Repair of retropatellar cartilage defects in the knee with microfracture and a cell-free polymer-based implant

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Abstract
Introduction To analyze magnetic resonance imaging (MRI) at 3T and the clinical outcome in a short-term pilot study after treatment of retropatellar cartilage defects with microfracturing and subsequent covering with the cell-free chondrotissue® polyglycolic acid–hyaluronan implant.
Methods Five consecutive patients after microfracturing and defect coverage with the chondrotissue® implant immersed with autologous serum were included. After a mean follow-up of 21 months (range 11–31 months), defect fill and repair tissue quality was assessed by 3-T MRI followed by applying established MRI scoring systems. The patients’ situation was assessed using the Knee injury and Osteoarthritis Outcome Score (KOOS) and a patients’ satisfaction questionnaire.
Results Magnetic resonance imaging showed good to excellent defect fill with complete integration. The mean MOCART score was 61 (range 50–75) points. The mean Henderson score was 7 (range 6–9) points. All patients showed subchondral bone alterations. The KOOS showed good values in all sub-categories in 4 out of 5 patients and a mean overall score of 73 (range 40–90) points. Two patients rated the outcome as excellent, two as good and one as fair. All patients would have the procedure again and recommend it.

Conclusions In this small case series, the coverage of symptomatic retropatellar cartilage defects with the chondrotissue® implant after microfracturing was safe and feasible with improvement of the patients’ situation at short-term follow-up.

Level of evidence IV, case series.

Keywords Cartilage repair · Patella · Microfracture · Polymer-based implant · Polyglycolic acid · Magnetic resonance imaging

Introduction

Cartilage defects do not heal spontaneously, are a common injury of the knee joint caused by trauma, inflammation and/or biomechanical dysfunction. Cartilage damage is a major health problem and may progress to severe osteoarthritis in symptomatic knees [1]. Retrospective analysis of knee arthroscopies revealed that up to 60 % of patients who have been subjected to arthroscopy show chondral or osteochondral defects. Defects of the patella are considered to be the most common, representing 11–37 % of all diagnosed chondral defects of the knee [2–5]. As a matter of fact, the complex architecture of the patellofemoral joint, the demanding compression and shear forces and the frequent association of patella defects with malalignment and instabilities make repair of cartilage defects of the patella very challenging [6, 7]. Treatment options for cartilage defects comprise microfracture or other bone marrow stimulating techniques and more complex procedures such as autologous chondrocyte implantation or osteochondral graft transfer. However, in the patella, the clinical efficacy of these procedures is variable and the outcome may be less predictable [8–11].
The microfracture technique is an easy to perform and cost effective common first-line treatment option for cartilage defects. During a mini-open or arthroscopic procedure, the defective cartilage is removed and perforation of the subchondral bone is performed to provoke bleeding into the defect and access to the subchondral bone marrow and its mesenchymal progenitor cells. A blood clot forms and in-growth of progenitor cells occurs with subsequent formation of a fibrous to fibro-cartilage-like repair tissue [12, 13]. However, clinical studies showed that the procedure is effective in the short-term but the clinical outcome may deteriorate in the mid- to long-term and may lead to degeneration [14–16].

As a consequence, one-step procedures have been developed that aim at improving the microfracture and/or bone marrow stimulating techniques by covering the defect with resorbable biomaterials or membranes that have been ‘bio-activated’ with blood derivatives. These approaches follow the route that covering of the microfractured defect may help to keep mesenchymal progenitor cells and probably growth factors released from the subchondral bone or synovial fluid in the defect and thereby improve the formation of cartilage repair tissue [17]. For instance, the AMIC procedure is based on closing the microfractured defect with fibrin glue mixed with autologous serum or PRP, followed by covering with a porcine collagen membrane. Clinical studies have shown that the procedure is safe and effective for cartilage repair but long-term effectiveness remains to be shown [18–20]. Another approach favors the use of a chitosan gel mixed with glycerophosphate and autologous whole blood (BST-CarGel) for filling microfractured cartilage defects. In a randomized trial, BST-CarGel has been shown to lead to better defect filling and repair tissue formation than microfracturing alone after 1 year, while the clinical outcome was significantly improved in both groups with no differences between the treatments [21].

