Evaluation of a Screening Dixon sequence for detecting presence of iron/ fat in patients with chronic liver disease

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Purpose: Magnetic resonance imaging (MRI) has been recognized as a non-invasive method for detection and quantification of fat and iron deposition in the liver. In-opposed-phase and multi-echo GRE are validated sequences with high accuracy for fat and iron detection respectively (1,2). Recently, a two-point automated dual-ratio Dixon discrimination technique with automatic liver segmentation, dubbed screening Dixon (SD), has emerged as a potential method for screening and discrimination of fat and iron signals (3). In this study, we aimed to investigate this technique for detecting fat/ iron liver deposition in patients with chronic liver disease waiting for hepatic transplantation. This group was chosen because of its higher expected prevalence iron overload (related to siderotic liver nodules) when compared to the general population, and associated diffuse steatosis. The purpose was to evaluate the accuracy of the SD sequence with automatic estimation of fat/ iron contents in this population and compare them with the results of our routine quantitative sequences as the reference standards (RS).

Materials and Methods: 82 patients who had undergone abdominal MRI were enrolled retrospectively. The study was approved by the local institutional review board. All MRI exams were performed on a 1.5T scanner (MAGNETOM Espree, Siemens, Erlangen, Germany) using a body matrix and the table-mounted spine coil. An in-/opposed-phase 3D VIBE sequence (TE 2.38/4.76ms, TR 7.48ms) with two-point Dixon reconstruction using the SD algorithm was applied. To serve as the RS for iron overload, a fat-saturated GRE sequence with 12 echoes was performed (TE 1.33-14.78ms, TR 200ms). As the RS for liver fat quantification, a four-echo 2D GRE Dixon was performed to generate fat percentage (FP) maps with $T2^*$ correction (TE 2.38/4.76/9.52/11.9ms, TR 400ms). MR images of SD were evaluated qualitatively by radiologist for the correctness of the automatic liver segmentation. Patients were categorized by SD report as normal or according to the presence of iron deposition (ID), fat deposition (FD) or both (CD). Reference $T2^*$ and FP values were measured on an external workstation (General Electric, Milwaukee, USA). On the 12-echo GRE images, a region of interest (ROI) was drawn in the right liver lobe and the $T2^*$ value was fitted. The same ROI was used to measure the FP value on the FP maps. A normal $T2^*$ was considered as above 15ms and a normal FP was considered as below 5.6%. SPSS (IBM Corp,Armonk, NY, USA) was used for statistical analysis.

Results: Of the 82 patients enrolled initially, 9 were excluded due to poor targeting of SD liver segmentation, 1 due to the presence of artifacts in the fat RS sequence and 2 due to technical problems. Therefore the final study group included 70 patients. Example resultant images of the SD sequence and the RS sequences are shown in Figure 1. Considering only the presence (altered) or absence (normal) of disease, SD demonstrates 100%, 86.96% and 91.43% for SD sensitivity, specificity and accuracy, respectively. Table 1 shows concordance between SD and RS sequences considering the four categorizations classes. The overall concordance (accuracy) was 76% (Kappa = 0.580/ standard error = 0.072). SD was capable of correctly identifying all normal patients (40/40). There was agreement between SD and RS sequences in 87% (7/8) for FD, 37% (6/16) for ID and none (0/6) for CD. Among the mischaracterized cases, 3 were considered as ID by SD and as FD by RS, and 6 as ID by SD and as CD by RS. In addition, 1 patient was classified as ID by SD and as normal by RS, 1 as FD by SD and as normal by RS, 2 as CD by SD and FD by RS and 4 as CD by SD and as normal by RS. When we considered only presence or absence of FD, SD was more specific (90.38%) than sensitive (50%). When we considered only the presence or absence of ID, SD was 100% sensitive, with specificity of 82.76% and accuracy of 85.71%.

Discussion: Our results suggest that SD is an efficient, highly sensitive method since no normal patient was misdiagnosed. Regarding the number of disagreement between SD and RS sequences (17/70), 9 cases are more relevant, since the SD report generated wrong recommendations and lead to an inadequate protocol performance. From this group, 3 cases were totally discordant and the disease would be missed if we would follow only the SD report recommendation. In the other 6 cases, 5 had high iron overload with low FP. One case showed a relevant FP value but also a very high ID with a very short $T2^*$. Although considered as an error, SD was capable to detect the worst disease. For the other 8 disagreement cases, the consequence was an unnecessary sequence for the patient, which we considered result of the high sensitivity of the method. We believe that our results can provide improvement suggestions for the SD algorithm development with respect to the population studied. One limitation of this study was that histopathological analysis was not performed yet, to a non-MR RS. We expect to perform that comparison in future studies.

Conclusion: Although the type of deposition is not perfectly discriminated, SD is an accurate method for detecting presence or absence of fat/iron deposition in the liver, being adequate as a screening technique in general MRI abdominal studies.

References: 1. Wood JC. *Curr Opin Hematol.* 2007;14: 183. 2. Dixon WT. *Radiology.* 1984;153:189. 3. Bashir MR, et al.. *Eur J Radiol.* 2012;(81)101.
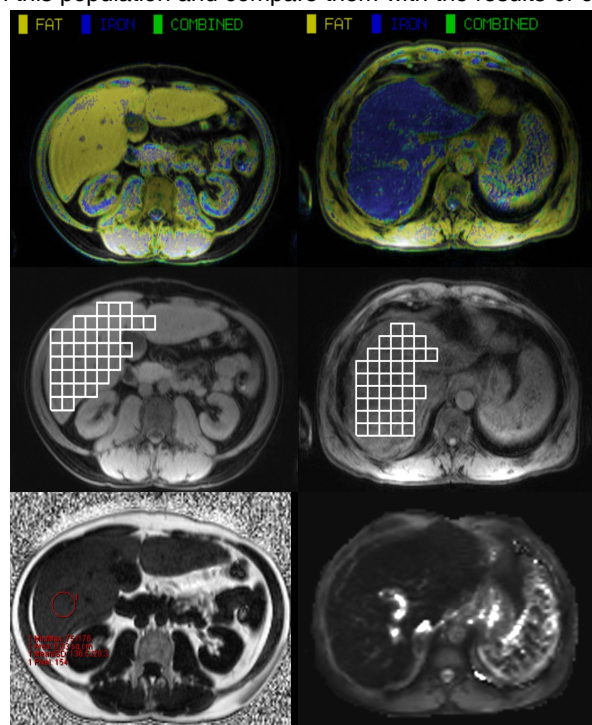
Figure 1: Two different patients with hepatic steatosis (left column) and iron overload (right column). Upper row show color overlaid SD images (yellow for fat, blue for iron), middle row automatic liver segmentation, lower row FP and $T2^*$ map.

SD		Reference Standard				
		Normal	ID	FD	CD	Total
	Normal	40	0	0	0	40
	ID	1	6	3	6	16
	FD	1	0	7	0	8
	CD	4	0	2	0	6
	Total	46	6	12	6	70

Table 1: Concordance between SD and RS considering categorization classes