President’s Report
Ryan Niederkohr, MD
PET CoE President

New hybrid imaging systems may offer advantages over existing technology, but clinical use of these innovations require provider training and ongoing education. This issue of the newsletter focuses on PET/MRI. The introduction covers upcoming educational opportunities and announces the center’s new PET/MRI working group. It is followed by two case reviews and an article on attenuation correction.

The SNMMI Annual Meeting in Denver will have a number of PET CoE-sponsored sessions, including one on PET/MRI, cosponsored with the International Society of Magnetic Resonance in Medicine. Be sure to check out all the offerings in the PET CoE News section of this newsletter.

SNMMI’s PET CoE website needs your help. We’re seeking contributors to update the pages with new material. To make this a worthwhile endeavor, we’re devising a system for contributors to earn academic credit. So, stay tuned for updates and let us know if you are interested in participating.

During my tenure as president of the PET Center of Excellence, the field of nuclear medicine has experienced a renaissance with several exciting developments: new radiotracers approved by the FDA and CMS, with more in the pipeline, as well as expansion from purely diagnostic services into delivering and monitoring therapy.

Now, as my term as president comes to an end, I want to thank the members of the Board of Directors for their time and commitment to the center’s activities, the SNMMI staff for their continuous support, and the entire membership for their interest in advancing the value and appropriate use of PET imaging in clinical practice. It has truly been an honor to serve as PET CoE president. Katherine Zukotynski, MD, will assume the role of PET CoE president at the Annual Meeting this June.

PET/ MRI in the Spotlight
Thomas A. Hope, MD, University of California, San Francisco

This issue of newsletter focuses on PET/MRI, a unique imaging modality that requires disparate skill sets with users who are trained in both nuclear medicine and magnetic resonance imaging (MRI). PET/MRI’s unique nature requires education and training collaborations between multiple organizations, bringing together expertise in nuclear medicine and diagnostic radiology.

Consider taking advantage of upcoming PET/MRI educational sessions and opportunities to advance its use in clinical practice:

SNMMI- ISMRM Co-Sponsored Annual Meeting Session
SNMMI has collaborated with the International Society of Magnetic Resonance in Medicine (ISMRM) over the past four years, which has resulted in yearly cosponsored sessions at the ISMRM and SNMMI annual meetings. This year, there will be a daylong session (Saturday, June 10) at the SNMMI Annual Meeting in Denver focused on clinical applications of PET/MRI in oncology, with multiple talks on brain tumors and prostate cancer. This exciting session will culminate in a debate between Johannes Czernin, MD, from UCLA and Ambros Beer, MD, from Ulm University on the pros and cons of using PET/MRI for oncologic applications.

SNMMI- ISMRM PET/ MRI Workshop
The first PET/MRI workshop co-sponsored by SNMMI and ISMRM will be held October 27-29, 2017, in Chicago at the Renaissance Blackstone. It will encompass a number of educational activities as well as research presentations. Talks will cover the clinical use of PET/MRI, with case sessions reviewing how to read the studies. The workshop also includes joint sessions that combine presentations of research abstracts with expert overviews of the field.

(Continued on page 2. See PET/MRI in the Spotlight.)
For technologists, there will be a series of talks focusing on PET/MRI required skills and accreditation, as well as workflow. The overall goal of the conference is to bring together technologists, physicians and physicists from both the PET and MRI worlds to educate and to build lasting collaborations. We hope that many of you will join us and participate in making this a successful inaugural PET/MRI workshop, hopefully setting the stage for a long-term successful collaboration between ISMRM and SNMMI.

Center of Excellence: PET/MRI Working Group

An SNMMI working group dedicated to PET/MRI has been created within the PET Center of Excellence (PET CoE). It will serve as a central hub for collaborative development of educational programs on this hybrid modality. PET CoE; as leader of this group, hopes to have as much participation as possible from SNMMI members interested in the development of PET/MRI use in clinical practice.

