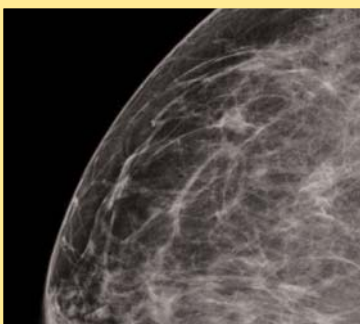
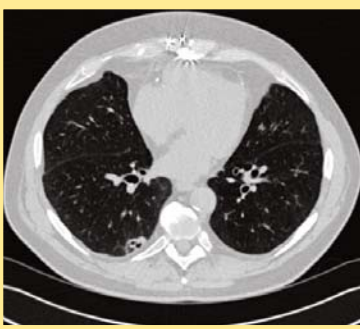




# ACRIN at RSNA: Presentations and Clinical Trials Update



**2010 Radiological Society of North America  
Annual Meeting**

**McCormick Place - Chicago, IL  
November 28 - December 3**

**ACRIN<sup>®</sup>**  
AMERICAN COLLEGE OF  
**RADIOLOGY**  
IMAGING NETWORK

# Table of Contents

<b>ACRIN PRESENTATIONS SCHEDULE</b>	<b>2</b>
<b>SPECIAL ACRIN ACTIVITIES</b>	<b>3</b>
<b>ABSTRACT PRESENTATIONS</b>	<b>4</b>
<b>SCIENTIFIC OBJECTIVES AND LEADERSHIP</b>	<b>9</b>
<b>ACRIN PARTICIPATION</b>	<b>11</b>
<b>TRIALS SEEKING SITE PARTICIPATION</b>	<b>12</b>
<b>SPONSORS AND CONTRIBUTORS</b>	<b>16</b>



# ACRIN Presentations Schedule

*Sunday, November 28*

**11:45 am, Room N228**

**Title:** Increased Progression with T2-based Imaging during Anti-VEGF Therapy in Glioblastoma: ACRIN 6677 / RTOG 0625

**Authors:** Sorensen G; Zhang Z; Boxerman J; Safriel Y; Gimpel J; Snyder B; Girardi V; Larvie M; Gilbert M.

[Page 4](#)

*Monday, November 29*

**3:30 pm, Room S403B**

**Title:** Effective Dose Assessment for Participants in the National Lung Screening Trial Receiving Posterior-Anterior (PA) Chest X-ray Examinations

**Authors:** Kruger R; Judy P; Flynn M; Cagnon C; Seibert A.

[Page 5](#)

**4:30 pm, Room S406B**

**Title:** The National Lung Screening Trial Initial Results Presentation

**Presenters:** The NLST Research Team

[Page 3](#)

*Tuesday, November 30*

**3:00 pm, Room E450A**

**Title:** Multiple Bilateral Similar Masses on Ultrasound: Results of ACRIN 6666

**Authors:** Berg W; Zhang Z; Yeh M; Mendelson E.

[Page 6](#)

*Friday, December 3*

**10:30 am, Room E450B**

**Title:** Annual Screening Strategies in BRCA1 Gene Mutation Carriers: A Comparative Effectiveness Analysis

**Authors:** Lowry K; Lee J; Kong C; McMahon P; Gilmore M; Pisano E; Gatsonis C; Ryan P; Ozanne E; Gazelle G.

[Page 7](#)

**10:40 am, Room E450B**

**Title:** Multiple Bilateral Similar Findings on Mammography: Results of ACRIN 6666

**Authors:** Berg W; Zhang Z; Adams A; Mendelson E.

[Page 8](#)

*Sunday, November 28 – Friday, December 3*

**Lakeside Learning Center, Hall E**

**Title:** The Quantitative Imaging Reading Room: Open-Source Tools to Analyze, Report, and Communicate Radiology Results in the Quantitative Imaging Era (exhibit # LL-QRR3022)

**Project Demonstration Lead:** Rubin, D.

[Page 3](#)

# Special ACRIN Activities

## Initial Results of the National Lung Screening Trial

**Monday, September 29**

**4:30-6:00 pm, Room S406B**

1. Trial Design and Initial Results  
Presenter: Denise Aberle, MD  
*NLST ACRIN National Principal Investigator, UCLA*
2. Imaging Technique and X-ray Dose Considerations  
Presenter: Frederick Larke, MS, DABR  
*NLST LSS Physicist, University of Colorado*
3. False Positive Rate and the Evaluation of a Positive Scan  
Presenter: David Gierada, MD  
*NLST LSS Site Radiologist, Washington University*
4. Future Analyses  
Presenter: Constantine Gatsonis, PhD  
*Director, ACRIN Biostatistics and Data Management Center, Brown University*
5. Question and Answer Session  
Moderators: Christine Berg, MD  
*NLST LSS Project Officer, National Cancer Institute*  
Denise Aberle, MD  
*NLST ACRIN National Principal Investigator, UCLA*

For more information about the NLST study results, visit [www.acrin.org](http://www.acrin.org). For more information about the NLST design and methods, visit <http://radiology.rsna.org/cgi/content/abstract/radiol.10091808> to access the recently published paper "The National Lung Screening Trial: Overview and Study Design."

