Robust Cardiac BOLD MRI using an fMRI-like approach with Repeated Stress Paradigms

Aurelien F. Stalder[1], Michaela Schmidt[1], Andreas Greiser[1], Peter Speier[1], Jens Guehring[1], Matthias G Friedrich[2,3], and Edgar Mueller[1]

[1]*Siemens AG Healthcare Sector, Erlangen, Germany,* [2]*Departments of Cardiology and Radiology, Montreal Heart Institute, Université de Montréal, Montreal, QC, Canada,* [3]*Departments of Cardiac Sciences and Radiology, University of Calgary, Calgary, AB, Canada*

Introduction: BOLD MRI uses the different magnetic properties of oxygenated and deoxygenated hemoglobin to measure oxygenation changes in vivo. Nonetheless, BOLD signal variations are within a few percent and thus of the order of magnitude of noise, motion-induced signal variations, hardware instabilities, or physiological effects. Consequently, the BOLD contrast-to-noise ratio is typically low and interpreting individual BOLD images is unreliable. To overcome this challenge, functional MRI (fMRI) uses repeated paradigms to modulate oxygenation and statistical tools - often the general linear model – to isolate the signal variation induced by a specific paradigm. Cardiac BOLD MRI has already been used to assess ischemia, coronary stenosis (1–3), edema (4) or scar tissue (5). While these results are encouraging, the diagnostic accuracy remains moderate (2), and methodological improvements with respect to robustness and sensitivity are still needed to allow clinical use (3,6). Generally, BOLD imaging is difficult in the myocardium due to low BOLD CNR, potential image artifacts as well as cardiac and respiratory motion (7).

Purpose: Use repeated stress paradigms, motion correction and an approach taken from neurological BOLD fMRI to derive robust cardiac BOLD measurements.

Materials and Methods: Data were acquired on a 1.5T MR scanner (Magnetom Aera, Siemens AG Healthcare Sector, Erlangen, Germany) using a multiple-repetition, single-shot, ECG-triggered, bSSFP sequence prototype (res. 2.3 x 1.8 mm^2, 8 mm slice thickness) with adiabatic non-selective T2-preparation pulses (duration = 55 ms). Images were acquired continuously during repeated long breath-holds in 13 volunteers. The healthy participants (claimed breath-holding ability of at least 45 s) were asked to hold their breath at end-expiration as long as possible during 5 to 14 successive apneas (free recovery 30 to 90 s). Non-rigid motion correction (8) was applied to the acquired data which was then analyzed using a general linear model (GLM) taking into account the effects of the breath-hold duration (linear model), RR interval (variable recovery time between acquisitions due to ECG gating), motion (based on the motion correction deformation field) and baseline variations (Fig. 1, left). Both voxel- and ROI-based analyses were performed.

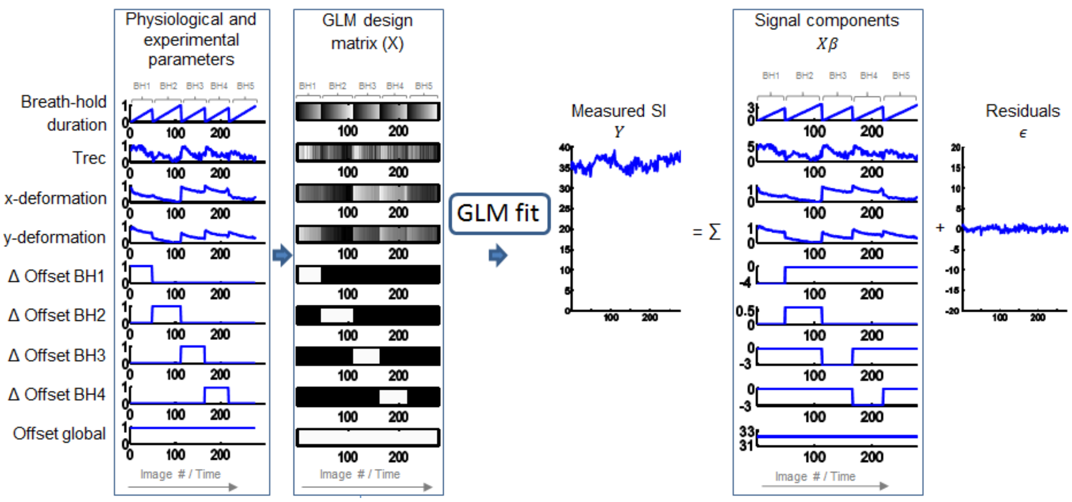

Fig. 1 Definition of the GLM design matrix and individual GLM components in the myocardium of one volunteer after 5 breath-holds. The physiological and experimental parameters as well as the GLM design matrix were scaled between 0 and 1. The GLM fit provides the measured SI as the sum of the individual signal components and of the residuals.

