Histologic and Immunohistochemical Characteristics of Failed Articular Cartilage Resurfacing Procedures for Osteochondritis of the Knee

A Case Series

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Background: The histologic appearance of the repair tissue after articular cartilage resurfacing procedures in humans is not well documented.

Hypothesis: The histologic and immunohistochemical appearance of the repair tissues in failed articular cartilage resurfacing procedures will be similar, regardless of the procedure that was done, and will not resemble normal articular cartilage.

Study Design: Case series; Level of evidence, 4.

Methods: Graft tissue from 10 patients who underwent an autologous chondrocyte implantation (n = 6), microfracture (n = 3), or periosteal transplantation (n = 1) procedure to treat symptomatic osteochondritis dissecans of the medial femoral condyle was processed for histologic examination after failure of the articular cartilage resurfacing procedure. Serial sections from all slabs were stained with hematoxylin and eosin and toluidine blue and were immunostained using antibodies directed against types I, II, and X collagen.

Results: Specimens from all 3 types of repair procedures were composed primarily of fibrous connective tissue and fibrocartilage. None of the sections stained positively for type X collagen. All 10 cases stained positively for type I collagen (range, 7%-97% of tissue area). Staining for type II collagen was positive in 4 of 6 autologous chondrocyte implantation cases, 3 of 3 microfracture cases, and the periosteal transplant case (range, 2%-65% of tissue area). In 8 of 10 cases, the percentage of the section area exhibiting positive staining for type I collagen was higher than for type II collagen (6 of 6 autologous chondrocyte implantation; 1 of 3 microfracture; 1 periosteal transplant).

Conclusion: The histologic appearance of the repair tissue of 3 different failed articular cartilage resurfacing procedures was similar and did not resemble normal articular cartilage.

Keywords: autologous chondrocyte implantation; microfracture; periosteal transplantation; dislodged cartilage grafts; histology; immunohistochemistry

Articular cartilage damage to the knee joint is very common, with chondral defects being reported in up to 66% of knee arthroscopies.[1,8] In 1 prospective study, 11% of patients had localized full-thickness chondral defects that were potentially treatable with current technology.[1] The precise cause of articular cartilage defects is largely unknown, and the condition is most likely multifactorial.[9,12] Multiple procedures have been introduced to resurface articular cartilage defects, but none have resulted in restoration of tissue that closely resembles normal articular cartilage.[6,10,14,16,19,24,28,30]

Autologous chondrocyte implantation (ACI),[3,13,16,19,24] microfracture,[13,28] and periosteal transplantation[7,19] are

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TABLE 1
Graft Histology Results of Patients With Failed Articular Cartilage Replacement Procedures[a]

Patient	Implant Type	Gross Dimensions, mm	No. of Slabs Evaluated	Graft Composition	Graft Surfaces	Chondrocyte Necrosis	Foci of Hypertrophic Cartilage	Areas of Toluidine Blue–Positive Matrix	Comments
1	ACI	8 × 15 × 6	4	FC/FT	Fibrous rim	0	3+	3+	
2	ACI	10 × 15 × 6	3	FC/FT	Fibrous rim	0	0	0	
3	ACI	15 × 11 × 5	8	FC/FT	Fibrous rim	1+	1+	0	
4	ACI	9 × 11 × 7	2	FC/FT	Fibrillated	0	0	0	
5	ACI	22 × 15 × 5	2	FC/FT	Fibrous rim	0	1+	1+	
6	ACI	14 × 10 × 5	2	FC/FT	Fibrillated	1+	0	0	
7	MF	24 × 11 × 5	6	FC/FT	Fibrillated	0	0	0	
8	MF	10 × 4 × 1.5	2	FC/FT	Fibrillated	0	2+	2+	
9	MF	13 × 10 × 2	2	FC/FT	Fibrillated	1+	1+	1+	NSB
10	PT	15 × 9 × 4	4	FC/FT[b]	Fibrillated	3+	0	2+	
ACI mean		13.0 × 12.8 × 5.7	3.5			0.33+	0.83+	0.67+	
MF mean		15.7 × 8.3 × 2.8	3.3			0.33+	1.0+	1.0+	
Overall mean		13.9 × 11.3 × 4.7	3.4			0.60+	0.80+	0.90+	

[a]ACI, autologous chondrocyte implantation; FC, fibrocartilage; FT, fibrous tissue; MF, microfracture; NSB, necrosis of subchondral bone; PT, periosteal transplant.
[b]This specimen was composed of an admixture of highly cellular and vascularized fibrocartilage and multiple foci of necrotic chondrocytes as well as small foci of necrotic bone.

procedures that are currently used to treat symptomatic full-thickness articular cartilage defects of the femoral condyles. As part of our treatment and referral practice, we have noted a number of patients with treatment failures who previously had undergone these procedures.

Our hypothesis is that the histologic and immunohistochemical appearance of failed articular cartilage resurfacing procedures would be similar and would not resemble normal articular cartilage. The purpose of the present study was to evaluate the histologic appearance of the repair site after failed articular cartilage resurfacing procedures.

