A new approach for automatic motion compensation for improved estimation of perfusion quantification parameters in ultrasound imaging

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Abstract

This work presents a new approach for automatic motion compensation in the context of ultrasound contrast imaging. Image registration is obtained by performing a rigid transformation on the basis of a similarity criterion between a reference image and the images to be realigned. Mutual information was found to be the most suitable and robust similarity criterion in the presence of changes in contrast occurring during the ultrasound contrast agent wash-in and wash-out phases. A series of optimization strategies is also presented in order to maximize processing speed, such as a predictive-motion model and adaptive spatial sub-sampling, taking into account the image content. Parametric perfusion imaging computed on motion-compensated sequences shows substantial improvements, both in accuracy and in spatial resolution of the parameter estimates, compared to the results obtained on original image sequences. Examples using in-vivo sequences demonstrate the potential of this approach, which will undoubtedly play an increasing role in the future of ultrasound contrast imaging in radiological applications.

I. INTRODUCTION

In medical ultrasound imaging, the assessment of perfusion with ultrasound contrast agents (UCA) is beneficial in several diagnostic applications, covering both radiology and cardiology. A UCA is made of a suspension of micro-bubbles, which is administered intravenously to a patient, either as a bolus or as an infusion. As UCA micro-bubbles have sizes comparable to red blood cells, they cross the lung microcirculation (capillaries of at most 8 µm in diameter), and reach the arterial system and thus all organs to be examined by ultrasound imaging. The scattering cross-section is much higher for micron-size bubbles than for physiological structure with similar sizes, such as red blood cells. Moreover, micro-bubbles respond to ultrasound waves in a non-linear way [1]. Most medical ultrasound systems are now equipped with contrast-specific imaging techniques exploiting the non-linear response of micro-bubbles. SonoVue® is a UCA presently commercialized by Bracco, and consists of micro-bubbles containing sulphur hexafluoride (SF₆) gas encapsulated within a phospholipid monolayer shell [2,3,4].

One of the main limitations of current perfusion assessment techniques with UCA is that motion present in an image sequence, due to internal organ movement (breathing etc.) or to slight probe movements, causes degradation in the quality of the estimated perfusion parameters. This degradation occurs in the case of quantification within user-defined regions of interest, as well as in the case of parametric imaging where quantification is assessed on a pixel-by-pixel basis. Manual alignment of the individual images is extremely time-consuming and thus not practical.

Motion compensation has two major benefits for the assessment of perfusion. The first benefit concerns the quality of estimates of perfusion parameters, such as those that can be derived from replenishment kinetics following UCA destruction. Figure 1 shows an example of tissue re-perfusion by the UCA destruction-replenishment technique at low Mechanical Index, where the time intensity curves D(t) are the raw video intensity signals and Df(t) their corresponding best-fit signals, fitted by a mono-exponential model. In Figure 1(a), the motion results in a low frequency component (~ 0.5 Hz) in D(t). The application of motion compensation drastically reduces this low frequency component, as shown on Figure 1(b). The accuracy of curve fitting is clearly improved. The second benefit is especially clear in parametric perfusion imaging: when computed on compensated sequences, parametric imaging is substantially improved, compared to parametric imaging on uncompensated sequences, in terms of both accuracy and spatial resolution.

In this paper, a new approach for automatic motion compensation is described in the context of ultrasound contrast imaging. Section II presents the technical choices related to the motion compensation methodology. Section III discusses the validation approach and the results obtained.
with the new method, whereas Section IV discusses the pros and cons of this approach, with prospects for new avenues of research.

II. METHOD
This Section describes the methodology and comprises four parts: definition of image registration, multi-mask method, image registration setup and processing-speed improvements.

A. Definition of image registration
In the context of ultrasound imaging, automatic image registration describes a technique to compensate probe or patient movements within the imaging plane. Automatic image registration is thus the establishment of a spatial correspondence between two or more images, with the aim of improving the assessment of local blood perfusion. One image is selected in a sequence as a reference image; the other images are considered as floating images (to be realigned). The image registration aims at determining the optimal geometrical transformation of a floating image with respect to the reference. When followed by automatic registration, the analysis of an image sequence provides an improved assessment of local blood perfusion, compared to what may be achieved without registration.

B. Multiple-mask method
In the present image registration approach, multiple masks are considered. As shown on Figure 2(a), this method implies manual drawing of two regions:

- a delimitation mask, \( M_d \), to delimit the image portion to be realigned, including the total excursion of the motion; and
- a feature mask, \( M_f \), to delimit an image portion where anatomical features of the organ are well identified.

One advantage of the double-mask method is the fact that it allows improved registration accuracy, thanks to the operator’s knowledge of anatomy. Indeed, the feature mask is defined on the reference image and has to delimit a portion of image corresponding to anatomical features in the organ to be realigned.

