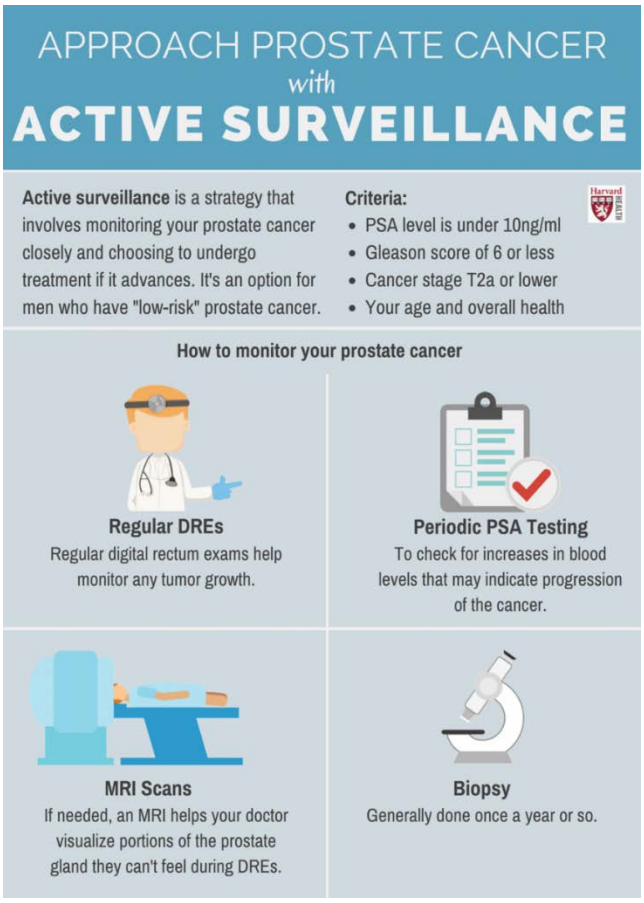
To treat or not to treat prostate cancer? A question for which answers are evolving.

Paul F. Schellhammer, M.D.

The word cancer strikes fear in the hearts of all humans. It is often whispered as the “big C”. Therefore, we can understand the anxiety of a gentleman who was told by his primary care physician that he has an elevated blood test that might suggest a prostate cancer diagnosis. That anxiety is heightened when he is sent to an urologist for discussion of diagnosis by a rather uncomfortable sounding procedure that will involve a probe placed in the rectum to direct 12 or more needle punctures into the prostate to obtain tissue for examination under a microscope. Anxiety reaches a fever pitch when a phone call is made to arrange an appointment to discuss abnormal findings. So when the patient, and very frequently his family, arrives for consultation and is told that the diagnosis of prostate cancer has been made, a decision by the patient has already been made to do something. After all, cancer societies emphasize early diagnosis of cancer and prompt treatment for best outcome. In the discussion that follows on this first office visit, and the subsequent visits that will be necessary, education and counseling will be more important than an immediate path to action. It will be necessary to ‘reset’ preconceived notions and expectations. If the cancer is identified “aggressive”, a decision as to which treatments might be appropriate (surgery, the various types of radiation therapy, the addition of “hormone” therapy) will be necessary. If the cancer is labeled “indolent/nonaggressive” than a decision to delay treatment and enter “active surveillance” is necessary. How are these identifiers of aggressive vs nonaggressive determined?



A number of characteristics garnered from the prostate biopsy will direct discussions down these two quite different pathways. Factors include, but are not limited to, the appearance of the cancer under the microscope, the extent of involvement of each of the tissue specimens, the relationship of the size of the prostate to the PSA level, and the evaluation of patient’s health, family history, age, and race. If the characteristics of tumor indicate that the benefits of treatment in the “benefits versus risk equation” outweigh the risks and side effects of therapy, then clearly “doing something”, and receiving treatment, will become the focus of education and action. This

recommendation for immediate active therapy is one that patients and families are expecting, understand and usually agree to pursue.

