

SURGERY UPDATE LEADING THE WAY

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Cure for the Broken Heart



ROBERT B. LOVE, M.D.
Professor, Cardiothoracic Surgery
Chief, Adult Cardiac Surgery

Department of Surgery

*Dedicated to Clinical Care,
Research and Education*

- Cardiothoracic Surgery
- Colorectal Surgery
- Community Surgery
- Surgical Education
- General Surgery
- Pediatric Surgery
- Surgical Oncology
- Transplant Surgery
- Trauma and Critical Care
- Vascular Surgery

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Editors: Dr. Rebecca C. Anderson and Dana Schmidman. Dana can be reached at 414-805-5602, or dschmidm@mcw.edu.

Leading the Way is written for physicians for medical education purposes only. It does not provide a complete overview of the topics covered and should not replace the independent judgment of a physician about the appropriateness or risks of a procedure for a given patient.

In December of 2012, the Medical College of Wisconsin Advanced Heart Failure Program became the first in the United States, outside of a clinical trial, to implant the U.S. Food and Drug Administration (FDA)-approved HeartWare® Ventricular Assist Device System. The HeartWare® Ventricular Assist System obtained FDA market approval as a bridge-to-transplant therapy for patients with advanced stage heart failure. The HeartWare® System has been commercially available in other global markets including Europe and Australia since 2009. To date, more than 2,500 patients have been treated worldwide with the HeartWare® Ventricular Assist System. The MCW team was pleased to be the first center in the United States to implant the device following FDA approval. The recipient of the device is recovering and remains actively listed for a heart transplant. This is the first continuous flow device available for implantation.

Heart failure is a degenerative and ultimately terminal disease affecting greater than 20 million patients worldwide. Heart transplantation is a proven option for treating Class IV heart failure patients, however, a limited number of donor hearts become available annually. Ventricular assist devices can offer circulatory support until a donor heart becomes available, making the device serve as a bridge-to-transplant or provide long-term circulatory support as an alternative to transplantation, referred to as destination therapy. The HeartWare® miniaturized ventricular assist device, called the HVAD Pump, is designed to be implanted next to the heart in the pericardial space avoiding more invasive surgical procedures required with previous Left Ventricular Assist Device (LVAD) technology.

The HeartWare® HVAD is much smaller in size and is placed into the pericardial space after implantation. This is a significant step toward making miniaturized circulatory support (MCS) available for smaller patients. Previous devices were so large that the pump had to be placed in the abdomen or left upper quadrant. Further advancements in miniaturization are expected within the next 12 months, making this type of device available to pediatric patients. This technology will extend MCS as a treatment for medically refractory heart failure to thousands of patients previously on palliative medical therapy, and will also dramatically affect heart transplantation. With the continued shortage of donor hearts, most patients awaiting heart transplant will have a VAD implanted to stabilize their heart failure while on the wait list. •

FOR ADDITIONAL INFORMATION on this topic, visit mcw.edu/surgery or contact Dr. Love at 414-955-6939, rlove@mcw.edu or Dr. Claudius Mahr at 414-955-6737, cmahr@mcw.edu.



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Mass-Casualty Incidents: Preparation and Multidisciplinary Management



TRAVIS WEBB, MD, MHPE
Division of Trauma/Critical Care



TERRI DEROON-CASSINI, PhD
Division of Trauma/Critical Care



REBECCA C. ANDERSON, PhD
Division of Transplant Surgery

Managing Mass Casualties

Recently, our institution and specifically, our Level One Trauma Center came into the national spotlight under unfortunate circumstances. Dealing with mass-casualty incidents is not a particularly desirable goal for a trauma surgeon or any healthcare provider. However, we must always be prepared to respond with swift precision when these events do occur, and we can learn from the experience to improve our care following such tragedies.

As acute care surgeons, we are all too familiar with managing multiple gunshot victims in the middle of the night with limited resources at our immediate disposal. However, mass-casualty incidents, characterized by a large influx of patients arriving in rapid succession and ultimately overwhelming routine medical care resources, raise the bar for preparedness and planning. The principles of Advanced Trauma Life Support and triage guide us as we make decisions regarding the severity of injuries and survivability of the injured patients. These principles become of utmost importance during a mass-casualty situation. The surgeon must quickly identify patients who can wait for further treatment and differentiate them from those who require immediate lifesaving surgical interventions. Appropriate triage has the greatest impact on patient outcomes and ultimate resource utilization. Studies using historical data and computer modeling have analyzed triage decisions to assist in identifying the best method for triage during mass-casualty incidents, but over-triage and under-triage remain problematic in real life.^{1,2}

We have learned some lessons from experiences dealing with mass-casualty incidents. First, it is important to become involved in the planning and understand your hospital's disaster plan. The surgeon must know what will happen when an event occurs and the resources that will be available to the trauma leader. Do you know who will be called for help and how you will be involved in this communication? Most surgeons have not been intimately involved in this planning and have only a cursory understanding of their hospital's disaster response plan.³ Second, as the trauma expert, you will be placed in a position of leadership requiring you to direct the allocation of resources well beyond your routine responsibilities. You must provide direction and be willing to multitask and provide oversight of those providing direct care to injured patients. On many levels, communication skills will be put to the test.

The Department of Surgery and specifically the Division of Trauma/Critical Care is proud of our institution's response to recent mass-casualty events. Though we would prefer to avoid seeing these types of senseless tragedies again, we rest assured that we have learned from our experiences and are better prepared for the future.

Coping with Mass Trauma

It is difficult for one to truly comprehend the reasons that might drive someone to break into a school with the intent to injure or murder children. The news of the Sandy Hook Elementary shooting left many people asking that very question—Why? If only we knew the why behind what drove the suspect to do this, maybe, in some small way, it could help us to gain a sense of understanding of the incomprehensible—to put this horrible and tragic event into perspective. Our thoughts lead us to ask several questions: Severe mental illness? Exposure to guns and violent video games? Or, in the case of the Sikh Temple shooting or the mass shooting at the Azana Spa, prejudice? Ignorance? Domestic violence? No matter the reason, it seems nothing guides us to truly gain an understanding of the motivation of those who plan and execute intentional and egregious acts of violence, rendering many individuals feeling helpless.

The unbelievable and malicious nature of intentional mass casualty can have a far-reaching societal impact. Seminal work by Janoff-Bullman discusses shattered assumptions after trauma, the idea being that most people believe that if one works hard in life, and treats others fairly, one can expect the same in return.⁴ When inexplicable intentional casualty occurs, it shatters those assumptions and changes how one views the world. Also, studies on Terror Management Theory, particularly after 9/11, have suggested that when mass casualty occurs, one's own mortality salience increases, even for those who are not directly impacted by or in close proximity to the trauma.⁵ Both of these phenomena are known to occur on a large scale, leaving people, communities, and nations feeling



vulnerable. This is particularly true when violence occurs in places that are generally perceived as safe, such as a place of worship, a salon/spa, or a school.

