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STANDARDS

ENETS standardized (synoptic) reporting for radiological imaging in neuroendocrine tumours

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Abstract

This expert consensus document represents an initiative by the European Neuroendocrine Tumor Society (ENETS) to provide guidance for synoptic reporting of radiological examinations critical to the diagnosis, grading, staging and treatment of neuroendocrine neoplasms (NENs). Template drafts for initial tumor staging and follow-up by computed tomography (CT) and magnetic resonance imaging (MRI) were established, based on existing institutional and organisational reporting templates relevant for NEN imaging, and applying the RadLex lexicon of radiological information (Radiological Society of North America), for consistency regarding the radiological terms. During the ENETS Scientific Advisory Board meeting 2018, the template drafts were subject to iterative interdisciplinary discussions among experts in imaging, surgery, gastroenterology, oncology and pathology. Members of the imaging group stated a strong preference for a combination of limited and standardised options by way of drop-down menus. Separate templates were produced for the

initial work-up and for follow-up, respectively. To provide a detailed description of the radiological findings of the primary tumor and its local extension and spread, different templates were developed for bronchial, pancreatic and gastrointestinal NENs for CT and MRI, respectively. Each template was structured in 10 sections: clinical details, comparative imaging modality, acquisition technique, primary tumor findings, regional lymph node metastases, distant metastases, TNM classification, reference lesions according to RECIST 1.1, additional findings and conclusion. Two templates were developed for follow-up, for CT and MRI, respectively, and were specifically focused on assessment of therapy response. These included a qualitative response assessment, such as decrease of vascularisation and presence of necrosis, and a quantitative assessment according to RECIST 1.1 and the modified RECIST (mRECIST) for assessing tumor response following transarterial chemoembolisation.

KEYWORDS

CT, MRI, neuroendocrine neoplasia, synoptic reporting

1 | INTRODUCTION

Radiology reports have a key role in diagnostic work-up, therapeutic management guidance and follow-up of neuroendocrine neoplasm (NEN) patients. By convention, radiology reports comprise free-text narratives, which are very variable in length, structure, content and clarity. As a result of their different informative qualities, they are also prone to omission of important data required by managing clinicians to determine optimal care pathways for their patients. Adoption of synoptic reporting should lead to improved standardisation of diagnostic criteria and terminology, thereby enhancing clarity, readability and consistency in clinical reports. This is likely to improve satisfaction among referring clinicians, including primary physicians, surgeons, oncologists, endocrinologists and gastroenterologists, and contribute to improvement of clinical care. Furthermore, synoptic reporting provides a checklist that ensures a more complete reporting of the essential findings, particularly by readers who are less experienced in reporting findings relevant to NEN. Finally, synoptic reporting also denotes a means to populate structured databases, which facilitate data exchange and analysis for quality assurance, cancer epidemiology and research. Potential benefits of structured reporting in radiology have been outlined at the American College of Radiology (ACR) 2007 Intersociety Conference.[1]

This expert consensus document represents an initiative by the European Neuroendocrine Tumor Society (ENETS) to provide guidance for synoptic reporting of radiological examinations. Through publication of standards-of-care consensus guidelines, the ENETS promotes writing and updating guidelines for all aspects of NET care, including diagnosis, treatment and standard of care.[2] In parallel with development of practice guidelines, ENETS have developed standards for accreditation of ENETS Centre of Excellence (CoE).

During the annual Scientific Advisory Board (SAB) Meeting in November 2018, the European Neuroendocrine Tumor Society (ENETS) initiated expert working groups to develop guidelines for the synoptic reporting of gastroenterology procedures, pathology, radiology and molecular imaging for patients with NEN. This paper describes the process and consensus outcomes of the radiology panel.

2 | MATERIALS AND METHODS

In 2018, imaging experts of the scientific advisory board of ENETS were invited to initiate a working group to provide synoptic reporting on imaging for NEN initial staging and follow-up.

As an initial step, they identified existing institutional or organisational reporting templates that might be relevant for computed tomography (CT) and magnetic resonance imaging (MRI) examinations of NEN patients. Four initial draft templates were established as the basis for preliminary interdisciplinary discussions: two templates for initial staging on CT and MRI and two templates for follow-up on CT and MRI. The RadLex lexicon, a lexicon of radiological information produced by the Radiological Society of North America (RSNA), was used to unify radiology terms (http://www.radlex.org).