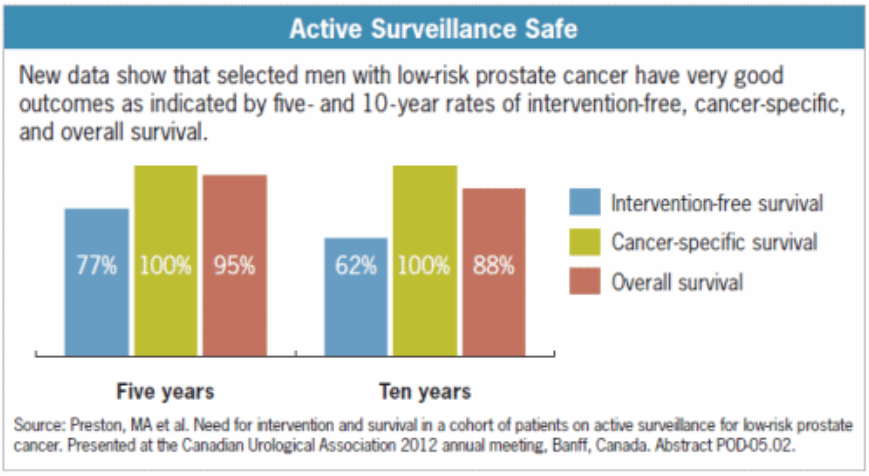
However, the recommendation of no immediate treatment, because benefits do not outweigh the risks and side effects of treatment in the “benefits versus risks equation”, is quite foreign and unsettling to patients and families. A series of questions arise:

Why is a biopsy done if no action is to be taken?

The biopsy is obtained more to determine if aggressive cancer is present rather than if any sign of cancer is present. Tissue under the microscope is necessary for the pathologist to name the cancer as indolent, slow-growing and very unlikely life threatening, versus aggressive, quickly growing and life threatening.

Are we just going to ignore and forget about this problem?

Absolutely not. The operative word in the recommendation for no immediate therapy is immediate. Your urologist will actively monitor your prostate by doing periodic PSA tests, examinations, and repeat biopsies. Genomic tests have been developed that can provide further information to support a “no immediate treatment” decision.

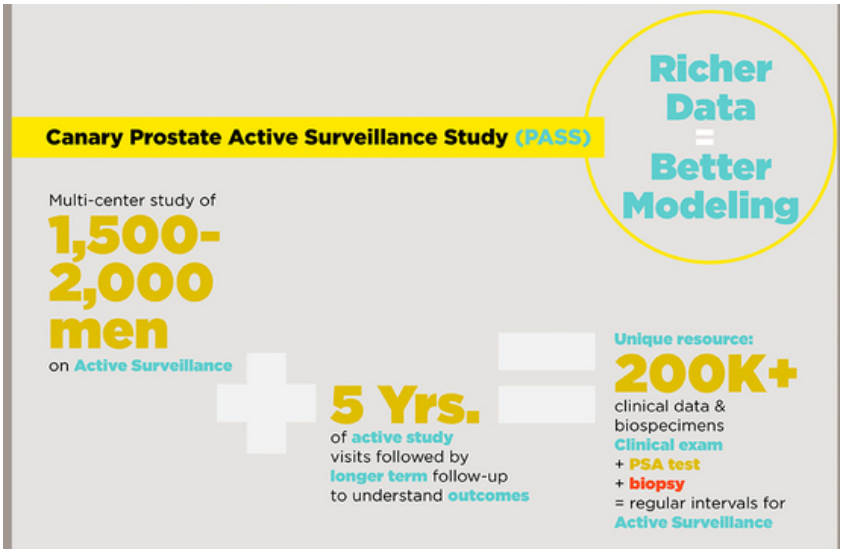


Why not just take the tiger by the tail, have therapy and avoid this monitoring and anxiety?

