

ACRIN NEWSLETTER

Advancing Clinical Care Through Imaging Research

March 2011

From the Network Chair NCI Cooperative Group Program Restructuring



Mitchell Schnall, MD, PhD, ACRIN Network Chair

In the last issue, ACRIN network chair Mitchell Schnall, MD, PhD shared his perspective on the Institute of Medicine (IOM) report that offered broad recommendations for reinvigorating the National Cancer Institute (NCI) Cooperative Group Program and improving the clinical trials system. Here, he weighs in on the November 2010 NCI announcement of specific approaches to implement these recommendations.

The release by NCI of “Transforming the NCI’s Clinical Trial System” signals comprehensive changes are ahead for the Cooperative Group Program. Meetings with NCI staff

and other Cooperative Group members have clarified two major aspects of the proposed plans: (1) NCI envisions the resulting new structure to look more like a network of closely interacting research organizations rather than separate institutional groups competing with each other, and (2) collaboration and coordination among the members of this network will be critical to its success. NCI seeks, through a consolidated network, to leverage the unique strengths of each existing group, and facilitate the consolidation by issuing funding opportunity announcements (FOAs) for the various components of the restructured network. The most competitive applications will come from scientifically diverse and multimodality groups conducting a wide range of trials. ACRIN, and other smaller organizations with more focused agendas, will need to pursue strategies for collaborating with other groups in the process of competing to be a part of one of the four Cooperative Groups designed to be the end result of the consolidation.

ACRIN leadership is involved in ongoing talks with several groups and exploring options for forming a group with the potential to submit a strong FOA application. A key discussion point has focused on whether the new network should include an imaging core to support the activities of quality assurance, site qualification, and relevance of certain imaging procedures. Although ACRIN believes such a core is necessary to ensure that the quality of imaging done across the network is sufficiently high, opportunities are not provided within the FOA process for any existing Cooperative Group to define its role within the restructured network.

Major considerations for ACRIN in these collaborative discussions address what is best for the science we’re engaged in and for keeping our infrastructure intact. Thus, our focus is on helping to ensure that the imaging science we feel so passionate about is well reflected in the reorganized network and that the infrastructure we built with our own sweat will play a similar ongoing role.

“Major considerations for ACRIN in these collaborative discussions address what is best for the science we’re engaged in and for keeping our infrastructure intact.”

- Mitchell Schnall, MD, PhD
ACRIN Network Chair

(continued on page 3)

NCI-Proposed Time Line for Cooperative Group Restructuring

Below is the time line proposed by the NCI for the cooperative group program restructuring. The target dates below highlight key points in the restructuring process, including the development of a new Funding Opportunity Announcement (FOA), the application submission and review process, and receipt of NCI funding awards.

December 2010 – July 2011:

Gather input from stakeholders for the new FOA

August 2011 – March 2012:

FOA development within NCI

March 2012 – July 2012:

NIH review processes

July 2012:

FOA published

November 2012:

Receipt of competing applications

February 2013 - May 2013:

Review of competing applications

After October 2013:

Rollout of awards for FY 2014

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IMAGING NETWORK

Perspectives of Constantine Gatsonis, PhD

Overview

Comparative effectiveness research (CER) has been a major focus of recent national policy initiatives. As defined by the US Department of Health and Human Services, CER aims to improve health outcomes by developing and disseminating evidence-based information to patients, clinicians, and other decision makers about which interventions are most effective for which patients under specific circumstances. The Patient Protection and Affordable Care Act of 2009 mandated the establishment of the Patient-Centered Outcomes Research Institute (PCORI) to set priorities and conduct or support CER. In support of these efforts, the American Recovery and Reinvestment Act (ARRA) of 2009 provided \$1.1 billion in CER funding across three federal health agencies: National Institute of Health (NIH), Health and Human Services (HHS), and Agency for Healthcare Research and Quality (AHRQ).

