Speakers (Title and Abstracts) at the 2014 San Francisco Chapter of the AAPM Young Investigator's Symposium

1. Katherine Walker, Graduate Student (Mentor: Simon Cherry, Professor, UC Davis Biomedical Engineering)

Title: Flexible Geometry, High-Sensitivity, Single-Photon Imaging System for Small Animals and Plants

Abstract: In preclinical single-photon emission computed tomography (SPECT) system development, the primary objective has been to improve spatial resolution by using novel parallel-hole or multi-pinhole collimator geometries. However, such high-resolution systems have relatively poor-sensitivity, often less than 0.1%. In contrast, a system that does not use collimators, can achieve very high-sensitivity. The absence of any collimation takes the sensitivity and resolution tradeoff for single-photon imaging to one of its limits and represents an underexplored performance regime. Here we present a flexible geometry, high-sensitivity, un-collimated detector single-photon imaging system for the imaging of both small animals and plants. The scanner consists of two thin, closely spaced, pixelated scintillation detectors of NaI(Tl), CsI(Na), or BGO. The detectors may be interchanged to optimize system efficiency for a wide range of gamma-ray energies. The performance of the system has been characterized using the metrics of sensitivity, spatial resolution, linearity and detection limits, and uniformity. With ^{99m}Tc (140 keV) in the center of the field of view, we measure a sensitivity of 37.7% using the NaI(Tl) detectors and 45.8% with CsI(Na). The best spatial resolution (FWHM when the image formed as the geometrical mean of the two detector heads, 20 mm detector separation) is: 19.0 mm for NaI(Tl) and 11.9 mm for CsI(Na) at 140 keV, and 13.6 mm for BGO at 511 keV. We find quantitative accuracy of linearity and detection limits is better than 2% down to activity levels of 100 nCi. Two *in vivo* animal studies (a renal scan using ^{99m}Tc MAG-3 and a thyroid scan with ^{123}I) and one plant study (a $^{99m}TcO_4^-$ xylem transport study) highlight the unique capabilities of this un-collimated system: high-sensitivity, high-throughput screening, and dynamic imaging where very good temporal resolution is critical. From the renal scan, we observe a 1000-fold increase in sensitivity compared to the Siemens Inveon SPECT/CT scanner. This un-collimated detector system is useful for many imaging tasks that do not require excellent spatial resolution, such as simple radiotracer uptake studies in tumor xenografts, counting of radiolabeled cells *in vitro*, *in vivo* imaging of easily saturated receptor systems, or *in planta* imaging of radioisotopes at low concentrations.

2. Brian Neal, PhD, Clinical Physics Resident (Mentor: Tokihiro Yamamoto, PhD, Assistant Professor, UC Davis Radiation Oncology)

Title: Novel technique for dynamic lung ventilation imaging based on wide coverage 4D CT

Abstract: An emerging lung ventilation imaging method based on conventional 4D CT has a high translational potential and advantages over other competing modalities, however suffers from binning artifacts and irregular breathing during a scan. We propose a novel technique to compute dynamic ventilation based upon wide coverage 320-slice 4D CT, which provides high spatial and

temporal resolution and binning artifact-free images. Methods: Wide coverage 4D CT images were acquired using a commercial 320-slice CT scanner, with 160 mm craniocaudal coverage and 0.35 s rotation time, during tidal breathing for five patients with thoracic cancer. The image at each of 51 time points was deformably registered to a peak-exhalation phase image using B-spline deformable image registration (DIR). For each time-point, the Jacobian determinant of deformation acted as a surrogate for regional ventilation. Dynamic ventilation was then computed by comparing time-resolved ventilation images. The accuracy of DIR was quantified by calculating target registration errors (TREs) of 100 anatomic landmarks per patient. Results: The proposed technique provided regional ventilation information of high spatial and temporal resolution. The average TRE of five patients was 1.4±1.3 mm. Dynamic properties of regional ventilation were found to be spatially heterogeneous. For example, ventilation increased during inhalation and decreased during exhalation in well-ventilated normal lung regions. However, in poorly-ventilated emphysematous regions, ventilation showed relatively minor changes with time around zero. Furthermore, ventilation resolved at this timescale demonstrated a signal that appeared to come from the heartbeat, especially in proximity to the heart.
Conclusion: 320-slice 4D CT-based ventilation imaging provides regional ventilation information of high spatial and temporal resolution. Dynamic ventilation information obtained by this technique may be useful in creating a model of dynamic ventilation that could be used to compensate for errors in conventional 4D CT-based ventilation imaging, and may also provide new insights into respiratory physiology.

