

INTRAOPERATIVE ULTRASOUND OF THE LIVER

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RESUME: Intraoperative ultrasound has become an essential tool for the surgeon in the field of hepatobiliary surgery. No preoperative study has been able to duplicate the sensitivity and specificity of intraoperative ultrasound (IOUS) in the identification of occult lesions. With recent improvements in technology, IOUS has now become an indispensable means of defining the extent of disease and respectability, and providing a guide to anatomic and nonanatomic hepatic resections and minimally invasive and percutaneous ablative techniques. The contrast-enhanced intraoperative ultrasound (CE-IOUS) makes IOUS more accurate, thus enhancing the impact of this technique on operative decision-making for liver tumors. The concept of intraoperative ultrasound (IOUS) was first introduced in the mid-1960s and was used primarily in evaluating choledocholithiasis. More advanced applications were not pursued until the early 1980s, secondary to the limitations of ultrasound technology, which involved large bulky transducers and a relatively poor image quality [1]. Presently, IOUS is a mainstay in all oncologic hepatobiliary procedures. Despite all of these technical advances, preoperative detection of preoperative liver lesions remains 60% to 80%. As a reflection of these shortcomings, false negative rates with CT and MRI range from 40% to 70% Table 1 summarizes these findings, the significance of which are demonstrated by several groups citing that in 27% to 49% of cases the operative plan will be changed based on new IOUS findings. These conclusions hold true even in the modern era of advanced preoperative staging. As a result, IOUS has now become a standard part of almost allhepatobiliary cases.

An understanding of normal ultrasound anatomy is essential in performing IOUS because it enables the surgeon to plan segmental resection and define resectability. (Table 1) On rare occasions, the three veins enter the inferior vena cava as a single trunk; more often, the right hepatic vein enters the cava separately while the middle and left form a single trunk or enter separately. Other occasional variants include a separate right superior hepatic vein that drains the upper portion of the liver bound by the coronary ligament, or an accessory inferior right hepatic vein that drains into the cava 2 to 3 cm distal to the hepatic vein confluence. On occasion the portal vein may be ventral to the hepatic artery, duplicated, congenitally absent, or branch intrahepatically.

ULTRASOUND SIGNS OF HEPATIC TUMORS

Tumors are best characterized as being an-, hyper-, or hypoechoic when compared with normal hepatic parenchyma (Table 1).

Table 1

Hypoechoic lesions	Hyperechoic lesions	Anechoic lesions
Hepatocellular carcinoma	Most commonly benign	Biliary cyst
Metastases of extra-abdominal origin	Gastrointestinal metastases	Hydatid cysts
Hyperplastic nodule	Hepatocellular carcinoma	
Regenerative nodule	Hemangioma	
Adenomatous hyperplasia	Fatty metamorphosis	
Small cysts		
Areas without fatty infiltration in a fatty liver		

TECHNICAL ASPECTS OF INTRAOPERATIVE ULTRASOUND

A complete evaluation of the liver can be performed through most incisions and with minimal mobilization of the liver. There are a variety of IOUS systems available. It is also possible to use standard transabdominal equipment, but it has limitations in resolution, the near field of view, and the bulkiness of the probe [1]. IOUS is best performed using a real-time B-mode electronic scanner system with a 5-MHz or 7.5-MHz side-fire T-shaped linear array probe or a convex-array end-fire probe. Either probe can be cradled in the palm of the hand and directly applied to the surface of the liver without gel or acoustic coupling agent. The convex probe reaches all areas of the liver even if full mobilization has not been performed, and allows greater visualization of the deep liver as compared with the linear array. Regardless of the type of system used, a methodical, systematic approach must be used in all cases. The use of overlapping fields is essential to assess completely the entire liver. We scan the liver with overlapping fields from the dome to the caudal edge, proceeding from left to right through the entire organ in a sequential manner. Scanning at a frequency of 5 MHz allows a depth of penetration of up to 10 to 12 cm, while the 7.5-MHz probe provides a shallower depth of penetration. For deeper lesions, the probe can be placed on the posterior surface of the liver. During the entire survey, the transducer is palmed in the hand of the surgeon such that it never loses contact with the surface of the liver and the surgeon is able to maintain tactile sense of location and prevent skipping areas. To ensure thorough examination of the liver parenchyma, a systematic approach based on the intrahepatic vascular anatomy is mandatory. This examination is broken into four steps, with each stage sharing three objectives: (1) identify tumors, (2) identify tumor thrombi and vascular invasion, and (3) define the relation of these lesions with respect to the vascular anatomy. The examination starts with identifying the hepatic veins as they arise from the inferior vena cava and following each vein out to its peripheral tributary branches (Fig. 2). The next step is to identify the left portal pedical to segments 2, 3, and 4 (Fig. 3) and the right portal pedicles to segments 5, 6, 7, and 8 (Fig. 4). Finally, the porta hepatis is evaluated.

