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TAKE HOME *Messages*

Following are summaries of the Take Home Messages delivered on the final day of this year's AUA meeting. The purpose of these messages is to provide an overview of presentations on select topics. Abstract numbers are in parentheses (J Urol, suppl., 2018; **199**: e1-e1250).

Kidney Cancer

Brian McNeil, MD
Brooklyn, New York

The Program Planning Committee for the 113th AUA Annual Meeting organized a thought-provoking scientific program. The Kidney Cancer program incorporated 1 video session, 8 podium sessions and 8 moderated poster sessions in addition to plenary sessions highlighting current controversies in kidney cancer. A total of 258 abstracts were presented.

Common themes discussed during the epidemiology and evaluation/staging sessions were renal biopsy, risk stratification and perioperative kidney function trends. In a review of preoperative trends in kidney function in a Veterans Affairs cohort, the preoperative trend was independently associated with postoperative chronic kidney disease following radical or partial nephrectomy when looking at 5 or more measurements in a 2-year period (MP28-15).

In a validation of a previously reported nomogram predicting the 12-year probability of metastatic renal cancer, the addition of a targeted sequencing panel of common genes mutated in clear cell renal cell carcinoma (RCC) helped improve risk prediction (MP36-09).

Sessions on surgical therapy for localized disease highlighted shifting practice patterns and risk based surveillance. Open, laparoscopic and robotic partial and radical nephrectomy practice patterns and the new standard of care were analyzed using a statewide database (PD16-03). More evidence was revealed that minimally invasive robotic approaches are being used more often for radical and partial nephrectomy. Patients are traveling less outside of their health service areas with the regional dissemination of robotic surgery.

In a prognostic evaluation of perinephric fat, renal sinus fat and renal venous invasion in pathologic stage T3a clear cell RCC, investigators reported their experience with patients undergoing radical nephrectomy during a 30-year period (PD16-12). Isolated extrarenal extension involving perinephric fat, renal sinus fat or a renal venous structure carried similar prognostic weight. The presence of multiple pT3a patterns of extrarenal extension was associated with worse oncologic outcomes.

The active surveillance for localized disease session featured current perspectives regarding surveillance of complex cystic masses. In an analysis of the management of genetically defined renal tumors using size based risk stratification, 3 cm represents a clinically meaningful threshold for deciding between active surveillance and surgical management in patients with von Hippel-Lindau, hereditary papillary renal carcinoma and Birt-Hogg-Dubé associated renal tumors

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Pediatrics

Emilie K. Johnson, MD, MPH
Chicago, Illinois

Introduction

Pediatric urology was featured at AUA2018 in several venues. The Societies for Pediatric Urology (SPU) meeting included 78 podium presentations and 61 posters covering a variety of salient topics. This year, Health Services and Population Research was a separate section for the first time.

The SPU meeting also featured many notable special talks. The audience was particularly enthused by Dr. David Miller's presentation on how quality improvement methodology developed in adult urology could apply to pediatrics. Prof. Philip Ransley's perspective on the evolution of the field of pediatric urology, "Pediatric Urology Grows Up," was also a highlight.

At the main AUA2018 meeting a full day of pediatric programming included a lively plenary session, 2 moderated poster sessions and viewing of surgical videos. Among other wonderful talks the plenary participants enjoyed a panel discussion about fertility preservation for pediatric oncology patients, a debate about regionalization of care for complex cases (eg bladder exstrophy) and a lecture on cancer screening after

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Take Home Messages—Westney

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beta-lactamase agents highlights the need to identify alternate strategies to interrupt the infectious process. Several presentations focused on different aspects of host-bacterial interactions resulting in adherence (MP23-01, MP23-02, MP23-03).

The 2-step verification process required for type I pilus assembly was detailed in one presentation, demonstrating that successful disruption would block the attachment of uropathogenic Escherichia coli to urothelium (MP23-01) (fig. 1).

Microbiome

Many groups explored the characteristics of the urinary and/or fecal microbiome to gain insights into antibiotic resistance, CPPS/interstitial cystitis (IC) phenotyping, inflammatory conditions and neovaginal microflora in male to female transsexuals (MP15-09, MP15-10, MP15-12, MP23-10).

