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Imaging in neuroendocrine tumors: an update for the clinician

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Abstract

Neuroendocrine tumors are a heterogeneous group of neoplasms that are best worked up and managed using a variety of clinical and imaging studies. They are often diagnosed after they have already metastasized, though this does not necessarily preclude an attempt at curative surgical treatment or surgical debulking. Tumor burden assessment often requires use of multiple imaging modalities including computed tomography, magnetic resonance imaging and ultrasound. Somatostatin receptor-based imaging is also of great utility in looking for primaries and determining the extent of metastatic disease. This paper will review the most common imaging modalities used in the diagnosis and treatment of neuroendocrine tumors.

Keywords

⁶⁸Ga-DOTANOC; ⁶⁸Ga-DOTATOC; CT; MRI; NET; neuroendocrine tumor; OctreoScan; PET; somatostatin imaging; ultrasound

Neuroendocrine tumors (NETs) arise from the diffuse neuroendocrine system, which is comprised of 17 different cell types that reside in skin, lung, the hepatobiliary system, the urogenital tract, thyroid and the gastrointestinal tract [1]. Though these tumors can arise in any of the aforementioned tissues, the most common primary sites are the lung, rectum and small bowel [2]. The hallmark of these tumors is their propensity for hormone secretion, which may cause symptoms such as diarrhea or flushing, and serve as biologic markers of the disease.

Historically, these tumors were thought to be extremely rare, though many recent studies have shown an increasing incidence [2–4]. This increase has been ascribed, in part, to improved methods of diagnosis and greater disease awareness [3]. Innovations in somatostatin receptor-based technologies have also pushed NET molecular diagnostics and therapeutics forward, improving the quality of life for many patients [5,6].

This review will focus on the imaging techniques used in the diagnosis, staging and follow-up of neuroendocrine tumors. A short review of conventional imaging techniques such as computed tomography (CT), magnetic resonance imaging (MRI), ultrasound (US) and ¹⁸F-FDG-PET will precede a more extensive review of the somatostatin-based imaging techniques that make the workup of NET patients unique.

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Conventional imaging techniques

Computed tomography

CT scans are often the initial imaging study for a patient presenting with signs or symptoms suggestive of a NET. These studies are most useful for disease staging and surgical planning as they provide excellent anatomic detail of the tumors themselves and surrounding structures. Primary NETs (GI and lung NETs) and their metastases are generally hyperenhancing with IV contrast and are best seen in the arterial phase of a triple phase CT scan (Figure 1) [7,8].

In primary NETs, the average sensitivity of a CT scan is 73% [9]. This modality is also useful when the primary tumor site is unknown. In a single-institution retrospective study, it was the most common study ordered to look for an unknown primary tumor site and was able to uncover the primary in 95% of cases [10]. CT scans have even better sensitivity in detecting NET metastases, as they demonstrate 80% sensitivity for hepatic metastases [9,11] and 75% sensitivity for extrahepatic metastases [9].

Magnetic resonance imaging

MRI is the best conventional study to detail hepatic metastases in NETs (Figure 2) [12]. It is not as useful as CT for the detection of primary small bowel lesions or their associated lymphadenopathy, but is good for the detection of primary pancreatic NETs. A study comparing MRI, CT and standard somatostatin receptor-based imaging (OctreoScan) reported 95.2% sensitivity for MRI, 78.5% sensitivity for CT and 49.3% sensitivity for the OctreoScan in detecting hepatic metastases. MRI also detected significantly more liver lesions than the other two modalities ($p = 0.02$ vs CT, $p < 10^{-4}$ vs OctreoScan) [13].

Ultrasound

The primary role of conventional ultrasound in neuroendocrine disease is detection of hepatic metastases and estimation of total hepatic tumor burden. This technique has the advantages of near-universal availability, intraoperative utility, minimal expense and lack of radiation. Most US examinations are performed without contrast, which limits their sensitivity (compared with CT and MRI). A recent study showed that the use of a microbubble contrast agent improved the sensitivity of conventional US from 68 to 99% in detection of individual hepatic NET metastases ($p < 0.0001$) and reduced the rate of false positive calls [14].

