SHILO: Simultaneous High/Low spatial/temporal resolution dual-imaging acquisition for improved parameters quantification in dynamic contrast enhanced (DCE) MRI of atherosclerosis

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Background: High-risk/vulnerable atherosclerotic plaques are often unrecognized before dramatic clinical events (stroke, myocardial infarction or sudden death). The knowledge that plaque inflammation (presence of inflammatory cells and neovascularization) is a histological hallmark of plaque vulnerability has stimulated extensive research of surrogate non-invasive markers for its detection(1). Dynamic contrast enhanced (DCE) MRI with kinetic modeling has recently been applied to quantify and characterize plaques' neovessels (2,3). Despite initial encouraging results, many challenges still hinder accurate quantification of plaque neovasculature. The reliability of DCE-MRI measurements in atherosclerosis depends on accurate sampling (high SNR and time resolution) of both arterial input function (AIF, the concentration of contrast agent in the blood plasma) and vessel wall enhancement curve. This imposes almost opposite requirements in terms of imaging parameters, thus making the development of acquisition protocols challenging (**Table 1**). For example, vessel wall imaging requirements can be met if slower time resolutions are accepted. However, this can compromise adequate AIF sampling. By reaching a compromise between these different requirements, current imaging protocols fail to address these specific challenges. This may significantly impact accurate parameter quantification.

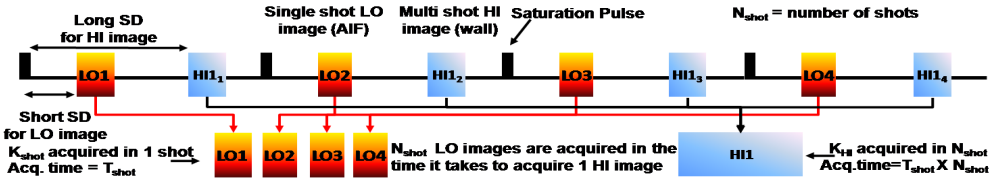

Figure 1: SHILO sequence diagram. The time resolution of LO is 4 times faster than the one HI, that however have 4 times higher spatial resolution.

SHILO, (**S**imultaneous **H**igh **Lo**w), **a newly proposed dual imaging sequence**: First pass perfusion imaging of the myocardium shares some of the challenges of DCE-MRI of atherosclerosis. Kim et al (4) developed a multi-slice dual imaging method to improve quantification of myocardial perfusion. Their approach consists of a hybrid echo-planar imaging (EPI) sequence which allows for simultaneous acquisition of the AIF and the vessel wall time course after a single saturation pulse. In this case both images are acquired in one shot, but at two different delays after saturation (the shorter one optimal for AIF acquisition, the longer one adequate for vessel wall acquisition). Building upon their work, we modified a spoiled, multi-shot, saturation prepared turbo field echo (TFE) sequence into a dual-imaging sequence for DCE-MRI of atherosclerosis. However, differently from Kim et al we will acquire a low spatial/high temporal resolution single-shot AIF image (referred to as "**LO**") and simultaneously a high spatial/low temporal resolution multi-shot vessel wall image (referred to as "**HI**") as detailed in **Figure 1**.

Implementation: We will illustrate the sequence implementation with an example: assume 120 k-space lines (K_{HI}) are to be acquired for vessel wall imaging (**HI**) in 4 shots (30 k-space lines per shot, K_{shot}). For a given TR, the acquisition time for a shot is TR x 30 k-space lines (T_{shot}), while **HI** acquisition time will be TR x 120 k-space lines. If a saturation pulse is applied before the first excitation of each shot, and the saturation delay (SD) before acquisition of **HI** is longer than T_{shot}, an additional shot can be acquired during this delay (**Figure 1**). If K_{shot} is enough, the image from the inserted shot (**LO**, acquired at a shorter, optimal delay after saturation) could be used for AIF data acquisition. **By inserting the acquisition of the LO image after the saturation pulse, but before the acquisition of the HI image, it is possible to acquire two images with different dynamic signal range, different spatial and temporal resolution within the same acquisition.** The different dynamic signal range derives from the shorter (LO, AIF) and longer (HI, vessel wall) delay after the saturation pulse. The different spatial resolution derives from different number of k-space lines acquired (30 lines, LO image; 120 lines, HI image). The different temporal resolution derives from the fact that LO is acquired as single-shot (one image after every saturation pulse applied), while HI is acquired as multi-shot. For every HI (vessel wall) image, 4 LO (AIF) images will be acquired in this case, with an acceleration factor determined by the number of shots necessary to acquire the HI image. We refer to this approach as **SHILO** (**S**imultaneous **H**igh **Lo**w).

