

ACRIN NEWSLETTER

Advancing Clinical Care Through Imaging Research

American College of Radiology Imaging Network

MAY 2007



ACRIN CHAIR'S COLUMN

Bruce J. Hillman, MD

When we speak of "personalized medicine," the idea is that we are no longer simply treating a "disease" but rather tailoring treatment to how the disease interacts with a patient's individual genetic and environmental makeup. It follows then that a certain treatment will be more or less effective in different patients—and indeed, that is the case. To optimize treatment, physicians have to determine which of a plethora of old and newer treatments—alone or in combination—work best for particular patients.

How to do this? The current approach is to identify "biomarkers," which are a representation of physiologic or metabolic processes. With respect to cancer, we are looking for biomarkers that imply what treatment may be most effective. In prospect, imaging can serve in this regard, particularly metabolic and functional imaging techniques like PET, DCE-MRI, and MRS. Preliminary studies, mostly in small cohorts accrued in single institutional studies, have shown that imaging may perform the critical roles of predicting which treatment may be most effective for a given patient, and, once treatment has begun, telling us earlier and more accurately whether treatment is having a positive effect.

One of the problems in bringing imaging biomarkers to clinical care is a lack of standardization in how molecular imaging technologies are employed. To begin to address this, ACRIN will soon initiate a trial of FDG-PET imaging for non-operable lung cancer, which is being co-funded by the NCI and the Biomarkers Consortium. The Biomarkers Consortium is a collaboration of industry, advocacy groups, the NIH, FDA, and CMS. The trial-ACRIN 6678, led by Dr. Wolfgang Weber of UCLA is the first venture of the newly formed Consortium. The goals of the trial are to demonstrate, based on imaging response, the ability of PET to effectively determine the subset of patients in whom the treatment regimen will produce a more desirable outcome, as well as to show that standardized use of PET is achievable across institutions. Ultimately, we hope that the trial will inform the development of standards that can be employed for this purpose in the clinical environment. If successful, ACRIN 6678 will support the goals of the Biomarkers Consortium to develop biomarkers that will be applicable in the clinical environment and that will speed the assessment of new therapeutic agents through regulatory approval and into clinical use.

ACRIN 6678 is one of several ACRIN trials that are being performed to establish the value of various imaging technologies as biomarkers of the response to treatment. This is a crucial area of cancer research. Progress is essential if imaging is to play a role in making cancer care more efficient, less injurious to patients, and more affordable.

UPCOMING EVENTS

May 3 and 4:

Innoventures 2007

ACRIN will have a booth at *Innoventures 2007*, a science and business exposition designed to showcase innovation occurring in a variety of industries in central Pennsylvania. ACRIN investigator Timothy Mosher, MD, from Penn State University will present an abstract regarding his work on MRI image markers for knee articular cartilage damage from osteoarthritis.

May 19 - 23:

ACR Annual Meeting and Chapter Leadership Conference

ACRIN staff will be on hand to talk with ACR members about new clinical trials, research results, and an NOPR update.

June 21:

Grant Renewal Site Visit

NCI grant review team will conduct a site review in Philadelphia that will allow ACRIN investigators to highlight the work completed during the past NCI funding cycle and the new research strategy planned for implementation beginning in January 2008.

September 27 - 30:

ACRIN Fall Meeting

Mark your calendar for the ACRIN Fall Meeting to be held at the Ritz Carlton-Pentagon City, in Arlington, VA. Information about submission of award nominations for the Outstanding Contribution Awards and the Jo-Ann D'Amato Award of Excellence will be coming soon.

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ACRIN CORE LABORATORIES PROVIDE RESEARCH SUPPORT



Mark Rosen, MD, PhD, director of the ACRIN MRI/CT Core Lab, reviews images with Mostafa Atri, MD, trial PI for ACRIN's cervical cancer study.

New ACRIN core laboratories support both ACRIN's research and the cancer research community as a whole. A core laboratory for outcomes research develops trial components such as quality of life and cost-effectiveness. Imaging core laboratories provide comprehensive image management and quality-control infrastructure for clinical trials and related research. The laboratories will standardize some aspects of ACRIN's research, and they will also move ACRIN in the direction of becoming a service-oriented organization capable of sharing imaging expertise with the broader medical community.

The PET Core Laboratory, directed by Barry Siegel, MD, was the first to open at ACRIN's Philadelphia headquarters. "The PET Core Laboratory is designed to assist the ACRIN disease site committees in the development of ACRIN trials, as well as provide expertise to other cooperative groups," says Siegel. "Already, the PET Core Laboratory has helped develop quantitative endpoints for imaging trials and standardized procedures for imaging

acquisition and analysis. Our goal is to perform innovative PET research that will help the medical community provide better treatment and patient care."

