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Case Reports and Series

Complex Osteochondral Lesions of the Talus Treated With a Novel Bi-Phasic Aragonite-based Implant

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ABSTRACT

To present initial results of a novel, bi-phasic, porous, biodegrade, and cell-free aragonite-based scaffold for treating complex osteochondral lesions of the talus (OLT). Four subjects (2 males and 2 females; 34-61 years old) were operated on their ankles due to chronic and deep OLT-Hepple grades 4 or 5 (1.8-2.2 cm^2). Three subjects had OLT on the medial central trochlea, and 1 had a combined medial and lateral lesions. OLT were exposed through medial malleolus osteotomy, with an additional lateral arthrotomy in the combined lesions. Bi-phasic porous osteochondral scaffolds (single implant or 2 implants) were implanted in a press-fit manner using a designated surgical toolset. Treatment outcome was followed clinically (Foot and Ankle Outcome Score, EQ-5D 3L, Tegner activity scale) and by medical imaging (radiographs, magnetic resonance imaging) from 18 to 32 months. All Foot and Ankle Outcome Score values increased from preoperative to final follow-up values (Symptoms 62 to 71, Pain 53 to 84, ADL 60 to 89, Sport 19 to 65, and QoL 18 to 47). EQ-5D 3L increased from 0.59 to 0.76, and Tegner activity values increased from 1.5 to 3. Kellgren-Lawrence ankle radiographic scores remained stable (2 to 2). Postoperative MR evaluation demonstrated cartilage defect fill of 75% to 100% respect to the native cartilage in 3 subjects (4 OLTs), while 1 lesion was filled 25% to 50%. No graft related serious adverse events or graft failures were reported. The use of a bi-phasic osteochondral biodegradable aragonite-based scaffold in the treatment of complex OLT during the reported period presented positive and promising clinical and radiologic outcome, without serious adverse events or graft failures.

Osteochondral defects of the talus (OLT) are joint surface lesions affecting both parts of the osteochondral unit, the cartilage and its underlying subchondral bone that may cause debilitating symptoms and – if left untreated – present a risk factor for the development of secondary osteoarthritis (1). The ultimate goal of treating OLT is to achieve hyaline cartilage restoration integrated with surrounding cartilage and underlying bone of good quality (2). Arthroscopic lesion debridement and bone marrow stimulation represents the most common therapeutic modality for uncomplicated lesions (3). Complex cases, such as deep lesions, cystic lesions, and revision surgeries, often require open surgical intervention via medial malleolar osteotomy (4). In such cases, osteochondral autografts, allografts, osteochondral scaffolds, or partial metal implants may be utilized (5). Certain disadvantages in their applications, such as donor site morbidity of autograft cylinders harvested from the knee, availability and low biologic potential of allografts, nonoptimal subchondral bone restoration of available scaffolds, and metal implant loosening, required search for a novel osteochondral repair device. Due to increasing awareness that subchondral bone restoration is essential for high quality durable cartilage

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repair, a novel aragonite-based bi-phasic scaffold was developed (Agili-C™, CartiHeal) (6). The implant demonstrated excellent preclinical results and has already shown to enhance hyaline cartilage and subchondral bone restoration in the knee (7-12). Herein we present the first clinical and imaging results of this novel aragonite bi-phasic scaffold when used for treating complex OLT.

Case Reports

The study was designed as a *pilot* case series, and the clinical investigational plan was approved by the National Medical Ethics Committee (permit No. 0120-99/2019/4). Adult subjects with symptomatic, complex OLT, classified as Hepple 4 or 5, were enrolled (13). Presence of mild ankle osteoarthritis (radiographic classification by Kellgren-Lawrence ≤2) was permitted (14). Exclusion criteria were inability to comply with required postoperative regimen and associated general medical conditions (infection, neoplastic, metabolic, or inflammatory).

