

Urology Research Review™

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Issue 61 - 2023

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Abbreviations used in this issue:

AUC = area under the receiver operating characteristic curve;
CI = confidence interval; **ICSI** = intracytoplasmic sperm injection;
ISUP = International Society of Urological Pathology;
IVF = *in vitro* fertilisation; **MRI** = magnetic resonance imaging;
mTESE = microdissection testicular sperm extraction; **OR** = odds ratio;
PDE5 = phosphodiesterase-5; **PLND** = pelvic lymph node dissection;
PSA = prostate-specific antigen;
VI-RADS = Vesical Imaging-Reporting and Data System.

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Welcome to Issue 61 of Urology Research Review.

In a retrospective study from China we discover that a radiomics model is useful in the diagnosis of muscle invasion of bladder cancer. Following on, virtual and in-person training using a three-step simulation training platform for neonatal circumcision shows potential as a useful resource. Other topics covered in this issue include safety outcomes for the Infla10® inflatable penile prosthesis, validation of the Pelvic Pain Map, disparities and trends in US genitourinary cancer incidence and mortality, ureteral injuries from ureteral access sheath insertion, a safety valve for prevention of catheter balloon inflation injury, and vaginoscopy with laser treatment of upper vaginal mesh exposure.

We hope you find our selection of articles for this review interesting and welcome your feedback.

Kind Regards,

Professor Eric Chung

eric.chung@researchreview.com.au

Integrating radiomics with the vesical imaging-reporting and data system to predict muscle invasion of bladder cancer

Authors: Wang W et al.

Summary: This retrospective study used data from 192 patients (training set n = 85; validation set n = 36; testing set n = 70) to assess predictive models for determining muscle invasion of bladder cancer based on integration of radiomics (high-b-value diffusion weighted images MRI) and VI-RADS. The radiomics model had AUC values of 0.801 in the training set, 0.867 in the validation set, and 0.806 in the testing set. VI-RADS scores of two independent radiologists had AUC values of 0.831/0.781, 0.909/0.815, and 0.871/0.776 in the training, validation, and testing sets. The integrated clinical-radiomics model had AUC values of 0.889/0.854, 0.961/0.919, and 0.881/0.844 in the training, validation, and testing sets. Performance of the clinical-radiomics model was better than the VI-RADS score for an inexperienced radiologist ($p < 0.05$).

Comment: Radiomics, by its inherent ability to integrate critical data signatures from large image bases pertinent to a pathology, may bridge the gap of missing parameters that preclude radiologists from being unable to provide a diagnosis conclusively. In this unique study, the radiomics model showed the clinical-radiomics model for readers one/two revealed AUC values of 0.889/0.854, 0.961/0.919, and 0.881/0.844 in the training, validation, and testing sets, respectively and the performance of the clinical-radiomics model was improved compared to the VI-RADS score for inexperienced reader two. While radiomics appears to be better than conventional radiological investigative modality, it has yet to gain widespread use given construction of a radiomic model is not simple and may not be easily reproducible. Nonetheless, radiomics can be combined new imaging biomarkers and machine-learning algorithms to transform clinical evaluation. Future studies should be made to break down the limitations caused by technology deficiencies, and inherent problems during the process of radiomics analysis, as well as the quality of present studies.

Reference: *Urol Oncol.* 2023;41(6):294.e1-294.e8

[Abstract](#)

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Circumcision learning experience using simulation: A pilot learning platform for safe neonatal circumcision training offered either virtually or in person

Authors: Dos Santos J et al.

Summary: The CIRCumcision Learning Experience Using Simulation (CIRCLES) study assessed the use of virtual and in-person training using a three-step simulation training platform for neonatal circumcision. The simulation training platform improved knowledge, skills, and confidence in neonatal circumcision in both virtual and in-person learners.