Looking ahead, keep an eye out for announcements on new online journal clubs focused on PET/MRI!

For a better understanding of PET/MRI, I refer you to the two articles in this issue:
• PET/MRI: Two Cases
• Attenuation Correction in PET/MRI

PET/MRI: Two Cases

Samuel J. Galgano, MD, and Jonathan McConathy, MD, PhD, University of Alabama at Birmingham

Simultaneous PET/MRI is a new hybrid imaging technique that has applications for oncologic and cardiovascular imaging, as well as neuroimaging. At the University of Alabama at Birmingham (UAB), we have recently begun performing PET/MRI for selected clinical cases. We have found that the high soft-tissue contrast and local tumor assessment provided by MRI, combined with the specificity and whole-body staging capabilities of PET, to be helpful for certain clinical applications of cancer imaging. Typically, clinical PET/MRI is performed in patients who have indications for standard of care MRI and standard of care PET examinations. Here, we present two clinical oncology cases where the combination of FDG-PET and MRI helped in the diagnostic evaluation and treatment planning for our patients.

Case 1

The patient is a 53-year-old woman who initially presented to the gastroenterologist after developing right upper quadrant pain, jaundice, and 15 lb. weight loss. She initially underwent imaging with CT and ultrasound without a clear diagnosis of malignancy.

Initial liver MRI images demonstrated ill-defined enhancement around the portal confluence and intrahepatic biliary ductal dilation that abruptly terminated in the hilum. Subsequently, the patient underwent endoscopic retrograde cholangiopancreatography and endoscopic ultrasound, all with negative pathology for malignancy. However, due to the pattern of biliary ductal dilation and the enhancement seen on MRI, she underwent partial hepatectomy and hepaticojejunostomy for suspected malignancy. The patient subsequently underwent right hepatic trisegmentectomy, and surgical pathology demonstrated a well-defined cholangiocarcinoma with periductal and perineural invasion.

Given the patient’s complete surgical resection with negative margins, adjuvant chemotherapy or radiation therapy were not offered at that time. The patient was monitored for disease recurrence with serum CA 19-9 values. The patient was disease free for four years following the partial hepatectomy, but the patient’s CA 19-9 eventually began to rise. Conventional imaging with CT and MRI were unrevealing, but a PET/CT scan demonstrated increased FDG uptake at the resection margin. After discussion by the hepatobiliary tumor board, the decision was made to perform an FDG-PET/MRI to again evaluate the liver with MRI and to localize the site of suspected potential recurrence with FDG and MRI.

PET/MRI demonstrated increased FDG uptake adjacent to the resection margin, which correlated to an area of diffusion-restriction (Figure 1).

Figure 1: A – maximum intensity projection; B and C – hepatobiliary phase MRI without and with fusion; D and E – diffusion-weighted images without and with fusion

(Continued on page 3. See PET/MRI: Two Cases.)
Because of the extrahepatic location of this recurrence and lack of distant metastases, the patient was treated with a combination of radiation and chemotherapy, rather than another resection or chemotherapy alone.

**Case 2**

The patient is a 46-year-old woman who initially presented to her gynecologist with abnormal uterine bleeding. Pelvic exam at the initial visit demonstrated a bleeding, fungating mass at the cervix. Biopsy demonstrated a squamous cell carcinoma of the cervix with lymphatic invasion. Subsequent CT of the abdomen and pelvis demonstrated obstruction of the left ureter by the cervical mass and enlarged lymph nodes in the periaortic, pericaval and bilateral iliac nodal stations. Given the findings on the CT and physical exam, the patient was not deemed to be a surgical candidate and was instead referred to radiation oncology for chemotherapy and radiation treatment.

As part of the patient’s planning for radiation therapy, an FDG-PET/MRI exam was ordered to better evaluate the extent of pelvic disease and for whole-body staging. PET/MRI demonstrated a markedly hypermetabolic cervical mass and hypermetabolic pelvic/retroperitoneal adenopathy (Figure 2: A – D), but was also notable for left supraclavicular adenopathy with increased FDG uptake (Figure 2: E) and increased FDG uptake within the right pubic body. Incidentally, diffusely increased FDG uptake in the colon is likely related to concurrent metformin treatment.

