European Urology Today

EAU21 Congress News

36th Annual Congress of the European Association of Urology

8-12 July 2021
Virtual

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Will we ever meet in person again? YES!

In the lead up to EAU21 Virtual, the EAU Executive Committee looks back at the past 1.5 years

In this special EAU21 congress edition of European Urology Today, we open with a brief look back at the extraordinary year we have seen. We asked the members of our Executive Committee what their experiences have been and what their expectations are for the future of our association and for your daily clinical practices.

IIn the past 18 months, the EAU Executive Committee has not met in person due to all travel restrictions, but that hasn't stopped its members from successfully developing educational programmes, stimulating scientific exchanges, and transforming existing services for our members to the fully digital era. Before they will, hopefully, come together in our studio from where multiple sessions of the 36th Annual EAU Congress (EAU21 Virtual) will be broadcast, all five executive members, Profs. Christopher Chapple (GB), Hein Van Poppel (BE), Arnulf Stenzl (DE), Manfred Wirth (DE), and Jens Sønksen (DK), share their personal lessons learned and their thoughts on what the lasting impact of the pandemic will be.

No travel

The past 1.5 years will be remembered as, among other things, the time of no travel, which is quite unusual for this quintet used to travelling around the world. Prof. Chapple commences: "Not seeing my patients at the hospital but having to deal with them by either tele- or videoconferencing was one of the major issues. Even though one can do tele- and videoconferences, it can be quite frustrating not being able to examine and treat patients and just to see the waiting lists for surgery growing."

Prof. Wirth states that not seeing friends and family was the biggest sacrifice. "Especially my grandchildren who don't live nearby. Luckily there is Facetime, but it is just not the same." For Prof. Stenzl, the world came through his 15" screen of his computer. "Throughout the pandemic, I spent almost every weekend at home, meeting friends and colleagues virtually. I became much humbler about the good things in life such as live concerts, theatres, movies, visits to friends, and parties, which were part of our daily lives but all of a sudden were not possible anymore."

Prof. Van Poppel adds that he learned how to read from people's eyes what they think and what their state of mind is. "Whether they are happy, disappointed, the eyes will tell it all." Also Prof. Sønksen mentions the psychological aspects of the pandemic. "I have noted a lot of uncertainty, because you didn't know what the future was going to bring."

To the question how the pandemic has affected our society, all agree that this disruption made everyone more critical of how to spend their time and what formats are the most beneficial financially and in terms of efficiency in gaining knowledge. "From the very beginning, it was clear that we had limited possibilities to plan because of the many unknown factors", says Prof. Sønksen.

"Our physical meetings were cancelled, so we had to make the shift to virtual meetings really fast. In no time, the team at the Central Office had built a completely new platform from scratch and we were giving webinars twice a week before we knew it."

Prof. Chapple agrees that by the use of tele- and videoconferencing the EAU has managed to keep up to date with everything and continued contributing to its sister associations across the world. "Within the association, we have managed to continue to work on our objectives thanks to the amazing support from the Central Office, who have had significant challenges but have shown great resilience in adapting our complete portfolio to a virtual setting." Prof. Van Poppel adds that working hours have intensified. "Instead of travelling to a nice place to attend a meeting for one day and work together for the day having a nice dinner, we now do virtual meetings with the same agenda in a couple of hours, preferably in the weekends or evenings. So we worked harder, more efficiently."

Lessons learned

In terms of lessons learned, Prof. Wirth is very clear: "We can omit a lot of travelling. It saves you time and money, it is better for our environment and will make our lives easier in a lot of ways. Also when looking at education, the online equivalents offer many advantages." Prof. Van Poppel, too, has fully adapted to working remotely and has integrated virtual meetings in his 'new normal' professional life.

Prof. Sønksen, however, is cautious: "The stop of physical meetings has led to a deteriorating and poor education of the residents, at least around me. We should be better prepared for crises like this in the future. Especially when you look at education, not only within the EAU but urology in general, you should really have some kind of back-up for your educational plans." Prof. Chapple foresees an enormous problem over the next few years in terms of catching up on the backlog as well as maintaining the management of existing problems within our clinical setting.

Another personal lesson learned by Prof. Stenzl relates to adapting to a new way of interacting during virtual meetings. "I've learned to always think about putting on the microphone before speaking, which made me more cautious of contributing with useful comments, clearing the bookshelf behind your head before turning on the camera and not to yawn when your camera is on."

All men are positive about our future and see many possibilities in the digital front. Both Prof. Chapple and Prof. Stenzl recognise that the use of tele- and videoconferencing with patients will remain in the future as it facilitates treatment, particularly for monitoring and follow-up. "There is an increasing number of companies organising online doctor visits", says Prof. Stenzl. Prof. Wirth adds:

The EAU Executive Committee: Prof. Arnulf Stenzl, Prof. Hein Van Poppel, Prof. Manfred Wirth (standing from left to right), Prof. Jens Sønksen, and Prof. Christopher Chapple (sitting from left to right). Photo taken in 2019.

"Telemedicine is not only here to stay, it will also improve the patient communication as it is much easier and faster." Many patients seem to be happy with a Zoom meeting with their doctor, according to Prof. Sønksen. Prof. Wirth agrees: "They benefit from easier second opinions and quicker access to the right treatment."

The improved access to education at a global scale is another aspect that, according to all executive members, will not likely disappear when we go back to normal. Prof. Stenzl says: "Many of the smaller topic-oriented educational meetings and masterclasses will be virtual and shorter." Prof. Wirth is also convinced that online education will increase. "We will have less face-to-face meetings, and smaller meetings will be more and more transformed into an online equivalent, allowing us to reach a broader audience outside Europe."

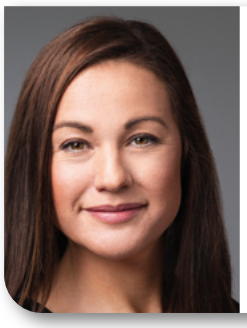
To the final question whether we will ever meet in person again, the answer is a wholeheartedly *yes!* We will travel less, but we need to meet at a regular basis, although not completely in the same way as we used to do, according to Prof. Van Poppel. "We have had a fantastic number of years where everything was possible, and we must be grateful for that. However, the 'old normal' is very unlikely to ever come back. Hugs, cuddles, and kisses will be gone for ever." Prof. Chapple concludes that, "Over the last year, we have learned a tremendous amount and that will be reflected in the upcoming virtual Annual Congress."

"With a scientific programme that will not make any concessions compared to our previous physical congresses, we look forward to welcoming many colleagues from all around the world to EAU21 while we also hope to meet each other in person again next year."

This is a special EAU21 Virtual edition of *European Urology Today* (EUT). EAU21 Virtual will be taking place from 8 to 12 July 2021 and promises to be one of the scientific highlights of the year. This 48-page EUT features all quality scientific content written by speakers, interviews with award winners, the full scientific programme, including all the sessions coming live from our studio, and much more.

The PIONEER Big Data platform:

How does it apply to prostate cancer?



Dr. Susan Evans Axelsson
Clinical Coordinator
PIONEER
Malmö (SE)

susan.evans_axelsson@med.lu.se

To transform prostate cancer (PCa) outcomes we must do things differently. We have not seen a pragmatic change in the treatment of PCa in the last 10 years, thus PIONEER was formed to address this problem and more. PIONEER is one of four Innovative Medicine Initiatives disease-specific Big Data for Better Outcomes (BD4BO) projects. Its focus is on BD4BO in prostate cancer while the other three focus on Alzheimer's disease (ROADMAP), haematologic malignancies (HARMONY) and cardiovascular disease (BigData@Heart).

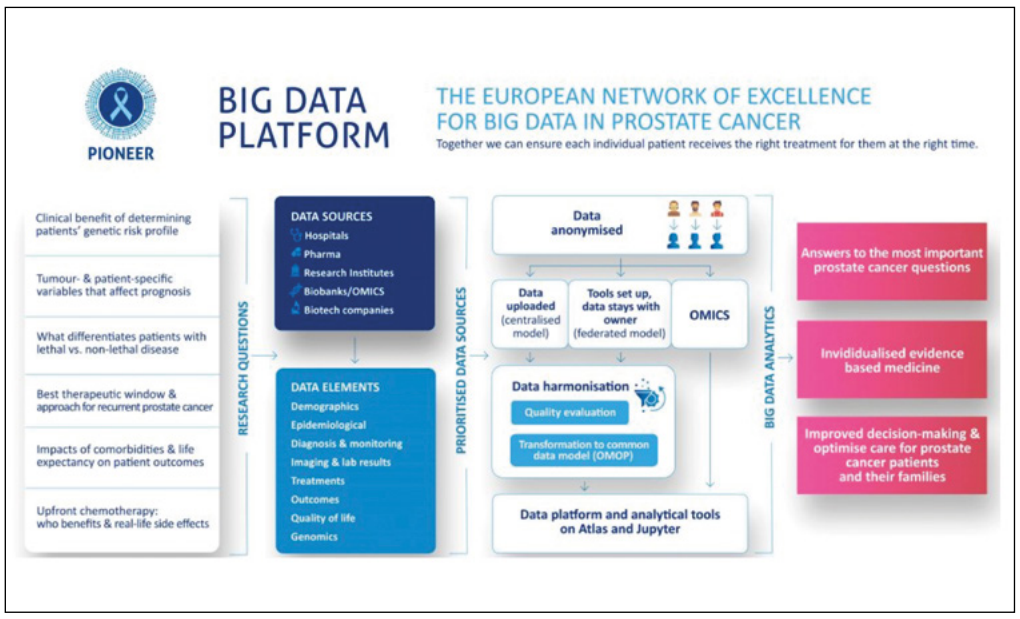


Figure 2: An infographic on the workings of PIONEER

Though these are disease-specific projects, they are all focused on the same themes, namely:

- to design sets of standard outcomes and demonstrate value
- to increase access to high-quality outcomes data
- to use data to improve value of health care delivery
- to increase patient engagement through digital solutions

The projects share the same goal: to maximise the potential of Big Data to empower meaningful improvement in clinical practice, disease-related outcomes, and healthcare systems across Europe.

PIONEER is the 'youngest' of the four BD4BO programmes and thus has had the opportunity to build on the successes and learn from the failures of other projects. Because of this, PIONEER is building a stable and sustainable platform that will assemble, standardise, harmonise, and analyse high-quality big data from diverse populations of prostate cancer patients across all stages of the disease to provide evidence-based results for improving decision-making by key stakeholders and strengthen prostate cancer care and management.

Patients have been involved from the very beginning.

Prior to the start of PIONEER, the members of the EAU Prostate Cancer Guidelines panel and other prostate cancer key opinion leaders identified 44 questions as important knowledge gaps in the field of prostate cancer. Based on these questions, a prioritisation survey was conducted among key opinion leaders including healthcare professionals, pharmaceutical companies, and prostate cancer patients. In the first round, 73 healthcare professionals and 57 patients participated. For the second round, 12 questions were added, and the survey was translated from English into French, German, Italian and Spanish. 49 healthcare professionals and 169 patients replied in the second round, highlighting patients' willingness to be actively involved in what they feel are crucial gaps in their healthcare and to become the ultimate beneficiaries of improvements. This survey resulted in **56 prioritised and re-ordered research questions covering all stages of prostate cancer, ranked according to the highest percentage for 'critically important'.**

Different research questions require different types of data. To ensure the PIONEER database holds information relevant to PIONEER's aims, we ask each data holder to fill in a PIONEER Study Fact Sheet. With these fact sheets we are able to get a better understanding of the data contained in each dataset. The Study Fact Sheet questions what key data (if any) is available concerning the following topics: clinical, treatment, lab results, imaging, epidemiologic, economic, and genomic. As of May 2021, **PIONEER has collected 44 fact sheets from potential data partners.**

"PIONEER's potential impact to change the clinical practice and fuel a new era in prostate cancer care and management is immeasurable."

Data sharing models

Flexibility is key! In order to offer more flexibility to the data providers, the PIONEER consortium has chosen to utilise a mix of both the federated (remote data) and central (importable data) data sharing models and will ask the data provider to choose which model they prefer to use or are required to use by local law or other restrictions/regulations. Importantly, PIONEER will only accept anonymised data in the federated and central models and thus no original patient level data leaves the site. All data is anonymised and standardised to the OHDSI OMOP-common data model behind the data providers firewall to facilitate analysis. The anonymised data is then moved to a central repository for research (in case of the central model), or the analytical code is sent to the data source where it is run locally in their own safe haven and from where only aggregated results are shared (in case of the federated model). Regardless of the chosen model, data contributors have the right to decide which studies they want to participate in and thus also have the right to opt out of studies.

PIONEER is contributing to the paradigm shift in the care and management of men with prostate cancer across Europe by collecting and collating high-quality datasets from European and non-European data providers. Data sources include hospitals, pharma, research institutes, biobanks/OMICS, and biotech companies. Ninety-five data sources have been identified as possible contributors to the platform. As of May 2021, **11 datasets are available in the PIONEER platform and 21 datasets are in the process of being converted to the OHDSI OMOP-common data model or do not require conversion to be added to the platform.**

Within PIONEER, we are developing a unique analytical toolkit for the analysis of a variety of data sources containing clinical studies, claims data, electronic health records, etc. to produce data descriptions, statistics, data visualisations and predictive models to answer the identified research questions. Bringing big data into an environment where it can easily be queried in a scientifically valid method to address these critical questions about how patient management impacts patient outcomes is essential for the future health care delivery model.

Study-a-thon

In March 2021, PIONEER, together with European Health Data & Evidence Network (EHDEN) and Observational Health Data Sciences and Informatics (OHDSI) joined forces to kickstart the process of answering PIONEER research questions by holding a five-day study-a-thon. The aim was to use big data and big data analytics to determine the real natural history of prostate cancer patients managed with watchful waiting. This event attracted 245 participants from 20 countries and combined results from at least 19 datasets (>two million prostate cancer patients from PIONEER and non-PIONEER data through the OHDSI community) to answer this question. This first study-a-thon demonstrated that we can create standardised operational definitions of clinically relevant concepts across datasets that will become the fundamental building blocks for future analyses (e.g. watchful waiting, active surveillance, disease progressions, etc.). This will ultimately speed up the analysis and facilitate the replication of analyses across multiple datasets leading to the generation of bodies of publishable and meaningful evidence that will support guideline development and revisions and changes in clinical practice.

As the PIONEER platform continues to grow with more high-quality big data from diverse populations of prostate cancer patients across different stages of the disease, its potential impact to change the clinical practice and fuel a new era in prostate cancer care and management is immeasurable.

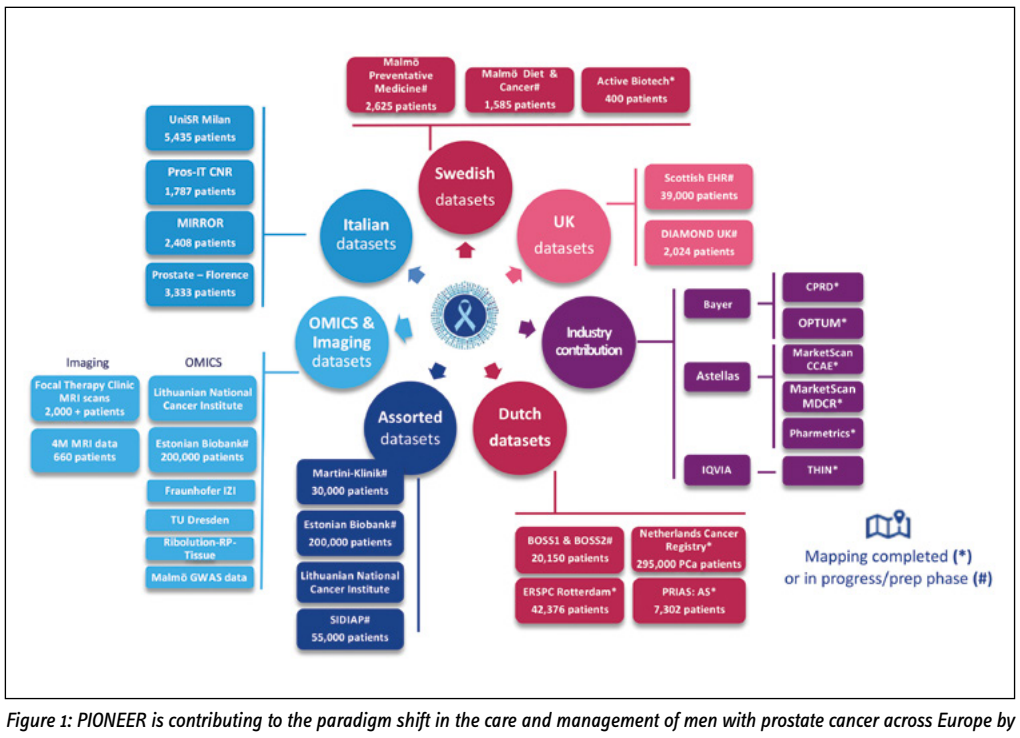


Figure 1: PIONEER is contributing to the paradigm shift in the care and management of men with prostate cancer across Europe by collecting and collating high-quality datasets from European and non-European data providers

Monday 12 July, 14.30 – 15.30 CEST
EAU Specialty Session
PIONEER prostate cancer platform
Virtual Room 5

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Award

EAU Willy Gregoir Medal

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

2020 - 2021
M. Wirth
Dresden, Germany

EAU Frans Debruyne Life Time Achievement Award

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

2020 - 2021
H. Van Poppel
Leuven, Belgium

EAU Crystal Matula Award

For a young promising European urologist

2021
V. Phé
Paris, France

2020
D. Tilki
Hamburg, Germany

Supported by LABORIE

New EAU Honorary Members **2020 - 2021**

For an important influence on European urology

W. Artibani
Verona, Italy

D. Castro Diaz
Tenerife, Spain

R. Sylvester
Brussels, Belgium

T. Tammela
Tampere, Finland

L-P. Xie
Hangzhou, China

Best Papers published in Urological Literature Awards **2021**

Best Paper on Fundamental Research

Bladder Tumor Subtype Commitment Occurs in Carcinoma In Situ Driven by Key Signaling Pathways Including ECM Remodeling
Cancer Research; doi: 10.1158/0008-5472.CAN-20-2336

A. Wullweber, R. Strick, F. Lange, D. Sikic, H. Taubert, S. Wach, B. Wullich, S. Bertz, V. Weyerer, R. Stoehr, J. Breyer, M. Burger, A. Hartmann, P. Strissel, M. Eckstein (Düsseldorf, Erlangen, Regensburg, Germany)

Best Paper on Clinical Research

Hybrid Indocyanine Green–99mTc-nanocolloid for Single-photon Emission Computed Tomography and Combined Radio- and Fluorescence-guided Sentinel Node Biopsy in Penile Cancer: Results of 740 Inguinal Basins Assessed at a Single Institution
European Urology 78 (2020) Pages 865-872

P. Dell'Oglio, H. de Vries, E. Mazzone, G. KleinJan, M. Donswijk, H. van der Poel, S. Horenblas, F. van Leeuwen, O. Brouwer (Milan, Italy; Amsterdam, Leiden, The Netherlands)

European Urology® Awards **2021**

Best Scientific Paper

The DaBlaCa-13 Study: Short-term, Intensive Chemoresection Versus Standard Adjuvant Intravesical Instillations in Non-muscle-invasive Bladder Cancer - A Randomised Controlled Trial
European Urology, Volume 78, Issue 6, Pages 856–862

M. Lindgren, P. Bue, N. Azawi, L. Blichert-Refsgaard, M. Sundelin, L. Dyrskjøt, J. Jensen

Supported by ELSEVIER

Best Scientific Paper on Fundamental Research

Gut Bacteria Composition Drives Primary Resistance to Cancer Immunotherapy in Renal Cell Carcinoma Patients
European Urology, Volume 78, Issue 2, Pages 195-206

L. Derosa, B. Routy, M. Fidelle, V. Iebba, L. Edoardo Pasolli, N. Segata, A. Desnoyer, F. Pietrantonio, G. Ferrere, J-E. Fahrner, E. Le Chatellier, N. Pons, N. Galleron, H. Roume, C. Duong, L. Mondragón, K. Iribarren, M. Bonvalet, S. Terrisse, C. Rauber, A-G. Goubet, R. Daillère, F. Lemaitre, A. Reni, B. Casu, M. Tidjani Alou, C. Alves Costa Silva, D. Raoult, K. Fizazi, B. Escudier, G. Kroemer, L. Albiges, L. Zitvogel

Supported by ELSEVIER

Best Scientific Paper on Clinical Research

Treatment of High-grade Non-muscle-invasive Bladder Carcinoma by Standard Number and Dose of BCG Instillations Versus Reduced Number and Standard Dose of BCG Instillations: Results of the European Association of Urology Research Foundation Randomised Phase III Clinical Trial "NIMBUS"
European Urology, Volume 78, Issue 5, Pages 690–698

M-O. Grimm, A. van der Heijden, M. Colombel, T. Muilwijk, L. Martínez-Piñeiro, M. Babjuk, L. Türkeri, J. Palou, A. Patel, A. Bjartell, C. Caris, R. Schipper, W. Witjes for the EAU Research Foundation NIMBUS Study Group

Supported by ELSEVIER

Best Scientific Paper on Oncology

Effect of Antibiotic Use on Outcomes with Systemic Therapies in Metastatic Renal Cell Carcinoma
European Urology Oncology, Volume 3, Issue 3, Pages 372–381

A-K. Lalani, W. Xie, D. Braun, M. Kaymakcalan, D. Bossé, J. Steinharter, D. Martini, R. Simantov, X. Lin, X. Wei, B. McGregor, R. McKay, L. Harshman, T. Choueiri

Supported by ELSEVIER

Best Scientific Paper on Robotic Surgery

Outcomes of Gender Affirming Peritoneal Flap Vaginoplasty Using the Da Vinci Single Port Versus Xi Robotic Systems
European Urology, Volume 79, Issue 5, Pages 676–683

G. Dy, M. Suk Jun, G. Blasdel, R. Bluebond-Langner, L. Zhao

Supported by the VATTIKUTI FOUNDATION

European Urology® Awards **2021**

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

The Clinicopathologic and Molecular Landscape of Clear Cell Papillary Renal Cell Carcinoma: Implications in Diagnosis and Management
European Urology, Volume 79, Issue 4, Pages 468–477

S. Weng, R. DiNatale, A. Silagy, R. Mano, K. Attalla, M. Kashani, K. Weiss, N. Benfante, A. Winer, J. Coleman, V. Reuter, P. Russo, E. Reznik, S. Tickoo, A. Hakimi

Supported by BOSTON SCIENTIFIC

Platinum Awards

M. Cooperberg, San Francisco, United States of America
A. D'Amico, Boston, United States of America
E. Zabor, Cleveland, United States of America

Top 5 Best Patient Poster Awards **2021**

Patient-reported experience of diagnosis, management, and burden of renal cell carcinomas: Results from a global patient survey in 41 countries
Abstract Nr. 2223

R. Giles, D. Maskens, R. Martinez, K. Kastrati, C. Castro, J. Julián Mauro, R. Bick, M. Packer, D. Heng, J. Larkin, A. Bex, E. Jonasch, S. Maclennan, M. Jewett (Duivendrecht, The Netherlands; Toronto, Calgary, Canada; Mountain View, Houston, USA; Wölfersheim, Germany; Mexico City, Mexico; Madrid, Spain; Guildford, London, Aberdeen, United Kingdom)

Sexual function of men undergoing invasive prostate cancer treatment versus active surveillance – results of the EUPROMS study
Abstract Nr. 1286

L. Venderbos, A. Deschamps, E-G. Carl, J. Dowling, S. Remmers, M. Roobol (Rotterdam, The Netherlands; Antwerp, Belgium)

Remote consultations: Experiences of patients with prostate cancer
Abstract Nr. 2015

R. Leszczynski, S. Allen, R. Persad, T. Page, W. Cross, E. Craske, H. Lovett, K. Stalbow (London, Bristol, Newcastle upon Tyne, Leeds, United Kingdom)

Cancer care during COVID-19: Data from 157 patient organisations
Abstract Nr. 2225

R. Giles, E. Baugh, F. Cordoso, A. Filicevas, J. Fox, K. Oliver, F. Reid, L. Warwick, C. Mackay (Duivendrecht, The Netherlands; Toronto, Mississauga, Canada; Lisbon, Portugal; Brussels, Belgium; Liverpool, London, United Kingdom)

Ten years' experience of peer support by specifically trained prostate cancer patients
Abstract Nr. 3072

V. Griesser (Geneva, Switzerland)

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Colophon

European Association of Urology

Gallery

EAU Hans Marberger Award

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

2021
A. Gallioli
Barcelona, Spain

Learning Curve in Robot-assisted Kidney Transplantation: Results from the European Robotic Urological Society Working Group
European Urology 78 (2020) 239-247

2020
A. Larcher
Milan, Italy

The ERUS Curriculum for Robot-assisted Partial Nephrectomy: Structure Definition and Pilot Clinical Validation
European Urology 75 (2019) 1023-1031

Supported by KARL STORZ SE & CO.KG

EAU Prostate Cancer Research Award

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

2021
W. Fendler
Essen, Germany

Prostate-Specific Membrane Antigen Ligand Positron Emission Tomography in Men with Nonmetastatic Castration-Resistant Prostate Cancer
Clinical Cancer Research; DOI: 10.1158/1078-0432.CCR-19-1050

2020
D. Osses
Rotterdam, The Netherlands

Results of Prostate Cancer Screening in a Unique Cohort at 19 yr of Follow-up
European Urology 75 (2019) 374-377

Supported by the FRITZ H. SCHRÖDER FOUNDATION

EAU Innovators in Urology Award

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

2020 - 2021
J. Barentsz
Nijmegen, The Netherlands

EAU Ernest Desnos Prize

For extraordinary contributions to the History of Urology

2020 - 2021
M. Moran
Tucson, United States of America

European Urological Scholarship Programme Awards **2021**

EUSP Best Clinical Scholar Award

Detailing sexual outcomes after focal therapy for localised prostate cancer

G. Fiard, Brie et Angonnes, France

EUSP Best Research Scholar Award

Study on next-generation sequencing in the identification of predictive biomarkers for neoadjuvant cisplatin-based chemotherapy in bladder cancer patients

I. Lysenko, St. Petersburg, Russia

Young Academic Urologists Awards **2021**

Best Paper by YAU

Clinical Efficacy of Serenoa repens Versus Placebo Versus Alpha-blockers for the Treatment of Lower Urinary Tract Symptoms/Benign Prostatic Enlargement: A Systematic Review and Network Meta-analysis of Randomized Placebo-controlled Clinical Trials

G. Russo, C. Scandura, M. Di Mauro, G. Cacciamani, M. Albersen, G. Hatzichristodoulou, M. Fode, P. Capogrosso, S. Cimino, T. Marcelissen, J-N. Cornu, M. Gacci, A. Minervini, A. Cocci (Catania, Nicolosi, Milan, Florence, Italy; Los Angeles, USA; Leuven, Belgium; Nurnberg, Germany; Herlev, Denmark; Maastricht, The Netherlands; Rouen, France)

Best Poster by YAU

Survival outcomes after radical cystectomy versus conservative management for clinical T1 high grade non-muscle invasive micropapillary bladder cancer: a multicenter collaboration by the European Association of Urology–Young Academic Urologists

M. Moschini, C. Lonati, P. Baumeister, L. Afferi, A. Mari, A. Minervini, W. Krajewski, S. Einerhand, F. Montorsi, A. Briganti, A. Antonelli, M. Rouprêt, A. Masson-Lecomte, S. Shariat, D. D'Andrea, F. Soria, R. Hurle, M. Mir, S. Zamboni, C. Simeone, T. Klatte, J. Teoh, G. Schulz, A. Mattei (Lucerne, Switzerland; Brescia, Florence, Milan, Verona, Turin, Rozzano, Italy; Wroclaw, Poland; Amsterdam, The Netherlands; Paris, France; Vienna, Austria; Valencia, Spain; Bournemouth, United Kingdom; Hong Kong, China; Munich, Germany)

Best Reviewer YAU

R. Campi, Florence, Italy

Best Abstract Awards Non-Oncology **2021**

First Prize

Efficacy and safety of the sublingual bacterial vaccine MV140 in women with recurrent urinary tract infections: An European phase III, multicentre, randomized, double-blind, placebo-controlled trial
Abstract Nr. P0130

M. Lorenzo Gomez, S. Foley, J. Nickel, B. Padilla-Fernández, I. González-Casado, M. Martínez-Huélamo, B. Yang, P. Saz-Leal, M. Casanovas, M. García-Cenador (Salamanca, Tenerife, Alcalá de Henares, Spain; Reading, United Kingdom; Kingston, Canada)

Second Prize

Simulation in urological training and Education (SIMULATE): A randomised controlled clinical and educational trial to determine the effect of simulation-based surgical training
Abstract Nr. P0961

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

Best Abstract Awards Oncology **2021**

First Prize

Prostate cancer screening using prostate-specific antigen, a multiplex blood-test, magnetic resonance imaging and targeted prostate biopsies: The STHLM3MRI trial
Abstract Nr. P1014

T. Nordström, A. Discacciati, M. Bergman, M. Aly, M. Annerstedt, A. Glaessgen, S. Carlsson, F. Jäderling, M. Eklund, H. Grönberg (Stockholm, Sweden)

Second Prize

Prevalence and spectrum of germline cancer susceptibility gene mutations among patients with renal cell carcinoma
Abstract Nr. P0541

W. Kong, Y. Tongtong, H. Wang, H. Liu, M. Li, X. Liang, W. Wang, F. Lou, S. Cao, J. Zhang (Shanghai, Beijing, China)

Third Prize

Should the follow-up schedule after radical nephroureterectomy be revised? An analysis on the timing and location of recurrences
Abstract Nr. P0779

A. Martini, C. Lonati, A. Stabile, A. Necchi, A. Briganti, F. Montorsi, A. Mattei, S. Shariat, M. Moschini (Milan, Italy; Lucerne, Switzerland; Vienna, Austria)

Best Abstracts by Residents-in-Urology Awards **2021**

First Prize

Visioning - Evaluation of a solely MRI-based, PSA-free prostate cancer screening program
Abstract Nr. P0991

M. Matthias, C. Wetterauer, H. Pueschel, L. Bubendorf, D. Boll, E. Merkle, H. Seifert, C. Rentsch (Basel, Switzerland)

Second Prize

En-bloc versus conventional transurethral resection of bladder tumors: Interim analysis of a single-center prospective randomized trial
Abstract Nr. P0759

M. Fontana, P. Diana, A. Territo, A. Gallioli, A. Piana, A. Mercadé, S. Fontanet, F. Algaba, Ó. Rodriguez-Faba, J. Gaya Sopena, J. Palou, A. Breda (Barcelona, Spain)

Third Prize

Robot-assisted laparoscopic radical cystectomy with intracorporeal ileal conduit diversion versus open radical cystectomy with ileal conduit in an ERAS setup (BORARC): A double-blinded, randomised feasibility study
Abstract Nr. P0813

S. Maibom, M. Røder, E. Aasvang, M. Rohrsted, P. Thind, P. Bagi, T. Kistorp, A. Poulsen, L. Salling, H. Kehlet, K. Brasso, U. Joensen (Copenhagen, Denmark)

Best Video Abstract Awards **2021**

First Prize

New technologies in robot-assisted kidney transplantation: Improving surgical performances, expanding the indication
V24

A. Piana, A. Territo, A. Gallioli, M. Fontana, P. Diana, J. Gaya, O. Rodríguez Faba, J. Huguet, P. Gavrilov, A. Mercadé, J.D. Subiela, L. Guirado, C. Facundo, A. Bellin, D. Amparore, J. Palou, F. Porpiglia, A. Breda (Barcelona, Spain; Turin, Italy)

Second Prize

Indocyanine green guidance during 3D augmented reality robot assisted partial nephrectomy: A step towards the "automatic" overlapping
V23

F. Porpiglia, D. Amparore, F. Piramide, E. Checcucci, P. Verri, G. Volpi, S. De Cillis, A. Piana, P. Piazzolla, A. Bellin, M. Manfredi, E. Vezzetti, C. Fiori (Turin, Italy)

Third Prize

Robot-assisted partial nephrectomy with 3D preoperative surgical planning: Video presentation of the florentine experience
V22

A. Grosso, F. Di Maida, R. Tellini, A. Mari, S. Sforza, R. Campi, F. Valastro, L. Lambertini, P. Polverino, P. Verrienti, M. Presutti, L. Masieri, M. Carini, A. Minervini (Florence, Italy)

Prof. Derya Tilki wins 2020 EAU Crystal Matula Award

"To be selected is an honour; not only for me, but also for all the people I have been trained by"

By Juul Seesing

She received medical education in Germany and the United States. She is currently faculty member of the Martini-Klinik in Hamburg (DE), where she works in collaboration with several international research institutes around the globe. In a world of ongoing international collaboration, she is a symbol of future urology. Prof. Derya Tilki (DE) was therefore selected as the recipient of the 2020 EAU Crystal Matula Award, awarded to a young promising European urologist aged 40 or under who has the potential to become one of the future leaders in academic European urology. The award was scheduled to be bestowed at EAU20 in Amsterdam and was instead given to Prof. Tilki in the build-up to EAU21 Virtual.

Prof. Derya Tilki

Previous winners of the EAU Crystal Matula Award: Prof. Mesrur Selçuk Silay (TR, left, 2018) and Dr. Maarten Albersen (NL, 2019)

"Global research projects provide more heterogeneity not only of patients and diseases we are studying, but also regarding differences in how urologists think, construct methodology to answer a question, and interpret data," Prof. Tilki says about the several international collaborations she has been part of. "I did my urological oncology fellowship at the UC Davis Medical Center (US) and saw many new ways to address a question."

"Global research projects provide more heterogeneity not only of patients and diseases we are studying, but also regarding differences in how urologists think."

What does winning the EAU Crystal Matula Award mean to you?
Prof. Tilki: "I feel incredibly honoured. Every year, there are many qualified and deserving applicants. To be elected is an honour; not only for me, but also for all the people I have been trained by, currently work with, and those who I am mentoring now and will be mentoring in the years to come."

Your main clinical interests are diagnosis and treatment of prostate cancer, while your research focusses on prostate cancer outcomes and biomarker research. Could you say something about how and why you chose this path?
"During medical school, I did my medical thesis on tumour angiogenesis. The project I was working on was related to prostate and bladder cancer, which included a collaboration with the urology department. This was the reason I chose the field of urology. The ability to investigate clinical questions with tools to better help patients and physicians was a natural fit."

You also concentrate on translational research. What new developments do you see in the field of prostate cancer?
"Some of the most exciting developments at present include new biomarkers in prostate cancer, new imaging modalities and their influence on treatment decisions, and new agents in metastatic prostate cancer. Each one of these has a potentially profound impact to benefit patients."

"Find an area that you are passionate about and focus on it."

You attended among others Harvard Medical School (US), Weill Cornell Medical College (US), and UC Davis Medical Center (US). What experience was most helpful for you on the journey to winning the EAU Crystal Matula Award?
"I attended these places during different times of my career: Harvard during medical school, Weill Cornell Medical College during residency, and UC Davis Medical Center for my clinical fellowship. The combination of them has contributed to my journey in total and created the foundation for my achievements."

You are actively involved in the EAU, for instance as member of the EAU Prostate Cancer Guidelines Panel. What did you learn from your involvement in the EAU so far?
"I learned the importance of collaboration and group research as a mechanism to broaden my knowledge as well as to share it."

What advice would you give to a young urologist starting out now?
"Find an area that you are passionate about and focus on it. Also, always have a mentor. Ultimately, that mentor should become a collaborator."

Prof. Arnulf Stenzl (DE), Adjunct Secretary General of the EAU, bestowed the EAU Crystal Matula Award on Prof. Tilki in Tübingen (DE). Visit the EAU21 Congress Platform and watch the video!

"You have to be ambitious and daring; nothing is innate"

Barrier-breaking Prof. Véronique Phé wins the 2021 EAU Crystal Matula Award

By Juul Seesing

The EAU Crystal Matula Award is presented to a young promising European urologist aged 40 or under who has the potential to become one of the future leaders of academic European urology. By winning this prize, Prof. Véronique Phé (FR) has taken her next step on the EAU ladder. It was only seven years ago that she won a European Urological Scholarship Programme (EUSP) grant, which gave her the opportunity to spend a one-year fellowship in the Department of Uro-Neurology at the National Hospital for Neurology and Neurosurgery and the UCL Institute of Neurology in London (GB). "This fellowship definitely changed my career," she relates.

"You can imagine that it was even more difficult when you are a woman, mother, and born in a foreign country."

"It gave me the opportunity to create international collaborations, which have been maintained to this day, and to get to know fellows from different countries. I also learned humility while working in a foreign country and not to be afraid of ambition."

Indeed, it was a milestone in her journey toward earning the 2021 EAU Crystal Matula Award, which was granted to her especially for her work in the field of neuro-urology and functional urology. She became the first female urologist to reach the academic position of professor of urology in France through her appointment at the Pitié-Salpêtrière Hospital in Paris (FR) in September 2020.

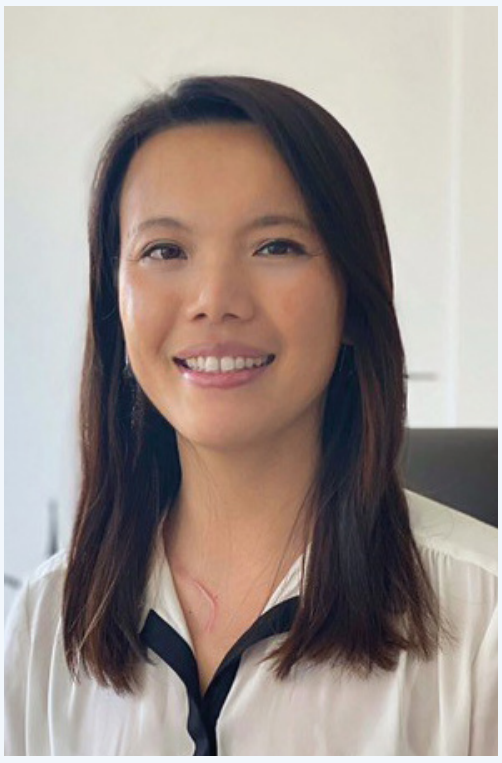
"Becoming a full academic professor of surgery in France is extremely difficult," she describes. "There are many requirements: from having recognised clinical and surgical expertise to being efficient in producing scientific publications; from having supervised teams to being a good teacher. Your academic projects and perspectives have to be exceptional. Understanding these challenging aspects also mean gaining maturity with time. In the end, you can imagine that it was even more difficult when you are a woman, mother, and born in a foreign country [Prof. Phé was born in Thailand, Ed.]."

Ongoing pursuit of excellence

Prof. Phé regards it as a "tremendous honour" to be presented with the EAU Crystal Matula Award. "It is the most prestigious international award for a young urologist. To me, it means that you have gained recognition from your colleagues both in your home country and at an international level thanks to work, determination, and integrity. These are the values that drive me in life. I believe in meritocracy. Winning the award delivers a positive message to all young academic urologists who want to pursue this pathway. The previous winners of the Crystal Matula have become established leaders within the field. This is a great inspiration for my ongoing pursuit of excellence."

"Work, determination, and integrity. These are the values that drive me in life."

This pursuit of excellence will mainly take place in the field of neuro-urology and functional urology, where Prof. Phé's clinical practice and academic interest is focussed on. "Strictly speaking, we do not save the lives of patients, but we alleviate their urinary handicap by giving them quality of life, autonomy, dignity, and self-esteem. I like to start from a complex clinical situation and dismantle it in a way that makes it simple, understandable, and solvent. The relationship with a patient is strong, lasting, and also unique as it requires a result contract with the patient. I feel like I am useful and that I have done my duty when a patient tells me, 'Thank you, doctor. I am living again,' or, 'You have given me an acceptable life.'"



Prof. Véronique Phé

Mentor

In answer to our question about her main goal for the future, Prof. Phé's response is short but sweet: "Creating my own school of urology to share my surgical techniques, thoughts, and ideas across the world."

"Teaching has always had my interest. I have been involved in UROwebinars, and I hope that one day I will be able to participate in the European Urology Residents Education Programme (EUREP) as a teacher."

However, she already has a word of advice she would like to share with young urologists: "You have to identify your field of interest early and pick your curriculum as soon as possible, because the journey is long and strewn with pitfalls. You have to be ambitious and daring; nothing is innate. At best, you have a mentor who teaches you what they know, helps you to the top, and lifts you up when you have fallen down. Furthermore, I am convinced that hard work and integrity go hand in hand."

"I feel like I am useful and that I have done my duty when a patient tells me, 'Thank you, doctor. I am living again."

"Young people should be encouraged to pursue an academic career in urology. This is essential for the sustainability of our specialty. This is one of the roles academic professors should fulfil. This must be done with benevolence while maintaining a high level of requirement."

Prof. Morgan Rouprêt (FR), chairman of the EAU Section of Oncological Urology (ESOU), met with Prof. Phé to present her with the EAU Crystal Matula Award. Go to the EAU21 Congress Platform and check out the video!

Urine biomarkers for treatment response

Considerable unmet biomarker potential exists in the treatment of bladder cancer

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Of the various sources of biomarker material available for prognostic and predictive investigation in bladder cancer (BCa), urine has the strongest rationale for study. It is readily available, easy to collect in large quantities, and provides a non-invasive source with direct tumour contact. This has led to a deluge of urine-based biomarkers, but most have been developed for the diagnosis and surveillance of BCa, with relatively few having sufficient accuracy to predict therapeutic response.

Intravesical immunotherapy with Bacille Calmette-Guérin (BCG) is in most need of a 'marker of treatment response.' BCG is the mainstay treatment for intermediate and high-risk non-muscle-invasive BCa (NMIBC). While highly effective when used correctly[1], there are various nuances that clinicians need to be aware of when using BCG to obtain the best result for our patients, including appropriate dosing and scheduling, and how to tailor the therapy to avoid unnecessary toxicity. A marker of response to BCG would thus be invaluable and many have worked towards this goal. Unfortunately, as recognised in a recent review, an international panel concluded that the best markers of response remain clinicopathologic factors such as tumour stage, grade, size, presence or absence of carcinoma in situ, focality and recurrence history. [2]

A recent advance in NMIBC has been the adoption by the US Food and Drug Administration (FDA) of unified definitions to aid in novel, bladder-sparing therapeutic developments and single-arm trials in high-risk NMIBC [3,4]. The occurrence of high-grade disease within 6-12 months after receiving adequate BCG denotes a BCG 'unresponsive' state. [3,4] As drugs are studied and approved during this advance, markers of treatment response become ever more important to allow us to appropriately select personalised treatments for patients.

"Significant progress has been made in identifying immunohistochemistry-based protein signatures in pre-neoadjuvant chemotherapy-treated MIBC specimens."

Cytokines

Several candidate markers studied in the preclinical setting primarily exploited the mechanism of BCG therapeutic response. [5] Interleukin (IL)-8 is one of the first cytokines expressed in the urine after BCG therapy. In a pilot study of 20 patients with NMIBC or upper tract urothelial carcinoma, Thalmann et al. profiled IL-8 expression in voided urine at 6 hours post-BCG instillation. Patients with high IL-8 expression had lower rates of recurrence and progression. [6] These findings were confirmed in a subsequent study, which identified IL-18 as another candidate cytokine with predictive capacity for BCG outcomes. [7] Additionally, when investigators profiled urinary Th1 response after BCG [8], failure to detect IL-2 during induction was associated with a shorter time to recurrence and progression.

