Intraoperative Ultrasonographic Localization of Islet Cell Tumors

A Prospective Comparison to Palpation

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The purpose of the present study was to evaluate prospectively the value of intraoperative ultrasound scanning (IOUS) in localizing islet cell tumors by comparing results of IOUS to those of palpation during 44 consecutive laparotomies for gastrinoma (36) or insulinoma (8). All patients had preoperative radiographic imaging studies and selective venous sampling for hormones, which guided the subsequent laparotomy. Any suspicious finding by palpation and/or IOUS was resected. Pathologic evidence of islet cell neoplasm served as the reference standard. Five patients were excluded from analysis because neither palpation nor IOUS had suspicious findings and no islet cell tumor was found. Seven pancreatic insulinomas were found in seven patients. IOUS was as sensitive as palpation at localizing insulinomas. Twenty-three pancreatic gastrinomas were found in 19 patients. IOUS was equal to palpation in the ability to localize gastrinomas. Gastrinomas that were successfully imaged by IOUS were significantly larger than gastrinomas that were not imaged. Twelve extrapancreatic gastrinomas were found in nine patients, and palpation was more sensitive than IOUS at localizing these small duodenal wall tumors. Five patients (11%) had their surgical management changed by IOUS. Two patients had pancreatic tumors (one gastrinoma and insulinoma) enucleated that would not have been found without IOUS, and three patients had resections of pathologically proven malignant islet cell tumors based on sonographic findings. All five patients were *cured* with short follow-up. The present results demonstrate that palpation and IOUS are complementary because IOUS can image tumors that are not palpable and IOUS can provide additional information concerning malignant potential not detected by palpation.

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TUMOR LOCALIZATION is a major problem associated with endocrine tumors. Small islet cell tumors produce hormones that lead to early diagnosis and potential surgical intervention. Despite careful search at laparotomy, insulinomas and gastrinomas are occult and elusive. Blind subtotal pancreatectomy with the increased morbidity and mortality rate is necessary when an insulinoma cannot be found.[1] Gastrinomas are more elusive than insulinomas and have been localized in only 60–73% of laparotomies for Zollinger-Ellison syndrome (ZES).[2–4] Preoperative localization procedures, including selective arteriography,[5] CT scanning with contrast,[6] and transhepatic portal venous sampling for hormones,[7] have not solved the problem of islet cell tumor localization.

In 1982 the use of high-resolution B-mode IOUS scanning to image an insulinoma[8] and a gastrinoma[9] was first reported. In 1985 operative sonography successfully localized a small insulinoma, which had not been palpable in the pancreatic head.[10] We have had a large experience with insulinoma[11] and gastrinoma.[12] To evaluate the potential usefulness of IOUS to find small, surgically curable insulinomas and gastrinomas, we instituted a prospective comparison of IOUS to palpation in 1983. We have briefly described the first 10 gastrinoma patients.[13] We now analyze our results in 44 consecutive patients: 36 patients with gastrinoma and 8 patients with insulinoma.

Methods

In October 1983, a prospective study of the ability of IOUS to localize islet cell neoplasms in patients with either insulinoma or gastrinoma was instituted. All patients were treated at the National Institutes of Health using approved protocols.

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The diagnosis of insulinoma was established by an inappropriate elevation of serum insulin level and hypoglycemia following a fast.[11] The diagnosis of ZES was established using the following criteria: (1) elevated fasting serum gastrin concentration (>100 pg/mL); (2) basal acid output greater than 15 mEq/h (no previous gastric surgery); and (3) abnormal provocative secretin or calcium test defined as an increase in serum gastrin concentration of greater than 200 pg/mL following the I.V. administration of 2 U/kg of GIH secretin or greater than 395 pg/mL after calcium (5 mg/kg/h × 3 hours).[4]

All patients had preoperative localization studies, namely, ultrasound, computed tomography, selective ateriography, and percutaneous transhepatic portal venous sampling (PVS).[4–8] A hormone (either gastrin or insulin) gradient of 50% (selective portal venous hormone concentration/simultaneous peripheral venous concentration) was considered to be regionally localizing to the head, body, or tail of the pancreas.[7] As outlined previously,[4] all patients with metastatic tumor to the liver or with multiple endocrine neoplasia type I without positive results from imaging studies were excluded from this study. Final surgical pathology served as the reference standard for all intraoperative localization maneuvers.

All operations were performed as previously described.[4] The liver, pelvis, small intestine, pancreas, stomach, duodenum, mesenteric, and retroperitoneal regions were carefully explored. The pancreas was examined visually and by palpation. The pancreatic head was inspected after an extended Kocher maneuver. The pancreatic body and tail were inspected by opening the lesser sac along the avascular plane of the transverse colon. The inferior border of the pancreas was dissected free, so the body and tail could be palpated between two fingers. The entire duodenum was carefully palpated. The same extensive search was made regardless of the preoperative localization information or the operative findings. Knowledge of the preoperative imaging and localization studies did guide the exploration in that a general exploration was performed on all patients, but specific areas were focused based on preoperative imaging. Any suspicious finding by palpation was noted, and subsequently following ultrasound was excised or resected for pathologic analysis.