3. **Peymon Gazi, Graduate Student (Mentor: John Boone, Professor, UC Davis, Department of Biomedical Engineering, Breast Tomography Research Lab, Department of Radiology)**

Title: High resolution dedicated breast CT for breast cancer screening: A replacement of digital mammography?

Abstract: In recent years, prototype breast CT (bCT) scanners have been designed and developed at several institutions. As a fully tomographic modality, bCT overcomes the superimposition effects found in mammography, where overlying normal breast tissue can obscure a lesion, thereby hindering detection, or cause summation artifacts leading to false positives, recalls, and additional studies. On the other hand, bCT used as a screening modality, has limitations in detecting micro-calcifications. Multiple clinical studies show despite the fact that compared to mammography, bCT is a better screening modality in finding mass lesions, mammography still outperforms breast CT in detecting micro-calcifications.
In this study, we have designed and implemented a fourth-generation bCT system to improve the spatial resolution characteristics of dedicated cone-beam breast CT, in order to improve detection of micro-calcifications. The results of MTF experiments demonstrate a significant improvement in spatial resolution characteristics. In the new bCT system, the pixel pitch of the flat-panel x-ray detector is 2.6 times smaller than the similar detector binning modes used in the previous generations of bCT. Also, the x-rays were generated in only 15% of each projection acquisition. The magnification was reduced 27% to achieve the same FOV as the previous generations of bCT. The MTF analysis of the new prototype bCT shows that using the new hardware and control structure results in a significant improvement in visualization of finer details. These

results suggest that the visualization of the micro-calcifications during breast cancer screening will be significantly improved.

4. Andrea Ferrero, Graduate student (Mentor, Ramsey Badawi, PhD, UCD Radiology/BME)

Title: Initial clinical experience with the UC Davis dedicated breast and extremity PET/CT scanner

Abstract: Neoadjuvant (primary) chemotherapy (NAC) is being used increasingly in the treatment of patients with locally advanced breast cancer aiming to reduce tumor size and prevent metastasis. The preliminary results from 8 patients enrolled in a clinical trial aiming at defining the potential of high resolution, dedicated breast PET/CT in predicting tumor response at an early stage are presented. In order to validate *in vivo* findings from novel, high resolution imaging devices there is a need to have accurate spatial correlation with the current gold standard in tumor diagnosis and staging, i.e. pathology. Efforts toward providing sub-cm spatial correlation between *in vivo* PET/CT images of the breast and histopathological samples are reported. Finally, the design and preliminary performance characterization of a second generation breast PET/CT prototype under development at our institution are presented.

5. Kuan Lu, Graduate Student (UC Berkeley: Mentor: Steven Conolly, Professor, UC Berkeley Imaging Systems Laboratory)

Title: Experimental demonstration of multichannel magnetic particle imaging for improved resolution.

Abstract: Magnetic particle imaging (MPI) is a promising imaging technique for a great number of clinical and scientific applications ranging from angiography to stem cell tracking. However, with a conventional single channel excitation, the inherently MPI resolution is anisotropic, which is not ideal for clinical diagnosis. In this work, we explored the physics of the anisotropy of MPI resolution, developed theory, hardware and imaging reconstruction algorithms, and experimentally demonstrated that with multichannel orthogonal excitation, we can achieve isotropic resolution without sacrificing the signal to noise ratio (SNR) of the image.

6. Patrick W. Goodwill, PhD, Postdoctoral Researcher, (UC Berkeley: Mentor: Steven Conolly, Professor, UC Berkeley Imaging Systems Laboratory)

Title: Kidney-safe, Radiation-free Interventional Imaging using Magnetic Particle Imaging

Abstract: The fluoroscopic imaging during percutaneous cardiac interventions has two major weaknesses, the relatively dangerous iodine contrast agent and the radiation exposure to the patient and the clinician. The iodine contrast agent poses a significant risk to the 25% of patients that present to the angiography suite with Chronic Kidney Disease (CKD), as exposure these agents frequently leads to contrast induced nephropathy (CIN) and can even induce kidney failure. The radiation exposure to the patient and clinician can also be significant.

We are developing a new imaging modality, Magnetic Particle Imaging (MPI), that is potentially capable of interventional imaging using kidney-safe iron-oxide tracers and without radiation. The technique is not based on MRI, and cannot be performed in any existing imaging scanner. In this talk, I will discuss multiple generations of MPI imagers we have developed at UC Berkeley, the basic image processing necessary to produce an image, and a demonstration of MPI imaging of interventional angiography balloons and biological samples.

