Imaging Diffuse Liver Disease – Part II

by Pierre Vassallo

CT scan protocols for the liver may be classified single-, dual- or triple-phase techniques. An initial non-contrast enhanced scan is obtained with all three techniques. In the case of a single phase technique, the nonenhanced scan is followed by a scan in the portal venous phase (40 seconds after the peak aortic enhancement). In the dual-phase technique, scans are obtained in the late hepatic arterial phase (20 seconds after peak aortic enhancement) and in the portal venous phase. In the triple-phase technique, late arterial and late portal venous scans are followed by a hepatic venous phase scan (60 seconds after peak aortic enhancement).

Single phase scans are practical when whole body scans are required usually for cancer staging. Single phase scans acquire images of the liver prior to contrast injection and during the portal venous phase (ie 40 seconds after peak aortic enhancement) (Figure 1).

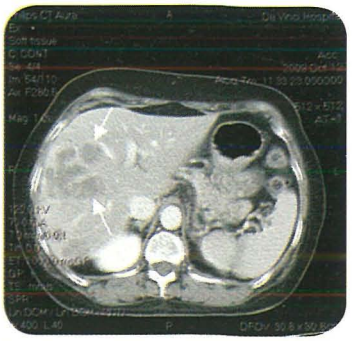


Figure 1
Part of a whole body scan to stage colon cancer, liver metastases are present (arrows).

Dual phase scans are performed in cases with a known or suspected hypervascular primary neoplasm outside the liver for which hypervascular hepatic metastases are suspected. Confirmed or suspected diagnoses of breast carcinoma, renal cell carcinoma, melanoma, neuroendocrine tumors, and thyroid carcinoma would call for the dual-phase hepatic imaging protocol (Figure 2).

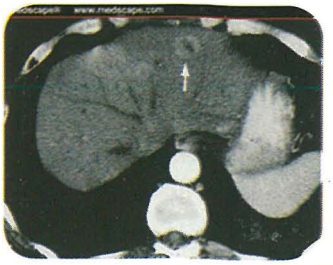


Figure 2
Dual phase scanning allows better demonstration of hypervascular metastasis (arrow).

Triple phase scans are used in cases of known or suspected cirrhosis or hepatocellular carcinoma as well as suspected benign primary liver lesions such as focal nodular hyperplasia or hepatic adenoma. A further delayed phase performed 10–15 minutes after peak aortic enhancement; this will demonstrate the pathophysiologic phenomenon of delayed contrast agent washin and washout that occurs in these lesions allowing them to appear denser than normal liver parenchyma during this phase (Figure 3).

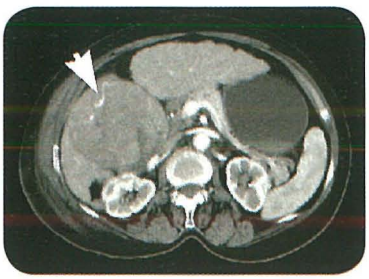


Figure 3
Primary hepatic tumors demonstrate delayed washout (arrow) on this delayed phase image from a triple phase scan.

The most common indication for liver CT is to exclude, confirm or monitor hepatic metastatic disease; single and in some cases dual phase scans are adequate for such cases. Triple phase scans are reserved for particular cases where information about a primary hepatic lesion or diffuse liver disease is required. Below I will discuss some of the more common indications of a triple phase CT scan.

Storage Diseases

Hepatic steatosis represents the excessive accumulation of triglycerides within the hepatocytes, a phenomenon that can affect hepatic parenchyma focally or diffusely. At the hepatocellular level, three underlying pathophysiologic phenomena have been identified that contribute to fatty infiltration of hepatic parenchyma: decreased mitochondrial fatty acid beta-oxidation, increased endogenous fatty acid synthesis or enhanced alimentary delivery of fatty acids leading to hypertriglyceridemia, and deficient incorporation or export of lipoproteins. Fatty liver disease can cover a severity spectrum ranging from dormant noninflammatory fatty liver, to steatohepatitis with inflammation, fibrosis, and eventually cirrhosis.

