A Comparison of the Outcomes for Cartilage Defects of the Knee Treated With Either Biologic Resurfacing Versus Focal Metallic Implants

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Purpose: To compare the results of focal metallic resurfacing with biologic procedures in patients more than 35 years of age with isolated, full thickness defects of the femoral condyle. **Methods:** A total of 61 patients met the selection criteria resulting in 30 patients treated with biological procedures, including debridement, microfracture, osteochondral autograft transplantation, osteochondral allograft, and autologous chondrocyte implantation (BIO group), and 32 patients treated with focal metallic resurfacing (CAP group). The BIO and CAP groups were matched according to treatment location, defect grade and size, and age profile. Outcomes included Western Ontario and McMaster Osteoarthritis Index (WOMAC), Short Form-12, and satisfaction. The primary combination endpoint was determined as a 20% improvement (minimum clinically important difference-20) on WOMAC pain and function at 2 years and no additional index lesion-related surgical intervention. Safety and effectiveness were also reported. **Results:** Thirty patients in the BIO group (mean age of 44.6, range 35-64) had an average follow-up of 2.6 years and 32 patients in the CAP group (mean age 47.9, range 37-68) were followed for 2.0 years. Fifty-three percent in the BIO group and 75% in the CAP group achieved success per the endpoint definition. The mean total WOMAC score improved significantly for both groups (BIO: 57-78; $P < .001$) (CAP: 41-86; $P < .001$). The physical component score (Short Form-12 PCS) improved significantly in the CAP group only (30-36.4; $P < .001$). Good to excellent patient satisfaction was achieved by 80% in BIO and 91% in CAP. There were 4 secondary procedures on the index lesion in the BIO group and 2 in the CAP group. **Conclusions:** Careful patient selection can achieve high satisfaction rates with both biological and focal metal resurfacing procedures for the treatment of isolated focal chondral lesions of the femoral condyle in the knee. Focal metallic resurfacing results in similar clinical outcomes and provides excellent success rates at short-term follow-up. **Level of Evidence:** Level III comparative study.

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Arthritis of the knee joint is a major debilitating musculoskeletal condition in our modern society. Both unicondylar and total knee replacements are the mainstay of patient care for advanced stages of arthritis. Although there are many factors causing arthritic degeneration of the knee, focal articular full thickness and osteochondral defects of the femoral condyle frequently result in severe and persistent pain and functional impairment.[1] Despite the limited defect size, the symptoms suffered by these patients can match those who are scheduled for knee arthroplasty.[1] Focal chondral lesions are of high prevalence in the young adult population.[2,3] If left untreated, these lesions will most likely progress to osteoarthritis.[4-13]

Biological treatments for chondral lesions such as debridement, abrasion, microfracture, osteochondral autograft or allograft, and various other cell-based strategies have shown good results in young patients. However with increasing age, results have been less

Table 1. Inclusion and Exclusion Criteria

Inclusion Criteria	Exclusion Criteria
• Twenty-four-month follow-up • Age 35-60 yr • Grade IV (International Cartilage Repair Society [ICRS]) articular surface defect located on the medial or lateral femoral condyle • Good joint stability in the affected joint, with grade 1 Lachman or less, with no pivot shift for anterior instability and no posterior translation of more than grade 1 • Passive motion deficit measured as a lack of extension less than 10°	• More than one grade IV (ICRS) articular surface defect on the medial or lateral femoral condyle • Varus or valgus joint malalignment greater than 7° from the neutral mechanical axis in the affected limb • Evidence of metabolic disorders that may impair the formation or healing of bone • Evidence of infections at remote sites, which may spread to the implant site • Evidence of rheumatoid arthritis, gross joint destruction, infectious/crystal arthropathies, or bone resorption visible on radiographs • Evidence of chronic instability or deficient soft tissues, vascular, or muscular insufficiency • A history of prior meniscal allograft or a failed osteochondral graft with the presence of cysts or partial joint replacement • Irresolvable joint pain or loss of function with an undeterminable cause • Medial or lateral femoral condyle defect is nonfocal or very large (greater than 20 mm) • Medial or lateral femoral condyle articular surface defect is not located relatively central to the femoral condyle so that the resurfacing implant would extend beyond the lateral or medial aspect of the condyle • Widespread degenerative or inflammatory conditions in the joint that would make pain mitigation as a result of the implant difficult to measure or insignificant • Significant damage (defined as worse than grade II changes) to the articular surface opposing the implant on the tibia • Significant damage (defined as worse than grade II changes) to articular surfaces in other compartments within the affected joint • Severely compromised soft-tissue support structures in the joint. Irregularly shaped or grossly degenerated femoral condyle, where restoration of a smooth continuous articular surface is not possible such as skeletal dysplasia, mal united fracture, osteochondrosis, or nonfocal lesions

encouraging with recurring symptoms and sometimes poor or little pain relief or functional improvement.[14-16] Older patients tend to have larger chondral lesions and early signs of osteoarthritis.[9] Contained, focal defects with healthy articular perimeters do not lend themselves to traditional arthroplasty procedures because the risk of revision surgery remains highest in patients younger than 50.[14,17-21] In this population, focal metallic cartilage resurfacing could be a suitable treatment option before considering unicompartmental (UKR) or total knee replacement.

Until the development of focal metallic cartilage resurfacing, the transition from biological procedures to primary arthroplasty has not provided an intermediary step that maintains focal character while offering an unaffected exit into conventional joint replacement. This resurfacing procedure, under investigational device exemption (IDE) investigation in the United States, offers the advantage of contoured surface reconstruction and primary implant stability seen with arthroplasty while preserving healthy tissues through its focal nature.

