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Cartilage repair in the knee with subchondral drilling augmented with a platelet-rich plasma-immersed polymer-based implant

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Abstract
Purpose The aim of our study was to analyse the clinical and histological outcome after the treatment of focal cartilage defects in non-degenerative and degenerative knees with bone marrow stimulation and subsequent covering with a cell-free resorbable polyglycolic acid–hyaluronan (PGA-HA) implant immersed with autologous platelet-rich plasma (PRP).
Methods Fifty-two patients (mean age 44 years) with focal chondral defects in radiologically confirmed non-degenerative or degenerative knees were subjected to subchondral drilling arthroscopically. Subsequently, defects were covered with the PGA-HA implant immersed with autologous PRP. At 2-year follow-up, the patients' situation was assessed using the Knee Injury and Osteoarthritis Outcome Score (KOOS) and compared to the preoperative situation and 3–12-month follow-up. Biopsies ($n = 4$) were harvested at 18–24 months after implantation and were analysed by histology and collagen type II immune staining.
Results At 1- and 2-year follow-up, the KOOS showed clinically meaningful and significant ($p < 0.05$) improvement in all subcategories compared to baseline and to 3-month follow-up. There were no differences in KOOS data obtained after 2 years compared to 1 year after the treatment. Histological analysis of the biopsy tissue showed hyaline-like to hyaline cartilage repair tissue that was rich in cells with a chondrocyte morphology, proteoglycans and type II collagen.
Conclusions Covering of focal cartilage defects with the PGA-HA implant and PRP after bone marrow stimulation improves the patients' situation and has the potential to regenerate hyaline-like cartilage.
Level of evidence Case series, Level IV.

Keywords Cartilage repair · Knee · Arthroscopy · Regenerative medicine · PGA-HA scaffold · Platelet-rich plasma · Microfracture · Bone marrow stimulation · Polymer-based implant · Polyglycolic acid

Introduction

Focal cartilage lesions of the knee occur frequently, are a major health problem and may progress to severe osteoarthritis in symptomatic knees. Frequently used first-line treatment options for focal cartilage defects are bone marrow-stimulating techniques, like drilling or the

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microfracture technique [33, 38, 39]. In microfracture, the clinical outcome may be variable due to, for example, the size of the lesion and age/activity of the patient as well as due to uncertain long-term functional improvements [26, 35, 37]. Compared to other advanced cartilage repair options like autologous chondrocyte implantation, the microfracture technique is cost effective, does not need two interventions and shows good to excellent short-term clinical results in particular in patients aged 40-45 and younger [20, 22, 37]. However, the repair tissue induced by bone marrow stimulation is known to be predominantly of a hyaline to fibrous appearance.

In recent years, one-step cartilage repair approaches based on covering the microfractured defect with resorbable scaffolds combined with blood derivatives have been developed. In autologous matrix-induced chondrogenesis (AMIC), a porcine collagen type I/III membrane is used with fibrin glue and autologous serum or platelet-rich plasma to cover the microfractured defect [3, 5, 11]. Newer approaches favour the use of synthetic, textile polyglycolic acid–hyaluronan (PGA-HA) implants for covering microfractured defects. In the ovine model, these implants immersed with autologous serum have been shown to enhance cartilage repair compared to microfracture and to regenerate a hyaline-like cartilage repair tissue [13, 14]. First pilot studies have shown that covering of microfractured cartilage defects with PGA-HA implants (chondrotissue®) immersed with autologous serum or PRP is safe, improves the patients' situation and leads to defect filling with the potential to regenerate hyaline-like cartilaginous repair tissue [12, 30, 36, 41].

Platelet-rich plasma (PRP) is known as a source of autologous growths factors [1, 28]. In cartilage repair, PRP has been shown to induce the migration and chondrogenic differentiation of subchondral progenitor cells known from microfracture [24]. In a study including 100 consecutive patients, the injection of PRP in knees with chronic degenerative symptoms showed that PRP has the potential to reduce pain and to improve knee function in younger patients with a low degree of degeneration, at 6–12-month follow-up [21]. Using a scaffold-based one-step approach in twenty patients with osteochondral lesions, PRP combined with bone marrow concentrate and a hyaluronan scaffold significantly improved the patients' situation at 2-year follow-up as assessed by the IKDC (International Knee Documentation Committee) questionnaire and KOOS [7].

Recently, we have shown in a case series with 52 patients that implantation of the PGA-HA implants immersed with autologous PRP after drilling results in significant improvement of the patients' situation as assessed by KOOS and in the formation of hyaline-like cartilage repair tissue, at a 1 year follow-up [36]. We hypothesize that the 2-year clinical outcome in the same patient cohort is improved compared to the pre-operative situation and shows no differences regarding subgroups with treated cartilage defects in non-degenerative and degenerative knees. Clinical evaluation and analysis of the newly formed repair tissue in four biopsies at 18–24-month follow-up was assessed by the validated KOOS and by histological staining of key cartilage matrix components.

