Injury, Int. J. Care Injured 47S6 (2016) S27–S32

Contents lists available at ScienceDirect

Injury

journal homepage: www. elsevier.com/locate/Injury

A novel aragonite-based scaffold for osteochondral regeneration: early experience on human implants and technical developments

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KEYWORDS

Cartilage
Osteochondral repair
Biphasic
Aragonite
Scaffold
Knee

ABSTRACT

Introduction: Chondral and osteochondral lesions represent a debilitating disease. Untreated lesions remain a risk factor for more extensive joint damage. The objective of this clinical study is to evaluate safety and early results of an aragonite-based scaffold used for osteochondral unit repair, by analysing both clinical outcome and MRI results, as well as the benefits of the procedure optimization through novel tapered shaped implants.
Methods: A crystalline aragonite bi-phasic scaffold was implanted in patients affected by focal chondral-osteochondral knee lesions of the condyle and trochlea. Twenty-one patients (17 men, 4 women with a mean age of 31.0 ± 8.6 years) without severe OA received tapered shaped implants for the treatment of 2.5 ± 1.7 cm^2 sized defects. The control group consisted of 76 patients selected according to the same criteria from a database of patients who previously underwent implantation of cylindrical-shaped implants.
The clinical outcome of all patients was evaluated with the IKDC subjective score, the Lysholm score, and all 5 KOOS subscales administered preoperatively and at 6 and 12 months after surgery, while MRI evaluation was performed at the 12 month follow-up.
Results: A statistically significant improvement in all clinical scores was documented both in the tapered implants and the cylindrical group. No difference could be detected in the comparison between the improvement obtained with the two implant types, neither in the clinical nor in imaging evaluations. A difference could be detected instead in terms of revision rate, which was lower in the tapered implant group with no implant removal – 0% vs 8/76–10.5% failures in the cylindrical implants.
Conclusions: This study highlighted both safety and potential of a novel aragonite-based scaffold for the treatment of chondral and osteochondral lesions in humans. A tapered shape relative to the cylindrical shaped implant design, improved the scaffold's safety profile. Tapered scaffolds maintain the clinical improvement observed in cylindrical implants while reducing the postoperative risk of revision surgery. This aragonite-based implant was associated with a significant clinical improvement at the 12 month follow-up. Moreover, MRI findings revealed graft integration with good bone and cartilage formation.

Introduction

Chondral and osteochondral lesions represent a debilitating disease, which if left untreated would progress to more extensive joint damage eventually leading to the development of osteoarthritis [1]. Clinical and research activities are ongoing in an effort to improve outcomes and over the years different surgical techniques have been suggested [2]. Among these, regenerative scaffold-based procedures are emerging as a potential therapeutic option, with an increasing number of publications every year on *in vitro*, preclinical animal studies and clinical applications [3,4], but none has shown tissue healing with biomechanical properties that match the physiological condition.

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Lately, the awareness of the involvement of subchondral bone in many of these lesions, resulted in the development of cell-free treatment strategies focused on the entire osteochondral unit [5–7], and currently heterogeneous scaffolds have been proposed that combine distinct but integrated layers corresponding to the cartilage and bone regions to regenerate both components of the osteochondral unit to restore the articular surface [8–11].

Most scaffolds attempt to regenerate the articular cartilage by implantation of soft biomaterials to act as a cartilage surrogate that is supposed to allow surface reconstitution. Recent literature described a different approach to target osteochondral regeneration: an aragonite-based bi-phasic scaffold, which showed promise in the preclinical model [12,13]. To date, only a preliminary report in humans has been published, with positive results at 24 months for the treatment of a patient affected by a chronic posttraumatic cartilage lesion of the knee [14]. However, prior to wide range clinical application, it is important to document both safety and feasibility of this procedure, which is based on the implant of a scaffold relying on a press-fit fixation. Considering that sufficient attachment and graft stability in the early period are essential for the successful outcome of any technique, since an insufficient graft fixation may facilitate the detachment of the transplanted biomaterial and lead to treatment failure [15], we focused on the stability evaluation of this procedure, which has been first developed with cylindrical implants and recently optimized through a new shape for tapered implants. To document the early postoperative adherence rate in humans, invasive approaches are not appropriate due to patient safety concerns and disruption of the primary stability. Thus, magnetic resonance imaging (MRI) is useful as a non-invasive technique for the analysis of the morphological status of cartilage defects and the repair tissue throughout the postoperative period [16,17]. In the current work, we evaluated both early clinical results as well as MRI imaging of a pilot group of patients undergoing implantation of the tapered aragonite-based scaffold with the objective to compare the results of treatment to a historical control of patients who previously underwent cylindrical scaffold implantation.

