Heterogeneity of BOLD-indexed Myocardial Perfusion Reserve

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Introduction: The potential of MR to characterize myocardial perfusion reserve, as indexed by the Blood Oxygenation Level Dependent (BOLD) response to maximal pharmacological vasodilation, has been documented [1-3]. The implications of regional variability of the BOLD indexed perfusion reserve for the detection of segmental myocardial disease, such as coronary artery disease (CAD), have received less attention. In this study we explore regional heterogeneity of BOLD perfusion reserve in healthy human subjects.

Methods: *Sequence*: Apparent transverse relaxation rate ($R_2^* = 1/T_2^*$) was estimated using a gated, segmented, spoiled gradient-echo sequence on a Signa 1.5T scanner (GE Medical Systems, Milwaukee, WI) with a surface coil receiver. Saturation pulses were applied to basal and apical slabs before end systole to null signal arising from blood within the atria and ventricles, thereby reducing flow artifact.

Datasets of nine images with equally spaced TEs over the range of 2.05-25.7ms were acquired in a single 20-25s breath-hold. Five RF excitations, each followed by a nine-echo readout train, were played during each cardiac cycle. Data were acquired in a 138ms window in mid to late diastole. Parameters for one echo train were TR/α/RBW = 27.6ms/30°/±62.5kHz, with a matrix of 256x120, and FOV 400x400mm (1.56x3.33x10mm).

Infusion Protocol: At least 8 datasets were acquired to establish a baseline. Dipyridamole was then administered at a dose of 0.56mg/kg over 4 min. Post-infusion datasets were acquired approximately every minute for twenty minutes.

Analysis: Each dataset of 9 images was combined to generate R_2^* estimates at each time point. For regional assessment, eight regions of interest (ROIs) of approx. 22 pixels were selected within the central myocardium (Fig. 1a) and manually registered through time. R_2^* for each ROI was calculated using a logarithmic fit of the mean signal intensity at each time point. ΔR_2^* relative to mean baseline was calculated for each time point. Peak values were calculated using 4 contiguous time points (Fig. 1b). As a measure of regional heterogeneity, the coefficient of variation (S.D./mean) among ROIs was calculated. For global assessment, R_2^* values were pooled to obtain a mean time-course for each individual (Fig 1c). T_2^* pixel-by-pixel maps for each time point were generated, and pixels with correlation coefficient less than 0.95 were rejected. All baseline maps were manually segmented, visually aligned, and averaged to generate a composite baseline T_2^* map. Likewise, six contiguous time points at peak effect were combined to generate a stress T_2^* map (Fig. 2).

Results: Typical regional peak ΔR_2^* results are shown in Fig. 1b. Global (all ROIs) peak ΔR_2^* was -4.3±1.2s^{-1} (n=2 subjects). In Fig. 1c, we display results obtained when rejecting ROIs with dephasing due to the posterior cardiac vein [4] (ΔR_2^* = -8.6±2.6s^{-1}). Average coefficient of variation among regions was 48±10%. An example of pixel-by-pixel composite baseline and stress maps demonstrating the dipyridamole-induced BOLD change can be seen in Fig 2. This effect was verified using a pixel histogram.

Discussion: Based on experience with clinical thallium imaging, if one accounts for attenuation artifacts, perfusion reserve is regionally uniform in normal hearts [5]. There are multiple

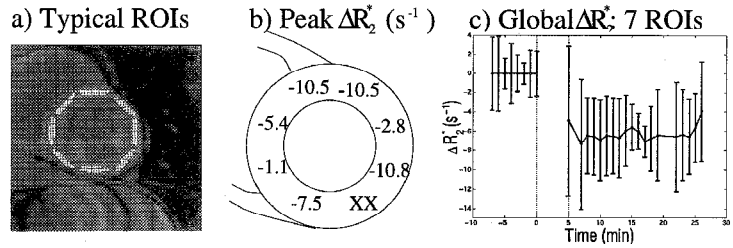

Figure 1: a) Regional ROIs in one subject. Corresponding b) regional peak ΔR_2^* values depicting heterogeneity, and c) global ΔR_2^* time course. ROI XX corresponds to the posterior cardiac vein and was excluded from global analysis.

sources for the origin of the observed regional heterogeneity of BOLD perfusion reserve. Measurement-related factors, including artifact arising from the blood-pool [6], can contribute to this heterogeneity. However, the BOLD mechanism is dependent on blood volume, among other factors, and resting blood volume is known to be heterogeneous [7]. Thus, it is not surprising that dipyridamole hyperemia would result in heterogeneous changes in blood volume and therefore in ΔR_2^*. Our global ΔR_2^* in healthy subjects is consistent with published data [1]. Given the observed variability, to classify a segment as abnormal using a threshold of twice the coefficient of variation [8], would require a 96% reduction in segmental ΔR_2^* from the mean value. This suggests that while the present method may be adequate for the detection of global reductions of perfusion reserve, to detect segmental disease the variability will need to be reduced by a factor of 2 [5,9].

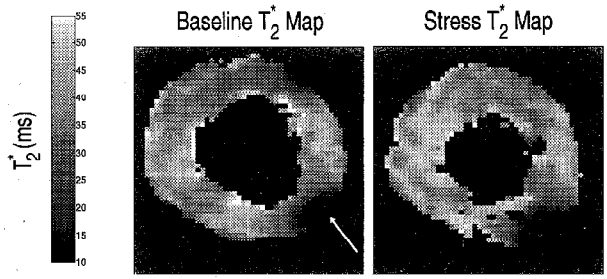

Figure 2: Sample composite pixel-by-pixel T_2^* maps pre- and post-stress. Papillary muscles are segmented out. Differences in configuration relate to imaging in slightly different phases in diastole. Note dephasing due to the posterior cardiac vein (arrow). The dipyridamole-induced change in T_2^* was confirmed by histogram analysis.

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