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Localisation of neuroendocrine tumours of the upper gastrointestinal tract

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Abstract

In order to localise neuroendocrine tumours of the foregut type (that is, of the stomach, duodenum, and pancreas), 18 patients were studied prospectively by endoscopic ultrasonography, computed tomography, transabdominal ultrasonography, magnetic resonance imaging, and somatostatin receptor scintigraphy. These 18 patients had a total of 25 primary tumour lesions which were verified histologically in tissue obtained by surgery or by ultrasound or endoscopy guided biopsy. Tumours were found in the stomach (n=1), duodenum (n=6), pancreas (n=17), and liver (n=1). Endoscopic ultrasonography had the highest sensitivity for tumour detection, followed by somatostatin receptor scintigraphy, computed tomography, transabdominal ultrasonography, and magnetic resonance imaging (88%, 52%, 36%, 32%, and 24% respectively). Endoscopic ultrasonography was especially sensitive in tumours smaller than 2 cm in diameter (88% *v* somatostatin receptor scintigraphy 35%; computed tomography 12%; transabdominal ultrasonography 6%; and magnetic resonance imaging 0%). Of 17 tumours located in the pancreas, endoscopic ultrasonography showed a sensitivity of 94% (somatostatin receptor scintigraphy 47%; computed tomography 47%; transabdominal ultrasonography 41%; and magnetic resonance imaging 29%). Of eight extrapancreatic tumours, six were identified by endoscopic ultrasonography, five by somatostatin receptor scintigraphy, and only one by computed tomography, transabdominal ultrasonography, and magnetic resonance imaging. One neuroendocrine tumour that was not detected by endoscopic ultrasonography was correctly identified by somatostatin receptor scintigraphy. Endoscopic ultrasound allowed correct determination of the tumour size and tumour spread into parapancreatic structures, especially the large vessels (T stage), in all 14 patients operated upon. The lymph node stage (N stage) was correctly determined in 10 of these 14 patients. In summary, endoscopic ultrasonography and somatostatin receptor scintigraphy were the most sensitive imaging methods for the localisation of these tumours and should be used as early diagnostic procedures to accurately stage neuroendocrine tumours of the foregut type.

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Neuroendocrine tumours of the foregut type constitute a subgroup of tumours that are mainly located in the pancreas, stomach, and duodenum.[1] Because functionally active neuroendocrine tumours are associated with well-characterised clinical symptoms (for example, Zollinger-Ellison and carcinoid syndromes), they can often be diagnosed when they are still resectable and the patient has not yet developed metastatic disease.[2] In contrast, functionally inactive tumours are often diagnosed when they have already metastised.[1] Localisation of primary tumours of the pancreas, intestinal wall, or paraintestinal lymph nodes by conventional imaging methods is difficult, mainly because of their small size and their proximity to hollow organs.[3]

Depending on their size, functional neuroendocrine tumours can be diagnosed preoperatively by imaging procedures such as transabdominal ultrasonography (US), computed tomography (CT), angiography, and magnetic resonance imaging (MRI), at best in 40–60% of all cases.[4–13] As far as non-functional, small (<2 cm in diameter), pancreatic and extrapancreatic neuroendocrine tumours of the foregut are concerned, only limited data for conventional imaging methods exist.[8 9 12 14 15] Recent studies using two new imaging techniques, endoscopic US and somatostatin receptor scintigraphy (SRS), indicated that these might be more sensitive than the conventional methods.[16 17] SRS uses ^{123}I- or ^{111}In-labelled somatostatin analogues to identify somatostatin receptors in vivo. So far, two studies, as well as a study by our group, have shown that neuroendocrine tumour tissue can be visualised in patients who are negative by conventional methods.[16 18 19] Also, in contrast to conventional imaging techniques, endoscopic US detects pancreatic ductal carcinomas as well as functional neuroendocrine tumours of the pancreas correctly in 80–100%.[17 20–26] Experience with endoscopic US in patients with gastroenteropancreatic, non-functional neuroendocrine tumours of the foregut type, and especially those located in the gastrointestinal wall, is limited.[24 25] Furthermore, a direct comparison between endoscopic US and SRS and conventional imaging methods is lacking.

In view of these new methods, we have carried out a prospective, comparative study. The value of the imaging procedures endoscopic US, SRS, US, CT, and MRI in the diagnosis of primary tumour lesions and local spread of neuroendocrine tumours of the foregut type were investigated.

