

ACRIN NEWSLETTER

Advancing Clinical Care Through Imaging Research

American College of Radiology Imaging Network

Fall 2009



*Mitchell Schnall, MD, PhD,
ACRIN Network Chair*

From the Network Chair: ACRIN Looks to Expanded Research Agenda at 10-Year Anniversary

by Mitchell Schnall, MD, PhD

The 2009 Fall Meeting provides an opportunity to collectively take stock of the successes of our first 10 years of operation. It is also an exciting time to look forward and envision the potential accomplishments of the next 10 years especially given ACRIN's evolution into an expanded model of supporting the conduct of imaging clinical trials. This evolution should have significant impact on ACRIN's future scientific achievements.

Although a noticeable expansion involves trials examining the role of imaging in diseases other than cancer, ACRIN's NCI-funded oncology research has certainly benefitted from an expanded focus as well. In particular, there has been a shift from clinical validation of mature imaging technology (e.g. mammography) to researching emerging technology with more of a functional and molecular focus.

No comprehensive funding source currently exists to support the introduction and management of trials that examine how imaging technology can be used in the treatment of other diseases. Therefore, it has been necessary to pursue smaller grants from a variety of sources for these ACRIN initiatives. In the area of cardiovascular (CV) disease, for example, the ACRIN trial of CT coronary angiography (CTA) for evaluating patients presenting to the ER with chest pains is funded by grants from the state of Pennsylvania, the ACRIN Foundation, and the National Institute of Health (NIH). Additional funding applications have been submitted to support studies of the use of CTA in other populations at risk for CV disease and in the evaluation of technological factors that influence the outcome of CV treatments (e.g. patient dose).

The ACRIN Neurosciences Committee, headed by Greg Sorensen, MD (Head and Neck/Neuro Committee Chair), is in the early stages of reviewing the current science regarding the role of imaging in neurological diagnosis and treatment and prioritizing its research goals. Here, as with all ACRIN trial planning, the process begins with, and is grounded in, the science and expert opinions of the committee members.

ACRIN Projects, a title used to describe miscellaneous ACRIN research activities not connected with a disease site committee, have also expanded in number and in level of technological advancement. See the article in this issue about the exciting projects being facilitated through the newly designed ACRIN Imaging Core Laboratory.

The Pennsylvania Department of Health provides another source of financial support for both cancer and noncancer-related trials (referred to as the ACRIN PA Network) through the Master Settlement Agreement in 1998 with the tobacco companies. This has provided an opportunity for ACRIN scientific committees to collaborate in ACRIN-PA protocols. For example, a trial of breast tomosynthesis is being explored by the Breast Committee to carry out through the ACRIN PA network.

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ACRIN Trials Opening In 2009

Activated trials:

ACRIN 6682: Cervical Cancer: ⁶⁴Cu-ATSM PET/CT Assessment of Tumor Hypoxia

ACRIN 6684: Assessment of Tumor Hypoxia in Glioblastoma with PET and MRI

ACRIN 6687: ¹⁸F-Fluoride PET as a Biomarker for Prostate Cancer and Bone Metastases

ACRIN 6688: Phase II Study of FLT PET in Invasive Breast Cancer

ACRIN PA 4003 / ACRIN PA 4004: Evaluation of a Novel PET Radiopharmaceutical to Identify Patients with Alzheimer's Disease

ACRIN PA 4005: CT Coronary Angiogram vs Traditional Care for Low-Risk ED Patients with Potential Acute Coronary Syndromes

Also to open this year:

ACRIN 6681: Evaluating CTC Computer-Aided Detection Technology

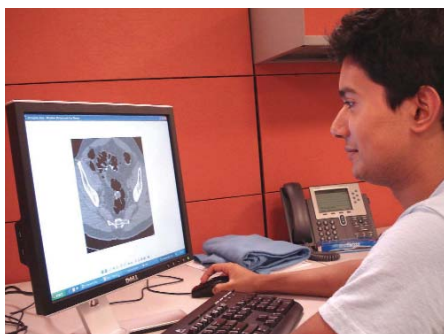
ACRIN 6685: FDG-PET/CT: Staging of Head and Neck Cancer and its Impact on N0 Neck Surgical Treatment

ACRIN 6686: Substudy of Advanced MRI Techniques Evaluating Newly Diagnosed Glioblastoma

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Interns Pursue Rigorous Research Projects

This summer ACRIN was fortunate to fund two Princeton Internships in Civic Service that allowed interns Shihab Ali and Chris Baldassano to complete projects that furthered ACRIN research endeavors. Ali and Baldassano describe their internships below. The internships are made available to ACRIN through Princeton University alumnus Bruce Hillman, MD.



