A Bright Future for Nuclear Endocrinology

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As supplement editors, it is our pleasure to introduce you to the *Journal of Nuclear Medicine* (*JNM*) supplement on the application of molecular imaging to endocrinology. Nuclear medicine has always been an important component of endocrinology and continues to expand the understanding of endocrine diseases. Improvements in instrumentation and new radiopharmaceuticals have expanded the scope and use of nuclear endocrinology. The diversity of molecular targets uniquely expressed by endocrine tumors provides opportunities for enhanced characterization of these tumors (e.g., hormone synthesis, transporter expression, and receptor expression), mirroring histologic classification on a whole-body, in vivo scale. These imaging phenotypes reflect the diverse genetic landscape of endocrine disorders. Radiopharmaceuticals in endocrine applications serve not only as diagnostic agents but also as a platform to treat patients with matched radionuclide therapy agents, using the so-called theranostic approach. This *JNM* supplement focuses on the most novel approaches and cutting-edge clinical and scientific information regarding diagnostic nuclear imaging for several endocrine disorders, except for gastroenteropancreatic neuroendocrine tumors, which were fully addressed within the last few months. Following is a summary of the topics included in this supplement.

Radioiodine has been recognized as the earliest nuclear medicine theranostic molecule and has been a mainstay for thyroid disease since the pioneering works of Saul Hertz. In the 21st century, the use of radioiodine remains vital for the subtyping of hyperthyroidism and the treatment of hyperthyroid and thyroid cancer patients. Results from quantitative ^{123}I thyroid scintigraphy provide unique insights for the classification of various forms of thyroid functional autonomy (TFA) that lead to hyperthyroidism. Pharmacologic manipulation of uptake and dosimetry provide tools for treating Graves disease and TFA with curativelike outcomes. In this supplement, Giovanella et al. (*1*) review this important area of practice.

In contrast, the evaluation of nonfunctioning thyroid nodules has changed in recent decades, switching from thyroid scintigraphy as the primary diagnostic modality to neck ultrasonography with fine-needle aspiration, when needed. Bernet et al. (*2*) provide an overview of the clinically useful tools—including molecular markers (classifiers)—for cancer risk prediction that serves as an adjunct for diagnosis, limiting unnecessary thyroid surgery. The relative high cost of molecular assays (discussed in this supplement) may, however, limit their use in various parts of the world. Radiomics might also bring new opportunities for the molecular imaging of thyroid nodules, despite some concerns regarding reproducibility.

Future discoveries about the pathogenesis of endocrine malignancies—together with the introduction of new radiopharmaceuticals—will advance the goal of personalized medicine, for the benefit of patients. This concept is illustrated by Sundin et al. (*3*) in their review of the imaging of adrenal cortical and medullary tumors. Emerging PET tracers not only offer higher diagnostic accuracy and lower patient dosimetry than classical protocols but also enable significantly shorter imaging protocols.

Another example of advances based on novel diagnostic targets is the development of agents for imaging the receptor for glucagonlike peptide 1. This protein is expressed by pancreatic β-cells and has the potential to guide insulinoma localization, which can be very challenging. Wild et al. (*4*) cover this area and discuss how to move into clinical application. ^{68}Ga-labeled exendin was shown to be more sensitive for insulinoma detection than ^{111}In-labeled exendin as well as conventional imaging techniques. Combining glucagonlike peptide 1 receptor PET with triple-phase CT would be an important step toward the implantation of a 1-step procedure for the detection of insulinomas. States et al. (*5*) review complementary approaches for the imaging of neonatal hyperinsulinism with special emphasis on comparing ^{18}F-DOPA PET with ^{68}Ga-exendin PET.

PET imaging provides some notable advantages over scintigraphy, often leading to improved diagnostic accuracy. However, in considering PET as an alternative to scintigraphy, it is crucial to ensure that the paradigms that have been validated with scintigraphy are still valuable with PET. This issue is clearly illustrated in the diagnosis of primary hyperparathyroidism. During the past decades, the surgical strategy for primary hyperparathyroidism has progressively switched from bilateral cervical exploration to minimally invasive parathyroidectomy. Preoperative imaging plays an essential role in selecting patients who are likely to benefit from minimally invasive parathyroidectomy, ruling out multiglandular disease and ectopic gland inaccessible via a cervical route. However, patient selection must be very reliable because the alterative (using bilateral cervicotomy) has a success rate of >95% with low morbidity.

^{18}F-fluorocholine PET/CT has played an increasing role in preoperative workup and is increasingly being viewed as the leading imaging procedure in centers that have implemented this approach. Hindié et al. (*6*) review this topic and describe a need for large,

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well-designed studies comparing ^{18}F-fluorocholine PET/CT with the standard scintigraphy protocol (subtraction ^{123}I/^{99m}Tc-sestamibi) for impact on patient management and surgical outcomes, with the goal of drawing firm conclusions about the benefit of PET imaging for primary hyperparathyroidism.

What is perhaps not as widely known is that molecular imaging can play a role in patients with pituitary adenomas. MRI is essential for guiding effective decision making in patients with pituitary adenomas. However, there is an important subgroup of patients with negative or equivocal findings on MRI (e.g., microadenomas and residual/recurrent disease). Bashari et al. (*7*) show that pituitary molecular imaging with various PET tracers (e.g., ^{11}C-methionine) coregistered with volumetric MRI can complement standard cross-sectional imaging to allow more precise localization of the disease and, in so doing, enable an important subgroup of patients to be offered (further) surgery or radiosurgery with curative intent.

Although brown adipose tissue is also not a classical target for clinical nuclear medicine, it has received considerable attention in the discipline of nuclear endocrinology during the past 15 y. Analysis of the amount of metabolically active brown adipose tissue (the primary organ for heat production) in people, with the idea of increasing its activity, has attracted much interest with regard to the treatment of diabetes and obesity. Crandall and Wahl (*8*) close the supplement by providing an overview of preclinical and clinical imaging for brown adipose tissue.

PET has helped test a diversity of targets (e.g., glucose uptake; oxidative and fatty acid metabolism; and adenosine, norepinephrine, and cannabinoid receptors) during various experimental temperature exposures. The future use of PET depends on the development of well-tolerated and effective therapeutic approaches.

In conclusion, the future for nuclear endocrinology is bright. Only a handful of PET-specific tracers have been approved for clinical use up to now. The clinical translation of new radiopharmaceuticals, together with PET technologic improvements (including PET/MRI), will lead to advances in the care of patients with endocrine disorders. Advances in nuclear endocrinology will be used together with state-of-the-art proteomics, functional genomics, and systems biology approaches to identify new targets that will improve diagnosis, offer new treatments, and expand understanding of these diseases. This *JNM* supplement is dedicated to nuclear endocrinology and provides comprehensive and up-to-date knowledge about diagnostic nuclear medicine approaches to endocrine tumors in a new spirit of precision medicine. We hope that it will serve as a helpful resource to practicing physicians, including nuclear medicine specialists, radiologists, endocrinologists, oncologists, and many others, as well as fellows in training, students, and other health care professionals.

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