the evolving prostate cancer treatment landscape

17.45 - 18.45 **Merck (MSD)**
Adjuvant Treatment of Patients with Locoregional Renal Cell Carcinoma

17.45 - 19.15 **Medac (by Medscape)**
NMIBC Master Class: Best practice for treatment of all risk classes

18.15 - 19.15 **Intuitive (industry workshop)**
Pushing boundaries with 4th Generation systems, advanced technologies and digital offering – What does that mean for me as a surgeon ?

What's new in the EAU Guidelines 2022 on Urolithiasis?

Radiation exposure and protection, urinary stones, and new algorithms

Dr. Kay Thomas
Department of Urology
Guy's and St Thomas' NHS Foundation Trust
London (GB)

kay.thomas@gstt.nhs.uk

The European Association of Urology (EAU) Urolithiasis Guidelines were first published in 2000. The guidelines cover most aspects of the disease, which is still a cause of significant morbidity despite technological and scientific advances. Every year an international group of clinicians with expertise in urolithiasis scrutinise the available evidence, discuss the updates to the guidelines and identify areas that require more detailed analysis and refreshing.

In addition, topics are proposed to the Central Guidelines Office for consideration of systematic review. The purpose of the guidelines is to help urologists assess evidence-based management of stones/calculi in the urinary tract and incorporate recommendations into clinical practice. The full text version of the guidelines is available online and can be accessed through the EAU website: **www.uroweb.org/guidelines/urolithiasis.** An abridged version intended as a quick reference document (EAU Pocket Guidelines) is also available, both in print and as an app for iOS and Android devices.

Summary of changes
As always, the literature for the entire previous guideline document (2021) has been checked, and wherever relevant, updated with references and supporting text. For 2022, two new sections have been added; radiation exposure and protection during endourology, and the follow-up of urinary stones. Throughout the text, passages on best clinical practice for the use of different interventions have been added to the relevant sections. In addition, medical expulsive therapy has been thoroughly revised, and the bladder stones guideline (previously a separate document), has been integrated into this text.

Four new algorithms have also been added this year:
- Follow-up duration of urinary stone patients after treatments (Fig. 1)
- Consensus on follow-up frequency and imaging modality to use after treatment (Fig. 2)
- Diagnostic algorithm for calcium oxalate stones (Fig. 3 available upon request)
- Diagnostic algorithm for uric acid stones (Fig. 4 available upon request)

New sections
Radiation exposure and protection during endourology
The diagnosis and treatment of urolithiasis is associated with high levels of ionising radiation exposure to patients. Currently there are no studies estimating the lifetime radiation exposure of stone formers, or the subsequent risk of malignancy development. The radiation exposure of endourologists has been extensively studied, but there are no studies assessing the risk of radiation-induced malignancies in urologists or operating theatre staff members.

Current evidence from atomic bomb patients, retrospective epidemiological data on medical exposure and modelling studies suggest an age and dose dependent risk of secondary malignancy from ionising radiation. The International Commission on Radiological Protection (ICRP) recommends a maximum annual occupational exposure of 50mSv. However, the risk of radiation-induced malignancy follows a stochastic model having no known safe threshold of exposure. Taking this into consideration, as well as the length of a urologists career, the upper limit of 50mSv is still highly concerning.

Availability of fluoroscopy is mandatory for endourological procedures. There is an increasing interest on fluoroless and fluoroscopy-free operations in urology. Several RCTs have been published showing a good outcome in means of stone free and complication rates. These trials have been limited to non-complex cases and they were not sufficiently powered to show non-inferiority of fluoroscopy in PNL or superiority of ultrasound in URS.

Table 1 shows the EAU Urolithiasis Guidelines Panel recommended protection methods to reduce radiation exposure to patients, surgical, anaesthesiologic and nursing staff.

Follow-up of urinary stones
Patients suffering from urolithiasis have a predisposition to develop symptoms, complications, and recurrence of stones. Despite the rich literature published on urolithiasis, very little has been written about how patients should be monitored after their treatment. There is no general agreement on whether and when stone patients should be released from their follow-up, nor when and how follow-up should occur for patients who need it.

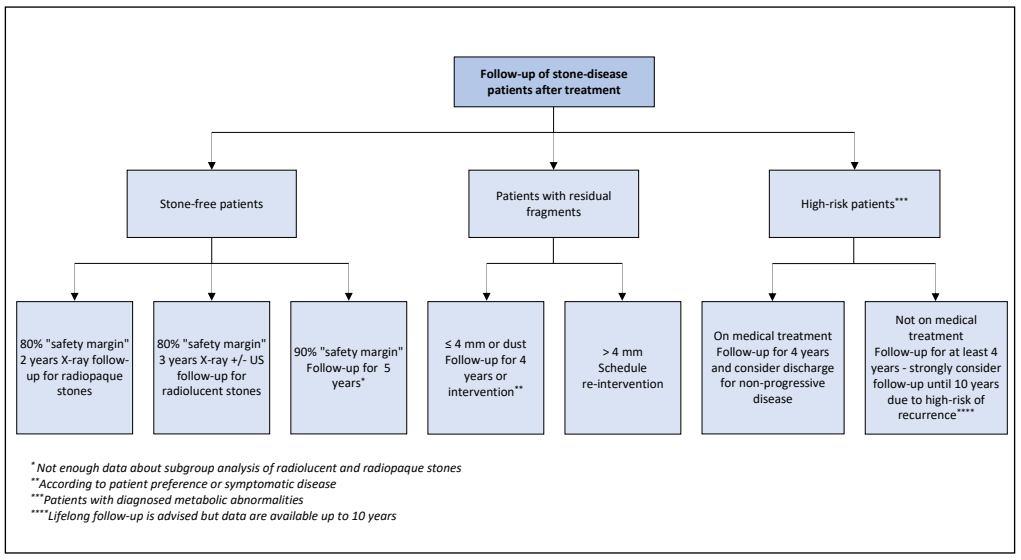

Figure 1: Follow-up duration of urinary stone patients after treatments

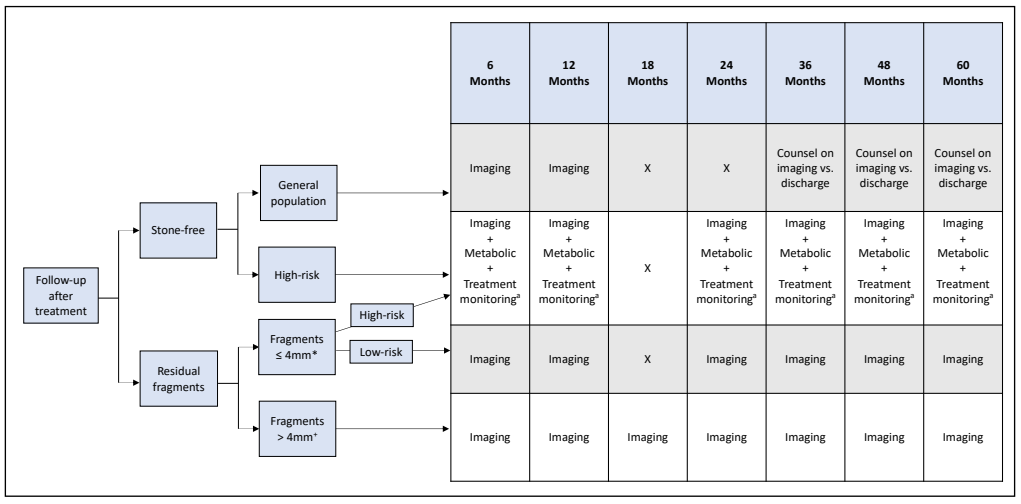

Figure 2: Consensus on follow-up frequency and imaging modality to use after treatment

Table 1: Radiation protection measures

• Limit studies or intervention involving radiation exposure to those that are strictly medically necessary.
• Implement a patient electronic record of medical imaging.
• Make use of imaging studies with lower radiation doses (US, KUB, digital tomosynthesis, low-dose and ultra-low dose CT scan).
• Create and follow a precise radiation exposure protection protocol in your department.
• Act in accordance with the as low as reasonably achievable (ALARA) principle.
• Measure and report fluoroscopy time to the operative surgeon (use dosimeters and perform monthly calculations).
• Technical measures to reduce radiation exposure include: ▪ Reducing fluoroscopy time; ▪ Limiting time adjacent to patient; ▪ Using low-dose radiation; ▪ Irradiating only to observe motion; ▪ Intra-operative use of pulsed fluoroscopy; ▪ Reduced fluoroscopy pulse rate; ▪ Collimated fields; ▪ Avoid digital image acquisition and rely on last image hold and instant replay technology.
• Use radiation protection instruments (chest, pelvic and thyroid shields, lead or lead-free gloves, protective glasses, lead protection under the operating table between the x-ray source and the surgeon).
• The radiation protection instruments must be cared for appropriately as any damage decreases effectiveness and increases exposure risk. They should be monitored and measured regularly to ensure integrity.
• Proper surgeon and operating room setup should be observed (follow the inverse square law, use the x-ray source underneath the patient's body, decrease the x-ray source to patient distance, reduce magnification, avoid field overlap by not turning the C-arm in extreme angles, operate in the standing rather than the seated position).

The main reason for this lack of agreement is the great clinical heterogeneity of stone disease among patients. The EAU Urolithiasis Guidelines Panel performed a systematic review questioning the benefits and harms of scheduled follow-up for patients who underwent definitive treatment (extracorporeal shock wave lithotripsy, ureteroscopy, percutaneous nephrolithotomy, medical chemoprophylaxis).

The panel aimed to answer three main questions regarding urolithiasis follow-up:
1. In patients with no residual fragments, does imaging follow-up after treatment for upper urinary tract stones offer more clinical benefits than harms compared with no scheduled follow-up?
2. In patients with residual fragments, does imaging follow-up after treatment for upper urinary tract stones offer more clinical benefits than harms compared with no scheduled follow-up after treatment?
3. Does biochemical urine analysis follow-up after treatment for upper urinary tract stones offer more clinical benefits than harms compared with no scheduled follow-up?

The panel used data from the eligible observational and randomised studies included in the systematic review to identify the time of patient discharge after follow-up according to stone disease status (stone-free patients, patients with residual stones, patients with metabolic abnormalities), and to come to a consensus on frequency of follow-up and use of investigations.

From a pooled analysis of 5,467 stone-free patients, the panel estimated that for a safety margin of 80%, patients should be followed-up using imaging, for at least two years (radiopaque stones), or at least three years (radiolucent stones) before discharge, while for a safety margin of 90%, patients should be discharged after five years of no recurrence.

Regarding residual disease, patients with fragments < 4mm could be offered either surveillance for up to four years, based on intervention rates ranging between 17-29%, disease progression between 9-34% and spontaneous passage between 21-34% at 49 months. Patients with larger residual fragments should be offered further definitive intervention, since intervention rates are high (24-100%).

Insufficient data exists for high-risk patients, but current literature dictates that patients who are adherent to targeted medical treatment seem to experience less stone growth or re-growth of residual fragments and may be discharged after 36-48 months of non-progressive disease on imaging. (See Fig. 1)

Conclusion
A panel consensus was reached after extensive discussion of data regarding frequency of follow-up. In the stone-free general population, the vast majority of patients remained stone-free during the 1st year, in contrast with patients with metabolic abnormalities not under targeted medical treatment, < 40% were stone-free after three years of follow-up. Therefore, a more extensive follow-up is proposed for patients with metabolic abnormalities.

Patients with small residual fragments < 4 mm, showed a spontaneous expulsion at 17.9-46.5% and growth rate at 10.1-40.7% during the 1st year, while patients with larger fragments (> 4 mm) had only 9% of spontaneous expulsion at three years.

Therefore, patients with small < 4mm, asymptomatic fragments should be followed-up or scheduled for an intervention according to patient preference, while those with larger stones should primarily be offered re-intervention. Proposed imaging consists of plain X-ray KUB and/or US, based on stone characteristics and clinicians' preferences. Computed tomography scan should be reserved for symptomatic disease or pre-operative imaging, in order to avoid extensive radiation exposure. (See Fig. 2)

New algorithms
Due to space constraints, Figures 3 and 4 are available upon request via: communications@uroweb.org

Conclusion
The 2022 EAU Guidelines have seen some significant changes and new sections added. This is part of the constant drive to improve the guidelines and provide recommendations and best clinical practice advice for colleagues based on the newest and highest levels of evidence possible.

For the 2023 text update we have the following aims:
- Evaluate the highest evidence for best clinical practice in endourology
- Perform a systematic review on patient and personnel radiation protection during endourology
- Question the accuracy of stone size as the surrogate index on deciding the treatment of urinary stones.

Monday, 4 July 10:30 - 12:00
Thematic Session 11
Grey Area, eURO Auditorium 2

GET ON BOARD
TO APPRECIATE THE INFLUENCE OF PSMA ON PROSTATE CANCER MANAGEMENT

SYMPOSIUM PROGRAM

Improvements in metastatic prostate cancer: Focus on imaging and treament

CHAIR: **DR ALICIA MORGANS**

→ PROF STEFANO FANTI — 20 min
DIRECTOR OF NUCLEAR MEDICINE DIVISION AND OF PET UNIT AT S. ORSOLA POLYCLINIC HOSPITAL IN BOLOGNA, ITALY
What is PSMA all about?

→ PROF JOCHEN WALZ — 20 min
HEAD OF THE DEPARTMENT OF UROLOGY AT THE INSTITUT PAOLI-CALMETTES CANCER CENTRE IN MARSEILLE, FRANCE
When does PSMA help me?

→ DR ALICIA MORGANS — 20 min
MEDICAL DIRECTOR OF THE SURVIVORSHIP PROGRAM AT DANA-FARBER CANCER INSTITUTE IN BOSTON, USA
The future of prostate cancer management

→ **Patient cases discussion and roundtable** — 30 min

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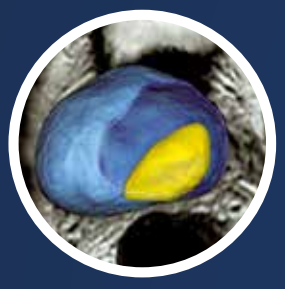

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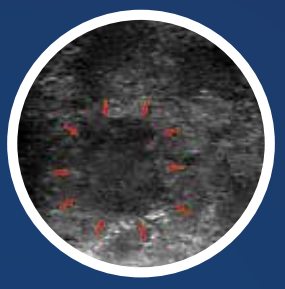
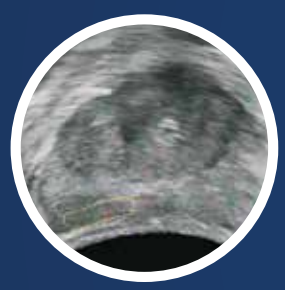
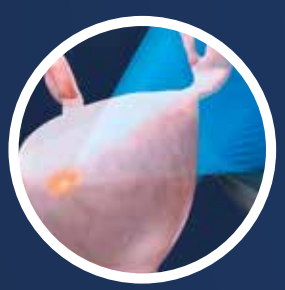


Precise Planning
· Anatomical contouring
· Urologist-centered interface



Transperineal or
Transrectal Approaches
All-in-one platform with 15-minute protocol for standard and targeted biopsies in the hands of the urologist



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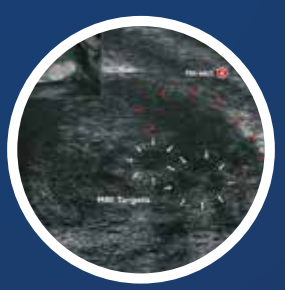

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Revival of shock wave treatment

Why it is meant to stay

Prof. Kemal Sarica
MD, PhD
Professor of Urology
Department of Urology
Biruni University, Medical School
Istanbul, TURKEY

Following its first clinical introduction with Dornier HM-3 lithotriptor in the early 1980s, Shock Wave Lithotripsy (SWL) was proven as a safe and effective alternative in treatment of urinary tract stones. [1,2] At present, SWL is the only non-invasive method in the "true non-invasive" management of urinary stones that requires no anaesthesia and hospitalization both in adults as well as particularly in children. This procedure is currently one of the most recommended treatment options for small- and medium-sized stones in most guidelines. Although other minimal invasive stone removal procedures may be associated with varying grades of complications (minor to severe) SWL related complications are practically insignificant and the procedure can be easily be repeated after a few days in case of failure or partial success. Regarding this issue, although radiation exposure seems to be a major risk factor during all available stone treatment modalities which needs to be seriously taken into account, increasing experience in the use of sonography in the majority of urological applications enabled radiation-free localization and monitoring of stones during SWL procedures. This approach will certainly reduce fluoroscopy duration, decrease the total radiation dose and increase stone fragmentation efficacy as a valuable imaging modality. Morover, this modality allows the identification of radiolucent calculi, real-time feedback on stone fragmentation, and better targeting accuracy for ureteric calculi. [3-5]

However, despite evident the advantages stated above, SWL appeared to lose its popularity due to the clinical introduction of minimally invasive stone disintegration and removal procedures namely percutaneous nephrolithotomy (PNL) and flexible ureteroscopic laser treatment (fURS) of renal stones in the last two to three decades. Miniaturization of the instruments has decreased the well-known invasive nature of PNL to a certain extent and the evolution of these two modalities in stone management have changed the treatment of relatively large stones (> 20mm) within this period. [5-7] Accumulated experience so far have shown that these more invasive modalities (when compared with SWL) did change our approaches in large and complex stones with significantly higher stone free rates noted. As a result of the results obtained with PNL and fURS, a certain feeling among endourologists emerged as " SWL is dying". However, current AUA-EAU guidelines-based approach states well that when the patient and stone selection criteria are strictly applied, SWL will not be regarded as "dead" and will be applied as preferred treatment modality for stones less than 15mm in size. SWL is still active and effective; it remains as a valuable option for a certain percentage of all stones in experienced hands.
A well-planned case selection (based on stone and patient related factors), dedicated team performing the procedure by an experienced urologist and performance of the procedure in the light of the tips and tricks stated in the "manual book" will produce high success rates with limited or no complications.

On the other hand ESWL was first used successfully by Newman in 1986 for the treatment of pediatric urolithiasis and following this first application, many clinical studies with adequate numbers of pediatric cases treated demonstrate the effectiveness and safety of ESWL in older children as well as in infants. Although general anesthesia needs to be performed in younger children, in the light of the accumulated experience over the past three to four decades, currently adjusted doses of ketamine and midazolam combination are considered as effective and safe for ESWL procedures in both preschool and school pediatric patients. This combination seems suitable for busy procedural settings without any significant side effects and hospitalization requirements. Thus, SWL is the first treatment option in the majority of upper tract stones in children due to the body habitus of the cases,early mobilization after the procedure and the more elastic nature of ureter in these patients. [8]

SWL in COVID-19 era : Reconsideration of its clinical value
The unprecedented introduction of COVID-19 in February 2020 has dramatically influenced all parts of medicine and changed our practice patterns in stone management to a certain extent. Although the urologists did not know how to act in the very beginning of the pandemic without any certain preparations, based on the experience obtained over time recommendations were made to select the best approach particularly in urgent cases and postpone and/or reschedule elective procedures to limit the risk of infection spread.

"Based on the facts and evident changes in the practice patterns, elective stone procedures such as RIRS and PCNL needed to be postponed during the outbreak of the pandemic. Regarding the treatment of obstructive ureteral stones, ureteral stents and nephrostomy tubes insertion were commonly preferred to drain the system in an urgent and effective manner."

Experience gained during COVID-19 period has clearly demonstrated that the routine treatment protocols for stone management were reported to be altered by the vast majority of the urologists. The possible reasons for such an alteration can be listed as follows:
First of all, the elective surgeries were not allowed in most of the hospitals and non-emergent stone interventions were cancelled. Secondly, the anesthesia during the operation could be considered as an important a risk factor for the dissemination of the viral infection not only for the patient but also for the health care professionals. Another important reason could be the possible unexplained risk of infection from the body fluids and secretions of the infected individuals. Furthermore, during the hospitalization of these patients, there may be an increased risk of infection in the hospital wards through the health care professionals and relatives, visitors of the patients.

