INTRAOPERATIVE ULTRASONOGRAPHIC EVALUATION OF INSULINOMAS: AN UPDATE*

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Abstract **The authors review the literature about intraoperative ultrasonography for evaluation of pancreatic insulinomas. Results of intraoperative ultrasound, preoperative ultrasound and computed tomography are discussed, as well as results of inspection and palpation of the pancreas during surgery, reported in the literature.**
Keywords: Insulinoma; Ultrasonography; Intraoperative ultrasonography.

Resumo *Avaliação dos insulinomas pela ultra-sonografia intra-operatória: estado atual do tema.*
Os autores fazem uma revisão da literatura sobre a utilização da ultra-sonografia intra-operatória para a avaliação dos insulinomas pancreáticos. São referidos os resultados da ultra-sonografia intra-operatória, ultra-sonografia e tomografia computadorizada realizadas no pré-operatório, e os resultados da inspeção e palpação do pâncreas realizadas durante procedimentos cirúrgicos referidos na literatura.
Unitermos: Insulinoma; Ultra-sonografia; Ultra-sonografia intra-operatória.

INTRODUCTION

The pancreas is a solid organ and should be easily demonstrated by ultrasonography[(1)]. However, because of its retroperineal localization with anteposition of hollow viscera, the gas present in the viscera may complicate its study by means of ultrasound [(2)].

During abdominal surgeries, the bowel loops can be manually moved apart, and the transducer can be placed directly on the pancreas surface, resulting in an increment of the image quality[(2)].

In this article, the authors review the role of the intraoperative ultrasonography (IOUS) in the evaluation of pancreatic insulinomas, comparing its applicability with that of other methods like ultrasound (US) and computed tomography (CT), as well as establishing a correlation with surgical staging data.

DISCUSSION

Hormone-secreting pancreatic tumors with clinical repercussions are rarely seen. The occurrence of these tumors is estimated in about four to five cases per million inhabitants[(3)]. However, they awake a great clinical interest because of the different syndromes they may produce as a result of their excessive hormone production[(3)]. The treatment of these lesions has caught both clinicians and surgeons´ attention, and, currently, the most appropriate approach is the multidisciplinary one, involving endocrinologists, gastroenterologists, surgeons and oncologists[(3)]. Usually the therapy is aimed at controlling the increased hormone secretion, and the tumor resection afterwards. In case of metastasis, chemotherapy represents an alternative attempt to control the disease[(3)].

In the literature, one may find that endocrine cells of the digestive system are derived from neural crest cells and present common features in relation to biochemical and ultrastructural aspects related to the synthesis of amines and peptides[(3,4)]. These cells are considered as pertaining to the APUD (amine precursor uptake and decarboxilation)[(3)].

It should be reported that there are experimental evidences discussing the origin of the gastroenteropancreatic APUD cells in the neural crest[(5)]. Notwithstanding, in spite of this controversy, the application of the APUD system concept explains the diversity of syndromes associated with endocrine pancreatic tumors[(3)].

The term APUD originates from the three initial letters of the words in English designating three important characteristics of these cells: 1) high amines concentration; 2) amine precursor uptake capacity; 3) presence of an amino acid descarboxylase[(3)]. They are widely distributed in different locations of the organism such us central nervous system, thyroid (parafollicular cells), pancreas, bowel, supra-renal medulla and urogenital tract[(3)].

Tumors originating from APUD cells may be called “apudomas”. Endocrine pancreatic tumors contain APUD system cells and, therefore, may be considered as apudomas[(3)].

At least five types of pancreatic islet cells are found in the normal pancreas. Each type produces a different peptide or

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amine. Beta cells produce insulin, alpha cells produce glucagon; gamma cells, somatostatine; F cells, pancreatic polypeptide; and enterochromafin cells produce serotonine[6].

Insulinomas are the most frequent neuroendocrine pancreatic tumors and usually are of benign nature[7]. Gastrinoma is the second more frequent neuroendocrine pancreatic tumor, and 60% of them, or more, may be of malignant nature[8].

