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STANDARDS

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ENETS standardized (synoptic) reporting for molecular imaging studies in neuroendocrine tumours

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Abstract

The European Neuroendocrine Tumor Society (ENETS) promotes practices and procedures that aim to improve the standard of care delivered to patients diagnosed with or suspected of having neuroendocrine neoplasia (NEN). At its annual Scientific Advisory Board Meeting in 2018, experts in imaging, pathology and clinical care of patients with NEN drafted guidance for the standardised reporting of diagnostic studies critical to the diagnosis, grading, staging and treatment of NEN. These included pathology, radiology, endoscopy and molecular imaging procedures. In an iterative

process, a synoptic reporting template for molecular imaging procedures was developed to guide personalised therapies. Following pilot implementation and refinement within the ENETS Center of Excellence network, harmonisation with specialist imaging societies including the Society of Nuclear Medicine, European Association of Nuclear Medicine and the International Cancer Imaging Society will be pursued.

KEYWORDS
neuroendocrine neoplasia, PET, synoptic reporting

1 | INTRODUCTION

The concept of harmonisation of medical practice is well-established in many domains. The goal is to improve the quality and consistency of the information to be relayed to referring clinicians aiming to inform management decisions and thereby increase the likelihood of optimal patient care. For example, in nuclear medicine, there have been coordinated efforts to achieve consistent acquisition, processing and analysis of molecular imaging studies.[1]

Beyond acquisition of the primary data related to diagnostic procedures, the formal reporting of results is increasingly being subjected to standardisation in the form of synoptic templates, replacing a more narrative format. This has been largely led by the pathology community, which has recognised that narrative reporting can cause misinterpretation as a result of a lack of critical data and inconsistent structure.[2,3] Prospective, randomised control trials assessing the impact of implementation of synoptic reporting on patient outcomes are lacking. Such trials are inevitably difficult to perform given that multiple other factors contribute to endpoints like overall survival. Nevertheless, capture of key data elements and enhanced ability to integrate these into searchable databases are proposed advantages of this approach. Specialist imaging societies have also started to make recommendations regarding the standardised reporting of diagnostic studies. For example, the European Association of Nuclear Medicine (EANM) recently published guidelines for the use of molecular imaging studies in the evaluation of neuroendocrine neoplasia (NEN), which included general advice from experts in the field on the reporting of scans without defining specific data elements for inclusion or recommending formal synoptic reporting.[4] Similarly, the International Cancer Imaging Society has recently supported a series of reviews that provide guidance on the acquisition and reporting of imaging studies in oncology,[5] including ^{18}fluorodeoxyglucose (FDG) positron emission tomography (PET)/computed tomography (CT).[6] However, these reflect expert opinion rather than providing a consensus on the optimal data that might be included in a synoptic report.

To harmonise the diagnostic and therapeutic approaches of NEN, the European Neuroendocrine Tumor Society (ENETS) promotes practices and procedures through publication of standards-of-care consensus guidelines, with the ultimate goal of improving patient outcomes. For example, detailed guidelines on the imaging of NEN have been published.[7] Although these guidelines focused primarily on the acquisition and interpretation of these scans, no recommendations were made regarding the formatting of reports into a synoptic format.

In parallel with development of practice guidelines, ENETS has established an accreditation framework to identify healthcare facilities that provide comprehensive and high-quality care to patients diagnosed with NEN. The ENETS Center of Excellence (CoE) network performs a detailed audit of practices, including patient referral numbers, compliance with ENETS standard-operating-procedures and involvement in research activities that are needed to advance the field. An aspirational goal of ENETS is to integrate information on diagnostic inputs, therapeutics and patient outcomes into searchable, pseudonymised databases.

Although feasible using artificial intelligence methodologies, narrative reports of pathology and imaging, as key inputs into prognostic stratification and treatment selection pathways, are difficult to integrate into databases without significant human oversight. The ENETS Executive Committee determined that this process may be facilitated by introduction of synoptic reporting of pathology, radiology and molecular imaging investigations. Accordingly, at its annual Scientific Advisory Board (SAB) Meeting in November 2018, experts in imaging, pathology and clinical care of patients with NEN were commissioned to develop guidance for the synoptic reporting of diagnostic studies critical to the diagnosis, grading, staging and ultimately therapy of patients with NEN. This report describes the process and consensus outcomes of the molecular imaging panel with input from the chairs of the radiology committee and meeting convenors.