Based on the facts and evident changes in the practice patterns, elective stone procedures such as RIRS and PCNL needed be postponed during the outbreak of the pandemic. Regarding the treatment of obstructive ureteral stones, ureteral stents and nephrostomy tubes insertion were commonly preferred to drain the system in an urgent and effective manner. As the majority of the stone cases refer to the emergency department, management of these cases has also been altered in more majority of the patients during this period due to the absence of elective surgery chance and also occupation of these departments by COVID-19 infected cases. While timely management of these cases in the emergency department is crucial other urgent solutions including medical management to some extent and widespread application of SWL (on an outpatient based manner) gained more importance. SWL was the only treatment choice which allowed stone management without any anesthesia and relevant risks for the spread of the infection.

In the light of all facts experienced during unexpected COVID-19 period, as a non-invasive, anaesthesia-free procedure "emergency SWL" (allowing an efficient social-surgical distance for the patient and the endourologist) began to be applied more commonly than ever with safe and highly succesful outcomes. [9-13]

Future perspectives : Emerging technologies
Since the introduction of the Dornier HM-3 lithotripter, changes in focal zone area, energy, and delivery rate, as well as, imaging modalities for monitoring stone fragmentation were made to improve results. However, the future of lithotripsy seems to move toward the improvement in safety and fragmentation such as microbubble technology will seems to increase the stone disintegration rates in a meaninful manner when applied in an appropriate manner. Additionally, newer technology lithotripters, such as histotripsy and burst wave lithotripsy, work by varying the delivery of ultrasound waves to a stone.

Related with this issue, microbubble technology is emerging as a potential adjunct to ESWL. In this approach, microbubbles can be modified with binding domains, which allow them to attach onto calcium stones. Experiments in animals [14] used a 5-F ureteric catheter to introduce modified microbubbles every 90 seconds during ESWL treatment. Using the microbubble technology, stone fragmentation was faster at lower energy levels than without microbubbles. Furthermore, histological evaluation of the renal and ureteric parenchyma post-treatment showed no evidence of tissue injury. Therefore, microbubbles have the potential to improve the safety and efficacy of all ESWL devices by lowering the energy required to achieve fragmentation.

Application of "burst wave technology" will enable the endourologist to relocate the stones prior to the procedure (particularly from the lower pole to renal pelvis) in an attempt to disintegrate well and increase the chance of spontaneos passage. Related with this issue, Harper and associates developed an innovative technique that utilizes short bursts of focused ultrasonic pulses to transcutaneously reposition stones within the renal collecting system and ureter. Future applications include repositioning stones prior to treatment, expediting the expulsion of residual fragments following ureteroscopy or SWL, and moving obstructing ureteropelvic junction (UPJ) stones into the kidney (to alleviate acute renal colic). The technology is currently being enhanced, and future directions include fusion of the technology with burst wave lithotripsy and stone – specific ultrasound imaging algorithms. [15] These technologies seem to hold the future of extracorporeal shockwave treatment.

Wide focal zone shock wave generators
Lithotripters differ based on their acoustic output (i.e. the dimensions and pressures of the focal zone (F2). In cases with multiple renal stones, the efficacy was reduced when compared to the former gold standard, Dornier HM3. [16] Currently, the evidence indicates that a wide focal zone provides more efficient fragmentation [17,18] while high peak pressures (i.e. high energy flux densities) result in increased tissue injury. [19] Improvements to the design of the acoustic lens of a contemporary.

Dual pulse lithotripter
Distributing the shock wave energy on two applicators is the basis for the dual – EHL system (Direx Duet, Direx Corp, Israel). As shock waves can be delivered along separate paths, the use of dual shock sources has the potential advantage of reducing treatment time. Twin sources can be operated so that shockwaves are fired simultaneously (synchronous or simultaneous mode) or in sequence (alternating mode). Since this method can manipulate the acoustic field, it also has the potential to improve stone breakage. [20] The limited clinical data available indicates safe application with no advantage over single – source SWL. The main challenge with this approach is creating adequate coupling to the stone. [21]

Last but not least, precise and reliable identification of stone(s) located in the kidney is essential in delivering shock waves to the desired focal point and achieving higher stone-free rates. Our findings demonstrated that using the specially designed imaging modality OptiVision was significantly helpful in identifying and localizing stones with high-quality images before SWL for effective stone disintegration during this procedure. [22]

Conclusions
During the last three decades, SWL technology has advanced in terms of shock wave generation, focusing, patient coupling and stone localization. The implementation of multifunctional lithotripters has made SWL available to urology departments worldwide. Indications for SWL have evolved as well. Although endoscopic treatment techniques have improved significantly and seem to take the lead in stone therapy in the western countries due to high stone-free rates, SWL continues to be considered as the first-line therapy for the treatment of most intra-renal stones and many ureteral stones.
If urologists make use of a more comprehensive understanding of the pathophysiology and physics of shock waves, much better results could be achieved in the future. This may lead to a renaissance and encourage SWL as first-line therapy for urolithiasis in times of rapid progress in endoscopic treatment modalities.

"The implementation of multifunctional lithotripters has made SWL available to urology departments worldwide."

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Saturday, 2 July 14:15 - 17:45
Meeting of the EAU Section of Urolithiasis (EULIS)
Yellow Area, Room Forum

Highlights: What went wrong with PSA and PCa?

The proposed algorithm is a useful tool for a risk-adapted strategy

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Prostate Specific Antigen (PSA) was originally meant to be a diagnostic and follow-up tool for prostate cancer, but not a screening tool. The research on an antigen in the human semen started in the 1970's and it was Dr. T. Ming Chu (US) at Roswell Park Memorial Institute who discovered a "purified human prostate antigen" in 1984. However, in the early 1990s, PSA was introduced as a screening tool. The test was not expensive and required only minimal investment.

Dr. W.J. Catalona (US) published research in 1991 on PSA testing for the detection and staging of prostate cancer. It was clear that PSA was prostate specific but not prostate cancer specific. After a visit from Dr. Catalona to the Erasmus Medical Centre in Rotterdam, Prof. Fritz Schröder (NL) and Prof. Louis Denis (BE) designed a European Randomised PSA-based Prostate Cancer Screening Trial, later called the ERSPC. Eight centres across Europe joined; coordination was with Prof. Monique Roobol (NL) from Erasmus University, with participation from Belgium, Finland, France, Italy, Spain, Sweden, Switzerland and the Netherlands. In the United States, the PLCO (prostate-, lung-, colorectal- and ovary) screening trial was setup in 1993.

The ERSPC study showed a significant reduction in prostate cancer mortality. After the first analysis the PLCO did not, because of contamination in the non-screening arm where most men had at least undergone one PSA test during the trial. However, in the end both these historical trials provided evidence of a very significant reduction in prostate cancer mortality.

Over diagnosis issue
Along with the screening trials, the number of prostate cancers detected increased rapidly in the general population between 1985 and 1995, as PSA testing became popular. This rise in incidence was obviously related to over diagnosis (up to 50% in the screening trials) of cancers that would never harm, cause symptoms or lead to prostate cancer death. It is indeed well documented that microscopic prostate cancer can be found in autopsy studies of our male population in around 80% of 80-year-old men. For this reason, a campaign against widespread PSA testing was initiated after the recommendations by the United States Preventive Services Task Force (USPSTF) in 2008 and 2012. Similar advice was issued by the UK National Screening Committee and by the German Institute for Qualität und Wirtschaftlichkeit. These recommendations were based on systematic reviews and metanalyses highlighting that the harms (unnecessary biopsies, unnecessary treatments and their complications) of population-based PSA screening outweigh the benefits (saving lives and improving quality of life).

While the decrease in mortality from cancer has been shown to be the most significant for prostate cancer as compared to all other malignant tumours in the years 2005-2009, the over diagnosis and overtreatment issue has meant that PSA testing was generally discouraged. This in turn led to the end of the steady decrease in prostate cancer mortality in the USA, and even a small increase was recorded five-years after the recommendations against PSA testing. In fact, in the USA and in Germany, more men die today from prostate than from colorectal cancer, and in the UK (where an increase of 17% in prostate cancer deaths was seen in the last 10 years), more men die from prostate cancer than women from breast cancer.

Late diagnosis
The increase in deaths has occurred because when less PSA testing is done, prostate cancers are detected more often in an advanced or metastatic stage, a phenomenon called "reverse stage migration."
As a consequence, prostate cancer is now the most fatal male cancer in Sweden and the number two in an increasing number of countries in the European Union.

While EU level guidance on cancer screening programs were recommended in 2003 by the European Council for breast-, cervical- and colorectal cancer, these recommendations have never been updated and thus up-to-date guidance on prostate cancer (or other major life-threatening cancers, e.g. lung) is still not included.

It is not acceptable that more and more men are diagnosed too late, and that despite better diagnostic and therapeutic tools, the mortality from prostate cancer is increasing. COVID-19 has caused delays in the diagnosis of cancer in general and of prostate cancer in particular. As an example, in Belgium since the beginning of the pandemic, 15% less prostate cancers were diagnosed. A number of these will become locally advanced or metastatic when diagnosed later.

Finally, we learned from the past that PSA testing in uninformed men and opportunistic (wild) screening, most importantly in age categories that do not profit from early detection, should not be advocated. This is because European men are now better informed about prostate and prostate cancer and they will ask their primary care physicians or general practitioner to test their PSA. It was clearly shown that this unorganised opportunistic screening does not significantly impact on prostate cancer mortality and, more importantly, does not avoid over-diagnosis and eventually overtreatment.

The need for screening recommendations
The European Commission launched the Europe's Beat Cancer Plan in February 2021. If Europe wants to beat cancer, it seems unacceptable that early detection of prostate cancer would not be included in the new version on the European Council's Recommendations that are expected to be made public in Q3 of 2022. PSA has fallen victim of its own success, but we have learned how to better use it in a way that significant cancers are timely detected and can be treated with curative intent. At the same time we can avoid over-diagnosis and over-treatment by the use of risk stratification. Therefore, we need to propose not a blind population-based PSA testing in all healthy men of a certain age category, but rather a population-based risk-adapted early detection strategy, starting with a PSA test in well-informed men as from 50 years of age up till an age where they still have a 15-year life expectancy.

Proposed algorithm
The EAU has therefore prepared, in collaboration with multiple stakeholders, epidemiologists, decision makers and patient organisations, an algorithm where overdiagnosis can be dramatically reduced, while significant cancers will be detected in time and can be offered curative treatment with better preservation of the patient's quality of life.

The proposed algorithm should be implemented without further delay to stop the ongoing opportunistic screening and halt the increasing numbers of diagnoses discovered too late. Opponents will insist to have new clinical trials to prove its efficacy and to include new risk stratification tools. However, waiting for the outcomes of new trials would take at least another decade.

The Future
Today in Sweden, two of the 21 regions have started a coordinated organised screening program based on the general principles of the algorithm with inclusion of risk calculators and MRI. During 2022, three other regions will start doing the same, aiming at a national Swedish early detection programme to be in place by 2025. By registering and following up on the results, further improvements can be made.

There are new urine and blood biomarkers and technologies that have become available that will allow an ever-improving risk adapted approach. These early detection tests show great potential in differentiating further between significant and insignificant cancers.

The tools to implement a risk adapted strategy for the early detection of prostate cancer in healthy well-informed men are available. The 2022 EU council recommendation on screening fits perfectly in the Europe's Beating Cancer Plan and provides an excellent opportunity for the European Union to address this challenge. Political will and support will be necessary from EU member states and regions to implement this strategy. A major effort will be needed to inform our healthy male population and to update our general practitioners and primary care physicians, based on the new European guidelines on early detection.

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Friday, 1 July 10:30 - 13:30
Special Session Prostate Cancer
Orange Area, eURO Auditorium 1

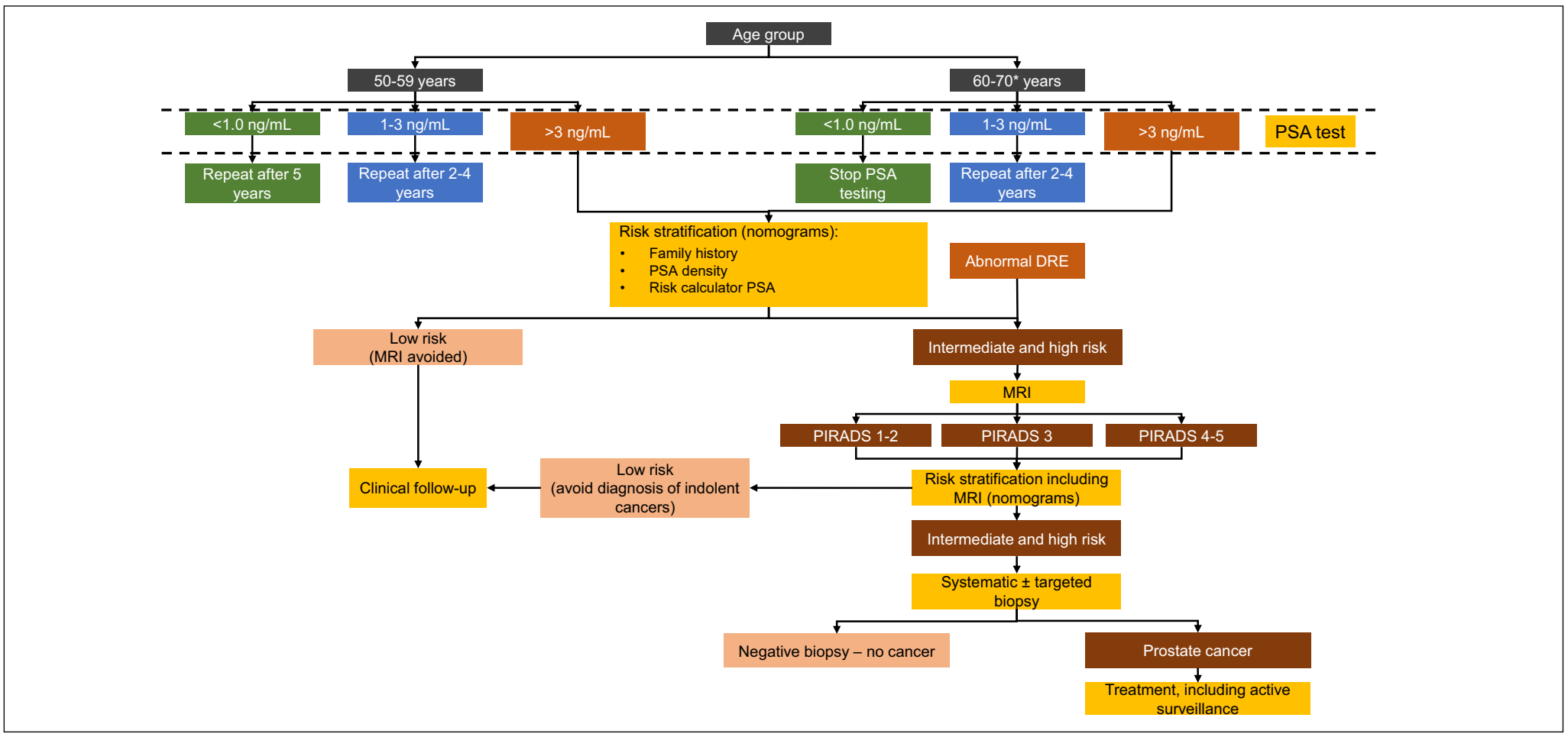

Figure 1: algorithm to illustrate the EAU's risk adapted strategy for the early detection of prostate cancer in well-informed men(3).

- *Risk-adapted algorithm for the early detection of prostate cancer, adapted based on prostate cancer guidelines published by the EAU. The patient's values and preferences should always be taken into account as part of a shared decision-making process.*
- *DRE = digital rectal examination; EAU = European Association of Urology; MRI = magnetic resonance imaging; PIRADS = Prostate Imaging Reporting and Data System; PSA = prostate-specific antigen.*
- **Healthy men >70 yr without important comorbidities and a life expectancy of >10-15 yr may continue PSA testing.*

Management of testicular non-germ cell tumours

Treatment and follow-up recommendations

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Most testicular tumours are germ cell tumours (GCTs), whereas sex cord–stromal tumours represent the second largest group of primary testicular tumours and include Leydig, Sertoli, Granulosa or unspecified subtypes. [1] Another rare subgroup of testicular tumours are the previously called 'spermatocytic seminomas', which have been reclassified as spermatocytic tumours. [2] Further rare testicular histologies are mesothelial tumours, including malignant mesothelioma [3] or the usually benign tumours of the thecoma/fibroma group. [1,4]

Although those non-GCT tumours are rare testicular tumours, they are seen periodically in urology and oncology departments, and published data to guide treatment is scarce. For example, only 76 Leydig cell tumours were coded in the National Cancer Institute's Surveillance, Epidemiology and End Results (SEER) programme. [5]

Our group therefore performed several systematic reviews and meta-analyses of published case reports in non-GCT. However, such reviews are prone to publication bias and offer only limited long-term oncological outcomes. Nevertheless, those analyses provide the largest assimilation of data in the field and hence the best available information on which to base treatment and follow-up recommendations. Based mainly on those reviews, the chapter on rare adult para-/testicular tumours in the testicular cancer EAU Guideline was amended. [6]

To improve the status quo in the future, we initiated the OrphAn Testis Histologies (OATH) registry to provide more conclusive recommendations regarding clinical management and follow-up of these rare entities. We encourage collaborators to contribute data regarding patients with rare testis cancer histology.

Leydig cell tumours
Leydig cell tumours are estimated to be 20 times less common than GCTs, [7] and the incidence of metastases has previously been thought to be as high as 10%. [8] This 10% figure for metastasis has been questioned more recently in a retrospective study of 204 cases. Follow-up was available for 60 men, [7] and only one (<2%) experienced recurrence during a follow-up of 112 months (IQR 14–145 months). Leydig cell tumours may present with hormonal manifestations, including gynaecomastia and more rarely accompanied by Cushing's syndrome. [1] With testis-sparing surgery, a local recurrence rate of 7% has been reported. [9] Several risk factors for metastatic disease have been proposed which may be useful for image-guided follow-up intensity. [9]

Survival of men with metastatic Leydig cell tumours is poor, but occasional responses to surgical and systemic treatment have been reported. [9] Two editorial comments suggest adjuvant retroperitoneal lymph node dissection (RPLND) for patients with stage I disease and the presence of pathological risk factors. [10,11] This conclusion was based on experience in several high-volume centres and is supported by our findings because our review indicated that men with visible metastatic Leydig cell tumours have a particularly poor prognosis and that the retroperitoneum represents the primary landing zone in two thirds of oligometastatic cases.

Therefore, RPLND is thought to cure micro metastatic disease in the retroperitoneum, but the indication depends heavily on the pathology report, which requires a dedicated and experienced uropathologist. Furthermore, RPLND should only be performed in centres with adequate expertise regardless of whether it is minimally invasive or open.

Sertoli cell tumours
Sertoli cell tumours account for approximately 1% of testicular neoplasms. [1] The risk of metastases is unclear. With testis-sparing surgery, a local recurrence rate of <1% has been reported, although no adjuvant treatment options can be recommended. [12] Several risk factors for metastatic disease have been proposed which may aid in image-guided follow-up intensity. [12] Survival of men with metastatic disease is poor, although response to surgery has been occasionally reported. [12] Therefore, adjuvant RPLND for patients with stage I disease and the presence of pathological risk factors may also be indicated in selected men with Sertoli cell tumours.

Granulosa cell tumours
Whereas metastatic disease has never been reported in juvenile Granulosa cell tumours, men with the adult type may occasionally present with metastatic disease. [13] Survival of men with metastatic Granulosa cell tumours is poor, although rare instances of response to surgical or systemic treatment have been reported. [13] Therefore, again, adjuvant RPLND for patients with stage I disease and the presence of pathological risk factors may also be indicated in selected men with Granulosa cell tumours. With testis-sparing surgery, a local recurrence rate of 5% has been reported.

