Liver steatosis may induce various imaging appearances and some of these changes may cause confusion particularly in cancer patients (1–4). Previous studies have demonstrated the value of magnetic resonance imaging (MRI) over computed tomography (CT) and ultrasonography (US) in the evaluation of fatty liver (5–7). Fat spared areas, hypersteatotis, and patchy areas of fat infiltration can be easily diagnosed by in- and opposed-phase images. Although these changes could be easily identified by liver MRI, the metabolic effect of steatosis on liver may cause confusion on positron emission tomography-computed tomography (PET-CT) scans (8, 9).

It is known that liver steatosis may induce liver fibrosis and decreased parenchymal function in chronic and severe cases. Impaired liver function is a serious complication; however, it could be recognized on the hepatobiliary phase of gadolinium-ethoxybenzyl-diethylenetriamine pentaacetic acid (Gd-EOB-DTPA) enhanced liver magnetic resonance imaging. The metabolic effect of steatosis on liver may cause confusion on positron emission tomography-computed tomography (PET-CT) scans (8, 9).

Nevertheless fat spared areas in the liver may induce increased signal intensity on HBP images due to increased fluorodeoxyglucose (FDG) uptake compared with suppressed steatotic background liver (8, 9).

You may cite this article as: Ünal E, İdilman İS, Karaosmanoğlu AD, Özmen MN, Akata D, Karcaaltıncaba M. Hyperintensity at fat spared area in steatotic liver on the hepatobiliary phase MRI. Diagn Interv Radiol 2019; DOI 10.5152/dir.2019.18535.
Signal intensity characteristics of fat spared areas on liver MRI in patients who received Gd-EOB-DTPA have not been previously analyzed. Therefore, we aimed to investigate the reasons of hyperintensity at fat spared area on hepatobiliary phase of Gd-EOB-DTPA enhanced liver MRI.

**Methods**

**Study population**

A total of 22 consecutive patients with a focal fat spared area demonstrating increased signal intensity on Gd-EOB-DTPA enhanced liver MRI were included in the study (Fig. 1). This was a retrospective analysis of a database prospectively collected between 2014 and 2017. This retrospective study has been approved by the local ethics committee. Informed consent was waived.

**MRI examinations**

The MRI examinations were performed on a 1.5T HDxt MRI system (GE Healthcare). An 8-channel phased array body coil was used for MRI acquisitions. The patients were examined in the supine position. Gadoxetate disodium (Primovist, Bayer Schering Pharma) was injected intravenously at a dose of 0.025 mmol/kg. A three-dimensional gradient-echo (LAVA) sequence was used for dynamic liver examination. Consequently, the hepatobiliary phase images were obtained 20 minutes after the contrast material injection.

**Image processing**

The acquired images were analyzed on PACS station (GE Healthcare). An elliptic (~1 cm²) region of interest (ROI) was placed on in- and opposed-phase images at focal fat spared area and background steatotic liver parenchyma by avoiding major vessels and bile ducts to measure the fat fraction. The measurement was also performed on precontrast fat suppressed T1-weighted and hepatobiliary phase images, while maintaining the same section plane for fat spared area and liver parenchyma. The signal intensities (SI) of spleen, kidney, erector spinae muscle, intervertebral disc, and spinal cord on precontrast fat-suppressed T1-weighted and hepatobiliary phase images were also recorded.

The fat fraction was calculated for the liver parenchyma and fat spared area according to the following formula: Fat fraction = In phase SI – opposed phase SI / 2 × In phase SI (14). The difference of fat fraction between liver parenchyma and fat spared area was defined as delta fat fraction. The relative enhancement ratio for the liver parenchyma and fat spared area was calculated with the following equation: (HBP-SI) – (Precontrast-SI) / (Precontrast-SI).

The intensity ratios were measured for both the liver parenchyma and fat spared area with the following equation: (HBP-SI of liver or fat spared area / HBP-SI of other body part) / (Precontrast-SI of liver or fat spared area / Precontrast-SI of other body part) (15, 16). The measurements were made by a single radiologist who had 8 years of experience in reading liver MRI examinations.

**Statistical analysis**

All statistical analyses were performed using descriptive summaries. Means and standard deviations or median and range were computed for all continuous data. The Kolmogorov-Smirnov test was used to test the normal distribution of variables. Comparison between two groups in terms of continuous variables was assessed by repeated measures ANOVA, paired Student t-test or Wilcoxon signed rank test, where applicable.

The degree of association between continuous variables was calculated by Pearson test. For all tests, a two-tailed $P$ value of $<0.05$ was considered statistically significant.