¹⁸F¹⁸FDG positron emission scanning

18-fluoro-deoxy-glucose PET (FDG PET) is used to detect malignancy for a variety of tumor types. Unfortunately, its utility has not been borne out in NETs, as the majority of NETs tend to be relatively metabolically inactive and fail to take up the tracer well [15]. However, high-grade NETs are more likely to demonstrate avid uptake of ¹⁸FDG, giving these scans utility in identifying tumors likely to display more aggressive behavior [16]. The advantages and disadvantages of various imaging modalities are summarized in Table 1.

Somatostatin receptor-based imaging techniques

Somatostatin is an endogenous peptide that is secreted by neuroendocrine cells, activated immune cells and inflammatory cells [17]. It affects its antiproliferative and antisecretory functions by binding to one of five types of somatostatin receptors (SSTR1- SSTR5). These are G-protein coupled receptors and are normally distributed in the brain, pituitary, pancreas, thyroid, spleen, kidney, gastrointestinal tract, vasculature, peripheral nervous system and on immune cells [18]. Expression of SSTRs is highest on well-differentiated NETs. Somatostatin receptor type 2 is the most highly expressed subtype, followed by SSTRs 1 and 5, SSTR3 and SSTR4.

The ubiquity of SSTRs on NET cell surfaces makes them ideal targets for treatment and imaging [19]. There are two primary types of somatostatin receptorbased imaging available. The most common is the OctreoScan, which uses the ligand ^{111}In -DPTA-D-Phe-1-octreotide and binds primarily to SSTR2 and SSTR5 [18]. In its original form, it provided a planar, full body image (Figure 3A). In modern practice, this image is fused with single photon emission computed tomography (SPECT) and CT (Figure 3B). This takes advantage of the specificity of the OctreoScan and the anatomic detail provided by SPECT/CT, improving OctreoScan's diagnostic accuracy [20]. The newest somatostatin receptor-based imaging modality uses the positron emitter ^{68}Ga to label various somatostatin analogs. The most common of these labeled analogs are ^{68}Ga -DOTATOC (Figure 4), ^{68}Ga -DOTANOC and ^{68}Ga -DOTATATE [21]. These PET images are fused with CT to enhance the anatomic resolution of the study (Figure 3C & D) [22].

The indications for somatostatin receptor-based imaging are: detection and localization of primary NETs and their metastases, staging, follow-up for disease recurrence and to select patients for peptide receptor radionuclide therapy (PRRT). Long acting octreotide should be discontinued 4 to 6 weeks prior to imaging and the patient should be transitioned to a short acting regimen. For OctreoScan, patients need only to void prior to image acquisition. Though if the abdomen is the area of interest, use of an over-the-counter laxative the night prior to imaging may minimize the amount of nonpathologic uptake in the bowel, as approximately 2% of the labeled somatostatin analog is cleared via the hepatobiliary system and will end up in the intestine. The OctreoScan images are obtained 4 and 24 h after intravenous injection of the ligand [18,23]. The newer DOTA PET images are acquired once, at 60 min after radiotracer injection [22].

Octreotide analog studies

The first iteration of somatostatin receptor-based imaging used ^{123}I -Tyr-3-octreotide as its SSTR-specific ligand. This radiotracer was tested *in vivo* in a small group of patients (n = 10) in 1989. Investigators reported that 50% of primary tumors from a variety of sites were identified correctly. In two patients, previously undetected metastases were demonstrated. These scans also appeared to predict whether patients would benefit from treatment with octreotide. Patients who had responded had positive scans and those that were considered nonresponders to octreotide had negative scans [24]. There were a few problems with this initial ligand. Not only was it difficult to prepare, but it had a short half-life and accumulated at high levels in the small intestine, limiting its utility for GI NETs.

