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:** 2 - Development and Analysis of an Infrastructure for Review of Modern Clinical Trials that Include Radiotherapy

7. **Start and End Date of Research Project:** 1/1/2009 – 12/31/2012

8. **Name of Principal Investigator for the Research Project:** Elizabeth O'Meara, BS, CCRP, ARRT (R), (T)

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:

   $ 340,464.90

   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
O'Meara	Principle Investigator	5% Yr 1;10% Yr 2	$14,891.75
Xiao	Co-Investigator	2% Yrs 2-4	$22,406.5
Galvin	Co-Investigator	5% Yrs 2-4	$37,344.17
Presley	Dosimetrist	14% Yr 3; 12% Yr 4	$28,746.80
Cui	Post-Doc	10% Yrs 3-4	$18,672.09
Chen	Post-Doc	10% Yrs 3-4	$18,672.09

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
None		

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
None		

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___X_____

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

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___X_____ 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:
Imaging and Radiation Oncology Core (IROC)*	☒ NIH ☐ Other federal (specify:_____) ☐ Nonfederal source (specify:_)	Jan 2013	$14,000,000**	Not reviewed yet
NRG Oncology Center of Innovative Radiation Oncology*	☒ NIH ☐ Other federal (specify:_____) ☐ Nonfederal source (specify:_)	Jan 2013	$10,000**	Not reviewed yet

* Results from the CURE grant were included in the application.
**Amount in Column D is the year one funding for the research that references work completed under the CURE grant. Total funds requested for the grant maybe higher.

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

Yes_____ No____X_____

If yes, please describe your plans:

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

Incorporate the research outcome from this project to the proposed NCI clinical trial network (NCTN) conduct and investigations with multiple investigators.

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___X_____ No_____

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

	Undergraduate	Masters	Pre-doc	Post-doc
Male				2
Female				
Unknown				
Total				**2**

	Undergraduate	Masters	Pre-doc	Post-doc
Hispanic				
Non-Hispanic				2
Unknown				
Total				**2**

	Undergraduate	Masters	Pre-doc	Post-doc
White				
Black				
Asian				2
Other				
Unknown				
Total				**2**

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

    Yes_____ No___X_____

    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____X_____ No_____

    If yes, describe how improvements in infrastructure, the addition of new investigators, and other resources have led to more and better research.
    .
    We have developed, for investigators, an infrastructure for review of modern clinical trials that include Radiotherapy and have trained these investigators on these tools.

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___X_____ No_____

If yes, please describe the collaborations:

The following sites collaborated in piloting the tools for review of clinical trials utilizing radiation therapy as a treatment modality.

Fudan, Shanghai, China
MAASTRO, Netherlands
Duke University

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

Yes_____ No____X_____

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_____X_____

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.

This project resulted in the development of an infrastructure for review of clinical trials, that includes Radiotherapy.

1. System acquisition and upgrade

We acquired three review systems that were needed for the clinical trial cases, in order to utilize the latest technologies. The systems acquired for the Radiation Therapy RT Core Laboratory included, Elekta IMPAC MOSAIQ/MOSAIQ PACs electronic medical records, Varian ARIA Oncology Information System/Eclipse Treatment Planning System, MiMvista (MIM) deformable dose accumulation and fusion.

MIMcontouring (MIM) is software that provides advanced multi-modality image review manipulation, analysis, and fusion. Contouring tools aid in the definition of target volumes and normal tissue using fast, 3D methods for Positron Emission Tomography (PET), Singe Photon emission Tomography (SPECT), Computed Tomography (CT), and Magnetic Resonance Imaging (MRI). Velocity AI (Advanced Imaging) is an imaging informatics software with image registration and contouring capabilities is an application that features multi-modality image registration and automated tumor contouring technology. This allows various scans such as PET, CT, MR and SPECT to be overlaid, used and assessed together.

We acquired Matlab licenses for numerical computations with matrices and vectors. Mathwork's MATLAB is a high-level language and interactive environment that enables you to perform computationally intensive tasks faster than with traditional programming languages such as C, C++, and Fortran.

We also acquired:

- Elekta Monaco Workstation with IMRT and VMAT Software.
- Stand-alone radiation therapy & medical image viewing and treatment planning platform with Monte Carlo and Pencil Beam dose algorithms,
- Biologically-based optimization, smart sequencing,
- Voxel Definition Controls, Multi-Plan Viewing - Compare Dose distributions and

- DVH for up to three alternative plans simultaneously,
- Dose Cursor Tool, Summation and subtraction of dose plans,
- Contouring Tools including Auto-Segmentation, 3D Variable, Margin and Unique Drawing assistant.
- Real-Time Imaging for final beam arrangement with dose approval,
- Function, Imaging Tools including Window and Level controls, Synchronized Zoom and Pan with independent Transverse, Sagittal and Coronal viewing.
- View DVH, Ports Real-time, high resolution Digitally Reconstructed Radiographs including Maximum Intensity Projection (Virtual fluoroscopy).
- The Visual tools for Isocenter, Beam entry, Gantry, Collimator placement and MLC run on Windows XP or later operating systems.
- We've also acquired Nucletron Oncentra where we will be evaluating Proton plans which include CT images, structures, and dose constraints.

After their acquisition, upgrades were performed for the following systems, with the goal of implementing and testing the improvements needed to meet the demands of the cooperative group protocols that utilize advanced technologies, and related to our strategic plan of gathering and analyzing data on the effectiveness of tools for case review.

- *Monaco® treatment planning system (Elekta CMS, Maryland Heights, MO)*
- *Oncentra® MasterPlan treatment planning system (Elekta Nucletron, Veenendaal, The Netherlands)*
- *VelocityAI (Velocity Medical Solutions, Atlanta, GA)*

2. IGRT Credentialing

With our Image Guided Radiation Therapy (IGRT) Reviews we created IGRT instructional documents for each process to streamline the processes.

An IGRT data integrity checklist below was developed to:

1. Verify that data was anonymized properly (i.e. date info is preserved in DICOM)
2. Confirm IGRT credentialing.
3. Verify the 2D IGRT**:** 2D registration screen captures were included. Two orthogonal images with corresponding DRRs in DICOM RT format were optional. The number of daily treatment images was protocol specific. The number is usually 5 if not otherwise indicated in protocol.
4. Confirm that Pre- shift images / screen captures (and post- shift images only if specified in the protocol) were submitted. Confirm that all 2D IGRT data was copied to protocol Sharepoint.
5. Verify the 3D IGRT**:** 3D in-room images (e.g. kV CBCT, MV CT) were included together with the planning CT, RT PLAN, RT STRUCT, and RT DOSE. . The number of daily treatment images was protocol specific. This number is usually 5 if not otherwise indicated in protocol.
6. Confirm that all 3D IGRT data was submitted to the assigned protocol SFTP site.

IGRT Credentialing May-2010: The institutions downloaded this new IGRT credentialing form for their IGRT data submission.

IGRT Review Instruction May-2010: Each Physics PI, were notified that there were new IGRT cases waiting for them to review.

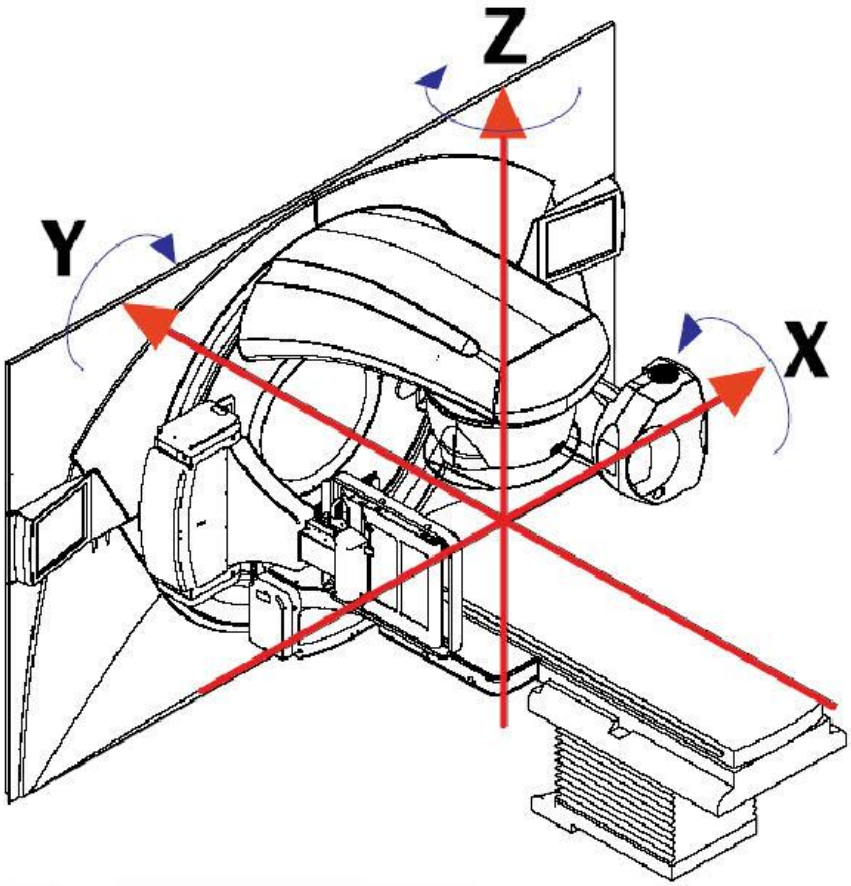
IGRT Review Worksheet May-2010: We created a document "Instruction for preparing the IGRT data for the reviewers.doc" regarding how to use this worksheet. This worksheet was designed to convert the registration shifts and rotations derived from MIM to the shifts and rotations designated by IGRT Credentialing Spreadsheet.

