Published in final edited form as:

Nucl Med Commun. 2019 July ; 40(7): 727–733. doi:10.1097/MNM.0000000000001022.

Prevalence and Quantitative Analysis of In-111 pentetreotide (Octreoscan) Uptake in the Pancreatic Head on SPECT/CT Imaging: Establishing an ROI-based Pathological Uptake Threshold

Jamal J. Derakhshan, MD, PhD¹ and Michael D. Farwell, MD²

¹Mallinckrodt Institute of Radiology, Washington University School of Medicine, St. Louis, MO

²Department of Radiology, Hospital of the University of Pennsylvania, Philadelphia, PA

Abstract

Objective—Determine the prevalence of benign In-111 pentetreotide uptake in the pancreatic head and determine if a semi-quantitative method can be used to differentiate physiologic from pathologic uptake.

Methods—IRB-approved, HIPAA-compliant retrospective review of 197 somatostatin receptor scintigraphy studies performed in 136 patients, from December 2012 to November 2013 at a large academic medical center. The pancreatic head uptake was visually graded and for all positive cases, 2D and 3D ratios of pancreatic head to normal liver uptake were calculated. Statistical analysis using paired and 2 sample T-tests was performed.

Results—19/129 (14.7%) patients had benign In-111 pentetreotide uptake in the pancreatic head. 7/7 (100%) patients with neuroendocrine tumors had definite visual uptake. Uptake was 2.7× more likely benign than malignant. Using a 3D ROI method, the pancreatic head to liver ratio was 0.91 ± 0.38 (0.37-1.63) for benign uptake and 8.2 ± 7.3 (1.79-23.6) for pathologic uptake ($p < 0.001$). A threshold of 1.67 provided 100% accuracy for determining presence or absence of a pancreatic head neuroendocrine tumor. Using a 2D ROI method, the uptake ratio was 0.88 ± 0.37 (0.28-1.73) for benign and 7.5 ± 6.2 (1.85-19.6) for pathologic uptake ($p < 0.001$); a ratio threshold of 1.62 provided 97% accuracy. There was no difference between the uptake ratios at 4 and 24 hours.

Conclusions—In-111 pentetreotide uptake in the pancreatic head is common and more frequently benign than malignant. Using simple ROI ratio methods helps to differentiate benign physiologic from malignant neuroendocrine tumor uptake.

Keywords

Somatostatin receptor scintigraphy (SRS); In-111 pentetreotide; SPECT/CT; pancreatic head; quantitative

INTRODUCTION

Somatostatin Receptor Scintigraphy (SRS) is commonly used to detect, stage, and provide surveillance and therapy monitoring of neuroendocrine tumors by imaging gamma rays emitted by either In-111 or Tc-99m labeled octreotide, a long-acting analogue of somatostatin (1). Due to the low rate of proliferation and metabolism, neuroendocrine tumors are not reliably identified with FDG PET. The vast majority of neuroendocrine tumors overexpress the somatostatin receptor (2); however, there is variable expression of somatostatin receptors physiologically, including types 1-3 and 5 in the endocrine pancreas (3). Cross-sectional SRS studies have confirmed benign uptake in the pancreatic head. In a recently-published study using In-111 DTPA octreotide (pentetreotide), 26% of patients showed benign uptake in the pancreatic head (4). In a smaller study using Tc-99m labeled octreotide, 19% of patients showed benign uptake in the pancreatic head (5). Visually, the majority of the benign uptake has been rated as less than or equal to liver parenchyma, while some is greater.

Case reports have detailed the significance of false positive somatostatin receptor scintigraphy results in the pancreatic head (6, 7). For example, postoperative imaging for staging after resection of a duodenal gastrin-producing tumor demonstrated focal In-111 pentetreotide uptake in the pancreatic head, which was thought to represent a neuroendocrine tumor and resulted in a Whipple procedure. The surgery was complicated by bile leak and ultimately death, only to find no pancreatic head tumor at pathology, but rather hyperplasia of polypeptide cells expressing the somatostatin receptor 2a (7). Recent studies using high throughput immunohistochemistry techniques have shown that there is wide variation in the composition of cells of the islets of Langerhans in the uncinate process of the pancreas, with 0-90% of the islets being composed of polypeptide cells, which have a high expression of somatostatin receptor (8). Thus, benign uptake of radiolabeled octreotide is likely due to the variable presence of polypeptide cells in the uncinate process. Interestingly, human serum pancreatic polypeptide levels are known to increase with age (9) and can fluctuate, temporarily increasing with infectious or inflammatory processes (10).

