Sygnatura: Pol J Radiol, 2006; 71(1): 72-77

Polish Journal of Radiology
www.PolRadiol.com
REVIEW ARTICLE

Otrzymano: 2005.12.20
Zaakceptowano: 2006.01.12

Imaging of the fatty liver

Diagnostyka obrazowa stłuszczenia wątroby

Eugeniusz Tarasów[1], Jacek Janica[1], Jerzy Walecki[2]

[1] Department of Radiology, Medical University Hospital, Bialystok, Poland
[2] Department of Radiology Postgraduate Medical Cluter, Warsaw, Poland

Adres autora: Tarasów Eugeniusz, Department of Radiology, Medical University Hospital, Sklodowskiej 24a Str., 15-276 Bialystok, Poland, e-mail: etarasow@interia.pl

Summary

The global emergence of obesity as an epidemic has made fatty liver disease a public health problem. The net consequence of hepatic steatosis is progresses to steatohepatitis and cirrhosis. Although liver biopsy is currently the gold standard for diagnosis, there is a need for less invasive methods. Imaging by ultrasound, computerized tomography and magnetic resonance are all able to demonstrate liver steatosis. In this paper, these imaging techniques are critically assessed.

Key words: Liver • lipids • steatosis • imaging

PDF file: http://www.polradiol.com/pub/pjr/vol_71/nr_1/8629.pdf

Liver steatosis is referred to as the state of liver parenchyma when excessive accumulation of fat takes place in hepatocytes. Triacyloglyceroles are usually the major compound, but sfingolipides, pfospholipides, cholesterol and its esters may also occur. In physiologic conditions the liver weights about 1600 g in adult males and about 1400 g in adult females and accounts for 1,8–3,1% body weight. The normal liver contains small droplets of fat in hepatocyte cytoplasm; however, they are invisible on histologic examination. It is agreed that if over 5% of hepatocytes exhibits signs of lipid accumulation, the state may be referred to as steatosis [1]. The definition is not widely accepted however, because some authors maintain that liver steatosis should be diagnosed when not less than 50% of hepatocytes are affected by fat accumulation or lipid mass exceeds 5% of the liver weight [2].

Confirmative diagnosis of fatty liver is primarily based on imaging examination, e.g. ustrasonography, computed tomography and magnetic resonance. All these imaging techniques permit diagnosis of liver steatosis; however, evaluation of lipid content or degree of steatosis is qualitative rather, than quantitative. Histopathologic examination is rarely used for confirmation of liver steatosis, although in view of development of alcoholic hepatitis or NASH, its role is very crucial [3]. It is noteworthy that biopsy is an invasive technique burdened with 0.1–0.6% risk of complications (bleeding, pneumothorax, biliary peritonitis) and 0.001–0.003% mortality due to haemoperitoneum [4].

Assessment of liver steatosis in imaging examinations

Ultrasonography (US)

In patients with liver steatosis minor or medium enlargement of the organ is found on ultrasonographic examination [5]. Accumulation of lipid compounds results in diffuse changes in echogenicity of the liver with the presence of hyperechoic areas on the US examination which cause limited imaging of the diaphragm and blood vessels [6]. According to Scatarige et al. [7], three stages of steatosis are defined. Stage I: enhanced echogenicity of the parenchyma with normal image of the vessels and the diaphragm boundaries. Stage II: higher number of minor and diffuse echoes in the parenchyma, poorer imaging of the vessels and the diaphragm boundaries. Stage III: significant number of diffuse echoes in the parenchyma and weak or absent imaging of the vessels, diaphragm and the distal part of the right lobe of the liver.

On experimantal examination of the toxic liver lesion in dogs, steatosis related changes on the US imaging (enlargement,

higher echogenicity, lower echogenicity of the portal vein) are found as early as in the second day of the lesion. The most prominent changes were found between the days 2 and 5 of the lesion. Furthermore, correlation between degree of changes in the sonographic images of the liver and histopathologic examination were found [8].

Relatively low sensitivity and specificity of the US are reported in diffuse lesions of the liver [9]. On the other hand, sonography is sensitive in 89% and specific in 93% in diagnosis of the fatty liver, which was confirmed by histopathologic examination [10, 11]. Also on comparative CT and US imaging a close correlation between the high echogenicity and CT attenuation was demonstrated [12, 13].

