A Fully Quantitative Pixel Based Approach for Measuring Myocardial Blood Flow in First-Pass Contrast-Enhanced Perfusion MRI: Microspheres Validation in Dogs and Feasibility Study in Humans

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Introduction:

Quantitative analysis of myocardial perfusion using first-pass Gadolinium-enhanced magnetic resonance (MR) imaging compares well with microsphere measures of absolute myocardial blood flow (MBF) in animals [1]. Quantification of myocardial perfusion is routinely performed on a sector-by-sector basis that inherently downgrades the resolution of perfusion information to the size of a sector. In this study we present a method to quantify MBF from the first-pass MR perfusion images at the pixel level. Fully quantitative MBF was estimated for each pixel in the myocardial regions of interest by a model constrained deconvolution technique. The results of the fully quantitative MBF estimates from the MR perfusion images were validated with absolute MBF as determined by microspheres measurements in animals. The feasibility of the method was tested in human perfusion MR images to estimate pixel-wise MBF at rest and during stress.

Methods:

Local hyperemia of MBF in the left anterior descending coronary artery distribution was induced in 7 dogs through intracoronary adenosine infusion. Fluorescent microspheres were used as the reference standard to determine the absolute MBF in ml/g/min on 16 sectors (8 endocardial and 8 epicardial) of a mid ventricular slice. The MR perfusion image data was acquired with a Siemens Avanto 1.5T scanner using a steady-state free precession (SSFP) sequence with saturation recovery magnetization preparation. A dual-bolus contrast technique was used which consists of two concentrations of gadolinium-DTPA at 0.005 mmol/kg and 0.1 mmol/kg. Typical imaging parameters included a non slice-selective saturation preparation pulse at 90° flip angle, read out flip angle 50°, saturation recovery time 90 ms, TR 2.4 ms, TE 1.2 ms, field of view 260 x 179 mm, acquisition matrix 128 x 80, slice thickness 8 mm. Parallel imaging with an accelerating factor of 2 was used. At the beginning of each perfusion scan, two proton density weighted images were also acquired. For sector level perfusion MBF quantification, the myocardial regions of interest were defined by manual tracing endocardial and epicardial borders in all MR perfusion images. Time signal intensity curves were analyzed based on 8 equal-divided transmural sectors of a mid ventricular slice, which were sub-divided into 16 (8 endocardial and 8 epicardial) sectors. Fully quantitative MBF of each sector was estimated using a model constrained deconvolution based on a logistic impulse response function [2]. The results of MR estimated sector-wise MBF were then compared against the microsphere reference. For pixel-wise perfusion MBF quantification, all images were first corrected for surface coil intensity profile by using a bias field estimated from the PD image. All images were then corrected for spatial motion by using a non-rigid body image warping. This was implemented by matching all endocardial and epicardial border points to two corresponding concentric circles. A closest distance measure was used to obtain the corresponding points of myocardial borders and the concentric circles. The myocardial regions of interest of the perfusion images were processed by a thin plate spline warping to improve the consistency of pixel-wise time signal intensity curves. MR time intensity curves were then analyzed on a pixel-by-pixel basis and converted to MBF maps using the model constrained deconvolution.

Results:

The sector-wise MBF estimates from MR closely correlated with absolute microsphere MBF measurements. Average MBF from microsphere measurements were 5.1±1.5 ml/g/min in hyperemic sectors and 1.3±0.7 ml/g/min in control zones. For transmural sector averages, MBF matched well between MR and microspheres measurement (R=0.89). For subsector comparison, both endocardial sectors (R=0.91) and epicardial sectors (R=0.85) showed good correlations with microspheres MBF. Bland Altman analysis confirmed there was no significant bias as a function of MBF in all comparisons. For a pixel-by-pixel based analysis, Figure-1 shows an example of colorized MR perfusion pixel map from a dog with corresponding microsphere MBF on the same absolute color scale. Qualitatively, color perfusion maps were comparable to microsphere bull's-eye plots in all animals. Regional hyperemic blood flow was clearly seen in all animals. Perfusion pixel maps had a higher spatial resolution than sector-wise microsphere measurements. Figure-2 shows an example of the method applied to clinical perfusion MRI at rest and during stress. Pixel-wise perfusion maps showed easily differentiated rest and stress MBF in a patient with normal perfusion. However, the perfusion pixel map of another patient shows a moderate subendocardial defect in the mid anterior wall and anteroseptal wall during stress study but a homogeneous resting blood flow which correlated spatially to a moderate stenosis by the coronary angiography.

Discussion:

We demonstrate an approach to generate comprehensive pixel-wise MBF maps for high resolution quantitative visualization of first-pass contrast-enhanced perfusion MR images. A sector-wise comparison shows the results of MBF estimates in MRI are closely correlated with the absolute microsphere measurements in a wide range of MBF values. The results of pixel-wise perfusion maps displayed on a calibrated color scale are also qualitatively comparable to microsphere MBF bullseye plots. This method could improve the objectivity of quantification in first-pass perfusion MRI for diagnosing coronary artery disease. One limitation of the current method is the need for manual tracing of myocardial borders, a time-consuming step. However, when done well, these myocardial borders constrain perfusion image quantification only to regions of high information content and minimize motion related artifacts.

References: [1] Christian TF, et al. Radiology 2004;232:677-684.
[2] Hsu L, et al., Proc. ISMRM 2009;3769.

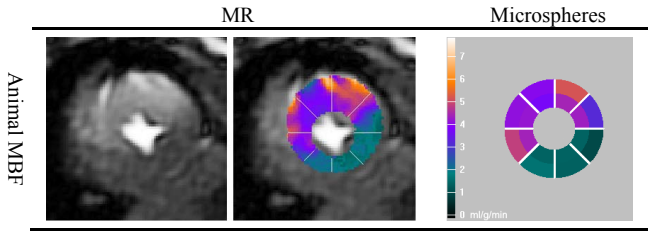

Figure-1

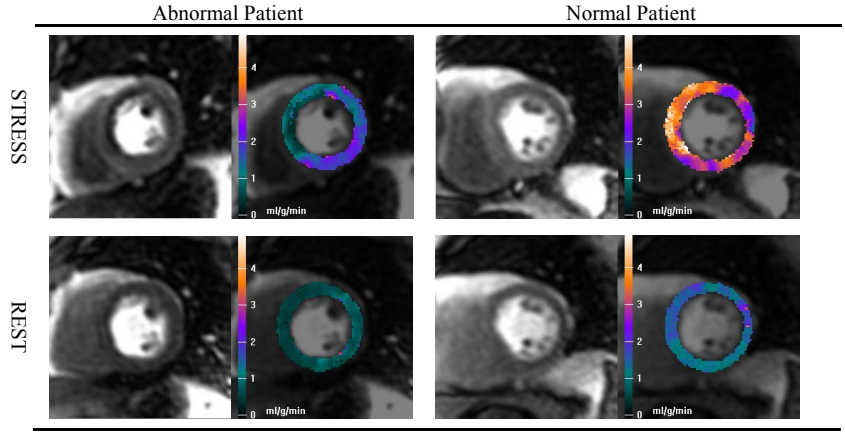

Figure-2