Ultrasonography of the Liver

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Diagnostics series on liver diseases for the physician with a special interest in hepatology

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Ultrasound of the liver is painless, radiation-free, repeatable and widely available. It is therefore the investigation of first choice when liver disease is suspected. The disadvantage is the necessity to establish the findings during the examination, the high dependency on the experience of the examiner and the non-standardized image documentation. Table 1 shows the type of questions that can be elucidated by liver ultrasoundography. In combination with colour Doppler ultrasound and the numerous ultrasound-guided diagnostic and therapeutic procedures, the range of indications has broadened considerably. Great experience is required in order to make full use of these additional possibilities.

If there are positive findings, the question of appropriate and above all economical supplementary diagnostic investigation arises. This is where a high degree of knowledge about the accuracy and costs of the individ-

### Table 1: Indications for ultrasound examination.

- Diffuse liver disorders
- Focal liver lesions
- Biliary disease
- Suspected vascular processes
- Upper abdominal symptoms
- TMN classification of malignant tumors
- Orientation before surgery (anatomy, segment classification, variants of normal)
- Monitoring and follow-up
- Ultrasound-guided diagnostic and therapeutic procedures
ual investigation methods is required of the ultrasound examiner. In general, early biopsy should be considered when an abnormality is found on ultrasound, as it can shorten the diagnostic process economically (Pasha et al., 1998).
“Curved array” transducers have the advantage of a fan-shaped echo propagation with a relatively small contact surface. For routine purposes a 3.5 MHz transducer is used, and in very slender persons, a 5 MHz transducer may be useful. Modern machines have “tunable” transducers that allow different frequencies. Both the depth of penetration and the resolution can be improved by technical refinements such as “harmonic imaging” or the combination of fundamental sound and the “compound scan” method. Very good artefact suppression is also achieved with these techniques. The availability of colour Doppler equipment is ideal; this has opened up a new domain in ultrasonography of the liver (Seitz et al., 1997). The sector transducer, which offers a good view into the liver with a minimal contact area, especially transcostally, has also proven its worth. The sector transducer is essential in patients after surgery with large dressings or scars (e.g. during follow-up after liver transplantation).

Ultrasound examination of the liver takes place with the patient in supine position. Examination in the left lateral position can improve visibility of the liver and especially of the hilum in the presence of ascites. Examination of the seated patient from behind can also be useful when the anterior view is restricted.

During the examination, the size of the liver, which is usually measured in the midclavicular line, is recorded. The examiner also assesses the deformability of the liver during inspiration and expiration and during one-finger palpation. The shape of the liver, the caudal margin of the lobes of the liver and the echo texture and sound transmission are analyzed. The branches of the portal vein, the arteries, the intra- and extrahepatic bile ducts, the hepatic veins and the gallbladder are also assessed. The area around the liver (in the re-
region of the hepatoduodenal ligament) is examined for lymph nodes, ascites and collateral veins. The size of the spleen is also determined. Measurement of the diameter of the hilum has proved useful, where values under 5 cm are usually considered normal. The liver is examined systematically in different planes as shown in figure 1. Starting with a longitudinal scan to the left of the xiphoid process (A in figure 1), the transducer is then moved further to the right parallel to the long axis of the body. The patient is asked to inspire as deeply as possible in case the left or right lobe of the liver is initially beneath the costal arch. When the transducer is moved further to the right as far as the right flank, where the size, shape, internal structure and mobility of the right hepatic lobe can be assessed; furthermore, the gallbladder, porta hepatis with portal vein, the common bile duct and hepatic artery become visible, along with the kidney at the extreme right. The echo texture of the liver and kidney can now be compared, which is important in diagnosing fatty liver and cirrhosis.

This is followed by transverse scans in the epigastrium (B), when the transducer is moved parallel to the costal margin. Using a curved array transducer, it is possible to examine high into the dome of the diaphragm by tilting it in a cranial direction with gentle pressure under the costal margin and with deep inspiration. By tilting it in the postero-inferior direction, the stellate hepatic vein confluence, the right branch of the portal vein and the gallbladder become visible in succession. If this tilt is applied at the extreme right, the right kidney can usually be imaged in cross section with the liver as acoustic window. The intercostal scans (C in figure 1) are used to show the subphrenic areas of the right hepatic lobe. When the diaphragm is ele-
Fig. 1: Scanning sequence in liver examination.
vated, e.g. in the case of meteorism, ascites and/or atelectasis of the right lung, the liver can be displaced cranially under the right costal margin, so that it is difficult to image it using the subcostal scan. In these cases, the intercostal scans offer a way of assessing larger areas of the right lobe of the liver and the gallbladder.

It is also important to examine dynamically in different intercostal spaces both from cranial to caudal and from ventral to dorsal during inspiration and expiration. In some cases, an incomplete left lateral decubitus position may be helpful; this causes the liver to “drop” medial and caudal to the ribs.

**Segmental anatomy of the liver**

The Couinaud system of liver segments (figure 2), which can be removed deliberately surgically, is used predominately today. Localizing space-occupying lesions according to their segmental anatomy affects the surgical procedure. The lines of separation are formed by the sites of intersection of branches of the portal and hepatic veins. Because of the strictly horizontal scanning, segmental classification is easier on computed tomography. A detailed description of the segmental anatomy can be found in Frank (1992) and Takayasu and Okuda (1997).

Typical scans are shown below in the other illustrations. In each case, diagrams explain the represented structures and the segments. Figure 3 shows a longitudinal scan over the inferior vena cava. The caudate lobe is separated from the left lobe of the liver by a fine
The size of the caudate lobe (segment I) is assessed when cirrhosis or Budd-Chiari syndrome is suspected. The ligamentum teres (LT) is normally the obliterated remnant of the umbilical vein, which can be reopened in portal hypertension (see below).

Figure 4 shows a longitudinal scan in the axis of the left main branch of the portal vein. Portal veins are easy to distinguish from hepatic veins, as they have strong wall reflections which derive from the accompanying bile ducts and arteries. High-resolution transducers separate these wall reflections and must not be mistaken for the “double barrelled phenomenon” found in mechanical cholestasis.

Figure 5 shows an almost strict longitudinal scan over the gallbladder. Here, the degree of filling, the wall thickness, the contents (stones, polyps, tumor) and possible tenderness are examined.
Fig. 3:
VCI = IVC
ARD = RRA

Longitudinal scan over the inferior vena cava (IVC) which appears dorsally at the level of the right renal artery (RRA). I = segment I, corresponding to the caudate lobe. The left main branch of the portal vein is continued in the ligamentum teres (LT). PV designates the extra-hepatic portal vein, P the partially shown junction of the head and body of the pancreas.
Fig. 4:
Longitudinal scan over the left main portal vein (LP). It separates segments II and III of the left lobe of the liver on the left. IVC (VCI) = inferior vena cava, LHV (LLV) = left hepatic vein.
Fig. 5:
Longitudinal scan over the gallbladder (GB). RPV = right main portal vein,
VCI = inferior vena cava.
Figure 6 shows a transverse section at the level of the right main portal vein, which usually follows a horizontal course. Under good acoustic conditions, this scan offers a wealth of information. It can show segments IV, V and VI and a cross section of the right kidney.

Figure 7 shows a view of the costal margin in deep inspiration. This shows the “hepatic venous star”. The width of the hepatic veins, which can be identified easily by the absence of the reflection from the wall, varies greatly. Nevertheless, their width in the vicinity of the inferior vena cava is seldom greater than 1 cm. They usually have an extended course, and the vena cava demonstrates double pulsations. In cirrhosis (see below) and severe fatty liver, the hepatic veins are compressed, and in Budd-Chiari syndrome they are occluded by thrombosis.

Figure 8 shows a slightly oblique scan, to demonstrate the gallbladder bed and the left main portal vein. Segment IV (quadrate lobe) is bounded by these structures. A reduction in the size of the segment is said to be a sign of cirrhosis. The transverse diameter is measured at the point where the left portal vein is joined by the branch from segment IV.

Figure 9 shows an intercostal scan taken relatively cranially. The white line passes through the transversely encountered right hepatic vein (RH) and the branching of the right portal vein (RP). This marks the boundary of segments V and VIII.

Figure 10 also shows an intercostal scan, which demonstrates the right kidney and segment VI.
Fig. 6:
Transverse scan in the axis of the right portal vein (RPV). LL = left lobe of the liver, PS (PT) = tail of pancreas, SMA (AMS) = superior mesenteric artery, Ao = aorta, Sp (WS) = spinal column, RK (RN) = right kidney, VCI = inferior vena cava, segments IV (quadrate lobe), V and VI.
Fig. 7:
Transverse scan along the right costal margin to show the “hepatic venous star”, which determines the corresponding segments. Dorsal to the right hepatic vein lies segment VII, segment VIII lies between the right and middle hepatic veins, and segment IV between the two branches of the middle hepatic vein. VCI = inferior vena cava, H (C) = heart.
Fig. 8:
Demonstration of segment IV, which is bounded by the gallbladder bed (arrow) and the left portal vein. The measurement line runs at the level of segmental branch IV and is normal at 5 cm (RK [RN] = right kidney).
Fig. 9:
Cranially positioned intercostal scan. Branching of the right portal vein (RP), right hepatic vein (RH) [RL], VCI = inferior vena cava.
Fig. 10: Intercostal scan over the right kidney (RK) [RN]. Parts of segment VI are becoming visible.
Liver size and variation

Measurement of the vertical and deep diameters in the right midclavicular line (MCL) is usually adequate to determine the size of the liver. The vertical diameter is normally 12 ± 3 cm, and the deep diameter 9 ± 1 cm. However, marked individual variation can be observed. For instance, the vertical diameter of the liver in the MCL can be greater than 15 cm in a person of asthenic habitus; if it is a slender organ with a small deep diameter, the total size of the liver is still entirely normal. The Riedel lobe is a normal variant. This can cause the right lobe of the liver to extend far in a caudal direction. When the liver is up to 13 cm in the MCL, about 93% of those examined have a normal liver. Only with a length greater than 15 cm in the MCL is there definite hepatomegaly, usually as a result of liver damage (Gosink and Leymaster, 1981). The shape of the liver is also variable.
Diffuse liver disorders

The size and shape, consistency, surface, internal structure and the intrahepatic vessels and bile ducts are used in the investigation of diffuse liver disorders. Determination of the size is of little value as it depends on the measurement parameters and, for instance, on the patient’s height. These may be supplemented by findings outside the liver, especially signs of portal hypertension when cirrhosis is suspected or the syndrome of hypersplenism or lymph nodes in the region of the hepatoduodenal ligament in viral hepatitis (Schwerk, 1987; Forsberg et al., 1987).

Table 2 and figure 11 list syndromes associated with diffuse liver changes and the expected findings on ultrasonography.

The sensitivity of ultrasound in diffuse liver disease depends greatly on the gold standard employed. Biopsy has a sensitivity of only 60–70% in cirrhosis compared to laparoscopy with targeted tissue sampling (Cardi et al., 1997). Reasons for the inferiority of biopsy alone include aspiration from areas which are only slightly altered and insufficiently large biopsies, which do not allow fibrosis to be distinguished from complete cirrhotic transformation. A biopsy optimally should contain ten portal areas.
Diffuse disorder | Comment
--- | ---
Fatty liver | Characteristically echogenic liver with at least 30% fatty infiltration of the hepatocytes. Increasing dorsal echo attenuation.
Acute and chronic hepatitis | No definite sonographic correlate, but acute tends to be hypoechoic, and signs of portal hypertension are possible in fulminant hepatitis. There is an increased incidence of detection of lymph nodes in the hepatoduodenal ligament and fatty infiltration in hepatitis C.
Acute and chronic hepatic congestion | Ascites and distended hepatic veins are characteristic, and fibrosis or cirrhosis develops when long-standing.
Vascular disorders | Nonhomogeneous and more echogenic areas and enlargement of the caudate lobe in Budd-Chiari syndrome, ectatic vessels in Osler’s disease.
Fibrosis | Uncharacteristically coarse and uneven internal echoes are possible. Distinction from fatty infiltration and cirrhosis difficult. (Fibroscan®?)
Cirrhosis | Irregular surface and signs of portal hypertension are very sensitive and specific, and liver size correlates directly with the prognosis.

