Urologic Oncology Highlights Report 2016

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Message from the Chairman

Welcome to the 2016 update from the UPMC Department of Urology. Since becoming a department in 1999, our goal has remained the same: to become outstanding through focused clinical expertise, active clinical investigations, and exemplary basic science pursuits. In this report, our focus on urologic oncology will be evident in all three domains. Our emphasis on urological malignancies is comprehensive both in terms of the number of fellowship-trained urologic oncologists and in the programs we support. In this report, we highlight the efforts of three of our faculty members in the areas of prostate cancer, kidney cancer, and bladder cancer.

Jodi Maranchie, MD, is a true translational investigator in the treatment of kidney cancer. She was the first to identify the importance of NOX4 in the pathogenesis of prostate cancer, in addition to the critical role of HIF1-alpha in von Hippel-Lindau (VHL) mutated kidney cancer. She has translated these observations into clinical trials of hydroxychloroquine combined with IL-2 in treatment. Currently, Dr. Maranchie is examining the role of novel immunotherapy using PD-L1 inhibitors perioperatively in cases of high-risk kidney cancer. Recognizing the treatment of life-threatening kidney cancer is more than simply a task of surgeons, Dr. Maranchie has led our multidisciplinary kidney cancer clinic. Understanding both high-risk disease — through systematic evaluation of familial kidney cancer — and low-risk disease — through an active surveillance program, Dr. Maranchie has taken the plurality of this disease and developed a thoughtful approach to its management.

Benjamin Davies, MD, leads our Society of Urologic Oncology Fellowship Program. He has taken the thoughtful approach of not following the crowd, examining the practice of urologic oncology to find better ways of providing care. As multiparametric magnetic resonance imaging (mpMRI) seems to have replaced digital rectal exam in the staging of prostate cancer, Dr. Davies openly questions its global use. Indeed, he emphasizes mpMRI should be limited to men with a previous negative prostate needle biopsy with continued concerns for undiagnosed prostate cancer, and for men who have appropriately chosen active surveillance for their low-risk prostate cancer. He has been examining the best way to manage patients in the perioperative period, through our Enhanced Recovery After Surgery (ERAS) program, and by looking nationally at the cost and availability of drugs to treat urological cancer patients. Dr. Davies doesn't follow the crowd; he follows the evidence and data, precisely the approach that distinguishes the UPMC Department of Urology.

Tatum Tarin, MD, is both an innovator and educator in bladder cancer. His appointments in the University of Pittsburgh Swanson School of Engineering and the McGowan Institute for Regenerative Medicine have fueled his efforts in the noninvasive diagnosis of urothelial malignancies. He and colleagues are developing a highly sensitive — in the picomolar range — assay for gelatinase, a protein that should only be detected in invading cells. Additionally, Dr. Tarin is developing a steerable laser for the treatment of upper-tract cancers, yet another technology that may add to his seven biomedical patents. He has recognized what is widely known: radical cystectomy is a significant surgical undertaking, often in patients without the reserve to withstand its physiologic challenge. He has been systematically studying the use of nutritional supplements with high-arginine content to improve their outcomes. Dr. Tarin has shown that the fad of vaping, through e-cigarettes, is not innocuous. The levels of 6-toluidine and 2-naphthylamine, compounds associated with bladder cancer, are significantly higher in e-cigarette vapors than controls. Again, a comprehensive approach to urological malignancies is evident through the work of Dr. Tarin.

At the Department of Urology at UPMC, we remain committed to our original mandate. Our success is not only measured by our national reputation, it is seen through the programs and care we provide to our patients. I hope you will enjoy reading more about the work of our program.

Respectfully,

Joel B. Nelson, MD

Frederic N. Schwentker Professor and Chairman, Department of Urology

Chief Clinical Officer, UPMC Health Services Division

Renal Cell Carcinoma: New Findings in Basic Biology and Genetics

Jodi K. Maranchie, MD, FACS, associate professor of urology, is a fellowship-trained urologist specializing in urologic oncology. Dr. Maranchie's surgical practice covers cancers of the kidney, bladder and testis, and her basic science and clinical research is focused on kidney cancer.

Research by Dr. Maranchie has led to a better understanding of some of the genetic underpinnings of clear cell renal carcinoma, notably the implication of NOX4 induction of HIF-alpha. In several ongoing clinical correlations studies, she is pursuing therapies aimed at not only modulating NOX4 but investigating inhibitors of tumor cell autophagy, in particular with the immune-modulating compound hydroxychloroquine.

Dr. Maranchie's basic science research has set the stage for some of these ongoing clinical trials aimed at suppressing aspects of clear cell renal carcinoma tumor growth and metastatic disease courses.

Research by Jodi K. Maranchie, MD, FACS, has led to a better understanding of some of the genetic underpinnings of clear cell renal carcinoma.

"We showed that when NOX4 is absent, kidney cancer cells are unable to grow and their behavior is reverted back to that of normal, noncancerous cells."