Our approach uses a resorbable, textile polyglycolic acid–hyaluronan implant (chondrotissue®) for cartilage repair to cover microfractured defects. The implant has been shown to improve repair tissue formation and quality compared to microfracturing alone, in the ovine model [22, 23]. Clinical effectiveness with up to 5-year follow-up, safety of the procedure as well as formation of hyaline-like cartilage repair tissue and good defect fill have already been reported by other groups that combined the implant with autologous serum, platelet-rich plasma or bone marrow aspirate for the repair of tibial and femoral cartilage defects of the knee [24–29].

Since effective treatment options for cartilage defects of the patella are demanded and information about the outcome of the chondrotissue® treatment in patellar cartilage defects is scarce, we retrospectively determined the magnetic resonance images (MRI) and clinical outcome within a short-term pilot study with five patients who have been treated with microfracturing and the chondrotissue® implant for retropatellar cartilage repair. We hypothesized that this procedure is safe, leads to good cartilage fill on MRI and satisfactory clinical outcomes as assessed by self-administered patients questionnaires.

Materials and methods

Patients

From October 2011 to June 2013, five consecutive patients with symptomatic full thickness chondral defects of the patella were treated arthroscopically with the cell-free polyglycolic acid–hyaluronan (PGA-HA) implant (chondrotissue®, BioTissue AG, Zurich, Switzerland) immersed with autologous serum. All patients gave informed consent and were recalled after a mean follow-up of 21 months (range 11–31 months after surgery). All data were obtained from medical records and MRI. Characteristics of patients (2 females, 3 males) are given in Table 1. The average age of the patients was 27 years (range 15–40 years). The mean defect size was 4.0 cm² (range 3.0–5.0 cm²). All defects were classified as Outerbridge grade IV defects [30]. In three patients, additional concomitant realignment surgical procedures were necessary. In two patients, additional microfracture on the lateral femoral condyle was performed. Four of the patients have not been subjected to previous surgeries. One patient had undergone arthroscopic plica resection and cartilage shaving.

Surgical procedure

Retropatellar microfracturing followed by the implantation of the chondrotissue® implants were performed using an open approach (Fig. 1). The damaged cartilage (Fig. 1a) was debrided down to the subchondral bone with a curette and a shaver. Microfracturing was performed using a chondroprick awl (Fig. 1b), according to the protocol by Steadman et al. [13]. The implants were immersed in 2–3 mL autologous serum that had been prepared from venous blood pre-operatively. Implants were cut to fit the size of the defect and fixated using 3–4 SmartNail® (ConMed Deutschland GmbH, Groß-Gerau, Germany), as described previously [24] (Fig. 1c). In one patient, the implant margins were additionally covered with fibrin glue (Tissucol, Baxter, Germany). The rehabilitation plan included limited weight bearing to no more than 15 kg on crutches for the first 6 weeks and gradual increase of range of motion from the third day after surgery by 30° every 2 weeks protected by a brace in all patients. After 6 weeks, patients increased weight bearing and mobility to full body
weight and full range of motion. Gentle exertion was allowed after 2 (cycling) to 6 months (running), and more strenuous activities and contact sports (such as tennis or football) after 9 months.

**Magnetic resonance imaging**

Cartilage repair tissue assessment was done using a 3-T magnetic resonance imager (Discovery MR750, GE Healthcare, Milwaukee, WI, USA) with a maximum gradient strength of 50 mT/m and 200 T/m/s slew rate using an 8-channel (phased array) knee coil. Sagittal and axial isotropic 3-dimensional (3D) gradient echo fast imaging employing steady-state acquisition (FIESTA) and proton density fat-suppressed fast-spin echo (PD-FSE) were performed. Images were evaluated by a board-certified orthopedic surgeon and radiologist. Discrepancies in interpretation were settled by consensus. Magnetic resonance observation of cartilage repair tissue (MOCART) scoring [31] was performed to assess (1) degree of defect