Spermatocytic tumours
These tumours are unrelated to germ cell neoplasia in situ (GCNIS) and show a unique amplification of chromosome 9 corresponding to the DMRT1 gene. [2] Men with spermatocytic tumours predominantly do not exhibit elevated serum tumour markers. [2] As those tumours cannot be differentiated from seminoma GCT by frozen section analysis, radical orchiectomy is the standard treatment option. Outcomes after testis-sparing surgery or adjuvant treatment are unknown and therefore not recommended. [14] Metastatic disease is very rare and typically presents at or soon after initial diagnosis with limited survival. [14]

Mesothelioma of the tunica vaginalis testis
Mesothelioma of the tunica vaginalis testis is a rare but aggressive disease. [15] Aside from older age, larger tumour size, presence of necrosis, angiolymphatic invasion or a high mitotic index, the only modifiable risk factor for metastases is local recurrence. Therefore, aggressive local treatment with hemiscrotectomy is recommended. No clear suggestion can be made regarding adjuvant treatment. In the case of metastatic disease, the median overall survival is only a few months, and multimodal treatment could be considered.

Follow-up
After local surgical treatment is completed, attention turns to follow-up strategies with the aim of detecting recurrence or secondary cancers at a stage when further curative procedures are possible, whilst minimising the burden of follow-up, the potential for over-treatment and concomitant treatment toxicity. Traditional, fixed follow-up schedules, including visits to a cancer specialist for examinations with cross-sectional imaging are expensive, expose patients to contrast and radiation and may be burdensome for the patient. The impact on prognosis and patient-reported outcomes of more or less intense follow-up schedules – either specialist- or non-specialist-led – is of limited value in most cancers. [16] This fact is particularly relevant in rare non-GCTs of the testis with a natural history of being generally indolent but which have a rare predilection to progress more widely. In a recent review, we provide the best available clinical data about the recurrence rates of these rare tumours during follow-up, to discuss the risks and benefits of follow-up with cross-sectional imaging and to provide follow-up recommendations. [17]

Paratesticular tumours
In contrast to testicular tumours, the majority of paratesticular/epididymal masses are benign cystic or inflammatory conditions. Solid epididymal tumours are rare and comprise numerous benign and neoplastic lesions. In the only population-based analyses, [18] the majority of neoplastic lesions of the epididymis or spermatic cord were sarcomas, metastases from other organs or primary adenocarcinomas similar to proportions reported in institutional studies.[19,20]

Benign lesions, which may comprise the majority in clinical practice, include lipomas, adenomatoid tumours leiomyomas and papillary cystadenomas. Robust criteria to differentiate between paratesticular malignant and benign lesions preoperatively have not been defined, although ultrasonography with or without fine needle aspiration, [21] magnetic resonance imaging [22,23] and surgical exploration with frozen section analyses or histopathological confirmation can be considered. No clear recommendation can be provided regarding surgical approach, the extent of resection and neo- or adjuvant treatment.

In conclusion, given the rarity of those rare para-/testicular cancers together with the poor prognosis in the metastatic setting, I suggest referral of these cases for multidisciplinary discussion including central imaging and pathology review.

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Sunday, 3 July 10:30 - 12:00
Thematic Session 03
Green Area, Room 1

Penile epispadias reconstruction techniques

An update from 326 patients treated from 2013 to 2021

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Epispadias is very rare and most complex congenital anomaly of the penis, and its treatment presents a real challenge for many experienced surgeons; ideal functional and aesthetic result is still hard to achieve. It can be found isolated or joined with bladder exstrophy.

Contrary to traditional view that epispadias is only a urethral problem, in reality all penile structures are deviant: cavernosal bodies are triangular, separated and dorsally curved with reduced upper length; neuro-vascular body (NVB) is also split by urethral plate that is widely open dorsally and placed between cavernosal bodies; it continues into the dorsally opened glans; in proximal and majority of middle forms bladder neck is widely opened anteriorly and incompetent; penile skin is missing dorsally and is widely spread between scrotum and penile base ventrally; in rare cases of isolated epispadias symphyseal diastasis is present and bladder can be small.

During treatment all of mentioned problems should be faced and treated in order to create as normal as possible penis, which is somewhat shorter in majority of patients. (Fig. 1)

Long-term results of epispadias repair showed many remaining problems in adults who underwent repair in childhood - poor aesthetic outcome with multiple scars, severe dorsal curvature with penile entrapment; this makes sexual intercourse difficult and painful, sometimes even impossible. Glans, cavernosal bodies and/or penile skin necrosis caused by previous surgeries are not rare.

In our previous study we precisely described all anatomical features of epispadiac penis, which was the basis for our further investigation and improvement of surgical technique using our radical total disassembly technique.

Materials and methods
In the period from January 2013 till October 2021 we treated surgically 326 male epispadias and exstrophy patients (393 surgeries, excluding small procedures and endoscopies) aged between two days and 59 years. Penile reconstruction was done in 274 of them; 58 had isolated epispadias (11 distal, 15 midshaft and 32 proximal), 47 epispadias were corrected after previous bladder closure, 161 during full exstrophy correction (12 in primary repair and 149 re-do) and eight patients with cloacal exstrophy. Out of these, 187 were children younger than 14, and the remaining 87 were older children and adults (with adult size genitals). Timing of penile surgery in primary epispadias and in children after primary bladder closure was between second and third year of age or later, and in re-do cases we did it after the first year. In all younger children with small penile size preoperative testosterone treatment was advised – 2% dihydrotestosterone gel or intramuscular testosterone injections in fully incontinent children.

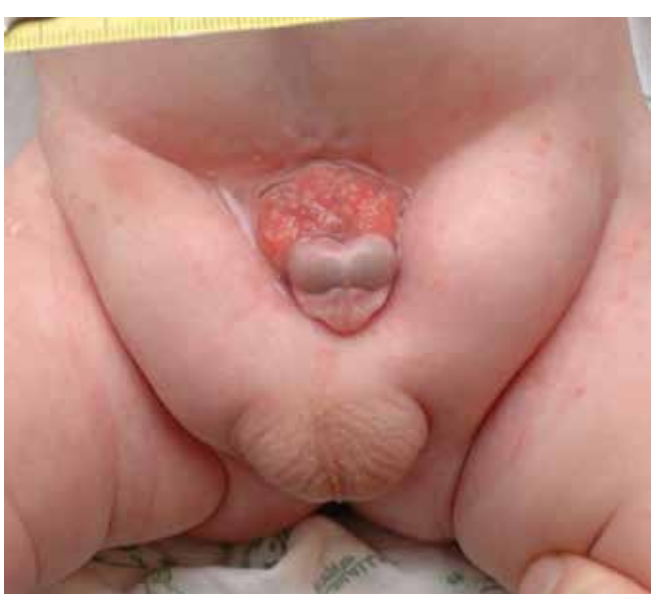

Figure 1: Epispadias-exstrophy complex

Surgical technique
The main surgical techniques that are present nowadays for epispadias repair are the Cantwell-Ransley and Mitchell techniques. Due to lack of satisfactory outcome, we started to make some changes in order to achieve improvements, all based on a deeper insight into anatomy achieved by radical penile disassembly. Surgery begins with wide penile degloving, leaving around 1cm of the prepuce and continuing para-urethraly and laterally until scrotum. Skin is released from non-elastic deep dartos fascia to create wide elastic flap, taking care to preserve its vascularity provided by superficial and deep external pudendal vessels.

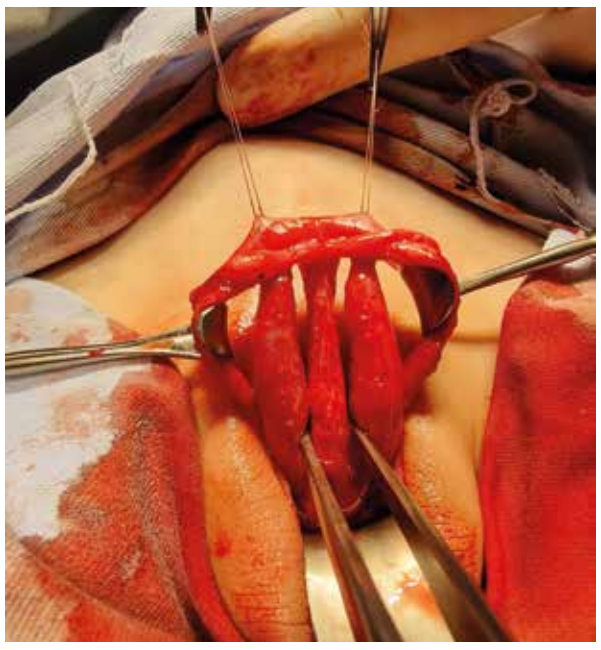

Figure 2: Total penile disassembly

Figure 3: Satisfactory outcome in epispadias

The penis, including whole depth of cavernosal crura and urethral bulb is fully released. Dissection continues dorsally deep under symphysis and partially under pubic rami with obligatory preservation of cavernosal arteries and elements of the NVBs. Both NVBs and urethra are radically mobilised off the cavernosal bodies using combined sharp and blunt dissection. Then follows separation of the urethral plate from NVBs with careful excision of tight non-elastic fibers that are found between them, which greatly increase their elasticity and lengthening of the dorsal side of corpora. Separation continues deep into the glans in the plane of Buck's fascia, creating widely mobile glans wings. (Fig. 2)

The bladder neck is reconstructed in all incontinent children with appropriate bladder size the urethra is tubularised over sillicone Foley catheter (size depends on patient's age). Severity and points of dorsal curvatures are checked in artificial erection bilaterally and thickened dorsal triangular ridge of tunical albuginea is carefully excised; cavernosal bodies are additionally straightened by multiple transversal incisions of only superficial tunical layer dorso-laterally, taking care to preserve inner circular layer and cavernosal membrane; cavernosal bodies are rotated externally and joined, transposing previously tubularised urethra ventrally.

After excision of uneven medial mucosal tags, the glans is reconstructed in a few layers to avoid dorsal grove formation. NVBs are fixed paraurethraly and joined dorsally, forming normal anatomical relations of the penis. Then follows reconstruction of the penile skin, which is tacked to the base of the penis, wrapped around and joined dorsally. A compressive dressing is applied and changed every two to three days for two weeks, when the Foley catheter is usually removed. Patients are advised to use vacuum device for postoperative penile stretching for six months, to maintain penile straightening and lengthening achieved by tunical attenuation.

Results
Follow-up was 6 months to 8 years (mean 45 months). Since a great majority of patients were from abroad, we are following them up for years by being regularly sent photos, videos while voiding and all necessary results/images by e-mail. This way showed to be sufficient for assessment of both aesthetic appearance (glans, penile skin, size, straightness and relationship with surrounded structures) and urine stream. (Fig. 3)

There was clear difference in outcome between primary and re-do repair, and also between epispadias and exstrophy patients (due to corporal divergence caused by diasthasis). Scarring and tissue damage caused by previous surgeries (especially on dorsal side) made dissection in some cases extremely difficult. Considering all anatomical features of epispadiac penis we achieved good functional and aesthetic outcome in majority of patients.

However, we also had many problems: different degree of penile curvature or rotation remained in 24 patients. Urethral stricture was present in 16 and fistula in eight patients. Partial penile skin necrosis was present in 32 patients, that was treated by frequent application of ointments which enable slow reepithelization. Thirteen exstrophy patients had postoperative glanular venous stasis with dark glans due to compression of NVB, which was treated aggressively by frequent postoperative glanular puncturing with small bore needle to release trapped venous blood and prevent its coagulation and necrosis for a few days until glans color return to normal. Eventually, there were no necrosis of glans or corpora in our series; erection is preserved in all patients. Additional small corrective surgery was done in 29 patients.

Conclusions
New insight into anatomical features of epispadiac penis revealed several important particularities, which enabled us to understand better all underlying problems and find a better solutions. Radical mobilisation of all penile entities is crucial to provide appropriate access for correction of all mentioned abnormalities and their re-arrangement into normal, tension free relations. Dissection is often very difficult with high risk of serious damage of neurovascular structures with devastating consequences, reconstruction can be equally complex. Glans and penile skin appearance are the most important for final aesthetic outcome. This kind of surgery should be reserved for highly specialised centres.

Saturday, 2 July 10:30 - 14:00
Joint meeting of the ESTU, ESOU and the ESGURS
Grey Area, Room Emerald

Two hands in one glove

The "discovery" of the cavernous nerves

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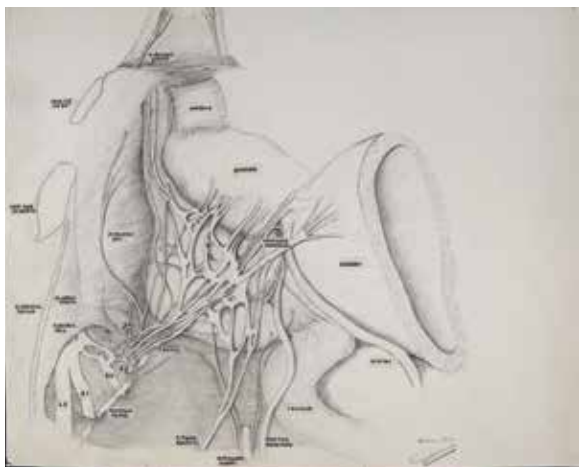


Drawing of dissection of left pelvic plexus in male newborn

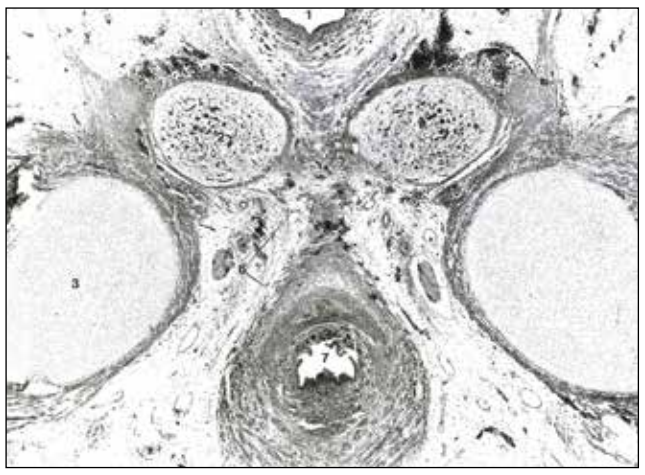


Image of transverse section through male foetus in the Walsh-Donker publication (1982)

In the past, the anatomy of the pelvis has been described in several anatomical atlases in detail, but before the 1980s this "old" anatomical knowledge had not contributed to the (radical) surgical approach of the prostate. This procedure was unpopular because of the abundant, sometimes life-threatening, blood loss from the plexus of Santorini (the dorsal vein complex of the prostate). Radical prostatectomy was therefore performed with little enthusiasm. This hurdle, as I will explain later, was only overcome after modifications of this procedure by, among others, Patrick C. Walsh, professor at the James Buchanan Brady Institute of Urology at Johns Hopkins in Baltimore (US). The next hurdle was another problem of the procedure, the injury to the neurovascular bundles. Intact bundle(s) are a prerequisite for normal erections (nervi erigenti). This is what Pieter Donker, emeritus professor of urology at the University of Leiden (NL) at that time, should be credited for.

Who was this Pieter Donker. Donker was born on March 2, 1914 in Schellinkhout, a small village in the province of North-Holland (NL). After completing secondary school in Hoorn, he studied medicine at the Municipal University of Amsterdam and began his surgical and internal training in 1938 at the Maria Foundation in Haarlem, interrupted by the mobilization of WWII in 1939. In 1942, Donker continued the training in the "Johannes de Deo" in Haarlem. He then went to the St. Franciscus Gasthuis in Rotterdam to complete his training (under the supervision of the surgeon P.A. de Vos).

In 1945, Donker left for Indonesia (a Dutch colony at that time) as a volunteer doctor. He was initially stationed in Jakarta as head of the surgical department. Then in 1946, he was stationed in Surabaya in the Marine Hospital as head of the surgical department.

In 1948, he returned to the Netherlands but was unable to practice his profession for a year due to an illness. Since the profession as a general surgeon was probably too arduous, fortunately, Donker decided to specialise in urology.

In 1949, Donker started training at J.A. Weijtlandt in Amsterdam. In 1951, he obtained his doctorate with Prof. Dr. I. Boerema in Amsterdam on the thesis "The treatment of perforating abdominal injuries". In the same year, he established himself as a urologist at the St. Franciscus Gasthuis (1951-1965) and Eudokia Hospital (1951-1962) in Rotterdam and became a member of the Dutch Urological Association (DUA), which had 19 members at the time. In the 1950's he became a trainer in urology.

On April 1, 1962, Donker started as an extraordinary lecturer in Leiden. Three years later, he became an extraordinary professor of urology. In 1968, he was appointed full professor of urology. Donker retired in 1979 and presented his farewell lecture "Cost control in clinical medicine" on September 21 of the same year. This was not the end of his interest in urology and anatomy.

Since then, Donker devoted himself to the dissection of the small pelvis in the laboratory for Embryology and Anatomy in Leiden. At this stage, Walsh, whom Donker was already in contact with, visited Donker and used his findings to develop the nerve-sparing radical prostatectomy.

How something small can result in big consequences is clear from the landmark article in the Journal of Urology of 2007, in which Walsh described how he came to his ground-breaking technique of nerve-sparing prostatectomy.

In 1977, Walsh had already adapted his technique (the binding of the dorsal vein complex of the prostate) in such a way that it became possible to perform a radical prostatectomy without too much blood loss. That same year, Walsh entered the American Association of Genitourinary Surgeons for the first time. The night before a convention, Walsh went to a restaurant with his wife and "Standing in the shadows behind the maître d', I spotted an older man. Impetuously I asked if he was also attending the meeting and whether he would like to join us for dinner." The older man was Donker. This meeting was the beginning of a friendship.

A few years later in February 1981, Walsh attended a Boerhaave symposium in Leiden by invitation. The symposium was quite intensive for Walsh due to lectures and demonstrations in the OR. Nonetheless, he still wanted to see a bit of Leiden. Professor Udo Jonas, professor of urology in Leiden at the time, asked Donker, if he would show Walsh around but it never came to that; Walsh wanted to know what Donker was doing in his spare time instead.

Donker worked in the anatomical laboratory trying to map the innervation of the bladder in male foetuses. Upon learning this, Walsh was eager to see Donker's work and asked him if he also prepared the innervation of the corpora cavernosa. Up until then, Donker had not looked for it. Three hours later, both saw that these nerve pathways (contrary to what had been claimed) which laid outside the capsule and fascia of the prostate, an essential find for future nerve-sparing procedures! Armed with this knowledge, Walsh returned to the United States and laid the foundation for his well-known nerve-sparing technique of radical retropubic prostatectomy. In his articles, Walsh has always credited Donker for his contributions.

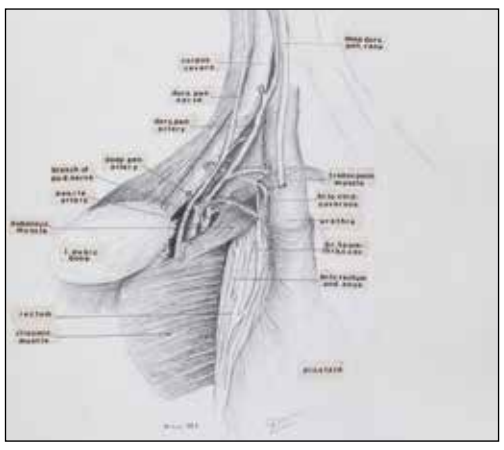
The drawings used for the original publication in the Journal of Urology in 1982 were considered lost. In 2010, thanks to Donker's son, these beautiful pencil drawings of the male pelvis were discovered behind a cupboard when Donker's widow moved out of their house!

