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EDITORIAL

Current experts' views on precision nuclear medicine imaging of phaeochromocytoma and paraganglioma

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Abstract
The EANM/SNMMI 2019 guidelines for radionuclide imaging of phaeochromocytoma and paraganglioma (PPGL) describe the current experts' views on molecular imaging in the era of precision medicine, and contain all of the information needed by nuclear physicians for performing, interpreting, and reporting the results of imaging investigations. This editorial, from a clinician's perspective, describes the first-choice radiopharmaceutical for a particular clinical setting as an important element of the revised guidelines. It also gives new evidence-based data showing the steadily growing role of nuclear imaging in PPGL phenotyping and assessment of their clinical characteristics and outcomes.

Imaging of patients with confirmed or suspected phaeochromocytoma/paraganglioma (PPGL) is important in every step of their management. The choice of radiopharmaceutical depends heavily on tumour biology, which is tightly linked with tumour location (from sympathetic vs parasympathetic paraganglia; adrenal vs extra-adrenal), genetic status, biochemical phenotype, and size, with all being intimately interconnected. The European Association of Nuclear Medicine Practice Guideline/Society of Nuclear Medicine and Molecular Imaging Procedure Standard 2019 for radionuclide imaging of phaeochromocytoma and paraganglioma is based on the most novel approaches and cutting-edge clinical and scientific information regarding the diagnosis of PPGL. It represents a unique collaborative effort between EANM and SNMMI, assembling a very experienced international team of clinicians and nuclear physicians in this area. By choosing gallium-68-labelled somatostatin receptor analogues ([^{68}Ga]SSTs) as the first-intention tracers in imaging of PPGL, EANM/SNMMI recommendations propose a simplified imaging approach in most PPGLs, which is also tightly connected to the use of targeted radionuclide therapy in metastatic or inoperable PPGLs. However, PPGLs related to *VHL* and *HIF2A* mutations remain an exception to the rule and should be explored first by [^{18}F]FDOPA. For sporadic phaeochromocytomas or those associated with mutations in *NF1*/*RET*/*MAX*, the use of [^{18}F]FDOPA rather than [^{68}Ga]SSTs is proposed, mainly due to the optimal tumour-to-adrenal uptake ratio that facilitate their detection. This is very important, since these tumours can be very small and often multifocal or recurrent. We also considered that [^{123}I]MIBG could be used for imaging of presumed sporadic and benign phaeochromocytomas. Additionally, we propose second- and third-intention diagnostic strategies that take into consideration the technical or legislative limitations for certain radiotracers in some countries (Table 3 in the Guidelines). These recommendations come to complement those proposed by the EANM clinical decision support system (endocrine system-PPGL) that are more general. They recommend using [^{18}F]FDOPA or [^{68}Ga]SSTs PET/CT as first intention in all situations (diagnosis, post-treatment evaluation, staging, suspicion of relapse), while highlighting the superiority of [^{68}Ga]SSTs in *SDHD*-related head and neck PPGLs. Therefore, new EANM/SNMMI recommendations provide a more personalized and fine-tuned approach. They also complement those of the European Nuclear Medicine guide, which, under the Oncology section, suggests the different

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PET radiopharmaceuticals and their general indications without describing the optimal acquisition protocols for each indication and performance in the setting of PPGL.

For all these reasons, our expert-based views suggest that all these tools/recommendations are complementary, and that the 2019 EANM/SNMMI guidelines provide very up-to-date information for nuclear physicians encountering patients with PPGL.

Beyond practical recommendations, the future of PPGL imaging by virtue of phenotyping disease will depend on the identification of new PPGL susceptibility genes, metabolites, cell membrane-specific targets, and signalling pathways. It is anticipated that future combinations of current and new specific radiopharmaceuticals, together with the identification of robust and reproducible new imaging biomarkers, will continue to provide crucial information for understanding this rare, fascinating, and potentially curable disease.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval This article does not contain any studies with human participants performed by any of the authors.