7**. Bo Zheng, MS, Graduate Student (UC Berkeley: Mentor: Steven Conolly, Professor, UC Berkeley Imaging Systems Laboratory)**

Title: High-sensitivity Magnetic Particle Imaging for in vivo cell therapy tracking

Abstract: Magnetic Particle Imaging (MPI) recently emerged as a new technique for safer angiography and cell therapy tracking with unparalleled image contrast. However, the fundamental physical limit of sensitivity in MPI, which has strong implications for imaging speed and necessary tracer concentration, has not yet been explored. In this work, we investigated fundamental sources of interference and noise mechanisms in MPI and demonstrate a 40-fold improvement in the signal-noise ratio through interference suppression and preamplifier matching. We further demonstrate the first use of MPI for in vivo cell therapy tracking over three months in the rat brain.

UCSF:

8. Atchar Sudhyadhom, PhD - Medical Physics Resident (Mentor: Jean Pouliot, Professor, UCSF, Department of Radiation Oncology)

Title: Inaccurate Dosimetry of FFF Beams for SRS and SBRT: What's the worst that could happen?

Abstract: Flattening Filter Free (FFF) photon beams are increasingly being employed in the treatment of small lesions for SRS and SBRT. Some of the characteristics that make these FFF beams favorable also pose new challenges for accurate dosimetric measurement. The aim of this work was to quantitatively assess a set of dosimetric errors specific to this treatment modality and introduce potential methods to mitigate them.

Dose measurements were taken on two machines (a Varian TrueBeam STx and Accuray CyberKnife VSI) using the three available FFF beams (TB 6XFFF, TB 10XFFF, and CK 6XFFF). Dosimetric uncertainties due to ion recombination, volume averaging, and small fields effects were all examined. Multiple types and models of dosimeters were studied in this work including ion chambers, diodes, film, and a scintillator. Correction factors for the aforementioned effects were determined and applied as appropriate and used to determine relative errors.

Errors in measurement due to choice of dosimeter may be substantial. Errors of close to 2% may be possible in absolute dose calibration and relative dose measurement of PDDs in large open fields. In the measurement of small fields, output factors measured between various dosimeters varied by up to 16%. Proper application of correction factors dramatically reduced the dosimetric variation caused by these effects. The proper choice of dosimeter is essential in the measurement of FFF beams especially when applied to small fields for SRS and SBRT.

9. Mareike Held, MS - PhD Candidate (Mentor: Jean Pouliot, Professor, UCSF, Department of Radiation Oncology)

Title: Urgent Treatments: Can we use MV CBCT for Expeditious Dose Planning and Delivery?

Abstract: Unlike scheduled treatments, emergency cases require immediate radiation. Consequently, the treatment plans are kept very simple and are often based on film, which is far behind today's digital capabilities. Doctors are increasingly reluctant to treat patients without sufficient image guidance to avoid delivering high doses to normal tissues. However, developing an accurate and conformal image-guided emergency plan for urgent care can lead to rushed treatments and increases the chance of errors.

We have developed an integrated CT-based on-line radiotherapy workflow that uses the in-room imaging system for patient simulation. To evaluate the feasibility of this workflow, we built a case library of 29 clinical megavoltage cone beam CT (MVCBCT) of all anatomical sites. The images were categorized into four groups (head and neck, thorax/spine, pelvis and extremities). To assess the dose-planning accuracies on MVCBCT, we created a simple emergency treatment plan on each MVCBCT and copied it to its reference CT. The agreement between the dose distributions of each image pair was evaluated by the mean dose difference of the dose volume and the gamma index of the central 2D axial plane. We also evaluated an array of popular urgent and palliative cases for imaging component clearance and field-of-view.

We found that the MVCBCT based dose planning and delivery approach is feasible in many treatment cases. Dose distributions for head and neck patients are unrestrictedly predictable. The limited FOV becomes an issue for large pelvis patients and imaging clearance is difficult for cases where the tumor is positioned far off midline. Further, we found that lung tissue is most challenging for accurate dose calculations given the current imaging filters and corrections. Yet, this study presents a wide range of feasible treatments that can benefit from the clinical implementation of an integrated CT-based on-line radiotherapy workflow for urgent treatments.

10. Serena Scott, PhD - Research Specialist (Mentor: Jean Pouliot, Professor, UCSF, Department of Radiation Oncology)

Title: Interstitial ultrasound for image-guided thermal ablation in the vertebrae

Abstract: The objectives of this study are to theoretically and experimentally assess the feasibility of image-guided interstitial ultrasound ablation of tumors within and near the spine, and to identify potential treatment delivery strategies in and near the spine.