Materials and methods

Fifty-two patients with traumatic and degenerative full-thickness chondral defects of the knee joint were treated with a cell-free polyglycolic acid–hyaluronan (PGA-HA) implant (chondrotissue®, BioTissue AG, Zurich, Switzerland) immersed with autologous platelet-rich plasma (PRP). In a previous report, patients' characteristics, inclusion and exclusion criteria as well as the surgical procedure and the clinical outcome at 1 year follow-up were described in detail [36]. All patients were recalled for this study at the 24-month follow-up, and all data were obtained from medical records and radiographs. Radiographs were taken pre-operatively and osteoarthritic degenerations were evaluated using the Kellgren–Lawrence (KL) scoring system. A Kellgren–Lawrence score of ≥ 2 defines osteoarthritis [18] and was found in 26 patients, designated degenerative group. Patients with a Kellgren–Lawrence score of <2 were assigned to the non-degenerative group. The level of evidence is therapeutic study, level IV.

Characteristics of patients with cartilage defects in non-degenerative and degenerative knees are given in Table 1. The average age of patients in the non-degenerative (KL score 0 and 1) group (15 females, 11 males; mean body mass index (BMI) 25 ranging from 19 to 31) was 41 years (31–55 years). The mean age of patients (17 females, 9 males, BMI 23 ranging from 19 to 28) in the degenerative group (KL score 2 and 3) was 46 years (33–65 years). The mean defect size in the non-degenerative group was 2.7 cm^2 (1.5–5.0 cm^2), while the mean defect size in the degenerative group was 3.4 cm^2 (2.0–5.0 cm^2). All defects were classified as ICRS class III or IV defects [6] and were located, in the non-degenerative group, on the femoral condyle ($n = 6$) or tibial condyle ($n = 20$). Defects in the degenerative group were located at the medial femoral condyle ($n = 6$), on the medial tibial condyle ($n = 15$) or on the lateral tibial condyle ($n = 5$). There were no concomitant and no previous surgeries.

Surgical procedure

Bone marrow stimulation followed by the implantation of the PGA-HA implants was performed arthroscopically (Fig. 1). The damaged and/or degenerated cartilage was

Table 1 Patients' characteristics

Characteristic	Patients' data	Kellgren–Lawrence grade 0–1	Kellgren–Lawrence grade 2–3
Total (n)	52 female ($n = 32$), male ($n = 20$)	26 female ($n = 15$), male ($n = 11$)	26 female ($n = 17$), male ($n = 9$)
Sex			
Median age (years)	44.5 (range 31–65)	42 (range 31–55)	46 (range 33–65)
Median height (cm)	168 (range 154–190)	168 (range 155–190)	167 (range 154–182)
Median weight (kg)	65 (range 50–108)	65 (range 53–108)	65 (range 50–94)
Median body mass index (BMI)	24 (range 19–31)	25 (range 19–31)	23 (range 19–28)
Kellgren–Lawrence score	Kellgren–Lawrence 0 ($n = 5$)	Kellgren–Lawrence 0 ($n = 5$)	Kellgren–Lawrence 2 ($n = 15$)
	Kellgren–Lawrence 1 ($n = 21$)	Kellgren–Lawrence 1 ($n = 21$)	Kellgren–Lawrence 3 ($n = 11$)
	Kellgren–Lawrence 2 ($n = 15$)		
	Kellgren–Lawrence 3 ($n = 11$)		
Median defect size (cm^2)	3.0 (range 1.5–5.0)	2.0 (range 1.5–5.0)	3.5 (range 2.0–5.0)
ICRS classification	III ($n = 16$)	III ($n = 12$)	III ($n = 4$)
	IV ($n = 36$)	IV ($n = 14$)	IV ($n = 22$)
Localization	Medial femoral condyle ($n = 12$),	Medial femoral condyle ($n = 6$),	Medial femoral condyle ($n = 6$),
	medial tibial condyle ($n = 31$),	medial tibial condyle ($n = 16$),	medial tibial condyle ($n = 15$),
	lateral tibial condyle ($n = 9$),	lateral tibial condyle ($n = 4$),	lateral tibial condyle ($n = 5$),
Concomitant surgeries	None	None	None
Previous surgical procedures	None	None	None

debrided down to the subchondral bone with a sharp spoon and a shaver. Perforations of ~2 cm depth were drilled into the subchondral bone using a K-wire with a thickness of 1.8 mm (Fig. 1a). The PGA-HA scaffolds were immersed in 3 mL autologous PRP (not conditioned PRP; mean concentration, 832.1×10^3 platelets/μL; 6.1×10^3 leucocytes/μL) for 5–10 min. The implants were cut to fit the size of the defect and fixated in femoral defects using Smart Nails® (ConMed Linvatec Italy, Milano, Italy) as previously described [36, 41]. For fixation of implants in tibial defects, an adhesive 'fibrin glue'-like adhesive made of autologous PRP gelled by calcium gluconate and thrombin additives was used. The adhesive was applied on the cartilage rim, and the defect was covered with the implant immersed with PRP (Fig. 1b). Subsequently, the whole implant was covered with the autologous PRP glue (Fig. 1c). The rehabilitation regime was reported previously [36].

