And Now for Something Slightly Different: When Traveling to Japan...

Twyla Bartel, DO, MBA, FACNM; PET CoE Board Member

Of course, traveling to Japan is much easier if, like me, you grew up there for 17 years and speak the language—but here are a few suggestions and tips if you ever plan to go to this wonderful country. However, first of all, I would like to sum up the recent Japan Society of Nuclear Medicine (JSNM) meeting that occurred in November 2018.

The 58th Annual Scientific Meeting of the JSNM occurred in Okinawa, Japan, in combination with the 38th Annual Meeting of the Japanese Society of Nuclear Medicine Technology at the Okinawa Convention Center in Ginowan City, Okinawa. JSNM President Jun Hatazawa was a very gracious host. SNMMI President Satoshi Minoshima was a featured speaker at this meeting, with one of his talks on the topic of artificial intelligence for nuclear medicine. I was also a speaker, representing the American College of Nuclear Medicine (ACNM) at this meeting, giving my talk in both English and Japanese. There were several talks related to PET imaging, including quantification and standardization, whole-body and/or dynamic imaging, dementia and other neurology-related titles, and oncology. The meeting was excellent, as were the President’s and Congress receptions.

Now, on to the suggestions and tips.

• There are no immunization or visa requirements for U.S. citizens when travelling to Japan, just a U.S. passport.
• In most of Japan, you can find individuals who speak a decent amount of English if you stay in areas most visited. Google Translate is also a handy tool.
• It is highly recommended to rent a pocket WIFI if you are planning to explore beyond a meeting or hotel site, and several devices can be

(Continued on page 3. See Traveling to Japan.)
On the diplomatic front, among many stories to be told, relations between Russia, the EU, Canada, and the U.S. were under the microscope. After 18 years at Germany’s helm, Angela Merkel announced she would not seek re-election. Theresa May and Brexit encountered more issues. Irish voters favored repealing the abortion ban. China’s parliament changed the country’s constitution to allow President Xi Jinping to rule for life. Kim Jong Un reached out to South Korean President Moon-Jae, and a hotline was initiated. The U.S. moved its embassy to Jerusalem and sent the National Guard to secure the Mexican border. Tariffs were discussed, imposed, and renegotiated. Supreme Court Justice Anthony Kennedy retired, to be replaced by Justice Brett Kavanaugh, sparking heated discussion. The midterm elections came and went with changes on the horizon. Cuba recognized private property under their constitution. Saudi Arabia started the year with an anticorruption purge, seizing nearly $100 billion and ended the year amid international turmoil. The gay sex ban in India was rejected. Pope Francis called for a day of prayer and peace, declared the death penalty unacceptable, and grappled with issues of sexual misconduct in the Church. El Chapo, the suspected infamous Mexican drug lord, was prosecuted. Legalization of recreational marijuana expanded. Thousands of the suspected infamous Mexican drug lord, was prosecuted. Legalization of recreational marijuana expanded. Thousands of artifacts were returned to their rightful owners, including the 800-year-old heart of Laurence O’Toole, first Irish archbishop of Dublin. The National Museum of Brazil burned down, losing countless artifacts. Meghan and Prince Harry were married at Windsor Castle, and Queen Elizabeth threw a 70th birthday party for her son.

In technology, AT&T announced plans for a 5th generation (5G) wireless network. Amazon proposed an automated grocery store, chose New York and Northern Virginia as their Headquarters 2, and taught Alexa sign language. Apple’s worth reached $1 trillion. Elon Musk sent his Roadster into space via a SpaceX rocket and gave up control of Tesla. The possibility of flying and talking vehicles was discussed. Nokia and Vodafone plotted a mobile phone network for the moon, and NASA launched missions to Mars and to the Sun. On a somber note, a woman was killed by a self-driving Uber in Arizona, thousands downloaded a 3D-printed gun blueprint, hackers scored, people had information improperly used by Facebook, Twitter suspended accounts in an effort to decrease misinformation, and Sears (an empire of days gone by) declared bankruptcy.

