

# Registration of Cardiac Magnetic Resonance Perfusion Data as a Basis for Quantification of Myocardial Perfusion

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## Abstract

*Quantification of cardiac magnetic resonance (CMR) myocardial perfusion remains time consuming since it requires manual intervention to compensate for motion. Thus, the aim of this study was to test an automated registration method. We studied 10 patients who had rest and stress CMR perfusion exams. For both exams, three short-axis slices were selected. Then, a rigid edge based registration algorithm was performed. Its quality was assessed 1) qualitatively by comparing the k-means clustering maps obtained before and after registration. 2) quantitatively by estimating noise amplitude within the myocardium. Registration substantially improved myocardial symmetry and heart structures identification on the k-means maps in 12/16 slices at rest and 22/27 slices at stress. It reduced noise amplitude from  $48 \pm 26$  to  $28 \pm 10$  at rest ( $p < 0.05$ ) and from  $53 \pm 13$  to  $31 \pm 10$  during stress ( $p < 0.05$ ). Our method performed successfully on both rest and stress CMR perfusion data.*

## 1. Introduction

Cardiac magnetic resonance (CMR) myocardial perfusion imaging is an essential addition to the noninvasive cardiac imaging tools for the diagnosis and the follow-up of patients with coronary artery disease (CAD). Several studies showed the potential usefulness of CMR against conventional techniques used in clinical routine for the diagnosis and the evaluation of CAD such as PET and SPECT myocardial perfusion imaging [1].

First-pass CMR myocardial perfusion is mostly evaluated using visual analysis of dynamic contrast enhanced sequences. This visual interpretation is subjective and is strongly hampered by the presence of artifacts such as respiratory motion related artifacts. Several attempts for objective quantification of CMR myocardial perfusion have been proposed [1,2].

However, because of respiratory motion, manual shifts of a region of interest on consecutive images were used to track a consistent part of the myocardium [1,2]. This repositioning is time consuming, and is a potential source of inter and intra observer variability.

In this paper a semi-automated registration technique which was previously used to compensate for respiratory motion in dynamic contrast enhanced renal series [3] was adapted to myocardial perfusion series and was tested on both resting and stress data. Its efficiency was evaluated qualitatively and quantitatively on 60 dynamic sequences (30 resting and 30 stress series). For the qualitative evaluation, the analysis of k-means clustering maps obtained on the registered and non registered datasets was performed while considering the ability to clearly identify heart structures and to observe myocardial symmetry. For the quantitative analysis, the improvement induced by the registration process was quantified by calculating the random noise amplitude within the myocardium, before and after registration. In addition to these two evaluations which aimed at highlighting the improvement carried out by the registration a manual reference was used to confirm the goodness of our registration process.

## 2. Methods

We studied 10 non selected patients (5 men, 5 women, age:  $66 \pm 12$  years) who undergone CMR clinical exam for the evaluation of CAD. Imaging was performed using a Phillips 1.5T system (Gyrosan Intera, Philips, Best, the Netherland) device. For perfusion imaging, an intravenous bolus dose of 0.1 mmol/kg Gd-DTPA was administered. Perfusion imaging was then performed using the following imaging parameters at both stress and rest: repetition time (TR) 2.5 ms, echo time (TE) 1.25 ms, flip angle 15°, pixel spacing 1.4 mm x 1.4 mm, slice thickness 10 mm. The number of frames in each dynamic sequence varied between 35 images and 98 images.

## 2.1. Reference image

For each slice, an image on which the three main anatomical structures of the heart (LV, RV, and myocardium) are enhanced was defined as the reference image ( $I_r$ ) to be used for the registration process. It was also used for drawing a ROI around the heart. Binary masks generated from each ROI were dilated using a rectangular structuring element for which  $x$  and  $y$  dimensions were fixed by the operator and defined as the maximal authorized translations during registration. To avoid boundaries associated artifact during registration, the dilated ROI was filtered by a spatial low pass resulting in a dilated and edge blurred mask.

