MRI-Based Quantification of Myocardial Perfusion at Rest and Stress Using Automated Frame-by-Frame Segmentation and Non-Rigid Registration

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Abstract

We developed a method for automated quantification of myocardial perfusion from cardiac magnetic resonance (CMR) images. Our approach uses region-based and edge-based level set techniques for endocardial and epicardial border detection combined with non-rigid registration achieved by a 2D multi-scale cross-correlation and contour adaptation. This method was tested on 66 short-axis image sequences (Philips 1.5T) obtained in 11 patients at rest and during vasodilator stress at 3 levels of the left ventricle during first pass of a Gadolinium-DTPA bolus. Myocardial ROIs were automatically defined and contrast enhancement curves were constructed throughout the image sequence. Analysis of one sequence required <1 min and resulted in endo- and epicardial boundaries that were judged accurate. Curves obtained during stress showed the typical pattern of first-pass perfusion with SNR of 19±4, as well as increased contrast inflow rate (0.031±0.013 vs 0.014±0.004 sec^{-1}) and higher peak-to-peak amplitude (0.20±0.05 vs 0.14±0.03) compared to resting curves. Despite the extreme dynamic nature of contrast enhanced image sequences and respiratory motion, fast automated detection of myocardial segments and quantification of tissue contrast results in time curves with excellent noise levels, which reflect the expected effects of stress.

1. Introduction

Quantification of first-pass myocardial perfusion from contrast-enhanced cardiac magnetic resonance (CMR) images relies on the definition of myocardial regions of interest (ROI). This is usually achieved by manually drawing ROIs in one frame and then adjusting their position on subsequent frames to compensate for cardiac translation due to respiration [1]. This tedious, time-consuming and potentially inaccurate methodology has been hindering widespread clinical application of imaging-based quantification of myocardial perfusion. However, the development of automated techniques has been difficult because of the extreme dynamic nature of contrast-enhanced image sequences and out-of-plane cardiac motion. Recently, analysis of image noise density distribution proved as a useful tool for automated dynamic endocardial border detection [2]. The goals of the present study were: (i) to use this approach to develop an automated technique for identification and registration of myocardial ROIs, and (ii) to test the feasibility of using this technique for perfusion quantification from images obtained in patients undergoing pharmacological stress CMR testing.

2. Methods

2.1. Population

Eleven adult subjects (age 56±17 yrs, 7 males) were studied using CMR imaging. Exclusion criteria were: (i) standard contraindications to MRI with Gadolinium contrast, (ii) ischemic heart disease evidenced by perfusion abnormalities or delayed Gd enhancement.

2.2. Imaging

Short-axis images (Achieva, Philips 1.5T) were obtained at three levels of the left ventricle during first pass of a Gadolinium-DTPA bolus (0.075 to 0.10 mmol/kg at 4 to 5 ml/ sec). Images were acquired using a hybrid gradient echo/ echo planar imaging sequence (nonselective 90° saturation pulse followed by a 80 ms delay, voxel size ~2.5x2.5mm, acquisition time=83 ms per slice, slice thickness 10mm, flip angle 20°, TR=5.9 ms, TE=2.7 ms, EPI factor 5, and SENSE factor 2). Patients were instructed to hold their breath as long as possible starting just prior to the administration of contrast. Imaging was performed starting 2 minutes after injection of A_{2A} specific vasodilator stress agent regadenoson (Lexiscan; Astellas Pharmaceutical) and then repeated 15 minutes after injection of aminophylline under resting conditions.

