# Image Processing and Informatics Laboratory

# ANNUAL PROGRESS REPORT
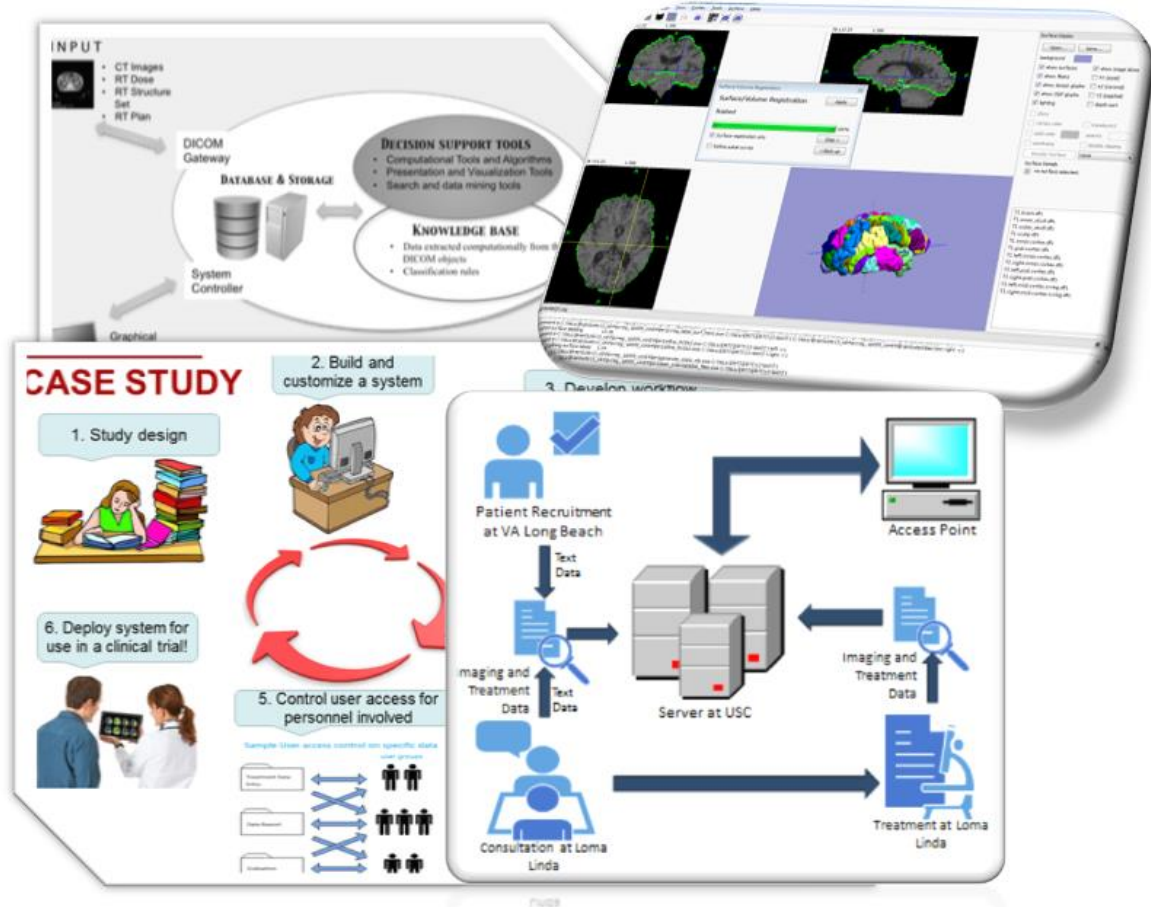
*February 2014*



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DEPARTMENT OF BIOMEDICAL ENGINEERING
VITERBI SCHOOL OF ENGINEERING
UNIVERSITY OF SOUTHERN CALIFORNIA

# 2014 Annual Report

## Image Processing and Informatics Laboratory

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# SUMMARY

The Image Processing and Informatics Laboratory (IPILab) is currently located at the Annenberg Research Park at 734 W. Adams Blvd. in the Kerckhoff Hall near the University Park Campus. During this year, IPILab has continued its vision and course to provide a bridge of collaboration between the two schools - Viterbi School of Engineering and the Keck School of Medicine - establishing new collaborations and research funding and hosting visitors interested in Imaging Informatics training and research.

Last year's milestones for past IPILab members include the following:

One of our previousT32 Predoctoral Fellow from our Training Grant from the NIBIB/NIH) entitled: "Biomedical Imaging Informatics Training Program", Syed Ashrafulla completed his PhD in EE student in the Viterbi School of Engineering.  Additionally, one of our past IPILab trainees, Anh Le, PhD, completed her Oncology residency program at the University of Pittsburgh Medical Center (UPMC). The USC Summer Undergraduate Research Program continues to fund our efforts to recruit and foster bright young undergraduate students searching for future academic research directions and we recruited two undergraduate researchers.  We also had two MS graduate students from the BME program who participated in research training activities and has since found professional positions. Currently within the IPILab, two former Provost Fellow PhD students Ruchi Deshpande and Ximing Wang, former T32 trainee Kevin Ma, and PhD student Sneha Verma - all from the BME graduate program - have continued their PhD research with IPILab. Both Ruchi and Ximing plan to advance to PhD candidacy in the next few months while Kevin Ma plans to complete his studies during the summer.

We have continued in our areas of Medical Imaging Informatics research with a transition to new frontier areas of research: 1) The development of an eFolder System for Multiple Sclerosis Patients 2) A multimedia cloud-based ePR system to support the large-scale OPTT-RERC "Rehabilitation Engineering Research Center for Technologies for Successful Aging with Disability" multi-media data; 3) The development of imaging informatics core for large-scale stroke rehab clinical trials (eg, Interdisciplinary Comprehensive Arm Rehabilitation Evaluations – ICARE); 4) Continued development of data mining of DICOM-RT objects in conventional radiation therapy of prostate cancer patients; 5) An ePR to provide decision support in evaluating does optimization in Stroke Rehabilitation (DOSE);6 ) An ePR-based system for Spinal Cord Injury patients for treating pain with Proton Therapy Radiosurgery. Once again, we attended the RSNA conference in December 2013 with a total of 5 presentations. Some of the research work continues to be supported by extramural finds including NIH, DOE/NIDRR, VA, U.S. Army Medical Research and Materiel Command, and the private industry. We are continuing to transition to areas in Rehabilitative Science and Physical Therapy since multi-media data is utilized in the research field in addition to patient-related imaging informatics data.

In the Table of Contents, this 2014 Annual Report includes materials related to the IPILab, IPILab R & D plans and current results, selected published and in-press peer-reviewed

papers during the year, as well as preprints to appear in the *Proceedings of the International Society for Optical Engineering (SPIE) in Medical Imaging*, San Diego, CA, February 19-20, 2014.

## Our research has been supported by:

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# STAFF AND COLLABORATORS

| Faculty and Administration | Academic Collaborators |
|---|---|
| **Norberto M. Grzywacz, PhD**<br>Professor and Chairman,<br>Department of Biomedical Engineering (BME) | **Carolee Winstein, PhD**<br>Professor, Biokinesiology and Physical Therapy |
| **Brent J. Liu, PhD**<br>Associate Professor of BME<br>Director, IPILab | **Ewa Pietka, PhD, DSc**<br>Professor, Technical University of Silesia, Poland<br>*Visiting Professor of Radiology* |
| **H.K. Huang, DSc, FRCR (Hon.), FAIMBE**<br>Professor Emeritus of Radiology & BME | **Edward V. Grant, MD, FACR**<br>Professor and Chairman, Department of Radiology |
| **James Sayre, PhD**<br>Professor of Biostatistics and Radiological Science,<br>UCLA *Consultant* | **Michael Khoo, PhD**<br>Professor of BME, Co-PI, NIBIB Training Grant |
| **Heinz U. Lemke, Professor**<br>Technical University Berlin | **Sophia Chun, MD**<br>Chief, SCI at Veterans Health Administration |
| **Jianguo Zhang, PhD**<br>Professor, Shanghai Institute of Technical Physics,<br>The Chinese Academy of Science<br>Visiting Professor of Radiology | **James Slater, MD**<br>Radiation Medicine, Loma Linda University |
| | **Lilyana Amezcua, MD**<br>Assistant Professor of Neurology, Keck Hospital of USC |
| **Maria YY Law, MPhil, BRS, PhD**<br>Consultant (Medical Imaging and Radiotherapy)<br>Hong Kong Sanatorium and Hospital<br>Professor of Radiation Therapy<br>Tung Wah College, Hong Kong<br>Visiting Associate Professor of Radiology at USC | **Meng Law, MD, MBBS, FRACR**<br>Director of Neuroradiology, Keck Hospital of USC |
| | **Alexander Lerner, MD**<br>Visiting Assistant Professor of Clinical Radiology,<br>Keck Hospital of USC |
| | **Jorge Documet, PhD**<br>Software Engineer ,MedQIA |

| Postdoctoral and Visiting Fellows | |
|---|---|
| **Paymann Moin, MD**<br>Radiologist, Advanced Imaging Center, Valencia, CA | **Richard Lee, MD**<br>Radiology Resident |
| **Anh Le, PhD**<br>Faculty, University of Texas Dallas | **Jasper Lee, PhD**<br>R&D Manager, SCImage, Los Altos |
| **Ali Maziad, MD**<br>Spine Deformity Fellow at Hospital for Special Surgery | **James Fernandez, MD**<br>Radiology Resident |
| **Marco A. Gutierrez, PhD**<br>Invited Professor, Heart Institute of University of San Paulo | **Kathleen Garrison, PhD**<br>Associate Post-Doctoral Fellow Department of Psychiatry, Yale University |

| Graduate Student Assistants | |
|---|---|
| **Kevin Ma, MS** | **Sneha Verma, MS** |
| **Ruchi Deshpande, MS** | **Ximing Wang, MS** |
| **Jing Wang, MS** | |

| Undergraduate Students | |
|---|---|
| **Jonathan Wong** | **Mark Zhong** |

## IPILab Collaborations

International    National

**ABBREVIATIONS**
**IPILab**: Image Processing and Informatics Laboratory, USC
**BME**: Biomedical Engineering Department, USC
**HCC2**: Healthcare Consultation Center 2, USC
**KSM**: Keck School of Medicine, USC
**UCLA**: Dept. of Radiological Sciences, UCLA
**VHA**: Veterans Health Administration, Long Beach
**WRAMC**: Walter Reed Army Medical Center

Division of Biomedical Electronics Silesian University of Technology Gliwice, Poland

Department of Radiology University of Pisa Pisa, Italy

PACS Laboratory & Image Management Laboratory Hong Kong, China

Iranian Society of Radiology Tehran, Iran

Medical Imaging Informatics Laboratory Shanghai, China

Incor Heart Institute Univ. of San Paulo San Paulo, Brazil

**IPILab**
**Los Angeles, CA**

WRAMC

VHA

UCLA

USC BME

USC KSM

USC HCC2

University of Southern California

*Image Processing and Informatics Lab*

USC **Viterbi** School of Engineering

KECK SCHOOL OF MEDICINE USC

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### About Us



The Image Processing and Informatics Laboratory (IPI) is located at Annenberg Research Park, 734 West Adams Blvd. Los Angeles, California 90089..

Our research facility includes PACS Simulator, Fault-tolerance Server, Data Grid, PACS workstations, CAD servers, and connections to two clinical PACS.

Reseach topics include:

- Computer Aided Detection and Diagnosis
- Data Grid and Image Archival
- Imaging Informatics Technology
- PDA Application in Clinical Environment
- Radiation Therapy Informatics
- Clinical Workflow Model
- CAD - PACS Integration Toolkit
- EPR for a surgical environment
- Multimedia ePR for Rehabilitation
- eFolder for Multiple Sclerosis Decision Support
- Spinal Cord Injury Pain Classification

### NEWS AND EVENTS

#### IPILab Update: RSNA 2013
August 20th, 2013

The IPILab have 4 abstracts accepted to RSNA (Radiological Society of North America) 2013.

The list is as follows:
**Web-based DICOM-SR Viewer for CAD data of multiple sclerosis lesions in an imaging informatics-based eFolder**
Authors: *Brent Liu, Kevin Ma, Jeff Zhang*

**An open source, rich-client web application for visualizing DICOM RT data**
Authors: *Brent J. Liu, Ruchi R. Deshpande, David Clunie, John DeMarco, Jorge Documet*

**Web-based neurological pain classifier tool utilizing Bayesian decision theory for pain classification in spinal cord injury patients.**
Authors: *Sneha K. Verma, Sophia Chun, Brent J. Liu*

**An imaging informatics-based system with a novel intelligent workflow engine to support rehabilitation clinical trial research**
Authors: *Brent Liu, Ximing Wang, Clarisa Martinez, Carolee Winstein*

*We would appreciate your interests in our topics.*

#### IPILab Update: RSNA 2011
August 24th, 2011

IPILab have 10 abstracts accepted to RSNA (Radiological Society of North America) 2011, as well as two abstracts from our collaborators.

The list is as follows:

- Extending Imaging Informatics beyond Radiology: A Web-based Multimedia System to Improve Decision Support through Movement Analysis of Elite Athletes [Educational Exhibit]
- Clinical Experiences and Challenges from the Implementation of a Zero Footprint Mobile DICOM WADO Display Solution for Smartphones and Tablets [Poster]
- A Novel Multimedia Electronic Patient Record (ePR) system to Enhance the Workflow, Accuracy, and Management of Various Types of Image-assisted (IA) Surgery [Computer Exhibit]
- Data Mining Utilizing DICOM RT Objects for Knowledge Discovery in Radiation Therapy for Prostate Cancer.[Poster]
- Spatial Normalization of Lesioned Brains: Impact on fMRI Region of Interest Analyses. [Poster]
- A Comprehensive Online Imaging Informatics Systems for a Large Scale Clinical Stroke Rehabilitation Trial.[Computer Exhibit]
- An Automatic Multiple Sclerosis Lesion Tracking Tool for Longitudinal MRI Studies. [Educational Exhibit]
- Evaluation of Stereoscopic 3D Digital Mammography on Lesion Assessment and Confidence Levels: A Preliminary Study [Poster]
- A Dynamic Online Radiology Directory and Request Queuing System to Increase Efficiency and Enhance Clinician-Radiologist Communication Workflow. [Poster]
- A timeline widget correlating MRI lesion load and EDSS parameters in a large cohort for MS patients. [Computer Exhibit]

Tow abstracts from Collaborators:

Maria Law, PhD, Hong Kong University :

- The Efficacy of Lingzhi (Ganoderma Lucidum) on Radiation Side Effects and Quality of Life in Patients with Nasopharyngeal Cancer Undergoing Radiotherapy [Poster and Presentation]

Anh Le, PhD, University of Florida:

- Automatic Treatment Plan Evaluation Utilizing a Web-based Electronic Patient Record (ePR) System and a Computer-aided Evaluation (CAE) for Intensity Modulated Radiation Therapy (IMRT) Plans [Poster]

We would appreciate your interests in our topics.

News Archive

Last Updated: 2012-01-05

# RSNA 2013 POSTERS

## Imaging Informatics System Utilizing DICOM Objects for
## Treating Pain in Spinal Cord Injury Patients Utilizing Proton Beam Radiotherapy

Sneha K. Verma, MS[1]; Sophia Chun, MD[2]; Brent Liu, PhD[1]; Ruchi Deshpande,MS[1]; Jing Wang, BS[1]; Daila S. Gridley, PhD[3];

[1]Image Processing and Informatics Lab, Dept. of Biomedical Engineering, Viterbi School of Engineering, USC
[2]VA Long Beach, [3]Loma Linda University

### Overall Goal of Study:

This project aims to determine the effectiveness of radiation therapy targeting the dorsal horn synapse in managing Spinal cord Injury(SCI)-related Neuropathic Pain (NP) as an alternative to invasive surgical lesioning.

### Relevance of Research:

- Many US combat personnel have sustained nervous tissue trauma during service.
- Neuropathic pain is often difficult to manage which is often developed as a result of trauma.
- In select patients, synapse lesioning can provide significant pain control and improved quality of life.

### Collaborations:

1. IPILab at USC
2. Loma Linda University
3. VA Long Beach



### Learning Challenges:

- Need of a smart knowledge based decision support system to support clinical protocols for treating SCI-related NP study.
- Need of system like ePR, that can incorporate multimedia data, together with DICOM based information.

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### Clinical Study Overall workflow



**Animal Studies** — Phase 1: Animal (Pig) treated with proton beam radiotherapy.

**SCI Patient Recruitment** — Phase 2: Patients with neuropathic pain are recruited.

**Pain Classification Module** — Phase 3: Pain Classification module is developed using machine learning algorithms.

**Human Studies** — Phase 4: Patients will be treated with proton beam radiotherapy

**Treatment Evaluation** — Phase 5: Treatment evaluations will be dose once patients are treated.

### Dataflow/ System Architecture
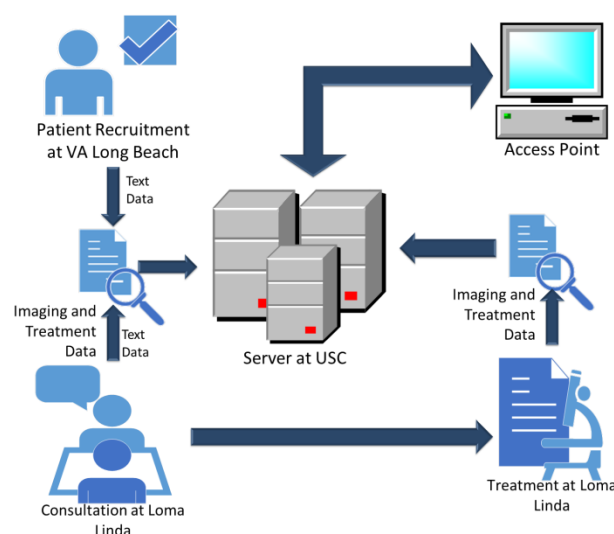


Patient Recruitment at VA Long Beach

Text Data

Access Point

Imaging and Treatment Data

Text Data

Server at USC

Imaging and Treatment Data

Consultation at Loma Linda

Treatment at Loma Linda

USC University of Southern California

# An imaging informatics-based system with a novel intelligent workflow engine and workflow builder to support imaging-based clinical trials

X Wang, MS[1], Los Angeles, CA, B J Liu, PhD[1], Clarisa Martinez PhD[2], C J Winstein, PhD[2]

1-Image Processing and Informatics Lab, Department of Biomedical Engineering, Viterbi School of Engineering, University of Southern California, Los Angeles, CA 90089
2-Division of Biokinesiology & Physical Therapy, University of Southern California, Los Angeles, CA 90089

**Aim:** Present an imaging informatics-based system with a customizable workflow engine to support specific clinical workflows and imaging related data within a clinical trial.

## Background and Challenges

Complex clinical research workflows deal with multimedia data at various stages within the workflow

The data management needs of clinical trials are typically addressed with custom-built & one-off systems.

The challenge arises when customizing system for workflows require additional software development

Workflow engines can benefit the complex clinical trial research workflows and facilitate data management

## Learning Objectives

Understand what is a workflow engine and how workflow engines can enhance clinical trials

Discover what challenges with workflows are met in imaging data-related clinical trial

Observe how a system with an intelligent workflow engine can be customized easily

A hands-on experience of building the clinical trial research workflow and rules for the workflow engine
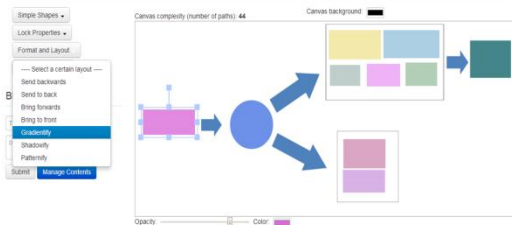
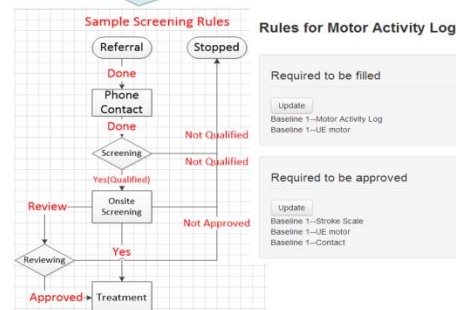---

# CASE STUDY

1. Study design
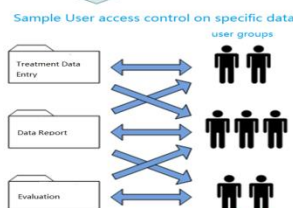
2. Build and customize a system

3. Develop workflow



4. Set up workflow engine rules

6. Deploy system for use in a clinical trial!

5. Control user access for personnel involved

# An open source, rich-client web application for visualizing DICOM RT data

Brent Liu, PhD[1], Ruchi Deshpande, MS[1]; John DeMarco, PhD[2]; Wanwara Thuptimdang[1], B.S., Jorge Documet[3], PhD

1 – Department of Biomedical Engineering, Viterbi School of Engineering, University of Southern California, Los Angeles, CA;
2- Department of Radiation Oncology, University of California, Los Angeles, CA
3 – MedQIA, Los Angeles, CA

## OVERVIEW

Radiation Therapy Informatics systems may be oriented towards either:

**Research**
[E.g. Comparing competing protocols, evaluating new technologies, discovering disease patterns, etc.]

**Clinical Service**
[E.g. Outside consultation, Data Management, Decision Support, etc.]

## LEARNING OBJECTIVES

1. Understand the need for a web-based, rich-client toolset for processing DICOM RT data.
2. Understand and observe how different RT data objects such as Region of Interest (ROI) contours, Isodose overlays and Dose Volume Histograms can be displayed interactively in a browser.
3. Understand what technical components are required to build such tools.

| Requirements for RT Informatics Systems | Solution |
|---|---|
| Ability to work with data from different treatment planning system vendors | DICOM ensures vendor neutrality |
| Remote access, centralization of data | Web-based approach |
| Ability to comprehend RT data objects for manipulation and processing | DICOM Parser |
| User friendly data presentation | Visualization Tools |
| Ability to read and process data on the client side to avoid HIPAA complications | Web Based Parser & Visualization |



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## Data Flow and Order of Operations on the Client-side

### PARSER

- Parser creates pointers to various data elements
- Retrieve Pixel Data
- Extract Coordinates for Region of Interest (ROI) Contours
- Get Dose Grid and Grid Frame Offset Vector

### CONTROL MODULE

- Retrieve user-selected files from the system and send to the parser
- Rescale, Reformat, sort by z-Index. Save pixels & z-indices in the buffer
- Assign contours to associated CT slices
- Set thresholds and generate isodose curves
- Assign contours to associated CT slices

### VISUALIZATION MODULE

- Put pixels onto the Canvas
- User scrolls on canvas and triggers mousewheel event
- User selects ROI/ Isodose
- Draw Contours on the CT pixels

Control module (right side of visualization):
- Return pixels for the first CT Image from the buffer
- Extract appropriate CT Image pixels based on the browser event
- Do contours exist for the current CT Slice? If yes, extract from buffer and return

### BUFFER

| | | | | |
|---|---|---|---|---|
| Z-Axis Index | $z_1$ | $z_2$ | ... | $z_3$ |
| CT Pixel Data | $[i_1,i_2,...i_{nm}]$ | $[i_1,i_2,...i_{nm}]$ | ... | $[i_1,i_2,...i_{nm}]$ |
| ROI #1 Contour Coordinates | $(x_1,y_1)$ $(x_2,y_2)$ . | $(x_1,y_1)$ $(x_2,y_2)$ .. | .. | $(x_1,y_1)$ $(x_2,y_2)$ .. |
| ... | ... | ... | ... | ... |
| ROI #n Contour Coordinates | $(x_1,y_1)$ $(x_2,y_2)$ . | $(x_1,y_1)$ $(x_2,y_2)$ .. | ... | $(x_1,y_1)$ $(x_2,y_2)$ .. |
| 40% Isodose Coordinates | $(x_1,y_1)$ $(x_2,y_2)$ . | $(x_1,y_1)$ $(x_2,y_2)$ .. | ... | $(x_1,y_1)$ $(x_2,y_2)$ .. |
| ... | ... | ... | ... | |
| 95% Isodose Coordinates | $(x_1,y_1)$ $(x_2,y_2)$ . | $(x_1,y_1)$ $(x_2,y_2)$ .. | ... | $(x_1,y_1)$ $(x_2,y_2)$ .. |

# Cloud computation of anatomical features from imaging studies to discover radiation toxicity trends using a DICOM-based decision support system

R. Deshpande, MS[1]; J. DeMarco, PhD[2]; A. Le, PhD[3]; B. J. Liu, PhD[1], Jing Wang, BS[1]

1 – Department of Biomedical Engineering, Viterbi School of Engineering, University of Southern California, Los Angeles, CA
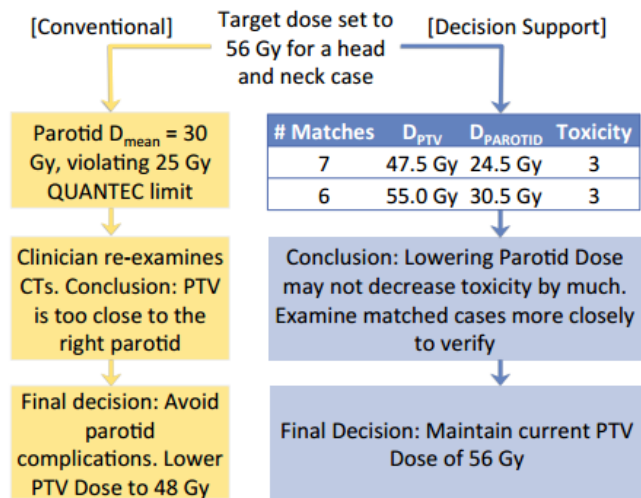2 - Department of Radiation Oncology, University of California, Los Angeles, CA
3 – Department of Radiation Oncology, University of Pittsburgh Medical Center, Pittsburgh, PA
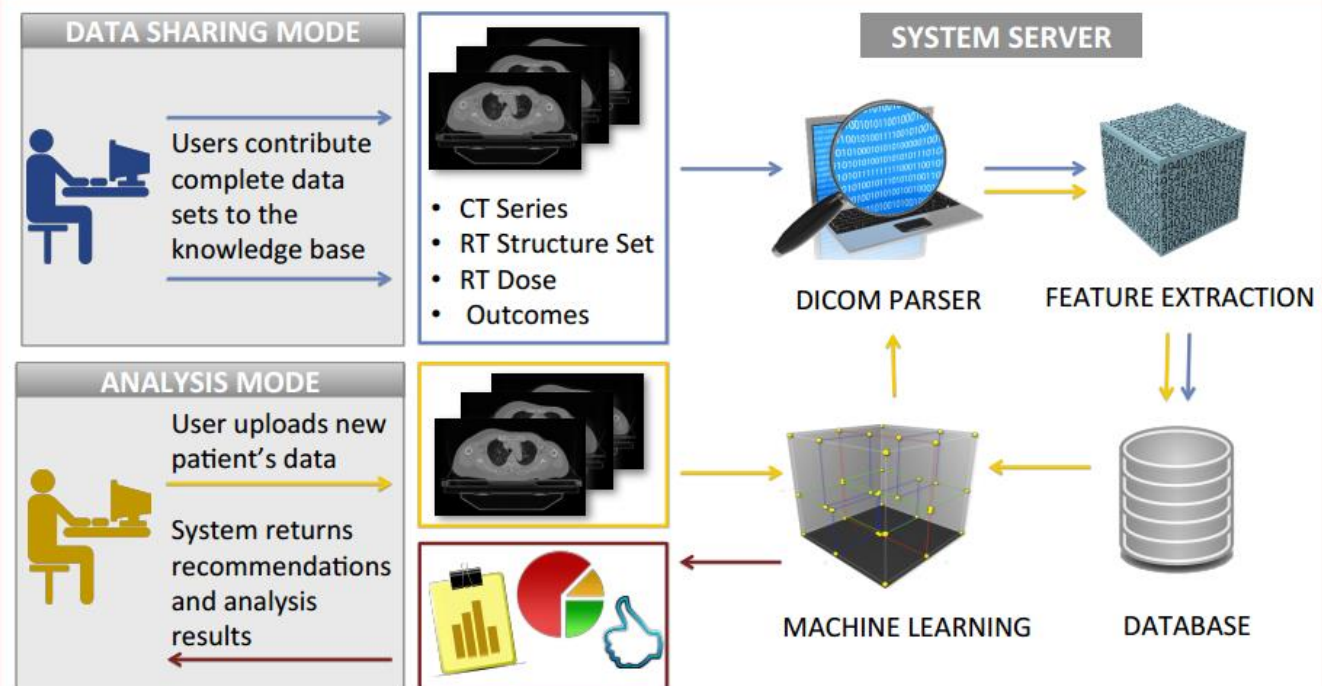
## OVERVIEW

- Maximize target dose, minimize normal tissue exposure.
- Standard guidelines recommend safe yet effective treatment parameters.
- Anatomical variation amongst patients puts a limit on the applicability of universal guidelines and standards.
- Clinicians assess these variations subjectively by examining imaging studies visually and determine reasonable deviations from these standards based on their experience and knowledge of "what works best".
- Decision Support System:
  - Quantifies the spatial relationship between targets and their surrounding organs at risk (OAR).
  - Maintains a database of retrospective patients
  - Searches the database for every incoming patient to find past patients with similar PTV-OAR configurations
  - Uses outcomes data of closest matches to pick the best results to serve as templates for the current patient.

## DECISION SUPPORT WORKFLOW

Target dose set to 56 Gy for a head and neck case

[Conventional]

Parotid $D_{mean}$ = 30 Gy, violating 25 Gy QUANTEC limit

Clinician re-examines CTs. Conclusion: PTV is too close to the right parotid

Final decision: Avoid parotid complications. Lower PTV Dose to 48 Gy

[Decision Support]

| # Matches | $D_{PTV}$ | $D_{PAROTID}$ | Toxicity |
|-----------|-----------|---------------|----------|
| 7 | 47.5 Gy | 24.5 Gy | 3 |
| 6 | 55.0 Gy | 30.5 Gy | 3 |

Conclusion: Lowering Parotid Dose may not decrease toxicity by much. Examine matched cases more closely to verify

Final Decision: Maintain current PTV Dose of 56 Gy

## SYSTEM ARCHITECTURE AND DATA FLOW



**DATA SHARING MODE**

Users contribute complete data sets to the knowledge base

- CT Series
- RT Structure Set
- RT Dose
- Outcomes

**ANALYSIS MODE**

User uploads new patient's data

System returns recommendations and analysis results

**SYSTEM SERVER**

DICOM PARSER

FEATURE EXTRACTION

MACHINE LEARNING

DATABASE
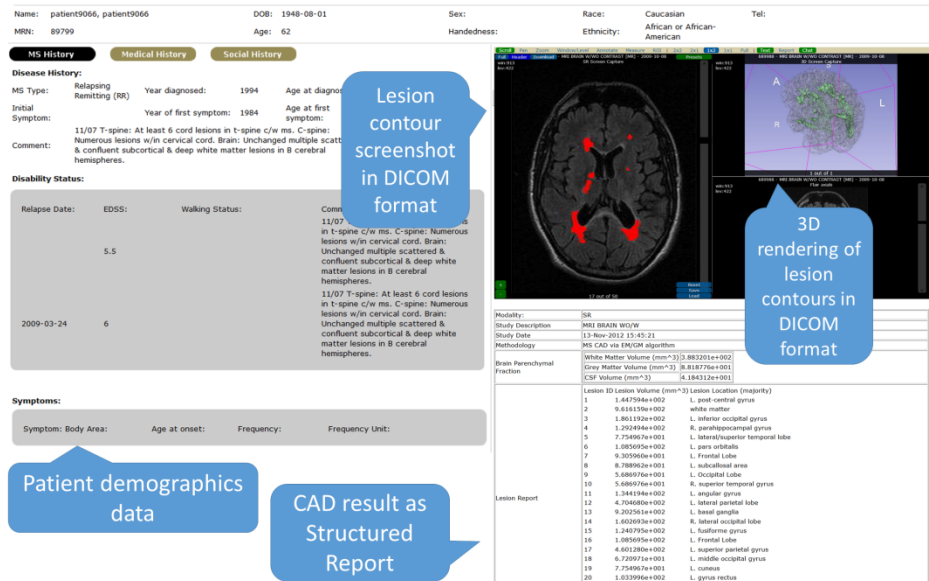
*Image Processing and Informatics Laboratory*

# Web-based DICOM-SR Viewer for CAD data of multiple sclerosis lesions in an imaging informatics-based eFolder

Kevin Ma, MS; Jeff Zhang; Mark Zhong; Jon Wong; Brent Liu, PhD

*Image Processing and Informatics Lab, Dept. of Biomedical Engineering, Viterbi School of Engineering, USC*

**Learning Objectives:**

- How to implement a DICOM-SR display module in an eFolder system
- How to display secondary capture as DICOM objects in a WADO image viewer
- How to integrate MS patient demographic data with imaging and CAD lesion analysis
- How to store and display MS lesion identification, localization, and quantification results as DICOM-SR objects
- How to design an IHE-compliant eFolder system that can be integrated in a clinical workflow

**SPIE 2014 PREPRINTS**

# Development of a user customizable imaging informatics-based intelligent workflow engine system to enhance rehabilitation clinical trials

Ximing Wang[a], Clarisa Martinez[b], Jing Wang[a], Ye Liu[a], Brent Liu[a]

[a]Image Processing and Informatics Lab, University of Southern California, 734 W Adams Blvd, Los Angeles, CA 90089
[b]Motor Behavior and Neurorehabilitation Lab, Div. of Biokinesiology and Physical Therapy, USC

## ABSTRACT

Clinical trials usually have a demand to collect, track and analyze multimedia data according to the workflow. Currently, the clinical trial data management requirements are normally addressed with custom-built systems. Challenges occur in the workflow design within different trials. The traditional pre-defined custom-built system is usually limited to a specific clinical trial and normally requires time-consuming and resource-intensive software development. To provide a solution, we present a user customizable imaging informatics-based intelligent workflow engine system for managing stroke rehabilitation clinical trials with intelligent workflow. The intelligent workflow engine provides flexibility in building and tailoring the workflow in various stages of clinical trials. By providing a solution to tailor and automate the workflow, the system will save time and reduce errors for clinical trials. Although our system is designed for clinical trials for rehabilitation, it may be extended to other imaging based clinical trials as well.

**Keywords:** Workflow Engine, Rehabilitation Engineering, electronic Medical Record (eMR), Clinical Service

## 1. INTRODUCTION

With the dramatic changes in technology in the past decade, the present-day stroke rehabilitation clinical trials are equipped with modern technology that can produce massive amounts of multimedia data [1]. Consequently, the organization and management of large volumes of generated data can be complex. For example, clinical trials in stroke rehabilitation may include: biomechanics, behavioral, physiological, psychophysical, imaging (such as Magnetic Resonance Imaging(MRI), computed tomography(CT)), transcranial magnetic stimulation(TMS), kinetics, video, electromyography (EMG), and survey/questionnaire items that may reside in various devices, such as hospital picture archiving and communication system (PACS) and hardcopy paper forms. The collection of multimedia data typically involves complex workflows and teams of staff. Thus, efficient management of the clinical trial workflow is crucial. Although the concept of rehabilitation informatics has already been introduced, it has not traditionally focused on the needs of the clinical trial workflow, presenting an opportunity for further exploration.

Different from conventional database management experience, clinical trials typically require that data be collected, tracked, presented and analyzed in accordance with a study's workflow and protocol. At present, the clinical trial data management requirements are usually serviced by a custom-built system. However, each trial typically has unique needs associated with its respective workflow and research questions, including the types of data collected and the structure/content of data collection forms. Even within a single trial, the workflow and forms may change significantly during various research stages. For example, a change of data management staff, a refinement of research goals, and the appearance of new ideas or technologies can lead to a change of the workflow. Thus, such changes to the workflow may render the pre-defined custom-built system obsolete. However, system updates may require additional software development, which is a step that can be time-consuming, resource-intensive and can negatively impact the data collection and analysis. Therefore, flexibility in the workflow design in clinical trials is crucial, and a solution that can provide efficient workflow, data management, and decision support to serve the rehabilitation clinical trials, is urgently needed.

The concept of the workflow engine has been present for decades and the workflow engine has proven to enhance the efficiency of business through process automation. Complex clinical trial workflows, such as those of stroke

rehabilitation clinical trials, can also benefit from the workflow engine by allowing for efficient collection, analysis and release of multimedia data at various stages of the workflow. In this paper, we present an intelligent workflow engine core informatics system for complex randomized control trials. It is first applied to a stroke rehabilitation clinical trial designed to understand the best dose of a principle-based rehabilitation intervention for stroke (Dose Optimization for Stroke Evaluation, DOSE). The objective of the DOSE clinical trial is to determine prospectively the optimal dose of therapy that will lead to further improvements of upper extremity use for individual patients who have had a stroke. The trial aims to recruit 60 subjects. Each subject is recruited, enrolled, and randomized into the trial and undergoes 10 months of therapy. A variety of data will be collected, including rehabilitation evaluation and clinical test data in forms, MRI studies with DTI and Transcranial magnetic stimulation (TMS), and wearable sensor data.

## 2. METHODOLOGY

**System Components**

The alpha prototype system is developed in PHP, Javascript, HTML 5 and MySQL on an Apache server. As shown in figure 1, the base level of the system is comprised of an image viewing system and the database and file systems. The image viewing system is adapted from a Web Access to DICOM Objects (WADO) viewer developed by the Image Processing and Informatics Lab at the University of Southern California.[3] The image viewing system is composed of an image uploader, DICOM anonymizer, DICOM parser and a zero footprint vendor neutral WADO viewer. Beyond the imaging data, all clinical information is stored in a centralized MySQL database and all multimedia data is stored in the file storage systems. The software is built in an Ubuntu 12.10 environment.

The upper tier of the software consists of a workflow designer and a system generator. As shown in the figure 1, a project manager is able to use the workflow designer to draw the workflow and deploy the system based on the specific workflow. The second component, system generator, is able to create a customized system designed by the project manager. The workflow designer is developed on the HTML 5 standard [8] and an open source library fabricjs[9].

**Scenario of the application of the software**

The system allows the project coordinator to build a data collection and management system customized to the research protocol workflow. This is achieved through a graphical user interface for users to pick tools to build a workflow specifically designed for the clinical trial. A library of tasks can be added to each phase of the workflow. The available tasks include questionnaires, assessment form templates, a web-based DICOM viewer with annotation tools for visualization of brain images, DICOM uploader with anonymizer and parser, and multimedia video player. The assessment form templates are designed for common tests such as Motor Activity Log (MAL), Wolf Motor Function Test (WMFT) and Stroke Impact Scale (SIS). A graphical tool is also available for the user to create a web-based questionnaire form or modify the form based on the templates. The web-based DICOM viewer allows the user to view, download images, mark ROI, measure the length of the lesion, store the annotation and ROI into database, and compare images of same patient in the studies from different timeframe, which is useful to track the lesion location and size.

