Intraoperative and Laparoscopic Ultrasound During Liver Surgery

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Intraoperative ultrasound (IOUS) was used primarily in 1960 to localize renal calculi during surgery for nephrolithotomy [1]. The first application of IOUS in hepatobiliary surgery was described by Yamakawa in 1951 to detect cholelithiasis using A-mode ultrasound [2]. With the progress in ultrasound technology and the refinement of instruments, by the mid-1970s, real-time two-dimensional B-mode imaging systems became available. In 1977, Makuuchi was the first to use an electronic linear array (2.5- and 3.5-MHz transducers) for IOUS examination of the liver and pancreas [3]. Since then, IOUS of the liver has become an essential tool for hepatobiliary surgery and is essential in planning surgical strategies. Current applications of intraoperative ultrasound include assessment of tumor(s) and vascular involvement in addition to guidance of hepatic resection, whole or split-liver transplantation, and tumor ablation. Traditional ultrasound does not provide information about tumor vascularity and tissue microcirculation; however, contrast agents are becoming available to allow this evaluation [4, 5].

The purpose of this chapter is to explain how to perform IOUS of the liver. Normal anatomy and anatomic variations, typical features of hepatic tumors, and the different applications of IOUS will be discussed.

Technique

Equipment

Dedicated transducers should be used for IOUS of the liver. The frequency of the probe is inversely proportional to the depth of penetration, but proportional to the image definition. The ideal probe is therefore a compromise between depth and detail. The most common probes are the multifrequency (5, 7.5, 10 MHz) T-probe linear or curvilinear array, T-style finger-grip, and I-style finger-grip and should have color Doppler capability. The probe should fit comfortably in the palm of the hand and between the fingers to easily explore the upper part and the right lateral segments of the liver (Fig. 15.1). If the probe is not sterilizable, a condom sheath can be used to provide sterility of the probe. The sheath must be long at least 2 m to make sure that the entire length of the electric supply cord is covered, and it should snugly fit to the

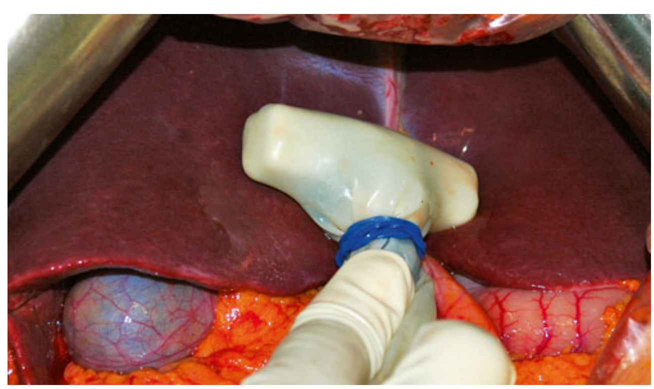

Fig. 15.1 T-style finger-grip intraoperative probe

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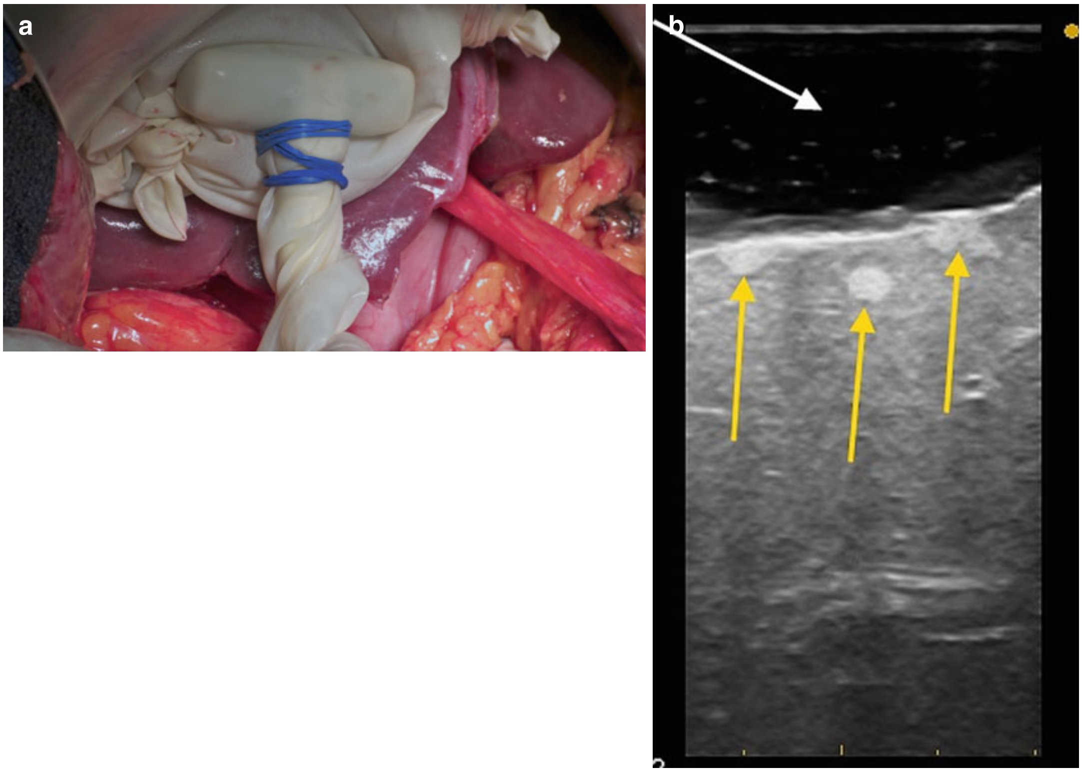

Fig. 15.2 (**a**) Probe standoff technique: a saline-filled glove is placed between the probe and the liver in order to examine the superficial aspect of the liver. (**b**) Probe standoff (*white arrow* indicates saline interface) allows better visualization of superficial lesions (*yellow arrows* indicate lesions)

transducer to avoid artifacts. The covered cord must be kept off the ground and away from all equipment.

IOUS of the Liver

Open Approach

The ultrasound scanner and monitor screen are placed to the right of the patient. The surgeon can begin with a small incision as it is easy to slide the hand between the liver and the diaphragm. If there are no contraindications to the planned operation, the incision can be extended and the liver mobilized to perform a complete IOUS.

The probe is placed directly on the surface of the liver. Typically, no gel is required, as the natural surface moisture of the liver is adequate for acoustic coupling. In some cases, however, some moisture on the liver surface is required. Only light pressure should be applied to the liver surface to avoid vascular compression. It is important to note that there is decreased resolution for about the first 5 mm between the probe and liver surface. In order to explore this area, probe standoff can be used with saline immersion (Fig. 15.2a, b) (refer to “Probe standoff scanning” for further information). The probe is moved in different directions by making small rotational movements around its axis. A standardized approach and technique is essential in order to ensure complete exploration of the organ. The liver is scanned completely from the upper to the caudal edge, moving from the left to the right through the entire organ in a systematic manner in order not to leave any area unexplored.

Aims of the liver ultrasound exploration are:

- To identify tumors
- To discover tumor thrombi and vascular invasion
- To define the relation of these lesions with respect to the vascular anatomy

The initial step of IOUS of the liver is to identify each hepatic vein as it arises from the inferior vena cava. The probe is held in a transverse midline position on the anterior surface of the liver and angled toward the beating heart (Fig. 15.3). All three hepatic veins must be followed to their peripheral tributary branches by moving the probe along the hepatic veins’ axes.

The next step is to identify and follow the portal pedicles in order to define segmental anatomy of the liver. This is best achieved by placing the transducer on the surface of the liver, at the level of the segment IV, and angling the transducer toward the porta hepatis. Beginning from the left of the round ligament, the left portal branches for segments 2, 3, and 4 are identified and followed. Thereafter, moving over to the right side of the round ligament, the anterior and the posterior branches of the right portal vein and the feeding vessels for segments 5, 6, 7, and 8 are identified and followed. By using the intraoperative Doppler and color flow setting, dilated bile ducts can be discriminated from adjacent vascular structures

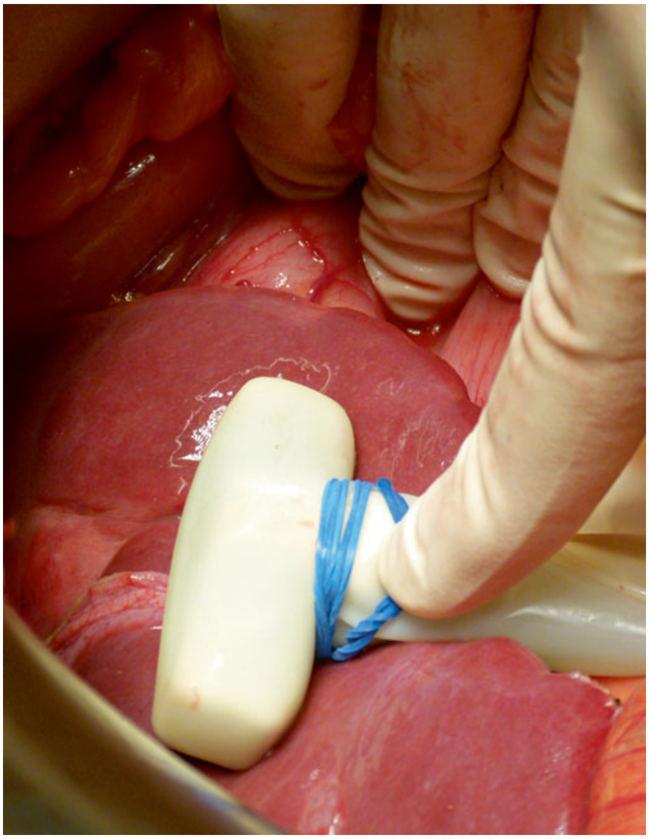

Fig. 15.3 The probe is angled toward the heart in order to identify hepatic veins

Fig. 15.4 (**a**) The laparoscopic ultrasound probe with a flexible tip. (**b**). Angulation of the laparoscopic ultrasound probe allows for better exploration of the liver surface

and define the flow direction. The examination is completed with ultrasound of gallbladder and the porta hepatis.