Ga-68 labeled octreotide analogs have been introduced as a more sensitive method for somatostatin receptor imaging using PET. These studies have shown a high rate of benign uptake in the pancreatic head ranging from 16-70% (11-16). In one study, an SUV_{max} threshold of 17.1 provided 90.0% sensitivity and 93.6% specificity for differentiating physiologic from pathologic tumor uptake (17). SPECT is typically considered a non-quantitative imaging technique as calibrations needed for direct quantitation (MBq/ml) are not routinely performed (18). However, the ratio of uptake between tissues can be used as a semi-quantitative surrogate, as system offsets are eliminated with a ratio (19).

Somatostatin receptor scintigraphy remains a widely used functional method for neuroendocrine tumor imaging; the current study was performed for two purposes. The first was to determine the prevalence of In-111 pentetreotide uptake in the pancreatic head in our patient population. The second purpose was to determine whether a semi-quantitative ratiometric method could be used to reliably differentiate physiologic from pathologic

uptake using somatostatin receptor scintigraphy since visual assessment alone might be insufficient.

MATERIALS AND METHODS

A retrospective review of all 359 In-111 pentetreotide scans obtained from 161 consecutive patients over a one-year period (from December 1, 2012 to November 31, 2013) at a large academic medical center was performed in an IRB-approved, HIPAA-compliant study. Whole-body anterior and posterior projection planar images were obtained at 4 and 24 hours after intravenous injection of 222 MBq In-111 pentetreotide (Octreoscan) as well as SPECT/CT images of the abdomen at 4 hours (prior to significant bowel excretion) and of the chest at 24 hours. For each study, the patient age, sex, indication and pertinent history were recorded. 25 patients were excluded: 11 due to absent pancreatic head (either due to prior Whipple surgery or total pancreatectomy), 9 due to repeat studies (only the first was included), 2 due to lack of concurrent CT scan, 1 due to significant distortion of anatomy confounding origin of uptake, 1 due to diffuse liver metastases (could not assess normal liver uptake), and 1 due to an incomplete study.

A blinded senior radiology resident and fellowship-trained nuclear medicine attending radiologist visually graded the uptake in the pancreatic head on all SPECT studies as 0 (absent), 1 (faint or mildly above adjacent background) or 2 (definite or clearly above surrounding background), in consensus. Uptake in the mid-abdomen at the level of the kidneys was detected on the attenuation-corrected SPECT scan using a narrow window and correlated to the available fused SPECT/CT image to ensure that the center of uptake reasonably co-localized to the pancreatic head parenchyma on the CT scan, as opposed to being clearly from adjacent bowel or lymph nodes. For the cases graded as faint or definite uptake, two methods were used for semi-quantitative analysis. In the 2D method, using a standard PACS workstation, a small circular region of interest (ROI) was drawn around the uptake in the pancreatic head on the slices where the uptake appeared highest and the maximum attenuation-corrected value from the ROI on the slice with highest uptake was recorded. The maximum value was chosen as opposed to the mean to eliminate ROI size as a confounding factor. The maximum value was not appreciably greater than the mean in the small ROIs, so noise was not dominant. A second larger elliptical ROI was placed in an area of uniform normal liver parenchyma (taking care not to include regions of increased uptake in hepatic metastases) and the mean value in the larger hepatic ROI was recorded. The ratio of the maximum uptake in the pancreatic head to mean uptake in the liver was calculated. In the second 3D method, the attenuation-corrected SPECT and CT data were imported, fused and analyzed using MIM Encore (Cleveland, OH). A 1cm spherical ROI was centered on the maximal uptake in the pancreatic head and the mean uptake in the ROI was recorded. A second 4cm diameter spherical ROI was centered in the liver, again avoiding any area of metastasis, and the mean uptake was recorded. A ratio of mean pancreatic to mean liver uptake was calculated in Microsoft Excel (Redmond, WA). The ratiometric data were then imported and analyzed in Matlab (Mathworks, Natick, MA). For statistical analysis two-sample and paired T-tests were used (as appropriate), with significance determined by $p < 0.05$.

