USANZ 2024 Conference Review™

Making Education Easy

24-27 February, 2024

In this review:

Abbreviations used in this review:

AE = adverse effect; **BoNT/A** = onabotulinumtoxinA; **CQI** = clinical quality indicator; **CSS** = cancer-specific survival; **ED** = erectile dysfunction; **HR** = hazard ratio; **mCRPC** = metastatic castration-resistant prostate cancer; **MIST** = minimally invasive surgical therapy; **OS** = overall survival; **PC** = prostate cancer; **PFP** = pelvic floor procedure; **PROM** = patient-reported outcome measure; **PSA** = prostate-specific antigen; **PSMA** = prostate-specific membrane antigen; **VOC** = volatile organic compound; **%fPSA** = percentage of free PSA.

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Welcome to our review of the 2024 Urological Society of Australia and NZ (USANZ) Annual Scientific Meeting held in Adelaide, Australia.

This year USANZ hosted a rich programme dedicated to enhancing all aspects of urology care. In this review, I begin by discussing six noteworthy abstracts which were granted awards, many of which explored the use of innovative technologies. The Villis Marshall Prize was given to a study which found that ChatGPT achieved numerically, though not significantly poorer pass rates and scores than human trainees when writing answers for the FRACS Urology exam, and the BAUS Trophy Award went to a trial of the Prostafix Water Electrolysis System - a promising, minimally invasive day treatment for lower urinary tract symptoms secondary to benign prostatic hyperplasia. A fascinating study on a novel, male contraceptive coined ADAM™ showed encouraging safety outcomes and received the AZ Platinum Trophy Award; as a non-hormonal, reversible male contraception, this technology has great potential, and we eagerly await the long-term safety and efficacy data.

Detailed abstracts for the presentations can be located here.

I trust that you will find these and the other abstracts in this review interesting and informative, and I look forward to reading your comments.

Kind Regards,

Professor Eric Chung
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Keith Kirkland's Prize: Percentage of free PSA as a predictive biomarker for men with metastatic castration-resistant prostate cancer

Speaker: Dr Andrew Silagy (Austin Health, Heidelberg, Australia)

Summary: These investigators analysed prospective data to determine whether the percentage of free PSA (%fPSA), a cost-effective and accessible metric, is a predictor of outcomes in metastatic castration-resistant prostate cancer (mCRPC) when measured at the time of diagnosis. Over a follow-up of 25.6 months, 254 patients were evaluated, 63% of whom had %fPSA >15, 48% were treated with docetaxel and 43% with abiraterone acetate/enzalutamide in the first-line setting. The median OS was 44.5 months and median CSS 46.0 months. Multivariable analysis revealed that patients with poorer OS included those with %fPSA >15 (HR 1.55; 95% CI 1.02—2.36; p=0.042) and those who received docetaxel (HR 1.75; 95% CI 1.14—2.68; p=0.01). Subgroup analysis found that %fPSA >15 was associated with shorter OS in patients who received docetaxel, yet there was no association with abiraterone acetate/enzalutamide. Investigators noted that %fPSA may be an effective biomarker to inform physicians' selection of appropriate doublet therapy.

Comment: The treatment landscape of advanced prostate cancer has completely changed during the last few decades, with the old backbone of androgen-deprivation monotherapy being disrupted in the hormone-sensitive setting, and new drugs such as chemotherapy, androgen-receptor signalling inhibitors, immunotherapy and radioisotopes revolutionising the management of mCRPC. These medical advances, along with an improved understanding of the adaptive responses to and predictors of outcomes concerning various treatments, are catalysing the development of more effective therapeutic strategies in advanced cancer. In this abstract, %fPSA appeared to predict treatment response in patients on docetaxel over abiraterone or enzalutamide in the mCRPC setting. Improved disease management with prognostic determinant biomarkers is important to select the optimal treatment and maximise treatment benefits in patients with mCRPC.