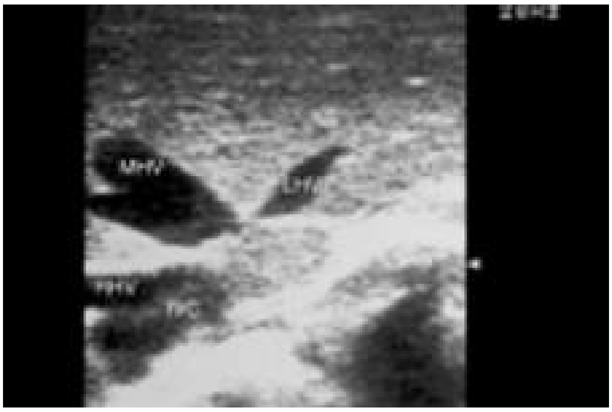

Fig. 1. Ultrasonograpic view of the confluence of the right (RHV), middle (MHV) and left (LHV) hepatic veins with the inferior vena cava (IVC).

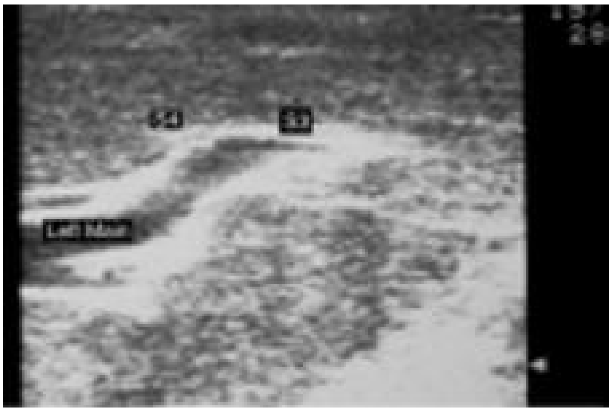

Fig. 2. Ultrasonographic view of the left portal vessel (left main) and its branches to the Couinaud segments 3 (S3) and 4 (S4).

By adhering to this regimen, a thorough examination of the entire liver will be accomplished. With intraoperative Doppler and color flow studies, one is able to differentiate dilated bile ducts from adjacent vascular structures during the survey. This technology can identify smaller thrombi that are frequently missed by preoperative studies [1]. If a lesion is encountered, it should be examined in both transverse and longitudinal directions to determine its full extent. Its proximity and extension to neighboring vessels should be determined, as well as the best ''window'' to visualize the lesion. Such windows are useful for guidance of ablative techniques and biopsy instruments. Careful inspection of the lesion will also help differentiate malignant lesions from nonmalignant lesions. Nonmalignant lesions are typically soft, and will be deformable visually by palpation and compression when using a bimanual technique. Particular care should be given to the detection of superficial lesions that may be missed with a 5-MHz probe because of near-field artifacts in the first 1 cm of the image. Use of higher frequency probes (7.5–10 MHz) may help compensate for this; another approach, however, is to examine the superficial surface of the dome and anterior liver surface by placing the probe posteriorly, increasing the depth of penetration, and performing a complete examination using overlapping fields. An additional method would be to place the probe in a sterile glove filled with saline to serve as a water standoff. Subcapsular lesions may still be difficult to image, but in most cases they are palpable and easily biopsied, making excessive attempts of imaging unnecessary [1].

APPLICATIONS OF INTRAOPERATIVE ULTRASOUND

Assessment of tumor burden and localization of occult lesions The wide acceptance of IOUS in hepatobiliary surgery is based on its sensitivity in identifying lesions and defining their relation to vital intrahepatic structures. Despite adequate imaging preoperatively, localization of lesions intraoperatively may be difficult in identifying HCC lesions and in cases of recurrences or in previously resected livers [1,2]. A review of 154 hepatic lesions at Deaconess Hospital revealed that 51 of these lesions were identified intraoperatively [1]. Of these 51 lesions, 65% were detected by ultrasound alone. More specific reviews have demonstrated that nearly 30% of HCC lesions are nonpalpable and that 10% to 40% of colorectal carcinoma metastases will not be palpable. In 51% of these cases, the planned procedure may be changed due to IOUS findings. An additional review by Brower and colleagues reveals that the sensitivity, specificity, and accuracy of IOUS (78%, 100%, and 84%, respectively) are superior to those of arteriography, CT, preoperative ultrasound, and palpation. In this review, 15% to 25% of surgical plans were modified based on IOUS findings in both HCC and colorectal metastases cases [4]. Clarke and colleagues have demonstrated that IOUS has detected an additional 25% to 35% of hepatic lesions while performing resection and staging of colorectal carcinomas. In a series of 250 patients, Machi and colleagues demonstrated that the overall accuracy of IOUS was 94.2% compared with 73%, 75%, and 80% of preoperative ultrasound, preoperative CT scan, and surgical exploration, respectively. Similar superior results were seen for IOUS when considering sensitivity, specificity, and positive and negative predictive values. In a review of 12 studies by Kolecki and colleagues, the detection rate of occult metastases by IOUS alone ranged from 3.5% to 14%. These findings have led some investigators to include IOUS of the liver as a standard procedure during the primary resection of colorectal carcinomas. In a series of 58 patients by Stone and colleagues, occult metastases were found in 5% of all patients undergoing primary colorectal resections. This yield was increased to 10% if limited to T3 and T4 lesions. The false-negative findings were 13% overall, 0% in T1 and T2 lesions, and 7% in T3 N0 lesions. While some groups have demonstrated conflicting results, a reduction in hepatic recurrence to 7% from the expected 20% has been noted using IOUS at the time of primary resection. These data suggest that the routine use of IOUS may improve the therapeutic impact of hepatic resection in these patients, and that proper patient selection may improve overall yield.