What is less known is that Donker also mapped the innervation of the pelvic floor and internal genital organs of women. The surgical anatomy of the innervation of the female pelvis was not well known in the 1980s. At that time, the then unknown drawings of the female pelvis were a great find and fortunately, these were fully appreciated when these were discovered during the cleaning of the old anatomical laboratory. These exquisite drawings were printed in 2008 in the anniversary book of the DUA when the association celebrated its 100th anniversary.

For his services to the Dutch urology, the DUA has honoured Donker posthumously by instituting the *Pieter Donker lecture* which is held annually under the auspices of the Scientific Committee, on topics related to the experimental or clinical urology.

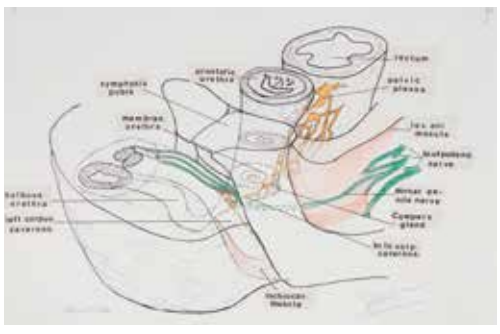
Due to space constraints, the entire reference list can be made available to interested readers upon request by sending an email to: communications@uroweb.org.

Saturday, 2 July 11.00 - 13.30
EAU History office
Grey Area, Room G107

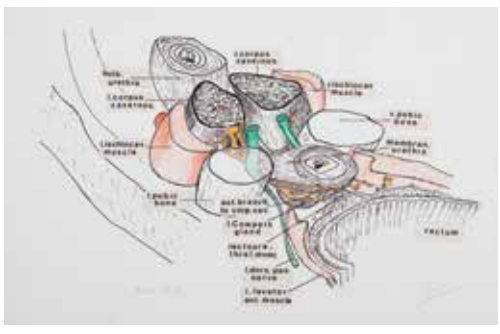


Drawing of dissection of caudal and ventral part of left pelvic plexus in male newborn

Professor Pieter Donker (1914-1999)



Drawing of male foetus 11 cm. crown-rump length, composition of microscopic sections



Drawing of male foetus 20 cm. crown-rump length, composition of microscopic sections

The right dose of antimicrobials

For patients with renal transplants or renal dysfunction

Prof. Suzanne Geerlings
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Adequate antibiotic drug exposure in patients treated for bacterial infections is of high importance because underexposure is associated with therapeutic failure and the development of antibiotic resistance, while overexposure may lead to toxicity [1]. Reducing the dose of renally cleared antibiotics for patients with impaired renal function is standard of care as incorporated in all clinical guidelines, aiming to prevent accumulation of the drug and to achieve antibiotic drug exposure equivalent to that in patients with adequate renal function receiving the regular dose [2,3].

However, significantly increased therapeutic failure and death were observed in patients with impaired renal function treated with recommended reduced doses of antibiotics [4]. Additionally, multiple antibiotics recently approved by the US Food and Drug Administration (FDA) carry precautionary statements in their labelling for reduced clinical response in patients with impaired renal function [5]. In clinical practice, prescribers often do not apply recommended dose reductions for patients with impaired renal function because they worry about underexposure [6]. Particularly patients in the intensive care unit (ICU) are almost always treated with regular doses instead of recommended reduced doses because underexposure is a big problem in these patients [7,8,9]. Also, inconsistency exists between different guidelines in the cutoff value of renal function below which the dose per antibiotic should be reduced and in the degree of the dose reduction [10].

Efficacy of antimicrobial dosing
Pharmacokinetics (PK) describe the time course of antimicrobial concentrations in the body, while pharmacodyamics (PD) describe the relationship between these concentrations and the antimicrobial effect.

The primary measure of antimicrobial effect is the minimum inhibitory concentration (MIC). The MIC is the lowest concentration of an antibiotic that prevents visible growth of bacteria in vitro. While the MIC is a good indicator of the potency of an antimicrobial, it indicates nothing about the time course of antimicrobial activity.

PK-parameters quantify the serum level time course of an antimicrobial. The three pharmacokinetic parameters that are most important for evaluating antibiotic efficacy are:

1. The peak concentration (C_{max})
2. The trough concentration (C_{min})
3. The area under the concentration-time curve (AUC)

While these parameters quantify the serum level time course, they do not describe the killing activity of an antibiotic. Integrating PK-parameters with the MIC gives us the opportunity to quantify the activity of an antimicrobial within PK/PD targets [11].

Systematic review on antimicrobial dosing
We wondered whether the recommended dose reduction of renally cleared antibiotics for patients with impaired renal function was adequate and whether they have been validated in clinical practice. Therefore, we performed a systematic review to summarise the available evidence on drug exposure or on PK/PD target attainment after dose reduction of antibiotics in patients with impaired renal function.

We systematically searched Ovid Medline and Embase from inception (respectively 1946 and 1947) through July 2019 for all studies reporting antibiotic drug exposure and/or PK/PD target attainment after dose reduction of antibiotics in patients with impaired renal function.

The reduced dose was considered adequate when the most relevant parameters of drug exposure or PK/PD target attainment in patients with impaired renal function were within a range of 80% to 125% compared to patients with adequate renal function receiving a regular dose (reference) or when PK/PD target attainment was attained in at least 90% of the patients with impaired renal function, regardless of the lack of a reference group.

Twenty-seven of the 4,202 identified studies were included. The quality of 15 of 27 studies was fair, and most studies were of β-lactams (12/27). The best evidence was available for meropenem: four studies were included, of which two studies were of good quality. Drug exposure for meropenem is 158% to 286% higher in patients with impaired renal function receiving reduced doses compared to patients with adequate renal function receiving regular doses. For all other antibiotics, a maximum of one good-quality study could be identified.

To conclude, no good-quality evidence on the recommended dose reduction of renally cleared antibiotics in patients with impaired renal function is present, with the exception of meropenem [12].

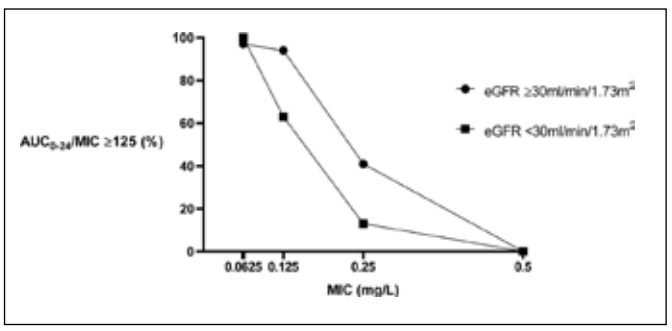
Ciprofloxacin
The fluoroquinolone antibiotic ciprofloxacin is frequently prescribed both in inpatient and outpatient settings and its activity mainly includes Gram-negative bacteria, of which Enterobacterales and *Pseudomonas aeruginosa* are the most clinically relevant. It is frequently used in the treatment of urinary tract infections.

Ciprofloxacin is primarily eliminated renally. Therefore, dose reductions are recommended for patients with an eGFR of <30 mL/min/1.73m2. These dose reductions are based on extrapolations from small studies mostly investigating the PKs of ciprofloxacin after a single, full, unadjusted dose in volunteers with impaired renal function, but without an infection. However, ciprofloxacin is also metabolised and partly excreted through the biliary system. This alternative elimination pathway may compensate for reduced elimination through the kidneys in patients with impaired renal function. Therefore, the correlation between eGFR and total clearance of ciprofloxacin might not be directly proportional.

For ciprofloxacin, the PK/PD target is defined as the ratio of the area under the concentration–time curve (AUC) over the minimum inhibitory concentration (MIC) of the causative microorganisms. Attaining the PK/PD target of AUC/MIC ≥125 for total ciprofloxacin exposure is associated with clinical and microbiological cure of lower respiratory tract infections, bacteraemia, wound and soft tissue infections, and complicated urinary tract infections, mainly caused by *P. aeruginosa* or other Gram-negative bacteria [13,14]. However, it has been shown that AUC/MIC ≥125 is often not attained in critically ill patients or in patients on general wards treated with recommended doses of ciprofloxacin (200–1500 mg/day).

Therefore, we investigated:
1. PK/PD target attainment of ciprofloxacin (AUC/MIC ≥125 in the first 24 hours of treatment in adult patients on general wards with adequate and impaired renal function receiving regular and reduced doses of ciprofloxacin, respectively.

2. Drug exposure for patients with impaired renal function receiving the guideline-recommended dose reduction of ciprofloxacin compared to drug exposure in patients with adequate renal function receiving the regular dose.



Percentage of patients attaining the PK/PD target of AUC0–24/MIC ≥125 at different MIC values (0.0625, 0.125, 0.25 and 0.5 mg/L) for patients with adequate renal function (eGFR ≥30 mL/min/1.73m2) and for patients with impaired renal function (eGFR <30 mL/min/1.73m2)

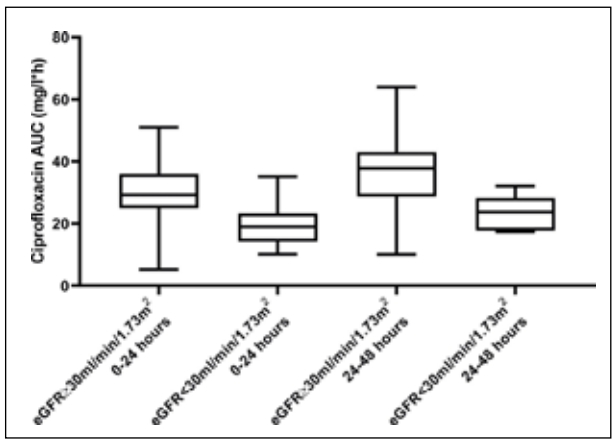
We obtained three blood samples per patient for ciprofloxacin concentration measurement. Individual AUCs were calculated using a population PK model developed by non-linear mixed-effects modelling (NONMEM).

Forty patients were included, of whom eight had impaired renal function and were treated with a guideline-recommended reduced dose. Using the clinical breakpoint MIC of the most isolated bacteria (Escherichia coli, 0.25 mg/L), AUC_{0-24}/MIC ≥125 was attained in 13/32 (41%) patients with adequate renal function receiving regular doses and in 1/8 (13%) patients with impaired renal function receiving reduced doses.

Median drug exposure (AUC_{0-24}) for patients with impaired renal function was 19.0 [interquartile range (IQR) 14.2–23.3] mg/L•h, which was statistically significantly lower than that for patients with adequate renal function [29.3 (IQR 25.0–36.0) mg/L•h] (P < 0.01).

To conclude, AUC_{0-24}/MIC ≥125 is not attained in the majority of adult patients on general wards for clinically relevant bacteria with MICs at or just below the clinical breakpoint. The risk of not attaining the target appears to be highest in patients with impaired renal function receiving guideline-recommended reduced doses, as drug exposure is significantly lower in these patients [15].

New dosing simulations of ciprofloxacin
The rationale behind the guideline recommended dose reduction of ciprofloxacin in patients with impaired renal function is to achieve bioequivalence, defined as drug exposure equivalent to exposure in patients with adequate renal function receiving a regular dose. However, results from the above presented study by our research group showed that drug exposure is not equivalent, but statistically significant lower in patients with impaired renal function (eGFR 30 ml/min/1.73m2).



Median ciprofloxacin exposure in the first 24-h (AUC_{0-24}) and 24–48 h (AUC_{24-48}) after treatment with ciprofloxacin for patients with adequate renal function (eGFR ≥30 mL/min/1.73m2) and for patients with impaired renal function (eGFR <30 mL/min/1.73m2)

Therefore, we simulated alternative dosing recommendations of ciprofloxacin for patients with impaired renal function. Results of these simulations show that a daily dose of ciprofloxacin of 750 mg orally and 600 mg intravenously (instead of the currently recommended daily dose of 500 mg orally and 400 mg iv), should lead to equivalent drug exposure and better PK/PD target attainment in patients with impaired renal function, (eGFR 30ml/min/1.73m2) as in patients with adequate renal function receiving a regular dose.

We are now performing a prospective cohort study to validate these new dosing recommendations of ciprofloxacin for patients with impaired renal function.

Due to space constraints, the entire reference list can be made available to interested readers upon request by sending an email to: communications@uroweb.org.

Saturday, 2 July 14:15 - 17:50
Meeting of the EAU Section of Infections in Urology (ESIU)
Grey Area, Room Emerald

Urinary tract infections of viral origin

Viral orchitis, epididymitis and transplanted immunocompromised patients

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The COVID-19 (coronavirus disease 2019) pandemic has shown that infectious diseases, especially viruses, have an enormous impact on the healthcare system and beyond. [1,2,3] Patients present with viral infections are associated with numerous diseases in daily urological practice. Unfortunately, the therapeutic options in urological viral infections are often limited to symptomatic approaches or immunomodulation. That is why vaccination prevention could be an essential option for viral urinary tract infections, so further research on that topic is vital. [3]

Viral urological infections can appear very heterogeneously, reaching from recent reports that severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) can cause kidney failure or thromboembolic complications like priapism, prostate- or kidney infarction [3-11] to the association of human papillomavirus (HPV) with penile cancer. [12] However, urologists will mainly be confronted with viral infections in two cases: firstly, in viral orchitis or epididymitis and secondly, in transplanted immunocompromised patients.

Consequently, this article summarises the main facts of those two cases.

Acute, symptomatic urogenital infections – viral orchitis and epididymitis

Acute, symptomatic viral infections in the male genital tract have only been described in orchitis or epididymitis. [3,13] Different viruses are related to this disease, but most data are available for mumps. [3,13-16] Historical data show that orchitis appears in nearly 18% of the cases five to ten days following parotitis. [16] Since the introduction of vaccination, mumps orchitis has been a rare disease, but it is still possible even with a lower rate of symptoms. [15] Furthermore, it has been described that Coxsackie viruses can cause orchitis. [17] However, many studies only describe imprecise if it is only orchitis, epididymitis or epididymorchitis because they only rely on palpation. A more precise method would be duplex-sonography, but two studies also describe an epididymitis in mumps orchitis in 33% or 56% of the cases. [18,19]

Conversely, in 60% of initial bacterial epididymitis, the testis is involved. [20] Unfortunately, only a few studies investigate a viral origin of epididymitis or only analyse mumps serology. [13,21,22] Only one study investigated polymerase chain reaction (PCR) in urine, blood and semen 23 different viruses. In two of 150 patients, enteroviruses were prevalent in the semen, which were no longer detectable after healing the disease. [21] In summary, further research about viral origins in epididymorchitis is necessary.

Viral urological infections in transplantation medicine – significance of BK polyomavirus (BKPyV) for urology

Urologists are often involved with viral infections in kidney transplantation. Viral infections are a very relevant problem in these immunocompromised patients. Relevant viruses are herpes virus (HSV), cytomegalovirus (CMV), Epstein Barr virus (EBV) and BK polyomavirus (BKPyV), but even influenza or parainfluenza viruses are important. [3,23] Interestingly, CMV is one of the most severe viral infections in kidney transplant recipients, but luckily with adequate prophylaxis, the incidence is very low (< 1%) in most transplantation programmes. [24] Without adequate CMV prophylaxis, there is an incidence up to 70%, often leading to early graft failure. [25] Since CMV infections are mostly asymptomatic, it is essential to differentiate them from organ rejection so that kidney biopsies are frequently necessary. This is also why CMV plasma viral load should be detected via PCR during every hospital readmission in the first year following transplantation. [26] Therapy of CMV infection is applied according to the KDIGO (Kidney Disease Improving Global Outcome) guidelines. [27]

Polyomaviruses are of particular interest to kidney transplant recipients. They are small DNA viruses that were first discovered in 1971. At present, 13 different types are recognised, but the most significant for renal transplant patients is BKPyV, the cause of BKPyV associated nephropathy (BKVAN). Furthermore, this virus can lead to hemorrhagic cystitis and ureter stenosis. [28,29,30] To put it in a nutshell, BKPyV is the most important polyomavirus affecting renal transplant recipients, and adequate management of this infection may significantly impact allograft survival.

The general population is exposed to BKPyV during childhood, and 80 – 95% of the adults are seropositive. The virus persists in different cells from which it can be reactivated. Sometimes the infection may be transmitted with the allograft. [29] Although BKPyV has been detected in patients with heart or liver transplantation and patients with human-immunodeficiency virus (HIV) infection or intestinal inflammatory disease, BKVAN is mainly described in renal transplant recipients. [29,31-34] BKVAN is seen in approximately 5% of renal transplant recipients and can lead to chronic allograft failure or even graft loss in up to 50% of cases.

Some of the proposed risk factors include older age due to waning of immunity, human leukocyte antigen (HLA) mismatches, acute rejection, steroid therapy and maintenance immunosuppression with tacrolimus. [29,35] However, the common surrogate to all these factors is BKPyV viremia. [29,36] The infection (also reactivation is possible) is initially asymptomatic, so surveillance programmes are essential. The diagnosis then is based on quantitative PCR in plasma (viremia) and urine (viruria) in the presence of acute renal failure. Unfortunately, no effective therapy is available, and screening remains the cornerstone for tackling BKPyV disease. [28,29]

Implications for further research

In summary, many questions in urinary tract infections of viral origin are open, and further research is essential since especially high-quality research is sparse. Promising new targets for further evaluation in research are virus-specific T cells and targeting the viral immune response or even the development of vaccination since these therapies might have less collateral damage than the classical antivirals, which also affect the host.

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Saturday, 2 July 14:15 - 18:00
Meeting of the EAU Section of Infections in Urology (ESIU)
Grey Area, Room Emerald

Transgender and gender non-conforming health care today

The role of gender-defining surgery

Dr. Wietse Claeys
Urology resident,
PhD researcher
Ghent University
Hospital
Ghent (BE)

Prof. Piet Hoebeke
Urologist
Ghent University
Hospital
Ghent (BE)

Transgender and gender non-conforming individuals experience gender dysphoria or gender incongruence. This refers to a mental unrest resulting from an incongruity between the assigned biological sex and the mentally experienced gender or gender identity. [1] These individuals may seek care directly related to their gender dysphoria. They may seek psychological counselling that supports them in dealing with their feelings of gender incongruence or helps them in considering further steps in a gender transitioning process and its possible implications on relationships, employment, and social acceptance. Young and teenage individuals may benefit from treatments suppressing the effects of their body's own hormones and secondary sexual characteristics. This gives them time to evaluate and explore a more ambiguous gender identity before shifting to treatments with permanent effects. Alternatively, older adolescents and adults may search for masculinizing or feminizing hormonal therapies to bring their anatomical characteristic more in line with their perceived gender identity. These hormonal treatments may be accompanied or followed by surgical steps to further define the external appearance.

Today, the care provided to transgender and gender non-conforming individuals is no longer a provider but rather a patient-based programme. The dichotomous perspective on gender is no longer considered to be the centre of care. Current treatment regiments aim to provide the patient what they wish for rather than what the provider assumes is the ideal. In this way, transgender care is presented more as a menu from which patients themselves can determine what their goals in the care process should be. Logically then, a large part of the care requests lie in a spectrum between the binary gender idea.

The model by which transgender care should be provided is a topic of discussion. One might argue that, in an effort to further include gender variant individuals in the daily society, general assessments should be attended in the primary care setting without deviating from any care standards for cisgender individuals that seek psychological counseling. [2] In this setting, care providers could assess for hormone and surgery need and/or readiness alongside providing support in social exploration and transition. First-line treatment like mental health support and evidence-based information could already be provided. Given the high need for education and training in such care models, most transgender healthcare centres today are centres of expertise that offer care in different subspecialties such as psychology, endocrinology, voice therapy and otorhinolaryngology, gynecology, urology, and plastic surgery under one roof.

