

Surgery Update

NEWS FROM THE MEDICAL COLLEGE OF WISCONSIN DEPARTMENT OF SURGERY

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Message from the Chairman

by Douglas B. Evans, MD

*Donald C. Ausman Family Foundation Professor of Surgery;
Chairman, Department of Surgery, The Medical College of Wisconsin*

The featured picture in this issue of *Surgery Update* captures David Lal, MD, and Thomas Sato, MD, along with Terry Derks, PA-C, in the operating room. Dr. Sato and I both had the opportunity of working for Kurt Newman, MD, this year's Eberbach Visiting Professor. Dr. Newman is Chair of Surgery at Children's National Medical Center in Washington, D.C.; Dr. Sato worked with him as a fellow, and I worked with him as a lowly third year resident when Dr. Newman was the pediatric surgery fellow (Tom Sato and I both survived – barely). The Eberbach Visiting Professor marks the end of our academic year and signals the graduation of chief surgical residents. Rachel Ebel, MD, Robb Edwards, MD, and Matt Cox, MD, will be leaving us for the private practice of general surgery; Ciarán Bradley, MD, MA, will begin a surgical oncology fellowship at Memorial Sloan-Kettering Cancer Center, and Rachel Greenup, MD, MPH, will begin a breast surgery fellowship at Massachusetts General Hospital. We wish them all the very best and are most appreciative of their many extra efforts on behalf of the Medical College of Wisconsin, our department, and our affiliate institutions.

Carl W. Eberbach, MD, was Chairman of the Department of Surgery at the Medical College of Wisconsin (actually, Marquette University School of Medicine at that time) from 1950 to 1958. His clinical expertise was legendary and ranged from hepatobiliary surgery to the management of breast cancer. He was instrumental in the recruitment of Edward Ellison, MD, from Ohio State in 1958. The first Eberbach Visiting Professor was Ronald Malt, MD, from Massachusetts General Hospital in 1978, and Eberbach Visiting Professors since that time have included Oliver Behrs, MD, (Mayo Clinic), John Mannick, MD, (Brigham and Women's Hospital, Boston), Tom DeMeester, MD, (University of Southern California), Julie Freischlag, MD, (Johns Hopkins University), Layton Rikkers, MD, (University of Wisconsin) and as you all know, Sam Wells, MD, (currently at the National Institutes of Health after retiring as Chair of Surgery at Washington University) was our Eberbach Professor last year. The opportunity to celebrate the graduation of our chief residents and share our department with such distinguished guests is one of the many joys of academic medicine.

Please review this issue of *Surgery Update*. We are fortunate to have a number of excellent contributions with great relevance to the daily practice of surgery.



*(left to right) David Lal, MD,
Thomas Sato, MD, Terry Derks, PA-C*

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SAFETY OF LIVER RESECTION IN THE ELDERLY: HOW IMPORTANT IS AGE?

For more information on the Froedtert & The Medical College of Wisconsin Liver Cancer Program, please refer to mcw.edu/surgicaloncology.htm, or call 414-805-5020.

By **T. Clark Gamblin, MD, MS**
Associate Professor, Department of Surgery
Stuart D. Wilson Chair in Surgical Oncology
Chief, Division of Surgical Oncology

Surgical resection is an established treatment modality for a variety of benign and malignant lesions of the liver. Recent advances in operative techniques and peri-operative care have significantly reduced morbidity and mortality of major liver resection.^{1,2} However, with the aging of the population, more elderly patients with significant co-morbidities are being referred for major liver resection. Therefore, selecting appropriate surgical candidates is crucial to maximizing the benefit derived from surgery.³ It is not clear whether advanced age itself alters risk/benefit ratio of surgery, or whether age-independent variables are associated with higher operative risk.

We recently reported a series of liver resections in the elderly population. Specifically, we hypothesized that the age of patients alone is not associated with increased rate and severity of post-operative complications, but that specific variables of individual patients are the major determinants of operative morbidity and mortality. In addition, we sought to elucidate factors associated with higher surgical risk in elderly patients.

A retrospective case-matched study was performed to compare the rates and severity of post-operative complications of liver resection in two different age groups. Patients ages 70 or older (Group E) who underwent liver resection were matched with those younger than 70 (Group Y) by the extent of liver resection performed and by diagnosis. The study included only those who underwent liver resection of at least two Couinaud segments. Data were collected on: patient demographics, co-morbidities, American Society of Anesthesiologists (ASA) physical status classification, pre-operative laboratory values, operative procedures, diagnosis, operative time, packed red blood cell (PRBC) transfusion, length of hospital stay, post-operative complications and discharge destinations.

From a consecutive series of 497 liver resections, we identified 75 patients aged 70 or older with liver resection of at least two Couinaud segments who were then matched with 75 control patients younger than 70 with similar types of liver resection and with similar indications for surgery. Cases involving additional procedures such as ablation therapy were excluded.

Characteristics of patients showed the older age group was associated with a higher rate of cardiovascular co-morbidities such as

coronary artery disease (p=0.001), cardiac arrhythmias (p=0.037) and hypertension (p=0.023). There were also significant differences in terms of ASA class (p=0.001), diabetes (p=0.01) and creatinine levels (p=0.01), favoring the younger group. However, there were no differences in terms of congestive heart failure, stroke, pre-operative use of chemotherapy, smoking, liver cirrhosis, COPD, BMI, preoperative total bilirubin, albumin, alanine transaminase and INR.

Table 1. Demographics and Co-morbidities of Patients Undergoing Liver Resection

	Group E	Group Y	p value
No.	75	75	
Sex (M:F)	33:42	33:42	
Age			
Median	76	52	
Range	70-87	25-67	
Body Mass Index			
Median	26	25.9	0.842
Range	17.6-39.1	15.1-53.1	
Coronary artery disease (n)	20	4	0.001
Cardiac arrhythmias (n)	6	0	0.037
Congestive heart failure (n)	7	2	0.169
Stroke (n)	7	1	0.069
Hypertension (n)	44	14	0.023
Diabetes (n)	17	6	0.01
Liver cirrhosis (n)	2	5	0.439
COPD (n)	4	1	0.363
Smoking (n)	43	40	0.646
Prior history of malignancy (n)	42	28	0.033
Pre-operative chemotherapy (n)	31	28	0.738
ASA status (n)			0.001
1	1	3	
2	12	46	
3	59	25	
4	3	1	
5	0	0	
Hematocrit (%)			0.03
Median	37.5	39.8	
Range	25.4-49.0	24.4-48	
Albumin (g/dL)			0.445
Median	3.9	4.0	
Range	1.5-5.1	2.6-5.2	
Creatinine (mg/dL)			0.01
Median	1.0	0.8	
Range	0.6-3.1	0.5-6.1	
INR			0.545
Median	1.0	1.0	
Range	0.9-1.3	0.9-1.5	
Bilirubin (mg/dL)			0.508
Median	0.4	0.5	
Range	0.1-4.4	0.1-8.4	
Alanine transaminase (unit/L)			0.408
Median	29	32	
Range	11-417	12-332	

Table 2. Indications for Liver Resection

	Group E	Group Y
Colorectal carcinoma metastases	31	32
Hepatocellular carcinoma	8	7
Metastectomy	8	8
Gallbladder carcinoma	8	8
Cholangiocarcinoma	4	3
Hepatic cyst	4	4
Hemangioma/FNH	7	7
Others	5	6

Table 3. Operative Procedures

	Group E	Group Y
Extended hepatectomy	4	4
Right/left hepatectomy	24	23
Left lateral sectionectomy (seg 2 and 3)	8	8
Central hepatectomy (seg 4b and 5)	15	15
Other partial hepatectomy	24	25
Laparoscopic liver resection	(9)	(9)
Total	75	75

The two groups were well matched for indications for liver resection and operative procedures performed.