Evaluation of clinical results

For evaluation of clinical results after implantation of the PGA-HA implant, the KOOS (Knee injury and Osteoarthritis Outcome Score, www.koos.nu) [34] was applied pre-operatively and at 3-, 12- and 24-month post-operatively. The pre-operative data as well as the 3- and 12-month follow-up data were used for comparison and were reported previously [36]. The KOOS is a patient-administered score and is divided into subcategories such as pain, symptoms, activities of daily living (ADL), sports and recreation function (sport&recr), and knee-related quality of life (QoL). Each subcategory 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 minimal detectable changes in patients with knee injuries/knee OA are as follows [10]: pain (6.0–6.1/13.4), symptoms (5.0–8.5/15.5), ADL (7.0–8.0/15.4), sport&recr (5.8–12.0) and QoL (7.0–7.2/21.1). The test–retest liability or interclass correlation of KOOS in patients with knee injuries/knee OA is as follows [10]: pain (0.85–0.93/0.80–0.97), symptoms (0.83–0.95/0.74–0.94), ADL (0.75–0.91/0.84–0.94), sport&recr (0.61–0.89/0.65–0.92) and QoL (0.83–0.95/0.60–0.91). The minimal, clinically important change (ΔKOOS) is currently suggested to be 8–10.

At 1-year follow-up, repair tissue formation was monitored by second-look using the InnerVue™ Diagnostic Scope System (Biomet Inc., Warzaw, USA), see supplemental material. To assess cartilage repair and repair tissue quality, 4 patients gave consent to additional magnet resonance imaging (MRI) and biopsy harvest. MRI was performed 1 year after the surgery. The repair tissue biopsies were taken from the central defect region at 18–24-month follow-up. Biopsies were taken with a standard 2.5-mm diameter Jamshidi needle. The specimens were placed in 4 % formalin and were subjected to histological analysis.

Histology

For histological and immuno-histochemical analyses, biopsies were fixed in 4 % formalin in phosphate-buffered

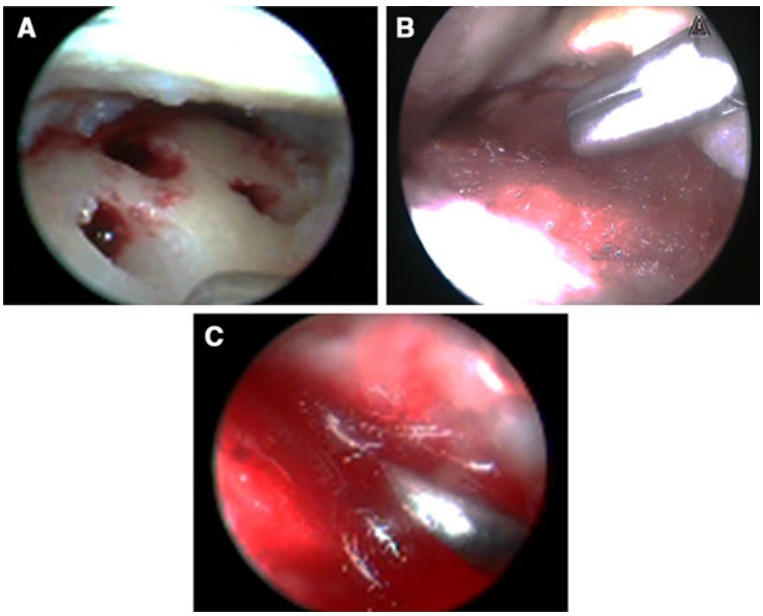

Fig. 1 Arthroscopic implantation of the PGA-HA implant. The defective cartilage is removed down to the subchondral bone and microfractures were introduced by drilling (**a**). The PGA-HA implant was immersed with PRP and used to cover the defect (**b**). Fixation was performed by applying autologous PRP 'fibrin glue'-like adhesive onto the PGA-HA implant (**c**)

