Signal Intensity Normalization for Serial Vessel Wall Imaging

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Synopsis

This study aims to establish an approach for normalizing serial magnetic resonance imaging (MRI) of popliteal arteries in order to evaluate vessel wall signal changes quantitively. We developed histogram-based measurements combined with a machine learning technique, selecting the surrounding muscle in the knee as a landmark for normalization. This was verified as both biologically reasonable and technically feasible based on scans of 4,796 subjects. This approach may be applied to provide information in vascular research, such as giving assistance in vascular disease diagnosis and identifying high risk atherosclerotic lesions.

Introduction

MRI is commonly used to assess vascular diseases. However, because the displayed value of MR images are based on an arbitrary unit, interpretation of pathological abnormalities in vessel wall regions by the signal intensity varies across different subjects and prevent automated analysis. Several methods have been previously developed for brain intensity normalization. However, these methods are either based on brain tissues or neglecting the great differences between patients, such as abnormal pathological representation that changes the image histogram. These problems prohibit application for analysis of vessel walls in knee images by signal intensity, such as the vessel wall data from the Osteoarthritis Initiative dataset that contains MR scans of popliteal artery vessel wall from 4796 subjects with abundant vascular information. To address these issues, we introduce a normalization method that uses muscle as landmark and applies different approaches to validate the results.

Imaging Data

- The Osteoarthritis Initiative (OAI) is a multi-center, ten-year observational study, sponsored by the National Institutes of Health.
- Imaging parameters for the knees (3D DESS) are: TR/TE:16.32/4.71 ms, in-plane resolution: 0.36×0.36 mm, spacing between images: 1.5 mm, field of view: 140×140 mm.
- Validation set: 17 cases that are scanned twice at the same time point, from the OAI dataset.
- Test set: we identified two groups of subjects who, on the basis of baseline clinical and demographic information, had either low or high risk for cardiovascular disease. Test set consists of 200 subjects from the high risk group and 200 subjects from the low risk group.

Normalization Algorithm

Muscle is a tissue that is relatively unaffected by vascular disease and is consistent within the entire knee, making it comparable within the dataset. We propose a histogram-based method in order to segment muscle from the knee as our landmark for normalization. Most of pixels belonging to muscle have a higher signal intensity in the histogram of the knee, which generates a second peak, as Figure 1 shows. In practice, we set \( \mu \) as the peak value for the second peak, then let \( F(x) \) be the cumulative distribution function (CDF) of the MR image inside the muscle mask.

\[
F(x) = P(I(x) \leq I(x))
\]

Define \( \tau = 5\% \) (this value is selected after sensitivity analysis), then the muscle mask is defined as the set

\[
\Omega = I(x)|F^*(F(\mu) - \tau) < I(x) < F^*(F(\mu) + \tau)
\]

where \( F^*(x) = F^{-1}(x) \). Histogram-based segmentation results are shown in Figure 1. For those cases without the second peak (the difference between the first peak and the second peak is less than 5), fuzzy c-means are applied, which allows one piece of data to belong to two or more clusters through an iterative optimization of a designed function.

Let \( \sigma \) be the standard deviation associated with \( I(x) \). Finally, we apply z-score to all pixels in the whole image.

\[
I'(x) = (I(x) - \mu)/\sigma
\]
After vessel wall is segmented, the validation is based on the maximum intensity and average intensity of whole vessel wall in knee and the maximum value in each slice. We plotted the data and calculated the correlation coefficient and coefficient of determination to verify the result.

For clinical analysis, we calculated the maximum signal intensity for the vessel wall for 200 cases in each group of the test set. A T-test was used for comparing the feature differences between the two groups.

**Results**

For validation, before normalization, the coefficient of determination for the validation set is 0.0704 (p value<0.3), which indicates that the dots are distributed randomly. After normalization, the coefficients of determination were 0.6006 and 0.8008 (p value>0.3), therefore most of the dots fit in the same line. More importantly, the slopes of the lines are 0.9716 and 0.9213, as Figure 2 shows. This proves that values for the same spot from two scans on the same person are in the same range after normalization, verifying the normalization.

After signal normalization, we found that the maximum signal intensity and standard deviation for vessel walls in the high risk group was higher than that of the low risk group as Figure 3 shows (p value: 6.32*10^{-7} and 8.55*10^{-4}). In addition, the histogram for the high risk group was much more complex than that of the low risk group. As Figure 4 shows, the histogram of the high risk group has more peaks than the low risk group.

**Discussion and Conclusion**

Using our method, one can analyze vessel wall features from MRI images of knees based on the signal intensity of tissues across different subjects. Signal intensity of the high risk group was significantly different from the low risk group (Figure 3). The maximum signal intensity of vessel walls after normalization may thus be useful when assessing the risk of vascular diseases. Histograms of the high risk group tended to have multiple peaks, while the low risk group only had one or two peaks. It is likely that vessel walls belonging to the high risk group tended to have various tissues and lesions leading to different signal intensity peaks in the histogram compared to the low risk group with simple structures and few lesions.

In conclusion, we introduced a robust normalization methodology for MRI of the knee using segmented muscles as the reference. The intensity features may be useful for risk assessments from vessel walls in MR knee scans.

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**References**


Figures

Figure 1 Original image (left). Histogram of a whole knee signal intensity(middle). Horizontal axis is the value of signal intensity and vertical axis is the number of pixel in the value. From the histogram we can see that there are two peaks. Segmented pixels in the second peak generates the third graph (right).

Figure 2 Verification of normalization. Plot 1 (left) is the maximum intensity for each slice from two different scans of the same person. Plot 2 (right) is the maximum intensity of entire vessel wall for two different scans of the same person. Dots in plot 1 (left) represent different slices and dots in plot 2 (right) represent different cases.

Figure 3 Maximum signal intensity of high risk group and low risk groups after signal normalization using the proposed method.
Figure 4 Histogram of vessel wall in knee after normalization of high risk group (left) and low risk group (right). The two images beneath the histogram are examples of the original knee MRI image. Arrows point to the vessel wall. A direct observation is that the signal of vessel wall in the high risk group appears to be more complex than low risk group.