There were no significant differences in terms of operative time, estimated blood loss (EBL), use of Pringle maneuver and intra-operative PRBC transfusion requirement. However, a significantly higher number of patients in Group E than in Group Y required ICU stay ($p=0.028$). The median length of hospital stay was also significantly longer in Group E than in Group Y (7 days vs. 6 days; $p=0.01$).

There was no mortality within the 90 days post-operative period in either group. Overall complication rates were 44 percent in Group E and 33.3 percent in Group Y, and this difference was not significant ($p=0.241$; odds ratio=1.57; 95% CI=0.81-3.05). Sixteen percent of patients suffered from complications requiring invasive interventions (Clavien classification grade $\geq 3a$) in Group E, compared to 14.7 percent in Group Y, and this was not significantly different ($p=0.744$; odds ratio=1.11; 95% CI=0.46-2.70).

In terms of specific complications, post-operative confusion was significantly more common in Group E than Group Y ($p=0.022$). These were successfully dealt with by medical management. Post-operative peak total bilirubin and peak AST of elderly patients with confusion were statistically similar to those without confusion ($p=0.290$ and $p=0.318$, respectively).

Univariate relationships between possible predictors of post-operative complications in elderly patients were tested. History of systemic chemotherapy

before surgery ($p=0.01$) and a longer operative time ($p=0.004$) were found to be predictive of postoperative complications. There were trends toward higher morbidity in those with higher BMI and lower preoperative hematocrit ($p=0.073$ and $p=0.052$, respectively). In addition, patients with complications had a longer length of stay ($p=0.001$), and longer ICU stay ($p=0.01$) than those who did not.

Furthermore, we showed that advanced age itself is not the major determinant of the incidence and severity of post-operative complications. This provides

important evidence to dispel the common misconception that all elderly patients belong to a high surgical risk group by their advanced age alone. After liver resection, elderly patients derive as much benefit as younger counterparts, as evidenced by an increasing number of studies which report equivalent survival benefits after liver resection of colorectal metastasis as well as of hepatocellular carcinoma.^{4,5}

We demonstrated that the majority of the post-operative complications in the elderly were minor and successfully treated with medical management only (grade 1 and 2). Furthermore, advanced age was not associated with more severe complications requiring invasive procedures when compared to the younger group. The only age-specific complication we found was post-operative confusion, which was significantly more common in the elderly than the young. In addition, elderly patients with post-operative confusion did not have higher peak total bilirubin and peak AST than those without confusion. In view of these findings, we did not find any evidence that elderly patients were more susceptible to liver insufficiency than younger patients.

In conclusion, we report that liver resection can be performed safely in carefully selected elderly patients in a tertiary liver cancer center and suggest that advanced age alone should not be considered a contraindication for hepatic resection. However, elderly patients who received pre-operative systemic chemotherapy are at risk for higher morbidity, and efforts should be made to coordinate its duration and timing with medical oncologists in order to optimize surgical outcome.

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Table 4. Operative Details and Hospital Course

	Group E	Group Y	p value
Operative time (minutes)			0.203
Median	269	301	
Range	115-815	78-792	
Estimated blood loss (ml)			0.513
Median	200	200	
Range	0-5000	0-4000	
Intra-operative PRBC transfusion (n)	20	16	0.566
Pringle maneuver employed (n)	11	9	0.810
Peak post-operative total bilirubin (mg/dL)			0.735
Median	1.2	1.1	
Range	0.2-13.1	0.4-8.1	
Peak post-operative AST (Unit/L)			0.892
Median	349	349	
Range	46-2409	49-5070	
Peak post-operative INR			0.218
Median	1.2	1.2	
Range	0.9-3.8	1.0-2.6	
No. of patients requiring ICU stay (n)	27	14	0.028
Length of hospital stay (day)			0.01
Median	7	6	
Range	1-24	1-25	
Discharge destination (n)			0.001
Home	59	74	
Rehabilitation facility	16	1	
Readmission within 30 days of discharge (n)	4	5	0.889

RISK-REDUCING SURGERY FOR WOMEN WITH BRCA MUTATIONS SAVES LIVES

BRCA1 (chromosome 17) and BRCA2 (chromosome 13) are tumor suppressor genes which, when mutated, result in an increased risk of breast and ovarian cancer.

By **Tina W.F. Yen, MD, MS**
*Associate Professor, Department of Surgery
Division of Surgical Oncology*

Breast cancer is the most prevalent type of cancer in women in the United States and is the second leading cause of death. Approximately 10 percent of breast cancers are hereditary, and the majority of these familial cases are due to specific mutations in the *BRCA1* or *BRCA2* genes. In the Sept. 1, 2010 issue of the *Journal of the American Medical Association* (JAMA), Domchek and colleagues¹ present their findings confirming the benefits of risk-reducing surgeries for women who are *BRCA* mutation carriers. This prospective, multicenter study conducted in Europe and North America involved almost 2,500 women with known *BRCA1* or *BRCA2* mutations who were followed for an average of four years. Approximately 40 percent underwent risk-reducing salpingo-oophorectomy and 10 percent underwent risk-reducing mastectomy, while more than 50 percent opted for surveillance. The results substantiate that risk-reducing mastectomy is a highly effective strategy for breast cancer risk reduction;^{2,3} none of the women who underwent risk-reducing mastectomy developed breast cancer, while 7 percent of those who did not undergo risk-reducing mastectomy developed breast cancer. In women with no prior history of breast cancer, risk-reducing

salpingo-oophorectomy was associated with a 37 percent and 64 percent breast cancer risk reduction in *BRCA1* and *BRCA2* mutation carriers, respectively. Furthermore, only 1.1 percent of women who underwent risk-reducing salpingo-oophorectomy developed ovarian cancer. Most importantly, risk-reducing salpingo-oophorectomy was associated with a reduction in all-cause mortality (10 percent vs. 3 percent), breast cancer-specific mortality (6 percent vs. 2 percent), and ovarian cancer-specific mortality (3 percent vs. 0.4 percent), confirming prior work in this cohort.⁴