**Results**

In all patients (11 men, 11 women), focal fat spared area appeared hyperintense at hepatobiliary phase of liver MRI (Figs. 2, 3).

**Main points**

- Liver steatosis may induce liver fibrosis and decrease parenchymal function.
- Impaired liver function could be recognized on the hepatobiliary phase of Gd-EOB-DTPA enhanced liver MRI, as areas of decreased contrast enhancement due to reduced number or function of hepatocytes.
- Fat spared areas in the liver may induce increased signal intensity on HBP images due to preserved or even increased parenchymal function.
- Increased or preserved parenchymal function at fat spared area could be a potential pitfall for false positive PET-CT due to relatively increased metabolic activity.

---

**Figure 1.** The flow chart of patient selection.
The mean age of the participants was 49.9 years (range, 18–70 years). There was no patient with liver cirrhosis or elevated liver enzymes in our study. There was no signal alteration in fat spared areas on T2-weighted and diffusion-weighted images, indicating absence of focal nodular hyperplasia, adenoma or hemangioma.

Focal fat spared area was present at segment 4 (n=16), caudate lobe (n=4), adjacent to gallbladder (n=1), and subcapsular liver parenchyma (n=1). The mean fat fraction of the liver and fat spared areas was 24.86% (range, 8%–46%) and 8.41% (range, 1%–34%), respectively. There was a statistically significant difference between fat fraction of the liver and fat spared areas (P < 0.001, paired t-test). The mean signal intensity of liver and fat spared areas on precontrast fat-suppressed T1-weighted images was 330 (range, 78–890) and 405 (range, 105–904) with statistically significant difference (P < 0.001, paired Student t-test). The mean signal intensity of liver and fat spared areas on hepatobiliary phase images was 602 (range, 208–1436) and 799 (range, 319–1957) (P < 0.001, paired Student t-test).

The mean relative enhancement ratio of liver and fat spared areas was 0.98 (range, 0.05–1.90) and 1.15 (range, 0.22–2.03), respectively (P < 0.001, paired Student t-test). However, in 6 out of 22 patients, the mean relative enhancement ratios of liver (1.11) and fat spared areas (1.13) were almost equal (slightly increased at fat spared area) (Fig. 4).

The mean delta fat fraction was 16.55% (range, 4.7%–38.9%). There was a significant and positive correlation between liver parenchyma fat fraction and delta fat fraction (r=0.74, P < 0.001, Pearson test) (Fig. 5). There was no statistically significant correlation between fat fraction of liver or fat spared areas and the signal intensities of both parameters before contrast (r=-0.01, P = 0.96, and r=-0.01, P = 0.53, respectively, Pearson test), after contrast (r=0.06, P = 0.78, and r=-0.01, P = 0.55, respectively, Pearson test), and in terms of relative enhancement ratio (r=0.18, P = 0.42, and r=-0.01, P = 0.95, respectively, Pearson test).

The median liver to muscle and fat spared areas to muscle intensity ratio was 2.05 (range, 1.67–3.98) and 2.25 (range, 2–4), respectively (P = 0.048, Wilcoxon signed rank test). The median liver to spinal cord and fat spared areas to spinal cord intensity ratio was 2.34 (range, 0–3) and 2.47 (range, 0–4), respectively.
respectively ($P = 0.034$, Wilcoxon signed rank test). The median liver to spleen and fat spared areas to spleen intensity ratio was 1.78 (range, 1–3) and 1.87 (range, 1–3), respectively ($P = 0.18$, Wilcoxon signed rank test). The median liver to intervertebral disc and fat spared areas to intervertebral disc intensity ratio was 2.14 (range, 1–4) and 2.24 (range, 1–5), respectively ($P = 0.21$, Wilcoxon signed rank test).