“The concept of CER has been with us for awhile,” states Constantine Gatsonis, PhD, Director of the Center for Statistical Sciences at Brown University and ACRIN Group Statistician. According to Gatsonis, “CER, as applied to diagnostic imaging, refers to research that evaluates and compares how diagnostic tests affect patient outcome, such as mortality, morbidity, cost, and quality of life.” The current CER policy focus emphasizes assessment of comprehensive health-related outcomes for diverse patient populations and subgroups, the use of a variety of data sources and methods to assess effectiveness, and active dissemination of the results.

Priorities and Challenges for Imaging

“The goal of CER is to assess how diagnostic procedures work in real-world settings and to

provide information to help individuals decide whether to undergo a procedure, to help physicians make clinical decisions, and to help payers decide whether to cover a procedure,” remarks Gatsonis. “That’s a tall order;” he continues, “considering how broad the mandate is and how rapidly new imaging technologies disseminate and become usual care.” Many ACRIN trials, for example, the Digital Mammographic Imaging Screening Trial (DMIST) and the National CT Colonography Trial, have been designed primarily to evaluate the accuracy of an imaging test, rather than the ultimate effects on patients. These studies have included data collection of some outcomes, such as patient experience with the procedure, quality of life, and cost. These data, together with the estimates of test accuracy were used to develop models for projecting the impact of tests and assessing cost effectiveness. However, with the exception of the National Lung Screening Trial (a randomized study), they have not assessed directly the impact of screening on mortality or morbidity.

“The change for ACRIN is to assess how something works in a real-world setting.”

-Constantine Gatsonis, PhD
ACRIN Group Statistician

Imaging CER presents a variety of challenges. Fundamentally, testing is situated further from patient outcomes than therapy. Without a randomized study, it is difficult to link a test with patient outcome, because of the intervening therapy decisions and interventions. And, in order to study the impact of tests on outcomes using available databases, the investigators need to assess health outcomes occurring years or decades after the initial imaging studies. As Gatsonis summarizes, “once image data are sent to a clini-

cian, radiology professionals have no control over whether that information is used or not used, how it is used, and whether it produces a desired outcome in a specific patient.”

In spring 2009, Gatsonis served on an Institute of Medicine CER committee charged with identifying 100 national CER priorities (IOM Report). Resulting imaging-related priorities included comparisons of breast cancer screening modalities in community practice for high-risk women; traditional risk stratification vs. noninvasive imaging for coronary artery disease; and imaging technologies in diagnosing, staging, and monitoring patients with cancer. Gatsonis led the organizing of the workshop “CER for Diagnostic Imaging” last year cosponsored by the Radiological Society of North America (RSNA) and the National Institute of Biomedical Imaging and Bioengineering (NIBIB); a white paper detailing the results of the workshop is expected.

Advancing diagnostic imaging technology in the absence of effective treatment modalities for specific cancers is an additional dilemma that must be addressed. According to Gatsonis, “showing the impact of a test to diagnose a condition is not easy if available therapy doesn’t help the patient.” However, imaging may well be ahead of therapy in identifying disease, for example as it happens in the case of DCIS.

Future ACRIN CER Initiatives

Given that CER has become a national health care priority, ACRIN is developing its research portfolio in this area. Articles in future issues of the *ACRIN Newsletter* will explore such protocols in more detail. An example is the recently activated RESCUE trial (see sidebar), which directly addresses one of the imaging research priorities highlighted in the IOM Report.

ACRIN 4701: RESCUE (Randomized Evaluation of Patients with Stable Angina Comparing Utilization of Noninvasive Examinations)

- Conducted through the ACRIN Cardiovascular Committee and funded by the Agency for Healthcare Quality and Research
- Multicenter clinical trial to evaluate how two diagnostic imaging procedures affect outcomes in patients with stable angina who are at moderate risk of coronary artery disease (CAD):
- Single photon emission computed tomography-myocardial perfusion imaging (SPECT-MPI) and Cardiac computed tomography angiography (CCTA)
- A total of 4300 study participants to be enrolled at up to 80 institutions internationally

For more information visit www.acrin.org/RESCUE_protocol.aspx or contact project manager Cynthia Olson (215-574-3234; colson@acr.org).

