# Non-Rigid Motion Compensation in Free-Breathing Myocardial Perfusion Magnetic Resonance Imaging

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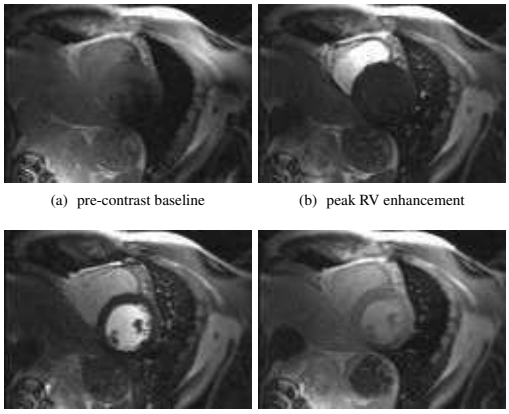
## Abstract

*Breathing movements during the image acquisition of first-pass gadolinium enhanced,* Magnetic Resonance Imaging *(MRI) hinder a direct automatic analysis of the myocardial perfusion. In addition, a qualitative readout by visual tracking is also more difficult as well. Non-rigid registration can be used to compensate for these movements in the image series. Because of the local contrast and intensity change over time, the registration method needs to be chosen carefully. We propose to make use of the periodicity of the breathing movement when patients are allowed to breath freely during image acquisition. Specifically, we propose to first identify a subset of the images that corresponds to the same phase of the breathing cycle and register these to compensate for the residual differences. By using a combination of Normalised Gradient Fields and the Sum of Squared Differences we circumvent the problems arising from the change of intensity. Then, for each of the remaining images, reference images of a similar intensity distribution are created by a linear combination of images from the align subset. In the last step, registration is achieved by minimising the Sum of Squared Differences. Our first experiments show that this approach is well suited to compensate for the breathing movements.*

## 1. Introduction

First-pass gadolinium enhanced *magnetic resonance imaging* (MRI) can be used to observe and quantify perfusion of the different regions of the myocardium. Ultimately, such observation can lead to diagnosis and staging of coronary artery disease that causes narrowing of the coronary arteries leading to reduced blood flow to the heart muscle.

A typical imaging sequence includes a pre-contrast baseline image, the full cycle of contrast agent first entering the right heart ventricle (RV), then the left ventricle (LV), and finally, the agent perfusing into the LV myocardium (Fig. 1). Acquisition protocols of first-pass gadolinium enhanced, myocardial perfusion Magnetic Resonance Imaging (MRI) are too long for the average patient to hold their breath. Therefore, breathing movements are normally present in the image series. However, for the automatic analysis of the regional myocardial perfusion, a proper alignment of the heart structures over the whole sequence is desired.



(a) pre-contrast baseline (b) peak RV enhancement

(c) peak LV enhancement (d) peak myocardial enhancement

Figure 1. Images from a first-pass gadolinium enhanced, myocardial perfusion MRI study.

### 1.1. State of the art

The challenge in achieving alignment of the contrast enhanced perfusion imaged is that the contrast and intensity of the images change locally over time, especially in the region of interest, the left ventricular myocardium. Various registration methods have been proposed to compensate the breathing movement of the heart structures in the

whole sequence [1].

Some approaches use rigid registration only: Breeuwer and Spreeuwers [2] use a translation/rotation based registration with normalised cross-correlation as a similarity measure. Milles et al. [3] proposed to identify three images (base-line, peak RV enhancement, peak LV enhancement) by using *independent component analysis* (ICA) of the intensity curve within the left and the right ventricle. These three images then form a vector base that is used to create a reference image for each time step by a weighted linear combination, hopefully exhibiting a similar intensity distribution like the according original image to be registered. Image registration of each original image to its composed reference image is then done by a rigid transformation minimising the *sum of squared differences* (SSD). However, it is not clear, how the displacements between the three base images are corrected (if at all), and how their mis-alignment might influence the overall registration. Apart from that, using rigid registration only does not account for the non-rigid deformations of the heart.

