Advance (Summer 2014) - Stethoscopes and Pocket Protectors: Research Collaborations Reveal New Vistas for Patient Care

University of Tennessee Medical Center

University of Tennessee Graduate School of Medicine

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On the Horizon:
Finding Novel Ways to Use the World’s Best Imaging

Research Spotlight:
Engineering and Medicine Build a Tiny Wireless Camera for Abdominal Close-ups

Studies in Brief:
• Understanding Blood Inside and Out
• Using Gold to Control Effectiveness of Biomarkers

Clinical Trials
Spirit of Discovery...
This edition of *Advance* highlights the emphasis on research that ultimately affects patient care and clinical outcomes in areas where we have exceptional medical expertise that has earned regional and national recognition. The research in the core laboratories of biomedical engineering, vascular diseases and molecular imaging are closely allied to and support advanced and skilled clinical care given in the Stroke Center, the Brain and Spine Institute, The Heart, Lung, Vascular Institute, Neonatal Intensive Care Unit, and the Cancer Institute. Other efforts, such as the anesthesia clotting laboratory, have contributed significantly to how we address clotting abnormalities in massive trauma injuries, post-partum hemorrhage and other situations where appropriate blood component replacement is necessary. Nikki Zite, M.D., and Audrey Barry, M.D., highlight geographic location of patients and subsequent cost factors that play a role in access to medical care, underlining a major socioeconomic impediment to the delivery of obstetrical care seen in the Women’s Center. Stephen Kennel, Ph.D., is exploring more effective ways to treat cancer through modern nanotechnology. Many of the highlighted efforts represent work that is done in collaboration with other nationally recognized institutions while others are singular to our institution. All of these areas of research will have an impact on how we care for patients, putting University of Tennessee Medical Center on track to delve into the kind of advanced medical care that attracts national attention.

This recognition leads not only to better care for our patients, but it also helps recruit physicians who give expert care and who are on the forefront of innovations leading to better care. Additionally, it helps recruit higher quality residents and students who ask questions that make us uncomfortable with the status quo in some areas and force us to look for new solutions. Someone once suggested to me, that a physician who taught or did research only did so because he or she couldn’t give proper clinical care. On the contrary, the physicians at UTMCK do all three expertly. Our clinicians practice, teach and seek solutions for the complex problems presented by clinical situations.

Mitchell H. Goldman, M.D.  
Professor and Chairman, Department of Surgery  
Assistant Dean of Research  
University of Tennessee, Graduate School of Medicine

This is the final issue under the direction of Amanda Johnson as managing editor. We would like to recognize her for her professionalism, creativity and editorial expertise. She was a credit to the Graduate School of Medicine and will be missed. We wish her well in her new position. Kristen Bass and Brittany Nauta will take over editorial duties.
She was a chief resident far from home and passionate about women's health. He was a third-year medical student transplanted from Knoxville and eager to excel. In the midst of the caffeine-rich environment of medical school and residency training, these two determined young professionals met.

“It sounds much more ‘Grey’s Anatomy’ than it actually was,” laughs Nikki Zite, M.D., about the popular television drama.

Without Hollywood’s help, the two met, and a collaboration of the truest kind began.

“We were engaged by the time I finished medical school,” remembers Wes White, M.D.

Today, Zite is an associate professor and residency program director in the Department of Obstetrics/Gynecology. White is an assistant professor in the Department of Surgery and director of the Division of Laparoscopic and Robotic Surgery in the Department of Urology.

At the end of the day, though, they become just husband and wife, mom and dad.

Zite and White sit comfortably together on the squishy sofa on their porch. Their two boys, Jackson, 6, and Grayson, 4, topple onto their laps, keen to hear about their parents’ experiences at work. Cleo, their black Labrador retriever, demonstrates her enthusiasm.

In this familial chaos and after spending a day delivering babies, performing surgery and advancing research and educational programs, Zite and White are calm and attentive, even with Cleo.

Their backgrounds and medical specialties differ, but one thing is identical: Both physicians are avid about the patients they care for, the residents they teach and the research they conduct.