## The Quantitative Imaging Reading Room

**Exhibit title:** Open-Source Tools to Analyze, Report, and Communicate Radiology Results in the Quantitative Imaging Era (exhibit # LL-QRR3022)

**Lakeside Learning Center, Hall E**

**Sunday, November 28 – Friday, December 3**

**Exhibit hours:** Sun. 8:00 am - 6:00 pm; Mon. - Thurs. 7:00 am - 10:00 pm; Fri. 7:00 am - 12:45 pm

The Quantitative Imaging Reading Room will showcase products that integrate quantitative analysis of images into the imaging workflow. Attendees will be able to learn about these applications (products) through hands-on exhibits featuring informational posters, computer-based demonstrations and Meet-the-Experts presentations scheduled throughout the week.

Daniel Rubin, MD, MS (Stanford University), chair of the ACRIN Biomedical Imaging Informatics Committee, leads the development of iPAD (image Physician Annotation Device). iPAD is an open-source tool that serves as a bridge linking the semantic content of a radiologic image with the image itself, enabling physicians to annotate images such that descriptions are recorded into the computer in a machine-accessible way. Dr. Rubin and ACRIN staff will be available to assist in hands-on demonstrations of the iPAD tool.

# Abstract Presentations

Sunday, November 28

**Title:** Increased Progression with T2-based Imaging during Anti-VEGF Therapy in Glioblastoma: ACRIN 6677 / RTOG 0625

**Authors:** Sorensen G; Zhang Z; Boxerman J; Safriel Y; Gimpel J; Snyder B; Girardi V; Larvie M; Gilbert M.

**Time:** 11:45 am

**Location:** Room N228

**Background/Purpose:** Bevacizumab, an anti-VEGF antibody, was recently approved by the FDA for recurrent glioblastoma, the first new drug treatment for this disease in more than a decade. Central radiology review was key in the FDA's decision. However, the two radiology reviewers disagreed about progression (25% increase in size) in ~50% of MRI scans. Furthermore, VEGF blockade might diminish tumor enhancement despite tumor growth concern, and so T2-weighted imaging may be needed to assess progression. We undertook central radiological review in ACRIN 6677 with specific attention to these two key issues.

**Materials/Methods:** RTOG 0625 / ACRIN 6677 is a randomized Phase II trial of bevacizumab with either irinotecan or dose-dense temozolomide in recurrent glioblastoma (GBM). Central radiology review was performed by performing WHO-style bidimensional radiographic assessment of progression, and assessment of serial 3D volume, both on T1-weighted post-contrast images; and 3D volume assessments of T2-weighted images. Two readers and an adjudicator (all CAQ'd neuroradiologists) were trained using a customized presentation and tested for comprehension. The six month progression-free survival (PFS-6) rate was calculated for 2D, 3D-T1, and 3D-T2 as well as combinations. Adjudication rates were assessed for each measurement method.

**Results:** Of 121 patients enrolled, central review has been completed to date on 51 cases. Adjudication rates were 33% for 2D (n=48), 29% for 3D-T1 (n=34), and 33% for 3D-T2 (n=43), substantially lower than the published figure of 44 to 47% in previous bevacizumab trials, suggesting the benefits of careful training and testing before undertaking central review. PFS-6 was similar for all three methods: 2D: 33%; 3D-T1: 32%; 3D-T2: 26%. The addition of T2 to T1 imaging identified progression in 36/48 cases for 2D T1 imaging (PFS-6=16.7%) and 27/34 cases for 3D-T1 imaging (PFS6=17.7%). Combining all three led to PFS-6 of 12% (all changes  $p < 0.002$ ).

**Conclusions:** Training appears to improve central radiological review agreement. Addition of T2 imaging increases detection of progression rates in recurrent GBM patients being treated with anti-VEGF therapy.