The objective of this study was to compare the results of focal metallic resurfacing with biologic procedures in patients who are 35 years and older with isolated, full thickness defects of the femoral condyle. Our hypothesis was that focal resurfacing would result in similar clinical outcomes when compared with biologic procedures in a matched group of patients.

Methods

Design

This is a population-matched, comparative cohort study. The study endpoint and patient selection criteria for the CAP group were predetermined by the IDE approved protocol. The BIO group followed the same selection and endpoint criteria.

Eligibility Criteria

Both groups (BIO and CAP) included patients with complete preoperative and final 2-year follow-up data sets who met the inclusion and exclusion criteria for this study (Table 1). The CAP group was based on consecutive 2-year endpoint data in a Phase II IDE investigation. Any patient converted to traditional joint replacement before the 2-year endpoint was not followed after his or her revision procedure and was not included in the analysis. They were however included in the evaluation of failures and revision surgery.

All study activities were approved by governing institutional review boards and all participants signed an informed consent form. Patient level data were anonymized for the purpose of this investigation.

Selection Bias

To offset the drawback of a nonconcurrent multicenter investigation, the study placed emphasis on selection bias through various mechanisms to promote

Table 2. Selection Bias

	BIO	CAP
Outcomes	Retrospective (with baseline)	Prospective enrollment
Inclusion/exclusion criteria	Established before subject enrollment	Established before subject enrollment
Symptoms	All patients presenting with symptoms of a focal, isolated defect were included	All patients presenting with symptoms of a focal, isolated defect were included
Loss to follow-up	Follow-up with all patients at regular intervals (3, 6, 12, and 24 mo)	Follow-up with all patients at regular intervals (3, 6, 12, and 24 mo)
Analysis at 2 yr postoperative	Closely matching final assessment time point	A priori decision
Questionnaires	Predetermined assessment forms for all subjects	Predetermined assessment forms for all subjects
Patient accountability	Completed for all subjects	Completed for all subjects
Prognostic factors	Similar defect age < 24 mo: 75%, significantly different, $P = .2$	Similar defect age < 24 mo: 60%
Success criteria	Based on published literature recommendations. Matching the FDA determined combination endpoint	Based on published literature recommendations. FDA determined combination endpoint

NOTE. Selection bias was controlled in both studies by a number of conditions.
BIO, patients treated with biological procedures; CAP, patients treated with focal metallic resurfacing; FDA, U.S. Food and Drug Administration.

similar distribution of prognostic factors among the 2 groups (Table 2).

Participants and Interventions

BIO Group. From 2003 to 2006, 1,138 consecutive cartilage knee procedures were performed at one center and recorded in the institutional cartilage registry. All surgeons performing the operations had many years of experience with the biological procedures. Of those 1,138 procedures, 499 were performed on patients 35 years and older. On review of intraoperative criteria such as lesion location, size, grade, and other eligibility criteria, 109 subjects qualified for this study. Of the 109 patients, 44 had complete preoperative outcomes data. Of the 44 subjects, 30 consented to participate in the study and provide both baseline and 2-year follow-up data. BIO patients were treated arthroscopically for a single symptomatic chondral lesion using one of 5 biological procedures (microfracture n = 15; osteochondral autograft transplantation [OAT] n = 2; debridement n = 2; autologous chondrocyte implantation [ACI] n = 1, or osteochondral allograft n = 10).

CAP Group. Between 2004 and 2006, 32 patients from 8 US centers were treated with the HemiCAP focal femoral condyle resurfacing prosthesis (Arthrosurface, Franklin, MA) by 12 surgeons and followed for 2 years. One of the 32 patients was converted from a focal resurfacing implant to a unicondylar knee replacement 6 months after the index procedure at which point the patient reached the study endpoint per protocol and was not included in the baseline to follow-up comparison, but was factored into the overall success evaluation. The surgical technique has been described in several publications.[1-3,14]

Demographics and Surgical History. Both groups were alike across baseline demographic parameters, except that the BIO patients had a significantly higher body mass index ($P = .03$) (Table 3). The groups were also alike with respect to their index lesion and duration of symptoms. Indications to perform a biological cartilage procedure or resurfacing were similar.

Nineteen patients (63%) in the BIO group had one or more prior procedures in the index knee; the remainder (37%) were treated with a primary biological procedure. The surgical history included 3 microfracture procedures, 10 debridements, 4 meniscectomies, 1 drilling, 2 anterior cruciate ligament reconstructions, and 1 hardware removal. Twenty-seven patients in the CAP group (84%) had undergone a total of 82 previous surgical procedures to their index knee including multiple interventions using the same technique. These consisted of 36 debridements, 1 osteochondral allograft, 10 microfractures, 1 ACI, 7 abrasion arthroplasties, 20 meniscectomies, 2 meniscal repairs, 2 anterior cruciate ligament reconstructions, and 3 other procedures (Table 4). Five patients (16%) were treated as a primary resurfacing procedure.

Outcome Measurements

Definition of Success: Primary Combination Endpoint. The protocol for the CAP group determined

Table 3. Demographics of the BIO and CAP Groups

	BIO (n = 30)	CAP (n = 32)	*P* Value
Age, yr (range)	44.6 ± 8.5 (35-64)	47.9 ± 8.3 (37-68)	.7
Body mass index (range)	30.4 ± 7.8 (18.4-50.3)	26.7 ± 3.67 (19.0-33.5)	.03*
Gender	60% M 40% F	66% M 34% F	.65
Smoker	90% No 10% Yes	75% No 25% Yes	.12
Involved knee	47% R 53% L	31% R 69% L	.3
Last follow-up, yr	2.6 ± 0.6	2.0 ± 0.00	.0002

BIO, patients treated with biological procedures; CAP, patients treated with focal metallic resurfacing.
*Significant.

