Innovators in Translational & Quantitative Imaging
When I came to Duke in 2000, I was given an office and targets for funding and publication. (I was also given a mandate to watch Duke basketball games!) I set to work relentlessly to meet those challenges. In the process, I took advantage of the many resources and people that this great institution has to offer. We formed research teams to achieve common goals. Some of these teams worked great. Others were resounding failures. I always wondered (and am still wondering) what makes a good team. I outline here some answers to this question that I have come to thus far, with the hope that some may find them useful.

First ingredient: Individual responsibility. What is often called “shared responsibility” is badly misunderstood. Team members are best motivated when we are given a discrete slice of responsibility to claim as our own. In that way, when we come together as a team, we each have our own claims, our own “victories,” and yet contribute towards the broader goal. Practically speaking, this requires moving from a mastermind/laborers/single goal model to a model in which multiple smaller (yet definitive) goals are designed for individual team members, who are empowered with the authority and the freedom to own and pursue their objective.

Second ingredient: Attitude. You have to have the right people with the right attitude. You need people who own the task, who care, who do not do things just because it is their job. We rarely do our best out of a sense of duty, but because of our passion. You of course need to have the skill and intelligence as well, but some deficit in either is redeemable; a deficit in attitude makes any effort futile. In making assignment, a team leader must consider the individual team member’s gifts and interests; at the same time, team members must be willing to adapt their passions and personal goals in order to truly own the tasks of a particular project.

Third ingredient: Communication. Research goals, goals that are worthwhile to be pursued, often require lots of back and forth, rethinking, revisiting of speculation, and so on. In these processes, you often need to brainstorm and renegotiate individual goals. For this type of interaction, you need to have people who are skilled in communication, people who listen, who can engage in substantive dialogue over intellectual content. “Communication” in its truest sense involves a genuine exchange, not one-way pronouncements. Without this fundamental communication, individual goals remain isolated and do not develop effectively towards the broader goal.

Incidentally, a good basketball team embodies many aspects of these attributes. Of course, it is easy to pontificate about the kind of people we want to have on our team, but let’s also not forget to ask if we have the attributes of a good team player ourselves!
Correlated-polarity Noise Reduction for Dose Reduction in CT

Considerable effort is currently underway to find means to reduce dose in imaging, particularly in CT. Various approaches have been investigated, including iterative reconstruction, technique optimization, intelligent beam profile modification, and also noise reduction strategies. The Dobbins lab has developed a novel noise reduction strategy called Correlated-Polarity Noise Reduction (CPNR) that recently has been applied for the first time to CT.

CPNR is a statistical noise reduction technique that reverses the process by which random fluctuations add to the variance of pixel values. The technique works by subtracting random numbers from pixels in the image, but with the important distinction that the polarity of the noise to be subtracted matches the polarity of noise actually in each pixel. Thus, if a given pixel has positive noise relative to the true unknown mean, then a positive random number is subtracted. If the noise is negative, then a negative random number is subtracted. The requirements for this technique are that the width of the overall noise distribution must be measured (a relatively easy task), and the polarity of noise must be estimated at each pixel. Novel methods have been developed to estimate polarity of noise in pixels, with about 70-85% accuracy. The net result is that roughly a 20% reduction of standard deviation is possible per iteration with this technique. Application to radiography has shown that up to a three-fold reduction in dose may be possible with only minimal impact on image quality [1].

The CPNR technique has recently been applied to CT for the first time by performing CPNR on the projection images prior to reconstruction [2]. These images were simulated using the XCAT computer-generated phantom of the Segars lab, and the resulting reconstructed CT image at half of normal dose with CPNR shows virtually identical image quality to conventional full-dose CT reconstructions (Fig. 1). These results are very encouraging, but additional work is needed to characterize the image quality quantitatively and to evaluate CPNR in conjunction with iterative CT reconstruction methods as well as with filtered back projection (FBP).

This work was presented at the SPIE Physics of Medical Imaging Conference in February 2013 and constitutes an important part of the dissertation work of PhD student Jered Wells.


Research Updates

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. The model is capable of realistically simulating the normal electromechanical function of the human heart. The next step in the project is to simulate abnormal states of the heart due to cardiovascular disease.

