Final Progress Report for Research Projects Funded by Health Research Grants

Instructions: Please complete all of the items as instructed. Do not delete instructions. Do not leave any items blank; responses must be provided for all items. If your response to an item is "None", please specify "None" as your response. "Not applicable" is not an acceptable response for any of the items. There is no limit to the length of your response to any question. Responses should be single-spaced, no smaller than 12-point type. The report **must be completed using MS Word**. Submitted reports must be Word documents; they should not be converted to pdf format. Questions? Contact Health Research Program staff at 717-783-2548.

1. **Grantee Institution:** American College of Radiology

2. **Reporting Period (start and end date of grant award period):** 1/1/2009– 12/31/2012

3. **Grant Contact Person (First Name, M.I., Last Name, Degrees):** Marcia Fogle, RN, CCRC

4. **Grant Contact Person's Telephone Number:** 215-940-8898

5. **Grant SAP Number:** 4100047624

6. **Project Number and Title of Research Project:** 7 - Quantitative Imaging Biomarker Tools

7. **Start and End Date of Research Project:** 10/15/2010 – 12/31/2012

8. **Name of Principal Investigator for the Research Project:** Mitchell Schnall, MD, PhD

9. **Research Project Expenses**.

   9(A) Please provide the amount of health research grant funds spent on this project for the entire duration of the grant, including any interest earned that was spent:

   $ 1,241,075.77

   9(B) Provide the last names (include first initial if multiple individuals with the same last name are listed) of **all** persons who worked on this research project and were supported with health research funds. Include position titles (Principal Investigator, Graduate Assistant, Post-doctoral Fellow, etc.), percent of effort on project and total health research funds expended for the position. For multiple year projects, if percent of effort varied from year to year, report in the % of Effort column the effort by year 1, 2, 3, etc. of the project (x% Yr 1; z% Yr 2-3).

Last Name	Position Title	% of Effort on Project	Cost
Apgar	Sr Dir ACRIN	1% Yr 3	$1,335.01
Bauza	Technologist	2% Yr 3	$2,435.74
Boudhar	Statistician	1% Yr 3; 32% yr 4	$38,662.35
Gimpel	Imaging Analyst	16% Yr 3;21% Yr 4	$45,406.32
Harbison	Project Manager	6% Yr3; 7% Yr4	$11,932.10
Levering	Asst Dir Imaging	4% Yr 3; 1% Yr 4	$6,798.73
Price	Technologist	1% Yr 3	$904.83
Fogle	Project Manager	5% Yr 3; 4% Yr 4	$9,752.74
Gaeta	Dir IT Image Technology	16% Yr ; 27% Yr 4	$82,362.57
Ryan	PACS Admin	22% Yr 4	$29,437.99

9(C) Provide the names of **all** persons who worked on this research project, but who *were not* supported with health research funds. Include position titles (Research Assistant, Administrative Assistant, etc.) and percent of effort on project. For multiple year projects, if percent of effort varied from year to year, report in the % of Effort column the effort by year 1, 2, 3, etc. of the project (x% Yr 1; z% Yr 2-3).

Last Name	Position Title	% of Effort on Project
Schnall	ACRIN Group Chair	<1%
Rubin	Investigator	2.5%

9(D) Provide a list of **all** scientific equipment purchased as part of this research grant, a short description of the value (benefit) derived by the institution from this equipment, and the cost of the equipment.

Type of Scientific Equipment	Value Derived	Cost
EMC Celerra NS-G2 platform	EMC Celerra NS-G2 platform extended the value of our existing EMC CX700 storage array. This device delivered a comprehensive, consolidated storage solution that added Network Attached Storage which enabled us to manage file systems with multi-protocol access. This device enabled us to build CIFS shares to better manage our image data. The image data was able to be mirrored via EMC's Replication manager to our Reston data center to ensure data availability and integrity. Along with mirroring data the device allowed us to institute snapshots via EMC SnapSure. The snapshot technology allows for quick and efficient recovery of data elements to ensure availability for ongoing clinical trials.	$84,915.69

10. Co-funding of Research Project during Health Research Grant Award Period. Did this research project receive funding from any other source during the project period when it was supported by the health research grant?

Yes____✓_____ No_____

If yes, please indicate the source and amount of other funds:

Dr. Rubin provided leadership to this project as an expansion of his duties as ACRIN Informatics Chair which is funded by the NIH.

11. Leveraging of Additional Funds

11(A) As a result of the health research funds provided for this research project, were you able to apply for and/or obtain funding from other sources to continue or expand the research?

Yes_____ No____✓_____

If yes, please list the applications submitted (column A), the funding agency (National Institutes of Health—NIH, or other source in column B), the month and year when the application was submitted (column C), and the amount of funds requested (column D). If you have received a notice that the grant will be funded, please indicate the amount of funds to be awarded (column E). If the grant was not funded, insert "not funded" in column E.

Do not include funding from your own institution or from CURE (tobacco settlement funds). Do not include grants submitted prior to the start date of the grant as shown in Question 2. If you list grants submitted within 1-6 months of the start date of this grant, add a statement below the table indicating how the data/results from this project were used to secure that grant.

A. Title of research project on grant application	B. Funding agency (check those that apply)	C. Month and Year Submitted	D. Amount of funds requested:	E. Amount of funds to be awarded:
None	☐NIH ☐ Other federal (specify:_____) ☐ Nonfederal source (specify:_)		$	$

11(B) Are you planning to apply for additional funding in the future to continue or expand the research?

Yes____✓_____ No_____

If yes, please describe your plans:

Dr. Rosen, co-investigator of the project, has applied for funding for the ACR Imaging Core Laboratory to pursue continued efforts for the application of imaging biomarker extraction and analysis in support of clinical oncology trials. This funding effort is part of a larger consortium, the Imaging and Radiation Oncology Consortium (IROC), which has submitted a request for funding in response a National Cancer Institute funding notice (RFA-CA-12-014).

Dr. Schnall, leader of the ACR Imaging Network and PI for the formula grant has applied for funding in response to RFA-CA-12-010 as co-PI with Robert Comis, MD, to form the ECOG-ACRIN partnership co-operative group for clinical oncology and advanced imaging trials.

12. Future of Research Project. What are the future plans for this research project?

We are currently working to refine the Annotation and Image Markup (AIM) electronic physician annotation device (ePAD) web-interface to improve workflow. Future plans include [1] integration of AIM from ePAD with the ACRIN TRIAD (image archive) system and data warehouse; and [2] extend ePAD to enable quantitative evaluation of PET/CT (PERCIST response criteria), including development of a PERCIST template modeled after the RECIST template described later in this report. These efforts will allow the ACR Imaging Core Laboratory to improve internal operations and efficiency for extracting meaningful quantitative metrics for imaging data.

13. New Investigator Training and Development. Did students participate in project supported internships or graduate or post-graduate training for at least one semester or one summer?

Yes____✓_____ No_____

If yes, how many students? Please specify in the tables below:

	Undergraduate	Masters	Pre-doc	Post-doc
Male		1		
Female				
Unknown				
Total		**1**		

	Undergraduate	Masters	Pre-doc	Post-doc
Hispanic		1		
Non-Hispanic				
Unknown				
Total		**1**		

	Undergraduate	Masters	Pre-doc	Post-doc
White		1		
Black				
Asian				
Other				
Unknown				
Total		**1**		

14. Recruitment of Out-of–State Researchers. Did you bring researchers into Pennsylvania to carry out this research project?