The response to these problems was development of ^{111}In -DTPA-D-Phe-1-octreotide, which is the ligand used by the modern OctreoScan. This tracer was easier to prepare, cleared primarily by the kidneys (solving the problem of accumulation within the GI tract), and had a much longer half-life (optimal image acquisition occurs at 24 h postinjection of the radiotracer). A small comparison study of the two tracers showed identical results in 4 of 6 patients. In the remaining 2 patients, the new ^{111}In tracer was able to identify an insulinoma that the ^{123}I tracer missed, and identified a greater total number of ‘carcinoid deposits’ compared with its predecessor [25].

A much larger series published by the same group in 1993 solidified ^{111}In -DTPA-D-Phe-1-octreotide’s role as the best ligand for nuclear imaging. In this report, 735 patients had an OctreoScan using ^{111}In -DTPA-D-Phe-1-octreotide and complete records available to confirm the findings of the study. Investigators found that the OctreoScan localized 86% of carcinoids, 89% of neuroblastomas, 86% of pheochromocytomas, 94% of paragangliomas and 80% of PNETs. It was less useful in detecting medullary thyroid carcinomas and pituitary tumors. No patient experienced adverse side effects from radiotracer injection [26].

In most centers, OctreoScan is combined with SPECT or SPECT/CT to improve its anatomic localization [27]. These fused images are obtained in thin slices, which minimizes obfuscation of the tumor by radioactivity emitted from surrounding normal tissues [28]. These improvements have been shown to alter the management in approximately 15% of cases, compared with planar OctreoScan images [29]. The sensitivity of the fused modality is comparable to standard imaging, though a wide range exists. In primary tumors, the OctreoScan’s sensitivity ranges from 35 to 80% [11,30–32], with its performance for unknown primary tumors dipping beneath the lower end of that range (24%) [11]. Its ability to detect the primary is limited by the size but not SSTR2 expression, as tumors less than 2 cm are significantly more likely not to localize but do not have significantly different SSTR2 expression than their larger counterparts [32].

One of the benefits to incorporating the OctreoScan into a workup for NETs is the ability to survey the entire body for metastases with a single study. The OctreoScan performs better in the detection of liver metastases than it does in primary tumor detection, and demonstrates sensitivities ranging from 49 to 91% in this context [11,13,31,33–34]. This compares relatively favorably with MRI (80 – 95%), the gold standard of liver lesion characterization [13,33]. Similar to the situation with primary tumor detection, the OctreoScan’s sensitivity appears to be limited by tumor size [13]. Due to OctreoScan being a functional (i.e., SSTR-specific) full body scan, it can often identify lesions that were missed by CT or MRI. Chiti *et al.* found that OctreoScan identified new lesions in 28% of patients [11]. In two studies focusing on identification of NET metastases, the OctreoScan identified new lesions in 47% [33] and 4.6% [13] of patients, respectively, whose lesions were otherwise missed by CT or MRI. A study performed in a set of 31 patients with bronchial carcinoids showed comparable results. In 22 cases, the OctreoScan results were identical to conventional imaging studies. Previously undiscovered lesions were detected by OctreoScan in 6 of 31 cases, and in 2 cases, the OctreoScan was the only modality to detect these lesions [35].

The OctreoScan is a useful adjunct in the workup of NETs, especially when fused with SPECT and CT, and is likely the most commonly used imaging study in the diagnosis and work up of NETs. It has moderate sensitivity as a stand-alone study, but excellent specificity and has the advantage of being the only functional imaging study available for the majority of these tumors. Further, its whole-body acquisition allows much information to be gathered with a straightforward protocol. Its advantages maintain its role in the workup of these tumors, while its disadvantages have prompted continued innovations to further improve utility. These include high uptake in the liver making smaller metastases difficult to visualize, excretion into the GI tract, insensitivity for small primaries, and low anatomic detail that limits its value in planning operations.