Being in tune to how our patients are coping and how we as providers are dealing with such inexplicable events is imperative. Whether your patient is a trauma survivor who experiences the news of a mass shooting as a trigger, or someone who is returning for a post-operative follow-up for a non-trauma related procedure, normalizing feelings of vulnerability and helplessness can be tremendously supportive. For healthcare workers who strive day in and day out to save the lives of trauma survivors, feelings such as anger toward the perpetrator can be particularly salient. Whether for our patients or ourselves, individual and community resilience can be fostered when there is connection with others. Volunteering to discuss safety at schools, initiating conversations with others about gun safety, advocating for more mental health treatment, or reaching out to neighbors in your community who might have been particularly impacted by a mass trauma might bring a sense of “doing something” to help. Whatever the connection one makes with others, when a sense of purpose develops out of trauma, this new meaning in life can be individually healing and collectively transformative. •

Photos above used with permission: *Milwaukee Journal Sentinel*/Rick Wood

FOR ADDITIONAL INFORMATION on this topic, see references, visit mcw.edu/surgery, or contact Dr. deRoos-Cassini at tcassini@mcw.edu or Dr. Travis Webb at trwebb@mcw.edu.

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Dr. Lewis to serve as Interim Director of Curriculum and Evaluation



Dr. Brian Lewis

Brian Lewis, MD, Associate Professor of Surgery, has been named Interim Director of the Curriculum and Evaluation Committee (CEC) at MCW. This Committee is composed of 17 faculty members representing multiple departments and is responsible for oversight of the medical school curriculum. Oversight activities include ongoing monitoring of existing courses, clerkships, sub-internships, electives, and Pathways, as well as the approval of new courses and electives, including the Discovery Curriculum. The Committee works closely with the offices of Curriculum and Educational Services in Academic Affairs to ensure that the curriculum meets LCME accreditation standards and provides a high-quality educational experience for our students.

In addition to his role on the CEC, Dr. Lewis serves as Student Clerkship Director and Associate Post-Graduate Physician Assistant Program Director in the Department of Surgery. He continues to be actively involved with resident, fellow, and student education, while remaining clinically active at Froedtert and the VA. He has twice been presented with the Department of Surgery Golden Cane award for medical student teaching (2006 and 2007). Dr. Lewis was also the recipient of the MCW Edward J. Lennon Endowed Clinical Teaching Award in 2009 recognizing his exceptional contribution to teaching and has received the annual MCW Outstanding Medical Student Teacher award twice (2010 and 2012).

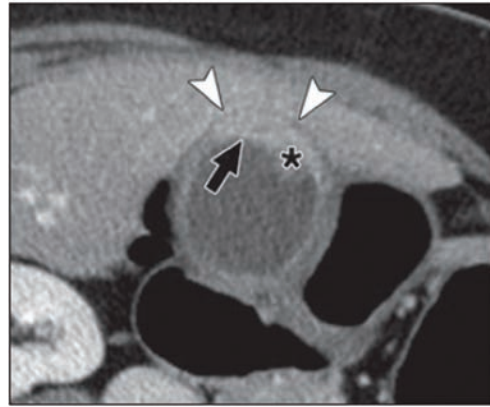
Imaging of Gallbladder Cancer



CHARLES H.C. PILGRIM, MD, PhD
HPB Fellow
Division of Surgical Oncology



T. CLARK GAMBLIN, MD, MS
Chief of Surgical Oncology
Stuart D. Wilson Chair in Surgery



A subtle gall bladder cancer in a 54-year-old female. This was already a T3 lesion on final pathology.⁷

In the United States, the appropriate operation for gallbladder cancer is frequently not performed, largely due to the failure of surgeons to consider the diagnosis before and during cholecystectomy. A more careful consideration of preoperative imaging should allow for the identification of at-risk patients, reducing the rate of “incidental gallbladder cancer,” which would translate to more patients referred for appropriate oncologic management. The nature of gallbladder wall thickening is particularly interesting. Computed tomography (CT) or magnetic resonance imaging (MRI) features are capable of establishing the differential diagnosis of gallbladder cancer based on descriptions of wall characteristics and thickness. A greater number of patients with suspicious lesions on ultrasound (US) should proceed to these imaging investigations to identify the diagnosis preoperatively.

Controversy surrounding risk of malignancy of gallbladder polyps continues. However, the vast majority of gallbladder cancer does not arise from adenomatous polyps, and the vast majority of polyps are not adenomatous. Identifying the rare polyp that harbors malignant potential remains difficult, but should not be the ongoing focus of attention in detecting early-stage gallbladder cancer. Instead, attention should focus on non-specific gallbladder wall thickening and the assessment of this US-finding with cross-sectional imaging.

Polyps

Gallbladder polyps >10mm warrant cholecystectomy to reduce the incidence of malignancy. However, the majority of polyps are simple hyperplastic lesions and are not adenomatous. Furthermore, the majority of adenomatous polyps do not become gallbladder cancer, which more commonly arises from dysplastic lesions.¹

A cohort of 346 patients followed up clinically or with US demonstrated the benign nature of virtually all gallbladder polyps in Western patients. Of 149 who underwent US scanning, only one polyp increased in size (from 3 mm to 5 mm), and more than 1/3 were not present on subsequent scans. Of those who proceeded to surgery, more than 2/3 did not have a polyp of any

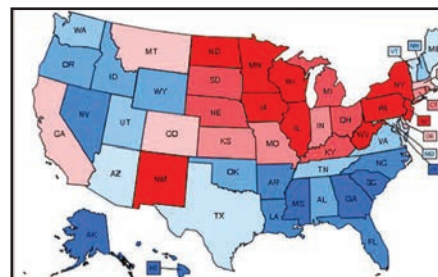
kind on final pathology. The authors concluded that the presence of gallbladder cancer resulting from, or associated with, incidentally detected polyps is extremely low, and that incidental polyps <6 mm do not require follow up.²

Identifying which polyps are of concern is difficult. Endoscopic US (EUS) is considered superior to conventional US because of its higher operating frequency, which enables higher resolution imaging of small lesions.^{3,4} However, EUS performs poorly for lesions <10 mm, with only 40% accuracy. For lesions >10 mm, the diagnostic accuracy of EUS (86%) is not better than that of newer, high-resolution transabdominal US (HRUS, 90%).

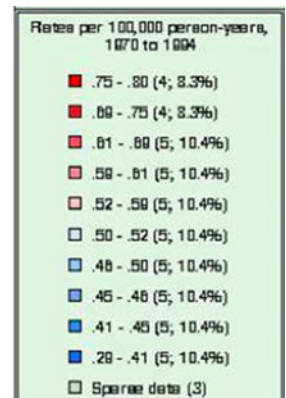
Gallbladder lesions do not need to be removed simply because they are polypoid, especially if they are small. However, if they display features suggestive of malignancy, such as local invasion, vascularity, sessile shape, or are associated with enlarged regional lymph nodes, they should be treated as cancer rather than as a polyp, necessitating further imaging investigation and appropriate oncologic surgery.

