

University of Wisconsin Urology



A semi-annual publication for alumni and friends of the UW Program in Urology.

Winter 2005¹

Message from the Chair



It is with great anticipation that we present the first issue of *Wisconsin Urology*, a newsletter for alumni and friends of the University of Wisconsin, Division of Urology. It has been another banner year here in Madison, highlighted by the Fourth Annual Uehling Lectureship, which featured **E. Darracott Vaughan, MD**, from New York

Hospital. Dr. Vaughan spoke on renal cancer, BPH and adrenal disease, and his erudite comments and mastery of nearly all domains of urology was appreciated by all in attendance. Our former endourology fellow, Dr. Patrick Lowry, was also a visiting speaker. Dr. Lowry is currently Assistant Professor at Scott and White in Texas. The 2004 Uehling Lectures also emphasized David Uehling's absence in Madison, as he returned from his new retirement home in South Carolina for the event.

This year marks more **academic milestones** in Madison. Drs. Wade Bushman and Walt Hopkins secured more funding for research in areas of the prostate and urinary tract infections. Our O'Brien Center Program Project grant is progressing well, and Dr. Bushman held an outstanding research symposia in Madison this year. Dr. David Jarrard's laboratory remains highly productive in the UW Comprehensive Cancer Center. We are anxiously awaiting ground breaking for the new Interdisciplinary Research Complex, which achieved state approval this year. Our laboratories will be moving to this state-of-the-art facility in the coming years.

New initiatives include the recent groundbreaking for the American Family Children's Hospital. With our rapidly growing practice in pediatric urology, I am pleased to announce we have recruited a second pediatric urologist, Dr. Bruce Slaughenhaupt from Louisville, Kentucky. This year also marks the first full year of videourodynamics at UW, and the bladder group led by Dr. Bushman has begun to offer Interstim procedures to select patients in Wisconsin.

The residency program is doing better than ever. This past June, our program was reviewed by the ACGME and the program earned full accreditation status for five years. Kudos to Nancy Hawkins, our program coordinator, and all those involved! This year we sent two residents to the North Central Section Meeting in Florida; this meeting also marked the beginning of my three-year tenure as Secretary of the Section. Of course, we will be holding our **Annual UW Alumni Reception at the AUA** again in San Antonio. This spring, Drs. Dean Assimos, Steve Docimo and John Mulhall will all be visiting professors at the UW; please see the "Upcoming Events" section for all details.

I sincerely hope you enjoy receiving and reading *Wisconsin Urology*, and on behalf of all our faculty, I hope to see you more in Madison. Please join us at the Uehling Lectures, the AUA, other meetings, grand rounds, or just here in the hallway!

Stephen Y. Nakada, MD

New Initiatives in Wisconsin

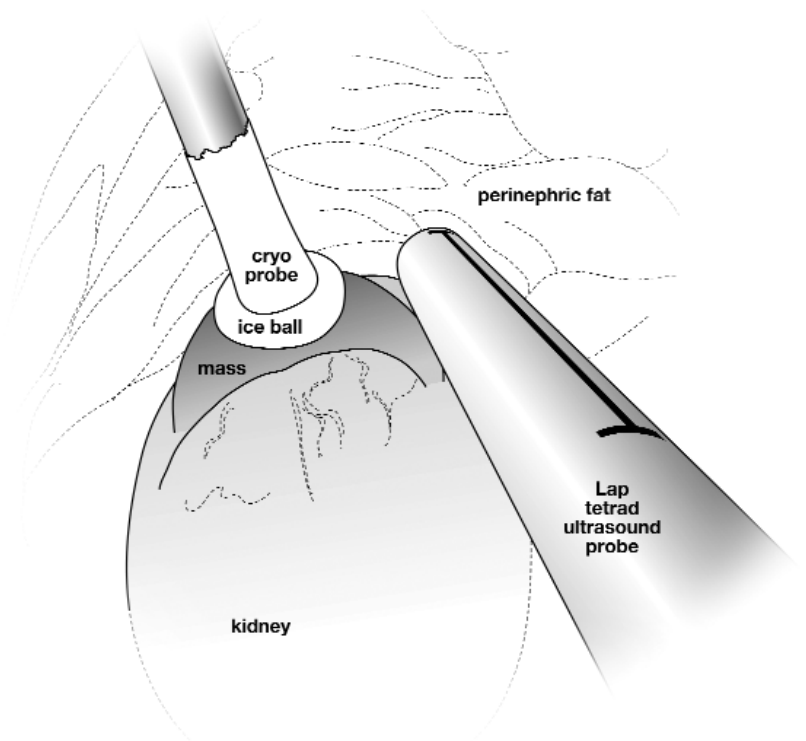
New Treatments for Small Kidney Tumors

Wade Bushman, MD, PhD
Associate Professor

Advances in imaging modalities are allowing physicians to find renal tumors at a very early stage. Sometimes, these tumors are found incidentally when a CT scan or MRI is performed for another reason. The small size of these lesions, between 1-3 cm, makes them a different challenge than the typically larger renal tumors that are removed by standard surgery. Minimally invasive renal surgery is a rapidly developing area that's changing the face of surgery for renal tumors – particularly small, incidentally discovered masses.

