Science News from the SNMMI 2020 Annual Meeting

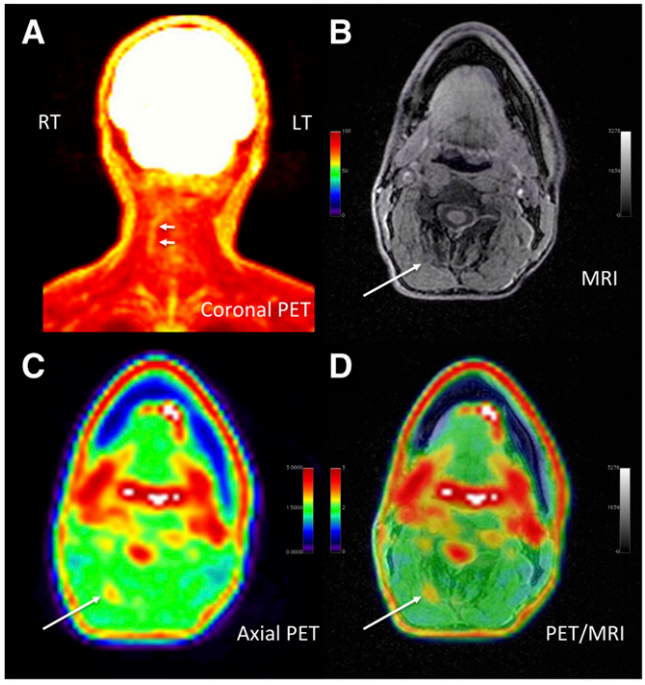
The SNMMI 2020 Annual Meeting, held virtually through live and recorded events from July 11 to 14, maintained the society's long tradition of presenting carefully selected state-of-the-art clinical, translational, and basic science investigations from around the world. Many of these presentations and their authors were featured in international media reports highlighting the most recent advances in nuclear and molecular imaging and therapy. The following selected summaries include relevant abstract numbers in brackets, and abstracts can be accessed in *The Journal of Nuclear Medicine* special issue at http://jnm.snmjournals.org/site/misc/JNM_Meeting_Abstracts_Info.xhtml.

PET/MRI and Localization of Chronic Pain

Cipriano et al. from Stanford University (CA) reported that "^{18}F-FDG PET/MRI of patients with chronic pain alters management" [399]. The goal of the study was to develop a clinical PET/MRI method to accurately localize sites of increased inflammation related to sources of pain and to look at whether such imaging results would affect management decisions. "In the past few decades, we have confirmed that anatomic-based imaging approaches, such as conventional MRI, are unhelpful in identifying chronic pain generators," said Sandip Biswal, MD, senior author of the study. "We know that ^{18}F-FDG PET has the ability to accurately evaluate increased glucose metabolism that arises from acute or chronic pain generators. As such, in our study we examined PET/MRI as a potential solution to determine the exact molecular underpinnings of one's pain."

The study included 65 patients referred for chronic pain who underwent head-to-foot imaging on a GE SIGNA PET/MRI system. Maximum SUVs and target-to-background ratios were measured, and images were evaluated by 2 radiologists to determine whether increased ^{18}F-FDG uptake occurred at the site of symptoms or in other areas of the body. Imaging results were discussed with referring physicians. Increased uptake in affected nerves and muscle was identified at the site of pain and in other areas of the body in 58 patients. This resulted in a mild modification of management plan (e.g., additional diagnostic tests) for 16 patients and a significant modification (e.g., new invasive procedure suggested or ordered) for 36 patients. New management plans were implemented for a total of 40 patients.

"The results of this study show that better outcomes are possible for those suffering from chronic pain," said Biswal. "This clinical molecular imaging approach is addressing a tremendous unmet clinical need, and I am hopeful that this work will lay the groundwork for the birth of a new subspecialty in nuclear medicine and radiology. Using this approach will require knowledge and expertise not only in nuclear medicine but also in musculoskeletal imaging, neuroradiology, and potentially other fields, such as body imaging and pediatric radiology, where pain syndromes are important clinical problems."