These results provide valuable information for women with *BRCA* mutations who have a 56 percent to 84 percent lifetime risk of developing breast cancer and an estimated risk of developing ovarian cancer ranging from 36 percent to 63 percent in *BRCA1* mutation carriers and 10 percent to 27 percent for *BRCA2* mutation carriers. We not only need to counsel these women with strong genetic predispositions for breast and ovarian cancer about their risks and options, but we also need to properly identify those women at risk of harboring a *BRCA* mutation and increase the awareness of genetic testing. Women with a personal history of breast cancer diagnosed at the age of 45 years or younger and women with a family history of breast and/or ovarian cancer, especially in family members diagnosed before the age of 50 years, should be offered the opportunity to meet with a genetic counselor prior to

undergoing *BRCA* testing.⁵ Genetic counseling provides women with a better understanding of their risk of harboring a *BRCA* mutation, as well as the opportunity to discuss the implications associated with undergoing testing, including the Genetic Information Nondiscrimination Act of 2008 which protects from insurance and employer discrimination based on genetic test results.^{5,6}

Once identified as a *BRCA* mutation carrier, a woman should be counseled on her cancer risk management options. Breast cancer screening with annual mammography and breast magnetic resonance imaging (MRI) should be performed.^{5,7} Measurement of serum CA-125 levels and transvaginal ultrasonography every six months should be considered, although ovarian cancer screening is poor.⁵ Risk-reducing salpingo-oophorectomy is recommended once child-bearing is completed. Chemoprevention with tamoxifen or raloxifene (in postmenopausal women) may be considered in those who elect not to undergo risk-reducing surgery. Domchek and others clearly demonstrate the benefits of mastectomy and salpingo-oophorectomy in reducing the risk of breast and ovarian cancer in *BRCA* mutation carriers.^{2-4,8} The JAMA study shows that this reduction in breast and ovarian cancer after risk-reducing salpingo-oophorectomy translates into a survival benefit.

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SAFETY OF LIVER RESECTION IN THE ELDERLY *continued from page 3*

For additional information on this topic, see references, visit mcw.edu/surgery, or contact the author: 414-805-5020 or tcgamblin@mcw.edu.

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BALANCING CANCER STAGING AND PROGNOSIS WITH PERIOPERATIVE CARDIAC RISK: THE IMPORTANCE OF A MULTIDISCIPLINARY APPROACH

As the population ages, the management of medical co-morbidities (especially cardiac) will become an increasingly important part of perioperative patient care.

By **Timothy D. Woods, MD**

*Associate Professor, Department of Medicine
Division of Cardiovascular Medicine*

The circumstances for which preoperative cardiac testing is needed before non-cardiac surgery remain controversial. Time urgency and hematologic effects of chemotherapy further complicate cardiac decision making in the treatment of cancer.¹ Once pursued, non-invasive stress tests available to identify coronary disease have excellent negative predictive value, but low positive predictive value for a peri-operative event. These studies are also subject to false positive and negative results. Finally, once obstructive coronary disease is confirmed as present, the literature suggests there are few circumstances in which coronary revascularization alters operative risk beyond best medical management.

Case

A 54-year-old gentleman at another institution was diagnosed with pancreatic cancer, and referred for consideration of a pancreaticoduodenectomy. Early in the course of his preoperative evaluation, the development of fever, elevated WBC and a new murmur led to a diagnosis of enterococcal aortic valve endocarditis. He remained clinically stable, and was successfully treated with a six week course of ampicillin and gentamicin. During this time, he also underwent neoadjuvant chemotherapy using gemcitabine and tarceva as part of an American College of Surgeons Oncology Group clinical trial (Protocol Z5041).

Near the conclusion of his antibiotic course, he developed chest pain and exertional dyspnea, and was admitted to the cardiology service. On admission, he was noted to have a significant new anemia (hemoglobin 7.5 g/dl), as well as renal failure (creatinine 2.7 mg/ml). There was no enzyme or EKG evidence of acute myocardial infarction. Although the new exertional pattern of chest pain he described was classic for unstable angina, a subsequent regadenoson nuclear perfusion stress test demonstrated no fixed or reversible defects. However, the ECG portion of the test appeared positive

for ischemia, and he continued to have significant exertional chest discomfort. The nuclear perfusion imaging was suspected as a false negative based on his symptoms and stress EKG, but his renal failure prevented elective cardiac catheterization. He was transfused blood as a palliative approach to his angina, which brought improvement, but not resolution of his symptoms. Surgical Oncology, Medical Oncology and Cardiology reviewed the complexities of the case together, and agreed the best approach was a waiting period until anticipated improvement of drug-induced renal function permitted cardiac catheterization. During this waiting period, he underwent neo-adjuvant 5FU-based chemotherapy and radiation therapy for his tumor.

The renal function improved, and he subsequently underwent elective outpatient cardiac catheterization two months later, at which time two-vessel severe coronary disease, including proximal LAD, was identified. A multidisciplinary discussion again ensued, and given his continued exertional symptoms, revascularization was felt prudent prior to his surgical tumor resection.

He subsequently underwent uncomplicated two-vessel coronary bypass grafting, and aortic valve replacement with a bioprosthesis. Clinically, he did well, and was discharged to recover in preparation for the anticipated Whipple surgery.

Approximately three weeks later, he was admitted for acute cholecystitis, requiring placement of a cholecystostomy tube. CT scanning during this hospitalization identified a suspicious bladder mass. A week later, he subsequently underwent a successful cystourethroscopically guided papillary bladder tumor resection.

Approximately seven months after his initial diagnosis of pancreatic cancer, he underwent successful pancreaticoduodenectomy, with negative margins. There was no evidence of metastatic disease at the time of surgery, and there were no cardiac complications. He remains cancer free and clinically asymptomatic as of June 2011.

Discussion

This case emphasizes the importance of a multidisciplinary approach to complex cases. Additionally, the importance of persistence is demonstrated.

Although the need to perform preoperative stress testing is necessary in only select individuals,² once a stress test is ordered, the findings must be interpreted with caution. All stress test modalities have pitfalls, and failure to detect severe multi-vessel CAD is a well-described weakness of nuclear perfusion imaging as seen in this case. Imaging results must always be interpreted in the context of the clinical findings, and the EKG portion of the study must never be dismissed as an unimportant component of the exam.

Given that most cancer surgeries are considered no higher than moderate risk, the majority of patients will be able to complete their surgery without complications despite the presence of known but clinically stable coronary disease.³⁻⁵ Attempted percutaneous revascularization of obstructive CAD potentially delays the surgery, and introduces new risks of perioperative stent thrombosis, even if bare metal stents are used. Surgical revascularization carries its own risks, and delays the needed non-cardiac surgery for at least four weeks. In the patient described, the stage of the pancreatic tumor and persistent symptoms of unstable angina were the primary motivation for recommending coronary revascularization prior to tumor resection. In this case, the need for coronary revascularization was further complicated by recent post-endocarditis aortic regurgitation.

The combined chemotherapy and radiation approach, followed by a tumor resection with a Whipple after coronary revascularization resulted in a successful initial result for this patient. Lengthy follow-up will determine if a long-term cure was obtained.

For additional information on this topic, see references, visit mcw.edu/surgery, or contact the author: 414-805-0010 or twoods@mcw.edu.

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GENETIC COUNSELING FOR PANCREATIC CANCER RISK ASSESSMENT

From the Multidisciplinary Pancreatic Cancer Program at Froedtert & The Medical College of Wisconsin.