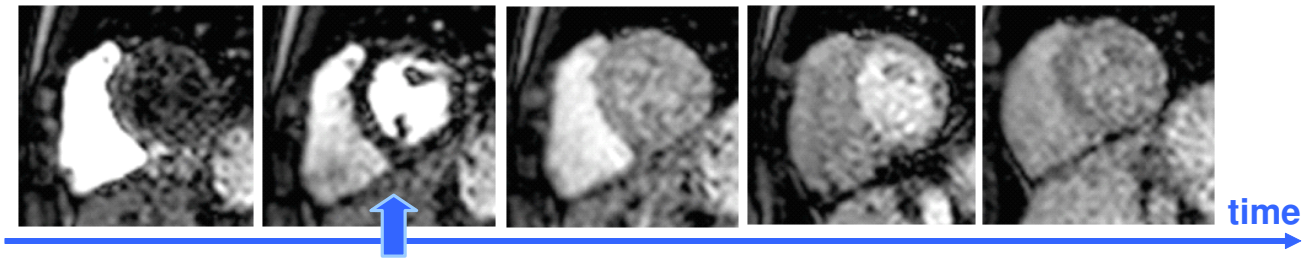

Figure 1. Automated selection of the frame for endo- and epicardial detection is achieved by tracking over time the pixel intensity in the vicinity of the seed point inside the LV cavity and identifying the frame in which the intensity reaches 95% of its maximum (arrow). This frame shows optimal left and right ventricular cavity opacification, as well as a certain level of myocardial enhancement, which are all helpful for endo- and epicardial detection. Of note, this usually occurs early in the sequence, when the patient is still in apnea.

2.3. Image segmentation

For each slice, the first step of analysis is manual placement of a single point inside the LV cavity. This is done in a single frame. The second step is the automated selection of the best frame for endo- and epicardial detection (figure 1). In this reference frame, first, the endocardial boundary is automatically detected (figures 2A and 2B). Unlike most previously used techniques that are based on thresholding pixel intensity, our approach is based on the assumption that noise distribution in the blood pool is different from that in the myocardium.

This assumption allows us to use a region-based level set technique to partition the heart into maximally homogeneous regions taking into account the local noise patterns. From a mathematical point of view, we first define a curve C as the zero level set of an implicit real function φ taking values on the image domain Ω:

$$C = \{(x, y) \in \Omega: \varphi(x, y) = 0\}$$

This curve C undergoes an evolution in time in order to maximize the following functional F:

$$F(I,C) = \varepsilon \cdot lenght(C) + \int_{\Omega_i(C)} \log p(I)\, dxdy + \int_{\Omega_o(C)} \log p(I)\, dxdy$$

I is the gray level intensity image, $\Omega_i(C)$ and $\Omega_o(C)$ are the regions inside and outside C, and $\varepsilon \cdot length(C)$ is a regularization term [3]. $p(I)$ represents the probability density distribution of the gray levels in MRI images, which can be approximated with a Gaussian distribution under fairly reasonable conditions:

$$p(I) = \frac{1}{\sqrt{2\pi}\sigma} \exp\left(-\frac{1}{2}\left(\frac{I(x,y) - \mu}{\sigma} \right)^2 \right)$$

where μ and σ are the average and variance of I, respectively.

The final step of endocardial detection is boundary regularization achieved using curvature motion [4] that does not allow curvature above certain level and was designed to automatically include the papillary muscles in the LV cavity (figure 2B). We then use the classical edge-based level-set model [5] to search the image from the endocardium outwards and identify the epicardial boundary (figure 2C). The equation that drives the evolution is the well-known Malladi-Sethian model for active contour evolution including a dependence of the speed on the curvature, a propagation expansion speed and an advection speed based on the image gradient

$$\partial_t \phi = g(\varepsilon K - 1)|\nabla \phi| + \nu \nabla g \cdot \nabla \phi$$

with adequate boundary conditions and the previously computed endocardium contour as initial condition. At the end of this step, the epicardial boundary is also regularized with modified curvature motion.

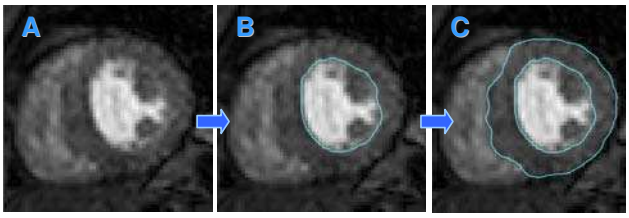

Figure 2. After optimal frame is automatically selected (A), LV endocardial boundary is detected using a region-based level set technique taking into account the local noise patterns (B). Then, the epicardial boundary is detected using classical edge-based level-set model that searches from the endocardial boundary outwards (C).