Patients and methods

Between March 1991 and March 1993, 18 consecutive patients (seven men and 11 women, aged 8–76 years, mean 54) with histologically verified neuroendocrine tumours (n=8) or suspected neuroendocrine tumours based on

clinical signs and laboratory tests (n=10) were examined in parallel by endoscopic US, transabdominal US, CT, MRI, and SRS. All examinations were done within four weeks for each patient.

Before the imaging procedures, histological confirmation of metastatic liver tissues was obtained by US or CT guided biopsies in four cases, and of primary tumour tissues via an endoscopic route in four cases (stomach, n=1; duodenum, n=3). One patient whose primary tumour (duodenum) had been removed 12 months previously, was re-evaluated because of a suspected recurrence of primary tumour tissue. Based on clinical signs and laboratory tests, four insulinomas (positive fasting tests), four gastrinomas (positive secretin tests), and one carcinoid tumour (intermittant flush with high serum serotonin values and increased 5-hydroxyindolic acid in the urine) were diagnosed. After all five imaging procedures had been performed, 14 patients were operated on, and a direct comparison between the imaging results and the intraoperative findings including histological verification was made.

Endoscopic US was carried out with an Olympus GF UM3 echoendoscope. Patients were examined in the left lateral decubitus position. After introducing the echoendoscope into the descending duodenum, various parts of the pancreas, duodenal, and gastric wall were carefully scanned by slowly withdrawing the instrument. A water filled balloon at the tip of the instrument and filling of the stomach with about 400 ml of water were necessary to provide a fluid interface between the transducer and gastrointestinal wall.

Transabdominal US was performed with a Picker LSC 7000 scanner, using a 3·5 MHz and, if necessary, a 5 MHz mechanical sector scanner.

CT scanning was performed with a Siemens DRG scanner, before and after intravenous and oral administration of contrast material. The total abdomen was scanned in 8 mm sections. In addition, the pancreatic region was scanned in 4 mm sections. All images were obtained in transaxial plane.

MRI was done with an 1,5 Tesla Siemens Magnetom superconducting imaging system. Two pulse sequences were employed: A T_1 weighed spin-echo sequence (SE 500/15) and a T_2 weighed spin-echo sequence (SE 2.300/90). Additionally, all patients were imaged with fast T_1 weighed rapid multisection imaging (GRE 160/5/80°). All images were aquired in transaxial plane with a section thickness of 8 mm.

SRS was performed by the use of a Siemens Orbiter 7500 gamma camera. For examination, a dosage between 100 to 200 MBq ^{111}Indium-labelled pentetreotide was given as a bolus intravenous injection. All patients underwent anterior and posterior whole body static scintigraphy 4, 24, and (only in selected cases) 48 hours after injection. Images were obtained both in an analogue and digital manner. Additionally, single photon emission computed tomography (SPECT) was done 24 hours after injection in 11 patients.

TABLE I *Characteristics of patients with neuroendocrine tumours (NET) and their primary tumour lesions by imaging and surgical procedures*

Patient no	*No of primary tumours*	*Confirmation by*	*Localisation of primary tumours*	*Maximum diameter (cm)*	*Functional state*
1	2	Surgery	Pancreas (h)	4	F (gastrinoma)
			Duodenum	1	F (gastrinoma)
2	1	Surgery	Pancreas (h)	6	Nf
3	1	Surgery	Pancreas (t)	2	F (insulinoma)
4	1	Surgery	Pancreas (h)	1·5	F (insulinoma)
5	5	Surgery	Pancreas (t)	1·5	F (insulinoma)
			Pancreas (t)	2	F (insulinoma)
			Pancreas (t)	2	F (insulinoma)
			Pancreas (b)	1·5	F (insulinoma)
			Pancreas (b)	0·8	F (insulinoma)
6	1	Surgery	Pancreas (h)	5	F (carcinoid)
7	2	Surgery	Pancreas (h)	0·8	Nf
			Duodenum	0·2	Nf
8	1	Biopsy	Duodenum	1	Nf
9	1	Biopsy	Pancreas (b)	2	F (insulinoma)
10	1	Surgery	Stomach	0·6	Nf
11	1	Surgery	Pancreas (h)	6	F (gastrinoma)
12	2	Surgery	Pancreas (h)	0·8	Nf
			Pancreas (b)	2	Nf
13	1	Biopsy	Pancreas (t)	3	Nf
14	1	Biopsy	Duodenum	1	Nf
15	1	Surgery	Papilla minor	1·5	Nf
16	1	Surgery	Pancreas (h)	3	Nf
17	1	Surgery	Duodenum	4	F (gastrinoma)
18	1	Surgery	Liver	3	F (gastrinoma)

F=functional NET; Nf=non-functional NET; h=head; b=body; t=tail of pancreas.