Spreadsheet for IGRT Credentialing Data Collection for Anonymized Patients

Date	Tr #	IGRT technique[2]	Iso-center shift X (mm)[1]	Iso-center shift Y (mm)[1]	Iso-center shift Z (mm)[1]	Couch rot-ation around X (◦)[1]	Couch rot-ation around Y (◦)[1]	Couch rot-ation around Z (◦)[1]	IGRT time pt[3]	Was a reposi-tioning made pre-rx?[4]

Process:
The definition of XYZ translations and rotations in MIM: (with the patient lying in the conventional (supine) position with head towards gantry).

1. Record shift and rotation numbers according to the following definition of the dimensions: (Please make sure to use correct positive or negative sign. Note that the shifts are defined as the difference between planned isocenter and imaging center, i.e. shift = planned isocenter – imaging center. For example, if the imaging center is 1.0 cm in the positive X direction from the isocenter, this should be reported as an X shift of -1.0cm or -10mm)



Definition of XYZ dimension (arrowheads indicate positive directions for shifts & rotations)

2. An institution should have a primary means of IGRT.
   KVCB = KV Cone Beam CT scan
   MVCB = MV Cone Beam CT scan
   KVCT = KV Fan Beam CT scan (e.g., in-room diagnostic CT)
   MVCT = MV Fan Beam CT scan (e.g., Tomotherapy)
   MVorth = MV orthogonal images
   KVorth = KV orthogonal images

However, an institution may use a backup system for IGRT if necessary – for example if an institution's KVCB is not working one day, they may use MVorth. Portal imaging with radiographic film (MVForth) can be used for backup only.

3. When the Images were obtained relative to treatment.
   A = Prior to treatment -- Immediately after immobilizing patient using marks on mask – no prior imaging;
   B = Re-imaging -- Prior to treatment but after a previous positioning and/or imaging procedure.
   C = Post-treatment imaging.

Note that, although only “A” is required normally, “B” or “C” may be requested when the repositioning shift is ≥ 2 cm in any direction. For the 5-day pre-treatment images required for IGRT credentialing, both “A” and “B” or “C” for at least two days should be submitted.

4. If a repositioning was made and the shift was ≥ 2 cm in any direction, either Re-imaging or Post treatment imaging should be obtained (thus the patient will have two IGRT datasets for that day’s treatment).

3. Systems supporting clinical trials and analysis

We’ve focused our efforts with this research project, on the evaluation of systems to support clinical trials, with further upgrading of the Velocity Advanced Imaging Informatics Software System with image registration and contouring capabilities and launched XenApp for web-based access to Core Lab applications. This XenApp is the latest Citrix technology for distributed, web-based access. It enables cross-platform delivery (access from desktops, laptops, PDAs). It leverages local graphics processor, multi-monitor and 5.8 megapixel display.

For a Phase II trial of Hippocampal Avoidance during whole Brain Radiotheapy for Brain Metastases, we evaluated these systems: MIMvista, Velocity AI, MOSAIQ, and CERR for functions for contouring evaluation and dose/volume evaluation. We identified the systems for the review process and software tools developed (Figure 1).

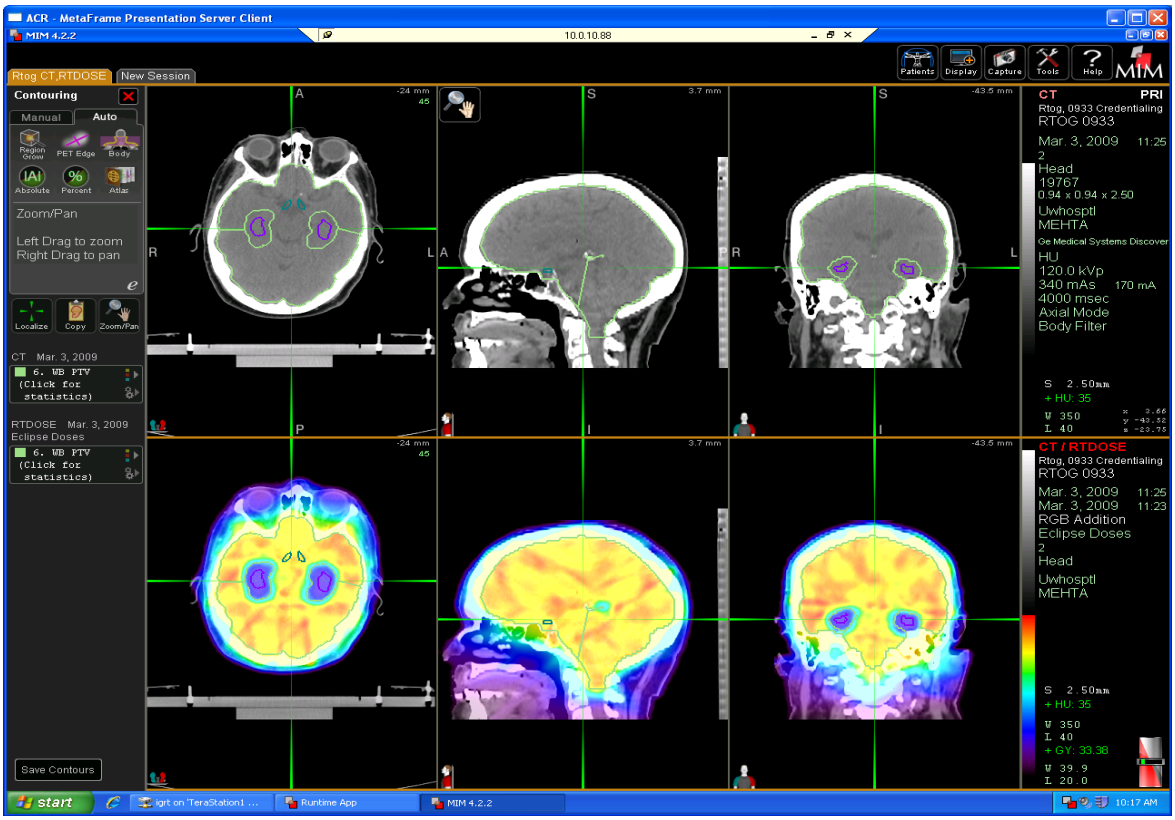


Figure 1a. Evaluating hippocampus contours using MIMvista

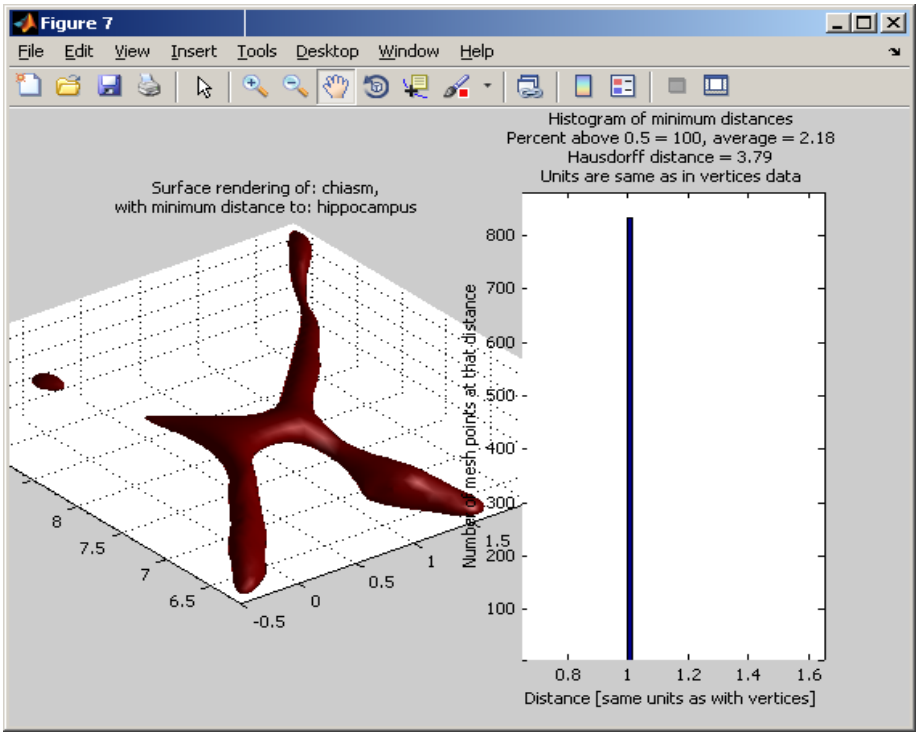


Figure 1b. Compare physician's hippocampus contour with gold standard contour by calculating Hausdorff distance between them using a MATLAB program

For a Phase III trial evaluating both Erlotinib and Chemoradiaiton as adjuvant treatment for patients with resected head of Pancreas Adenocarcinoma we evaluated these systems: MIMvista, Velocity AI, MOSAIQ, and CERR for functions for contouring evaluation and dose/volume evaluation. We've identified the system for the review process (Figure 2).

