Published in final edited form as:

Urology. 2015 December ; 86(6): 1200–1205. doi:10.1016/j.urology.2015.07.008.

Rapid Identification of Rectal Multi-Drug Resistant *E. coli* Prior to Transrectal Prostate Biopsy

Veronika L. Tchesnokova¹, Linda L. Otelly², Kyoko Sakamoto^{2,3}, Joshua Fierer^{2,4}, Evgeni Sokurenko^{3,5}, and Michael A. Liss⁶

¹VA Healthcare System Minneapolis, Minneapolis, MN

²VA Healthcare System San Diego, San Diego, CA

³University of California, San Diego School of Medicine, Department of Urology, La Jolla, CA

⁴University of California, San Diego School of Medicine, Departments of Medicine, and Pathology, La Jolla, CA

⁵University of Washington, Department of Microbiology, Seattle, WA

⁶University of Texas Health Science Center San Antonio, Department of Urology, San Antonio, TX

Abstract

Objective—To develop and evaluated a rapid multiplex-qPCR to identify fecal carriers of multi-drug resistant extra-intestinal pathogenic *E. coli* clonal groups.

Methods—Men presenting for transrectal prostate biopsy (TPB) at the San Diego Veterans Affairs Medical Center underwent rectal culture immediately prior to TPB. Rectal swabs were streaked ciprofloxacin-supplemented (4 mg/L) MacConkey agar plates, identified, and susceptibility tested. The same swab was sent to the University of Washington for qPCR test (EST200) targeting two major MDR-ExPEC clonal groups – ST131 and ST69 that combined were expected to represent majority of fluoroquinolone as well as trimethoprim-sulfamethoxazole resistant *E. coli*. We calculate test characteristics including the area under the receiver operative curve (AUC).

Results—We enrolled 104 men from 11/5/2013 to 6/10/2014. Fluoroquinolone - resistant *E. coli* were cultured from 19.2% (20/104) of rectal swabs and 26% (27/104) of all swabs were positive for EST200 by PCR. The test characteristics comparing the EST200 to the culture-based detection

Corresponding Author: Michael A. Liss M.D., M.A.S., Assistant Professor, University of Texas Health Science Center San Antonio, Department of Urology, 7703 Floyd Curl Drive, San Antonio, TX, 78225.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

This manuscript won “Best Abstract” at the American Urological Association annual meeting on May 16, 2015 in New Orleans, LA, USA.

Conflicts of Interest: None

of fluoroquinolone-resistance were 75%, 86%, 94%, and 56%, respectively. The AUC was 0.84 for the EST200 to detect fluoroquinolone resistance prior to TPB.

Conclusions—Compared to the reference standard rectal culture, EST200 was able to detect majority of fluoroquinolone resistant *E. coli* on rectal swabs prior to prostate biopsy.

Introduction

Prostate cancer remains the most common cancer diagnosis among men and is most commonly diagnosed by a trans-rectal prostate biopsy.(1) Infectious complications from prostate biopsy include urinary tract infection, epididymitis, orchitis, prostatitis, and sepsis. (2, 3) The current incidence of infection in larger studies is about 4% (0.1–7%), most commonly due to extra-intestinal pathogenic *Escherichia coli* (ExPEC).(2–14) Based on level 1b evidence, the American Urological Association Best Practices Statement for Antibacterial Prophylaxis recommends use of a fluoroquinolone (FQ) as prophylaxis of infection from transrectal prostate biopsy and some urologists advocate for trimethoprim/sulfamethoxazole (T/S) as well.(15)

Recent studies revealed that infection rates have increased four-fold over the last decade largely due to FQ resistance.(3, 7, 14, 16–19) Detecting FQ resistant *E. coli* in feces prior to biopsy would identify men who at higher risk of infection from introduction of ExPEC into the prostate and bloodstream during the biopsy (20). These men would be candidates for alternative or additional antibiotic prophylaxis.(14, 21) While this can be done by culture, that approach requires at least 48h lead-time and may involve an initial investment of coordination between laboratories, infectious disease clinicians, and urologists.