## 2.2. Registration process

Gradient images provided by Sobel filter were estimated for each masked image of the dynamic sequence. The edge magnitude and orientation (Figure 1) were noted  $M_r$  and  $\theta_r$  for the reference image and  $M_c$  and  $\theta_c$  for any current image. Assuming that the motion of the LV was dominated by the respiratory motion, only in-plane rigid translation ( $dx$ ,  $dy$ ) were considered here. The similarity function between the reference image and any current image ( $I_c$ ) translated by ( $dx$ ,  $dy$ ) was defined by:

$$S(dx, dy) = \frac{\sum_p A_p(dx, dy) \cdot \cos(2 \cdot \alpha_p(dx, dy))}{\sum_p A_p(dx, dy)}$$

Where  $p$  is a pixel location,  $A_p$  is a local weighting coefficient and  $\alpha_p$  is the local angle difference:

$$A_p(dx, dy) = M_c(x_p + dx, y_p + dy) \cdot M_r(x_p, y_p)$$

$$\alpha_p(dx, dy) = \theta_c(x_p + dx, y_p + dy) - \theta_r(x_p, y_p)$$

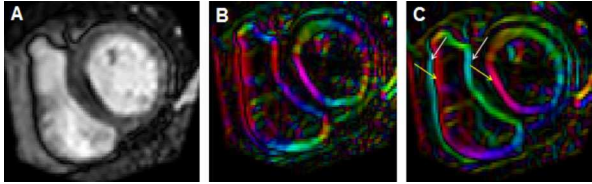


Figure 1. Gradient maps corresponding to the reference image (A); without the orientation information (B) and with the orientation information (C).

At the difference of morphological data, in which anatomical structures are characterized by a fixed gray level along time, structures in DCE-data have variable gray levels during acquisition caused by the transition of the contrast agent. Thus, inversion of contrast can occur between any structure and its neighborhood, inducing an inversion of the gradient angle between the reference and the current image  $\theta_c$  ( $\theta_c = \theta_r + \pi$ ). By multiplying  $\alpha_p$  by 2, the effect of this inversion is canceled, resulting in  $\alpha_p$  conservation ( $2 \cdot \theta_c = 2 \cdot \theta_r + 2\pi$ ). The pair ( $dx_{opt}$ ,  $dy_{opt}$ ) maximizing the similarity function indicated the optimal

in-plane translation to be applied to the current image.

## 2.3. Evaluation of registration efficiency

The registration efficiency was assessed by comparing registered dataset against original dataset using qualitative and quantitative evaluation. Qualitative evaluation was based on a visual analysis of k-means clustering maps. The k-means clustering algorithm was used to classify signal intensity curves of the pixels included in the previously defined ROIs. The clusters number was set to six to identify the following features: LV and RV cavities and myocardial enhancements, the background and two additional clusters for characterizing motion when it occurs or partial volume. k-means maps obtained before and after registration were visually reviewed by an independent operator who was asked to evaluate the effect of registration on the symmetry of the myocardial shape and on the identification of the 3 main heart structures.

For quantitative evaluation, the endocardial and the epicardial contours were manually traced on the “reference image” which, by definition, was common to both registered and none registered datasets. Then, the noise amplitude was estimated within the myocardium on both datasets. This estimation was performed pixel by pixel by using an autocorrelation-based technique [4]. The principle of this technique consists in separating noise and informative components of any signal intensity curves, in terms of magnitude. Because of the nature of DCE-data, noise was assumed to be random while the informative component was assumed to be correlated in the temporal dimension [4]. For each slice, the resulting local noise amplitude was averaged for all myocardial pixels. Averaged values of noise amplitude obtained before and after registration were used for comparisons.

## 2.4. Comparison against manual reference

For each registered dataset, the manually drawn endocardial and epicardial contours were superimposed on each image. Then, a manual motion correction based on in plane translations in both directions ( $x, y$ ) was performed to reach the optimal superimposition of the myocardial contours on each image. The  $dx_m$  and  $dy_m$  translations were expressed in pixels and millimeters and were averaged for each slice representing the automated registration error.

## 2.5. Statistical analysis

Mean values and standard deviations were provided for both noise amplitude and registration errors at rest and during pharmacological stress. Noise amplitudes estimated before and after registration were compared using a Student t-test, a  $p$ -value  $< 0.05$  was significant.

All tools, including automated registration, k-means mapping, noise amplitude assessment, manual correction were integrated in custom software developed on Matlab (Mathworks, Natick, USA).

### 3. Results

Relative and absolute evaluations of the automated registration technique were achieved. Relative evaluation consisted in comparing the original and the automatically registered datasets to qualitatively and quantitatively assess the improvement carried out by the registration. Absolute evaluation was achieved using a manual reference; it consisted in estimating the additional manual shifts required to reach the optimal correction of the respiratory motion.

