REGISTRATION OF ULTRASOUND IMAGE SEQUENCES FOR PERFUSION ANALYSIS

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ABSTRACT

This paper describes a method for registration of images in ultrasound sequences when contrast agent is administrated in blood stream. The proposed method is based on mutual information, image enhancement and automatic selection of multi-reference images. The registration process and the properties of the normalized mutual information are investigated and tested on real ultrasound contrast sequences from myocardial perfusion application.

1. INTRODUCTION

Multimodal image registration is a fundamental step in many areas of medical image processing. The main aim of this process is to transform the images taken by different imaging modalities in one spatial coordinate system. This is usually used as the first step in fusion of various types of medical images such as magnetic resonance image (MRI), computer tomography (CT), single photon emission computed tomography (SPECT), positron emission tomography (PET) and ultrasound (US) [2]. Fused images increase diagnostic possibilities of imaging systems.

Another application of some imaging systems (MRI, US) is the perfusion analysis [1]. The imaging systems are used to acquire sequence of images during contrast agent propagation through the analyzed organ or tissue. Due to the movement of patient, breathing, peristalsis or probe movement in ultrasound perfusion analysis, the registration process is required to align images in sequence. Multimodal registration methods must be used, because the presence of the contrast agent causes changes of image properties (mainly contrast and intensity). Many registration methods for various medical imaging modalities have been developed and published, but there are still many issues [14]. Especially, the registration of ultrasound images is a quite difficult task due to low signal-noise ratio, speckle pattern (frequency dependent noise) and spatial variant resolution [3]. In this paper the multimodal registration method based on mutual information (MI) measure [9] is utilized for multi-reference image registration.

2. DATA PROPERTIES

The used ultrasound image sequences were acquired using echocardiography application on ultrasound imaging system ATL Philips HDI5000 with 2.5ml bolus of SonoVue contrast agent injected into the blood stream of a healthy volunteer followed by 10ml saline flush bolus. The recording was ECG gated (end-diastolic heart phase - end of T-wave).

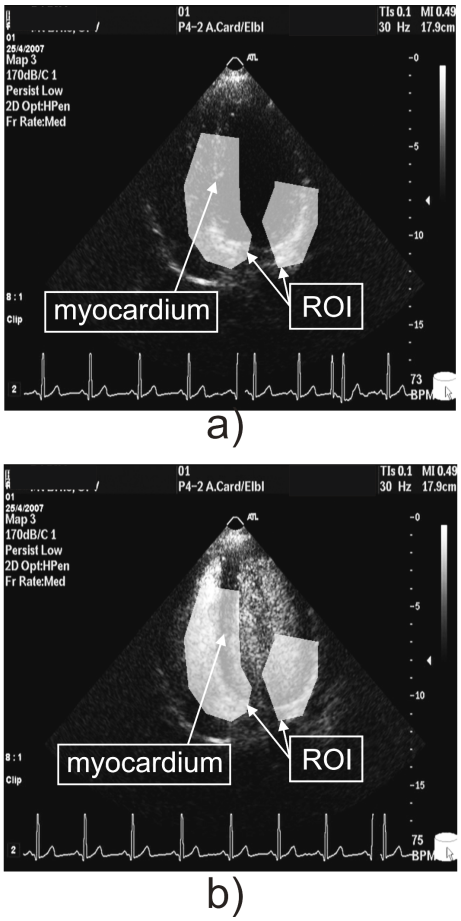


Figure 1: Image of a) pre-contrast and b) contrast phase. Myocardium and multiROI for image registration are pointed by arrows.

The tested sequence contains 78 images. The contrast of images in the sequence is varying, which corresponds to ultrasound contrast agent propagation through the heart cavities and myocardium microcirculation during the measure-

ment. The sequence can be classified to three main parts. In the first pre-contrast phase the contrast agent is not present and myocardium is brighter than cavities, see Figure 1. a). In the second contrast part, the concentration of ultrasound contrast agent is maximal and myocardium is darker than cavities, see Figure 1. b). In the third phase the contrast agent is washing out. Noise and speckle pattern is also highly changing during the sequence acquisition. Misalignments between images are marginally caused by patient breathing, heart and probe movement, assumption of no movement out of the tomographic plane.

