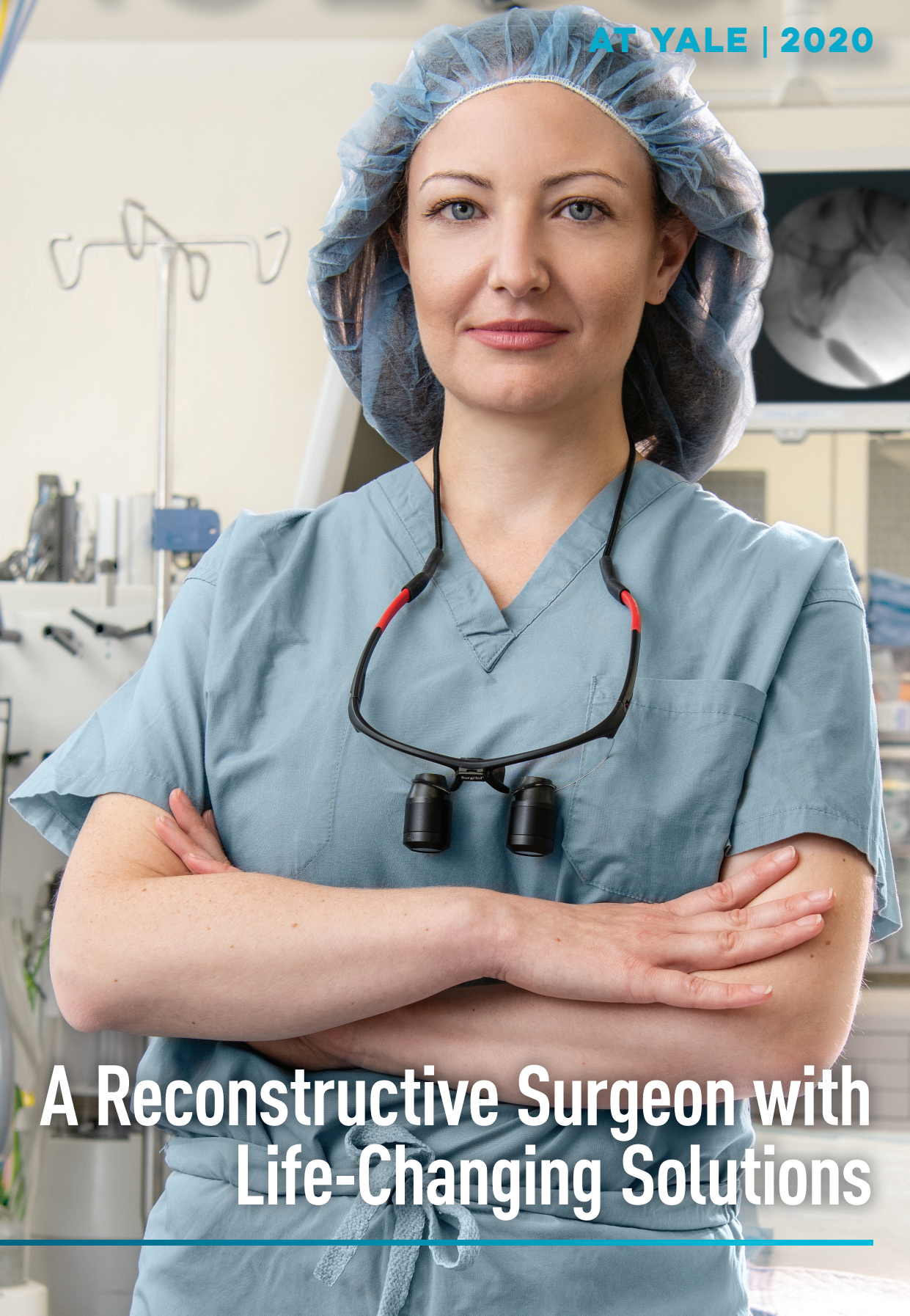


UROLOGY

AT YALE | 2020



**A Reconstructive Surgeon with
Life-Changing Solutions**

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As the only male genitourinary reconstructive surgeon in Connecticut, Jaime Cavallo, MD, MPH, considers it a privilege to help men regain their confidence and quality of life. Repairing debilitating genitourinary disorders, whether urinary or sexual, requires elite skill but also, open communication with the patient and often their partner.

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A leader in drug development and a major player in identifying new chemotherapy agents that are getting better results for patients with prostate, bladder, and other cancers, Dr. Daniel Petrylak is often the person surgeons and other oncologists turn to to discuss cases. His expertise in the field has helped countless patients, mentored trainees, and he is continually pushing to develop new treatments.

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Typically, men with extremely enlarged prostates have limited, often morbid, options for treatment. Now, Yale New Haven Hospital is the first medical center in Connecticut to offer a minimally invasive procedure known as HoLEP, bringing men relief with faster recovery time.

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“While we continue to refine and expand our goals, our commitment to patient-centric, innovative care remains steadfast.” – Peter G. Schulam, MD, PhD

2019 was filled with opportunity and growth across our clinical practices and throughout the Yale Department of Urology. We continued to expand our footprint into new communities across Connecticut and into Rhode Island; we welcomed six new faculty, adding to our already talented pool of physicians and researchers; and we introduced new technologies and tools to help care for our patients in an effort to continually improve outcomes.

In this issue of Urology at Yale, I am pleased to share stories representing some of the impressive research and clinical transformations from our department and how they are making an impact in our local communities and beyond.

Our cover story features one of our newest faculty members to join Yale Urology, Dr. Jaime Cavallo, who brings a wealth of experience in the specialized area of male reconstructive surgery. As the only such surgeon in Connecticut, Dr. Cavallo shares her unique approach to improving the lives of her patients. Dr. Daniel Petrylak is


highlighted on the heels of his groundbreaking clinical research, which led to the FDA approval of the drug enfortumab vedotin for bladder cancer. A highly-respected member of the department who provides faculty with mentorship and guidance when needed, Dr. Petrylak is a thought leader advancing patient care worldwide.

