This has been an exciting quarter for the community of Nuclear Medicine and Molecular Imaging. New PSMA-targeting therapy and diagnostic agents have been approved for clinical use for the treatment and management of patients suffering from prostate cancer. The SNMMI has been a forefront of advancing theranostics, and we, as the community of physicians, scientists, healthcare workers, industry, staff, and all stakeholders, are truly excited about our new value of patient care. Thank you so much for your support of the SNMMI Value Initiative.

To further enhance our efforts, the SNMMI is conducting a strategic planning effort for the next 3-5 years, one that ties directly to the work of the Value Initiative's five domains. Through 21 interviews with key leaders and stakeholders, physicians, scientists, technologists, and industry; 18 qualitative responses to an environmental scan; and a full membership survey, a team of SNMMI leaders consolidated the findings to flesh out the needs, trends, and priorities of the field moving forward.

Some key findings and observations reinforced the core work of the Value Initiative. Throughout the strategic planning process, themes emerged around our continued need to improve quality of practice, research and discovery, the workforce pipeline, advocacy, and outreach. The field is thriving, and we have an abundance of opportunity.

The VI and staff have worked hard to increase the visibility of Nuclear Medicine with the public and have had some excellent mainstream media coverage, and work remains to be done. We also received a great deal of feedback that we need to continue to find ways to communicate to many audiences about the work we are doing, showcasing our progress.

The SWOT analysis identified the ongoing need for not only technical reimbursement, but also physician reimbursement, and agility as the field grows, and more Nuclear Medicine physicians engage in the practice. Expansion of therapies and theranostics is a clear trend. SNMMI has a wealth of resources in theranostics and will continue to consolidate and make them easily accessible on the Radiopharmaceutical Therapy Central website. Training, education, development and expansion of the workforce, and patient-centered care and practice for clinicians are top needs as nuclear medicine advances. Collaboration throughout the field with other societies, industry, and beyond was another big theme. Our work with other societies and outreach to referring physicians

Continued on page 12. See Reflection, Renewal, Resolve.
Usage of blood volume testing for inpatient and outpatient use within nuclear medicine facilities is growing, driven by the demand from heart failure and critical care practitioners who struggle with readmissions, mortality and resource utilization. Published data show reductions in mortality, length of stay, and hospital readmissions have been achieved by care informed by direct intravascular volume measurements to ensure adequate decongestion and anemia treatment in heart failure, and optimal resuscitation in critical care.

These tests have been administered utilizing Daxor BVA-100® (Blood Volume Analyzer), the first diagnostic blood test cleared by the FDA to provide safe, 98% accurate, objective quantification of total intravascular blood, red blood cell and plasma volume compared to patient-specific norms. The test is based on the indicator dilution technique, the gold standard methodology for blood volume measurement. Volumex™ Albumin I-131 tracer is injected intravascularly at the bedside and a series of blood samples are drawn and sent to the nuclear medicine laboratory for processing with results achievable within 1 hour. The BVA-100 automatically calculates volumes by measuring tracer concentration in the blood samples and generates a report showing deviations in total blood, red blood cell, and plasma volume from the patient’s ideal volume values. (Figures 1 & 2)

BVA applied as an early diagnostic provides clinicians with patient-specific information to create an informed fluid management care plan that helps avoid over or under treatment, and prevent risky therapeutic missteps. Today, BVA-100 tests are performed routinely for both in and outpatient care with reimbursement by both public and private insurers.

Achieving Better Outcomes That Help Hospitals Improve Quality Metrics

A propensity-score matched outcome analysis published in the Journal American College Cardiology - Heart Failure studied outcomes of 245 consecutive acute heart failure admissions with mixed ejection fractions which used BVA measurement to guide in-hospital care. This study demonstrated significantly improved outcomes with BVA-guided treatment: 82% reduction in 30-day mortality (2.0% vs. 11.1%; p < 0.001), an 86% reduction in 365-day mortality (4.9% vs. 35.5%; p < 0.001) and a 56% reduction in 30-day readmissions (12.2% vs. 27.7%; p < 0.001). (Figure 3) Many hospitals have prioritized improving 30-day outcomes as a key quality metric tracked by The Centers

Continued on page 13. See HSA-I 131 Test For Blood Volume.
Overcoming Lutetium-177 Production and Supply Challenges

BY ISOTOPIA NUCLEAR MEDICINE, A SNMMI VALUE INITIATIVE PRINCIPAL MEMBER

Lutathera and Lutetium-PSMA 617 are FDA-approved therapeutic radiotracers used to treat neuroendocrine tumors and prostate cancer. As the demand for radioisotopes increases, producers are challenged to supply the market with sufficient product to accommodate the heightened demand without compromising product quality and patient health. In addition, several clinical studies in different clinical development stages are ongoing adding to commercial demand.

Taking the above into consideration, the importance of Lutetium-177 in cancer treatment cannot be overstated. In fact, over 40 million nuclear medicine procedures are performed every year, and the demand for radioisotopes is increasing rapidly.

Lutetium-177 is a medium-energy β-emitter (490 keV) with a long physical half-life of 6.7 days, which is helpful for synthesis and transport, and an average beta–particle range in the soft tissue of 670 nm and maximal tissue penetration of 1-2 mm. Another benefit of Lu-177 is that it produces low-energy gammas (113 keV, 208 keV), suitable for imaging purposes, allowing biodistribution and excretion kinetics to be monitored and calculated dosimetry with SPECT-CT. Lutetium-177 has favorable chemistry for chelation. Therefore, it is gaining popularity for therapy applications.