Because BCG immunogenicity is complex and nonspecific, single candidate markers alone may be unreliable prognostic tools. We thus measured levels of 12 mechanistically relevant urinary cytokines in 130 patients with intermediate and high-risk NMIBC at our institution using an enzyme-linked immunosorbent assay (ELISA) at baseline and at specified time points throughout BCG therapy. [9] The final Cytokine Panel for Response to Intravesical Therapy (CyPRIT) nomogram was generated, including 9 inducible cytokines after BCG instillation (IL-2, IL-6, IL-8, IL-18, IL-1ra, TRAIL, IFN-γ, IL-12[p70], and TNF-α), which predicted the likelihood of recurrence with 85.5% accuracy (95% CI 77.9-93.1%).

"Use of UroVysion FISH is supported by the AUA Guidelines for assessing the response to intravesical BCG."

In addition to induced cytokine expression in the acute phase after BCG therapy, it has also been proposed that high-baseline, pre-treatment levels of certain cytokines may promote tumorigenesis and progression. We profiled a broad panel of cytokine expression in urine samples and peripheral blood leukocytes at baseline prior to BCG. [10] Indeed, expression of IL-8 in urine was associated with recurrence in BCG-treated patients, with patients who had higher baseline urinary IL-8 levels experiencing a 4-fold increased risk of tumour recurrence (HR 3.72, 95% CI 1.49-9.28, P=0.005). High-baseline IL-8 expression in peripheral blood leukocytes similarly correlated with disease recurrence. This predictive capacity of urinary IL-8 was subsequently verified independently in a separate pilot trial of NMIBC patients treated with BCG ± intradermal HS-410. [11] Taken together, these studies confirm IL-8 as a putative negative pre-treatment prognostic marker for BCG response.

FISH assay

A fluorescence in situ hybridisation (FISH) assay which detects aneuploidy in chromosomes 3, 7, and 17 and loss of the 9p21 locus in voided urine samples (UroVysion®) has been approved by the FDA as an adjunct to cystoscopy for screening patients with haematuria as well as for the surveillance of patients with a history of BCa. Investigators at the Mayo Clinic (US) studied 37 patients primarily receiving BCG for NMIBC: all 12 patients with positive post-treatment UroVysion FISH suffered a tumour recurrence, with over half being muscle-invasive (MIBC). [12] Positive post-treatment UroVysion was confirmed to be a predictor of recurrence in several other independent studies with variable adjuvant intravesical agents for NMIBC. [13-16]

Our group subsequently investigated the role of FISH as a dynamic marker at various time points to predict recurrence and progression in NMIBC patients treated with induction and maintenance BCG. In a cohort of 126 patients, those who had a positive FISH result during therapy were 3-5 times more likely to develop recurrence and 5-13 times more likely to be faced with progression in comparison with patients with negative mid-treatment FISH. [17] This was subsequently validated in an independent, multi-centre trial where FISH was predictive of recurrence and/or progression events at baseline (HR 2.59, 95% CI 1.42-4.73) prior to the 6th induction instillation (HR 1.94, 95% CI 1.04-3.59) and at 3-month follow-up (HR 3.22, 95% CI 1.65-6.27). [18] While not specifically FDA-approved for this indication, use of UroVysion FISH is supported by the AUA Guidelines for assessing the response to intravesical BCG. [19]

The identification of so-called 'molecular BCG failure' patients, defined as positive FISH at 6 weeks and 3 months with negative 3-month cystoscopy, has tremendous clinical relevance to the identification of those at the highest risk of BCG failure with continued therapy. Patients with such a molecular BCG failure have significantly higher rates of recurrence and progression than patients with a negative FISH and may be candidates for early enrolment into clinical trials that compare novel agents with the continued standard of care BCG therapy. [20]

Unmet needs and future directions

Despite the candidate predictive urine markers mentioned above, considerable unmet biomarker potential exists in the treatment of BCa. Clearly in times of BCG shortage, alternative intravesical therapies such as with chemotherapy are increasing in use. Additionally, with emerging intravesical and systemic therapeutic options for BCG unresponsive disease, as well as immunotherapeutics and antibody-drug conjugates with proven efficacy in earlier disease states, there is an obvious need for growth in our biomarker armamentarium.

A viable option is to translate available tissue-based predictive protein and molecular biomarkers into urine assays. Targeted exon sequencing of pre-treatment NMIBC tumours identified ARID1A mutations as being predictive of BCG failure. [21] Additionally, recent thorough molecular classification of NMIBC has correlated candidate molecular subtypes to innate sensitivity and resistance to BCG therapy. [22] This is in addition to the well-characterised molecular subtypes of MIBC with the ability to predict response to systemic chemotherapy. [23] Sensitive biomarkers to predict complete clinical response to intravesical and systemic therapies would have tremendous implications on bladder preservation. The Southwest Oncology Group (SWOG) 1314 trial prospectively profiled the ability of the COXEN tissue-based genetic classifier to predict complete pathologic response to neoadjuvant cisplatin-based chemotherapy. [24] As sequencing technology becomes more refined and clinically applicable, urine-based genetic material (exfoliated tumour cells, cell-free DNA, exosomes, etc.) may prove a viable source for molecular subtyping and predictive biomarker development.

Using the clinical cohort from our CyPRIT study, collaborators at Cedars Sinai (Los Angeles, US) studied the Oncuria™ test, which measures 10 cancer-associated biomarkers. [25] They found that pre-treatment urinary concentrations of MMP9, VEGFA, CA9, SDC1, PAI1, APOE, A1AT, ANG and MMP10 were increased in subjects with disease recurrence. A combinatorial predictive model of treatment outcomes reached an area under the receiver operating curve of 0.89 (95% CI: 0.80 – 0.99), outperforming any single biomarker, with a test sensitivity of 81.8% and a specificity of 84.9%. Patients with higher urinary levels of ANG, CA9 and MMP10 had a significantly higher risk of disease recurrence.

"As novel agents transition from (...) systemic therapies with nonspecific targets and host responses to targeted therapeutics, we expect biomarkers to become equally predictable."

Additionally, significant progress has been made in identifying immunohistochemistry (IHC)-based protein signatures in pre-neoadjuvant chemotherapy-treated MIBC specimens. These signatures that are predictive of pathologic response [26] could rationally be profiled in pre-treatment urine specimens using high-fidelity ELISA-based platforms.

Lastly, we can presume there exists a predictive biomarker rationale for characterising the expression and molecular constitution of therapeutic targets. For example, UroSEEK is a urine-based molecular assay designed for detection and surveillance of BCa. It detects alterations in 11 commonly mutated genes, including TERT, FGFR3, PIK3CA, TP53, HRAS, KRAS, ERBB2, CDKN2A, MET, MLL, and VHL [27], most of which are druggable targets with agents that have been actively studied in clinical trials or that have recently received FDA approval.

Conclusions

There are no current urine biomarkers FDA-approved for predicting therapeutic response along the spectrum of NMIBC or MIBC. Off-label use of the FISH assay (UroVysion®) in voided specimens of patients with NMIBC undergoing treatment with intravesical BCG has a predictive capacity and is supported by the AUA Guidelines. The most promising preclinical evidence of urine-based predictive biomarker potential in the NMIBC setting involves the profiling of baseline-and-elicited-cytokine response to BCG therapy. As novel agents transition from intravesical and systemic therapies with nonspecific targets and host responses (i.e. BCG and cytotoxic chemotherapies) to targeted therapeutics (monoclonal antibodies and antibody-drug conjugates), we expect biomarkers to become equally predictable and precise.

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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.

Saturday 10 July, 13.15 – 14.15 CEST
Live from the studio: Thematic Session 09
Urinary biomarkers: Are we there yet?
Virtual room 3

Systemic Treatment:

How to choose the right treatment for the right patient

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As a result of the publication of the Stampede trial's data from its "Docetaxel Comparison", 2015 was a vintage year for patients with newly presenting metastatic prostate cancer (mHNPC). This confirmed the positive effects of combination treatment with Androgen Deprivation Therapy (ADT), shown previously by the CHAARTED trial but not supported by the previously published GETUG-15 trial. Stampede's "tie breaker" effect changed the international standard of care for patients with mHNPC who are fit to receive chemotherapy.

Further "vintages" have followed year-on-year, with serial high-quality publications from international trials confirming the benefit of combining ADT with Novel Hormonal Agents (NHA) using Abiraterone (+prednisone), Enzalutamide and Apalutamide. It is now clear that there is substantial benefit for most patients with this condition when they receive combination treatment as a first-line therapy. However, the question, currently unresolved is "which agent should be combined with standard ADT for which patient?"

Systemic Agents in Clinical M0 Disease
In men with newly-diagnosed, high-risk clinically localised prostate cancer (M0N0/N+) the case for additional systemic therapy is currently unproven. The GETUG-12 trial of ADT+Docetaxel reported an 8% benefit for metastasis-free survival (MFS), a direct surrogate for actual survival, at 12 years but the question remains, should this justify treatment for all high-risk M0 cases given the known toxicities of the therapy?

Stampede's M0 Doetaxel comparison has also reported its findings at the 6.5 year point. The hazard ratio for benefit was virtually identical to that for GETUG-12 but survival was not significant as the trial was too immature. The suggestion is that both studies will ultimately show similar long-term results. Therefore, at the current time the general use of this therapy for clinical M0 patients is not supported by the available evidence. For NHAs in this setting the data from trials is awaited. These hold the promise of future benefit and since the studies in this area have focused on a two year treatment window in addition to standard of care (SOC) radiotherapy+ADT, treatments should be well tolerated. The first results from these studies are expected in 2021, with the tantalising prospect that the SOC may change yet again in high-risk M0 CaP.

"Differential toxicities are an important consideration in choosing therapy."

Men with M0 disease exhibiting castrate resistance (M0CRPC) who have a rapid PSA doubling-time(PSADT) have a high risk of early M1 progression. The information from three large-scale trials studying the effects of early vs delayed intervention in this condition have shown that the early addition of NHA is beneficial. The "SPA" studies (Spartan: Apalutamide, Prosper: Enzalutamide and Aramis: Darolutamide) showed separately that the early addition of NHA extended the time to treatment failure and improved survival. This treatment approach is licensed and is now recommended by international guidelines. An important consideration here is the definition of "M0" CaP when choosing this therapeutic approach: in selecting patients all three trials used standard imaging with isotope bone scan and CT, not PSMA-based imaging. In the Spartan trial a post-hoc analysis showed that a high proportion of men had PSMA positivity but the benefit of treatment was sustained notwithstanding when the bone scan/CT was negative. It is therefore important to base treatment decisions in this setting on conventional imaging, not novel PSMA-based methods.

Systemic Therapy in M1HNPC
The clinical efficacy of combination treatments in M1CaP whether with Docetaxel or NHAs is at its greatest in the hormone naïve state rather than the castrate resistant setting. Serial studies have confirmed that the early use of ADT combinations in mHNPC confers a survival benefit of approximately 16 to 18 months. When similar combinations are used following hormone escape this benefit is much smaller, being between 2.5-4.5 months. Thus, early combined treatment either with Docetaxel or NHAs is now the international standard of care for M1HNPC. However, the decision as to which combination should be used is less clear, depending on various factors, including relative drug efficacy, toxicity, duration of therapy, drug cost/availability, licence indications and importantly, patient/clinician preference.

Drug Efficacy
The two trials with the greatest statistical power using Docetaxel, CHAARTED and Stampede both showed clear benefit for ADT+Docetaxel but their selection criteria were different. CHAARTED had a "volume" criterion based on a critical number of 4 bone metastases with a requirement for one metastasis to be outside the axial skeleton (but without recognition of lymph-node status). In addition, a significant proportion of the trial population were drawn from men whose disease had progressed, having failed radical local treatment.

By contrast, Stampede's Docetaxel comparison recruited "all-comers" without volume/burden consideration and >90% were untreated primary M1 cases. Both trials showed substantial survival benefit accompanied by other reductions in important clinical events such as clinical SRE's. These results were consolidated and confirmed by a subsequent individual patient data meta-analysis of all 3 aforementioned Docetaxel trials. [1] But what of the "volume/burden" question? This was resolved by a post-hoc study of Stampede data involving a process of centralisation, analysis and categorisation of all M1 staging scans using CHAARTED criteria. This showed that there was no "volume/burden" effect: patients in both categories accrued benefit and furthermore, using such criteria excluded approximately 40% of patients from treatment which would otherwise have been potentially beneficial. [2]

NHAs have also been shown to have a clear benefit in newly presenting M1 patients. The first studies, Latitude and Stampede, published synchronously in 2017, showed clear benefit and these have been followed by similarly positive studies using Enzalutamide and Apalutamide. The comparative benefit with use of these agents is remarkably similar, with results showing clear benefit for survival and other important clinical events including failure-free survival and clinical SRE's. These agents clearly work and they are generally well-tolerated, albeit with inter-individually different side-effects when compared to chemotherapy.

The controversy relating to eligibility using "risk" profiling in NHA's was similar in many regards to that with Docetaxel and "volume/burden". In the Latitude trial using Abiraterone, inclusion was predicated on an arbitrarily-chosen risk stratification: patients had to have 2 of 3 of either bone metastases, Gleason score 8-10 or visceral disease. Stampede's Arm G abiraterone comparison had no such bar to inclusion. A further post-hoc analysis of Stampede's imaging data applying Latitude and CHAARTED risk criteria confirmed that the benefit from ADT/Abiraterone was seen across the board irrespective of "risk/volume" and again, approximately 40% of patients would have been excluded from treatment benefit had exclusion been applied. [3]

"CHAARTED and Stampede confirmed that men receiving a combination of SOC ADT with Docetaxel had a fall in QoL during the period of active treatment but this recovered within one year."

The systemic therapy "risk/volume" aspect was considered in further trials of the "amide" NHAs in a pre-specified analysis, confirming, as with Abiraterone, that there was potential benefit for all patients. Thus, patients suitable for treatment with NHAs should be offered this option irrespective of any risk/burden/volume categorisation.

The efficacy of both chemotherapy and NHAs raises the difficult question of which is best. There are unfortunately, no direct comparisons of the relative benefits of one therapy over the other. The best available data is from an opportunistic comparison within Stampede, rendered possible by the fact that the trial's Docetaxel and Abiraterone comparisons were recruiting simultaneously for a period, and from patients with similar M1 trial-entry characteristics. [4] Whilst this was not a direct "head-to-head" comparison its results have helped to inform practice, showing that when using Abiraterone PSA failure occurred significantly later than with Docetaxel. However, when considering other major clinical effects, notably metastatic progression and survival there was therapeutic equipoise (Fig 1). Thus, in practical terms, both treatments are equivalent but in reality there is one difference which may be influential: second-line treatment changes are often triggered by PSA progression. Therefore, treatment switches are likely to occur later with androgen-linked therapies than with chemotherapy. That said, the final choice of agent rests on consideration of patient eligibility for treatment and a decision about the duration of primary treatment that a patient wishes to have, given that Docetaxel has a shorter duration and that NHAs are given for a longer period of time until secondary progression. Added to this there are other considerations including relative toxicity, QoL, and cost/availability.

Drug Toxicity
Differential toxicities are an important consideration in choosing therapy. Neutropenia, with potential for sepsis occurs in approximately 8% of patients in Docetaxel trials and has been reported at a higher rate in real-world use. Its incidence can however be virtually negated by use of G-CSF. Effects on nails/hair are also prevalent, as is the significant rate of peripheral neuropathy. However, Docetaxel is very well-tolerated, it has a finite dose schedule (six 3-weekly cycles) and QoL returns virtually to normal in most men within 1 year. It is also safe to give this therapy to older men.

"Whatever the new dilemmas we now have to resolve, the improved survival and QoL engendered by these new systemic options is greatly welcomed."

For NHAs there are specific exclusions and some relative cautions. For the "Amides" a history of a cerebral event with a potential augmented seizure-risk is a contra-indication. Darolutamide is a relative exception to this: its different chemical structure is thought to reduce its ability to cross the blood-brain barrier. These drugs can also induce hypertension and fatigue is another problem for some men.

For Abiraterone the presence of hepatic dysfunction is a contraindication and because of the steroid requirement, weight gain, diabetes and other long-term steroid-related complications must be considered. Hepatic function must also be tested regularly whilst on treatment and because of the heightened ACTH effect sodium and potassium balance needs to be monitored. All NHAs will induce loss of bone and muscle mass with long-term use and bone protective agents should be used concomitantly, particularly when there is a high risk of osteoporosis. If NHAs are chosen, it should be understood that the duration of therapy is long-term i.e. until progression to CRPC or death, whichever occurs first. This is a significant consideration for patients and for the overall cost of therapy.

Systemic Treatment and QoL
In M1CaP, a condition which is ultimately fatal in most men, maintenance of QoL is fundamentally important. The number of studies reporting this long-term in mHNPC using Docetaxel or NHAs are relatively few but there are three important ones for consideration here. The first two, from CHAARTED and Stampede confirmed that men receiving a combination of SOC ADT with Docetaxel had a fall in QoL during the period of active treatment but this recovered within one year. In the third [5] QoL was compared between the Docetaxel and Abiraterone arms of Stampede. The recovery of QoL for Docetaxel confirmed its return, with substantial recovery within 12 months. However, the return to baseline QoL in Abiraterone patients was significantly better in the long-term. Similar studies using the amide-type NHAs are currently awaited.

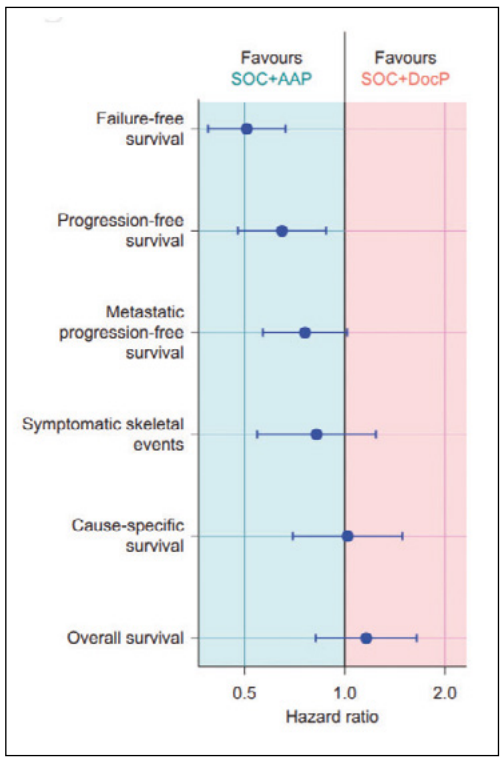

Figure 1: The relative effects of abiraterone and prednisone vs docetaxel in M1HNPC in the Stampede trial (ref: Sydes M et al Annal of Oncology 2018)

Summary
Since 2015 the options for effective systemic treatment of potentially lethal prostate cancer have changed serially, with better therapies and an improved understanding of how to sub-categorise patients and direct treatment. This new-found opportunity has brought with it uncertainty regarding which therapy to use. In some cases the choice is clear and straightforward but for the majority it is nuanced, depending on multiple factors predicated on clinical and social factors and the availability of specific agents in different health-care systems.

Whatever the new dilemmas we now have to resolve, the improved survival and QoL engendered by these new systemic options is greatly welcomed. And of course, there are new "vintages" on the way, with the prospect of early PARP inhibition and PSMA radionuclide-linked therapies emerging on the horizon. Clinicians and patients alike welcome these positive steps and the continued improvement in understanding and treating this common and distressing condition.

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Sunday 11 July, 11.45 – 13.15 CEST
Live from the studio: Plenary session 05
Treatment for metastatic hormone-sensitive prostate cancer
Virtual room 1

Telemedicine in office and outpatient urology

Considerations for urologists as pandemic has accelerated adoption

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The current COVID-19 pandemic caused a rapid and grievous global health emergency. That led to an enormous pressure on our healthcare systems, disturbance of our professional activities with severe economic consequences, and dramatic changes in our daily lives. Strict controls on movement and socialising have been enforced by many countries in an effort to control virus dissemination. These measures had an inevitable impact on the way we practice clinical medicine and the expectations of our patients.

The vaccination programme against COVID-19 throughout Europe is expected to bring a great relief to this unparalleled public health, social, and economic condition. Still, our priorities as urologists even under this unprecedented situation are to prevent our patients from COVID-19 contamination, protect ourselves as healthcare professionals, and deliver optimal urological care. A great part of urological diseases concern patients at the highest risk of adverse outcomes from COVID-19 due to advanced age and male gender.[1] Avoiding unnecessary medical visits in the office, outpatient clinics, and home emergency calls appears a reasonable alternative. That would reduce unneeded contacts, protect patients, and decrease the burden of care and consumption of resources.

In this regard, one of the more appealing solutions has been the increasing interest in telemedicine. According to the WHO, telemedicine focuses on the distance as a critical factor for delivery of individual health care services using technologies.[2] It offers a broad range of applications and possibilities, including live videoconferencing, transmission of recorded data, and remote patient monitoring supported by mobile devices such as cell phones, tablet computers, or wearable devices. Accordingly, telemedicine may transform a part of the standard face-to-face health care to a distance delivery of health care services with the same efficiency and, hopefully, with reduced healthcare costs. [3]

On the other hand, the "Virtual Urologist" needs to conquer the trust and thus the acceptance of urology patients, especially the more elderly who face adaptation issues with the new technologies. Moreover, some technical aspects of telemedicine need to be evolved and many ethical, legal, privacy, and billing issues are involved and need to be settled. Our aim as ESUO is to provide practical recommendations for appropriate and effective use of technology tools in urological telemedicine.

Applications and acceptance of telemedicine in outpatient and office urology

While a telephone consultation was the "non plus ultra" for many office urologists until the corona pandemic, the pandemic has changed many things. It has significantly increased patients' need for non-contact, virtual and internet-based communication. Additionally, the overload of telephones in many offices requires internet-based relief. The prerequisite is not only ease of use but also compliance with national and European data protection regulations. Here we report on practical experiences in our own office.

After several frustrating attempts with net-based appointment scheduling (too expensive and too complicated), we introduced a system for video consultation and data-protected chat in the wake of the pandemic. The access is done either by an invitation by the urologist which allows the patient to create a password-protected account or by a widget on the office-homepage. This request must be confirmed by the urologist. Then, within the framework of a chat function, things like findings and laboratory value transmissions are possible in a data-protected manner. The patient can also request a video appointment, which is then assigned by the office. The system can be used by doctors and office staff via separate accesses with different authorizations, so that appointment requests can be processed by the office-staff.

This also leads to a relief of the eternally busy telephone. The acceptance of this system by patients, and not only the younger ones, is high. Above all, the independence from office hours and telephone is very much appreciated. Within a few weeks, we had enrolled over 200 patients in the system. For documentation purposes, the chat history can be transferred to a "Word" document with just a few clicks, which is then saved in the electronic patient file or printed out.

We also use the system to communicate with other offices: sending patient reports, laboratory results or ultrasound and X-ray images. Here, too, the system has proven to be fast and unproblematic. The communication with hospitals is much more difficult, because the firewalls used often do not allow any communication and the Electronic Data Processing (EDP) department is very skeptical about such systems. Unfortunately, clinics in Germany prefer to fax and phone. Another possible application has been found in communication with representatives of the pharmaceutical industry. Such systems are also conceivable for conducting online conferences or a virtual tumour board.

Overall, the introduction of internet-based and virtual communication in urological practice has proven its worth. Acceptance by patients is high, as is the potential relief for physicians and staff. However, the data protection and professional guidelines must be guaranteed. Furthermore, electronic and paperless office management is a great advantage.

Technical aspects: making the pieces work together

Telemedicine includes several different levels of interaction between the physician/surgeon and the patient, ranging from the simple remote consultancy and up to tele-surgery.[4] The more interaction, the higher complexity of the system required and relative technical requirements. Providing a remote consultation may rely on a simple phone call or, more recently, on web-conferencing software. In the fully developed, "ideal" telesurgery system, the surgeon should be provided with a sense of touch and might also project his appearance in that location, as if he was present in a different place.

In any case, a remote communication requires two systems to be connected and data to be transferred between them. As the data packages grow in volume, data-transfer rates need to be increased in order to avoid lag in the telecommunication. This is a technical aspect that is nowadays driving the wide spread of this technology, as long-distance connections rely on internet bandwidth and speed. Some telemedicine services like Babylon Health [5] rely on artificial intelligence to provide early diagnostics and optimise the workflow, even before being connected to an actual physician. While lag would be not relevant during a diagnostic conversation, it might be highly problematic during a remotely driven surgical procedure, where having enough bandwidth becomes critical.

The introduction of 5G is bringing today fresh air in this field, thanks to its transfer capability of 10Gbps (Gigabits per second), opposed to the actual 1Gbps offered by full band optic fiber connection. The possibility of performing remote surgery might open novel scenarios in the medical field. In a world that is facing a never-seen-before shortage of doctors [6, 7], challenging cases could be indeed operated with the active remote assistance of an expert. On the other hand, *teletraining* [4] is allowing the wide spread of high-quality education, which could increase the overall competence of young surgeons, thus providing more safety to patients on an unprecedented scale.

Use in the pre- and postoperative course for in-hospital patients

Telemedicine offers a variety of opportunities for patient-doctor interaction in the pre-, peri- and postoperative course for patients undergoing urological surgery.

During the current COVID-19 pandemic, telemedicine has been used for preoperative prioritization and triage of patients undergoing urological surgery. Bi-directional information flow has been necessary both for doctors following up on their patients' condition as well as for patients understanding their individual risk and the need for prioritised scheduling of surgeries. Prior to the pandemic, telemedicine had been explored for preoperative patient counseling. In a series of 32 patients that had undergone emergency treatment for urolithiasis, telemedicine consultation led to an alteration of the initial treatment plan in 12 patients (37.5%).

In the perioperative course, telemedicine has been explored for telementoring and telesurgery in minimally-invasive procedures. Most recently, a series on aquablation surgery found no differences for the main outcomes operative time, time to Foley catheter removal, hemoglobin drops, urinary retention, and adverse events between 21 telementor-guided and 38 on-site guided surgeries. In another recent feasibility study on telementoring for patients undergoing transurethral enucleation of the prostate, high evaluation scores were found for safety, efficacy, learning and connection quality of telementoring by both the mentor and the trainee.

In the early perioperative period, telerounds have been used by surgeons performing percutaneous nephrolithotomy. Satisfaction rates were reported as high by both surgeons (91%) and patients (73%).

In the postoperative course, telemedicine remote video visits for postprostatectomy patients have been compared to traditional on-site visits for efficiency, satisfaction, and costs. Equivalent efficacy was noted as measured by patient–provider face time. No significant differences were reported in patient perception of visit confidentiality, efficiency, education quality, or overall satisfaction. Video visits incurred lower costs, including distance traveled, travel time, missed work, and money spent on travel.

Taken together, telemedicine has successfully been implemented in selected scenarios in the course of in-hospital patients. While the current pandemic will give a significant boost, more robust data on its long-term efficacy, safety and health economics is needed.

Ethical and legal aspects

The advanced deployment of novel services has formed ethical and legal queries related to telemedicine. [8] The regulations vary among European countries, and an additional challenge for healthcare providers is the necessity to remain compliant with pre-existing laws and medical ethics codes. [9] While telemedicine itself is a rapidly growing sector of the healthcare industry in the era of COVID-19 pandemic, practitioners should follow applicable practice regulations at the facility, regional, and country levels. [10]

A flood of legislative activity has recently surrounded telemedicine. [11] Generally speaking, the same ethical and legal obligations exist for practicing telemedicine as for practicing in-person medicine, while any doubts arising during e-visit should deserve a traditional patient's appointment [12].

Major legal and regulatory considerations cover the following topics: a) informed consent to be obtained in real time prior any encounter (to information sharing, confidentiality, privacy and data protection, information security management), b) national or regional licensing (practicing across countries or districts), c) privacy and security of transmission and software (e.g. software vendors, storage providers, adequate patient's identification), d) proper electronic medical documentation and solutions in case of technological failures, e) conflicts of interest, f) malpractice insurance and reimbursement, g) protected health information (confidentiality and other aspects of the patient–professional relationship) [10-15]. As a consequence, there is a general tendency to first initiate an in-person visit with a patient to establish care (e.g. physical examination) prior to a telemedicine encounter taking place. There was also a position of telepresenter proposed, who is a healthcare provider (e.g., registered nurse or physician) physically available at the patient's location during a non-stationery visit. [11]

It is important to note, however, that some telemedicine papers have demonstrated no benefit and even harm, e.g. telemedicine providers prescribed more broad-spectrum antibiotics as reported by Uscher-Pines et al. [11, 16] Thus, telemedicine progress can be better measured when legal frameworks are introduced, national regulations are developed, more practitioners are trained, regular funding is committed, and long-term plans are developed [13].The use of telemedicine in developing countries has also been questioned ethically. [17] Clearly, using telemedicine in underserved countries to increase access to care brings great benefit, but it is questionable if it is the most effective use of scarce resources. [15]

Financial and practical considerations

The aspects of billing and coding are directly related to the legislative issues of telemedicine. Before the COVID-19 pandemic, the urologists' reimbursement was the most significant obstacle to the widespread adoption of telemedicine. [18] Over the course of last year, patients or insurance companies, almost universally, have provided payment for telemedicine services, usually comparable to an in-office consultation. It is uncertain the extent to which this practice will be continued post-pandemic.

Urologists usually charge patients directly or have special contracts with insurance companies on a fee-for-service basis. The physician must know that private insurance companies have individual coverage policies, and there is a limited number of patients that can enjoy all telehealth benefits.

Most outpatient and office urologists routinely perform an in-office ultrasound for urinary system surveillance as part of conventional patient care. Patients undergoing telemedicine visits have their surveillance studies done outside of the urologist's office, leading to loss of revenue from ancillary services, such as laboratory and radiology.

During the COVID-19 pandemic, the use of telemedicine reduced the direct contact between patients and urologists. Office urologists had already included telemedical approaches in their daily routine and used them more frequently than urologists from the hospital sector. [19] Outpatient urologists might thus consider expanding their services during the pandemic to take care of urological patients who would have been treated in the hospital under normal conditions. [20] By performing video visits urologists can reduce the financial strain on office practices during the pandemic.

In highly integrated healthcare systems in which fee for service medicine does not apply, telemedicine is provided to save money and increase efficiency or access. The majority of the reports estimating expenses demonstrated advantages for telehealth, [21-23] whereas a single trial reported a minimal difference favouring standard care. [24] Furthermore, telemedicine can limit patients' travelling, producing a meaningful decrease in carbon dioxide emissions and other atmospheric pollutants.

Conclusions

It is difficult to predict the long-term consequences of the pandemic on our social and occupational life. Social distancing may become a general rule for a long time and this situation, hopefully with a lower level of emergency, will likely affect and modify the organisation of our health care facilities of any type. In this context telemedicine constitutes a quite appealing alternative for the foreseeable future. Especially in urology, telemedicine appears to offer many potential advantages such as fewer patient contacts, lower infection rates among the health care staff, patient convenience and a reduction in transportation-related emissions. The acceptance by the patients and the potential relief for physicians and staff appear to be high. Moreover, there might be also economic benefits for the healthcare system.

However, the data protection and professional guidelines must be guaranteed. Our role is to define the position of telemedicine in everyday urological practice and to get familiar with all the needed technologies and provided tools for its optimal effectuation.

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

Saturday 10 July, 16.30 – 17.30 CEST
Thematic Session 13
Telemedicine in urology
Virtual Room 4

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Date of preparation: June 2021 CP-23983

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]

Genetics in male infertility

Determining underlying genetic basis for solution development

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Male infertility refers to a male's inability to cause pregnancy in a fertile female. It accounts for 40–50% of infertility cases and affects approximately 7% of men. The condition is multifactorial and presents heterogeneous phenotypic features.

Genetic factors are responsible for up to 15% of male infertility cases. It is necessary to determine the underlying genetic basis of male factor infertility to develop appropriate screens for abnormal phenotypes, and to discover more effective solutions for the problems of infertile couples. The most common genetic causes of male infertility include sex chromosome aneuploidies, Y chromosome microdeletions, gene polymorphisms and congenital absence of the vas deferens.

Klinefelter syndrome
Klinefelter syndrome is one of the most frequent cytogenetic anomalies found in infertile men. The most frequent type of karyotype present in men with Klinefelter syndrome is 47, XXY. The syndrome can also be related to mosaicism 46XY/47 XXY; also higher number of X chromosomes such as 48, XXXY; 48, XXYY or even 49, XXXXY and structurally abnormalities in sex chromosomes can be found. Notably, men with Klinefelter syndrome present hypogonadism, azoospermia, small testes, erectile dysfunction, and higher gonadotropin levels compared to normal and fertile men.

Patients with XX male syndrome (46, XX) are less common than Klinefelter syndrome. Uneven crossing over between X and Y chromosomes may result in an additional X chromosome bearing the SRY gene through a translocation process. Patients with XX male syndrome are infertile and may develop male external genitalia, micropenis, hypospadias and cryptorchidism.

Klinefelter syndrome is easily detected through conventional cytogenetic analysis but XX male syndrome requires molecular cytogenetic with SRY probe to be performed. Also, several X chromosome linked genes, such as AKAP4 and TGIF2LX, affect the ability of a man to have children.

"Klinefelter syndrome is easily detected through conventional cytogenetic analysis but XX male syndrome requires molecular cytogenetic with SRY probe to be performed."

Sperm aneuploidy
Male infertility is commonly due to deficiencies in the semen, and semen quality is used as a surrogate measure of male fecundity. However, the role of sperm chromosome level in male infertility remains unclear.

Normal karyotyping of blood cells, sperm DNA fragmentation and routine semen analysis cannot exclude the presence of chromosomal abnormalities in spermatozoa. The evaluation of autosome and sex chromosome aneuploidy in sperm of men with history of infertility and/or recurrent pregnancy loss (RPL) and/or failed in vitro fertilization (IVF) should be done routinely. Fluorescence in situ hybridization (FISH) technique based screening is recommended for investigating sperm aneuploidy in 13, 18, 21, X, and Y chromosomes.

Recent studies have focused in RPL, which affects 1–2% of couples. The ESHRE Guidelines defines RPL as having two or more consecutive pregnancy losses before week 20 of gestation. Dr. Ranjith Ramasamy and co-authors found that men with RPL had a greater percentage of sperm aneuploidy within the sex chromosomes and chromosomes 13,18, 21 (1.04% vs. 0.38%; 0.18% vs. 0.03%; 0.26% vs. 0.08%). In total, 40% of men with normal sperm density and motility had abnormal sperm aneuploidy in all the chromosomes analysed. Men with abnormal sperm density and motility had a higher proportion of sperm sex chromosome aneuploidy than men with normal density/motility (62% vs. 45%). Men with normal strict morphology (>4%) had lower rates of sex chromosome and sperm aneuploidy than men with abnormal strict morphology (28% vs. 57%). There was no association between sperm DNA fragmentation and sperm aneuploidy.

The conclusions of the study are:

- Men in couples with RPL have increased sperm aneuploidy compared with controls.
- A total of 40% of men with RPL and normal sperm density/motility had abnormal sperm aneuploidy.
- Men with oligoasthenozoospermia and abnormal strict morphology had a greater percentage of sperm aneuploidy compared with men with normal semen parameters.

"It is necessary to determine the underlying genetic basis of male factor infertility to develop appropriate screens for abnormal phenotypes."

Furthermore, it is important to identify reasons for failure after IVF and intracytoplasmic sperm injection (ICSI). One of the greatest challenges with ICSI is the identification of "normal sperm" for micro-manipulation. Selection of euploid spermatozoa could possibly improve the chances of these couples of successfully carrying a pregnancy to term. However, as yet no such technique is available. With current technologies, we can only identify sperm with grossly abnormal morphology rather than detecting underlying genetic abnormalities such as aneuploidy.

Preimplantation genetic screening (PGS) could also be useful in managing sperm aneuploidy by screening for genetically normal embryos that improve chances of successful implantation and pregnancy. Therefore, men presenting with recurrent pregnancy loss or recurrent unexplained failure with assisted reproductive techniques (ART) should consider sperm aneuploidy testing to determine an underlying etiology to enable better and informed reproductive choices.

FISH can detect the rate of aneuploidy in different samples including ejaculated, epididymal, and testicular sperm for diagnostic purposes in male infertility. Clinically, results from this screening tool can be used in genetic counselling of couples suffering from male factor infertility to make informed decisions concerning their ART cycles.

Y chromosome microdeletion
Mammalian sex chromosomes evolved from autosomes at least 180 million years ago. The first step in differentiation of the Y chromosome involved the acquisition of the testis determining gene followed by large-scale inversions and sequential suppression of recombination between the X and Y chromosomes in a stepwise fashion.

Human Y is an acrocentric chromosome composed of two pseudoautosomal regions (PARs), a short arm (Yp) and the long arm (Yq) that are separated by a centromere. The Y chromosome is an obvious area of interest in the study of male factor infertility because it contains many of the genes that are critical for spermatogenesis and the development of male gonads.

"It is critical that azoospermic and severely oligozoospermic men be tested for microdeletions, both for accurate diagnosis and genetic counseling before performing ART."

The AZF gene is one of the most investigated Y chromosome genes related to infertility. The prevalence of microdeletions in azoospermic men was found to range from 10%–15%, in oligozoospermic men the prevalence of microdeletions was 5%–10%. Infertile patients with AZF deletions showing at least minimal levels of spermatogenesis could have children through sperm aspiration followed by intracytoplasmic sperm injection. Unfortunately, the AZF deletion is inherited by the male offspring (AZFc region microdeletion). AZFc deletions cause approximately 12% of nonobstructive azoospermia and 6% of severe oligozoospermia. It is critical that azoospermic and severely oligozoospermic men be tested for microdeletions both for accurate diagnosis and genetic counseling before performing ART.

"Careful clinical observations coupled with detailed genetic information will give a different perspective to the field of androgenetics."

Translocations
Translocations can cause the loss of genetic material at the break points of genes, which can corrupt the genetic message. Autosomal translocations were found to be four to 10 times more likely in infertile males in comparison with normal males. Robertsonian translocations, which occur when two acrocentric chromosomes fuse, are the most frequent structural chromosomal abnormalities in humans, and they affect fertility in one out of 1,000 men. Although the prevalence of Robertsonian translocations is only 0.8% in infertile males (oligozoospermic and azoospermic men with rates of 1.6% and 0.09% respectively), this figure is nine times higher than in the general population. The translocations can result in a variety of sperm production phenotypes from normal spermatogenesis to an inability to produce spermatogonia. Due to the risk of passing on the translocation to offspring, fluorescent in situ hybridization, with additional probes added for common translocations, is recommended to determine the chromosomal composition of the sperm.

CFTR gene
The CFTR gene, located on chromosome 7, is mutated in 60%–90% of patients with congenital bilateral absence of the vas deferens (CBAVD). Sperm aspiration and ICSI are useful methods of treatment for men with the CFTR mutation as long as the female does not also carry the CFTR mutation. Partners who both carry the mutation should be advised to have PGD to avoid passing the abnormality to their offspring.

Careful clinical observations coupled with detailed genetic information will provide important insights into these unanswered basic questions and give a different perspective to the field of androgenetics.

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Monday 12 July, 12:00 - 13:00 CEST
Meeting of the EAU Section of Outpatient and Office Urology (ESUO)
Andrological tips and tricks for outpatient and office urologists
Virtual Room 3

Antimicrobial resistance: How to deal with the pandemic

The relevance of antimicrobial stewardship programmes

Dr. José Medina-Polo
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A primary concern for worldwide healthcare systems is the increasing prevalence of antibiotic resistance in hospital and outpatient settings. An estimated 700,000 mortalities occur annually due to unsuccessful antibiotic treatments, and that number is surging. The World Health Organization has declared that antimicrobial resistance is one of the top 10 global public health threats facing humanity. Antibiotics' widespread use is one of the reasons for the outbreak of microorganisms resistant to antibiotics. The highest antibiotic resistance is reported in low middle-income countries (LMICs), which have the highest antibiotic consumption.

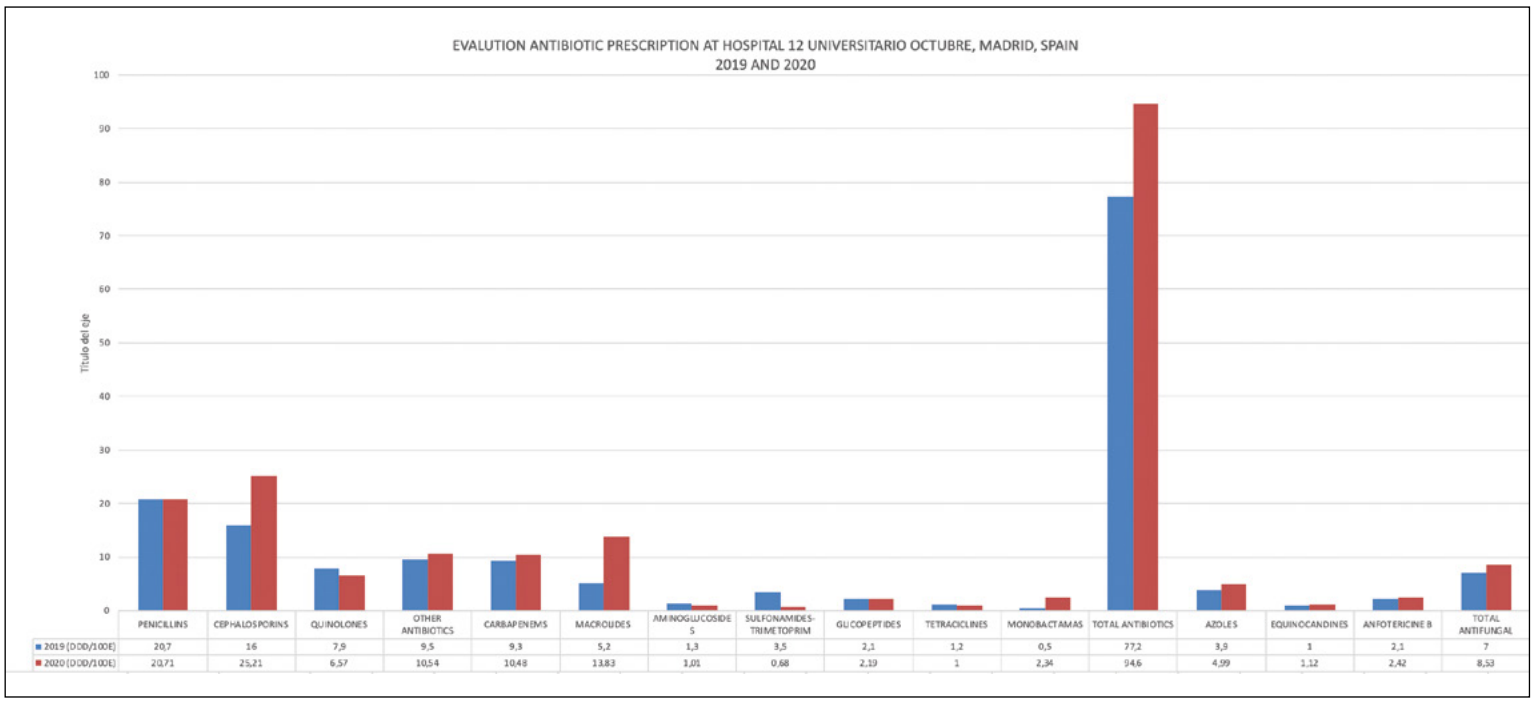

Figure 1: The evaluation antibiotic prescription at Hospital Universitario 12 de Octubre from 2019 to 2020

Furthermore, the SARS-CoVID-2 pandemic exacerbated the antimicrobial resistance pandemic, leading to higher consumption of antibiotics. It was estimated that more than 70% of patients hospitalised due to a COVID-19 infection, received antibiotics to treat secondary bacterial infections that represent a significant risk factor for adverse COVID-19 outcomes.

Enterobacteriaceae is among the most frequently isolated bacteria and the main bacteria isolated in urology. To treat infections caused by Enterobacteriaceae, systemic empiric antibiotic treatment with third-generation cephalosporins is commonly recommended. This group of antibiotics is also commonly prescribed for urinary tract infections (UTIs).