### Table 1 Patients' characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Patient No. 1</th>
<th>Patient No. 2</th>
<th>Patient No. 3</th>
<th>Patient No. 4</th>
<th>Patient No. 5</th>
</tr>
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<tbody>
<tr>
<td>Sex</td>
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<td>Male</td>
<td>Female</td>
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<td>Male</td>
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<tr>
<td>Age (years) at surgery</td>
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<td>19</td>
<td>39</td>
<td>25</td>
<td>40</td>
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<tr>
<td>Follow-up (months)</td>
<td>29</td>
<td>23</td>
<td>11</td>
<td>31</td>
<td>13</td>
</tr>
<tr>
<td>Retropatellar defect location</td>
<td>Mediodistal + patellar ridge</td>
<td>Mediodistal + patellar ridge</td>
<td>Central + distal patella</td>
<td>Mediodistal + patellar ridge</td>
<td>Laterodistal + patellar ridge</td>
</tr>
<tr>
<td>Defect size (cm²)</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>Outerbridge classification</td>
<td>IV</td>
<td>IV</td>
<td>IV</td>
<td>IV</td>
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<tr>
<td>Implant fixation</td>
<td>SmartNail®</td>
<td>SmartNail® + fibrin glue</td>
<td>SmartNail®</td>
<td>SmartNail®</td>
<td>SmartNail®</td>
</tr>
<tr>
<td>Concomitant surgeries</td>
<td>Medial patellofemoral ligament reconstruction</td>
<td>Medial patellofemoral ligament reconstruction, anteromedialization tibial tuberosity, lateral femoral condyle microfracturing</td>
<td>Lateral release, lateral femoral condyle microfracturing</td>
<td></td>
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<tr>
<td>Previous surgical procedures</td>
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<td>None</td>
<td>None</td>
<td>Plica resection, shaving</td>
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</tr>
</tbody>
</table>

**Fig. 1** Open implantation of the chondrotissue® polyglycolic acid–hyaluronan implant in a large retropatellar cartilage defect (patient No. 3) (a). The degenerative cartilage has been removed down to the subchondral bone and microfractures were introduced (b). The PGA-HA implant was immersed with autologous serum and used to cover the defect. Fixation was performed by using resorbable nails (c)
repair and filling, (2) integration to border zone, (3) surface of the repair tissue, (4) structure of the repair tissue, (5) subchondral bone alterations, (6) signal intensity of the repair tissue, and (7) effusion. The Henderson score \[32\] was applied to assess (1) defect filling, (2) MRI signal of the repair tissue, (3) bone marrow edema, and (4) effusion. The overall Henderson score is the sum of all items (minimum 4 points, maximum 16 points). A score of 4 represents normal cartilage, a score of 5–8 shows nearly normal cartilage, while a score of 9–12 shows abnormal and a score of 13–16 severely abnormal cartilage.

**Evaluation of clinical results**

For evaluation of clinical results, the KOOS (Knee injury and Osteoarthritis Outcome Score, http://www.koos.nu) \[33\] was applied. The KOOS is a patient-administered score and is divided into the sub-categories pain, symptoms, activities of daily living (ADL), sports and recreation function (sport&recr), and knee-related quality of life (QoL). Each sub-category was calculated as the sum of all included items. A score of a maximum of 100 represents no knee problems, while a score of 0 represents severe knee problems. The overall KOOS represents the mean KOOS value calculated from all sub-categories. Patients’ satisfaction with the procedure was monitored by a standardized questionnaire regarding the use of analgetics, self-assessment of the clinical outcome, willingness to have the procedure again and to recommend the surgical procedure.

**Results**

**MRI evaluation of cartilage repair**

Pre-operative MRI showed prominent medial and/or distal cartilage defects of the patella (Fig. 2, black arrows). At follow-up, the defect areas showed good to excellent cartilage repair with good defect coverage and fill as well as complete integration of the repair tissue in all cases. In two cases, intra-lesional osteophyte formation was observed (Fig. 2, black arrowhead). Three out of five cases showed subchondral alterations (Fig. 2, white arrow) in the area of the SmartNail® fixation. In all cases, intraosseous residua of the SmartNail® or drill holes (Fig. 2, black double arrows) were evident. In the patient with medial patellofemoral ligament reconstruction, the screw channel was visible (Fig. 2, white arrowhead). Two patients developed unstructured, hypertrophic tissue in areas without contralateral surfaces (Fig. 2, white double arrows). The mean MOCART score was 61 (range 50–75) points (Table 2) and the mean Henderson score was 7 (range 6–9) points (Table 2). Three patients showed complete and two patients had >50 % cartilage repair. All patients showed a complete integration of the repair tissue to the adjacent cartilage, and the cartilage signal of the repair tissue was nearly normal. The surface of the repair tissue was intact in two patients, while three patients showed some surface damage <50 % of depth. The repair tissue appeared to be homogenous in two out of five patients. All patients showed alterations of the subchondral lamina and the subchondral bone. Bone marrow edema was mild in two patients and moderate in three patients. There were no signs of effusion and some adhesions were present in four out of five cases.

