SNR enhancement of highly-accelerated real-time cardiac MRI acquisitions based on non-local means algorithm

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Real-time cardiac MRI appears as a promising technique to evaluate the mechanical function of the heart. However, ultra-fast MRI acquisitions come with an important signal-to-noise ratio (SNR) penalty, which drastically reduces the image quality. Hence, a real-time denoising approach would be desirable for SNR amelioration. In the clinical context of cardiac dysfunction assessment, long acquisitions are required and for most patients the acquisition takes place with free breathing. Hence, it is necessary to compensate respiratory motion in real-time.

In this article, a real-time and interactive method for sequential registration and denoising of real-time cardiac MRI images is presented. The method has been experimented on 60 fast MRI acquisitions in five healthy volunteers and five patients. These experiments assessed the feasibility of the method in a real-time context.

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1. Introduction

In clinical routine cardiac MR examinations, high-quality temporal series of images are obtained during breath hold acquisitions by combining information from several heart cycles. The electrocardiogram (ECG) signal is used as a reference to pool data corresponding to each level of contraction into a corresponding high-resolution image: the "segmented cine" breath hold technique (Sakuma et al., 1993). The segmented cine technique yields high quality dynamic MR series of images, which enables accurate measurements of end-systolic and end-diastolic volumes, ejection fraction, and wall thickening. Besides these quantitative measures, the direct visualisation of the heart contraction can provide the clinician with important information about myocardium motion being normal, hypokinetic, akinetic, or dyskinetic. While providing high quality images of cardiac contraction with a large number of cardiac contraction phases, the segmented cine technique is less robust in the presence of arrhythmia or unreliable ECG signals. Moreover, cardiac patients often have difficulties with holding their breath during the acquisition. Therefore, a recent proposal in cardiac function evaluation with MRI is the use of real-time imaging (Schalla et al., 2001; Hori et al., 2003; Francone et al., 2005; Nayak, 2005). With real-time imaging, an entire image is acquired at each contraction phase. Thus, the ECG synchronization is no longer necessary to pool the different segments into one reconstructed image. Real-time MR images need to be acquired during time intervals of 100 ms or less to avoid intra-scan motion and thus suffer from significantly degraded signal-to-noise ratio (SNR) and lower spatial resolution.

In this work, we propose a novel approach for SNR enhancement of real-time cardiac images based on the NL-means algorithm (Buades et al., 2005) applied to high temporal resolution non-triggered free-breathing MRI acquisitions. This method does not require a pre-recorded ECG or a self-gating (Thompson and McVeigh, 2006) procedure. Prior to the application of the denoising algorithm, the respiratory motion displacements are reduced efficiently by using a robust rigid registration algorithm. The method is used in a clinical context to qualitatively evaluate cardiac function in real-time and thus assess its clinical usefulness.

This paper is organized as follows. Section 2 describes prior works related to cardiac MRI registration and denoising. The proposed algorithm for image registration and denoising is presented in Section 3. Section 4 establishes criteria for the evaluation of the algorithm. Experiments and results are presented in Section 5. We conclude the paper with a discussion in Sections 6 and 7.

2. Related work

New technical developments and especially the advent of multi-element receive coils and associated parallel MR imaging has
made possible real-time cardiac imaging with reasonable spatial resolution. The acceleration is provided by undersampling techniques such as GRAPPA (Wintersperger et al., 2003). Image acquisition acceleration is needed to capture sufficient phases of the full cardiac contraction including the end-diastolic and end-systolic phases, while maintaining acceptable spatial resolution. In order to maintain the relative deviation of the end-systolic and end-diastolic volumes from reference measurements below 7%, it is necessary to sample up to the 8th harmonic of the contraction waveform at the Nyquist rate (Setser et al., 2000). For a heart rate of 130 bpm, this corresponds to a contraction cycle sampling frequency of 35 Hz, or to an acquisition time/image of 29 ms.

Recently, it was suggested that the TSENSE (Kellman et al., 2001) parallel imaging technique may be well-suited for real-time cardiac imaging (Guttman et al., 2003), as it provides adaptive coil sensitivity profile calculations. With a TSENSE acceleration factor of 5, images with true (non-interpolated) temporal resolution of 29 ms and sampling matrices of 64 × 64 points can be obtained. For image contrast, a balanced steady state free precession (b-SSFP) sequence is typically used, as it achieves maximum signal-to-noise ratio (SNR) and blood-myocardium contrast (Scheffler and Lehnardt, 2003). However, high TSENSE acceleration factors degrade the SNR significantly. This image quality degradation combined with respiratory motion renders the real-time visualisation of potential myocardial dyskinesia difficult for the clinician, limiting the interest of performing real-time acquisitions. Thus, sequential registration and denoising techniques are needed.