Laparoscopic Approach

As the use of laparoscopic procedures and minimally invasive surgery continues to increase, the role of IOUS during laparoscopy has become even more important. The laparoscopic approach has some limits as the surgeon is unable to palpate the liver and potential lesions. The technique of laparoscopic IOUS is similar to the open approach. The probe is introduced through a 12-mm epigastric or umbilical port for longitudinal imaging and a lateral abdominal port for transverse imaging. We use a 7.5-MHz linear-array transducer. A flexible probe is preferable as it allows better contact with the liver surface, which is limited by using a rigid probe (Fig. 15.4a, b). As in the open IOUS, the posterior segments of the liver are difficult to visualize. To explore this "blind area," it is essential to obtain maximal medial displacement of the liver by placing the patient in the semilateral position with the right side elevated.

Contrast-Enhanced Intraoperative Ultrasound (CE-IOUS)

There are limitations in liver ultrasound. In cirrhotic patients, IOUS is able to identify new lesions in 15–33 % of patient with hepatocellular carcinoma (HCC), which can change the surgical strategy [4, 6, 7]. On the other hand, tiny metastases from colorectal cancer may be not detected during IOUS [5].

Contrast-enhanced intraoperative ultrasound (CE-IOUS) has improved the ultrasound capability in detection and characterization of hepatic nodules [8]. Second-generation microbubble contrast agents have further improved the sensitivity of CE-IOUS [9, 10]. The microbubble is an ideal ultrasound contrast agent as it is extremely echogenic, as well as biocompatible, multifunctional, and inexpensive. Microbubbles are gas spheres between 0.1 and 10 μm in diameter and are much smaller than the wavelength of diagnostic ultrasound, which is typically 100–1,000 μm [11]. The gas core has a low density and is highly compressible, allowing it to shrink and expand

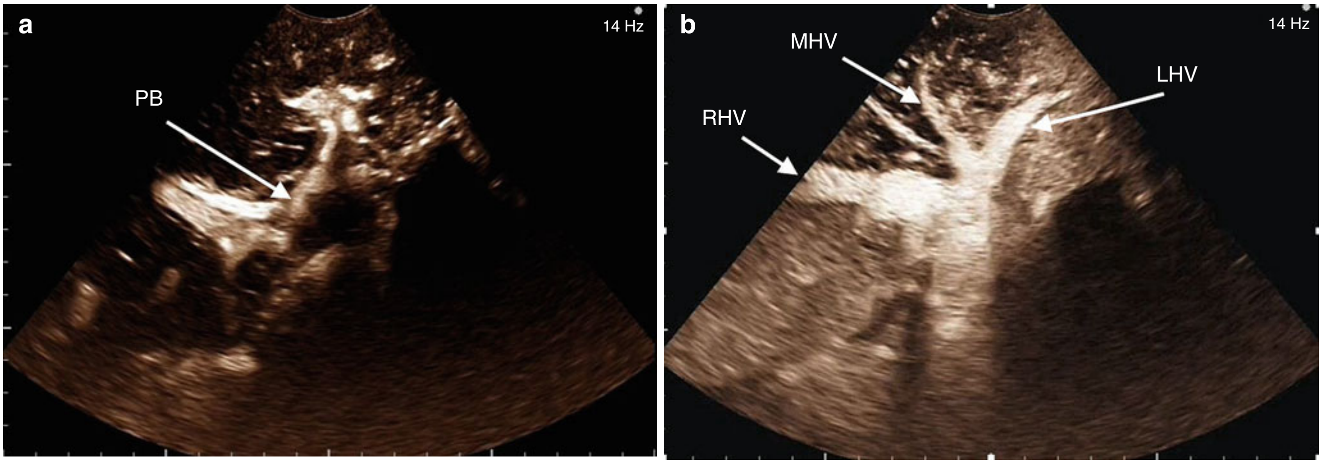

Fig. 15.5 Contrast-enhanced intraoperative ultrasound (CE-IOUS). (**a**) Arterial and portal features after injection of SonoVue. Portal bifurcation (*PB*) is showed by *white arrow*. (**b**) Hepatic veins in the late phase of CE-IOUS: right hepatic vein (*RHV*), middle hepatic vein (*MHV*), and left hepatic vein (*LHV*)

with the passage of an acoustic wave. The most widely used contrast agent is SonoVue (Bracco Imaging, Milan, Italy®) commercialized in Italy since the end of 2001. It is a pure intravascular contrast agent made of stabilized microbubbles containing sulfur hexafluoride, an echogenic and poorly soluble gas. Microbubbles have approximately the same size of red blood cells and are able to move into the vessels, but not through the vascular endothelium into the interstitial space. Recently, a new ultrasound contrast agent, Sonazoid (GE Healthcare, Oslo, Norway ®), has been developed, but it is not available in every country. It accumulates in hepatic Kupffer cells, providing a parenchyma-specific image in addition to demonstrating tumor vascularity [12, 13]. IOUS is initially performed in order to search for new nodules and to establish a surgical strategy. Following IOUS, CE-IOUS is performed in order to detect new nodules. CE-IOUS is also performed at the end of restorative face of liver transplantation (LT) in order to check the vascular anastomoses patency and the parenchyma perfusion. We use a dedicated probe for CE-IOUS and utilize SonoVue as contrast agent. The anesthesiologist injects 4.8 ml of SonoVue through a peripheral vein, which is followed by 10 ml of normal saline. The ultrasound is then performed using an US machine, which has contrast-specific software. Each phase of the ultrasound examination is recorded (arterial phase, portal phase, and late phase) (Fig. 15.5a, b). (Refer to section "Intraoperative contrast-enhanced ultrasound" in Chap. 23, for further information.)

Normal Anatomy

Knowledge of the anatomy of the liver is very important in order to understand and analyze under ultrasound the different aspects of the hepatic parenchyma, segmental anatomy, and structures, such as the vessels and biliary tract.

Ultrasound Anatomy of the Liver

The normal liver parenchyma is of a medium echogenicity and is made of many thin spots creating a homogenous appearance. In comparison to the kidney, the liver is less echogenic. However, in the case of steatosis, there is an increase in liver echogenicity as compared to the kidney. The liver surface is normally very smooth. Irregular and nodular appearance with protrusions or indentations are typical features found in liver cirrhosis.

Segmental Anatomy of the Liver

The liver is a large organ without many landmarks. Its blood vessels are not identified or defined on the surface. These difficulties in defining liver anatomy and its vasculature can be resolved by performing IOUS. The importance of the intrahepatic vasculature as a guide for the recognition of the segmental anatomy of the liver is extremely important for liver resection and, in particular, for repeat liver resection. In cases of repeat liver resection, the liver surface is different and IOUS is paramount in defining the segmental anatomy and vasculature. IOUS is also very useful for marking vessels on the liver surface to guide the resection and to perform anatomic hepatectomies. To obtain the most useful information by performing IOUS, the surgeon must be familiar with the relevant intraoperative and vascular anatomy and the spectrum of normal and abnormal findings.

Segmental anatomy of the liver is based on the hepatic veins and the intrahepatic branches of portal system. As described by Healy and Schroy, hepatic territories are defined as Glissonian segments, which are based on Glissonian pedicles with an arterial branch, portal branch,

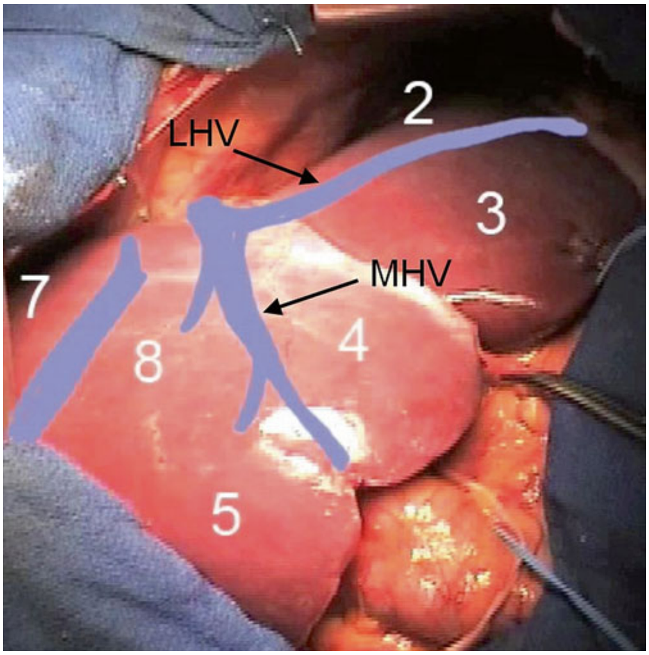

Fig. 15.6 Liver anatomy according to Couinaud segmentation. The middle hepatic vein (*MHV*) divides the right and left livers. The left hepatic vein (*LHV*) runs between segments *2* and *3*