⁶⁸Ga-labeled studies

The newest advance in somatostatin receptor-based imaging is the introduction of ⁶⁸Ga-labeled radioligands, whose uptake is measured by PET scan (Figure 4). These peptides are easier and cheaper to synthesize than standard octreotide-analog based ligands, boast single time point image acquisition (1 h postinjection vs OctreoScan, which requires patients to be scanned at 4 and 24 h postinjection), and allow for quantifying the uptake of the ligand within the lesions. Its superior spatial resolution derives from the fact that it measures the radiation from two photons coincidentally. SPECT, in comparison, measures the gamma radiation emitted from one photon directly. This results in different limitations of detection – millimeters for ⁶⁸Ga-PET compared with 1 cm or more for SPECT [28]. There are a few choices of ligands with this type of imaging, but the differences lie primarily in their SSTR affinities – all of the ligands bind with great affinity to SSTR2 and SSTR5. ⁶⁸Ga-DOTANOC also binds to SSTR3. Despite these differences, no single ⁶⁸Ga ligand has stood out as the clear choice for use in NETs [22]. As with standard somatostatin receptor-based imaging, these ⁶⁸Ga-PET studies are fused with CT to improve anatomic localization.

Comparison studies between ⁶⁸Ga-PET and standard imaging techniques (CT, OctreoScan) have universally demonstrated the superiority of ⁶⁸Ga-PET in detection of NET primary tumors and metastases. Two early studies compared ⁶⁸Ga-DOTATOC to standard somatostatin imaging (SRS)-SPECT and CT. Buchmann *et al.* reported that ⁶⁸Ga-DOTATOC detected more than 279 NET lesions in 27 patients with histologically proven NETs, whereas SRS-SPECT detected only 157. The greatest number of lesions were detected in the liver. ⁶⁸Ga-DOTATOC found more than 152 hepatic lesions, while SRS-SPECT found only 105, resulting in a 66% concordance rate between the two modalities. The concordance for abdominal lymph nodes was worse at 40.1%. In this set of patients, the greater sensitivity of ⁶⁸Ga-DOTATOC resulted in an altered surgical plan in one patient [36].

Gabriel *et al.* reported similar conclusions to Buchmann *et al.* in their comparison study of ⁶⁸Ga-DOTATOC, SRS-SPECT and CT in 84 patients. They found the sensitivity and specificity of ⁶⁸Ga-DOTATOC to be 97 and 92%, respectively. For SRS-SPECT, the sensitivity was 52% and specificity 92%. The difference in sensitivities between these two modalities was statistically significant ($p < 0.001$). ⁶⁸Ga-DOTATOC provided new clinical

information in 21.4% of patients, which resulted in altered surgical plans in three patients (surgery declined due to previously unknown widespread metastases) [37].

Studies have also compared ^{68}Ga -DOTANOC to standard imaging (CT, MRI, US, OctreoScan). In the smaller of these studies ($n = 19$), ^{68}Ga -DOTANOC was compared with OctreoScan. In general, ^{68}Ga -DOTANOC detected more numerous lesions than OctreoScan, but there were a fair number that were missed by ^{68}Ga -DOTANOC and detected by OctreoScan [38]. In a larger study ($n = 109$), the sensitivity of ^{68}Ga -DOTANOC was superior to CT, MRI, and US by almost every measure. In primary tumors, the sensitivity of ^{68}Ga -DOTANOC was 78.3% compared with 63.8% sensitivity with conventional imaging (CT, MRI, US) ($p < 0.001$). In metastases, ^{68}Ga -DOTANOC had a sensitivity of 97.4%, while conventional imaging demonstrated a sensitivity of 81.8%. Broken down by metastasis type, ^{68}Ga -DOTANOC was significantly better at detecting lymph node metastases than conventional imaging ($p < 0.0001$), though there was no difference in these studies' abilities to detect liver metastases ($p = 1$). ^{68}Ga -DOTANOC improved the care of 19% of patients included in the study. The primary tumor was detected in 5.5% of patients where it was otherwise missed, which led to surgery in these patients. In 6.4%, a more extensive surgery was planned, as additional metastases were uncovered. Three patients were spared surgery because ^{68}Ga -DOTANOC demonstrated more extensive metastatic disease than did conventional imaging [39].