Although they collaborate on an ongoing study about kidney stones during pregnancy, their
research rarely intertwines. Zite focuses her research on contraception, sterilization and health disparities; while White researches robotics, laparoscopy and laparoendoscopic single-site surgery.

“I have a built-in sounding board,” White says of his wife who in addition to being a medical doctor is trained in public health. “It’s nice to be able to sit on the sofa and read my research to Nikki. She’s good with study design.”

White, the first Urology resident at the Graduate School of Medicine in 2004, says he wants to give back to a program that was good to him. He dedicates each Friday to research and seeks novel perspectives from which to approach a medical issue. Currently, he is working with the UT Knoxville College of Business to build a predictive model to determine patient outcomes, particularly in relation to prostate cancer diagnosis and treatment.

About her work, Zite says, “I really like taking care of patients, and working on improving public health issues. I hope to continue to do research until we figure out a better way to provide care for women with socioeconomic limitations.” [See related story page 11.]

Zite researches ways to debunk myths from the 1970s about the safety of IUDs (intrauterine devices) in women who have never delivered a baby, and she promotes sterilization for women on Medicaid/TennCare who opt for the procedure.

“It’s a national issue,” Zite says. “We are working to get the attention of the right people.” Just then Jackson’s ball goes off course, and Grayson stomps into the room, temporarily upset.

So, do these doctors/researchers/teachers/parents want their children to become doctors?

“Statistics tell us one of them probably will,” says the dad, reluctantly.

To which the mom adds calmly, “We want them to do what fulfills them.”
Collaborative New Institute Bridges Engineering and Medicine

There's a new collaboration in town. This partnership joins pocket protectors and stethoscopes, data and diagnoses. The collaboration, called the Institute of Biomedical Engineering, aligns the best of the UT College of Engineering with the Graduate School of Medicine and College of Veterinary Medicine to develop unique approaches to patient care.

Skeptical? Keep reading.

**Physics and Lower Back Pain**

Lower back pain is not just a pain in the neck; it’s also the second leading cause for physician visits in the U.S., reports the American Chiropractic Association. The most popular diagnostic method is imaging, but x-ray, CT and MRI scans are static and cannot provide quantitative dynamic information. For anyone who suffers from recurrent lower back pain, an undiagnosed source of the pain rapidly deteriorates quality of life.

About five years ago, Mohamed Mahfouz, Ph.D., the director of the Institute of Biomedical Engineering and professor of biomedical engineering, received funding from the National Institutes of Health to develop a tool to diagnose lower back pain. His device is smaller than a cell phone, noninvasive and analyzes patterns of motion in everyday movement.

For the rest of the story, visit http://gsm.utmck.edu/research/ibme/main.cfm

**Pushing Ultrasound Beyond the Boundaries**

Mahfouz and team also are expanding the boundaries of ultrasound, transforming a helpful 2D image into a revealing 3D image, and anyone who receives injections in their joints will welcome this technology.

Ultrasound is often preferred because it does not use radiation, and it provides immediate feedback. Its limited imaging capability,
Why this matters:
Looking beyond conventional medical care takes courage and innovative thinking. These collaborative efforts will both accelerate and improve medical solutions for patients in ways rarely conceived before.

however, can create difficulties for certain medical procedures. To address this need, the team created innovative software that combines the radiofrequency signal of ultrasound with an original algorithm and knowledge of anatomy to “complete the picture.” Where ultrasound doesn’t see, the software fills in the bone’s image, even if the bone is malformed.

For the rest of the story, visit http://gsm.utmck.edu/research/ibme/main.cfm

Approaching Personalized Medicine

Collaborations between engineering and medicine don’t only address direct patient care. One collaboration is examining ways to optimize the healthcare process to maximize resources and increase the likelihood of positive outcomes for patients.