Dr. Daniel Kellner, a male urologist, has made significant strides when it comes to helping men with benign prostatic hyperplasia (BPH). Dr. Kellner’s specialized training in the HoLEP procedure has brought relief to many men who have exhausted standard of care options. Technology continues to provide benefits to patients. Dr. John Onofrey is using his coding expertise to develop artificial intelligence and improve upon prostate imaging for more precise biopsies when cancer is suspected. Our telehealth program is using technology to give the gift of time back to our patients through video visits with their physician.

And lastly, the generous support of our advisory group has been a valuable asset to our growth and

our ability to support unfunded missions within the department. Their feedback and funding has provided our faculty with numerous opportunities and we are so grateful for their involvement now and for the future.

While we continue to refine and expand our goals, our commitment to patient-centric, innovative care remains steadfast. I hope you enjoy this issue of Urology at Yale and I look forward to sharing our new advances and breakthroughs in the year to come.

Most sincerely,

Peter G. Schulam, MD, PhD
Chair, Department of Urology
Yale School of Medicine
Chief of Urology
Yale New Haven Hospital

Telehealth Visits Channel Care Directly to Patients at Home



The post-op period can be a delicate time for urology patients. They may be in pain, on medication, and unable to get around easily. To accommodate patients’ needs during this sensitive period in their recovery, Yale Urology now offers a telehealth service. These secure, password-protected video visits using a smart phone or computer for communication between a doctor and patient provide a high level of care for post-op appointments but enable patients to remain in the comfort and convenience of their own home or office.

When Yale Urology launched its telehealth service early in 2019, it joined an institution-wide implementation across Yale Medicine to provide patients with easier, faster access to healthcare. “We felt it was very important for us to offer this service to our patients,” said Patrick Kenney, MD, Clinical Vice Chair, Department of Urology. Dr. Kenney spearheaded the launch with urologist Marianne Passarelli, MD, the physician lead. “Our goals were to not only address the patient experience, but to be able to provide truly outstanding care in an efficient way that decreases the barriers that can exist between patients and their providers.”

Telehealth offers multiple benefits for patients—starting with a tremendous time and cost savings. “We share our patients’ concerns about the total cost of care, including missed days from work and travel time,” Dr. Kenney said. “We know that our average in-person follow-up visit, which is a 15-minute visit, takes several hours of a patient’s day.” In contrast, patients can schedule the brief telehealth appointment during their lunch or coffee break and then continue on with their day. A survey of Yale Medicine telehealth patients found that 100 percent of patients saved at least 30 minutes by having a video visit; the majority saved two to three hours.

The convenience of telehealth is especially important during the post-op period. “After surgery, some patients can’t drive and there may not be a family

member available to bring them to the office,” Dr. Kenney explained. “They might still be having pain that makes riding in a car uncomfortable. The principal aspects of a post-op visit—discussing a pathology report, learning about their symptoms, setting a plan for the future—can just as well be accomplished through a telehealth visit as it can in the office. And since this is a video visit, we can still see the patient, get a sense of their overall well-being, and visually inspect the appearance of their surgical site.”

That convenience extends to the scheduling process. Patients can schedule their telehealth visits through their MyChart portal, which they already use for arranging in-office visits and communicating with their care team. “From the physician’s perspective, it’s relatively seamless,” Dr. Kenney said. “It’s incorporated within existing workflows. The patient has a defined visit time and we see them just as we would if they were coming to the office.”

Dr. Kenney compares the telehealth visits to FaceTime and Skype calls and has found the technology to be easy to use for patients of all ages. “Some people might wonder whether telehealth is better suited for millennials,” he said, “but I care for people from a wide range of ages, and there are plenty of retirees and older folks who are very tech savvy and able to reap the benefits of telehealth.”

The response to telehealth from patients of Yale Urology and across Yale Medicine has been resoundingly positive. More than 200 video visits have been completed across Yale Medicine. Ninety-six percent of patients surveyed strongly agreed that video visits were easy and quality of care was the same as an in-office visit.

“Telehealth is an important instrument in our tool chest we can use in our commitment to patient-centered care,” Dr. Kenney said. “It is changing the paradigm of care, and I’m confident that this is part of the future of medicine.”

A Reconstructive Surgeon with Life-Changing Solutions

Jaime Cavallo, MD, MPH

“It’s a privilege to discuss these very personal issues with patients, address their concerns, and offer them potentially life-changing solutions.”

Genitourinary reconstructive surgery can offer hope to men when other treatments fail. Obstructive voiding, urinary incontinence, or sexual dysfunction can resist behavioral and pharmaceutical therapies, and yet, fellowship-trained surgeons who can manage these complex cases are uncommon. With the arrival of Dr. Jaime Cavallo to Yale Urology, a fellowship-trained surgeon from the Lahey Clinic and the only male genitourinary reconstructive surgeon in Connecticut, her skill promises to be life-changing for patients.

“The ability to make a very dramatic improvement in a patient’s quality of life” is why Dr. Cavallo chose genitourinary reconstructive surgery. “There are many aspects of these genitourinary disorders, whether they be urinary or sexual or both, that can be debilitating and even embarrassing to the patient. And so, for me, it’s a privilege to discuss these very personal issues with patients, address their concerns, and offer them potentially life-changing solutions.”

“A physician must be able to engage patients in that discussion, to help them to feel comfortable talking about it, and to encourage them to be honest and open in their communication about these issues. The more information patients share with me, the more individualized a care plan I can make for them,” she said.

Men, and sometimes their partners, usually have many questions and concerns when they inquire about reconstructive surgery. The types of urologic disorders



We always start with the patients expressing what their concerns are and then

I have the opportunity to educate them about what we're capable of achieving together.

— Dr. Jaime Cavallo

Dr. Cavallo treats include urethral strictures, urinary incontinence, Peyronie's disease, erectile dysfunction, and buried penis. Ultimately, Dr. Cavallo knows that for her elite skills to make a difference, she has to help her patients navigate their options.