New Working Group Addresses Benefits and Risks of Radiation Safety in ACRIN Clinical Trials

ACRIN has established a Radiation Safety Working Group whose goal is to provide information and resources about radiation exposure specific to ACRIN clinical trials.

Developed as an initiative of the ACRIN Patient Advocacy Committee, the working group comprises patient advocates, radiologists, medical physicists, research associates, and representatives from the ACRIN imaging core laboratory.

The first project completed by the working group was the creation of an ACRIN Web page which includes and will be updated with resources and tools for patients, physicians, and other individuals who are interested in learning more about radiation exposure in ACRIN clinical trials. “The Web page goes a long way to provide information on radiation and radiation protection to many individuals, including patients,” says group member and radiologist Donald Frush, MD (Duke University). “It also represents the profession's efforts in improving accountability and advocacy when medical imaging with ionizing radiation is involved in patient care, including scientific investigations.” Resources on the new Web page include general information about radiation safety. Cancer-specific resources will be posted as identified and approved by the committee. In addition to exploring the patient resources provided on the Web page, patients are invited also

to navigate the resources developed for physicians to learn more technical information. For example, a featured resource includes a link to Duke University's Radiation Safety Web site, where patients and physicians can conceptualize how radiation exposure compares to things they encounter in everyday life, such as natural background radiation exposure and travel by air. Radiologist Robert Reiman, MSPH, MD (Duke University) from the working group adds: “At Duke, we have developed a Web site designed to help clinical investigators write ‘radiation risks’ paragraphs for many radiological exams for inclusion in their informed consent forms. I am pleased that ACRIN has featured our site, which is available to all interested researchers.” Consent language included on Duke's University's Radiation Safety Web site is appropriate for inclusion in future ACRIN consent materials, and permission to use Duke's consent language has been reviewed and approved by ACRIN legal counsel.

Materials on the Web page are organized by the following categories:

- Resources for patients and the general public
- Resources for physicians, technologists, and research associates
- Radiation safety publications
- Radiation safety in the news

Members of the working group will vet new materials identified before they are posted for their appropriateness to post to the Web page. Just recently, a link to an episode of the Dr. Oz Show was added to the Web page, which features ACRIN investigator and Radiological Society of North America (RSNA) Public Information Committee Chair Mary Mahoney, MD (Univ. of Cincinnati) as a guest panelist to discuss the benefits and risks of radiation exposure. During her appearance, Dr. Mahoney addressed the benefits and risks of medical imaging exams.

We invite readers to view the newly created page at: www.acrin.org/AboutRadiationBenefitsandRisks.aspx.

“ I am extremely impressed with the efficient approach that the group has taken toward its mission of providing patients and the public with thorough and balanced information about the benefits and risks of radiation.”

- Ann Kolker, Liaison
Gynecologic Committee
ACRIN Patient Advocacy Committee

Network Chair...(continued from page 1)

Support for a prominent ACRIN role in the oncology research network has been forthcoming from imaging organizations, including the Academy of Radiology Research, and ACRIN has actively engaged that community in the advocacy process.

Maximizing the opportunities for dialogue in the near term is integral to shaping ACRIN's network integration: a workshop sponsored by the American Society of Clinical Oncology and the IOM will bring stakeholders together to promote a collaborative approach for instituting change; NCI has established an open process for ongoing discussions with Cooperative Group leadership; the Group chairs continue to meet; and the Group statisticians also are convening their own discussion meetings. Finally, the ACRIN leadership retreat held earlier this month provided significant guidance in shaping a strategy for going forward.

Viewing the proposed changes from a “glass half-full” perspective, we recognize the opportunity afforded us to better integrate our efforts in a broader clinical context so that we have stronger studies and our studies have better appeal to broader clinical practitioners. We need to reach out to work with others, not in an effort to preserve ACRIN as an independent, semiautonomous functioning organization, but to figure out how to make what we do better.

