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An automated image-processing strategy to analyze dynamic arterial spin labeling perfusion studies. Application to human skeletal muscle under stress

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Abstract

Arterial spin labeling (ASL) perfusion measurements allow the follow-up of muscle perfusion with high temporal resolution during a stress test. Automated image processing is proposed to estimate perfusion maps from ASL images. It is based on two successive analyses: at first, automated rejection of the image pairs between which a large displacement is detected is performed, followed by factor analysis of the dynamic data and cluster analysis to classify pixels with large signal variation characteristic of vessels. Then, after masking these "vascular" pixels, factor analysis and cluster analysis are further applied to separate the different muscles between low or high perfusion increase, yielding a functional map of the leg. Data from 10 subjects (five normal volunteers and five elite sportsmen) had been analyzed. Resulting time perfusion curves from a region of interest (ROI) in active muscles show a good accordance whether extracted with automated processing or with manual processing. This method of functional segmentation allows automated suppression of vessels and fast visualization of muscles with high, medium or low perfusion, without any a priori knowledge.

Keywords: Image processing; Perfusion; Arterial spin labeling; Skeletal muscle

1. Introduction

The adaptation of perfusion is a key factor for adequate supply of O_2 and substrates to organs. The quantification of perfusion, if performed with adequate temporal and spatial resolutions, is a challenge for studies of high metabolism organs such as the brain, heart, kidney and muscle. NMR arterial spin labeling (ASL) techniques [1,2] give access to absolute perfusion quantification with high temporal resolution. Arterial spin labeling techniques are increasingly applied to quantify brain perfusion [3–6] and are now being developed to quantify myocardium perfusion [7–10]. Arterial spin labeling techniques applied early to exercised human muscle [11] have been progressively refined [12–14] to perform faster perfusion quantification, without contamination by the variations of water content and oxygenation induced by intense exercise in skeletal muscle [15]. Recently, ASL perfusion maps have been applied to the comparison of elite sportsmen under specific training [16].

Arterial spin labeling perfusion maps are obtained from the subtraction of images acquired consecutively with and without preliminary tagging of the arterial water which then flows through the tissue capillaries and exchanges magnetization with tissue water. This can be done by performing alternately either nonselective slab inversion enclosing the slice under study and its arterial feeding (before acquisition of a tagged image) or selective inversion of the imaged slice itself (before acquisition of an untagged image), which is the basis of the FAIR method [17].

Several factors limit the accuracy of perfusion measurements performed with ASL.

First, a high signal-to-noise ratio is needed for native tagged and untagged images since for value of perfusion

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around 50 ml 100 ml^{-1} min^{-1}, the fractional contribution of perfusion to the NMR signal is about 1.5%, so that the signal-to-noise ratio of perfusion maps is intrinsically low. In the muscle, the short value of water T2 is unfavorable.

The second factor is the contamination of tissue signal by macroscopic vessel signal. On untagged images, blood vessels contain fresh magnetization entering the slice and are clearly visible on subtraction image. Vascular artifacts extending out of vessels are created when using fast imaging technique with low number of phase encoding steps. As illustrated further, systematic overestimation of perfusion may be induced by small- or middle-size vessels, or by artifacts propagated out of larger vessels. Several authors have proposed and tested strategies that decrease the undesirable contribution of blood magnetization in vessels to perfusion measurement, relying upon the destruction of vessel blood signal by magnetic field gradient pulses [18,19], with the penalty of increased echo time. Gradient pulses that dephase flowing blood signal shortly before image acquisition are thought to interfere weakly with the exchange between capillary and tissue water magnetization, while decreasing strongly intravascular signal. Recently, Norris and Schwarzbauer [20] and Wong et al. [21] have proposed to measure perfusion by a velocity selective ASL technique which partly obviates the influence of displacement of the imaged slice. However, application in our case would be impeded by the large range of variation of blood arterial velocity during a stress test.

The third factor is motion during or between image acquisition. The registration of successive images based upon correction of in-plane displacements may then be useful. However, if strong out-of-plane motion occurs between two paired images, no such correction is possible since the selectively inverted slice and the image slice are no more congruent.

The fourth factor is the contamination of perfusion measurements by oxygenation variations in muscle after an ischemic stress test. This contamination, which occurs when oxygenation variations modify the tagged and untagged images by a different factor, is here minimized by the short interval between acquisitions.

Automated image processing has the potential to detect zones with high perfusion independently of the operator. Efficient handling of motion artifacts (through image rejection) and of vascular artifacts (through image processing) may improve the accuracy of perfusion measurement.

In this paper, we propose a strategy for functional segmentation and automated treatment of perfusion maps, based upon three steps of data processing: (1) the rejection of the image pairs for which the amplitude of the displacement reaches several pixels; (2) the factor analysis of a temporal sequence of images, (3) the *K*-means clustering of the resulting factor images. This strategy is tested upon muscle perfusion maps. We illustrate this methodology by applying it to the quantification of leg muscle perfusion variations induced by a stress test consisting of ischemic exercise. Examinations of five normal volunteers and five elite sportsmen were processed, in order to perform a test upon two different classes of subjects who have different perfusion responses. We show the potentialities and limitations of this processing strategy, which is compared to the manual strategy previously used for extraction of perfusion values in active muscles [13].

2. Material and methods

2.1. Experimental protocol

2.1.1. NMR Protocol

Measurements of perfusion in leg muscles were performed at 4 T, in a 17-cm-diameter TEM coil, using a dedicated sequence of ASL termed SATIR, combined with single-shot half-Fourier fast spin echo for image acquisition. This technique, derived from FAIR, has been fully described by Raynaud et al. [13] who validated it against venous occlusion plethysmography on 21 volunteers. Untagged and tagged images, acquired respectively after selective and nonselective inversion of arterial water, were obtained in 170 ms every 1.5 s, so that effective temporal resolution of perfusion maps was 3 s. Spatial resolution was 1.7×2 mm^2, imaging slice thickness and selectively inverted slice thickness were 6 and 18 mm, respectively.

2.1.2. Exercise protocol

The leg exercise consisted of plantar foot flexions performed by the gastrocnemii and soleus muscles. The exercise protocol, monitored by using a pneumatic ergometer [22], was done under ischemia induced by inflation of a pneumatic cuff at 250 mm Hg, during 120–200 s up to exhaustion [16]. Measurements began at the immediate end of exercise, and cuff pressure was released 28 s later. The increase of perfusion induced by leg muscle ischemic exercise was followed during 15 min, and 600 images were acquired.

The data obtained with this protocol on five healthy nonsportive volunteers aged 27 ± 4 (three males, two females) and five elite sportsmen aged 32 ± 5 (five males) trained for endurance [16], respectively termed as control and trained subjects, were analysed. All subjects worked until exhaustion. The elite sportsmen had higher production of work at the end of exercise, and they are known to exhibit higher perfusion variations.

2.2. Automated image processing strategy

2.2.1. Hypotheses for image processing

The computation was performed on a pixel-by-pixel basis to extract the different time courses of perfusion. The approach was based on the following hypotheses.

(1) Each pixel represents the same volume of interest during the length of acquisition. To fulfill this condition, the images where there is a significant displacement must be rejected.