

Physician Update

FOR HOPKINS CLINICAL FACULTY AND REFERRING PHYSICIANS

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When Prostate Removal Goes High Tech

It's one thing to learn robotic-assisted laparoscopic prostatectomy. It's quite another to perform the operation in the department where your mentor is Patrick Walsh, the surgeon who proved to the world that a cancerous prostate can be removed without destroying the nerves that govern erections and urinary control.

"Patrick Walsh has an understanding of prostatic anatomy better than anyone I know," says **Li-Ming Su**, director of laparoscopic and robotic urologic surgery at Hopkins' Brady Urological Institute. "Five years ago, our department began to evaluate laparoscopic radical prostatectomy as a minimally invasive treatment for prostate cancer. We had to prove that our outcomes with this approach would be equivalent to that of the open procedure before accepting it as a standard of care for men with clinically localized prostate cancer."

For patients, who often assume that technology like the surgical robot must be better, Su's diligence is welcome news. While it's true that laparoscopic operations in general come with less postoperative pain and shorter recovery, the clinical results of any new technique, says Su, should be closely monitored and compared to those of more established techniques before becoming mainstream. Nerve-sparing prostatectomy is daunting enough with the standard, 5- to 10-inch abdominal incision. The objective—to



Li-Ming Su and the operating arms of the surgical robot.

excise the malignant gland with clean margins while avoiding the delicate nerve bundles that run alongside it—becomes even more challenging when the surgeon operates without touching the internal anatomy and instead relies on images projected from a camera and telescopic lens inserted into one of the five half-inch keyhole incisions that provide access to the surgical field.

Su and colleague **Christian Pavlovich** have performed over 700 non-robotic laparoscopic prostatectomies since 2001. "The goal has always been to replicate the technique of open nerve-sparing radi-

cal prostatectomy," Su says. "As Dr. Walsh continues to find ways to improve the outcomes and minimize the side effects of radical prostatectomy, we've incorporated many of his advances into the laparoscopic approach." As a result, at one year, 90 percent of Hopkins laparoscopic prostatectomy patients are continent, and in those who received bilateral nerve-sparing surgery, 75 percent reported successful sexual intercourse—outcomes comparable to open prostatectomy. Now, having performed more than 120 cases in the last year using the robot, Su has found similar outcomes by prospectively track-

ing his patients with validated quality-of-life surveys.

Among the robot's attributes is its ability to provide intensely illuminated, 3-D images magnified tenfold. Furthermore, the instrumentation allows the surgeon to operate, dissect, manipulate and suture with the dexterity of a human wrist. "These two advantages," says Su, "make the robotic operation superior to the conventional laparoscopic approach. In skilled hands, I believe the robotic, laparoscopic and open techniques offer very similar outcomes, but with the first two there's less blood loss and perhaps

Get a PSA at 40?

For years, 50 has been the recommended age for most men to have their first prostate-specific antigen level measurement. What's been debated is the PSA level that should trigger a biopsy. Going below the long-accepted threshold of 4.0 ng/mL, as some urologists have urged, could increase detection of curable prostate cancers. It could also lead to overdiagnosis and overtreatment. Yet sticking with the higher level before ordering a biopsy could mean missing a biologically important cancer.

To get beyond the impasse, **H. Balentine Carter**, director of Hopkins' Division of Adult Urology, and investigators at the Baltimore Longitudinal Study of Aging (BLSA) looked at PSA velocity—how fast the blood serum level of the protein changes over time—as a marker for life-threatening cancers. Using BLSA samples, they determined PSA velocity in 980 study participants and found that not only could it predict death from prostate cancer, but that it could signal the risk 10 to 15 years ahead of diagnosis. Among their findings: In men with a PSA velocity above 0.35 ng/mL per year, there was significantly lower prostate cancer-specific survival at 25 years when compared to men with a PSA velocity of 0.35 ng/mL per year or lower.

As a result, Carter says men should have their first PSA test at age 40, when levels are usually lower and prostate enlargement isn't a confounding factor. Establishing this early baseline, he argues, will help clinicians more easily detect patients with small but dangerous rises in PSA levels, even when the level itself is still low. Equally important, PSA velocity could identify men with slow-growing prostate cancer that may never require treatment.

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shorter convalescence. Here, we have experts in all three approaches. The robotic technique is here to stay and will likely play a more dominant role in the surgical treatment of prostate cancer in the future."

