Over the past year, our urology faculty have made great strides in understanding the mechanisms underlying urologic diseases and advancing treatments.

Among our many bench-to-bedside advances, our department is at the forefront of exploring new options for the screening, detection, and treatment of prostate cancer. Following one of the largest studies of its kind, our researchers report on the importance of conservative management as a strategy for low-risk disease, and we look at our recent experience performing focal ablation as well as radical prostatectomy. We are also testing novel compounds against prostate cancer cells, including a new type of molecule that blocks the action of genes involved in treatment-resistant prostate cancer. Other advances include innovations in reconstructive surgery as well as novel treatments for voiding dysfunction. Read on to learn more about our achievements and their potential impact on patient care.
Fewer Veterans Opting for Aggressive Treatment of Low-Risk Prostate Cancer

A recent study led by NYU School of Medicine and Manhattan VA NY Harbor Healthcare System researchers reveals that conservative management has become the preferred management option for U.S. veterans with low-risk prostate cancer.

The findings signal a reversal after decades of overtreatment for low-grade tumors and suggest that more physicians are heeding best practice guidelines.

MORE GUIDELINES-CONCORDANT CARE

The investigation was led by Stacy Loeb, MD, MSc, assistant professor of urology and population health at NYU Langone Health, an attending urologist at the Manhattan VA, and a member of Perlmutter Cancer Center at NYU Langone Health. Her team found that patients with low-grade tumors were far less likely to pursue aggressive treatment in 2015 than in 2005—a period when prostate-specific antigen (PSA) testing came under increasing criticism for inducing over-diagnosis leading to unnecessary treatments. Findings were published online in the May 2018 issue of Journal of the American Medical Association.

The study, one of the largest to date examining U.S. treatment patterns for low-risk disease, was based on an analysis of more than 125,000 patient records contained in the VA’s Central Data Warehouse. Patients had a mean age of 64 and mean PSA of 5.4 ng/mL.

CONSERVATIVE MANAGEMENT INCREASING IN ALL AGE GROUPS

Researchers noted a substantial rise in the use of active surveillance during the study period across all age groups. During the study period, the percentage of men younger than age 65 who opted for watchful waiting or active surveillance over surgery jumped from 27 percent to 72 percent, with a similar increase seen among older patients.

Associated with greater odds of conservative management were increasing age, black race, unmarried status, higher PSA, increasing comorbidity, and geographic region. Among men choosing conservative management, those older than 75 years, with higher PSA scores, and with greater comorbidity were more likely to receive watchful waiting as opposed to active surveillance.

This marks a historic reversal, at least at the VA, in the decades-long overtreatment of men with prostate cancers least likely to cause harm. It brings their care more in line with the latest best practice guidelines, such as those of the American Society of Clinical Oncology and American Urological Association, which discourage aggressive therapy for low-grade tumors.”

—Stacy Loeb, MD, MSc

During the study period, the percentage of men younger than age 65 who opted for watchful waiting or active surveillance over surgery jumped from 27% to 72% with a similar increase seen among older patients.
Despite the trend toward best practice adherence, certain circumstances may lead patients to prefer immediate treatment, such as an infection following the initial biopsy, says Dr. Loeb. The important point, she stresses, is for physicians and patients to carefully review all options and risks upfront and engage in shared decision-making.

“The main conclusion to be drawn from the data is that most veterans with low-risk prostate cancer are now adopting conservative management, and other American men might follow suit if counseled on the potential benefits,” says Dr. Loeb. With funding from the Prostate Cancer Foundation, Dr. Loeb and her team are creating additional tools and online education materials to improve active surveillance.