Psychological support

The first pillar of care for transgender and gender non-conforming individuals lies on psychological assessment, guidance and, if needed, therapy. Through this process, gender variant individuals can be given support in accepting and exploring their gender incongruent feelings and take steps in a possible transition process.

The latest version of the standards of care of the World Professional Association on Transgender Health (WPATH) states that for any further treatments (hormonal and surgical), patients must present with persistent and well-documented gender dysphoria, must be of legal age and must be able to provide an informed consent to treatment. Furthermore, if significant mental, medical of social problems co-exist in these individuals, they should be addressed and managed properly before starting any further treatment. These criteria should be documented by a mental health professional experienced in transgender care. Currently, the standards of care state the need for one recommendation letter to apply for hormonal treatments and chest surgery. Two referrals by independent care providers are warranted to qualify for genital surgery. [3] In our centre, we work in a multidisciplinary specialist team setting with shared medical files and discuss cases with all relevant members of the team present. This direct communication abolishes the need for recommendation letters.

Secondary sex characteristics

The second pillar of care consists of providing masculinizing or feminizing treatments to emphasise the secondary sex characteristics towards the preferred gender. This can be done by use of hormonal (suppressing) agents as well as surgical interventions.

A first goal here is to suppress the natal sex differentiating hormones using a variety of hormone blocking agents such as spironolactone, cyproterone acetate or gonadotropin releasing hormone (GnRH) analogues or antagonists and thus suppress the clinical effect of these natal hormones on the bodily development of typical natal gender characteristics. An alternative to providing hormone blocking agents is to remove the ovaries or testicles as they produce the natal sex differentiating hormones.

Ideally, discussions on gamete storage and thus the possibility of having biological offspring are held before starting any hormonal treatments as long-term use of cross-sex hormonal therapy is associated with lower chances fertility recovery. [4]

The second goal is to emphasize the secondary sex characteristics towards the desired gender using feminizing or masculinizing hormones. As for individuals seeking more feminine characteristics, different estrogen formulations are prescribed. These exist under the form of tablets or transdermal patches and creams. Dosing of these agents is based on plasma levels, side effects and wishes of the patient. Usually, physiological levels of natal women are targeted. Feminizing hormone therapy has several effects on the secondary sex characteristics. A list of effects and time of onset after start of hormonal treatment can be found in the WPATH guidelines. [3] Most transgender women will seek permanent hair removal to reduce facial and body hair as this is not appropriately achieved by hormonal therapy alone. Usually, these therapies are more effective after feminizing hormonal treatment has been started.

Individuals seeking more masculine characteristics, a variety of testosterone preparations is on the market. Transdermal gels and a recently FDA-approved tablet formulation are prescribed. Most often however, testosterone is administered as a longer acting intramuscular injection. Again, dosing is done based on plasma levels of natal men and effect on secondary sex characteristics.

Third, surgically feminizing or masculinizing chest, voice and general appearance interventions may be performed. Most individuals who pursue a more feminine appearance will fill the bosom. When breast development through use of feminizing hormonal treatments did not provide the desired volume and shape, this may be further accentuated by breast augmentation. This can be performed using autologous fat transplantation, implant placement, or a combination of both. Those people seeking a more male appearance will usually bind their existing breast development to flatten the chest area. This may be a good temporal solution. However, most female-to-male individuals will seek mastectomy to promote a more masculine image. The techniques used vary widely on the volume of breast development, elasticity of the skin, and the preferences of the patient. [5]

Speech and language therapy has an important role in patients transitioning to another gender identity. [6] The goal is to achieve a more masculine or feminine pitch without straining of the vocal cords. If voice therapy alone cannot result in the desired phonation, surgical measures can be undertaken to physically alter the tension and length of the vocal cords.

Transgender women may want to further accentuate a feminine appearance with surgery. Facial feminization surgery is a group of procedures in which the soft and bony structures of the face are altered to create a more feminine shape. These consist of forehead contouring, reduction of frontal bossing, reduction rhinoplasty, and jaw and chin reduction. Other therapies include brow and lip lift, thyroid shaving, and hairline re-contouring. Specific masculinizing aesthetic surgery is rarely performed but may consist of various implants in the face and rest of the body.

Primary sex characteristics

The third pillar of care is to provide the possibility of altering the primary sex characteristics of individuals. This involves the removal of the natal reproductive organs and in some cases (part of) the natal external genitalia. These can be replaced by surrogate genitalia while maintaining urological and sexual function.

In transgender men, genital surgery can consist of hysterectomy and oophorectomy, which are usually performed before any further steps to diminish risks of complications. In the second stage, phallic and scrotal construction together with masculinizing monsplasty can be performed with or without vaginectomy and urethral lengthening. The neophallus can be created by phalloplasty or metoidioplasty.

In phalloplasty, the aim is to create an anatomically sized penis using skin and subcutaneous tissue transfers from various regions of the body. Many different pedicled and free flap transfers have been described. The most robust and generally used flaps are the radial forearm free flap (RFF) and the anterolateral thigh flap (ALT). Both of these meet many of the ideal requirements of phalloplasty put forward by Gilbert and Hage. [7,8] Nerve anastomoses between the cutaneous flap branches and the dorsal clitoral nerve and/or the ilio-inguinal nerve can be performed to account for penile sensation. If desired, a tube-within-tube design can be performed to allow for urethral lengthening and micturition while standing. Even though donor site morbidity is relatively low in these options, patients are left with a considerable and possibly stigmatizing set of scars.

In metoidioplasty, a micropenis is created by releasing hormonally hypertrophied clitoris form its supporting ligaments and surrounding fatty tissue. [9] Here too, urethral lengthening can be performed by use of various local flaps. However, due to the high variability in clitoral hypertrophy and thus final penile length, not all patients will be able to void while standing. Recovery is faster and scars from this procedure are usually non-visible and confined to the genital area. It is a simpler solution for individuals not seeking penetrative intercourse. The scrotum is constructed through caudal dissection and medial advancement of the labia majora. These are then sutured on themselves, creating an empty scrotum. [10] Further refinements of this technique include a prepubic monsplasty with pedicled fat dissection creating a filled scrotum (M. Özer, personal communication, August 11-13, 2021, Fourth European Professional Association on Transgender Health Congress).

Placement of erectile and testicular prostheses are usually reserved for the third stage to reduce the risk of prosthetic infection. Over the past few years, two types of penile prostheses were designed specifically for phalloplasty patients. [11,12] Although severe complications of phalloplasty and metoidioplasty are rare (<0.5% - bladder/rectal perforation, complete flap necrosis), the overall complication rates of finalised results in phalloplasty and metoidioplasty are high. [13] The biggest culprit of these is urethral lengthening, resulting in urologic complications (strictures and fistulas) in around 40% of cases, followed by prosthesis-related complications in up to 30%.

Transgender women seeking genital surgery can opt for orchidectomy, penectomy, construction of a female urethral meatus, clitoral and labial reconstruction and vaginoplasty. Vaginal depth is initially created by turning the penile skin inside out after penectomy is performed and a neovaginal cavity is created in the plane between the prostate and bladder anteriorly and rectum posteriorly. In most instances however, the penis is sub optimally developed due to early start of hormonal blocking agents. In such cases, further gaining of depth may be needed using scrotal flaps or intestinal interposition for the creation of a cavity of at least 10cm. [14]

To prevent postoperative vaginal stenosis, all cases of vaginoplasty require lifelong self-dilation. Patients preferring only an aesthetically pleasing result without the possibility of penetrative vaginal intercourse can undergo vulvoplasty without vaginoplasty. This makes the procedure less invasive and abolishes the need for lifelong vaginal dilation. The clitoris and labia minora are constructed using the variously reduced penile glans with part of the prepuce pedicled on the dorsal penile neurovascular bundle. [15] Right beneath, a ventrally spatulated bulbar urethra is positioned. The labia majora are constructed using the remainder of the scrotal tissue. Complications after vaginoplasty lay around 10% and consist of rectovaginal fistula (1%) and urethral meatal stenosis (5%). [14] When dilation is performed properly, neovaginal stenosis is rare.

Outcomes

Ever growing bodies of data suggest positive effects on quality of life, satisfaction with general and neo-genital appearance, and sexual function if gender-confirming treatments are provided and administered properly. [16–19]. Although hormonal therapy and gender-confirmation surgery will reduce complaints of gender dysphoria and concurring mental health issues, transgender and gender non-conforming individuals need lifelong follow-up to reduce risks of cardiovascular disease, recurrence of mental health issues, and suicide which are higher than in a cisgender population. [20,21]

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Saturday, 2 July 14:15 - 18:00
Meeting of the EAU Section of Genitourinary Reconstructive Surgeons (ESGURS)
Green Area, Room 4

Penile prosthesis in Peyronie's disease: An update

Techniques for penile straightening and lengthening

Mr. Wai Gin Lee
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Erectile dysfunction (ED) is commonly associated with Peyronie's disease (PD) (in over half of patients). [1] Direct ingrowth of fibrosis and plaque formation is thought to impair adjacent cavernosal arterial inflow. PD is also frequently associated with other risk factors for ED such as diabetes, hypercholesterolaemia, hypertension and hypogonadism. [2] Progressive cavernosal fibrosis also shortens the penis and these factors in combination cause the significant psychological morbidity experienced by men with PD.

The standard of care for men with concomitant PD and ED refractory to medical therapy is a penile prosthesis (inflatable or malleable). In some situations, a penile prosthesis may be the ideal early option and it should no longer be considered as the treatment of last resort only. [3] However, the decision to insert a penile prosthesis is irreversible and men should be fully counselled and understand what is achievable (and what is not).

The aim of a penile prosthesis is to give the man a strong erection and straighten (or improve) the penile curvature to allow sexual intercourse. Historical techniques primarily focused on ameliorating these concerns but more recently, novel approaches for penile lengthening have been developed to better address the loss of penile length associated with PD. Additionally, substitute grafting materials and no-grafting techniques have been proposed. These advances are briefly described in the following article.

Techniques for penile straightening

The process of inserting a penile prosthesis may straighten the penis although the success rate is dependent on the severity of the initial curvature. [4] Modelling the penis is currently the preferred technique to further straighten a residual curvature. [5] Briefly, rubber shods are placed on the tubing to the pump after inflating the prosthesis. Manual pressure is then applied in the opposite direction of the curvature and held for 90 seconds. Traditionally, this is done twice, and no further intervention is necessary if the residual curvature is less than 30˚ because the penis will straighten with continued use and cycling of the device. Durability of the penile prosthesis is maintained but there is a small but significant risk (4%) of urethral injury. [6] The risk may be mitigated by compression of the distal urethra and fossa navicularis during the modelling process. The penis may be safely modelled multiple times provided this "chicken choke" adaptation is used. [7] Another useful adjunct is to weaken the plaque internally (for example, the "scratch" technique [8]) prior to modelling.

A small study showed that components of an inflatable penile prosthesis may be more likely to fail following manual modelling. [9] The same study also found that inserting a penile prosthesis for PD independently predicted device failure. These risks were not identified in the much larger cohort studies of manual modelling but do warrant further investigation in a prospective study.

Some patients (and surgeons) prefer to have a straight penis at the conclusion of the operation. The options are plicate the penis or incise the plaque. Plication sutures are placed before inserting the penile prosthesis and various techniques have been adapted (including the 16-dot technique). Plication does shorten the penis in a significant number of patients (73%) but counter-intuitively, plication may result in fewer palpable nodules following surgery. [10]

Alternatively, the Peyronie's plaque can be incised at the point of maximum curvature. This was the preferred technique for penile straightening before the advent of manual modelling. Since then, plaque incision is usually reserved for a significant residual curvature after modelling. Grafting is recommended if there is a tunical defect greater than 2cm after incising the plaque. Many allografts, xenografts, synthetic grafts and autologous grafts have been reported but no clinical differences in efficacy or outcome were found on systematic review of the literature. [11]

The newest graft that is gaining in popularity is the collagen fleece. The PICS (Penile Implant in Combination with Sealing) technique is quicker because there is no need to suture the collagen fleece in place (and it is cheaper). [12] Early results are encouraging but comparative medium- to long-term follow-up data are currently lacking. [13] Buck's fascia must be closed well to provide support for the collagen fleece and the device should be left semi-inflated for an extended period.

More recent advances

The first description for "maximal" penile lengthening was in 1995 where a circumferential tunical incision was shown to increase the penile length by an average of 1.5cm. [14] Complications were common with 1 out of 5 men (20%) developing penile necrosis and 2 others (40%) required removal of their penile prosthesis due to infection. This highlights the technical difficulties associated with penile lengthening. More recent reports where the circumferential incision was made at the point of maximal curvature showed a length gain of 2.8cm but 20% of men complained that glans sensitivity was reduced after the procedure. [15]

The "sliding" technique gained a lot of interest as an option to lengthen the penis when it was proposed in 2012. [16] The technique improved on the concept of a circumferential incision. Instead, a dorso-ventral incision is made in the tunica albuginea after the penis is disassembled. The penis is then stretched to maximal length (usually limited by the neurovascular bundle) before inserting a penile prosthesis. The tunical defects are closed with grafts resulting in an average increase in length of 3.2cm.

The modified sliding technique (MOST) added complementary relaxing longitudinal incisions (to restore girth) and closed the tunical defects with Buck's fascia only (no graft). [17] Compression dressing is required for a week and the inflatable prosthesis is kept partially inflated for 2 to 3 weeks due to the high haematoma risk.

The MOST technique subsequently evolved into the "multiple-slit" technique (MUST). [18] The technique still requires some penile disassembly, but the urethra is only mobilised over the distal half of the penis. Multiple semi-circular tunical incisions are then made on the concave (shorter) aspect of the penis. Grafting is not required. Multiple small longitudinal slits on the tunica albuginea at areas of narrowing can also be used to restore girth. Mean gain in penile length was 3.1cm.

The most recent evolution of the sliding technique by Prof. Dr. Paulo Egydio is the tunical expansion procedures (TEP). [19] The penis is degloved and disassembled. Multiple transverse tunical incisions of between 5mm-8mm are performed spaced in a predefined mathematical formula. Vertical incisions can be made in areas of narrowing. No glans necrosis was reported in a large sample of 416 patients and a 3.3cm average gain in penile length was found.

Lastly, a novel approach to the sliding technique may reduce the risk of ischaemic complications. [20] The non-degloving approach via a peno-scrotal incision (no sub-coronal incision) may maintain vascularity to the glans by preserving the continuity of skin and dartos (in addition to the neurovascular bundle and urethra). Grafting is not required. Preliminary results in 12 patients show a mean penile length gain of 2.6cm with no vascular complications.

Caution is required

Most implanters will know that men commonly request a longer penis, especially those with PD. Therefore, the temptation to offer these techniques is strong but caution is required. Disassembling the penis is technically challenging and complications occur even in experienced hands. Complications include glans necrosis (or more extensive penile loss), impaired glans sensitivity and difficulty achieving orgasm. Infection and explant of the penile prosthesis is low in published reports (possibly because these procedures are being performed at high volume centres of excellence).

Previous penile surgery with sliding technique was identified in 33% of men who subsequently developed glans necrosis. [21] The risk is highest in men with multiple risk factors for glans necrosis including (in descending order of prevalence) previous subcoronal incision, atherosclerotic cardiovascular disease, diabetes mellitus, smoking, previous penile prosthesis explantation and previous radiotherapy. Men considering penile lengthening surgery should be assessed for these risk factors and strongly discouraged if any are identified.

In general, penile prosthesis insertion for PD has high satisfaction rates. Preliminary results from the Prospective Registry of Outcomes with Penile Prosthesis for Erectile Restoration (PROPPER) database confirm this with satisfaction of >80% with 2-year follow-up. [22] Interestingly, patient-reported depression in 19.3% of men falling to 10.9% of men after 2 years.

Conclusions

Insertion of a penile prosthesis for concomitant ED and PD can be challenging. Men are bothered not only by the penile curvature but also the loss of penile length that is pathognomonic of PD. There is no single technique that would address every individual's concerns and in practice, a breadth of techniques should be offered. It is therefore vital that great care is taken to understand what an individual's concerns are and that they understand the risks and benefits of their preferred option.

Penile lengthening operations are technically challenging and come with a risk for catastrophic complications including glans or penile necrosis and the loss of sensation. These techniques should only be offered to men who are willing to accept the risk (for potentially limited benefit) and even then, by a surgeon who is proficient in the techniques required.

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Saturday, 2 July 14:15 - 18:00
Meeting of the EAU Section of Genitourinary Reconstructive Surgeons (ESGURS)
Green Area, Room 4

Management of recto-urinary fistulas

Surgical approaches and multidisciplinary teamwork

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Recto-urinary fistulas are a rare complication that occur after radical prostatectomy, colorectal surgery, and cryosurgery. Recto-urinary fistulas are also observed in patients with Crohn's disease or diverticular disease.

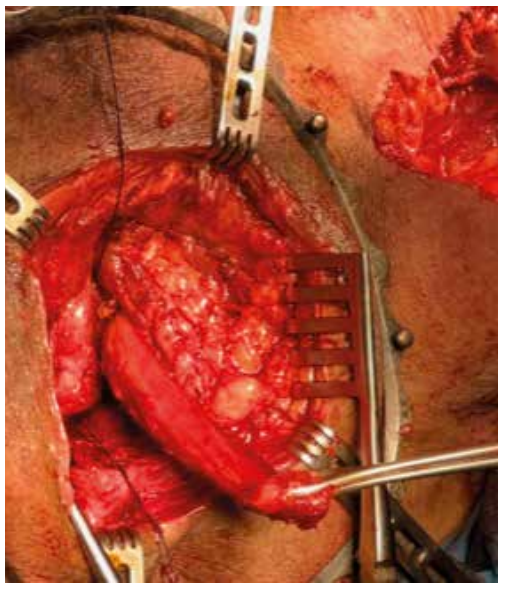
After radical prostatectomy, the estimated incidence is lower than 2%, and rectourethral fistula is the most common type with the highest percentage in case of combined treatment for prostate cancer with surgery and pelvic irradiation. Radiotherapy or lesion of the rectal wall during radical prostatectomy are the leading causes. If a fistula occurs during the surgery, primary closure is needed. However, in some cases, the urinary-rectal fistula is diagnosed in the postoperative period.

The management acquired recto-urinary fistulas represent a challenging task. A surgical repair is required in most of the cases. Several surgical procedures were described, including resection of the fistula tract and direct closure of the fistula with a perineal approach, mucosal flaps, instillation of fibrin glue, endorectal advancement flap, a York-Mason operation, and fistula closure with an abdominal approach. The less aggressive procedures report good outcomes but not in complex fistulas. However, complex fistulas with previous surgeries or in patients with prior radiotherapy may require the interposition of tissues in the management of fistula to achieve fistula closure and reduce the incidence of recurrence.

Among the tissues used for transposition in the recto-urethral fistula are gracilis muscle, rectus abdominis, omentum, dartos, gluteus maximus, and latissimus dorsi. The abdominal approach has the advantages of placing healthy well-vascularized tissue in the affected area. On the other hand, the abdominal approach has potentially significant perioperative adverse sequelae. Gracilis interposition allows a well-vascularized tissue via a perineal approach. Repair of perineal fistulas with gracilis muscle interposition was first described by Garlock et al. in 1928. In 1952, Igelman-Sundberg described the technique in patients with vesicovaginal fistulas. The interposition of gracilis muscle is one of the procedures that provide satisfactory outcomes with limited functional limitation in the donor area as gracilis muscle has an only vestigial function. Transposition of a gracilis muscle flap may be used for the surgical management of rectovaginal, rectourethral, pouch-vaginal and pouch-urethral fistula.

"The management acquired recto-urinary fistulas represent a challenging task. A surgical repair is required in most of the cases... The less aggressive procedures report good outcomes but not in complex fistulas."