A faster approach could be detection of the resistant bacteria by using molecular diagnostics like quantitative polymerase chain reaction (PCR). While the resistance mechanisms even to same antibiotics are highly diverse, it had been determined that drug-resistance in ExPEC is clonal in nature, i.e. the isolates with a distinct resistance profile are grouping into closely-related genetic families – Sequence Types (STs). Among MDR-ExPEC, two STs are of particular clinical prevalence – ST69 (aka Clonal Group A) and ST131. The majority of both STs are resistant to trim/sulfa (T/S) and majority of ST131 isolates are also resistant to FQ. *E. coli* ST131 accounts for up to 70% of the fluoroquinolone resistant *E. coli* found at the time of prostate biopsy.(22–24) It has been recently shown that vast majority of the FQ-resistant ST131 isolates belong to its sub-clone H30 (ST131-H30). The clonal nature of drug-resistant ExPEC provides a potential way for to detect the bacteria that are most likely to be multidrug-resistant ExPEC using qPCR targeting clone-specific genetic markers.

Here, we test a rapid qPCR-based clonal typing test to identify the FQ as well as T/S resistant *E. coli* in rectal swabs from men prior to prostate biopsy by single-tube multi-plex test that include probes for the major multi-drug resistant clonal groups of ExPEC - ST69 and ST131, with a separate probe against ST131-H30. The results show that a rapid test could individualize antibiotic augmentation as an alternative to the potentially cumbersome logistics surrounding rectal culture in clinical practice.

Methods

Population

After IRB approval and materials transfer agreement, men presenting for TPB at the San Diego Veterans Affairs Medical Center underwent pre-transrectal prostate biopsy (TPB) rectal culture. The standard pre-TPB prophylaxis regimen included a sodium phosphate enema the morning of the biopsy and one dose of ciprofloxacin 750 mg taken approximately 1 hour prior to TPB. The provider performing the TPB collected a rectal swab from the patient immediately before placement of the rectal ultrasound probe for prostate biopsy.

Infection Identification

Surveillance for post biopsy infections included a phone call to the patient from a nurse 2–3 days after the procedure. Additionally, medical records were reviewed using a standardized instrument to extract epidemiological data and to identify infectious complications. Epidemiological data included age, race, presence of diabetes, body mass index, history of previous ciprofloxacin use, previous hospital admission, and additional antibiotics at time of biopsy. Post-TPB infection was defined as presentation to an emergency department with lower urinary tract symptoms, plus fever and/or chills, within 7 days after prostate biopsy.

Rectal Culture and Bacterial Isolation

Rectal swabs were streaked onto locally prepared ciprofloxacin-supplemented (4 mg/L) MacConkey agar plates, which were quality-controlled using fluoroquinolone-susceptible and resistant *E. coli* isolates (20). A representative culture of each distinct colonial morphotype was selected for identification and susceptibility using the Vitek 2 instrument (BioMerieux, Durham, NC) GN identification cards based on the Clinical and Laboratory Standards Institute interpretative criteria.(25) The result from the San Diego Healthcare System was used as the reference standard and was blinded to the University of Washington microbiology laboratory. The swabs used for culture were refrigerated and then mailed overnight to the University of Washington where the swabs were re-cultured for confirmation and PCR analysis. No patient identifiers were sent.

Rapid detection of *E. coli* clonal groups by the qPCR clonotyping test

The swab tip was re-suspended in 300 uL of sterile water, heated 10 min at 98°C and centrifuged at 10,000 rpm for 2 min. The supernatant was used in qPCR on Rotor-Gene Q instrument (Qiagen, Germany) in 10 uL reaction volume with 1 ul of sample added as follows: (a) Presence and load of *Escherichia coli* DNA in the fecal sample was detected with *uidA* specific primers (PrF 5'-tcttgccgttttcgtcgta, PrR 5'-cacgccgtatgttattgccg) using Rotor-Gene™ SYBR-Green qPCR (Qiagen), (b) Specific probes for *E.coli* clonal groups ST131, its sub-clone ST131-H30, and ST69 were used to detect respective *E.coli* clones in a multiplex reaction using QuantiFast® Probe PCR Kit (Qiagen) (Supplementary Table 1). Upon confirmatory culture of the swab, single colony typing was performed by sequencing *fumC* and *fimH* gene, a two-loci alternative to the MLST-based clonotyping. On average, 4 colonies were chosen for the sequence typing.

