

SURGERY UPDATE

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From the Chairman

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This issue of *Surgery Update* contains too much information to cover in a short introduction. I hope you all have time to read the excellent articles by Drs. Peschman (PGY2), Kastenmeier (joined our faculty on September 1; see page 12), Calkins, Rossi, and Termuhlen. The primary goal of *Surgery Update* is to provide brief, scientific contributions from MCW faculty and residents that highlight recent innovations, translational research, and clinical information useful in the daily practice of medicine and surgery. This issue is a bit unique due to the amount of additional information that we felt important to include (especially for our alumni). The excitement of a new academic year (chief residents appear on pages 4-5) has been quieted by the sudden and most untimely death of Dr. Bob Ausman, a longtime faculty member and loyal supporter of the Department of Surgery and MCW. Please read the brief summary of Bob's work in support of MCW on page 15; he was a wonderful man, a talented scientist, and an insightful advisor for many of us – we hope to have the Simulation Center be a lasting memory of his many contributions to our department.

The picture on this page captures Dr. Allan Roza, who was recently awarded the “Golden Cane Award” for teaching excellence by the senior medical students (page 15). Allan is pictured in the operating room with Rachel Harris (PGY3) who is currently doing molecular biology research in the laboratory of Dr. Gary Gallick at M. D. Anderson Cancer Center (Houston) as part of the T32 grant program. In fact, Dr. Paula Termuhlen, our new residency program director, also worked in the Gallick lab during her residency (please refer to Paula's article on melanoma and the MSLT-II trial on page 8). Congratulations also to Drs. Travis Webb and Kevin Packman (Aprahamian Faculty Teaching Awards) and Dr. Dean Klinger (Professionalism Award), all of whom were chosen by our residents and recognized at the Eberbach Banquet (page 15).

Lastly, it is with deep gratitude that Dr. Clark Gamblin and I acknowledge the generosity of Sharon Wadina in her support of the Division of Surgical Oncology and the creation of the Wadina Chair (page 13). Drs. Gamblin and (Sam) Pappas were among the physician team that cared for Mrs. Wadina during her recent surgery for soft tissue sarcoma. Under the direction of Dr. Pappas, her contribution to cancer research will make a meaningful difference. Congratulations to Dr. Sam Pappas, the inaugural holder of the Wadina Chair. •



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Fetal Surgery: Maternal-Fetal Intervention



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The practice of pediatric general and thoracic surgery predominantly focuses on the care of surgical conditions encountered from birth through the teenage years. However, a multitude of advances have allowed practitioners to diagnose and treat some conditions prior to birth. Fetal intervention involves the utilization of techniques aimed to ameliorate fetal conditions that may be incompatible with life, or improving upon such conditions to ensure a live birth and enabling a post-natal intervention to address such ailments.¹ However, while many surgical conditions can now be accurately diagnosed before birth, only a few are amenable to fetal intervention. In addition, *fetal intervention* is more accurately *maternal-fetal intervention* as the most important consideration to the fetus is the well-being and safety of the mother.

Counseling

Perhaps *the* most important role of the pediatric surgeon in addressing a fetal anomaly is the act of counseling the mother and the family. Prenatal pediatric surgical consultations have a significant impact on the perinatal management of a fetus with a congenital anomaly by providing obstetric and perinatology colleagues and families with valuable information regarding the surgical management of the problem. The most common anomalies referred for prenatal pediatric surgical consultation are listed in Table 1. The utilization of contemporary therapy for a fetus or a neonate has made survival possible for many infants with serious congenital anomalies, however, the ethical considerations regarding the deployment of advanced fetal and neonatal care can be complex in some instances. A pediatric surgeon from our group meets with the family and members of our multidisciplinary team prenatally to ensure the optimal care of a neonate – whether a fetal intervention is indicated or not. Mothers are *often, but not always*, encouraged to deliver at the **Maternal Fetal Care Center at Froedtert Hospital**, which is in immediate physical proximity to the Level

Table 1: Common anomalies referred for prenatal pediatric surgical consultation.

Congenital lung lesions (i.e. CPAM, a.k.a. CCAM)
Congenital Diaphragmatic Hernia (CDH)
Esophageal Atresia/Tracheoesophageal Fistula (TEF)
Intestinal Atresias (Duodenal Atresia and Jejunoileal Atresia)
Abdominal Wall Defects (Gastroschisis and Omphalocele)
Sacroccygeal Teratoma
Cystic Abdominal or Pelvic Masses

III NICU and operating rooms at **Children’s Hospital of Wisconsin**. As the mother recovers, a care plan is developed to provide for the surgical care of the neonate – much of which has been determined prior to delivery. An integrated approach with care coordination among specialists limits stress on both parents and infant, while minimizing separation between the family and their newborn.

What anomalies are amenable to fetal intervention and what techniques are utilized?

A host of congenital anomalies have been treated by several different types of fetal interventions. Table 2 lists a current compendium of anomalies that may be considered for fetal intervention depending on a variety of individual circumstances. In general, there are three approaches to fetal intervention.

Table 2: Congenital anomalies that may be amenable to fetal intervention

Type	Examples
OPEN FETAL SURGERY	<ul style="list-style-type: none"> • SCT – Resection • MMC – Repair • EXIT <ul style="list-style-type: none"> ○ Tracheal occlusion ○ Neck tumors ○ Large CCAM (EXIT to lobectomy)
FETAL ENDOSCOPIC SURGERY	<ul style="list-style-type: none"> • Balloon Occlusion of Trachea (for CDH) • Laser Ablation of Vessels (for TTTS) • Cord Ligation/Division • Cystoscopic Ablation Posterior Urethral Valves • Amniotic Bands Division
FETAL IMAGE GUIDED SURGERY	<ul style="list-style-type: none"> • Amnioreduction/Infusion • Fetal Blood Sampling • RFA Anomalous Twins • Vesico/Pleuro - Amniotic Shunts • Cord Monopolar Cautery • Balloon Dilation Aortic Stenosis

The most definitive yet most invasive is *open fetal surgery*. In this technique, the mother is anesthetized, a lower abdominal incision is made to expose the uterus and create a hysterotomy, surgical repair of the fetal anomaly is completed, the uterus and maternal abdominal wall are closed, and the mother is awakened. This requires future cesarean delivery of this and subsequent pregnancies, and often results in preterm labor and delivery. Most recently, a randomized trial comparing open fetal surgery to traditional postnatal management of myelomeningocele (MMC) was completed demonstrating a statistically significant decreased need for postnatal ventriculoperitoneal shunting in the fetal treatment group. The long-term benefits of this type of open fetal surgery are still to yet to be realized.²