"Patients with severe erectile dysfunction often feel embarrassed and disconnected from their partner. Their self-esteem declines. Some may not respond to pharmaceutical therapy and this can exacerbate how they feel," she said. "It's really gratifying to know that you can offer men a procedure that, for even the most refractory cases, can allow them to have erections again. In doing so, they can reestablish connections with their partner and their quality of life improves dramatically and fairly immediately."

Among the specialized procedures Dr. Cavallo provides to patients is urethroplasty, a definitive treatment for urethral strictures. Urethral strictures are narrowings of the urethra from scar tissue that can make it difficult and painful to urinate. This scar tissue can be the result of prior interventions, inflammation, infection, injury, or other causes. The most common treatments are endoscopic procedures, such as urethral dilation and direct vision internal urethrotomy (DVIU), but these tend to be temporary remedies because they open but do not remove the scar tissue. Instead, Dr. Cavallo rebuilds the urethra using a tissue graft from the patient's own mucosa.

The treatment standard is that patients with bulbar urethral strictures less than 2 centimeters in

length should have only one endoscopic treatment before undergoing urethral reconstruction. Patients with all other types of urethral strictures should proceed directly to urethral reconstruction. Dr. Cavallo plans to focus on areas of Connecticut where patients are having multiple endoscopic treatments and will do educational outreach to physicians in those areas to update them on the permanent reconstructive solutions available to their patients.

All of the surgeries that Dr. Cavallo performs address quality of life, something she would like to see tracked using validated instruments and recorded in electronic health records—both to improve individual clinical care and to support research endeavors. Using the quality of life data, she aims to analyze the comparative effectiveness and comparative cost of available therapies. For example, some patients with Peyronie's disease, an acquired curvature of the penis, qualify for treatment with either an injectable pharmaceutical or surgery. To best inform patients about their therapeutic options, Dr. Cavallo believes that the treatments should be compared with respect to cost as well as effectiveness using both objective measurements and patient-reported outcomes. Only then can treatment options be placed in the context of a patient's personal goals of care.

Dr. Cavallo completed a prestigious National Institutes of Health (NIH)-funded KM1 Comparative Effectiveness Research Career Development Award and is interested in evaluating

the comparative success of various interventions in urology, where new techniques and devices are abundant. As a health services researcher, Dr. Cavallo also studies how to use study results to inform physician-patient shared decision-making, and how to disseminate and implement changes in clinical practice guidelines to practitioners nationwide to eliminate practice variation.

Dr. Cavallo is the eighth woman to join the Urology faculty at Yale. Since her arrival, third-year Urology resident, Dr. Marianne Casilla-Lennon, has begun to consider a career in male genitourinary reconstructive surgery. "She's an amazing mentor, and I'm very happy she's here," said Dr. Casilla-Lennon, who will have the opportunity to assist Dr. Cavallo in surgery. She will also collaborate with Dr. Cavallo on research, including a look at the representation of women within the field of urology. "There were some places I interviewed that had zero women on faculty," said Dr. Casilla-Lennon.

For Dr. Cavallo, as the first person in her family to attend college, teaching residents is a joy, as is teaching patients. She has a unique interest in educating patients with various levels of health literacy about their urologic disorders and their treatment options.

"We always start with the patients expressing what their concerns are, and then I have the opportunity to educate them about what we're capable of achieving together," she said.

Those achievements are what drive her practice. "It can be life-changing," Dr. Cavallo said. **Y**

THE DISCOVERIES ARE BIG but the applications are nuanced

When Dr. Daniel Petrylak graduated from medical school in 1985, there was little to offer in the way of chemotherapy to patients with genitourinary cancers. "For bladder cancer, there was no effective treatment," he recalled. Likewise, oncologists struggled to find treatments that were effective against prostate cancer. Three years later, as a fellow at Memorial Sloan Kettering Cancer Center, it was Dr. Alan Yagoda, acclaimed oncologist and researcher, who steered his mentee, Dr. Petrylak, towards research in prostate cancer. His influence made a career in medical oncology with a focus on genitourinary cancers particularly appealing.

"You work in areas where there's a need, and that's one of the reasons why I chose prostate cancer initially," he said. "The population is aging, and there weren't a lot of effective treatments. The need for research and advances was really apparent."

Years later, in 2012, Dr. Petrylak brought his expertise in genitourinary (GU) cancers to Yale. He is a leader in drug development and has played a major role in identifying new chemotherapy agents that are getting better results for patients with prostate, bladder, and other cancers. His wide-ranging role at Yale as Professor of Urology and of Medicine and co-director of the Cancer Signaling Networks Research Program at Yale Cancer Center, allows for the opportunity to pursue research with the hope and excitement of new discoveries and new cures. One of the most important meetings of the week for Dr. Petrylak is when the Genitourinary Tumor Board convenes, a multispecialty group of physicians who work together to develop care plans for complex patient cases. He views a multidisciplinary approach to GU malignancies as critical to personalized patient care, but the consultations do not end then.

Dr. Petrylak's patient schedule is frequently comprised of international patients from across Europe and the Middle East who fly to the U.S. for a consultation. His international role in



Daniel Petrylak, MD

cancer research has him traveling around the world to confer with colleagues and addressing symposia. As a result, the international exposure he has gained has also expanded his portfolio of patients, each of whom is seeking his experience and advice.

In addition to making big discoveries, Dr. Petrylak is especially adept at discerning small differences between patients’ diagnoses and then working with other physicians to chart optimal courses of treatment.