After full operative exposure and completion of manual palpation, realtime IOUS was performed using a Diasonics ultrasound scanner (model DRF 1; Diasonics Inc., Milipitas, CA) and a 10 MHz mechanical-sectoring transducer. Realtime studies were recorded on videotape. The transducer was inserted into a long, sterile, plastic sleeve containing methylcellulose gel at the distal tip. The abdominal cavity was filled with warm saline to provide additional acoustic coupling. The pancreas was

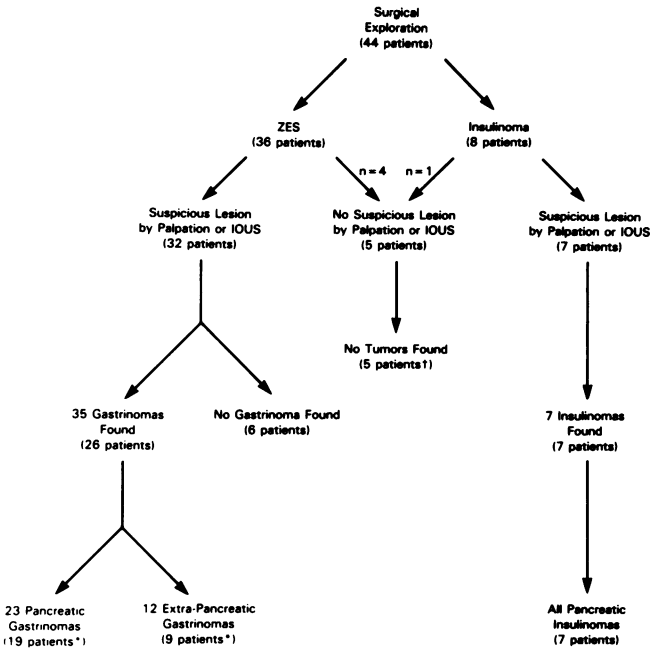

FIG. 1. Flow diagram describing the number of patients in the study divided into tumor types, suspicious operative findings, and the numbers of tumors proven pathologically in different patients. †Five patients were excluded from analysis because no tumors were found and no suspicious operative findings were identified by palpation or IOUS. *Two patients had gastrinomas found both within and outside of the pancreas.

scanned by passing the probe from the pancreatic head across the body to the tail, visualizing the pancreas in the longitudinal (sagittal) scanning plane. Several parallel passes were necessary for complete examination of the pancreas. Next, the pancreatic head, uncinate process, and duodenum were manually manipulated for optimal exposure and ultrasound visualization. All suspicious findings from palpation were carefully delineated by IOUS examination. The IOUS study was considered positive for islet cell tumor if a sonolucent mass lesion could be detected in both transverse and longitudinal imaging planes. After completion of the IOUS examination, the pancreas and peripancreatic tissues were again carefully palpated. Duodenal nodules were better exposed by opening the duodenal wall. Any suspicious pancreatic, stomach, duodenal, bowel, peripancreatic nodule, or lymph node, whether detected by palpation or intraoperative ultrasound, was biopsied. In the bowel or stomach wall, a suspected tumor was excised with a full thickness rim of normal tissue around the tumor. In the pancreatic head or adjacent lymph node areas, suspected tumors were enucleated. In the pancreatic body and tail, a pancreatic resection or enucleation was performed dependent on the size and appearance of the tumor. Lesions thought to be malignant were resected by subtotal or distal pancreatectomy and splenectomy.