The gracilis muscle is situated at the thigh's medial part from the ischiopubic branch to its tibial insertion forming the goosefoot. It is the most medial and superficial muscle of the inner thigh, fulfilling adduction functions, internal rotation, and flexion of the hip. The gracilis muscle has a very proximal pedicle consisting of the circumflex medial femoral artery, which allows adequate transposition to the perineal area. There is also a distal vascular pedicle from the deep femoral artery, which can be



Gracilis muscle used to repair a complex fistula

divided and ligated to achieve the flap's correct rotation. Other minor pedicles can be dissected. The main advantages of a flap with the gracilis muscle include there is enough tissue provided from the donor site to correct interposition, limited functional loss, and low morbidity in the donor site. Moreover, when the procedure is carried out by an experienced surgeon, the dissection of the gracilis muscle is a simple technique.

When a complex urinary-rectal fistula is diagnosed, a faecal and urinary diversion is recommended. At the beginning of the procedure, ureteral catheterization may be performed as the fistula's orifice may be close to the ureteral meatus. The surgical procedure with transposition of gracilis muscle consists of a perineal approach with dissection above the transversus perineum muscle and below the bulbocavernosus muscle. The dissection is carried out until the identification of the fistula. The edges of the fistula are resected to leave soft, viable tissue for the closure of the fistula. The rectal wall and the urethra is closed with absorbable stitches closed. The suture must be done using healthy tissues.

The gracilis muscle is dissected from the non-dominant leg and transposed to the perineum to preserve the proximal pedicle through a subcutaneous tunnel. For the gracilis muscle, harvesting an incision at the medial thigh is made immediately from the posterior to the saphenous vein from 4 to 8 fingerbreadths distal to the anterior superior iliac spine. The gracilis muscle is then interposed between the rectal and urethral closure of the fistula and fixed with absorbable suture. The surgery is associated with a complication rate of 0% to 49%. The most common complication is perineal wound infection or delayed healing.

Although the donor site morbidity of the gracilis muscle harvesting site is low, adequate control of the donor site in the thigh is essential during the postoperative procedure. This is to minimise the incidence of wound infection or delayed healing. It is necessary to inform the patients beforehand that urinary incontinence and faecal incontinence during the postoperative period are reported in 14% and 4.2% of patients, respectively.

The surgery must be carried out by a multidisciplinary team which includes a urologist, colorectal surgeons, and urological reconstructive surgeons with specific surgical skills in the perineal surgery. Repair of the urinary-rectal fistula with transposition of the gracilis muscle is challenging as many patients have received prior radiotherapy and have had previous failed attempt to repair the fistula.

Monday, 4 July 10:30 - 12:00
Thematic Session 13
Purple Area, Room Elicium 2

Circumcision practices in monotheistic religions

History, cultural beliefs and practices

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Male circumcision is one of the most common surgeries performed worldwide. According to the World Health Organization (WHO), approximately one third of the male population (1.2 billion) is reported to be circumcised [1]. Today, in the United States, around 1.2 million newborns are circumcised in community hospitals annually [2]. However, the true number is expected to be higher due to unreported circumcisions in private clinics. The Muslims are the most commonly circumcised community wherein 70% are circumcised.

In many regions of the world, circumcision is performed based on religious or cultural purposes. In some others, it is performed for medical purposes for better hygiene or protection against AIDS and other sexually transmitted diseases (STDs). Whatever the reason is, circumcision is still one of the most debated topics in medical conferences and political platforms such as the European Council.

In this article, we aimed to review the literature regarding male circumcision history in monotheistic religions, including Islam, Judaism and Christianity. Historical perspective is the main target of this review and the medical or political perspectives are beyond our objectives.

Methodology
A non-systematic review was performed for the existing literature for male circumcision history in monotheistic religions. A comprehensive search was performed through PubMed and Google databases; and the results were analysed and synthesized.

Circumcision history
Beyond the contemporary discussions, male circumcision is one of the oldest surgeries in history. It is forgotten or underreported in the literature why or how this operation began. Anthropologists and historians do not agree on the origin of male circumcision. There are several theories about its initiation period.

The English Egyptologist Sir Grafton Elliot Smith proposed that circumcision originated from the heliolithic culture about 15,000 years ago and spread worldwide afterwards [3]. Some believed it has originated independently in different cultures. When Christopher Columbus found the "New World", he observed that many of the male natives were circumcised. In the meantime, circumcision was also being performed in other continents including Africa, Australia, Middle East and Asia.

The wall paintings of the Egyptian history (5000 BC) clearly demonstrate and even describe how the circumcision was performed. Circumcision is performed at birth in some of the African tribes. In monotheistic religions including Judaism, Christianity and Islam, circumcision is attributed to Prophet Abraham's tradition. In Judaism, it is performed on the 8th day after birth. In Muslim, the timing varies from one culture to the another but usually before puberty and as a rite of passage from childhood to young adulthood. In ancient Egypt, circumcision is believed to be a mark of slavery. This procedure is then evolved and performed as a ritual in many other cultures.

In summary, the real origin of circumcision will probably never be known exactly. However, the truth can only be elucidated when all the theories are gathered together.

Circumcision in Judaism
Prophet Abraham himself was circumcised at the age of 99 while his son Ismael was circumcised at 13 years old. It is also believed that Prophet Abraham circumcised his son Isaac when he was only eight days old. The Jews continued this tradition by circumcising their sons on the 8th day after birth.

The same tradition has been transmitted from one generation to the next and now, it has become contemporary practice. Jewish circumcision is being performed by a non-medical practitioner such as the father or more frequently, by a Mohel. Unlike in Islam, it is not an option to refuse circumcision but it is a commandment from God called "Brit Milah". Therefore, there is no debate within Judaism.

Even when death penalty was imposed on the Jews for performing circumcision in ancient Greece and Rome, and also during the Soviet Union period when circumcision was supressed, the Jews continued to practice it. This clearly shows that circumcision is a vital component of Judaism.

Circumcision in Christianity
Jesus Christ himself was circumcised on the 8th day after his birth. However, it is not a common procedure in Christianity since it is believed that physical circumcision is not mandatory. This anti-circumcision position was confirmed at the first Council of Jerusalem in 48 AD and a new rite or sacrament was created to take its place: Baptism. In Christian philosophy, the spiritual circumcision of the heart triumphed over the physical circumcision of the foreskin. This was also the standpoint later adopted by Martin Luther and John Calvin.

In Victorian times, due to increasing numbers of STDs, an awareness about circumcision arose in the Anglo-Saxon populations. It was performed to improve hygiene and to protect individuals from STDs.

Today in the United States, male circumcision is a common practice especially in newborns for medical purposes. The American Academy of Pediatrics states that "the benefits of male circumcision outweigh the risks" in its latest published policy statement in 2012. In the United Kingdom, however, circumcision is more common among the well-educated upper-class.

After the rising prevalence of AIDS in 1980s, male circumcision became popular again and it was widely performed in Sub-Saharan Africa to prevent AIDS [4]. There have been also other calls from the United Kingdom and Australia about initiating infant circumcision for long-term benefits [5, 6, 7].

On the contrary, nowadays there are anti-circumcision policies being set by some European countries. In Cologne, Germany, circumcision is banned if performed on a young male under 14 years of age. This is to give a young male the chance to make his own decision with regard to his penis. It is also considered as his right of physical integrity.

The activists supporting this idea suggest that circumcision adversely affects the sensation of the penis and also diminishes sexual activity. There is no clear data supporting these; however, there is also no clear data supporting routine circumcision in existing literature backed by by evidence-based medicine.

Figure 1: A painting depicts the circumcision of Jesus Christ

Circumcision in Islam
Circumcision was a common practice in pre-Islamic period in the Arabic world. The Arabic word used for circumcision for males is "khitan". It is now certain that circumcision did not start with Islam but was performed previously. When looking into the chapters of Holy Quran, circumcision is not mentioned in any of the pages. However, there is strong evidence that Prophet Mohammed recognised and advocated this procedure in his sayings which is called "hadith". For that reason, although circumcision is not obligatory to become a Muslim, it is considered as "Sunnah" which means "Prophet's tradition".

Prophet Mohammed circumcised his grandsons Hasan and Huseyin on the 7th day after birth. Although the Holy Quran is the main reference for Muslims, the "hadith" is also considered as another main reference especially for the practical way of living Islam. Therefore, circumcision is considered as a condition of becoming Muslim by Islamic communities. Again, if a non-circumcised non-Muslim man converts to Islam, and if he does not get circumcised, that does not exclude him out of Islam.

The age at circumcision in Islamic world significantly varies between different regions. There is no standard period of circumcision, however the vast majority of males are circumcised before puberty. In general, circumcision is performed by non-medical professionals but there is an increasing trend and awareness of medical doctors performing circumcisions to decrease complications.

In 2015, the Turkish Ministry of Health banned circumcision by non-medical professionals and is now only performed by medical doctors However, unlawful circumcision is still performed occasionally in some rural areas.

Conclusions
Circumcision is one of the most common surgical procedures performed all over the world. In Islam and Judaism circumcision is widely performed for religious and cultural reasons. Although it is not mandatory in Islam to get circumcised, it is widely being performed at different ages before puberty. In Judaism, it is mandatory to get circumcised and it is believed that it is a commandment from God. In Christianity, although Jesus Christ himself was circumcised, circumcision is not a rule for the believers and only performed for medical purposes if necessitated.

Figure 2: Historical circumcision knife from Jewish Museum, London

References

1. World Health Organization/UNAIDS. Male circumcision: Global trends and determinants of prevalence, safety and acceptability. http://whqlibdoc.who.int/publications/2007/9789241596169_eng.pdf. World Health Organization, Geneva, 2007.
2. Merrill CT, Nagamine M, Steiner C: Circumcisions Performed in U.S. Community Hospitals, 2005: Statistical Brief #45. Healthcare Cost and Utilization Project; http://www.ncbi.nlm.nih.gov/books/NBK56311/ 2008:1–9.
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6. Cooper DA, Wodak AD, Morris BJ: The case for boosting infant male circumcision in the face of rising heterosexual transmission of HIV. Med J Aust 2010, 193:318–319.
7. Weiss HA, Dickson KE, Agot K, Hankins CA: Male circumcision for HIV prevention: current research and programmatic issues. AIDS 2010, 24(Suppl 4):S61–S69.

Sunday, 3 July 14:00 - 15:30
Thematic Session 08
Green Area, Room 1

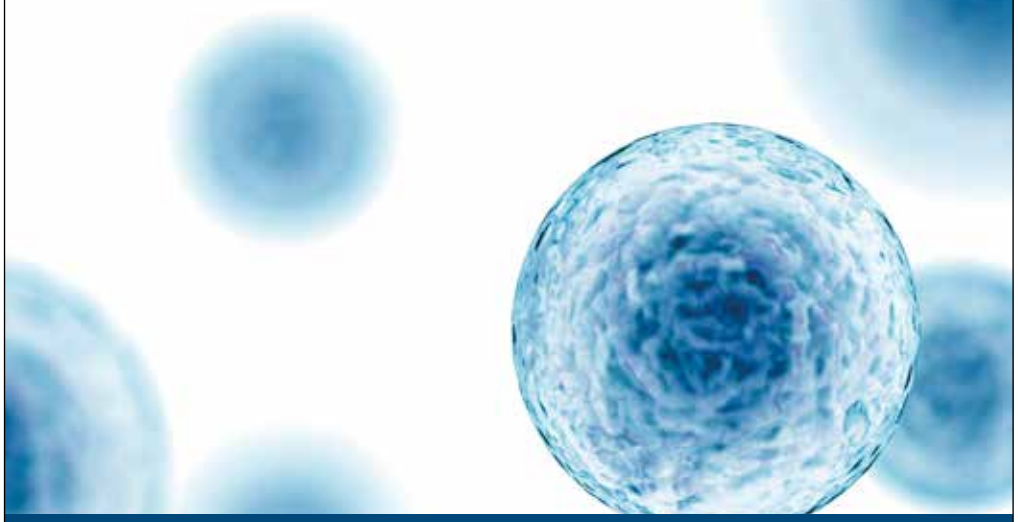
ESUR22

28th Meeting of the EAU Section of Urological Research

13-15 October 2022, Innsbruck, Austria

In collaboration with the EAU Section of Uropathology (ESUP)

www.esur22.org



Abstract submission deadline: 11 July 2022

An application has been made to the EACCME® for CME accreditation of this event

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ESGURS22

12th Meeting of the EAU Section of Genito-Urinary Reconstructive Surgeons

20-21 October 2022, Madrid, Spain

www.esgurs22.org

Abstract deadline: 21 July 2022

An application has been made to the EACCME® for CME accreditation of this event

esgurs eau European Association of Urology

ERUS22

19th Meeting of the EAU Robotic Urology Section

26-28 October 2022, Barcelona, Spain

www.erus22.org

An application has been made to the EACCME® for CME accreditation of this event

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ESUI22

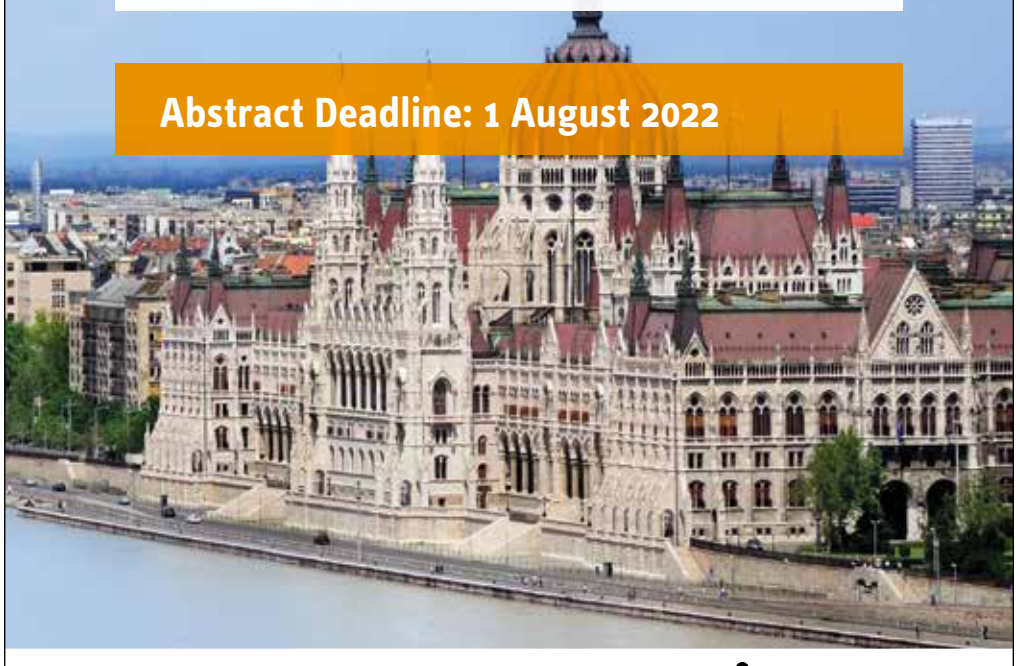
10th Meeting of the EAU Section of Urological Imaging

10 November 2022, Budapest, Hungary

www.esui22.org

In conjunction with the 14th European Multidisciplinary Congress on Urological Cancers ⚙ EMUC22

Abstract Deadline: 1 August 2022



An application has been made to the EACCME® for CME accreditation of this event

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Today's European Urology Events

Best Paper Awards 2022

Friday July 1st
11.30 - 12.00, Green Area side wall
Green Room 5 / Ground Floor

BEST SCIENTIFIC PAPER AWARD

The Additive Diagnostic Value of Prostate-specific Membrane Antigen Positron Emission Tomography Computed Tomography to Multiparametric Magnetic Resonance Imaging Triage in the Diagnosis of Prostate Cancer (PRIMARY): A Prospective Multicentre Study

Louise Emmett, Buteau J., Papa N., Moon D., Thompson J., Roberts M.J., Rasiah K., Pattison D.A., Yaxley J., Thomas P., Hutton A.C., Agrawal S., Amin A., Blazevski A., Chalasani V., Ho B., Nguyen A., Liu V., Lee J., Sheehan-Dare G., Kooner R., Coughlin G., Chan L., Cusick T., Namdarian B., Kapoor J., Alghazo O., Woo H.H., Lawrentschuk N., Murphy D., Hofman M.S., Stricker P.

Volume 80, Issue 6 - Pages 682-689

BEST PAPER AWARD - CLINICAL RESEARCH

Shockwave Lithotripsy Versus Ureteroscopic Treatment as Therapeutic Interventions for Stones of the Ureter (TISU): A Multicentre Randomised Controlled Non-Inferiority Trial

Ranan Dasgupta, Cameron S., Aucott L., MacLennan G., Thomas R.E., Kilonzo M.M., Lam T.B.L., N'Dow J., Norrie J., Anson K., Burgess N., Clark C.T., Keeley F.X., MacLennan S.J., Starr K., McClinton S.

Volume 80, Issue 1 - Pages 46-54

BEST PAPER AWARD - FUNDAMENTAL RESEARCH

Integrated Expression of Circulating miR375 and miR371 to Identify Teratoma and Active Germ Cell Malignancy Components in Malignant Germ Cell Tumors

Lucia Nappi, Thi M., Adra N., Hamilton R.J., Leao R., Lavoie J.-M., Soleimani M., Eigl B.J., Chi K., Gleave M., So A., Black P.C., Bell R., Daneshmand S., Cary C., Masterson T., Einhorn L., Nichols C., Kollmannsberger C.

Volume 79, Issue 1 - Pages 16-19

BEST PAPER AWARD - ROBOTIC SURGERY

A DROP-IN Gamma Probe for Robot-assisted Radioguided Surgery of Lymph Nodes During Radical Prostatectomy

Paolo Dell'Oglio, Meershoek P., Maurer T., Wit E.M.K., van Leeuwen P.J., van der Poel H.G., van Leeuwen F.W.B., van Oosterom M.N.

Volume 79, Issue 1 - Pages 124-132

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Today's European Urology Events

ESU Course 07

Saturday July 2nd, 8.30 – 10.30, Grey Area, Room G104

How to write the introduction and methods

Learning Objectives:
Understand how to construct a well written introduction and methods section for your manuscript. Learn how to work through examples of good and bad practices, and understand key points when writing. Obtain insight from editors on what they expect to see.

- To understand what makes a good introduction.
- To understand what makes a good methods section.
- To understand about systematic reviews and meta-analysis.
- To learn from experienced editors.

1 Welcome
2 Writing the introduction
Sarah Psutka, Seattle (US)
3 How to write the methods section
Giacomo Novara, Padova (IT)
4 Key features for a systematic review
Gianluca Giannarini, Udine (IT)
5 What to look for in the statistics section
Rodney Dunn, Ann Arbor (US)

ESU Course 13

Saturday July 2nd, 12:00 – 14:00, Grey Area, Room G104

How to write results and discussion

Learning objectives:
Learn the best way to draft the results and discussion section of a scientific paper. Understand how to work through examples of good and bad practices, to find the key points of the manuscript. Obtain insight from editors on what they expect to see.

- To understand what makes good results section and how best to present your data.
- To understand what makes a good discussion.
- To learn from experienced editors.

1 Welcome
2 Choosing and presenting your statistical analysis
Rodney Dunn, Ann Arbor (US)
3 How to write the results section
Jean-Nicolas Cornu, Rouen (FR)
4 Writing the discussion section
Malte Rieken, Zürich (CH)
5 What the editor looks for when reviewing the results and discussion
Giacomo Novara, Padova (IT)

Residents' Corner Awards

Saturday July 2nd, 16:45 - 17:00
Room 1, Green Area

Is There a Detrimental Effect of Antibiotic Therapy in Patients with Muscle-invasive Bladder Cancer Treated with Neoadjuvant Pembrolizumab?

