

gagCEST MRI: A potential biomarker for post-surgery follow-up of patients with anterior cruciate ligament reconstruction

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Target Audience:

Scientists interested in CEST imaging.

Purpose:

Nowadays, tendon and ligament disease and injury result in instability of the knee. Its incidence is very high and represents a major health – care burden¹. Anterior cruciate ligament (ACL) reconstruction has become a common procedure for injuries of the ACL. Recently introduced Glycosaminoglycan Chemical Exchange Saturation Transfer (gagCEST) MR technique has shown to be sensitive to alterations in the biochemical composition of cartilage in the knee in patients following cartilage repair surgery as well as in vertebral disks^{2,3}. The purpose of this study was to investigate the feasibility of gagCEST imaging and T2* mapping in post-surgery monitoring of biochemical and morphological properties of reconstructed tissue in the patients with ACL substitution.

Subjects and Methods:

Seven patients (mean age 27±7 years) with previous history of ACL reconstruction were examined in early post surgery phase (0-12 months) and late post surgery phase (12 - 24 months). Institutional Review Board (IRB) approval as well as written informed consent from patients were obtained prior the measurements. Imaging was performed on a 7T MRI scanner (Siemens Medical Solutions, Erlangen, Germany) using a 28-channel Tx/Rx knee coil (QED, OH, USA). For gagCEST imaging, CEST effects were prepared by a train of Gaussian RF pulses followed by signal readout with a 3D RF spoiled GRE sequence. The saturation parameters were: B1-CWAE (continuous wave amplitude equivalent) = 0.8 μ T, pulse duration PD = 99 ms, interpulse delay IPD = 100 ms, number of CEST pulses = 5. The GRE imaging parameters were: FOV = 132 x 170 mm², slice thickness = 3 mm, TR/TE = 7.9 ms /3.5 ms, spatial resolution = 0.7 mm x 0.7 mm, flip angle = 9°, acquisition duration (min:sec) = 11:17. The CEST curves were calculated for each pixel and were shifted for the water resonance to appear at 0 ppm of the Z-Spectrum. MTRasym (δ) was calculated as $MTR(+\delta) - MTR(-\delta)$ integrated over the offset range δ from 0.5 to 2ppm, which corresponds to the resonance frequencies of exchangeable hydroxyl protons of glycosaminoglycans. The GRE sequence parameters were as follows: TR = 23 ms, 25 echoes with TEs from 1.2 to 16.9 ms, FOV = 119 x 225 mm², slice thickness = 1 mm, flip angle 11°, acquisition time (min:sec) = 13:33. T2* maps for all patients were calculated offline, using a custom-written script in IDL 6.0 (Interactive Data Language, Research Systems, Inc., Boulder, CO, USA). A mono-exponential fitting procedure was performed on all MR data sets on a pixel-by-pixel basis. For mono-exponential fitting, a two-parametric function was used to fit the signal intensity $SI = A_0 \cdot \exp(-TE/A_1)$ where A_0 corresponds to the proton density, A_1 corresponds to the actual T2*. CEST effect and T2* were evaluated by placing the regions of interest (ROIs) at three areas (in the regions of tunnels in distal femur (I), tibia (II) and region in-between (III)) and statistical evaluation was performed (Paired – Samples T test; SPSS16; Chicago, IL, USA).

Results:

Measured gagCEST effects and T2* relaxation times values in three different regions of reconstructed ACL are summarized in Table 1. Results showed a significant difference in gagCEST effect between early and late postsurgery phase in all regions (CI = 95% , (I: p=0.009; II: p=0.032 ; III: p=0.044)). CEST effect showed an increase in time in six patients and in all regions (Fig.1-a). In only one patient CEST value was lower in region III comparing in two post-surgery phases. T2* maps showed a decrease in all individual patients, which was statistically significant during post-surgery period (CI = 95%, (I: p=0.002; II: p=0.011 ; III: p=0.013)) (Fig.1-b).

Table: 1. Calculated mean CEST values and T2* relaxation times and corresponding standard deviations for three different region in early and late post-surgery phase after ACL reconstruction

Region	CEST \pm SD [au]		T2* \pm SD [ms]	
	early	late	early	late
I	7.7±0.6	11.9±1.4	6.3±0.8	4.5±0.8
II	7.6±0.2	12.8±1.2	5.7±0.9	4.5±0.4
III	8.0±0.5	11.0±1.5	6.4±0.9	5.3±1.0

Discussion:

Our results showed an increase of gagCEST values during the post-surgery period. This can be related to the change in the total GAGs content in the tissue. T2* relaxation time, affected by alterations in collagen architecture network and/or water content over the time after surgery, showed a significant decrease. This can be attributed to the changes in morphologic and biochemical properties of tendon tissue during „ligamentization“ process.

Conclusion:

Preliminary results of this study show that gagCEST has a great potential as a biomarker in the post surgery monitoring of biochemical properties of newly developed ligament tissue in patients after ACL reconstruction.

References:

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- [2] Schmitt et al. *Radiology*. 2011;260(1):257–264.
- [3] Kim et al. *NMR Biomed*. 2011;24(9):1137–1144.

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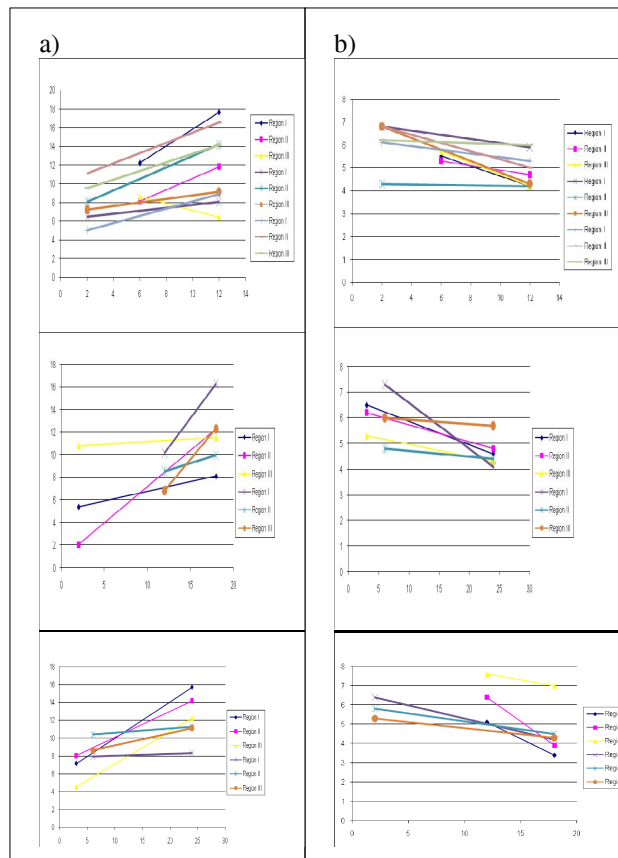


Figure 1. Graphical presentation of (a) CEST values (b) T2* relaxation times obtained from all ROIs in 3 different regions (I, II, III) of new ligament tissue during post-surgery follow up.