^{1}H MRS assessment of hepatic steatosis in overweight children and adolescents: comparison between 3T and open 1T MR-systems

Elizaveta Chabanova,[1] Dorthe S. Bille,[2,4] Ebbe Thisted,[2] Jens-Christian Holm,[2,3] Henrik S. Thomsen[1,5]

[1]Department of Diagnostic Radiology, Copenhagen University Hospital Herlev, 54E2, Herlev Ringvej 75, 2730 Herlev, Denmark
[2]Department of Pediatrics, The Children's Obesity Clinic, Holbaek Hospital, 4300 Holbaek, Denmark
[3]Faculty of Health Sciences, University of Copenhagen, 2200 Copenhagen, Denmark
[4]Section of Metabolic Genetics, Faculty of Health Sciences, The Novo Nordisk Foundation Center for Basic Metabolic Research, University of Copenhagen, 2200 Copenhagen, Denmark
[5]Department of Diagnostic Sciences, Faculty of Health Sciences, University of Copenhagen, 2200 Copenhagen, Denmark

Abstract

Purpose: In recent years, proton magnetic resonance spectroscopy (MRS) has emerged as a non-invasive technique for measurement of fat content in the liver. The technique is often applied for overweight and obese patients. However, excessively obese patients cannot be examined in most conventional magnetic resonance systems due to limited space. The purpose of this study was to examine the ability of open 1T system to monitor liver fat with proton MRS and to compare hepatic fat fractions (HFFs) obtained using an open 1T system with assessment with 3T proton MRS.
Methods: The study included 23 children and adolescents up to 20 years of age with a body mass index above the 97th percentile according to age and gender. Proton MRS for each patient was performed in both 1T and 3T using point resolved spectroscopy sequence in a single volume positioned in the right liver lobe.
Results: Average T2 relaxation times obtained for an open 1T system (55 ± 7 ms for water and 85 ± 11 ms for fat) were higher than average T2 relaxation times obtained for a 3T system (31 ± 4 ms for water and 66 ± 10 ms for fat). HFFs measured using an open 1T system showed strong correlation with HFFs measured using a 3T system ($r = 0.99$, $P < 0.0001$).

Conclusions: Proton MRS measurements of HFF with an open 1T system are feasible. Open 1T system may reliably replace 3T magnetic resonance system for the assessment of liver fat.

Key words: Magnetic resonance—Spectroscopy—Relaxation time—Children—Non-alcoholic fatty liver disease—Obesity

In recent years, obesity has become a growing problem all over the world beginning at early age in children and progressing into adulthood [1, 2]. One of the major complications caused and worsened by obesity is non-alcoholic fatty liver disease (NAFLD). NAFLD ranges from simple steatosis through steatohepatitis to end-stage liver disease (cirrhosis) and is defined as triglyceride accumulation in hepatocytes exceeding 5 % of the liver weight [3, 4]. It is hard to predict who are going to develop steatohepatitis and liver function impairment. Liver biopsy is the gold standard of diagnosis and severity assessment of NAFLD [5, 6]. However, it is an invasive procedure associated with serious risks. Obese children are frequently affected by NAFLD, which cannot be predicted by liver enzymes, clinical and/or anthropometrical findings [7]. Magnetic resonance spectroscopy (MRS) is a valid alternative for the detection of accumulation of fat in livers in obese children [8].

Correspondence to: Elizaveta Chabanova; *email:* elizaveta.chabanova@regionh.dk

MRS is a unique technique that allows the study of the metabolic tissue content in vivo noninvasively [4, 8]. Proton MRS (^{1}H MRS) can measure the triglyceride content in liver cells directly and can analyze the hepatic fat fraction (HFF) quantitatively in the liver [9, 10]. ^{1}H MRS is more accurate in the detection of fatty liver than computed tomography (CT) and exhibits higher sensitivity in the detection of liver fat content than conventional MR imaging and ultrasound investigations [11, 12].