For all cases with visual uptake, the patient folder in the picture archiving and communication system (PACS) was used to identify recent diagnostic contrast-enhanced (CE) MRI or CT to corroborate the presence or absence of a pancreatic head mass. The studies were independently reviewed and the official read was consulted to establish any abnormality in the pancreas. For the cases with neuroendocrine tumors, biochemical markers were recorded (gastrin, pancreatic polypeptide (PP) and chromogranin A levels) along with any relevant pathology or endoscopic ultrasound results.

RESULTS

Demographic details of the study population and visual uptake results are summarized in Table 1. 129/136 patients (95%) had no evidence of pancreatic head mass while 7/136 (5%) had imaging as well as biochemical evidence of pancreatic head neuroendocrine tumors (Table 2). There were studies from 135 patients including the pancreatic head at the 4hr time point and from 62 at the 24hr time point (as the pancreatic head is at the bottom edge of the thoracic field of view and therefore often excluded at the later time point). The prevalence of pancreatic head uptake in patients without a pancreatic head mass was 19/129 or 14.7% (6/129 or 4.7% with mild and 13/129 or 10.1% definite visual uptake). There was similar prevalence at 4 hours and 24 hours. Only one patient was rated differently at 4 vs. 24 hours, having been rated as 1 (faint) at the 4hr time point and 0 (none) at the 24hr time point. Of the 19 patients with benign uptake, 15 (79%) had a very recent prior (less than two months) and/or subsequent diagnostic contrast-enhanced CT or MRI confirming the absence of enhancing or suspicious pancreatic head mass, 1 (5.3%) had no abnormal uptake on a recent FDG PET/CT scan, 1 (5.3%) had no mass on a subsequent abdominal ultrasound, and 3 (15.8%) had no mass on the accompanying unenhanced CT scan (1×1×5mm resolution) but no other imaging. Figure 1 shows SPECT/CT and CE MRI images of the patient with the highest level of benign uptake in the uncinate process of the pancreas.

7 studies were performed in patients with known pancreatic head tumors. All 7/7 (100%) studies with known pancreatic head neuroendocrine tumors were graded as showing definite uptake. There was 2.7-fold higher likelihood of benign pancreatic head uptake than malignant (19 vs. 7, respectively). Figure 2 shows SPECT/CT images from the patient with the smallest neuroendocrine tumor (1.1cm), along with MRI correlation.

Table 3 provides the 3D ROI based pancreas to liver uptake ratio results. There was no significant difference in the uptake ratios between 4hr and 24hr time points, either for patients with benign or malignant uptake. Average pancreas to liver uptake ratio was 0.91 ± 0.38 in patients without a pancreatic head mass (range = 0.37-1.63, 93% confidence interval). Average uptake ratio in patients with a mass was 8.2 ± 7.3 (range 1.79-23.6, 83% confidence interval). The difference in uptake ratios in patients without and with a pancreatic head mass was highly significant ($p < 0.001$). Defining an abnormal uptake ratio as the mean uptake ratio + 2 standard deviations in patients without a mass provides a threshold of $0.91 + 2 \times 0.38 = 1.67$. This threshold provided 100% accuracy in determining the presence of a pancreatic head mass (see Figure 3). Figure 4 shows the uptake ratio variation from 4 to 24 hours for all patients using the 3D ROI method. There was no trend to an increased uptake ratio at 24 hours in patients without a pancreatic head mass. In those with a mass there was a

trend to an increased uptake ratio, however, this was predominately due to the absence of two of the lower uptake masses at the 24hr time point, with only one of four masses showing considerably increased uptake at the later time point.