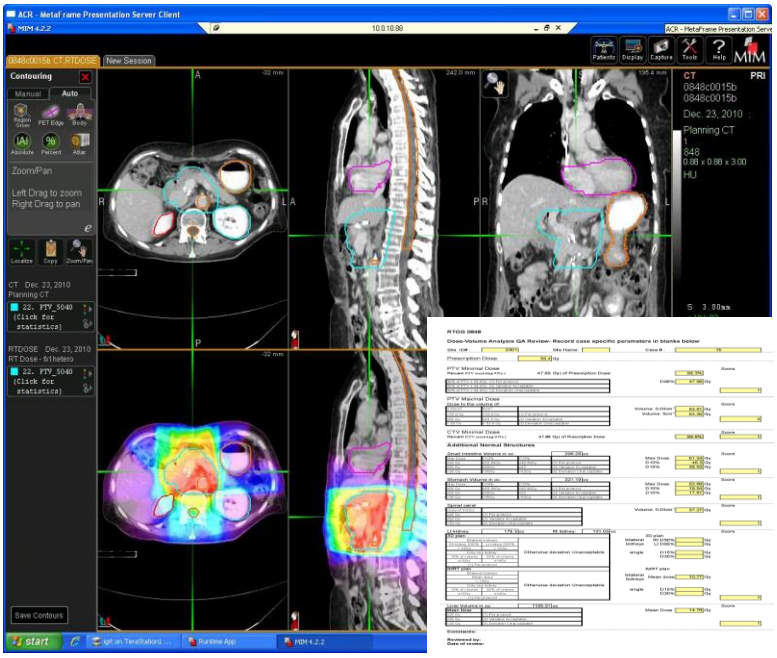


Figure 2. Treatment plan review with MIMvista and Dose-Volume Analysis form

For an Image Guided approval process, we evaluated systems: MiMvista, Velocity AI, MOSAIQ, and CERR for functions for 3D and 2D registration accuracy (Figure 3).

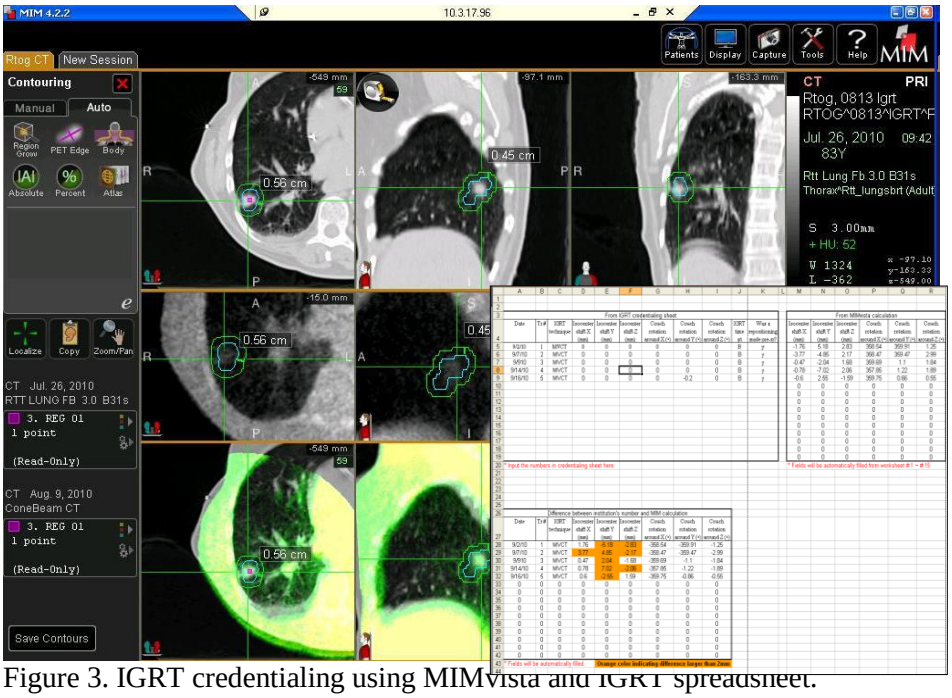


Figure 3. IGRT credentialing using MIMvista and IGRT spreadsheet.

For a Randomized Phase II trial of Individualized Adaptive Radiation used during treatment FDG-PET/CT and modern Radiation Technology to dose escalated in locally advanced Non-Small Cell Lung Cancer (NSCLC), we evaluated: Pinnacle, XiO, Eclipse and CERR for contour evaluation, planning technique and optimization. Figure 4

Figure 4. Analyzing RTOG 1106 dry run cases with MIMvista and CERR

With the IT infrastructure, we integrated imaging/RT systems for onsite and remote usage and the evaluation of devices and systems with physician and medical physics support to further scientific investigation (Figure 5).

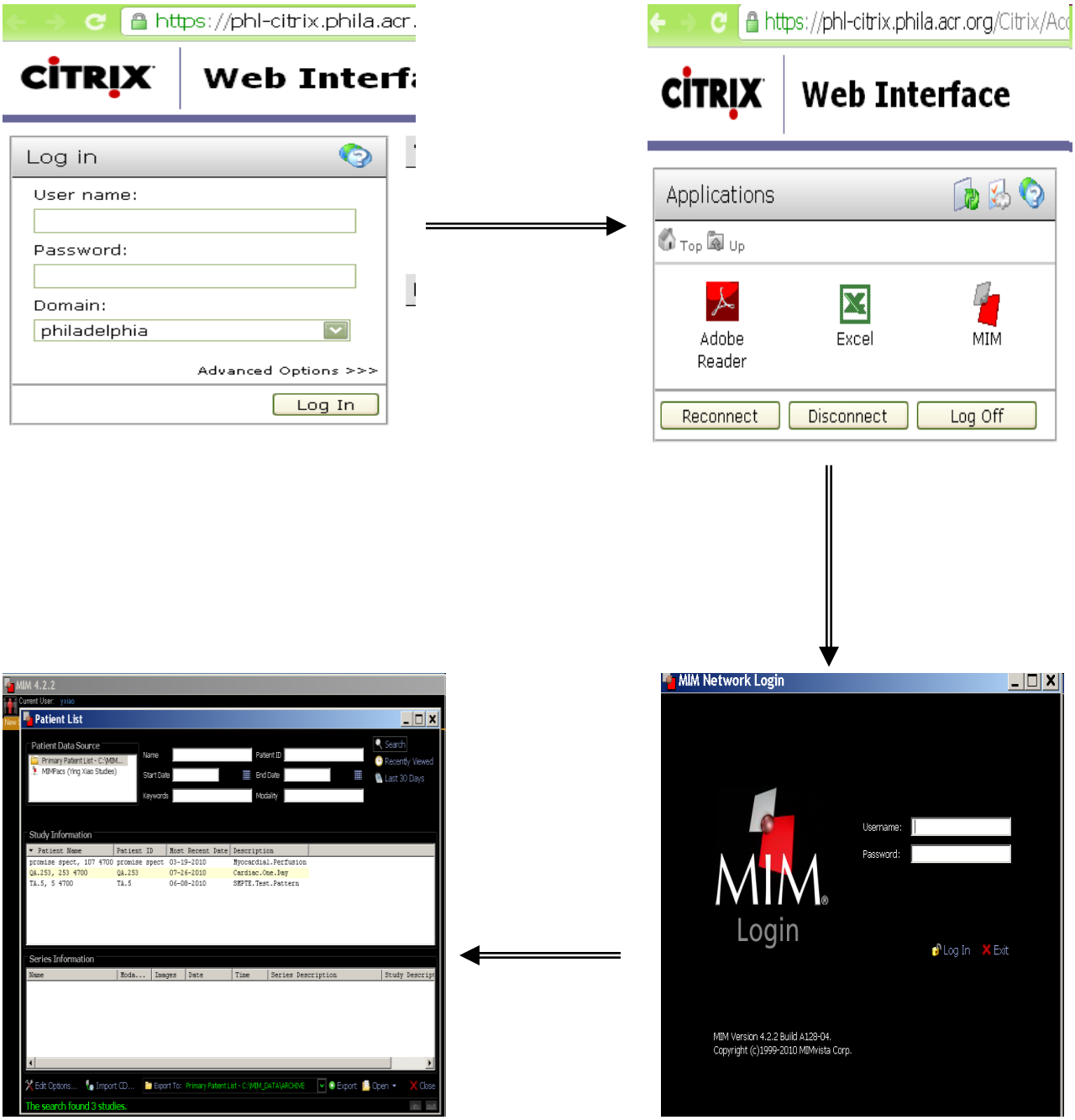


Figure 5. Utilizing Citrix server for remote review

There were two abstracts presented at the 2011 American Society for Radiation Oncology (ASTRO) Annual Meeting based on these applications. One of them is titled “Using During-RT

PET to Individualize Adaptive RT for Patients with Stage III NSCLC: A RTOG Planning Study", and another is "Initial Experience With A Pre-Clinical Trial Process for A Dosimetric Feasibility Study of Adaptive Radiotherapy for Patients With Stage III NSCLC".

4. Establishing the Computer Assisted Theragnostics (CAT) network at RTOG - A rapid learning community

This study provided a feasible solution to the data sharing issues between institutions and organizations who work on data analysis. Firewalls and political barriers that prevent institutions from sharing data with another party, hampers the ability of a PI to review cases at will and hinders data analysis from being done. The strategy of the CAT network overcame this issue and also demonstrated a good example of gathering and analyzing data on the effectiveness tool.