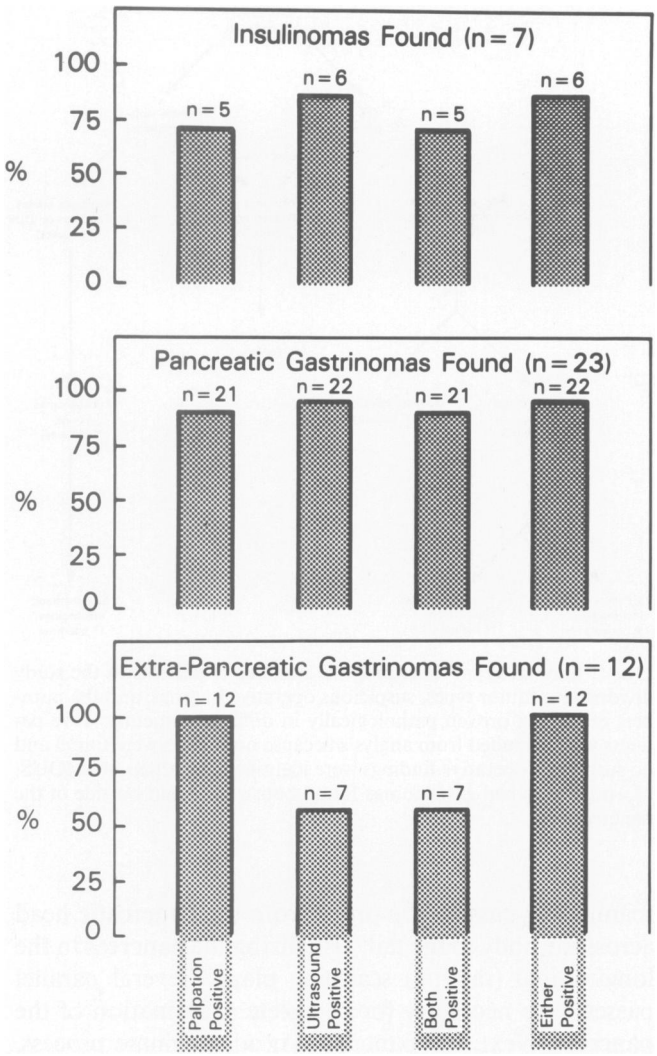

FIG. 2. Percentages for true-positives of operative localization methods including palpation alone, ultrasound alone, both combined and either positive in finding pancreatic insulinomas, pancreatic gastrinomas, and extrapancreatic gastrinomas. Statistically, both operative methods are comparable in finding pancreatic insulinomas and gastrinomas. Palpation is significantly better at localizing extrapancreatic gastrinomas than ultrasound ($p < 0.01$).

Results of intraoperative localization procedures (palpation and ultrasound) were compared to the final surgical, pathologic, and diagnostic proof of islet cell tumor. A decision analysis was performed on the results of intraoperative localization procedures using a method described by Weinstein and Fineberg.[14] After the pathologic results of the operation were known, manual palpation, or IOUS, were rated as true-positive, true-negative, false-positive, or false-negative. A true-positive result was defined as one in which an islet cell tumor was found in the exact location suggested by the intraoperative procedure. A true-negative result was one in which one localization maneuver suggested that no tumor was present in a given location, while the other localization maneuver suggested that tumor was present and no tumor was identified on biopsy. False-positive results were defined as erroneous tumor locations indicated by intraoperative maneuvers. False-negative results were defined as failure to image or palpate a tumor that was subsequently found. Sensitivity of the two methods was calculated by dividing true-positive results by the sum of true-positive and false-positive results. Sensitivity percentages were compared statistically by the Fischer's exact test. Size of tumors detected and not detected by IOUS were compared by unpaired t-test.

Results

Forty-four patients entered this study. Thirty-six patients had the diagnosis of ZES and eight patients had the diagnosis of insulinoma. All patients underwent exploratory laparotomy for tumor resection. Five patients (one insulinoma, four ZES) were excluded from this analysis because intraoperative localization procedures produced no suspicious findings and islet cell tumors were not found (Fig. 1). Suspicious lesions were identified by palpation and/or operative ultrasound in 39 patients (32 ZES, seven insulinoma) who formed the basis of the present analysis. Seven insulinomas (proven pathologically) were detected in the seven patients with a clinical diagnosis of insulinoma, and all tumors were within the pancreas. Six patients with ZES who had suspicious lesions by operative ultrasound and/or palpation had no gastrinomas proven pathologically. In 26 patients with ZES, 35 gastrinomas were proven pathologically. In 19 patients with ZES, 23 gastrinomas were found within the pancreas and in 9 patients, 12 gastrinomas were extrapancreatic. Two patients with ZES had gastrinomas both within and outside of the pancreas (Fig. 1).

TABLE 1. *Palpation* versus *IOUS in Localizing Insulinomas and Gastrinomas*

	Insulinoma (7)		Gastrinoma (35)	
	Palpation	IOUS	Palpation	IOUS
True-positive	5	6	33	29
True-negative	0	1	5	3
False-positive	1	0	9	11
False-negative	2	1	2	6
Sensitivity* (%)	71	86	94	83

Values in parentheses are the total no. of tumors proven pathologically.

* Sensitivity of palpation *vs.* IOUS at localizing gastrinomas or insulinomas is not significantly different.

