culture (Fig. 3). In addition, we also demonstrated that the pellet of MSC-magnetic bead complexes could differentiate along the chondrogenic lineage even in a three-dimensional culture system against gravity and under the influence of an external magnetic force (Figs. 4 and 5).

Recently, we investigated the efficacy of a magnetic drug delivery system (DDS). We demonstrated successfully that the combined treatment of a topical injection of magnetic liposomes containing magnetite (Fe_3O_4; mean diameter: 10 nm) and cytokines, such as recombinant human bone morphogenetic protein-2 (rhBMP-2) and TGF-β1, together with a magnet implanted at the target defect site is effective for bone formation in a segmental bone defect rat model and for promotion of chondrogenesis in the osteochondral defect rat model.[18,19] These studies led to the use of an external magnetic force, which is less invasive and more useful than the surgical implantation of a magnet. We modified this magnetic DDS and demonstrated that this magnetic stem cell delivery system could direct MSC-magnetic bead complexes to the desired location. We had previously performed a pilot study demonstrating the clinical application of this system, in which a cartilage defect in the bilateral femoral condyle of a rabbit was placed between two magnetic poles after an intra-articular injection of MSC-magnetic bead complexes.[1] In this model, the accumulation of the MSC-magnetic bead complexes in the defects after 60 min was markedly higher in the group exposed to an external magnetic force than the group that was not exposed to a magnetic force.[1] In contrast, in another *in vitro* experimental model, we had found that the chondrogenic potential of the complexes was slightly reduced compared to that of normal rat MSCs.[6] On the basis of these previous results, we tried to control the concentration of TGF-β at the local site under an external magnetic force by using TGF-β-immobilized magnetic beads to form a denser cartilage matrix. Consequently, we found that as long as the CDM was supplemented with 10 μL/mL TGF-β-immobilized magnetic beads (TGF-β concentration: 1 ng/mL) and these TGF-β-immobilized magnetic beads were localized under an external magnetic force, the MSC-magnetic bead complexes could differentiate along the chondrogenic lineage even in three-dimensional culture systems in CDM lacking TGF-β.

In this study, Ferri Sphere 100C® magnetic beads were used. As this model has potential for clinical application, but several investigators have shown that micro-sized magnetic beads are phagocytosed by some cells such as active dendritic cells[20] or CD8-positive lymphocytes,[21] we speculated that mediator-immobilized magnetic beads may be taken up by cells such as macrophages once released from the cell surface[6] or from an external magnetic force.

The mechanism underlying the action of the TGF-β-immobilized magnetic beads remains unknown. The TGF-β superfamily contains multifunctional growth factors that are responsible for many cellular processes such as differentiation, proliferation, and apoptosis.[22,23] However, the effects of TGF-β during chondrogenesis are still unclear. Chondrocyte differentiation is regulated by the conflicting effects of TGF-β. TGF-β promotes the differentiation of embryonic chick limb cartilage.[24] MSC-derived primary chondrogenesis needs TGF-β signals.[7] TGF-β activates the TGF-β type I receptor by forming a ligand-receptor complex with the type II receptor. Several TGF-β responsive pathways, such as the Smad2/3 and mitogen-activated protein kinase (MAPK) pathways, have been identified as key signaling processes and are regulated by the activation of the TGF-β receptor.[25–27] We speculate that the TGF-β-immobilized magnetic beads linked to the MSCs might stimulate the Smad2/3 signaling pathway and therefore produce Smad 2 and Smad 3, which are phosphorylated and translocated into nuclei along with nonlabeled TGF-β.[28] Studies that focus on the function of TGF-β-regulated Smads (Smad2/3) during chondrogenesis from MSCs are required to further investigate the mechanism underlying the action of the TGF-β-immobilized magnetic beads.

In conclusion, we have demonstrated that our novel TGF-β-immobilized magnetic beads could lower the concentration of TGF-β necessary for chondrogenesis of MSC-magnetic bead complexes. Our cell and growth factor delivery systems, which can be influenced by an external magnetic force *in vitro*, has the potential to support minimally invasive cartilage repair such as intra-articular cell transplantation without scaffolds. Our results suggest that the use of TGF-β-immobilized magnetic beads under an external magnetic field can enhance chondrogenesis of MSC and decrease the incidence of side effects caused by injection of TGF-β directly into the joint. However, further studies will be necessary to evaluate the effectiveness of our new stem cell and growth factor delivery system for cartilage repair *in vivo*.

A part of this study won the Best Poster Presentation at the 20th Annual Research Meeting of the Japanese Orthopedic Association, October 20-21, 2005.

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TRAUMA SURGERY

Repair of a large osteochondral defect in the knee joint using autologous and artificial bone graft combined with motion preserving distraction arthroplasty: a case report

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Abstract The biological reconstruction of a large osteochondral defect in the weight-bearing area of the knee joint has long been a challenge to orthopedic surgeons. We present a case of a large posttraumatic defect in the weight-bearing area of knee joint treated with a novel distraction arthroplasty device after reconstruction of the joint surface using combined autologous and artificial bone graft.