Yes_____ No____✓_____

If yes, please list the name and degree of each researcher and his/her previous affiliation:

15. Impact on Research Capacity and Quality. Did the health research project enhance the quality and/or capacity of research at your institution?

Yes____✓_____ No_____

If yes, describe how improvements in infrastructure, the addition of new investigators, and other resources have led to more and better research.

Through the efforts funded by this formula grant, the ACR Imaging Core Laboratory has developed streamlined methods for extracting quantitative information from imaging studies as derived from annotations provided by radiologists and other expert image analysis personnel. Improvements in efficiency will enable a larger number of reader studies at lower cost in the ACR Imaging Core Laboratory.

16. Collaboration, business and community involvement.

16(A) Did the health research funds lead to collaboration with research partners outside of your institution (e.g., entire university, entire hospital system)?

Yes____✓_____ No_____

If yes, please describe the collaborations:

Daniel Rubin, MD, of Stanford University, led the research team and oversaw the programming efforts of the ACRIN and Stanford programmers (Alan Snyder and Debra Willet). The following radiologists served as readers for the reader study: Rupesh Kalthia, MD, Stanford University; Bhavik Patel, MD, Stanford University; Mark Rosen, MD, PhD, University of Pennsylvania; and Drew Torigian, MD, University of

Pennsylvania.

16(B) Did the research project result in commercial development of any research products?

Yes_____ No____✓_____

If yes, please describe commercial development activities that resulted from the research project:

16(C) Did the research lead to new involvement with the community?

Yes_____ No____✓_____

If yes, please describe involvement with community groups that resulted from the research project:

17. Progress in Achieving Research Goals, Objectives and Aims.

List the project goals, objectives and specific aims (as contained in the grant application's strategic plan). Summarize the progress made in achieving these goals, objectives and aims for the period that the project was funded (i.e., from project start date through end date). Indicate whether or not each goal/objective/aim was achieved; if something was not achieved, note the reasons why. Describe the methods used. If changes were made to the research goals/objectives/aims, methods, design or timeline since the original grant application was submitted, please describe the changes. Provide detailed results of the project. Include evidence of the data that was generated and analyzed, and provide tables, graphs, and figures of the data. List published abstracts, poster presentations and scientific meeting presentations at the end of the summary of progress; peer-reviewed publications should be listed under item 20.

This response should be a DETAILED report of the methods and findings. It is not sufficient to state that the work was completed. Insufficient information may result in an unfavorable performance review, which may jeopardize future funding. If research findings are pending publication you must still include enough detail for the expert peer reviewers to evaluate the progress during the course of the project.

Health research grants funded under the Tobacco Settlement Act will be evaluated via a performance review by an expert panel of researchers and clinicians who will assess project work using this Final Progress Report, all project Annual Reports and the project's strategic plan. After the final performance review of each project is complete, approximately 12-16 months after the end of the grant, this Final Progress Report, as well as the Final Performance Review Report containing the comments of the expert review panel, and the grantee's written response to the Final Performance Review Report, will be posted on the CURE Web site.

There is no limit to the length of your response. Responses must be single-spaced below, no smaller than 12-point type. If you cut and paste text from a publication, be sure symbols print properly, e.g., the Greek symbol for alpha (α) and beta (ß) should not print as boxes (□) and include the appropriate citation(s). DO NOT DELETE THESE INSTRUCTIONS.

Quantitative Imaging Biomarker Tools

The purpose of this study is to evaluate, develop, and unify software tools that are used to collect, record, and analyze quantitative imaging data in order to discover imaging biomarkers for more accurate analysis of image results collected in clinical trials. At present, the assessment of cancer treatment response based on image assessment is a key component of the assessment of treatment efficacy in cancer clinical trials. However, this process is cumbersome, with few freely available tools for measuring and capturing vital image meta-data required for this assessment. Our outcome will bridge these barriers and advance the field by improving the efficiency of response assessment evaluation on images. Our ultimate goal for developing these tools is to facilitate assessment of treatment response and clinical decision-making in cancer. Our unified tools will enable cancer researchers to derive quantitative measurements of patient responses to cancer therapies from imaging data. Our work will enable oncologists to make better treatment choices for their cancer patients – a potential benefit to over 1.4 million patients with new cancers annually.

Aim 1: Analyze and refine tools to determine if enabling automated extraction of quantitative imaging biomarkers will improve the efficiency of the analysis of imaging data.

We began with an assessment of the major quantitative imaging tools available and in use in the ACRIN core laboratory. In addition to identifying which tools provide open programming interfaces, this assessment included an inventory of all quantitative software applications including the vendor, version, operating system, imaging applications, current ACRIN uses (by application and ACRIN trial), Digital Imaging and Communications in Medicine (DICOM) compatibility, type of layer/annotation management, and type of Region of Interest (ROI) export. We then conducted a detailed gap analysis, provided as Appendix 1. This analysis was performed by working with core laboratory imaging analysts and radiologists to identify what features are used and what features are missing in terms of tools and workflow for each of the following reader scenarios – Response Evaluation Criteria in Solid Tumors (RECIST) assessments, positron emission tomography (PET) assessments, and dynamic contrast enhanced-magnetic resonance imaging (DCE-MRI) assessments.

Our ability to refine currently available tools were hampered due to the differences in the fundamental structure of these applications for sharing analytic outputs, as well as the ability to capture semantic or descriptive language regarding disease presentation. Therefore, work performed in support of enabling meaningful and standardized automated extraction of quantitative imaging biomarkers was performed in concert with extending the functionality of the web-based electronic physician annotation device (ePAD) and developing a tumor assessment template, per the Response Evaluation Criteria in Solid Tumors (RECIST 1.1), criteria as described below in Aim 2.

Aim 2: Develop a standards-based software platform to unify quantitative imaging tools for efficient image evaluation and data interoperability.

In tandem to extending functionality of the ePAD tool, as discussed in Aim 1 above, we developed a web-based platform. The platform stores all image data according to the National Cancer Institute's (NCI) cancer Biomedical Informatics Grid (caBIG) Annotation and Image Markup (AIM) standards to maximize interoperability. AIM is a "standard" means of capturing descriptive information added to the image in the clinical environment. The first few months of this effort were devoted to assessing and then implementing the appropriate infrastructure and firewall updates required for deployment of a web-based platform. We set up and tested project-specific DICOM servers populated with test cases. Together, the ACRIN and Stanford team installed and tested ePAD with the DICOM servers at ACRIN. ePAD was successfully configured to interface with both the ClearCanvas and dcm4chee servers. The dcm4chee server is an open source DICOM- compliant and Health Level Seven (HL7)-compliant image manager/archive which provides many robust and scalable services and can be accessed by the Stanford team via a web interface. In connection with this, we are currently communicating with the Northwestern University AIM team regarding implementation/development of AIM on ClearCanvas.

We chose to focus on improving the efficiency and analysis of RECIST assessments. Code was written to support unambiguous identification of target lesions and automated tracking (matching) of images across various time points. We then worked to define the user requirements and technical specifications for the Extensible Markup Language (XML) database and query interface to support queries and extraction of AIM data. Once the database requirements were well defined the programming team developed the database. A significant level of effort was spent testing and refining the image annotation database and data output of the ePAD RECIST Template. The ePAD RECIST Template provides a standardized workflow and methodology for recording, calculating and summarizing quantitative measurements. Testing and programming efforts continued for the RECIST table and graph. The RECIST table, in addition to providing a summary display of RECIST measurements made by the user at each imaging time point, now allows users to navigate directly to a given lesion and timepoint. This should provide added efficiency to the image review process and thereby, the overall quantitative image analysis (we evaluate the impact on reader performance below). We also developed an instruction manual this report period. Screenshots of the ePAD template for RECIST are shown in the attached Reader Study Instruction Manual (Appendix 2).