Comment: The Plastibell, Gomco, and Mogen devices are commonly used for neonatal male circumcision. Nonetheless, several controversies and ethical issues continue to exist regarding neonatal circumcision outside of religious contexts or indications for high-risk neonates. Simulation has emerged as an effective solution to increasing modern constraints in surgical training and may remove the (at times steep) learning curve out of the operating theatre and facilitate training in a safe and pressure-free environment whilst focusing on patient safety. In this interesting CIRCLES study, it is reported that simulation training platforms can be associated with significant improvement in learners' knowledge, skills, and confidence. The cost of simulation is not insignificant, especially up-front, and requires ongoing financial commitment in funding, human resources, and service logistics. With the ever-growing range of simulators and more innovative technological advancements, simulation training may offer a "simpler", cheaper, and safer training model for repetitive learning, especially in the current medicolegal climate where patient safety and best clinical care are paramount.

Reference: *Front Urol.* 2023;3:1199194

[Abstract](#)

Initial safety outcomes for the Rigicon Infla10® inflatable penile prosthesis

Authors: Wilson SK et al.

Summary: This retrospective review (2019-21) of patient information forms submitted to the manufacturer, assessed the early outcomes from an inflatable penile prosthesis, the Rigicon Infla10® in 319 patients (mean age 58.5 years). Over a mean follow-up of 21.2 months, 4.4% of devices required removal or revision and complications included mechanical failure (2.5%) and component migration (0.7%). There were no infections observed. Revision for inadequate straightening of Peyronie's disease was required in one (0.4%) patient and three (0.9%) patients requested removal because of dissatisfaction. Overall, 21 months after implantation, 95.6% of devices were free from explant or revision. Rates of cumulative survival were 95.6% at 12 months, 94.7% at 24 months, and 93.7% at 36 months, based on Kaplan-Meier analysis.

Comment: It was in 1973 when Dr Scott published his landmark paper on modern inflatable penile prosthesis implants. Over the past 50 years, there have been significant advances made in device technology and innovative surgical techniques. To date, Boston Scientific AMS 700™ and the Coloplast Titan® series have worldwide commercial monopoly. This new Rigicon Infla10® study showed the device to be mechanically durable with the rates of cumulative survival of the device at 12, 24, and 36 months of 95.6%, 94.7%, and 93.7%, while reported complications were rare (0% infection rate, 2.5% mechanical failure and 0.7% component migration). The addition of the Rigicon Infla10® device invariably brings excitement and "stiff" competition. In turn, hopefully, it will stimulate further research and development to advance the penile prosthetics world.

Reference: *BJU Int.* 2023;131(6):729-733

[Abstract](#)

Validation of the 'Pelvic Pain Map': A new self-assessment tool for chronic pelvic pain localisation

Authors: Aibel K & Moldwin R

Summary: This study assessed the validity of the Pelvic Pain Map, single, front-facing images of the male and female pelvis incorporating abdominal and perineal views, generated by 12 chronic pelvic pain experts, and assessed using a retrospective cohort of patients with chronic pelvic pain syndrome who completed the maps. Test-retest reliability for individual map zones was moderate to excellent (Cohen's kappa 0.28-0.64) and for total map zones was excellent (intraclass correlation coefficient 0.90). Individual map zones convergent validity with location from the Genitourinary Pain Index (GPI) was strong (phi coefficients 0.26-0.79) and for total map zones was moderate ($r = 0.56$). Total map zones discriminant validity, using separate but related constructs from the GPI and Pain Catastrophising Scale (PCS-6) was weakly positive ($r 0.27-0.32$).

Comment: Body maps can be helpful adjuncts to verbal descriptions of pain and may serve a role in phenotyping what is known to be a heterogeneous patient population. Pelvic body mapping demonstrated that different forms of chronic pelvic pain syndrome displayed different distributions of pain, but mapping was not predictive of any diagnostic group. This Pelvic Pain Map combined input from 12 chronic pelvic pain experts and patient feedback to assess face validity. Test-retest for individual map zones demonstrated moderate to excellent reliability (Cohen's kappa coefficients ranging from 0.28 to 0.64) and for total map zones demonstrated high reliability (intraclass correlation coefficient = 0.90 with Spearman's correlation coefficient = 0.56). While the pelvic body map is useful in identifying precise locations of pain and may help uncover regions of pain that cannot be easily communicated, outcomes from the Multidisciplinary Approach to the Study of Chronic Pelvic Pain Research Network showed that urologic chronic pelvic pain syndrome pain and urinary symptoms often co-vary, and that symptom flares are common and can differ considerably in intensity, duration, and influence on quality of life. Hence, more objective phenotypic abnormalities and distinct biological characteristics identification are needed to answer this difficult diagnostics and management dilemma.