Table 2: “Diffuse” parenchymal liver disorders.
Fig. 11: Diagram of the changes in diffuse liver parenchymal alterations which can be observed sonographically.

Normal liver:
Sharp edges, fine homogeneous internal echoes, 12–15 cm in the midclavicular line (MCL)

Fatty liver:
Blunt edges, enlarged up to 20 cm in the MCL, echogenic internal structure, dorsal echo attenuation, hepatic veins barely distinguishable

Cirrhosis:
In the initial stage enlarged, finely to coarsely nodular surface, coarse internal echoes, poorly distinguished hepatic veins
Ultrasound reports very often contain diagnoses such as “diffuse liver parenchymal damage” or descriptions such as “rounded inferior margin”. There are hardly any normal reports among beginners. Our own investigations showed that alterations of shape alone, increased echogenicity or the use of the concept of “diffuse liver parenchymal damage” are seldom associated with genuine liver pathology, when biopsy or the transaminases are used for comparison (Ochs et al., 1994). Only when a definitive diagnosis such as fatty liver, hepatic congestion or cirrhosis is made sonographically does this correlate with real pathological changes in more than 70% of cases.

**Fatty liver**

Fatty infiltration of the liver can be found when there is at least 30% fatty infiltration of hepatocytes (Joseph et al., 1991; Saverymuttu et al., 1986). A fatty liver is usually enlarged with blunt edges and increased echogenicity. There is posterior echo attenuation, so that the diaphragm cannot be visualized with older equipment even with the gain turned up. The hepatic veins are more difficult to identify than in the normal liver (figures 12 and 13). With severe fatty liver hepatitis, portal hypertension can occur. Regionally, there can be reversed flow in the intrahepatic portal veins. A fatty liver can be compressed by finger palpation under vision. Ultrasound is superior to enzyme measurement in diagnosing fatty liver (Petritsch et al., 1987; Steinmaurer et al., 1984). The degree of fatty infiltration can be estimated very well on ultrasound (Ricci et al., 1997).
Fig. 12: Transverse scan through a markedly fatty liver. The echogenic internal hepatic structure, the increasing posterior echo attenuation and the poorly demarcated hepatic veins are characteristic.

Fig. 13: Transverse scan of a fatty liver showing the right kidney (N = K) and the gallbladder (GB). Markedly increased echogenicity of the liver parenchyma compared to the kidney.
Sonography is also an important building block in establishing the diagnosis of non-alcoholic fatty liver (Ahima, 2007). Nonhomogeneous greater or lesser degrees of fatty infiltration can be mistaken for focal lesions and may induce complex investigations for diagnosis. Focal disorders of fat distribution are found in metabolic disorders (diabetes mellitus, obesity, alcohol abuse), after chemotherapy and with vascular alterations in the liver. Echo-poor or echogenic areas are usually not sharply demarcated and are localized around the blood vessels or gallbladder (figure 14). They have a dynamic course. Occasionally computed tomography or biopsy is necessary if a tumor is suspected (see also pseudotumors of the liver).

Fig. 14: Fatty liver with regional variation in the degree of fat infiltration in a patient with obesity and diabetes mellitus.
Acute and chronic hepatitis

In acute hepatitis, the ultrasound appearance is uncharacteristic. The importance of ultrasonography lies in excluding mechanical cholestasis or a chronic liver disorder (tumor, cirrhosis). The liver is enlarged and the edge is blunt. The internal structure is homogeneous and shows fine loosely distributed individual reflections. The echogenicity is normal or somewhat reduced. It may be accompanied by moderate splenomegaly and a contracted gallbladder with thickened wall. Ascites can occur when the disease is severe, indicating incipient portal hypertension. Lymph nodes in the region of the hepatoduodenal ligament (Forsberg et al., 1987) are said to correlate with the activity of chronic hepatitis C (Dietrich et al., 1997). In chronic hepatitis, the individual reflections are coarser, leading to an increase in echogenicity. In chronic hepatitis C, increased echogenicity on ultrasound corresponds to fatty infiltration on biopsy. There is no sonographic substrate for the extent of the inflammatory activity or fibrosis (Dietrich et al., 1998). Nonhomogeneity can occur subsequently, which can extend to nodular changes. Analyses of texture, even computer-aided, have not hitherto become clinical routine (Taylor et al., 1986).
Hepatic congestion

Acute and chronic hepatic congestion can be characterized well on ultrasound. Figure 15 shows widely congested hepatic veins and ascites. When it is long-standing, fibrosis or cirrhosis can develop (cardiac cirrhosis). Ascites is nearly always present. Protein measurement in ascites gives levels of 4 g/100 ml or more. Colour Doppler ultrasound shows slow but undulating flow in the portal vein. Figure 15 shows acute hepatic congestion with distended hepatic veins. Figure 16 shows chronic hepatic congestion, early cirrhosis is possible.

Fig. 15:
Acute hepatic congestion with distended hepatic veins and noncollapsing inferior vena cava (VCI).
A = ascites, HV (LV) = hepatic veins
Fibrosis and cirrhosis

The sonographic appearance in fibrosis and cirrhosis is variable depending on the degree of the pathological anatomical changes. Early cirrhosis may not be apparent on ultrasound. However, it is also possible that hepatomegaly, a rounded edge and increased echogenicity with coarsening of the individual reflections are present, giving a sonographic appearance similar to that found with fatty infiltration. The transition from fibrosis (reversible) to cirrhosis (irreversible) is continuous. When several non-invasive parameters are included (ultrasound findings, serum fibrosis markers), a sensitivity of 87% for diagnosing cirrhosis can be achieved (Oberti et al., 1997; Gaiani et al., 1997; Di Lelio et al., 1989). The severity of the fibrosis or cirrhosis can be determined with a method of determining liver stiffness known as transient elastography. The correlation of

Fig. 16: Chronic hepatic congestion in cardiomyopathy due to secondary hemochromatosis. The inferior vena cava does not collapse, the inferior edge of the liver is blunted, and there is ascites (A). The cirrhosis has possibly developed because of the congestion and hemochromatosis; however, there is obvious undulation of flow in the portal vein on colour Doppler ultrasound.
Fibroscan® with liver histology is particularly good in homogeneous conditions such as hepatitis C; even the degree of portal hypertension can be deduced (Vizzutti et al., 2007).

Table 3 and figure 17 reproduce important direct and indirect signs. Each sign on its own usually has low sensitivity and specificity. Considered overall, an experienced examiner assisted by color Doppler sonography can make diagnoses which exceed the quality of biopsy. The gold standard in the diagnosis of cirrhosis continues to be laparoscopy. In cirrhosis induced by hepatitis C, the diagnosis is made by biopsy alone in only 60–70% of cases. Further studies of Fibroscan® must be conducted before biopsy can be omitted. Obesity and ascites limit this method (Friedrich-Rust and Zeuzem, 2007).

Table 3

Sonographic criteria of cirrhosis:
Liver size variable
Enlargement: early cirrhosis
“Shrunken liver”: end stage
Irregular surface
Nonhomogeneous internal structure
Coarse echo texture
Compressed hepatic veins
Irregular calibre of the intrahepatic portal vein branches
Pseudo double-barrelled appearance (prominent arteries)
Narrowing of segment IV
Enlargement of the caudate lobe
Thickening of the wall of the gall-bladder
Lax gallbladder (often with stones)
Fig. 17: Findings in cirrhosis which can be made with conventional ultrasound.
Irregular surface

The irregularity of the hepatic surface can be demonstrated (with high-resolution transducers) even without ascites (Di Lelio et al., 1989). This irregularity has a high positive predictive value of up to 84% in viral cirrhosis (Oberti et al., 1997; Gaiani et al., 1997). Ultrasound parameters can be combined with serum parameters. Here, measurement of the hyaluronic acid appears to give additional information with regard to fibrosing activity. The diagnosis of cirrhosis is easy when there is ascites and a grossly altered surface (figure 18).

Coarse internal echoes are an expression of fatty infiltration, fibrosis or regenerative nodules. Various liver segment diameters have also been utilized. For instance, the transverse diameter of segment IV (quadrate lobe, figure 8) is thought to be only $28 \pm 9$ mm in cirrhosis, and $43 \pm 8$ mm in normal persons.

Fig. 18: Decompensated liver cirrhosis. The irregular surface and nonhomogeneous internal structure are striking.
(Lafortune et al., 1998). The relationship of the caudate lobe to the left lobe of the liver is also regarded as a sign of cirrhosis (figure 19) (Giorgio et al., 1986). An enlarged cirrhotic liver has a favourable prognosis in contrast to the small coarsely nodular liver (Zoli et al., 1990).

Thickening of the gallbladder wall is observed with and without ascites (figure 20). A wall thickness greater than 4 mm is found in more than half of patients with cirrhosis. The wall thickness correlates with the Child-Pugh class and with the presence of ascites (Wang et al., 1997). On colour Doppler ultrasound, gallbladder varices can sometimes be detected as the cause of the wall thickening.

Fig. 19: Markedly enlarged caudate lobe (LC) (segment I) in cirrhosis.
Portal hypertension

The detection of signs of portal hypertension increases the accuracy of the diagnosis of cirrhosis on ultrasound (Vilgrain et al., 1990). Figure 17 and table 4 give a summary of the signs and parameters of portal hypertension. Only some cases of cirrhosis are associated with portal hypertension; the reasons for this are unclear. If colour Doppler ultrasonography is available, portal hypertension can be best quantified by the congestion index, which includes the velocity of flow in the portal vein and the cross-sectional area of the portal vein (Moriyasu et al., 1986). However, this has not become accepted as routine.

Portal hypertension is often accompanied by splenomegaly (figure 21). However, splenomegaly is not essential. A normal-sized or only slightly enlarged spleen does

Fig. 20:
Markedly thickened gallbladder wall in cirrhosis and ascites. Collateral vessels were found on colour Doppler sonography.
### Table 4: Sonographically detectable signs of portal hypertension (CDU = colour Doppler ultrasound).

- Splenomegaly
- Ascites
- Distension of the portal vein (> 1.3 cm) and veins draining into it (splenic vein, superior mesenteric vein)
- Pathological congestion index (CDU)
- Absence of respiratory fluctuations in diameter (< 10 %)
- Absence of compressibility of these vessels
- Increase in diameter of portal vein at the hilum of the liver
- Portosystemic collaterals (ventricular coronary vein)
- Patent umbilical vein
- Thickening of gastric wall
- Thickening of gallbladder wall
- Spontaneous splenorenal shunt
not exclude hypersplenism or portal hypertension. Particularly marked splenomegaly of over 8 cm in the region of the hilum should suggest splenic vein thrombosis, an additional hematological disorder, idiopathic non-cirrhotic portal hypertension or schistosomiasis.

In portal hypertension, the portal vein is usually distended to over 1.3 cm. The splenic vein (figure 22) or superior mesenteric vein no longer demonstrate compressibility and the fluctuation in size with respiration is less than 15%.

Fig. 21:
Indirect sign of cirrhosis: marked splenomegaly with a diameter at the hilum of 7.3 cm (normal up to 4.5 cm).
Fig. 22:
Indirect sign of cirrhosis due to finding of portal hypertension with splenic vein up to 1.6 cm in diameter projected onto the pancreas.