Attempts of semiquantitative evaluation of steatosis degree in sonographic imaging are also made. Osawa at al. [14] evaluated US sensitivity at 91.3% based on histograms of semiquantitaive US images of the liver and the kidneys with different echogenicity ≥ 7 dB.

On sonographic Doppler imaging a negative correlation between steatosis and perfusion index is found as a proportion of arterial flow to total liver flow [15]. Hamato et al. (16) found statistically significant changes in flow indices in the hepatic artery in patients with steatosis, chronic hepatitis and hepatic cirrhosis. Based on the Doppler imaging, steatosis and fibrosis changes in the liver were also significantly correlated with changes in flow parameters in the hepatic veins [17].

CT imaging (CT)

CT attenuation (CTA) of the normal hepatic parenchyma at CT imaging with no contrast enhancement amounts to about 65±5 Hounsfield's units (HU) and is higher than attenuation of other visceral organs and muscles. Structures containing blood or bile (blood vessels and bile tracts) are visible as hypodense areas on non-enhanced background of the liver parenchyma. CT scan of the liver is usually performed in several phases. Scanning without contrast enhancement (CE) is combined with a repeated examination of the same area after i.v. contrast enhancement: in the arterial phase, the portal phase and occasionally in the late phase. The examination protocol containing a contrast enhancement dosing, the rate of its administration and time delays are crucial for optimum quality images. The maximum enhancement of the aorta, hepatic artery and its branches is observed 12–17 s. after bolus CE (usually 3 ml/kg body weight, using an automatic syringe) and imaging in the arterial phase should be performed at this delay. The consecutive scanning in the portal phase is performed at the delay of 40–60 s. after contrast enhancement. At this time range, the portal circulation vessels and the liver parenchyma are visualised. Absorption of the contrasted parenchyma at the peak enhancement increases at about 20–25 HU in relation to examination without CE. Elimination of contrast media from the parenchyma is relatively quick and after 5 mins 50% decrease in CT density is observed [18].

Hepatic accumulation of lipids results in a decrease of CT attenuation in the parenchyma without CE, because the adipose tissue has negative CT density values – from -70 HU to -100 HU. With a significant steatosis a contrast reversal can be observed, manifesting itself with hyperdense vessels on the hypodense parenchyma background. The main advantage of CT imaging is a possibility of density measurement at an optional area. The measurements are employed in semiquantitative evaluation of steatosis stages. A basis for this evaluation was developed in many experimental and clinical investigations in 1970s and 1980s. Kawata et al. [19] found significant correlations between triglycerides, cholesterol and cholesterol esters content and liver attenuation on CT examinations in the rats. Similar correlations were also found between histologically assessed steatosis stage and CT density of the liver. Ducommun et al. [20] found that 12–20 HU decrease in CT density is associated with an accumulation of 20–40 mg lipids per 1 gram of the liver tissue.

The correlation between the hepatic lipid content and CT density of the liver was also confirmed in clinical studies. Yajima et al. [21] evaluated the liver attenuation in CT examinations in patients with different diffuse liver lesions.

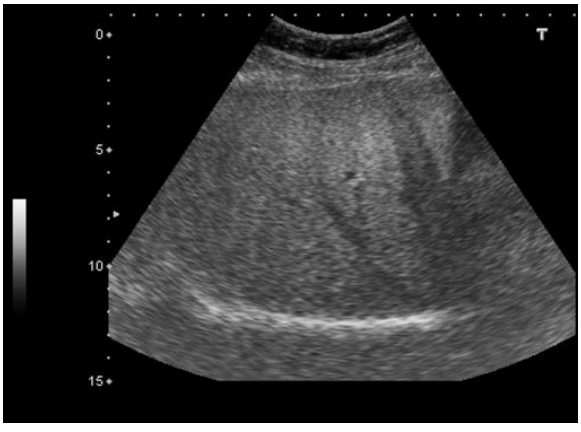

Figure 1. Stage I liver steatosis in US examination; enhanced echogenicity of the liver parenchyma.
Rycina 1. Stłuszczenie wątroby I stopnia w badaniu USG; zwiększona echogeniczność miąższu wątroby.