**Clinical outcome**

No intra- or post-operative complications were observed. None of the patients needed further operative treatment during the follow-up period. During the follow-up period, there were no clinical signs of knee joint infection or inflammation. There were no allergic reactions, no foreign body reactions, and no abnormal knee joint effusion or swelling. Temporary blocking was not reported and there were no signs for ablation of the implant or loosening of the repair tissue.

Clinical scoring and analysis of KOOS values at follow-up showed good scores in all subgroups in four out of five patients (Table 2). At follow-up, the subgroup ‘pain’ showed a mean of 83 (range 50–94) points, ‘symptoms’ 74 (range 36–89) points, ‘activities of daily living’ 90 (range 63–100) points, ‘sport & recreation’ 66 (range 20–85) points, and the subgroup ‘quality of life’ showed a mean of 51 (range 44–81) points. The average overall KOOS showed 73 (range 40–90) points, post-operatively.

Corresponding to the evaluation of the patients’ situation using the KOOS, the standardized questionnaire about patients’ satisfaction showed that four out of five patients needed no analgetics or only once a month and the treatment effect was ranked ‘very good’ to ‘excellent’. The patient with the lowest KOOS values (patient No. 2) needed analgetics regularly on a weekly basis and reported that the treatment effect was fair. All patients were willing to have the surgery again if needed and would recommend the surgery to other patients.

**Discussion**

The most important finding of the present pilot study is that implantation of the cell-free chondrotissue® polyglycolic acid–hyaluronan implant combined with microfracturing appears to be safe for the treatment of patellofemoral cartilage defects and leads to a good clinical outcome as assessed by magnetic resonance imaging and validated
KOOS. There were no adverse events and no complications during surgery and follow-up.

Microfracturing is known to be a cost-effective first-line treatment option that leads to good results in the short-term but cartilage repair deteriorates in the mid to long-term [14, 15]. Two-step procedures such as autologous chondrocyte implantation (ACI) have been shown to be clinically effective. However, these procedures need two interventions, may lead to donor site morbidity and are time and cost-intensive. Clinical data suggest that superiority of the ACI procedure compared to microfracturing is still controversial [34–36]. In consequence, one-step procedures for the treatment of chondral defects have been developed that combine microfracturing and covering of the defect with resorbable matrices for improvement of the procedure. The common concept of these procedures is that in-growth of subchondral mesenchymal progenitor or stem cells into the cartilage defect is stimulated by microfracturing, and that the matrix immersed with autologous blood derivatives keeps the cells in place and guides cartilage repair tissue formation. In general, clinical effectiveness of such one-step procedures has been shown in pilot studies with low to moderate numbers of patients [20, 21, 37]. In line with our current results in the patella, implantation of the chondrotissue® implant bio-activated with blood-derived products or bone marrow aspirate in femoral and tibial defects of the knee pre-treated with microfracturing or drilling has been reported previously to be clinically safe, to improve the patients’ situation and to lead to good defect fill with hyaline-like cartilage repair tissue [27–29].

In the current study, the overall KOOS at follow-up showed a mean score of 73 points. This is lower than the overall KOOS score of 83 points that has been reported at 2-year follow-up after repair of patellar and femoral cartilage defects with the chondrotissue implant immersed with platelet-rich plasma [26]. However, treatment of patellofemoral cartilage defects with alternative one-step procedures or ACI resulted in comparable or lower KOOS at 2-year follow-up, compared to our approach. In a prospective case series with ten patients, the autologous matrix-induced chondrogenesis (AMIC) procedure has been shown to lead to an overall KOOS of 49 points after repair of patellofemoral cartilage defects at 2-year follow-up [38]. The DeNovo NT procedure that uses particulated juvenile articular cartilage allografts led to a mean overall KOOS of 76 points in 13 patients with patellar cartilage defects and a follow-up of in mean 28.8 months [39]. The ACI procedure has been reported to result in an overall KOOS of 71 points at 2-year follow-up and 74 points at 4-year follow-up, after treatment of cartilage defects in the patellofemoral joint. It has to be noted that the authors did not stratify the data by patellar or trochlear defects [40].