Fig. 23:
Large-diameter collaterals projected onto the head of the pancreas. Duodenal varices were seen endoscopically. Con = confluence, C = collaterals, LL = left hepatic lobe.
Collateral vessels can also be demonstrated if sought precisely even without colour Doppler ultrasound. At the splenic hilum, they can be equivalent to a spontaneous splenorenal shunt or gastric varices. The ventricular coronary vein or other collateral vessels can sometimes be demonstrated originating from the confluence (figure 23). The finding of a patent umbilical vein (Cruveilhier-Baumgarten syndrome, figure 24) or of paraumbilical veins is proof of portal hypertension. Grape-like collaterals going in the retroperitoneal direction can be the source of severe intra-abdominal hemorrhage (figure 25).

A fresh portal vein thrombosis shows an extension of the vessel, filled with echogenic material, while the so-called cavernomatous transformation develops subsequently (see vascular alterations).
Ultrastronography of ascites

Small volumes of ascites are identified as a narrow perihepatic or perisplenic echo-free rim. When ascites is first detected and complications are suspected, diagnostic paracentesis should be performed.

Sonographic detection of ascites is greatly superior to percussion. In 80% of cases, ascites has a hepatic cause. In 10% of cases, there is an underlying malignancy. The remaining 10% are distributed through renal, pancreatic, tuberculous, cardiac and other rare causes. Fibrin threads indicate an inflammatory process. They are also observed in patients on peritoneal dialysis. Sedimentations can be found following hemorrhage after ruptured spleen, ascites aspiration and bursting of intra-abdominal collaterals or spontaneously ruptured hepatocellular carcinoma. Diagnostic paracentesis gives important information.

Fig. 25:
Large collaterals projected on to the right renal hilum. Flow in the dorsal direction was found on colour Doppler ultrasound. In addition, ascites is present.
Spontaneous bacterial peritonitis (SBP) is a complication of ascites. The diagnosis is also made by diagnostic paracentesis. The ascites can appear sonographically as non-echofree (figure 26). After frequent paracentesis or after operations with peritonitis, compartments can form which make further paracentesis impossible (figure 27).

Fig. 26:
Non-echofree ascites as expression of SBP. The patient complained acutely of abdominal pain. Aspiration yielded a leucocyte count of 6000/µl.
DS = BL = bowel loop.
Vascular alterations of the liver

*Budd-Chiari syndrome (BCS)*

This syndrome consists of postsinusoidal portal hypertension, due to occlusion or displacement of the hepatic veins. The principal pathological mechanism in our latitudes is thrombotic occlusion due to hematological disorders or genetic coagulation defects (Menon et al., 2004). There is also an increased incidence in female smokers taking contraceptives. Obstruction of hepatic veins by membranes (“webs”) is seen rarely in Western Europe. Other causes are compression due to primary tumors or metastases. Rarely, there is a primary sarcoma of the hepatic veins or inferior vena cava.

Fig. 27:
Loculated ascites in a cirrhotic patient as a consequence of a complicated cholecystectomy. There are honeycombed compartments under the right diaphragm.
The clinical syndrome is fulminant in the form of hepatic and renal failure with ascites or subacute or chronic. In the latter case, cirrhosis is often diagnosed incorrectly. Complete and incomplete causes of BCS are being diagnosed increasingly frequently by ultrasound and especially by colour Doppler sonography.

BCS can be identified on conventional ultrasound also (Braun et al. 1983). The criteria are summarized in table 5. Brancatelli et al. have compiled a collection of characteristic imaging findings (2007). Figures 28–30 show examples of BCS. The caudate lobe can appear hypoechoic like a tumor and compress the inferior vena cava, leading to thrombosis in this region.

### Table 5: Ultrasound findings in BCS.

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<td>Enlargement of the liver (acutely painful)</td>
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<td>Absence of imaging of hepatic veins</td>
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<td>Enlarged caudate lobe (with compression of the inferior vena cava)</td>
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<td>Intrahepatic portal venous shunts</td>
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<td>Tumor-like parenchymal nonhomogeneity (regeneration nodules, nodular regenerative hyperplasia)</td>
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Fig. 28: Subacute BCS with ascites, narrowed echogenic hepatic veins (LV = HV) and thickened gallbladder wall (GB).

Fig. 29: Acute BCS. Longitudinal scan over the inferior vena cava (VCI) which is greatly compressed by the acutely enlarged caudate lobe. This led to obstruction of flow beneath it. The problem was relieved fully by a transjugular portosystemic stent shunt (TIPS).
Veno-occlusive disease (VOD)

VOD has a similar clinical appearance to Budd-Chiari syndrome. However, the large hepatic veins are patent. Toxic and autoimmune processes lead to fibrotic and inflammatory occlusion of small hepatic veins. There is usually icterus and ascites clinically. Multiorgan failure can develop rapidly. VOD is found in up to 50% of patients after allogenic bone marrow transplantation. The diagnosis is difficult on conventional sonography. Hepatosplenomegaly, thickening of the gallbladder wall, a wide portal vein, small hepatic veins, ascites and a patent umbilical vein are typical. Colour Doppler ultrasound can detect the portal hypertension and, in particular, the reversed intrahepatic portal vein flow. Flow in the portal vein is demodulated and the RI of the hepatic arteries is over 0.75 (Lassau et al., 1997). The diagnosis is made by biopsy. A transjugular biopsy

Fig. 30:
Longitudinal scan over the inferior vena cava (VCI = IVC). BCS for six months. The caudate lobe (LC = CL) has large veins and thus partially compensates the abnormal venous outflow. (Con = confluence).
can be taken in liver failure and if therapeutically indicated. An important differential diagnosis is toxic cardiac damage. Raised transaminases, ascites and hepatomegaly are found in this situation also. However, the hepatic veins and the vena cava are congested. The portal vein demonstrates reduced but pulsatile flow indicating unimpeded sinusoidal perfusion.

**Portal vein thrombosis (PVT)**

A complete or incomplete occlusion can be found acutely or subclinically in patients with and without cirrhosis (figure 31). In patients with cirrhosis, acute portal vein thrombosis is always suspicious for the presence of a hepatocellular carcinoma (HCC) until proven otherwise. If vessels are found in the thrombus by Doppler ultrasound, the diagnosis of HCC can be regarded as confirmed.

Fig. 31: Fresh incomplete portal vein thrombosis. Even without colour Doppler ultrasound, echogenic areas can be found in the portal vein.
In non-cirrhotic PVT, there is an increased incidence of genetic coagulation factors (e.g. factor V disease, see also Budd-Chiari syndrome). The extent of the thrombosis is divided into four stages, depending on the degree of thrombosis. In stage IV, the portal vein, splenic vein and superior mesenteric vein are occluded. There is little information about the natural course of PVT. Smaller intrahepatic thromboses can resolve or can become the origin of periportal fibrosis. This is how non-cirrhotic portal hypertension is believed to develop. Larger thromboses can progress to cavernomatous transformation within a few weeks (figure 32, Braun et al., 1984). If this has occurred, a liver transplant or surgical shunt procedure can become technically impossible. The liver then receives its portal supply through collaterals (e.g. gallbladder wall) or capsular vessels. The main blood supply then comes from the arteries. The transformation can involve the splenic and mesenteric veins. There is then a danger of fundal variceal bleeding. Collaterals in the region of the splenic hilum in the form of a gastroportal or gastrocaval shunt or a spontaneous splenorenal shunt can sometimes be shown with conventional ultrasound and particularly well with colour Doppler sonography (Seitz et al., 1997).
Osler-Weber-Rendu disease

This is a rare hereditary disorder in which multiple angiodysplasias occur, which usually become apparent in the gastrointestinal tract. Corkscrew-like vascular malformations can be detectable in the liver (figure 33). Large arteriovenous shunts can develop, leading to heart failure. Cirrhosis can develop as a result of this disorder. The syndrome of hypersplenism can produce severe hemorrhage, including intracranial bleeding, due to thrombocytopenia. Hepatic involvement can be diagnosed when the diameter of the common hepatic artery is more than 1 cm (Caselitz et al., 2003).

Fig. 32:
Cavernomatous transformation of the portal vein. This oblique scan over the hepatoduodenal ligament does not show any echo-free vascular structure. The portal vein rather is replaced by echogenic material. On colour Doppler sonography, numerous collaterals could be seen over the liver capsule and around the former portal vein.
Fig. 33: Typical intrahepatic vascular malformations in Osler’s disease. Colour-coded ultrasonography shows numerous arteriovenous shunts.
The search for focal lesions and the interpretation of focal abnormalities with their diagnostic and therapeutic consequences represent the main task of liver ultrasonography. Figure 34 shows the variety of possible focal lesions. Focal lesions can be demonstrated according to their frequency, their ultrasonographic appearance or their histological classification. No system entirely meets the real situation. In the concrete case, the examiner is faced with two situations:

- the search for a liver focus
- finding a liver focus.

Algorithms are given below for both sets of problems. The basic question in looking for a liver lesion is whether there is a metastasis from a known primary tumor. A hepatic space-occupying lesion is also sought in conditions which suggest a tumor or in the case of recent cholestasis. If a lesion is found, investigation can often be shortened by ultrasound-guided biopsy. If no lesion is found when there is a high degree of suspicion, the examiner must initiate the next useful investigations.

The incidental finding of a hepatic lesion is usually followed by a “wait and see” attitude if the focus lacks signs of malignancy. Thus, the examiner must consider whether he can give a firm diagnosis using ultrasound. This decision depends greatly on the examiner’s experience. As figure 34 shows, multiple histological conditions (Altman, 1994) contrast with only few unequivocal ultrasonographic appearances in differential diagnosis.

The finding of a focal hepatic lesion in principle always opens up the entire range of differential diagnosis. In practice, however, the findings are limited to a few differential diagnoses. Table 6 shows that the majority of detected focal lesions are metastases or cysts, which do not cause problems in the
Fig. 34:
Tumors and tumor-like lesions of the liver, classified according to histological criteria. The findings which are encountered most frequently are shaded in pink.
180 hepatic lesions were unclear initially. Further investigation then resulted predominantly in metastases, cysts or hemangiomas. The finding of hepatic lesions is also greatly dependent on the patient groups investigated. In liver centres, hepatocellular carcinomas are seen very frequently, while they are a rarity in a general practice.

The introduction of echo contrast enhancers has brought about a revolution in ultrasoundography, especially in the area of the liver (Wermcke, 2006).

Great progress was achieved with echo contrast or echo signal enhancers (CEUS) in the improved detection and characterization of space-occupying lesions. There are two echo signal enhancer products on the market, Levovist® und Sonovue®, and others are in the pipeline. With corresponding hardware, which works with phase-inverted sound application, the reflections are extinguished

<table>
<thead>
<tr>
<th>Total</th>
<th>75,840</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liver focal lesions</td>
<td>180</td>
</tr>
<tr>
<td>No abnormality on repeat examination</td>
<td>35 20%</td>
</tr>
<tr>
<td>Metastases</td>
<td>59 33%</td>
</tr>
<tr>
<td>Hemangiomas</td>
<td>24 14%</td>
</tr>
<tr>
<td>Cysts</td>
<td>26 14%</td>
</tr>
<tr>
<td>HCC</td>
<td>8 4.4%</td>
</tr>
<tr>
<td>Adenomas</td>
<td>5 2.8%</td>
</tr>
<tr>
<td>Echinococcus/abscesses</td>
<td>3 1.5%</td>
</tr>
<tr>
<td>Other lesions</td>
<td>20 11%</td>
</tr>
</tbody>
</table>

Table 6:
Frequency of causes of 180 initially unclarified focal lesions (Weiss 1987) in 75,840 ultrasound scans.
on linear reflectors such as liver cells and give a virtually absent signal. The gas bubbles of the echo signal enhancers are non-linear reflectors that are stimulated to vibrate by the sound waves. They reflect non-linearly as the compression and expression have slight differences. Because of this, the reflections are not extinguished and give a signal. Levovist® can be sonicated only with high sound energy (high mechanical index, MI); when the transducer is swivelled, the bubbles burst, producing what is known as a burst. An examination with low MI is possible with Sonovue®; the bubbles only vibrate and remain detectable for minutes. Thus, observation of the perfusion of both the liver and the space-occupying lesion is possible. Triple-phase examination is also used in computed tomography, with a so-called spiral “driven” in each phase with corresponding radiation burden. Figure 35 a shows these phases. The arteries appear about 15 sec after injection of an echo signal enhancer. This phase is important in cirrhosis, adenoma and in metastases and hepatocellular carcinoma (HCC). Metastases can “wash out” the contrast in the portal venous phase, which occurs in the late phase or parenchymal phase at the latest. In hepatic tissue there are sinusoids in which the bubbles can persist for a long time. Non-hepatic tissue does not have these sinusoids so that these lesions are apparent as spaces in the late phase.