Table 1	AIF	Vessel Wall
Spatial Resolution	Low	High
Time Resolution	Fast	Slow
Slice Coverage	Limited	Extensive
Concentration	High	Low

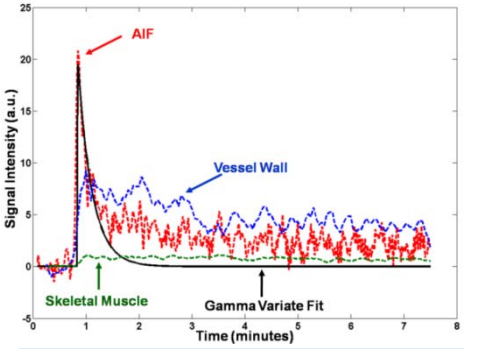

Figure 3: Signal intensity curves from SHILO. Red, AIF (LO). Blue, Vessel wall (HI). Green, Skeletal muscle (HI). Black, AIF gamma variate fit. x axis, time (min). y axis, signal intensity

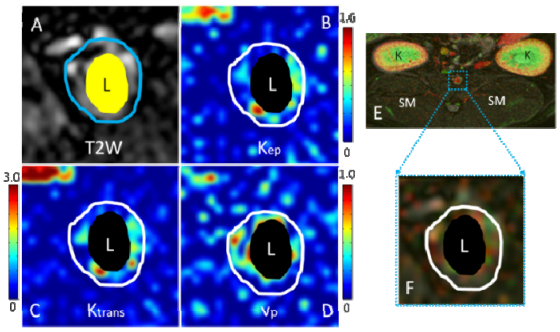

Figure 2: Kinetic parameters maps of aortic vessel wall calculated from SHILO acquisition. (A) T2W image for anatomical reference, (B)K_{ep} map. (C)K^{trans} map. (D) v_p map.L: vessel lumen. (E) Fused anatomical T2W, with color coded K^{trans}(green) and v_p (red) maps(full view). K: kidneys,. SM: skeletal muscle.(F) Zoomed in view of E. Lumen is colored black or yellow for better clarity.

Results: *Image Acquisition*: Two atherosclerotic rabbits and two subjects with carotid artery disease were imaged for preliminary testing on a 3T clinical system, using a conventional knee coil for rabbits and a dedicated 8-channel carotid coil for the human carotids. Following standard TOF and black blood T1, T2 and PDW imaging for plaque identification and characterization, SHILO DCE-MRI was performed on one selected axial slice (imaging parameters: TR, 9.6 ms; TE, 2.4 ms; flip angle 12 degrees; FOV, 16X16cm; matrix size, 320X320; spatial resolution, 1 mm in plane for LO, 0.5 mm in plane for HI; echo train length, 80; 4 shots). Time resolution for LO was ~ 1s, while for HI was ~ 4s. *Image Analysis*: A linear correlation was assumed between signal intensity and contrast agent concentration. Kinetic modeling was performed with a modified Tofts model using linear least squares procedures (5). Figure 2 shows examples of anatomical images and parameters maps of the aortic vessel wall of one atherosclerotic rabbit calculated from SHILO acquisition. Figure 3 shows time curves for AIF, vessel wall and skeletal muscle from SHILO.

Conclusions: In this preliminary study, we successfully demonstrated the use of **SHILO** for accurate AIF sampling (LO), and adequate spatial resolution images for vessel wall acquisition in both atherosclerotic rabbits and human subjects.

References:

1. Sanz J et al. Nature 2008, 2. Calcagno C et al, ATVB, 2008, 3. Kerwin WS et al, MRM 2008, 4. Kim D et al, JMRI 2006, 5. Murase et al MRM 2004