Performance of 16S rRNA amplicon sequencing performed on rectal swabs demonstrated an alteration in the fecal microbiome of patients with fluoroquinolone resistant E. coli organisms, with overgrowth of Enterobacteriaceae and a relative absence of Aeromonadaceae (MP15-12).

Prophylactic Antibiotics for Prostate Biopsy

The discussion regarding the best strategies for selecting prophylaxis for prostate biopsies to minimize infectious complications continued in this year's sessions. One group reported on the use of next generation DNA sequencing to test rectal swabs for the purpose of tailoring the prebiopsy antibiotic regimen (MP15-14). Infectious complications were avoided in 23 of 24 patients, with only a single patient having cystitis 3 weeks after biopsy.

While this strategy allows for complete coverage of all organisms, multiple agents including antifungals may be required to address all the generated sensitivities. Targeted antimicrobial prophylaxis has not been universally successful at eliminating septic events (MP15-15). In addition, 2 studies focused on the judicious use of local and hospital antibiograms to supplement empirical antibiotic selection (MP15-18, MP15-20).

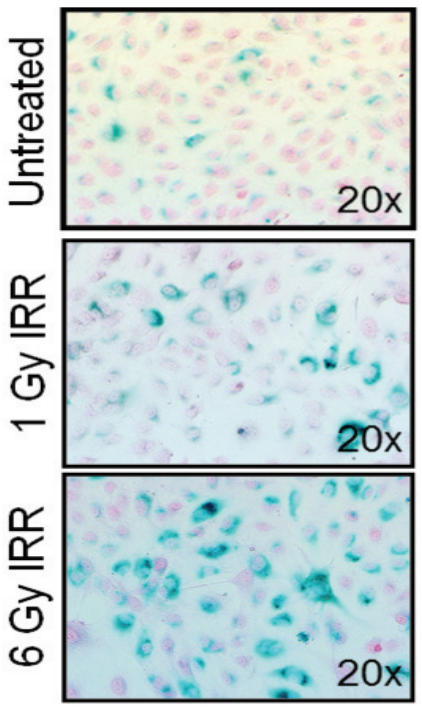


Figure 3. HUVEC cells demonstrating increased β-galactosidase staining, reflecting increased senescent cell population with higher irradiation dose. Reprinted with permission, MP10-08.

Hemorrhagic Cystitis

Hemorrhagic cystitis related to radiation and chemotherapy has long been a source of patient morbidity.

An elegant study demonstrated specific endothelial aberrations when exposing HUVEC (human umbilical vein endothelial cells) to radiation, namely significant decreases in cell proliferation and migratory capability, combined with an increased proportion of senescent cells (MP10-08) (figs. 2 and 3). Research along these lines bolsters future efforts to prevent functional consequences of radiation cystitis.

Another study highlighted a protein product of Schistosoma haematobium that may be more effective than Mesna in preventing acrolein related hemorrhagic cystitis (MP39-15). A single dose of H-IPSE^{H06} acting by potentiating the anti-inflammtory effects of interleukin-4 was at least equivalent to 3 doses of Mesna.

Urologic CPPS (UCPPS)/IC Phenotyping

The UCPPS/IC session focused on phenotyping of pain and interstitial cystitis subtypes to place patients in appropriate treatment groups and facilitate stratification noninvasively. Further work from the MAPP (Multidisciplinary Approach to the Study of Chronic Pelvic Pain) research group examined the characteristics of subjects with genital pain, noting that increasing sites and severity of pain co-localized with other pain syndromes (headache, myalgia), depression and poorer psychosocial/overall health (MP39-18).

There was considerable progress in the identification of Hunner's ulcer subtypes with a combination of urinary biomarkers and pain scores. The ability to recognize these patients without inflicting additional discomfort will be of considerable value (MP39-11).