MATERIALS AND METHODS

Patients

All patients who were seen between January 1, 2002, and June 30, 2003, with failed articular cartilage resurfacing procedures had a histologic and immunohistochemical analysis of the failed repair tissues. For ACI patients, the dislodged or partially dislodged tissues were removed arthroscopically. For the microfracture and periosteal transplant patients, the entire area of the repair tissue was removed with osteotome en bloc at the time of a fresh osteoarticular allograft procedure.

Histology/Immunohistochemistry

The excised tissues were fixed in 4% paraformaldehyde; briefly decalcified in 10% ethylenediamine tetraacetic acid, pH 6.2, when necessary; and sectioned into 2- to 3-mm-thick slabs with a scalpel blade. Each case consisted of a variable number of slabs, depending on the size of the retrieved specimen (range, 2-8 slabs) (Table 1). Each slab was embedded in paraffin and sectioned at 4 m. Serial sections from each slab were stained routinely with hematoxylin and eosin (H&E), toluidine blue, and trichrome stains (Gomori's 1-step trichrome), and additional serial sections were immunostained for types I, II, and X collagen. Deparaffinization and rehydration were followed by enzymatic pretreatment and protein blocking (Dako Serum-Free Protein Block, Dako, Carpinteria, Calif) before application of the primary antibody.

Sections stained for type I collagen were pretreated with pronase 1 mg/mL in Tris buffer, pH 7.6, for 15 minutes at 25 C, and the mouse antihuman collagen I (Sigma, St Louis, Mo) was diluted at 1:350. Type II collagen-stained sections were pretreated with pepsin 1 mg/mL in 100 mM Tris HCl, pH 2.0, for 15 minutes at 25 C, and mouse antihuman collagen II (Iowa Hybridoma Bank, Iowa City, Iowa) was diluted at 1:10. Sections for type X collagen were pretreated with hyaluronidase at 1 mg/mL in Tris buffer, pH 7.6, for 20 minutes at 25 C, and mouse antihuman type X collagen (gift from Dr Paul DiCesare, Hospital for Joint Diseases, New York, NY) was diluted at 1:1000. Sections were incubated with primary antibodies overnight at 4 C and were detected using antimouse link and streptavidin label from the Super Sensitive Alkaline Phosphatase Kit from BioGenex (San Ramon, Calif), followed by Vector Red alkaline phosphatase substrate (Vector Laboratories, Burlingame, Calif). All sections were counterstained with Mayer's hematoxylin. Sections of normal adult human articular cartilage and subchondral bone from a freshly collected medial femoral condyle of a 22-year-old man were used as positive controls for type I (subchondral bone) and type II (articular cartilage) collagen, whereas sections of distal femur from an immature cynomolgus monkey (open growth plate) served as positive controls for type X collagen. Positive controls were incubated with the primary antibody at the specified dilution. The primary antibody was substituted with negative control serum for super sensitive mouse antibodies (BioGenex) for all negative control sections.

TABLE 2
Characteristics of Patients With Failed Articular Cartilage Replacement Procedures[a]

Patient	Age, y	Sex	Initial Diagnosis	Implant Type	Period From Primary Procedure to Symptom Recurrence, mo	Mechanism of Reinjury	Period From Primary Procedure to Reoperation, mo	Failure Treatment
1	36	F	L MFC; OCD	ACI	19	Fell on ice	27	FOA
2	33	M	R MFC; OCD	ACI	22	Rising from a chair	32	LBR
3	37	M	L MFC; OCD	ACI	41	Twisted playing soccer	47	FOA
4	24	F	R MFC; OCD	ACI	20	NKI	23	LBR
5	34	M	R MFC; OCD	ACI	46	NKI	46	LBR
6	23	M	R MFC; OCD	ACI	54	Pain appeared while riding bike	59	LBR
7	20	F	L MFC; OCD	MF	9	Twisted playing basketball	15	FOA + PTO
8	28	M	L MFC; OCD	MF	8	NKI	18	FOA
9	45	M	R MFC; OCD	MF	51	NKI	59	FOA
10	18	M	L MFC; OCD	PT	5	Landed on the knee while dancing	9	FOA + PTO
ACI mean (range)	31.2 (23-37)				33.7 (19-54)		39.0 (23-59)	
MF mean (range)	31 (20-45)				22.7 (8-51)		30.7 (15-59)	
Overall mean	29.8				27.5		33.5	

[a]ACI, autologous chondrocyte implantation; F, female; FOA, fresh osteoarticular allograft; L, left; LBR, loose body removal; M, male; MF, microfracture; MFC, medial femoral condyle; NKI, no known injury; OCD, osteochondritis dissecans; PT, periosteal transplant; PTO, proximal tibial osteotomy; R, right.

All H&E–, toluidine blue–, and Gomori's trichrome–stained sections for each case were graded with the reviewer blinded to the type of failed cartilage repair procedure, and the results were tabulated (Table 1). The presence and extent of chondrocyte necrosis, foci of cartilage with a hypertrophic appearance (increased size of chondrocytes, sometimes associated with mineralization of the adjacent matrix), and areas of toluidine blue positive matrix were graded as follows: 0, feature absent; 1+, minimal; 2+, mild; 3+, moderate; and 4+, marked.