All severities of fatty liver disease can be associated with the use of alcohol. In the absence of alcohol consumption, nonalcoholic fatty liver disease is most commonly associated with obesity, type 2 diabetes mellitus, and dyslipidemia. It can also manifest as an aggressive subtype characterized by hepatocyte ballooning and necrosis, with and without Mallory hyaline and fibrosis, called nonalcoholic steatohepatitis

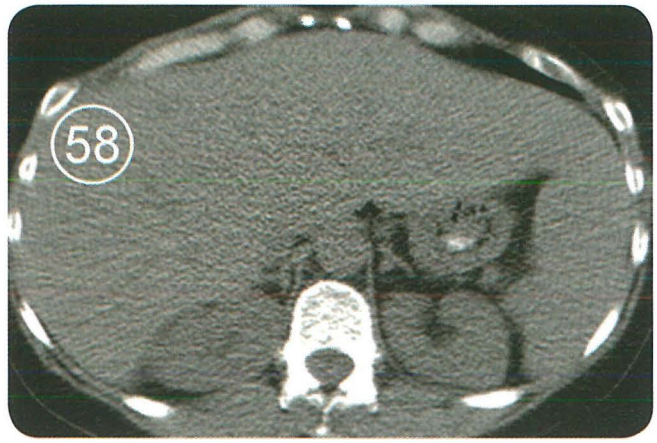


Figure 4a

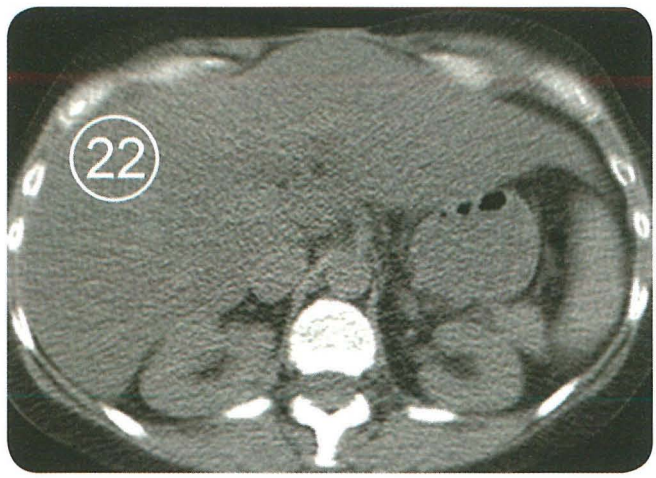


Figure 4b

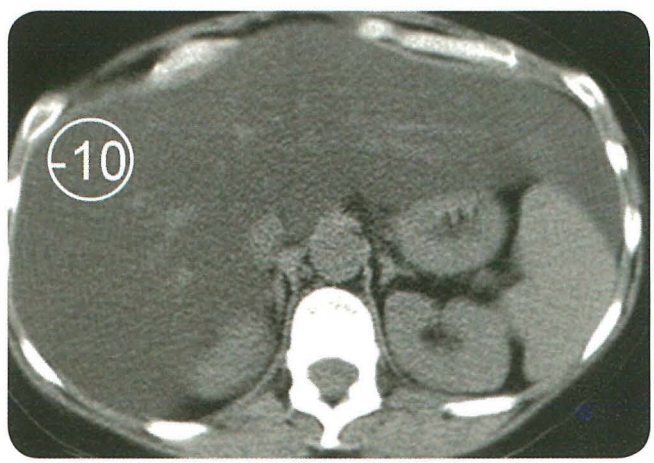


Figure 4c

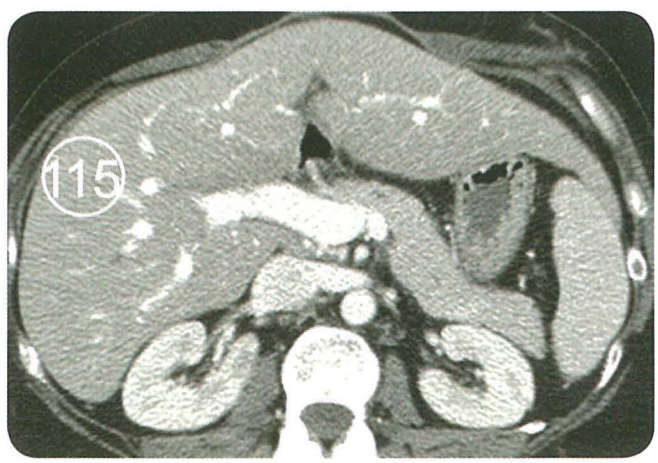


Figure 4d

Figure 4
Fatty infiltration of the liver parenchyma in a 46-year-old woman with ovarian cancer who was undergoing chemotherapy. Sequential nonenhanced (a–c) and portal venous perfusion phase contrast material–enhanced (d–f) CT scans obtained at 3-month intervals show a progressive decrease in hepatic attenuation. Circle = region of density measurement, number = attenuation in Hounsfield units.