Aim 3: We will assess our platform in a study requiring evaluation of quantitative imaging data.

We undertook a formal reader study to assess the impact of using the ePAD tool on the efficiency of reader evaluation of quantitative imaging studies. Reader training was conducted in parallel to the above described testing, and was completed mid-September, 2012. Reader training included a review of the RECIST 1.1 criteria and review of two test patient image sets as test cases using the ePAD RECIST tool to familiarize themselves with the RECIST template workflow and ePad software mechanics.

The reader study commenced immediately upon completion of the final testing. The reader study consisted of twenty (20) cases with metastatic carcinoid tumor archived by ACRIN in the course of a central reader analysis for a phase III treatment trial co-sponsored by the Southwest Oncology Group (SWOG) and Genentech. Each case consisted of Chest, Abdomen and/or Pelvis CT scans across four (4) time points, baseline and three (3) follow-up studies. Target lesions and new lesions were defined and measured per the RECIST 1.1 criteria. Non-target lesions were not identified nor measured for purposes of this evaluation, in concert with our goals of maximizing the automatated analysis of quantitative (lesion diameter) metrics. Each case was reviewed by four (4) radiologist readers experienced in thoracic/abdominal radiology. Readers were un-blinded to time point order. The primary measurement variables were the times of review both with and without the use of the AIM-enabled tool in the ePad environment. A facilitator was present for all reads to assist the radiologist and oversee timing of the review.

ASSISTED READS

The readers first reviewed each case using the ePAD RECIST 1.1 tool. During this "assisted read", the readers created linear measurement markups of target lesions in accordance with RECIST 1.1 criteria and the ePAD interface facilitated the completion of a simple electronic form capturing lesion size, location and time point. The tool then calculated progression versus response at each time point based on the sums of the diameters of target lesions identified by the readers according to the criteria.

The ePAD RECIST tool includes a defined workflow ensuring that each review is conducted in a standardized manner and per the RECIST 1.1 response criteria, thereby helping to ensure accurate and comparable data are collected for study endpoints. The methods and workflow for the "assisted reads" is described below.

Image Display:

Readers log into the ePAD application using a secure log-in and password. The reader begins by selecting the case and the image sets to be reviewed. Once the images are loaded, the facilitator/timer starts the stopwatch and documents the "Begin" time on the field log.

- By default, there is a 2 x 2 hanging protocol (4 viewports) so that as the reader proceeds to review the follow-up image sets all 4 time points can be viewed at the same time – this helps ensure that the same lesions are measured over all time points.
- The reader is able to adjust the window/level settings for optimal visualization by using dynamic-range, click-drag functionality of the mouse and/or also by using pre-set window/level hotkeys programmed to lung, bone and soft tissue windows, with additional hot keys for pan/zoom image control.

Baseline Assessment: The first step in the RECIST workflow is to identify the baseline target lesion(s). The reader performs a linear measurement of the longest diameter of the first target lesion (or short axis in the case of lymph nodes) according to RECIST 1.1 criteria. The system labels the first target Lesion1 (the second as Lesion 2, the third as Lesion 3, etc.) by default but this label is freely editable by the reader. The application then displays an electronic form corresponding to Lesion1 which contains fields to classify the lesion further according to the

RECIST criteria. These fields include drop-down lists for the reader to identify the lesion per the standardized AIM ontology.

- Lesion Location: per Radlex ontology (http://www.radlex.org/) (supported by AIM)
- Lesion Type:
    - Target Lesion
    - Non-target Lesion
    - New Lesion
    - Resolved Lesion

The reader identifies and measures each additional baseline target lesion, as described for Lesion 1 above. The sum of the diameters of all target lesions measured is totaled by, and tracked within, the ePad application. The reader alerts the facilitator upon completion of the baseline review, the stopwatch is stopped, and the elapsed time in seconds is recorded as "End 1" on the field log.

Follow-Up Assessments: The second step in the RECIST workflow is to review and measure the same target lesions identified at baseline on the next sequential follow-up exam. The review time for each follow up time point is timed in the same manner as the baseline review and documented on the field log ("Start 2", "End 2", "Start 3", etc.).

Lesion ID (default label or reader-specified label), Lesion Location and Lesion Type from the baseline review is displayed helping to ensure the same lesions are followed across all time points as specified by the response criteria. The reader performs a linear measurement of each target lesion and any new lesions (lesion not present at baseline). The reader clicks on the measurement to pull up a lesion-specific electronic form to provide Lesion Location and Lesion Type. Upon measurement and classification of all target lesions the sum of the diameters is totaled by, and tracked within, the ePAD application. The application compares the sum of the diameters of the follow-up and baseline time points, figure in the presence of new lesions, and provide an automated response assessment (PR, CR, SD, or PD) as defined by the RECIST 1.1 criteria. This process is repeated for each follow-up time point. The reader confirms the accuracy of longest diameters and the RECIST tool output.

The reader is able to recall any of the target lesions from a list which will identify the target lesion number and time point (by case). The image corresponding to the markup of the lesion shall display when queried retrospectively from a list within the ePad interface. All markups are saved automatically and the reader can proceed to the next case.

The data from each time point is displayed in a table; this can be printed or exported for upload to the Clinical Trial Management System. The application can also display a graph showing the sum of the longest diameters and response assessment by time point.

UNASSISTED READS

Following a 30-day washout period to negate recall bias, the cases were read again by the readers in the same environment, but in an "unassisted" fashion without the use of the ePAD RECIST tool. The readers instead recorded their findings with the use of a standard paper case report form. The time to complete each read, including the calculation of progression vs. response, was

again recorded and compared with the times recorded during the preceding assisted review.

Readers initially undertook the "assisted" reads, followed by the thirty-day washout period. After this the "unassisted" reads were performed. This order was maintained for each of the four readers, to ensure that any effects of a "learning curve" would be biased in favor of the "unassisted" read. In this manner, any time savings a reader experienced with the assistance of the ePAD plug-in could not be attributable to learning curve effects on improved efficiency.

ANALYSIS

Dataset

Exams were selected from 20 subjects who had one baseline and three consecutive follow-up imaging exams. Four radiologists were recruited to perform replicate quantitative assessments of these exams. Exams were read initially with the aid of the ePAD tool ("assisted read"). After a thirty-day washout period, the exams were re-read but without the AIM plug-in ("unassisted read"). The reading time is measured in minutes. One of the readers ("A") had completed unassisted read on 19 subjects.

Statistical Method

Mean and standard deviations of each reader's reading time for both assisted read and unassisted read are calculated. Reader average reading times for both reading modes are calculated as well. Paired t-tests are used to compare the reading time from both reading modes for each reader separately. Overall time savings for using "assisted read" is analyzed using linear mixed model with random intercept and treating reading mode and reader as nested random effect.