Transient biothermal finite element models of interstitial ultrasound ablation involving bone were validated using invasive and MR-based temperature measurements in ex vivo tissues. 7 MHz directional applicators with tubular transducers were considered (1.5 mm outer diameter, 0.5-1.5 cm long). Parametric and patient-specific assessments of the impact of tumor and bone properties on necessary treatment parameters were performed, with consideration of CO_2 insulation. 3D patient-specific models were generated based on segmented CT scans for nine representative patient cases selected to bracket a range of clinical interest, with tumors (10-27 mm diameter, 10-43 mm long) within or near the vertebrae.

Preferential ultrasound absorption and heating at bone surfaces allowed for faster, more effective

ablations. Numerical models using simplified approximations produced temperature profiles closely matching experimental measurements. 100% of the volumes of five simulated tumors located 4.3-14 mm from the spinal canal and 94.6-99.9% of the volumes of four simulated tumors 0-4.5 mm from the spinal canal could be ablated (>240 EM43°C) within 15 min without damaging (<6 EM43°C) critical nerves. 3-5 mm of normal cortical bone was found sufficient to insulate untargeted sensitive tissues, while sensitive tissues closer to targeted tumors could be protected through directional power control and CO2 insulation.
Parametric and patient-specific studies demonstrated the feasibility of interstitial ultrasound ablation of paraspinal tumors and osteolytic tumors within the spine. Preferential absorption of ultrasound by bone may provide improved localization, faster treatment times, and larger treatment zones in highly osteolytic and soft tissue tumors in and near the spine, as compared to other heating modalities. (Support: NIH R44CA112852).

11. Vickie Y. Zhang - PhD Candidate (Mentor: Jean Pouliot, Professor, UCSF, Department of Radiology and Biomedical Imaging)

Title: Hyperpolarized 13 C Biomarkers of Response to Prostate Cancer Radiation Therapy

Abstract: Clinical studies have demonstrated radiation dose escalation with hypofractionated radiation therapy regimens significantly improve disease-free survival for high-risk prostate cancer patients. Accurate assessment of early tumor response to treatment is crucial in determining whether to continue current therapy or switch to an alternative therapy. We investigated the physiologic and metabolic changes in TRAMP tumors (total 13 mice) following radiation therapy using both clinical ^{1}H MR imaging approach, including DCE and diffusion weighted imaging, and a clinical translatable hyperpolarized ^{13}C technique, and interrogated the histopathological and biochemical basis of the multi-parametric MRI data and their relationship to tumor response to a range of radiation dose levels.

12. Moiz Ahmad (Postdoctoral Fellow, Mentor: Lei Xing, Department of Radiation Oncology Stanford University School of Medicine)

Title: Order of Magnitude Sensitivity Increase in X-ray Fluorescence Computed Tomography (XFCT)

Abstract: **Purpose:** To improve the sensitivity of X-ray fluorescence computed tomography (XFCT) for *in vivo* molecular imaging. Is the maximum sensitivity achieved with an isotropic (4-pi) detector geometry? We prove that this is not necessarily true, and that a greater sensitivity is possible with anisotropic detector configuration. **Methods:** We performed both computer simulations and experimental XFCT imaging studies to assess the sensitivity improvement with our optimized configuration. The simulation used a Monte Carlo model of scanning of a gold-containing phantom with an x-ray pencil beam, and the subsequent acquisition of emitted XF photons with arrays of photon-counting detectors. In the experimental validation, an XFCT imaging system was constructed consisting of 1) a collimated pencil beam x-ray source using a fluoroscopy grade x-ray tube; 2) a CdTe x-ray photon counting detector to detect fluorescent x-rays; and 3) a rotation/translation stage for tomographic imaging. We created a 6.5-cm diameter water phantom with 2-cm inserts of low gold concentration (2.5–10 mg/mL) to simulate tumors