Other authors target for non-rigid registration and use *mutual information* (MI) based criteria as image similarity measures [4, 5], but the evaluation of MI is quite expensive in computational terms.

In an earlier work [6], we employed a combination of modified *Normalised Gradient Fields* (NGF) [7] and the *Sum of Squared Differences* (SDD) as registration criterion. However, by using a serial registration scheme, where only pairs of neighbouring images are registered, errors in one registration propagate and due to the change in intensity registering all images to only one reference is not reliable and depends a lot on the choice of the reference.

### 1.2. Our contribution

Currently, the patient is usually asked to hold his breath as long as possible, resulting in well aligned structures in the first part of the image sequence. However, when the patient can't hold it anymore, a strong respiratory movement occurs in the second half of the sequence which still needs to be compensated. We propose, to let the patient breath freely and to exploit the periodicity of the respiratory movement when aligning the heart structures. We first identify and align a subset of the imaging sequence that corresponds to the same movement phase, and then align the remaining images. To avoid the difficulties in registration induced by the local contrast change in the phase-aligned images, we rely on our earlier work [6] using a modified version of *Normalised Gradient Fields* (NGF) in combination with the *Sum of Squared Differences* (SSD) as registration criterion. For each of the remaining images, we create a reference image by linearly combining the two closest registered images of the phase-aligned subset. This reference image will exhibit a similar intensity distribution like its corresponding original image making it possible to employ SSD as registration criterion.

In the remainder of this paper, we shortly review the NGF+SSD based cost measure, then we discuss the identification of the phase aligned subset and their registration as well as the registration of the remaining images. Finally, we present and discuss results of experiments done on real data sets and sketched future work.

## 2. Methods

### 2.1. Similarity measures

The *sum of squared differences* is a well established similarity measure that can be used to compare images that exhibit the same intensity distribution

$$F_{\text{SSD}} := \int_{\Omega} \left(S(\mathbf{x}) - \mathbf{R}(\mathbf{x})\right)^2 d\mathbf{x}. \tag{1}$$

The use of *normalised gradient fields* (NGF) for image registration has been proposed by Haber and Modersitzki [7]. Given an image $I(\mathbf{x})$ $\mathbf{x} \in \mathbf{\Omega}$ and its noise level $\eta$, a measure $\epsilon$ for boundary "jumps" (locations with a high gradient) can be defined as

$$\epsilon := \eta \frac{\int_{\Omega} |\nabla I(\mathbf{x})| \mathbf{dx}}{\int_{\Omega} d\mathbf{x}}, \tag{2}$$

and with

$$\|\nabla I(\mathbf{x})\|_{\epsilon} := \sqrt{\sum_{\mathbf{i=1}}^{\mathbf{d}} \mathbf{x_i^2} + \boldsymbol{\epsilon}^{\mathbf{2}}}, \tag{3}$$

the NGF of an image $I$ is defined as follows:

$$\mathbf{n}_{\epsilon}(\mathbf{I}, \mathbf{x}) := \frac{\nabla \mathbf{I}(\mathbf{x})}{\|\nabla \mathbf{I}(\mathbf{x})\|_{\epsilon}}. \tag{4}$$

A NGF based similarity measure for the image registration of a test image $S$ to a reference image $R$ can be formulated based on the scalar product of the vectors of the NGF [7]:

$$F^{(\cdot)}_{\text{NGF}}(S, R) := -\frac{1}{2} \int_{\Omega} \|\mathbf{n}_{\epsilon}(\mathbf{R}, \mathbf{x}) \cdot \mathbf{n}_{\epsilon}(\mathbf{S}, \mathbf{x})\|^{\mathbf{2}} \mathbf{dx} \tag{5}$$