# Abstract Presentations

Monday, November 29

**Title:** Effective Dose Assessment for Participants in the National Lung Screening Trial Receiving Posterior-Anterior (PA) Chest X-ray Examinations

**Authors:** Kruger R; Judy P; Flynn M; Cagnon C; Seibert A.

**Time:** 3:30 pm

**Location:** Room S403B

**Background/Purpose:** The National Lung Screening Trial (NLST) was designed to compare lung cancer specific mortality in its two arms, one of which received low-dose computed tomography (CT), the other PA chest x-rays. Assessment of participant's effective dose is crucial to an accurate radiation risk assessment. The objective of this study is to determine the effective radiation dose associated with individual NLST chest x-ray examinations.

**Materials/Methods:** During the NLST screening period of 2002-2007, a total of 73,733 chest x-ray exams were performed, 67,641 examinations were included in this assessment. Acquisition parameters included the tube potential (kVp), exposure time-current product (mAs), and detector system. Participant specific information (gender, height and weight) was also obtained. Annual measurements of radiation output (mR/mAs) and half-value layer for the nominal kVp of the chest x-ray were performed on the x-ray systems used at each of the 33 NLST screening sites. The entrance skin air kerma of NLST participants' chest x-ray exams was estimated and used in this analysis. The effective dose per entrance skin air kerma for each exam was determined using a Monte Carlo-based program (PCXMC: PC program for X-ray Monte Carlo, STUK - Radiation and Nuclear Safety Authority, Helsinki, Finland).

**Results:** This study found a median participant effective dose of 0.0344 mSv, a 95th percentile value of 0.1150 mSv and a 5th percentile value of 0.0104 mSv.

**Conclusions:** A significant concern associated with either a CT or chest x-ray examination is the potential for adverse biological effect to the subject including an increase in the risk of cancer. Radiation risk is commonly assessed by determining the whole body dose that is equivalent to the dose delivered to portions of the body by a radiological procedure. This involves determination of the dose delivered to specific organs and the computation of a weighted average dose, or effective dose that accounts for the varying radio-sensitivity of different organs. The findings of this study are consistent with previous investigations reported in the scientific literature.

**Clinical Relevance/Application:** This study reports the effective dose for individual NLST chest x-ray examinations and is of specific interest in relation to that associated with the NLST CT examinations.

# Abstract Presentations

Tuesday, November 30

**Title:** Multiple Bilateral Similar Masses on Ultrasound: Results of ACRIN 6666

**Authors:** Berg W; Zhang Z; Yeh M; Mendelson E.

**Time:** 3:00 pm

**Location:** Room E450A

**Background/Purpose:** To determine rates of malignancy of multiple bilateral similar masses on ultrasound and compare those rates to lesions otherwise described by the same features excluding the descriptor “multiple bilateral”.

**Materials/Methods:** 2662 Participants at elevated risk of breast cancer with at least heterogeneously dense breasts underwent three rounds of screening with mammography and physician-performed whole breast ultrasound with reference standard truth of 11 full months of imaging and/or clinical follow-up or diagnosis of cancer at 21 different institutions in this IRB-approved, HIPAA-compliant protocol. In 1630 participants, sonographic findings were identified and prospectively recorded using standard BI-RADS terminology, with addition of the descriptor “multiple bilateral” (M-B) for “similar benign-appearing findings in both breasts”, i.e. at least two in one breast and one in the other. Rates of malignancy for M-B lesions were compared to solitary findings with the same descriptors. We distinguished shapes of two or three gentle lobulations from oval, though in the BI-RADS, these are synonymous.

**Results:** 144 unique participants had 152 unique mass “lesions” reported as “multiple bilateral” (M-B) complicated cysts (n=100), solid, circumscribed oval masses (n= 43), solid masses with two or three gentle lobulations (n=5), or clustered microcysts (n=4); 1114 participants had 1837 non-M-B sonographic masses. Mean age of participants was 55 yrs (range 25-86). Women with a personal history of breast cancer were less likely to have M-B lesions than those without prior breast cancer (34/941, 3.6%, vs. 119/689, 17.3%,  $p < .0001$ ). There were no malignancies among such M-B lesions. Of 359 non M-B lesions described as complicated cysts, one (0.3%) proved malignant, as did 1/125 (0.8%) clustered microcysts, 3/498 (0.6%) circumscribed oval solid masses, 3/162 (1.9%) circumscribed masses with two or three gentle lobulations, 1/109 (0.9%) lymph nodes, 0/17 (0%) intraductal masses, and 1/67 (1.5%) circumscribed round solid masses. As expected, the malignancy rate was  $> 2\%$  for the following non-M-B lesions: 3/91 (3.3%) oval, not circumscribed lesions were malignant as were 1/31 (3.2%) with two or three gentle lobulations, not circumscribed; 2/37 (5.4%) round, not circumscribed; 2/21 (9.5%) irregular shape but circumscribed; and 38/320 (11.9%) irregular not circumscribed.