The published results addressing the problem of heart registration and SNR enhancement from real-time cardiac MRI sequences remain limited. To our knowledge, no work has addressed the problem of real-time processing of such sequences. The closest related works are (Kellman et al., 2007, 2008) in which the authors propose a method to enhance SNR from real-time cardiac sequences based on an averaging of corresponding cardiac phases after non-rigid registration with an algorithm proposed in (Ledesma-Carbayo et al., 2007). However, this is not a real-time method: the processing is done retrospectively.

In the broader field of cardiac MRI, some works address registration methods in various contexts (Mäkelä et al., 2002; Dornier et al., 2003; Stegmann et al., 2005; Smolíková-Wachowiak et al., 2005; Ledesma-Carbayo et al., 2007).

As far as image denoising is concerned, it is desirable to remove noise without blurring edges. Several noise-removing techniques have been proposed to achieve this in the context of MRI: wavelet-based (Nowak, 1999; Placidi et al., 2003; Leung and Tsotsos, 2005; Delakis et al., 2007), anisotropic filtering-based (Positano et al., 2000; Samsonov and Johnson, 2004), and NL-means-based methods (Coupé et al., 2006; Coupé et al., 2008; Manjón et al., 2008).

The idea of wavelet-based methods is to attenuate the wavelet coefficients which contain more noise than signal while avoiding the blurring of image contours. These methods are usually based on extraction of the edges from the original image using various techniques (Canny or Sobel), filtering of the image in the wavelet space and finally restoring the original edges. However, this type of filters may introduce characteristic artifacts.

Anisotropic filtering is a method widely used to suppress noise without blurring contours. This method is based on an iterative pixel averaging in the orthogonal fully-automated noise suppression direction of the gradient. A systematic quantitative comparison of multiple noise suppression filters has been conducted in (Montillo et al., 2003). The purpose was to evaluate fully-automated noise suppression methods in the context of breath-hold tagged MRI. Methods based on adaptive Wiener and anisotropic diffusion filters were compared. While the adaptive Wiener may be suitable for real-time implementation, some diffusion filters require many iterations, which may not achieve the level of real-time speed we seek in this paper.

The Non-Local means (NL-means) algorithm has been introduced by Buades (Buades et al., 2005) and is an evolution of the Yaroslavsky filter (Yaroslavsky, 1985). The principle is to use the natural redundancy present in an image to suppress noise. Its main limitation being the complexity of the algorithm, some strategies have been proposed to overcome this drawback (Coupé et al., 2006; Coupé et al., 2008; Manjón et al., 2008). Some studies suggest that NL-means outperforms other denoising methods, either in a general context (Buades et al., 2005) or specifically applied to MRI (Coupé et al., 2006; Coupé et al., 2008; Manjón et al., 2008). Moreover, this method is particularly suited for real-time applications, since the computation can be implemented in a parallel manner.

3. Methods

In this section we present our method for real-time registration and SNR enhancement of real-time cardiac sequences. The algorithm provides user interaction, therefore allowing the clinician to adjust in real-time the parameters summarized in Table 1. The different steps of the method are illustrated in Fig. 1.

In a first step, a region of interest enclosing the heart region is determined interactively and can be updated in real-time. Then the registration step enables the compensation of the respiratory motion by performing a rigid registration inside the region of interest. A denoising algorithm is then performed inside the registered region of interest.

3.1. Region of interest

An interactive step enables the definition of a rectangular region of interest (ROI) enclosing the cardiac region. The ROI center is determined by clicking on a graphical interface showing the current image and by adjusting a zoom factor in real-time. The image on which the ROI selection is performed also becomes the reference image for subsequent registration.

3.2. Correction of respiratory motion

The heart displacement caused by respiratory motion is reduced by using a rigid registration method. This method provides an estimate of the translation and rotation parameters (t_x, t_y, t_z) of the current ROI with respect to the reference image determined interactively (see preceding subsection).

