Foot and Ankle Surgery 26 (2020) 669–675

Contents lists available at ScienceDirect

Foot and Ankle Surgery

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

Comparison Matrix-Associated Stem Cell Transplantation (MAST) with Autologous Matrix Induced Chondrogenesis plus Peripheral Blood Concentrate (AMIC + PBC) in chondral lesions at the ankle—A clinical matched-patient analysis

Martinus Richter[1,*], Stefan Zech, Stefan Meissner, Issam Naef

Department for Foot and Ankle Surgery Rummelsberg and Nuremberg, Germany

ARTICLE INFO

Article history:
Received 22 May 2019
Received in revised form 1 August 2019
Accepted 19 August 2019

Keywords:
Chondral lesion
Matrix-Associated Stem Cell Transplantation (MAST)
Autologous Matrix Induced Chondrogenesis (AMIC)
Peripheral Blood Concentrate (PBC)
Ankle

ABSTRACT

Background: The aim of the study was to compare Matrix-Associated Stem Cell Transplantation (MAST) with Autologous Matrix Induced Chondrogenesis plus Peripheral Blood Concentrate (AMIC + PBC) in chondral lesions at the ankle.

Methods: In a matched-patient clinical follow-up study, patients with chondral lesion at the ankle that were treated with MAST from April 1, 2009 to July 15, 2016, and patients that were treated with AMIC + PBC from July 17, 2016 to May 31, 2017 were included and compared. Size and location of the chondral lesions and the Visual-Analogue-Scale Foot and Ankle (VAS FA) before treatment and at follow-up were analysed. Bone Marrow Aspirate Concentrate (BMAC) was used for MAST and Peripheral Blood Concentrate (PBC) for AMIC + PBC to impregnate a collagen I/III matrix (Chondro-Gide, Wollhusen, Switzerland) that was fixed into the chondral lesion with fibrin glue.

Results: One hundred and twenty-nine patients with 136 chondral lesions were included in both groups. The chondral lesions were located as follows (MAST/AMIC + PBC, n (%)), medial talar shoulder only, 59 (43)/62 (46); lateral talar shoulder only, 44 (32)/42 (31); medial and lateral talar shoulder, 7 (10)/7 (10); tibia, 19 (14)/18 (13). The lesion size was 1.6/1.8 cm^2 on average and VAS FA was 46.9/45.7 (MAST/AMIC + PBC). For MAST/AMIC + PBC groups, 107 (83%)/105 (81%) with 112/110 previous chondral lesions completed the defined 2-year-follow-up after 24.4/23.8 months on average. VAS FA improved to 82.3/79.8 (MAST/AMIC + PBC). No parameter significantly differed between MAST and AMIC + PBC groups.

Conclusions: MAST and AMIC + PBC as part of a complex surgical approach led to improved and high validated outcome scores in 2-year-follow-up. MAST and AMIC + PBC showed similar results.

1. Introduction

Matrix-Associated Stem Cell Transplantation (MAST) is a modification of Autologous Matrix Induced Chondrogenesis (AMIC) with a potentially higher concentration of stem cells (from Bone Marrow Aspirate Concentrate (BMAC)) in the implanted matrix [1–4]. MAST led to improved and high validated outcome scores in the mid-term-follow-up as part of a complex surgical approach [1,5,6]. No method related complications were registered [1,5,6]. Even though a control group was missing in all studies, the authors concluded that MAST as part of a complex surgical approach is an effective method for the treatment of chondral lesions of the ankle for at least five years [1,5,6]. However, in 2017, the local government authorities re-categorized MAST, i.e. the included BMAC for impregnation of the matrix, as stem call manufacturing and heterologous transplantation [1]. Consequently, MAST and all other procedures including BMAC were not "subject to disclosure" as before but "subject to authorization". The authors' institution was not authorized to perform MAST after July 16, 2016, and applied for authorization shortly after. The authorization process is still pending (status September 2019), and no approval for MAST, or any other procedure involving BMAC has been approved in the entire country. Meanwhile, the authors' institution changed the treatment of chondral lesions by replacing BMAC as part of MAST to Peripheral Blood Concentrate (PBC) resulting in AMIC + PBC. The effect of replacing MAST (including BMAC) by AMIC + PBC is unclear. Therefore, we conducted a study

* Corresponding author at: Department for Foot and Ankle Surgery Rummelsberg and Nuremberg, Location Hospital Rummelsberg, Rummelsberg 71, 90592 Schwarzenbruck, Germany.
E-mail address: martinus.richter@sana.de (M. Richter).
[1] Homepage: www.foot-surgery.eu.

https://doi.org/10.1016/j.fas.2019.08.009

to compare MAST with AMIC + PBC. As we used MAST before July 16, 2016, and AMIC + PBC after, we could not conduct a prospective controlled study. Consequently, a matched-patient follow-up analysis was performed.