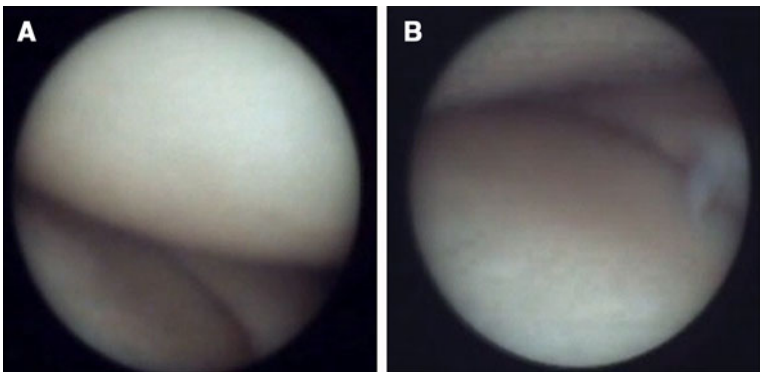

Fig. 2 Macroscopic appearance of the repair tissue 1 year after the implantation of the PGA-HA implant. The repair tissue formed in femoral (**a**) and tibial (**b**) showed good defect filling and appeared to be as white to more whitish, compared to the surrounding tissue. Please see supplemental material for video documentation

saline (PBS), washed twice in PBS for 15 min, dehydrated in graded ethanol series and then paraffin-embedded. Cross-sections (5 µm thickness) were cut, de-waxed and stained with hematoxylin and eosin (H&E). Acidic mucopolysaccharides (proteoglycans) were visualized by Alcian blue staining at pH 2.5. For immuno-histochemical analysis, serial sections of paraffin-embedded samples were de-waxed and treated with methanol: H_2O_2 (49:1) for 30 min to inhibit endogenous peroxidases. Sections were then treated with 1 mg/ml hyaluronidase in PBS, pH 6.0, for 30 min at 37 °C and washed with PBS. Slices were then incubated with goat serum for 1 h to reduce non-specific binding. Type II collagen antibody (CIICI anti-COLLII, DSHB, University of Iowa, USA) staining as well as negative control staining with omitted primary antibody (in duplicates using section from independent biopsies) was performed as described previously [36].

Statistical analysis

To compare pre- and post-operative KOOS values, the *t* test and the Mann–Whitney rank sum test were performed, depending on the normal distribution of data. All tests were performed using the statistical software SigmaStat 3.5 (Statcon, Witzenhausen, Germany). Values are given as mean and standard deviation. A ΔKOOS of >10 is considered clinically meaningful, and p value of <0.05 is considered statistically significant.

Results

The cell-free PGA-HA implant was implanted in focal cartilage defects in non-degenerative and degenerative knees arthroscopically. To assess the degree of degenera-

tive changes, pre-operative radiographs were scored according to Kellgren–Lawrence. In the non-degenerative group, the radiographs showed a Kellgren–Lawrence score of 0–1 with no obvious degenerative changes. The radiographs of knees in the degenerative group showed osteoarthritic degeneration and a Kellgren–Lawrence score of 2–3 with constriction of the joint space and/or formation of osteophytes.

Clinical outcome

At 2-year post-operatively, there were no clinical signs of persistent knee joint infection or inflammation, allergic reactions, foreign body reactions, nor knee joint effusion or swelling. There was no temporary blocking, and signs for ablation of the implant or loosening of the newly formed repair tissue were not evident. One year after implantation of the PGA-HA scaffold, a second-look inspection of all operated knees was performed and showed newly formed repair tissue in the weight-bearing zone (Fig. 2). The colour of the repair tissue appeared to be as white to more whitish, compared to the surrounding tissue. The repair tissue was of a cartilaginous appearance with good integration and bonding in femoral (Fig. 2a, supplemental material video 1) and tibial defects (Fig. 2b, supplemental material video 2).

Clinical evaluation of surgical results 2 years after the implantation of the PGA-HA implant

Clinical scoring and analysis of KOOS values derived from the whole study population showed a clinically meaningful (ΔKOOS > 10) and significant ($p < 0.001$) improvement in all KOOS subcategories at 3-, 12- and 24-month follow-up, compared to the pre-operative situation (Fig. 3). At 12- and 24-month follow-up, the scores were clinically meaningful and significantly improved compared to the scores obtained at 3-month follow-up. There was no difference between the KOOS at 12-month follow-up and 24-month follow-up. The overall KOOS was in mean 50.3 at baseline and increased to in mean 82.9 at 2-year follow-up. There was no difference in overall KOOS at 24-month follow-up and ΔKOOS between the group with tibial defects that received an implant and fixation by gluing (50.0 at baseline to 82.4; ΔKOOS 32.6) and the group with femoral defects and implants fixated with resorbable nails (51.1 at baseline to 83.8; ΔKOOS 32.7).