For evaluation of the immunostained sections, the total area (millimeters squared) of each tissue section was measured with the Osteomeasure Bone Morphometry System (Osteometrics, Decatur, Ga) using a 1× objective. All areas of positive immunostaining, regardless of staining intensity, were measured using the same system, and the percentage of positively stained tissue in each section was determined. Each section was evaluated independently (L.B.), and the examiner was blinded to the type of failed cartilage repair procedure. The results from all sections (1 section/slab) for each case were averaged to determine the mean percentage of positively stained tissue area for each case.

RESULTS

Patients

Ten patients with symptomatic full-thickness grade 4 chondromalacia because of osteochondritis dissecans (OCD) of the medial femoral condyle[22] developed failures of articular cartilage replacement procedures and were seen at our institution over a period of 18 months (Table 2). The procedures these patients had undergone included ACI (n = 6), microfracture (n = 3), and periosteal transplant (n = 1). The 6 ACI patients were treated originally at our institution, whereas the other 4 individuals were referral patients who were originally treated elsewhere.

During the period of time that the 6 ACI failure patients underwent their primary ACI procedures, a total of 38 patients (including the 6 failure patients) underwent ACI procedures at our institution. The ACI failures in this study all occurred in patients with a primary diagnosis of OCD of the medial femoral condyle (6/9 total), and none had an associated bone graft procedure.

At presentation, all 10 patients reported symptoms of pain and joint effusion with activity and were found to have normal articular cartilage of the opposing medial tibial plateau and a normal medial meniscus. Eight patients, including all 6 ACI patients and 2 of the microfracture patients, had normal anatomical alignment of the lower extremity on long leg standing radiographs before the surgical procedure. The remaining 2 patients (patient No. 7, microfracture; patient No. 10, periosteal transplant) did not obtain preoperative alignment radiographs before their initial surgeries and were noted to have coronal plane varus alignments on long leg standing radiographs on presentation to our center.

The postoperative cartilage resurfacing rehabilitation protocol was similar for all 10 patients and consisted of no weightbearing for 6 weeks along with the use of a continuous passive motion machine for a minimum of 6 hours daily during this time. Progressive weightbearing after the initial 6-week period was allowed based on

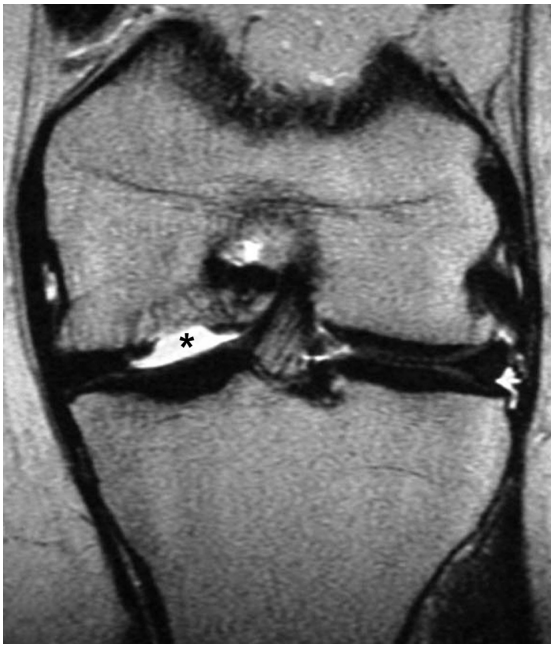

Figure 1. Magnetic resonance imaging arthrogram with intra-articular gadolinium demonstrating a dislodged autologous chondrocyte implantation graft and the recurrent chondral defect (asterisk) of the medial femoral condyle of a patient with a dislodged autologous chondrocyte implantation graft (left knee, coronal view).

symptoms, and patients were allowed to wean off their crutches when they were without pain and could walk without a limp (at a mean of approximately 10 weeks postoperatively).

The 6 ACI failure patients experienced symptoms of recurrent pain or of a loose body at a mean of 33.7 months (range, 19-54 months) after their primary ACI procedures. Before the onset of symptoms, all patients had been doing well with no complaints of knee pain. An MRI arthrogram with intra-articular gadolinium demonstrated either a loose chondral flap or a chondral defect of the medial femoral condyle with an associated loose body in the painful knee (Figure 1). These patients all underwent an arthroscopic evaluation of their knees, which confirmed a complete or partial dislodgement of the ACI graft. The loose or dislodged portion of the ACI graft was removed and fixed in 4% paraformaldehyde for histologic analysis. The mean age at the time of arthroscopy and graft removal was 31.2 years (range, 23-37 years), and the mean time from the primary ACI surgery to the arthroscopic evaluation was 39 months (range, 23-59 months) (Table 2). The mean period of time from recurrence of symptoms to arthroscopy was 5.3 months (range, 1-10 months).

