in the experimental group of animals. One group was implanted with autologous tissue grafts engineered from scaffold and articular chondrocytes. In one group cell free scaffolds were implanted while last group served as negative control in which only conversion of defect was performed, but it was left untreated. Animals were sacrificed and tissue analysis was performed at three different time points: 6 weeks, 3 months and 12 months after the implantation. Tissue analysis included macroscopic, microscopic and molecular evaluation. Microscopic analysis included different stains (hematoxylin-eosin, safranin O, picrosirius) and immunohistochemistry (collagen I, II and aggrecan). Semi-quantitative data of morphology were obtained with histological score ICRS II. ELISA and DMMB assays were performed to quantify the amount of collagen I, II and glycosaminoglycans in repair tissue.

Results confirmed the feasibility of production of autologous cartilage tissue grafts from nasal septum chondrocyte for treatment of condyle cartilage defects. Furthermore, nasal chondrocyte grafts showed promising results in restoration of damaged articular cartilage.

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CARTILAGE TISSUE ENGINEERING FROM NOSE2KNEE: 12-MONTHS RESULTS OF A PHASE 1 CLINICAL TRIAL

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Purpose

As compared to commonly used cell based treatments for articular cartilage repair, grafting of cartilage tissues, engineered in vitro to reach a mature stage, could result in more durable repair. To reduce the variability in the quality of the engineered tissue grafts, nasal chondrocytes were used as a cell source with reproducible chondrogenic capacity. The purpose of this phase-1 study was to demonstrate safety and feasibility of the procedure. Preliminary indications on efficacy after 12 months are also presented.

Material and methods

Ten patients with symptomatic, post-traumatic full-thickness cartilage lesions (2-8cm2) on the femoral condyle/ trochlea were treated. Patients underwent nasal

septum cartilage biopsy in an outpatient procedure. Autologous nasal chondrocytes were isolated, expanded, seeded and cultured in collagen sponges (Chondrogide®, Geistlich) according to Good Manufacturing Practice (GMP) regulations. After four weeks production, the engineered nasal cartilage graft was implanted via mini-arthrotomy.

Patients were followed up radiologically by MRI (MOCART score), delayed Gadolinium Enhanced MRI (dGEMRIC, for assessment of glycosaminoglycans content) and clinically (IKDC score).

Results

No complications occurred by nasal cartilage biopsying or implantation of the engineered tissues,

10 patients with 12 cartilage defects reached 12 months follow up so far. One patient with 1 defect partially lost the graft due to new sports injury and was excluded from analysis. The MOCART score 12 months post-surgery was 41.3 (5-60). The dGEMRIC revealed a relative ΔR1 of 1.40 (0.78-2.17). The IKDC pre-surgery and 12 months post-surgery was 46.5 and 75.6 respectively. The KOOS pre-surgery and 12 months post-surgery was 63.9 and 81.3 (Symptoms), 70.4 and 88.9 (Pain), 76.1 and 93.2 (ADL), 36.1 and 69.4 (Sport), 41.7 and 57.0 (QoL).

Conclusion

These early results demonstrate safety and feasibility of the method and indicate that engineered nasal cartilage grafts can participate to the repair of articular cartilage defects in the knee. The mean relative ΔR1 of 1.40 (1.0 for native cartilage) suggests that hyaline repair tissue can be achieved, possibly to a higher extent than MACT (2.18, Trattnig+, 2008) or ACT (2.40, Trattnig+, 2007). Our results demonstrate safety and feasibility of the method and indicate that patients can benefit from this therapy.

This study opens a new approach in biological cartilage regeneration, based on engineering of mature cartilage tissues using autologous nasal chondrocytes.

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