Subjects

Five OLT in 4 subjects (2 men and 2 women) were included in this case series. The mean age was 42 (12) years and mean BMI was 33.6 (4.4) kg/m^2. Three subjects had a lesion on the medial trochlea shoulder, and 1 subject had combined medial and lateral lesions. Two subjects had undergone previous failed surgeries to treat their cartilage defects. Symptom duration in all subjects was over 1 year. Details on the subject demographics, medical history, and surgical procedures are shown in Table 1.

Surgical Intervention

Medial malleolus osteotomy exposure was used in all subjects, and an additional lateral arthrotomy was used in subject with combined lesions. Total lesion size ranged from 1.8 to 2.2 cm^2. An additional lesion of the opposite tibial plafond was bone grafted in one case, while lateral ligament reconstruction was performed in another. One to 2 bi-phasic, biodegradable, osteochondral implants (Agili-C™, CartiHeal, Israel) were used to treat the lesions. The implant diameters ranged from 7.5 to 15 mm, and 10 mm in depth. A designated surgical toolset was used (CartiHeal, Israel) as per the following surgical technique: (1) guide wire positioning via the perpendicular aligner in the centre of lesion without penetration into the subtalar joint, (2) perpendicular drilling over the guide wire to the designated depth in order to assure implant positioning 2-mm below the articular surface, (3) a shaper was used to adjust the lesion diameter, (4) gentle manual implant insertion with slight implant tapping to ensure press-fit fixation below the articular surface. A technical note – when OLT is centred over the talus shoulder, the device was positioned obliquely, approximately 45° respect to both adjacent articular surfaces, in a fully contained manner. Prerequisites for using this aragonite bi-phasic implant were contained lesion with preserved surrounding bone circumference, maximal lesion depth (including cyst) of 8 mm, and a preserved bony bridge of 5 mm between 2 implants. Refer to Table 1 for subject and surgery details.

Rehabilitation

Postoperative the subjects were restrained from weight-bearing for 6 to 8 weeks until the malleolar osteotomy healed. In addition, during the first 2 weeks they were immobilized in a *removable posterior short leg plastic splint* and performed only passive machine-driven range of motion exercise. From 3 weeks onward, the subjects were allowed active and passive dorsal/plantar exercises without side motion. Stationary cycling was allowed after 1 month. At 2 months, they discontinued using crutches, and progressed to proprioceptive exercise, aquatic rehabilitation, and gait training. After 3 months they were allowed strength training, including elliptical trainers, and Nordic walking *(an activity that involves walking across country with the aid of long poles resembling ski sticks)* on stable ground. Eight months after surgery (if the ankle's functional status permitted), they were allowed activities on uneven ground, including easy jogging. Return to full activities was allowed only one year after the procedure.

Clinical and Radiologic Evaluation

The subjects were clinically followed using standard subjective outcome measures: Foot and Ankle Outcome Score (FAOS) (15), European quality of life in 5 dimensions (EQ-5D 3L) (16), and the Tegner activity scale (17). Additionally, graft failures (defined as revision surgery to the lesion) and serious adverse events (defined as any hospitalisation or revision surgery) were recorded. Standard weight-bearing anteroposterior and lateral ankle radiographs were taken before and after the procedure. Osteoarthritis grade was assessed according to Kellgren-Lawrence classification (14). Prior to procedure, and at final follow-up, routine ankle magnetic resonance imaging was performed on a Philips, Achieva, 3.0 T scanner. The lesion's defect fill at final follow-up was calculated *by the radiologist* from the postoperative MR images by comparing the amount of cartilage defect fill compared to the native articular cartilage. All data is presented as mean (SD). In some cases, ranges are listed. Descriptive statistical analysis was performed using statistical software IBM SPSS® Statistics V22.0 (IBM Corp, Armonk, NY).