Gallbladder Wall Thickening

Gallbladder cancer presents more commonly as non-specific gallbladder wall thickening. The diagnosis in this context is rarely considered, given the commonness of acute and chronic cholecystitis. Multi-detector CT is ideally suited to careful scrutiny of gallbladder wall thickening, and will frequently document evidence of distant nodal or metastatic spread.



Mortality for white females from gallbladder cancer (1970–1994). The Midwest, including Wisconsin, has some of the country's highest mortality from gallbladder cancer.⁸



	DESCRIPTION	MOST COMMON DIAGNOSIS
Type 1	Heterogeneously enhancing thick one layer	Gallbladder cancer
Type 2	Strongly enhancing thick inner layer (≥ 2.6 mm) weakly enhancing/nonenhancing thin outer layer (≤ 3.4 mm)	Gallbladder cancer
Type 3	Borderline pattern	Adenomyomatosis
Type 4	Weakly enhancing thin inner layer/nonenhancing thin outer layer	Chronic cholecystitis
Type 5	Weakly enhancing thin inner layer nonenhancing thick outer layer	Acute cholecystitis

Table 1—CT features of gallbladder wall thickening with likely differential diagnosis⁵

Kim *et al* described five distinct patterns of wall enhancement on CT that correlate well with gallbladder cancer, adenomyomatosis, or acute or chronic cholecystitis (Table 1).⁵ MRI-HASTE imaging (the source images for magnetic resonance cholangiography) can also describe four distinct layered patterns (Table 2).

Thickness per se also appears to be an important overlooked feature. Mean gallbladder wall thickness was 6.5 mm vs. 19.4 mm for nonneoplastic and neoplastic gallbladder wall thickening on EUS. Similarly, the mean wall thickness of gallbladder cancer measured by CT was 13.6 mm vs. 6.6 mm for benign conditions.

With careful observation of cross-sectional imaging features, even early-stage tumors may be anticipated prior to their penetration into the deeper muscular layers of the gallbladder. This area truly represents an opportunity for clinicians to improve regarding earlier diagnosis of gallbladder cancer.

Established Gallbladder Cancer

In those cases where the diagnosis of gallbladder cancer is established preoperatively, an accurate assessment of T, N, and M stage is critical to plan treatment and surgery.

US has a relatively high sensitivity for detection of advanced tumors but is limited in the diagnosis of early lesions and is unreliable for staging. Accurate diagnosis of early-stage disease is performed more reliably with CT. The significance of local nodal disease on postoperative scanning is difficult to ascertain. The differentiation of malignant nodal involvement from inflammation is almost impossible. Paraaortic nodal involvement is, however, much less likely to be attributable to the postoperative state in this context. The presence of enlarged nodes prior to surgery is more ominous for malignancy.

Conclusions

With a more critical evaluation of the common US finding of gallbladder wall thickness, and a more liberal approach to CT or MRI for patients with abnormal US examinations, we may increase the detection of early stage gallbladder cancer. Attention should focus on wall thickening, rather than the often unnecessary concern over small polyps that rarely become malignant. Clinicians should realize that a gallbladder wall >10 mm should be treated

	DESCRIPTION	MOST COMMON DIAGNOSIS
Type 1	Two layers Thin hypointense inner layer Thick hyperintense outer layer	Chronic cholecystitis
Type 2	Two layers Ill-defined margins	Acute cholecystitis
Type 3	Multiple hyperintense cystic spaces in wall	Adenomyomatosis
Type 4	Diffuse nodular thickening without layering	Gallbladder cancer

Table 2—MRI features of gallbladder wall thickening with likely differential diagnosis⁶

with the same suspicion for harboring malignancy as the 10 mm gallbladder polyp and be aware that there are defined CT and MRI descriptions of wall changes that can differentiate gallbladder cancer from benign acute and chronic cholecystitis. •

FOR ADDITIONAL INFORMATION on this topic, see references, visit mcw.edu/surgery, or contact Dr. Gamblin at 414-805-5020; tcgamblin@mcw.edu.

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Developing Cell Lines to Study Mechanisms of Gemcitabine Resistance in Pancreatic Cancer



RACHEL MORRIS, MD
General Surgery Research Resident
Medical College of Wisconsin



GARY GALICK, PhD
Senior Scientist, University of Texas
M. D. Anderson Cancer Center

Pancreas cancer is the fourth leading cause of adult cancer death, with an average survival of 9–12 months. The poor survival rate is due to late presentation and lack of effective chemotherapeutic agents. Less than 20% of patients are surgical candidates due to advanced disease at diagnosis.¹ Gemcitabine, the current standard of care for many patients, offers a modest improvement in progression-free survival due to the rapid development of resistance.² If the molecular alterations of gemcitabine resistance were better understood, combination therapies

could be developed to decrease resistance and improve tumor response. Changes in the tumor and microenvironment are thought to contribute to resistance, leading to increases in growth, proliferation, invasion and changes in drug transport, metabolism, apoptosis and angiogenesis.³ AKT, NFκB, c-Met, Notch, and MAPK are among the key signaling molecules suspected to be involved in these pathway changes.⁴ However, inhibiting these targets has failed to substantially improve combination therapy. Even less understood genetic changes in tumor cells could be essential in decreasing gemcitabine resistance.

Given the current limited knowledge of resistance mechanisms, we developed two gemcitabine-resistant cell lines from parental pancreatic cell lines L3.6 and Aspc-1. Parental cell lines were treated with 25 nm and 100 nm gemcitabine, respectively. Greater than 80% of cells died. Upon outgrowth of remaining live cells, gemcitabine concentration was serially increased, and this selection was repeated with increasing concentrations of gemcitabine. Cells are currently resistant to 1000 nm (L3.6) and 2000 nm (Aspc-1) after 11 months of selection. Kill curves reveal that the gemcitabine resistant cell lines' IC50s are greater 100 times that of the parental cell lines (Figure 1). The resistant cell lines also show increased mesenchymal characteristics, including increased vimentin and decreased E-cadherin (Figure 2). As MET is overexpressed in pancreatic cancer cells and implicated in chemoresistance in other cancer cells, we determined if the MET inhibitor cabozantinib, currently in a clinical trial, would increase the sensitivity of the resistant cells to gemcitabine.⁵ Unfortunately, cells remained resistant to gemcitabine.

