MR spectroscopy of prostate metabolism

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Synopsis: MR spectroscopy of the human prostate provides metabolic information, valuable in the diagnosis of cancer (1,2). Citrate is a major metabolite in the prostate accumulating in large amounts , but knowledge about its metabolism is limited. The signal for citrate decreases in tumor tissue while the signal for choline compounds increases. Despite the clinical potential of MRS its application is hampered by the limited robustness of the current measurement methods. We will present new approaches to overcome the limitation of these methods. In addition we will present new ^{13}C tracking data providing a quantitative view of prostate cell metabolism supporting citrate synthesis.

Adiabatic pulses. Volume selection in ^{1}H MR spectroscopic imaging (MRSI) of the prostate at 3T is commonly performed with a PRESS sequence using low-bandwidth refocusing pulses. However, their large chemical shift displacement error (CSDE) causes lipid signal contamination. As the application of high-bandwidth adiabatic pulses is limited by RF power we equipped a semi-LASER sequence with low RF power demanding Gradient-modulated Offset-Independent Adiabaticity (GOIA) refocusing pulses with WURST(16,4) modulation. These GOIA pulses select slices with a flat top, sharp edges and minimal CSDE. The sequence was tuned to an optimal citrate signal shape. High quality spectra with reduced lipid artifacts were obtained from the whole prostate. Compared to PRESS acquisition the SNR of citrate is increased up to 2.6 and choline up to 1.3. Thus prostate MRSI is possible with limited lipid contamination and improved SNR, facilitating routine clinical acquisition of metabolic data. We also demonstrate that this is possible without water signal suppression.

Spiral k-space sampling: Cartesian k-space sampling in 3D MRSI limits the selection of voxel size and acquisition time. Therefore, large prostates are often scanned at reduced spatial resolutions to stay within acceptable measurement times. We modified a GOIA- sLASER sequence with spiral k-space acquisition (GOIA-sLASER-Spiral) for fast prostate MRSI with enhanced resolution and extended matrix sizes. This acquisition allowed to obtain MR spectra in ~5min comparable to those acquired with a Cartesian PRESS protocol in ~9min, or at an enhanced spatial resolution showing more precise tissue allocation of metabolites. The flexibility of spiral sampling enables prostate MRSI with variable resolutions and FOVs without increases in acquisition times and is suitable for routine clinical exams.

No endorectal coil: Prostate 3D ^{1}H-MRSI is commonly applied with an endorectal coil. However, currently in prostate MRI this is replaced by more comfortable multichannel body coils. We demonstrate that thanks to an increased SNR it is possible to apply a GOIA-sLASER for volume selection in ^{1}H MRSI with good quality spectra at a clinical useful spatial resolution within 10 minutes

Carbon sources & pathways for secreted citrate. We mapped these in citrate-producing human prostate cancer metastasis cell lines using ^{13}C substrates to track ^{13}C labeling of citrate by ^{1}H and ^{13}C NMR spectroscopy. We provide direct evidence that glucose and glutamine are main carbon sources for secreted citrate. Pyruvate partly enters the Krebs cycle via pyruvate carboxylase. Glutamine contributes to citrate partly via reductive carboxylation. A probabilistic model to describe citrate metabolism, indicated that less than 50% of citrate leaves the Krebs cycle at every turn. Citrate ^{13}C ratios in this model may serve as biomarkers for epithelial cell metabolism and cancer.

1. In vivo MR spectroscopic imaging of the prostate, from application to interpretation. Tayari N, Heerschap A, Scheenen TWJ, Kobus T. Anal Biochem. 2017 Jul 15;529:158-170..
2. Mapping of prostate cancer by ^{1}H MRSI. Kobus T, Wright AJ, Scheenen TW, Heerschap A. NMR Biomed. 2014 Jan;27(1):39-52.