# UCEPR: Ultrafast Localized CEST Spectroscopy with PRESS

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**INTRODUCTION**: Chemical Exchange Saturation Transfer (CEST) contrast is used to detect endogenous or exogenous molecules containing exchangeable protons by selectively saturating these protons. The saturation is transferred to the bulk water via chemical exchange, leading to the decreased water signal, thus producing a contrast.[1] Often, a series of images or spectra is acquired as a function of a frequency offset of the saturating irradiation (Z-spectrum). Typically, for each point in the Z-spectrum, a whole spectrum or image acquisition is required. Such acquisition is time-consuming due to the long saturation pulse, the large number of frequency offsets and/or the long TRs. This limits applications of CEST, especially *in-vivo* and in clinical setting. Recently, a method for the ultrafast acquisition of the Z-spectra was introduced (UFZ [2,3]), which is based on a modified spectroscopy sequence that employs a gradient during the saturation pulse and a readout gradient during the acquisition.[4] The technique allows acquisition of the whole Z-spectra with only two scans (saturation scan and reference scan). While the original publication relied on non-localized UFZ, the expansion of the technique to imaging is possible, but may require prolong acquisition times as well, since the dimension used to encode saturation information is already "occupied" by the imaging. However, in many *in-vivo* cases localized information is desired. For example, when the suspicious lesion is identified using standard imaging methods, a localized Z-spectrum from the lesion may allow for assessing tumor stage[5] or differentiation from necrosis[6].

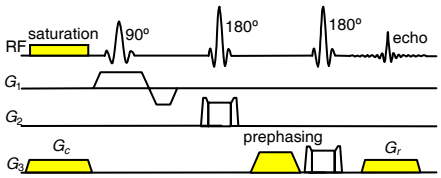


***Fig.1*** *Pulse sequence of UCEPR.* The ultra fast CEST elements are highlighted in yellow.

Here we develop the method allowing ultrafast **localized** Z-spectroscopy, via combination of the ultrafast CEST with volume localization using PRESS: UCEPR.

**SEQUENCE**: UCEPR pulse sequence is shown in Fig.1. Concurrent application of a gradient during saturation ($G_c$) allows broadband saturation. PRESS volume localization follows. In order to resolve the spectral information of saturation, readout gradient with strength $G_r$ along the saturation direction is applied during the signal acquisition. The Z-spectrum is generated by Fourier transform of the sampled data. The effective saturation frequency range of the volume (and thus the width of the Z-spectrum) is determined by $BW_c^{eff} = \gamma G_c \Delta d / 2\pi$, where $\Delta d$ is the volume size along the direction of saturation. The $BW_c^{eff}$ is different from the non-localized UFZ, since it incorporates the voxel size. Once $G_c$ is set, higher voxel volume will lead to higher Z-spectrum bandwidth. The saturation BW is connected to readout BW via: $BW_c^{eff} \le G_c / G_r \cdot BW_r$, similar to non-localized UFZ. The resolution of Z-spectrum is given by $BW_c^{eff}/N$, where $N$ is the number of samples. Lower resolution (smaller $N$) would result in reduced acquisition and echo times thus potentially improving SNR. Moreover, the spatial resolution along saturation dimension decreases with decreasing $N$ thus also improving the SNR. The reference scan (without saturation) is required to account for potential intrinsic volume non-uniformity.