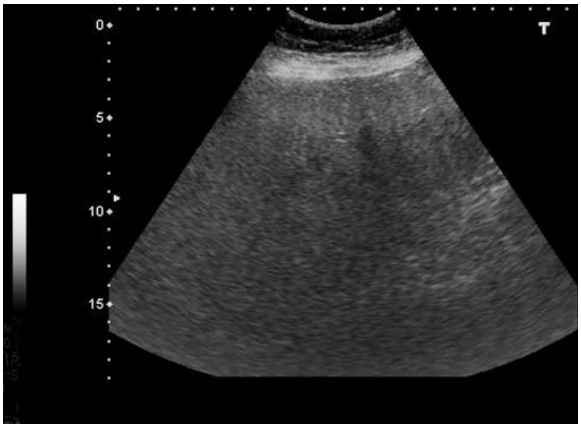

Figure 2. Stage III liver steatosis in US examination; significant enhanced echogenicity and weak imaging of the vessels.
Rycina 2. III stopień stłuszczenia wątroby w badaniu USG; znacznie zwiększona echogeniczność miąższu, słabe uwidocznienie naczyń wątrobowych.

Both in the group of patients with cirrhosis and with chronic hepatitis, respectively, minor insignificant decrease in the CT density was noted. In patients with fatty liver, statistically significant decrease in CT attenuation below 50 HU was found. Moreover, statistically significant correlation between the lipid content and CT density was noted. Assuming that steatosis occurs at the lipid content above 100 mg/g fresh tissue, the authors suggest that a decrease of CT attenuation below 48 HU anables unequivocal diagnosis of the liver steatosis. Pamilo et al. [22] found that in mild steatosis (below 10%) CT density amounts to 39–60 HU, at the lipid content of 10–25% it decreases to 4–46 HU, and at the severe steatosis (above 25% lipid content) it may be negative (-6) - (+19) HU. The correlation between the histologically assessed steatosis grade and CT attenuation was also confirmed by Bydder et al. [23] in a group of patients with alcoholic fatty liver.

As the spleen displays a lower CT values (45±5 HU) in non-enhancement CT scans compared with that of the liver, the assessment of the liver steatosis is also based on the liver/spleen index (L/S) expressed as the difference between the liver and the spleen attenuation (CTA_L-CTA_S) or their quotient (CTA_L/CTA_S). The liver/spleen index was found to correlate positively with the liver steatosis stage at the histo-morphometric examination [24]. Also, Ricci et al. [25] found there exists statistically significant correlations between CTA values of the liver, the L/S index and the lipid content based on the histo-morphometric examination in patients with the liver steatosis. Occasionally, the muscle tissue is used as the internal standard to compare the CTA values of the liver [26].

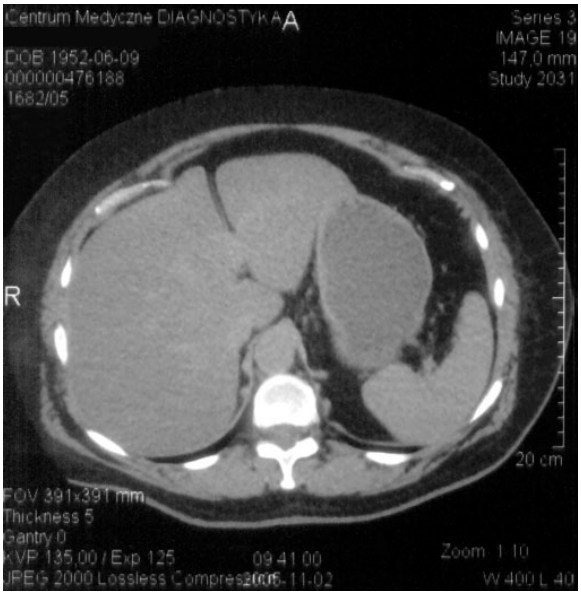

Figure 3. Liver steatosis in CT; marked decrease of the liver CT attenuation compared to spleen and contrast reversal sign - hyperdense liver vessels on the hypodense parenchyma background.

Rycina 3. Stłuszczenie wątroby w obrazie TK; znaczne obniżenie osłabiania wątroby w porównaniu ze śledzioną oraz obraz odwrócenia kontrastowego – hiperdensyjne naczynia wątrobowe widoczne na tle hipodensyjnego miąższu wątroby.

Additionally, attempts to develop a noninvasive method for the quantification of the hepatic fat content in vivo based on CT scans with the use of phantoms and callibration curves. Ricci et al. [25] found statistically significant correlations between CTA values and terbutyl alcohol content in phantoms with different concentrations of the alcohol. CTA values of terbutyl alcohol used in the experiment are comparable to these of the adipose tissue. The authors found a close correlation between the liver lipid content in patients with the fatty liver based on callibrated CT scans and histomorphometric assessment. The authors emphasize the particular value of this method in patients with a mild steatosis.