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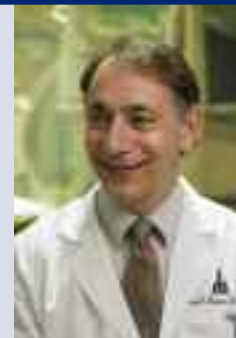
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Ovarian Tumors That Are Neither Fish Nor Fowl

The growth on Stephanie Garagozzo's ovary made its presence known four years ago when the New Jersey internist had a routine ultrasound examination during her first pregnancy. Told that the mass appeared to be a complex but benign cyst, Garagozzo later decided to have it removed. And then her fear set in.

"I'd never heard of a borderline ovarian tumor," she says of the diagnosis on her full pathology report. "Even my physician friends didn't know about it. With other tumors, *borderline* means that it's likely to progress to cancer. I was 33 years old; my daughter wasn't even 2. I was terrified that I wouldn't be around to see her grow up."

Garagozzo's physician recommended removing the ovary right away. Instead, Garagozzo went online and found, she says, that Hopkins' director of gynecologic pathology, **Robert Kurman**, "is *the* guy for borderlines in the United States." When she realized that the terminology in her pathology report didn't match Kurman's, she headed straight for Baltimore.



Stephanie Garagozzo, left, is convinced that had Ginger Gardner not been determined to preserve her fertility, there'd be no such person as 4-month-old Lela Francesca. "There aren't many physicians who deal with borderline tumors like I had," says Garagozzo. "With Ginger, I was finally comfortable to just be the patient."

Kurman has spent nearly three decades characterizing ovarian tumors (there are over 100 types, more than occur in any other organ), so he's no stranger to the confusion that surrounds those known as borderlines. "They're somewhere in Never-Never Land," Kurman says, "neither fish nor fowl." Unlike true ovarian

cancers, which invade the ovary, so-called borderline tumors are usually benign and noninvasive, and even when they do spread are unlikely to be life threatening. Yet the still-lingering *borderline* moniker—given in the early 1970s when little was known about them—suggests that they require aggressive treat-

ment. "That's why I don't call them *borderline*," explains Kurman. "I call them *atypical* because nothing in that says *cancer*." Still, he says, these tumors can't be ignored.

Kurman's non-alarmist approach began to ease Garagozzo's anxiety, and gynecologic oncologist **Ginger Gardner** completed the turnaround. Gardner, who directs minimally invasive surgery in Hopkins' Ovarian Cancer Center of Excellence, explained that "even in the worst-case scenario, these tumors are very treatable."

As with other ovarian masses, atypical tumors must be staged, which usually requires a big, open laparotomy. Gardner, however, performed all staging biopsies (results were negative) and removed the remainder of Garagozzo's one ovary, the regional lymph nodes and her appendix in a laparoscopic procedure that allowed her patient to leave the hospital the next day.

"Because of her cell type and age," Gardner says, "we could spare her other ovary and her uterus," an outcome important not only for hormonal health and pelvic-floor support, but for future childbearing.

"From the moment I went to Hopkins," Garagozzo says, "I knew I'd be OK. I had the surgery in March 2005, and my second daughter was born a year later. That is huge."

☎ 410-955-8240 to learn more. ■

Pediatric ERCP: When and Why

If there's one misconception that interventional gastroenterologist **Patrick Okolo** is out to dispel, it's that endoscopic retrograde cholangiopancreatography shouldn't be performed in children. "It does require a significant level of dexterity," says the new chief of GI endoscopy. "But ERCP can be done with great safety *and* favorable outcomes. The goal is to make the correct diagnosis with the least invasive technique and avoid unnecessary procedures."

In neonates and infants, who must be examined with a special, small-caliber scope, diagnosing congenital bile-duct abnormalities is the most common indication, Okolo says. Most jaundice can be evaluated noninvasively, but with biliary atresia being a cardinal issue in newborns, the diagnostic details that ERCP reveals can either obviate surgery or help plan it.



Scoping expert Patrick Okolo.

By the time children reach 12 months of age, acquired conditions join congenital problems in the diagnostic mix, and in many cases, ERCP not only aids diagnosis but can correct the problem. With choledochal cysts, for example, although surgical management is tailored to the type of bile duct dilatation, ERCP can be used to map out the operation and often relieve the obstruction. It can also restore bile duct integrity in children who develop biliary leaks following a liver transplant and re-establish lumen size in sclerosing cholangitis by allowing placement of a balloon and / or stent in the dominant strictures.