#### 3.1. Qualitative evaluation

At rest, visualization of the k-means maps derived from the original dataset enabled identification of heart structures and myocardial symmetry in 14/30 slices. In these cases, symmetry and structures identification were conserved after the automated registration. On the remaining slices (16/30), registration provided an improvement in symmetry and structure identification in 16/16 slices. This improvement was substantial in 12/16 and moderate in 4/16 slices.

Figure 2 shows an example of k-means maps obtained before and after registration at rest. The clustering maps highlight the improvement in myocardial symmetry carried out by the automated registration. An example of contrast enhanced kinetics observed in the anterior wall before and after registration confirmed this improvement.

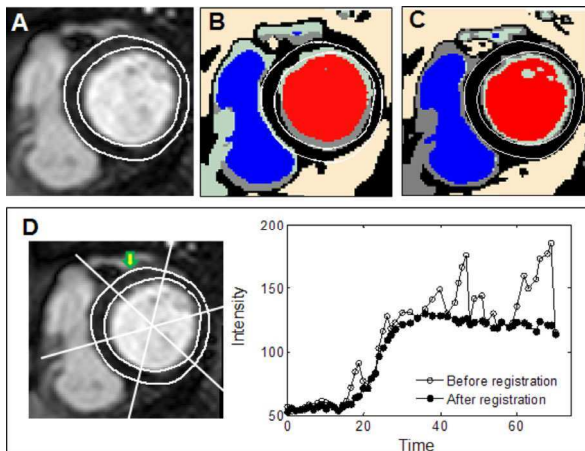


Figure 2. Original frame of a resting dataset (A), k-means maps before (B) and after (C) registration. (D) Contrast enhancement kinetics within the anterior wall before and after registration.

During stress, visualization of the k-means maps

derived from the original dataset enabled identification of heart structures and myocardial symmetry in only 3/30 slices. In these cases, symmetry and structures identification were conserved after the automated registration. On the remaining slices, registration provided an improvement in symmetry and structure identification in 27/27 slices. This improvement was substantial in 22/27 and moderate in 5/27 slices. Figure 3 shows an example of k-means clustering maps obtained before and after registration of a dynamic sequence acquired during stress. The clustering maps highlight a substantial improvement in structures (LV, RV cavities and the myocardium) identification and myocardial symmetry carried out by the automated registration. Besides, a better superimposition of the myocardial borders manually drawn on the reference image was noted on the k-means map computed from the registered dataset. An example of contrast enhanced kinetics observed in the inferior wall before and after registration confirmed this improvement.

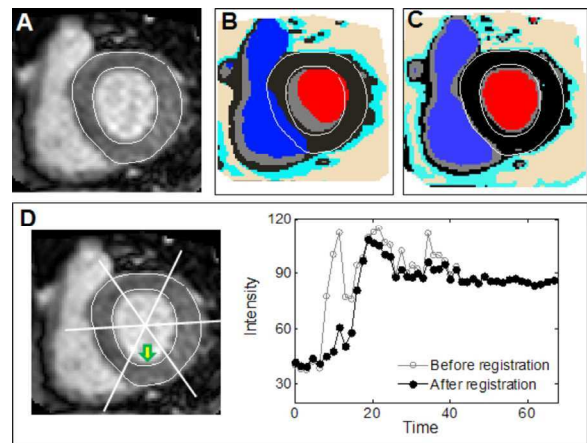


Figure 3. Original frame of a stress dataset (A), k-means maps before (B) and after (C) registration. (D) Contrast enhancement kinetics within the inferior wall before and after registration.

#### 3.2. Quantitative evaluation

At rest, noise amplitude averaged over the 30 slices was  $49 \pm 26$  before registration; it decreased to  $29 \pm 11$ . This decrease was statistically significant ( $p < 0.05$ ). During stress, it decreased significantly ( $p < 0.05$ ) from  $52 \pm 14$  to  $30 \pm 10$  with registration. Moreover, the noise reduction ratio (amplitude before registration divided by amplitude after registration) was in agreement with the independent qualitative evaluation. For both rest and stress, this ratio was higher in the slices for which the registration was judged to improve the symmetry of the heart structures on the k-means maps (Table 1).

	Noise reduction ratio	
	Rest	Stress
Qualitative improvement	2.05 ± 0.48 (n=16)	1.81 ± 0.39 (n=27)
Qualitative conservation	1.25 ± 0.26 (n=14)	1.36 ± 0.36 (n=3)

Table 1. Agreement between qualitative and quantitative evaluations.

