Introduction

The aim of contemporary knee surgery is to minimize the complications following cartilage injury and to renovate the continuity of the articular surface, especially of the weight-bearing areas. The clinical pictures of various chondral lesion types differ according to their localization and defect thickness.

A plethora of recommended treatment methods have been described (2, 3, 13, 15, 24, 26, 31). Use of abrasive techniques dominated in the eighties (Pridie drilling, Steadman’s microfracture techniques, Ficat spongialisation), (10, 27, 28). These methods are based on the presumption that subchondral bone penetration stimulates formation of new reparative tissue. Subchondral bone penetration in full-thickness cartilage defects affects the subchondral vessels and leads to the formation of a fibrin clot and migration of undifferentiated mesenchymal cells. The so-called subchondral abrasion technique described by JOHNSON (17), a modification of the previous methods, is the most widely used nowadays. However, the resulting tissue healed via this technique is predominantly of a fibrous nature, containing varying numbers of chondrocytes and fibrocytes in an unorganized matrix. The fibrocartilage-like reparative tissue resulting from abrasive techniques lacks the biomechanical and viscoelastic characteristics of normal hyaline cartilage, and long-term clinical outcomes are unpredictable. These factors represent the main reasons for the continued search of newer methods affording replacement of injured cartilage with reparative tissue more closely resembling the original hyaline cartilage. Newer options for tissue replacement with cultivated cell transplantation have been investigated. The authors present an orig-
inal method of chondrograft preparation based on autologous cultivated chondrocytes in a three-dimensional carrier—fibrin glue (Tissucol, Baxter, Austria).

**Materials and methods**

Between 1999 and 2002 a total number of 50 patients were included in a prospective randomised study. Randomisation was done using the envelope method. Group I comprised of 25 patients (18 males, 7 females) with an average age of 29.48 years (range 18-50 years). Group II comprised of 25 patients (16 males, 9 females) with an average age 32.20 years (range 21-50 years).

In group I the cause of injury was trauma in 20 cases; 4 cases were diagnosed with osteochondritis dissecans and one case with Ahlback syndrome. In group II the cause of injury was trauma in 23 cases and two cases were diagnosed as osteochondritis dissecans. The defects in group I were treated using autologous chondrograft transplantation and in group II by abrasive techniques according to Johnson.

All patients suffered moderate to large (2.0-10.0 cm²) full thickness (Noyes-Stabler grade III.a. or III.b.) chondral defects of the knee and had severe symptoms (22). The average size of cartilage defect in group I was 4.08 cm², ranging from 2.0 to 10.0 cm²; and in group II was 3.36 cm², ranging from 2.0 to 8.8 cm².

In group I, the chondral defect was localised in the weight bearing area of the medial femoral condyle in 16 patients, on the lateral femoral condyle in five cases, on the tibial plateau in two cases, and on the patella in 6 cases. Four cases of double defects were diagnosed and a total number of 29 cartilage defects were treated in group I. The chondral defect was localised in group II in the weight bearing area of medial femoral condyle in 17 cases, on the lateral femoral condyle in 6 cases, on the tibial plateau in three cases and on the patella in five cases. Six cases of double defects were diagnosed and a total number of 31 cartilage defects were treated in group II.

In group I, concomitant injuries of the soft knee were found in 22 cases, and monotrauma of the cartilage occurred in only three cases. In group II we observed concomitant injuries of the soft knee in 19 cases, and in six cases, monotrauma of the cartilage. Concomitant injuries were treated during chondral transplantation or during abrasive techniques.

Additional surgeries performed on patients in group I:

- ACL replacement in seven cases (3 cases with patellar tendon graft; 4 cases with semitendinosus graft).
- Partial meniscectomy in 13 cases; suture of the meniscus in 3 cases.
- Lateral release in five patients.

In group II, we performed:

- ACL replacement in three cases (two cases with patellar tendon graft; one case with semitendinosus graft).
- Partial meniscectomy in 10 cases; suture of meniscus in 3 cases.
- Lateral release in four cases.

Statistical evaluation of inclusion criteria (age, chondral defect size and localization, concomitant injuries) certified homogeneity of the study groups of patients with deep chondral defect on the weight-bearing area of the knee. (ANOVA, Kruskal-Wallis, χ²-test).

**Defect treatment of patients in group I — chondrograft preparation and implantation**

Upon diagnosing a defect during arthroscopy, the size of lesion was assessed and cartilage samples were taken (in the amount of 300-500 mg from the upper minor weight-bearing area of the medial femoral condyle) for cultivation. The slivers of cartilage were immersed in a cold salt solution (0.9% NaCl) with antibiotics. Cell isolation was initiated within 8 hours of surgery. Samples were cleaned and cut into small pieces and digested using trypsin and collagenase enzymes. This chondrocyte suspension was inoculated into flasks and cultured in the incubator at 37°C in a CO₂ environment. The culture medium was exchanged every 48 hours. Proliferation of chondrocytes was monitored using light microscopy. Successful primocultivation resulted in a cell monolayer. The required number of cells (5-10 million of cells per ml) was obtained through successive subcultivations. A detailed description of the chondrocyte cultivation method is published by Peterson (25).