Research Into Renal Cell Carcinoma: NOX4 and HIF-2a

Dr. Maranchie has applied significant effort as part of her research to unlocking some of the cellular and genetic pathways leading to renal cell carcinoma. Her lab was responsible for the discovery[1,2] of a basic pathway promoting clear cell renal cell carcinoma (ccRCC), which appears to be dependent upon reactive oxygen production through a gene called NOX4. "We showed that when NOX4 is absent, kidney cancer cells are unable to grow and their behavior is reverted back to that of normal, noncancerous cells," explains Dr. Maranchie.

In addition to investigating the role of NOX4 in renal cell carcinoma, Dr. Maranchie has also studied the related HIF-2a pathway. HIF-alpha, or hypoxia inducible factor alpha, appears to be quite important in the development of most clear cell renal carcinoma (approximately 85 percent of all kidney cancers are clear cell). "In clear cell renal carcinoma, HIF-alpha is oncogenic, responsible for tumor development and progression. The von Hippel-Lindau (VHL) gene is ordinarily responsible for maintaining very low levels of HIF-alpha. When VHL is lost or mutated, HIF-alpha accumulates in the cells," says Dr. Maranchie. This in turn starts the machinery to transcribe a number of other genes (more than 100) that ordinarily would not function outside of embryonic growth or cellular stress.

In a natural stress situation, such as when an organism is suddenly robbed of oxygen, the normal biological response is to express HIF-alpha, which in turn activates all the genes needed to survive without oxygen. It orchestrates creation of new blood vessels, recruitment of existing blood vessels, and a conversion to anaerobic metabolism. "This is an important survival mechanism for individual cells under stress, but when these features are turned on in a normal cell living in the close community of an organism, they result in unchecked cell division and survival. In the kidney, activation of this HIF-alpha pathway leads to kidney cancer," says Dr. Maranchie.

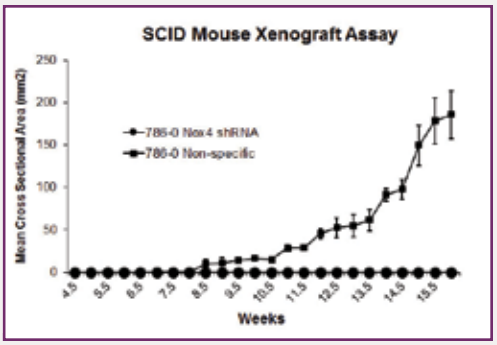
To date, clinicians have targeted specific genes regulated by HIF-alpha, notably the VEGF gene responsible for blood vessel recruitment within the tumor. Multiple agents that target VEGF are used clinically. They prevent tumor growth by limiting the delivery of blood but typically don't kill the cancer cells. This is because VEGF is just one component of HIF-alpha enhanced survival.

"I've always believed that if you could target HIF-alpha directly, you could potentially reverse the entire genetic defect supporting the cancer. It is somewhat more complicated than that, because in 2002 we showed that of the different variants of HIF-alpha, HIF-2 alpha appears to be the more relevant to kidney cancer. The big news in the past year is that we now have, from a company called Peloton Therapeutics, specific HIF-2 alpha inhibitors that can be tested in multicenter clinical trials here and around the world," says Dr. Maranchie.

Clinical Correlation Studies — Looking for Answers

Dr. Maranchie is currently conducting a number of clinical trials in renal cell carcinoma. One such trial (see references at the end of this article) was initiated by her and others at the University of Pittsburgh that is looking at cellular autophagy as a tumor survival mechanism. A phase III clinical trial is studying a combination of I-L2, an immune-stimulating cytokine with

Inhibition of xenograft tumor growth after Nox4 silencing.



the drug hydroxychloroquine, which is an inhibitor of autophagy. "In this ongoing trial, we are using this combination therapy in the setting of metastatic kidney cancer. Preliminary results are promising, and we are very optimistic of this approach as the trial progresses," says Dr. Maranchie. Preliminary results of this study will be presented at the 2017 GU ASCO Symposium.

Another group of trials that Dr. Maranchie is involved with are exploring the roles of immune checkpoint inhibitors in genitourinary cancers. Tumor cells express the checkpoint protein, PD-L1, which binds to PD-1 on T cells to block recognition by the immune system. In essence, PD-L1 acts as a cloaking device for the tumor cells. "Anti-PD-1/PD-L1 checkpoint inhibitors, if given systemically, can uncloak the tumor and allow the immune system to see it and kill it." Dr. Maranchie comments that the PD-1 inhibitors are an exciting front in renal carcinoma research right now. Two trials of PD-1 inhibitors are currently open, and three more will open in the near future. "We will hopefully be able to offer these trials to patients at every stage of the disease — before, instead of, or after surgery, or for those with metastatic disease."

One of these trials, currently open at University of Pittsburgh, is investigating atezolizumab in the adjuvant setting. This trial is for patients with aggressive kidney cancer who have been treated by surgical nephrectomy. "In these patients, we don't see signs of cancer but we know that there is a high risk for recurrence. By giving them the agent immediately after surgery, we hope to uncloak any cancer cells that may be remaining so that the immune system can find and destroy them," says Dr. Maranchie.