To understand the mechanisms of resistance in these new resistant cell lines, we will take an unbiased approach using a cDNA gene array of both cell lines and use the results of this array to find greater than twofold gene expression changes between the parental and resistant cell lines. The goal of this approach will be to discover new drug targets that confer decreased resistance to gemcitabine. These resulting targets will be tested for their effects on gemcitabine resistance using inhibitors as well as employing a knock-down strategy to determine if loss of expression of the gene product will increase gemcitabine sensitivity. *In vivo*, knock-down tumors will be treated with gemcitabine and responsiveness compared to parental cell tumors and resistant tumors. We hope this will be the first step in the development of a novel therapeutic agent to be used as combination therapy with gemcitabine for pancreatic cancer. •

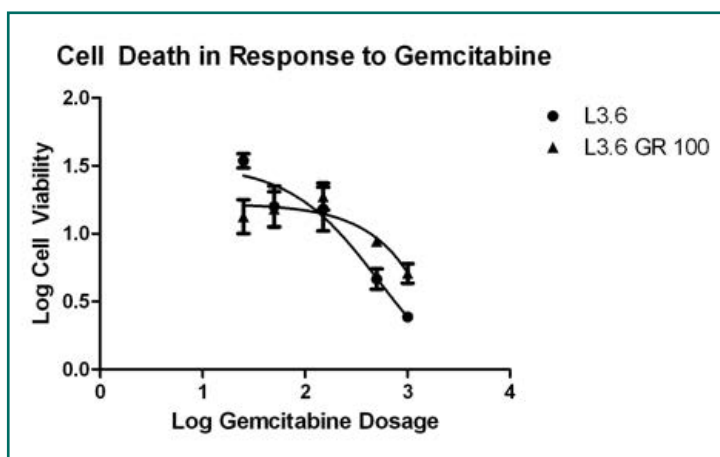
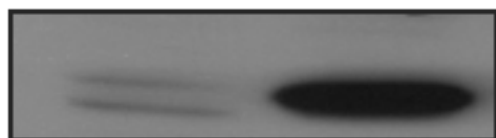


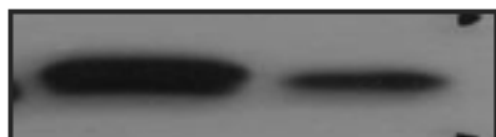
Figure 1: L3.6 IC50 523 nm Gemcitabine
L3.6 GR100 IC50 562,087 nm Gemcitabine

mechanisms of Adenocarcinoma

Figure 2: Markers of Resistance



E-cadherin



Vimentin



Vinculin

Dr. Rachel Morris is in her second year of research under the direction of Dr. Gary E. Gallick, a senior scientist at The University of Texas M. D. Anderson Cancer Center. Dr. Morris began her research fellowship after completing two years of surgical training at MCW.

FOR ADDITIONAL INFORMATION on her basic science studies of pancreatic cancer, see references, or contact Dr. Morris at rcharris@mcw.edu.

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Dr. Termuhlen to Lead MCW Community Medical Education Program



Dr. Paula Termuhlen

To address the need for primary care physicians in underserved communities across Wisconsin, the Medical College of Wisconsin has implemented a community medical education program. This program will include two medical campuses located throughout the state; Green

Bay and Wausau have been selected as sites for the new medical schools.

We are pleased to inform our readers that Paula Termuhlen, MD, Professor of Surgery and General Surgery Residency Program Director, has been named the Faculty Leader and Director of MCW's Community Medical Education Program. She will provide leadership in developing a comprehensive model for the community-based medical education program and facilitates the Steering Committee.

The Steering Committee is charged with “conceptualizing and developing a comprehensive model for community medical education programs designed to prepare high-quality, community-based physicians with competencies in team-based care and improving quality and outcomes in statewide populations while decreasing the cost of care.”

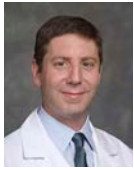
Congratulations, Dr. Termuhlen! •

Please Update Your Address

The Medical College of Wisconsin Department of Surgery wants to stay in touch.

Please contact Dana Schmidman at dschmidm@mcw.edu to update your contact information.

Safety and Efficacy of CT-Guided Hookwire Localization of Small Pulmonary Nodules Prior to Video-Assisted Thoracoscopic Surgery



DARYL P. PEARLSTEIN, MD
Division of Cardiothoracic Surgery

“Other things being equal, the simplest solution is most often the correct one.”
— Occam’s Razor

Background

Small pulmonary nodules (defined as nodules <15 mm for the purposes of this article) are a challenge for all general thoracic surgeons in 2013. With thin slice thoracic computed tomography (CT) scans becoming increasingly prevalent, patient referrals for small, asymptomatic pulmonary nodules are commonplace. Many of these nodules, although small, are suspicious for malignancy for a variety of reasons: either they demonstrate increasing size over sequential scans, they are found in patients with extensive smoking histories, or they show increased metabolic activity on PET scans. Further complicating matters, as far as thoracic surgeons are concerned, many of these patients have comorbidities, especially chronic obstructive pulmonary disease (COPD), which make pulmonary interventions risky. While surgical resection using minimally invasive techniques is often the treatment of choice, these small nodules can be challenging to palpate and identify during video assisted thoracoscopic surgery (VATS).

Several techniques for localizing small pulmonary nodules are emerging or have been described previously. These techniques include tattooing with blue dye (either percutaneously or bronchoscopically),¹ injection of radiotracer² or radiopaque material,³ the use of preoperative electromagnetic navigation bronchoscopy to place easily palpable fiducial markers, and intraoperative CT fluoroscopy. Many of these techniques are cumbersome, utilize multiple steps that are difficult to coordinate, or require expensive equipment.

A previously described technique of localizing small or non-solid pulmonary nodules with a CT-guided hookwire has been shown to be straightforward, easy to duplicate, and very successful.^{4,5} Non-solid pulmonary nodules are similar in density to the surrounding lung parenchyma. They are suspicious for bronchioloalveolar carcinoma (a low-grade lung cancer). Even though they appear distinct from the surrounding lung on CT, they are difficult to feel during thoracoscopy. Wire localization is an ideal way to mark these lesions to ensure a complete resection during thoracoscopy. However, caution is often exercised in performing this technique, especially in patients with COPD for fear of causing hazardous pneumothoraces, or the dislodgement of the wire from the lung that continues to move as the patient breathes. Therefore, we attempted to create a framework that would be feasible for interventional radiologists to localize small pulmonary nodules, (as well as non-solid nodules which

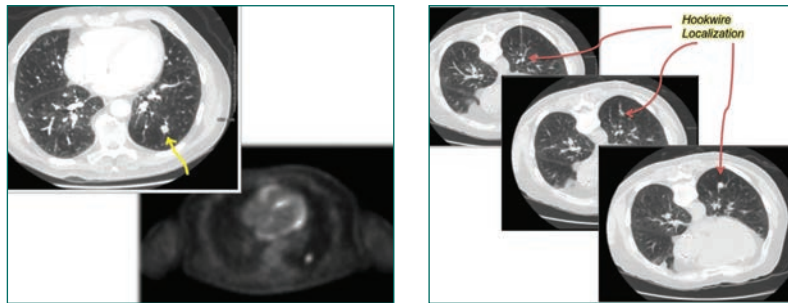


Figure 1 (left): Patient with COPD and asymptomatic pulmonary nodule. FEV1: 1.1L (36% predicted DLCO: (39%).

