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ANKLE

Autologous collagen-induced chondrogenesis technique (ACIC) for the treatment of chondral lesions of the talus

P. Volpi · C. Bait · A. Quaglia · A. Redaelli · E. Prospero · M. Cervellin · D. Stanco · L. de Girolamo

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Abstract
Purpose Autologous collagen-induced chondrogenesis technique (ACIC) combines microfractures with the use of an injectable atelocollagen matrix that allows performing the whole cartilage repair treatment arthroscopically. The aim of this study was to evaluate the in vitro cytocompatibility of this biomaterial using human bone marrow mesenchymal stem cells and human chondrocytes. Moreover, the preliminary data of five patients affected by chondral lesion of the talus treated with the ACIC technique are shown.
Methods Human bone marrow mesenchymal stem cells and human chondrocytes were seeded on solid and pre-solid atelocollagen scaffolds. Cell–scaffold constructs were cultured for 7 days and then prepared for histological analyses. Arthroscopic ACIC was performed in five patients affected by chondral lesions of the talus; they were clinically evaluated with AOFAS, VAS and Tegner score before and then after 6 months from surgery.
Results In vitro results showed that both bone marrow mesenchymal stem cells and chondrocytes were able to efficiently colonize the whole construct, from the surface to the core, only when seeded on the pre-solid atelocollagen scaffold, but not on its solid form. No adverse events were observed in the patients treated with the ACIC technique; a significant improvement in VAS pain scale and in AOFAS score was found at 6 months follow up.
Conclusion Injectable atelocollagen can be considered a feasible scaffold for cartilage repair treatment, in particular if used in its pre-solid form. ACIC leads to good clinical results in the treatment for chondral lesions of the talus even if longer follow-up and a higher number of patients are necessary to confirm these data.
Level of evidence IV.

Keywords Chondral lesions · Talus · Cartilage repair · Autologous collagen-induced chondrogenesis (ACIC) · Bone marrow mesenchymal stem cells

Introduction

Due to this limited ability of regeneration in response to injury, symptomatic chondral and osteochondral ankle defects often require surgical treatment. These defects can cause pain, as well as impaired function, limited range of motion, stiffness, catching, locking and swelling [35]. Due to their high incidence among people, in particular sports persons, chondral and osteochondral lesions of the talus have a crucial clinical relevance. The recent technological improvements have allowed to ameliorate the outcome of the chondral defects treatment, although several aspects still remain not completely solved. Indeed, over the last years, many therapeutic strategies were set up, starting from conservative treatments, useful only for symptom relief, to one-step surgical treatments such as cartilage debridement [1], microfractures [2, 27] and osteochondral autograft transfer system (OATS) [14], or two-step approaches including autologous chondrocyte implantation (ACI) [8] and matrix-induced autologous chondrocytes

P. Volpi (✉) · C. Bait · A. Quaglia · A. Redaelli · E. Prospero · M. Cervellin
Istituto Clinico Humanitas, Via Manzoni 56, Rozzano, Italy
e-mail: volpi.piero@libero.it

D. Stanco · L. de Girolamo
Orthopaedic Biotechnology Laboratory, IRCCS Istituto Ortopedico Galeazzi, Milan, Italy

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transplantation (MACI) [22]. Still more recently, platelet-rich plasma, hyaluronic acid injections and osteochondral scaffolds have also been employed for treating talar cartilage defects [13, 19].

