The Value of Nuclear Medicine and Molecular Imaging in the Time of COVID

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The state of nuclear medicine and molecular imaging is strong. Despite the global COVID-19 pandemic, signs of the sector’s strength abound. Cancer care–related molecular imaging (MI) procedures stayed strong, and FDG-PET procedure volume has regained the pre-pandemic level of use worldwide. Compared to other diagnostic modalities such as CT and MR, MI procedure volume remained relatively high during the pandemic.

During this challenging time, it is so exciting to all of us that new tracers are being approved. The U.S. Food and Drug Administration approved the use of a tau PET agent (TAVID™) to help dementia patients, and an estrogen receptor agent (Cerianna) has been approved for use in patients with recurrent or metastatic breast cancer as an adjunct to biopsy. These are clear signs of the value of our field and contributions to patient care.

As we move through the global COVID-19 pandemic, the strategic vision of SNMMI’s Value Initiative 2.0 is more important than ever to help diagnose and treat diseases. We have not slowed down in our efforts or in our plans. Thanks to our members, councils, centers of excellence and industry partners, highlights of the 2020 Value Initiative achievements include:

- **Advocacy:** Continue to hold targeted virtual fly-ins. So far met with close to 50 U.S. legislators/staff from both House and Senate to advocate and build momentum for HR 3772 and secure appropriate reimbursement. We have 22 co-sponsors in the House and are now working on a Senate companion bill.
- **Outreach:** Created a coalition of 9 patient advocacy groups and 21 medical societies to advance patient care during the pandemic.
- **Research and Discovery:** Completed the “Mars Shot” Nuclear Medicine Vision Document and formed Artificial Intelligence and Dosimetry Task Forces to capitalize on opportunities in the field.
- **Workforce Pipeline and Lifelong Learning:** Held a virtual meeting/webinar with nuclear medicine/nuclear radiology program directors, certification boards and other thought leaders to discuss radionuclide therapy training during nuclear medicine/nuclear radiology residency.
- **Quality of Practice:** Began development of 2 new appropriate use criteria—lymphoscintigraphy and brain imaging, including amyloid and tau PET.

In the SNMMI VI 2.0, we will reach out to and engage every member of our society—chapters, councils, and centers—to advance our contributions to outstanding patient care. As we envision the future of nuclear medicine and molecular imaging, let us continue to share ideas, be bold in our questions and jointly move toward an exciting future—remembering that, as Sam Gambhir would say, “There is no elevator to success, we must take the stairs.”
Over 15 years ago, we started to develop and manufacture radiopharmaceuticals at ITM. Since then we have had one very specific objective in mind: to significantly improve the treatment outcome and quality of life of cancer patients.

We are fully aware how precious every moment in life is and of the freedom to enjoy those moments to the fullest. Targeted Radionuclide Therapy stands out as a promising treatment option – which is why we are doing everything in our power to ensure that as many patients as possible can benefit from this precise approach and have been intensively working on the development of a proprietary portfolio of Targeted Radionuclide Therapies.

Targeted Radionuclide Therapy as a platform technology enables us to address a range of cancers such as neuroendocrine tumors, glioblastoma, osteosarcoma and bone metastases, as well as folate receptor α positive tumors such as lung, ovarian or breast cancer. In a theranostic approach, which combines therapy and diagnostics, we are able to offer patients a precise diagnosis and subsequent treatment using a well-tolerated procedure.

In our international phase III clinical trial COMPETE, we are investigating the therapeutic radiopharmaceutical no-carrier-added (n.c.a.) Lutetium-177-Edotreotide for the treatment of neuroendocrine tumors, targeting somatostatin receptor type 2 and 5. In order to diagnose these rare tumors, we recently launched the companion diagnostic, ready-to-use radiopharmaceutical Gallium-68-Edotreotide (TOCscan®) in Germany, Austria and France, and are aiming for an EMA approval.

Improving treatment of osteosarcoma and osteoblastic bone metastases, we are working in a preclinical project on radiolabeled Zoledronate. Many patients with non-metastatic osteosarcoma can survive long-term. However, a high proportion do not respond well to standard of care treatments or recurs, resulting in the need for alternative options such us Targeted Radionuclide Therapy.

For patients suffering from glioblastoma we are developing a novel n.c.a. Lutetium-177 based intra-cavitary immunoradiotherapy (iRIT) partnering with Helmholtz Zentrum München (HZM), Glioblastoma is a complex tumor which has so far been very difficult to treat. iRIT aims to circumvent the blood-brain-barrier by direct injection of pharmaceuticals into the tumor lumen during brain surgery.