In detail, a rapid learning health care system has been proposed to supplement or even drive clinical trials in personalised medicine. In such a system, routine clinical data is used to extract and continuously update knowledge. But the sharing of routine clinical data is hampered by political, administrative and ethical barriers. In this study we aimed to describe a rapid learning community that has overcome these barriers and shares routine patient data. We hypothesize that the knowledge extracted from this community is better than knowledge extracted from individual institutes. In detail, a rapid learning community was formed based on the Computer Assisted Theragnostics (CAT) system. This system meets three high level requirements: a) individual patient data never leaves the hospital, b) analysis comes to the data, is transparent and is statistical in nature, and c) full semantic interoperability is achieved for all patients with limited resources. The CAT system was used to learn a prediction model for two-year survival of head and neck cancer patients treated with radiation therapy. We compared learning the model in individual institutes to community learning, in which the model was learned in a distributed manner in data from two community members. The CAT system was reviewed and approved by seven institutes and review boards from five countries (Netherlands, Belgium, Italy, Germany and USA). As a result, community learning led to a prediction model that performed markedly and significantly better than a model based on learning the model from data from individual institutes (Table 1). In conclusion, a rapid learning community is feasible when it is supported by a system that addresses administrative, ethical and political barriers to sharing data. Such a community can be used to extract knowledge which is more accurate than the knowledge gained by individual centres.

Table 1. Area-Under the Curve (AUC) discriminatory performance for models learned at MAASTRO ($M_{MAASTRO}$), RTOG (M_{RTOG}) and in both ($M_{COMMUNITY}$).

	$M_{MAASTRO}$	M_{RTOG}	$M_{COMMUNITY}$
Validated in MAASTRO	0.68* (0.62-0.74)	0.62* (0.56-0.68)	0.68* (0.62-0.74)
Validated in RTOG	0.62* (0.56-0.68)	0.68* (0.62-0.74)	0.68* (0.62-0.74)
Validated in COMMUNITY	0.64* (0.58-0.70)	0.64* (0.58-0.70)	0.68* (0.62-0.74)

* different from random; (confidence interval) determined by bootstrapping.

5. Equip Core Lab with tools for latest technology and apply these tools for technology analysis - a planning study and surface dose verification for breast tangential treatment plan using flattening filter free beams

This research study related to the goal of implementing and testing the improvements needed to meet the demands of the cooperative group protocols that utilize advanced technologies. The latest flattening filter free beams were modelled in the treatment planning system in the Core Lab to provide a tool to review and analyze cases planed with this new technology. It relates to our strategic plan of gathering and analyzing data on the effectiveness of tools for case review.

The study aimed to evaluate the feasibility of using flattening filter free (FFF) beams (Figure 6) for tangential supine whole breast radiotherapy and to describe the dosimetric characteristics for supine whole breast tangential-field treatment plans using flattening filter (FF) beams with dynamic wedges. The study also performed surface dose measurements for FFF beams. In detail, supine breast cancer plans of ten patients were analyzed for the feasibility planning study. Two half-beam (with and without flattening filter, and one non-divergent edge) tangential treatment plans were created on a treatment planning system (TPS) for each patient. This study compared plan features including, target dose, dose distribution to the organ at risk (OAR) and the unspecified tissue, as well as average monitor unit (MU) and beam-on time for plans with FFF and with FF beams. A Rando phantom and InLightTM nanoDots Optically stimulated luminescence dosimetry (OSLD) system were used to measure surface doses at medial, apex and lateral locations from central plane, as well as positions from caudal and cranial regions of plans with FFF beams. As the results showed, all of the FFF plans were clinically acceptable (Figure 7). The wedge angles of FF plans ranged between 25° to 45°. For target dose homogeneity, the average reduction of V105% was on average 21.91% (standard deviation 7.43%) when FFF beams were used. Both FF and FFF tangential plans predicted similar low doses to the ipsilateral lung and to the heart of left breast cancer patients (Figure 8). Compared with FF plans, The FFF plans predicted lower dose to unspecified tissue outside the field and shorter beam-on time. Surface dose of FFF plans were 2.2%-4.7% lower than those with flattened beams with wedges, when doses at deeper depth from central axis stay close in value (Figure 9). In the apex region of central plane, the OSLD readouts are 6.1%-7.9% higher than calculated values. In the caudal and cranial regions, TPS underestimated the surface dose from 3.8%-5.1%. In the medial and lateral regions are 14.6%-17.5% (Table 2). In conclusion, tangential plans with FFF beams showed superior dosimetric quality for breast cancer treatment, lower surface dose and lower dose to unspecified tissue outside the target. Higher dose rate is also a factor to significantly reduce beam-on time, potentially minimizing the effect of organ motion and potentially simplifying the use of motion management techniques for critical structure dose reduction.

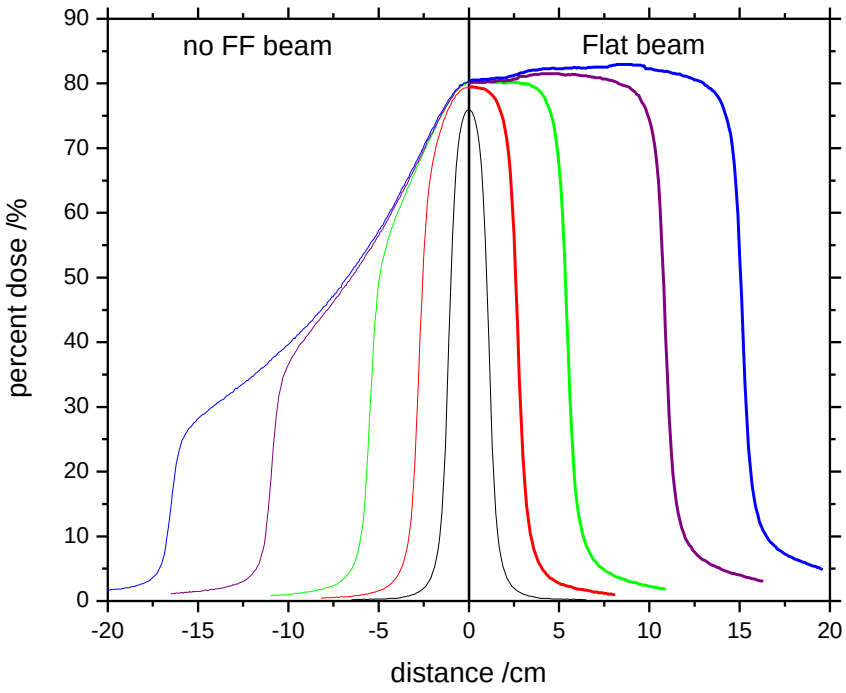


Figure 6. Profile from FFF beam

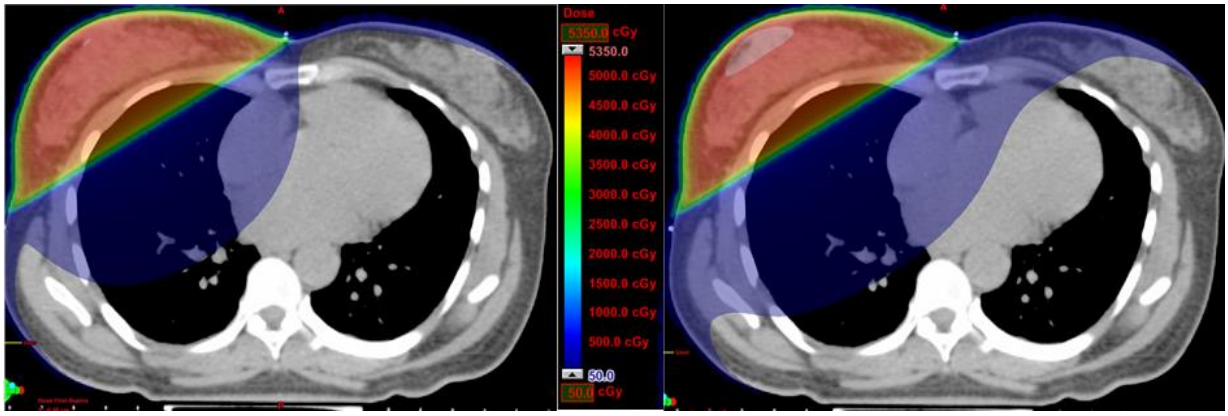
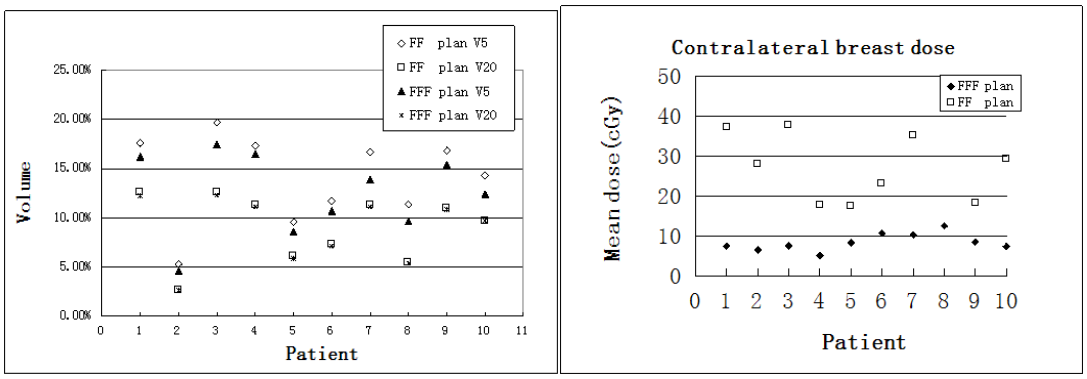


Figure 7. Dose distribution on patient. The FFF plan on the left is similar to the FF plan on the right. The low dose region in normal tissue is reduced for FFF plan.