The PET Core Laboratory is currently supporting many ACRIN trials involving PET. One notable example is ACRIN 6678: FDG-PET/CT as a Predictive Marker of Tumor Response and Patient Outcome, a new trial of non-small-cell lung cancer that opened this spring. The trial, which examines whether FDG-PET/CT can be used to determine the effectiveness of chemotherapy after just one or two cycles, is the first clinical trial supported by the Biomarkers Consortium, a public-private partnership launched in October 2006. ACRIN's PET Core Laboratory will provide crucial support for site accreditation, image acquisition, and image analysis. According to Siegel, "ACRIN 6678 represents a very significant investment by NCI and its partners to confirm, in a rigorous, multicenter setting, the validity of FDG-PET as a biomarker for tumor response. This study presents several challenges to the ACRIN Core

Laboratory, but we are excited to have the opportunity to participate in this important trial."

ACRIN will provide core laboratory expertise for other modalities as well. The new MRI/CT Core Laboratory, directed by Mark Rosen, MD, PhD, has already been involved with several ACRIN trials. "The MRI/CT Core Laboratory brings ACRIN and the cancer research community specialized expertise with these modalities, both from physicians and imaging technologists," Rosen explains. "Our lab will standardize image acquisition protocols for morphologic and functional imaging, aid trial principal investigators in developing quality-control measures, and perform quantitative analyses to explore the use of imaging biomarkers. As ACRIN develops new trials, it is critical to have highly specialized personnel in place to facilitate the quality review and analysis of medical imaging."

The ACRIN Newsletter is published by ACRIN Headquarters and distributed to participants and others interested in the Network.

ACRIN is supported by Grant CA80098 from the National Cancer Institute.

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EXPERIMENTAL IMAGING COMMITTEE FOCUSES ON INNOVATIVE RESEARCH



David Mankoff, MD, PhD, Chair of ACRIN's new Experimental Imaging Committee.

A new ACRIN committee will help further the ACRIN scientific objectives by pursuing cutting-edge imaging research. The Experimental Imaging Committee will work with the disease site committees to investigate developing modalities, new uses for established modalities, and new or untested equipment. "Studies

undertaken by the committee will likely be somewhat different from prior ACRIN studies," says David Mankoff, MD, chair of the committee. "The focus is going to be early studies of advanced cancer imaging approaches, and working out the 'kinks' of new image acquisition and analysis approaches in small pilot multicenter trials. We may also look at a more quantitative or detailed version of current procedures, such as 3-D spectroscopic imaging or dynamic FDG-PET."

"We hope many of the studies will be directed towards novel, individualized cancer treatment."

— David Mankoff, MD, PhD
Assistant Professor of Nuclear Medicine
University of Washington Medical Center

The committee, which is still in the formative stage, will be further discussed at the ACRIN Fall Meeting and developed as part of ACRIN's grant

renewal application. Committee members will have a broad range of expertise, from researchers specializing in cancer biology to experts in radiopharmaceuticals and other diagnostic imaging agents. Committee members will work closely with the ACRIN Outcomes Core Laboratory and the Biostatistics Center at Brown University. Mankoff says, "This is a brand-new start for me with ACRIN and cooperative trials. I'm looking forward to working with everyone."

The trials developed in the committee will have common patient entry criteria and standardized imaging procedures, and they will include 2-4 sites. "The pathway for taking some of these new imaging techniques through initial development and into multicenter clinical trials involves a long cycle of development," explains Mankoff. "This committee's job will be to facilitate and shorten the process. Studies will also match current trends in cancer treatment; we hope many of the studies will be directed towards novel, individualized cancer treatment."

ACRIN FUND FOR IMAGING INNOVATION

The ACRIN Fund for Imaging Innovation has a new advocate: Tony Covington, the new director of development and corporate relations for the American College of Radiology (ACR). Covington will serve as the point of contact for all donors and future donors of the Fund, keep members of the ACR up to date on the campaign, and raise additional funding for ACR and ACR Foundation projects.

He comes to the ACR with years of development experience at the American Heart Association in Tampa, Florida. He says, "I am excited to be a part of an organization that is dedicated both to making a difference with new technologies that save lives and

to helping advance the profession and practice of radiology."

On behalf of the ACR, Covington would like to thank all of the contributors who have helped ACRIN continue to have a direct impact on patient care by advancing clinical trials. He adds, "ACRIN is indeed poised to grow in a new direction, and you, our 'Friends of ACRIN,' have helped to pave the way. Although the campaign has reached its target goal, it is not too late to contribute. Remember, your dollars will make a tremendous impact on imaging research, and there is still much work to be done." Covington can be reached at the ACR office in Reston, Virginia at 703-476-1129, or by e-mail at tcovington@acr.org.