While not comprehensive, this summary features high quality and meaningful research relating to many other focus areas within urology. I look foward to seeing the progression next year in Chicago. ◆

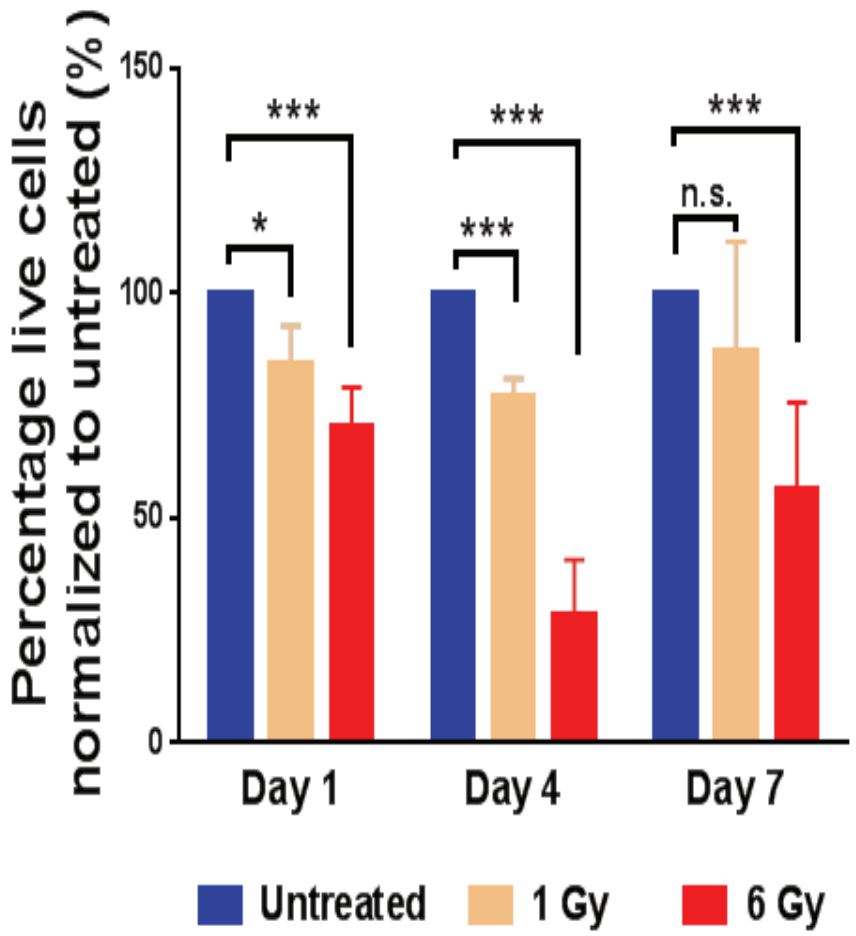


Figure 2. Signficant proliferation reduction in HUVEC cells with dose and time response to radiation exposure. Reprinted with permission, MP10-08.

Appendix. Comparison of urine culture and bacterial stone aggregation with or without bioflim presence collected from 23 PCNL cases (MP10-07)

ID	Stone[a]	Bacteriological Culture		Biofilm-SEM[b]
		Urine	Stone	
03	Ca Ox, Ca Ph	*Enterococcus faecalis*	*E. coli*	Absent
04	Ca Ph	*Pseudomonas aeruginosa*	*E. coli*	Present
08	Uric acid	*E. coli*	*E. coli*	Present
12	Uric acid, Ca Ph	Negative	*Proteus mirabilis*	Absent
13	Ca Ox, Ca Ph	Negative	*E. coli*	Present
16	Ca Ca, Ca Ph	*Staphylococcus*	*Proteus mirabilis*	Present
17	Ca Ox, Ca Ph	Negative	*Proteus mirabilis*	Present
18	Uric acid, Ca Ox	Negative	*Pseudomonas aeruginosa*	Present
19	Ca Ph	*Enterococcus faecalis*	*E. coli*	Present

[a]Ca, calcium; Ox, oxalate; Ph, phosphate; Ca, carbonate; and [b]SEM, scanning electron microscopy.

THE VALUE OF NEXT GENERATION DNA SEQUENCING TESTING OF RECTAL SWABS BEFORE TRANSRECTAL PROSTATE BIOPSY FOR INDIVIDUALIZED AND TARGETED PROPHYLAXIS OF URINARY TRACT INFECTION

V. Mouraviev[1], M.McDonald[2], C.Skinner[3], S.Vourganti[4], D.Albala[5], F.M.E. Wagenlehner[6], K. G. Naber[7], T.E. Bjerklund Johansen[8]