Shihab Ali reviews one of the CTC test cases

CT Colonography Education: Developing Teaching and Test Sets

By Shihab Ali

During my 10-week ACRIN internship, I worked on the development of a CT colonography teaching and testing project with C. Daniel Johnson, MD of the Mayo Clinic in Scottsdale, Ariz. I was responsible for developing individualized CT colonography (CTC) instruction and evaluation materials. A sample of CTC cases from ACRIN 6664 that were representative of the full spectrum commonly encountered in clinical practice were to form the basis of two teaching and two test sets.

The ACRIN Data Management and Biostatistics Center generated a preliminary list of 135 cases using criteria we initially established to ensure representative variety. All identifying markers were removed from the collected cases using the Clinical Trial Processing (CTP) software, an endeavor in which Sereivutha Chao from the Imaging Core

Laboratory was invaluable. Next, lesion data (e.g. size, morphology, histology, colonic segment) were recorded from the various ACRIN 6664 protocol forms. Dr. Johnson and I then reviewed each of the positive cases, identifying the colonic lesions, recording additional data (e.g. slice numbers), capturing images of the lesions, and writing teaching points for the cases. The cases were carefully assigned to one of the four sets so that each set would demonstrate various important aspects of CTC and demand a variety of interpretation techniques from readers. Finally, accompanying workbooks were generated, each including an answer key with verified data for the lesions in each case, pictures of the lesions, and custom teaching points describing the important aspects of CTC interpretation demonstrated by each case.

These CTC Educational Teaching and Testing Sets will soon be made available for distribution. We hope they will provide radiologists with an easily accessible, comprehensive, and user-friendly resource for learning CTC and validating their skills.

Expanding Informatics Tools

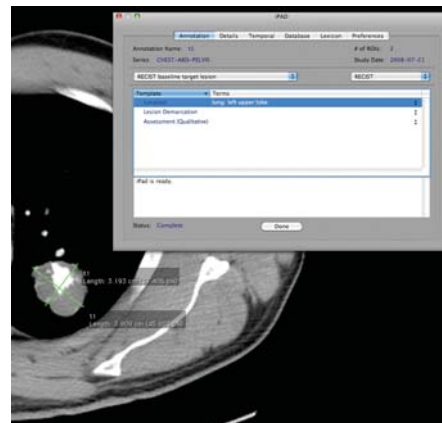
By Chris Baldassano

Following my graduation from Princeton University with a degree in Electrical Engineering, I completed an ACRIN summer internship. My project was directed by Biomedical Imaging Informatics Committee Chair, Daniel Rubin, MD, MS, and done in collaboration with biomedical informatics researchers at Stanford University, where I will be starting a PhD program in computer science this fall.

My work focused on extending iPad, an open-source plug-in for OsiriX (a free digital imaging and communications in medicine [DICOM] image processing application). iPad was originally developed to allow explicit, machine-read-

able text to be added to images, according to the Annotation Imaging Markup (AIM) standard developed by the Cancer Biomedical Informatics Grid (caBIG). Regions of interest (e.g. circles or lines) can be created, modified, or deleted directly using OsiriX's native tools, with the relevant measurements being automatically updated within the AIM annotation. This allows a user to access a single image for individual annotation or to simultaneously display all images for a specific annotation name.

One application for iPad involves the Response Evaluation Criteria in Solid Tumors (RECIST) evaluations, in which response is currently computed manually. iPad's electronic database is able to immediately capture lesion length information and automatically calculate and display the RECIST evaluation as a graph describing the patient's progress. This offers radiologists a tool for quickly overviewing a patient's history that facilitates storage, communication, and comparison among multiple readers.



