Evaluation of superparamagnetic iron oxide (SPIO) particles for MR imaging of nonalcoholic steatohepatitis (NASH)

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Introduction: In patients with nonalcoholic fatty liver disease (NAFLD), a liver biopsy remains the only reliable method for differentiating simple steatosis from nonalcoholic steatohepatitis (NASH). It has been documented that both enhanced release of cytokines from hepatic Kupffer cells (KC) and a concomitant decrease in the phagocytic activity of KCs may play crucial roles in the pathogenesis of NASH (1-2). We determined whether superparamagnetic iron oxide (SPIO)-enhanced MR imaging could be a noninvasive imaging test for the diagnosis of NASH.

Methods: Nineteen consecutive patients with suspected NAFLD at the time of liver biopsy underwent MR imaging at 1.5 T (Signa HD; GE Healthcare). Transverse T2W-FSE (3200/92) images, T2*W-GRE (200/20/20°) images, and GRE echo planar imaging (EPI; 2000/20/45°) images were obtained using a torso array coil. Following the precontrast baseline, SPIO (ferucarbotran: 0.016 ml/kg body weight) was intravenously injected. GRE-EPI [a set of serial 15 phases (totally 30 seconds breath hold)] was acquired immediately after the beginning of SPIO administration, and repeated up to 10 minutes with a short interval. We analyzed the signal intensity decay on GRE-EPI obtained within 10 min of the bolus injection of SPIO as follows: $S(t) = So \cdot \exp(-t/\tau)$. The values of τ were calculated based on the exponential function approximations. T2*W-GRE and T2W-FSE were obtained more than 10 minutes after SPIO administration, and the relative signal decrease [%T2 and %T2*: (S.I.pre – S.I.post) / S.I.pre · 100 (%)] was calculated. An experienced pathologist established histological diagnoses using H&E and Mallory staining sections from liver biopsies, according to the NAFLD scoring system (3). The NAFLD activity score is the unweighted sum of the steatosis [score 0-3], lobular inflammation [0-3], and hepatocellular ballooning [0-2]. A NAFLD activity score ≥ 5 corresponded to a diagnosis of "definitive NASH," a score of 3-4 corresponded to "borderline NASH," and a score ≤ 2 corresponded to "not NASH."

Results: There was a statistically significant relationship between the histological NAFLD activity scores and the τ values ($r = 0.66$, $P = 0.002$, Figure left), and %T2 ($r = -0.58$, $P = 0.009$, Figure right). The NAFLD activity score had only a tendency to correlate with the values of %T2* ($r = -0.45$, $P = 0.051$). The τ values were significantly larger for the patients with "definitive NASH" [62.5 ± 18.4 (sec)] compared with the patients with "not-definitive NASH" ("borderline NASH" + "not NASH") [39.4 ± 23.5 (sec), $P = 0.028$]. The values of %T2 were significantly lower for the patients with "definitive NASH" [30.4 ± 12.3] than "not-definitive NASH" (45.2 ± 9.4; $P = 0.009$), but no significant differences were found between two group in the values of %T2* (74.3 ± 10.7 versus 31.0 ± 2.8; $P = 0.087$).

Discussion: The present study showed that the T2 relaxation effect of SPIO was significantly weaker in "definitive NASH" than in "not-definitive NASH". Although the T2* relaxation effect of SPIO had only a tendency to negatively correlate with the NAFLD activity score, no significant difference %T2* was found between two groups. Our data and these results suggest that there may have been significantly fewer small intracellular SPIO particles in the livers of "definitive NASH" patients compared with livers of patients that did not have definitive NASH, whereas the numbers of large SPIO particles may have been similar in these two patient groups (4-5). Noninvasive SPIO-enhanced MR imaging is a reliable tool for the identification of NASH patients among the numerous patients with suspected NAFLD. The values of %T2 and τ on SPIO-enhanced MRI are useful markers for NASH. We are planning a larger series of studies to develop this imaging test.

References

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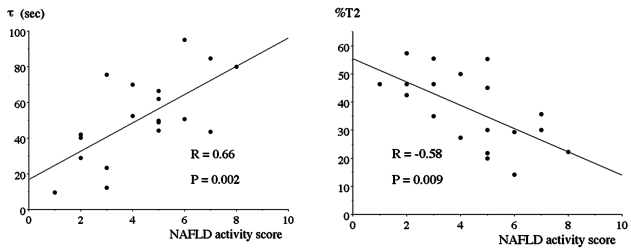

Figure: Relationship between the NAFLD activity score and the MR parameters