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Biological Reconstruction after Excision of Juxta-articular Osteosarcoma around the Knee: A New Classification System

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Abstract. *Background: A new classification system for juxta-articular osteosarcoma around the knee joint was developed to allow biological reconstructions using distraction osteogenesis or frozen autograft containing tumors treated with liquid nitrogen. Type I: Tumor has metaphyseal extension to a maximum of 2 cm from the epiphyseal cartilage plate. Type II: Tumor extends to at least half the circumference of the epiphyseal cartilage plate. Type III: Extension to the whole circumference of the epiphyseal cartilage plate. Type IV: Tumor extends to part of the epiphysis through any point of the epiphyseal cartilage plate 10 mm from the joint line. Type V: Tumor extends to half or less of the epiphysis. Type VI: Extension of the tumor to more than half of the epiphysis. Patients and Methods: Twenty patients with juxta-articular osteosarcoma around the knee joint were treated according to this classification system. The cohort comprised 12 males and 8 females with a mean age of 20 years. The tumors were located in the femur in 12 patients and in the tibia in 8 patients. Results: The tumors were Type II in 1 patient, Type III in 8 patients, Type IV in 2 patients, Type V in 3 patients and Type VI in 6 patients. Reconstruction after tumor excision was performed using distraction osteogenesis in 13 patients and using frozen autografts in 7 patients. The mean follow-up in the series was 54 months, ranging from 5 to 103 months. Conclusion: The classification system may act as a guide to appropriate decision-making in cases of juxta-articular osteosarcoma around the knee joint. Biological reconstruction, using distraction osteogenesis or frozen autografts, may yield good functional results without leading to an increase in the incidence of local recurrence.*

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A juxta-articular tumor around the knee joint usually represents a surgical challenge as no joint replacement can function identically to the intact knee (1, 2). The knee joint represents a special site for endoprosthetic replacement because of its subcutaneous nature and repair of the extensor mechanism to the prosthesis is often difficult (1). To keep the reconstruction biological, autoclaved allografts or autografts, or sometimes vascularized fibular grafts, are used. Joint instability and incongruity are major problems with osteoarticular allografts in children. Multi-directional joint instability persists despite ligamentous reconstruction, and these patients require permanent use of a supporting brace (3). The disadvantages of autoclaved bone are that it takes a long time to revascularize and incorporate into the bone, and the bone itself is brittle (1). Further, high rates of complications, such as infection, bone resorption and fracture, were reported after use of massive autoclaved allografts and autografts for limb salvage surgery (4). Previously, we reported excision of juxta-articular osteosarcomas while preserving the epiphysis, joint surface, ligaments and neurovascular structures under effective chemotherapy. Then, reconstruction of the bony defect was achieved with the patient's own living bone tissue regenerated by distraction osteogenesis. Thus, normal limb functions in cases of juxta-articular osteosarcoma can be restored by this technique, which should be considered the most conservative method of limb-saving surgery presently available for juxta-articular osteosarcoma around the knee joint in both pediatric and adult patients (5-9). However, some cases present late and thus, conservative surgery cannot be performed. To overcome problems of autoclaved autografts for reconstruction after tumor excision, we devised a method for treating autografts that utilizes the hypothermic effect of liquid nitrogen (10, 11). Further, we developed a new classification system to facilitate decision-making in cases of juxta-articular osteosarcoma around the knee joint. The aim of this classification is to provide a guide for the resection margins and the available methods of biological reconstruction of the bone defect.