Results

As shown in table 1 below, for unassisted reads, the mean(sd) review time per patient for each of the four readers was 11.4(2.6), 12.2(3.9), 8.8(2.5) and 9.3(2.8) minutes (average 10.4 minutes), while for the assisted reads, the mean(sd) time required for each of the same four readers was 8.6(2.7), 10.0(3.4), 7.5(2.5) and 11.7(3.6) minutes (average 9.5 minutes), respectively. On three of the four readers, ePAD generated significant time savings. However, for the fourth reader, ePAD assisted reading time is significantly longer than that of the unassisted read ($p<0.0001$). On average across all four readers, the use of ePAD produced a savings of 0.9 minutes (95% CI: -3.2 to 1.3 minutes, $p=0.48$) per patient, representing a net increase in reader efficiency of 9%. However, this reduction is not statistically significant.

Table 1: Reading time (min) as shown by mean (sd), by reader and reading mode. The reading time between the two reading modes were compared by the difference in time (min) with 95% CI and p-values from paired t-test (for individual reader) or linear mixed model (for average).

Reader	Unassisted Read	Assisted Read	Assisted – Unassisted Read	p-value
A	11.4(2.6)	8.6(2.7)	-2.6(-4.0, -1.3)	0.0005
B	12.2(3.9)	10.0(3.4)	-2.1(-3.1, -1.1)	0.0002
C	8.8(2.5)	7.5(2.5)	-1.3(-2.6, -0.1)	0.037
D	9.3(2.8)	11.7(3.6)	2.4(1.7, 3.1)	<0.0001
Average	10.4(1.8)	9.5(1.6)	-0.9(-3.2, 1.3)	0.48

Noting the outlier status of reader "D", this reader was queried as to the methodology of imaging evaluation used by this reader during both "assisted" and "unassisted" reading sessions. This reader indicated that he recalled that no new lesions were identified in any of the twenty patient data sets in the course of the initial ("assisted") read. Recalling this fact, the reader indicated that during the subsequent "unassisted" read the reader did not devote time to evaluating for any new lesions. It should also be noted that this reader D experienced the longest average read time per patient (11.7 minutes). We therefore conclude that the results from this reader may have been affected by this recall bias. As such, despite the overall lack of statistical significance between assisted and unassisted reading session times, we believe the data supports the use of the software tool to improve overall reader time for data analysis.

18. Extent of Clinical Activities Initiated and Completed. Items 18(A) and 18(B) should be completed for all research projects. If the project was restricted to secondary analysis of clinical data or data analysis of clinical research, then responses to 18(A) and 18(B) should be "No."

18(A) Did you initiate a study that involved the testing of treatment, prevention or diagnostic procedures on human subjects?

_____Yes
__✓___No

18(B) Did you complete a study that involved the testing of treatment, prevention or diagnostic procedures on human subjects?

_____Yes
__✓___No

If "Yes" to either 18(A) or 18(B), items 18(C) – (F) must also be completed. (Do NOT complete 18(C-F) if 18(A) and 18(B) are both "No.")

18(C) How many hospital and health care professionals were involved in the research project?

_____Number of hospital and health care professionals involved in the research project

18(D) How many subjects were included in the study compared to targeted goals?

_____Number of subjects originally targeted to be included in the study
_____Number of subjects enrolled in the study

Note: Studies that fall dramatically short on recruitment are encouraged to provide the details of their recruitment efforts in Item 17, Progress in Achieving Research Goals, Objectives and Aims. For example, the number of eligible subjects approached, the number that refused to participate and the reasons for

refusal. Without this information it is difficult to discern whether eligibility criteria were too restrictive or the study simply did not appeal to subjects.

18(E) How many subjects were enrolled in the study by gender, ethnicity and race?

Gender:
_____Males
_____Females
_____Unknown

Ethnicity:
_____Latinos or Hispanics
_____Not Latinos or Hispanics
_____Unknown

Race:
_____American Indian or Alaska Native
_____Asian
_____Blacks or African American
_____Native Hawaiian or Other Pacific Islander
_____White
_____Other, specify:_____
_____Unknown

18(F) Where was the research study conducted? (List the county where the research study was conducted. If the treatment, prevention and diagnostic tests were offered in more than one county, list all of the counties where the research study was conducted.)

19. Human Embryonic Stem Cell Research. Item 19(A) should be completed for all research projects. If the research project involved human embryonic stem cells, items 19(B) and 19(C) must also be completed.

19(A) Did this project involve, in any capacity, human embryonic stem cells?
_____Yes
__✓___No

19(B) Were these stem cell lines NIH-approved lines that were derived outside of Pennsylvania?
_____Yes
_____No

19(C) Please describe how this project involved human embryonic stem cells:

20. Articles Submitted to Peer-Reviewed Publications.

20(A) Identify all publications that resulted from the research performed during the funding period and that have been submitted to peer-reviewed publications. Do not list journal abstracts or presentations at professional meetings; abstract and meeting presentations should be listed at the end of item 17. **Include only those publications that acknowledge the Pennsylvania Department of Health as a funding source** (as required in the grant agreement). List the title of the journal article, the authors, the name of the peer-reviewed publication, the month and year when it was submitted, and the status of publication (submitted for publication, accepted for publication or published.). Submit an electronic copy of each publication or paper submitted for publication, listed in the table, in a PDF version 5.0.5 (or greater) format, 1,200 dpi. Filenames for each publication should include the number of the research project, the last name of the PI, the number of the publication and an abbreviated research project title. For example, if you submit two publications for PI Smith for the "Cognition and MRI in Older Adults" research project (Project 1), and two publications for PI Zhang for the "Lung Cancer" research project (Project 3), the filenames should be:

Project 1 – Smith – Publication 1 – Cognition and MRI
Project 1 – Smith – Publication 2 – Cognition and MRI
Project 3 – Zhang – Publication 1 – Lung Cancer
Project 3 – Zhang – Publication 2 – Lung Cancer

If the publication is not available electronically, provide 5 paper copies of the publication.

Note: The grant agreement requires that recipients acknowledge the Pennsylvania Department of Health funding in all publications. Please ensure that all publications listed acknowledge the Department of Health funding. If a publication does not acknowledge the funding from the Commonwealth, do not list the publication.

Title of Journal Article:	Authors:	Name of Peer-reviewed Publication:	Month and Year Submitted:	Publication Status (check appropriate box below):
1. None				☐Submitted ☐Accepted ☐Published

20(B) Based on this project, are you planning to submit articles to peer-reviewed publications in the future?

Yes__✓___ No_____

If yes, please describe your plans:

We are continuing our analysis of the results for the reader study, and comparing these results to those from an earlier reader study of our ePAD platform. We presented results from our prior version of the tool, iPAD, at RSNA [Rubin D, et al., " Tools for Quantitative

Imaging Assessment of Treatment Response in the American College of Radiology Imaging Network (ACRIN). Paper presented at: Radiologic Society of North America Annual Meeting 2012; Chicago, Ill.]

21. Changes in Outcome, Impact and Effectiveness Attributable to the Research Project. Describe the outcome, impact, and effectiveness of the research project by summarizing its impact on the incidence of disease, death from disease, stage of disease at time of diagnosis, or other relevant measures of outcome, impact or effectiveness of the research project. If there were no changes, insert "None"; do not use "Not applicable." Responses must be single-spaced below, and no smaller than 12-point type. DO NOT DELETE THESE INSTRUCTIONS. There is no limit to the length of your response.

Based on the results of our studies, we are pursuing broader implementation of the ePAD tool interface in our reader studies. These will continue to impact our RECIST analyses in oncology trials, but will be expanded into other areas of quantitative imaging analysis, particularly in PET analysis (e.g. "PERCIST" and other standardized PET response criteria). Successful implementation of these tools into the routine of the ACR Core Laboratory will greatly enhance the ability of the Core Lab to facilitate the process of centralized reader studies in oncology trials.