Reference: *BJU Int.* 2023;131(6):763-769

[Abstract](#)

Disparities and trends in genitourinary cancer incidence and mortality in the USA

Authors: Schafer EJ et al.

Summary: This retrospective study (1990-2020) used data from the US Surveillance, Epidemiology and End Results (SEER) database to determine disparities and trends in incidence and mortality of major genitourinary cancers (bladder, kidney, prostate, testis). Bladder and kidney cancers incidence and mortality rates were two- to four-fold higher for men than for women. Among non-Hispanic Whites, the highest incidence rates for bladder cancer occurred in the Northeast and for kidney cancer occurred in Appalachia. The highest prostate cancer death rates occurred in the West. Incidence rates for kidney, testicular and advanced-stage prostate cancers increased in almost all racial/ethnic populations and for bladder cancer increased in the American Indian and native Alaskan populations. Death rates in the Hispanic population increased for testicular cancer, while prostate cancer rates in White and Asian American/Pacific Islander men stabilised after a decline since the early 1990s.

Comment: Kidney, bladder, and prostate cancers are the most common genitourinary cancers and previous epidemiological studies have reported considerable heterogeneity in the temporal trend of disease burden across geographic locations and socio-demographic index levels. Along with the aging population and socioeconomic changes, the incidence and mortality of genitourinary cancers have changed significantly in recent decades. Based on the incidence data from several cancer databases, the incidence and death rates for bladder and kidney cancers continued to be two- to four-fold higher for men than for women, while prostate cancer incidence and mortality rates continued to be highest for Black men. Interestingly, incidence rates increased for kidney and testicular cancer and advanced-stage prostate cancer in all groups and for bladder cancer increased in American Indians/Alaska Native populations. There are many reasons to explain the estimated differences in risk factors such as cigarette smoking, diet, medical co-morbidities, and access to the healthcare system. The findings of increasing incidence or death rates and persistent racial and ethnic disparities in genitourinary cancers will have significant implications for healthcare services, especially among at-risk populations. Further research is needed to elucidate the reasons for these patterns to better plan appropriate interventions, mitigate the sociodemographic disparities and promote better healthcare system access.

Reference: *Eur Urol.* 2023;84(1):117-126

[Abstract](#)

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Abbreviations: ADT: androgen deprivation therapy; HR: hazard ratio; mHSPC: metastatic hormone-sensitive prostate cancer; OS: overall survival; PBS: Pharmaceutical Benefits Scheme. References: 1. PBS Schedule of Pharmaceutical Benefits. 2023. Available at: <https://www.pbs.gov.au/pbs/home> 2. Chi K *et al. J Clin Oncol* 2021;39:2294–2303. Further information is available on request from Janssen-Cilag Pty Ltd, ABN 47 000 129 975, 1-5 Khartoum Road, Macquarie Park NSW 2113. Ph: 1800 226 334. ERLYAND® is a registered trademark of Janssen-Cilag Pty Ltd CP-387406 EMVERL0239 Date of preparation: May 2023.

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Evaluation of ureteral injuries caused by ureteral access sheath insertion during ureteroscopic lithotripsy

Authors: Taguchi M et al.

Summary: This Japanese study assessed ureteral injuries caused by 13-Fr ureteral access sheath (UAS) insertion during ureteroscopic lithotripsy in 109 patients and sought to identify factors predictive of ureteral injury. Overall, 21 UAS-related injuries were identified, including 11 grade 2 cases and 10 grade 3 cases. The ureteral injury occurred in the proximal ureter in 20 cases and the middle ureter in one case. Multivariate analysis identified predictive factors for ureteral injury including male sex (OR 5.19; 95% CI 1.11-24.3; $p = 0.037$) and smaller stone diameter (OR 0.83; 95% CI 0.71-0.97; $p = 0.02$). There were no cases of postoperative ureteral stricture.