In the context of real-time cardiac imaging where intra-subject registration is performed and no significant intensity change is assumed for corresponding pixels, the sum of squared errors is taken as similarity measure. For this purpose we use an efficient rigid registration algorithm described in (Thévenaz et al., 1998). This method performs a rigid registration of a test image into a reference image based on pixels intensity and a criterion defined as

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>ROI coordinates</td>
<td>Coordinates of region of interest</td>
</tr>
<tr>
<td>Reference frame</td>
<td>Frame used as reference for registration</td>
</tr>
<tr>
<td>h</td>
<td>Decay parameter</td>
</tr>
<tr>
<td>D</td>
<td>Size of the similarity window</td>
</tr>
<tr>
<td>M</td>
<td>Size of squared neighborhood V_i</td>
</tr>
<tr>
<td>T</td>
<td>Number of preceding frames used in the search space</td>
</tr>
<tr>
<td>μ</td>
<td>Pixel selection optimization parameter</td>
</tr>
<tr>
<td>σ^2</td>
<td>Pixel selection optimization parameter</td>
</tr>
</tbody>
</table>

Table 1
Algorithm parameters.
\[ e^2 = \|f_k(x) - Q_p[f_j(x)]\|^2, \]

where \( f_k(x) \) is the reference image and \( Q_p[f_j(x)] \) is the rotated and translated test image. An optimized Levenberg-Marquardt algorithm is used to minimize this criterion with respect to registration parameters (translations and rotation). Registration is performed on different scales in a multi-resolution scheme. An efficient interpolation method based on splines (Unser, 1999; Thévenaz et al., 2000) allows for sub-pixel precision.

In the context of real-time cardiac imaging, a rigid approach to registration has been preferred to a non-rigid one for several reasons. Firstly, in a clinical context, image content should not be altered, meaning that heart movement and myocardial edge information should be preserved. Secondly, due to the free-breathing acquisition, unavoidable through-plane motion may occur. Therefore, using a deformable registration algorithm may lead to the computation of an image deformation which attempts to put in correspondence different cardiac planes, which is not desirable. Finally, rigid registration can be implemented using efficient algorithms allowing fast processing.

Rigid registration implies establishing a correspondence between image pixels whose movement is induced only by the respiratory motion. Therefore, this approach requires to define a region of interest enclosing the heart and containing several pixels whose movement is only due to the respiratory motion. However, it is not a problem in practice to define such a ROI.

3.3. Sequence denoising

MRI protocols enabling fast imaging involve undersampling of the spatial frequencies of the image (k-space), which leads to spatial aliasing in the conjugate image domain. The elimination of spatial aliasing through reconstruction approaches that use the multiple reception coil element sensitivity spatial profiles is imperfect, introducing both noise and artifacts, and thus reducing the image SNR. It is well known that MRI noise follows a Rician distribution. However, when parallel imaging is used the noise is no longer Rician and varies spatially, therefore preventing assumptions on the noise statistics of real-time MRI sequences. In this context, where no estimation on the nature of noise is available, the NL-means filter, introduced by Buades (Buades et al., 2005), is well-suited.

3.3.1. The NL-means filter

The principal assumption of NL-means filter is that each local configuration or “image patch” around a pixel occurs multiple times in an image. This redundancy is used to retrieve in a noisy image the expected pixel values of the original image. This is achieved by performing a weighted averaging of a pixel with all other pixels of the image, where the weights depend on the similarity between pixels. The similarity is calculated using a distance weighted by a Gaussian kernel. Indeed, this distance preserves, in expectation, the order of similarity between pixels under the presence of additive white noise (Buades et al., 2005).

Given an image \( u: E \rightarrow \mathbb{Z} \) where \( E \) represents the image grid, the principle of NL-means is to restore each point \( x_i \in E \) with the value:

\[ NL(u)(x_i) = \sum_{x_j \in E} w(x_i, x_j) u(x_j). \]

The weight assigned to \( u(x_j) \) for the restoration of \( x_i \) is defined by:

\[ w(x_i, x_j) = \frac{1}{Z(h)} \frac{e^{-\frac{\|\mathbf{w}(x_i-x_j)\|^2}{\sigma^2}}}{\sigma}, \]

where \( \mathbf{w}(N_i) \) denotes the vector containing the intensities of \( u \) in the square neighborhood centered on \( x_i \) of size \( 2D + 1 \), \( \| \cdot \|_a^2 \) denotes the Euclidean distance weighted by a Gaussian kernel of standard deviation \( a \), \( Z(h) = \sum e^{-\frac{\|\mathbf{w}(x_i-x_j)\|^2}{\sigma^2}} \) is the normalizing factor. The parameter \( h \) controls the decay of the exponential function and therefore the decay of the weights, as a function of the Euclidean distance. The window used to compute the similarity index is generally taken as a squared neighborhood of size \( 2D + 1 \) centered on the pixel.