Hormone secreting tumors, like insulinomas, gastrinomas and glucagonomas, may produce identifiable clinical syndromes as a consequence of the excessive hormones production[9]. The presence of these symptoms determines an earlier presentation than the usual presentation of other pancreatic neoplasms. So, usually, these tumors are small, frequently measuring less than 1.5 cm.[9,10].

On the other hand, somatostatinomas and neuroendocrine tumors producing pancreatic polypeptide define the presentation of no or few symptoms, although, at the moment of diagnosis, they may present large dimensions[9].

The insulinomas were the first pancreatic neuroendocrine tumors to be identified, as reported by Whipple & Frantz[11]. The most important finding in cases of insulinomas is the prevalence of high levels of autonomous insulin secretion in the presence of concurrent hypoglycemia. This behavior leads to a diagnosis based on the finding of high fasting (72 hours) levels of plasmatic insulin[12]. Consequently, they cause hypoglycemia and symptoms characteristic of the hypoglycemic syndrome[3]. A wide variety of symptoms may occur, including tremor, flutter, irritability, weakness, hunger, sweating, tachycardia and, occasionally, nauseas and emesis. Additionally, behavioral and consciousness disturbances may occur[3]. More severe cases may progress to unconsciousness and coma as a result of hypoglycemia[3]. As a result of these behavioral disturbances, about 20% of patients are initially misdiagnosed with psychiatric or neurological disorders[13].

Insulinomas may occur at any age range, but the greatest majority occurs between 30 and 60 years of age[14]. Similarly, Machado *et al*.[15] report a casuistic with 54.2% of patients in this age range, with 94.8% with less than 60 years[15,16].

As regards sex, insulinomas would have a slight incidence in females[16–18]. Other authors, like Norton *et al*.[19], have observed an even higher (about 83%) incidence in females.

Most of insulinomas are benign and small, and in 80%-90% of cases are solitary lesions[3]. Comi *et al*.[20] also report that insulinomas usually are intrapancreatic (about 100%) and small (less than 2 cm). Others report benign insulinomas with less than 1.5 cm in 70% of cases[10]. Approximately 10% of insulinomas are malignant and present with metastasis at the moment of diagnosis[3,21].

Multiple and benign lesions may occur in about 10% of cases, and are more frequent in patients with MEN type I syndrome (multiple endocrine neoplasm)[3]. Some authors, like Welbourn *et al*.[22], report that the number of patients with MEN type 1 would correspond to 5% of all the patients with insulinomas.

Benign insulinomas have no predilection to a specific site within the pancreas[19], and have been usually identified with the same frequency in different portions of the pancreas: head (30%), body (35%) and tail (35%)[3].

The tumors may be on the surface of the gland or within the pancreatic parenchyma[3]. The majority of lesions is covered by a layer of pancreatic parenchyma and is typically firmer than the normal pancreas[3].

As regards patients with MEN-1, Demeure *et al*.[23] report the significance of a careful evaluation of these patients, considering the higher possibility of malignancy (about 20%) when compared with non-MEN-1-related sporadic insulinomas (malignancy in about 10% of cases). They have observed that in patients with MEN-1 insulinomas were multiple in 76% of cases.

Machado *et al*.[16] have described cases where multiple insulinomas in patients with MEN-1 were localized in the pancreatic body and tail in 87%. In this study, the patients underwent left pancreatectomy (caudal body) associated with enucleation in cases of concurrent cephalic lesions. This surgical alternative had already been previously proposed with excellent results[24–26].

At US, insulinomas, in 90% of cases are small, well-defined, round, homogeneous and hypoechogenic lesions[9,10] (Figures 1, 2, 3, 4 and 5). The pancreatic tail presents a special difficulty for insulinomas localization[9]. Calcifications, configured as areas of higher echogenicity may, occasionally, be identified [9].

Norton *et al*.[19] and Lo *et al*.[7] have observed that insulinomas may be of difficult localization due their small dimensions, and their correct identification, both preoperatively and during the surgical procedure is of paramount importance for their therapeutic management[19].

Machado *et al*.[16] have described the IOUS as an extremely useful method for insulinomas management, routinely utilized by the authors for allowing an adequate localization of lesions, with a correct definition of the pancreatic anatomy and for avoiding extensive pancreatic resections, besides identifying small-sized lesions usually missed by preoperative examinations.