Figure 2(b) shows a third mask, called computation mask, \( M_c \), resulting from the intersection between the transformed delimitation mask, \( T(M_d) \), and the feature mask, where \( T(\cdot) \) designates a geometrical transform operator. The computation mask delimitates a computation region where a similarity criterion between the transformed floating image and the reference image is calculated. The principle of the motion estimation is an iterative process; the computation mask changes at each iteration. The iterative process consists in minimizing the differences between two images, i.e. maximizing a similarity criterion, in order to reach the best geometrical transformation compensating the displacement of the floating image with respect to the reference image. The multi-mask method is the keystone of the algorithm, because it also controls the boundary conditions.

Figure 2: Schematic outline of the double-mask method. (a) Delimitation mask, \( M_d \), and feature mask, \( M_f \), delineations. (b) Transformed delimitation mask, \( T(M_d) \), and computation mask, \( M_c \), delineations. The computation mask is defined as the intersection between the transformed delimitation mask and the feature mask.

C. Image registration setup
Various methods of image registration exist and all of them include similar features. There are four such features: type of transformation, registration category, similarity criterion, and optimization. The best solution is found by a judicious choice of each feature and by taking into account the requirements of the imaging context. Theses technical choices are discussed below in the case of perfusion assessment in ultrasound contrast imaging.

Type of transformation
Geometric transformations may be classified into two types: rigid and non-rigid. A rigid transformation is one that changes position and orientation without changing shape or size [5]. There are three degrees of freedom for rigid transformation in a plane: two translations and one rotation. Only rigid transformations are considered here, because non-rigid transformations (involving spatial distortion) can produce meaningless results, especially when out-of-plane motion is present.

Registration categories
Two main categories of automatic registration may be distinguished [6]. The first one is based on geometric image features such as anatomical landmarks. The second one is based on pixel similarity measures. Ultrasound images are characterized by heavy speckle patterns, caused by interferences of the coherent ultrasound beam with scatterers present in tissue. It is thus extremely difficult to identify anatomical landmarks automatically. Therefore, the second approach of pixel-based similarity criterion was chosen.

Similarity criterion
The choice of a similarity criterion is one of the most important elements. Mutual information (MI) [7] was found to be the most suitable and robust similarity criterion in the presence of changes in contrast. Formally, the MI is calculated over the computation mask, \( M_c \), between the reference image, \( R \), and the transformed floating image, \( F \), can be defined as:
\[ MI(R, F) = \sum_{r \in R_{\text{ref}}} \sum_{f \in F_{\text{ref}}} p(r, f) \log \frac{p(r, f)}{p(r) p(f)} \]  

where \( p(r,f) \) is the joint histogram and \( p(r) \) and \( p(f) \) are the marginal histograms of the reference and the transformed floating image, respectively. MI can be quantitatively considered as a measure of image alignment. In other words, MI reaches its maximum value when the alignment is optimal. The higher the MI, the better the alignment.

**Optimization**

An exhaustive search to find a global maximum of the MI is usually too computationally extensive. For instance, Powell [8] or Simplex [9] methods are the most often used. Even though they are not optimal, they are faster than an exhaustive search. The steepest gradient descent optimization yielded more accurate results. In most cases, robust registration of individual images is achieved in less than five iterations, using the steepest gradient descent on MI.

**D. Processing-speed improvements**

To be practically useful in the clinical environment, computation time must be kept at a strict minimum. Ideally, the processing time for registering several hundred images should not exceed one minute. The challenge is then to optimize processing while maintaining both robustness and accuracy. In order to fulfill this objective, three types of improvements were developed:

- an adaptive spatial sub-sampling,
- a predictive motion model, and
- a fast computation of the MI.

**Adaptive spatial sub-sampling**

The adaptive spatial sub-sampling consists in reducing the volume of data to be processed. It is based on a speckle reduction filter which sub-samples the data according to its spatial frequency content. The sub-sampling rate follows the speckle grain size. The speckle grain size assessment is performed by a spatial frequency analysis on the reference image. For instance, a speckle grain size of 3x2 pixels, results in a gain in processing-speed of 6.

**Predictive motion model**

The predictive motion model allows a reduction of the total number of images to be processed for estimating the motion. For example, by skipping every second image, the gain in processing speed is a factor of two. The motion estimation is performed only on selected images, by initializing the search with a linear predictive motion model. Whereas the geometrical transformation of skipped images is interpolated.

**Fast computation of the MI**

The computation of the similarity criterion is a critical point, because it occurs for each iteration of the motion estimation algorithm. Considering a sequence of 1000 images with an average convergence of five iterations per image, the similarity criterion will be computed 5000 times. This explains the motivation for decreasing its computation time. Here, the improvement consists in accelerating the source code with the use of custom-made routines. The similarity criterion is the mutual information as defined in (1). The main custom-made routine is a tabulation of logarithm operator in 512 discrete values. The tabulated logarithm is about two times faster than its calculation in double precision floating point.