Figure 2 (right): CT-guided hookwire localization.

would be difficult to feel) safely with CT-guided hookwires. Our hypothesis was that if the localization procedure (performed by the radiologist in the CT scanner) was coordinated with the surgical team so that the patient was taken back to the operating room shortly after the wire was placed, there would be little risk to the patient, even if they had COPD and/or developed a pneumothorax. Additionally, we asked the interventional radiologists to cut the end of the hookwire flush with the chest wall of the patient after they marked the skin at the point of insertion. We felt this step would lessen the likelihood of the wire dislodging. Immediately after wire placement, patients would be taken to the operating room for VATS surgery and “wedge” resection of the lesion using endoscopic linear staplers.

Methods

Fifty consecutive patients with 51 suspicious pulmonary nodules that would be difficult to palpate during VATS due to their small size (44; size 10.2 ± 3.4 mm) or non-solid nature (7) were scheduled for preoperative localization with a CT-guided hookwire. (For images of a representative patient, see Figure 1.) In each case, a Ghiatas Beaded breast localization wire, 20G x 9 cm (Bard Biopsy Systems, Tempe, AZ) was used for localization. CT fluoroscopy was utilized for all localization procedures and moderate sedation with midazolam and fentanyl was offered (Figure 2). A total of 26 patients had COPD (10 mild, 13 moderate, three severe). Once the hookwire was placed, the radiologist marked the skin at the point of insertion and then cut the tail of the wire flush with the chest wall. Immediately after localization, patients went to the operating room for

Hookwire Localization of Pulmonary Lobectomy (VATS) Resection

resection (Figure 3). A total of 10 interventional radiologists at two different hospitals performed the wire localizations. All resections were performed by the same surgeon.

Results

A total of 47 patients successfully underwent CT-guided hookwire localization of a suspicious nodule. Four patients demonstrated regression noticed by the radiologist on the CT obtained prior to beginning their procedure, and localizations were cancelled. The time of localization procedures was 27 ± 10.5 minutes. The average time between the end of the localization procedure and the start of the operation was 44.8 ± 23.3 minutes (range 15–123 minutes). All lesions were successfully resected by VATS without conversion. Mean operative time for VATS wedge resection was 47 ± 3.2 minutes. No pre-operative chest tubes were necessary and there were no complications related to wire localization. Wire dislodgement was noted in three cases, but in each of these cases, the skin mark where the wire was inserted, combined with the mark on the visceral pleura where the wire penetrated the lung, allowed the surgeon to easily identify the nodule. Final diagnoses included 18 non-small cell lung cancers, 10 metastases, one lymphoma, and 18 benign lesions. Twelve patients underwent additional procedures including five VATS lobectomies and seven brachytherapy mesh insertions. Mean chest tube duration was 2.1 days and mean hospital stay was 2.5 days.

Discussion

With lung cancer screening being performed and the increased use of high-resolution thoracic CT for a variety of reasons, small suspicious pulmonary nodules are being found with increasing prevalence. Many of the patients in whom these nodules are identified have comorbidities, including COPD. Because these nodules are often difficult to palpate during thoracoscopy, it is important that thoracic surgeons develop strategies to localize these lesions prior to minimally invasive (VATS) resection. Of course, it is important that these techniques are safe and effective. CT-guided hookwire localization

is an effective way to identify suspicious pulmonary lesions that may be difficult to palpate during VATS and appears safe even in patients with COPD. Demonstrated benefits include efficient operating times and no thoracotomy conversions. Furthermore, our results suggest that success is reproducible among multiple interventional radiologists. One of the main factors in assuring patient safety seems to be coordinating the schedule between the interventional radiology team and the surgical team so there is very little lag time between the end of the localization procedure and the start of the operation. Our goal was to keep this time below one hour, but on nine occasions, we encountered delays of greater than 60 minutes (longest 123 minutes) without incident. A small percentage of lesions (7.8%) regressed between the time of the patient's preoperative CT scan and their preoperative localization surgery. These lesions presumably are benign and represent the expected false-positive rate of current imaging studies. Consequently we were able to withhold unnecessary surgical intervention in this subset of patients. Although further experience is necessary, our hope is that this technique eventually may be more widely utilized to resect small suspicious pulmonary nodules. •

**Presented at the 50th Annual Meeting of the Eastern Cardiothoracic Surgical Society, Naples, Florida, October 4–6, 2012.*

FOR ADDITIONAL INFORMATION on this topic, see references, visit mcw.edu/surgery, or contact Dr. Pearlstein at 414-955-6969; dpearlstein@mcw.edu.

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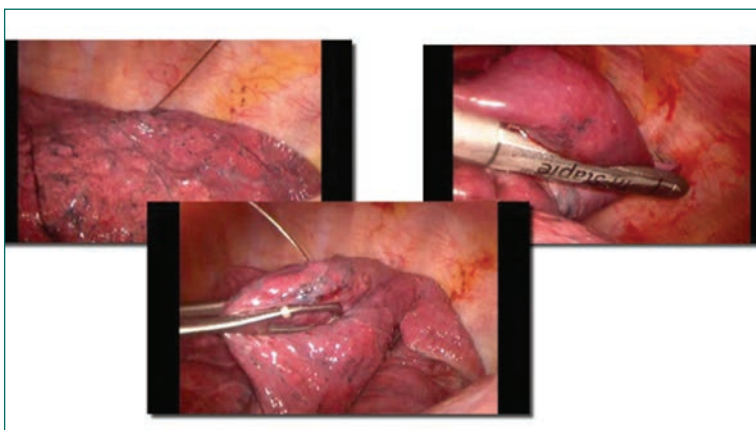


Figure 3: Surgical resection of wire-localized lesion

Contralateral Prophylactic Mastectomies: Who Benefits?