Prostate Cancer Foundation 2018 Young Investigator Awards

Danil H., Makarov, MD
assistant professor of urology and population health and director of surgical research, Department of Population Health:
Exploring Contextual Factors Associated With Effectiveness of a Physician-Centered Behavioral Intervention To De-Implement Guideline-Dissonant Prostate Cancer Imaging

David R. Wise, MD, PhD
assistant professor of medicine and urology:
Overcoming Immune Evasion in Androgen Receptor-Independent Prostate Cancer through Targeting Dickkopf-1 (DKK1)

Disclosures: All authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Dr. Loeb reported consulting for Lilly, MDxHealth, GenomeDx, and General Electric, and receiving personal fees from Astellas, Sanofi, Minomic, and Boehringer Ingelheim. Dr. Makarov reported consulting for the U.S. Food and Drug Administration. Dr. Lepor reported previously holding shares in SonaCare Medical and receiving research support from and serving on the advisory board for Genomic Health. No other disclosures were reported.
The treatment paradigm we’re currently following isn’t very effective; as a medical community, we could be doing a better job with the management of these patients—and now we have the needed insight to effectively and safely get them the deep, restorative sleep they need.”

Benjamin M. Brucker, MD
OPTIONS FOR OVERACTIVE BLADDER IN PATIENTS WITH PARKINSON’S DISEASE

Dr. Brucker also led two retrospective studies investigating alternative treatments for OAB in patients with Parkinson’s disease. Patients with overactive bladder often have distressing urinary incontinence. When patients have a neurological basis for their bladder dysfunction, the efficacy of available treatments can be difficult to assess.

To shed light on the efficacy and safety of potential treatments, Dr. Brucker and a team of researchers including Nirit Rosenblum, MD, clinical associate professor of urology and obstetrics and gynecology, and co-director of the Female Pelvic Medicine Fellowship Program, examined two therapies that have been used in OAB patients without Parkinson’s disease; one study investigated mirabegron, a novel Beta adrenoceptor agonist approved for OAB in 2012; the other examined onabotulinum toxin A injections (Botox; Allergan). While both treatments have been shown to be safe and effective for OAB, anticholinergic drugs—which increase the risk of cognitive dysfunction and adverse events—remain the standard of care for patients with Parkinson’s disease, due to lack of clinical studies.

In the first study, investigators examined records of 50 Parkinson’s patients who received daily doses of mirabegron between 2012 and 2017. After six weeks of treatment, 50 percent of patients experienced improvement, and 11 percent reported complete resolution of their OAB symptoms. The therapy was well tolerated, and median time to discontinuation (17 months) was longer than that observed in other OAB patients.

In the onabotulinum toxin A study, researchers analyzed outcomes for a cohort of Parkinson’s patients who underwent 100U injections between 2010 and 2017. Over a four week period, 79.2 percent of patients showed improved symptoms after the initial injection, increasing to 87.5 percent with repeat injection. About 12 percent of patients required clean, intermittent catheterization for urinary retention after the first injection.

The study findings were published online in May 2018 in Neurourology and Urodynamics and online in July 2018 in Parkinsonism and Related Disorders, respectively. Considering their more favorable side-effect profile compared with anticholinergics, both treatments merit further consideration as viable therapies in Parkinson’s patients with OAB, the researchers concluded.

Disclosure: Dr. Brucker is an advisor and speaker for Avadel (maker of AVOO2) as well as a speaker, advisor, and investigator for Allergan (maker of BOTOX®). He is also an investigator for ISPEN (makes medication similar to Botox) and an advisor for Watkins-Conti Products, Inc. (nothing related to these studies).

Exploring New Options for Prostate Cancer Detection and Treatment

To meet the challenges of treating prostate cancer while reducing associated risks, NYU Langone continues to lead research identifying new applications for focal ablation.
Exploring New Options for Prostate Cancer Detection and Treatment

Focal ablation, the promising minimally invasive alternative to radical prostatectomy and radiation therapy, causes fewer treatment-related complications, and may be the optimal management choice for a select group of men with clinically localized prostate cancer.

RESEARCH HOMES IN ON OPTIMAL FOCAL ABLATION CANDIDATES

Optimal management of the spectrum of prostate cancers includes a range of options, from active surveillance to whole-gland removal. In select cases, recent research points to focal ablation (FA) as a viable alternative option that can potentially control disease while preserving the patient’s sexual function.