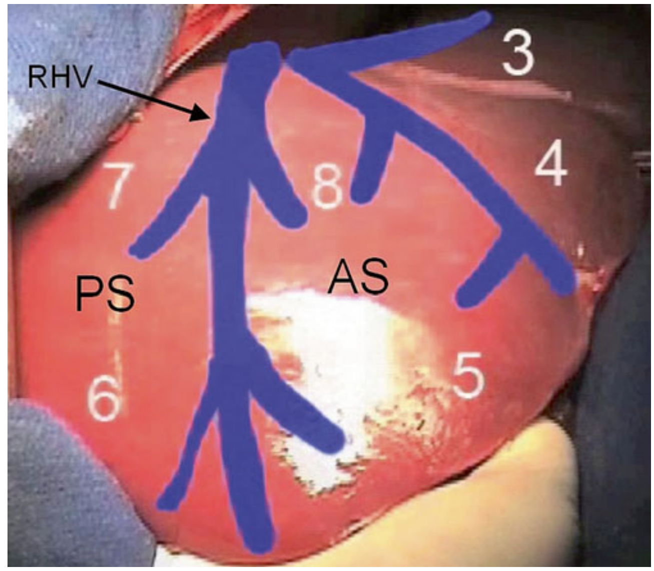

Fig. 15.7 The right liver is divided by the right hepatic vein (*RHV*): the anterior sector (*AS*) and the posterior sector (*PS*)

and intrahepatic bile duct [14]. The pedicles are surrounded by the intrahepatic extension of the Glisson's capsule that covers the liver surface. Alternatively, Couinaud described eight liver segments, whereby the left liver consists of segments 2, 3, and 4 and the right liver consists of segments 5, 6, 7, and 8 [15]. Note that in this terminology, the left lobe consists of segments 2 and 3 and the right lobe consists of the right liver (segments 5, 6, 7, and 8) and segment 4. The left hepatic vein travels between segments 2 and 3 in the left lobe. The middle hepatic vein divides the left and the right livers, whereby the right hepatic vein divides the right liver into the anterior sector (5 and 8) and the posterior sector (6 and 7) (Figs. 15.6 and 15.7).

The hepatic veins are identified beginning at their junctions with the IVC and are followed along their main axes. The hepatic veins divide the liver into different sectors. The plane between the middle hepatic vein and the IVC (inferior vena cava) divides the right (supplied by the right portal vein) and the left hepatic parenchymas (supplied by the left portal vein) (Fig. 15.6). The junction between the IVC and hepatic veins is easy to identify (Fig. 15.8). Since they are not surrounded by Glisson's capsule, the walls of the hepatic veins are recognized as a thin echogenic line. Typically, the left and the middle hepatic veins have a common trunk (Fig. 15.8). Several branches including one large posterior and some small anterior tributaries usually form the left hepatic vein. Two anterior veins from segments 4 and 5 form the middle hepatic vein. Less frequently, there are small veins draining the upper part of the segment 4 and segment 8

Fig. 15.8 The common trunk (*CT*) is formed by the left (*LHV*) and middle (*MHV*) hepatic veins to empty into the inferior vena cava (*IVC*)

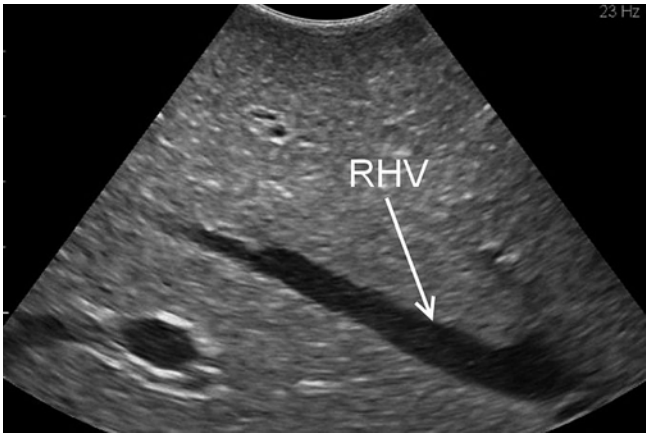

Fig. 15.9 The right hepatic vein (*RHV*) divides the right liver in the anterior and posterior sectors

Fig. 15.11 Portal bifurcation at the hepatic hilum

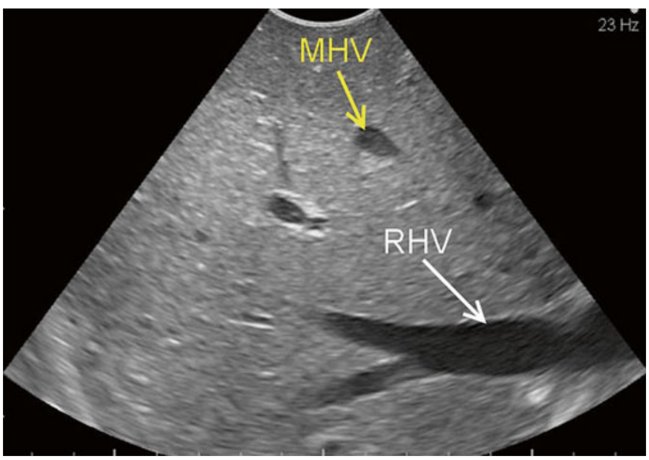

Fig. 15.10 Here, depicted are the right hepatic vein (*RHV*, *white arrow*) and the middle hepatic vein (*MHV*, *yellow arrow*)

into the middle hepatic vein. As indicated above, the plane between the IVC and the middle hepatic vein splits the liver in two different parts, each with its own portal supply. The line passing through this plane is called main portal scissure and is very useful to discriminate the limit between the right and left hepatectomies.

The junction between the IVC and the right hepatic vein is located on the right side of the IVC and typically (70 %) consists of a single large trunk (Figs. 15.9 and 15.10). There are usually three or four hepatic veins which drain segment 1 and very difficult to recognize due to their small size. The surgeon should also recognize the location of accessory hepatic veins, as this can be clinically important. For example, a right accessory hepatic vein draining the inferior right liver allows the surgeon to preserve the inferior portion of the right liver (segments 5, 6), even in case of ligature of the right hepatic vein [16, 17]. This vein is present in 13 % and joins the IVC directly at the level of the hepatic hilum.

The portal vein is the most important element of the hepatic hilum, and the intrahepatic branches are used to determine the segmental anatomy. The portal bifurcation is easily detectable under ultrasound by placing the probe transversely over the lower portion of segment 4 targeted on the hilum and through a horizontal plane. The arterial branch and the biliary system are typically anterior and superior to the portal system and can be difficult to identify (Fig. 15.11).

Keeping the probe in the same plane and moving it toward the left side, the extrahepatic portion of the left branch of the portal vein (i.e., the horizontal portion of the left portal vein) is followed. At this level, in the posterior plane, the segment 1 portal branches are identified. The left portal vein then turns anteriorly (i.e., the umbilical portion of the left portal vein) and extends to the round ligament, where the round ligament appears as a well-defined hyperechoic zone. Here, the left portal vein terminates in a cul-de-sac named the recess of Rex (Fig. 15.12a–d). At the "elbow" of the left portal vein, the branch to segment 2 arises (Fig. 15.13). At the level of the recess of Rex, the left portal vein terminates into two branches to segment 3 (to the left) and to segment 4 (to the right) (Fig. 15.14).

The right branch of the portal vein is short as it divides early into its anterior and posterior branches (Fig. 15.15). The anterior branch of the right portal vein is located between the right and middle hepatic veins and supplies the anterior sector of the right liver with separate branches to segments 5 and 8. The posterior trunk of the right portal vein supplies the posterior sector of the right liver but is more variable as it supplies multiple branches to segments 6 and 7. One of the most important anatomic variations of the portal system is the trifurcation of the portal vein, where the main portal vein divides into the left, right anterior, and right posterior branches. Also important is the "slipping" of the right anterior branch, where this branch arises from the left portal vein.

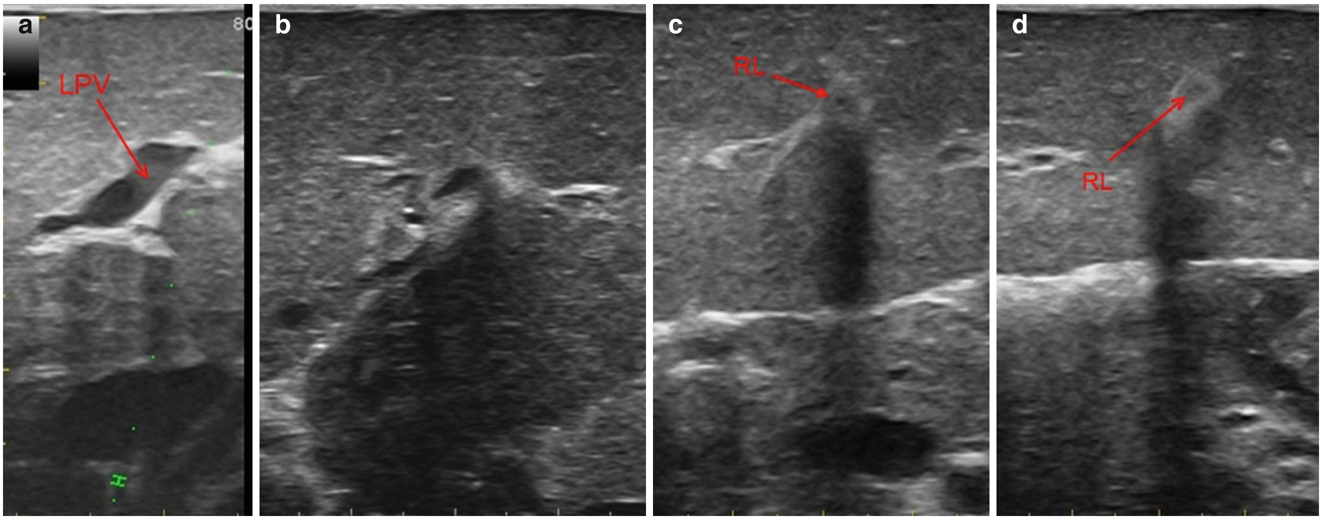

Fig. 15.12 (**a–d**) This series of images shows the left portal vein (*LPV*) (**a**) where it extends to the round ligament and as it terminates in the recess of Rex (**b**) at the round ligament (*RL*). The round ligament appears as a well-defined hyperechoic zone (**c**, **d**)