Villis Marshall Prize: Can ChatGPT pass the FRACS Urology Examination? Exploring artificial intelligence's capabilities and limitations in surgical specialty training assessment

Speaker: Dr Kathleen Lockhart (Roual North Shore Hospital, St Leonards, Australia)

Summary: In this case control study, the performance of ChatGPT in the FRACS Urology exam was compared against human urology trainees. Under exam conditions, ten trainees completed 20 written-based essay questions over 4 hours, which had been compiled from previous fellowship exams. ChatGPT was prompted to answer the same questions with instructions regarding exam parameters; five exams were completed by ChatGPT version 3.5 and five exams by version 4.0. The exams were marked by five blinded urologists. A greater proportion of trainees passed the exam compared to ChatGPT, although the difference was not statistically significant (90% vs. 60%, respectively; p=0.30). The majority of failed ChatGPT exams (75%) were completed by version 3.5. Trainees achieved a numerically higher proportion of pass marks than ChatGPT (89.4% vs. 80.9%) and higher raw aggregate scores (79.2% vs. 78.12%), however neither of these reached significance (p=0.22; p=0.79). Urologists incorrectly assumed that two trainee exams were completed by ChatGPT. The sensitivity, specificity and overall accuracy of identifying ChatGPT were 100%, 83.3% and 91.7%, respectively.

Comment: When using detailed prompts and providing the context of the chosen study, ChatGPT can generate appropriate responses to questions and complete discussions on its own as it draws information from various sources on the internet, although this raises concerns about the integrity of the paper when using AI-generated text. This abstract showed that ChatGPT performed more poorly compared to human trainees in the FRACS Urology written exam, although the differences observed in pass marks and raw aggregate scores were not statistically significant. It is important to note that humans are the experts, and ChatGPT is a helpful tool. Nonetheless, the functionality of AI text generators for scientific research, and the quality of content, is improving with every new software update and more advanced technology. There is a need for comprehensive discussions on the potential uses, threats and limitations of these tools, emphasising the importance of ethical and academic principles.

Alban Gee Prize: Volatile organic urinary compounds in the diagnosis of prostate cancer

Speaker: Dr Omid Yassaie (Wellington Hospital, NZ)

Summary: Volatile organic compounds (VOCs) which are created by secretions such as urine, breath and sweat, have been investigated in ovary, lung and bladder cancers, as well as inflammatory bowel disease. The objective of this preliminary study was to identify a urinary VOC biomarker for prostate cancer (PC), and to explore whether acidic or alkali conditions improve the detection of VOCs. A total of 242 patients provided urine samples, 120 of whom had PC, while 122 did not. Samples were paired with sulphuric acid or sodium hydroxide. VOCs were more readily detected within acified samples than alkaline ($p<0.05$), regardless of PC status. Overall, 189 VOCs were identified. Researchers noted that 18 VOCs were more commonly detected among patients with PC, however none were a strong biomarker for PC.

Comment: The odour signature of urine is produced by substances known as volatile organic compounds (VOCs), which can be separated and identified by gas chromatography/mass spectroscopy. Following the proof-of-concept studies in dogs, researchers have tested "*electronic nose*" technology to discriminate the odour of urine from patients with PC and controls. In this study, it appeared that acidic urine is favourable compared to alkali for the detection of VOC in urine in patients with PC, although ROC curve analysis did not identify any compounds which would be a strong biomarker for PC. While VOC profiling of urine headspace is encouraging, a multiplatform method that combines volatile analyses with analyses of non-volatile compounds (using nuclear magnetic resonance spectroscopy or high-performance liquid chromatography/mass spectrometry-based approaches) will likely achieve a more comprehensive understanding of the metabolic characteristics of PC. Furthermore, more work is to be undertaken to identify and validate these metabolic avenues in PC.

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Low-Arnold Award in female and functional urology: Bladder botulinum toxin 19-year discontinuation rates in Australian single-surgeon private practice

Speaker: Dr Samantha Pillay (Continence Matters, North Adelaide, Australia)

Summary: This presentation shared prospective data on patients treated with onabotulinumtoxinA (BoNT/A) injections as a third-line treatment for overactive bladder. Over 19 years (2004-23), at a single-surgeon centre, 353 patients (95% female; mean age 69 years) received 1631 injections (63% under sedation, 33% local anaesthetic, 4% general anaesthetic). One patient received 27 treatments. A total of 164 patients (46%) discontinued treatment, of whom 34% elected other treatment options, 29% described a lack of efficacy, 21% reported the issue as resolved and 12% stopped due to other reasons such as frailty or terminal illness. On average, patients underwent 2.84 treatments before discontinuation.

