Chemical Exchange Saturation Transfer Angiography - CESTA

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Target audience: Researchers and physicians that are interested in CEST, non-contrast-enhanced MRA techniques, and vascular anomalies that present with slow or complex flow patterns.

Purpose: Non-contrast-enhanced magnetic resonance angiography (MRA) has been widely accepted as a reliable diagnostic imaging method. However, the same physical principles that generate blood contrast make these angiography methods sensitive to slow or complex flow patterns[1]. As a result, neurovascular diseases that present with slow or complex flow may not be fully appreciated using these methods. In this report, the feasibility of using Chemical Exchange Transfer Saturation (CEST)[2] as an angiography method is investigated. Since contrast in CEST imaging is generated by the exchangeable protons in solute and not by utilization of blood flow or velocity, it is suggested that CEST angiography (CESTA) will be less sensitive to slow or complex flow.

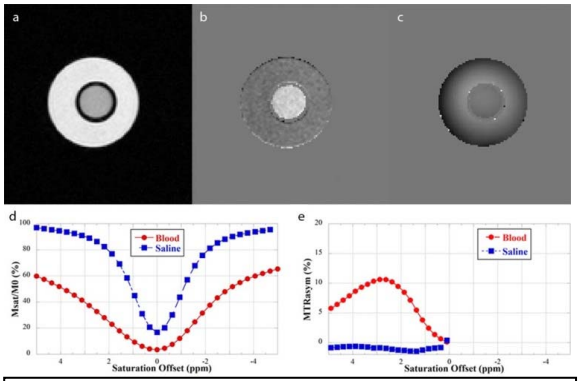

Fig 1. CEST data of blood samples. Proton density image (a), CEST image at 3 ppm (b), WASSR shift map (c), corresponding Z-spectra (d) and MTR_{asym} graphs (e) from blood and saline.

Methods: Porcine whole blood in acid citrate dextrose was placed in cylindrical tubes and emerged in saline for *ex vivo* imaging. MRI experiments were performed on a 3.0 T whole-body MR scanner (Philips Healthcare, Best, the Netherlands) and a custom-made solenoid T/R coil. A WASSR method[3] was used to correct for B0 inhomogeneities. WASSR data was obtained by varying the offset frequency relative to bulk water from 32 Hz to -32 Hz. CEST data was acquired at offset frequency ranging from 640 Hz to -640 Hz. Image data was acquired using a single slice parallel to the short axis of the cylindrical tube with a slice thickness of 3 mm and a field of view (FOV) of 60mm × 60mm with matrix size of 120 × 112 (TR/TE = 3000/8.1ms, TSE-factor = 16, low-high scan order, NSA = 1). *In vivo* CESTA imaging was performed on the right upper leg of a healthy volunteer, because of its simple anatomy. Axial single slice WASSR and CEST images consisting the femoral artery were acquired by using an 8-element receive-only SENSE knee coil and a turbo field echo (TFE) sequence with a slice thickness of 5 mm, a FOV of 180 mm × 180 mm, and matrix size = 128 × 110, and (TFE factor = 29, SENSE factor = 2; shot interval= 3000ms; TR/TE = 7.1/4.2 ms, flip angle (FA) = 20°, NSA = 4 and 6 for WASSR and CEST, respectively). Seventeen dynamics were acquired using a frequency offset range of 640 Hz to -640 Hz and a 3.5 μT pre-saturation pulse of 500 ms. Regions of interest (ROIs) were manually drawn in WASSR data and automatically copied to corresponding CEST data. Normalized Z-spectra were generated using the mean values per ROI and were filtered for noise and corrected for B0 inhomogeneities using WASSR. To quantify the generated CEST contrast, MTR_{asym} was used[2].

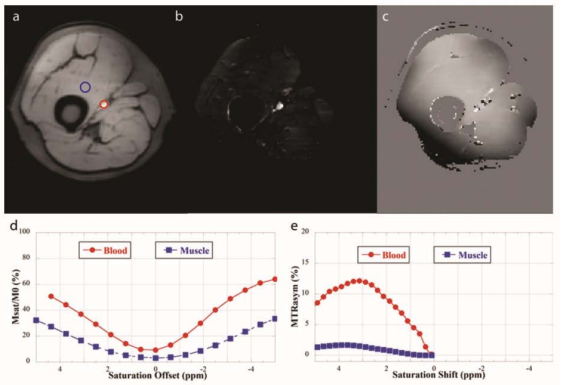

Fig 2. CESTA results of in vivo experiments. Anatomic Proton image with ROIs (a), CEST image at 3 ppm (b), WASSR shift map (c), Z-spectra (d) and MTR_{asym} graphs (e) corresponding to ROIs in (a).

Results: In Figure 1, a proton-density image and corresponding CEST image and WASSR-shift map of a blood sample are shown. The CEST image was generated by calculating the MTR_{asym} value for all pixels using a fixed pre-saturation offset of 3 ppm and a pixel-wise implementation of the WASSR and CEST data processing. Blood appears hyperintense compared to surrounding saline solution. Figure 2 shows the anatomical and CEST image (3 ppm) of the upper leg of a volunteer and the Z-spectrum and MTR_{asym} plot corresponding to ROIs drawn in the lumen of the femoral artery and muscle tissue. Maximum MTR_{asym} values of blood and muscle were about 12.0% and 1.7%, respectively.

Discussion: This preliminary study demonstrates that CEST can be used as a non-invasive angiographic technique. Unlike currently available MR angiography techniques, our proposed method is based on the measurement of the labile protons which are associated with various amino acids, proteins, peptides and other molecules that are naturally present in blood. As a proof-of-principle, the upper leg and femoral artery was used for CEST imaging because of the relative simple and homogeneous anatomic structure. To limit scanning time, only a single slice 2D sequence was used for imaging which on average took 12 minutes. This is caused by the fact that a full Z-spectrum was acquired, which is not required to generate a CEST image.

Conclusion: Although there are substantial challenges that need to be resolved before CESTA can be used as full-fledged angiography technique, we have shown that blood is a feasible CEST agent that provides sufficient contrast to noise ratio relative to surrounding tissue. Our future research will consist of pulse sequence optimization and to address challenges such as imaging time and B0- and B1 inhomogeneities.

References: [1] Bernstein MA *et al. Magn Reson Med.* 2001;46:955-962 [2] van Zijl PCM *et al. Magn Reson Med.* 2011;65:927-948 [3] Kim M *Magn Reson Med.* 2009;61:1441-1450.