Table 4. Prior Procedures to the Index Lesion

Treatment	BIO, n	CAP, n
Microfracture	3	10
Debridement	10	36
Drilling	1	0
Osteochondral allograft	0	1
ACI	0	1
Abrasion arthroplasty	0	7

ACI, autologous chondrocyte implantation; BIO, patients treated with biological procedures; CAP, patients treated with focal metallic resurfacing.

the overall success definition for a focal cartilage procedure. Clinical parameters were combined with the need for subsequent interventions over the course of 2 years. To effectively compare both groups, the BIO group followed the same criteria. Success was defined according to previously published parameters using the minimum clinically important difference-20 from baseline.[22] Patients were considered a success if they improved by at least 20% in the Western Ontario and McMaster Osteoarthritis Index (WOMAC) pain and function subdomains in the study knee and did not undergo any subsequent defect or implant-related procedures during the course of a 2-year follow-up period.[23,24]

Secondary Effectiveness Comparison. Secondary outcome parameters included WOMAC scores,[25-27] Short Form-12 (SF-12),[28] satisfaction, and adverse events. For ease of interpretation and comparison, the WOMAC scores for each group were converted to normalized scores out of 100.[23,29,30]

In the BIO group, WOMAC scores were derived from the registry Knee Injury and Osteoarthritis Outcome Score (KOOS) questionnaire.[30] The WOMAC Likert 3.1[23] items are included in the KOOS subscales of pain, symptoms, and activities of daily living. Likert scores for each domain were totaled (Pain 20, Stiffness 8, Function 68, and Total 96). The scores were then converted to scores out of 100 with 100 being the best and 0 being the worst, using the following formula: 100 − (actual raw score × 100)/possible raw score range.[23,29,30]

In the CAP group, the visual analog scale version of the WOMAC questionnaire was used and scores for each domain were calculated (Pain 500, Stiffness 200, Function 1700, and Total 2400). Results were then converted to a normalized score out of 100 with 100 being the best and 0 being the worst by the same formula above.

The standard calculation for the SF-12 from the development handbook[28] was used to calculate the SF-12 scores. Both the physical component score (PCS) and mental component score (MCS) were used in the comparisons.

A satisfaction questionnaire was presented by the surgeon at the final follow-up asking the patients if they were satisfied with the resolution of their symptoms and their overall satisfaction. Surgeons were also asked about their overall satisfaction with the surgery. All questions were graded on the scale of 10 = excellent, 8 = very good, 6 = good, 4 = fair, and 2 = poor.

Statistical Analysis

Both groups were assessed at similar time points: 3, 6, 12, and 24 months; however, the BIO group completed the questionnaires only preoperatively and at the 24 months of follow-up. Therefore baseline data and the 2-year endpoint follow-up visit for both groups were used for analysis. Both data sets were checked and found to be normally distributed. Fisher's exact test was used to analyze the difference between the groups for the proportion of patients with at least one reoperation. A Cox's proportional hazards model for comparison of the survivorship curves could not be performed because of the low proportion of patients who underwent reoperation. Statistical comparison of the mean rating scores using the independent *t*-test was performed to evaluate the pre- and postoperative results for each group and the improvement between the groups. The primary endpoint of success as well as satisfaction was compared between each group at the last follow-up using the independent *t*-test. The *P* value for significance level was determined a priori to be $\leq .05$.

Secondary Safety Comparison: Adverse Events

The prospective study design in the CAP study provided stringent adverse event data through continuous prospective follow-up intervals and data monitoring during the course of the 2-year multicenter IDE investigation. As a registry-based study, reoperations and adverse event data for the BIO group were collected based on patient records and history. The secondary safety comparison was based on knee-related adverse events at 24 months of follow-up.

Results

Primary Outcome

On the basis of the study success definition, the CAP group showed a significantly better clinical success compared with the BIO group ($P < .001$). The overall success rate for the CAP group was 75% (n = 24 of 32) compared with 53% (n = 16 of 30) in the BIO group. In the BIO group, 47% (14 of 30) did not reach the predefined success criteria: 3 patients underwent a revision of microfracture with an osteochondral allograft; 1 patient was converted from an osteochondral allograft to unicompartmental arthroplasty; 10 patients did not improve beyond the 20% mark on WOMAC pain or function. In the CAP group, 25% (8 of 32) did not reach the predefined success criteria: 1 patient was converted to unicompartmental arthroplasty, 1 patient underwent periprosthetic debridement, and 6 patients did not

Table 5. Improvement in WOMAC Scores

	(A) BIO Group		
	BIO Preop	BIO Postop	*P* Value
Pain	56.2 ± 16.3 (30-85), 50.34-62.00	74.9 ± 21.0 (35-100), 67.4-82.44	<.001
Stiffness	57.5 ± 21.7 (12.5-100), 49.74-65.26	72.9 ± 22.5 (25-100), 64.86-80.98	.009
Function	59.2 ± 21.2 (11.67-98.5), 48.93-65.21	79.8 ± 19.5 (25-100), 72.74-86.72	<.001
Total	58.5 ± 19.0 (19.32-93.75), 50.88-64.94	78.2 ± 19.3 (31.25-100), 71.09-84.99	.001
	(B) CAP Group		
	CAP Preop	CAP Postop	*P* Value
Pain	40.9 ± 16.4 (6.5-64.8), 35.1-46.64	86.2 ± 19.5 (24.1-100), 79.35-93.05	>.001
Stiffness	36.8 ± 23.9 (4.0-90.9), 28.41-45.23	81.5 ± 25.4 (6.1-100), 72.59-90.47	>.001
Function	42.8 ± 22.9 (0-95.1), 34.71-50.85	87.0 ± 18.0 (22.7-100), 80.68-93.38	>.001
Total	41.9 ± 20.0 (10.7-87.2), 34.82-48.9	86.4 ± 18.6 (21.6-100), 79.84-92.94	>.001

NOTE. Data shown as mean ± standard deviation (range), 95% confidence interval.