As children get older, pancreatic disease—particularly idiopathic recurrent pancreatitis—becomes more common. Here, Okolo says, ERCP is invaluable in differentiating among such conditions as

microlithiasis, sphincter of Oddi syndrome and annular pancreas (which ERCP can confirm when noninvasive imaging shows nothing). And for children who've sustained injuries from contact sports or other trauma, ERCP can identify disruptions to pancreatic duct integrity and potentially treat them, usually with a stent placed across areas of leakage.

"Whenever children present with jaundice, unexplained blood biochemistry abnormalities, growth failure or pancreatitis, the cause needs to be identified," Okolo says. "It's not merely that untreated biliary obstruction and recurrent pancreatitis can result in significant morbidity and mortality. We also need to remember the effect of the 'sick role' on the child's psychology."

☎ 410-502-6761 to learn more. ■

Shorter Breast Cancer Treatment, Happier Patients

For some members of Hopkins' institutional review board, the clinical trial **Richard Zellars** proposed was going to be a tough sell. Among those scrutinizing his protocol were physicians who remembered reports from the early days of chemotherapy and radiation for breast cancer—how attempting to combine the treatments was deemed dangerously toxic.

“Thirty years ago,” says Zellars, a radiation oncologist, “the whole breast was irradiated, and when that was simultaneously added to chemotherapy, the result was worse-than-third-degree burns.” As a consequence, breast cancer patients who need both chemo and radiation following surgery have been treated sequentially in a regimen that can stretch on for six months. Zellars, though, was convinced that the time had come to give simultaneous treatment another go.

Among the evidence he marshaled was literature showing that in patients who've had a lumpectomy for cancer limited to the breast, any major tumor recurrence tends to appear in the same breast quadrant as the original lesion. As a result, U.S. and European researchers now have been targeting the radiation needed to prevent local recurrence to only the area of the lumpectomy plus a small margin. Furthermore, studies in other cancers have shown that there's

greater tumor cell “kill” when chemo is added to radiation. Finally, under Zellars' proposal, the duration of each treatment would be trimmed, decreasing both delays and toxicity. Instead of being given standard doses of chemo (Adriamycin plus Cytosin) every three weeks for up to four and a half months, patients would instead receive the same doses at two-week intervals for a total of seven weeks. Likewise, radiation treatments overlapping chemotherapy would be condensed to three weeks or less, not the usual six.

Zellars, whose rationale won over the IRB's skeptics, began enrolling patients two years ago for the phase I/II trial. “More than 80 percent of the women we've offered it to have accepted,” he says. “They're excited about getting their treatment over within seven weeks.”

Viola Collier Jones is among the 15



Radiation oncologist Richard Zellars: “We've made great strides in treating breast cancer—now it behooves us to see if we can make treatment more patient friendly.”

women who've so far completed the trial. A 55-year-old Washington, D.C., resident who underwent a lumpectomy at Hopkins in April 2005 for cancer

that involved one lymph node, Jones signed on for Zellars' abbreviated chemo-radiation regimen that June and was finished by August. She acknowledges going into a temporary tailspin at the thought of losing her below-the-shoulders hair, but when it did come out about half-way through treatment, she says, “I was at peace—I looked in the mirror and I didn't go berserk.”

Like most women in Zellars' study, Jones experienced little to no breast discoloration. (Grade 1 reddening has occurred in three patients, he says—not even close to the grade 4 that halted trials years ago.) In fact, the only side effect that really bothered Jones was chemo-induced fatigue, managed with the same prophylactic growth factors prescribed during traditional treatment. “If I had to do it all over again,” she says, “I would definitely choose that clinical trial.”

“We're still enrolling patients,” Zellars says, “but we've already shown that the combination is safe. The next goal is to establish long-term efficacy.”

☎ 410-502-1421 to learn more. ■

CARDIOLOGY

Making Peace Between Heart Devices and MRI

After electrophysiologist **Henry Halperin** decided to challenge the dogma that magnetic resonance imaging can't be done in patients with pacemakers or implanted cardioverter defibrillators, he wasn't exactly surprised when the positive results his team reported two years ago ignited fierce debate. Yet by combining carefully worked-out adjustments to both the MR scanner and the heart devices, Halperin and his group now have scanned more than 100 patients who had no imaging alternatives.

To prevent misfires, they reprogram each device so that its electronics won't mistake the MR radiofrequency for an arrhythmia. They also turn off a defibrillator's shocking function for the 30 to 60 minutes needed to do an MR scan. In addition, they halve the amount of energy used at peak scanning, reducing the strength of the



Halperin, undaunted by naysayers.

electromagnetic field from as much as 4 watts per kilogram to 2 watts per kilogram per patient. And during the scan, they closely monitor every patient using electrocardiography and pulse oximetry.