New ACR Director of Development and Corporate Relations Tony Covington.

D'AMATO AWARD OF EXCELLENCE

The ACRIN Research Associate Core Committee established the annual Jo-Ann D'Amato Award of Excellence to recognize a research associate whose dedicated involvement in furthering ACRIN's research and other community service programs exemplifies Jo-Ann's devotion to her work and community. The first award was presented at the ACRIN 2006 Fall Meeting.



Diane Evans, holding the award plaque that is displayed at ACRIN HQ.

Diane Evans, a study coordinator at St. Elizabeth Health Center's Department of Research, is the first recipient of the D'Amato Award of Excellence, presented at the ACRIN 2006 Fall Meeting. Diane's hard work and dedication to the field of clinical research, compassion for patients, and involvement in community service exemplify the values representative of the award.

2006 OUTSTANDING CONTRIBUTION AWARDS

The 2006 ACRIN Outstanding Contribution Awards were presented by ACRIN Network Chair Bruce Hillman, MD, at the Fall Meeting. The awards recognize the extraordinary work of site researchers, staff at ACRIN Headquarters, staff at the Biostatistics and Data Management Center, and ACRIN leaders.

Site Awards

Mary Pollock, RN is the principal RA for the National Lung Screening Trial (NLST) at Beth

Israel Medical Center in Boston. She has worked long hours and put forth great personal effort on behalf of both her co-workers and the trial's participants.

Elizabeth Mickels, CCRC works on multiple ACRIN trials at Scottsdale Medical Imaging, and she helped Scottsdale become the top accruer for ACRIN 6664. She took over this trial shortly before the site audit, and her dedication to quality produced excellent results.

Daniel Lehrer, MD is the site PI for the ACRIN 6666 trial at the CERIM breast imaging center in Buenos Aires. Despite a late start due to obstacles to establishing an ACRIN site outside the U.S., Dan's leadership resulted in CERIM's being the second largest accruer to this trial.

Lisa Hinshaw, study coordinator for NLST at Wake Forest, has helped her site accrue well and have one of the highest participant retention rates. To ensure timely follow up, she finds delinquent participants by writing letters to the Social Security Administration, the U.S. Postal Service, and local voter registration.

Pradeep Mutalik, MD, and Svetlana Vassilieva, MD, clinical research coordinators at Yale University, have helped their site perform well in ACRIN 6664 despite many obstacles. Thanks to their willingness to work long hours and visit potential subjects in their homes when necessary, this site became one of the highest accruers.

Shannon Williams, RN helped Ochsner continue its strong participation in NLST in the aftermath of Hurricane Katrina. Despite the migration of New Orleans residents caused by the storm, more than 450 of Ochsner's 500 accrued subjects remain in the trial.

ACRIN Headquarters and the Biostatistics and Data Management Center

Quentin McMullen, AB became administrative manager of the Biostatistics Center this year and has done a superb job in his new position. He has helped standardize operating procedures, improve the reliability and effectiveness of operations, and promote the development of informatics tools to enhance efficiency.

Brad Snyder, MS is singularly responsible for the analysis and reports for ACRIN 6651. His capacity for independent work and his effectiveness and productivity have been remarkable. In addition to the work in 6651, he has taken on major new responsibilities in NLST and other ACRIN studies.

Sharon Hartson provided extraordinary leadership in bringing to life the National Oncologic PET Registry. Her attention to detail has resulted in facility registrations and completed cases far exceeding expectations.

Maria Oh, BA has made critical regulatory contributions to both the National Oncologic PET Registry and the NLST. She provides excellent support for protocol development and advises protocol teams about regulatory issues for all ongoing ACRIN clinical trials.

Cynthia Olson, MBA, MHS has worked on ACRIN-PA, the initial foray into emerging technology trials employing Pennsylvania Tobacco Settlement Funds. Cynthia has been instrumental in coordinating study team activities for two trials and developing a subnetwork of ACRIN Pennsylvania sites.

ACRIN Leadership

Barry Siegel, MD, involved in ACRIN since its founding, has outdone himself this past year. The National Oncologic PET Registry has improved access to PET for cancer patients, won ACRIN recognition, and created a potential source of funding for ACRIN.

Donald Mitchell, MD, chair of ACRIN's GYN Committee, has been a force both in the completion of the work of the ACRIN 6651 trial team and in the implementation of ACRIN 6671. His efforts have strengthened the critical link between ACRIN and the Gynecology Oncology Group.

Denise Aberle, MD has been in the spotlight as the principal investigator of ACRIN's highest profile trial, the National Lung Screening Trial. Throughout the course of this large trial, her leadership has helped move forward NLST-associated projects.