Stratifying the patients' KOOS data according to the degenerative nature of treated knee (Fig. 4) showed that implantation of the PGA-HA implant improved the situation of patients in the non-degenerative group (Fig. 4a) as well as of patients with defects in degenerative knees with a Kellgren–Lawrence score of 2 or 3 (Fig. 4b). The improvement in all subcategories of KOOS was significant

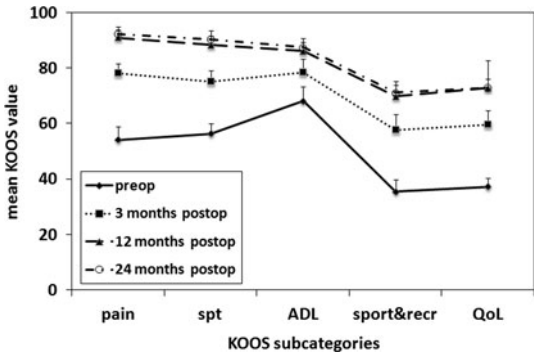

Fig. 3 Clinical outcome after 2 years as assessed by the Knee injury and Osteoarthritis Outcome Score (KOOS). The KOOS profiles prior to and up to 2 years after the implantation of the PGA-HA implant are presented as mean value ($n = 52$). *Error bars* define standard deviation. *spt* symptoms, *ADL* activities of daily living, *sport&recr* sports and recreation, *QoL* quality of life. Pre-operative, 3- and 12-month KOOS raw data were taken from a previous report [36]

($p < 0.001$) and clinically meaningful (ΔKOOS > 10) at 3-, 12- and 24-month follow-up. There was no difference between the KOOS at 12-month follow-up and 24-month follow-up, in the non-degenerative and in the degenerative group. There was no significant difference in the ΔKOOS found in all subcategories at 24-month follow-up compared to the pre-operative situation between the non-degenerative and the degenerative groups (Fig. 4c).

Evaluation of the repair tissue after the implantation of the PGA-HA implant

Biopsies were obtained from 4 patients 18–24 months after the implantation of the PGA-HA implant (Fig. 5, full chondral biopsy view after hematoxylin staining is given in supplemental material Fig. 1). Hematoxylin staining (Fig. 5a–d) showed that the repair tissue is rich in round-shaped cells of a chondrocytic appearance. The repair tissues showed cells either isolated (Fig. 5a, b) or in small cluster (Fig. 5c) occasionally in a columnar distribution (Fig. 5d, arrows). The extracellular matrix appeared rough (Fig. 5b) to well structured and smooth (Fig. 5a, c, d). There were no remnants of the PGA-HA implant and no signs of foreign body reaction or necrosis. Alcian blue staining showed that the repair tissue was rich in proteoglycan and chondrocytic cells (Fig. 5e–h). Staining of collagen type II (Fig. 5i–l) showed positive staining of cells and the extracellular matrix and proofed hyaline-like to hyaline repair tissue formation 18–24 months after the implantation of the PGA-HA implant. Controls for type II immune staining (Fig. 5m, n) were negative and showed specificity of the staining of type II collagen.

Figure 6 shows MRI for this group of 4 patients at 1 year after the implantation of the PGA-HA implant. The repair tissue showed good defect filling, and the cartilage

