ACRIN NEWSLETTER
Advancing Clinical Care Through Imaging Research

ACRIN’s Research Pipeline

by Mitchell Schnall, MD, PhD

The spring and fall ACRIN meetings give ACRIN leadership the opportunity to review the current portfolio of clinical trials and chart ACRIN's course for the future. At this fall's meeting, ACRIN's leaders and members of the scientific committees will use the ACRIN objectives to guide the development and execution of ACRIN's clinical trials.

ACRIN's scientific objectives for 2008 - 2012 all relate to an overarching goal of targeted cancer care. The objectives are as follows: 1) to develop appropriate and effective strategies for implementing imaging in the surveillance of populations at high risk for cancer; 2) to establish imaging approaches to the characterization of disease anatomy, physiology, and molecular biology in order to guide the administration of targeted therapies; and 3) to identify, standardize, and validate biomarkers of therapeutic response for implementation in clinical trials and clinical care of cancer patients.

The first objective focuses on screening for cancer. Targeted and effective screening helps us identify cancers as soon and as quickly as possible. ACRIN will continue to investigate the use of biologic indicators to determine who is most at risk for certain cancers and thus which populations stand to benefit from screening. We must also determine the best screening intervals for testing and evaluate new screening technology. ACRIN 6666, Screening Breast Ultrasound for High-Risk Women, fits well with this objective; in this trial, Principal Investigator Wendie Berg has been working to determine whether ultrasound is an effective screening modality for women at high risk for breast cancer. In the future, ACRIN will evaluate other modalities, such as the use of tomosynthesis, as we continue to determine the best screening options for women at high risk for breast cancer and other cancers.

The second objective focuses on characterization of different cancers. We need to learn more about the types of cancer that can be identified through biomarkers such as FDG uptake and angiogenesis so that doctors and patients can choose the best course of treatment. ACRIN 6671, for example, will evaluate the diagnostic sensitivity and specificity of preoperative FDG-PET/CT imaging in identifying metastases to pelvic lymph nodes in patients with cervical cancer. The ACRIN Head and Neck Committee currently has two trials in development that will fit with this objective: one, led by Val Lowe, MD, will explore the role of FDG-PET/CT imaging in nodal staging head and neck cancer, while the other, led by Greg Sorensen, MD, will investigate the assessment of tumor hypoxia in glioblastoma with PET and MRI.

The third objective focuses on response markers for treatment. We will work to identify biomarkers that can be used to determine whether or not a specific treatment is effective. As more chemotherapy treatments are becoming available, this research is particularly important; it can enable doctors and patients to make better choices—and to choose more quickly—among all the available options. ACRIN 6668 and 6678, for example, will determine whether FDG-PET can be used to assess treatment response for lung cancer. ACRIN 6676 will determine whether MRI can be used to predict response in patients with renal cell carcinoma.

This is an exciting time for ACRIN's research. Our fall meeting will allow us to build on our existing strengths and expertise to make sure our research pipeline contains trials that focus on our three key objectives and move us forward into the future of targeted cancer care.

Leadership Update

The chairs of ACRIN committees and the leaders of ACRIN's core laboratories play a crucial role in shaping research. As ACRIN has grown, several new committees and core laboratories have been formed to enhance and expand ACRIN's mission.

We thank the leaders who have stepped down from their chair positions in the past year and are grateful for their service.

C. Craig Blackmore, MD, MPH
Outcomes and Economics Committee

Robert Greenes, MD, PhD
Informatics Committee

Donald Mitchell, MD
Gynecological Committee

With the start of the 2008 - 2012 grant cycle, ACRIN has welcomed a cadre of new leaders, many who have exciting projects well underway. Also, the previous network chair has assumed an exciting new role.

William Black, MD
Outcomes and Economics Core Laboratory

Bruce Hillman, MD
Industry Relations Committee

David Mankoff, MD
Experimental Imaging Sciences Committee

Daniel Reuben, MD, MS
Informatics Committee

Mark Rosen, MD, PhD, MR/CT
Core Laboratory

Anthony Shields, MD, PhD
Oncology Committee

Pamela Woodard, MD
Cardiovascular Imaging Committee
ACRIN Launches New TRIAD System

ACRIN’s new image acquisition and management system for medical imaging clinical trials, TRIAD, is now fully operational at more than 55 ACRIN sites. TRIAD replaces the Preview-32 system to allow the transfer of image data between sites and ACRIN headquarters.