Fetal endoscopic surgery was developed in the 1990s with the principal intent of minimizing the incidence of preterm labor. The



Figure 1: A fetus delivered by EXIT at Children’s Hospital of Wisconsin who was prenatally diagnosed with a large cervical teratoma. A tracheostomy was performed after traditional airway intubation proved impossible. The fetus was delivered, and the cervical teratoma eventually resected two days later. The infant had a subsequent uneventful recovery and is alive and well 18 months following birth.

combination of using image-guided techniques along with in-utero endoscopy has proved to be useful in treating a number of conditions. Fetoscopic intervention can be done either percutaneously or through a small opening in the mother’s abdomen (mini-laparotomy). Although this technique is less invasive than open fetal surgery, it has not eliminated the problem of preterm labor. It has proven particularly useful for treating problems with the placenta, such as twin-to-twin transfusion syndrome (TTTS).³

Fetal Image-Guided Surgery (FIGS) describes the method of manipulating the fetus without an incision in the uterus. The manipulation is done entirely utilizing real-time sonography. It can often be performed under either a regional anesthetic such as an epidural or a spinal, or local anesthesia. This is the least invasive of the fetal access techniques and, therefore, causes the least degree of maternal discomfort and risk of preterm labor, although it has not completely eliminated the problem of preterm labor. Image-guided intervention was first used for amniocentesis and fetal blood sampling, but now has been used successfully for a variety of fetal manipulations, including placement of catheter-shunts in the chest, abdomen, or bladder, radio frequency ablation (RFA) to solve problems with anomalous twins, and even for cardiac manipulation.⁴ It is also important to remember that the fetus can be accessed non-invasively through the mother’s circulation. For example, in the treatment of fetal cardiac arrhythmias, medicines and nutrients can be delivered to the fetus by administering them to the mother and letting them cross the placenta.⁵

The EXIT procedure

The EXIT (“EX-utero Intrapartum Therapy”) procedure is a specific type of open fetal surgical intervention performed with the intent of operating on a fetus while maintaining placental blood flow, with the ultimate goal of delivering the fetus once the intervention has been completed. It is primarily used in cases whereby the fetal airway is obstructed. Congenital High Airway Obstruction Syndrome (“CHAOS”) is defined either by an

intrinsic airway anomaly such as tracheal atresia, or an extrinsic lesion that may render immediate postnatal airway access untenable and life threatening (i.e., a cervical teratoma – Figure 1). The goal of the EXIT procedure is to provide the fetus with a functioning airway so that oxygen can be delivered to the lungs after the fetus is separated from the placenta. The EXIT procedure is a planned, specialized intervention and delivery that requires a large multidisciplinary team consisting of pediatric surgeons, obstetricians, anesthesiologists, and neonatologists. The procedure is begun similar to a Cesarean delivery, however unlike a classic Cesarean in which the aim is to deliver the fetus quickly, the mother is placed under general anesthesia in order to ensure that the uterus is completely relaxed while the intervention on the fetus is performed. The fetal head and neck are delivered, and the surgeon uses a multitude of techniques to secure a durable endotracheal airway. If this is successful, and oxygen is being delivered to the fetus, the infant is delivered and the umbilical cord cut. If an endotracheal tube cannot be passed through the obstruction, the surgeon performs a tracheostomy, and inserts a tube directly into the trachea, bypassing the blockage. Once the tube is placed, and the surgeon is confident that oxygen is being delivered to the baby, the infant is delivered and the lesion is addressed once the infant is removed from placental support.⁶

Conclusion

Many types of fetal intervention remain novel, yet may afford an option when the lack of intervention would otherwise prove fatal for the fetus. In weighing the risks versus the benefits of an intervention, the most important considerations are the mother, her health, her family, and her ability to have other children. When faced with a prenatal diagnosis that may be amenable to such techniques, our multidisciplinary team of caregivers assembles to ascertain whether or not an intervention may be warranted, and in many cases, can carry out the intervention here on the MCW campus allowing families to remain close to home. •

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FOR ADDITIONAL INFORMATION on this topic, see references, visit mcw.edu/surgery, or contact the author at 414-266-6558; calkins@chw.org.

Does Age Play a Role in Trauma Admission?



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As America ages, the overall utilization of health resources continues to rise. This will likely affect trauma centers, an area of the health-care system that typically has a young patient population. Based on data from the Centers for Disease Control and Prevention and National Center for Injury Prevention and Control, more than 21.9 million people suffered traumatic injuries in 2008. Of these, approximately 3.3 million (roughly 15%) occurred in people age 65 or older.¹ Between the increasing proportion of the elderly in the population and advances in health care that improve quality and quantity of life, the number of elderly patients experiencing traumatic injuries will continue to increase.

The goal of our study was to examine the geriatric admission practices of our Level 1 Trauma Center, with the specific aim of determining whether age independently increased the likelihood of admission. We constructed a database from our trauma registry from January 1, 2005 to December 31, 2006,

which included 5,202 (1,970 discharged, 3,232 admitted) patients. Many demographic, physiologic, and injury-related variables were included in the analysis. The data was rigorously analyzed with multivariable logistic regression to determine if age alone was an independent variable for admission.

Over the two year period, approximately 62.2% of the overall trauma population were

admitted for further care. That number was significantly higher for patients age 65 or older (86.7%;² = 126.64, $p < 0.001$). Binomial regression identified several independent factors that had significant correlation ($p < 0.001$) predicting hospital admission including age greater than 64 (OR 3.76), presence of head injury (OR 5.3), moderate (≥ 15) injury severity score (ISS) (OR 17.5),

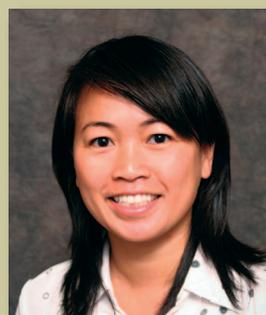
Table 1. Admission Rates for Defined Age Groups

Age Range (yrs)	Median of Age Range (yrs)	Discharged Patients	Admitted Patients	Total Patients	Admission Rate (%)
≤24	19	601	731	1332	54.9
25-34	30	511	668	1179	56.7
35-44	40	416	613	1029	59.6
45-54	50	262	553	815	67.9
55-64	60	116	275	391	70.3
<65	35	1906	2840	4746	59.8
≥65	82	60	391	451	86.7