[1]Central Florida Cancer Institute, Davenport, FL, Nova Southeastren University, Fort Lauderdale, FL, U.S.A.; [2]Florida Hospital Celebration Health, Celebration, FL, U.S.A.; [3] University of Central Florida, Orlando, FL,U.S.A., [4] Dept. of Urology, Rush University, Chicago, IL, U.S.A.; [5] Associated Medical Professionals of New York, U.S.A., [6] Dept. of Urology, Justus -Liebig University Giessen, Germany; [7]Technical University Munich, Germany; [8]Dept. of Urology, Oslo University Hospital, Norway

Abstract

INTRODUCTION AND OBJECTIVES. Despite the implementation of new antibiotic regimens, the rate of severe febrile urinary tract infection (UTI)/urosepsis after transrectal prostate biopsy remains unchanged over recent years at approximately 3% of all cases. Such complications require urgent hospitalization with intravenous antibiotic administration. The introduction of next generation sequencing (NGS) allows a comprehensive analysis of the genomic profile of rectal microbiota including the detection of resistance genes for the most frequently used antibiotics for empiric prophylaxis. The aim of our study was to evaluate NGS of rectal swabs in a pilot study in patients before transrectal biopsy of prostate aimed to prevent severe UTI.

METHODS. Between June 2017 and April 2018, 50 patients were entered into this study before scheduled prostate biopsy for elevated PSA or abnormal DRE or multiparametric MRI. Two types of molecular microbial diagnostic testing levels are performed. The Level 1 Panel, received within 24 hours, is a quantitative real-time Polymerase chain reaction (PCR) test for bacteria and fungi, and assessment of genetic factors conferring resistance to bacteria. The Level 2 test, received within 3-5 business days, detects virtually all microbial organisms and fungal pathogens that may be present in patient specimens based on the database of 25,000 species. The rectal swabs were processed by MicroGen^{DX}, a CAP and CLIA certified laboratory in the U.S.A. performing diagnostics via NGS. The determination of the population of bacterial species, including antibiotic resistance genes, provides for a susceptibility determination that clinicians can adjust using local antibiograms and/or clinical references. Standard protocol for prevention of infection included levofloxacin 0.5 g orally and 1 gr. ceftriaxone intramuscularly before biopsy with adjustment for targeted prophylaxis for each case.

RESULTS. In all 50 patients multiple species were reported with median 9 (range: 1-16). The predominant flora was Bacteroides spp (dorei, fragilis, caccae and vulgaris) – in 20 men, Escherichia coli in 13, Prevotella copri – in 7, Faecalibacterium prausnitzii – in 3, Citrobacter (koseri and freudii) – in 2, and Corynebacterium striatum, Klebsiella pneumoniae, Fenollaria timonensis, Streptococcus agalactiae, Campylobacter hominis – each in 1 patient, respectively. In 35 of 50 (70%) cases multiple drug resistance genes were detected, and 24 (48%) were to fluoroquinolones. These data allowed us to modify our empiric prophylaxis in those 24 patients to alternative antibiotic(s) rather than levofloxacin. In 17 cases, fungal species were detected (11 of whom harbored multiple fungal spp) which was used as an indication to supplement prophylaxis with an antifungal agent. This microbiome genome-sequence guided prophylaxis strategy was associated with avoidance of serious infectious complications in all patients within 30 days after biopsy.

CONCLUSIONS. NGS testing allowed the implementation of truly individualized and targeted prophylaxis of patients undergoing transrectal biopsy. Further phase II-III studies will be required to compare the efficacy of NGS vs. standard methods of culture and sensitivity of rectal swabs.