TRIAD offers many advantages. TRIAD has a Web-based graphic user interface that facilitates image search, view, and download, and it also includes advanced image management and user management functions. The new “click-once” technology allows installation of TRIAD by site personnel without a visit from ACRIN staff, and system updates are automatic. At ACRIN sites, server and client applications can be installed on the same workstation.

Anthony Levering, assistant director, Diagnostic Imaging for ACRIN, says of the new system, "TRIAD provides us with all the capabilities necessary to effectively collect images from any participating researcher. We're very excited about the vision for future TRIAD enhancements, which will extend the capabilities in areas of image annotation, manipulation, and viewing."

Sites are encouraged to use TRIAD for any trials in which they are actively participating (for more information about contacting the TRIAD support team, see sidebar). Alternate media, such as CDs, will continue to be an acceptable substitute for electronic submission, but ACRIN is committed to making electronic submission the standard for the future; this is consistent with ACRIN's overall strategy to be an electronic data collection and management organization.

Levering says that sites that wish to install TRIAD can do so by completing all the steps in the readiness checklist that is sent out by ACRIN headquarters. Sites should also identify an IT person who will help with the process. Representatives at the site will need to be able to access TRIAD with a username and password assigned by ACRIN. When sites have completed those steps, they are ready to work with ACRIN staff via phone on the installation process.

"With TRIAD, we're taking an industry leadership position," says Charles Apgar, senior director of ACRIN Administration. "This system has gone through a rigorous validation process that meets industry standards for documentation and backup procedures. It gives us a very high degree of certainty as far as data integrity. We've seen interest from outside of ACRIN in this technology. There's also the potential to use this system for ACR accreditation or education in the future."
ACRIN UPDATE

ACRIN Fund Projects Underway

Two New Projects

The ACRIN Fund for Imaging Innovation was designed to help offset the fluctuating funding levels from ACRIN’s principal sponsor, the National Cancer Institute, and to allow for the expansion of ACRIN’s research scope and infrastructure. To date, the ACRIN Fund has received commitments of more than $7 million dollars from corporations and individuals in the imaging community. The first two projects confirmed by the Research Selection Committee offer exciting—but very different—opportunities for imaging research.

Creation of Cardiovascular Imaging Committee

ACRIN will move beyond cancer imaging with the creation of a Cardiovascular Imaging Committee. The purpose of the Cardiovascular Imaging Committee is to provide answers to clinical cardiac questions that impact patient care. The committee is composed of people selected for their expertise and dedication to cardiovascular research and imaging, regardless of specialty.

The committee is headed by Pamela Woodard, MD, current president of the North American Society for Cardiovascular Imaging. Woodard, who has been involved in cardiac imaging research since 1995, has focused on cardiac MRI and, more recently, coronary CT angiography. She has been involved with numerous multi-center clinical trials and has served as a principal investigator for two National Institutes of Health grants.

Woodard is enthusiastic about her committee’s research. She says, “What excites me most about the opportunity to lead ACRIN’s cardiovascular imaging committee is the ability to identify questions in cardiac CT imaging and MRI and to shape patient care by providing a means to answer them.”

The committee hopes to have one or two proposals for randomized, controlled trials ready for consideration at the ACRIN Fall Meeting. Several possibilities have been discussed. One trial the committee hopes to pursue will explore how chemotherapy affects heart function, particularly left ventricular (LV) function. The committee would partner with other cooperative groups that are currently engaged in a treatment trial. Another possible trial would look at using CT coronary angiography versus traditional care for low-risk patients who are present in the emergency department with potential acute coronary syndromes.

Evaluating CAD for Digital Mammography

The second project approved for support is a computer-aided detection (CAD) study of full-field digital mammography headed by Etta Pisano, MD, FACR, chair of ACRIN’s Breast Scientific Committee and the principal investigator of ACRIN’s high-profile Digital Mammographic Imaging Screening Trial (DMIST). The CAD study, which is already underway, will engage 45 board-certified radiologists specializing in mammography to determine whether radiologists interpreting digital mammography exams using CAD have greater diagnostic accuracy than without using this tool. Researchers

(continued on page 4)

ACRIN Intern Researches Biomarkers

This summer, Will Pickering had the opportunity to work at ACRIN’s Philadelphia headquarters for an internship established by the Princeton Class of 1969’s Community Service Fund. The internship was created by Princeton alumnus Bruce Hillman, MD, the former Network chair and the current chair of the Industry Relations Committee.