22. Major Discoveries, New Drugs, and New Approaches for Prevention Diagnosis and Treatment. Describe major discoveries, new drugs, and new approaches for prevention, diagnosis and treatment that are attributable to the completed research project. If there were no major discoveries, drugs or approaches, insert "None"; do not use "Not applicable." Responses must be single-spaced below, and no smaller than 12-point type. DO NOT DELETE THESE INSTRUCTIONS. There is no limit to the length of your response.

None.

23. Inventions, Patents and Commercial Development Opportunities.

23(A) Were any inventions, which may be patentable or otherwise protectable under Title 35 of the United States Code, conceived or first actually reduced to practice in the performance of work under this health research grant? Yes_____ No____✓_____

If "Yes" to 23(A), complete items a – g below for each invention. (Do NOT complete items a - g if 23(A) is "No.")

a. Title of Invention:

b. Name of Inventor(s):

c. Technical Description of Invention (describe nature, purpose, operation and physical, chemical, biological or electrical characteristics of the invention):

d. Was a patent filed for the invention conceived or first actually reduced to practice in the performance of work under this health research grant?
Yes_____ No____

If yes, indicate date patent was filed:

e. Was a patent issued for the invention conceived or first actually reduced to practice in the performance of work under this health research grant?
Yes_____ No____
If yes, indicate number of patent, title and date issued:
Patent number:
Title of patent:
Date issued:

f. Were any licenses granted for the patent obtained as a result of work performed under this health research grant? Yes_____ No____

If yes, how many licenses were granted?_____

g. Were any commercial development activities taken to develop the invention into a commercial product or service for manufacture or sale? Yes___ No____

If yes, describe the commercial development activities:

23(B) Based on the results of this project, are you planning to file for any licenses or patents, or undertake any commercial development opportunities in the future?

Yes_____ No_____✓_____

If yes, please describe your plans:

24. Key Investigator Qualifications. Briefly describe the education, research interests and experience and professional commitments of the Principal Investigator and all other key investigators. In place of narrative you may insert the NIH biosketch form here; however, please limit each biosketch to 1-2 pages.

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors in the order listed on Form Page 2.
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME	POSITION TITLE
Daniel Rubin, M.D.	Assistant Professor, Radiology and Medicine (Biomedical Informatics Research)
eRA COMMONS USER NAME (credential, e.g., agency login) DANIEL.RUBIN	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	MM/YY	FIELD OF STUDY
Stanford University, Stanford, CA B.S.	B.S.	1980	Biology
Stanford University Medical School	M.D.	1985	Medicine
Stanford University, Department of Medicine	Internship	1985-86	Medicine
Stanford University, Department of Radiology	Residency	1986-90	Radiology
Stanford University, Department of Radiology	Fellowship	1990-1991	Radiology
Stanford University, Stanford, CA	M.S.	2000	Biomedical Informatics

A. Personal Statement

As Biomedical Imaging Informatics Committee Chair of the American College of Radiology Imaging Network (ACRIN), Dr. Rubin led the team of researchers that developed the standards-based informatics tool to streamline the collection and evaluation of quantitative imaging data in its clinical trials. He is also the Assistant Professor in the Department of Radiology at Stanford University. His research uses computational methods to leverage the information in radiology images to enable biomedical discovery and to guide physicians in personalized care. Dr. Rubin's innovative methods will enhance ECOG – ACRIN's translational research platform by making the content in images computable and to electronically correlate images with other clinical data such as pathology and molecular data.

B. Positions and Honors.

Positions and Employment

1991 -1994	Consultant, Diagnostic Imaging Board of Scientific Advisors, Sterling Winthrop Inc., Malvern, PA
1991 -1995	Staff Radiologist, Good Samaritan Hospital of Santa Clara Valley, San Jose, CA
1995 -2000	Consultant to Pharmaceutical Industry, consulting activities with Nycomed Inc. (Wayne, PA), Bracco Diagnostics, Inc. (Princeton, NJ) and Berlex Laboratories (Princeton, NJ).
1998 -1999	Assistant Clinical Professor, Department of Radiology, SF School of Medicine, San Francisco, CA
1991 - 2008	Clinical Assistant Professor, Department of Radiology, Stanford University School of Medicine, Stanford, CA
1994 - 2001	Founder and Principal Investigator, Center for Diagnostic Imaging Research, Staff Physician, Columbia Good Samaritan Hospital, San Jose, CA
1995, 1997-1998	Staff Radiologist, San Francisco Veteran's Administration Hospital, San Francisco, CA.

2000 - 2008	Research Scientist, Stanford Center for Biomedical Informatics Research, Stanford University, Stanford, CA.
2008 -	Assistant Professor, Department of Radiology, Stanford University School of Medicine.
2011 -	Assistant Professor, Department of Medicine (Biomedical Informatics Research), Stanford University School of Medicine.

Honors:

1979 Phi Beta Kappa, Stanford University Chapter, junior electee.
1980 Los Angeles Area Chamber of Commerce Youth Vision Award.
1985 Research Honors Award in Diagnostic Radiology, Stanford University School of Medicine.
1990 Lauterbur Award for Magnetic Resonance Imaging Research, Society of Computed Body Tomography.
1991, 93 Editor's Recognition Award with Special Distinction for Reviewing Radiology manuscripts.
2004 Certificate of Merit, "A Web-based Decision Support System for Mammography." RSNA 2004.
2005 Certificate of Merit, "What are ontologies, and how are they useful to radiology?" RSNA 2005.
2006 Distinguished Paper Award, Rubin DL, et al., "Ontology-Based Representation of Simulation Models of Physiology," American Medical Informatics Association (AMIA) Annual Symposium.
2006 Cum Laude Award, Educational Exhibit, "Data Warehousing in Radiology." RSNA 2006.
2006 Certificate of Merit, Educational Exhibit, "Steering Radiology onto the Information Superhighway: A Primer on the Semantic Web." RSNA 2006.
2007 IMIA Yearbook of Medical Informatics 2007 "the best of medical informatics" paper selection: Rubin DL, et. al, "Using ontologies linked with geometric models to reason about penetrating injuries."
2008 Cum Laude Award, Educational Exhibit, "Annotation and Image Markup in Radiology." RSNA 2008. 2009 Certificate of Merit, Educational Exhibit, "J-Viewer: A Free Javascript Library for Creating Web (and iPhone) Teaching Files with Simple PACS Functionality," RSNA 2009.
2009 Certificate of Merit, Educational Exhibit, "Xrayhead MSK Online: A Radiology Teaching File Based on RSNA's RadLex," RSNA 2009.
2010 Cancer Biomedical Informatics Grid (caBIG) Connecting Collaborators Award, National Cancer Institute.
2010 Cum Laude Award, Educational Exhibit, "Natural Language Processing in Radiology." RSNA 2010.
2010 Distinguished Paper Award, Rubin DL, et al., "Natural Language Processing for Lines and Devices in Portable Chest X-Rays," AMIA Annual Symposium, 2010.
2011 Cum Laude Award, Educational Exhibit, "The caBIG Annotation and Image Markup (AIM) Version 4.0." RSNA 2011.
2011 Cum Laude Award, Educational Exhibit, "An Open Sourced Web-based Application for Viewing, Annotating, and Capturing Quantitative Data in Medical Images." RSNA 2011.
2012 RSNA Honored Educator Award, Radiological Society of North America.
2012 Best Paper, Journal of Digital Imaging: Rubin DL, et al., "Ontology-assisted Analysis of Web Queries to Determine the Knowledge Radiologists Seek." (JDI Volume 24 (1): 160-164, 2011.