2018 was the year of the Winter Olympics in PyeongChang and its many awe-inspiring performances, but also a year where many cities opted out of hosting future games due to unbearable costs. It was also the year France recaptured the FIFA World Cup, the Eagles won the Super Bowl, the Washington Capitals won their first-ever Stanley Cup (after 45 years of existence, against the inaugural Vegas Golden Knights), and the Red Sox won the World Series. Among other hotly discussed stories, the NFL announced teams would be fined if players knelt during the national anthem, and the Cleveland Indians removed the “Chief Wahoo” logo from their uniforms.

On the medical side, there were outbreaks of cholera, listeria, and Ebola in Malawi, South Africa, and the Congo, respectively. Salmonella and E. coli were seen in the U.S., the flu had its worst run in the past decade, and polio-like neurological cases were confirmed by the Centers for Disease Control and Prevention.

The 2018 Nobel Prize in physics was awarded to Arthur Ashkin, Gerard Mourou, and Donna Strickland for their work on lasers. The Nobel Prize in chemistry was awarded to Frances Arnold, George Smith, and Sir Gregory Winter for their work on enzymes, peptides, and antibodies. The Nobel Prize in medicine went to James Allison and Tasuku Honjo for their discovery of cancer therapy inhibition of negative immune regulation. The Nobel Peace Prize went to Denis Mukwege and Nadia Murad for their work giving greater visibility to war-time sexual violence so that the perpetrators can be held accountable. The Nobel Prize in economics was awarded to William Nordhaus and Paul Romer for integrating climate change and technological innovations respectively into long-run macroeconomic analysis. There was no Nobel Prize in literature due to an ongoing scandal. The Turing Award (computing) went to former Stanford University President John Hennessy and his close colleague David Patterson for their work in computer architectures. Per tradition, there were four Fields Medal (mathematics) recipients in 2018: Caucher Birkar, Alessio Figalli, Peter Scholze, and Akshay Venkatesh, all under 40 years of age. Regarding the Grammy Awards, the Album of 2018 was 24K Magic by Bruno Mars. Regarding the Golden Globe Awards, the best miniseries was Big Little Lies; the best crime-drama film was Three Billboards Outside Ebbing, Missouri; the best Comedy-Drama was Lady Bird; and the best animated feature film was Coco.

Several names exist in memory, although the people are in our world no more. To mention but a few: lunar astronaut John Young; Republican Senator John McCain; President George H.W. Bush and First Lady Barbara Bush; fashion designers Hubert de Givenchy and Kate Spade; chef Anthony Bourdain; author and columnist Charles Krauthammer; Aretha Franklin, singer and queen of soul; Neil Simon, writer known for “Barefoot in the Park” and “The Odd Couple”; William Golding, writer known for “Butch Cassidy and the Sundance Kid” and “All the President’s Men”; actor Burt Reynolds; Microsoft co-founder Paul Allen; Prince Henrik of Denmark; and theoretical physicist Stephen Hawking. From within our community, voices that exist no more also include: Hsieh-Fu Cheng (PhD), Anna Geddie (CNMT), Joseph McNally (MD), Carl Neufeld (DO), and Anthony Vasilas (MD), among others.

And, for a twisted smile, 2018 was also the year United Airlines refused to accept an “emotional support peacock” on a flight due to its weight and size. The swimsuit competition was dropped from Miss America, and California announced a new law requiring coffee be served with a cancer warning since acrylamide, a possible cancer-carrying byproduct of roasting coffee beans, can be found within.

In terms of the PET CoE, the Mid-Winter Meeting was held in January 2018 in Orlando, Florida, and included talks on (Continued on page 6. See President’s Report.)
connected at once. You can reserve one online before your trip for pick-up at the airport or your hotel. When leaving Japan, you can arrange to have this left at your hotel or at the airport, or you can drop it off at a local post office (return envelope and postage usually provided).