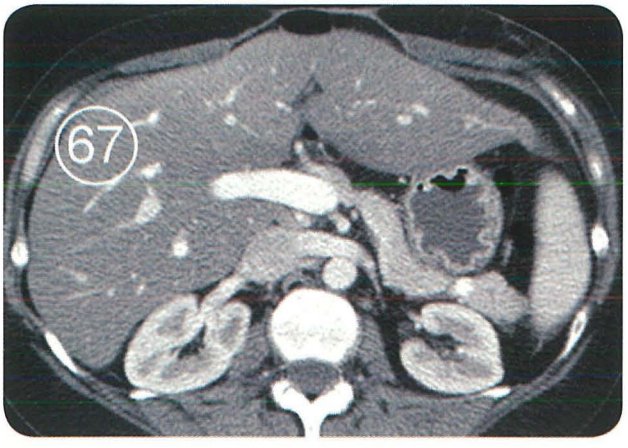


Figure 4e

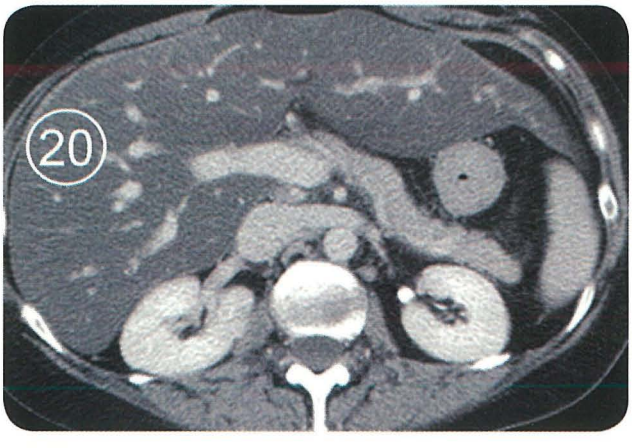


Figure 4f

(NASH). Several other clinical disorders and scenarios including malnutrition, severe hepatitis, corticosteroid use, pregnancy, drug toxic effects, malaria, kwashiorkor, Reye syndrome, and chemotherapy also lead to fatty liver disease (Figure 4).

At unenhanced hepatic CT, fatty infiltration results in a lowering of the attenuation of the liver parenchyma. In normal adults, the attenuation value of the liver is consistently higher than that of the spleen. Mild degrees of diffuse fatty infiltration can be diagnosed when the attenuation value of the liver parenchyma is slightly less than that of the spleen; marked steatosis hepatis leads to attenuation levels lower than that of the intrahepatic blood vessels. Contrast enhanced CT scans are less reliable in detecting fatty infiltration of the liver. After contrast material administration, significant fatty infiltration can be suggested if the liver attenuation is less than that of muscle.

Wilson's disease is an autosomal recessive disease characterized by increased intestinal uptake of copper and subsequent deposition, predominantly in the liver and basal ganglia. Wilson's disease can manifest as acute and even fulminant hepatitis with rapid progression into mostly macronodular-type cirrhosis. Clinically, patients present with very low levels of ceruloplasmin. Rarely malignant transformation into hepatocellular carcinoma may occur.

Hepatic CT may demonstrate nonspecific increased liver parenchymal density related to the copper deposition (Figure 5). However, Wilson's disease may also be accompanied by diffuse fatty infiltration, which decreases the attenuation at hepatic CT. Clinical correlation and rarely ultrasound guided liver biopsy may be required for confirmation in these cases.

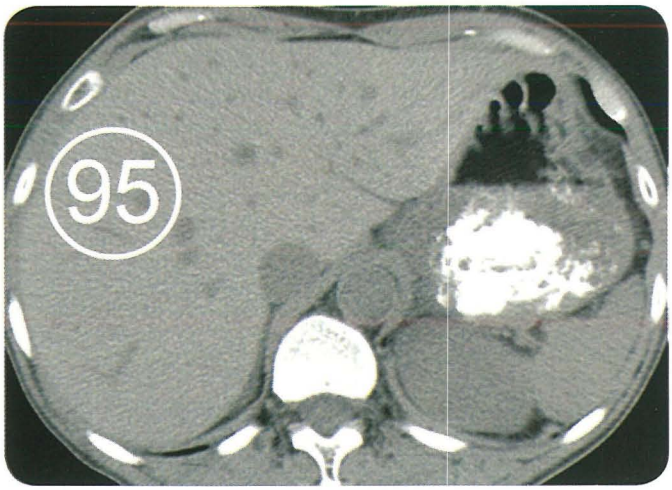
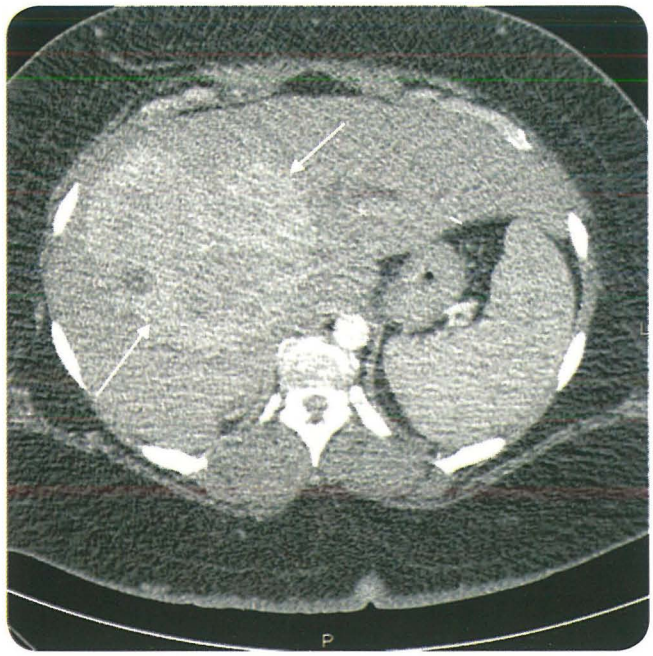