2. Methods

2.1. Techniques

The indication for surgery as such with potential inclusion of MAST/AMIC + PBC was based on clinical symptoms as for example pain or instability and MRI-findings [6,7]. The definite indication for MAST/AMIC + PBC procedures during the surgery was subjectively made by the surgeon made during initial arthroscopy for instable, fragmented or missing cartilage [1,6]. MAST was performed as previously described [1]. AMIC + PBC was performed in similar fashion except using PBC instead of BMAC for the impregnation of the matrix (detailed description below). The other procedures included joint preserving measures such as synovectomy, lateral ligament reconstruction, peroneal tendon debridement/tenolysis, gastrocnemius tendon lengthening and others [1,8–10]. A gastrocnemius tendon lengthening was performed if ankle dorsiflexion was less than 10° with positive Silverskiöld-test [8–10]. A longitudinal medial 3 cm-skin incision was performed above the origin of the gastrocnemius tendon [11]. The fascia was longitudinally incised, and the entire gastrocnemius tendon was cut directly at the origin of the tendon [11]. The lengthened tendon was secured with a single suture in the lengthened position. The MAST/AMIC + PBC procedure was performed through a medial approach for medial chondral lesions and through a lateral approach for lateral or central lesions (Fig. 1a–c) [6]. When the chondral lesion could not be reached without, additional malleolar osteotomy was performed [6]. Medial malleolar and anterior tibial osteotomies were performed as single oblique saw cut [6]. Lateral malleolar osteotomies were performed as anterior window cut with the anterior syndesmotic ligament attached to the cut-out fragment and the central and posterior syndesmotic ligaments attached to the remaining main fragment [6]. The osteotomized fragments were later fixed with lag screws [6]. The chondral lesion was debrided until stable surrounding cartilage was present. Subchondral cysts (MRI-stage 5, Hepple and Winson/Bristol classification) were cleared out [6,7]. Microfracturing with a 1.6 mm Kirschner wire was performed at intact subchondral bone, and at the ground of subchondral bone defects and cysts [6]. Bone defects of more than 3 mm depth (cysts and others) were filled with autologous cancellous bone harvested from the distal tibia not exceeding the surrounding subchondral bone level.

2.2. BMAC versus PBC

For MAST including BMAC, 15cc stem cell-rich blood was harvested during the procedure from the ipsilateral pelvic bone marrow with a Jamshidi needle (10 × 3 mm, Cardinal, Dublin, OH, USA) and a special syringe (Arthrex-ACP, Arthrex, Naples, FL, USA) through a stab incision [6]. For AMIC + PBC, 15cc peripheral venous blood was harvested with the same special syringe (Arthrex-ACP, Arthrex, Naples, FL, USA). For both, MAST including BMAC and AMIC + PBC, the syringe was centrifuged (10 min, 1,500 rotations per minute) [6]. After centrifugation, the supernatant was aspirated including the entire fluid layer directly above the erythrocyte layer. Thus, PBC is a modification of Platelet Rich Plasma (PRP) and Autologous Conditioned Plasma (ACP) [12–14]. The difference of PBC to PRP is that for PBC no addition of an anticoagulant, such as citrate dextrose A to prevent platelet activation prior to its use as for PRP [14]. The difference of PBC to ACP is that for PBC the aspirated supernatant (after centrifugation) included the entire fluid layer directly above the erythrocyte layer, whereas ACP includes the only the clear fluid above [12].

2.3. Preparation of the matrix

The supernatant was used to impregnate a collagen I/III matrix (Chondro-Gide, Geistlich, Wollhusen, Switzerland) by submerging the matrix completely into the supernatant for 3 min (impregnation) [6]. The matrix was cut to the size of the cartilage lesion roughly before and more exact after the impregnation [6]. The impregnated matrix was fixed into the chondral lesion with fibrin glue (Tissucoll or Tisseel, Baxter, Deerfield, IL, USA) (Fig. 1b) [6]. The matrix fixation was tested by moving the joint several times [6]. Adequate fixation was approved when the matrix stayed in place in the chondral lesion [6].

The postoperative treatment included partial weight bearing with 15 kg with orthosis (Vacuped, Oped, Valley, Germany) [6]. Motion of the joint was restricted for two days, and joint motion in the orthosis, i.e. approximately 10° range of motion, was started at day three after surgery [6]. Postoperative consultations were performed at 6 weeks, 3, 12, and 24 months [6].

2.4. Study design

2.4.1. Inclusion criteria

For the AMIC + PBC group, all patients with chondral lesion at the ankle that were treated with AMIC + PBC from July 17, 2016 to May 31, 2017 were considered for inclusion prospectively and consecutively (n = 141). As basis for the matched-patient group, all patients treated with MAST from April 1, 2009 to July 15, 2016 were included (MAST cohort, n = 824) [5,6]. This data was gathered prospectively and continuously [1,5,6].

