Iopamidol CEST for pH measurements on a clinical 3T scanner: phantom and first human in vivo study

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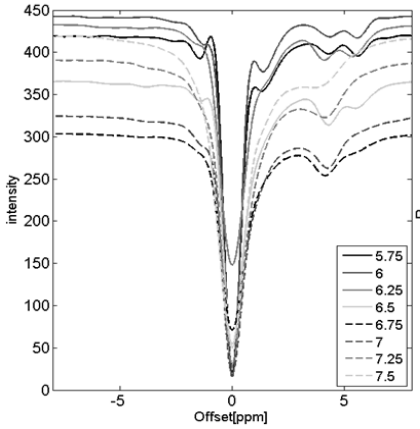

Fig. 1: CEST curves of a 200mM Iopamidol solution with pH values from 5.75 to 7.5

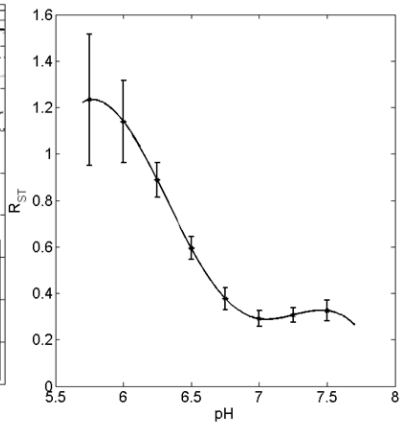

Fig. 2: Calibration curve for pH quantification obtained by 20 in vitro measurements.

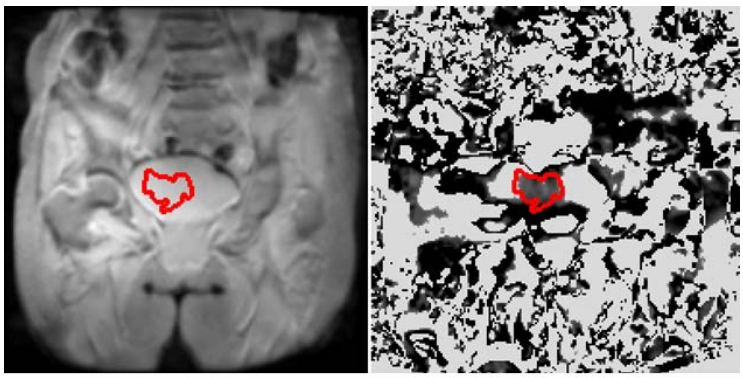

Fig. 3: Anatomical image and pH map of the human bladder.

Target Audience: People interested in chemical exchange saturation transfer MR imaging (CEST) and in vivo pH quantification at clinical MR scanners.

Purpose: Several pathologies are associated with altered pH values like acidic extracellular pH in tumours [1,2] and perturbation of renal parenchyma[1,3]. Up to now, in vivo pH determination with Iopamidol as CEST contrast agent was only performed in animals[1]. New approaches exist using pulse train saturation, which is applicable at clinical MR scanners[4].The aim of this study was to determine pH values in vitro and in the human bladder with Iopamidol on a clinical 3T scanner.

Methods: An CEST preparation module with pulsed saturation RF pulses was applied followed by a 2D RF-spoiled GRE readout of a single slice on a 3T clinical MR scanner (Siemens Magnetom Trio). The CEST parameters were: B1-CWAE (continuous-wave amplitude equivalent) = 0.4 µT, pulse duration PD and interpulse delay IPD = 100 ms, number of CEST pulses = 10. In order to determine the pH value, a phantom was used with 8 tubes filled with a 100 mM Iopamidol solution with pH values in the range of 5.75 to 7.5 with an interval of 0.25. The CEST curves were determined and the saturation transfer of both Iopamidol peaks at 4.2 ppm and 5.5 ppm were calculated in order to determine the ratiometric saturation transfer R_{ST} according to Longo et al [1]. 20 measurements were performed to derive a calibration curve, which enables the determination of pH values. One patient (female, 66 years old), who had previously undergone a contrast-enhanced CT scan with Iopamidol, was measured with the Iopamidol-CEST-sequence at 3T. During post-processing, a R_{ST} image was calculated and converted into a pH map. The region in the image including an appropriate amount of Iopamidol was automatically recognized and the pH value in this region was determined. Afterwards, the pH of the urine was determined with a pH-meter (Mettler Toledo).

Results: Fig. 1 shows the CEST curves for different pH values. At low pH values, both Iopamidol peaks are clearly visible. Especially the first peak increases with increasing pH values. At high pH values, both peaks broaden and the peak at 5.5 ppm vanishes. Fig. 2 shows the calibration curve for the pH values in dependence of the R_{ST}. From pH = 5.75 to pH = 7, a decrease of R_{ST} values is clearly visible, thus enabling the determination of pH in this range. Fig. 3 shows the anatomical as well as the pH map obtained from in vivo CEST imaging of the bladder. Only in the red encircled region, a sufficient amount of Iopamidol was detected by an automatic algorithm. The average pH value of the ROI was 6.66 ± 0.34. The pH value measured by the pH-meter in urine was 6.72.

Discussion: The phantom results show, that a pH determination with Iopamidol in the range of 5.75 to 7 is possible. The first human in vivo measurements in the human bladder support this result.

Conclusion: CEST MR imaging using Iopamidol as a contrast agent seems to be a suitable quantitative in-vivo pH imaging method. Further studies in humans are required to determine the potential diagnostic value of this technique, as for example in patients with cancer or renal diseases.

References:

1. Longo DL, Dastrù W, Digilio G, et al. Iopamidol as a responsive MRI-chemical exchange saturation transfer contrast agent for pH mapping of kidneys: In vivo studies in mice at 7 T. *Magn Reson Med*. 2011;65(1):202–211.
2. Gillies RJ, Raghunand N, Garcia-Martin ML, Gatenby RA. pH imaging. A review of pH measurement methods and applications in cancers. *IEEE Eng Med Biol Mag*. 2004;23(5):57–64.
3. Miranda DM, Oliveira EA, Silva ACSE. Molecular pathophysiology of renal tubular acidosis. *Curr. Genomics*. 2009;10(1):51–59.
4. Schmitt B, Zaiß M, Zhou J, Bachert P. Optimization of pulse train presaturation for CEST imaging in clinical scanners. *Magnetic Resonance in Medicine*. 2011;65(6):1620–1629.