

Differentiation of Pre-Ablation and Post-Ablation Late Gadolinium-Enhanced Cardiac MRI Scans of Longstanding Persistent Atrial Fibrillation Patients

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ABSTRACT

Late Gadolinium-Enhanced Cardiac MRI (LGE CMRI) is an emerging non-invasive technique to image and quantify pre-ablation native and post-ablation atrial scarring. Previous studies have reported that enhanced image intensities of the atrial scarring in the LGE CMRI inversely correlate with the left atrial endocardial voltage invasively obtained by electro-anatomical mapping. However, the reported reproducibility of using LGE CMRI to identify and quantify atrial scarring is variable. This may be due to two reasons: first, delineation of the left atrium (LA) and pulmonary veins (PVs) anatomy generally relies on manual operation that is highly subjective, and this could substantially affect the subsequent atrial scarring segmentation; second, simple intensity based image features may not be good enough to detect subtle changes in atrial scarring. In this study, we hypothesized that texture analysis can provide reliable image features for the LGE CMRI images subject to accurate and objective delineation of the heart anatomy based on a fully-automated whole heart segmentation (WHS) method. We tested the extracted texture features to differentiate between pre-ablation and post-ablation LGE CMRI studies in longstanding persistent atrial fibrillation patients. These patients often have extensive native scarring and differentiation from post-ablation scarring can be difficult. Quantification results showed that our method is capable of solving this classification task, and we can envisage further deployment of this texture analysis based method for other clinical problems using LGE CMRI.

Keywords: Atlas Propagation, Multi-Scale Patch, Local Atlas Ranking, Whole Heart Segmentation, Texture Analysis, Cardiac MRI, Classification, Machine Learning, Computer-Aided Diagnosis, Medical Imaging Analysis, Image Processing

1. INTRODUCTION

Late Gadolinium-Enhanced Cardiac MRI (LGE CMRI) is a promising technique to identify pre-ablation native and post-ablation induced atrial scars. Compared to the current gold standard, i.e., electro-anatomical mapping (EAM), which is performed during an invasive electrophysiological (EP) study¹, LGE CMRI is non-invasive, uses no ionizing radiation, and has reported higher accuracy of localization of the atrial scars². Although some studies have demonstrated that there is an inverse correlation between the enhanced atrial scarring regions extracted from the LGE CMRI and left atrial endocardial voltage obtained from the EAM, the reproducibility of these findings is still debatable³. This may be due, firstly, to the previous delineation of left atrium (LA) and pulmonary veins (PVs) anatomy relying on operators' manual drawing which is highly subjective⁴; and secondly, simple intensity based image features or volumetric ratio between enhanced and non-enhanced voxels are over-simplified for the quantification of the atrial scarring. We hypothesized that, first, the LA and PVs anatomy can be accurately determined via a multi-atlas propagation based fully-automated whole heart segmentation (WHS); and second, that texture analysis on the extracted LA wall and PVs can provide more robust features for the LGE CMRI images than simple intensity-based measures. We validated our method by using it to differentiate pre-ablation LGE CMRI scans from post-ablation ones in cases of long-standing persistent atrial fibrillation patients. Cross validation results on 20 LGE CMRI scans of longstanding persistent atrial fibrillation (AF) patients showed dramatic improvement on the classification accuracy. And we can envisage the application of this technique for other cardiovascular clinical studies using LGE CMRI particularly in patients that atrial fibrosis can be quantified.

2. METHODOLOGY

2.1 Multi-Atlas Propagation Based Fully-Automated Whole Heart Segmentation (WHS)

Visualization of atrial scarring is performed by superimposing the enhanced signals derived from an LGE CMRI acquisition onto a 3D model of the LA and PV anatomy derived from a CMRI roadmap acquisition. Delineation of the heart anatomy in the CMRI roadmap study is a very challenging task and has generally been done using manual drawing by experienced operators. This suffers from two major pitfalls: first, the procedure is time-consuming and second, the manual segmentation is subjective and might not be reproducible. To automate this procedure, co-registration and a multi-atlas propagation based segmentation (MAS) method was proposed to accomplish the task⁵. Previous studies have shown that the multi-atlas can be built from just labeling LA and PVs⁶ or labeling all the whole heart substructures including four chambers, major vessels and PVs⁵. The former method might be easier for atlas construction, but the segmentation accuracy of LA and PVs anatomy could be sacrificed without considering variances and deformation of surrounding substructures⁶; therefore, whole heart substructures were used in our atlas construction. In this study, we developed a MAS technique followed by a multi-scale patch