AIM Annotation: iPad is shown in the OsiriX environment during the creation of a new annotation

Currently, most annotations are captured only as free text and are often not linked to the images they describe. Machine-readable annotations would

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Expanded Core Laboratory Services in Demand



Image review session in the new imaging core laboratory

The results of the 10-year evolution of the diagnostic imaging core laboratory supporting ACRIN research are immediately visible to anyone visiting the newly expanded facilities at the Philadelphia ACR office. To meet the need for integration of more technically sophisticated processes into research protocols, the core lab now includes multimonitor, ergonomically designed workstations with specialized image processing software capabilities; advanced acoustics, temperature control, and ambient lighting; independent reading rooms; and LCD wall monitor-equipped training rooms.

"The core laboratory has moved from providing imaging archival and transmission services for large clinical trials to performing advanced image data extraction and quantification functions," explains Mehdi Adineh, PhD, the core laboratory operations administrator. The updated facilities now support the functions of investigator, reader and staff training, standardizing new imaging and treatment planning techniques, and conducting quality assurance activities.

The months following the April 2009 grand opening have been an exciting time for the core laboratory, according to its assistant director, Anthony Levering. "It's been rewarding to be a part of integrating new and cutting-edge software into clinical studies," he

notes. Recent protocols making use of the lab's facilities include ACRIN 6668, which is examining whether the standard uptake value (SUV) measurement from FDG-PET imaging shortly after treatment is a useful predictor of long-term clinical outcome (survival) after definitive chemoradiotherapy for locally advanced non-small cell lung cancer. The core lab worked with University

of Pennsylvania medical staff to develop a software extension capable of automatically identifying the hottest pixel, indicating the peak SUV. The lab has hosted a nuclear medicine physician on a continuing basis for this protocol, for which the reader study has been completed and the wrap-up phase is currently underway.

A 3-day blinded reader study was recently conducted by radiologists in conjunction with ACRIN 6673 to estimate the proportion of participants undergoing radiofrequency ablation whose livers have no identifiable tumor by CT scan at 18 months. The core lab was instrumental in facilitating the necessary tumor analysis with measurements.



Clockwise from top: ACRIN investigators Terry Wong, MD, PhD, Barry Siegel, MD, and Mark Rosen, MD, PhD test drive some recently acquired software in the core lab

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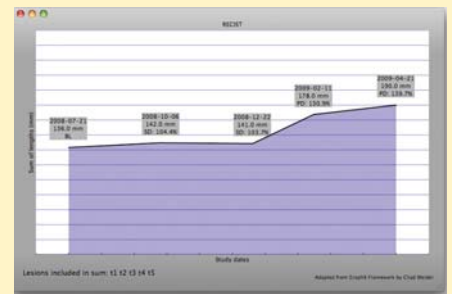
(Network Chair... continued from page 1)

How does this expansion affect ACRIN's mission, if at all? Ultimately, the fundamental mission of ACRIN to conduct rigorous clinical trials of diagnostic imaging and image-guided therapeutic technologies remains the same. The research activities initially directed to cancer are now simply being extended to other diseases as well.

Given this expansion, ACRIN's corollary aims of serving the larger clinical imaging community become even more salient. These include setting the standard for good clinical research for other collaborative groups and developing a pathway for the testing of clinical imaging technology.

(Interns... continued from page 2)

allow for the creation of searchable imaging databases and open the door to the application of new artificial intelligence and machine learning algorithms.



RECIST: When a RECIST analysis is performed, the patient's progress is graphed and the study dates are labeled according to the RECIST criteria (BL = "Baseline", SD = "Stable Disease", PD = "Progressive Disease"). RECIST = Response Evaluation Criteria in Solid Tumors

Various individuals at ACRIN were asked to share their personal thoughts and experiences during their respected tenure with the organization. Each one of their responses provides a unique and valuable perspective about the progress and accomplishments that ACRIN has made over the past 10 years.

“It has been inspiring to lead a research project that has required so many people to pull together over the past 8 years to accomplish an enormous task. The National Lung Screening Trial will conclude data collection this year and move into the phase of analyzing this rich data source.”