Computational Breast Phantoms
The labs of Paul Segars, James Dobbins and Ehsan Samei have been working together to create a series of detailed 3D computational breast phantoms for breast imaging research as part of NIH grant RO1-CA134658. The groups are refining the segmentation procedures used in creating the phantoms.

Modeling Breast and Breast Imaging
As an inter-laboratory activity of RAI Labs, a group of investigators have worked closely to devise clinically-derived anthropomorphic breast phantoms for three dimensional breast imaging (Fig. 1). The first of such phantoms was fabricated using a 3D printer. The phantom has demonstrated many desirable attributes and is currently being studied by the FDA and breast groups in EU as a basis of QC metrology for breast tomosynthesis.

Quantitative Optimization of Breast Tomosynthesis
Joseph Lo and Ehsan Samei are collaborating on this ambitious project to optimize the new modality of breast tomosynthesis imaging. By combining physical measurements with observer modeling techniques, Lynda Ikejimba evaluated the performance of different imaging paradigms, such as comparing 2D vs 3D, temporal vs dual-energy subtraction, and the presence or absence of contrast materials. Nooshin Kiarashi made parallel comparisons using a suite of virtual and physical breast phantoms that are highly realistic because they are based on human breast CT data. Adam Nolte is helping Nooshin to develop the next generation of the physical phantoms by exploring different phantom materials and 3D printing technologies (see above). Ravi Mahadevan is working with Yuan Lin to develop fast GPU-accelerated reconstruction algorithms to assess how these algorithms affect image quality.

FDA Clinical Trial for Breast Tomosynthesis
Drs. Baker and Lo are now in the second year of a multi-site clinical trial to collect breast tomosynthesis images for Siemens Healthcare premarket approval submission to the FDA. Over a hundred human subject cases have been accrued to date on this trial. They will soon close out the separate clinical trial that accrued 385 subjects over the past 8 years as part of Lo’s NIH grant.

Knowledge-Based Radiation Therapy Planning
In collaboration with Shiva Das of radiation oncology, Joseph Lo has led a team of students in RAILabs to develop new external beam radiation treatment plans for prostate cancer and head and neck cancer. In 2012, the prostate cancer research has led to 3 MS theses for Christopher Busselburg, Deon Dick, and David Good. Christopher explored ways to improve the current 2D treatment planning approach by using an advanced 3D image registration algorithm. Deon demonstrated robustness of our approach for many types of patients by developing new treatment plans for 101 cases of prostate cancer from Duke. Her new, semi-automated plans were consistently comparable or better than the original clinical plans that were generated via a laborious, manual process. David showed that this approach can improve treatment plan quality and patient safety not just at Duke, but also for a cohort of 54 cases from an independent outside institution. Currently, Matt Schmidt, Shelby Grzetic, and Carly Lutzky are working on adapting these techniques to the much more challenging cases of head and neck cancer.

Qualitimersics
In cooperation with the Clinical Imaging Physics Group, the Samei group has added a new section and additional features to a new phantom (Fig. 2, top) designed to characterize CT performance as a function of patient size. The phantom represents four patient sizes and provides information for characterizing resolution and noise as a function of patient size and contrast level. A software platform (Fig. 2, bottom) has also been developed to supplement the phantom to enable robust evaluation of those attributes in an automated fashion.
Human Modeling and Radiometrics

The Samei and Segars groups, in collaboration with Dr. Frush, have continued the development of detailed 4D computational phantoms realistically representing a wide population of subjects as part of NIH grant RO1-EB001838. 150+ human models have been developed thus far (Fig. 3). Newest development in that front has been the assessment of dose metrics across a multiplicity of protocols. Additional work includes the incorporation of dose metrology for auto mA protocols.

**Computer-Aided Adaptive Radiology Education**

Dr. Mazurowski’s group is making progress in the area of computer-aided adaptive education in mammography. The goal of these efforts is to construct a system that automatically recognizes areas that need improvement in each trainee and proposes a training plan that addresses his or her individual needs. This goal is achieved through application of machine learning and collaborative filtering algorithms that recognize and model patterns in the trainees’ error making. The collaborators on this project include Drs. Baker, Maxfield, Yoon, Ghate from Duke and Dr. Kuzmiak from the UNC Chapel Hill. The research is supported the Department of Defense (PI: Mazurowski) and will be supported by the very recently recommended for funding Duke GME Innovation Grant (PIs: Maxfield and Mazurowski).