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Molecular radiotherapy (MRT) seems the perfect solution to kill cancer cells with minimal harm to surrounding healthy tissue. But the complexities of tailoring the treatment to each individual patient present a challenge to both clinical departments and software companies. In this article, Erin Ross, Principal Nuclear Medicine Physicist at University Hospitals Birmingham NHS FT in the UK and Helena McMeekin, Clinical Applications Scientist at Hermes Medical Solutions, describe a collaborative effort to overcome the challenges and deliver the optimal treatment for patients.

The development of planning and treatment delivery evaluation for MRT lags as much as 30 years behind external beam radiotherapy and brachytherapy. External beam radiotherapy is delivered using high energy X-ray beams that are precision guided from the radiotherapy machine onto a target tumour in the patient. These X-ray beams can be turned on and off via control switch with beams being shaped to ensure optimal coverage of the target tumour whilst minimising radiation dose to adjacent radiosensitive organs at risk (OARs). In brachytherapy, sealed radioactive sources are placed into body cavities or directly into tissues, the effect of the radiation on the adjacent tissue is predicted using planning software to maximise damage to tumour tissues. Until such software becomes commercially available for MRT, dose planning and evaluation will remain in the research domain with many local variations. Hermes Medical Solutions is proud to lead the way with the FDA 510(k) cleared and CE marked Voxel Dosimetry™ software.
An important research area, in which we collaborate with Merck KGaA, is the treatment of non-small-cell lung carcinoma, ovarian cancer or triple negative breast cancer. These cancers show folate receptor α overexpression. In this early phase project we took advantage of this fact and developed a diagnostic radiopharmaceutical, which is currently in Phase I, and a therapeutic radiopharmaceutical in preclinical stage.

In addition to our extensive R&D focus, we manufacture high-quality medical radioisotopes for our numerous partners in the pharmaceutical industry, for the direct supply of our clinical partners as well as for our own rapidly growing pipeline. Our key product, the highly pure therapeutic precursor n.c.a. Lutetium-177, is available under the brand name EndolucinBeta® and distributed via our global supply network and exclusive technology transfer partners. With marketing authorization in the EU and a DMF in the US, EndolucinBeta® is widely used in Targeted Radionuclide Therapy for severe forms of cancer. To meet the growing need for our radiopharmaceuticals and medical radioisotopes, we are also building a new state-of-the-art GMP production facility near our headquarters that will strongly increase production capacities.

In addition to working with our industrial and clinical partners, we value our collaboration with various research institutions around the world. These partnerships open up the opportunity to transfer the extensive academic know-how to our industrial development in order to offer our patients the most innovative therapies in the end. The project FORActinium is one current example of a joint venture with a research facility, the Technical University of Munich (TUM), focusing on the development of a industrial manufacturing process for the therapeutic radioisotope Actinium-225, which is so specific that it could be used to treat micrometastases or leukemia.

SNMMI’s VI Launches Artificial Intelligence (AI) Taskforce

Enhancing research on how artificial intelligence, machine-learning, and deep learning can be applied to nuclear medicine and molecular imaging is a goal defined the SNMMI Board of Directors in the Value Initiative. The Research and Discovery Domain formed an Artificial Intelligence (AI) Task Force to identify opportunities for the use of and gaps in the resources needed to develop and deploy AI in nuclear medicine and molecular imaging. The task force comprises scientists and physicians from academia and industry with experience in artificial intelligence.

Our holistic approach to both developing in-house solutions as well as supporting our partners by providing high-quality radiopharmaceutical precursors, creates synergy effects and essentially contributes to the development of urgently needed drugs. A strong commitment to collaborations not only within the industry, but also on an academic level, helps ensure promising treatment options. We believe that partnerships are the key to success, especially when it comes to dealing with state-of-the-art technology in order to help patients. Primary market dynamics aside, pharmaceutical companies regardless of their size and market share must never forget where they began and whom they are serving: human beings. When you embed this notion into a business’s DNA, growth and success come naturally.
Blue Earth Diagnostics develops and provides PET diagnostic imaging and therapeutic radiopharmaceutical products to help people with serious disease, such as cancer. COVID-19 has brought unprecedented changes to our world. Amid the challenges of COVID-19, Blue Earth Diagnostics stands committed to supporting those parts of life that matter most: health and well-being.