Results

Subjects were clinically and radiologically followed for a mean of 26 (7) months. No graft failures were recorded during this period. One serious adverse event (osteotomy screws electively removed at 30 months postoperatively) was classified – not related to the implant. All FAOS values increased from pre-operative to final follow-up values: Symptoms from 62 (29) to 71 (22), Pain from 53 (17) to 84 (12), ADL from 60 (20) to 89 (13), Sport from 19 (21) to 65 (31), and QoL from 18

Table 1
Demographic data and surgical details of subjects (N = 4) treated with an aragonite osteochondral scaffold on the talus

Age (Years)	Gender	BMI (kg/m^2)	Previous Surgeries	Lesion Location	Total Lesion Size (cm^2)	Lesion Depth	Implants Size (mm Diameter)	Conjoined Procedures
35	male	29.9	none	medial and lateral trochlea	2.2	Grade 5	Agili-C lateral 10 medial 12.5	medial malleolus osteotomy, lateral arthrotomy
34	male	31.3	microfractures	medial trochlea	2.0	Grade 4	Agili-C 10	medial malleolus osteotomy, lateral ligament reconstruction, mfx of posterior lesion part
61	female	33.2	lesion bone grafting	medial trochlea and medial tibia plafond subchondral cyst	1.8	Grade 5	Agili-C 15	medial malleolus osteotomy, tibial plafond bone grafting
39	female	39.9	none	medial trochlea	2.0	Grade 4	Agili-C 2 × 7.5	medial malleolus osteotomy

(14) to 47 (23). EQ-5D 3L indicated improved quality of life with an increase from 0.59 (0.02) preoperatively to 0.76 (0.18) at final postoperative evaluation. The Tegner activity values averages increased from 1.5 (0.6) preoperatively to 3.0 (1.2) postoperatively. Kellgren-Lawrence ankle radiographic scores remained constant: preoperative 2 (0) to postoperative 2 (0). Postoperative MR evaluation demonstrated articular cartilage defect fill of 75% to 100% in 4 of 5 lesions (3 subjects), and 25% to 50% in 1 of 5 lesions (1 subject). Refer to Table 2 for individual clinical results. The opportunity of osteotomy screws removal was used to conduct 1 second look arthroscopy – excellent cartilage-like repair tissue, of full thickness at the level with native surrounding cartilage, with full continuum from the surrounding native cartilage, and no visible gap was noted. The articular surface was white and silky, only the surface on the center of the implant was slightly softer on palpation with minor fibrillations – Nearly Normal (11/12 points - Ib 4/II 4/III 3) according to Arthroscopic ICRS Cartilage Repair Assessment. This subject`s images, intraoperative view, and second-look arthroscopy are presented in Figure.

Discussion

The main finding of this *pilot* case series was that a bi-phasic absorbable osteochondral aragonite implant proved to be an adequate treatment option for complex OLT. Clinical and imaging measures improved markedly during the 2-year follow-up period, and no graft related serious adverse events or graft failures were recorded.