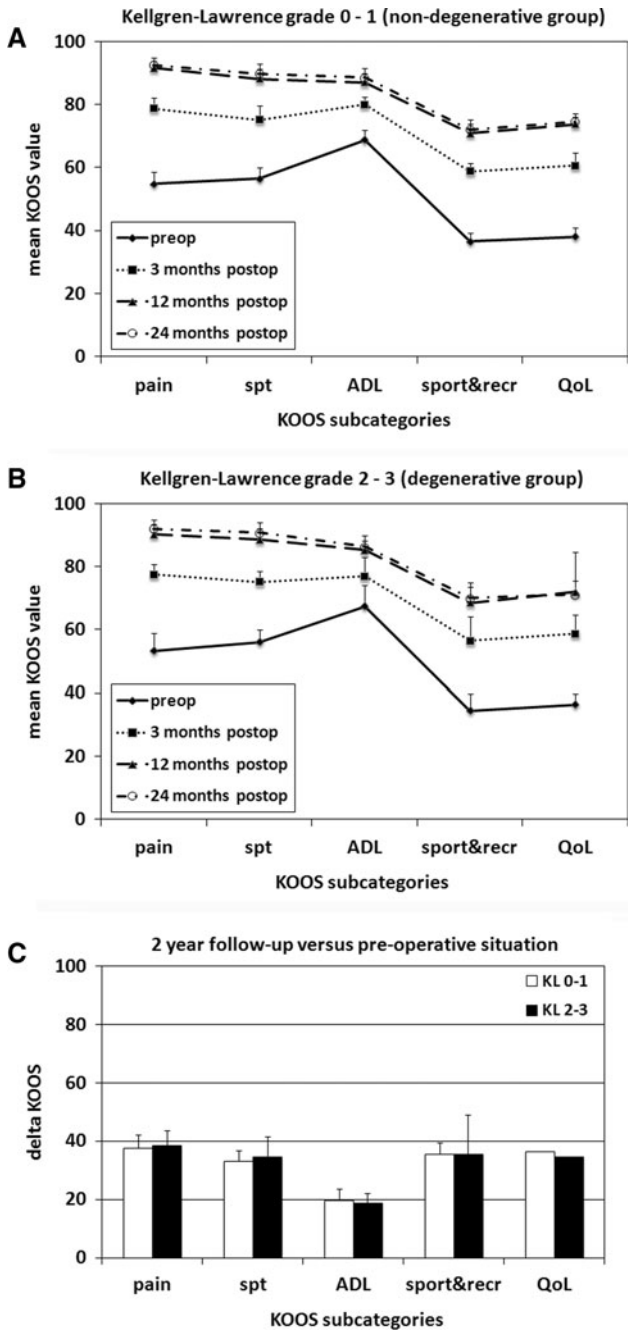

Fig. 4 Clinical outcome of patients with cartilage defects in non-degenerated and degenerated knees after 2 years as assessed by the Knee injury and Osteoarthritis Outcome Score (KOOS). The KOOS profiles of patients in the non-degenerative (**a**, Kellgren–Lawrence score of 0–1) and degenerative group (**b**, Kellgren–Lawrence score of 2–3) are presented. The KOOS improvement, compared to the preoperative situation, in both groups after 2-year follow-up showed no significant differences (**c**). The KOOS is presented as a mean value, and *error bars* define standard deviation. spt, symptoms; ADL, activities of daily living; sport&recr, sports and recreation; QoL, quality of life. Pre-operative, 3- and 12-month KOOS raw data were taken from a previous report [36]

signal was iso- to hyperintense compared with the adjacent cartilage. There is still some bone signal evident that may due to bone remodelling and/or the drilling procedure.

Discussion

The most important finding of the present study was that the validated KOOS score showed clinically meaningful and significant improvement 2 years after the implantation of the PGA-HA implant in full-thickness cartilage defects in non-degenerative and degenerative knees, compared to the pre-operative situation. We have shown the benefit and reliability of the use of the cell-free PGA-HA implant chondrotissue® immersed with autologous PRP after subchondral drilling for the treatment of full-thickness cartilage defects in non-degenerative and degenerative knees. Histological analysis of repair tissue obtained 18–24 months after the surgery proofed the formation of hyaline-like to hyaline cartilaginous tissue.

Autologous chondrocyte-based approaches for cartilage repair using expanded chondrocytes alone or in combination with different scaffolds like collagen, hyaluronan or resorbable polymer-based materials have been shown to be clinically effective in repairing chondral defects of the knee [4, 23, 25, 29, 32, 35, 40]. However, these two-step procedures need, for example, two interventions, may lead to donor site morbidity and are time and cost intensive. Recently, one-step cartilage repair procedures have been developed for the treatment of chondral defects and the improvement of the microfracture procedure [5, 11, 15, 30]. The main concept of these procedures is that subchondral progenitor cells are 'activated' and released into the defect by bone marrow stimulation and that the defect is covered with different types of matrices augmented with blood derivatives for cartilage repair tissue formation. We used the subchondral drilling procedure to produce deep perforations that allow for having good access to the subchondral bone marrow and in turn to the subchondral progenitor cells. In a rabbit model, it has been shown that deeper subchondral drilling leads to greater defect fill, larger regions of repairing/bone remodelling and improved cartilage repair [8, 9].

Up to now, the clinical effectiveness of one-step procedures is shown mainly in pilot studies with low to moderate number of patients. In a pilot study with five patients, microfracture and a PGA-HA matrix immersed with autologous serum were used that showed noticeable clinical improvement in KOOS (mean overall KOOS of 33 pre-operatively to 79 at 2-year follow-up). However,