Comment: OnabotulinumtoxinA (BoNT/A) has been injected into the bladder for more than two decades now, and is proven to be safe and effective in overactive bladder patients. However, we are still not completely aware of how it acts at a molecular level to improve sensory symptoms in urinary urgency. This long-term, single surgeon's retrospective series reported that close to half (46%) of patients discontinued treatment in the long term (over 19 years of follow-up) with more than a third of patients electing for other therapeutic options either due to lack of clinical efficacy, or wanting more definitive treatment. A lot of work has gone into innovating ways to improve the delivery of BoNT/A in bladders, to reduce the risk of deleterious effects (such as urinary retention) and to provide less invasive methods of treatment (including liposomes, low-energy shock waves and inert hydrogels). While BoNT/A remains a valid minimally invasive treatment for overactive bladder, neuromodulation is rapidly gaining traction as a 'better' therapy since it may alter the underlying disease process, rather than providing symptomatic relief.

BAUS Trophy Award: Evaluating the efficacy and safety of the Prostafix Water Electrolysis System for treating benign prostatic hyperplasia

Speaker: Professor Peter Gilling (Tauranga Public Hospital, NZ)

Summary: The Prostafix Water Electrolysis System is indicated as a minimally invasive treatment for lower urinary tract symptoms secondary to benign prostatic hyperplasia. It ablates prostate tissue by directing current energy with interstitial needles, which induces water electrolysis and pH changes. This study assessed the safety and efficacy of the Prostafix System in a day setting using only topical anaesthesia among 49 men across three sites in NZ and Singapore. Most men (84.8%) required no catheter or <24-hour catheterisation, while one required catheterisation for >3 days. At 3 months of follow-up, men showed a mean decrease in IPSS of 9.5 points (43.8%). The procedure was well-tolerated; 91.1% of AEs were mild and 68.8% of these were unrelated to the device of the procedure. The most common AEs included worsening of lower urinary tract symptoms (16.5%) and hypertonic bladder (7.6%).

Comment: In recent times, it has become evident that the preservation of various male sexual function domains such as erectile and ejaculatory functions are of paramount importance for many sexually active men who are contemplating benign prostatic hyperplasia surgery. Various innovative MISTs have been shown to improve various parameters in voiding domains while minimising sexual dysfunction. This early data on the Prostafix system showed promising results, with patients reporting a 43.8% decrease in IPSS, and most patients (84.8%) requiring no catheter or less than 24-hour catheterisation. Perhaps the discussion should not be centred on whether this technology is unique or effective, but on how the Prostafix system compares to similar ablative technologies (such as Rezum) and on the cost-effectiveness analysis modelling in adopting this technology in the current MIST environment.

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AU-15023. October 2022.

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AZ Platinum Trophy Award: Preliminary safety results of a first in human clinical trial of ADAM™, a vas-occlusive hydrogel designed for male contraception

Speaker: Professor Nathan Lawrentschuk (University of Melbourne, Australia)

Summary: ADAM™ is a novel method of non-permanent, non-hormonal male contraception which involves injecting a proprietary biocompatible hydrogel into the vas deferens. Professor Lawrentschuk presented the initial safety results of ADAM™ from a first-in-human, single-arm, prospective, open-label, multicentre, dose-ranging clinical trial. Eligible men (n=13; mean age 35 years) with normal semen parameters were implanted with ADAM™ under general anaesthesia, using one of three doses of hydrogel. All implantations were carried out successfully. No AEs occurred during the procedures and to date, no serious AEs have been reported. Of the 45 reported AEs, 91.8% have been mild, and 85.7% resolved within 30 days of implantation. There was no difference in AEs between the various dosages, and no AEs have been related to the ADAM™ hydrogel. The recovery pathway and AEs after implantation were comparable to those seen in men following a no-scalpel vasectomy. Men will be monitored for a minimum of 12 months, and the trial is ongoing.

Comment: For the past several decades, extensive research has been undertaken to explore the feasibility of hormonal male contraception ranging from exploitation of the hypothalamic-pituitary-gonadal (HPG) axis to suppress spermatogenesis, to non-hormonal occlusive materials and devices such as polyurethane and silicone polymers to block sperm transport in the vas deferens. The concerns of vas-occlusive contraception technology centres on actual effectiveness, its reversible nature and potential (long-term) spermicidal action. The ADAM™ hydrogel study reported a comparable safety and recovery profile to vasectomy, and most AEs were mild and temporary in nature. The ideal vas-occlusive contraceptive material should have the following properties: namely, it should be easily administered, have rapid action, not migrate, effectively block the passage of sperm, be easily reversed and have no significant (permanent) histological effects on the vas deferens, sperm or genitourinary tissues. If these criteria are fulfilled, the ADAM™ hydrogel vas-occlusive technology has great potential to become the first in a class of long-lasting, non-hormonal and reversible male contraceptives.