A second trial, using the related agent nivolumab, will be given to patients for four weeks before surgery and then for one year after surgery. "The rationale for giving it before surgery is to ramp up the immune system while plenty of cancer cells are still present. There is a theoretical concern that if you remove the tumor first and then apply the PD-1 inhibitor, there is not really anything there for the immune system to see. It's unclear to us right now whether this is a valid concern or not, and hence our interest in both trials," explains Dr. Maranchie.

The Multidisciplinary Kidney Center

For renal cell carcinoma patients, the Multidisciplinary Kidney Center brings together services and care for patients who will require both medical oncology and surgery. The clinic, co-directed by Drs. Maranchie and Leonard Appleman, MD, affords patients the opportunity to be seen by clinicians from both areas during one coordinated visit. "We facilitate the medical encounter and make it as easy as possible for patients and their families by addressing all

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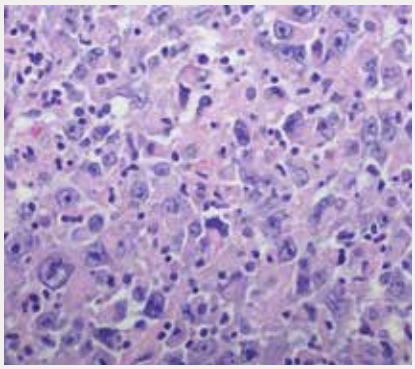
Renal cell carcinoma.



aspects of their care plan between the Department of Urology and the UPMC CancerCenter," indicates Dr. Maranchie.

For complex kidney cancer patients, having input from both sides of the care spectrum is essential. Cases are then presented at a multidisciplinary tumor board with participation from radiation oncology, pathology, and radiology. Team members, along with residents and fellows, meet regularly to review cases and discuss the best plans of care for individual patients.

Familial Renal Cancer Syndrome

One particular clinical specialty of Dr. Maranchie is patients with familial renal cancer syndrome. Approximately five percent of all patients with kidney cancer have a germ-line genetic defect that predisposes them to form kidney tumors. These patients are typically younger at presentation and often have multiple tumors involving both kidneys, which makes early diagnosis so important. "We work very closely with our cancer geneticists at UPMC CancerCenter when we suspect a patient might carry a familial cancer," says Dr. Maranchie. They assist with patient counseling and genetic testing. Identification of a germ-line defect changes patient management considerably. Because the risk of forming new tumors will last for decades, Dr. Maranchie indicates that she is very aggressive about sparing normal kidney cells and removing only the cancers. She also explains that there is a desire to avoid too many surgical procedures. "We follow the 3 cm rule established by the National Cancer Institute, observing small cancers without intervention until they reach a 3 cm threshold," says Dr. Maranchie. The goal of this approach is to strike a balance between the risk of metastasis, which is rarely seen before 4 cm in diameter, and the risk of repeated surgical procedures under anesthesia with associated loss of functioning kidney tissue.

There are, however, exceptions to this rule. Individuals diagnosed with Hereditary Leiomyomatosis and Renal Cell Cancer (HLRCC), a rare familial syndrome, must be treated aggressively and as early as possible. "If we suspect HLRCC in a patient, we proceed to surgery immediately regardless of tumor size, because this variant has been known to metastasize very early and is often lethal. We have to be vigilant of signs that might lead us to suspect a case of HLRCC," says Dr. Maranchie.

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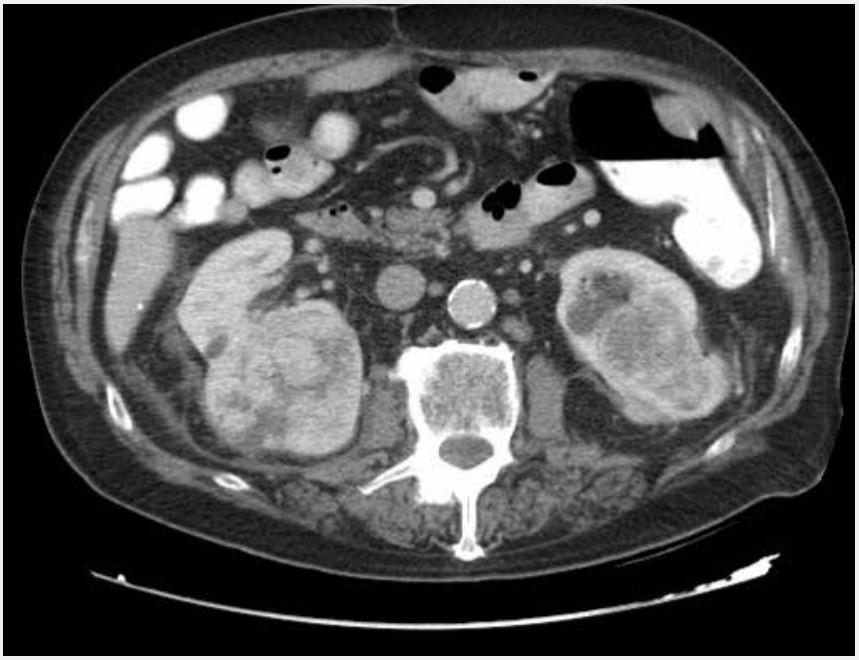

CT image of patient with familial renal cancer showing bilateral renal masses.