**Textured Phantom for CT Metrology**

In the presence of non-linear image processing, imaging performance can change whether an assessment is being performed in a uniform background or a textured one. The Samei group has been developing a new CT phantom with anthropomorphic textures to enable the assessment of imaging performance for CT in the presence of such processes.

**Homeland Security**

In collaboration with David Brady in Electrical Engineering, the Samei and Kapadia groups are devising a technique to use scatter signatures to develop a method to differentiate material for homeland security applications. The main challenge has been devising an apparatus that maximizes the extraction of scatter data with the highest level of sensitivity so that the data can be reconstructed efficiently.

**Emerging Quantitative Imaging Techniques**

Greeshma Agasthya and Anuj Kapadia demonstrated the use of time-resolved neutron imaging to detect liver cancers in the body. Using the technique, a 3D image of the liver can be generated without tomographic angular rotation of the source around the patient. This method represents a critical step towards the clinical translation of the NSECT technique. Greeshma Agasthya completed her PhD dissertation on this topic.

Rodrigo Viana and Anuj Kapadia demonstrated the first fully 3-D images from an NSECT scan of the kidney. The images (Fig. 5) showed the 3D distribution of elements in renal cell carcinoma and indicated the location of a tumor with high precision and dose levels comparable to clinical CT scans.

Manu Lakshmanan and Anuj Kapadia demonstrated the use of nuclear resonance fluorescence to detect breast cancer in vivo through 2D imaging methods. The lesion and breasts were imaged based on the differences in sodium and potassium between the healthy and cancerous breast tissue. The results indicate the potential for the nuclear resonance technique to be used for detecting human diseases in vivo.

**Quantitative CT**

The Samei group has continued its studies focused on how CT can be more quantitative. The newest work in that direction includes the development of a new formulation for an estimability index ($e'$). In a validation study, $e'$ was proved to correlate with precision of volume estimation in CT across a variety of dose levels, reconstruction methods, and slice thicknesses. The metrology is envisioned as a way to access the compliance of facilities and methods with quantitative standards.
While features like shape, structure, arrangements etc. are visually apparent from an image, their statistical analysis can be challenging because quantitative characterization is often not straightforward. However, visualization can prove inadequate when we have to summarize information across many images: for instance, what is the average shape of an organ? Where in a cell does a particular organelle typically reside? Are there morphological differences between neurons that reside in different parts of the brain? The work of Kingshuk Roy Choudhury and his students addresses questions in this area. A lot of his work has been in the area of cellular imaging, where fluorescent markers enable quantification of individual cellular components. In the illustration below, they compare the distribution of two different varieties of calcium ion channels: Cav 1.2 and AB70. Calcium channels are known to act as a conduit for cellular signaling. Despite the high degree of variability within and across cells, their analysis suggests significant differences in the intra-cellular distribution of these two channel sub-types, particularly at the nuclear boundary. Since form follows function in nature, they hypothesize that their roles in the cell may be different too.

![Fig. 1: Analysis of the distribution of a calcium channel in cellular nuclei. (a) Confocal fluorescence microscopy image of neuroblastoma nuclei: blue in a chromatin marker (DAPI), red is a nuclear boundary marker (Emerin), green is marker of calcium channel (Cav 1.2) (b) Cellular shape contours for radial density mapping (c) Radial density profiles of Cav 1.2 and Emerin. The x-axis is distance from nucleus center, with 1 representing the boundary of the nucleus. The y-axis is the (normalized) expression of the marker. Each line corresponds to a cell in (a). (d) Average expression profiles for two different calcium channels Cav 1.2 and AB70. The dotted lines denote a 95% confidence band. Notice that the distribution of the channels is significantly different at the boundary of the nucleus (p-value < 0.001). Joint work with John Mackrill, Dept. of Physiology, University College Cork, Ireland.](image)

**Statistical Characterization of Image Features**

by Kingshuk Roy Choudhury, PhD

The Clinical Imaging Physics Group continues to make a positive impact on the clinical imaging operations at Duke University Medical Center. During this past year, the group played a lead role in the successful renewal of the American College of Radiology accreditation for the CT, MRI, US, NM and Mammography departments. The CIPG also assisted with the relocation of the mammography department from the South Clinic to its beautiful new location in the Duke Cancer Center (Suite 2-1).