Statistical Analysis

The primary outcome was detection of fluoroquinolone resistant *E. coli* with the primary predictor variable as the rapid qPCR for the major MDR-ExPEC clonal groups. The new microbiologic test is compared to the reference standard culture result. We compare amount of bacteria present on MacConkey plates to amount noted on qPCR (colony forming units/mL) to determine correlation of the amount of resistant bacteria between the two methods using a Pearson correlation coefficient. From previous studies we know that 30% of fluoroquinolone resistant bacteria are not ST131; therefore, these bacteria will not test positive with only performing the qPCR and we expect a sensitivity of approximately 70%. (22) We calculate sensitivity, specificity, negative predictive value, positive predictive value, likelihood ratios, and an area under the receiver operative curve (AUC).

Future Clinical Utility

The clone-specific probes were initially selected due to the resistance patterns noted in urinary cultures that were not related to prostate biopsies. *E. coli* that were resistant to FQ and trimethoprim/sulfamethoxazole (T/S) were most frequently identified as clonotype ST131 and ST69. This suggested that the EST200 test could be used to identify carriers of the two clonotypes that are responsible for most Ciprofloxacin-resistance and thus identify men who need alternative prophylaxis. We also compared the resistance profiles obtained from each sequence type on rectal culture to an existing database representing 2,795 *E. coli* isolated from clinical human urine samples collected over last 5 years at hospitals worldwide.(26) The Fisher's Exact test was used to determine proportional differences regarding resistance profiles of the sequence types (rectal vs. urine isolates).

Results

Detection of *E. coli* clonal groups in fecal samples by the qPCR

We enrolled 104 men at the San Diego VA Healthcare System from 11/5/2013 to 6/10/2014. Demographics are displayed in Table 1. The qPCR test was positive in 27 of those samples and negative in all culture-negative samples (Table 2). The timing for the positive identification by qPCR was on average 30 minutes (range between 25 and 45 minutes), including 10 minutes clinical sample preparation and loading time. There were no correlation between the level of signal of the qPCR and the bacterial density on the MacConkey plate ($R^2=.04$; Supplemental Figure 1A), indicating that the tested clonotypes do not necessarily predominate in the intestinal *E. coli* populations.

Among the samples that yielded positive result in the qPCR clonotyping test, 9 were positive for ST69, 12 for ST131-H30 and 6 for ST131-non-H30 (Table 2). No samples were positive for both *E. coli* ST131 and ST69 clonal groups in any given single sample. Subsequent screening of single colonies from the agar cultures by sequence typing, confirmed presence of the *E. coli* of detected clonal groups in all but one sample (PCR-positive for ST131-non-H30). Only one sample of the 27 PCR-positives yielded two separate ST131 sub-clones - H30 and one of non-H30 sub-clones (H41). In a total of 10 samples, presence of clonotypes other than those tested by qPCR were also detected by the single colony screening (not

shown). Out of 29 *E. coli* cultures that were negative for any of qPCR clonal probes, only one yielded a test-specific clone (ST69) by the single colony screening.

Detection of fluoroquinolone resistant *E. coli*

By culture, FQ resistance was noted in 19.2% (20/104) patients. Fifteen of these samples (75%) yielded positive results in the qPCR – 4 ST69- and 11 ST131-H30-positive, with the clonal identity of the FQ-resistant bacteria confirmed by single colony screening for all but one sample (positive for ST69). In every one of the 14 confirmed samples, but one, all colonies tested from the same plate were of same clonal identity, indicating presence of a single dominant FQ-resistant strain. Indeed, in cases when the tested clonotype was FQ-resistant, there was a strong correlation ($R^2=.62$; Supplemental Figure 1B) between the bacterial load on MacConkey+FQ plate and the qPCR response level. The overall AUC of the qPCR test is 0.804. The positive and negative predictive values of the presence of FQ-resistant *E. coli* for each clonotyping probe are presented in Supplementary Table 2.