EVALUATION OF INTRAHEPATIC VASCULATURE

Following the identification of occult lesions, IOUS can evaluate intrahepatic vessel patency, the presence of tumor thrombus, and tumor invasion. The proximity and extension of tumor into the hepatic veins, inferior vena cava, and the portal venous system influence the type and extent of resection performed. These considerations are crucial in patients with HCC because it spreads principally by way of the portal venous branches supplying the tumor. Therefore, tumor thrombi may propagate and give rise to ‘‘daughter lesions.’’ Radical resection in these cases must include the entire portal region supplying the tumor. This is often difficult to ascertain clinically in the cirrhotic liver because of changes in topography, and is facilitated by the use of IOUS Intravascular tumor thrombus has been found in as many as 20% of cases of HCC. These findings are often missed by preoperative studies. Guidance of intraoperative and percutaneous radiofrequency ablation and other ablative techniques Local tumor ablative techniques were developed as an alternative treatment for unresectable lesions. These techniques include ethanol injection, cryoablation, interstitial photocoagulation, and microwave tumor coagulation. The most recent technique, radiofrequency ablation, destroys tumors by generating heat within the lesion. The application of this technology was first described in 1911. Radiofrequency ablation has now become the method of choice for ablative therapy at most centers, and would not be possible for nonpalpable lesions without the use of IOUS. IOUS also provides a reliable means of obtaining pretreatment size of lesions to determine if they can be ablated and gives a sense of the extent of ablation performed posttreatment. Lesions are routinely identified using IOUS, the ablation probe is positioned under direct visualization of the ultrasound probe, and ablation is performed under direct visualization of the ultrasound probe. Once a cycle of ablation is completed, the lesion is then reaccessed to determine adequate kill and the absence of grossly viable tumor.

BILIARY DISEASE

Intraoperative US is used to image extrahepatic bile duct abnormalities, including retained stones, and to locate cystic duct insertion sites. In addition, many intrahepatic biliary abnormalities occur that can be thoroughly evaluated with US (6). Intraoperative US may be performed to define ductal anatomy and to locate the site of confluence of the right and left hepatic ducts in patients with resectable cholangiocarcinoma; to locate and characterize bile duct strictures; and to define the extent of segmental involvement in patients with chronic inflammatory changes, Caroli disease, or recurrent pyogenic cholangiohepatitis. Color Doppler imaging is used to distinguish dilated ducts from vessels and intrabiliary sludge from tumors. Chronic inflammatory changes of the gallbladder and bile ducts are difficult to distinguish from malignancies with the use of intraoperative US, but the modality nonetheless plays a particularly useful role in guiding resection. Most commonly, it is used to exclude metastases in patients who are undergoing a trisegmental resection for treatment of cholangiocarcinoma. The common bile duct can be fully evaluated in 97% of cases (Level II).4,5 For identifying choledocholithiasis, the sensitivity is 90%-96% and specificity 100% (Level II).

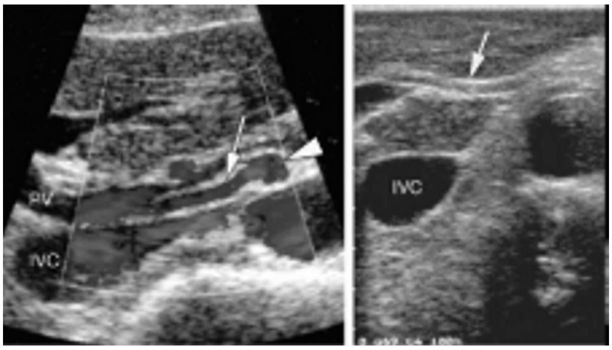

Fig. 4. Replaced right hepatic artery. Intraoperative color Doppler US image shows a replaced artery (arrow) that arises from the superior mesenteric artery (arrowhead) and courses between the portal vein (PV), which is anterior to it, and the more posteriorly located vena cava (IVC).