Prescription of antibiotics is not the only reason for the increase in antimicrobial resistance. Biocide-based products such as hand sanitisers and surface cleaners could also cause increased rates of antimicrobial resistance.

Cleaning hands is necessary. However, biocide products may affect the prevalence of antimicrobial resistance. Data from our hospital in Madrid which report the increase in antibiotic prescription and antimicrobial resistance during the pandemic are summarised in figures 1 and 2.

Multidrug-resistant organisms

Although multidrug-resistant organisms (MDROs) are increasing globally; healthcare-associated infections (HAIs) and MDRO infections must be evaluated locally. The revision of incidence must be carried out in each centre due to the variability of resistance with essential differences between continents, countries, and even centres in the same region. Therefore, based on clinical practice guidelines, each centre has to collect its data on the prevalence of MDRO and design protocols to prescribe empirical antibiotic therapy. These measures help optimise treatments and reduce complications and provide a better understanding of the development of resistance.

Urologists must be aware that MDRO infections are common and becoming increasingly familiar. One of the main activities in urology is to assess the characteristics of HAIs through studies such as the Global Prevalence in Infections in Urology (GPIU) and SERPENS which are developed and carried out by the EAU Section of Infections in urology (ESIU).

Treating MDRO infections is a challenging task and may require a multidisciplinary team. When managing patient treatment, urologists have to involve all diagnostic and therapeutic measures. Therefore, it is optimal to have urologists integrated into a multidisciplinary antimicrobial stewardship team comprised of the following:

- Urologists who are experts in the diagnosis and treatment of UTIs
- Nurses with expertise in the diagnosis and treatment of UTIs
- Clinical experts in the diagnosis and treatment of infectious diseases
- Microbiologist
- Hospital pharmacist with a specific training in infectious pathology, antimicrobial optimisation, and calculation of indicators on the consumption of antimicrobials

The team must develop a programme with continuous monitorisation of infections as this has demonstrated that it may optimise the management of infections. According to the standard regulating the implementation of the plan for the optimisation of the use of antimicrobials (PROA) in patients hospitalised in the Hospital Universitario 12 de Octubre from 2019 to 2021, the following measures are recommended:

1. Improve the clinical results of patients with UTIs
2. Minimise adverse events associated with the use of antimicrobials, including resistances
3. Reduce the consumption of antimicrobials, adapt the prescription to the infectious process, and optimise the duration of treatment
4. Reduce the incidence of multi-resistant strains
5. Make physicians aware of the importance of the correct use of antimicrobials
6. Promote the development of research projects
7. Promote the improvement of activities related to infection control, the use of antibiotics, and the appearance and spread of multi-resistant strains.
8. Optimise antibiotic use by ensuring that the appropriate antibiotic is administered at the correct dose and for the right duration

In our department, we have developed a programme with continuous monitoring and prevention of infections (figure 3). The observational study has led to a decrease in the global prevalence of HAIs in patients admitted in the urology ward, from 7.3% in 2012 to figures below 5% in 2019 and 2020.

Dealing with antimicrobial resistance

However, our data report a high prevalence of MDRO, up to 22.8% of cultures from the urology ward. Urologists have to play an essential role in implementing measures to deal with antimicrobial resistance pandemic in the context of antimicrobial stewardship programs. Antimicrobial stewardship programmes have the following principles:

- Regular training of staff in the best use of antimicrobial agents
- Ensure adherence to local, national or international guidelines
- Regular ward visits and consultation with infectious diseases physicians and clinical microbiologists
- Audit of adherence and treatment outcomes
- Regular monitoring and feedback to prescribers of their performance and local pathogen resistance profiles.

The improvement in the use of antibiotics has reduced the development of antimicrobial resistance, but also reduces the cost associated with hospitalisation and the pharmaceutical cost. An effort to control antimicrobial resistance and prescribe antibiotics more precisely is also recognised as a quality programme contributing excellence to daily clinical care.

The prescription of antibiotics has implications in antibiotic prophylaxis as well. Prophylaxis must be prescribed according to the type of surgery, the degree of contamination in the surgical field, and the risk factors for infections. An adequate indication and selection of prophylaxis are not only associated with a lower incidence of infection but also show lower antibiotic prescription costs.

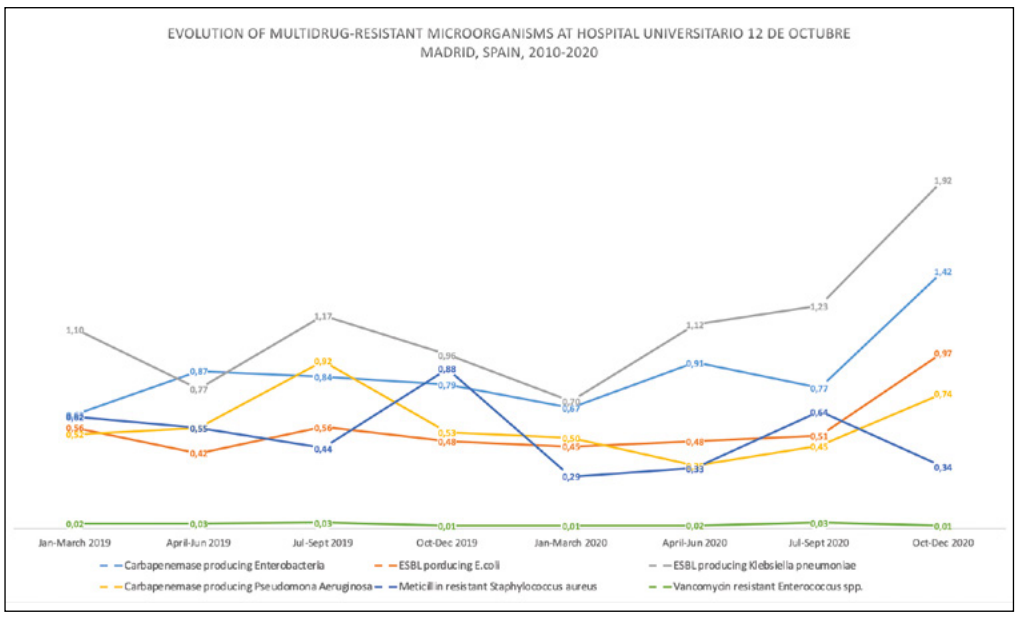

Figure 2: The evolution of MDROs at Hospital Universitario 12 de Octubre from 2010 to 2020

One of the main issues when dealing with MDRO is the prescription of adequate empirical treatment. Therefore, the management of antimicrobial resistance pandemic in a urological setting requires knowing risk factors for antimicrobial resistance microorganisms isolation, which may determine empirical antimicrobial therapy. In urological patients, immunosuppression, diabetes mellitus or high anaesthetic risk (ASA score III-IV), prior urinary infections and urinary catheter in the upper urinary tract are risk factors for presenting MDRO infections. Among urological patients, those with a catheter in the upper urinary tract (ureteral double-J stent, nephrostomy tube or percutaneous internal-external nephrostomy catheter) require special attention and show the highest prevalence of infections due to MDRO.

In conclusion, the urologist must be aware of the antimicrobial resistance pandemic and collaborate in antimicrobial stewardship programmes. The main actions to implement may be summarised in the following points:

- Review antimicrobial prescriptions and recommend adjustment
- Examine the evolution of microbial resistance
- Evaluate the results of the measures implemented
- Update and promote protocols for the treatment of the most frequent infectious conditions to contribute to optimising antimicrobial prescription
- Training of health professionals in the prevention and treatment of infections as proper use of antimicrobials
- Promote research related to infection and the use of antimicrobial
- Prepare an annual report with the outcomes of the indicators obtained, the evaluation of the results and proposal of new measures.

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

Saturday 10 July, 15.15 – 16.15 CEST
Thematic Session 12
Emerging threats by infectious diseases
Virtual Room 3

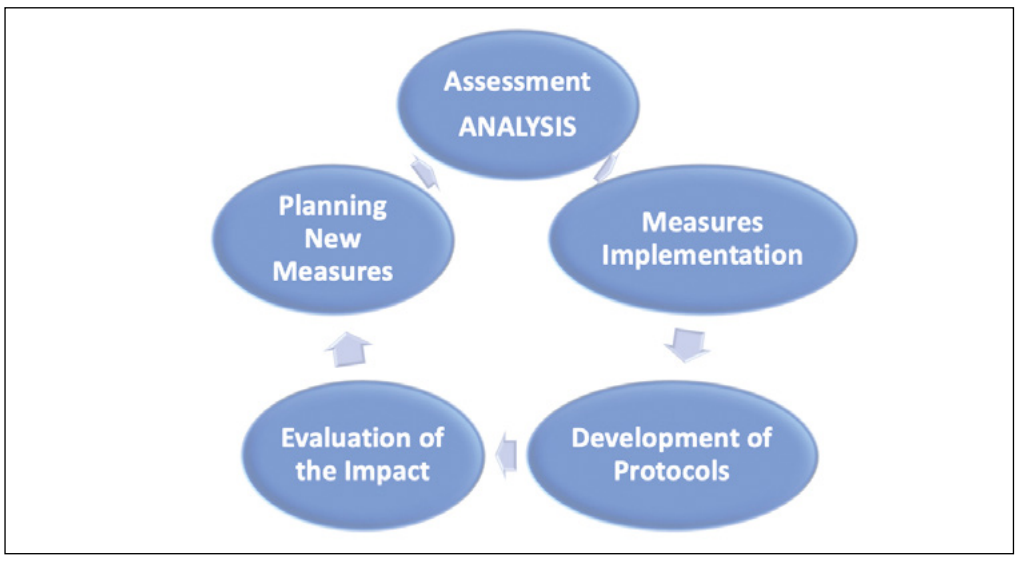

Figure 3: Continuous monitoring and prevention of infections

Transforming lives through sustainable business practices:

Surprising results from study comparing carbon footprint of single-use and reusable scopes

Research published in *The Journal of Endourology*, has shown that the carbon footprint of single-use scopes is comparable to reusable scopes[1].

The study analysed the typical life cycle and carbon footprint of the LithoVue™ Single-Use Digital Flexible Ureteroscope compared to a reusable flexible ureteroscope; obtaining data on product manufacturing, disposal, repairs and replacements. The results showed that the carbon footprint of LithoVue™ was 4.43 kg of CO2 per endourologic case compared to 4.47 kg of CO2 per endourologic case for the reusable scope.

"It did surprise me to learn that single-use scopes could have an equivalent carbon footprint to reusables. With a scarcity of data in this area, it's perhaps not surprising that such myths exist today, and we need to do more to educate ourselves on the true impact of our practices on the environment." **Michele Talso, Consultant Urologist, ASST Fatebenefratelli Sacco – Polo Universitario Ospedale Luigi Sacco Urology Department, Italy.**

Sharing data on the carbon footprint equivalence of single-use and reusable ureteroscopes is just one of the ways at Boston Scientific we believe challenging the status quo can help advance the discussion on climate change.

We are dedicated to transforming lives through innovative medical solutions that improve the health of patients around the world. That is why, our commitment to improving patient health comes with a responsibility to safeguard the planet. As we work to solve healthcare's challenges, we are taking action to reduce our environmental impacts, whilst continuing to develop innovative products to meet the needs of our customers and the patients they serve.

Our global commitment
Our goal is to achieve carbon neutrality across our manufacturing and key distribution sites by 2030, and we have set aggressive environmental targets, aligned to the United Nations Sustainable Development Goals, to cut our carbon emissions and reduce our climate impact.

Already, since 2017, we have reduced our global carbon footprint by 50 per cent and, by 2024, we expect to source or generate 100 percent of our electricity from renewable energy sources, significantly reducing levels of carbon dioxide and other greenhouse gas emissions that are linked to climate change.[2]

Sustainability at the product level
Whilst our life-saving products help millions of people worldwide, we recognise that they also have a carbon footprint.

Our C[3] strategy of cutting harmful emissions, converting to renewables and compensating for unavoidable emissions has helped us systematise our approach to make steady and significant improvements over the long term.

At our manufacturing sites, we adhere to internationally recognised programs such as Leadership in Energy and Environmental Design (LEED) or the ISO 50001 energy management system. Today, 42% of our global real estate is green.[2]

In Europe, all electrical power for our main distribution centre in the Netherlands, is sourced from renewable energy; resulting in significant decarbonisation of energy use in how we distribute our single-use products.

While our primary focus is on cutting energy use and converting to clean energy sources in our business operations, we are also piloting compensation projects for unavoidable emissions. Recently, we joined forces with Treedom, to offset the carbon emissions for all single-use scopes used by our customers in the EMEA region this year. To date, over 15,000 trees have been planted in Kenya, offsetting over 3,940 tonnes of CO2 over 10 years, whilst benefitting local communities.

Partnering on our journey
Although we are on track to achieving carbon neutrality by 2030, there is still a long way to go. It is only by sharing data with each other and working together with our sustainably-minded customers and partners, that we can achieve this goal.

Our Impact: 2020 Global Snapshot

- 67% reduction in greenhouse gas emissions since 2009
- 71% of purchased electricity from renewable sources
- 94% of solid waste diverted from landfills

Boston Scientific 2020 Performance Report

Boston Scientific
Advancing science for life™

Trees planted in Kenya provide source of local income and cleaner air for all

References:

1. Davis et al. 2018. Carbon Footprint in Flexible Ureteroscopy: A Comparative Study on the Environmental Impact of Reusable and Single-Use Ureteroscopes. Journal of Endourology Volume 32, Number 3. The comparative study did not include product packaging.
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Wirth: "This is my legacy"

An interview with the 2020 Willy Gregoir Medal Winner

By Loek Keizer

Prof. Manfred Wirth (DE) was the 2020 winner of the Willy Gregoir Medal for a significant contribution to the development of the urological specialty in Europe. The medal had previously been awarded to only the biggest names in urology, most recently Freddie Hamdy (2019), Vincenzo Mirone (2018) and Paul Abrams (2017).

This year, Prof. Wirth is also retiring from the EAU's Executive Committee, where he served as Treasurer and was in charge of the EAU's communications since 2004. We spoke to Prof. Wirth on this momentous occasion, after over fifteen years at the heart of the Association.

How did you first become involved in the EAU?
"I first got involved with the EAU when then-Secretary General Frans Debruyne approached me in the early 1990s. I already knew Frans well from the different urology meetings that we had both attended in previous years."

"In the summer of 1992 I was invited to join a meeting in Paris that would determine the long-term strategy of the EAU, to make it the association that it is today. Frans and his team must have thought that I would be of value to the Association!"

"I'm proud that we have not just the best urology journal in the world but a whole family of quality journals."

"From that point on, I was involved in the EAU's activities, working for its research section and the Video Committee. In 2004 I joined the Executive Committee as Treasurer."

How do you look back on your time on the Executive?
"With regards to my role as treasurer, I'm happy that the EAU is financially completely independent, able to finance an excellent central office, world-class and annually updated Guidelines, a whole range of meetings, specialised sections and also a Research Foundation. We made big steps to financial security since 2004."

"Over time, we managed to hold on to our money and invest in the right things. I have to thank Executive Manager of Business Affairs Maurice Schlief and his team for rising to the challenge and doing an excellent job supporting the EAU's ambitions."

"Regarding the EAU's communications: I'm proud that we have not just the best urology journal in the world but a whole family of quality journals."

"We recently saw the launch of the new journal EU Open Access, which is a significant development in how our scientific content is published and distributed."

"Being responsible for communications has also made me an ex-officio member of the EAU History Office. I'm proud of the research project that investigated the fate of our Jewish colleagues during the Second World War in *Urology Under the Swastika* (2017)."

"This was my idea, started at the DGU as a strictly German topic we brought it to EAU an enlarging its scope. This is something I'm particularly proud of, and it's an important and dark chapter in our profession's history that we must face."

The Willy Gregoir Medal is for significant contributions to urology in Europe. What is your proudest achievement in your field?

"This is very difficult to say. As an academic and a teacher, I'm proud to have worked with excellent colleagues, to have trained them to become masters in the field, heads of university departments, clinics and excellent researchers. Over the years I've motivated and guided people to prominent positions. I've trained more than fifty urologists. I think this is my legacy."

"It is a great honour to win this award, to join this group of esteemed colleagues. But I'm not retiring yet: I will keep working at Dresden University as a senior professor, and as a clinical consultant. I want to serve both patients and my younger colleagues with my longstanding experience, expertise, and practical knowledge."

"I might be going back to academia, but I also look forward to spend more time with my wife, our four children and our six grandchildren. My wife is happy that I will have a bit more time, and I'm happy too."

Watch the video of Prof. Wirth receiving the Willy Gregoir Medal by visiting our EAU21 Congress Platform!

Van Poppel: Champion of education and patient involvement

An interview with the Frans Debruyne Lifetime Achievement Award winner

By Loek Keizer

The 2020 winner of the Frans Debruyne Lifetime Achievement Award was Prof. Hendrik Van Poppel (Leuven, BE). The award is given for longstanding and important contributions to the activities and development of the EAU. Prof. Van Poppel most recently served on the EAU Executive as Adjunct Secretary General responsible for Education (2012-2021), and as Chairman of the European School of Urology (ESU) before that (2004-2012). We spoke to him on the occasion of his retirement from the EAU Executive and receiving this honour from the Association.

When and how did your involvement with the EAU start?
Then-Secretary General Frans Debruyne approached me when I attended a Davos winter symposium in 1997. I obviously knew Frans, who did his Medical School at my University in Leuven, beforehand from the EORTC GU group where he was Chairman for a couple of years and I was Treasurer. He invited me and engaged me in EAU teaching activities like Tenerife, Davos, and various ESU courses. He started the Guidelines Initiative with Bernard Lobel and Claude Abbou, where I got appointed in the Prostate cancer panel. I started to participate in the EBU-organised 'Rome course' that the EAU would transform into the current, fantastic EUREP, organised every year in Prague.

How do you look back on your time as Adjunct Secretary General?
I started under Per-Anders Abrahamsson, with Chris Chapple, Manfred Wirth and Walter Artibani in 2012. I quickly realised how the EAU really functioned, and I learned to value the hard work of a wonderful team of motivated enthusiastic people in the Central Office, professionally managed and coached by Executive managers Jacqueline Roelofswaard and Maurice Schlief. I felt it was like working together as a group of friends in the many face-to-face meetings and in up to three hour-long video-conferences.

As Adjunct Secretary General for Education I had the privilege to work with my great successor as ESU Chairman, Joan Palou, who together with EAU Education Office Manager Jacobijn Sedelaar-Maaskant did not really need my supervision but regularly came up with critical points to discuss in order to expand and strengthen the School's educational programme to the big well-oiled machine that is has become since. I also cherish the privilege to have worked with EAU Guidelines Office Chairman James N'Dow (and Guidelines Office Manager Karin Plass) who in no time restructured the Guidelines Office and upgraded it to where the EAU Guidelines are today: the best evidence-based urology guidelines in the world. I am also pleased to have been able to support him in allowing his Office to receive the financial support its work deserves.

I look back on the privilege of working with EU-ACME chairman Rien Nijman and EU-ACME office manager Beata Adamczyk who successfully elaborated on the EU-ACME system where he increased not only the numbers of participants among our members but also the quality of the educational sessions of the EAU. I was also privileged to work with EUSP chairman Vincenzo Mirone and EUSP coordinator Angela Terberg at the Scholarship program (EUSP), who defended and secured financial support from our treasurer for an expanding number of short visits, fellowships, and fostering collaboration with other organisations.

Last but not least, I look back fondly on working with Michiel Sedelaar who successfully integrated the ESRU into the Young Urology Office, investigated the undergraduate curriculum, steered the YAU and started a training initiative for future academic leaders in urology.

Will you remain involved in urology in the coming years?
When looking at other successful professional organisations like ESMO, I started to pay more and more attention to the involvement of the patients and their empowerment through their patient advocates and patient coalitions. Throughout Europe, many of these patient groups are well established for GU cancers, much less for non-oncological urological diseases. This is how we founded, with the help of Patient information senior coordinator Esther Robijn, the EAU Patient Advocacy Group (EPAG) where the major European patient organisations became members, like ECPC, EUomo, World Bladder Cancer Patient Coalition (WBCPC), International Kidney Cancer Coalition (IKCC), the World Federation for Incontinence and Pelvic Problems (WFIPP), the European Reference Network eUROGEN and others.

With Thorsten Bach and Esther Robijn the Patient Information Initiative (PII) was born: a group of young volunteers that spent their free time to adapt the Guidelines into lay language suitable for patients, and also to translate them into many European languages. The PII also features a number of absolutely superb animated videos. Together, EPAG and PII can start to increase patient involvement in our educational activities, something we are exploring at the moment.

The second issue to receive my attention in recent years is influencing policymakers, raising awareness of Urology and GU cancers in Brussels in the European Parliament and pressing the European Commission on the need of early detection of prostate cancer in well-informed healthy men. Patient support is crucial if we want to gain political support for our efforts to decrease the number of men that die from prostate cancer in the EU every year (i.e. 107,000 men). The aim is to get prostate cancer in the European Commission's Europe's Beating Cancer Plan, as led by Commissioner Stella Kyriakides. So, I am committed in the coming years to further elaborate and prepare the instalment of a formal EAU Patient Office and I will be devoted to EAU's European affairs by leading the EAU's newly-created EU Policy Office.

What are your thoughts on winning this award? You will join previous winners like Francesco Montorsi, Per-Anders Abrahamsson and Laurent Boccon-Gibod:

I am very much humbled when I see my name added to this list of remarkable and globally-renowned scientists and experts. I see there are two former Secretary Generals, and only one Adjunct Secretary General, so I am the second to receive this award in that function. And the third Belgian... Many others would deserve a Frans Debruyne Life Achievement award, and I am really honoured and most pleased to receive this award, with the name of the Godfather of the modern EAU, and... a good friend of mine, Frans Debruyne.

Prof. Frans Debruyne (BE) himself bestowed the Frans Debruyne Lifetime Achievement Award on Prof. Van Poppel. Visit the EAU21 Congress Platform and watch the video!

What is the role of TUR in MIBC?

Going forward in the field of advanced bladder cancer in 2021

Dr. Alejandro R. Rodríguez
Secretary General
Confederación Americana de Urología (CAU)
Rochester (US)

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Bladder cancer is the 10th most diagnosed cancer worldwide, with approximately 573,000 new cases and 213,000 deaths. It is more common in men than in women, with a respective incidence and mortality rate of 9.5 and 3.3 per 100,000 men globally, approximately 4 times more than among women. [1]

In 2021, there will be an estimated 83,730 new cases and 17,200 new deaths due to bladder cancer in the USA. It is the 4th most common cause of cancer in men just behind prostate, lung/bronchus, and colon/rectum cancer. [2]

"TUR for MIBC will not only give you the clinical stage and grade of the primary tumour, but it will also play an important role in identifying the type of histology."

Given that the median age at diagnosis is 73 years, medical comorbidities are a frequent consideration in patient management. The clinical spectrum of bladder cancer can be divided into 3 categories that differ in prognosis, management and therapeutic aims. The first category consists of non-muscle-invasive diseases, for which treatment is directed at reducing recurrences and preventing progression to a more advance stage. The second group encompasses muscle-invasive diseases. As for patients in this group, it should be determined whether the bladder should be removed or if it can be preserved without compromising survival and whether the primary lesion can be managed independently or whether the patient is at high risk for distant spread requiring systemic approaches to improve the likelihood of cure. The critical concern for the third group, which consists of metastatic lesions, is how to prolong and maintain quality of life.

Bladder cancer staging
The goal of transurethral resection of bladder tumour (TURBT) is to correctly identify the clinical stage and grade of disease while completely resecting all visible tumour. Therefore, an adequate sample that includes bladder muscle should be obtained in the resection specimen. A small fragment of tumour with few muscle fibres is inadequate for assessing the depth of invasion and guiding treatment recommendations.

The most used staging system is the tumour, node and metastasis (TNM) staging system by the American Joint Committee on Cancer (AJCC). [3] Approximately 75% of newly detected cases are non-muscle-invasive disease (NMIBC) and 25% are muscle invasive (MIBC). Clinical investigation of the specimen obtained by TURBT is an important step in the diagnosis and subsequent management of bladder cancer. The modifier "c" before the "stage" refers to clinical staging based on bimanual exam under anaesthesia, TURBT and imaging studies. A modifier "p" would refer to pathologic staging based on cystectomy and lymph node dissection.

Muscle-invasive bladder cancer (MIBC)
MIBC (T2) is defined as a malignant extension into the detrusor muscle while perivesical tissue involvement defines a T3 disease. Extravesical invasion into the surrounding organs (the prostatic stroma, seminal vesicles, uterus, vagina, pelvic wall, abdominal wall) delineates T4 disease. The depth of invasion is the most important determinant of prognosis and treatment for localised bladder cancer.

Several workup procedures are recommended to accurately determine the clinical stage of MIBC. Laboratory studies, such as a complete blood cell count and chemistry profile, including alkaline phosphatase, must be performed, and the patient should be assessed for the presence of regional or distant metastases. This evaluation should include chest imaging (CT, x-ray, or FDG-PET/CT) and evaluation for suspected bone metastasis in patients with symptoms or clinical suspicion of bone metastasis (elevated alkaline phosphatase, focal bone pain). Chest imaging with CT is preferred over chest imaging with X-ray. This is based on studies that showed a better sensitivity of CT for detection of metastatic disease. Bone imaging may include a bone scan, MRI, or FDG-PET/CT. Imaging studies help assess the extent of the tumour spread to the lymph nodes or the distant and regional extent of the disease. Unfortunately, CT-scans, ultrasounds and MRIs cannot accurately predict the true depth of invasion (see figure 1 and 2).

ROLE of TUR in MIBC
Although the overwhelming majority of muscle-invasive tumours are high-grade urothelial cancer, TUR for MIBC will not only give you the clinical stage and grade of the primary tumour, but it will also play an important role in identifying the type of histology (especially variant histology) that could change your management approaches to MIBC. We need to remember that approximately 10% of the bladder tumours are non-urothelial (non-transitional) carcinoma. These pathologic entities include mixed-histology, pure squamous, adenocarcinoma, small-cell tumours, urachal carcinoma, or primary bladder sarcoma. The presence of histologic variants in urothelial carcinoma should be documented as data suggest that the subtype may reflect the risk of disease progression and a different genetic etiology and may subsequently determine whether a more aggressive treatment approach should be considered. In some cases with a mixed histology, systemic treatment may only target cells of urothelial origin and the non-urothelial component can remain. The 4th edition of the World Health Organization (WHO) classification of tumours has classified these histologic subtypes into the following: nested, including large nested; microcystic; micropapillary; lymphoepithelioma-like, plasmacytoid/signet ring cell/diffuse; sarcomatoid; giant cell; poorly differentiated; lipid-rich; clear cell; infiltrating urothelial carcinoma with divergent differentiation. [4]

For MIBC of urothelial origin, further treatment following initial TURBT is often required, although selected patients may be treated with TURBT alone. TURBT alone may be an option for patients with stage-II disease who are not candidates for cystectomy. TURBT alone may be curative in selected cases that include solitary lesions less than 2 cm in size that have minimally invaded the muscle. These cases should also have no associated in situ component, palpable mass or associated hydronephrosis. If primary treatment consists of TURBT alone, patients should undergo an aggressive re-resection of the site within 4 weeks of the primary procedure to ensure that no residual disease is present. If repeat TURBT is negative for residual tumour, the patient can be managed conservatively with repeat endoscopic evaluations and cytologies every 3 months until a relapse is documented. The stage of the lesion documented at relapse would determine further management decisions. [5-7]

"This modality is endorsed by multiple international organisations that have developed evidence-based consensus guidelines and recommendations."

TUR for MIBC is also important in bladder preservation options. All bladder-sparing approaches are based on the principle that not all cases require an immediate cystectomy, and the decision to remove the bladder can be deferred until the response to organ-sparing therapy is assessed. Bladder-preserving approaches are reasonable alternatives to cystectomy for patients who are medically unfit for surgery and those seeking an alternative to radical cystectomy.

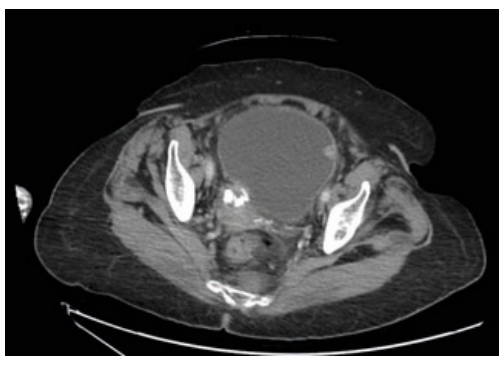

Figure 1: A bladder tumour of 2 cm. Seemed non-invasive; however, it was a T2 high-grade

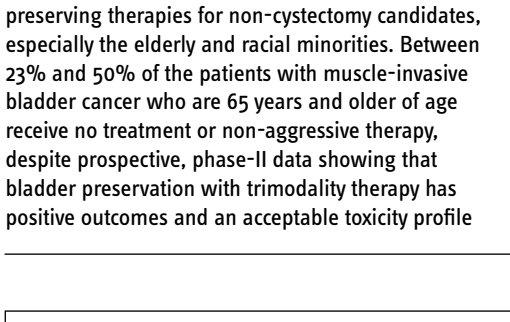

Figure 2: A bladder tumour of 8 cm. Seemed muscle-invasive; however, it was a Ta low-grade

The decision to use a bladder-preserving approach should be partially based on the location of the lesion, depth of the invasion, size of the tumour, status of the "uninvolved" urothelium, and status of the patient (bladder capacity, bladder function, comorbidities). Bladder preservation as an alternative to cystectomy is generally reserved for patients with smaller solitary tumours, negative nodes, no extensive or multifocal CIS, no tumour-related hydronephrosis, and a good pre-treatment bladder function. Maximal TUR with concurrent chemoradiotherapy should be given as a primary treatment to these patients.

This modality is endorsed by multiple international organisations that have developed evidence-based consensus guidelines and recommendations, including the International Consultation on Urologic Disease-European Association of Urology (ICUD-EAU), UK National Institute for Health and Care Excellence (NICE) and the AUA/ASCO/ASTRO/SUO. There is an apparent underutilisation of aggressive bladder-preserving therapies for non-cystectomy candidates, especially the elderly and racial minorities. Between 23% and 50% of the patients with muscle-invasive bladder cancer who are 65 years and older of age receive no treatment or non-aggressive therapy, despite prospective, phase-II data showing that bladder preservation with trimodality therapy has positive outcomes and an acceptable toxicity profile for patients >=65 years of age, with a 2-year OS of 94.4% and 2-year DFS of 72.6%. [8]

"Chest imaging with CT is preferred over chest imaging with X-ray. This is based on studies that showed a better sensitivity of CT for detection of metastatic disease."

Summary
The role of TUR in MIBC is to obtain tissue for the histopathological diagnosis, grading and clinical staging of the tumour. TUR for MIBC should also achieve macroscopic clearance where possible. In a select few patients, TUR alone for MIBC may be a reasonable alternative to other more invasive options. Maximal TUR with concurrent chemoradiotherapy may be given as a real primary treatment to patients that look for bladder preservation as an alternative to radical cystectomy.

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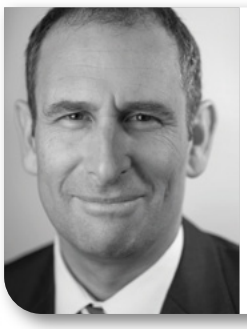
Due to space constraints, the entire reference list can be made available to interested readers upon request by sending an email to: communications@uroweb.org.

Saturday 10 July, 11.00 - 12.30 CEST
Live from the studio: Plenary Session 03
Advanced bladder cancer in 2021: Going forward?
Virtual room 1

cN+ = pN+?

The future of prostate cancer staging



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cN+ = pN+? Or, in English, does clinical lymph node (LN) positivity equal pathological node positivity? Well, generally speaking, the answer is: yes. Regardless of the imaging modality used, specificity is high at 82-99%. [1-4] In other words, when pelvic LNs are seen as suspicious on imaging, there's a very high chance they are indeed prostate cancer metastases.

But there are two arguably much more important questions to consider. First, what exactly does N+ mean in prostate cancer staging these days? And second, does clinical LN *negativity* equal pathological LN *negativity* (cN- = pN-)?

To refresh your memory, N1 in TNM classification of prostate cancer only refers to any positive regional (pelvic) LNs, where the short axis of the nodes is >8mm on CT. Any positive LNs outside the pelvis are designated M1a (bone scan is the other traditional imaging modality in prostate cancer staging but is of course not relevant for lymph node assessment).

But now we have a new player in this field called PSMA PET, and, to push the sporting analogy further, it's hitting CT out of the park! Any PSMA avidity in pelvic LNs on PSMA PET is also N1. But we'll come back to PSMA PET in a moment.

CT
It is well known that CT scanning for LN staging in prostate cancer has been woefully inadequate. Back in 2008, Hovels et al.'s meta-analysis included 18 studies using CT in over 1,000 patients. Pooled **sensitivity of CT was 42%**. [1] The authors didn't hide their frustration, stating that CT is "far too insensitive" in its ability to detect nodal metastases and "should not be used in its current form."

"The authors didn't hide their frustration, stating that CT is 'far too insensitive' in its ability to detect nodal metastases and 'should not be used in its current form'."

In another study of over 1,000 patients undergoing radical prostatectomy with pelvic LN dissection in 2016, Gabriele et al. found the **sensitivity of CT to be just 8.8%** and that it provided no additional predictive value over other pre-operative risk factors. [2] Furthermore, the detection of positive LNs on CT is less than 1% when PSA < 20 or ISUP Grade Group < 4. [5-7]

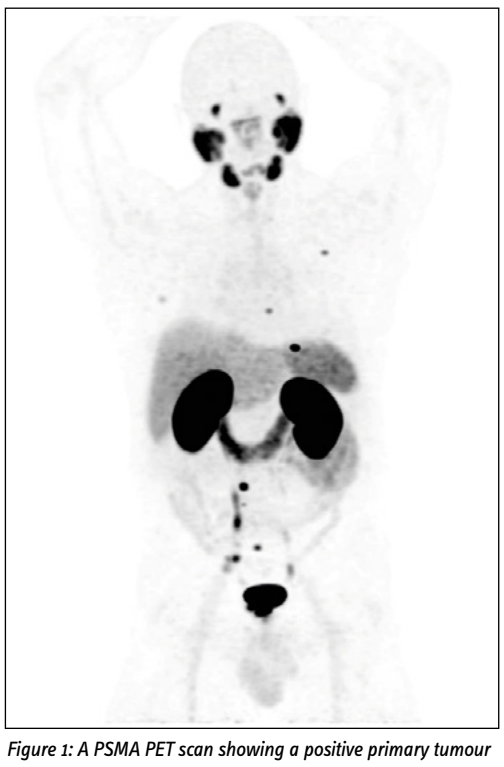

Figure 1: A PSMA PET scan showing a positive primary tumour and multiple positive lymph nodes

The problem, of course, is that as a result of such low sensitivity, many patients with true metastatic disease to (and/or beyond) pelvic LNs are only being treated locally, without any certainty that all pelvic LNs will be included in their treatments, either by a surgical dissection template or within the radiation field. Furthermore, even if visibly positive pelvic LNs are effectively treated themselves, they portend a high risk of microscopic disease, not visible on any current imaging modality, further afield.

Risk calculators
Due to CT's poor sensitivity in pelvic LN staging, risk calculators have been developed using typical clinical risk factors, but these are far from perfect as well. First, previous models were based on systematic biopsy only. And second, whilst the more recent models do incorporate pre-biopsy MRI, which is now the recommended standard of care, and their use could avoid unnecessary LN dissection in more than half of the patients, doing so would miss 2.6% of LN metastases. [8]

"Overall, when including both pelvic LNs and distant metastases, there was an absolute difference in sensitivity of 47%(!) in favour of PSMA PET."

PSMA PET
Fast forward to 2021 and we finally have a staging modality with far higher sensitivity: PSMA PET. In their landmark randomised controlled trial proPSMA, Hofman et al. studied 302 men, clinically high-risk patients with biopsy-proven prostate cancer, comparing conventional imaging with CT and bone scan versus Ga-68 PSMA-11 PET. [3] Overall, when including both pelvic LNs and distant metastases, there was an **absolute difference in sensitivity of 47%(!) (38% vs 85%)** in favour of PSMA PET.
A sub-analysis of pelvic LNs was performed, and, calculating from the raw data that was provided, sensitivity of CT vs PSMA PET was **22.5% (9/40) vs 82.9% (29/35),** respectively. Even when equivocal LNs were subsequently designated as positive in a sensitivity analysis, the sensitivity of CT increased only to 27.5% (11/40) but that for PSMA PET remained the same at **82.9%** (29/35). The specificity of PSMA PET was as high as 98%.

In the same year, Perera et al. published a systematic review and meta-analysis of Ga-68 PSMA PET using 37 articles with 4790 patients, including 5 studies (244 patients) on primary staging. [4] The pooled-per-patient **sensitivity of PSMA PET for overall metastatic disease was 77%,** but a sub-analysis of pelvic LN sensitivity was not performed. Overall specificity was again extremely high at 97%.

Summary
When pelvic LNs are deemed positive on imaging, they are highly likely to be truly positive if on CT and almost certainly truly positive if on PSMA PET, i.e. cN+ usually = pN+. As specificity is high regardless, this is not much of a clinical issue.

It should be clear, however, from the above recent high-level data that cN- by no means equals pN-. However, **PSMA PET is far more likely to detect pelvic LNs than CT.** So cN- is far more likely to equal pN- when PSMA PET is used for primary staging of higher-risk prostate cancer. This is reflected in the current EAU Guidelines summary of evidence (see figure 2). [9]

"As there are no outcome data based on trials using staging with PSMA PET yet, our dilemma now is: what exactly is that optimal treatment...?"

PSMA PET is not yet widely available outside Australia, Germany and the UK, but one question worth considering, given the marked disparity between cN status using CT versus PSMA PET, is whether cN status should be divided accordingly. For example, perhaps pelvic LN positivity on PSMA PET only could be designated cN1a, but cN1b could be considered for CT? This might prove useful in reducing the confusion that now occurs due to the large stage shift caused by PSMA PET's vastly superior accuracy.

5.3.5 *Summary of evidence and guidelines for staging of prostate cancer*

Summary of evidence	LE
PSMA PET/CT is more accurate for staging than CT and bone scan but to date no outcome data exist to inform subsequent management.	1b

Figure 2: Section 5.3.5 of the 2021 EAU Guidelines on Prostate Cancer

To conclude, PSMA PET represents a major advance in our ability to more accurately stage prostate cancer. As has been the case throughout medical history, the more accurate the staging for cancer, the more likely it is that the optimal management will be chosen. As there are no outcome data based on trials using staging with PSMA PET yet, our dilemma now is: what exactly is that optimal treatment...?

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Sunday 11 July, 15.00 – 16.00 CEST
Live from the studio: Thematic Session 14
Guideline Session II: Prostate cancer - cN+ in newly diagnosed patients
Virtual room 2

Incontinence mesh removal surgery in women

Multidisciplinary management, surgical terminology and outcomes

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Mesh-augmented surgery for stress urinary incontinence (SUI) in women using minimally invasive surgical techniques and polypropylene mesh were widely used in the 1990s [1] including retropubic (TVT) and transobturator tapes (TOT). Randomised controlled trials showed the effectiveness of mesh surgery compared with conventional surgery, in particular colposuspension. [2] However, the majority of these trials did not report long-term complications.

In a large retrospective study of over 92,000 women in England, complications have been reported in 9.8% of cases at 5 years. [3] Mesh exposure has been reported in 2.7–4.4%, voiding dysfunction requiring surgery in up to 3%, urinary tract infections (UTIs) in 10.7–17.1%, neurological symptoms in 5.4–9.7% [4], and pain in 4.5%, reaching 9% in some series. [5] All these complications may lead to reoperation in 2.2% of cases [6], and most of the time, multiple operations are required before the mesh is entirely removed. [7] Indeed, some authors reported the need for a median of two revision surgeries (range 1-9) to remove the mesh. [8]

Recommended pre-operative assessment

There are currently no guidelines on pre-operative assessment in case of incontinence mesh complications. A complete medical history and examination are needed. Multidisciplinary evaluation is encouraged, especially if there are other symptoms related to mesh such as pain or musculoskeletal issues. [9] There are currently no mesh-specific validated outcome questionnaires. [9] Vaginal and pelvic examination are mandatory as they may reveal vaginal erosion, trigger points for pain or tender areas. We recently published a diagnostic pathway for incontinence mesh complications (Fig 1) [9] and investigations are targeted towards the mesh complication.

Mesh complications classification and standardization

There is a lack of standardization in terminology to describe mesh complications, as well as, surgical mesh removal terminology. IUGA/ICS has proposed a comprehensive calculator. [10] However, this classification can be complex to use routinely and seems to be more suitable for research. Therefore, we recommend making a detailed report with the complete history, the reported symptoms and the results of the clinical examination. In case of mesh removal surgery, a comprehensive and detailed description of the procedure is mandatory including measurement, recording of the length and photos of the mesh removed. [9] This is helpful if further surgery is required and may be useful for medico-legal purposes too.

The terminology proposed by AUGS-IUGA [11] to describe the surgical procedure may be confusing, therefore we proposed to use the following terminology for mesh removal [9]:

- Covering of the mesh with vaginal tissue: this does not involve removal or division of the mesh and only involves dissection of the vaginal tissue and using that to cover the exposed mesh
- Division of the mesh: this involves cutting the mesh without removing any part of it and is usually used in those with voiding dysfunction.
- Partial removal/excision of the mesh: this involves removing only part of the mesh. The site and length of the mesh removed will have to be specified.
- Full removal of the mesh: removing all the mesh from one end to the other.
- Completion removal of the mesh: this is where they had a previous partial removal and the rest of the mesh needed to be removed fully.

Incontinence mesh removal surgery: When and how?

Whatever the complication, a tailored individualised treatment must be proposed to the patients. Before planning surgery, it is crucial to collect the patient's expectations and goals. Patients must be aware of the benefits and harms of the mesh removal surgery, notably the failure to remove the entire mesh, no change or worsening of the predominant symptom, and the risk of stress urinary incontinence (SUI) recurrence. They also may be aware of the possibility of needing more than one procedure. NICE have developed a patient decision aid for mesh removal [12] which are given to patients.

A multidisciplinary management may be considered, depending on the complication. For example, in cases of pain, pain specialists, psychologists/psychiatrists and physiotherapists have a key role in patient management. Other surgeons may be involved, depending on the type of complication. For example, orthopaedic surgeons may be included in cases of needing groin dissection for TOT removals or colorectal surgeons may be involved in case of bowel complications. Finally, in the UK, NICE also recommends to discuss all mesh removal surgeries cases in a regional multidisciplinary team meeting. [13]

Vaginal erosion

In case of asymptomatic vaginal erosion, with an area of exposed mesh less than 1cm2, initial conservative treatment using topical vaginal oestrogen for at least 3 months before surgical options are considered may be tried. [13] There is some evidence of a higher risk of failure compared with surgery as an initial step, and up to 59.3% of women managed initially conservatively will eventually need surgical treatment. [9] Surgery may be proposed in case of symptomatic vaginal erosion, or failure of conservative treatment: removal of all the vaginal portion is at higher risk of SUI recurrence than removing part of the vaginal component, however the risk of exposure in the latter is lower. [9] In case of adherent mesh to the urethra and per-operative urethral injury, tissue interposition with Martius labial fat pad graft may be required.

"Multidisciplinary management is encouraged for patients with mesh complications and joint/shared decision-making is crucial when offering mesh removal surgery using patient-decision aids."