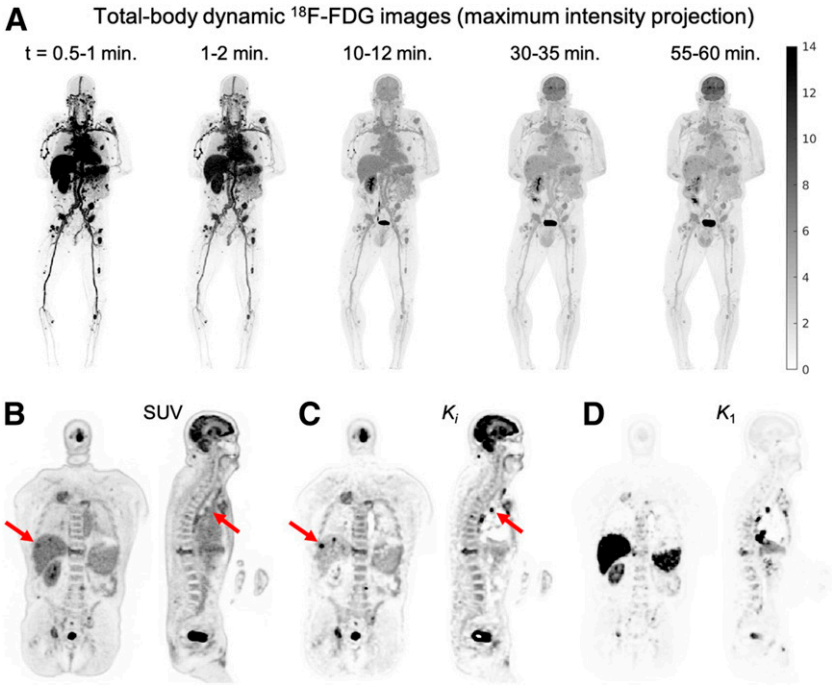


Adult male with decades of right neck pain, discomfort, and tightening following birth injury. Multiple standard therapeutic maneuvers had failed before ^{18}F-FDG PET/MR imaging, which showed abnormally elevated uptake (white arrows; SUV_{max} = 1.2) in a linear pattern in the posterolateral right neck, between the oblique capitis inferior and the semispinalis capitis muscles, where the greater occipital nerve resides. By comparison, the same region on the contralateral, asymptomatic side of the neck had an SUV_{max} = 0.7. This result encouraged a surgeon to explore the area of uptake. The surgeon ultimately found a collection of small arteries wrapped around the nerve. The small arteries underwent lysis, and the patient reported relief of symptoms. (A) Coronal thick-slab multiple-intensity projection ^{18}F-FDG PET. (B) Axial LAVA FLEX MRI through cervical spine. (C) Axial PET at the same slice as the axial MRI. (D) Fused axial PET/MRI.

Total-Body Dynamic PET and Metastatic Cancer

Wang et al. from the University of California Davis (Davis and Sacramento) and Imperial College London (UK) presented "Total-body dynamic PET of metastatic cancer: First patient results" [208]. The study used the uEXPLORER, an ultra-high-resolution digital PET/CT with a 194-cm axial field of view for total-body imaging, in a patient with metastatic renal cell carcinoma. "The focus of our study was to test the capability of uEXPLORER for kinetic modeling and parametric imaging of cancer," said Wang. "Different kinetic parameters can be used in combination to understand the behavior of both tumor metastases and organs of interest such as the spleen and bone marrow. Thus, both tumor response and therapy side-effects can be assessed using the same scan."

A patient with metastatic renal cell carcinoma was injected with ^{18}F-FDG and scanned on the uEXPLORER.



uEXPLORER total-body dynamic ^{18}F-FDG PET imaging allowed monitoring of the spatiotemporal distribution of glucose concentration in metastatic tumors from injection to 60 min (a). Compared to a typical clinical SUV image (b), the parametric image of tracer influx rate (K_i) (c) can achieve higher lesion-to-background contrast. In addition to glucose metabolism imaging by K_i, total-body dynamic PET also enables multiparametric characterization of tumors and organs using additional physiologically important parameters (e.g., glucose transport rate K_1 [d]) across the entire body.

The static PET SUV was calculated, and kinetic modeling was performed for regional quantification in 16 regions of interest, including major organs and multiple metastases. The glucose influx rate was calculated, and additional kinetic modeling was implemented to generate parametric images. The kinetic data were then used to explore tumor detection and tumor characterization.

Multiple metastases were identified on dynamic PET/CT, confirming the feasibility of total-body kinetic modeling and parametric imaging of metastatic cancer. Parametric images of glucose influx rate showed improved tumor contrast over SUV in general and specifically led to improved lesion detection in the liver. Total-body kinetic quantification also provided multiparametric characterization of tumor metastases and organs of interest.

