1 Traditional evidence acquisition powered by Big Data is the next generational paradigm shift in urology

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N'Dow J.

University of Aberdeen, Academic Urology Unit, Aberdeen, United Kingdom

Introduction & Objectives: Our purpose as a global urological community is the improvement of patient care that is evidence-based, patient-centred, cost-effective and data-driven towards value-based healthcare provision. 10 years ago, the EAU Guidelines started a mini-revolution, to transform the Guidelines from eminence-based to being evidence-based with the introduction of Cochrane methods and ensuring that guideline recommendations are underpinned by systematic reviews (SRs). During the first 5 years, many of the recommendations were still underpinned by low level evidence because the primary studies were not good enough and the dependence on expert opinion was still prevalent.

Materials & Methods: 5 years ago, the EAU decided to step into the new world of Big Data (Real World Data; RWD) as a new source of evidence acquisition to complement traditional published clinical trials and SRs. Today, the EAU is coordinator of two large Big Data consortia funded by the European Commission's Innovative Medicines Initiative (PIONEER €12M funded 2018 and more recently OPTIMA €21.3M funded 2021). Invaluable lessons learnt from the Big Data experiment has confirmed that the time is right for a generational paradigm shift in evidence acquisition strategies that is powered by Big Data which goes beyond retrospective RWD with the additional incorporation of large scale prospective big data capture. This would entail full mobilisation of the collective will of the EAU membership, KOLs and all other urologists wherever they may be.

Results: Urologists, patients, healthcare providers, funders, and other key stakeholders benefit from reliably captured data on patient outcomes, practice variations, guideline adherence, and the impact of adherence & non-adherence on outcomes and cost. RWD is central to all of this and will be an essential contributor to new knowledge that fills significant evidence gaps in guideline recommendations and urological practice as well as inform healthcare prioritisation and policy. Building an ecosystem that allows traditional evidence acquisition to co-exist and be complemented by RWD would allow urologists to start to gain much needed confidence in the estimates of effects generated by RWD analytics. It would enable researchers and clinicians to further characterise urological conditions, increasing understanding of the pathophysiology of the conditions and to identify novel treatments. It will allow predicting of disease course and drug response for patients reliably. Ultimately, this would result in tools to rapidly select the most promising personalised treatment strategy for a particular individual patient. Delivering insights that will allow healthcare systems to ensure that the patient is truly at the centre of decision-making, with health outcomes that matter and resources focused on treatments that really make a difference. The next generational paradigm shift has started.

2 Risk-adapted screening for prostate cancer in young men – First results of the PROBASE trial

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Albers P. , PROBASE Trial Study Group

Düsseldorf University, Dept. of Urology, Dusseldorf, Germany

Introduction & Objectives: Prostate-specific antigen (PSA) – based screening has proven to significantly reduce prostate cancer (PCa) mortality. However, population-based screening for PCa suffers from a high rate of overdiagnosis followed by overtreatment. A digital rectal examination (DRE) still represents the mainstay of the German statutory early detection program. In contrast, risk-adapted approaches have been suggested to improve the accuracy. Here we report on updated results of the risk-adapted PROBASE screening trial for PCa.

Materials & Methods: From February 2014 to December 2019, PROBASE recruited and randomized 46,642 men in Germany at age 45 to receive either an immediate PSA test (arm A) or a delayed PSA test at age 50 (arm B). Participants in arm B were offered a DRE at the time of enrolment instead of a PSA test. PSA tests classified participants in arm A into a low (<1.5 ng/ml), intermediate (1.5-2.99 ng/ml) or high (>3 ng/ml) risk category. In cases of confirmed PSA values >3 ng/ml participants were recommended a prostate biopsy based on upfront multiparametric magnetic resonance imaging.

Results: Baseline PSA tests categorized the 23,301 participants of arm A into low (89.2%) and intermediate (9.3%) risk. With confirmed PSA >3ng/ml 186 (0.8%) men were at high risk of whom 120 (64.5%) underwent a biopsy with detection of 48 prostate cancers (overall prevalence 0.2%). Only four patients had International Society of Uropathology (ISUP) grade group (GG) >3 cancers (overall prevalence 0.02%). In arm B, 23,194 participants were enrolled and 6,537 underwent a DRE with 57 suspicious findings. Two of which showed ISUP GG 1 PCa corresponding to a detection rate by DRE of 0.03% (2/6,537). Adherence to the protocol was excellent with a so-called PSA contamination rate of at most 25%. Analysis of tumors detected will be presented.

Conclusions: The majority of men (about 90%) at age 45 presents with a PSA below 1.5 ng/mg which implies a very low risk to develop prostate cancer. The prevalence of screen-detected clinically significant PCa in 45-year-old men is very low. Moreover, the rate of aggressive cancers (ISUP GG 3-5) is even lower. DRE did not turn out effective for early detection of PCa.

3

First in-men evaluation of OTL78, a near-infrared fluorescent prostate-specific membrane antigen-targeting probe, in prostate cancer patients undergoing radical prostatectomy

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Van Der Poel H.G.[1], De Barros H.[1], Stibbe J.[2], Vahrmeijer A.[3], Burrgraaf K.[2]

[1]Netherlands Cancer Institute, Dept. of Urology, Amsterdam, The Netherlands, [2]CHDR, LUMC, Leiden, The Netherlands, [3]LUMC, Dept. of Surgery, Leiden, The Netherlands

Introduction & Objectives: Improved prostate cancer (PCa) visualization during radical prostatectomy can increase the rate of complete surgical resections while preserving the periprostatic nerves. We evaluated the feasibility of OTL78, a high-affinity Prostate-Specific Membrane Antigen (PSMA)-targeting ligand labeled with a fluorophore (S0456) for the real-time near-infrared (NIR) intraoperative detection of PCa.

Materials & Methods: In this single-center, prospective, open-label, single-arm, phase I/II clinical trial, we enrolled patients with biopsy-confirmed PCa scheduled to undergo a robot-assisted radical prostatectomy (RARP). A concomitant extended pelvic lymph node dissection (ePLND) was performed in patients at an increased risk of lymph node metastasis (LNM). Patients were sequentially enrolled into three different dose cohorts (DC) of a single IV infusion of OTL78: 0.06 mg/kg 1-2 hours before surgery, 0.03 mg/kg 1-2 hours before surgery, and 0.03 mg/kg 24 hours before surgery. The VisionSense NIR imaging system (Medtronic) was used for in- and ex vivo fluorescence imaging. The primary objective was to determine the optimal dose and dose interval of OTL78 for the real-time identification of PCa as measured by the signal-to-background ratio (SBR), in which a SBR ≥ 1.5 was considered sufficient for the distinction between lesion and background.

Results: Eighteen PCa patients were enrolled between June 2020, and April 2021. No serious adverse events attributed to OTL78 occurred. The median in vivo SBR was 1.0 (IQR 1.0-1.6) in DC1, 1.3 (IQR 1.0 – 1.7) in DC 2 and 1.9 (IQR 1.0 – 2.3) in DC3. Sixty-five (42%) prostate regions contained PCa on histology. The in vivo sensitivity and specificity per dose group were 33% and 53% in DC1, 49% and 87% in DC2, and 68% and 100% in DC3, respectively. The ex vivo visibility of tumors on prostate whole mounts with NIR fluorescence imaging was predominantly dependent on tumor volume (the detection rate of lesions < 0.5 cm^3 versus ≥ 0.5 cm^3 was 36% and 92%, respectively), the dose and timing of OTL78 (the detection rate was 23% in DC1, 34% in DC2 and 65% in DC3), the ISUP grade (25% of ISUP 1-2 lesions versus 51% of ISUP ³ 3 lesions were detected), and the PSMA expression on immunohistochemistry (the detection rate of lesions with weak, moderate and intense PSMA expression was 11%, 25%, and 49%, respectively). NIR imaging also provided in vivo visualization of LNMs in 4 (22%) patients (median metastasis size of 2.8 mm [IQR 1.3-23.4]).

Conclusions: This first-in-men study demonstrates the safety and feasibility of optimally dosed OTL78 (i.e., 0.03 mg/kg administered 24 hours preoperatively) for the intraoperative visualization of PCa. PSMA-directed intraoperative fluorescence imaging visualized positive surgical margins, nodal metastases, and remnant PCa in the prostate resection bed.

4 Development, multi-institutional external validation, and algorithmic audit of SEPERA – An artificial intelligence-based side-specific extra-prostatic extension risk assessment tool for patients undergoing radical prostatectomy

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Kwong J.C.C.[1], Adree K.[2], Meng E.[3], Taylor N.[2], Kuk C.[4], Perlis N.[1], Kulkarni G.S.[1], Hamilton R.J.[1], Fleshner N.E.[1], Finelli A.[1], Van Der Kwast T.H.[5], Ali A.[6], Jamal M.[1], Papanikolaou F.[1], Short T.[1], Srigley J.[7], Colinet V.[8], Peltier A.[8], Diamand R.[8], Lefebvre Y.[8], Mandoorah Q.[9], Sanchez-Salas R.[9], Macek P.[9], Cathelineau X.[9], Eklund M.[10], Johnson A.E.W.[11], Feifer A.[1], Zlotta A.R.[4]

[1]University of Toronto, Dept. of Surgery, Urology, Toronto, Canada, [2]University of Toronto, Temerty Faculty of Medicine, Toronto, Canada, [3]Queen's University, Faculty of Medicine, Kingston, Canada, [4]Sinai Health System, Dept. of Surgery, Urology, Toronto, Canada, [5]University Health Network, Dept. of Pathology, Toronto, Canada, [6]Trillium Health Partners, Institute for Better Health, Mississauga, Canada, [7]University of Toronto, Dept. of Laboratory Medicine and Pathobiology, Toronto, Canada, [8]Jules Bordet Institute, Dept. of Urology, Brussels, Belgium, [9]L'Institut Mutualiste Montsouris, Dept. of Urology, Paris, France, [10]Karolinska Institutet, Dept. of Medical Epidemiology and Biostatistics, Stockholm, Sweden, [11]University of Toronto, Temerty Centre for AI Research and Education in Medicine, Toronto, Canada

Introduction & Objectives: Accurate prediction of side-specific extraprostatic extension (ssEPE) is critical for performing nerve-sparing surgery in order to mitigate treatment-related side effects such as impotence and incontinence in patients with localized prostate cancer. Artificial intelligence (AI) may provide robust and personalized ssEPE predictions to better inform nerve-sparing strategy during radical prostatectomy.