We used the fibrin tissue glue Tissucol (Baxter, Austria) as a three dimensional carrier for the chondrocyte culture. Excellent viability of chondrocytes along with ability migrate over the Tissucol surface was documented (30). Preclinical tests on cadavres demonstrated the chondrograft’s ability to fill up the chondral defect completely and renew the anatomical surface of the joint cartilage (29). Tests on pigs demonstrated good healing after chondrocyte transplantation. Follow-up histological examination evinced a hyaline-like cartilage 3 months postop (11).

After serial preclinical tests we decided to try chondrograft transplantation in humans. When adequate chondrocytes counts were reached from cultivation samples (mean interval of 21 to 28 days of cultivation), the patient was prepared for transplantation. The chondrocyte suspension was mixed with fibrin glue to form a matrix prior to surgery (Fig. 1). With patients under general or spinal anesthesia, a medial or lateral parapatellar arthrotomy was performed in a tourniquet-controlled
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Clinical Evaluations

Four scoring systems were used to quantify the clinical status of the patients: the Lysholm knee score, the IKDC (International Knee Documentation Committee) subjective knee score, the Tegner activity score and the reparation assessment using the ICRS (International Cartilage Repair Society) score (25).

Additional Investigations

Second look arthroscopy and additional procedures (shaving of adhesions in the knee) were done in 4 patients. The quality of tissue repair was assessed using the ICRS repair score for macroscopic appearance of the cartilage surface. This scoring system included evaluation of defect remodeling, integration with surrounding cartilage and surface mechanical characteristics. Biopsy specimens were obtained from the centre of defects and samples were examined by conventional light and electron microscopy (transmission and scanning). Immunohistochemical staining for Type II collagen was performed with a monoclonal antibody detecting native Type II collagen.

Statistic evaluations

The results were subjected to the \( \chi^2 \)-test and its modifications (MANTEL-HAENSZEL, YATES, FISCHER), KRUSKAL-WALLIS analysis as a non-parametric test for distribution-free data and ANOVA analysis of normally distributed data were also done.

Results

Lysholm knee score

The preoperative value of Lysholm knee score in group I was 47.60 points (SD 10.71, range 19-63) ; 77.20 points (SD 11.15, range 48-93) 5 months after surgery ; and 86.48 points (SD 8.88, range 57-100) 12 months after surgery. Excellent results according to the Lysholm score were obtained in six patients after 12 months ; good results were seen in 12 patients ; sufficient results in six patients ; and a fair result was observed in one patient. Good and excellent results were obtained in 72% of patients.

The preoperative value of the Lysholm knee score in group II was 52.60 points (SD 11.46, range 30-68) ; 69.20 points (SD 11.15, range 48-93) 5 months after surgery ; and 74.48 points (SD 8.88, range 57-100) 12 months after surgery. Excellent results according to the Lysholm score were obtained in no patient following surgery using the abrasive technique; good results were seen in 10 patients ; sufficient results in 11 patients ; and a fair results were observed in

bloodless field. Chondral lesion debridement was performed (subchondral bone penetration). Capillary bleeding from the defect base was compressed for a few minutes and a microlayer of Tissucol was applied locally. The prepared chondrograft was remoulded and transplanted into the defect. Fixation was secured via agglutination with fibrin glue (Fig. 2).

Defect treatment of patients in group II — abrasive technique sec. Johnson

The method is based on ablation of sclerotic bone layers at the base of the defect with a shaver (abrader) to open the haversian canals. Abrasion is done to a depth of 1-2 mm and the defects are sharply margined. The advantage to this method is in the miniinvasive arthroscopic approach and one step procedure when compared to transplantation.

Fig. 1
Chondral lesion before transplantation.

Fig. 2
Chondral lesion after transplantation.
4 patients. Good results were obtained in 40% of patients.

Results 12 months after surgery were significantly better in group I as compared to group II (p < 0.001, ANOVA, KRUSKAL-WALLIS) (table 1).

**IKDC subjective knee score**

The preoperative value of IKDC subjective score in group I was 41.28 points (SD 11.65, range 11-58); 67.00 points (SD 12.57, range 35-84) 5 months after surgery; and 76.48 points (SD 12.87, range 45-96) 12 months after surgery. Average improvement after 5 months was 25.72 points, and after 12 months, 35.20 points.