The system is able to create distinct user groups that allows specific rights and access to various data—a crucial component in maintaining data safety and integrity. The data presentation component of the system can create data reports for online viewing and downloading. By using this system, users can customize workflow according to their specific needs without any knowledge of software development.
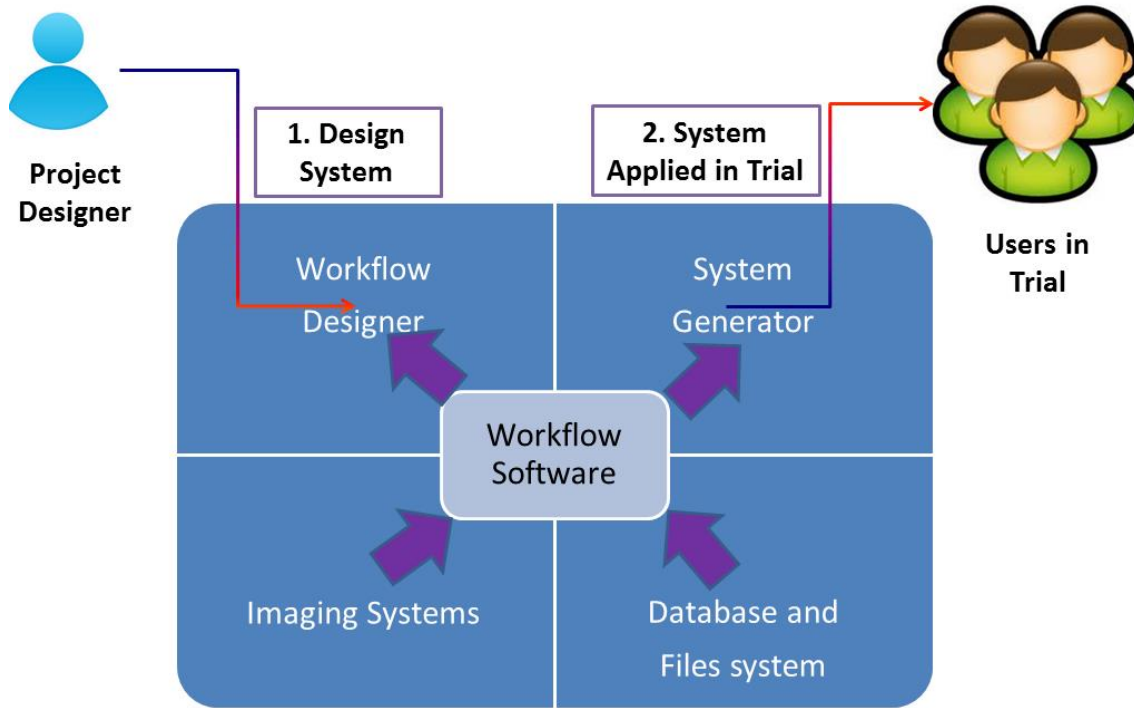
Figure 1 Software Components. The upper tier of the software consists of a workflow designer and a system generator. A project designer is able to use the workflow designer to draw the workflow and deploy the system based on the specific workflow. The second component, system generator, is able to create a customized system designed by the project leader.

## 3. RESULT

**Workflow Designer**

An alpha version of the prototype system was developed at IPILab, University of Southern California. The system is a web-based system with two modules included. The workflow designer and system generator both have a distinct uniform resource locator (URL). In the workflow designer module, the user is able to design the workflow by a web-based HTML5 tool shown in figure 2. The designer tool provides simple shapes, such as rectangle, circle and arrow to choose from. The user can drag a shape and drop it on the canvas. These shapes represent a group of tasks in the workflow. The canvas allows user to group several tasks together to form a workflow stage within the trial. After designing the workflow, the user can edit the title and description of each task group. By managing contents of each task group, the user is able to assign tasks such as imaging viewer, textual forms to each group. The last step is setting up engine rules for the workflow. The rules specify prerequisite requirements for access of specific modules. The requirements include completeness or approval of a specific form, or uploading of imaging data.
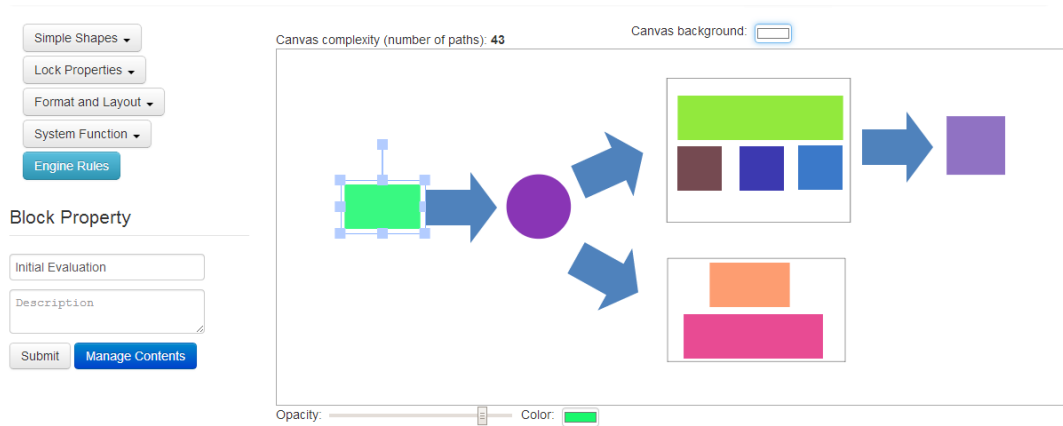
Figure 2 HTML5 workflow designer. The user is able to pick simple shapes and drop on canvas, change the format and the layout of the canvas, and change background, color, and opacity of the canvas. Once the workflow is designed, user can set the contents for each block and set the engine rules for the workflow.

**System Generator**

Once the user completes designing the workflow, the system generator module will deploy a new imaging informatics based clinical trial system based on the workflow designer. In the generated system, the system allows user to enroll new patients, collect data based on the workflow and retrieve collected data. The system shows a profile page for each patient and a workflow associated with the patients. As shown in figure 3, the workflow is shown in the patient profile page. In each stage of the workflow, there is a small number illustrating the number of tasks in each block and the number of tasks that have been completed. Choosing the stage in the workflow will lead to a popup window with all tasks in that stage. Users can collect the data through the modules in the window. If the engine rules are defined with a task in workflow designer, the task will be unavailable to access unless all requirements have been satisfied.
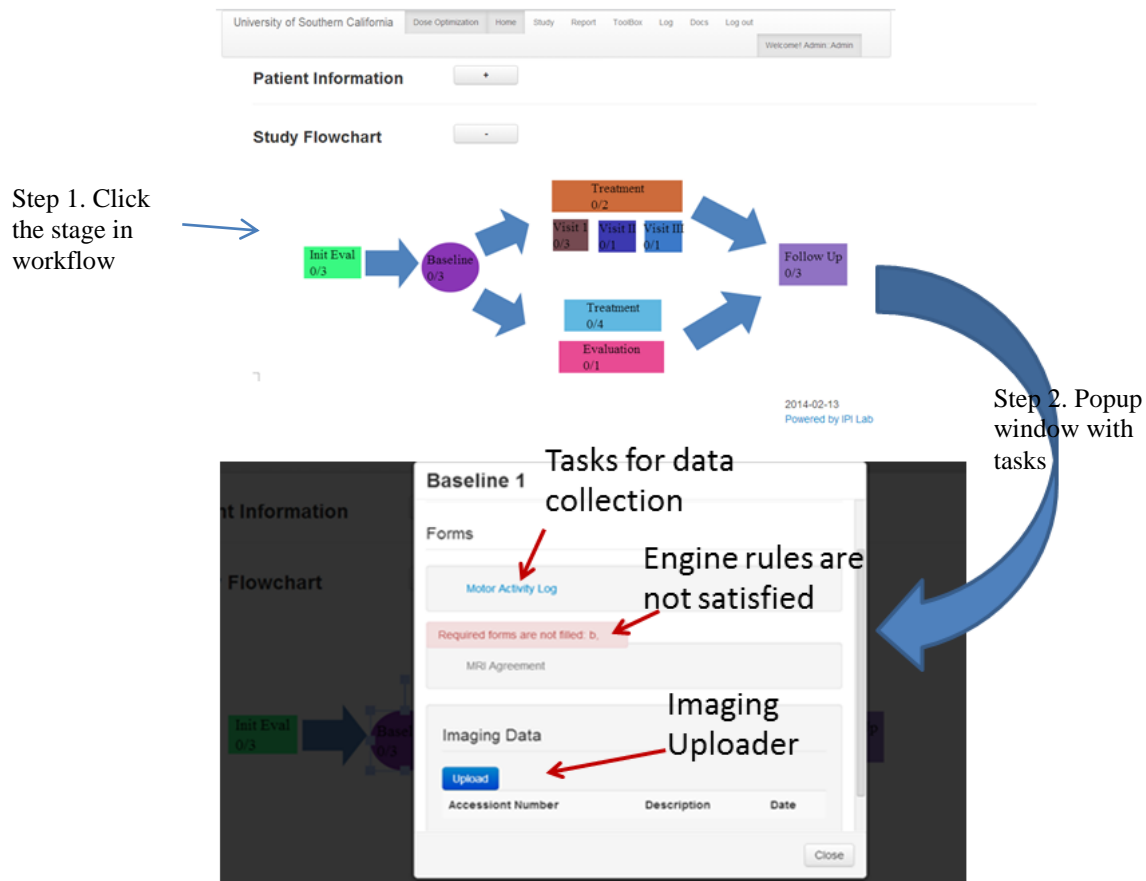
Figure 3 Patient profile page in the system. Clicking a stage in the workflow will lead to a popup window with all tasks in that stage. Users can collect the data through the tasks in the window. The module will be unavailable to access if the engine rules are not satisfied.

Once the user uploads the DICOM files into the system through the imaging uploader, the user is able to view the images through a web access to DICOM objects (WADO) viewer. The viewer enables the user to scroll, pan, zoom and change the window/level of the images. The user is also able to make annotations, mark ROI and measure distance between two points. More details of this viewer were discussed by X. Wang et al in 2012. [3]
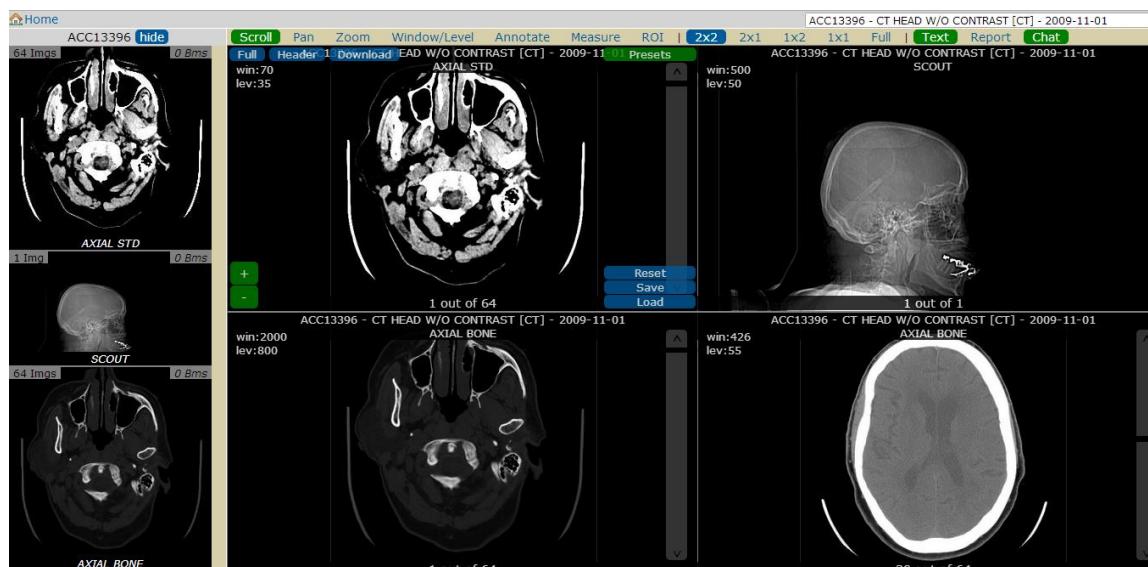
Figure 4 Web based DICOM viewer integrated with the system The viewer enables users to scroll, pan, zoom and change the window/level of the images. The user is also able to make annotations, mark ROI and measure distances between two points.

The alpha system has already been developed and currently being tested. To provide a fully functional system for managing clinical trial data, a beta version is currently under development. The beta version aims to improve the robustness of the program and provide new tasks such as multimedia data player into the workflow.

## 4. FUTURE WORK and CONCLUSION

Based on the experiences gained by the alpha version, the beta system will be developed and applied to the Dose Optimization for Stroke Evaluation clinical trial. A preliminary evaluation of the system will be conducted in the DOSE clinical trial with data from the subjects enrolled in the DOSE trial. The trial has enrolled 18 subjects and target enrollment is 60 subjects during a four year period. The system will be evaluated by researchers, therapists, and evaluators in the DOSE trial based on these subjects enrolled. Evaluation will be conducted on adaptability to workflow, usability, cost-reduction, user-interaction and user's satisfaction. Questionnaires from the users will also be collected.

In summary, we have developed a prototype alpha informatics system with the intelligent workflow engine. The system aims to provide flexibility in building and tailoring the workflow in various stages of clinical trials. By providing a solution to tailor and automate the workflow, the system can save time and reduce errors for clinical trials. Although our system is designed for a clinical trial in stroke rehabilitation, it may be extended to all other imaging based clinical trials.

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# Development of a Web-based DICOM-SR Viewer for CAD data of multiple sclerosis lesions in an imaging informatics-based eFolder

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## ABSTRACT

In the past, we have presented an imaging-informatics based eFolder system for managing and analyzing imaging and lesion data of multiple sclerosis (MS) patients, which allows for data storage, data analysis, and data mining in clinical and research settings. The system integrates the patient's clinical data with imaging studies and a computer-aided detection (CAD) algorithm for quantifying MS lesion volume, lesion contour, locations, and sizes in brain MRI studies. For compliance with IHE integration protocols, long-term storage in PACS, and data query and display in a DICOM compliant clinical setting, CAD results need to be converted into DICOM-Structured Report (SR) format. Open-source dcmtk and customized XML templates are used to convert quantitative MS CAD results from MATLAB to DICOM-SR format. A web-based GUI based on our existing web-accessible DICOM object (WADO) image viewer has been designed to display the CAD results from generated SR files. The GUI is able to parse DICOM-SR files and extract SR document data, then display lesion volume, location, and brain matter volume along with the referenced DICOM imaging study. In addition, the GUI supports lesion contour overlay, which matches a detected MS lesion with its corresponding DICOM-SR data when a user selects either the lesion or the data. The methodology of converting CAD data in native MATLAB format to DICOM-SR and displaying the tabulated DICOM-SR along with the patient's clinical information, and relevant study images in the GUI will be demonstrated. The developed SR conversion model and GUI support aim to further demonstrate how to incorporate CAD post-processing components in a PACS and imaging informatics-based environment.

**Keywords:** multiple sclerosis, system integration, structured reporting, DICOM, wado

## 1. INTRODUCTION

This manuscript presents new advancements in a disease-centric patient record and data management system for Multiple Sclerosis patients. The eFolder project has expanded to be applicable in full DICOM-compliant clinical and research environments. The manuscript also explains the methodology of converting a computer-aided detection (CAD) result from raw image processing data to a structured report format fit to the DICOM standard (DICOM-SR). The SR document, along with MR images and patient data, are displayed via a web accessible DICOM object (WADO) viewer. The result offers an example of how to integrate and view post-processing data in both clinical and research environments via the current web technology.

### 1.1. Multiple Sclerosis research

Multiple Sclerosis (MS) is an autoimmune neurological disease that affects approximately 2.5 million people worldwide, and proximately 200 new patients are diagnosed with MS each week in the United States. The body's own immune system attacked the central nervous system, causing damages and scar tissues (called lesions) in brain parenchyma, spinal cord, and optic nerves[1]. There is no known cure for MS, and thus treatments for MS include disease management, reducing number and severity of attacks, and improve patients' ability to function in daily lives[2, 3]. Therefore, longitudinal disease tracking of patients become key in MS treatment.

Magnetic Resonance Imaging (MRI) is a commonly-used tool in diagnosing and monitoring MS by visually displaying lesions[4]. In longitudinal tracking, existing individual MS lesions need to be identified and quantified for monitoring

patients' responses to treatments as well as disease progress. To solve these challenges, an imaging-informatics based eFolder has been designed to store and display MS patient data with MR images and MS lesion quantification results. The benefits of the eFolder include integrated patient data repository, an automatic lesion detection and quantification system to allow disease tracking on MR, and a data mining tool for both clinical and research purposes.

## 1.2. The MS eFolder project

The MS eFolder is a disease-centric, imaging informatics based electronic system that allows management of patient data, imaging data, and post-processing data. The purpose is to integrate patient's neurological examinations, demographic data, and disease history with patient's radiological images to help track a patient's disease profile and disease progression. The MS eFolder system has three main design components: database, graphical user interface, and a computer-aided detection (CAD) system that can quantify lesion volume and number of lesions. The CAD system is used to detect disease changes on the imaging level, including changes in quantity and size of 3-dimensional lesions and changes in brain parenchyma ratio, and correlate MS lesion characteristics (size, number, location) with patient's demographic data for research purposes.

### 1.2.1. eFolder Database

The eFolder database stores text data such as patient history, MR image locations, and lesion quantification results. Database schema has been developed in MySQL The database structure is built such that one single patient has a unique data entry regarding demographics and social data, has a list of all MR studies regarding to MS, and a list of all post processing results available for that patient. The data therefore is patient-centric and allows quick access to a patient's historical data. Patient demographic data is collected and designed via physicians' survey forms. The imaging database follows the DICOM structure to store metadata from headers. The CAD results database stores quantified lesion statistics on both study and image level. The purpose of the database design is to allow patient lookup and query/retrieve of images based on disease profiles and MS lesion characteristics.

### 1.2.2. Computer-aided Lesion Detection (CAD) and quantification system

The MS CAD algorithm is designed to output lesion volumes, lesion locations, and total lesion load. The detailed algorithm design splits up into three parts: preprocessing, lesion voxel identification by probability thresholding, and lesion quantification. The algorithm has been prototyped in MATLAB and has been refined to increase post-processing efficiency by reducing processing time.

The CAD algorithm is designed on 3-D MRI brain images. It uses T1 and FLAIR (Fluid attenuated inversion recovery) axial sequences. The algorithm converts the series of MR images into a three-dimensional matrix for 3-D lesion analysis. Lesion voxel classification is based on Statistical Parametric Mapping (SPM) brain image analysis toolkit for MATLAB[4]. Grey matter and white matter are first segmented, and an expectation minimization algorithm for k multidimensional Gaussian mixture[5] is applied to the brain images. The estimation results are used to determine the likelihood of a lesion voxel based on whether the voxel intensity is outside the predetermined normal range. The normal range is current set at within 3 standard deviations of normal FLAIR intensities.

The results from the voxel classification algorithm is then clustered and quantified based on DICOM values, and the final output includes individual lesion volumes in 3D, lesion locations in coordinate space, and total lesion load for the study.

## 1.3. IHE Post-processing workflow with MS eFolder

Last year, we presented a workflow profile and simulation for MS eFolder within a clinical environment. The workflow is designed based on the Integrating the Healthcare Enterprise (IHE) post-processing workflow profile[6,7]. Figure 1 shows how the MS eFolder is hit in the clinical workflow.
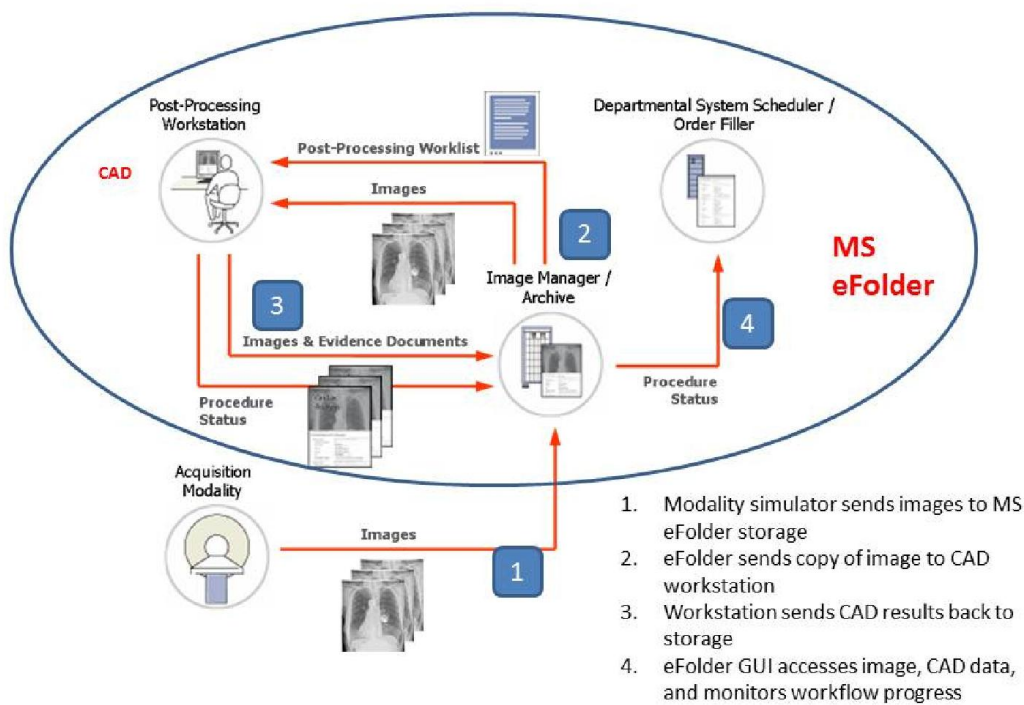
Figure 1. MS eFolder workflow diagram with IHE postprocessing profile. The blue circle indicates all of the components included in the eFolder. The steps 1 through 4 indicates the order of workflow of the demonstration.

The workflow for MS eFolder integration is defined in four steps:
1. MR images are sent from modality simulator to the eFolder server for archiving
2. The eFolder server sends a copy of the images to the CAD Workstation for postprocessing analysis
3. The CAD Workstation sends the completed CAD report back to eFolder server for archiving
4. At the completion of each of the previous steps, a status tracking tool inside eFolder displays alerts of the study progress to the user

The workflow was demonstrated successfully in the laboratory environment. The last step of this workflow is to let users view post-processing data on the eFolder web-based GUI. Therefore, converting post-processing data (which was in MATLAB results format) into a DICOM-compliant format and display was the next step in eFolder integration.

## 1.4. DICOM SR

A structured report (SR) is by definition a radiological report in a tabulated format. Instead of radiologists' dictations on a particular study, the report is converted to a tabulated format. A DICOM SR is a structured report object that is treated the same as DICOM image objects, conforming to the DICOM standard in archiving, transferring, and managing of studies[8]. Figure 2 shows how the DICOM SR structure fits in a real-world model[9].
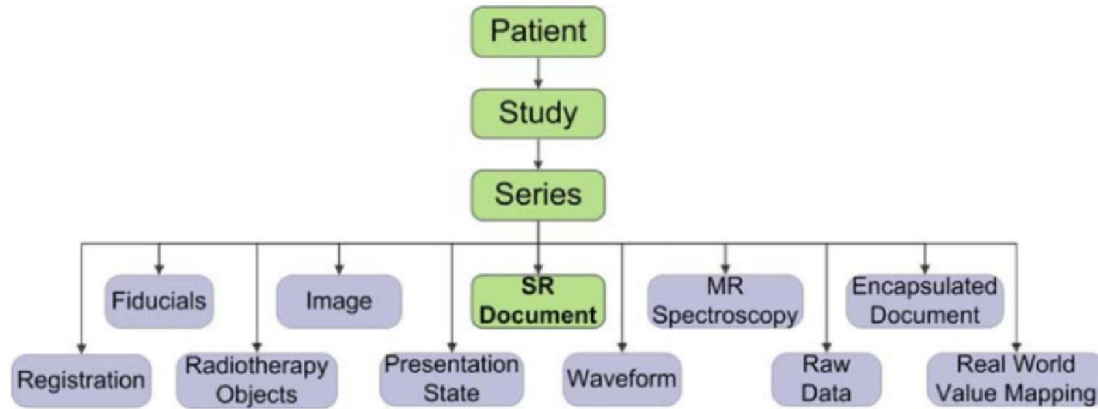
Figure 2. DICOM SR objects in the DICOM model of the real world. CAD results are saved in the SR document on the same level as the DICOM images, under the DICOM series.

The advantages of DICOM SR include consistent report contents throughout the system, linking with DICOM study origins and linking of key images, allowing data mining, and provide better support to automatically generated content from a CAD application. These benefits highlight the motivation of converting CAD result generated by the MS eFolder to DICOM SR.

After the CAD results are converted to DICOM-SR, users need to be able to view the SR data along with the DICOM images. The MS eFolder has a web-based GUI to display DICOM images and patient's clinical and demographical data. The goal is to parse SR documents on the server side, and display the DICOM SR document contents by a web browser to complete the eFolder's comprehensive GUI.

## 2. METHODS

In this section, the methodology of creating a DICOM-SR web-based viewer is explained. This includes data collection and how the CAD data is generated, converting the CAD data into DICOM SR objects, and how to parse and integrate SR objects into web-compliant format for display.

### 2.1. Data collection

Image and patient data used in the MS eFolder setup is the same as existing eFolder data that has been collected over 3 years. A total of 72 patients are collected: 36 Hispanic and 36 Caucasian patients. The patients of two groups are matched by gender, age (within 5 years), disease duration (within 5 years), and disease type (all are relapse-remitting). All brain MR studies are collected at University of Southern California Academic Medical Center and Los Angeles County Hospital. MR images are in DICOM format and anonymized. All studies contain noncontrast T1 and FLAIR axial slices as required by the MS CAD algorithm.

### 2.1.1. CAD data

The CAD algorithm has been performed on all 72 studies. In addition, lesion contours by neuroradiologists at USC have been collected to act as gold standard for lesion detection. The contours were done manually by two neuroradiologists on Fuji Synapse 3D post-processing client in the clinical environment. Currently the manual contours are used in this project, as the CAD algorithm is still being refined for more consistent accuracy in its results. Figure 3 shows the MATLAB results of a sample data.

Figure 3. Raw MATLAB output of MS CAD. Left: original FLAIR axial image. Middle: lesion contour overlaid on the FLAIR image. Right: MATLAB outputs. lesionLoad includes individual lesion volumes, numberOfLesions indicates that there are 22 unique lesion bodies in this study, and totalLesionLoad is the sum of all lesion volumes.

### 2.1.2. Brain matter volume quantification

Whole brain atrophy is related to MS disease progression[10]. The loss of white matter and grey matter volume is directly related to disease severity and can be tracked to measure treatment's effectiveness. An often-used indicator for this is the brain parenchymal fraction, or the fraction of brain matter volume over the whole brain volume (brain matter and CSF). In order to track BPF in MS patients, the eFolder utilizes BrainSuite's segmentation methodology[11]. The BrainSuite toolset is a free-to-use brain MR image processing software developed from a combined effort of UCLA and USC. Brain segmentation from BrainSuite utilizes patient's T1 axial series to perform a number of tasks, including skull stripping, tissue classification, pial surface generation, etc. to identify brain matter structures. The usage of 3rd-party software like BrainSuite is to quickly propotype the new CAD features and generate comprehensive CAD results for DICOM-SR objects. Figure 4 shows BrainSuite GUI and results of brain segmentation of a sample study.
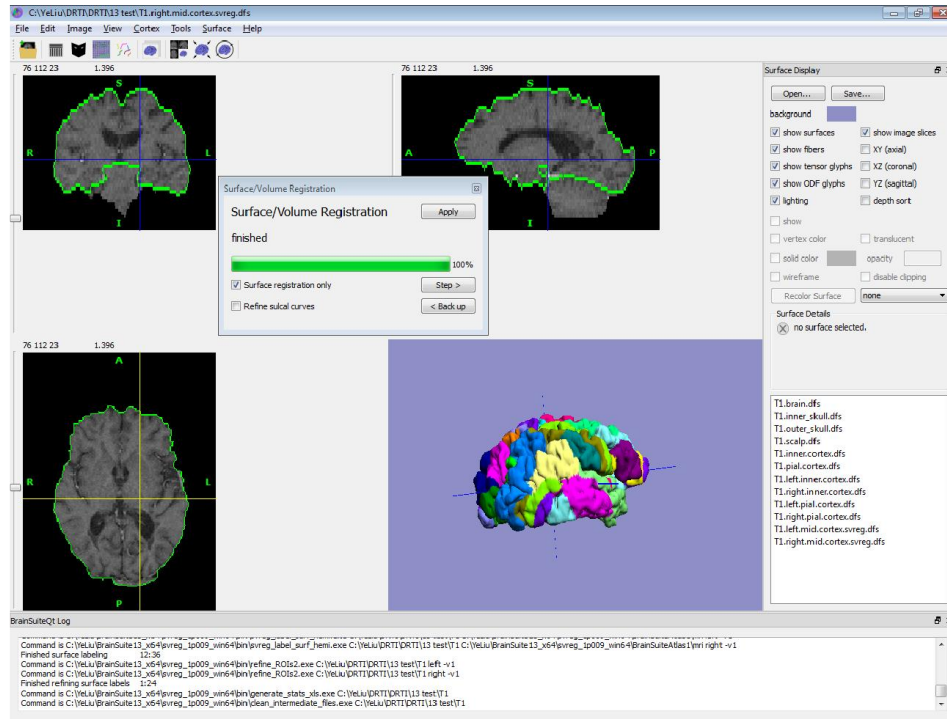
Figure 4. BrainSuite GUI for brain volume segnmentation and registration.

The output of the BrainSuite analysis is quantified via MS eFolder CAD software to calculate white matter volume, grey matter volume, and CSF volume. The results are saved and included in the DICOM-SR documents.

### 2.1.3. Lesion Location identification

The lesion location data for MS eFolder CAD is obtained from BrainSuite's surface and volume registration toolkit (SVG)[12]. The purpose of the SVG toolkit is to spatially map the segmented brain parenchyma (surface models from the previous section) into a brain template, which in turn allows anatomical labelling of the segmented brain. Using this knowledge, the eFolder is able to map a patient's lesion coordinates to the registered brain of the same study, thus identifying anatomical location of MS lesions. In the above Figure 4, results from the SVG toolkit can be seen on the bottom-right panel of the 4x4 window.

### 2.2. DICOM-SR methodology

### 2.2.1. Creating DICOM-SR objects from MS CAD

The workflow of converting CAD results from MATLAB to DICOM-SR, then converting to web-based display format is shown in Figure 5.
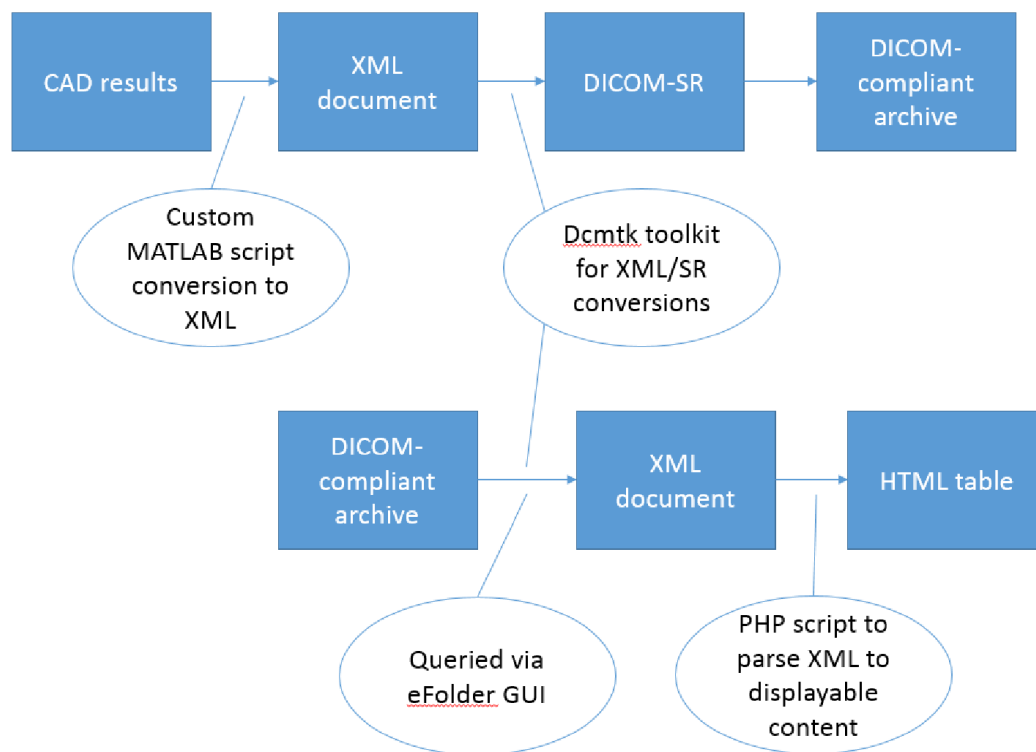
Figure 5. Workflow diagram for DICOM-SR conversion and display. Top row: converting MS CAD results to DICOM-SR for storage. Bottom row: querying and displaying information within DICOM-SR objects

The first step is to convert CAD results to an XML document, which then is converted to DICOM-SR via the dcmtk open-source toolkit. In order to generate the correct XML document, sample DICOM SR files are downloaded from D. Clunie's website[13] and converted to XML. The XML template then is modified and customized to store the CAD quantification values. A MATLAB script is used to convert CAD output from a study to the XML file according to the customized template. Figure 6 shows a partial screenshot of the resultant XML document.

```xml
<?xml version="1.0" encoding="UTF-8"?>
- <report type="Basic Text SR">
    <sopclass uid="1.2.840.███████████████">BasicTextSRStorage</sopclass>
    <modality>SR</modality>
  - <patient>
      <id>C001</id>
    - <name>
        <first>C001</first>
        <last>C001</last>
      </name>
      <sex>F</sex>
    </patient>
  - <study studytime="███████" studydate="███████████" InstanceUID="█████████">
      <description>MRI BRAIN WO/W</description>
    </study>
  - <series uid="1.2.840████████████████████████████████">
      <description>Ax T2 FLAIR</description>
    </series>
  - <document>
      <completion flag="PARTIAL"/>
      <verification flag="UNVERIFIED"/>
    - <content>
        <date>███████████████</date>
      - <container flag="SEPARATE">
        - <concept>
            <value>DT.04</value>
          - <scheme>
              <designator>99_OFFIS_DCMTK</designator>
            </scheme>
            <meaning>Report</meaning>
          </concept>
        - <text>
            <relationship>CONTAINS</relationship>
          - <concept>
              <value>RE.01</value>
              <scheme/>
              <meaning>Lesion Report</meaning>
            </concept>
          - <value>
            - <lesion id="1">
                <load>1.447594e+002</load>
              </lesion>
            - <lesion id="2">
                <load>9.616159e+002</load>
              </lesion>
            - <lesion id="3">
                <load>1.861192e+002</load>
              </lesion>
            - <lesion id="4">
                <load>1.292494e+002</load>
              </lesion>
            - <lesion id="5">
                <load>7.754967e+001</load>
              </lesion>
```

Figure 6. XML document to store MS CAD analysis results based on DICOM SR template

The DICOM-SR object is created by dcmtk's *xml2dsr* function[14] and is sent to archive via DICOM protocol.

### 2.2.2. Creating DICOM-SC objects

DICOM secondary capture, or DICOM-SC, are DICOM image objects generated by post-processing clients and software packages. In the eFolder project, DICOM SC are image captures of MS CAD contour results. DICOM-SC,

along with SR, aids users to visualize MS lesion contours in both 2D and 3D space. The secondary captures of MS CAD results are converted to the DICOM format for storage and display from a DICOM image viewer, for streamlining the DICOM-compliant workflow in the MS eFolder system.

For 2D image captures, a MATLAB script is used to overlay 2D lesion contours on top of the FLAIR axial images to create a new series under the DICOM study. An example of the overlay technique is shown previously in Figure 3. DICOM-SCs are stored in the archive and can be viewed alongside the original DICOM images in the DICOM web-based viewer. Figure 7 shows how the DICOM images and SCs are viewed in a WADO (web accessible DICOM objects) viewer.
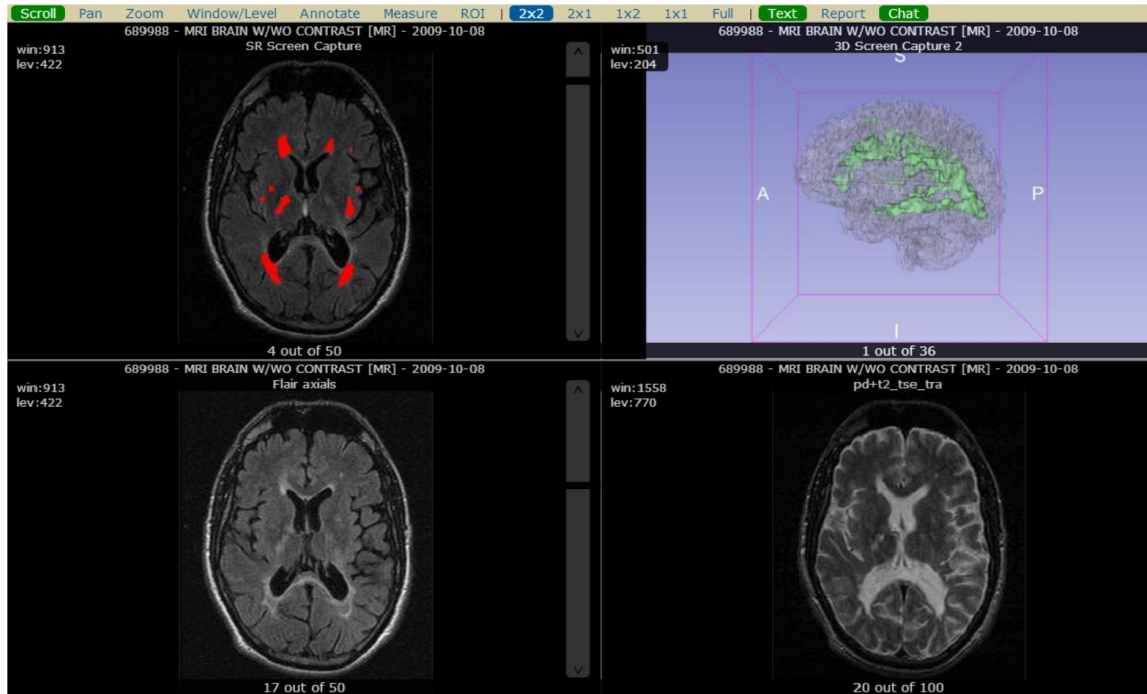


Figure 7. Screenshot of WADO viewer displaying DICOM images and DICOM-SC for the MS eFolder. Upper left panel displays the 2D contour overlay, upper right panel displays the 3D lesion rendering from different angles.