MEDICAL COLLEGE OF WISCONSIN DEPARTMENT OF



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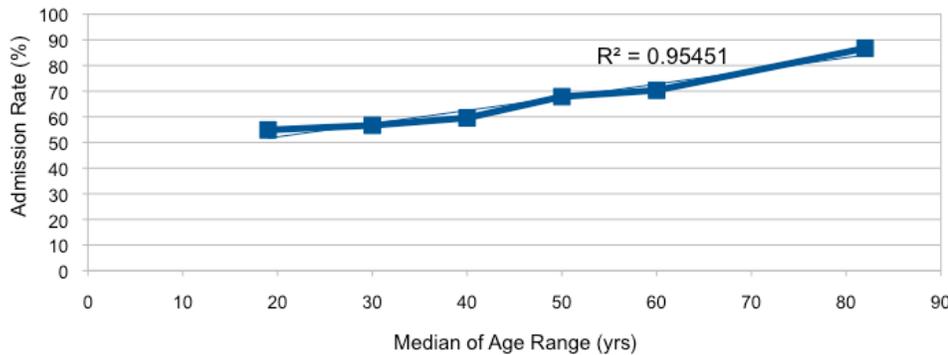


Sara Mijal, MD



Anthony Nelson, MD

Figure 1: Admission Rate vs. Median of Age Range



Glasgow coma scale on arrival to hospital (OR 0.753), and initial hospital systolic blood pressure (OR 0.987). Examination of specific age groups, treating age as a continuous variable, also demonstrated a trend correlating with increasing admission rates as age increased ($R^2 = 0.95$).

For the admitted population, the average ISS was 12.92 (SD 9.74), Intensive Care Unit (ICU) admission rate was 41.2%, and length of hospital stay (LOS) was 6.85 days (SD 9.27). Elderly patients had a higher ISS (14.87 vs. 12.66) and longer LOS (8.03 days vs. 6.69 days) than those < 65 years of age. Elderly patients were also admitted to the SICU at a higher rate (60.9 vs. 38.5, $z = 69.92$, $p < 0.001$) and were more likely to remain there for a longer period of time.

We found that patients age 65 or older are nearly four times more likely to be admitted than younger patients with similar injuries.

Additionally, the admission trends identified appear to indicate that age may be a continuous variable rather than a specific cut off at age 65. This effect was found to be independent of several other factors including presence of a head injury, GCS at initial trauma evaluation, ISS, and other physiologic parameters. This is especially important as this trend exists despite the fact that trauma centers do not provide the same outcome benefit for the elderly as they do for younger patients.² Our data also demonstrated that geriatric patients are admitted to the ICU at a greater frequency. More than 60% of geriatric trauma patients were admitted to the ICU, compared to 38.5% of the rest of the adult population. This may be the result of specific practice patterns related to geriatric patients. For instance, rib fractures are known to increase mortality in geriatric populations compared with younger patients. Thus, our practice is to admit geriatric patients

with rib fractures to the ICU independent of their physiologic status.³

Our data indicates that age alone is an independent predictor of admission after traumatic injury. Ultimately, in order to assure that we are providing the best possible care, further investigation is needed to ensure we are admitting these patients because they require inpatient care, and not solely based on their age. This should eventually lead to proper selection of patients that are safe to go home after minor trauma and reduce the morbidity of hospitalization and the associated expense while appropriately treating those who do require higher levels of inpatient care. •

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FOR ADDITIONAL INFORMATION on this topic, see references, visit mcw.edu/surgery, or contact the authors 815-325-6299; jpeschma@mcw.edu 414-805-8624; kbrasel@mcw.edu 414-805-8624; tneideen@mcw.edu.

SURGERY WELCOMES CHIEF RESIDENTS 2011–2012



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Allegra Saving, MD



Jill Whitehouse, MD



Personalized Medicine for Pancreatic Cancer

Rationale and the New Clinical Trial Available at the Medical College of Wisconsin



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Pancreatic adenocarcinoma is the fourth leading cause of adult cancer mortality and its incidence is on the rise. As lifestyle modifications (smoking cessation) and screening practices (colonoscopy, mammography) become more common place, it is anticipated that pancreatic cancer will approach breast and colon cancer as a dominant health concern. Unfortunately, our treatments to date have been relatively ineffective with less than 10% of all patients surviving five years. This is because the overwhelming majority of patients have metastatic disease (even if radiographically occult) at the time of diagnosis, including those whose primary tumor appears localized to the pancreas and potentially resectable (AJCC Stages 1 and 2). For this reason, there has been growing enthusiasm for multimodality therapy to include neoadjuvant therapy (chemotherapy, chemoradiation) even for patients with potentially resectable disease. In fact, the Medical College of Wisconsin is one of a small number of institutions that have participated in the first multi-institutional trial of neoadjuvant therapy supported by the American College of Surgeons Oncology Group (ACOSOG). The Medical College of Wisconsin Pancreatic Cancer study group is one of the top enrolling institutions into this trial which involves the delivery of gemcitabine and erlotinib before and after pancreaticoduodenectomy. While this represents the evolution of single institution experiences in the cooperative group

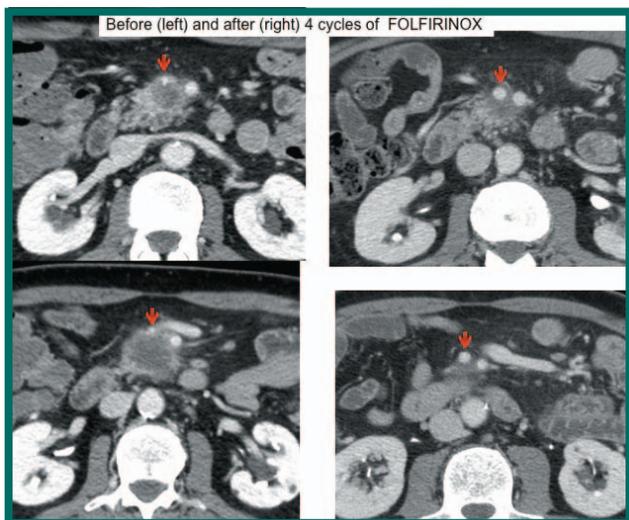
setting, it treats all patients with the same therapy; namely gemcitabine and erlotinib. Unfortunately, all pancreatic cancers are not the same as there are patients who appear to respond dramatically, and some who do not respond at all.

