# Evaluation of a collagen-gel based cartilage repair method using zonal variation in T2-mapping and dGEMRIC

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**Target audience**

Musculoskeletal radiologists, OA scientists

**Purpose**

CaReS® (Arthro Kinetics Biotechnology GmbH, Krems, Austria) is an available matrix associated autologous chondrocyte transplantation (MACT) product, based on collagen type I gel [1]. Quantitative MRI methods like T2-mapping and delayed Gadolinium-Enhanced-MRI of Cartilage (dGEMRIC), play an important role in the evaluation of cartilage repair tissue (RT). The purpose of this study was to investigate the RT structure after MACT with CaReS in the knee. To our best knowledge, this is the first study that includes zonal dGEMRIC evaluation in the follow up of CaReS®.

**Methods**

Fourteen knees of 14 patients (mean age 38.1±10.0) with a mean follow-up of 2.0±0.9 years were included in this cross sectional study. All MRI examinations were performed on a 3.0-Tesla MRI-unit (Tim Trio, Siemens Healthcare, Erlangen, Germany) using a dedicated eight-channel knee coil (Invivo, Gainsville, FL, USA). For morphological evaluation a PD FSE sequence in the sagittal plane (TR/TE 2670/36 ms; FOV 120 mm; Matrix 512*512; resolution 0.2*0.2*2.0 mm; slice thickness 2.0; acquisition time 06:53 min) and an isotropic T2 weighted True-FISP sequence in the sagittal plane (TR/TE 7.7/3.9 ms; FOV 192*192 mm; Matrix 384*384; resolution 0.5*0.5*0.5 mm; slice thickness 0.5; acquisition time 06:03 min) was applied. Quantitative T2-mapping was done with a multi echo spin echo sequence (TR/TE 1200/13.8, 27.6, 41.4, 55.2, 69.0, 82.8 ms; FOV 160*160 mm; Matrix 320; resolution 0.5*0.5*3.0 mm; slice thickness 3.0; acquisition time 03:40 min). For quantitative T1 mapping (dGEMRIC) a 3D gradient echo based dual flip angle sequence (VIBE) was applied (TR/TE 15/2.0 ms; FOV 160*160 mm; Matrix 384*384; resolution 0.4*0.4*3.0 mm; slice thickness 3.0; acquisition time 06:28 min). The same sequence was used both before and after intravenous administration of anionic Gadolinium-DTPA. The dGEMRIC protocol reported by Burstein et al. was followed [2]. Regions of interests (ROI) were manually selected by a senior radiologist with a special interest in musculoskeletal MRI within the RT and the native surrounding cartilage (NC) on three continuous slices to cover the whole repair site in T2-maps, and pre- and post-contrast T1-maps. The deep and the superficial layer were measured separately, both in T2-maps and in dGEMRIC images (Fig. 1). For morphological assessment, the MOCART score was used [3]. The clinical evaluation was performed preoperatively and on the day of the MRI using the International Knee Documentation Committee (IKDC) subjective form, Lysholm score, and a modified Cincinnati rating.

**Results**

A significant difference in T2-values of the RT and the NC was not detected, but a significant difference in the mean dGEMRIC index was found (Table 1). A significant difference in zonal values in T2-values as well as in dGEMRIC index in both, the RT and the NC (Table 1) was observed. The mean MOCART score was 81.1 ± 9.8 points. All clinical scores improved significantly (Table 2).

| | T2-map | T1-map |
|---|---|---|
| **Repair Tissue** | 37.3 ± 5.9 | 564.1 ± 137.2 |
| **Native Cartilage** | 39.6 ± 5.1 | 790.9 ± 196.3 |
| **p-value** | = 0.281 | = 0.002 |
| **RT – deep** | 34.8 ± 6.7 | 630 ± 170 |
| **RT – superficial** | 39.8 ± 5.7 | 499 ± 114 |
| **p-value** | = 0.003 | < 0.001 |
| **NC – deep** | 38.5 ± 5.1 | 885 ± 236 |
| **NC – superficial** | 40.7 ± 5.4 | 697 ± 162 |
| **p-value** | < 0.001 | < 0.001 |

Table 1: T2-values and dGEMRIC index in the RT and the NC as well as zonal variation

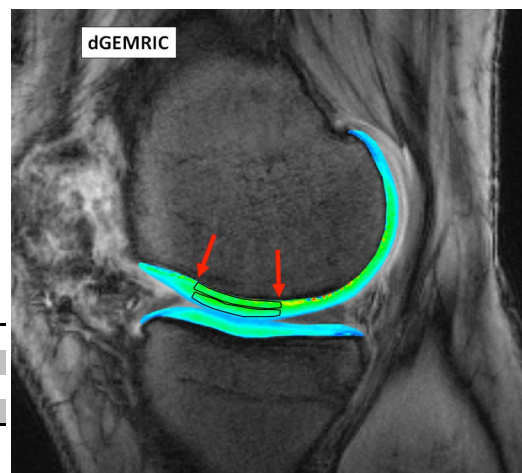| | preOP | postOP | p-value |
|---|---|---|---|
| **Subj. IKDC** | 57.5 | 68.3 | 0.041 |
| **Lysholm** | 60 | 85.5 | 0.041 |
| **Mod. Cincinnati** | 4 | 7.5 | 0.019 |

Table 2: Median values of the assessed scoring systems



Figure 1: Example dGEMRIC map with zonal evaluation

**Discussion**

The T2-mapping results suggest a similar water content and collagen structure in the RT compared to the surrounding NC. Not only T2 but also the dGEMRIC results demonstrate zonal differences, with lower values in the superficial layer and higher values in the deep layer. This suggests a gradual increase in proteoglycan content of repair tissue from the superficial to the deep layer.

**Conclusion**

Our results suggest a zonal organization of repair tissue after MACT with CaReS similar to native cartilage, with zonal differences in collagen structure, and proteoglycan content.

**References:**

1. Schneider, U. et al.: A prospective multicenter study on the outcome of type I collagen hydrogel-based autologous chondrocyte implantation (CaReS) for the repair of articular cartilage defects in the knee. Am J Sports Med. 39, 2558–2565 (2011).
2. Burstein, D. et al.: Protocol issues for delayed Gd(DTPA)(2-)-enhanced MRI (dGEMRIC) for clinical evaluation of articular cartilage. Magn Reson Med. 45, 36–41 (2001).
3. Marlovits, S. et al.: Magnetic resonance observation of cartilage repair tissue (MOCART) for the evaluation of autologous chondrocyte transplantation: determination of interobserver variability and correlation to clinical outcome after 2 years. Eur J Radiol. 57, 16–23 (2006).