RAI NEWS

A Newsletter of the Carl E. Ravin Advanced Imaging Laboratories

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Innovators in Translational & Quantitative Imaging

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A Call To Originality

In the course of a normal academic life, there are so many tasks to attend to: data to acquire and analyze, programs to develop, papers and reports to write (and rewrite), meetings to attend, presentations to give, collaborations to manage, emails (lots of them!) and personal interaction issues to address (an integral part of any human enterprise). The breadth of what we do is not limited to academia; doing too many things seems to be a feature of our time and our culture. But whatever the underlying cause, in the midst of these activities, “clutter” you might call them, it is easy to lose sight of the real purpose of our activities. I submit to you that the aim of our academic activities should be originality. Let me explain what I mean. I believe the first and foremost calling of an academician (whether faculty, student, postdoc, or staff) is not to be a “user” of technologies or resources (even though we use many technological tools and resources for our purposes), nor to implement new technologies (even though we try many new ideas). In our particular discipline, our primary purpose is to envision technologies and applications that are new, things that have not been materialized by others before. We are further to demonstrate their utility and applicability, that the envisioned entity is not just a “pie in the sky,” but something that has true clinical and research utility, functionality, and applicability. Our job is not to develop the idea into a product – that is what companies are set up to do with better efficiency – ours is to just do enough demonstration to convince those companies, others, and ourselves that the envisioned entity can provide true value, to the clinical work or to the research enterprise, and it is reasonably implementable. In other words, our job, first and foremost, is being scientists, creators of ideas, not those who implement them in the most practical and pragmatic manner. Limited implementation and clinical demonstration are of course in order, but only to the extent that they provide a proof of concept. I believe knowing our exact calling in this way can clarify what our focus should be and, in the natural progression of an idea, where we need to stop. Perhaps this clarification might be of value in anchoring our place and orientation in the natural “clutter” of our academic activities.
Certain diseases in the human body show changes in element concentrations corresponding to the disease severity. However, despite this knowledge, such diagnostic methods of element quantification in deep-seated organs have not been clinically feasible yet due to the lack of a suitable measurement method. Neutron Stimulated Emission Computed Tomography (NSECT), a technique pioneered at RAILabs, aims to fulfill this need by diagnosing element-related disorders using quasi-monochromatic neutron beams. The NSECT device measures gamma photons emitted from an organ irradiated with fast neutrons. Due to the engineering limitations of the neutron source and gamma detectors that are currently available, a typical NSECT imaging acquisition requires physical movement of the beam at a multitude of angles around the sample one position at a time. As a result, a single imaging study performed with the current hardware can require as much as 24 hours per scan - an impossible scenario for a clinical setting.

To overcome this challenge, Anuj Kapadia and Greeshma Agasthya developed a novel acquisition approach that reduces the scan time and radiation dose by an order of magnitude. The approach involves the use of time-resolved gamma detectors to measure the arrival time of the neutron-induced signal in addition to the energy. This process enables back tracing of the detected gamma photons to their point of origination within the tissue based on their arrival time in the detectors. Exploiting the monochromatic nature of the specialized neutron sources, the time stamp of the detected gamma photons can be used to generate an image of the anatomical structure of the tissue without the need for multiple angular rotations. The concept was demonstrated successfully using Monte-Carlo simulations developed in GEANT4, and the results were presented at the IEEE Medical Imaging Conference in Valencia, Spain (Agasthya G. A., et al. Neutron time-of-flight spectroscopy for depth-resolved quantification through NSECT. NSS/MIC, 2011 IEEE).

A demonstration of the technique with different combinations of time-sensitive detectors is shown below.