Despite its many benefits, manufacturing radioisotopes such as Lutetium-177 is a complex process requiring a deep level of expertise and logistical processes. From technical capabilities and infrastructure to reliable manufacturing and distribution, each phase of the process needs to be carefully orchestrated to ensure optimal quality and “on time” supply to patients.

Choosing the right isotope supplier with a scalable solution that follows GMP practices is essential. The right supplier should also have deep regulatory expertise, and the infrastructure to meet tight deadlines.

Lu-177 Transportation Challenges

One of the main challenges remaining is the transportation of Lutetium-177 over long distances. For even the most experienced pharmaceutical companies, this remains a massive hurdle. The successful transport of radioactive materials is vested primarily in logistics capabilities. That being said, especially during Covid, being closer to the customers helps de-risk logistics to ensure safe delivery for each patient. To solve this challenge in North America, Isotopia set up a manufacturing site in partnership with The Centre for Probe Development and Commercialization (CPDC) in Hamilton, Canada which began commercial supply of n.c.a. Lutetium-177 in March 2022.

Production in Canada is designed to serve customers in North America and address the growing need for Lu-177, and of course, save costs, transportation, and shorten patient arrival time.

Learning From the Past

Although most therapeutic radionuclides are produced in nuclear reactors, only a few nuclear reactors produce therapeutic radionuclides. Commercial production of radionuclides occurs in research reactors, which are also used for several other research or industrial applications.

Between 2008 and 2010, several reactors were temporarily shut down during what was known as the Moly crisis, during which technical glitches at a Dutch nuclear reactor that produces medical isotopes lead to rationing of medical tests and treatments globally.

More recently, a shutdown at a nuclear reactor in Petten, in the Netherlands, impacted global supplies of molybdenum-99 (Mo-99) and lutetium-177 (Lu-177) for medical use. These unexpected dips in supply led to reduced shipments of medical isotopes to many hospitals.

Considering these issues from the past, seeking a supplier with a proven supply and a network backed by long-term agreements is key. The ability to maintain weekly Lutetium-177 production ensures that future demand is covered. A stable supplier such as Isotopia is wisely engaged with a network of reactors around the globe to back up each

Continued on page 12. See Overcoming Lutetium-177 Production and Supply Challenges.
PYLARIFY® (piflufolastat F 18) Injection and PYLARIFY AI™: From Innovation and Regulatory Submission to FDA Approval and Market Adoption

VINCENT A. DIPIPPO, PhD, SENIOR DIRECTOR, CLINICAL SCIENCE COMMUNICATIONS LANTHEUS HOLDINGS, INC., PARENT COMPANY OF PROGENICS PHARMACEUTICALS, INC.

Figure 1: PYLARIFY PET/CT study analyzed using PYLARIFY AI showing multiple prostate and regional lymph node lesions. The software automatically detects, quantifies and labels by stage and anatomical location hotspots consistent with prostate cancer disease, and outputs summary PSMA scores on patient and regional levels to help physicians track disease burden over time.

PYLARIFY New Drug Application Approval

It was on May 27, 2021, just under six months after NDA submission, when Lantheus Holdings, Inc. (North Billerica, MA) announced FDA approval of PYLARIFY® (piflufolastat F18; previously referred to as 18F-DCFPyL).

PYLARIFY, a fluorinated small molecule prostate-specific membrane antigen (PSMA)-targeted positron emission tomography (PET) imaging agent, enables visualization of the prostate, prostatic bed, lymph nodes, bone, and soft tissue to detect recurrent and/or metastatic prostate cancer. The recommended imaging dose is 333 MBq (9 mCi; range: 296-370 MBq or 8-10 mCi), administered as an IV injection.1 With FDA approval, PYLARIFY became the first commercially available PSMA-targeted PET imaging agent for prostate cancer for both men with recurrent prostate cancer and those with suspected metastasis prior to initial definitive therapy such as radical prostatectomy and/or radiation therapy.1 This novel imaging modality can provide more accurate and earlier detection of disease than conventional imaging such that more informed treatment decisions may be made between physicians and their patients.

PYLARIFY’s regulatory approval was based on two pivotal studies (OSPREY and CONDOR) that established its safety and diagnostic performance in both the high-risk and biochemically recurrent prostate cancer patient populations, respectively.2,3 OSPREY (Cohort A) results showed improvements in specificity and positive predictive value (PPV) compared to conventional imaging and CONDOR results demonstrated high correct localization and detection rates in patients with recurring disease at low PSA values (median PSA 0.8 ng/mL). In both studies, PYLARIFY was well tolerated with headache, dysgeusia and fatigue being the most common adverse events (≤ 2% of patients).

In recognition of this paradigm shifting moment in prostate cancer imaging, in September 2021, the Society of Nuclear Medicine and Molecular Imaging (SNMMI), in collaboration with a number of key medical groups including the American Urological Association (AUA) and American Society of Clinical Oncology (ASCO), developed a new set of appropriate use criteria for PSMA-targeted imaging technology. In addition, that same month PSMA PET imaging with PYLARIFY was included in the updated National Comprehensive Cancer Network (NCCN) Guidelines for prostate cancer, a widely recognized and adopted standard for clinical...
Capintec and Biodex Brands Merge Under Mirion Technologies

BY MIRION, A SNMMI VALUE INITIATIVE PRINCIPAL MEMBER

Anyone familiar with the manufacturing space for nuclear medicine technology and supplies would have noticed significant changes to in recent months. As of the start of 2022, two leading brands of nuclear medicine products and technology, Capintec™ and Biodex™, have joined forces to provide customers with a more streamlined, efficient buying process for all their nuclear medicine instrumentation and supply needs.

Over the last several months, the two divisions have worked to consolidate their product assortment under one roof in an effort to strengthen the overall experience for the customer.