Urinary tract extrusion

Extrusion into the urinary tract requires surgical removal as the mesh can cause infection, lower urinary tract symptoms (LUTS), stones and/or pain. A systematic review including 20 articles, reported that endoscopic treatment is an effective minimal invasive option, with an initial success rate of 67 % for laser excision and 80% for endoscopic excision. [14] However, between 18 to 25% of patients required at least one additional procedure, some of them with an open approach. Moreover, this technique did not prevent SUI recurrence (around 20% of the patients). [14] In cases of non-endoscopic management, the risk of SUI recurrence is higher with complete than with partial mesh removal. [13] The type of removal has to be discussed with the patient, and risks and benefits discussed carefully. In cases of urinary tract extrusions, it is best that women are managed in specialised centres. [13]

Pain

The incidence of chronic postoperative pain after placement of sub-urethral tape for incontinence varies between 0 and 30% depending on the study. A higher incidence is also observed after transobturator surgery compared with retropubic surgery. [15,16] The chronology of pain occurring after the surgical procedure is a major factor to establish a causal link between surgery, placement of prosthetic material and the patient's symptoms. [17] A detailed analysis of the patient's symptoms can then help to define the type of lesion: myofascial, neuropathic, and/or autonomic. Indeed, the pain may be due to somatic nerve lesions or decompensated neuropathic pain,

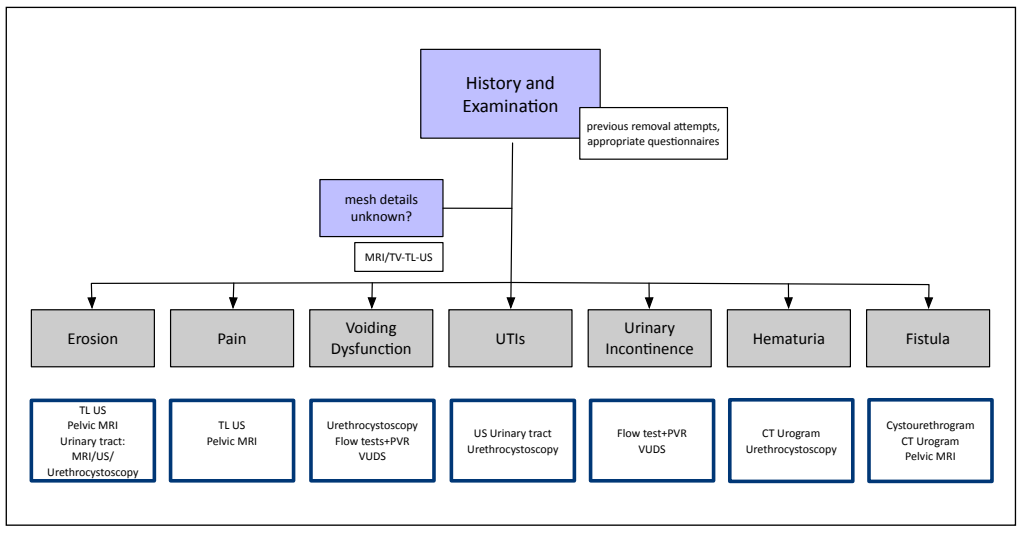

Figure 1: Diagnostic pathway (modified from Bueno Garcia Reyes P. (9))
CT, computed tomography; MRI, magnetic resonance imaging; PVR, post-void residual; TL, translabial; TV, transvaginal; US, ultrasound; UTIs, urinary tract infections; VUDS, videourodynamics

muscle pain due to direct injury or reactive pain, or finally much more diffuse pain accompanied by urinary, gastrointestinal or sexual symptoms in a context of pelvic sensitization. [17,18]

If no mesh abnormality is found, non-surgical treatment is initiated, and if no improvement is achieved, advice from the mesh multidisciplinary team must be sought before any surgical treatment is decided. Trigger point injections with local anaesthetic, as a trial of treatment can be useful and can also help establish an association with mesh. [9] Partial mesh excision may be considered only if pain is related to a specific component of the sling. [9] Therefore, some authors suggest performing groin incision only in patients with associated preoperative obturator neuralgia, for the removal of the prosthetic material and obturator nerve release. [17]

In patients with myofascial pain, section of the material to release excessive tension phenomena, without complete removal, may sometimes be sufficient. [15] However partial removals make future removals of any remnant mesh more difficult due to scarring and retraction of the mesh. [9]

Full mesh removal improves pain in around 60% of cases [9,17] and may reach more than 80% of cases. [19] Persistent pain may be a major cause of dissatisfaction, and patients must be made aware of this risk. In cases of persistent pain after complete mesh removal, the patient should be referred to a pain management centre for global pain management, with multimodal treatments. [17]

Lower Urinary Tract Symptoms (LUTS)

Chronic voiding symptoms is one of the most frequent complication of tapes, with reported rates ranging between 2.8 to 34.7%. [19] If retention is the only complication from sling insertion, sub-urethral mesh division or partial excision may be enough, with high resolution rates after surgery. [20,21]

Laparoscopic or open approach?

Laparoscopic approaches have been published for mesh removals. However, to the best of our knowledge, there are no studies comparing abdominal open versus laparoscopic approaches. In our experience, laparoscopic surgery does not remove the mesh fully in retropubic tapes, especially the supra-fascial/subdermal portion of the mesh, but may be facilitated by using a robot. In the transobturator route, it is often difficult to get the mesh out from within the muscle fibres in the obturator foramen. [9] However, some authors state that obturator nerve release may also be performed via laparoscopic approach to access the pelvic course of the nerve and may be indicated in case of obturator neuralgia. [17]

Outcomes of mesh removals

Functional outcomes

Mesh removal surgery can lead to a complete resolution of symptoms in about 60%-70% [19,21-23] except for chronic storage symptoms (urgency, frequency, urgency urinary incontinence) which may have a lower success rate. The higher success rate is when the mesh removal surgery is indicated for voiding dysfunction. [20] SUI recurrence after mesh removal is a common adverse event, with 20 to 50% of the patients concerned [9,17,24,25], whatever the indication for removal, and is more prevalent in cases of full removal. [24]

Quality of life outcomes

There is a scarcity of data focusing on quality of life, as well as sexual life after incontinence mesh removal surgery. Our results on functional and quality of life outcomes after TOT removal [26] showed satisfaction rate was high (86%). 81% of the patients considered the surgery successful, 93% would still have the surgery if they were in the same situation again, and 95% would recommend this surgery. Moreover, 70% returned to having a sexual life after surgery, with 80% considering it about the same, a bit better or much better than before the surgery.

Conclusion/ implication for practice

Multidisciplinary management is encouraged for patients with mesh complications and joint/shared decision-making is crucial when offering mesh removal surgery using patient-decision aids.

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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.

Friday 9 July, 13.45 – 14.45 CEST
Live from the studio: Thematic Session 01
Guideline Session I: Urethral strictures and female UI
Virtual Room 4

Tuberculosis: The leading infectious killer

UGTB definition, effects, diagnosis and treatment strategies

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Tuberculosis (TB) is a communicable disease that is one of the top 10 global causes of death, and the leading cause of death from a single infectious agent, ranking above HIV/AIDS. This was the case before the COVID-19 pandemic started in March 2020. In 2019, 10 million people developed TB and 1.4 million died from the disease (see figure 1).

Throughout history, TB has claimed lives; even now it accounts for 5,000 deaths on a daily basis. TB kills more young and adults than any other infectious disease. Many well-known and distinguished persons were victims of TB: Pharaoh Tutankhamun (1358 - 1340 BC), Cardinal Richelieu (1581 - 1642), Baruch Spinoza (1632 - 1677), Anders Celsius (1701 - 1744), Jean-Jacques Rousseau (1712 - 1778), Robert Burns (1759 - 1796), Frederic Chopin (1810 - 1849), Napoleon II of France (1811 - 1832), Anton Chekhov (1860 - 1904), Amedeo Modigliani (1884 - 1920), George Orwell (1903 - 1950), Anna Eleanor Roosevelt (1884 - 1962) Franz Kafka (1883 - 1924), Vivien Leigh (1913 - 1967) and many, many others.

According to the World Health Organization's (WHO) latest global TB report, an estimated 1.8 million people could die from TB in 2020 (numbers were last seen in 2012). The statistics were based on WHO's modelling which estimated an additional 200,000 to 400,000 TB deaths in 2020 if the number of people with TB detected and treated falls by 25% to 50% over a three-month period. In 2019, an estimated 1.4 million people died from TB-related illnesses.

The WHO emphasised that the COVID-19 pandemic threatens to reverse recent progress in reducing the global burden of TB disease. The global number of TB deaths could increase by around 0.2–0.4 million in 2020 if health services are disrupted and the number of people who are treated for TB falls by 25–50% over a period of 3 months. [1]

Urogenital tuberculosis

TB is caused by the bacillus Mycobacterium tuberculosis (Mtb). The disease typically affects the lungs (pulmonary TB) but can also affect other parts of the body (extrapulmonary TB).

TB can affect anyone but most people who develop the disease (about 90%) are adults. Of those who fell sick with TB in 2019, 87% were in one of 30 high TB-burden countries. [1] The risk of TB is significantly increased in chronic kidney disease. The link between chronic kidney disease and TB has been known for more than 40 years, but the pathophysiological interaction between these two diseases is still poorly understood. Dialysis and renal transplant patients appear to be at a higher risk of TB, in part related to immunosuppression along with socioeconomic, demographic, and comorbid factors.

In some regions of high TB-burden countries, urogenital tuberculosis (UGTB) is the second most common form of TB and in other regions, the third most common form of TB. A large proportion of patients is underdiagnosed; hence, untreated. The continuing spread of multidrug-resistant TB (MDR-TB) is also a growing concern. According to WHO, only 38% of the estimated number of people with MDR-TB were enrolled in treatment programmes in 2019. [2]

UGTB includes urinary tract TB and genital TB and is associated with pulmonary or other localizations of TB in 40 - 65% of cases. Male genital tuberculosis (MGTB) is associated with pulmonary or renal TB in 50% of cases, but isolated forms also occur. Usually the epididymis and prostate are involved together. [3-4] Diagnosis of UGTB remains an enigma; sometimes it is even more art than science. The related symptoms are nonspecific, including frequency, microscopic haematuria, flank pain, and acidic urine; also urinary TB showed a wide variety of findings on x-ray examination. [5] If there is no other evidence of Mtb, UGTB may be diagnosed based on skin-test, histological picture, caverns revealed by urography and sterile pyuria, but last point has more and more contraversions.

'Since symptoms are non-specific, UGTB often hides under a mask of another disease. This is a reason why UGTB is often called as "great imitator", "great mystificator", or "great hoaxer".'

In the past, the diagnosis may have been based on sterile pyuria – but now the paradigm has changed: the detection of bacteria in patients with no urinary tract infections indicated that the dogma that "urine is sterile" was false. We have found non-specific microbes in 75% patients with UGTB. Although acid fast bacilli microscopy and Lowenstein-Jensen culture remains the cornerstone of the diagnosis of TB as whole, these traditional bacteriological methods are either slow or their sensitivity is low, especially with clinical samples like urine that contain small number of micro-organisms. [6]

UGTB is followed by a number of problems and paradoxes. There is no consensus on a terminology, diagnostic criteria and criteria of healing. Since symptoms are non-specific, UGTB often hides under a mask of another disease. This is a reason why UGTB is often called as "great imitator", "great mystificator", or "great hoaxer". [7] Clinical features, diagnostic tools, and possibilities of anti-Tb therapy and surgery for UGTB have changed during last decades significantly. Surgery for UGTB patients may be performed in department of general urology, but neoadjuvant anti-TB therapy for at least two months should be provided. MC "Avicenna" in Novosibirsk, Siberia, performed laparoscopic operations for UGTB patients alongside with Novosibirsk Research TB Institute.

We would like to illustrate challenges in urogenital TB with the following case [4]:

A 60-year old female patient had her first episode of gross haematuria in 2015. The symptoms cleared on their own. For two years she had no complaints. In 2017, haematuria, dysuria and flank pain appeared on her right side. A cystoscopy revealed strong inflammation and therefore, a biopsy of the bladder wall was performed. Histological investigation showed TB granuloma; DNA Mtb was found in urine by polymerase chain reaction. The x-ray examination revealed stricture of the right ureter, destruction of renal parenchyma and hydronephrosis on the right kidney, an afunctional left kidney, and Microcystis.

The diagnosis was: UGTB, kidney TB 4th stage on left, kidney TB 3rd stage on right, bilateral TB of ureter, bladder TB 4th stage. To preserve the right kidney, nephrostomy was performed. Standard anti-TB therapy with four drugs was prescribed for four months, then Dr. Kholtobin performed nephroureterectomy on the left kidney, cystectomy and enteroplasty by laparoscopy.

What lesson can we learn from this clinical case? Although the first symptoms reoccurred after two years, the patient was not fully examined and UGTB was not suspected despite her living in a TB-epidemic region. Gross haematuria may be the only manifestation of renal TB, and UGTB should be suspected especially in a patient who, without any other reason, has the symptoms and lives in a TB-epidemic region.

For two years, the patient appeared well and had no complaints, but latent torpid TB inflammation severely damaged her kidney and bladder. She had the so-called "open form" of UGTB; she was contagious and possibly infected her family as well.

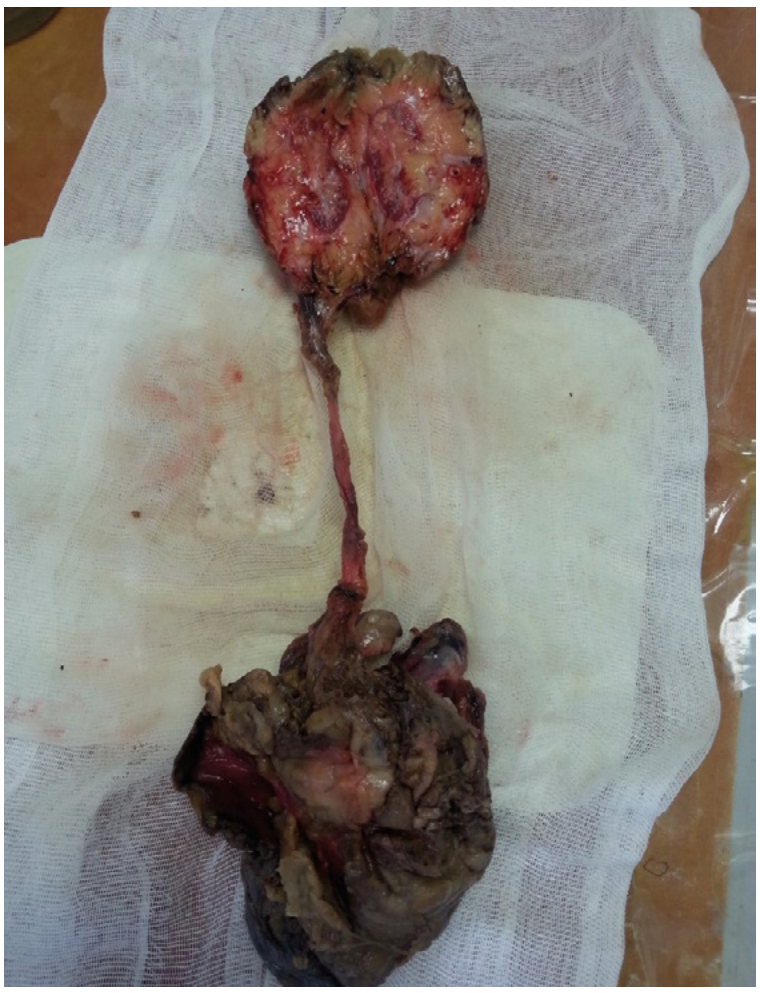

Figure 2: A kidney and a bladder affected by UGTB

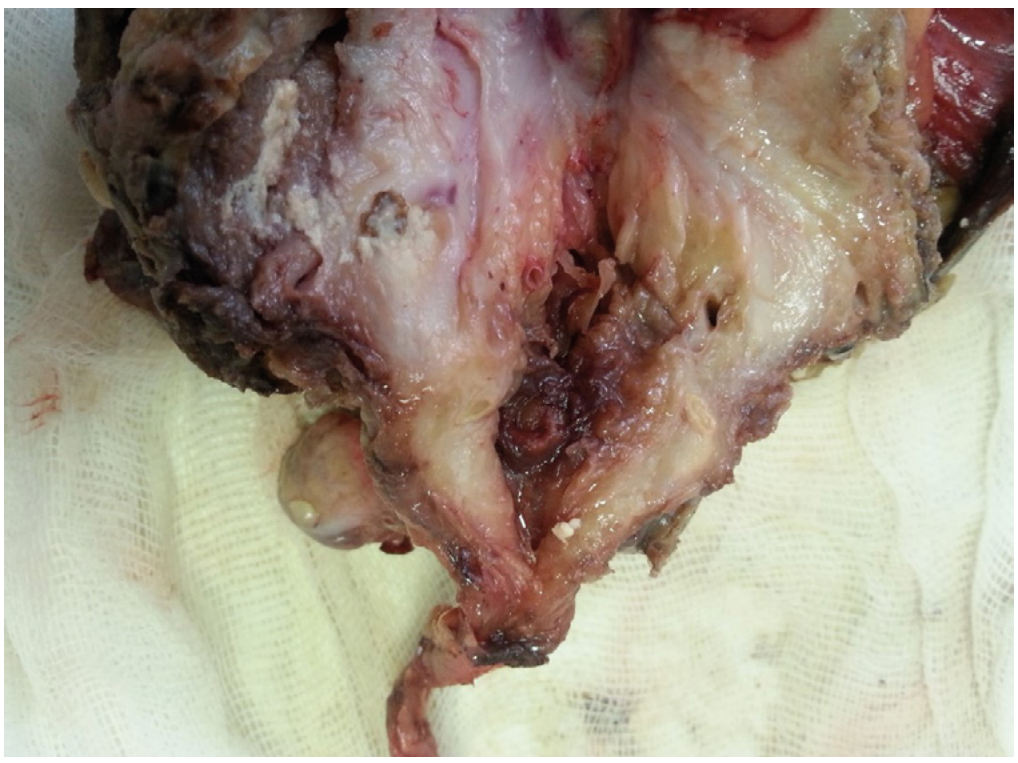

Figure 3: A section of the TB bladder in figure 2 showing total fibrosis and obliteration of the bladder

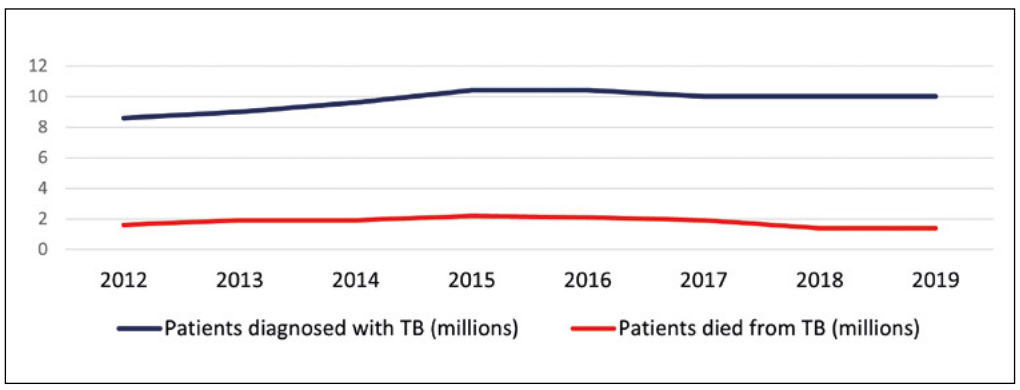

Figure 1: The dynamic of the incidence and mortality rate of TB worldwide

References:

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2. WHO consolidated guidelines on tuberculosis 2020. Module 4: treatment. Available on https://www.who.int/publications/i/item/9789240007048
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4. Kulchavenya E, Kholtobin D, Shevchenko S. Challenges in urogenital tuberculosis. World J Urol. 2020 Jan;38(1):89-94. doi: 10.1007/s00345-019-02767-x.
5. Sallami S, Ghariani R, Hichri A, Zrayer O. Imaging findings of urinary tuberculosis on computerized tomography versus excretory urography: through 46 confirmed cases. Tunis Med. 2014 Dec;92(12):743-7.
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7. Choreño Parra JA, Martínez Zúñiga N, Salinas Lara C. Tuberculosis "the great imitator": False healing and subclinical activity. Indian J Tuberc. 2017; 64(4):345-348. doi: 10.1016/j.ijtb.2017.05.006.

Saturday 10 July, 15.15 – 16.15 CEST
Thematic Session 12
Emerging threats by infectious diseases
Virtual Room 5

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Semi-live Surgery

Thursday 8th July | VIRTUAL ROOM 1 |

In partnership with COOK MEDICAL

1) 11:10 - 11:20
Anatomical Enucleation of the Prostate with Thulium Fiber Laser
L. Tunc, Ankara (TR)

2) 11:20 - 11:30
FURS L. Ajayi, London (GB)

3) 13:00 - 13:10
Endoscopic combined intrarenal surgery (ECIRS)
O. Angerri Feu, Barcelona (ES) E. Emiliani, Barcelona (ES)

4) 13:20 - 13:30
Thulium Laser Enucleation of the Prostate (ThuLEP)
G. Bozzini, Busto Arsizio (IT)

Check for **all semi-live surgeries** and **abstracts at EAU 2021** with Quanta System devices

5) 16:00 - 16:10
Retrograde intra renal surgery (RIRS) for stones
O. Traxer, Paris (FR)

6) 16:40 - 16:50
Holmium Laser Enucleation of the Prostate (HoLEP) using the two-lobe technique
C.R. Brunken, Reinbek (DE)

7) 17:30 - 17:40
HoLEP procedure using special emission mode (Virtual Basket)
F. Gomez Sancha, Madrid (ES)

8) 18:20 - 18:30
Combined Holmium Procedures
E. Liatsikos, Patras (GR)

9) 18:30 - 18:40
Enbloc laser enucleation of the prostate (HoLEP)
P. Kallidonis, Patras (GR)

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The Desnos Medal: "Protecting the legacy of urology"

An interview with the fifth curator of the AUA's William P. Didusch Center for Urologic History

By Loek Keizer

The EAU History Office is proud to award Prof. Michael E. Moran (US) the 2020/21 Ernest Desnos Medal for his extraordinary contributions to the field of urological history. Mike Moran is a Professor of Urology at the University of South Carolina and was curator of the American Urological Association's William P. Didusch Center for Urologic History for ten years, recently stepping down from the position.

It was for his work as the Didusch Center's curator and his own achievements in the field that the EAU is honouring Prof. Moran, joining earlier winners like medical historian Prof. Sergio Musitelli and the Karl Storz endoscope company.

Can you tell us about your work as curator?
"The AUA, just like the EAU and other medical societies, has always had a historical collection of artifacts. From its foundation in 1902, there were urologists collecting. In 1909, they organised a literal museum at the AUA headquarters in Baltimore. Bill Didusch was the first curator, and the museum was subsequently named after him."

"It's great to keep history palpable."

"The AUA was always loosely affiliated with Johns Hopkins, from its earliest days. Artifacts were being accumulated by Hugh Hampton Young himself. We have a lot of early stuff from that time. Throughout the 1920s and 30s the collection grew as people started donating their own collections. We have early transurethral instruments, early batteries and the first incandescent cystoscope bulbs. We also have more general items like early microscopes."

"Every year we receive donations from retiring or deceased colleagues. We also sometimes receive remarkable items from non-urologists. For example, we have the only existing prototype of the Wales cystoscope, which was made by surgeon general during civil war. By accepting these donations we're doing our part to protect the legacy of American urology, and European urology too, as we own several items from the UK, Germany and the Netherlands, among others."

"We have to make a concerted effort to attract new people to take an interest in history."

"As a curator, I would of course maintain items, and manage the collection. After more than a century, it's quite a large collection of instruments and books. The whole AUA headquarters has display cases. It's great to keep history palpable. People can come visit and indeed we've had high schools or college students come by to learn about medical history or do an internship on curating."

"My immediate predecessor Reiner Engel had close ties with Europe because of his German background. One of my goals when I took over, was affiliating with more international societies, hoping that they would start museums of their own. Finances are always the limiting factor, running a museum can get expensive!"

What kind of developments did you see over the course of your ten-year tenure?
"Since I started, we've seen more emphasis on information technology to manage and share our collection, of course. We also have to make a concerted effort to attract new people to take an interest in history. We set up a prize, the Retrospectoscope Award to encourage historical research."

Due to the Covid-19 pandemic, Prof. Michael E. Moran has already received the EAU Ernest Desnos Medal

"The manhours required for inputting data and maintaining the site are a large cost. Industry funding is also controlled more strictly than it used to be. With the worldwide pandemic, museums are really taking it on the chin. At the moment the curator position is vacant, apart from when a themed exhibition is held at the AUA's annual congress."

"I never expected to win a prize named after Desnos."

"The collection is going to continue to grow from donations and acquisitions. But unfortunately we do miss out on occasion, when collections are being sold piecemeal, and we simply cannot compete with private buyers. That's always difficult."

Over the years you've always contributed to the EAU's historical publications. Will you continue writing now that your tenure as curator is finished?
"Yes, I have several books in the pipeline that I now have more time for. A new one that will soon be coming out: *Vital Signs: History and Physical*, on the history of the physical exam and how it's changed. I've also nearly finished a "History of Genius" and the impact on medical history. I'm working on a book on the history of international urology meetings, from when they first started in the early twentieth century. I'm also working on a comprehensive, updated history of urology (two volumes) that I think our field is long overdue."

What are your thoughts on winning the EAU's Ernest Desnos Medal?
"I'm overwhelmed to win this prize! The first book I bought as a urology resident was the Desnos-Murphy book History of Urology. Anything affiliated with that name, it's overwhelming to me. I never expected to win a prize named after Desnos. The people who won before me, they're titans in the field. I can think of so many people deserving of this recognition, over me."

EAU21 | VIRTUAL 8-12 July

EAU21 Virtual Scientific Programme

This session is live from the studio!

Thursday, 8 July

EAU Specialty Session

7:45 - 8:00 **Welcome to the EAU21 Virtual Congress**

Urology beyond Europe

8:00 - 10:00 Joint Session of the European Association of Urology (EAU) and the Urological Society of Australia and New Zealand (USANZ)
8:00 - 10:00 Joint Session of the European Association of Urology (EAU) and the Federation of ASEAN Urological Associations (FAUA)
8:00 - 10:00 Joint Session of the European Association of Urology (EAU) and Russian Society of Urology (RSU)
10:00 - 12:00 Joint Session of the European Association of Urology (EAU) and the Japanese Urological Association (JUA)
10:00 - 12:00 Joint Session of the European Association of Urology (EAU) and the Korean Urological Association (KUA)
10:00 - 12:00 Joint Session of the European Association of Urology (EAU) and the Taiwan Urological Association (TUA)
13:00 - 15:00 Joint Session of the European Association of Urology (EAU) and the Iranian Urological Association (IUA)
13:00 - 15:00 Joint Session of the European Association of Urology (EAU) and the Pakistan Association of Urological Surgeons (PAUS)
13:00 - 15:00 Joint Session of the European Association of Urology (EAU) and the Caucasus/Central Asian countries
15:00 - 17:00 Joint Session of the European Association of Urology (EAU) and the Société Internationale d'Urologie (SIU)
15:00 - 17:00 Joint Session of the European Association of Urology (EAU) and the Arab Association of Urology (AAU)
15:00 - 17:00 Joint Session of the European Association of Urology (EAU) and the Urological Society of India (USI)
15:00 - 17:00 Joint Session of the European Association of Urology (EAU) and the Maghreb Union Countries
17:00 - 19:00 Joint Session of the European Association of Urology (EAU) and the Confederación Americana de Urología (CAU)
17:00 - 19:00 Joint Session of the European Association of Urology (EAU) and the Canadian Urological Association (CUA)
17:00 - 19:00 Joint Session of the European Association of Urology (EAU) and the Pan-African Urological Surgeons Association (PAUSA)

Poster Sessions

8:00 - 9:00 **Poster Session 01:** Basic research and clinical developments in chronic pelvic pain, OAB and neurogenic bladder
9:00 - 10:00 **Poster Session 02:** Step by step management LUTS/BPO: From drug treatment to minimally invasive therapies
10:00 - 11:00 **Poster Session 03:** Ablative BPO surgery - The world of lasers
11:00 - 12:00 **Poster Session 04:** Male and female stress urinary incontinence - Evaluation and surgical solutions
12:00 - 13:00 **Poster Session 05:** Urinary tract infections: Screening and diagnosis
13:00 - 14:00 **Poster Session 06:** Urinary tract infections: Treatment and follow-up

EAU Section Meeting

10:15 - 19:00 **Meeting of the EAU Section of Uro-Technology (ESUT), in cooperation with the EAU Robotic Urology Section (ERUS) and the EAU Section of Urolithiasis (EULIS)**
Technology development never ends!

Friday, 9 July

Plenary Sessions

10:00 - 10:30 **Game Changing Session 2**
10:30 - 12:00 **Plenary Session 01:** Nightmare session: PCa early detection
10:15 - 10:30 **Game Changing Session 1**
10:30 - 12:00 **Plenary Session 02:** Optimal management of incontinence in the elderly patient

Thematic Sessions

13:45 - 14:45 **Thematic Session 01:** Guideline Session I: Urethral strictures and female UI
13:45 - 14:45 **Thematic Session 02:** Semi-live I: Penile surgery
15:00 - 16:00 **Thematic Session 03:** Basic research in prostate cancer and potential clinical impact
15:15 - 16:15 **Thematic Session 04:** Seminal discoveries in male infertility: From diagnosis to treatment
15:00 - 16:00 **Thematic Session 05:** Urological trauma: What's new, what's controversial?
16:15 - 17:15 **Thematic Session 06:** Semi-Live II: Benign female surgery
16:15 - 17:15 **Thematic Session 07:** Treating Peyronie's disease and erectile dysfunction: It's not that hard!

Special Sessions

11:30 - 12:30 **Patient Information Session:** Prostate Cancer
12:30 - 13:30 **Patient Information Session:** Bladder cancer
13:30 - 14:30 **Patient Information Session:** Kidney cancer
13:45 - 14:45 **Special Session:** Update on prostate cancer screening 2021
14:30 - 15:30 **Patient Information Session:** Life After Cancer Treatment
15:30 - 16:30 **Patient Information Session:** Funtional Urology
16:30 - 17:30 **Special Session:** Active Surveillance for intermediate risk prostate cancer: What urologist and patients should know
16:30 - 17:40 **Patient Information Session:** Patient poster presentations
18:00 - 19:00 **Patient Information Session:** Round table: The road to successful intervention

Poster Sessions

10:00 - 11:00 **Poster Session 07:** Patient engagement
11:00 - 12:00 **Poster Session 08:** Urolithiasis: Research, new technology and stents
12:00 - 13:00 **Poster Session 09:** Urolithiasis: Epidemiology, imaging and conservative management
13:00 - 14:00 **Poster Session 10:** Urolithiasis: Endourology and ESWL
14:00 - 15:00 **Poster Session 11:** Guidelines
15:00 - 16:00 **Poster Session 12:** Renal transplantation: Expanding donors' indications, optimising recipients' outcomes
16:00 - 17:00 **Poster Session 13:** Urinary tract reconstruction, including pelvic organ prolapse and fistula repair
17:00 - 18:00 **Poster Session 14:** Striking features of urethral strictures
18:00 - 19:00 **Poster Session 15:** Cell biology, biomarkers and novel therapies in prostate cancer

Video Sessions

12:00 - 12:45 **Video Session 01:** Techniques to evolve radical prostatectomy
12:00 - 12:45 **Video Session 02:** Progress in sacrocolpopexy
12:00 - 12:45 **Video Session 03:** Innovative training and novel technologies
17:15 - 18:00 **Video Session 04:** Avoiding and managing complications
17:15 - 18:00 **Video Session 05:** Alternative approaches to bladder outlet obstruction
17:15 - 18:00 **Video Session 06:** Challenges in genital cancer surgery

Saturday, 10 July

Plenary Sessions

10:30 - 11:00 **Game Changing Session 3**
10:45 - 11:00 **Game Changing Session 4**
11:00 - 12:30 **Plenary Session 03:** Advanced bladder cancer in 2021: Going forward?
11:00 - 12:30 **Plenary session 04:** Renal cancer: From localised to metastatic disease

Thematic Sessions

13:15 - 14:15 **Thematic Session 08:** Germline genetic testing and clinical consequences for patients and relatives in onco-urology
13:15 - 14:15 **Thematic Session 09:** Urinary biomarkers: Are we there yet?
15:15 - 16:15 **Thematic Session 10:** Immunotherapy in urothelial cancer
15:15 - 16:15 **Thematic Session 11:** Testis Cancer: Innovations by biomarkers and surgery
15:15 - 16:15 **Thematic Session 12:** Emerging threats by infectious diseases
16:30 - 17:30 **Thematic Session 13:** Telemedicine in urology

Special Sessions

15:15 - 17:15 **EAU Specialty Sessions:** YUORDay21: EAU Young Urologists Office (YUO) & European Society of Residents in Urology (ESRU)
16:45 - 18:15 **Special Session:** Controversies in Bladder Cancer 2021: Rapid-fire debates

Poster Sessions

10:00 - 11:00 **Poster Session 16:** Novel biomarkers, subtypes, and disease models in urothelial cancer
11:00 - 12:00 **Poster Session 17:** Male sexual dysfunction
12:00 - 13:00 **Poster Session 18:** Male infertility and hypogonadism
13:00 - 14:00 **Poster Session 19:** Liquid biopsies, biomarkers, and novel therapies in renal tumours
14:00 - 15:00 **Poster Session 20:** Nephron-sparing treatment in localised kidney cancer
15:00 - 16:00 **Poster Session 21:** Localised renal tumour diagnosis and prognosis in the digitalised era
16:00 - 17:00 **Abstract session:** Best of EAU21 poster abstracts
17:00 - 18:00 **Poster Session 22:** Renal tumours: Locally advanced and metastatic disease
18:15 - 19:15 **Poster Session 23:** Miscellaneous: Rare and complex urology and all about adrenals
18:15 - 19:15 **Poster Session 24:** Penile and testis cancer

Video Sessions

12:30 - 13:15 **Video Session 07:** Improving outcomes following robotic cystectomy
12:30 - 13:15 **Video Session 08:** Award winning video session
12:30 - 13:15 **Video Session 09:** Challenging retroperitoneal surgery for testicular disease
17:45 - 18:30 **Video Session 10:** New perspectives in inguinal and pelvic lymph node dissection
17:45 - 18:30 **Video Session 11:** A tale of three kidneys: Complex and salvage robotic kidney surgery
17:45 - 18:30 **Video Session 12:** Robotic partial nephrectomy - get your clamp off!

Sunday, 11 July

Plenary Sessions

11:15 - 11:45 **Game Changing Session 5**
11:45 - 13:15 **Plenary session 05:** Treatment for metastatic hormone-sensitive prostate cancer
11:30 - 11:45 **Game Changing Session 6**
11:45 - 13:15 **Plenary Session 06:** Reconstructive surgery: Did the robot take over?

Thematic Sessions

15:00 - 16:00 **Thematic Session 14:** Guideline Session II: Prostate cancer - cN+ in newly diagnosed patients
15:00 - 16:00 **Thematic Session 15:** Complications/solutions of robot-assisted urologic surgery: Quick answers
15:00 - 16:00 **Thematic Session 16:** How machine learning is transforming diagnostics
16:30 - 17:30 **Thematic Session 17:** Treatment sequencing in metastatic prostate cancer
16:15 - 17:15 **Thematic Session 18:** Semi-Live III: Laparoscopic and robotic surgery for malignant diseases

Poster Sessions

12:00 - 13:00 **Poster Session 25:** NMIBC: New insights for the diagnosis, management and follow-up
13:00 - 14:00 **Poster Session 26:** NMIBC: Treatment and prognosis
14:00 - 15:00 **Poster Session 27:** UTUC: Molecular characterisation and modern management
15:00 - 16:00 **Poster Session 28:** MIBC: Evolution of surgical management and morbidity
16:00 - 17:00 **Poster Session 29:** Metastatic prostate cancer
17:00 - 17:30 **Poster Session 30:** Clinical trials
18:00 - 19:00 **Poster Session 31:** Affordable urology, instruments and disposables and trauma

Video Sessions

13:15 - 14:00 **Video Session 13:** Interesting techniques in urethral stricture management
13:15 - 14:00 **Video Session 14:** Salvage robotic pelvic surgery
13:15 - 14:00 **Video Session 15:** Pushing the boundaries in female reconstructive surgery
17:15 - 18:00 **Video Session 16:** Robotic reconstructions
17:15 - 18:00 **Video Session 17:** Augmented reality in robotic urological surgery
17:15 - 18:00 **Video Session 18:** Interesting techniques for management of upper tract obstruction

Cutting-edge Science at Europe's largest Urology Congress

*The **36th Annual EAU Congress, Arnhem, Netherlands, 08/07/2021-12/07/2021** has been accredited by the European Accreditation Council for Continuing Medical Education (EACCME®) with 40 European CME credits (ECMEC®s). Each medical specialist should claim only those hours of credit that he/she actually spent in the educational activity."*

Monday, 12 July

Plenary Session

8:00 - 9:30 **Plenary Session 07:** Stones: Keeping with tradition or time for new concepts?

Thematic Sessions

10:00 - 11:00 **Thematic Session 19:** Kidney transplantation in 2021

10:00 - 11:00 **Thematic Session 20:** Semi-Live IV: New standards in endourology

10:00 - 11:00 **Thematic Session 21:** Latest developments in paediatric urology

Special Sessions

9:45 - 10:45 Controversies on EAU Guidelines - Session I

11:00 - 12:00 Controversies on EAU Guidelines - Session II

11.00 - 12.00 History of urology at a glance

12:00 - 13:00 Joint session of the EAU and the Advanced Prostate Cancer Consensus (APCCC)

12:30 - 13:30 Meeting of the Young Academic Urologists (YAU)

13:30 - 14:30 7th ESO Prostate Cancer observatory: Innovations and care in the next 12 months

14:30 - 15:30 PIONEER prostate cancer platform

15:30 - 16:30 European Urology: Surgery-in-Motion session

16:30 - 17:30 ERN eUROGEN 2021: Update on rare and complex urology

17:30 - 19:30 Best of EAU 2021 session

19:30 - 20:30 EAU General Assembly

Poster Sessions

9:30 - 10:30 **Poster Session 32:** Prostate cancer detection by MR, PET and Micro-US imaging

10:30 - 11:30 **Poster Session 33:** Prostate cancer biopsy protocols and methods of targeting

11:00 - 12:00 **Poster Session 34:** Education and training models in urology and E-health

11:30 - 12:30 **Poster Session 35:** Prostate cancer screening, biopsy indication protocols and markers

12:00 - 12:30 **Poster Session 36:** History and histories

12:30 - 13:30 **Poster Session 37:** Active surveillance and focal therapy: Evolving concepts and long term outcome

13:30 - 14:30 **Poster Session 38:** Paediatric urology

13:30 - 14:30 **Poster Session 39:** Radical prostatectomy: Long-term outcome and how we can do better

14:30 - 15:30 **Poster Session 40:** Transgender and adult and paediatric genital surgery

14:30 - 15:30 **Poster Session 41:** Functional outcome of radical prostatectomy and how we can do better

15:30 - 16:30 **Poster Session 42:** Detection of recurrence and salvage treatment options after primary treatment for prostate cancer

16:30 - 17:30 **Poster Session 43:** How to manage high risk and advanced prostate cancer?

Video Sessions

13:00 - 13:30 **Video Session 19:** Minimally invasive techniques in adrenal surgery

15:30 - 16:00 **Video Session 20:** Focal diagnosis and treatment

15:30 - 16:00 **Video Session 21:** Mini-PCNL for paediatric stones

15:30 - 16:15 **Video Session 22:** Contemporary robotic kidney transplantation

EAU Section Meetings

11:00 - 12:00 **Meeting of the EAU Section of Infections in Urology (ESIU):** The threat of urogenital infections

12:00 - 13:00 **Meeting of the EAU Section of Genitourinary Reconstructive Surgeons (ESGURS):** Contemporary urogenital reconstruction and continence restoration: A practical guide

12:00 - 13:00 **Meeting of the EAU Section of Outpatient and Office Urology (ESUO):** Andrological tips and tricks for outpatient and office urologists

13:30 - 14:30 **Meeting of the EAU Section of Andrological Urology (ESAU):** Unanswered questions in andrology

13:30 - 14:30 **Meeting of the EAU Section of Urolithiasis (EULIS):** Pathophysiology and management of urolithiasis: New perspectives and approaches in 2021

14:30 - 15:30 **Meeting of the EAU Robotic Urology Section (ERUS):** State of the art in robotic surgery: ERUS 2021

14:30 - 15:30 **Meeting of the EAU Section of Transplantation Urology (ESTU):** Surgical matters in kidney transplantation

16:00 - 17:30 **Joint meeting of the EAU Section of Oncological Urology (ESOU) and the EAU Robotic Urology Section (ERUS) in conjunction with ESMO and ESTRO:** Controversies in onco-urology

16:00 - 17:30 **Joint meeting of the EAU Section of Urological Imaging (ESUI), the EAU Section of Uropathology (ESUP) and the EAU Section of Urological Research (ESUR):** Ready for take-off: Molecular markers for clinical management of urological malignancies

16:15 - 17:15 **Meeting of the EAU Section of Female and Functional Urology (ESFFU):** Functional urology in 2021: What did we miss at EAU20 and what is essential?

Please note that all session times and virtual rooms listed in this EUT edition are subject to change. For the latest and most up-to-date programme, visit: **www.eau2021.org/programme**

Schedule of ESU Courses at EAU21

Thursday, 8 July 2021

08:00 - 10:00 **ESU Course 1** Surgical management of prolapse and urinary incontinence/female pelvic floor disorders

11:00 - 13:00 **ESU Course 2** Practical aspects of cancer pathology for urologists. The 2021 WHO novelties

14:00 - 16:00 **ESU Course 3** Andrology and infertility update

17:00 - 19:00 **ESU Course 4** Ultrasound in urology

Friday, 9 July 2021

08:00 - 10:00 **ESU Course 5** Renal transplantation: Technical aspects, diagnosis and management of early and late urological complications

11.00 - 13.00 **ESU Course 6** Flexible ureterorenoscopy and retrograde intrarenal surgery: Instrumentation, technique, tips and tricks and indications

14.00 - 16.00 **ESU Course 7** Management of lower urinary tract dysfunction and BPO: From urodynamics to medical and surgical treatment

17:00 - 19:00 **ESU Course 8** Metabolic workup and non-surgical management of urinary stone disease

Saturday, 10 July 2021

08:00 - 10:00 **ESU Course 10** Advanced course on urethral stricture surgery

10:30 - 12:30 **ESU Course 11** Prostate cancer imaging and biopsy

13:00 - 15:00 **ESU Course 12** Prostate cancer screening and active surveillance: Where are we now?

15:30 - 17:30 **ESU Course 13** Urinary tract and genital trauma

18:00 - 20:00 **ESU Course 14** Robot-assisted laparoscopic radical cystectomy: Intracorporeal urinary diversions and nerve-sparing techniques. Surgical tricks and management of complications

Sunday, 11 July 2021

08:00 - 10:00 **ESU Course 15** Practical management of non-muscle invasive bladder cancer (NMIBC)

10:30 - 12:30 **ESU Course 16** Current concepts and controversy in the diagnosis and management of upper tract urothelial carcinoma (UTUC)

13:00 - 15:00 **ESU Course 17** Management of invasive and locally or metastatic bladder cancer: From bladder sparing to cystectomy and systemic treatment

15:30 - 17:30 **ESU Course 18** Percutaneous nephrolithotripsy (PCNL)

18:00 - 20:00 **ESU Course 19** Metastatic prostate cancer: Systemic treatments and options of local treatment in case of oligometastatic disease

Monday, 12 July 2021

08:00 - 10:00 **ESU Course 20** Robotic surgery and ablative treatment of renal tumours

11:00 - 13:00 **ESU Course 21** Laparoscopy for beginners

14:15 - 16:15 **ESU Course 22** Prosthetic surgery in urology

17:30 - 19:30 **ESU Course 23** Recent advances in robotic urology of the prostate

How to register

Participation in the ESU courses is subject to availability and only limited virtual seats are available! Don't miss out and sign up for the courses now.