Because selected chemotherapy regimens appear to work in some patients and do not help in others, there has been growing enthusiasm for a more detailed analysis of the tumor itself at a molecular level. This is already being done in colon cancer, where patients receive cetuximab (a monoclonal antibody directed at the epidermal growth factor receptor [EGFR]) if they are found to have a wild type (normal) *KRAS* gene in the tumor. Because *KRAS* is downstream from EGFR, a mutant *KRAS* will prevent the therapeutic effect of cetuximab in blocking EGFR. In patients with lung cancer, erlotinib (Tarceva; small molecule tyrosine kinase inhibitor) is used in the presence of EGFR-activating mutations in those patients who also have a wild type *KRAS* gene. In contrast to colon and lung cancer, the molecular biology of pancreatic cancer is even more complex. However, there appear to be individual examples which illustrate that not every pancreatic cancer is biologically the same and that the points of vulnerability are different for different tumors. This is the obvious explanation for why some patients respond well to a given therapeutic regimen and other patients do not respond at all.

Figure 1 contains CT scans of a patient who responded dramatically to systemic therapy. This patient was found to be a carrier of a *BRCA1* germ line mutation and was treated with FOLFIRINOX (5FU, leucovorin, irinotecan, oxaliplatin). One can see the dramatic response to induction therapy. The *BRCA* tumor suppressor genes are associated with an increased risk of breast and ovarian cancer and are present in up to 7% of patients with pancreatic cancer. In patients with familial pancreatic cancer, the frequency of *BRCA* mutation carriers is approaching 15-20%. Loss of function of the *BRCA1* or 2 proteins inhibit the cell from repairing double stranded DNA breaks by homologous recombination. Therefore, alkylating agents which induce double stranded DNA breaks are particularly more effective. In this patient, we were able to match the chemotherapy most likely to result in a meaningful response with the molecular vulnerability of the tumor. This same logic can be applied to other genes and other chemotherapeutic agents.

Our current trial, which has now been IRB approved, incorporates advanced technology in interventional gastroenterology (Drs. Dua, Khan and Oh) with emerging technology in the molecular pathology laboratory of Dr. Craig Mackinnon. A panel of biomarkers is analyzed from material obtained at fine needle aspiration (FNA) biopsy performed during endoscopic ultrasound (EUS). Once the diagnosis of adenocarcinoma is made at a cytologic level, the remainder of the tumor aspirate is submitted for biomarker analysis. The results of the molecular

Figure 1: CT scans of a patient who responded to systemic therapy.



analysis are then used to tailor the chemotherapy program for each individual patient. To our knowledge, this represents the first attempt at personalized medicine for patients with early stage pancreas cancer.

As part of this trial, patients will receive chemotherapy before and after surgery and radiation therapy is used selectively. Patients are eligible for this trial if they have resectable or borderline resectable (tumor artery abutment) disease and can undergo EUS-guided FNA biopsy. Importantly, patients can receive their chemotherapy at any institution assuming their physicians will agree with the chemotherapy regimen that is based on molecular profiling. Radiographic imaging will include PET scanning as well as diffusion weighted MRI imaging. Translational laboratory studies will include a comprehensive xenograft system to allow expansion of tumors in immunocompromised mice for a series of detailed laboratory studies under the direction of Dr. Tsai.

Most new patients seen at the Medical College of Wisconsin Clinical Cancer Center by members of the Pancreatic Cancer Program are

reviewed weekly at our Friday, 7:00 a.m. conference. The benefit of interactive multimodality discussion for clinical trial development, as well as off protocol therapy, cannot be overstated. Having physicians of different specialties reach consensus on treatment recommendations requires that they have meaningful interchange. The multidisciplinary conference provides that venue while at the same time offering detailed re-review of complicated radiographic images and a thorough discussion of challenging cytopathologic diagnoses. We invite anyone interested to join us on Friday, at 7:00 a.m. in the Dean Roe Auditorium at Froedtert Hospital for our multidisciplinary conference. •

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FOR ADDITIONAL INFORMATION regarding this trial as well as additional information on pancreatic cancer, please refer to www.mcw.edu/surgery/targetedtherapy.

To refer a patient or request a transfer/consultation, please use these numbers:

**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

What is MSLT-II and how will it help patients with melanoma? *Evidence-based surgical care at its best*



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Residency Program Director

Melanoma is a common malignancy and has been rising in incidence annually since 1975. With a median age at presentation of 60 years, more than 68,000 cases are diagnosed annually.¹ However, melanoma can affect patients across the age spectrum including the pediatric population. While melanoma is primarily found in Caucasian individuals, people of color also can be affected.

Research into the management of melanoma is one of the best examples of evidence-based care in surgery. The most common treatment of melanoma is wide excision of skin surrounding the primary lesion. The width of the margin necessary to completely excise a melanoma, and to lower the chance of local recurrence, has been the focus of intense study for many years. After the completion of multiple carefully controlled, international, randomized trials, it has been recognized that a 1-2 cm margin is adequate to achieve local control and complete excision.^{2,3} The specific determination of these margins is based on the depth and individual characteristics of each tumor.

Patients with tumors that are 1 mm in depth or thicker, or who have thinner tumors with adverse features, have a higher risk of metastases to regional lymph nodes in addition to local recurrence. Prior to the mid-1990s, patients with these types of tumors and clinically negative lymph node basins would undergo either elective lymphadenectomy or observation, depending on the individual

treating surgeon's philosophy regarding the importance of identifying early metastatic disease. The subsequent morbidity of a complete lymphadenectomy in the axilla or groin raised the question of the risk versus benefit of the procedure. In 1992, sentinel lymph node biopsy was established for use in these patients at risk for lymph node metastases. The technique uses filtration by the lymphatics of technetium labeled sulfur colloid and vital blue dye injected at the primary site to identify the first, or sentinel, regional lymph nodes that receive lymphatic drainage from the area. Typically, this technique removes only 1-4 lymph nodes, instead of 20 or more as occurs with a complete lymphadenectomy. Sentinel lymph node biopsy was quickly adopted for use in melanoma patients, since the morbidity of the procedure was relatively minor in comparison. Sentinel lymph node biopsy has become the most common way that lymph node basins are assessed in melanoma patients.

However, as is often the case in clinical care, the confirmation of effectiveness followed the adoption of technique. While the highest volume centers clearly could identify sentinel lymph nodes, concern was raised as to its accuracy in broader practice. In 1994, while using the principles developed in the earlier clinical trials, Dr. Donald Morton at the John Wayne Cancer Institute and investigators from around the globe created the Phase III Multicenter Selective Lymphadenectomy Trial (MSLT-I). Patients were randomized to one of two treatment approaches:

- 1) wide excision plus lymphatic mapping and sentinel node biopsy with completion lymphadenectomy for metastases, or
- 2) wide excision with postoperative observation and delayed completion lymphadenectomy for subsequent clinically

identified nodal disease. The results of the study, published in 2005, demonstrated increased accuracy of sentinel lymph node identification after 25 cases, suggesting a modest learning curve for the technique. A complication rate of 37% after completion lymphadenectomy versus 10% with sentinel node biopsy alone raised further concern about the morbidity of completion lymphadenectomy. Additionally, it was noted that only 10-20% of patients with tumor-positive sentinel lymph nodes have tumor-positive non-sentinel nodes identified during completion lymphadenectomy.⁴ Determination of tumor-specific factors to help predict additional positive non-sentinel nodes remains unclear, but potential candidates have been proposed.⁵ In aggregate, this information has helped to set the stage for MSLT-II.