Materials & Methods: 4936 prostatic lobes (cases) were included in this study. SEPERA, a Side-specific Extra-Prostatic Extension Risk Assessment tool, was trained on 1022 cases from a community hospital network, Trillium Health Partners, Canada. SEPERA was externally validated on 3914 cases across three academic centers: Princess Margaret Cancer Centre, Canada; L'Institut Mutualiste Montsouris, France; and Jules Bordet Institute, Belgium. Model performance was characterized by area under the receiver-operating characteristic curve (AUROC), area under the precision-recall curve (AUPRC), calibration, and net benefit. An algorithmic audit was performed to assess model bias and identify common patient characteristics among predictive errors. SEPERA was compared against contemporary nomograms, as well as a separate logistic regression model using the same variables included in SEPERA.

Results: SEPERA was well calibrated and had the best performance across all validation cohorts (pooled AUROC 0.77, pooled AUPRC 0.61). It had the highest net benefit, enabling more patients to safely undergo nerve-sparing. No significant difference in AUROC was observed when stratified by race, biopsy year, age, biopsy type (systematic only vs systematic and MRI-targeted), biopsy location (academic vs community), and D'Amico risk group. In patients with pathological ssEPE despite benign ipsilateral biopsies, SEPERA correctly predicted ssEPE in 68% of cases, compared to 0-44% for the other models. The most common errors were false positives, particularly for older patients with higher risk disease. No aggressive tumours (i.e., > Grade Group 2 or high-risk disease) were found among false negatives.

Conclusions: We demonstrate the accuracy, safety, and generalizability of using SEPERA to personalize nerve-sparing approaches during radical prostatectomy.

5 Predictors of urinary incontinence after radical prostatectomy based on high-volume center cohort and a systematic review

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Grivas N.[1], Wit E.[1], Boellaard T.[2], Heijmink S.[2], Van Der Poel H.[1]

[1]The Netherlands Cancer Institute-Antoni van Leeuwenhoek Hospital, Dept. of Urology, Amsterdam, The Netherlands, [2]The Netherlands Cancer Institute-Antoni van Leeuwenhoek Hospital, Dept. of Radiology, Amsterdam, The Netherlands

Introduction & Objectives: There are multiple preoperative, intraoperative, and postoperative factors at both patient and surgeon levels which affect urinary incontinence (UI). Aim of our study was to determine patient- and tumour-related prognostic factors for postoperative UI based on the database of a high-volume academic center and the findings of a systematic review.

Materials & Methods: 439 men from a high-volume academic center with PCa treated with robot-assisted radical prostatectomy (RARP) underwent preoperative staging MRI to determine periprostatic fascia thickness (FT), membranours urethra length (MUL) and inner levator distance (ILD) while fascia/nerve preservation (FP) was intraoperatively assessed. The following variables were also recorded: age, prostate size, body mass index, preoperative PSA, Gleason sum score and clinical stage (cT). The systematic review was performed according to PRISMA guidelines. English language articles published from 1990 to 2020 were included. All types of studies exclusively investigating patient and tumour-related prognostic factors for postoperative UI in a univariable (UVA) or multivariable analysis (MVA) were included.

Results: Based on our patient's database, the predictors of shorter continence recovery time were a longer MUL (OR 1.309; CI 1.211, 1.415; P < 0.0001) and shorter ILD (OR 0.904; CI 0.850, 0.961; P = 0.001). In the logistic regression analysis longer MUL (OR 1.565; CI 1.362, 1.798; P < 0.0001), shorter ILD (OR 0.819, CI 0.742, 0.904; P < 0.0001), and higher FP score (OR 1.089, CI 1.011, 1.172; P = 0.024) were independent predictors of continence outcome. In the developed predictive model, maximal nerve preservation (FP score = 12) improved the continence recovery by 5-30% points for all measures of MUL. The risk calculator of our model predicted continence recovery between 1.3% and 99% on a patient level. In the systematic review a total of 119 studies with 131.379 patients were included. Significant prognostic factors for postoperative UI within 3 mo after RP were age (OR per yearly increase 1.04, 95% CI 1.03–1.05), MUL (OR per 1-mm increase 0.81, 95% CI 0.74–0.88), prostate volume (OR per 1-ml increase 1.005, 95% CI 1.000–1.011), and Charlson comorbidity index (CCI, OR 1.28, 95% CI 1.09–1.50). Regarding the role of other patient-related factors, we found no evidence that BMI or PSA were meaningfully associated with postoperative UI, while there were insufficient data available to draw any conclusions for the role of biopsy Gleason score and cT stage.

Conclusions: Based on the analysis of our data and the findings of the systematic review we found that increasing age, shorter MUL, shorter ILD, maximal nerve preservation, greater prostate volume and higher CCI are major prognostic factors for UI. These findings and the developed risk calculator can inform clinicians and patients in treatment decision-making and guide further research.

6 Ex-vivo confocal fluorescence microscopy (VivaScope) at the time of renal tumour biopsy

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Mir Maresma M.C.

IMED, Dept. of Urology, Valencia, Spain

Introduction & Objectives: Renal mass biopsy (RMB) has been underused as a diagnostic tool due to the high rates of non-diagnostic biopsies (20%). Confocal Fluorescence Microscopy (CFM) allows for real-time imaging of specimens with detection of tissue alterations. Our study aimed to demonstrate the utility of CFM on RMB in a daily urological practice. The primary endpoint was to evaluate the ability of CFM to discriminate between good-poor quality cores. As a secondary endpoint, we aimed to assess the agreement for identification of tumoral features in RMB between CFM and standard histopathology diagnosis.

Materials & Methods: From May 2019 to May 2020, 18 RMB were performed at our institution and prospectively included in our study. RMB were performed following a state-of-the-art technique, with a minimum of two quality cores obtained for each case. The definition of good quality renal cores included those with at least 0.5 cm of length, not detached or torn. Specimens were first examined using a confocal scanning microscope after appropriate CFM processing, within 15 minutes of biopsy. Tissue architecture was then assessed, classifying tissue alterations as tumoral, fibrotic, necrotic or normal renal parenchyma If normal or insufficient tissue was reported, then rebiopsy was performed on same day. After completion of ex-vivo CFM imaging, all specimens underwent 5% formalin-fixed paraffin tissue processing and were examined by an expert uro-pathologist. Continuous variables were reported as medians and interquartile ranges (IQR), qualitative variables were reported as frequencies and percentages (%).

Results: Median age at diagnosis of RM was 66 years old.Median tumor size was 2.5 cm (IQR: 2.2-4.2). Renal mass staging was cT1a in 10 patients (55%) and cT1b in 8 patients (44%). Median RENAL score was 7. Standard histopathologic analysis of biopsies revealed oncocytoma in 5 cases (28%), clear cell RCC (ccRCC) in 9 cases (50%), non-ccRCC in 3 cases (17%) and urothelial carcinoma in 1 case (6%). All the biopsy core specimens, previously examined by CFM, were sufficient for standard histologic analysis. Real time identification of normal tissue by CFM led to instant rebiopsy in one patient. The overall detection rate of tumoral tissue by CFM was 100%, in agreement with histopathologic analysis. The median percent of tumor involvement in confocal specimens was 70% (IQR 30-80).

Conclusions: CFM was able to identify core quality in 100% of cases. We reported a diagnostic accuracy of 100 % for CFM, in agreement with standard histopathologic analysis. This supports our hypothesis that CFM performed at the time of RMB allows selection of excellent quality renal cores, and instantly discriminates between normal/tumoral tissue. This would benefit our clinical practice by decreasing the odds of a second renal diagnostic biopsy.

7

Similarities and differences of selected gene expression in metastasizing and differentiation of renal cell carcinoma

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Apanovich V.[1], Matveev V.[2], Apanovich V.[1], Korotaeva A.[1], Kipkeeva M.[1], Muzaffarova T.[1], Khalmurzaev A.[2], Matveev V.[2], Karpukhin A.[1]

[1]Bochkov Research Centre for Medical Genetics, Laboratory of Molecular Genetics, Moscow, Russia, [2]N.N. Blokhin National Medical Research Center of Oncology, Dept. of Urology, Moscow, Russia

Introduction & Objectives: Metastasizing and degree of differentiation refer to the main clinical characteristics of malignant tumors. Both listed features need an in-depth study that can lead to an understanding of the mechanisms for the occurrence of certain state of cancer cells. The objective of our study was to assess the correlation between metastasis and differentiation of clear cell renal cell carcinoma (ccRCC), and panel of selected gene expression.

Materials & Methods: The levels of expression of ten genes in 65 paired samples were studied (ccRCC tumor tissue and the normal kidney tissue) by the real-time polymerase chain reaction.