Obese patients over 120 kg often exceed the gantry or bore diameter of MR-system because of their girth and therefore cannot be examined in most conventional MR-systems. New open MR-systems with greater table weight capacity and larger gaps can be used for MR-imaging examination and can diagnose excessively obese patients offering sufficient image quality to impact the therapy [13]. The purpose of this study was to examine the ability of an open 1T system to monitor liver fat by ^{1}H MRS technique and to compare HFF obtained using an open 1T system with assessment with 3T proton ^{1}H MRS.

Materials and methods

Patients

23 children and adolescents (16 girls and 7 boys; mean age 14 ± 3; range 8.1–19.3 years) included in childhood obesity treatment [14] participated in the study. The patients had a body mass index (BMI) above the 97th percentile according to Danish age and gender adjusted BMI charts [15]. Mean BMI was 31 ± 6 (range 22.2–48.4, weight/height squared).

Written informed consent was obtained from all patients older than 18 years of age and from parents of children with an age younger than 18 years. The study was approved by the institutional review board (ID-no.: SJ-104 and SJ-98), by the data protection agency, and by ClinicalTrials.gov (ID-no.: NCT00823277 and NCT 00928473).

Magnetic resonance examination

MR measurements were performed for each patient in 3T Achieva MR-imaging system (Philips Medical Systems, Best, the Netherlands) and in open 1T Panorama HFO MR-imaging system (Philips Medical Systems, Best, the Netherlands) with 5-30 min between the examinations. Each examination took about 30 min. Patients were examined in the supine position. No respiratory triggering was used.

MR measurements at the 3T system were performed with a Sense Cardiac coil. T2-weighted turbo spin echo (TSE) coronal and axial slices through the upper abdomen were acquired for positioning the spectroscopy volume of interest (VOI). Parameters for the TSE sequence were: TSE factor = 93, repetition time (TR) = 2182 ms, slice thickness = 7 mm, echo time (TE) = 80 ms. Spectroscopy VOI (11 mm × 11 mm × 11 mm) was positioned in the right lobe of the liver avoiding major blood vessels and intrahepatic bile ducts according to TSE images. A single voxel spectrum without water saturation was recorded using a point resolved spectroscopy (PRESS) sequence with the parameters: TR = 4000 ms, TE = 75 ms, spectral bandwidth = 2000 Hz, 1024 points, 32 averages. A series of TE = 45, 60, 75, 90, and 105 ms was applied for measuring HFF compensated for T2 relaxation, and T2 relaxation times of water and of fat.

MR measurements at the open 1T system were performed with a Sense Body Large or XLarge coil. A balanced fast field echo survey scan (20 slices, 4-mm slice thickness, TR = 3.8 ms, TE = 1.9 ms) in three orthogonal directions was used for positioning VOI. Spectroscopy VOI (14 mm × 14 mm × 14 mm) was positioned in the right lobe of the liver. A single voxel spectrum without water saturation was recorded using a PRESS sequence with the parameters: TR = 4000 ms, TE = 75 ms, spectral bandwidth = 1000 Hz, 1024 points, 32 averages. A series of TE = 65, 95, 125, 155, and 185 ms was applied for measuring HFF compensated for T2 relaxation, and T2 relaxation times of water and of fat.

Measurement of hepatic fat fraction

The water (4.7 ppm) and fat (1.3 ppm) peaks of the acquired spectra were fitted to obtain their areas using a standard post-processing protocol for fitting metabolite peak areas available at the MR-imaging systems.

HFF was calculated according to the equation

$$\text{HFF} = \big(\text{fat peak area}/\big(\text{fat peak area} + \text{water peak area}\big)\big) *100.$$

For comparison, HFF was calculated for the two different MR-systems from the single spectra at TE = 75 ms. HFF obtained at TE = 75 ms is overestimated due to T2 relaxation effects [9]. Water and fat T2 relaxation times and HFF corrected for T2 relaxation effects (HFF at TE = 0 ms) were calculated using an exponential least-square fitting algorithm to the peak areas with the series of TE as described earlier [9]. The T2 relaxation calculations for the fat peak were performed when the fat peak was sufficiently large (HFF > 5 % at TE = 75 ms).