Despite good performances for image denoising, this method leads to a high algorithmic complexity \( O(N^2(2D + 1)^2) \), where \( N^2 \) is image size and \( (2D + 1)^2 \) is the size of the similarity window and therefore introduces a high computational burden. In order to have acceptable computation times, some simplifications and optimizations must be used.

Generally, the pixels used for weighting are chosen in a subset \( V \) of the image domain \( E \), called the search space. This subset is generally taken as a square of size \( 2M + 1 \) centered on the processed pixel \( x_i \). Reducing the size of the search space obviously improves the computation efficiency, but reduces the probability of finding similar patches, therefore diminishing the denoising quality.

An optimization based on pixel selection has been proposed in Coupé et al. (2006), Coupé et al. (2008). The idea is to reduce locally
the size of the search space by discarding pixels being too dissimilar from the current pixel: only pixels having similar statistics are selected for distance computation. Using first order moments (mean and standard-deviation) enables the computation of these values for each pixel only once prior to the filter computation. Using this optimization, the weighting can be redefined by:

\[
W(x_i, x_j) = \begin{cases} 
\frac{1}{Z(x_i)} e^{-\frac{\|x_i - x_j\|^2}{\sigma^2}} & \text{if } \mu_i, \sigma_i \leq \mu_{N_i}, \sigma_{N_i} < \frac{1}{p_1} \\
0 & \text{otherwise}
\end{cases}
\]

where \(\mu_{N_i}\) and \(\sigma_{N_i}\) denote respectively the mean and the variance of \(u(N_i)\) and the parameters \(0 \leq \mu, \sigma \leq 1\) control the number of pixel selected.

Moreover, NL-means algorithm based on this optimization seems to better preserve the detailed regions (Coupé et al., 2006; Coupé et al., 2008). Indeed, since dissimilar pixels are discarded from the distance computation, this avoids the blurring of pixels having several dissimilar pixels in their search space.

Another way of reducing computational time is the parallelization of the weights computation, since each pixel comparison is independent from the others.

### 3.3.2. Extended Non-Local means (ENL-Means) filter

We present an extension of the Non-Local means filter adapted to the context of real-time cardiac MRI, allowing to improve both denoising quality and computation efficiency.

The two main ideas of this extension rely on the use of redundancy between successive frames to optimize the search space and on a recursive scheme, consisting in reusing the filtered images to compute the weights. This way, the filter progressively enhances image SNR while preserving fine details.

Let \(s_n : E \rightarrow \mathbb{Z}\) be the \(n^{th}\) frame of an image sequence. The extended NL-means filter is defined recursively by:

\[
ENL(s_n)(x_i) = \begin{cases} 
\sum_{x_i \in V_i} w(x_i, x_j)s_0(x_j) & \text{if } n \leq 0 \\
\sum_{k=1}^{T} \sum_{x_i \in V_i} w(x_i, x_j)ENL(s_{n-k})(x_j) & \text{if } n > 0
\end{cases}
\]

where \(V_i\) represents the local neighborhood of pixel \(x_i\).

The preceding denoising frames \(ENL(s_{n-k})\) are used to restore the frame \(s_n\). The pixel selection optimization described above is used for computing the weights. The parameters related to the ENL filter are:

- \(h\): the decay parameter. This parameter should be related to the image noise standard deviation \(\sigma\). Usually, \(h\) is chosen to be equal to 3\(\sigma\) or 4\(\sigma\) (Buades et al., 2005);
- \(D\): the size of the similarity window;
- \(M\): the size of the square neighborhood \(V_i\) centered on \(x_i\);
- \(T\): the number of preceding frames used in the search space;
- \(\mu\) and \(\sigma^2\): parameters related to the pixel selection optimization.

### 4. Evaluation methodology

#### 4.1. Respiratory motion correction

The registration results were evaluated quantitatively by considering the position of the endocardial borders in end-diastolic phase. For both types of real-time free breathing acquisitions, the
endocardial borders were extracted before and after registration (before filtering step) using a semi-automatic segmentation method. This method is based on a connected thresholding, which is implemented using a component-tree structure (Najman and Couplet, 2006). Given an image $u$, the connected component of the threshold set $X_t = \{ x \in E \mid u(x) \geq t \}$ containing $p$ is retrieved (in mathematical morphology, this is equivalent to performing a geodesic reconstruction by dilation of the impulse function $p$ in the original image (Soille, 2003)).