Christopher Stephens, Ph.D., an assistant professor and research director for iBME; Eman Abdel Fatah, Ph.D., post-doctoral research associate at the UT College of Engineering; and others are leading the effort, with support from Paul Terry, Ph.D., M.P.H., an associate professor in the College of Education, Health and Human Sciences. Simultaneously, Stephens and Fatah are creating clinical pathways models to understand the steps in a patient’s treatment process while Terry is directing research in clinical end points to ensure efficiencies result in better patient safety and care.

For the rest of the story, visit http://gsm.utmck.edu/research/ibme/main.cfm

Knoxville, Meet the Future

Jindong Tan, Ph.D., an associate professor in Mechanical, Aerospace and Biomedical Engineering, specializes in robots and medical imaging and devices. The National Science Foundation recently recognized the value of the innovation and awarded $400,000 for further development.

Surgeons have long relied on camera-tipped instruments in minimally invasive surgeries. These, however, are restricted by inflexibility, immobility or inability to see beyond organs. They are even less functional with the newer single-incision and natural-orifice surgical techniques.

The sCam is different. This small capsule is equipped with big technology: A spherical magnetic head for locomotion; an illumination and vision subsystem; a wireless communication subsystem; an inertial sensing system; and a battery and battery-management system.

For the rest of the story, visit http://gsm.utmck.edu/research/ibme/main.cfm

The future of surgical imaging is being developed today, and it’s about the size of an almond. The sCam, a novel wireless laparoscopic surgical camera system, is small technology with enormous impact.
The collaboration of Yong Bradley, M.D., an associate professor in Radiology and chief of the Division of Nuclear Medicine, and Dustin Osborne, Ph.D., an assistant professor in Radiology and clinical research director of the Molecular Imaging and Translational Research Program, is making a difference in the lives of patients and causing heads to turn toward Knoxville.

Recently, the doctors oversaw the installation at The University of Tennessee Medical Center of a new and immensely more powerful PET/CT scanner, called the Biograph mCT. This imaging technology is the only one of its kind in the region and sees smaller lesions with more clarity and reduces image defects that are not related to the anatomical/molecular image captured by the mCT scanner. It also accommodates timing issues between recorded measurements, making resulting scans more accurate.

Not only is the new technology currently in diagnostic use, but is also part of the national clinical trials network of the Society of Nuclear Medicine. This network provides improved access to clinical trials and expands access to clinical research mechanisms that might otherwise be unavailable.

One research program involves beta testing (final stage of testing) a new clinical software that is FDA-approved for use in PET-CT imaging.

“Testing of this new technology took place in only two sites in the world, and one is here,” says Osborne.

Using technology called “continuous bed motion” (CBM), lesion-detection capabilities and patient workflow are greatly improved by...
Dustin Osborne, Ph.D., and Yong Bradley, M.D., investigate innovative uses of the powerful mCT scanner. The new continuous bed motion technology results in improved scans (right), as compared to the traditional step-and-shoot imaging, providing a more fluid image with fewer overlaps. The imaging technologist has better control of the scan length, which leads to reduced scan times and up to 5% reduction in radiation dose.

“The technology allows us more flexibility and reduces the radiation burden for the patient,” says Bradley.

Since March, more than 100 patients have benefitted from the new CBM technology, and in May, the team combined CBM technology with high-definition chest imaging, becoming the first facility in the world to make this connection. Chest imaging using this technology results in tailored patient workflows and improved diagnostic image quality.

Bradley and Osborne also are beginning to use a better imaging agent, fluorocholine (FCH), with patients who have pancreatic cancer. Unlike other glucose-based agents, FCH is absorbed only by cells that show an increase in choline production, leading to more focused imaging. This compound has generally only been used in prostate cancer imaging.

“Many believe that an unusually high incidence of pancreatic cancer exists in our region,” Bradley says. He and Osborne are collaborating with Keith Gray, M.D., an assistant professor in the Department of Surgery and chief of the Division of Surgical Oncology, and the Appalachian Regional Commission to identify contributing factors of this high incidence rate. They are looking at socioeconomic information, treatment compliance and social trends of the people in the region.