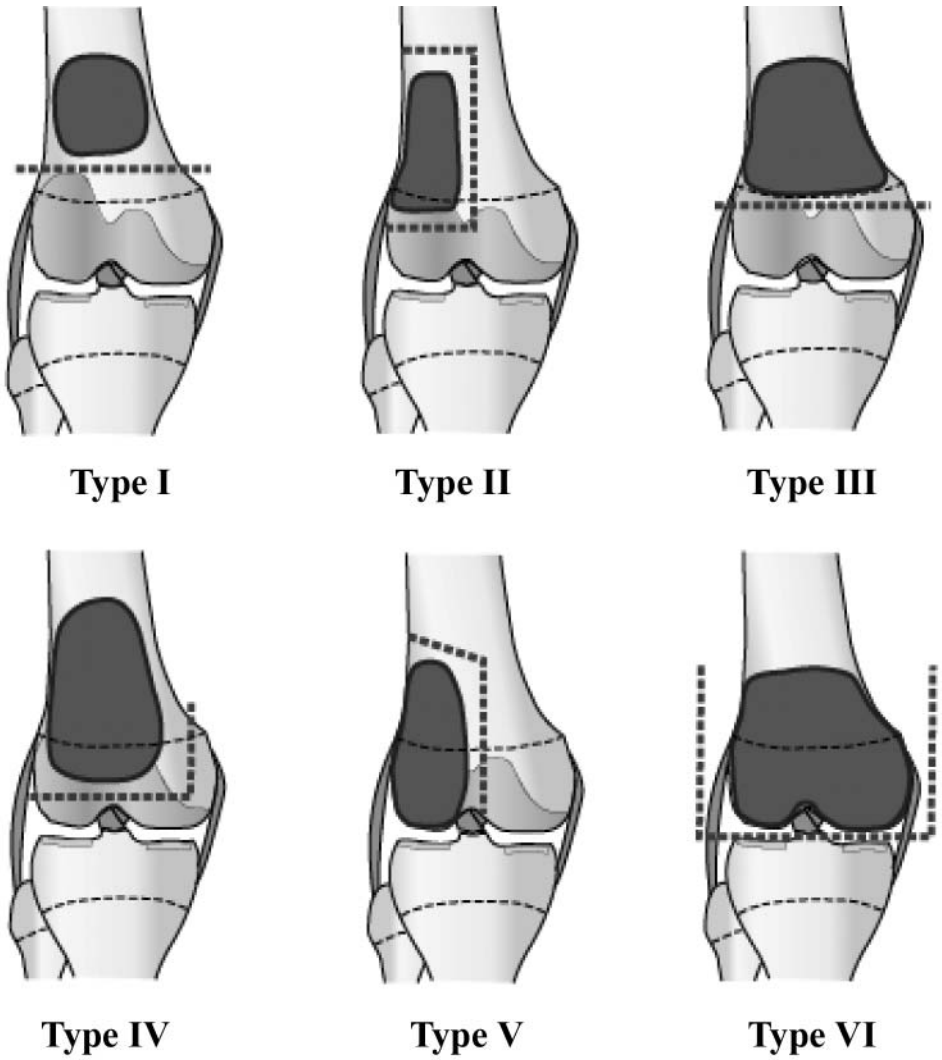

Figure 1. *Classification of osteosarcoma around the knee.*

Classification of juxta-articular osteosarcoma around the knee joint (Figure 1)

Type I: The tumor has metaphyseal extension to a maximum of 2 cm from the epiphyseal cartilage plate. These tumors can be excised and the bone defect reconstructed by Type 1 reconstruction (diaphyseal reconstruction) using distraction osteogenesis. Intercalary allografts, vascularized fibular grafts and frozen autografts are also options for reconstruction. However, when the tumor is osteolytic, frozen autografts cannot be used.

Type II: The tumor extends to at least half of the circumference of the epiphyseal cartilage plate. Excision of a maximum of half the epiphyseal cartilage plate is mandatory. There is a possibility of joint preservation and reconstruction of the bone defect by distraction osteogenesis. However, there is also a possibility of joint deformity due to unequal growth. Frozen autograft reconstruction is another option.

Type III: Extension to the whole circumference of the epiphyseal cartilage plate. In these patients, the epiphyseal cartilage plate is fully excised and bone reconstruction can be achieved through distraction osteogenesis. However, limb length discrepancies are anticipated in young patients, which may be managed surgically if necessary. Frozen autografts are also available when rigid fixation is feasible.