AMANDA L. KONG, MD, MS
Division of Surgical Oncology

Although lung cancer is the leading cause of cancer death in women, breast cancer is the most commonly diagnosed malignancy in the United States.¹ From radical mastectomies to modified radical mastectomies to lumpectomies with radiation, surgical interventions for breast cancer have become less invasive, as it has been shown in the National Surgical Adjuvant Breast and Bowel Project (NSABP) trials that there is no survival benefit from maximally invasive surgery.²

However, there has been a national trend toward performing mastectomies including contralateral prophylactic mastectomies (CPM) for the prevention of contralateral breast cancer. Using SEER data, Tuttle *et al* found that the rate of CPM in patients with ductal carcinoma *in situ* (DCIS) increased from 6.4% to 18.4%³ from 1998 to 2005, and the rate of CPM in patients with invasive breast cancer increased from 4.2% to 11% from 1998 to 2003.⁴ These findings are surprising given the risk of developing contralateral breast cancer. Gao *et al* used SEER data examining women diagnosed with unilateral DCIS or Stage I or II breast cancer from 1973 to 1996 and has reported that the incidence of contralateral breast cancer is approximately 6% and 12% at 10 and 20 years, respectively, with an annual incidence of 0.5–0.75% a year⁵. These numbers are likely even lower today given the improvement in systemic therapy available. The group of women who are most at risk for developing contralateral breast cancer are those with BRCA1 and BRCA2 mutation carriers who have 4.5 fold and 3.4 fold increased risks of contralateral breast cancer, respectively, compared to non-carriers as well as those who have undergone mantle irradiation during childhood and adolescence.⁶

At the American Society of Clinical Oncology's Quality Care Symposium in San Diego this year, Hawley and colleagues from the University of Michigan Medical School presented data that demonstrated that many women considered CPM despite the fact that very few of them had a clinically significant risk of developing contralateral breast cancer. In fact, most of the women they surveyed did not have a clinical indication for considering CPM and thus, were not expected to benefit from the procedure in terms of disease-free survival.⁷

The group surveyed 2,245 women with newly diagnosed breast cancer using the Detroit and Los Angeles SEER registries from June 2005–February 2007. They then re-surveyed these women approximately four years after their diagnosis. The primary outcome of the study was the receipt of CPM. The authors found that of the 1,446 women who had not had a recurrence

of breast cancer at the time of the second survey, 35% considered CPM and 7.4% received it. Of the women who received a mastectomy to treat their initial breast cancer, 53% considered CPM and 19% received it. Approximately 70% of the patients who received CPM were at very low risk for contralateral disease, and 90% of those who received CPM reported being very worried about recurrence when making their treatment decision. On multivariate analysis, receipt of CPM was associated with having a family history of breast cancer and a positive genetic test, but was also associated with greater worry about recurrence. The authors concluded that more research must be conducted to determine the underlying factors driving the decision making process for contralateral prophylactic mastectomies.

A recent Cochrane review concluded that CPM decreased the incidence of contralateral breast cancer, but was not associated with survival benefit, and should be considered by those at very high risk for breast cancer.⁸ Other single-institution reports have found that CPM is associated with a small improvement in breast cancer-specific survival in younger women with early ER-negative breast cancer⁹ or improved overall survival and disease-free survival in those with early stage breast cancer who have a family history of breast cancer.¹⁰

It is unknown why there is an increasing trend of CPM. Potential reasons include improvements in mastectomy and breast reconstruction techniques, availability of genetic testing, desire for balance and symmetry, increased use of MRI, physician recommendation, and fear of recurrence. However, CPM is not without risk. Patients may develop post-surgical complications, which may lead to delays in treatment, poor cosmetic outcome, and a diminished sense of sexuality.¹¹

Further studies are needed to elucidate which populations may derive a survival benefit from CPMs and why an increasing number of women are opting for this surgical approach. Until then, it is important for physicians to discuss and educate their patients on the risk of cancer recurrence versus developing a new primary in the non-affected breast when developing an individualized treatment plan. •

FOR ADDITIONAL INFORMATION on this topic, see references, visit mcw.edu/surgery, or contact Dr. Kong at akong@mcw.edu or 414.805.5815.

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Department of Surgery Welcomes New Faculty

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Dr. Husam Balkhy

The Department of Surgery and the Division of Cardiothoracic Surgery are pleased to announce that Dr. Husam ‘Sam’ Balkhy joined the Division of Cardiothoracic Surgery on September 1, 2012. Dr. Balkhy is a graduate of King Abdulaziz University College of Medicine in Saudi Arabia. He completed a residency in general surgery at Tufts New England Medical Center and then completed a fellowship in vascular surgery at the Lahey Clinic before returning to Tufts to complete his cardiothoracic surgical training.

Dr. Balkhy has been in practice in Milwaukee since 1997. He has held leadership positions at hospitals in the Milwaukee metro area, most notably the Wisconsin Heart Hospital where he has served as Chairman of the Department of Cardiothoracic Surgery and Director of the Center for Robotic and Minimally Invasive Cardiac Surgery.

Dr. Balkhy has a broad range of clinical interests in cardiac surgery, especially robotic and minimally invasive cardiac surgery, the surgical treatment of atrial fibrillation, and off-pump coronary surgery. He has made substantial contributions to the development of minimally invasive cardiac surgery and robotic technology. We welcome Dr. Balkhy to the full-time faculty.



Dr. Muthusamy
Kunnimalaiyaan

The Department of Surgery and the Division of Surgical Oncology are pleased to welcome Dr. Muthusamy Kunnimalaiyaan to the faculty as an Assistant Professor of Surgery. Dr. Kunni was previously a senior scientist in the Department of Surgery at the University of Wisconsin where he was the Director of the Endocrine Surgery Research Laboratories. He has received numerous awards and mentored many students and residents in addition to serving on the editorial board of several outstanding journals. He is funded by the NIH and his previous work focused on neuroendocrine and pancreatic cancer. With 65 peer-reviewed publications and more than 100 presentations, his addition represents an important recruitment for the division. He is accompanied by his wife, Selvi, who works as a researcher, and their young son, Navin. Dr. Kunni’s successful recruitment will provide an outstanding bridge for basic science research. •

Reoperative Parathyroid Surgery: Utility of Intraoperative Localization from Bilateral Internal Jugular Veins in Patients with Persistent Hyperparathyroidism



AZADEH A. CARR, MD
Endocrine Surgery Fellow
Division of Surgical Oncology



TRACY S. WANG, MD, MPH
Division of Surgical Oncology



DOUGLAS B. EVANS, MD
Chairman, Department of Surgery

Primarily hyperparathyroidism (PHPT) occurs as a result of excess production of parathyroid hormone (PTH), leading to elevated serum calcium levels. The only curative treatment for PHPT is surgical resection of the abnormal parathyroid gland(s). Surgical techniques include bilateral cervical exploration or minimally invasive parathyroidectomy, a focused approach that uses preoperative localization studies and intraoperative PTH (IOPTH) monitoring. Both have been shown to have success rates of 95-98%.¹

Persistent PHPT is defined as elevated serum calcium levels within six months of initial surgery and is usually due to failure to find the abnormal parathyroid gland at the initial operation or rarely unrecognized multiglandular disease. In the majority of cases of persistent PHPT, the parathyroid adenoma is eventually located in expected locations rather than at ectopic sites.^{2,3} Recurrent PHPT refers to elevated serum calcium levels after more than six months of normocalcemia and implies a successful initial operation.