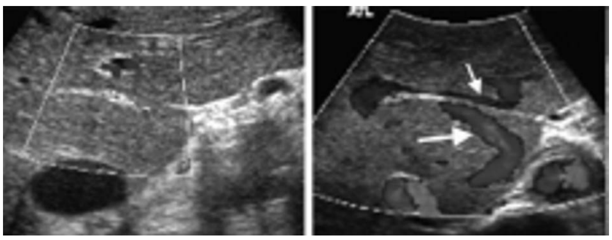

Fig. 5. (5) Replaced hepatic artery. a) Intraoperative gray-scale US image shows a replaced artery that courses through the ligamentum venosum (arrow), which is located anterior to the caudate love and vena cava (IVC). b) Intraoperative Doppler US image demonstrates the presence of flow through the replaced vessel, which arises from the left hepatic artery. c) Intraoperative Doppler US image shows not only the replaced artery (small arrow) that courses through the echogenic ligamentum venosum but also a potentially significant collateral vessel (large arrow) that connects the portal vein with the vena cava in the caudate lobe. The depiction of such vessel is important for the planning of any surgical resection in this anatomic region.

HEPATIC PSEUDOLESIONS

Foci of fatty infiltration that occur in cirrhosis or in patients undergoing chemotherapy may appear quite discrete in the intraoperative setting, when US image resolution is far better than at transcutaneous examination.

BLIND AREAS OF THE LIVER

Imaging of certain areas of the liver is particularly challenging in the intraoperative setting. These areas include the high dome of the lateral right lobe, access to which frequently requires dissection of the falciform and triangular ligaments. The posterior subdiaphragmatic bare area of the liver may be difficult to image, and surface lesions, typically hamartomas, are also difficult to identify, especially when the transducer provides poor near-field resolution or the depth of field or focal zone is not adequately altered. In these situations, the operator should consider using a water standoff (Fig 4) or scanning from the opposite surface of the liver.

EXTRAHEPATIC DISEASE

When the liver is imaged, abnormalities may be identified in adjacent structures. For example, lymph nodes are frequently visible near the porta hepatis, and tumors may extend into the diaphragm, right atrium, or vena cava.

LAPAROSCOPIC TECHNIQUES

As the use of laparoscopic and minimally invasive surgery continues to increase, the role of IOUS during laparoscopy has become even more important. Laparoscopy has obvious shortcomings in evaluating the liver because it eliminates the surgeon's ability to palpate structures and lesions. IOUS attempts to restore some of this tactile feedback while providing important information as seen in open procedures. The technique of laparoscopic ultrasound is well described and it has a better sensitivity than most preoperative studies. When compared with open IOUS, laparoscopic IOUS has a similar sensitivity and specificity. Some authors have suggested the routine use of laparoscopic IOUS in laparoscopic colorectal cancer surgery and before laparotomy for planned hepatic resection. In such cases with known hepatic disease, nearly 64% of patients could be spared a laparotomy incision based on laparoscopic findings. Several series have also suggested the role of laparoscopic ultrasound in the ablation of hepatic lesions. The advantages of this technique over percutaneous ablation include direct visualization of the peritoneal cavity, detection of occult lesions, and decreased risk of injury to adjacent organs. In comparison to open ablation, laparoscopic techniques may require more advanced technical skills and localizing lesions in segments 7 and 8 may be more difficult. To ovecome this difficulty, a hand-assisted technique has been suggested. When technically feasible, however, the laparoscopic approach has the benefit of a shorter recovery and greater patient satisfaction.

DL, with the addition of LUS for colon and rectal metastasis or hepatocellular cancer staging, identifies 10%-25% more additional tumors than preoperative CT (Level II-III). However, DL can be restricted in 13% of cases and not possible in 3% due to adhesions (Level II). DL with LUS changes the management in up to 49% of cases, and LUS alone added additional staging information in 42% of cases (Level II). DL with LUS has specificity of 75%-90% and sensitivity of 80%-100%, with a positive predictive value of 85% (Level III). Unnecessary open surgery for missed disease was uncommon, and avoidance of open surgery due to unresectability was 16%-25% (Level II-III) In pancreatic cancer, DL with LUS was 100% sensitive and specific (Level III).

SURGERY-SPECIFIC US FEATURES

At intraoperative US of the liver, certain features may appear that the radiologist should be aware of. The cut margin of a liver segment is often echogenic because of small amounts of gas that enter the parenchyma and sinusoids after cautery or sonication, techniques commonly used for segmental resection. The cut margin of partially resected tumors also may appear echogenic because of gas bubbles in the tumor remnant. Imaging during cautery produces bandlike artifacts. Accumulations of air adjacent to the vena cava, in the gallbladder fossa or in surgical packing material may simulate intravenous air or produce acoustic shadowing. Palpation of the posterior surface of the liver, which is frequently used to maneuver the liver for better imaging, also may result in acoustic shadowing that simulates mucinous metastases. Cautery on the liver surface, which is often performed to mark subjacent lesions, produces acoustic shadowing that must be distinguished from that produced by superficial tumors.