Machado *et al*.[16] have also observed that, notwithstanding the progress of diagnostic methods during the latest years, the identification of insulinomas remains a difficult clinical problem both for clinicians and surgeons.

According to Norton *et al*.[19] the main advantages of the IOUS for the treatment of benign insulinomas include: precise operative localization; enucleation of nonpalpable, nonvisible tumors; and avoidance of ductal and vascular injuries as well as injuries to other vital structures by precise localization of adjacent vital structures. These authors have observed that the IOUS is capable of accurately identifying insulinomas in a higher number than those identified by palpation.

Norton *et al*.[19] have described a benign insulinoma presenting at IOUS as typically hypoechoic and well-defined lesions in relation to the adjacent pancreatic parenchyma. Notwithstanding, these authors have described a case of an insulinoma appearing to have an echogenicity pattern similar to the surrounding pancreas, thus making it difficult to visualize. On the other hand, even this isoechogenic tumor presented a sonolucent peripheral rim that allowed it to be successfully visualized.

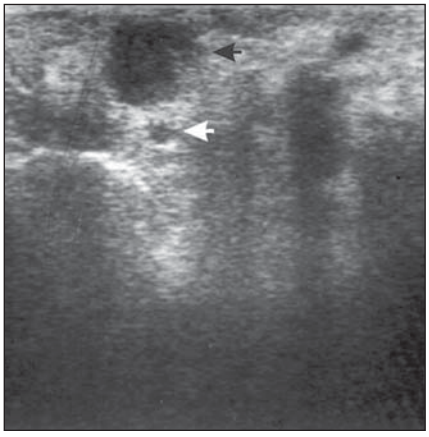

Figure 1. Hypoechogenic nodules (insulinomas) with 1.5 cm (black arrow) and 0.3 cm (white arrow).

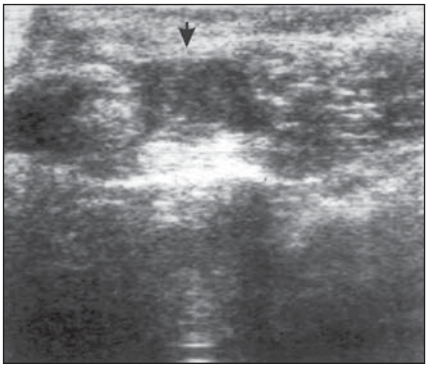

Figure 2. Hypoechogenic nodule (insulinoma) with 1.5 cm (arrow).

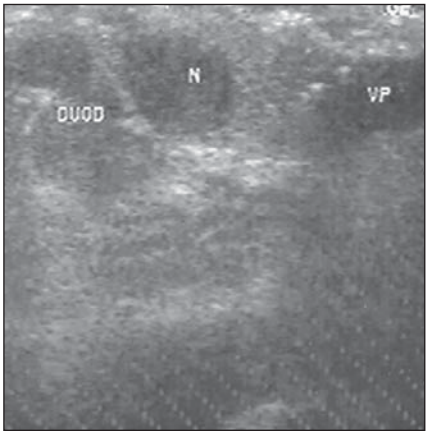

Figure 3. Hypoechogenic nodule (insulinoma) with 0.6 cm. (N, insulinoma; DUOD, duodenum; VP, portal vein).

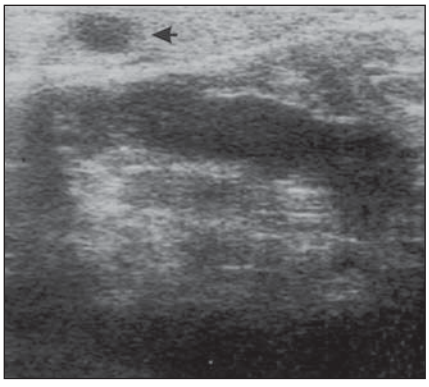

Figure 4. Hypoechogenic nodule (insulinoma) with 0.4 cm (arrow) localized in the pancreatic tail.