The studies have found that FA not only achieves acceptable disease control in select patients, but also results in far fewer treatment-related complications, such as urinary, gastrointestinal, and sexual side effects, that frequently accompany radical prostatectomy or radiation therapy.

Selecting candidates for FA is based on detecting lesions with magnetic resonance imaging (MRI), which does not detect very small low-risk disease. However, MRI has been shown to identify the index (or most aggressive) tumor accurately in 93 percent of candidates for FA who underwent radical prostatectomy, according to a study led by Dr. Lepor. The study, presented at the American Urological Association Annual Meeting and published in the February 2018 issue of Urology, reported on 59 men who underwent radical prostatectomy and met the criteria for FA. Dr. Lepor found that only a small proportion of very low volume intermediate-risk cancers would have been left untreated if the men had received FA.

More recently, Dr. Lepor turned his attention to further defining oncological control following FA, an area of unmet need when it comes to evidence-based counselling for men considering FA. Dr. Lepor and his colleague James S. Wysock, MD, assistant professor of urology, acknowledged the lack of data in a comprehensive review published in the June 2018 issue of Reviews in Urology.

“More research is needed on whether untreated disease within or beyond the ablation zone will become life-threatening over time,” says Dr. Lepor.

IMPORTANCE OF FOLLOW-UP CARE CONFIRMED BY STUDY

New findings from Dr. Lepor and colleagues represent the first published data on follow-up care beyond one year in the context of FA treatment. The research, published in the June 2018 issue of European Urology Oncology, reports on quality of life and disease recurrence in 32 men who underwent PSA testing and MRI at six months and two years following laser FA.

At the two-year mark, MRI reliably identified recurrence of intermediate-risk disease in the ablation zone, investigators reported, providing compelling evidence that patients should undergo interval MRI and biopsy upon positive findings. The procedure had virtually no adverse impact on urinary or sexual function.

It can be challenging to define what constitutes significant or aggressive disease following FA, notes Dr. Lepor. For this study, investigators targeted at least four biopsies in and around the ablation zone and assigned risk based on National Comprehensive Cancer Network guidelines, as follows:

- Intermediate risk: Gleason pattern 4
- Low risk: Gleason 6 with <50 percent core involvement
- Very low risk: Gleason 6 with ≤50 percent core involvement and fewer than three positive cores.

In the study, eight patients with positive MRI were found to have cancer in the ablation zone. Of these, six were intermediate-, one low-, and one very low-risk. In patients with negative MRI findings, intermediate-risk disease was rarely detected, notes Dr. Lepor.

“The decision to perform biopsy in MRI-negative patients should be guided by whether finding low-risk disease would influence management,” he concludes.

CONCLUSIONS YIELD NEW QUESTIONS

While more research is needed, it’s clear that ongoing monitoring and testing are essential following FA, says Dr. Lepor.

“Our study provides compelling evidence that many men with a negative biopsy at six months may develop in-field recurrences at two years,” he says. “A positive MRI scan should prompt a biopsy, preferably one that is MRI-guided to the ablation zone.”

The recent follow-up study also highlights the need to refine how FA is performed and how men should be followed, notes Samir S. Taneja, MD, the James M. Neissa and Janet Riha Neissa Professor of Urologic Oncology; professor of urology, radiology, and biomedical engineering; director of urologic oncology and vice chair, Department of Urology, and genitourinary oncology program leader, Perlmutter Cancer Center.

“The fact that almost 30 percent of men in our study developed intermediate-risk prostate cancer in the ablation zone within two years is disconcerting,” Dr. Taneja says. “It suggests that the extent of the ablation zone or delivery of laser energy is inadequate and needs refining. This is consistent with data we have previously published demonstrating that MRI underrepresents the extent and size of many tumors, suggesting that MRI-targeted ablations must incorporate an adequate margin to ensure complete tumor destruction.” To that end, NYU Langone urologists now employ cryo-–ablation and high intensity focused ultrasound (HIFU) as preferred energy sources to destroy regions of the prostate harboring cancer, because they allow for reliable incorporation of wider margins around the targeted tumor.
Case Study: Innovative Robotic Approach for Managing Proximal Ureteral Strictures

Urologists at NYU Langone lead the field with expertise in the use of robotic assistance during laparoscopic repair of ureteral strictures.