Introducing Sanford Jeames A Voice for Abdominal Cancer Patients and Underserved Populations



Sanford Jeames, DHA, ACRIN Abdominal Advocate

Sanford gained a significant understanding about treatment of various abdominal cancers while serving in the United States Army as a surgical technician. During his clinical experience in the army, Sanford developed a desire to learn more about cancer, which led him to seek advocate opportunities that combined his clinical and educational experience. One of his earlier advocate activities was serving as an ambassador with the American Cancer Society (ACS) where he participated in lobbying activities in Washington, D.C.; Montgomery, AL; and New Orleans, LA.

Much of Sanford's experience with abdominal cancer is directly related to his role as caregiver to his parents, who were both diagnosed with colon cancer—his mother when he was five years old, and his father in 1994. His father passed away in 2010 from complications associated with the disease. "My parents' diagnosis and struggle with the disease increased my interest in cancer prevention, screening, treatment, and survivorship. This experience, combined with my work in the health care setting, provided me with the motivation to try and help families and patients affected by the disease."

Concurrent with his membership on the ACRIN Patient Advocacy Committee, Sanford also maintains a number of other advocacy roles, including serving as: a cancer support group facilitator for US TOO International Prostate Cancer Support Groups and the ACS's Man to Man Prostate Cancer Support group in Springfield, MA; a member of the Society of Urological Surgical Associates; and a patient advocate with the National Cancer Institute Sub-Committee for review of cooperative group cancer protocols; and advocate review trainer for the Lance Armstrong Foundation.

Sanford's unique perspective on abdominal cancer outreach and education will be valuable during the development of ACRIN abdominal trials. "My priority as a patient advocate is to voice the concerns of cancer patients, especially for minorities and underserved populations who are affected by cancer. I also am interested in expanding the role of community-based participatory research in the national atmosphere of cancer research. It is imperative that national and international cooperative groups design clinical trials that address the widening disparities of the incidences of cancer within the population."

In April 2010, the ACRIN Patient Advocacy Committee welcomed Sanford Jeames, DHA, as the new abdominal patient advocate. Sanford, who is currently a senior program manager at the University of Massachusetts Donahue Institute, has been a patient advocate since 1998, when he served as the patient education coordinator and clinic coordinator at the University of Alabama, Birmingham (UAB) (Prostate Clinic). His advocacy role at UAB primarily focused on patient outreach and education where he met with new patients and conducted follow-up interviews.

Sanford gained a significant understanding about treatment of various abdominal cancers while serving in the United States Army as a surgical technician.

“ My priority as a patient advocate is to voice the concerns of cancer patients, especially for minorities and underserved populations who are affected by cancer.”

- Sanford Jeames, DHA, Liaison
Abdominal Committee
ACRIN Patient Advocacy Committee

ACRIN Protocols Seeking Site Participation

Abdominal

6690: Comparison of Multiphase Contrast-Enhanced CT and MRI for Diagnosis of HCC and Liver Transplant Allocation

Breast

6688: Phase II Study of FLT in Invasive Breast Cancer

Cardiovascular

4701: Randomized Evaluation of Patients with Stable Angina Comparing Utilization of Noninvasive Examinations (RESCUE)

Gynecologic

6671: Cervical and Endometrial Cancers: Staging with PET/CT

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

Head / Neck / Neuro

6685: FDG-PET/CT Staging of Head and Neck Cancer and its Impact on the NO Neck

6686: Newly Diagnosed Glioblastoma: Tumor Assessment with Advanced MRI (A substudy of RTOG 0825)

6689: Newly Diagnosed Glioblastoma: Tumor Assessment with FLT PET and DCE MRI and MRS (A substudy of RTOG 0837)

Thoracic

6678: Non-small Cell Lung Cancer: FDG-PET/CT as a Predictive Marker of Tumor Response and Patient Outcome

For contact information and for more information on ACRIN trials, visit the ACRIN Protocol Summary Table at: www.acrin.org/CurrentProtocols.aspx.