Eq. 5 is minimal if the gradients in $S$ are parallel to the gradients in $R$. Homogeneous areas in either of the images at one point $\mathbf{x}$ result in no contribution to the cost function. In order to improve its properties for image registration, we proposed a modification to (5) that we use in our registration approach (cf. [6]):

$$d(\mathbf{a}, \mathbf{b}) := \begin{cases} \mathbf{a} - \mathbf{b}, \text{if } \mathbf{a} \cdot \mathbf{b} > \mathbf{0}, \\ \mathbf{a} + \mathbf{b}, \text{otherwise} \end{cases} \tag{6}$$

$$F_{\mathrm{NGF}}(S,R) := \frac{1}{2}\int_{\Omega} \|\mathbf{n}_\epsilon(\mathbf{R},\mathbf{x}) \cdot \mathbf{d}(\mathbf{n}_\epsilon(\mathbf{R},\mathbf{x}),\mathbf{n}_\epsilon(\mathbf{S},\mathbf{x}))\|^2 \mathbf{dx}. \quad (7)$$

## 2.2. The registration method

Normal free breathing results in a periodic movement that we exploit in our registration approach.

In order to compensate this periodic movement, first a subset of images is identified selecting those images that correspond to the same breathing phase that are, therefore, already quite well aligned. In order to do so, a reference image $R$ from the middle of the sequence is picked, and for all images $S \in \mathbb{S}$ $F^{(\cdot)}_{\mathrm{NGF}}(S,R)$ is evaluated to obtain a similarity profile over the image sequence. Then, the images that exhibit local minima in the similarity profile are selected as the subset belonging to the same phase in the breathing cycle as the reference image.

As can be seen from Fig. 2 the image which is selected as reference strongly influences how easy it is to identify a phase aligned subset. Currently, we evaluate similarity profiles for several references, and pick one that shows clearly the periodic minima.

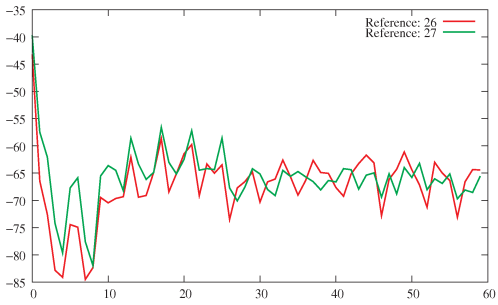


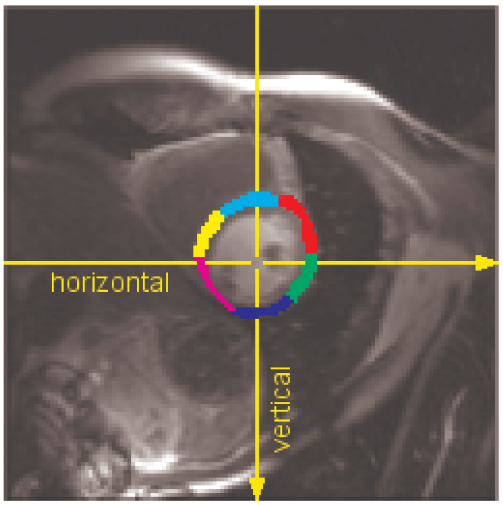

Figure 2. Similarity profiles of an unregistered image sequence. Note, for obtaining a phase-aligned subset of images a good reference image needs to be selected. Here, image 26 is a better choice as a reference.

The images of this subset are then registered non-rigidly to the reference image $R$ of the series by minimising $F_{\mathrm{NGF}} + 0.1 * F_{\mathrm{SSD}}$ . Here, $F_{\mathrm{NGF}}$ takes precedence in the image areas with strong gradients, and $F_{\mathrm{SSD}}$ maintains a registering force in areas with low gradients. The transformation model to based on B-Spline and additional smoothness is ensured by a Laplacian regularizer. As minimiser we use a Levenberg-Marquardt optimiser [8]. The registration is sped up be employing a multi-resolution scheme.