2.4.2. Exclusion criteria

Patients with bilateral treatment, i.e. both ankles (n = 54 (7%)/3 (2%) (MAST/AMIC + PBC)) and/or MAST/AMIC + PBC at more than one joint surface, i.e. talus and tibia (n = 67 (8%)/9 (10%)(MAST/AMIC + PBC)) were excluded from the study. No other exclusion criteria were defined. One-hundred and twenty-nine patients were eligible for the AMIC + PBC group, and 703 for the MAST group before matching.

2.4.3. Matching

Age, sex, chondral lesion size and location, additional procedures, and follow-up time were considered for the matching, i.e. for each patient from the AMIC-PBC group the most similar patient from the entire MAST cohort was chosen. The matched-patient MAST group comprised 129 patients, i.e. 574 patients (82%) from the entire MAST cohort were not included.

2.4.4. Parameter

Before surgery and at follow-up, radiographs (bilateral views (dorsoplantar and lateral) with full weight bearing) or Weight-bearing Computed Tomography (WBCT) scan based on the availability of WBCT after July 2012 were obtained [15]. Magnetic resonance imaging (MRI) was also obtained before surgery and at follow-up. Two-year-follow-up was aimed for and was defined as follow-up between 22 and 26 months postoperatively. Before July 2014, "standard" MRI imaging with slice thickness of 3 mm was obtained [6]. From July 2014, MRI with so-called “Cartilage-mapping” with slice thickness of 0.4 mm was obtained (Fig. 1e) [16]. Visual Analogue Scale Foot and Ankle (VAS FA) was registered [17]. The lesions were preoperatively classified based on MRI based