TABLE II *Comparison of sensitivities of various imaging procedures in detecting primary tumour lesions of neuroendocrine tumours depending on size and location (no (%))*

	Endoscopic US	*US*	*CT*	*NMR*	*SRS*
Sensitivity total	22/25 (88)	8/25 (32)	9/25 (36)	6/25 (24)	13/25 (52)
Sensitivity <2 cm	15/17 (88)	1/17 (6)	2/17 (12)	0/17 (0)	6/17 (35)
Sensitivity >2 cm	7/8 (87)	7/8 (87)	7/8 (87)	6/8 (75)	7/8 (87)
Sensitivity pancreas	16/17 (94)	7/17 (41)	8/17 (47)	5/17 (29)	8/17 (47)
Sensitivity extrapancreatic	6/8 (75)	1/8 (12)	1/8 (12)	1/8 (12)	5/8 (62)

US=ultrasound; CT=computed tomography; NMR=nuclear magnetic resonance imaging; SRS=somatostatin receptor scintigraphy.

Results

Altogether 25 tumour lesions were identified in the pancreas (head, n=8; body, n=4; tail, n=5), duodenum/papilla minor (n=5/n=1), liver (n=1), and stomach (n=1) in the 18 patients studied. The patients' characteristics are given in Table I. After surgery (n=14) or biopsies via endoscopy (n=2) or US guidance (n=2), tumour lesions identified by imaging methods could be verified by histological and immunohistological means. Most of the 25 tumours (17) were less than 2 cm in diameter. There were 11 non-functional tumours, eight insulinomas, five gastrinomas, and one carcinoid. Non-functional tumours were operationally defined as neuroendocrine tumours that did not cause any classic clinical symptoms.

Endoscopic US was able to identify 22 of all 25 neuroendocrine tumours found in the pancreas, duodenum, and stomach (88%). SRS identified 13 of 25 (52%), CT nine of 25 (36%), US eight of 25 (32%), and MRI six of 25 (24%) (Table II). Separate analysis of the 17 tumours localised in the pancreas showed a sensitivity of 94% for endoscopic US, 47% for SRS, 47% for CT, 41% for US, and 29% for MRI (Table II). Of the eight tumours localised in the duodenum, stomach, and liver, endoscopic US detected six (75%) and SRS five (62%), whereas CT, US, and MRI were able to detect only one (12%), a tumour that was localised in the liver and turned out to be a gastrinoma of the liver (Table II).

The tumours undetected by endoscopic US were:

TABLE III *Comparison of sensitivities of various imaging procedures in detecting primary tumour lesions of neuroendocrine tumours depending on functional state (no (%))*

	Endoscopic US	*US*	*CT*	*NMR*	*SRS*
Sensitivity total	22/25 (88)	8/25 (32)	9/25 (36)	6/25 (24)	13/25 (52)
Sensitivity gastrinomas	4/5 (80)	3/5 (60)	3/5 (60)	3/5 (60)	5/5 (100)
Sensitivity insulinomas	7/8 (87)	0/8 (0)	1/8 (12)	0/8 (0)	1/8 (12)
Sensitivity carcinoid	1/1 (100)	1/1 (100)	1/1 (100)	1/1 (100)	1/1 (100)
Sensitivity non-functional tumours	10/11(91)	4/11 (36)	4/11 (36)	2/11 (18)	6/11 (54)

US=ultrasound; CT=computed tomography; NMR=nuclear magnetic resonance imaging; SRS=somatostatin receptor scintigraphy.

TABLE IV *Accuracy of endoscopic ultrasound (US) and angiography in determining T stage, N stage, and vascular status in patients with neuroendocrine tumours (no (%))*

Accuracy	*Endoscopic US*	*Angiography*
T stage	14/14 (100)	-
N stage	10/14 (71)	-
Vascular status	14/14 (100)	10/11 (91)

Fourteen patients were studied by endoscopic US and underwent surgery: 11 of them underwent preoperative angiography.