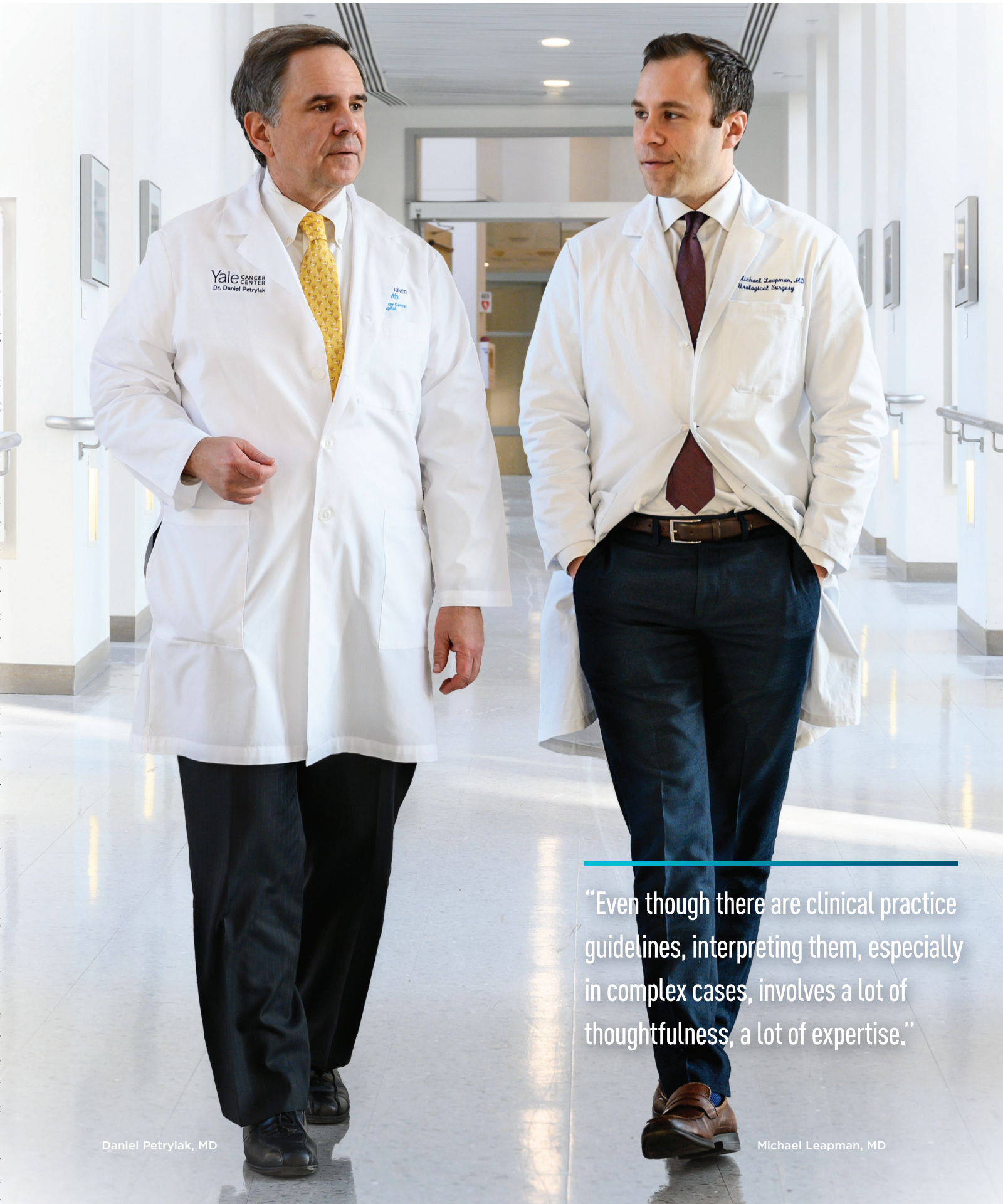
“Even though there are clinical practice guidelines, interpreting them, especially in complex cases, involves a lot of thoughtfulness, a lot of expertise,” said Dr. Michael Leapman, a Yale Urology surgeon. He described a recent patient with bladder cancer. “Because this patient was not able to receive conventional chemotherapy after surgery, Dr. Petrylak was able to enroll him on a clinical trial of a promising drug that may reduce his risk of cancer recurrence,” he said. Surgeons throughout the department share similar stories of Dr. Petrylak making a decision that was not initially obvious, but was ultimately more beneficial for a patient. Those good outcomes are exactly what Dr. Petrylak was looking for when he began his career. “It’s rewarding to see people who had a poor prognosis just a few years ago live longer,” he said.

Dr. Petrylak has access to clinical trials, led by himself or by colleagues, that may be an appropriate option for patients when conventional therapies are failing. “They do offer hope,” said Dr. John Colberg, a surgeon who specializes in prostate and bladder cancers. Dr. Colberg sends his patients to Dr. Petrylak for a consultation. Even if there isn’t a current trial, new studies tend to emerge in a matter of months providing patients with more possibilities. “Dr. Petrylak is so well-connected in the research world that he will always know of relevant trials,” Dr. Colberg said.

“In the evenings, back in the office, the faculty are all talking to Dan,” said Dr. Peter Schulam, Chair of Urology. “Some colleagues are seeking mentorship on research projects; others, on clinical cases.”

Being a resource to his colleagues at Yale while conducting national and international research collaborations takes a great deal of flexibility. “Fortunately, his phone works everywhere,” said Dr. Schulam. He spoke about texting Dr. Petrylak on a Friday, when he was just arriving in Calgary for the Annual Global Summit on Genitourinary Malignancies. They spoke and emailed over the weekend about two cases and met the following Monday at the Tumor Board. “He didn’t miss a beat,” said Dr. Schulam. “Really what surgeons want is the same thing that patients want—accessibility.”

The collaboration between medical oncologists like Dr. Petrylak and surgeons is part of a larger story that shapes the care patients with genitourinary cancers at Smilow Cancer Hospital receive. “If you’re looking



Daniel Petrylak, MD

Michael Leapman, MD

“Even though there are clinical practice guidelines, interpreting them, especially in complex cases, involves a lot of thoughtfulness, a lot of expertise.”

for great care, you’re looking for a team, not an individual,” Dr. Schulam explained. Urologists, radiologists, interventional radiologists, pathologists, medical oncologists, and surgeons must all be outstanding if patients are going to receive top-notch care. He noted that Dr. Peter Humphrey, Director of Genitourinary Pathology at Yale, is one of the foremost diagnosticians in the world. “We are all only as good as the information that we have to work with,” Dr. Schulam said.