Approaching the patient with persistent or recurrent PHPT takes special consideration, given the risks associated with reoperative parathyroid surgery, including the risks of permanent hypoparathyroidism and recurrent laryngeal nerve injury. These factors make preoperative localization imperative. In addition to standard preoperative imaging modalities of cervical ultrasound, 99-technetium Sestamibi with single photon emission computed tomography (MIBI-SPECT), and 4D-CT; more invasive localization methods, such as preoperative selective venous sampling and preoperative or intraoperative ultrasound guided bilateral

internal jugular (IJ) venous sampling for PTH have been employed to achieve accurate preoperative localization.

The MCW Endocrine Surgery protocol for preoperative localization in patients with PHPT includes routine MIBI-SPECT and ultrasound; 4D-CT is performed for patients with discordant or negative imaging. All patients with persistent or recurrent PHPT who are considered for reoperative parathyroidectomy routinely undergo 4D-CT in addition to MIBI-SPECT and ultrasound. All operations are performed with IOPTH monitoring with intraoperative success defined as a final post-excision PTH level >50% below the baseline level and within the normal range.

In cases of negative or discordant imaging, bilateral IJ PTH sampling can be a useful adjunct. This can be performed under ultrasound guidance in the office or intraoperatively, either percutaneously after induction of general anesthesia or via the cervical neck incision. In 2007 Ito *et al* analyzed 152 patients with PHPT at a single institution who underwent bilateral IJ PTH sampling intraoperatively.⁴ They defined lateralization as a >5% difference between the right and left IJ samples, and found a sensitivity of 80% and positive predictive value of 71%, compared to 72% and 71% for MIBI. Of the 45 patients with negative preoperative imaging, bilateral IJ PTH sampling successfully localized the abnormal parathyroid glands in 26 cases (58%) and confirmed bilateral disease in five cases (11%). In 2009, Carneiro-Pla reported office-based bilateral IJ PTH sampling in 21 patients with negative MIBI and lateralization was defined as >10% difference (right to left).⁵ Sampling was correct in indicating the side of the abnormal gland in 17 (81%) of 21 patients.

To refer a patient or request a transfer/consultation, please use the references below:

**Froedtert & The Medical
College of Wisconsin**
Referrals: 800-272-3666
Transfers/Consultations:
877-804-4700
mcw.edu/surgery

Clinical Cancer Center
Referrals: 866-680-0505
Transfers/Consultations:
877-804-4700

**Children's Hospital
of Wisconsin**
Referrals/Transfers/
Consultations: 800-266-0366
Acute Care Surgery:
414-266-7858

Intraoperative Parathyroid Hormone Sampling with Negative Preoperative Imaging

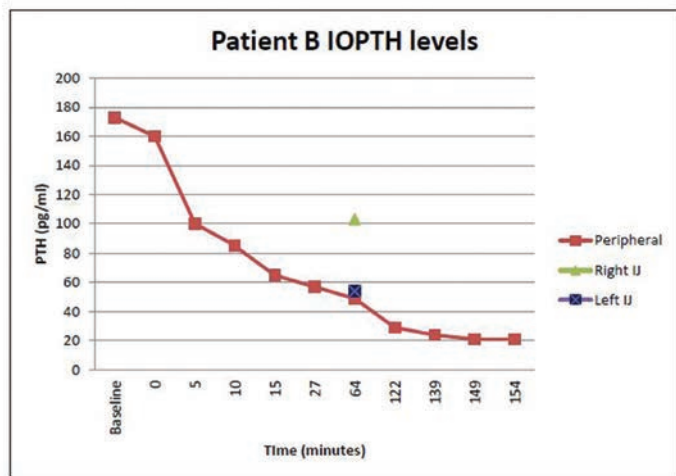


Figure 1: Time 0: right inferior parathyroid removed; Time 122: right thyroid lobectomy completed

Two of our recent reoperative cases at MCW in which intraoperative bilateral IJ PTH sampling aided in identifying the side of the abnormal parathyroid are discussed below to demonstrate the potential utility of this technique.

Patient A is a 74-year-old woman with persistent PHPT who previously underwent bilateral cervical exploration with reported visualization of all four parathyroid glands and resection of a histologically normal right parathyroid gland. Prior to re-exploration, preoperative imaging was repeated, as per the MCW protocol described above, but no obvious parathyroid adenoma was identified. The operative plan was to obtain bilateral intraoperative IJ PTH samples prior to incision as a guide for exploration. The baseline PTH level was 76 pg/mL, the right IJ PTH was 89, and the left IJ PTH was 75 (>10% difference, favoring the right side). Unilateral exploration of the right side was performed, with no evident parathyroid adenoma. Based on the differential IJ samples, a right thyroid lobectomy was performed, removing all attached soft tissue to the right of midline and leaving only trachea, esophagus, and right recurrent laryngeal nerve. Post resection peripheral PTH samples declined appropriately to 17 pg/mL at 10 minutes and final pathology confirmed a parathyroid gland in the surgical specimen.

Patient B is a 74-year-old woman with recurrent PHPT who had undergone bilateral cervical exploration for PHPT 40 years ago with successful parathyroidectomy reported as the removal of a single adenoma. Prior to reoperative parathyroidectomy, a right inferior parathyroid adenoma was identified on 4D-CT. At the time of surgery, the right inferior parathyroid gland was identified and resected, and IOPTH levels decreased from a baseline of 173 to 65 pg/mL at 15 minutes post-

excision; remaining at 57 pg/mL at 27 minutes. Failure of IOPTH levels to decline further raised concern for residual abnormal parathyroid tissue. Bilateral IJ PTH sampling was performed, showing the right side to be almost twice that on the left, perhaps stimulated by manipulation of an abnormal parathyroid in the right side of the neck (Figure 1). A right thyroid lobectomy with excision of all surrounding tissue on right side, including the entire thymic tongue was performed, with IOPTH levels decreasing to 21 pg/mL at 15 minutes post-excision. The final pathology was notable for multiple areas of parathyroid tissue within the resected right neck contents, indicating possible parathyromatosis (fracture of the parathyroid adenoma at the initial operation 40 years ago).

Both patients have been eucalcemic since surgery, suggestive of a durable biochemical cure from PHPT. Despite the accuracy of preoperative noninvasive imaging modalities in patients with PHPT, surgical outcomes may benefit from innovative techniques, such as bilateral IJ sampling, particularly in patients with persistent or recurrent parathyroid disease. Importantly, the decision to reoperate in these patients must be made in a multidisciplinary fashion, to include experienced endocrinologists for confirmation of the diagnosis, radiologists to properly perform and evaluate imaging studies, and endocrine surgeons with experience in parathyroid anatomy and the interpretation of IOPTH levels. •

FOR ADDITIONAL INFORMATION on this topic, please refer to the selected references, visit mcw.edu/surgery, or contact Drs. Carr or Wang at 414-805-5755; acarr@mcw.edu, tswang@mcw.edu.