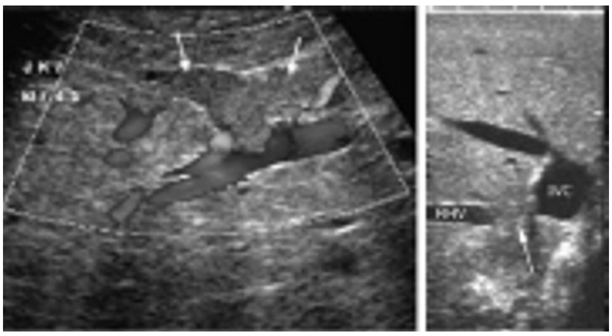

Fig. 6, 7. (6) Thrombus. Intraoperative color Doppler flow image obtained during US-guided metastasectomy in a patients with hepatocellular carcinoma shows a thrombus in the left portal vein (arrows). (7) Vascular invasion by metastasis. Intraoperative US image demonstrates a colorectal cancer metastasis (arrow) that has invaded the distal portion of the right hepatic vein (RHV) at its confluence with the adjacent vena cava (IVC). In this setting if resection is performed, segment VII (posterior to the right hepatic vein) and segment VIII (posterior to the right hepatic vein) of the liver are likely to be resected.

..Benign and malignant tumors frequently coexist. The radiologist should be aware that metastases that are similar in size and that arise from a single primary neoplasm typically have similar US appearances, whereas metastases of different sizes may have varying US appearances. Therefore, if two or more lesions of similar size have differing US appearances, it is likely that one set represents the neoplasm and the other set represents something else, such as hemangiomas.

LIVER TRANSPLANTATION

Intraoperative US is useful in cadaveric liver transplantations, in which the documentation of vessel patency and evaluation of anastomoses may be required. Intraoperative US is also helpful when there is inadvertent injury to the hepatic arteries, including dissection, or when interposition grafts are used to bridge recipient and donor vessels. Intraoperative US guidance is usually required during the harvesting phase of adult rightlobe split-liver transplantation, to help identify the relatively avascular resection plane 1–2 cm to the right of the middle hepatic vein. For these procedures, intraoperative US is also used to depict and localize the intrahepatic location of hepatic veins that drain segments V and VIII and to localize and characterize any accessory hepatic veins that may require the creation of separate anastomoses during implantation. In an implanted cadaveric liver, a thrombus may be identified in excluded vascular remnants such as the remnant vena cava, and the thrombus may even extend into adjacent hepatic veins. In this setting, intraoperative US is used for guidance of thrombectomy (Fig 8).

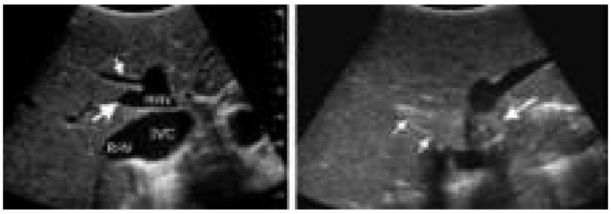

Fig. 7, 8 (7). Image obtained for planning of a living-related split-liver transplantation shows the relatively avascular plane between the right and left lobes of the liver (between segments VII and VIII); the insertion sites of the middle (MHV) and the right hepatic veins (RHV) into the vena cava (IVC); and the location and size of the veins that drain into the middle hepatic vein from segments V, VII and VIII (arrows). Intraoperative Us image shows a thrombus located between the confluence of the middle and right hepatic veins (small arrows) anteriorly and the recipient vena cava (large arrow) posteriorly, a finding that is not unusual in an implanted cadaveric liver. Extension of the thrombus into adjacent veins was ruled out before thrombectomy was performed.

ADDITIONAL VALUE OF CONTRAST ENHANCED INTRAOPERATIVE ULTRASOUND FOR COLORECTAL LIVER METASTASES

During surgery, intraoperative ultrasound (IOUS) is associated with the highest sensitivity (95-99%) and specificity (95-100%) concerning the number and localization of the liver lesions and their relation with major vascular and biliar structures.1,2,4,6

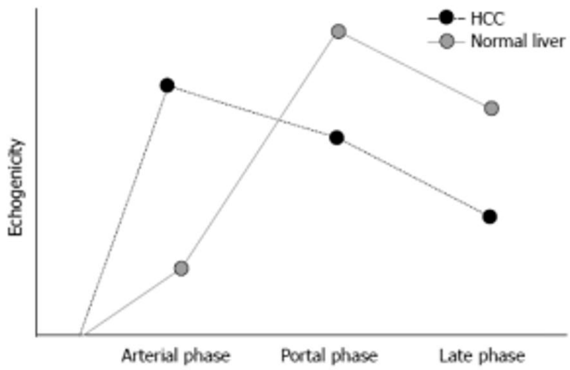

Fig. 9. It ilustrates the enhancing pattern of HCC and normal liver parenchyma. With more arterial supply, HCC appears hyperechoic in the arterial phase and the