2 | METHODS

As an initial step, a Pubmed search was performed with the keywords "synoptic" or "structured report" and "nuclear medicine", "PET", "positron emission tomography" or "scintigraphy" to ascertain whether any synoptic or structured reporting guidance existed. This failed to find any relevant papers at that time. Therefore, participants were invited in a preliminary teleconference or email contact to identify existing institutional or organisational reporting templates that might be relevant for reporting molecular imaging studies performed for the evaluation of NEN. A draft template used for reporting PET studies at the Peter MacCallum Cancer Centre,

an accredited ENETS CoE, was used as the basis for preliminary interdisciplinary discussions. The draft report template had five sections: clinical details, procedure, comparative imaging, findings and conclusion. Options for discussion included whether the template would be able to be implemented within an existing Radiology Information System (RIS), opportunities for standardisation of nomenclature, the level of detail required and whether reporting should be based on body region or conform to the TNM schema. Based on fruitful discussions within a subcommittee of the SAB, a refined template was presented to the broader group for feedback and further refinement. Through this iterative process, a proposed synoptic reporting template for molecular imaging procedures was developed.

3 | RESULTS

The clinicians involved stated a strong preference for, wherever possible, a combination of limited but standardised options (e.g., by way of drop-down menus) combined with a facility to enter additional relevant free-text pertinent to each field. For clinical details, the preferred fields included clinical indication, location of any known primary and pathological details, if known. The preferred terminology for options in these fields is detailed in Table 1. Additional pertinent information could be entered as free text included details of co-morbidities, prior and current treatment, and identification of any diagnostic dilemmas raised by prior investigations. Entering of information regarding tumour proliferation (Ki-67 or mitotic index), if available, should be included. However, for ENETS CoE sites using synoptic reporting of pathology, avoiding duplication of data entry was recommended.

The details of the procedure performed are considered critical for quality-assurance purposes and to allow reproducibility of methodology for follow-up studies. The imaging specialists indicated that, although of limited interest to referring clinicians, these data must be integrated into the final report because this is generally mandated by specialist imaging societies in their procedural guidelines. The requisite primary data are detailed in Table 2.

TABLE 1 Clinical details

Field	Template options
Indication	Diagnosis Staging-clinical vs. pathological TNM Treatment planning Suitability for radioligand therapy Therapy response Restaging (type of therapy)/surveillance with or without anticancer therapy Other (free text)
Primary location	Unknown Lung, thymus Pancreas Small intestine Appendix Right colon Left colon Rectum Other (free text)
Pathology	Typical carcinoid (lung, thymus) Atypical carcinoid (lung, thymus) GEP-NET G1 GEP-NET G2 GEP-NET G3 NEC MINEN Other
Inherited/clinical syndrome	None MEN-1 VHL Carcinoid Insulinoma Glucagonoma Gastrinoma VIPoma Other (free text)
Other relevant clinical information	Progressive disease (yes/no) Free text

TABLE 2 Procedure

Field	Options
Radiopharmaceutical	^{68}Ga DOTA-DPhe^{1}, Tyr^{3}-octreotate (DOTATATE) ^{68}Ga (DOTA(0)-Phe(1)-Tyr(3))octreotid (DOTATOC) ^{68}Ga DOTA-1-Nal^{3}-octreotide (DOTANOC) ^{111}In-pentetreotide (Octreoscan®) ^{18}F-FDG ^{18}F-DOPA ^{123}-MIBG ^{68}Ga-exendin-4 Other (free text)
Administered activity	(Insert) MBq
Uptake time	(insert) min h^{-1}
Scan-type	Planar Planar + SPECT/CT (insert region) SPECT SPECT/CT PET PET/CT PET/MRI
Image range	Total body Vertex to mid-thigh Other (free text)
Interventions	None Diuretic Insulin Sedation
Other relevant procedural information	Free text

Abbreviations: DOTA^{68}Ga 1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid; MIBG, metaiodobenzylguanidine.

TABLE 3 Comparative imaging

Field	Options	Sub-categories	Date
Modality	CT	Non-contrast Portal-venous Triple-phase	
	MRI	Eovist/Primovist Others	
	^{111}In-pentetreotide	Planar SPECT SPECT/CT	
	^{68}Ga-DOTATATE ^{68}Ga-DOTATOC ^{68}Ga-DOTANOC	PET PET/CT	
	FDG	PET PET/CT	
	Other (free text)		

Recognising that patients with NEN may undergo contemporaneous and serial imaging studies using the same or different modalities during the course of their disease, details of correlative imaging are important, especially for documentation of disease progression or therapeutic response. Suggested options are detailed in Table 3.