Please go to **https://eaucongress.uroweb.org/registration/** to register for EAU21 and enrol to the ESU courses of your choice.

The registration fees* for the courses are as follows:

EAU members	€ 25
Non-members	€ 35
Residents/nurses	€ 15

Fees Include 7.7% VAT.

EAU21 Industry Sessions

Thursday, 8 July

12.00 - 13.00 **Intuitive**

12:00 - 13:00 **BioTechne**

19.00 - 20.00 **Boston Scientific**

19.00 - 20.00 **Laborie**

Friday, 9 July

12.45 - 13.45 **Astellas**

12.45 - 13.45 **Janssen**

18.00 - 19.00 **AstraZeneca**

18.00 - 19.00 **GSK**

Saturday, 10 July

09.30 - 10.30 **Ipsen**

09.30 - 10.30 **Medac GMBH**

14.15 - 15.15 **Bristol-Myers Squibb**

14.15 - 15.15 **IBSA**

18.30 - 19.30 **Astellas**

Sunday, 11 July

10.15 - 11.15 **Astellas**

10.15 - 11.15 **Pierre Fabre**

14.00 - 15.00 **Bayer**

18.00 - 18.30 **Recordati**

This overview of the Industry Sessions planned during EAU21 Virtual, 8-12 July 2021 is subject to be changed. For the latest and most up-to-date programme, visit **eau2021.org**.

"Very special to be the first non-urologist to win this award"

Prof. Jelle Barentsz receives the EAU Innovators in Urology Award

By Juul Seesing

The year was 2006 when Prof. Jelle Barentsz (NL) sustained a partial paraplegia after an operation gone wrong. "I can walk well again – with some limitations," he says now, fifteen years later. "The recovery went excellently for me, and this made me humbler. I know what it is like to be a patient and to depend on your treating physician. That made me work even harder for the patient. When I feel that the interest of the patient is at stake, I can be a source of annoyance to my colleagues."

This determination has brought Prof. Barentsz, professor of radiology and chair of the Prostate MRI Reference Center at the Radboudumc in Nijmegen (NL), the EAU Innovators in Urology Award. This award was originally scheduled to be bestowed at EAU20 in Amsterdam and was eventually given to Prof. Barentsz in the build-up to EAU21 Virtual. The award is presented in recognition of the importance of inventions and clinical contributions with a major impact on the treatment and/or diagnosis of a urological disease. Prof. Barentsz won this award because of his ground-breaking achievements in functional and molecular imaging in the field of prostate cancer MRI. He and his team were responsible for the introduction of the Prostate Imaging - Reporting and Data System (PI-RADS), which is now considered best practice in prostate MRI and has found its way in clinical guidelines across the world, including the EAU Guidelines.

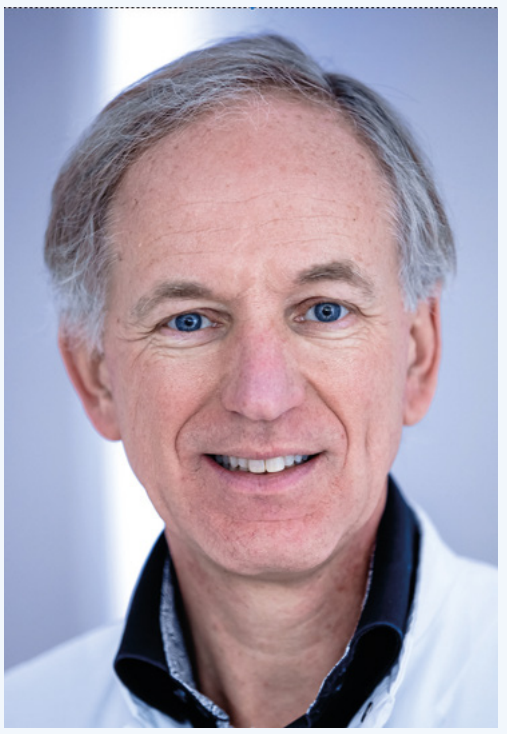
"Imaging can help clinicians find a way in the dark; it is a road map."

"MRI imaging has a huge positive effect on the treatment of the patient. It decreases side effects and increases the chances of cure," Prof. Barentsz says. "I have been awarded many prizes, among which the royal decoration of Knight in the Order of the Lion of the Netherlands, which is like knighthood in the UK. But the EAU Innovators in Urology Award is an even more important prize to me than that. Why? Because before me, this prize was granted to what I call the 'urological icons', such as John Wickham, who was a pioneer of extracorporeal shock-wave lithotripsy and laparoscopic nephrectomy. Being a radiologist, I am the first non-urologist who is granted this award. It is very special to get this kind of distinction from clinicians. This is a huge appreciation for and promotion of imaging. And that was my motivation to start in radiology: to promote imaging."

"I have been awarded the royal decoration of Knight in the Order of the Lion of the Netherlands. But the EAU Innovators in Urology Award is an even more important prize to me than that."

Not your or my but our patient

That motivation stemmed from Prof. Barentsz' experiences with colleagues who "didn't recognise the important impact imaging had on the treatment options for the patient." "Many clinicians, especially twenty to thirty years ago, did not appreciate radiology," he remembers. "Urologists were opposed to the idea to use MRI to detect clinically significant prostate cancer. Some of them still are. To them I would like to say: why are you against this? I personally only care about what I can do for the patient. This patient is not *yours* or *mine*; this is *our* patient. Consider what we can do for them if we collaborate with a mind open to new ideas. I am having a lot of discussions with prostate cancer patient societies, and they really want MRI. Imaging is one



Prof. Jelle Barentsz

piece of the puzzle in a patient's journey, a piece that is just as important as the treatment. Imaging can help clinicians find a way in the dark; it is a road map. That is my ultimate goal for imaging; that it is recognised as this important piece of the puzzle by all clinicians. Receiving this prize from the world-leading association in urology is a huge step toward achieving this."

Quality assurance

Another huge step would be a quality assurance for prostate MRI throughout Europe. Prof. Barentsz: "In many hospitals the MRI isn't good enough. In my country the Netherlands, we don't have enough MRI scanners to support the guidelines. We are working on that in the Radiological Society of the Netherlands (NVvR). The hurdles are financial and quality ones. The financial issue can be solved with the help of hospital directors, healthcare providers, insurance companies, and politicians. There needs to be a shift of money to MRI. As for the quality issue, we need to educate more radiologists using accreditation and certification. We are working on all of this, and the blueprints are there. For instance, the NVvR will soon discuss how to implement good-quality MRI with the Dutch Association of Urology (NVU) and the Dutch Association for Prostate Cancer Patients (PKS)."

"This patient is not yours or mine; this is our patient. Consider what we can do for them if we collaborate with a mind open to new ideas."

Many more developments are afoot – such as early detection of prostate cancer and the use of artificial intelligence in this (also see page 37) – but Prof. Barentsz cannot help but notice he is "gradually moving toward the age where people say you have to retire." But: "Fortunately, all those developments are not beyond but in front of the horizon. And I may be able to shift the horizon a bit further away from me."

Visit the EAU21 Congress Platform and watch the video of Prof. Frans Debruyne (BE) bestowing the EAU Innovators in Urology Award on Prof. Barentsz!

In focus: Dr. Daniël Osses

Prize winner of the 2020 EAU Prostate Cancer Research Award

By Erika De Groot

Every year, the European Association of Urology (EAU) bestows prestigious awards to clinicians for their pioneering research and outstanding performance in the field of urology. Dr. Daniël Osses (NL) of the Erasmus University Medical Center is the esteemed recipient of the 2020 EAU Prostate Cancer Research Award. In this article, he talked about the research that garnered the accolade, the inspiration behind his study's pursuit, and what lies ahead regarding his research.

The EAU launched the EAU Prostate Cancer Research Award to encourage innovative, exceptional research in prostate cancer (PCa). Together with the support of the Fritz H. Schröder Foundation, an expert jury selects and grants the best published paper on clinical or experimental studies in PCa with the award during the Annual EAU Congress.

In 2020, the recognition was bestowed upon Dr. Osses for his research which was entitled *"Results of Prostate Cancer Screening in a Unique Cohort at 19yr of Follow-up"*. His paper was initially published in the March 2019 edition of the acclaimed peer-reviewed journal *European Urology.*

Based on his research, long-term data predominantly coming from an era with hardly any prostate specific antigen (PSA) contamination show that PSA-based PCa screening could result in a considerable reduction of both metastatic disease and prostate-cancer-specific mortality. If confirmed in larger datasets, this could refuel the discussions on the harms and benefits of PCa screening.

When asked what inspired Dr. Osses to pursue this research topic, he explained, "Despite observed reductions in metastatic disease and prostate-cancer-specific mortality by PCa screening in previous studies, unnecessary testing and overdiagnosis still preclude PSA-based PCa screening from adoption as public health policy.

Dr. Daniël Osses

"Extended follow-up is required to better understand the long-term risks and benefits of PCa screening. Therefore my supervisor Prof. Dr. Monique Roobol (NL) had the excellent idea to assess the effect of PSA-based PCa screening in an European Randomized study of Screening for Prostate Cancer (ERSPC) Rotterdam study cohort (i.e. Pilot 1 study) with men randomised in the period of 1991 to 1992 (an era in which PSA testing was uncommon) and enabling us to report on the basis of long-term follow-up (median follow-up of 19 years). Additionally, because the main ERSPC trial does not have the availability of this long-term follow-up yet."

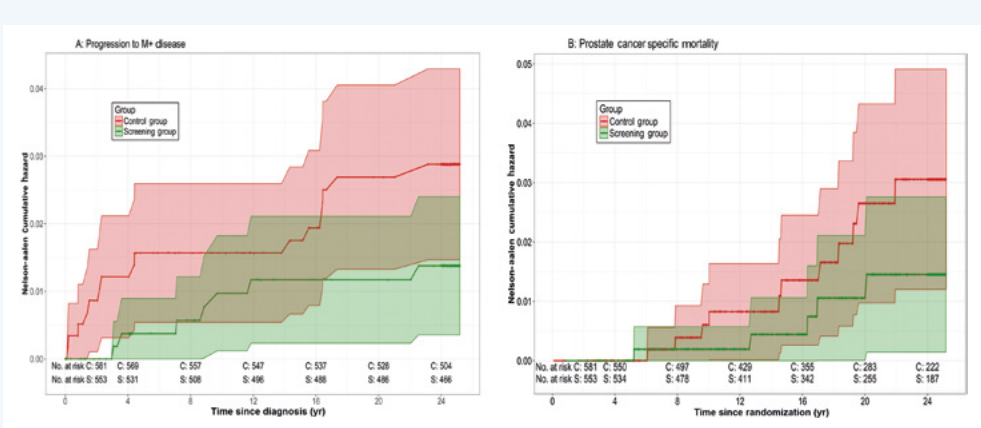


Figure 1: As stated in Dr. Osses's paper, descriptive statistics were used to evaluate patient/tumour characteristics. To get a better look at the statistics and to view the full paper, please go to www.europeanurology.com/article/S0302-2838(18)30851-0/fulltext

Next steps for his research
Dr. Osses stated that the collection of follow-up data in the main ERSPC trial is still an ongoing process. "These long-term data will provide us with more insights on the full effect of PCa screening, and will definitely trigger the discussions on the pros and cons of PCa screening."

Beginnings and aspirations
To know more about the man behind the achievements, we asked Dr. Osses when did he know that he wanted to be a urologist. He replied, "I knew that urology was going to be my calling when I had my internship at the Haga Teaching Hospital in The Hague, Netherlands back in 2014/2015."

He added that his biggest inspiration were his parents. "My Cuban mother and Chilean father, who built their lives in the Netherlands, gave my brother and I all the opportunities we could ever wish for." And what is Dr. Osses's greatest professional aspiration? He shared, "I want to further cultivate and build my knowledge and competencies as a urological clinician and researcher, and to also train the next generation of young doctors. A good friend and colleague of mine once taught me a valuable life lesson as he quoted Benjamin Franklin: 'By failing to prepare, you are preparing to fail.' In my opinion, to be able to provide optimal care for patients, as well as, to have a successful medical career, one must incorporate this important lesson in his/her daily practice."

Visit the EAU21 Congress Platform and watch the video of Prof. Monique Roobol (NL) bestowing the EAU Prostate Cancer Research Award on Dr. Osses!

Thinking outside the current staging categories

Prof. Wolfgang Fendler wins the 2021 EAU Prostate Cancer Research Award

By Juul Seesing

The findings of his and his co-authors' study have the potential to drastically impact the disease burden categorisation of non-metastatic castration-resistant prostate cancer (nmCRPC) patients. "The diagnostic landscape of prostate cancer has undergone rapid change with the introduction of next-generation molecular imaging," Prof. Wolfgang Fendler (Essen, DE) says. "Prostate-specific membrane antigen positron emission tomography (PSMA PET) spearheaded this development by demonstrating high-level evidence for superior accuracy in the settings of primary staging and biochemical recurrence. As a next step, we assessed the diagnostic accuracy of PSMA PET in patients with high-risk castration-resistant prostate cancer, non-metastatic by conventional imaging."

"The next step is to bring this to a level of clinical relevance; how can we use the higher accuracy of PSMA PET to guide treatments for prostate cancer to improve the patient outcomes?"

The results won Prof. Fendler the 2021 EAU Prostate Cancer Research Award for the paper "Prostate-Specific Membrane Antigen Ligand Positron Emission Tomography in Men with Nonmetastatic Castration-Resistant Prostate Cancer", originally published in *Clinical Cancer Research* in September 2019. The award is annually given to the best paper published on clinical or experimental studies in the field of prostate cancer.

Using PSMA PET, Prof. Fendler and his colleagues found metastatic disease in more than 50% of the 200 patients who participated in the study, again, while all these patients had been considered non-metastatic by conventional imaging. "Our findings have been confirmed in several subsequent studies. In the meantime, we have gathered more and more information on diagnostics, imaging, and how to describe different stages. The next step is to bring this to a level of clinical relevance; how can we use the higher accuracy of PSMA PET to guide treatments for prostate cancer to improve the patient outcomes?"

Nuclear medicine
Prof. Fendler won the EAU Prostate Cancer Research Award as a physician researcher working in the field of nuclear medicine, which made him feel even more honoured. "The award was given for a project focussed on nuclear medical imaging. Although this is highly relevant for prostate cancer and urology in general, I still see it as something very special to be acknowledged in this way, also because it comes from an association that has had a motivating influence on my career. Seeing the very stringent, high-quality clinical work by the EAU to change the clinical practice for improved outcomes of prostate cancer patients was a great motivation for all of us. The value of PSMA PET imaging for treatment guidance should now be tested in future studies, eventually influencing the EAU Guidelines, thus changing the practice and, indeed, improving the outcomes for patients."

"Only because current disease stages have been divided into several categories doesn't mean this will still be helpful in the future."

No common labels anymore
Prof. Fendler describes himself as an "active researcher, always actively pursuing hypotheses." "I don't necessarily observe. I create ideas in new fields as we did with this project. I like to take new steps. Instead of having very practice-oriented questions, I like to ask new questions that haven't been asked before and may be a bit provocative. With our findings of this study, for instance, we basically changed the name of the patient cohort we looked at. The fact that this so-called 'non-metastatic' cohort shifted to a higher, metastatic stage completely changes how to view and talk about these patients."

"Instead of having very practice-oriented questions, I like to ask new questions that haven't been asked before and may be a bit provocative."

Prof. Fendler comes across as determined; for instance, when asked about his career choices, he answers without a hint of doubt: "The field of nuclear medicine has always been my interest because of the technology and great methods for imaging and treatments with radionuclides that are available for many cancer entities." Also when asked for a word of advice for fellow researchers, the words come to him easily:

"One of our motivations behind this publication was to think outside the established categories, to think outside the current boxes we all have designed. There's always a different way of looking at patients. Only because current disease stages have been divided into several categories doesn't mean this will still be helpful in the future. It will be helpful to not put patients in a common label like nmCRPC anymore but to really look at them individually. New technologies such as PSMA PET provide us with the possibility to have that much information about a patient to really individualise care by designing a treatment that will most likely fit that specific patient. In the end, this might improve the outcomes for patients and the survival rates."

Prof. Wolfgang Fendler

Prof. Peter Albers (DE) presented Prof. Fendler with the EAU Prostate Cancer Research Award. Go to the EAU21 Congress Platform and watch the video!

ERN eUROGEN 2021: An update on rare and complex urology

Special Session at EAU21

Ms. Jen Tidman
ERN eUROGEN Business Support Manager
Nijmegen (NL)

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On Monday, 12 July (16:30 – 17:30) the ERN eUROGEN special session at EAU21 will update you on the European Reference Networks (ERNs), the recent largest healthcare innovation in Europe involving 30 million patients with a rare disease or complex condition.

ERN eUROGEN (www.eurogen-ern.eu) is the ERN for uro-recto-genital rare diseases and complex conditions and one of the 24 ERNs approved and co-funded by the European Commission. ERN eUROGEN aims to improve diagnosis, create more equitable access to high-quality treatment and care for patients with these rare diseases and conditions, and covers the whole spectrum from congenital anomalies, to lifelong care, complex functional urology, and rare urogenital tumours.

ERN eUROGEN now delivers virtual highly specialised advice to healthcare professionals across Europe using an innovative IT platform, the Clinical Patient Management System, provided by the European Commission. As a guest user of the system, you can refer a case to us and our multidisciplinary teams of experts are able to diagnose, suggest treatment or surgery, and provide advice for post-operative and transitional support.

ERN eUROGEN Registry

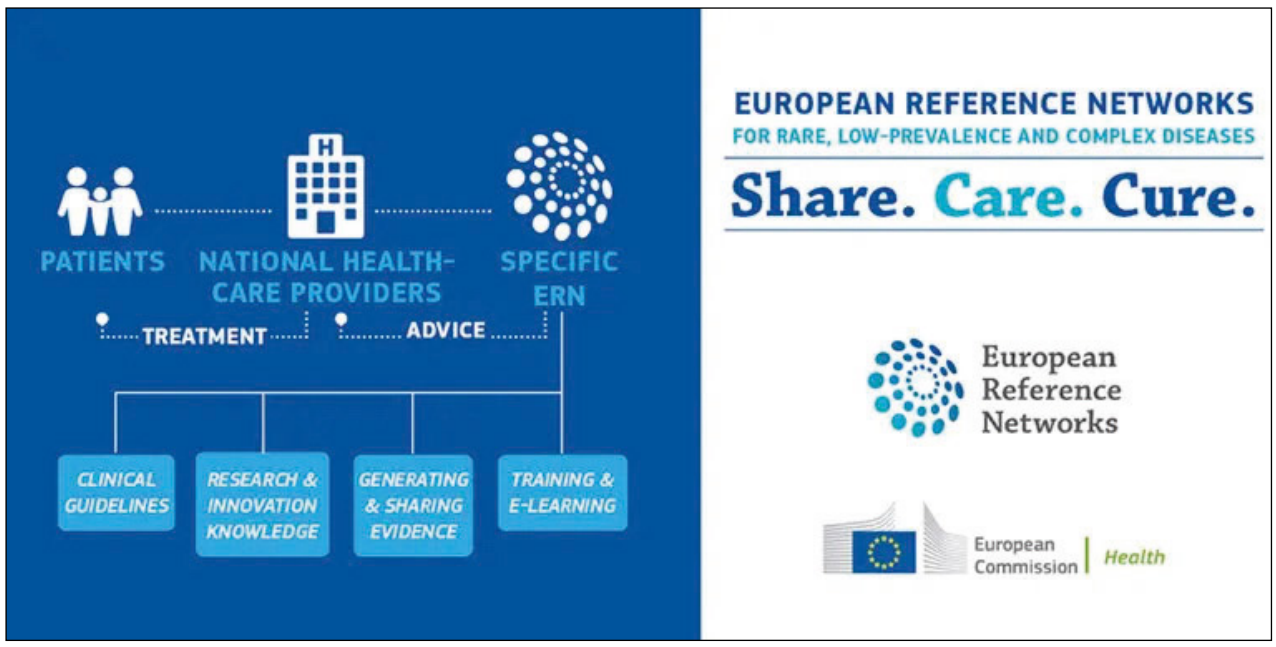
To begin the special session at EAU21, our Network Coordinator Prof. Wouter Feitz (NL) and our Programme Manager Ms. Michelle Battye (NL) will introduce the session and give an update on ERN eUROGEN, including its expansion both geographically and in terms of disease coverage. The network is also working hard on Sharing knowledge, Care programs and Cure innovations, clinical guidelines for patients with urological rare or complex conditions, the ERN eUROGEN Registry with 25 years of follow up, expert mobility, training and education, and research connections with different EU Infrastructures and organisations such as the EMA and European Health Data Space - all aimed at improving care for your patients.

ERN eUROGEN Registry Coordinator Dr. Loes Van Der Zanden (NL) will then present the recent ERN eUROGEN registry development, data, and future perspectives. At present, registries in the field of rare uro-recto-genital diseases lack uniformity. ERN eUROGEN wants to facilitate knowledge-sharing through the continuous and comprehensive collection of relevant clinical data. Therefore, the ERN eUROGEN registry (a large population registry on rare uro-recto-genital diseases and complex conditions with a long-term sustainable perspective of at least 25 years) is a top priority. The ERNs have an ambitious aim of including 500,000 patients with a rare disease or complex condition in the 24 ERN registries by 2025.

The ERN eUROGEN registry will collect common data elements defined by the EU Rare Disease Platform. These are common to all rare disease registries and will be the connecting point for all ERN databases. In addition, there will be clinical snapshots consisting of six disease-specific clinical questions. These two aspects of the registry will form the pilot phase where physicians from our current 39 healthcare provider members from 18 EU Member States will be asked to register their last 30 rare cases. This will allow users to understand how to use the registry and perform a clinical snapshot of current practices i.e. to compare clinical management among expert centres across Europe.

After the pilot phase, the disease-specific questions will be supplemented with additional follow-up questions. In addition, data from existing registries will be combined with the ERN eUROGEN Registry. In her presentation, Dr. Van Der Zanden will give an update on the status of the development of the ERN eUROGEN Registry.

The ERNs not only bring together the expertise of healthcare professionals within specialities, but they collaborate to enhance care for rare diseases and conditions that cross disciplines. As such, from Workstream 1 (rare congenital abnormalities) ERN eUROGEN collaborates with ERN ITHACA (the ERN for rare congenital malformation and syndromes with intellectual and other neurodevelopmental disorders) on a cross-ERN working group on spina bifida to allow multidisciplinary collaboration and the highest common standard in diagnosis and management, including access to new diagnostic tools and treatment.



In his presentation, Dr. Giovanni Mosiello (IT) will cover these joint activities and their current progress. He will discuss the development of three guidelines on the urological care of patients with spinal dysraphism (paediatric, transitional, and adult) and future education and training initiatives for clinicians and researchers, such as a two-day workshop for future research on innovative diagnostics and interdisciplinary treatments.

Lifelong care for patients

One of the aims of ERN eUROGEN is to provide lifelong care for patients (from cradle to end of life) and 17 ERNs include some form of highly specialised surgery as a treatment needed by patients with a rare disease or complex condition. As such, for the presentation from Workstream 2, Mr. Dan Wood (GB) will highlight the importance of transitional care in terms of adult urogenital reconstructive surgery.

In this context, transition is defined as the assumption of healthcare responsibility by a young adult as they move from a paediatric healthcare environment to adult healthcare. This is essential for children who have required childhood surgery and/or treatment for major urogenital anomalies. There are many adjustments for them to make: firstly, in better understanding their condition and treatment and, beyond that, discussing issues that are less easily addressed in a paediatric environment, such as sexual and reproductive function. It is also important to recognise that there may be predictors of long-term functional issues, for instance proteinuria in posterior urethral valves as a marker of risk to renal function.

Healthcare teams working in this field of medicine need to understand the paediatric condition and its prior management. This is important not only from a clinical perspective but also for recognition that patients often have a very clear understanding of their own condition and if their clinician is not able to show that they also have this, patients will quickly lose trust. Mr. Wood's talk will therefore focus on some of the avenues for formulating care in this field of urology with these factors in mind.

The third workstream within ERN eUROGEN focuses on rare urogenital tumours (penile and testicular cancer, adrenal tumours, abdominopelvic sarcoma, and rare renal tumour surgery). Although Prof. Vijay Sangar (GB) had to step down as Workstream 3 Lead unfortunately due to Brexit, he will still give the presentation *"Rare oncological urology and metrics: Our road to success"* at EAU21.

Rare urogenital cancers have come to the forefront in recent years. Producing quality science, outcome data and sharing patient management experience is pivotal in any healthcare system. The ERN eUROGEN rare cancer workstream includes some of Europe's largest providers and is growing. Our current data outputs will be presented showing how we have progressed and what the future will hold for collaborative working.

Patients are at the heart of ERN eUROGEN and the ERNs in general. Our European Patient Advocacy Groups (ePAGs) and their representatives are a crucial and highly valued part of our activities, and we endeavour to make sure their voices are heard.

During the EAU21 special session Mrs. Nicole Schwarzer (DE) and Mr. Michel Haanen (NL) will present a talk, which has been prepared together with Mrs. Dalia Aminoff (IT), emphasising once again the important topic of transition: this time, from a patient perspective.

They will consider what it would look like if transition was well organised and documented, not only for patients but also for healthcare professionals. They will cover the perspective of ePAGs and chairpersons of patient organizations, as well as the perspective of patients with anorectal malformations themselves. They will review whether there have been any changes since their last presentation at the ERN eUROGEN Annual Strategic Board Meeting in Noordwijk, the Netherlands in 2019 or indeed over the past 20 years.

In addition, Mr. Haanen will provide a case report of his own individual experiences, what is needed to upgrade transition and the results for patients in daily practice, what harm can be avoided for patients, and what benefits there are for healthcare professionals.

The session will include three opportunities for live questions and answers on ERN eUROGEN developments, workstreams and specific diseases, and patients and future perspectives. We look forward to seeing you there and hope for a lively discussion about these important issues.

Monday 12 July, 16.30 - 17.30 CEST
Special Session
ERN eUROGEN 2021: Update on rare and complex urology
Virtual room 8

Urine biomarkers in non-muscle-invasive bladder cancer

Biomarkers for diagnosis, follow-up, and recurrence

Ass. Prof. Joost Boormans
Associate Professor of Urology
Erasmus MC – Cancer Institute
Rotterdam (NL)

Twitter: @joostboormans

Current guidelines recommend doing a cystoscopy to rule out the presence of a bladder tumour in patients with haematuria. However, in only 3% of the patients with microscopic haematuria is a bladder tumour present, versus 28% of the patients with gross haematuria. Consequently, the vast majority of patients presenting with haematuria do not have cancer and performing cystoscopies in all patients poses an important burden to the healthcare system. In addition, patients under surveillance following an initial diagnosis of non-muscle-invasive bladder cancer (NMIBC) are subjected to regular cystoscopies for years, which has a significant impact on the patient's quality of life.

A urine assay with good diagnostic performance for the detection of urothelial cancer in the primary or surveillance setting can be of importance to clinical decision-making. First, the diagnostic performance of the cystoscopy is enhanced with additional information provided by the urine assay. Previously it was shown that the sensitivity of cystoscopy increases when the urologist is aware of a positive urine test: a so-called diagnostic review bias. [1] Secondly, cystoscopy visualises the bladder and urethra but not the upper urinary tract, whereas a urine assay has the ability to detect both upper and lower urinary tract localisations of urothelial cancer. A positive urine test combined with a negative cystoscopy encourages accelerated upper tract imaging leading to a shorter delay in upper tract tumour diagnosis. In addition, studies have shown that a positive urine marker test sometimes does not correlate with the presence of a tumour at cystoscopy but that it does correlate with a higher rate of recurrences over time in patients under surveillance. This indicates that a urine test might pick up recurrences sooner, even before a lesion is visible at cystoscopy, which is called the anticipatory effect. [2] Lastly, a negative urine assay potentially reduces the number of non-informative cystoscopies.

Many urine assays have been reported in the literature; an overview is summarised below. To interpret the diagnostic performance of such assays, it is important to highlight the quality parameters of a diagnostic test: sensitivity, specificity, negative predictive value (NPV), and positive predictive value (PPV). Sensitivity, the proportion of diseased persons who had received a positive test result, and specificity, the proportion of healthy persons who received a negative test result, are not affected by the prevalence of a disease. However, the NPV and PPV are impacted by disease prevalence and test sensitivity (see table 1). Therefore, it is of importance to realise that the diagnostic accuracy of a urine assay in the primary diagnostic setting cannot be compared between micro- and macrohematuria populations as the prevalence of urothelial cancer is 3% versus almost 30%.

"Urine assays show promise for future use in urological practice."

Furthermore, the objective of the urine assay should be taken into account. Is the test used to rule out a patient for cystoscopy in order to reduce the number of unnecessary cystoscopies? Such a test necessitates a high NPV, a high sensitivity, and a high specificity: the lower the NPV, the higher the risk that a patient with a negative test result will turn out to be a diseased patient missed. In addition, the lower the sensitivity, the more affected patients will receive a false negative test result and the lower the specificity, the more unaffected patients will receive a false positive test result. Conversely, if the test is used to rule in patients with high-risk urothelial cancer, then a high PPV and a high specificity are mandatory, because the lower the PPV, the more tests will incorrectly label unaffected patients as affected and the lower the specificity, the more unaffected patients will receive a false positive test result.

Lastly, the performance of most urine assays is measured in relation to cystoscopy, which is considered to be the gold standard; however, the sensitivity and specificity of standard white-light cystoscopy is not 100%. [3]

Cell-based urine assays
A well-known cell-based urine assay is voided urine cytology, which is the only urinary marker recommended in current guidelines. Its use is strongly recommended as an adjunct to cystoscopy for the detection of high-grade (HG) urothelial carcinoma or *carcinoma in situ* of the bladder in both the primary and surveillance setting. Urine cytology results in a very low number of false positives; however, it has a moderate sensitivity for the detection of HG cancers (HG sensitivity = 38-84%) and a low sensitivity for low-grade (LG) cancers (LG sensitivity = 12-26%) [4], leading to a high proportion of false negative test results. In addition, the operator-dependent assessment is significant with variable results across institutions. [5] Urine cytology is further hampered by a high rate of inconclusive results especially in patients with urinary tract infections. [6] It is also laborious and as a result expensive.

Other cell-based urines assays are Immunocyt and Urovysion, which are both FDA approved – but Immunocyt was recently withdrawn from the market. Urovysion's sensitivity was 79% for HG disease versus 53% for LG disease with a specificity of 80% in the surveillance setting. [7]

"It is important to stress that all available urine assays have significant limitations and lack validation in a real-world setting."

Protein-based urine assays
A potential advantage of protein in the urine is that the proteome can be directly linked to a bladder cancer phenotype. Examples of protein-based assays are NMP22 and BTA TRAK, which are amongst the most studied assays and have been approved by the FDA for use in surveillance and detection of disease in high-risk populations. [8,9] The reported sensitivity of both assays was higher than cytology, especially for LG disease with an overall sensitivity of 47-76%. However, test results are influenced by the presence of haematuria or stones, instrumentation of the urinary tract, and urinary tract infections, which compromises the specificity. The specificity of the assays ranged between 75-93%.

The ADx assay is an ELISA test targeting the MCM5 protein. In a study involving 856 patients with haematuria with a prevalence of bladder cancer of 8.6%, the ADx assay had a sensitivity of 65%, a specificity of 68%, the NPV was 96% and the PPV was not reported. [10] In the surveillance setting, including 1431 NMIBC patients with a recurrence prevalence of 8.6% (HG recurrence: 2.6%), the sensitivity was 45%, specificity 71%, the NPV was 92% and the PPV was not reported.

DNA-based urine assays
Many DNA aberrations, such as oncogenic mutations, have been targeted for the development of urine assays. The detection of an oncogenic mutation in the urine is a very strong indicator for the presence of cancer in the urinary tract. However, the clinical implementation of DNA-based assays is hampered by processing time. Plus, a low DNA yield in single urine samples impedes the production of reliable test results. The Bladder EpiCheck assay combines a panel of 15 methylation markers, and it was shown in a prospective trial involving 440 patients in the surveillance setting (recurrence prevalence = 12.2%) that EpiCheck had an overall sensitivity of 68%, a specificity of 88%, a NPV of 94% and a PPV of 45%. [11] The performance was better in the subgroup of patients who had had a previous diagnosis of a HG tumour (52%), with a sensitivity of 86% and a NPV of 99%.

The AssureMDx assay combines oncogenic mutations in the genes *FGFR3, TERT,* and *HRAS* and the methylations of the genes *ONECUT2, OTX1,* and *TWIST1*. In two retrospective case-enriched discovery series, the test had a sensitivity of 93-97%, a specificity of 83-86%, and a NPV of 99% for an estimated 5-10% prevalence of bladder cancer in the populations investigated. [12,13] The assay was further validated in a prospective population-based cohort of 1003 patients referred for gross or microscopic haematuria. The sensitivity here reached 93%, the specificity was 81% and the NPV 99%. [14].

Sensitivity	Prevalence	NPV
95%	5%	100%
0%	5%	94%
95%	30%	98%

Table 1: The impact of a change in the sensitivity of a diagnostic test and in the prevalence of the disease on the Negative Predictive Value (NPV)

RNA-based urine assays
RNA-based urine assays have short turnaround times, but the challenge is to obtain RNA of a sufficient high quality from urine. Abstracting RNA from bladder washings gives a significantly better yield of high-quality RNA; however, this is not feasible to be implemented in clinical practice.

The Cxbladder Monitor is an RNA-based assay, measuring the expression of the genes *IGFBP5, HOXA13, MDK, CDK1,* and *CXCR2*. In a prospective trial including 485 patients with gross haematuria and a bladder cancer prevalence of 13.6%, the sensitivity and specificity was 82% and 85%, but the NPV and PPV were not reported. [15] Kavalieris et al. reported on a cohort of 763 patients under surveillance with a recurrence rate of 15.1%. The sensitivity and NPV rate were 92% and 96% respectively. However, the specificity was only 32% and the PPV was not reported. [16]

The Xpert assay measures the expression of *ABL1, CRH, IGF2, UPK1B,* and *ANXA10*. In the diagnostic setting including 895 patients without a history of bladder cancer, the sensitivity was 78%, specificity 84%, and the NPV 98%. [17] The prevalence of bladder cancer was not reported. In the surveillance setting (n=239) with a recurrence rate of 18%, sensitivity was 74%, specificity was 80%, the NPV was 93%, and PPV was 44%. [18]

"When analysing the diagnostic performance of a urine test, one should take into account the characteristics of the population tested, as well as the quality parameters of the test itself."

Conclusions
To summarise, urine assays show promise for future use in urological practice. Urine is easy to obtain, the assays are not costly, and they have the potential to reduce the number of invasive cystoscopies and upper tract imaging. However, it is important to stress that all available urine assays have significant limitations and lack validation in a real-world setting, both in the primary diagnostic and surveillance setting of patients with urothelial cancer.

When analysing the diagnostic performance of a urine test, one should take into account the characteristics of the population tested, as well as the quality parameters of the test itself. If the goal is to **rule in** patients for primary or recurrent bladder cancer, a high PPV and specificity of a urine assay are of importance. For UroVysion, ADxBladdr, Xpert Bladder Detect, and Cx Detect, the PPV was not reported (NR) and for the AssureMDx the PPV was 34%. The specificity of Xpert Detect and Cx Detect were both highest being 85%. In the surveillance setting, the reported specificity of ADxBladder, Xpert Monitor, Cx Monitor, and Bladder EpiCheck, was 71%, 80%, 32%, and 86%, whereas the PPV was NR, 44%, NR, and 45%, respectively.

If the objective is to **rule out** patients to reduce the number of unnecessary cystoscopies, a high NPV, a high sensitivity, and a high specificity of the test are mandatory. Currently, none of the tests reported in the literature has an accurate performance on all three parameters. However, in the surveillance setting of patients with HG disease all tests have better sensitivity than urine cytology at the cost of a lower specificity.

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Saturday 10 July, 13:15 - 14:15 CEST
Live from the studio: Thematic Session 09
Urinary biomarkers: Are we there yet?
Virtual Room 3

RPLND for chemo-resistant disease

Examining different options for different patients

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In addition to systemic chemotherapy, salvage surgery represents a mainstay of multimodality therapy for those rare patients. The options of salvage surgery, desperation surgery and surgery for late relapses will be discussed.

Patients with persistent or relapsing elevated serum tumour markers (STMs) following induction chemotherapy are considered to have residual germ cell tumour elements and second-line chemotherapy is the standard management of choice.[1] Following salvage chemotherapy, patients have a higher rate of malignancy in residual tumour specimens so that a postsalvage chemotherapy retroperitoneal lymph node dissection (RPLND) is recommended for all patients with residual lesions independent of their size. Still the overall long-term survival rates are poor at 15–40%. [2,3]

Surgery of patients with rising or STM persistence following second or third-line chemotherapy indicates the presence of chemorefractory disease and complete surgical resection will result in long-term cure rates of 35–75%. [2,3] When referring to salvage surgery in mTGCT, one has to differentiate the terms salvage, late relapse and desperation surgery.

"All patients with enlarged residual masses should undergo salvage RPLND due to the 55% frequency of active cancer."

Salvage RPLND
Salvage RPLND usually defines a patient with an enlarged mass and normalized STMs following salvage chemotherapy. All patients with enlarged residual masses should undergo salvage RPLND due to the 55% frequency of active cancer. [4] Salvage RPLND is always performed with a curative intent so that even in the presence of multiple sites, all efforts should be taken to resecting all residual disease.

There is a histological discordance between the histology of the RP and extraretroperitoneal sites in about 30% of cases indicating that all residual masses need to be resected. [4,5] There is, however, a 90% histological concordance between RP and lung lesions so that expectant management can be considered in patients with necrosis/fibrosis in the RP specimen in order to reduce treatment associated morbidity. Salvage surgery by itself is more complicated and it requires a higher frequency of adjunctive procedures such as vascular, intestinal or even skeletal surgeries so that it should only be performed in highly experienced centers only. [6,7] Long-term survival is reported in the range of 75% following salvage chemotherapy and about 65% following high-dose chemotherapy [1,4,7].

There are reliable predictive markers associated with viable cancer or teratoma although persistently elevated STMs have a higher chance of finding active cancer in the resected specimens. It also has been demonstrated that basically all patients with high elevated ß-hCG levels will relapse after salvage RPLND and that high ß-hCG levels represent a predictor for disease-free survival. [8-10] Especially for patients with elevated ß-hCG salvage, RPLND should only be performed if the residual masses are completely resectable.

Furthermore, the location of the masses seems to be associated with oncological outcome: 82 and 57% with retroperitoneal/mediastinal masses and visceral disease achieved complete resection, respectively. [10] Postoperative normalization of STMs has a long-term prognostic value so far, that STM persistence results in 5-year survival of 8% as compared to 95% in normalized STMs. [11]

"Repeat RPLND itself represents a poor risk factor associated with a significantly lower 5-year survival rate of only 55% as compared to 86% in the group of patients undergoing adequate PC-RPLND."

Desperation surgery or RPLND
This describes the clinical situation of elevated or rising STMs during or within 4 weeks after completion of systemic therapy and those patients harbour chemorefractory GCT, which only can be cured by complete surgical resection.

Despite the fact that STMs are rising, about 50% of patients harbour teratoma or necrosis only in the final specimen. [2,3, 12-14] Therefore, all men with completely resectable lesions should undergo surgery resulting in a partial remission rate and long-term cure rate of 50–60% and 20–30%, respectively. However, there are several criteria to identify those patients who might benefit most from desperation surgery. The 5-year OS is 93, 60, and 23% in men with normalized, stable or rising STMs, respectively. [14] In addition, slowly rising STMs are associated with the long-term cure, especially if only alpha-fetoprotein (AFP) is involved. Resectable masses in less than three sites are additional criteria predicting long-term benefit from surgery. Respectively. [11] Postoperative normalization of STMs has a long-term prognostic value so far, that STM persistence results in 5-year survival of 8% as compared to 95% in normalized STMs.[12] In recent series, increasing preoperative ß-hCG, elevated AFP, redo RPLND and incomplete resection had been indentified as negative risk factors associated with poor survival. [13, 14]

Late relapse surgery
This kind of surgery is defined for patients with relapses > 2 years after completion of first line chemotherapy and it is observed in about 3.2% and 1.4% of patients with nonseminomas or seminomas, respectively. [15,16] The majority of relapses develops in the retroperitroneum only and 80% harbor viable GCT with yolk sac tumour elements representing the most common histology. [17] In addition, many lesions contain somatic malignant transformation so that surgery remains the therapeutic approach of choice if the mass is completely resectable.

Systemic chemotherapy is associated with an inferior oncological outcome because a complete remission can only be achieved in 26% and relapse-free survival without surgery of only 3%. [17,18] In patients with extensive disease at the time of late relapse not amenable for upfront surgery, systemic chemotherapy followed by surgical resection will result in complete remission of 50% and a median overall survival of 23.9 months. [18]

Repeat RPLND after previous retroperitoneal surgery
Although rare, a subset of patients' needs repeat RPLND due to metastatic tumour recurrence after primary RPLND or PC-RPLND because of incomplete tumour resection during initial surgery. [19-25]

Repeat RPLND itself represents a poor risk factor associated with a significantly lower 5-year survival rate of only 55% as compared to 86% in the group of patients undergoing adequate PC-RPLND. The long-term outcome after repeat RPLND relies on the complete resection of all residual retroperitoneal masses, which will harbour viable cancer and mature teratoma in 20–25 and 35–40%, respectively. Whereas the cure rate for those with mature teratoma only approaches 100%, it decreases significantly to 44% and 20% in the presence of viable cancer and teratoma with malignant transformation, respectively.

Repeat RPLND is a challenging surgical procedure associated with higher rates of adjunctive surgical procedures, with ipsilateral nephrectomy and vascular procedures being the most frequent adjunctive surgeries.

Repeat RPLND often represents the last chance of cure for patients with in-field recurrences and it usually can be performed with acceptable morbidity. Repeat RPLND will result in long-term survival of 67–75%; if patients present with in-field recurrences and elevated markers, systemic chemotherapy followed by PC-RPLND should be initiated. In patients with negative markers, immediate RPLND should be performed since most masses will harbour mature teratoma only.

"Depending on the International Germ Cell Cancer Classification Group risk classification, 10–50% of metastatic testis cancer patients relapse."

Adjunctive surgery in patients undergoing PC-RPLND
Additional surgical procedures of adjacent vascular or visceral structures might be necessary in up to 25% of the patients undergoing PC-RPLND in order to achieve complete resection of the residual masses. [26] En-bloc nephrectomy represents the most common type of adjunctive surgery for complete tumour clearance. Additional vascular procedures such as aortic replacement and resection of the inferior vena cava due to tumour infiltration will be necessary for about 1.5 and 10%, respectively.

Our group compared the outcome of standard PC-RPLND versus complex PC-RPLND with a variety of adjunctive vascular, visceral or skeletal surgeries. [27] It was demonstrated that the extensive surgeries resulted in an identical high cure rate as compared to the standard PC-RPLND. Besides, in patients undergoing pancreaticoduodenal surgeries, we did encounter a significantly increased frequency or severity of surgery-related complications.

