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Quantitative 3D MRI as a Valid Endpoint for Randomized Clinical Trials in Cartilage Repair and its Correlation with Repair Tissue Collagen Architecture

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Summary:

Standardized quantitative 3D MRI was used in a multicenter clinical trial and demonstrated structural superiority of BST-CarGel® treatment over microfracture with regards to both the quantity and quality of repair cartilage. Such improved repair cartilage structure may predict superior durability and sustained clinical benefit. T2 MRI correlated with both PLM and the degree of lesion filling.

Abstract:

Purpose:

Cartilage repair clinical trials should evaluate repair tissue structure as well as clinical benefit to assess biomechanical function of the repair and the potential for long term durability. Newer MRI techniques offer non-invasive quantification of both quantity and quality of repair. A standardized quantitative 3-dimensional (3D) MRI was used as the primary endpoint (repair tissue quantity and quality) of a cartilage repair RCT comparing BST-CarGel[®] (Piramal Healthcare (Canada) Ltd.) treatment to the microfracture control.

Materials and Methods:

A multicenter trial comparing BST-CarGel[®] treatment[1] to microfracture enrolled 80 patients (BST-CarGel[®] n=41, MFX n=39), with grade III/IV focal lesions on the femoral condyles. Standardized MRI scans were obtained from each patient using 3D fat-suppressed SPGR and 3D-GRE for morphological analysis, and fat-suppressed Dual Echo Spin Echo for T2 mapping. Condyles were reconstructed in 3D with semi-automated (radiologist corrected) morphological segmentation using an anatomical atlas and validated methodologies.[2] Co-registration of 1 month to 12 month scans permitted Lesion % Fill to be calculated from the ratio of new repair tissue volume at 12-months to the baseline cartilage lesion volume at 1-month post-treatment. Average T2 values at 12 months, which reflect collagen macromolecular content, organization and tissue hydration, were derived from the entire repair tissue volume as well as from separate zones representing the top and bottom halves of the repair tissue. Histological sections from 13-month elective osteochondral biopsies (BST-CarGel[®] n=21, MFX n=17) were evaluated using a validated PLM score[3-4] for collagen architecture and zonal stratification. Pre-specified linear and non-linear statistical models were applied to investigate potential associations between matched T2, PLM scores and Lesion % Fill.



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Results / Discussion:

Blinded MRI analysis revealed a significant improvement in Lesion % Fill (p=0.0105) for BST-CarGel® treatment compared to microfracture as well as more native cartilage-like average T2 values (p=0.0330). BST-CarGel treatment also resulted in improved repair tissue stratification. This improvement in repair cartilage structure may predict superior durability and sustained clinical benefit. ANCOVA found that both PLM and Lesion % Fill were significant co-factors in explaining the T2 response (p=0.02, 0.003 respectively), revealing a multiple correlation coefficient of R=0.62. Importantly, this correlation was not dependent on treatment.

Conclusion:

Standardized quantitative MRI was able to accurately detect repair tissue structural differences in the context of a multicenter clinical trial. The superiority of BST-CarGel® treatment over microfracture with regards to both the quantity and quality of the repair cartilage was demonstrated, which may predict superior durability and sustained clinical benefit. Furthermore, T2 MRI was shown to be an intrinsic, multifactorial measure of repair tissue quality, which may depend on both repair tissue quality (PLM) and quantity (% Fill).

1) Shive et al., in Operative Techniques in Orthopaedics, Chap. 16, 271-8 (2006)

- 2) Tamez-Peña JG et al., IEEE Trans Biomed Eng, 59(4), 1177-1786 (2012) 3) Changoor et al., Osteoarthritis Cartilage, 19(1):126-35 (2011)
- 4) Changoor et al., Osteoarthritis Cartilage, 19(12):1458-68 (2011)