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based label fusion (MSP-LF)⁷. The developed WHS technique was applied to our CMRI roadmap whole-heart acquisition, and the LA and PVs anatomy was extracted (Figure 1). As both CMRI roadmap and LGE CMRI sequences are ECG gated, we can apply the extracted LA and PVs segmentation from the CMRI roadmap directly on to the LGE CMRI images (Figure 1). Further refinement of the PVs segmentation might be achieved via prior information provided by contrast-enhanced MR angiography or manual editing; however, non-gated MR angiography can cause mis-registration to the ECG gated LGE CMRI and further complicate the segmentation procedure. In this study, we focused on a fully automated WHS method for the delineation of LA and PVs without further manual intervention.

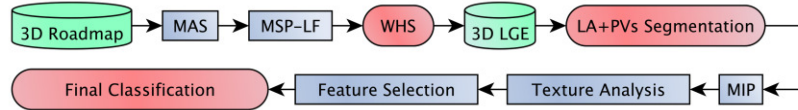


Figure 1: Flowchart of our fully automated WHS, texture analysis and classification workflow.

2.2 Maximum Intensity Projection and Feature Extraction via Texture Analysis

Following the WHS derived LA blood pool and PVs anatomy, we aim to extract information on possible atrial scarring in the LA wall and around PVs. Morphological dilation was applied to the derived LA blood pool and PVs to an extent of 3mm which is assumed to be the thickness of the LA wall⁸. Previous clinical-focused studies only considered intensity-based features, e.g., enhanced intensity or ratio between enhanced and overall LA wall and PVs regions⁹.