Surveillance for Small Renal Masses

Another front of special interest to Dr. Maranchie is surveillance for small renal masses. Recognizing that a large number of renal masses less than 2 cm in diameter are either benign or so indolent that they will never grow into a clinically significant cancer, Dr. Maranchie and her department colleagues rely on a surveillance approach. Rather than removing every small mass, she recommends to many patients a period of surveillance.

"This surveillance period helps us to distinguish which of these small masses are aggressive and require surgical intervention," says Dr. Maranchie. This approach has obvious benefits by avoiding surgeries, complications, and costs for those individuals unlikely to be affected.

The efforts of Dr. Maranchie and the Department of Urology are paving new roads in the understanding of renal cancers, and how best to treat and, in some cases, avoid overtreatment of the patients in their care.

References and Reading Resources

Specific research papers authored by Dr. Maranchie and discussed in this article are listed below.

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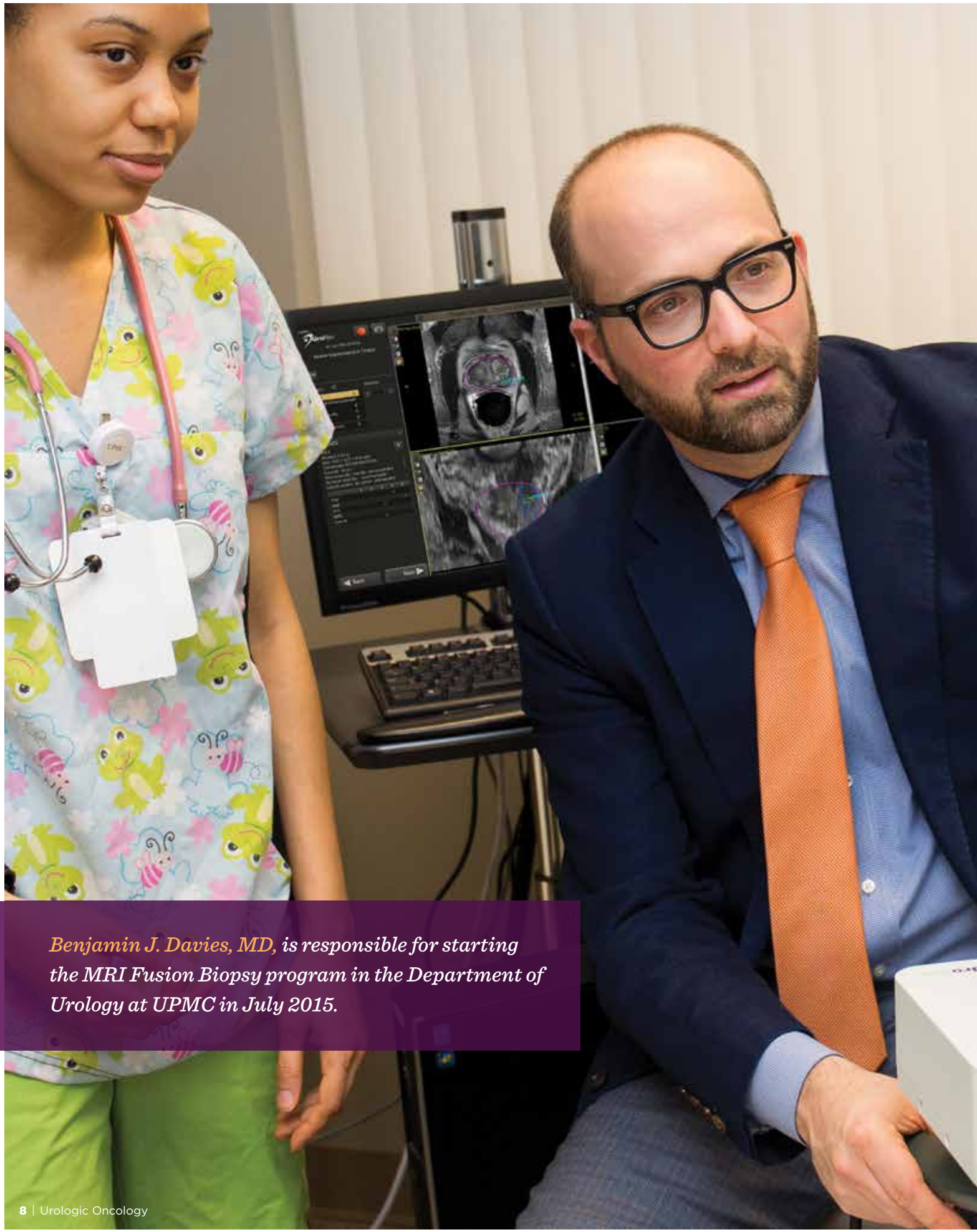


Benjamin J. Davies, MD, is responsible for starting the MRI Fusion Biopsy program in the Department of Urology at UPMC in July 2015.