Since two-step techniques are associated with higher costs, patient's discomfort and length of the procedure, the attention has been focused again on one-step procedures, most of which, including microfractures, are based on mesenchymal stem cell (MSC) potential. MSCs are adult progenitor cells with a good proliferative potential and a multilineage differentiation ability, including the chondrogenic one [24]. Moreover, they have been found to secrete a variety of cytokines with anti-inflammatory activity that makes them able to restore the joint homeostasis [21, 23]. For these reasons, MSCs are able to contribute to cartilage regeneration, both by directly replacing damaged cells, thanks to their chondrogenic potential, and by the inflammatory response modulation [20, 21]. As known, microfracturing and drilling techniques promote the release of growth factors and the infiltration of bone marrow-derived cells in the chondral lesion. Although some authors reported encouraging results at mid-term follow-up after microfractures of the talus [2], a further development of this approach called matrix-assisted microfracture technique has been recently proposed [30, 34]. The main advantage of the combination of microfractures with the use of a biological matrix is represented by the ability of the matrix to stabilize and maintain the blood clot in the lesion site, forming a "regeneration chamber" inside which MSCs from subchondral bone can promote the cartilage regeneration. However, in most of the cases, an arthrotomy approach is needed to place the matrix. The autologous collagen-induced chondrogenesis technique (ACIC) seems to be particularly promising since it can be performed completely arthroscopically as the matrix is made of injectable atelocollagen that polymerizes once placed on the lesion. The aim of this in vitro study was to evaluate the cytocompatibility and the ability to be colonized by cells of the collagen gel-based matrix (Cartifill^{TM}, Regenerative Medicine System), before and after the polymerization process, using both human bone marrow mesenchymal stem cells (BMSCs) and chondrocytes (CHs). Although several in vitro and preclinical studies concerning the injectable atelocollagen matrix have been performed, still very few clinical data are available, none of which about the use in the ankle. For this reason, the preliminary data of five patients affected by an osteochondral lesion of the talus treated with the arthroscopical ACIC technique are discussed here.

Materials and methods

In vitro cytocompatibility

Cell culture and seeding of the atelocollagen scaffolds

Primary bone marrow mesenchymal stem cells (BMSCs) and articular chondrocytes (CHs) were used in this experiment. BMSCs and CHs were isolated from bone marrow of the waste femoral compartment of two patients undergoing total hip replacement and from cartilage of the femoral head of the same donors, respectively. BMSCs were isolated from bone marrow by plastic adherence, whereas cartilage was digested with collagenase II as previously reported [16]. Both cell populations were cultured in complete medium composed of DMEM, 10 % foetal bovine serum (FBS; Sigma-Aldrich), 2 mM L glutamine, 100 U/ml penicillin and 100 µg/ml streptomycin (Sigma-Aldrich) added with 5 ng/ml FGF-2 and 1 ng/ml TGFβ (this last supplement was just used for CHs) (PeproTech, Rocky Hill, NJ, USA). BMSCs and CHs were maintained at 37 °C in humidified atmosphere with 5 % CO_2, changing medium every 3 days; when the cells reached 80–90 % of confluence, they were detached with trypsin/EDTA (0.5 % trypsin/0.2 % EDTA; Sigma-Aldrich) and cultured at 3×10^3 cells/cm^2 of density until passage 3. At this passage, both BMSCs and CHs were seeded at two different cell densities (0.5×10^5 or 10^5/scaffold) on Cartifill^{TM} scaffold made of thick filaments of swine atelocollagen and of a stabilizer-supplying stable environment for cellular activities, including MSC proliferation. Atelocollagen is a highly purified type I collagen obtained by following the treatment of skin dermis with pepsin and telopeptide removal, making it nonimmunogenic [26]. Cartifill^{TM} remains as a gel until it is mixed in 1:1 ratio with fibrin glue, which provokes its solidification, as reported by the manufacturer's sheet. The cell seeding was performed both before (pre-solid state) and after the complete polymerization (solid state). Each scaffold sample had a final volume of 250 µl and after solidification appeared as a small sphere. Cell–scaffold constructs were cultured for 7 days in the same culture medium, changing the medium every 3 days.

Histological analysis

After the culture period, the samples were prepared for the histological analyses. Scaffolds were fixed in 10 % neutral-buffered formalin, embedded in paraffin and sectioned at 4 µm. The sections were stained with haematoxylin–eosin (Sigma-Aldrich) for the morphological examination and with Alcian blue (pH 2.5, Sigma-Aldrich) to evaluate the

deposition of extracellular matrix and glycosaminoglycans (GAGs). In order to assess the presence of collagen II in the extracellular matrix, sections from each sample were immunostained with a primary mouse monoclonal antibody against collagen II antigen (Abcam, #ab54237, Cambridge, UK). For each sample, serial sections incubated with a 10 % solution of normal horse serum served as negative controls. All sections were evaluated under light microscope (Fig. 1).