MSLT-II has been designed to study the outcomes of patients who undergo completion lymphadenectomy immediately following the identification of sentinel lymph node metastases, compared to a group who is observed with ultrasound surveillance of the lymph node basin.⁶ The trial opened in 2006 with a target accrual of 4,500 patients, in which the primary outcome measure is melanoma-specific survival with secondary endpoints of disease-free survival and recurrence over a 10 year period. Again, an international group of investigators from the United States, Australia, Canada, Finland, Germany, Ireland, Israel, Italy, Netherlands, Spain, Sweden, Switzerland, and the United Kingdom have joined forces to further the science of melanoma care. Patients with melanoma can be reassured that surgeons across the globe will soon be able to better identify individuals who do not need to be subjected to the potential morbidity of completion lymphadenectomy. Stay tuned. •

Venous Thromboembolic Disease (VTE)

It's not just heparin and warfarin any more



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FOR ADDITIONAL INFORMATION

on this topic, see references, visit mcw.edu/surgery, or contact the author 414-805-5929; ptermuhlen@mcw.edu.

The management of deep vein thrombosis (DVT) and pulmonary embolism (PE) has undergone dramatic change in the last 10 years. The traditional treatment consisted of intravenous unfractionated heparin (UFH), followed by transition to oral vitamin K antagonists (VKA, i.e. warfarin). Inferior vena cava (IVC) filters have been reserved as adjunctive therapy for patients failing anticoagulation or at high risk for complications from anticoagulant use. The introduction of catheter-directed thrombolysis (CDT) has been promising for some patients, but its optimal use has yet to be defined.

DVT and PE are significant causes of morbidity and mortality every year in the United States, where yearly, 650,000 PE will occur resulting in nearly 20,000 deaths.¹ Sixty to eighty percent of all patients diagnosed with a DVT will ultimately develop a PE, and PE is second only to myocardial infarction as a cause of sudden death in the U.S. It would logically follow that new methods of therapy for DVT to prevent its complications could prevent significant morbidity and possibly provide substantial cost savings. PE is not the only possible consequence of DVT. Patients with iliofemoral or femoropopliteal DVT are prone to develop the post-thrombotic syndrome (PTS), a potentially devastating condition with chronic leg ulceration and even limb amputation as a long-term result.

While PE is a common and well-known consequence of DVT, PTS is not as well recognized but is a major source of morbidity and has a significant economic impact. Up to 60% of patients with DVT that are treated with anticoagulation as a primary therapy develop PTS, which can include chronic skin ulceration (Figure 1), limb swelling, and severe difficulty with ambulation.²

Up to 2 million work days are lost yearly in the U.S. due to this condition. Clearly, alternative treatment to simple anticoagulation would be desirable.

Symptoms of DVT generally include asymmetric limb swelling with or without limb pain. The diagnosis is often confirmed by duplex ultrasonography with compression, which is very sensitive and specific. Duplex ultrasound may not be diagnostic in patients with pelvic vein thrombosis, in which case computed tomography (CT) venogram or magnetic resonance (MR) venogram may be necessary. Treatment for uncomplicated, minimally symptomatic DVT is anticoagulation with intravenous UFH or subcutaneous low molecular weight heparin (LMWH), followed by transition to VKA as described in the American College of Chest

Figure 1: Chronic skin ulceration



VTE

CONTINUED FROM PAGE 9

Physicians guidelines.³ Outpatient treatment for uncomplicated DVT is recommended over inpatient therapy whenever possible. It is important to determine the cause of thrombosis for ongoing management, i.e., whether it is physiologic (Table 1), or anatomic (i.e., vein compression as seen in May-Thurner syndrome or Paget-Schroetter syndrome).

Table 1: Systemic causes of Venous Thromboembolism

Prothrombin gene mutation
Protein C deficiency
Protein S deficiency
Antithrombin deficiency
Antiphospholipid antibody syndrome
Nephrotic syndrome
Factor V Leiden mutation

Escalating therapy may be necessary when symptoms are severe, when patients fail to improve with anticoagulation, or have complications from anticoagulation. Inferior vena cava filters have been used to prevent PE in patients with DVT, and for prophylaxis in patients at high risk for developing DVT. These filters may be permanent or temporary. However, these devices do not treat the DVT and certainly do not alleviate the symptoms; in fact, over time they can be associated with thrombosis of the inferior vena cava.

Over the last 10 years, CDT has become a popular means of treating a severely symptomatic DVT. This technique generally involves percutaneous access of a vein peripheral to the site of thrombosis, passage of a wire beyond the occlusion, and placement of a catheter across the occlusion with the infusion of a thrombolytic agent (either over the course of several days, or in a single session with adjunctive means of pharmacomechanical thrombolysis). The results with this technique have been encouraging. In Figure 2, an acute femoropopliteal venous thrombosis is demonstrated, which is drastically improved after overnight CDT (Figure 3). The patient's symptoms resolved almost completely within 48 hours, and he was subsequently anticoagulated with heparin and transitioned to oral warfarin.

The American College of Chest Physicians guidelines for the management of DVT and PE currently list CDT as a class IIb recommendation, as long term data regarding safety and efficacy are lacking.³ Medical College of Wisconsin physicians in the divisions of Vascular Surgery and Interventional Radiology are jointly participating in a phase III randomized, multicenter trial to assess the safety, cost effectiveness, and long-term outcomes of catheter directed thrombolysis for patients with iliofemoral and femoropopliteal DVT. Known as the ATTRACT trial (Acute Venous Thrombosis: Thrombus Removal with Adjunctive Catheter-directed Thrombolysis), 692 patients will be randomized at between 30 and 50 hospitals over two to three years. In general, this treatment will be most effective if it can be initiated within seven days of the onset of symptoms.

Figure 2: acute femoropopliteal venous thrombosis



Figure 3: improved venous thrombosis after CDT



The management of lower extremity DVT is evolving rapidly. CDT is a promising technique, and its effectiveness in preventing post-thrombotic syndrome is encouraging. Clinical trials are ongoing to determine the optimal use of this adjunctive therapy. •

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FOR ADDITIONAL INFORMATION on this topic, see references, visit mcw.edu/surgery, or contact the author at 414-805-9160; prossi@mcw.edu.