The presentation of scan findings was the most vigorously debated aspect of template development. Although some of the imaging specialists initially had preference for a report based on body-region, reflecting the systematic review process generally performed by most radiologists and some nuclear medicine imaging specialists, the benefits of TNM-based reporting were adopted as being preferable, particularly given support for this by the clinicians involved. Detailing the findings with respect to the primary tumour, relevant nodal stations and distant metastatic disease by organ system provides a consistent structure of the report that helps clinicians select patients for locoregional versus systemic therapies. Description by organ system is especially relevant for skeletal lesions, which can involve all anatomical zones. Pertinent positive and negative findings should also be recorded. In addition to findings directly related to NEN, incidental findings on both molecular imaging and correlative anatomical imaging should be integrated into the report. Table 4 provides a framework for synoptic reporting of scan findings. Both clinicians and imaging specialists supported the concept of integrating a table identifying target lesions, organised by body region, with relevant measurements for comparison with future studies to assess disease progression or monitor therapeutic response using any of the relevant response criteria including RECIST and PERCIST.[8] Such tables would also facilitate correlation with CT or magnetic resonance imaging (MRI) studies performed as part of patient follow-up.

The conclusion is less easily amenable to synoptic reporting because it ideally requires the reporting specialist to integrate the information above into a cogent answer to the specific clinical

TABLE 4 Findings

Field	Options	Sub-categories
Primary location	Not identified Lung Thymus Oesophagus Stomach Pancreas Duodenum Small intestine Appendix Colon Rectum Other (free text)	None/resected RUL/RML/RLL/LUL/LLL Proximal/mid/distal Head/body/tail Jejenum/ileum Ascending/transverse/descending
Primary avidity	Low/no Mild Moderate Intense Very intense Reference (spleen, liver)	Krenning score* 0 (< blood pool) Krenning score 1 (< liver) Krenning score 2 (= liver) Krenning score 3 (> liver but < spleen) Krenning score 4 (= or > spleen) *Relevant to somatostatin receptor imaging
Primary size	() cm	
Primary characteristics	Free text	
Nodes	None Locoregional Distant	
Nodal characteristics	Free text (size, location)	
Metastases	None Present	
Metastases locations	Liver Bone Lungs Peritoneum Other (free text)	
Metastases characteristics	Free text (e.g., size, number or heterogeneity/necrosis)	Overall lesion intensity (e.g., Krenning score)

question posed by the managing clinician or team. When the diagnosis of a specific lesion is uncertain and would influence stage, an opinion regarding the likelihood of NEN and further investigation or follow-up options may be relevant. For patients being monitored for known metastatic disease, stability of disease and expression of therapeutic targets may be more pertinent to management decisions. Accordingly, it is proposed that conclusion should be primarily free text.

Based on these discussions, a template with pull-down menus was created for distribution and testing at ENETS CoEs. In discussion with the radiology working group, the need for consistent nomenclature was agreed to be desirable. In parallel, alignment of the lexicon with data fields in the International ENETS Registry will facilitate extraction of imaging data directly from the synoptic report into the patient's pseudonymised health record. Accordingly, the template may require adaptation to local information technology platforms in use. A subsequent interdisciplinary discussion between the imaging subcommittee chairs (RJH, VP, AS and CD) identified that future iterations of the template may be required for PET/CT reporting performed by nuclear medicine physicians without radiology credentialing, dual trained nuclear medicine specialists providing an integrated PET and diagnostic CT report, and combined reading by a nuclear medicine specialist co-reading with a radiologist. In the latter circumstance, a single integrated and co-signed report was considered advisable.

4 | DISCUSSION

The advantages of synoptic reporting in pathology have prompted other fields, including imaging, to enhance the ease of information integration into clinical management planning. The aims of such an approach are generally to facilitate intra- and inter-reader consistency and facilitate inter- and intra-institutional data-sharing for either research or multicentric clinical trials quality assurance. One approach to standardisation of reporting criteria has been the