^{68}Ga -DOTA PET has also proven its utility in special situations, such as detection of unique NETs and in cases of unknown primary NETs. Neuroendocrine tumors can arise in a variety of tissues. Rare subtypes are frequently excluded from large series, and so little is known about how standard NET workup and treatments perform in these cases. Fanti *et al.* examined the question of how well ^{68}Ga -DOTANOC detected 'unique' NET primaries in 2008. The study included 13 patients with NETs originating from uterus ($n = 3$), ovary ($n = 1$), kidney ($n = 1$), prostate ($n = 3$), breast ($n = 1$), ear ($n = 1$), as well as paragangliomas ($n = 3$). In this set, ^{68}Ga -DOTANOC was deemed to have added useful clinical information in 50% of cases. In 57% of cases, the study was 'the determinant of management.' The study concluded that in the setting of unusual NET primaries, ^{68}Ga -DOTANOC can add useful information to many clinical situations but that it is most useful for patients with paragangliomas [40].

For unknown primary sites, ^{68}Ga -DOTANOC was able to localize the primary tumor in 35 of 59 patients (59%) with known neuroendocrine metastases. Primary sites (confirmed at surgery or by other imaging modalities) included pancreas ($n = 16$), small bowel ($n = 15$), lung ($n = 2$), rectum/colon ($n = 2$) and a paraganglioma ($n = 1$). CT localized the primary tumor in only 20% of patients [41]. In another study of patients with elevated serum markers and suspected NETs ($n = 131$), ^{68}Ga -DOTANOC was true positive in 17 cases, true negative in 112 cases and false negative in 2 cases [42]. Taken together, these studies suggest that when a patient has histologically proven neuroendocrine disease, but prior workup has failed to uncover the primary, ^{68}Ga -PET imaging has a high likelihood of uncovering the primary compared with conventional imaging. When neuroendocrine disease is suspected but not histologically proven, ^{68}Ga -PET should not be used as the primary imaging modality, given its expense and the likelihood that it has a high probability of being (true) negative in

patients with elevated serum markers as the only indication of disease [42]. Physiologic uptake in the uncinate process of the pancreas, pituitary, spleen (or accessory spleen) and kidneys may be misconstrued as a false positive result [43]. Its true utility lies in its ability to supplement the information gathered via clinical investigations and standard imaging (CT, OctreoScan) [42].

Just as the OctreoScan has been used to select patients for treatment with Octreotide, ^{68}Ga -DOTA PET imaging can be used to determine which patients might benefit from Octreotide and PRRT. The benefit is determined not just by whether or not the tumors take up the radioligand. A recent report suggests that patients can be stratified into 'responders' or 'non-responders' to PRRT, based on their pretreatment maximum standard uptake value (SUVmax), where 'responders' have an SUVmax of greater than 17.9 [44]. However, this is not a universal finding, as in 2009, Gabriel *et al.* found that SUVmax was a poor measure of treatment response [45]. Larger studies will be required to resolve this issue.

Beyond prediction of treatment response, there have been questions as to how PRRT may affect the uptake of ^{68}Ga radioligand in follow-up studies in normal and cancerous tissues, and possibly diminish its utility as a follow-up study. Quantitative differences in ^{68}Ga uptake can be determined by comparing pre- and post-treatment maximum standard uptake values (SUVmax). The general conclusions from two recent studies were that treatment with PRRT did not seem to affect the accuracy of the follow-up ^{68}Ga -PET studies. In one study, there was no significant difference in SUVmax in any of the tissues evaluated [46], and in the other, a significant difference in SUVmax was seen pre- and post-treatment in liver metastases ($p < 0.02$), but the uptake in benign liver tissue remained so low that the study maintained its clinical utility for these lesions [43].