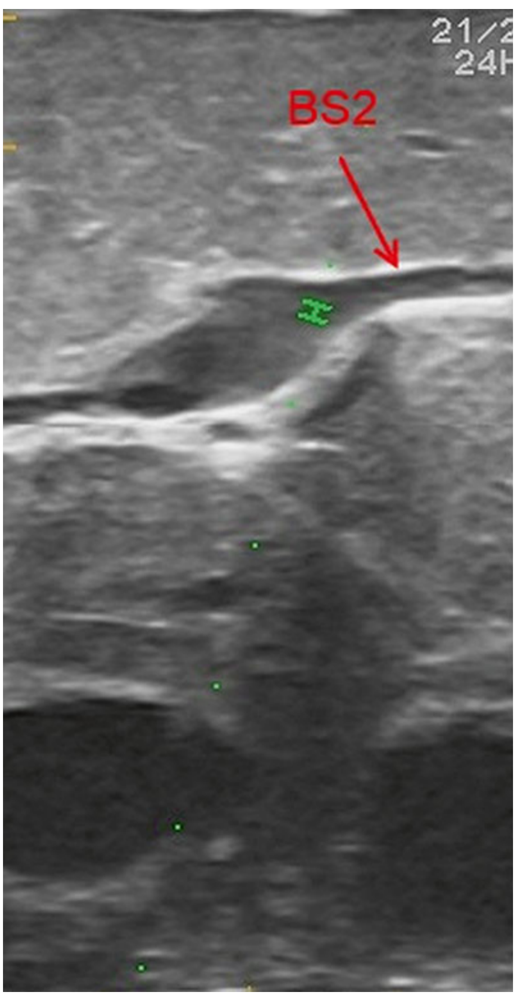

Fig. 15.13 The picture shows the origin of the portal branch to segment 2 (*BS2*)

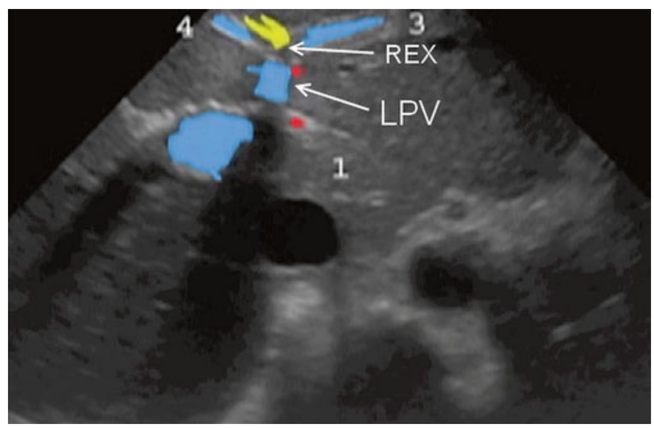

Fig. 15.14 Left portal vein (*LPV*). Portal branches to segments 3 (*3*) and 4 (*4*) can be recognized at the level of the recess of Rex (*REX*). Also seen here is the portal branch to segment 1 (*1*)

An arterial variation that is frequently relevant is a replaced right hepatic artery, which arises from the superior mesenteric artery and travels posterior to the portal vein. A replaced or accessory left hepatic artery arising from the left gastric artery and running through the ligamentum venosum may also be encountered. Intrahepatic arteries are not usually visible but may be enlarged in the case of arterialization of the liver (pathological finding) or after a major hepatectomy. The right and left bile ducts, as well as their confluence, are normally identifiable and their typical diameter is approximately 5 mm. The peripheral bile channels are not evident unless they are dilated for pathological reasons, such as in biliary obstruction.

The exploration of some areas of the liver is particularly challenging in the intraoperative setting.

Fig. 15.15 Right portal vein (*RPV*) and its anterior (*AB-RPV*) and posterior branches (*PB-RPV*). Also seen here is the anterior branch of right hepatic artery (*AB-RHA*)

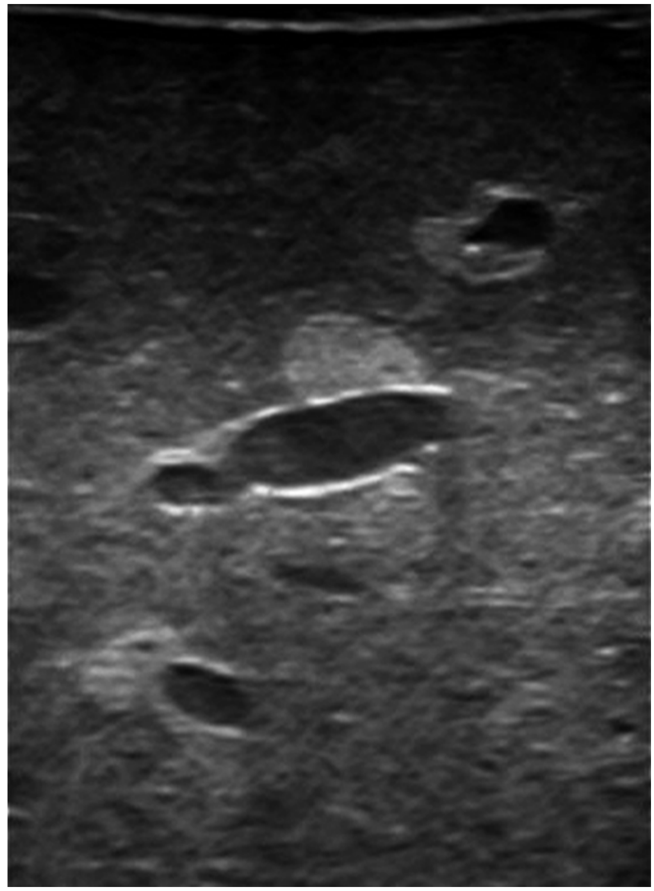

Fig. 15.16 Hepatic adenoma. It appears as a hyperechoic round lesion placed side to hepatic vein without any signs of compression

For example, upper and lateral aspects of the right liver, whose access typically requires dissection of the falciform and triangular ligaments, can be difficult to image. In that case, it might be necessary to place the probe on the inferior surface of the liver. Lesions very close to the liver surface can also be difficult to image. In this case, a probe standoff technique, as discussed earlier, can be used or placing the probe on the opposite surface of the liver can image the lesion.

Ultrasound Features of Hepatic Tumors

IOUS can identify certain hepatic tumors due to different sonographic characteristics as compared to the normal liver parenchyma. Tumors are characterized as being an-, hyper-, or hypoechoic when compared to normal hepatic parenchyma. Anechoic (appears black) lesions are typically cystic and may be, for example, biliary cysts or hydatid cysts. Hyperechoic (appears brighter than the background liver) lesions are more commonly benign tumors such as hemangiomas and adenomas (Fig. 15.16). Less frequently, malignant lesions are hyperechoic. Finally, hypoechoic (appears darker than the background liver) lesions are typically malignant tumors (Fig. 15.17a–c), such as colorectal liver metastasis (CRLM), neuroendocrine tumor, or HCC. Homogenous isoechoic tumors are the most difficult to recognize. They may be identified only by their mass effect on neighboring vascular structures or by the presence of a hypoechoic border. Tumors may be either homo- or heterogeneous (mixed), compared to normal parenchyma, and the ultrasound beam beyond the lesion may be attenuated, increased, or completely absent. The usefulness of IOUS is even more important for unknown lesions detected intraoperatively. In this section, the ultrasound features of CRLM, HCC, and benign tumors as well as the role of IOUS in the detection of the primary and metastatic tumors will be discussed.