## 2.3. Integration of SR with web-based GUI

In order to access DICOM-SR object and display on the web-based GUI, the GUI automatically queries the SR and images from the DICOM archive when the user accesses a patient's profile in the eFolder. While the DICOM studies are loaded into the WADO viewer, the SR document is displayed separately in an HTML table. The SR object is converted back to the original XML document, and a custom XML-parser is built in PHP to read the document and extract data in a tabulated format. The eFolder simultaneously displays the patient's clinical data, the WADO image viewer, and the SR document viewer. Figure 8 shows the eFolder GUI with all the information available.

Figure 8. Screenshot of comprehensive MS eFolder web-based GUI. Left panel: patient's clinical and demographic data. Right top panel: WADO image viewer embedded in eFolder GUI. Right bottom panel: SR document content in tabulated format.

## 3. RESULTS AND DISCUSSIONS

The comprehensive eFolder GUI has been successfully completed and is available for viewing on the web. The DICOM-SR conversion workflow has been completed and successfully tested within the system. Lesion location and BPF 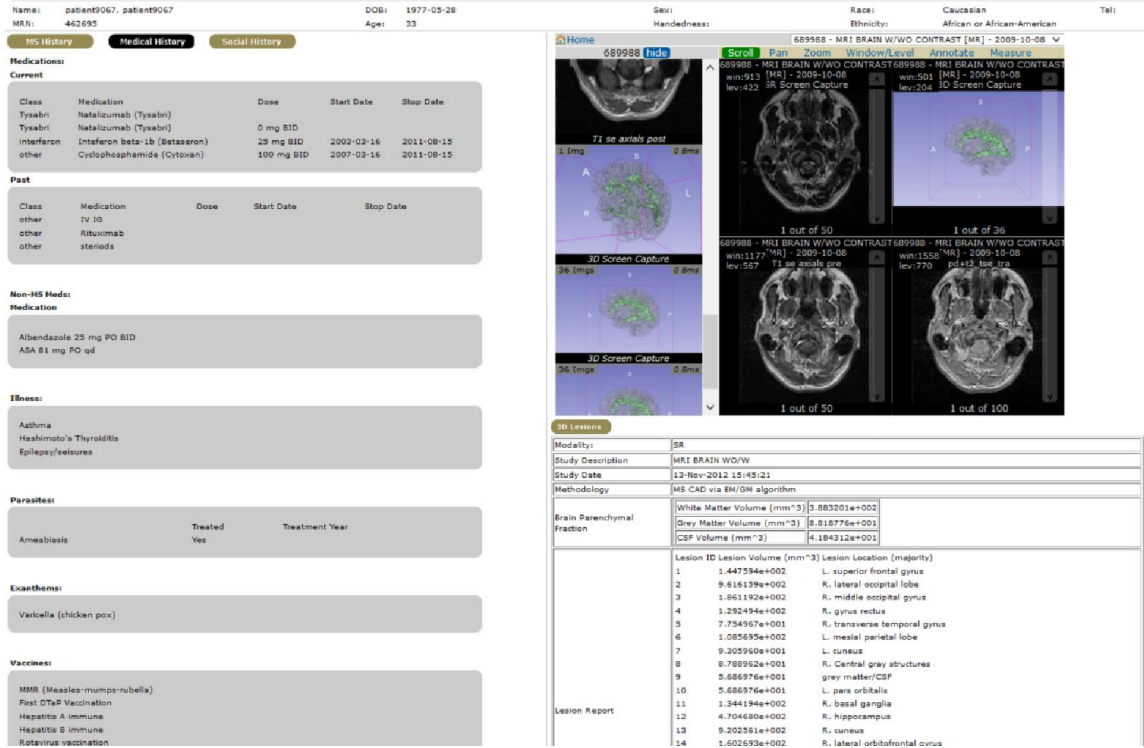measurement features have been tested with all available data from data collection. Overall, the comprehensive GUI design and layout to display CAD data in DICOM-SR has been completed.

There are a few areas of the eFolder DICOM-SR GUI and the eFolder system that need further work and is currently under development:

1. CAD process is currently not automated. While the original CAD based on MATLAB can be run and stored automatically, the BPF measurement and lesion location analysis involve a different software and thus the workflow needs manual inputs to run. In addition, BPF measurements and lesion location identification through BrainSuite toolkit do not work on all of the cases due to image quality from archived PACS studies. Adjustments of calculation parameters and modifications of images are being considered to solve the current roadblock. Future plan is to streamline the CAD process by including BPF and lesion location calculation within the CAD algorithm.
2. Generating the DICOM-SC objects also requires manual input and currently not automated due to involvement of different software toolkits. Future work can include researching on displaying 3D objects by a WADO-compliant viewer directly.
3. The completed eFolder system with IHE post-processing workflow will also need to be completed and evaluated in a real clinical setting. Performance evaluations and user feedbacks will be used to improve system performance and GUI design. The current GUI can be also more interactive to include dynamic referencing on individual lesions in wado viewer and DICOM-SR viewer. Additional features will be discussed and planned according to user feedback.

## 4. CONCLUSION

There are advantages of using DICOM structured reporting to store and present computer-aided detection data in a DICOM-compliant environment. Last year, an implementation of MS eFolder workflow according IHE post-processing workflow profile was presented. In order to display post-processing data in this workflow, the MS CAD data was converted into DICOM SR documents via XML conversions. Additionally, brain parenchymal fraction and lesion location information has been stored along with lesion volumes and numbers of lesions on MR. The conversion methodology has been completed and tested, and results are successfully shown on the MS eFolder web-based GUI. Future work involves automating the entire DICOM SR workflow, completing the MS eFolder system in the clinical environment, and collecting evaluation results in intended day-to-day operations.

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# A collaborative framework for contributing DICOM RT PHI (Protected Health Information) to augment data mining in clinical decision support

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## ABSTRACT

We have built a decision support system that provides recommendations for customizing radiation therapy treatment plans, based on patient models generated from a database of retrospective planning data. This database consists of relevant metadata and information derived from the following DICOM objects - CT images, RT Structure Set, RT Dose and RT Plan. The usefulness and accuracy of such patient models partly depends on the sample size of the learning data set. Our current goal is to increase this sample size by expanding our decision support system into a collaborative framework to include contributions from multiple collaborators. Potential collaborators are often reluctant to upload even anonymized patient files to repositories outside their local organizational network in order to avoid any conflicts with HIPAA Privacy and Security Rules. We have circumvented this problem by developing a tool that can parse DICOM files on the client's side and extract de-identified numeric and text data from DICOM RT headers for uploading to a centralized system. As a result, the DICOM files containing PHI remain local to the client side. This is a novel workflow that results in adding only relevant yet valuable data from DICOM files to the centralized decision support knowledge base in such a way that the DICOM files never leave the contributor's local workstation in a cloud-based environment. Such a workflow serves to encourage clinicians to contribute data for research endeavors by ensuring protection of electronic patient data.

**Keywords:** Cancer Registry, Radiation Therapy, Radiation Oncology, IMRT, Imaging Informatics, Prostate Cancer, DICOM RT

## 1. INTRODUCTION

The primary goal in radiation therapy for cancer is to expose the tumor to as much radiation as possible, while curtailing the dose delivered to critical organs and structures surrounding the tumor. The radiation target, known as the 'Planning target Volume', is generated during treatment planning, and includes a buffer around the tumor to account for organ movement and planning uncertainties. The critical structures surrounding the tumor are called 'Organs At Risk', or OARs. OARs involved in prostate cancer include the bladder and the rectum, since they are situated in close proximity to the prostate. Head and neck cancer OARs include the parotid glands, the mandible, tongue, brainstem, cochlea, etc. Oftentimes, the boundary of the PTV encroaches on some of the surrounding critical structures, or is situated too close to the PTV, resulting in excessive dose being delivered to the OARs. Different types of tissue have different tolerance doses. Research and evidence-based medicine lead to the development of guidelines that should be followed and determination of OAR dose limits that should not be exceeded. Doses in excess of these recommended amounts may lead to undesirable complications and toxicity. However, in order to sufficiently destroy the tumor, some OARs simply cannot be spared and are exposed to more radiation dose than is recommended to avoid severe complications. Currently, there are very few quantitative methods that can assist in the determination of how much sparing is possible without compromising PTV dose coverage. Usually, a patient's internal anatomy places limits on the amount of sparing that is possible for certain critical structures. The spatial inter-relations between the PTV and surrounding OARs can be quantified in terms of distances, overlap [1, 2] and orientation and then a database of retrospective patients with quantified anatomical features can be used to provide estimates of practical dose parameters for new patients. This technique extracts those historical patients who had anatomical features similar to the current patient, but had the best

dose parameters for the OARs as well as the PTV. The treatment plans for these patients can then be used as a reference for carrying out treatment planning for the new patient.

## 1.1 Workflow

Before designing a clinical decision support system, or any other medical imaging informatics system, it is essential to analyze the clinical workflow. The next step is to determine where the new system fits into the clinical workflow, and analyze the effect it will have on normal clinical operations. Figure 1 shows the clinical workflow in Radiation Therapy Treatment Planning. It assumes that the patient has already been enrolled for Radiation Therapy, and depicts the steps that follow. These steps are summarized below:

- <u>CT Simulation and Portal Image</u>: Generation of the CT images that are used for treatment planning.

- <u>ROI Contouring</u>: All relevant ROIs are contoured slice-by-slice on the Treatment Planning System (TPS).

- <u>Initial Parameters</u>: Selection and placement of fields, number and direction of beams, etc.

- <u>Dose Grid Computation</u>: The TPS calculates the dose grid.

- <u>Plan Evaluation</u>: Review of Dose Volume Histograms, isodose contours, dose homogeneity, etc.

- <u>Plan Approval</u>: The radiation oncologist either approves or rejects the plan based on the evaluation results

- <u>Re-adjustments and fine-tuning</u>: Further adjustments to resolve inadequacies (if any) found in the evaluation.
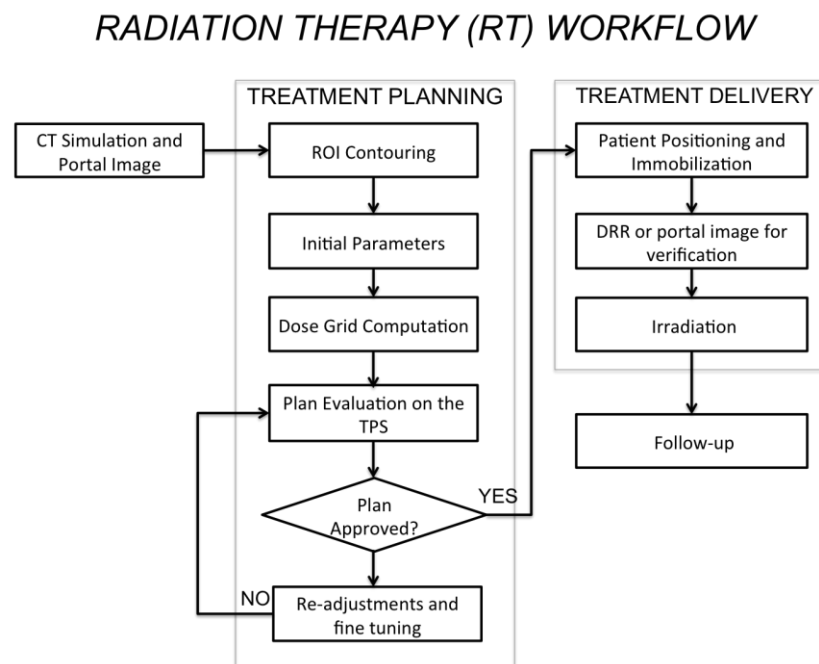


Figure 1. Radiation Therapy Workflow [5, 3]

The decision support system benefits the clinical workflow by potentially reducing the number of iterations of the treatment evaluation loop. Not only can it reduce the number of iterations, but also provides the most optimized evaluation results in very few iterations. This helps to increase workflow efficiency, and to facilitate development of treatment plans that are practical as well as more optimal.

## 1.2 The Decision Support System and Challenges in Implementation

The main goal of the decision support system is to provide clinicians with feedback regarding how other similar patients have been treated and then facilitating the clinician to use those treatment plans that had the best dose parameters. In this context, the system should be able to take relevant input from users, record user input methodically in a database, carry

out machine learning procedures, perform ranking algorithms as well as present information in a familiar and user-friendly fashion. Since the core application is that of a decision-support system, the quality, variety and amount of training data dictate the performance of the system. To accomplish this objective, it is important for the system to recruit data from multiple institutions and multiple treatment planning systems. The follow strategies may be employed in order to help fulfill this requirement:

1. Adoption of DICOM [4,5]: Integrating data from systems built by different vendors either requires a universally accepted standard, or complicated data consolidation and recoding techniques. Fortunately, DICOM provides very reliable definitions for DICOM Radiation Therapy objects, and is also supported by most major Treatment Planning System vendors. As a result, we have chosen to build our data model around the DICOM standard, and so the system can accept DICOM RT [5] objects such as Structure Set, Plan, etc. This allows data from multiple sources to be merged into a single, central repository.

2. A web-based approach: A web-based system allows users to access the system from any location in a cloud-based environment. Since the application is designed to run in web browsers, this also allows it to be platform independent up to a certain extent. Data from multiple sources can thus be collected efficiently, and every user can now draw upon the wealth of the entire aggregated data pool.

3. Client-side DICOM Parsing Protocol in a cloud-based environment: Potential collaborators are often reluctant to upload even anonymized patient files to repositories outside their local organizational network in order to avoid any conflicts with HIPAA Privacy and Security Rules. This problem can be circumvented by developing a tool that can parse DICOM files on the client's side and extract de-identified numeric and text data from DICOM RT headers for uploading to a centralized system. As a result, the DICOM files containing PHI remain local to the client side. This results in extracting only relevant yet valuable and unidentifiable data from DICOM files in such a way that the DICOM files never leave the contributor's local workstation. Such a workflow serves to encourage clinicians to contribute data for research endeavors by ensuring protection of electronic patient data.

## 1.3 The Data Model

This section describes the DICOM data model used in the decision support system. As mentioned previously, we have adopted the DICOM standard as the backbone of our system. The data model leading up to the actual database lays the foundation for all future applications by ensuring efficient data accessibility. Proper organization and good data accessibility is essential in making the machine learning and data processing tools feasible. A good understanding of the structure and the relationship between the principal data elements facilitates proper implementation. The four main types of data objects that the system deals with are: DICOM RT Structure Set, DICOM RT Dose, DICOM RT Plan, DICOM CT Images. Figure 2 shows where each of these objects fit into the data model. The DICOM RT Structure Set object defines the various structures of relevance, or 'Regions Of Interest' (ROIs) such as the radiation target (the tumor) as well as surrounding Organs at Risk (OARs). It also provides the coordinates of the contours that outline these ROIs. The DICOM RT Dose object contains a three-dimensional dose grid, as well as Dose Volume Histogram sequences for all the ROIs defined in the Structure Set object. The DICOM RT Plan object contains technical parameters and details regarding the treatment beams and fields such as shape, number, energy, etc. The CT images are the CT simulation images that are used specifically for treatment planning. The RT objects all fall under a special type of series – the RT series. Figure 3 shows the relationship between the different elements in the Structure Set objects and Figure 4 shows similar relationships, but for the dose object.
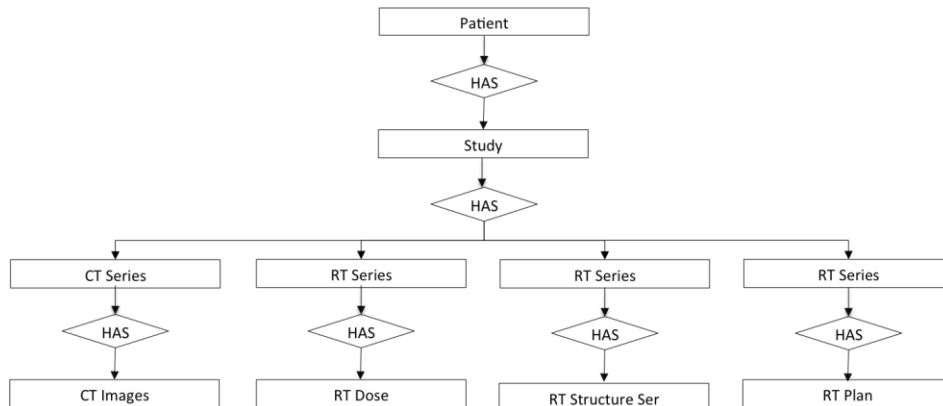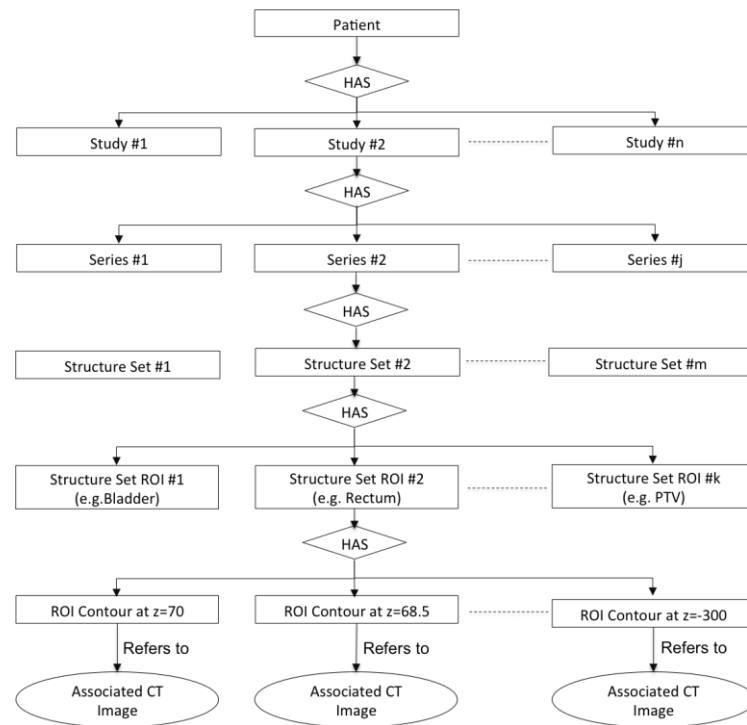
Figure 2. DICOM RT objects in the DICOM data model



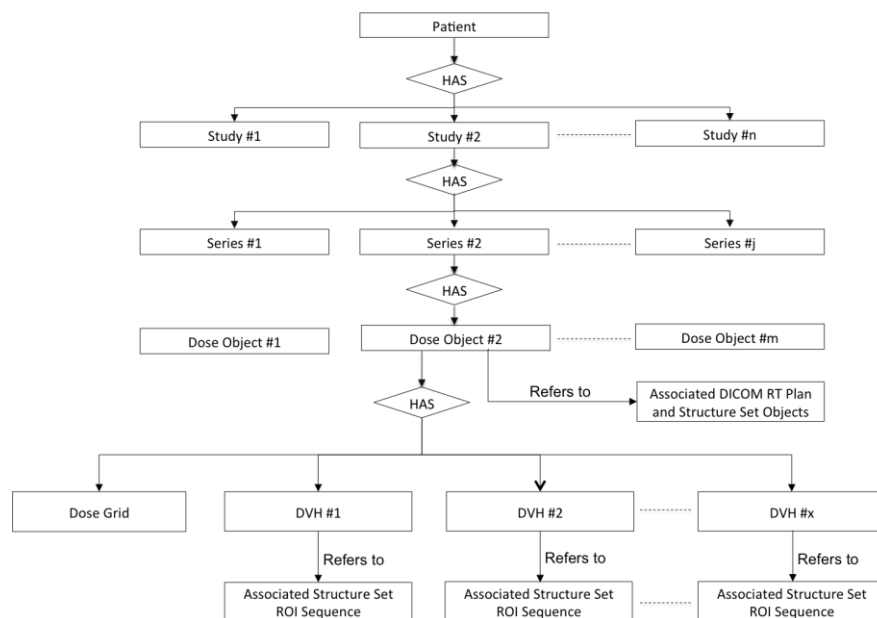Figure 3. Data Model of the RT Structure Set Object



Figure 4. Data Model of the RT Dose Object

## 2. METHODS

The following sections describe the system architecture and components as well as the client-side parsing protocol for data sharing and collection. Proper design and implementation are essential in order to fulfill system goals.

### 2.1 System Architecture

Figure 5 depicts the system architecture and inter-connections between the various components. The main components of the system are describes below:

1) The <u>DICOM Gateway</u>: This component is responsible for reception and management of incoming DICOM data. It can operate in one of two modes. The first is server-side parsing, wherein the files are uploaded after anonymization, and then parsed on the server by a python script. The second is client side parsing, where the DICOM files do not leave the client's machine at all, and a JavaScript parser accesses these files through a browser and extracts only certain pre-defined attributes that are known to be anonymous. The gateway also catalogs all the DICOM metadata that it receives into the database.

2) The <u>Database</u>: The database records all relevant metadata associated with various DICOM objects, as well as data that are extracted from the DICOM metadata after processing. Our decision support system uses MySQL, which is an open-source relational database management system.

3) The Web-based Zero-Footprint <u>Graphical User Interface</u>: The GUI is responsible for presentation and visualization of the results of system analysis, as well as clinical data objects such as CT images, ROI overlays, isodose curves, etc. The GUI is written using HTML and JavaScript.

4) The <u>Decision Support module</u>:  This module carries out all the data processing and machine learning tasks such as extraction of anatomical features, similarity searches, regression model predictions, etc. Some of these functions have only been prototyped in MATLAB so far, but are in the process of being ported to Python scripts that can be integrated directly with the system.  The algorithms are performed on the server-side while the results are displayed through the web-based GUI.

5) The <u>Knowledge Base</u>: This consists of information that is derived from the raw DICOM data after data processing. This is a specialized subset of the database, which is physically contained within the database, but is conceptually more specific. For instance, it contains the overlap volume histogram [3][4], which is computed from the DICOM RT Dose, RT Structure Set and CT images.

6) The <u>System Controller</u>: This controls the flow of data and operations according to the user's needs and requirements. It acts as the link between the different system components, and schedules and coordinates tasks.
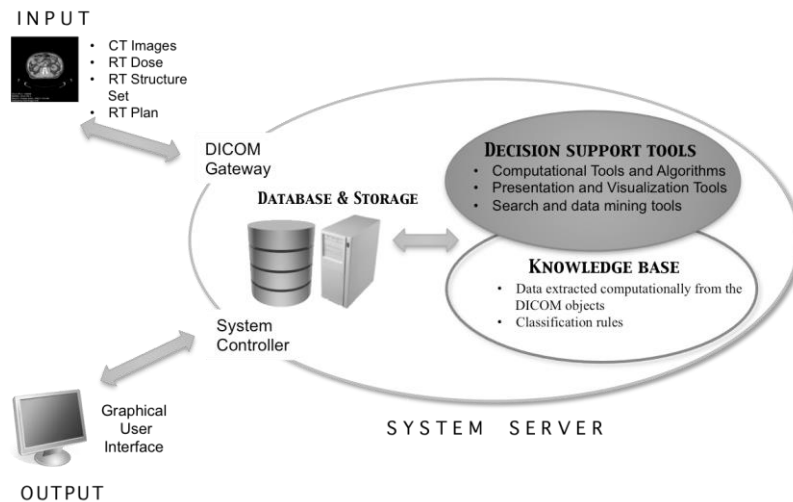


Figure 5. System Component and Architecture diagram

## 2.2 Client-Side Parser

In order to make the system a collaborative initiative that encourages more participants to contribute data from their institutions, we have enabled the system to work in a local client-side parsing mode. This protocol ensures that the user's DICOM files never leave the client machine. Only those fields that have been pre-selected and verified for anonymity are extracted from the DICOM files that the user selects. This extracted metadata is not identifiable, and thus fulfills HIPAA requirements.

This client-side parser is written in JavaScript, and will soon be available as an open source toolkit for imaging informatics developers. The functions of this toolkit run purely on the client's machine, facilitated by a web browser. The user interface prompts users to select a folder from their local file system. All the DICOM files associated with the treatment data that the user wishes to contribute must be available in this folder. The parser will then associate each data element with an attribute. For e.g. the parser will determine exactly which bytes in the data stream belong to the attribute 'Number of Rows'. Once this mapping is in place, another component of the toolkit will extract data elements for a list of pre-determined attributes, encapsulate this information in a format compatible to the server, and send this encapsulated data to the server.

The client-side DICOM parser was developed at the Image Processing and Informatics Lab of the University of Southern California, and is enabled to deal with complex DICOM objects such as radiation therapy files, which include multi-level nested sequences. The list of attributes that are required was determined based on the input parameters for all the data processing algorithms that are run on the server in the decision support module.

## 3. RESULTS

The implementation of this new client-side DICOM parsing workflow is still in progress. However, we have developed a data sharing workflow that demonstrates how this new protocol can be put to practical use. Currently, the client-side DICOM parser has been fully developed and tested and has been shown to preserve the integrity of the data being extracted. It was tested with a dataset of 10 treatment plans associated with 10 different patients. Each dataset included CT images, DICOM RT Structure Set and DICOM RT Dose. A subject matter expert in Radiation Therapy performed verification of the results. DICOM RT Plan is yet to be tested. Figure 6 shows the workflow of this new data sharing protocol for research applications.
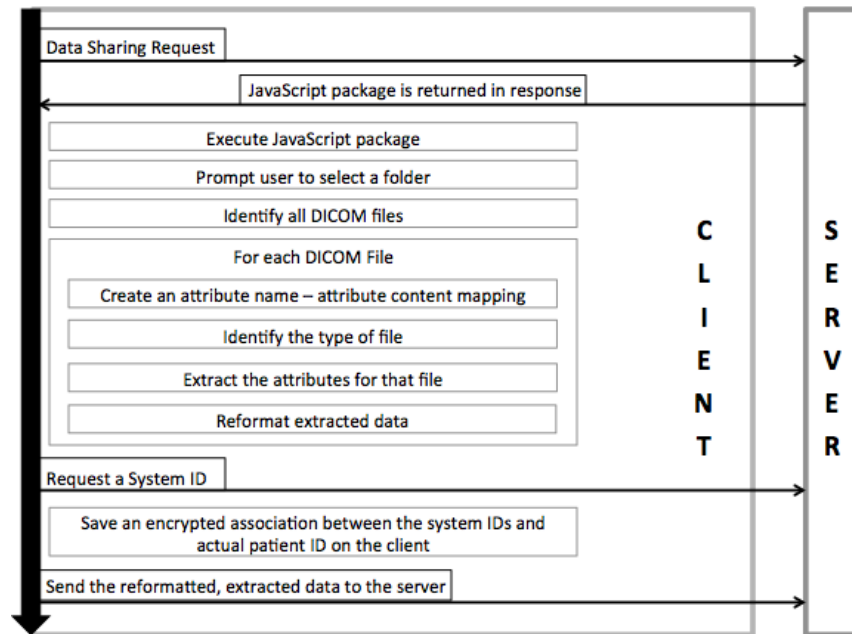


Figure 6. Data Sharing Protocol Workflow in a Cloud-based Environment

(1) The user must first initiate a data sharing protocol with the server. This is a notification to the server that a client wishes to upload data.

(2) The server then returns an acknowledgement and transfers resources back to the client in the form of a JavaScript package that is executed by the client's web browser.

(3) The user is first prompted to select a folder containing all the DICOM files to be processed.

(4) The parser identifies all the DICOM and non-DICOM files stored within sub-folders in the main selected folder. For every DICOM file encountered, the file type is first identified.

(5) Based on the type of file, the parser selects a set of pre-determined attributes to extract since a different set of attributes is associated with each file type.

(6) The values or content for those attributes are extracted and reformatted.

(7) Next, the JavaScript tool sends a request to the server for a new system ID to associate the data with.

(8) This system ID is then stored in a mapping with the true patient ID of the dataset. This mapping is stored in an encrypted format on the client's machine, and can be loaded the next time the user wants to upload follow-up information for the same patient.

(9) The de-identified, reformatted data is then transferred to the server for storage.

## 4. DISCUSSION

Our ultimate aim is to develop a data sharing and collaboration workflow that encourages clinicians to contribute clinical data to our centralized knowledge repository. This data fuels machine learning and data mining applications leading to the development of decision support tools and knowledge discovery of disease patterns, biomarkers, efficacy of treatment protocols, etc. One of the major hurdles is that clinicians are hesitant to contribute data for research purposes out of fear of HIPAA violations. HIPAA regulations are often not well understood, and clinicians often have no time to consult with experts, anonymize files for sharing or to verify the anonymization procedure with a statistician or other expert (which is a HIPAA requirement). This often makes them reluctant to share data, since the procedure is cumbersome and complicated. Offering a simple system that facilitates HIPAA compliance by default will make them more willing and able to share their data. Our system ensures that the DICOM files never leave the user's workstation. Only fixed and selected fields are parsed. Experts have already verified that these fields contain only de-identified data. As a result only de-identified data leaves the user's workstation. This is better than providing an anonymization tool to be executed on the clinician's workstation. However, there is no guarantee that every possible field that has de-identified data, including private tags, will get anonymized. It is better to simply identify a set of 'safe' fields, and then parse those fields only.

## 5. CONCLUSION

We have presented the concept of a novel cloud-based data sharing and collaboration workflow that simplifies the process of contributing clinical data for research purposes, in full compliance with HIPAA regulations. We have described the components of this new data sharing methodology, and described the workflow that demonstrates how this tool may be used in practice. Further development and testing is required to verify the usefulness and usability of this tool.

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# A web-based neurological pain classifier tool utilizing Bayesian decision theory for pain classification in spinal cord injury patients

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## Abstract

Pain is a common complication after spinal cord injury with prevalence estimates ranging 77% to 81%, which highly affects a patient's lifestyle and well-being. In the current clinical setting paper-based forms are used to classify pain correctly, however, the accuracy of diagnoses and optimal management of pain largely depend on the expert reviewer, which in many cases is not possible because of very few experts in this field. The need for a clinical decision support system that can be used by expert and non-expert clinicians has been cited in literature, but such a system has not been developed. We have designed and developed a stand-alone tool for correctly classifying pain type in spinal cord injury (SCI) patients, using Bayesian decision theory. Various machine learning simulation methods are used to verify the algorithm using a pilot study data set, which consists of 48 patients data set. The data set consists of the paper-based forms, collected at Long Beach VA clinic with pain classification done by expert in the field. Using the WEKA as the machine learning tool we have tested on the 48 patient dataset that the hypothesis that attributes collected on the forms and the pain location marked by patients have very significant impact on the pain type classification. This tool will be integrated with an imaging informatics system to support a clinical study that will test the effectiveness of using Proton Beam radiotherapy for treating spinal cord injury (SCI) related neuropathic pain as an alternative to invasive surgical lesioning.

## Introduction

Spinal cord injury (SCI) affects more than 200,000 people in the United States with 12,000 new cases each year. Approximately 70% of the SCI patients suffer from chronic pain, and in 30% the pain is classified as severe. Chronic pain is a serious consequence of SCI and can be a significant factor affecting the level of function and quality of life. It is also associated with lower general health and well-being, and with higher levels of depression. Managing this pain is a challenging problem as neuropathic syndromes tends to be severe and often refractory to pharmacologic management. There are various studies, in which significant effects of drugs could be demonstrated, but these effects are rated as only partially effective and a substantially large fraction of SCI patients do not benefit from it. In this paper we will discuss a web-based neurological pain classifier tool, which is part of a project that focuses on utilizing Proton Beam, radiotherapy for treating SCI related neuropathic pain. This research is a joint collaboration of University of Southern California (USC), Spinal Cord Institute VA Healthcare System, Long Beach, and Loma Linda University. However, for success of any treatment option, it is very crucial that the pain type is correctly classified. Pain classification is an important factor in determination of the source of pain. There are currently various paper-based tools, which have been developed by many experts over the past few decades that are being used in current clinical setting to classify pain. Unfortunately, these tools have not proven to improve pain management of SCI in a significant way. One of the limitations of these tools is that they often require an expert to review collected data. Therefore, current pain classification tools largely depend on the expert reviewer's personal experience and availability, which in many cases may vary. This paper, discusses the development of web based pain classifier system which utilizes Bayesian decision theory algorithms in order to classify pain types in a user friendly and efficient way. Not only is the pain classification tool developed for this particular clinical study, but it can also be extended as a standalone tool for evaluating and classifying pain for all SCI patients.

## Methods

**SCI Pain Treatment & Management:**

Spinal cord injury often results in chronic pain, which is difficult to manage for patients while doing day-to-day activities. In order to properly treat SCI pain, the correct classification of pain type is highly imperative. However, the clinical picture of pain associated with SCI is highly complex in that multiple pains with different characteristics may be experienced simultaneously in different regions of the body. A group of SCI pain researchers has presented their effort to

classify pain in a systematic way, which is shown in Figure 1. The classification organizes SCI pain hierarchically into three tiers:

- **The first tier**: This includes the types of nociceptive pain, neuropathic pain, and other and unknown pain.
- **The second tier:** This includes for the neuropathic and nociceptive categories various subtypes of pain identifies in previous SCI classification.
- **The third tier:** This is used to specify the primary pain source at the organ level as well as pathology, of either is known. For the other pain category, this tier is used to specify distinct reorganized pain entities or syndromes, which do not fulfill the criteria for nociceptive or neuropathic pain.
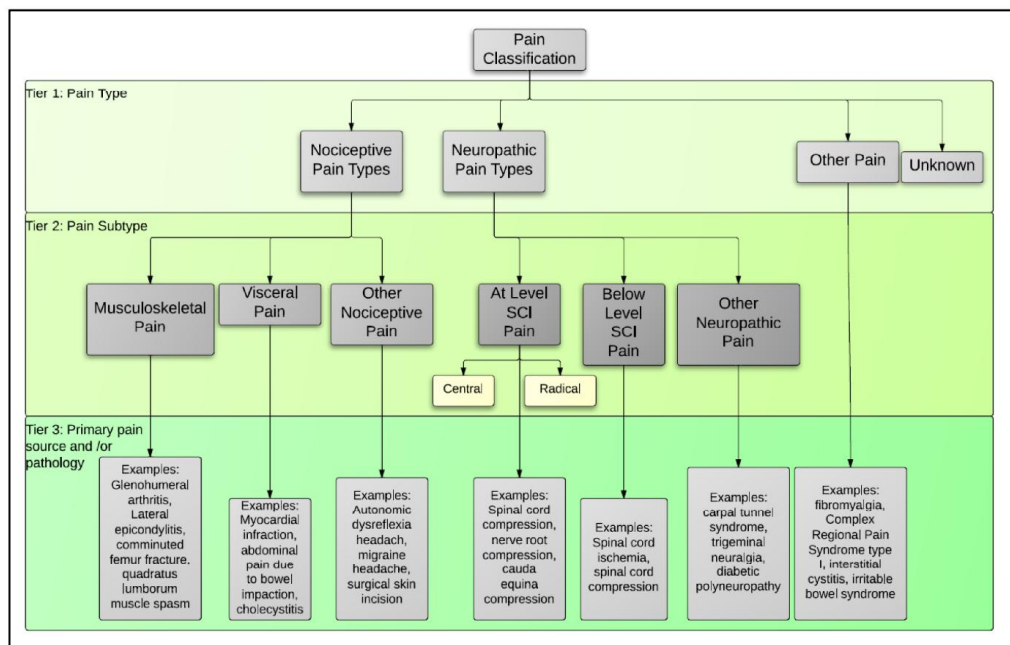


**Figure 1 Pain Classification Tree**

From Figure 1, some of the different pain types will be discussed briefly. Nociceptive is a pain arising from activation of nociceptor, where a nociceptor is defined as a peripheral nerve ending or a sensory receptor that is capable of transducing and encoding noxious stimuli, Musculoskeletal pain refers to pain occurring in a region where there is atleast some preserved sensation and that is believed to be arising from nociceptors within musculoskeletal structure (muscles, tendons, ligaments, joints, bones). Visceral pain refers to pain located (usually) in the thorax, abdomen or pelvis, which is generated in visceral structures. Other nociceptive pain refers to nociceptive pain that do not fall into musculoskeletal or visceral categories. Neuropathic pain is caused by a lesion or disease of the somatosensory nervous system. At level SCI pain refers to neuropathic pain that is electric and shooting pain and is hypersensitive in dermatomes close to the level of injury. Below level SCI pain refers to pain with the same burning, shooting, electric qualities as the previous type of pain but it is located diffusely below the level of injury usually bilaterally in the buttocks and legs. Other neuropathic pain refers to neuropathic pain that is present above, at or below the neurological level of injury but pathologically is not related to the SCI. Other pain types defined as pain that occurs when there is no identifiable noxious stimulus nor any detectable inflammation or damage to the nervous system responsible for the pain. It is also described as dysfunctional pain. Unknown pain refers only to pain of unknown etiology and not to pain of seemingly mixed etiology that is a pain with both nociceptive and neuropathic qualities.

SCI Pain can present as a combination of nociceptive pain, primary neuropathic pain, or involve other pain syndromes such as complex regional pain or secondary processes related to syrinx formation or compressive neuropathies. Managing and treating pain that is developed as a consequence of SCI is very difficult regardless of etiology. However,

developing a good the pain classification is an imperative step in developing effective treatment of pain. Pain that is not classified correctly cannot be assessed and treated appropriately

Regardless of the current treatment options available, managing SCI pain is a challenging problem and it has been shown in various researches that the pain management using drugs has not been as effective in the long term for patients. Studies have concluded that there is an inadequacy of available options to manage chronic pain related to SCI. Several surgical approaches provide some pain control, at least initially, although the long-term results in treating SCI related pain is very disappointing. Loma Linda University has been funded a clinical study to develop a radiosurgical treatment option for SCI related pain using proton beam. Figure 2, shows a general overview of the study, and Figure 3 shows different types of data collected over different phases.
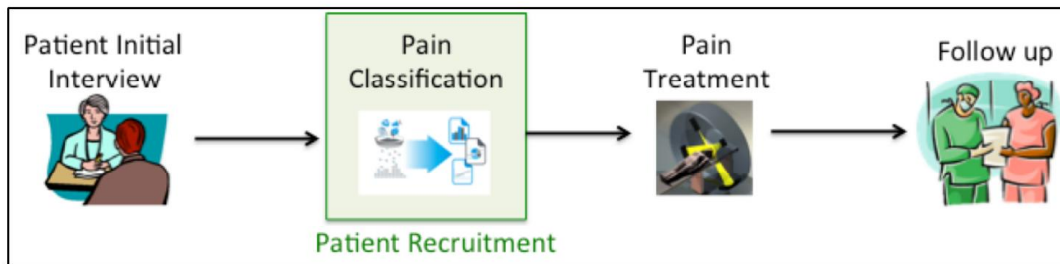


**Figure 2: Clinical study overview**

As shown in Figure 2, there are four stages of this clinical study. First, during the Patient Initial Interview stage, a provider will meet with the patient in order to collect information about injury and pain. This step involves the collection of text-based data as shown in Figure 3. The second stage is Patient Recruitment where pain is classified so that source of pain can be determined in a systematic way and later enrolled in the clinical study. The pain classification tool discussed in this paper is utilized to determine which particular SCI patients will be recruited into the study. The third stage is Pain Treatment, which involves the actual treatment planning, and delivery of proton beam radiosurgery. The fourth and final stage is Follow Up where the subjects are evaluated post-treatment to determine whether the procedures were successful. Figure 3 shows the different kinds of data elements, which get collected at various stages.
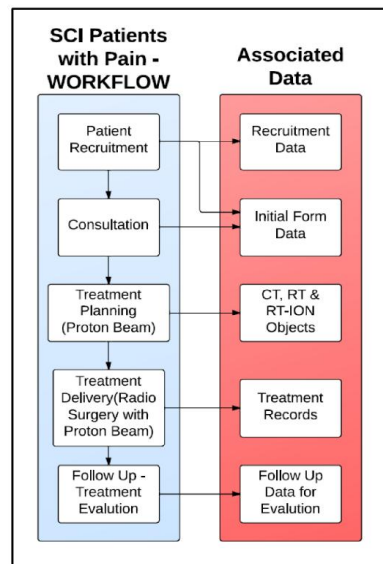


**Figure 3: Data Model**

Over the past few decades researchers and clinicians have developed over 29 SCI pain classification systems, including a recently validated International Spinal Cord Injury Pain Classification. Despite major efforts in SCI pain classification, advances in the management of SCI pain have been fairly insignificant. There are many limitations of currently available pain classification systems, such as:

- Pain associated with SCI is complex and particularly problematic because several types of pain may exist simultaneously and many of these pains are refractory to currently available treatments.
- Standard set of questions can be frustrating for both physicians and patients to answer, which results in poor diagnosis of pain.
- Mostly all pain classifiers need an expert to review data collected, which might not be possible as there are very few experts in this field.

