Rigid Registration of Delayed-Enhancement and Cine Cardiac MR Images using 3D Normalized Mutual Information

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Abstract

For the viability assessment in patients with infarcts, myocardial hyperenhancement on Delayed-Enhancement Cardiac MRI (DE) can be anatomically localized using Cine Cardiac MRI (Cine). An automatic rigid registration method, using the Normalized Mutual Information (NMI) maximization was proposed to refine the registration of the functional (DE) and anatomical (Cine) images. The full process including: 1) a coarse DE/Cine spatio-temporal alignment, 2) a refined DE/Cine registration, 3) a GVF-Snakes segmentation of myocardial contours on Cine images and 4) a myocardial infarction extent (MIE) quantification using a fuzzy c-means algorithm, was applied to ten patients with myocardial infarction. The qualitative and quantitative evaluation of the registration method showed high-quality alignment. The comparison between visual and automatic MIE quantification agreement (±1 grade) showed an improvement from 86% before to 91% after the refined registration step.

1. Introduction

Multimodal image registration is of prime importance in medical image analysis, to combine functional and anatomical information. The fundamental role of DE imaging in predicting myocardial viability is nowadays well established (1). For the viability assessment in patients with infarcts, myocardial hyperenhancement on DE images can be accurately quantified, provided that the myocardium could be separated from the blood cavities, through accurate contours delimitation. In clinical routine, MIE is visually assessed by experimented cardiologists or radiologists. However, the hyper-enhancement reduces the contrast between the myocardium and the left ventricular (LV) cavity, making difficult myocardial contours delineation and accurate image interpretation.

In this work, we propose to extract the epicardial and endocardial (epi/endo) contours from the Cine images which present a high intensity contrast between muscle and LV cavity and superimpose them on the DE images in order to quantify the hyperenhancement inside the myocardium. This requires inevitably a preliminary robust registration of the functional and anatomical images. The geometrical transformation can in this case be approximated by a rigid registration. An automated rigid registration method was consequently developed and applied to register the 3D DE and Cine cardiac images. As the DE images contain different gray levels compared to the Cine images, due to noise and infarcted zones enhancement, a robust intensity-based similarity criterion was used for the registration. Recently, methods based on the information theory emerged and are now intensively used for inter-modality registration. Among them, the mutual information (MI) was exploited with good results, for intra as well as inter-modality registration (2, 3).

The automated processing retained in this work included four steps. Firstly, a coarse DE/Cine spatiotemporal alignment was performed. Then, an automatic rigid registration method, using the maximization of 3D-NMI was then developed and applied to refine the first registration and correct for spatial misalignment resulting from patient motion between the two acquisitions. Thirdly, epi/endo contours were segmented from the Cine images and superimposed on the DE images, to localize the hyperenhancement inside the myocardium. Finally, the MIE was automatically quantified on myocardial segments, each slice being divided into 18 segments by a computer-assisted method, based on a fuzzy c-means algorithm (4). The described process was applied to ten patients with proven myocardial infarction. Because of ground-truth lack in practice, the rigid registration method was qualitatively evaluated by counting the number of well superimposed epi/endo contours after registration and by measuring the agreement between automatic and visual MIE quantification. The refined registration showed high-quality alignment and a notable improvement of the concordance between automatic and visual segmental quantification grades after the refined registration.

2. Materials and methods

For this study, 10 patients with clinically proven myocardial infarction underwent Cine and DE exams, during the same imaging session. 3D+t Cine exams (512x512 pixels; 12 to 15 slices, 35 phases) with ECG gating were performed on a 1.5T MR-scanner (GE Medical Systems). Patients were told to hold their breath. Short-axis (SA) views were acquired using Fast Imaging Employing STeady-state Acquisition (FIESTA). Slice thickness and spacing between slices were of 8 mm and pixel size varied from 0.72x0.72 mm^2 to 0.86x0.86 mm^2. 3D DE images (256x256 pixels; 24 to 44 slices) were obtained at 5, 6 and 7 min after Gadolinium injection, using phase sensitive inversion recovery sequences. SA views were acquired during the diastolic phase to minimize cardiac movement artifacts. Slice thickness was of 6-7 mm; spacing between slices was of 3-3.5 mm and pixel size varied from 1.36x1.36 mm^2 to 1.48x1.48 mm^2.