Table 4 tabulates the pancreatic head to liver ratios using the 2D ROI method. Once again, there were highly significant differences between patients without and with a pancreatic head mass at all time points and no difference between 4hr and 24hr time points, similar to the 3D method. The average uptake ratio in patients without a mass was 0.88 ± 0.37 , very similar to the 3D method (with a slightly larger range of uptake, 0.28-1.73). The average uptake ratio in patients with a mass was 7.5 ± 6.2 (range 1.85-19.6). The threshold for abnormal uptake with the 2D method is $0.88 + 2 \times 0.37 = 1.62$, which provided 97% accuracy for determining the presence of a pancreatic head mass (100% sensitivity and 96% specificity). Figure 5 is a plot of the pancreas to liver ratio obtained in 2D vs. 3D ROI methods. There is no bias in the ratio, with a good fit to the line of unity. Paired T-test did not show a significant difference in uptake ratio calculated using 2D or 3D methods ($p = 0.47$ overall comparison ($n=39$) and $p = 0.35, 0.45, 0.69$ and 0.77 for each group; groups included: no pancreatic head neuroendocrine (NE) tumor 4hr ($n=18$), pancreatic head NE tumor 4hr ($n=7$), no pancreatic head NE tumor 24hr ($n=10$) and pancreatic head NE tumor 24hr ($n=4$), respectively).

DISCUSSION

This study determined the prevalence of benign pancreatic head uptake to be 14.7% in a cohort of patients imaged for oncological purposes. This rate is lower than the 26% prevalence recently reported in another similar sized study with the same radiopharmaceutical(4). At that institution, In-111 pentetreotide studies were also performed in patients with suspected inflammatory disorders; these patients are known to have higher levels of serum pancreatic polypeptide(10), which may explain the higher prevalence of visual uptake in that cohort. The prevalence of uptake in this study (15%) is similar to a smaller cohort (36 patients) previously reported from a ^{99m}Tc -HYNIC-TOC SPECT/CT study (19%). These prevalence values of benign physiological pancreatic head uptake in SPECT/CT are similar to the lower end of reported physiological uptake in Ga-68 labeled octreotide PET/CT studies (16-70%)(11–16), which may be due to different affinities of the tracers to somatostatin receptors as well as the known higher sensitivity of PET. Nevertheless, In-111 pentetreotide uptake in the pancreatic head is common, and was observed in approximately 1 in 7 studies performed. In a large academic institution with a large number of syndromic oncologic patients, there is $2.7\times$ higher likelihood of benign than malignant uptake. Therefore, awareness of the prevalence of this finding is critical to accurate interpretation of In-111 pentetreotide studies in both academic centers and private practice, to avoid the expense and concern created by a false positive finding.

In the qualitative portion of this study, the presence vs. absence of visual uptake in the head of the pancreas was assessed. A semi-quantitative approach was then used to characterize the amount of uptake, which allowed threshold, accuracy and reference range determination. A 93% confidence interval for benign uptake could be provided due to the large sample size of patients without a pancreatic head mass but with visual uptake; therefore, accurate

thresholds for abnormal uptake are proposed. Semi-quantitative analysis using these thresholds is important given the close proximity of benign and malignant uptake ranges, making visual assessment alone insufficient. Using these thresholds, prediction of benign and malignant uptake was possible with high accuracy. The ratio of the threshold for abnormal uptake determined in this study compared to the mean benign uptake level [$1.67/0.91=1.84$ (3D) and $1.62/0.88=1.84$ (2D)] can be compared to a similar ratio extrapolated from two prior PET studies [$17.1/9.2 = 1.86$; values provided in references (17) and (13), respectively]. The equality of the 2D and 3D ratios demonstrates the correlation of both techniques, while the similarity to prior PET work validates the accuracy of the semi-quantitative approach. The malignant uptake ranges observed in this study (1.79-23.6) are also comparable to the uptake in neuroendocrine tumors found in prior studies throughout the body (1.8-7.3; 54 lesions in 26 patients) (19).