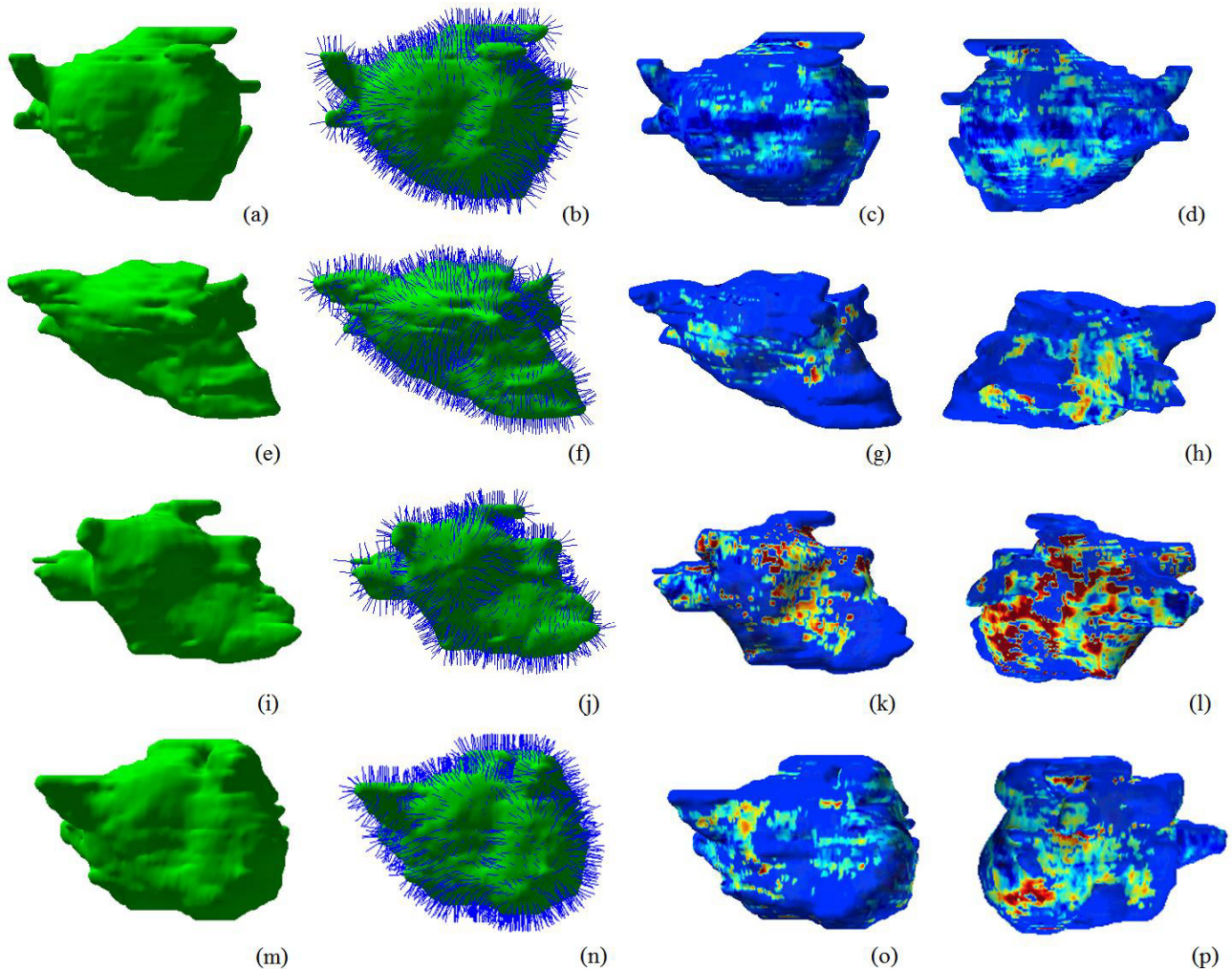


Figure 2: Visualization of the WHS results for two pre-ablation cases (a-d) and (e-h) and two post-ablation cases (i-l) and (m-p). First column: 3D surface rendering of the WHS results of LA and PVs; second column: the computed normals (blue lines) perpendicular to the segmented surface; Last two columns: anteroposterior and posteroanterior views of the 3D MIP showing the atrial scarring.

In this study, we employed texture based features for further quantification. Texture analysis has been successfully applied for the enhanced regions derived from LGE CMRI but for the infarction tissues in left ventricle only, which has much thicker myocardium¹⁰. It is very challenging to perform the texture analysis for the LA wall and PVs because the LA wall thickness is

small and the voxel size is relatively large (1.5mm×1.5mm×4mm reconstructed to 0.75mm×0.75mm×2mm). Previous studies have used 3D maximum intensity projection (MIP, Figure 2) ⁶, and texture analysis can be performed after surface flattening ¹¹; however, this can introduce artifacts after interpolation. Considering previous limitations and challenges, we performed 2D MIPs for each WHS, with two projections being performed for each patient (from the central slice to the most superior and to the most inferior slices as shown in Figure 3 (a) and (b)). Multi-level Gabor wavelet filters based texture analysis has been adopted to extract robust image features (Figure 3 (c)) ¹² and minimum redundancy maximum relevance (mRMR) was applied for further feature selection ¹². Ten selected texture features were used for the final classification task.

2.3 Classification and Evaluation

The classification performance was evaluated by (i) Leave-One-Patient-Out (LOO) cross validation, which is an unbiased predictor and is capable of creating sufficient training data for studies with small sample size ¹³; (ii) the area under the receiver operating characteristic (ROC) curve (AUC); (iii) the classification accuracy, sensitivity and specificity at the operating point on the ROC curve using the both naïve Bayes (NB) and decision tree (DT) based classifiers ^{14,15}.