By **Jennifer Geurts, MS, CGC**

Genetic Counselor, Department of Surgery

The purpose of identifying individuals at increased risk for pancreatic cancer is to offer a chance at early detection and prevention of this devastating disease. Dr. Lerch best expressed his empathy with the reality these individuals face in this commentary: “To be born into a family with familial pancreatic cancer ... has various implications for an individual’s life – and none is fortunate.”¹ Pancreatic cancer is one of the most deadly cancers, with an overall five year survival rate of 6 percent.² This poor outcome is attributed to late stage at clinical presentation and relative resistance to standard systemic therapies. Despite enhanced medical technologies over the past decade in imaging, surgical techniques and adjuvant therapies, which have improved the survival of individuals with other cancer types, statistics for pancreatic cancer remain grim. Currently, endoscopic ultrasound (EUS) and magnetic resonance imaging (MRI) based screening protocols are offering hope for individuals at increased risk for developing pancreatic cancer.

Inherited genetic factors contribute to approximately 10 percent of pancreatic cancer incidence. Known inherited genetic cancer syndromes that increase the risk for pancreatic cancer include: hereditary breast and ovarian cancer syndrome (HBOC), Lynch syndrome (also known as HNPCC), cutaneous malignant melanoma syndrome (also known as familial atypical mole-malignant melanoma syndrome), and Peutz-Jeghers syndrome (PJS).

Hereditary Breast and Ovarian Cancer Syndrome

To date, the genes associated with hereditary breast and ovarian cancer syndrome (HBOC) are the *BRCA1*, *BRCA2* and *PALB2* genes. These gene products are integral in the Fanconi anemia pathway, which functions to repair DNA double strand breaks. HBOC is most recognized by a significantly increased risk for breast cancer (up to 80 percent) and ovarian cancer (up to 40 percent). However, an increased risk for cancers of the prostate, gallbladder, bile duct, stomach and malignant melanoma have also been observed in these families. Mutations in the *BRCA2*, *PALB2* genes and

to a lesser extent, *BRCA1*, have all conferred an increased risk for pancreatic cancer. In HBOC families, the lifetime pancreatic cancer risk for individuals may be up to 5 percent, depending on family history and the gene involved.³ Importantly, some families with *BRCA2* and *PALB2* gene mutations may only present with pancreatic cancer; breast and ovarian cancer may not be noted in the family history. However, mutation carriers should be considered at increased risk for breast and ovarian cancer regardless of the presence or absence of these cancers in the family.

Lynch Syndrome

Lynch syndrome is an under-recognized hereditary cancer syndrome due to DNA mismatch repair defects which lead to microsatellite instability (MSI). Mutations in the *MLH1*, *MSH2*, *MSH6*, *PMS2* and *EpCAM (TACSTD1)* genes are implicated in this condition. Hallmark cancers of Lynch syndrome include colorectal, endometrial, ovarian and stomach cancers. However, there is also an increased risk in some families for pancreatic cancer, biliary tract cancer, brain cancer, urinary tract cancer, kidney cancer, small bowel cancer, and sebaceous adenomas. The risk for pancreatic cancer in Lynch syndrome is moderate – up to a 3.68 percent risk by the age of 70 years.⁴ The diagnosis of Lynch syndrome can be challenging in a pancreatic patient, since the utility of microsatellite instability (MSI) testing in pancreatic tumors has yet to be proven.

Cutaneous Malignant Melanoma Syndrome

Approximately 2 percent of all melanoma cases are attributed to hereditary mutations in the *CDKN2A* (p16) gene. The risk of developing melanoma in this

syndrome is highly variable and is modified by family history, ethnicity and environmental exposures. The estimated risk for developing pancreatic cancer is also variable, with relative risk estimates ranging from 9.4 percent to 47.8 percent in some families.⁵ Characteristics of cutaneous malignant melanoma syndrome include melanoma diagnosed at a young age (mean of 35 years), multiple primary melanomas in one individual, having multiple family members with melanoma, and a family history of melanoma and pancreatic cancer. Additionally, some families with *CDKN2A* mutations exhibit atypical nevi and dysplastic nevi.

Peutz-Jeghers Syndrome

Patients with Peutz-Jeghers syndrome (PJS) face one of the highest risks for developing some type of cancer over their lifetime (up to 85 percent). The risk for cancer involves gastrointestinal related and non-gastrointestinal related cancers, with a lifetime risk for pancreatic cancer of 36 percent.⁶ Features of PJS also include mucocutaneous hyperpigmentation and intestinal hamartomatous polyps. The tumor suppressor gene *STK11 (LKB1)*, which is involved in regulating cell polarity and cell division, is the only gene known to be associated with PJS.

Familial Pancreatic Cancer

The vast majority of genes contributing to the inherited risk for pancreatic cancer remain unknown. Familial pancreatic cancer families display an autosomal dominant pattern of transmission with reduced penetrance. Having at least two first-degree relatives with pancreatic cancer, outside of a known inherited syndrome, confers an 8 percent to 12 percent lifetime risk for developing pancreatic cancer. In stronger

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Indications for Referral to Genetic Counseling for Pancreatic Cancer Risk Assessment

- Two or more family members with pancreatic cancer
- A family history of pancreatic cancer and ovarian cancer
- A family history of pancreatic cancer and young onset breast cancer
- A family history of pancreatic cancer and young onset colorectal cancer
- History suggestive of Peutz-Jeghers syndrome with mucocutaneous hyperpigmentation, and/or intestinal hamartomatous polyps
- Two or more family members with melanoma
- A family history of pancreatic cancer and melanoma

NEW FACULTY JOIN DEPARTMENT OF SURGERY

The Medical College of Wisconsin and the Department of Surgery are excited to announce the successful recruitment of three new surgeons to our faculty. For more information, visit mcw.edu/surgery.



Jon C. Gould, MD

Jon C. Gould, MD, will join us on August 1, 2011 as Associate Professor and Chief of the Division of General Surgery. He will hold the Alonzo P. Walker Chair in Surgery and will be Senior Medical Director of Clinical Operations for Froedtert Hospital. Dr. Gould is currently Section Head of Minimally Invasive and Bariatric Surgery at the University of Wisconsin Hospital and Clinics (UW) in Madison, Wis. He is also Medical Director of the Clinical Simulation Program and Surgical Skills Training Laboratory in the Department of Surgery at UW. It is a true privilege for the Department of Surgery and The Medical College of Wisconsin to have Jon join our faculty.



David W. Johnstone, MD

David W. Johnstone, MD, has joined the Division of Cardiothoracic Surgery as Director of the Lung Cancer Program. Dr. Johnstone assumed this position on July 1, 2011. He is currently Director of the Comprehensive Thoracic Oncology Program at Dartmouth Medical School and the Norris Cotton Cancer Center. Since 2007, he has been Chief of the Division of Thoracic Surgery at Dartmouth. Dr. Johnstone brings with him 20 years of experience in thoracic oncology, most notably, the multidisciplinary management of lung cancer. The Division of Cardiothoracic Surgery is honored to have David join our faculty and the Multidisciplinary Thoracic Oncology Program.