This study compared two semi-quantitative approaches for determining the pancreatic head uptake, using 3D and 2D ROI methods. Both methods provided similar results, without bias or statistically significant differences in the ratios. However, the 3D method performed better, providing 100% accuracy as compared to 97% for the 2D method (one false positive result). The 2D method may be simpler and/or faster for readers without access to or accustomed to dedicated quantitative analysis software packages and can be used with a standard PACS workstation. However, the 3D method did perform better and its use is encouraged, especially among subspecialty nuclear medicine physicians who may already use similar dedicated analysis software packages in routine assessment of nuclear medicine studies.

Recent studies have shown the superiority of Ga-68 DOTATATE PET/CT over In-111 pentetreotide SRS, due to increased sensitivity for gastroenterohepatic NET (95.1% vs. 30.9%, respectively), greater convenience (one day as opposed to two day scan) and lower radiation exposure (20) leading to FDA approval of the Ga-68 DOTATATE agent on June 1, 2016. Therefore, there has been increased usage of Ga-68 DOTATATE PET/CT over In-111 pentetreotide SPECT/CT. However, In-111 pentetreotide remains within clinical algorithms for gastroenterohepatic NET when Ga-68 DOTATATE is not available (21), and it is still the primary diagnostic agent at many institutions. Also, information from this study may be relevant to peptide receptor radionuclide therapy (PRRT), which also utilizes longer-lived radiometals (22).

A potential limitation of the semi-quantitative technique is that a pancreatic head NE tumor that is small or has low somatostatin receptor expression could fall within the benign uptake range. Thus, correlation with contrast enhanced CT or MRI, endoscopy and/or subsequent imaging would be helpful to confirm that the uptake is indeed benign. If however, the uptake ratio is above the benign range established here using the 2D or preferably 3D technique, this should be highly suspicious for underlying pathology leading to further work-up.

CONCLUSION

In-111 pentetreotide uptake in the pancreatic head is common, observed in 14.7% of all patients in an oncologic cohort. In a large academic medical center, In-111 pentetreotide

uptake in the pancreatic head is 2.7× more likely to be benign than malignant. Thresholds for abnormal In-111 pentetreotide uptake have been established using a semi-quantitative approach. Using a pancreas to liver threshold of 1.67 and 3D ROI based method, 100% accuracy was possible for differentiating benign from malignant uptake.

ACKNOWLEDGEMENTS

David A. Mankoff, MD, PhD for helpful discussions regarding data analysis.

Conflicts of Interest and Source of Funding: JJD has received grants from the Radiological Society of North America (Siemens Healthineers/RSNA Research Fellow Grant) and NIH (T32 EB004311), and MDF has received a grant from the Radiological Society of North America (RSNA Research Scholar Grant).

