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FULL PAPER

Quantitative pixelwise myocardial perfusion maps from first-pass perfusion MRI

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Objective: To calculate and evaluate absolute quantitative myocardial perfusion maps from rest first-pass perfusion MRI.

Methods: 10 patients after revascularization of myocardial infarction underwent cardiac rest first-pass perfusion MRI. Additionally, perfusion examinations were performed in 12 healthy volunteers. Quantitative myocardial perfusion maps were calculated by using a deconvolution technique, and results were compared with the findings of a sector-based quantification.

Results: Maps were typically calculated within 3 min per slice. For the volunteers, myocardial blood flow values of the maps were $0.51 \pm 0.16 \text{ ml g}^{-1}$ per minute, whereas sector-based evaluation delivered $0.52 \pm 0.15 \text{ ml g}^{-1}$ per minute. A *t*-test revealed no statistical difference

between the two sets of values. For the patients, all perfusion defects visually detected in the dynamic perfusion series could be correctly reproduced in the maps.

Conclusion: Calculation of quantitative perfusion maps from myocardial perfusion MRI examinations is feasible. The absolute quantitative maps provide additional information on the transmural extent of perfusion defects compared with the visual evaluation of the perfusion series and offer a convenient way to present perfusion MRI findings.

Advances in knowledge: Voxelwise analysis of myocardial perfusion helps clinicians to assess the degree of tissue damage, and the resulting maps are a good tool to present findings to patients.

MRI is widely used for the evaluation of myocardial perfusion. Advantages of perfusion MRI are a higher spatial resolution compared with positron emission tomography (PET)^{1,2} and single photon emission CT³ and the lack of exposure to radiation. Great efforts have been made to use MRI for quantitative evaluation of myocardial perfusion in the past years.^{4,5} In clinical routine, however, evaluation of MRI perfusion examinations is performed by the visual analysis of the acquired images depicting areas remaining hypo-intense during the passage of the contrast agent bolus. One main reason for not quantifying myocardial perfusion is the sometimes-excessive user interaction time required for manual segmentation of the acquired images in the quantification process.

If myocardial perfusion is quantified, in most studies, the high spatial resolution of the acquired MR images is not maintained. Instead, a sector-based evaluation is performed.^{6,7} First attempts have been made to calculate myocardial perfusion maps to evaluate regional myocardial perfusion.^{3,8–10} However, until now, these studies were

performed in animals^{8–10} or perfusion was only evaluated semiquantitatively.³ Recently, our group has published an automatic post-processing tool for quantitative perfusion evaluation.¹¹ That study focused on the automation of post-processing but confined itself on sectors of the myocardium. The next and consequent step is to evolve this technique to work on a pixel-by-pixel basis. Therefore, it was the goal of this study to develop and test a method that calculates pixelwise quantitative perfusion maps from myocardial perfusion MRI examinations. These maps might help the clinician in making a diagnosis by decreasing the number of images to be examined, because a pixelwise quantitative perfusion map demonstrates the information of a whole series of images obtained in a first-pass perfusion examination clearly arranged.

METHODS AND MATERIALS

The study was approved by the local ethics committee, and written informed consent was obtained from every participant.

Rest first-pass perfusion MRI

All examinations were performed in supine position on a 1.5-T scanner [Symphony Quantum (8 channels); Siemens Healthcare AG, Erlangen, Germany] using a steady-state free precession saturation-recovery true fast imaging with steady state precession (true-FISP) sequence with the following parameters: repetition time = 2.6 ms; echo time = 1.1 ms; inversion time = 110 ms; flip angle = 50°; three-fourths Fourier acquisition, number of phase encoding lines = 60; field of view = 340 mm with reduction to three-fourths (*i.e.* 255 mm) in the phase encoding direction; in-plane resolution 1.8×1.8 mm; and slice thickness = 8 mm. Using electrocardiogram (ECG)-gating and short-axis double-oblique angulation, 40 images of three slices of the left ventricular myocardium were acquired in 40 consecutive heart beats. Subjects were told to hold their breath from the beginning of the measurement for as long as possible and to breathe shallowly afterwards.

To allow for quantification and to improve the signal-to-noise ratio in the myocardium, a pre-bolus technique was used with 1/4 ml gadolinium-based contrast agent.^{12,13} To obtain a non-saturated arterial input function, a bolus of 1 ml was injected followed by a flush of 20 ml saline to prevent bolus dispersion. After a short break of approximately 1 min, a second bolus of 4 ml contrast agent was administered, again followed by a flush of 20 ml saline, to achieve a sufficient signal-to-noise ratio in the myocardium.