Type IV: The tumor extends to part of the epiphysis through any point of the epiphyseal cartilage plate 10 mm from the joint line. Joint preservation and bone reconstruction by distraction osteogenesis is still possible, but limb shortening is anticipated. Osteoarticular frozen autografts are an available option.

Table I. *Summary of data of juxta-articular osteosarcoma around the knee joint treated according to our classification system.*

Patient	Age/Sex	Grade	Bone	Classification	Technique	Time to healing (months)	End result (months)
1	13/F	High	Femur	III	SD	15	CDF 103 months
2	43/F	High	Tibia	IV	BT	11	CDF 94 months
3	22/M	High	Femur	V	SD with IMN	9	CDF 90 months
4	20/M	Low	Tibia	III	SD	5	CDF 81 months
5	34/F	Low	Femur	III	SD with IMN	4	CDF 78 months
6	15/M	High	Tibia	III	BT	12	CDF 77 months
7	13/F	High	Femur	VI	FA	11	NED 75 months
8	9/F	High	Femur	III	SD with IMN	3	CDF 70 months
9	14/M	High	Tibia	V	FA	9	NED 63 months
10	16/M	High	Tibia	III	BT	9	DUD 49 months
11	26/F	Low	Femur	II	BT	7	CDF 55 months
12	38/M	High	Femur	VI	FA	5	CDF 54 months
13	13/F	High	Tibia	III	BT	6	CDF 43 months
14	9/M	High	Femur	III	BT	12	CDF 37 months
15	22/M	High	Femur	VI	FA	2	CDF 36 months
16	19/M	High	Femur	VI	FA	7	CDF 31 months
17	17/M	High	Tibia	V	BT	10	DOD 14 months
18	15/M	High	Tibia	VI	FA	2	CDF 28 months
19	38/M	High	Femur	IV	BT with IMN	6	DOD 13 months
20	17/M	High	Femur	VI	FA	non-union	DOD 5 months

M= Male; F=Female; SD=shortening-distraction; BT=bone transport; FA=frozen autograft; IMN=intramedullary nailing; CDF=continuously disease-free; NED=no evidence of disease; DUD=dead of unrelated disease; DOD=dead of disease.

Type V: The tumor extends to half or less of the epiphysis. There is no possibility of preservation of the whole joint. After resection of the hemicondyle, options for reconstruction include frozen autografts or utilization of the patellar articular cartilage with or without bone. Osteoarticular frozen autografts are another option.

Type VI: Extension of the tumor to more than half of the epiphysis. For these patients, the options available for reconstruction include arthrodesis (using distraction osteogenesis or vascularized fibular grafts), osteoarticular allografts, or frozen autografts (if the tumor is osteoblastic). In addition, a combination of frozen grafts and surface arthroplasty is available.

Patients and Methods

Twenty patients with juxta-articular osteosarcoma around the knee joint were treated according to this classification system. The cohort comprised 12 males and 8 females with a mean age of 20 (range; 9-43) years. The tumors were located in the femur in 12 patients and in the tibia in 8 patients (Table I). Intra-arterial cisplatin and caffeine with doxorubicin were administered 3 to 5 times preoperatively. After a good response was observed in at least 2 out of 4 radiological examinations, *i.e.*, plain radiography, angiogram, magnetic resonance (MR) imaging and Thallium-201 scanning, limb salvage surgery was conducted by the intentional marginal procedure. Evidence of good chemotherapeutic response consisted of sclerotic changes or good margination of the tumor observed on plain radiographs, marked shrinkage of tumors extending into soft tissue on MR images, disappearance of tumor stains on angiograms, or the disappearance of abnormal accumulation on Thallium-201 scintigrams. Wide excision was indicated when a poor clinical response to chemotherapy was detected on radiographic evaluation. The operative technique consisted of *en bloc* tumor excision with preservation of the epiphysis, articular surface and the maximum amounts of healthy tissues for responders. For reconstruction using distraction osteogenesis, an external fixator was applied. Intramedullary nailing, if feasible, was also used to shorten the external fixation time. Bone regeneration was accomplished by either bone transport or shortening-distraction that set 1 to 2 weeks after the operation. Gradual distraction was applied at a speed of 1 mm/day (5-9). The histological response to preoperative chemotherapy was evaluated in the resected tumors with the grading system of Rosen *et al.* (6).