**METHODS:** All the experiments were performed on a Philips Achieva 3T scanner using 32-channel phased array head coil. The method was tested in a phantom containing 25ml tubes filled with Isovue-300 (Iopamidol, Bracco) at pH=6.0, 6.5, 7.0, 7.5, 8.0. The UCEPR signals were acquired from each tube by using a voxel of size 11.5×11.5×30 mm$^3$. Six Z-spectra were acquired by six scans (each scan contains two dynamics: with and without RF saturation), with TE/TR= 99/5000 ms, $BW_r$=8000Hz, $G_c$=5600uT/m, $G_r$=-1400uT/m, to ensure that $BW_c^{eff} \approx 2600Hz(20ppm)$. Number of Scan Averages NSA=8 to improve SNR with total scan time of 80sec. Z-spectra were also acquired by conventional CEST method using EPI with TE/TR=6/5000ms, matrix size=128x128, slice thickness=4 mm, total scan time is 215s. $B_0$ inhomogeneity was corrected using WASSR (WAter Saturation Shift Referencing), requiring additional 115s. No $B_0$ correction was used in UCEPR. All the spectra were interpolated to 1001 points. Pulsed saturation was used (sinc shape and alternating parallel transmit in standard; sinc-gauss and single transmit in UCEPR) with identical average $B_1$=1.4uT and $t_{sat}$=1s.

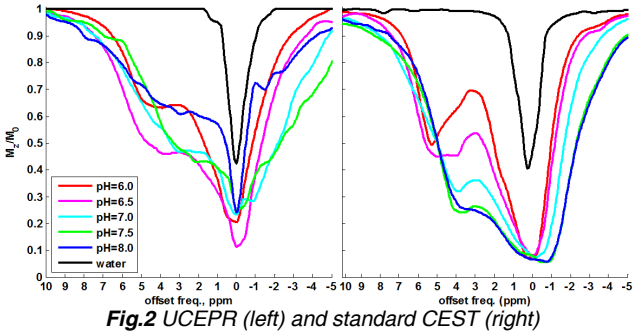


***Fig.2*** *UCEPR (left) and standard CEST (right)*

**RESULTS AND DISCUSSION**: Figs. 2 and 3 display the results acquired by the proposed ultrafast and the conventional CEST methods. A good agreement between the results obtained using UCEPR and standard CEST is observed. The lower saturation observed in UCEPR is due to the less efficient saturation scheme (alternating parallel transmit vs single channel transmit). In addition, some differences may rise from the different effective TE times. Importantly, UCEPR displays analogous dependence on pH (Fig.3).

Currently, UCEPR acquisition is about four times faster than the standard imaging CEST. We are working on the ways to improve the SNR of these scans and decreasing the NSA from 8 to 1. Note that the ultrafast scans have inherently lower SNR, since, effectively, only a small portion of the volume contributes to a given frequency. While we show results from voxel localization only, the method also allowed slice- or bar- localization. In addition any saturation direction can be chosen.

**CONCLUSION**: We have introduced a method providing **localized** CEST information in ultrafast way. The method is straightforward to implement on a clinical scanner. We have demonstrated the application using PRESS but other localization methods, e.g. STEAM can be used. We are working on ways to improve SNR, increase saturation achieved in UCEPR and test the sequence performance *in-vivo*.

The standard CEST methods allow visualization of spatial distribution but often require long times. The localized ultrafast CEST described here would allow fast assessment of suspicions areas and could become important tool in clinical setting. It would offer localized assessment of metabolites or physiology on the time scale unattainable to standard methods, allowing, for instance, dynamic processes monitoring. Moreover, it is possible to implement quantification methods, e.g. omega-plots in relatively fast fashion. We envision that the sequence will complement imaging and spectroscopy methods used *in-vivo* today.

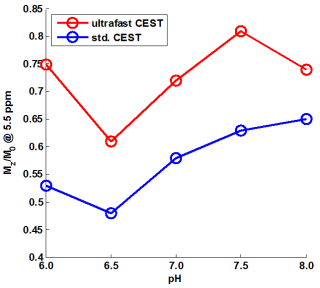


***Fig.3*** *Mz/M0 at 5.5ppm vs pH*

**REFERENCES**: **1**. Ward KM, et al, *JMR* 2000; **2**. Xu X, et al, *Angew. Chem. Int.* 2013; **3**. Jorg D, et al, *JMR* 2013; **4**. Swanson S D, *JMR* 1991; **5.** Zhou J, *et al, MRM* 2008; **6.** Zhou J, *et al, Nature Med* 2011.