Greg A. Ekblom, MD

Greg A. Ekblom, MD, has joined The Medical College of Wisconsin Department of Surgery effective June 1, 2011. His primary appointment will be in the Division of Community Surgery, and he will have a joint appointment in the Division of Surgical Oncology (breast surgery). Dr. Ekblom completed his general surgery residency at the Medical College of Wisconsin, which included six months at the Radcliffe Infirmary in Oxford, England. He has been an Assistant Clinical Professor (community teaching faculty) of this department since 1982. Dr. Ekblom's practice is devoted exclusively to benign and malignant diseases of the breast. We are thrilled to announce Dr. Ekblom as the fifth faculty member in our growing Division of Community Surgery.

HERSHEL RAFF, PHD, HONORED FOR THIRD YEAR WITH HARRY BECKMAN BASIC SCIENCE TEACHING AWARD



Hershel Raff, PhD

The Department of Surgery congratulates Hershel Raff, PhD, on winning the 2011 Harry Beckman Basic Science Teaching Award. This award is given to a professor who teaches one of the basic science courses during the first two years of the medical school curriculum and is seen by the students as "a distinguished teacher." The award is determined by vote of the graduating class. This is the third time Dr. Raff has won the honor. Dr. Raff holds a joint appointment in the Department of Surgery.

CANCER STAGING

continued from page 5

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The Medical College of Wisconsin Department of Surgery

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*Effective July 2011; ** Effective Aug. 2011

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GENETIC COUNSELING *continued from page 6*

family histories of three or more relatives with pancreatic cancer, the lifetime risk may be as high as 40 percent.⁷

Cancer Risk Assessment

Genetic counseling is crucial in identifying families at increased risk for pancreatic cancer. Genetic counselors elicit a detailed family history and offer genetic testing when appropriate, steps which are essential for calculating cancer risk. The genetic testing discussion includes informed consent elements of risk, benefits and limitations of testing. The communication of cancer risk is framed for the patient's expressed needs and concerns. Additionally, modifiable risk factors for pancreatic cancer, such as smoking cessation, are emphasized in a counseling session.

Most health insurance companies provide coverage for genetic testing when medically indicated. Importantly, state and federal laws protect people from health insurance discrimination and employment discrimination based on genetic test results. Ideally, genetic testing is first performed on the individual in the family with cancer. If initial tests reveal a causative mutation, subsequent family members can be offered site-specific genetic testing for the familial mutation to determine their risk status.

For additional information on this topic, see references, visit mcw.edu/surgery, or contact the author: 414-456-5889 or jgeurts@mcw.edu.

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RESIDENTS HEAD TO THE LAB

Three surgical residents will engage in laboratory work in 2011.

Liver Disease

Ryan Groeschl, MD, will work in the laboratory of T. Clark Gamblin, MD, MS. Dr. Gamblin's lab is engaged in translational research examining benign and malignant diseases of the liver.

Acute Lung Injury

Paul Jeziorczak, MD, will work in the laboratory of John Densmore, MD, studying the role of endothelial microparticle induced inflammation in acute lung injury.

Pancreatic and Colon Cancers

Rachel Harris, MD, will work in the laboratory of Gary E. Gallick, MD, at The University of Texas, M. D. Anderson Cancer Center. Dr. Harris is supported by the T32 grant and will study the molecular biology of pancreatic and colon cancers.

RISK-REDUCING SURGERY FOR WOMEN *continued from page 4*

Although risk-reducing surgery is a relatively low-risk procedure, it significantly reduces breast and ovarian cancer risk and reduces mortality, the cosmetic, psychological and medical issues (health risks associated with early menopause after salpingo-oophorectomy) associated with these surgeries must also be considered during the decision-making process. The decision to proceed with risk-reducing surgery is a very difficult and personal one. The results of this study add to the growing body of literature that should assist women with *BRCA* mutations and their clinicians in making a more informed decision about their cancer risk management strategy.

Genetic counseling and testing services are offered at the Froedtert & The Medical College of Wisconsin Clinical Cancer Center through the Cancer Genetics Screening Program. To schedule an appointment, call the Clinical Cancer Center at 414-805-0505, 866-680-0505, or 414-805-0572.

For additional information on this topic, see references, visit mcw.edu/surgery, or contact the author: 414-805-5495 or tyen@mcw.edu.

Complete article source: Yen TW. Genetic Testing for *BRCA* Mutations Can Save Lives. *Arch Surg* 2011 April; 146(4):479-480.

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IMAGING ADVANCES FOR PERITONEAL CARCINOMATOSIS

For additional information on the Regional Cancer Therapy Program, please refer to mcw.edu/surgicaloncology.htm, or call 414-805-5078.

By **Kiran K. Turaga, MD, MPH**

*Assistant Professor, Department of Surgery
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Stuart D. Wilson Professor of Surgery*

Peritoneal carcinomatosis poses a significant global health burden with more than 16,000 cases diagnosed every year in the U.S. alone. Treatment of such patients has been palliative/supportive until the introduction of cytoreductive surgery and hyperthermic chemoperfusion (CRS+HIPEC), which includes complete removal of these tumors in conjunction with circulation of hyperthermic chemotherapy at 108°F in the peritoneal cavity. Peritoneal carcinomatosis from colorectal cancer treated with chemotherapy alone results in median survival of five to 13 months, whereas CRS with HIPEC for early peritoneal carcinomatosis from colorectal cancer has shown a significantly increased median survival (with current data showing a median survival of 48 to 63 months and five year survival of 51 percent), which has been demonstrated in randomized clinical trials.¹ Currently, the only accurate way to measure burden of disease is using the peritoneal carcinomatosis index (PCI), which is measured during laparoscopy/laparotomy/surgery using the size of implants (0, 0-0.5cm, 0.5-5cm, and >5cm) in 13 regions of the abdomen yielding a maximum score of 39.² The accurate measure of burden of disease in patients with peritoneal carcinomatosis is important in prediction of completion of CRS+HIPEC. In addition, burden of disease has been validated as a measure of survival in this select subgroup of patients. Patients with peritoneal carcinomatosis with colorectal primary lesions with a PCI score of ≥ 19 have a consistently worse survival³ than those with lower PCI scores. Earlier identification of patients with a high burden of disease would prevent laparotomies for staging purposes alone and promote alternate therapies, including clinical trials.

Surveillance of patients with peritoneal carcinomatosis is extremely difficult given the small diameter disease which is relatively inconspicuous on conventional cross-sectional imaging. The detection of small metastases versus no evidence of disease carries vital prognostic information. Also, in the evaluation of recurrence, distinction between localized and multifocal disease is a critical factor in determining the need for secondary cytoreduction.