For reconstruction using frozen autografts, the excised bone was treated with liquid nitrogen in a cycle of 45 min: immersion in liquid nitrogen for 20 min, leaving the bone in room temperature air for 15 min, followed by immersion of the bone in distilled water for 10 min. Then, the bone was re-implanted and fixed with internal fixation (10, 11).

Postoperative chemotherapy was performed on a neoadjuvant basis. Two chemotherapy protocols were used: the K1 and K2 protocols (12). The function of the affected limb was evaluated using the evaluation system of Enneking *et al.* (13).

Figure 2. *A case treated with distraction osteogenesis. In a 15-year-old boy (case 6) with a Type III osteosarcoma in the proximal tibia. a: MRI (T1-weighted image)), the epiphysis and medial cortical bone were preserved by intentional marginal procedure; b): then, a bone cylinder was taken from the diaphysis and the subarticular structure was reconstructed immediately (c); the newly created diaphyseal defect was reconstructed by bone transport (d); a radiograph 2 years after surgery shows excellent bone formation (e); and 8 years after surgery excellent remodeling of the tibia (f).*

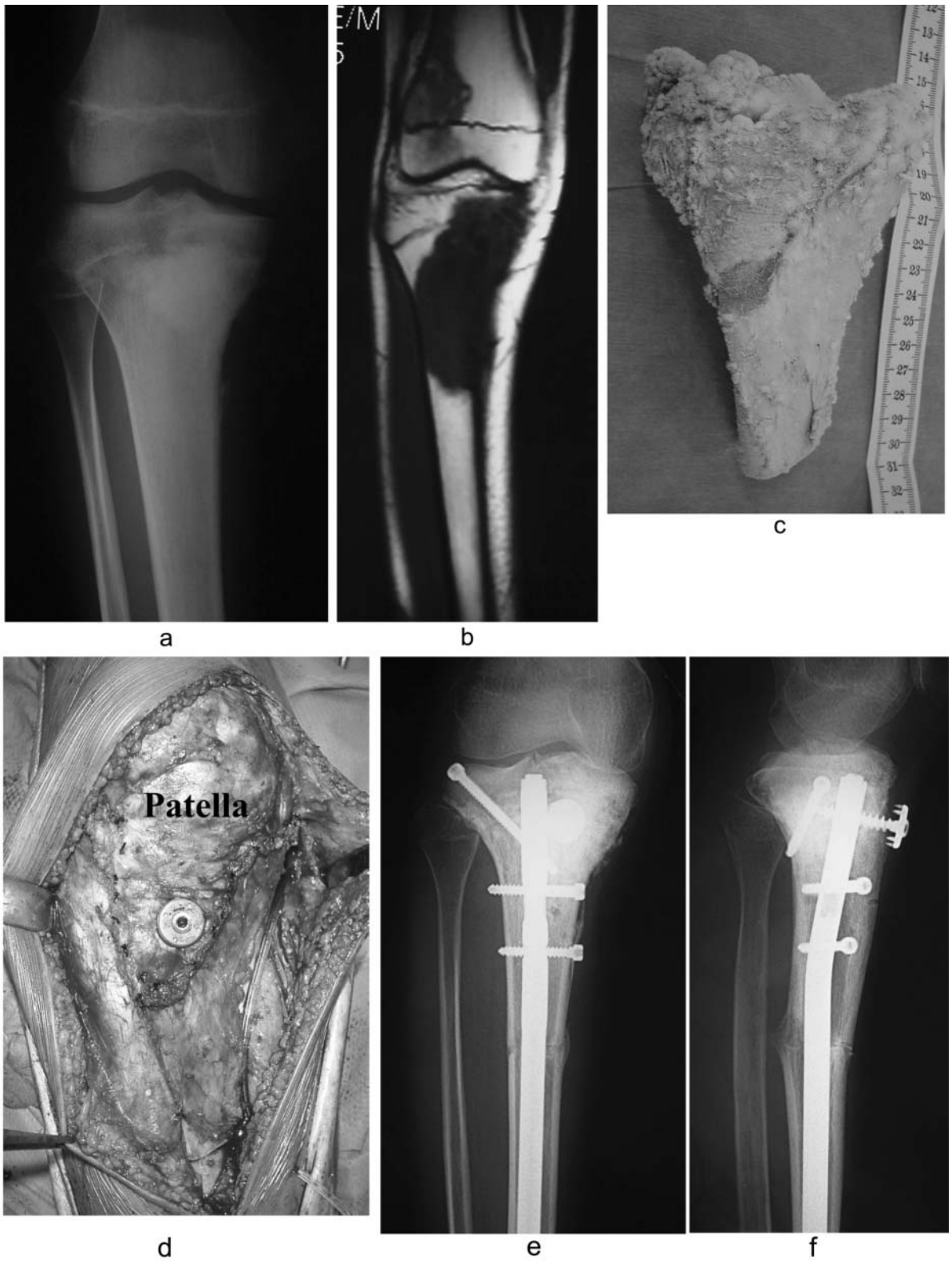

Figure 3. *A case treated with frozen autograft. A 14-year-old boy (case 9) with a. Type V osteosarcoma in the proximal tibia. a: a plain radiograph; b: MRI (T1-weighted image)) was treated by intentional marginal procedure and reconstruction with frozen autograft; c: resected specimen treated with liquid nitrogen for 20 minutes. The patella tendon was reattached to the frozen autograft with a spike washer (d) and intramedullary nail fixation was carried out. The junction between the frozen autograft and host bone was united completely on the radiograph 2 years after surgery (e.f.).*

Results

The tumors examined in the present study were Type II in 1 patient, Type III in 8 patients, Type IV in 2 patients, Type V in 3 patients and Type VI in 6 patients. Reconstruction after tumor excision was performed by distraction osteogenesis (Figure 2) in 13 patients and frozen autografts in 7 patients. The mean follow-up in the whole series was 54 months, ranging from 5 to 103 months.