^{123}I -MIBG imaging

Radioiodinated (^{123}I) metaiodobenzylguanidine (MIBG) is an analog of norepinephrine that is used to image catecholamine-secreting NETs such as pheochromocytomas, paragangliomas and glomus tumors [47]. In patients with functional pheochromocytomas or paragangliomas, this modality has a sensitivity of 90% [48,49] and positive predictive value of 100% [49]. However, it has limited use in GI NETs, as this modality was positive in only 49.1% of patients. In the same cohort of patients, OctreoScan was positive in 91.2% [50]. As an imaging tool, this study is best used to confirm a diagnosis of pheochromocytoma or paraganglioma and define the extent of metastatic disease in these tumors [51]. Its most practical use in GI NETs may be to determine whether patients with metastases may benefit from treatment with ^{131}I -MIBG.

Conclusion

Neuroendocrine tumors are a unique malignant entity that can be evaluated by imaging in a variety of ways. Conventional imaging modalities such as CT, US, MRI and the OctreoScan are excellent initial studies to locate the primary tumor, evaluate extent of disease and plan for surgical management. However, in cases where these studies do not provide the detail required to make more complex management decisions, the ^{68}Ga -PET studies have

demonstrated their utility as excellent confirmatory studies, and have the capability to alter clinical decision making due to their superior sensitivity.

Future perspective

There are likely two areas in NET-specific imaging that will see improvement in the coming years. The first is access to PET imaging with ^{68}Ga -DOTA octreopeptides. Though this modality is available in the majority of European centers, lack of FDA approval for the ^{68}Ga radiotracer has hindered its use in the USA. However, as more randomized controlled trials are performed and clinical experience increases with this valuable modality, FDA approval for the ^{68}Ga labeled octreotide analogs is expected. This approval will likely result in ^{68}Ga -PET imaging supplanting the standard OctreoScan as the somatostatin-receptor based imaging modality of choice. The second area of interest in this field is discovery of novel targets for NET-specific imaging. Not all NETs have high expression of SSTR and may thus be missed by current somatostatin-based imaging. As molecular investigations of NETs have increased, there have been some recent advances in this area [52], but no doubt more are likely to come.

Executive summary

Conventional imaging techniques

- Contrast-enhanced CT scans are useful in the preoperative setting, as they provide excellent anatomic characterization of both malignant and normal tissues. Hepatic metastases are best visualized in the arterial phase, and will wash out in subsequent phases.
- MRI is the ideal study to differentiate between malignant and benign hepatic lesions.
- Ultrasound is a useful adjunct to CT and is used to identify hepatic metastases. Its advantages are its low cost, widespread availability and use as an intraoperative tool.
- ^{18}F FDG PET may identify high grade neuroendocrine tumors, as they tend to be more metabolically active.

Somatostatin-based imaging

- OctreoScan is the current standard in somatostatin-based imaging. It can be fused with SPECT and CT to provide both functional and anatomic information.
- ^{68}Ga -PET imaging has greater sensitivity detecting NETs than the OctreoScan. It is fused with CT to provide anatomic details. Despite its superior spatial resolution, it is only available in a small number of centers around the USA.

Conclusion

- Optimal work up of neuroendocrine tumors requires use of a combination of conventional and somatostatin-based imaging techniques.

- ⁶⁸Ga-PET imaging may supplant OctreoScan as the somatostatin-based imaging modality of choice, once FDA approval of the ⁶⁸Ga radiotracer allows for greater access throughout the USA.