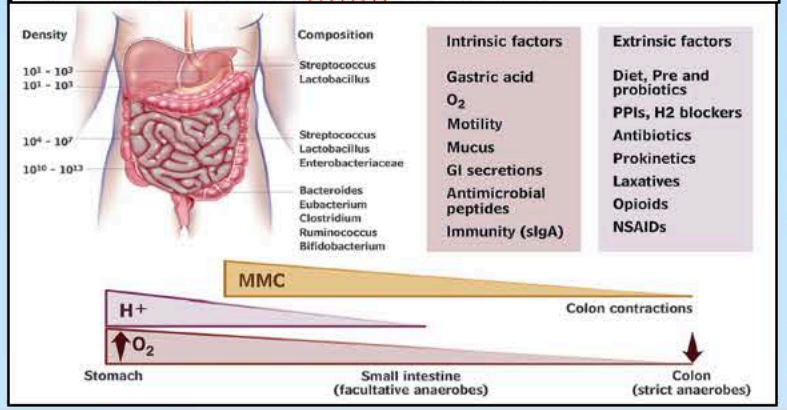
Introduction and Objectives

- Despite the implementation of new antibiotic regimens, the rate of severe febrile urinary tract infection (UTI)/urosepsis after transrectal prostate biopsy remains unchanged over recent years at approximately 3% of all cases.
- The introduction of next generation sequencing (NGS) allows a comprehensive analysis of the genomic profile of rectal microbiota including the detection of resistance genes for the most frequently used antibiotics for empiric prophylaxis.
- The aim of our study was to evaluate NGS of rectal swabs in a pilot study in patients before transrectal biopsy of prostate aimed to prevent severe UTI.

Methods

Between June 2017 and April 2018, 50 patients were studied prior to elective prostate biopsy for suspected prostate cancer (elevated PSA, abnormal DRE, multiparametric MRI with PIRADS v2 score ≥3) by rectal swab. The rectal swabs were processed by MicroGen^{DX}, a US based CLIA certified laboratory providing diagnosis via NGS. Two methods of molecular microbial diagnostic testing were performed: Level 1 Panel is a quantitative real-time PCR test for bacterial and fungal genes with specific assay for presence of antimicrobial drug resistance genes. The Level 2 Panel is a comprehensive NGS of all genomic DNA present in the patient specimen which aims to catalog all microbial and fungal pathogens present. Standard protocol for prevention of infection included levofloxacin 0.5 g orally and 1 g ceftriaxone intramuscularly before biopsy with adjustment for targeted prophylaxis for each case based on NGS findings. Random biopsy was performed using systematic 12-core scheme under TRUS-guidance plus selectively targeted cognitive MRI-TRUS guided in 9 patients.

Fig.1 Gut microbiome (Simren et al.,2017)



Results

Table 1. Dominant flora and resistance

Bacteria	50 Pats
Bacteroides spp (dorei, fragilis, vulgaris or caccae)	20
Escherichia coli	13
Prevotella copri	7
Faecalibacterium prausnitzil	3
Citrobacter koseri or freudii	2
Corynebacterium striatum	1
Klebsiella pneumonia	1
Campylobacter hominis	1
Fenollaria timonensis	1
Streptococcus agalactiae	1
Prophylactic drug resistance	35
Quinolone resistant	24
Fungi	**17 pats**
Candida albicans, glabrata, dubliniensis or zeylanoides	15
Saccharomyces cerevisiae	8
Aspergillus tubinges or foetidus	2
Prastagenesporum nodorum, Talomyces pinophileus, Cyberlindnera jadinii, Piskarozyma capsuligue, Penicilium echinulatum, Rotorinda nucilerginosa, Delaryomyces hansenii, Malassezia restricta	1
Multifungal association	11

Multiple microbial species were reported with median 9 microorganism spp from rectal microbiota (range: 1-16). The predominant flora was found to be Bacteroides – in 20 men; E. coli in 13, Prevotella – in 7; Faecalibacterium - in 3; Citrobacter - in 2; Corynebacterium, Klebsiella, Campylobacter, Fenollaria, Strep. agalactiae in 1 patient, respectively. In 35 of 50 (70%) cases multiple drug resistance genes were detected, and 24 (48%) of those were to fluoroquinolones. These data allowed us to modify our empiric prophylaxis in those 24 patients to alternative antibiotic(s) rather than levofloxacin. In 17 cases, fungal species were detected (11 of whom harbored multiple fungal spp) which was used as an indication to supplement prophylaxis with an antifungal agent. This microbiome genome-sequence guided prophylaxis strategy was associated with avoidance of serious infectious complications in all patients within 30 days after biopsy, including some men with high risk of UTI development (previous history of biopsy related sepsis, immunodeficiency, or diabetes).

Conclusion

NGS testing allowed the implementation of truly individualized and targeted prophylaxis for patients undergoing transrectal prostate biopsy. Further phase II-III studies will be required to compare the efficacy of NGS vs. standard methods of culture and sensitivity of rectal swabs.