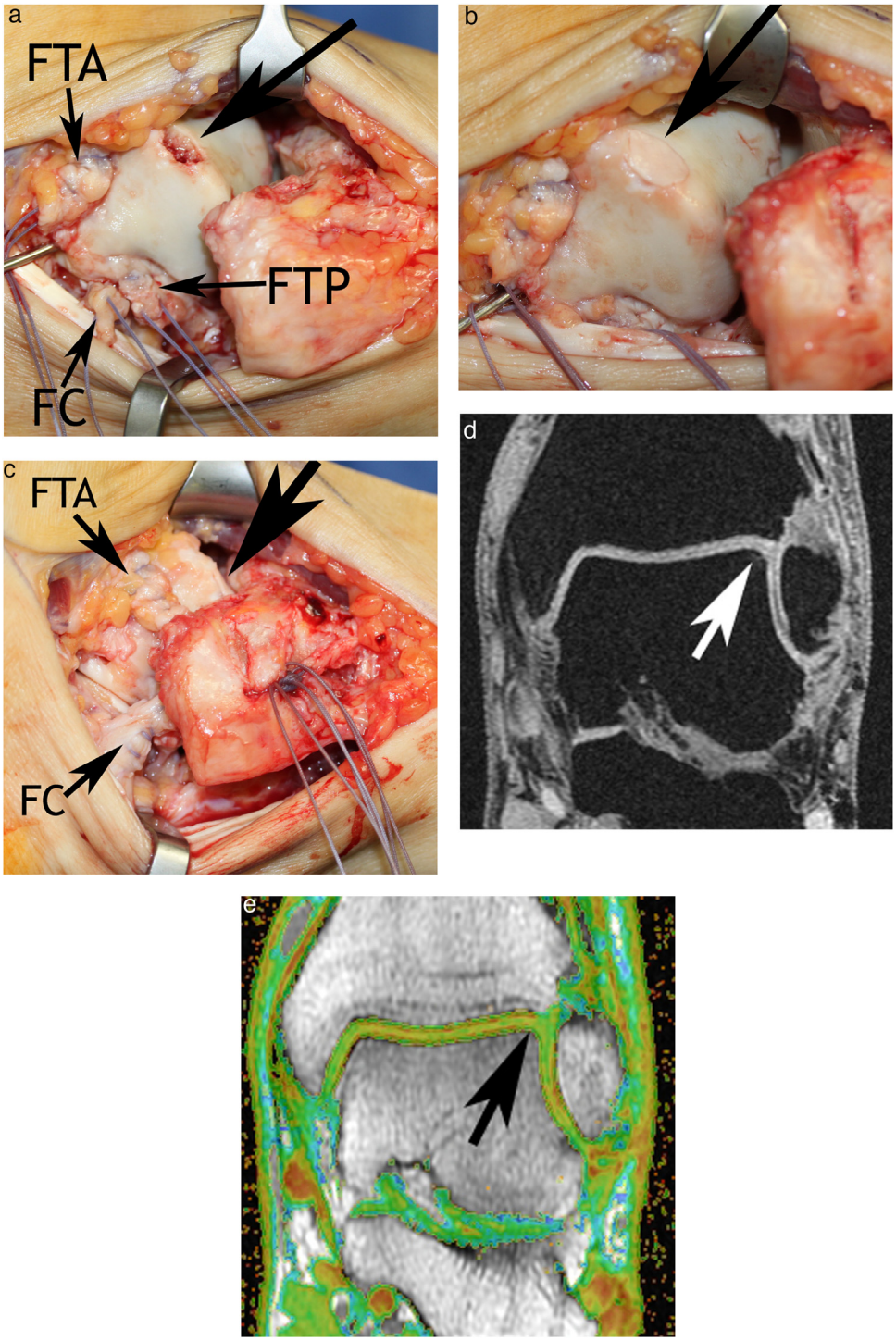

Fig. 1. a–e. AMIC + PBC at left lateral talar shoulder in a 43-year-old male patient. The VAS FA preoperatively was 52.6. Fig. 1a shows the chondral lesion (large black arrow). The size of the lesion was 1.4 × 1.8 cm (2.5 cm^2), and the maximal depth 0.8 cm. All three lateral ligaments (Fibulocalcaneal (FC), anterior and posterior tibiotalar (FTA and FTP) were elongated and partly dystopic. The ligaments were detached from the fibula, the dystopic parts were debrided and remaining ligaments were sheathed with a suture (Orthocord, DepuySynthes, Raynham, MA, USA). A 2.0 mm Kirschner wire was inserted in the talus as joystick. Fig. 1b shows the chondral lesion after AMIC + PBC (large black arrow) including autologous cancellous bone transplantation into the subchondral bone lesion, harvested from the distal tibia. Fig. 1c shows the situs after reinsertion of the lateral ligaments. 4.5 mm drill holes were drilled from the origins of the three ligaments (FTA, FC, FTP) towards proximal and lateral. The sheathed ligaments were pulled into these holes, and the sutures were knot at the proximal end of the holes. The patient completed follow-up at 24.2 months. The VAS FA was 89.6. Fig. 1d shows a coronal MRI reformation of "Cartilage-mapping" T2 specification with 0.4 mm slice thickness at follow-up. At the lateral talar shoulder (arrow, location of earlier chondral lesion), the cartilage is clearly visible as well as the minimal joint gap between the tibial and talar cartilage despite minimal irregular surface of the subchondral bone. No subchondral bone oedema is visible (MRI-stage for chondral or osteochondral lesion negative) [7]. Fig. 1e shows a colour coded visualization of the cartilage at follow-up. At the lateral talar shoulder (arrow, location of earlier chondral lesion), the fluid percentage/content is not increased (green colour). An increased fluid percentage/content would be a sign for chondral damage which often precedes morphologically visible damage [6]. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

on the Hepple and Winson/Bristol classification (Fig. 1d–e) [7]. Intraoperatively, the actual lesion size was measured and the lesion location specified. Complications and treatment failure, as for example conversion to ankle joint replacement of arthrodesis were registered.

2.5. Statistical analysis

The data was analysed with SPSS software (IBM SPSS Statistics 25, IBM, Armonk, NY, USA). An unpaired t-test was used for statistical comparison of VAS FA preoperatively and at follow-up and between groups. Before using the paired t-test, the data were investigated regarding the distribution and the data were proven to be normally distributed. Chi^2-test was used to compare the different MRI stages preoperatively versus follow-up and between groups. ANOVA (potential Scheffe Post Hoc test) was used to analyse differences of the follow-up scores for different lesion location, size (lesion size $\leq$2 cm or >2 cm) and MRI-stage and between groups. The significance level was defined as $p < 0.05$). A power analysis that was carried out before each specific statistical justified sufficient power (>0.8).

3. Results

3.1. Patients

One hundred and twenty-nine patients with 136 chondral lesions were included in the study for both MAST and AMIC + PBC groups. Table 1 shows the demographic parameter, preoperative VAS FA and suspected cause and mechanism of the chondral lesions.

3.2. Chondral lesions

The chondral lesions were located as follows (MAST/AMIC PBC, n (%)), medial talar shoulder only, 59 (43)/62 (46); lateral talar shoulder only, 44 (32)/42 (31); medial and lateral talar shoulder, 7 (10)/7 (10)(7 lesions medial plus 7 lesions lateral = 14 lesions, i.e. 10% of all lesions); tibia, 19 (14)/18 (13). The lesion size was 1.6/1.8 cm^2 on average (range, .8–3.6/.6–4 cm^2) (MAST/AMIC + PBC). Table 2 shows the MRI-stage of the lesions. Most common stages were 1 (cartilage lesion only) in 52/54 cases (38%/36%) (MAST/AMIC + PBC).

3.3. Additional surgical procedures

Table 3 shows the additional surgical procedures. Synovectomy was performed in all cases, lateral ligament reconstruction in 93/99% and gastrocnemius tendon lengthening in 73/93% (MAST/AMIC + PBC).