Figure 1: (A) Top view of a simulated phantom containing lesions with focal iron deposits. The yellow ellipse shows the torso containing adipose tissue; the white solid circle is the spine containing skeletal tissue; and the pink outlined organ is the liver containing focal iron deposits. Figures 1B and 1C show the resulting time-resolved images corresponding to $^{12}\text{C}$ and $^{56}\text{Fe}$ in the sample acquired using an order of magnitude fewer neutrons than previous scanning methods. The X-axis shows time in nanoseconds, and the Y-axis shows the beam position (along the arrow in Fig 1A). The image from carbon (Fig. 1B) shows an intensity gradient corresponding to the high $^{12}\text{C}$ content of adipose tissue and lower content within the liver volume. Similarly, the image from iron (Fig. 1C) shows an intensity gradient corresponding to iron deposits within the liver. A close-up of the iron deposits is shown in Fig 2 below.

Figure 2: Time-resolved images of iron ($^{56}\text{Fe}$) superimposed on carbon ($^{12}\text{C}$) simulated using a realistic germanium detector. The gray color bar represents the $^{12}\text{C}$ image pixel intensities, and the red or ‘hot’ color bar corresponds to $^{56}\text{Fe}$ image pixel intensities.

This method has strong potential in bringing the NSECT technology to the clinic. In addition to reducing the scan time by an order of magnitude, it significantly lowers the radiation dose to the patient and improves the detection sensitivity of the technique. Dr. Kapadia and Ms. Agasthya are now working on an advanced reconstruction algorithm to combine the anatomical and quantitative information extracted from multiple detectors into a single high-resolution image generated without any angular rotations around the object.

Anuj Kapadia is an Assistant Professor of Radiology at RAILabs. He received his PhD in Biomedical Engineering from Duke University. Dr. Kapadia’s research focuses on developing innovative neutron and gamma-based imaging modalities for tomographic imaging of trace elements in the human body.
Patient-and cohort- specific Conversion Coefficients for Radiation Dose and Risk in Pediatric CT
By Rachel Tian

Recently, the increasing usage of computer tomography (CT) have led to concerns about CT-induced radiation exposure, especially for pediatric patients. To manage dose and optimize protocols, an accurate method to estimate dose and risk is crucial. Such dose and risk information can be included in a patient’s dosimetry medical record, enable the health care provider to track radiation exposure history from medical imaging, and assist risk-benefit study of a certain CT scan.

Rachel Tian, Xiang Li, Ehsan Samei, Paul Segars, and Donald Frush studied patient- and cohort- specific radiation dose and risk for pediatric CT. A pre-validated Monte Carlo based program was used to simulate the dose deposited by multiple CT scanners (GE LightSpeed and Siemens DefinationFlash). In collaboration with Duke Medical Center and John Hopkins University, a library of patient computer anatomical models encompassing all age and weight percentiles was built in our laboratory. Using the Monte Carlo program and computational phantoms, organ dose, effective dose, and cancer risk were estimated for 42 patients.

Two protocols (chest and abdominopelvic) were simulated in the study. The relationship between organ dose, effective dose, and cancer risk and patient anatomical characteristics (age, size, and gender) was evaluated. We further compared discrepancy across scan models for normalized dose and risk values. The average discrepancy for normalize organ dose (within scan range), effective dose, and cancer risk, was less than 10%. Given the small discrepancy, it might be possible to generate universal dose and risk conversion coefficients across scanner models. Based on that, the patient- and cohort- specific dose and risk values could be estimated for any given patient and any given scanner.

Iterative Reconstruction in Quantitative CT
By Baiyu Chen

CT imaging is moving towards quantification by extracting numerical information (volume, concentration, density, etc.) from the image to help diagnose and stage the disease. The precision of quantifications (stability and reliability of measurements from repeated scans), however, is technique dependent, and thus requires protocol-specific evaluations. CT imaging is also moving towards iterative reconstruction algorithms (IR), which greatly reduce noise while preserving edges, and potentially provide better quantification precision.