Palpation Versus *IOUS to Localize Islet Cell Tumors*

IOUS correctly identified six of seven insulinomas, while palpation only identified five (Fig. 2, Table 1). One insulinoma was not detected by palpation or IOUS and was found following a blind distal pancreatectomy in a patient with a selective insulin gradient in the distal pancreas detected by PVS. The IOUS appearance of most islet cell tumors typically demonstrated a sonolucent mass lesion with discrete echogenic borders (Fig. 3) as described previously.[8-10] Palpation correctly identified 33 of 35 gastrinomas while IOUS only identified 29 (Table 1, Fig. 2). Both methods were equal (sensitivity) in their ability to localize insulinomas and gastrinomas

TABLE 2. *Palpation* versus *IOUS in Localizing Pancreatic and Extrapancreatic Gastrinomas*

	Pancreatic Gastrinoma (23)		Extrapancreatic Gastrinoma (12)	
	Palpation	IOUS	Palpation	IOUS
True-positive	21	22	12	7
True-negative	5	1	0	2
False-positive	4	8	5	3
False-negative	2	1	0	5
Sensitivity (%)	91	95	100	58*

Values in parentheses are the total no. of tumors proven pathologically.

* Palpation is more sensitive than IOUS at localizing extrapancreatic gastrinomas ($p < 0.01$), but the two methods are equal at localizing pancreatic gastrinomas.

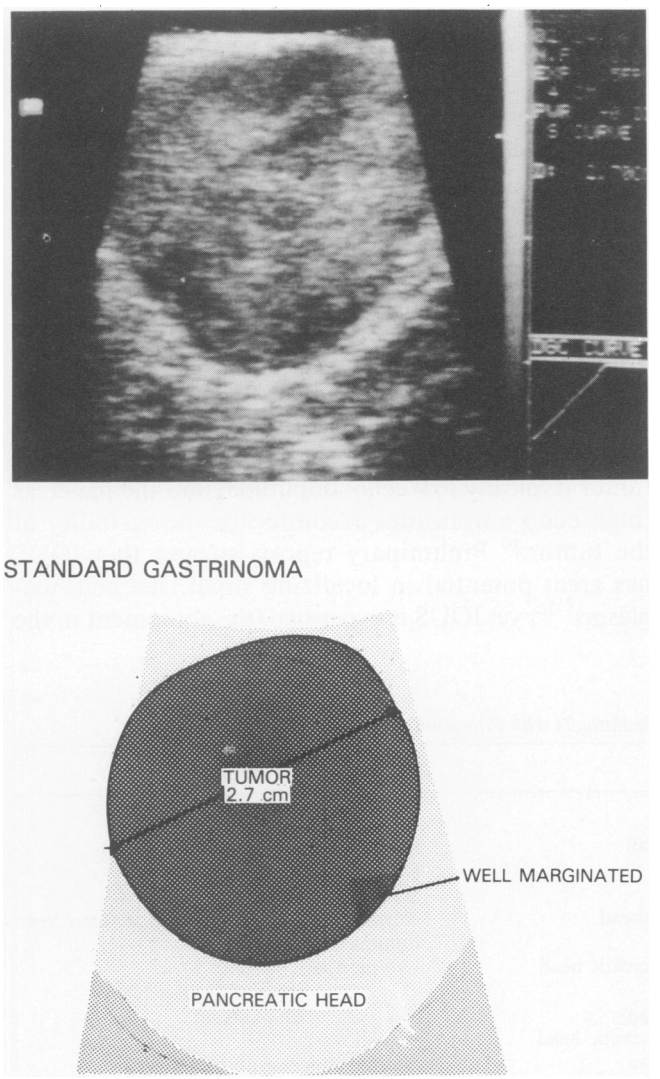

FIG. 3. Operative sonographic appearance of a typical islet cell tumor. The tumor is sonolucent compared to the surrounding pancreas, which is more echogenic. The margin of the tumor and the pancreas is discrete with an echogenic rim around the entire tumor. This appearance is consistent with a benign islet cell neoplasm.

(Table 1). Each method individually was similar to either method alone or both methods together in ability to detect insulinomas or pancreatic gastrinomas (Table 2, Fig. 2). Extrapancreatic gastrinomas were identified better by palpation (12 of 12, sensitivity = 100%) than IOUS (7 of 12, sensitivity = 58%) ($p < 0.01$) (Fig. 2, Table 2).

When one combines the pancreatic gastrinomas and insulinomas, 30 islet cell tumors were found within the pancreas. Palpation had 26 true positive findings and IOUS had 28 (Table 3). Sensitivity for palpation (87%) was again similar to sensitivity for IOUS (93%).

False-positive and False-negative Results

False-positive and false-negative localization occurred with both palpation and IOUS for both insulinomas and gastrinomas (Table 1). Whereas the overall rate of either false-positive or false-negative results for palpation and IOUS was not significantly different (Table 3) ($p > 0.1$), analysis of the false-positive cases (Table 4) or false-negative cases (Table 5) demonstrates a number of important features. The duodenum is a common location for gastrinoma, but it was also a common location for ectopic pancreas (three cases) (Table 4), which was identified as a positive tumor in each case by palpation and in one case by IOUS. A 0.5–1.0 cm mass in the pancreatic head area was identified as a gastrinoma in four cases by IOUS and confirmed in one case by palpation, but was found to be a normal intrapancreatic lymph node in the four patients (Table 4). Normal pancreas, scar tissue from previous ulcer disease, and dilated pancreatic ducts were also sources of false-positives (Table 4).