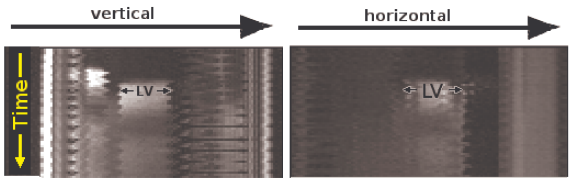
Finally, for each of the remaining images of the series an individual reference image is created by linearly combining the two closest registered images of the above, phase-aligned subset. This individual reference image will exhibit a a similar intensity distribution as the image to be registered. Hence, registration is done by minimising the sum of squared differences, and applying the same transformation and regularizer previously described.

## 3. Experiments & results

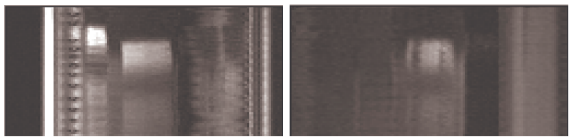
First pass contrast enhanced myocardial perfusion imaging data was acquired during free-breathing. Motion compensation was performed for four distinct slices of one patient data set covering different levels of the LV-myocardium.




(a) Reference slice with areas of interest and location of horizontal and vertical profiles.




(b) Original image series



(c) Registration result

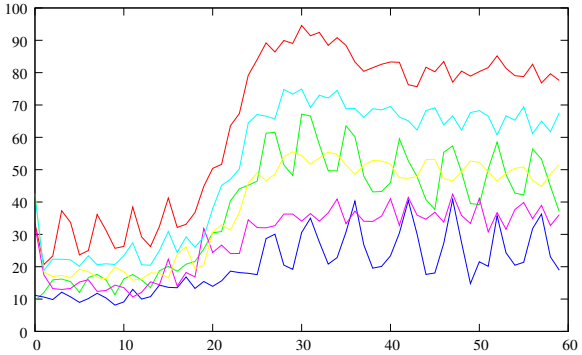
Figure 3. Reference slice and registration results.

The quality of the registration was assessed visually observing videos as well as horizontal and vertical profiles through the time-series stack. An example of the profiles and their location is given in Fig. 3.

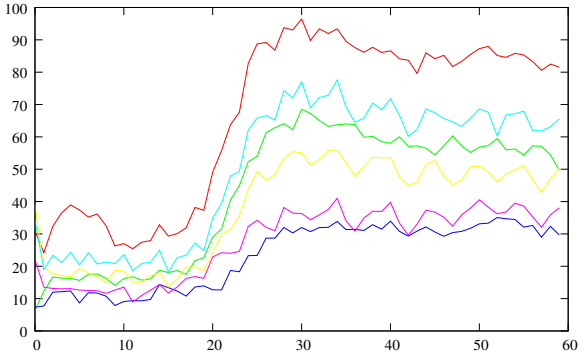
Following this scheme, a good reduction of the breathing motion was achieved for all four slices. The best registration results were actually obtained using 3 multi-

resolution levels, a B-spline knot-spacing of $16mm$ in each spacial direction, and a regularizer of weight 2.0. However, for the forth slice near the apex, we had to select a different reference image, and hence, a different pre-aligned set to compensate for the strong out-of-plane motion.

The good registration results were confirmed by observing the (average) signal intensities time courses in different regions of the myocardium. Fig. 4 show the corresponding intensity curves of the ROIs represented in Fig. 3(a). A clear improvement is observed for the blue and the green region, making a further automatic analysis of the blood flow possible and visual inspection easier.




(a) Original intensity profiles




(b) Intensity profiles after registration

Figure 4. Comparison of intensity change before and after registration in the areas of interest with the corresponding colours as given in Fig. 3 (a). The patient is suffering from chronic MI in the mid-posterior region (inferior to inferolateral).

## 4. Discussion and conclusions

The proposed registration procedure minimises the influence of the contrast-agent induced intensity change on the registration as a whole. In addition, letting the patients breath freely has some advantages over asking the patients to hold their breath: On one hand, the procedure is easier for the patient. On the other hand, normal free breathing typically results in smaller, more predictable and more readily compensated respiratory motion than breath holding in situations when the patient can no longer hold their breath and take a large gasp.

Future work include a thorough validation of the registration method and a comparison with other methods.

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