development of so-called imaging-reporting and data systems, which has been primarily a cooperative effort of the American College of Radiology. The first of these was BI-RADS, which sought to assign a likelihood of breast cancer on the basis of mammographic features using a common lexicon.[9] Similar schemes have been developed for reporting of liver lesions using a range of modalities (LI-RADS)[10] and prostate abnormalities on multiparametric MRI (PI-RADS).[11] A suggestion has been advanced that this approach might also be applicable to molecular imaging results. This has been termed the molecular imaging-reporting and data system (MI-RADS).[12] The so-called PETNET scoring system that compares the intensity and distribution of somatostatin receptor and ^{18}FDG PET finding has also been proposed,[13] reflecting the utility of these scans in defining suitability for peptide receptor radionuclide therapy[14] and their prognostic significance.[15] Although providing clinicians with a number that conveys the level of confidence that the imaging specialist has regarding the likelihood of malignancy based on standard imaging characteristics, the RADS generally lack the depth of information that would be needed for searchable data extraction, or to otherwise guide clinical management. They are also primarily used for assigning the likelihood of malignancy prior to biopsy confirmation of disease. They do not convey information about disease extent, which is vital for staging and prognostic stratification.

Similarly, there have been attempts to standardise assessment of response using qualitative scoring systems, such as the five-point score used for lymphoma,[16] or semi-quantitative measures, such as the PERCIST schema.[8] Although helpful for reporting of results within clinical trials, these sometimes lack the nuances involved in narrative reporting and the associated value of an expert clinician's insight into weighting of findings with respect to the likelihood of malignancy or in recommending what further investigations might be helpful to approach an adequate level of diagnostic certainty to facilitate robust management decisions. A combination of synoptic reporting incorporating data sufficient to create, for example, a minimum imaging dataset and free text to allow a narrative component potentially provides an optimal compromise. The proposed template for the reporting of molecular imaging studies in NEN represents the aspirations of nuclear medicine specialists to convey the key information to referring clinicians and their imaging colleagues, who might need to correlate independent diagnostic examinations. Most importantly, the aim is to meet the expectations of clinicians with respect to providing the information they need to plan management of their patients.

The most hotly debated aspect of the process undertaken by the ENETS SAB was whether the report should be formatted according to body region or according to a TNM schema. With the advent of multiplanar formatting, radiologists generally scroll through the transaxial plane as an initial method of review, and then correlate their findings on coronal or sagittal planes. Orthogonal review in transaxial, sagittal and coronal reconstructions is increasingly available on modern imaging review software. Some organs are better evaluated in either the coronal or sagittal plane. Systematically reviewing all images using multiple display windows maximises the chances of detecting abnormalities in regions with complex anatomy. Extrapolating this technique to hybrid imaging with single photon emission computed tomography/CT or PET/CT thus has some attractions. However, one of the advantages of molecular imaging is the ability to represent the data as a truly whole-body image, generally with high contrast and relatively low complexity. A whole-body pseudo-planar representation, known as the maximum intensity projection (MIP) image, can be rotated continuously or displayed in a particular orientation (e.g., anterior, posterior, left and right lateral) and provides an immediate gestalt of the distribution of tracer within the body, and also provides a reference matrix for triangulation of abnormalities for review of raw molecular imaging data, fused molecular and anatomical information or stand-alone anatomical information using any desired display format. For example, identification of a focus of activity in the thorax on a MIP image could be localised to the lung, characterised for avidity, measured precisely on anatomical imaging, and characterised for shape, calcification or other radiological features on the anatomical component by alternating between soft tissue and lung windows. This use of the whole-body or MIP image as the guide for review lends itself to TNM template reporting. Figures 1 and 2 show two different PET/CT protocols: one without iodine containing contrast media and the other with full diagnostic contrast enhanced three phase CT. Apart from differences in CT protocol, the colour scale depicted in the two images also represent two different approaches. The colour scale of Figure 1 is more directed towards depicting tumor avidity of somatostatin receptor radioligands, thereby allowing visual scaling of radioactivity analogue to Krenning's scale, which is of special interest for peptide receptor radionuclide therapy. On the other hand, the dichotomous colour scale in Figure 2 is more binary and has higher sensitivity (e.g., useful in surgical planning). The approach has been used at the Peter MacCallum Cancer Centre for the reporting of ^{18}FDG PET/CT for more than two decades[6] and is strongly embraced by oncologists and surgeons in Australia.

Other nuclear medicine specialists on the panel also reported using a similar approach. Synoptic reporting is a logical extension of this approach. However, others were equally adamant that local reporting guidance mandate description of disease by body region. It is important to stress at this point that MIP images should be considered as an adjunct to the multiplanar images, especially considering the fact that discordance between PET and CT or MRI images can exist. Furthermore, in regions of higher background activity, lesions may only be appreciated on multiplanar images. Accordingly, detailed evaluation of all imaging data should also be reviewed by scrolling through the available image sets, usually in the transaxial, but, by individual preference, also potentially in the coronal or sagittal planes. Clinically relevant non-oncological findings also should be given appropriate weighting in any synoptic reporting. A compromise to the body-region reporting technique that was felt to have merit by the committee was the potential inclusion in tabular format of reference findings to facilitate future comparison and assessment of disease progression or response to therapy (Table 5).