Recently, Baiyu Chen, Ehsan Samei and Samuel Richard have investigated the impact of iterative reconstructions on the precision of nodule volume quantifications. To physically measure the precision, synthetic spherical nodules embedded in an anthropomorphic chest phantom were first scanned under a variety of protocols, with their volumes quantified from the image using commercial software. The precision of the volume quantifications were then calculated for various protocols. Compared to FBP, iterative reconstruction (MBIR) greatly improves the precision of quantification, and has the potential of reaching the same precision at a dose 20-60% lower. In addition to measuring quantitative precision via physical measurements, we have further developed a mathematical predictor of precision [estimability index (e’)] based on 1) the task-dependent resolution of the system, 2) the texture and magnitude of the system noise, and 3) the lesion to be quantified. Results show that e’ strongly correlates with measured precision, indicating e’ as a promising predictor of quantitative precision. Ongoing work includes extending e’ to incorporate variations from stationarity, nodule characteristics, and segmentation software.

“CT imaging is moving towards quantification. CT imaging is also moving towards iterative reconstructions. We measure, model, and predict the impact of iterative reconstructions on the precision of CT nodule volume quantification.”
- Baiyu Chen

“When a diagnostic procedure is to be performed, a balance should be observed between acceptable image quality and potential associated risk. Accurate estimation of CT-induced radiation dose and risk is a first step to achieve dose optimization.”
- Rachel Tian
**Research Updates**

**Computer-Aided Diagnosis — Chest Imaging**
Qiang Li and Wei Guo developed a new CAD system to significantly improve the performance of computerized nodule detection in chest CT images. They decompose a 3D nodule candidate into a series of effective 2D reformatted images which allows for reliable distinction between true nodules and false positives. With this new technique, they were able to remove 84.4% false positives at a sensitivity of 85% compared to a conventional CAD.

**Computer-Aided Diagnosis — BCI**
Qiang Li, Wei Guo, Sarah Boyce, and Ehsan Samei developed a computerized system to detect lung nodules in three-view chest radiography (BCI). The system fuses information from three images of the same patient from three views to remove false positives. By use of this information fusion technique, their CAD system can both reduce the number of false positives significantly and improve the detection sensitivity for true nodules. Their manuscript on this project has been tentatively accepted for publication by Medical Physics.

**Computer-Aided Diagnosis — Brain Imaging**
Qiang Li, Xiaohua Qian, and James Provenzale, M.D. are developing a new technique to enhance acute ischemic stroke on brain CT image. They compared brain parenchyma of the two brain hemispheres to enhance the suspicious locations that were significantly different the contralateral hemispheres. They were able to enhance subtle acute ischemic strokes in their preliminary results.

**Simulation Tools for 3D and 4D CT and Dosimetry**
Paul Segars and Ehsan Samei continue their work on developing a library of detailed 4D computational phantoms realistically representing a wide population of subjects as part of NIH grant R01-EB001838. One hundred anatomically variable models have been created to date. These models are being used to develop methods to accurately estimate patient-specific CT dose (both effective dose and organ dose) and associated radiation risk.

**Multi-scale Model of the Human Heart**
In collaboration with the University of California San Diego, the Segars lab has been working on creating a four chambered finite-element (FE) heart model for imaging research. They are currently finalizing and testing the biomechanics of the model to see if it accurately simulates the normal beating heart.

**Breast Phantoms**
James Dobbins, Paul Segars and Christina Li have created a series of detailed 3D computational breast phantoms for breast imaging research as part of NIH grant R01-CA134658. To date, one hundred anatomically variable breast models have been created based on breast CT data.

Ehsan Samei and Nooshin Kiarashi have instituted a new study to extend the module for contrast-based imaging.

**Emerging Quantitative Imaging Techniques**
Manu Lakshmanan and Anuj Kapadia have developed a Monte Carlo simulation of the nuclear resonance fluorescence (NRF) reaction. In the NRF reaction, an incident gamma photon of specific energy triggers resonant excitation in a target nucleus. The excited nucleus then emits gamma-rays in a known de-excitation pattern, just as in neutron inelastic scattering, the reaction upon which NSECT (Neutron Stimulated Emission Computed Tomography) is based. Manu will apply the NRF reaction for tomographic imaging of isotope distribution in the human breast and liver. The imaging technique is called GSECT (gamma-ray stimulated emission computed tomography).