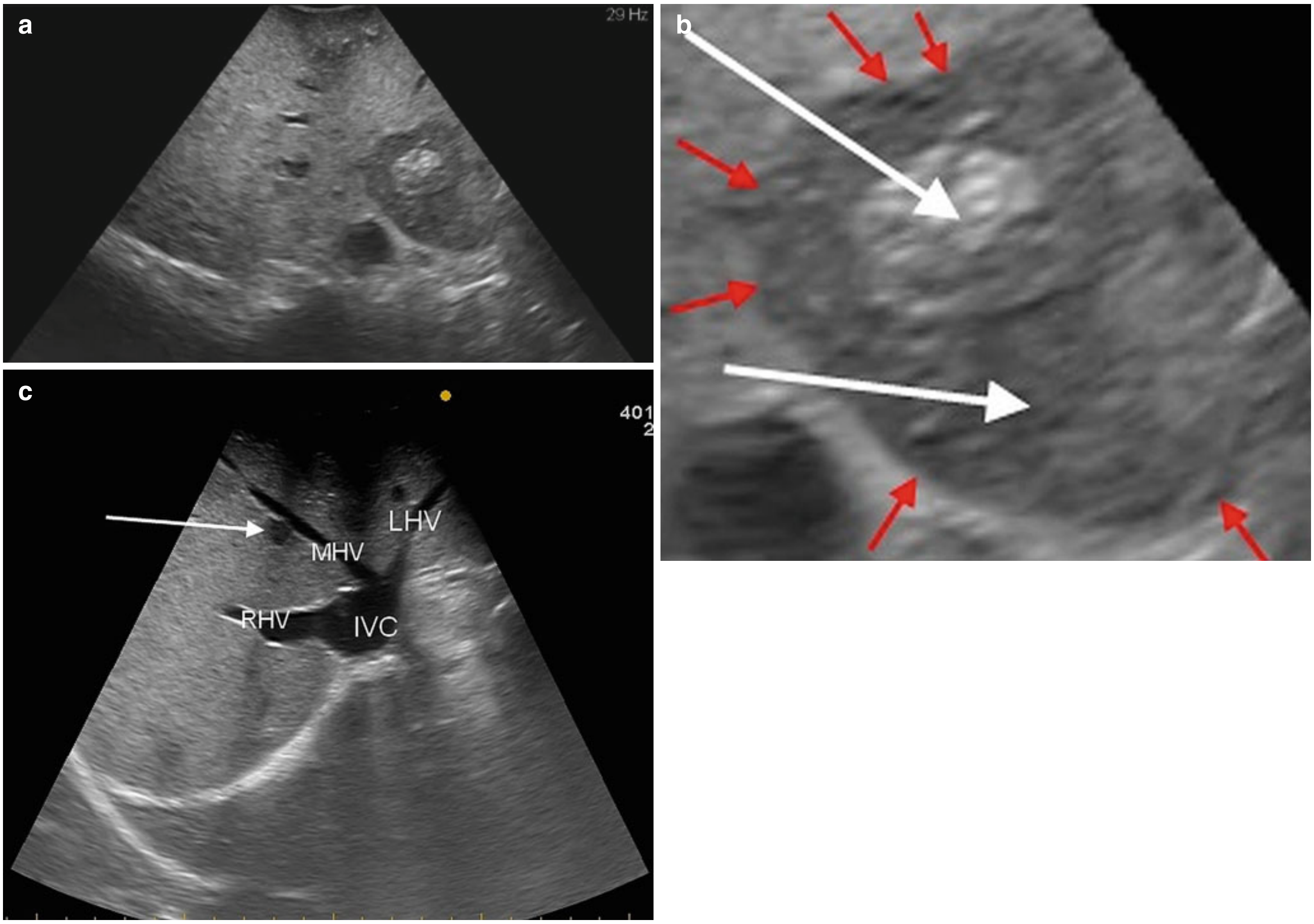

Fig. 15.17 Liver metastases. (**a**, **b**) The ultrasound characteristics of a lesion may be influenced by the degree of necrosis in response to chemotherapy. (**a**) This post-chemotherapy-treated colorectal liver metastasis is a heterogeneous lesion, which is predominantly hypoechoic with a central hyperechoic zone. The hyperechoic zone may represent calcification. (**b**) The border of the lesion is irregular as showed by *red arrows. White arrows* indicate the hypo- and hyperechoic characteristics of this lesion. (**c**) This hypoechoic lesion corresponds to a liver metastasis from neuroendocrine tumor. Note the proximity to the middle hepatic vein (*MHV*). *RHV* right hepatic vein, *MHV* median hepatic vein, *LHV* left hepatic vein, *IVC* inferior vena cava

Liver Metastasis

Approximately half of patients with colorectal cancer develop liver metastases [18, 19]. The only potentially curative option for these patients is surgical resection in order to reach a 5-year survival rate of 25–58 % [20, 21]. Intraoperative ultrasound has been recognized for years to be beneficial in those undergoing liver resection for colorectal liver metastases (CRLM). In particular, IOUS allows the surgeon to detect additional small CRLM not seen on preoperative cross-sectional imaging, typically those less than 2 cm and those metastases which have “disappeared” following chemotherapy (i.e., “missing” metastases). Several reports identify the additional detection rate of IOUS to be as high as 10–20 % [22, 23]. Sensitivity of more than 90 % has been reported with positive and negative predictive values of 90 and 70 %, respectively [24, 25]. Recent studies have suggested that with the improvement of preoperative imaging, there is no additional benefit of IOUS. However, Van Vledder and colleagues have demonstrated that IOUS leads to the detection of additional lesions in 10 % of patients and subsequently changes the surgical strategy in 9 % of patients [26]. Furthermore, they found that the probability of finding additional metastases varied considerably based on specific clinical and ultrasound features. Those who had more than four metastases or those who had hypoechoic lesions were found to have a higher chance of identifying additional lesions in 26 and 18 %, respectively. The detection of additional lesions may change the surgical approach and may contribute to improved outcomes. Recently, D’Hondt et al. reported that IOUS could change the operative strategy in 16.5 % of patients [27]. Furthermore, IOUS is useful to detect metastases, which have “disappeared” after chemotherapy. To improve surgical outcomes, there is an increasing trend to administer preoperative chemotherapy to patients with resectable CRLM. This leads to more patients who have a major radiological response but also leads to liver metastases which

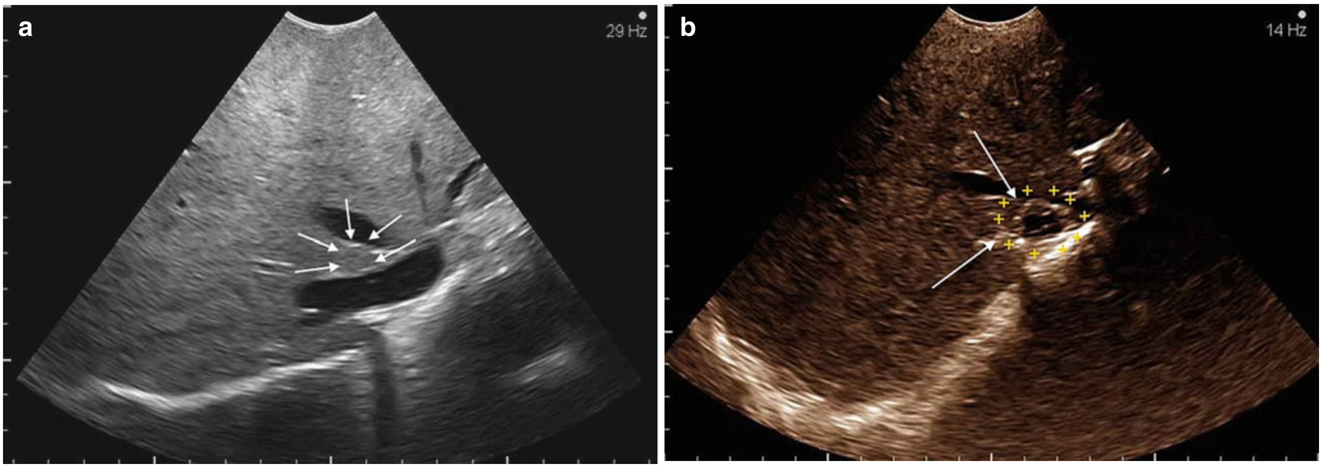

Fig. 15.18 Contrast-enhanced ultrasound. (**a**) IOUS is unable to detect this isoechoic lesion. The lesion is marked by the *white arrows*. (**b**) Following injection of contrast medium, the liver metastasis appears (*white arrows* and *yellow* +). This particular lesion had disappeared on the preoperative imaging following chemotherapy. This demonstrates the utility of CE-IOUS during standard IOUS, especially in those "missing" metastases following chemotherapy

"disappear" after chemotherapy. A recent paper reports that IOUS increases the intraoperative detection of these "disappearing" metastases in more than 50 % of cases [28]. The ability of IOUS to detect additional metastases is also improved by the use of contrast agents (Fig. 15.18a, b). CE-IOUS is more sensitive than conventional IOUS for detecting CRLM [32], with a sensitivity rate reported around of 97 % [29]. Recent papers have shown that CE-IOUS leads to a change in the surgical strategy in 14–30 % of CRLM cases [30, 31].

Hepatocellular Carcinoma

HCC is the fifth most common malignancy and represents the principal cause of death of cirrhotic patients [33–35]. Among the local treatments available, surgical resection is the most radical approach [36–39]. Intraoperative ultrasound enables identification of new occult lesions in 15–33 % of patients with HCC, and it is responsible for a change in operative strategy in more than 15 % of cases [27, 40] (Fig. 15.19).

IOUS is very important in those with cirrhosis and HCC. The hard and irregular surface of the cirrhotic liver makes detection of liver lesions by palpation very difficult, especially in the case of deep and small HCC [49]. Furthermore, atrophy or hypertrophy of the cirrhotic liver can make the localization of liver lesions and the definition of the liver vascularization more difficult. The use of IOUS allows for parenchymal-sparing resection and limits the number of patients undergoing major hepatectomy [50, 51].

However, IOUS has some limitations. In cirrhotic patients, less than half of the new lesions detected by IOUS are HCC.

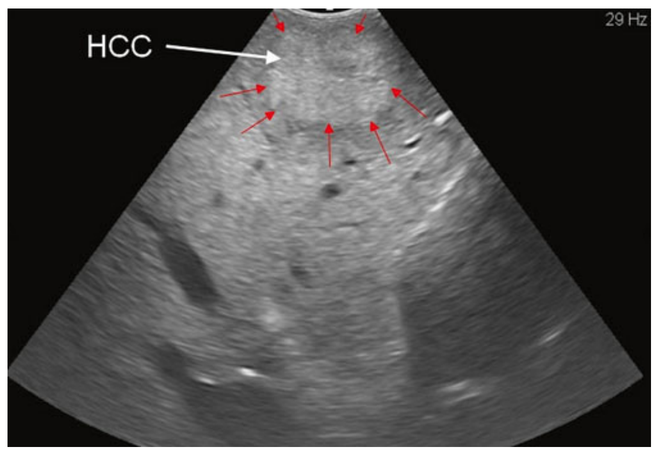

Fig. 15.19 Hepatocellular carcinoma. Note that it is isoechoic (*white arrow*) with a hypoechoic irregular rim (*red arrows*)

These lesions may be benign, which include regenerative and dysplastic nodules. The diagnosis of HCC is a critical point in cirrhotic patients to avoid resection and sacrifice of functioning parenchyma. In those with cirrhosis, the possibility to assess the vascularity of nodules detected by IOUS may improve the ability in discriminating malignant from benign lesions. In fact, except for those nodules with a mosaic ultrasound pattern, which are malignant in 80 % of cases, only 24–30 % of hypoechoic and 0–1 % of hyperechoic nodules are malignant when evaluating for HCC [4, 6]. A needle biopsy of a new lesion can be performed, but the false-negative rate is as high as 30 % [40–42]. Furthermore, a needle biopsy can lead to tumor seeding and ultimately may worsen the prognosis of a patient [43–45]. The analysis of a nodule's vascularity may provide the crucial information for differentiation.