We denote $\partial B_i$ the set of contour points of the left ventricle border extracted in end-diastole of the $i$-th cycle of the sequence. To quantify the differences between the borders, we used the Hausdorff distance which is well-suited for comparing distance between sets (Huttenlocher et al., 1993). For two compact subsets $A$ and $B$ of a metric space, the Hausdorff distance is defined as follows:

$$H(A, B) = \max(h(A, B), h(B, A)),$$

where

$$h(a, B) = \max_{a \in A} d(a, B),$$

$$h(B, A) = \min_{b \in B} d(B, a),$$

and $d$ is the Euclidian distance. $h(A, B)$ is called the directed Hausdorff distance, while $h(a, B)$ is called the “point-to-set” distance, which represents the smallest distance between a point $a \in A$ and all the points of set $B$. The Hausdorff distance being very sensitive to a single outlier (i.e. a point being far from the reference set), we also used the mean and the standard deviation of point-to-set distances. We define the mean point-to-set distance between two sets as:

$$d_{\mu}(A, B) = \frac{\sum_{a \in A} h(a, B) + \sum_{b \in B} h(B, A)}{\text{card}(A) + \text{card}(B)}$$

and the standard deviation as:

$$d_{\sigma}(A, B) = \frac{\sum_{a \in A} (h(a, B) - d_{\mu}(A, B))^2 + \sum_{b \in B} (h(B, A) - d_{\mu}(A, B))^2}{\text{card}(A) + \text{card}(B)}$$

The contour $\partial B_1$ (i.e. the first extracted border of the left-ventricular in end-diastole phase of the sequence) was chosen as reference and compared to all others. For each border $(\partial B_i \mid i > 1)$, $H(\partial B_1, \partial B_i)$, $d_{\mu}(\partial B_1, \partial B_i)$ and $d_{\sigma}(\partial B_1, \partial B_i)$ was computed before and after the registration step.

### Table 2
Parameter values used in the experiments.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>NL-means experiments</th>
<th>ENL-means experiments</th>
</tr>
</thead>
<tbody>
<tr>
<td>$h$</td>
<td>50</td>
<td>30–50</td>
</tr>
<tr>
<td>$D$</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>$M$</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>$T$</td>
<td>-</td>
<td>5</td>
</tr>
<tr>
<td>$\mu$</td>
<td>0.8</td>
<td>0.8</td>
</tr>
<tr>
<td>$\sigma$</td>
<td>0.5</td>
<td>0.5</td>
</tr>
</tbody>
</table>

![Fig. 3](image3.png)

**Fig. 3.** Evolution of a vertical line crossing the left ventricle from a MRI sequence along the time axis. This image represents a vertical line of the $n$th frame ($y$-axis) versus the frame number ($x$-axis). (a) Before registration. (b) After registration.

![Fig. 4](image4.png)

**Fig. 4.** Evaluation of registration accuracy by comparison of endocardial borders extracted from two distinct end-diastolic phases (in white and grey). Superposition of the contours before registration (a) and after registration (b). On this case, Hausdorff distance between these two contours is 8.13 mm before registration and 2.03 mm after registration. Mean point-to-set distance is $3.64 \pm 2.17$ mm before registration and $0.65 \pm 0.95$ mm after registration. Since the pixel spacing is 2.03 mm, the mean error is inferior to one pixel.

![Fig. 5](image5.png)

**Fig. 5.** Mean point-to-set distances (in millimeters) between reference left ventricle contour (obtained from first cardiac cycle) and all other cardiac cycles. The vertical bar denotes the standard deviation. (a) Averaged for 30 GRAPPA sequences. (b) Averaged for 30 TSENSE sequences.

#### 4.2. Sequence denoising

The denoising step was evaluated quantitatively by measuring the SNR enhancement in a region of interest selected in the left ventricular (LV) cavity and by assessing the edge strength of the endocardial borders.

Each measurement was performed in four different images:

1. the original image;
2. the image denoised with the NL-means algorithm;
3. the image denoised with the ENL-means algorithm;
4. the image denoised with a simple averaging filter.

4.2.1. SNR enhancement
The SNR is defined as: $\frac{\mu_{ROI}}{\sigma_{ROI}}$, where $\mu_{ROI}$ and $\sigma_{ROI}$ denote respectively the mean and the standard deviation of the intensities into the region of interest. The region of interest was delineated manually inside the homogeneous zone of the LV cavity and SNR was computed before and after processing.

4.2.2. Edge strength preservation
SNR enhancement of a homogeneous zone is not the only criterion to evaluate the performance of a denoising method. The algorithm should also preserve and potentially improve the edge strength of the endocardial borders after processing. As in Montillo et al. (2003), an evaluation of edge strength along the endocardial borders was done by taking the maximum of the gradient image along a line orthogonal to manually defined contours. The maximum of the gradient in the processed image was normalized with respect to the maximum of the gradient in the original image. This way, only the variation of edge strength relative to the original image was calculated. The mean and standard deviation of the gradient maximum along four lines orthogonal to endocardial borders were computed and used as edge strength measurement.