BIO, patients treated with biological procedures; CAP, patients treated with focal metallic resurfacing; WOMAC, Western Ontario and McMaster Osteoarthritis Index.

improve past the 20% mark on WOMAC pain or function.

Secondary Outcome

Patients in both groups improved significantly in all domains of the WOMAC score when comparing the preoperative score with the postoperative score within each group (Table 5A BIO Group, Table 5B CAP group). When comparing the scores for each domain of the WOMAC score, the patients in the CAP group had significantly worse symptoms (lower score) at baseline compared with patients in the BIO group. At the last follow-up, despite the CAP group having better scores across all domains, the difference between the 2 groups was only significant for the WOMAC pain domain ($P = .03$; Fig 1).

BIO group patients without a previous procedure to the index knee improved on average from 62.7 to 88.1 on the total WOMAC score; those with a prior surgical history improved from 55.1 to 72.2. CAP group patients without a prior procedure to the index knee improved on average from 43.6 to 94.7; those with a prior procedure improved from 40.5 to 85.2 on the total WOMAC score.

Within both groups, the pre- and postoperative scores of the SF-12 showed no significant improvement in the MCS; however, there was a significant difference in the PCS subscore for both groups (Table 6A BIO, $P = .002$;

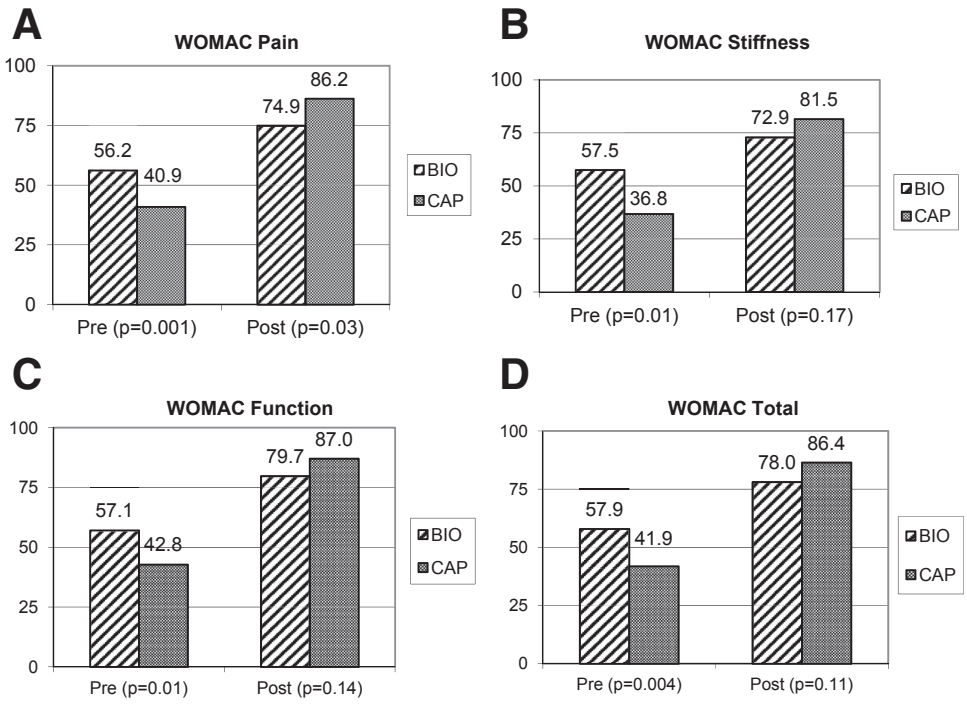

Fig 1. Pre- and postoperative Western Ontario and McMaster Osteoarthritis Index (WOMAC) scores for each domain: (A) Pain, (B) stiffness, (C) function, (D) total. (BIO, patients treated with biological procedures; CAP, patients treated with focal metallic resurfacing.)

Table 6. Improvement in SF-12 Scores

	(A) BIO Group		
	BIO Preop	BIO Postop	*P* Value
PCS score (range) 95% CI	34.5 ± 15.4 (15.9-56.8) 29, 40	42.93 ± 11.1 (25.3-57.9) 38.9, 46.9	.002*
MCS score (range) 95% CI	52.2 ± 11.1 (32.6-71.4) 4.2, 56.2	53.2 ± 7.9 (35.3-64.2) 50.4, 56.03	.69
	(B) CAP Group		
	CAP Preop	CAP Postop	*P* Value
PCS score (range) 95% CI	30.0 ± 4.4 (22.0-38.4) 28.5,31.6	36.4 ± 5.6 (21.9-48) 34.4, 38.4	<.001*
MCS score (range) 95% CI	50.2 ± 6.9 (35.3-62.9) 47.8,52.6	50.8 ± 6 (31.8-60.7) 48.7, 52.9	.72

BIO, patients treated with biological procedures; CAP, patients treated with focal metallic resurfacing; CI, confidence interval; MCS, mental component score; PCS, physical component score; SF-12, Short Form-12.
*Statistically significant.

Table 6B CAP $P < .001$). When comparing the preoperative and postoperative scores between the 2 groups, there was no significant difference in the MCS subscores (pre $P = .4$; post $P = .2$); however, there was a significant difference in both the preoperative and postoperative scores for the PCS subdomain (pre $P = .03$; post $P = .006$) (Fig 2).