Recently, CE-IOUS has been reported to evaluate tumor vascularization as is done with other contrast imaging modalities [46, 47]. CE-IOUS using SonoVue has been advocated as an alternative to differentiate HCC from benign lesions found during IOUS [7]. Using CE-IOUS, a change in the surgical strategy has been reported in 35–79 % of cases [7, 48]. Even using the newer contrast agent Sonazoid, CE-IOUS is able to detect new lesions in more than 20 % of cirrhotic patients. In a prospective study, Arita and colleagues showed that the sensitivity and specificity of CE-IOUS with Sonazoid for differentiating HCC were 65 and 94 %, respectively, and with an accuracy of 87 % [40]. (Refer to section "Intraoperative contrast-enhanced ultrasound" in Chap. 23, for further information.)

Using CE-IOUS, hypoechoic or hyperechoic nodules are considered malignant if the lesion [52]:

- Becomes hyperechoic (i.e., full enhancement) in the arterial phase and becomes hypoechoic in the delayed portal and late phase
- Remains hypoechoic with thin vessels supplying the nodule in the arterial and delayed phases
- Does not show early enhancement (i.e., full enhancement on the arterial phase) but remains hypoechoic in the delayed phases without peripheral and/or intralesional neovascularization (refer to section "Intraoperative contrast-enhanced ultrasound" in Chap. 23, for further information)

IOUS allows an accurate three-dimensional reconstruction of the relationship between the tumor, the portal branches, and the hepatic veins: This is a fundamental step in the definition of the proper surgical strategy. It remains unclear whether hepatectomy for HCC should be performed as anatomic resection or nonanatomic resection. The majority of recurrences occur in the liver as a result of subclinical metastases, which originate from the primary tumor through microscopic vascular invasion and peripheral spread along the intrasegmental branches. This is the most important factor associated with a poor prognosis [53–55].

On this basis, the routine removal of the hepatic segment fed by tumor-bearing portal tributaries (i.e., the entire functional unit through an anatomic resection) has been suggested to be more effective for tumor eradication [56]. On the other hand, most surgeons prefer, in cirrhotic patients, to preserve functional liver parenchyma with a nonanatomic resection in order to reduce the risk of postoperative liver failure. Two recent meta-analyses of observational studies addressed this still debated topic. The meta-analysis of Zhou et al. [57] found that disease-free survival was better in those undergoing anatomic resection as compared to nonanatomic resection. Chen and colleagues [58] demonstrated similar results in terms of disease-free survival in their meta-analysis, however found no difference in overall survival between the two groups. Improved disease-free and overall survival in those undergoing anatomic as opposed to nonanatomic resection was also found by Cucchetti and colleagues [59]. However, in this meta-analysis, the nonanatomic resection group had a higher proportion of cirrhosis, which affected both disease-free and overall survival. These meta-analyses are limited as they include only retrospective observational studies and not randomized studies. Limited resection guided by IOUS is simpler than the routine segmentectomy as there is no need to identify and ligate the portal branch, which supplies the area of the liver to be resected. If resection is not feasible, either because of the extent of the tumor or because of a high risk of postoperative liver failure, percutaneous ultrasound-guided embolization of the portal branch supplying the tumor may be performed. Embolization can prevent a massive portal invasion that may further increase the preexistent portal hypertension and lead to a GI bleeding.

Benign Tumors

The most important role of IOUS in the benign tumors is to discriminate between them from malignant lesions. Usually, metastases that arise from the same primary malignancy have a similar size and similar ultrasound appearance. Therefore, if two or more lesions of similar size have different ultrasound appearances, it is possible that one lesion represents malignancy while the other may represent a different diagnosis, such as a benign lesion. Hemangiomas vary widely in appearance, but are typically soft. On Doppler ultrasound, hemangiomas do not have increased flow as compared to the adjacent liver parenchyma. They are solitary in 90 % of cases and are typically hyperechoic. Among the other solid tumors, such as adenoma and focal nodular hyperplasia, an ultrasound-guided biopsy is necessary if the diagnosis is in doubt.

Applications in the Hepatic Surgery

Hepatectomy

Certain steps should be followed in performing IOUS of the liver prior to liver resection. First, the tumor must be localized after performing a meticulous ultrasound. The probe should be moved slowly and gain should be modified to better characterize the tumor. The use of probe standoff with saline immersion, as described earlier, is useful to localize superficial lesions as is the placement of the probe on the opposite face of the liver. Secondly, anatomic variations should be noted and taken into consideration prior to liver resection. The hepatic and portal venous systems must be evaluated, especially since hepatocellular carcinomas frequently invade major vessels as can colorectal cancer metastases. Once the tumor is localized and all segments of the liver have been evaluated, the relationship of the tumor and vessels in terms of vascular proximity, occlusion, and invasion is integrated by the surgeon. Color flow and Doppler US are frequently used to discriminate dilated bile ducts and blood vessels. If a vascular thrombus is identified, it may be important to distinguish between a tumor-associated thrombus, which is avascular, and a tumor thrombus, which has an arterial waveform at pulsed Doppler evaluation. It is always important to exclude the presence of a thrombus in critical areas such as the hepatic venous confluence.

Once a full evaluation of the liver anatomy and tumor features is complete, the best surgical strategy is chosen. In cases of deep lesions, the liver capsule can be marked with cautery overlying the lesion under ultrasound. Furthermore, the hepatic veins and portal branches can be marked to define the limits of resection. Ultrasound can be used during parenchymal resection to confirm the resection line and to ensure completeness of resection. During parenchymal transection, the air bubbles within the resection line are visible under ultrasound. A wet compress within the resection line also allows ultrasound visualization of the resection margin. Thus, during resection, the correct resection line can be verified using ultrasound.

Intraoperative ultrasound is imperative to evaluate the extent of the tumor in the liver. Ultrasound findings in the operating room can lead to a change in the surgical strategy or a contraindication of the planned surgery. For example, consider a CRLM case where the preoperative imaging demonstrates disease to be localized to the right liver; however, IOUS demonstrates disease to extend to the left liver and compress the left hepatic vein. Here, the planned resection is contradicted. On the other hand, consider a case where a small metastasis is found to be abutting or invading a segmental portal branch by IOUS; a parenchymal-sparing, such as segmentectomy or subsegmentectomy, may be undertaken [60]. Lastly, if multiple metastases of colorectal cancer are found to be bilateral under IOUS, consideration can be given to a two-stage hepatectomy (classic or ALPPS) [61–64].

Biopsy

Despite the improvement of preoperative imaging, the diagnosis of a lesion may be difficult to establish, such as in the case of small lesions in cirrhotic patients. If IOUS or CE-IOUS fails to discriminate between a benign and malignant diagnosis, an ultrasound-guided biopsy of the lesion is preferable (Fig. 15.20). Biopsy under ultrasound guidance can be performed and the specimen is analyzed as a fresh frozen section by pathology. We prefer to biopsy using a Menghini or Tru-Cut needle, which obtains a specimen that measures up to 2 mm of diameter.

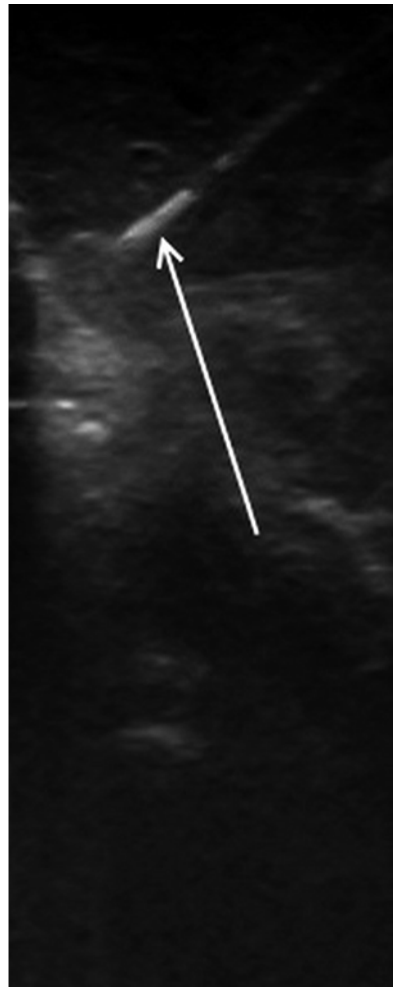

Fig. 15.20 A practical application of intraoperative ultrasound is biopsy. Depicted here is the intraoperative biopsy of a hypoechoic lesion (*white arrow*: biopsy needle)

To avoid hemorrhage, the biopsy needle is passed through normal parenchyma to reach the tumor for biopsy. If the biopsy demonstrates malignancy, resection of the liver parenchyma between the liver surface and the lesion where the needle passed during biopsy is necessary. This is to ensure completeness of resection as tumor seeding via the needle track can occur during biopsy.