Multi-slice contrast-enhanced computed tomography (CT) is the most commonly used preoperative staging investigation in primary CRC for detecting metastases. The sensitivity of CT for CLM is reported to be 73–85%.9,10 Previously undetected liver metastases are still diagnosed at laparotomy in a significant proportion of patients. However, metastases are often missed at laparotomy, either because they are too small or too deep to palpate or because they are located in a liver segment inaccessible to view. The routine use of intraoperative ultrasound (IOUS) of the liver during primary CRC surgery is effective for detecting additional lesions.11–13 However, around 15–20% of patients with a negative IOUS develop liver metastases within 2 years of followup. [11,13] Although some of this later disease may be microscopic at the time of IOUS, it is likely that some macroscopic lesions are missed as a result of their small size or atypical characteristics, because they mimic benign lesions or because they are iso-echoic with the hepatic parenchyma and thus invisible. An imaging modality with increased sensitivity and the capacity to distinguish benign from malignant with more clarity (and simplicity) is needed. Contrast agents have long been used to improve CT and magnetic resonance imaging (MRI). Contrast-enhanced transabdominal ultrasound is now available for routine use. Data recorded for each lesion included ultrasound characteristics, liver segment(s) involved, a detailed description of the relationships of the lesion to anatomical landmarks, an impression as to the benign ormalignant nature of the lesion and comments regarding correlation with the CT data. Particular attention was paid to the classical three phases of ultrasound contrast: the arterial phase (the initial 30 s); the porto-venous phase (30 s to 2 min), and the delayed parenchymal phase (2–5 min). The CE-IOUS was performed using a standard mechanical index of 0.18. The frequency of the probe was set at 4.3 MHz in contrast-specific mode. The entire scanning period of 5 min was recorded in digital video format. The use of MRI with liver-specific contrast also served two clinical purposes. Firstly, it provided a roadmap of the metastases to aid in treatment planning. Secondly, it provided a baseline from which to assess response to chemotherapy with subsequent MRI. Patients without suspicious or new standard screening with trans-abdominal ultrasound at 3 and 6 months with serum carcino-embryonic antigen levels and a CT scan at 1 year. None of the preoperative staging modalities used in CRC are as accurate or sensitive as IOUS of the liver. This includes CT,13,18 positron emission tomography (PET)19 and probably MRI.20,21 One reason for this is a lack of ultrasound training for colorectal surgeons. In our own experience, even when a combined resection is not to be considered, an accurate description of intraoperative findings by the colorectal surgeon is invaluable when considering cases for future liver resection. The contrast agent was SonoVue (Bracco Imaging, Milan, Italy) which consists of sulphur hexafluoride microbubbles stabilized by a phospholipid shell; 4.8 mL of SonoVue per exploration was injected intravenously through a peripheral vein. A low mechanical index (MI < 0.1) mode was used. All phases of contrast enhancement, including arterial (10-20 s to 25-35 s after injection), portal (30-45 s to 120 s) and late parenchymal (>120 s) phases were recorded and analyzed[13]. HCC is characterized by arterial phase hyper-enhancing and wash out of microbubbles during the portal and late phase, while benign solid lesions are characterized by persistence of contrast enhancement during the portal and late phase[15].

SUMMARY

Intraoperative ultrasound has become an essential tool for the surgeon in the field of hepatobiliary surgery. No preoperative study has been able to duplicate the sensitivity and specificity of IOUS in the identification of occult lesions. With recent improvements in technology, IOUS has now become an indispensable means of defining the extent of disease and respectability, and providing a guide to anatomic and nonanatomic hepatic resections and minimally invasive and percutaneous ablative techniques.

The success of this alternative technique for hepatectomies translates into lower mortality rates; mortality rates are up to 5 times lower using ultrasound guided techniques than with traditional techniques.

Intraoperative US provides crucial diagnostic and staging information to the surgeon during surgery. The technique has a demonstrated positive effect on patient care, surgical planning, and clinical outcome. As hepatic surgical procedures become more innovative, and with the increasingly frequent use of metastasectomy, we expect an increased future demand for access to and use of intraoperative US.