In order to overcome these shortcomings, we have developed a classification system utilizing Bayesian decision theory, which is discussed in next section.

**Bayesian decision theory for pain classification:**

Over the years, clinical decision support systems (CDSS) have been proven to be very useful as an aid to physicians. Furthermore, use of Bayesian networks and their variants has been a successful approach to handling uncertainty in decision support application. [9,10,11] The objective for the development of this tool was to leverage an innovative web-based SCI Pain decision support tool to classify pains helping both experts and non-experts. In order to develop such decision support tool, it is very necessary to understand how pain is classified currently in a clinical setting. When a patient visits healthcare provider with complain history of SCI a general interview is conducted to collect as much information of injury and pain description. During this interview, patients are asked to either fill out forms or answers question directly to the provider. Generally, all pain interview focus on collecting following information from the patient:

- Pain locations.
- Dermatome covered in pain areas
- If the pain area is a joint or not
- Pain description (time, intensity etc)

After collecting all this information, an expert looks back on the logical relations between these factors and then on his/her own experience of dealing with similar cases. For example, an expert will know which pain locations can't be related to one another, as opposed to the pain locations which are directly related and have a same source. He/she will also be able to relate the case at hand with any similar case they had diagnosed previously. On the other hand, with computerized decision support systems, knowledge based systems often use IF-THEN rules, which sometimes cause problems, as clinical problems might vary a lot from specified rules. In order to resolve this conflict, many decision support systems rely on pattern detection. For example, if the clinician is not able to find or remember the exact case from previous years, he will use his experience from the most relatable case. Therefore, the algorithm should look for the best possible option while it tries to classify pain. Based on these design requirements, Figure 4 shows how the probabilities are calculate and related from the above information obtained during an interview
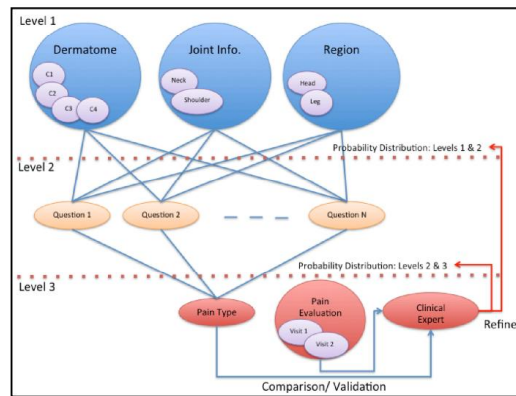


**Figure 4: Bayesian Network for Pain Classification.**

We have been able to implement a tree based pain classification model derived from four layers of knowledge as follows:

1. **Dermatome (Parameter 1)** – This represents which dermatome each pain location belongs to.
2. **Anatomical Region (Parameter 2)** – This indicates which anatomical region each pain location belongs to.
3. **Joint or non-Joint Location (Parameter 3) –** This indicates if the pain location is a joint or not.
4. **Pain related questions (Parameter 4)** – This are the questions which are asked to describe pain

In order to determine values to the first three parameters (1, 2, 3), the three templates are merged into a single image as shown in the figure 5 below. Once the user (patient or physician) selects a location, all three parameters have corresponding values. Pain marking is followed by a set of questions. Prototype of this interface can be seen in figure 5. We have implemented an interactive form for collecting this information, which is shown in results section.
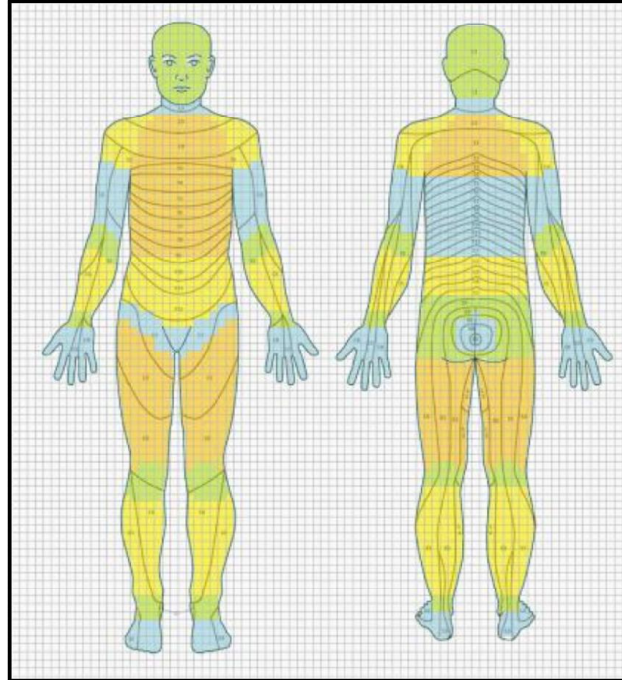


**Figure 5: Three layers of information, anatomical regions, and dermatome and joint information merged in a single image.**

# Results

Data was collected from two sources for a small retrospective pilot study to evaluate the initial pain classification decision support module prototype by performing data analysis and validation. Table 1 below summarizes data after some minor data integrity checks and pre-processing to clean up and normalize for the prototype.

**Table 1 Retrospective data collected in order to validate our hypothesis.**

| | Total number collected | Total number used for analysis | Division of Pain type among used set | Total number of fields |
|---|---|---|---|---|
| Set 1 | 35 Pain locations from 35 Patients | 19 Pain Locations from 19 Patients | 13 Neuropathic; 6 nociceptive | 5 Attributes |
| Set 2 | 26 Pain Locations from 13 Patients | 20 Pain Locations from 9 Patients | 12 Neuropathic; 8 nociceptive | 16 Attributes |

For initial prototype development two algorithms were applied to both Set 1 & Set 2, which are variant of Bayesian decision theory. First one **Bayes Network,** which encodes joint probability distribution of different attributes, which eventually decides the pain type. Second variant of Bayesian Decision theory is **Naïve Bayes**, which is a simple probabilistic classifier, based on applying Bayes theorem (Bayes' Rule) with a strong independence (naïve) assumption. The purpose of using a Naïve Bayes as a second potential algorithm is based on the theory that factors on which a pain expert decides which pain type is classified are not necessarily related to each other. This would be considered a completely unbiased approach to pain classification. Initially we intend to determine which the better approach is: a fully independent decision support algorithm or a one with a priori knowledge embedded. However, we believe the latter will be the eventual successful design. In order to test the algorithms based on Bayes Network and Naïve Bayes, four separate evaluations were performed where tested both algorithms on Sets 1 and 2. We integrated Weka into our system prototype which is a popular machine-learning workbench written in Java. It contains a collection of visualization and algorithms for data analysis and predictive modeling. To avoid train/test split bias in the evaluation, a commonly used cross validation testing. Also we used same measures to monitor performance after each experiment in order to maintain uniformity of the study. We currently used correctly classified vs incorrectly classified pain types for the performance numbers obtained. Table 2 shows the success rates:

**Table 2 Pilot study results (% Correct SCI Pain Classification)**

|       | Bayes Network | Naïve Bayes |
|-------|---------------|-------------|
| Set 1 | 78%           | 63%         |
| Set 2 | 90%           | 60%         |

The first reason for low success rate of Set 1 is that it had many missing data elements and since the data set was small in nature to begin with, the missing elements had a major impact on the classification. We believed that with a full data set, the performance numbers would increase dramatically. Secondly, Set 1 and Set 2 have varying differences in the number of attributes used. Although both sets share similar attributes, the number of attributes in Set 2 is larger which also would impact the overall performance. It is important to note that both sets contain data that is crucial for the diagnosis of pain by the expert and one cannot be disregarded over the other. Therefore, our plan is to develop a new data set by merging both sets and their corresponding attributes. Our next step if to perform the same evaluation but on a larger scale to achieve the proper statistical power calculations.

**GUI Development**

The pain classifier tool is embedded in a web-based imaging informatics system, which makes it portable and easy to access for both patients and providers. Currently, the pain classification procedure involves the patient marking answers to relevant clinical questions and outlining pain locations by hand on a paper-based form. Filling out these paper based forms could be quite overwhelming in terms of the sheer quantity and complexity of the questions, as well as the precision required in answering them. This leads to considerable frustration, and as a result the data capture is prone to errors and inaccuracies. On the other hand, it is cumbersome for clinicians to sift through paper-based forms for making clinical diagnoses and for utilizing this data in performing research. A user-friendly and interactive graphical user interface can ease many of these workflow bottlenecks, and provide an integrated solution for carrying out pain classification.
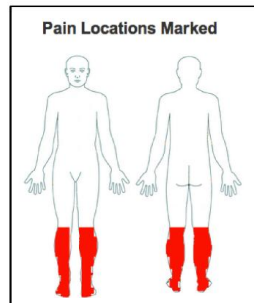


**Figure 6: Pain marking interface**

We have developed a GUI where patients or health care providers can mark locations specifying pain regions as shown in Figure 6. The human figure has been sub-divided into a digital grid as shown in Figure 5, and various grid regions have been labeled with anatomical information in the context of pain classification. Touching or clicking various parts of the screen activates and highlights different regions. This is demonstrated in Figure 6, where the lower leg has been highlighted in red, as the general pain location. Furthermore, this GUI has also been developed and tested for use on tablets and smart phones, making it more practically accessible to patients, and makes the system highly portable. All the text-based and numeric questions are also presented as interactive electronic form elements, some of which can be made mandatory and validated in the background. This reduces the risk of missing, incomplete or incompatible data, which can often have far reaching consequences in research.

Figure 7, shows an overview of what the pain classification interface looks once the data has been analyzed. Pain markings done by patients or providers are integrated in this view. Recorded answers for the pain classification questionnaires are displayed on the right in a manner that is easy to navigate. Pain classification results generated by our Bayesian algorithm are shown in lower left corner. It indicates percentage probability of a pain to be of a certain type. Our GUI has been developed using latest the web technologies, which makes user interactions very smooth and fast.

An expert clinician has validated the integrity of this system's data capture mechanism. Further, a qualitative analysis shows considerable promise and potential in optimizing the efficiency of research workflow.
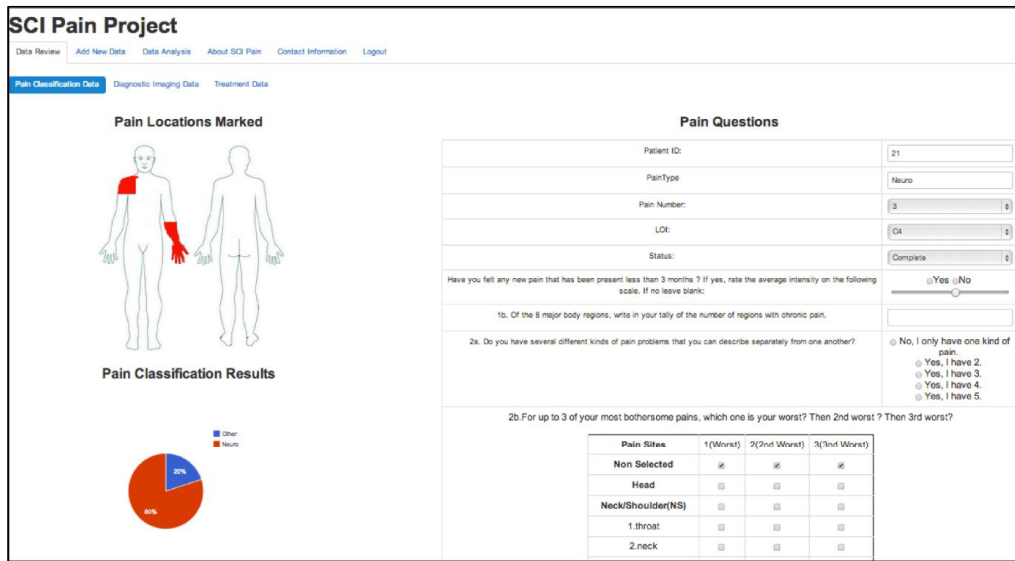


**Figure 7: Prototype of user interface**

## Conclusions & Future work

Over past few decades many clinical problems have been solved using Bayesian theory algorithms, but the field of pain classification remains untouched. We presented a web-based decision support tool, which not only promises to make pain classification process potentially more accurate and efficient, but also makes it possible to see patterns in a large-scale study. Initial results prove that Bayesian theories can be applied to pain classification. This prototype tool promises to take the spinal cord injury (SCI) pain classification to the next level by developing a valid and reliable, web-based decision support system, which encompasses a decision tree system to aid clinicians to accurately classify and manage SCI pain.

Next steps are to further develop this algorithm and test it with a larger data set and to evaluate this classifier integrated in a web-based environment with real time pain classification.

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# An Imaging Informatics-Based System Utilizing DICOM Objects for Treating Pain in Spinal Cord Injury Patients Utilizing Proton Beam Radiotherapy

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## Abstract

Many US combat personnel have sustained nervous tissue trauma during service, which often causes Neuropathic pain as a side effect and is difficult to manage. However in select patients, synapse lesioning can provide significant pain control. Our goal is to determine the effectiveness of using Proton Beam radiotherapy for treating spinal cord injury (SCI) related neuropathic pain as an alternative to invasive surgical lesioning. The project is a joint collaboration of USC, Spinal Cord Institute VA Healthcare System, Long Beach, and Loma Linda University. This is first system of its kind that supports integration and standardization of imaging informatics data in DICOM format; clinical evaluation forms outcomes data and treatment planning data from the Treatment planning station (TPS) utilized to administer the proton therapy in DICOM-RT format. It also supports evaluation of SCI subjects for recruitment into the clinical study, which includes the development, and integration of digital forms and tools for automatic evaluation and classification of SCI pain. Last year, we presented the concept for the patient recruitment module based on the principle of Bayesian decision theory. This year we are presenting the fully developed patient recruitment module and its integration to other modules. In addition, the DICOM module for integrating DICOM and DICOM-RT-ION data is also developed and integrated. This allows researchers to upload animal/patient study data into the system. The patient recruitment module has been tested using 25 retrospective patient data and DICOM data module is tested using 5 sets of animal data.

## Introduction

Many US combat personnel have sustained nervous tissue trauma during service, which results in neuropathic pain. Neuropathic pain is a significant factor affecting level of function and quality of life. Managing neuropathic pain is challenging problem, as neuropathic syndromes tends to be severe and often refractory to pharmacologic management. There are various studies in which significant effect of drugs could be demonstrated. However, these effects are rated, as partial and a substantial fraction of spinal cord injury (SCI) patients do not benefit from it. The main objective of this clinical study is to determine the effectiveness of using Proton Beam radiotherapy for treating spinal cord injury (SCI) related neuropathic pain as an alternative to invasive surgical lesioning. In select patients, synapse lesioning can provide significant pain control. In this paper, we will discuss an imaging informatics-based system, which utilizes DICOM objects for treating pain in SCI patients. This is the first system of its kind that supports integration and standardization of imaging informatics data in DICOM format; clinical evaluation forms outcomes data and treatment planning data from the Treatment planning station (TPS) utilized to administer the proton therapy in DICOM-RT format. It also supports evaluation of SCI subjects for recruitment into the clinical study, which includes the development, and integration of digital forms and tools for automatic evaluation and classification of SCI pain. This research is a joint collaboration of University of Southern California (USC), Spinal Cord Institute VA Healthcare System, Long Beach, and Loma Linda University. In the following sections we will discuss various stages involved in this study and the system architecture. Also, we will describe various independent modules (Pain classifier, WADO viewer), which are developed to support different stages of this study. We will also discuss the DICOM module for integrating DICOM and DICOM-RT-ION data.

## Methods

**Background on spinal cord injury related neuropathic pain:**

Pain continues to be a significant problem in people with SCI. Despite this there is little consensus regarding the nature, terminology and definitions of the various types of pain that occurs following SCI. This has led to large variation in the reported incidence and prevalence of pain following spinal cord injury. Treatment studies have been hampered by inconsistent and inaccurate identification of pain types. Recently, a group of researchers presented their effort to classify pain in a systematic way, which is shown in figure 1. The classification, organizes SCI pain hierarchically into three tiers:

- **The first tier** includes the types of nociceptive pain, neuropathic pain, and other and unknown pain.
- **The second tier** includes for the neuropathic and nociceptive categories various subtypes of pain identifies in previous SCI classification.
- **The third tier** is used to specify the primary pain source at the organ level as well as pathology, of either is known. For the "other" pain category, this tier is used to specify distinct reorganized pain entities or syndromes, which do not fulfill the criteria for nociceptive or neuropathic pain.
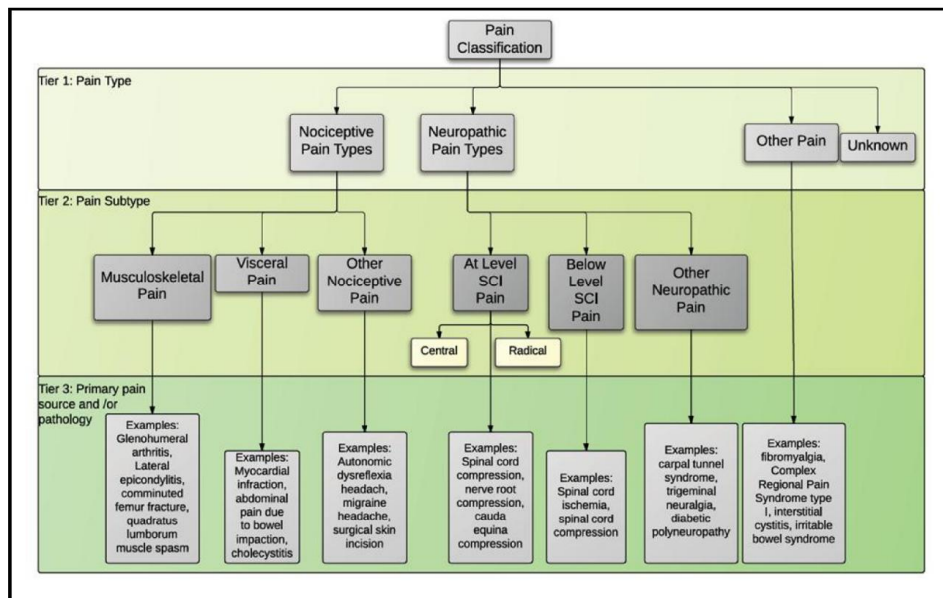


**Figure 1: Pain Classification**

**Pain Management:**

Management of chronic pain syndromes following SCI proves very difficult and unfortunately is often only partially effective. As already mentioned, when treating chronic pain, it is essential to comprehensively evaluate the types of pain and psychosocial factors contributing with emphasis on functional capabilities, behavioral responses to pain, adjustment to disability and degree of motivation. This is of great importance when selecting an appropriate combination of pharmacological, physical, and psychological and other treatment approaches. Treatable underlying pathology, such as local nerve root compression or post-traumatic syringomyelia (with expanding syrinx formation) must be excluded.

Neuropathic pain responds poorly to most available treatments including opioids. The drugs that have been demonstrated to be most effective are the anticonvulsants and tricyclic antidepressants. Anticonvulsants work by dampening abnormal neuronal activity in peripheral nerves and the central nervous system. Tricyclic antidepressants are thought to work by increasing the available amounts of the inhibitory transmitters serotonin and noradrenaline. Several surgical approaches (cordotomy, segmental cordectomy, deep brain stimulation) have been reported to provide some pain control, at least initially, although the long-term results in treating SCI-related neuropathic pain have been disappointing. Lesioning of dorsal root entry zone is generally recognized as the most effective surgical treatment for SCI related neuropathic pain. Therefore, a radio-surgical procedure targeting the synapses located in the dorsal root entry zone will a very good option for treating neuropathic pain.

**Overview of clinical workflow:** Below are the key stages of this clinical study, as shown in figure 2,
- **Patient recruitment at VA Long Beach**
  - ❖ Patient Initial Interview: This first stage is when patient meets the physician for the first time. Physician collects information related to injury (history, pain descriptions etc).
  - ❖ Pain classification: Pain information is used to classify cases with specific pain (neuropathic in this case).
- **Pain Treatment at Loma Linda University**

- ❖ Consultation: Once the patient's pain is identified as neuropathic pain, the physician will meet with the patients in order to consult about the treatment plan.
- ❖ Treatment planning: According to the patient needs, a treatment plan is designed for proton beam therapy. At this stage different DICOM objects will be captured which are described in the next section.
- ❖ Treatment delivery: Treatment will be delivered at this stage and treatment record will be generated.
- **Follow up / Treatment evaluation:** At this stage the improvement in patient condition will be accessed using potential imaging biomarkers.

Also there are two additional stages, which are:
- **Preclinical Animal Study:** Treatment is actually tested on animal first.
- **Preclinical Animal Study evaluation:** Effects of treatment are analyzed to find out if the desired effect if obtained.
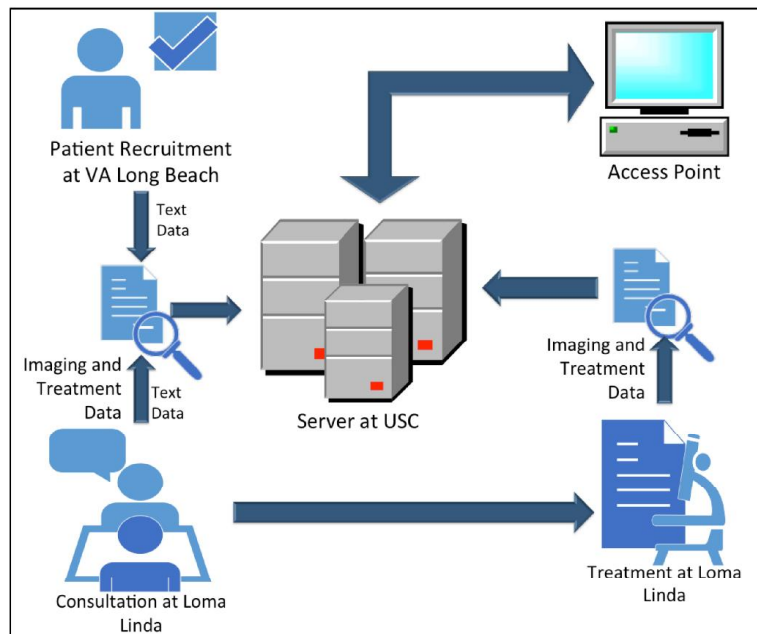


**Figure 2: Clinical Study Overview**

**Data Elements and Data Model:**
For efficient data mining algorithms and a computer support system to work, proper organization and accessibility of data is essential. Data from proton therapy is contained in various DICOM-RT objects as well as other data objects as described below:

- **RT Structure Set**: To carry out radiotherapy treatment planning, the target tissue and organs at risk (OAR) are defined. This process of segmentation of tomographic images or drawings contours of target tumor and OARs leads to a set of structure, which are defined by DICOM RT structure set object.
- **RT Dose**: Treatment planning systems calculate the radiation dose distribution as a matrix of points associated doses. These dose grid files are supported in the DICOM RT dose object. Definitions also exist in the DICOM RT dose specifications to store relationship between dose and structure through dose volume histograms and dose region of interest (ROI) statics.
- **RT Image**: The RT image objet addresses the requirement for image transfer found in general radiotherapy applications performed on conventional simulators, virtual simulations, and portal imaging devices. Such images may either be acquired directly from the device or digitized using a film digitizer.

- **RT ION Plan**: The RT Ion plan addresses the requirement for transfer of treatment plans generated by manual entry, a virtual simulation system, or a treatment planning system before or during a course of proton therapy treatment. Such plans may contain fractionation information, and define proton beams.
- **RT ION Beams treatment record**: The RT ion beams treatment record addresses the requirement for transfer of treatment session reports generated by a treatment verification system during a course of proton beam treatment, with optional cumulative summary information. It may also be used for transfer of treatment information during delivery
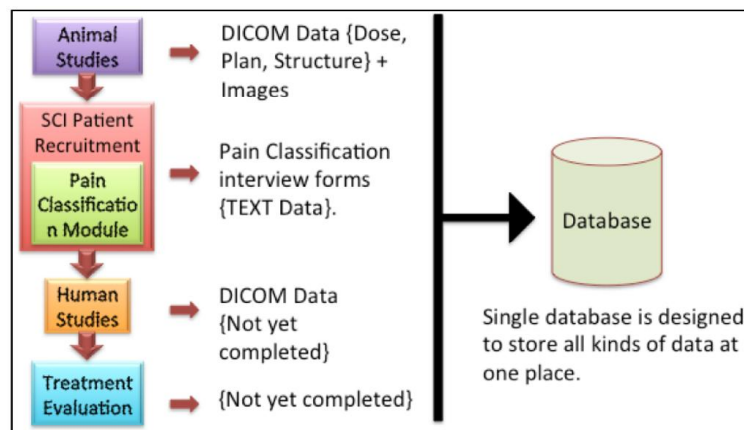


**Figure 3: Data Model**

- **SCI Pain Related Data**: SCI pain data is a holding place for all information regarding pain type. It contains location of pain, group's details, intensity of pain and all different kind of information that get generated during pain classification for patient recruitment and treatment evaluation phase.

**System Architecture:**
Based on various stages of clinical study, as shown in figure 1 and different data elements, we designed an informatics-based system as shown in figure 4. Key components for the system include:

- **Input Data** - It consists of different forms of data, which are either generated or collected at various stages in the workflow. It consists of following:

  o **Recruitment Data** – This data comprises of pain classification object. It contains information for pain sites such as dermatome level, anatomical region, joint related information, ASIA level etc. It also consists text data that indicates of anyone pain location is associated with any other pain location. If there is a relation between multiple pain locations than it also gives details about how they are related.

  o **Initial Form Data** – This consists of the text based form data that is collected during patient recruitment, treatment and follow up.

  o **CT, RT & RT-ION Objects** – This consists of CT images and DICOM objects such as RT structure set, RT Dose, RT Image, RT ION Plan, RT ION Beams treatment record. All are described in Data model section above.

  o **Treatment Records** – These are the records collected from the patient charts.
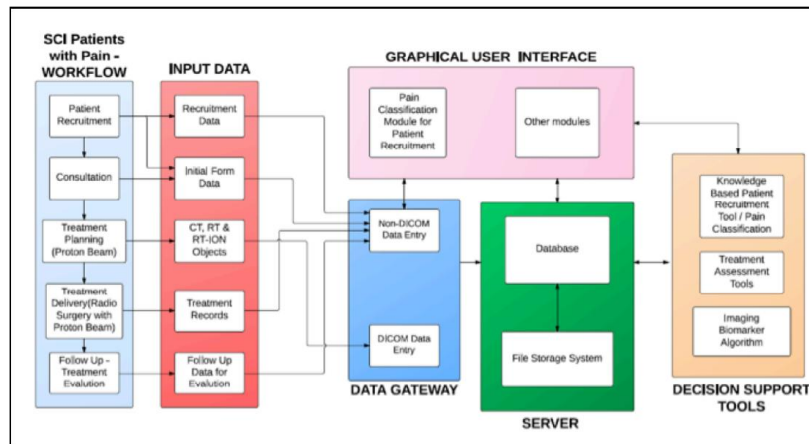
**Figure 4: System Architecture**

- **Data Gateway**- The data gateway is responsible to get DICOM and non-DICOM data, which is collected or generated at various stages of the work, flow, and store it properly inside the system database. Data gateway has two small modules as described below:

  o **DICOM Module** – The DICOM module allows the system to receive DICOM RT and DICOM RT ION objects from PACS or any TPS that can export DICOM Objects. This allows the data to be uploaded to the system through an upload web interface. Upon receiving the DICOM object the DICOM receiver transfers it to the server and triggers the DICOM extractor to update the database and obtain the knowledge information. Query/ Retrieve Tool, which will be available in future, will be able to provide user the ability to query and retrieve DICOM studies from PACS, TPS, or any DICOM storage node to the Server.

  o **Non-DICOM Module** – The non-DICOM module has two components: Text processing module and DICOM RT converter. The former is designed to handle clinical data in a non-DICOM format (text, Excel spreadsheet etc) and the later to convert data, which are defined in DICOM standard to DICOM objects.

- **Server** – The server provides computational power to other components of the system such as decision support tool, web interface and data gateway. All data, DICOM and non-DICOM, is stored and accessed using the central database. This database design is according to the DICOM data model, which is explained in previous section. The design of the database plays a major role as it affects the response time of the entire system as a whole. Also various data objects that are collected has to be stored in the file system using this data base, therefore it is necessary that all form of data is taken into consideration before designing and implementing it. File storage is a major physical memory holder, which contains entire data at one place.

- **Graphical User Interface** - This is the front end of the system, which allows users (patients, physicians and researchers) to interact with the system. Right now the system has a pain classifier developed and is under testing process. In the future, various modules for treatment assessment will also be available.

- **Decision Support Tools** - There are various decision support tools that can be built upon the knowledge that is contained in the server regarding patient history, pain information, treatment planning and outcomes. Our focus here is to collect all the information, and determine some efficient data-mining algorithm to train the system so that it can pull out information, which can later help in evaluation of the treatment. Also once it's working it can be used to improve the effectiveness of the treatment. Also for this project the decision support tools are very use full in the patient recruitment process. We have developed one such tool, for pain classification, which is explained in the next section.

**Pain Classification Module:**

A pain classifier for patient recruitment tool has been designed and has been implemented using simple tools such as jQuery and PHP. We have been able to implement a tree based pain classification model, which was described earlier in the pain classification background section. The pain classifier uses layers of information templates in order to classify any pain. Three layers of information are:

- **Dermatome (Parameter 1)** – This represents which dermatome each pain location belongs to.
- **Anatomical Region (Parameter 2)** – This indicates which anatomical region each pain location belongs to.
- **Joint or non-Joint Location (Parameter 3)** – This indicates if the pain location is a joint or not.

In order to determine values to the three parameters (1, 2, 3), the three templates are merged into a single image as shown in the figure 5 below. Once the user (patient or physician) selects a location, all three parameters gets corresponding values. After this the pain on multiple locations is grouped according the relative occurrence of the pain, or intensity of the pain. Based on this the pain is classified for each location for every patient. After this follow up questions are asked.
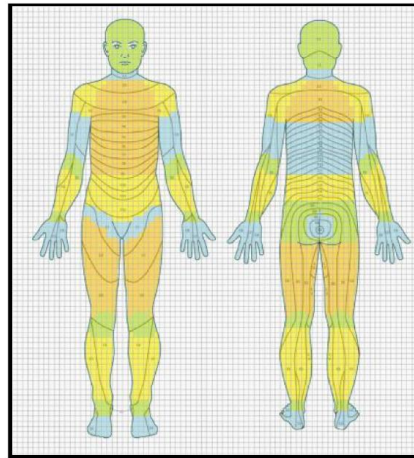


**Figure 5: Dermatome information merged with anatomical and joint information**

The key features of this pain classifier are:

- It is a web-based system.
- It asks follow up questions based on the classification of pain; therefore extra data is not recorded.
- Pain classification makes sure that the patients with the right kind of pain are getting recruited for the study.

**Web-based DICOM WADO Imaging Data Viewer:** As during pain treatment, imaging data will be generated, this module will make it possible for researchers and physicians to study images online.

**Web-based DICOM-RT Object Viewer:** Proton therapy data is contained in DICOM-RT objects, which show how much radiation is give to a patient, what area it is targeted and other related information. This module provides a way to view all this information through the web-based GUI.

## Results

A web based informatics system is designed and developed which is capable of integrating information from various phases of a large research project. The design of this system is such that it allows the development of all modules independently using various technologies including machine learning algorithms and DICOM data objects. Figure 6,7,8,9 shows screenshots from the prototype system.

**Figure 6: Pain Classification Module Interface (Input)**



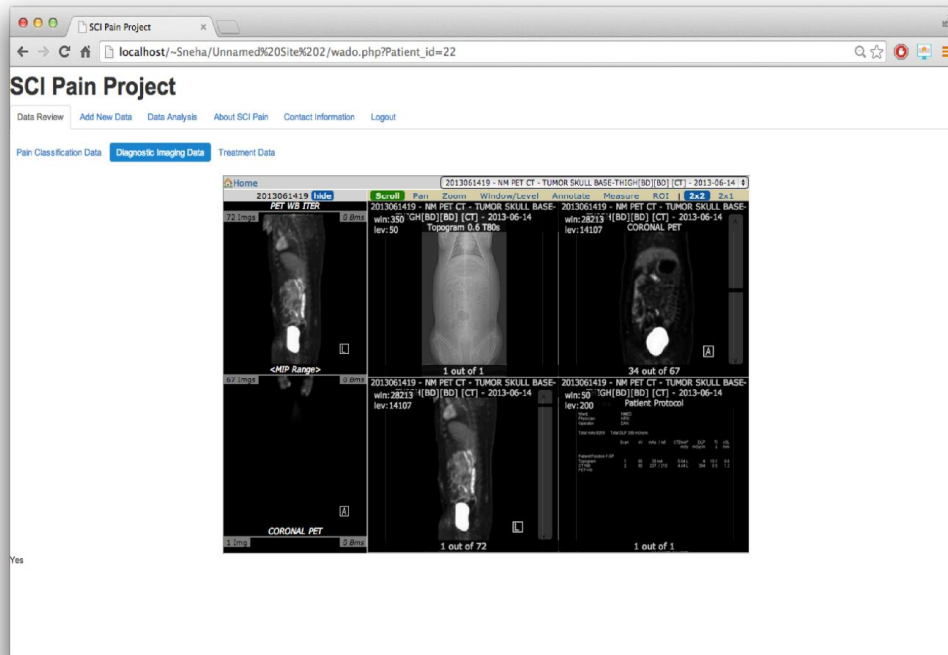**Figure 7: Pain Classification Module Interface (Output)**

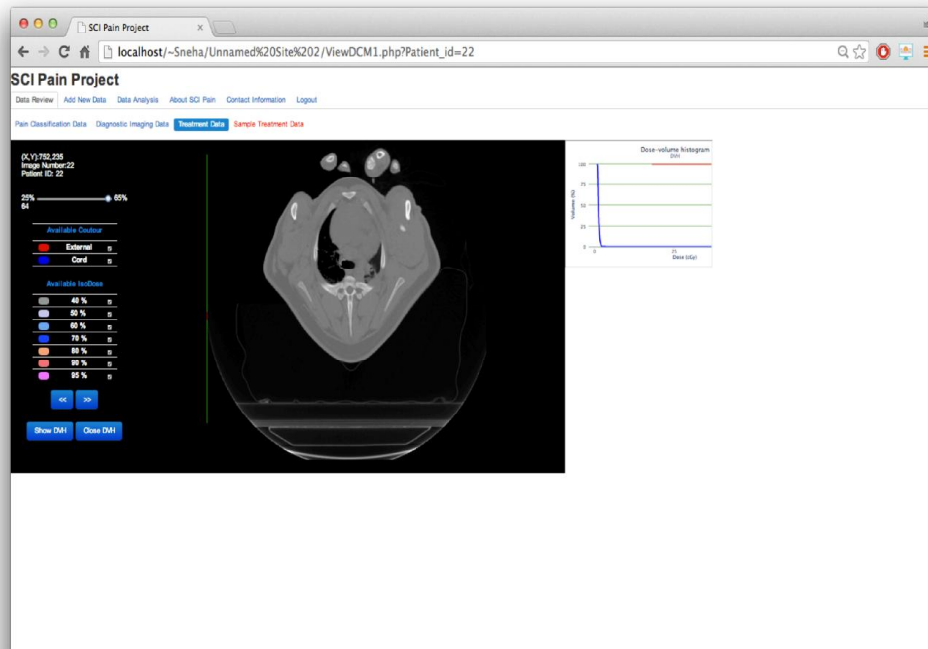**Figure 8: Imaging Data Viewer Module Interface**



**Figure 9: Treatment Data Reviewer Module Interface**

Figure 6 shows the interactive web based tool for pain classification, which is based on the three layers of knowledge, which were discussed in previous sections. The patients can enter pain information by marking on the human figure and also fill out pain related questions on the same page. Figure 7 shows how pain classification information is available once the patient answers all questions. It shows the probability of pain being a neuropathic versus other pain type. The current system is able to integrate information and run machine-learning algorithms on the data collected via various modules which includes patient recruitment data (demographics, pain history, pain location etc) collected using the pain classifier and DICOM data which are uploaded into the system using the DICOM up loader module. The interface for imaging data reviewer and DICOM object viewer is shown in Figure 8 & 9.The patient recruitment module was tested using 48 retrospective patient data and DICOM data module was tested using 5 sets of animal data. Table below shows what different data sets are integrated into the system as shown in table 1.

| Data Type | Integrated in the System |
|---|---|
| SCI Pain interview | 25 |
| Imaging Data | 5 |
| Treatment Data | 2 |
| Evaluation Data | 0 |

Table 1: Data integrated into the system

## Conclusions & Future work

This is the first system of its kind that integrates preclinical data, from animal studies and research related human studies, on one web-based platform with standardized DICOM data objects. It supports integration and standardization of imaging informatics data in DICOM format; clinical evaluation forms outcomes data and treatment planning data from the Treatment planning station (TPS) utilized to administer the radiation dose in DICOM-RT format. In addition, it supports evaluation of SCI subjects for recruitment into the clinical study, which includes the development, and integration of digital forms and tools for automatic subject evaluation and classification of SCI pain as well as a rules-based decision tree. This medical informatics system capable of integrating various data objects, such as patient recruitment information; preclinical studies, treatment related information utilizing the DICOM standard and implemented on single web-based platform.