B. Selected Peer-reviewed Publications (selected from 131 peer-reviewed publications)

1. Xu J, Napel S, Greenspan H, Beaulieu CF, Agrawal N, **Rubin DL**, Quantifying the Margin Sharpness of Lesions on Radiological Images for Content-Based Image Retrieval, Medical Physics 39(9):5405-18, 2012 (PMCID PMC3432101).

2. Mongkolwat P, Channin DS, Kleper V, **Rubin DL**, Informatics in Radiology: An Open-Source and Open-Access Cancer Biomedical Informatics Grid Annotation and Image Markup Template Builder, Radiographics 32(4):1223-32, 2012 (PMCID PMC3393884).
3. Nair VS, Gevaert O, Davidzon G, Napel S, Graves EE, Hoang CD, Shrager JB, Quon A, **Rubin DL**, and Plevritis SK, Prognostic PET 18F-FDG uptake imaging features are associated with major oncogenomic alterations in patients with resected non-small cell lung cancer, Cancer Research 72(15):3725-34, 2012 (PMID 22710433).
4. Abajian A, Levy M, **Rubin DL**, Informatics in Radiology: Improving Clinical Work Flow through an AIM Database: A Sample Web-based Lesion Tracking Application, Radiographics 32(5):1543-52, 2012 (PMCID PMC3439633).
5. **Rubin DL**, Finding the Meaning in Images: Annotation and Image Markup. Psychiatry and Psychology, 18(4), 2012 (ISSN: 1071-6076).
6. Xu J, Faruque J, Beaulieu CF, **Rubin DL** and Napel S, A Comprehensive Descriptor of Shape: Method and Application to Content-Based Retrieval of Similar Appearing Lesions in Medical Images. J Digit Imaging, 25(1):121-8, 2012 (PMID: 21547518).
7. Xu J, Greenspan H, Napel S and **Rubin DL**, Automated temporal tracking and segmentation of lymphoma on serial CT examinations. Med Phys 38(11): 5879-86, 2011 (PMCID: 1711418).
8. Levy MA and **Rubin DL**, Computational approaches to assist in the evaluation of cancer treatment response. Imaging in Medicine 3(2): 233-246, 2011 (DOI: http://dx.doi.org/10.2217/iim.11.8).
9. Liu YI, Kamaya A, Desser TS and **Rubin DL**, A bayesian network for differentiating benign from malignant thyroid nodules using sonographic and demographic features. AJR Am J Roentgenol 196(5): W598-605, 2011 (PMID: 21512051).
10. Levy MA and **Rubin DL**, Current and future trends in imaging informatics for oncology. Cancer J 17(4): 203-10, 2011 (PMID: 21799326).
11. Korenblum D, **Rubin DL**, Napel S, Rodriguez C and Beaulieu C, Managing biomedical image metadata for search and retrieval of similar images. J Digit Imaging 24(4): 739-48, 2011 (PMID 3138941).
12. Kahn CE, Jr., Langlotz CP, Channin DS and **Rubin DL**, Informatics in radiology: an information model of the DICOM standard. Radiographics 31(1): 295-304, 2011 (PMID: 20980665).
13. **Rubin DL**, Flanders A, Kim W, Siddiqui KM, Kahn CE, Ontology-Assisted Analysis of Web Queries to Determine the Knowledge Radiologists Seek (JDI Best Paper Award), J Digital Imaging 24(1):160-4, 2011 (PMCID: 3046796).
14. Wu AS, Do BH, Kim J, **Rubin DL**. Evaluation of Negation and Uncertainty Detection and its Impact on Precision and Recall in Search. J Digital Imaging 24(2):234-42, 2011 (PMCID: 3056979).
15. **Rubin DL**, Wang D, Chambers DA, Chambers JG, South BR and Goldstein MK, AMIA Natural language processing for lines and devices in portable chest x-rays (AMIA Distinguished Paper Award). AMIA Annu Symp Proc 2010: 692-6, 2010 (PMID 3041297).
16. Napel SA, Beaulieu CF, Rodriguez C, Cui J, Xu J, Gupta A, Korenblum D, Greenspan H, Ma Y and **Rubin DL**, Automated retrieval of CT images of liver lesions on the basis of image similarity: method and preliminary results. Radiology 256(1): 243-52, 2010 (PMCID: 2897688).
17. Do B, Wu A, Biswal B, Kamaya A, **Rubin DL**, Informatics in radiology, RADTF: a semantic search-enabled, natural language processor-generated radiology teaching file. Radiographics 30(7):2039-48, 2010 (PMID: 20801868).
18. **Rubin DL** and Napel S, Imaging informatics: toward capturing and processing semantic information in radiology images. Yearbook Med Inform 34-42, 2010 (PMID 20938568).
19. Cooper L, Kong J, Gutman D, Wang F, Cholleti S, Pan T, Widener P, Sharma A, Mikkelsen T, Flanders A, **Rubin DL**, Van Meir E, Kurc T, Moreno C, Brat D, and Saltz J, An Integrative Approach for In Silico Glioma Research. An integrative approach for in silico glioma research. IEEE Trans Biomed Eng 57(10):2617-21 (PMID: 20656651).

20. Channin DS, Mongkolwat P, Kleper V, **Rubin DL**, The annotation and image mark-up project. Radiology 253:590-592, 2009 (PMID: 19952021).
21. Channin DS, Mongkolwat P, Kleper V, Sepukar K and **Rubin DL**, The caBIG Annotation and Image Markup Project. J Digit Imaging, 23(2):217-25, 2009 (PMCID: 2837161).
22. Kahn CE, Jr., **Rubin DL**, Automated semantic indexing of figure captions to improve radiology image retrieval. J Am Med Inform Assoc 16:380-386, 2009 (PMCID: 2732225).
23. Levy MA, O'Connor MJ, **Rubin DL**, Semantic Reasoning with Image Annotations for Tumor Assessment. AMIA Annu Symp Proc 359-363, 2009 (PMCID: 2815449).
24. **Rubin DL**, Mongkolwat P and Channin DS, A Semantic Image Annotation Model to Enable Integrative Translational Research. In: AMIA Summit on Translational Bioinformatics, San Francisco, CA, pp 106-110, 2009 (PMCID: 3041574).
25. Liu YI, Kamaya A, Desser TD and **Rubin DL**, A Controlled Vocabulary to Represent Sonographic Features of the Thyroid and its application in a Bayesian Network to Predict Thyroid Nodule Malignancy. AMIA Summit on Translational Bioinformatics, pp 68-72, 2009 (PMCID: 3041558).
26. **Rubin DL**, Supekar K, Mongkolwat P, Kleper V and Channin DS, Annotation and Image Markup: Accessing and Interoperating with the Semantic Content in Medical Imaging. IEEE Intelligent Systems 24(1): 57-65, 2009 (PMCID: 2837161).
27. **Rubin DL**, Talos IF, Halle M, Musen MA and Kikinis R, Computational neuroanatomy: ontology-based representation of neural components and connectivity. BMC Bioinformatics 10 Suppl 2: S3, 2009 (PMCID: 2646240).
28. **Rubin DL**, Rodriguez C, Shah P and Beaulieu C, iPad: Semantic Annotation and Markup of Radiological Images. AMIA Annu Symp Proc: 626-30, 2008 (PMCID: 2655990).
29. Mejino JL, **Rubin DL** and Brinkley JF, FMA-RadLex: An Application Ontology of Radiological Anatomy derived from the Foundational Model of Anatomy Reference Ontology. AMIA Annu Symp Proc: 465-9, 2008 (PMCID: 2656009).
30. Liu YI, Kamaya A, Desser TD and **Rubin DL**, A Bayesian Classifier for Differentiating Benign versus Malignant Thyroid Nodules using Sonographic Features. AMIA Annu Symp Proc: 419-23, 2008 (PMCID: 2656040).
31. Levy MA and **Rubin DL**, Tool support to enable evaluation of the clinical response to treatment. AMIA Annu Symp Proc: 399-403, 2008 (PMCID: 2655986).
32. **Rubin DL**, Mongkolwat P, Kleper V, Supekar K and Channin DS, Medical Imaging on the Semantic Web: Annotation and Image Markup. In: 2008 AAAI Spring Symposium Series, Semantic Scientific Knowledge Integration, Stanford University, 2008 (PMCID: 2655990).
33. **Rubin DL** and Desser TS, A data warehouse for integrating radiologic and pathologic data. J Am Coll Radiol 5(3): 210-7, 2008 (PMID: 18312970).
34. **Rubin DL**, Creating and curating a terminology for radiology: ontology modeling and analysis. J Digit Imaging 21(4): 355-62, 2008 (PMCID: 3043845).