2.1. Data spatiotemporal synchronization

To compensate for the differences in the acquisition parameters between DE and Cine images, a temporal synchronization of the images was carried out by calculating a 3D mean Cine image in a temporal zone, corresponding to the DE volume acquisition phase (5). Then, a spatial scan alignment between the two data sets was performed using the image orientation and position parameters extracted from the DICOM fields of the original images (5). The images scales and voxel sizes were thus adjusted. This first step allowed achieving a coarse registration between the two data sets.

2.2. DE/Cine CMRI rigid registration

In a second step, a rigid registration method was developed and applied to register the synchronized DE and Cine images. Since both studies corresponded to the same diastolic phase, cardiac motion was considerably minimized. Assuming that the heart motion is reproducible from one cycle to another, we consider the hypothesis that the residual misalignment mainly results from the patient and respiratory movements. The relation between DE images position before and after registration can therefore be described as a rigid transformation:

$$\begin{bmatrix} x' \\ y' \\ z' \\ 1 \end{bmatrix} = \begin{bmatrix} 1 & 0 & 0 & 0 \\ 0 & \cos\theta & -\sin\theta & 0 \\ 0 & \sin\theta & \cos\theta & 0 \\ 0 & 0 & 0 & 1 \end{bmatrix} \circ \begin{bmatrix} 1 & 0 & 0 & t_x \\ 0 & 1 & 0 & t_y \\ 0 & 0 & 1 & t_z \\ 0 & 0 & 0 & 1 \end{bmatrix} \circ \begin{bmatrix} x \\ y \\ z \\ 1 \end{bmatrix}$$

with (x, y, z) and (x', y', z') the pixels coordinates, respectively before and after registration, (t_x, t_y, t_z) the translation components in the (x, y, z) directions and θ the planar rotation, since we only have SA slices.

The MI is a measure derived from the information theory which gives the mutual dependence of two variables A and B (6). To perform our intensity-based registration and to overcome problems resulting from different overlapping image sizes, we proposed to use Normalized MI (2), which can be expressed as follows: $NMI(A,B) = \frac{H(A)+H(B)}{H(A,B)}$, with $H(A)$ and $H(B)$ the entropies of A (respect. B) and $H(A,B)$ the joint entropy of A and B, given by: $H(A,B) = -\sum_{i,j} p(i,j) \cdot \log[p(i,j)]$, with $p(i,j)$ the joint probability of A and B and (i,j) the images gray intensities. Sub-volumes I and J constituted by regions of interest (ROI) limited to the heart zone were extracted and gray levels of the 3D regions were normalized between 0 and 1 before NMI computing. Matching the sub-volumes was then performed by estimating the rigid transform T (rotation, translation) minimizing the cost function: $C(T) = e^{-NMI(I,J,T)}$. The optimization was performed using the *Powell's* iterative method (7). The obtained optimal parameters were finally used to transform the whole DE volume to map the corresponding Cine volume and the transformed voxel values computation done using a trilinear interpolation. This second step constituted the refined registration step.

2.3. Myocardial segmentation using GVF-Snakes

Epi/endo contours of the LV cavity were segmented from the Cine images (Figure 1-(a)). A Gradient Vector Flow Snakes (GVF-Snakes) method was used to perform the segmentation on the SA slices. The images were previously filtered using connected filters. The segmentation allowed accurate myocardium detection and was robust to papillary muscles (8).

2.4. Infarction extent assessment

A computer-assisted method using a fuzzy c-means algorithm was applied to automatically quantify the MIE (4), according to a 5-point scale (0 if no infarction, 1 to 4 for a transmurality respectively: <25%, from 26% to 50%, from 51% to 75% and from 76% to 100%). For a precise regional analysis, Cine and DE SA slices (6 to 7/ patient) were divided into 18 myocardial segments (Figure 2). The origin of division was defined at the anterior insertion of the right ventricle into the interventricular septum and the next segments processed in a clockwise manner. All the segments were visually analyzed on the 7 min study by an expert. A transmurality index was attributed in both cases (auto and visual) to each myocardial segment, according to the 5-point scale.