References

1. Sundin A. Radiological and nuclear medicine imaging of gastroenteropancreatic neuroendocrine tumours. *Best Pract Res Clin Gastroenterol* 2012;26(6):803–18. [PubMed: 23582920]
2. Hankus J, Tomaszewska R. Neuroendocrine neoplasms and somatostatin receptor subtypes expression. *Nucl Med Rev Cent East Eur* 2016;19(2):111–7. [PubMed: 27479788]
3. Unger N, Ueberberg B, Schulz S, Saeger W, Mann K, Petersenn S. Differential expression of somatostatin receptor subtype 1-5 proteins in numerous human normal tissues. *Exp Clin Endocrinol Diabetes*. 2012;120(8):482–9. [PubMed: 22976314]
4. Brabander T, Teunissen J, Kwekkeboom D. Physiological Uptake in the Pancreatic Head on Somatostatin Receptor Scintigraphy Using [111In-DTPA]Octreotide: Incidence and Mechanism. *Clin Nucl Med* 2017;42(1):15–9. [PubMed: 27775943]
5. Yamaga LY, Neto GC, da Cunha ML, Osawa A, Oliveira JC, Fonseca RQ, et al. 99mTc-HYNIC-TOC increased uptake can mimic malignancy in the pancreas uncinate process at somatostatin receptor SPECT/CT. *Radiol Med* 2016;121(3):225–8. [PubMed: 26558391]
6. Albers MB, Maurer E, Kloppel G, Bartsch DK. Pancreatic polypeptide-rich islets in the posterior portion of the pancreatic head—a tumor mimic in somatostatin receptor scintigraphy. *Pancreas*. 2014;43(4):648–50. [PubMed: 24713672]
7. Bunning J, Merchant SH, Crooks LA, Hartshorne MF. Indium-111 pentetreotide uptake by pancreatic polypeptide cell hyperplasia: potential pitfall in somatostatin receptor scintigraphy. *Pancreas*. 2007;35(4):372–5. [PubMed: 18090246]
8. Wang X, Zielinski MC, Misawa R, Wen P, Wang TY, Wang CZ, et al. Quantitative analysis of pancreatic polypeptide cell distribution in the human pancreas. *PLoS One*. 2013;8(1):e55501. [PubMed: 23383206]
9. Floyd JC, Jr. Human pancreatic polypeptide. *Clin Endocrinol Metab* 1979;8(2):379–99. [PubMed: 225071]
10. Hallgren R, Lundqvist G. Elevated levels of circulating pancreatic polypeptide in inflammatory and infectious disorders. *Regul Pept* 1980;1(3):159–67. [PubMed: 7232771]
11. Al-Ibraheem A, Bundschuh RA, Notni J, Buck A, Winter A, Wester HJ, et al. Focal uptake of 68Ga-DOTATOC in the pancreas: pathological or physiological correlate in patients with neuroendocrine tumours? *Eur J Nucl Med Mol Imaging*. 2011;38(11):2005–13. [PubMed: 21792572]
12. Castellucci P, Pou Ucha J, Fuccio C, Rubello D, Ambrosini V, Montini GC, et al. Incidence of increased 68Ga-DOTANOC uptake in the pancreatic head in a large series of extrapancreatic NET patients studied with sequential PET/CT. *J Nucl Med* 2011;52(6):886–90. [PubMed: 21571796]
13. Jacobsson H, Larsson P, Jonsson C, Jussing E, Gryback P. Normal uptake of 68Ga-DOTA-TOC by the pancreas uncinate process mimicking malignancy at somatostatin receptor PET. *Clin Nucl Med* 2012;37(4):362–5. [PubMed: 22391705]
14. Krausz Y, Rubinstein R, Appelbaum L, Mishani E, Orevi M, Fraenkel M, et al. Ga-68 DOTA-NOC uptake in the pancreas: pathological and physiological patterns. *Clin Nucl Med* 2012;37(1):57–62. [PubMed: 22157030]

15. Kunikowska J, Krolicki L, Pawlak D, Zerizer I, Mikolajczak R. Semiquantitative analysis and characterization of physiological biodistribution of (68)Ga-DOTA-TATE PET/CT. *Clin Nucl Med* 2012;37(11):1052–7. [PubMed: 22996234]
16. Mapelli P, Tam HH, Sharma R, Aboagye EO, Al-Nahhas A. Frequency and significance of physiological versus pathological uptake of 68Ga-DOTATATE in the pancreas: validation with morphological imaging. *Nucl Med Commun* 2014;35(6):613–9. [PubMed: 24686250]
17. Kroiss A, Putzer D, Decristoforo C, Uprimny C, Warwitz B, Nilica B, et al. 68Ga-DOTA-TOC uptake in neuroendocrine tumour and healthy tissue: differentiation of physiological uptake and pathological processes in PET/CT. *Eur J Nucl Med Mol Imaging*. 2013;40(4):514–23. [PubMed: 23291643]
18. Bailey DL, Willowson KP. An evidence-based review of quantitative SPECT imaging and potential clinical applications. *J Nucl Med* 2013;54(1):83–9. [PubMed: 23283563]
19. Buchmann I, Henze M, Engelbrecht S, Eisenhut M, Runz A, Schafer M, et al. Comparison of 68Ga-DOTATOC PET and 111In-DTPAOC (Octreoscan) SPECT in patients with neuroendocrine tumours. *Eur J Nucl Med Mol Imaging*. 2007;34(10):1617–26. [PubMed: 17520251]
20. Sadowski SM, Neychev V, Millo C, Shih J, Nilubol N, Herscovitch P, et al. Prospective Study of 68Ga-DOTATATE Positron Emission Tomography/Computed Tomography for Detecting Gastro-Enteropancreatic Neuroendocrine Tumors and Unknown Primary Sites. *J Clin Oncol* 2016;34(6):588–96. [PubMed: 26712231]
21. Deroose CM, Hindie E, Kebebew E, Goichot B, Pacak K, Taieb D, et al. Molecular Imaging of Gastroenteropancreatic Neuroendocrine Tumors: Current Status and Future Directions. *J Nucl Med* 2016;57(12):1949–56. [PubMed: 27811124]
22. Cives M, Strosberg J. Radionuclide Therapy for Neuroendocrine Tumors. *Curr Oncol Rep* 2017;19(2):9. [PubMed: 28220446]