It may be that the anxiety level will not allow some patients to choose active surveillance. It is also important to recognize that careful monitoring after any therapy will be necessary. Therefore, the idea of “totally getting this problem out of my life” is not realistic. The rationale for active monitoring and avoiding immediate therapy is that any treatment for prostate cancer will impact quality of life in two very important areas --urinary and sexual function. It is in the discussion of these trade-offs that patient education, understanding and physician interaction is critical.

Are you alone in this situation?

Absolutely not. Urology of Virginia participates in a national program that has been established to interface with a number of other major centers in the country to enter patients appropriate for active surveillance to a registry. This program accumulates real time data and provides



feedback as to how to improve the accuracy/consistency of testing to assure best follow-up care. Patients who agree to participate are carefully monitored not only here at Urology of Virginia but by virtue of data sharing along with a large national population of patients receiving similar monitoring. In addition to Urology of Virginia and the Eastern Virginia Medical School, centers participating include The Fred Hutchinson Cancer Center at University of Washington, The University of California, San Francisco, The University of Michigan, the University of Texas Health Science Center in San Antonio, Emory University and Stanford University.

Is this active surveillance program going to become the standard for all prostate cancer patients?

Absolutely not! As we have already discussed, if the indicators point to aggressive disease where benefits of treatment outweigh the risks of treatment, then the urologist and patient discussion will focus on the effective immediate active therapy.

Dr. Langston Goes to Washington.
Josh Langston, M.D.

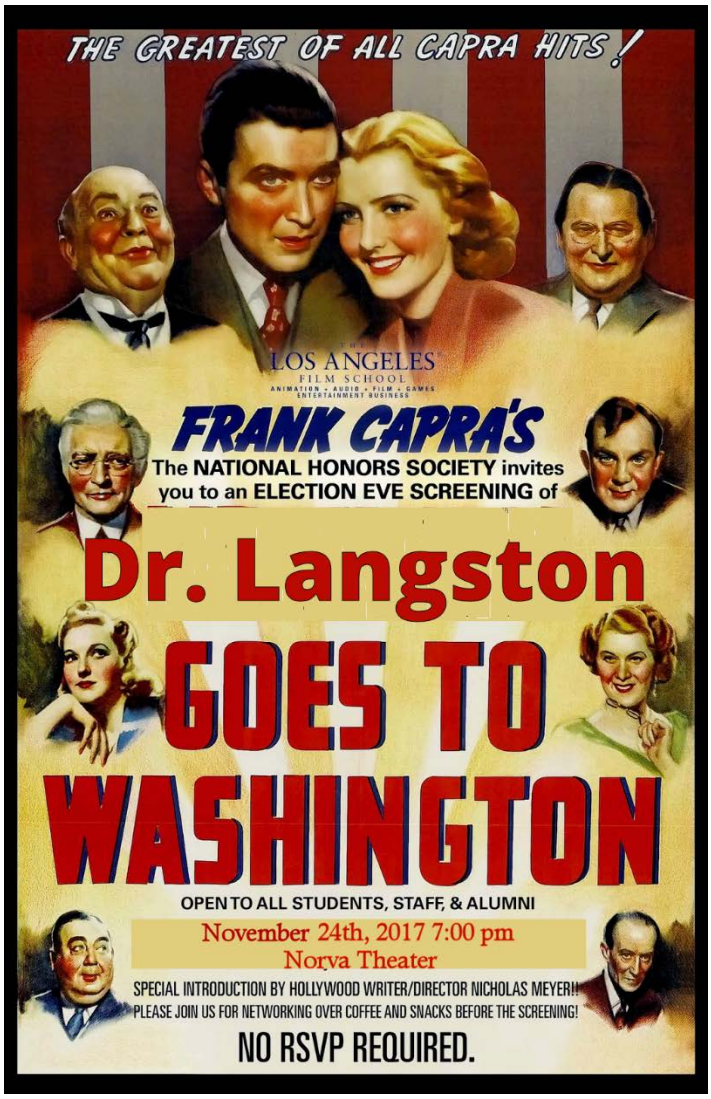
“Let’s go this way, they’re protesting me over there” Senator Cassidy said as we walked from his office to the Capitol. This was not the effect a gastroenterologist was used to having on people. Politics changes things.