Minimally Invasive Surgery and an Emerging Therapy for Achalasia: the Per-Oral Endoscopic Myotomy (POEM)



ANDREW S. KASTENMEIER, MD
Assistant Professor
General Surgery

In 1901, the German surgeon Gerog Kelling inserted a cystoscope through the abdominal wall and into the peritoneal cavity to visualize the organs within.¹ More than 80 years later, the French surgeons Phillipe Mouret, Francois Dubois, and Jacques Perissat began presenting their experiences with the laparoscopic cholecystectomy and initiated the laparoscopic era of surgery.¹ From that point forward, laparoscopy was quickly adopted and has since become the preferred technique for a multitude of operations.

Few innovations in surgery have had such a widespread and profound effect on patient care as laparoscopy. The rise of laparoscopy, however, has been more than a technical innovation. It has become the most successful example of a broader concept called minimally invasive surgery (MIS). MIS involves performing surgery with the least possible trauma to the human body. The intent is less morbidity, lower mortality, faster recovery, and increased patient satisfaction. Initially felt to provide a purely cosmetic advantage, laparoscopy has since shown how MIS can have a dramatic effect on patient outcomes. Although results vary depending on the type of surgery and the indication, laparoscopy generally results in lower pain scores, shorter hospital stays, faster recovery, reduced overall post-operative complications (wound infections, pneumonia, venous thromboembolism, and ileus).²

In a search for even less invasive ways to perform surgery, Dr. Anthony Kalloo and colleagues described the technique of Natural Orifice Translumenal Endoscopic Surgery (NOTES) in 2004.³ Rather than making incisions on the abdominal wall, this technique utilizes natural orifices (such as the mouth, anus, or vagina) as conduits into the abdominal and thoracic cavities. Surgery is then performed using

a flexible endoscope. In 2007, Drs. G.V. Rao and Nageshwar Reddy applied this technique and performed the first human NOTES procedure, a transgastric appendectomy. This convergence of surgery and flexible therapeutic endoscopy now shows great promise as the next frontier of MIS.

Some of the first applications of flexible endoscopic MIS are just beginning to emerge. One application generating great excitement is a new treatment for achalasia called the Per-Oral Endoscopic Myotomy (POEM). Achalasia is a primary motility disorder of the esophagus that remains incompletely understood. Neurodegeneration of uncertain etiology results in an aperistaltic esophagus and a hypertensive, nonrelaxing lower esophageal sphincter (LES). Patients subsequently develop a variety of

symptoms including dysphagia, odynophagia, chest pain, regurgitation, and weight loss. There is no cure for achalasia; therefore, current therapy aims to relieve symptoms and curb disease progression. The standard surgical therapy has been a laparoscopic Heller myotomy with a partial fundoplication. The myotomy disrupts the circular fibers of the LES allowing uninhibited esophageal clearance. A partial fundoplication is then performed to recreate an antireflux mechanism after the hiatal dissection and myotomy. Results have been favorable with 89% symptom relief at 3 years.⁴

Like many other procedures, the Heller myotomy improved significantly with regard

MINIMALLY INVASIVE
CONTINUED ON PAGE 12 >>

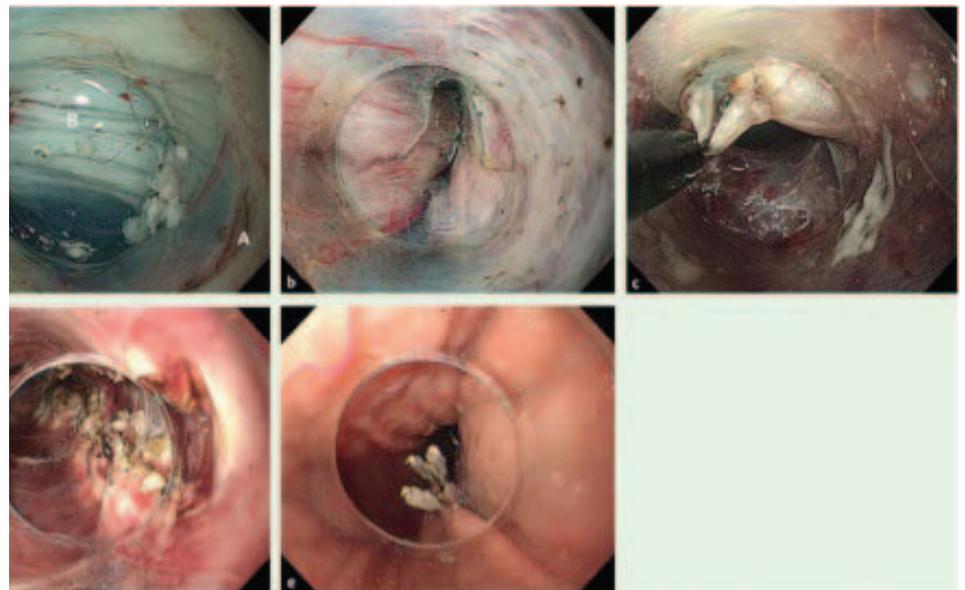


Figure 1: (a) The esophageal submucosal tunnel showing (A) the mucosal layer and (B) the circular fibers. (b) The esophageal submucosal tunnel at the gastroesophageal junction. (c) Endoscopic myotomy of the circular muscle fibers. (d) The completed endoscopic myotomy. (e) Closure of the mucosal defect with endoscopic clips.⁶

	Before POEM	After POEM	P
Dysphagia symptom score	10	1.3	0.0003*
LES pressure, mmHg	52.4 (14.3-80.5)	19.8 (9.3-42.7)	0.0001†

Figure 2: Initial results of the POEM procedure.⁶

*Wilcoxon signed-rank test † Paired Student's t-test

to patient outcomes when performed laparoscopically. Dr. Pankaj Pasricha and colleagues, however, felt that the disease perfectly lent itself to less invasive endoscopic therapy, and in 2007, they described the endoscopic myotomy in a porcine model.⁵ The authors described using flexible endoscopy to create a submucosal tunnel in the esophageal wall down to the LES. The circular fibers of the LES were then identified and selectively cut (Figure 1). Dr. Haruhiro Inoue, a pioneer of therapeutic endoscopy, then burst onto the scene in 2009 with the first endoscopic myotomy in humans and coined the term POEM.⁶ He followed with a series of 17 patients. The initial results have been impressive. At an average of five-month follow-up, dysphagia symptom scores and LES pressures improved dramatically (Figure 2), and no major complications have been reported. Interestingly, only one patient was found to have objective evidence of gastroesophageal reflux. It is suspected that because this less invasive approach preserves the longitudinal esophageal muscle fibers and the phrenoesophageal membrane, it also preserves enough of the natural antireflux anatomy to prevent reflux in the majority of patients, despite the exclusion of a formal antireflux procedure.