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A Disease-specific Pilot Program for Outpatient EPIC Referrals

The Medical College of Wisconsin Department of Surgery has initiated a pilot program for disease-specific, outpatient EPIC referrals for those programs previously placed via either the 'General Surgery' and/or the 'Clinical Cancer Center' referrals:

Bariatric/Minimally Invasive Surgery (RFSUC.002)

Bariatric Surgery, foregut surgery (achalasia, hiatal hernia, reflux surgery)

Breast Cancer Surgery (RFCCC.003)

For benign breast conditions, use the Breast Care Referral, Undiagnosed

Colorectal Surgery (RFSUC.003)

Anorectal disease, colorectal cancers, benign colorectal disease, inflammatory bowel disease

Condon Hernia Institute (RFSUC.005)

All abdominal wall defects/hernias including ventral, recurrent, incisional, inguinal, femoral

Endocrine Surgery (RFSUC.001)

Thyroid cancer, benign thyroid disease, parathyroid disease, adrenal tumors, carcinoid tumors, carcinoid disease, inherited endocrine tumors

General Surgery (RFSUC.000)

Abdominal pain, abdominal mass, gallbladder disease, soft tissue masses/nodules, feeding tubes

Hepatobiliary Surgery (RFSUC.004)

Liver tumors (benign and malignant), gallbladder disease, biliary tree disorders, bile duct cancers

Pancreatic Surgery (RFSUC.006)

Pancreatic cancer, benign pancreatic diseases (cysts, pancreatitis), pancreatic neuroendocrine tumors

Surgical Oncology (RFCCC.002)

Melanoma, retroperitoneal sarcoma, neuroendocrine tumors, carcinoid tumors, carcinoid disease, carcinomatosis, hyperthermic chemoperfusion therapy (HIPEC)

For urgent/emergent issues requiring same-day attention, please call the Acute Care Surgery service via the Froedtert Hospital operator (414-805-3000).

Leaving a Legacy

by Meg M. Bilicki, Director of Development for the Department of Surgery

When looking to define the word passionate, look no further than Claire L. Scheele, MD, FACS, '73, a general surgeon in Martinsville, Indiana. She is passionate about many things in her life, but two at the top of the list are medical research and the Medical College of Wisconsin.

In Dr. Scheele's eyes, it's simple. "Planned giving should be a part of everyone's estate planning. It is the type of gift that can help the College now and in the future." Dr. Scheele wants to ensure the next generation of medical students has the same opportunity. "Medicine is a calling," she said. "You never stop being a doctor. I was given the gift of a superior medical education and medical training. I have the best job in the world, and I have the best patients. It has just been a blessing to practice medicine."

"The outstanding legacy we, as alumni, leave is not only one of commitment to improving the health of our communities, but one that involves sharing time and resources with future physicians" said Dr. Scheele. "I want to impact the care of as many people as possible, so I'm supporting future physicians who will be caring for patients long after I leave the medical field. Making this commitment to the Medical College's Department of Surgery became a way for me to leave a legacy. I feel it's my responsibility to give back because of how much my time at the Medical College has impacted my career and my life."

Planned giving is a philanthropic approach to invest your money, often receiving benefits during your lifetime, and then bequeath remaining funds to the Medical College's Department of Surgery. To excel in the future, the Department of Surgery must continue to develop new financial resources that will advance our core missions of education, discovery, patient care, and community engagement.

Leaving a legacy is a great way for your generosity to last beyond your own lifetime. It's also an opportunity to leave a legacy of your own for your family and future generations.

The benefits of planned giving—now and later—are clear. Planned giving provides creative and flexible strategies for your estate and charitable planning. Some planned gifts provide you with income. Many of them can reduce your income or estate taxes. Whether as a charitable bequest, a charitable remainder trust or a charitable gift annuity, donors can be recognized during their lifetime for what they do as well as leave a legacy of which they can be proud. Your attorney can advise you on how best to accomplish your goals. The greatest gift, however, lies in knowing you are supporting the work of the Medical College's Department of Surgery now and in the future.

I would like to encourage our readership to consider the Medical College by including a bequest in your will, or by designating the Department of Surgery a beneficiary of your trust, insurance policy, retirement plan, bank account or security. With your planned gift, you may enjoy financial or tax benefits while also helping ensure that we are able to continue our important work for years to come.

If you have already included a gift to us in your estate or financial plans, please let us know so that we can ensure your future gift is directed to the programs you wish to support. You can also share your gift intentions with us and still remain anonymous.

To discuss the many ways that you can leave a legacy, please contact Meg Bilicki at (414) 805-5731 or mbilicki@mcw.edu. We are deeply grateful to each and every individual who supports the Medical College's Department of Surgery. Thank you for your thoughtful commitment to our future. •



Claire L. Scheele, MD, '73, GME '79.

Outstanding teachers honored

Congratulations to this year's Outstanding Medical Student Teachers. Several Department of Surgery faculty and residents have been selected as recipients. These recipients were formally recognized on Wednesday, October 17, between M&M and Grand Rounds. Please join us in thanking:

M2 Medical Ethics & Palliative Care

Marshall Beckman, MD

M3 Clerkships

John Aiken, MD

Ryan Berg, MD

George Haasler, MD

Jeremy Juern, MD

John Miura, MD

Gary Seabrook, MD

Kathleen Simon, MD

M4 Sub-Internships

Panna Codner, MD

Brian Lewis, MD

Susan Tsai, MD, MHS

Travis Webb, MD, MHPE

In the Fall 2012 Issue of *Leading the Way*, the author of the "In Memoriam" piece was omitted. Stuart D. Wilson, MD, was the author of that piece. We apologize for the omission.



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MARK YOUR CALENDARS

Upcoming Events

March 23, 2013: Updates in Gastrointestinal Oncology

This event will provide an update and summary of ASCO® GI presentations and a discussion of new developments in surgical oncology. Dr. Timothy Pawlik from Johns Hopkins Hospital will present.

April 3, 2013: Third Annual Vascular Access Symposium

This symposium features an exciting roster of expert clinicians who will speak to the immediate and real needs of patients with end-stage renal disease. This half-day symposium will be held in Conference Room M, located in the Cancer Center.

April 12, 2013: Acute Care Surgery: Trauma, Critical Care, and Emergency General Surgery Symposium

This day-long educational activity will provide updates and general information regarding the practice of emergency general surgery, surgical critical care, and trauma care.

May 3, 2013: Complex Abdominal Hernia Symposium

This event is designed to educate the community general and plastic surgeon about the latest techniques for complex abdominal wall reconstruction. Dr. Brent Matthews, of Washington University-St. Louis, will present.

May 10 & 11, 2013: MCW and University of Texas M. D. Anderson Cancer Center Endocrine Surgery Symposium

The 2013 symposium will highlight current issues in the management of disorders of the thyroid, parathyroid, and adrenal glands. Invited speakers include well-known academic physicians from Harvard Medical School, The Medical College of Wisconsin, and The University of Texas M. D. Anderson Cancer Center.