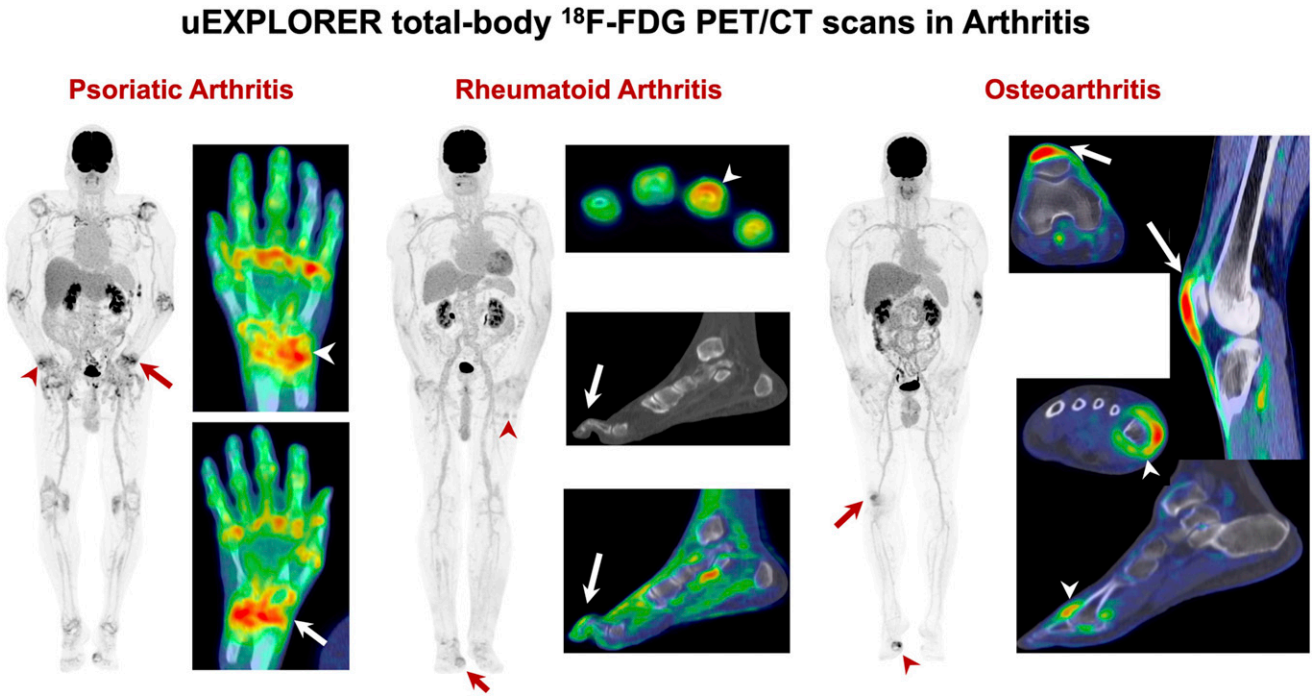
"Total-body dynamic imaging and kinetic modeling enabled by total-body PET have the potential to change nuclear medicine into a multiparametric imaging method, where many different aspects of tissue behavior can be assessed in the same clinical setting—much like the information gained from different sequences in an MRI scan," said Ramsey D. Badawi, PhD, senior author. "The total-body parametric imaging technique is not limited to ^{18}F-FDG; it is applicable to all radiotracers. It is also not limited to cancer but can be broadly applied to evaluate disease severity and organ interactions in many other systemic diseases. We expect a profound impact in the field of nuclear medicine and molecular imaging."

Systemic Inflammatory Arthritis and Total-Body PET/CT

The uExplorer was also the focus of a presentation reporting that "Total-body PET/CT captures full picture of systemic inflammatory arthritis" [331] by Abdelhafez, from the South Egypt Cancer Institute, and researchers from the University of California (Davis and Sacramento). The authors described initial findings from a prospective study in 14 patients with established rheumatoid arthritis, psoriatic arthritis, and osteoarthritis who underwent a single-timepoint total-body uEXPLORER ^{18}F-FDG PET/CT. Only 75.5 MBq ^{18}F-FDG PET were injected (~20% of conventional dose).

"In our research, we sought to examine the feasibility of assessing glucose metabolism both in normal and diseased joint tissues across the body as a means for quantifying systemic inflammatory burden for these conditions," said Abdelhafez. Participants with rheumatoid arthritis showed multiple, somewhat symmetric joint involvement, most often in the hands, with the joints of the feet less frequently affected. Other notable features for rheumatoid arthritis included radiotracer uptake patterns consistent with inflammation of the joint synovium. All participants with psoriatic arthritis had positive findings in large joints and demonstrated multiple sites of enthesitis, affecting the tendons of the hand and fingers, including the nail beds. Osteoarthritic participants showed unilateral enhanced uptake in at least 1 large joint (shoulder, elbow, or knee) and occasionally in a few small joints of the hand and feet and the quadriceps femoris tendon.

