Cine-EPI Can Be Used to Detect Adenosine-Induced Myocardial Oxygenation Changes in Canines

J. D. Green[1,2], M. Voehringer[2], J. A. Flewitt[2], S. Zuehlsdorff[3], J. V. Tyberg[2], and M. G. Friedrich[2]

[1]Siemens Healthcare, Calgary, Alberta, Canada, [2]University of Calgary, Calgary, Alberta, Canada, [3]Siemens Medical Solutions USA, Inc., Chicago, Illinois, United States

Introduction: Non-invasive assessment of myocardial ischemia is challenging. Because the BOLD (Blood Oxygen Level Dependent) effect mainly relies on endogenous contrast to differentiate ischemic from non-ischemic tissue, BOLD has the potential to directly assess myocardial oxygenation.

Though T_2*-weighting is easily achieved using triggered, mid-diastolic echo planar imaging (EPI), it can be sensitive to artifacts. However, by using a cine-EPI approach, it may be possible to use a lower effective TE (TE_{eff}), thereby reducing artifacts but maintaining BOLD sensitivity by averaging several mid-diastolic phases during analysis. Our hypothesis was that a cine-EPI sequence can be used to detect adenosine-induced oxygenation changes in a stenosis dog model.

Methods: We developed a cine EPI sequence with the goal of obtaining strong BOLD-weighted imaging but without significant image artifacts. Cine phases were acquired using prospective ECG-triggering, a breath hold (~12 s), a short echo train (4 echoes) with a segmented approach (8 lines/segment), and a bipolar readout. Radiofrequency pulses with a narrow bandwidth were used to avoid excitation of fat. All studies were performed on a 1.5T MAGNETOM Avanto (Siemens Healthcare, Germany) in canines (n=4) with a balloon catheter fluoroscopically guided into the left circumflex or left anterior descending coronary artery, to create stenoses as validated by simultaneous fractional flow reserve measurements.

We obtained cine-EPI images in a mid-ventricular slice, before and during an adenosine infusion of 140 μg/kg for two minutes. We repeated this process three times, once with no stenosis, once with a mid-grade stenosis and once with a high-grade stenosis. At the end of the study, we injected gadolinium (Gd) via our intracoronary catheter and ran a perfusion scan to verify the territory affected by the stenosed artery. We then injected Gd intravenously and performed late enhancement (LE) to verify the absence of myocardial infarction. Sequence parameters for cine-EPI: TR/TE_{eff}/flip angle=25 ms/15 ms/15°; echo train = 4; 8 lines/phase/cardiac cycle; FOV=300x300 mm^2; matrix=123x128; slice thickness=10 mm; temporal resolution=49 ms.

We analyzed the data using a clinically validated software package (cmr^{42}, Circle Cardiovascular Imaging Inc., Canada). We used the intracoronary perfusion images to identify the affected and remote myocardium. By averaging 4 phases corresponding to mid-diastole, we measured mean signal intensity (meanSI) in the affected and remote territory during no stenosis and the two stenosis levels, when the subject was at rest and during adenosine infusion. For each territory, we calculated the adenosine response as a percent change in image meanSI going from rest to stress ($\%\Delta SI_{aden}$) for each of the three stenosis levels (no stenosis, mid-grade stenosis, high-grade stenosis). We then compared $\%\Delta SI_{aden}$ in a particular territory for the different stenosis levels using a matched pairs t-test (α=0.05).

Results: A sample data set is shown in Figure 1. The quantitative results are summarized in the Figure 2. In the remote territory, mean $\%\Delta SI_{aden}$ at no, mid-grade, and high-grade stenosis (± standard error) was 12.3% ± 3%, 11.7% ± 4%, and 11.3% ± 3% respectively. In the affected territory, the same measurements were 12.0% ± 1%, 8.6% ± 1%, and 1.2% ± 1%. Looking at each stenosis level, there was only a statistically significant difference between the two territories for the high-grade stenosis. Looking at each territory, there was no statistically significant difference between the $\%\Delta SI_{aden}$ observed for the different stenosis levels in the remote territory. For the affected myocardial territory, there was a statistically significant decrease in $\%\Delta SI_{aden}$ going from baseline to either stenosis level, as well as going from mid- to high-grade stenosis. No LE was observed.

Discussion and Conclusion: We have shown that cine-EPI can accurately detect changes in adenosine response in myocardium affected by a high-grade stenosis. We could use a lower TE_{eff} than previously reported for EPI cardiac BOLD because we were able to signal average over several cardiac phases, which in turn reduced image artifacts. Cine-EPI shows promise for identifying regions of ischemia in CMR, simultaneous to functional assessment.

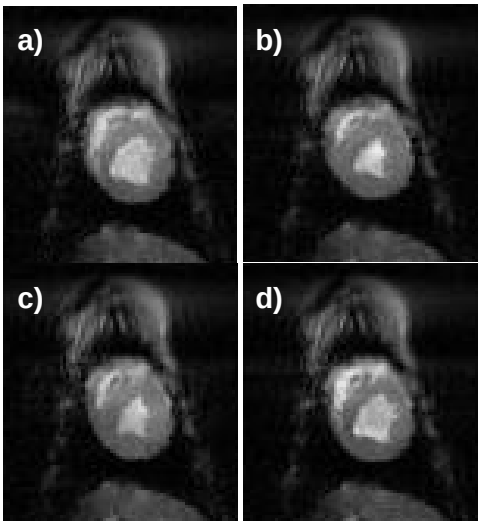

Figure 1: Typical stress images from one study during the high-grade stenosis, taken during **a)** early systole **b)** systole **c)** early diastole and **d)** diastole using cine-EPI.

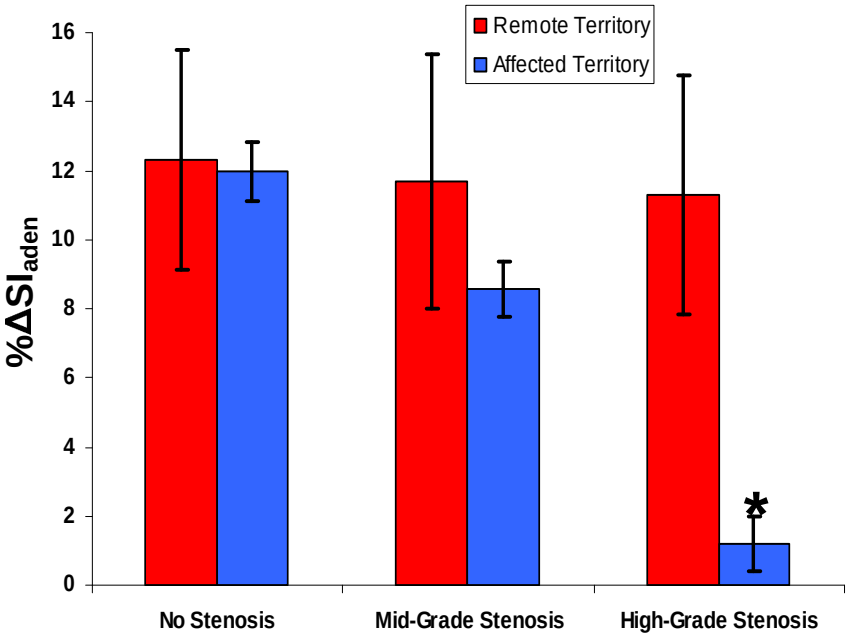

Figure 2: Plot of %ΔSIaden (%SI change from rest during adenosine infusion) for the affected territory and the remote territory for the three levels of coronary artery stenosis. Error bars represent ±1 SE. An * indicates a statistically significant difference ($p<0.05$).