

# IMPROVED T2\* ASSESSMENT IN LIVER IRON OVERLOAD BY 2D FUZZY C-MEAN CLUSTERING

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**Target Audience:** Researchers and Clinicians with interest in liver iron overload measurement by magnetic resonance imaging (MRI).

**Purpose:** The T2\* liver iron overload measurement is currently a clinical tool to assess and monitor iron concentration in Thalassemia patients<sup>1,2</sup>. The 1/T2\* or R2\* values can be further tabulated to liver iron concentration (LIC) data<sup>2</sup> and reported by its median and interquartile range (IQR)<sup>3,4</sup>. Such the data is clinically useful for monitoring the efficacy of the chelator agents. A low variability of such measurements is, thus, the most desirable factor. The liver T2\* measurement can be divided into two parts: the MR acquisition and post-processing analysis. Unlike the acquisition section, the analysis part still has some disagreements regarding the optimal method employed. There are, however, some studies<sup>2-4</sup> already demonstrated a method to lower the inter-observer variability. One study<sup>3</sup> further suggested an improvement to lower the variability (lower the IQR) by automatic separation of vessel pixels from parenchyma using a fuzzy c-mean (FCM) algorithm on the acquired images. In this study, we further investigate the usefulness of the FCM by hypothesized that the FCM calculated from a combination of an acquired image and its LIC map should further improve the segmentation result as compared to from the acquired image alone.

**Methods:** The manual and FCM segmentations were performed on the acquired multi-echo T2\* images and their calculated LIC maps of 60 thalassemia major patients<sup>4</sup>. All segmentations of vessel pixels from parenchyma were performed only inside the defined region of interest (ROI) of the whole liver. The manual segmentation of each patient was based on thresholding and morphology operated by an MR abdomen technologist on a selected high-contrast T2\* image and used its LIC map as the visualization feedback. The automatic segmentation, on the other hand, was based on a FCM algorithm (MATLAB software tools). The FCM clustering was utilized into two types: 1D- and 2D-FCM. The 1D-FCM method calculated the clustering on each T2\* echo image (e.g. Figure 1a) while the 2D-FCM method was on the combination with its LIC map (e.g. Figure 1a and 1b). The choice of fuzzy membership data were then defined by varying the clustering threshold from 0.02 to 1 with 0.02 increments. The FCM segmentation results were reported, as compared to the manual results, in percentage of correct and incorrect classifications of parenchyma and vessel pixels, respectively. The best possible segmentation result from all FCM clustering data of each patient (20-echo images and 50-thresholding levels: 1,000 realizations) was, hence, defined from the closest of its outcome as compared to the perfect classification (i.e. 100% corrected and 0% in-corrected segmentations of the parenchyma and vessel pixels, respectively, or the upper left corner point of Figure 2). The mixed method (MIX) which combines the best possible segmentation of the 1D- and 2D-FCM was also investigated. The usefulness of the segmentations to lower the variability was indicated from the percent of normalized IQR (IQR\*100/median(LIC)). The paired t-test was selected to evaluate the difference between data which  $P < 0.05$  was consider to be significant.

**Results:** Figure 2 shows the best possible classifications from the 1D-FCM, 2D-FCM, and MIX methods of the sixty thalassemia patients. Overall, both 1D- and 2D-FCM methods can successfully segment the parenchyma ( $95.2 \pm 3.3\%$  and  $95.7 \pm 7.9\%$ , respectively), but the 1D-FCM method has significantly higher in-corrected classification of the vessels pixels as compared to the 2D-FCM method ( $8.5 \pm 10.5\% \text{ vs } 1.5 \pm 2.4\%$ ,  $p < 0.01$ ). Both methods provide different outcomes such that about 12 of 60 cases (20%) from the 1D-FCM method are incorrectly segmented the vessel pixels by more than 10% while there are about 8% of the cases in the 2D-FCM method that only correctly segmented the parenchyma by less than 80%. Figure 1 displayed the differences of both segmentation outcomes. The first row is a case when the 1D-FCM method is inferior in excluding the vessel pixels while the second row show a case of 2D-FCM method with lower the inclusion of parenchyma. In this study, the MIX method can, then, further improve the segmentation result with  $98 \pm 2.6\%$  corrected and  $1 \pm 1.8\%$  in-corrected segments of the parenchyma and vessel pixels, respectively. In this study, there is no specific thresholding level nor a T2\* echo number to obtain the best classification results.