**Conclusions:** In this prospective multicenter trial, there were no malignancies among multiple bilateral benign-appearing masses seen on whole breast screening ultrasound. Further, the rate of malignancy for isolated complicated cysts, clustered microcysts, or solid oval or round circumscribed masses was  $< 2\%$ .

**Clinical Relevance/Application:** Our results validate our approach of a BI-RADS 2, benign assessment for multiple bilateral complicated cysts or circumscribed, oval solid masses, and for both M-B and solitary clustered microcysts. A probably benign, BI-RADS 3, assessment is appropriate for solitary complicated cysts or circumscribed oval or round masses, including those with two or three gentle lobulations.

# Abstract Presentations

Friday, December 3

**Title:** Annual Screening Strategies in BRCA1 Gene Mutation Carriers: A Comparative Effectiveness Analysis

**Authors:** Lowry K; Lee J; Kong C; McMahon P; Gilmore M; Pisano E; Gatsonis C; Ryan P; Ozanne E; Gazelle G.

**Time:** 10:30 am

**Location:** Room E450B

**Background/Purpose:** To evaluate the comparative effectiveness of annual breast cancer screening strategies in BRCA1 gene mutation carriers using mammography (film or digital), alone or in combination with MRI.

**Materials/Methods:** We used a Markov Monte Carlo model of breast cancer (BC) to compare clinical surveillance without imaging to six annual screening strategies [film mammography (FM), digital mammography (DM), FM and MRI or DM and MRI contemporaneously, and alternating FM/MRI or DM/MRI at six-month intervals] starting at ages 25, 30, 35, and 40. Each strategy was evaluated without and with additional radiation-induced risk of breast cancer from mammography. We compared two models of excess relative risk (ERR): age-at-exposure (AE) and attained-age (AA). Input parameters were obtained from the medical literature, DMIST trial, and calibration. The primary outcome projected was life expectancy (LE).

**Results:** At all start ages, DM strategies provided higher LE than FM strategies, and alternating DM/MRI provided the highest LE. Without ERR, the optimal start age was 25, with LE = 73.76 yrs vs. clinical surveillance (71.75 yrs). With ERR, cumulative BC incidence increased slightly from 71.7% to 72.9% (AA model) or 73.1% (AE model). ERR effects were most pronounced when mammography screening started at age 25. The benefits of the alternating DM/MRI strategy between ages 25-30 were offset by radiation risk [LE = 73.54 yrs starting at 25 vs. 73.54 yrs starting at 30 (AA) and 73.55 yrs starting at 25 vs. 73.56 yrs starting at 30 (AE)]. Evaluation of additional strategies indicated that the strategy which maximized LE in the context of radiation exposure risks was annual MRI starting at 25 with alternating DM/MRI starting at age 30 [73.63 yrs (AA), 73.65 yrs (AE)].

**Conclusions:** Alternating DM/MRI at six month intervals is the most effective screening strategy in BRCA1 mutation carriers. When radiation-induced risk is modeled, cumulative BC incidence increases by <2% and the optimal strategy consists of MRI starting at age 25 with alternating DM/MRI starting at age 30.

**Clinical Relevance/Application:** When radiation-induced risk is modeled, the most effective breast cancer screening strategy for women with BRCA1 mutations is annual MRI starting at age 25 and alternating DM/MRI starting at age 30.

# Abstract Presentations

Friday, December 3

**Title:** Multiple Bilateral Similar Findings on Mammography: Results of ACRIN 6666

**Authors:** Berg W; Zhang Z; Adams A; Mendelson E.

**Time:** 10:40 am

**Location:** Room E450B

**Background/Purpose:** To prospectively determine malignancy rates for multiple bilateral similar findings on mammography and to compare those rates to lesions otherwise described by the same features excluding the descriptor “multiple bilateral”.

**Materials/Methods:** 2662 Participants at elevated risk of breast cancer with at least heterogeneously dense breasts were enrolled in an IRB-approved, HIPAA-compliant protocol at 21 sites and underwent up to three rounds of screening with mammography and physician-performed whole breast ultrasound with reference standard truth of 11 full months of imaging and/or clinical follow-up or diagnosis of cancer. We prospectively recorded mammographic findings using standard BI-RADS terminology, with the addition of the descriptor “multiple bilateral” (M-B) for “similar benign-appearing findings in both breasts”, i.e. at least two in one breast and one in the other. 1306/2662 (49.1%) participants had mammographic masses, asymmetries, and/or calcifications. Rates of malignancy for lesions so described were evaluated.