These templates were first presented during the annual SAB meeting in June 2018. During this meeting, a breakout session was organised in which an ENETS SAB subcommittee representing different medical specialties deliberated on the various specific aspects of radiology reports and conveyed their results to the board conference attendees. The working group included three radiologists, one surgeon, one oncologist, four gastrointestinal-endoscopists and one gastroenterologist.

Options for discussion included the target population likely to utilise these reporting templates (expert *vs* general radiologists), the field of application (clinical routine *vs* research), feasibility of integration of such a template within existing radiology information

systems (RIS), opportunities for standardisation of nomenclature, extent of imaging findings to be reported without overcrowding the final report, and whether reporting should be based on tumor location or not. Based on fruitful discussions within a subcommittee of the SAB, refined templates were presented to obtain feedback, using a sequential process; first, from the breakout group members and, second, from the SAB members. The group worked iteratively, with consensus agreement to define each of the data elements and refine the structure of the report. Through this iterative process, six synoptic reporting templates were developed: three templates for initial staging on CT exams for bronchial, digestive and pancreatic NEN, one template for initial staging on MRI exams, and two templates for follow up on CT and MRI exams. For each of the templates, pull-down menus were created for distribution and testing at ENETS CoEs.

3 | RESULTS

3.1 | General

The group chose a set of standardised RadLex terminology to maintain consistency between reporting templates and to ensure semantic clarity.

3.2 | Synoptic reporting for initial work-up

Following current clinical practice for radiologists, and to provide a detailed description of the radiological findings of the primary tumor and its local extension and spread, three different CT templates were developed for the most common primary tumor locations: bronchial NEN, pancreatic NEN and gastrointestinal NEN. An important reason for developing three specific templates, by tumor location, rather than only one, was that differences in surgical treatment between these primary tumors require specific descriptors within the imaging findings to guide the resectability.

Each template was structured in 10 sections: clinical details, comparative imaging modality, acquisition technique, primary tumor findings, regional lymph node metastases, distant metastases, TNM classification, reference lesions according to RECIST 1.1, additional findings and conclusion (see Supporting information, Appendix S1).

Members of the imaging group stated a strong preference for, wherever possible, a combination of limited and standardised options by way of drop-down menus.

For clinical details section, some items specific to NENs, such as location of the primary tumor, pathological differentiation and grade, as well as tumor predisposition syndrome, have been implemented in addition to the more common items such as indications and clinical symptoms (Table 1).

Sections on comparative imaging modality and acquisition technique sections corresponded to those routinely used in radiology reports (Table 2).

A minimal imaging acquisition reporting was considered critical for quality-assurance assessment. Particularly for CT examination, the acquisition of a late arterial phase in addition to the venous phase examination is an absolute must. Radiologists indicated the importance to document this information to allow for reproducibility of methodology in follow-up studies.

CT findings regarding the primary tumor comprised the only section that was different between the three templates developed for the initial staging. It was also the section for which the multidisciplinary approach of this initiative was the most fruitful. Each item was strongly debated between the different specialists of the group. The conclusions from the multidisciplinary debate are summed up in Tables 3-5. For the template of digestive NEN, an eleventh section with description of carcinoid heart disease findings was added.

For description of distant metastases, clinicians emphasised the clinical relevance to report lesions requiring a specific management (e.g., bone lesions compromising neurological function or with risk of instability and fracture, bowel obstruction as a result of mesenteric metastases and peritoneal implants) in addition to reporting the presence and absence of metastases in the different locations (Table 6).

Both clinicians and imaging specialists supported the concept of integrating a table identifying target lesions according to RECIST 1.1, the most commonly used criteria both in clinical trials and in the daily clinical routine, to assess therapy response[3] (Table 7).

The conclusion was less easily amenable to synoptic reporting because it more often than not requires a summary of most relevant information. In addition, conclusions generally tend to answer specific clinical question(s) posed by the referring physician. Accordingly, it was proposed that conclusions are reported as free text.

An example of a radiologic CT report for initial staging of a digestive NEN (Figures 1-4) is presented in the Supporting information (Appendix S2).