Keywords Large osteochondral defect repair · Knee · Distraction arthroplasty

Introduction

Large osteochondral defects are associated with mechanical instability and are accepted indications for surgical intervention to prevent development of degenerative joint disease.

Ideally, a large osteochondral defect should be repaired with a graft that can provide mechanical stability and allow early postoperative function under physiologic loading conditions [1].

Osteochondral defects in the weight-bearing area are difficult to treat effectively using biological methods [2, 3].

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The fragile repair tissue induced from the bone marrow is thought to be damaged by overloading. Furthermore, it is well known that joint motion promotes repair of osteochondral defects in the joint [5, 6]. Therefore, to minimize damage to the repaired tissue, long-term unloading with continuous passive motion was applied [1].

Distraction arthroplasty is a technique that has been used mostly at the elbow, hip, and ankle joints to preserve joint space and decrease the weight-bearing load. It delays the need for arthrodesis or joint replacement surgery [7–10].

The senior author [11] developed a new articulated arthroplasty device for the knee joint (Meira, Nagoya, Japan). In addition to the merits of previous devices, which include preservation of the joint surface and protection against overload on the regenerating fibrocartilage during weight bearing, this new articulated device permits smooth exercising of the joint during fixation [11].

We hypothesize that articulated joint distraction may be a useful treatment for osteochondral defects in the weight-bearing area. So we present a case of large osteochondral defect in the knee joint treated with a novel distraction arthroplasty (DA) device after reconstruction of the joint surface using combined autologous and artificial bone graft.

Case report

An 18-year-old female patient presented to us with her chief complaints: right knee pain with a limited range of motion, instability and deformity of the knee especially on weight bearing.

In March 2003, she was injured by traffic accident and resulting an open fracture of the right knee joint. Her plain X-rays revealed also a remarkable bone defect in the right

medial tibial condyle due to a markedly depressed fracture of the right medial tibial plateau (Schatzker classification type IV B, AO/ASIF type B2 pure depression) with a corresponding bony defect of the right medial femoral condyle due to an impacted compression fracture. Initial MRI demonstrated only medial meniscus tear and medial collateral ligament (MCL) injury. There were no associated neurovascular injuries. At this time, debridement and open reduction of the dislocation fracture, and bracing were carried out.

In mid-October, she was referred to our hospital for the purpose of the treatment of the large bone defect in the right knee joint as revealed in plain X-ray (Fig. 1a, b) as well as CT (Fig. 2).

On presentation; the wound on the anteromedial aspect of the knee was completely healed with no evidence of infection. There was limited range of motion of the affected knee from 0 to 50. Marked varus malalignment of the right lower limb could be attributable to the marked bony defect on the medial side of the knee, meanwhile there was no clinical, or MRI evidence of lateral collateral ligament (LCL), anterior cruciate ligament (ACL) or posterior cruciate ligament (PCL) injuries.

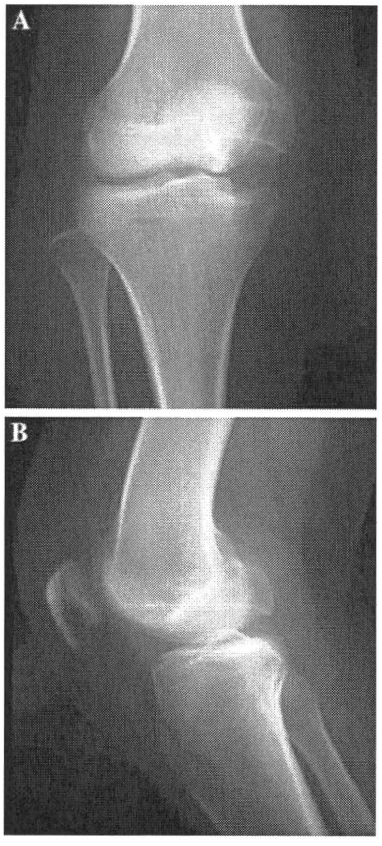

Fig. 1 Preoperative plain X-ray **a** AP view, **b** lateral view; revealing bony defect of the right medial femoral and tibial condyles

Surgical procedure

On exploration there was a large bony defect of the right medial tibial and femoral condyles, and irreparable complex injury of the medial meniscus.

The first step

The first step was reconstruction of the original shape of the medial femoral condyle using a combination of autologous iliac crest bone graft fixed by Herbert screws and artificial bone grafts shaped to the configuration of the remaining defect and consisting of hydroxyapatite ceramic with an interconnected porous structure (IP-CHA) (NEOBONE_, Toshiba Ceramics Co., Tokyo, Japan). Mesenchymal stem Cells and growth factors can readily penetrate the IP-CHA center to provide good osteoconduction in the early phase of the graft healing. This artificial bone was fixed by absorbable pins [poly-L-lactide (PLLA) pins of diameter 2 mm (Neofix; Gunze, Kyoto, Japan)] [12].