Contrast enhancement of the liver and the spleen is dependent on the contrast medium dose, the rate of its administration and the scaning delay. Consequently, the enhanced CT scans are largely dependent on the examination protocol employed. Notwithstanding, qualitative and quantitative criteria of the liver steatosis diagnostics following the enhanced CT scans were developed in clinical trials; however, CT attenuation values of the normal and fatty liver (and also the L/S index value) exhibit a slight overlap after enhancement [27]. Consequently, the enhanced CT scanning is not suggested as a diagnostic method in assessment of steatosis, and the nonenhanced CT remains as a method of choice [28]. However, in order to obtain a better assessment of the liver parenchyma and the stage of its steatosis, attempts are being made to administer media that are specifically bound by hepatocytes. Bergman et al. [29] found in their experimental research on rats, that the liver steatosis is accompanied by a decrease accumulation of FP 736-04 emulsion that is specifically bound by hepatocytes. The authors also suggest that the analysis of the liver attenuation after FP 736-04 administration may be employed in the assessment of the liver steatosis.

Magnetic resonance imaging (MRI)

In MRI diagnostics of the fatty liver special sequences of fast gradient echo are used [30] combined with Chemical Shift Imaging (CSI) technique [31, 32, 33, 34]. Other methods of choice include gradient sequences „in-phase" and „in out-phase" [35, 36] and magnetisation transfer imaging (MT). Alanen et al. [37] found out that the value of relative proton fat density in the latter method is significantly correlated with a proportion of steatosed hepatocytes in histologic examination.

Contrast media are uncommonly used in diagnostics of the liver steatosis. Contrast media of paramagnetics group (Gd-DTPA – gadopentetate dimeglumine) or supraparamagnetics group are used for diagnostics of steatosis-related focal changes and differentiating from other types of focal changes [38]. Thus, the employment of organ-specific contrast media, e.g. Mn-DPDP (manganese-DPDP) or Gd-BOPTA/dimeg (gadobenate dimeglumine) serves diagnostics and differentiating of focal changes in cases of fatty liver [39].

It is commonly accepted that liver steatosis is accopmanied by shortened time of lingitudinal relaxation (T_1) due to triglyceride accumulation. However, results of relaxation time measurements T_1 and T_2 (transverse relaxation time)

are divergent in studies of different authors. Chai et al. [40] evaluated the relaxation times and magnetisation transfer phenomenon in two experimental models of fatty liver in rats. In cases of the acute steatosis the authors recorded increased relaxation times T_1 and T_2 and weaker effect of magnetisation transfer compared with the control group. Chronic liver steatosis was characterised by shortened values of T_1 and T_2 and stronger effect of magnetisation transfer. Kreft et al. [39] found out that in simple liver steatosis in rats T_1 is shortened by 15%, whereas steatosis with hepatocyte degeneration results in increase of T_1 by 12%. On the other hand, T_2 in both exparimental models correlated positively with the steatosis grade. The authors also found a significant correlation between a signal intensity at conventional imaging in T1-weighted images, CSI images and the steatosis grade.

Other imaging methods

Single proton emission computed tomography (SPECT) and planar scintigraphy (PS) occasionally were used as diagnostic methods in liver steatosia assessment. Delcourt et al. [41] demonstrated a high specificity of SPECT and planar scintigraphy in diagnostics of alcoholic liver steatosis.

Antropometric indices in diagnostics of steatosis

Body mass index (BMI) may be used as a simple index indicating a risk of liver steatosis. Rinella et al. [42] found no signs of liver steatosis in patients with BMI below 25. On the other hand, incodence of liver steatosis increased with BMI, from 33% at BMI of 25–28 to 76% at BMI above 28. The authors found a statistically significant correlation between BMI and incidence of the biopsy confirmed steatosis in a group of potential liver donors.

However, all above-mentioned imaging techniques enable diagnosis of liver steatosis, assessment of lipid content and, consequently degree of the steatosis is qualitative rather than quantitative. Moreover, on CT and MRI examinations a certain percentage of false negative results is noted. This is confirmed by by Rinella et al. [42] in their comparative studies in patients with MRI and CT diagnosed and subsequently biopsy confirmed fatty liver. However, in some cases of the biopsy-confirmed steatosis imaging studies gave negative results: 24% and 30% patients diagnosed by CT and MRI, respectively. This is also confirmed by observations by Ricci et al. [43] who found normal values of L/S index on CT scans in a significant proportion of patients with increased hepatic liver content based on histomorphometric assessment.