Conventional anatomical cross-sectional imaging with CT scans and functional imaging with PET scans have shown sub-optimal sensitivity and specificity in detecting disease.⁴ The shortcomings of conventional cross-sectional imaging techniques with regard to the contrast between tumor and normal tissue can be overcome with diffusion-weighted imaging. Diffusion-weighted imaging translates the restrictive effect of tissue structure on the

Figure 1:

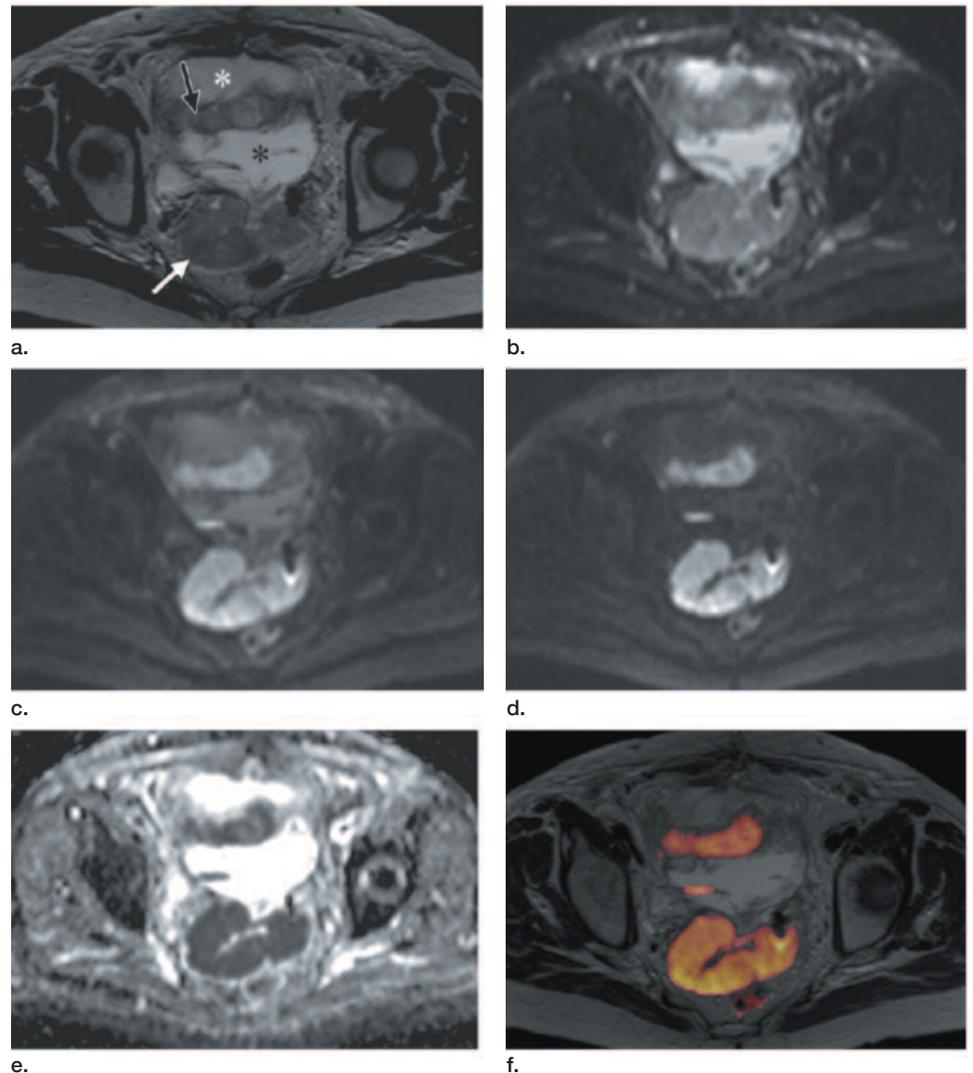


Figure 1: a) Axial T2-weighted MR image shows a bulky tumor in the rectovaginal space (white arrow), a malignant deposit (black arrow) infiltrating the posterior-superior wall of the bladder (white *), and ascites (black *). b) Axial diffusion-weighted fat-suppressed images acquired with b values of 0 (b), 600 (c), and 1050 (d) sec/mm² show cumulative loss of signal from fluid and normal tissue (vessels, lymph nodes, and uninvolved peritoneal membranes), whereas areas of malignancy retain high signal intensity denoting impeded diffusivity. (e) ADC map depicts restricted diffusion (low ADC values) in the tumor. (f) Fused MR image obtained with co-registration of gray-scale data from T2-weighted imaging and color-coded data from diffusion-weighted imaging (b = 1050 sec/mm²) provides advantages similar to those obtained by merging a positron emission tomography (PET) dataset with a CT dataset. (reproduced from deSouza, et. al.⁴).

†ADC: apparent diffusion coefficient, b-value: index of diffusion weighting

Figure 2:

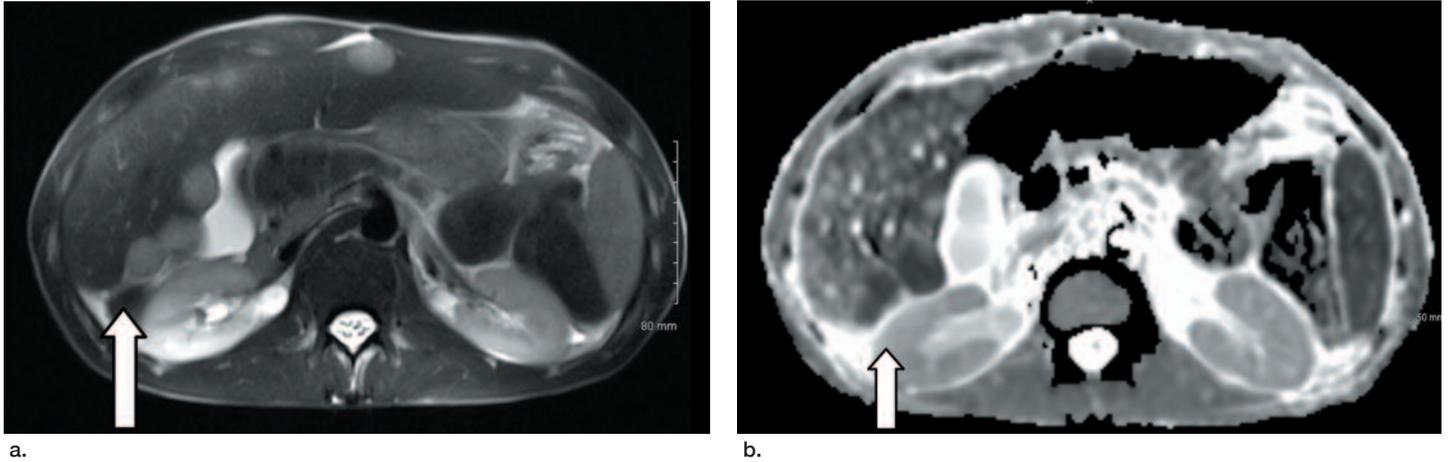


Figure 2 a) MRI T2 weighted imaging of the abdomen showing peritoneal metastases along glissons capsule of the liver b) An apparent diffusion coefficient map derived from diffusion-weighted imaging showing restricted diffusion in the tumor deposits.

mobility of water molecules into visible signal intensity or contrast. Its ability to provide qualitative and quantitative information about tissue cellularity is increasingly used in oncologic imaging for lesion detection and characterization and for monitoring response to treatment. The integration of diffusion-weighted imaging with conventional imaging has been shown to increase the accuracy in the staging of ovarian cancer, but the value of this modality for patients with peritoneal carcinomatosis is unknown.⁴

The morphological pattern of peritoneal carcinomatosis is varied, reflecting the diverse biology of tumors. Tumor deposits can vary from nodules 5-20 mm in size, to bulky intraperitoneal masses or plaques lining the peritoneum and mesenteric surfaces. A diffuse pattern of spread is often noted in the omentum, where replacement of normal fat by tumor may range from subtle micronodularity to solid omental caking. Early infiltration of the perivascular and perilymphatic spaces in the small bowel mesentery increases their attenuation and may produce stranding. Infiltration of the mesentery also sometimes manifests with a pleated pattern produced by stiffening of the connective tissue, with resultant tethering and crowding of the mesenteric vessels and separation and angulation of small bowel loops. Involvement of the bowel serosa can range from segmental mural thickening to endoluminal obstructive masses. Discrimination of these morphological subtypes is essential in prognostication of disease.