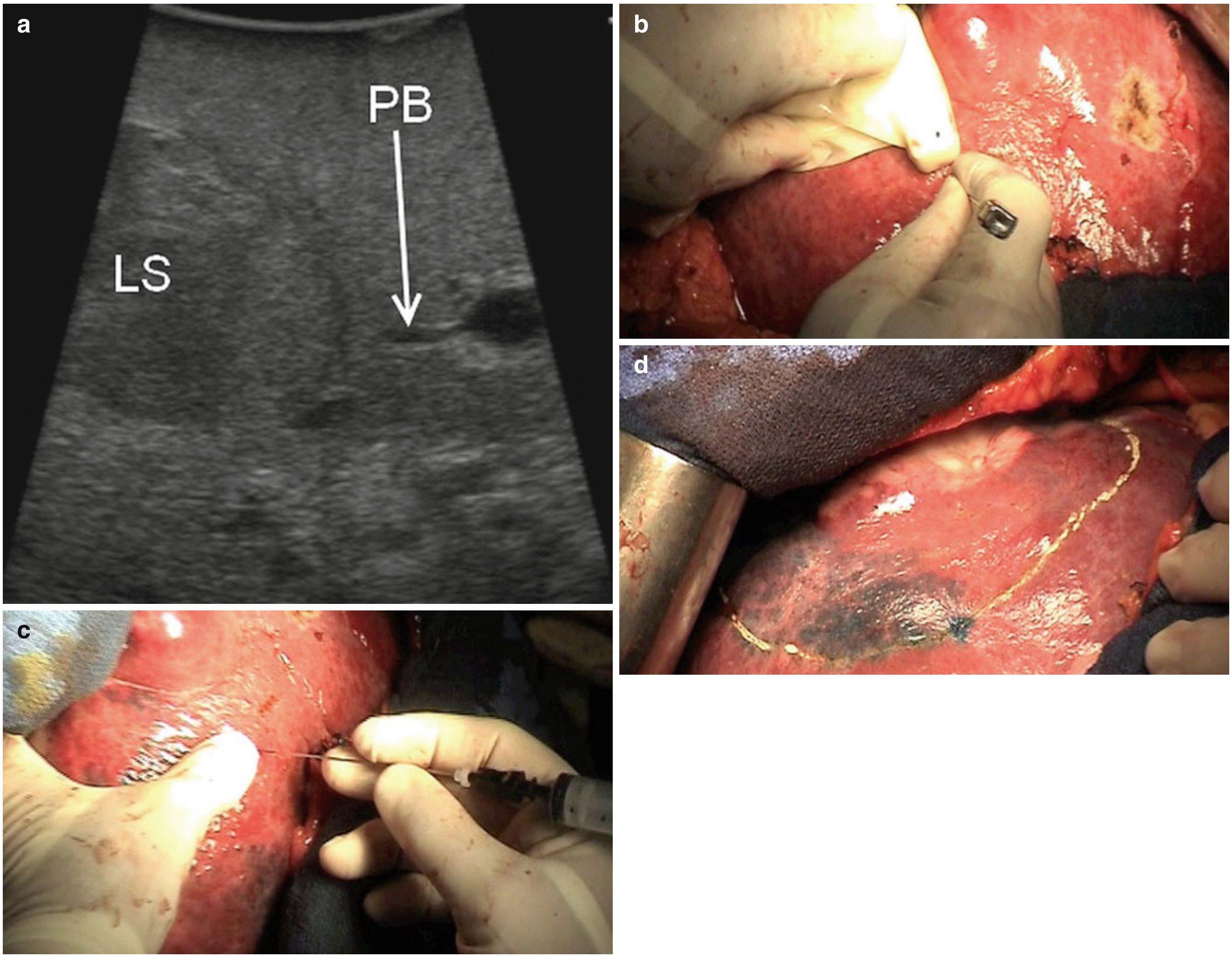

Fig. 15.21 Ultrasound-guided anatomic hepatectomy by dye injection. (**a**). Using US, the lesion (*LS*) with feeding portal branch (*PB*) is identified. (**b**) A Chiba needle is inserted under US guidance into the portal vein supplying the tumor. (**c**) Injection of methylene blue via the Chiba needle into the portal vein. (**d**) Methylene blue marks the extent of resection required by the portal supply

Ultrasound-Guided Anatomic Hepatectomy by Dye Injection

As described above, HCC can invade the portal venous branches either by direct invasion or by spread of cancer cells via the portal vein, which supplies the tumor. In patients with impaired hepatic function, a limited resection should be carried out in order to prevent postoperative hepatic failure. Therefore, in cirrhotic patients, a complete resection limited to the portal space containing the tumor is mandatory. This type of resection can be carried out by using blue dye injection guided by IOUS and is termed subsegmentectomy by a Japanese team [65]. After the tumor is identified by IOUS, the portal vein supplying the tumor is accessed under ultrasound and blue dye (methylene blue) is injected. The stained area defines the limits of the resection and is marked by electric cautery. In patients with HCC, an arterial-portal shunt is not uncommon, and, therefore, hepatic artery branch should be occluded during injection. This will ensure containment of the blue dye to the portal unit requiring resection (Fig. 15.21).

Ultrasound-Guided Vessel Compression

It is generally considered that for anatomic sectionectomy, preventive division of the sectional vascular pedicles by an extrahepatic approach is required for definition of the hepatic area to be resected. However, many of the proposed techniques are technically demanding and time consuming and have associated drawbacks [66–71]. According to Torzilli and colleagues, IOUS-targeted bimanual liver compression can be an effective method to identify subsegmental and segmental areas of the liver and to remove them in an anatomic fashion [72, 73]. IOUS and, if needed, CE-IOUS are performed before using the US-guided vessel compression technique. Once the tumor is identified, the most peripheral portal pedicle supplying the tumor is located under IOUS. The hemiliver where the lesion is located is partially mobilized. The surgeon's left or right hand is placed below the right or the left hemiliver, respectively, while the IOUS probe, handled by the surgeon's other hand, is placed above the liver. Both hands are positioned at the level of interest under IOUS, which is at the most distal portion of the vessel, but proximal to the tumor to be removed. The surgeon uses his/her fingertips and the IOUS probe to compress bilaterally the liver at the targeted position. This results in compression of the portal pedicle supplying the tumor, as previously identified. This maneuver is constantly monitored by real-time US. The IOUS probe is maintained on the liver surface until discoloration is noted. Once the first assistant marks the discolored area with the electrocautery, the compression is released. Due to the thickness and the shape of the liver profile, bimanual compression is more difficult to apply for lesions located in segments 1, 8, or superior 4. These areas should be demarcated by compressing the segmental branches of the adjacent segment, section, or hemiliver. Once the area is demarcated, IOUS is used to guide liver resection.

The main advantage of this technique is that it is not invasive, as it does not require any additional vascular access, dissection, or clamping. The technique is always feasible and totally reversible. It does not require vascular division, injection, or ablation. Once the compression is released, there is full return of the liver to the initial condition. Mobilization of the liver to accomplish the targeted compression may be required to perform the liver dissection. Furthermore, this maneuver can minimize the area of resection by choosing, under IOUS, the most peripheral and suitable level of compression of the feeding portal and arterial branches. This has the potential added value of further sparing liver parenchyma, as compared with a complete segmentectomy. It may be potentially applied in each segment of liver as long as the thickness of the parenchyma and the anatomy of liver are suitable [60]. This technique has even been described for resection of segment 8 [74].

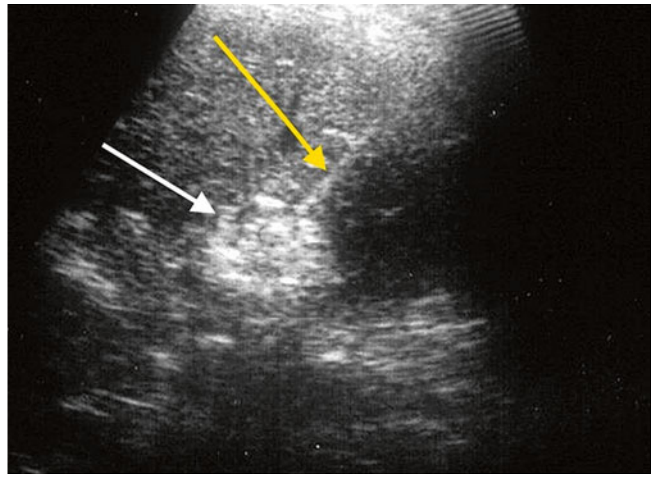

Fig. 15.22 Radiofrequency (RFA) liver tumor ablation. The radiofrequency needle (*yellow arrow*) is inserted into the lesion (*white arrow*) under US guidance. Once the radiofrequency energy is applied, the efficacity of the procedure can be monitored by the appearance of a hyperechoic rim around the lesion

Guidance of Intraoperative and Percutaneous Radiofrequency Ablation and Other Ablative Techniques

Hepatic resection is the most effective treatment for patients with primary or metastatic hepatic malignancies. Unfortunately, liver resection can be limited by a poor functional reserve of the remnant liver in cirrhosis and by the presence of multifocal bilateral lesions in metastatic disease. Nowadays, radiofrequency ablation (RFA) has been accepted as a treatment for primary and liver metastases when liver resection is contraindicated. Four prospective randomized studies showed superiority of RFA compared to ethanol injection in terms of local recurrence and overall survival in those with HCC [75–78]. Furthermore, there are now at least five reports, including one randomized trial, comparing RFA with resection for HCC. RFA has been shown to have similar local tumor control with a lower rate of complication for small HCC [79–83]. IOUS guidance during RFA is useful to identify the tumor, to guide the RFA needle into the tumor, and to check the efficacity of ablation (Fig. 15.22). (Refer to Chap. 17 for further information.)