Drs. Stephen Nakada, Timothy Moon, and Sean Hedican have collaborated with Dr. Fred Lee (Radiology) to put UW at the forefront of minimally invasive renal surgery in the greater Midwest region. Using two different techniques, cryoablation and radio frequency ablation, tumors are destroyed without the need for open surgery. Cryoablation utilizes super-cooled needle probes to freeze the tumor achieving temperatures that destroy cancer cells. Radio frequency ablation uses a heat emitting needle probe to destroy the tumor. Both techniques can be performed through a laproscope or percutaneous approach with ultrasound or CT guidance. Since 1999, nearly 50 people have been treated with few major complications. The cure rates thus far are equal to those of standard surgery. And, recovery is much quicker, with most patients staying overnight.

For some patients these approaches are not just easier – they are essential. Patients with Von Hippel Lindau disease often develop multiple tumors in both kidneys. Standard surgical approaches often damage normal renal tissue with loss of renal function and could result in a need for dialysis. These minimally invasive techniques allow the tumors to be treated with limited injury to the normal kidney tissue and preservation of renal function. Other patients may specifically benefit from the low morbidity of ablation procedures, such as those with systemic illnesses that preclude major open surgery or patients who develop a tumor in a transplant kidney. The surgeons at UW were the first in the nation to treat a tumor in a transplant kidney using cryoablation. They continue to be at the forefront of this work. As part of this effort, the division of Urology is one of the country's centers that provides advanced fellowship training for young urologists who wish to pursue a career in minimally invasive surgery.



Research Breakthroughs at UW

What does a one-eyed sheep have to do with prostate cancer?

David Jarrard, MD
Associate Professor

The answer to this question may hold new promise for men with advanced prostate cancer. A chemical found in meadow flowers that produced birth defects in sheep grazing on the plants has been shown to block prostate cancer growth in mice and is leading to the generation of new treatments for advanced prostate cancer.

The insights that led to this discovery stem from the work of Dr. Wade Bushman, a member of the department of urology. Eight years ago, Dr. Bushman began studying the role of an oddly named protein, Sonic Hedgehog, in growth of the prostate during fetal development. He was the first to describe the role of this protein in normal prostate development and show that blocking this protein's action prevented prostate development. Further work by Dr. Bushman done in collaboration with Curis Inc. (Cambridge) then showed that the Sonic Hedgehog protein is also active in prostate cancer and that it makes tumors grow faster. This work, published in August in the *Journal of Endocrinology*, was the first description of



Dr. Bushman's lab group

the role of Sonic Hedgehog in prostate cancer. Three other papers have been published since then and all show a central role for Sonic Hedgehog in tumor growth and a promising target for anti-tumor therapy.



... so what about the one-eyed sheep? When pregnant ewes consumed the meadow flower *Veratrum californicum*, their offspring showed a number of defects including cyclopia (one eye). The effect was traced to a specific chemical in the plant that was named cyclopamine. Biochemical studies showed that cyclopamine causes these birth defects because it blocks the function of the Sonic Hedgehog protein. Using this compound, Dr. Bushman showed that prostate development could be blocked by cyclopamine and this generated the idea of using such a compound to treat prostate cancer. This seems to be possible. In work recently published by Dr. Berman and colleagues at Johns Hopkins, cyclopamine administration blocked tumor growth in animal models of prostate cancer.

Work is currently being done by Curis in combination with Genentech (San Francisco) developing high potency analogs of cyclopamine for use in treating cancer. It is hoped that clinical trials with these compounds may begin as early as next year. Since Sonic Hedgehog is not active in most adult tissues, the expectation is that these compounds will inhibit tumor growth while having minimal toxicity (side effects). For patients with advanced prostate cancer, this holds the promise of providing an effective therapy to slow or arrest tumor growth while maintaining a high quality of life.

Program News

Congratulations to the 2005 PGY-1 Urology Residents:

Matthew Christian, MD (Tufts University)

Christopher Manakas, MD (Indiana University)



2005 Minimally Invasive Urology Fellow

Charles Wen, MD

Dr. Wen received his MD from Boston University Medical School in 2000.

He completed his Urology residency at Boston University Medical School in 2005. Dr. Wen also has a strong background in engineering.

Notable and Newsworthy

- A proposal by **Jason Gee, MD**, entitled "Evaluation of NM404 PET-CT in Prostate Cancer Patients as a Tumor-Selective Imaging Technique" was approved in the amount of \$40,000 by George Wilding, M.D and the UW Comprehensive Cancer Center.
- **Travis Jerde**, working in Dr. Nakada's lab, was chosen to receive the prestigious *2004 Dr. Razia Zaman/Dr. Sbahanara Zaman Saroya Graduate Student Award* for Excellence in Research and Scholarship.
- **Stephen Nakada, MD** was awarded National Institutes of Health (NIH) Funding for his lab's studies entitled, "Stretch-induced COX-2 in Urothelial Cells."
- **Murali Ankem, MD**, our 2004 endourology fellow, received third prize in the Endourology Essay Contest for his paper on prostaglandin E2 receptor modulation in the ureter. Look for it in the *Journal of Endourology*.
- **Xudong Shi, PhD**, a post-doc in Dr. Wade Bushman's lab, received funding as an American Foundation of Urologic Disease scholar.