There is more work to be done in defining the safety and efficacy of the POEM when compared to the laparoscopic Heller myotomy. The POEM, however, represents a highly applicable NOTES procedure that extends the frontier of MIS. The Division of General Surgery at the Medical College of Wisconsin aspires to be on this MIS frontier through the development, investigation, and utilization of novel techniques for treating human disease in a minimally invasive manner. Through surgical innovation and research our focus is to provide our patients with the most current and effective therapeutic options available. •

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Andrew S. Kastenmeier, MD, joins Department of Surgery Faculty



On behalf of Dr. Jon Gould, Division Chief of General Surgery, and the Department of Surgery faculty, we are pleased to announce the successful recruitment of Andrew S. Kastenmeier, MD. Dr. Kastenmeier joined the Division of General Surgery on September 1. His recruitment was made possible by the Division of General Surgery, the Minimally Invasive Surgery and Bariatric Surgery Program, and the Condon Hernia Institute. Dr. Kastenmeier is a graduate of the University of Wisconsin and also attended medical school at

UW. While in medical school, he studied outcomes research under the direction of Dr. Sharon Weber in the section of Surgical Oncology. Andrew completed his surgical training at the University of Utah, including one year in the laboratory of Dr. David Bull, where he studied myocardial ischemia and the application of gene therapy to the treatment of ischemic heart disease. Following his chief resident year in Utah, he entered the well-known Minimally Invasive Surgery and Foregut Fellowship at Legacy Health in Portland, Oregon under the direction of Dr. Lee Swanstrom. During his fellowship, Andrew acquired extensive experience in the latest minimally invasive and endoscopic surgical procedures.

Dr. Kastenmeier will join our expanding program in Minimally Invasive Surgery to include Drs. Gould, Wallace, and Goldblatt. The mission of the Minimally Invasive Surgery Program is to provide cutting-edge technology to patients of today and to develop the innovations and advanced therapies that are so very important for the patients of tomorrow. For Andrew, this is a return to home as he attended high school in Mequon and his family remains in the Milwaukee area. We are thrilled with the opportunity of having Andrew Kastenmeier join our department and look forward to his many contributions to Minimally Invasive and Acute Care Surgery. Andrew can be reached at akastenm@mcw.edu. •

FOR ADDITIONAL INFORMATION
on this topic, see references, visit mcw.edu/surgery, or contact the author at 414-805-5026; akastenm@mcw.edu.

Dr. Sam Pappas to receive the Sharon K. Wadina Chair in Sarcoma Research

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

Sharon K. Wadina is donating \$1 million to The Medical College of Wisconsin for research in the Division of Surgical Oncology that advances the understanding and treatment of sarcoma tumors, one of the rarest forms of cancer. Her gift establishes a research fund and endows the Sharon K. Wadina Chair of Sarcoma Research, to be held by Sam Pappas, MD, Assistant Professor of Surgical Oncology.

Mrs. Wadina was diagnosed with soft tissue sarcoma in the summer of 2010. She says her experience inspired her to make this gift to expand research and develop innovative treatments to improve outcomes for patients.

“When you get diagnosed and realize there is almost nothing out there for treatment options, and you think you have limited time, it makes you think about your plans,” Wadina said. “Because of my situation, because of the lack of research, because of the reputation of the MCW Cancer Center and because of Dr. Pappas, I wanted to support this. I feel I’ve gotten excellent care.”

As a Medical College surgical faculty member since 2007, Dr. Pappas is known for his expertise in surgical oncology. He is investigating how the molecular profile of sarcoma tumors can identify patients most likely to benefit from alternative chemotherapy regimens. The use of more advanced molecular profiling of individual tumors might allow for a tailored treatment regimen based on the specific characteristics of the individual tumor.

Dr. Pappas will use Mrs. Wadina’s gift to launch a pilot study to gather data on molecular profiling. Having an internal funding source available for these kinds of projects is critical to advancing medical discovery and new treatments for patients.

“We are very fortunate to have Mrs. Wadina’s support, and will be working diligently on this research so that we can promptly report results,” Dr. Pappas said. “Sarcomas are rare tumors, and research to date has not made significant impact on the management of sarcomas before and after surgery. We need to know more about the biology of these tumors to enhance current and future treatment approaches.”

As a cancer affecting a relatively small number of patients, investigations into sarcoma attract fewer research dollars than other diseases. In cases like



Sam Pappas, MD, Assistant Professor of Surgical Oncology, Sharon K. Wadina, and T. Clark Gamblin, MD, MS, the Stuart D. Wilson Professor and Chief of the Division of Surgical Oncology

this, private philanthropy is an important source of funding that can uncover new patient treatments. Academic medical centers are ideal settings for this sort of research, as physicians and surgeons can work closely with basic scientists on problems observed directly in the clinic and during patient encounters.

“In addition to being a significant form of recognition, endowed chairs, like the Sharon K. Wadina Chair, provide vital resources for research endeavors,” said T. Clark Gamblin, MD, MS, the Stuart D. Wilson Professor and Chief of Surgical Oncology. “The Sharon K. Wadina Chair in Sarcoma Research is incredibly important as Dr. Pappas strives to further our understanding of tumor biology and define more effective treatments for sarcoma patients. An endowed chair is an unusual opportunity for an assistant professor, and we are indebted to Mrs. Wadina for her vision and gift.”

Before having her two sons, Mrs. Wadina worked as a nurse in a VA hospital in California and at the Clement J. Zablocki VA Medical Center. Her husband, the late Gerald Wadina, MD, was a 1965 Marquette/Medical College of Wisconsin alumnus and served as an Associate Clinical Professor at the Medical College for more than 20 years. •

Second Recipient Honored with the Surgery Schmitz Scholarship



Betsy Appel, MD is the second recipient of the Maryann Zwaska Schmitz Endowed Scholarship. This endowment scholarship was established to recognize in-state students who have demonstrated merit and proficiency in surgery. The Maryann Zwaska Schmitz scholarship represents the value of one year of full tuition. Selection of the recipient for this award is made by the Office of Student Financial Services, with the assistance and approval of the Department of Surgery.

Dr. Appel graduated from The Medical College of Wisconsin on May 20, 2011 and we were very fortunate to successfully recruit her into the general surgery residency in the Department of Surgery at the Medical College of Wisconsin. Congratulations Dr. Appel.

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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.