An Opportunity to Offer the Best of the Best

The move comes following the joining of the two brands under Mirion Technologies, a global company specializing in technological solutions for radiation detection, protection and measurement. With the strength of this powerhouse behind them, there was an opportunity to integrate the two product lines in a way that would highlight the top product innovations from each brand.

The Capintec brand has been a leading worldwide supplier of nuclear medicine instrumentation for over 50 years. Their Captus® Thyroid Uptake System and CRC® line of dose calibrators are known and trusted for their safety and high quality. Biodex contributions have been equally groundbreaking. Their radiation safety and shielding innovations, including their top-quality line of customizable lead-lined furniture, has a more than 60-year history of serving the medical community.

By offering all nuclear medicine products and accessories from both product lines through Capintec.com, customers can now benefit from one-stop shopping for all their supply needs.

Stronger Together Under Mirion

Capintec was acquired by Mirion in July 2019. Biodex was then brought into the Mirion fold a year later in September 2020. Seeing the individual strengths of the two companies, Mirion saw them as an appropriate fit to join their growing medical division.

The Mirion mission is “To harness our unrivaled knowledge of ionizing radiation for the greater good of humanity.” With all the significant contributions the two brands have made over the last several decades to further safety and proficiency in nuclear medicine and molecular imaging practice, what they’ve always stood for is well aligned with the Mirion vision for the future.

With the added support of Mirion, the teams behind Biodex and Capintec nuclear medicine solutions can look forward to an expanded product line, more resources and a more streamlined buying experience for industry professionals.

What Does this Mean for Customers?

Understanding that the merging of the Capintec and Biodex nuclear medicine product lines is a big change for many, the company is committed to keeping consumers informed every step of the way.

Here is what customers can expect:

Having successfully completed the integration of the Capintec and Biodex product lines, all nuclear medicine products can be found on Capintec.com, searchable by product category or model number.

Continued on page 19. See Capintec and Biodex Brands Merge.
JOIN US FOR THE 2022
ANNUAL SCIENTIFIC MEETING IN
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www.canm-acmn.ca
Focus on Actinium-225
BY DR. RICHARD ZIMMERMANN AND TALA ALLAHHAM, THE ONCIDIUM FOUNDATION

The oncology world is just discovering the benefits of Lutetium-177 (177Lu) that already other promising radionuclides are emerging. Amongst them, Actinium-225 (225Ac), an alpha particle emitter, is presenting new and different advantages that bring renewed hope for patient treatment.

Grasping the potential

The time between the identification of interesting new radionuclides and their availability at the industrial scale has been typically spanning over decades. For instance, the story of 177Lu really started around 1998, with the availability and the preliminary publications of animal therapy and it took until 2017 for EMA and 2018 for FDA approval of the first marketed drug, 177Lu-Oxodotreotide, to reach the market. Actinium has been known and tested in human for more than 20 years, and it is now anticipated that the first 225Ac-labeled drug may reach the market by 2026 at best.

Nowadays, new radiopharmaceuticals develop successfully around a new radionuclide only if an industrial key player believes and decides to invest in it. As long as a radionuclide is not available with a guarantee of easy large-scale production and affordable price, the attempts to develop associated radiopharmaceuticals remain in the realm of academic research. What’s more, to be taken seriously, any new radionuclide must show some advantages compared to the existing “standard”. So, what is so interesting about 225Ac?

What is so interesting about 225Ac?

225Ac has been known for a while now but was only considered when physicians discovered that Lutetium is not the only solution and that some tumors would need something “stronger” in terms of cancer cell destructive potential. An alpha emitter should do the job, meaning, in other words, that an alpha particle could destroy what an array of beta particles cannot. By replacing 177Lu with 225Ac in a molecule that has already proven a certain efficacy (such as the PSMA peptides or somatostatin analogues for example), superiority might be established in non-responder or relapsing patients. This became the real starting point of all this narrative, even though precursors such as radiolabeled antibodies (225Ac-Lintuzumab, 225Ac-Daratumumab, developed by Actinium Pharma) have been of high interest for some time already. When it became obvious that the substitution of Ac for Lu was feasible in many Lu-labeled molecule, the level of interest in the production of 225Ac in the industry was triggered.

Challenges regarding implementation

Around 2015, the worldwide capacity of 225Ac reached about 1.5 Ci. Even considering that single dose amounts needed per patient with alpha emitters compared to beta-emitters will be far lower (10 µCi for 225Ac vs 100-150 mCi for 177Lu), this total available amount would considerably limit access for a high number of patients. Researchers associated with the industry decided to tackle the problem and among the almost 10 different methods to produce 225Ac, the four most efficient methods were selected and investigated.

The original process and presently the only method leading to 225Ac available for development programs is based on a generator. This historical source is obtained through the natural decay of Thorium-229 (half-life 7,340 years) itself a decay product from Uranium-233. Unfortunately, the precursor is considered as strategic material, and the extraction of thorium is cumbersome. Only a few curies of 229Th are currently available for decay product extraction. Furthermore, there are only three sites (USA, Germany and Russia) presently able to produce today a maximum of 1.7 Ci of pure 225Ac per year. Two of them intend to increase their capacity over the next years but this is likely to be limited to less than 5 Ci. Even though a new company stepped in recently (TerraPower, USA) is expected to increase the availability (estimated beyond 100 Ci over the next

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What’s the Difference Between Increased Access and Equal Access When It Comes to PET/CT?

BY UNITED IMAGING, A SNMMI VALUE INITIATIVE PRINCIPAL MEMBER

“Access” has become an industry buzzword. Lots of us talk about it, some act on it, and generally speaking, it’s good news for patients that there’s a conversation about it.