Prostate Cancer and Fusion MRI Biopsy: The Next Generation in Diagnostic Testing

The world of prostate cancer diagnosis and treatment has undergone a series of significant changes over the last 10 years. Understanding who is most at risk, who should be screened and when, and even who should be treated when a tumor is detected have undergone re-evaluations, with corresponding changes in guidelines published in 2010 by the American Cancer Society, United States Preventative Task Force in 2012, and the American Urologic Association in 2012.

Technology for screening and diagnosing prostate cancer has advanced in recent years, using both DNA-level and radiographic technologies. The relatively new process of fusion biopsy, which combines both multiparametric magnetic resonance imaging (mpMRI) with ultrasound imaging to guide biopsies of specific areas of the prostate suspected to contain lesions, is changing how, and to what degree, urologists are able to accurately screen and confirm the presence of cancer from suspected tumors.

Benjamin J. Davies, MD, associate professor of Urology, chief of Urology at UPMC Shadyside, and program director of the Urologic Oncology Fellowship Program, is responsible for starting the MRI Fusion Biopsy program in the Department of Urology at UPMC in July 2015.

"Fusion MRI in prostate cancer diagnosis is really the new frontier in how to diagnose the condition, find the troublesome tumors most likely to cause a patient harm, and rule out or help us decide which patients may not need any type of intervention due to the nature of their disease."

Multiparametric MRI and Fusion Biopsy: How It Works

While the technology appears to be relatively straightforward, the benefits of prostate fusion biopsy are significant. Prostate fusion biopsy combines several elements together to more accurately diagnose the condition, and at the same time help to eliminate overdiagnosis and unnecessary treatments.

Candidate patients for the screening first have a multiparametric MRI (mpMRI) done of their prostate gland. This MRI is conducted with contrast to aid in the evaluation process. This type of MRI produces both a functional and anatomic scan of the prostate. "Essentially, what we obtain with the mpMRI scan is a phased look at the prostate, and it more accurately gives us indications of where there are potential tumors in the prostate," says Dr. Davies. "It is imperative that the mpMRI be done by experienced radiologists, which we have at UPMC."

These MRI scans capture anatomic images in the sagittal, axial, and coronal planes, and functional images and information are obtained through diffusion-weighted imaging that provides information on Brownian motion in the tissues, and dynamic contrast-enhanced images that provide an idea on tumor vascularity, among other characteristics.

Once the patient has completed the MRI scans, the urologist obtains those images and combines them with real-time ultrasound imaging during the actual biopsy procedure performed in the office or clinic. It is this combination, or fusion, of the MRI scans with the active ultrasound imaging that precisely guides which areas should be biopsied based on the suspect areas seen on the MRI scan. In the case of Dr. Davies and UPMC, the system used to conduct the procedure includes software able to "fuse" the MRI and ultrasound images together with the UroNav® EM sensor. Using a transrectal ultrasonography (TRUS) probe, the images and biopsy are conducted using the UroNav Workspot station by the urologist performing the procedure.

"This technique finds the tumors we are most interested in, but it also allows us to much more accurately differentiate those that are unlikely to be of concern for one reason or another. Fusion MRI biopsy moves us from the world of basically blind biopsies to highly targeted ones with a number of advantages for both the urologist and the patient," says Dr. Davies.

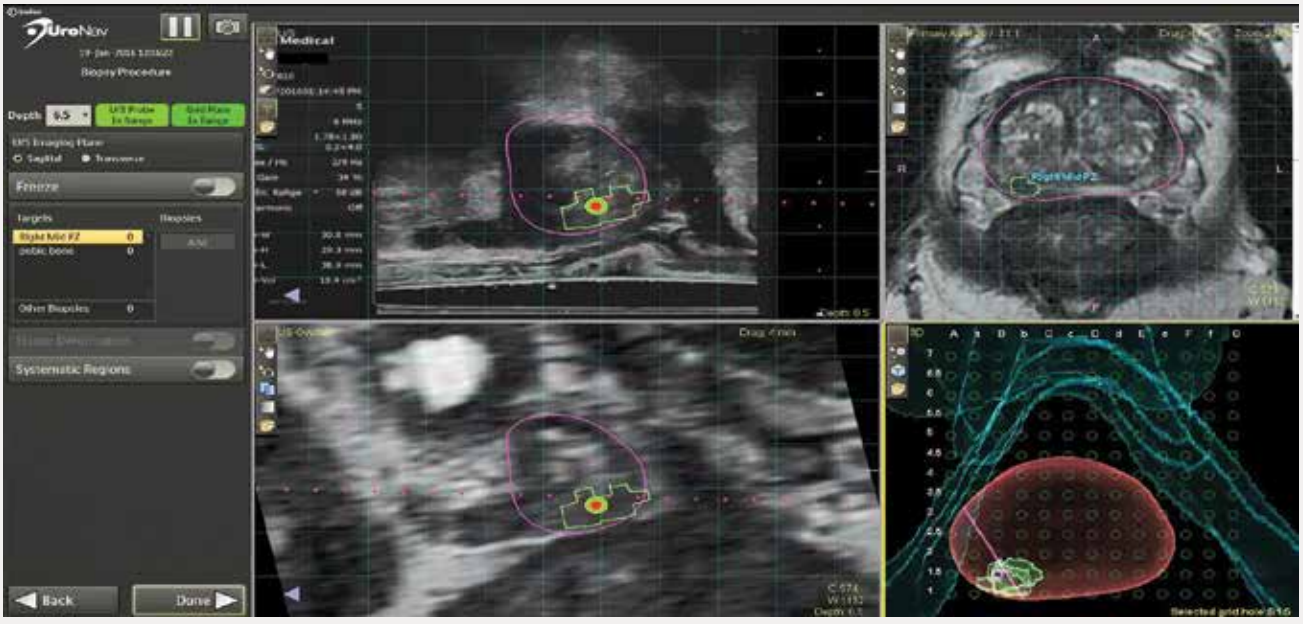
When Is Fusion Biopsy Appropriate?