A subsequent ultrasound-guided biopsy of the left supraclavicular adenopathy demonstrated metastatic squamous cell carcinoma. This case illustrates the ability of FDG-PET/MRI to provide important whole-body staging information while also providing excellent regional staging for pelvic malignancies in a single imaging session.

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**Figure 2: A & B – axial T2 weighted non-fat saturated with and without fusion; C & D – sagittal T2 fat-saturated with and without fusion; E – maximum-intensity projection**

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**PET CoE News**

**Looking forward to the 2017 SNMMI Annual Meeting**

PET CoE is sponsoring a host of great sessions at the 2017 Annual Meeting in Denver, Colorado (June 10-14), including one categorical session on June 10, two CE sessions organized solely by PET CoE, and two CE sessions organized with other organizations. Build your schedule online or download the meeting app for easy access!

**Here’s a preview of a few of the sessions:**

**CAT5: PET/MRI: A Focus on Oncology (June 10, 8 AM – 4 PM; separate registration required)** – Jointly organized with the International Society for Magnetic Resonance in Medicine (ISMRM), this session will cover the role of PET/MR in oncologic imaging, with a focus on prostate cancer and neuro-oncology. Participants will learn about current clinical applications and possible roles for PET/MRI in the future.

**CE58: PET/CT and Immune Modulation Therapy Assessment (June 13, 8 – 9:30 AM)** – This session will provide basic information on immune modulation therapies and describe the challenges of using RECIST or PERCIST in assessing immune modulation therapy. Case examples will be used to illustrate the value and pitfalls of PET/CT in assessing immune modulation therapy.

**CE62: Peter E. Valk, MD, Memorial Award and Lecture (June 13, 8 – 9:30 AM)** – George M. Segall, MD, FACNM, FSNMMI, will be honored with the 2017 Peter E. Valk, MD, Memorial Award during this session. He will present a lecture entitled PET/CT and Patient Outcomes.

PET CoE members are also encouraged to attend the PET Center of Excellence Business and Board of Directors Meeting on June 12 at 6:45 AM.

**Mark your Calendar!**

**ISMRM-SNMMI Co-Provided Workshop on PET MR**

October 26 – 29, 2017

Renaissance Blackstone Hotel, Chicago, Illinois
Attenuation Correction in PET/MRI

Peder Larson, PhD, and Andrew Leynes, MS, University of California, San Francisco

Accurate uptake estimation is important for tumor staging and treatment response monitoring, and is especially so for quantitative imaging studies. This accuracy is important clinically when comparing across PET/CT and PET/MR systems or between vendors. For PET/MRI, spatial accuracy will be very important to compare MRI parameters, for example from diffusion-weighted imaging, with PET parameters.

Quantitative accuracy in PET relies on attenuation correction. In PET/CT, measurement of attenuation maps is straightforward, as the CT component measures electron density directly. In PET/MRI, however, there is no direct method for measuring attenuation maps, as MRI measures nuclear spin properties, not electron density. Specialized methods are required for generating accurate attenuation correction maps for PET/MRI to provide quantitative PET accuracy.

The development and evaluation of PET/MRI attenuation correction methods is a very active area of research, where several promising solutions have emerged. These include atlas-based methods, fat/water imaging, and ultra-short echo time (UTE) or zero-echo-time (ZTE) imaging. These methods are typically tailored to specific regions, such as head, chest and body (Figure 1).

In the head, current commercial products rely on atlas-based methods, where MRI data is registered to an imaging atlas that includes attenuation information. These approaches require relatively simple MRI scans, placing the burden on post-processing methods to generate attenuation maps. The main challenge of atlas-based methods is that they do not completely account for patient-specific variations in bone structure and density.