(a) (b)

Figure 8. Comparison of (a) ipsilateral lung dose and (b) contralateral breast dose.

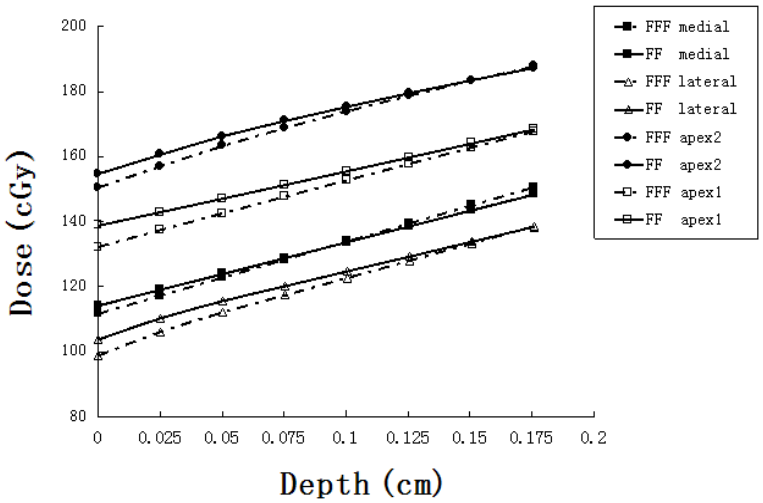


Figure 9. Surface dose validation

Table 2. Measurement validation from OSLD.

Position	Measured (cGy)	Calculated (cGy)	Deviation (%)
Apex 1	151.87±1.23%	142.60±1.93%	6.1
Apex 2	177.35±0.56%	163.26±1.88%	7.9
Medial	149.35±1.50%	122.81±0.63%	17.5
Lateral	131.30±1.39%	112.10±1.95%	14.6
Cranial	136.98±0.91%	130.90±5.53%	5.1
Caudal	143.03±1.12%	137.60±3.99%	3.8

6. An automated plan-quality evaluation program for multi-institutional clinical trials

The aim of this study was to develop a plan-quality evaluation program for multi-institutional clinical trials so that the overall evaluation efficiency and accuracy were improved.

In multi-institutional clinical trials evaluating the plan-quality is a time-consuming and labor-intensive process. The commonly used method for the evaluation is to compare the dosimetry parameters with preset criteria. Normally this is carried out manually by reading the parameters from the dose volume histogram (DVH). For a large amount of institutional data and rapid case reviews, human errors can be readily introduced into the process. We developed an automatic plan-quality evaluation program which combined the virtues of MIM, which is an innovative web-based solution for remote image access and secure storage. MIM workstation software provides clinicians with easy access to their patient's images, as well as short-term or long-term data storage, Java/MATLAB, which is a high-level technical computing language and interactive environment for algorithm development, data visualization, data analysis, and numerical computation and extensible markup language (XML). More specifically, MIM was used for data visualize; Java and its powerful function library are implemented for calculating dosimetry parameters; to improve the clarity of the index definitions, XML was applied. Figure 10 shows the workflow of this program's algorithm.

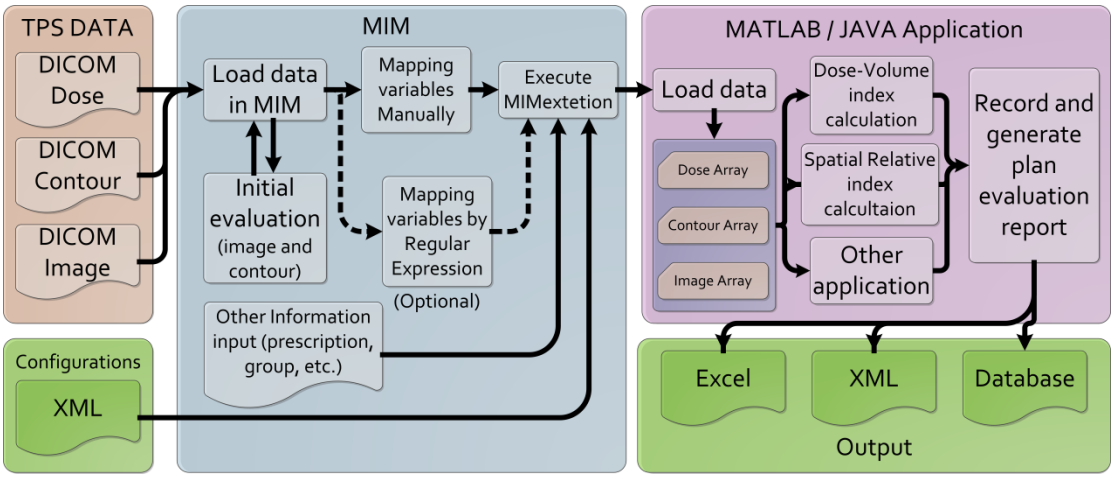


Figure 10. The workflow of the algorithm.

The accuracy and the efficiency of the program were evaluated by comparing the automated program to manual recording for two RTOG protocols (1005 and 1016). ROTG 1005 is a breast radiotherapy trial with 2 arms including a boost dose which means that each patient has two dose distributions. Some criteria in this protocol are related to the prescription which is variable between patients. The full protocol has 18 indices. RTOG 1016 is a head and neck trial protocol which has 9 indices. Table 1 shows a section of the dose-volume index of those two protocols. We selected 11 patients (5 from 1005, 6 from 1016) from the database to test the accuracy and the efficiency of this tool. The manual recording data was obtained from MIM. The manual recording processing was executed by a physicist who had a full understanding of the indices and protocol. All times for calculating the efficiency of each method were established by using the computer's clock.

A slight difference between the automatic program and manual recording was observed (Figure 11). Most of the differences were less than 0.2% or 0.2Gy except the minimum dose which had the maximum difference of about 0.6Gy. According to the criteria of index defined in the XML setting file, there was minimal differences between the two methods.

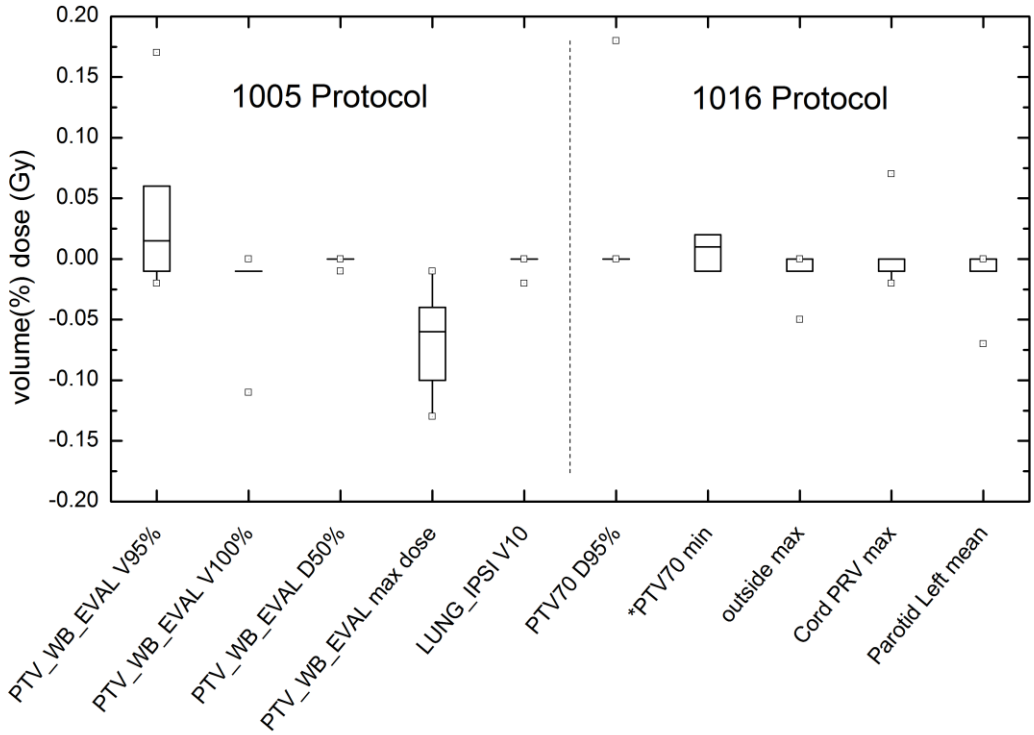


Figure 11. Differences between the automatic result and manual recording (the unit for volume is percent and the unit for dose is Gy).

The accuracy and the efficiency of the program were evaluated by comparing the results of the program with the manually recorded results in two RTOG trials. ROTG 1005 is breast radiotherapy trial in which 18 indexes were recorded. RTOG 1016 is head and neck trial which has 9 indexes. We selected 11 institutions (5 from RTOG 1005, 6 from ROTG 1016) from the database to test the accuracy and the efficiency of our program. The manual recording process was executed by a physicist.

The average time for the automatic program to generate the report for protocol 1016 is 2 minutes (range 1.9-2.1 minutes) which includes manual contour name mapping and program calculation. The average time to manually record a case is about 10.3 minutes (range 9.0-12.1 minutes) for protocol 1016. The average time for the automatic program to generate the report for protocol 1005 is 2 minutes (range 1.9-2.1 minutes) as well. It requires 20.5 minutes (range 19.1-22.1 minutes) manually. The protocol 1005 is more complex than protocol 1016 so the time needed for manual recording was much longer. For the automatic program evaluation, no significant time difference between two protocols was observed ($p=0.946$, T-test).