targeted by gold nano-particles. XFCT imaging was performed at three different detector positions (60°, 90°, 145°) to determine the impact of forward-scatter, side-scatter, and back-scatter on imaging performance. The three data sets were also combined to estimate the imaging performance with an isotropic detector. **Results:** In the Monte Carlo simulation, the optimized configuration had a 10 times greater sensitivity than the isotropic configuration. In the experimental study, the highest sensitivity was achieved when the XF detector was in the back-scatter 145° configuration (2.5 mg/mL), and only the optimized configuration could detect this concentration. For this concentration, the optimized configuration had a higher signal-to-noise ratio (SNR = 5.5) than the isotropic configuration (SNR = 2.4). The corresponding SNRs were 1.4 and 0 for 60° and 90° configurations, respectively. The imaging dose was 14 mGy, which is in the range of typical clinical x-ray imaging doses. **Conclusion:** This study experimentally proves, for the fist time, the Anisotropic Detection Principle in XF imaging, which holds that optimized anisotropic x-ray fluorescence detection provides greater sensitivity than complete isotropic detection. The optimized detection arrangement was used to improve the sensitivity of the XFCT experiment, and the achieved XFCT sensitivity is the highest ever for a phantom at least this large using a benchtop x-ray source, which is an important step toward clinical XFCT molecular imaging.

13. Amy Yu, PhD (Resident, Mentor: Peter G. Maxim, PhD, Department of Radiation Oncology Stanford University School of Medicine)

Title: Anatomic Optimization of Lung Tumor Stereotactic Ablative Radiotherapy

Abstract:

The aim of this study is to demonstrate proof of principle that anatomic optimization by selecting the degree of breath hold could result in dosimetrically superior stereotactic ablative radiotherapy (SABR) treatment plans. **Methods and Materials** Thirty patients with 41 plans were included in this planned secondary analysis of a prospective trial. Simulation included free breathing four-dimensional computed tomography (4DCT) and deep inspiration breath hold (DIBH) CT. Fifteen plans were treated in natural end exhale (NEE) and 26 plans were treated in DIBH. To evaluate whether the original treatment plan was dosimetrically optimal, we re-planned on the opposite respiratory state using the same beam configuration as the original plan. A treatment plan was deemed superior if it met protocol constraints while the other did not. If both plans met or violated the constraints, the plans were deemed equivalent irrespective of the magnitude of the dose difference. **Results**For patients originally planned on DIBH, re-planning on NEE resulted in a dosimetrically superior plan for three out of 26 treatment plans. For 22 treatment plans in this group, they were dosimetrically equivalent; while one treatment plan on DIBH was dosimetrically superior. For patients originally planned on NEE, four out of 15 treatment plans had dosimetrically superior plans on NEE, while two treatment plans were dosimetrically superior on DIBH and nine plans were dosimetrically equivalent. Thus, ten out of 41 plans, one respiratory state was superior to the other. **Conclusions** In order to obtain uniformly optimal plans, individual anatomic optimization would be needed. Our results demonstrate proof of principle that a ‘one size fits it all’ approach is not adequate

14. Mohammadreza Negahdar (Postdoctoral Fellow, Mentor: Peter G. Maxim, Department of Radiation Oncology Stanford University School of Medicine)

Title: First in Human High-Resolution Imaging of Regional Lung Function by Single Energy Xenon CT Compared to Ventilation SPECT

Abstract:

For many pulmonary diseases it would be valuable to map the function of different portions of the lung, but clinically available tools to do so are limited. Pulmonary function testing measures whole lung function, but not of specific lung regions. We are developing an imaging method based on widely available CT scanning that quantifies regional lung function in three-dimensional detail. Patients would breathe xenon gas, which can be seen on CT so its distribution can be measured. We propose a pilot clinical study of Xe CT in patients receiving radiation therapy and compare Xe CT to ventilation SPECT, which is the current clinical reference. Xe CT could be valuable for diagnosis and monitoring of diseases such as COPD and ARDS, and for directing biopsies and planning treatments like surgery and radiation therapy.

15. Scott Hsieh, PhD (Postdoctoral Fellow, Mentor: Norbert J. Pelc, Department of Radiology, Stanford University School of Medicine)

Title: Dynamic attenuators for CT systems

Abstract:

CT scans are now responsible for 25% of the radiation dose delivered to the U.S. We propose dynamic attenuation, or flux control, of CT. Flux control is ubiquitous in radiation therapy with devices such as the multileaf collimator. The challenge in introducing similar devices in CT is that imaging artifacts may be introduced as side effects. Our proposed dynamic attenuator consists of movable triangular wedges which produce a time-varying, piecewise-linear thickness profile. The geometry of the attenuator mitigates artifacts by virtue of a smoothly varying attenuation profile. Simulations indicate that the attenuator reduces radiation dose by 30% without increasing peak noise, with further benefits for targeted scans, and a significant reduction in dynamic range, which could enable next-generation, photon-counting detectors. We will also discuss control algorithms for the dynamic attenuator and an early prototype system.