To be widely implemented, synoptic reporting needs to be time-efficient for imaging specialists and to help clinicians develop accurate

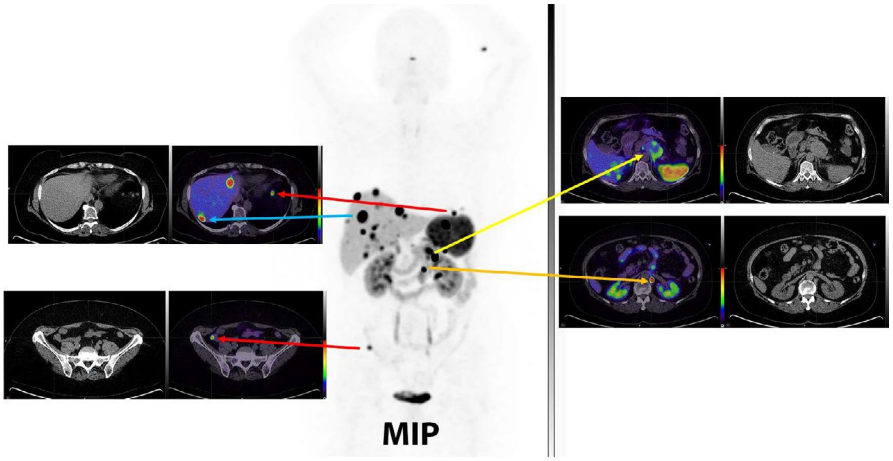

FIGURE 1 The maximum intensity projection (MIP) image of ^{68}Ga-DOTA-octreotate uptake provides immediate recognition of widespread disease with uptake above the left kidney confirmed on fused PET/CT images to reflect a mass lesion in the body of the pancreas (yellow arrow). Central photopaenia suggests possible tumour necrosis. Correlative CT provides improved anatomical relations and size measurement providing T-staging. A small focus of activity medial to the primary indicates regional nodal disease (N-staging). More distant nodal disease in the left para-aortic station at the level of the renal vein indicates distant nodal involvement. Multifocal hepatic metastases can be localized on fused PET/CT images (blue arrow) and in the peritoneum (red arrows; M-staging). No bone disease is identified

