Liver disease is any disturbance of liver function that causes illness. In the US up to 20% of adult liver patients have non-alcoholic fatty liver disease (NAFLD) or non-alcoholic steatohepatitis (NASH) [1]. The current monitoring of these patients is liver biopsy. MR is offering some promising techniques for fat and iron evaluation in routine clinical liver diagnostics. Siemens’ LiverLab offers a comprehensive package for liver fat evaluation. LiverLab provides clinically relevant biomarkers: Fat signal fraction, which correlates with hepatic steatosis, and $R^2*$ of water, which correlates with iron content. The purpose of this article is to share the knowledge of implementing LiverLab at my sites.

LiverLab consists of three sequences incorporated into the Abdomen Dot Engine protocol. The $t_1$ vibe e-Dixon (First look Dixon), vibe q-Dixon (Multi-echo Dixon), and the HISTO (breath-hold spectroscopy) sequences are usually performed in conjunction with routine liver examination. LiverLab must be performed as a Dot Engine.

The $t_1$ vibe e-Dixon (or First look Dixon) is a single breath-hold 3D acquisition that provides whole-liver coverage and generates opposed and in-phase images as well as fat and water images. It is a two-point Dixon technique. After image acquisition the system performs Inline Liver Segmentation and suggests a region-of-interest (ROI) placement for the subsequent evaluation protocol. It is important to check the Liver Segmentation for quality since it cannot be corrected. This segmentation is used again for the q- or Multi-echo Dixon sequence. It is not repeated for the q-Dixon, and therefore the patient must follow the same breath-hold instructions very carefully. Based on a dual ratio analysis, the system performs and assigns a voxel classification of either normal liver tissue, fat deposition, iron deposition or combined deposition. Based on these findings the system determines an evaluation recommendation for further evaluation. It is important to note this is not a diagnosis. If the recommendation comes back as normal, it only means that if further evaluation were to be performed it would very likely come back with normal MR values.

It has been my experience that if the patient is being referred for fat/iron evaluation we will proceed with further evaluation (q-Dixon and HISTO) even if the system comes back with a normal tissue classification.
e- or First look Dixon generates six series in the patient browser: the in-phase, opposed-phase, fat, water, water with segmentation, and the report. In some cases to display the segmentation on the PACS system I have saved them as RGB images.

The q-Dixon (or Multi-echo Dixon) is a single breath-hold VIBE Dixon with multiple, typically six echoes that provides whole-liver coverage. The q-Dixon should be performed with the same breath-hold instructions as the e-Dixon sequence to properly project the liver segmentation from e-Dixon to q-Dixon. The system opens the sequence with a suggested position for the ROI, but you can reposition it. The ROI should be positioned in liver tissue not over vessels or the gallbladder.

q-Dixon provides mean fat signal fraction and R2* values for both a region-of-interest and the segmented liver volume. The liver segmentation must be checked for quality. If liver segmentation fails the segmentation Fat Fraction and R2* values will not be accurate, since they may include non-liver tissue; in those cases, a properly placed ROI will provide better results.

In addition multi-echo VIBE Dixon provides volumetric fat fraction, R2* maps, T2* maps, water fraction, and a goodness-of-fit map. R2* values are corrected for fat effects and the fat percentage is corrected for the T2* effects. R2* is the inverse of T2*. A higher R2* value correlates with a higher iron content whereas a lower T2* value correlates with a higher iron content. q-Dixon will generate eight series in the patient browser: water, fat, fat percentage, goodness-of-fit, R2* map, T2* map, and water percentage. The fat fraction, R2* and goodness-of-fit datasets will show the segmentation and the ROI position. The goodness-of-fit is an indication of fitting residual errors of the fat percentage and the R2* results. The smaller the value, the better and more reliable the results. To check the goodness-of-fit, draw a ROI over liver tissue on the goodness-of-fit map to get a mean value. The fit error values are also part of the DICOM report, on top of the fat fraction and R2* values. The goodness-of-fit percentage is the mean value multiplied by 0.1. Goodness-of-fit should be 5% or less. For example a mean value of 43.7 would be a fit of 4.37%.
The q-Dixon Evaluation Report will have two color bars. The top color bar is for fat fraction and the bottom is for R2* (iron). Each bar will provide a segmentation value (whole-liver volume from segmentation of liver) and a ROI value. For fat it will show a percent and for R2* it will show a value of seconds to the inverse of 1 (sec\(^{-1}\)). R2* is sensitive to iron deposition and is the preferred clinical biomarker. However, if there is too much iron then the signal of the gradient echo sequence can be very low or even zero (below the noise floor) and then the R2* value will not be reliable. In rare instances the fat and water images provided by Dixon can swap, thereby giving an inaccurate value for fat percentage.