Lee C. Zhao, MD, first described the technique of robotic ureteroplasty with buccal mucosal graft for management of a proximal ureteral stricture in the September 2015 issue of *Urology*.

In a current case, a 40-year-old male patient was referred to NYU Langone after undergoing multiple procedures that failed to resolve a 4 cm proximal ureteral stricture that had developed as a result of treatment with ureteroscopy and laser lithotripsy for an impacted ureteral stone. Before seeking treatment at NYU Langone, the patient underwent ureteral dilatation, endoureterotomy, and placement of a stent. After stent removal, he developed pain and hydronephrosis, necessitating nephrostomy placement at the outside institution. Using robot-assisted laparoscopy, NYU Langone urologists successfully achieved ureteral reconstruction with a buccal mucosa onlay graft.

LOCATION AND EXTENT OF STRICTURE GUIDE

SURGICAL MANAGEMENT

“At NYU Langone, we typically perform ureteroneocystostomy in patients who have distal ureteral strictures,” explains Lee C. Zhao, MD, MS, assistant professor of urology, director of male reconstructive surgery, and co-director, Transgender Reconstructive Surgery. “If the patient has a mid-ureteral stricture with sufficient bladder capacity, a Boari flap can be utilized. In patients with proximal ureteral strictures where a direct connection from the ureter to the renal pelvis is possible, pyeloplasty is performed,” Dr. Zhao continues.

“Display of buccal mucosa or an appendix flap can be used for ureteral reconstruction in large proximal strictures. If a long segment of the ureter is missing, ideal ureter transposition is a potential option, but potential bowel complications include ileus and metabolic acidosis,” he says.

“Autotransplantation may provide a solution as a last resort, although it is associated with the risk of vascular injury to the recipient vessels.”

70% of ureteral strictures are benign and iatrogenic. Most benign strictures are related to ureteral calculi.”

—Lee C. Zhao, MD

Lee C. Zhao, MD, and plastic surgeon Rachel Bluebond-Langner, MD (Photo credit: Sasha Nialla)
Preoperative anatomic assessment of the stricture includes evaluation of the degree of obstruction, relative renal function, and surrounding vascular anatomy. In this case, antegrade and retrograde pyelograms were performed to delineate the patient’s 4 cm proximal stricture (Figure 1).

“A stent may obscure the delineation between the normal ureteral segment and the stricture,” Dr. Zhao explains, “so we remove the ureteral stent before reconstruction, to allow the stricture to mature. If the patient is dependent upon a ureteral stent, we place a nephrostomy tube before stent removal.”

INTRAOPERATIVE IDENTIFICATION OF DISEASED TISSUE IS CRITICAL TO SUCCESS

After transport to the OR, the patient was placed in the flank position with the ureter exposed. Four robotic trocars were placed. Intraoperative ureteroscopy with FireFly® fluorescence imaging was performed to identify the location of the stricture (Figure 2). An incision was performed on the anterior surface of the narrowed segment of the ureter until a 4 cm opening was achieved (Figure 3).

BUCCAL MUCOSA TISSUE CHARACTERISTICS ARE IDEAL FOR URINARY TRACT RECONSTRUCTION

After measurement of the defect, a buccal mucosal graft of appropriate size was harvested from the cheek and passed into the abdomen. Buccal mucosa has a thick epithelium, and the lamina propria is highly vascularized, making it a good choice for repair of ureteral strictures.

The graft was sutured on as an onlay until the ureteral defect was covered entirely (Figure 4). An omental flap, which had been mobilized during the initial dissection, was then secured around the anastomosis at the psoas muscle and sutured to the graft to provide vascularity.