“We will be one of the first to use FCH to image pancreatic cancer,” Bradley says. “These images can help determine treatment strategies and diagnose the cancer at an earlier stage. We believe it also can be used in other cancers and to potentially determine fast- and slow-growing lesions in prostate cancer. The use of FCH coupled with our expanding work with fluorothymidine (FLT) opens new imaging possibilities.”

The team also is working to determine if FLT and FCH do a better job of imaging prostate and biliary tract cancers.

**Why this matters:**

As we are able to find more ways to use the best technology in the world in concert with keen minds and curiosity, we are able to provide better care for patients.
Why this matters:

Medical advancements are possible in part because of clinical trials, and patients can feel assured that clinical trials are safe and stringently monitored for adherence to federal regulations.

All research studies using human volunteers must follow stringent federal regulations and be reviewed by an Institutional Review Board (IRB) before being approved. An IRB Committee, comprised of physicians, pharmacists, scientists, researchers and non-scientific community representatives, review research protocol to ensure federal protections are in place for people volunteering in the study.

The IRB at the UT Graduate School of Medicine oversees clinical trials, which provide therapeutic, diagnostic and translational information. Trials help bring treatments more rapidly to patients.

Craig Towers, M.D., Maternal-Fetal Medicine, and others are collaborating with physicians at the University of South Alabama Medical Center to investigate whether preservatives (parabens and triclosans) from cosmetics, lotions and some foods cross the placenta and if ethnicity plays a role. This is the first study of its kind in the country. For more information, contact the Department of Obstetrics/Gynecology at 865-305-9306.

Rajiv Dhand, M.D., Department of Medicine, and co-investigators are part of a multi-center clinical trial to determine if adding inhaled antibiotics to conventional therapy with intravenous antibiotics for mechanically ventilated patients with Gram-negative pneumonia will improve clinical outcomes. This study is enrolling. Call Lauren Davis at 865-305-7975.

Melissa Phillips, M.D., Department of Surgery, is recruiting patients for a post-market observational study to collect data on the performance of a new ventral hernia graft technology when used to reinforce or bridge the abdominal wall for the repair of ventral hernias. Visit www.clinicaltrials.gov and search “Hybrid Graft for Ventral Hernia Repair.” The Department of Surgery also has two additional hernia-repair trials upcoming. For more information, call the department at 865-305-9227.

A comprehensive list of clinical trials being conducted nationwide can be found at www.clinicaltrials.gov.
Anesthesiologists know blood, inside and out. They administer more blood to patients than any other group of medical specialists.

For a decade, anesthesiologists at the UT Graduate School of Medicine have researched platelet and whole blood functions to find better care for their patients. Recently, a collaborative team led by Robert M. Craft, M.D., a professor and residency program director in the Department of Anesthesiology, has been investigating blood coagulation in a variety of clinical situations.

“Traditional tests examine the coagulation properties of blood’s individual components but not how they work together,” Craft says. “The coagulation cascade cannot be adequately assessed by isolating the parts.”

The team, which also includes, Roger Carroll Ph.D., and Russell Langdon M.D., is now studying a process called thromboelastography (TEG) that determines the rigidity of blood during coagulation. “TEG can tell us which aspect of the coagulation cascade is at fault and allows us to get these assessments in real time,” Craft explains.

Craft and team members from various medical specialties also are using TEG to investigate care in:

• Pregnancy and safety with epidurals
• Preconception anticoagulation screenings
• Coagulopathy in massive blood transfusions
• Testing of anticoagulants used for atrial fibrillation
• Coagulation profiles of ischemic and hemorrhagic stroke
• Anticoagulation inside the brain
• Effect of controlled hypothermia on coagulation

“Our care affects all branches of medicine, so our research reflects this,” Craft says of the collaborative spirit evident in the diversity of research in his department.

Anesthesiologists must understand the actions and reactions of blood during medical procedures, and collaborative research led by anesthesiologists will bolster that understanding to bring about improved patient safety, better care and more promising outcomes.
Revealing basic-science research at the UT Graduate School of Medicine is indicating how testosterone affects the body’s response to vascular intervention.