3.4. Complications/revisions

No complications (Neuropraxia, stiffness, wound healing delay, thrombosis, infection) were registered until follow-up. Four patients (3%) of the MAST group underwent another joint preserving ankle surgery after 9, 12, 14 and 18 months including another MAST (three patients) or AMIC + PBC (one patient) procedure. Three patients (2%) of the AMIC + PBC group underwent another joint preserving ankle surgery after 8, 13 and 16 months including another AMIC + PBC procedure. Each patient reported subsequent ankle sprains before the second surgery. All seven patients completed follow-up.

3.5. Follow-up

From MAST/AMIC + PBC groups, 107 (83%)/105 (81%) with 112/110 previous chondral lesions completed the defined 2-year-follow-up after 24.4/23.8 months on average (range, 22–26/22–25 months). VAS FA improved to 82.3/79.8 (range, 52.1–100/43.8–100; t-test, $p < .01$ each) (MAST/AMIC + PBC). The MRI stage improved (Table 2; Chi^2, each $p < .01$). In 52/42 of the previous lesion locations (47/38%) (MAST/AMIC + PBC), no lesion was visible in the MRI at follow-up (MRI-stage for chondral or osteochondral lesion negative) [7]. Different lesion location (medial/lateral talar shoulder, tibia), lesion size ($\leq$2 cm or >2 cm) or MRI-stage did not lead to different VAS FA at follow-up (ANOVA, all $p > .05$, Post Hoc test not applicable). Highest scores were registered in lesions located at the Tibia, size $\leq$ 2 cm, and MRI-stage 1. The seven patients with second surgery before follow-up did not differ significantly regarding VAS FA or other parameter from the remaining patients (data not shown).

3.6. Comparison MAST versus AMIC + PBC

The following parameters did not significantly differ between AMIC + PBC, age at the time of surgery, gender, preoperative VAS

Table 1
Demographic parameter, preoperative VAS FA, cause and suspected mechanism of chondral lesions (patient based analysis, i.e. 129 patients in total for each group).

	MAST	AMIC + PBC	Test, p
Age (average, range)	35.3 (18–69)	35.6 (13–68)	t-test, .98
Gender (male; n (%))	76 (59)	77 (60)	Chi^2, .87
VAS FA (average, range)	46.9 (18.3–81.2)	45.7 (17.5–78.9)	t-test, .89
Cause (n (%))			
Vehicular accident	8 (6)	5 (5)	Chi^2, .92
Sports-related trauma	64 (50)	62 (48)	
Non-vehicular/sports-related trauma	41 (32)	43 (33)	
Deformity without trauma	6 (5)	7 (5)	
Hindfoot/ankle varus	4 (3)	4 (3)	
Hindfoot/ankle valgus	2 (2)	3 (2)	
Other	6 (5)	5 (4)	
Unknown	4 (3)	5 (4)	
Mechanism (n (%))			
Fracture	9 (7)	7 (5)	Chi^2, .88
Single sprain	23 (18)	21 (16)	
Multiple sprains	68 (53)	70 (54)	
Other	2 (2)	3 (2)	
Unknown	27 (21)	28 (22)	

Cause and mechanism are independently listed.

Table 2
MRI based classification of 129 patients with 136 chondral lesions.

Stage and stage description	MAST		AMIC-PBC	
	Preop n (%)	FU n (%)	Preop n (%)	FU n (%)
1 cartilage lesion only	52 (38)	34 (31)	54 (40)	40 (36)
2a subchondral fracture with surrounding bone edema	46 (34)	12 (11)	43 (32)	19 (17)
2b subchondral fracture with no surrounding bone edema	8 (6)	2 (2)	9 (7)	1 (1)
3 detached but undisplaced fragment	5 (4)	3 (3)	7 (5)	3 (3)
4 displaced fragment	6 (4)	2 (2)	7 (5)	1 (1)
5 subchondral cyst	18 (13)	5 (5)	16 (12)	6 (5)
MRI-stage for chondral or osteo-chondral lesion negative (no lesion visible)	1 (1)	52 (47)	0 (0)	42 (38)

Preop, preoperatively. FU, follow-up.
Lesion based analysis, MAST preop, n = 136; MAST FU, n = 110; AMIC + PBC preop, n = 136; AMIC + PBC FU, n = 112. Distribution preop versus FU; Chi^2, $p < 0.01$ (MAST and AMIC-PBC). Distribution preop MAST versus AMIC + PBC, Chi^2, p = .86. Distribution FU MAST versus AMIC + PBC, Chi^2, p = .52.

Table 3
Additional procedures performed during surgery.

Procedure	MAST n (%)	AMIC + PBC n (%)
Arthroscopy	129 (100)	129 (100)
Synovectomy	129 (100)	129 (100)
Debridement/tenolysis peroneal tendons	120 (93)	128 (99)
Lateral ligament reconstruction/augmentation	120 (93)	128 (99)
Gastrocnemius tendon lengthening	94 (73)	120 (93)
Medial malleolus osteotomy	14(11)	17 (13)
Lateral malleolus osteotomy	0 (0)	1 (1)
Anterior tibial osteotomy	1 (1)	1 (1)
Autologous cancellous bone transplantation (under MAST)	25 (19)	34 (26)
Correction of malalignment	5 (4)	3 (2)
Correction above ankle	1 (1)	0 (0)
Correction below ankle	4 (3)	3 (2)

Case (patient) based analysis.