Filippo Pederzoli, Bandini M., Raggi D., Marandino L., Basile G., Alfano M., Colombo R., Salonia A., Briganti A., Gallina A., Montorsi F., Necchi A.
Volume 80, Issue - Pages 319-322

Effect of Simulation-based Training on Surgical Proficiency and Patient Outcomes: A Randomised Controlled Clinical and Educational Trial

Abdullatif Aydin, Ahmed K., Abe T., Raison N., Van Hemelrijck M., Garmo H., Ahmed H.U., Mukhtar F., Al-Jabir A., Brunckhorst O., Shinohara N., Zhu W., Zeng G., Sfakianos J.P., Gupta M., Tewari A., Gozen A.S., Rassweiler J., Skolarikos A., Kunit T., Knoll T., Moltzahn F., Thalmann G.N., Lantz Powers A.G., Chew B.H., Sarica K., Shamim Khan M., Dasgupta P.

Volume 81, Issue 4 - Pages 385-393

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SATURN Registry reaches target of 1000 recruited patients

European Registry evaluates the cure rate of surgical procedures for Male SUI

Introduction
Stress Urinary Incontinence (SUI) after surgical prostate treatment is an important and common problem in men with a potential detrimental impact on quality of life. If conservative therapy fails, implantation of the artificial urinary sphincter (AUS) is the recommended surgical procedure for men who have troublesome SUI. Nowadays, the AMS 800 device (Boston Scientific, Minnetonka, MN, USA) is most commonly used, even though there are alternative devices available. In recent years male slings have become a popular alternative surgery for male SUI. Male slings (fixed and adjustable) offer a minimally invasive treatment option and do not require the manual dexterity and sufficient mental function necessary to operate an AUS properly. With the advent of rapidly introduced new surgical options, the current management of male SUI often lacks science-based evidence since it is not clear which patient should get which procedure.

SATURN registry
The objectives of the SATURN registry are to evaluate the effects of surgical treatment of SUI with current available devices in common urological practice and to determine prognostic factors which may help to identify clinical and surgical variables that correlate with (un)favourable outcomes. Patient Reported Outcome Measures (PROMS), quality of life (QoL); incontinence, and clinical data are collected from study visits at baseline, before surgery; at the time of surgery; 6 weeks (activation of AUS); 12 weeks and 1 year post-surgery. Mid- and long-term follow-up consists of annual patient contacts after one year post-surgery up to year 10.

Study update
Nine countries (The Netherlands, Belgium, Czech Republic, Germany, The United Kingdom, Norway, Spain, Italy, Finland) are participating with a total of 28 centres.

Despite potential setbacks due to COVID-19 restrictions, patient recruitment was completed ahead of time on the 30th November 2021 after the surgery of the 1000th eligible patient was recorded in the eCRF. Patients (54) that signed the Informed Consent (IC) before the 30th November 2021 but did not have their surgery yet, were still allowed to be included in the registry.

An interim analysis of baseline data was performed based on a data export of October 5th 2021. At that date 980 patients gave IC of which 915 underwent surgery. On average, 11% of centers recruited > 25 cases/year, whilst 46% of recruiting centers included <10 cases/ year. Average inclusion was 18 patients/ month. Implanted devices included 2 types of AUS (AMS800 (66%), VICTO(+) (3%)), non-adjustable Advance XP (20%), 3 adjustable implants (ProAct (3%), Argus (1%), ATOMS (6%)) and miscellaneous (1%). The primary cause of SUI was radical prostatectomy (81%), of which 56% robot-assisted and 32% adjuvant radiotherapy (RT). Further, primary RT (5%), endoscopic LUTS treatments (10%), and others (e.g. neurological) (4%) were documented. Prior to study inclusion, 15% received one and 6% two or more previous SUI surgeries. In total, 90 patients had urethral stricture and 87% of these received an AUS. Previous RT was noted in 39% of AUS patients, while this was 7% for advanced XP and 22% for adjustable devices.

We want to congratulate all participating investigators and their staf members for reaching (despite the COVID-19 crisis) the target of 1000 inclusions. Thank you for all your efforts and dedications that will make the SATURN Registry a great success!

For more information, please visit the EAU RF website http://uroweb.org/research/projects/.

Country	Investigator	City	Hospital	# Eligible Patients with surgery performed	# Eligible Patients with pending surgery
BE	Frank Van der Aa	Leuven	UHs Leuven	200	
BE	Karel Everaert	Ghent	UH Ghent	14	
BE	Koen Van Renterghem	Hasselt	Jessa Hospital	66	
BE	Siska Van Bruwaene	Kortrijk	UH Groeninge	16	
BE	Stefan de Wachter	Antwerpen	UH Antwerpen	5	1
CZ	Roman Zachoval	Prague	Thomayer Hospital	57	
DE	Tanja Hüsch	Mainz	UH Mainz	2	
DE	Fabian Queißert	Münster	UH Münster	4	
DE	Margit Fisch	Hamburg	Asklepios Klinik Harburg	3	
ES	Juan Martinez-Salamanca	Madrid	UH P.De Hierro-Majadahonda	31	
ES	Javier Romero-Otero	Madrid	UH 12 Octubre	57	
ES	David Castro Diaz	Tenerife	UH de Canarias	16	7
ES	Ignacio Puche-Saz	Granada	UH Virgen de las Nieves	10	2
ES	José Gago	Barcelona	UH Germans Trias i Pujol	18	4
ES	Enrique Lledó	Madrid	UGH Gregorio Marañón	2	
ES	Salvador Landis	Valencia	UHI La Fe	11	
ES	Agustín Fraile Poblador	Madrid	UH Ramón y Cajal	19	
ES	Antoni Romero Hoyuela	Murcia	GH Morales Meseguer	32	
ES	José Miguel Gómez de Vicente	Madrid	Hospital La Paz	12	1
FI	Mika Matikainen	Helsinki	UCH Helsinki	6	1
GB	Rizwan Hamid	London	RNI Orthopaedic Hospital	9	
GB	Nikesh Thiruchelvam	Cambridge	CUH-Addenbrooke's Hospital	20	
GB	Arun Sahai	London	Guy's & Thomas's Hospital	19	
IT	Emilio Sacco	Rome	FPU Agostino Gemelli IRCCS	49	5
NL	John Heesakker/Frank Martens	Nijmegen	Radboudumc	133	2
NL	Laetitia de Korte	Utrecht	UMC Utrecht	47	2
NO	Ole Jacob Nilsen	Oslo	Rikshospitalet	147	3
NO	John Martin Pedersen	Narvik	UNN Narvik	14	7
			Total	**1019**	**35**

Collaborator
Boston Scientific Corporation

Steering Committee:
- Rizwan Hamid, United Kingdom, Principal Investigator
- Nikesh Thiruchelvam, United Kingdom
- Frank Van Der Aa, Belgium
- John Heesakkers, The Netherlands
- Frank Martens, The Netherlands
- Wim Witjes, EAU Research Foundation, The Netherlands

EAU Research Foundation
- Wim Witjes, Scientific and Clinical Research Director
- Raymond Schipper, Clinical Project Manager
- Joni Kats, Clinical Project and Data Manager
- Christien Caris, Clinical Project Manager
- Joke Van Egmond, Clinical Data Manager
- Hans Noordzij, Marvin system assistant

Recruitment rate for VENUS registry is accelerating

Prospective registry evaluates the cure rate of AUS implantation surgery for female SUI due to ISD

Introduction:
The VENUS registry is a prospective non-controlled cohort study evaluating the outcomes of artificial urinary sphincter (AUS) implantation surgery (Robot-assisted, Laparoscopic, Open or other) in female patients for the treatment of stress urinary incontinence (SUI) due to intrinsic sphincter deficiency (ISD).

The goal of this registry is to get insight into the clinical daily practice of AUS implantation surgeries and the short and long term follow-up outcomes e.g. efficacy, complications, quality of live, urodynamic parameters and sexual functioning within female patients with SUI due to ISD.

The main outcome will be the cure rate of AUS implantation surgeries, with cure rate defined as urinary continence with no pads used or use of 1 light security pad.

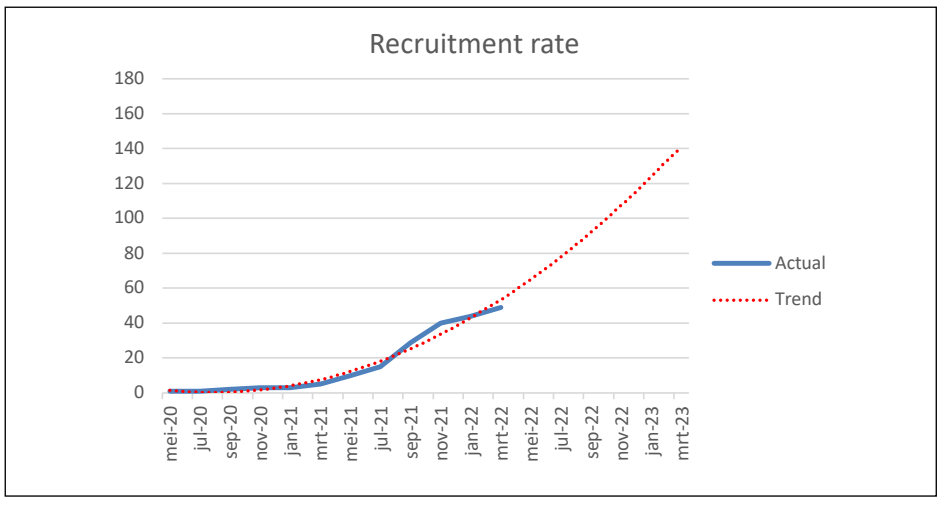
A total of 150 patients will be recruited within 3 years whereafter patients will be followed until the end of the registry.

Study update:
Due to the COVID-19 pandemic it is challenging to recruit patients for the VENUS registry as for most centres AUS implantation is considered non urgent and surgeries are postponed or halted.

Nevertheless the previous months the inclusion of patients accelerated. On the day of writing (cut-off date 31 March 2022), 13 centres started recruitment and included 49 patients in the eCRF (recruited patients who are not yet entered in the eCRF are not taken into account). It is expected that this inclusion rate will be maintained as an additional 9 centres are initiated and ready to start including patients, further 5 other centres are in the initiation process or filing for ethical committee approval.

Interested to join the VENUS Registry? Please fill in the Feasibility Questionnaire at https://www.surveymonkey.com/r/5YZPG8W or send an email to researchfoundation@uroweb.org.

Country	Investigator	City	Hospital	Status	# Patients included
BE	Frank van der Aa	Leuven	University Hospitals Leuven	Recruiting	**6**
BE	Karel Everaert	Gent	Universitair Ziekenhuis Gent	Initiated	**0**
BE	Stephan de Wachter	Antwerpen	Universitair Ziekenhuis Antwerpen	Initiated	**0**
CZ	Roman Zachoval	Prague	Thomayer Hospital	Initiated	**0**
DE	Karl-Dietrich Sievert	Detmold	Klinikum Lippe	Recruiting	**1**
DE	Justine Hein	Magdeburg	Klinikum Magdeburg	In Submission	
ES	Mercedes Ruiz Hernández	Madrid	Hospital Ramón y Cajal. Madrid	Recruiting	**4**
ES	Luis López-Fando Lavalle	Madrid	Hospital de La Princesa	Initiated	**0**
FR	Benoit Peyronnet	Rennes	University of Rennes	Recruiting	**9**
FR	Aurelien Descazeaud	Limoges	CHU de Limoges	Recruiting	**1**
FR	Georges Fournier	Brest	Hopital de la Cavale Blanche	To be initiated	
FR	Xavier Biardeau	Lille	CHU de Lille	Recruiting	**3**
FR	Adrien Vidart	Suresnes	Hopital Foch	Initiated	**0**
FR	Xavier Game	Toulouse	CHU Rangueil	Initiated	**0**
FR	Vincent Cardot	Meudon	Pole de Sante du Plateau	Initiated	**0**
FR	Pierre Lecoanet	Vandoeuvre Les	CHU Nancy	Recruiting	**1**
FR	Olivier Belas	Le Mans	Pole sante sud	Initiated	**0**
FR	Grégoire Capon	Bordeaux	University Hospital Bordeaux	Recruiting	**1**
FR	Laurent Wagner	Nimes	University Hospital of Nimes	Recruiting	**7**
FR	Emmanuel Chartier-Kastler	Paris	Hôpital de la Pitié-Salpêtrière	Recruiting	**10**
FR	Alain Ruffion	Lyon	Hôpital Lyon Sud	Initiated	**0**
FR	Gilles Karsenty	Marseille	Hôpital la Conception	Recruiting	**1**
FR	Jean-Nicolas Cornu	Rouen	Hôpital Charles Nicolle	To be initiated	
FR	Marie Aimee Perrouin Verbe	Nantes	Nantes University	Recruiting	**3**
GB	Nikesh Thiruchelvam	Cambridge	Addenbrooks Hospital, Cambridge	Recruiting	**2**
GB	Tamsin Greenwell	London	University College London Hospital	In Submission	
NL	Gommert van Koeveringe	Maastricht	Maastricht UMC+	In Submission	
				Total	**49**



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- Benoit Peyronnet, France
- Frank Van der Aa, Belgium
- Wim Witjes, The Netherlands

EAU Research Foundation:
Wim Witjes, Scientific and Clinical Research Director
Christien Caris, Clinical Project Manager
Joni Kats, Clinical Project and Data Manager
Joke van Egmond, Clinical Data Manager
Hans Noordzij, Marvin system assistant

ERN eUROGEN Special Session at EAU22

Update on Rare and Complex Urology

Jen Tidman
ERN eUROGEN Business Support Manager
Nijmegen (NL)

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ERN eUROGEN, the European Reference Network (ERN) for rare urogenital diseases and complex conditions requiring highly specialised surgery, will once again coordinate a *Special Session* on rare and complex urology at the 2022 Annual European Association of Urology Congress.

Network update

Programme Manager Michelle Battye (NL), will present an **"Update on ERN eUROGEN Developments"** as well as co-chairing the session with Network Coordinator Prof. Wout Feitz (NL).

As part of her update, she will note that on 1 January 2022, ERN eUROGEN has nearly doubled in size, with 29 full healthcare provider members joining following the 2019 call for applications to join existing ERNs. On 14 January 2022, the European Commission adopted the second 2022 EU4Health work programme, giving a budget of €26 million to the 24 ERNs (€1,083,333 each). This will support specialised healthcare for rare diseases, clinical practice guidelines and clinical decision support tools, education and training (including our webinar and exchange visit programmes), research, our patient registry, and virtual multi-disciplinary consultations using the Clinical Patient Management System.

Lecture by Patient Advocacy Group

Patients are at the heart of everything the ERNs do, with a mission to "Share. Care. Cure." In a lecture on **"Penile cancer – the way forward?"** our European Patient Advocacy Group (ePAG) will give an overview on their new initiatives. The speakers are advocates John Osborne (GB) and Kenneth Manzie (GB), and male cancer information nurse specialist Rob Cornes (GB).

Penile cancer affects around 36,000 men globally each year. Due to its rarity, it is often difficult to provide a level of peer and psychosocial support following treatment, comparable with more common cancers. Working in conjunction with ERN eUROGEN the above ePAG advocates have provided a perspective of the patient journey and highlighted key areas of improvement.

In addition, a new global penile cancer steering group is being developed, made up of allied health care professionals and survivors from around the world. The aim of this group is to create a global network and resource for information and virtual support, for anyone who has been affected by the disease or who is working within the field of penile cancer.

ERN eUROGEN has also organised lectures for their three workstreams, each encompassing several expertise areas:

***Workstream 1* – Paediatric: Rare congenital urorectogenital anomalies and their transition to adult follow-up**

Dr. Giovanni Mosiello (IT) will present a lecture on **"Congenital neurogenic bladder dysfunction – What the adult urologist needs to know."** He will look at the causes of neurogenic bladder dysfunction (NBD) in children and adolescents, which are different to causes in adults.

Spinal dysraphism (SD) is the most common cause, with defects such as occult SD and myelomeningocele. NBD in SD is variable and may occur at any time; in occult SD, most cases present later, in adolescence, with back pain, absence of perineal sensation, and lower urinary tract dysfunction. Other causes of NBD include sacral agenesis or caudal regression syndrome, often associated with anorectal malformation (ARM). ARM may occur as an isolated malformation or with other malformations (e.g., VATER/VACTERL association) and both bowel and bladder dysfunctions may be present. NBD is observed in cerebral palsy or Down syndrome but is often misdiagnosed or dismissed because of coexisting disabilities. NBD is reported in other genetical syndromes as Williams-Beuren and in congenital muscular dystrophies.

Due to the increased life expectancy of all these children, and considering acquired forms of paediatric onset (trauma, infection, iatrogenic), adult urologists must be aware that patients with paediatric NBD, who require lifelong supervision, will increase in the future.

The EAU and ESPU guidelines are helpful, but tailored guidelines for each pathology would be useful in these rare and complex diseases, particularly for surgery and defining specific transitional care programmes with a multidisciplinary approach, using cross-ERN activities.

***Workstream 2* – functional urogenital conditions requiring highly specialised surgery**

In this presentation, Dr. Mariangela Mancini (IT), will consider **"Vesicovaginal fistula: Management strategies and keys to successful treatment."** As a large, pan-European network, ERN eUROGEN represents a new opportunity for centres of expertise to provide and share advice for the management of vesicovaginal fistulas (VVF).

Aetiology, incontinence score, fistula size, and timing of surgery are not correlated with successful VVF repair, although size is strictly associated with the length of the fistulous tract. When bladder reconstruction is necessary, the abdominal approach allows a definitive cure even in the most challenging cases and an extraperitoneal trans-vesical approach is safe and successful in most cases. Maximal results can be expected in centres of experience on the first attempt in a previously non-treated patient. When properly performed, minimally invasive techniques such as laparoscopy or robotic surgery can reduce the invasiveness of the traditional approach. The key to success is the standardisation of surgical key points based on experience and the centralisation of care in referral centres, connected in international networks of expertise such as ERN eUROGEN.

***Workstream 3* – Rare urogenital tumours**

Assoc. Prof. Hans Langenhuijsen (NL) will present a lecture on **"Expansion of the network with tremendous opportunities for rare urogenital tumours."** He will show that oncological treatment is optimised by the cross-border sharing of clinical knowledge, specialist education involving both experts and patient representatives, and research activities on large patient populations.

These cancers have an annual incidence of ≤ 5:100.000 and present a challenge to clinical management and research. At present, ERN eUROGEN covers four rare cancer expertise areas: penile cancer, testicular cancer, adrenal tumours, and abdominopelvic sarcoma.

In 2021, ERN eUROGEN included 29 full-member and 16 affiliated partner healthcare providers across 19 EU Member States (MS). Ten of the healthcare providers, one patient organisation and two supporting partners (EAU and ESPU) were actively involved in rare urogenital tumours. The cumulative patient population was 10,000 and the annual number of new patients increased from 484 in 2013, to 1,377 in 2020. Three live educational webinars were broadcast, and eight publications appeared in peer-reviewed journals in 2019-2020. Due to the COVID-19 pandemic, the annual number of new patients flattened, and the UK's exit from the EU resulted in the withdrawal of six members in 2019. Fortunately, the 29 new full members are now being integrated, which expands the network to 57 healthcare providers in 20 MS.

This offers tremendous opportunities for creating large long-term registries facilitating research and clinical guideline development. The ERN eUROGEN registry went live at the beginning of 2022 and the healthcare providers in the network are beginning to seek informed consent from their patients to include their data in the new registry. Furthermore, new initiatives aimed at improving patient care, such as cross-ERN collaborations, will be explored.

COVID-19 impact

As mentioned previously, the coronavirus pandemic has impacted healthcare systems worldwide and brought elective surgical activity to a minimum. During the ERN eUROGEN Special Session, Prof. Magdalena Fossum (DK), on behalf of her co-authors across Europe, will present **"The COVID-19 Pandemic: Patient impact in 10 European centres for urorectogenital care."** Her presentation will give insight into the effect of changes in health care prioritisations on paediatric urology waiting lists, and how European centres dealt with the challenge in terms of logistic and financial prioritisations.