Figure 35 b shows in diagram form the following echo signal enhancers.

**Hemangioma:** There is so-called globular enhancement in the early arterial phase. Later the lesion “flows” from without inwards (iris phenomenon). Non-stained parts can correspond to scars or thrombi.
Fig. 35 a: Dynamics in triple-phase sonography with echo contrast enhancers. As in computed tomography, three phases of contrast uptake can be distinguished. Examples of characterization of space-occupying lesions are shown.

Fig. 35 b: Behavior of different lesions after echo signal enhancers. Native or fundamental mode on the left, then the arterial, portal venous, and late phase (see also figure 35 a).
Adenoma: the domain of CEUS. It is important that the lesions are sometimes visible only for seconds in the early arterial contrast phase and later become isoechogenic with the surrounding liver tissue. They thus become invisible.

Focal nodular hyperplasia (FNH): Spoke-like arteries are strongly enhanced in the early arterial phase. The lesion fills early with contrast and usually remains somewhat more echogenic than the surrounding parenchyma in the late phase.

Abscess: The native scan shows hypoechoic to anechoic cystic areas. After echo signal enhancers the margin can take up contrast, while the lacunar areas inside the abscess always remain anechoic and appear punched out.

Metastases: They have only one arterial inflow and one venous outflow. They can take up contrast arterially. In the portal venous phase and at the latest in the parenchymal phase, the metastases “wash out” the contrast and become anechoic. The metastases of neuroendocrine tumors stain particularly highly arterially. If there is a high chromogranin A in the blood, the diagnosis of such a tumor is highly likely.

Focal lesions appear ultrasonographically when they are distinguished from the surrounding hepatic tissue by their echo texture. Space-occupying lesions can become apparent indirectly by alterations in liver size, compression of blood vessels or biliary ducts or irregularity of the surface. Calcifications are apparent above about 3 mm, cysts above 3–5 mm, solid lesions above 5 mm. However, identification depends not only on the size of the lesion but also on
the equipment employed, the investigator’s experience and the location of the lesion. Lesions that are directly lateral or subdiaphragmatic or located at the caudal margin of the liver are difficult to detect. The detection of focal lesions through echo signal enhancers is now comparable to computed tomography, and the two methods are partially complementary.

**Pseudotumors**

With the introduction of imaging, localized parenchymal alterations which sometimes have no anatomical pathological correlate became visible. Table 7 gives a summary of ultrasonographically detectable phenomena which can look like focal lesions or imitate malignant processes. Occasionally, calcifications are found in the liver, which are distinguished from echogenic hepatic lesions by their posterior echo extinction. Such calcifications are often then found in other organs also, especially in the spleen. They can usually be attributed to previous infections such as tuberculosis. Aerobilia or hepatolithiasis must be considered in the differential diagnosis. Calcification of regressed metastases, hepatocellular carcinoma or in the wall of echinococcal cysts is also found occasionally. Focal major or minor fatty infiltration is sometimes mistaken for a tumor. Increased focal fatty infiltration is often found particularly around the falciform ligament or around branches of the portal vein; focal minor fatty infiltration is also associated with certain vascular areas and with the caudate lobe (figure 14). Nonhomogeneous fat distribution is found in patients with alcoholic disease, diabetes mellitus, non-alcoholic steatohepatitis (NASH) or during chemo- or hormone therapy. On computed tomography, areas with different Hounsfield...
<table>
<thead>
<tr>
<th>In metabolic disorders, chemotherapy or hormone therapy:</th>
<th>Vascular alterations:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nonhomogeneous fatty infiltration</td>
<td>Nodular regenerative hyperplasia in Budd-Chiari syndrome (BCS)</td>
</tr>
<tr>
<td>Focal lesions in Wilson’s disease</td>
<td>Nonhomogeneous enlargement of the caudate lobe in BCS</td>
</tr>
<tr>
<td>Alpha-1-antitrypsin deficiency</td>
<td>Pseudoaneurysm of the portal vein</td>
</tr>
<tr>
<td>Type I tyrosinemia</td>
<td>Aneurysm of the hepatic arteries</td>
</tr>
<tr>
<td>Gaucher’s disease</td>
<td>Intrahepatic shunts</td>
</tr>
<tr>
<td>Porphyrias</td>
<td>Focal lesions in Osler-Weber-Rendu disease</td>
</tr>
<tr>
<td>Anatomical structures:</td>
<td>Map-like changes in HELLP syndrome</td>
</tr>
<tr>
<td>Ligamentum teres, Zahn’s grooves</td>
<td>Peliosis hepatis</td>
</tr>
<tr>
<td>Postoperative conditions, trauma:</td>
<td>Liver infarct (very rare)</td>
</tr>
<tr>
<td>Needle biopsy, endoscopy, spontaneous</td>
<td>Fibrosis/cirrhosis:</td>
</tr>
<tr>
<td>Scars after cholecystectomy</td>
<td>Macronodular regenerative nodules</td>
</tr>
<tr>
<td>Defect after resection</td>
<td>Confluent focal fibrosis</td>
</tr>
<tr>
<td>Clips</td>
<td>Irregular surface</td>
</tr>
<tr>
<td>Aerobilia</td>
<td>Biliary tract abnormalities:</td>
</tr>
<tr>
<td>Seroma</td>
<td>Hepatolithiasis</td>
</tr>
<tr>
<td>Bilioma</td>
<td>Caroli’s syndrome</td>
</tr>
<tr>
<td>Gas in the portal vein</td>
<td>Bile duct abscesses</td>
</tr>
<tr>
<td>Hematoma/bleeding into lesion</td>
<td>Tumors:</td>
</tr>
<tr>
<td></td>
<td>Extrahepatic tumors</td>
</tr>
</tbody>
</table>

Table 7: Alterations which can cause problems in differential diagnosis, appearing on ultrasound as circumscribed space-occupying lesions.
units are found. If biopsy is performed, areas of variable echogenicity should be aspirated. Ideally, a margin between major and minor fatty infiltration will then be visible histologically. Observation is feasible in the case of incidental findings. The nonhomogeneous areas are dynamic, for instance, with better control of diabetes mellitus or abstinence from alcohol (see also p. 27, fig. 14). It can be shown with echo signal enhancers that these areas take up contrast identically in the parenchymal phase so that they do not correspond to metastases.

**Hematomas**

Hematomas in the liver are usually echo-free initially and when they liquefy subsequently. They usually follow the anatomy and therefore have irregular outlines. Typically, they occur following trauma (figure 36) or after

---

**Fig. 36:** Subcapsular, relatively fresh hematoma after diagnostic laparotomy and cholecystectomy. At the same time, there is cavernous transformation (CVT) of the portal vein, which had the appearance of a biliary tract tumor on CT, leading to laparotomy.
invasive diagnostic procedures. However, spontaneous bleeding occurs with coagulation disorders or in the presence of pre-existing liver lesions. The lesions become more echogenic and better demarcated at first and can be demonstrable for weeks after the trauma. When they liquefy, there is again a change in the pattern of echogenicity. Residual conditions have the appearance of cysts.

**Rare examples**

An appearance similar to metastases can occur in Wilson’s disease (figure 37). These changes correspond histologically to fatty infiltration and fibrosis, which make the liver appear echogenic. There are hypoechoic islands of normal hepatic tissue in between. This appearance is believed to indicate a favourable prognosis for treated Wilson’s disease (Vogel et al., 1988).

**Fig. 37:** Multiple hypoechoic lesions in a liver with Wilson’s disease. No evidence of malignancy was found on biopsy.
Cystic processes

Liver cysts

Dysontogenetic liver cysts are found at up to 0.15% of autopsies and on up to 3% of liver ultrasound scans. The typical liver cyst (figure 38) has a soft edge, a typical dorsal echo enhancement and a completely echo-free interior. If these criteria are met and this is a coincidental finding, no further investigations are necessary. It is called a polycystic liver when there are more than 10–15 cysts. Hepatic metabolic functions are preserved intact for a long time even with multiple cysts. The sensitivity of ultrasound is comparable to that of CT and MRI. The finding of hemorrhage in polycystic syndromes is best made with MRI. Liver cysts are often associated with cysts in other organs (kidney, pancreas, spleen). This combination is observed in the Hippel-Lindau syndrome. Larger cysts over approx. 5–10 cm can cause

Fig. 38:
Typical cyst of the liver. The interior is echo-free, the wall is thin, and there is posterior echo enhancement.
symptoms and lead to slightly raised parameters of cholestasis (figure 38 a + b). They can be sclerosed under ultrasound control with ethanol or saline (see interventional therapy). The differential diagnosis of cysts includes Echinococcus cysticus, early, almost echo-free metastases (melanoma, lymphoma, ovarian and esophageal carcinoma, carcinoid, cystadenoma, cystadenocarcinoma), Caroli’s syndrome, liquefied hematomas and abscesses. Diagnostic aspiration is sometimes required to aid diagnosis.

Fig. 38 a: Very large liver cyst with a diameter of 17 cm which gave rise to upper abdominal symptoms (N = right kidney).
Echinococcosis:
Echinococcus cysticus is relatively rare in Germany. In the typical case, several daughter cysts are found in a cyst bordered by a relatively echogenic rim. Echinococcal cysts are occasionally found in other organs. Classification of stage can be deduced from the sonomorphology (Lewall, 1998; Strohm and Weimer, 1997; Di Matteo et al., 1996; Caremani et al., 1996; Richter et al., 2003). Sonomorphology is relatively typical so that in experienced hands the correct diagnosis can be made rapidly together with the serology. The WHO has proposed a classification for cystic lesions (figure 39). In this overview, the typical cyst (CL) is seen on the left. This is followed by the stages of Echinococcus cysticus:

CE1 Ovular cysts with thicker wall than dysontogenetic cysts, but at this initial stage, they can be mistaken for liver cysts (figure 39).
Cysts with daughter cysts (figure 39 and 40). CE1 and CE2 are regarded as the active form.

Honeycomb structure or pathognomonic wheel spoke structure (figure 39, 41 and 42). In this case, the ability to maintain the pressure in the cysts was lost; as a result, the membranes are floating in the main cyst. The activity is transitional.

Solid tumor with possible calcifications. Degenerative late stage, where the solid parts are possibly due to earlier bacterial superinfections. Cyst walls lying close together give the appearance of double membranes.

Up to a few years ago, surgery was regarded as the treatment of choice of cysts. Today, less invasive therapies such as (ultrasound-guided) puncture, aspiration, injection and reaspiration (PAIR, McManus et al., 2003) are preferred in the cystic stages. The cysts are sclerosed with 95% ethanol. Solid manifestations can be converted to cystic forms by medications in some cases and then treated by PAIR. Radiofrequency thermoablation has also been used.