Patient Satisfaction

The satisfaction profile showed very good to excellent results in the CAP group, whereas the BIO group profile was more classified as good to very good. Overall, good to excellent results for patients rating their resolution of symptoms was achieved by 66% in the BIO and 91% in the CAP group, good to excellent overall satisfaction was achieved by 80% of patients in the BIO and 91% in the CAP group, and good to excellent surgeon satisfaction was reported in 89% for the BIO and 97% in the CAP group. When these results were compared, the CAP group showed statistically better results for each question ($P < .001$) (Fig 3).

Safety

BIO Group. Of the 30 patients in the BIO study, 16 (53.3%) reported having an adverse event all of which reported persistent knee pain after the initial procedure. Ten of the patients reported more than one event receiving multiple treatments that included nonoperative management such as intra-articular corticoid injection, pain medication, femoral nerve block, and physical therapy, as well as secondary operative interventions such as osteochondral allografting and diagnostic arthroscopy. One patient had a reactive muscle spasm treated with pain medication. One patient presented with a postoperative thrombophlebitis that did not require anticoagulation.

CAP Group. Of the 32 patients in the CAP study, 21 (66%) reported a knee-related adverse event. Six patients had more than one event. Only 3 of the 25 events were considered possibly related to the implant device: 1 drainage of portal site resolved with medication, 1 clicking resolved with no treatment, and 1 knee pain resolved with physiotherapy.

Subsequent Procedures and Effectiveness

In total, 4 patients (13.3%) in the BIO study needed a subsequent procedure on the index lesion and therefore were considered a failure. Of those, 1 was

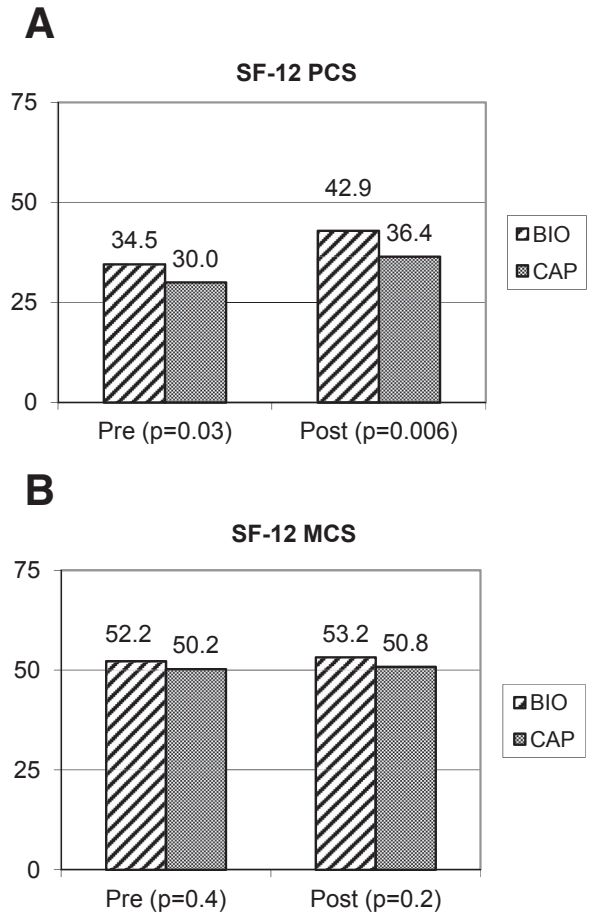

Fig 2. Pre- and postoperative Short Form-12 (SF-12) for each domain: (A) physical component score (PCS); (B) mental component score (MCS). (BIO, patients treated with biological procedures; CAP, patients treated with focal metallic resurfacing.)

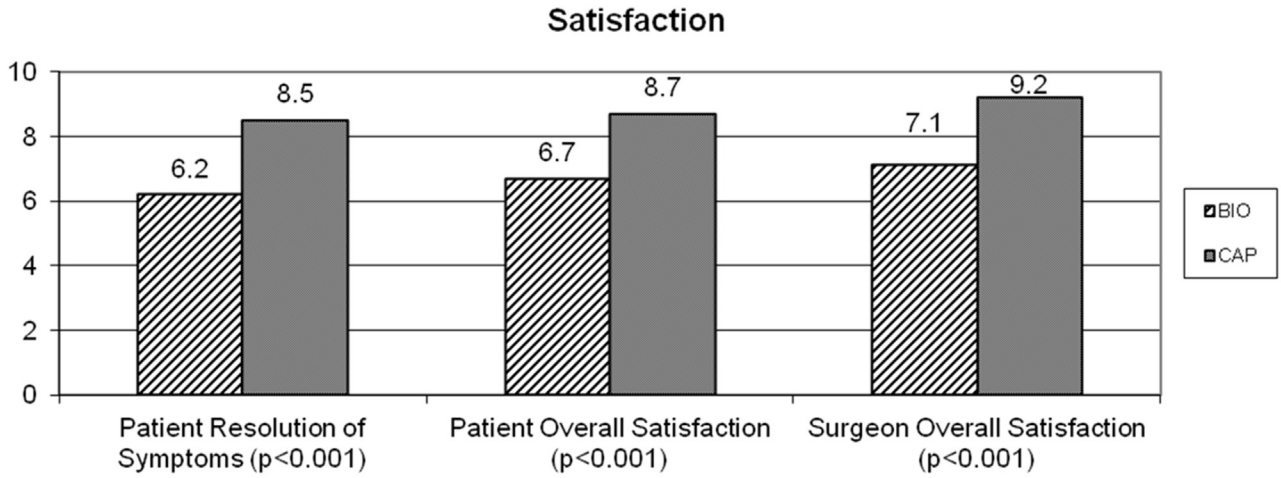

Fig 3. Satisfaction per group. 10 = excellent, 8 = very good, 6 = good, 4 = fair, and 2 = poor. (BIO, patients treated with biological procedures; CAP, patients treated with focal metallic resurfacing.)

converted to a unicondylar knee replacement and 3 received an osteochondral allograft. The reason for all subsequent procedures was persistent knee pain.