2.4. Image registration

Non-rigid image registration was achieved by a multi-scale extension of two-dimensional cross-correlation to compensate for cardiac translation and deformation as a result of out-of-plane motion. To this effect, we defined a first template image of the left ventricle in the reference frame, and five additional template images created by resizing this template to different degrees (1 pixel difference at a time). Then cross-correlation between each consecutive frame and each of the six templates was calculated and the new size and position of both endo- and epicardial boundaries were determined by finding the

largest cross-correlation peak among the six combinations. Subsequently, contour adaptation was performed as a final step of boundary refinement using again the edge-based level-set model (figure 3). Templates were updated for each consecutive frame to take into account the changes in pixel intensity occurring during the passage of the contrast bolus.

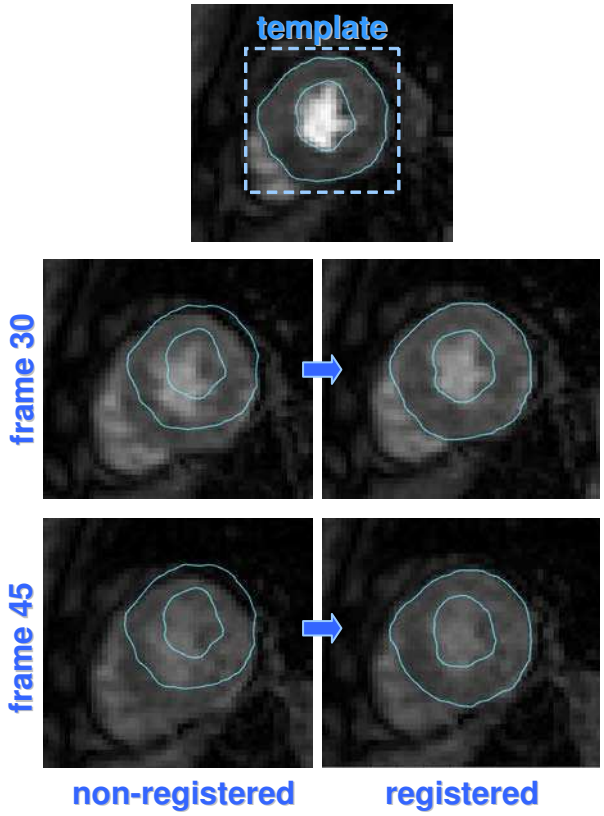

Figure 3. Image registration uses a template obtained from the reference frame (top). The endo- and epicardial contours are shifted and deformed in each consecutive frame to match the position and shape of the left ventricle.

2.5. Quantification of contrast dynamics

To allow analysis of regional myocardial perfusion, the myocardial ROI, defined as the area between the endo- and epicardial contours, was divided into 6 wedge-shaped segments, according to the standard segmentation model (figure 4, left). For anatomically correct orientation, the user manually identified the anterior junction of the right ventricular free wall with the inter-ventricular septum. Then pixel intensity was measured in each segment over time, resulting in contrast enhancement curves throughout the image sequence (figure 4, right). From each curve, the slope of the contrast enhancement phase, reflecting inflow rate, was calculated using the linear regression analysis of the upslope portion of the curve. In addition, the peak-to-peak amplitude, reflecting the concentration of Gadolinium per unit volume, was calculated.

2.6. Performance testing

This approach was tested by: (i) visually judging frame-by-frame the accuracy of endo- and epicardial boundary positions, and (ii) calculating for each segment the ratio between the peak-to-peak amplitude of the contrast enhancement curve and the SD of the plateau phase (SNR). In addition, the slope of the contrast enhancement phase and the peak-to-peak amplitude in each segment were compared between rest and stress, to test the ability of our technique to quantify the expected effects of stress.

3. Results

Time required for automated analysis of a complete perfusion sequence in one slice was less than 1 minute on a personal computer and resulted in endo- and epicardial boundaries that were judged accurate in all image sequences (figure 3, right). Contrast enhancement curves clearly showed the typical pattern of first-pass perfusion (figure 4, right), in all images sequences obtained at both rest and stress. Mean SNR was 15±5 at rest and 19±4