Surgical treatment: ACIC technique

In addition to the in vitro study, five patients (3 males, 2 females) affected by chondral lesions of the talus (2.5–4 cm^2, grade III–IV according to International Cartilage Repair Society scale [12]) were treated with the ACIC technique (Figs. 2, 3) by the same senior surgeon. All the patients gave informed consent to this procedure. Inclusion criteria were both sex, age <40 years and pre-treatment VAS pain scale ≥5. Those with arthritis of the ankle joint, "kissing" lesions, untreated ankle instability or misalignment, tendon tears of ankle joint, previous surgery at the same ankle, rheumatoid arthritis, any other inflammatory arthropathy and therapy, as well as heavy smokers or alcohol abusers were excluded.

The entire procedures were performed arthroscopically, using antero-medial and antero-lateral portal approaches for the ankle and thigh tourniquet for all patients at 250 mm/Hg. After the usual preparation of the lesion for this kind of treatment [5], microfractures were performed using a 4–5-mm angled chondral pick, placed 3–4 mm apart from each other [7, 25] (Figs. 4, 5). Then, tourniquet was removed, water was replaced by carbon dioxide (CO_2) in order to maintain the same joint distension and to avoid the dilution of the injectable matrix (Fig. 6). To allow its polymerization, Cartifill^{TM} was combined with synthetic fibrin glue, in 1:1 ratio as reported in the manufacturer's sheet. The mix of these two components was guaranteed by a pre-filled two-way syringe connected with a needle and that was introduced into the joint using the arthroscopic portal. After being introduced and spread on the lesion, Cartifill^{TM} polymerized within 5–8 min (Fig. 7). All the patients were discharged the day after surgery and were instructed to follow the usual post-operative rehabilitation protocol for this kind of procedure [31], without any use of cast or walker boot. Patients were clinically evaluated during follow-up in order to monitor possible adverse events. Before surgery and six months from surgery, AOFAS [4, 11, 15, 18], Tegner [17, 29] and VAS Pain scale scores [3] were recorded for each patient.

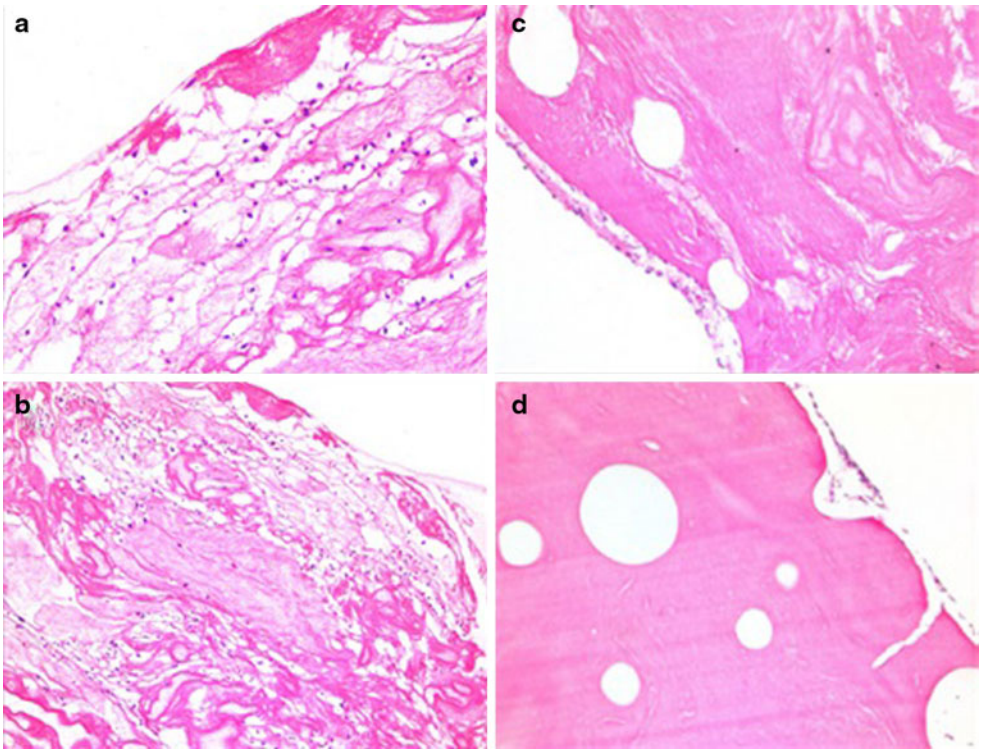

Fig. 1 Histological evaluation stained with haematoxylin–eosin of atelocollagen scaffold at pre-solid state (**a**, **b**) and after polymerization (**c**, **d**), seeded with BMSCs (**a**–**c**) and CHs (**b**–**d**) at a concentration of 10^5 cells/scaffold