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

These referrals include:

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)

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In Memory *Robert K. Ausman, MD*

It is with extreme sadness that we report the death of Robert K. Ausman, MD, who was a close friend and long-time faculty member of the Department of Surgery at the Medical College of Wisconsin. Bob and his family (Ausman Family Foundation) were extremely generous with both time and resources in their devotion to the Department of Surgery. We are all deeply saddened by the sudden and untimely passing of Bob Ausman.

We know that his spirit will remain in Helfaer Auditorium to ensure our faculty's commitment to education, science, and clinical excellence.

Bob graduated from Marquette University School of Medicine in 1957 and continued his training as a surgical resident under Dr. Owen Wangenstein. He began his research career as a Damon Runyon Scholar and then received his PhD from the University of Minnesota in 1961. His first faculty position was as Director of Health Research at Roswell Park Memorial Cancer Institute in Buffalo, New York, where he stayed until being recruited to Baxter Laboratories as Director of Clinical Research in 1970. This began a two-decade-long career at Baxter Healthcare Corporation in Illinois, which allowed him to collaborate with the Department of Surgery as a Clinical Professor from 1970 to the present. Bob had a unique skill set, an incredibly inquisitive mind, and was a prodigious reader of all things medical. He pioneered isolated organ perfusion for cancer and presented his work on isolated perfusion of the liver at the Surgical Forum in 1959. He then published a series of manuscripts (many with Ed Quebbeman) on both the science of organ perfusion as well as pharmacology and clinical

effectiveness of prolonged infusion of 5-fluorouracil. In addition, Dr. Ausman was instrumental in the development of total parenteral nutrition and its proper application, long before we had worked out the best technology for central venous access. He then helped develop the safe and efficient intravenous pump systems now used.

Dr. Ausman's dedication to the Department of Surgery at The Medical College of Wisconsin is impossible to accurately describe in words. His thoughtful comments at our conferences as well as his insight into everything from department strategy to the politics of greater Milwaukee will be impossible to replace. His most recent passion in the arena of surgical education involves simulation training. Through the Ausman Family Foundation, he made a very generous gift to launch efforts at creating a world-class simulation center. This will come to fruition quite soon, but sadly not soon enough for Bob to participate to the degree that we all would have liked. The effect of Bob Ausman on the Department of Surgery and its faculty will be long-lasting, and his seat at our weekly Grand Rounds and M&M Conference will not be empty; we know that his spirit will remain in Helfaer Auditorium to ensure our faculty's commitment to education, science, and clinical excellence. •

Douglas B. Evans, MD

Stuart D. Wilson, MD

Edward J. Quebbeman, MD, PhD



Robert K. Ausman, MD
January 31, 1933–August 7, 2011

2011 Eberbach Banquet Award Winners



Dr. Roza

The Eberbach Banquet represents an opportunity to honor our graduating residents and acknowledge our outstanding faculty and resident educators. At this year's annual Eberbach banquet, **Allan M. Roza, MD** was awarded the Golden Cane Award which originated in 1987, by Mark B. Adams MD, in recognition of the outstanding faculty teacher. The nominees are voted on by the Junior and Senior medical students. A beautiful wooden cane with a gold handle, engraved with "Golden Cane Award" and the honoree's name and date of award was presented to Dr. Roza.

Dean Klingner, MD was awarded the Professionalism Award. This award is given to a faculty member who best exemplifies outstanding professionalism. Dr. Mark Adams implemented this award in 2005 to recognize faculty professionalism. Dr. Klingner was chosen by a vote of all current surgery residents.

Dr. Travis Webb of The Medical College of Wisconsin and **Dr. Kevin Packman** of Wheaton Franciscan-St. Joseph were awarded the Arahamian Faculty Teaching Awards (initiated in 1986). This award recognizes two outstanding faculty teachers, one internal to FMLH/MCWAH and the other from an affiliated institution. The graduating chief residents selected Drs. Webb and Packman.

Our congratulations go out to these talented and dedicated educators for their efforts in training our medical students and residents. We also want to acknowledge the hard work of our entire teaching faculty.



Dr. Klingner



Dr. Webb



Dr. Packman



Department of Surgery
9200 West Wisconsin Avenue
Milwaukee, WI 53226



MARK YOUR CALENDARS

Recent Event

The 25th Annual C. Morrison Schroeder Lectureship Welcomed Visiting Professor Keith D. Lillemoe, MD

The 25th Schroeder Lectureship was held on September 13, 2011. The lectureship welcomed Keith D. Lillemoe, MD, Surgeon-in-Chief and Chair of the Massachusetts General Hospital Department of Surgery. Prior to his new position at MGH, he was the surgeon-in-chief at Indiana University Hospital, and the Jay L. Grosfeld Professor of Surgery and chairman of the Department of Surgery at Indiana University School of Medicine.

Upcoming Events

October 15, 2011: Get Your Rear in Gear[®] 5K Run/Walk

Please encourage your patients to join us for **Get your Rear in Gear[®]** a 5K run/walk to raise colon cancer awareness. It will be held Sat., Oct. 15, 2011 at Hart Park in Wauwatosa, WI. This Colon Cancer Coalition event is presented in partnership with The Medical College of Wisconsin. For more information, please visit getyourrearingear.com, or e-mail Lynn Fischer at lfischer@mcw.edu.

October 24, 2011: Reception at American College of Surgeons Clinical Congress, San Francisco, Calif.

Plan to join us at the MCW Department of Surgery/Marquette Medical Alumni Association reception during the American College of Surgeons 97th Annual Clinical Congress on Monday, October 24, 2011. The reception will be held from 6:00 p.m. to 8:00 p.m. at The City Club of San Francisco, 155 Sansome Street.

February 3–4, 2012: Third Annual Liver Pancreas Symposium

The first day will be an open house during which physicians can visit endoscopy, interventional radiology, and surgery. The following day will offer lectures in the evolving management of liver and pancreatic disease featuring Dr. Michael Soulen, University of Pennsylvania, who will speak on hepatic artery directed therapy for liver cancer. Under the direction of Dr. Kathleen Christians, Dr. Bill Rilling, and Dr. Jim Thomas, this upcoming event promises to provide new and exciting developments in the fields of liver and pancreas disease. Please plan to join us for this Symposium held at The Medical College of Wisconsin. For more information, see www.mcw.edu/surgery.

June 29–30, 2012: Fourth Annual Medical College of Wisconsin and University of Texas M. D. Anderson Cancer Center Endocrine Surgery Symposium

This symposium will be held at The Cape Codder, Hyannis, MA, with invited speakers from Massachusetts General Hospital, Brigham and Women's Hospital, and New York University Medical Center. For more information, see www.mcw.edu/surgery.