Detection of trim/sulfa resistant *E. coli*

T/S resistant bacteria were identified in 19 *E. coli* positive samples, with 12 samples yielding both T/S and FQ-resistant bacteria. Among the T/S resistant samples, 14 were positive in the qPCR test – 5 for ST69, 6 for ST131-H30 and 3 for ST131-non-H30 only. Single colony screening confirmed that the T/S-resistance was at least in part due to the tested clonotype in 4 out of 5 ST69-positive samples, all 3 ST131-non-H30 and in 5 out of 6 ST131-H30 positive samples. There were no strong correlation between the qPCR signal and the load of bacteria on MacConkey+T/S plate ($R=0.06$, Supplementary Table 1C). The overall AUC of the qPCR test to predict T/S sensitivity is 0.794. The positive and negative predictive values of the presence of T/S-resistant *E. coli* in fecal sample for each clonotyping probe are presented in Supplementary Table 2.

Correspondence of the resistance profiles between rectal and external urinary isolates

Besides the resistance to FQ and T/S, we determined resistance of the clonal fecal isolates to ceftriaxone, fosfomycin, and gentamicin, antibiotics suggested for adjunctive or alternative prophylaxis. We noted no difference resistance profiles were then compared between the fecal bacteria obtained prior to prostate biopsy compared to patients presented with urinary tract infection from a separate cohort (all $p>0.05$, Table 3). According to the profiles of both groups, ST131-H30 was almost completely (>90%) resistant to FQ, followed by intermediate (17–33%) resistance of ST69 and low (<10%) resistance of ST131-non-H30. About half of isolates in each clonal group were resistant to T/S.

Among other antibiotics, it was notable that ST131 bacteria showed intermediate (23–31%) resistance to gentamicin in both isolation groups, while 11% of ST69 were resistant to gentamicin. None of the bacteria from the tested clones were resistant to fosfomycin. Using this information to guide prostate individualized prostate biopsy prophylaxis, we constructed a hypothetical antibiotic selection chart based on bacterial clonal predicted susceptibility rates (Figure 1).

Post biopsy infection

Post prostate biopsy infection occurred in three patients in the study. One patient presented to an outside hospital and necessitated intensive care treatment due to sepsis caused by FQ-resistant *E. coli*. For this patient the pre-biopsy qPCR test was negative, with a culture screen positive for FQ-resistant *E. coli*. The second patient presented to the VA Healthcare medical center emergency department with lower urinary tract symptoms and fever. He was treated with IV antibiotics and was not admitted. He was positive on both culture and qPCR testing for ST131-H30 *E. coli*. The third patient presented to the emergency department with syncope and a positive urine culture and was admitted. The rectal culture was negative for FQ-resistant *E. coli*; however, the qPCR test was positive for the ST131-non-H30 *E. coli*.

Discussion

The qPCR technique for the identification of ST 131H30 *E. coli* has combined sensitivity and specificity for detecting FQ resistant (75%, 86%) as well as T/S resistant (74%, 85%) *E. coli* from the rectum immediately prior to transrectal prostate biopsy. We plan to investigate additional PCR probes to enhance the tests accuracy. The technology may serve as a near-patient based screening tool to predict patient's antibiotic susceptibilities to multiple antibiotics in the future. We envision a multiplex PCR test could potentially recommend patient-tailored antibiotic prophylaxis. Using the data from our pilot study we compared the resistance rates to urinary infection isolates much like an antibiogram would be used (Table 3). The information would then guide the antibiotic prophylaxis based common clonal resistance patterns based on patient specific *E. coli* clones, rather than general trends.