— **Denise R. Aberle, MD**
ACRIN Deputy Co-Chair

“I have been particularly impressed by the growth and development of the ACRIN headquarters staff and am proud to work alongside them and witness their incredible dedication and loyalty to ACRIN on a daily basis. ACRIN has also afforded me the opportunity to work closely with inspirational scientific leaders who have created an environment which is intellectually challenging, consistently supportive, and truly collaborative. My time at ACRIN has been a professional highlight in my career and I look forward to the continued success of the organization.”

— **Charles Apgar, MBA**
Senior Director,
ACRIN Administration

“Although many organizations now have advocate members, ACRIN actually incorporates their suggestions and recommendations on a routine basis. ACRIN is a leader in the field of providing patient-centered clinical trials!”

— **Peggy Devine, CLS**
Deputy Chair,
ACRIN Patient Advocate Committee

“As a co-founder of ACRIN, I am naturally proud that we have built an internationally known network conducting definitive studies of cancer imaging and serving as a paradigm for the clinical evaluation of imaging in general. When a group of imaging researchers at an overseas meeting asked me for advice on how to develop a similar network in their country, I responded with all the usual description of science and organization. I also added that none of this can be done without the gusto and dedication of the colleagues we have had in ACRIN's core organization and at our participating sites over the years. With such fine colleagues, I look forward to ACRIN's next decade.”

— **Constantine Gatsonis, PhD**
Director, ACRIN
Biostatistics Center

“One of ACRIN's original mandates was to be nimble, a term that in retrospect has meant not only that we were to develop trials rapidly, but also that our portfolio would include amazingly diverse studies. At times I found the diversity, which meant that few components of one study could be recycled in the next, overwhelming; now I believe it gave us creative energy.”

— **Lucy Hanna, MS MAT**
Biostatistician

“In my 10 years at ACRIN, I have experienced such growth and am grateful for such an opportunity to be involved in cancer imaging research. One of my most memorable moments is completing the ACRIN 6664 National CT Colonography Trial. It was a wonderful experience and opportunity to be part of the protocol team with Dr. Johnson.”

— **Donna Hartfeil, RN, BSN**
Senior Project Manager

“In the beginning, we were just a handful of highly motivated people striving to create a successful imaging group, but now, 10 years later, after our numbers have swelled and we have solidly established ourselves as the imaging cooperative group, it is exhilarating to note that that same dedication, that same motivation, that same belief in the importance of our work drives everyone in ACRIN to maintain our high standards, to strive to make ACRIN the best it can be, and to do our part to fight cancer every day.”

— **Ben Herman, SM**
Biostatistician

“Being the founding chair and playing an important role in developing ACRIN was the most exciting professional activity of my life. There are so many things that occurred, sometimes seemingly serendipitously, during my nine year tenure that were critical in those fragile early years. One thing that stands out was about 4-5 years into getting going. We were starting to see some positive trial results, but money was very tight and it appeared we were going to have to back off developing new trials. Dan Sullivan and I reserved an hour to present ACRIN's case directly to then NCI Director Andy von Eschenbach. At the end, he asked me what I felt we needed. I said another \$2 million a year. He said "yes," and Barbara Galen made sure it was added to our base so that we would see it annually into the future. At the time, it made all the difference between regressing and continuing to move forward.”

— **Dr. Bruce J. Hillman, MD**
Chair, Industry Relations Committee

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“It’s been rewarding being part of the team that has supported research that has changed the practice of imaging and an extraordinary career opportunity to work with the best and the brightest in the field. Over the past ten years, we’ve evolved from a one-room reading area with two workstations to a large, multi-function environment that allows for training, education, image quality control and case review with 24 workstations and sophisticated software. I look forward to the next ten years being equally exciting.”

— **Anthony Levering, RT (R)
(CT) (MR), CIIP
Assistant Director,
Diagnostic Imaging**

“During the past 8 years, a tremendous amount of infrastructure has been developed to carry out the National Lung Screening Trial (NLST). Along the way, we’ve learned so much about participant recruitment and retention strategies, medical abstraction and endpoint verification processes, bio-repository practices and equipment quality control. It has been exciting to be part of this work and to realize these major NLST milestones have far ranging implications for future ACRIN research.”