**NSECT and CT Simulations in GEANT4**
Matthew Belley and Anuj Kapadia developed a simulation of an X-ray CT scanner using the GEANT4 Application for Tomographic Emission (GATE) toolkit. The goal of this research is to generate limited-angle CT reconstructed images of high-resolution phantoms of the human body, which will be used for anatomical co-registration of NSECT images. Although NSECT images exhibit excellent specificity and quantitation for different elements, their spatial resolution is considerably lower than that of CT. Hence, co-registration of the NSECT image with a higher-resolution CT image significantly improves the anatomic precision with which elements can be identified. Potential lesions can be identified with NSECT and located within the body using X-ray CT. The CT simulations were performed on whole-body and breast phantoms developed by Paul Segars.”
**Q:** What's new with our collaboration with Siemens in the area of breast imaging?

**JYL:** We are very excited to be running two simultaneous studies with Siemens Healthcare in breast tomosynthesis. A few months ago, we started the long awaited clinical trial to collect data that Siemens will use to gain FDA approval for their breast tomo system. Dr. Jay Baker and I are running this study together, with Anne Jarvis handling the hard work of recruiting subjects and all the important paperwork associated with FDA trials. Duke is just one of many sites in the US. Thanks to our previous experience accruing nearly 400 subjects under the NIH/Siemens study, everything is going smoothly and we can't wait to see the results!

In addition, Dr. Ehsan Samei, Dr. Sujata Ghate, and I are running a second study on contrast-enhanced dual-energy tomo, or just CEDET for short. This is the continuation of our long-standing relationship with Siemens that goes all the way back to 2003. Siemens has provided us with a second breast tomo unit, which has been modified to allow us to shoot at up to 49 kVp in order to image iodine contrast. We will be exploring the capabilities of this new unit in the coming year.

**Q:** What do you think contrast-enhanced dual-energy tomo (CEDET) will provide that conventional tomo or mammography does not?

**SG:** CEDET enables fast, high resolution 3D functional imaging of the breast. Unlike conventional tomo or mammography, CEDET provides information about tumor morphology as well as kinetics, similar to MRI. Potential advantages of CEDET compared to MRI include higher spatial resolution, more immediate availability and lower cost.

**Q:** What are some possible clinical applications of CEDET?

**SG:** I can think of three applications right away. First, CEDET may allow us to define the extent of disease in patients with a known breast malignancy. Second, once a woman undergoes treatment, CEDET may be able to help us monitor chemotherapy response. Third, CEDET has the potential to distinguish benign from malignant lesions, thus reducing false positive biopsies. Each of these are roles currently served by MRI, so it will be exciting to see how CEDET can contribute to the clinical workflow.

**Q:** What do you think the biggest challenge will be for this research?

**SG:** As with any x-ray based imaging modality, it will be important to optimize image quality at the lowest possible dose. In addition, we will also need to optimize the temporal acquisition protocols.

**JYL:** I agree. Although we call it CEDET for short, this technology really has much broader potential capabilities. We can use this system to do both mammography and tomosynthesis, at low and high energies, with or without the use of IV contrast, and finally to perform dual energy or temporal subtraction at one or more time points. The large number of possible combinations is both exciting and daunting, so currently we are working hard on optimizing all these options. Our students Lynda Ikejimba and Nooshin Kiarashi are tackling this problem from two different directions, using empirical measurements and virtual simulated phantoms, respectively. They will each present a talk at the upcoming SPIE conference in February. If all goes well, in the coming months we will likely begin human subject trials, so stay tuned!

**Clinical Imaging Physics Group** marked three years since its launch to address the imaging physics needs of clinical operations at Duke University Medical Center. The vision of the CIPG is to provide clinical physics support in such a way that is scientifically-informed by findings and methods at Duke and beyond, relevant to clinical practice, team-based, and impactful to the science of clinical physics at large.