- If you are flying directly to Tokyo, there are two airports, Haneda and Narita. Narita is the primary international airport and is located approximately 37 miles east of Tokyo. If you are staying in or starting your travels in Tokyo, you can reach your hotel from Narita via taxi, bus, rental car, or train; my preference is by train or bus. I really do not recommend driving a car in Tokyo. Uber is available in Tokyo only, but there is no significant difference in cost if you take a regular taxi. A taxi to your hotel is likely going to be just under $200, very expensive and a long drive. Although it is a long ride to Tokyo, I prefer an airport limousine bus, which may drop you off directly at your hotel (depending upon where you are staying) and is much less expensive at about $30. You can book this service online before arriving in Japan. Another good option is the Narita Express train, which takes you directly from the Narita airport to Tokyo. Once in Tokyo, plan to do a LOT of walking. There is also extensive train service and routes that can get you most anywhere in and around Tokyo. If you cannot understand how to use an electronic ticketing machine at a train station, there are always counters where you can talk to individuals in person for help. Hyperdia is an excellent app for determining train routes and times throughout Japan.

- If you plan to explore many other areas in Japan, I highly recommend the Shinkansen or bullet train. One very good option when using the Shinkansen is to purchase a Japan Rail Pass (also called JR Pass), which is solely available for overseas visitors to Japan. This can also be purchased ahead of your trip with shipment directly to your office or home before you leave. The advantages include discounted ticket prices and the ability to get on and off the train as many times as you would like without additional charge within a certain time period. There are routes to almost any area of Japan you would like to visit (Okinawa is the exception). My preference is to reserve my seats online ahead of time; however, this is not necessary.

- To get to Okinawa, you can travel by boat or airplane. If you plan to explore beyond your meeting site or hotel in Okinawa, a rental car is a very good idea. There are also several islands off the main Okinawa island that are accessible by bridge, boat, or airplane. You will need to obtain an international driver's license at least two weeks prior to your departure to Japan if you plan to drive. This can be obtained through a local U.S. AAA office. I have found that Google Maps on my iPad or cell phone (via the rented pocket WIFI) is more useful than GPS navigation in a rental car.

- As far as lodging, there are many good options. There are chain hotels close to most airports and/or train and bus stops, one example being the budget Toyoko Inn. If you want to get close to the Japanese culture, I would recommend renting, such as with Airbnb or hostels. Of course, there are also many resorts and higher-end hotels.

- Please remember that you do not tip in Japan. Also, the prices stated on items already includes the tax.

- To communicate with your friends, colleagues, or family overseas, I recommend using WhatsApp or something similar. You can text, talk, or even video talk without additional charge whenever you have WIFI access.

I hope you are able to travel to Japan in your future!
History

A 10-year-old boy presented with café au lait spots, Lisch nodules, and pain in his left posterior thigh and pelvis. An x-ray revealed a left gluteal soft tissue mass with bony infiltration of the left hemipelvis, in keeping with a plexiform neurofibroma (pNF). He was subsequently diagnosed with neurofibromatosis type 1 (NF1). He was followed by MR imaging once a year, which eventually demonstrated additional pNFs in the neural foramina throughout the spine and progression of disease in the left hemipelvis and bilateral lower extremities.

Four years following initial diagnosis, a baseline PET/CT scan was performed to characterize the progressive disease (Figure 1). Imaging findings demonstrated intense FDG avidity in the known soft tissue masses in the left hemipelvis extending down along the sciatic nerve to the left thigh (Figure 1A). The pNFs in the right thigh were minimally avid, as seen in the maximum intensity projection (MIP) (Figure 1B), and no abnormal FDG activity was seen in paravertebral pNFs. No other focal abnormality was seen in the remainder of the body. A biopsy of the left pNF confirmed the diagnosis of NF1 without malignant transformation. The patient continued to be followed with PET/CT and MRI.

A follow-up PET/CT scan performed six years later showed dramatic progression of disease. Markedly increased metabolic activity in the lower limbs is seen on coronal (Figure 2A), and frontal and lateral MIP views (Figure 2B). Mildly increased avidity was also identified in a left occipital pNF, as shown on the MIP and axial views of the head (Figure 2B-C). A biopsy of the left upper thigh confirmed transformation into a malignant peripheral nerve sheath tumor. The patient underwent radiation and surgery. Unfortunately, he later developed pulmonary metastases and succumbed to his disease.

Discussion

NF1 is one of the most common genetic diseases of the nervous system. Plexiform neurofibromas manifest in up to 50% of these patients and have a 5-10 percent risk of eventual malignant transformation. The literature suggests any pNF with a maximum standardized uptake value (SUVmax) above 3.5 on delayed imaging with FDG PET/CT is likely malignant and should be verified with biopsy. However, there is generally no optimal SUVmax to determine malignancy since there is a large overlap in SUVmax of benign versus malignant lesions.