The system will make a note on the report that the fat percentage is unusually high and the arrows on the top color bar will not be seen.

**Note:**
The normal fat percentage result and the result where fat and water are swapped. The fat and water images will also give a clear indication that a fat and water swap has occurred. If fat and water swap does occur the HISTO sequence will provide accurate fat fraction. A FOV that is too small might cause this. Use a slightly larger FOV for signal. Avoid changing the TEs of the optimized multi echo sequence as delivered, as Dixon relies on specific TE values to calculate fat and water.

**Note:**
The image labeled water is fat and the image labeled fat is water.
If liver segmentation fails or if the physician desires, the fat fraction or R2* map can be loaded into viewing and additional ROIs or manual segmentation can be drawn using the ROI tool or the Freehand ROI Tool. Multiply the mean value by 1 to get the seconds to the inverse of 1 (sec⁻¹). For manual segmentation the ROI would have to be drawn out for each slice and then the value averaged together. This is very useful as even if the ROI had not been placed in a desired location there is no need to repeat the series; the ROI can be drawn as post processing on the R2* map. LiverLab does not provide an iron quant value (liver iron concentration or LIC usually obtained from the liver biopsy). There are studies that support taking the R2* value and converting to iron quant value. These differ in acquisition and parameter fitting, and hence the calibration equations are slightly different. To date, there is no published iron calibration specifically for R2* from multi-echo VIBE Dixon, so if previously published calibrations are used, care must be taken. See ‘Iron quantification with LiverLab’ (page 44).

The HISTO sequence is a 15 second breath-hold (STEAM) spectroscopy sequence. It is a single voxel spectroscopy with typically a 3 x 3 x 3 cm³ voxel size. The system will recommend a location for the voxel size but it can be repositioned in liver tissue not over vessels or the gallbladder. When the HISTO sequence is opened the system will take the sequence in the active graphic segment and create a new series without distortion correction. I recommend you ensure that the e-dixon vibe (Screening Dixon) sequence is in the active box prior to opening the sequence. From there I right click and select series and load that non-distortion corrected series into Applications 3D MPR, and then generate coronal and sagittal reformat which can be dragged into the graphic segments from the browser for positioning the voxel in all 3 planes. With the axial image active, the scroll nearest tool will select the coronal and sagittal image closest to the voxel position on the axial much the same as normal spectroscopy.

Note: The mean value and the notation at the bottom for what factor to multiply the mean value by.
positioning. HISTO provides Proton Density Fat Fraction (PDFF) that has been corrected for fat and water transverse relaxation. Since this is a spin echo sequence R2 values are provided rather than R2* values (R2* is calculated from GRE sequences). The color bar map will show fat at the top in percent and R2 water with a value in seconds inverted over 1. The fit value (rsq fit “R-squared”) should be as close to 1 as possible, preferably >0.95. For additional Quality Control there is a T2 relaxation curve for water and fat with the lowest TE value scanned showing a spectral peak above it showing fat at 1.3 ppm (red) and water at 4.7 ppm (blue).

For patients with very high iron content there is a second HISTO sequence in the Siemens library with shorter TE values. Under Siemens-Abdomen-library-3d you will find two HISTO sequences. The primary sequence has echo times of 12, 24, 36, 48, and 72. The secondary sequence is for patients that have higher iron content where the TEs are shorter 12, 15, 18, 21, and 24 so that the signal is not destroyed by the higher TEs due to the higher iron content.

References
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