With efforts primarily focused on the safety and quality of clinical operation, the group provides baseline physics evaluations (including acceptance testing and annual inspections), quality control services, and initiatives oriented towards improving imaging operations. The group further provides educational opportunities for residents, students, and technologists, and is involved with research projects with immediate clinical application. This past year, CIPG assumed oversight of mammographic and fluoroscopic systems in addition to CR, DR, CT, NM, MRI, and display devices, which were already under CIPG’s supervision. The group also expanded into Duke Primary Care facilities; launched a new internal publication, Clinical Technical Notes, to inform imaging operations; and made major strides in the monitoring and maintaining radiation dose and imaging protocol definitions at Duke. CIPG was also integrally involved with the launch of the new Duke Cancer Center.

 Interested in Dr. Ghate’s research? Contact her via email: sujata.ghate@dm.duke.edu
New Junior Faculty

“My formal training is in Electrical Engineering with focus on machine learning. I also have an MA degree in Philosophy. I very much enjoy formulating and solving challenging problems knowing that the solutions can potentially have a real impact on health care and therefore on people’s lives. I would like to continue exploring applications of modern data-driven approaches such as machine learning and data mining to decision support, decision modeling, education, workflow, human-computer interaction and other decision-related aspects of radiology. Currently I am working on development of an adaptive computer system for radiology education. The user models will capture strengths and weaknesses of each trainee. I am looking forward to many more exciting discoveries in this area.”

New Research Grants

- Ehsan Samei and David Brady received a $1,156,502 grant from DHS to develop a computational adaptive X-ray imaging system for explosive detection in homeland security applications. The subcontract focuses on the physical modeling of the system and the development of the first prototype.

- Ehsan Samei’s research on “Optimization of protocols employing advanced reconstruction algorithms” was awarded a $91,288 grant from General Electric. The grant aims to develop task specific metrics of image quality calibrated with clinical data for the optimization of CT protocols utilizing iterative reconstructions.

- Ehsan Samei was awarded a grant from NIH/RSNA titled “Development of assessment and predictive metrics for quantitative imaging in chest CT.” The aim of this sub-contracted grant is to develop predictive models for quantitative CT imaging based on phantom and theoretical techniques, and use the outcome to develop a calibration and verification method for quantitative applications.

- Ehsan Samei received a grant from Siemens Medical Solutions for his research titled, “Clinical evaluation of Auto-kV dose optimization schemes in pediatric and adult patients”, which will aim to evaluate and optimize a new Auto-kV CT protocol technique for improved image quality and reduction of patient dose.

- Ehsan Samei was awarded a grant from RSNA and AAPM titled “Clinical residency education in imaging” to support the establishment of a clinical residency program in diagnostic imaging physics.

- Joseph Lo and Ehsan Samei received a $90,000 grant from Siemens Medical Systems to develop a contrast-enhanced dual energy breast tomosynthesis imaging system for improved detection of breast cancer.

Awards & Honors

- Qiang Li is the lead editor of the first book in the field of computer-aided diagnosis, entitled “Computer-aided Detection and Diagnosis in Medical Imaging.” This book will be published in June of 2012 and is expected to have great impact in the CAD field.

- Qiang Li is the lead editor for a Special Issue on Advances in Computer-Aided Detection and Diagnosis, to be published by the International Journal of Biomedical Imaging in 2012.

- Christina Hsu, Mark Palmeri, Paul Segars, and James Dobbins were co-authors on a publication selected by the American Physical Society and American Institute of Physics to appear in the Virtual Journal of Biological Physics Research, a compilation of specially selected articles considered to cover focused areas of frontier research. The citation is: Hsu CM, Palmeri ML, Segars WP, Dobbins JT III: An analysis of the mechanical parameters used for finite element compression of a high-resolution 3D breast phantom. Medical Physics 38(10):5756-5770, 2011.

- James Dobbins served as Chair of the Board of Directors of the Society of Directors of Academic Medical Physics Programs, Inc this year. SDAMPP is an international professional society, founded by Drs. Dobbins and Ehsan Samei, to improve education in medical physics. It currently has over 100 members from most of the major graduate programs in the U.S. and Canada, and members from a number of residency training programs.