Figure 1. Benign In-111 pentetreotide uptake in the uncinus process of the pancreas in a 64 y/o woman with elevated Chromogranin level. **(a)** Fused SPECT/CT scan at 4hrs after injection. Arrow denotes physiological uptake in the uncinus process of the pancreas. The 2D and 3D pancreas to liver uptake ratios were 1.58 and 1.63, respectively (both below the pathologic thresholds). **(b)** Arterial phase contrast enhanced T1w MRI image demonstrating a normal uncinus process without any mass.

Figure 2.

52 y/o woman with multiple endocrine neoplasia type 1 (MEN1) and Zollinger-Ellison (ZE) syndrome with biochemical evidence of neuroendocrine tumor: Chromogranin A 43 (normal <15ng/ml), pancreatic polypeptide >1600 (normal 67-1319 pg/ml), gastrin 128 (normal 100 pg/ml). **(a)** Fused 4hr In-111 pentetreotide SPECT/CT scan showing uptake in the pancreatic head (arrow). The pancreas lesion to liver ratio was 2.29 using 3D ROI and 2.50 using 2D ROI methods, both above the pathologic thresholds. **(b)** Arterial phase T1w contrast-enhanced MRI performed the same date showing 12 × 8mm enhancing mass in the uncinate process of the pancreatic head consistent with a neuroendocrine tumor (arrow).

Figure 3.

3D ROI based mean pancreatic head to liver uptake ratios in all patients with visually identifiable pancreatic head uptake. Group 1 are patients without a pancreatic head lesion at 4 hours, group 2 are patients without a pancreatic head lesion at 24 hours, group 3 are patients with a pancreatic head mass at 4 hours, and group 4 are patients with a pancreatic head mass at 24 hours. The line represents a threshold ratio of 1.67, which predicts the presence or absence of a mass with 100% accuracy. The range of ratios for patients with physiological uptake (groups 1 and 2) was 0.37 – 1.63, and the range of ratios for patients with a neuroendocrine tumor (groups 3 and 4) was 1.79 – 23.6.

Figure 4. Comparison of 4hr and 24hr pancreatic head to liver uptake ratio using 3D volumetric ROIs in patients without (a) and with (b) a pancreatic head mass. Each line connects the values from the same patient at two time points.

TABLE 1.

Patient characteristics and qualitative pancreatic head In-111 pentetreotide uptake results.

	No Pancreatic Head Mass	Pancreatic Head NE Tumor	Total
Patients	129	7	136
Age (range)	57.1 ± 14.4 (22-94)*	51.0 ± 14.1 (26-66)*	56.7 ± 14.4 (22-94)
Female sex	75 (58.1%)	3 (42.9%)	78 (57.4%)
4 hour studies	128	7	135
24 hour studies	58	4	62
4 hour ratings			
No uptake	110 (85.9%)		
Mild Uptake	6 (4.7%)		
Definite Uptake	12 (9.4%)	7 (100%)	
24 hour ratings			
No uptake	48 (82.8%)		
Mild Uptake	2 (3.4%)		
Definite Uptake	8 (13.8%)	4 (100%)	
Overall			
No uptake	110 (85.3%)		110
Mild Uptake	6 (4.7%)		6
Definite Uptake	13 (10.1%)	7 (100%)	20

TABLE 2.

Clinical, imaging and biochemical characteristics of pancreatic head NE tumor cases.