The remaining 4 patients had initially been treated with either a microfracture (n = 3) or a periosteal transplantation (n = 1) procedure and were referred to our clinic for consultation because of continued knee pain after the initial procedure. All 4 of these patients had a physical examination, a high-resolution (1.5-T) MRI scan with intra-articular gadolinium, and a long leg alignment radiograph as part of their workups to determine the cause of their continued medial joint line pain. The mean time from the primary procedure to the first recurrence of the symptoms (medial joint line pain and effusions with activity) for the microfracture patients was 22.7 months (range, 8-51 months) (Table 2). The mean age of these patients at the time of arthroscopy and graft removal was 31.0 years (range, 20-45 years), and the mean time from primary surgery to revision surgery and graft removal was 30.7 months (range, 15-59 months). The periosteal transplantation patient was 18 years old, had symptoms of recurrence at 5 months postoperatively, and had surgery and graft removal performed 9 months after the initial procedure (Table 2).

As noted previously, 2 of the patients (patient No. 7, microfracture; patient No. 10, periosteal transplant) had genu varus alignments on long leg radiographs. In both patients, a concurrent proximal tibial opening wedge osteotomy and fresh osteoarticular allograft to the medial femoral condyle were performed. A fresh osteoarticular allograft to the medial femoral condyle procedure alone was performed in the remaining 2 microfracture cases.

Gross Examination

The partial or complete ACI dislodgement tissues were qualitatively noted to be shiny white (Figure 2) and appeared slightly lighter in gross appearance at the time of arthroscopy than was the remaining native articular cartilage. These specimens were subjectively firm on palpation, had mildly irregular surfaces, and ranged in size from 693 mm^3 to 1650 mm^3 (Table 1). At surgery, the tissue in the area of the microfracture and periosteal transplantation procedures also appeared qualitatively to be whiter and was subjectively softer on gross examination than was the surrounding native articular cartilage, and the surfaces of these specimens also were mildly irregular. These specimens ranged in size from 60 mm^3 to 1320 mm^3 (Table 1).

Specimen Microstructure

All tissue sections were composed either primarily or completely of an admixture of fibrous connective tissue and fibrocartilage (Table 1), and with the exception of the periosteal transplant case (patient No. 10), the appearance of this tissue was remarkably similar from section to section and case to case. The areas of fibrocartilage/fibrous connective tissue contained matrix that was loosely arranged in some areas and tightly packed in others. Trichrome staining ranged from very pale blue in areas where the matrix was loosely arranged to dark blue in areas where the matrix was tightly packed. In 4 cases (all ACI repairs), the repair tissue was roughly ovoid in shape and was surrounded by an outer rim of fibrous connective tissue. In the remaining 6 cases (2 ACI, 3 microfracture, and 1 periosteal transplant), the repair tissue was irregular in shape and had fibrillated margins. Some sections from the ACI and microfracture repairs had areas containing hypertrophic chondrocytes in lacunae; however, the majority of the chondrocytes in all sections were small and quiescent (resembling resting chondrocytes) in appearance. Some sections from all repair types had areas that stained positively with

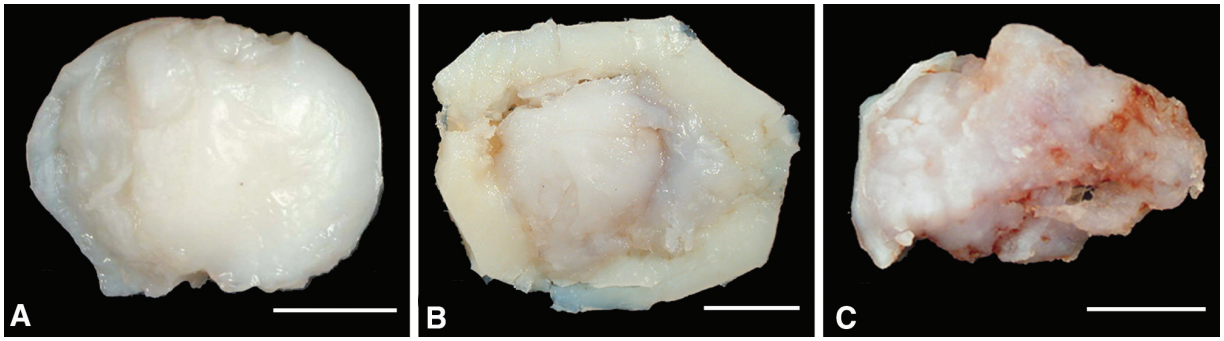

Figure 2. Gross images of representative tissue from each primary procedure: A, autologous chondrocyte implantation; B, microfracture; C, periosteal transplant. Bar = 0.5 cm.