An analysis of the false-negative responses demonstrates that both the size and location of the gastrinoma were important variables (Table 5). The size of the gastrinomas missed by IOUS was significantly smaller than

TABLE 3. *Palpation* versus *IOUS in to Localizing Intrapancreatic Islet Cell Tumors*

	Intrapancreatic Islet Cell Tumors (gastrinomas and insulinomas) (30)	
	Palpation	IOUS
True-positive	26	28
True-negative	5	2
False-positive	5	8
False-negative	4	2
Sensitivity (%)	87	93*

Value in parentheses is the total no. of tumors proven pathologically.
* There is no significant difference between IOUS and palpation.

the size of the gastrinomas correctly identified (0.4 ± 0.05 *vs.* 1.9 ± 0.4 cm, $p < 0.05$, Table 5). Location was important because extrapancreatic gastrinomas were more frequently missed by IOUS than pancreatic gastrinomas (Table 5). Specifically, 1 of 23 pancreatic gastrinomas and 5 of 12 extrapancreatic gastrinomas were missed by IOUS ($p < 0.01$, Table 5). Of the five extrapancreatic gastrinomas missed by IOUS, all five were in the duodenum (Table 5).

Surgical Impact of IOUS

IOUS affected the intraoperative decision process or the ability to find an islet cell tumor in 5 of 44 patients (11%). In three patients (two ZES, one insulinoma), IOUS correctly suggested a malignant gastrinoma that was not obvious by palpation (patients 1, 2, and 5, Table 6). In these patients IOUS demonstrated indistinct margins of the tumor with extension into adjacent pancreas (Fig. 4) and obliteration of the pancreatic duct (Fig. 5). Pancreatic resections were performed based on IOUS findings (Table 6). In two other patients (patients 3 and 4, Table 6) (one with gastrinoma and one with insulinoma), tumors would not have been identified without IOUS. One patient with occult insulinoma in the pancreatic head, which was identified only by IOUS, had been described in detail previously.[10] The other patient with ZES was similar. Portal venous sampling for gastrin suggested that a gastrinoma was located in the pancreatic head region. Careful operative palpation revealed no tumor and a Whipple pancreaticoduodenectomy was not believed to be a reasonable surgical option. Operative ultrasonography revealed a 1-cm sonolucent mass in the posterior head of the pancreas near the common bile duct. The gastrinoma was enucleated with intraoperative ultrasound guidance, and a pancreatic resection was not done. Follow-up of all five patients indicates that each has no evidence of recurrent islet cell tumor.

Discussion

Although IOUS is a recent addition to surgical practice, it is clear that islet cell tumors of the pancreas can be detected intraoperatively by realtime B-mode ultrasonography.[15] The sonographic appearance of islet cell tumors at operation is identical to that described for these tumors detected by ultrasound preoperatively (Fig. 3).[16] The difference in echogenicity between the tumor (typically low echo amplitude) and the pancreas (high echo amplitude) accounts for the visibility of the tumor.[10] Preliminary reports suggest that IOUS has great potential in localizing small islet cell neoplasms[8-10]; yet IOUS is expensive (the equipment in the

TABLE 4. *False-positive Results for Gastrinoma Patients with Palpation and/or IOUS*

Palpation (N = 10)	IOUS (N = 11)	Pathology
2-cm pancreatic tail nodule	2-cm sonolucent lesion	Normal pancreas (no tumor)
Nodule in pyloric wall	Sonolucent 4-mm nodule pyloric wall	Ectopic pancreas (no tumor)
Nodule in duodenal wall	Negative	Ectopic pancreas (no tumor)
Nodule in jejunal wall	Sonolucent 5-mm nodule	Scar from prior ulcer
Negative	Sonolucent 5-mm lesion pancreatic head	Normal lymph node within pancreatic head
Nodule in duodenal wall	Sonolucent nodule duodenal wall	Lipoma duodenal wall
Nodule in posterior pancreatic head	Sonolucent nodule in posterior pancreatic head	Lymph node
Negative	Sonolucent nodule in pancreatic head	Scar tissue with pancreas
Negative	1-cm sonolucent nodule within pancreatic head	Lymph node
Negative	Sonolucent nodule in pancreatic head	Normal pancreas no tumor seen
Nodule in pancreatic tail	Negative	Normal pancreas
Negative	8-mm sonolucent lesion in pancreatic head	Lymph node
0.5-cm nodule in pancreatic body	Sonolucent lesion in pancreatic body	Dilated ectopic pancreatic duct
Nodule in duodenal wall	Negative	Ectopic pancreas
Nodule body of pancreas	Negative	Normal pancreas

TABLE 5. *IOUS Result as a Function of Gastrinoma Size and Location*

IOUS Result	Gastrinomas Found	Diameter* (cm)	Location					
			Pancreas (N = 23)			Extrapancreatic (N = 12)		
			Head	Body	Tail	Duodenal Wall	Jejunal Wall	Other
Positive	29	1.9 ± .4 (0.4–10.0)	14	3	5	4	2	1 (ovary)
Negative	6	0.4 ± .05† (0.2–0.6)	—	—	1	5	—	—
Total	35	—	14	3	6	9	2	1

* Value for diameter is mean ± SEM; other numbers are total number.