TABLE V *Endosonographic features of the 22 neuroendocrine tumours detected in pancreas, stomach, and duodenum by endoscopic ultrasound*

Feature	*No of tumours*
Sonographic pattern*	
Homogenous	12
Echo-poor	16
Echo-rich	6
Inhomogenous	10
Tumour margin	
Smooth	12
Irregular	10

*In comparison with the liver.

(1) A non-functional tumour of the duodenal wall, 2 mm in size;

(2) An insulinoma of the pancreatic tail, 8 mm in diameter, and;

(3) A 3 cm gastrinoma of the lower part of duodenal wall that could not be reached with the echoendoscope. This tumour could be visualised by SRS.

Endoscopic US localised seven of eight insulinomas (87%), four of five gastrinomas (80%), the single carcinoid (100%), and 10 of 11 non-functional tumours (91%) (Table III).

SRS localised one of eight insulinomas (12·5%), five of five gastrinomas (100%), the single carcinoid tumour (100%), and six of 11 non-functional tumours (54%) (Table III).

Neuroendocrine tumours not detected by planar images were not found by SPECT either. As shown in Table II, neuroendocrine tumours less than 2 cm in diameter could only be identified by endoscopic US and also, in part, by SRS.

In contrast, only one of 17 tumours smaller than 2 cm in diameter, could be detected by conventional imaging methods. CT, US, and MRI were unable to detect any of the seven tumours in the stomach and duodenal wall. Small insulinomas and non-functional tumours were also hardly detected by conventional methods (Table III).

Endosconographic determination of tumour size, T stage (especially tumour spread into large vessels), and N stage could be directly compared in 14 patients who were operated on consecutively. At surgery, 15 tumours were found in the pancreas, one in the papilla minor, three in the duodenum, one in the stomach, and one in the liver (Table I). Endoscopic US predicted correctly the T stage in all cases and the N stage in 10 of 14 patients (Table IV). There were three false positive findings, and one false negative finding, however, with regard to the former, in one patient an adenoma of the left adrenal gland was falsely interpreted by endoscopic US as an infiltrated lymph node. In two other cases, only enlarged lymph nodes without malignant cell infiltration were found. In the case of the false negative, malignant lymph nodes were found in the area of the ligament of Treitz at surgery, but were not detected by endoscopic US.

In 11 of these patients, angiography was carried out preoperatively to determine the tumour vascularisation and spread into large vessels. In eight cases, the tumour location was correctly identified by angiography. A possible vascular infiltration was correctly detected in 10 of 11 cases studied by angiography (Table IV).

The ultrasonographic features of the tumours studied, were variable and did not differ between functional and non-functional neuroendocrine tumours (Table V). In addition, tumours that caused a similar hormonal syndrome, for example, insulinomas, showed different ultrasonographic patterns within this tumour subtype (Fig 1 (A) and (B)). Most tumours showed poor