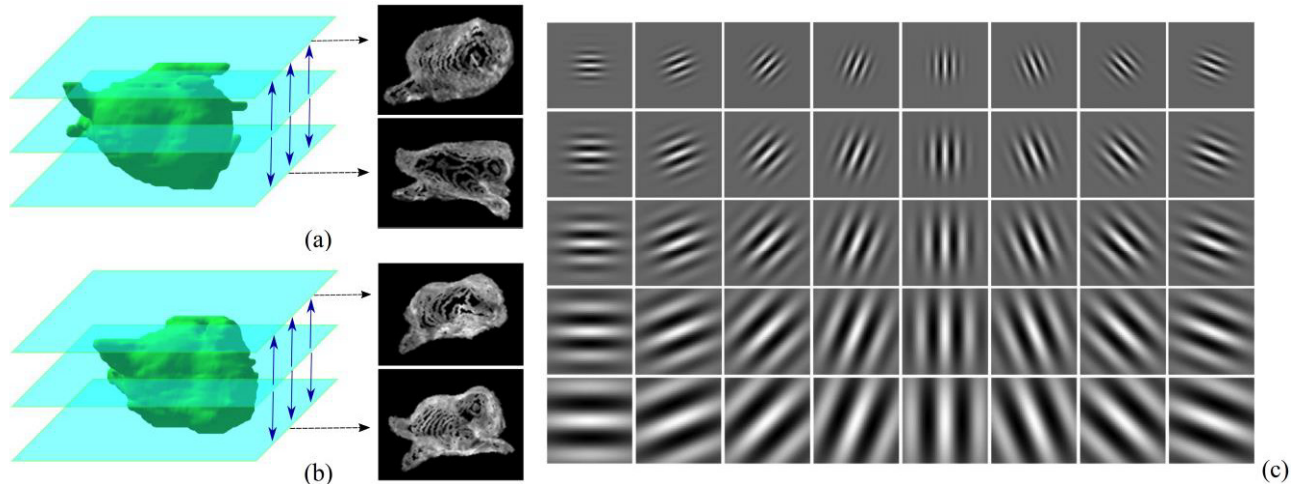


Figure 3: (a) Two 2D MIPs from the central slice to the most superior and to the most inferior slices for a pre-ablation case (blue arrows show the projection directions); (b) As (a) but applied for a post-ablation case; (c) Multi-level Gabor wavelet filters: 5 scales with 8 directions.

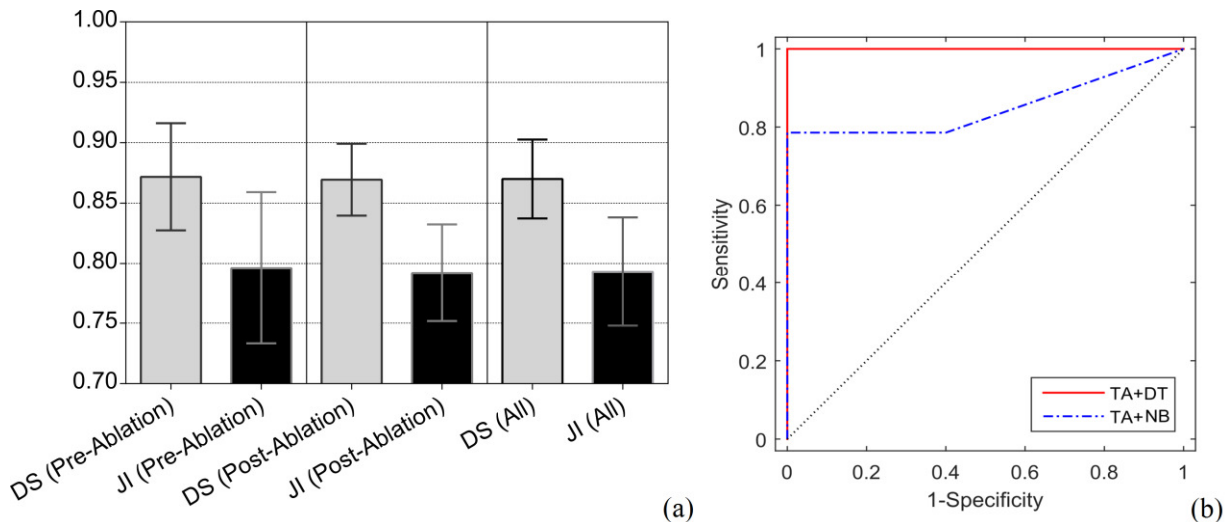


Figure 4: (a) WHS accuracy measured via Dice score (DS) and Jaccard Index (JI) for both pre-ablation cases, post-ablation cases and all the cases; (b) Comparison of the ROC for the texture analysis with naïve Bayes (TA+NB) or decision tree (TA+DT) classifiers.