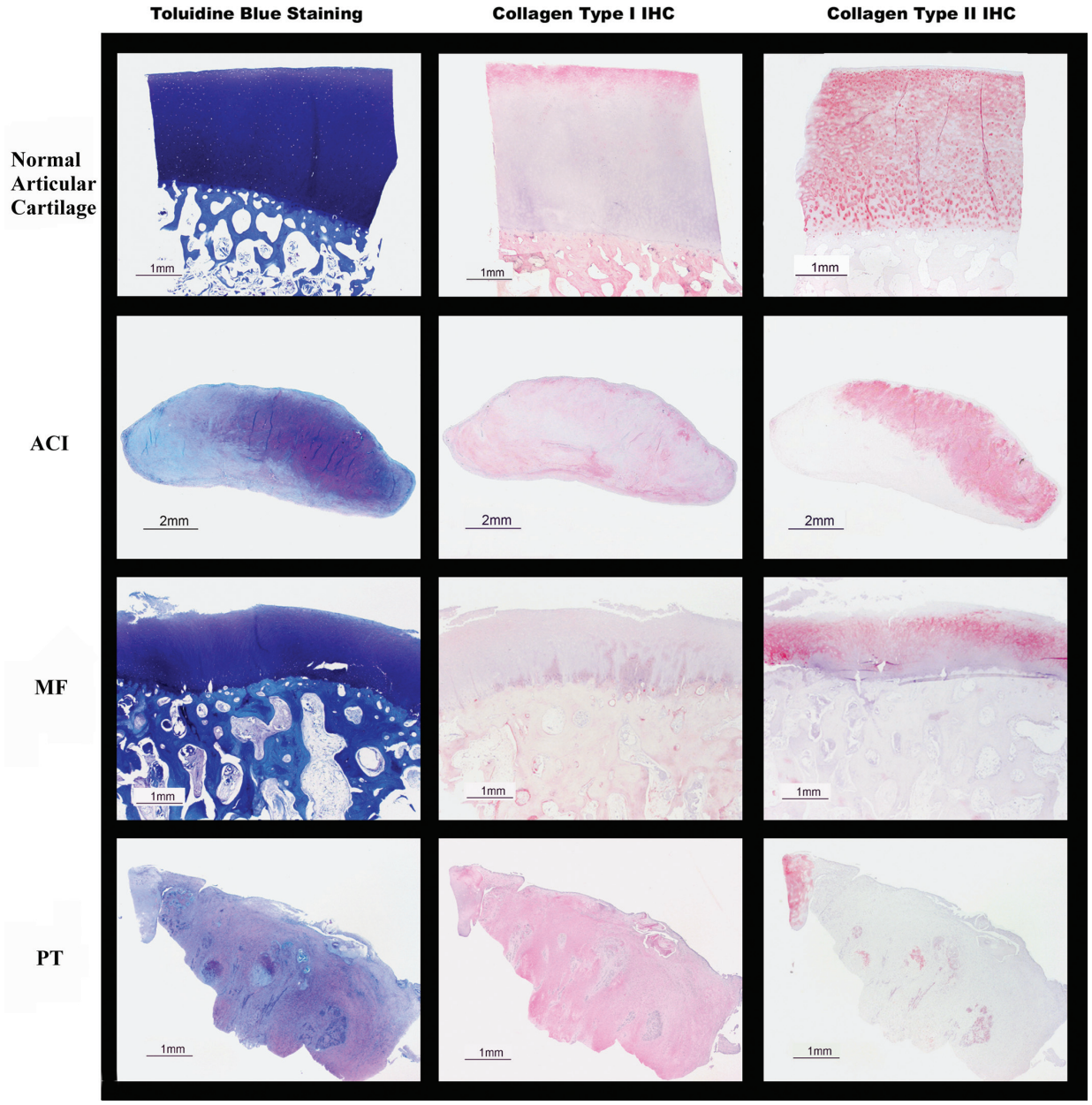

Figure 3. Histologic and immunohistochemical staining of representative sections of normal human articular cartilage, autologous chondrocyte implantation (ACI), microfracture (MF), and periosteal transplant (PT) demonstrating toluidine blue, type I collagen, and type II collagen staining patterns. The immunohistochemical (IHC) reaction product for type I and type II collagen is red.