Results: The expression of 7 genes: CA9, NDUFA4L2, VWF, IGFBP3, BHLHE41, ANGPTL4, and EGLN3 gene were associated both with the degree of differentiation and with the synchronous metastasis of ccRCC. C1QA expression was associated only with metastasis. An ambiguous level of FN1 and CSF1R gene expression was not essential for ccRCC metastasis process, but may have a certain role for differentiation of tumor cells. Poorly differentiated tumors had almost five times higher rate of metastases at one year than well differentiated tumors (odds ratio 4.94). A low correlation of selected gene expression in poorly differentiated tumors was revealed, as opposed to their high co-expression in well differentiated tumors.

Conclusions: A significant part of genes substantial for the development of ccRCC is associated with both metastasis and the degree of differentiation of the ccRCC, which is due to the similarity of functional changes that stimulate both of these processes. For poorly differentiated tumors the number of genes with correlated expression is less than in well differentiated tumors. This may be due to disorganization of gene expression.

8

Is Calcium Oxalate Dihydrate indicative of hypercalciuria in stone patients?

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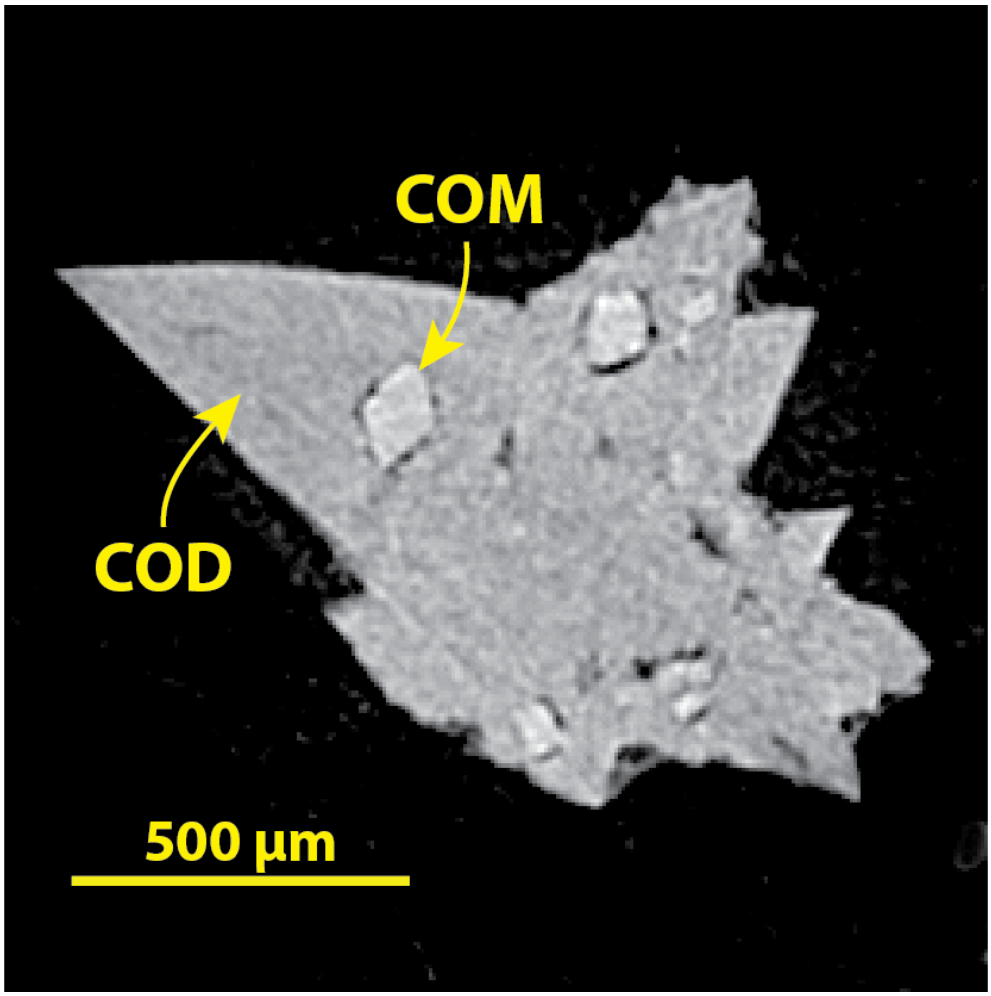
Hesselholt M.S.[1], Osther P.J.S.[1], Lingeman J.E.[2], Williams J.C.[3]

[1]University Hospital of Southern Denmark, Dept. of Urology, Vejle, Denmark, [2]Indiana University School of Medicine, Dept. of Urology, Indianapolis, United States of America, [3]Indiana University School of Medicine, Dept. of Anatomy and Cell Biology, Indianapolis, United States of America

Introduction & Objectives: Calcium oxalate (CaOx) is recoqnized as the most common component in kidney stones. CaOx occurs mainly in two forms, CaOx Dihydrate (COD) and CaOx Monohydrate (COM). The two crystal types have very different morphological characteristics and can easily be distinguished. A large French series has pointed toward hypercalciuria as the main risk factor in COD and hyperoxaluria in COM stone formation. Through meta-analysis we aimed to confirm the possibility that in a kidney stone, COD might be suggestive of hypercalciuria, and to explore why the natural conversion of COD to COM may confuse usage of traditional stone analysis as a tool for stone prevention.

Materials & Methods: The literature search was focused on identifying reports of 24-hour urine calcium measurements and concomitant determination of COM/COD content in kidney stones. Searches of Pubmed and Web of Science databases were performed. Additionally, examples of urinary stones composed of COD, COM, and COD converting to COM, were scanned by micro computed tomographic imaging (micro CT) to examine microscopic structure.

Results: Six published studies have reported both COD and COM content in stones along with numerical data for urine calcium, representing a total of 844 patients, 655 being classified as COM, 119 as COD, and 67 as mixed COM/COD stones. The pooled results revealed that COD stone formers had significantly higher urinary calcium excretion compared to COM stone formers. The mean difference between COD and COM stones formers was 2.63 mmol/24 hours (95% CI 1.78-3.47 mmol/24 hours)($p<0.001$). Micro CT examination of stones revealed how stones that are initially formed as COD can convert to COM, suggesting that stone morphology in addition to stone composition as an aid to identify patients with hypercalciuria may add important knowledge for stone prevention strategies (Fig).



Conclusions: High urinary excretion of calcium seems to correlate with COD content in a kidney stone. This correlation probably also extends to stones primarily formed ad COD, which over time is converted to COM. Adding stone morphology to stone analysis, simply by recognizing COD crystals on the surface of the stone, could add additional predictive value for hypercalciuria in stone patients, which potentially would be valuable for both understanding the pathophysiology of stone formation and clinical management.

9 The role of extracorporeal shock wave therapy in urology

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Rassweiler J.

Danube Private University, Chair of Urology and Andrology, Krems, Austria

Introduction & Objectives: Extracorporeal shock wave lithotripsy has been a game-changer of stone treatment, however, recently with decreasing treatment numbers due to the developments in endourology. Extracorporeal shock wave therapy using different energy levels and application systems have been developed during the last ten years mainly in the field of orthopaedics and surgery, but recently also in neurology and cardiology. The presentation should update the actual situation and perspectives of ESWT in Urology.

Materials & Methods: Based personal experience with ESWT for urologic indications since 1998 and a review of the recent literature, the technical basis of low-intensity shock wave therapy (Li-ESWT) is presented focussing on the main indications (Peyronie`s disease, Erectile Dysfunction, Pelvic Pain Syndrome). Additionally, early promising experiences with new indications (ie. postoperative management of. Fournier`s gangrene) are shown.

Results: Whereas extracorporeal shock wave lithotripsy needs high levels of shock wave energy ranging from 1 to 3 mJ/mm^2) are required, for orthopaedic indications apart from pseudarthrosis much less energy levels are significantly lower (0.05 to 0.55). Also, the focal depth is much lower to reach the target. This resulted in the development of special devices for Li-ESWT (ie. Storz Duolith SD, Dornier Epos Ultra, HMT Ossatron, Wolf Piezoson 300). These devices differ in the type of shock wave generation and focal size. In urology, despite excellent studies for Peyronie`s disease, ESWT is only approved in EAU-guidelines for treatment of pain, whereas EAU-guidelines recommend Li-ESWT for treatment of vasculogenic ED based on existing meta-analyses. Also, for treatment of PPS, randomized trials proved efficacy. New indications could be Li-ESWT after RALP to improve penile rehabilitation. Based on previous Li-ESWT-studies on wound healing, we were able to close secondary and primary wounds after radical excision of the affected area. This resulted in complete restoration of the scrotal and penile skin.

Conclusions: The medical application of shock waves started in urology. Now after more than 40 years, Li-ESWT may play an important role in regenerative medicine also for urologic indications.

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Proteomic profiling of muscle invasive bladder cancer treated with neoadjuvant chemotherapy

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Contreras-Sanz A.[1], Reike M.J.[1], Negri G.L.[2], Oo H.Z.[1], Spencer Miko S.[2], Nielsen K.[2], Roberts M.E.[1], Scurll J.[1], Ikeda K.[1], Wang G.[3], Seiler R.[1], Morin G.B.[2], Black P.[1]

[1]University of British Columbia, Dept. of Urologic Sciences, Vancouver, Canada, [2]University of British Columbia, British Columbia Cancer Research Institute, Vancouver, Canada, [3]University of British Columbia, Dept. of Pathology and Laboratory Medicine, Vancouver, Canada

Introduction & Objectives: While genomic alterations and transcriptomic classifiers have previously been employed to predict response of muscle invasive bladder cancer (MIBC) to neoadjuvant chemotherapy (NAC), proteomic analysis in this context is lacking. We aimed to analyze the proteome of MIBC before and after NAC to identify potential novel biomarkers of response and study the biology of chemoresistance.