Access in molecular imaging has traditionally meant getting technology into the hands of more rural healthcare providers. The need is significant. According to The Journal of the American Medical Association (JAMA), “nearly 20% of U.S. residents, about 65 million people, live in small towns and sparsely populated areas...”1 Not all rural hospitals and imaging centers are the same, and not all rural patient populations are the same. But people generally travel further in rural areas than in cities to get scanned, resulting in more time and expense – and healthcare providers that serve them are often under budget pressure and don’t have the most modern, versatile technologies.

Why is “access” not enough? Why isn’t it enough to get more scanners into the hands of more hospitals and imaging centers, so that more patients can access those services?

The focus the industry needs is on Equal access. In the case of PET/CT, for example, an article in The Journal of Nuclear Medicine Technology says: “The superiority of PET/CT...in cancer assessment has created the need in rural community hospitals to acquire this technology.”2 The point is not just to make technology accessible – the point is to make state-of-the-art technology accessible.

Consider the uEXPLORER®, a first-of-its kind, ultra-high-resolution digital PET/CT with a 194 cm axial PET FOV that enables the total body to be scanned in one bed position. In use at UC Davis Health and select other institutions, it’s groundbreaking technology. Not every healthcare provider can accommodate it. However, United Imaging takes uEXPLORER technology and embeds it in other molecular imaging scanners up and down the portfolio. That ensures no matter which PET/CT scanners a healthcare provider purchases, they get the same core innovations that the highest-end scanner offers. Unique in the industry, our uMI 550 in particular allows that sophisticated technology to show up in a small hospital in Manhattan, Kansas just as easily as it could show up in an academic institution in Manhattan, New York. To extend this commitment even further, United Imaging innovated state-of-the-art digital PET/CT in a mobile configuration, bringing uEXPLORER technology to even more rural areas.

That approach, taking the most sophisticated core innovations and embedding them in technology at all budget levels, is what makes Equal access possible. It’s not a new concept in product development. However, in medical imaging traditionally, it’s not the most common. It can be enabled by vertical integration, where a manufacturer exerts substantial control over the innovation process, manufacturing process, and supply chain. It’s also enabled by a commitment to platform design that applies the same technology across systems and focuses R&D investment on new innovation, not redesign for lower cost platforms. United Imaging took that approach

Continued on page 17. See What’s the Difference.
How Imaging Advancements Are Helping Cardiologists Prevent Unnecessary Cardiac Catheterizations

BY MARTY SHIRLEY, CNMT, DIGIRAD

While cardiac imaging has seen drastic advancements in image quality, inconclusive scans still happen. When they do, cardiac catheterization is the next step. When faced with a questionable scan, the risk of a false negative far outweighs the potential of a false positive.

While false positives are a fact of life, unnecessary catheterizations are frustrating for all. They are invasive, add unnecessary radiation exposure, and increase costs to the system. The good news is that technology is available to give interpreting physicians more diagnostic confidence about their images.

The Source of “Grey Area” Scans

Scans that are clearly positive or negative are not the problem – it’s images that could go either way that cause false positives. Images that fall into a “grey area” are read as indeterminate and are often the source of serious issues for interpreting and referring physicians when making life-sustaining decisions for their patients.

Many times, the source of the “grey area” is attenuation within the image. Any material that blocks the heart can be responsible for attenuation. It could be caused by anything from a large abdomen or breast tissue to the physical location of the patients’ diaphragm or even bone. The artifacts created can appear as fixed defects suggestive of myocardial infarction or as reversible and, therefore, suggestive of ischemia.

Ultimately, if you want clearer, more conclusive images, you need to remove the potential obstruction (attenuation) to clearly see the heart’s tracer uptake. Using imaging equipment with actual attenuation correction (AC) technology is a proven way to create clearer images and improve clinical confidence in the images.

Cardiac Imaging with Attenuation Correction

While the concept of Attenuation Correction has existed in cardiology for decades, technology has evolved considerably over the last few years. Older, scanning line source methods have been replaced with state-of-the-art, fluorescence-based technology making SPECT MPI with actual attenuation correction cost-effective and easy to implement in nuclear cardiology labs.

As a point of comparison, Positron Emission Tomography (PET) imaging has always incorporated AC and, in many ways, is why PET shows higher accuracy and fewer false positives than SPECT cameras (that do not have AC). SPECT MPI with Fluorescence AC combines solid-state SPECT scan advancements with actual AC technology to create precise, more conclusive SPECT images. By adding Fluorescence AC to traditional SPECT MPI studies, cardiologists can enhance clarity over standard MPI studies.

SPECT with Attenuation Correction

New SPECT MPI technology is now available that brings the benefit of actual AC into traditional SPECT imaging. Cameras such as the Digirad X-ACT+ leverage a technology called Fluorescence AC to create an added level of clarity.

Fluorescence AC is a method based on CT technology. It utilizes a fluorescence x-ray, resulting in tracer distribution clarity. FAC results in much lower radiation exposure to the patient. By combining FAC technology with SPECT, cardiologists can identify and remove attenuation artifacts and capture the accurate distribution of the imaging agent, thus allowing for higher reading confidence and diagnostic accuracy.

Currently, fluorescence ACT is only available in conjunction with the Digirad X-ACT+ camera. The X-ACT+ camera utilizes a unique combination of full-field, solid-state detectors, the FAC technology and software to deliver image clarity – True Attenuation Correction.

Using Attenuation Correction to Reduce False Positives

Ultimately, the way to reduce the number of false positives is to produce clearer images that allow for a more definitive diagnosis. Attenuation correction is a proven

SPECT imaging has been the most commonly used technology for diagnosing coronary artery disease and guiding the appropriate therapeutic strategy for decades. However, its benefits have been tempered by image attenuation artifacts. When SPECT images are generated by the emission and detection of photons from a radiotracer, tissue encountered on its pathway to the detector is absorbed or scattered. This causes a portion of the detected photons to be attenuated, or weakened, causing artifacts in the image.