Pickering, a rising sophomore, grew up in Chattanooga, Tennessee, before heading to Princeton to study math. While at school, Pickering volunteers at the Robert Wood Johnson Hospital in the pediatric cancer wing. “These kids are so positive and enthusiastic when you consider their situation,” he says. He also writes regular editorial columns for The Daily Princetonian. Pickering hopes to go to medical school after graduation, and he was attracted to the ACRIN internship because he liked the idea of applying his theoretical math skills to a medical setting.

Pickering’s main project while at ACRIN dealt with finding new quantitative ways to analyze tumors. He worked with ACRIN researchers Daniel Reuben, MD, MS, and Mark Rosen, MD, PhD, to design a study that would determine which biomarkers change over the course of treatment. On a test set of PET images, he traced the perimeter of tumors and highlighted their interior to separate them from the healthy tissue, a process known as lesion segmentation, and then

(continued on page 4)
ACRIN Trials Recruiting New Institutions

Several ACRIN trials are seeking additional institutions. Interested site personnel can contact the project manager listed for each trial. More information is also available on the ACRIN Web site www.acrin.org. Click on the “Protocol Summary Table” and select the protocol of interest.

ACRIN 6668 (in collaboration with RTOG 0235): Lung Cancer: Predicting Treatment Response with PET

The main objective of this trial is to determine if the post-treatment glucose update as measured by FDG-PET is a useful predictor of survival after definitive chemoradiotherapy. Participants are individuals with clinical stage IIB/III non-small cell lung cancer who are being planned for definitive concurrent chemoradiotherapy.

**Project Manager:** Irene Mahon (215-574-3249; imahon@phila.acr.org)

ACRIN 6671 (in collaboration with GOG): Cervical Cancer: Staging with Combidex MRI and PET/CT

The primary objectives of this trial are to evaluate the diagnostic sensitivity and specificity of preoperative FDG-PET/CT imaging in identifying metastases to abdominal lymph nodes in patients with locoregionally advanced cervical cancer, and to evaluate the diagnostic sensitivity and specificity of preoperative ferumoxtran-10 (Combidex) MRI scanning in finding metastases to abdominal lymph nodes. Participants must have previously untreated, locoregionally advanced invasive cervical cancer and must be appropriate surgical candidates to undergo extra-peritoneal or laparoscopic lymph node sampling.

**Project Manager:** Bernadine Dunning (215-574-3228; bdunning@phila.acr.org)

ACRIN 6676 (a substudy of ECOG 2804): Renal Cell Carcinoma: Predicting Treatment Response

This trial has three objectives: 1) to relate changes in tumor perfusion and vascular permeability on serial dynamic contrast-enhanced (DCE) MRI to clinical outcome and radiologic regression detected by other standard methods; 2) to assess the potential of DCE-MRI imaging as a biomarker for response to therapy and/or as a prognostic indicator of disease progression; and 3) to assess site readiness and ability in acquiring DCE-MRI data. Participants will be patients enrolled into the ECOG E2804 trial.

**Project Manager:** Donna Hartfeil (215-717-2765; dhartfeil@phila.acr.org)

ACRIN 6678: Lung Cancer: Evaluation of Treatment Response with PET

This trial has four main objectives: 1) to test whether a metabolic response provides early prediction of tumor response and patient survival; 2) to determine the test-retest reproducibility of quantitative assessment of tumor FDG uptake by SUVs; 3) to study the time course of treatment induced changes in tumor FDG uptake; and 4) to evaluate in an exploratory analysis changes in tumor volume during chemotherapy by multislice CT. Participants will be patients with advanced NSCLC who meet the eligibility criteria, and who will receive platinum-based doublet chemotherapy.

**Project Manager:** Donna Hartfeil (215-717-2765; dhartfeil@phila.acr.org)