Ultrasonics 54 (2014) 1289–1299

Contents lists available at ScienceDirect

Ultrasonics

journal homepage: www.elsevier.com/locate/ultras

Dual-mode registration of dynamic contrast-enhanced ultrasound combining tissue and contrast sequences

Nizar Bouhlel [a,b,1], Alain Coron [a,b,*], Guillaume Barrois [a,b], Olivier Lucidarme [c], S. Lori Bridal [a,b]

[a] UPMC Univ Paris 06, UMR 7623, LIP, F-75005, Paris, France
[b] CNRS, UMR 7623, LIP, F-75006, Paris, France
[c] AP-HP, Hôpital Pitié-Salpêtrière, Service de radiologie, F-75013, Paris, France

ARTICLE INFO

Article history:
Received 3 April 2013
Received in revised form 2 December 2013
Accepted 2 January 2014
Available online 18 January 2014

Keywords:
Registration
Motion compensation
Dynamic contrast-enhanced ultrasound
Contrast image
Maximum distance

ABSTRACT

This study proposes a new method for automatic, iterative image registration in the context of dynamic contrast-enhanced ultrasound (DCE-US) imaging. By constructing a cost function of image registration using a combination of the tissue and contrast-microbubble responses, this new method, referred to as dual-mode registration, performs alignment based on both tissue and vascular structures. Data from five focal liver lesions (FLLs) were used for the evaluation. Automatic registration based on the dual-mode registration technique and tissue-mode registration obtained using the linear response image sequence alone were compared to manual alignment of the sequence by an expert. Comparison of the maximum distance between the transformations applied by the automatic registration techniques and those from expert manual registration reference showed that the dual-mode registration provided better precision than the tissue-mode registration for all cases. The reduction of maximum distance ranged from 0.25 to 9.3 mm. Dual-mode registration is also significantly better than tissue-mode registration for the five sequences with p-values lower than 0.03. The improved sequence alignment is also demonstrated visually by comparison of images from the sequences and the video playbacks of the motion-corrected sequences. This new registration technique better maintains a selected region of interest (ROI) within a fixed position of the image plane throughout the DCE-US sequence. This should reduce motion-related variability of the echo-power estimations and, thus, contribute to more robust perfusion quantification with DCE-US.

1. Introduction

Dynamic contrast-enhanced ultrasound (DCE-US) uses non-linear imaging techniques to specifically detect harmonic components from contrast microbubbles and suppress the linear response from the surrounding tissue. The echo-power level from a voxel of tissue in the contrast DCE-US images is proportional to the concentration of contrast microbubbles present in the corresponding volume of tissue. The echo-power estimated in a region of interest (ROI) of each image in an acquired sequence can be fit to mathematical models derived from indicator-dilution theory [1,2] to describe the relative blood volume and flow rate within a region of an organ or tumor. Slight motion of the hand-held probe or respiratory motions of the internal organs can cause the location of the analyzed structures within the imaged plane to move from frame to frame. In some cases, out-of-plane motion can cause well-defined structures or regions to completely disappear from the imaged plane. For these reasons, a ROI selected in a reference image from the sequence can be corrupted by neighboring tissues or reflective interfaces. Such movement-related effects can undermine the robustness of blood flow estimates from DCE-US.

It is important, therefore, to insure that echo-power is estimated from a fixed region and plane of the tissue as a function of time. To do this, three principle strategies have been investigated: breath-holding, gating and registration. Acquisition of DCE-US data for evaluation of the micro-vascularization typically lasts from 20 s to 2 min which can be too long to recommend breath-holding throughout the examination. Sequence gating has also been proposed to select a subset of image frames acquired at times when the anatomical structures of interest are well-positioned. Selection of a subset of imaging planes from a sequence can be used to extract frames which maintain the position of

* Corresponding author at: Laboratoire d'Imagerie Paramétrique UMR 7623, 15 rue de l'Ecole de Médecine, 75006 Paris, France. Tel.: +33 1 44 41 96 10; fax: +33 1 46 33 56 73.
E-mail addresses: nizar.bouhlel@u-paris10.fr (N. Bouhlel), alain.coron@upmc.fr (A. Coron), guillaume.barrois@upmc.fr (G. Barrois), olivier.lucidarme@psl.aphp.fr (O. Lucidarme), lori.bridal@upmc.fr (S.L. Bridal).
[1] Permanent address: Univ Tunis El Manar, ENIT, Laboratory U2S, 1002 Tunis, Tunisia.

http://dx.doi.org/10.1016/j.ultras.2014.01.005
0041-624X/

structures of interest. Such image-subset selection provides a useful solution if the periodicity of the motion used to select images provides adequate sampling of contrast modifications with time. This choice imposes, however, a reduction of the temporal resolution of the data. To select two subsets of images corresponding, respectively, to end of expiration and end of inspiration frames an *a posteriori* automatic gating solution for motion-elimination has been proposed by Renault et al. [3] based on Independent Component Analysis (ICA) of the contrast frames. In 2011, Zhang et al. [4] proposed a strategy to select and register a subset of the contrast-mode images of a sequence acquired using dual-mode display. The strategy took into account the duration of the respiratory cycle to limit the number of selected images and the similarity between the registered tissue images and the reference tissue image. Another solution was proposed by Mulé et al. [5] based on *a priori* knowledge of the frequency of the respiratory cycle and on Principal Component Analysis (PCA) of the tissue frames of a dual-mode sequence. Averkiou et al. [6] also advocated gating. Their solution consisted in choosing a reference image, which included a noticeable echogenic interface and then manually rejecting all the images where the echogenic interface deviates from its reference position.