† Significantly less than diameter of positive result ($p < 0.05$).

present study costs $80,000), requires expertise, and adds time to the operation. Until the present study, no prospective evaluation of IOUS compared to traditional operative techniques such as palpation had been done. The present study demonstrates no overall difference between palpation and ultrasound in the ability to intraoperatively localize pancreatic islet cell tumors; however, it demonstrates that in 11% of patients IOUS provides information not provided by palpation that affects surgical management. For localizing extrapancreatic islet cell tumors, palpation is significantly better than IOUS.

The observed equality between palpation and IOUS in the ability to find pancreatic islet cell tumors was unexpected in light of a number of preliminary reports[8–10,15,17] that IOUS might frequently localize islet

TABLE 6. *IOUS Affected Surgical Decision-making or Ability to Find Islet Cell Tumor*

Patient (N = 5) (11%)	Diagnosis	Impression Postpalpation	IOUS Finding	Surgical Procedure	Pathologic Analysis	Follow-up
1	ZES	Well-defined 2-cm tumor pancreatic tail	2-cm tumor with indistinct margins and extension outside pancreatic tail	Distal pancreatectomy splenectomy	Malignant gastrinoma with vascular invasion and extension outside pancreas into fat	Cured at 6 months
2	ZES	Well-defined 2-cm tumor midpancreatic body	Same 2-cm tumor with invasion into pancreas and extension outside pancreas	Subtotal pancreatectomy splenectomy	Malignant gastrinoma with extension into peripancreatic fat and vascular invasion	Cured at 6 months
3	ZES	No tumor palpable	1-cm well-demarcated tumor in posterior pancreatic head near common duct	Enucleation	1-cm gastrinoma from pancreatic head	Cured at 6 months
4	Insulinoma	No tumor palpable	7-mm well-demarcated tumor in pancreatic head	Enucleation	7-mm insulinoma from pancreatic head	Cured at 3 years
5	Insulinoma	Well-defined 1.5-cm tumor midpancreatic body	1.5-cm tumor without distinct margins and extension into adjacent pancreas	Subtotal pancreatectomy splenectomy	2.0-cm insulinoma with vascular invasion and invasion into adjacent pancreas	Cured at 2 years