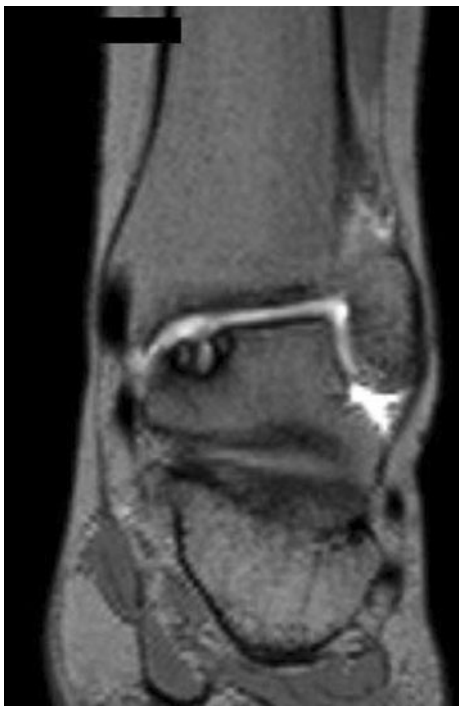

Fig. 2 Coronal ankle MRI of a patient included in the study

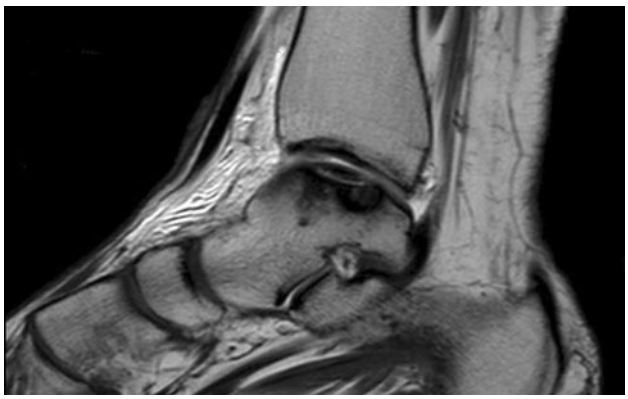

Fig. 3 Sagittal ankle MRI of a patient included in the study

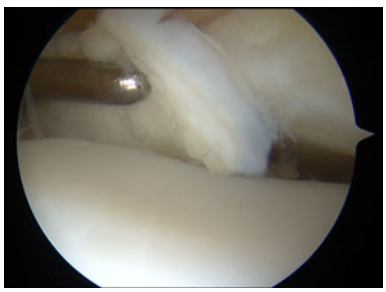

Fig. 4 Arthroscopic view of chondral lesion of the talus

All the procedures were carried out with the Institutional Review Board approval (Galeazzi Orthopaedic Institute, M-SPER-014.ver7- 03.01.2013).