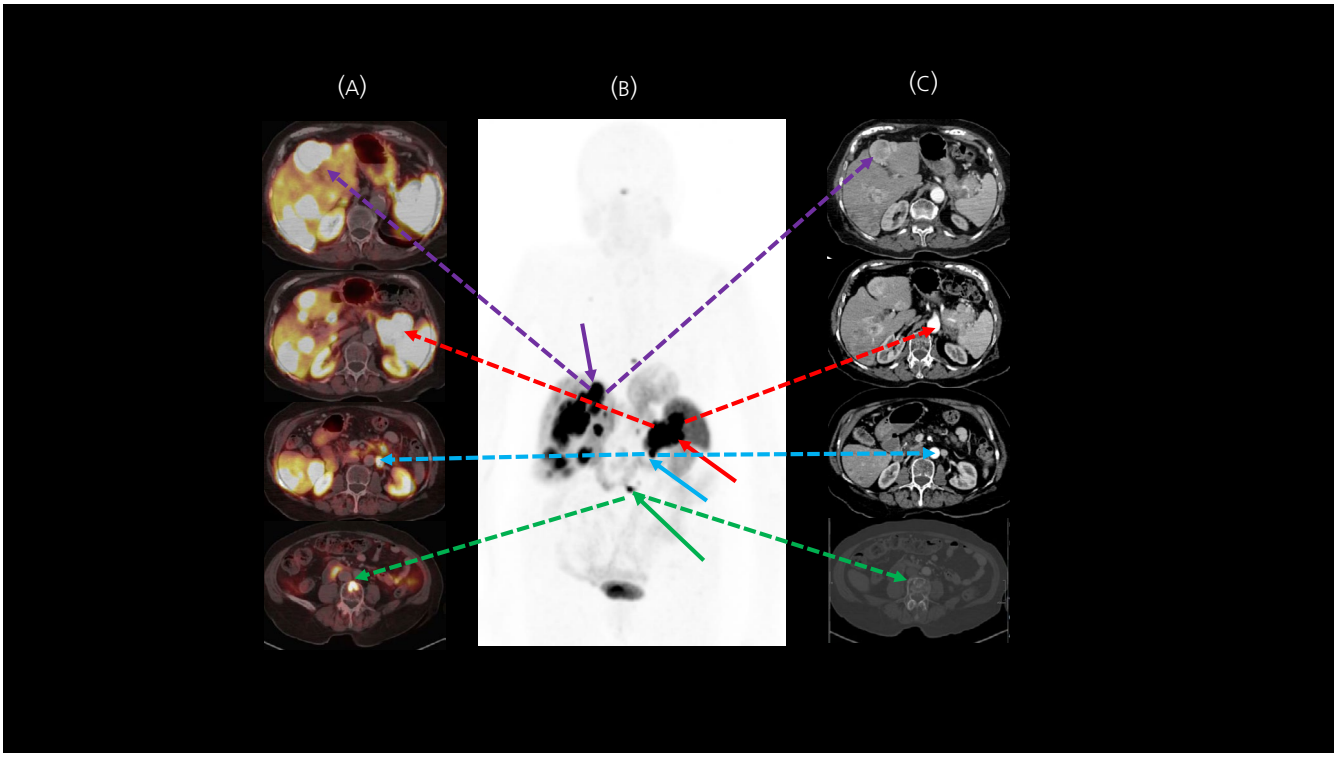

FIGURE 2 The central maximum intensity projection image (B) provides an overview of disease distribution enabling an immediate impression of possible primary sites including, in this case of a ^{68}Ga-DOTATATE PET/CT, the pancreas (red arrow), regional nodes (blue arrow), hepatic (purple arrow) and bone (green arrow) metastases, which can be secondarily reviewed as orthogonal tomographic images displayed with appropriate windowing of hybrid (A) and anatomical (C) data (dotted lines)

and timely diagnoses on which to advance precision medicine. To achieve these goals, a process of testing and refinement of the proposed template will be undertaken within the ENETS CoE network. Further evolution of these templates will need consultation with other specialist societies involved in the delivery of imaging in cancer patients. Particularly in the context of molecular imaging templates, EANM, Society of Nuclear Medicine and International Cancer Imaging Society endorsement will be sought. The ability to incorporate reporting templates into existing RIS varies and may require vendor engagement for more routine implementation. It should be noted that the

TABLE 5 Reference lesions

Region	Lesion descriptor (location)	Visual avidity (e.g., Krenning score)	Semiquantit-ative avidity (e.g., SUV_{max})	Tumor to spleen SUV_{max} ratio	Somatostatin Receptor-FDG relationship	Size (uni- or bidimensional)
Head and Neck						
Thorax						
Abdomen						
Pelvis						
Appendicular						

Abbreviation: SUV_{max}maximum standard unit value.

current template does not include the facility for integrated reporting of imaging using more than one molecular imaging tracer (e.g., ^{68}GA DOTATATE and ^{18}FDG PET/CT or ^{123}I-MIBG and ^{68}Ga DOTATATE). Differing report templates may also be relevant for imaging specialists with different levels of modality credentialling. Thus, ongoing refinement of the synoptic templates are likely to be required as incorporation of molecular imaging phenotyping into treatment planning becomes more routinely available and clinically accepted.

5 | CONCLUSIONS

After a wide-ranging discussion and review of available literature, our multidisciplinary panel has developed a template for synoptic reporting of molecular imaging studies pertinent to the diagnosis, characterisation, staging and therapeutic approaches of NEN. We realise that these represent preliminary steps in establishing a framework for synoptic reporting and look forward to feedback and further refinement of this template through engagement of ENETS CoEs and specialist imaging societies. It is recognised that local accreditation standards may mandate reporting requirements that are not included in the current template and RIS implementation may prove problematic at some sites. Nevertheless, reporting clinicians are encouraged to implement as many elements of the current template as possible within these constraints.

This article is part of a special issue on standised (synoptic) reporting of neuroendocrine tumours (see editorial[17] and articles[18-21]).

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CONFLICT OF INTERESTS

The authors declare that they have no conflicts of interest.

AUTHOR CONTRIBUTIONS

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DATA AVAILABILITY

Data sharing is not applicable to this article because no datasets were generated or analysed during the current study.

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APPENDIX ENETS

ADVISORY BOARD MEETING PARTICIPANTS IN 2018

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