In the body, current commercial products rely on fat/water imaging (also known as “Dixon MRI”) methods (1). These methods can rapidly provide accurate maps of the fractions of fat versus water soft-tissues, which are in turn converted into attenuation maps based on the expected attenuation of these tissue types. In the chest, the lung is typically segmented out and given its own attenuation coefficient.

The main drawback of fat/water imaging methods is that they do not capture the attenuation effects of bone. This is because conventional MRI does not detect any signal from bone, due to its very short T2* relaxation time. This can lead to 10-20 percent underestimation of uptake, particularly for lesions in and around bone (Figure 2).

(Continued on page 5. See Attenuation Correction in PET/MRI.)

Figure 1: ZTE-based attenuation correction results in a five-fold reduction in quantification error compared to the standard atlas based reconstruction. MR data is acquired using a zero-echo time (ZTE) sequence. The ZTE images are then post processed to make a ZTE-based attenuation correction map directly from the patient specific imaging data. Using ZTE-based attenuation correction maps, Amyvid (florbetapir) PET data is reconstructed.
PET in the News

The international literature on PET, PET/CT and PET/MR continues to grow at a pace that challenges both researchers and clinicians. The media has recognized the value of these modalities and regularly features advances in research and technology in the news. In each issue, the PET CoE Newsletter presents a tomographic slice of the breadth of PET media coverage that appears in publications around the world. Additional news articles can be found online at www.snmmi.org under “MI: Making a Difference.”

FDG-PET/CT scoring system aids in cervical cancer prognosis
Aunt Minnie

World’s first full-body PET scanner could aid drug development, monitor environmental toxins
Science Magazine

FDG-PET/CT can direct biopsies for pediatric cancer
Aunt Minnie

Monitoring Cardiac Sarcoidosis Patients with Repeated PET Scans Could Help Set Best Treatment Course
Sarcoidosis News

Comparison of standard and delayed imaging to improve the detection rate of [(68)Ga]PSMA I&T PET/CT in patients with biochemical recurrence or prostate-specific antigen persistence after primary therapy for prostate cancer
UroToday

Humans have three times more brown body fat: A study of 3,000 PET-scans yields new data on the proportion of brown fat
Science Daily

Multimodal Imaging Ties Tau to Neurodegeneration, and Symptoms
Alzforum

A ‘portable’ approach to studying the brain unveiled at American Association for the Advancement of Science meeting in Boston
MassLive

From Alzheimer’s to autism, nuclear neurology could launch revolution in diagnosing and treating brain diseases
MedicalXpress

PET Shines Light on Early-Stage Alzheimer Disease
Psychiatric Times

Automated fluorine radiolabelling moves closer to the clinic
Chemistry World

(Continued from page 7. See Attenuation Correction in PET/MRI.)

Figure 2. MR attenuation-correction (MRAC) methods in the body currently use Dixon fat/water separation techniques that neglect bone, which leads to substantial errors (>10 percent) for lesions within bone or soft tissues of the pelvis, due to extensive surrounding bone. Preliminary results indicate that bone density can be accurately estimated from zero-echo-time (ZTE) MRI using a hybrid ZTE/Dixon method for pseudoCT (top left) and that PET standardized uptake values (SUV) are more accurate than Dixon alone compared with gold-standard CT attenuation correction maps (bottom left). Preliminary results also indicate that these techniques can reduce average SUVmax errors of bony and soft tissue pelvic lesions to less than 5 percent (right).

(Attenuation Correction in PET/MRI. Continued from page 4.)
Researchers have used positron emission tomography (PET) to successfully identify genetic cell mutations that can cause lung cancer. The research, published in the featured article of the April 2017 issue of *The Journal of Nuclear Medicine*, shows that an advanced image analysis technique, radiomics, can non-invasively identify underlying cell mutations in patients with non-small cell lung cancer (NSCLC). More people in the United States die from lung cancer than from any other type of cancer, and NSCLC is the most common form.