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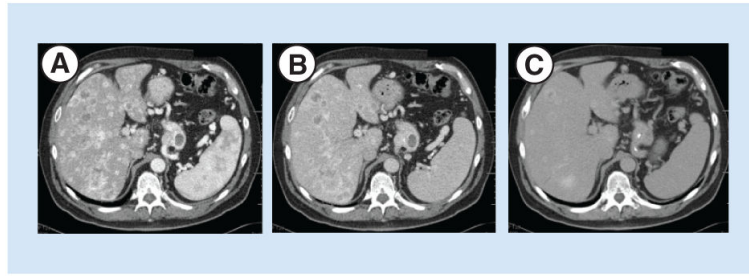


Figure 1. Triple phase CT scan demonstrating approximately 70% replacement of the liver by enhancing neuroendocrine tumor metastases

(A) Arterial phase, (B) venous phase and (C) equilibrium phase of delayed images. Note that hyperenhancing lesions are most clearly seen on arterial phase.

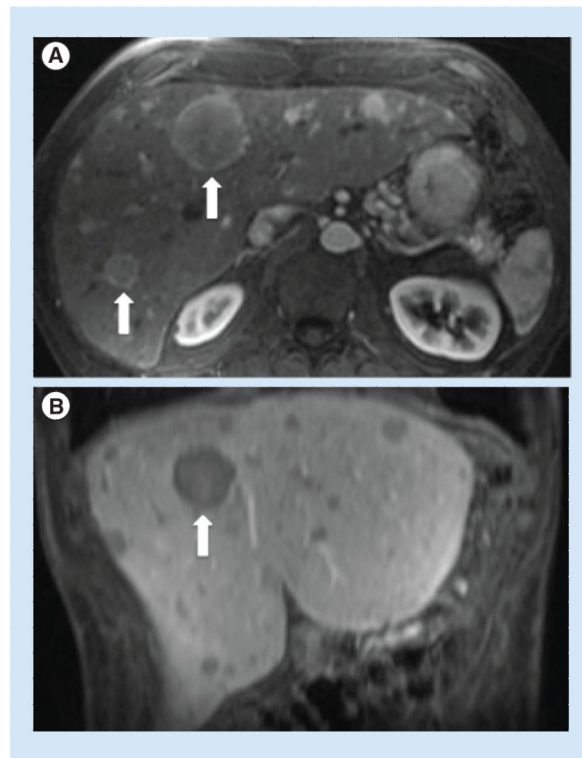


Figure 2. Hepatic neuroendocrine tumor metastases demonstrated on axial T1 weighted fat-suppressed postgadolinium images
(A) Axial image, early arterial phase and (B) coronal image, portal venous phase. Arrows indicate large hepatic metastases.

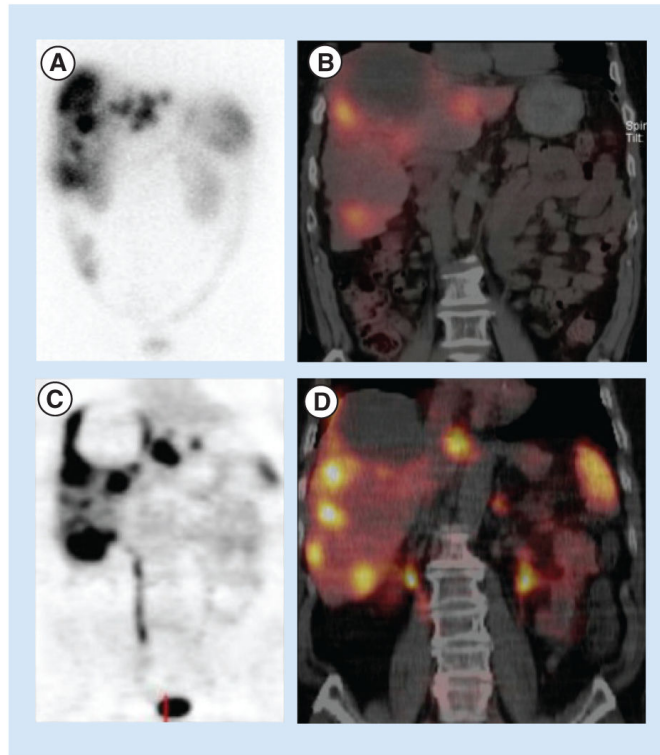


Figure 3. Comparison of (A) planar OctreoScan, (B) fused OctreoScan/SPECT/CT, (C) planar ⁶⁸Ga-DOTATOC PET and (D) ⁶⁸Ga-DOTATOC PET/CT in the same patient
The patient has approximately 33% of their liver replaced by neuroendocrine tumor metastases. The images in (C) and (D) provide more precise delineation of lesions, compared with (A) and (B).