For MRI reporting, the template followed the same sections and same terminology as for CT. The main difference compared to the CT templates comprised the section including MRI specific technical information, such as MRI acquisition sequences. Based on surgeons' suggestions, and also taking into consideration the fact that most of the MRI examinations for NEN work-up are performed to rule out or diagnose liver metastases, a specific section with more detailed description of liver metastases was also added.

3.3 | Synoptic reporting for follow-up

Two templates were developed for follow-up, one for CT and one for MRI, and were targeted specifically to assess the response to treatment. Conversely, a part was added in the clinical detail section to register treatment information (type of therapy, date of start and date of nadir) to facilitate comparison with the most appropriate previous examination and choice of proper criteria for tumor response evaluation.

TABLE 1 Clinical details

Field	Template options
Indication	Diagnosis Staging Treatment planning Other (free text)
Location	Free text
Pathology type	Typical lung – NET Atypical lung – NET NEC – large cell NEC – small cell Mixed tumor Unknown
Pathology differentiation	Well differentiated Poorly differentiated Unknown
Pathology grade	Grade 1 Grade 2 Grade 3 Unknown
Tumor-predisposition syndrome	None MEN-1 VHL Carcinoid Insulinoma Glucagonoma Gastrinoma VIPoma Other (free text)
Clinical symptoms	Hormone-related symptoms No hormone-related symptoms If yes, describe (free text)
Other relevant clinical information	Free text

Abbreviations: MEN-1: Multiple endocrine neoplasia type 1, NEC: neuroendocrine carcinoma, NET: neuroendocrine tumor, VHL: von Hippel Lindau, VIPoma: vasoactive intestinal peptide tumor.

The presentation on therapy response was organised in two steps: first, a qualitative assessment evaluating the changes in tumor phenotypes, such as decrease of vascularisation and presence of necrosis, and, second, a quantitative assessment using specific criteria developed for treatment response assessment. Both clinicians and imaging specialists recognised that, despite its limitations, RECIST 1.1 is still the most clinically relevant criteria to evaluate treatment response. Because these criteria assess changes in tumor size and do not account for development of tumor necrosis, the treatment response may be underestimated, in particular for some systemic targeted therapies and transarterial (chemo)embolisation (TACE). Consequently, following the recommendations of the European Association for the Study of Liver (EASL), the panel of experts proposed to consider the modified RECIST (mRECIST), which considers the concept of tumor viability based on arterial enhancement, instead of the RECIST 1.1 for radiologically evaluating tumor response during TACE.[4,5]

For research purposes only, two additional criteria were proposed, the CHOI criteria for CT and the apparent diffusion coefficient (ADC) measurement for MRI, respectively. The CHOI criteria, defining a tumor partial response by either a 10% reduction in size or a 15% reduction in attenuation (Hounsfield units) on venous phase CT images, were proposed as an alternative to RECIST 1.1 for response evaluation of targeted therapies.[6] The ADC (mean and minimum) on diffusion-weighted MRI may indicate treatment-related tumor necrosis.[7] Until such a time as immune check-point inhibitors therapy is established for the treatment of NEN, immune-modified RECIST (imRECIST) was not incorporated into the current templates.

The different templates of synoptic reporting for initial and follow-up work-up for CT and MRI are presented in the Supporting information (Appendix S1).

4 | DISCUSSION

Radiology reports play a key role in diagnostic work-up and consequent therapeutic selection, as well as in post-treatment surveillance of every cancer patient. Key parameters to ensure the quality of radiological reporting include appropriate description, completeness, conformance with current agreed standards, and consistency and timeliness. A major advantage of synoptic over narrative reporting

TABLE 2 Comparative imaging

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

Abbreviations: CT: computed tomography, DOTANOC: 68Ga DOTA-1-Nal3-octreotide, DOTATATE: 68Ga DOTA-DPhe1, Tyr3-octreotate, DOTATOC: 68Ga (DOTA(0)-Phe(1)-Tyr(3))octreotid, FDG: (18)F-fluorodeoxyglucose, MRI: magnetic resonance imaging, PET: positron emission tomography, SPECT: single photon emission computed tomography.