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# SELECTED PEER REVIEW REPRINTS
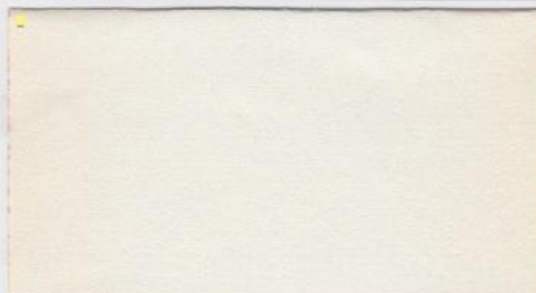
**Purpose**

A minimally invasive spinal surgery (MISS) electronic Patient Record (ePR) system was developed in 2007 and was deployed for clinical operation in 2009. This system had been used on over 300 patients for image-assisted spinal surgery with encouraged qualitative results over the conventional MISS procedure. Among them are: (1) the system saves the surgical team operation time per patient, (2) automatic digital operation during pre-surgical operation (pre-op) and real-time intra-surgical operation (intra-op) provide accurate on-line imaging data display and archive, and (3) the pre-op and post-surgery operation (post-op) authoring toolkit allows surgeons to systematically generate a timely efficient surgical reports. However, this system was a first attempt to test the effective and efficacy of using such a digital system for surgery targeting only for MISS. Its design was far from perfect in terms of system efficiency, effectiveness and reliability. In addition, it is difficult to expand the system to other types of surgery because the rigidity software was designed only for MISS. This presentation describes a second generation design of an integrated image-assisted surgery system (IAS) to minimize the aforementioned drawbacks. The design for neurosurgery IAS was used as an example.

**Methods**

Basic IAS Platform and Customized Components. The concept of an integrated IAS surgical system is based on two steps. First step is to identify common hardware and software components required by most neurosurgical procedures to form a basic IAS platform. For a
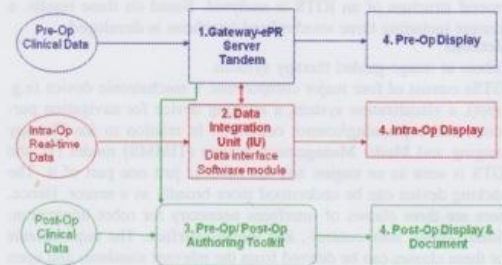


**Fig. 1** Three time phases shown in the first (*Blue*, pre-op), second (*red*, intra-op) and third row (*green*, post-op). Numerals 1, 2, 3 and 4 are the four basic system components
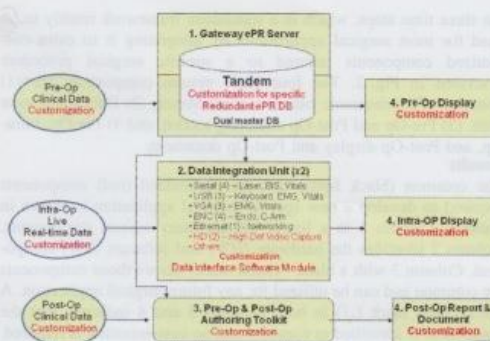
**Fig. 2** Common components (*black*) of the IAS platform and customized components (*red*) for a specific image-assisted surgical procedure. *DB* database

**Table 1** Comparison between the IAS platform basic common components in black (columns 3 and 4) and the customized components in red in column 2 (SW) and column 4 (C) for a specific surgical application

| IAS platform common components | Hardware/ software | Common components | Customized (C) components by modifying the IAS platform for a specific application |
|---|---|---|---|
| Data interface software module | SW | | C |
| Basic data input ports | HW | ✔ | ✔ |
| High Def (HD) input ports | HW | ✔ | ✔ |
| Mobile IU | HW | ✔ | ✔ |
| Gateway | HW | ✔ | ✔ |
| ePR | HW | ✔ | ✔ |
| Basic surgical DB | SW | ✔ | ✔ |
| Customized surgical DB | SW | | C |
| Pre- and Post-Op authoring toolkit | SW | | C |
| Pre-Op and Intra-OP display | SW | | C |
| Post-Op reports | SW | | C |

*HW* hardware, *SW* software. √: Available in the IAS infrastructure

given type of neurosurgery, other specific customized components would also be needed. These customized components would then be integrated to the platform to form a specific type of neurosurgery IAS. In the process of integration, imaging and informatics data of a patient acquired would cover the entire surgical workflow continuum from pre-op, intra-op to post-op based on the DICOM (Digital imaging and communications in medicine) standard data model. To develop another specific type of neurosurgery, the basic IAS platform can be identical, only customized components would need to be changed.

*Image-assisted Surgery Workflow.* The IAS system is based on three time-phases workflow, pre-op, intra-op, and post-op. Figure 1 shows

the three time steps, which is a standalone framework readily to be used for most surgical applications by integrating it to extra customized components tailored to a specific surgical procedure described in Fig. 2. The four basic system components are (1) Gateway ePR (electronic patient record) Server, (2) Data Integration Unit, (3) Pre-Op and Post-Op authoring toolkit, and 4) Pre-Op, Intra-Op, and Post-Op display and Post-Op document.

**Results**

The common (black fonts) and the customized (red) components required to develop a new specific surgical application is shown in Table 1. Column 1 is a list of all necessary system components. Column 2 identifies the hardware (HW) and software (SW) component. Column 3 with a black "check mark" shows those components are common and can be utilized for any future surgical application. A black check mark ($\sqrt{}$) in both columns 3 and 4 indicates that the component is identified as common and no customization is required. Column 4 with a red C shows the component is required for customization for a specific surgical application. This table demonstrates that all new customized components are software; however, system integration software is not listed because each integration requires a specific description.
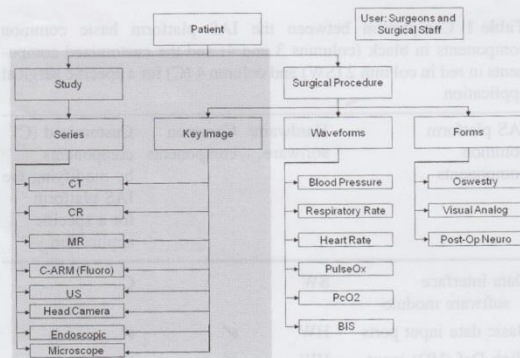


**Fig. 3** Data model of the IAS infrastructure based on DICOM standard. The *left Grey* background color column designates image data, and *right white* background column designates waveform and form data. The endoscope and microscope channels (*bottom left*) can also be used for surgical cameras
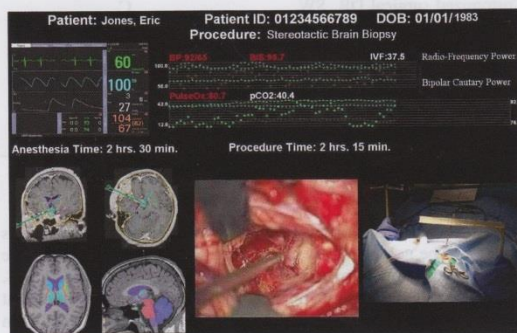


**Fig. 4** A mock-up intra-op screenshot mimicking neurosurgery display window. Additional real-time imaging data shown in the bottom are neuro-navigation system output with 3D images on the left, microscopic image in the middle and overhead surgical camera image on the right

*Data Model*. The general data model of the IAS is based on DICOM Standard shown in Fig. 3. The left column depicts the DICOM image inputs, and the right column illustrates surgical and clinical inputs including waveforms and forms. The surgical database tables and schema described in this section is designed based on this model.

*A mock-up intra-op neurosurgery*. The design of the intra-op display is shown in Fig. 4. The upper row is for patient real time vital signs (common components). The bottom row shows the intra-op displays of the neurosurgery system connected to three customized surgical related external systems (left to right): the neuro-navigation, microscopic and surgical cameras. The system interface software for these three cameras to integrate with the IAS is not listed in Table 1.

**Conclusion**

This presentation discusses the design of a second generation integrated image-assisted surgery system (IAS) for neurosurgery application. Dividing the IAS into two components, common and customized, can be better to organize the system and to simplify system integration process. The common component can be easily used for implementing other specific image-assisted neurosurgery systems. Data shown in the results section have been completed; a single brain tumor excision surgery has been identified as the prototype system development because of its relatively simpler surgical procedure [1].

**Reference**

[1] Chiu J, Huang HK, (2012) Surgical Data Monitoring and Display System. US Trademark: 079977-0015: SURGMATIX; Canadian No. 1,423,071, 2010. US Patent 8,313,432 B2.

# Medical imaging informatics simulators: a tutorial

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Anh H. Le · Jasper Lee · Kevin Ma · Brent J. Liu

## Abstract

*Purpose* A medical imaging informatics infrastructure (MIII) platform is an organized method of selecting tools and synthesizing data from HIS/RIS/PACS/ePR systems with the aim of developing an imaging-based diagnosis or treatment system. Evaluation and analysis of these systems can be made more efficient by designing and implementing imaging informatics simulators. This tutorial introduces the MIII platform and provides the definition of treatment/diagnosis systems, while primarily focusing on the development of the related simulators.

*Methods* A medical imaging informatics (MII) simulator in this context is defined as a system integration of many selected imaging and data components from the MIII platform and clinical treatment protocols, which can be used to simulate patient workflow and data flow starting from diagnostic procedures to the completion of treatment. In these processes, DICOM and HL-7 standards, IHE workflow profiles, and Web-based tools are emphasized. From the information collected in the database of a specific simulator, evidence-based medicine can be hypothesized to choose and integrate optimal clinical decision support components.

Other relevant, selected clinical resources in addition to data and tools from the HIS/RIS/PACS and ePRs platform may also be tailored to develop the simulator. These resources can include image content indexing, 3D rendering with visualization, data grid and cloud computing, computer-aided diagnosis (CAD) methods, specialized image-assisted surgical, and radiation therapy technologies.

*Results* Five simulators will be discussed in this tutorial. The PACS–ePR simulator with image distribution is the cradle of the other simulators. It supplies the necessary PACS-based ingredients and data security for the development of four other simulators: the data grid simulator for molecular imaging, CAD–PACS, radiation therapy simulator, and image-assisted surgery simulator. The purpose and benefits of each simulator with respect to its clinical relevance are presented.

*Conclusion* The concept, design, and development of these five simulators have been implemented in laboratory settings for education and training. Some of them have been extended to clinical applications in hospital environments.

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## Abbreviations

| | |
|---|---|
| AMS | Acquisition modality simulator |
| CAD | Computer-aided diagnosis and detection |
| CT | Computed tomography |
| DCU | DICOM conversion unit |
| DG | Data grid |
| DGS | Data grid simulator |

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| DICOM | Digital imaging and communications in medicine |
| DHA | Digital hand atlas |
| DICOM SR | DICOM structured report |
| DVH | Dose–volume histogram |
| ePR | Electronic patient record |
| GUI | Graphical user interface |
| HIS | Hospital information system |
| IAS | Image-assisted surgery |
| IAT | Image-assisted therapy |
| IHE | Integrating the healthcare enterprise |
| IHE XDS-I | IHE cross-enterprise document sharing for imaging |
| ITPN | Intelligent treatment plan navigator |
| KB | Knowledge base |
| MIDG | Molecular imaging data grid |
| MIII | Medical imaging informatics infrastructure |
| MISS | Minimally invasive spinal surgery |
| OGSA | Open grid services architecture |
| PACS | Picture archiving and communications system |
| PET | Positron emission tomography |
| PPM | Preprocessing manager |
| Q/R | Query/retrieve |
| RIS | Radiology information system |
| RSNA | Radiological Society of North America |
| RT | Radiation therapy |
| TPS | Treatment planning system |
| US | Ultrasound |
| WS | Work station |

## Introduction

Medical imaging informatics (MII) emphasizes the study of medical images and data. The prevalent medical imaging and data-related systems are 'Picture Archiving and Communication Systems' (PACS), Hospital Information Systems (HIS), Radiology Information Systems (RIS), electronic patient records (ePR) with image and data distribution, data grid (DG), and cloud computing technologies for archive. Some MII methods for imaging-based diagnosis and treatment are computer-aided diagnosis and detection (CAD), image-assisted surgery (IAS), and image-assisted therapy (IAT). The medical imaging informatics infrastructure (MIII) platform is an organized method of collecting these data and technologies to develop a certain clinical diagnosis or treatment application. In the process of integrating the images/data, tools and technologies, the 'Digital Imaging and Communication in Medicine' (DICOM), and 'Health Level Seven' (HL7) standards, 'Integrating the Healthcare Enterprise'

(IHE) workflow profiles and Web-based tools are normally used. Figure 1 shows the organization of this integration [1].

A medical imaging informatics (MII) simulator in this context is defined as a system integration of many appropriable selected image and data components from the MIII platform, along with certain clinical protocols, that can be assembled together to simulate the patient workflow and data flow starting from diagnostic procedures to the completion of a treatment. For examples, a PACS simulator can be used to predict how the PACS would function under a given clinical environment, and a CAD–PACS simulator can be used to predict how a CAD method would function in a given PACS environment. Similarly, other imaging informatics simulators can be used to predict certain outcomes before a clinical system is developed. The advantage of using the MIII platform is that once the platform is established, it can be expanded to develop other similar types of simulators.

In order to develop MII simulators, one must study the operations of MII system components in the real clinical environment and mimic their functions in a laboratory environment. Most of the imaging informatics systems described in the manuscript are novel research systems that are constantly evolving. Apart from the PACS simulator, every other simulator is built with the intention of trying to simulate new and innovative research-engendered informatics systems in order to examine their interactions and integration with *existing* informatics systems such as HIS, RIS, and PACS as well as to analyze their performance in order to evaluate their effectiveness without disrupting actual clinical operations.

The MII simulators mentioned in our paper do not attempt to carry out system evaluation, but rather enable and facilitate researchers and clinicians to evaluate MII systems more efficiently by providing tools to enhance research workflow. Readers are encouraged to peruse the publications referenced throughout the manuscript for a detailed evaluation of the associated systems being simulated. The aim of this manuscript is to point out the rationale behind developing imaging informatics simulators, to describe how such simulators can be developed, and to explain their benefits and applications. A thorough description of the methods involved in implementing MII simulators will empower readers to use such simulators for testing their specific applications.

## PACS–ePR simulator

### What is a PACS–ePR simulator?

The PACS–ePR simulator is a comprehensive training tool designed to emulate a 24/7 clinical PACS system in a laboratory environment. It allows the user to learn basic PACS–ePR concepts and provides the opportunity for hands-on experi-

**Fig. 1** Relationship between HIS/RIS/PACS dataflow (*upper, red*) and the imaging informatics platform (*middle, green*), and MII simulators (*blue*). DICOM images and data are transmitted from the PACS server to the imaging informatics server as well as the Web-based ePR system. Processed data from the medical imaging informatics platform are transmitted to the MII simulator for the proper application
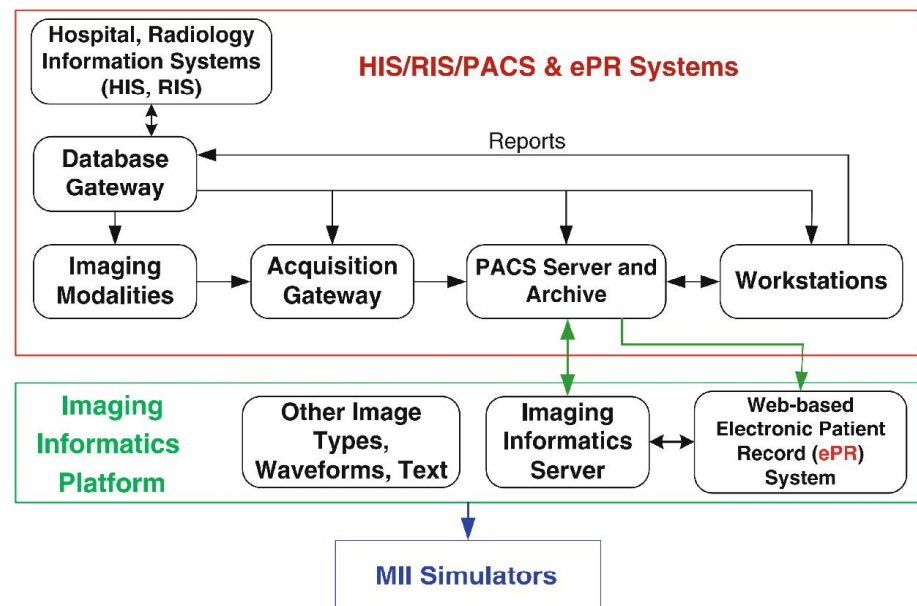


ence without compromising the stability and security of the clinical PACS–ePR system.

What does it do?

The function and data flow of the PACS–ePR simulator begins with the acquisition modality simulator (AMS). The AMS simulates the acquisition of various medical images types (computed tomography or CT, magnetic resonance imaging or MRI, computed radiography or CR, and ultrasound or US) and stores DICOM examinations in the DICOM gateway, and then the PACS server. In addition to storing and archiving the images, the PACS server also distributes the examinations to the viewing workstation via a query/retrieve function. The workstation archives the examinations into a local database and can also distribute them to a Web-based ePR server.

PACS–ePR simulator components and data flow

The simulator consists of four main components that represent the essential functions of a typical clinical PACS–ePR:

(1) RIS and acquisition modality simulator (AMS),
(2) DICOM gateway,
(3) PACS server and ePR server
(4) Workstations

Through these components, trainees can observe clinical PACS–ePR operations, trace the data flow step by step, and identify possible image data flow bottlenecks. Because the PACS–ePR simulator is stand-alone, users can also manually induce failures to any component and observe the impact on the PACS–ePR operation. This provides trainees with a

better understanding of the system workflow in a safe, simulated learning environment, without impacting the clinical workflow of the actual systems. Figure 2 depicts the PACS–ePR simulator shown during several 'Radiological Society of North America' (RSNA) annual scientific exhibits.

Using the PACS–ePR simulator as the basis for developing other imaging informatics simulators

The PACS–ePR simulator encompasses a large segment of the image/data and tools used for imaging informatics applications. It forms the basis for the other four simulators discussed in this paper. The data grid simulator replaces the PACS archive server using data grid technology to achieve storage fault tolerance and to reduce its cost. The CAD–PACS simulator integrates CAD results to act as a secondary reader in the PACS data flow to assist the radiologist during the diagnostic process. Image-assisted surgery and radiation therapy simulators extract subsets of PACS patients who require surgery or radiation therapy, respectively, forming the image data sources of the two clinical Web-based ePR systems. These four simulators use the PACS–ePR image/data, data grid, CAD methods, and surgical and radiation therapy treatment protocols to form the basis for specific imaging informatics applications.

**Data grid simulator**

What is a data grid simulator?

Data grid (DG) is used for large-scale enterprise PACS–ePR and imaging informatics system operations. It utilizes storage

**Fig. 2** The PACS–ePR simulator shown at an RSNA exhibits. *Left* to *right* RIS simulator, modality simulator, DICOM gateway, monitoring system of the data flow of the PACS–ePR simulator operation, PACS simulator, PACS WS, and Web-based ePR simulator and WS [2,3]
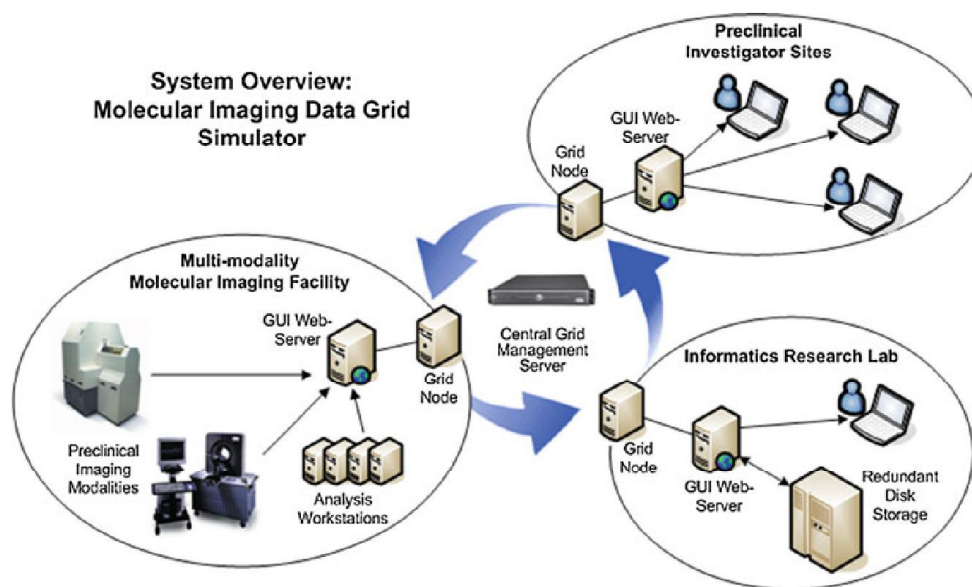


**Fig. 3** MIDG simulator workflow and system overview. A molecular imaging facility typically has three major components: preclinical researchers at various remote sites (*upper right*), molecular animal imaging modalities (*lower left*), and the imaging informatics facility (*lower right*)

from multiple sites in the enterprise to share the primary and backup image/data archives of the entire system. In order to achieve storage fault tolerance, three copies of every image are normally used. Combining DG with cloud computing technology, the storage locations can be remotely hosted by professional enterprise archive centers. In this case, availability of reliable high-speed networking is essential.

### Data grid simulator (DGS) components and their connectivity

Depending upon the application of the data grid simulator (DGS), its components and their connections can vary. The DGS is designed to emulate a specific PACS–ePR or an imaging informatics data archive application. The DICOM standard is used as the data structure and format. Three major functions of the data grid simulator are archive and backup, query/retrieve, and disaster recovery. Some applications of DGS are DG for fault-tolerant image archive, image-based

multiple site clinical trials, data migration from the backup to the primary archive, dedicated breast MRI enterprise DG, and molecular imaging DG [4–7]. For example, a PACS–ePR DGS with multiple simulated sites can have the following functions: to support the archive, backup, and disaster recovery for all sites, and to allow a work station (WS) from a site to retrieve and review image/data from any other sites.

### Molecular imaging data grid (MIDG) simulator

MIDG provides data archiving, management, and distribution for small animal (preclinical) imaging facilities [8]. The system utilizes grid technologies and a custom graphical user interface (GUI) to promote experimental data sharing and to expedite data management workflows by imaging informatics technologies. The simulator consists of three major components shown in Fig. 3: A general small animal facility with many researchers performing experiments at multiple sites (upper right) sharing the imaging equipment (lower

**Fig. 4** Typical imaging modalities in a small animal imaging research facility
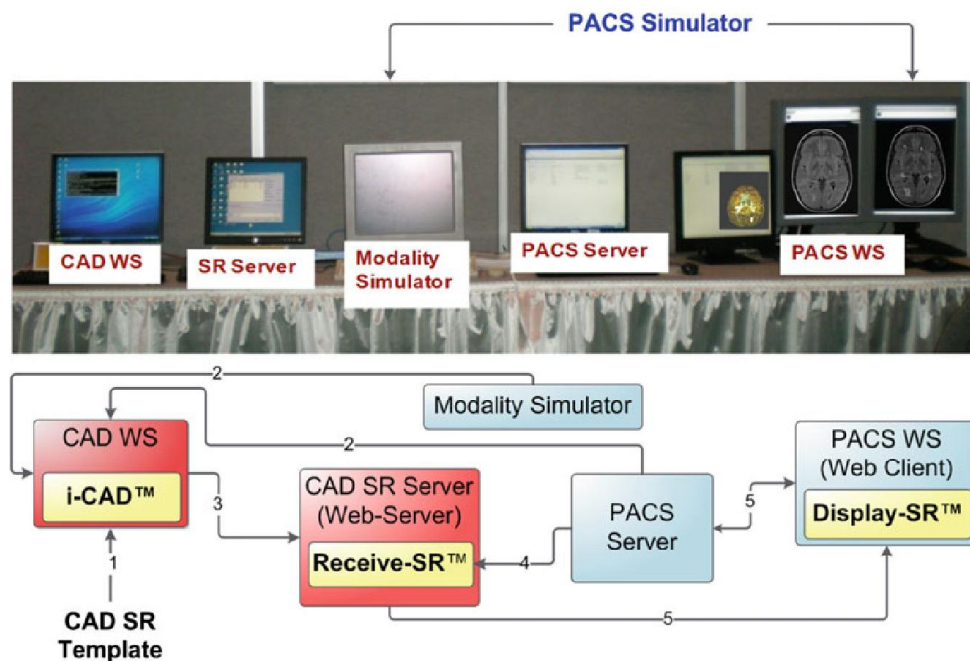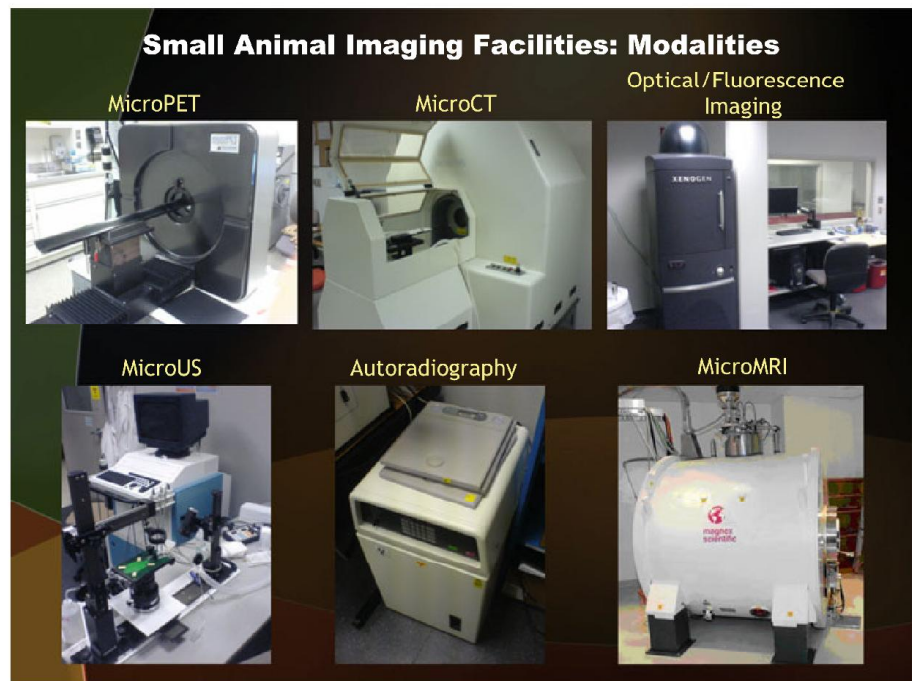




**Fig. 5** Evaluation of an automatic detection and quantification method of multiple sclerosis (MS) on MRI—configuration of the CAD–PACS simulator and its data flow. *Top* The CAD–PACS simulator displayed at the 2007 RSNA annual scientific exhibit [16]. The PACS WSs (*right*) also show the MRI images and 3D CAD result (*color*). *Bottom* The CAD–PACS integration and workflow steps (*numerals*). *Blue* PACS simulator components. *Red* CAD components. *Yellow* CAD–PACS toolkit modules

left, see also Fig. 4) and imaging informatics resource including archive, retrieval, and processing (lower right). In order to facilitate data sharing between researcher sites and the multimodality small animal imaging facility, images are first converted to the DICOM format. The standardization allows data to be distributed through the grid infrastructure via the grid node server at each participating site connected to the DG [9].

Current trends in imaging informatics data grid
with cloud computing design

*OGSA and IHE XDS-I*

Existing medical data grid (DG) takes advantage of the
open source Global toolkits [6]; however, it has two major
drawbacks—the lack of easy to use documentation and heavy
overhead of the software. For medical imaging applications,
the trends are to continue taking advantage of the open grid
services architecture (OGSA) principles [7–9], but to aban-
don the Globus toolkit that has been used commonly in most
current data grid designs. The MIDG simulator was origi-
nally designed using the Globus toolkit, but has been imple-
mented based on the OGSA and IHE workflow profiles, in
particular the 'cross-enterprise document sharing for imag-
ing' (XDS-I) profile. The result was a replacement of the
Globus toolkit with a DICOM-handling infrastructure based
on Web services. Performing a study registration, replication
or retrieval no longer requires DICOM middleware to make
a call first to the Globus toolkit for file delivery responsibil-
ities. Furthermore, the DICOM metadata database and file
localization databases are now a single database leading to
fewer and less complex database queries. Finding all meta-
data relevant to a study, including its physical storage loca-
tion within the MIDG, is now done in a single filtered query.
This centralized architecture culminates in a more extensible
design that can support system-wide process monitoring and
rules-based data backup policies.

The use of cloud computing services in the archive
architecture

The open grid services architecture (OGSA) principles
require enterprise partners contributing storage to the data
grid. With the readily available archive infrastructure in
cloud computing services, storage contribution by data grid
partners in the enterprise PACS–ePR becomes less impor-
tant. Examples of available Internet-based scalable and fault-
tolerant Blobstore data management are Google app engine
(GAE) [10], Microsoft Windows Azure [11], Amazon Web
Services (AWS) [12], and Eucalyptus [13]. The blob is
unstructured data (value) stored in a container, and the lookup
is performed through a text key. For multimedia PACS–ePR
data, Blobstore is very attractive for its storage application.
Once the storage is secured using the Blobstore through a
service provider, a PACS–ePR system will no longer need
a local archive component. Conceptually, the use of cloud
computing for PACS–ePR is simple; the cloud computing
services replace the data grid. However, in order to do so at
this point of time, the concept of the OGSA principles still
needs to be augmented in the cloud services for DICOM-
based PACS–ePR applications [14].

**CAD–PACS simulator**

The concept of CAD–PACS integration

Computer-aided detection and diagnosis (CAD) systems
and PACS are separate standalone systems, requiring pro-
prietary software to view CAD results or separate CAD-
specific workstations. Integrating CAD with PACS means
integrating the CAD results with the PACS workflow,
thereby enabling the clinician to view CAD results on a
PACS WS [15]. The workflow consists of the following
steps:

1. Integrating the CAD system within the PACS workflow.
2. The CAD result is treated as a new imaging modality
   in the DICOM data model and is then integrated in the
   PACS workflow.
3. The clinician uses DICOM structured report (SR) to
   retrieve and view CAD results at the PACS WS where
   the CAD results would overlay on the relevant diagnos-
   tic images.
4. CAD–PACS integration toolkit is available in the litera-
   ture [16]. To use, it would require the modification of the
   existing preprocessing manager (PPM) software of the
   PACS server and the use of the DICOM SR.

The CAD–PACS simulator

The CAD–PACS simulator can be used to learn how to inte-
grate a CAD system with a PACS that complies with DICOM
and SR standards. The simulator possesses the following
characteristics:

1. The integration process uses standardized imaging infor-
   matics methodology.
2. The PACS DICOM data model and workflow treat the
   CAD output as an individual surrogate imaging modality.
3. The utilization of DICOM–SR and 'Integrating the
   Healthcare Enterprise' (IHE) integration profiles are used
   to display CAD output in the PACS WS environment.

The CAD–PACS simulator can simulate and validate an
automated workflow of integrating CAD systems in clinical
PACS environments using standardized imaging informatics
methodology. The simulator utilizes DICOM SR (structured
reporting) and 'Integrating the Healthcare Enterprise' (IHE)
integration profiles to display CAD output in the PACS envi-
ronment.

Components and functions

1. PACS simulator

**Fig. 6** CAD results shown on the PACS WS. *Left* DICOM SR describing the multiple sclerosis. *Bottom middle* An MRI image of a patient with multiple sclerosis (MS) and *bottom right* The 3D CAD results of MS in the brain. See also Fig. 5—the CAD–PACS integration components for the MRI images and CAD result shown on the *right*
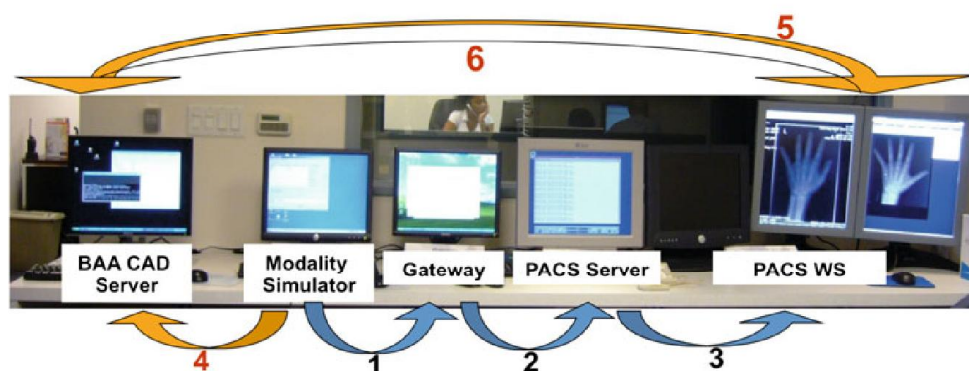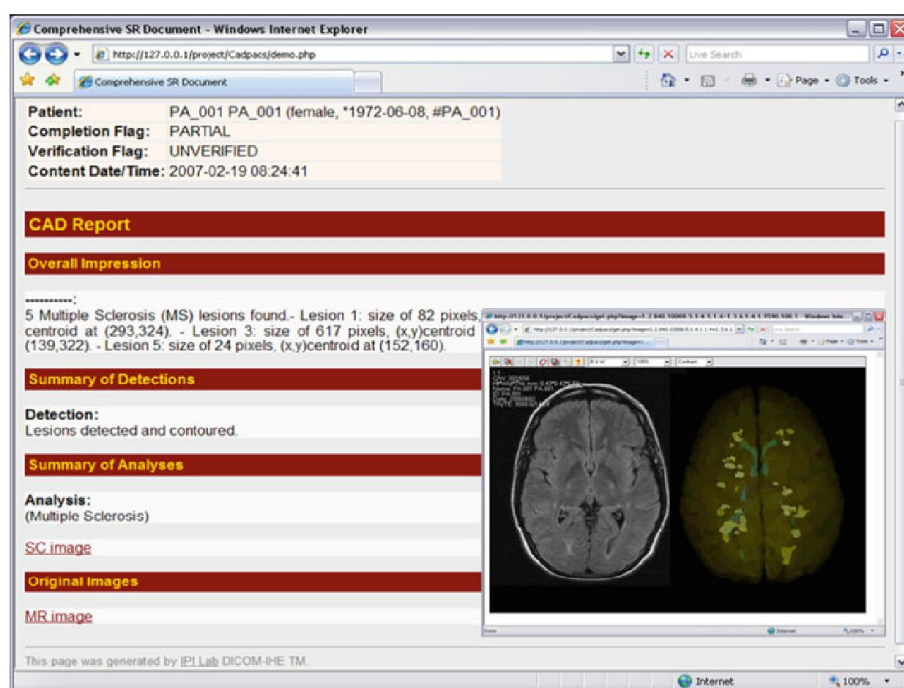




**Fig. 7** CAD–PACS simulator in a laboratory environment (see also Fig. 5) *Black fonts* Normal clinical workflow. *Red* BAA using the CAD–PACS simulator, *Numeral 4* a second copy of the hand image is sent from the PACS to the CAD server; *Numeral 5* radiologist also reviews CAD results at the PACS WS; *Numeral 6* result is saved both at PACS and CAD server

a. Modality simulator
b. PACS–ePR archive simulator
c. Display workstation

2. CAD server (on virtual machine)
3. SR server (on virtual machine)

The CAD–PACS simulator consists of three system components: PACS–ePR simulator, CAD server and workstation (WS), and SR server and PACS display workstation (WS). The top of Fig. 5 shows the CAD–PACS simulator displayed at a Computer Exhibit at RSNA 2007. The CAD–PACS simulator is equipped with the CAD–PACS toolkit [16] to handle the integration between the CAD components and PACS, including the creation of DICOM SR objects based on a customized template for each CAD application, as well as data exchange (send/query/retrieve) and Web-based display of DICOM SR objects.

Using a CAD–PACS simulator to facilitate the evaluation of CAD algorithms

The workflow for evaluating a CAD algorithm can be enhanced by integrating it with the PACS–ePR simulator using three available software modules: i-CAD, Receive-SR, and Display-SR [16]. This integration workflow is shown at the bottom of Fig. 5. The simulator furnishes researchers and clinicians with valuable tools to assist in evaluating the CAD algorithm more efficiently. For instance, data collec-

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1. CR sends a second image copy to the CAD server
2. CAD server receives the DICOM image, performs BAA and record results in database
3. Web server looks into database to locate CAD result and original image, as well as best-matched DHA image (determined by CAD)
4. GUI displays images and guides radiologist through validation steps

**Fig. 8** CAD–PACS simulator in the clinical environment. Population statistics database has been embedded in the clinical workflow. The bone age of the child is compared directly with the database for eval-uating the health of the child, elevating the role of the simulator. *DHA* Digital Hand Atlas

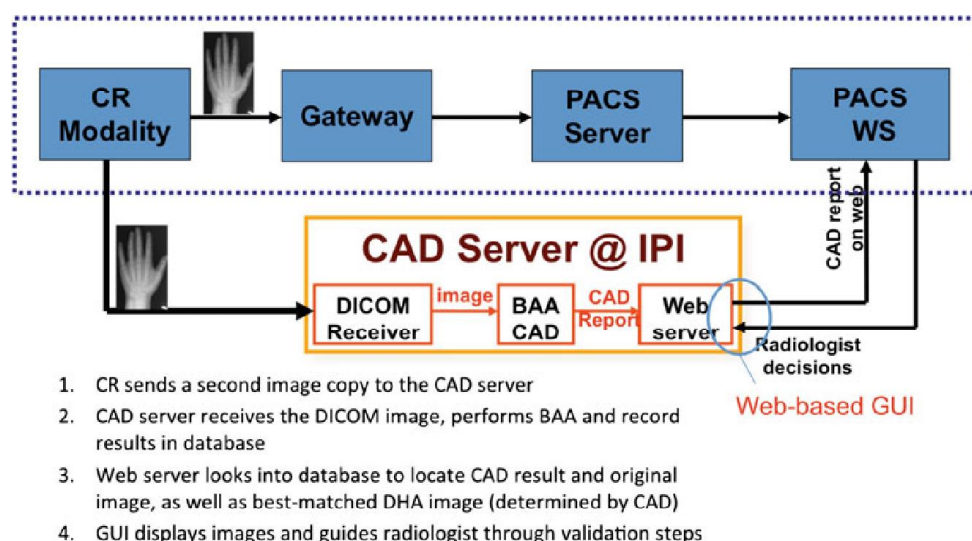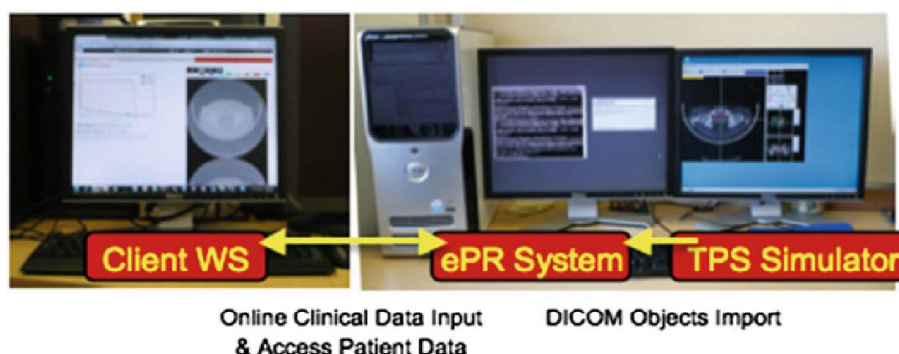**Fig. 9** System components of the RT ePR simulator in a laboratory environment. From the *right* to *left* TPS simulator, ePR system, and client WS, the *yellow arrows* represent the data flow and the direction of data flow



tion efficiency is much improved by enabling a communications interface between the CAD server and both the input sources—the modality simulator and the PACS server. In addition, the SR server enables the storage of CAD results as DICOM SR, a standardized format. This allows the CAD results to be displayed on DICOM compliant workstations for review by clinicians. Figure 6 shows CAD results displayed on the PACS WS (right) and DICOM SR (left). The example presents an automatic detection and quantification method of multiple sclerosis (MS) on MRI.