The attenuation correction process compensates for these artifacts, and it has been shown to increase the accuracy of interpretation and enable absolute quantification. However, using conventional Anger camera systems, attenuation correction requires a supplementary computed tomography (CT) transmission scan or two-position imaging, using upright and supine or prone, to mitigate attenuation artifacts. This multi-step process increases the procedure time for the patient and the imaging department, and requires additional radiation dose.

Spectrum Dynamics, the company that introduced the digital D-SPECT® CZT-detector dedicated cardiac system to the market in 2007, has continued its passion for nuclear cardiology innovations. Its most recent development is a new solution for attenuation correction that eliminates the need for a CT scan and additional radiation — TruCorr® Attenuation Correction.

Transforming Workflow and Patient Experience

TruCorr® is a new available technology applying a Deep Learning approach for attenuation correction of myocardial perfusion scans acquired in the D-SPECT scanner. It uses the SPECT data from a single acquisition, with no additional scan time beyond D-SPECT standard clinical protocols. Using the patient’s emission data, TruCorr generates an attenuation map and reconstructs the data to create an attenuation corrected dataset. TruCorr® Attenuation Correction technology is expected to increase the specificity of cardiac imaging and enable more accurate quantitative analysis. As it is a software approach, it can be applied within the typical workflow of any laboratory. TruCorr will be particularly beneficial for sites performing dual position scans, sites where there is no hybrid scanner available, or where staffing issues make it difficult to schedule time to scan and process an additional CT-based transmission scan. It creates workflow optimization possibilities, potentially eliminating the need for rest imaging in low likelihood patients.

Applying Deep Learning to Diagnostics

TruCorr® technology is based on Deep Learning, a type of artificial intelligence that has brought significant advancements to health care in the areas of data analysis and image classification. A particular benefit is that it requires less guidance from humans and is able to self-verify its decisions. In fact, some convolutional neural networks (CNNs) have demonstrated similar or superior accuracy to humans in diagnostic imaging studies.

The TruCorr® algorithm is based on a CNN that was trained to assess reconstructed emission data and provide an attenuation map. The development of the deep learning attenuation correction algorithm involved thousands of slabs (input) extracted randomly from the reconstruction of myocardial perfusion SPECT imaging studies that also included a corresponding CT scan for comparison. The data analysis found TruCorr corrected images were similar to CT attenuation corrected images.

Increasing Confidence

“In our experience, TruCorr has dramatically reduced the perceived necessity to proceed with a rest image,” said Dr. Timothy Bateman, co-director of the Cardiovascular Radiologic Imaging Program at St.
Artificial intelligence (AI) based methods are becoming increasingly popular in PET imaging, mostly in the form of deep convolutional neural networks (DCNNs). These networks can be trained to benefit from the large volumes of acquired PET data for a given imaging scenario but they can also extract useful features from individual images without any prior training. These unique properties which do not exist in other analytical or statistical image reconstruction approaches make artificial intelligence based methods very attractive for PET.

In a working group at Canon and UC Davis we explore uses of artificial intelligence covering the entire image reconstruction chain. Intelligent devices can know which region of the body to scan for how long and later categorize datasets as those with high probabilities of having lesions. Intelligent algorithms can then reconstruct these datasets and the resulting images can be processed in the final step to assist doctors in making clinical decisions. In this article, we will mainly discuss the image reconstruction applications of AI.

The most common use of AI methods in PET are in the form of DCNNs for image denoising. These neural networks can be multilayer convolutional networks, can have U-net architectures or can be generative adversarial networks. Figure 1 shows the 8-layer residual neural network that is used in Canon for image denoising. This network is trained using a combination of real and simulated datasets corresponding to a wide range of activity distributions and count levels. The goal of this approach was to ensure that the network produced a good quality, low noise image regardless of the patient size, activity distribution or noise level. Figure 2 shows a representative image comparison between DCNN and standard (event driven, time-of-flight) OSEM. The training approach can be further refined by so-called “feature oriented training” where regions of interest are manually assigned higher weights during the training process so that lesions can be better preserved when new images are processed. Neural networks such as the one presented here greatly smooth background regions while leaving lesion activity levels mostly unchanged; depending on how they are applied, they may achieve higher signal-to-noise by reducing image noise compared to unfiltered OSEM or by maintaining resolution and local quantification better than conventional, postfiltered OSEM.

Artificial Intelligence Applications for PET Image Reconstruction

BY EVREN ASMA1, TIANTIAN LI2, ZHAOHENG XIE2 AND JINYI QI2

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The role of AI in PET imaging is much broader than just image denoising and AI can be applied to all the physical correction steps as well as processes such as data gating. Figure 3 shows an example of the use of a neural network for data gating. In this particular example, the network essentially operates as an autoencoder to extract features from the images reconstructed from very short duration datasets. These images are obtained by very rough reconstructions without any physical corrections to speed up the process. Once the latent feature vectors are extracted from the images, they are clustered using K-means clustering to determine the temporal frames that belong to the same gate. This results in data being gated not according to traditional phase or amplitude information but according to three-dimensional feature vector information extracted by the network. Figure 4 shows representative gated images as well as the gate histogram for a clinical dataset showing the number of counts in each gate.

Another exciting application of neural networks is in data and physical corrections such as attenuation,
must continue. Ultimately, our “why” is to advance patient care, and the Value Initiative’s collaborative dialogue is more important than ever to improve what our work is ultimately about: improving the clinical outcomes and lives of patients.