— **Irene Mahon, RN, MPH
NLST Project Manager**

“One of my most memorable moments is of my first ACRIN meetings. As a new biostatistician, I was eager to learn about the workings of ACRIN out in the field. In one of the RA sessions, I introduced myself and asked if any of the RAs would be willing to talk with me about their day-to-day ACRIN work and processes. I was overwhelmed by the response I received. So many committed individuals happy to educate me about their work on ACRIN. And throughout my years at ACRIN, I have been repeatedly inspired by the dedication of so many members of the ACRIN community.”

— **Quentin McMullen, AB
ACRIN Biostatistics Center
Administrative Manager**

“Working on the original grant submission and now looking back 10 years, it is amazing how far ACRIN has come, thanks to the efforts of some very dedicated and special colleagues. I’m grateful for the opportunity to continue to be involved!”

— **Cynthia B. Olson, MBA, MHS
Project Manager**

“It was really gratifying seeing the ACRIN team pull together in preparation for the grant renewal. The superb score that we received on our application demonstrates that our network of investigators and ACRIN staff are committed to producing scientific results that will have a significant impact on patient care.”

— **Mitchell Schnall, MD, PhD
ACRIN Network Chair**

“A number of years ago, I realized that the use of PET in oncology could not really enter the mainstream unless it was validated and then incorporated into multicenter clinical trials. Over the past decade, I have been privileged to work with many colleagues at ACRIN to help achieve this goal. Especially gratifying to me personally was the critical role that ACRIN staff and infrastructure have played in the success of the National Oncologic PET Registry—a project that has had tremendous impact on access of Medicare beneficiaries to PET and PET/CT.”

— **Barry A. Siegel, MD
ACRIN Deputy Co-chair**

“It’s been gratifying to be a part of ACRIN for the last 10 years especially working with the RA committee in building a strong community of support for ACRIN RAs and seeing how that support has contributed to ACRIN’s success.”

— **Wendy Smith, RT
ACRIN Research Associate**

More ACRIN History

The history of ACRIN’s development and a timeline of major milestones achieved during the past 10 years are available on the ACRIN Web site at:

www.acrin.org/ACRIN_History.aspx

ACRIN at Ten Years

Clinical trials activated:

31 trials

Images stored in the image archive:

20 terabytes

Primary aim papers published:

9 papers

Reader studies conducted:

15 studies

Requests for ACRIN images and data fulfilled:

12 requests

Trial participants accrued:

76,672 participants

Facilities participating in the National Oncologic PET Registry (NOPR):

1,898 facilities

Scans reimbursed through NOPR:

126,039 scans

NOPR results publications:

6 publications

(Expanded Core Lab... continued from page 5)



Imaging Analyst Jim Gimpel, RT(R)(MR), on the right, demonstrates new MRI techniques to a guest attending the core laboratory open house held on June 8. (Photo courtesy of Wendell Christie.)

Radiologists in the collaborative SWOG 0518/ACRIN 6680 trial are making use of the core lab to obtain RECIST measurements of one or more carcinoid tumors in a patient over various time points to determine response, stability, or progression following treatment. This

protocol is designed to assess and compare the prognostic and predictive value of the combination of In-111 pentetreotide somatostatin-receptor scintigraphy (SRS) and CT vs. CT.

ACRIN 6677 is designed to assess the potential role of perfusion MRI and MR spectroscopy imag-

ing as an early indicator of treatment response and as a prognostic indicator based on images over time during treatment with bevacizumab for glioblastoma brain tumors. The core lab's specialized imaging software has facilitated volumetric measurements for this study

that are based on segmenting the tumor according to pixel intensity.

The core lab is also supporting the early phases of an image collection and quality control project (ACRIN 6686/RTOG 0825) designed to collect images from MRI examinations and CT scans. A reader study has just been completed for ACRIN 6666 in which the core lab assisted in a qualitative review of ultrasound, mammography, and MRI in the screening of women at high risk for breast cancer.

Future initiatives for the core lab include providing the software infrastructure to host internal applications on a central server and to allow for remote Web-based viewing of images, developing closer relationships with image equipment suppliers, and the increased use of radiology reading rooms.



Left to right: Walter Curran, Jr., MD; Harvey Neiman, MD; Steven King, MS, FACHE; Sen. Robert P. Casey, Jr.; and Mitchell Schnall, MD, PhD during a walkthrough of the Imaging Core Laboratory

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