Materials and methods

Scaffold characteristics and implantation procedure

The implant (Agili-C™, CartiHeal, Israel) consists of a natural crystalline aragonite, derived from corals, to which hyaluronic acid (HA) is added. The natural aragonite, possess a nano-rough structure as well as interconnecting porosity that allows to stimulate cell adhesion and proliferation as well as matrix production [18]. A square grid pattern of 2 mm deep drilled channels is made in the top part, using Bungard CCD, a CNC drilling and routing machine and an appropriate drill-bit as described in US patent application 20120177702 & 20120189669. HA is added to the top part of the implant. A preliminary preclinical study in a goat model showed the benefit of a scaffold configuration with mechanical modification through micro-drilling of the top layer and HA added to it [12]; the early potential of both bone and cartilage formation at 6 months was confirmed by a subsequent study of the same model at 12-month follow-up with scaffold degradation and osteochondral regeneration [13]. Thus this scaffold configuration was used and developed in the shape of cylinders for the treatment of both chondral and osteochondral defects in humans. Recently, a tapered version of the implants, with an angle of 2 degrees from the longitudinal axis, has been designed to improve the press-fit implantation (Figure 1). Before the clinical application, an extensive purification process is performed to treat and remove trapped particles, debris and organic remnants, and the implants are sterilized by 25 kGy gamma radiation.

The surgical procedure is performed with the patient under anesthesia and in the supine position. A pneumatic tourniquet is placed on the proximal thigh and a mini arthrotomy medial or lateral parapatellar approach is used to expose the lesions. The defect is then prepared using proprietary surgical toolset (Cartiheal, Israel). A perpendicular aligner is used to center the lesions and place a K-wire, which is used to correctly position a drill sleeve where a motorized drill is inserted to prepare the defect up to the desired depth. A reamer is then inserted to ensure the correct depth is obtained and a shaper is introduced to finalize the lesion with the correct wall inclination. Then the peripheral cartilage is trimmed and, after debris removal, the tapered implant is inserted manually and subsequently gently impacted to a position 2 mm below the surface of the articular cartilage through a silicone-covered tamper. The stability of the transplant is tested by cyclic bending of the knee while the graft is under direct vision, both before and after tourniquet removal.

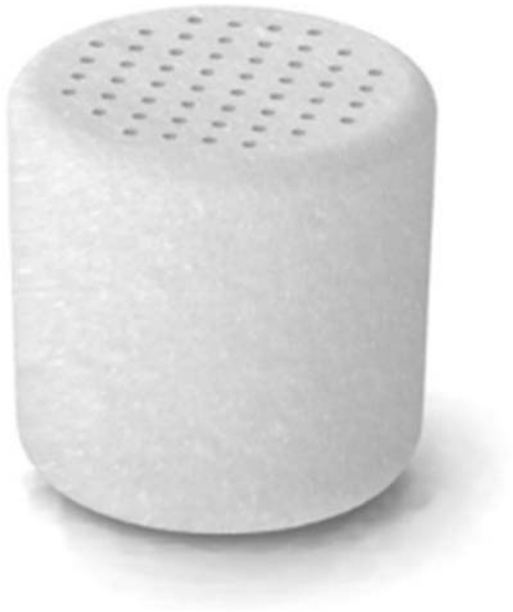

Fig. 1. Tapered aragonite-based implant.

The rehabilitation program includes toe-touch weight bearing (with no significant amount of weight) using crutches for 4 weeks, with increasing partial weight bearing reaching full weight bearing after 6 weeks. During the first 48 hours cryotherapy in conjunction with a continuous-passive-motion (CPM) device are applied and carried on for 3 weeks, together with active assisted range-of-motion exercises. Quadriceps isometric sets and electrostimulation are initiated immediately after surgery. Stationary cycling is introduced at 4 weeks, when the patient reaches knee flexion of 100°. Hydrotherapy is advised immediately after suture removal. Resistance muscle-strengthening exercises are initiated after the third month. Outdoor cycling activity and skiing are allowed not earlier than 6 months after the operation, while repetitive joint impact activities are allowed after 1 year.

Patients' selection and evaluation

The study involves patients enrolled, treated, and prospectively followed after Hospital Ethics Committee and Internal Review Board approvals. Inclusion criteria for the selection of patients for this pilot evaluation were: patients affected by focal chondral-osteochondral knee lesions ICRS grade III-IV of the condyle and trochlea, with Kellgren Lawrence lower than 3 and age younger than 50 years. Exclusion criteria were: concomitant ICRS grade 4 lesions on the patella or tibial plateau, multiple lesions and evidence of severe joint degeneration at the pre-operative X-Ray of Kellgren Lawrence >2, and patients with non-corrected misalignment or instability of the knee (patients who