This was one of the many unique experiences I had during my month working for the physician turned Senator from Louisiana. I was honored to receive the 2017 American Urological Association Holtgrewe Legislative Fellowship, and with the gracious support of the partners at Urology of Virginia I was able to take a month away from my practice to live and work in Washington. Unexpectedly, luck also had me there the month that Cassidy and Senator Lindsey Graham chose to introduce their healthcare replacement bill.

From day one the pace was intense. The bill had only 3 weeks to pass and came with an incredible number of procedural hurdles because of the budget reconciliation process they were attempting to use. This meant seemingly endless tweaks to the bill to satisfy parliamentary rules, adjust the funding model, and most importantly accommodate the concerns of colleagues on the fence.

I jumped in immediately as the staffers scrambled to crunch numbers on endless spreadsheets. I learned quickly that your iPhone calculator is useless in D.C. It doesn’t go above billions, which was the minimum dollar amount on our financial calculations. I found a useful niche as an

interpreter between the policy and press teams, and spent several days translating policy to answer reporter's questions and writing responses to criticism.



Most notable through all of this was how well Senator Cassidy knew the details of the bill. His days seemed to be split between digging through spreadsheets and then explaining and selling the bill to colleagues and the media. His knowledge of the minutiae of the bill was incredible. It was clear that his background as an academic and intellectual produced a very different type of politician. This was clear in committee hearings as well. I was told that most senators don't care much for the subject matter of a hearing, they are just looking to get a good clip for the evening news or YouTube. Senator Cassidy however loved to ask detailed questions and get into the "weeds" on an issue. This was highly unusual according to the staff, but refreshing for me to see the physician-scientist mindset applied in a different forum.

The ugly side of politics set in quickly. As initial drafts of the bill were released, analyses were done by partisan groups who knew what they wanted the message to be before they looked at the bill. Worse yet were the supposed thought leaders, like former CMS administrator Andy Slavitt, who parroted clearly false narratives to disparage the bill. It became clear that there was no premium on accuracy or truth, just on finding a way to create the story that your side wants to hear. Some of this is to be expected in politics, but when it comes to healthcare it is particularly toxic.

The bill, in brief, worked off of the idea that states knew better than the federal government how to manage the needs of their people. Further, states control much of the regulation of healthcare, as we feel often here in Virginia, so it makes sense to incentivize them to align regulations to drive down costs. The bill centered on "block grants" or a set annual amount of funding from the federal government based on a state's low-income population. It was up to the state how to structure the care it provided. The concept was based on the successful welfare reform from the Clinton era that used similar structure.

Ultimately the bill did not have the support needed to go for a vote before the deadline, but the debate over the future of healthcare in America is far from over. During my time with Senator Cassidy I accompanied him to a CNN-hosted debate, along with Senator Lindsey Graham, against Senators Bernie Sanders and Amy Klobuchar on the potential for single-payer healthcare in America versus the Cassidy plan. Ultimately, all sides care about Americans having access to affordable healthcare, but in keeping with their differing political views on the role of government they come up with different solutions. Time will tell what has the potential to work, and more importantly what Americans will support.

In my final week after things calmed down I was able to push the office toward introduction of a bi-partisan Senate bill to reform the U.S. Preventative Services Taskforce. The Taskforce is a government organization that evaluates and determines the usefulness of various screenings tests, including prostate and breast cancer, as well as other diseases. Over the decades their role has evolved to have significant impact over what is recommended and covered by Medicare and private insurance, but their structure and oversight has not mirrored this change. The calls for reform have largely been from patient and physician groups, through phone calls, letter writing, and occasionally marching in the streets! It was very clear that the Senator and his staff were attune to the voice of those advocating for the bill and motivating its progression through the political process. Momentum is hard to achieve in Congress and not possible without our voice!