Upcoming Events in Wisconsin

2005 Winter/Spring Urology Grand Rounds Visiting Professors

March 10, 2005 - John P. Mulhall, MD

Dr. John Mulhall will give a lecture on sexual dysfunction. Dr. Mulhall is an Associate Professor of Urology and Director of the Sexual Medicine Program at Weill Medical College of Cornell University. He also holds a joint appointment with the Department of Urology at Memorial Sloan Kettering Cancer Center, New York, New York.

April 28, 2005 - Dean G. Assimos, MD

Dr. Dean Assimos will be speaking on the medical and surgical management of stones. Dr. Assimos is a Professor in the Department of Urology at Wake Forest University Medical Center, Winston-Salem, North Carolina. His clinical interests include kidney cancer, kidney stones, reconstructive renal surgery, ureteral stones, transplant urology, laparoscopy, and ureteral strictures.

June 2, 2005 - Steven G. Docimo, MD

Dr. Steven Docimo will give a lecture on pediatric urology. Dr. Docimo is Professor and Chief of the Division of Pediatric Urology at the University of Pittsburgh Medical Center and the Children's Hospital of Pittsburgh in Pittsburgh, Pennsylvania.

Watch for these UW Urology AUA Events

UW Alumni Reception

The UW Urology Alumni Reception will take place on Sunday, May 22, 2005 from 5:00-7:00 pm. Check at the AUA Information Desk for exact room location.

UW Faculty at the AUA

Dr. Reginald Bruskewitz will be serving as a Point-Counterpoint Debater at the Plenary Program for the session entitled "Should All Men With Symptomatic BPH Have UD Studies Before Treatment?" scheduled on Monday, May 23, 2005. Dr. Bruskewitz will also serve as a faculty member on an AUA Office of Education Course entitled "Management of BPH" on Monday, May 23, 2005.

Dr. Stephen Nakada will serve as an AUA Office of Education Course Co-director on a course entitled "Decision-making in Endourology: An Outcomes-based Approach." The course is scheduled to take place on Sunday, May 22, 2005. Dr. Nakada will also moderate a session entitled "SWL and Invasive Therapy Including Utereroscopy" on May 25, 2005.

2005 Uehling Lectures

The UW Division of Urology will be holding its annual David T. Uehling Lectures on October 21-22, 2005 at the Monona Terrace Community and Convention Center in Madison. Our keynote speaker this year is **Alan W. Partin, MD, PhD** from The Johns Hopkins Medical Institutions in Baltimore, Maryland. Dr. Partin is the David Hall McConnell Professor and Chair of the Department of Urology and the Brady Urological Institute and Urologist-in-Chief at The Johns Hopkins Hospital. The brochure for this exciting conference will be mailed this summer.

Clinical Trials in Wisconsin

John Wegenke, MD
Associate Professor

New medications must be discovered, engineered, purified, and tested before use in humans. Cell studies are often the first stage of testing new drugs for their effect on living systems. Animal studies are then carried out to test for the toxicity and the effect these drugs have in vivo. The most promising drugs are then tested in human trials for clinical use. About 1 in 1,000 potential drugs are tested before one reaches approval. The phases of clinical trial testing are outlined in Table 1.

The government, pharmaceutical industry or private foundations

typically fund studies. The average cost of developing a new medication for use in humans is approximately \$800 million.

Thousands of people volunteer each year to participate in clinical trials to help themselves and millions of other patients benefit from these innovative drugs.

The urology division at the University of Wisconsin participates in a variety of these studies at various levels.

Current studies being conducted in the Urology division at the Highland and South Park Campus are for the treatment of overactive bladder, stress

incontinence, benign prostatic hypertrophy with urinary urge incontinence, and fracture prevention in hormone treated prostate cancer patients. Pending studies will evaluate antibiotics in complicated urinary tract infection, the usage of stents in treating stone disease as well as treatment of overactive bladder with medication and behavior modification.

We plan to elaborate on the ongoing studies in future newsletters.

Table 1. Phases of Clinical Trials

	I	II	III	IV
		Pre-marketing		Post-marketing
Length of study	1 week to several years	several months to 2 years	several months to 4 years	several months to several years
Number of subjects	10 to 100	50 to several hundred	several hundred to several thousand	50 to several hundred
Purpose	Determining pharmacology, pharmacokinetics, toxicity and safety dosage in humans	Determine safety and efficacy in a limited number of patients	Compare safety and clinical effectiveness of drug to standard therapy in a large population	Provide additional information on the efficacy or safety profile



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