Comment: Controversy continues to exist on whether to use or not to routinely use UAS during retrograde intrarenal surgery. The UAS allows multiple passes of uretero-pyeloscopy to reduce operative times, improve visualisation and maintain a safe intrarenal pressure. This study from Japan analysed 109 patients who underwent the insertion of a 13-Fr UAS and there were 21 cases of UAS-related ureteral injury. Multiple logistic regression analysis showed that male sex and smaller stone diameter were significant predictive factors for ureteral injury. Interestingly, postoperative ureteral stricture did not occur in any cases. It is postulated that UAS use is associated with higher complication rates through direct ureter/renal pelvis injury or the theoretical risk of inducing ureteral ischemia. Furthermore, the severity of the ureteral injury was not related to ureteral stricture progression in the setting of pre-stenting patients. Animal models have shown that despite the presence of inflammation during the early postoperative period, there was no observed chronic histological effect, and this may explain the absence of postoperative ureteral stricture in this study.

Reference: *Int J Urol.* 2023;30(6):554-558

[Abstract](#)

Unilateral pelvic lymph node dissection in prostate cancer patients diagnosed in the era of magnetic resonance imaging-targeted biopsy: A study that challenges the dogma

Authors: Martini A et al.

Summary: The multicentre analysis assessed the feasibility of unilateral extended pelvic lymph node dissection (PLND) in the era of modern prostate cancer MRI imaging and targeted biopsies in 2253 men with cN0 disease. Lymph node invasion occurred in 302 (13%) patients and 83 (4%) patients had lymph node invasion in the contralateral side to the dominant prostatic lobe. Using a model that included PSA, maximum index lesion diameter, seminal vesicle invasion on MRI, ISUP grade on the nondominant side, and percentage of positive cores on the nondominant side, the AUC was 84% after internal validation. Using contralateral lymph node invasion cut-off of 1%, 27% of contralateral PLNDs could be omitted with 1.2% of lymph node invasion missed.

Comment: PLND is the most reliable procedure for lymph node staging. However, the therapeutic benefit remains unproven, although most radical surgery of prostate cancer is often accompanied by PLND despite the lack of clear consensus regarding the optimal anatomical extent of PLND. In this study of 2253 patients, lymph node invasion was documented in 13% of patients with 4% of patients having lymph node invasion contralateral to the dominant prostatic lobe. Based on the PLND modelling with a cut-off of contralateral lymph node invasion of 1%, 27% of contralateral PLNDs would be omitted with only one lymph node invasion missed. In recent years, improved imaging technology, and a greater understanding of the biology of prostate cancer have led to many urologists advocating for a limited anatomical template for PLND in a select group of patients at risk of unfavourable pathology, given the higher risk of complications reported in extended PLND. Radiomics and genomics represent two of the most promising fields of cancer research and will improve the risk stratification and hopefully solve the conundrum on PLND.

Reference: *J Urol.* 2023;210(1):117-127

[Abstract](#)

Platelet-rich plasma for the treatment of erectile dysfunction: A prospective, randomized, double-blind, placebo-controlled clinical trial

Authors: Masterson TA et al.

Summary: This prospective, randomised, double-blind, placebo-controlled clinical trial examined the use of two injections of platelet-rich plasma (PRP) in 61 men with mild-to-moderate erectile dysfunction (ED). After 1 month there was no difference between PRP recipients and placebo recipients in the primary endpoint minimum clinically important difference (58.3% vs 53.6%). Mean International Index of Erectile Function-Erectile Function domain (secondary endpoint) changed from 17.4 (95% CI 15.8-19.0) to 21 (17.9-24.0) in PRP recipients versus 18.6 (95% CI 17.3-19.8) to 21.6 (95% CI 19.1-24.1) in placebo recipients with no difference between groups. There were no major adverse events.