Echinococcus alveolaris must be distinguished from the cystic form; it appears more like a diffusely infiltrating tumor and is not anechoic (figure 43).

The region of the hilum is usually affected, and E. alveolaris cannot be distinguished in appearance from a central bile duct carcinoma. The diagnosis is often made only at diagnostic laparotomy. If the diagnosis is made in time, treatment is medical in order to limit spread as much as possible. The

The serological test (an IgG ELISA) reaches a sensitivity of 85–94% and a specificity of 99%.
Fig. 39:
Summary of the cystic lesions according to the WHO. CL = cystic lesion. CE1 and CE2 correspond to the active form of Echinococcus cysticus. Large solitary cysts can be mistaken for harmless dysontogenetic cysts. Stage CE3 is designated as transitional. CE4 and CE5 are regarded as inactive.
Fig. 40:
Echinococcus cysticus, stage CE2. There are daughter cysts in the main cyst.
Fig. 41: Stage CE3: The honeycomb structure predominates.

Fig. 42: The honeycomb structure of stage CE3 is also shown well by computed tomography.
most radical surgery possible is accompanied by two-year follow-up treatment with albendazole (McManus et al., 2003).

**Abscesses**

Two large groups can be distinguished: pyogenic and parasitic abscesses. There is an increased incidence of pyogenic abscesses in the 5th to 7th decades, especially in immunosuppressed (AIDS, chemotherapy) or operated patients (biliary procedures, biliary malignancies, interventions). Diverticulitis or other foci can be the source. The ascending biliary form predominates (up to 70%), compared to hematogenous dissemination (up to 30%). Pyogenic abscesses are solitary in only half of cases (figure 44) and 70% of them are found in the right lobe. Aspiration provides a microbiological result in 80% of cases (usually E. coli, Klebsiellas, also enterococci, streptococci). Mortality is up to
11–25% and is particularly high in the case of multiple abscesses (figure 45). Pyrexia and abdominal pain are almost always present.

Table 8 shows the approach with pyogenic abscesses. In about 10–20% of cases, the origin of the infection is not found. There are several kinds of sonographic appearance. At an early phase, no capsule has yet formed and the abscess can be overlooked. The abscesses are usually echo-poor and show dorsal echo enhancement (figure 44). A capsule with dorsal echo enhancement appear later (figure 45), and the internal echoes are variable. On contrast-enhanced computed tomography, colouring of the capsule is pathognomonic. However, this effect can be absent. Abscesses can be shown excellently with echo signal enhancers. The hyperemic margin can be seen in the capillary or portal venous phase (Bauditz et al., 2007).

Fig. 44: Liver abscess. There is a hypoechoic space-occupying lesion with a suggestion of dorsal acoustic enhancement. The origin was severe infectious colitis. Treatment was with drainage and antibiotics.
Fig. 45: Multiple abscesses in a patient with a bile duct carcinoma. Placement of a stent in the common bile duct brought temporary improvement.
Table 8: Algorithm for pyogenic abscess.

Therapy

Antibiotics

Small abscesses

Drainage

a) abscess < 4 cm: single aspiration and irrigation with saline, antibiotics for three weeks

b) abscess > 4 cm: drain through pigtailed catheter

Operation

when drainage has been unsuccessful
With mixed infections and air inclusions, there is a complex picture, and the abscess may be mistaken for a tumor, especially when the classical clinical signs with pyrexia are absent.

Younger patients who give a history of spending time in the tropics often suffer from an amebic abscess. Pyrexia and upper abdominal symptoms can occur weeks after the return from tropical regions. Diarrhea due to the amebas can have a relatively bland clinical course. Solitary abscesses with homogeneous contents predominate (figure 46). Sedimentation can appear in this case also; there is dorsal echo enhancement. Abscesses which are superinfected have complex internal echoes (figure 47).

The diagnosis can be made from the history and the typical ultrasound appearance. The hemagglutination test is nearly always positive. Blood cultures typically are sterile. Diagnostic aspiration (usually not necessary) yields an odourless brownish cocoa-like liquid. Treatment is mainly conservative. It can take months before the abscesses disappear. If there is a risk of rupture or vicinity to the pericardium, drainage or surgical evacuation can be necessary. Since there are usually no severe concomitant illnesses in this group of patients, the prognosis is good.
Fig. 46: Amebic abscess in the right lobe of the liver 10 cm in diameter after a sojourn in the tropics. There are fine internal echoes which appeared with a change of patient position.

Fig. 47: No longer fresh amebic abscess 4 weeks after antibiotic therapy. The patient had only become ill with pyrexia 8 weeks after her return from India. The complex internal structure and the initial absence of a response to metronidazole suggested bacterial superinfection.
Benign liver tumors

Hemangioma

The commonest benign liver tumor is the cavernous hemangioma. It is found at 1–7% of autopsies. Women are affected five times more often. A growth-promoting effect of estrogens and progesterone is suspected. The ratio of solitary to multiple hemangiomas is 4–9:1. Complications are rare. Calcifications are found in 10% of cases. A hemangioma consists histologically of lacuna-like distended capillaries, through which flow is slow. A reticuloendothelial system is absent, so that the hemangioma remains unenhanced on colloid isotope scintigraphy. With increasing size, there is a tendency to thrombosis, fibrosis, cystic degeneration or calcification. The typical ultrasound appearance is of a strongly echogenic tumor with relatively smooth margins (snowball). The numerous impedance leaps of blood and vessel walls give rise to strong echoes, which can lead to repeat echoes posterior to the lesion (reverberations). There is usually an inflow or outflow vessel directly connected to the hemangioma (figure 48). The listed characteristics are typical of the capillary hemangioma, which seldom becomes bigger than 3 cm. The sonographic appearance can be extraordinarily varied in the case of hemangiomas greater than 3 cm (figure 49, 51). Most are of the cavernous type with sometimes wide vessel lacune. Hypoechoic structures can correspond to a thrombosis or fibrosis. In case of doubt, further investigation is performed, usually a spiral CT with biphasic contrast injection (table 9). On contrast CT, the surrounding parenchyma first becomes coloured, while the hemangioma appears as a gap. Small spots of contrast can be visible at this early phase in the region of the margin. Because of the slow
Fig. 48: Typical hemangiomas. Echogenic, relatively sharply demarcated lesions in the right lobe of the liver. A vessel can be seen in the upper part of the larger hemangioma.

Fig. 49: Atypical hemangioma 4.2 x 3 cm in diameter, with rather few internal echoes. However, on CT the lesion demonstrates a typical iris phenomenon. The echo-poor interior possibly corresponds to thrombosis.
Table 9: Findings and accuracy of various imaging techniques for hemangioma.

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ultrasound</td>
<td>80 %</td>
<td>up to 100 %</td>
<td>Problems in the event of thrombosis and with giant hemangiomas, and with echo-poor hemangiomas in a fatty liver. In nearly 80 % the iris phenomenon can be demonstrated with echo signal enhancers.</td>
</tr>
<tr>
<td>CT</td>
<td>85–95 %</td>
<td></td>
<td>Native: hypodense, after contrast iris phenomenon.</td>
</tr>
<tr>
<td>MRI</td>
<td>95 %</td>
<td></td>
<td>T1: hypointense, T2: native hyperintense, T2 with contrast iris phenomenon. MRI pattern little disturbed by fibrosis and thrombosis</td>
</tr>
</tbody>
</table>
blood flow, the hemangioma fills slowly from the margin towards the centre (iris phenomenon), while the contrast agent has already flowed out of the rest of the liver (figure 50). However, this behaviour of the contrast is also seen with metastases from a mammary carcinoma. Alternatively, MRI can be performed. Blood pool scintigraphy has become less important. On colour Doppler sonography, hemangiomas under 3 cm diameter do not give any colour signals in the interior or periphery. If colour signals are obtained and if a pulsatile signal is found particularly in the interior of the lesion, a hepatocellular carcinoma or metastasis should be suspected (vide infra). In 3% of small hemangiomas, nevertheless, arterial signals are found in the interior of the lesion with modern colour Doppler ultrasound equipment (Wachberg and Jilani, 1999). Contrast-enhanced colour Doppler sonography can also demonstrate the phases of so-called globular enhancement and the iris phenomenon (Wermke and Gassmann, 1998; Dietrich et al., 2007). The iris phenomenon occurs within 180 sec in 78% of cases of biopsied hemangiomas (Dietrich et al., 2007) and is therefore highly reliable (figure 51 left).

Hemangiomas can be aspirated (Brambs and Spamer, 1985; Dietrich et al., 2007). In doubtful cases, diagnosis can be hastened in this way and costs saved. As with all lesions, there should be a rim of normal hepatic tissue between the liver surface and the presumed hemangioma.

Differential diagnosis: echogenic metastases (colon carcinoma, neuroendocrine tumors) (Zimmer et al., 1995), focal nodular hyperplasia, lipomas, (rarely angiomyolipomas, e.g, in tuberous sclerosis) (Nonomura et al., 1996). In case of doubt, it is very helpful if comparison with earlier scans is possible.
Fig. 50: Contrast behaviour on CT. The native hemangioma is hypo- or isodense (arrow). After injection of contrast, the hemangioma fills from outside inwards (iris phenomenon, arrow, right side), while in the rest of the liver the parenchyma has become decoloured.
Fig. 51:
On the left is a hemangioma after injection of an echo signal enhancer. The border of the hemangioma shows nodular enhancement (red circle). In the right-hand picture, a typical hemangioma can be seen with a blood vessel in a congested liver in a patient with global cardiac failure. (A = ascites).
Progress: There is no tendency to malignant transformation. Growth in size can occur under hormonal influence. At sizes over 15 cm, a consumption coagulopathy is possible. Rupture is very rare and seen only with very large hemangiomas. An operation may be necessary in this situation. Asymptomatic giant hemangiomas are observed. Symptomatic hemangiomas can be operated, and no recurrence has been described. Individual case reports also recommend transarterial embolization.

**Liver cell adenoma**

The liver cell adenoma is a genuine epithelial tumor which has increased in incidence. It is found in fewer than 0.5 % of autopsies. Women are affected nine times as often as men. Growth occurs with steroid treatment. Men should be asked about anabolic steroids. It also occurs more frequently in the glycogenoses. The typical age for the disorder is 15–45 years. In 30 % it is a coincidental finding, and in up to 50 % it is found because of abdominal symptoms. There are complications in up to 30 % of cases, such as bleeding into the tumor or rupture, so that an emergency operation is required. In 90 % of cases, the tumor is solitary (Bleck et al., 1997).

Histologically, it consists of hepatocytes, portal areas and bile ducts, and Kupffer cells are usually but not always absent. The adenoma is often surrounded by a pseudocapsule. The adenoma can be difficult to distinguish histologically from normal hepatic tissue or from a highly differentiated hepatocellular carcinoma.

The ultrasound appearance is variable and not diagnostic. It is usually echo-poor, but it can also be echogenic, have complex echoes (figure 52) or demarcation from surrounding tissue may not be possible. With
Echogenic signal enhancers imaging is most successful in the early arterial phase. CEUS even appears to be superior to other methods. Occasionally, only a projection of the liver surface suggests the diagnosis. Since a malignancy cannot be excluded by any form of imaging, biopsy is required. The other imaging methods are also non-specific. The appearance is variable, and partly dependent on the fat content. Since malignant degeneration occurs, the current opinion is that adenomas should be removed surgically. Even histologically, distinction from a highly differentiated hepatocellular carcinoma can be difficult (De Carlis et al., 1997).

Differential diagnosis: hepatocellular carcinoma, fibrolamellar carcinoma, metastases, focal nodular hyperplasia.