**Results:** 353 Unique participants had 364 unique “lesions” reported as “multiple bilateral” (M-B), and 1101 participants had 1590 non-M-B mammographic lesions (148 of whom also had M-B lesions). Mean age was 56 years (range 25-87). Of 321 M-B calcifications, none were malignant, regardless of distribution, including: 2 branching/fine-linear; 1 pleomorphic; 14 amorphous/indistinct; 25 coarse heterogeneous; 108 punctate; 11 milk of calcium; and 160 coarse, typically benign. None of 187 diffuse/scattered non-M-B calcification lesions were malignant, regardless of morphology. Of remaining distributions, 0/6 milk-of-calcium and 1/152 (0.7 %) of coarse, typically benign non-M-B calcifications proved malignant, as did 6/140 (4.3%) punctate, 3/47 (6.4%) coarse heterogeneous, 7/129 (5.4%) amorphous/indistinct, 20/60 (33%) pleomorphic, and 5/12 (42%) branching/fine-linear. None of 39 lesions described as M-B circumscribed or obscured masses were malignant, whereas for non-M-B-lesions, 2/225 (0.9%) of isolated circumscribed and 2/87 (2.3%) of isolated obscured masses were malignant. None of 3 M-B circumscribed fat-containing nor 67 isolated circumscribed fat-containing masses were malignant.

**Conclusions:** In this prospective multicenter trial, there were no malignancies among multiple bilateral similar benign-appearing masses or calcifications or among unilateral diffuse, scattered calcifications.

**Clinical Relevance/Application:** When analyzing mammographic findings and determining management, morphology and distribution of calcifications should be considered, as well as whether or not the finding is multiple, bilateral, and similar. Multiple bilateral circumscribed or obscured masses were all benign, whereas such findings in isolation had 0.9 to 2.3% rates of malignancy, consistent with prior studies.

# Scientific Objectives and Leadership

## Research Goal

The American College of Radiology Imaging Network (ACRIN) is an integrated group of imaging researchers, other physician specialists, and basic and clinical scientists, patient advocates and a wide array of research support personnel. ACRIN seeks to develop information through clinical trials of diagnostic imaging and image-guided therapeutics technologies that lengthen and improve the quality of patients' lives.

## Primary Research Objective

### Oncologic

As a National Cancer Institute cooperative group member, ACRIN has three primary research objectives that drive scientific strategy and clinical trial development during the current funding period. These objectives support ACRIN's broad goal by establishing imaging as an important tool in the development and monitoring of targeted interventions for cancer treatment and prevention.

1. Screening of populations at high risk for cancer
2. Diagnosing and staging disease to guide targeted therapy
3. Investigations of biomarkers of treatment response

### Cardiovascular

1. Determining the appropriate use of diagnostic CV imaging tests
2. Evaluating the risks, benefits, clinical impact and costs of CV imaging diagnostic tests and algorithms
3. Examining these variables in representative populations and settings

### Neuroscience

1. Assessing the use of imaging for the measurement of extent of disease and for monitoring therapeutic response
2. Developing and validating functional imaging markers for response to therapy for neurologic disease
3. Discussing the feasibility of using imaging in the management of intravenous thrombolysis in acute ischemic stroke

## Network Leadership

**Network Chair:** Mitchell Schnall, MD, PhD  
University of Pennsylvania

**Deputy Co-chair:** Denise Aberle, MD  
University of California, Los Angeles

**Deputy Co-chair:** Barry Siegel, MD  
Washington University

**Network Statistician:** Constantine Gatsonis, PhD  
Brown University

# Scientific Objectives and Leadership

## Scientific Committees

ACRIN's eight scientific committees develop research strategies that encompass both the network's overarching research agenda and critical imaging questions related to specific diseases. Information about the specific strategies of the committees listed below can be found on the ACRIN Web site at [www.acrin.org](http://www.acrin.org).