Brian Freeman, M.D., a third-year surgical resident, took a year to study testosterone in the Vascular Research Laboratory. This lab, led by Deidra Mountain, Ph.D., already has made impressive findings on the effect of estrogen on vascular recovery after intervention.

Freeman’s research in collaboration with the Division of Urology specifically examines the role of testosterone deficiency and testosterone supplementation in the development of intimal hyperplasia (thickening of the vascular wall) through abnormal remodeling of the cells using certain enzymes.

“Although still in the very early stages, our study could identify low testosterone levels as a predictor of the incidence of restenosis in patients prior to vascular intervention,” Freeman says. “This knowledge would help physicians and patients make decisions about care pre- and post-intervention.”

Valerie Sams, M.D., a surgical resident, avidly pursues research. A recent project involved collaboration with the Division of Orthopedics and UT College of Pharmacy.

“Clinicians and surgeons strive to provide pain control to patients while avoiding use of opiates. Many orthopedic surgeons, however, believe non-opiate NSAIDs [non-steroidal anti-inflammatory drugs] impair healing,” Sams explains.

The team investigated whether the use of NSAIDs after surgery of traumatic long-bone fractures could result in poor healing of bone and increase the chance of infection. In their retrospective study, the team incorporated the variable of smoking and controlled for other factors.

Findings showed patients with long-bone fractures who received NSAIDs perioperatively were more than twice as likely and smokers more than three times as likely to suffer complications, such as non- or mal-union of the bone or infection.
In a 2011 study released by the Centers for Disease Control and Prevention, 49% of pregnancies in the U.S. in 2006 were unintended. Two physicians at the UT Graduate School of Medicine are seeking causes.

Audrey Barry, M.D., a fourth-year resident in the Department of Obstetrics and Gynecology; Nikki Zite, M.D., an associate professor and Ob-Gyn residency program director; and Lorraine Wallace, Ph.D., now at The Ohio State University, are studying disparities in health care, particularly disparities in costs for prescription contraceptives. They presented their findings at a recent meeting of the American College of Obstetricians and Gynecologists (ACOG).

“Access to health care, especially access to contraceptives, is a leading problem for many women,” says Barry, as reported by ACOG. “We believe there is a correlation between high cost of contraceptives for low-income women and unintended-pregnancy rates.”

Barry and Zite surveyed costs of the seven most common prescription contraceptives in the state of Florida using the website, MyFloridax.com. Comparing this with census data, they were able to compare prices for each zip code with income levels.

“Virtually all of the prescription contraceptives we surveyed were more expensive in the low-income zip codes,” Barry says, “and for two of the contraceptives, higher-income residents paid significantly less.”

Although a limited study, Zite believes cost is a significant barrier to contraceptive use, contributing to the high unintended-pregnancy rate in the U.S. “Ensuring that costs of contraceptives are equivalent among socioeconomic groups could improve access for all women and result in a healthier community,” she says.

**Why this matters:**

Uncovering disparities in access to health care improves the healthcare system and helps physicians as advocates for their patients. When fewer disparities exist, patients can make wiser choices for their long-term health and the health of their families.
For more than 20 years, Stephen Kennel, Ph.D., an associate professor of Departments of Medicine and Radiology, has sought a better way to deliver radioisotopes for the treatment of cancer, and recently, he and colleagues hit on a golden idea.

Previously, targeted radiotherapy (using radioactive isotopes injected into the body to kill targeted cancer cells) used beta agents, which have limited potency. Kennel and Saed Mirzadeh, Ph.D., a senior scientist at the Oak Ridge National Laboratory, and other medical researchers believed using alpha-emitting radioisotopes, which kill more efficiently, would improve results.

“When many of the alpha-emitting radioisotopes decay, however, they produce ‘daughters’, generated by the original ‘parent’ radioisotope,” Kennel says. “The radioactive daughters stray from the parent and can damage surrounding normal tissue.”