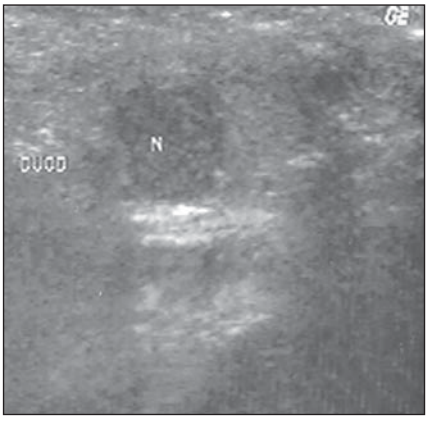

Figure 5. Hypoechogenic nodule (insulinoma) with 0.5 cm (N, insulinoma; DUOD, duodenum).

These authors have reaffirmed that the pancreas evaluation should be precisely performed, with perpendicular and oblique insonation of pancreatic regions in order to maximizing the US scanning results, identifying pancreatic insulinomas. This careful and systematic evaluation allows the visualization of lesions with high diagnostic difficulty, as it can be observed in this case of an isoechogenic insulinoma reported by the authors[19].

Norton *et al*.[19] have also demonstrated that IOUS has affected the surgical procedure, facilitating the excision of occult insulinomas, and in about 41% of cases the IOUS has allowed enucleation of cephalic insulinomas which could not be removed except by means of higher morbidity methods like duodenopancreatectomy. In these 41% of cases reported by the authors, IOUS has defined the incision, determining the most direct and shorter route to the tumor, without traversing the pancreatic duct or other vascular structures. Also, according these authors, after the surgical incision, the shortest route was continually reconfirmed by IOUS up to the complete enucleation of the lesion.

Doherty *et al*.[27], in a study with 25 patients, have concluded that IOUS was particularly useful for identifying cephalic pancreatic tumors detected in all the cases, and for definition of the relationship between the tumor and the pancreatic duct in the 25 patients evaluated. Additionally, IOUS was utilized to guide the dissection during enucleation both in cases of palpable and nonpalpable lesions. Also, they have affirmed that the higher significance of the IOUS is not in the fact of identifying lesions, but rather in the utility of this information for the success of the surgical procedure. Grant *et al*.[10] have corroborated such IOUS relevance, demonstrating its influence on the surgical conduct in 62% of the patients with insulinoma, also for the finding of nonpalpable lesions in the head of the pancreas in four of 29 patients.

In any of the surgical alternatives available for approaching insulinomas, it is defined that IOUS is of paramount significance for the evaluation of the pancreatic parenchyma, since it may guide the characterization of the pancreatic ducts and vascular structures[28], resulting in reliable anatomical information for definition of the surgical strategy.

It is very important to highlight that the major breakthrough in the localization of occult insulinomas is the use of IOUS. Some authors have reported their concern related to the results of the blind resection, a method until recently utilized. According to Norton *et al*.[19], in cases where insulinomas could not be identified, blind (distal, subtotal or even total) pancreatectomy would be performed with high morbidity, possibly resulting in pancreatitis, pancreatic fistulas, pancreatic abscesses and even progress to exocrine pancreatic failure and diabetes mellitus. On the other hand, Kaplan *et al*.[29] also have observed that blind distal pancreatic resections (caudal bodies) would have a 33% chance of not removing the insulinoma because some occult insulinomas will be in the pancreatic head. Norton *et al*.[19], reported a casuistic with 45% of cephalic insulinomas which would have not been successfully removed by blind distal pancreatectomy.

All of these difficulties were resolved with the utilization of IOUS to identify occult insulinomas, probably in association with a careful palpation of the pancreas.

Demeure *et al*.[23] reported the possibility of demonstrating malignant and ectopic extrapancreatic insulinomas. Extrapancreatic insulinomas would occur in less than 1% cases.

Brazilian and foreign authors concern in searching for a more accurate method for identifying pancreatic insulinomas is a result of the poor diagnostic capacity of preoperative examinations (US and CT) when compared with IOUS[10,16,27,30–34]. Many series report varied frequencies of preoperative US detection rates for insulinomas of 0%[32], 26%[27], 28.1%[16], 29.5%[33], 59%[10] and 62%[31]. Preoperative CT detection rates also vary, with some authors identifying low rates like those reported by Doherty *et al*.[27], of 17%. Machado *et al*.[16] have reported rates of about 25% and Grant *et al*.[10], of 36%. However, other studies report higher values, like those of Stark *et al*.[30], ranging between 50% and 60%.