A prospective trial to assess the initial diagnostic accuracy of FDG-PET compared to PSMA-PET for newly diagnosed high risk prostate cancer prior to treatment

Speaker: Dr Matthew Roberts (Royal Brisbane & Women's Hospital, Australia)

Summary: This prospective, multicentre trial evaluated the additive diagnostic value of FDG PET-CT to PSMA PET-CT in 32 patients (median age 69 years; median PSA 14ug/L) with newly diagnosed, high-risk PC. According to physician interpretation, FDG-PET imaging did not provide any additional definite or probable metastasis information to PSMA PET. Researchers were unable to identify any patient subgroups who would benefit from FDG-PET imaging.

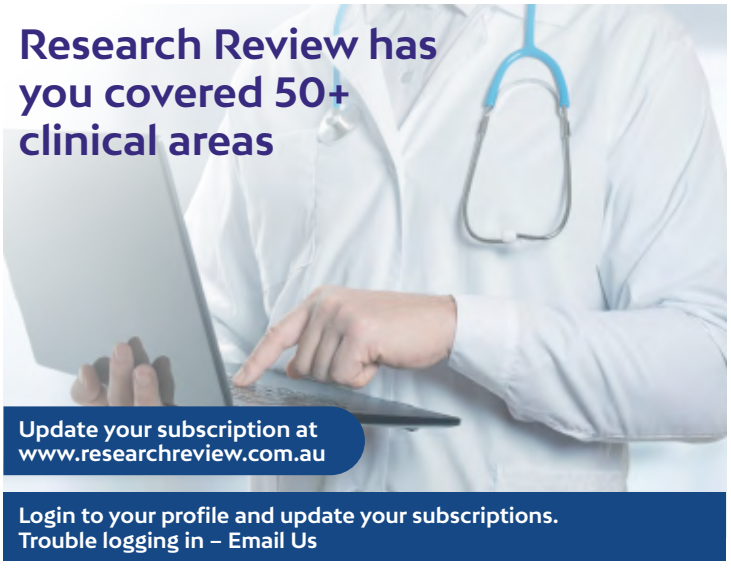
Comment: Although FDG PET-CT is useful for detecting different types of malignant tumours, it is less frequently used in PC imaging because of its low sensitivity compared to PSMA PET-CT. Nonetheless, several studies have demonstrated the diagnostic value of performing both FDG and PSMA PET-CT, especially in patients on androgen deprivation therapy, which could reduce the PSMA uptake and the visibility of tumour lesions in castration-sensitive prostate cancer. This quasi-RCT showed that FDG-PET imaging does not appear to provide additive staging information above PSMA-PET for newly diagnosed, high-risk prostate cancer patients, and the exact patient subgroups who will benefit from combined FDG-PET and PSMA-PET remain unknown at this stage. Perhaps the utility of FDG-PET resides in the detection of metastatic disease in a small fraction of men with biochemical failure with scan sensitivity that increases with increasing serum PSA level, in the assessment of the extent of metabolically-active, castrate-resistant metastatic disease, in monitoring response to androgen deprivation therapy and in other treatments and prognostication.

A randomised, single-dose, bioavailability, and safety phase 1/2 clinical study on novel SDS-089 nasal Vardenafil 4 mg spray solution in comparison to oral Vardenafil tablet 10 mg in healthy volunteers

Speaker: Professor Eric Chung (Androurology Centre, Brisbane, Australia)

Summary: Vardenafil (VDF; SDS-089) has been developed as an intranasal spray for the treatment of erectile dysfunction (ED). This clinical study randomly assigned eligible men (n=13) to either VDF spray (4mg) or a VDF oral tablet (10mg), to compare the bioavailability and safety of the two treatment methods. Blood samples were collected up to 10 hours after administration. VDF (SDS-089) spray and the oral VDF tablet were comparable in terms of half-life (2.52 vs. 2.46 hours), peak time (0.17 vs. 0.97 hours) and peak concentration (9.21 vs. 11.24ng/mL). AEs occurred more frequently with the nasal spray than with the oral tablet (33 vs. 9); these were predominantly transient headaches and were well-tolerated.