In summary, we developed a plan-quality evaluation program for multi-institutional clinical trials, and the overall evaluation efficiency and accuracy are improved.

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
___X__No

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

_____Yes
___X__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
___X_ 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. Multi-System Verification Of Registrations For Image-Guided Radiotherapy In Clinical Trials	Yunfeng Cui, James Galvin, William Straube, Walter Bosch, James Purdy, Allen Li, Ying Xiao	International Journal of Radiation Oncology, Biology, Physics	March 2010	☐Submitted ☐Accepted ☒Published

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

Yes____X_____ No_____

If yes, please describe your plans:

From this research, we plan to submit articles so other investigators can be informed of the needs for an infrastructure for review of modern clinical trials that include Radiotherapy.

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.

The research from this study led to a design and implementation of multi-institutional quality assurance system for image-guided radiation therapy. This process potentially reduces the major uncertainty associated with patient positioning during radiotherapy treatment, thereby enabling more dose to target and less dose to critical structures. This concentration of dose to tumor may lead to better survival and better quality of life.

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.

We have built a novel data-sharing infrastructure for investigations. We designed and implemented a new system for quality assurance of image-guided radiotherapy for multi-institutional clinical trials. We have introduced innovative mathematics methodology for uncertainty evaluation.

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___X_____

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____X_____

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 Elizabeth A. O'Meara	POSITION TITLE Senior Director, Radiation Oncology Services
eRA COMMONS USER NAME (credential, e.g., agency login)	

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 St. Francis, Joliet, IL	B.S.	1995 –1999	Health Arts
Albert Einstein Medical Center, Philadelphia, PA	RT (R)	1974-1976	Radiologic Technology
Cooper Hospital/University Med Ctr, Camden. NJ	RT(T)	1984-1985	Radiation Therapy
Hahnemann University Hospital, Philadelphia, PA	CMD	1985-19986	Dosimetry/radiation Phy
Society of Clinical Research Associates	CCRP	2000-2002	Clinical Research

A. Personal Statement

As Senior Director of Radiation Oncology Services at Radiation Therapy Oncology Group I have the opportunity to participate in this important clinical research. I have extension knowledge of radiation dosimetry, radiation dosimetry quality assurance and the application of these concepts to the cooperative clinical trial setting. The goal of the proposed research is to assure the NCI Nation that the radiation doses delivered in clinical trials to patients are accurate with minimal uncertainty. My professional experience and expertise in the clinical trial setting will be instrumental with the IROC group.

B. Positions and Honors

Positions and Employment

2011-present	Senior Director, Radiation Oncology Services, American College of Radiology, Philadelphia PA
2008-2011	Director, RT Quality Assurance and Core Lab Operations, American College of Radiology, Philadelphia, PA
1999-2008	Director, RT Quality Assurance, American College of Radiology, Philadelphia, PA
1997-1999	Chief Dosimetrist, RTQA, American College of Radiology, Philadelphia, PA
1993-1997	Dosimetrist, RTQA, American College of Radiology, Philadelphia, PA
1990-1993	Administrative Manager, R.T. Temps, Inc., Philadelphia, PA

1981-1990	Dosimetrist/Radiation Therapist, Hahnemann University Hospital, Philadelphia, PA
1977-1981	Simulation Technologist, Hahnemann University Hospital, Philadelphia, PA
1975-1977	Staff Radiologic Technologist, Albert Einstein Medical Center, Philadelphia, PA

Honors

1985	Varian Award for Clinical Excellence, Cooper Hospital/University
1976	Women's League for Medical Research, Albert Einstein Medical Center, ND

C. Selected Peer-reviewed Publications

1. Michalski, J., Winter, K., Purdy, J., Martin, E., Gillin, M. and Curran Jr, W.: Image Guided Radiation Therapy in the RTOG. 4th S Takahashi Int'l Workshop on 3D Conformal RT, Nagoya, Japan, Int J Radiat Oncol Biol Phys, pg. Abs. 2004.
2. Young, B. K., Martin, E., Hoffman, W., Wudarski, T., King, S., Brasteter, H., Galvin, J. and Curran Jr, W.: Adaptive Protocol Development And Trial Initiation: RTOG's Experience In The Current Clinical Trials Environment. Proc Amer Soc Thera Rad Onc (ASTRO), Philadelphia, PA, Int J Rad Onc Bio Phys, 2006.
3. O'Meara, E.A, Machtay, M., Moughan, J., McIlvaine, J., Galvin, J., Forastiere, A., Trotti, A., Garden, A., Cooper, J., Ang, K.: Associations between Radiation Doses to Pharyngeal Regions and Severe Late Toxicity in Head and Neck Cancer Patients Treated with Concurrent Chemoradiotherapy -- An RTOG Analysis. Amer Soc Thera Rad Onc (ASTRO), Los Angeles, CA.
4. Bosch, W.R., Straube, W.L., Matthews, J.W., Michalski, J., Deasy, J., Young, B., O'Meara, E., Curran, W.J., Cox, J., Purdy, J.: A Survey of the ITC Volumetric Treatment Planning Data Archive Supporting RTOG Advanced Technology Clinical Trials. Amer Soc Thera Rad Onc (ASTRO), Los Angeles, CA.
5. Martin, E., Lustig, R., Harris, J., Dunning, B., Lu, J., Huq, S., Curran, W.: Validation of the Sampling Technique Used in the Radiation Therapy Oncology Group's (RTOG) Quality Assurance Program. Society for Clinical Trials, Anaheim, CA.

D. Research Support - Ongoing Research Support

5 U10 CA021661-32 Curran (PI) 1/1/02-12/31/08
NIH/DC
Radiation Therapy Oncology Group (RTOG)
Main Goal: RTOG is an NCI-funded cooperative group seeking to improve upon the outcome of selected cancer patients through well-executed clinical trials.
Role: Chief Dosimetrist & RT QA Director

Development and Analysis of an Infrastructure for Review of Modern Clinical Trials that Include Radiotherapy
State of Pennsylvania, Radiation Therapy Oncology Group (RTOG), 2009-2013
Overall goals: Designing the review tools needed for future cooperative group protocols that might include one or more advanced technology

Responsibility: Design and implement review systems and tools for advanced technology for RTOG core lab
Role: Senior Director, Radiation Oncology Services

Radiation Therapy Oncology Group – IROC Group Transition Supplement
NIH/NCI, 2012
Overall goals: Transition and re-organization of clinical trial and QA groups
Responsibility: grant preparation for the transition
Role: Senior Director, Radiation Oncology Services

Completed Research Support

ME 02-290 Curran (PI) 7/01/97 - 6/30/05
Pennsylvania Department of Health
Main Goal: Cancer Center Support for Clinical Science Division, Cancer Prevention and Control Division, and Cancer Advocacy and Survivorship Program of the cancer center.
Role: Chief Dosimetrist & RT QA Director

2 U24 CA 081647-07 Purdy (PI) 7/22/01-6/30/07
NCI/DCTD
Advanced Technology QA Center
Main Goal: To capitalize on the infrastructure and strengths of the existing national quality assurance programs to create an Advanced Technology Radiation Therapy Clinical Trials Support QA Consortium
Role: Chief Dosimetrist & RT QA Director

BIOGRAPHICAL SKETCH

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

NAME Ying Xiao, PhD	POSITION TITLE Professor, Department of Radiation Oncology, Jefferson Medical College
eRA COMMONS USER NAME (credential, e.g., agency login)	

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
Tsinghua University, Beijing, China	BS	July 1989	Optical engineering
Temple University, Philadelphia, PA	MS	May 1992	Physics
Temple University, Philadelphia, PA	PhD	May 1996	Physics
Los Alamos National Laboratory, Los Alamos, NM	n/a	1992-1996	Physics
Jefferson Medical College, Philadelphia, PA	n/a	1998-1999	Instructor, RadOnc

INSTITUTION AND LOCATION	DEGREE (*if applicable*)	MM/YY	FIELD OF STUDY
Tsinghua University, Beijing, China	BS	July 1989	Optical engineering
Temple University, Philadelphia, PA	MS	May 1992	Physics
Temple University, Philadelphia, PA	PhD	May 1996	Physics
Los Alamos National Laboratory, Los Alamos, NM	n/a	1992-1996	Physics
Jefferson Medical College, Philadelphia, PA	n/a	1998-1999	Instructor, RadOnc

A. Personal Statement

I have been the designated physicist for Radiotherapy core laboratory of American College of Radiology (ACR) since 2006. I have directed the construction of the Radiation Oncology Therapy Group (RTOG) quality assurance core laboratory, evaluating and implementing latest technologies and systems to meet ever- evolving needs. As PI or co-Investigator on a number of federal or state funded projects on radiotherapy clinical trial quality, I have accumulated the experience for the proposed research by developing effective research methodologies relevant to the proposed research. I have a demonstrated record of accomplished and productive research projects in an area of high relevance for this project, and my expertise and experience have prepared me to play a significant role in this project. I will serve as the co-chair of IROC QA research subcommittee.