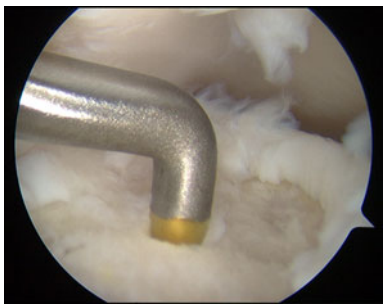

Fig. 5 Arthroscopic view of the chondral pick used to perform microfractures

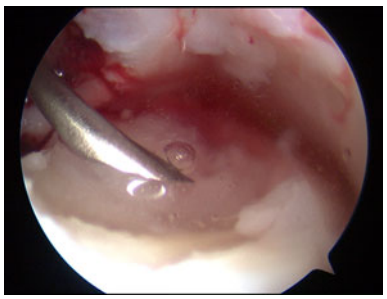

Fig. 6 Covering of the lesion with Cartifill^{TM}

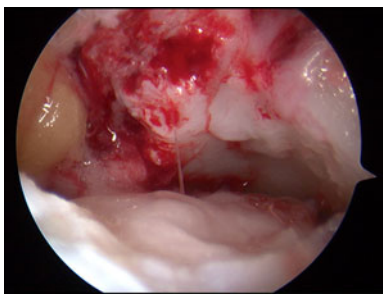

Fig. 7 Final arthroscopic view

Statistical analysis

All the clinical data were collected by the same clinician (AQ). All the results were expressed as mean ± standard deviation; range was also reported where appropriate. A Wilcoxon test for paired data was performed to compare variables before and after surgery. A p-value <0.05 was considered statistically significant.

Results

In vitro cytocompatibility

After 7 days of culture of both BMSCs and CHs, histological evaluation of cell–scaffold construct was performed (Fig. 1). Haematoxylin–eosin revealed that both BMSCs and CHs

seeded on pre-solid atelocollagen scaffold, independently from the cell concentration used, were able to colonize the whole sphere, from the surface to the core, (Fig. 1a, b). On the contrary, BMSCs and CHs seeded on solid scaffolds were not able to migrate within the scaffold but just adhered on the surface; also in this case similar results were observed for both the two cell densities, 0.5×10^5 and 10^5 (Fig. 1c, d). Morphologically, CHs cells appeared to have a smaller size (approximately 15–20 μm in diameter) and rounded, while BMSCs were spindled to stellate. No GAGs or collagen II deposition were found in the examined samples, probably due to the too short period of culture.

In vivo surgical results

Background population data are reported in Table 1. All the patients presented a VAS score >5; the mean age was 25.6 ± 6.6 years old and the mean lesion size 3.1 ± 0.6. They all had a rapid recovery after surgery. No adverse events or complication such as infections, nerve palsies, synovitis and allergic reactions were found during follow-up.

A significant improvement was observed in VAS pain scale, which passed from 6.6 ± 1.1 pre-operatively to 1.6 ± 1.5 at final follow-up ($p < 0.05$). The difference between pre-operative and 6 months follow-up AOFAS scores was also statistically significant (53.8 ± 15.1 and 86 ± 9, respectively, $p < 0.05$) (Table 2). Tegner activity scale showed different results among patients: in two of them, a value decreasing from 9 to 5 at pre-operative assessment and at 6 months follow-up, respectively, was observed. Other two patients had an improvement of their activity level after surgery (from 2 to 3 and from 4 to 6, respectively); finally, in one case at 6 months follow-up, Tegner score was the same as the pre-operative one. However, overall no statistically significant differences were observed between the mean pre-operative and 6 months follow-up score in term of Tegner score (n.s) (Table 2).

Discussion

The most important finding of the in vitro study was that both BMSCs and CHs were able to colonize the surface and the core of the pre-solid but not of the solid atelocollagen scaffold, independently from the cell seeding density. Indeed, cells seeded on scaffold after solidification remained localized on the surface and were not able to migrate towards its core. GAGs evaluation was negative in all samples probably because the culture period was too short to allow mature matrix formation. To clarify this aspect and to evaluate the quality of the matrix produced by both the types of cells seeded on the scaffold, it would be useful to culture cells on scaffold for longer period. Moreover, a limitation of this in vitro investigation is that cell culture were performed in a static setting; perfusion bioreactor or other types of dynamic culture could give more complete informations concerning the ability of these cells to colonize the atelocollagen, above all in its solid state.