In this case, PET/CT was useful in providing preliminary findings suggestive of malignancy in NF1 with pNF manifestation. These findings helped determine the sites for biopsy that would provide the most accurate results based on metabolic activity quantified by SUVmax. PET/CT may be able to detect malignant transformation of NF1 in early stages and allow for treatment as early as possible to increase the patient's chance of cure.

References

1. Neurofibromatosis Therapeutic Acceleration Program (NTAP). NF1 and Plexiform Neurofibromas [Internet]. USA: Neurofibromatosis Therapeutic Acceleration Program (NTAP); [cited 2018 Jul 18]. Available from: http://www.n-tap.org/plexiform-neurofibromas/
PET/MR Imaging: A Brief History and Development

Nicole Nardecchia, MBA, CNMT, PET, RT(CT)(MR)

PET/MR is innovative hybrid technology that combines two leading imaging modalities into one: PET, which involves the physiologic and localized metabolic data, and MR, which shows us an anatomical view of the patient complete with soft-tissue differentiation, cellular density, and contrast-weighted imaging. These PET and MR images are superimposed over one another to give a greatly detailed picture of both anatomy and physiologic function. In 2007, the first PET/MR scanners began to appear in the clinical setting, used primarily for neurological applications.

Practical Applications

In the research setting, advocates for PET/MR are working to identify ideal patient and disease candidates for the most practical and useful applications for this technology. The most common uses for PET/MR scans include oncology, neurology, and cardiology. In oncology PET/MR has the potential to provide more precise tumor localization that helps plan treatments and exposes patients to less radiation than a typical PET/CT. In addition, combining these high-value modalities may reduce the number of scans the patient must have, thus providing a convenient service for patients as well as highly detailed images.

Neurology is another area where PET/MR imaging is very useful, as we are able to view the metabolic brain function from PET along with the detailed anatomic mapping from MR. In cardiology it has been written that “PET/MRI scanners enable tissue characterization, morphology and ventricular function visualization. The complex algorithms of image analysis software can detect even subtle changes in tissue composition. Particularly, synergetic images can be promising for diagnosing and treating sarcoidosis, myocarditis and myocardial infarction.”

Technology

PET/MR technology is currently manufactured by many of our industry leaders, such as GE, Philips, and Siemens. Many of these scanners are used in the research setting to help identify staging, disease processes, and ideal patient candidates for this type of imaging. There are several technological challenges with PET/MR scanners. Scintillation crystals often include bismuth germanium oxide and lutetium oxyorthosilicate. Photomultiplier tubes (PMTs) must be designed that can function in a magnetic field. Long optical fiber tubes permit PMTs to be placed outside the fringe field. Because of the long fibers, image degradation may occur as some energy from the light transferring will be lost. Any electronics should be properly shielded for protection against the magnetic field.

Attenuation correction has long been a challenge for this technology. “Attenuation correction is required to account for the differences in photon absorption in different tissue of the human body, which is necessary to allow correct quantification of PET radiotracer activity. In PET/computed tomography (CT) this information is obtained from the CT data, whereas in MR imaging the attenuation map has to be generated using these specific MR imaging sequences and segmentation models for body tissues such as air, lung, fat, soft tissue, and cortical bone.” Of course, funding is another challenge when it comes to PET/MR scanners. The cost to any capital budget will be significant for this piece of equipment, with little immediate clinical return on the investment, as we are still largely in a research stage.

Nicole Nardecchia is the winner of the 2018 SNMMI Ursula Mary Kocemba-Slosky, PhD, Professional Relations Fellowship. She is the first technologist to win the award.

References

PET CoE News

SNMMI Mid-Winter Meeting

It is not too late to register! Online registration ends on January 14.

The 2019 SNMMI Mid-Winter and ACNM Annual Meeting will be held January 17-19 at the Renaissance Palm Springs in Palm Springs, CA.

The PET Center of Excellence is sponsoring:

- ONE session in collaboration with the Correlative Imaging Council (CIC): Cardiac PET/CT
- TWO sessions in collaboration with the Clinical Trials Network and Therapy Center of Excellence: Theranostic Agents: What’s New and What’s on the Horizon and Nuts and Bolts of Using PRRT

Check the program for times and locations.