Reconstruction was performed by distraction osteogenesis in 13 patients – 7 males and 6 females, ranging in age from 9 to 43 years (mean, 21.2 years). The tumor sites were the distal femur in 7 patients and proximal tibia in 6 patients. Tumors were Type II in 1 patient, Type III in 8 patients, Type IV in 2 patients and Type V in 2 patients. Histopathological examination of the tumor tissues after biopsy rated the tumors as high-grade in 10 patients and low-grade in 3 patients. Preoperative chemotherapy had not been used for the low-grade tumors and was performed for 10 cases with high-grade tumors using the K2 chemotherapy protocol, consisting of 5 courses of intraarterial cisplatin, caffeine and doxorubicin at 3-week intervals.

An Ilizarov ring fixator was applied in 11 patients and an Orthofix unilateral fixator was applied in 2 patients. In addition, intramedullary nails were used in 4 patients. Bone transport was used in 8 patients and shortening-distraction was used in 5 patients. Reconstruction was Type 2 (metaphyseal reconstruction) in 9 patients, Type 3 (epiphyseal reconstruction) in 2 patients and Type 4 (subarticular reconstruction) in 2 patients. The external fixation time was 302±121.7 days. The post-operative limb function was rated as excellent in 10 patients, good in 1 and fair in 2. Nine complications were encountered in 7 patients, namely delayed healing (2), superficial infection (1), deep infection (1), fracture after frame removal (1), common peroneal nerve injury (1) and equines deformity (1). No local recurrence had been encountered by the end of follow-up. At the end of follow-up, 2 patients had died due to their disease after 13 and 14 months, 1 patient died due to hepatitis 49 months after the operation, while 10 patients are still alive after a mean of 73 months ranging from 37 to 103 months. The mean follow-up of the series was 62 months, ranging from 5 to 103 months.