The preoperative value of IKDC subjective score in group II was 45.00 points (SD 11.34, range 20-61); 62.28 points (SD 8.95, range 32-73) 5 months after surgery; and 68.08 points (SD 10.21, range 35-81) 12 months after surgery. Average improvement after 5 months was 17.28 points and after 12 months 23.10 points.

Results 12 months after surgery were significantly better in group I when compared to group II (p < 0.05, ANOVA), (table 2).

**Tegner activity score**

Follow up of patients evaluated by Tegner score was provided retrospectively before injury, before chondrograft transplantation, and 12 months after surgery (in 13 patients from group I and 10 patients from group II). The average value of Tegner score in group I before injury was 7.85 points (SD 1.0 points); before surgery 3.23 points (SD 0.8 points); and 12 months after surgery 5.92 points (SD 0.8 points). Average activity decrease after injury was five points and average activity improvement one year after transplantation was 3 points.

Second look arthroscopy was performed in four patients from group I 3-5 months after chondrograft transplantation. In two patients, complete healing of graft was observed. Two cases of partial chondrograft degeneration (30% of graft area) were documented. Graft surface was evaluated according to cartilage repair assessment system (ICRS-cartilage score) (table 4). Average ICRS cartilage’s score was 8.5 points (almost normal graft surface), (SD 2.38, range 6-11). During second-look arthroscopy samples for conventional light and electron microscopy were obtained. Microscopic evaluation showed presence of hyaline-like cartilage in the healing defect (presence of typical spherical chondrocytes, extracellular collagenous filaments, formation of typical isogenetic cellular groups). Immunohistochemical staining for Type II collagen was positive. In those cases with partial graft degeneration (fissuration), we documented neovascularisation of reparative tissue with presence of fibroblast-like cells.

**Postoperative follow-up**

No serious clinical complications were observed in either group during the postoperative period. Reactive synovitis with exudation was documented in 20% of patients after chondrograft transplantation. Clinical

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**Table 1**

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<thead>
<tr>
<th>Lysholm knee score according to time interval after surgery</th>
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<tbody>
<tr>
<td><strong>Lysholm knee score (points)</strong></td>
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<tr>
<td>Group I</td>
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<td>Group II</td>
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* NS  ± p < 0.05  ± ± p < 0.001

**Table 2**

<table>
<thead>
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<th>IKDC subjective score according to time interval from surgery</th>
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<tr>
<td><strong>IKDC subjective score (points)</strong></td>
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<tr>
<td>Group I</td>
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<td>Group II</td>
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* NS  ± p < 0.05

**Table 3**

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<th>Tegner score after surgery</th>
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<tr>
<td><strong>Tegner score (points)</strong></td>
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<tr>
<td>Group I</td>
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<td>Group II</td>
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* NS  ± p < 0.01

Average values of the Tegner score in group II before injury was 7.10 points (SD 1.1 points); before surgery 2.30 points (SD 1.1 points); and 12 months after surgery 4.20 points (SD 1.1 points). Average activity decrease after injury was 5 points and average activity improvement one year after surgery was 2 points.

Results 12 months after surgery were significantly better in group I when compared to group II (p < 0.01, KRUSKAL-WALLIS) (table 3).

**ICRS repair score**

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**Table 4**

<table>
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<tr>
<th>ICRS repair score during second look arthroscopy</th>
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<tr>
<td><strong>ICRS repair score (points)</strong></td>
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<tr>
<td>Patient No. 1</td>
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<td>Patient No. 2</td>
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<td>Patient No. 3</td>
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<td>Patient No. 4</td>
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<td>Average</td>
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symptoms disappeared after NSAID administration within 4 weeks. Mechanical load was eliminated for 3 weeks and full weight-bearing was allowed only after 6-8 weeks. Intensive rehabilitation was an obligatory part of postoperative care.

**Discussion**

Full-thickness cartilage defects represent a common and serious problem in knee surgery today. The limited ability of the cartilage to repair the injured surface is generally known. Clinical symptoms in patients with full-thickness defects are severe and lead to the premature development of osteoarthritis. The occurrence of osteochondral defects in acute haemarthrosis varies between 8-11% (Haridakis 8%, Butler 11%, Gillquist 10%, Noyes 10%), (6, 7, 12, 14, 22). We have evaluated a total number of 651 patients with acute haemarthrosis between the years 1996 and 1998. Chondral defects of 3.A. or 3.B. type (according to Noyes-Stabler) were found in 11.5% patients.

The gravity of deep chondral defect complications has led to a gamut of proposed treatment methods (5, 8, 16, 19). Abrasive techniques were introduced, and dominated during the 1980s. Two of the described abrasive techniques currently remain in clinical practice: the subchondral plane abrasion according to Johnson and the microfracture technique according to Steadman (17, 27). According to the majority of studies, abrasive techniques result in good and excellent results in 50-74% of cases, and the treatment effect lasts for 5 years in most patients (9).