In the CAP group, 1 patient continued to have serious knee pain leading to implant removal and conversion to UKR at 6 months after the index procedure and was considered a treatment failure. The patient reached the study endpoint at this time and no further data were collected. One additional patient underwent arthroscopic debridement anterior to the implant and was considered a failure because of a defect-related secondary procedure.

Discussion

The study showed that focal metallic resurfacing resulted in similar clinical outcomes when compared with biologic procedures for the treatment of focal chondral lesions of the femoral condyle in a matched group of patients. However, compared with the BIO group, the CAP group showed significantly better clinical success and required fewer subsequent procedures.

Full thickness articular cartilage lesions in patients more than 35 years of age present greater treatment challenges than those encountered in younger patients. Frequently, previous surgical interventions and nonlocalized or multiple lesions are encountered leading to the question of when to transition from biology to arthroplasty.

Management of full thickness focal articular cartilage defects of the femoral condyles requires a highly individualized treatment approach that benefits from patient profiling.[14] Surgical decision making may vary from patient to patient based on patient age, defect-related surgical history, lesion size, opposing articular surfaces, meniscal function, mechanical alignment, ligament instability, body mass index, and recovery expectations.[14,31-33]

A 35- to 40-year-old patient with normal alignment and no surgical history will typically undergo biological treatment options initially, in particular when rehabilitation demands can be met. The same patient with an extensive surgical history of debridement, microfracture, OAT, ACI, or allograft procedures becomes more challenging when symptoms return or the procedure did not provide adequate pain relief and functional improvement. With increasing age, biological repeat procedures oftentimes lack sustainable treatment results, yet at the same time, conventional arthroplasty is relatively contraindicated because of the relative young patient age and continued isolated pathology.[34,35]

A recent publication by Bedi et al.[31] provided an evidence-based review of different methods of treating chondral defects in the knee. They concluded that bone-marrow stimulating techniques and whole tissue transplantation of allografts and autografts provide favorable outcomes but are not without their complications and disadvantages.

Microfracture is the most frequently used bone-marrow stimulating technique. Steadman et al.[36] in a long-term (11-year) follow-up found that although patients who were less than 45 years of age had a significant improvement after microfracture, only 32% were pain free. The patients, however, had to adjust their activity levels to match the condition of their knee. Microfracture was also most effective as a first-line procedure, although its results in a salvage situation were less predictable.[37,38]

Fifty percent of the patients in the BIO group were treated with microfracture (n = 15). Only one of these patients had a prior cartilage procedure to the index lesion (debridement); all others were treated with a primary intervention. Despite the literature evidence of declining success in this age group, this study showed that microfracture can provide very satisfactory results at 2 years of follow-up.

Osteochondral allograft implantation is considered a second-line treatment in cartilage restoration. Of the 10

BIO group patients treated with an osteochondral allograft, 9 had prior cartilage treatments. As a biological revision procedure, osteochondral allografting allowed for continuation of focal repair with a biological method that uses viable cartilage and structural bone. Preoperative baseline symptoms for this treatment group were most severe within the BIO group that was reflected by the lowest function and total WOMAC scores in this group. At the last follow-up, clinical scores were inferior to primary procedures such as microfracture, but patients showed the highest functional improvement within the BIO group at a level similar to the CAP group. Recently, Chahal et al.[39] performed a systematic review for outcomes of osteochondral allograft transplantation in the knee across 19 studies. They reported good clinical outcomes with a high satisfaction rate at a mean follow-up of 5 years. The mean age across all investigations was 37 years, which compares favorably with the current study with a higher mean age of 43 years within the osteochondral allograft group.

Enrollment into a tightly monitored prospective IDE investigation ensured a highly homogeneous multicenter group. Despite significant baseline symptoms and corresponding low scores, final results showed excellent improvement levels across all WOMAC domains and satisfaction rates. The clinical value becomes particularly apparent when comparing the percent improvement rates of the CAP group with the BIO group. As a first-line arthroplasty intervention, CAP patients were older on average and had a larger number of prior procedures supporting a transition into focal metallic resurfacing. These results are similar to reports from Bollars et al.,[40] who showed a close match to normative scores in a well-selected group of focal femoral condyle resurfacing patients. Results from this investigation confirm the importance of patient profiling and an individual treatment approach for successful outcomes. The longest follow-up for focal inlay resurfacing has been reported by Becher et al.[41] After 5 to 6 years, the procedure achieved radiographic joint space preservation and significant improvements on KOOS domains, Tegner, and SF-36 scores. One patient was converted to a UKR; 2 of 21 patients had subsequent procedures on the index knee but retained the focal prosthesis.

Both the osteochondral allograft and CAP patients had considerable baseline symptoms reflected by the lowest total WOMAC scores before the index procedure. As such, they presented greater challenges for postoperative improvement. In our study, inlay resurfacing showed more favorable results than osteochondral allografting.

Several studies have been published on secondary and tertiary biological interventions. Vijayan et al.[42] reported on revision cartilage transplantation after primary ACI and matrix autologous chondrocyte implantation in a young group (mean 37.4 years) yielding 63% of good to excellent clinical outcomes and continued joint preservation at 5.4 years of follow-up. In 2014, Minas et al.[43] published long-term results (mean 12 $\pm$ 2 years) of ACI and reported an overall graft survival of 79% at 5 years, 71% at 10 years, and 71% at 15 years. Graft survival for primary procedures was 79% compared with 44% in knees that underwent prior microfracture. Horton et al.[44] reported on osteochondral allografts with a minimum follow-up of 2 years. Tertiary treatment with revision allograft implantation resulted in 61% survival at 10 years; 39% failed at 5.5 years.