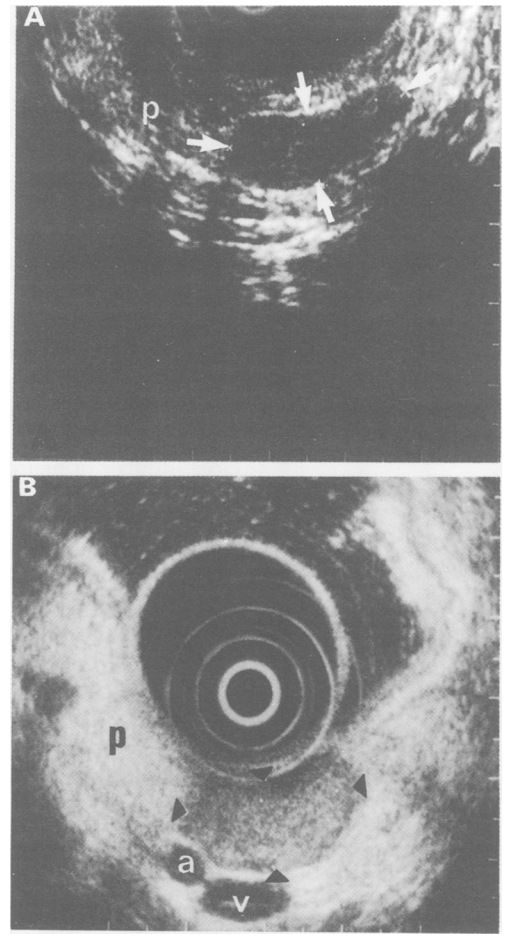

Figure 1: Endosonographic images of insulinomas located in the tail of the pancreas. Tumours show a smooth margin and a homogenous but variable echopattern. In (A) the tumour is echo-poor (white arrows), whereas in (B) the tumour is echo-rich (black arrowheads). p=pancreas; a=splenic artery; v=splenic vein.

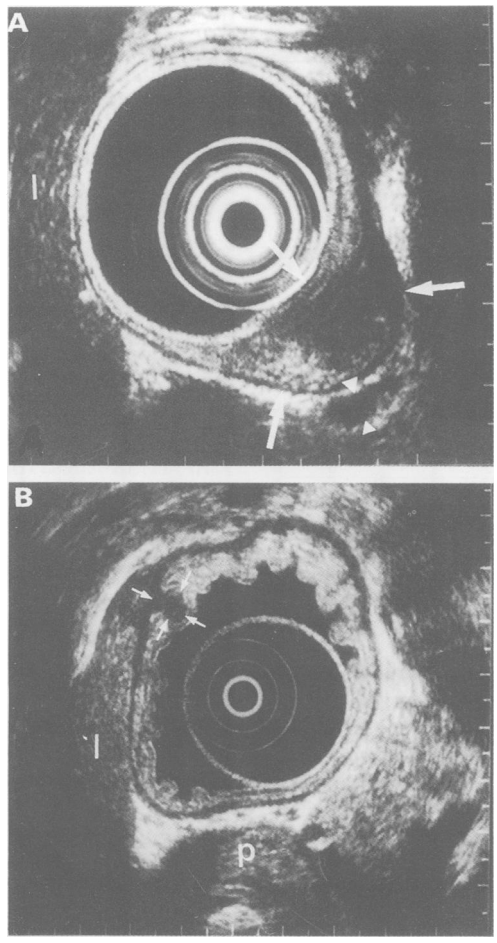

Figure 2: Endosonographic images of two non-functional neuroendocrine tumours (NET) of the intestinal wall. In (A) a NET of the minor papilla with an inhomogenous, ehco-poor pattern is shown (arrows). Note, that the tumour lies within the duodenal wall and does not infiltrate periduodenal tissue or the pancreatic duct (arrowheads). In (B) a small (6 mm in diameter) NET of the stomach with an homogenous, echo-poor pattern and irregular margin is shown (arrows). Note, that the tumour lies within the gastric wall and does not infiltrate perigastral tissues or organs. l=left lobe of liver; p=pancreas.

and relatively uniform echogenicities (Fig 2), with regular or irregular margins. With increasing size, the tumours became inhomogenous.

Discussion

This is the first study investigating prospectively the diagnostic value of the combined use of endoscopic US and SRS in the localisation of neuroendocrine tumours of the upper gastrointestinal tract by comparing these new techniques with conventional imaging methods. Furthermore, our study considers a relatively large number of neuroendocrine tumours of the foregut type with both, a location in the gastrointestinal wall[24 25] and a non-functional state.[17 23-26]

Because of our selection criteria we had no negative controls and were unable to work out the specifity of any tested diagnostic method. Whereas almost all neuroendocrine tumours were visualised by endoscopic US together with SRS, only a few could be identified by conventional methods (Table II). The high sensitivity of endoscopic US in imaging pancreatic tumours is consistent with previous results for pancreatic ductal carcinomas[20 22] and pancreatic, functional neuroendocrine tumours.[17 23-26] Thus far, data on non-functional, gastroenteropancreatic neuroendocrine tumours, especially those located in the gastrointestinal wall, are limited.[24 25] In the present study, a total of seven tumours of the gastrointestinal wall (two gastrinomas and five non-functional tumours) were studied, most of which (five of seven) could be detected correctly by endoscopic US. In addition endoscopic US shows a high sensitivity in detecting tumours, independently of their functional state and size. In tumour staging, endoscopic US also showed a high level of diagnostic accuracy in determining tumour infiltration of neighbouring tissue, including large blood vessels (T stage) and lymph nodes (N stage). The accuracy in our study is comparable with previous investigations on periampullar and pancreatic ductal carcinomas.[20 22] Determination of N stage by endoscopic US resulted in three false positive interpretations. As has already been shown in previous studies on carcinomas of the oesophagus, stomach, and rectum, endoscopic US can detect enlarged lymph nodes very well, but no absolute sonographic features exist to differentiate between lymph nodes containing a bulk of tumour or inflammatory cells.[27 28] Furthermore, structures such as lymph nodes nearby the ligament of Treitz cannot be seen by endoscopic US, since they are located outside the reach and imaging field of the instrument.