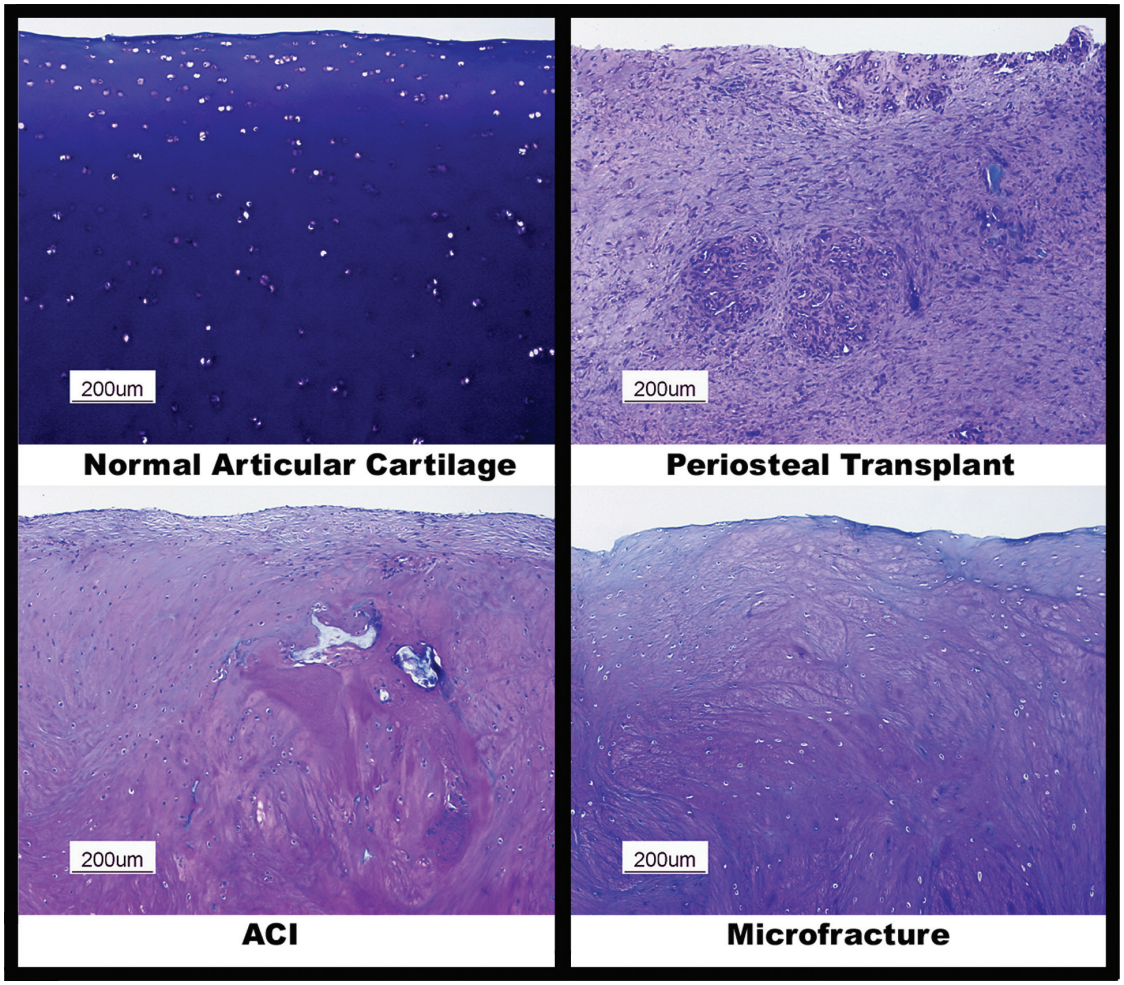

Figure 4. High magnification images of toluidine blue–stained serial sections of normal cartilage and periosteal transplant, autologous chondrocyte implantation (ACI), and microfracture repair tissues, demonstrating loss of toluidine blue staining and fibrillated nature of all repair tissues compared with normal cartilage.

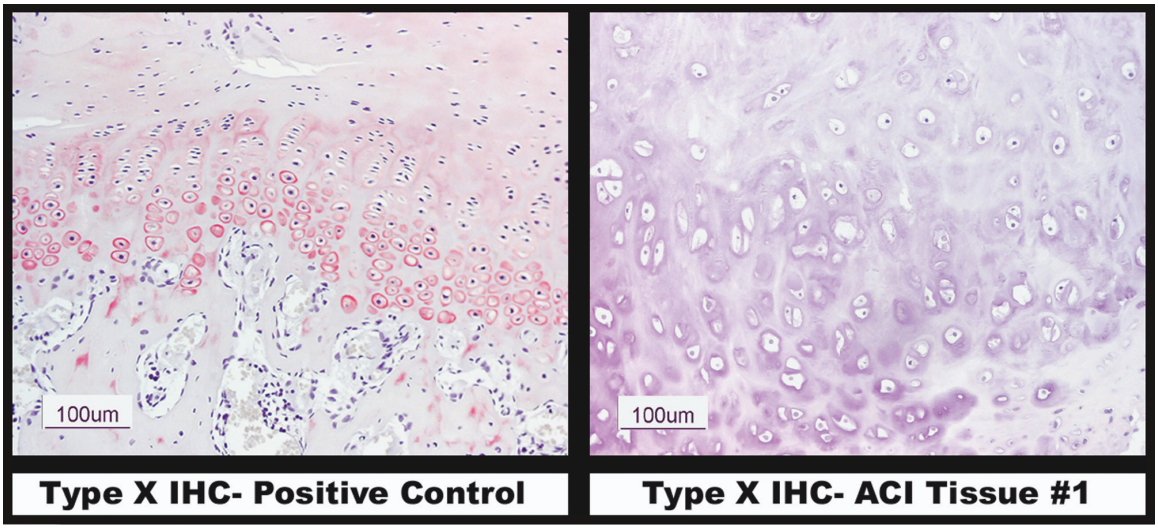

Figure 5. Type X collagen immunostaining of autologous chondrocyte implantation (ACI) tissue demonstrating lack of positivity in hypertrophic chondrocytes (right). Positive control tissue (left) demonstrates positive immunostaining (red reaction product) localized to hypertrophic chondrocytes in femoral physeal cartilage from a cynomolgus monkey (positive control). IHC, immunohistochemical.