C. Research Support.

Ongoing

National Institutes of Health U01 CA142555 (Rubin) 05/01/10 – 04/30/15

Title: *Computerized Quantitative Imaging Assessment of Tumor Burden*
Goal: The major goals of this project are to develop software infrastructure to evaluate tumor burden and treatment response.
Role: Principal Investigator

Radiological Society of North America (Rubin) 09/30/08 – 09/29/13
Title: *Enriching the RadLex Ontology to Enable Biomedical Imaging Research in Neuroimaging*

Goal: The major goals of this project are to develop an ontology of radiology to enable research in functional neuroimaging and other domains in radiology.
Role: Principal Investigator

General Electric Medical Systems (Rubin)
06/01/12 – 05/31/13
Title: *Next –Generation PACS 2.0: Content –Based Image Retrieval in Centricity System*
Goal: The major goals of this project are to develop a prototype system for retrieving images of similar-appearing images on the PACS.
Role: Principal Investigator

American College of Radiology -CA80098 (Rubin) 01/01/11 – 12/31/12
Title: *American College of Radiology Imaging Network (ACRIN) Committee Agreement*
Goal: The major goals of this project are to develop and implement emerging informatics standards to enable research in a large imaging research cooperative group.
Role: Principal Investigator

Brigham and Women's Hospital (Rubin)
06/01/12–5/31/13
NIH Prime 5P41 RR013218-12 (PI: Kikinis)
Title: *Neuroimaging Analysis Center (NAC)*
Goal: The major goals of this project are to create a functional-ontology-enhanced, three-dimensional brain atlas, by integrating ontologically modeled knowledge of brain function with geometric information
Role: Principal Investigator

National Institutes of Health R01 CA160251 (Napel/Plevritis) 09/15/11 – 07/31/16

Title: *Tools for Linking and Mining Image and Genomic Data in Non-Small Cell Lung Cancer*
Goal: The major goals of this project are to develop informatics methods of linking quantitative imaging data in lung cancer, integrating it with molecular data, and predicting clinical outcome and molecular events based on imaging data.
Role: Co-Investigator

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors in the order listed on Form Page 2.

Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME Mitchell D. Schnall, M.D., Ph.D.	POSITION TITLE Professor of Radiology
eRA COMMONS USER NAME (credential, e.g., agency login) schnallm	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	MM/YY	FIELD OF STUDY
University of Pennsylvania	BA	1981	Physics
University of Pennsylvania	MD	1986	Medicine
University of Pennsylvania	PhD	1986	Biophysics

A. Personal Statement

Dr. Schnall is the Eugene P Pendergrass Professor of Radiology, and the Chair of the Radiology Department at the Perelman School of Medicine at the University of Pennsylvania. Dr. Schnall is an international leader in translational biomedical imaging research. Through his career he has worked across the interface between basic imaging science and clinical medicine. His work has lead to fundamental changes in the imaging approaches to breast and prostate cancer. In addition, he has had a significant influence on emerging technologies such as optical imaging. Dr. Schnall has played a critical role in efforts to organize cancer clinical and translational imaging research in the US. He has been the principal investigator of numerous team science initiatives. He served ACRIN Deputy Chair from 1999-2007. In 2008 he assumed the role of ACRIN Chair. Among the important trials ACRIN completed under his leadership is the landmark National Lung Cancer Screening trial that demonstrated the ability of low done lung cancer screening to reduce lung cancer mortality by 20% in high risk patients. Dr. Schnall has been elected as a member of the American Society for Clinical Investigation, Association of American Physicians and the IOM. He is ideal to serve as Co-Chair of the merged ECOG-ACRIN Cancer Research group.

B. Positions and Honors

Positions and Employment

2012 Eugene P. Pendergrass Professor of Radiology, of Pennsylvania School of Medicine, Phila.
2008- American College of Radiology Imaging Network (ACRIN) –Chair
2004-08 American College of Radiology Imaging Network (ACRIN) – Deputy Chair
2002 Professor of Radiology
2001 Matthew J. Wilson Professor of Research Radiology
1998 Associate Professor with tenure
1994 Associate Professor, Department of Radiology, University of Pennsylvania School of

Medicine
1991 Assistant Professor, Department of Radiology, University of Pennsylvania School of Medicine, Phila.
1987 Assistant Instructor, Department of Radiology, University of Pennsylvania School of Medicine, Phila.
1987 Radiology Resident, Department of Radiology, Hospital of the University of Pennsylvania, Phila., PA
1986-87 Medical Internship, Lankenau Hospital, Wynnewood, PA
1982-86 NIH Medical Scientist Training Program Fellowship, University of Pennsylvania, Philadelphia, PA

Other Experience and Professional Memberships

1987- Radiological Society of North America
1990- International Society for Magnetic Resonance in Medicine
1995- American College of Radiology
2003- American Association for Cancer Research
2006- The American Society for Clinical Investigation (ASCI)
2007- RSNA Clinical Trials Methodology Workshop – Organizer
2009-2013 Member – Clinical Trials & Translational Research Advisory Committee (CTAC) of the NCI

Honors

2008 The American Society for Clinical Investigation (ASCI)
2009 The Association of American Physicians (AAP)
2010 Fellow in the American College of Radiology
2012 Elected to the IOM