Overall it was a great month to witness the internal process of lawmaking and to see the unique impact that a physician like Senator Cassidy can have in Congress. I hope the perspectives gained will benefit our group and our specialty going forward, and am very grateful to the physicians at Urology of Virginia for allowing me this opportunity.

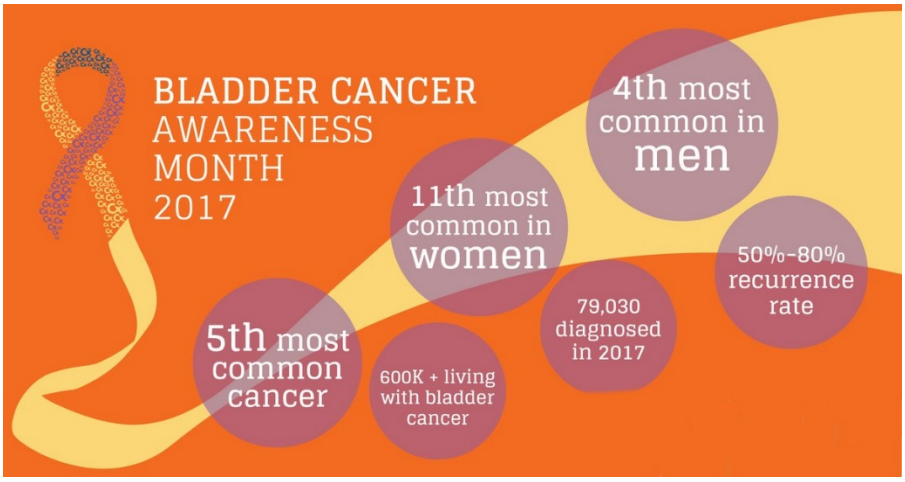
Bladder Cancer: A significant leap in outcomes on the horizon

Michael B. Williams, M.D.

When I first discuss a diagnosis of bladder cancer with a patient in clinic, they are often unaware as to the significant number of people in the United States affected by this disease. In 2017, bladder cancer ranks as the 4th most common cancer diagnosis in men and accounts for the 8th most common cause of cancer death. It uniquely affects men more than women, but this gap is closing over the last several years. Bladder cancer is a disease that has one very important risk factor: smoking. This lone factor can increase a person’s chance of becoming affected by the disease by 3-5 fold over the rest of the population.

Bladder cancer is subdivided into two different categories: non-muscle invasive, which affects the cells lining the inside of the bladder, and muscle invasive, which affects the deeper tissue of the bladder. Non-muscle invasive bladder cancer is the most common type of bladder cancer

diagnosed, accounting for ~75% of all diagnoses. It may be successfully treated by placing an active anticancer solution into the bladder. However, ~30% of patients with this type of disease will ultimately have recurrence of their bladder tumors. There have been few treatments available for them beyond bladder removal, e.g. cystectomy. A new clinical trial utilizes a completely new drug delivery system to focus on better treatment for this recurrent disease. The drug called rAd-IFNα/Syn3 (Instiladrin) utilizes interferon placed within an adenovirus (what commonly causes the common cold) to infect bladder cancer cells. Urology of Virginia is currently enrolling patients with recurrent non-muscle invasive bladder cancer into this clinical trial to determine long-term effects and survival benefits.