Our study is the first to describe this concept relating to prostate biopsy and future probes will be necessary. Using current probes, the combined sensitivity was 74–75%, specificity of 85–86%, and AUC of 0.84 for the FQ and T/S resistance detection are acceptable but need improvement. The qPCR is not currently designed to detect all FQ or T/S resistant *E. coli*, only those of the particularly common multi-drug resistant sequence types 69 and 131.(24) The qPCR test captured two of the three infections in the cohort and can be modified to include additional clonal groups.

The qPCR is the latest attempt to provide real-time antibiotic resistance probabilities to urologists to guide appropriate antibiotic selection and improve antibiotic stewardship. The current concern over prostate biopsy infections has lead a number of urologic groups to use more than one antibiotic as their prophylactic regimen. Currently, nearly 30% of urologists in a recent study admit to using two or more antibiotics for their prostate biopsy patients. (27) This practice is likely lead to worsening antibiotic resistant profiles in the future and a concerted effort should be undertaken to limit additional antibiotic to those patients at high risk of carrying MDR-ExPEC.

To this end, several studies have now shown that rectal culture is one way to improve the detection of men with colonization of resistant bacteria in the rectum prior to the prostate biopsy.(17, 19) The use of rectal culture tailored prophylaxis selection termed “targeted prophylaxis” has been tested in multiple groups and has had promising results.(28) Unfortunately, obtaining a rectal culture prior to prostate biopsy can be logistically

challenging for some practices. The optimal interval between culture and biopsy has not been established, patients may have to make an additional office visit to get cultured and this may be a hardship, and urologists will have to make a concerted effort with the clinical microbiology laboratory to have the cultures done properly and promptly in order to obtain meaningful results.

The intent of developing this qPCR based assay was to create a screening test for MDR-ExPEC that would eliminate the lag time inherent in performing rectal cultures. Understanding that culture will likely pick up most if not all of the resistant bacteria, and the qPCR will likely miss more resistant strains than culture because it is specifically targeting only the two most prevalent Cipro-resistant clones. However, ST131 accounts for 70% of the FQ resistant *E. coli* found on rectal culture in patients undergoing transrectal prostate biopsy.(22) The qPCR information would still be very useful as it provides a more individualized infection risk stratification. While not as accurate as rectal culture, we consider PCR to be an improvement to currently used hospital antibiograms. The antibiogram supplied by the nearest hospitals, and this may not be relevant to the patients undergoing prostate biopsy.

The clonal nature of resistant ExPEC provides an alternative way to predict the bacterial resistance by using clone-specific PCR markers as a surrogate for resistance testing. The latter is easier to design for robust performance in fecal swabs than detecting the mutations or the genes responsible for the resistance as there are many possible genotypes that encode a resistance phenotype.

Another advantage of clone-based vs. gene-based diagnostics is that detection of the clonal identity allows predicting not a single resistance factor but susceptibility profile to multiple antibiotics that is associated with the clonotype as was exemplified in our study (see Table 3). One antibiotic that had favorable sensitivities to the majority of clones was fosfomycin. Recent studies have indicated that fosfomycin can reach therapeutic levels in the prostate 1–4 hours after oral ingestion and may be appropriate for prostate biopsy prophylaxis.(29, 30)

Limitations of the study include the limited number of patients. However, this is a pilot study for a microbiologic test using the patients themselves as their own control in a prospective fashion. The qPCR test had to be performed at the University of Washington and, therefore, transport of cultures could result in altered results if the colony was contaminated or died in transit. The culture was obtained immediately prior to the prostate biopsy but after ciprofloxacin was taken for prophylaxis approximately 1–2 hours prior that could have biased results. The ST200 test in its current state only has a sensitivity of 75% to predict ciprofloxacin resistance and will need to be further modified to guide clinical prophylaxis regimens.