To be eligible, patients must have one of the 24 modern heart devices the Hopkins physicians have already tested—pacemakers made after 1996 and defibrillators manufactured after 2000—which are made of titanium and thus better protected from radiofrequency energy. Halperin says they also found in earlier research that device leads on the surface of the heart or those

capped with metal are prone to overheating, so only patients with leads embedded in blood vessels or connected to the device battery have been allowed to undergo MR imaging. Among the patients who've been scanned at Hopkins, lead sensing didn't fluctuate or change during the MRIs, the scans didn't alter battery charges, and the devices performed successfully after the scans without any premature firing or false alarms.

The overarching goal, of course, is to gather needed clinical information, and Halperin reports that physicians here have been able to make definitive diagnoses in all the patients they've scanned who had nonthoracic conditions and in 93 percent of those with problems involving the heart and upper body. They've planned artery-opening procedures, measured tumor growth, detected strokes and a brain mass, and diagnosed a blood clot in the spine that had been missed by CT scanning.

Halperin cautions that there are still risks. “But,” he adds, “our results show that with appropriate precautions, MRI is a safe and effective diagnostic tool in patients with modern implanted heart devices. We've turned a once exceptional procedure into one that's now routine at Hopkins.”

☎ 410-502-0550 to learn more. ■

An Ear Operation that Sets the World Straight Again



Lloyd Minor with a patient who's no longer dizzy.

and his colleagues had to find the cause. They've also created a solution.

Starting with the fact that their patients' dizziness was clearly related to the vestibular-ocular reflex linking the eye and the inner ear, they remembered a century-old study in pigeons that had connected specific eye movements with damage to particular canals of the inner ear. "We monitored the eye twitches of our two patients," says Minor, "and then took the problem to the lab." There, they compared CT scans of the patients' vestibular structures and, after adding evidence from hundreds of preserved inner-ear bones, realized they were looking at tiny holes in the uppermost part of the ear's three-canal balance system. They

named the previously undescribed condition superior canal dehiscence.

Minor and his group also collected sporadic case reports (including one involving a French horn player for whom "the world seemed to tilt by 15 degrees" when he played a certain note) and examined dozens more patients firsthand. Their efforts made clear that SCD produces a range of symptoms, often evoked by such mundane events as sneezing, laughing or lifting a heavy object. In addition to sudden dizziness, loss of balance, falling down and nausea, some patients have reported being able to hear

their heart beating or their eyes moving in their sockets.

Minor believes SCD's underlying cause is failure of the upper semicircular canal bone to reach normal thickness. In some people, it may erode over time due to the pressure of the brain; in others, it tears after a blow to the head, for example, or a violent bout of coughing. The open balance canal is then abnormally activated by sounds and pressure, which are in turn interpreted by the brain as head movement.

The key to ending patients' misery was obvious: Plug the hole. Yet reaching the toothpick-wide superior canal—in a dime-size area that can only be exposed by opening the skull and moving aside part of the brain—would be the easy part. The real challenge was inventing the patch

The key to ending patients' misery was obvious: Plug the hole.

itself. Testing their concept in chinchillas, whose inner-ear structures are easily accessible, Minor and his team succeeded with a mixture of bone chips and fibrous tissue taken from the area of the skull incision. After the concoction is wedged into place, a bone graft completes the four- to six-hour procedure.

It's not for every SCD patient, says Minor, who estimates that only about a third of those afflicted have symptoms that are controlling their lives. So far, 39 of his patients have reached that point, and in what's believed to be the largest follow-up analysis of those who've opted for the operation, he and his team have shown that it works. "It can put a stop to even severe symptoms," Minor says, "and allow patients to return to their normal daily activities."

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Your Vital Links

Johns Hopkins Medicine offers the following links to physicians in the surrounding community. It also urges M.D.'s to use its Physician Liaison Service to offer suggestions and comments. Good communication, we believe, is vital.

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Hopkins Access Line (HAL): Physician-Only Line for Consultations, Referrals and Patient Transfers

1-800-765-5447 (Continental United States)

410-955-9444 (Baltimore area and international calls)

Online Referral Directory
www.hopkinsmedicine.org

Physician Liaison Service: Concerns or Suggestions for Hopkins Medicine

1-800-759-7734 (Continental United States)

410-502-2737 (Baltimore area and international calls) jhmcares@jhmi.edu

CME Program Information

www.hopkinscme.org

Information: 410-955-3169

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Clinical Trials Information

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