B. Positions and Honors

First Affiliate High School of HuaZhong Normal University, Wuhan, China

1983 First Prize, Composition Competition

1984 First Prize, Mathematics Competition

Tsinghua University, Beijing, China

1985 Third Prize, Mathematics Competition, Tsinghua University

1986 First Prize, English Competition, Tsinghua University

1987 First Prize, French Competition, Tsinghua University

Jefferson Medical College, Philadelphia, PA

1999-2006 Assistant professor, Department of Radiation Oncology

2006-2011 Clinical Director, Medical Physics Division, Department of Radiation Oncology

2006-2012	Associate professor, Department of Radiation Oncology
2011-present	Director, International Fellowships Medical Physics Division, Dept of Radiation Oncology
2012-present	Professor, Department of Radiation Oncology

Other

2010	Mid-Career Women Faculty Professional Development Seminar Award
2011	Varian Visiting Scholar to RTOG
2011	The John S. Laughlin Science Council Research Symposium Presentation Award, AAPM
2012	Fellow, American Association of Physicists in Medicine

Specialty certification

2002	Certification by the American Board of Radiology in Therapy Radiation Physics

Scientific and Professional Society Memberships

American Physical Society
American Association of Physicists in Medicine (AAPM)
Computer Society, The Institute of Electrical and Electronics Engineers (IEEE)
Delaware Valley Chapter of AAPM
American Society for Radiation Oncology (ASTRO)
The Institute of Physics and Engineering in Medicine (IPEM)

Professional and Scientific Committees

American Association of Physicists in Medicine (AAPM)

2005-2008	Member, Therapy Physics Committee
2005-2009	Chair, Task Group on IMRT QA
2005-present	Chair, Work Group on IMRT
2005-present	Member, Treatment Delivery Subcommittee
2008-present	Member, Therapy Emerging Technology Assessment Work Group
2010-present	Member, Summer School Scholarships Subcommittee
2010-present	Member, Women's Professional Subcommittee
2010-present	Member, TG180 Modeling and Accounting for the Imaging Guidance Radiation Doses to Radiotherapy Patients in Treatment Planning
2011-present	Chair, Radiation Oncology Medical Physics Education Subcommittee
2011-present	Member, Medical Physics Education of Physicians
2011-present	Board Member, Chapter Representative, Delaware Chapter
2011-present	Member, Radiation Dosimetry & Treatment Planning Subcommittee
2011-present	Member, TG219 (Independent Dose and MU Verification for IMRT Patient-Specific Quality Assurance)
2003, 2005, 2010, 2011	Session co-chair

American Society for Radiation Oncology (ASTRO)

2009-present	Chair, Physics Core Curriculum Subcommittee, Research Council
2008-present	Member, Radiation Physics Committee of the Research Council
2010	Annual meeting session co-chair

Sino-American Network for Therapeutic Radiology and Oncology (SANTRO)

2009-present	Member, Executive Committee
2010	Session co-chair

American College of Radiology (ACR)

2011-present	Chair, Bioinformatics Work Group

Editorial positions

2002-present	Referee for *Medical Physics*
2002-present	Referee for *Physics in Medicine and Biology*
2002-present	Referee for International Journal of Radiation Oncology*Biology*Physics
2002-present	Annual meeting abstract reviewer, AAPM
2005	Reviewer, Encyclopedia of Medical Devices and Instrumentation
2009-present	Reviewer, Abstracts for ASTRO annual meeting
2009-present	Editorial Board member, *World Journal of Radiology*
2010-present	Referee for *Journal of Applied Clinical Medical Physics*
March 2010	Reviewer, RSNA Education Study Section
June 2009,	Reviewer, NIH SBIR
2007, 2011, 2012	Associate Editor (invited), *Medical Physics*

C. Selected Peer-reviewed Publications

1. Xiao Y, Galvin J, Hossain M, Valicenti R. 2000. “An optimized forward-planning technique for intensity modulated radiation therapy.” *Medical Physics*; 27: 2093-9. PMID: 11011738
2. Xiao Y, Michalski D, Censor Y, Galvin JM. 2004. “Inherent Smoothness of Intensity Patterns for Intensity Modulated Radiation Therapy Generated by a Simultaneous Projection Algorithm,” *Physics in Medicine and Biology*; 49(14): 3227-45. PMID: 15357194
3. Censor Y, Ben-Israel A, Xiao Y, Galvin J. 2008. “On linear infeasibility arising in intensity-modulated radiation therapy inverse planning,” *Linear Algebra and its Applications* IMRT special edition; 428(5-6): 1406-20. PMID: 19562040
4. Showalter TN, Nawaz AO, Xiao Y, Galvin JM, Valicenti RK. 2008. “A cone beam CT-based study for clinical target definition using pelvic anatomy during postprostatectomy radiotherapy.” *International Journal of Radiation Oncology*Biology*Physics*; 70: 431-6. PMID: 17869021
5. Galvin JM, Xiao Y, Curran WJ, Jr. 2008. “Re: Intensity-modulated radiation therapy dose prescription, recording, and delivery: Patterns of variability among institutions and treatment planning systems.” *Journal of the National Cancer Institute*; 100:1264. PMID: 18728287
6. Xiao Y, Papiez L, Paulus R, et al. 2009. “Dosimetric evaluation of heterogeneity corrections for RTOG 0236: Stereotactic body radiotherapy of inoperable stage I-II Non–Small-cell lung cancer.” *International Journal of Radiation Oncology*Biology*Physics*; 73:1235-42. PMID: 19251095
7. Ezzell GA, Burmeister JW, Dogan N, LoSasso TJ, Mechalakos JG, Mihailidis D, Molineu A, Paltav JR, Ramsey CR, Salter BJ, Shi J, Xia P, Yue NJ, Xiao Y. 2009. "IMRT

Commissioning: Multiple Institution Planning and Dosimetry Comparisons: A Report from AAPM Task Group 119," *Medical Physics*; 36: 5359-73. PMID: 19994544
8. Den RB, Doemer A, Kubicek V, Bednarz G, Galvin JM, Keane KM, Xiao Y, Machtay. M. 2010. "Daily Image Guidance with Cone-Beam Computed Tomography for Head-and-Neck Cancer Intensity-Modulated Radiotherapy: A Prospective Study," *International Journal of Radiation Oncology*Biology*Physics*; 76(5):1353-1359 PMID: 19540071
9. Studenski MT, Xiao Y. 2010. "Proton therapy dosimetry using positron emission tomography", *World Journal of* Radiology; 2(4):135 -42. PMID: 21160579
10. Cui Y, Galvin JM, Straube WL, Bosch WR, Purdy JA, Li XA, Xiao Y. 2011. "Multi-System Verification of Registrations for Image-Guided Radiotherapy in Clinical Trials," *International Journal of Radiation Oncology*Biology*Physics*; 81(1): 301-12. PMID: 21236596
11. Cui Y, Piper JW, Harrison AS, Showalter TN, Yu Y, Galvin JM, Xiao Y. 2011. "Deformable Dose Accumulation with Image Guided Radiotherapy for Final Dose Evaluation in Pelvic Cases", *Journal of Nuclear Medicine & Radiation Therapy*; S3:e001. doi:10.4172/2155-9619.S3-e001.
12. Werner-Wasik M, Nelson ND, Choi W, Arai Y, Faulhaber PF, Kang P, Almeida FD, Xiao Y, Ohri N, Brockway KD, Piper JW, Nelson AS. 2012. "What Is the Best Way to Contour Lung Tumors on PET Scans? Multiobserver Validation of a Gradient-Based Method Using a NSCLC Digital PET Phantom," *International Journal of Radiation Oncology*Biology*Physics*; 82(3):1164-71. PMID: 21531085
13. Giaddui T, Cui Y, Galvin J, Chen W, Yu Y, Xiao Y. 2012. "Characteristics Of Gafchromic Xrqa2 Films For Kv Image Dose Measurement," *Medical Physics*; 39(2): 842. PMID: 22320794
14. Li J, Galvin J, Harrison A, Timmerman R, Yu Y, Xiao Y. 2012. "Dosimetric Verification Using Monte Carlo Calculations for Tissue Heterogeneity-corrected Conformal Treatment Plans Following RTOG 0813 Dosimetric Criteria for Lung Cancer Stereotactic Body Radiotherapy", *International Journal of Radiation Oncology*Biology*Physics*; 84(2): 508-13. PMID: 22365630
15. Chen W, Cui Y, Yanyan H, Yu Y, Galvin J, Hussaini Y, Xiao Y. 2012. "Application of Dempster–Shafer theory in dose response outcome analysis." *Physics in Medicine and Biology*; 57: 5575–85. PMID: 22892545

D. Research Support

Ongoing

Development and Analysis of an Infrastructure for Review of Modern Clinical Trials that Include Radiotherapy
State of Pennsylvania, Radiation Therapy Oncology Group (RTOG), 2009-2013
Role: Co-PI $320,000
Overall goals: Designing the review tools needed for future cooperative group protocols that might include one or more advanced technology
Responsibility: Design and implement review systems and tools for advanced technology for RTOG core laboratory

Development of Methods and Strategies to Incorporate Radiotherapy
Delivery Uncertainties in Clinical Trials Outcome Analysis
State of Pennsylvania, Radiation Therapy Oncology Group (RTOG), 2009-2013

Role: PI $300,000
Overall goals: Explore theoretical methodologies for critical assessment and propagation of uncertainties of radiation deliveries as a complement to current clinical trial analysis. Developed methods to incorporated uncertainties into clinical trial outcome
Responsibility: Oversee the conduct of the project

Radiation Therapy Oncology Group – IROC Group Transition Supplement
NIH/NCI, 2012
Role: PI subcontract $80,000
Overall goals: Transition and re-organization of clinical trial and QA groups
Responsibility: grant preparation for the transition

Quantitative Uncertainty Investigations for Clinical Trial Protocols, RTOG 0617
RTOG, CURE, PA Department of Health, 2012-2015
Role: PI $400,000
Overall goals: Investigate the unexpected result from RTOG 0617
Responsibility: oversee the conduct of the project