**Discussion**

Focal fat spared areas in a steatotic liver can demonstrate increased signal intensity on HBP images. We found relatively increased function in fat spared areas (mean relative enhancement ratio of 1.15) compared with background liver (mean relative enhancement ratio of 0.98, $P < 0.001$). In the studies evaluating the effectiveness of Gd-EOB-DTPA enhanced MRI in differentiation of normal liver from the fibrotic or cirrhotic livers, authors reported higher enhancement ratios and signal intensity values on HBP images in normal livers or in low stage of liver fibrosis compared with severe fibrotic livers (11, 17–20). In addition, steatohepatitis has also been reported to induce decreased parenchymal intensity related to fibrosis state as a consequence of hepatocyte dysfunction (11, 21). Based on our results, we suggest that fat spared area demonstrating hyperintensity on HBP images may contain hyperfunctioning hepatocytes compared with background liver. Therefore fat spared area may exhibit more hyperintensity compared with steatotic liver parenchyma on HBP images. However, we cannot rule out the effect of fibrosis level differences between fat spared area and rest of liver parenchyma due to lack of histopathologic examination in our study. Nevertheless, we observed a significant and positive correlation between the liver parenchyma fat fraction and delta fat fraction ($r=0.775$, $P < 0.001$), which indicates that higher fat accumulation in the liver increases the gap between fat fraction of fat spared area and background liver parenchyma. Liver steatosis may induce various imaging appearances particularly on CT and US (1–4, 22). Liver MRI could be used as a problem solving tool in the assessment of focal liver lesions detected in a steatotic liver by CT and US. However, great attention should be given to assessment of PET-CT scan in a steatotic liver. Focal areas of fat infiltration could be misinterpreted as metastases on CT or US; however, focal fat does not usually cause confusion on PET-CT scans because these areas are usually not hypermetabolic. We demonstrated higher signal intensity in focal fat spared areas on hepatobiliary phase images can be due to relatively increased hepatocyte function or basal hyperintensity on precontrast T1-weighted MRI.

Figure 4. a–d. A 45-year-old man with significant liver steatosis. In-phase (a) and opposed-phase (b) images demonstrate liver steatosis (fat fraction of 35%) and fat spared area (fat fraction of 19%) located anterior to main portal vein. The hyperintensity at focal fat spared area on hepatobiliary phase image (c) was due to influence of existing hyperintensity on precontrast T1-weighted image (d). The relative enhancement ratio difference between liver parenchyma (0.222) and focal fat spared area (0.227) was negligible.

Figure 5. Scatterplot shows the correlation between hepatic steatosis and delta hepatic fat fraction ($r=0.741$, $P < 0.001$).
Hyperintense appearing focal fat spared areas in patients with relatively increased function are potential pitfalls for false positive PET-CT scans (8, 9). We also found that these areas exhibit increased signal intensity values on precontrast fat suppressed T1-weighted images as a consequence of suppressed signal of background steatotic liver on a fat suppressed sequence and in patients with relative enhancement ratio difference was negligible. Therefore, a focal fat spared area should not be interpreted as a space occupying liver lesion due to T1 shortening effect on precontrast fat suppressed T1-weighted image. Focal nodular hyperplasia may also result in hyperintensity on hepatobiliary phase images; however, lack of contrast enhancement on dynamic postcontrast sequences may enable differentiation of FNH from fat spared area.

In the literature, various MRI-derived indices obtained by measuring the signal intensity of liver and other organs on HBP images, were investigated for predicting liver fibrosis stage or to differentiate normal liver from cirrhosis (16, 23–26). Nojiri et al. (16) reported that the best correlation between MRI and the liver biopsy was achieved with liver-to-intervertebral disc ratio, followed by relative liver enhancement and with liver-to-spleen ratio being the least accurate for discriminating liver fibrosis. Kukuk et al. (23) concluded that liver to spleen contrast ratio and relative liver enhancement were significantly correlated with liver function tests. Moreover, Kumazawa et al. (24) reported that the intensity ratio of the enhanced liver to spinal cord was the most suitable method among other MRI-derived indices to predict liver fibrosis. In our study, relative enhancement ratio and signal intensity values on hepatobiliary phase images demonstrated statistically significant difference between fat spared area and steatotic liver. We could not find statistically significant correlation between fat fraction of liver or fat spared areas and relative enhancement ratio. This may be due to lack of patients with cirrhosis or severely fibrotic liver in our study.

Our study had several limitations that should be addressed. First, it was a retrospective analysis. Second, the number of study cohort was small. Third, fibrosis level difference between fat spared areas and liver parenchyma was not histopathologically confirmed. Fourth, FDG-PET-CT scans of the patients were not obtained. Therefore, we cannot conclude, but may suggest that fat spared area in a steatotic liver could be responsible for false positive PET-CT results, due to increased relative enhancement ratio which reflects hyperfunctioning liver parenchyma.

In conclusion, focal fat spared area can appear hyperintense on hepatobiliary phase MRI due to two reasons: (i) influence of existing hyperintensity on precontrast T1-weighted images, (ii) relatively increased parenchymal enhancement (function). The latter might be a potential pitfall for false positive PET-CT due to relatively increased metabolic activity.

Conflict of interest disclosure

The authors declared no conflicts of interest.

References

7. Park VY, Choi JY, Chung YE, et al. Dynamic enhancement pattern of HCC smaller than 3 cm in diameter on gadoxetic acid-enhanced MRI: comparison with multiphasic MDCT. Liver Int 2014; 34:1593–1602. [CrossRef]