3. EXPERIMENTS AND RESULTS

We applied the classification and cross validation on 20 LGE CMRI scans of longstanding persistent AF patients. Figure 2 shows the 3D rendering of the WHS results (LA and PVs), and the 3D MIP of the enhanced atrial scarring. Figure 3 demonstrates the 2D MIP procedure and multi-level Gabor wavelet filters adopted. Figure 4 (a) summarizes the accuracy of our WHS evaluated by both Dice score and Jaccard index. Figure 4 (b) shows the ROC curve of the classification results, and we compared the performance of using NB and DT based classifiers on texture features. We compared our method with using

intensity based features: (i) using statistics (minimum, maximum, mean, median and standard deviation) extracted from image intensities of the segmented LA wall and PVs regions, and (ii) segmenting the enhanced scar regions using x-standard deviation method ($x=2, 3, 4$ or 6)⁴, and the ratio between the enhanced volume and overall LA wall and PVs volume was then used as classification feature. According to a benchmark work⁴, there is no significant difference obtained from various segmentation methods for atrial scarring delineation; therefore, in this work we used the classic standard deviation method to extract the atrial scarring and performed the comparison studies. Table 1 shows the comparison results of the classification using intensity based features and texture analysis derived features. LOO results showed that texture analysis with DT classifier achieved 100% accuracy, and significantly outperformed the results obtained by using the intensity based features.

Table 1: Quantitative results of the classification (IF+NB: intensity features with naïve Bayes classifier; IF+DT: intensity features with decision tree classifier; x-SD+NB: x-standard deviation and with naïve Bayes classifier; x-SD+DT: x-standard deviation and with decision tree classifier; TA+NB: texture analysis with naïve Bayes; TA+DT: texture analysis with decision tree classifier).

Method	Sensitivity	Specificity	PPV	NPV	Accuracy	AUC
IF+NB	40.00	93.33	66.67	82.35	80.00	0.67
IF+DT	40.00	86.67	50.00	81.25	75.00	0.75
2-SD+NB	40.00	93.33	66.67	82.35	80.00	0.37
2-SD+DT	40.00	100.00	100.00	83.33	85.00	0.52
3-SD+NB	40.00	100.00	100.00	83.33	85.00	0.40
3-SD+DT	40.00	100.00	100.00	83.33	85.00	0.53
Method	Sensitivity	Specificity	PPV	NPV	Accuracy	AUC
4-SD+NB	40.00	93.33	66.67	82.35	80.00	0.39
4-SD+DT	20.00	93.33	50.00	77.78	75.00	0.53
6-SD+NB	20.00	93.33	50.00	77.78	75.00	0.53
6-SD+DT	60.00	93.33	75.00	87.50	85.00	0.67
TA+NB	100.00	73.33	55.56	100.00	84.21	0.85
TA+DT	100.00	100.00	100.00	100.00	100.00	1.00

4. CONCLUSION

In this study, we proposed a fully automated workflow to process LGE CMRI images including objective delineation of LA and PVs anatomy and texture analysis based feature extraction. The designed workflow was applied to distinguish pre-ablation cases from post-ablation scans acquired by LGE CMRI. Such a task can be very difficult as all our patients suffered from longstanding persistent AF, and pre-ablation native atrial scarring can be quite extensive. We hypothesized that texture analysis can extract robust features for this challenging task subject to accurate anatomy segmentation. Our experimental results have demonstrated the high efficacy of our workflow and we can expect our method to be deployed for other clinical problems using LGE CMRI. In particular, it may be able to improve the classification of patients pre-ablation, which is currently based on intensity based parameters which would provide increased guidance for the invasive ablation strategy. Upon the acceptance of this initial submitted abstract, in the final manuscript, we will provide a more detailed description of the proposed method with mathematical equations and elaborated steps of experiments. Finally, we will provide a full discussion including merits and limitations of our workflow. Also, we herein confirm that this submission is our latest research work and has not published elsewhere.

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