Another focus of the CIPG has been tracking patient dose; not only to identify problems leading to excessive and insufficient radiation exposures, but also aid in optimizing clinical protocols. In the past year, the Dose Tracker program, created by CIPG physicist Olav Christianson, has been modified to include several metrics relating to CT image quality including image noise, tube current modulation, and reconstruction algorithm to further facilitate protocol optimization. The program has also expanded its coverage to include every CT scan conducted at DUMC and Duke Regional Hospital. Data collected from Dose Tracker has contributed to modifications of several CT clinical protocols including the addition of size-specific CTDI reference levels for all CT protocols. Also of note is the ACR has incorporated the Dose Tracker algorithm for measuring patient thickness into their automated Dose Index Registry program (a national data registry which allows facilities to submit and compare their CT dose indices to regional and national values).

In an attempt to maintain consistency throughout the CT department, CIPG physicists worked closely with Radiology faculty and clinical staff to create an electronic protocol database which is viewable at every CT scanner throughout DUMC. Prior to performing patient scans, the CT technologists are now able to easily double check technique settings and compare the scanner predicted CTDI scan value against a size-specific expected range of values, generated from the Dose Tracker program, to help ensure a reasonable balance between image quality and patient safety.

The CIPG has also been hard at work developing image quality metrics and automated analysis programs for phantoms in clinical use. In CT, an automated program was developed to perform regular quality control using the ACR phantom. In addition to the routine physics tests, the program also measures the MTF and NPS and automatically identifies common CT artifacts. Additionally, advanced image quality analysis is now routinely performed during annual CT evaluation using the Mercury phantom developed last year by CIPG physicist Josh Wilson and RAI Labs alum Sam Richard.

In NM, CIPG physicist Jeff Nelson directed the development of a new metric for analyzing uniformity, the Artifact Index, capable of detecting subtle patterns that would otherwise compromise the usefulness of clinical images. Additionally, a method to measure the MTF from bar phantom images was implemented. Both of these metrics were incorporated into an automated analysis, reporting, and alert quality control program.

Finally, the CIPG has also recently put into clinical use an algorithm created by RAI Labs member Yuan Lin which analyses 10 image quality factors in chest radiographs. This exciting project will enable image quality evaluation on a per image basis allowing quality control on a level previously unimaginable. The algorithm is currently running on chest x-ray exams performed at DUMC and Duke Primary Care clinics.

**Clinical Imaging Physics Group**

by Jeff Nelson & CIPG Team
NEW RESEARCH GRANTS

Ehsan Samei was awarded a two year $150,000 grant from Carestream Health titled “Image quality in digital radiography.” The study aims to validate and implement an automated image quality assessment method for clinical digital chest radiographs.

Ehsan Samei received a $199,680 grant from Siemens Medical Solutions for his research titled, “Evaluation and optimization of iterative reconstruction methods.” The study aims to evaluate and optimize the latest iterative reconstruction techniques aimed to reduce radiation dose in CT.

AWARDS & HONORS

Greeshma Agasthya and Manu Lakshmanan both received the 2012 IEEE NSS/MIC/RTSD Trainee Grant. The grant is presented to select outstanding graduate students for attending the IEEE NSS/MIC conference. Greeshma has received this award fourth time in a row.

Jim Dobbins has been appointed Vice-Chair of the Education Council at AAPM. The Education Council is the primary means by which AAPM influences the content of educational activities for medical physicists at the graduate and residency levels, as well as educating the general public and radiology and radiation oncology residents about physics in medicine.

Jim Dobbins has been appointed to a 4-year term as Chair of the Misconduct in Research Committee at Duke University.

Jim Dobbins was one of three finalists for the position of Editor-in-Chief of the journal Medical Physics.

Jim Dobbins has been working with the Provost's office and other leaders in the Medical Physics Graduate Program to complete a proposal for a new graduate program in medical physics in Kunshan, China.