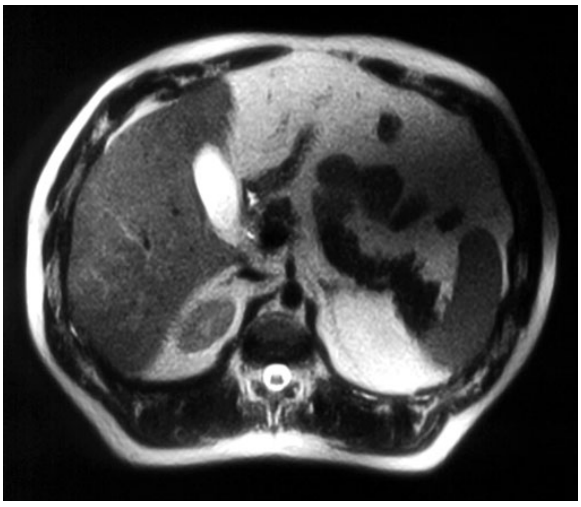

Figure 4. Fatty liver in MR examination. Hiperintense liver parenchyma in T2-weigthed axial image.

Rycina 4. Stłuszczenie wątroby w badaniu MR. Hiperintensywny miąższ wątroby w obrazach T2-zależnych w płaszczyźnie poprzecznej.

1H MR spectroscopy in assessment of liver steatosis (1H MRS)

A high usefulness of 1H MR spectroscopy in assessment of lipid compounds content in the liver is confirmed by Szczepaniak et al. [44]. The authors in experimental investigations evaluated lipid content in the livers of dogs and rats and the influence of norepinephrine stimulation on changes of their levels. After norepinephrine administration, which enhances tissue lypolysis, a significant increase in hepatic liver content was found. The results indicated high

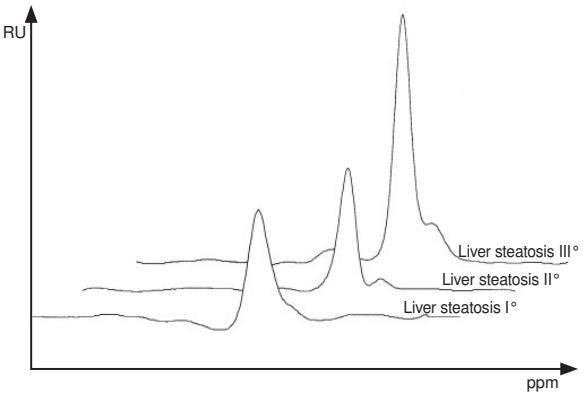

Figure 5. 1H MR spectra from healthy liver and patients with various stages of liver steatosis.

Rycina 5. Widma spektroskopii 1H MR wątroby osoby zdrowej oraz chorych z różnymi stopniami stłuszczenia.

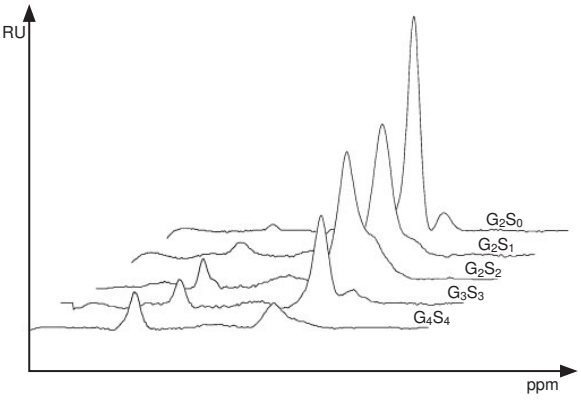

Figure 6. 1 H MR spectra from patients with chronic hepatitis with different inflammatory activity stage (G-grading) and fibrosis advancement (S-staging).

Rycina 6. Widma 1H MRS chorych z przewlekłym wirusowym zapaleniem wątroby z różnymi stopniami aktywności zapalnej (G-grading) oraz różnym zaawansowaniem włóknienia (S-staging).