TABLE 3
Collagen I and II Immunohistochemistry Evaluation of Patients With Failed Articular Cartilage Replacement Procedures[a]

		Collagen I			Collagen II			
Specimen	Implant Type	Total Tissue Area, mm^2	Positive Tissue Area, mm^2	Percentage Positive	Total Tissue Area, mm^2	Positive Tissue Area, mm^2	Percentage Positive	Percentage Collagen II Positive/Percentage Collagen I Positive
1	ACI	208.79	177.98	85.24	241.32	57.65	23.89	0.28
2	ACI	197.17	13.63	6.91	197.85	0.00	0.00	0.00
3	ACI	240.70	71.19	29.58	323.78	1.86	0.58	0.02
4	ACI	59.79	43.10	72.08	62.11	0.00	0.00	0.00
5	ACI	91.85	88.84	96.72	100.82	65.19	64.66	0.67
6	ACI	69.21	48.92	70.69	65.38	19.33	29.56	0.42
7	MF	155.03	17.30	11.16	181.41	39.44	21.74	1.95
8	MF	8.76	6.53	74.60	7.90	1.95	24.76	0.33
9	MF	20.43	5.38	26.34	23.37	13.30	56.91	2.16
10	PT	64.34	50.69	78.78	60.60	2.15	3.55	0.05
ACI mean		144.58	73.94	60.20	165.21	24.01	19.78	0.23
MF mean		61.41	9.74	37.37	70.89	18.23	34.47	1.48
Overall mean		111.61	52.36	55.21	126.45	20.09	22.57	0.59

[a]For tissue area and collagen I and II positive tissue area, each value represents the total area of all specimens evaluated in each particular patient; for percentage of collagen I and II positive area, each value represents the mean percentage of all specimens evaluated in each particular patient. ACI, autologous chondrocyte implantation; MF, microfracture; PT, periosteal transplant.

TABLE 4
Ranges of Percentage Immunopositivity (Relative to Total Area of Tissue Section) for Type I and Type II Collagen in Sections of Serial Slabs[a]

			Percentage Collagen I		Percentage Collagen II	
Specimen	Implant Type	No. of Slabs Evaluated	Minimum	Maximum	Minimum	Maximum
1	ACI	4	72.34	92.46	3.94	42.79
2	ACI	3	3.37	14.03	0.00	0.00
3	ACI	8	8.66	46.24	0.00	4.76
4	ACI	2	64.04	77.47	0.00	0.00
5	ACI	2	95.68	98.40	51.63	72.69
6	ACI	2	63.41	77.87	23.59	34.20
7	MF	6	0.00	85.49	0.00	50.46
8	MF	2	65.92	83.72	22.08	27.52
9	MF	2	19.58	32.43	49.83	62.86
10	PT	4	48.54	96.53	0.00	11.82

[a]Mean values are reported in Table 3. ACI, autologous chondrocyte implantation; MF, microfracture; PT, periosteal transplant.

toluidine blue stain; however, the majority of the tissue area in most sections was toluidine blue negative. In areas that stained positively with toluidine blue stain, the matrix had a fibrous rather than a hyaline appearance (Figures 3 and 4).

None of the tissue sections contained cells or matrix areas that stained positively for type X collagen (Figure 5). In contrast, 10 of 10 cases (100%) and 8 of 10 cases (80%) contained areas of positive matrix staining for type I and type II collagen, respectively (Table 3). The 2 cases that did not stain positively for type II collagen were both from patients who had undergone ACI. From comparison of serial sections, some specimens were identified that contained tissue areas that stained positively for both collagen types. In 8 of 10 cases (excluding patient No. 7 and patient No. 9, who were both microfracture patients), the percentage of positive staining for type I collagen (mean, 49.72%; range, 6.9%-96.7%) was higher than was the percentage of staining for type II collagen (mean, 25.69%; range, 0%-64.7%), whereas in patients No. 7 and No. 9, this was reversed. Seven cases (4 ACI, 2 microfractures, and 1 periosteal transplant) had >50% of tissue area that stained positively for type I collagen, and 3 cases (1 ACI and 2 microfractures) had >50% of tissue that stained positively for type II collagen (Table 3). The range in positively stained tissue area for both type I and type II collagen varied widely among the sections (Table 4).

Similar to the ACI and microfracture cases, histologic sections from the periosteal transplant case (patient No. 10) were composed primarily of an admixture of fibrous connective tissue and fibrocartilage; however, these sections were highly cellular and contained many small blood

vessels, areas of necrotic cartilage, and small foci of necrotic bone (Figure 3).

DISCUSSION

The histologic appearances of the failed repair sites for ACI, microfracture, and periosteal transplantation were all similar. None of these repair tissues had either a histologic or immunohistochemical resemblance to normal articular cartilage. The results of the present study demonstrate that failed articular cartilage implantation grafts do not resemble normal hyaline cartilage, being composed primarily of a mixture of fibrous connective tissue and fibrocartilage. These results are similar to those of Nehrer et al,[21] in which the predominant tissue retrieved from 6 failed ACI repairs was composed predominantly of fibrous tissue and "transition tissue," with immunopositivity being weak to moderate for type I collagen, weak to absent for type II collagen, and absent for type X collagen. It is unclear whether the appearance of the failed ACI specimens is representative of all ACI grafts or only the failures; however, in follow-up biopsies performed 2 years after cartilage repair surgery, Knutsen et al[13] found some hyaline cartilage present in only 39% of their ACI and microfracture patients, whereas 43% of cases had fibrocartilage throughout most of their depth. This suggests that even clinically successful cases may often have abnormal histologic findings 2 years after the initial procedure. In contrast to our findings, Roberts et al[26] found that all 10 punch biopsy samples taken from ACI graft failures had areas that stained positively for type II collagen, including 2 samples that were composed primarily of fibrocartilaginous tissue. In fact, in 8 of 10 of the samples in that study, between 54% and 96% of the cartilage area stained positively for type II collagen; however, immunostaining for type I collagen was not done for comparison. Although the histologic appearance of the tissue from slab to slab in a given specimen was quite similar in the present study, the percentage of tissue area that stained positively for type I or type II collagen was quite variable depending on the tissue slab examined (Table 4). It is clear from our results that the examination of a small biopsy sample may not produce immunostaining results that are representative of the larger tissue area.