Fig. 52:
Adenoma in segment IV confirmed by biopsy. The internal structure has complex echoes and does not allow precise diagnosis. At the same time, the patient who refused operation has a cavernomatous transformation of the portal vein with a congenital abnormality of coagulation. GB = gallbladder
Focal nodular hyperplasia (FNH)

Focal nodular hyperplasia (FNH) is a benign hepatic tumor and is found in 0.1–1% of autopsies. Women are affected twice as often. Steroid hormones are not regarded as causes but appear to promote growth so that it has hitherto been considered correct to discontinue them following diagnosis of FNH. This view has recently been challenged in a large series of 216 women with FNH (Mathieu et al., 2000). In this study the size and number of FNH was not influenced by use of oral contraceptives; in addition, pregnancy was not associated with FNH changes or complications. The typical age is 20–50 years. In 80% there is only one focus. Ruptures occur much more seldom than in the case of adenoma. In 45–80% it is a coincidental finding. One third of patients complain of abdominal pain (Kojiro et al., 1996; Bartlett et al., 1996).

All of the liver’s cell types are represented histologically. However, the bile ducts are rarefied and impaired in function. A few pathologists regard FNH as a hamartoma in association with vascular malformations (Takayasu and Okuda, 1997; Wanless, 1990). Others describe FNH as localized cirrhosis or regenerative nodules. The ultrasound appearance can be highly varied (figure 53 and 54). Small lesions are homogeneous, but over 3 cm a stellate scar can usually be detected. Connective tissue septa with arteries are arranged in the form of a star, thus producing the characteristic wheel spoke pattern on arteriography and colour Doppler sonography. The wheel spoke structure can be demonstrated well using echo contrast or in power mode (figure 55). After echo signal enhancement, FNH “stains” strongly in the early arterial and portal venous phases (figure 55). In the late phase, FNH often remains more highly stained with
Fig. 53: FNH nearly 10 cm in diameter confirmed by biopsy. A definite scar star is not visible.

Fig. 54: FNH over 6 cm of the right lobe. A wheel spoke pattern is suggested.
echo signal enhancers than the surrounding tissue, which distinguishes them from metastases (Wermke and Gassmann, 1998; Wermke, 2006).

Until recently, hepatobiliary sequence scintigraphy was regarded as the gold standard in imaging FNH. Since FNH contains all cell types but the correct architecture of the liver lobe is lost, there is delayed uptake and delayed biliary excretion of the tracer (Sciuk and Schober, 1997). If the perfusion, parenchymal and late phases are evaluated adequately in this investigation, cholescintigraphy achieves a sensitivity of 90% and a specificity of 100% in differentiating it from hepatocellular carcinoma (Gratz and Weimann, 1998). On CT, there is brief massive enhancement and delayed contrast equilibrium with the surrounding hepatic tissue. The stellate scar is not always present (Schild et al., 1987).

Fig. 55: FNH approx. 30 sec after injection of an echo signal enhancer. The FNH is already taking it up while the surrounding parenchymas does not yet appear completely echogenic.
Ultrasound-guided needle biopsy shortens the diagnostic process. It is usually done to differentiate from adenoma. Asymptomatic FNH is observed. Malignant transformation has not been described (Bennett and Bova, 1990). When there is clear evidence of FNH on CEUS, biopsy can be omitted.

**Nodular regenerative hyperplasia**

Multiple benign lesions in the form of nodular regenerative hyperplasia (NRH) often pose a considerable problem in differential diagnosis (figure 56). One theory states that hyperplastic or hepatocellular lesions form as after chemical carcinogens. Wanless (1990) considers NRH to be a compensation mechanism after local atrophy of liver tissue. Micronodular nodules remain invisible on ultrasound. However, they become visible when they are the size of the regenerative nodules of cirrhosis. NRH is found in

![Fig. 56: Nodular regenerative hyperplasia in a 42 year old patient with an unclarified systemic illness (eosinophilia). Multiple echogenic nodules with a diameter of up to 1.5 cm are seen throughout the entire liver (confirmed by biopsy).](image)
systemic illness (vasculitis), and during hormone and chemotherapy and in myelo- and lymphoproliferative disorders. NRH can be accompanied by portal hypertension. The ultrasound appearance is variable, and only biopsy allows the diagnosis to be made.

**Rare benign liver tumors**

Lipoma, angiomyolipoma, hamartoma and many other benign tumors all have no pathognomonic appearance. Lipomas are echogenic and can be mistaken for a hemangioma.

**Malignant tumors**

**Metastases**

Metastases are the commonest cause of focal lesions seen on ultrasound. Table 10 lists the possible questions that ultrasonography can answer when looking for and evaluating metastases. Metastases are very variable in appearance. Table 11 and figures 57–60 represent possible imaging forms. Focal metastases over a diameter of 5 to 10 mm can usually be identified. However, identification depends on the echogenicity, the site of the lesion, the quality of the equipment and the experience of the examiner. In unfavourable sites (metastases in subphrenic area, superior left lobe, extreme lateral right lobe), CT is superior. With the newest generation equipment, metastases 5 to 10 mm in size can be detected (Seemann et al. 1998). Only limited conclusions
Lesions typical of metastases detected:

- Secure diagnosis
- Possibility of biopsy
- Number, site (segment classification) and size with reference to resection
- Lymph node involvement or infiltration of neighbouring organs
- Number, site, size and ultrasound appearance with regard to follow-up during treatment (reference lesions)
- Recommendation of other necessary investigations (with limited echo quality, small lesions)

No lesion detected:

- How accurately could the liver be examined?
- What other investigations are recommended?

Table 10:
Questions answered by ultrasound in the case of metastases.
Nodular micrometastases – invisible on ultrasound
Diffuse infiltration – invisible on ultrasound
Diffuse infiltration with hepatomegaly
Nodular metastases with the same echogenicity as hepatic tissue:
Visible – due to irregularity of liver surface
– displacement or compression of vessels
– changes in echogenicity subsequently
Map-like infiltration
Focal appearance: Anechoic with dorsal echo enhancement
Hypoechoic with and without a rim
Echogenic with and without a rim
Echo-complex with echo-free or echogenic internal interior
(spontaneous or as a result of therapy)
Regressive changes (scar, calcification, necrosis)

| Table 11: Ultrasound appearance of liver metastases. |
about the primary tumor can be drawn from the ultrasound appearance of the lesions. The sensitivity of ultrasound for the detection of metastases is approx. 60–70 %. When highly suspected but ultrasound is negative, the next useful investigation is contrast-enhanced ultrasound (if available) or computed tomography (Bidlingsmaier et al., 1999; Fröhlich et al., 1997). Comparative studies show that a sensitivity of over 90 % can be achieved with modern high-end devices. Computed tomography can be regarded as complementary as different focal lesions can be shown in both. In CEUS metastases “wash out” in the late phase as they are not hepatic tissue and thus have no sinusoids and therefore they cannot “store” the echo signal enhancer (figure 58). This “washout” in the portal venous phase results in a sensitivity of 100 % for malignancy (Mörk et al., 2007). In a multicenter study, basic ultrasound had a sensitivity of 84.6 % and specificity of 78 %. The values were increased by CEUS to 88.5 % and 94 % respectively compared to contrast-supported spiral computed tomography of 92.3 % and 89.2 % respectively (Dietrich et al., 2006). However, caution is warranted in the case of metastases of neuroendocrine tumors. They have very high arterial perfusion but can also acquire the characteristics of hemangiomas.

Metastases can also be monitored ultrasonographically. Early metastases tend to be echo-poor and are therefore easily identifiable only in a fatty liver. In the case of lymphomas or melanoma, the metastases can be mistaken for cysts (figure 57).
Fig. 57: Appearance of metastases. Early metastases appear echo-poor or anechoic, and they can demonstrate dorsal echo enhancement (malignant melanoma, diameter < 1 cm, 1). Somewhat larger metastases tend to be echo-poor, and a rim is absent in this case (breast cancer, 2). Typical echo-poor rim, target type (small cell bronchial carcinoma, 1.5 cm diameter, 3). Echogenic metastasis, typical of gastrointestinal primary tumors, can be mistaken for a hemangioma (here colorectal carcinoma, 4). Larger echogenic lesion of a colorectal carcinoma, echo-poor rim, echogenic ring, echo-poor interior, “bull’s eye” (5).
The detection of an echo-poor rim around a slightly more echogenic centre (target) has a sensitivity and specificity for the presence of metastases of 84 to 90%. The rim is thus highly suspicious but no proof. It is not yet clear whether this is tumor tissue or a reaction by the area surrounding the metastasis.

Very small metastases not detectable ultrasonographically are found particularly often with small cell bronchial carcinoma (Schölmerich et al., 1984 and 1987). Laparoscopy should be considered when therapeutically indicated. Breast cancer and melanoma also often have small hypoechoic or ultrasonographically undetectable metastases. The diagnosis becomes easier as the disease progresses. Figure 59 shows diffuse interspersion with small hypoechoic metastases (some of target type) in malignant melanoma.

Fig. 58:
Metastases with a punched-out appearance in the late phase of CEUS.
In the clinical course metastases may become confluent and will show a map-type phenotype (figure 59).

Ultrasound is used widely today to monitor tumor disease. There are two situations: monitoring in patients initially free from metastases, and monitoring during treatment. Depending on the indication, a rational examination interval and actual therapeutic consequences in discovering focal lesions should be ensured. The high psychological stress on patients of excessively frequent follow-up examinations should be considered along with the possibility of an unsatisfactory result when repeat examinations are performed too frequently during therapy. In monitoring progress, planimetry or even volumetry of space-occupying lesions is superior to measuring the transverse and longitudinal diameters. On the other hand, this is more time consuming and the accuracy of reproducibility of the same measurement direction is questionable. Investigations have shown that progression or regression can be reported only when the
change is greater than 30% (Schölmerich and Gross 1997). Measurements using spiral CT are more precise, but the method is more complex. Not only the size but also the appearance of the metastases can alter spontaneously or during treatment. As the diameter increases, areas of spontaneous necrosis develop. This can be regarded as success during chemotherapy, and necrosis occurs even with small diameter lesions. Metastases can disappear completely on treatment or can undergo fibrous or calcified degeneration (figure 60).

If primary resection is possible, exact diagnosis of the number and site of the metastases is necessary. CT arterioprtography (CTAP) can be used preoperatively. An arterial catheter is inserted and the behaviour of the contrast agent during the arterial (through the hepatic or superior mesenteric artery) or portal venous phase (through the splenic artery) is studied by computed tomography. The disadvantage of the method is its invasiveness and the necessity of using contrast. However, the gold standard is intraoperative ultrasound. The operative plan still has to be changed or the operation halted in up to 40% of cases nowadays because of the intraoperative detection of further metastases or other sites. Contrast-enhanced MRI is being improved constantly, but the selection of examination parameters and interpretation of the findings is considerably more complex.
Fig. 60:
Progress of echogenic metastases in colon carcinoma. (1) Large echogenic lesion initially. (2) Necrotic areas appear subsequently during chemotherapy. (3) Regressively altered areas with calcification after chemotherapy for colorectal carcinoma.
**Lymphomas**

Lymphomas of the liver can produce diffusely infiltrating and focal changes in the liver (figure 61 and 62). The ultrasound appearance is not pathognomonic. Focal lesions are usually echo-poor or almost anechoic, so that it is possible to mistake them for cysts. Extrahepatic manifestations of lymphoma (splenomegaly, mesenteric lymphomas) support the suspected diagnosis of lymphomatous infiltration of the liver, but only histology is confirmative.