Materials & Methods: Pre-NAC tissue was included from 107 MIBC patients who received NAC followed by radical cystectomy. Residual tumor (≥ypT1N0-3) in the cystectomy specimen was present in 62% of patients after NAC, and was available for analysis in 55 (51%) patients. Multiregional sampling was conducted in 37/107 pre-NAC and 15/55 post-NAC samples. Benign ureter was used as control. SP3-Clinical Tissue Proteomics (SP3-CTP) on formalin-fixed paraffin-embedded tissue and bioinformatic analysis were performed.

Results: We quantified 9769 proteins across all samples. Unsupervised clustering of pre-NAC tissue established four clusters with distinct survival outcomes, but no difference in ypT stage: CC1, with high metabolic activity and a luminal profile; CC2, with high nuclear activity; CC3 with high immune infiltration and basal characteristics; and CC4, with high immune infiltration and increased lipid metabolism. CC3 showed worse overall survival ($p<0.01$) and aligned with the RNA-based basal subtype. Multivariable analysis adjusting for prognostic variables identified novel favorable (MAPK9 and MTIF) and unfavorable (DVL2 and NES) biomarkers. Matched analysis of pre- and post-NAC tissue identified markers indicative of NAC resistance (AZGP1 and ORM1). Multiregional analysis showed distinct proteomic tumor profiles in selected pre- and post-NAC matched samples. Findings for some individual proteins were validated by immunohistochemistry in a tissue microarray.

Conclusions: We described four proteomic clusters with distinct biology and survival, as well as novel prognostic protein biomarkers. Ongoing studies in patients treated without NAC will determine if the markers are specifically predictive of outcome after NAC.

11 Cytotoxic effect of cannabinoids on bladder urothelial carcinoma

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Ramon J., Anis O.

Sheba Medical Center and Tel Aviv University, Dept. of Urology, Tel Aviv, Israel

Introduction & Objectives: A large retrospective epidemiological study revealed that cannabis use among the general population is associated with a lower incidence of bladder cancer. This association remains unexplained. In a previous work, we have shown that certain cannabis extracts and cannabinoids, in particular cannabichromene (CBC) with delta-9-tetrahydrocannabinol (THC), have cytotoxic activity against the survival of urothelial carcinoma (UC) cell lines. The purpose of the current study is to further examine the effect of cannabis-derived compounds on in vitro and ex vivo models.

Materials & Methods: Medically available cannabis extracts and clean standards of CBC and THC were tested. Using two commercial UC cell lines (T24, HTB-9), XTT assay, scratch assay and annexin-PI were performed to evaluate cell survival, cell motility, and apoptosis, respectively. Cannabis extracts with a proven effect on the survival of UC cell lines were further analyzed for composition definition. Ex vivo organ cultures (EVOCs) were performed to evaluate the effect of the same extracts and cannabinoids on UC tumors, using tumor samples taken from patients in our institute. The effect of cannabis-derived compounds was tested using continuous exposure and repeated exposure 2 hours daily, at a concentration of 100µg/ml. The survival of EVOC tumor cells was evaluated by a pathologist, who was unaware of the treatment. Drug related cell death was assessed in Hematoxylin & Eosin stain.

Results: Certain cannabis extracts showed an antitumor effect on urothelial carcinoma cell lines and EVOCs. The extracts containing CBC and the THC and synthetic composition of these cannabinoids (85% CBC, 15% THC) caused inhibition of cell survival, cell motility and initiated cell cycle arrest and apoptosis in cell line models. Inhibition concentration of 50% of cells (IC50%) was 13-13.5µg/ml for both cell lines. Eighteen bladder UC patients were enrolled, of them, 12 EVOCs survived the assay. Six EVOCs were treated with cannabis sativa extracts and six with synthetic cannabinoids. Among the EVOCs treated with cannabis extracts, all tissues showed drug related tumor cell death (10% to 100% of tumor cells, mean 81%). Among EVOCs treated with CBC+THC, all tissues with high-grade UC showed drug related tumor cells death (55% to 100% of tumor cells, mean 88.5%). EVOC with low-grade UC showed a drug-related response of 5% of tumor cells. Four normal bladder samples were treated with synthetic cannabinoids, showed no drug-related tissue damage. Tumor tissues exposed to cannabis-derived treatment did not present stromal or muscle layer tissue necrosis.

Conclusions: Cannabis-derived compounds initiate UC tumor cell death, both in cell lines and tumor tissue cultures. High grade tumors are mostly affected. These results represent a potential therapeutic approach for bladder cancer. Further studies are required.

12

Robot-assisted radical cystectomy with neobladder in females: Safety profile and functional outcomes

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Walz J., Andrea A., Caviglia A., Branger N., Maubon T., Pignot G.

Institut Paoli-Calmettes Cancer Center, Dept. of Urology, Marseille, France

Introduction & Objectives: Radical cystectomy (RC) is standard treatment for localized muscle invasive bladder cancer and high-risk non muscle invasive bladder cancer. In women traditionally RC is performed with hystero-adnexectomy and resection of the anterior vaginal wall, often resulting in sexual disorders. Vaginal sparing techniques have been developed to improve functional outcomes. This analysis explores the safety and the functional outcome of this approach.

Materials & Methods: We retrospectively analyzed all consecutive female patients undergoing robot assisted RC (RARC) with neobladder diversion between October 2017 and February 2022. Unless contraindicated, patients with muscle invasive bladder cancer received neoadjuvant chemotherapy (MVAC or Gem-Cis). The indications for vaginal-sparing RC were absence of tumor on bladder neck or urethra and no sign of infiltration of posterior bladder wall at preoperative staging on MRI. Functional results were evaluated with the aid of 5 questions out of the Bladder Cancer Index (BCI) questionnaire. For functional results, only patients with an age < 75 years at surgery and who underwent a procedure with total or partial genital preservation were included. Complications were reported according to Calvien-Dindo and cancer control was evaluated for recurrence free and cancer specific survival.

Results: A total of 22 female patients underwent RARC with neobladder. Mean age was 62 (IQR 57-66) years, and Charlson Comorbidity Index was 3 or more in 11 patients (50%). Preoperative pathology showed pT2 disease in 20 (91%) patients, and Cis in 3 (14%) cases. Neoadjuvant chemotherapy was given in 17 (77%) cases. Clavien-Dindo III-IV complications occurred in 4 (18%) cases. After a mean follow-up of 29 (IRQ 16-44) months, 6 patients (27%) developed distant metastases and 1 woman (5%) local relapse. A total of 3 patients (14%) died during the follow up period, all of bladder cancer. Sexual-sparing surgery was performed in 19 (86%) patients, in the others the anterior vaginal wall was resected, but neobladder was still performed. A total of 15 patients were included in the functional outcomes analysis. During daytime no patients reported total incontinence, and 73% reported total continence or only occasional leaks. Night-time continence outcomes showed total incontinence in 20% of patients, and 47% reported total continence or only occasional leaks. Of all patients, 13% needed self-catheterization for incomplete and 20% for complete urinary retention. Sexual results showed that 47% of women regained sexual activity after surgery, with a quality reported as “good” or “very good” in 40% of all 19 cases.

Conclusions: Robot assisted radical cystectomy in female with anterior vaginal wall preservation is feasible. The approach showed a good safety profile, with satisfying functional results. This sexual-sparing approach should be carried out after correct patient selection.

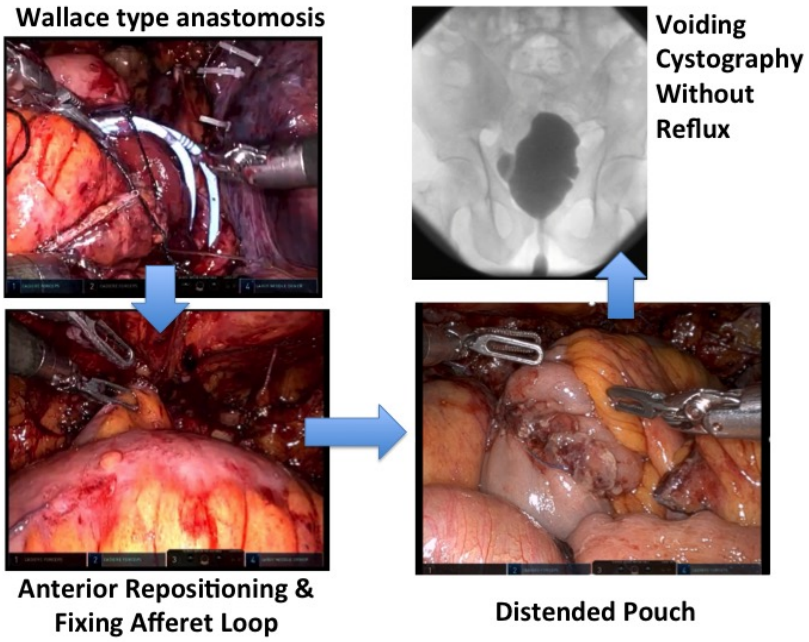
13 Intracorporeal ileal neobladder with enhanced antireflux mechanism achieved by anterior repositioning of the afferent loop during robotic radical cystectomy with endopelvic fascia sparing approach

Eur Urol Open Sci 2023;48(Suppl 1):S14

Balbay M.D.[1], Canda A.E.[1], Koseoglu E.[1], Ozkan A.[1], Kilic M.[2], Musaoglu A.[2], Aykanat I.C.[1]

[1]Koç University Hospital, Dept. of Urology, Istanbul, Turkey, [2]American Hospital, Dept. of Urology, Istanbul, Turkey

Introduction & Objectives: We developed and performed an intracorporeal ileal neobladder(INB) with enhanced antireflux mechanism(ARM) achieved by anterior repositioning of the afferent loop during endopelvic fascia sparing(EPFS) RARC.