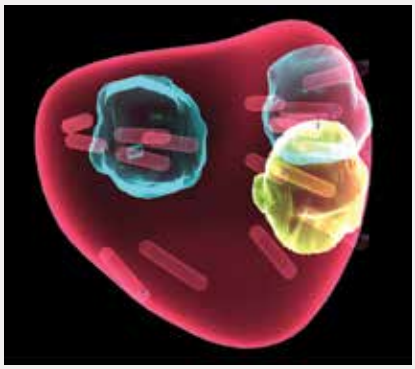
Fusion biopsy, while a powerful new diagnostic tool, is not applicable for every case of suspected prostate cancer. Certain individuals can benefit the most from the procedure. These include those individuals who have had a previous negative biopsy but have rising prostate-specific antigen (PSA) levels, and for use in cases of active surveillance. "There is a vocal group in our profession who think mpMRI should be used on everyone who has an abnormal PSA. However, as a department, we have not come to that conclusion and highly doubt this global use will be necessary," says Dr. Davies.

UroNav system used by Dr. Davies for procedures.

"Multiparametric MRI and fusion biopsy fit very well into our approach of active surveillance of tumors that we are suspicious of, but are waiting to see what happens before intervening or recommending some type of invasive treatment option for the patient. The approach of active surveillance, coupled with mpMRI and Fusion biopsy, really is able to assist us in determining who we should treat and who we should not," says Dr. Davies. This has obvious implications related to overdiagnosis, eliminating unnecessary, costly surgeries or interventions, and, again, puts the focus on those cases of prostate cancer that must be treated.

Dr. Davies, along with colleagues from the department, have recently conducted research[1] on the characteristics of biopsies and which patients are the best candidates for an active surveillance approach. "Fusion biopsy and mpMRI, in conjunction with these types of research efforts, can better help us decide who we are going to watch closely. Specifically, mpMRI does two important things for active surveillance patients. First, a negative scan is comforting since the negative predictive value of having a serious tumor is extremely low with a negative scan. Second, if there is a small tumor that is low grade, it can be followed with scans over time. It is this second idea — of following tumors on mpMRI — that is under active investigation here at UPMC and by other large research institutions. At this time, it appears safe, although we are anticipating some studies soon that will make it clearer," says Dr. Davies.





Prostate scan review image with biopsy target areas.

Measuring Efficacy of Fusion Biopsy

Dr. Davies has been collecting data on cases of fusion biopsy that he and several of his colleagues in the department have conducted since beginning the program. As of March 2017, data has been collected on 225 fusion biopsy cases.

The data being collected has two purposes. "The most important one is that it allows for more open communication and meetings with our Radiology colleagues to make sure the quality of our work is being met at the highest possible order. Second, we want to be able to quantify the type of lesions we are measuring, and whether or not they are, in fact, cancer," says Dr. Davies.