Dr. Petrylak agrees. He believes that advanced diagnostics are the key to better outcomes in genitourinary cancers. “I think that all patients will soon have their tumors profiled molecularly, and once that’s done we can select the appropriate treatment. I think that’s where the future’s going to be,” he said.

Though his colleagues value his mentorship and collaboration, his proudest moment as a researcher came from being extremely independent. He believed that docetaxel had the potential to help men with metastatic prostate cancer. “That was a concept nobody wanted to touch,” he recalled. The manufacturer did not share his enthusiasm and declined to fund a study. So, Dr. Petrylak pieced together funding from other sources and went forward. “I was confident because of what I was seeing in the laboratory,” he said, adding with a laugh: “I know how to pick ‘em.” The drug showed a survival benefit and now has FDA approval as a prostate cancer treatment.

A certain boldness pays off. “It’s important that ideas move forward, but there are also a lot of failures. It’s difficult to predict what’s going to happen,” he said. But he added that even when patients do not respond, there is still much to learn. “The important thing is to figure out why,” he said.

Dr. Roy Herbst, Chief of Medical Oncology at Yale Cancer Center and Smilow Cancer Hospital, along with Dr. Schulam, recruited Dr. Petrylak to Yale with a vision toward making it a center for world-class research and clinical care in genitourinary cancers. Dr. Petrylak’s skill and reputation as an international leader in his field is helping to bring even more clinical and research capacity to Yale, said Dr. Herbst. Junior medical oncologists are working closely with Dr. Petrylak and developing their own programs of research with his mentorship. “It raises their game. They are working with a luminary in the field, and he certainly is that,” said Dr. Herbst.

Dr. Petrylak is “a wise voice on clinical research even outside his area,” Dr. Herbst noted. He consults with colleagues about everything from regulatory issues to managing patients in large trials.

For Dr. Petrylak, discovering treatments is an ongoing passion. Targeted therapy and immunotherapy options for genitourinary cancers need to continue to increase so that patients who do not respond to current drugs have more options. “It gives people hope,” he said. **Y**

A New Solution for BPH

When it comes to treatment of the prostate, most patients typically want to avoid invasive procedures. But when Daniel Kellner, MD, Assistant Professor of Clinical Urology at Yale School of Medicine told Max Sabrin that he would undergo HoLEP (Holmium laser enucleation of the prostate), a promising newer technique for treating benign prostatic hyperplasia (BPH), Sabrin, 66, was more than game.

“For a decade, I’d been getting up to urinate two times a night, three times a night, then, as the years passed, five times a night. I was becoming a zombie,” Mr. Sabrin, who lives with his wife in Old Saybrook, Connecticut, said. Though he tried alpha blockers, which are the standard medication for BPH, he didn’t like the side effects; they gave him headaches and made him feel congested and tired. “I even tried herbal supplements. Maybe they help some people, but for me, it was just wishful thinking.”

The fact that medication had not worked well for Mr. Sabrin doesn’t surprise Dr. Kellner. “Medical treatment for BPH fails a large proportion of patients,” he explained. Yet getting treatment for BPH can be crucial, despite the fact that the condition is considered benign. Besides causing frequent urination, irregular or weak flow, and other disruptive symptoms over time, BPH can also result in bladder damage. That was the case for Mr. Sabrin. After looking at MRI scans of his prostate, Dr. Kellner told him that his bladder was being damaged—perhaps irreversibly—because it was not emptying fully. Mr. Sabrin said, “For me, that was the point of no return.”

Typically, a normal prostate is about the size of a walnut, weighing about 20 grams. But with BPH, the prostate can get as big as a grapefruit and weigh as much as 300 to 500 grams, choking off the urethra, “like a bagel stuffed with dough in

the middle,” so the urine cannot flow normally, said Dr. Kellner. Despite its prevalence—BPH affects 50 percent of men between the ages of 51 and 60 and up to 90 percent of men older than 80—many of the current minimally invasive procedures available to treat the condition don’t work well for men with very large prostates, including the most common, so-called gold standard surgical treatment for the condition, known as TURP (for transurethral resection of the prostate). “With TURP and other procedures, you are limited as to how big a prostate you can operate on,” said Dr. Kellner. “For one thing, there can be a lot of bleeding during the TURP scraping procedure. Second, as the body absorbs all that fluid, the patient’s salt level can drop,” he explained. The bottom line: “It’s very difficult to cut away adequate tissue when you’re dealing with a very large prostate.”

There are other ways to surgically treat BPH, including open surgery, a prostatectomy. “But that’s also a very complicated procedure, and it often means spending five days or so in the hospital,” said Dr. Kellner. Instead, Dr. Kellner recommended that Mr. Sabrin choose a newer minimally invasive procedure known as HoLEP. How it works: A surgical laser is inserted through the urethra and used to remove the excess prostate tissue in a process Dr. Kellner likens to ‘peeling an orange from the inside,’ then working the tissue up and into the bladder. “This creates a generous opening, and during the process it’s easy for the surgeon to see the blood vessels and to coagulate the largest ones with the laser. That makes for a lot less bleeding—it’s a different level of control,” he explained. Next, a second instrument, known as a morcellator, cuts the tissue into smaller fragments and removes them from the bladder.

“The advantage with HoLEP is that you can

treat any size prostate, with no incisions, less bleeding, a shorter hospital stay, and better results,” said Dr. Kellner. “The excess tissue is also removed more completely than with TURP, which means there is less need for follow up treatment.” Indeed, while the retreatment rate for TURP is over 7 percent, “with HoLEP, it approaches zero,” said Dr. Kellner.

Yet, despite these advantages, surgeons in the U.S. have been slow to adopt HoLEP. “It has a steep learning curve,” explained Dr. Kellner. “Besides needing special equipment, it is a different technique than most surgeons are accustomed to, and it can be disorienting.” With TURP, surgeons can see certain landmarks with a camera which helps them check their position. In contrast, HoLEP requires the surgeon to adjust to a new orientation. “You need to be able to read the texture of the tissue—like being able to tell the orange peel from the pulp,” Dr. Kellner explained. “It takes time and dedication to get used to it.”