Results: The GLM model was able to isolate the component of the BOLD signal arising from the breath-holds and separate it from the background effects due to heart rate variations, motion and baselines (Fig.1, right; Fig. 2). A significant ($p<0.05$) BOLD signal increase was observed in the myocardium of healthy volunteers in 11/13 volunteers. In one volunteer, the analysis was not successful due to very different positions of the diaphragm between breath-holds. In another volunteer, the analysis was not statistically significant due to some motion being correlated with the breath-hold duration.

Discussion: Using an elastic motion correction algorithm and fast acquisition techniques, it was possible to apply fMRI-like strategies for cardiac BOLD MRI in volunteers and derive robust BOLD measurements. The observed slight but significant oxygenation increase in the myocardium of volunteers might be explained by the vasodilator effect of increased CO_2 concentration under apnea (9). Detection of such small physiological changes in volunteers performing breath-holds demonstrates that the method could have potential in identifying low oxygenation regions in the myocardium of patients during stress tests. Breath-hold was chosen in this study as stress paradigm mostly because of its non-invasiveness. However, such long breath-holds may not be feasible in patients. Nonetheless, the same method with repeated paradigms can be applied as well with other stress agents (e.g. pharmaceutical, physical exercise, inhaled gases alteration) which may potentially have a stronger effect on the oxygenation of the myocardium. Oxygenation-sensitive CMR as a non-invasive contrast-free technique has the potential to become an alternative to current diagnostic tools in patients with suspected CAD.

References: 1. Wacker CM et al. MAGMA 1999;8:48–54. 2. Arnold JR et al. J. Am. Coll. Cardiol. 2012;59:1954–64. 3. Friedrich MG et al. Circulation 2003;108:2219–23. 4. Giri S et al. J Cardiovasc Magn Reson 2009;11:56. 5. Egred M et al. Heart 2003;89:738–44. 6. Friedrich MG et al. J Cardiovasc Magn Reson 2013;15:43. 7. Fieno DS et al. Circulation 2004;110:1284–90. 8. Guetter C et al. In: IEEE; 2011. pp. 590–593. 9. Guensch DP et al. PLoS One 2013;8:e53282.

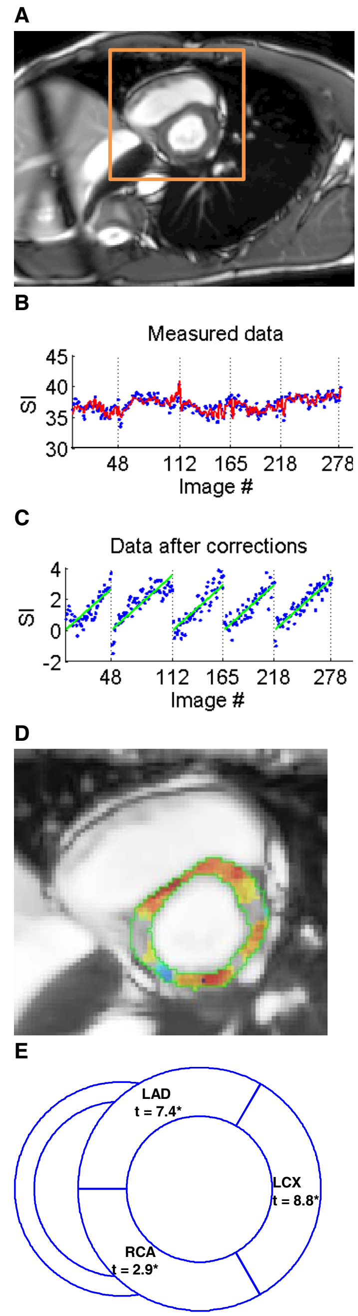

Fig. 2 GLM analysis for the volunteer of Fig. 1 (5 apneas). **A:** Motion-corrected average image, **B:** average measured SI and global GLM SI in the myocardium, **C:** SI after correction for the unwanted effects from the RR interval, motion and baseline, **D:** t-statistics map of the correlation with the apnea duration, and **E:** segmental analysis in the myocardium.