Fig. 61:
Focal manifestation of a high-grade non-Hodgkin’s lymphoma of the liver. The focus cannot be distinguished from a metastasis from an epithelial tumor.
Primary malignant liver tumors:

*Hepatocellular carcinoma (HCC)*

The hepatocellular carcinoma is the commonest malignant tumor worldwide, due to the high prevalence of hepatitis B in countries of the Third World. In Germany, the incidence is comparatively lower. Cirrhosis is present in 80% of cases. The annual incidence in cirrhosis is 3–6%. In particular, patients with hepatitis B and C, alcoholic cirrhosis and genetic hemochromatosis are at high risk and require close screening, consisting of liver ultrasound and measurement of the alpha-1-fetoprotein every 6 months. It is still unclear whether this improves the prognosis or whether the tumor is only discovered sooner.

Fig. 62:
B-cell non-Hodgkin’s lymphoma. Apart from a lesion typical of metastasis, there are further echo-poor lesions and one echogenic focus.
The manifestation of a HCC can be diffuse, focal or pedunculated. The ultrasound appearance is very variable, and several echo qualities, i.e. echo-poor and echo-rich areas, can occur in a tumor nodule (mosaic pattern, figure 63; Takayasu and Okuda, 1997). A connective tissue capsule is believed to indicate a better prognosis.

On colour Doppler sonography, lesions less than 3 cm give signals at the periphery (basket sign) or in the interior (tumor vessel, spot sign, figure 64) in up to 80% of cases. The detection of internal flow signals increases in power mode (Lin et al. 1997). If these have a pulsatile spectrum, a hepatocellular carcinoma is present with a high degree of probability, especially in the presence of cirrhosis, when metastases are rare. A central continuous spectrum is believed to indicate regenerative nodules or adenomatous hyperplasia. On CEUS 90% of HCCs show ring enhancement, but only 30% of...
Dysplastic regenerative nodules. 100% of HCCs but only 10% of regenerative nodules demonstrate chaotic perfusion and centripetal uptake of echo signal enhancers (Rickes et al., 2002). Washout in the parenchymal phase can be observed with echo signal enhancers as a criterion of malignancy, and this is more marked with Levovist® than with Sonovue® (von Herbay et al., 2007). However, in the individual case, distinguishing a HCC from a regenerative nodule can be very difficult even histologically. In general, biopsy is recommended in the case of doubt unless transplantation is planned anyway. Whether a biopsy can then be omitted must be agreed with the respective center.

HCC can be divided into stages together with clinical parameters, signs of portal hypertension and taking liver function into account. There are different staging systems, and the Barcelona Clinic Liver Cancer stag-

Fig. 64: Diagram of the findings which can be made with colour Doppler ultrasound (see text).
The Barcelona Clinic Liver Cancer (BCLC) staging system comes closest to clinical requirements. It takes into account liver function, portal hypertension, the extent of the HCC, and any vascular invasion. Therapy allocation is according to stage and extends from resection and transplantation in early stages to palliative procedures such as ethanol injection (PEI) or radiofrequency thermoablation (RFTA) (Schacherer et al., 2007).

The CEUS does not show a clear picture. Distinction from regenerative nodules is difficult. Table 12 lists comparative studies. With the current spiral CT a sensitivity of 54–70% and specificity of 70–93% can be achieved. For MRI, the sensitivity is between 57 and 85% and the specificity is between 21 and 82% (Schacherer et al., 2007).

An increased alpha-1-fetoprotein of more than 500 ng/ml and the finding of a corresponding lesion on ultrasound are regarded today as adequate proof of a HCC. Typical signs also include tumor thrombosis of the portal vein and its branches. If arterial vessels are found in the thrombus, malignancy is confirmed (figure 65).

Fig. 65:
Tumor thrombosis of the portal vein in alcoholic cirrhosis. The right lobe of the liver is diffusely infiltrated and there is perihepatic ascites.
In contrast to earlier pessimism, a range of possible treatments is available today, which make a differentiated procedure necessary (see algorithm). The aim is the earliest possible diagnosis of the HCC by the screening of high-risk groups described above (figure 71). Table 12 shows the usefulness of different imaging methods. Ultimately, no method is capable of distinguishing between a hyperplastic regenerative nodule and a small HCC. On contrast-enhanced spiral CT, HCC can be seen particularly in the early arterial phase. The value of Lipiodol\textsuperscript{®} CT is controversial. The selective accumulation of Lipiodol\textsuperscript{®} in the HCC is utilised also in transarterial chemoembolization (TACE), when Lipiodol\textsuperscript{®} can be mixed with chemotherapeutic agents.

The diagnostic and therapeutic procedure also depends on hepatic function. This is taken into account in Okuda’s classification (Takayasu and Okuda, 1997). Ultrasound-guided diagnostic and therapeutic aspiration is used in palliative procedures (see therapeutic interventions). CT shows the relationship to adjacent organs and the size of the lesion better (figure 66).
### Table 12:
Sensitivity (%) of imaging of hepatocellular carcinoma. *Small carcinomas. (US = ultrasound, CT = computed tomography, MRI = magnetic resonance imaging, DSA = digital subtraction angiography).

<table>
<thead>
<tr>
<th>Study</th>
<th>US</th>
<th>CT</th>
<th>Lipiodol®-CT</th>
<th>MRI</th>
<th>DSA</th>
<th>Intra-operative US</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nagasue et al. (1989)</td>
<td>91</td>
<td>92</td>
<td></td>
<td></td>
<td>93</td>
<td>98</td>
</tr>
<tr>
<td>Choi et al. (1991)</td>
<td>73</td>
<td>82</td>
<td>96</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Takayasu et al. (1990)*</td>
<td>84</td>
<td>84</td>
<td>93</td>
<td></td>
<td>81</td>
<td>96</td>
</tr>
<tr>
<td>Shibata et al. (1991)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>De Santis et al. (1992)*</td>
<td>67</td>
<td>50</td>
<td>93</td>
<td>63</td>
<td>74</td>
<td></td>
</tr>
</tbody>
</table>
Fig. 66:
Large HCC in segment III with cirrhosis due to hepatitis C. Left, CT, right, ultrasound. The patient recovered well from resection of this initially solitary lesion. However, several new foci of HCC appeared in the remaining liver eight months later.
Cholangiocellular carcinoma (CCC)

These rare tumors are divided into peripheral and hilar types (Klatskin tumors). The peripheral carcinomas cannot be distinguished ultrasonographically from other primary or secondary carcinomas (figure 67). Central hilar tumors often remain invisible on ultrasound and are apparent only indirectly through congestion of the bile ducts (figure 68). Again it is CEUS that can show the tumor spaces in the late phase in the case of Klatskin tumors (Bauditz et al., 2007). ERCP is performed today for diagnosis and placement of a palliative stent. Whether MRCP (magnetic resonance cholangiopancreatography) will improve early diagnosis remains to be investigated.

In the past, the thorium used as the X-ray contrast agent Thorotrast® represented an important risk factor for a CCC. It has not been used since 1950. The last patient in Freiburg with Thorotrast®-induced CCC died in 1989.

A risk group for the development of a CCC today is represented particularly by patients with primary sclerosing cholangitis. There is no useful screening test. The prognosis is good only when the CCC is discovered as an incidental finding during transplantation. Echinococcus alveolaris is an important differential diagnosis in CCC, which can also show as diffuse hilar infiltration with blockage of the bile ducts (cf. figure 43).

Rare primary tumors

Hemangioendotheliosarcoma, angiosarcoma, fibrolamellar carcinoma and hepatoma in childhood do not have a typical ultrasound appearance and can only be confirmed by histology.
Fig. 67: CCC of peripheral type. Locally blocked bile ducts and ascites (A) can be seen in addition to echogenic, poorly demarcated areas of tumor (T).

Fig. 68: CCC of central type (Klatskin tumor). The bile ducts are clearly distended. A diffusely infiltrating process is suspected in the area of the hilum.
The following pages contain suggestions for the procedure in certain situations using tables and algorithms.

**Diffuse parenchymal disorders**

Fatty liver, cardiac hepatic congestion and cirrhosis can be diagnosed well today by ultrasound, if several signs coincide and the examiner has the appropriate experience. Beginners often diagnose “diffuse parenchymal damage” which is associated with pathological liver tests in no more than 30% of cases (Ochs et al., 1994). Using colour Doppler sonography, portal vein thrombosis, Budd-Chiari syndrome and portal hypertension can also be diagnosed (Haag et al., 1999).

However, the gold standard is still biopsy and laparoscopy. Biopsy will always be attempted in the case of treatable causes of liver disease (hepatitis C, Wilson’s disease, hemochromatosis, alpha-1-antitrypsin deficiency, autoimmune hepatitis, primary biliary cirrhosis etc.). In ascites or severe coagulation disorders, transjugular biopsy can also be attempted.

**Focal liver lesions**

Innumerable algorithms have been proposed to investigate focal lesions of the liver (Brambs, 1996; Feuerbach et al., 1997; Fröhlich et al., 1997; Gerok, 1988; Helmerger et al., 1998; Lihart et al., 1998; Lise et al., 1996; Lock et al., 1997; Rettenmaier, 1988; Strohm and Weimer, 1997; Weismann et al., 1997; Weiss, 1991). The complexity of the possible differential diagnoses contrasts with the frequency distribution of the findings.
Metastases account for up to 70% of cases, which appear as such and can be confirmed rapidly by needle aspiration, if a more accessible tumor site is not available. Table 13 gives a synopsis of current imaging methods with the typical findings and their accuracy.

As discussed, two situations arise:
- the procedure with an incidentally detected lesion
- the procedure when tumor is suspected

Before working through each of these algorithms, an attempt should be made to obtain a second opinion from an experienced examiner (Fröhlich et al., 1997).

If a focal lesion is found on ultrasound and clear classification is not possible, biopsy is an economical way of shortening further procedure. No other imaging method will give a histological diagnosis.

Figure 69 shows an algorithm for the incidental finding of a focal lesion. Five ultrasound diagnoses can be regarded as definite, if they meet classic criteria:
- cysts
- hemangioma
- mild fatty infiltration
- classical Echinococcus cysticus
- metastases

With CEUS, FNH and adenoma can be diagnosed highly visibly along with metastases.

Figure 70 shows the procedure when looking for hepatic lesions. These are usually patients with a known or highly suspected malignancy on initial investigation or follow-up. This algorithm differs from figure 69 in that unclear findings are biopsied much sooner and a hemangioma or cyst is kept under observation only with quite unequivocal evidence.
<table>
<thead>
<tr>
<th>Focal lesion</th>
<th>Gold standard</th>
<th>Ultrasound (fundamental)</th>
<th>Colour Doppler ultrasound (CEUS)</th>
<th>Spiral CT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemangioma</td>
<td>Ultrasound in typical hemangiomas</td>
<td>Echogenic, feeding vessel</td>
<td>Iris phenomenon and nodular enhancement</td>
<td>Iris phenomenon and nodular enhancement</td>
</tr>
<tr>
<td>Cysts</td>
<td>Ultrasound</td>
<td>Anechoic, posterior acoustic enhancement</td>
<td>No additional information</td>
<td>Hypodense</td>
</tr>
<tr>
<td>Adenoma</td>
<td>Biopsy, CEUS</td>
<td>Hypoechoic or slightly more echogenic than the surroundings, uncharacteristic</td>
<td>Readily demonstrable early arterial enhancement</td>
<td>Hypodense with hyperdense areas of bleeding</td>
</tr>
<tr>
<td>Focal nodular hyperplasia</td>
<td>CEUS, CT, MRI, (biopsy)</td>
<td>Sharp margins, usually hypoechoic, wheel spoke structure sometimes visible</td>
<td>Wheel spoke appearance of the vessels (with or without CEUS)</td>
<td>Hypodense with centrifugal enhancement (“blush”)</td>
</tr>
<tr>
<td>Metastases</td>
<td>Spiral CT with contrast, CEUS, MRI, biopsy</td>
<td>Hypoechoic halo typical but not obligatory, hypoechoic, echogenic</td>
<td>CEUS: washout in the late phase</td>
<td>Hypodense, nonhomogeneous due to necrosis or scarring or bleeding</td>
</tr>
<tr>
<td>Hepatocellular carcinoma</td>
<td>Biopsy? AFP and detection of focal lesion in cirrhosis (refer there, contrast CT, MRI, CEUS)</td>
<td>Signs of cirrhosis in 80 %, hypoechoic and echogenic, “mosaic pattern”, tumor thrombus</td>
<td>Evidence of tumor thrombi, arterial fistulas, pathological arterial flow profile</td>
<td>Early arterial margin enhancement, irregularly hypodense, (Lipiodol® storage 14 days after administration)</td>
</tr>
</tbody>
</table>