Autologous cultured chondrocyte transplantation has become an advancement in the treatment of chondral knee lesions in the last decade. Most authors analyse treatment outcome of defects in size ranging from 4 to 6 cm², localised mostly on the medial femoral condyle (65-80% cases). Excellent and good results have been observed in 75-85% patients (1). In our study group excellent and good results according to Lysholm score were seen in 72% of patients. The lower success rate of our study group was most likely influenced by the high incidence of severe concomitant injuries. Concomitant injuries had an important impact on the total value of the Lysholm knee score. From the patient’s viewpoint we found the results obtained to be very good for our cohort.

MINAS analysed a group of 169 patients one and two years (21) after surgery using cultivated chondrocytes covered by periostue. The average cartilage defect size was 4.3 cm², and documented improvement was observed in 87% patients. During second look arthroscopy MINAS demonstrated findings of arthrofibrosis in 5% of patients and periostal hypertrophy in 20% patients. Symptoms of arthrofibrosis developed quite early – up to 3 months after transplantation and symptoms of periostal hypertrophy developed after 4 to 9 months. Both complications were resolved by arthroscopic shaving. Follow up biopsies showed the following 4 cartilage layers:

- Fibrous periostal remnant cover.
- Transitional repair tissue.
- Deep hyaline-like repair tissue.
- Calcified layer.

Histological evaluation of our follow up samples demonstrated only two layers:

- Hyaline-like cartilage.
- Calcified layer.

Differing histological findings between the technique we used and MINAS can be explained by the different surgical technique, where the first two layers in MINAS technique developed as a consequence of periostal use for chondrocyte fixation.

A hallmark study of cultivated chondrocytes under periostue was published by Peterson in 2000 (25). He evaluated two- to nine-year outcomes after autologous chondrocyte transplantation in 101 patients, where the chondral defect size varied from 1.5 cm² to large 12 cm² full thickness chondral defects. Patients were divided retrospectively into five groups and good to excellent clinical results were seen as follows: isolated femoral condyle lesion (92%), multiple lesion (67%), osteochondritis dissecans (89%), patella (65%), and femoral condyle with anterior cruciate ligament repair (75%). Our sample size is too small to be divided into these 5 groups. Our cohort most closely resembles Peterson’s subdivision of chondral lesions with concurrent anterior cruciate ligament repair. Under this comparison our results are in agreement. In the Peterson study 53 patients underwent second look arthroscopy. Hypertrophic response of the periostue was seen under arthroscopy in 26 patients, while graft failure occurred in seven patients. Histological analysis of 37 biopsy specimens showed hyaline-like tissue (positive staining for Type II collagen). Both studies by MINAS and Peterson describe a high occurrence of periostal hypertrophy as the principal complication of the operative techniques.

The goal of present tissue engineering is to find an optimal three-dimensional carrier for the autologous chondrocyte culture (18, 31). A new type of carrier based on hyaluronic acid – Hyalograft C was presented by Maracci (20). Results published from the first 20 clinical cases using Hyalograft C have not reported any complications with the method used. Subjective improvement after 12 months was observed, but detailed evaluation using the functional scoring systems has not yet been published. Our chondrograft technique repre-
sents an alternative method when compared to the method described by Marccoli.

Indications for the use of different chondral repair techniques also represent a subject for this investigator’s discussion. Use of the newly described methods of mosaicplasty or chondrocyte transplantation is limited by biological age of the knee joint. The reasons to indicate mosaicplasty or chondrocyte transplantation have not yet been determined. We have established 2 cm² as the decisive defect size in method indicated. The same critical size was published by Britberg (4). Defects of 2 cm² or less are corrected via mosaicplasty. Chondrocyte transplantation avoids the use of the periosteal flap thereby simplifying the surgical procedure. Thus, complications such as hypertrophy or ossification of periosteal flap are extremely reduced. Their indications are becoming more stringent. Their outcome in patients treated using autologous chondrocyte transplantation are better as compared to the one treated using chondrograft transplantation. Europ J of Trauma, 2002, S(1): 170-1 (P 111).

References

The results obtained have statistically confirmed a better outcome in patients treated using autologous chondrocyte transplantation. Previous methods, such as the subchondral bone penetration, are being replaced by newer methods enabling better options for articular surface reparation. The aforesaid methods are still used, but their indications are becoming more stringent. Their value is determined by the character of the cartilage defect and also by the degree of biological age of the knee, by body weight and other factors.

The second generation of autologous-tissue engineered cartilage transplantation avoids the use of the periosteal flap thereby simplifying the surgical procedure. Thus, complications such as hypertrophy or ossification of periosteal flap are avoided, and surgical morbidity and patient recovery time are extremely reduced. The original method we have described was found to be just as effective as standard procedures, and we therefore recommend its use in the clinical arena.

Conclusions

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References