Conclusions

Compared to the reference standard rectal culture, the qPCR based test was able to provide recognition of FQ and T/S resistance prior to prostate biopsy. Probes against additional drug-resistant *E. coli* clones may be needed to improve the test characteristics and

prospective clinical trials to determine if the use of qPCR can reduce prostate biopsy infection are warranted.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements

This work was supported by the National Institutes of Health (grant no. R01AI106007) and University of Washington, Department of Microbiology (Sokurenko lab budget no. 75-5533).

References

1. Siegel R, Ward E, Brawley O, Jemal A. Cancer statistics, 2011: the impact of eliminating socioeconomic and racial disparities on premature cancer deaths. *CA Cancer J Clin.* 2011; 61(4): 212–236. [PubMed: 21685461]
2. Tal R, Livne PM, Lask DM, Baniel J. Empirical management of urinary tract infections complicating transrectal ultrasound guided prostate biopsy. *J Urol.* 2003; 169(5):1762–1765. [PubMed: 12686828]
3. Nam RK, Saskin R, Lee Y, et al. Increasing hospital admission rates for urological complications after transrectal ultrasound guided prostate biopsy. *J Urol.* 2010; 183(3):963–968. [PubMed: 20089283]
4. Patel U, Kirby R. Infections after prostate biopsy and antibiotic resistance. *BJU Int.* 2008; 101(10): 1201–1202. [PubMed: 18336605]
5. Sieber PR, Rommel FM, Agusta VE, et al. Antibiotic prophylaxis in ultrasound guided transrectal prostate biopsy. *J Urol.* 1997; 157(6):2199–2200. [PubMed: 9146614]
6. Kapoor DA, Klimberg IW, Malek GH, et al. Single-dose oral ciprofloxacin versus placebo for prophylaxis during transrectal prostate biopsy. *Urology.* 1998; 52(4):552–558. [PubMed: 9763070]
7. Feliciano J, Teper E, Ferrandino M, et al. The incidence of fluoroquinolone resistant infections after prostate biopsy--are fluoroquinolones still effective prophylaxis? *J Urol.* 2008; 179(3):952–955. discussion 5. [PubMed: 18207185]
8. Djavan B, Waldert M, Zlotta A, et al. Safety and morbidity of first and repeat transrectal ultrasound guided prostate needle biopsies: results of a prospective European prostate cancer detection study. *J Urol.* 2001; 166(3):856–860. [PubMed: 11490233]
9. Lange D, Zappavigna C, Hamidzadeh R, et al. Bacterial sepsis after prostate biopsy--a new perspective. *Urology.* 2009; 74(6):1200–1205. [PubMed: 19815258]
10. Young JL, Liss MA, Szabo RJ. Sepsis due to fluoroquinolone-resistant *Escherichia coli* after transrectal ultrasound-guided prostate needle biopsy. *Urology.* 2009; 74(2):332–338. [PubMed: 19464041]
11. Ozden E, Bostanci Y, Yakupoglu KY, et al. Incidence of acute prostatitis caused by extended-spectrum beta-lactamase-producing *Escherichia coli* after transrectal prostate biopsy. *Urology.* 2009; 74(1):119–123. [PubMed: 19464043]
12. Shigehara K, Miyagi T, Nakashima T, Shimamura M. Acute bacterial prostatitis after transrectal prostate needle biopsy: clinical analysis. *J Infect Chemother.* 2008; 14(1):40–43. [PubMed: 18297448]
13. Raaijmakers R, Kirkels WJ, Roobol MJ, et al. Complication rates and risk factors of 5802 transrectal ultrasound-guided sextant biopsies of the prostate within a population-based screening program. *Urology.* 2002; 60(5):826–830. [PubMed: 12429309]
14. Batura D, Rao GG, Nielsen PB. Prevalence of antimicrobial resistance in intestinal flora of patients undergoing prostatic biopsy: implications for prophylaxis and treatment of infections after biopsy. *BJU Int.* 2010; 106(7):1017–1020. [PubMed: 20346055]