In this study, first-pass perfusion data of 10 patients examined within 7 days after revascularization of myocardial infarction were evaluated. For comparison, perfusion examinations of 12 healthy volunteers were performed.

Data post-processing

Post-processing was performed on a standard personal computer (PC) (OS, SUSE LINUX 10.1, SUSE LINUX Products GmbH, Nürnberg, Germany; CPU, 1.7 GHz; and working memory, 2.0 GB) using bespoke in-house written software implemented in interactive data language (Exelis Visual Information Solutions, Gilching, Germany). Possible motion of the heart caused by breathing or cardiac motion was corrected by using a modified implementation¹¹ of Adluru's registration algorithm.¹⁴ This algorithm circumvents the problem of variable contrast over time by calculating a model image for each single time frame and afterwards registering the original images to the

corresponding models by rigid transformation, that is, the original images were shifted in the x and y directions to minimize the χ^2 error between the model images and the original images. As a result, the heart is found in the same position on every image of the perfusion series, which is crucial for a stable map calculation.

After motion correction, a region of interest (ROI) centred at the left ventricular blood pool and comprising the complete left ventricular myocardium and at least a part of the right ventricular blood pool was selected manually. This reduced the number of signal intensity (SI) time courses to be evaluated.

A correction of the SI time courses for partial volume errors¹⁵ was performed to correct for spillover from the blood pools. This spillover might arise from not perfectly corrected motion, from the limited spatial resolution resulting in voxels containing both blood and myocardium or from slices not perpendicular to the myocardium. Therefore, the user had to choose a pixel in the right ventricular blood pool. The left ventricular blood pool was obtained automatically as the centre of the ROIs. A baseline correction¹² converted the SI time courses to courses of relative SI change.

The corrected courses were deconvolved with the arterial input function from the left ventricular blood pool to obtain absolute perfusion values¹² for every pixel inside the ROI. The values were exported as standard digital imaging and communications in medicine (DICOM) files and presented as colour-coded perfusion maps. The maps also contained a colour bar for direct interrogation of the perfusion value in every pixel. For comparison purposes, myocardial perfusion was additionally quantified in eight equiangular sectors of the myocardial ring as proposed previously.¹⁶ This small difference to the American Heart Association (AHA) model might provide a slightly more accurate analysis of the myocardium and was already implemented in the in-house written software.

Data analysis

To evaluate the calculated perfusion maps, first, a visual inspection was carried out comparing the maps to the perfusion series. Additionally, the quantitative maps were compared with the sector-based quantitative evaluation. Histograms were calculated to visualize the distribution of the blood flow values both for sector-based and pixelwise evaluations. Since the

Figure 1. Map (right) and corresponding mid-chamber short-axis image of the perfusion series (left) of a healthy volunteer.

Figure 2. Cumulative frequency curves of the myocardial perfusion values in the healthy volunteers obtained with the maps (dashed line) and with sector-based evaluation (solid line).

number of values differs between sector-based ($n = 288$) and pixelwise ($n = 33,107$) evaluations, relative cumulative frequency curves have been calculated for the values obtained from the healthy volunteers.

Finally, a standard t -test was applied to check for differences between the two sets of values.

Data of the patients were evaluated by visual comparison of the dynamic perfusion series and the calculated maps with respect to general visibility and the degree of transmural perfusion defects. Therefore, perfusion defects were categorized to affect either $\leq 50\%$ or $> 50\%$ of the myocardial wall.

A physician (12 years of cardiac MRI experience) was asked to investigate the presence of perfusion defects in the dynamic perfusion series, while a natural scientist (7 years of cardiac MRI experience) checked the pixelwise perfusion maps for perfusion defects. Both observers were asked to categorize perfusion defects having a degree of transmural perfusion of $\leq 50\%$ or $> 50\%$.

RESULTS

Quantitative perfusion maps were successfully calculated for all 66 acquired slices, *i.e.* 30 slices from patient studies and 36 slices

from volunteer studies. The typical calculation time for one map was 3 min on a standard PC.

The maps of the healthy volunteers showed good homogeneity throughout the myocardium. Values comparable to previous MR perfusion studies^{16–19} could be calculated. Figure 1 shows the perfusion map of one healthy volunteer. The corresponding image from the perfusion series is presented in the left column. Mean perfusion value in the myocardium of the map presented in Figure 1 was $0.65 \pm 0.19 \text{ ml g}^{-1}$ per minute.

Mean perfusion values of the myocardium in all maps of the volunteers were $0.51 \pm 0.16 \text{ ml g}^{-1}$ per minute, whereas, for the sector-based evaluation, values of $0.52 \pm 0.14 \text{ ml g}^{-1}$ per minute were obtained.