Materials & Methods: We applied our technique on 2 men (64 and 57 years old) with bladder cancer(cT2N0M0). Cystectomy was done with Balbay's EPFS technique followed by construction of INB with enhanced ARM. Firstly, a 90° counter clockwise twisted ileal urethral anastomosis was performed at the 10th cm from the distal cut edge of the segregated ileal segment and urethral stump. Twisted urethral INB anastomosis was neutralized by turning the INB 90° counter clockwise and suture fixing its anterior wall to the pubic periosteum at this position. Probable increased tension due to stretch at the ureteral Wallace plate and ileal anastomosis as a result of INB rotation was reduced by using a longer(20 cm) afferent loop. At the conclusion of the construction, afferent loop is fixed to the INB and positioned between it posteriorly and abdominal wall anteriorly.

Results: Mean follow-up was 3.5 months. Final pathology was pT1aN0 in both patients with clear surgical margins. Mean LN yield was 34.5. Mean operative time, median estimated blood loss, median duration of hospital stay were 510 min, 625 ml, 11 days, respectively. Urethral catheter was removed at postoperative 4 weeks following cystography, confirming no leakage and no upper urinary tract reflux(UUTR). On uroflowmetry; mean Qmax, Qave, mean voided urine volume and post-voided residual urine volume were 15.5 ml/sec, 6.5 ml/sec, 180 ml and 0 ml, respectively. Both patients were fully continent during day-time (no pad) and had mild incontinence (1 pad) during night-time in one month of catheter withdrawal.

Voiding cystography at 3 months confirmed no UUTR. Both patients had erectile functional recovery with PDE5 inhibitor use, sufficient for penetration.

Conclusions: Utilizing this new technique, it is assumed that as the INB is filled with urine produced or intraabdominal pressure is increased while straining to void, afferent loop lumen would be compressed against its free wall and/or anterior abdominal wall both of which would prevent UUTR. Expected long term implications are prevention/reduction of hydronephrosis, pyelonephritis and renal functional loss.

14 Understanding prostate cancer biology and treatment: The value of combining big data with basic and translational science

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Clarke N.W.

The Christie Hospital, Dept. of Surgery, Manchester, United Kingdom

Introduction & Objectives: Understanding prostate cancer biology and optimising treatment is evolving but matching large-scale trials with publicly-collected, accessible datasets facilitates this evolution. Allied to translational science the power of this integrated analytical approach is strengthened and confidence in subsequent published evidence is stronger, enabling development of robust diagnostic and treatment guidelines based on level-1 evidence.

Materials & Methods: The hierarchy of medical evidence has its apotheosis in the randomised trial, strengthened further by Independent Patient Data(IPD) Meta-analysis. The exemplar is in hormone sensitive prostate cancer(HSPC), where large national/international trials have changed practice serially, particularly since 2015, with results demonstrating marked improvement in clinical outcome, consolidated by IPD Meta-analysis initiatives such as the UK MRC's StopCaP and the international IceCaP programmes. In the latter their 24,000 patient meta-analysis of M0CaP trials established metastatic progression free survival(MFS) as a new trial end-point, enabling foreshortening of ongoing trials, with earlier analysis of data, as in the recent Stampede Abiraterone M0 study. Linkage of treatment to real-world national/international datasets enables rational translation of trial data to populations "at scale", evaluating existing and novel approaches to diagnosis, treatment and prediction of outcome, unselected for fitness, demography and ethnicity. An example is the UK National Prostate Cancer Audit(www.npca.org.uk), established in England and Wales in 2013, collecting incident and treatment data annually on all prostate cancers presenting in those countries for 10 years (approximately 450,000 patients). Linking nationally recorded hospital episode statistics (HES) it is now possible tracking the effects of prostate cancer treatment over extended periods, establishing "real world" evidence of benefits and complications arising from common therapies, including long-term fracture and cardiac toxicities from systemic/local interventions for CaP.

Results: Linking large scale trial datasets to sophisticated basic and translational science is now possible, facilitating detailed analysis of fluids, tissue and imaging linked to diagnosis, staging and treatment. The Stratosphere and Biomedical Imaging Group(BIG) initiatives in Stampede exemplify this: tissue from high-risk CaP patients has been collected centrally and integrated with low-pass genome sequencing, revealing important differences in genomic profiles of HSPC factored for metastatic load/disease distribution and prediction of adverse outcome in high-risk M0 disease. Detailed image analysis by the Stampede BIG team has also defined disease burden and distribution in M1CaP and by centralising >24,000 stampede-related scans is matching trial and long-term HES data, identifying significant Musculo-skeletal effects arising years after initiation of common and widely used treatments.

Conclusions: Future national/international collaboration are both important and possible but it does require collaboration, resource and endeavour to bridge the academic/commercial divide and link basic science and public health initiatives/resource. This process of "triangulation" has now started: it has much further to go but the rewards for patients, if this is achieved, will be considerable.

15

Efficacy and safety of intralesional injection of Hyaluronic Acid for the treatment of chronic phase Peyronie's Disease (PD): Preliminary results from a pilot study

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Verze P.[1], Capece M.[2]

[1]University of Salerno, Dept. of Medicine, Surgery and Dentistry Scuola Medica Salernitana, Urology Unit, Baronissi, Italy, [2]University of Naples Federico II, Dept. of Neurosciences, Reproductive Medicine, Odontostomatology, Urology Unit, Naples, Italy

Introduction & Objectives: HA proved effective in interfering with scar formation and modeling. Intralesional injections of HA (IIHA) have been proposed in acute phase PD because able to improve pain, curvature and erectile function. Herein we report, for the first time ever, our findings in terms of safety and efficacy of IIHA in the treatment of chronic phase PD.

Materials & Methods: All consecutive chronic phase PD patients were proposed to be enrolled in this prospective, non-randomized and uncontrolled pilot study. At baseline, an objective assessment of penile curvature with intra-cavernous injection of alprostadil was performed. All patients completed the Peyronie's Disease Questionnaire (PDQ) and the International Index of Erectile Function (IIEF) questionnaires. Exclusion criteria were previous local treatment for PD and stabilization phase of the disease less than 12 months. Our treatment protocol included: a. IIHA (under penile block of 15 mL plain mepivacaine 1%) that were performed by the same operator (MC) every other week for a total of 3 injections in six weeks; b. penile modeling performed by the operator after each injection; c. daily use of the vacuum erection device (VED) combined with self modeling and stretching. At week 8 all patients were re-assessed for penile curvature, PDQ and IIEF tools and in addition they completed the Global Assessment of Peyronie's Disease (GAPD) tool.

Results: Overall, 23 patients were recruited in this pilot study. Two patients were excluded from this preliminary analysis because they did not correctly perform the home protocol indicated after the injections. The median penile curvature degree at baseline was 55° (IQR= 45 - 65), with a significant improvement at the follow-up visit after 8 weeks, when resulted 40° (IQR = 35 – 50) ($p<0.001$). Nineteen out of 21 patients (90%) showed a reduction in the degree of curvature by a mean of 11.9 ± 7.3 degrees. A statistically significant improvement in IIEF - Intercourse satisfaction domain (from baseline: 6.41 ± 3.8 to 8 week: 8.76 ± 2.8; $p<0.001$) and PDQ- Symptoms Bother domain (from baseline: 8.75 ± 4.1 to 8 week: 7.4 ± 3.3; $p<0.001$) was also detected. Regarding the GAPD questionnaire, 18/21 patients reported an improvement of their condition at the end of the protocol, 2 patients reported no changes and one patient claimed there was a worsening of the disease. In all cases IIHA were well tolerated and no complication was reported.

Conclusions: The findings of our pilot study show that IIHA combined with the use of VED, modeling and stretching can significantly reduce penile curvature in chronic phase PD patients. Our intent is to continue the study further to better understand the impact that IIHA therapy can have on the management of the stabilized PD in terms of patient satisfaction and reduction in the need for surgery.

16 Does the detection of human papillomavirus (HPV) DNA in penile carcinoma hold prognostic information regarding patient survival?

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Moen C.A.[1], Thorkelsen T.K.[1], Bostad L.[2], Rio O.E.[3], Honore A.[1], Chaudhry A.A.[1], Juliebø-Jones P.[1], Beisland C.[1]

[1]Haukeland University Hospital, Dept. of Urology, Bergen, Norway, [2]Haukeland University Hospital, Dept. of Pathology, Bergen, Norway, [3]Haukeland University Hospital, Section for Cancer Genomics, Dept. of Laboratory Medicine and Pathology, Bergen, Norway

Introduction & Objectives: Penile Cancer (PeCa) is a rare disease and approximately 60 new cases are reported annually to the Cancer Registry of Norway (population ≈ 5.5 M). Human papillomavirus (HPV) infection is a known risk factor for PeCa development. However, it remains inconclusive as to whether patients with HPV-related PeCa have a different prognosis than those without. The aim of this study was to investigate the prevalence of HPV positive penile squamous-cell carcinoma (SCC) in Western Norway as well as the relationship between HPV status and survival.

Materials & Methods: In this ethically approved study, analysis of hospital records between 1973-2020, identified 178 patients diagnosed with invasive CaPe and 42 with penile intra-epithelial neoplasia (PeIN). Of the 178 CaPe patients, 173 were treated surgically. Clinical variables, treatment and follow-up were recorded. The local diagnostic biobank was screened for stored tissue samples. All pathological tissue samples were then re-evaluated by a pathologist. Staging was performed in accordance with the 2016 UICC TNM-system and grading/subtype was performed in line with the WHO recommendations. Tissue blocks were available for 170 patients with invasive CaPe and these underwent testing for HPV-status by polymerase chain reaction (PCR) test.