3. REGISTRATION FRAMEWORK

3.1 Metric

Registration methods based on the MI measure are universal methods used for monomodal and mainly multimodal image registration [9]. In medical imaging MI measure is used in various applications e.g. registration of MRI and CT, SPECT/PET and MRI images. Here we adopt the registration method for registration of ultrasound sequences for perfusion analysis.

Mutual information of images A and B, $MI(A,B)$, represents the degree of dependence between these images. The definition of MI is [11]:

$$MI(A,B) = H(A) + H(B) + H(A,B), \tag{1}$$

where $H(A)$ and $H(B)$ are the Shanon entropies of the image A and B and $H(A,B)$ is the joint entropy.

Another form of definition is related to Kullback-Leibler distance, which is defined as $\sum_i p(i) \log \frac{q(i)}{r(i)}$, for two distributions q and r. The MI can be expressed as [9]:

$$MI(A,B) = \sum_{(a,b)} p(a,b) \cdot \log \frac{p(a,b)}{p(a)p(b)}, \tag{2}$$

where $p(a)$ and $p(b)$ are marginal probability density functions and $p(a,b)$ is the joint probability density function. The basic MI definition is for overlapping images, but the MI value can be also evaluated for a defined region of interest (ROI). Multiple ROIs can also be used to select various structures, see Figure 1.

The most robust and convenient definition of MI for image registration is the normalized mutual information (NMI), which suppresses the problems caused by a small overlapping area and the problem of noisy overlapping regions. The NMI is defined as [12]:

$$NMI(A,B) = \frac{H(A) + H(B)}{H(A,B)}. \tag{3}$$

3.2 Spatial transformation

Usually a flexible spatial transformation is used for registration of medical images especially for images of the heart. For perfusion analysis is crucial to register only part of organ or tissue which is analyzed. In this case the rigid transformation model is more fast and robust.

The frames in the sequence are aligned using the rigid transformation model, which is described by three parameters of transformation: vertical and horizontal translation t_x, t_y in pixels and rotation angle φ in degrees.

3.3 Preprocessing

The image preprocessing is one of the most important steps in the presented registration framework. Here, we apply two preprocessing steps. The first step is suppression of speckle pattern. The basic method for speckle suppression is based on median filtering and its modification with adaptive weights [6]. More complex methods are based for example on deconvolution [4] or geometrical filters [5]. The disadvantage of these methods is computation intensity. Therefore, the simple median filtering (window size 7×7) has been used in our application with satisfactory results [3].

The second preprocessing step is focused on edge enhancement to make our method more robust with respect to the hazy edges in images. Two edges operators are used, h_y for vertical edges and h_x for horizontal edges. The operators are created as:

$$h_y = \vec{a}' \times \{ \ -1 \quad 0 \quad 1 \ \} \tag{4}$$

$$h_x = h_y', \tag{5}$$

where $\vec{a}$ is a vector of ones with the length l. The length l roughly corresponds to the mean size of speckles. In our case, the length $l = 9$ was empirically set. *Parametric* images with enhanced edges E_x (resp. E_y) were computed as:

$$E_x = |h_x \star P| ; E_y = \left| h_y \star P \right| \tag{6}$$

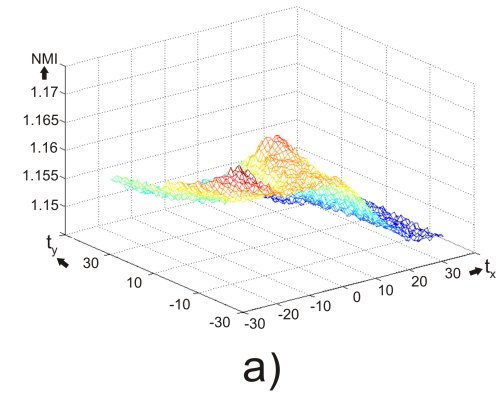
where P is the image.