SRS was shown to be a simple and sensitive method for imaging neuroendocrine tumours in the upper gastrointestinal tract. Compared with previous data, however, the sensitivity for the identification of these tumours was lower in this study.[18 19] This is probably because relatively small tumours were evaluated and only tumours of the foregut type were studied. Tumours of the foregut more often yield negative results by SRS midgut tumours.[16] In comparison with abdominal US, CT, MRI, and endoscopic US, the sensitivity of SRS was independent of the localisation of the tumours but dependent on their functional state (insulinomas<non-functional tumours<gastrinomas) and size (Tables II and III).

In summary, low sensitivities of US, CT, and MRI for the detection of gastroenteropancreatic neuroendocrine tumours are observed. We show, furthermore, that tumours less than 2 cm in diameter, and especially those located in the gastrointestinal wall, are rarely visualised by conventional methods but are detected by endoscopic US and, in part, by SRS. For the detection and staging of gastrinomas especially, the combination of SRS and endoscopic US gives a very high accuracy in localising tumours within the pancreas and duodenal and gastric walls. In addition, it represents a sensitive method of identifying lymph nodes and blood vessels infiltrated by tumour tissue.

We conclude that endoscopic US and SRS are the most sensitive imaging methods for gastroenteropancreatic neuroendocrine tumours and should therefore be used early to determine the primary tumours as well as the local spread, especially infiltration of large vessels and involvement of regional lymph nodes.

1 Lloyd RV. Neuroendocrine cells and neoplasms of the gastrointestinal tract. In: Lloyd RV, ed. *Endocrine pathology*. New York: Springer Verlag, 1990: 111–27.
2 Lloyd RV. Endocrine pancreas. In: Lloyd RV, ed. *Endocrine pathology*. New York: Springer Verlag, 1990: 85–109.
3 Pipeleers-Marichal M, Somers G, Willems G, Foulis A, Imrie C, Bishop AE, *et al*. Gastrinomas in the duodenums of patients with multiple endocrine neoplasia type 1 and the Zollinger-Ellison syndrome. *N Engl J Med* 1990; **322**: 723–7.