It didn’t faze Mr. Sabrin that this was a newer procedure to Yale. “Dr. Kellner was very matter of fact and reassuring,” said Mr. Sabrin. Indeed, Dr. Kellner trained with experts across the country, then brought the procedure to Yale New Haven Hospital, the only medical center in the state of Connecticut to offer it. “Now we are able to treat large prostates in a minimally-invasive way. We’re filling a void in terms of treatment options for men with enlarged prostates.”

Dr. Kellner performed HoLEP on Mr. Sabrin, who was released from the hospital the next day. Within two weeks or so, he was mostly back to normal, with few side effects. Best of all, six months after his surgery, Mr. Sabrin says he now gets up only once a night to urinate. “I have a clean bill of health and I’m sleeping well now,” he said. “It’s a whole new world for me.” **Y**



“HoLEP...[is] filling a void in terms of treatment options for men with enlarged prostates.”



Using AI to Make Prostate Biopsies More Accurate

John Onofrey, PhD, is on the vanguard of a new kind of precision medicine: Using machine learning to make up for the limitations of imaging technology and improve cancer detection.

Prostate cancer is the second leading cause of cancer death in men in the U.S.—which means that when a malignancy is suspected, getting an accurate biopsy is crucial. Yet the standard method for urologists to biopsy for the disease is not as accurate as it could be. Typically, a urologist will use trans-rectal ultrasound (TRUS) imaging technology to guide the needle as they do the biopsy. “But with ultrasound imaging, cancerous lesions in the prostate don’t tend to show up well,” said John Onofrey, PhD, Assistant Professor of Urology and of Radiology and Biomedical Imaging. To make up for the limitations of the ultrasound image, a urologist will generally take 12 small biopsy samples along the prostate in a 4 X 3 grid. That may seem all-encompassing, but it accounts for less than 0.5% of the volume of the prostate, explained Dr. Onofrey. “Some researchers have likened this process to a game of chance in terms of whether this technique is actually going to be able to detect cancer in a clinically significant way.”

Blame the nature of human anatomy—and of the prostate. “It’s a squishy gland,” said Dr. Onofrey. On an ultrasound, it looks different depending on how a patient moves, breathes or whether their rectum is filled with air or with stool. “That means the same features you see in an MRI show up looking completely different on an ultrasound—there’s not a one-to-one correspondence there,” said Dr. Onofrey. “Think of the prostate as a rubber ball that you can flatten out—the urologist is often left trying

to align one image from the MRI machine with a totally different ‘deformed’ image from the ultrasound. Even though the images come from the same person, they look nothing alike.”

That’s where Dr. Onofrey’s research comes in. With the right algorithms, he and his post-doctoral advisor, Xenophon Papademetris, PhD, Professor of Radiology and Biomedical Imaging and Biomedical Engineering at Yale’s School of Engineering and Applied Science, surmised that it might be possible to predict those differences—and ignore them, taking them out of the equation altogether so the two images align. To that end, Dr. Onofrey developed an algorithm based on ultrasound data from the biopsies of more than 100 patients. “Our aim was to come up with a model that could withstand the errors in the ultrasound—that would be robust in spite of those errors.”

The model they came up with, known as a non-rigid “deformation model,” acts as a template prostate, one that serves as a kind of atlas “of how the prostate changes shape between the MRI image and the ultrasound without worrying about someone’s prostate actually changing shape,” he shared. In a 2017 NIH-funded study published in the journal *Medical Image Analysis*, Drs. Onofrey and Papademetris, along with their co-authors, found that this model was “significantly robust to increasing levels of noise”—meaning that it was able to set aside inaccuracies in the image due to the ever-changing shape of the prostate gland.

More recently, in a 2019 pilot study with 20 patients at Yale and 20 patients at Stanford University, Dr. Onofrey tested his model in the clinic, alongside men undergoing prostate biopsies. For this, Dr. Onofrey collaborated with

Preston Sprenkle, MD, Associate Professor of Urology, who performs image-guided biopsies weekly at Yale. “To our knowledge, it’s the first time anyone has been able to test an algorithm right in the clinic,” he said. The advantage is that urologists can see, in real time, if what they come up with manually matches the model.

This model benefits patients by helping to ensure that urologists take their biopsy samples from the correct sections of the prostate gland, rather than a game-of-chance approach. During the pilot study, when Dr. Onofrey’s computer-generated model and the fusion model were in agreement as to the likely location of a lesion, “the urologist felt very comfortable sampling that area,” he said. And when the two methods yielded wildly different results? “That’s when the urologist could conceivably sample a wider area.”

Dr. Onofrey eventually hopes to use the data from hundreds and even thousands of prostate images to improve the accuracy of his model—and to expand its use. “There’s real power in using machine learning and artificial intelligence not to replace human beings, but to help them make more accurate decisions.” This kind of work, he says, gets to the heart of personalized, precision medicine. “It would be great to one day be able to predict patient outcomes based on what their personal history looks like, and even to be able to figure out what side effects someone might experience.”

For the time being, however, his goal is narrower, though just as significant: “To marshal the resources of Yale and all its expertise in machine learning and image processing to improve our ability to diagnose prostate cancer.” **Y**

Turning Ideas into Action: The Urology Advisory Group



Michael and Gale Silverberg

“What if?” is one of the most exciting and powerful questions in medicine. It opens minds and open doors to new opportunities, new approaches, and new treatments to benefit patients.

Over the past six years, the Urology Advisory Group has been assisting Yale Urology in transforming the “What if?” questions into action plans by supporting its strategic and philanthropic goals and raising funds for unfunded urology missions. The group’s efforts—under the leadership of chairman Michael Silverberg—have enabled Yale urologists to share their expertise with underserved patients in the New Haven community and as far afield as Uganda.

“When we started the group in December 2013, we wanted to accomplish two goals,” said Mr. Silverberg, a patient of Yale Urology and an insurance advisor in West Hartford, Connecticut. “We wanted to get the name of Yale Urology out into the community so that people know that Yale is a place to get care equal to or better than what they’d find in Boston or New York. And we wanted to raise money for situations where current Yale funding is not available. I think we’ve done a pretty good job at both.”