Comment: Contemporary non-surgical ED therapies include oral PDE5 inhibitors, intra-cavernosal injection, or vacuum erection devices. However, these treatments offer only temporary symptomatic relief, do not influence disease progression and patients require lifelong treatment. PRP is an exciting biotechnology, and it is postulated that PRP injections may modify key pathophysiologic mechanisms leading to ED through anti-inflammatory, reparative, neuroprotective, and neurotrophic effects. In this prospective, double-blind, randomised, placebo-controlled clinical trial between 28 patients receiving PRP and 33 patients on placebo, there was no difference between groups in the percentage of men meeting minimum clinically important difference at 1 month and in the mean change in International Index of Erectile Function-Erectile Function domain. While there were no major adverse events and only one minor adverse event in each group, no changes in penile Doppler parameters from baseline to 6 months were observed. There are significant barriers in the actual translation from the positive animal models to human clinical trials. Furthermore, the current medical hype of this regenerative technology promised to this vulnerable demographic really needs proper clinical governance in addition to more robust clinical studies to identify the optimal dose and duration of PRP treatment, the ideal patient population, and whether other adjunctive measures can improve clinical outcomes.

Reference: *J Urol.* 2023;210(1):154-161

[Abstract](#)

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A prospective multi-institutional study using a novel safety valve for the prevention of catheter balloon inflation injury of the urethra

Authors: O'Connor EM et al.

Summary: This European, multinational, prospective, study examined a transurethral catheterisation safety valve for the prevention of urethral catheter balloon injury during 994 urethral catheterisations. Over 12 months, 22 (2.2%) episodes of safety valve venting occurred, with no urethral injuries. In an embedded 3-month study, 18 catheter balloon injuries (5.5/1,000 catheterisations) were recorded in catheterisations not using the safety valve.

Comment: Iatrogenic urethral catheter injuries (IUCIs) can occur by several mechanisms such as inadvertent inflation of the retention balloon in the urethra, creation of a false passage, and removal of the catheter with the balloon still inflated, causing significant pain, infection, haemorrhage, urinary retention, and complex stricture disease. In this prospective, multi-institutional study using a safety valve during urinary catheterisation that allows fluid in the catheter system to vent through a pressure relief valve if attempted intraurethral inflation of the catheter's anchoring balloon occurs, it was found that 22 episodes of safety valve venting were recorded but no urethral injuries occurred in these patients during the overall 12-month device study phase. In the embedded 3-month study, 18 catheter balloon injuries were recorded in association with catheterisations performed without the safety valve. Previous attempts at minimising the risk of IUCI have included training and educational workshops for providers with varying levels of success. While proper instruction on catheter insertion is critical, it does not eliminate the risk of IUCI, and it can be quite difficult to ensure competency. While the result of this study appears promising, it does not resolve the inherent risk of current catheter designs against human errors. Further testing is needed to compare the safety and efficacy of this device to the current indwelling and standard catheter practice.

Reference: *J Urol.* 2023;210(1):179-185

[Abstract](#)

Vaginotomy with laser treatment of symptomatic upper vaginal mesh exposure after prior mesh sacrocolpopexy

Authors: Chen JY & Zimmern PE

Summary: This retrospective study (2013-22) examined vaginotomy with Holmium:YAG and Thulium laser treatment of upper vaginal mesh exposure after mesh sacrocolpopexy in five patients (six surgeries). The symptomatic mesh was exposed at the vaginal apex, which was tented up and difficult to access through traditional transvaginal mesh excision. Vaginal mesh treatment with laser resulted in no further vaginal mesh exposure on follow-up exam or vaginotomy; one patient had a small recurrence at 4 months, underwent a second procedure and had negative findings at 7.9 months post-operative vaginotomy.