A TR of 4 s was considered sufficiently long to avoid influence of T1 relaxation in the post-processing calculations.

Statistical analysis

Mathematical and statistical calculations were performed using MATLAB software. Quantitative variables were processed to give group mean values,

Fig. 1. **A** ¹H MR spectra at TE = 75 ms in 1T and 3T MR-▶ systems in a 12-year-old. The water peak is visible at a frequency of 4.7 ppm, the fat (methylene) peak is visible at a frequency of 1.3 ppm. **B**, **C** Comparison between T2 relaxation decays. Intensities are normalized so that initial intensities at TE = 0 ms are equal to 100. **B** Water peak area (3T fit: $y = 100^*\exp(-0.037^*x)$, $R^2 = 0.99$; 1T fit: $y = 100^*\exp(-0.021^*x)$, $R^2 = 0.99$). **C** Fat peak area (3T fit: $y = 100^*\exp(-0.021^*x)$, $R^2 = 0.97$; 1T fit: $y = 100^*\exp(-0.011^*x)$, $R^2 = 0.99$).

Table 1. T2 relaxation times of water and fat components for 1T and 3T MR-systems

	T2 of water (ms)		T2 of fat (ms)	
	3T	1T	3T	1T
Mean	31	55	66	85
Standard deviation	4	7	10	11
Minimum	22	45	48	67
Maximum	38	71	83	104

T2 relaxation times of water were calculated for the 23 patients. T2 relaxation times of fat were calculated for the 7 patients when the fat peak was sufficiently large (HFF > 5 % at 1T, TE = 75 ms)

standard deviations, a minimum and a maximum. Pearson's correlation coefficient r was used to describe correlation. Statistical significance was described by a P value below 0.05.
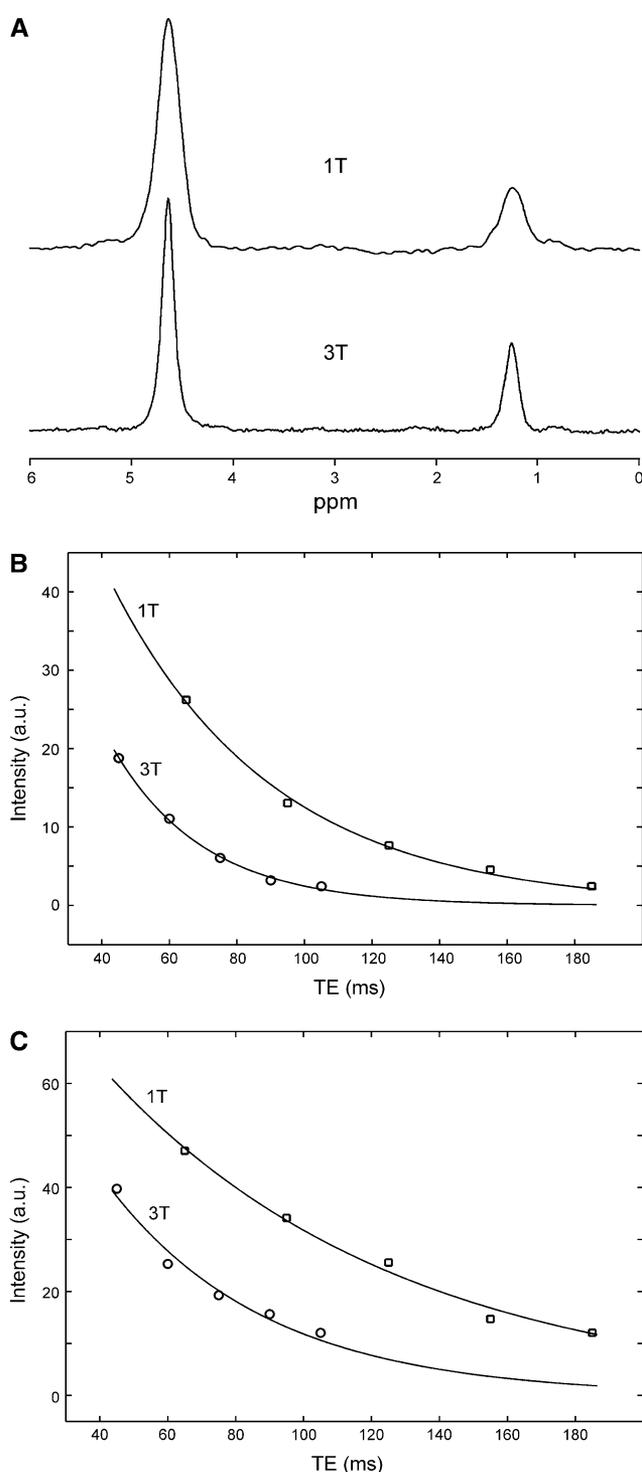
Results

