Nasal chondrocyte-engineered implants: a functional treatment for severe articular cartilage lesions?

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INTRODUCTION:

Cartilage lesions of the knee joint are injuries classified according to the degree of their severity. Acute lesions have a favorable prognostic outcome, therefore can be healed to a certain degree with a number of available cell-based treatments or bioengineered implants. Chronic, more complex lesions, such as ”kissing” cartilage lesions formed on two opposite sides of the joint have been so far classified untreatable, as they are considered an early degenerative pathology of a high risk for osteoarthritis development.

Chondrocytes isolated from nasal septum cartilage have been shown *in vitro* to possess a greater chondrogenic potential over traditional cell sources as articular chondrocytes or stem cells. This alternative cell source was used to design a bio-implant of excellent stability and capacity for articular cartilage healing, as demonstrated in recent preclinical and clinical studies (Mumme *et al.*, 2016a; Mumme *et al.*, 2016b).

We have investigated in a preclinical study the potential of the implant in repair of the articular “kissing” cartilage lesions. Moreover, we have generated a higher maturity-grade-implant to examine its effect on integration to native cartilage and quality of the repair process.

METHODS:

The preclinical investigation was conducted under the authorization of ethics committee (approval HR-POK-020), using 20 sheep. Osteochondral kissing lesions of 6 mm diameter and 2 mm depth were first introduced on two opposite sides of the patellofemoral joint, in trochlea (Fig. 1A) and patella. Immediately after, autologous nasal septum chondrocytes seeded on a collagen scaffold and cultured for 2 days and 2 weeks generating immature or mature tissue, respectively, were implanted and retained in the defect for 6 weeks or 6 months. Efficacy of the repair was first evaluated macroscopically (Fig. 1B), scoring the ICRS scale I. Statistical significance was evaluated by Student’s t-test for comparison between two groups. Osteochondral explants were further assessed histologically through the morphology analysis of repaired tissue and its matrix content, evidenced by staining and immunohistochemistry.

RESULTS SECTION:

Our results so far obtained on three to five sheep per group show that 6 weeks after the implantation, immature and mature implants are retained and well integrated within the adjacent native cartilage in the majority of created defects. As evidenced from the morphology, an early cartilage healing is initiated in a high number of sheep, regardless of the implant type. The quantification of overall macroscopic repair suggests a significant improvement in quality of the repaired cartilage, 6 months after the treatment. In these sheep, all the defects are filled with a newly formed repair tissue, lacking the proper structural organization typical of native cartilage. However, notable collagen type II, aggrecan and glycosaminoglycan matrix content, and a low amount of fibrous collagen type I, particularly within the group treated with immature implant, reveal a significant cartilage repair in both sites of the “kissing” lesion (Fig. 1C).

DISCUSSION:

We have demonstrated a great regenerative potential of the cartilage implant engineered from nasal chondrocytes in healing of articular “kissing” cartilage lesions. The cartilage defects introduced in the knee joint of sheep were replaced by a tissue of the matrix composition highly similar to healthy articular cartilage. However, the quality of the repair could not be further improved by a prolonged *in vitro* culturing of the bio-implant. The reached repair point will be additionally assessed by MRI analysis and microscopic quantification of the repair.

As the relatively short duration of the treatment was not sufficient for the newly formed cartilage to express its native structural properties, a longer endpoint study will be necessary to predict a veritable quality of the repair process. Considering the ability of collagen scaffold to repair the cartilage, an additional study applying scaffold treatment only is under investigation in our laboratory.

SIGNIFICANCE/CLINICAL RELEVANCE:

The nasal chondrocyte-based implant tested in our preclinical study has a high potential to be used as a novel efficient treatment for both acute and chronic lesions, thus overcoming limitations of the existing treatments designed for acute lesions only. This prosperous therapy may affect thousands of patients currently in line for a successful treatment of severely damaged cartilages.

REFERENCES:

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IMAGES AND TABLES:

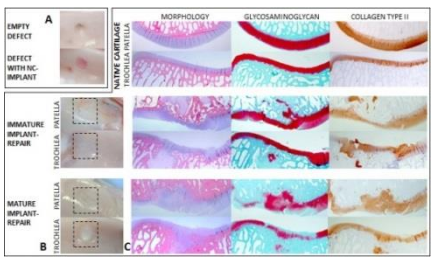

Figure 1.

A) Appearance of the “kissing” lesion defect in trochlea – empty and when filled with nasal chondrocyte (NC)-engineered implant.

B) The highest macroscopic degree of cartilage repair in the “kissing” lesion of patella and trochlea evidenced after the 6-month treatment with immature and mature NC implant. The repaired defect is placed inside the marked square.

C) Microscopic quality of the repair assessed from the morphology and matrix composition analyses of glycosaminoglycan and collagen type II, as compared to healthy, native cartilage in sheep. The evaluated parameters were evidenced by hematoxylin and eosin staining, safranin-O staining and immunohistochemistry, respectively.