Application in Liver Transplantation

IOUS has an important role in liver transplantation (LT). It is routinely used to assess the status of vascular anastomoses. Pulsed and color Doppler evaluation of the hepatic

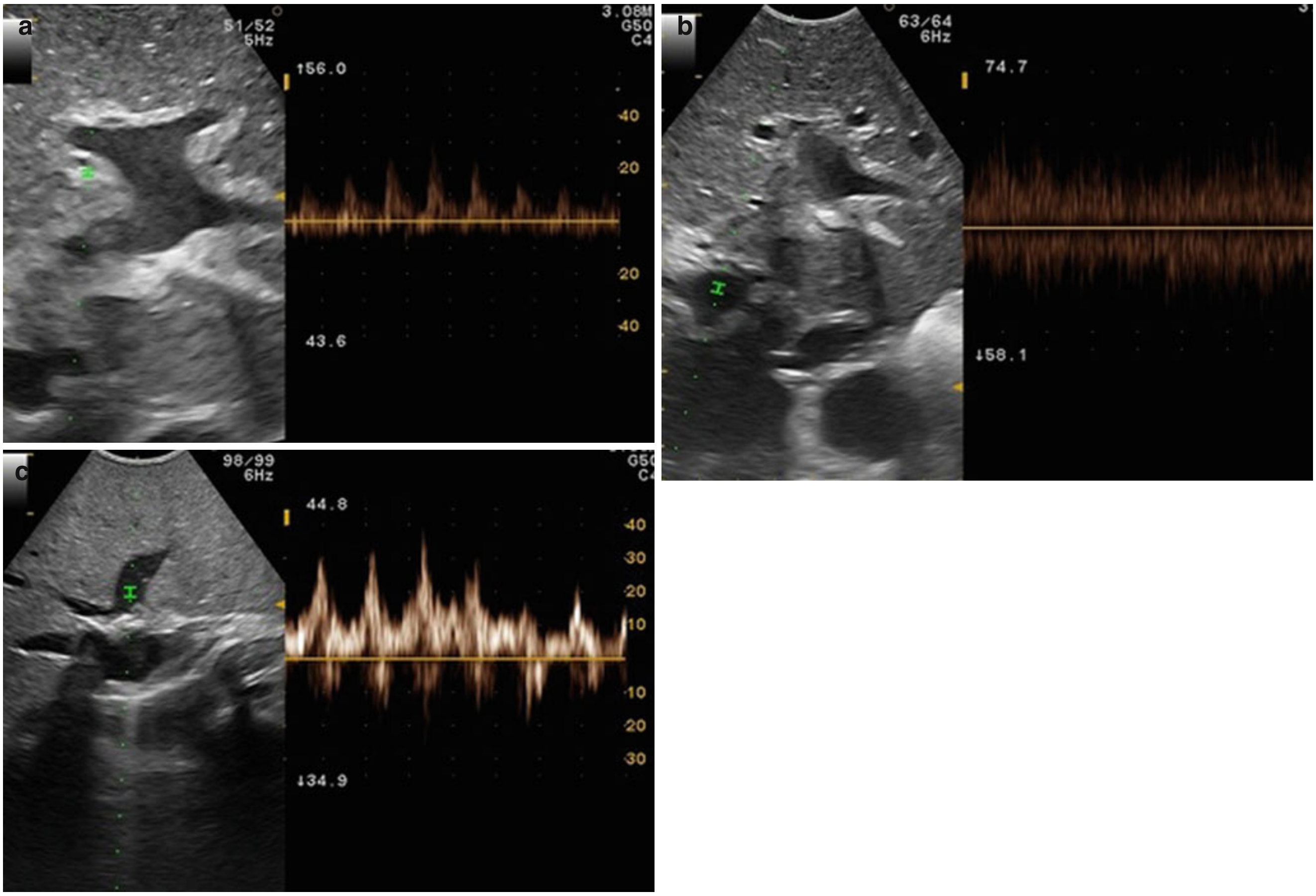

Fig. 15.23 Intraoperative ultrasound during liver transplantation. Each vessel is evaluated using Doppler in this series of figures. (**a**) The arterial flow, (**b**) portal flow, and (**c**) hepatic venous flow are verified. In each slide, the green notch indicates the vessel being assessed

artery as well as the study of the portal vein and the inferior vena cava (IVC) should be included in the ultrasound exam.

Sometimes, primary graft nonfunction is related to vascular complications, which can be addressed during the operation. Therefore, its detection during LT is extremely important.

We perform color Doppler IOUS (CE-IOUS) once the vascular anastomoses are done. A complete examination should show good flow within the main hepatic artery, proximal and distal to the anastomosis, as well as in the right and left hepatic branches (Fig. 15.23a–c). Usually, the hepatic artery has low-impedance waveform pattern with flow during the diastolic phase. The absence of flow in the hepatic artery would suggest a hepatic artery thrombosis (HAT). The normal hepatic vein waveform pattern shows cyclical variations of flow velocity during inspiration and flow reversal flow the contraction of the right heart. Nonphasic hepatic vein waveforms can be found in vena caval stenosis or thrombosis (i.e., Budd-Chiari syndrome). The typical pattern of the portal vein demonstrates almost continuous flow, with variations related to breathing movements.

CE-IOUS at the end of LT has been useful for us to better evaluate portal, arterial, and hepatic venous flow. CE-IOUS can be useful to detect arterial flow where classic IOUS has failed to demonstrate flow. On the other hand, in patients with normal flow on IOUS, altered arterial perfusion may be detected by CE-IOUS (Fig. 15.24a–c). IOUS examination is also required during the harvesting phase of living donor liver transplantation (LDLT). Ultrasound examination of the hepatic veins is essential in planning and guiding resection during LDLT.

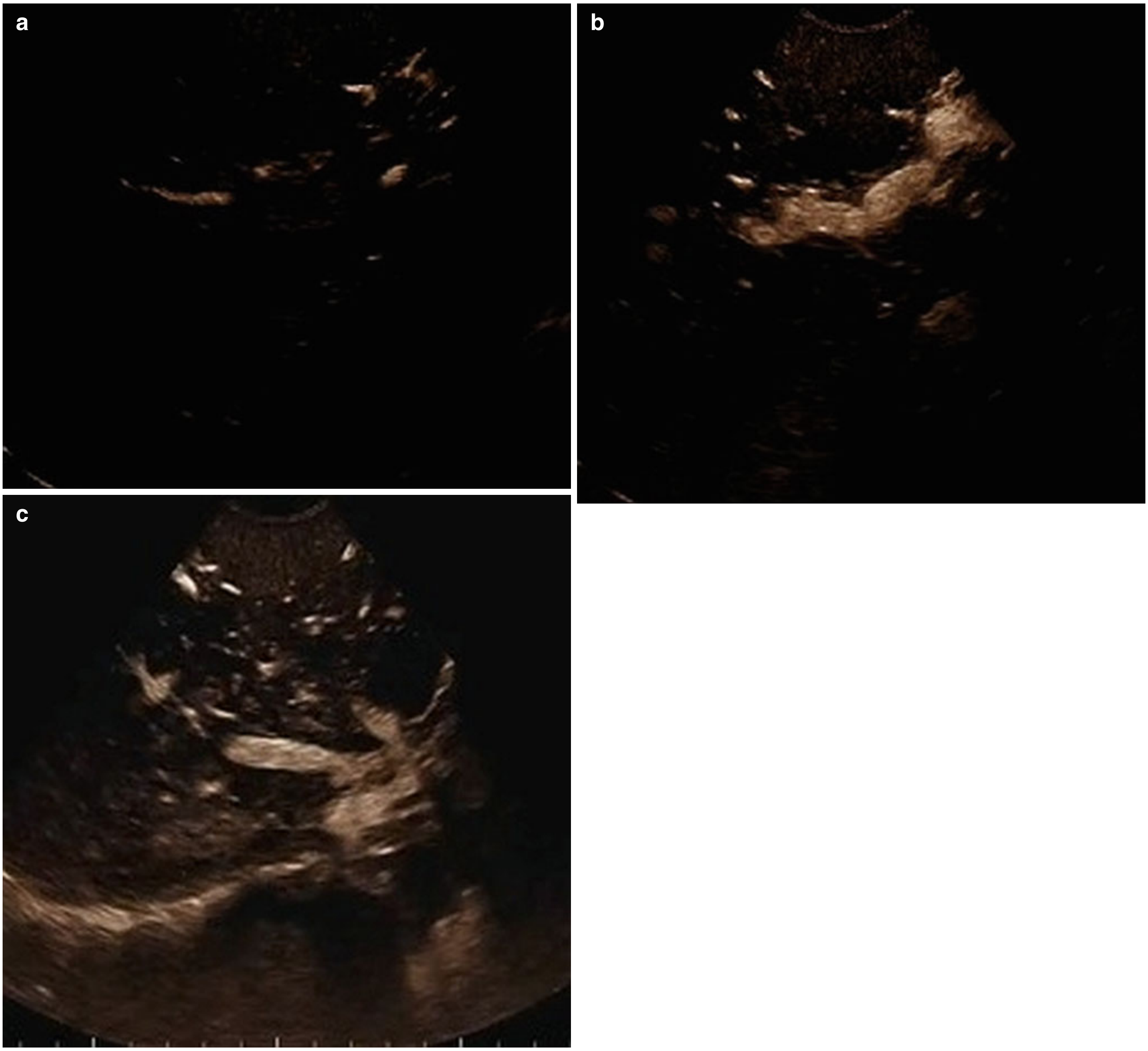

Fig. 15.24 CE-IOUS during liver transplantation. CE-IOUS is performed at the end of liver transplantation to verify patency of the (**a**) arterial, (**b**) portal, and (**c**) hepatic venous phases

Conclusion

IOUS provides crucial diagnostic and staging information to the surgeon during liver surgery.

The use of IOUS is mandatory during hepatic surgery and should be part of surgeons' professional training and experience. Despite the high quality of preoperative imaging, IOUS is still an essential tool in detecting lesions and planning and executing the surgical strategy.

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