**Total gain in speed**

By cumulating processing-speed improvements described above, with a spatial sub-sampling of 4x2, a predictive motion skipping every second image and a faster computation MI, the total gain in processing speed may reach 24 (3x2x2x2).

**III. RESULTS AND DISCUSSION**

This Section shows and discusses results. It comprises three parts: parametric imaging, validation approach and results.

**A. Parametric imaging**

From the analysis of a time sequence of contrast images, perfusion parameters may be calculated, such as relative blood volume (rBV), mean transit time (mTT), perfusion index (rBV/mTT) and goodness- or quality-of-fit (QOF). The perfusion parameters are defined in a model function. A parametric image is a spatial distribution of any parameter, and may enhance perfusion information content for diagnostic purpose. The parametric image of QOF is discussed first. When QOF is too low, the related perfusion parameters cannot be considered as reliable.

Formally, the QOF parameter is a statistical value, defined in percent, which measures the difference between an experimental signal, \( D(t) \), and its corresponding fitted signal, \( D_f(t) \), according to a given model function. The QOF index is defined as:

\[ QOF = 100 \cdot \left(1 - \frac{SSR}{SST}\right), \]

where \( SSR \) is the sum of squared residuals,

\[ SSR = \sum_{i=1}^{N} \left[D(t) - D_f(t)\right]^2, \]

with \( N \) the number of samples and \( t \) the sample index, and \( SST \) is the sum of the squared differences about the mean, defined as

\[ SST = \sum_{i=1}^{N} \left[D(t) - \bar{D}_f\right]^2. \]
B. Validation approach

Defining a reliable validation is not a trivial task. Several approaches may be considered. Firstly, the motion compensation may be validated qualitatively by visual inspection. This approach lacks accuracy, and is totally subjective. Secondly, a manual validation may be considered, by placing landmarks on each image. The resulting motion estimation can then be compared with the automatic one. This approach needs a representative number of sequences for performing a validation on a statistically significant scale. Thirdly, an artificial and known motion may be added to a sequence to test its automatic registration. Unfortunately, this approach is not realistic in ultrasound imaging, because it does not reproduce the speckle-pattern changes that occur with relative movements of the beam and scattering sources in tissue.

All these approaches are thus inappropriate. Instead, a full automatic and quantitative validation is introduced, based on parametric imaging of the QOF index. The mean QOF should be improved by motion compensation, and the validation results are discussed below.

C. Results

Figures 3 and 4 depict the QOF validation on two sequences of contrast imaging at low mechanical index, using two administration modes: destruction-replenishment under UCA infusion, and a wash-in/wash-out sequences with a UCA bolus.

Figure 3 shows the benefit of motion compensation on kidney reperfusion by the destruction-replenishment technique. Panel (a) shows the reference image, where the outer and inner regions are the delimitation and feature masks, respectively. Panel (b) shows a floating image at the maximum lateral excursion with respect to the reference. Following motion estimation, the maxima are 82 pixels in horizontal translation, 9 pixels in vertical translation, and 9 degrees in rotation. Panels (c) and (d) show parametric images of QOF in the upper-left part of the cortex, for the uncompensated and compensated sequences, respectively. The mean QOF is 39% for (c) and 54% for (d). With such a large improvement in mean QOF, a significantly improved assessment of perfusion is expected.

Figure 4 shows the benefit of motion compensation on a liver perfusion sequence with a UCA bolus. Panels (a) and (b) show parametric images of QOF, where (a) and (b) are the uncompensated and compensated sequences, respectively. The mean QOF is 17% for (a) and 28% for (b). Panels (c) and (d) are parametric images of the mean transit time parameter in an area including a hyper-vascular tumour surrounded by normal parenchyma. The tumour exhibits a shorter mean transit time (<25 sec.) than normal parenchyma. Thus, the tumour is significantly more conspicuous on the compensated sequence (d) than on the uncompensated one (c).
IV. SUMMARY AND CONCLUSION

In summary, our automatic ultrasound contrast imaging registration technique performs a rigid transformation with a multi-mask method; it is based on the steepest gradient descent optimization of the MI similarity criterion. The QOF validation demonstrates the ability of automatic motion compensation to improve the accuracy of parametric images. The ultimate validation, however, would be with manual alignment. It will be subject to further studies.

Two avenues of further possible improvements may be explored. Firstly, the spatial sub-sampling applied may mask slight motions. A multiple resolution approach could be a worthwhile approach to be studied. The motion estimation at low resolution could thus be used to initialize the one to be computed in full resolution, with an improved final estimation. Secondly, further work could be the extension of automatic registration to three-dimensional ultrasound imaging. In the case of volume registration, the problem of out-of-plane motion is eliminated. However, the computational burden is heavy and a practically usable implementation shall require advanced processing-speed improvements.

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References


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