Biological and focal prosthetic resurfacing both follow the clinical paradigm of treatment limited to the defect area, preserving bone, healthy cartilage surfaces, and soft tissues to achieve joint preservation in the long-term management of knee arthrosis and arthritis. Examination of the various treatment algorithms for the treatment of chondral injury illustrates the complex decision-making process that may confront an orthopaedic surgeon when determining the appropriate treatment method for his or her patient.

Limitations

The nonconcurrent nature of the study presents limitations; however, it allowed an effective match across both groups using strict selection criteria; demographics and defect-specific findings showed a good match among the 2 treatment groups. Enrolling appropriate study participants in this age group who show isolated lesions within the selection criteria is challenging; a registry-based study therefore provided the most suitable approach to perform this comparative investigation.

Another limitation of the study was the mix of surgical procedures performed in the BIO group with small numbers particularly for OAT, debridement, and ACI thereby limiting subgroup analysis. Half (50%) of the patients in the BIO group received microfracture, which could bias the overall results. Although clinical results with microfracture have been encouraging, significantly better outcomes have been reported in patients treated with OAT.[45]

The study was limited to baseline and 2 years of follow-up comparison; interim follow-up data would have strengthened the results.

The nonconcurrent study design may have introduced some degree of selection bias as evidenced by lower baseline scores for the CAP group. However, a higher number of prior chondral procedures to the index lesion are expected for a focal metallic salvage procedure (Table 4).

Another limiting factor was the number of surgeons performing the procedures that could potentially affect

the results. Nevertheless, all surgeons were fellowship trained and had many years of experience performing the various treatments in the study.

Overall, longer follow-up and larger patient groups are necessary to further strengthen the assessment of these procedures in the targeted patient population.

Conclusions

Careful patient selection can achieve high satisfaction rates with both biological and focal metal resurfacing procedures for the treatment of isolated focal chondral lesions of the femoral condyle in the knee. Focal metallic resurfacing results in similar clinical outcomes and provides excellent success rates at short-term follow-up.

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References

1. Heir S, Nerhus TK, Rotterud JH, et al. Focal cartilage defects in the knee impair quality of life as much as severe osteoarthritis. *Am J Sports Med* 2010;38:231-237.
2. Curl WW, Krome J, Gordon SE, Rushing J, Smith BP, Poehling G. Cartilage injuries: A review of 31,516 knee arthroscopies. *Arthroscopy* 1997;13:456-460.
3. Widuchowski W, Widuchowski J, Trzaska T. Articular cartilage defects: Study of 25,124 knee arthroscopies. *Knee* 2007;14:177-182.
4. Blevins FT, Steadman JR, Rodrigo JJ, Silliman J. Treatment of articular cartilage defects in athletes: An analysis of functional outcome and lesion appearance. *Orthopedics* 1998;21:761-768.
5. Buckwalter JA, Mankin HJ. Articular cartilage: Part II. Degeneration and osteoarthrosis, repair, regeneration, and transplantation. *J Bone Joint Surg Am* 1997;79:612-632.
6. Cole BJ, D'Amato M. Autologous chondrocyte implantation. *Oper Tech Orthop* 2001;11:115-131.
7. Jackson DW, Lalor PA, Aberman HM, Simon TM. Spontaneous repair of full thickness defects of articular cartilage in a goat model. *J Bone Joint Surg Am* 2001;83A:53-64.
8. Kish G, Modis L, Hangody L. Osteochondral mosaicplasty for the treatment of focal chondral and osteochondral lesions of the knee and talus in the athlete. Rationale, indications, techniques and results. *Clin Sports Med* 1999;18:45-66.
9. Linden B. Osteochondritis dissecans of the femoral condyles: A long-term follow-up study. *J Bone Joint Surg Am* 1977;59:769-776.
10. Messner K, Maletius W. The long-term prognosis of severe damage to weight-bearing cartilage in the knee: A 14-year clinical and radiographic follow-up in 28 young athletes. *Acta Orthop Scand* 1996;67:165-168.
11. Minas T. Chondrocyte implantation in the repair of chondral lesions of the knee: Economics and quality of life. *Am J Orthop* 1998;27:739-744.
12. O'Driscoll S. The healing and regeneration of articular cartilage. *J Bone Joint Surg Am* 1998;80:1795-1812.
13. Hjelle K, Solheim E, Strand T, Muri R, Brittberg M. Articular cartilage defects in 1,000 knee arthroscopies. *Arthroscopy* 2002;28:730-734.
14. DeWindt TS, Bekkers JEJ, Creemers LB, Dhert WJA, Daris DBF. Patient profiling in cartilage regeneration. *Am J Sports Med* 2009;37:58S-62S.
15. Bentley G, Biant LC, Carrington RW, et al. A prospective, randomised comparison of autologous chondrocyte implantation versus mosaicplasty for osteochondral defects in the knee. *J Bone Joint Surg Br* 2003;85B:223-230.
16. Williams RJ III, Ranawat AS, Potter HG, Carter T, Warren RF. Fresh stored allografts for the treatment of osteochondral defects of the knee. *J Bone Joint Surg Am* 2007;89A:718-726.
17. Insall JN, Binazzi R, Soudry M, Mestriner LA. Total knee arthroplasty. *Clin Orthop Relat Res* 1985;192:13-22.
18. Julin J, Jämsen E, Puolakka T, Konttinen YT, Moilanen T. Younger age increases the risk of early prosthesis failure following primary total knee replacement for osteoarthritis. *Acta Orthop* 2010;81:413-419.
19. Pagnano MW, Clarke HD, Jacofsky DJ, Amendola A, Repicci JA. Surgical treatment of the middle-aged patient with arthritic knees. *Instr Course Lect* 2005;54:251-259.
20. Rand JA, Ilstrup DM. Survivorship analysis of total knee arthroplasty: Cumulative rates of survival of 9200 total knee arthroplasties. *J Bone Joint Surg Am* 1991;73:397-409.
21. W-Dahl A, Robertsson O, Lidgren L. Surgery for knee osteoarthritis in younger patients. *Acta Orthop* 2010;81:161-164.
22. Tubach F, Ravaud P, Baron G, et al. Evaluation of clinically relevant changes in patient reported outcomes in knee and hip osteoarthritis: The minimally clinically important improvement. *Ann Rheum Dis* 2005;64:29-33.
23. Bellamy N, Bell MJ, Goldsmith CH, et al. Evaluation of WOMAC 20, 50, 70 response criteria in patients treated with hylan G-F 20 for knee osteoarthritis. *Ann Rheum Dis* 2005;64:881-885.
24. Raymaud J-P, Torrance GW, Band PA, et al. A prospective, randomized, pragmatic, health outcomes trial evaluating the incorporation of hylan G-F 20 into the treatment paradigm for patients with knee osteoarthritis (Part1 and 2): Clinical results. *Osteoarthr Cart* 2002;10:506-517.
25. Bellamy N, Buchanan WW, Goldsmith CH, Campbell J, Stitt LW. Validation study of WOMAC: A health status instrument for measuring clinically important patient relevant outcomes to antirheumatic drug therapy in patients with osteoarthritis of the hip or knee. *J Rheumatol* 1988;15:1833-1840.