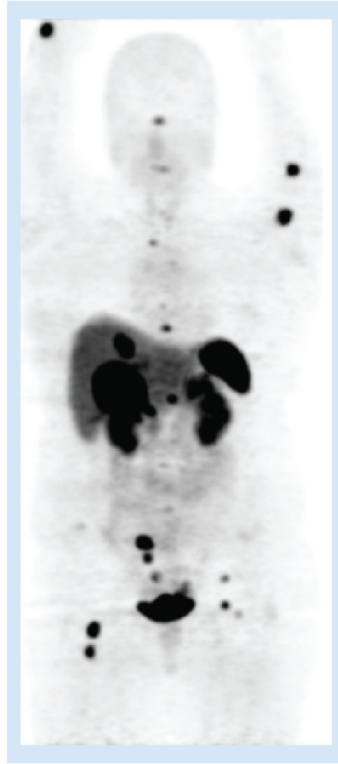


Figure 4. ^{68}Ga -DOTATOC demonstrating multiple metastases in the upper and lower extremities, liver and right lower quadrant in a patient with an SBNET primary. Physiologic uptake is seen in the pituitary, kidneys, spleen and bladder.

Table 1

Comparison of the advantages and disadvantages of the major imaging modalities used in neuroendocrine

Modality	Advantages	Disadvantages
CT	<ul style="list-style-type: none"> High anatomic resolution of liver, pancreas, mesenteric lesions, abdominal/retroperitoneal lymph nodes Useful for operative planning, disease staging 	<ul style="list-style-type: none"> High radiation exposure Optimal imaging of NETs requires IV contrast Not a functional study
MRI	<ul style="list-style-type: none"> Best modality to detail hepatic lesions Good pancreatic resolution No radiation exposure Gadolinium contrast is safer if renal dysfunction 	<ul style="list-style-type: none"> Poorer resolution of GI tract, mesenteric lesions Cannot image patients with metal implants Not a functional study
Ultrasound	<ul style="list-style-type: none"> Useful for estimating hepatic tumor burden Inexpensive Available at the majority of institutions No radiation exposure 	<ul style="list-style-type: none"> Study quality dependent upon the skill of the US technician Limited sensitivity if performed without microbubble contrast
Octreoscan	<ul style="list-style-type: none"> Functional study Level of uptake can be graded Provides whole body image Predicts response to therapy 	<ul style="list-style-type: none"> High background in GI tract, which may obscure midgut NETs Patient must be scanned twice in 24 h Low anatomic detail Need to hold Octreotide prior to scan
MIBG	<ul style="list-style-type: none"> Functional study High specificity for pheochromocytoma, paraganglioma, and glomus tumors Provides whole body image Predicts response to therapy 	<ul style="list-style-type: none"> High background Low anatomic detail Many medications can interfere with the scan and must therefore be held Thyroid must be blocked prior to scan Patient scanned 24 h after contrast administration
FDG-PET	<ul style="list-style-type: none"> Good for high grade NETs Good anatomic resolution 	<ul style="list-style-type: none"> Uptake unlikely in low-grade NETs
DOTA-PET	<ul style="list-style-type: none"> Functional study Uptake can be quantified Good anatomic resolution Provides whole body image Image acquired over 2 h Predicts response to therapy 	<ul style="list-style-type: none"> Physiologic uptake in uncinate process, pituitary, spleen and kidneys may be confused for tumor uptake Need to hold Octreotide prior to scan Available at a limited number of centers in the USA