Call for Volunteers

The PET Center of Excellence seeks volunteers for two key initiatives. If you are interested in participating in these working committees, please email K. Malaika Walton (mwalton@snmmi.org), associate director of governance. Please include a one paragraph statement of interest and your CV.

PET/MRI Working Group

The PET Center of Excellence has launched a PET/MR working group that will bring together members from across SNMMI. PET/MRI is an emerging imaging modality that requires significant development to realize its full potential in research and clinical care. The objective of the SNMMI PET/MRI working group is to support the development of PET/MRI and to educate physicians, researchers, and technologists. It will support educational activities at the SNMMI Annual Meeting, webinars, and workshops jointly sponsored with other organizations. PET/MRI is truly an intersociety modality requiring input from multiple organizations to help accelerate its development and clinical adoption. The new PET/MR group will work with the SNMMI community to address member needs and help advance PET/MRI.

Theranostics Task Force

The purpose of this committee is to focus on the utility of PET for therapy—specifically, to evaluate, educate about, and promote the use of PET as an adjunct to therapies. While the primary therapeutic focus is targeted radionuclide therapies, this working group will focus more largely on any role of PET related to therapies (i.e., patient selection and/or radiation treatment planning). Current projects are examining the role of $^{68}$Ga-DOTATATE for $^{177}$Lu-DOTATATE therapy in NETs and the role of $^{18}$F-FDG in radiation treatment planning.

Call for Volunteers (Continued from page 2.)

novel PET radiopharmaceuticals such as PSMA for prostate and non-prostate cancer and somatostatin receptor agents for neuroendocrine tumors. It was during this meeting that the FDA announced approval of Lutathera ($^{177}$Lu-DOTATATE). The Annual Meeting was held in June in Philadelphia, Pennsylvania, and we hosted several continuing education (CE) sessions on aspects related to PET, including a categorical on Practical PET/CT. It was during this meeting that we announced that Peter Conti, MD, PhD, had won the PET CoE Valk Award for his contributions to PET over the years.

We have tried to make our newsletters informative by devoting issues to Axumin, somatostatin receptor PET, FDG PET/CT in infection imaging, FDG PET/CT for imaging noninfectious causes of fever of unknown origin, and, most recently, the use of contrast media in PET/CT imaging (this last lead article provides CE credit as well). Additional articles and cases covered interpretative criteria for PSMA PET, PET/MR, radiation safety, and pediatrics, among others. Please do not hesitate to contact Malaika Walton at MWalton@snmmi.org should you wish to see a prior issue that you may not have had access to.

In terms of upcoming meetings, we are planning to co-host CE sessions at the 2019 Mid-Winter Meeting, to be held January 17–19 in Palm Springs, CA, including Theranostic Agents Beyond Lutathera: What’s New and What’s on the Horizon as well as Nuts and Bolts of Using PRRT and a Cardiac PET/CT Workshop. We will also be involved with categorical sessions and an array of CE events at the Annual Meeting, June 22–25 in Anaheim, CA. More to follow. We hope 2019 will also see a PET/MR symposium as well as webinars for our members.

Although it has been said that “Tomorrow, and tomorrow, and tomorrow creeps in this petty pace from day to day to the last syllable of recorded time,” for me, at least, the years go by faster and faster. For some, 2018 will have been the most important year of their lives, and for others it will be just a blur. There were dark moments, but also moments of true joy. There are too many stories, by far, to tell them all, and what I have written just scratched the surface. If I have missed your own highlight of the year, I am sorry. Of this, however, I am sure: What was true in the beginning remains true at the end. The PET CoE would not exist without the help and devotion of those who support us, and we would be far poorer without you. So thank you! Also, I do believe that there is always a way, although the path might be ever so obscure.

So then, I shall conclude the year with much the same words with which I began it. Our world moves forward, spurred by those who live in the now wishing for a better tomorrow. Although it has been said many times and many ways, no matter your age, may you continue to dream through the years…and I hope your dreams come true!
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.