Thank you so much for being a part of the SNMMI Value Initiative.

Establishing a Global Footprint

On September 8th, 2020, The Centre for Probe Development and Commercialization (CPDC), a global leader in the development, production, and commercialization of radiopharmaceuticals, announced a collaboration with Isotopia Molecular Imaging for the production of n.c.a. Lutetium-177 and distribution in North America.

Isotopia’s CEO & Co-Founder Dr. Eli Shalom stated “The CPDC manufacturing site is the first step towards Isotopia’s global footprint plan to ensure efficient production of n.c.a. Lutetium-177 and will be added to its existing Drug Master File (DMF). CPDC’s strategic location in Southern Ontario, its professional and enthusiastic personnel, renowned expertise in logistics, and just-in-time delivery will enhance the distribution of Isotopia’s n.c.a. Lutetium-177 and secure supply for our radiopharmaceutical and CMO clients in North America.”

Communication is Key

Communication is vital for time-critical materials such as isotopes. The “just in time” nature of the supply chain can be achieved through various channels of communication. Suppliers should be a point of contact for everything from billing administration, and logistics to training.

Lutetium-177 suppliers should maintain a policy of open communication. When changes are required, especially in our dynamic climate, having open communication allows for a more collaborative and streamlined process, affecting all touchpoints.

To summarize

The future of nuclear medicine is promising, and the research being done now stands to extend further our ability to diagnose and treat disease. With continued investment in nuclear medicine research, radiotracers will continue to become more specific and effective at treating disease.

Overcoming supply and production challenges to the use of Lutetium-177 is the most important action to ensure the successful implementation of this promising medical innovation.
for Medicare & Medicaid Services.

In a randomized control trial published in the journal *Shock*, SICU patients at a Level-1 trauma center suffering predominantly from ARDS/sepsis/septic shock/hemorrhagic shock who received BVA guided care showed significant benefits including a 66% lower mortality rate (P<0.03). Analysis showed 44% of BVA test results led to a change in treatment strategy (P=0.004) and 36-hour earlier treatment decisions that care teams would not have performed absent the data from the BVA test. (Figure 4)

Data published in the journal *Critical Care* showed the BVA-100 test provided insights into the pathophysiology of volume derangements and capillary distress in critically ill COVID-19 patients enabling improved care. The research letter titled “Blood volume and albumin transudation in critically-ill COVID-19 patients” studied the abnormal blood volume profiles in mechanically ventilated patients admitted to the ICU. The data showed that COVID-19 patients suffer from significant capillary damage and blood volume deficits that care teams became aware of through the use of the BVA-100 test. (3)

Excellent Value in Healthcare

A recent study titled, “Cost-effectiveness Analysis of Early Blood Volume-Guided Management in Hospitalized Heart Failure Patients” showed BVA to be “extremely cost-effective” with a cost 80% less than other heart failure therapies that are considered “good value” by common quality metrics. The data also revealed an average life-extension of 2.32 quality-adjusted life years (QALYs) in addition to the cost savings. (4) (Figure 5)

Make A Difference Throughout The Hospital

In an era focused on value-based care, a cost-effective and precise diagnostic that provides immediate actionable data, describes the essence of value-based care. By offering the BVA-100 test, nuclear medicine departments can provide safe, accurate, comprehensive data to help clinicians optimize treatment plans and individualize care, improving outcomes and reducing duration and cost of care.

“We have been offering the BVA-100 test for over a decade and have found it simple to perform and interpret. It provides our clinicians with additional information to supplement their clinical assessments and traditional quantitative tests. It is rewarding that we play an integral and valued role in the management of patients.” - Hung Dam, M.D. Chief, Section of Nuclear Medicine, Department of Radiology, ChristianaCare

To learn more about blood volume analysis visit daxor.com.

REFERENCES

oncology decision making.\(^4,5\)

Upon approval, PYLARIFY was available to imaging centers in parts of the mid-Atlantic and southern regions of the US but quickly became broadly available nationwide with 23 activated PET manufacturing facilities as of March 2022. Lantheus’ objective is to maximize the availability of PYLARIFY across the country to more men and their health care providers thus providing access to this game changing imaging agent. The successful adoption of this strategy has resulted in thousands of men receiving a PYLARIFY PET/CT scan by the end of 2021.

**PYLARIFY AI\(\text{TM}\)**

PYLARIFY PET/CT provides valuable disease state information for physicians and yet it is also of critical importance that PSMA-targeted imaging has a consistent and standardized platform to efficiently and accurately identify and quantify PSMA uptake at the lesion level for prostate cancer patients. To this end, in July 2021 Lantheus announced that its subsidiary, EXINI Diagnostics (Lund, Sweden), was granted 510(k) clearance by the FDA for its new medical device software, aPROMISE\(\text{TM}\) (automated PROstate Cancer Molecular Imaging Standardized Evaluation), the first and only FDA cleared artificial intelligence (AI) enabled PSMA digital application. Once the FDA cleared aPROMISE, the PYLARIFY AI\(\text{TM}\) brand name was adopted. Using a deep learning algorithm, PYLARIFY AI was trained and validated using more than 3,000 PSMA images and subsequently launched in November 2021. As described in the FDA clearance notification, “aPROMISE is intended to be used by healthcare professionals and researchers for acceptance, transfer, storage, image display, manipulation, quantification and reporting of digital medical images. The system is intended to be used with images acquired using nuclear medicine (NM) imaging using PSMA PET/CT. The device provides general Picture Archiving and Communications System (PACS) tools as well as a clinical application for oncology including marking of regions of interest and quantitative analysis.”\(^6\)

Established by the foremost experts in prostate cancer imaging, PROMISE criteria were developed to standardize quantitative evaluation of prostate cancer lesions by location using PSMA PET/CT.\(^7\) PYLARIFY AI rapidly and robustly facilitates this quantification process in the appropriate anatomical context, thus enabling clinicians to make routine use of an automated approach to patient evaluation.