Ten European centres participated by gathering waiting list data for predetermined procedures over a one-year period, starting March 2020. Centres were surveyed at three-month intervals about operating room capacity and funding. Retrospectively, centres reported on total surgery and outpatient activity from 2019-2021. Outcome measurements and statistical analysis were based on waiting list tendencies, in both numbers of patients and time waiting.

The authors found a decrease in surgery and outpatient activity in spring 2020. Some paediatric urology centres were able to increase their budget (15%) and staff working hours (20%) during part of the study period. However, all centres increased the total number of patients waiting (11%), and accumulated days on waiting lists (73%), yielding a total of 6,102 accumulated waiting days in the study population. These results add to the ongoing debate about the morbidity and negative socioeconomic effects on paediatric urology patients and their caregivers in future healthcare crises.

Panel discussion

To finish the *Special Session*, all presenters will take part in a panel discussion giving their views on **"Rare Diseases in 2030."**

ERN eUROGEN will also be present in the EAU22 Exhibition Centre with a shared stand at the EAU booth. Please do come to this fascinating *Special Session* and if you have any questions, then come and chat with us at the stand. In the meantime, for further information about the network, please visit our website: **www.eurogen-ern.eu**

Update on rare and complex urology
ERN eUROGEN

Date:	Sunday 3 July, 15:45 - 17:15
Location:	Orange Area, Room 2
Chairs:	M. Battye, Nijmegen (NL) W.F.J. Feitz, Nijmegen (NL)

15:45 - 15:55	Programme manager presentation Update on ERN eUROGEN developments
15:55 - 16:10	ERN Patient Advocacy Group (ePAG) lecture Penile cancer: The way forward?
16:10 - 16:25	Workstream 1 (rare congenital uro-recto-genital anomalies) lecture Congenital neurogenic bladder dysfunction: What the adult urologist needs to know
16:25 - 16:40	Workstream 2 (functional urogenital conditions requiring highly specialised surgery) lecture Vesico-vaginal fistula: Management strategies and keys to successful treatment
16:40 - 16:55	Workstream 3 (rare urogenital tumours) lecture Expansion of the network with tremendous opportunities for rare urogenital tumours
16:55 - 17:05	The COVID-19 pandemic Patient impact in 10 European centers for uro-rectogenital care
17:05 - 17:15	Panel discussion Presenters' views on rare diseases in 2030

When we all help one another, everybody wins

Urology nurses need the help and support of all urologists and urological departments

Paula Allchorne, RN
Executive MBA - Health Service Management
Chair EAUN
London (GB)

p.allchorne@eaun.org

Dear Surgeons and EAU members,

I'm taking this opportunity to introduce myself as the new chair of the European Association of Urology Nurses (EAUN) and I'm asking for your help. The EAUN's main role is to standardise the quality of urological nursing care across Europe. This was a similar reason the EAU was originally formed, as a platform for urologists to standardise practice in urological surgery.

For modern urological care to be improved, nurses need to be involved. But whilst most Urology departments have a number of EAU members, only a minority support their nurses to join the EAUN. This is a serious barrier to the development of true holistic care in urology and something every EAU member can change by encouraging or ideally funding at least one nurse from their department to join the EAUN.

EAUN membership offers opportunities that can benefit both the individual nurse and their Urology department:

Fellowship Programme
Nurses looking to develop their practice or learn from service improvements in other countries may benefit from partaking in this programme. It provides an opportunity to visit a host institution to observe nursing care in another country. Eligibility and details of how to apply can be found in the Education section of the EAUN website.

Special Interest Groups (SIGs)
For nurses with a special knowledge about specific urological issues to exchange experiences and investigate urological nursing issues related to their topic group. The SIGs help develop guidelines, deliver state-of-the-art sessions at conference, run ESUN (European School of Urology Nursing) courses and webinars.

Guidelines
The opportunity to join guideline panels. Building on the success of the previous guidelines which are used all over the world to standardised care.

Annual meeting
Attend a 3-day nursing meeting and share papers on Research or Improvement. The nurses also have access to the EAU Congress. Allowing nurses to increase their knowledge and share this knowledge within their team.

Education
EAUN run webinars, e-courses & urological updates, recent ones include: bladder cancer care, catheter care, effects of androgen deprivation therapy (ADT), the role of exercise in prostate cancer patient care and shared decision-making in prostate cancer care. We also run ESUN courses (European School of Urology Nursing) – where 25 nurses across the world attended with the aim to return to their departments, share the knowledge and improve patient care.

EFUN (Educational Framework for Urological Nursing)
EAUN, BAUN and ANZUNS are developing an Educational framework for urological nursing. This collaboration across the world aims to standardise and improve nursing skills within the profession, develop urology care and the provision of research-based practice.

These initiatives will only work with the help of urologists and every urological department, supporting their nurses. We have some excellent Urology departments in Europe that are already doing outstanding work, leading the way in holistic multidisciplinary patient centred care. But this needs to be shared so that it quickly becomes the standard of care throughout Europe.

Please encourage your nurses to join the EAUN, membership is 35 euros per year. There is also the option of group membership via national nurses societies. For further information on membership please contact Hanneke Lurvink via eaun@uroweb.org. The EAUN website can be found at **www.eaun.uroweb.org**

"If everyone is moving forward together, then success takes care of itself."

EAUN22: Nurse led clinics

Highlighting clinics for benign conditions

By Robert McConkey, SCO Member, Galway, Ireland

The ever-growing workload in urology has resulted in changes to the way urological care has traditionally been delivered. In many countries, nurse led clinics in urology manage and deliver holistic patient centred care for a variety of benign conditions within the multidisciplinary team.

These can range from lower urinary tract assessment and treatment clinics, including trial without catheter clinics, performing invasive and non-invasive urodynamics, continence assessment and treatment clinics, intermittent self-catheterisation education, intravesical instillations, diagnostic cystoscopy and therapeutic intravesical botox injections, amongst others.

Nurses with differing levels of autonomy may deliver these services. The scope of practice and level of responsibility of the nurse delivering the service is associated with their grade. The grade of the nurse, or role title, which carries with it a certain level of autonomy in decision-making, is related to their experience, education, and training. This however is not standardised internationally, and a myriad of role titles and levels of autonomy exist which may cause confusion. While role titles, grades, and bands of nurses, may have different meaning in different countries, the important consideration for nurses is that they work within their scope of practice.

On Saturday, 2 July at 15:45, State-of-the-art lecture 1 will examine the role of the nurse in delivering nurse led clinics to assess, treat, educate patients, and manage common benign urological conditions to improve patient's quality of life. Ms. Margaret Tiernan, Continence Advisor in the Primary Care Centre in Roscommon, Ireland, will outline the functioning of her clinic and the pathways that she uses to manage continence issues in the community. Following this, Ms. Angie Rantell, Lead Nurse, Urogynaecology at King's College Hospital, NHS Foundation Trust, London, UK, will explain the methods she utilises to meet patients expectations in relation to overactive bladder in her nurse led clinic. These nurse led clinics will demonstrate the valuable role that specialist nurses contribute to the management of benign urological conditions.

Saturday, 2 July, 15:45 - 16:15
State-of-the-art Lecture 1, 22nd EAUN Meeting
Nurse led clinics in benign urology
Yellow Area, Room E102

Syndromic infertility and cancer predisposition

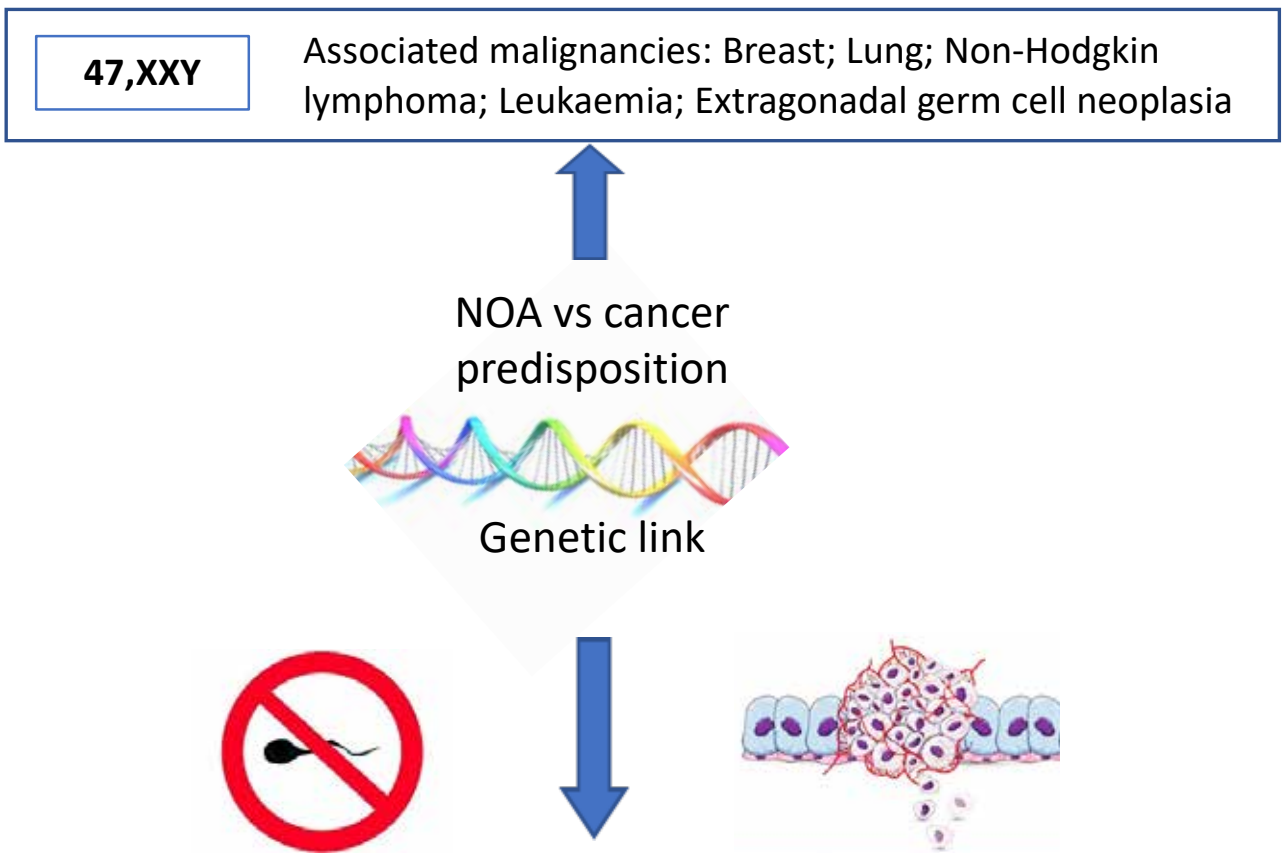
The link between azoospermia and gene mutations involved in DNA repair

Dr. Csilla Krausz
President of the European Academy of Andrology
University of Florence (IT)

Impaired reproductive function is clinically heterogeneous and may manifest as an isolated or a syndromic condition. Azoospermia is the severest form of male infertility and it affects about 1% of men in the general population. It can be the consequence of various aetiologies: (i) hypothalamic–pituitary axis dysfunction, (ii) primary quantitative spermatogenic disturbances, and (iii) urogenital duct obstruction. [1]

The large majority (75%) of Non-obstructive azoospermia (NOA) cases is due to primary testicular failure, which may derive from different testicular histologies: i) complete absence of germ cells i.e. Sertoli Cell only Syndrome (SCOS); ii) spermatogenic arrest; iii) hypospermatogenesis.

"Besides Klinefelter syndrome, monogenic disorders may also lead to non-obstructive azoospermia (NOA) and impaired general health, especially when mutations in DNA repair genes are diagnosed."



Epidemiological studies suggest that NOA is associated with reduced life expectancy and higher morbidity, including cancer. [2] The pathogenic mechanism for the above observations is likely to be related to endocrine and/or genetic factors, which may affect not only reproductive function but also general health. In the Klinefelter syndrome (KS), both low testosterone and altered gene dosage are involved in the pathogenesis of general health problems.

Besides KS, monogenic disorders may also lead to NOA and impaired general health, especially when mutations in DNA repair genes are diagnosed. [3,4]

The Klinefelter syndrome

KS is a numerical karyotype anomaly (47, XXY), which in 10–20% of cases may present higher-grade aneuploidies (48,XXXY or 48,XXYY), structurally abnormal X chromosome (47,iXq,Y) or mosaicisms (47,XXY/46,XY). Its frequency is around 10–14% in azoospermic subjects. The clinical phenotype of KS males may vary from mild to severe forms depending on the number of supernumerary X chromosome, the presence of mosaicism, testosterone level and the number of CAG repeats in the androgen receptor.

The reproductive phenotype is characterised by very small and firm testes and in over 95% of cases by azoospermia. There is a progressive deterioration of the germinal epithelium and the testosterone producing Leydig cells. Nearly all patients show elevated LH levels and have either a subclinical or overt hypogonadism. According to recent meta-analysis, the success rate for the recovery of spermatozoa through microsurgical TESE (m-TESE) in KS men is 34–44%. [5] Sperm retrieval rates by TESE in adolescents with KS aged 15 to 19 years old are comparable with those reported in young adults who are aged 20 to 30 years old. [6,7]

In KS we can observe a wide spectrum of comorbidities, some of them clearly attributable to hypoandrogenism (e.g. metabolic syndrome, osteopenia/osteoporosis, anaemia etc). X-linked gene dosage effect or epigenetic factors related to the supernumerary X chromosome are most likely the cause of higher risk for deep vein thrombosis, lung embolism, autoimmune diseases, and some typical cancers.

Among the solid cancers, breast and lung cancer are more frequent in KS than in 46,XY individuals. Regarding breast cancer, KS patients have a 4-30 fold increased incidence, but the absolute risk remains low given that male breast cancer is very rare. Moreover, it has an earlier onset in KS (58 years) compared to men with normal karyotype (67 years). According to the recent EAA Guidelines, it is recommended to perform breast examination (including mammary gland ultrasonography if necessary) and then a tailored follow-up as preventive measure. [7] In addition, haematological malignancies such as leukaemia and non-Hodgkin lymphoma are significantly more frequent (standardised incidence ratio [SIR] of 3.02 for NHL and a SIR of 3.62 for leukaemia).

Finally, an increased incidence of extragonadal germ cells neoplasia (usually non-seminomas), mainly located in the mediastinum, have been observed in KS patients. These lesions may present with thorax symptoms and in younger boys with precocious puberty due to hCG production. No increased incidence of testicular germ cells tumours has been documented.

Andrologists should be aware of the increased risk of the above-mentioned cancers allowing an early detection and treatment of such malignancies in KS patients.

"Recent Whole Exome Sequencing studies allowed the discovery of genes involved in NOA with proven role in cancer prone syndromes such as Fanconi anaemia or with potential role in cancer predisposition."

NOA and cancer-prone syndromes

As stated above, even 46,XY NOA patients seem to be at increased risk for various cancers. Both epidemiological and bioinformatic studies suggest significant genetic overlap between male infertility and particular types of cancer, including urologic neoplasms/carcinomas and B-cell lymphoma.

It is plausible that spermatogenesis and tumorigenesis may share common genetic factors, especially those involved in stem cell renewal/differentiation, mismatch repair mechanisms, and apoptosis. Particularly, germline alterations in DNA repair genes, which are fundamental for maintaining the genomic integrity and stability in the early stages of the male germline, may confer hereditable predisposition to impaired spermatogenesis and cancer. [3,4]

Spermatogenesis shares common biological pathways also with haematopoiesis and in fact, patients affected by bone marrow failure syndromes often have spermatogenic failure as well. It has been hypothesized that if DNA repair is defective during replication of stem cells then a progressive depletion of both the hematopoietic and spermatogenic stem cells, may occur leading to anaemia and NOA, respectively.

Fanconi Anemia (FA) is a rare genetic disease. In the majority of cases, the clinical manifestations of FA appear during childhood. However, in 10% of patients the diagnosis is delayed until adulthood due to slow progressive Bone Marrow Failure (BMF). Late diagnosis may occur especially when individuals have no symptoms or present subtle findings that may be overlooked. In these patients the diagnosis is usually made because of the appearance of FA-related cancers. Therefore, diagnosing "occult" FA before the appearance of neoplasia has a relevance for cancer prevention/early surveillance.

FANCA is the most commonly mutated gene in FA. Starting from Whole Exome Sequencing (WES) followed by targeted gene sequencing, we have identified recessive FANCA mutations in 3/29 idiopathic NOA patients with SCOS and with slightly altered/borderline haematological parameters i.e. with no-overt anaemia. [8] None of these "occult" FA cases presented FA-related cancers at the time of the diagnosis but thanks to the genetic diagnosis they are under strict surveillance by oncohematologists.
The SCOS phenotype reflects the lack of spermatogonial stem cells, which is the testicular equivalent of the bone marrow stem cell depletion. This finding indicates that andrological evaluation, especially in SCOS patients, should not only include hormone measurement but also blood exam since this specific subgroup of patients are at higher risk for "occult" FA.

Apart from FANCA, there are 21 genes known to take part in the so-called FA pathway, and involved in DNA double-strand break (DBS) repair. Mutations in other FA pathway genes have also been recently reported in NOA. Among them, the testis-enhanced FANCM mutations were identified in patients affected by SCOS and oligoasthenozoospermia (for review see 4). It is interesting to note that the Fancm mutant mice displayed SCO tubules and a progressive loss of germ cells overtime; hence, it is likely that FANCM mutations may be a new cause of progressive impairment of spermatogenesis with clinical implications such as preventive sperm cryopreservation.

Other examples of shared NOA/cancer predisposing genes are MCM8 and TEX15, two other DNA DSB repair genes, and the X-linked WNK3 gene, involved in cell signalling, survival and proliferation. [4]
DNA repair genes are also important for meiotic progression and in fact, in a selected group of patients with meiotic arrest, we identified mutations in TERB1, MSH4 RAD21L1 and MEIOB, all involved in the maintenance of genome integrity. [9] Long-term follow-up of these patients will be necessary to prove the concept about the potential genetic link between NOA and cancer predisposition (fig 1).

In conclusion, recent WES studies allowed the discovery of genes involved in NOA with proven role in cancer prone syndromes such as FA or with potential role in cancer predisposition. The clinical impact of discovering such "hidden" genetic factors is important not only in relationship with the reproductive function but also for the general health status of these men and their offspring.

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Saturday, 2 July 10:30 - 14:00
Meeting of the EAU Section of Andrological Urology (ESAU)
Purple Area, Room Elicium 1

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PRESCRIBING INFORMATION ADVERSE EVENT REPORTING

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1. ERLEADA®. Summary of Product Characteristics (January, 2022). Janssen-Cilag International NV. Available at: https://www.ema.europa.eu/en/documents/product-information/erleada-epar-product-information_en.pdf. Accessed: January 2022. **2.** Chi KN, *et al. J Clin Oncol* 2021 Apr 29:JCO2003488. doi: 10.1200/JCO.20.03488. **3.** Chi KN, *et al. N Engl J Med* 2019;381:13–24.

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ADT, androgen deprivation therapy. CI, confidence interval. HR, hazard ratio. mHSPC, metastatic hormone-sensitive prostate cancer. OS, overall survival. rPFS, radiographic progression-free survival.
*ERLEADA® (apalutamide) is indicated in adult men for the treatment of metastatic hormone-sensitive prostate cancer (mHSPC), in combination with ADT.[1]
†Median OS not yet reached with ERLEADA® + ADT: the majority of patients were still alive at the time of the final analysis (after adjustment for crossover); HR: 0.52 (95% CI: 0.42–0.64) p<0.0001.[2]
‡rPFS: time from randomisation to first imaging-based documentation of progressive disease or death, whichever occurred first. Median rPFS could not be estimated for ERLEADA® + ADT vs. 22.1 months with placebo + ADT; HR: 0.48 (95% CI: 0.39–0.60) p<0.001.[3]