To our knowledge, this is the first clinical report about the use of an injectable atelocollagen matrix for the treatment of chondral lesions of the talus. The same technique was used in the knee with good results [26]. In this retrospective study, ten patients affected by ICRS grade III or IV chondral lesions were treated arthroscopically with microdrilling and atelocollagen application. Magnetic resonance imaging shows good cartilage defect filling, as well as it suggests the presence of a hyaline-like repair tissue at two-year follow-up [26]. Our preliminary data on five patients just allow to make some general considerations about this technique in the ankle. The surgical time was not significantly increased in comparison with standard microfractures, and no adverse events or complications were observed. All the patients had severe pain at pre-operative level, associated to a very poor AOFAS score in most of

Table 2 Post-operative (6 months follow-up) values of AOFAS, Tegner and VAS pain scale

	Pre-operative	Post-operative	*P* value
VAS pain scale	6.6 ± 1.1 (5–8)	1.6 ± 1.5 (0–4)	0.0412
AOFAS score	53.8 ± 15.1 (33–68)	86 ± 9 (71–95)	0.0431
Tegner score	6 ± 3.1 (2–9)	5.1 ± 1.3 (3–6)	n.s.

Data are expressed as mean ± SD (range)

P values are referred to the statistical difference between pre- and post-operative scores

Table 1 Patient background data

ID	Sex	Age	Lesion size (cm^2)	AOFAS pre-op	Tegner pre-op	VAS pre-op
1	M	20	2.5	68	9	8
2	M	19	2.5	43	9	5
3	F	24	3	64	2	7
4	F	33	4	61	6	7
5	M	32	3.5	33	4	6
Mean ± SD	/	25.6 ± 6.6	3.1 ± 0.6	53.8 ± 15.1	6 ± 3.1	6.6 ± 1.1

them. Six months after the procedure, significant improvements in terms of both VAS pain scale and AOFAS score were observed. On the other hand, Tegner score lightly decreased after the surgical procedure but not in a significant way; these results can be explained since usually patients return to sport later than 6 months from this kind of surgery. Indeed, two patients had very high pre-operative Tegner score, and both of them, at the time of evaluation, had not returned to their original activities yet, although they were very satisfy of their progressive recovery. In the other three patients, presenting moderate or low pre-operative Tegner score, an improvement or, at least, a maintenance of the same level was observed at 6 months follow up in comparison with the pre-operative levels. These results can be considered comparable with previously published findings concerning microfractures: unsatisfactory results were reported in 14 % of patients affected by osteochondral lesion of the talus treated with microfractures technique [32]; in another study, 20 % of persistent pain was found in a similar population after microfractures of the talus [10]. AMIC technique (autologous matrix-induced chondrogenesis), involving the use of a solid type I/III collagen matrix, was the first matrix-assisted microfracture technique to be developed in 2003 [6, 9, 28]. Recently, the results of this technique in the treatment of osteochondral lesions of the talus have been published [30, 33, 34]. Wiewiorski et al. [33] reported a case of a young male patient with a large osteochondral lesion of the medial talar edge treated with drilling of the subchondral bone and a type I/III collagen matrix, filling the bone defect with an autologous bone grafting. At one-year follow-up, the patient was free of pain; even during sport activities, no sign of instability was reported. The same group more recently reported the results at a minimum of 24 months after surgery of 26 patients who underwent the repair of osteochondral lesions using autologous bone grafting sealed by a collagen matrix, without drilling of the subchondral bone. All the clinical scores significantly improved, as well as the MOCART score for cartilage repair tissue on post-operative magnetic resonance was considered good [28]. However, a standard antero-medial or antero-lateral approach for arthrotomy was used in both cases. The use of an injectable matrix could overcome this needing, thus allowing a less invasive surgical procedure. However, to better compare this new approach to these more traditional procedures, controlled trials with a longer follow-up and with a bigger population are needed. Indeed, the main limitation of the present study is the low number of the patients and the short follow-up. Moreover, an accurate MRI study is lacking, and thus, no information about the quality of the neo-formed cartilage is available. However, it has to be intended as a preliminary report of our experience with ACIC in the talus needs to be confirmed at longer follow-up. The more relevant finding of our investigation derives from the in vitro study: in order to allow a homogenous cellular distribution within the a-telocollagen matrix, bleeding from microfracture holes should be allowed before the complete solidification of Cartifill^{TM}. So, in case of use of tourniquet, it should be removed immediately before applying the injectable matrix.