4.3. Clinical evaluation
A comparison of diagnostic assessment before and after processing was done, as well as a subjective evaluation of image quality. Overall image quality and artifacts for all subjects were assessed by two experts using a 4-point scale. The artifacts score measure from 0 (no artifacts) to 3, the number and the intensity of the artifacts through the image sequence. For overall image quality, the rating was based on SNR, ability to evaluate global and regional function and visibility of fine details in the image (e.g. trabeculations). The score range from 0 (non-diagnostic or barely diagnostic quality) to 3 (excellent).

Finally, in order to assess the potential influence of application of our algorithm on clinical measures (such as the partial ejection fraction), the variability encountered in the manual delineation of LV contours before and after processing was measured.

5. Experiments and results
5.1. Data
Five healthy volunteers and five patients with an acute or chronic myocardial infarct and an abnormal cardiac function underwent real-time cardiac MRI with a b-SSFP pulse sequence on a 3T MR system (Trio, Siemens Medical Solutions, Erlangen, Germany). All the patients presented a severe regional contraction deficit such as a dyskinesia or an akinnesia. Real-time sequences of 128 images were acquired without ECG gating at three short-axis slice levels (basal, mid-ventricular and apical) during free-breathing. Two parallel imaging acceleration methods were used: GRAPPA with an acceleration factor of 3, resulting in an acquisition time of 65–70 ms per image and TSENSE with an acceleration factor of 5, resulting in an acquisition time of 25–30 ms per image. GRAPPA sequences contained seven complete cardiac cycles in average, while TSENSE sequences contained three cardiac cycles, as a result of a fixed number of acquired images per real-time sequence. The pixel size of GRAPPA and TSENSE sequences was adapted to the patient chest size (between 1.56 mm and 2.34 mm), and the reconstructed matrix size was $128 \times 128$.

Our test database was hence composed of 3 GRAPPA and 3 TSENSE sequences per subject at basal, mid-ventricular and apical slice levels, giving six sequences per subject for a total of 60 sequences. Examples of images obtained with GRAPPA and TSENSE techniques are shown in Fig. 2.

For the clinical evaluation, two experts delineated manually endocardial contours in the same end-diastolic (ED) and end-systolic (ES) phases in order to quantify ED and ES cavity surfaces.

5.2. Implementation
The proposed method was implemented in C++ under the Linux operating system, embedded into a graphical user interface based...
on Qt\textsuperscript{1}. Dicom images were retrieved using the GDCM library\textsuperscript{2}. Rigid registration was performed using Thévenaz’s ANSI C routine\textsuperscript{3}. The algorithm implementation was optimized in order to enable a real-time processing. The computer used for validations was composed of a 3.2 GHz Intel Pentium IV with 2 GB of memory.

5.3. Experiments

The experiments were performed by emulating a real-time processing using the off-line sequences of pre-acquired images. Two experiments have been made on all the 60 sequences. In the first experiment, the denoising step was based on the NL-means algorithm. In the second one, the denoising step was based on the proposed ENL-means method.

The ROI coordinates and the reference image were set interactively for each sequence using the graphical interface. The ROI size was inferior to 60 × 60 pixels in all sequences. To assess the versatility of the method, all parameters were left unchanged for all the experiments, except for the parameter $h$. This parameter was set to 50 for all experiments using the NL-means algorithm. However, in some marginal cases using the ENL-means algorithm and mostly with noisy TSENSE sequences, the parameter $h$ was lowered down to 30 in order to reduce the denoising strength. In practice this is not an issue since this parameter can be set interactively and very fastly, in a real-time fashion, until a satisfactory result is obtained.

Table 2 summarizes the parameter values used within the two experiments.

5.4. Algorithm evaluation results

5.4.1. Respiratory motion correction

Fig. 3 shows the temporal evolution of the same vertical line of pixels crossing the left ventricle in each image (frame) in the temporal MRI sequence. On this representation, it can easily be observed that respiratory movement in free breathing sequences is significantly reduced. Based on this representation, the qualitative evaluation performed on all the 60 sequences suggested that the respiratory effect was corrected.

For the quantitative evaluation, an example of the comparison of endocardial borders extracted from two distinct end-diastolic phases is illustrated in Fig. 4.