Simulator: from the laboratory environment to clinical evaluation

Using a simulator, a CAD algorithm can first be tested in the laboratory setting and continue to be evaluated in the clinical environment. The "bone age assessment of children" [17–20] is used as an example to present the CAD–PACS simulator system workflow. A routine health examination of children's growth needs certain normal growth and development stan-

dards for comparison. A left hand and wrist radiograph provides a dependable indicator of developmental status through bone growth observations of a child. Bone age assessment (BAA) is a clinical procedure in pediatric radiology to evaluate the stage of skeletal maturity based on a left hand and wrist radiograph. Figure 7 depicts the bone age assessment of a hand radiograph in the laboratory seating. Figure 8 shows that the simulator has been integrated with the PACS clinical workflow, where the CAD bone age result has been incorporated in the clinical assessment with the population health statistics.

**Radiation therapy (RT) ePR simulator**

Concept of the RT ePR simulator

The radiation therapy electronic patient record (RT ePR) simulator emulates a clinical scenario where a system could improve the efficiency of data integration and data mining
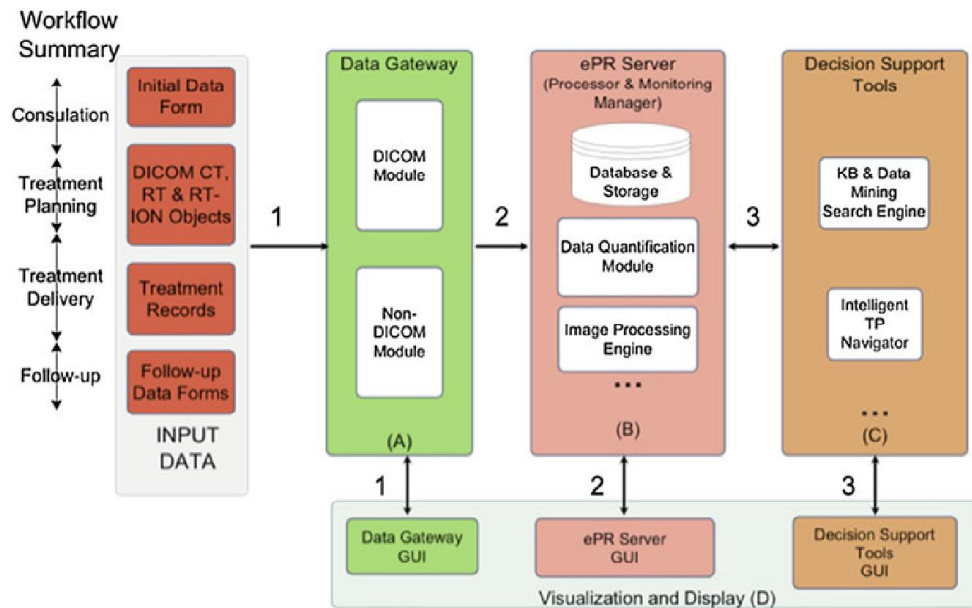
**Fig. 10** Architecture and dataflow of the RT ePR system. **a** The data gateway is used to receive data. **b** The ePR server has the storage and database to archive and quantify stored data. **c** The decision support tools give users the ability to analyze and interact with treatment plans and patient data to improve treatment for future patient. **d** The visualiza- tion module contains all GUIs for user interaction in data acquisition, data storage, data display, and for decision support tools. The *numerals* represent the dataflow steps. *KB* knowledge base, *GUI* graphical user interface



**Fig. 11** Improving treatment for a new patient based on treatment plans of previous patients. It shows step-by-step simulation of knowledge discovery based on the previous patients' treatment plans
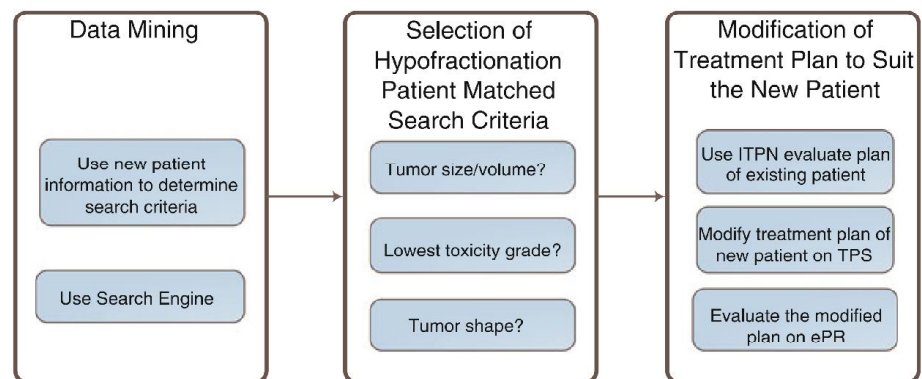
in the research related to outcomes analysis and new treatment protocols in radiation therapy. The RT ePR centralizes all relevant clinical and treatment plan data from all four main steps in radiation therapy: consultation, treatment planning, treatment delivery, and follow-up [21]. Currently, the RT ePR simulator utilizes data from prostate cancer patients treated with hypofractionation dose protocol proton beam therapy. Each data set includes an initial data form, DICOM files (CT images, RT, and RT-ION DICOM objects), and patient follow-up data forms.

## Components and features

Figure 9 shows the system components of the RT ePR, which consists of three subsystems: (1) the treatment planning sys-

tem (TPS) simulator, (2) the ePR system, and (3) the client WS. The TPS simulator, which is the Odyssey treatment planning software non-clinical version 4.2, simulates the data flow of DICOM objects to the ePR system [21]. The ePR system is the main component of the RT ePR simulator and responsible for data input, storage, quantification, display, and distribution. The client workstation allows users to perform online clinical data input and to access patient data through the Web interface and test the functionalities of the simulator [22,23].

## RT ePR simulator architecture

The RT ePR is a Web-based system that could also be used to complement the current treatment planning system (TPS)

in a radiotherapy department. The RT ePR simulator consists of four main components: the data gateway, the ePR server, decision support tools, and visualization and display tools, shown in Fig. 10.

The three steps of data flow in the RT ePR System (numerals in Fig. 10):

1. The data are first obtained from each treatment step and then imported to the Data Gateway
2. After the data are received, it will be transferred to the ePR server for archive and further quantification, and
3. The quantified data from DICOM RT objects and clinical data are then used by decision support tools to perform data mining and knowledge discovery functions. At each step of the dataflow, the user could interact with the system using the GUIs provided by the visualization and display component.

## Simulation of knowledge discovery

The RT ePR simulator can study several clinical outcomes. This example discusses how the simulator retrieves knowledge from previous patients data through data mining. Figure 11 describes the step-by-step simulation of knowledge discovery utilizing the RT ePR system to improve the treatment plan of a new patient based on previous patients treatment plans.

## An example of using the simulator to improve a patient's treatment plan based on knowledge discovery

Figure 12 shows a screenshot of results obtained from the RT ePR simulator. Based on the knowledge discovery, the beam margin has been modified from 10 to 7 mm, resulting in reduced doses to two critical organs and yet maintaining the dose delivered to the target volume.

## Role of the RT ePR simulator

The RT ePR simulator discussed here plays the role of a radiation treatment planning decision support method based on knowledge accumulated from previous patient treatments in the database. This add-on knowledge can help the oncologist to prescribe a better treatment plan for a new patient under the similar treatment by maximizing the target volume dose and at the same time minimizing the dose to critical organs. In addition, the method may also reduce the normal time required to finalize the treatment plan. Although the
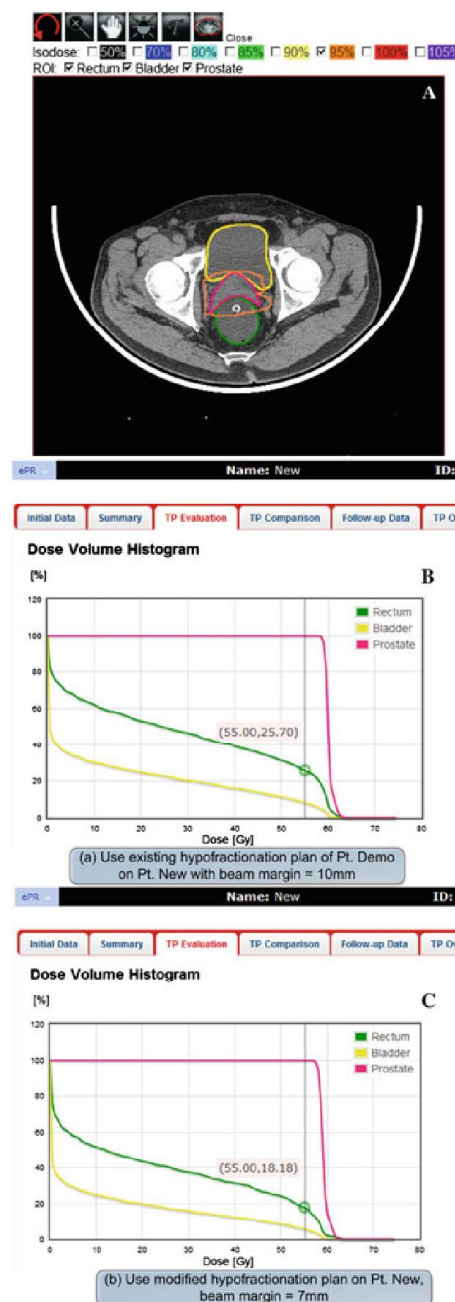


**Fig. 12 a** A screenshot of the intelligent treatment plan navigator (ITPN) shows the overlapping region of the 95 % isodose curve (*orange*), the target prostate (*pink*), and two critical organs: the bladder (*yellow*) and the rectum (*green*). Utilization of knowledge discovery results for this patient led to a modification of the original 10 mm beam margin to a smaller 7 mm margin. **b** The dose–volume histogram (DVH) for the original treatment plan with a beam margin of 10 mm shows that 25.70 % of the rectum receives 55 Gy dose. **c** The DVH of the modified treatment plan incorporating a reduced beam margin of 7 mm shows that the volume of the rectum receiving 55 Gy dose has reduced from the original 25.70–18.18 %, while maintaining the original dose of 55 Gy to 100 % of the prostate

**Fig. 13** Dataflow of the image-assisted surgery (IAS) ePR simulator. Minimally invasive spinal surgery (MISS) is used as an example. There are three surgical operation phases: pre-op, intra-op, and post-op, each phase with four data flow steps. *Numerals* indicate the dataflow steps through the three phases of operation
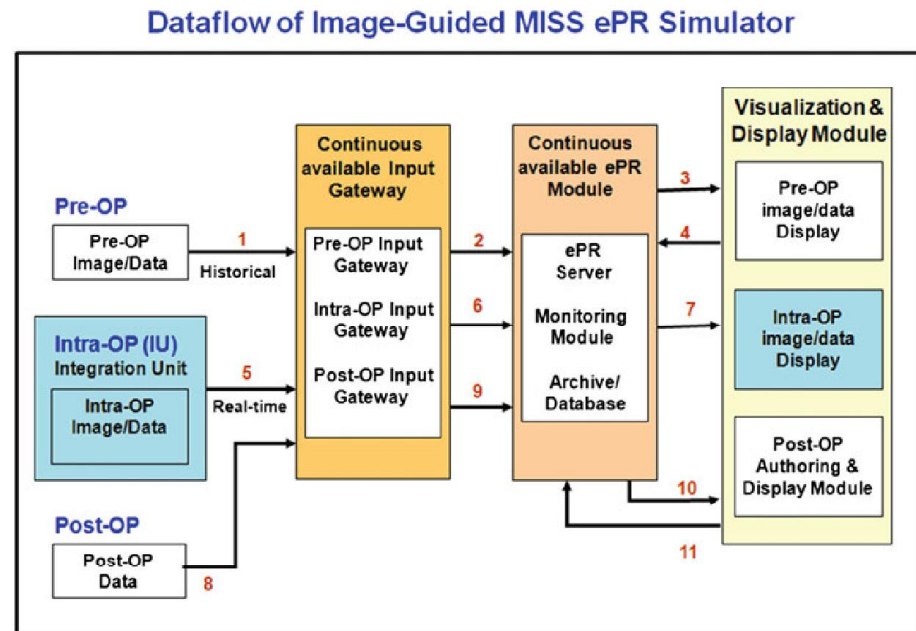


data shown in this example were proton beam therapy data, the simulator can also be used for other types of radiation therapy beams.

## Image-assisted surgery (IAS) ePR simulator

Role of the ePR simulator in image-assisted surgery

Currently, following weaknesses exists in image-assisted surgery:

1. Patient clinical forms and data from surgical devices in the operation room, including various pre- and postsurgical textual data, waveforms, and multiple sources of images and video are scattered.
2. The pre-op, intra-op, and post-op workflows do not have a single system guided by a master time clock during data acquisition, management, and distribution.
3. There is no systematic method to analyze patient outcomes based on surgical workflow.
4. There are no data organization and image display system to record the live real-time intra-operation data.

The IAS ePR simulator can be used to minimize these shortcomings. [24]

IAS ePR simulator dataflow

The surgical data workflow of the IAS ePR simulator is shown in Fig. 13. It has three time phases (first column: pre-op, intra-op, and post-op), each with four data flow steps:



**Fig. 14** The IAS ePR simulator in the laboratory environment simulating the pre-op and intra-op of a MISS surgery. *Right* to *left* two pre-op displays, an intra-op live display and two DVD devices feeding simulating data to the intra-op display

data collection, data standardization and preprocessing at the Gateway, fault tolerance ePR archive and monitoring operations, and image/data visualization.

Workflow of the simulator

The IAS ePR simulator (minimally invasive spinal surgery is used as an example) has three time phases:

1. Pre-op phase: It is the phase before the operation, which includes patient consultations and planning of the surgery. Features of this phase include patient registra-

Fig. 15 a The MISS operation room before the installation of the ePR System. b A snapshot from the real-time intra-op display monitor of the MISS ePR system
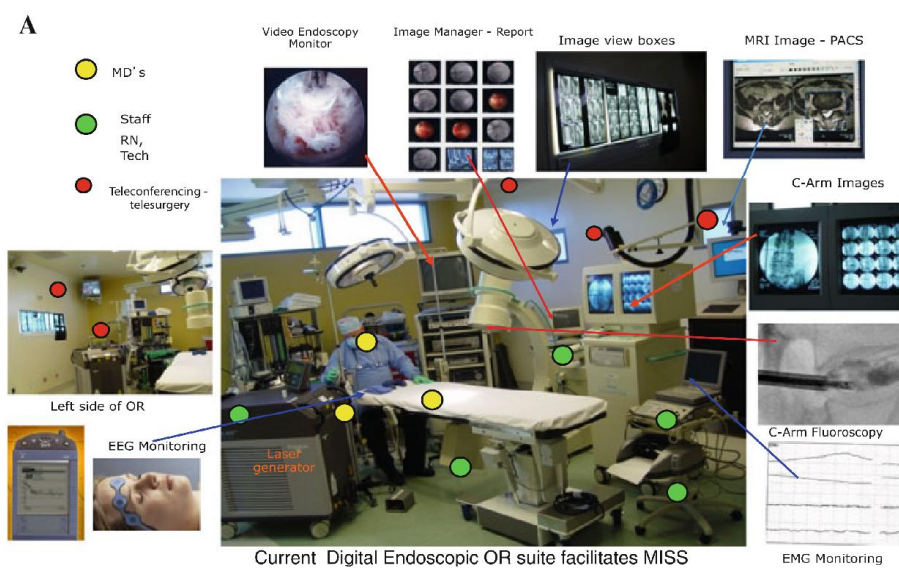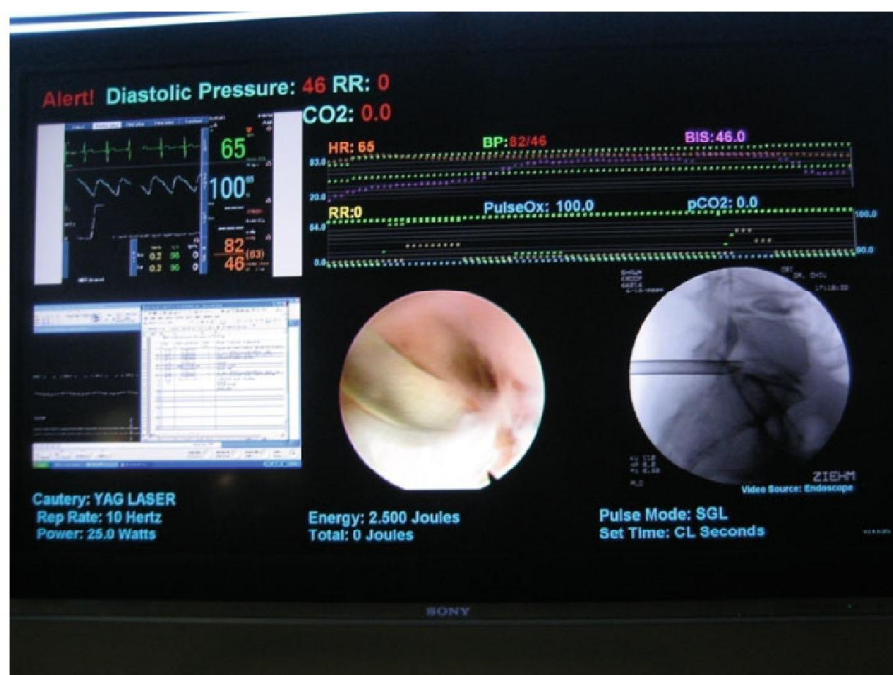


tion, PACS image acquisition, surgical procedure creation and scheduling, preparation of navigation tools, key image selection and annotations, surgical whiteboard data, and pain surveys.

2. Intra-op phase: This phase occurs during the operation. The system acquires, archives, and displays various live data from peripheral surgically related devices in real time. Some of the archived information during pre-op will also be used for later review and surgical documentation. These data include biometric verification of patients just

prior to surgery, real-time alerts of vital signs using a rules-based system, digital acquisition and integration of video, images, and waveform data from various input devices. Some of these selected data are recorded in real time in a digital storage device, which will be used to emulate the data collection during the intra-op phase of the simulator.

3. Post-op phase: This phase is for the creation of a clinical report of the surgical procedure from the data gathered in the pre-op and intra-op phases. Clinical reports can

**Fig. 16 a** Pre-op. *Left* patient records, *right* MRI, and red depicts the lesion to be operated on. **b** Intra-op. *Top* Live real-time waveforms with inserted labels. *Top-left* vital signs waveforms with synthesized data per second, and the automatic alert signal. *Middle Left*, EMG. *Middle* to *right* endoscopic and C-arm images. All data are recorded in real time, synced by a system master time clock. IU—integration unit, Pulse OX—pulse oximeter. **c** An automatic screenshot from the intra-op real-time data taken during a specific time (see *bottom green marker* overlaid by *blue* on the time axis) prepared for the patient surgical document during the post-op. *Top left* to *right*, an endoscopic image along with some corresponding digital vital signs. *Bottom* time axis showing the duration of the operation time. *Red marks* automatic default data collection time. *Blue* Surgeon's requests during the operation via a foot paddle. *Larger green* time of screenshot capture. Some corresponding vital waveforms are also recorded

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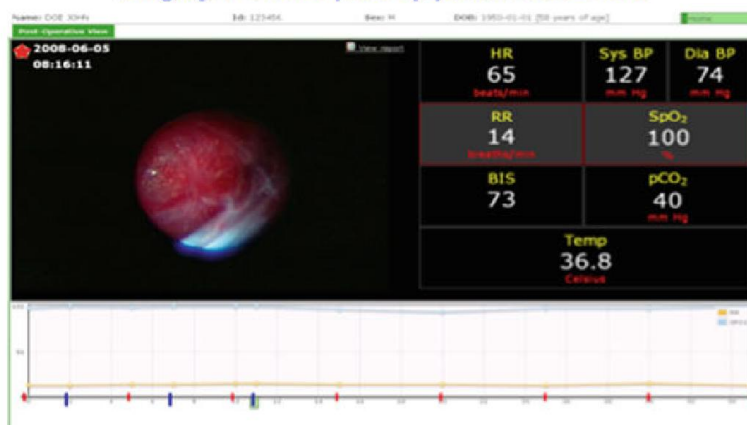
be generated from the post-op authoring module using these data. Vital signs and pain survey data can also be collected during the post-op phases.

## The IAS ePR simulator in a laboratory environment

Figure 14 shows a portion of the simulator laboratory in the IPILab at USC, depicting the major components of the IAS ePR simulator. The simulator was enabled to simulate the operation of two phases: pre-op (two large display monitors on the right) and intra-op (one larger monitor in the corner of the room). The two leftmost smaller monitors are two DVD devices, one of which fed simulated EMG and vital signs and the other fed endoscopic video and C-arm radiographs to the intra-op display monitor. A master time clock manages the data flow during the operation. The simulated data used were recorded during a minimally invasive spinal surgery (MISS) patient surgery from the live MISS ePR system.

## From IAS ePR simulator to the clinical MISS ePR System

The IAS ePR simulator was developed in 2009. Since then, a MISS ePR system has been implemented for daily clinical use at the California Spine Center starting in 2010. The MISS system was designed based on a more robust simulator architecture. Figure 15a shows the clinical environment of the spinal surgery operation room before the IAS ePR System was installed, and Figure 15b depicts a snapshot of the intra-op 52" display monitor showing a real-time capture from the MISS ePR system [25]. Figure 16a–c presents the snapshots of some pre-op data, intra-op live images and waveforms, and post-op patient documentation, respectively.

## Other potential IAS ePR simulators

The first IAS ePR simulator was developed for MISS. Several versions later, a clinical MISS ePR system was implemented for daily use. The concept and infrastructure of the IAS ePR simulator can be used to develop other specific IAS ePR systems. Examples are knee arthroscopic ePR, IAS maxillo-facial ePR, and image-assisted neurosurgery ePR. In these potential IAS ePR systems, the dataflow shown in Fig. 13 can be followed closely and modified according to each specific clinical workflow. However, four overall components will need to be modified: image input devices, the ePR surgical database, display, and graphical user interface. The degree of difficulty in system development among these three IAS systems is in ascending order, especially in neurosurgery because complex image navigation and guidance systems will be involved [26].

## Summary

A medical imaging informatics (MII) simulator in this context is defined as a system integration of many imaging and treatment components, which can be used to simulate a segment of the patient workflow and data flow, starting from diagnostic processes to the completion of a specific treatment. In this clinical continuum, it may sometimes be easier and more advantageous to develop only a subsection of the complete dataflow for particular applications.

The concept of an imaging informatics simulator originates from the diagnostic PACS–ePR simulator in the 90s, which was developed as an educational tool for learning the basics of PACS and ePR with image distribution. Use of the data grid technology for primary and backup image archives in PACS prompts an extension of the PACS–ePR simulator to emphasize the fault tolerance data archive, which leads to the data grid simulator development. With the introduction of cloud computing, the necessity of on-site storage components of the data grid becomes less important, as it can be replaced by cloud storage service.

CAD has been accepted as a potential secondary diagnostic reader in current radiology. Combining CAD results with PACS–ePR images in the diagnostic workflow would facilitate the viewing process, hence the need of CAD and PACS integration. The CAD–PACS simulator was thus introduced by augmenting the DICOM structured reporting and IHE workflow profiles.

In order to complete the clinical continuum, the scope of medical imaging informatics simulators must be expanded to include specific treatment applications. Two examples are presented—the radiation therapy (RT) ePR simulator and the image-assisted surgery (IAS) ePR simulator. Since every clinical treatment is patient-specific, a treatment-related simulator is best developed based on an ePR platform, for example the RT ePR simulator and IAS ePR simulator.

Each of the five simulators presented in this paper can be used to improve the education and learning of medical imaging informatics. They cover the spectrum from data collection to clinical diagnosis and treatment. Trainees equipped with this new vocabulary and knowledge may take advantage of them to innovate more effective and efficient diagnostic tools and image-guided treatments for better clinical service and research advancement.

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# Medical imaging, PACS, and imaging informatics: retrospective

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## Abstract

Historical reviews of PACS (picture archiving and communication system) and imaging informatics development from different points of view have been published in the past (Huang in Euro J Radiol 78:163–176, *2011*; Lemke in Euro J Radiol 78:177–183, *2011*; Inamura and Jong in Euro J Radiol 78:184–189, *2011*). This retrospective attempts to look at the topic from a different angle by identifying certain basic medical imaging inventions in the 1960s and 1970s which had conceptually defined basic components of PACS guiding its course of development in the 1980s and 1990s, as well as subsequent imaging informatics research in the 2000s. In medical imaging, the emphasis was on the innovations at Georgetown University in Washington, DC, in the 1960s and 1970s. During the 1980s and 1990s, research and training support from US government agencies and public and private medical imaging manufacturers became available for training of young talents in biomedical physics and for developing the key components required for PACS development. In the 2000s, computer hardware and software as well as communication networks advanced by leaps and bounds, opening the door for medical imaging informatics to flourish. Because

many key components required for the PACS operation were developed by the UCLA PACS Team and its collaborative partners in the 1980s, this presentation is centered on that aspect. During this period, substantial collaborative research efforts by many individual teams in the US and in Japan were highlighted. Credits are due particularly to the Pattern Recognition Laboratory at Georgetown University, and the computed radiography (CR) development at the Fuji Electric Corp. in collaboration with Stanford University in the 1970s; the Image Processing Laboratory at UCLA in the 1980s–1990s; as well as the early PACS development at the Hokkaido University, Sapporo, Japan, in the late 1970s, and film scanner and digital radiography developed by Konishiroku Photo Ind. Co. Ltd. (Konica-Minolta), Japan, in the 1980–1990s. Major support from the US National Institutes of Health and other federal agencies and private medical imaging industry are appreciated. The NATO (North Atlantic Treaty Organization) Advanced Study Institute (ASI) sponsored the International PACS Conference at Evian, France, in 1990, the contents and presentations of which convinced a half dozen high-level US military healthcare personnel, including surgeons and radiologists, that PACS was feasible and would greatly streamline the current military healthcare services. The impact of the post-conference summary by these individuals to their superiors opened the doors for long-term support of PACS development by the US Military Healthcare Services. PACS and imaging informatics have thus emerged as a daily clinical necessity.

**Keywords**  Medical imaging – PCAS – History of PACS – Imaging informatics

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# 1  Medical imaging

## 1.1  The Pattern Recognition Laboratory and Professor Robert S. Ledley

In the early medical imaging research in the 1960s–1970s, the two most important innovations allowing the possible development of PACS are probably the digitizer (or scanner), which converts an analog to a digital image and the whole-body CT scanner. The former development allowed the conversion of analog medical images to digital ones, with the latter replacing conventional 2-D X-ray procedures with the use of direct digital acquisition of 3-D body images. As to scanners, successful developments included the 35-mm film flying-spot scanner, the X-ray film drum scanner, and the microscopic slide scanner. Among other medical imaging researchers, Prof. Robert S. Ledley can be singled out

as a pioneer in this area of research. Ledley was Professor of Physiology and Biophysics and Professor of Radiology at the Georgetown University Medical School, pioneering in the use of electronic digital computers in biology and medicine. This section is dedicated to Dr. Ledley's lifetime accomplishments.

Ledley had a colorful career in research related to medical imaging. He contributed two influential articles in *Science*: "Reasoning Foundations of Medical Diagnosis" in 1959 [4] and "Digital Electronic Computers in Biomedical Science" in 1964 [5]. In 1965, he published the fundamental "Use of Computers in Biology and Medicine" book that became a classic in early medical imaging research (Fig. 1) [6]. In 1960, he founded the National Biomedical Research Foundation (NBRF) to promote the use of computers and electronic equipment in biomedical research. At the NBRF, Ledley pursued several major innovative projects to convert analog to digital images including the FIDAC (Film Input to Digital Automatic Computer) for 35-mm slides in the 1960s (Fig. 2a), and the DRIDAC (Drum Input to Digital Automatic Computer) for X-ray films (Fig. 2b) in the 1970s. In microscopic slides, the SPIDAC (Specimen Input to Digital Automatic Computer) automated the analysis of chromosomes in the late 1970s (Fig. 2c). He established the Pattern Recognition Laboratory at the NBRF which housed this equipment (Fig. 3). (See also Fig. 2c and Sect. 6.2.)

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Robert Steven Ledley (June 28, 1926 – July 24, 2012), Professor Emeritus of Physiology and Biophysics, Georgetown University. In 1965, he published *Use of Computers in Biology and Medicine* and established the Biomedical Research Foundation (NBRF).

**Fig. 1**

Robert Steven Ledley (June 28, 1926–July 24, 2012, aged 86)
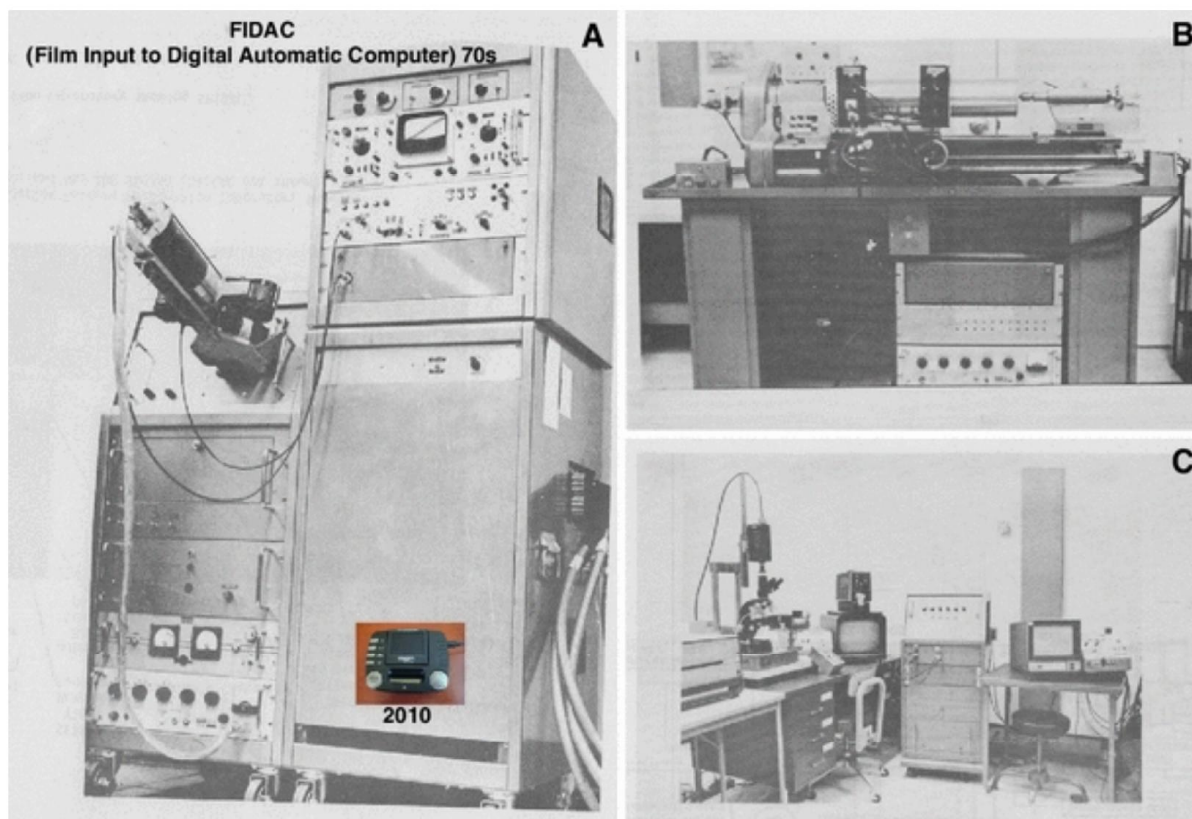
**Fig. 2**

Innovative medical imaging components in the Pattern Recognition Laboratory in the mid 1970s: **a** FIDAC (Film Input to Digital Automatic Computer), **b** DRIDAC (Drum Input to Digital Automatic Computer). **c** SPIDAC (Specimen Input to Digital Automatic Computer)
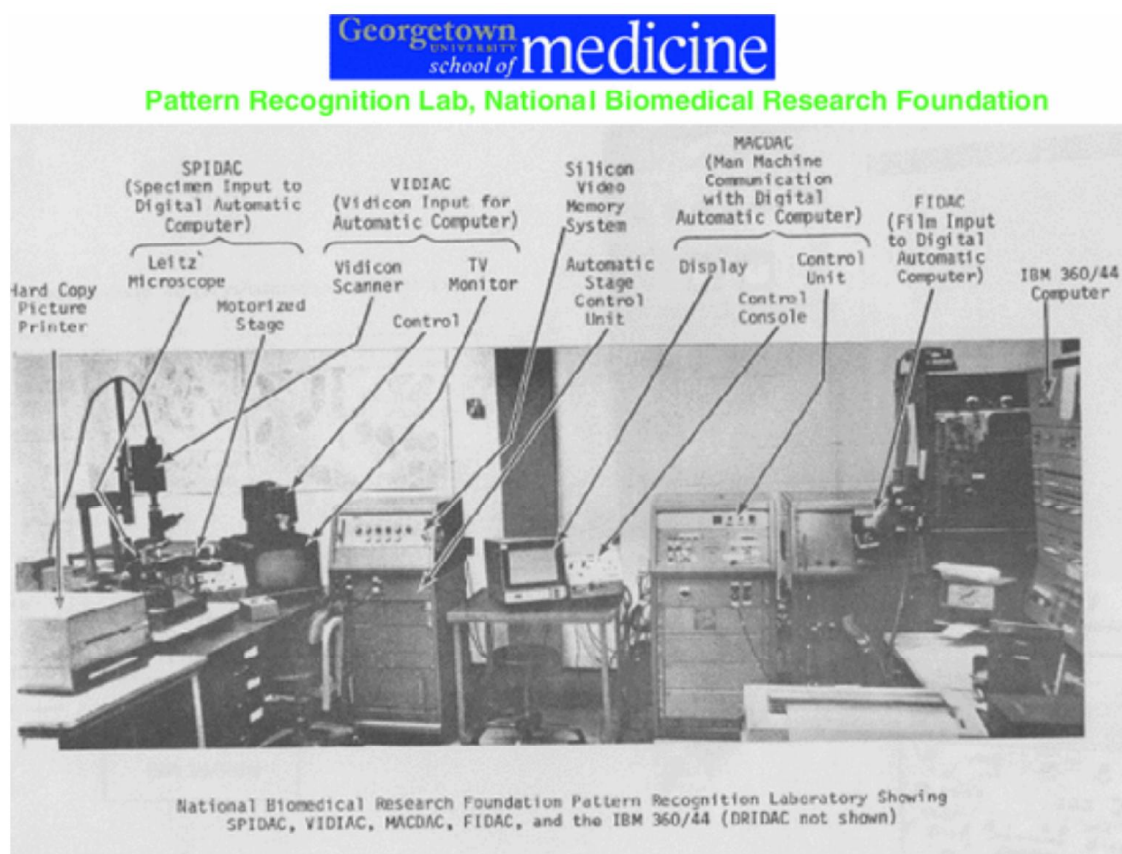
**Fig. 3**

Pattern Recognition Laboratory, National Biomedical Research Foundation

## 1.2  The ACTA: the whole-body CT scanner

When Sir Godfrey N. Hounsfield, Nobel laureate, invented the head CT scanner at EMI, England, in the early 1970s [7], Dr. Ledley was also developing the ACTA (automatic computerized transverse axial) scanner, the first whole-body CT scanner, in the middle 1970s (Fig. 4). In the first available cross-sectional anatomy textbook, published by Williams and Wilkins in 1997, the sectional images in the textbook were obtained from the ACTA scanner at Georgetown University [8]. NBRF was affiliated with the Georgetown University Medical School in Washington, DC, in the late 1960s as a research laboratory. Ledley became an Emeritus Professor in 2010. Through the years, he had provided opportunities to many young-multidisciplinary open-mind trainees to explore the use of computers and electronics in medicine by luring them to participate in his Pattern Recognition Laboratory as interns or research scientists (Fig. 3). The author, H.K. Huang, was one of the fortunate individuals,

who had given up his dream to become an astronomer, and was later mentored by Professor Ledley.



**Fig. 4**

The ACTA, with Professor Ledley, the first whole-body CT scanner, with two slices per scan in 4½ min

## 1.3 Dr. Ledley's lifetime accomplishments

Among many other accomplishments and awards, the first ACTA prototype scanner was displayed at the Smithsonian's National Museum of American History in Washington, DC. The museum also established an archive with relevant materials related to the development of the ACTA. Ledley was inducted into the National Inventors Hall of Fame, sponsored by the US Patent and Trademark Office, in 1990. And for pioneering his contributions to biomedical computing and engineering, including the invention of the whole-body CT scanner which revolutionized the practice of radiology, and for his role in developing automated chromosome analysis for prenatal diagnosis of birth defects (see Sect. 6.2), he was awarded the National Medal of Technology and Innovation by the US President Bill Clinton in 1997. The National Institutes of Health honored him with a public lecture in 2008: "A Lifetime of Biomedical Computing: A Conversation with Robert Ledley".

Ledley initiated and remained as the Editor-in-chief of four scientific journals from the 1970s until 2012: "Pattern Recognition", "Computers in Biology and Medicine", "Computer Languages, Systems and Structures", and "Computerized Medical Imaging and Graphics".

These journals are still in publication today.