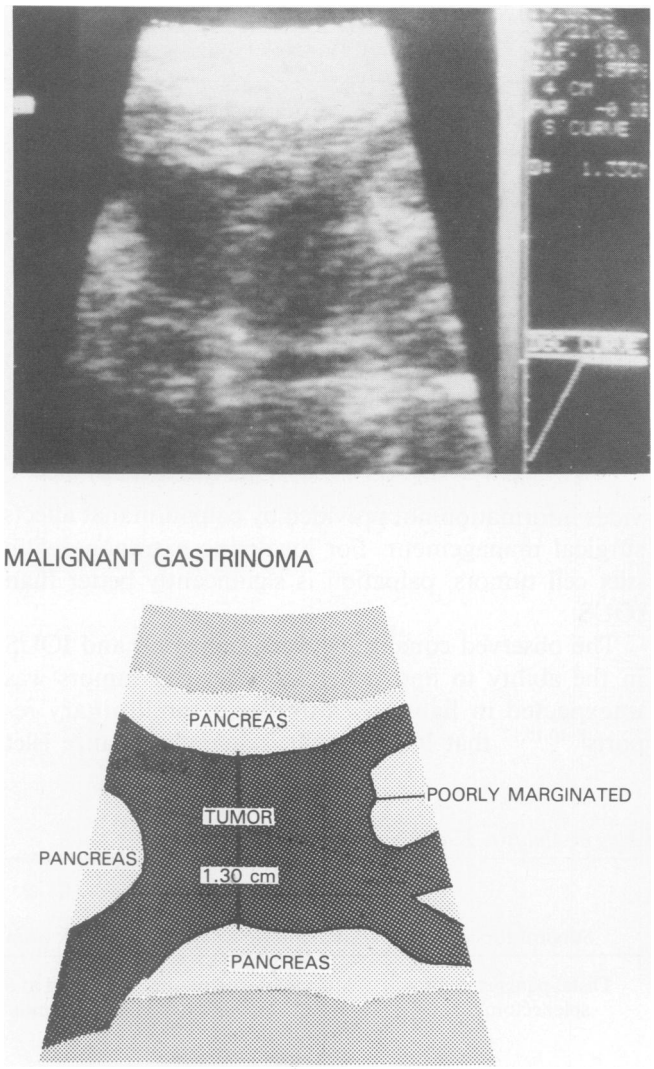

FIG. 4. Operative sonographic appearance of an islet cell tumor that was subsequently resected and proven to have malignant features pathologically. The tumor was sonolucent compared to the echogenic surrounding pancreas, but the border of the tumor was not clearly marginated and there was extension into surrounding pancreas. This sonographic appearance was consistent with a malignant islet cell neoplasm.

cell tumors not identified by palpation. A number of factors could contribute to our results. The difference in our results from those suggested in preliminary reports was unlikely to be due to a difference in expertise or the IOUS equipment used. In the present study, state-of-the-art IOUS equipment with a 10 MHz transducer was used to give the greatest possible resolution, whereas in earlier studies either 5 or 7.5 MHz[9,15] transducers were used. Although a learning curve exists for IOUS, at all operations an untrasonographer with extensive experience with ultrasound identification of islet cell tumors was present.[16] Furthermore, the sensitivity of detecting all pancreatic islet cell tumors in the present study was 93% (Table 3), which agrees closely with the sensitivity of 86% recently reported by another group with considerable expertise with IOUS localization of insulinomas.[17] It could be argued that the extensive preoperative localization studies (imaging studies, PVS), in fact, contributed disproportionally in increasing the sensitivity of palpation, which was 87% in the present study. This cannot be excluded; however, this information was available for both palpation and IOUS and should have affected the result from each procedure equally. Last, it cannot be excluded that in other centers with less experience with islet cell tumors, that IOUS may, in fact, contribute significantly more than found in the present

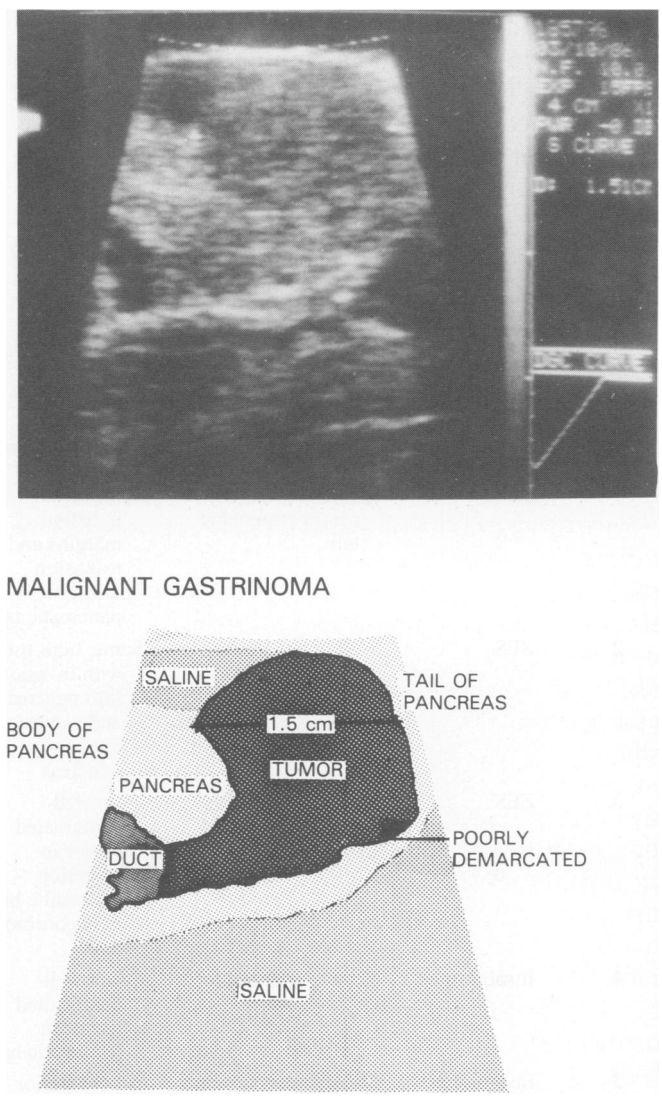

FIG. 5. Operative sonographic appearance of an islet cell tumor that was subsequently resected and proven to have malignant features pathologically. Again, the border of the pancreas and the tumor was not clearly marginated and there was total blockage of the pancreatic duct by direct invasion. This sonographic appearance was consistent with a malignant islet cell neoplasm.

study. In the present study, all patients have extensive exploration with kocherization of the duodenum, complete mobilization of the pancreatic tail, and frequently opening the duodenum even though more than one third have had previous upper abdominal surgery. This is possible because of the ability to control gastric acid hypersecretion at the time of surgery, and this allows for extensive palpation of all areas; whereas in centers with less experience, either because of adhesions from previous surgery or the inability to control hypersecretion of gastric acid, a thorough exploration may not be done, in which case IOUS may be even more valuable. Furthermore, the operating surgeon in the present study has had significant experience recognizing and palpating islet cell tumors that may have contributed to the high sensitivity of palpation.