The mean point-to-set distances for each cardiac cycle was averaged with respect to all 60 sequences and the result is depicted before and after registration in Fig. 5. The variation of the mean distances between endocardial borders in the original sequences follows the respiratory cycle. It can be observed that it is well-compensated by the registration algorithm in the processed sequences.

The mean point-to-set distances averaged with respect to all cardiac cycles obtained before and after registration for the 10 subjects are presented in Fig. 6. These results show that, for each modality (GRAPPA or TSENSE), the registration algorithm enables significant reduction of the mean point-to-set distance between the contours. Thus, the registration drastically reduces the left ventricular motion caused by the respiration. The improvement is larger for basal short-axis sequences, since respiratory motion is more important in these sequences.

All these results must be compared with the pixel spacing of each acquisition, which varies between 1.56 mm and 2.34 mm. Indeed the results obtained for the averaged mean point-to-set distances measurements (between 0.5 and 1 mm after registration for GRAPPA and between 0.7 and 1.7 mm after registration for TSENSE) are inferior or close to these values, showing that subpixel precision is achieved in our experiments.

5.4.2. Sequence denoising

Qualitatively, the proposed method provides noise suppression in large homogeneous regions without significant contour alterations for all 60 sequences. Fig. 7 illustrates some representative results obtained for GRAPPA and TSENSE sequences.

5.4.2.1. SNR enhancement. Fig. 8 summarizes the averaged SNR measurements obtained for each of the image types described in Section 4.

For both GRAPPA and TSENSE modalities, the SNR enhancement for ENL-means method increases with the cycle number. This progressive enhancement is due to the recursive definition of ENL-means. The SNR enhancement is greater for ENL-means than for NL-means. For comparison, the SNR enhancement observed for the mean filter is also depicted. The mean filter increases the original SNR, but is less efficient than NL-means or ENL-means.

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{fig7.png}
\caption{Example of denoising results. (a–d) GRAPPA sequences. (e–h) TSENSE sequences. Left: Before processing. Right: After processing.}
\end{figure}

\begin{table}[h]
\centering
\begin{tabular}{|c|c|}
\hline
Parameter & Value \\
\hline
\hline
\end{tabular}
\caption{Parameter values used within the two experiments.}
\end{table}
5.4.2.2. Edge strength preservation. Fig. 9 illustrates an example of edge strength measurement. On this example, it can be seen that gradient profile from ENL-means is close to the one obtained from the original image. NL-means profile is slightly under the ENL-means one. Obviously, in the mean image, the maximum of the gradient profile is significantly reduced, due to the averaging effect. Table 3 summarizes the results obtained for the edge strength evaluation. The experimental results show that the mean filter provides a significant loss in edge strength (up to 40%). On the contrary, the denoising methods based on NL-means or ENL-means tend to preserve the edge of the left ventricle.

Based on these results, there are no significant differences in terms of edge preservation between NL-means and ENL-means, even if the ratio observed for ENL-means is close to 100% of the original edge maximal gradient.

5.5. Clinical evaluation

The image quality was $1.1 \pm 1.21$ before and $1.95 \pm 0.83$ after processing. The artifacts score was $1.3 \pm 0.8$ before and $0.4 \pm 0.6$ after processing. Fig. 10 shows the distribution of these measures.

The two experts observed a subjective improvement in the denoised images to the detection of the regional contraction deficits in the patients. Enhancement of trabeculations was clearly seen on denoised images and modified the perception of the endocardial contour (see Fig. 7e and f, where the lateral wall of the processed image has a significant sharper but irregular endocardial contour compared to the raw data).

For the comparison of the variability encountered in the manual delineation of LV contours before and after processing, the Bland–Altman comparison of observer 1 versus observer 2 gave a
mean difference of −0.30 ± 1.84 cm² before processing and a mean difference of 0.47 ± 1.25 cm² after processing (see Fig. 11). Our experiments show that the bias before and after processing does not affect the measurement of the clinical relevant ejection fraction. The combined results on all the data showed that the inter-observer variability in LV cavity surface manual measurements in ED and ES was reduced on the filtered images.

Finally, Fig. 12 provides a visual comparison between a conventional segmented cine sequence, real-time TSENSE and denoised TSENSE sequence.