Reconstruction was performed using frozen autografts (Figure 3) in 7 patients, 5 males and 2 females with a mean age of 18 years (range, 13-38 years). The tumors were located in the distal femur in 5 patients and in the proximal tibia in 2 patients. According to our classification system, the tumors were Type V in 1 patient and Type VI in 6 patients. Bone healing was achieved in all but 1 case after a mean of 6 months (range, 2-11 months). At the end of follow-up, 1 patient had died due to the original disease after 5 months, while 6 patients are still alive after a mean of 41 months, ranging from 5 to 75 months. No evidence of local recurrence was noted in any of the 7 patients (Table I).

Discussion

Efficient chemotherapy has made long survival possible after excision of osteosarcoma and has helped to minimize the surgical margins. After effective preoperative chemotherapy, osteosarcoma can be excised with the preservation of a maximum of healthy tissue, such as ligaments and tendons. We introduced caffeine-potentiated chemotherapy, which is highly effective due to its inhibitory effects against DNA repair. The marginal excisions associated with caffeine-potentiated chemotherapy do not lead to an increased incidence of local recurrence (5, 7-9, 12).

There are several methods for biological reconstruction after excision of peri-articular osteosarcomas around the knee joint, including distraction osteogenesis, intercalary allograft, vascularized fibular graft, frozen autograft, or osteoarticular allograft. We classified juxta-articular osteosarcoma around the knee with reference to the epiphyseal cartilage plate and articular cartilage into 6 types. This classification served as a guide for the resection margins and the available methods of biological reconstruction of the bone defect. The results showed that this classification can be successfully used as a guide for appropriate decision-making in all cases. In our classification, our choices were kept as biological as possible. Thus, prosthetic replacement was excluded from the available options. A previous study indicated that prosthetic survival rates for large segment replacements for high-grade bone sarcoma were 83% at 5 years and 67% at 10 years (14). Reconstruction by distraction osteogenesis has clear advantages over other biological reconstruction techniques. Normal limb functions are restored. Once the reconstruction has taken place, it can be expected to remain permanent. Moreover, the growing part of the bone can be preserved, ensuring normal limb growth in some cases. Even if shortening does occur, simple lengthening can solve the problem. The prerequisites for using this technique are as follows: tumors of Type I-IV according to our classification system, not more than 15 cm in length, and low- or high-grade tumors which respond well to chemotherapy. The prognosis should generally be good and lung metastases should be considered as a relative contraindication for using this technique. If these prerequisites cannot be fulfilled, we usually prefer reconstruction using frozen autografts, as this method has advantages over the other options available, such as osteoarticular allografts, intercalary allografts, or vascularized fibular grafts. However, prosthetic replacement may be used if the prognosis is poor as in cases with lung metastases.

Frozen autografts contain autogenous protein, growth factors and cytokines, and do not elicit an immune reaction. Therefore, frozen autografts may possess advantages of early bone union and a low risk of bone resorption. However, frozen autografts may have some complications similar to allografts, such as infection, fracture, nonunion, graft failure or, occasionally, local recurrence (11). Of 28 tumors treated using the frozen autograft technique at Kanazawa University Hospital, Japan, we experienced local recurrence in 2 cases that occurred in the soft-tissue and probably represented satellite lesions. Cartilage frozen with liquid nitrogen may cause osteoarthritic changes over time, and surface total knee replacement may be necessary in the future. Nevertheless, as bioengineering evolves, it may become possible to restore or repair cartilage in the near future.

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