Recent Research Efforts

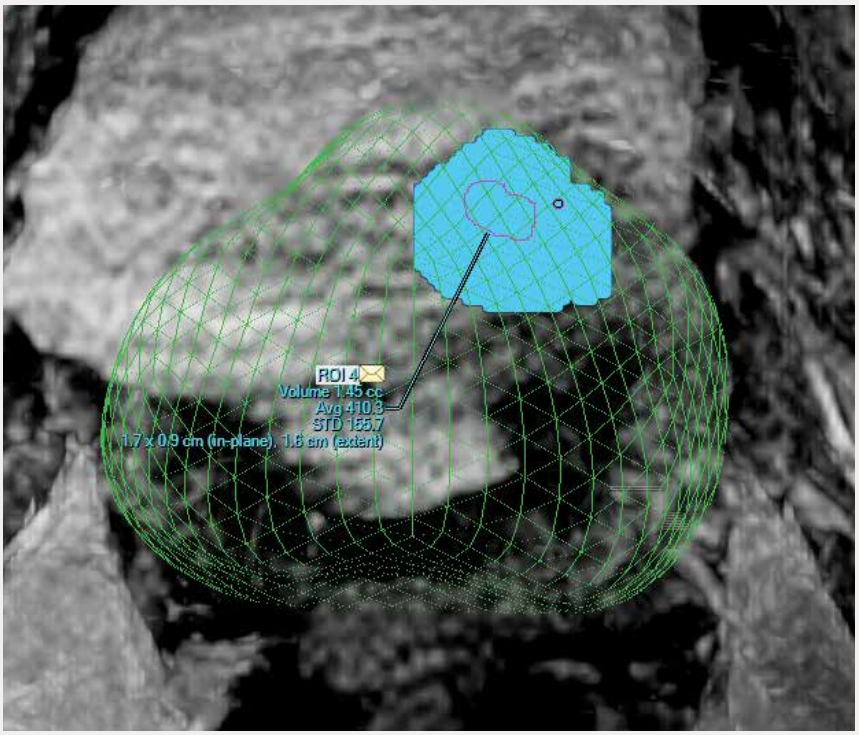
Dr. Davies has a broad range of research interests and has worked on other projects within the department to continue the evolution of urologic patient care. One such program has been the implementation of enhanced recovery after surgery (ERAS) protocols for cystectomy patients at UPMC Shadyside. This effort was started only

There is a vocal group in our profession who think mpMRI should be used on everyone who has an abnormal PSA. However, as a department, we have not come to that conclusion and highly doubt this global use will be necessary."

several months ago, but preliminary results have been encouraging thus far. Related to his ERAS adoption efforts for cystectomy patients, Dr. Davies is working on an IRB-approved opioid reduction program, designed to quantify opioid use in patients and see if usage can be reduced.

More broadly, Dr. Davies has recently completed research on generic drug pricing, describing the rise in generic pricing for bladder cancer drugs in concert with drug shortages. Dr. Davies has recently published these findings in the *New England Journal of Medicine*.

Separately, Dr. Davies is conducting two newly funded studies, the first of which is using population statistics to describe the growing disparity of care for bladder cancer between the African-American and Caucasian population in the United States. A second unrelated study is underway examining the overuse of radiology in bladder cancer patients and what the financial impact of this may be over the long term.



Biopsy scan detail with mesh overlay.

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Improving the Odds Against Bladder Cancer

Bladder cancer is at the top of the list in terms of the associated treatment costs for affected individuals. There are numerous reasons for this, including necessary long-term monitoring and a high frequency of recurrent cases. Postsurgical complications also are far too prevalent for this condition.

Tatum V. Tarin, MD, assistant professor of Urology and director of Urologic Oncology at UPMC Mercy (along with secondary appointments in the Swanson School of Engineering and the McGowan Institute for Regenerative Medicine), is applying his expertise along several fronts to improve treatment options and outcomes for bladder cancer and other urologic oncology conditions.

In addition to his clinical and research duties, Dr. Tarin also serves as the director of Medical Student Education for the Department of Urology, working extensively to teach and train new students and residents. In the recent past, Dr. Tarin established a robotic surgery development curriculum at UPMC Mercy and was the 2014 recipient of the Resident Teaching Award for his ongoing work and dedication to education and mentorship.

Tatum V. Tarin, MD, is applying his expertise along several fronts to improve treatment options and outcomes for bladder cancer and other urologic oncology conditions.

"In this trial, we are providing radical cystectomy patients with a preoperative high-arginine supplement. This approach is essentially a kind of prerehabilitative intervention for a high-risk patient cohort."

Tackling Complications of Bladder Cancer Surgery

Postsurgical complications from bladder cancer surgery occur frequently, and their monetary and physical costs can be significant. As Dr. Tarin explains, the typical bladder cancer patient cohort tends to be older and less healthy, and a large percentage of these patients are smokers. Beyond this, radical cystectomy procedures are by their very nature complex operations. "Oftentimes we are working on multiple organ systems, creating urinary diversions and removing lymph nodes; this all makes for complicated surgery. And in a population of unhealthy patients, they are more susceptible to postsurgical complications," says Dr. Tarin.

One approach to decreasing the incidence of postsurgical complications in radical cystectomy is to look for, and devise, approaches to address modifiable risk factors. One such area under investigation by Dr. Tarin is a phase two prospective clinical trial investigating the use of a presurgical nutritional supplement as a means to support and modify the immune system to reduce infection complication rates.

"In this trial, we are providing radical cystectomy patients with a preoperative high-arginine supplement. This approach is essentially a kind of prerehabilitative intervention for a high-risk patient cohort. There is evidence in the literature with colorectal surgery patients reporting lower rates of infection, and this may be a viable approach to reduce complications for our bladder cancer patients," says Dr. Tarin.

Goals of the study include measuring the safety, tolerability, and patient adherence to the supplement regimen, as well as tracking infection and complication rates 90-days post-surgery, and hospital length of stay after surgery.

Dr. Tarin's study ended in December 2016, and he and his colleagues are currently finishing data analysis and preparing to submit their results for publication in the early part of 2017. However, Dr. Tarin indicates that based on their findings from this study, plans are in progress to continue investigating this therapeutic presurgical intervention with a full, randomized clinical trial in the near future.