If the original images have edges primarily in one direction, only one edge operator can be used. The vertical edges of myocardium are significant in ultrasound images of heart when using apical view. Hence, the edges are enhanced only in one direction using the edge operator h_y. The image E_y is normalized to the range from 0 to 255 and the final image, which is used in registration process, is computed as a summation of the original image I and the parametric image E_y in the ratio $0.7 : 0.3$ ($I : E_y$). This ratio has been set empirically.

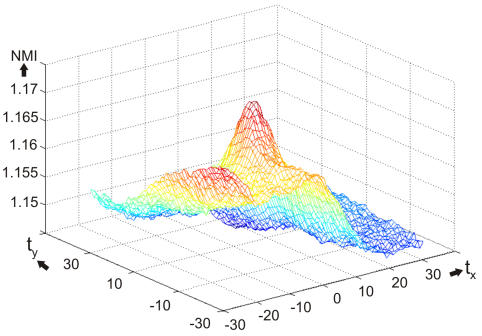
The positive influence of these preprocessing steps on the NMI values has explored. The NMI values were computed in the grid defined by boundaries $t_x \in (-30, 30)$ pixels, $t_y \in (-30, 30)$ pixels for the original pair of images and for the preprocessed pair. The step size was set to 1 pixel. The positive influence of preprocessing on the global maximum of the NMI surface can be seen in Figure 2 b). The global maximum is significantly clearer and local extremes are suppresed.

3.4 Registration strategy

Selection of the reference image in registration of the contrast sequence is one of the main problems. The first possibility is based on floating reference image: the second image is registered to first image; the third image is registered to the second image etc. The problem of this approach is the propagation of misalignment errors. The second basic possibility is to set only one reference image and other images in the sequence are registered with respect to this fixed image. The main problem of this approach is highly changing properties of the images. We propose a different method based on registration of subsequences. The original sequence is automatically divided to subsequences based on contrast values.



a)



b)

Figure 2: a) The values of NMI computed for two original images for translation from -30 pixels to 30 pixel in horizontal and vertical direction and for $\varphi = 0°$. b) The same situation for preprocessed images.

These are evaluated for each image within the ROI as [8]:

$$C_{ROI} = \sqrt{\frac{1}{M} \sum_{i,j \in ROI} (X_{i,j} - \bar{X})^2}, \tag{7}$$

where $X_{i,j}$ is the pixel intensity at position i, j in the ROI and $\bar{X}$ is the average intensity of all pixels in the ROI. The intensity values are normalized to the range $[0,1]$. The time progression of C_{ROI} in the echocardiography sequence, during ultrasound contrast agent propagation, is shown in Figure 3. The subsequences are determined as follows: the boundary image of subsequence $I.$ is the first image in order with C_{ROI} value higher than $C_I = 0.7(max(C_{ROI}) - min(C_{ROI}))$ (maximum and minimum calculated through the whole sequence). The boundary image of subsequence $II.$ is the first image in order with C_{ROI} value lower than C_I. The boundary image of subsequence $III.$ is the image in order, which has C_{ROI} value lower than the mean value of C_{ROI} computed from remaining images.

In each subsequence one image with the highest value of C_{ROI} is set as reference. The registration can be speed up by using parallel processing approach, because it leads to registration of many pairs of images (reference and moving image from appropriate subsequence). The registration of these pairs can be done in parallel threads using standard optimization approach (global optimization method based on simulated annealing [10] was finally used).

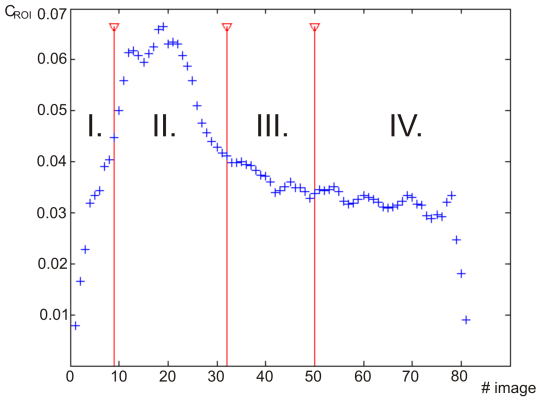


Figure 3: Progression of contrast C_{ROI} in dependence on image order in sequence. Subsequences I. - IV. are set.