As regards palpation, Kuzin *et al*.[33] have reported a 90% detection rate with this procedure. The precise localization of insulinomas by inspection/palpation depends on the surgeon experience. Doherty *et al*.[27] have identified 64% of insulinomas by means of palpation. Machado *et al*.[16] have reported the detection of 98.2% of cases by means of inspection/palpation, a result similar to those of other authors[35–37].

The literature review demonstrates that smaller the lesions to be evaluated, the greater will be the limitations of preoperative examinations. For insulinomas < 1.00 cm , authors[33] have demonstrated IOUS detection rate of about 10%, and 20% for preoperative CT. Kuzin *et al*.[33], considering only < 1.00 cm insulinomas, have reported a 82% detection rate with palpation.

In a recent study, Machado *et al*.[16], showed that IOUS, in association with palpation, allows a precise localization of in 100% of cases, as previously reported in the literature by authors like Van Heerden *et al*.[38] and Kisker *et al*.[37].

The clinicians and surgeons´ confidence in the IOUS capacity of identifying pancreatic insulinomas has been publicized in several recent publications[16,34].

As a matter of fact, Machado *et al*.[16] have affirmed that patients with a confirmed diagnosis for hyperinsulinism could be evaluated exclusively with conventional abdominal US associated with inspection/palpation during the surgery for insulinomas resection in association with IOUS, virtually succeeding in all the cases. Later complications, like diabetes, could be avoided by preserving a larger amount of pancreatic tissue.

Zeiger *et al*.[39] have confirmed that IOUS is an unique and safe method for assisting in the localization of insulinomas and is supplementary and additional to the other diagnostic methods. As a result of the practice, the IOUS may reduce the use of other imaging methods, influence the decision making and the surgical conduct, allowing a complete resection of the primary pancreatic lesion and even the resection of possible associated metastases.

It is important to mention that some of our studies have been developed with the first publications in 1997, evidencing the applicability of the vídeolaparoscopic intraoperative ultrasound or conventional (non-videolaparoscopic) IOUS (with an open abdominal cavity – laparotomy) in the hepatobiliarypancreatic surgical procedures[40–49].

CONCLUSIONS

The authors conclude that IOUS presents higher accuracy for identification of insulinomas when compared with other methods of preoperative staging, proving to be of high value during surgeries, effectively supplementing the surgical staging (palpation) itself.