Autologous collagen-induced chondrogenesis (ACIC) technique proved to be safe, and it does not add any potential risk to a common ankle arthroscopy. It is a feasible and easy technique that can be completely performed arthroscopically. This feature makes ACIC technique very suitable for joints characterized by difficult surgical access such as the ankle and especially for the treatment of chondral lesions of the talus that often requires open surgical procedures. Moreover, as the other one-step surgical procedure, it is characterized by a lower donor-site morbidity with respect to autologous chondrocyte implantation and by a ready availability.

Conclusions

Cartifill^{TM} proved to be cytocompatible, and in the pre-solid state, it allows an uniform cellular distribution of both BMSCs and CHs. The microfractures technique associated with the use of injectable matrices in the treatment of chondral lesions might be a remarkable advantage because it is less invasive, especially in the talus, as it is a fully arthroscopic technique. This preliminary pilot study shows that no major adverse event occurred within 6 months and symptoms were improved in all the patients. Longer follow-up, higher number of patients and comparative studies with other techniques will be necessary to confirm the validity of this new surgical approach.

References

1. Barnes CJ, Ferkel RD (2003) Arthroscopic debridement and drilling of osteochondral lesion of the talus. Foot Ankle Clin 8:243–257
2. Becher C, Becher C, Driessen A, Hess T, Longo UG, Maffulli N, Thermann H (2010) Microfracture for chondral defects of the talus: maintenance of early results at midterm follow-up. Knee Surg Sports Traumatol Arthrosc 18:656–663
3. Carlsson AM (1983) Assessment of chronic pain. I. Aspects of the reliability and validity of the visual analogue scale. Pain 16:87–101
4. Chen CY, Huang PJ, Kao KF, Chen JC, Cheng YM, Chiang HC, Lin CY (2004) Surgical reconstruction for chronic lateral instability of the ankle. Injury 35:809–813
5. de Girolamo L, Bertolini G, Cervellin M, Sozzi G, Volpi P (2010) Treatment of chondral defects of the knee with one step matrix-