For patients that have advanced bladder cancer that has spread to other parts of their body, standard regimens include platinum-based chemotherapy that can have significant adverse side effects. Recently, however, a new class of agents, known as checkpoint inhibitors, has begun to change the tide for patients in this advanced setting. Two agents are currently on the market and have demonstrated improvements in survival as compared to chemotherapy with much improved durable responses. Both work on a specific molecule that affects whether the cancer cell is “seen” by the immune system. The new medicines, called Keytruda® and Tecentreq® block these regions allowing the body’s own immune defense system to attack the cancer cells. The two molecules targeted are the program death protein-1 (PD-1) and the program death ligand-1 (PD-L1). Toxicity, as compared to chemotherapy in the second line setting, was significantly lower. Overall, both agents have demonstrated a dramatic improvement for patients suffering from metastatic bladder cancer.

In summary, though bladder cancer remains a very common cancer in the United States, there remains a significant need for further research. Fortunately, with the development of newer agents that unlock the body’s ability to target and destroy cancer cells, we are starting to see the tide change for this difficult disease.

For more information about bladder cancer, please check the informative site: http://bcan.org, sponsored by the Bladder Cancer Advocacy Network.

Current bladder cancer clinical trials enrolling at Urology of Virginia

For non-muscle invasive bladder cancer:

Spectrum CONQUER (Qapzola™)--This is a randomized, multicenter, two-arm, double-blind, placebo-controlled study of Qapzola™ in patients with low- to intermediate-risk non-muscle invasive bladder cancer. Patients will receive either Qapzola™ or placebo (2:1 randomization) at the time of tumor resection. Enrolled patients will be followed for five years with routine cystoscopies and cytologies. The study will evaluate the time to recurrence. *

FKD Instiladrin® (rAd-IFN)/Syn3) A Study to Evaluate **INSTILADRIN®** in Patients With High Grade, Bacillus Calmette-Guerin (BCG) Unresponsive Non-muscle Invasive Bladder Cancer. All enrolled subjects will receive Instiladrin® with the purpose to evaluate the incidence of event-free survival at 12 months, where event-free survival is defined as high-grade recurrence free survival.*

For muscle invasive bladder cancer:

A new study is forthcoming using the TARIS TAR-200. From the TARIS website, "TAR-200 is a drug-device combination product designed to release gemcitabine continuously into the bladder over 7 days. Gemcitabine is commonly used to treat multiple cancers alone and in combination with other chemotherapeutic drugs."*

For upper tract urothelial cancer:

Urogen OLYMPUS-- A Phase 3 Multicenter Trial Evaluating the Efficacy and Safety of MitoGel™ on Ablation of Upper Urinary Tract Urothelial Carcinoma. The study is investigating the ability of **UroGen's** MitoGel™ procedure to treat urothelial carcinoma tumors from the upper urinary tract. If this treatment will prove to be effective this will lead to the development of a new treatment approach for patients suffering from Low Grade Upper Urinary Urothelial Carcinoma (UTUC).*

For information about bladder cancer clinical trials at Urology of Virginia, please contact the research department at research@urologyofva.net.

Third Annual End of Prostate Cancer 5K

On Sunday, November 19, 2017, Urology of Virginia and ZERO--The End of Prostate Cancer hosted the 3rd Annual 5K Run/Walk at the 24th Street Park in Virginia Beach, VA. In addition to the 5K run, the event included a 1 mile walk, Kids Superhero Dash for Dad, and a virtual Snooze for Dudes program.

Although the morning started with drizzles of rain and was quite chilly, the participants and volunteers showed up ready to have a great time! The race began at 8:30AM with the first runner crossing the finish line in just over 19 minutes. Our youngest runners enjoyed a 200 yard Kids Dash on the boardwalk with Salty Dog, the Norfolk Admirals hockey team mascot, with each runner receiving a Super Hero medal at the finish line.

Participants and volunteers enjoyed food, beverages, face painting, music provided by two DJs, and many displays from vendors.

This year ZERO's Heroes, men who are diagnosed with prostate cancer and identify as survivors or patients, were recognized by receiving ZERO Hero hats from our Urology of Virginia Physicians. In turn, caregivers of these ZERO's Heroes were also recognized by their "Hero" with a special sash for their dedication and support.