TABLE 3 Findings for bronchial neuroendocrine neoplasms

Field	Options
Location	Endobronchial Perihilar Peripheral
Lung lobe	Right upper lobe Right middle lobe Right lower lobe Left upper lobe Left lower lobe
Lung atelectasis	Yes/No
Size of each lesion	() mm
Calcifications	Yes/No
Suspected DIPNECH	Yes/No

is an increase in completeness of data and findings, as demonstrated by a number of studies across various cancer types, including colorectal, lung, breast and prostate cancer, as well as cutaneous malignant melanoma.[8] Synoptic reporting not only ensures that all reports contain essential parameters, but also reduces the inter-reader variability and improves the communication with clinicians. Given the multidisciplinary nature of the management of NENs, radiology reports have many users relying on different types of information. These end-users include, but are not limited to, surgeons, medical oncologists, radiation oncologists, endocrinologists, gastroenterologists, interventional radiologists, nuclear medicine specialists and pathologists. Thus, the clinical relevance and clarity of the report should seriously be taken into consideration. The multidisciplinary approach of the process initiated by the ENETS ensured that the proposed structured radiology reports contain not only a description of radiological features, but also important and comprehensive information required for patient care as guided by experts in the management of NEN.

The first aspect debated by the ENETS SAB members was to define the appropriate degree of data structuration, ranging from a traditional unformatted narrative report without standardised content, to a completely standardised dataset and electronic implementation with binding terminology.[9] Our proposed synoptic reporting positions itself in the middle between these extremes regarding the degree to which data are structured and classified. Indeed, the goal was to set up a specific reporting format with a check list of important data, but not necessarily requiring software implementation.

The terminology used in drafting is also an important parameter of structured reports. We mainly used the RadLex lexicon produced by the Radiology Society of North America (RSNA) based on a structured radiology-specific ontology, with more than 30,000 terms.[10] Moreover, the structure of reporting and terminology used were defined in consensus with the molecular imaging group in order to provide templates as similar as possible. It was recognised that many molecular imaging studies are now combined with acquisition of diagnostic quality CT and either co-reported by a radiologist and nuclear medicine physician or by dual-trained radiologists. Therefore, integration of synoptic CT reporting into a combined PET-CT report would be aided by this process.

The most debated items were the radiologic features of the primary tumor. The main difficulty was to find the right balance between completeness of data and the time needed to complete the report. Each item was carefully selected to meet specific criteria: (1) to focus on the radiological findings most relevant for patient management; (2) to emphasise imaging findings specific to NENs; and (3) to communicate relevant findings clearly to referring physicians in order to assist them in creating treatment plans.

Specific templates were also developed for follow-up to standardise assessment of response to treatment. Although RECIST 1.1 is intended for use in the clinical trial setting, oncologists increasingly rely on RECIST 1.1 based tumor measurements to make clinical management and therapeutic decisions in daily clinical practice.

TABLE 4 Findings for digestive neuroendocrine neoplasms

Field	Options	Subcategories
Number	Solitary Multiple (add number)	
Location (s)	Free text	
Size of each lesion	() mm	
Pattern	Not detectable Enhancing polyp Plaque-like mass	
Calcifications	Yes/No	
Signs of obstruction	Yes/No	
Mesenteric LN involvement	Yes/No Size	Stage 1: Nodes near bowel Stage 2: Involvement of the SMA branches Stage 3: Involvement of SMA without involvement of the superior jejunal artery Stage 4: involvement of the root of the SMA
Entrapped loops of the small bowel	Yes/No	If yes, length of the entrapped loops: () cm
Desmoplastic reaction (retractile mesenteritis)	Yes/No	Vascular ectasia (Yes/No) Bowel wall thickening and enhancement (Yes/No) Small bowel submucosal edema (target sign): (Yes/No)

Abbreviations: SMA: Superior mesenteric artery.

