Pancreatic neuroendocrine tumours (pNETs) are rare tumours that arise from the neuroendocrine cells of the pancreas (1). They are less than 3% of pancreatic tumours, with a growing annual incidence of one case per 100,000 individuals (1-3). pNETs can be an isolate phenomenon or a part of a hereditary syndrome like von Hippel-Lindau syndrome or neurofibromatosis-1. The incidence has increased in the last years, also because of the improvement of cross-sectional imaging. Computed tomography (CT), magnetic resonance imaging (MRI) and functional imaging are the mainstream imaging modalities used for tumour detection and disease extension assessment, due to easy availability and better contrast/spatial resolution. Radiological imaging plays a fundamental role in detection, characterization and surveillance of pNETs and is involved in almost every stage of patients' management. Moreover, with specific indications and techniques, interventional radiology can also play a role in therapeutic management. Surgery is the treatment of choice, consisting of either partial pancreatectomy or enucleation of the primary tumour. This article reviews the radiologic features of different pNETs as well as imaging mimics, in order to help radiologists to avoid potential pitfalls, to reach the correct diagnosis and to support the multidisciplinary team in establishing the right treatment.

Keywords: Neuroendocrine tumour (NET); computed tomography (CT); magnetic resonance; radiomics


doi: 10.21037/gs-20-537

View this article at: http://dx.doi.org/10.21037/gs-20-537
oncological pathology either for the initial assessment, the
treatment planning, and the follow-up after therapy (14). A
lot of imaging methods can be useful including ultrasound
(US), computed tomography (CT), magnetic resonance
imaging (MRI) and functional/nuclear imaging such as
somatostatin receptor imaging and positron emission
tomography (PET). The association between PET and
CT (PET/CT) with different tracers can be particularly
important during staging and search of metastases (15).
Radiological imaging plays a fundamental contributory role
in detection, characterization and surveillance of pNETs and
is involved in almost every stage of patients’ management
and can be useful both for diagnosis and surgical or medical
therapy. Moreover, with specific indications and techniques,
interventional radiology can also play a role in therapeutic
management (16,17).

In this article, we reviewed the different radiological
findings at CT and MRI related to the different patterns
of pNETs. Radiologists should be aware of these potential
accidental findings and collaborate with clinicians to reach
an accurate diagnosis and to decide the right therapy.
We present the following article in accordance with the
Narrative Review reporting checklist (available at http://
dx.doi.org/10.21037/gs-20-537).

**Non-functioning tumours**

Non-functioning tumours are 60–80% of pNETs and
approximately 50–90% of them are malignant at
presentation also because they tend to manifest late and
often larger in size (1,18). Abdominal US has low sensitivity
and specificity for detecting pancreatic solid nodules or
masses but can help in finding liver metastases (19,20).

Recently, contrast-enhanced US (CEUS) improves the
accuracy of analysis of focal pancreatic lesions through the
use of US contrast medium (20). In fact, the bloody supply
to the pancreas is entirely arterial and enhancement of
the gland is well recognized through CEUS examination:
similarly to CT exam as explained below, also pancreatic
CEUS shows a hyperenhancing arterial phase in
pNETs (21). CT is the imaging method of choice for the
evaluation of various pancreatic diseases and is often the
initial diagnostic technique, also because of its high spatial
resolution and short acquisition time (22). Both an arterial
angiographic phase, after 20–30 seconds, or a pancreatic
one, 20 seconds later than the first, can be used, followed,
after 60–80 seconds by a portal-venous phase (23,24). The
arterial phase is considered the gold standard in localizing
pNETs, as they are usually hypervascular, and because of
their contrast washout in the venous phase, that makes the
tumour isodense respect to the surrounding parenchyma.
Referring to this particular behaviour, pNETs tend to be
a well-defined and homogeneously enhanced lesions on
arterial-phase CT, due to their copious capillary pathway,
and hypo-iso or hyperdense on portal phase, in contrast
with pancreatic parenchyma (Figure 1) (25). A lot of research
has been made to search a way to differentiate tumour
grades both with CT and MRI (26,27). Zamboni et al. in
their retrospective study, tried to differentiate various grades
of pNETs in 148 patients using CT, and demonstrated
that the parameters with better performance in G1–G2
tumours were the hypervascular aspect in the arterial phase,
hyperdensity in the venous phase and well-defined margins.
On the other hand, they affirmed that G3 tumours are larger
ones, non-hypervascular in the arterial phase and hypodense
in the venous phase and tend to be more invasive (26).