Figure 5
Histologically proved Wilson disease in a 41-year-old man. Nonenhanced CT scan shows increased attenuation of the hepatic parenchyma.

All known variants of identified glycogen storage diseases are inherited autosomal recessive disorders and are characterized by absence or deficiency of one of the enzymes responsible for producing or metabolizing glycogen. Different enzyme deficiencies cause either abnormal concentrations of glycogen or abnormally formed glycogen. Different subtypes of glycogen storage disease involve the liver, musculature, haematopoietic system, myocardium, and kidneys. Types Ia (von Gierke), Ib, II (Pompe), III (Forbes), IV (Anderson), VI, and IX have the cardinal symptom of hepatomegaly.

Types Ia and Ib have the potential to undergo malignant transformation to form hepatocellular carcinomas, whereas types III and IV progress to development of cirrhosis. In types Ia, Ib, and III, an increased prevalence of hepatic adenomas has been observed (Figure 6).
In all children in whom hepatomegaly in combination with hypoglycemia, growth retardation, and disproportional distribution of body fat is detected, the diagnosis of glycogen storage disease should be considered.

Figure 6
Hepatic adenoma (arrows) in type 1a (von Gierke) glycogen storage disease.



Lipid storage diseases represent a diverse family of diseases that result from an enzymatic deficiency of a lysosomal hydrolase. This leads to lysosomal accumulation of sphingolipids. Sphingolipid substrate storage in visceral cells can lead to organomegaly. However, the main target organ is the central nervous system, the feature responsible for the predominantly neurodegenerative course of lipid storage diseases. Numerous subtypes of lipid storage diseases have been identified that are classified according which enzyme is deficient: GM1 and GM2 gangliosidosis, Gaucher disease, Niemann- Pick disease, Fabry disease, Schindler disease to name a few. Most of these diseases may manifest as an enlarged liver due to lipid and cholesterol deposition, leading to cirrhosis and chronic liver failure before adulthood). CT imaging of the liver shows hepatomegaly with accompanying steatosis hepatis as nonspecific imaging findings (Figure 7). Deficient activity of the enzymes regulating the catabolism of glucosamine glycans leads to the accumulation of excess mucopolysaccharides in tissues, as well as excretion of specific metabolites in the urine. The more common mucopolysaccharidoses including type I (Hurler), type II (Hunter), type III (San Filippo), type VI (Maroteaux-Lamy), type VIIb all have hepatic manifestations. At pathomorphologic analysis, hepatomegaly, diffuse fibrosis and a micronodular cirrhotic pattern can be observed. CT imaging of the liver shows cirrhotic changes as a nonspecific imaging finding.

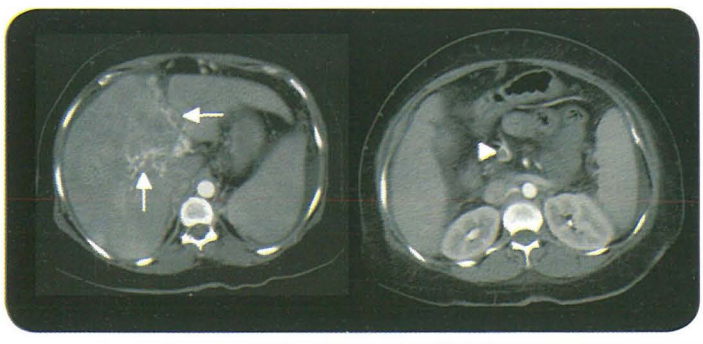


Figure 7 Niemann-Pick disease in an 11-year-old girl. Portal venous phase image shows hepatomegaly and splenomegaly.