4 Böttger TC, Weber W, Beyer J, Junginger T. Value of tumor localization in patients with insulinoma. *World J Surg* 1990; **14:** 107–14.
5 Broughan TA, Leslie JD, Soto JM, Hermann RE. Pancreatic islet cell tumors. *Surgery* 1986; **99:** 671–8.
6 Galiber AK, Reading CC, Charboneau JW, Sheedy PF, James EM, Gorman B, *et al.* Localization of pancreatic insulinoma: comparison of pre- and intraoperative US with CT and angiography. *Radiology* 1988; **166:** 405–8.
7 Günther RW, Klose KJ, Rückert K, Kuhn FP, Beyer J, Klotter HJ, *et al.* Islet-cell tumors: detection of small lesions with computed tomography and ultrasound. *Radiology* 1983; **148:** 485–8.
8 Hemmingsson A, Lindgren PG, Lörelius LE, Öberg K. Diagnosis of endocrine gastrointestinal tumours. *Acta Radiol* 1981; **22:** 657–61.
9 Krudy AG, Doppman JL, Jensen RT, Norton JA, Collen MJ, Shawker TH, *et al.* Localization of islet cell tumors by dynamic CT. Comparison with plain CT, arteriography, sonography, and venous sampling. *AJR* 1984; **143:** 585–9.
10 Norton JA, Doppman JL, Collen MJ. Prospective study of gastrinoma localization and resection in patients with Zollinger-Ellison syndrome. *Ann Surg* 1986; **204:** 468–79.
11 Päivansalo M, Mäkäräinen H, Sinuluoto T, Stahlberg M, Jalovaara P. Ultrasound compared with computed tomography and pancreatic arteriography in the detection of endocrine tumours of the pancreas. *Europ J Radiol* 1989; **9:** 173–8.
12 Stark DD, Moss AA, Goldberg HJ, Deveney CW. CT of pancreatic islet cell tumors. *Radiology* 1984; **150:** 491–4.
13 Wank SA, Doppman JL, Miller DL, Collen MJ, Maton PN, Vinayek R, *et al.* Prospective study of the ability of computed axial tomography to localize gastrinomas in patients with Zollinger-Ellison syndrome. *Gastroenterology* 1987; **92:** 905–12.
14 Frucht HF, Doppman JL, Norton JA, Miller DL, Dwyer AJ, Frank JA, *et al.* Gastrinomas: comparison of MR imaging with CT, angiography, and US. *Radiology* 1989; **171:** 713–7.
15 Frucht HF, Norton JA, London JF, Vinayek R, Doppman JL, Gardner JD, *et al.* Detection of duodenal gastrinomas by operative endoscopic transillumination. *Gastroenterology* 1990; **99:** 1622–7.
16 Scherübl H, Bäder M, Fett U, Hamm B, Schmidt-Gayk R, Koppenhagen K, *et al.* Somatostatin-receptor imaging of neuroendocrine tumors. A new, diagnostically relevant procedure. *Gastroenterology* 1993; **105:** 1705–9.
17 Rösch T, Lightdale CJ, Botet JF, Boyce GA, Sivak MV, Yasuda K, *et al.* Localization of pancreatic endocrine tumors by endoscopic ultrasonography. *N Engl J Med* 1992; **326:** 1721–6.
18 Krenning EP, Kwekkeboom DJ, Oei HY, Reubi JC, Van Hagen PM, Kooij PPM, *et al.* Somatostatin receptor imaging of endocrine gastrointestinal tumors. *Schweiz Med Wochenschr* 1992; **122:** 634–7.
19 Lamberts SWJ, Bakker WH, Reubi JC, Krenning EP. Somatostatin receptor imaging in the localization of endocrine tumors. *N Engl J Med* 1990; **323:** 1246–9.
20 Rösch T, Dittler HJ, Lorenz R, Braig C, Gain T, Feuerbach S, *et al.* Endosonographisches Staging des Pankreaskarzinoms. *Dtsch Med Wochenschr* 1992; **117:** 563–9.
21 Rösch T, Braig C, Gain T, Feuerback S, Siewert JR, Schusdtiarra V, *et al.* Staging of pancreatic and ampullary carcinoma by endoscopic ultrasonography. *Gastroenterology* 1992; **102:** 188–99.
22 Yasuda K, Hidekazu M, Fujimoto S, Masatsugu N, Kawai K. The diagnosis of pancreatic cancer by endoscopic ultrasonography. *Gastrointest Endosc* 1988; **34:** 1–8.
23 Glover JR, Shorvon PJ, Lees WR. Endoscopic ultrasound for localisation of islet cell tumours. *Gut* 1992; **33:** 108–10.
24 Lightdale CJ, Botet JF, Woodruff JM, Brennan M. Localization of Endocrine tumors of the pancreas with endoscopic ultrasonography. *Cancer* 1991; **68:** 1815–20.
25 Ruszniewski P, Amoyal P, Combes R, Amoyal G, Grange JD, Bernades P, *et al.* Endoscopic ultrasonography (EUS) is useful for the localization of primary gastrinomas. *Gastroenterology* 1991; **100** (suppl): A297.
26 Yamada M, Komoto E, Naito Y, Tsukamoto Y, Mitake M. Endoscopic ultrasonography in the diagnosis of pancreatic islet cell tumors. *J Ultrasound Med* 1991; **10:** 271–6.
27 Aibe T, Ito T, Yoshida T. Endoscopic ultrasonography of lymph nodes surrounding the upper GI tract. *Scand J Gastroenterol* 1986; **21:** 158–63.
28 Tio TL, Tytgat GNJ. Endoscopic ultrasonography in analyzing periintestinal lymph node abnormality. Preliminary results of studies in vitro and in vivo. *Scand J Gastroenterol* 1986; **21:** 158–63.