![Figure 1](image_url) Hypervascular pNET with hypovascular metastases. CT images in (A,B,C) show a hyperenhancing pancreatic nodule in the body-tail of the organ (arrows). Please note the atypical hepatic metastases in the right lobe that are hypovascular in arterial, pancreatic and venous phase. pNET, pancreatic neuroendocrine tumour; CT, computed tomography.
A similar study was made by Takumi et al. evaluating multiple parameters such as tumour’s margin, presence of peripancreatic vascular involvement, ductal dilatation, metastasis (lymph nodal N or distant ones M), cystic or necrotic aspects. They found that G1 and G2 have no great difference referring to tumour morphology, vascular involvement, ductal dilatation, or N involvement; instead, G2 are more often larger in size (≥ 20 mm) and show no hyper-attenuation during the portal phase (28). It is easy to understand from these studies how limited is the possibility to differentiate G1 from G2, being only few radiological characteristics related with tumour grade.

With the advent of Radiomics, the new method in which the information is “hidden” inside the radiological images and can be extracted using advanced texture and shape analysis, it has been possible to extract lots of information regarding the structure we need to study (29-31). Zhao et al. tried to overcome these limits using radiomics features on CT images to identify some discriminant features for G1 and G2 tumours: he found that six features, using both non-enhanced and portal-venous phases, can be useful in differentiating grade G1/G2 in non-functional pNETs (32).

More information in the characterization of these different grades can be obtained with MRI imaging (15). The pancreas has a hyperintense signal on T1-weighted imaging, because of the amount of protein inside the parenchyma, therefore pNETs tend to appear hypointense in contrast with pancreatic parenchyma on un-enhanced T1-weighted images. On T2-weighted images, pNETs can be hyperintense, even if a lower signal can also be present. On post-contrast images, tumours show vivid contrast enhancement, that can be both homogeneous or heterogeneous, ring- or target-like (Figure 2). Diffusion weighted imaging (DWI) may also help in tumour detection (33,34). Guo et al. studied a total of 59 lesions trying to identify the MRI features in differentiating pNETs G1/G2 and pancreatic neuroendocrine carcinoma G3; G1/G2 tumours had well-circumscribed border compared with G3 (35). G3 tend to be bigger in size, often associated with metastases and duct dilatation, low-moderate enhancement also because of necrotic phenomena, and high DWI signal intensity, with lower apparent diffusion coefficient (ADC) values than G1/G2 (35). They concluded that the presence of metastases and the different ADC value between grades

Figure 2 CT and MRI imaging. A large pNET (arrows) in a young woman that underwent a CT exam [(A) axial arterial, (B) axial portal phases and (C) coronal arterial reconstruction] and MRI [(D) T1-weighted, (E) T2-weighted imaging and (F) coronal T2 reconstruction]. Note the non-homogeneous vascularization of the lesion and the relatively hyperintensity in T2 weighted phase. CT, computed tomography; MRI, magnetic resonance imaging; pNET, pancreatic neuroendocrine tumour.
can be useful in distinguishing G3 from G1/G2 pNETs. Also, Mebis et al. tried to find the connection between ADC value on MRI and histopathologic WHO-grades of NET. They found interesting and important differences between low (G1–G2), with higher values of ADC, and high grade (G3) pNETs (36). The lower ADC values on ADC map in high grade pNETs may be caused by the high cellularity with less extracellular space and cytoplasm, reducing the possibilities of water molecules to move (37). Also, fibrosis can be involved in generating lower ADC values, above all in some low grade, well-differentiated tumours (38). De Robertis et al. tried to improve the use of MRI in association with histogram analysis parameters finding that, in the analysis of 42 pNETs >1 cm, the whole-tumour histogram analysis of ADC maps may be used as a predictor of tumour grade, vascular invasion and nodal or liver metastases. Furthermore, ADC entropy and ADC kurtosis resulted as the most significant parameters in discerning tumours with malignant behaviour (39).