15. Wolf JS Jr, Bennett CJ, Dmochowski RR, et al. Best practice policy statement on urologic surgery antimicrobial prophylaxis. *J Urol*. 2008; 179(4):1379–1390. [PubMed: 18280509]
16. Lee K, Kim YA, Park YJ, et al. Increasing prevalence of vancomycin-resistant enterococci, and cefoxitin-, imipenem- and fluoroquinolone-resistant gram-negative bacilli: a KONSAR study in 2002. *Yonsei Med J*. 2004; 45(4):598–608. [PubMed: 15344199]
17. Liss MA, Chang A, Santos R, et al. Prevalence and significance of fluoroquinolone resistant *Escherichia coli* in patients undergoing transrectal ultrasound guided prostate needle biopsy. *J Urol*. 2011; 185(4):1283–1288. [PubMed: 21334021]
18. Hadway P, Barrett LK, Waghorn DJ, et al. Urosepsis and bacteraemia caused by antibiotic-resistant organisms after transrectal ultrasonography-guided prostate biopsy. *BJU Int*. 2009; 104(11):1556–1558. [PubMed: 20053186]
19. Taylor S, Margolick J, Abughosh Z, et al. Ciprofloxacin resistance in the faecal carriage of patients undergoing transrectal ultrasound guided prostate biopsy. *BJU Int*. 2013
20. Liss MA, Johnson JR, Porter SB, et al. Clinical and Microbiological Determinants of Infection After Transrectal Prostate Biopsy. *Clinical infectious diseases : an official publication of the Infectious Diseases Society of America*. 2014
21. Lindert KA, Kabalin JN, Terris MK. Bacteremia and bacteriuria after transrectal ultrasound guided prostate biopsy. *J Urol*. 2000; 164(1):76–80. [PubMed: 10840428]
22. Liss MA, Peterson EM, Johnston B, et al. Prevalence of ST131 among fluoroquinolone-resistant *Escherichia coli* obtained from rectal swabs before transrectal prostate biopsy. *Urology*. 2013; 81(3):548–555. [PubMed: 23333000]
23. Johnson JR, Tchesnokova V, Johnston B, et al. Abrupt emergence of a single dominant multidrug-resistant strain of *Escherichia coli*. *The Journal of infectious diseases*. 2013; 207(6):919–928. [PubMed: 23288927]
24. Lopez-Cerero L, Navarro MD, Bellido M, et al. *Escherichia coli* belonging to the worldwide emerging epidemic clonal group O25b/ST131: risk factors and clinical implications. *The Journal of antimicrobial chemotherapy*. 2014; 69(3):809–814. [PubMed: 24123431]
25. Performance Standards for Antimicrobial Susceptibility Testing: 20th Informational Supplement M100-S20. Wayne, Pa: Clinical and Laboratory Standards Institute, NCCLS; 2010.
26. Tchesnokova V, Billig M, Chattopadhyay S, et al. Predictive diagnostics for *Escherichia coli* infections based on the clonal association of antimicrobial resistance and clinical outcome. *Journal of clinical microbiology*. 2013; 51(9):2991–2999. [PubMed: 23843485]
27. Hillelsohn JH, Duty B, Blute ML Jr, et al. Variability of transrectal ultrasound-guided prostate biopsy prophylactic measures. *The Canadian journal of urology*. 2012; 19(6):6573–6577. [PubMed: 23228295]
28. Roberts MJ, Williamson DA, Hadway P, et al. Baseline prevalence of antimicrobial resistance and subsequent infection following prostate biopsy using empirical or altered prophylaxis: A bias-adjusted meta-analysis. *International journal of antimicrobial agents*. 2014; 43(4):301–309. [PubMed: 24630305]
29. Rhodes NJ, Gardiner BJ, Neely MN, et al. Optimal timing of oral fosfomycin administration for pre-prostate biopsy prophylaxis. *The Journal of antimicrobial chemotherapy*. 2015
30. Lista F, Redondo C, Meilan E, et al. Efficacy and safety of fosfomycin trometamol in the prophylaxis for transrectal prostate biopsy. Prospective randomized comparison with ciprofloxacin. *Actas urológicas españolas*. 2014; 38(6):391–396. [PubMed: 24775812]