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# 2  PACS and its development

## 2.1  PACS

PACS, based on digital communication, display, and information technology, has revolutionized the practice of radiology, and, when combined with medical imaging informatics, it greatly enhances clinical practice. The first international conference and workshop on picture archiving and communication systems (PACS) was held at Newport Beach, California, in January 1982, sponsored by SPIE (International Society for Optical Engineering). Major components of PACS consist of an image and data acquisition gateway accepting images from various modalities, a PACS server and archive for management and storage, and display workstations, connected by digital networks. PACS is usually integrated with other healthcare information systems through database gateways, for example, HIS (Hospital Information System) and RIS (Radiology Information System), to communicate and manage patient information related to imaging examinations. The top of Fig. 5 depicts the general HIS/RIS/PACS system.
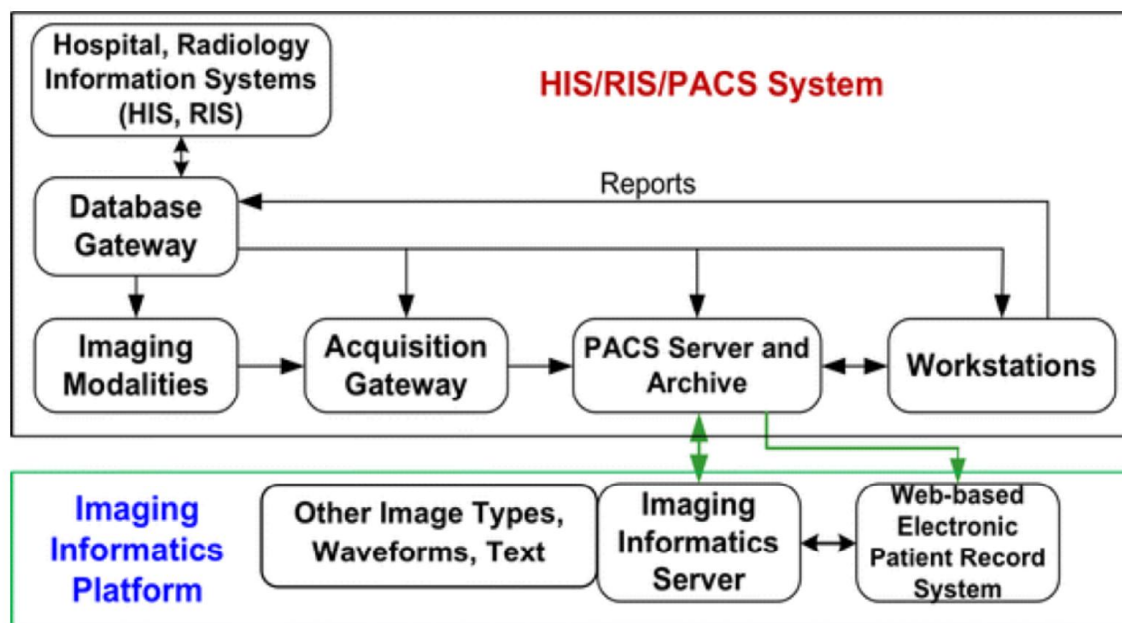


**Fig. 5**

*Top* PACS system and components. *Bottom* imaging informatics platform

This retrospective attempts to identify some of the major components in the early days of PACS development, contributed by the UCLA PACS Team and its collaborators, that played major roles in the later success of PACS. Some of these components could be traced back to Professor Ledley's innovations in his Pattern Recognition Laboratory (PRL) at Georgetown University. Others were the Laser film digitizer, computed and digital radiography, direct digital image input to computer memory, interactive display workstations, and the concept of imaging informatics (discussed later in Sect. 6). In order to present these innovations, and the cutting-edge technologies, Sects. 2.2, and 2.3 are used as background material to facilitate the subsequent presentation, followed by Sects. 3, 4, and 5: Sect. 2.2, the Department of Radiological Sciences and the Biomedical Physics Graduate Program, UCLA; Sect. 2.3, the Image Processing Laboratory; Sect. 3, development of computer and software, storage, and communication networks-related key technologies; Sect. 4, development of medical imaging-related key technologies; Sect. 5, collaboration with government agencies, industry, and medical imaging associations.

## 2.2 The Department of Radiological Sciences and the Biomedical Physics Graduate Program, UCLA (data based in 1987, when PACS was developed at UCLA)

The UCLA Medical Center is situated on the south side of the UCLA campus in Westwood Village, California, a community in the Santa Monica foothills, a few miles from the Pacific Ocean. The Medical Center is the primary training facility for diagnostic radiology, including a 4-year resident training program. The Medical Center had over 700 beds, and performed 200000 diagnostic radiological and nuclear medicine procedures annually in the1980s. Another facility adjacent to the hospital, the Medical Plaza, provides a resource for training in outpatient radiology. The department had 23 professors, 7 emeritus professors, 6 associate professors, 16 assistant professors and many adjunct faculty members. Faculty members include both medical professional and basic scientists.

The Medical Center also has a Biomedical Physics Graduate Program under the auspices of the Department of Radiological Sciences that trains MS and PhD candidates in four specialties: Biophysics, Medical Imaging, Medical Physics, and Radiation Biology, covering students from three clinical science departments. Two pioneers, Professor Moses Greenfield,

Director of the Biomedical Physics Graduate Program, and Professor Hooshang Kangarloo, Chairman of Radiological Sciences, championed the development of PACS at UCLA that led to the success of its implementation.

## 2.2.1 Professor Moses Greenfield (March 8, 1916–July 26, 2012, 97 years)

Professor M. Greenfield (Fig. 6a), Professor Emeritus of Radiological Sciences, was the founder of the Medical Physics PhD program at UCLA. In 1948, UCLA established the Department of Radiological Science, and Greenfield was recruited to establish the Clinical Physics Laboratory inside a clinical department of the Medical School. He later formed and was appointed as the Director of the well-known Medical Physics PhD Program at UCLA from 1960–1982. After he retired, Professor H.K. Huang was recruited to be mentored by Greenfield, who was instrumental in expanding the graduate program and adopted a new name, Biomedical Physics Graduate Program to signify a broadened scope by offering four subspecialties in Biophysics/Nuclear Medicine, Medical Imaging, Radiobiology and Experimental Radiation Oncology, and Therapeutic Medical Physics. H.K. Huang was the Director of the Graduate Program from 1982 to 1992. Greenfield was asked to assume the position of Acting Director of the Graduate Program from 1992 to 1996. After he became Professor Emeritus, Professor Greenfield continued to participate in the training program until 2010. During his tenure at UCLA, Greenfield co-founded the American Association of Physicists in Medicine (AAPM) and the American College of Medical Physics. He received the William D. Coolidge Award, AAPM, in 1991. The *Journal of Applied Clinical Medical Physics* (JACMP), 2005, issue was dedicated to his accomplishments in this field.
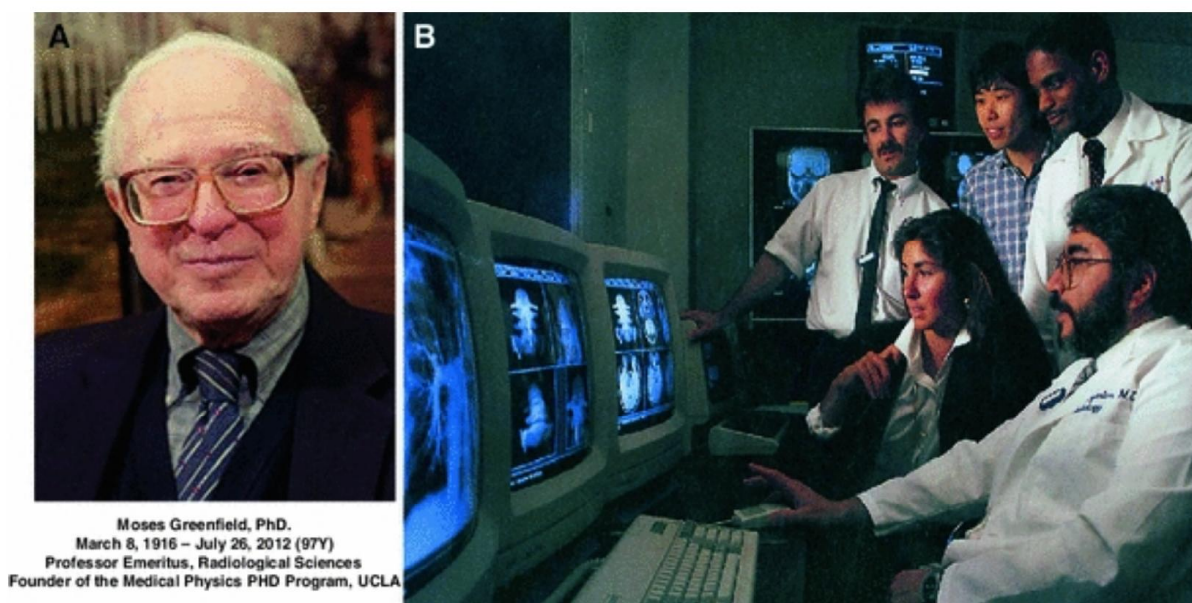
**Fig. 6**

**a** Professor Moses Greenfield. **b** Professor Hooshang Kangarloo and his faculty and residents in the pediatric radiology reading room using the PACS three 1K × 1K monitor viewing workstation

Greenfield received an NIH (National Institutes of Health) Training Grant in Medical Physics in the late 1970s. With the graduate program broadened to "Biomedical Physics" in the 1980s, the training grant was renewed. The training grant continues to be renewed by the succeeding Directors of the Graduate Program, each as the Principal Investigator, one of the longest training grants in this field supported by NIH. The UCLA Biomedical Physics Program gave more than 266 MS and PhD degrees (as of 2010), a major contribution to the medical physics profession. Many of the graduates have dedicated their careers to the fields of medical imaging, PACS, and imaging informatics, continuing the research and development efforts.

Dr. Greenfield's contribution to PACS and imaging informatics development helps to establish the quality of trainees in the biomedical physics program that provides a pool of young scientists to participate in these fields of research.

## 2.2.2 Professor Hooshang Kangarloo (Dec 24, 1944–May 15, 2012, 67 years)

Professor H. Kangarloo was Professor of Pediatrics, Radiology, and Bioengineering at UCLA. He was section head of Pediatric Imaging from 1978 to 1987, director of residency

training from 1984 to 1986, and became the first Leo G. Rigler Chair of the Department of Radiological Sciences from 1986 to 1995. Under his chairmanship, UCLA became renowned as a major innovator in PACS. Using integrated computed radiography, CT, MR, and US images, the PACS displayed them on three multiple 1K × 1K monitors, the pediatric PACS was online for daily clinical use in the late 1980s. From 1984 to 2005, Kangarloo was the principal investigator of five NIH-funded R01 grants, a training grant from the National Library of Medicine (NLM) in medical imaging informatics, and a continuously funded Program Project Grant in digital imaging, PACS, and informatics that spanned over 20 years. He became Emeritus Professor and Chairman, Department of Radiological Sciences, in 2005 and continued leading the research and training program in PACS and medical imaging informatics until 2012.

The major contributions of Professor Kangarloo to PACS and imaging informatics are as follows: as the chair of the Department of Radiological Sciences, he persuaded the clinical faculty to buy into the concept of PACS, and he moved the department from film reading to PACS reading. When he was the division chief, his pediatric radiology division was the first clinical division to use total digital PACS to read radiologic examinations. He mandated that radiology resident training had to include a 2-week rotation in the Image Processing Laboratory for learning PACS. He also encouraged faculty and residents to participate in PACS and imaging informatics research. Figure 6b shows Professor Kangarloo with his faculty and residents using the PACS system in the pediatric radiology reading room.

## 2.3  The Image Processing Laboratory (IPL) at UCLA

Professor HK Huang was recruited from the Georgetown University to establish the future Image Processing Laboratory (IPL) at UCLA in 1982, supported by the Department of Radiological Sciences. While he was waiting for the position to be vacated by Professor Greenfield's retirement from UCLA, he set up a smaller-scale image processing laboratory at the Bioengineering Department and the Department of Radiology at the University of Iowa, Iowa City, Iowa, from September 1980 to April 1982. The original purpose of the UCLA IPL was to assist residents to learn the basic image-processing terminology commonly used in diagnostic radiology. After Professor Huang joined UCLA, the department's research direction gradually shifted to PACS research and development. As a result, the IPL grew steadily. In 1987, the IPL had received several grants related to PACS development from the NIH, collaborative research support from five major imaging equipment manufacturers, and

some matching funds from the Department of Radiological Sciences. Many Biomedical Physics Graduate Program's Post-doctorates (PDs) and PhD students joined the laboratory, as did 5–6 post-doctoral fellows from foreign countries. The IPL gradually matured as a research and education laboratory; its members became faculty and researchers and PhD students in the Division of Medical Imaging of the Biomedical Physics Graduate Program. The laboratory also offered a formal training program to radiology residents. Table 1 is a list of the equipment in the IPL, and Fig. 7 depicts system components of the laboratory and clinical equipment supporting the PACS operation (data were collected in 1987). The IPL hosted annual visits for participants of the SPIE Annual PACS Conference, Newport Beach, CA, from 1987 to 1991 (see Sect. 5.6).

**Table 1**

Equipment in the IPL Laboratory and PACS components in clinical sites at the UCLA Medical Center, 1987

| |
|---|
| VAX-11/750 computer A (7 Mb) and B (6 Mb) |
| Gould IP8500 image processor A: the Gould IP8500 has 12 512 × 512 image memories, a real-time (1/30 s) image digitizer, and an image array processor |
| Gould IP8500 image processor B: same as A but has 20 Mb image memory (80 512 × 512 images). |
| Storage: data storage includes six magnetic disk drives (10, 121, 205 and three 456 Mb), two optical storage systems, one optical library (166 gigabytes), and a high-speed dual-density magnetic tape drive |
| Video scanner: one video scanner together with the IP8500 can digitize an analog image into a 512 × 512 × 8 digital image in 1/30 s; a Mitsubishi 1440 × 1440 × 8 video scanner is attached to its own image processor |
| Laser scanner/printer: two laser scanners—one can digitize a 14 × 17″ X-ray to a 2000 × 2400 × 10 bit digital image, and the other to a 1440 × 1440 × 8 image. The laser printer can write one or more images into a 4000 × 5000 pixel area on 8 × 10 and 14 × 17″ film |
| CT image-processing system: this system consists of PDP-11/44 computer, dual AP-500 array processors, hardwired back-projector. 160 Mb disk, tape drive and a multi-format camera |
| PIXAR image computer: this 1024 color state-of-the-art image computer is connected to a SUN computer |
| Mitsubishi 2048 image processor: this image processor is connected to a laser film scanner and two 2048 monitor display station |
| Picture archiving and communication system: one broadband and one baseband Ethernet communication system connect the laboratory to remote facilities and diagnostic imaging equipment located throughout the department |
| Viewing stations: there are five multiple monitor viewing stations with 512, 1024, and 2048 resolutions |
| All computers and image-processing equipment are connected through an Ethernet communication system |
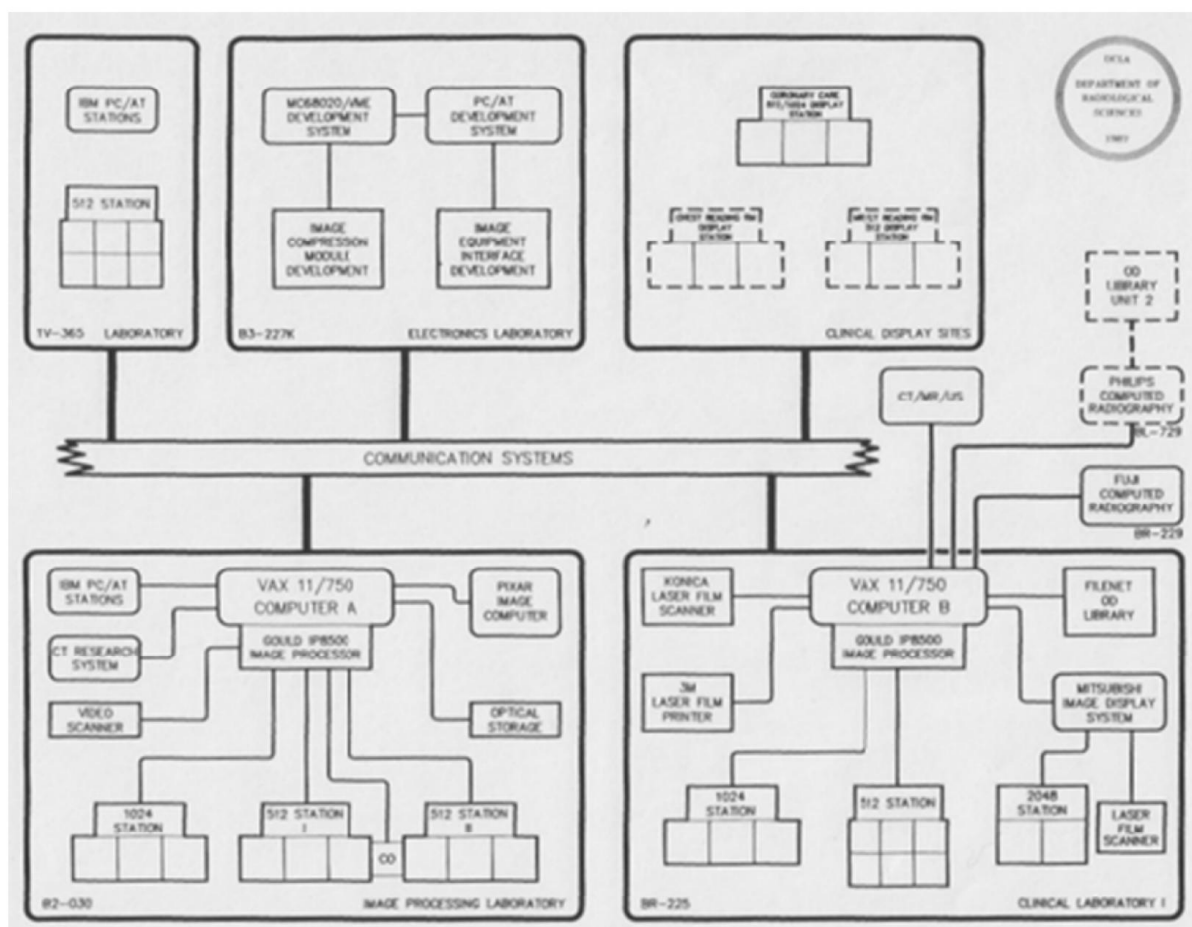
**Fig. 7**

Research and clinical components at IPL connected by the Ethernet Communication System. *Bottom left* IPL. *Right* clinical laboratory. *Top* PACS workstations at three experimental laboratories. This equipment was the Beta version of the PACS workstations later installed in the clinical sites

# 3 Key technologies: computer and software, storage, and communication networks

Many key technologies were not in existence during the early 1980s, but PACS required them for its development. Although most of them have been improved/replaced gradually by more up-to-date technologies, it is instructive for historical purposes to review some of them. For details, see [*9–11*]. This section presents a set of computer and software, data storage, and communication networks technologies which were not originally developed for PACS, but were modified for PACS applications. Section 4 describes a second set of key

technologies developed solely for PACS [*12*]. In the presentation of these two sets of new key technologies, credit is given to those individuals and/or manufacturers who contributed to the novelty of the accomplishment.

## 3.1 The VAX 11/750 computer system

The VAX 11/750 computer system was partially supported by the Digital Equipment Corporation (DEC) in 1984, running the VMS operating system, the most advanced mini-computer at that time (Fig. 8, left, and Fig. 7, bottom left and right).



VAX 750 computer (Left) driving the Goluld DeAnza 1K color display controller (blue), 1986
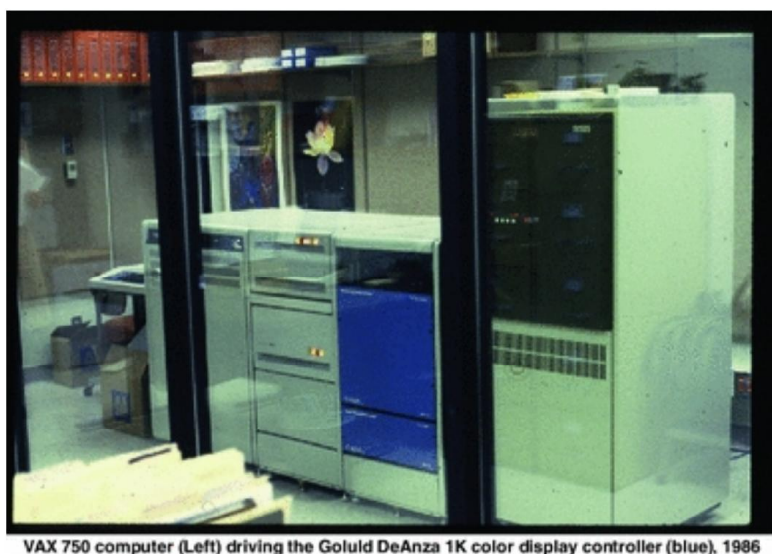
**Fig. 8**

The VAX/11 750 computer. *Left* the Gould DeAnza multiple display controller (*middle, blue*)

## 3.2 Multiple display controller

The Image Processing Controller hardware that could drive a color 1024 monitor (Fig. 7 lower left and right, and Fig. 8 middle, blue, and Fig. 14 right) was supported by Dr. Harold Rutherford of the Gould DeAnza Corp. from January 1984 to January 1989. The controller was modified by the UCLA PACS Team to drive three 1024 black and white monitors to display three different 1K × 1K PACS (black and white) images simultaneously. Hence, it becomes a high-resolution multimodality image display system.

## 3.3 Hierarchical storage system

This project was carried out in collaboration with Kodak, USA, from April 1988 to March 1995 to integrate a large-capacity computer Jukebox with many optical disks (14″) (Fig. 9 left) with the then innovative redundant array of inexpensive disks (RAID) by use of AMASS software (Fig. 9 right) which was designed by the UCLA PACS Team. This system was still running the UCLA legacy PACS for archiving of historical images until the early 2000s.
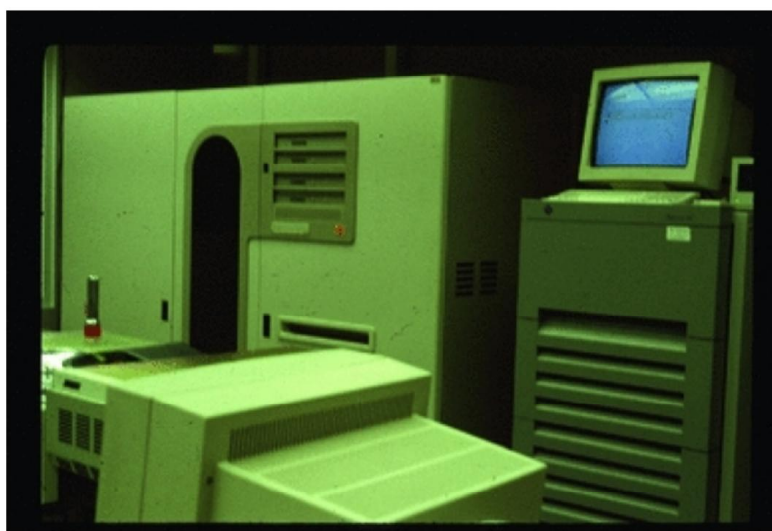


PACS Two-tier Storage: RAID (Right, Hitachi) and
optical disk jukebox with a Juke box (Left,
Kodak), UCLA, 1990

**Fig. 9**

Large-capacity Optical Disk Jukebox by Kodak and the RAID disks running the AMASS software (*right*)

## 3.4 Personal image filing system

This two-phase collaborative project with Maxell Hitachi, Japan, ran from October 1988 to September 1990, and from October 1992 to September 1994, for development of an information system using designated storage areas for retrieving/converting data and directories of different-format image archiving in optical and magnetic storage. The result was a US patent awarded to the UCLA Team with two Japanese scientists, Sonobe Takeo and Toru Shinagawa, of Maxell Hitachi in 1995 [*13*].

## 3.5 Image compression

This project was supported by IBM with its massive computer center at San Jose, CA, from August 1984 to August 1985, with continuous extension for running of computational intensive image compression algorithms which ultimately resulted in the development of the 3-D wavelet compression method for medical images [*14*, *15*].

## 3.6  Laser film printer for X-ray images

This project was sponsored by 3M Corp., Minneapolis, Minnesota, from October 1986 to September 1988 for printing of PACS output images on films. In the early days of PACS operation, printing of PACS images on films was still necessary for image quality comparison and as an established tradition in clinical wards. For these reasons, the availability of film copy was still required in the beginning of the PACS operation.

## 3.7  Asynchronous transfer mode (ATM) communication technology

This 2-year collaborative project with Pacific Bell, CalREN (California Research and Education Network), USA, from March 1994 to December 1996, was used for merging of the local area network with the ATM, the then high-speed wide area network (155 mbits/s) for PACS application in teleradiology. The location of the operation was at the Laboratory for Radiological Informatics, University of California, San Francisco [*16*].

## 4  Key technologies: medical imaging related

Five key technologies in medical imaging required for PACS operation are summarized. All were developed in long-term collaboration with major medical imaging manufacturers.

## 4.1  Laser film scanner

In order to convert millions of already archived X-ray films in every radiology department to digital format for PACS operation, high-resolution 2K × 2K × 12 bits laser film scanners were necessary. The UCLA PACS Team collaborated with three major film scanner manufacturers for many years. The first one developed for clinical use was by Konishiroku Photo Ind. Co. Ltd. (it changed its name to Konica in the 1980–1990s, and most recently to

Konica-Minolta), Japan. The collaborative research between Konica and UCLA was very extensive and is described in Sect. 5.5 in more detail. Figure 10 shows the first laser film scanner delivered by Konica at UCLA.
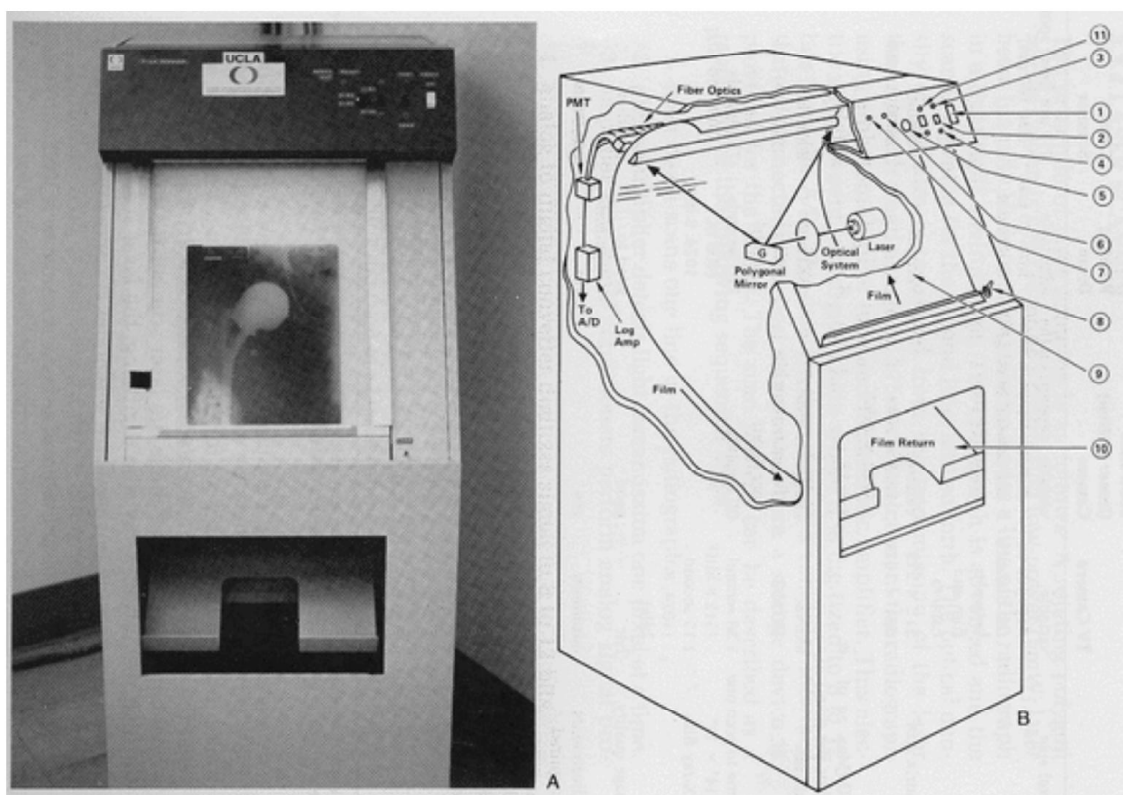


**The first Laser film scanner by Konica at UCLA**

**Fig. 10**

The first Konica laser film scanner at UCLA, 1984

In late 1964, Mr. Toshio Abe left Konishiroku, and he formed his own company in 1967, named Abe Sekkei, Tokyo, Japan. He had developed the micro-densitometer (1969), drum scanner (1975), and imaging camera for medical application (1977) (also compared with Professor Ledley's development of scanners discussed in Sect. 1.1). Abe had also developed one of the best laser film scanners for X-ray films and the digital radiography system dominating the Japanese laser scanner market. Since its establishment, Abe Sekkei has maintained a long-term working relationship with the UCLA PACS Team.

The UCLA Team also collaborated with Lumisys, Silicon Valley, CA. The scanner was used for digitizing of archived X-ray films and for comparison of digitized image quality with other scanners.

## 4.2 Computed radiography (CR)

In the late 1970s and early 1980s, Fuji Electric Corp. was developing a 2-D computed radiography system in Japan. H. Kado, the chief engineer, was collaborating with Stanford University, Stanford, CA, on its further clinical applications [*17*, *18*]. Fuji started to sell its CR in Japan in the early 1980s as a different method of generating an X-ray image by using a laser-stimulated luminescence phosphor plate. However, its output was still printed on laser Fuji film. Dr. Bill Angus, the late Senior Vice President of Philips Medical Systems of North America (PMS), USA, initiated the negotiations to obtain the license for Philips to sell the Fuji CR in Europe and in America under PMS's name. As a result, a similar Fuji CR system was called PMS CR on both continents. The first Fuji CR-101 installed in the US was at the Ochsner Clinics (now Health System), New Orleans, LA (Fig. 11). With the assistance of Dr. Angus, Fuji also installed the second Fuji CR-101 system in the US at UCLA, because Philips was not ready to deliver. Several members of the UCLA PACS Team were trained at the Ochsner Clinics by Philips CR physicists. UCLA used the CR-101 in its pediatric radiology section. Later, PMS installed the PR-701, PCR-901, and PCR-9000 at UCLA.



CR-101

First commercial Computed Radiography (CR) system in US at Ochsner Clinics, NO, 1985
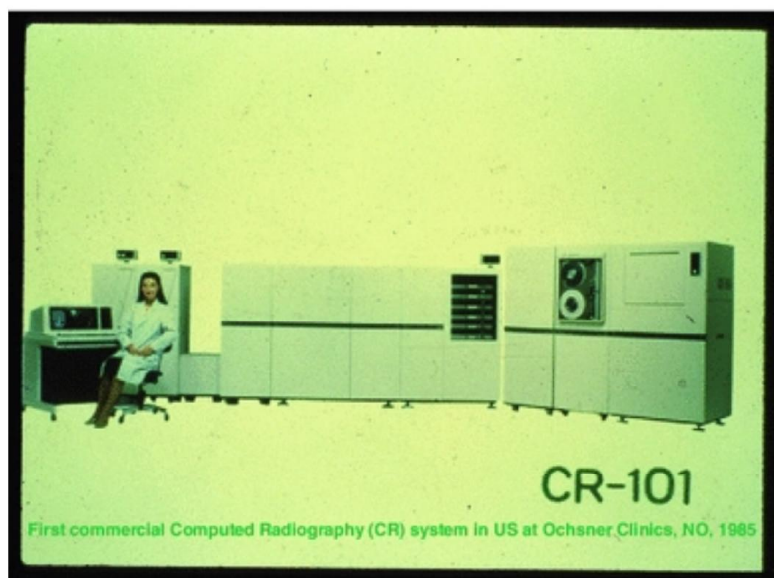
**Fig. 11**

The first Fuji computed radiography (CR) system in the US was installed at the Ochsner Clinics, New Orleans; the second CR system was installed at UCLA in late 1985

## 4.3 Direct digital input from CR to PACS

The reason UCLA wanted to install the Fuji CR system was not because a laser-stimulated luminescence phosphor could potentially produce a better quality image on a Fuji film. It was because UCLA contemplated the potential of obtaining a direct digital image from the output of the Fuji CR without going through a film. The advantage was immediately obvious for PACS application. However, several negotiations with Fuji failed to allow the UCLA Team to obtain the direct digital image output from the Fuji CR, due to industry confidentiality. Several months later, through the influence of Dr. Angus of PMS, UCLA developed a long-term research collaboration with PMS from which the UCLA Team learned the digital data characteristic of the Fuji CR. This knowledge opened the gate for direct digital images from a CR system that might eliminate the use of a film scanner to scan future X-rays films. This success was a key turning point for shortening the development time of the PACS system. Figure 12a shows the black box with two cable ribbons, one connected to the Fuji CR system and the second to the PACS image acquisition computer [19]. This project involved in-depth industry collaboration; some of its collaborative arrangements are presented in Sect. 5.5 (Fig. 12).
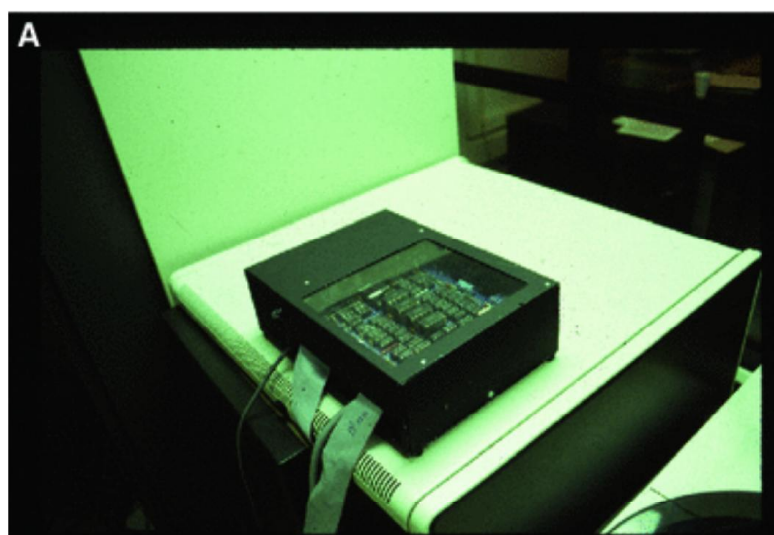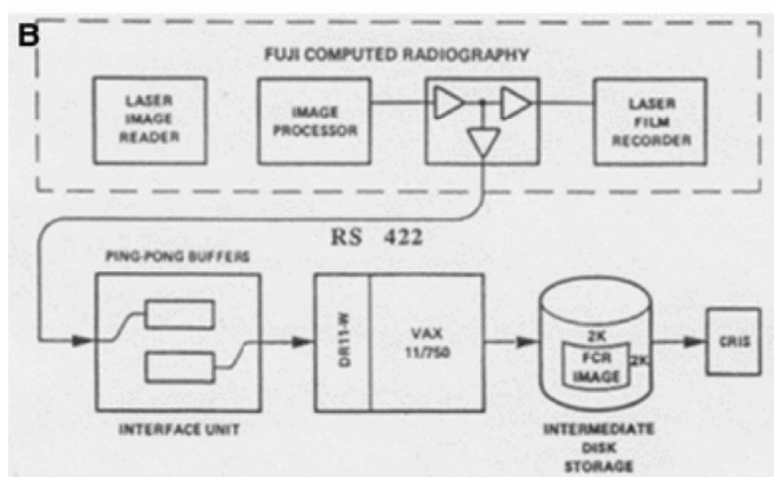
**Fig. 12**

The first digital interface unit using a ping-pong buffer and the DR11-W interface technology to transmit CR images in real time to the outside of the CR reader. It was designed and implemented by the UCLA PACS Team. The *black box* is shown in **a**. The architecture module was a gateway to the PACS input system (**b**). The novelty of the design at that time was the use of the ping-pong buffers to allow the continuous Fuji image data transfer to both the laser film recorder as well as the direct digital capture mechanism of the VAX 11/750 computer

## 4.4 Digital radiography

Konica used a laser-stimulated luminescence phosphor plate to develop a prototype digital radiography (DR) system in Japan and shipped it to UCLA for further research and development for clinical use (Fig. 13). The difference between the Fuji CR and the Konica

DR system at that time was that the early Fuji CR required four steps for obtaining a CR image. First, the unexposed laser-stimulated luminescence phosphor plate was exposed to form an X-ray image, a laser beam was used to scan the exposed plate to obtain light photons which formed a light image, and then the CR film image was produced. The residual light energy in the plate was erased by use of a high-intensity floodlight. These steps occurred in sequence, and hence a massive instrument was required to house the FCR-101 system, as shown in Fig 11. The Konica prototype DR system used the indirect image capture method with a semiconductor laser to scan the plate to collect light photons, and a PMT (photomultiplier tube) and an A/D (analog to digital conversion) coupled together to convert the light photos to form a digital image. There were three imaging plates inside the system, allowing three X-ray exposures per examination. Figure 13 depicts the Konica system. Several Konica engineers from Japan and a few UCLA PACS Team members worked together to modify the DR system to be a prototype clinical system. Later, Konica developed a new DR system for clinical trials.
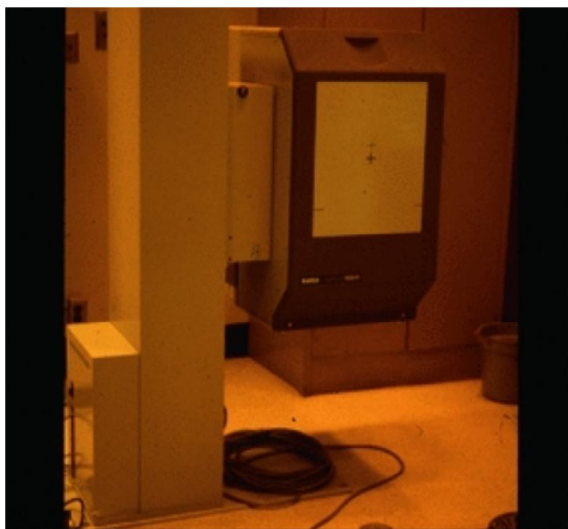


**A prototype DR system, Konica and UCLA**

**Fig. 13**

The prototype Konica digital radiography system at the UCLA PACS Clinical Laboratory. There were three imaging plates in the housing, allowing three consecutive exposures in one examination

## 4.5  Interactive display with multiple monitors

In order to understand the resolution requirement and the number of images needed to display for a given type of radiographic examination, the UCLA Team developed

workstations of various resolutions and with various display monitors. This ambitious endeavor required many workstations of different kinds. Through the generous support by many image workstation manufacturers, a workstation laboratory was established. Most of the time, the manufacturer loaned the hardware to UCLA, and their engineers worked together with the PCAS Team to develop the display and controller software. These workstations included two sets of six $512 \times 512$ monitors (the architecture of this display system was later adopted by Siemens Gammasonics, Inc., Chicago, IL. for their PACS system installed at the Danube Hospital, Vienna, Austria, 1990), three $1024 \times 1014$ monitors (supported by Gould DeAnza), one 1400-line monitor (supported by Mitsubishi, Japan), and two $2048 \times 2048$ monitors (supported by Megascan, USA). Figure 14 depicts the multiple viewing workstations laboratory at UCLA.
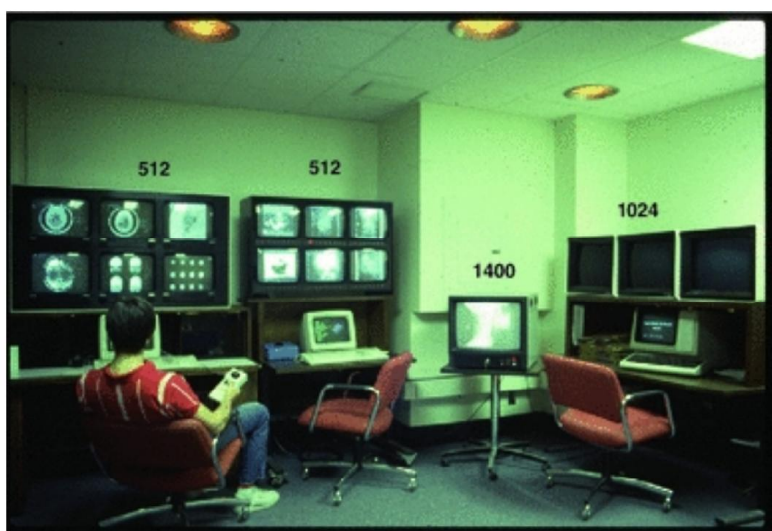


Multiple viewing workstations at the UCLA viewing room, 1990

**Fig. 14**

The multiple viewing workstations laboratory at UCLA with multiple-resolution workstations, including two six-monitor display systems (512 × 512), one 1400 line single-monitor system, and one three-monitor display system (1K × 1K). This workstation room was used for the first large-scale study on the quality of image display with different spatial and density resolutions

# 5 Collaboration with government agencies, industry, and medical imaging associations

In addition to the pioneering work of medical imaging by Professor Robert Ledley,

Georgetown University; Professor Moses Greenfield's development of the biomedical physics training program; and Professor Hooshang Kangarloo, as both a clinician and scientist to champion PACS R&D; and the PACS Team at the Department of Radiological Sciences at UCLA, the success of rapid development of key PACS technologies during the first 10 years had been due to the collaboration with government agencies, industry, and medical imaging associations. Among them were contributions from national and international government agencies, private medical imaging industry, scientific societies, colleagues from academia, and many individuals from these organizations, as described in previous sections. This retrospective section attempts to organize their contributions systematically.