A registration method was implemented on a Siemens Sequoia diagnostic ultrasound machine by Gardner et al. [7] using the Axius™ Autotracking Contrast Quantification package (Siemens Medical Solutions, Mountain View, USA), to divide the linear tissue response images into blocks. The motion for each block was then estimated between successive pairs of frames by minimizing the sum-of-absolute differences, and the motion between each frame and the reference frame was used for contrast sequence registration. A registration solution proposed by Rognin et al. [8–10] proposed use of a reference image and two masks: a feature mask and a delimitation mask on a contrast reference image. All the other images of the sequence were motion-compensated with respect to the reference image. Normalized mutual information was chosen as a robust criteria. Their approach was validated on parametric perfusion imaging, and it improved the accuracy of the parameter estimates compared to those from non-corrected image sequences. It is implemented in VueBox™ (Bracco Suisse SA, Geneva, Switzerland). Harabis et al. proposed another method [11] also based on normalised mutual information and rigid transformation. Because the information within a contrast image varies strongly during the sequence, they considered that choosing a single reference image was not adequate. Thus, an automatic multi-reference frame image registration strategy was presented.

With the exception of the two-level reference image technique presented by Harabis et al. [11], motion-compensation of DCE-US sequences has generally been performed based on tissue response image sequences. Tissue response sequences have been preferred because two, randomly-chosen tissue images acquired from the same plane share many more common features than two, randomly-chosen images from a contrast image sequence. On the tissue response sequence, prominent structures visible before contrast agent arrival are usually also visible after. On the other hand, microvascular structures under assessment with DCE-US may only be visible during certain phases of the contrast imaging sequences. These temporally-variable landmarks perturb existing techniques for image registration, and, for the few cases where contrast sequences have been considered in image registration, complex strategies have been needed to compensate for these time-dependent variations in image contrast [11].

This work presents a new, iterative and automatic image registration approach for dual-mode DCE-US that uses both the tissue and the contrast image sequences. This automatic dual-mode method is compared to registration based on the tissue image sequence alone for DCE-US sequences acquired with 5 focal liver lesions (FLLs). It is also compared with respect to manual registration of the sequences by an expert. Section 2 describes the data, the proposed registration technique and the method for comparison of the new technique relative to tissue and manual registration techniques. Quantitative results are presented in Section 3, and the comparison is completed by videos permitting visual assessment of the achieved motion-correction. Results and perspectives are discussed in the last section (Section 4).

2. Materials and methods

2.1. Image sequence acquisition

Five hepatic DCE-US sequences were acquired from patients with colorectal cancer presenting FLLs. A bolus of SonoVue® (Bracco SpA, Milan, Italy) contrast agent was injected intravenously and a contrast ultrasound sequence was acquired during 35–50 s (340–480 images). Images were acquired at a low mechanical index of 0.15 with a curved phased-array transducer 4C1-S connected to a Sequoia 512 ultrasound scanner (Acuson, Siemens Medical Solutions, Mountain View, USA). Dual-mode imaging provided a set of conventional (linear tissue responses) and cadence CPS (Cadence Contrast Pulse Sequencing) images [12,13]. The CPS is a multiple-pulse, non-linear imaging mode designed to detect additional non-linear energy from contrast agent in the fundamental frequency band. A ROI was selected by an expert to delimit the tumor region. Each acquisition can be divided into three main parts: dark CPS images during the initial pre-contrast phase before UCA arrives at the region of the imaged plane, intensely brightened CPS images during the UCA bolus passage and progressively reduced brightness with modified speckle characteristics in the CPS images during the wash-out phase.

2.2. Image registration approach

In the following, x denotes the cartesian coordinates on the image plane. Registering a moving image $I_M(x)$ with a fixed image $I_F(x)$ consists in finding the best spatial transformation $\mathcal{T}$, such that $I_M(\mathcal{T}(x))$ and $I_F(x)$ are spatially aligned [14–17].

From a mathematical point of view, it is an optimization problem in which a cost function $\mathcal{C}$ associated with a similarity measure is minimized via the transformation $\mathcal{T}$:

$$\widehat{\mathcal{T}} = \arg\min_{\mathcal{T}} \mathcal{C}(\mathcal{T}; I_F, I_M)$$

Usually the tumor is the ROI, and only the tumor and its vicinity have to be aligned prior to quantification. Thus, M_F, a fixed image mask is introduced that is equal to 1 in the tumor and its immediate surrounding area and 0 outside. With such a mask, the computation of the cost function $\mathcal{C}$ is restricted to the region where $M_F(x) = 1$ instead of the whole fixed image. A moving image mask M_M could also be associated with the moving image but has not been explicitly introduced in this study.

Registering a sequence of N images I_k with $k \in \{1, \ldots, N\}$ consists in finding the best transformations $\mathcal{T}_k$ such that each image $I_k(\mathcal{T}_k)$ is spatially aligned with all the other images of the sequence. In order to combine tissue and contrast information, we consider the ultrasound sequence as a collection of two-channel images $I_k = \left(I_k^{\mathrm{T}}, I_k^{\mathrm{C}}\right)$ with I_k^{T} and I_k^{C} the tissue-mode image and the contrast-mode image acquired at time t_k.

To automatically register the sequence, a time reference t_R and the associated image $I_R = \left(I_R^{\mathrm{T}}, I_R^{\mathrm{C}}\right)$ are chosen as well as the ROI to be aligned and its associated mask M_R. Then starting from I_R, images are iteratively registered forward that is from I_{R+1} to I_N and backward