Survey Results: PET Imaging Use During COVID-19

TERRI WILSON, CHIEF COMMERCIAL OFFICER, BLUE EARTH DIAGNOSTICS, A BRACCO COMPANY

Commitment in the Face of COVID-19

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Data on the Use of PET/CT and Other Imaging Services During the COVID-19 Pandemic

Numerous online webinars have been organized by SNMMI and other organizations in an attempt to measure the impact of COVID-19 on imaging practices. One overarching takeaway is that the frequency of PET/CT scanning has been less impacted than some other imaging modalities, indicating its potential value to help physicians make informed patient management decisions for serious medical conditions. In one such recent webinar entitled, “COVID-19 Business Impact on Medical Imaging,” hosted by IMV, part of Science and Medicine Group, results of a survey that included nearly 500 responses from U.S. imaging facilities were reported. The survey was conducted at the peak of the COVID-19 pandemic, April 10 – April 27, 2020, and reflected a 92% decline in imaging procedures being performed by imaging facilities. As pictured below, the survey found that the impact of COVID-19 on PET/CT scans was much lower than the impact on MRI (~25% vs ~47% decrease). For full survey results please visit IMV’s website at https://imvinfo.com/covid-19-impact-on-imaging-facilities-tracker/#toggle-id-1.

Blue Earth Diagnostics Imaging Center Survey and Results

Blue Earth Diagnostics conducted a survey of ~350 imaging facilities from May 15 – June 1, 2020, in order to gain insight into how the COVID-19 pandemic has affected our customers’ clinical practice involving the use of Axumin® (fluciclovine F 18) injection PET/CT scans and how their use may be impacted in the future.

Survey Results

Nearly sixty percent (60%) of imaging centers surveyed report there was no delay in scheduling patients for Axumin scans. Of the nearly forty percent (40%) that did report a delay, the decision to cancel or delay was primarily driven by the patients, followed by the healthcare providers (HCP).

The survey showed that patients and HCPs were typically the key

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In MRT, radiopharmaceuticals can be delivered systemically, making use of biological processes to ensure radiation is only delivered directly into tumour cells. Alternatively, radiation can be selectively delivered to specifically targeted tumours by making use of the blood vessels directly supplying tumours. There is no on/off switch for the radiation associated with MRT. Planning and then evaluation of dose delivery requires consideration of the biological and physical half-life of the radiopharmaceutical used; the method of uptake by the tumour cells; excretion pathways of excess radiopharmaceutical not taken up in tumours; residence time of that radiopharmaceutical in different organs; and its proximity to other radiosensitive organs.

The first steps towards dosimetry for MRT is to make better use of the quantitative nature of nuclear medicine imaging. Conventional SPECT/CT images can be made quantitative by following a simple phantom calibration process and using advanced, vendor neutral reconstruction software: Hermes SUV SPECT®. For Lu-177 DOTATATE MRT, post therapy imaging using Hermes SUV SPECT® allows the radiologist to evaluate MRT uptake and treatment response. SUV scaled images provide instant comparison between follow up scans, removing the need for the radiologist to subjectively threshold each image before starting their comparison.

A further benefit to using SUV SPECT® is that dosimetry can be performed directly on the images. Hermes Voxel Dosimetry® or Hermes Organ Dosimetry® can be used to determine the dose delivered to tumour volumes and OARs. Hermes Voxel Dosimetry® produces a 3D dose map by running a full photon Monte-Carlo dose simulation using the SUV SPECT® recon and the patient’s CT; electron dose is modelled by local absorption. The development and validation of this innovative software was the subject of a PhD thesis and several peer reviewed publications, underlining Hermes Medical Solutions’ commitment to research and development. Hermes Organ Dosimetry® relies on the industry standard OLINDA/EXM® engine to calculate organ doses according to the MIRD model.

Dr. Ross and a multi-disciplinary team at University Hospitals Birmingham NHS FT, with the support of Hermes Medical Solutions, are undertaking a project to evaluate the dose delivered to patients receiving the fixed treatment regime of 4 cycles of 7.4GBq Lu-177 DOTATATE MRT. The aim is to build a tumour dose-response relationship and determine MRT specific dose limits for OARs, facilitating activity prescription on an individual patient basis rather than a standardised regime.

In comparison to external beam radiotherapy and brachytherapy, the field of personalised dosimetry in MRT is in its infancy. Nuclear medicine is a quantitative imaging modality and software is now available to carry out dosimetry and evaluate treatment response. We owe it to the patients to optimise this powerful tool in the fight against cancer.

4 cycles Lu-177

Post therapy images for 4 cycles of Lu-177 DOTATATE therapy reconstructed with Hermes SUV SPECT®
decision makers when it came to cancelling or delaying Axumin PET/CT scans. This finding is not surprising, since accessing Axumin in the hospital setting may be of concern for patients who are immunocompromised or vulnerable due to age or co-morbidities associated with higher COVID-19 mortality rates. In anticipation of this potential concern, Blue Earth Diagnostics is encouraging non-hospital imaging facilities that perform Axumin PET/CT scans to list their sites on the Axumin Imaging Center Locator Tool (www.AxuminImagingCenter.com).