Team building was a primary focus this year. We campaigned and encouraged friends and family to join together to support creating Generation ZERO—a generation with zero incidence of prostate cancer. The Top 3 Largest Teams - Team Bunch O Nuts, Team DIVA and Team Ham answered the call. Together with the Top 3 Fundraising Teams – Team Bunch O Nuts, Team Ham and Theta Chi – ODU and the Top 3 Individual Fundraiser Participants – Chaz Heron, Daniel Wagoner and Janice Sadler, a significant amount of money was raised and enthusiasm and excitement were felt throughout the race course.

We challenged the Hampton Roads business community to support our mission, and they really stepped up to the challenge! Local sponsors not only provided financial support and in-kind donations, they also volunteered on race day. Some even ran! Sponsors included pharmaceutical reps, banks, hospital systems, medical practices, attorneys, and printers.

With the help of over 450 registered participants, volunteers and donors, this year's event exceeded our fundraising goal! The funds raised from the ZERO Prostate Cancer Run/Walk are invested around the country to provide research for new treatments, free prostate cancer testing, and educating men and families about prostate cancer. A portion of the proceeds will be used

locally to benefit the Schellhammer Urological Research Foundation (SURF) as well as The Hampton Roads Prostate Health Forum. Donations will be accepted through December 31st. Many thanks to the volunteers, participants, donors, sponsors, friends, family, and the community for supporting such a worthy cause.

For more information, please visit: www.zeroprostatecancerrun.org/hamptonroads

Volunteer Mission Update

Kurt McCammon, M.D.

The philanthropic mission of SURF has continued throughout the year with trips to Zimbabwe, Senegal and most recently to San Fernando General Hospital in Trinidad.

During our trip to Zimbabwe we were able to start working on collaborations with the department of urology at the University Of Zimbabwe College Of Health Sciences in Harare. This will allow us to move forward to increase our presence and training for the attendings and residents at their medical school.

Our annual trip to Hoggy Hospital in Dakar, Senegal continued to be productive. We were able to review outcomes for patients undergoing urethral reconstruction and found out that our workshops and training have increased the success rates in surgical management of these patients by 300%. There is still a lot to do but it is very rewarding to see this improvement! Our next step is to help the physicians there set up treatment pathways that we are sure will continue to increase patient care. \Finally, we recently returned from our annual workshop in Trinidad at San Fernando Hospital. This workshop focused on the care of female patients with urinary incontinence and pelvic organ prolapse. These quality of life issues are largely ignored and in the past, these patients were not treated.

With the gracious support of SURF, we were very excited to have Erin Glace, MS.PT. join us on this trip. Erin is a pelvic floor physiotherapist, with expertise in pelvic floor dysfunction, who has worked with patients at Urology of Virginia for greater than 17 years.

Erin met with the urologists and physiotherapists in San Fernando hospital, and gave several lectures on the treatment of these conditions. Pelvic floor therapy is a non-invasive treatment option that is infrequently used in low and middle-income countries. Our hope is that we will start improving the quality of life of many of these women who in the past had to live with their distressing conditions.

We are grateful to SURF for the support that allows us to continue our volunteer mission.

Help Support our Mission

The Schellhammer Urological Research Foundation (SURF) is a leading 501-C-3 non-profit organization whose mission is to improve urological care in our community and beyond through excellence in research, education and compassionate innovative health care.

Your donations to the SURF are greatly appreciated!
All donations are tax-deductible to the extent permitted by law.

Donations may be made online or via a downloadable form at http://surf-1.org/donate.html.

Donations may be mailed to:
SURF
225 Clearfield Ave.
Virginia Beach, VA 23462-1815

Attention: Kurt McCammon, M.D.

If you would like additional information, please call Laurie Jackson at (757) 452-3461.