Since the role of the subchondral bone in the etiopathogenesis of OLT has been confirmed, restoration of the entire osteochondral unit has gained a lot of traction (18). Following this rationale, a bi-phasic scaffold capable of reproducing favourable biological, mechanical and structural properties of the subchondral bone and articular cartilage could provide a novel approach for successful treatment of these complex lesions (19). Rapid progress in biomaterial science has led to the development of several multilayered scaffolds, some of which showed potential to regenerate damaged tissue without prior cell addition, thus enabling single-stage surgical treatment of OLT (20). Such scaffolds serve as surgical augmentation to bone marrow stimulating techniques, as they stabilize mesenchymal stem/stromal cells derived from bone marrow and provide a suitable environment for cell differentiation into the desired chondrogenic and osteogenic phenotypes of the regenerating osteochondral unit (21). Even though such cell-free off-the-shelf implants capable of inducing in situ osteochondral regeneration are considered as ideal grafts, both from surgical and commercial standpoints, only 2 multilayered scaffolds have been previously clinically used (6). Studies regarding the effectiveness of polymeric PLGA-PGA and calcium-sulfate bi-layered scaffold showed controversial results, both from the clinical and imaging perspectives, so the device usage was discontinued (22). A second acellular multilayered scaffold available in clinical practice (collagen-hydroxyapatite bi- or tri-layered scaffolds) showed excellent outcome in almost all initial studies (23-25). However, mid-term studies with ongoing good clinical outcomes, raised questions regarding insufficient subchondral bone restoration after 4 to 5 years follow-up (26). Moreover, Albano et al observed a relatively high failure rate (31%) of osteochondral treatment with this scaffold and Christensen et al confirmed poor results in terms of cartilage and bone restoration, despite observing significant clinical improvement (27,28). Based on this, further developments should be made to successfully implement this promising treatment strategy of in situ osteochondral regeneration with cell-free off-the-shelf multilayered scaffolds into clinical practice. The current study uses a new and novel aragonite-based, bi-phasic scaffold. The implant consists of natural crystalline aragonite derived from coral exoskeleton. It is capable of recruiting bone-marrow mesenchymal stem cells which differentiate into the desired chondrogenic and osteogenic phenotypes (7-12).

Table 2
Clinical outcome of subjects (N = 4) treated with an aragonite-based osteochondral scaffold on the talus

Preoperative Values								Follow-up (Months)	Postoperative Values							
FAOS Sympt	FAOS Pain	FAOS ADL	FAOS Sport	FAOS QoL	Tegner Activity	EQ-5D 3L	Xray KL Scale		FAOS Sympt	FAOS Pain	FAOS ADL	FAOS Sport	FAOS QoL	Tegner Activity	EQ-5D 3L	Xray KL Scale	MRI Defect fill
93	70	85	45	13	1	0.59	2	22	96	97	100	100	56	4	1	2	75%-100%*
71	61	65	25	13	1	0.61	2	32	57	83	81	50	31	2	0.59	2	75%-100%
25	36	40	5	6	2	0.56	2	32	50	69	76	30	25	4	0.67	2	25%-50%
57	42	49	0	38	2	0.59	2	18	82	86	100	80	75	2	0.77	2	75%-100%
61.5 (28.5)	52.8 (16.7)	59.8 (19.8)	18.8 (20.6)	17.5 (14.1)	1.5 (0.6)	0.59 (0.02)	2 (0)	26.0 (7.1)	71.3 (21.5)	83.8 (11.5)	89.3 (12.6)	65.0 (31.1)	46.8 (23.1)	3.0 (1.2)	0.76 (0.18)	2 (0)	4 x grade IV 1 x grade I

Abbreviations: EQ-5D 3L European Quality of Life in 5 dimensions 3 level questionnaire; FAOS, Foot and Ankle Outcome Score; Xray KL, Ankle AP radiographs evaluated according to Kellgren-Lawrence criteria.
* Medial and lateral lesions showed same result.