Kennel and Mirzadeh, along with researchers at the University of Missouri tested a theory: Entrap the radioisotope alpha emitter inside of a salt-like crystal to contain the daughters. This provided about 50% containment, so the team added layers of salt-like shell around the crystal. This worked better, but not well enough.

Then they had the golden idea.

“The Missouri team placed a shell of gold around the entire particle,” Kennel explains, “and we’ve seen about 90 percent containment of the destructive daughters.”

In preclinical testing, Kennel added a binding agent to the gold shell to allow attachment of an antibody, which directed the particle containing the radioisotope to the targeted site, and injected it into a preclinical model of breast cancer metastasis.

“In the model, breast cancer tumor cells growing as metastatic colonies in the lung were killed,” Kennel says. “We are a long way from use in the clinic, but this concept is significant. Learning to bury an isotope in a gold-plated crystal preventing the escape of radioactive daughters and subsequent off-target damage is valuable to further cancer studies.”

**Golden Idea: Groundbreaking Radiation Therapy Research**

**Why this matters:**
Medical breakthroughs often come on the shoulders of research done at the basic-science level, and this finding can lead to better ways to target cancer cells without damaging surrounding organs.
**Nutrition Research Funding Renewed**

Christy M. Lawson, M.D., an assistant professor in the Department of Surgery, recently presented the initial phase results of her Norman Yoshimura Grant by B Braun and the Aesculap Academy research award from the Rhoads Foundation of the American Society of Parenteral and Enteral Nutrition at Clinical Nutrition Week in Phoenix, Ariz. Her ongoing project was funded for another year based upon the exciting results of “Cross Talk Between Renin and Angiotensin in Burn Trauma.” A co-investigator is Michael Karlstad, Ph.D., a professor in the Department of Surgery.

**Concussion Research Links Genetic Markers**

Ongoing and important research on concussion is the first to link two genetic markers to post-concussion neurocognitive function and outcome. Tom Terrell, M.D., an associate professor in the department of Family Medicine Sports Medicine Program, studied more than 3,000 college football and soccer athletes and believes this is a step closer to understanding the link between genetic factors and neurocognitive outcome for concussion in contact-sport athletes, as reported by the American Medical Society of Sports Medicine. The research received funding from the National Operating Committee on Standards for Athletic Equipment.

**Collaboration Garners Top Finish**

Collaboration in the Physionet 2012 competition, one of the premier events focusing on computer applications in clinical cardiology and cardiovascular research, generated a top finish. The team comprised of University of Tennessee, Knoxville, representatives Henian Xia, Xiaoping Zhao and Adam Petrie, and UT Graduate School of Medicine Professor of Surgery Brian Daley, M.D., combined clinical and engineering expertise to develop a model for mortality prediction based on a new and blinded outcome ICU data set. The project’s results are published in Computing in Cardiology.

**Radiology Residents’ Research Awarded**

Residents in the Department of Radiology earned first-place finishes in recent research presentations. Katherine Frederick-Dyer, M.D., was awarded a first place trainee award by the Association of University Radiologists for her project “The Effect on Patient Radiation Dose of a Formal Fluoroscopy Privileging Program in First Fluoroscopy Rotations.” Austin Bourgeois, M.D., placed first for his presentation “Increased Accuracy in Lumbar Pedicle Screw Placement Using Three-Dimensional Image Guidance” at the 2013 American Society of Spinal Radiology Annual Meeting.

**Dhand Re-elected to International Society**

Rajiv Dhand, M.D., chair of the Department of Medicine, recently was re-elected to the Executive Board of the International Society of Aerosols in Medicine.

**Your Chance to Advance**

The people at the UT Graduate School of Medicine would be happy to discuss our research programs and how your support can help advance health care. For information about philanthropic giving to the UT Graduate School of Medicine Office of Research, please contact the development office at 865-305-6611 or development@utmck.edu.

If you would like more information about any of the research programs described in this issue of Advance, please contact the UT Graduate School of Medicine at 865-305-9290 or visit us online: [http://gsm.utmck.edu/research/main.cfm](http://gsm.utmck.edu/research/main.cfm).

Thank you.