Age	Sex	History	Imaging	Biochemical	Clinical
52	F	MEN1, ZE syndrome	1.2cm enhancing uncinate process mass on MRI, 0.9mm EUS hypoechoic mass one year prior	Gastrin 128 (H), PP > 1600 (H), Chromogranin A 43 (H)	Prior pancreatic head and tail enucleations 11 years prior with NE tumor
26	F	MEN1, ZE syndrome	1.1cm enhancing and restricting pancreatic head mass on MRI, 1.2cm hypoechoic pancreatic head mass on intraoperative US	Gastrin 620 (H), PP 559 (H), Chromogranin A 229 (H)	subsequent uncinectomy with 1.1cm well differentiated NE tumor, low grade
61	M	MEN1, ZE syndrome	2.2cm pancreatic head mass with T1 shortening and enhancement on MRI; 2.1×1.3cm hypoechoic pancreatic head mass on EUS	Gastrin 110 (H), PP >1600 (H), Chromogranin A 184 (H)	Observation, prior distal pancreatectomy
56	M	MEN1, ZE syndrome	1.4cm pancreatic neck mass MRI; 1.5×1.5cm hypoechoic pancreatic mass on EUS	Gastrin 127 (H), PP 1740 (H), Chromogranin A 680 (H)	Slow growing (8mm in 15 years), managed with esomeprazole
66	M	MEN1	Hypoechoic 3.7cm pancreatic head mass on MRI, Rim calcification on CT	PP 51 (N), Chromogranin A 41 (N)	Liver metastases s/p TACE
58	F	MEN1	3.6cm heterogeneously enhancing exophytic pancreatic head mass on MRI	Chromogranin A 263 (H)	Biopsy proven liver metastases, well-differentiated NE tumor
38	M	TS	2.9cm enhancing pancreatic head mass on MRI	PP 427 (H), chromogranin A 24 (H)	Observed due to Tuberous Sclerosis

Normal ranges varied: [gastrin] pg/ml, [PP = pancreatic polypeptide] pg/ml, [Chromogranin A] ng/ml; H=high, N=normal (in comparison to lab normal ranges, which were variable)

EUS = endoscopic ultrasound; TACE=transarterial chemo-embolization; NE=neuro endocrine; MEN1 = multiple endocrine neoplasia type 1; ZE = Zollinger-Ellison syndrome; TS = Tuberous Sclerosis.

TABLE 3.

Quantitative Results using 3D spherical volumetric ROIs.

	No Pancreatic Head Mass	Pancreatic Head Mass	P-value
Pancreas-to-liver 4hr	0.91 ± 0.40 (0.37-1.63) [†] N=18	6.8 ± 5.3 (2.3-14.9) N=7	<0.001
Pancreas-to-liver 24hr	0.91 ± 0.38 (0.39-1.38) N=10	10.6 ± 10.4 (1.79-23.6) N=4	0.009
P-value (grouped, paired)	0.96, 0.32	0.81, 0.32	
Pancreas-to-liver all	0.91 ± 0.38 (0.37-1.63) [†] N=28	8.2 ± 7.3 (1.79-23.6) [§] N=11	<0.001

Confidence intervals:

[†]89%[†]93%[§]83%.

Paired t-test comparison for all 4hr vs. 24hr studies (n=13) = 0.33

TABLE 4.

Quantitative results for 2D slice-based ellipse ROI analysis.

	No Pancreatic Head Mass	Pancreatic Head Mass	P-value
Pancreas-to-liver 4hr	0.87 ± 0.40 (0.35-1.73) [†] N=18	6.3 ± 4.5 (2.4-13.4) N=7	<0.001
Pancreas-to-liver 24hr	0.89 ± 0.33 (0.28-1.27) N=10	9.7 ± 8.7 (1.85-19.6) N=4	0.005
P-value (grouped, paired)	0.93, 0.44	0.40, 0.24	
Pancreas-to-liver all	0.88 ± 0.37 (0.28-1.73) [†] N=28	7.5 ± 6.2 (1.85-19.6) [§] N=11	<0.001

Confidence intervals:

[†]89%[†]93%[§]83%.

Paired t-test comparison for all 4hr vs. 24hr studies (n=13) = 0.28