Imaging AI spots and predicts Alzheimer’s signs 6 years early in PET scan study
Fierce Biotech

Researchers identify a mechanism that fuels cancer cells’ growth
Medical Xpress

Imaging Tool Quickly Measures Brain Cancer Treatment Effectiveness
Alliance of Advanced Biomedical Engineering News

PET Ready To Expand Into Sports Medicine And Beyond
Imaging Technology News

Brain Scans Suggest Pain of Fibromyalgia Isn’t Imaginary
HealthDay

PET-CT Responses After First-Line Immunotherapy in Follicular Lymphoma
Cancer Network

Scientists show change in beliefs associated with dopamine in brain
Medical Xpress

PET Scan “Hot Spots” Help Visualize Inflammatory Complication of HIV
NIH News and Events

Tau PET Tracer Called Accurate for Alzheimer’s Diagnosis—But role in patient care still uncertain
MedPage Today

Benefits of Exercise for Parkinson’s Patients Linked to Increased Dopamine Release, Study Suggests
Parkinson’s News Today

ATTEND A PET CENTER OF EXCELLENCE SPONSORED CATEGORICAL SEMINAR AT THE SNMMI 2019 ANNUAL MEETING

Join more than 5,000 members of the profession at the SNMMI 2019 Annual Meeting—June 22-25 in Anaheim, California—to learn about the techniques and research helping provide a tailored approach to the identification, diagnosis, and treatment of disease.

Get a Comprehensive Overview on a Topic of Critical Interest to You and Your Practice.

Add a full-day PET Center Sponsored Pre-Meeting Categorical Seminar to your registration:

- Image Guided Decision Making and Therapy for Optimal Cardiovascular Patient Care, sponsored by the Cardiovascular Council and PET Center of Excellence
- PET Imaging of Autoimmunity and Immune Checkpoint Inhibition Efficacy, sponsored by the Center for Molecular Imaging Innovation and Translation, Radiopharmaceutical Sciences Council, and PET Center of Excellence

Register today!
www.snmmi.org/AM2019
Novel Tracer Developed for Precision Targeting of Non-Small Cell Lung Cancer

Researchers have developed a new nuclear medicine tracer that could improve diagnosis and treatment of non–small cell lung cancer. Research published in the November issue of The Journal of Nuclear Medicine found that the new tracer, $^{99m}$Tc-HYNIC-cMBP, produced clearer images in less time than currently used tracers and was more rapidly eliminated from the body, reducing radiation exposure.

The c-Met receptor—a promising therapeutic target for this disease—is a tyrosine kinase receptor that promotes the growth of cancer cells, particularly in NSCLC. When c-Met receptors are elevated, cells may be resistant to EGFR-targeted therapy. However, with precise targeting of the c-Met receptor, physicians may be able to more effectively treat this disease.

In the study, the novel radiotracer was developed and cultured in two NSCLC cell lines, H1993 (high c-Met expression) and H1299 (no c-Met expression), and the activity and uptake of the $^{99m}$Tc-HYNIC-cMBP tracer was assessed. These tumor cells were then transplanted into mice, and in vivo tumor specificity was measured by SPECT at various intervals after injection of the tracer. Blocking assays, biodistribution and autoradiography also were conducted to determine the tracer’s specificity.

The authors found the preparation of the $^{99m}$Tc-HYNIC-cMBP imaging agent to be simple, providing a high yield of the tracer with few associated costs. Biodistribution and autoradiography showed significantly higher accumulation of $^{99m}$Tc-HYNIC-cMBP in H1993 tumors than in H1299 tumors. In addition, the H1993 tumors were clearly visualized after only a half hour in SPECT images, while the H1299 tumors were not observed at any time. The tracer was also cleared rapidly, which is favorable for reducing exposure to radiation, background noise and long delays between treatment and imaging readout.

“To the best of our knowledge, there are no other c-Met–targeted imaging studies in NSCLC using peptide-based radiotracer to date,” noted Baozhong Shen, MD, PhD, professor of medical imaging and nuclear medicine and the first president of the Fourth Hospital of Harbin Medical University. “Our research results confirmed the feasibility of detecting c-Met expression in NSCLC with the novel SPECT tracer. Upon further optimization, the SPECT tracer may be translated into clinical use for screening and monitoring therapeutic response in NSCLC patients.”
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