### Abdominal Committee

**Chair:** Terence Wong, MD, PhD  
Duke University  
[wong0015@mc.duke.edu](mailto:wong0015@mc.duke.edu)

### Breast Committee

**Chair:** Constance Lehman, MD, PhD  
University of Washington  
[lehman@u.washington.edu](mailto:lehman@u.washington.edu)

### Cardiovascular Committee

**Chair:** Pamela Woodard, MD  
Washington University  
[woodardp@mir.wustl.edu](mailto:woodardp@mir.wustl.edu)

### Experimental Imaging Sciences Committee

**Chair:** David Mankoff, MD, PhD  
University of Washington  
[dam@u.washington.edu](mailto:dam@u.washington.edu)

### Gynecologic Committee

**Chair:** Susanna Lee, MD, PhD  
Massachusetts General Hospital  
[slee0@partners.org](mailto:slee0@partners.org)

### Head and Neck/Neuro

**Chair:** Gregory Sorensen, MD  
Massachusetts General Hospital  
[sorensen@nmr.mgh.harvard.edu](mailto:sorensen@nmr.mgh.harvard.edu)

### Neuroscience Committee

**Chair:** Gregory Sorensen, MD  
Massachusetts General Hospital  
[sorensen@nmr.mgh.harvard.edu](mailto:sorensen@nmr.mgh.harvard.edu)

### Thoracic Committee

**Chair:** Caroline Chiles, MD  
Wake Forest University  
[cchiles@wfubmc.edu](mailto:cchiles@wfubmc.edu)

# ACRIN Participation

ACRIN has established a dynamic clinical trials infrastructure and developed numerous protocols since its establishment in 1999 as a National Cancer Institute (NCI) clinical trials cooperative group. These trials have the potential to alter and expand the role of medical imaging and image-guided therapy in the diagnosis and treatment of cancer. More recently, ACRIN has expanded its imaging research focus to include clinical trials related to other disease processes such as cardiovascular, osteoarthritis, and Alzheimer's disease.

Investigators from all imaging settings and researchers from other disciplines with an interest in imaging are encouraged to participate in ACRIN research activities. Currently, nearly 100 academic and community-based medical facilities in the United States regularly participate in ACRIN clinical trials.

## Participation Benefits

In addition to supporting research to enhance the practice of imaging, other rewards of ACRIN participation include the:

- Option to participate in one or several trials—depending upon an imaging interests and facility resources
- Potential for improving local medical care
- Opportunity to promote participation in cutting edge research
- Access to multicenter data for performing ancillary research
- Development of new or honing of existing skills
- Collaboration with international leaders in the field
- Enhancement of practice revenue
- Opportunity to advance research ideas

## Who can Participate

ACRIN's network brings together a wide range of professionals:

- Imagers from academic centers, community hospitals, and freestanding facilities
- Other specialty clinicians and methodologists with an interest in imaging
- Clinical research associates and imaging technologists
- Other cooperative groups
- Representatives of industry
- Health insurance payers

## How to Participate

Visit ACRIN's Web site ([www.acrin.org](http://www.acrin.org)) to learn how you can:

- Participate in one or more of ACRIN's clinical trials
- Join an ACRIN committee and learn about the goals of the various scientific and scientific support committees
- Attend the ACRIN Annual Meeting that is open to all who are interested

# ACRIN Trials Seeking Site Participation

Below are summaries of trials for which ACRIN is currently recruiting sites. For information on site participation, contact the ACRIN project manager or recruitment specialist listed after each trial summary. For more information about ACRIN trials, visit <http://www.acrin.org/CurrentProtocols.aspx> to access the ACRIN Protocol Summary Table.

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

**Principal Investigator:** Arthur Stillman, MD, PhD

**Status:** Soon to Open

**Overview:** The RESCUE trial is funded by a grant for comparative-effectiveness research from the Agency for Healthcare Research and Quality ([www.ahrq.gov](http://www.ahrq.gov)). This randomized, controlled, diagnostic, multicenter, phase III trial will assess two imaging technologies—coronary computed tomography angiography (CCTA) and single positron emission tomography (SPECT) myocardial perfusion imaging (MPI)—in diagnosing cardiac disease in patients with stable angina or angina equivalent. Results from diagnostic imaging assessment will guide subsequent therapeutic approach. Participants with positive cardiac findings on diagnosis will be guided to optimal medical therapy (OMT) or diagnostic invasive coronary angiography (ICA) and possible revascularization, depending on extent and location of disease. Participants will be followed to collect healthcare utilization data, cardiac events, and quality-of-life questionnaires.

**Main Objective:** The primary endpoint of the study is a combined endpoint of occurrence of major adverse cardiac events (MACE), comprising cardiac-related death or acute myocardial infarction, and revascularization. We will calculate differences in the combined MACE/revascularization endpoint between the CCTA and SPECT MPI arms.

**Participants:** Patients 40 years and older presenting to ACRIN-qualified institutions with symptoms of stable angina CCS Class I to III or angina equivalent, with or without known coronary artery disease (CAD), and eligible to undergo non-invasive imaging for diagnosis may enroll into the study.