The use of diffusion-weighted imaging in detecting disease burden in patients with ovarian cancer was suggested by deSouza, et. al, in 2010⁴. The pattern of peritoneal

carcinomatosis from epithelial ovarian cancer is similar in morphology to carcinomatosis from colorectal and other gastrointestinal primary tumors. This is an evolving field of ongoing research (Figure 1).

The Medical College of Wisconsin Division of Surgical Oncology recently established the Regional Cancer Therapy Program (RCTP). This team has provided multidisciplinary novel therapies for patients with peritoneal carcinomatosis and has led to the establishment of evidence-based care for patients with peritoneal disease. Diffusion-weighted MRI imaging is currently being investigated in the setting of peritoneal carcinomatosis with promising preliminary results (Figure 2).

Patients referred to the RCTP routinely undergo contrast enhanced CT scan imaging and PET-CT fusion scanning unless the patient has been referred with the above imaging modalities, which are satisfactory. Patients then undergo diffusion-weighted MRI imaging to determine the extent of peritoneal carcinomatosis. The major barrier to MR imaging of the peritoneum is motion artifact. We have been able to optimize the utilization of navigator pulse on the cancer center scanner to make sure the patient is imaged repeatedly at the same point in the respiratory cycle, which eliminates respiratory motion from our non-breath hold sequences. In addition, our IM glucagon protocol has proven to be quite robust in limiting/preventing bowel peristalsis for the duration of the exam. This allows us to obtain high quality diffusion-weighted images and ADC maps which are much like what we have already seen done for MR imaging of pancreatic cancer. Our initial concerns

Figure 3:

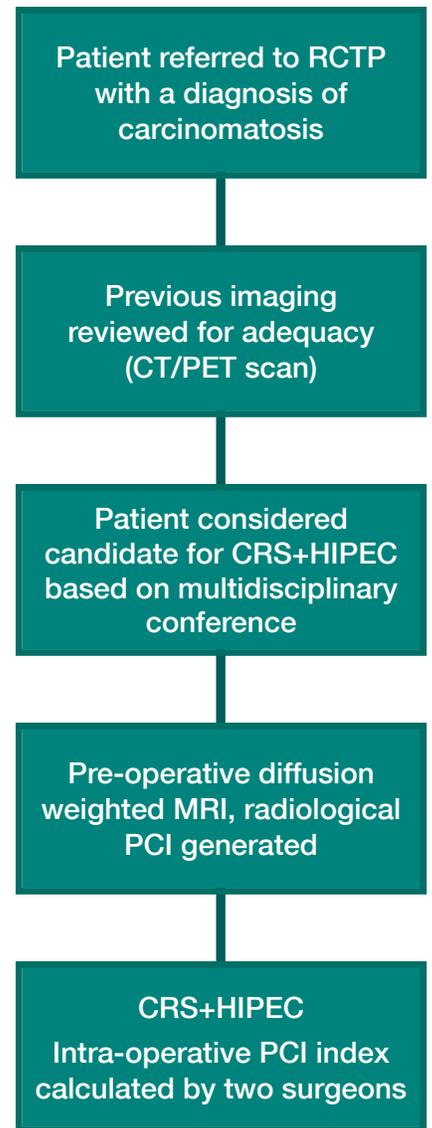


Figure 3: Workflow of patients undergoing diffusion weighted MRI imaging.

continued on page 12

regarding dielectric effect/standing wave artifact associated with ascites at 3 Tesla have not been a problem.

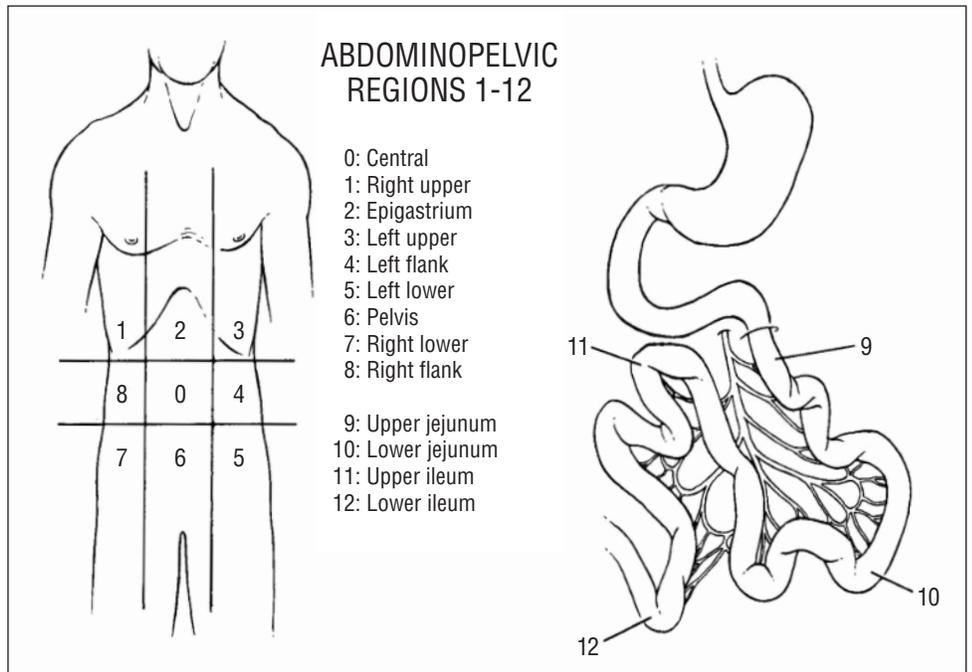
Diffusion-weighted MR imaging can be used to identify the sites of disease and the largest size of the tumor deposit in the 13 zones of the abdomen as defined by the peritoneal carcinomatosis index (PCI) (Figure 4). Specific attention is paid to the mesenteric surfaces and mesenteric foreshortening is noted. A PCI score is then generated based on the MRI imaging. Currently, we are in the process of validating the MRI-generated PCI score with the intraoperative score.

Conclusions

Diffusion-weighted MR imaging offers an attractive way to assess the burden of disease from peritoneal carcinomatosis, but needs prospective validation. The ability to assess the burden of disease non-invasively can help prognosticate, decide therapeutics and facilitate surveillance. Further imaging improvements are essential in advancing the study of peritoneal carcinomatosis.

For additional information on this topic, see references, visit mcw.edu/surgery, or contact the authors: 414-805-5078; kturaga@mcw.edu; 414-805-5828; spappas@mcw.edu; 414-805-3258; pknechtges@mcw.edu; 414-805-5020; tcgamblin@mcw.edu.