## 5.1 The US NIH, NSF, FAA, NCHS

The Department of Radiological Sciences, UCLA, was fortunate to receive substantial support from the US NIH (National Institutes of Health), NSF (National Science Foundation), FAA (Federal Aviation Administration), and NCHS (National Center for Health Statistics) for PACS-related research during the first 10 years of PACS development, as follows: (1) from the National Cancer Institute (NCI), NIH: Digital Viewing Stations for Diagnostic Images (6/84-6/87, 8/87-7/92 and 8/92-95), Radiological Image Compression (7/86-6/89), Program Project Grant: PACS in Radiology (5/90-4/95), and Biomedical Physics Training (9/87-8/92, and 9/92-8/97); 2) The National Science Foundation: Parallel Computing Algorithms for 3-D Imaging (7/92-6/94); 3) The Federal Aviation Administration: Image Processing for Automated X-ray Experimental System (12/83-12/84) and New Detection Concept (9/85-12/87); and 4) National Center for Health Statistics: Film Digitization (5/90-10/97).

Dr. Matti Al-Aish, of the Radiation Research Program, NCI (National Cancer Institute), who was the Program Administrator of the UCLA Program Project Grant on behalf of the NCI, presented his impression of UCLA PACS R&D development at the NATO (North Atlantic Treaty Organization), ASI (Advanced Science Institute) meeting, "Picture Archiving and Communication Systems (PACS) in Medicine", Evian, France, October 14–26, 1990 (see also Sect. 5.3) [20]:

> At the University of California in Los Angeles (UCLA) ... research is in progress
> on many aspects of PACS in radiology...

*In conclusion, The UCLA Team is striving to design and develop an accurate diagnostic imaging system with rapid throughput of patients, timely reporting and efficient retrieval of patients' radiological examinations. They are investing six years of experience in PACS research in this major undertaking. So far, they have successfully implemented two PACS prototype systems in pediatric radiology and coronary care units. These systems have been used for the past two years in the daily routine of patients' examinations. This success encourages them to plan five additional PACS modules in intensive care units, neuroradiology, urology, and chest radiology. It is heartening to say that upon completion of this project, 35 % of the total examination procedure at the department of radiology at UCLA will be converted to PACS digital imaging systems.*

*The anticipated success of this research project will usher in a new era in radiological examination, improved patient care, and health care costs.*

## 5.2  The Netherlands National Foundation and the UCLA PACS

Professor A.R. Bakker of the University of Leiden was also the Director of BAZIS, a non-profit organization that developed and supported the integrated hospital information system (HIS) in the Netherlands. This HIS was one of the best systems in the world in the 1980s; it was in use in 7 out of 8 university hospitals and some 30 general hospitals in the country. The UCLA PACS Team benefited from Professor Bakker, who shared this technology with the Team and explained the importance of the integration of PACS with HIS in the future of PACS development. Professor Bakker, however, cautioned about the difficulty for the Netherlands and other European countries to develop a PACS system, for two reasons: (1) the initial investment was too huge a burden for a European country, and (2) in the 1980s and 1990s, no major imaging manufacturers in Europe would invest in this application [21]. He forecasts that the cost of PACS could not be justified for any Netherlands hospitals to install until the year 2000, when its cost would be equivalent to that of a film-based system. For these reasons, during the first decade of PACS development in Europe, the focus would be on research of PACS components. Professor Bakker encouraged the UCLA Team to apply for travel lectureship funds from the National Science Foundation of the Netherlands as a means of exchanging information on PACS technology development during the years ahead.

Through his suggestion and assistance, the UCLA PACS Team was successful in receiving two 2-week lecture grants from the Netherlands: (1) Information System in National Science, "Digital Radiology in Netherlands Lectures" (10/1985); and (2) National Science Foundation of Netherlands (10/1988), "Boerhaave Lectures". In each trip during the time of these lectures, the UCLA PACS Team toured universities in the Netherlands, other research laboratories, and the Philips Medical Systems, exchanging the Team's experience in PACS system integration with the hosts' specialties in PACS component development. In these two lecture tours, the UCLA Team always included several members who themselves were visitors to UCLA from different manufacturers, and/or from universities of different countries.

## 5.3  The NATO Advanced Science Institute (ASI), and the UCLA PACS

Among several major PACS international conferences during the first 10 years of PACS development, two deeply influenced the development of PACS. The first was the SPIE Medical Imaging Conference at Newport Beach, CA, in 1982, where the name "PACS" was coined. The second was the NATO (North Atlantic Treaty Organization) Advanced Study Institute (ASI)-sponsored picture archiving and communication systems (PACS) in medicine conference held in Evian, France, October 14–26,1990 [22]. The ASI supported NATO countries to conduct innovative research and development projects in the form of sponsoring conferences in a NATO country. The UCLA PACS Team, in coordination with Professor Osman Ratib, Digital Imaging Unit, Center of Medical Informatics, University Hospital of Geneva, Switzerland (a cardiologist by training, he also received a PhD degree in Medical Imaging at UCLA), applied to NATO ASI to host an international conference on PACS. During the second round of the application in 1989, the grant was awarded to the UCLA Medical Imaging Division: NATO Advanced Study Institute, 8/1990, PACS in Medicine. The grant was able to support travel expenses for 2 weeks for 100 participants who had made contributions to PACS-related research in the past, and no admission fee to the ASI was required. The site had to be in one of the NATO countries, and Evian, France, was chosen. More than 150 participants joined the conference; 1/3 of them paid their own travel expenses. There were altogether 68 presentations and many small-group workshops. The highlights are:

*1.*  The conference hall had only one public telephone, and there were no TVs or phones in the surrounding dormitory rooms. Each room was spacious and comfortable with private

shower. Evian was famous for its excellent drinking water. This countryside accommodation environment resulted in drawing the participants close together and having more time for discussions in individual groups. The evening atmosphere was always friendly and candid, with frank discussions on the pros and cons of PACS in medical practice. The NATO Conference created a memorable fraternity of PACS research and development (R&D) in these early days.

*2.* Almost 75 % of the participants had R&D experience in PACS, and 50 % of them remained in this area of work 10 years after the NATO Conference. Many of them became leaders in their own area of expertise in PACS and imaging informatics, and in the future PACS operation or management.

*3.* Many chief engineers and management personnel in PACS R&D of major medical imaging manufacturers from Japan and Korea, European countries, and the US joined the conference, but no commercial advertising was done during the meeting.

*4.* Many presentations summarized the PACS development in a specific country. The Proceedings of the NATO Conference published by the Springer-Verlag (Berlin and Heidelberg, Germany) in 1991 was one of the most complete documents related to PACS development in each country at that time, with the pros and cons detailed by the presenters. As an example, Professor Walter Hruby's presentation on "The Vienna SMZO Project" hinted that his project was almost complete [23]. In April 1992, Professor Hruby opened a new and completely digital radiology department at the Danube Hospital, Vienna, showcasing his PACS system installed by Siemens Gammasonics. Many of the NATO participants were Professor Hruby's guests of honor, subsequently, during the opening ceremony of the digital radiology department of the Danube Hospital.

*5.* Japan was leading in PACS development during the first 10 years. Two main reasons might be (1) the pioneering work of Fuji's CR system and Konica's film scanner, and CR and DR systems, and (2) the PACS project was jointly supported by the Japanese government and the manufacturers. Many Japanese researchers from the universities supported by the government teamed up with their respective supporting manufacturers, to install PACS systems in their affiliated university hospitals. In the NATO conference, they presented their PACS development and experience [22, 25, 26].

*6.* Colonel Fred Goeringer, Medical Diagnostic Imaging Support Systems for Military Medicine, and many other military officers, of colonel rank, from various healthcare

services in the US, also participated. The Digital Imaging Network and Picture Archiving and Communications System (DIN/PACS), RFP (request for proposal) announced in 1986 encouraged the US universities to compete for funding support [24]. After the NATO ASI, Col. Goeringer immediately implemented the Army MDIS (Medical Diagnostic Imaging Support Systems) project, which resulted in several large-scale military PACS installations. The MDIS also injected a major stimulus into the PACS industry in the US and Europe, which led to continuous large-scale PACS R&D efforts.

## 5.4  Collaboration of the UCLA Team with the US medical imaging industry

Sections 3 and 4 had presented some key PACS technologies in which the UCLA Team collaborated with the US medical imaging industry. In order to appreciate the support of industries, this section summarizes their contribution to the UCLA PACS project systematically in chronological order.

1. Technicare Corporation: CT Image Input to PACS (1/84-1/89)

2. Light Signatures, Inc.: Image Processing Research (1/84-1/86)

3. Gould/DeAnza Inc.: Image Processing Equipment Evaluation (1/84-1/89)

4. 3M: Laser Film Printer (10/86-9/88)

5. Virtual Imaging: Image Station (5/87-1/89)

6. Polaroid Corporation: Quality Assurance of Laser Imager (7/95-12/96)

7. Pacific Bell, CalREN: ATM High Speed WAN (3/94-12/96)

8. IBM, Folder Manager and PACS Related Research Topics (84-85 and cont., 1/93-1/95)

9. Kodak: Hierarchical Storage System (4/88-3/95)

10. Philips Medical Systems: Computed Radiography Systems and CR Equipment (7/85-12/86, 5/87-3/89, 9/89-8/92)

11. Megascan: 2K × 2K Workstation (9/87-9/90)

12. Lumisys: high-resolution laser digitizer (9/94-9/99)

## 5.5  Japan medical imaging technology and the UCLA PACS

The UCLA Team had had a very close collaboration with both Japan academia and the medical imaging industry, including Konica (1984–1993), Mitsubishi Electronic Co. (1985–1989), Maxell Hitachi (1988–1990 and 1992–1994), and Abe Sekkei (1988–2013).

In 1984, Konishiroku (Konica) Photo Ind. Co. Ltd., delivered the first laser film scanner to the IPL (Image Processing Laboratory), UCLA, followed by a computed radiography, then a digital radiography system. Many research engineers from Konica also came to work with the PACS Team not only on PACS, but also on its clinical operation at various time intervals during the first 10 years of PCAS research. The upper management of Konica signed a long-term collaborative contract with the Department of Radiological Sciences at UCLA. Konica wanted their technical key employees to be inspired by some of the western research spirit and methodology. Through the years from 1982 to the 1990s, the following senior engineers stayed at UCLA for at least 2 years: Dr. Hiroshi Takeuchi (post-doctoral fellow in medical imaging), and M. Kimura, PhD (post-doctor in medical imaging), Yoshiyuki Ishimitsu (received his PhD degree in medical imaging at UCLA).

After the late Dr. Bill Angus, senior VP of Philips Medical Systems (PMS), North America, obtained the right for PMS to sell the Fuji FCR system in Europe and North America in 1984, he single-handedly established a working relationship between the UCLA PACS Team and Fuji, Japan. Since then, the PACS Team has had a license to work with both Konica and Fuji to benefit from using both companies' CR systems for PACS application. The UCLA Team, with Konica and Fuji engineers, abides by a certain set of guidelines, respecting each company's confidentiality, working together without any conflicts or problems. This arrangement led to a tremendous advance in PACS development from 1982 to 1992.

During this collaboration between Konica and Fuji within UCLA, and the Team's working relationship with other Japanese medical imaging manufacturers, the Team visited Japan often and attended national conferences. The Team was very well received by the Japanese elite PACS research groups, and they learned a tremendous amount about the Japanese PACS philosophy and methodology [25, 26].

Many academic faculty members in Japan contributed much to the PACS development during the 1980s, as evidenced by publications in the *Journal of the Japan Association of Medical Imaging Technology* (JAMIT, 1983, 1986). Among these members, three deeply influenced the thoughts of the Team in developing PACS at UCLA: Morio Onoe, Professor Emeritus, University of Tokyo, in his Opening Special Lecture at the Fifth Symposium on Medical Imaging Technology in Japan, 1986, "Facets of PACS" [27]. He clearly identified

four major key technological issues in PACS: (1) short-term and long-term image archive; (2) high-speed image transmission; (3) a more sophisticated image workstation; and (4) standardization. The UCLA Team closely followed his thought processes and guidance during the years of PACS development. In the US, we have been fortunate to have Professor Steve Horii at the University of Pennsylvania (before, he was at Georgetown University), who has taken up the challenge on (4) standardization, and has since spent his lifetime to teach and perfect the DICOM (Digital Imaging and Communications in Medicine) Standard which PACS had adopted for years as the standard for all medical images used in PACS.

The second person was Professor Goro Irie, Radiology Department, Hokkaido University Hospital, Sapporo. The UCLA Team had visited his hospital several times in the 1980s, when Professor Irie was developing his MIS in HU (Hokkaido University Medical Information System), in which PACS was connected to HIS (Hospital Information System) and the Medical Record System, as shown in the bottom of Fig. 15. He predicted that PACS had to be connected with the HIS and MIS in order to be accepted as a fully functional digital data healthcare delivery system. Professor Irie lectured to the Team on this concept, and some of the Team members took his advice seriously. Professor Irie presented his concept, "Clinical Experience—16 months of HU-PACS", during the NATO ASI [28]. Unfortunately, the UCLA Team was unable to carry out such a large-scale project in the 1980s. Instead, the Team focused first on the PACS development, followed by connecting the PACS to the RIS (Radiology Information System), then to the HIS in the 1990s. True fulfilling of Professor Irie's concept did not occur until after 1999, when some UCLA Team members were relocated to other institutions, and they had designed a total integration system for the Hong Kong Hospital Authority with 43 public hospitals in the early 2000s. The design included Professor Irie's original concept, and several years later the total integration system was gradually implemented. The paper: "From PACS to Web-based ePR system with image distribution for enterprise-level filmless healthcare delivery" was published in this Journal in July 2011 (about 20 hospitals were online then) [29]. The number of online hospitals has continuously been added to (see Ref. [29]; Figs 5, 6, 7).
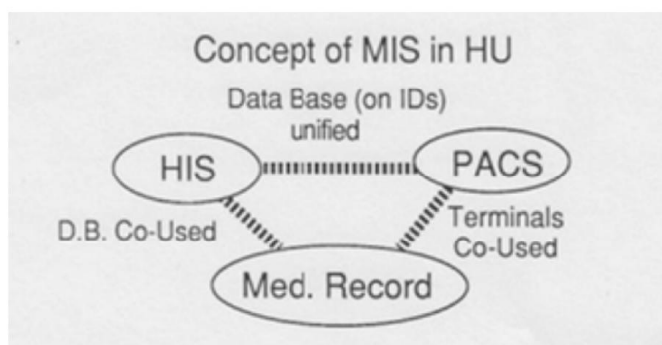
**Fig. 15**

Adopted from Professor Irie's Concept of Medical Record System (MIS) in Hokkadio University Hospital [*28*, see also *29*]

The third person was Mr. Koyo Matsuda, who worked at Konishiroku (Konica) Photo Ind. Co. Ltd., and left the company in 1984 to work at Abe Sekkei (see Sect. 4.1). He established a life-long working relationship and friendship between Abe Sekkei and the UCLA PACS Team members. A new company, Array Corporation, branched out from Abe Sekkei to extend its business to include computer software in 1991. In 1998, the Array Corporation merged with Abe Sekkei, where Mr. Toshio Abe and his son Satoshi have been the Chairman and the President, respectively, and Mr. Matsuda remains in the merged company. Many original UCLA PACS Team members, even though they might have changed careers or relocated to different positions, remain in contact with Array, either in business or friendship.

## 5.6 SPIE, EuroPACS, CARS, and UCLA PACS Team

In addition to working with the Japanese medical imaging industry, the UCLA PACS Team also worked very closely with three professional conferences, starting when they established the PACS emphasis in their conferences: SPIE (the International Society for Optical Engineering), Medical Imaging Conferences and Courses (1982), The International European PACS Meeting (EuroPACS, 1982), and the computer-assisted radiology and surgery (CARS) International Congress and Exhibit (1985).

### 5.6.1 SPIE

The first SPIE PACS Conference started in 1982 at Newport Beach, CA. The meeting was held there until the venue changed to San Diego, CA, in the early 2000s, then has alternated between San Diego, CA, and Orlando, FL, every other year since the late 2010s. In the early

1980s, when UCLA started its PACS R&D efforts, many participants of SPIE Conferences came to visit the UCLA IPL and the PACS Laboratory. In the mid 1980s, SPIE discussed with the UCLA IPL organizing these visits to become an annual event attached to the SPIE PACS Conference, compliments of the IPL. On a selected evening during the SPIE conference, a tour bus would take a carload of SPIE visitors to UCLA, Westwood, for an evening with show-and-tell and visit all related laboratories, followed by a light snack and open discussion. The bus would take them back to Newport Beach, where their conference hotels were located. Good will, friendship, and fellowship were generated during this evening event.

## 5.6.2 EuroPACS

EuroPACS was launched in 1982 as the European PACS Society. Its membership was open to any individual, hospital, or university in Europe. The Europe PACS philosophy at that time was quite different from that in Japan or the US, where system integration was the priority. European PACS development was mostly in modeling, simulation, or individual components during the 1980s and early 1990s. The membership of the society was limited. A different host country took turns to sponsor an annual meeting during a summer month. Because of the small membership, the meetings tended to be close-knit; almost all members and their families met at least once a year, and everybody knew each other well. The discussion was very open, and each country learned what other countries were planning and executing to help each other to progress. Researchers from outside Europe could join as guest members or could be elected as Honorary Members of the EuroPACS Board. The UCLA PACS Team began its association with the EuroPACS in 1982, and some members were elected as Honoray Board Members. It was very important for the UCLA PACS members to join the EuroPACS because they learned much about the philosophy of the EuroPACS and their emphasis and progress. EuroPACS merged in the late1990s–early 2000s with CARS and became one of the International Congress and Exhibit members. As of today, many original EuroPACS members still have a good relationship with the original UCLA PACS Team members.

## 5.6.3 CARS

CARS (computer-assisted radiology and surgery) was established in 1985. Its original name was CAR (computed-assisted radiology); later, the specialty surgery joined the CAR to

become CARS. The CARS headquarters was near the Black Forest, Germany, and the Congress met every year, one year always being in Germany (Berlin or other cities), and the other year in a different country, including Japan and the US. CARS had an annual attendance of about 1000, including the host country's participants. The CARS Congress includes other conferences: International Society for Computer-Aided Surgery (IACAS), EuroPACS Meeting, Workshop on Computer-Aided Diagnosis (CAD), and the Computed Maxillofacial Imaging Congress (CMI). The UCLA PACS Team joined the Program Committee of CARS in 1985, when it was established and has since contributed substantially to its activities including: scientific presentations, workshop and tutorial presenters, session chairmen, and as the CARS Congress Annual President. CARS allowed the Team members to gain more depth in the knowledge of PACS, and also to learn other image-assisted specialties that are necessary for imaging informatics research and development.

## 5.7  Patents and copyrights

The UCLA PACS Team has collaborated with many US and other countries' academic institutions, professional societies, and manufacturers since 1982. Many of these collaborations were tightly coupled with the PACS development. Thus, sometimes it was difficult to distinguish which partners should own what intellectual properties, copyrights and/or patents. The Team had waived its right to apply for any copyrights and/or patents related to PACS project research and development in the 1980s; and their partners had a free hand to pursue their own applications. The first of two examples was interfacing the Fuji CR to the outside world; it was a novel development (see the black box in Fig. 12 with its caption). Several years later, Fuji used a similar concept to develop its own interface. The second example was the six-monitor display workstation used by Siemens Gammasonics in Professor Hruby's SMZO PACS project, in 1992, as described in Sect. 5.3, (4). The original design of the workstation was by the UCLA Team in 1987, shown in Fig. 14 with its caption, in the UCLA Workstation Laboratory.

The only exception where the UCLA PACS Team applied for a patent was the US Patent No. 5410676, April 25, 1995. Some Team members received the patent award with collaborators from Maxell Hitachi, the topic of which was not related to PACS, but was related to a computer software data storage algorithm [13].

# 6  Medical imaging informatics

## 6.1  Biomedical informatics

Biomedical informatics (BMI) is loosely categorized into four levels of study: bioinformatics (molecular level), imaging informatics (cellular, tissue, and organ system level), clinical informatics (personal healthcare level), and public health informatics (population level) [30]. Some rudimentary biomedical informatics research and development started as early as in the 1990s. However, because medical imaging informatics research requires large-scale medical image/data from PACS (not available until in the late 1980s and the1990s), enterprise PACS, and integration of PACS with HIS and RIS (not available until in the late 1990s and early 2000s), systematic medical imaging informatics research did not start until the middle of the 2000s. The only exception was the automatic chromosome karyotyping imaging informatics system developed by Professor Robert Ledley in the 1970s. He was able to develop such an imaging informatics system for research because he did not use radiologic images as input data. Instead, in order to acquire a large number of digital images, Ledley used the microscopic analog light images from glass slides, and his SPIDAC system to covert the analog images to digital images.

## 6.2  The 1970s concept: chromosome karyotyping

In the early1970s, Professor Ledley developed the SPIDAC (Specimen Input to Digital Automatics Computer) in his Pattern Recognition Laboratory (PRL, see Sect. 1.1) and applied it to automatic chromosome karyotyping and analysis. This endeavor could probably be considered as the first systematic medical imaging informatics application. Chromosome karyotypes describe the number, shapes, bands, and contents of chromosomes in a metaphase cell, and how they look under a light microscope. In human genetics, chromosomes karyotyping is used to determine whether the chromosomes in the metaphase cell of the mother are normal or abnormal. The results can lead to prenatal diagnosis of birth defects.

A systematic medical imaging informatics platform normally includes two major components: (1) the PACS for images and data acquisition, archive, communications, display, and management; and (2) the new knowledge discovery from the PACS data.

In Professor Ledley's PRL, integration of SPIDAC with the VIDAC (video memory) + MACDAC (man machine interface to digital automatic computer) + IBM360/44

computer could scan a microscopic glass slide (Fig. 16, left), select (Fig. 16, upper middle, detected two metaphase cells at low resolution and chromosomes at high resolution), acquire (upper right), display (lower left), and manage metaphase cells. These functions in the 1970s were almost equivalent to the basic components of an early Pathology PACS in the 2000s (including all steps shown in Fig. 16). The medical imaging informatics component included image processing to analyze and karyotype all chromosomes (Fig. 16, lower right) in the cell and the intelligent component to determine whether the cell was normal based on information from its chromosome karyotyping, which is the new knowledge discovery component extracted from the image informatics data.
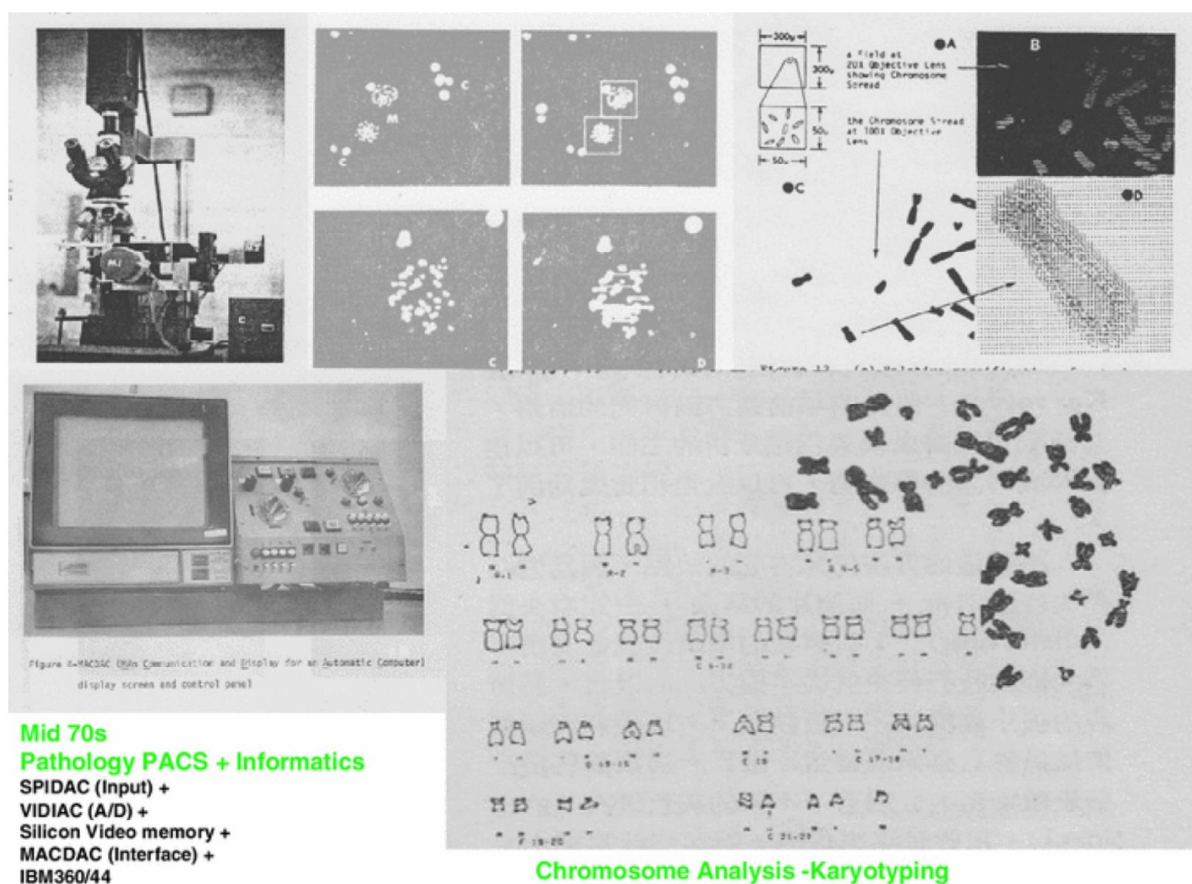


**Mid 70s**
**Pathology PACS + Informatics**
SPIDAC (Input) +
VIDIAC (A/D) +
Silicon Video memory +
MACDAC (Interface) +
IBM360/44

**Chromosome Analysis -Karyotyping**

**Fig. 16**

Automatic chromosome karyotyping innovation by Professor Ledley in the 1970s, probably the earliest concept in systematic medical imaging informatics. Process steps included medical image acquisition, metaphase cell determination, patient data, interactive display, automatic measurement of chromosomes and karyotyping, the determination of normal vs. abnormal chromosomes that led to the final diagnosis. PACS components including MACDAC (Man Machine Interface to Digital Automatic Computer. SPIDAC + VIDAC (video memory) + MACDAC (interface) + IBM360/44 were equivalent of today's Pathology PACS. The new knowledge discovery component showed an example of automatic chromosome analysis—microscopic scanning, detecting two metaphase cells

(low resolution) and chromosomes (high), analyzing each chromosome, and karyotyping that could lead to the prenatal diagnosis of birth defects

## 6.3  Medical imaging informatics today

Figure 17 gives three examples of today's medical imaging informatics system components platform that can lead to different types of specific applications: (1) image-assisted neurosurgery; (2) neuro-rehabilitation engineering, and (3) radiation therapy for prostate cancer [*30*]. In all cases, the upper rectangle in the figure represents the PACS components, whereas the lower rectangle depicts the medical imaging informatics components, including image detection and processing, as well as the new knowledge discovery from the PACS data.
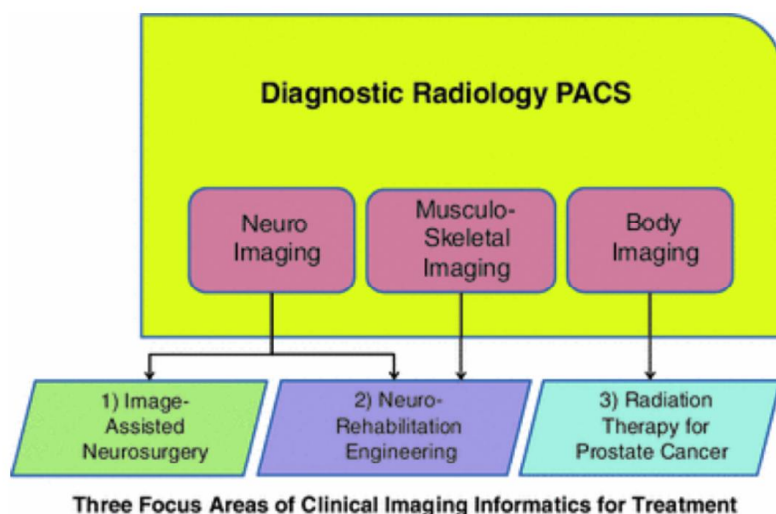


**Fig. 17**

Examples of today's medical imaging informatics applications include three types of patient treatment—surgery, rehabilitation, and radiation therapy. *Upper row* use of the images from various body segments for three different applications. *Lower row* for image-assisted surgery, neuro-rehabilitation, and radiation therapy for cancer treatment

# 7  Conclusion

The possibility of PACS development during the first 10 years in the 1980s and 1990s was ignited by three pioneers' innovations and dedication. In this retrospective review, we started

by introducing the background of three pioneers and explaining their influence on the success of PACS research and developmental efforts, followed by the opportunity of UCLA receiving research support from US federal government agencies. The UCLA PACS Team also established a close collaboration with many medical imaging partners in private industry. The time was ripe for the UCLA PACS Team to attempt the implementation of PACS components in a clinical system for daily healthcare use.

The influence of three pioneers: (1) Professor Robert Ledley established his Pattern Recognition Laboratory, invented various types of medical imaging scanners, introduced the concept of medical imaging informatics application, and led a group of "can-do followers" in the 1960s and 1970s. (2) Professor Moses Greenfield, who formed and ran the Biomedical Physics Graduate Program, UCLA, for more than 40 years where he trained more than 200 graduate students, many of whom selected PACS and imaging informatics as their career path. (3) Dr. Hooshang Kangarloo, Professor of Pediatrics, Radiology and Bioengineering, Chairman of Radiological Sciences at UCLA, championed PACS as representing the future of radiology and the future of digital practice in healthcare delivery. He dared to convert his Pediatric Radiology Division from a film to a PACS operation; this has become the first clinical site for clinical service with PACS.

## 7.1 The golden era of medical technology research support

The 1980s and 1990s were the golden era of receiving support from US government agencies for innovative research and training, especially related to medical high-technology development. The funding opportunity was even better if a university could set up a matching program, in the sense that the university would match a certain percentage of the federal amounts. The Department of Radiological Science at UCLA was a well-established and wealthy department in the 1980s and 1990s. With Professor Kangarloo as the chairman who championed the development of PACS, it would not be too difficult for him to convince the department's financial committee to accept the PACS concept and agree to support the developmental effort. Once the federal government funded the UCLA PACS R&D program with the additional departmental support, the US and Japanese medical imaging industry contemplated the opportunity of future collaboration with UCLA, and they also contributed to the program. Another major factor in the success of the PACS implementation at UCLA was Professor Greenfield's Biomedical Physics Graduate Program, which recruited many young talents who had physics, engineering, or other physical science majors, and a

biomedical science minor. They could either enroll in the graduate program to obtain a PhD degree or join the post-doctoral program to expand their horizon to become faculty members either at UCLA or at other US universities, or they returned to their motherlands to seek opportunities. The R&D and training resources in the Department of Radiological Sciences were able to support the Graduate Program without much difficulty.

The time was ripe for the implementation of PCAS components in a system for daily clinical use. The reasons were as follows: first, the R&D personnel of PACS developers were ready for its implementation. The primary users of PACS were radiology faculty and residents at UCLA. They had been convinced by the PACS champion, Dr. Kangarloo, and were eager to try it out. In addition, they had taken the mandatory 2-week PACS training class in the Biomedical Physics Graduate Program. The result was that several PACS modules were clinically online in the late 1980s, and the radiology users had not looked back to read a case based on X-ray films for making the radiologic diagnosis.

## 7.2  After the first 10 years of PACS

After several PACS modules were online for daily clinical use at UCLA, the question was, "Now what?" During the first wave when PACS started in the 1980s, much R&D work was contributed by the UCLA PACS Team and its collaborators. With enough resources for PACS R&D and with excellent personnel, the time was ripe for the Team to expand the PACS capacity to include PACS for the multiple-hospital enterprise, PACS integration with HIS and RIS, PACS with the Web server for image distribution, and integration of PACS with the patient record system [30]. However, as the scope of PACS increased, the UCLA PACS Team could not handle such multifaceted interests, demands, and requirements. Many of them were too technically mature to be confined to a group project like the PACS, original designed at UCLA. It was time for the Team to move on or to let private industry take over the continuation of development. Individuals started to pursue their own interests and domain, and they also sought other career ventures. Other experts from outside UCLA had different talents and were most definitely qualified to take on some aforementioned PACS applications to flourish.

## 7.3  The PACS end users

As for the end users of PACS, radiologists and radiology personnel, what was their perspective? Before the high-technology scanners and the 1980s and 1990s PACS era,

radiology had been a self-sufficient, low-key, but vital clinical service department supporting physicians by performing radiological procedures and making diagnoses from X-ray-related examinations. With the advent of US, nuclear medicine, CT, and then MRI developed by the radiological science specialists, and the successful use of these scanners for medical diagnoses, the prestige of the radiology profession was elevated among healthcare colleagues. Those radiologists who led the development of these scanners had become leaders in their profession, and the majority of these leaders agreed that PACS technology, if refined and polished, could one day be another new valuable clinical tool for radiology to contribute to healthcare delivery.

When PACS was first introduced as a clinical tool, because of its cost, because it did not have good methods for training the users, human inertia of avoiding to learn new technics, and individual xenophobia, PACS was not well accepted by general radiologists. In addition, PACS still presented many operational handicaps, including image quality on soft copy, archive capacity, image transmission speed, and data security. But leaders in the radiology community felt that the "time was ripe for the push" to support PACS development. At every annual RSNA (Radiology Society of North America) Assembly since the 1990s, they promoted PACS diligently and formed many subcommittees to resolve the aforementioned shortcomings. Examples of the contributions were in the training of their fellows, residents, and participants in the RSNA assembly in the technology and usage of PACS, setting up the DICOM (Digital Imaging and Communications in Medicine) Standard and IHE (Integrating of Healthcare Enterprise) Workflow Profiles, defining long-term and short-term archives, requiring HIPAA compliance (Health Insurance Portability and Accountability Act), including data definition and privacy, security, and integrity, system fault tolerance, and continuous availability. Because of competition, the vendors lowered the cost of the PACS system. The radiology leaders, as a group, contemplated that the time was ripe for their attempt to contribute substantially to the continuing development of PACS.

## 7.4 The diligent contributors

The PCAS banner has been carried successfully by many other experts with different skills and backgrounds that led to today's benchmarks for PACS as the daily healthcare baseline tool for data and image distribution to every clinical service in hospitals and by medical practitioners. They are the diligent contributors to PACS. With them, medical imaging informatics promises to be the next wave to be recognized and nurtured to success in the near

future.

## Prelude and acknowledgments

When my former two mentors, Professor Ledley at Georgetown University, and Professor Greenfield at UCLA, as well as Emeritus Chairman and Professor Kangarloo at UCLA passed away in the same year, 2012, in memory of these pioneers I delivered a special presentation: "In memory of three pioneers in Biomedical Imaging, Medical Physics, and PACS and Informatics [31], during the SPIE Annual Medical Imaging Conference—Advanced PACS-based imaging informatics and therapeutic applications, at Lake Buena Vista, Florida, USA. To my surprise, though it was the last day afternoon session, many colleagues with whom we had been working during the past 40 years showed up for the talk. After the meeting, several of them mentioned that I should write a paper to publicize the past contributions of the pioneers in these fields. I took their advice and searched for a suitable journal. Since the beginning of PACS, I had learned so much from my many Japanese colleagues, and I always felt that, without their early PACS concepts, the film scanner, CR and DR, PACS progress would not have moved so speedily, I contacted Professor Kunio Doi on May 9, 2013, and asked whether the journal "Radiological Physics and Technology", published by Springer with its base in Japan, of which he is the Editor-in-Chief, would be interested in receiving such a "Pioneers" manuscript for review. He thought about my suggestion, and the following was his response on May 13 this year:

*"Regarding your proposal about memory of pioneers, I agree that these would be a proper topic for our Journal of RPT. However, I have another suggestion for you to consider. Would you be able to consider the materials you will have and also your own activities at UCLA toward historical review on development of PACS and informatics? I believe that research activities at UCLA at that time were very influential to many researchers, and thus it would be useful to learn from historical review on PACS and informatics at that time.*

*You can include many aspects related to memory of pioneers in this format. I believe that with this format, you can describe also many of your activities at UCLA, which would be very informative to many readers of RPT."*

I took Professor Doi's wisdom, suggestions, and guidelines, after several revisions, to come up with this manuscript for submission. For this reason, I deeply appreciate Professor Doi's original idea that has definitely enriched the horizon of the current manuscript compared to the basic original "Pioneers" contents. In addition, it also brought in another aspect, which had often been neglected by other historical reviews, of Japan's tremendous contribution to the basic conceptual technology development

that led to facilitating the successful implementation of PACS in the 1990s. I would also like to thank Mrs. EF Lanzl for her meticuous editing.

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