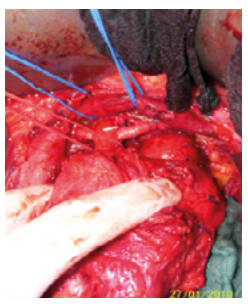
Preoperative imaging studies
All types of salvage surgery are more complicated and require more adjunctive surgeries than a typical post-chemotherapy RPLND. [1,2] Therefore, a complete metastatic workup is mandatory, using different imaging modalities to identify potential pitfalls of the intended resection and in order to allow early identification of multidisciplinary teams. Especially in patients with large residual masses, imaging studies should allow an adequate assessment of the retroperitoneal vascular structures since the involvement of the inferior vena cava (IVC) and the abdominal aorta can be expected in about 6–10 and 2%, respectively. [28]

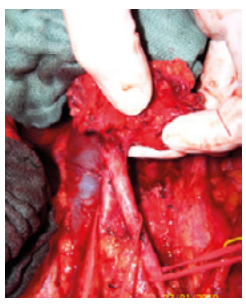
"All patients with residual lesions need to undergo post-chemotherapy residual tumour resection of all residual lesions."

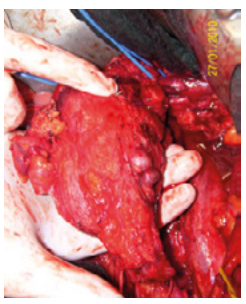
Magnetic resonance imaging represents the most appropriate imaging technique to predict infiltrations of the vessel wall and the presence of an intracaval tumour thrombus. Infiltrations of the IVC wall or IVC thrombi should be completely resected since about two thirds of the patients harbor vital cancer or mature teratoma in the infiltrating masses. Usually, intraoperative reconstruction or replacement of the IVC is not necessary since chronic venous sequelae are to be expected in less than 5% of all patients. [28] The necessity for aortic replacement is rare and usually accompanied by large residual masses involving additional adjacent structures and making additional surgical procedures necessary such as nephrectomy, IVC resection, small bowel resection and hepatic resection. In the majority of cases, mature teratoma or vital carcinoma was identified in the aortic wall.

Summary
Depending on the International Germ Cell Cancer Classification Group risk classification, 10–50% of metastatic testis cancer patients relapse. Tumour marker negative late relapses are best treated by a surgical approach when complete resection of metastatic sites is possible. Tumour marker positive relapses are initially managed by systemic salvage second-line or high dose chemotherapy depending on the prognostic risk score.

All patients with residual lesions need to undergo post-chemotherapy residual tumour resection of all residual lesions. Patients with early rising markers during or within 4 weeks after completion of salvage chemotherapy are best treated by desperation surgery if the masses can be resected completely. All those systemic and surgical are reserved for specialised centres only.







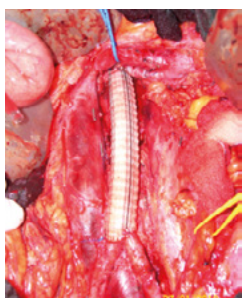
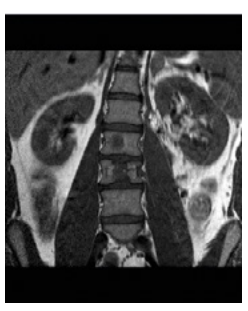


Photo 1A – 1D: A complete resection of a large retroperitoneal mass with a step-by-step dissection and securing of the major retroperitoneal vessels followed by an en-bloc resection of the mass and the infrarenal aorta, which was replaced by an aortic prosthesis



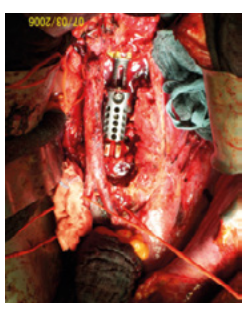
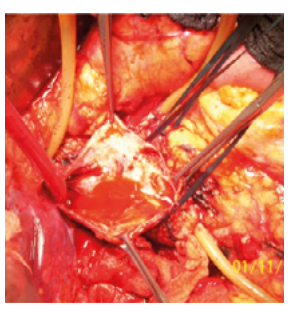


Photo 2A and 2B: A complete resection of two skeletal metastases in the lumbar spine; replacement of vertebral bodies with a cage



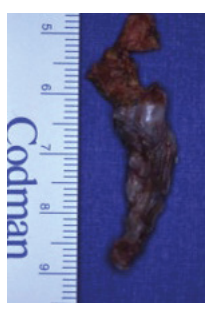


Photo 3A and 3B: A complete resection of an intracaval tumour thrombus-harbouring mature teratoma

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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.

Saturday 10 July, 15.15 – 16.15 CEST
Live from the studio: Thematic Session 11
Testis Cancer: Innovations by biomarkers and surgery
Virtual Room 3

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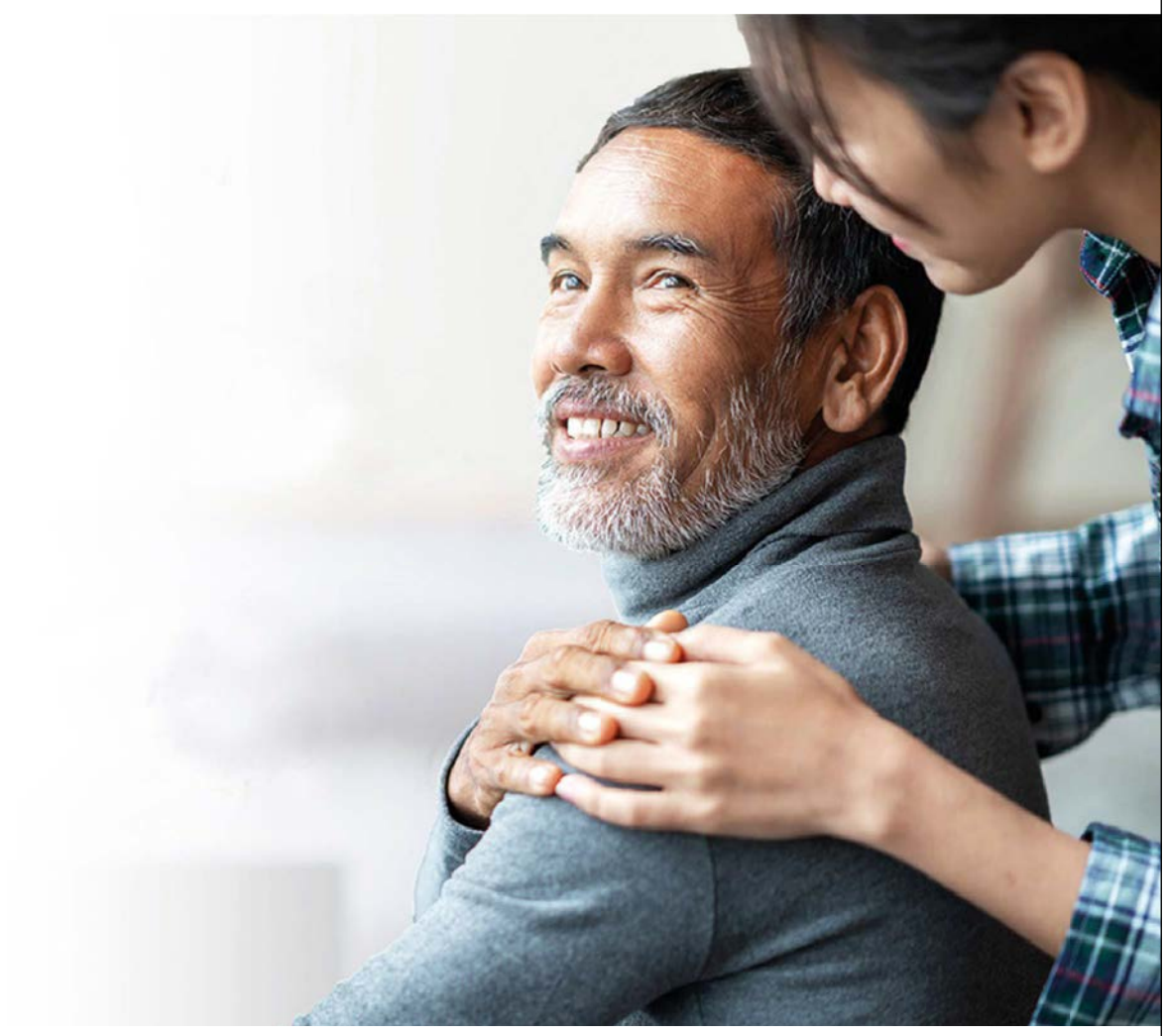
PN1087191 EU-RevA 06/2021



Using pharmacotherapy for OAB

What drug interactions to be aware of

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The average patient seeking treatment for overactive bladder (OAB) is in his/her 60s. Most patients in this age group suffer from multiple diseases and, accordingly, receive multiple medications. This creates a potential for drug-drug interactions (DDIs) that may lead to altered efficacy and/or increased side effects. While urologists are trained to select medical treatment for OAB and other conditions for an optimal balance between efficacy and tolerability, the impact of comedications is often overlooked.

The prevalence of many diseases increases with age, for instance, OAB, benign prostatic hyperplasia (BPH), coronary heart disease, type 2 diabetes, or most types of cancer. Thus, older people are likely to suffer from multiple concomitant diseases. Most of them are treated at least partly by medication. Accordingly, the concomitant use of multiple drugs is frequent, and the prevalence of receiving multiple drugs concomitantly increases by age. For instance, based on the 2019 German claims data, only 6.5% of subjects aged 65 and older did not receive any prescription medicine. However, the median number of drugs used in this age group was seven (interquartile range 4-11), and 72.6% of patients received at least five different medications, i.e. exhibited polypharmacy. [4]

As patients receiving OAB medication by average are in their 60s, about half of all patients receiving OAB belong to the age group having by average seven different medications. This creates a major potential for DDIs. DDI can have a major impact on health: For instance, meta-analysis has shown that DDI account for 22.2% of all adverse event-related and 1.2% of total hospital admissions. [2]

"Consultation with other physicians treating a patient is required to optimally address medical needs arising from drug-drug interactions."

DDI comes in two forms: pharmacodynamic and pharmacokinetic DDI. The former occurs if two or more drugs act on the same physiological system. Depending on what the drugs do, this can lead to greater or smaller effects. This can affect both efficacy and tolerability of the interacting drugs. Such interaction can be intentional when we use multiple drugs acting on the same organ (but mostly on a different molecular target) in many medical conditions to increase efficacy. An example of this is when treating urinary tract infections with a combination of antibiotics or bladder cancer with a treatment regimen based on multiple drugs. However, such combinations can also attenuate drug efficacy. For instance, acetylcholinesterase inhibitors are used in the symptomatic treatment of dementia. These inhibitors prevent the inactivation of acetylcholine which in turn, may enhance existing bladder overactivity and thereby limit the efficacy of OAB medications. Pharmacodynamic DDI typically affects all drugs using the same mechanism of action in a similar way.

Pharmacokinetic DDI occurs when one medication affects the absorption, distribution, metabolism, or excretion of another drug. The most frequent form of this is one drug being metabolised by enzymes of the cytochrome P450 (CYP) system and another drug either inducing such enzymes or inhibiting them. This leads to reduced and enhanced exposure of the first drug, respectively. For instance, the anti-epileptic drug carbamazepine induces CYP3A4 which in turn, metabolises the immunosuppressant drug, cyclosporine. Cases have been reported where concomitant use of carbamazepine and cyclosporine led to underdosing of cyclosporine and loss of a kidney transplant. Pharmacokinetic DDI is not generalizable within a drug class, but specific for individual drugs (Table 1).

Muscarinic antagonists

Muscarinic receptor antagonists are the mainstay of medical OAB treatment. Side effects such as dry mouth and, to a lesser degree, constipation are frequent and unpleasant and often lead to premature discontinuation of treatment. Perhaps even more relevant are the cognitive side effects of muscarinic antagonists. [3]

While specific studies for such drugs in OAB are missing, it is generally accepted that the risk for side effects increases with the total number of medications having antimuscarinic effects. These include analgesics, antiarrhythmic drugs, antiemetics, antihistamines, antihypertensives, antiparkinsonian agents, antispasmodics, bronchodilators, ulcer drugs, many antidepressants and schizophrenia drugs. Generally, the higher the number of drugs with muscarinic antagonist properties, the greater the anticholinergic load and associated risk of cognitive impairment. [1]
A comprehensive medication history is key to detect potential sources of pharmacodynamic DDI and prevent or reverse corresponding side effects.

While there are no known pharmacokinetic DDI for trospium, all other muscarinic antagonists are metabolised by CYP2D6 and/or CYP3A4. Concomitant use of medications that inhibit these enzymes can increase exposure to the antimuscarinics. This leads to specific recommendations on adjusted dosing schemes in the presence of such comedication (Table 1). Frequently used inhibitors of CYP2D6 include anti-viral protease inhibitors such as indinavir and selective serotonin uptake inhibitors such as fluoxetine or paroxetine (Table 2). Potent inhibitors of CYP3A4 include azole-antimycotics (e.g. ketoconazole), macrolide antibiotics (e.g. erythromycin), protease inhibitors and some selective serotonin-uptake inhibitors but also grapefruit juice (Table 2). For instance, concomitant use of such drugs can increase the exposure to darifenacin 10-fold. [5]

β3-Adrenoceptor agonists

The only β3-adrenoceptor agonist currently approved in Europe is mirabegron. In contrast, to muscarinic antagonists, mirabegron has little risk for clinically relevant pharmacodynamic DDI. Concomitant use of potent CYP3A4 inhibitors can increase exposure to mirabegron, but the extent of this interaction is of limited clinical relevance in patients with normal renal function. However, in case of concomitant minor to moderate impairments of renal function (GFR 60-89 or 30-59 ml/min/1.73 m^2, respectively), the mirabegron dose should be limited to 25 mg if potent CYP3A4 inhibitors are used.

Table 1: Drug-drug interactions with muscarinic antagonists. Adapted from (5).

Drug	Comedication	Consequence
Darifenacin (7.5/15 mg)	CYP2D6 inhibitors Moderate CYP3A4 inhibitors Potent CYP3A4 inhibitors	Starting dose 7.5 mg; titrate to 15 mg if well tolerated Starting dose 7.5 mg Do not use
Fesoterodine (4/8 mg)	CYP2D6 inhibitors Potent CYP3A4 inhibitors	Starting dose 4 mg Maximum dose 4 mg
Oxybutynin (5-30 mg)	Potent and moderate CYP3A4 inhibitors	Caution
Propiverine (5/15 IR/30/45 mg ER)	Potent CYP3A4 inhibitors	No studies available but in-vitro data point to possible interactions
Solifenacin (5/10 mg)	Potent CYP3A4 inhibitors	Maximum dose 5 mg
Tolterodine (1/2/4 mg)	Potent CYP3A4 inhibitions	Maximum dose 2x1 mg IR or 2 mg ER
Trospium (40 mg)	No pharmacokinetic interactions identified	

Table 2: Examples of drugs causing DDI by inhibiting CYP2D6 or CYP3A4

Class	Drug	CYP2D6	CYP3A4
Anti-infectives	Ketoconazole	-	+++
	Itraconazole	-	+++
	Erythromycin	-	++
	Clarithromycin	-	++
	Indinavir	++	+++
	Ritonavir	++	+++
Anti-depressants	Fluoxetine	+++	+
	Paroxetine	+++	+
Foods	Grapefruit juice	-	++

Consequences

OAB patients are in an age group where multiple comorbidities and comedications are likely. Dedicated research on DDI has largely focused on the interaction between two drugs. While the specific evidence on what happens if three or more drugs are used concomitantly remains scarce, it is safe to assume that the risk for clinically relevant DDI increases with increasing numbers of concomitantly prescribed drugs. There are two pragmatic key defences against DDI: a comprehensive medication history and staying alert for any sudden change in efficacy or tolerability of drugs and their possible association with a change in comedications.

The greatest risk for clinically relevant DDI in the treatment of OAB comes from muscarinic antagonists. While the risk for pharmacodynamic DDI applies to the entire drug class, that for pharmacokinetic DDI depends on the specific compound in question.

When a pharmacokinetic DDI is suspected, it can be helpful to switch to an antimuscarinic that is metabolised/excreted by other pathways and less vulnerable to a specific interacting medication (Table 1). If this is not possible or if a pharmacodynamic DDI is suspected, switching to a β3-adrenoceptor agonist can be considered. If the result of the DDI is highly relevant and neither approach is feasible, it should be considered to stop one of the medications being involved. Such decisions should be based on an exchange with the colleague responsible for the prescription of the other drug. Drugs prescribed by other physicians should not be discontinued without consultation with the prescribing colleague.

Tips for clinical practice

The important pointers to keep in mind are the following:

- A complete medication history is key to the prevention, detection, and management of DDI.
- If the efficacy or tolerability of a drug changes, changes of medication regimen should be checked.
- Consultation with other physicians treating a patient is required to optimally address medical needs arising from DDI.

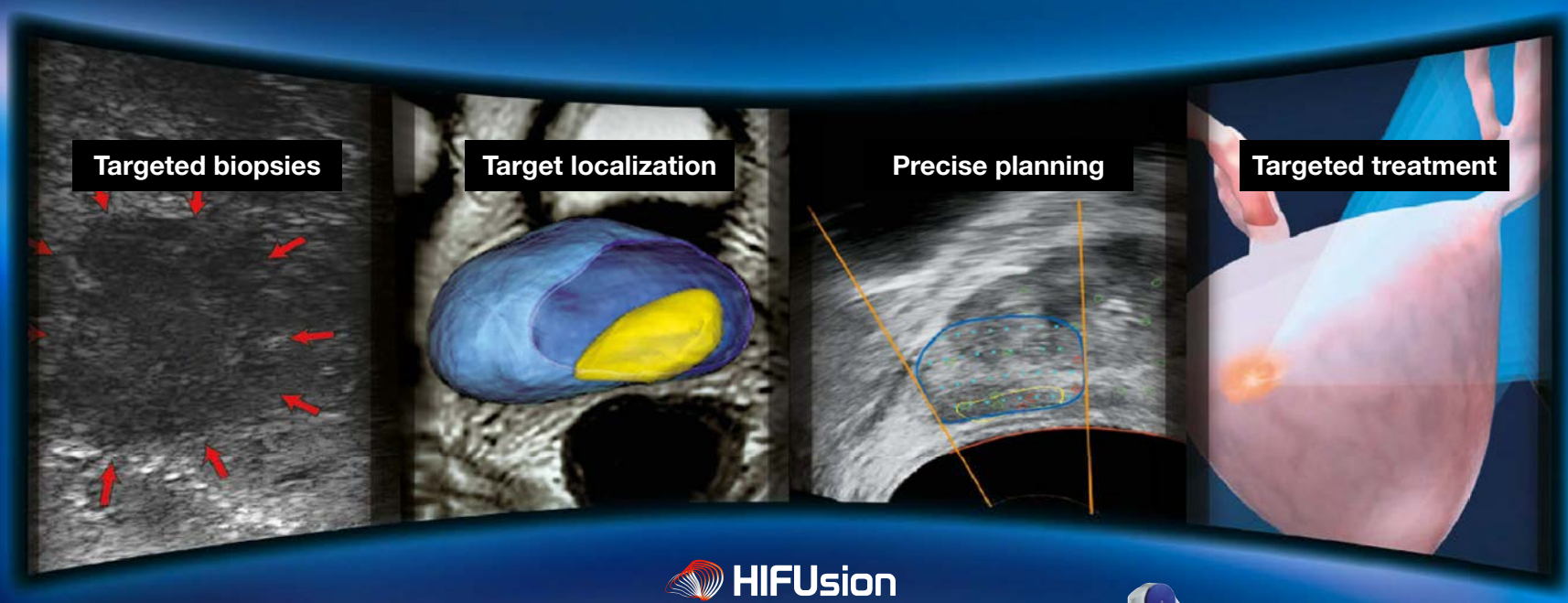
Due to space constraints, the reference list can be made available to interested readers upon request by sending an email to: communications@uroweb.org.

Friday 9 July, 10.30 - 12.00 CEST
Live from the studio: Plenary Session 02
Optimal management of incontinence in the elderly patient
Virtual room 3

by edap tms

End-to-end Management of Prostate Cancer

from targeted biopsies to focal therapy



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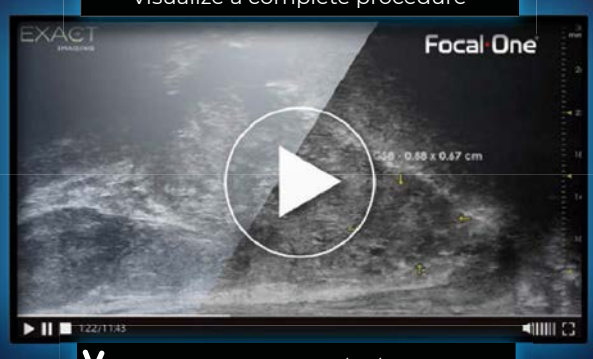

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Bringing New Horizons to Therapy

Prof. Enrico Dormia: The man, the urologist and his basket

An ode to innovation in urology, with great transformative consequences for the field

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Every day, a urologist somewhere in the world asks the operative nurse for a Dormia Basket. We are so used to do this, but do we really know who Dormia was?

The name Dormia is not of a manufacturer but rather the name of a renowned Italian Urologist who was active until 20 years ago. Prof. Enrico Dormia MD, a giant in the field of urology, passed away on February 20th 2009.

Born in 1928 in Bormio, a tiny village in the Italian Alps, Enrico Dormia graduated from the University of Milan in 1952. He went on to complete his fellowship training in Milan, was promoted to Professor and became an active member of the staff at the Urology Clinic of the University of Milan. During his stay in the Urology Clinic, under the direction of Prof. Luigi Pisani, who was President of the International Society of Urology and one out of three full professors of Urology in Italy, Dormia worked hard and studied urinary stones in depth.

At that time, until the early eighties, the only active therapy for ureteral or kidney stones was open surgery. In fact, it was only in 1978 that Arthur Smith established a new specialty in Urology and chose the name "endourology", defining it as a "closed and controlled manipulation of the genitourinary tract". After this date, in Europe, ureterorenoscopy by Perez Castro, PCNL by P. Alken and ESWL by C. Chaussy started and blossomed.

In the early 1950s, Enrico Dormia had started to study how to apply to stones the concept popularized by another Italian great physician Umberto Veronesi 30 years later: "from the maximum treatment possible to the minimum efficacious one", stressing the concept of minimally invasive therapy in urology. Dormia dedicated his efforts to ideate and develop systems to extract ureteral stones from the lumen of the ureter and to the possibility of dissolving the stones in the renal cavities. They would then be washed out with solutions invented for this purpose, producing significant scientific and clinical work in the field of chemolysis.

"The concept of putting together a ureteral catheter and the thinnest string of a guitar."

The basket and the metallic tricep

In 1958 Dormia published the first paper in Italian on two new instruments to remove stones from the ureter: the basket and the metallic tricep. Dormia, a bright and creative man, developed the concept of putting together a ureteral catheter and the thinnest string of a guitar to create the prototype of the world famous Dormia Basket: a 5 Ch catheter containing a metal wire that -pushed out of the tip of the catheter- was able to spring 3 or 4 wires fixed to each other on the tip and arranged in an helicoidal shape. The basket was able -when sprung out- to dilate the ureter, capture and extract the stone (see figure 2).

Figure 1: Prof Enrico Dormia

The second instrument was a metallic tricep, 8 Ch in size, actuated by a handle with three fingers. Both instruments had to be inserted in the ureter in cystoscopy and under radiological control. The basket had to pass over the stone and had to be adjusted with gentle movements towards the stone until this was "in" the basket, whereas the second instrument had to touch the stone and then had to be opened to allow the tricep to embrace the stone (see figure 3). The release of the stone was more difficult with the basket than with the triceps. However, some historical extractions are reported in the literature at the beginning of the basket tale (see figure 4).

I had the lucky opportunity to be taught by Prof Dormia to extract ureteral stones by means of the basket under radiological control. The rules were simple:

1) The stone should be located in the pelvic ureter no more than 7 cm from the papilla.
2) The bladder had to be empty.
3) The traction had to be continuous and gentle.
4) The direction of the traction had to be towards the opposite side and upwards.
5) Sometimes an electrical papillotomy had to be performed before the extraction.

"Only in Dormia's hands could the basket be employed in stones above the iliac vessels."

Only in Dormia's hands could the basket be employed in stones above the iliac vessels: in these cases a small weight was attached to the basket (usually some Italian coins) and the progression of the stone was observed radiologically for some days. The Dormia basket was presented in Paris during an international congress. It was patented, acquired and commercialized by Porges in the Coloplast group, which owns the brand name "Dormia Basket". The prototype of the Dormia basket is exhibited in the History of Medicine Museum in Vienna, Austria.

Dormia planted the seeds

Nowadays the original extraction technique, which was safe in Enrico Dormia's hands and was a well-established technique, has been abandoned. The EAU Guidelines forbid the blind extraction of ureteral stones and recommend to do that under direct vision. However, without any doubt, Dormia planted the seeds of the extraordinary future development of endourology.

In 1962, a few years after the basket presentation, Enrico Dormia proposed his technique to dissolve stones by chemolysis. He studied for a long time with a chemist, Ottavio Zardini, a solution called Doria-Zardini (DZ Solution), which was able to dissolve calcium stones both in vitro and in vivo. Dormia created a system to irrigate the kidney with high flows and low pressures through a two-way ureteral catheter (see figure 5). The technique, which was tricky in some ways, was reserved for fragile patients (single kidney, pluri-operated, etc.). It required long times to accomplish good but often partial results, but it was the only alternative new surgical procedure.

"Enrico Dormia was also an outstanding surgeon mainly in the field of kidney stones."

In such a productive time, Dormia got married, had two children and discovered to be a loving father, spending the little time away from urology with his family. His second son Guido -urologist as well- was his successor as Chief in San Carlo Hospital in Milan.

In 1969 Dormia was appointed as Chief of the Urology Department at the Alessandro Manzoni Hospital in Lecco. In 1973, he started an intense program in renal transplantation and applied chemolysis to residual stones post-ESWL. In 1991, he moved to Milan as Chief of the Department of Urology at the San Carlo Hospital and retired in 1998.

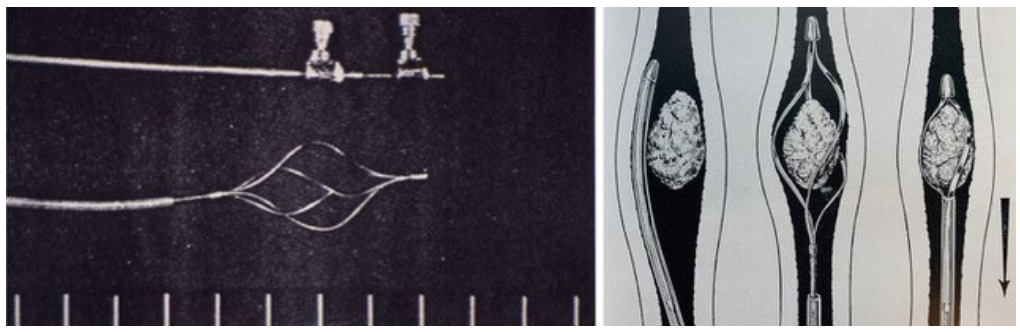

Figure 2: The basket was able -when sprung out- to dilate the ureter, capture and extract the stone

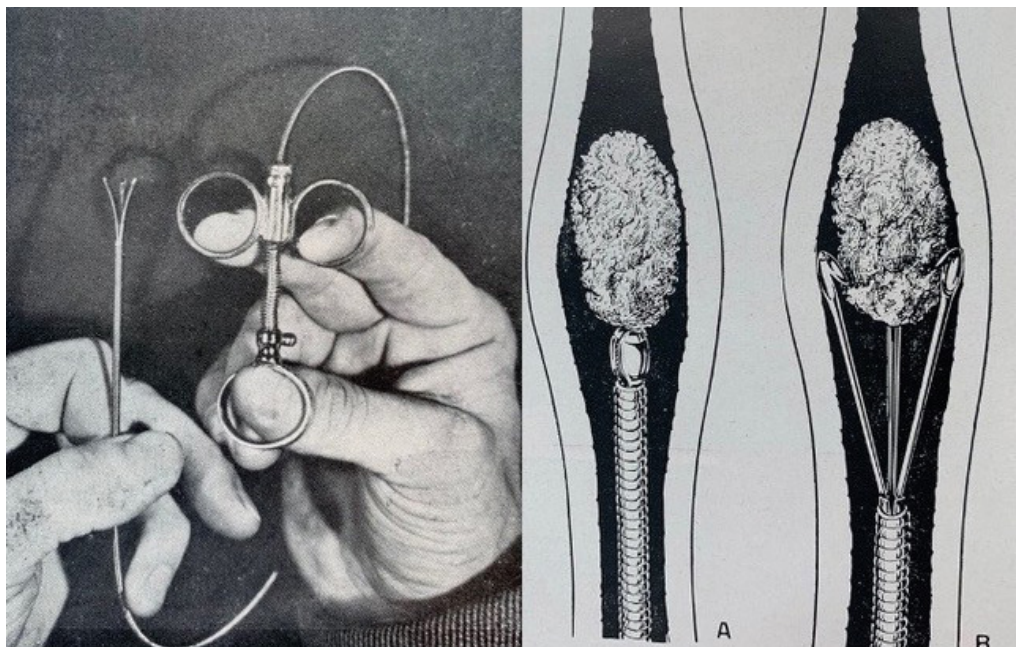

Figure 3: The basket had to pass over the stone and had to be adjusted with gentle movements towards the stone until this was "in" the basket, whereas the metallic tricep had to touch the stone and then had to be opened to allow the tricep to embrace the stone

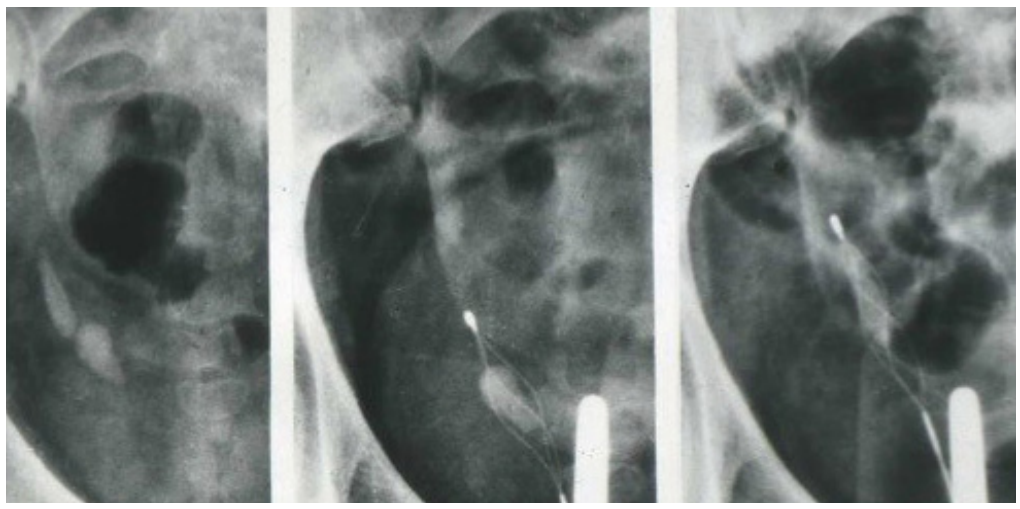

Figure 4: Some historical extractions are reported in the literature at the beginning of the basket tale

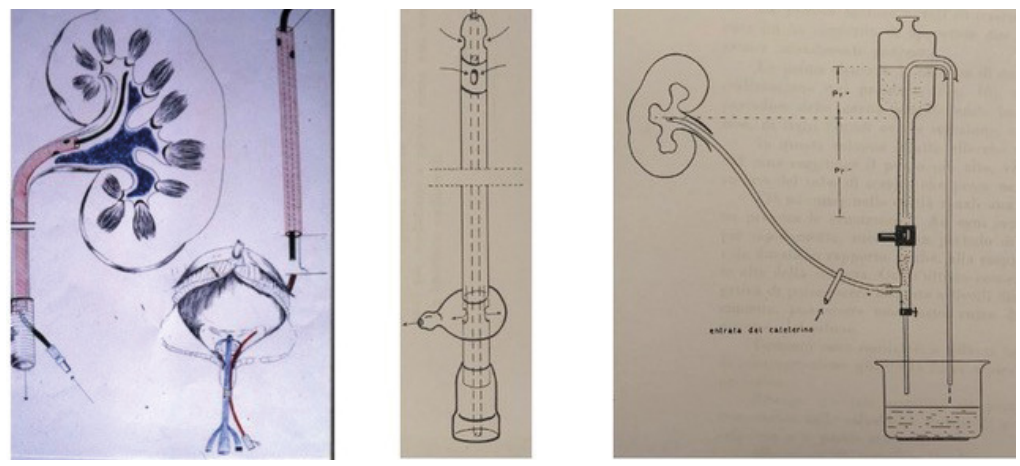

Figure 5: Dormia created a system to irrigate the kidney with high flows and low pressures through a two-way ureteral catheter

Prof. Dormia was a member of the Italian Society of Urology for more than 50 years and honorary member of the urological Society of Argentina for more than 30 years. He is considered in Italy to be the first minimally-invasive surgeon in the endourological field: for that distinction he was named an Honorary Member of the Italian Society of Endourology. Enrico Dormia was also an outstanding surgeon mainly in the field of kidney stones and he was recognized in 1983 by the American Urological Association for his activity in this field.

I worked in the Urology Clinic of the University of Milan from 1984 till 2003 and then in 2016 I came back to chair the institution where Dormia worked. His memory is still well alive and he is considered the pride of our Institution.

Monday 12 July, 11.00 – 12.00 CEST
EAU Specialty Session
History of urology at a glance
Virtual Room 6

The EAU History Office recently received a first-generation Dormia basket as a donation for its collection of instruments. If you are interested in donating or selling historically significant or antique urological instruments, please contact: history@uroweb.org.

Immunotherapy for metastatic urothelial cancer

New agents are expected to significantly improve overall prognosis

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Bladder cancer is one of the most diagnosed cancers worldwide, with an age standardised incidence rate of 9.5/100,000 in men and 2.4/100,000 in women in 2020. [1] Although the introduction of new drugs, most importantly immune checkpoint inhibitors (ICIs), in the treatment landscape of metastatic urothelial cancer (mUC) has improved the prognosis in some regions with unlimited access to ICIs, mortality rates in Europe for 2030 are expected to increase by as much as 20% [2]; however, a recent article announced an expectation of a reduction in the bladder cancer death rate in the USA: a reduction of 10,000 cases by 2040 from 2020 levels, to be precise. [3] New agents and strategies like the antibody drug conjugates (ADC) enfortumab vedontin [4] and sacituzumab govitecan [5], as well as switch maintenance with an anti-PDL-1 antibody, are expected to significantly improve the overall prognosis in this highly aggressive disease. [6]

Immunotherapy after failure of platinum-based chemotherapy

The first revolutionary step towards an improvement of the prognosis of our patients with mUC came with the data of anti-PD-1 and anti-PDL-1 drugs in second-line therapy after failure of platinum-based chemotherapy (CHT). Of 5 ICIs, three (pembrolizumab [7], atezolizumab [8] and nivolumab [9]) have received approval from the European Medicines Agency (EMA) with a level-IA evidence only for pembrolizumab, reporting positive overall survival (OS) improvement in a phase-III trial [7] compared to chemotherapy with paclitaxel, docetaxel, or vinflunine. The question arises, "Who will respond to these immune-oncology drugs?" But even in 2021, four years after the first positive phase-III trial, this question remains unanswered.

PDL-1 expression after platinum-based CHT failure does not give us guidance on the patient population that would benefit the most. There have been attempts to study the prognostic models already established for CHT. Two atezolizumab trials were pooled and a post-hoc analysis was performed to create and then validate a prognostic model for patients receiving this PDL-1 inhibitor (IMvigor210: n=310 [8], phase1a PCD4989g n=95 [10]). Six risk factors were identified (higher ECOG, elevated platelet count, presence of liver metastasis, elevated LDH, increased lymphocyte neutrophil ratio, and anaemia). Patients with zero or one risk factor(s) had a median OS of 20 months, patients with more risk factors less than 3 months. This raises the question, "Should patients with a high score (four factors or more) even be considered for second-line treatment or should they receive best supportive care [11]?"

Immunotherapy in first-line cisplatin-ineligible patients

The second-line approval of checkpoint inhibitors (CPIs) pushed investigations and trial designs to the first-line setting, where there was a clear unmet need for improvement. Two phase-II trials in cisplatin-ineligible patients (IMvigor210 [12] and KEYNOTE-052 [13]) showed a remarkable progression-free survival (PFS) improvement that led to the approval for first-line cisplatin-ineligible patients. The authorisation was restricted to PDL-1-positive patients in some countries after the interim analysis of the IMvigor130 trial demonstrated a significantly worse performance of PDL-1 negative patients in the monotherapy arm with atezolizumab. At ASCO 2021, a five-year follow-up of the KEYNOTE-052 was presented, which demonstrated that patients with a CPS ≥ 10 had better outcomes (OS, duration of response and confirmed ORR), which underlines the necessity to reserve that treatment for cisplatin-ineligible patients with a high PDL-1 expression. [14] A post-hoc analysis of a subgroup from the IMvigor130, presented at ASCO GU 2021, reported an OS benefit (HR 0.53; 95% CI: 0.30-0.94) Arm B (Atezolizumab) vs. Arm C (platinum/gemcitabine) in atezolizumab-treated cisplatin-ineligible IC2/3 patients. [15]

Immunotherapy in first-line chemo-immuno and immuno-oncology combinations

The approval of CPIs in two treatment lines in mUC and the encouraging data of the triplet combination in metastatic lung cancer provided a rationale for similar trial designs in patients with mUC. Two three-arm randomised controlled phase-III trials, IMvigor130 and KEYNOTE-361 (platinum-based CHT plus anti-PD1/PDL-1 vs anti-PD1/PDL-1 mono vs platinum-based CHT mono) showed disappointing results as they were not positive for OS improvement [16,17]. Similar in all these trials was the detrimental performance of the CPI monotherapy in the first weeks of treatment, with the typical infinity symbol shaping survival curves that showed inferiority of the IO monotherapy compared to platinum-based CHT in the PDL-1 negative groups. Even the PDL-1, high-population durvalumab and pembrolizumab arms were inferior to CHT in the first 9 to 12 months of follow-up and could not statistically outperform CHT in the longer follow-up both in the DANUBE and KEYNOTE-361 phase-III trials. [17, 18]

The implementation of a cytotoxic T-lymphocyte-associated protein-4 (CTLA-4) inhibitor plus an anti-PD-1 antibody in first-line trial designs failed to demonstrate an improved OS over classic platinum-based CHT, as reported by the DANUBE trial with the combination of durvalumab and tremelimumab. [18] Overall response rates (ORR) were lower in the durvalumab/tremelimumab combination (36%) compared to CHT (49%) and roughly equal (47 vs. 48%) in the PDL-1-high population. The results from CheckMate-901, which investigated ipilimumab and nivolumab in a three-arm design, are still anticipated. The doses of the CTLA4/PD-1 combination in this trial were chosen as approved for melanoma (Ipilimumab 3 mg/kg, Nivolumab 1 mg/kg), since data from the phase-II study [19] in platinum pre-treated patients was encouraging for the higher Ipilimumab dose and is thus more toxic while mUC patients tend to be more frail.

Switch to maintenance instead of sequencing

Prof. Powles and colleagues presented an OS of 21.4 months (HR 0.69 (95% CI: 0.56, 0.86)), the longest ever reported in a first-line phase-III trial in advanced or metastatic UC, at the ASCO meeting only a year ago [6], of note, with patients having responded on first-line platinum-based chemotherapy. The JAVELIN-Bladder 100 phase-III trial investigated the efficacy of maintenance with anti-PDL-1 inhibition with Avelumab plus best supportive care (BSC) or BSC alone in patients not progressing during four to six cycles of platinum-based CHT (either cisplatin or carboplatin). Most subgroups were in favour of Avelumab + BSC. Moreover, quality of life did not decline in the Avelumab + BSC arm. [20]

This data leads to a change in the terminology of selection criteria of first-line treatment choice from cisplatin-eligible to CHT-ineligible since the OS benefit was shown to be independent of cisplatin or carboplatin-based CHT. Important to note, though, is that cisplatin remains the standard choice over carboplatin in cisplatin-eligible patients. Hence, the JAVELIN Bladder 100 data resulted in the immediate implementation of the maintenance strategy in the EAU and ESMO guidelines for first-line-chemotherapy-fit patients with a category-IA recommendation. Avelumab has been approved by both the Food and Drug Administration (FDA) and the EMA. The number of platinum-based CHT cycles needed will be another interesting field for investigation since a post-hoc analysis presented by Prof. Loriot at ASCO GU 2021 demonstrated non-inferiority of four versus six cycles. [21]

What is the role of immunotherapy in histologic variants?

All reported trials on immune-oncology drugs allowed patients with a partial component of histologic variants to be enrolled, predominant or pure variants excluded. The primary location of urothelial cancer was not restricted to the bladder, therefore recommendations and guidelines also apply to upper tract metastatic tumours.

Biomarkers for immunotherapy in advanced or mUC

PDL-1 has not been established as a predictive biomarker for response in second-line treatment but seems to have an impact on PFS with anti-PDL-1 treatment in first-line cisplatin-ineligible patients. More precisely, we have convincing results that PDL-1 negative patients are at risk of rapid progression if treated with CPI. Other approaches to identify biomarkers include circulating tumour DNA (ctDNA). The results from an exploratory analysis of the IMvigor010 trial were encouraging for ctDNA in patients that derive the most benefit from adjuvant atezolizumab after cystectomy. The trial itself did not reach its primary endpoint for the ITT population. [22] In mUC, ctDNA has been reported as predictive for response to anti-PD-1/PDL-1 antibodies in small subsets of patients in retrospective analyses. [23-25]

Table 1: Phase-III trials including immunotherapy (anti-PDL-1 or anti-CTLA4) in metastatic or advanced urothelial cancer (recruiting, data not yet reported as of 05.2021)

	Treatments	Disease Setting	Primary endpoint
EV-203 NCT04223856 n=760	Pembrolizumab + Enfortumab Vedontin vs. Cis/Gem or Carbo/Gem	untreated metastatic or locally advanced	PFS, OS
CHECKMATE-901 NCT03036098 n=1290	Nivolumab + Ipilimumab vs. Nivolumab + Cis/Gem vs. Cis/Gem or Carbo/Gem	untreated inoperable or metastatic UC	PFS (BICR in Cis-eligible), OS (in Cis eligible and ineligible, PDL-1 pos)
THOR NCT03390504 n=631	Erdafitinib vs. Docetaxel or Pembrolizumab or Vinflunine	FGFR mut/alt failure of 1 or 2 prior lines (cohort 1 prior anti- PD1, cohort 2 not anti-PD1 pretreated)	OS
NILE NCT03682068 n=1434	Durvalumab + Cis/Gem or Carbo/Gem vs. Durvalumab + Tremelimumab + Cis or Carb/Gem vs. Cis or Carbo/Gem	untreated metastatic or locally advanced	OS OS in pts with high PD-L1 expression for arm 1 vs arm 3 and arm 2 vs arm 3

BICR= blinded independent central review; Cis=Cisplatin, Carbo=Carboplatin, Gem=Gemcitabine, PFS= progression-free survival, PD1 (programmed cell death ligand 1), OS= overall survival

The future outlook for immunotherapy in advanced and mUC

Strategies based on immunotherapy in the first-line setting, either in combination or as a monotherapy, have not shown convincing OS benefits so far, although positive results for the PDL-1 positive subgroup have been reported in the exploratory analysis of IMVigor 130. Therefore, there might be a subgroup of patients benefiting from this approach, and further investigating these patient subgroups remains crucial. Second-line treatment with anti-PDL-1/PD-1 antibodies improves survival compared to CHT; however, it might be too late for most patients who are faced with progression after first-line CHT. Therefore, a maintenance strategy with avelumab for patients without progression during initial platinum-based CHT has achieved the highest level of evidence and thus has to be regarded as the standard of care.