Table 13: Different focal lesions and their typical appearance in different imaging procedures (modified from Bidlingsmaier et al., 1999 and Fröhlich et al., 1997). Nuclear medicine and angiographic methods have lost much of their importance.
<table>
<thead>
<tr>
<th>Focal lesion</th>
<th>Magnetic resonance imaging</th>
<th>Nuclear medicine</th>
<th>Angiography</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemangioma</td>
<td>T1: hypointense T2: hyperintense</td>
<td>Blood pool scintigraphy has become less important</td>
<td>Contrast pooling “cotton wool” sign</td>
</tr>
<tr>
<td>Cysts</td>
<td>T1: hypointense T2: hyperintense</td>
<td>No importance</td>
<td>No importance</td>
</tr>
<tr>
<td>Adenoma</td>
<td>T1: hyperintense T2: iso-hypointense, non-specific</td>
<td>Sulfur colloid: 80 % defect, 20 % staining, has become less important</td>
<td>Hypervascular, non-specific</td>
</tr>
<tr>
<td>Focal nodular hyperplasia</td>
<td>T1: isointense T2: iso-hyperintense, centrally hyperintense</td>
<td>Hepatobida scan: delayed staining, delayed biliary outflow</td>
<td>Hypervascular, wheel spoke structure</td>
</tr>
<tr>
<td>Metastases</td>
<td>T1: usually hypointense (hemorrhage, necrosis) T2: usually hyperintense (hemorrhage, necrosis)</td>
<td>Somatostatin receptor scintigraphy in GEP-NET. Positron emission tomography</td>
<td>Hypovascular apart from GEP-NET</td>
</tr>
<tr>
<td>Hepatocellular carcinoma</td>
<td>T1: usually hypointense (hemorrhage, necrosis) T2: usually hyperintense (hemorrhage, necrosis)</td>
<td>Similar staining as in FNH possible on hepatobida scan, arteriovenous shunts</td>
<td>Hypervascular, pathological arteries, arterioportal or arteriovenous fistulas</td>
</tr>
</tbody>
</table>

CEUS = contrast enhanced ultrasound, GEP-NET = gastroenteral-pancreatic neuroendocrine tumors, MRI = magnetic resonance imaging, grey type: low clinical significance
Focal lesion as incidental ultrasound finding

- **Cyst**
  - Monitoring or treatment
  - yes
  - no

- **Hemangioma**
  - Benign appearance
  - yes
  - CEUS
  - Spiral CT with contrast (MRI)

- **FNH, abscess**
  - Benign appearance
  - unclear

- **Suspected metastasis? Adenoma? HCC, CCC?**
  - yes
  - Search for primary tumor
  - Biopsy

Fig. 69: Procedure for the incidental finding of a focal lesion. HCC = hepatocellular carcinoma, CCC = cholangiocellular carcinoma.
Procedure when searching for a hepatic focus, usually in patients with a known primary tumor. This also allows for the situation when no hepatic foci are shown despite high clinical suspicion. A biopsy should always be performed always if a better extrahepatic biopsy site does not offer itself.
A particular situation arises when looking for a HCC. Cirrhosis is usually present, so that the important differential diagnosis is regenerative nodules. The therapeutic procedure will depend on the extent of hepatocellular insufficiency and tumor size (figure 71). Monitoring of cirrhosis patients is also included (Ruelas-Villavicencio and Vargas-Vorácková, 2004).

**Diagnostic approach in cholestasis**

No algorithm is given for this situation. Distended bile ducts can usually be detected easily on ultrasound, but detection of the cause of the blockage and its precise site is not always successful. The sensitivity of ultrasound for choledocholithiasis is thus no greater than 70%. It can be supplemented by endosonography, ERCP or MRCP when there are grounds for suspecting mechanical cholestasis. ERCP and transcatheteraneous transhepatic bile duct puncture and drainage are available for palliative treatment. The diagnosis of Klatskin tumors is made possible by CEUS. In the late phase the extent of the tumor infiltration surrounding the bile ducts can be demonstrated well (Bauditz et al., 2007).

**Ultrasound-guided diagnostic and therapeutic procedures**

**Diagnostic aspiration**

Hepatic lesions over 1–2 cm in size can usually be aspirated under sonographic guidance. Aspiration of a liver lesion is indicated when knowledge of its significance will have consequences for therapy. Ultrasound-guided fine needle aspiration allows tissue to be obtained with little burden for the patient and usually saves further investigation. Cytological opinion only is possible with
Fig. 71: Procedure with hepatic lesions suspicious for HCC.
very fine needles. Tissue cores obtained with cutting biopsy needles (e.g. Truecut®) can be assessed histologically. Contraindications must be noted (table 14). Figure 72 shows the various possible aspiration methods. In Freiburg, ultrasound-guided aspiration through a perforated curved array transducer is preferred.

Serious complications after ultrasound-guided needle biopsy of hepatic lesions are rare. The mortality is 0.08%. Complications such as bleeding, bile peritonitis, dissemination of tumor cells, hematoma or peritonitis of other origin was described in 0.5% of all aspirations. The overall rate, including minor complications, is 5% (Spamer et al., 1986). Dissemination of tumor cells along the needle track occurs very rarely (0.05%) and does not lead to decreased life expectancy of the patient. Echinococcus should be excluded serologically before aspiration, as anaphylactic reactions are possible. How-

| **Severe coagulation disorders**  
| **(Echinococcus cysticus)**  
| **Ascites (relative)**  

Table 14: Contraindications to ultrasound-guided aspiration of focal hepatic lesions.

ever, the risk of such a reaction is overestimated. In many cases, ultrasound-guided PAIR is also used today as treatment (refer there).

**Ultrasound-guided therapy**

**Aspiration of ascites and pleural effusion**

Even small volumes of ascites or pleural effusions can be aspirated diagnostically after ultrasound localization.
Fig. 72:
Ultrasound-guided biopsy. Left, needle aspiration through a perforated transducer. The probable route of aspiration is shown on the monitor by guidelines (A), which allows exact adjustment of the focus (B). On the right, the needle is guided “freehand” in the case of large lesions (C).
Percutaneous cholangiography/drainage

If percutaneous transhepatic cholangiography and drainage (PTCD) proves necessary, puncture especially of the left bile duct system can be undertaken under ultrasound control. Imaging with contrast and the insertion of guidewires then takes place in combination with radiology.

Abscess and cyst drainage, sclerotherapy

Figure 73 shows the procedure of cyst sclerotherapy. Symptomatic cysts can be sclerosed with ethoxysclerol, 10% saline or 95% ethanol. Ethoxysclerol has the advantage of an additional local anesthetic effect. A single aspiration will not be successful, since these are genuine cysts with a secreting epithelial covering. The cyst is first aspirated under local anesthesia and ultrasound control. The cyst contents can be withdrawn for diagnostic purposes. Using the Seldinger technique, a guide wire is inserted. This is followed by dilatation and the insertion of a 5–7F pigtailed catheter. The cyst is drained for at least 24 h and during this time 1000 to 2000 ml of fluid can be secreted. The cyst wall is then sclerosed by one of the substances listed above with approx. 10% of the cyst contents. Permanent success is achieved in 70%, and a 50% reduction in size is usually obtained in the remaining 30%. Echinococcus cysts are treated similarly (PAIR).

Larger abscesses can also be drained by the same technique. Often the reduction in size by short-term drainage is enough to allow rapid healing with antibiotic therapy.
Fig. 73:
Procedure of cyst sclerotherapy. Ultrasound-guided aspiration (A) of the cyst and insertion of a pigtailed catheter (B). Drainage of the cyst for at least 24 h. The cyst wall is then sclerosed by a concentrated solution (see text). After 8 weeks, cyst volume is markedly reduced.
Percutaneous therapy of primary tumors and metastases

Primary and secondary malignancies of the liver are being treated increasingly under ultrasound control. The size and number of the lesions are important for the success of therapy. Lesions up to 3 cm in size can be treated by targeting them with percutaneous ethanol injection (PEI) (Allgaier et al., 1996). 3–4 sessions are usually needed. Radiofrequency thermoablation (RFTA) represents another method. A needle is inserted into the tumor under ultrasound control, at the tip of which curved metal wires are extruded in which local heat is produced by a high frequency generator. As a rule, only one session is necessary. Lesions up to over 4 cm can be treated this way. The complication rate is higher than with PEI. A life-prolonging effect has not been confirmed hitherto.

Guidance of TIPS

Placing a transjugular intrahepatic portosystemic stent shunt without ultrasound guidance when the anatomy is complicated can no longer be imagined today. The aspirating needle can be guided from the hepatic vein into the portal vein. In particular, the anterior or posterior direction of aspiration, which is not visible on fluoroscopy, can be predicted by ultrasound.
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Ursofalk® 500mg film-coated tablets, Ursofalk® 250mg capsules, Ursofalk® 250mg/5ml suspension. Active ingredient: ursodeoxycholic acid. **Composition:** One film-coated tablet contains: active ingredient: 500 mg of ursodeoxycholic acid. Other ingredients: magnesium stearate, polysorbate 80, povidone K25, microcrystalline cellulose, silica colloidal anhydrous, crospovidone (type A), talc, hypromellose, macrogol 6000. One hard capsule or 5 ml of suspension contains: active ingredient: 250 mg of ursodeoxycholic acid. Other ingredients: hard capsules: magnesium stearate (Ph.Eur.), titanium dioxide (E171), maize starch, colloidal silica anhydrous, gelatin, sodium dodecyl sulfate, purified water. Suspension: benzoic acid, citric acid, glycerol, microcrystalline cellulose, carboxymethylcellulose sodium, sodium chloride, sodium citrate 2H2O, sodium cyclamate, propylene glycol, purified water, xylitol, lemon flavouring. **Indications:** 1. Symptomatic treatment of primary biliary cirrhosis provided no decompensated liver cirrhosis is present. 2. Dissolution of cholesterol gallstones in the gallbladder. The gallstones must not be larger than 15 mm, must be radiolucent (not show up on x-ray) and the gallbladder must be functioning despite of (a) gallstone(s). 3. Biliary reflux gastritis (only Ursofalk® 250mg capsules). **Dosage:** For 1: 14 ± 2 mg/kg body weight daily. For 2: approx. 10 mg/kg body weight daily before going to bed. For 3: 1 hard capsule daily before going to bed. **Contraindications:** acute inflammation of the gallbladder and bile ducts; obstruction of the biliary tract (common bile duct or cystic duct), frequent biliary colic, radio-opaque calcified gallstones, disturbed contractility of the gallbladder, hypersensitivity to bile acids or to any other ingredient, pregnancy, breast-feeding. **Side effects:** Pasty stools or diarrhea are common. Very rarely: severe right-side upper abdominal pain, calcification of gallstones, urticaria. During therapy of advanced stages of primary biliary cirrhosis, in very rare cases decompensation of hepatic cirrhosis (reversible). Ursofalk® 250mg/5ml suspension contains benzoic acid. **Interactions:** see patient information leaflet. Available on prescription only. Date of information: 05/2011.