<u>Completed</u>
Extraction of Imaging Dose from kV Panel Projections
State of Pennsylvania, Radiation Therapy Oncology Group (RTOG), 2008-2010
Role: Co-PI $250,000
Overall goals: To evaluate dose deposition from IGRT process via measurements and theoretical reconstructions
Responsibility: Calculate and measure imaging dose from IGRT processes

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 Galvin, James M.	POSITION TITLE Professor, Medical Physics
eRA COMMONS USER NAME (credential, e.g., agency login)	

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 Cincinnati, Ohio	B.S.	1959-63	Physics
University of Cincinnati, Ohio	M.S.	1963-66	Nuclear Engineering
University of Cincinnati, Ohio	M.S.	1966-68	Medical Physics
Harvard University, Boston, MA	D.Sc.	1970-75	Medical Physics

A. Personal Statement

After 35 years working in a number of different capacities relating to clinical medical physics as applied to radiation oncology, I adjusted my activities to concentrate more on clinical trials that use radiation to treat cancer. My efforts over the past 10 years have concentrated on designing and implementing National Cancer Institute (NCI) funded studies that use advanced technologies and treatment techniques to manage cancer patient care. My area of expertise within this activity relates to the quality assurance (QA) needed to ensure the integrity of the results of these studies. The recent challenging aspect of this activity is the complete reorganization of the NCI funded National Clinical Trials Network (NCTN). This major undertaking combines nine existing clinical trials groups into five. In addition to this undertaking, six existing clinical trials QA Centers are being combined into a single group. I am currently involved in both parts of this consolidation by helping prepare responses to the Funding Opportunity Announcements for the formation of the NCTN and Imaging and Radiation Therapy Core QA Services.

B. Positions and Honors

Positions and Employment

1963-68 Fellow, Radiological Science, University of Cincinnati General Hospital, Cincinnati, OH
1968-70 Head of Clinical Physics, Joint Center for Radiation Therapy, Harvard Medical School, Boston, MA
1969-70 Associate in Radiation Therapy, Dept. of Radiation Therapy, Harvard Medical School, Boston, MA
1970-75 Fellow, Medical Physics, Harvard School of Public Health, Boston, MA
1974-75 Director of Physics, Radiation Therapy Department, Salem Hospital, Salem, MA
1976-77 Research Associate, Joint Center for Radiation Therapy, Harvard Medical School, Boston, MA
1977-85 Senior Clinical Physicist, Radiation Oncology, Univ. of Pennsylvania Medical Sch., Philadelphia, PA
1977-87 Assistant Professor of Radiation Physics, Radiation Oncology, Univ of Pennsylvania, PA

1980-87 Secondary Appointment, Assistant Professor of Biomedical Engineering, Univ of Penn of Engineering
1985-92 Associate Professor and Section Chief - Clinical Physics, Department of Radiation Oncology, University of Pennsylvania Medical School, Philadelphia, PA
1992-97 Associate Professor and Director of Physics, Radiation Oncology, Tisch Hospital, NYU Medical Center, New York, NY
1997- 2007 Professor and Director, Medical Physics Division, Dept. of Radiation Oncology Thomas Jefferson University Hospital, Philadelphia, PA
2008- Professor, Medical Physics Division, Dept. of Radiation Oncology Thomas Jefferson University Hospital, Philadelphia, PA
2008- Headquarters QA Physicist, Radiation Therapy Oncology Group, Philadelphia, PA

Membership in Professional and Scientific Societies:

American Association of Physicists in Medicine (Previous Executive Committee Member)
American Society of Therapeutic Radiology & Oncology (Previous Board of Directors Member)
American College of Radiology

C. Selected peer-reviewed publications

1. Galvin, J., Ezzell, G., Eisbrauch, A., Yu, C., Butler, B., Xiao, Y., Rosen, I., Rosenman, J., Sharpe, M., Xing, L., Xia, P., Lomax, T., Low, D.A., Palta, J.: Implementing IMRT in clinical practice: A joint document of the American Society for Therapeutic Radiology and Oncology and the American Association of Physicists in Medicine. Intl. J. of Radiat. Oncol. Biol.Phys. 58(5), 1616-1634, 2004.
2. Xiao, Y., Michalski, D., Censor, Y., Galvin, J.M. Inherent smoothness of intensity patterns for m intensity modulated radiation therapy generated by simultaneous projection algorithms. Phys. Med. Biol. 49, 3227- 3245, 2004.
3. Xiao, Y., Werner-Wasik, M., Michalski, D., Houser, C., Bednarz, G., Curran, W., Galvin, J. Comparison of three IMRT inverse planning techniques that allow for partial esophagus sparing in patients receiving thoracic radiation therapy for lung cancer. Medical Dosimetry, 29:3, 210-216, 2004.
4. Timmerman, R., Galvin, J.M., Michalski, J. et al. Accreditation and quality assurance for radiation therapy oncology group: Multicenter clinical trials using stereotactic body radiation therapy in lung cancer. Acta Oncologica, 2006; 45(7): 779-786, 2006.
5. Galvin, J.M., De Neve, W. Intensity modulating and other radiation therapy devices for dose painting. Journal of Clinical Oncology, 25(8):924-930, 2007.
6. Showalter, T., Nawaz, A.O., Xiao, Y., Galvin, J.M., Valicenti, R.K. A Cone beam CT-based study for clinical target definition using pelvic anatomy during postprostatectomy radiotherapy. Int. J.Radiat. Oncol. Biol.Phys. Vol. 70, 431-436, 2007.
7. Galvin, J.M., Bednarz, G., Quality Assurance Procedures for Stereotactic Body Radiation Therapy. J. Rad. Oncol. Biol. Phys. 71(1 Suppl): S122-S125. 2008
8. Censor, Y., Ben-Israel, A., Xiao, Y., Galvin, J.M. On linear infeasibility arising in intenstity-modulated radiation therapy inverse planning. Linear Algebra and its Applications, Vol. 428, Issues 5-6 (1406-1420), March 2008.
9. Bednarz, G., Machtay, M., Downes, B., Bogner, J., Hyslop, T., Galvin, J., Evans, J., Curran, Jr., W. , Andrews, D., Report on a randomized trial comparing two forms of immobilization

of the head for fractionated stereotactic radiotherapy. Med. Phys. 36(1) , 12-17, January 2009.

10. Timmerman, R., Paulus, R., Galvin, J., Michalski, J., Straube, W., Bradley, J., Fakiris, A., Bezjak, A., Videtic, G., Johnstone, D., Fowler, J., Gore, E., Choy, H. Stereotactic Body Radiation Therapy for Inoperable Early Stage Lung Cancer. Journal of American Medical Association, 303 (11), 1070-1076, 2010.
11. Chen W, Cui Y, Yanyan H, Yu Y, Galvin J, Hussaini Y, Xiao Y. Application of Dempster–Shafer theory in dose response outcome analysis. Phys. Med. Biol. 57 (2012) 5575–5585

D. Research Support

Active Support

080-34000-Z52601 (Curran) 01/01/2009 – Present
5U10CA021661-34 RTOG/NIH through American College of Radiology
The main goal is to undertake clinical trials and other cooperative studies in an endeavor to advance knowledge in the curative and palliative management of cancer through the cooperative group mechanism of the Radiation Therapy Oncology Group (RTOG)
Role: Physicist Chair

080-34000-G12401 (Xiao) 01/01/2009 – 12/31/2011
PA Department of Health thru ACR, Commonwealth Universal Research Enhancement (C.U.R.E.)
Research Project #1: Development and Analysis of an Infrastructure for Review of Modern Clinical Trials that Include Radiotherapy $320,000
The main goal is improving the tools available for radiation therapy dose distribution review will also improve the efficiency of case review for patients entered on cooperative group protocols while maintaining or even increasing the level of accuracy achieved historically
Role: Co-Investigator

080-34000-G12801 (Xiao) 01/01/2009 – 12/31/2013
PA Department of Health thru ACR, Commonwealth Universal Research Enhancement (C.U.R.E.)
Research Project #1: Methods and Strategies to Incorporate Radiotherapy Delivery Unicertainties in Clinical Trial Outcome Analysis $300,000
The objectives of this study is to bridge a gap between present radiotherapy related clinical trials, where essential delivery uncertainties are not included in the outcome analysis, and computational implementation that has the ability to propagate these uncertainties through the analysis process.
Role: Co-Investigator

Radiation Therapy Oncology Group – IROC Group Transition Supplement
NIH/NCI, 2012
Role: PI subcontract $80,000
Overall goals: Transition and re-organization of clinical trial and QA groups
Responsibility: grant preparation for the transition

Quantitative Uncertainty Investigations for Clinical Trial Protocols, RTOG 0617
RTOG, CURE, PA Department of Health, 2012-2015
Role: PI $400,000
Overall goals: Investigate the unexpected result from RTOG 0617
Responsibility: oversee the conduct of the project

Completed
080-34000-G10601 (Galvin) 01/01/2008 – 12/31/2011
PA Department of Health thru ACR, Commonwealth Universal Research Enhancement (C.U.R.E.)
Research Project #2: Controlling Patient Dose Resulting from the Use of Frequent Image Guidance in RTOG Protocols (Exhibit A)
The purpose of this study is to quantify the radiation dose the patient receives to various parts of the body as a result of the frequent use of image guidance, and to devise techniques that will limit the imaging dose the patient receives.
Role: PI