The characteristics of metabolic tumors have been quantified by PET radiomics, but little is known about the relationship between these characteristics, or phenotypes, and the underlying mutations that cause them. This information is key to precision medicine—selecting the therapy that will work best for a particular patient.

“To our knowledge, this is the first study to investigate the relationship between somatic mutations and the metabolic phenotypes, which may provide valuable information for developing non-invasive imaging biomarkers for determining mutation status,” explains Stephen Yip, PhD, Harvard Medical School, Boston, Massachusetts. “Identifying mutation status in NSCLC patients is an important component of selecting an optimal treatment plan for the patient. The current standard of care uses molecular testing based on biopsies of tumor tissue or surgical resection to identify mutation status. Molecular testing, however, can be limited by invasive procedures and long processing times. In addition, tissue samples are not always readily available.”

For the study, 348 NSCLC patients underwent diagnostic F-18-fluorodeoxyglucose PET (F-18-FDG PET) scans and were tested for genetic mutations. Of those patients, 13 percent (44/348) and 28 percent (96/348) were found to harbor an epidermal growth factor receptor (EGFR) or Kirsten rat sarcoma viral (KRAS) mutations, respectively. The analysis evaluated 21 imaging features: 19 independent radiomic features quantifying phenotypic traits and 2 conventional features (metabolic tumor volume and maximum standard uptake value).

The results indicate that EGFR mutations may drive different metabolic tumor phenotypes that are captured in PET images, whereas KRAS-mutated tumors do not. This proof-of-concept study sheds light on genotype-phenotype interactions using radiomics to capture and describe the phenotype.

Yip notes, “This study may thus help develop an imaging biomarker that can non-invasively and accurately identify EGFR mutation status using PET imaging to complement, but not to replace, molecular testing.”

*The authors of “Associations between somatic mutations and metabolic imaging phenotypes in non-small cell lung cancer” include Stephen S.F. Yip, Thibaud P. Coroller, Chintan Parmar, Emmanuel Rios Velazquez, Elizabeth Huynh, Raymond H. Mak and Hugo J.W.L. Aerts, Dana-Farber Cancer Institute, Brigham and Women’s Hospital, and Harvard Medical School, Boston, Massachusetts, and John Kim, University of Michigan Health System, Ann Arbor, Michigan.*

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**LINK TO PDF OF THE FULL JNM ARTICLE**

**Advanced FDG-PET Image Analysis Identifies Cell Mutations in Cancer Patients**

![Figure: Tumors harbor different somatic mutations. From left to right are patients with EGFR mutation, KRAS mutation, and EGFR– and KRAS– tumors, respectively. Stage I and III tumors are shown in the top and bottom rows, respectively. Arrows indicate the locations of the lung tumors. Credit: Stephen S.F. Yip, PhD, and Hugo Aerts, PhD, Dana-Farber Cancer Institute, Brigham and Women’s Hospital, and Harvard Medical School, Boston Massachusetts; John Kim, MD, University of Michigan Health System, Ann Arbor, Michigan](image)
To capture patient-specific bone information for MRAC, methods based on ultrashort echo-time (UTE) and zero-echo-time (ZTE) pulse sequences have been proposed. These specialized acquisitions can capture the rapidly decaying bone signals, which in turn can be used to provide an estimate of bone density in individual patients. In the head and pelvis, these methods have been shown to reduce SUV errors to less than 5 percent across a range of patients and lesions (2). These methods will be integrated into future commercial products.

PET/MRI will also require new approaches for standardization across PET/MRI systems that account for the specialized approaches to PET/MRI attenuation correction. This will include the development of specialized PET/MRI phantoms that can provide the appropriate attenuation and MRI properties that are exploited by MR attenuation correction methods. This standardization along with robust attenuation correction methods will allow PET/MRI to be included in multicenter clinical trials and ensure that the uptake that we measure is accurate and can, therefore, be appropriately used for precision medicine applications.

References