In a technologic age, it is tempting to discount traditional operative methods like visualization and palpation in favor of expensive high technology equipment that can penetrate into structures in a noninvasive manner. However, our data clearly indicate that there are no significant differences between the two methods in detecting pancreatic islet cell tumors and that cost-effective palpation is significantly better at detecting extrapancreatic tumors. The results suggest that basic time-honored operative techniques such as palpation and visualization should not be replaced by IOUS in the search for islet cell tumors especially ones that are extrapancreatic in location. However, the results also indicate that IOUS does contribute in a fraction of patients, and in fact, is complementary to palpation.

Analysis of the false-negative and false-positive results for both palpation and IOUS provide a number of important insights. Analysis demonstrates that both the size of the islet cell tumor and location are important determinants of the false-negative rate for IOUS. Specifically, IOUS is less likely to detect an extrapancreatic gastrinoma than a pancreatic gastrinoma or insulinoma, whereas there is no difference for palpation. Furthermore, the size of gastrinomas detected with IOUS is significantly different from those not detected. Detection of sonolucent islet cell tumors by IOUS is clearer against a homogeneous echogenic background such as the pancreas than a mixed (gas-liquid-solid) background like the bowel. Small tumors (0.2–0.6 cm) in the duodenum have a higher likelihood of not being imaged, not because the 10 MHz transducer lacks resolution, but because resolution depends on the homogeneity of the background. Because in some series up to 50% of gastrinomas are extrapancreatic,[4,18,19] these results suggest that IOUS may be generally more helpful in localizing insulinomas than gastrinomas. Another difficult region to accurately image is the pancreatic tail because it is difficult to position the transducer under the left costal margin. This technical problem may be solved by mobilizing the tail of the pancreas and the spleen out of the retroperitoneum for examination, or by using a right angle high-resolution transducer (which was not available during this study). However, routine mobilization of the spleen in this manner may increase the risk of splenic injury and splenectomy. Finally, ultrasound detected some nonpalpable small false-positive images in the pancreatic head that appeared as sonolucent mass lesions similar to islet cell tumors. These lesions are normal lymph nodes within the pancreas. False-positives and false-negatives limit the present utility of IOUS and with more observer experience may be partially resolved.

A newly described advantage of IOUS is that it appears to differentiate malignant islet cell tumors from benign tumors. Benign tumors are very well demarcated with distinct hyperechoic borders (Fig. 3). Three tumors had indistinct borders, suggesting invasion into adjacent pancreas and pancreatic duct (Fig. 4 and 5), presumptive signs of malignancy. One tumor (Fig. 5) was small with ductal invasion; thus, size alone does not predict malignant potential. These tumors were resected based on IOUS results, and were found to have malignant features on pathologic analysis. Further instances and observations from other groups will be necessary to see how reliable the ultrasonic appearance of tumors predicts invasiveness and malignancy. Because up to 60–90% of gastrinomas are malignant,[12,19] whereas up to 80–90% of insulinomas are benign,[11] if, in fact, with greater experience it can be verified that IOUS can identify invasiveness, this suggests that IOUS will be more useful with gastrinomas than insulinomas to assess malignancy.

The most important consideration with any new technique is outcome. Operative sonography had clear impact on the final outcome of five patients (11%) in this study. It enabled the surgeon to find and remove two tumors that would not have been found or removed without it. It advised the surgeon to resect (instead of enucleate) three tumors with pathologic evidence of malignant invasion. All five patients in whom IOUS altered the surgical procedure are cured, albeit with short follow-up. The observation that IOUS can improve the ability of an experienced surgeon to find some nonpalpable islet cell tumors and can provide additional valuable information about invasiveness, allows us to make a strong recommendation for its use during explorations for islet cell neoplasms.

This study combined with other reports[17] indicates that IOUS is useful during abdominal explorations for pancreatic islet cell tumors. A sonolucent pancreatic mass imaged by IOUS should not be ignored because in some instances, pancreatic islet cell neoplasms will be

detected that may not be palpable or visible. The appearance of islet cell tumors and their interaction with adjacent pancreas and structures can provide evidence for malignant potential and rational resection.

In conclusion, even though palpation was the single best localization method because of equal sensitivity within the pancreas and better sensitivity outside the pancreas, the present results demonstrate that, in fact, palpation and IOUS are complementary because IOUS detects some tumors that are not palpated and can provide information concerning malignant potential not detected by palpation.

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