Numerous trials continue to investigate the future role of immuno-oncology drugs, in combination with emerging drugs and conventional CHT (see table 1), in advanced and metastatic UC. This will soon shed light on the as yet unanswered questions.

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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.

Saturday 10 July, 15.15 – 16.15 CEST
Live from the studio: Thematic Session 10
Immunotherapy in urothelial cancer
Virtual room 2

Risk stratification and artificial intelligence

In MRI-based early detection of prostate cancer

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Early detection of prostate cancer
Screening in a formal sense is not used for prostate cancer (PCa). Already in 2012, the United States Preventive Services Task Force recommended against the use of a serum prostate-specific-antigen (PSA)-based screening program for PCa, because the expected disadvantages outweighed the possible advantages [1]. It was advised not to use the PSA test until men would be well informed. Similar recommendations were stated in the European Association of Urology (EAU) Guidelines [2]. However, these recommendations were based on a conventional non-imaging-based diagnostic strategy; a pathway in which systematic transrectal ultrasound (TRUS)-guided biopsies were used to find the cause of the elevated PSA levels, without using risk-stratification tools such as multivariate risk-calculators or prostate MRI.

In recent years, magnetic resonance imaging (MRI) has transformed the PCa diagnostic pathway, based on multiple high level studies [3-7]. Taken together, the evidence indicates that MRI before biopsy can allow one-third of men to avoid an immediate biopsy and reduce overdiagnoses, with 40% fewer clinically indolent PCa and approximately 15% more clinically significant PCa detected. In the recent EAU Guidelines, MRI now plays an upfront role prior to prostate biopsies [8]. If a suspicious lesion is found on MRI, the subsequent biopsy can be targeted.

"AI does not only have the potential to improve the detection of clinically significant PCa but can also play a role in the other steps in the diagnostic pathway of PCa."

Given the changes in the PCa pathway with prostate MRI prior to biopsies, a sharp increase is expected in the number of men who will undergo prostate MRI. This will lead to a challenge: providing good image quality and diagnostic accuracy while meeting the demands of the expected high workload. In this article, we provide a brief overview of the possible solutions to this challenge. These include better pre-imaging risk stratification and adaptations of the MRI pathway with shorter and faster MRI protocols. We will also discuss the role Artificial Intelligence (AI) might play in this specific clinical setting.

Strategies to maintain diagnostic high quality and reduce workload
Better upfront patient selection
A first step to overcome this challenge is to use better pre-imaging risk-stratification tools. In an opinion paper by Prof. Van Poppel and colleagues, an intelligible diagnostic pathway with personalised risk stratification was proposed for early detection of PCa in well-informed men as a so-called "PCa Screening 2.0" [9]. By using this pathway, a more favourable balance between the harms and benefits of early detection is expected. The initial step is to use a PSA test in well-informed men, using age-based PSA interval testing. In case of a PSA elevation, men will be further stratified by using risk calculators [10]. If there is an increased risk of PCa, MRI will be performed. Targeted biopsy is only performed in men with PI-RADS 4 or 5 lesions and in PI-RADS 3 lesions with an unfavourable clinical setting (PSA >10 ng/ml and/or PSA density >0.15). Increasing evidence shows that in case of a negative (PI-RADS 1 or 2) or equivocal MRI (PI-RADS 3) without increased risk (PSA level, family history, age, digital rectal examination), systematic biopsies can be avoided [11].

Risk stratification will never be perfect and will have the consequence of missing clinically significant PCa [12]. It is a challenge to find the optimal balance between a more costly pathway with an increased MRI burden and a more affordable pathway with less MRIs and less unnecessary biopsies, but with missing a few more significant cancers. Cost-effectiveness analyses might be helpful for the different stakeholders, such as policymakers and clinicians, in taking well-informed decisions about the best diagnostic strategies [14].

Better radiology workflow
It is evident that with the changing guidelines there will be an increase in the number of men who will have a prostate MRI. This will lead to an increased pressure especially on the regular radiology programme. One of the solutions is to shorten and simplify prostate-MRI protocols. The omission of a dynamic contrast-enhanced MRI (DCE), resulting in a so-called biparametric (bp)MRI, results in shorter scan times and thus decreased capacity problems. Emerging evidence shows that omitting contrast series does not necessarily lead to missing clinically significant PCa [16]. The most important caveats for the bpMRI protocol are that the studies that have been performed to date have been carried out in expert centres with high-quality scans. Especially in less experienced readers, DCE can be of added value as it can reduce uncertainty, detect more significant cancers, and serve as an extra 'safety net' [21].

The role of Artificial Intelligence in the diagnostic pathway of prostate cancer
Artificial Intelligence (AI) can potentially improve the diagnostic quality and reduce the workload. AI is a rapidly emerging technology and has gained massive interest in medical imaging research, mainly in a preclinical setting [22, 23].

AI does not only have the potential to improve the detection of clinically significant PCa, which is generally considered as the most obvious benefit, but can also play a role in the other steps in the diagnostic pathway of PCa: from MR-image acquisition to generating the radiology report (see Figure 1).

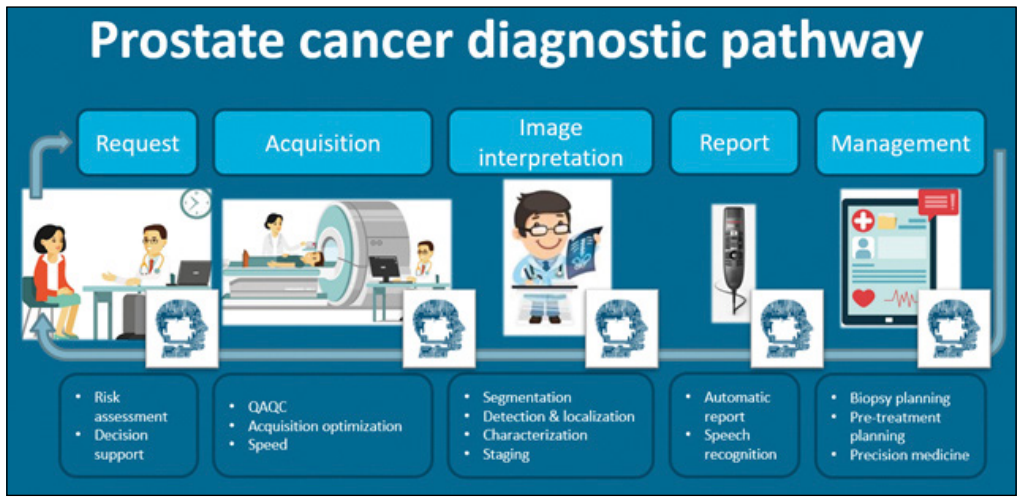

Figure 1: Artificial Intelligence can potentially play a role in all parts of the diagnostic pathway for prostate cancer: from the pre-imaging phase to generating a report. QAQC = quality assurance and quality control

Acquisition
Several studies show that AI can speed up the acquisition of MR images and thus can potentially help solve capacity problems. To date, there are no AI solutions for prostate-MRI image acquisition that can be directly implemented into the clinical workflow; however, in the research field of other body parts, examples do exist. For instance, in musculoskeletal radiology knee MR images can be acquired almost two-fold faster instead of the conventional acquisition technique, with similar or even better image quality [24]. Similar AI solutions for prostate MRI are expected in the future.

Image-quality assurance and quality control
Image-quality assurance and quality control are other potential applications of AI. An international radiological and urological prostate-MRI expert panel considers it mandatory for a radiologist to assess the image quality of each prostate-MR examination and mentions this in the report [25]. To enable this, prostate-image quality (PI-QUAL) assessment criteria for evaluation of a prostate MRI are under development [26, 27]. AI may help to generate a more objective score and to automatically evaluate the image quality during scanning so that technicians may repeat a sequence when it has an inferior quality.

Workflow
Many studies are performed to classify pre-annotated lesions into insignificant versus significant cancer and benign versus malignant lesions [29]. Also, more advanced algorithms are aimed at automated detection and classification of PCa lesions. Promising results are reported. However, it should be noted that most studies concern small cohorts, often without external validation, and have not been validated prospectively in a clinical workflow [30, 31].

Other AI applications
Other AI applications that are of interest are the ones that enable automated detection of 'normal' or obvious frequently appearing conditions such as BPH or prostatitis. More research on this topic has been done within breast imaging, where AI is utilised in a screening population to automatically filter out non-cancerous conditions with a high degree of accuracy [32]. Furthermore, AI as a 'second reader' could potentially improve the sensitivity of radiologists, which is of particular interest to less experienced radiologists.

Future applications of AI may, based on the combination of different (non-imaging) biomarkers, provide a prediction about which patients will benefit the most from imaging. AI could also predict which patients have a high chance to develop extracapsular extension, or a recurrence, and/or a metastasis, and thus it could allow for a more personalised treatment.

"The expected rise in the number of prostate MRIs requires solutions that come from different directions."

To summarise, the expected rise in the number of prostate MRIs requires solutions that come from different directions. An intelligible risk stratification (i.e. 'PCa Screening 2.0') is one of them. Also, other solutions like smarter and shorter MRI protocols need to be explored. In most of these solutions AI can play an important role. In this respect, the above-mentioned AI applications have the potential to improve the diagnostic quality of the prostate-MRI pathway and speed up the workflow. However, clinical validation of these tools is needed before fully exploiting their potential.

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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.

Sunday 11 July, 15.00 – 16.00 CEST
Thematic Session 16
How machine learning is transforming diagnostics
Virtual Room 5

Local treatment of cN1 M0 PCa:

Intensity-modulated radiotherapy and radical prostatectomy (in combination with long-term ADT)

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In lymph-node-metastasised prostate cancer (PCa) patients, options for local therapy and systemic therapies and their combinations should overlap. Approximately 5% to 10% of newly diagnosed PCa patients have synchronous suspected pelvic nodal metastases on conventional imaging (CT/bone scan) without bone or visceral metastases (cN1 M0 stage). Meta-analyses showed that PSMA-PET/CT prior to primary treatment in advanced PCa detects disease outside the prostate despite prior negative conventional imaging using bone scan and pelvic CT/MRI in 32% of the cases [Perera et al., 2020], thus leading to a stage shift with more cases classified as cN1, but with, on average, a lower nodal disease burden.

The management of cN1 PCa is mainly based on long-term androgen deprivation therapy (ADT) as systemic treatment. However, local tumour control is also of high importance for long-term disease control. This was clearly shown in a study on radiotherapy of localised PCa more than a decade ago. In a (retrospective) study with 1.469 patients, patients with a locally persistent tumour were at a significantly higher risk of distant metastases at ten years after radiotherapy. The prolonged time to the appearance of distant metastases in locally failed patients and an increasing hazard of distant metastases over time were consistent with a late wave of metastases from a locally persistent tumour in the prostate (Coen et al. 2002). In principle, this local control can be achieved with radiotherapy (RT) or radical prostatectomy (RP) (Bryant et al. 2018, Sarkar et al. 2019).

"The intensification and combination of systemic treatments in cN+ patients in combination with a local treatment remains an unsolved question and should be investigated in randomised clinical trials."

Benefits of local treatment

The benefit of adding local treatment has been assessed in various retrospective studies, summarised in one systematic review [Ventimiglia et al. 2019] including five retrospective studies dealing with cN1 M0 PCa patients [Tward et al. 2013, Lin et al. 2015, Seisen et al. 2017, James et al. 2016, Rusthoven et al. 2014]. The findings suggested an advantage in both overall survival (OS) and cause-specific survival (CSS) after local treatment (RT or RP) combined with ADT as compared to ADT alone. The majority of data came from studies on radiotherapy. The main limitations of this analysis were the lack of randomisation, of comparisons between RP and RT, as well as of the value of the extent of pelvic lymph node dissections (PLND) and of RT target volumes.

From another point of view, the STAMPEDE group reported results on 3D-planned RT to the primary tumour in 2061 men with oligometastatic PCa (M 1). They were able to show a significant overall survival benefit in patients with low-volume disease (even in the subgroup of M1a – i.e. lymphatic distant metastasis) (Ali et al. 2021). The oncologic situation cN1 M0 lied in between M 1 and locally advanced PCa (cT3/cT4 N0 M0), where a significant overall survival benefit for RT and long-term ADT was proven.

Only limited evidence exists supporting radical prostatectomy for cN+ patients. Moschini et al. compared the disease outcomes of 50 cN+ patients. These patients were part of a group of 252 patients with pN1 but had cN+ at preoperative staging. cN+ was not a significant predictor of CSS [Moschini et al. 2016].

Modern RT techniques

A special point of interest are more modern RT techniques like intensity-modulated radiotherapy in combination with image guidance, the current standard RT technique compared with those used in the older studies. These modern techniques allow for a higher total dose of RT to the primary tumour and the pelvic lymphatics, thus leading to improved disease control and an additional reduction of late side effects in the rectum and bladder. These came along with the integration of modern PSMA-PET/CTs in the clinical routine, which engenders a significant better detection of lymph-node metastases in locally advanced prostate cancer. All together, these techniques allow for giving such high doses as those of around 66 Gy as a boost to the lymph node metastases as a curative treatment option. Former doses of about 50 Gy to the pelvic lymphatics were sufficient to sterilise microscopic diseases only.

The intensification and combination of systemic treatments in cN+ patients (abiraterone acetate, docetaxel, zoledronic acid) in combination with a local treatment (RT or RP) remains an unsolved question and should be investigated in randomised clinical trials.

Taking into account the lack of grade-I evidence and with a consistent benefit seen in retrospective studies, local therapy (i.e. intensity-modulated radiotherapy in combination with image guidance or radical prostatectomy with pelvic lymphadenectomy) should be recommended in patients with cN1 disease at diagnosis in addition to long-term ADT.

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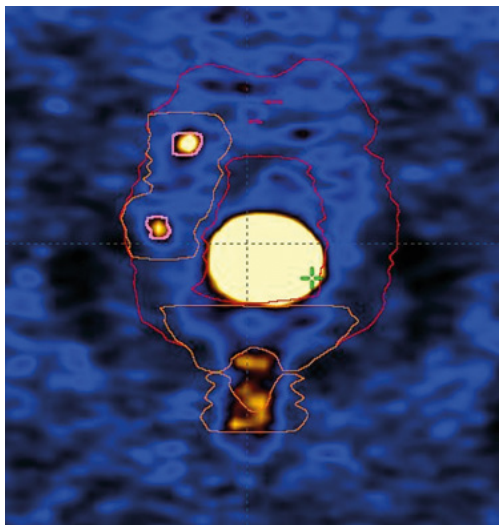

Figure 2: The same situation as in figure 1 showing the two positive lymph nodes on the Ga 68 PSMA-PET-CT integrated into the target volume delineation of RT

Ali A, Hoyle A, Haran ÁM, Brawley CD, Cook A, Amos C, Calvert J, Douis H, Mason MD, Dearnaley D, Attard G, Gillessen S, Parmar MKB, Parker CC, Sydes MR, James ND, Clarke NW. Association of Bone Metastatic Burden With Survival Benefit From Prostate Radiotherapy in Patients With Newly Diagnosed Metastatic Prostate Cancer: A Secondary Analysis of a Randomized Clinical Trial. JAMA Oncol. 2021 Apr 1;7(4):555-563. doi: 10.1001/jamaoncol.2020.7857. PMID: 33599706; PMCID: PMC7893550.

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Sunday 11 July, 15.00 – 16.00 CEST
Live from the studio: Thematic Session 14
Guideline Session II: Prostate cancer - cN+ in newly diagnosed patients
Virtual room 2

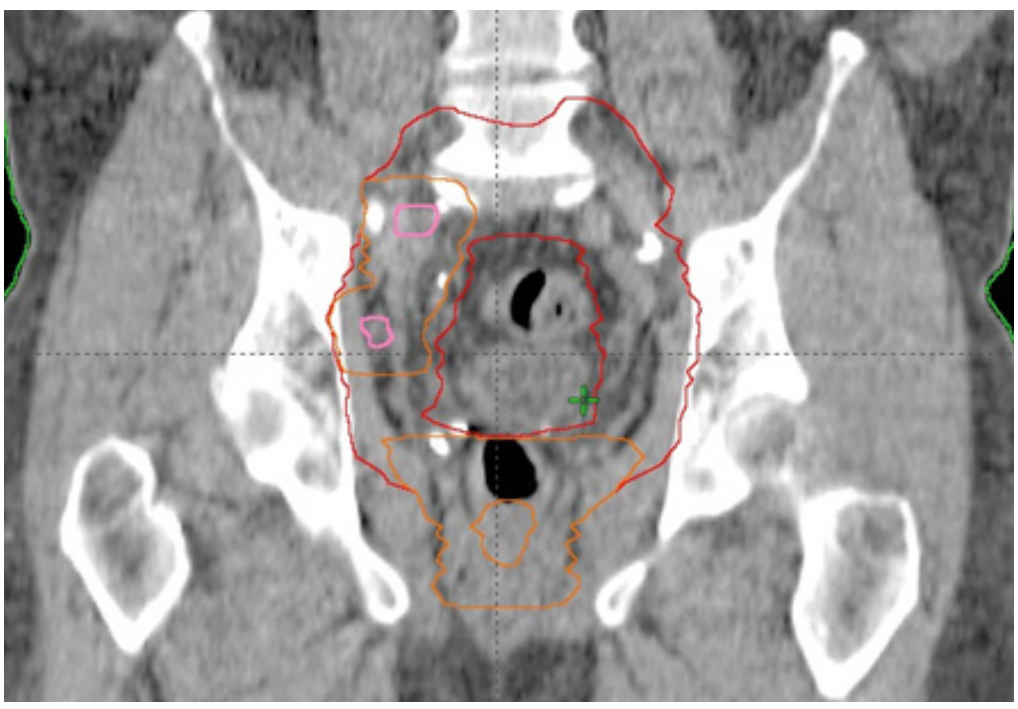

Figure 1: Planning CT before the start of radiotherapy in a patient with cN1 lymph node metastasis. In red: the target volume of the prostate and pelvic lymphatics. In orange: the target volume of the boost to the two positive nodes (total dose to the positive lymph nodes: 66.6 Gy)

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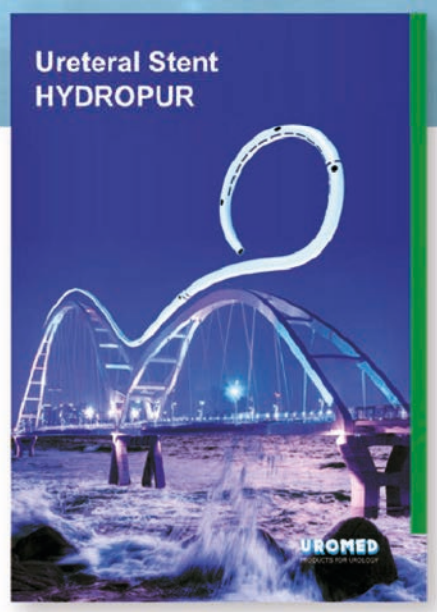

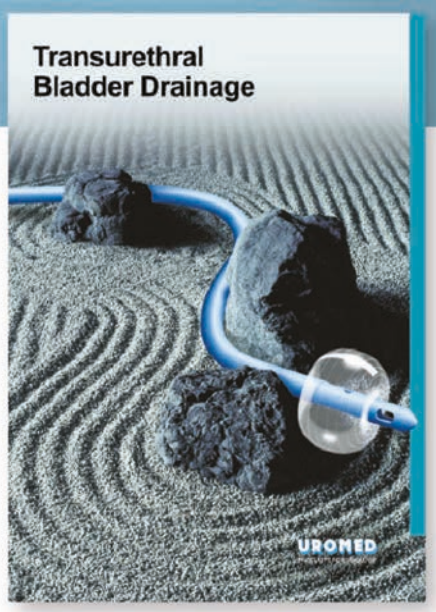

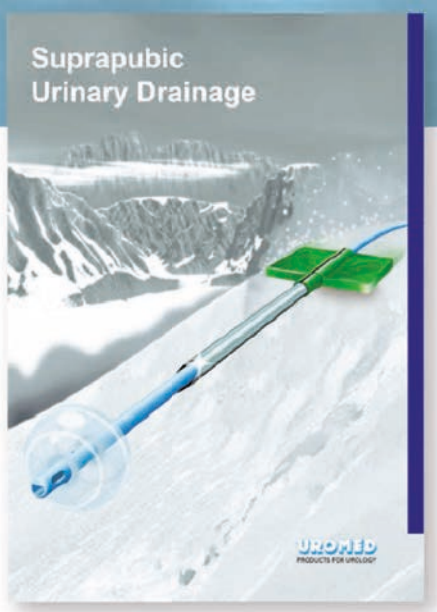

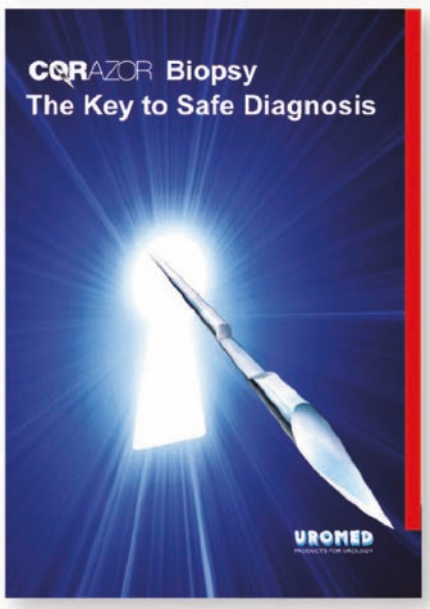

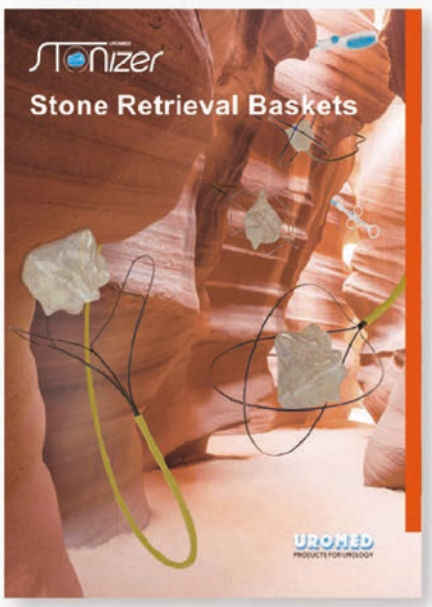

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Viral menace to male infertility

Effects and risks of viral infections on the sperm

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In male infertility, mumps (MuV), human immunodeficiency viruses (HIVs), adeno-associated virus (AAV), cytomegalovirus (HCMV), human papillomavirus (HPV), herpes simplex viruses (HSV), and Zika virus (ZIKV), are well-considered as risk-factor virals. It seems that in a delicate condition, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and coronavirus disease 2019 (COVID-19) entails risks as well. At present, screening is only performed in the evaluation of HIV, hepatitis B virus (HBV), and hepatitis C virus (HCV) for assisted reproduction techniques.

The negative influence of HPV, ZIKV in mouse testicular functions [1-2], abortion rate, fertilization, sperm parameters is demonstrable. [3]

The partners and newborns are in the risk of spreading horizontal or vertical dissemination. [4] We confer the main viruses and their effects on fertility and male reproductive system.

Sexually transmitted diseases (STDs) are stigmatized worldwide for problems in economy, community and heath. STDs endure the pregnancy complications and infertility [5] in 15% of reproductive-age couples and for 50% infertile male cases. The male reproductive system (MRS) is impaired due to inflammatory conditions of the testis and epididymis comparatively to accessory glands. [6] The impairment includes decreased motility, moderate sperm count and sperm death, production of icing inflammatory cytokines, and despairing male fertility. [7] Some mechanisms include:

1) Systemic acute or chronic infections [8]
2) Orchitis [9]
3) Urethral infections and male glands take part in male reproduction and fertility with a negative part [8]

Forward motility is low when HBV or HCV is found in semen [10] and also because of the rate of occurrence of sperm aneuploidy and DNA fragmentation. [11]

"The sperm alone can pass on the viral infection with an almost identical occurrence rate to sporadic sexual intercourse."

SARS – CoV was a health epidemic in 2003 as the Middle -East Respiratory Syndrome Corona Virus (MERS - CoV) was in 2012 [12] and COVID-19 in 2019. [13] For SARS-CoV and SARS-CoV-2 we have the identical human cell receptor, angiotensin-converting enzyme 2 (ACE2), but MERS CoV march to a different tune because of a receptor called dipeptidyl peptidase 4. [14] Cells with ACE2 receptor in dissimilar issues or other part of the body can be affected [15], as well as, lungs, intestine, kidney, testis, etc. [15-16].

We have to clarify the capacity of viruses to pass on vertically from the mothers to their neonates and vice versa.

On viruses and assisted reproduction
Found below are some of the aforementioned viruses and the sperm infections they cause.

Hepatitis B virus
The harmful spermatozoa of the HBV infection can cause male infertility. Lorusso et al. [10] established that sperm parameters (concentration, motility, morphology, viability) are notably enhanced in HBV seropositive patients. Kang et al. [17] manifested in vitro studies which revealed that HBV can persuade oxidative stress in sperm cells, as displayed by phosphatidylserine externalization, caspase activation, or DNA fragmentation. Qian et al. [18] demonstrated that quantitative real-time polymerase chain reaction (PCR) can inspect the viral load in the semen of HBV-infected patients during assisted reproduction. With fluorescence in situ hybridization (FISH), Huang et al. [19] proved that HBV DNA can be unified into the sperm chromosomes of HBV carriers and can vertically transmit via the germ cells.

Mumps virus
Acute orchitis in post-pubertal years can lead to male infertility. [20] Most are unilateral. Bilateral symbolize roughly 15% of the cases and can contribute to testicular atrophy-related subfertility and infertility. [21] The MuV infection can increase testicular temperature [22], lessen testosterone production, break apart the Leydig cell's function. [23]

Hepatitis C virus
The reduced motility and abnormal morphology of sperm have been linked to HCV infection. [10,24,25] Levy et al. (2002) showed changes in 30% of HCV-infected males before antiviral treatment. Also, mitochondrial membrane potential, chromatin compaction, and DNA fragmentation notably change in these patients. [8] Through in vitro fertilization (IVF) procedures, HCV transmission is possible via semen. [26] Sperm washing moderates the viral load in semen and the risk of transmission. [27] A new sperm washing device with double tube can be used for separating non-infected sperm. [28]

Human immunodeficiency virus
Orchitis and male infertility can be acquired from an HIV infection. [29] STDs play a role in the spread of HIV-1. There can be a high level of HIV-1 in seminal cells or seminal fluid that can be sexually transmitted when these patients are under antiretroviral therapy. [30] In HIV-positive men who are asymptomatic and have normal semen parameters [31], the progression of the disease can change the normal sperm morphology and motility. [32] We can use spermatozoa in procedures such as intrauterine insemination, IVF, or intracytoplasmic sperm injection (ICSI). [33]

Human papillomavirus
HPV is frequently detected in semen and urethral swabs from asymptomatic men. The data shown is contrasting, and the number of studies is low for HPV infection on sperm parameters. [34] We can find reduced sperm motility, moderate pH of seminal plasma but some authors comment that there are no clinically significant change on parameters.

Herpes simplex virus
In fertile and infertile topics and in semen has been found no difference in DNA of HSV-1 & 2. [35] The HSV DNA in semen can be accountable for some incidents of male infertility such as reduced sperm concentration and motility. [35] In vitro incubation had been performed for HSV-2 virus and had been found that it remains in the seminal fluid. [36]

Human cytomegalovirus
We can find HCMV DNA with frequency from 8% to 65% of the semen of fertile or infertile HCMV-seropositive patients. [35,37,38] Improvement is modest, just 5% of seropositive donors [39] with no serious object in infertility, semen quality, functional capacity of sperm, antisperm antibodies and seminal white blood cells [37,39]. In ICSI, we can still have virus transmission even when we use washing procedures for assisted reproduction techniques. [36]

Adeno-associated virus
On chromosome 19 we can find that the AAVS1 locality is supported by the testis tissue. [40] Infertile patients have more of AAV DNA in semen (20–40%) than normal patients (0–5%) and in couples, 3.8% in semen and endocervical examples. [41-42] We have identified a small risk of infection by AAV in genital tests. [43] In assisted reproduction, we have information about the infection of semen. [44]

Effect of SARS- CoV-2 in male fertility
Based on the fatality rates, men are more exposed to SARS- CoV-2 than women. Academic work in China and Italy has shown this. [45-46] In the United Kingdom, it has been reported that males represented 60% of the situation. [47] We must find the problems in acute or long form of this disease with regard to male fertility.

The systemic oxidative stress from SARS-CoV-2 can cause problems with testicular capacity. Hypogonadism has been observed. The angiotensin-converting enzymes 2 (ACE2) receptor is extremely manifested in testicular cells. The ACE2, together with the virus counter enzyme called Spike (S) glycoprotein, enter the virus. [48-49] A direct invasion can cause direct testicular damage, by immunological or inflammatory reactions. The young male patients and COVID-19 relate to high fever and for this reason, a multidimensional andrological translational research project was suggested. [50] It is investigated that the effect on semen parameters from febrile illnesses such as influenza. [51] A fever episode can improve sperm DNA fragmentation index together with modification of nuclear protein mixture of ejaculated spermatozoon. [52] SARS-CoV-2 may have an influence on the male reproductive organs and male infertility. Furthermore, we have to rate the risk of miscarriages.

Conclusive remarks
Male infertility has numerous pathophysiological mechanisms which can be influenced by infections caused by HBV, HCV, HIV, HPV, and HSV, but not by HCMV and AAV. At the semen level, some pathogens may be the source of untreatable or fatal infections, as well as, damage sperm parameters and functions. The SARS-CoV-2 virus can cause testicular damage together with infertility and this can be hypothetically explained. In light of these findings, we can state that the sperm alone can pass on the viral infection with an almost identical occurrence rate to sporadic sexual intercourse.

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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 12 July, 12.00 – 13.00 CEST
Meeting of the EAU Section of Outpatient and Office Urology (ESUO)
Andrological tips and tricks for outpatient and office urologists
Virtual Room 3

Microbiome and urolithiasis

Exploring the role of urinary tract microbiota

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Human microbiome understanding and its relationship with health has represented a revolution in biomedicine. It was facilitated by the emergence of new molecular microbiology techniques, specifically massive sequencing techniques, focused on the study of the gene content and the mRNA, along with proteomics.

The **microbiome** not only refers to the microorganisms present in a well-defined habitat but also includes the scenario where their activity takes place, resulting in specific ecosystem. The **microbiota** consists of the set of microorganisms belonging to different kingdoms, without considering their site of activity. The **metagenome** refers to the total microbial gene content resulting from the study and analysis of an environmental sample using new-generation sequencing techniques.

Gut microbiome
The intestinal microbiota presents incremental compositional and quantitative variation throughout the tract. The influence of the intestinal microbiome on digestive functions and nutrient absorption, either by direct action on them or by affecting the state of the mucosa, is well established.

Some conditions that may impact on factors associated with lithiasis are the use of dietary oxalate, inflammatory bowel disease caused or exacerbated by intestinal dysbiosis and derived malabsorption, dehydration due to chronic diarrhea caused by pathogenic bacteria, microbiota alterations associated with bariatric surgery, the influence on the composition of the vaginal and urinary microbiota as a consequence of a gut dysbiosis, and the impact of the intestinal microbiota on chronic low-grade inflammation and associated lesions at the renal tubule.

Other conditions affecting the composition of the microbiota and, therefore, influencing stone disease include the nutritional profile, the immune system, antibiotic consumption, age and gender.

Urobiome: the microbiome of the urinary system
The dogma of bladder urine sterility was broken by Wolfe et al, reporting the existence of microorganisms in the urine of healthy women sampled by suprapubic aspirate, by means of sequencing the 16S rRNA gene. Enhanced quantitative urine culture techniques (EQUC) were required to confirm the viability of the bacteria detected. The urobiome has been reported to be highly dependant on the vaginal microbiome, and determined by partial pressure of oxygen, the solutes dissolved in the urine (influenced by diet and metabolism), the presence of organic molecules (such as glycosaminoglycans (GAGs) of urothelial origin) and the urine pH, as well as by the consumption of antibiotics.

Dietary and behavioural indications, such as increasing water intake, minimise the likelihood of infections. Thus, dilution of both the solute concentration in the urine and the colonizing bacterial load of the bladder prevent this proliferation, in addition to facilitating their expulsion and preventing their ureteral ascent. Prebiotics, defined as molecules that, once ingested, selectively promote the development of beneficial microorganisms, can be useful in this setting when, either directly or their metabolites reach the urine.

Continued on page 42

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Bladder colonisation with microorganisms can facilitate migration to the upper urinary tract, where they act directly as nucleants in lithogenic processes, directly or indirectly as a cause of an increase in mucus production and of the resulting inflammatory reaction. In addition, the increased urinary pH associated with bacterial urease activity can lead to the formation of struvite and associated apatite stones.

Intestine-kidney axis
Most of the dietary oxalate is potentially metabolised by the intestinal microbiota as an energy source. Ever since *Oxalobacter formigenes* was demonstrated, the relationship between the intestinal microbiome and oxalocalcic lithiasis has become an important focus of research. Some studies show that there is a significant difference in favour of the presence of O. *formigenes* in healthy individuals, but results are very heterogeneous. In addition, it has been reported to have the ability to promote active transport of oxalate from the blood to the lumen of the intestine.

Being a strict anaerobic and oxalatrophic microorganism, the dietary restriction of foods by oxalate might not only affect its degree of colonisation but also jeopardise its efficacy in studies with patients who follow a strict oxalate-exclusive diet. Probiotic use of bacterial strains with a facultative oxalotrophic metabolism (with the possibility of using other energy sources) such as *Lactobacillus sp.*, or *Bifidobacterium sp* could be a potential therapeutic alternative. The existence of research projects involving animal models in which the transplantation of faecal material clearly and consistently modified urinary biochemistry reinforces this hypothesis.

The presence of a stable and diverse microbiota has been correlated with the absence of stone pathology. For this reason, it is advisable to preserve the microbiome of patients, both through dietary and lifestyle advice, as well as through prebiotic and probiotic supplements of proven efficacy. For this same reason, it is also of special importance to minimise the impact associated with the consumption of antibiotics, as they can lead to a dysbiotic microbiota with clinical implications.

Oxalate malabsorption is present with inflammatory bowel disease and bariatric surgery. In both cases, differences have been found in the composition of the microbiota as a result of changes in the physiology and intestinal state. Regarding oxalate, either due to a degradation of the intestinal epithelium or an increase in calcium absorption, the concentration of free luminal oxalate is increased, which, if not used by oxalatotrophic populations, will increase urinary oxalate. Fecal material transplantation from donors with a relevant profile can be a compassionate solution in highly recurrent patients.

Low-grade systemic inflammation and oxidative stress
Low-grade systemic inflammation presents multiple organic and metabolic dysfunctions. Thus, the development of chronic kidney disease, atherosclerosis, diabetes, or autoimmune diseases has been correlated with altered inflammatory markers and mediators. The impact of the microbiota on low-grade systemic inflammation has been intensively studied, given its influence on circulating levels of pro-inflammatory or anti-inflammatory immune factors, and in the specific case of stone disease, on tubular damage associated with promotion of the oxidative state. Even in situations of normal renal function, the toxin fraction absorbed, either due to an excessive presence of protein in the diet or due to a proteolytic microbiota, can increase and damage tubular cells.

High counts of *Proteobacteria* are associated with states of low-grade systemic inflammation. Maintaining the integrity and barrier function of the intestinal epithelium is of vital importance. The influence of the microbiota lies not only in the groups detected but also in the metabolites that result from interaction with food. Thus, the maintenance of a correct luminal pH (in the acid range) or the correct supply of short-chain fatty acids, especially butyric, will benefit the trophism of the epithelial cells, the presence of intercellular junctions (*tight junctions*) and a correct structure of the adjacent mucus layer, thereby maximizing the epithelial barrier function.

This scientific evidence reinforces the indication to reduce protein intake in the patient affected by calcium oxalate stones in order to minimise the lesions that act as nucleation spots.

Influence of the intestinal microbiota on the urogenital microbiota
The composition of the urobiota is strongly influenced by the intestinal microbiota, mainly in the form of contaminations of faecal origin through the perianal area, much more relevant in the female gender due to anatomical reasons, and it is easy to correlate a higher concentration of bacteria with uropathogenic potential at the distal areas of the bowel, with a higher probability of developing urinary infections.

Multiple investigations have focused on reducing this pathogenic burden with both probiotics (with direct antagonistic capacity or ecological superiority), or with prebiotics (fibers and oligosaccharides that selectively promote the growth of beneficial organisms). Moreover, promoting a eubiotic vaginal microbiota rich in lactic acid bacteria (which will allow the generation of an acidic environment (pH 4.5) and represent an ecological barrier for pathogens during their migration to the urinary system) will have the potential to reduce the potential negative impact of the urogenital microbiota.

"High counts of Proteobacteria are associated with states of low-grade systemic inflammation."

Urobiome and infectious stones
The formation of struvite stones is closely related to the presence of microorganisms with urease capacity in the urobiota. Preserving the structure and composition of the bladder urobiome, reducing the risk of colonization and proliferation of bacterial groups with high urease activity is especially relevant in patients with associated morbidities and those with a tendency for recurrent UTI. It can be expected that relevant alterations in the bladder bacterial ecosystem will translate into changes within the whole urinary system. Conditions that facilitate urinary stasis, as well as the implantation of urological devices, such as ureteral or urethral stents, are independent factors associated with a higher probability of developing infectious stones. Antibiotic-associated diarrhea can also facilitate contamination of the urogenital microbiome by gut microorganisms.

In order to reduce the burden of pathogenic bacteria, consumption of prebiotics and fibers with a high degree of polymerisation can be a very useful tool, as is preserving the structure of the genital microbiota, with special relevance at the vaginal level with vaginal probiotics reinforcing its physiological function both as a direct protection against vaginitis and vaginosis and as a reservoir of positive microorganisms that are indirectly provided to the urobiota. Another strategy is directly acting on the urobiota by instilling attenuated strains of pathogenic species such as E. Coli in what we could define as urobiota transplants. These options could be of interest in people affected with highly recurrent diseases or with permanent catheterization or fecal incontinence.

The urobiome in non-infectious stones
The Urobiome has been linked to non-infectious stones. Some studies confirm the presence of a urobiome in the upper urinary tract, with high similarity to the ecological structure found at the bladder level, and others point to certain micro-organisms in the nucleation and growth of oxalocalcic and apatitic phosphate stones. Furthermore, the secretion of inflammatory proteins as a tissue response to the presence of bacteria would act in a similar way to the Tamm-Horsfall protein, with ability to add crystals. Finally, the citrate lyase activity of certain bacterial groups could reduce this stone inhibitor, resulting in the formation of calcium-based stones.

Interventions on the microbiome seem to be an important source of new therapies for prevention and management of the stone disease. Consequently, study and analysis of the microbiome should be a factor to be considered in order to precisely determine the different factors that explain the etiology of nephrolithiasis.

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

Monday 12 July, 13.30 – 14.30 CEST
Meeting of the EAU Section of Urolithiasis (EULIS)
Pathophysiology and management of urolithiasis: New perspectives and approaches in 2021
Virtual room 2

EAUN21: Multidisciplinary collaboration forms the focal point

EAUN21 will be a not-to-be-missed event for nurses and allied healthcare professionals alike

For more than a year, we have faced up to the challenges posed by the COVID19 pandemic in both our professional and personal lives. The images of people directly impacted by the virus, as well as the burden and overwhelm on global healthcare systems when dealing with surges will be forever etched in our hearts and minds. Many nurses have been to the forefront in reconfiguring services to deliver safe, quality healthcare, often in new and innovative ways, in a changed environment.

While the EAUN meeting for 2020 in Amsterdam had to be cancelled, this year's event, which was scheduled to take place in Milan in March, is now scheduled as a virtual event on 3 and 4 September. EAUN21 will proceed in an era of hope, with vaccination rollouts underway globally, and with a sense of a return to a brighter future in the air.

The Scientific Congress Office of the EAUN, with support from the board, have been working hard to develop an educational meeting for delegates. The programme acknowledges the challenges that both patients and healthcare professionals have faced and brings together experts from the global urology family to deliver what we hope you will find to be an outstanding programme.

Register now for the early fee!
Deadline: 2 August 2021

The theme of multidisciplinary collaboration flows through this year's meeting and will be of interest to nurses and allied healthcare professionals working with patients with urological conditions. The 2-day programme provides an exciting and balanced series of educational presentations across the spectrum of both benign and uro-oncological disease. The impact of COVID-19 on the delivery of urological care will also be addressed.

Uro-oncology sessions
The uro-oncology sessions will include educational updates and presentations on prostate cancer, including PMSA scanning and Lu-PMSA treatment in castrate-resistant prostate cancer. The perspective of both the urologist and the nurse will be explored. A multi-professional approach to addressing skeletal issues in metastatic prostate cancer will also be discussed. Plus, managing erectile dysfunction post-prostate cancer treatment in a nurse-led clinic will be presented.

For the complete Scientific Programme visit www.eaun21.org

The bladder cancer series will include the ideal cystectomy pathway. It will consider the challenges in setting up a prehabilitation clinic, too, as well as how to involve the ward and inpatient services in the patient journey to recovery. The non-muscle-invasive-bladder-cancer session will look at emerging treatments, managing BCG side effects, BCG shortages, and the role of a dedicated bladder cancer patient support group.

Benign programme
The benign programme explores diverse topics such as an examination of nurse-led clinics in assessing and managing male lower urinary tract dysfunction including the role of virtual clinics. There will be presentations and learning opportunities in continence care, prevention of urinary tract infections, and a 3D animation of how to change a suprapubic catheter. The nursing solutions to difficult cases session will share the experience and problem-solving skills in managing complex issues that arise in practice. In addition, there will be updates on the Educational Framework for Urology Nursing, the EAUN catheterisation guidelines, and a presentation on (almost) everything you need to know about kidney function, plus many more interesting sessions and discussions.

Poster/video session and research competition
In addition, the very popular and interactive poster sessions give delegates the opportunity to learn from the experiences of their colleagues through dissemination of research findings, audits, and service developments, with prizes awarded across different categories. And the interactive nursing research project plan competition awards a prize to the best research plan to help fund the costs of carrying out the study.

Although this year's programme takes place in a virtual environment, advances in technology will facilitate an engaging and interactive programme. Delegates will have an opportunity in each session to pose questions to the panel or chairs of the session and engage in dialogue to enhance learning.

For an up-to-date overview of the EAUN21 scientific programme, please visit www.eaun21.org/scientific-programme/.

Access to EAU21
Nurses and EAUN Members registered for EAUN21 are automatically registered to EAU21. Make sure to register for EAUN21 before 7 July to be able to attend the EAU21 Virtual Congress for free!. Feel free to explore the EAU Congress' scientific programme via www.eau2021.org/programme.

Save the date!

How to register
Go to the registration webpage of the meeting www.eaun21.org/registration/ and sign up!
If you register before 7 July, you will also be able to attend the EAU21 Virtual Congress for free!

We look forward to welcoming you at EAU21 and EAUN21!

Jehovah's Witnesses and bloodless kidney transplants

Considering the ethical dilemmas transplantation urologists may face

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The Jehovah's Witnesses (JW) population refuses transfusions of homologous and autologous blood products that have been removed from continuity with the body. This refusal is based on their interpretation of the Bible. According to their beliefs, acceptance of blood or blood products will forfeit their chance for resurrection and eternal salvation.