Two key studies have been published describing the utility of PYLARIFY AI. First, in Nickols et al., a retrospective analysis was performed on PYLARIFY PET/CT images from 109 veterans with intermediate- or high-risk prostate cancer in order to validate the performance of PYLARIFY AI.\(^8\) Two independent nuclear medicine physicians conducted PYLARIFY AI-assisted reads resulting in standardized reports that both quantified individual prostate cancer lesions and staged patients. This was then compared with staging by conventional imaging. The analysis resulted in significant upstaging in patients with localized and regional disease at 23% (20/87) and 25% (2/8), respectively. This research also demonstrated PYLARIFY AI platform consistency between readers thus contributing to the broader standardization of PSMA imaging assessment and its potential clinical utility in patient management.

Separately, Johnsson et al. evaluated the analytical performance of PYLARIFY AI by investigating the automated segmentation of PYLARIFY PET/CT scans from 20 patients compared to manual segmentation.\(^9\) Potential lesions were evaluated in 339 prostate cancer patients who were enrolled in the OSPREY clinical trial.\(^2\) Sensitivity of detection of potential lesions was calculated by determining the percent of manually selected abnormal lesions that were automatically detected by PYLARIFY AI resulting in 91.5%, 90.6%, and 86.7% for regional lymph nodes, all lymph nodes, and bone, respectively, in metastatic patients. This study demonstrated segmentation accuracy of the deep learning algorithm, consistency in quantitative assessment across multiple readers, and high sensitivity in detecting potential lesions, providing the basis for clinical evaluation of PYLARIFY AI in standardized reporting of PSMA PET/CT.

Both PYLARIFY AI and Lantheus’ commitment to maximizing patient access to PYLARIFY PET/CT were heavily featured in the recent “SNMMI AI and Patient Access to and Health Disparities in Nuclear Medicine Procedures” symposium, of which Lantheus was the title sponsor.

This is an exciting and transformational time for prostate cancer imaging with PYLARIFY, along with the first FDA cleared AI-assisted platform, PYLARIFY AI, leading the way.

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INVASIVE LOBULAR BREAST CANCER (ILC)  
KNOW THE METASTATIC SITES

ILC can metastasize (spread) to common sites like the liver, lungs and bones as well as to less common sites, such as the GI tract and ovaries. ILC can metastasize many years after initial treatment.

SYMPTOMS (BEYOND USUAL ACHES AND PAINS) TO REPORT TO YOUR DOCTOR

- Unexplained bone pain that doesn’t go away, especially in the back, hips, ribs or thighs
- Unusual pelvic bleeding
- Abdominal pain, difficulty eating or abdominal distention and/or bloating
- Unexplained weight loss
- Unexplained shortness of breath or painful breathing
- Frequent headaches, dizziness, impaired intellectual function
- Swelling or lumps in the chest, armpit, neck or groin
- Change in skin color, lasting rash or firm nodule(s)
- New difficulty with your vision

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On the other hand, very large amounts of $^{225}$Ac can be produced with accelerators (linacs or rhodotrons) on the basis of a conversion of electrons from photons technology, in which $^{226}$Ra is transformed in $^{225}$Ac which decays in $^{225}$Ac in a very clean way with very high yields (several hundreds of curies per year). At least two of these sites have construction projects (Northstar, USA and SCK-CEN/IBA, Belgium) and there will be probably more to come. In other words, the industrial solution for producing high amounts of clean $^{225}$Ac is under construction, which paves the way for the development of an almost unlimited number of new $^{225}$Ac-labeled drugs, providing a solution will be found to get access to larger sources of the target material $^{226}$Ra, which production had been stopped in the 1950s.

With this increase of medical use of alpha-emitters, industries, together with authorities will also have to become creative in providing appropriate solutions for the handling of patients’ radioactive waste.

More than ten $^{225}$Ac-labeled drugs have already entered clinical trials and several of them ($^{225}$Ac-PSMA/Vipivotide, $^{225}$Ac-FPI-1434, $^{225}$Ac-Lintuzumab, $^{225}$Ac-DOTA-SP etc.) are becoming closer to reaching market authorization. While beta-emitter are long range radiation emitter ideal for destroying average size tumors through the cross-firing effect and alpha-emitters better for killing isolated tumor cells or micrometastases, it is highly expected that the sequential treatment of a $^{177}$Lu-drug followed by an $^{225}$Ac-drug to a patient could be substituted with a co-injection of $^{177}$Lu-labeled drug and the same $^{225}$Ac-labeled drug, showing much higher efficacy. The demonstration of this simultaneous effect on tumors and micrometastases will proportionally increase the interest for $^{225}$Ac. We hope we only have a few years to wait, just enough time to have access to sufficient amounts of $^{225}$Ac of high quality.

The Oncidium foundation’s role in striving for education

The foundation focuses its activities around three pillars: Access, Education and Hope, all three complementary, indissociable and equally important to carry out the mission to enhance worldwide access to radiotheranostics technologies for people living with cancer.

Through Education, the foundation strives to bring a better understanding of the functioning and benefits of radiotheranostics for cancer care and nuclear medicine in general but also to provide accurate and up-to-date information about radiopharmaceuticals for therapy. Indeed, an extensive list of marketed, under clinical development, early stage or even discontinued radiotherapeutics is available not only for experts Continued on page 17. See Focus on Actinium-225.
Focus on Actinium-225. Continued from page 16.

in the nuclear medicine field but also accessible for oncologists, general practitioners (thanks to a search by target) and even patients (through options according to cancer types). Thus, allowing to enhance Access to potentially life-saving information.