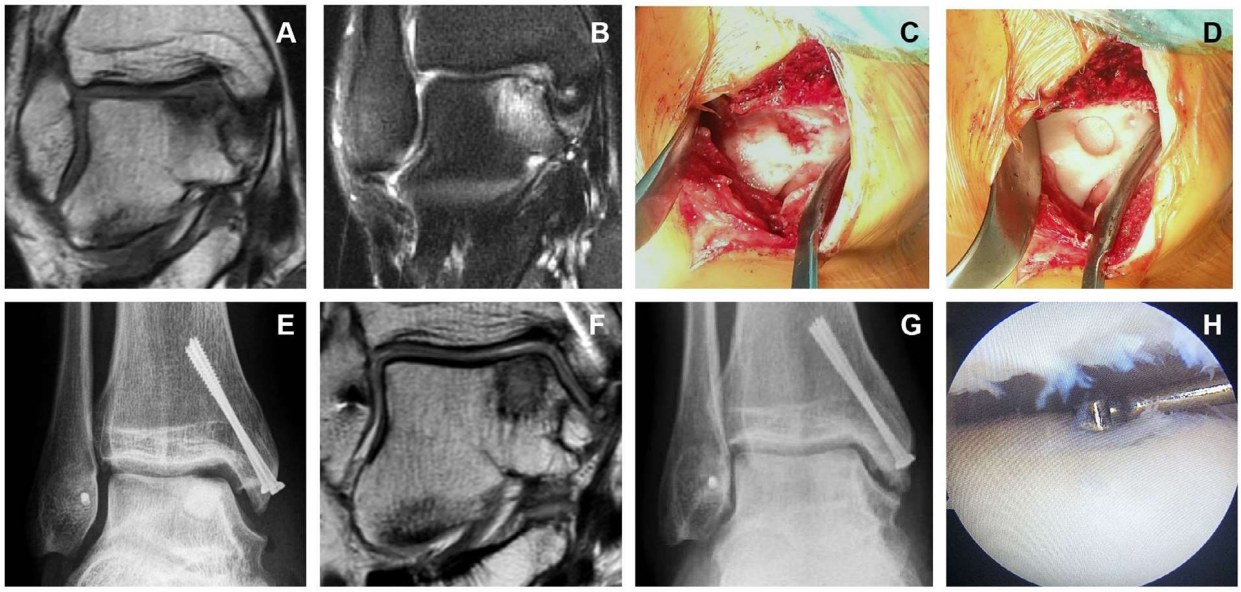

Fig. Imaging, intraoperative view, and second-look arthroscopy in a 40-year-old male patient treated with a single bi-phasic biodegradable aragonite-based osteochondral implant for a recurrent grade 4 OLT. (*A* and *B*) Preoperative ankle MRI, (*C*) Intraoperative view of the lesion, (*D*) Intraoperative view of the implantation, (*E*) Postoperative radiographs, (*F*) Follow-up MRI at 14 months, (*G*) Radiographs before hardware removal at 35 months, (*H*) Second look arthroscopy at 35 months.

Gradual resorption of the implant occurs proportional to the rate of cartilage and bone regeneration. Preclinical studies revealed its safety and good regenerative potential in promoting both bone and hyaline cartilage regeneration (without cell addition), which was further confirmed in humans in clinical study's studying its potential for treating osteochondral lesions in the knee (7-12).

Previously, clinical studies to test the ability of this aragonite-based scaffold to support osteochondral regeneration in the ankle were not performed. Although OLT are a common ankle pathology, successful treatment algorithms are still under investigation (29). Primary treatment of simple OLT, Hepple grades 2-3, relies mostly on arthroscopic intervention, such as debridement or bone-marrow stimulation that resulted in over 80% successful outcomes (30). However, complex OLT (grades 4 or 5) and lesions with a surface area over 1.5 cm^2 require a different approach with the prerequisite for subchondral bone restoration (1). Due to technical (harvesting of osteochondral autografts from the knee), biological (low vascularity and consequently low active stem/stromal cell count in the ankle), and logistical reasons (safety and availability of osteochondral allografts), a bi-phasic osteochondral off-the-shelf scaffold would be a major advantage in the treatment of complex OLT.

It should be emphasized that this case series was an initial "pilot study" and as such lacked necessary statistical power, average follow-up was rather short, lacked a control group, and conjoined procedures were used. However, based on the preliminary results, we can nevertheless conclude that the implantation of a novel aragonite-based bi-phasic scaffold is technically feasible for OLT and that accomplished results are positive. Observations in this limited series concur with experience gathered from large knee studies with this aragonite-based bi-phasic scaffold – endorsing cartilage restoration above and around its perimeter. This scaffold property is helpful to restore the cartilage geometry on talus shoulders, as the implant was recessed below the subchondral bone and repair tissue overgrowth was noted. Use of several small diameter implants, with an obligatory bone bridge in-between, is recommended instead of one large implant. Analogy was confirmed in current case series: a single 15 mm implant, which was required to cover the entire cystic OLT, demonstrated lower postoperative cartilage defect fill compared to the other 4 lesions that were treated with smaller implants, even when 2 implants were used to treat a lesion.