Comment: Numerous studies have found at least some degree of symptomatic improvement regardless of the amount of pelvic mesh removed. In this retrospective 10-year chart review of patients who underwent laser treatment of upper vaginal mesh exposure during vaginotomy at a single institution, five patients underwent vaginal mesh treatment with laser with no further vaginal mesh exposure on follow-up exam or vaginotomy, and one patient was found to have a small recurrence at 4 months and underwent a second treatment. For isolated mesh erosion, local measures such as laser mesh can be utilised with good success rate. Failures of local excision are counselled regarding the option of proceeding to complete removal of the remaining mesh versus continued attempts at local excision and the inherent risks of both approaches. An attempt for complete mesh excision is recommended for patients with diffuse vaginal pain, large mesh exposure, and extrusion of mesh into adjacent viscera. In patients who require complete mesh removal, it is important to counsel patients regarding possible complications of removal and the increased risk of recurrent stress urinary incontinence and pelvic organ prolapse postoperatively.

Reference: *Urology* 2023;176:69-73

[Abstract](#)

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Discordant bilateral testicular pathology does not affect sperm retrieval rate in bilateral microdissection testicular sperm extraction (mTESE)

Authors: Bole R et al.

Summary: This single-institutional retrospective review assessed the incidence of discordant testicular pathology and sperm retrieval rate in 114 non-obstructive azoospermia men undergoing bilateral microdissection testicular sperm extraction (mTESE; n = 132). Pathology specimens were available for 112 cases, among whom the success rate was 41.9%. Among 206 pathological reports, 52.4% were Sertoli cell only, 4.9% had Leydig cell hyperplasia, 8.7% had fibrosis, 16.5% maturation arrest, and 17.5% hypo-spermatogenesis; 12% of testicles had >1 pathology. Synchronous bilateral testicular pathology occurred in 66 men, of whom 11 (16.6%) had at least partially discordant pathology on initial review, and focused re-review by a genitourinary pathologist identified discordant pathology in seven (10.6%) cases, with a sperm retrieval rate of 57%.

Comment: The treatment of men with non-obstructive azoospermia has improved greatly over the past two decades in part due to the discovery of IVF/ICSI, but also due to improvements in surgical sperm retrieval methods, namely the development of mTESE. This procedure has revolutionised the field by allowing for the identification of favourable seminiferous tubules while simultaneously limiting the amount of testicular tissue removed. In this retrospective single-institutional review of all patients undergoing mTESE, 85% of cases had pathology specimens available, and within this specific cohort the success rate was 41.9% and 12% of testes had more than one pathologic diagnosis while 66 men had synchronous bilateral testicular pathology, of whom 16.6% had at least partially discordant pathology on initial review. Histopathology is one of the strongest predictors of sperm retrieval as it provides a direct snapshot of the testicular architecture. However, the performance of a testicular biopsy solely for diagnostic purposes is not routinely recommended because of its invasiveness. In addition, a diagnostic biopsy samples only a small section of the testicular tissue, so its predictive value is limited. Currently, sperm retrieval procedure remains highly dependent on surgeon experience, preoperative patient optimisation, and teamwork with laboratory personnel. Moving forward, new technologies for assisted reproduction, including microfluidics, cell sorting, or other micro-identification techniques could permit the identification of rare sperm and possibly the selection of optimal sperm from a limited pool to improve the likelihood of pregnancy success and live birth rate. Advanced imaging techniques to identify sites of sperm production preoperatively and better genetic screening could greatly enhance the application of surgical sperm retrieval.

Reference: *Urology* 2023;176:82-86

[Abstract](#)



Urology Research Review™

Independent commentary by Professor Eric Chung

Professor Eric Chung is a consultant urological surgeon at the Andro Urology Centre for Sexual, Urinary and Reproductive Excellence and holds academic appointments at the University of Queensland (Brisbane) and Macquarie University Hospital (Sydney). He is the Leader of male LUTS and Past Chair of Andrology section in the Urological Society of Australia and New Zealand (USANZ), the Secretary-General for the Asia Pacific Society of Sexual Medicine (APSSM) and Chairperson for the Prostate Cancer Survivorship committee at the International Consultation on Sexual Medicine (ICSM). He has been invited to speak and operate at many international meetings and has authored more than 100 peer-reviewed papers and book chapters.

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