FA, cause and suspected mechanism of chondral lesions, lesion size and location, preoperative MRI stage, additional surgical procedures, and rate of complications/revisions, follow-up rate, follow-up time, VAS FA at follow-up, and MRI stage at follow-up (each p > .05) (Tables 1–3).

4. Discussion

This is the first study comparing MAST with AMIC + PBC. The transition from MAST to AMIC + PBC was enforced by local regulations as described above. The enforced transition was seen very critical at the authors' institution and enormous efforts were undertaken to achieve authorization for performing MAST after July 2016 — without success until September 2019. However, the transition gave the opportunity to compare MAST with another method (AMIC + PBC) which was not planned before. Based on the good previous results of MAST, we did not expect that AMIC + PBC with potentially less "powerful" cells for matrix impregnation would achieve similar results [5,6].

We chose a clinical matched-patient analysis to compare AMIC + PBC with MAST. The high number of MAST procedures performed from April 2009 to July 2016 (n = 824) allowed for very accurate matching. An ongoing prospective data acquisition of all surgically treated patients including planned yearly follow-ups at the authors´ institution is the basis for this successful matching process. As result of the adequate matching process, the patient cohorts including demographic data, preoperative scores, and all characteristics of the chondral lesions (size, location, MRI-stage, cause and mechanism) were similar (Tables 1 and 2). Except the MAST/AMIC + PBC procedures, the additional surgical procedures did not significantly differ between groups (Table 2). We observed a trend towards a higher rate of lateral ligament reconstruction (99% versus 93%) and gastrocnemius lengthening (93% versus 73%) in the AMIC + PBC group (Table 2). The follow-up parameters did also not significantly differ between groups including follow-up rate, time and VAS FA score, and MRI stage of the chondral lesions (Tables 2 and 3). A trend to lower negative lesion visibility of the previous chondral lesion was observed in the AMIC + PBC group (38 versus 47%). The principal result of our study is that MAST and AMIC + PBC did not differ. Consequently, the main difference of both procedures, i.e. using BMAC or PBC had no influence on the results of this study. What does this mean? The use of BMAC and PBC as adjunct might not have an effect on the tissue development and/or the clinical outcome. If so, AMIC alone (without BMAC or PBC) would allow for the same results. As we did not perform AMIC alone, we tried to find comparable results from the literature [2,18–24]. The different studies with up to 47 cases and up to 8-year follow-up are difficult to compare because none of the studies included a validated outcome score as our study [2,18–24]. Our study also includes much more cases than all other current studies [2,18–24]. Our results are best comparable with the results of MAST from Murphy at al. [25]. We are (again) surprised about the low rate of deformities and instabilities from other studies [2,5,6,18–25]. Either, these pathologies were not present or were not registered. In our understanding deformity and above all instability is the most important and common prerequisite for chondral lesions at the ankle (see further below). AMIC + PBC shows comparable results as MAST on the basis of this and other studies [5,6,25]. Consequently, also no significant difference between PBC and BMAC as adjunct might exist. We used BMAC before to allow for a high concentration of mesenchymal stem cells [5,6,25]. The concentration of mesenchymal stem cells in PBC in comparison with BMAC is questionable. We did not investigate the content of BMAC or PBC cytologically and cannot answer this question. Another potential effect could be chemo tactical "attraction" of mesenchymal stem cell from PBC as described for PRP [14]. This is all unclear and debatable. We earlier reported about anecdotal histological investigations after MAST showing chondrocytes, and we suspect that the same would be observed after AMIC + PBC which is also debatable [5]. Our 2-year-follow-up results after MAST and AMIC + PBC at the ankle as part of a complex surgical approach are favourable and no adverse effects have been registered. We are aware that especially the high percentage and extent of additional procedures had influence on the study results and this issue will be discussed extensively below (see below, limitations). We observed a high percentage of lesions limited to the cartilage as before [5,6]. We could not detect follow-up score differences between different location, size or MRI-stage of the chondral lesions, as reported before [5,6]. We observed only a trend and no significance to higher follow-up scores towards smaller lesions, located at tibia and lower MRI-stages [5,6]. The follow-up scores

after MRI-stage V (subchondral cyst) were not the lowest as shown in other studies [5–7,26,27]. MAST and AMIC + PBC worked also for larger lesions and "higher" MRI-stages for two and for five years [5] AMIC + PBC.

4.1. Limitations

Limitations of the study are: subjective indication for treatment, unclear influence of associated procedures, missing control group, questionable visibility of lesions limited to the cartilage in the MRI, missing outcome parameter for the created tissue, and matched-patient instead of a "real" control group.