The presented pilot case series indicates the safety and potential of this novel aragonite-based bi-phasic scaffold for initiating and promoting bone and cartilage restoration. Promising early results with no implant related serious adverse events or graft failures during the short-term follow-up support further usage of this implant in the treatment of complex OLT.

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References

1. Looze CA, Capo J, Ryan MK, Begly JP, Chapman C, Swanson D, Singh BC, Strauss EJ. Evaluation and management of osteochondral lesions of the talus. Cartilage 2017;8:19–30.
2. Dhollander AAM, De Neve F, Almqvist KF, Verdonk R, Lambrecht S, Elewaut D, Verbruggen G, Verdonk PC. Autologous matrix-induced chondrogenesis combined with platelet-rich plasma gel: Technical description and a five pilot patients report. Knee Surg Sports Traumatol Arthrosc 2011;19:536–542.
3. Zengerink M, Struijs PA, Tol JL, Van Dijk CN. Treatment of osteochondral lesions of the talus: a systematic review. Knee Surg Sports Traumatol Arthrosc 2010;18:238–246.
4. Marcacci M, Filardo G, Kon E. Treatment of cartilage lesions: What works and why. Injury 2013;44(Suppl. 1):S11–S15.
5. Murawski CD, Kennedy JG. Operative treatment of osteochondral lesions of the talus. J Bone Joint Surg Am 2013;95:1045–1054.
6. Kon E, Filardo G, Perdisa F, Venieri G, Marcacci M. Clinical results of multilayered biomaterials for osteochondral regeneration. J Exp Orthop 2014;1:10.
7. Matta C, Szűcs-Somogyi C, Kon E, Robinson D, Neufeld T, Altschuler N, Berta A, Hangody L, Veréb Z, Zákány R. Osteogenic differentiation of human bone marrow-derived mesenchymal stem cells is enhanced by an aragonite scaffold. Differentiation 2019;107:24–34.
8. Kon E, Filardo G, Robinson D, Eisman JA, Levy A, Zaslav K, Shani J, Altschuler N. Osteochondral regeneration using a novel aragonite-hyaluronate bi-phasic scaffold in a goat model. Knee Surg Sports Traumatol Arthrosc 2014;22:1452–1464.
9. Kon E, Filardo G, Shani J, Altschuler N, Levy A, Zaslav K, Eisman JE, Robinson D. Osteochondral regeneration with a novel aragonite-hyaluronate biphasic scaffold: up to 12-month follow-up study in a goat model. J Orthop Surg Res 2015;10:81.
10. Chubinskaya S, Di Matteo B, Lovato L, Iacono F, Robinson D, Kon E. Agili-C implant promotes the regenerative capacity of articular cartilage defects in an ex vivo model. Knee Surg Sports Traumatol Arthrosc 2019;27:1953–1964.