5.6. Computational times

In our experiments the computation time for the registration step computed in a ROI whose dimensions are 60 × 60 pixels is less than 10 milliseconds per frame. Between 5 and 20 iterations are necessary for the optimized Levenberg–Marquardt algorithm (Thévenaz et al., 1998) to converge. The denoising step, including the computation of mean and variance images used for the optimization of the proposed ENL-means algorithm, is approximately 15 ms per frame. The whole processing time is inferior to 25 ms per frame, which is inferior to the image acquisition time (AT) of the fastest TSENSE sequences (26 ms). These processing times therefore allow a real-time processing on a standard computer. The denoising step based on the original optimized NL-means algo-

<table>
<thead>
<tr>
<th>Denoising method</th>
<th>Registration</th>
<th>Denoising</th>
<th>Total</th>
<th>Minimal AT</th>
</tr>
</thead>
<tbody>
<tr>
<td>NL-means</td>
<td>5 ms</td>
<td>60 ms</td>
<td>65 ms</td>
<td>26 ms</td>
</tr>
<tr>
<td>ENL-means</td>
<td>5 ms</td>
<td>20 ms</td>
<td>25 ms</td>
<td>26 ms</td>
</tr>
</tbody>
</table>

Fig. 10. Histograms of image quality scores (a) and artifacts density (b) for original and processed GRAPPA and TSENSE sequences.

Fig. 11. Bland–Altman comparison of ED and ES surface measurements obtained manually from two different operators on TSENSE and GRAPPA acquisitions. (a) Before processing. (b) After processing.

Fig. 12. (a) Conventional cine, (b) Original real-time TSENSE, (c) Processing of (b) using ENL-means.
rithm is 60 ms, which prevents in our experiments real-time processing for the fastest TSENSE sequences.

These processing times could however be further reduced by using more powerful dedicated systems. An interesting way to reduce computation times would be to parallelize the denoising step. Table 4 summarizes the computation times obtained for a ROI of 60 × 60 pixels using the two denoising methods.

6. Discussion

The experimental results showed that the rigid registration method reduces respiratory movement in real-time free-breathing cardiac MRI temporal sequences of images. On average, the mean point-to-set distance between extracted left-ventricular borders was inferior to one pixel. These results demonstrate the robustness of the registration algorithm in the presence of noise and complex motion. The rigid registration method does not alter or deform image content, which is desirable in clinical applications, where preservation of original left ventricle contours is needed for quantitative measurements.

A refinement of the ROI was necessary in some marginal cases where registration method gave instable results due to the lack of pixels moving under the respiratory motion only. The update of the ROI could be done very quickly using the graphical interface. However in most cases, the quality of the registration and denoising results are not sensitive to the choice of the ROI.

For the denoising method, the experimental results showed that ENL-means method, based on the redundancies of successive frames, allows SNR enhancement of real-time non-triggered cardiac MR temporal sequences, while preserving left ventricle contours and reducing processing time. Compared to the optimized NL-means algorithm applied frame by frame, the ENL-means method is more efficient for SNR enhancement and achieves improved preservation of the left ventricular borders. Furthermore, the ENL-means method is 2–3 times faster than the NL-means method, allowing a real-time implementation.

From a clinical point of view, no discrepancies were found between diagnostic based on denoised real-time images and standard cine acquisition, whereas 2 diagnostic of dyskinesia were missed with unprocessed real-time images. Moreover, the method allows the reduction in inter-observer variability in the manual delineation of left-ventricular borders, therefore leading to more reproducible measurements of partial ejection fraction and a more accurate diagnostic.

7. Conclusion

In this paper we have described a real-time and interactive processing algorithm providing respiratory motion compensation and enhanced image quality. The respiratory movement is reduced using a rigid registration algorithm and the image quality is enhanced by using the redundancy of the registered images over the heartbeat cycles, by using a modified NL-means denoising algorithm. The method is interactive and the processing is performed in real-time, enabling the user to set the region of interest in which the processing is performed and to adjust parameters of the denoising algorithm. The performance of the method was evaluated qualitatively and quantitatively and the clinical usefulness was assessed. Quantitative evaluation of the respiratory motion reduction showed that a sub-pixel precision can be achieved for the registration of the left-ventricular contours. For the denoising method, the proposed ENL-means method enables significant SNR enhancement inside the left-ventricular cavity while preserving edge strength. The results demonstrate that the overall image quality was increased and that the presence of artifacts was greatly reduced after processing. Moreover, inter-observer variability in the manual surface measurements of left-ventricular cavity was reduced. Therefore, the proposed denoising method is efficient for improving image quality and thus helps qualitative clinical evaluation of dyskinetic hearts, but also provides more accurate measurements of the LV cavity cross-sectional surface area. The presented method is fast and can be implemented in real-time, thus allowing registration and SNR enhancement of real-time MR imaging of myocardial contraction during clinical examinations, without the need for ECG synchronization or breath holds.

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