Physica Medica 30 (2014) 898–908

Contents lists available at ScienceDirect

Physica Medica

journal homepage: http://www.physicamedica.com

Original paper

The utility of deformable image registration for small artery visualisation in contrast-enhanced whole body MR angiography

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A R T I C L E I N F O

Article history:
Received 2 May 2014
Received in revised form
30 July 2014
Accepted 9 August 2014
Available online 31 August 2014

Keywords:
Deformable image registration
Atherosclerosis
Peripheral arterial disease
Whole body MR angiography
Contrast-enhanced
Normalised mutual information

A B S T R A C T

Purpose: An investigation was carried out into the effect of three image registration techniques on the diagnostic image quality of contrast-enhanced magnetic resonance angiography (CE-MRA) images.
Methods: Whole-body CE-MRA data from the lower legs of 27 patients recruited onto a study of asymptomatic atherosclerosis were processed using three deformable image registration algorithms. The resultant diagnostic image quality was evaluated qualitatively in a clinical evaluation by four expert observers, and quantitatively by measuring contrast-to-noise ratios and volumes of blood vessels, and assessing the techniques' ability to correct for varying degrees of motion.
Results: The first registration algorithm ('AIR') introduced significant stenosis-mimicking artefacts into the blood vessels' appearance, observed both qualitatively (clinical evaluation) and quantitatively (vessel volume measurements). The two other algorithms ('Slicer' and 'SEMI'), based on the normalised mutual information (NMI) concept and designed specifically to deal with variations in signal intensity as found in contrast-enhanced image data, did not suffer from this serious issue but were rather found to significantly improve the diagnostic image quality both qualitatively and quantitatively, and demonstrated a significantly improved ability to deal with the common problem of patient motion.
Conclusions: This work highlights both the significant benefits to be gained through the use of suitable registration algorithms and the deleterious effects of an inappropriate choice of algorithm for contrast-enhanced MRI data. The maximum benefit was found in the lower legs, where the small arterial vessel diameters and propensity for leg movement during image acquisitions posed considerable problems in making accurate diagnoses from the un-registered images.

Introduction

Peripheral arterial disease (PAD) is a manifestation of cardiovascular disease in the extremities of the body with reported incidences of 11–16% in persons over 55 years old [1]. PAD has been linked to a 6-fold increase in risk for myocardial infarction [2] and an at least 2-fold rise in the risk of ischaemic stroke [3], and hence the detection of this condition is critical for at-risk patients [4]. PAD involves the build-up of plaque in the arteries (a condition called atherosclerosis), and although patients usually present with a stenosis in one area (and hence diagnostic imaging tends to focus exclusively on that symptomatic area), it is likely that the disease will be manifest asymptomatically elsewhere in the body. The entire arterial system can, however, be investigated using a whole body contrast-enhanced magnetic resonance angiography (CE-MRA) approach, with a view to determining the extent of the disease and whether any asymptomatic PAD can be revealed. Whole body CE-MRA uses a moving table technique wherein the body is sub-divided into 4 or 5 "stations" which are sequentially

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http://dx.doi.org/10.1016/j.ejmp.2014.08.001
1120-1797/

scanned by automatically moving the anatomy covered by each station into the isocentre of the magnet. Initially, pre-contrast images are acquired at each station, followed by the rapid injection of a bolus of contrast agent and a re-acquisition of all images while chasing the bolus down the body. The respective pre- and post-contrast images are subtracted to accentuate visualisation of the arterial system.

However, mis-registration artefacts can cause significant deterioration of the resultant image quality, particularly evident when trying to visualise small vessels. This can occur due to patient motion, but also due to mis-alignment of the table following its movement in and out of the magnet between image acquisitions. In the bolus-chase method, the pre-contrast images are acquired feet first and finishing at the head, so that the post-contrast imaging commences where the contrast agent arrives first (i.e. upper body regions) and is chased down the body thereafter. As such, several minutes pass between the acquisition of the pre- and post-contrast images, particularly of the lower legs, while furthermore the table has twice moved the full extent of the body between acquisitions. Leg immobilisation techniques go some way towards preventing patient movement artefacts but do not eliminate this completely, particularly for patients with advanced PAD who have difficulty remaining still.