11. Kon E, Drobnic M, Davidson PA, Levy A, Zaslav K, Robinson D. Chronic posttraumatic cartilage lesion of the knee treated with an acellular osteochondral-regenerating implant: case history with rehabilitation guidelines. J Sport Rehabil 2014;23:270–275.
12. Kon E, Robinson D, Verdonk P, Drobnic M, Patrascu JM, Dulic O, Gavrilovic G, Filardo G. A novel aragonite-based scaffold for osteochondral regeneration: early experience on human implants and technical developments. Injury 2016;47(Suppl. 6):S27–S32.
13. Hepple S, Winson IG, Glew D. Osteochondral lesions of the talus: A revised classification. Foot Ankle Int 1999;20:789–793.
14. Kellgren JH, Lawrence JS. Radiological assessment of osteo-arthrosis. Ann Rheum Dis 1957;16:494–502.
15. Roos EM, Brandsson S, Karlsson J. Validation of the foot and ankle outcome score for ankle ligament reconstruction. Foot Ankle Int 2001;22:788–794.
16. Rupel VP, Srakar A, Rand K. Valuation of EQ-5D-3l Health States in Slovenia: VAS based and TTO based Value Sets. Slovenian J Public Health 2019;59:8–17.
17. Tegner Y, Lysholm J. Rating systems in the evaluation of knee ligament injuries. Clin Orthop Relat Res 1985;198:43–49.
18. Gomoll AH, Madry H, Knutsen G, van Dijk N, Seil R, Brittberg M, Kon E. The subchondral bone in articular cartilage repair: current problems in the surgical management. Knee Surg Sports Traumatol Arthrosc 2010;18:434–447.
19. O'Shea TM, Miao X. Bilayered scaffolds for osteochondral tissue engineering. Tiss Eng Part B Rev 2008;14:447–464.
20. Filardo G, Perdisa F, Gelinsky M, Despang F, Fini M, Marcacci M, Parrilli AP, Roffi A, Salamanna F, Sartori M, Schütz K, Kon E. Novel alginate biphasic scaffold for osteochondral regeneration: An in vivo evaluation in rabbit and sheep models. J Mater Sci Mater Med 2018;29:74.
21. Benthien JP, Behrens P. Autologous matrix-induced chondrogenesis (AMIC) combining microfracturing and a collagen I/III matrix for articular cartilage resurfacing. Cartilage 2010;1:65–68.
22. Hindle P, Hendry JL, Keating JF, Biant LC. Autologous osteochondral mosaicplasty or TruFit plugs for cartilage repair. Knee Surg Sports Traumatol Arthrosc 2014;22:1235–1240.
23. Kon E, Delcogliano M, Filardo G, Busacca M, Di Martino A, Marcacci M. Novel nanocomposite multilayered biomaterial for osteochondral regeneration: A pilot clinical trial. Am J Sports Med 2011;39:1180–1190.
24. Berruto M, Delcogliano M, de Caro F, Carimati G, Uboldi F, Ferrua P, Ziveri G, De Biase CF. Treatment of large knee osteochondral lesions with a biomimetic scaffold: Results of a multicenter study of 49 patients at 2-year follow-up. Am J Sports Med 2014;42:1607–1617.
25. Delcogliano M, de Caro F, Scaravella E, Ziveri G, De Biase CF, Marotta D, Marenghi P, Delcogliano A. Use of innovative biomimetic scaffold in the treatment for large osteochondral lesions of the knee. Knee Surg Sports Traumatol Arthrosc 2014;22:1260–1269.
26. Kon E, Filardo G, Di Martino A, Busacca M, Moio A, Perdisa F, Marcacci M. Clinical results and MRI evolution of a nano-composite multilayered biomaterial for osteochondral regeneration at 5 years. Am J Sports Med 2014;42:158–165.
27. Albano D, Martinelli N, Bianchi A, Messina C, Malerba F, Sconfienza LM. Clinical and imaging outcome of osteochondral lesions of the talus treated using autologous matrix-induced chondrogenesis technique with a biomimetic scaffold. BMC Musculoskelet Disord 2017;18:306.
28. Christensen BB, Foldager CB, Jensen J, Jensen NC, Lind M. Poor osteochondral repair by a biomimetic collagen scaffold: 1-to 3-year clinical and radiological follow-up. Knee Surg Sports Traumatol Arthrosc 2016;24:2380–2387.
29. Badekas T, Takvorian M, Souras N. Treatment principles for osteochondral lesions in foot and ankle. Int Orthop 2013;37:1697–1706.
30. Donnenwerth MP, Roukis TS. Outcome of arthroscopic debridement and microfracture as the primary treatment for osteochondral lesions of the talar dome. Arthroscopy 2012;28:1902–1907.