2.5. Registration evaluation

For each patient, rotation and translation values in the (x, y, z) directions were calculated. The registration accuracy evaluation was qualitatively performed by superimposing the segmented myocardial contours on the DE images and using Red Green (RG) superposition. The expert counted the well superimposed epi/endo contours after refined registration. To evaluate contribution of the refined registration in the transmurality quantification and to complete the quantitative evaluation, the automatically obtained MIE indexes were compared to the visually segmental grades obtained before and after registration, for the 3 DE studies. To exploit the three DE studies acquired at different times, combined segmental indexes were defined using a majority rule. If no majority index was available, automatic segmental index obtained at 7 min was considered. These segmental indexes were then compared to the visual gradation of the expert.

3. Results

The evaluation of the rigid registration method considering the expert counting of well superimposed contours showed high-quality alignment results for more than 92 % of the DE processed data. Regarding the 30 refined registered data sets (10 patients and 3 studies at 5, 6 and 7 minutes), we noted a mean absolute displacement value of 2.18±1.76 mm in the x direction, 2.37±2.04 mm in the y direction and 1.75±1.56 mm in the z direction. The mean absolute value of the planar rotation θ was of 0.73±0.86°. Real rotation and translation ranges, means and standard deviations are given in Table 1.

Table 1. Registration parameters ranges, mean values and SD obtained for the 30 registered DE volumes.

	Values (mm)			
ΔT	Min	Max	Mean	SD
Δx	-6.05	5.65	0.32	2.82
Δy	-2.14	6.78	1.98	2.43
Δz	-3.00	3.50	1.55	1.77
Δθ	-2.13	3.03	0.37	1.07

Figure 1 shows a qualitative registration evaluation example using myocardial contours superimposition on unregistered (Figure 1-(b)) and registered (Figure 1-(c)) DE images. Figures 1-(d) and 1-(e) shows the Cine/DE RG superposition respectively for unregistered and registered images. In both cases (contours and image superposition), the improvement brought by registration can be easily verified.

Figure 2 shows fuzzy c-means quantification results on apical and basal slices before (Figures 2-(a) and 2-(b)) and after (Figures 2-(c) and 2-(d)) the refined registration. Quantification errors due to the cavities inclusion in the myocardium segmentation are corrected after registration. Ischemic and healthy myocardium zones are thus better identified and quantified. Automatic and visual segmental transmurality indexes were matched in a total of 1044 segments corresponding to 58 SA slices (Tables 2 and 3).

Table 2. Automatic and visual segmental transmurality indexes concordance before the refined registration.

	Automatic segmental indexes				
Visual	0	1	2	3	4
0	737	19	35	5	9
1	38	1	6	1	8
2	34	4	8	2	17
3	8	2	8	1	23
4	18	2	9	2	47

Table 3. Automatic and visual segmental transmurality indexes concordance after the refined registration.

	Automatic segmental indexes				
Visual	0	1	2	3	4
0	761	26	12	2	4
1	39	6	5	1	3
2	27	5	25	1	7
3	5	3	14	1	19
4	7	3	20	2	46