In the next step the mean images from each registered subsequences are computed and these images are used for registration of subsequences together. Mean image with highest value of C_{ROI} is set as reference and another mean images are moving.

4. REGISTRATION EVALUATION

The mean image is computed from the registered sequence for evaluation purpose. It is expected that the mean image computed from the original or inaccurately registered sequence is more blurred than the mean image computed from the registered sequence. Therefore, the sharpness of these mean images can be used for registration evaluation.

The basic sharpness measure is based on the slopes of edges, which can be computed in randomly selected pixels laying on these edges. Slopes of significant edges are preferred for comparison.

A more complex evaluation method is based on edge detector [13]. To find strong and long edges, the modified Sobel horizontal and vertical operator was used [7]:

$$i_y = \begin{vmatrix} 1 & 1 & 1 & 1 & 2 & 2 & 2 & 1 & 1 & 1 & 1 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ -1 & -1 & -1 & -1 & -2 & -2 & -2 & -1 & -1 & -1 & -1 \end{vmatrix}, \tag{8}$$

$$i_x = i_y^T. \tag{9}$$

Vertical and horizontal edges can be computed using these two kernels I_x, I_y. Image of emphasized edges is computed as:

$$I = \sqrt{i_x^2 + i_y^2} \tag{10}$$

and thresholding is consequently applied:

$$I_T = \begin{cases} 1 & : \quad I > T \\ 0 & : \quad I \leq T \end{cases} \tag{11}$$

The threshold $T = 0.2$ was set empirically with respect to the image character.

This approach suppresses insignificant and short edges. The sharpness ratio SR is computed as:

$$SR = \frac{1}{n} \sum I_T \cdot 100[\%], \tag{12}$$

where n is the number of pixels of the image. The SR value represents the percentage of edges-area to image-area. Sharp and long edges therefore increases SR value. This also depends on the imaged structure, but in our case we use SR for comparison mean images of sequences obtained from the same structure - heart. To suppress the effect of the fan outline the SR was computed in area defined by mask and hence n in (12) represents area of this mask.

5. RESULTS AND CONCLUSION

Figure 4 shows the mean image computed from whole sequence. The mean image from the original (unregistered) sequence is blurred, see Figure 4 a), because of movements between images.

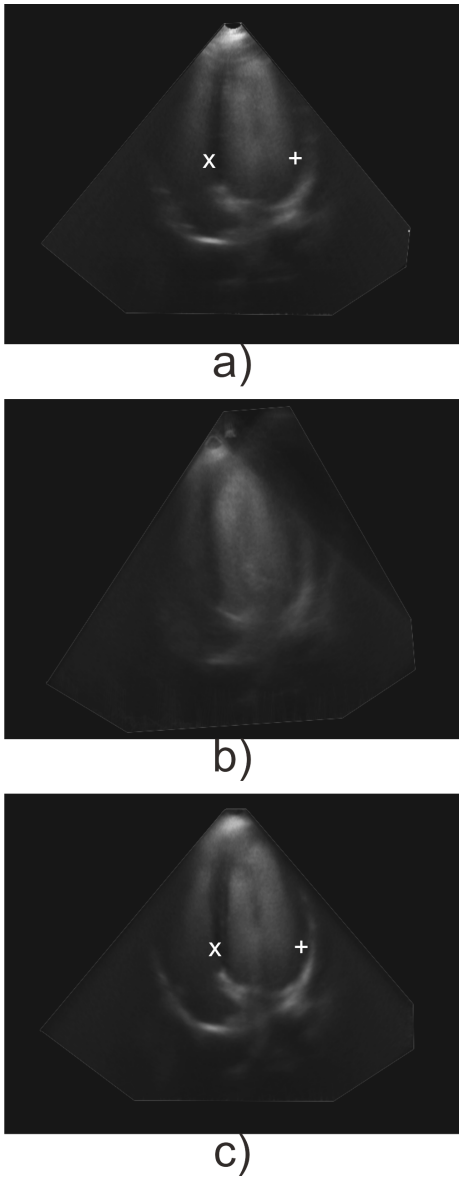


Figure 4: Mean image computed from a) original (unregistered) sequence, b) sequence registered using simple NMI method, c) sequence registered using our method.