- James Dobbins was co-director of a physics mini-course at RSNA on digital tomosynthesis. This was the third year that this refresher course was offered.

- Ehsan Samei received Award for Exceptional Leadership, Duke University Graduate School and Medical Physics Graduate Program, Duke University, May 2011.

- Anuj Kapadia was appointed as Chair of the Duke Medical Physics Graduate Program’s Recruitment Committee for a two-year term.

- Anuj Kapadia was invited to present a lecture at the Tata Institute of Fundamental Research in Mumbai, India on his Neutron and Gamma Imaging projects.

Christy Shafer successfully defended her PhD and has relocated to Madison, WI, to work for Epic Systems as a technical services engineer. (Yes, the same Epic that is redoing all of DUHS medical records software).

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**Alumni & Other News**

Adam Barnett is a third year medical student, who will be working with Dr. Joseph Lo and Dr. Maciej on breast imaging projects.

Erich Schnell has entered into a medical physics residency at Oklahoma University.

Congratulations & farewell to Gina Tourassi, PhD a long-term member of our community and an upstanding faculty member in Radiology and Medical Physics, is now the new Director of Biomedical Science and Engineering Center at Oak Ridge National Laboratories.

Greeshma Agasthya received the 2011 IEEE NSS/MIC/RTSD Trainee Grant presented to select outstanding graduate students who are first authors on abstracts selected for the IEEE NSS/MIC conference each year. Greeshma has received this grant for a third time in a row this year.

Gretchen Raterman joined RAILabs as an M.S. student in Medical Physics. She is advised by Dr. Kapadia.

Hyunkoo Chung is a junior in BME, joined the breast tomo quantitation project.

Jainil Shah, M.S., received the annual “Excellence in M.S. Studies” award presented by the Duke Biomedical Engineering Program at the Pratt School Graduation Ceremony. This award is presented annually to one M.S. student who demonstrates outstanding achievement in both research and academics.

Jorge Juan Suares-Cuenca completed his one-year research at RAILabs as a visiting scholar. He returned to Spain in February, 2011.

He is now a research associate at Santiago University in Spain.

Manu Lakshmanan, B.A., joined RAILabs as a Ph.D. student in Biomedical Engineering. He is co-advised by Dr. Kapadia (RAILabs) and Dr. Tornai (MMIL).

Nooshin Kiarashi joined Samei Lab and pursuing a Ph.D. in Electrical & Computer Engineering. The focus of her research is modeling of breast imaging systems.

Sylvia Hon is a 2nd year MS student also in BME, joined the breast tomo quantitation project.

Sam Richard, Ph.D. completed his post-doctoral tenure at Duke and joined Carestream Health as a Research Scientist.

Simon Murphy completed his Masters in Medical Physics and joined US Air Force as a Medical Physicist Officer.

Congratulations to Tuania Wright who earned her Masters in Business Administration, graduating Magna Cum Laude.

Vorakarn Chanyavanich successfully defended his PhD and is now a medical physics resident at Emory.

Wei Guo completed her two-year research at RAILabs as a visiting scholar. She returned to China in September, 2011. She is now a research associate at Northeastern University in China.

**Faces of RAI Labs**

**Visiting Scholars**

Dr. Quan Zhou is the Vice Chairman and Professor at Department of Radiology in the first Affiliated Hospital of Jinan University (Guanzhou, Guandong province). He has 22 years experience in x-ray, MRI, and CT. His main research interests include chest and orbital disease imaging diagnosis, functional MR imaging, and molecular imaging. He will be spending a year with us as a visiting scholar. We look forward to his scholarly contributions to our scientific enterprise.

Sukantadev Bag is working on developing statistical methods to recover and analyse information from cryo-electron microscopic images. This information is used to determine three-dimensional structure of a certain type of bacterial cellular inclusions. He is a PhD student in Statistics at the University College Cork, Ireland and currently visiting Duke as an exchange research scholar, supervised by Dr. Kingshuk Roy Choudhury.