REFERENCES

1. Francisco Neto MJ, Machado MM, Oliveira IRS, Cerri GG. Pâncreas. *In:* Cerri GG, Oliveira IRS, editores. Ultra-sonografia abdominal. São Paulo: Sarvier, 2002;261–294.
2. Luck AJ, Maddern GJ. Intraoperative abdominal ultrasonography. Br J Surg 1999;86:5–16.
3. Ellison EC, Wise SR, Johnson JA. Endocrine tumors of the pancreas. *In:* Moody FG, editor. Surgical treatment of digestive disease. 2nd ed. Chicago: Year Book Med Publ, 1990;545–598.
4. Welbourne RB, Polak JM, Bloom SR. Apudomas of the pancreas. *In:* Bloom SR, editor. Gut hormones. Edinburgh: Churchill Livingstone, 1978; 561–569.
5. Andrew A, Kramer B, Rawdon BB. Gut and pancreatic amine precursor uptake and decarboxylation cells are not neural crest derivatives. Gastroenterology 1983;84:429–431.
6. Kloppel G, Maillet B. Classification and staging of pancreatic nonendocrine tumors. Radiol Clin North Am 1989;27:105–119.
7. Lo CY, van Heerden JA, Thompson GB, Grant CS, Soreide JA, Harmsen WS. Islet cell carcinoma of the pancreas. World J Surg 1996;20:878–884.
8. Kisker O, Bastian D, Bartsch D, Nies C, Rothmund M. Localization, malignant potential, and surgical management of gastrinomas. World J Surg 1998;22:651–658.
9. Cosgrove DO. The pancreas. *In:* Meire H, Cosgrove DO, Dewbury K, Farrant P, editors. Abdominal and general ultrasound. 2nd ed. London: Churchill Livingstone, 2001;349–378.
10. Grant CS, van Heerden J, Charboneau JW, James EM, Reading CC. Insulinoma. The value of intraoperative ultrasonography. Arch Surg 1988; 123:843–848.
11. Whipple AO, Frantz VK. Adenoma of islet cells with hyperinsulinism. Ann Surg 1935;101:1299–1335.
12. Fajans SS, Vinik AI. Insulin-producing islet cell tumors. Endocrinol Metab Clin North Am 1980; 18:45–74.
13. Powers RD, Robb JF. Hypoglycemia due to insulinoma. An unusual cause of altered mental status in a young man. Minn Med 1983;66:13–15.
14. Galbut DL, Markowitz AM. Insulinoma: diagnosis, surgical management and long-term follow-up. Am J Surg 1980;139:682–690.
15. Machado MCC, Jukemura J, Monteiro da Cunha JE, *et al*. Tratamento cirúrgico dos insulinomas. Estudo de 59 casos. Rev Ass Med Brasil 1998;44: 159–166.
16. Machado MCC, Cunha JEM, Jukemura J, *et al*. Insulinoma: diagnostic strategies and surgical treatment. A 22–year experience. Hepatogastroenterology 2001;48:854–858.
17. Stefanini P, Carboni M, Patrassi N, Basoli A. Beta-islet cell tumors of the pancreas: results of a study on 1067 cases. Surgery 1974;75:597–609.
18. Service FJ, McMahon MM, O'Brien PC, Ballard DJ. Functioning insulinoma – incidence, recurrence, and long-term survival of patients: a 60-year study. Mayo Clin Proc 1991;66:711–719.
19. Norton JA, Shawker TH, Doppman JL, *et al*. Localization and surgical treatment of occult insulinomas. Ann Surg 1990;212:615–620.
20. Comi RJ, Gorden P, Doppman JL, Norton JA. Insulinoma. *In:* Go VLW, editor. The exocrine pancreas: biology, pathobiology and diseases. New York: Raven Press, 1986;745–761.
21. Reber HA, Way LW. Pancreas. *In:* Way LW, editor. Current surgical diagnosis & treatment. Connecticut: Appleton & Lange, 1994;345–359.
22. Welbourne RB, Wood SM, Polak JM, Bloom SR. Pancreatic endocrine tumors. *In:* Bloom SR, editor. Gut hormones. New York: Churchill Livingstone, 1981;547–554.
23. Demeure MJ, Klonoff DC, Karam JH, Duh QY, Clark OH. Insulinomas associated with multiple endocrine neoplasia type I: the need for a different surgical approach. Surgery 1991;110:998–1005.
24. Rasbach DA, van Heerden JA, Telander RL, Grant CS, Carney JA. Surgical management of hyperinsulinism in the multiple endocrine neopla-