The indication for AMIC + PBC was subjectively made by the surgeon during initial arthroscopy [5,6]. This is the typical decision-making process also in other studies but does still not follow objective parameters [5,6]. We believe that "surgical" decision-making is still better than indication based on any kind of imaging-based staging with the described limitations [5,6]. The indication for AMIC + PBC was not similar to the indication for surgery as such which was based on clinical symptoms as usual [5,6]. The simultaneous additional procedures (Table 3) confound the results as in all other studies we are aware of [5,26,28]. As stated this above, we consider this as a main limitation of this study [6]. These procedures were considered to be necessary to restore joint function (for example lateral ligament reconstruction in 93% or 99% or gastrocnemius tendon lengthening in 73% or 93%. Other procedures were performed on a regular basis (for example synovectomy in 100%). The percentage of gastrocnemius lengthening is high and even increasing in comparison with earlier studies [5,6]. The indication for gastrocnemius lengthening is not clearly defined and debatable [5,6]. This and other studies have shown more advantages like decreased joint load than disadvantages like decreased calf muscle strength as basis for the indication [5,6]. Performing MAST or AMIC + PBC as single procedure would allow for a much more specific study results and would allow for much stronger conclusions [6]. However, we did not notice a single patient with just a chondral lesion and no other pathologies [6]. Based on our experience and considering the literature, we doubt that isolated chondral lesions are common [6]. In our cohort, the main cause for the chondral lesion might have been post traumatic and/or ligamentous instability. Following this principle, treatment of the chondral lesion alone without treating the cause as for example the ligamentous instability would be inadequate [6]. In contrast, our treatment concept was and is still to address all pathologies in addition to the chondral lesion [6]. If we would exclude all patients with ligamentous repair and/or gastrocnemius lengthening from the study, we would exclude 99% of all patients. This would result in study cohort that does not reflect the real situation at least in our institution. A matched-patient study design is not as good as a prospective study with control group and at best randomized. However, we are not aware of any other prospective controlled (randomized) study. The presented matched-patient study design is superior to all other published designs as far as we know. Thus, we were very surprised about the results of a consensus meeting giving clear recommendations for treatment without real evidence [21].

Based our results, we do proceed with AMIC + PBC instead of MAST. We are not sure if we would return to MAST even if we would achieve approval again. Another task is fixation of the matrix in the chondral lesion without fibrin-glue to reduce cost, complexity and risk of infection since fibrin-glue is an allologous blood product [6]. We are working on different fixation possibilities beyond suture and glue.

In conclusion, MAST and AMIC + PBC as part of a complex surgical approach led to improved and high validated outcome scores in 2-year-follow-up. MAST and AMIC + PBC showed similar results. No method related complications were registered.

Conflict of interest

None of the authors or the authors' institution received funding in relation to this study.