Results: Common SCC, warty carcinoma and basaloid carcinoma were identified in 52%, 19% and 12% of the cohort, respectively. HPV DNA was detected in 45% (n=79) of the tumours, and the fraction of HPV positive tumours did not change significantly over the study period. HPV-16 was the most common subtype, occurring in 77% (n=61) of the HPV positive carcinomas. HPV-18 was second most common subtype, occurring in 7.9% (n=6) cases. Multiple HPV subtypes did not occur. Disease-specific 5-year survival in HPV-positive and HPV-negative patients was 70% vs. 83%, respectively (log-rank test p=0.09). In multivariable Cox regression with adjustment for age, grade, tumour stage and nodular stage, HPV status was not an independent predictor of survival (HR 1.23, 95% CI (0.62-2.45), p=0.6 for HPV positive vs. negative status).

Conclusions: The subtype distribution is in line with the literature. HPV DNA was found in approximately half of the investigated PeCa`s. HPV-16 was the most common subtype. There was no significant difference in disease-specific survival between patients with HPV positive and HPV negative tumours.

17 The effects of lifestyle modification on semen parameters and oxidative stress. A randomised, controlled interventional study

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Minhas S.[1], Papanikolaou N.[2], Abou Sherif S.[2], Dimakopoulou A.[2], Holterman O.[2], Brown A.[3], Sindi E.[2], Leeds A.[4], Frost G.[5], Dhillo W.J.[2], Jayasena C.N.[2]

[1]Imperial College London, Dept. of Urology and Section of Endocrinology and Investigative Medicine, London, United Kingdom, [2]Imperial College, Section of Endocrinology & Investigative Medicine, London, United Kingdom, [3]University College, Centre of Obesity Research, London, United Kingdom, [4]University of Copenhagen, Faculty of Life Sciences, Copenhagen, Denmark, [5]Imperial College London, Section for Nutrition Research, London, United Kingdom

Introduction & Objectives: Semen quality has been declining since the 1970s. Rising rates of obesity may be a causative factor to account for this decline. Although, poor semen quality is implicated in 50% of couples with infertility, there are no approved pharmacological therapies to optimise spermatogenesis. BMI is inversely correlated with poor sperm quality. Bariatric surgery has not been proven efficacious in improving semen parameters. Published uncontrolled studies have observed improvements in sperm concentration during dietary weight loss in men with obesity suggesting that lifestyle intervention is a potential, novel therapy for male infertility. However, the extent of dietary weight loss required to improve semen quality has not been investigated previously. We conducted two randomised, controlled interventional studies comparing the effects of low energy diet with basic healthy living advice in men with obesity and normal sperm count (Study A), and oligospermia (Study B).

Materials & Methods: Men aged 18-60 years with a BMI >30 kg/m^2 and normal sperm concentration (Study A) or oligospermia (Study B). Participants were randomised in a 1:1 ratio to either formula low energy diet (LED) providing 800 Kcal/day or NHS standard healthy living advice based on 'The Eatwell Guide' (NHS eat well) for 16 weeks. Thirty-six men completed study A and 43 men completed study B. We assessed anthropometrics and semen parameters including novel markers such as reactive oxygen species (ROS) using an established in-house chemiluminescence assay (performed in study A) and DNA fragmentation index (DFI) (performed in both studies) using TUNEL assay, at beginning (T0) and end of the protocol (T1).

Results: The men lost on average 17.6 Kg +/- 7.7 in study A and 14.4 Kg +/- 5.3 in study B in the LED group. Basic healthy living advice resulted in 6.3 Kg +/- 6.4 (study A) and 1.8 Kg +/- 4.2 (study B) weight loss. Total and progressive motility improved in both dietary interventions across both studies, although LED resulted in higher normalisation rate (TM NHS 36% vs LED 64%; PM NHS 30% vs LED 67%). Sperm concentration and volume did not change. DFI (T1) was significantly reduced in LED group compared to NHS (18.3% [14.3,21.05] NHS vs 4.1% [2.08,10.05] LED, p<0.001) in study A only, with a moderate inverse correlation (r= -0.56, p=0.005) between weight loss and DFI values at the end of the intervention. ROS (T1) had no statistically significant difference between the two interventions. Although in a subgroup of men with raised ROS at T0, 36% of men in the LED group normalised their ROS as compared to 10% in the NHS group.

Conclusions: Sperm motilities improve after lifestyle changes irrespective of the method of weight loss. However, LED resulted in a higher success rate of normalising the sperm motilities in men with asthenospermia. LED also decreased the DFI in men with obesity and normal semen parameters.

18 The role of the urologist in spinal cord injury: Lessons learned from the past

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Van Kerrebroeck Ph. E. V.

Life Expert Centre, Dept. of Urology, Antwerp, Belgium

Introduction & Objectives: Spinal injuries carried a fatal prognosis until the 20th century, mainly because of urological complications. Optimal management of the bladder is paramount for survival. How the urological approach evolved since WW II is of particular interest, and there are many lessons to be learned from the past.

Results: As a result of pioneering work started prior and during WW II, the situation of a patient with spinal cord injury has changed remarkably. In Europe, patients with an acute spinal injury are admitted to a specialised centre where all the facilities, including urological care, are available. Hence patients with spinal cord injury nowadays can expect a near normal life expectancy.
Prior to the first World War, traumatic spinal injuries were rare, but WW I was a conflict with many casualties with a spinal cord lesion. The majority of paraplegics died soon after injury, and those who survived long enough to reach a hospital, still had a 35% risk to die because of renal insufficiency following urinary tract infections. The method of managing the bladder was an indwelling catheter. Till 1944 the life expectancy for a patient with spinal cord injury remained low at only 3 months. This changed thanks to Ludwig Guttmann. Based on his clinical observations and his understanding of the autonomic reflexes upon bladder distension, he recognised the importance of bladder drainage and advocated no touch intermittent catheterisation (NTIC). Leading authorities at the time advocated rather the technique of cutaneous vesicostomy and dismissed NTIC as “certain to lead to disaster”. Guttmann presented the complications of cutaneous vesicostomy. He demonstrated that NTIC maintained the sterility of urine and reduced the complications of bladder calculi and fistulae. Guttmann's practice extended to the holistic care of his patients and recognised that sport and work could help with rehabilitation. He established the “Stoke Mandeville Games” which later became the Paralympics. In recent years, two other major steps influenced significantly the urological treatment of patients with spinal cord injury: the development of electrical bladder stimulation and the discovery of the beneficial effect of botulinum toxin on neurogenic bladder dysfunction.

Conclusions: The care for patients with spinal cord injury ameliorated significantly since WW II. The role of the urologist is paramount in terms of quality of life, but also guarantees life expectancy at the level of the population without spinal cord injury.

19 Phase I study of in-situ autologous vaccination for prostate cancer in a neo-adjuvant setting

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Tewari A.

Icahn School of Medicine at Mount Sinai, Dept. of Urology and Tisch Cancer Institute , New York, United States of America

Introduction & Objectives: Neoadjuvant therapies can potentially improve pathologic responses and oncological outcomes in prostate cancer patients. Immunotherapy is beneficial when administered in an early disease setting; however, the tumor microenvironment of PCa often impedes immune cell infiltration. Thus, there is an unmet need for neoadjuvant immunotherapy strategies to enhance immune cell infiltration favoring anti-cancer response. We used a novel “host targeted” in-situ “autovaccination” strategy using Poly-ICLC (Hiltonol®), Poly-ICLC was administered directly into the tumor.

Materials & Methods: This Phase I dose escalation study (NCT03262103) sought to determine a safe dose and schedule of intratumoral plus intramuscular Poly-ICLC before radical prostatectomy. Poly-ICLC was administered intratumorally (Artemis MRI-TRUS guided) and intramuscularly (e.g., deltoid muscle). Safety was measured by CTCAE. In addition, correlative studies were performed to characterize tissue and systemic biomarkers of response.

Results: 12 PCa (Gleason 7 – 10, cT2a – cT3b) patients were enrolled and treated. The median age and baseline PSA for the entire cohort were 62 (53-76) years and 7.81(4.62-22.9) ng/ml, respectively. Poly-ICLC was well tolerated (Safe) in all 12 patients, and the most frequent AE was grade 1, associated with soreness in the arm at injection site. Severe AE assessed as grade 3 was associated with grade 1 fever in one patient. This is a known risk-factor and did not occur more frequently than expected. Grade 4 related SAE observed in one patient in cohort 4, 48 days after the last administration of the investigational product (IP) was determined "unrelated to IP." 8 out of 12 patients (66.7 %) downgraded their biopsy Gleason scores and of the 6 with clinical staging of T3a or worse, 2 patients down staged to pT2 disease. In 11/12 patients who received all therapies the lymph nodes were negative. 2 out of 12 evaluable patients had biochemical recurrence after 2 years of prostatectomy. An increase in CD8+ T cells and activating immune checkpoints like PD1, TIGIT and TIMP3 on T-cell (CD4+, CD8+) and NK-cells were observed in RP specimens. Compared to baseline treatment resulted in significant upregulation of signatures associated with T-cell immune response, apoptosis and downregulation of signatures associated with DNA replication, cell division and metastasis. Additionally, we found that genes upregulated by treatment had better prognostic value. Early sequencing data revealed evidence of neoantigens. Post-vaccination immune infiltrates (CD4+/CD8+) were seen frequently in the tumor acini and in between the tumor cell (tumor acinitis).

Conclusions: Neoadjuvant Poly-ICLC is safe, and immunogenic, with promise for improving clinical outcomes. Larger Phase II studies will be required to evaluate the impact on long term clinical outcomes, and validation of response biomarkers.