Most JW accept crystalloid solutions, synthetic colloid solutions, haemoglobin substitutes as perfluorocarbons or artificial haemoglobin solutions, and recombinant proteins as erythropoietin or activated factor VII, while whole blood, red blood cells, platelets and plasma are unacceptable. Individual decisions need to be made regarding administration of purified fractions of plasma, as immunoglobulins and albumin, or solid organ transplants. Additionally, patients need to make personal decisions regarding (heart or venovenous) bypasses, haemodilution and intraoperative red cell salvage.

This request may be challenging for physicians, as blood products may be lifesaving in some severe medical conditions. On the other hand, the medical community has learned that blood products may submit patients to some risk of life-threatening incidents, of allergic reactions, and of various known (or unknown) blood-borne infections. These reasons, added to the costs and the scarcity of some blood components, have forced the development of blood product-free medical strategies.

That JW may refuse lifesaving blood transfusions is a morally accepted feature of contemporary medical practice. The principle of respect for autonomy supports this, and there is seldom reason to interfere with this choice because it rarely harms another individual. Advances in surgical technique have made it possible for transplant surgeons to perform bloodless organ transplants, enabling JW to benefit from this treatment. When the transplant organ is a directed donation from a family member or friend, no ethical dilemma arises.

Ethical dilemma

However, when a JW cannot identify a living donor and wishes to be listed for organ transplant, the transplant team may face an ethical dilemma. On the one hand, it wishes to provide care to the patient that is compatible with her or his preferences. On the other hand, the team may wonder if it is fair to other patients who need an organ and will accept blood transfusion to include the JW patient on a waiting list for a donated organ. If the JW patient is listed and receives an organ, then a patient who also needs an organ, and who is willing to accept all care to optimize the success of the transplant, may be denied an organ. To frame the ethical dilemma outlined above specially in the setting of a JW in urgent need of a kidney, is important to locate these programmes in high-volume centres, with multidisciplinary protocols, including medical, surgical, ethical and legal considerations.

It is necessary and probably time to review and update the evolution of the JW position on blood transfusion and the medical community's efforts to provide care that accommodates this religious commitment. If someone wants the Witnesses to be denied transplant in the name of justice, there must be an ethically sound reason. There are currently two rationales in the literature:

1) This attitude coming from a professional is unacceptable because it will cost lives.
2) Resources should be allocated to patients who comply with the standard of care.

It is evident to argue that neither apply to this dilemma. It is also important to emphasise the relevance of examining the data on outcomes of transplant with and without transfusion. A global interpretation of the published data on transplant without transfusion is that the outcomes are similar.

"In the absence of specific risk factors for the patient, it is not ethical to refuse to include a Jehovah's Witness patient on a waiting list for a kidney transplant."

However it is not a question of a "pendulum law": one extreme or the opposite. Patient-specific considerations must be taken into account preoperatively in order to balance the ethical and pure medical aspects to take the good decision. While organ transplantation can be performed safely in JW, there are multiple factors seen in some particular cases that warrant analysing:

1) The potential use of stricter transplant exclusionary criteria, given the specific recipient's advanced age and pre-existing co-morbidities, which likely increase risk of developing severe anaemia intra- or post-operatively
2) The recipient's emotional/psychological pre or post-operative state of high anxiety, which can be developed in the scenario of a hypothetical/objective anaemia

In hindsight, the anxiety level may be reduced if patients are also offered pre and/or post-operative psychological counselling sessions. Thus, it is of utmost importance to have strict enough criteria for proper selection of a JW candidate for kidney transplantation.

During recent decades, kidney transplant blood product requirements have significantly decreased in most centres, coinciding with better patient and graft survival rates. This improvement may be related to the better experience of the medical teams with operative recipient management, better surgical techniques, kidney transplantation indication and kidney graft use and preservation. Multidisciplinary transplant teams have also faced this situation, with different strategies to overcome problems and doubts. It is possible to increase haematocrit and platelet levels in patients awaiting kidney transplantation and be able to reduce the need of blood products during transplant procedures.

Kidney transplantation can be feasible and safe

In conclusion, kidney transplantation in selected end-stage renal disease JW patients can be feasible and safe, provided that it is carried out at experienced centres and according to a multidisciplinary approach, considering a complete preoperative discussion among professionals and -obviously- with the patients in order to evaluate all the expectations both subjective and objective.

In the absence of specific risk factors for the patient, it is not ethical to refuse to include a Jehovah's Witness patient on a waiting list for a kidney transplant. However, the evidence on the international heterogeneity in transplant institutes' polices for accepting Jehovah's Witness patients must be considered.

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

Monday 12 July, 10.00 – 11.00 CEST
Thematic Session 19
Kidney transplantation in 2021
Virtual Room 3

EAU Research Foundation presents...

Check out the EAU RF's presentations at this year's congress

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The EAU Research Foundation is giving an update on its projects at the 36th Annual EAU Congress.

One of these is the Phoenix registry. Phoenix is a registry entitled 'Prospective Registry for patients Undergoing Penile Prosthesis Implantation for Male Erectile Dysfunction'. The aim of the registry is to collect prospective data from 1000 patients with a penile prosthesis implant. The plan is to collect data from all Penile Prosthesis Implants (PPI) that are used in daily urological practice, so all surgeons who implant these prostheses are welcome to participate! This will enable us to create a synopsis on patient and partner satisfaction as well as assess the mechanical reliability of the different PPIs on the market.

The ultimate goal is to demonstrate that this therapeutic option is an excellent treatment in patients with refractory Erectile Dysfunction (ED) who did not respond to previous treatments. Furthermore it should be possible to identify clinical and surgical factors that correlate with patient outcome, surgical complications and mechanical reliability of the devices used in daily urological practice. With the results, treatment recommendations and guidelines can be further improved resulting in better care for this group of ED patients.

Within this registry various patient questionnaires related to sexual function, treatment satisfaction and quality of life will be used. Since not all questionnaires were available in the required languages, the questionnaires have been professionally translated according to the international ISPOR guidelines (the professional society for health economics and outcomes research), including forward and backward translation, as well as cognitive debriefing. Cognitive debriefing consists of testing the translated questionnaires on a small group of relevant patients in order to test alternative wording and to check understandability, interpretation, and cultural relevance of the translation. This testing was done by means of patient and partner interviews.

The Phoenix National Coordinators have identified a person within their department to conduct these interviews. Several meetings have taken place during which the interviewers were informed about the background of cognitive debriefing and were instructed how to conduct the interviews.

The Quality of Life and Sexuality with Penile Prosthesis questionnaire (QoLSPP), which was only available in Italian was translated to English first. The wording of the English translation was improved, in deliberation with the Italian designers of the questionnaire, based on comments provided during the interviewer instruction meetings. Following two rounds of patient interviews, the modified English QoLSPP was finalised and used for translation into the other required languages. These translations, together with the translated Erectile Dysfunction Inventory of Treatment Satisfaction (EDITS) questionnaire (patient and partner version), are being tested locally (and modified where needed) by means of patient interviews. Some countries have already finished the interviewing process, while others have some delay due to COVID-19, among other reasons. The progress of the translation and cross-cultural adaptation of the QoLSPP will be reported in **Poster Session 17 'Male sexual dysfunction' (P0499),** which will take place on **Saturday, 10 July 2021, 11.00 – 12.00 hours in Virtual Room 8.** Validation of the translated questionnaires will be part of the Phoenix project. Publications will be generated on the translation and validation process.

"We aim to include European centres who offer Penile Prosthesis Implants for their patients with erectile dysfunction."

For those countries where the interviews have been finished, the translated questionnaires can be finalized and implemented in the Phoenix database, which will allow these countries to start recruiting patients. We expect to first start enrollment in Italy, Belgium, the UK and Spain, followed at a later stage by Portugal, the Netherlands, Germany, Sweden and France. The EAU RF is very eager to start this interesting project.

Participating centres for our Registry still needed
We aim to include European Centres who offer PPI for their patients with erectile dysfunction. High as well as low volume centres can participate, in order to get a good representation of daily clinical practice. In this registry we will collect pre-defined parameters related to this kind of surgery. All registered devices that are used as implant in daily urological practice should be included. No extra visits will be required to collect the data, patients are seen on a regular basis according to standard clinical practice. Patient inclusion should be consecutive. Quite some centres have already shown interest in setting up such a registry and are willing to participate by contributing their patient data after receipt of the patient's consent. **ADDITIONAL CENTRES ARE WELCOME.** Should you be interested in participating in this registry, please inform the EAU RF by sending an email to C.Caris@uroweb.org.

Principal Investigators:
Dr. Koen Van Renterghem, Hasselt, Belgium
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Collaborators:
Boston Scientific Corporation
Coloplast Corporation

Sponsor: EAU Research Foundation

Novel update of SATURN Registry presented at EAU21
Artificial urinary sphincter (AUS) implantation has been the standard of care for refractory male stress urinary incontinence (SUI) for many years. Nowadays, new surgical procedures with devices like slings (fixed and adjustable) are increasingly used. Currently, there are no clear recommendations for which patient factors would identify the best surgical treatment options for SUI with either AUS or sling.

The objectives of the SATURN Registry are to evaluate the effects of surgical treatment of SUI with currently available devices and to determine prognostic factors which may help to identify clinical and surgical variables that correlate with (un)favourable outcomes.

The aim is to recruit 1000 male patients undergoing surgery for treatment of SUI with AUS or sling. Cure rate is defined as urinary continence with no need for use of pads or the use of one light security pad. PROMS (quality of life (QoL); incontinence) and clinical data are collected from study visits at baseline (BL) before surgery; at the time of surgery; six weeks (activation of AUS); 12 weeks and one year post-surgery. Mid-term follow up will consist of annual patient contacts after one year post-surgery, up to and including year 10.

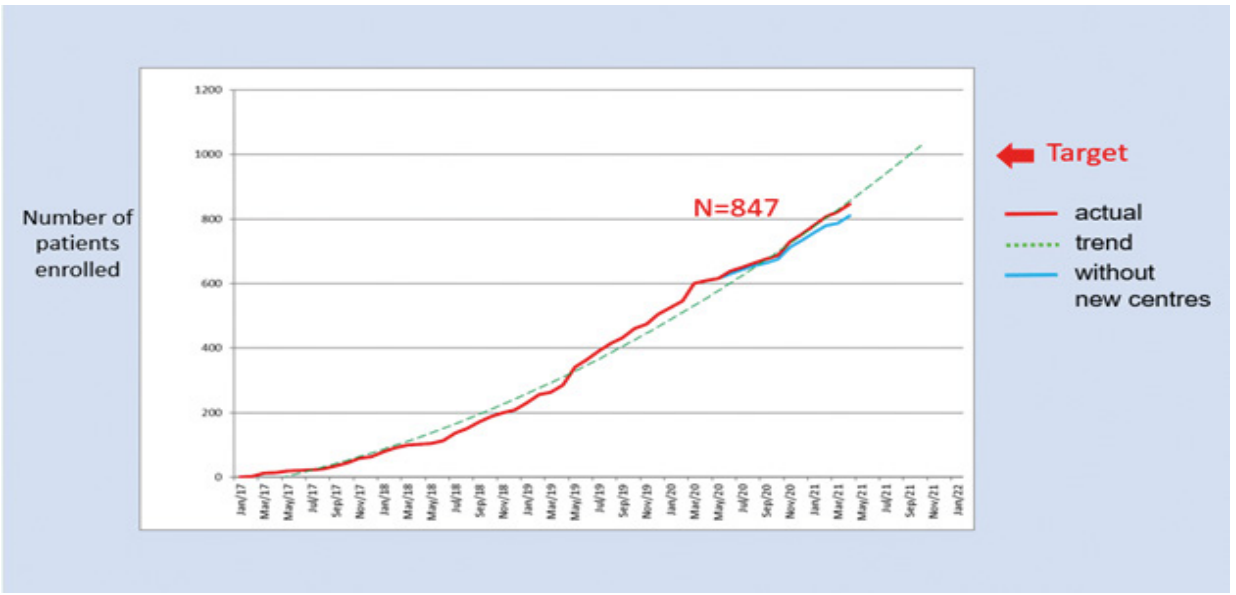

Figure 1: Inclusion rate of the SATURN Registry (cut-off date 20 April 2021). The blue line shows the recruitment rate if no new centers would have been added from February 2020

To date (cut-off date 20 April 2021), 847 patients have been recruited over a period of 50 months in centres from the Netherlands (2 centres, 159 patients), Belgium (5 centres, 258 patients), Czech Republic (1 centre, 48 patients), Spain (10 centres, 151 patients), Germany (3 centre, 10 patients), Norway (2 centres, 134 patients), the United Kingdom (3 centres, 47 patients), Italy (1 centre, 37 patients) and Finland (1 centre, 3 patients).

"Results reported will include (...) main causes of SUI, types of RP procedure, and (in)continence status after 3 months, 1 year and 2 years of follow-up."

Due to the COVID-19 pandemic, elective surgery has been limited over the past year. Inclusion at the centres that were already recruiting pre-COVID-19 (on which the expected trend was based) declined during COVID-19 (see Figure 1, blue line). However, with the addition of six new recruiting centres the current inclusion rate (see Figure 1, red line) is in accordance with the expectations/trend pre-COVID-19 to reach the target of 1000 included patients at the end of 2021 (see Figure 1, green dotted trend line).

The update of the SATURN Registry will be presented by Dr. Frank Martens (Nijmegen, NL) in **Poster Session 4 'Male and female stress urinary incontinence – evaluation and surgical solutions' (P0108),** which will take place on **Thursday 8 July 2021, 11.00 – 12.00 hours in Virtual Room 9.** Results reported will include types of devices implanted, main causes of SUI, types of RP procedure, and (in) continence status after 3 months, 1 year and 2 years of follow-up.

References:
Van der Aa F., Heesakkers J., Martens F., Thiruchelvam N., Bjartell A., Caris C., Schipper R., Witjes W., Hamid R. (2019). Prospective European registry for patients undergoing surgery for male stress urinary incontinence: An initial report of the registry 'SATURN'. European Urology Supplements. 18. e1063. DOI: 10.1016/S1569-9056(19)30767-5

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Collaborator:
Boston Scientific Corporation

Sponsor:
EAU Research Foundation

Thursday 8 July, 11.00 – 12.00 CEST
Poster Session 04
Male and female stress urinary incontinence - Evaluation and surgical solutions
Virtual Room 9

Saturday 10 July, 11.00 – 12.00 CEST
Poster Session 17
Male sexual dysfunction
Virtual Room 8

EAU21 Virtual Congress sees the premiere of Patient Day

Second day of the congress will feature one of its most important new elements

Mr. Eamonn T. Rogers
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So many new things are happening for EAU Patient Information (EAU PI) despite the global COVID-19 pandemic and its far-reaching impact on worldwide communities.

Due to technology advancing at an unprecedent rate since 2020, the European Association of Urology (EAU) has been able to successfully continue its long-standing congress tradition with the 36th Annual EAU Congress (EAU21 Virtual Congress). This virtual event premiers an EAU PI long-held vision of creating a larger and impactful presence at the annual EAU Congress. We are proud to present a virtual Patient Track solely devoted to patients, which will take centre stage for a day on Friday, 9 July 2021. This Patient Day will focus on engaging with patients, patient advocate organisations, and medical experts on a range of topics through different sessions and platforms.

"The Patient Day will focus on engaging with patients, patient advocate organisations, and medical experts on a range of topics."

Special thanks to our EAU Patient Advocacy Group (EPAG) members, in alphabetical order, Dr. Sara Badreh – European Cancer Patient Coalition (ECPC), Mrs. Serena Bartezzati - ERN eUROGEN, Ms. Antonella Cardone – European Cancer Patient Coalition (ECPC), Mr. Ernst Guenther Carl – Europa Uomo (EUomo), Mr. Phil Cornford – EAU Guidelines Office, Mr. John Dowling – Europa Uomo (EUomo), Dr. Rachel Giles - International Kidney Cancer Coalition (IKCC), Ms. Paulina Gono – European Cancer Patient Coalition (ECPC), Dr. Sara MacLennan – EAU Guidelines Office, Dr. Lydia Makaroff - World Bladder Cancer Patient Coalition (WBCPC), and Mrs. Mary Lynne Van Poelgeest-Pomfret - World Federation for Incontinence and Pelvic Problems (WFIPP), for their contributions and support in the development of the Patient Day programme.

Patient Information sessions – Friday, 9 July 11.30 – 16.30 (virtual rooms 9 and 10)
The Patient Day will start off with five different one-hour Patient Information sessions involving the patient advocate organisations EUomo, IKCC, WBCPC, and WFIPP together with medical experts and specialists. The topics for these sessions are prostate cancer, bladder cancer, kidney cancer, life after cancer treatment, and functional urology. The programme details for each session can be found at: EAU2021.org.

ADT Educational Programme – Friday, 9 July - PCa Session 11.30 – 12.30 (Virtual Room 10)
EAU PI will also introduce the Androgen Deprivation Therapy (ADT) Educational Programme. This is a collaboration with the authors of the ADT book *Androgen Deprivation Therapy: An essential guide for men with prostate cancer and their loved ones* and the founders of the Educational Programme in Canada: Dr. Richard Wassersug, Honorary Professor in the Department of Cellular and Physiological Sciences at the University of British Columbia (CA), Dr. Lauren Walker, a clinical psychologist and a Research Assistant Professor in the Department of Oncology at the University of Calgary (CA), and Dr. John Robinson, a clinical psychologist and a member of the Genital Urinary Program at the Tom Baker Cancer Centre in Calgary, Alberta (CA). The programme will be introduced together with the second-edition, European version of the book.

If you are not already familiar with the ADT Educational Programme, here is a brief insight into what it is and how it works. This programme helps prostate cancer patients manage the side effects of ADT through an interactive 1.5-hour class built around the ADT Book. The goal is to help prostate cancer patients improve their quality of life as well as maintain strong, intimate relationships while on ADT and to take appropriate actions to reduce, or avoid, the negative impact of ADT.

The ADT classes are planned to start in the near future with a small, selected number of hospitals in the UK and in Ireland. To prepare for these sessions, EAU PI is conducting a free virtual *Train-the-Trainer* course to a limited number of prostate cancer specialist nurses in the summer of 2021.

We conclude our premier Patient Day with the following activities:

Patient poster session – Friday, 9 July 16.30 – 17.40 (virtual room 9)
Our Patient poster session puts the spotlight on selected abstracts focussing on the theme Disconnect Between Patient and Physician. This disconnect can have far-reaching consequences in terms of side-effects, treatments, outcomes, and the level of quality of life, which impacts not only patients but also their circle of support. This session is aimed at starting a dialogue together with medical experts and patient advocates. It gives patient advocates a platform to present various aspects of patient-focussed research. By creating this forum, we hope to bring into focus any existing presumptions and to encourage patient perspectives.

Directly following the Patient poster session, the top-five best patient poster awards will be announced for the poster presentations. The awards will be presented by Mr. Eamonn Rogers (IE), EAU PI chairman, and Dr. Lydia Makaroff (BE) on behalf of WBCPC. The patient poster presentations will be available for viewing in the EAU21 Resource Centre.

Because of the unexpected number of patient topic abstract submissions for this year's congress, we have created an exclusive platform for presentations that we believe are of interest to viewers. A special, and specific, selection of patient topic poster presentations which aren't part of the congress programme will be published on the EAU PI website and in the EAU21 Resource Centre.

"The disconnect between patient and physician can have far-reaching consequences in terms of side-effects, treatments, outcomes, and the level of quality of life."

Roundtable: The Road to Successful Intervention – Friday, 9 July 18.00 – 19.00 (Virtual Room 2)
This session will be moderated live from a studio in the Netherlands. Medical experts, patients, and their loved ones come together to address the role of prostate cancer patients and HCPs. The session looks at four subjects on the topic: awareness, early detection, active surveillance, and treatment as it relates to shared responsibilities of both the healthcare provider and patient during a patient's care pathway. Do healthcare providers ask the right questions during intake? Do patients provide all the information the healthcare provider needs, such as a detailed medical history and anything that could be relevant to the decision-making process as to what care pathway to take?

At the end of each segment, there will be a live Question-and-Answer (Q&A) segment.

"Medical experts, patients, and their loved ones will come together to address the role of prostate cancer patients and HCPs."

The EAU is making it easy for patients and patient advocates to join EAU PI during the congress by offering a free full registration. A full registration includes:

- Online access to all sessions, which are live streamed, with the exception of the EAU General Assembly, ESU hands-on training sessions, and ESU-organised courses
- Access to the EAU Patient Day sessions
- Access to the Resource Centre for one year, which includes all scientific content (webcasts, abstracts, poster PDFs, and videos) presented at EAU21
- The EAU21 Mobile App

Even if you are not able to join in the full day's activities of EAU PI, we hope you will take a moment out of your day on 9 July to see some of what is happening during the EAU Patient Day premier.
For all the details regarding EAU PI activities during the EAU21 Virtual Congress, visit the EAU PI Congress webpage on the EAU PI website: **patients.uroweb.org/eau21/**, or the EAU Congress website: **eau2021.org**

Follow us on Twitter and Facebook and subscribe to our EAU PI Newsletters. You can contact us by e-mail via: **info.patientinformation@uroweb.org**.

Whether it be to re-connect or to make a new connection, we look forward to making a virtual connection with you during the EAU21 Virtual Congress!

Friday 9 July, 11.30 – 19.00 CEST
EAU Patient Day
Please view the scientific programme at eau2021.org to find all the up-to-date information on the EAU Patient Day sessions.

eau Patient Information

"I am honoured to be co-chairing the patient poster presentations at this year's conference. The EAU has been a world leader in ensuring that patient organisations are included within their congress. I am looking forward to seeing impactful presentations from around the world, demonstrating the value of patients and physicians working together to co-create better care pathways."

Dr. Lydia Makaroff
Vice-president World Bladder Cancer Patient Coalition (WBCPC)

"This is a fantastic opportunity to bring a well evaluated and high-quality programme to Europe which will benefit men with prostate cancer on ADT and their loved ones."

Louisa Fleure
PCa Specialist Nurse, Urology Centre
Guy's Hospital, London, UK, ADT Programme Coordinator Europe

Ms. Louisa Fleure on the ADT Educational Programme

Larcher wins the 2020 EAU Hans Marberger Award

First definition and clinical validation of a training curriculum for RAPN

By Loek Keizer

The 2020 EAU Hans Marberger Award was awarded to Dr. Alessandro Larcher of Milan (IT). His paper "The ERUS Curriculum for Robot-assisted Partial Nephrectomy: Structure Definition and Pilot Clinical Validation" was published in Issue 6, Vol. 75 of *European Urology* and was deemed the best European paper published on minimally-invasive surgery in urology.

The award, annually given since 2004, is named after Prof. Hans Marberger to honour his pioneering achievements and contributions to endourology and the development of urologic minimally invasive surgical procedures. Previous winners include Profs. Morgan Roupret (2011) and Jens Rassweiler (2013) and most recently Dr. Larcher's compatriot Dr. Giuseppe Simone (2019). The award is supported by a grant of €5,000 from KARL STORZ SE & CO.KG.

Dr. Larcher is a staff urologist at San Raffaele Hospital in Milan, having previously completed fellowships in Montreal (CA) and Aalst (BE). He is currently also Scientific Director at ORSI Academy in Melle, Belgium. Larcher has been involved with the EAU in several guises: his the Chair of the Junior ERUS/YAU working group on robot-assisted surgery and the Digital Media Associate Editor for *European Urology*.

The paper

Dr. Larcher's paper, co-written with many prominent robotic urologists, outlines and measures the efficacy of the recently established training curriculum for robot-assisted partial nephrectomy.
From the paper: "In urology, patients treated during the learning phase of the surgeon are at risk of inferior outcomes relative to those treated when adequate experience is accumulated in case of open, laparoscopic, or robot-assisted radical prostatectomy (RARP). To counter such suboptimal outcomes observed during the learning curve of radical prostatectomy, specific training programmes have been proposed and the European Association of Urology (EAU) Robotic Urology Section (ERUS) developed a curriculum based on theoretical knowledge, preclinical simulation, and interaction between mentor and trainee, allowing for the proficiency-based progression across modules with growing complexity."

"Although robot-assisted partial nephrectomy (RAPN) is another complex urological procedure with a non-negligible learning curve, no validated training programme is currently available for this procedure. To address this void, this study aims to define the structure of a curriculum for RAPN and to provide its pilot clinical validation, with the ultimate goal of improving patient's outcome during the learning curve of the surgeon."

"This study is the first definition and clinical validation of a training curriculum for RAPN. The ERUS curriculum for RAPN can protect patients from suboptimal outcome during the learning curve of the surgeons and can aid surgeons willing to start a RAPN programme. In the pilot phase of clinical validation, no evidence of any detriment with respect to patient's clinical outcomes was recorded and the programme allowed for the transition from the beginning of surgical experience through increasing responsibility to the independent completion of a full case. To ensure generalizability, the observed safety profile must be confirmed in a larger cohort of patients and the observed efficacy profile must be confirmed in a larger cohort of trainees in a multi-institutional setting."

Dr. Larcher spoke to *European Urology Today* on the occasion of his being awarded the Hans Marberger Award.

Congratulations on winning the award. Your paper both defined and assessed a curriculum for RAPN. Could you explain why this was a necessity?
"Human factors such as experience and training are key determinants of patient's outcome after surgery. Structured training programmes allow for better results in shorter time."

Its conclusions indicated that the curriculum is a success. How have these conclusions changed training for RAPN?
"The aim of the ERUS is to develop structured training programmes for robot-assisted surgery that can be taken as paradigm. The RAPN curriculum is a crucial piece of the larger puzzle."

What's next in the field of robotic training?
"ERUS will be expanding the curriculum with a training model for any renal surgery procedure such as pieloplasty, radical nephrectomy or nephroureterectomy."

Why do you think your paper was chosen for the award?
"The study design was innovative and unique. It is the first investigation in surgery studying the impact of a surgical training on patients' outcome and taking into consideration patient's outcomes."

How do you feel about your name being listed among the other award winners?
"It's such a privilege. It is a great honour to find my name among the giants of laparoscopy that have won the award since 2004."

Dr. Larcher receiving the 2020 EAU Hans Marberger Award from Prof. Francesco Montorsi in Milan. Watch the video on the EAU21 Congress Platform!

In the spotlight: Dr. Andrea Gallioli

The 2021 EAU Hans Marberger Award recipient

By Erika De Groot

Every year, the European Association of Urology (EAU) grants highly-coveted awards to exemplary urologists for their research and performance. This year, Dr. Andrea Gallioli (ES) of the Fundació Puigvert hospital receives the prestigious 2021 EAU Hans Marberger Award. In this interview, he shares the key findings of his award-winning research and shares the inspiration behind its inception.

The research and the accolade

The EAU Hans Marberger Award is given to the best published European paper on minimally-invasive surgery in urology. This year, Dr. Gallioli receives this recognition for his paper *"Learning Curve in Robot-assisted Kidney Transplantation: Results from the European Robotic Urological Society Working Group"* which was published in the August 2020 edition of the European Urology journal.

"We consider the learning curve of the technique crucial as one of the main issues of any new surgical technique relies on applicability and reproducibility among different surgeons."

Dr. Gallioli's research began during his fellowship at Fundació Puigvert under the guidance of Dr. Alberto Breda, Director of the Transplant Division and Uro-Oncology Unit at the institution and Chairman of the EAU Robotic Urology Section (ERUS).

"In 2015, Dr. Breda gathered a group of pioneer surgeons under the ERUS-RAKT Working Group to shed light on robot-assisted kidney transplantation. The group published several key studies on the topic. However, Dr. Breda and I observed that there wasn't any published study on the learning curve in robot-assisted kidney transplantation yet. We consider the learning curve of the technique crucial as one of the main issues of any new surgical technique relies on applicability and reproducibility among different surgeons.

"Together with Dr. Breda and other respected surgeons in the field such as Prof. Dr. Antonio Alcaraz, Prof. Dr. Karel Decaestecker, Prof. Dr. Sergio Serni, and Prof. Dr. Volkan Tuğcu, we studied the learning curve of this novel surgical technique in five centres with the highest volumes. We focused on the rewarming time, which is the time from the graft insertion in the abdominal cavity to the de-clamping of graft vessels," stated Dr. Gallioli.

The conclusions of the study are the following:

- Robot-assisted kidney transplantation requires a learning curve of 35 cases to achieve reproducibility in terms of timing, complications, and functional results.
- Synergy between the surgeon and the assistant is crucial to reduce rewarming time.
- High-grade complications and delayed graft function are rare after 10 surgeries.
- Hands-on training and proctorship are highly recommended.

When asked about the future plans about this study, Dr. Gallioli said, "Since the study focuses on learning curve, there is no need for a follow-up. However, the ERUS-RAKT Working Group is continuing to evaluate hot topics in robot-assisted kidney transplantation such as technological advancements in graft cooling systems, long-term outcomes of the surgery, and finally, a comparison with open kidney transplantation."

Dr. Andrea Gallioli

Urology as his calling

During the last two years of his medical education, Dr. Gallioli focused on oncologic abdominal surgery, particularly in general surgery. After graduation, he had the opportunity to gain more knowledge and experience at the Urology Unit of Fondazione IRCCS Ca' Granda – Ospedale Maggiore Policlinico in Milan. "It was there where I discovered a world of opportunities in a single specialty; urology offers the possibility to approach oncologic surgery, reconstructive and functional surgery, and endoscopy. Urology is an innovative specialty because of two main reasons: it comprises a part of surgery and a part of clinics, similarly to gynaecology and otolaryngology; moreover, urology is strongly associated with technological advancements and the pursuit for innovation," stated Dr. Gallioli.

Role models and inspirations

"My biggest role models include my parents, who are doctors as well. They were my inspiration in pursuing this profession and I'm truly grateful for their support. I was also fortunate to be under the tutelage of Prof. Emanuele Montanari, who was the Director of a residency programme in Milan. For five years, he imparted the principles of urology and encouraged me to join a fellowship abroad which I spent at Fundació Puigvert. There, I met Dr. Breda. His dedication to improving one's capabilities, whether in the surgical or research field, taught me that one should never stop learning.

"I would like to express my gratitude to Dr. Breda for including me in this research team which gave me a valuable experience and the opportunity to pursue the research on the learning curve in robot-assisted kidney transplantation. I would also like extend my appreciation to Prof. Joan Palou, who is Chairman of the Urology Department at Fundació Puigvert and Chairman of the European School of Urology, for giving me the chance to work on such interesting studies. Last but not least, I would also like to thank the whole team of authors who advised and helped during the development of the manuscript."

When asked what lies in the future for him, Dr. Gallioli shared, "My professional aspiration is to become a valuable surgeon and to pursue an academic career centred on oncologic urology and kidney transplantation. I hope to provide significant contributions that may help the urologic community in the coming years."

Prof. Joan Palou (ES) presented Dr. Gallioli with the EAU Hans Marberger Award. Go to the EAU21 Congress Platform and watch the video!

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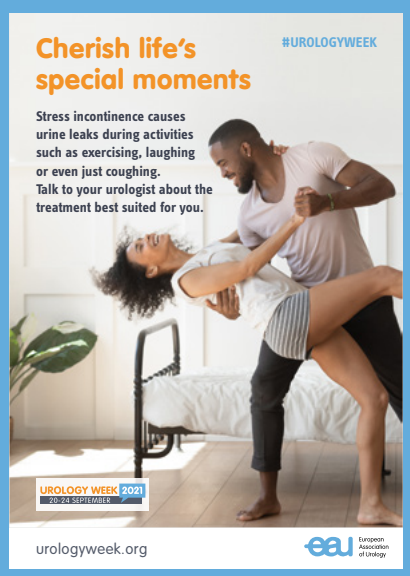

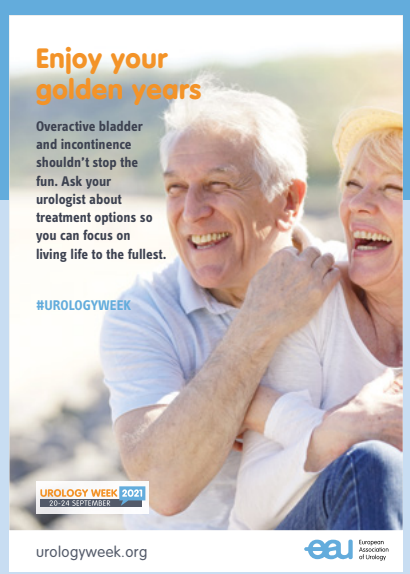

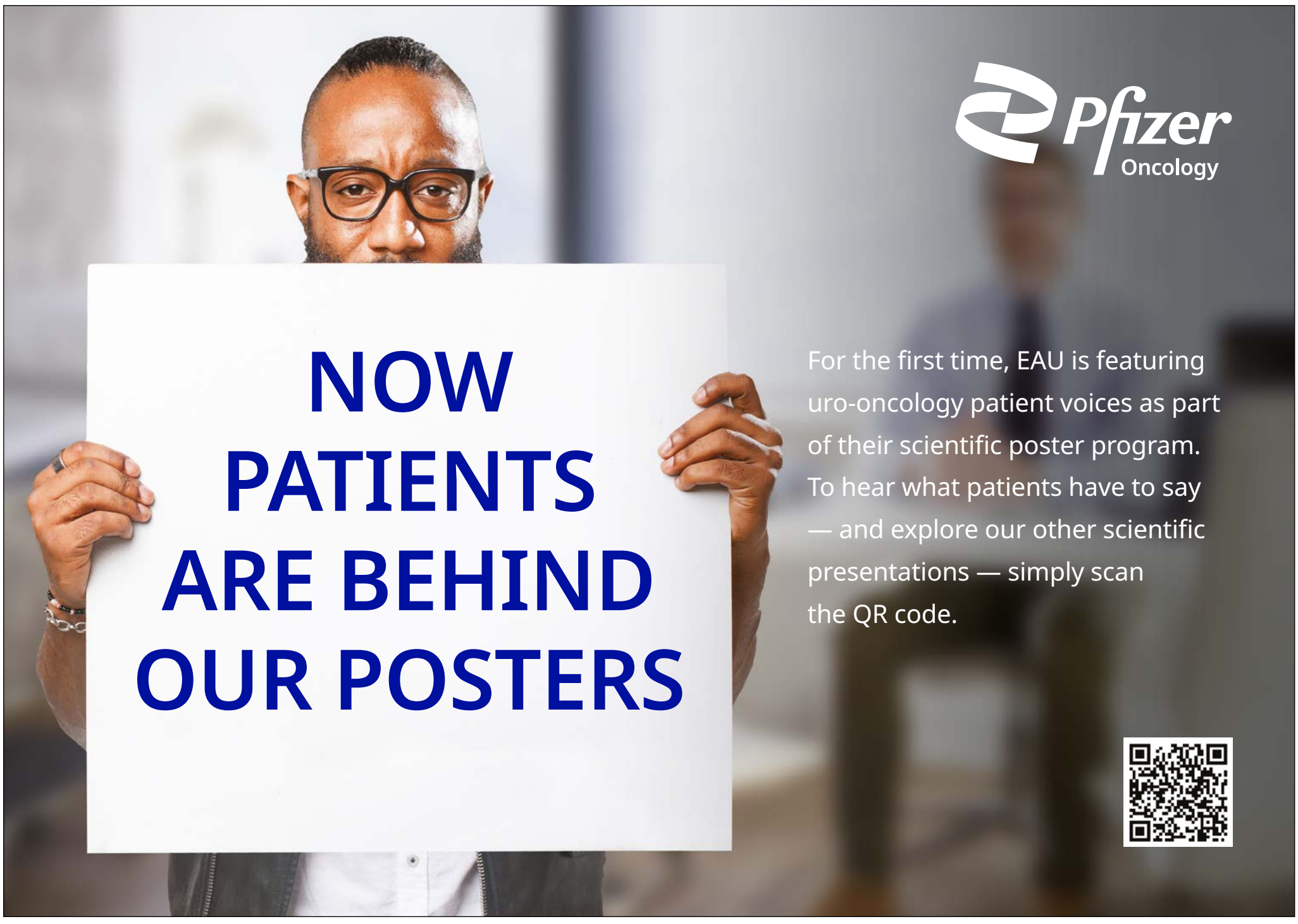

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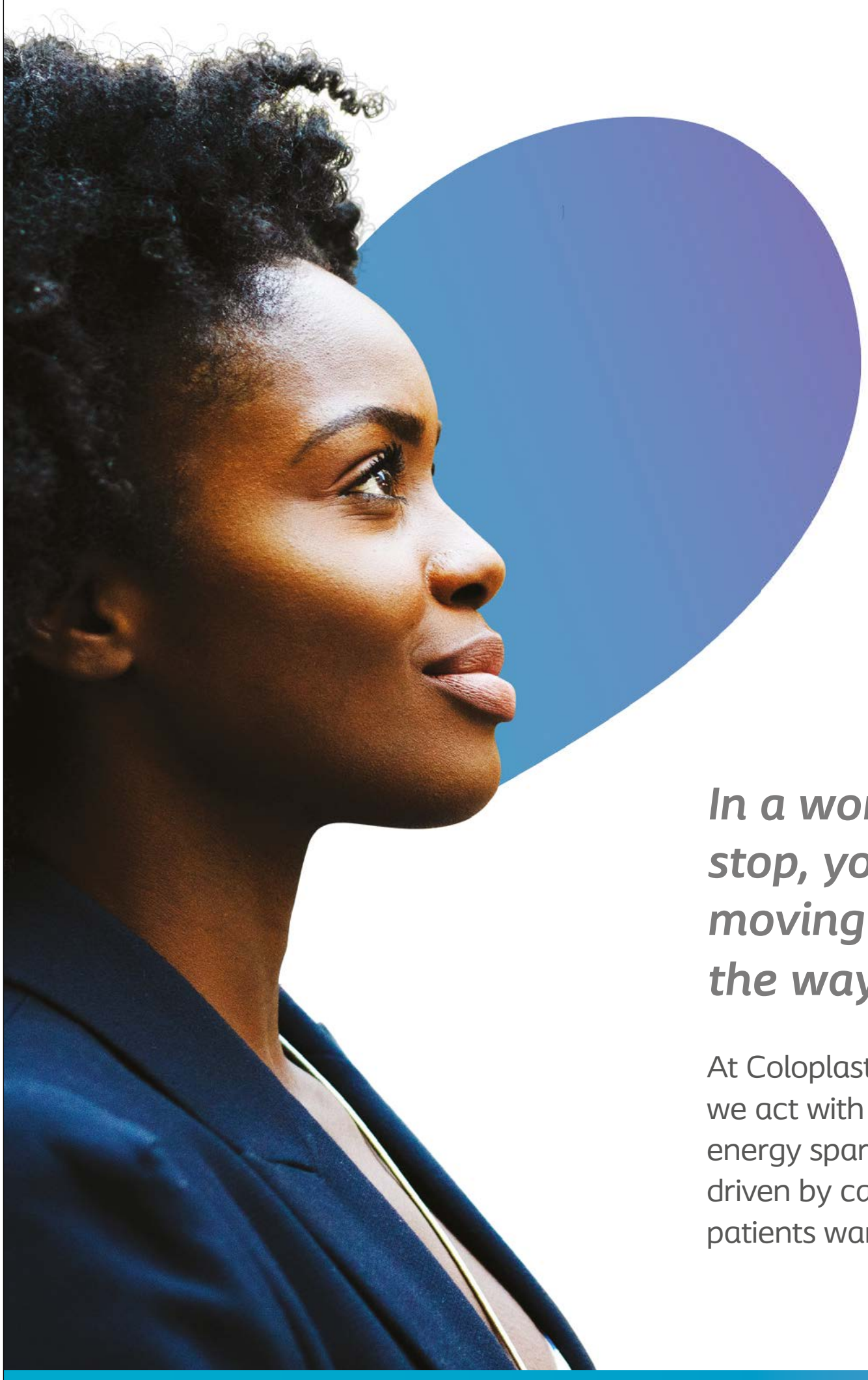

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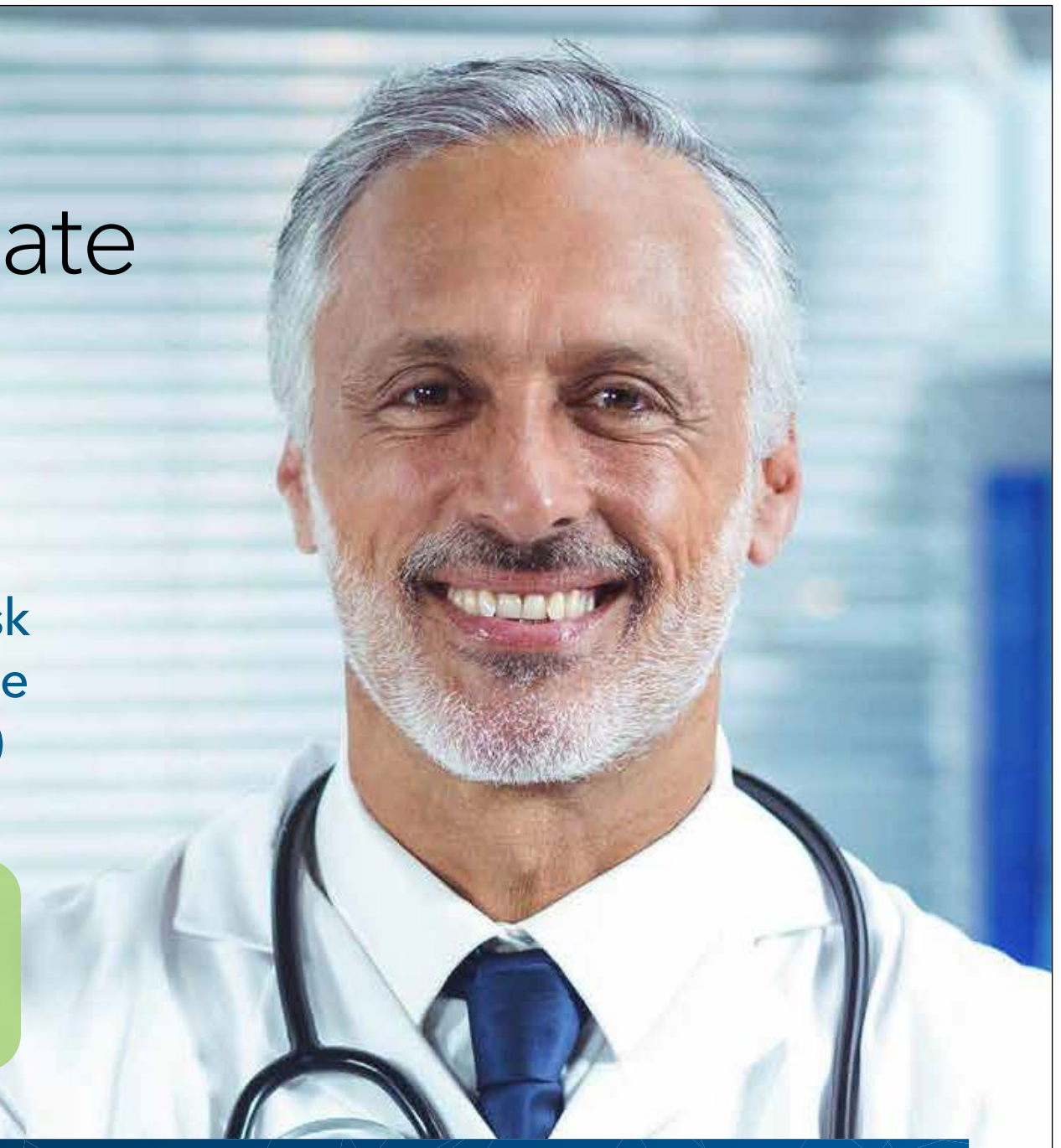

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What does the test score mean?

Cut point 15.6

0 — 100

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