“WE WANT TO HELP, NOT JUST BY GIVING MONEY BUT BY GIVING OUR SUPPORT IN WAYS THAT WILL BRING PEOPLE TO YALE UROLOGY’S DOORS.”

When Mr. Silverberg was diagnosed with an aggressive form of prostate cancer in spring 2013, there was no doubt in his mind where he would seek treatment. He has had a lifelong fondness for Yale. “I was born at Grace New Haven Hospital, where Smilow Cancer Hospital is today,” he said. “It was natural for me to go to Yale.”

Nostalgia aside, Mr. Silverberg knew he’d be in skilled hands at Yale. He and his wife, Gale, had contributed to the building fund for Smilow Cancer Hospital and knew of Yale’s vast resources for cancer care. Through his involvement with the Yale Cancer Center Director’s Advisory Board, he heard a presentation by Peter Schulam, MD, PhD, and was thoroughly impressed by Dr. Schulam’s expertise.

“When I told my daughter in Ohio that I was diagnosed with prostate cancer and getting

treatment at Yale, a urologist acquaintance of hers said, ‘Wow, how did Mike connect with Dr. Schulam?’” he recalled. “I knew I was fortunate to be dealing with a nationally renowned prostate and urological surgeon.”

Under Dr. Schulam’s leadership, Yale Urology has expanded from eight to more than 30 physicians at the forefront of their field. Mr. Silverberg benefitted from the team’s advanced skills. Preston Sprenkle, MD, a pioneer in advanced imaging techniques, conducted his MRI-guided biopsy. Mr. Silverberg underwent surgery with Dr. Schulam, an expert in minimally invasive surgery. After a course of radiation, trace amounts of cancer remain in his blood. As a result, he continues on hormone treatment and closely monitors his PSA levels under the watchful eye of Daniel Petrylak, MD, a leader in the research and development of new drugs and treatments to fight urological cancers. “My care has been exceptional,” Mr. Silverberg said. “Every person I have encountered has been friendly, efficient, and caring.”

Mr. Silverberg’s gratitude for his care at Yale Urology made it an easy “yes” when he was

asked by Dick Capobianco to help launch the Urology Advisory Group in late 2013. The group of 25 volunteers meets twice a year with Dr. Schulam to hear presentations about current—and prospective—developments in Yale Urology. “To hear doctors speak about their work on such an intimate basis is extremely meaningful,” Mr. Silverberg said. A key takeaway—and key talking point for when group members take their message to the public—is the wide range of conditions treated by Yale Urology. “It’s not just about prostate cancer,” Mr. Silverberg said. “There are serious pediatric and female urological problems as well that Yale Urology has the expertise to treat.”

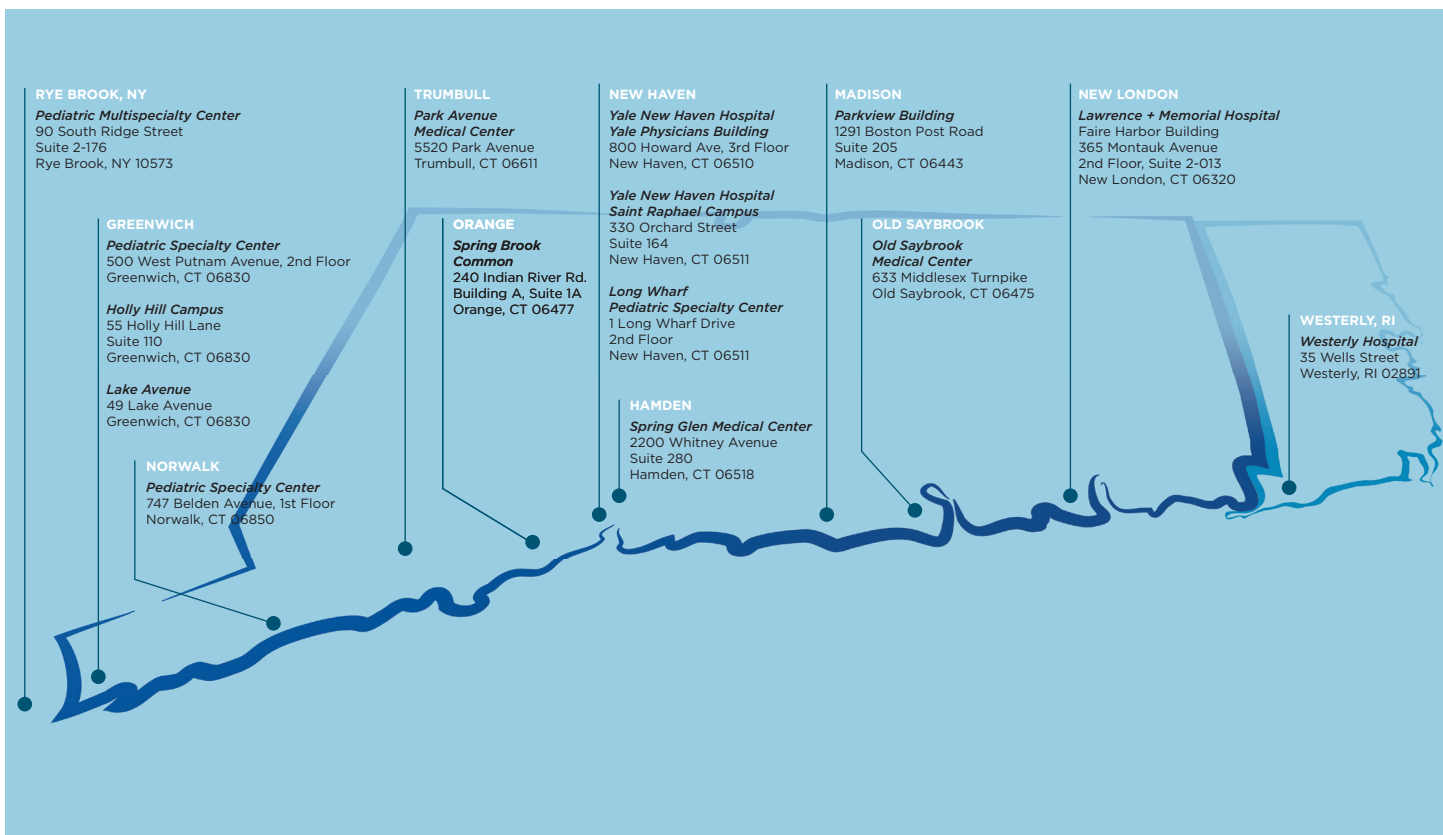
For example, one of the group’s first sponsorships was for a public information campaign about pelvic floor disorders championed by