REFER ENCES:

1. Kruskal JB, Kane RA. Intraoperative ultrasonography of the liver. *Crit Rev Diagn Imaging*. 1995;36:175–226
2. Staren ED, Gambla M, Deziel DJ, et al. Intraoperative ultrasound in the management of liver neoplasms. *Am Surg*. 1997;63:591–596
3. Makuuchi M, Hasegawa H, Yamazaki S. Interoperative ultrasonic examination for hepatectomy. *Jpn J Clin Oncol*. 1981;11:367–369
4. Fan MH, Chang AE. Resection of liver tumors: technical aspects. *Surg Oncol*. 2002;10:139–152
5. Rifkin MD, Rosato FE, Branhc HM, et al. Intraoperative ultrasound of the liver. An important adjunctive tool for decision making in the operating room. *Ann Surg*. 1987;205:466–470
6. Ravikumar TS, Buenaventura S, Salem RR, et al. Intraoperative ultrasonography of liver: detection of occult liver tumors and treatment by cryosurgery. *Cancer Detect Prev*. 1994;18:131–138
7. Wernecke K, Rummeny E, Bongartz G, et al. Detection of hepatic masses in patients with carcinoma: comparative sensitivities of sonography, CT, and MR imaging. *AJR Am J Roentgenol*. 1991;157:731–739
8. Clarke MP, Kane RA, Steele G, et al. Prospective comparison of preoperative imaging and intraoperative ultrasonography in the detection of liver tumors. *Surgery*. 1989;106:849–855
9. Knol JA, Marn CS, Francis IR, et al. Comparisons of dynamic infusion and delayed computed tomography, intraoperative ultrasound, and palpation in the diagnosis of liver metastases. *Am J Surg*. 1993;165:81–88
10. Ward BA, Miller DL, Frank JA, et al. Prospective evaluation of hepatic imaging studies in the detection of colorectal metastases: correlation with surgical findings. *Surgery*. 1989;105:180–187
11. Gunven P, Makuuchi M, Takayasu K, et al. Preoperative imaging of liver metastases. Comparison of angiography, CT scan, and ultrasonography. *Ann Surg*. 1985;202:573–579
12. Machi J, Sigel B. Operative ultrasound in general surgery. *Am J Surg*. 1996;172:15–20
13. Boggs RR, Rouch DA, Chua GT. Intraoperative ultrasound of hepatic tumors. *Indiana Med*. 1992;85:496–498
14. Bismuth H, Castaing D, Garden J. The use of intraoperative ultrasound in surgery of primary liver tumors. *World J Surg*.1987;11:610–614
15. Parker G, Lawrence W, Horsley S, et al. Intraoperative ultrasound of the liver affects operative decision making. *Ann Surg*.1989;209:569–577
16. Haider MA, Leonhardt C, Hanna SS, et al. The role of intraoperative ultrasonography in planning the resection of hepatic neoplasms. *Can Assoc Radiol J*. 1995;46:98–104
17. Cervone A, Sardi A, Conaway GL. Intraoperative ultrasound (IOUS) is essential in the management