26. Bellamy N, Buchanan WW. A preliminary evaluation of the dimensionality and clinical impact of pain and disability in osteoarthritis of the hip and knee. *Clin Rheum* 1986;5:231-241.
27. Bellamy N. Pain assessment in osteoarthritis: Experience with the WOMAC osteoarthritis index. *Semin Arthritis Rheum* 1989;18:14-17 (suppl 2).
28. Ware JE, Kosinski M, Keller SD. *SF-12: How to score the SF-12 physical and mental health summary scales*, Ed 2. Boston: Health Institute, New England Medical Center, 1995.
29. Bischoff-Ferrari HA, Bellamy N, Theiler R. Validation and patient acceptance of a computer touch screen version of the WOMAC 3.1 osteoarthritis index. *Ann Rheum Dis* 2005;64:80-84.
30. Roos EM, Roos HP, Lohmander LS, Ekdahl C, Beynnon BD. Knee Injury and Osteoarthritis Outcome Score (KOOS)—Development of a self-administered outcome measure. *J Orthop Sports Phys Ther* 1998;28:88-96.
31. Bedi A, Feeley BT, Williams RJ III. Management of articular cartilage defects in the knee. *J Bone Joint Surg Am* 2010;92:994-1009.
32. Niemeyer P, Salzmann GM, Hirschmüller A, Südkamp NP. Factors that influence clinical outcome following autologous chondrocyte implantation for cartilage defects of the knee. *Z Orthop Unfall* 2012;150:83-88.
33. Manek NJ, Lane NE. Osteoarthritis: Current concepts in diagnosis and management. *Am Fam Physician* 2000;61:1795-1804.
34. Browne JE, Branch TP. Surgical alternatives for treatment of articular cartilage lesions. *J Am Acad Orthop Surg* 2000;8:180-189.
35. Cole BJ, Pascual-Garrido C, Grumet RC. Surgical management of articular defects in the knee. *J Bone Joint Surg Am* 2009;91A:1778-1790.
36. Steadman JR, Briggs KK, Rodrigo JJ, Kocher MS, Gill TJ, Rodkey WG. Outcomes of microfracture for traumatic chondral defects of the knee. *Arthroscopy* 2003;19:477-484.
37. Gill TJ. The treatment of articular cartilage defects using microfracture and debridement. *Am J Knee Surg* 2000;13:33-40.
38. Mithoefer K, Williams RJ, Warren RF, Wickiewicz TL, Marx RG. High impact athletics after knee articular cartilage repair: A prospective evaluation of the microfracture technique. *Am J Sports Med* 2006;34:1413-1418.
39. Chahal J, Gross AE, Cross C, et al. Outcomes of osteochondral allograft transplantation in the knee. *Arthroscopy* 2013;29:575-588.
40. Bollars P, Bosquet M, Vandekerckhove B, Hardeman F, Bellemans J. Prosthetic inlay resurfacing for the treatment of focal, full thickness cartilage defects of the femoral condyle: A bridge between biologics and conventional arthroplasty. *Knee Surg Sports Traumatol Arthrosc* 2012;20:1753-1759.
41. Becher C, Kalbe C, Thermann H, et al. Minimum 5-year results of focal articular resurfacing for the treatment of full-thickness articular cartilage defects in the knee. *Arch Orthop Trauma Surg* 2011;131:1135-1143.
42. Vijayan S, Bentley G, Rahman J, Briggs TW, Skinner JA, Carrington RW. Revision cartilage cell transplantation for failed autologous chondrocyte transplantation in chronic osteochondral defects of the knee. *Bone Joint J* 2014;96-B:54-58.
43. Minas T, Von Keudell A, Bryant T, Gomoll AH. The John Insall Award: A minimum 10-year outcome study of autologous chondrocyte implantation. *Clin Orthop Relat Res* 2014;472:41-51.
44. Horton MT, Pulido PA, McCauley JC, Bugbee WD. Revision osteochondral allograft transplantations: Do they work? *Am J Sports Med* 2013;41:2507-2511.
45. Gudas R, Gudaite A, Pocius A, et al. Ten-year follow-up of a prospective, randomized clinical study of mosaic osteochondral autologous transplantation versus microfracture for the treatment of osteochondral defects in the knee joint of athletes. *Am J Sports Med* 2012;40:2499-2508.