TABLE 5 Findings for pancreatic neuroendocrine neoplasms

Field	Options	Subcategories
Number	Solitary Multiple (add number)	
Location (s)	MRI	
Size of each lesion	() mm	
Pattern	Enhancement at the arterial phase Enhancement at the delayed phase Cystic Mixed cystic and solid	
Margins	Well circumscribed Ill defined	
Calcifications	Yes/No	
Relationship of tumor and main pancreatic duct	> 3 mm distance < 3 mm distance without duct obstruction Tumor-related obstruction	
Tumor-related bile duct obstruction	> 3 mm distance < 3 mm distance without duct obstruction Tumor-related obstruction	
Adjacent organ involvement	Yes/No	If yes, which organ (free text)
Vessel involvement arteries	Celiac trunck Hepatic artery SMA	No contact Minimal contact Contact > 180° Obstruction Not assessable
Vessel involvement veins	Splenic vein Portal vein SMV	No contact Direct contact Stenosis/obstruction Tumor stenosis Not assessable

Abbreviations: SMA: Superior mesenteric artery, SMV: superior mesenteric vein.

TABLE 6 Metastases

Field	Options	If yes	Subcategories
Liver	Yes/No	% of liver involvement Pattern Type	<5 %; ≥ 5 < 25% ≥ 25 < 50% ≥ 50% Not assessable Hypovascular hypervascular Cystic Mixed
Mediastinal lymph nodes	Yes/No		
Abdominal lymph nodes	Yes/No		
Peritoneum	Yes/No	Bowel obstruction	Yes/No/Not assessable
Lung	Yes/No		
Bone	Yes/No	Neurologic risk Static instability Distribution of bone metastases	Yes/No Yes/No Localised; widespread, not applicable
Other	Yes/No	Location	

TABLE 7 Reference lesions according RECIST 1.1

Target lesion (TL)	Location	Size
TL1		
TL2		
TL3		
TL4		
TL5		
Sum of diameters		
% change from baseline or nadir		
Response target lesion		
Non-target lesions (NTL)	**Location**	**Evaluation**
NTL1		
NTL2		
NTL3		
NTL4		
NTL5		
Response non-target lesion		
New lesion		
Overall response		

Abbreviations: TL: Target lesion, NTL: non-target lesion.

Indeed, RECIST 1.1 provides a standardised set of rules for tumor size measurement and response assessment that are globally available and can be applied by most radiologist and clinicians. RECIST 1.1 provides a framework for reproducible analysis and offers a simple way of quantifying and communicating response assessment. Consequently, all members of the subcommittee, both radiologists and clinicians, agreed that RECIST 1.1 of 2009[3] should be implemented in the structured report for assessment of treatment response. Although RECIST 1.1 is suitable for most treatments, some limitations have been found in the assessment of loco-regional therapy and targeted therapy because these criteria do not account for therapy-induced tumor necrosis and devascularisation. In 2000, a panel of experts from the European Association for the Study of the Liver (EASL) agreed on specific response criteria for hepatocellular carcinoma, where the reduction in viable tumor size (defined as the contrast-enhancing part of the lesion), instead of the total tumor, was considered for assessment of the local therapy response.[11] Subsequently, similar advantages of using modified RECIST criteria (mRECIST) for loco-regional therapy in NENs have been reported, in particular for the assessment of TACE of liver metastases.[5] In addition, it has been suggested that the CHOI criteria, initially developed for the assessment of gastrointestinal stromal tumors treated with Imatinib, may be appropriate for tumor response assessment in NENs treated with either targeted therapies such as sunitinib and everolimus[12-14] or peptide receptor radionuclide therapy.[15] Finally, the ADC, measured on diffusion-weighted MRI, has also become a promising quantitative biomarker for prediction and monitoring of the therapeutic response. An increase in ADC has been correlated with necrosis and some studies have demonstrated ADC increases as a result of morphological changes associated with apoptosis.[7,16] Even though the level of evidence is low, the members of the subcommittee supported the more widely used of these criteria in addition of RECIST for research purposes.

It should be noted that the proposed templates do not include all types of primary NENs, but merely the most frequent. Thus, other templates are likely to be required. Another challenge is the implementation of these templates into existing radiology information systems (RIS) or picture archiving and communication systems (PACS) software used to generate radiology reports. Structured reporting is also an important step towards higher levels of data capture, which facilitate data collection for clinical and research registries, cancer epidemiology, and research and education.