of metastatic colorectal liver lesions. *Am Surg*. 2000;66:611–615
18. Bloed W, van Leeuwen MS, Borel Rinkes IH. Role of intraoperative ultrasound of the liver with improved preoperative hepatic imaging. *Eur J Surg*. 2000;166:691–695
19. Healy JE, Schroy PC. Anatomy of the biliary ducts within the human liver; analysis of prevailing pattern of branching and the major variations of the biliary ducts. *Arch Surg*. 1953;66:599–616
20. Couinard C. Lobes et segments hepatiques. *Presse Med*. 1954;62:709
21. Kanematus T, Sonoda T, Takenaka K, et al. The value of ultrasound in the diagnosis and treatment of small hepatocellular carcinoma. *Br J Surg*. 1985;72:23–25
22. Sheu J, Lee C, Sung J, et al. Intraoperative hepatic ultrasonography—an indispensable procedure in resection of small hepatocellular carcinomas. *Surgery*. 1985;97:97–103
23. Zhi-Zhang X. Real-time B mode ultrasonography in localization of subclinical hepatocellular carcinoma. In: Zhao-You T editors.Subclinical hepatocellular carcinoma. New York: Springer-Verlag; 1985;p. 12–20
24. Torzilli G, Makuuchi M. Intraoperative ultrasonography in liver cancer. *Surg Oncol Clin N Am*. 2003;12:91–104
25. Takigawa Y, Sugawara Y, Yamamoto J, et al. New lesions detected by intraoperative ultrasound during liver resection for hepatocellular carcinoma. *Ultrasound Med Biol*. 2001;27:151–156
26. Kokudo N, Bandai Y, Imanishi H, et al. Management of new hepatic nodules detected by intraoperative ultrasonography during hepatic resection for hepatocellular carcinoma. *Surgery*. 1996;119:634–640
27. Gruenberger T, Jourdan JL, Zhao J, et al. Echogenicity of liver metastases is an independent prognostic factor after potentially curative treatment. *Arch Surg*. 2000;135:1285–1290
28. Seifert J, Morris D. Pretreatment echogenicity of colorectal liver metastases predicts survival after hepatic cryotherapy. *Dis Colon Rectum*. 1999;42:43–49
29. Zhao-You T, Bing-Hui Y. Early detection of subclinical hepatocellular carcinoma. In: Zhao-You T editors. Subclinical hepatocellular carcinoma. New York: Springer-Verlag; 1985;p. 12–20
30. Kane RA, Hughes LA, Cua EJ, et al. The impact of intraoperative ultrasonography on surgery for liver neoplasms. *J Ultrasound Med*. 1994;13:1–6
31. Brower ST, Schwartz M, Miller C. Intraoperative ultrasound and liver tumors. *Cancer Treat Res*. 1994;69:197–220
32. Kolecki R, Schirmer B. Intraoperative and laparoscopic ultrasound. *Surg Clin North Am*. 1998;78:251–271
33. Meijer S, Paul MA, Cuesta MA, et al. Intra-operative ultrasound in the detection of liver metastases. *Eur J Cancer*.1995;31A:1210–1211
34. Charnley RM, Morris DL, Dennison AR, et al. Detection of colorectal liver metastases using intraoperative ultrasonography. *Br J Surg*. 1991;78:45–48
35. Stewart PJ, Chu JM, Kos SC, et al. Intraoperative ultrasound for the detection of metastases from colorectal cancer. *Aust N Z J Surg*. 1993;63:530–534
36. Machi J, Isomoto H, Kurohiji T, et al. Accuracy of intraoperative ultrasonography in diagnosing liver metastases from colorectal cancer: evaluation with postoperative follow-up results. *World J Surg*. 1991;15:551–556
37 Stone MD, Kane R, Bothe A, et al. Intraoperative ultrasound imaging of the liver at the time of colorectal cancer resection. *Arch Surg*. 1994;129:431–435
38. Leen E, Angerson WJ, O'Gorman P, et al. Intraoperative ultrasound in colorectal cancer patients undergoing apparently curative surgery: correlation with two year follow-up. *Clin Radiol*. 1996;51:157–159
39. Velasco JM, Montana L, Vallina V. Intraoperative endoscopy and ultrasonography. *Probl Gen Surg*. 1990;7:352–370
40. Makuuchi M, Hawgawa H, Yamazaki S, et al. The use of intraoperative ultrasound as an aid to liver resection in patients with hepatocellular carcinoma. *World J Surg*. 1987;11:615–621
41. Scudmore CH, Patterson EJ, Shapiro AMJ, et al. Liver tumor ablation techniques. *J Invest Surg*. 1997;10:157–164
42. Bezzi M, Merlino P, Orsi F, et al. Laparoscopic sonography during laparoscopic surgery: technique and imaging findings. *AJR Am J Roentgenol*. 1995;165:1193–1198
43. Machi J, Schwartz JH, Zaren HA, et al. Technique of laparoscopic ultrasound examination of the liver and pancreas. *Surg Endosc*. 1996;10:684–689
44. Cuschieri A. Laparoscopic management of cancer patients. *J R Coll Surg Edinb*. 1995;40:1–9
45. Hunderbein M, Rau B, Schlag PM. Laparoscopy and laparoscopic ultrasound for staging of upper gastrointestinal tumors. *Eur J Surg Oncol*. 1995;21:50–55
46. Gouma DJ, De Wit LT, Nieveen van Dijkum E, et al. Laparoscopic ultrasonography for staging of gastrointestinal malignancy.*Scand J Gastroenterol Suppl*. 1996;218:43–49
47. Goletti O, Buccianti P, Chiarugi M, et al. Laparoscopic sonography in screening metastases from gastrointestinal cancer: comparative accuracy with traditional procedures. *Surg Laparosc Endosc*. 1995;5:176–182
48. Tandan VR, Asch M, Margolis M, et al. Laparoscopic vs. open intraoperative ultrasound examination of the liver: a controlled study. *J Gastrointest Surg*. 1997;1:146–151
49. Hartley JE, Kumar H, Drew PJ, et al. Laparoscopic ultrasound for the detection of hepatic metastases during laparoscopic colorectal cancer surgery. *Dis Colon Rectum*. 2000;43:320–324
50. Barbot DJ, Marks JH, Feld RI, et al. Improved staging of liver tumors using laparoscopic

intraoperative ultrasound. *J Surg Oncol*.1997;64:63–67
51. John TG, Greig JD, Crosbie JL, et al. Superior staging of liver tumors with laparoscopy and laparoscopic ultrasound. *Ann Surg*.1994;220:711–719
52. Machi J, Oishi AJ, Mossing AJ, et al. Hand-assisted laparoscopic ultrasound-guided radiofrequency thermal ablation of liver tumors: a technical report. *Surg Laparosc Endosc Percutan Tech*. 2002;12:160–164
53. Cuschieri A, Bracken J, Boni L. Initial experience with laparoscopic ultrasound-guided radiofrequency thermal ablation of hepatic tumors. *Endoscopy*. 1999;31:318–321
54. Machi J, Uchida S, Sumida K, et al. Ultrasound-guided radiofrequency thermal ablation of liver tumors: percutaneous, laparoscopic, and open surgical approaches. *J Gastrointest Surg*. 2001;5:477–489