20

Combination of the PARP inhibitor olaparib with the vascular disrupting agent NOV202 reduces tumor growth in BRCA1/2 mutated prostate cancer xenografts

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Bjartell A.S.[1], Sereti E.[2], Evans Axelsson S.[3]

[1]Skåne University Hospital, Dept. of Urology, Malmö, Sweden, [2]Lund University, Translational Medicine, Urological Cancers, Lund, Sweden, [3]Lund University, Dept. of Translational Medicine, Urological Cancers, Lund, Sweden

Introduction & Objectives: The therapeutic landscape of metastatic prostate cancer evolved rapidly with intenstified and combination treatments. However, metastatic castration-resistant prostate cancer (mCRPC) remains an incurable malignancy with poor clinical outcome and three is a need for new therapies. Approximately 20-25% of mCRPC patients harbor homologous recombination repair (HRR) defects, with BRCA1/2 and ATM mutations representing the most frequent events. Recent clinical trials have shown that mCRPC patients with HRR deficiencies responded well to poly (ADP-ribose) polymerase inhibitors (PARPi). Olaparib significantly improved overall survival in mCRPC patients with BRCA1/2 or ATM mutations (Hussein et al NEJM 2020). However, there is a clinical need for novel combinational therapeutic approaches to improve the efficacy of PARPi and overcome treatment resistance. NOV202 is a microtubule destabilizer and a vascular disrupting agent (VDA) with strong anti-proliferative effect in a large panel of cancer cells. The aim of this study is to evaluate if NOV202 could improve the in vivo efficacy of olaparib in prostate cancer xenografts with and without BRCA1/2 mutations.

Materials & Methods: Prostate cancer-based xenografts were developed from luciferase-transfected human PC3 (BRCA1/2 wildtype) and DU145 (BRCA1/2 mutated) cell lines. Cells were inoculated subcutaneously in male NMRI nude mice and animals were treated with olaparib (100 mg/kg), NOV202 (30 mg/kg) or their combination for 21 days, followed by either 1 or 2 weeks of no treatment. Tumor growth and response to therapy were monitored by non-invasive bioluminescence optical imaging (BLI) and tumor size was measured by caliper. During the experiment, a 25-parameter blood analysis, including hemoglobin concentration, red and white blood cells, and neutrophil granulocytes was performed weekly.

Results: Olaparib and NOV202, as single drug treatments, induced tumor growth inhibition in both cell lines tested. The combination of olaparib with NOV202 exerted significant synergistic effect in the BRCA1/2 mutated xenograft (DU145) in contrast to the BRCA1/2 wildtype xenograft (PC3), where no significant synergistic effect was observed. The combinational effect continued for a 2-week post-treatment period.

Conclusions: Single agent treatment with NOV202 and with olaparib reduced tumor growth in prostate cancer xenografts regardless of the BRCA1/2 mutation status. Interestingly, the anticancer efficacy of olaparib was significantly increased when combined with NOV202 only in the BRCA1/2 mutated xenografts, which represents an option to increase the efficacy of PARPi in patients with BRCA1/2 mutations. A clinical trial of this combination is planned.

21

Attitude towards active surveillance for low-risk prostate cancer among the Polish urologists: Early results from a nation-wide survey study

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Sosnowski R.[1], Kamecki H.[1], Dobruch J.[2], Drewa T.[3] , Section of Urologic Oncology of the Polish Urological Association

[1]Maria Sklodowska-Curie National Research Institute of Oncology, Dept. of Uro-oncology, Warsaw, Poland, [2]Center of Postgraduate Medical Education, Dept. of Urology, Warsaw, Poland, [3]Collegium Medicum of Nicolaus Copernicus University, Clinic of General and Oncologic Urology, Bydgoszcz, Poland

Introduction & Objectives: Active surveillance (AS), the preferred management option for low-risk prostate cancer (LRPC), has been increasingly adopted during the last two decades, as demonstrated by studies from several countries. No such data have ever been reported for Poland. Our objective was to perform a pioneer nation-wide survey study addressed to the Polish urologists, aiming to assess the role of AS for LRPC in their clinical practice, as well as to study for possible barriers that could hinder adoption of AS.

Materials & Methods: A 37-factor, anonymous, cross-sectional, self-reported, open, web-based survey study was disseminated among members of the Polish Urological Association. Regular, independent decision making in LRPC patients was one of the inclusion criteria. Data was collected in regard to demographics, treated patient population characteristics, treatment offered, clinical judgement schemes, as well as own and perceived patient attitude toward AS. The survey consisted of open, multiple choice, and 5-point Likert scale questions. The variables were then studied for interdependencies.

Results: A total of 64 urologists (52 certified, 12 in-training) completed the survey (margin of error: 12%). 73% declared to offer primarily AS to LRPC patients. Primarily offering AS was associated with a declaration of LRPC comprising for > 40% of all PC patients treated ($p = 0.04$) but not with other variables, including declared familiarity with AS-protocols. The most common reason for avoiding AS was patient reluctance (88%) and own fear of risk-underassessment (63%). Urologists who do not primarily offer AS for LRPC agreed that a patient reluctant to AS is afraid of disease progression (mean: 4.7, 95%-confidence interval: 3.8-5.0). They disagreed with being limited by organizational barriers (1.6, 1.0-2.8).

Conclusions: Our study suggests that rate of adoption of AS in Poland may follow the worldwide trends. Proper patient education aimed at lowering the level of fear of progression might be a strategy to further decrease the number of men with LRPC unnecessarily undergoing definite therapy.

22

Experience with radical perineal prostatectomy at a single institution in the era of robotic-assisted laparoscopic prostatectomy

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Winebaum J.G., Rac G., Zheng Y., Sweeney T., Tanneru K., Grubb R.L., Keane T.E.

Medical University of South Carolina, Dept. of Urology, Charleston, United States of America

Introduction & Objectives: Radical perineal prostatectomy (RPP) and robotic assisted laparoscopic prostatectomy (RALP) are minimally invasive surgical options for clinically localized prostate cancer. We sought to update our oncologic and functional outcomes in prostate cancer patients who underwent radical prostatectomy (RP) at a single institution with expertise in both RPP and RALP.

Materials & Methods: We retrospectively reviewed the records of 625 patients who underwent RP at our institution between 1/2009 – 10/2017. 235 patients underwent RPP and 390 underwent RALP. We have data on an additional 226 patients since our previous report. The rates of biochemical recurrence (BCR), rates of salvage treatment, progression to metastatic disease and overall survival were determined, and the data was stratified by pre-operative AUA Risk Strata. Additionally, we compared urinary functional outcomes including International Prostate Symptom Score (IPSS), quantitative pad use, continence rates defined as no-pad use on follow-up visit, and voiding dysfunction interventions at 3, 6, 9, 12, 24 months within a subset of patients. Chi-squared tests were used with p-value cutoff of < 0.05 used to determine significance.

Results: The mean age of all patients in the cohort was 61.2 years old. The BCR rate for patients that underwent RP via RPP was 36.2% (8/235) which is higher than those who underwent RP via RALP at 28.2% (110/390; $p = 0.03$). When the patients were stratified by AUA Risk, there was no difference in the rate of BCR for any of the subgroups. We did note slightly higher proportionate rates of high risk and unfavorable intermediate risk disease in the RPP group, however, this was not statistically significant. There was no significant difference in rate of progression to metastatic disease between RPP (3.4%) and RALP (1.5%; $p = 0.34$), or in overall survival with deaths in RPP (1.7%) and RALP (2.8%), $p=0.78$. 421 men of this cohort were evaluated for functional outcomes. At all post-operative time points, IPSS scores were lower for RPP than RALP. Continence rates were greater for RPP vs RALP at all time points except 60 months, with lower mean pad use for RPP vs RALP. There was no significant difference between RPP and RALP in medical or surgical interventions for voiding dysfunction including anticholinergic use (46.2% vs 46.2%), cystoscopy (15.1% vs 11.8%), sling (0.8% vs 3.5%), or artificial urinary sphincter (0.4% vs 1.5%).

Conclusions: We updated our previous comparison of oncologic and functional data between RPP and RALP patients. We found RPP patients had a higher rate of BCR, however, the rate of progression to metastatic disease was not different between the groups, so the clinical significance of this finding is unclear. Functionally, we demonstrated RPP patients had better continence at all time points than RALP patients.

23 Neuro-urology: What do urologists need to know and what not?

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Kessler T.M.

Balgrist University Hospital, University of Zürich, Dept. of Neuro-urology, Zürich, Switzerland

Introduction & Objectives: Neurogenic urinary tract, sexual and bowel dysfunction is highly prevalent and affects the lives of millions of people worldwide. It has a major impact on quality of life and, besides the debilitating manifestations for patients, it also imposes a substantial economic burden on every healthcare system. Nevertheless, Neuro-Urology lacks the prestige of cancer or heart disease and it is still a urological “stepchild” shadowed by onco-urology. In this lecture, I will provide an overview on this rapidly developing and exciting sub-speciality bridging the fields of both Neurology and Urology. The aims of the neuro-urological management include preservation of upper urinary tract function, enhancing of quality of life, control of urinary tract infection and maintenance of a low-pressure bladder that is both continent and capable of emptying completely. The cornerstone to achieve these goals is an appropriate neuro-urological work-up. Urodynamics are essential to identify risk factors jeopardizing the upper and lower urinary tract as well as to guarantee an optimal patient-tailored treatment including bladder emptying measures, antimuscarinics, beta-3 agonists, intradetrusor onabotulinumtoxinA injections, neuromodulation, and reconstructive surgery in refractory cases. With risk- and patient-oriented neuro-urological care an optimised quality of life and life expectancy can be achieved. What brings the future? Changing the current strategy of treating symptoms and pathological urodynamic findings to a concept of “prevention before treatment” might constitute a major breakthrough in Neuro-Urology with the potential to revolutionize the field.