References

[1] Richter M, Zech S. Matrix-associated stem cell transplantation (MAST) in chondral defects of foot and ankle is effective. Foot Ankle Surg 2013;19(2):84–90.
[2] Walther M, Altenberger S, Kriegelstein S, Volkering C, Roser A. Reconstruction of focal cartilage defects in the talus with miniarthrotomy and collagen matrix. Oper Orthop Traumatol 2014;26(6):603–10.
[3] Giannini S, Buda R, Vannini F, Cavallo M, Grigolo B. One-step bone marrow-derived cell transplantation in talar osteochondral lesions. Clin Orthop Relat Res 2009;467(12):3307–20.
[4] Benthien JP, Behrens P. Autologous matrix-induced chondrogenesis (AMIC): combining microfracturing and a collagen I/III matrix for articular cartilage resurfacing. Cartilage 2010;1(1):65–8.
[5] Richter M, Zech S, Andreas Meissner S. Matrix-associated stem cell transplantation (MAST) in chondral defects of the ankle is safe and effective—2-year-followup in 130 patients. Foot Ankle Surg 2017;23(4):236–42.
[6] Richter M, Zech S. Matrix-associated stem cell transplantation (MAST) in chondral lesions at the ankle as part of a complex surgical approach—5-year-follow-up in 100 patients. Foot Ankle Surg 2019;25(3):264–71.
[7] Hepple S, Winson IG, Glew D. Osteochondral lesions of the talus: a revised classification. Foot Ankle Int 1999;20(12):789–93.
[8] Strayer LM. Recession of the gastrocnemius; an operation to relieve spastic contracture of the calf muscles. J Bone Joint Surg Am 1950;32-A(3):671–6.
[9] Pinney SJ, Sangeorzan BJ, Hansen Jr ST. Surgical anatomy of the gastrocnemius recession (Strayer procedure). Foot Ankle Int 2004;25(4):247–50.
[10] Richter M, Zech S. Arthrorisis with calcaneostop screw in children corrects Talo-1st Metatarsal-Index (TMT-Index). Foot Ankle Surg 2013;19(2):91–5.
[11] Richter M, Zech S. Lengthening osteotomy of the calcaneus and flexor digitorum longus tendon transfer in flexible flatfoot deformity improves talo-1st metatarsal-index, clinical outcome and pedographic parameter. Foot Ankle Surg 2013;19(1):56–61.
[12] Smith PA. Intra-articular autologous conditioned plasma injections provide safe and efficacious treatment for knee osteoarthritis: an FDA-sanctioned, randomized, double-blind, placebo-controlled clinical trial. Am J Sports Med 2016;44(4):884–91.
[13] Mei-Dan O, Carmont MR, Laver L, Mann G, Maffulli N, Nyska M. Platelet-rich plasma or hyaluronate in the management of osteochondral lesions of the talus. Am J Sports Med 2012;40(3):534–41.
[14] Dhurat R, Sukesh M. Principles and methods of preparation of platelet-rich plasma: a review and author's perspective. J Cutan Aesthet Surg 2014;7(4):189–97.
[15] Richter M, Seidl B, Zech S, Hahn S. PedCAT for 3D-imaging in standing position allows for more accurate bone position (angle) measurement than radiographs or CT. Foot Ankle Surg 2014;20:201–7.
[16] Richter M, Mittlmeier T, Rammelt S, Agren PH, Hahn S, Eschler A. Corrigendum to' Intramedullary fixation in severe Charcot osteo-neuroarthropathy with foot deformity results in adequate correction without loss of correction—results from a multi-centre study' [Foot Ankle Surg 21 (2015) 269-276]. Foot Ankle Surg 2016;22(4):289.
[17] Richter M, Zech S, Geerling J, Frink M, Knobloch K, Krettek C. A new foot and ankle outcome score: questionnaire based, subjective, visual-analogue-scale, validated and computerized. Foot Ankle Surg 2006;12(4):191–9.
[18] D'Ambrosi R, Maccario C, Ursino C, Serra N, Usuelli FG. Combining microfractures, autologous bone graft, and autologous matrix-induced chondrogenesis for the treatment of juvenile osteochondral talar lesions. Foot Ankle Int 2017;38(5):485–95.
[19] Usuelli FG, D'Ambrosi R, Maccario C, Boga M, de Girolamo L. All-arthroscopic AMIC(R) (AT-AMIC(R)) technique with autologous bone graft for talar osteochondral defects: clinical and radiological results. Knee Surg Sports Traumatol Arthrosc 2016;26(3):875–81.
[20] Weigelt L, Hartmann R, Pfirrmann C, Espinosa N, Wirth SH. Autologous matrix-induced chondrogenesis for osteochondral lesions of the talus: a clinical and radiological 2- to 8-year follow-up study. Am J Sports Med 2019363546519841574.
[21] Rothrauff BB, Murawski CD, Angthong C, Becher C, Nehrer S, Niemeyer P, et al. Scaffold-based therapies: proceedings of the international consensus meeting on cartilage repair of the ankle. Foot Ankle Int 2018;39(Suppl):41s–7s.
[22] Gottschalk O, Altenberger S, Baumbach S, Kriegelstein S, Dreyer F, Mehlhorn A, et al. Functional medium-term results after autologous matrix-induced chondrogenesis for osteochondral lesions of the talus: a 5-year prospective cohort study. J Foot Ankle Surg 2017;56(5):930–6.
[23] Galla M, Duensing I, Kahn TL, Barg A. Open reconstruction with autologous spongiosa grafts and matrix-induced chondrogenesis for osteochondral

lesions of the talus can be performed without medial malleolar osteotomy. Knee Surg Sports Traumatol Arthrosc 2018;27(9):2789–95.
[24] Baumfeld T, Baumfeld D, Prado M, Nery C. All-arthroscopic AMIC((R)) (AT-AMIC) for the treatment of talar osteochondral defects: a short follow-up case series. Foot (Edinburgh, Scotland) 2018;37:23–7.
[25] Murphy EP, Fenelon C, Egan C, Kearns SR. Matrix-associated stem cell transplantation is successful in treating talar osteochondral lesions. Knee Surg Sports Traumatol Arthrosc 2019;27(9):2737–43.
[26] Niemeyer P, Salzmann G, Schmal H, Mayr H, Sudkamp NP. Autologous chondrocyte implantation for the treatment of chondral and osteochondral defects of the talus: a meta-analysis of available evidence. Knee Surg Sports Traumatol Arthrosc 2011;20(9):1696–703.
[27] Aurich M, Venbrocks RA, Fuhrmann RA. Autologe chondrozytentransplantation am oberen sprunggelenk. Rational oder irrational? Orthopade 2008;37(3):188–95.
[28] Giannini S, Buda R, Cavallo M, Ruffilli A, Cenacchi A, Cavallo C, et al. Cartilage repair evolution in post-traumatic osteochondral lesions of the talus: from open field autologous chondrocyte to bone-marrow-derived cells transplantation. Injury 2010;41(11):1196–203.