A PROMISING ALTERNATIVE TREATMENT OPTION WITH A SUCCESSFUL OUTCOME

The patient was discharged on postoperative day 1, and the ureteral stent was removed after four weeks. The patient had complete resolution of flank pain. Subsequent renal ultrasound showed no hydronephrosis, and renal scan demonstrated good drainage. This case and other case reports and series demonstrate the expansion of treatment options and improved patient outcomes achieved through the use of laparoscopy with robotic assistance in the performance of challenging urologic surgeries.

Figure 1. Antegrade and retrograde pyelogram showing a 4 cm proximal ureteral stricture.
Figure 2. Ureteroscopy performed to identify the exact location of the stricture. Turning on FireFly® fluorescence imaging was performed to identify the location of the stricture (Figure 2). An incision was performed on the anterior surface of the narrowed segment of the ureter until a 4 cm opening was achieved (Figure 3).
Figure 3. Incision of the narrowed ureter reveals a 4 cm segment of stricture.
Figure 4. The buccal mucosa graft sutured as an onlay to reconstruct the ureteral segment.

A new type of molecule blocks the action of genes that drive the growth of therapy-resistant prostate cancer, a new study finds.
Rather than continue making compounds that are just like older drugs, the focus of our work has been to rethink the definition of what a drug-like molecule can be.”  
—Susan K. Logan, PhD

The researchers also wanted to show that their lead compound could block beta-catenin signals in a live animal. They chose zebrafish, in which rare genetic changes (mutations) that let beta-catenin build up are known to keep eyes from forming. In repeated experiments in fish with such mutations, the team found that their looping peptides—by blocking overactive beta-catenin:TCF interactions—similar to those affecting human prostate cancer—rescued eye development.

Furthermore, the treatment showed no toxicity in zebrafish at the rough equivalent of a dose that may work clinically in humans. Moving forward, the team will soon test their peptides on human prostate cancer cells grown in mice. In addition, tests are planned to see if the compound can block the beta-catenin:TCF interactions known to encourage growth in colon and breast cancers.
AWARDS & RECOGNITION

David S. Goldfarb, MD, holds several leadership positions in the field of nephrology. He is on the editorial board of the Clinical Journal of the American Society of Nephrology and a past president of the Research on Calculus Kinetics Society.

William C. Huang, MD, continues as co-director of the NYU Langone Robotic Urology Surgery Center. Dr. Huang uses robotic surgical techniques to minimally invasive surgeries to remove kidney, bladder, prostate, and testicular cancers with minimal side effects and improved quality of life for patients. Dr. Huang also serves on national and international committees that publish guidelines for the management of cancers of the urinary tract.

Herbert Lopor, MD, is a co-founder and the current editor-in-chief of Reviews in Urology and is on the editorial board of Urology.

Stacy Loeb, MD, MSc, is an Associate Editor for the Journal of Clinical Oncology, European Urology, Nature Reviews Urology and Reviews in Urology. Dr. Loeb hosts the Men’s Health Show on SiriusXM 149 satellite radio, and chairs the American Urological Association Social Media Work Group. She was also recently inducted into the Association of Academic Urologists.

Danil V. Mukherjee, MD, MHS, is a member of the Society for Medical Decision Making, a diplomate of the American Board of Urology, and chair of the White Paper Committee on Implementation of Shared Decision Making into Urologic Practice of the American Urological Association. He is also a consultant for the FDA’s Center for Devices and Radiological Health.

Samar S. Taneja, MD, is a consulting editor for the Urologic Clinics of North America and is on the editorial board of European Urology. He was recently inducted into the American Association of Genitourinary Surgeons.

Referenced Publications


ANNOUNCING

Tuition-Free Initiative Addresses High Student Debt

NYU School of Medicine announced in August 2018 that it will begin offering full-tuition scholarships to all current and future students in its MD degree program regardless of need or merit—a bold effort to simultaneously address the rising costs of medical education and still attract the best and brightest students to careers in medicine. “This decision recognizes a moral imperative that must be addressed,” says Robert I. Grossman, MD, the Saul J. Farber Dean of NYU School of Medicine and CEO of NYU Langone Health. “It addresses High Student Debt.”

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