Utility of conventional Dixon method for assessing fat deposition in the liver in a group of NASH patients, compared with PDFF analysis.

Poster No.: C-1564
Congress: ECR 2019
Type: Scientific Exhibit
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Keywords: Liver, Gastrointestinal tract, Abdomen, MR, Diagnostic procedure, Imaging sequences
DOI: 10.26044/ecr2019/C-1564

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Aims and objectives

The quantification of hepatic steatosis in recent years showed a great improvement, especially by magnetic resonance imaging (MRI), initially by the use of spectroscopy techniques and finally with proton density fat fraction (PDFF) sequence. This last technique allows the creation of a fat map, with correction of several factors, making it extremely easy and reliable to evaluate steatosis from pixel to pixel.

Among the main corrections of the PDFF analysis are the T1 and T2* relaxation. The latter correction allows the evaluation of iron deposits in the liver, obtained through a post-acquisition processing, without the need for additional sequences. The PDFF analysis can be obtained by the main commercial companies, but it is not broadly disseminated in most services in our country.

Our objective was to evaluate the efficacy of a conventional volumetric Dixon sequence (IN and OUT phase) in quantifying liver fat in a group of NASH patients exhibiting a range of steatosis and R2 values. The reason for this analysis was the greater availability of this sequence in most services and its comparison with more robust techniques such as PDFF.
Methods and materials

A total of 102 patients with NASH diagnosed by percutaneous biopsy were analyzed. Patients underwent a dedicated MRI study on a 3T device (Phillips Achieva) with a surface coil, less than 6 months after the biopsy. 14 volunteers with no history of liver disease and normal laboratory tests for hepatic function were also included.

The assessment of iron and fat deposition in the liver was made through a multi-spoiled gradient echo sequence (MSGE), where magnitude data were acquired. This sequence lasts around 13 seconds and is obtained during an apnea, involving the entire extension of the liver. After the acquisition, the images were processed by a specific software (Dive-In® - Magnepath - Perth, Australia), which calculates the percentage of triglycerides in the selected liver area, correcting for several confounding factors such as R2 *, T1 and the existing multiple fat peaks. The result is a percentage fat map of the liver, which can range from 0 to 100% (Fig 1).

A conventional volumetric Dixon sequence was also obtained during an apnea which resulted in IN-PHASE (IP), OUT-PHASE (OP), Water and Fat images, with similar parameters to those obtained in the above-mentioned MSGE sequence.

For the analysis of fat and iron, regions of interest (ROI's) involving the largest area of the liver in a sectional image were drawn, excluding major vessels, resulting in values of the fat fraction (FF, in%) and R2 * (in s-1). In the IP and OP images, the same ROI's were drawn (Fig 2) and fat deposition (FD) was calculated using the following equation (Fig 3):

We use Kolmogorov-Smirnov tests to evaluate the normality of the variables and the Spearman correlation coefficient to analyze the correlation between FF and FD. In order to assess the influence of R2 *, FF and FD, correlation tests were performed for four distinct strata of R2 *, based on their quartiles: <47.6, 47.6 | - 58.4, 58.4 | - 69.9, => 69.9 . All tests took into consideration a bidirectional # of 0.05 and 95% confidence interval (CI) and were performed with IBM SPSS 25 software (Statistical Package for the Social Sciences) and Excel 2010 (Microsoft Office).
The equation used to calculate the Fat Deposition in the liver using the values obtained with the conventional Dixon images - IP = IN-PHASE; OP = OUT-PHASE; FD = Fat Deposition

$$FD = 100 \times \left( \frac{(IP - OP)}{(2 \times IP)} \right)$$

**Fig. 3:** The equation used to calculate the Fat Deposition in the liver using the values obtained with the conventional Dixon images - IP = IN-PHASE; OP = OUT-PHASE; FD = Fat Deposition

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**Fig. 1:** Axial images showing Liver R2* map (left) and fat fraction map (right), showing abnormal results of iron, with an R2* of 167.3 s-1 (normal < 60 s-1) and steatosis, with 22.9% of fat (normal < 5%).

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Fig. 2: Results from a patient with high R2* (221.3 s⁻¹) and a FF of 23.1%, showing an estimated FD of 13.3% with the use of conventional Dixon method. The discrepancy is most probable related to the high iron content in the liver.

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Results

The mean FF value was 14.4% (SD = 9.2 / Min = 4.1% / Max = 54.8%). There was a good correlation between the degree of steatosis and the FF by the PDFF method, estimated in 0.72. The cut-off value considered ideal for steatosis was 5.4% with AROC of .98 for the distinction between normal and fat liver patients (Fig 4).

The mean value of R2* was 67.5 s⁻¹ (SD = 42 / Min = 34.5 s⁻¹ / Max = 384 s⁻¹). The ideal cutoff value for detection of siderosis (in correlation with histology) was 68.8 s⁻¹ (AUROC = .79).

The correlation between FF obtained by the PDFF method and FD by conventional Dixon was very high, estimated at 0.96, with p <0.01. A correlation between R2*, FF and FD was also identified, but with a low intensity, being estimated at 0.51 and 0.46, respectively. Regarding the influence of the R2* values in the analysis, there was an excellent correlation between the fat quantification methods in the first 3 quartiles (R2* <69.9 s⁻1), higher than 0.95 with p <0.001. Only for R2* values # 69.9 s⁻¹, the correlation was lower than the others, but still significant, with an estimated value of 0.87 and p <0.001 (Table 1).

These findings demonstrate a good correlation between conventional steatosis quantification methods using Dixon gradient echo sequences and advanced proton fat density methods, allowing the use of the former, if the latter are not available, as long as there are no signs of iron deposition in the hepatic parenchyma. This same quantification could be used in the control of these patients, even if more advanced techniques were acquired later.

It should be noted some important limitations in the study:

1. The study involved only NASH patients, which could limit its use in other patients, but this impact should be minimal, since patients' steatosis and R2* values were very broad.
2. Only one manufacturer's machine was used, which could impact the use of other Dixon sequences. This is related to variations among companies in the acquisition of three-dimensional Dixon sequences and could impact the correlation between more advanced techniques.
3. A 3T machine was used, which limits the results for this type of equipment, based on different R2* values in 1.5T MRI's. Generally, the values of R2* in 1.5T equipment are about a half of those obtained in 3T, which could imply a limit for the correlation in 1.5T of 35s⁻¹, but this aspect is only speculative at this point.
4. The values of $R_2^*$ used were obtained with the use of PDFF processed images, being different from those obtained in conventional relaxometry techniques, which could limit the threshold values used.

5. Only one FF postprocessing technique was used, but this aspect should have a small impact in the analysis, since there are already papers showing a good correlation between distinct methods of steatosis quantification with different PDFF techniques.
Steatosis grade normal cut off at 5.6%  
Specificity 93% - Sensitivity 92% - AUROC 0.98

Fig. 4: Plot comparing FF% obtained with PDFF sequences and the degree of steatosis in histology.

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Table 1: Correlation coefficients between FF and FD using distinct R2* quartiles

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Conclusion

The FF estimated from PDFF is very similar to the 3D Dixon technique in this group of NASH patients evaluated in a 3T machine.

The Correlation Coefficient between the techniques is only lower when the R2* is >69.9 s⁻¹.

This work shows the possibility of using conventional 3D Dixon techniques in steatosis quantification in patients without signs of iron deposition.
References