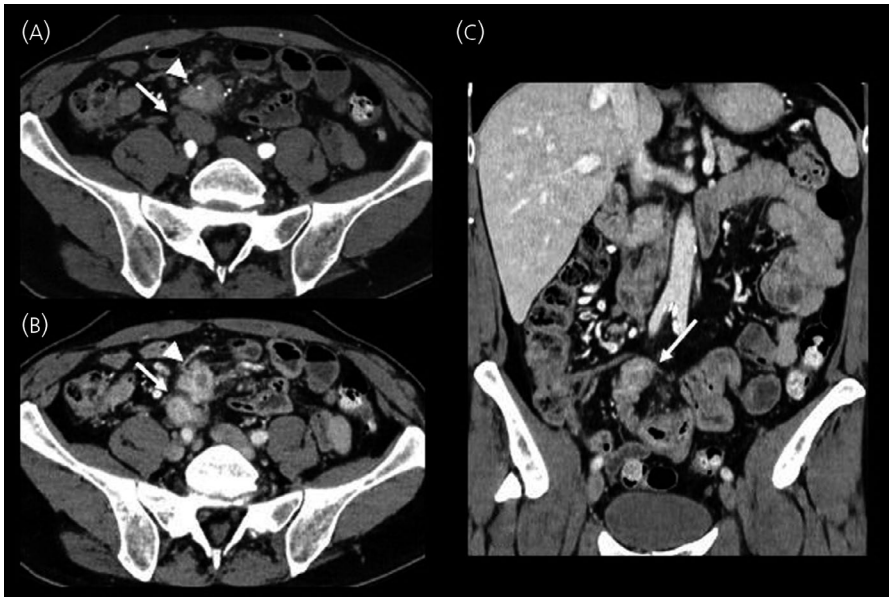

FIGURE 1 A 58 year-old patient with abdominal pains, nausea and postprandial vomiting. Transverse computed tomography images on arterial (A) and portal (B) phase with coronal reconstruction (C) show a enhancing mass in the ileum (arrows) with mesenteric lymph node involvement (arrowhead)

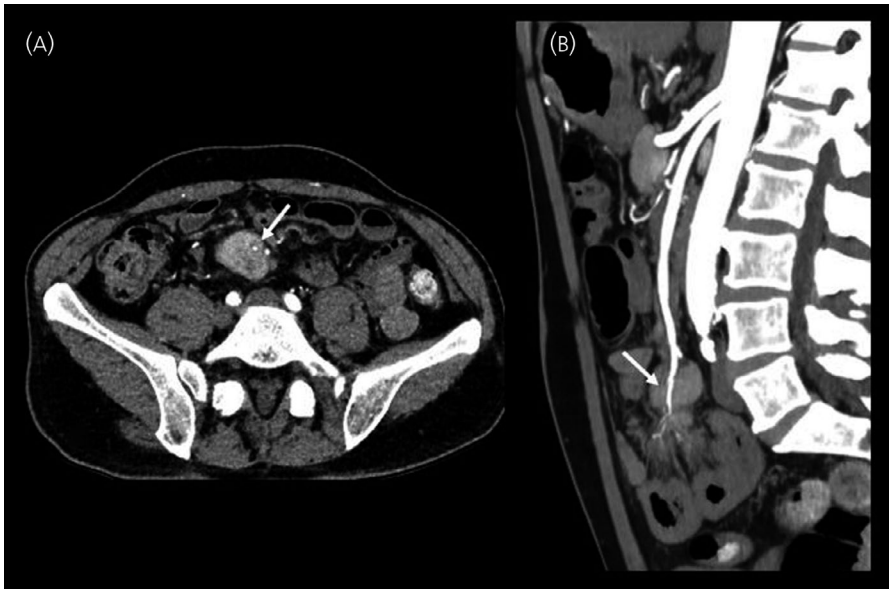

FIGURE 2 Transverse computed tomography images on arterial phase (A) with sagittal reconstruction using maximal intensity projection (B) show an involvement of the distal mesenteric artery branches (arrows) stage 2