Leslie Rickey, MD, MPH. Complications with bladder control, vaginal support, and bowel functions can happen for women at any age and be triggered by childbirth, menopause, or aging. Many women, however, do not seek treatment, either out of embarrassment, uncertainty about medical coverage, or a mistaken assumption that these conditions are a normal part of the aging process. “We helped Dr. Rickey get the word out to the general population in New Haven about these conditions and the treatment that’s available,” Mr. Silverberg said.

The Urology Advisory Group also sponsored the creation of a teaching and surgical program in Kenya that has since switched its base to Uganda. Twice per year, a Yale Urology faculty member and urology resident provide hands-on training in urological surgery to physicians in vastly under-resourced areas. The team also brings needed medical supplies. “The stories the urologists have brought back from Uganda have been unbelievable,” Mr. Silverberg said. “The types of tumors they see are staggering, but it’s what these people learn to live with because they don’t have urological care available to them.”

That outlook is now changing, thanks in large part to the support of the Urology Advisory Group. “It is a distinct pleasure working with Mike and everyone on the Urology Advisory Group,” said Dr. Schulam. “They are engaged and enthusiastic about our work and we are grateful for their support of the efforts of the physicians, researchers and staff of the Yale Urology.”

Mr. Silverberg always looks forward to hearing the next “What If?” question that Dr. Schulam might present at the upcoming Urology Advisory Group meeting. “Our members are a wonderful group of very generous, committed people who are very loyal to Yale Urology,” Mr. Silverberg said. “We want to help, not just by giving money but by giving our support in ways that will bring people to Yale Urology’s doors.”



Yale Urology Residents Fellowship placements (2012-present)

CLEVELAND CLINIC 2012
Christopher Starks, MD
Male Infertility/Microsurgery

INDIANA UNIVERSITY SCHOOL OF MEDICINE 2012
Hristos Kaimakliotis, MD
Urologic Oncology

NATIONAL CANCER INSTITUTE 2014
Amichai Kilchevsky, MD
Urologic Oncology

MEDICAL UNIVERSITY OF SOUTH CAROLINA 2014
Jaimin Shah, MD
Urologic Oncology

CITY OF HOPE COMPREHENSIVE CANCER CENTER 2015
Steven Kardos, MD
Urologic Oncology

HACKENSACK UNIVERSITY MEDICAL CENTER 2016
Gerald Portman, MD
Laproscopy/Robotics

UNIVERSITY OF MICHIGAN MEDICAL SCHOOL 2017
Nnenaya Agochukwu, MD
Health Services Research

VANDERBILT UNIVERSITY MEDICAL CENTER 2017
Sophia Delphe, MD
Female Pelvic Medicine

EMORY UNIVERSITY SCHOOL OF MEDICINE 2018
Qiaqia (Charlotte) Wu, MD
Pediatric Urology

BOSTON UNIVERSITY SCHOOL OF MEDICINE 2018
Shu Pan, MD
Reproductive Medicine

Faculty and Clinicians

Catherine M. Alonzo, MD
Angela M. Arlen, MD
Ryan Artigliere, PA
Charlotte Bell, APRN
Kelsey Bestall, PA
Leonid Bilenkin, PA
Lisa Boyd, PhD
Joseph M. Brito, III, MD
Thomas M. Buckley, MD
Marcy Cashman, PA
Jaime A. Cavallo, MD, MPH
Subha Chittamooru, PA
Jocelyn Cobb, PA
John W. Colberg, MD
Meaghan Conway, PA
Cynthia Curto, APRN
Juan DelPrado, PA
Ralph J. DeVito, MD
Erik G. Enquist, MD
Taryn Fabian, PA
Harris E. Foster, Jr., MD
Israel Franco, MD
Therese Gardere, APRN
Jenine Gesino, PA
George Hayner, PA
David G. Hesse, MD
Gillian Hepburn, PA

Adam B. Hittelman, MD, PhD
Stanton C. Honig, MD
Kristie Hotchkiss, APRN
Marissa Jacko, PA
Daniel S. Kellner, MD
Patrick A. Kenney, MD
Debra King, PhD
Megan Kolanovic, PA
Lou Kronisch, PA
Sarah M. Lambert, MD

Michael S. Leapman, MD
Franklin F. Leddy, MD
James Lunn, PA
Mary Grey Maher, MD
Rafaela Mangino, PA
Elizabeth Mann, PA
Darryl Martin, PhD
Thomas V. Martin, MD
Kaitlyn Murphy, APRN
Piruz Motamedinia, MD
Heather Nickerson, PA
Rebecca Orsulak, PA
Marianne G. Passarelli, MD, MBA
Courtney Peck, PA
Daniel P. Petrylak, MD
Brian Picciano, PA
Becky Pritchard, PA
Victor Quintanilla, PA
Thomas Rank, APRN
Joseph F. Renzulli, II, MD
Leslie M. Rickey, MD, MPH
James S. Rosoff, MD
Abbey Rumbold, PA
Heather Rynkowski, PA
Brittany Schnepf, PA
Peter G. Schulam, MD, PhD
Dinesh Singh, MD
Preston C. Sprenkle, MD
Nicholas Stroumbakis, MD
Ralph F. Stroup, MD
Marissa Sylvester, PA
Frank Toole, PA
Timothy Y. Tran, MD
Lee Venancio, PA
Robert M. Weiss, MD
Darrin Whited, PA
Dani Young, PA



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