To our knowledge, only 1 other study has evaluated the entire failed graft specimen,[21] with the remainder of the articular cartilage resurfacing studies reporting on the results from small (2-mm or equivalent) punch biopsy specimens.[2,4,11,13,20,23-27,29] An advantage of examining graft failures is that the entire specimen can be retrieved, avoiding concerns that the tissue that is examined is not representative of the entire site. In addition, ethical concerns regarding a second-look arthroscopic biopsy of an asymptomatic patient are avoided. However, although repair failures offer a much larger area of tissue for examination, it is unclear whether this tissue is representative of repair tissue in clinically functional grafts. In view of the small number of cases that had undergone microfracture or periosteal transplantation, comparisons among the various treatments should be made with caution.

We found that the histologic appearance of the failed microfracture repair tissue was similar to that of the failed ACI repairs. The patients with microfracture repair failures, however, presented a mean of 1 year earlier than did the ACI failures (Table 2). In addition, although the patients with ACI failures were asymptomatic during the period of time from initial repair to graft failure, the patients with microfracture failures had continued joint pain after their initial procedures.

The specimen from the failed periosteal transplant patient (patient No. 10) had the most unfavorable histologic appearance (Figure 3) in that it was highly vascular, contained areas of cartilage and bone necrosis, and had minimal tissue staining for either type I or type II cartilage. Unfortunately, because there was only 1 patient in this repair category in the present study, it is not possible to determine if this result is representative. In addition, the patient from whom this sample was taken had an underlying varus alignment, which may have been a contributing factor to the poor quality of the repair tissue in this case. Patient No. 7 (microfracture repair), however, also had a varus alignment, but the repair tissue from this patient was similar to that of the other 2 patients in this category who had normal anatomical alignment. To our knowledge, the histologic description of failed periosteal transplants in humans has not previously been reported.

Although the overall failure rate of the ACI procedure in our personal series, regardless of lesion type or anatomical location within the knee, was 15.8% (6/38), the ACI failure rate for patients with OCD lesions of the medial femoral condyle was 66.7% (6/9). The grafts from these individuals were composed of fibrous tissue/fibrocartilage and lacked evidence of incorporation with the surrounding tissue. These results suggest that the use of ACI procedures for the repair of OCD lesions of the medial femoral condyle may not be appropriate. Autologous chondrocyte implantation failure rates reported in other studies range from 5% to 14% and occur most commonly within 2 years of implantation.[13,15,17,18,23,24] At least 1 of these studies distinguished femoral condylar OCD patients from patients with other conditions, and this study reported the highest failure rate (14%).[23] Peterson et al[24] found an overall ACI failure rate of 7 of 101 (6.9%), with 2 failures in the 18 patients with OCD lesions, and reported that the grafts usually failed within 2 years of implantation. The mean time from primary procedure to symptom recurrence across all patients in the present study was 27.5 months, which is somewhat longer than is reported in other studies.[13,21,23]

One of the difficulties in comparing this study with others is the lack of consistency in methods and terminology in evaluating repair tissue biopsy specimens. Some reports refer to "hyaline-like" cartilage, but there does not appear to be a consistent definition of this phrase.[5,11,21,25,26] Because of the subjectivity involved in describing the histologic appearance of cartilage, we believe that immunohistochemistry procedures may be necessary to accurately assess this tissue. Special stains, such as trichrome (for fibrous tissue) and toluidine blue (for proteoglycans), also are useful, but the interpretation of these sections is at least somewhat subjective. We have found that positive immunostaining of cartilage for type II collagen is essential to verify the presence of hyaline cartilage. Positive immunostaining of cartilage for type I collagen verifies that

a fibrocartilage/fibrous tissue component is present. Measurement of positive areas of immunostaining for type I and type II collagen (relative to the total area of the section examined) in serial sections allows one to more accurately assess whether the tissue is predominantly fibrous or hyaline in a more objective manner than simply describing its histologic appearance. We also expected to see some areas of positive type X collagen immunostaining in the grafts, as has been described by others[21]; however, all tissue samples were negative, suggesting that these chondrocytes did not have a late hypertrophic/mineralizing phenotype.

In summary, these results demonstrate that the failed ACI, microfracture, and periosteal transplant repair tissues in this series were composed primarily of fibrous tissue/fibrocartilage and do not represent ideal articular cartilage repair tissue. Although the tissue in the present study was from failed articular cartilage repair procedures, the finding of variable cartilage repair in studies such as Knutsen et al[13] suggests that considerable improvements in cartilage repair procedures are warranted.

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