**Study Design Summary:** A total of 4300 patients will be randomized to CCTA or SPECT MPI/ICA for diagnostic assessment at up to 80 institutions internationally. All participants diagnosed with CAD by either strategy will be treated initially by OMT unless there is evidence of significant left main CAD ( $\geq 50\%$  stenosis) or markedly abnormal stress test, in which case they will undergo ICA and possibly revascularization as is standard practice. Follow up at the site level will comprise telephone participant/proxy contact at 2 weeks and 2 months after enrollment **only** for participants who have positive cardiac findings on diagnostic CCTA or SPECT MPI. **All** participants (or their proxies) will be contacted by telephone for additional medical information at 6-month intervals after enrollment for up to 24 months. Number of time points and duration of follow up depend on diagnostic results and timing of enrollment, respectively. Participant follow up will continue with medical records abstraction in the subset of participants who self-report MACE, revascularization, cardiac-related visits, or visits related to incidental findings associated with the diagnostic tests.

**Contact:** Cynthia Olson, project manager (215-574-3234; [colson@acr.org](mailto:colson@acr.org)); Suzanne Ahrens, recruitment specialist (215-574-3246; [sahrens-t@acr.org](mailto:sahrens-t@acr.org))

# ACRIN Trials Seeking Site Participation

## ***ACRIN 6678: FDG-PET/CT as a Predictive Marker of Tumor Response and Patient Outcome: Prospective Validation in Non-small Cell Lung Cancer***

**Principal Investigator:** Wolfgang Weber, MD

**Status:** Open

**Main Objectives:**

- To test whether a metabolic response, defined as a  $\geq 25\%$  decrease in peak tumor SUV post-cycle 1 of chemotherapy, provides early prediction of treatment outcome (tumor response and patient survival).
- To determine the test-retest reproducibility of quantitative assessment of tumor FDG uptake by SUVs.
- To evaluate in an exploratory analysis the time course of treatment induced changes in tumor FDG uptake.
- To evaluate in an exploratory analysis changes in tumor volume during chemotherapy by multislice CT.

**Participants:** Eligible participants for this trial are patients with advanced NSCLC (for Groups A and B: Stage IIIB with pleural effusion or Stage IV, who are scheduled to undergo palliative chemotherapy; for Group C, Stages IIIA, IIIB, or IV, with unspecified therapy) who meet the eligibility criteria. Patients with previously treated NSCLC may participate so long as they meet the eligibility criteria.

**Contact:** Donna Hartfeil (215-717-2765; [dhartfeil@acr.org](mailto:dhartfeil@acr.org))

## ***ACRIN 6684: Multicenter, Phase II Assessment of Tumor Hypoxia in Glioblastoma Using 18F-Fluoromisonidazole (FMISO) With PET and MRI***

**Principal Investigator:** A. Gregory Sorensen, MD

**Status:** Open

**Main Objective:** The objective of this study is to determine the association of FMISO PET uptake (tumor to blood ratio, hypoxic volume) and MRI parameters ( $K^{trans}$ , CBV) with overall survival, time to disease progression, and 6-month progression free survival in participants with newly diagnosed glioblastoma (GBM).

**Participants:** Adult patients newly diagnosed with GBM (World Health Organization grade IV) and visible residual disease (at least 4 cc of tissue volume on T1 gadolinium-contrast MRI) planned for initial treatment with radiation therapy and temozolomide, with or within anti-VEGF monotherapy, will be enrolled.

**Study Design Summary:** A total of 50 participants will be enrolled. The first 15 participants will have test/retest FMISO PET scans at baseline performed between 1 and 7 days apart (both scans completed prior to initiation of chemoradiation). FMISO MRI imaging will be conducted at baseline (within 2 weeks prior to initiation of chemoradiation), at week 4 (between cycle 1 and cycle 2), and at week 10 (after completion of chemoradiation). Follow up will be conducted up to 5 years following chemoradiation to assess for disease progression and survivorship.

**Contact:** Bernadine Dunning, project manager (215-574-3228; [bdunning@acr.org](mailto:bdunning@acr.org)); Heather Homick, recruitment specialist ([hhomick@acr.org](mailto:hhomick@acr.org); 215-574-3194)

# ACRIN Trials Seeking Site Participation

## ***ACRIN 6685: A Multicenter Trial of FDG-PET/CT Staging of Head and Neck Cancer and its Impact on the N0 Neck Surgical Treatment in Head and Neck Cancer Patients***

**Principal Investigators:** Val J. Lowe, MD and Brendan C. Stack, Jr., MD, FACS

**Status:** Open

**Main Objective:** The objective of this study is to determine the negative predictive value of PET/CT for the N0 neck based upon pathologic sampling of the neck lymph nodes and to determine PET/CT's potential to change treatment of the N0 neck.