### 3.3. Comparison against manual reference

At rest, the additional manual shifts required to reach the optimal correction of the respiratory motion were averaged over all images of the 30 datasets at rest and during stress. At rest, the total number of images was 1955 and the horizontal and vertical shift were  $dx_m = 0.05 \pm 0.09$  pixels ( $0.06 \pm 0.12$  mm) and  $dy_m = 0.03 \pm 0.06$  pixels ( $0.04 \pm 0.08$  mm). During stress, the total number of images was 1871 and the horizontal and vertical shift were  $dx_m = 0.23 \pm 0.51$  pixels ( $0.30 \pm 0.69$  mm) and  $dy_m = 0.20 \pm 0.39$  pixels ( $0.28 \pm 0.53$  mm).

## 4. Discussion and conclusions

Myocardial perfusion evaluation is crucial for the diagnosis, prognosis and management of patients with CAD. Despite the various technical developments in the area of CMR perfusion imaging, its usefulness in clinical routine remains limited because of technical issues and imaging artifacts. Among these artifacts, those induced by respiratory motion. Accordingly, developing an automated registration technique is necessary for the improvement of both visual comfort and quantitative evaluation of CMR perfusion data.

Several methods have been proposed for motion compensation [5]. Similarity function used is such techniques is affected by both noise and intensity variation caused by the contrast agent concentration. Recent technical developments allowed a substantial improvement in CMR myocardial perfusion contrast to noise ratio, increasing the usefulness of edges information based techniques against the use of intensity variation based techniques such as cross-correlation. Gradient information particularly the amplitude has been previously used for cardiac MR images registration [6]. To increase the robustness of such edge based registration, the gradient orientation was also used in the present study. Gradient orientation takes into account the shapes and the geometry of anatomical structures. However, in the case of contrast enhanced data, contrast inversion between phases results in changes in the sign of the gradient vector. One original feature of the used technique is the consideration of this vector inversion while defining our similarity function. These developments resulted in a fast technique (few seconds

for more than 60 frames) which is an important feature for clinical applications.

Also, original tools were proposed for the evaluation of registration efficiency. The k-means clustering maps provided a direct and fast visual control of the quality of motion compensation. Noise amplitude, which was accurately estimated by including the part of the noise due to motion and ignoring the correlated part of the signal related to contrast enhancement.

Finally, evaluation using myocardial borders rather than the center of mass [5] complies with the clinical requirement of myocardial perfusion evaluation. Indeed a correct quantification of segmental perfusion requires a perfect alignment of the myocardium.

At both stress and rest, noise amplitude within the myocardium was significantly reduced by the registration. In addition, only slight manual shifts were required to reach the optimal visual controlled registration. The proposed technique would prove clinical usefulness for quantitative and parametric evaluation of CMR perfusion.

## References

- [1] Schwitter J, Nanz D, Kneifel S, Bertschinger K, Buchi M, Knusel PR, Marincek B, Luscher TF, von Schulthess GK. Assessment of myocardial perfusion in coronary artery disease by magnetic resonance: a comparison with positron emission tomography and coronary angiography. *Circulation* 2001;103:2230-5
- [2] Hsu LY, Rhoads KL, Holly JE, Kellman P, Aletras AH, Arai AE. Quantitative myocardial perfusion analysis with a dual-bolus contrast-enhanced first-pass MRI technique in humans. *J Magn Reson Imaging* 2006;23:315-22
- [3] de Senneville BD, Mendichovszky IA, Roujol S, Gordon I, Moonen C, Grenier N. Improvement of MRI-functional measurement with automatic movement correction in native and transplanted kidneys. *J Magn Reson Imaging* 2008;28:970-8
- [4] Balvay D, Frouin F, Calmon G, Bessoud B, Kahn E, Siauve N, Clement O, Cuenod CA. New criteria for assessing fit quality in dynamic contrast-enhanced T1-weighted MRI for perfusion and permeability imaging. *Magn Reson Med* 2005;54:868-77
- [5] Milles J, van der Geest RJ, Jerosch-Herold M, Reiber JH, Lelieveldt BP. Fully automated motion correction in first-pass myocardial perfusion MR image sequences. *IEEE Trans Med Imaging* 2008;27:1611-21
- [6] Delzescaux T, Frouin F, De Cesare A, Philipp-Foliguet S, Zeboudj R, Janier M, Todd-Pokropek A, Herment A. Adaptive and self-evaluating registration method for myocardial perfusion assessment. *Magma* 2001;13:28-39

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