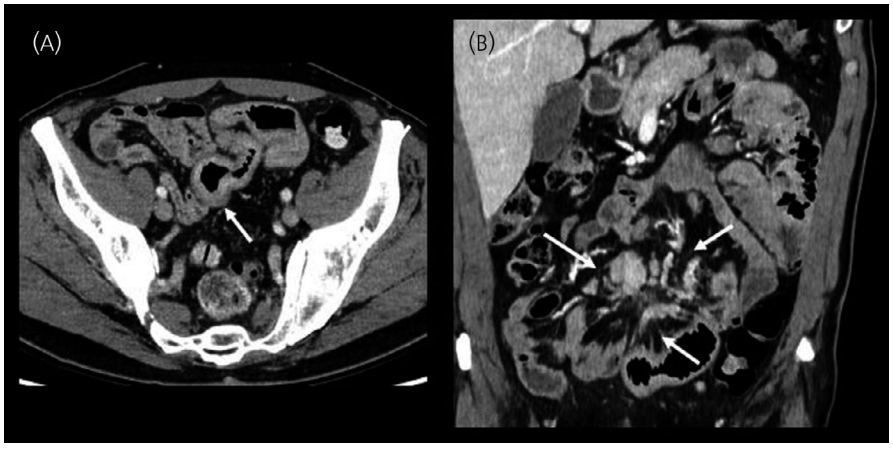

FIGURE 3 Transverse computed tomography images on portal phase in transverse (A) with coronal reconstruction (B) show a desmoplastic reaction of the mesentery (three arrows) and signs of ischemia, including vascular ectasia, bowel wall thickening with enhancement and target appearance (arrow)

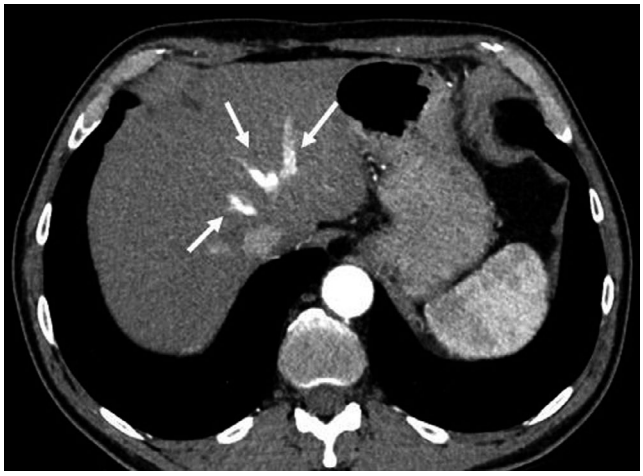

FIGURE 4 Transverse image on arterial phase shows a retrograde filling of hepatic veins (arrows) suggestive of a carcinoid heart disease

5 | CONCLUSIONS

From an ENETS initiative, a multidisciplinary panel of NEN experts has developed templates for synoptic reporting of radiology. After iterative interdisciplinary discussions among experts, six templates were developed for initial work-up for bronchial, pancreatic and gastrointestinal NEN, and for follow-up on CT and MRI.

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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AUTHOR CONTRIBUTIONS

Clarisse Dromain: Conceptualisation; Data curation; Formal analysis; Investigation; Methodology; Project administration; Validation; Writing – original draft; Writing – review & editing. **Marie – Pierre Vullierme:** Methodology; Validation; Writing – review & editing. **Rodney J. Hicks:** Conceptualisation; Data curation; Investigation; Methodology; Supervision; Validation; Writing – original draft; Writing – review & editing. **Vikas Prasad:** Conceptualisation; Data curation; Formal analysis; Investigation; Methodology; Project administration; Writing – original draft; Writing – review & editing. **Dermot O'Toole:** Conceptualisation; Methodology; Project administration; Resources; Writing – review & editing. **Wouter W. de Herder:** Conceptualisation; Writing – review & editing. **Marianne Pavel:** Conceptualisation; Writing – review & editing. **Antongiulio Faggiano:** Data curation; Investigation; Methodology; Writing – review & editing. **beata Kos – Kudla:** Data curation; Formal analysis; Methodology; Writing – review & editing. **Kjell Oberg:** Conceptualisation; Methodology; Resources; Writing – review & editing. **Guenter J. Krejs:** Data curation; Investigation; Writing – review & editing. **Enrique Grande:** Investigation; Methodology; Writing – review & editing. **Bruno Niederle:** Data curation; Investigation; Writing – review & editing. **Anders Sundin:** Conceptualisation; Formal analysis; Investigation; Methodology; Validation; Writing – original draft; Writing – review & editing.

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Data sharing is not applicable to this article.

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

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APPENDIX

ENETS ADVISORY BOARD MEETING PARTICIPANTS IN 2018

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