In addition to a clear understanding of current availabilities and options, the educational component enables to detect the opportunities that need to be addressed soon, especially those that aim at targeting indications that differ from the already crowded areas of Neuroendocrine Tumors and Prostate Cancer. It is through this endeavor that the foundation can build Hope, by understanding the needs and gaps first and then by supporting research and development and working towards their implementation, at a global scale, to help cancer patients live longer and with better lives.

For more information, visit our education page.


since its inception over a decade ago, and it’s enabled us to develop scanners that fulfill our mission of Equal Healthcare for All™.

Vertical integration has positioned United Imaging to offer other benefits to help providers protect their investment. Software Upgrades for Life™ means that all available software upgrades are delivered to our installed base free of cost for the life of each system, to help imaging centers and hospitals keep their equipment at its most modern. All-in Configurations™ means every scanner is delivered fully configured with all its capabilities, so the provider can expand capabilities as needed rather than having to buy add-on features. And, when United Imaging released the industry’s first AI-based PET reconstruction techniques to the market, they were made available to the entire installed base, instead of remaining in academia and the patients served by these institutions. Benefits like these are funded by United Imaging’s tight vertical integration and associated cost controls, and are immensely valuable to creating Equal access by helping rural healthcare providers maximize their investments and expand clinical capabilities.

Making it possible for providers to get not just any technology but the best technology should be the industry’s goal. For years the medical imaging community has built lower-performing, lesser systems in order to get more of them out to more areas; that’s a place to start, but it’s not a place to end. It’s a limited, short term strategy that creates access to unequal technology. Equal access should be the new standard, but it requires more manufacturers to change the way they’ve approached technology for many decades.

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Continued from page 11. See Artificial Intelligence Applications.

...energy correction, scatter or randoms correction. In particular, scatter correction is the most time-consuming correction and it also has the largest impact on final image quantitation. Neural networks that are intended for use in scatter correction are trained with input images that are non-scatter corrected, either with or without an attenuation map, and target images that are scatter corrected. As a result, the networks learn to produce images that look like scatter corrected images from non-corrected images. The difference between these scatter corrected image estimates and uncorrected images can also be forward projected to...

way to gain this clarity. Both new FAC SPECT technology and new PET technology utilize very similar base CT approaches to add this feature to your imaging department.

While the image quality of PET is considered higher, SPECT with FAC utilizes the benefits of actual attenuation correction technology as does PET to reduce false positives compared to standard SPECT MPI technology.

It’s also important to carefully evaluate both SPECT and PET cameras that claim to offer AC. Attenuation Correction technology with CT, FAC, or X-ray to produce the images have more than 30 years of peer-reviewed journal articles that give most readers great confidence. New software-only approaches, while interesting, are in their infancy and must stand the test of time in actual clinical imaging.

When taken into consideration with the overall costs of the camera, consumables, and reimbursement stability, SPECT with FAC is a solid option for organizations looking to upgrade their image quality.


Luke’s Hospital. “It creates greater uniformity in the images such that normal is easy to recognize and we can confidently determine the patient does not need to go on to have a rest image. I can imagine that for a typical patient, we would be seeing the whole test done on the order of 20 to 25 minutes, which is pretty powerful.”

Practices that leverage TruCorr emission-based attenuation correction for D-SPECT myocardial perfusion image data will see improvements in quality and efficiency. Departments that implement TruCorr will benefit from more time and resources to dedicate where they are needed most. Clinicians will also have more accurate imaging to guide their care decisions. By providing the highest quality care as quickly as possible, they may also find they have more satisfied patients.

REFERENCES


Capintec and Biodex Brands Merge. Continued from page 5.

Note that while some products may appear slightly different due to rebranding efforts, customers can trust that they are getting the same high-caliber quality and reliability.

In the event your desired product has been discontinued, customers may contact the Capintec office where a service professional will provide guidance on the best alternative.

“We understand that change is difficult for our employees and customers, and that facing uncertainty is always stressful,” says John Viscovic, Executive Vice President of Sales and Marketing at Mirion. He continues, “All organizational integrations are a gradual and interactive process, where people from two different teams learn to co-operate and transfer their strategic capabilities and knowledge. We are committed to remaining proactive, creative and persistent in order to bring the optimal value to our customers and patients through this process.”

A Look to the Future

The Capintec and Biodex teams look forward to seeing their customers again at upcoming conferences and meetings to reintroduce themselves as a new but familiar partner for all their nuclear medicine needs. Driven by an innovative spirit and a mission to advance human health, they plan to continue their commitment to excellence and pushing technology forward to better serve their customers.

If you have any questions, please contact capintec@mirion.com.

Continued from page 19. See Artificial Intelligence Applications.

produce a scatter sinogram estimate which can then be used in any image reconstruction algorithm. Figure 5 shows representative non scatter corrected images, images that are scatter corrected using physics-based single scatter simulation and images that are scatter corrected using neural networks. While there are still quantitative differences in hot spots and cold regions between single scatter simulation and neural network-based scatter correction, the neural network still generates a reasonably accurate scatter correction.

In this article, we gave some examples of the use of AI in the imaging chain and we would like to emphasize that AI can also be used in applications such as improving attenuation maps that might be noisy due to a low dose CT scan or those that lack direct attenuation information (e.g. from MR scans). Another exciting application is the joint estimation of motion information and activity images [5,6]. AI can also be used to extract quantitative features that can help evaluate new tracers or responses to therapy. With such a broad range of applications for AI in PET, a site can decide when the speed and performance provided by AI warrants its use at each step.

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