"Systemic joint evaluation of patients with inflammatory arthritis is indeed feasible with this total-body PET/CT scanner and feasible with low radiation dose," said Abdelhafez. "The evaluation of arthritic disease activity at all joints of the body could have direct implications for disease staging, risk stratification, treatment selection, and monitoring of treatment response. Furthermore, the impact of arthritis on other tissues of the body can be studied to better understand systemic disease burden." He added "Total-body molecular



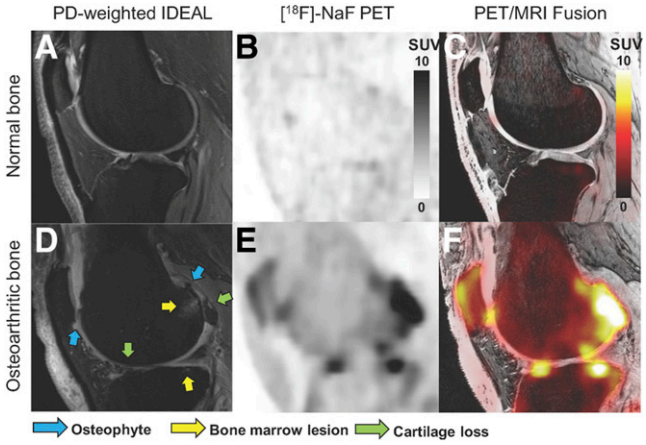
Left block of 3: Total-body PET/CT in psoriatic arthritis, with multiple joints affected: shoulders, elbows, wrists, knees, ankles, and small joints of hands/feet. Middle block of 3: Total-body PET/CT in rheumatoid arthritis, with multiple joints affected: right shoulder and small joints of the left hand. Arrowhead at the 4th proximal interphalangeal joint shows classic ring-like uptake pattern. Arrow on the foot demonstrates hammer toe deformity associated with big toe arthritis. Right block of 3: Total-body PET/CT in osteoarthritis, with affected joints including the left elbow, right knee, and right big toe.

imaging could provide currently unavailable, systemic, objective biomarkers that could help address the significant clinical challenges in managing inflammatory arthritic populations. These biomarkers may also have clear potential to accelerate arthritic drug discovery and development."

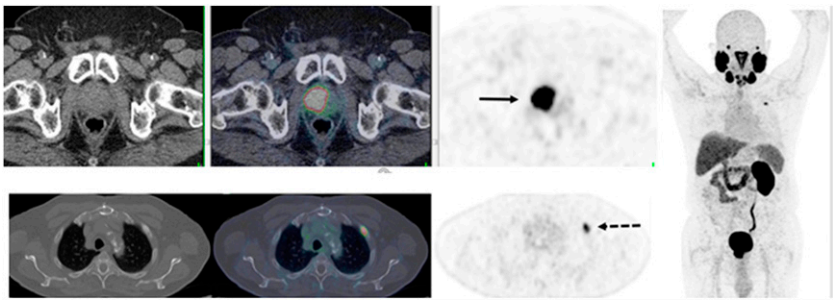
PET/MRI and Knee OA Progression

Watkins et al. from Stanford University (CA), the University of Cambridge (UK), and the Rigshospitalet (Copenhagen, Denmark) presented "Evaluating the relationship between dynamic Na[^{18}F] uptake parameters and MRI knee osteoarthritic findings" [182]. The authors evaluated correlations between observed structural changes in bone and cartilage on MRI and quantitative subchondral bone metabolic parameters using hybrid ^{18}F-fluoride PET/MRI. The study included 12 individuals with knee osteoarthritis who underwent serial imaging of both knees. "Osteoarthritis is not well understood, in part because we lack the tools to objectively evaluate early and reversible changes in key tissues," said Watkins. "While many MRI methods have been developed for assessment of early degenerative changes in cartilage, functional imaging of bone in the joint remains a major challenge."

MRI Osteoarthritis Knee Scores (MOAKS) and dynamic PET data were used to calculate the rates of bone perfusion, tissue clearance, and mineralization, as well as tracer extraction fraction and total bone uptake rate. Kinetic modeling was performed for regions of interest representing the subchondral bone of the patella, medial and lateral tibia, and anterior, central, and posterior regions of the medial and lateral femur. Abnormal bone metabolism in regions with bone marrow lesions, osteophytes, and adjacent cartilage lesions was found to be strongly associated with



Representative structural MRI (PD-weighted IDEAL images, A and D), ^{18}F-NaF PET SUV images (B and E), and fused images (C and F) of a healthy knee (top) and a knee with osteoarthritis (bottom). MOAKS scoring of MR images was used to identify size of osteophytes (blue arrows), bone marrow lesions (yellow arrows), and cartilage loss (green arrows) within bone regions in the patella, tibia, and femur.