In the mean image computed from the sequence, which was registered using the basic NMI method with one reference image from the contrast phase, Figure 4 b), significant misalignments can be observed in the sequence. Figure 4 c) shows the mean image computed from sequence, which is registered using the proposed method. The structures in this mean image are clearly visible and edges are sharper in comparison to Figure 4 a) (resp. 4 b)).

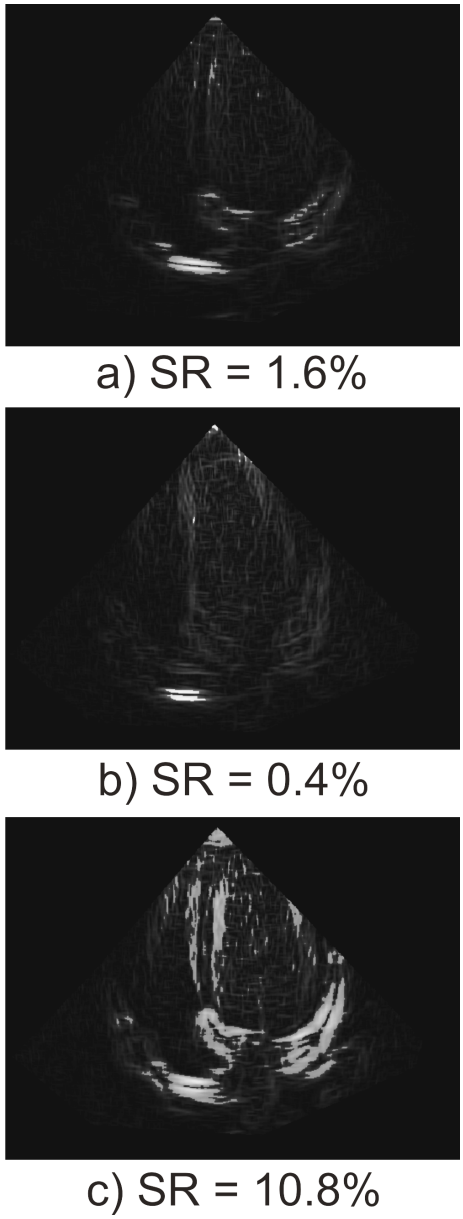


Figure 5: Significant edges marked by lighter areas in mean image computed from a) original (unregistered) sequence, b) sequence registered using simple NMI method, c) sequence registered using our method.

To evaluate objectively the registration results the slope of selected edges in the mean image was computed. In the mean images of the original (unregistered) and registered sequences the slopes of edges, marked as "X" and "+" in Figure 4 a), c), were computed. In the original mean image the slope of edge "X" is 0.92 and slope of edge "+" is 1.25. In

the registered mean image the slope of edges are higher, the slope of edge "X" is 1.64 and slope of edge "+" is 1.73. Figure 5 shows detected edges in the mean images. These edges are used for estimation of the *SR* value. It is clearly visible, that the highest value of $SR = 10.8\%$ is for the mean image computed from the sequence, which is registered by the proposed registration method, see Figure 5 c). The value of $SR = 1.6\%$ of the mean image from the original sequence, see Figure 5 a) is order of magnitude smaller. Figure 5 b) shows that the basic registration approach based on NMI and one reference image has failed. The number of edges in this mean image is significantly lower ($SR = 0.4\%$).

This paper presents the new approach of registration of ultrasound image sequences.The preprocessing and the modification of standard method based on NMI using the information about the edges showed positive influence on the shape of the metric surface in parametric space. The automatic divide to subsections minimize the influence of the reference image. The sharpness ratio as new criterion of sequence image registration evaluation is presented. Proposed approach was successfully tested on ultrasound sequence taken on healthy volunteer.

Acknowledgment

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