Image registration techniques are well established for dealing with patient movement artefacts, although routine clinical MRI applications focus predominately in the brain where robust registration techniques exist for a wide range of applications such as diffusion weighted/tensor imaging [5], functional MR [6], and serial imaging [7,8]. Nevertheless, this remains an area of active research, with the continued evolution of registration algorithms tailored for specific applications even within the brain [9] or between imaging modalities (for example, MRI and PET [10]). For an overview of the literature in MRI and other imaging modalities, including areas outside of the brain, the reader is referred to a recent comprehensive review [11].

Conventionally, registration techniques work through a direct analysis of pixel signal intensities or by identifying features within the two images to be registered, and hence a common assumption is that both images have the same signal intensities in corresponding anatomical structures which are simply displaced somewhat relative to each other. The earliest generation of registration algorithms were based on this rather simplistic approach, an example of which is the Automated Image Registration (AIR) algorithm originally described by Woods et al., in 1992 [12] and still widely used today [9,13,14].

An added complexity arises, however, in studies involving the administration of contrast agents whose purpose is specifically to change the localised signal intensity, whether in tumours in the case of dynamic contrast enhanced (DCE) studies [15], or blood vessels in CE-MRA examinations, rendering inaccurate the assumption of no signal changes between common image features the images to be registered. To this end, a new generation of registration techniques have been developed for application in DCE studies specifically to deal with such image intensity changes. The first such example was reported by Reuckert et al., in 1999 in a DCE study in the breast, where both signal intensity changes due to contrast agent and non-rigid tissue deformations were successfully corrected using a novel registration algorithm based on the concept of normalised mutual information (NMI) [16]. NMI stems from the field of information theory and expresses the amount of information that one image contains about another. Simply put, NMI postulates that two images will be optimally aligned when one of the images is “definable” by the other, in other words when the (normalised) mutual information between them is maximised. Hence, the registration problem reduces to shifting pixels such that the NMI between the resulting images is maximised. This approach is thus capable of dealing with signal intensity differences, and furthermore has been shown to accurately and robustly align images from different modalities where variable signal intensities may be expected [17]. It has been used in several DCE studies to good effect, including studies in the breast [18–20], lung [21], kidney [22], liver [23] and prostate [24]. A recently reported improvement on the mutual information approach involved introducing spatial information into the registration scheme, wherein the original image is sub-divided into an array of local regions, with the MI-maximisation procedure performed separately and independently over each sub-region [25]. This method demonstrated significant improvements in performance in brain, cardiac and contrast-enhanced liver datasets.

Many registration techniques designed to deal with signal intensity changes due to contrast agent uptake suffer from a particular misregistration artefact wherein enhancing regions undergo a volume change after the registration step [26]. Efforts to minimise this effect have focussed on imposing constraints on the allowable deformation, although this was achieved at the expense of the motion-correction performance [19]. A recent study comparing three registration algorithms found that an algorithm based on sequential elastic registration best preserved tumour volume and shape in 16 tumours distributed among the lung, liver, uterus and chest wall [27].

Despite the potential to improve the diagnostic image quality of CE-MRA images using registration techniques, there are very few studies reported in the literature in this field. Hipwell et al. reported a technique for registering MRA images with those obtained with X-ray digital subtraction angiography, however the aim was to provide complementary information from both modalities and no improvement was reported in the native MRA image quality [28]. In a separate study, an improvement in image quality was reported in CE-MRA images in the lower legs following registration using the AIR algorithm, with non-linear (deformable) registration found to perform slightly better than more simple linear approaches [29]. It should be noted that this algorithm was not intended to be used to register images with differing signal intensity values (as occurs, for example, when one of the images was acquired with a contrast agent in the vessels). To date, no applications of image registration algorithms designed specifically to deal with signal intensity changes in contrast-enhanced studies have been reported in CE-MRA.

The aim of the current study was to perform a critical evaluation of the performance of two NMI-based deformable registration algorithms for CE-MRA data in comparison to that of the AIR algorithm used in the previous study [29]. It was hypothesised that the AIR algorithm may not be suitable for this specific application, and that superior performance would be achieved with NMI-based algorithms, in particular with a novel NMI algorithm designed to incorporate spatial information into the registration scheme. Changes in image quality following application of each registration algorithm were evaluated qualitatively and quantitatively via a clinical evaluation of the diagnostic image quality and measurements of the contrast-to-noise ratio respectively. To check for inadvertent volume changes in enhancing regions, blood vessel volumes were also compared over identical sections in images generated using each algorithm.

Materials and methods

Data acquisition

A protocol was devised to acquire very high spatial and temporal resolution CE-MRA data of the first pass of a single bolus of