Conclusions: There is no uniform management in Neuro-Urology and a rather individualized, patient-tailored approach aiming to achieve an optimal quality of life and to protect the upper and lower urinary tract is needed for this special patient population. Regarding the increasingly aging population and the high prevalence of neurological diseases, it is our responsibility to pave the way for further clinical and scientific developments. The urological “stepchild” is getting more and more popular - depending on the perspective all becomes Neuro-Urology…

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Conservative management of male LUTS in primary care: A cluster randomised trial TRIUMPH

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Drake M.[1], Worthington J.[2], Frost J.[2], Sanderson E.[2], Cotterill N.[2], Fader M.[3], Hashim H.[4], Macaulay M.[3], Rees J.[5], Robles L.[2], Taylor G.[2], Taylor J.[2], Ridd M.[2], Macneill S.[2], Noble S.[2], Lane A.[2]

[1]Imperial College, Surgery and Cancer, London, United Kingdom, [2]University of Bristol, Bristol Trials Centre, Bristol, United Kingdom, [3]University of Southampton, Dept. of Nursing, Southampton, United Kingdom, [4]Southmead Hospital, Dept. of Urology, Bristol, United Kingdom, [5]Tyntesfield Medical Practice, GP, Bristol, United Kingdom

Introduction & Objectives: Conservative therapies are first-line treatment of LUTS, yet there is a lack of evidence on effectiveness. An NHS Evidence Update indicated a role for self-management, on post-hoc analysis of a small single centre RCT. NICE Clinical Guideline 97 recommended that a multicentre RCT determine effectiveness in clinical practice. The TRIUMPH study (TReatIng Urinary symptoms in Men in Primary Healthcare using non-pharmacological and non-surgical interventions) was funded by the UK National Institute of Heath Research accordingly (HTA 16/90/03). Objective: To determine whether a standardised and manualised intervention for Lower Urinary Tract Symptoms (LUTS) delivered in primary care achieves superior symptomatic improvement versus usual care.

Materials & Methods: Design: 2-arm cluster randomised controlled trial. Setting: 30 NHS General Practice sites in England. Participants: 1,077 adult men (≥18) with bothersome LUTS. 524 men consented at sites randomised (1:1 ratio) to the intervention arm (n=17) and 553 at sites in the usual care arm (n=13) between June 2018 to August 2019. Intervention: The TRIUMPH standardised printed advice booklet for self-management of LUTS was developed for the trial with patient and expert input. General practice or research nurses/healthcare assistants directed participants to relevant sections of the booklet following urinary symptom assessment (manualised element) and made follow-up contacts over 12 weeks to assist adherence. Main outcome measures: Primary outcome of the validated patient-reported International Prostate Symptom Score (IPSS) 12 months post-participant consent; secondary outcomes of patient reported quality of life, urinary symptoms and LUTS perception, referrals to hospital and adverse events. The primary analysis included 915 participants (85%). Trial registration: ISRCTN registry – ISRCTN11669964

Results: There was a lower mean IPSS score at 12 months in the intervention arm (adjusted mean difference of -1.81 points, 95% Confidence Interval (CI) -2.66 to -0.95) indicating less severe urinary symptoms. LUTS-specific quality of life, incontinence and LUTS-perceptions also showed evidence of a positive difference between the arms favouring the intervention. The proportion of urology referrals and numbers of adverse events were comparable between groups.

Conclusions: This study developed an intervention which provides a practical resource to support symptom assessment and conservative treatment for LUTS in primary care. The TRIUMPH intervention showed a sustained benefit (one year) for men's LUTS and quality of life across a range of outcome measures in a UK primary care setting. A follow on impact study is introducing these materials into standard GP consultation systems to make them routinely available in all consultations.

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The IMPROVE Trial: Surgical technique remains the most important factor associated with recovery of urinary continence after radical prostatectomy

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Sanchez-Salas R.[1], Tourinho-Barbosa R.[2], Sivaraman A.[3], Pascuali C.[2], Candela L.[4], Cathala N.[3], Mombet A.[3], Marra G.[5], Rodriguez Sanchez L.[3], Chahrazad Bey Boumezrag C.H.[3], Macek P.[3], Lanz C.[3], Korkes F.[2], Cathelineau X.[3]

[1]McGill University, Dept. of Surgery, Division of Urology, Montreal, Canada, [2]Faculdade de Medicina do ABC (ABC Medical School), Dept. of Urology, São Paulo, Brazil, [3]Institut Mutualiste Montsouris and Université Paris Descartes, Dept. of Urology, Paris, France, [4]San Raffaelle Hospital, Dept. of Urology, Milano, Italy, [5]University of Turin and Città della Salute e della Scienza, Dept. of Urology, Torino, Italy

Introduction & Objectives: Post-radical prostatectomy (RP) urinary incontinence (UI) is not uncommon. Both pelvic floor muscle training (PFMT) and duloxetine have been shown to be effective in improving post-RP UI in mostly retrospective series. To assess the efficacy of PFMT and duloxetine in urinary continence recovery (UCR) after robot-assisted RP (RARP).

Materials & Methods: We conducted a prospective, randomized controlled trial (NCT02367404) involving patients who experienced UI after RARP. Patients were randomized into 1 of 4 arms: (1) PMFT-biofeedback (BFB) only, (2) duloxetine only, (3) combined PMFT-BFB and duloxetine, and (4) control group. The PMFT program consisted of pelvic muscle contraction exercises conducted with electromyographic feedback weekly, for 3 months. Patients in duloxetine arms were instructed to take oral duloxetine at bedtime for 3 months. The primary end point was prevalence of continence at 6 months, defined as using no pad or only a security pad. Urinary symptoms and quality of life (QoL) were assessed by using a visual analog scale, the International Prostate Symptom Score questionnaire, and the King's Health Questionnaire.

Results: A total of 240 patients (60 in each arm) were included in the trial between 2015 and 2018. Overall, 89% of patients completed 1 year of follow-up. From the patients allocated to receive treatment, 89% (107 of 120) had completed the duloxetine treatment and 98% (117 of 120) attended the PMFT sessions. In the control group 96% of patients had achieved continence at 6 months, compared with 90% (P = .3) in the PMFT-BFB arm, 73% (P = .008) in the duloxetine arm, and 69% (P = .003) in the combined treatment arm. After accounting for other variables, complete preservation of neurovascular bundles (OR 2.95; P = .048) was the only perioperative intervention found to improve UCR. At 6 months, QoL was classified as uncomfortable or worse in 17% of patients in the control group, compared with 44% (p=0.01), 45% (p=0.008), and 34% (p=0.07) in the PMFT-BFB, duloxetine, and combined treatment arms, respectively.

Conclusions: PMFT-BFB and duloxetine do not improve UCR after RP, and may instead have a negative impact on QOL, thus they should not be routinely recommended. Early UCR after RARP is critically related to surgical aspects with emphasis on appropriate neurovascular bundle preservation .

26 Patient-specific 3D printed/virtual models from automated segmentation using MONAI labels

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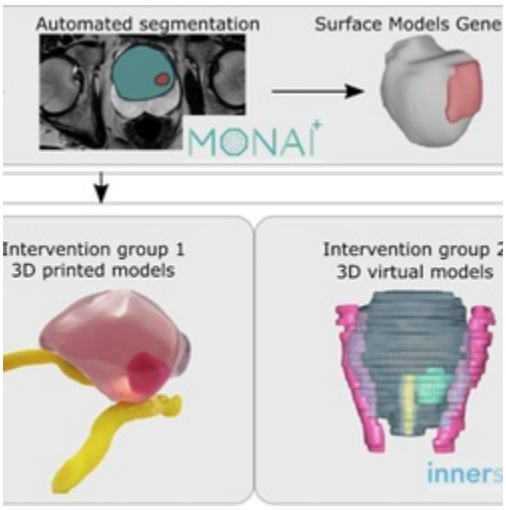
Antonelli M.[1], Diaz-Pinto A.[2], Mehta P.[1], Cardoso J.[1], Ourselin S.[1], Granados A.[1], Dasgupta P.[3]

[1]King's College London, Dept. of Surgical and Interventional Engineering, London, United Kingdom, [2]NVIDIA, Santa Clara, United States of America, [3]King's College London, King's Health Partners, Dept. of Surgery, London, United Kingdom

Introduction & Objectives: Recent evidence from an IDEAL Stage 2a study showed that the use of 3D printed or virtual models of the prostate during robotic assisted radical prostatectomy (RARP) can decrease positive margins rates (PSM) from 35% to 11%. In this process, manual segmentation of the prostate, significant cancers and neighbouring structures on mp-MRI is required. This is time-consuming and requires substantial radiological expertise. The aim of this study was to use artificial intelligence (AI) to perform this autonomously.

Materials & Methods: Using anonymised mp-MRI prostates, we describe substantial progress towards the automated segmentation of the prostate gland and cancer lesions using deep learning. We use MONAI a recent open source framework for deep learning in medical imaging, for the automated segmentation of prostate gland and cancer lesions. Specifically, we designed Auto-Prostate, a deep learning-powered framework for automatic MRI-based prostate segmentation and clinically significant lesion detection, and an extension of MONAI Labels called Click-Edit to allow for manual correction of errors in Auto-Prostate using active learning. These 3D printed models are compared to virtual 3D models of the prostate and surrounding structures derived from Innersight, a spin-out platform from our group.

Results: The accuracy of MONAI Labels is >90% with an error rate <1mm.



Conclusions: We have trained a deep learning model to automatically generate 3D models of the prostate, reducing radiological time and variability. An IDEAL Stage 2b study in RARP on 150 patients comparing standard of care, MONAI and Innersight has commenced.