Centers for Quantitative Imaging Excellence Update

Phase 2 of the National Cancer Institute's Centers for Quantitative Imaging Excellence (CQIE) program is now underway. The program, which is currently open only to the 59 NCI-designated cancer centers, began in August 2010. The purpose of the CQIE program is to qualify sites to participate in upcoming NCI-sponsored clinical trials that include a quantitative imaging component and is specifically aimed at body volumetric CT, brain volumetric MRI, body and brain DCE-MRI, and body and brain PET (or PET/CT).

Since the start of the CQIE program, 11 sites have been fully qualified and an additional 10 are currently in the process of meeting their final requirements for CQIE-qualification. With the launch of phase 2 of the CQIE program, the remaining cancer centers are now able begin the site qualification process.

"As with any new project, we experienced a few challenges early in the process. The ACRIN CQIE team has since gained significant experience regarding how best to assist the NCI-designated cancer centers to meet the site qualification requirements. Helping sites gain new imaging and research expertise that will be critical for successfully carrying out cutting-edge imaging clinical trials has been very gratifying," says the CQIE program manager Deborah Harbison. For more information, visit www.acrin.org/NCI-CQIE.aspx.

ACRIN Publications Update

NLST Presentation at RSNA 2010

The initial results of the National Lung Screening Trial (NLST [ACRIN 6654]) were presented during a special program session at the 2010 Radiological Society of North America annual meeting. The NLST initial results show that screening with low dose CT significantly reduces lung cancer death in people at high risk. Twenty percent fewer lung cancer deaths were seen among those screened with CT than with chest X-ray. Trial principal investigators, Denise Aberle, MD, and Christine Berg, MD, led members of the NLST research team during the panel discussion. The panel included Constantine Gatsonis, PhD; David Gierada, MD; and Fred Larke, MS, DABR.

"Everyone who participated in this trial has played an important role in providing hard evidence of a mortality benefit from CT screening for lung cancer as well as a road map for public policy development in the future"

**- Denise R. Aberle, MD
NLST-ACRIN National Principal Investigator
NLST Co-principal Investigator at UCLA**

"The National Lung Screening Trial: Overview and Study Design," by the NLST research team, was published in *Radiology* on November 2, 2010. The NLST primary aim paper is expected to be submitted for publication the first half of 2011.

ACRIN PA 4001 Publishes Primary Aim Manuscript

"Knee Articular Cartilage Damage in Osteoarthritis: Analysis of MR Image Biomarker Reproducibility in ACRIN PA 4001 Multicenter Trial," by the ACRIN PA 4001 research team, was published January 6 in *Radiology*. ACRIN PA trials are a network of Pennsylvania-based sites conducting research funded by the Pennsylvania Department of Health's Commonwealth Universal Research Enhancement (CURE) Program with funds from the Tobacco Settlement Act. This is the first ACRIN PA trial to publish primary aim results.

New Scientific Meetings Resource for ACRIN Investigators

A new Web page that lists the dates and locations of major scientific meetings and corresponding ACRIN publications-related deadlines was added to the ACRIN Web site. The Web page will serve to prompt ACRIN researchers to keep in mind deadlines for submission of abstracts and posters throughout the year.

NOPR Expands Coverage for F-18 Sodium Fluoride PET Scans

On February 7, 2011, the Centers for Medicare & Medicaid Services began reimbursing sites participating in the National Oncologic PET Registry for F-18 Sodium Fluoride- (NaF) PET scans. Physicians treating Medicare patients with known or suspected cancer metastatic to bone will be able to much more widely order PET scans using the radiotracer F-18 NaF to help formulate treatment plans.

The primary objective of the expanded NOPR is to assess the effect of NaF-PET on how physicians manage the care of their Medicare patients. "We've seen how the NOPR's contributions have been able to directly affect change in health care," says Joy Brown, NOPR project manager. All PET facilities currently participating in the NOPR are eligible to participate in the expanded program and new facilities are encouraged to join.

For more information, including a listing of NOPR results publications, visit the NOPR Web site at www.cancerPETregistry.org.

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