The cumulative frequency analysis of the perfusion data of the 12 volunteers for sector-based evaluation and for the quantitative maps is presented in Figure 2. Although the spatial resolution was tremendously increased in the pixel-based maps compared with that of the sector-based evaluation, the curves showed a similar distribution of the perfusion values in both methods. A t -test did not show a difference between the two value sets ($p = 0.3$).

By visual inspection of the dynamic perfusion series of the patients, 28 perfusion defects could be recognized by the experienced physician. The natural scientist recognized these 28 defects in the pixelwise perfusion maps. An agreement of 100% concerning the degree of transmural perfusion could be achieved. The quantitative map in Figure 3 (right) pictures a transmural perfusion defect of an infarcted patient after successful revascularization of right coronary artery (RCA) occlusion. While healthy tissue shows normal perfusion, the area in the posterolateral wall shows decreased myocardial blood flow values in the map also called no-reflow zone. This corresponds well to the hypo-intense area of the perfusion series (middle).

A second patient is presented in Figure 4. The calculated map (right) depicts a subendocardial, non-transmural perfusion defect in the posterior wall after revascularized non-ST-elevated myocardial infarction (NSTEMI) myocardial infarction. The correspondence to the image (left) of the perfusion series confirms the correctness of the map and reveals the potential of the

Figure 3. Calculated perfusion map (right), one image of the corresponding time series (middle) and the complete series (left) of a patient showing a transmural perfusion defect in the posterolateral wall. Arrows indicate the perfusion defect.

Figure 4. Calculated perfusion map (right), sector-based evaluation (middle) and corresponding perfusion image (left) of a patient showing a subendocardial perfusion defect in the posterior wall. Arrows indicate the perfusion defect.

quantitative perfusion maps. Sector-based evaluation (middle) only shows a decreased perfusion in the effected sectors, while the map depicts the correct extension of the perfusion defect and, in this case, states that there is still healthy tissue.

DISCUSSION

The presented work demonstrates the calculation of quantitative perfusion maps from MR first-pass perfusion examinations with good quality with a reasonable time and effort. The fact that only little user interaction is necessary for the calculation renders the technique almost completely user independent and may provide additional information during the diagnostic process in a clinical setting.

The maps contained absolute perfusion values close to those obtained with sector-based evaluation. The sharp transitions between the blood pools and the myocardium indicate that the correction for partial volume errors performed as expected: the typical spillover from the ventricles was corrected successfully. The calculated quantitative maps showed the same perfusion defects as the visual evaluation of the perfusion series by an experienced observer.

Quantitative maps make use of the high spatial resolution of the acquired MR image in contrast to a sector-based evaluation. As a consequence, the transmural extent of myocardial perfusion defects can be evaluated in more detail by use of pixelwise perfusion maps. The typical calculation time of 3 min per map and the possibility of exporting the maps as standard DICOM files provide the opportunity to integrate the maps in the clinical diagnostic process and to use them as a demonstration tool of diagnostic findings.

Figure 3 underlines the great advantage of pixelwise perfusion maps: the map (right) contains the same information as the whole time series (left). Thus, the number of images to be read by the physician can be greatly reduced.

A previous study by Panting *et al*³ also investigated myocardial perfusion in humans pixel by pixel. In contrast to the presented study, maps were calculated semiquantitatively for parameters like time to peak, peak intensity and upslope of the SI time courses. However, an absolute quantification of the myocardial perfusion has not been performed yet.

Other studies performed an absolute quantification on perfusion data in animals, *i.e.* pigs⁹ or dogs.⁸ While Goldstein *et al*⁸ could control breathing motion of the examined dogs from the operators side, this kind of motion did not interfere with data analysis. In addition, only healthy dogs were examined, and the performance regarding the detection of subendocardial and transmural perfusion defects could not be investigated. In contrast to Neyran *et al*⁹ where rather artificial study conditions (non-beating isolated pig heart) were used, this presented study uses data from a typical clinical setup.

For a future study, it will be interesting to compare delayed gadolinium enhancement to the quantitative pixelwise myocardial perfusion maps in patients with different diseases. However, this was beyond the scope of this work.

One limitation of this work is the determination of the accuracy of the calculated maps. Gold standard for the size of the perfusion defects of the patients were the acquired images. An evaluation with microspheres, as performed by Goldstein *et al*,⁸ is not possible in a human study. In the presented patients, PET examinations had not been performed. However, the applied technique for sector-based absolute quantification of myocardial blood flow from MRI data has already been validated in several studies.^{2,16,17,20}

Nonetheless, future work needs to be done to further optimize image registration and to speed up the calculation process of the maps. Additionally, studies need to be performed to evaluate the clinical value of absolute pixelwise quantitative myocardial perfusion maps in patients with different diseases.

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