Anuj Kapadia was selected as a Distinguished Nominee for the 2013 Hammers Teaching Award in the School of Medicine.

Xiang Li’s paper on the effect of protocol and obesity on CT dose received the 2012 Farrington Daniels Award for Best Article on Radiation Dosimetry published in Medical Physics.

Xiang Li & Ehsan Samei were appointed as co-chair of the new AAPM Task group TG23 defining Metrology for Computed Tomography.

Ehsan Samei was appointed a Council Member of the National Council of Radiation Protection and Measurements (NCRP).

Ehsan Samei received a Chapter Appreciation Award, Southeast Chapter of the American Association of Physicists in Medicine (SEAAPM) in April 2012.

Ehsan Samei served as chairman of the board for the Society of Directors of Academic Medical Physics Programs in 2012.

Ehsan Samei was appointed as the co-chair of the SPIE Medical Imaging Symposium in 2013 and 2014.

Jered Wells (Dobbins lab) was awarded the 2012-13 Carey E. Floyd Graduate Fellowship in Medical Physics. This award is the highest award given to PhD students in the medical physics graduate program at Duke.

Jered Wells was given the award for Excellence in Teaching Assistantship and Anuj Kapadia, Deon Dick, and Justin Solomon were given Director's Awards for Exemplary Service by the medical physics graduate program in May 2012.

Joshua Wilson received the following honors: SIIM Small Grant Program for Imaging Informatics Training, Principle Investigator; (2012); SEAAPM Chapter Meeting, Trainee Poster Award (2012); and IEEE NSS/MIC Trainee Grant (2012).

NEW ARRIVALS

Rodrigo Viana, M.S., joined RAILabs as an exchange research student scholar advised by Dr. Kapadia. He is supported by fellowships from the Government of Brazil.

Adam Nolte and Ravi Mahadevan are both BME junior Pratt Engineering Undergraduate Fellows that also began in 2012, working on the breast tomosynthesis imaging project.

Lars Grimm a 3rd year radiology resident, Zack Silber a junior BME undergraduate student and Jing Zhang, joined Mazurowski group.

Christopher Smitherman joined Samei group in 2012 his research focus is on CT optimization.

Shelby Grzetic began as 1st year MEDPHY M.S. student and Carly Lutzky as BME junior Pratt Engineering Undergraduate Fellow in 2012, both are working on knowledge based radiation therapy for head and neck cancers.

ALUMNI NEWS

Christina Hsu (Dobbins lab) completed a postdoc in BME at Duke and is now employed by McKinsey and Co.

Ying (Ada) Chen (Dobbins lab) has received tenure at Southern Illinois University.

Ka “Carl” Zhang received his BSE in BME in 2011, then remained in the lab for another year of post-graduate research. He is now a M.S. student in Biomanufacturing Program at North Carolina State University.

Sylvia Hon completed her M.S. in BME.

Christopher Busselburg completed his MEDPHY M.S. and is now a medical physics resident at Duke Radiation Oncology.

Deon Dick completed her MEDPHY M.S. and is now a medical physicist at Kingston Public Hospital, Kingston, Jamaica.

David Good completed his MEDPHY M.S. and is now a medical physics resident at Univ. of Indiana.

Bernice Addae is completing her Masters degree in physics at NCCU this spring and will be graduating from the Dobbins lab.

Jody Shen finished 2 years of research as a medical student, graduating with MD in 2013.

Greeshma Agasthya, completed her Ph.D. in BME and will join Emory radiology as a post doc.

Gretchen Raterman, M.S., successfully defended her M.S. thesis.

Stephanie Dudzinski, BME B.S.E., Pratt Engineering Undergraduate Fellow, will begin this fall at Vanderbilt Univ. in the MSTP MD/PhD program.


Matthew Schmidt completed his MEDPHY M.S. and will begin work at Varian as a medical physics instructor.

Yakun Zhang completed her MS in Medical Physics focusing on comparative patient dosimetry for chest CT, radiography, and tomosynthesis.

Joshua Johnson completed his MS in Medical Physics focusing on extracting patient dose value for clinical imaging.

Justin Solomon completed his MS in Medical Physics focusing on image quality metrology in CT and is now a Research Analyst with RAI Labs.
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