H.R. 3772 Interests in the Open Access Portion of the Survey: Take-Action!

As you may know, diagnostic radiopharmaceuticals are afforded a 2 – 3-year transitional pass-through period during which radiopharmaceuticals and PET scans are paid separately by Centers for Medicare & Medicaid Services (CMS). After this transitional pass-through period expires, diagnostic radiopharmaceutical payments become packaged in with the procedure payment in a manner that greatly reduces the hospital’s reimbursement for Original Medicare patients only. The loss of pass-through will not impact on the way outpatient imaging centers reimbursed under the Physician Fee for Service (PFS) are paid for radiopharmaceuticals by CMS. The transitional pass-through period for a number of diagnostic radiopharmaceuticals, including Axumin® (fluciclovine F 18) injection, expired on January 1, 2020.

A bill has recently been introduced in the U.S. House of Representatives – H.R. 3772 – to preserve Medicare beneficiary access to certain diagnostic radiopharmaceuticals under the Medicare hospital outpatient prospective payment system.

The Comments section of the survey indicated that many participants had interest in seeing H.R. 3772 passed. To address this important patient access issue, Blue Earth Diagnostics has been working with a coalition of professional societies and trade associations. Members of Congress are always interested in hearing directly from their constituents, particularly those that who care for these patients.

Please consider reaching out to your members of Congress in support of H.R. 3772. They prefer to hear about your personal experience and how it will impact you and your patients rather than receiving numerous pre-written letters. You can email your
members of Congress directly, or you can edit the suggested letter linked here before submitting.


On behalf of Blue Earth Diagnostics, our sincere appreciation goes out to all healthcare professionals who are fighting serious disease and helping to protect public health.

Healthcare professionals and the entire healthcare workforce are on the front lines in battling COVID-19, and we share our deepest thanks to all who are engaged in selfless efforts to help patients and protect the health of our communities. Blue Earth Diagnostics is committed to ensuring that we continue to support healthcare professionals throughout this time.

We are optimistic that the horizon of hope in overcoming COVID-19 will continue to expand, and that solutions and therapeutic approaches will emerge through the dedicated efforts of medical researchers and scientists around the world. As medical institutions lift restrictions on non-emergency procedures, including PET scans for patients with cancer that may have been delayed, Blue Earth Diagnostics is ready. We have active preparations underway for selective and well-considered re-opening activities in full accordance with national, regional, and local requirements, as well as those of individual institutions. All of our re-opening activities will be conducted with the safety and health of our employees, their families and loved ones, patients, healthcare workers and the communities where we live top of mind.

### Indication

Axumin® (fluciclovine F 18) injection is indicated for positron emission tomography (PET) imaging in men with suspected prostate cancer recurrence based on elevated blood prostate specific antigen (PSA) levels following prior treatment.

### Important Safety Information

- Image interpretation errors can occur with Axumin PET imaging. A negative image does not rule out recurrent prostate cancer and a positive image does not confirm its presence. The performance of Axumin seems to be affected by PSA levels. Axumin uptake may occur with other cancers and benign prostatic hypertrophy in primary prostate cancer. Clinical correlation, which may include histopathological evaluation, is recommended.

- Hypersensitivity reactions, including anaphylaxis, may occur in patients who receive Axumin. Emergency resuscitation equipment and personnel should be immediately available.

- Axumin use contributes to a patient’s overall long-term cumulative radiation exposure, which is associated with an increased risk of cancer. Safe handling practices should be used to minimize radiation exposure to the patient and health care providers.

- Adverse reactions were reported in ≤1% of subjects during clinical studies with Axumin. The most common adverse reactions were injection site pain, injection site erythema and dysgeusia.

To report suspected adverse reactions to Axumin, call 1-855-AXUMIN1 (1-855-298-6461) or contact FDA at 1-800-FDA-1088 or [www.fda.gov/medwatch](http://www.fda.gov/medwatch).

Please see [Axumin full Prescribing Information](http://www.snmmi.org/).
SNMMI’s Volunteer Leaders and Industry Partners Play an Indispensable Role in the Progress and Success of SNMMI Value Initiative Efforts

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Siemens presented to the Value Initiative Industry Alliance that procedure volume has, for the most part, recovered from the market dip in March and April.
SNMMI would like to thank our Value Initiative Industry Alliance Member Companies:

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The new $^{68}$Ge/$^{68}$Ga Generator GeGant® now available in the U.S.