**Participants:** People with newly diagnosed head and neck squamous cell carcinoma being considered for surgical resection, with at least one side of the neck clinically N0, and at risk for occult metastasis (when risk based on clinical data is felt to be greater than 30%).

**Study Design Summary:** A total of 292 participants will be enrolled from a minimum of 10 ACRIN-qualified institutions, enrolling for approximately 24 months.

**Contact:** Irene Mahon (215-574-3249; [imahon@acr.org](mailto:imahon@acr.org))

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

**RTOG Principal Investigator:** Mark R. Gilbert, MD

**ACRIN Principal Investigator:** A. Gregory Sorensen, MD

**Status:** Open

**Overview:** ACRIN 6686 is the advanced-imaging component of the RTOG 0825 trial. Prequalification of imaging scanners and images is required at RTOG sites wishing to participate in the advanced-imaging component. All eligible potential participants recruited at advanced-imaging sites must be asked to consent to advanced imaging. The advanced-imaging component comprises four (4) DSC- and DCE-MRI scans at baseline (T0), Week 3 (T1), Week 3 1 Day (T2), and Week 10 (T3).

**Main Objectives:** The main objectives of the ACRIN 6686 trial are to assess the association between overall survival and Ktrans change from T1 to T2 and to assess the association between overall survival and spin echo CBV changes from T1 to T2.

**Participants:** People with newly diagnosed, histopathologically-confirmed glioblastoma (WHO Grade IV) able to undergo MRI who are accrued to ACRIN-qualified, RTOG sites participating in the ACRIN 6686 advanced-imaging component.

**Study Design Summary:** A total of 264 participants from the 720 RTOG-study patients will be accrued to the ACRIN 6686 advanced-imaging component of the trial.

**Contact:** Bernadine Dunning (215-574-3228; [bdunning@acr.org](mailto:bdunning@acr.org))

# ACRIN Trials Seeking Site Participation

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

**RTOG Principal Investigator:** Tracy Batchelor, MD

**ACRIN Principal Investigator:** A. Gregory Sorensen, MD

**Status:** Open

**Overview:** ACRIN 6689 is the advanced-imaging component of the RTOG 0837 trial. Prequalification of MRI and PET scanners and images is required at RTOG sites wishing to participate in the advanced-imaging component. All eligible participants recruited at advanced-imaging sites must be consented to advanced imaging. The advanced-imaging component comprises seven (7) DSC- and DCE-MRI scans and four (4) FLT PET scans using this investigational imaging agent. See the protocol for specifics on timing for these scans. Pre-MRI blood collection and peri-PET blood sampling with same-day processing are required.

**Main Objectives:** The main objective of the ACRIN 6689 trial is to assess the association between overall survival and change in imaging biomarkers (Ktrans, gradient echo CBV, and [18F]FLT Ki and K1) from baseline imaging to imaging between doses of cediranib or placebo. Additional aims will assess progression-free survival and overall survival between these and other imaging time points, reproducibility of FLT PET imaging, relationships between FLT PET imaging biomarkers and tumor proliferation, and the "vascular normalization index".

**Participants:** People with newly diagnosed, histopathologically-confirmed glioblastoma (WHO Grade IV) able to undergo MRI and PET who are accrued to ACRIN-qualified, RTOG sites participating in the ACRIN 6689 advanced-imaging component.

**Study Design Summary:** A total of 51 participants from the 177 RTOG-study patients will be accrued to the ACRIN 6689 advanced-imaging component of the trial. A total of 25 participants will undergo a second FLT PET scan (Baseline #2) prior to initiation of chemotherapy; specifically, the first 5 participants from each advanced-imaging site will undergo the second FLT PET scan until 25 participants have completed advanced imaging.

**Contact:** Bernadine Dunning, project manager (215-574-3228; [bdunning@acr.org](mailto:bdunning@acr.org)); Heather Homick, recruitment specialist ([hhomick@acr.org](mailto:hhomick@acr.org); 215-574-3194)

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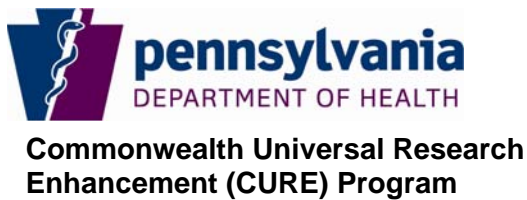
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