The median LIC from non-segmentation data is  $20.1 \pm 11.1 \text{ mg/g-dw}$  which is insignificant different as compared to the results from all segmentation methods. The IQR from the manual segmentation method, on the other hand, is significant lower than the non-segmentation one ( $22.0 \pm 8.2 \text{ vs } 14.9 \pm 8.1 \text{ mg/g-dw}$ ,  $p < 0.01$ ) but comparable to all other automatic segmentation methods ( $p = \text{NS}$ ), as shown in Figure 3.

**Discussion and Conclusion:** The 1D-FCM method in this study can classify the parenchyma correctly by about 95% while still has in-corrected segmentation of the vessel pixels by 8% which is different from the previous study<sup>3</sup> that can 100% correctly exclude the vessel pixels but only 47-60% correctly include the parenchyma. There are many factors to cause such differences. For an instance, in this study, the FCM was calculated from the acquired images as compared to the simulation data, and was compared to the manual segmentation using both the acquire image and LIC map. The 2D-FCM method is comparable to the 1D-FCM method on the classification of the parenchyma pixels, but has significantly lower of the misclassification of the vessel pixels (1.5% vs 8.5%). The high misclassification of the vessel pixels (>10%) in the later method happen in the cases with severe iron overload (LIC > 15 mg/g-dw) which should be due to the strong susceptibility effect in the T2\* echo images. The 2D-FCM method, on the other hand, can completely exclude the vessel pixels in these cases because of the improvement of the classification by LIC map which has the high contrast of vessel and parenchyma data. In the low or moderate overload ranges, however, the 2D-FCM method cannot effectively include the parenchyma pixels (< 80%) in 5 of 60 cases that might be due to various factors that requires further investigation. By combined the best possible classification of both 1D- and 2D-FCM methods, or MIX method, the segmentation results can be further improved to be 98% correct and 1% in-correct segmentation of parenchyma and vessel pixels, respectively. Such the combination can reduce the drawback of both methods. In this study, the exclusion of the vessel pixels from the parenchyma by manual or FCM segmentations can lower the variability, or IQR data, by 32% (22 vs 14.9 mg/g-dw) which the most reduction is in the server overload range, as shown in Figure 3. The 1D- and 2D-FCM segmentations also can provide the similar reduction as in the manual one without the offset of median LIC data. In this study, there is no exact T2\* echo image nor thresholding level found to give the best classification of the FCM methods which is different than the last echo and a thresholding of 0.5 suggested by previous study<sup>3</sup>. An further study should, therefore, investigate a criteria to optimize these two variables. In conclusion, the proposed 2D-FCM method calculated from the combination of an acquired image and its LIC map can improve the segmentation result as compared to the 1D-FCM which uses only the acquire image. Furthermore, the combination of both methods can further ameliorate the classification. Finding the optimal clustering variables, however, are necessary before it can be practically employed.

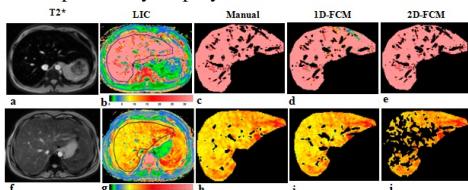


Figure 1. Two cases of manual, 1D- and 2D- FCM segmentations with their T2\* images and LIC maps

**References:** 1. Angelucci E, et al. Haematologica 2008;93(5):741-52.

3. Possitano V, et al. Magn Reson Imaging 2009;27(2):188-97.

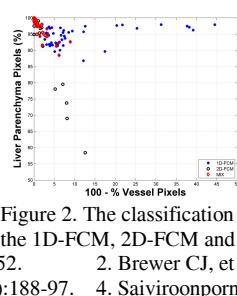


Figure 2. The classification results from the 1D-FCM, 2D-FCM and MIX methods

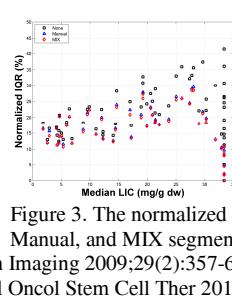


Figure 3. The normalized IQR of None, Manual, and MIX segmentation methods.