

## INDUCED PLURIPOTENT STEM CELLS IN CARTILAGE REPAIR

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The generation of functional cartilage tissue using stem cells is promising to be an important advance in regenerative medicine. Although progress has been made using adult mesenchymal stem cells, these cells suffer from limited accessibility, senescence upon expansion, donor and clonal variability and the generation of immature tissue. Investigating more potent stem cells such as human induced pluripotent stem cells (hiPSCs) could overcome a lot of those limitations but it also comes with its unique challenges. Whilst similar to embryonic stem cells they show differences in their epigenetic signature, suggesting different signalling requirements for differentiation. In-depth understanding of the signals that regulate cartilage development is paramount for harnessing the power of hiPSCs. We report a simple, chemically defined, efficient, scalable and reproducible protocol for the differentiation of hiPSCs toward chondrocytes that can be used to engineer mature cartilage *in vitro* and *in vivo*.

## IMPROVED MR SCORING SYSTEM FOR OUTCOME ANALYSIS OF CARTILAGE REPAIR PROCEDURES

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Articular cartilage and its supporting bone are tightly coupled and should be viewed as a connected unit. New treatments are emerging aiming at the regeneration of the entire osteochondral structure, but MRI evaluation scores are mainly focused on the superficial cartilaginous layer. The aim of this study is to analyze the MRIs obtained after transplantation of an osteochondral scaffold in order to develop a score for the assessment of the imaging appearance of the regenerated tissue quality, both at the cartilage and bone level, and its correlation with the clinical outcome.

Ninety-one MRIs of patients treated with a cell-free collagen-hydroxyapatite osteochondral scaffold for lesions of the knee articular surface were considered (71 men, 20 women, age at surgery  $31.2 \pm 11.5$  years, defect size  $2.8 \pm 1.6$  cm<sup>2</sup>, 38 affected by degenerative and 14 by traumatic cartilage lesions, and 39 by OCD). All MRIs were performed at 2 years of follow-up. MOCART, the most commonly applied MRI scoring system for cartilage evaluation, was used for developing the osteochondral imaging evaluation tool, by expanding the focus also on the subchondral structure and adapting the scores attributed to each parameter according to their correlation with the clinical outcome.

The MRI analysis showed no correlation between MOCART score and the clinical outcome (IKDC subjective score  $75.7 \pm 15.4$ ). The results of the multivariate analysis, performed to assess the correlation of each osteochondral score parameter with the clinical outcome, were used to attribute the score to each parameter to develop a 0-100 MRI score. Statistical analysis confirmed the correlation between the MRI results and the clinical outcome, both for the overall group and the patellar lesions ( $p=0.008$  and  $p=0.038$ , respectively). With a few exceptions, patients clinically successful with an IKDC > 80 also had an MRI osteochondral score of at least 70 ( $p=0.002$ ).

In conclusion, after reducing the parameters for cartilage layer evaluation and expanding the focus on the subchondral layer, 7 parameters were selected: degree of filling and integration, surface appearance, signal intensity with DP FAT-SAT, subchondral bone appearance and edema, effusion. The new osteochondral score correlated with the clinical outcome, proving to be an useful tool for the study of tissue maturation after the implantation of scaffolds for osteochondral regeneration.

## IMAGING TECHNOLOGIES IN TISSUE ENGINEERING

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### Introduction

Monitoring the parameters oxygen, pH or CO<sub>2</sub> is of great interest in many fields in cell biology and medical research. The knowledge on these parameters gives evidence on the metabolic status of cells, spheroids, engineered or native tissue. Ideally, a detection method should be non toxic and non invasive and at the same time the respective analyte should not be consumed during an online measurement. We