**Functioning tumours**

pNETs can be hyperfunctioning, with the production of a lot of different hormones such as insulin, glucagon, gastrin, vasoactive intestinal peptide (VIP) and somatostatin, that can create various clinical manifestation. This subtype of tumours tends to present earlier, with clinical signs and symptoms. Insulinomas are the most common functioning NET, representing the 40% of all functioning pNETs (40). Typically, insulinomas are located equally in all the anatomic sites of the pancreas, and they can be round-shaped, nodular or oval, usually with a diameter inferior to 15 mm. They can be isolate or multiple and both deep or superficial (41). At CT examination, these lesions are isodense at baseline, homogeneously hyperdense in the pancreatic phase, and hypodense in the venous one because of their washout phenomena (Figure 3). These aspects where confirmed by the study that included 53 patients with insulinoma, conducted by Fidler et al., demonstrating that most tumours were hyperenhancing compared with the pancreatic parenchyma on at least one of the phases; nevertheless three tumours were hypoattenuating on all phases and another three were isodense within the pancreatic parenchyma, but could be visualized because of their pedunculated morphology (42). In order to distinguish between typical and atypical insulinomas, multiphase imaging is essential: the latter is iso-hypoattenuating in the early phase at CT, and hypoattenuating in venous one, because of its higher stromal composition, its smaller dimensions and its structure with both amyloid and fibrohyaline components (43). MRI shows a homogeneously enhanced lesion with low signal on T1-weighted imaging and high signal on T2-weighted one (44). In their case report of a female patient with a clinical suspicion of insulinoma and an inconclusive contrast-enhanced CT and MRI, Anaye et al. underlined the usefulness of DWI sequences in detecting and localizing small insulinomas especially for those with no hypervascular pattern, with high signal intensity on DWI. Furthermore, ADC in that area was reduced as compared to the normal pancreatic parenchyma (45).

Gastrinomas are the second most common functioning pNETs. Their location is usually in the ‘gastrinoma triangle’ (90%) that is a virtual space marked superiorly by the cystic and common ducts, inferiorly by the 2nd and 3rd parts of the duodenum and medially by the connection between the neck and body of the pancreas (46). These tumours tend to

![Figure 3](image-url)
be smaller in size (0.3–3 cm), less vascular and with a higher probability than insulinomas to be extra-pancreatic (47). At CT examination, on baseline images they are hypodense, hyperattenuating in early enhanced phase and hypodense in the venous one. At MRI they show low signal intensity in T1-weighted images, high signal intensity in T2-weighted ones and enhancement in the pancreatic phase (48). In the study conducted by Semelka et al. analysing 22 pNETs, they found that gastrinomas are often different in appearance than other NETs as they usually have a ring-enhancement, whereas non-gastrinoma-non-insulinoma tumours usually enhance heterogeneously (49).

The others subtype of functioning pNETs represent 5% of this class, including glucagonoma, somatostatinoma, VIPoma, ACTHoma and PPoma. These functioning tumours have a low incidence and may show different clinical manifestations (47). They tend to be isolate lesions, larger than insulinomas, with non-specific and heterogeneous enhancement pattern that can be both hypodense or hyperdense, due to necrosis or haemorrhagic aspects. On MRI, they usually have low signal intensity on T1-weighted images and high signal intensity on T2-weighted ones. The article by Sofka et al. about a 2 cm VIPoma of the pancreatic tail demonstrated a moderate signal intensity of the lesion in T2-weighted images, suggesting that these tumours may have different aspects on T2-weighted sequences (50). Because of these variable imaging findings that may be present, above all for small hyperfunctioning ones, it seems that DWI may better depict and characterize small pNETs, due to its greater image contrast and functional information (51,52). Farchione et al. in their study affirmed that DWI will be particularly useful in those patients with clinical suspicion for pNETs and with negative or suspicious conventional imaging findings, or in those with contraindications to contrast medium injection (53). Brenner et al. found that using both high b-value diffusion-weighted and T2-weighted MR images improve detection of pNETs relative to either technique alone (54).