C. Selected Peer-reviewed Publications

1. Lehman CD, Isaacs C, **Schnall MD**, Pisano ED, Ascher SM, Weatherall PT, Bluemke DA, Bowen DJ, Marcom PK, Armstrong DK, Domchek SM, Tomlinson G, Skates SJ, Gatsonis C Cancer yield of mammography, MR, and US in high-risk women: prospective multi-institution breast cancer screening study. Radiology. 2007 Aug;244(2):381-8.
2. Saslow D, Boetes C, Burke W, Harms S, Leach MO, Lehman CD, Morris E, Pisano E, **Schnall M**, Sener S, Smith RA, Warner E, Yaffe M, Andrews KS, Russell CA; American Cancer Society Breast Cancer Advisory Group American Cancer Society guidelines for breast screening with MRI as an adjunct to mammography. CA Cancer J Clin. 2007 Mar-Apr;57(2):75-89. Erratum in: CA Cancer J Clin. 2007 May-Jun;57(3):185.
3. Lehman CD, Gatsonis C, Kuhl CK, Hendrick RE, Pisano ED, Hanna L, Peacock S, Smazal SF, Maki DD, Julian TB, DePeri ER, Bluemke DA, **Schnall MD**. ACRIN Trial 6667 Investigators Group. MRI evaluation of the contralateral breast in women with recently diagnosed breast cancer. N Engl J Med. 2007 Mar 29;356(13):1295-303.
4. Kumar R, Zhuang H, **Schnall M**, Conant E, Damia S, Weinstein S, Chandra P, Czerniecki B, Alavi A. FDG PET positive lymph nodes are highly predictive of metastasis in breast cancer. Nucl Med Commun. 2006 Mar;27(3):231-6.
5. Solin LJ, Orel SG, Hwang WT, Harris EE, **Schnall MD**. Relationship of breast magnetic resonance imaging to outcome after breast-conservation treatment with radiation for

women with early-stage invasive breast carcinoma or ductal carcinoma in situ. J Clin Oncol. 2008 Jan 20;26(3):386-91. (PMID: 18202414)

6. Boo-Kyung H, **Schnall MD**, Orel SG, Rosen M. Outcome of MRI-guided breast biopsy. AJR 2008 Dec; 191:1-7
7. Dorfman GS, Sullivan DC, **Schnall MD**, Matrisian LM; for the Translational Research Working Group. The Translational Research Working Group Developmental Pathway for Image-Based Assessment Modalities. Clin Cancer Res. 2008 Sep 15;14(18):5678-5684. (PMID: 18794075)
8. Kim DY, **Schnall MD**, Rosen MA, Connick T. Prostate MR imaging at 3T with a longitudinal array endorectal surface coil and phased array body coil. J Magn Reson Imaging. 2008 Jun;27(6):1327-30. (PMID: 18504745)
9. Choe R, Konecky SD, Corlu A, Lee K, Durduran T, Busch DR, Pathak S, Czerniecki BJ, Tchou J, Fraker DL, Demichele A, Chance B, Arridge SR, Schweiger M, Culver JP, **Schnall MD**, Putt ME, Rosen MA, Yodh AG. Differentiation of benign and malignant breast tumors by in-vivio three-dimensional parallel-plate diffuse optical tomography. J Biomed Opt. 2009 mar-apr; 14(2): 024020. (PMID: 19405750)
10. Carton AK, Gavenonis SC, Currivan JA, Conant EF, **Schnall MD**, Maidment AD. Dual-energy contrast-enhanced digital breast tomosynthesis – a feasibility study. Br J Radiol. 2009 June 8. (PMID: 19505964)
11. Zheng Y and Englander, E, Baloch S, Zacharaki EI, Fan Y, **Schnall MD**, Shen D. STEP: Spatiotemporal enhancement pattern for MR-based breast tumor diagnosis. Med. Phys. July 2009; 36 (7): 3192-3204. (PMID: 19673218)
12. Weinstein SP, Localio AR, Conant EF, Rosen M, Thomas KM, **Schnall MD**. Multimodality screening of high-risk women: a prospective cohort study. J Clin Oncol, Dec. 2009; 27(36): 6124-8. (PMID: 19884532)
13. Tchou J, Sonnad SS, Bergey MR, Basu S, Tomaszewski J, Alavi A, **Schnall M**. Degree of tumor FDG uptake correlates with proliferation index in triple negative breast cancer. Mol Imaging Biol. 2010 Dec;12(6):657-62. (PMID: 20012701)
14. Busch DR, Guo W, Choe R, Durduran T, Feldman MD, Mies C, Rosen MA, **Schnall MD**, Czerniecki BJ, Tchou J, DeMichele A, Putt ME, Yodh AG. Computer aided automatic detection of malignant lesion in diffuse optical mammography. Med Phys, Apr 2010; 37(4): 1840-9. (PMID: 20443506)
15. Weinstein SP, Hanna LG, Gatsonis C, **Schnall MD**, Rosen MA, Lehman CD. Frequency of malignancy seen in probably benign lesions of contrast-enhanced breast MR imaging: findings from ACRIN 6667. Radiology, Jun 2010; 255(3): 731-7. (PMID: 20501712)
16. National Lung Screening Trial Research Team. N Engl J Med, August 4, 2011; 365(5); 395-409 (PMID: 21714641)
17. Hylton NM, Blume JD, Bernreuter WK, Pisano ED, Rosen MA, Morris EA, Weatherall PT, Lehman CD, Newstead GM, Polin S, Marques HS, Esserman LJ, **Schnall MD**; ACRIN 6657 Trial Team and I-SPY 1 TRIAL Investigators. Locally advanced breast cancer: MR imaging for prediction of response to neoadjuvant chemotherapy--results from ACRIN 6657/I-SPY TRIAL. Radiology. 2012 Jun;263(3):663-72. (PMID:22623692

D. Research Support

Ongoing:

U54-CA163313-01	Armstrong, Katrina, M.D.	9/21/2011-8/31/2016

NIH
Penn Center for Innovation in Personalized Breast Screening
This proposal will advance a personalized breast cancer screening paradigm by developing a new tool (breast complexity index) for predicting individual screening outcomes.

P30-CA016520-36 Rev Dang, Chi, V. 7/13/2011-11/30/2015
NIH
Abramson Cancer Center Core Support Grant
This grant supports the cancer research effort of the Abramson Cancer Center of the University of Pennsylvania.

Commonwealth of PA Kung, Hank, Ph.D. 6/1/2012-5/31/2014
New PET Imaging Agents for Cancer Diagnosis

Delaware State Univ./DOD Maidment, Andrew, Ph.D. 4/1/2009-3/31/2013
Delaware State University/DOD
Image Based Biomarkers of Breast Cancer Risk: Analysis of Risk Disparity among Minority Populations

P41-EB015893-28 Reddy, Ravinder, Ph.D. 6/1/2010-5/31/2015
NIH
A Resource for Magnetic Resonance and Optical Imaging
To develop innovative MR and optical technologies for biomedical research.

R01-CA131333-03 Schmitz, Kathryn 7/1/2008-5/31/2013
NIH
WISER Sister

ACR Chair Agreement Schnall, Mitchell, M.D., Ph.D. 1/1/2004-12/31/2012

ACRIN Committee or Subcommittee Chair Agreement
To serve as Deputy Chair of the ACR Imaging Network.

UL1-RR024134-06 Schnall, Mitchell, M.D., Ph.D. 7/1/2011-6/30/2016
NIH
Institutional Clinical and Translational Science Award

R01-EB002109-15 Schnall, Mitchell/Yodh, Arjun 6/1/2009-4/30/2013
NIH
Multi-Spectral Parallel-Plate Diffuse Optical Breast Tomography

R01-CA125226-03 Song, Hee-Kwon, Ph.D. 2/13/2009-1/31/2013
NIH
Novel Radial MRI Methods for Fast, Motion Compensated DCE-MRI
To develop, implement, validate and apply novel strategies for improved quantification of tumor contrast kinetics