Average T2 relaxation times obtained for the open 1T system were higher than average T2 relaxation times obtained for the 3T system. T2 values for water and fat differed with a factor of almost 2 between the patients in each MR-system. The corresponding results are shown in Table 1. As an example, ¹H MR spectra and T2 relaxation decays measured with 1T and 3T MR-systems are shown in Fig. 1.

HFF obtained using the open 1T system showed strong correlation with HFF measured using the 3T system at both TE = 75 ms ($r = 0.99$, $P < 0.0001$) and TE = 0 ($r = 0.94$, $P = 0.002$). The corresponding results are shown in Fig. 2. HFF at TE = 75 ms were calculated for all patients. HFF corrected for T2 relaxation effects was calculated for the 7 patients with a sufficiently large fat peak (HFF > 5 % at TE = 75 ms).

Discussion

In recent years, proton MRS has emerged as a non-invasive technique for measurement of fat content in the liver [16–18]. For the determination of the true HFF, spectroscopic peak areas are usually corrected for T2 relaxations. Correction for T1 relaxation can be avoided by long TR. A number of studies [11, 17, 19–22] used average T2 values to correct for all patients. In the other studies [9, 23, 24], T2 values were calculated individually for each patient. Reported T2 values for 3T ranged from 12.4 to 54.3 ms with averages of 27 [24], 28 [9], and 34 ms [25] for water, and from 28 to 99 ms with averages of 61 [24], 64 [9], and 68 ms [25] for fat. The values for 3T are in line with the results obtained in this study. Average T2
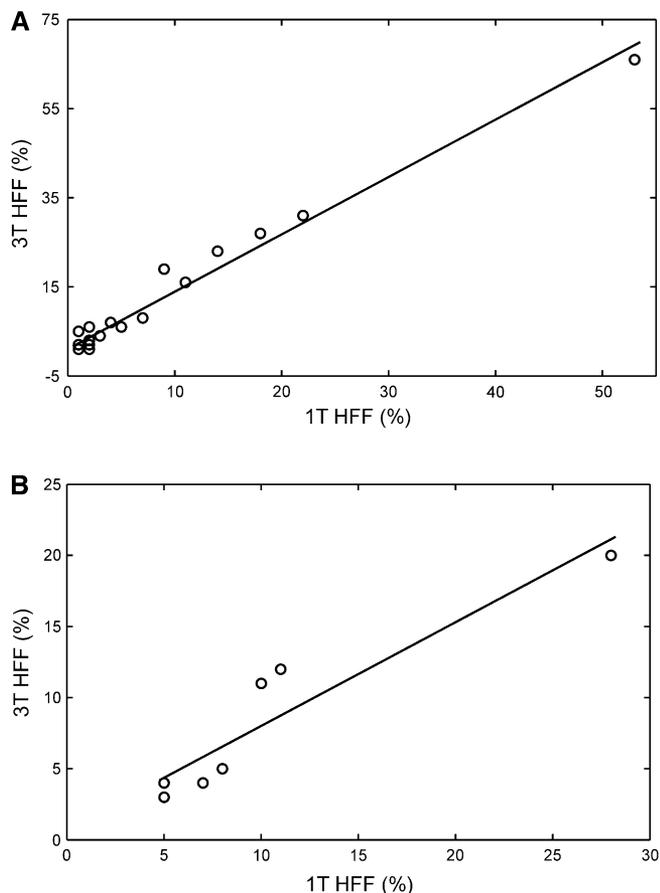
Fig. 2. Correlation between HFF values measured in 1T and 3T MR-systems. **A** HFF measured at TE = 75 ms ($r = 0.99$, $P < 0.0001$; fit: $y = 1.29 \cdot x + 1$, $R^2 = 0.98$). **B** HFF compensated for T2 relaxation (at TE = 0 ms) ($r = 0.94$, $P = 0.002$; fit: $y = 0.73 \cdot x + 0.72$, $R^2 = 0.85$).