Figure 4:



References:

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Development Corner

PINK PARTY TRAY RAISES FUNDS FOR BREAST CANCER RESEARCH

By **Meg M. Bilicki**
Director of Development
Department of Surgery

Tina W.F. Yen, MD, MS, Associate Professor of Surgery (Division of Surgical Oncology), has received research support from a Milwaukee company that raised funds and awareness for breast cancer with a customized product. Bardes Plastics, Inc., which creates stylish plastic packaging solutions, donated more than \$8,500 from the sale of a party tray shaped

like a pink ribbon to denote breast cancer awareness. The trays, made to contain fresh fruit and vegetables, were introduced in supermarkets nationwide.

“What began as a design to complement our line of colorful party trays has become a meaningful outreach program,” said Mary Strupp, chief executive officer of Bardes Plastics. “We are proud of our contribution and envision a yearly giving program to support breast cancer research.”

Dr. Yen assesses breast cancer outcomes to develop more effective treatment strategies and best practices. For example, her studies

of lymphedema – swelling of the arm and hand – have led to a better understanding of this complication after breast cancer treatment. “Outcomes research can lead to improved survival rates and improved quality of life for breast cancer survivors,” Dr. Yen said. “I am extremely appreciative of the funding from Bardes Plastics, Inc., which will allow me to further advocate my research.”

A variety of opportunities are available to support the Department of Surgery. For more information, please contact Meg M. Bilicki at mbilicki@mcw.edu or 414-805-5731.

WE HAVE A WINNER!

By **Stuart D. Wilson, MD**
Professor, Department of Surgery
Division of Surgical Oncology

We have a winner! John Denby, MD, identified all but two of the Ellison Era surgical house staff in the last issue of *Surgery Update*. They are standing in front of Milwaukee County Hospital. He also correctly named Larry Carey, MD, (1962-1963) as the resident who went on to become the Zollinger Professor and Chair of the Department of Surgery, Ohio State University Medical School.



In addition to winning this prize, John Denby, MD's other claim to fame was his position as "The Last Battleship Surgeon." Dr. Denby is pictured on the bridge of the BB-62 New Jersey, off shore DaNang, Vietnam, 1969, with visiting surgeon Stu Wilson, MD, who was stationed "on shore" with the 1st Med. BN, 1st Marine Division. He had hitched a chopper ride out for an "official consultation."

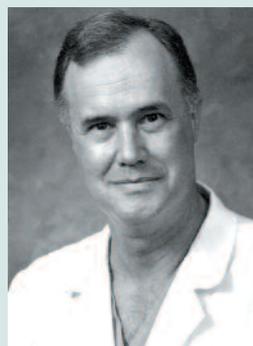


The house staff (left to right) are: George Cooper, MD, John Denby, MD, Cliff Starr, MD, Kopf, MD, Bill Schulte, MD, Bob Dawes, MD, Joe Williams, MD, "Jack" Foley, MD, Dudley Johnson, MD, Larry Carey, MD, Dave Trump, MD, Bill Evans, MD, Gene Snyder, MD, John Just, MD, Joe Gutierrez, MD, Plautz, MD, Loren Yount, MD, John McAnlis, MD, and John Riesch, MD. (Missing are Barnes, MD, Groessl, MD, Holden, MD, Earl Kitzerow, MD, Pete Parker MD, and Stu Wilson, MD).

CREATION OF THE MARK B. ADAMS CHAIR IN SURGERY

It is with great pleasure that the Department of Surgery at The Medical College of Wisconsin announces the creation of the Mark B. Adams Chair in Surgery. A search committee has been formed under the direction of Keith Oldham, MD, for recruitment of the inaugural holder of the Adams Chair who will also be the Service Line Director for Solid Organ Transplantation across The Medical College of Wisconsin - Froedtert Hospital - Children's Hospital of Wisconsin campus.

Dr. Adams was the Ausman Family Foundation Professor of Surgery and Department Chairman at The Medical College of Wisconsin from 2003 until his untimely death in 2007. A tremendously gifted surgeon and educator, Dr. Adams is credited with fostering the development of abdominal solid organ transplantation in Milwaukee. In 2001, he was honored with a Distinguished Service Award, The Medical College's highest honor, for his contributions in clinical excellence and teaching. He received the Faculty Teaching Award in 1981 and again in 1988 and was widely known for his extraordinary talents in clinical medicine and surgery.



Mark B. Adams, MD

Dr. Adams was a graduate of Reed College in Portland, Oregon and the University of Oregon Medical School. He came to Milwaukee in 1972 to join the Surgical Residency Program at The Medical College of Wisconsin. Following completion of his residency, he joined the faculty and was promoted to Professor in 1989. In 1987, he was appointed Chief of the Division of Transplantation and in 2003, was appointed Chair of the Department of Surgery. Dr.

Adams' research program was supported by VA merit reviews, industry sponsorship, and cooperative group funding. He authored or co-authored 168 manuscripts in the peer-reviewed literature, multiple book chapters, and numerous abstracts which were presented at regional and national meetings. Dr. Adams was a nationally known and respected leader in transplantation who displayed the highest level of integrity, the constant pursuit of excellence, and a deep commitment to his patients.

The creation of an endowed chair is the highest honor in the Department of Surgery. It is with tremendous pride and admiration that we announce the creation of the Mark B. Adams Chair in Surgery.



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CALENDAR OF EVENTS

RECENT EVENTS

The 51st Annual Carl B. Eberbach, MD, Lectureship Welcomed Visiting Professor Kurt Newman, MD

The 51st Eberbach lectureship was held on June 17, 2011. The lectureship welcomed Kurt D. Newman, MD, Senior Vice President and Surgeon-in-Chief, Children's National Medical Center, and The Joseph E. Roberts, Jr., Center for Surgical Care. Dr. Newman is a Professor of Surgery and Pediatrics at The George Washington University Medical Center.

The 10th Annual Marvin Glicklich Lectureship Welcomed Visiting Professor Thomas Krummel, MD

The 10th annual Glicklich Lectureship was held June 22, 2011 and featured Visiting Professor Thomas Krummel, MD. Dr. Krummel, a Medical College of Wisconsin alumnus, is the Emile Holman Professor and Chair in the Department of Surgery at Stanford University School of Medicine. Dr. Krummel is also the Susan B. Ford Surgeon-in-Chief at Lucile Packard Children's Hospital in Stanford, Calif.

UPCOMING EVENTS

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

The Medical College of Wisconsin welcomes Visiting Professor Keith D. Lillemoe, MD, as the 25th Annual C. Morrison Schroeder Lecturer, on September 14, 2011. Dr. Lillemoe is Surgeon-in-Chief and Chair of the Department of Surgery at Massachusetts General Hospital. Prior to his new position at Massachusetts General Hospital, he was 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.

Get Your Rear in Gear® Colorectal Cancer Awareness Event in October

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, Wis. This Colon Cancer Coalition event is presented in partnership with The Medical College of Wisconsin. For more information, please visit getyourrearingear.com or email Lynn Fischer: lfischer@mcw.edu.

Save the Date – October 24, 2011 – Reception at American College of Surgeons Clinical Congress, San Francisco, CA

We invite you to join us at The Medical College of Wisconsin 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.

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