PSMA PET/CT accurately detected recurrent prostate cancer in a 67-y-old man. Left: ^{18}F-DCFPyL-PSMA PET/CT showed extensive, intensely PSMA-avid local recurrence in prostate in keeping with the known tumor recurrence in the prostate. Right: PET showed extensive, intensely PSMA-avid local recurrence in prostate (top, solid arrow) and a solitary bone metastasis in left rib 2 (bottom, dotted arrow).

greater bone perfusion rates compared to bone that appeared normal on MRI. Strong spatial relationships between bone metabolic abnormalities and changes in overlying cartilage were also noted. The authors concluded that "kinetic parameters of ^{18}F-fluoride uptake in subchondral bone are objective measures of bone metabolism with potential to provide functional information that complements assessments of structural abnormalities observed on MRI."

"These findings show the utility and potential of PET imaging to study the role of bone physiology in degenerative joint disease," said Watkins. "This knowledge may help us understand the order of events leading to structural and functional degeneration of the knee. Further, this will help us to develop and quickly evaluate new interventions that target specific metabolic pathways to give us the best chance to slow or arrest the onset and progression of osteoarthritis."

PSMA PET and Recurrent Prostate Cancer Management

Metser et al. from the University of Toronto, McMaster University (Hamilton), Western University (London), Cancer Care Ontario (Toronto), and the University of Ottawa (all in Canada) presented "Preliminary results of a prospective, multicenter trial assessing the impact of ^{18}F-DCFPyl PET/CT on the management of patients with recurrent prostate cancer" [40]. The registry trial assessed disease detection rate and PET-directed changes in clinical management in 410 men with suspected limited recurrent prostate cancer after primary therapy who subsequently underwent ^{18}F-DCFPyl (prostate-specific membrane antigen [PSMA]) PET/CT. PSMA PET/CT identified disease in more than half of the men in whom CT and bone scan scintigraphy had been negative. Post-PSMA PET planned management was recorded in 341 participants. Of these, 66% had a documented PET-directed change in management. The most common change was conversion from observation or systemic therapy to surgery or radiation for locoregional (74) or oligometastatic disease (30) or the addition of nodal-directed therapy to salvage surgery or radiation (37).

"The identification of extent of recurrence and specific sites of recurrence is crucial in determining the most appropriate mode of therapy for these men," said Metser. "Findings from this study add to the body of evidence on the utility of PSMA PET in the management of prostate cancer patients. At this time, PSMA PET remains investigational in North American jurisdictions. Evidence generated from this study will help in seeking regulatory approvals to make molecular imaging with ^{18}F-DCFPyL widely available and will pave the way for clinical studies that incorporate PSMA PET as a treatment planning tool to assess ultimate impact on patient outcomes."

Visualizing Cardiac and Renal Inflammation After MI

Werner et al. from Children's Hospital/Hannover Medical School and the Technische Universität München (Garching, both in Germany) reported on "Imaging inflammation crosstalk along the cardio-renal axis after acute myocardial infarction" [28]. The authors speculated that inflammation contributes to the "crosstalk" or bidirectional interaction between the failing heart and the kidneys and used serial preclinical whole-body CXC chemokine receptor-4 (CXCR4)–targeted ^{68}Ga-pentixafor PET to explore this crosstalk after induced myocardial infarction. Images were acquired in mice 1, 3, and 7 d and 6 wk after coronary artery occlusion or sham surgery. Tracer retention was assessed in the kidneys and compared to infarct signal and cardiac function as measured independently by MRI.

The cardiac CXCR4 signal was found to be significantly elevated on the first day of imaging and returned to sham equivalents after 7 days. Renal CXCR4 signal was unchanged on the first day of imaging but, after 7 days, was reduced in comparison with sham levels. Cardiac and renal signals were directly correlated, suggesting an inflammatory link between the heart and kidneys. Ex vivo autoradiography confirmed a significant correlation between tracer retention in the infarct region and the kidneys.

"This study provides a foundation for simultaneous examination of heart and kidneys after myocardial infarction by using molecular imaging," said Werner. "It provides an impetus for the pursuit of systems-based multi-organ imaging to investigate systemic response to focal injury. Assessment of inflammation after myocardial infarction is beginning to be evaluated in clinical populations. With the growth of long-bore cameras with larger fields of view, the concept of multiorgan imaging will expand substantially in the next years."