assisted technique enhanced by autologous concentrated bone marrow: in vitro characterisation of mesenchymal stem cells from iliac crest and subchondral bone. Injury 41:1172–1177
6. Dhollander AA, De Neve F, Almqvist KF, Verdonk R, Lambrecht S, Elewaut D, Verbruggen G, Verdonk PC (2011) Autologous matrix-induced chondrogenesis combined with platelet-rich plasma gel: technical description and a five pilot patients report. Knee Surg Sports Traumatol Arthrosc 19:536–542
7. Frisbie DD, Oxford JT, Southwood L, Trotter GW, Rodkey WG, Steadman JR, Goodnight JL, McIlwraith CW (2003) Early events in cartilage repair after subchondral bone microfractures. Clin Orthop Relat Res 407:215–227
8. Giannini S, Buda R, Vannini F (2001) Autologous chondrocyte transplantation in osteochondral lesion of the ankle joint. Foot Ankle Int 22:513–517
9. Gille J, Schuseil E, Wimmer J, Gellissen J, Schulz AP, Behrens P (2010) Mid-term results of autologous matrix-induced chondrogenesis for treatment of focal cartilage defects in the knee. Knee Surg Sports Traumatol Arthrosc 18:1456–1464
10. Gobbi A, Francisco RA, Lubowitz JH, Allegra F, Canata G (2006) Osteochondral lesions of the talus: randomized controlled trial comparing chondroplasty, microfracture and osteochondral autograft transplantation. Arthroscopy 22:1085–1092
11. Gyton GP (2001) Theoretical limitations of AOFAS scoring system: an analysis using Monte Carlo modeling. Foot Ankle Int 22:779–787
12. Hjelle K, Soljeim E, Strand T, Muri R, Brittberg M (2002) Articular cartilage defects in 1,000 knee arthroscopies. Arthroscopy 18:730–734
13. Hui JHP, Buhary KS, Chowdhary A (2012) Implantation of orthobiologic, biodegradable scaffolds in osteochondral repair. Orthop Clin North Am 43:255–261
14. Imhoff AB, Paul J, Ottinger B, Wörtler K, Lämmle L, Spang J, Hinterwimmer S (2011) Osteochondral transplantation of the talus: long term clinical and magnetic resonance imaging evaluation. Am J Sports Med 39:1487–1493
15. Kitaoka HB, Patzer GL (1997) Analysis of clinical grading scales for the foot and ankle. Foot Ankle Int 18:443–446
16. Lopa S, Mercuri D, Colombini A, De Conti G, Segatti F, Zagra L, Moretti M (2013) Orthopedic bioactive implants: hydrogel enrichment of macroporous titanium for the delivery of mesenchymal stem cells and strontium. J Biomed Mater Res A 101:3396–3403
17. Lysholm J, Gillquist J (1982) Evaluation of knee ligament surgery results with special emphasis on use of a ascoring scale. Am J Sport Med 10:150–154
18. Madeley NJ, Wing KJ, Topliss C, Penner MJ, Glazebrook MA, Younger AS (2012) Responsiveness and validity of the SF-36, Ankle Osteoarthritis Scale, AOFAS Ankle Hindfoot Score, and Foot Function Index in end stage ankle arthritis. Foot Ankle Int 33:57–63
19. Mei-Dan O, Carmont MR, Laver L, Mann G, Maffulli N, Nyska M (2012) Platelet-rich plasma or hyaluronate in the management of osteochondral lesions of the talus. Am J Sports Med 40:534–541
20. Pelttari K, Steck E, Richter W (2008) The use of mesenchymal stem cells for chondrogenesis. Injury 39:S58–S65
21. Porada CD, Almeida-Porada G (2010) Mesenchymal stem cells ad therapeutics and vehicles for gene and drug delivery. Adv Drug Deliv Rev 62:1156–1166
22. Ronga M, Grassi FA (2005) Treatment of deep cartilage defects of the ankle with matrix-induced autologous chondrocyte implantation (MACI). Foot Ankle Surg 11:29–33
23. Schmitt A, van Griensven M, Imhoff AB, Buchmann S (2012) Application of stem cells in orthopedics. Stem Cells Int 2012:394962
24. Seo S, Na K (2011) Mesenchymal stem cell-based tissue engineering for chondrogenesis. J Biomed Biotechnol 2011:806891
25. Seo SS, Kim CW, Jung DW (2011) Management of focal chondral lesion in the knee joint. Knee Surg Relat Res 23:185–196
26. Shetty AA, Kim SJ, Bilagi P, Stelzeneder D (2013) Autologous collagen-induced chondrogenesis: single-stage arthroscopic cartilage repair technique. Orthopedics 36:e648–e652
27. Steadman JR, Rodkey WG, Rodrigo JJ (2001) Microfracture: surgical technique and rehabilitation to treat chondral defects. Clin Orthop Relat Res 391:S362–S369
28. Steinwachs MR, Guggi T, Kreuz PC (2008) Marrow stimulation techniques. Injury Suppl 1:S26–S31
29. Tegner Y, Lisholm J (1985) Rating systems in the evaluation of knee ligament injuries. Clin Orthop Relat Res 198:43–49
30. Valderrabano V, Miska M, Leumann A, Wiewiorski M (2013) Reconstruction of osteochondral lesion of the talus with autologous spongiosa graft and autologous matrix-induced chondogenesis. Am J Sports Med 41:519–527
31. van Eekeren IC, Reilingh ML, van Dijk CN (2012) Rehabilitation and return-to-sports activity after debridement and bone marrow stimulation of osteochondral talar defects. Sports Med 42:857–870
32. Verhagen RA, Struijs PA, Bossuyt PM, van Dijk NC (2003) Systematic review of treatment strategies for osteochondral defects of the talar dome. Foot Ankle Clin 8:233–242
33. Wiewiorski M, Leumann A, Buettner O, Pagenstert G, Horisberger M, Valderrabano V (2011) Autologous matrix-induced chondrogenesis aided reconstruction of a large focal osteochondral lesion of the talus. Arch Orthop Trauma Surg 131:293–296
34. Wiewiorski M, Barg A, Valderrabano V (2013) Autologous matrix-induced chondrogenesis in osteochondral lesions of the talus. Foot Ankle Clin 118:151–158
35. Zengerink M, Struijs PA, Tol JL, van Dijk CN (2010) Treatment of osteochondral lesions of the talus: a systematic review. Knee Surg Sports Traumatol Arthrosc 18:238–246