Comment: While oral PDE5i has been accepted as the standard of care and first-line medical treatment for males with ED, it has certain limitations. Intranasal Vardenafil (VDF; SDS-089) potentially offers a more timely and lower dose for the treatment of ED in patients who can tolerate transient local adverse reactions. The strength of this study is its randomised, crossover design. Because the study was conducted in 13 healthy young subjects, the results may not reflect those observed in elderly patients who may be likely to take VDF (SDS-089) for ED. Nevertheless, the changes in pharmacokinetic parameters in the present study are likely a reflection of the differences between intranasal and oral administration of the formulations. The present VDF (SDS-089) formulation, when administered intranasally, can achieve a more rapid but similar plasma concentration with only about one-third of the dose when compared with the oral administration, and it offers more convenient planning for ED treatment.



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ProFocal® – novel, cooled laser focal therapy

Speaker: Dr Jonathan Kam (Nepean Urology Research Group, Kingswood, Australia)

Summary: This session shared the final outcomes of PFLT-PC, the first-in-human trial of ProFocal® cooled laser focal ablation therapy for localised PC. The analysis included the first 100 men (median age 66 years; median PSA 5.9ng/mL) who underwent ablation as a day procedure. At a follow-up of 3 months, biopsies found no evidence of ISUP 2 or greater PC in 84% of patients. In the most recent 20 cases, 100% of men showed no infield recurrences, indicating a learning curve. Patients showed no significant worsening in quality-of-life scores, lower urinary tract symptoms or bowel function, although patient-reported sexual function scores decreased at the 3- and 6-month assessments.

Comment: Focal therapy for PC is gaining significant interest 'again' as a reasonably effective alternative to radical surgery in selected localised PC patients, but with potentially less adverse effects on continence and potency. Various energy sources have been used in focal therapy such as high-intensity focused ultrasound, irreversible electroporation, cryoablation, focal laser ablation, focal brachytherapy, photodynamic therapy and radiofrequency ablation. ProFocal® laser therapy is a new technology that originated in Australia, and this PFLT-PC trial reported promising oncological results (84% of patients having successful infield treatment), with excellent functional outcomes in terms of quality-of-life scores (SF-12), lower urinary tract symptoms (IPSS, EPIC- urinary domains) or bowel function, albeit with a decrease in sexual function (SHIM and EPIC-sexual domains) in the first 6 months. While this technology is a promising alternative treatment for localised PC, focal therapy still needs to show equivalent oncological outcomes to the current standard of care, and further studies are needed to better understand its safety and efficacy in PC treatment in the long term.

The Australasian Pelvic Floor Procedure Registry: monitoring device safety in women

Speaker: Professor Susannah Ahern (Monash University, Australia)

Summary: Professor Ahern discussed the role and significance of the Australasian Pelvic Floor Procedure Registry (APFPR), a clinical quality registry established to monitor and improve the quality and safety of procedures involving mesh and other prostheses for pelvic organ prolapse and stress urinary incontinence. At present, the APFPR is inviting surgeons and surgical sites to participate, with the aim of providing information and guidance on the effectiveness and safety of such procedures. A total of 702 patients have been recruited in the registry, and the opt-out rate is 2.7%. There are currently 30 participating sites who have carried out ≈500 procedures. To date, data for the clinical quality indicators (CQIs) are as follows: Among patients who underwent procedures for stress urinary incontinence and organ prolapse, 90.5% and 92.2%, respectively, had completed objective clinical assessments, 99.3% and 100% received intraoperative cystoscopy and 83.3% and 95.6% experienced improved outcomes. Furthermore, 0.3% and 0% of patients needed to return to theatre, 3.3% and 2% were readmitted within 30 days and 5.0% and 0% were catheterised on discharge. Patient-reported outcome measures (PROMs) are administered via email, text and phone at 6, 12 and 24 months after surgery, and the current response rate is ≈70%.

Comment: The APFPR was established following the 2018 Senate Committee Inquiry to track outcomes of pelvic floor procedures (PFPs) involving the use of devices and/or prostheses, to address systemic deficits in the collection, analysis and reporting of PFPs, establish early warning systems, and provide feedback to clinicians, hospitals, regulatory bodies and ultimately the public, regarding the status of pelvic floor interventions. It is the first registry to be established in Australia and NZ to routinely track and monitor PFPs and clinical outcomes to improve the health outcomes of women who undergo these procedures. Given the need for safe and high-quality treatments for PF devices, the APFPR can serve as a foundation to evaluate new prostheses and treatments available in the future for PFPs. Implementation of CQIs and PROMs, in addition to clinical outcomes, will enable the collection of vital information and support safety monitoring of mesh-related AEs in the long term, specifically those involving devices and/or prostheses, and add to our existing knowledge on pelvic floor disorder-related issues.

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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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