Novel Means of Detecting Potential Bladder Cancer

Over the last several years, Dr. Tarin has been in collaboration with Steven Little, PhD, chair of the Department of Chemical and Petroleum Engineering, and Abhinav Acharya, PhD, postdoctoral fellow in Dr. Little's department, to develop a new, highly sensitive testing technology that is able to detect trace quantities of target markers known to be important to bladder cancer.

"Working with Drs. Little and Acharya, we have been able to develop a new way to analyze bladder cancer markers in the urine. It's interesting because we have these known markers for bladder cancer, but we don't actually use them in clinical practice mainly because they have been difficult to test for, and the tests can be inaccurate," says Dr. Tarin.

This new technology, which replaces zymography and is based on combining the enzymatic activity of gelatinases in a chelated substrate, is designed to look for biomarkers in hematuria and is precise to picomolar concentrations. Current traditional screening options are problematic for reasons listed previously, not to mention the invasive nature of cystoscopy. "With this new technology, we can easily detect things at the picomolar concentration level, and we can conduct the test right in the office using a patient's urine sample," says Dr. Tarin.

Beyond the simplicity of the test, it is by any standard extremely inexpensive, costing approximately 43 cents to run. Dr. Tarin and his colleagues are working to continue development of the test, and the technology is pending patent.

This work builds off of previous research and development by the trio in a project titled, "Diagnosis of Aggressive Urologic Cancers Via Detection of MMP9 in Biological Fluids." This work, funded by the University of Pittsburgh Center for Medical Innovation, paved the way to improve and expand the technology for use as a bladder cancer screening test.

New Research — Electronic Cigarettes and Carcinogens

The number one risk factor for bladder cancer is cigarette smoking. However, little is known regarding the potential carcinogenic side effects of one of the newest products on the market, electronic cigarettes. Touted as a healthier alternative to regular cigarettes, these new devices are scarcely regulated, and even less is known about the potential health hazards they pose to their users.

"At this point, little is known about the effects of these devices and the risks involved. It's a public health concern not only for adults, but for kids who are doing it thinking it's a much safer alternative to tobacco products," says Dr. Tarin. Recently, Dr. Tarin has begun investigations, again collaborating with Steven Little and his lab, to see if they could identify any known bladder carcinogens in the urine of people using electronic cigarettes.

"At this point, little is known about the effects of these devices and the risks involved. It's a public health concern not only for adults, but for kids who are doing it thinking it's a much safer alternative to tobacco products."

"With our technology, we can steer the laser through the optical tip of the scope and control it using a computer, which allows for greater flexibility and manipulation of the device."

Dr. Tarin and his partners are among the first researchers to design such a study related to bladder cancer. Early research by this team has been able to positively identify at least two known carcinogens for bladder cancer in the urine of electronic cigarette users. Dr. Tarin is currently working on a manuscript of the research findings, and they continue to investigate the effects of electronic cigarette use in an attempt to further characterize the safety profile of the devices.

Improving Treatments With Better Device Designs

A significant area of research that Dr. Tarin has been involved with relates to the development and design of better medical technologies and devices. Dr. Tarin currently holds multiple U.S. and international patents.

One of his ongoing projects involves designing and testing the efficacy of a steerable laser device that can be used in a ureteroscope while maintaining the use of all of the other aspects of the device. "As urologists, we use a lot of scopes to treat diseases like kidney stones or tumors. The working channels of these scopes, being as tiny as they are, don't allow us to, for example, simultaneously use irrigation while using a laser to ablate a tumor we may find," says Dr. Tarin.

The new technology that Dr. Tarin and colleagues have designed allows for the laser to be used and fired through the existing optics of the ureteroscope, instead of using the one channel occupied with other features, such as irrigation. "With our technology, we can steer the laser through the optical tip of the scope and control it using a computer, which allows for greater flexibility and manipulation of the device." Testing and development of other aspects of the device are ongoing. However, if successful, this new technology will be a great leap forward in device design.

Shaping Tomorrow's Innovations and Innovators

As noted above, Dr. Tarin has a passion for innovation and technology, exploiting and improving such things as medical devices and diagnostic tests to better treat patients. One way that Dr. Tarin extends this part of his work is by helping other clinicians and students learn and advance the processes of design and commercialization of great ideas.

Dr. Tarin serves as the associate director of Clinical Affairs with the University of Pittsburgh's Center for Medical Innovation. The Center is a think tank, training ground, and research-funding body that aims to educate students, faculty, and clinicians in how to bring new biomedical ideas to fruition. The challenges and complexities of device development are numerous and sometimes daunting to individuals who have great ideas but lack the total background to navigate the multidisciplinary challenges of creating a new medical device. "One of the offerings of the center is a Master's-level graduate degree program, where we teach graduate students the entire process of medical device and technology innovation, from needs finding and brainstorming to management of intellectual property and, ultimately, commercialization," says Dr. Tarin.

References and Reading Resources

More information about Dr. Tarin's current and recent research can be found in the following publications.

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