Magnetic resonance imaging evaluation showed that patellar cartilage defect repair with the chondrotissue® implant resulted in good defect coverage and fill with nearly normal cartilage repair tissue that was well integrated into the surrounding tissue. The total MOCART score was between 50 and 75 points (mean 61) at follow-up. This is in line with results of another group that showed a total MOCART score of 53–54 points at 2-year follow-up, when the AMIC procedure was used for the treatment of patellar cartilage defects [37, 38] and a score of 58 points when the chondrotissue® implant was used in 5 patients for the treatment of femoral defects and cartilage defects involving the patellofemoral joint [28]. Two of our patients showed intra-lesional osteophyte formation and all

| Table 2 Patients’ imaging and clinical outcome data (SD Standard deviation) |
|---------------------------------|----------------|----------------|----------------|----------------|----------------|----------------|
|                                 | Patient No. 1 | Patient No. 2 | Patient No. 3 | Patient No. 4 | Patient No. 5 |
| MOCART                          | 65            | 50            | 50            | 65            | 75            |
| Henderson                       | 7             | 9             | 7             | 7             | 6             |
| Overall KOOS                    | 90            | 40            | 75            | 78            | 80            |
| KOOS sub-categories             |               |               |               |               |               |
| Pain                            | 94            | 50            | 83            | 92            | 94            |
| Symptoms                        | 89            | 36            | 75            | 82            | 86            |
| Activities of daily living      | 100           | 63            | 93            | 96            | 97            |
| Sports and recreation           | 85            | 20            | 75            | 70            | 80            |
| Quality of life                 | 81            | 31            | 50            | 50            | 44            |
| Patients’ satisfaction—rating of the result | Excellent | Fair         | Very good     | Excellent     | Very good     |
patients showed bone alterations at follow-up. Bone alteration and intra-lesional osteophyte formation are known to be associated with the microfracture treatment and has been shown to occur in up to 70% of the treated lesions [41, 42]. However, a recent MRI analysis of 78 patients that had been treated with microfracture-based procedures and showed intra-lesional bony overgrowth revealed that pre-existing bony overgrowth re-occurred in 36% of the patients and that presence of intra-lesional osteophytes did not correlate with clinical outcome. The authors concluded that intra-lesional bony overgrowth may not be as severe as previously believed [43]. Some subchondral changes could be related to the applied fixation nails. This potentially could be avoided by the use of fibrin glue for fixation of the implant. However, the risk of graft delamination in the retropatellar region is somewhat higher than on the femoral condyles due to increased shear forces on the implant, especially if the border of the adjacent healthy cartilage is not perfectly intact. Thus, we believe that the use of resorbable nails decreases the risk of delamination providing a more secure fixation of the implant.

The limitations of this case series are the small number of patients, the lack of a control group, missing pre-operative data due to the retrospective nature of the study and the short follow-up period. However, to our best knowledge, these are the first published data on the chondrotisue® implant in the treatment of retropatellar cartilage defects. Further studies are needed to show superiority of the procedure and long-term efficacy. The results of the clinical outcome measures in three patients may also be related to the additional procedures. However, especially realignment procedures are necessary in many cases to increase the probability for a success of cartilage repair in the patellofemoral joint [44]. A further limitation is that the structural architecture and cartilage specific extracellular matrix content of the repair tissue has not been evaluated histologically. Therefore, we cannot conclude that the repair tissue is hyaline cartilage that is suggested to be the most durable.

Conclusions

In this small case series, the imaging and clinical data of this pilot study suggest that microfracturing and the implantation of the cell-free chondrotisue® polyglycolic acid–hyaluronan implant immersed with serum in focal cartilage defects of the patella is safe and feasible with improvement of symptoms in this challenging group of patients at short-time follow-up.

Conflict of interest CK is a consultant of BioTissue AG. All other authors declare that there is no financial or other conflict of interest.

References