values at 1T have been reported based on 5 morbidly obese patients [25, 26]: T2 = 69 ms for water, and T2 = 60 ms for fat. Our study reports slightly different T2 values at 1T. The disagreement may be due to large range of T2 values in different patients and a small number of patients [26]. In general, T2 relaxation times are expected to be lower at higher field strengths [27]. This is in agreement with the present data.

The technique of using ¹H MRS for the evaluation of HFF is highly reproducible in the same spectroscopic volume [16, 19]. Although fat is not always equally distributed within the liver and HFF obtained in different positions can vary by up to 20 % [17, 19, 20, 28, 29], the present data show high correlation between the HFF obtained with 1T and 3T systems. It has recently been shown that measurements of HFF with ¹H MRS in an open 1T MR-system are in good correlation with clinical and histopathological results [26].

In conclusion, ¹H MRS measurements of HFF with an open 1T system are feasible. Open 1T system may reliably replace 3T system for the assessment of liver fat.

References

1. Harrison SA, Day CP (2007) Benefits of lifestyle modification in NAFLD. Gut 56:1760–1769
2. Bellentani S, Scaglioni F, Marino M, Bedogni G (2010) Epidemiology of non-alcoholic fatty liver disease. Dig Dis 28:155–161
3. Paradis V, Bedossa P (2008) Definition and natural history of metabolic steatosis: histology and cellular aspects. Diabetes Metab 34:638–642
4. Ma X, Holalkere NS, Kambadakone RA, et al. (2009) Imaging-based quantification of hepatic fat: methods and clinical applications. Radiographics 29:1253–1277
5. Patton HM, Lavine JE, Van Natta ML, et al. (2008) Clinical correlates of histopathology in pediatric nonalcoholic steatohepatitis. Gastroenterology 135:1961–1971
6. Wieckowska A, Feldstein AE (2008) Diagnosis of nonalcoholic fatty liver disease: invasive versus noninvasive. Semin Liver Dis 28:386–395
7. Radetti G, Kleon W, Stuefer J, Pittschieler K (2006) Non-alcoholic fatty liver disease in obese children evaluated by magnetic resonance imaging. Acta Paediatr 95:833–837
8. Fischbach F, Bruhn H (2008) Assessment of in vivo ¹H magnetic resonance spectroscopy in the liver: a review. Liver Int 28:297–307
9. Chabanova E, Bille DS, Thisted E, Holm J-C, Thomsen HS (2012) MR spectroscopy of liver in overweight children and adolescents: investigation of ¹H T2 relaxation times at 3T. Eur J Radiol 81:811–814
10. Reeder SB, Cruite I, Hamilton G, Sirlin CB (2011) Quantitative assessment of liver fat with magnetic resonance imaging and spectroscopy. J Magn Reson Imaging 34:729–749
11. Zhong L, Chen JJ, Chen J, et al. (2009) Non-alcoholic fatty liver disease: quantitative assessment of liver fat content by computed tomography, magnetic resonance imaging and proton magnetic resonance spectroscopy. J Dig Dis 10:315–320
12. Mehta SR, Louise Thomas E, Patel N, et al. (2010) Proton magnetic resonance spectroscopy and ultrasound for hepatic fat quantification. Hepatol Res 40:399–406
13. de Bucourt M, Streitparth F, Wonneberger U, Rump J, Teichgräber U (2011) Obese patients in an open MRI at 1.0 Tesla: image quality, diagnostic impact and feasibility. Eur Radiol 21:1004–1015