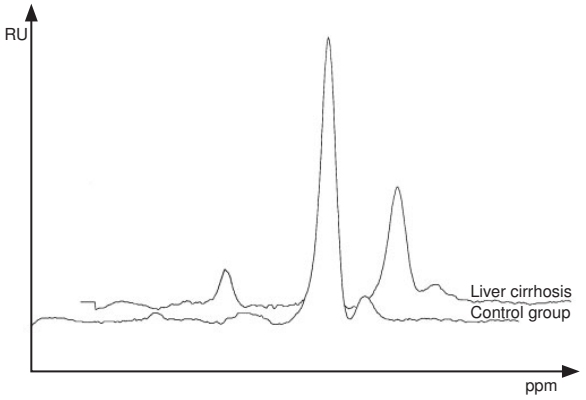

Figure 7. 1H MR spectra from patients with liver cirrhosis and control group.

Rycina 7. Widma 1H MRS wątroby chorego z marskością wątroby oraz osoby z grupy kontrolnej.

correlation between the lipid content evaluated by 1H MRS examination and biochemical and histological methods, both before and after norepinephrine administration. Also Choji at al. [45, 46] found correlations between lipid evaluation on 1H MRS examination and *in vitro* measurements in experimental model of liver steatosis in rats.

Application of 1H MR spectroscopy to assessment of lipid compounds in the liver has been described in scarce reports, hitherto. Thomsen et al. [47] found correlation between hepatic lipid content using 1H MRS examination *in vivo* and biochemical methods, in the liver bioptates of patients with alcoholic liver steatosis at various stages. Longo et al. [24, 48] assessed grade of liver steatosis by comparing results of 1H MRS spectroscopy, CT scanning and histological examinations. The authors found significant correlation between ratio of lipid signal to sum of lipid and water signal in 1H MRS spectroscopy and value of L/S attenuation index in CT scanning. Both the lipid content assessed by MR spectroscopy as well as L/S index on CT scans was significantly correlated with the steatosis assessed histologically. Also Choji et al. [45] found a high correlation between lipid content on 1H MRS and histological examinations in patients with fatty liver. According to the latter authors, sensitivity of 1H MRS in diagnostics of fatty liver amounted to 100%, specificity to 83% at accuracy of 81% (in comparison with CT – respectively, 43%, 90% and 81%). Also in our own examinations a high usefulness of 1H MR spectroscopy in assessment of hepatic lipids content in healthy subjects and patients with diffuse parenchymal diseases was demonstrated [49, 50, 51].

References:

1. Fromenty B, Berson A, Pessayre D: Microvesicular steatosis and steatohepatitis: role of mitochondrial dysfunction and lipid peroxidation. J Hepatol 1997; 26 Suppl 1: 13–22.
2. Sherlock S, Dooley J. Diseases of the liver and biliary system. Oxford: Blackwell Science; 1997.
3. Ueno T, Sugawara H, Sujaku K et al. Therapeutic effects of restricted diet and exercise in obese patients with fatty liver. J Hepatol 1997; 27: 103–7.
4. Piccinino F, Sagnelli E, Pasquale G, Giusti G: Complications following percutaneous liver biopsy. A multicentre retrospective study on 68,276 biopsies. J Hepatol 1986; 2: 165–73.
5. Doherty JF, Adam EJ, Griffin GE, Golden MH: Ultrasonographic assessment of the extent of hepatic steatosis in severe malnutrition. Arch Dis Child 1992; 67: 1348–52.
6. Quinn SF, Gosink BB: Characteristic sonographic signs of hepatic fatty infiltration. AJR Am J Roentgenol 1985; 145: 753–5.
6. Rzymski K. Atlas ultrasonografii. Poznań: UNI-DRUK, 1997.
7. Scatarige JC, Scott WW, Donovan PJ, Siegelman SS, Sanders RC: Fatty infiltration of the liver: ultrasonographic and computed tomographic correlation. J Ultrasound Med 1984; 3: 9–14.
8. Voros K, Albert M, Vetesi F, Harmat G, Binder K, Szaniszlo F: Hepatic ultrasonographic findings in experimental carbon tetrachloride intoxication of the dog. Acta Vet Hung 1997; 45: 137–50.
9. Cardi M, Muttillo IA, Amadori L et al: Superiority of laparoscopy compared to ultrasonography in diagnosis of widespread liver diseases. Dig Dis Sci 1997; 42: 546–8.
10. Caturelli E, Squillante MM, Andriulli A, Cedrone A, Cellerino C, Pompili M, Manoja ER, Rapaccini GL: Hypoechoic lesions in the 'bright liver': a reliable indicator of fatty change. A prospective study. J Gastroenterol Hepatol 1992; 7: 469–72.
11. Joseph AE, Saverymuttu SH, al-Sam S, Cook MG, Maxwell JD: Comparison of liver histology with ultrasonography in assessing diffuse parenchymal liver disease. Clin Radiol 1991; 43: 26–31.
12. Scatarige JC, Scott WW, Donovan PJ, Siegelman SS, Sanders RC: Fatty infiltration of the liver: ultrasonographic and computed tomographic correlation. J Ultrasound Med 1984; 3: 9–14.
13. Filippone A, Di Giandomenico V, Di Giandomenico E, Genovesi N, Bonomo L: Hepatic steatosis: combined echography-computerized tomography imaging. Radiol Med. 1991; 81: 16–21.
14. Osawa H, Mori Y: Sonographic diagnosis of fatty liver using a histogram technique that compares liver and renal cortical echo amplitudes. J Clin Ultrasound 1996; 24: 25–9.
15. Kakkos SK, Yarmenitis SD, Tsamandas AC, Gogos CA, Kalfarentzos F: Fatty liver in obesity: relation to Doppler perfusion index measurement of the liver. Scand J Gastroenterol 2000; 35: 976–80.
16. Hamato N, Moriyasu F, Someda H, Nishikawa K, Chiba T, Okuma M: Clinical application of hepatic venous hemodynamics by Doppler ultrasonography in chronic liver disease. Ultrasound Med Biol 1997; 23: 829–35.
17. Colli A, Cocciolo M, Riva C et al: Abnormalities of Doppler waveform of the hepatic veins in patients with chronic liver disease: correlation with histologic findings. AJR Am J Roentgenol 1994; 162: 833–7.
18. Wegener OH. Whole body computed tomography. 2nd ed. Boston (MA): Blackwell Scientific Publications Inc., 1993.
19. Kawata R, Sakata K, Kunieda T, Saji S, Doi H, Nozawa Y: Quantitative evaluation of fatty liver by computed tomography in rabbits. AJR Am J Roentgenol 1984; 142: 741–6.
20. Ducommun JC, Goldberg HI, Korobkin M, Moss AA, Kressel HY: The relation of liver fat to computed tomography numbers: a preliminary experimental study in rabbits. Radiology 1979; 130: 511–3.
21. Yajima Y, Narui T, Ishii M et al: Computed tomography in the diagnosis of fatty liver: total lipid content and computed tomography number. Tohoku J Exp Med 1982; 136: 337–42.
22. Pamilo M, Sotaniemi EA, Suramo I, Lahde S, Arranto AJ: Evaluation of liver steatotic and fibrous content by computerized tomography and ultrasound. Scand J Gastroenterol 1983; 18: 743–7.
23. Bydder GM, Chapman RW, Harry D, Bassan L, Sherlock S, Kreel L: Computed tomography attenuation values in fatty liver. Comput Tomogr 1981; 5: 33–5.
24. Longo R, Polesello P, Ricci C et al: Proton MR spectroscopy in quantitative in vivo determination of fat content in human liver steatosis. J Magn Reson Imaging 1995; 5: 281–5.
25. Ricci C, Longo R, Gioulis E et al: Noninvasive in vivo quantitative assessment of fat content in human liver. J Hepatol 1997; 27: 108–13.
26. Panicek DM, Giess CS, Schwartz LH: Qualitative assessment of liver for fatty infiltration on contrast-enhanced CT: is muscle a better standard of reference than spleen? J Comput Assist Tomogr 1997; 21: 699–705.
27. Jacobs JE, Birnbaum BA, Shapiro MA et al: Diagnostic criteria for fatty infiltration of the liver on contrast-enhanced helical CT. AJR Am J Roentgenol 1998; 171: 659–64.

