Theranostic Hybrid Molecular Imaging

Nuclear medicine has seen a very interesting evolution. Recently, different Nuclear Medicine Societies have addressed the issue of what is expected to be involved in our field of interest and the decision is that molecular imaging and therapy is what best defines us. From diagnosis to therapy, from radioactive probes to nonradioactive ones, there is a wide spectrum of imaging modalities included in its definition.

Once we define what we are, one of the next questions that can be asked is what are the future perspectives of nuclear medicine? And the answer is intimately connected to therapy with open sources and the concept of personalized diagnosis and treatment, theranosis. This concept is clearly illustrated by ^{68}Ga-DOTATATE and ^{177}Lu-DOTATATE in the treatment of neuroendocrine tumors (NETs).[1]

As our knowledge and comprehension of pathology advances we will be able to develop different tracers to perform personalized medicine as the standard of care. To make it possible we should aim to have a multimodality approach to theranosis. In this way, we should start thinking of incorporating optical imaging; in particular, optical imaging using near infrared (NIR) fluorescent light (700-900 nm). NIR light exhibits high tissue penetration (mm to cm deep) and low autoflorescence, which provides good contrast. To be able to detect NIR light, it is necessary to use a NIR camera, because we do not have photoreceptors sensitive to NIR light. Indocyanine green (ICG) is excited by NIR light and emits fluorescence that can be detected with a NIR camera. ICG was developed in the 1950s by Kodak Research Laboratories and has been approved by Food and Drug Administration for several clinical applications being retinal angiography one of the most common indications for ICG.

Recently, a hybrid tracer for sentinel node imaging was developed by the combination of two available and approved products such as technetium-99m (^{99m}Tc) nanocolloid and ICG.[2] These hybrid probes are used for preoperative scintigraphic or single-photon emission computed tomography/computed tomography imaging and transcutaneous evaluation with an ICG imaging system composed of an excitation system and a NIR camera in order to detect fluorescence emitted from the ICG present in the sentinel nodes the sentinel node. This information is useful to plan surgery. During surgery these probes allow identification of the sentinel node using real time imaging with both modalities through an intraoperative gamma camera and an ICG imaging system. An intraoperative ICG imaging system would have a complementary role to the one provided by the gamma camera and also aid the gamma probe. Intraoperative optical imaging would be able to give anatomic landmarks to spot the sentinel node more easily being particularly useful in complex anatomic regions were nerves and vessels must be preserved. If the injection site is near the sentinel node or if the migration of the particles hampers the identification of the sentinel node, the NIR camera can aid in its identification. Another item to take into consideration is that there are NIR fluorescence modules than can be used in laparoscopy, which can spot sentinel nodes that accumulate the hybrid tracer during laparoscopic surgeries such as during prostate cancer surgeries.[3] These hybrid probes can be used in open and laparoscopic surgeries and can be easily incorporated into routine sentinel node procedures. We have recently started to have our own hybrid experience with sentinel node procedures in melanoma and breast cancer using ICG ^{99m}Tc nanocolloid. Although there are several available NIR cameras for surgical settings, availability and costs have dictated that we construct our own camera taking into account the properties of ICG and its detection. Our results are encouraging and we plan to continue to apply this hybrid approach in sentinel node procedures.

Indocyanine green is considered a standard of NIR imaging, and can be compared to what 18 fluorodeoxyglucose (^{18}FDG) is to PET. ^{99m}Tc nanocolloid ICG has opened the path for clinical hybrid probes and has shown us the proof of concept, but new hybrid specific probes must be developed. Just think on how many tracers were developed after ^{18}FDG, hopefully the same will happen with these optical probes and also with hybrid probes. Maybe, we can imagine a nice synergy between ^{68}Ga-DOTATATE and a somatostatin analogue NIR probe to be used during surgery of NETs. We would be performing diagnosis with ^{68}Ga-DOTATATE and afterwards therapy during surgery looking at

Access this article online

Quick Response Code:

Website: www.wjnm.org

DOI: 10.4103/1450-1147.139129

the somatostatin analogue NIR probe to remove the tumor. In this way we would be taking a theranostic approach for the treatment of NETs using nuclear medicine and optical imaging. We can even think about the possibility of a hybrid probe, a NIR and positron emitting somatostatin analogue probe. This strategy could also be applied not only to cancer, but also to other pathologies that could benefit from this hybrid approach for diagnosis and treatment.

Nuclear medicine must get involved in optical imaging because the tracer concept is quite similar and surely much of the experience gained could be transferred to optical imaging. In this way, we could first think of optical analogues of nuclear medicine probes and afterwards hybrid ones. And as mentioned earlier, hybrid probes can have an important role to play not only in the diagnosis, but also in providing ways for safer and successful surgeries or biopsies being part of theranosis.

WARMTH worldwide can work through standard operating procedures[4] and make this hybrid tracer approach to therapy a reality. We need an interdisciplinary team that can be able to address this challenge. The 8th WARMTH International Conference on Radiopharmaceutical Therapy could be a nice opportunity to exchange ideas, broaden the field of theranostic nuclear medicine and molecular imaging incorporating theranostic hybrid alternatives and embrace optical imaging.

Juan Pablo Gambini

Nuclear Medicine Center, Clinical Hospital,
University of Uruguay, Montevideo, Uruguay
E-mail: jpgambini@gmail.com

References

1. Baum RP, Kulkarni HR. Theranostics: From molecular imaging using Ga-68 labeled tracers and PET/CT to personalized radionuclide therapy-The Bad Berka experience. Theranostics 2012;2:437-47.
2. Brouwer OR, Buckle T, Vermeeren L, Klop WM, Balm AJ, van der Poel HG, *et al*. Comparing the hybrid fluorescent-radioactive tracer indocyanine green-99mTc-nanocolloid with 99mTc-nanocolloid for sentinel node identification: A validation study using lymphoscintigraphy and SPECT/CT. J Nucl Med 2012;53:1034-40.
3. van der Poel HG, Buckle T, Brouwer OR, Valdés Olmos RA, van Leeuwen FW. Intraoperative laparoscopic fluorescence guidance to the sentinel lymph node in prostate cancer patients: Clinical proof of concept of an integrated functional imaging approach using a multimodal tracer. Eur Urol 2011;60:826-33.
4. Turner JH. Global WARMTH for patients with cancer. World J Nucl Med 2012;11:103-4.

How to cite this article: Gambini JP. Theranostic Hybrid Molecular Imaging. World J Nucl Med 2014;13:73-4.

Source of Support: Nil. **Conflict of Interest:** None declared.