14. Holm JC, Gamborg M, Bille DS, et al. (2011) Chronic care treatment of obese children and adolescents. Int J Pediatr Obes 6:188–196
15. Nysom K, Molgaard C, Hutchings B, Michaelsen KF (2001) Body mass index of 0 to 45-y-old Danes: reference values and comparison with published European reference values. Int J Obes Relat Metab Disord 25:177–184
16. Ishizaka K, Oyama N, Mito S, et al. (2011) Comparison of ¹H MR-spectroscopy, 3-point DIXON, and multi-echo gradient echo for measuring hepatic fat fraction. Magn Reson Med Sci 10:41–48
17. Hájek M, Dezortová M, Wagnerová D, et al. (2011) MR-spectroscopy as a tool for in vivo determination of steatosis in liver transplant recipients. MAGMA 24:297–304
18. Roldan-Valadez E, Favila R, Martínez-López M, et al. (2010) In vivo 3T spectroscopic quantification of liver fat content in non-alcoholic fatty liver disease: correlation with biochemical method and morphometry. J Hepatol 53:732–737
19. van Werven JR, Hoogduin JM, Nederveen AJ, et al. (2009) Reproducibility of 3.0 Tesla magnetic resonance spectroscopy for measuring hepatic fat content. J Magn Reson Imaging 30:444–448
20. Szczepaniak LS, Nurenberg P, Leonard D, et al. (2005) Magnetic resonance spectroscopy to measure hepatic triglyceride content: prevalence of hepatic steatosis in the general population. Am J Physiol Endocrinol Metab 288:E462–E468
21. van Werven JR, Schreuder TC, Nederveen AJ, et al. (2010) Hepatic unsaturated fatty acids in patients with non-alcoholic fatty liver disease assessed by 3.0T MR-spectroscopy. Eur J Radiol 75:e102–e107

22. Kotronen A, Peltonen M, Hakkarainen A, et al. (2009) Prediction of non-alcoholic fatty liver disease and liver fat using metabolic and genetic factors. Gastroenterology 137:865–872
23. Guiu B, Loffroy R, Petit JM, et al. (2009) Mapping of liver fat with triple-echo gradient echo imaging: validation against 3.0-T proton MR spectroscopy. Eur Radiol 19:1786–1793
24. Hamilton G, Middleton MS, Bydder M, et al. (2009) Effect of PRESS and STEAM sequences on magnetic resonance spectroscopic liver fat quantification. J Magn Reson Imaging 30:145–152
25. Bohte AE, Koot BG, van der Baan-Slootweg OH, et al. (2012) US cannot be used to predict the presence or severity of hepatic steatosis in severely obese adolescents. Radiology 262:327–334
26. van Werven JR, Schreuder TC, Aarts EO, et al. (2011) Hepatic steatosis in morbidly obese patients undergoing gastric bypass surgery: assessment with open-system [1]H-MR-spectroscopy. Am J Roentgenol 196:W736–W742
27. de Bazelaire CM, Duhamel GD, Rofsky NM, Alsop DC (2004) MR imaging relaxation times of abdominal and pelvic tissues measured in vivo at 3.0 T: preliminary results. Radiology 230:652–659
28. Cowin GJ, Jonsson JR, Bauer JD, et al. (2008) Magnetic resonance imaging and spectroscopy for monitoring liver steatosis. J Magn Reson Imaging 28:937–945
29. d'Assignies G, Ruel M, Khiat A, et al. (2008) Non-invasive quantitation of human liver steatosis using magnetic resonance and bioassay methods. Eur Radiol 19:2033–2040