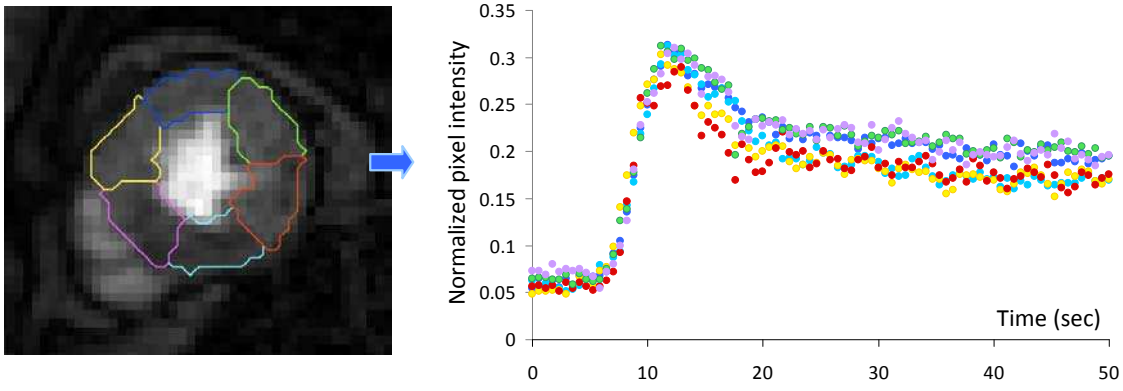

Figure 4. After myocardial ROIs were defined (left), regional contrast enhancement was plotted over time for each ROI. This example shows data obtained in a mid-ventricular slice during regadenoson stress.

during stress, reflecting excellent quality of the curves. As expected, during stress, the upslope phase of the curves was steeper in all myocardial segments in all patients (figure 5), indicating faster contrast inflow rate as part of the normal hyperemic response. This was reflected by the significantly higher slope, S, during stress: 0.031±0.013 vs 0.014±0.004 sec^{-1}.($p<0.05$) In addition, the stress-induced increase in pixel intensity, or the peak-to-peak amplitude of the curve, A, was also significantly higher during stress: 0.20±0.05 vs 0.14±0.03 ($p<0.05$), indicating increased intra-vascular blood volume (figure 5).

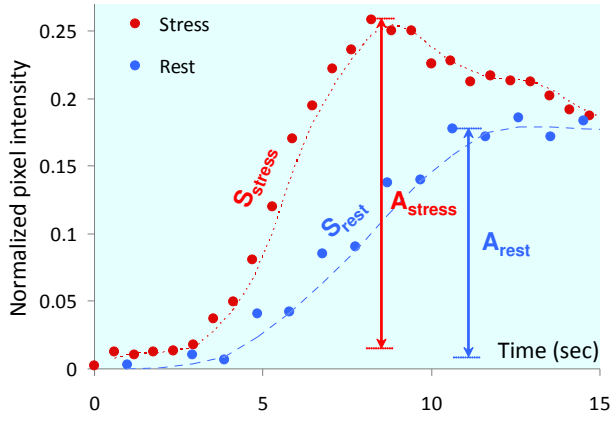

Figure 5. Example of contrast enhancement phase of the time curves obtained in the mid-inferior segment during rest (blue) and stress (red). Note the increase in both the slope and the peak-to-peak amplitude, reflecting the expected effects of stress.

4. Discussion and conclusions

This study was aimed at the development of an automated technique for the quantification of intra-myocardial contrast on CMR images, as an alternative to subjective, tedious and time-consuming manual tracing and frame-by-frame repositioning of multiple ROIs, which often takes 30 to 60 minutes per study. Typical CMR images acquired using perfusion-targeted pulse sequences are characterized by relatively low spatial resolution, high noise levels, and in- and out-of-plane cardiac motion, as well as rapid and extreme changes in brightness and contrast of the different image components. As a result, automated detection of the endo- and epicardial boundaries using conventional threshold based approaches is not feasible.

To the best of our knowledge, neither noise distribution nor non-rigid multi-scale registration have been previously used to segment contrast-enhanced CMR perfusion image sequences. Our results indicate that despite the extreme dynamic nature of contrast enhanced image sequences and respiratory motion, dynamic detection of myocardial segments and quantification of intra-myocardial contrast using this approach is feasible and is substantially faster than the current state of the art methodology. This approach results in regional contrast enhancement curves with excellent noise levels, which are necessary for reliable quantitative analysis of contrast dynamics. The comparisons of resting and stress data demonstrated the ability of this technique to reliably detect the expected effects of vasodilator stress.

In summary, our technique allows for the first time fast, automated, user-friendly and potentially more accurate measurement of intramyocardial contrast enhancement from CMR images, and may thus address the strong clinical need for quantitative evaluation of myocardial perfusion.

References

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