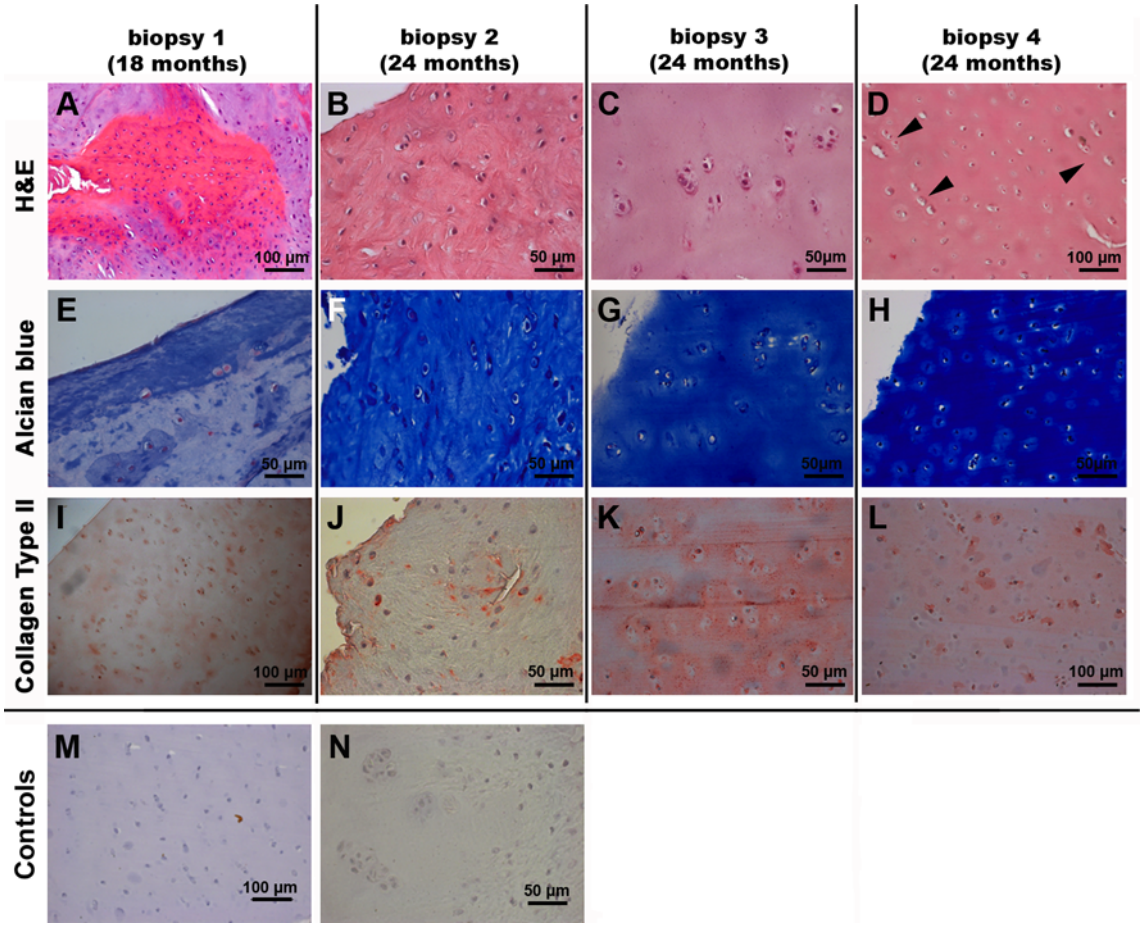

Fig. 5 Biopsies of repair tissue obtained after 18–24 months after the implantation of the PGA-HA implant immersed with PRP. Hematoxylin and eosin staining (**a**–**d**) showed chondrocytic cells and in part columnar distribution (**d**, *arrows*). Alcian blue staining (**e**–**h**) showed the presence of a cartilaginous matrix rich in proteoglycans. Immunostaining proofed the presence of collagen type II in all biopsies (**i**–**l**). Controls for collagen type II immune staining were negative (**m**, **n**)

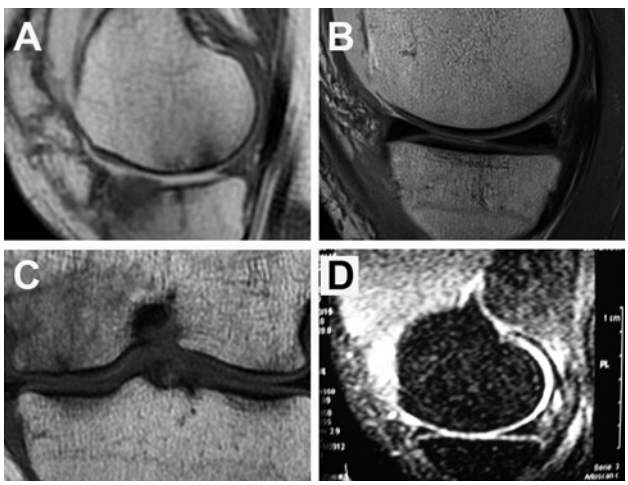

Fig. 6 MRI 12 months after the implantation of the PGA-HA implant immersed with PRP. Patients who gave consent to biopsies underwent MRI evaluation at 12-month follow-up. Femoral (**a**, **c**) and tibial (**b**, **d**) defects showed good defect filling with repair tissue of iso-to hyperintense signal compared to the adjacent cartilage and some bone signal

magnet resonance imaging (MRI) showed different percentages of incomplete filling, subchondral irregularities and intralesional osteophytes [12]. The same group showed in another five patients that the good clinical outcome obtained with the AMIC technique combined with a PRP gel did not match with the MRI improvement. At 2-year follow-up, the authors reported persistence of subchondral bone abnormalities, incomplete filling or hypertrophy of the repair tissue and intralesional osteophyte formation [11]. The AMIC (autologous matrix-induced chondrogenesis) technique, which uses a porcine collagen type I/III membrane with blood-fibrin glue to cover the microfractured defect, has been shown to lead to significant clinical improvement in 27 patients with moderate to complete defect filling, at an average of 37-month follow-up [16].