sia type I syndrome. Arch Surg 1985;120:584–589.
25. Skogseid B, Grama D, Rastad J, *et al*. Operative tumour yield obviates preoperative pancreatic tumour localization in multiple endocrine neoplasia type 1. J Intern Med 1995;238:281–288.
26. Thompson NW. The surgical management of hyperparathyroidism and endocrine disease of the pancreas in the multiple endocrine neoplasia type 1 patient. J Intern Med 1995;238:269–280.
27. Doherty GM, Doppman JL, Shawker TH, *et al*. Results of a prospective strategy to diagnose, localize, and resect insulinomas. Surgery 1991;110: 989–997.
28. Deixonne B, Lopez FM. Operative ultrasonography during hepatobiliary and pancreatic surgery. Berlin: Springer, 1988.
29. Kaplan EL, Arganini M, Kang SJ. Diagnosis and treatment of hypoglycemic disorders. Surg Clin North Am 1987;67:395–410.
30. Stark DD, Moss AA, Goldberg HI, Deveney CW, Way L. Computed tomography and nuclear magnetic resonance imaging of pancreatic islet cell tumors. Surgery 1983;94:1024–1027.
31. Bottger TC, Weber W, Beyer J, Junginger T. Value of tumor localization in patients with insulinoma. World J Surg 1990;14:107–114.
32. Vinik AI, Delbridge L, Moattari R, Cho K, Thompson N. Transhepatic portal vein catheterization for localization of insulinomas: a ten-year experience. Surgery 1991;109:1–11.
33. Kuzin NM, Egorov AV, Kondrashin SA, Lotov AN, Kuznetzov NS, Majorova JB. Preoperative and intraoperative topographic diagnosis of insulinomas. World J Surg 1998;22:593–598.
34. Machado MM. Ultra-sonografia intra-operatória (USIO) (Editorial). Radiol Bras 2001;34:V–VI.
35. Galiber AK, Reading CC, Charboneau JW, *et al*. Localization of pancreatic insulinoma: comparison of pre- and intraoperative US with CT and angiography. Radiology 1988;166:405–408.
36. Menegaux F, Schmitt G, Mercadier M, Chigot JP. Pancreatic insulinomas. Am J Surg 1993;165: 243–248.
37. Kisker O, Bastian D, Frank M, Rothmund M. Diagnostic localization of insulinomas. Experience with 25 patients with solitary tumors. Med Klin 1996;91:349–354.
38. van Heerden JA, Grant CS, Czako PF, Service FJ, Charboneau JW. Occult functioning insulinomas: which localizing studies are indicated? Surgery 1992;112:1010–1015.
39. Zeiger MA, Shawker TH, Norton JA. Use of intraoperative ultrasonography to localize islet cell tumors. World J Surg 1993;17:448–454.
40. Paula AL, Machado MM, Mota O, *et al*. Detecção de metástases hepáticas em tumores de cólon e reto com a utilização da ultra-sonografia intra-operatória vídeo-laparoscópica (IOUS-LAPA). Rev Bras Coloproc 1997;17 (Supl 1):30.
41. Paula AL, Machado MM, Mota O, *et al*. Metodização e racionalidade do emprego da ultra-sonografia intra-operatória vídeo-laparoscópica (IOUS-LAPA) na avaliação de metástases hepáticas de tumores colorretais. Rev Bras Coloproc 1997;17(Supl 1):67.
42. Machado MM, Paula AL, Mota O, *et al*. Ultrasonografia intra-operatória vídeo-laparoscópica. Estudo de sua evolução técnica e análise crítica de sua aplicabilidade em coloproctologia. Rev Bras Coloproc 1997;17 (Supl 1):67.
43. Machado MM, Cerri GG. Proposta de metodização da ultra-sonografia intra-operatória vídeo-laparoscópica (USIO-LAPA) no estadiamento do fígado em pacientes portadores de neoplasia gastrointestinal. Radiol Bras 1998;31:375–377.
44. Machado MM, Oliveira IRS, Cerri GG. Considerações sobre a evolução técnica dos transdutores na ultra-sonografia intra-operatória vídeo-laparoscópica (USIO-LAPA). Radiol Bras 1999;32: 85–87.
45. Machado MM, Cerri GG, Oliveira IRS, *et al*. Contribuição da ultra-sonografia intra-operatória (USIO) no estudo de pequenas imagens nodulares hipoatenuantes identificadas à tomografia computadorizada (TC) no exame pré-operatório de pacientes com adenocarcinoma colorretal e de pâncreas. Comunicação original. Radiol Bras 1999;32:255–258.
46. Machado MM, Rosa ACF, Barros N, Machado MCC, Cerri GG. Ultra-sonografia intra-operatória (USIO) do pâncreas e das vias biliares. Radiol Bras 2002;35:105–108.
47. Machado MM, Rosa ACF, Cerri GG. Ultra-sonografia intra-operatória (USIO). *In:* Cerri GG, Oliveira IRS, editores. Ultra-sonografia abdominal. Rio de Janeiro: Revinter, 2002;573–584.
48. Machado MM. Contribuição da ultra-sonografia intra-operatória (USIO) no estudo do fígado em pacientes candidatos à ressecção hepática por metástase de adenocarcinoma colorretal. (Tese de Doutorado). São Paulo: Universidade de São Paulo, 2002.
49. Rosa ACF. Contribuição da ultra-sonografia intra-operatória (USIO) no estudo dos insulinomas pancreáticos. (Tese de Doutorado). São Paulo: Universidade de São Paulo, 2004.