Metastasis and mimics

Non-functional pNETs are usually malignant (90%), approximately 50–60% of gastrinomas show these characteristics, whereas 90% of insulinomas are benign (55). They can generate metastases above all in lymph nodes, bones and liver (Figure 4). Hepatic metastases usually show hypointensity or isointensity on T1-weighted imaging in comparison with the surrounding parenchyma, hyperintensity on T2-weighted sequences. In some rare cases they can have a different presentation with both hyperintensity on T1 and hypointensity on T2-weighted images. The same characteristics may be seen at CT. Also baseline imaging is very important in the evaluation of these lesions, as their enhancement is usually higher during the arterial phase (Figure 5) (56). On the other hand, in the study of Armstrong et al. on 51 patients who underwent triple phase CT, 23 demonstrated hypoenhancement pattern, 18 a mixed one and only 10 showed a hyperenhancement in arterial phase (Figure 1) (57).

Bone metastases frequently involved axial skeleton. They can show both osteolytic or osteosclerotic aspects at traditional radiography; 10% are purely osteolytic (58). They are not uncommon, observed in 42% of patients at

![Figure 4](https://example.com/figure4.png) Hypervascular liver metastases. These axial CT images show a huge pNET (black arrowhead) with non-homogeneous arterial (A) and venous (B) enhancement. Liver metastases (white arrows) show the same dynamic contrast enhancement of the primary pancreatic lesion. CT, computed tomography; pNET, pancreatic neuroendocrine tumour.
Lesions are hypointense on T1-weighted images. Even if their predominant aspect is osteoblastic, they can show hyperintense and heterogeneous signal on T2-weighted images.

The differential diagnosis with pNETs, involve some other lesions (Table 1). For example, the metastases from renal cell carcinoma (RCC), are usually hyper-vascular and can be similar to the NETs (55). Gastrointestinal stromal tumours (GISTs), because of their position, arising from stomach or duodenum, and with their vivid contrast enhancement on arterial phase, with both cystic or necrotic phenomena are not easily discernible from a primary pancreatic tumour (9,60,61). pNETs can occasionally manifest as a primarily cystic tumours (for example mostly-solid serous cystadenoma) and differential diagnosis from other cystic neoplasms can be made through the evidence of their hypervascular rim (Figure 6) (62). It has to be remembered also that accessory spleens are commonly located in the pancreatic tail and with their high enhancement it can be difficult to distinguish them from pNETs (63). Zhang et al. reported two rare cases of paragangliomas of the pancreas, which are typically hypervascular, with cystic changes mimicking pNETs (64).

Furthermore, especially non-functioning pNETs that are bigger in size, may invade surrounding structures and present with biliary obstruction, as the classic presentation for pancreatic adenocarcinomas (65-68).

**Conclusions**

pNETs are rare tumours but their incidence is growing because of our better radiological detection especially...
through CT and MRI. The management of patients with pNET is multidisciplinary and often multimodal: this underlines the importance of the radiologists as a fundamental figure that must be aware of the typical/ atypical imaging findings or mimics of pNETs, according to up-to-date literature, in order to facilitate the initial diagnosis and to help in the management in patients with such pancreatic lesions.

Acknowledgments

Funding: None.

Footnote

Provenance and Peer Review: This article was commissioned by the Guest Editor (Antonio Barile) for the series “Multimodality Advanced Imaging and Intervention in Gland Diseases” published in Gland Surgery. The article has undergone external peer review.

Reporting Checklist: The authors have completed the Narrative Review reporting checklist. Available at http://dx.doi.org/10.21037/gs-20-537

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/gs-20-537). The series “Multimodality Advanced Imaging and Intervention in Gland Diseases” was commissioned by the editorial office without any funding or sponsorship. The authors have no other conflicts of interest to declare.

Ethical Statement: The authors are accountable for all the aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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