		Antibiotic Resistance Profile*			
Test Result		FQ	T/S	CTR	GM
Clone-specific qPCR	ST69-positive	17-33%	56-62%	5-9%	9-11%
	H30 negative	0-7%	44-57%	0-7%	29-31%
	H30 positive	91-92%	49-50%	0-17%	23-27%
	ST69- and ST131-negative	9%	18%	5%	5%

Figure 1. Hypothetical Prophylaxis Selection Algorithm

Using the individual components of the PCR and the likelihood of antibiotic resistance of those clones, an antibiotic selection profile can be made. The antibiotic selections could be made to suit the practice and practice location resistance patterns. The algorithm is hypothetical in that only 100 patients are tested in this study set and not all antibiotic were tested, such as oral cephalosporins. The likelihood of resistance comes from table 3. Green: 0–14%, Yellow: >15%, Red: 20%.

Table 1

Demographics

Demographic	Median (IQR)
Age	67 (63–70)
Body Mass Index	29.5 (25.6–32)
Prostate Specific Antigen (ng/mL)	5.62 (4.41–8.85)
Prostate Size on Ultrasound (cm ³)	53 (38.5–70)
N (%)	
Race	
White	66 (63.5)
Black	14 (13.5)
Hispanic	5 (4.8)
Asian	7 (6.7)
Other	12 (11.5)
Diabetes	20 (19.2)
Ciprofloxacin within last 6 months	13 (12.5)
Hospital Admission in the last year	9 (8.7)
Pre-biopsy Enema	103 (99.0)
Pre-biopsy Antibiotic is Ciprofloxacin	93 (89.4)
Fluoroquinolone Resistance on Rectal Culture	19 (18.3)
PCR Detected ST131 H30 E. Coli	13 (12.5)
Number of Infections	3 (2.9%)

Table 2

EST200 Test and Culture results from 104 study subjects.

Parameter	Total	ST131			ST69	Combined
		H30	Non-H30	All		
Patients	104 (100%)	12	6	18	9	
Average time of the qPCR	NA	20+/-4.2 min	20+/-4 min	NA	24+/-5.6 min	NA
MacConkey culture-positive	56 (100%)	12	6	18	9	27
Single colony confirmed	NA	12	7 ^a	18	9	27
Culture-negative	48	0	0	0	0	0
FQ plate culture-positive	20	11	0	11	4	15
FQ-R single colony confirmed	NA	11	0	11	3	14
T/S plate culture-positive	19	6	3	9	5	14
T/S-R single colony confirmed	NA	5 ^b	3 ^b	8	4	12

^a 1 sample was ST131-H30 positive in test, but had both types of single colony: ST131-H30 and ST131-other^b same sample as above had ST131-H30 T/S-S, but ST131-other T/S-

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

Table 3

E. coli clonal Antibigram

Antibiotic	SDVA Fecal Swab Isolates				Historical Multi-Institutional Urinary Tract Infection Isolates			
	ST69	ST131 H30+	ST131 H30–		ST69	ST131 H30+	ST131 H30–	Non ST69/ Non ST131
	N=11	N=13	N=7		N=133	N=186	N=89	N=1522
FQ	33%	92%	0%	0%	17%	91%	7%	9%
T/S	56%	50%	57%		62%	49%	44%	18%
CTR	9%	0%	0%		5%	17%	7%	5%
GM	9%	23%	29%		11%	27%	31%	5%
FOS	0%	0%	0%		0%	0%	0%	1%

Antibiotic resistance profiles from 104 study subjects rectal cultures compared to the collective resistance profiles of 2,795 *E. coli* isolated from clinical human urine samples over the last 5 years. There are no statistical differences between the two groups (all p>0.05).

FQ = Fluoroquinolone, T/S = Trimethoprim/Sulfamethoxazole, CTR = Ceftriaxone, GM = Gentamicin, FOS = Fosfomycin