28. Johnston RJ, Stamm ER, Lewin JM, Hendrick RE, Archer PG: Diagnosis of fatty infiltration of the liver on contrast enhanced CT: limitations of liver-minus-spleen attenuation difference measurements. Abdom Imaging 1998; 23: 409–15.
29. Bergman A, Sundin A, Karpe F, Magnusson A: CT with the hepatocyte-specific contrast medium FP 736-04 in an experimental model of liver steatosis. Acta Radiol 1997; 38: 405–9.
30. Fishbein MH, Stevens WR: Rapid MRI using a modified Dixon technique: a non-invasive and effective method for detection and monitoring of fatty metamorphosis of the liver. Pediatr Radiol 2001; 31: 806–9.
31. Brechtel K, Jacob S, Machann J et al: Acquired generalized lipoatrophy (AGL): highly selective MR lipid imaging and localized (1)H-MRS. J Magn Reson Imaging 2000; 12: 306–10.
32. Rosen BR, Carter AE, Pykett IL, Buchbinder BR, Brady TJ: Proton chemical shift imaging: An evaluation of its clinical potential using an in vivo fatty liver model. Radiology 1985; 154: 469–72.
33. Schertz LD, Lee JKT, Heiken JP, Molina PL, Totty WG: Proton spectroscopic imaging (Dixon method) of the liver: clinical utility. Radiology 1989, 173: 401–5.
34. Siegelman ES: MR imaging of diffuse liver disease. Hepatic fat and iron. Magn Reson Imaging Clin N Am 1997; 5: 347–65.
35. Kroncke TJ, Taupitz M, Kivelitz D et al: Multifocal nodular fatty infiltration of the liver mimicking metastatic disease on CT: imaging findings and diagnosis using MR imaging. Eur Radiol 2000; 10: 1095–100.
36. Martin J, Sentis M, Puig J et al: Comparison of in-phase and opposed-phase GRE and conventional SE MR pulse sequences in T1-weighted imaging of liver lesions. J Comput Assist Tomogr 1996; 20: 890–7.
37. Alanen A, Komu M, Leino R, Toikkanen S: MR and magnetisation transfer imaging in cirrhotic and fatty livers. Acta Radiol 1998; 39: 434–9.
38. Lwakatare F, Yamashita Y, Nakayama M, Takahashi M: SPIO-enhanced MR imaging of focal fatty liver lesions. Abdom Imaging 2001; 26: 157–60.
39. Kreft BP, Tanimoto A, Baba Y, Zhao L, Finn JP, Stark DD: Enhanced tumor detection in the presence of fatty liver disease: cell-specific contrast agents. J Magn Reson Imaging 1994; 4: 337–42.
40. Chai JW, Lin YC, Chen JH et al: In vivo magnetic resonance (MR) study of fatty liver: importance of intracellular ultrastructural alteration for MR tissue parameters change. J Magn Reson Imaging 2001; 14: 35–41.
41. Delcourt E, Vanhaeverbeek M, Binon JP et al: Emission tomography for assessment of diffuse alcoholic liver disease. J Nucl Med 1992; 33: 1337–44.
42. Rinella ME, Alonso E, Rao S et al: Body mass index as a predictor of hepatic steatosis in living liver donors. Liver Transpl 2001; 7: 409–14.
43. Ricci C, Longo R, Gioulis E et al: Noninvasive in vivo quantitative assessment of fat content in human liver. J Hepatol 1997; 27: 108–13.
44. Szczepaniak LS, Babcock EE, Schick F et al: Measurement of intracellular triglyceride stores by H spectroscopy: validation in vivo. Am J Physiol 1999; 276: E977–89.
45. Choji T, Honjou K, Suda H et al: Detection of intrahepatic lipids by 1H-MRS-studies by breath-holding & 1 cm3 VOI. Nippon Igaku Hoshasen Gakkai Zasshi 1992; 52: 107–9.
46. Choji T: Evaluation of fatty liver changes and fatty degeneration in liver tumors by 1H-MRS. Nippon Igaku Hoshasen Gakkai Zasshi 1993; 53: 1408–14.
47. Thomsen C, Becker U, Winkler K et al: Quantification of liver fat using magnetic resonance spectroscopy. Magn Reson Imaging 1994; 12: 487–95.
48. Longo R, Ricci C, Masutti F et al: Fatty infiltration of the liver. Quantification by 1H localized magnetic resonance spectroscopy and comparison with computed tomography. Invest Radiol 1993; 28: 297–302.
49. Tarasów E, Siergiejczyk L, Panasiuk A et al: MR proton spectroscopy in liver examinations of healthy individuals *in vivo*. Med Sci Monit 2002; 8: 36–40.
50. Tarasów E, Panasiuk A, Walecki J, Prokopowicz D: Metabolic profiles of liver parenchymal diseases. Pol J Radiol 2004; 69 Suppl 1: 96–7.
51. Tarasów E, Wiercińska-Drapało A, Jaroszewicz J et al: Metabolic disturbances in liver 1H MR spectroscopy in HIV and HCV coinfected patients as a potential marker of hepatocyte activation. Acta Radiol 2004, 45: 803–9.