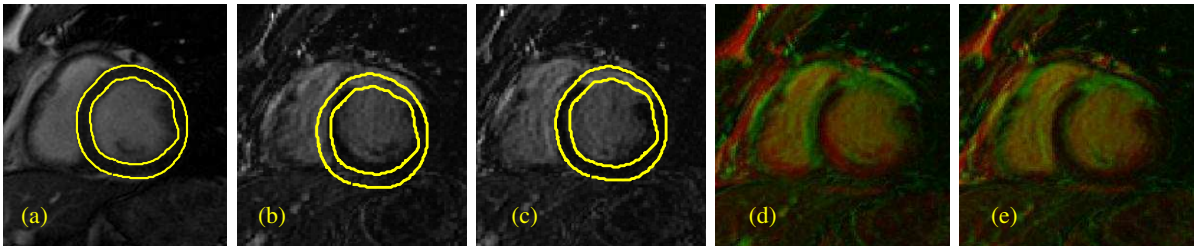

Figure 1. Extracted endocardic/epicardic contours from Cine-CMRI (a) and their superimposition on unregistered (b) and registered (c) corresponding DE image using the 3D-NMI rigid registration method. Cine and DE RG plans superposition for the same slice before (d) and after the refined registration (e).

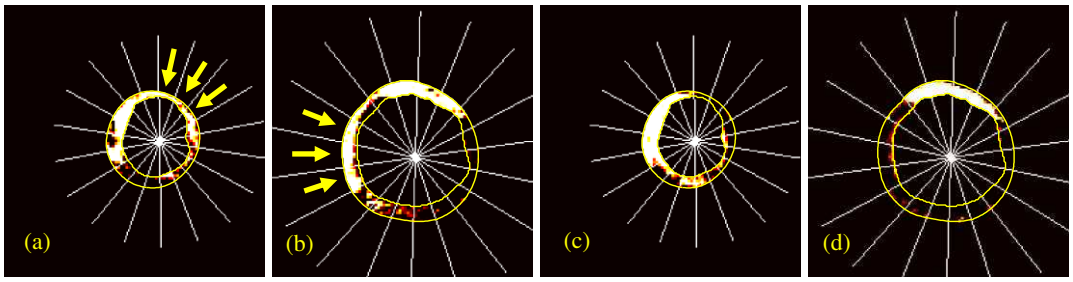

Figure 2. Fuzzy c-means quantification results on an apical and a basal slice before (a-b) and after (c-d) registration. Quantification errors (see arrows) due to the LV (a) and RV (b) cavities inclusion in the myocardium segmentation are corrected after the rigid registration. Ischemic and healthy myocardium zones are well identified and quantified.

Visual and automatic MIE quantification showed absolute agreement (identical gradation) of 76% before and 80% after the refined registration (respectively in 794/1044 and 839/1044 segments). The agreement with a tolerance of one grade of difference was of 86% before and 91% after registration (respectively in 896/1044 and 950/1044 segments). The number of highly discordant segments (>2 grades) decreased by more than half (52%) after the registration.

4. Discussion and conclusions

We proposed a rigid registration method using the NMI maximization and applied it to locally register 3D DE and Cine images. The aim of this study was to provide an accurate registration tool allowing detecting any changes in the images and thus reducing diagnosis errors and providing quantified approach of transmurality.

As the ground-truth is unknown, the registration accuracy evaluation was performed using visual criteria. The visual inspection relied both on myocardial segmented contours superimposition and on RG image superimposition. For the 10 patients, our results showed that the registration was visually systematically improved in all misaligned data (22/30 studies). Moreover, we showed that the agreement between expert reading and automatic MIE segmental quantification was significantly improved. The disagreement between the automatic and visual assessment can be explained by: 1) the difficulty of the expert to visually define the segments limits, 2) the poor segmentation results on a few noisy images (3 apical, 11 median slices), 3) involuntary patient motion during the acquisition, which could be at the origin of inter-slices misalignment of some images of the same volume. To confirm this hypothesis, a possible solution would be to compare the 3D registration to a slice-to-slice registration, allowing different images transformations in the same volume. This will be the subject of further research. One limitation of our method was that the segmentation step was time-consuming since: 1) it was semi-automatic and achieved slice by slice, 2) several filtering parameters were tested before finding the filtered image which give the best segmentation result. In addition, epicardial and endocardial contours were segmented separately, increasing the computing time.

In conclusion, we have proposed an accurate 3D-NMI rigid registration tool and showed the high-quality of the obtained images alignment results. We have further shown its positive contribution to the MIE quantification since it notably improved the automatic and visual gradation concordance after the refined registration.

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