Histogram Analysis to Evaluate Changes on Parametric Maps: Preliminary Application to Renal BOLD MRI

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INTRODUCTION

Parametric maps are being increasingly employed in radiologic investigations. However, regions of interest (ROI) analyses are most commonly used to evaluate them. While logistically simple and conceptually easier to interpret, ROI analysis only captures changes observed in relatively small regions defined by the user and does not fully evaluate the spatial distributions that are inherently available in images. ROI analysis is inherently operator dependent and may not be suitable for large scale clinical studies. ROI analysis also depends on the contrast between different regions that are of interest, *e.g.* cortex and medulla in renal applications. It is well known that in subjects with chronic kidney disease (CKD), the cortico-medullary differentiation is compromised [*J Magn Reson Imaging* 2007 Apr;25(4):790-5] making the choice of ROIs more challenging.

Here, we propose a simple histogram based analysis to evaluate changes observed on R2* maps used for intra-renal BOLD MRI (blood oxygen level dependent magnetic resonance imaging) that avoid the subjectivity associated with ROI analysis.

METHODS

All procedures were performed with IRB (Institutional Review Board) approval and written subject consent. All MRI data was acquired on a 3.0 T whole body scanner (Magnetom Verio, Siemens Healthcare, Erlangen, Germany). BOLD MRI data was acquired using breath-hold multiple gradient echo sequence with following parameters: Field of view (FOV) = 360 x 245mm, No. of Slice = 5, Slice thickness = 5.0mm, Matrix = 256 x 256, TR = 62ms, No. Echo = 8 equally spaced (3.09–32.3ms). NEX = 1. BOLD MRI measurements were acquired at baseline and after *iv* administration of 20 mg of furosemide, a common paradigm employed in functional renal imaging.

R2* maps and histogram analysis were performed on custom software developed using Matlab (Mathworks, Natick, MA). R2* maps were calculated on a pixel by pixel basis within the entire kidney by fitting a single exponential decay curve to the signal intensity *vs*. echo time data. From this map, a histogram was generated. The centroid for the histogram was then computed using standard equations [http://en.wikipedia.org/wiki/Centroid]

$$X_c = \frac{\sum_1^n X_i * m_i}{\sum_1^n m_i} \; ; Y_c = \frac{\sum_1^n Y_i * m_i}{\sum_1^n m_i},$$

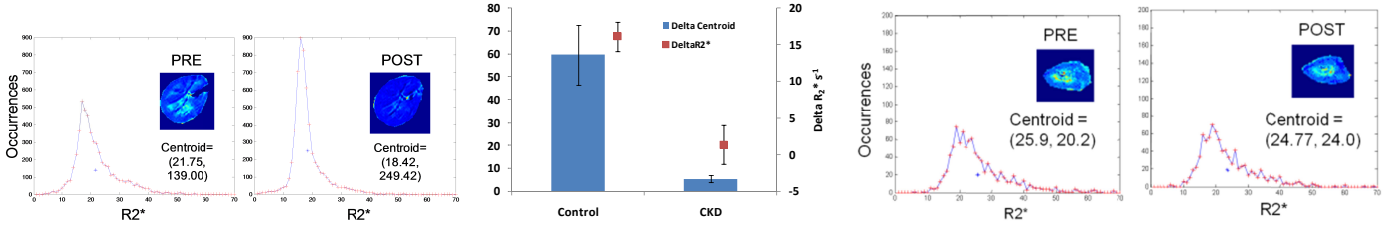
where X_i is the bin position, and m_i is the corresponding histogram value at that location, Y_i=m_i/2, and i ranges from 1 to n. The displacement of the geometric centroid was used to represent the change in R2* distribution before and after furosemide injection. The displacement was calculated using:

$$Delta\ Centroid = \sqrt{(X_1 - X_2)^2 + (Y_1 - Y_2)^2},$$

where (X_1,Y_1) and (X_2,Y_2) denote the coordinates of the centroids for the baseline and post-furosemide R2* histograms.

RESULTS

The figures below illustrates the technique. One clearly visualizes the change from pre- to post-furosemide on the R2* maps in control subjects (a) and the same is reflected in the histograms. On the other hand, very little change is observed in CKD (c). However, a numerical representation of this visual data is necessary for combining data from different subjects, usually necessary for performing statistical analysis. ROI analysis provides a simple numeric representation and is currently the method of choice. Our data suggests that alternate representation of the changes in histograms allow more comprehensive parameter that accounts for the numeric value and its spatial distribution. As shown below histogram centroids are used effectively to illustrate the changes observed pre- and post-furosemide and compared between two different groups of subjects (**b**).



(a) **(b)** **(c)**

Figure 1: is representative data from one kidney from a control subject **(a)** and a subject with CKD **(c)**. Included are R2* maps acquired before and after administration of furosemide. As is evident from the maps, there is a large response in the medulla of control subject, while minimal change is observed in the subject with CKD. The plots shown are histograms of R2* values within the kidney and represented by the geometric centroid. **(b)** is a plot of Delta Centroid in kidneys of control (n=6) and subjects with CKD (n=4). Also included are Delta Medullary R2* values computed using conventional ROI analysis. Note the similarity in the trends observed with either parameter. However, the scales are significantly different.

DISCUSSION AND CONCLUSION

The preliminary data provided here support the feasibility of using the proposed histogram analysis to characterize changes observed on functional images such as renal BOLD MRI. The choice of displacement in the geometric centroid as a measure of change shows similar trends compared to conventional ROI analysis. While the histogram analysis provides a more global view, ROI analysis allows for more selective regional view. Together, they may allow for a comprehensive evaluation of the observed change both in terms of the parameter and its spatial distribution. The histogram analysis inherently is more objective because it only needs trace of the kidney borders, and the whole kidney is used for analysis.

While the current work with small number of kidneys suggests higher sensitivity of the proposed histogram analysis compared to medullary R2* measurements by conventional ROI analysis, further studies with larger number of subjects is necessary. Since the displacement is inherently a vector quantity, it is not clear if the directionality provides additional information. It is also not clear if the centroid can be used to compare baseline differences between different cohorts. While the centroid is one intuitive representation of the histogram distribution, there may be other measures to consider in the future. It is possible that the baseline histogram can be resolved into two components, *viz*. cortex and medulla. These could be used to segment the R2* map which in turn can be used as masks to analyze regional differences.

The method could potentially be applied to any other parametric maps, *e.g.* T1, T2, ADC, magnetization transfer ratio (MTR) *etc.*.

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