In the present study, the use of the PGA-HA implant immersed with autologous PRP after bone marrow stimulation led to significant clinical improvement in a cohort of 52 patients with focal cartilage defects in a non-degenerative and degenerative environment, as assessed by KOOS

(overall mean KOOS at baseline 50.3–82.9 at 2-year follow-up). Histological analyses showed the formation of hyaline-like to hyaline cartilage repair tissue at 18–24-month follow-up. The original microfracture technique has been shown to lead to good short-term results but with limited hyaline repair tissue [26]. A recent meta-analysis showed that the rough estimate for the mean expected treatment effect achieved by microfracture is an increase in 22 overall KOOS points [27]. These data suggest that our cell-free approach using a PGA-HA implant and autologous PRP, which showed an improvement in overall KOOS of 32.6 points, leads to a good to excellent clinical outcome at 2-year follow-up. Nevertheless, randomized and controlled clinical trials have to show that such a cell-free one-step cartilage repair approach is superior to standard microfracture and/or autologous chondrocyte implantation in cartilage repair.

The limitations of our prospective study have been the lack of a control group or control groups, the missing of comprehensive MRI data for the evaluation of defect filling, a clear assessment with further osteoarthritis criteria whether cartilage lesions in the non-degenerative or degenerative environment are traumatic, post-traumatic and/or degenerative cartilage defects as well as that the clinical follow-up is limited to patients with a short-term 2-year follow-up and most repair methods may fail in the long term. A further limitation is that the biopsies obtained for histological analysis are taken from 4 patients. Therefore, we cannot say that the whole cohort developed hyaline-like to hyaline cartilaginous repair tissue. However, the results obtained after 2 years confirmed the good results found after 1 year [36] and may be promising for a good future outcome, since the results after 2 years are considered as an important indicator for the future outcome in autologous chondrocyte implantation [31]. Although the number of biopsies in this study (4 biopsies) and in our previous study (5 biopsies) [36] is low, we found uniformly hyaline-like to hyaline cartilaginous repair tissue formation, 9–24 months after the implantation of the PGA-HA implant immersed with PRP. Therefore, the percentage of hyaline-like repair tissue formation may somewhat higher than reported previously for other bone marrow stimulation techniques using scaffolds. Histological evaluation of biopsies obtained from five asymptomatic patients 1 year after microfracture treatment in combination with a collagen scaffold immersed with autologous bone marrow concentrate showed the formation of fibrocartilage (3 cases), mixed type hyaline-fibrocartilage (1 case) and hyaline-like (1 case) repair tissue [15]. However, a limitation of our current study is that the histological specimens show only chondral repair tissue and not the full osteochondral area as recommended by the ICRS histology group. Therefore, the information about the quality of the newly formed tissue (e.g. subchondral remodelling and bonding) is limited. However, staining of proteoglycan and type II collagen may indicate that our procedure has the potential to regenerate hyaline-like to hyaline cartilage repair tissue.

The treatment of patients with focal cartilage defects in a degenerative environment with the PGA-HA implant and PRP resulted in good clinical results and improvement of the patients' situation as assessed by KOOS at 2-year follow-up. Although moderate to severe degenerative or osteoarthritic defects are not indicated for current cartilage repair techniques, one-step procedures have been used in older patients with in part radiologically confirmed degenerative changes providing pain relief, increase in joint space and good histological results [2, 36]. The polymer-based PGA-HA implant is flexible, easy to cut to fit the size of the defect and can be securely fixated in the defect arthroscopically by gluing or pin/nail fixation [19, 41]. In addition, a recent biomechanical study has shown that covering a cartilage defect with the PGA-based matrix restores the joint compression forces towards forces found in normal joints [17]. Therefore, the stable felt-like structure of the implant may be favourable for arthroscopic approaches and for the treatment of defects that lack an intact cartilage rim. This study indicates that subchondral drilling followed by covering of the cartilage defects with PGA-HA implants is a promising alternative to the original bone marrow stimulation procedure in day-by-day clinical work. The PGA-HA implant has the potential to enhance cartilage repair and to broaden the indication for bone marrow stimulation to focal degenerative and osteoarthritic defects. However, further controlled clinical studies involving defined degenerative and/or osteoarthritic defects are needed, before the use of this one-step repair approach can be recommended unrestrictedly to this patient group.

Conclusions

Our clinical and histological data have suggested that subchondral drilling and the arthroscopic implantation of the PGA-HA implant immersed with PRP in focal cartilage defects leads to clinically meaningful and significant improvement of the patients' situation. The clinical and histological results obtained at 2-year follow-up confirmed the good findings obtained in short-term follow-up at 1 year and may suggest a good potential for future outcome.

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Conflict of interest All other authors declare that there is no financial or other conflict of interest.

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