A free breathing, retrospectively gated, saturation transfer encoded steady state cardiac cine method for preclinical chemical exchange saturation transfer imaging in the heart

Moriel Vandsburger[1], Avigdor Leftin[1], Senzeni Mpofu[1], and Michal Neeman[1]
[1]*Weizmann Institute of Science, Rehovot, None, Israel*

Introduction. Chemical exchange saturation transfer (CEST) imaging is emerging as a powerful MRI technique for selective visualization of a variety of targeted contrast agents and synthetic reporter genes (for full review see [1]). Prior CEST studies have overwhelmingly used rapid spin-echo acquisition schemes to obtain CEST weighted images. Subsequently, pre-clinical CEST studies have been largely performed in stationary organs (e.g. brain, kidney) or in cancer models, but never in the heart, where combined cardiac and respiratory motion obviate the use of rapid spin echo imaging. We developed a free breathing, retrospectively gated, CEST-encoded steady state gradient echo cardiac cine imaging sequence for the purpose of cardiac CEST imaging. **Methods.** A saturation transfer (ST) encoded - steady state gradient echo pulse sequence (Fig A) was developed in order to generate a series of ST-weighted images throughout the cardiac cycle. Saturation module parameters included a train (number of pulses = 28) of frequency selective Gaussian RF pulses (bandwidth = 200Hz, duration = 13.7ms) with dephasing gradient duration = 1ms, and inter-pulse delay = 5ms. Readout module parameters included TR/TE = 10.2/3.5ms, with a 1Khz bandwidth Gaussian excitation pulse (flip angle = 10°). In order to limit the effect of T_1 relaxation through exchange with macromolecules during image acquisition, the number of acquisitions was limited to 100 for each CEST preparation. The total number of sequence repetitions (saturation and readout modules) was 128. Specific imaging parameters were FOV=2.56x2.56cm, Matrix = 256x128, slices = 1, δ_x = 100µm and δ_y = 200µm, and slice thickness = 1mm. In order to obtain complete spectra, scans were performed by incrementing the saturation offset from -10ppm to 10ppm by 1ppm. In order to normalize for receiver coil sensitivity, a reference scan was performed with saturation flip angle = 10° and offset = -1ppm. Water saturation shift referencing (WASSR) correction was performed by acquiring a series of scans with offset = -0.5ppm by 0.1ppm to 0.5ppm, as described in [2]. Imaging was performed on a 9.4T Bruker Biospec (Ettlingen, Germany) scanner using a cylindrical volume coil for excitation and a single element surface coil for signal reception. Images were retrospectively reconstructed using the Bruker Intragate system, number of cine frames = 8, in order to remove respiratory artifact and perform cardiac gating. Image analysis was performed on end diastolic images by measuring signal intensity across the entire heart. Spectra were obtained by normalizing regional signal intensity to the corresponding reference scan. The asymmetric magnetization transfer ratio (MTRasym) was calculated for all offsets as MTRasym = $(S_+ - S_-)/S_{ref}$). Male, 8 week old, C57B6 mice (n=5) were imaged under 1.25% isoflurane anesthesia, with body temperature maintained using circulating thermostated water. **Results** Sample mid-ventricular end diastolic images at several offset frequencies, and the corresponding spectrum and MTRasym plot are shown in Fig B. Acquired cardiac spectra demonstrated mean on-resonance saturation efficiency of 69 ± 1.4% with full width half max of 1.0 ± 0.1ppm. The mean MTRasym value across all offsets was -0.008 ± 0.034 (A.U.). Direct saturation of the water signal, measured at ±6ppm from on-resonance, was 13.4 ± 2.4%. WASSR spectra revealed minimal resonant frequency variation within the heart (Fig B). **Discussion** By encoding the CEST effect into the steady state longitudinal magnetization of the readout module, CEST imaging can be performed without being limited by cardiac and respiratory motion. Further, by normalizing the measured signal intensity to that of a reference scan, pixel-wise CEST imaging can be performed without sensitivity to either regionally differing myocardial T_1 relaxation times, or the spatial profile of the receiver coil. Finally, because of the small size of the heart, WASSR correction of spectra may be unnecessary as the average WASSR shift was below the bandwidth of the saturation pulse. **Acknowledgements** Whitaker Postdoctoral Fellowship to MHV, Fullbright Award and NSF IRFP to AL, R01 CA75334 US National Cancer Institute, European Commission 7th Framework Integrated Project ENCITE, and European Research Council Advanced grant 232640-IMAGO to MN. **References** [1] Liu G. et al. Methods Mol Bio, 2011. [2] Kim et al. MRM. 2009.

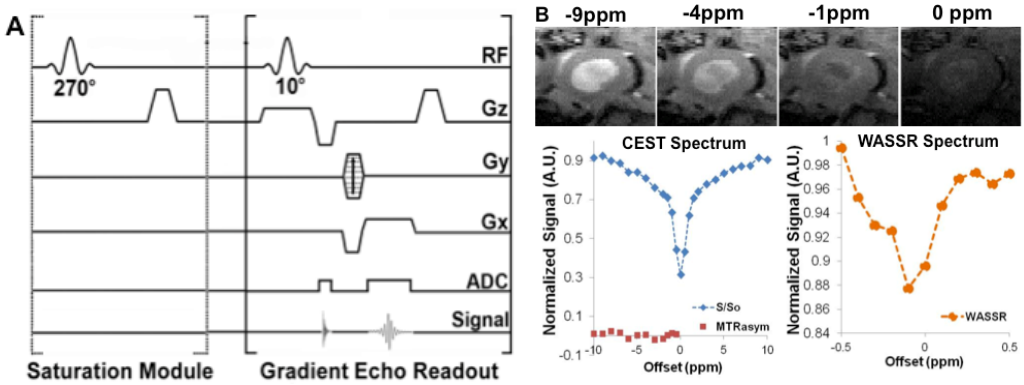

Figure. (A) Pulse sequence diagram for a ST-encoded steady state cardiac cine sequence. The saturation module is executed for 540ms, which encodes the CEST effect into the initial longitudinal magnetization of water. During the subsequent 1s of image acquisition, the short TR results in a CEST-encoded steady state longitudinal magnetization. **(B)** Representative images acquired with saturation offsets of -9, -4, -1, and 0 ppm demonstrate uniform saturation of the water signal throughout the myocardium. The resulting CEST spectrum and MTRasym plot of the heart demonstrate the ability to acquire clean spectra with minimal residual MTRasym in the heart. A representative WASSR spectrum reveals 0.1ppm (40 Hz at 9.4T) bias in water resonance.