Lastly, reconstruction of medial tibial plateau using the reformed bone retrieved from a free bone fragment, supplemented by iliac crest cortico-cancellous bone graft fixed with cancellous screws (Figs. 3, 4).

The second objective

The second objective was stimulating bone adhesion and cartilage regeneration by preserving the joint space and reducing the load, meanwhile preserving the joint motion and function. This could be accomplished through external fixation using a novel articulated distraction arthroplasty (DA) device that decreases the load to bone grafted area, meanwhile allowing early start of joint motion to get the advantage of the stimulating effect of continuous passive motion on cartilage regeneration (Fig. 5a, b).

Partial medial meniscectomy was performed due to the associated irreparable complex damage, while the associated MCL injury was managed conservatively.

Postoperatively continuous passive motion exercise commenced the day after surgery and was continued for approximately 2 weeks, partial weight bearing was encouraged 6 weeks after surgery, This articulated distraction devise was removed 3 months postoperative, full weight bearing was then encouraged. During the period of external fixation, the patient was encouraged to do range of motion (ROM) exercises at first passively by physiotherapist and then active ROM exercises as tolerated by the patient. The screws were removed 6 months postoperatively. Follow-up of the patient later on demonstrated satisfactory arthroscopic (Fig. 6a, b), as well as radiological results taken as late as 4.5 years postoperatively (Figs. 7, 8, 9).

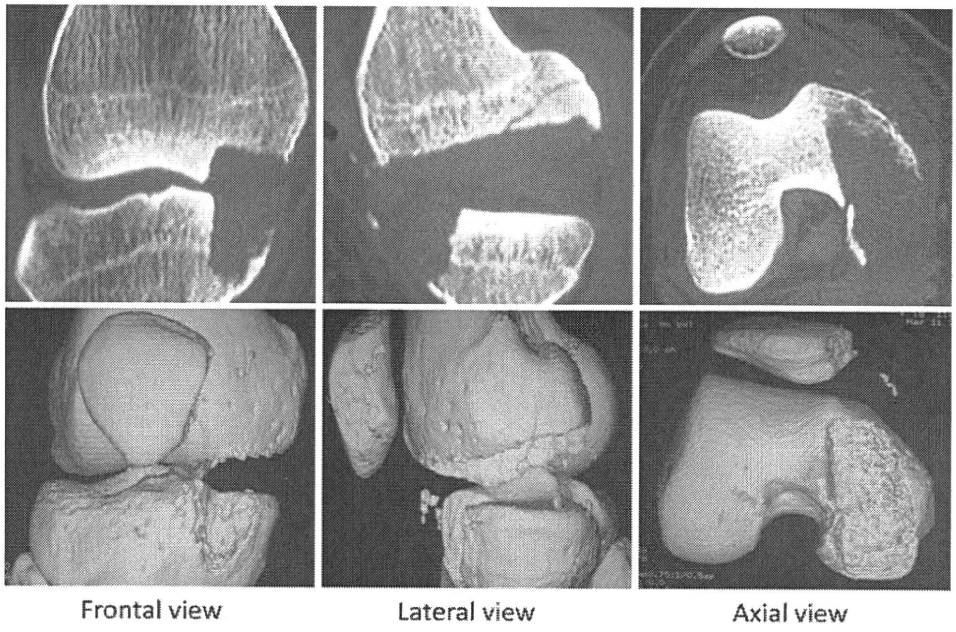

Fig. 2 Preoperative CT with three dimensional reconstruction showing a large osteochondral defect of the right medial femoral and tibial condyles

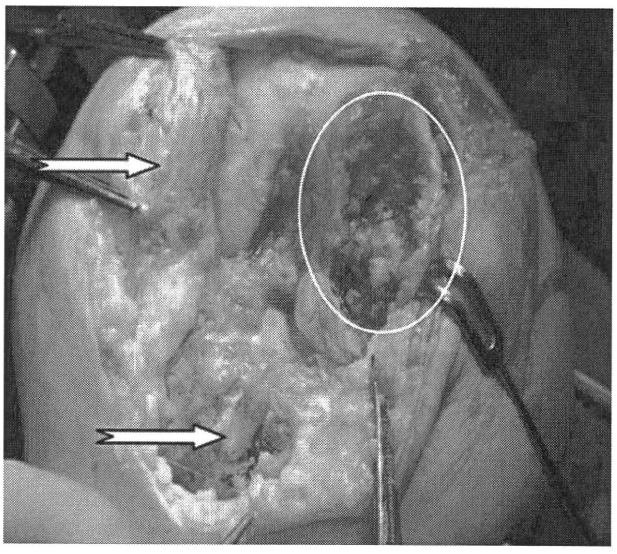

Fig. 3 Shows the bone defect in the medial femoral condyle (within the *white circle*), bone defect of the right medial tibial plateau (*white arrow*), patella (*yellow arrow*)

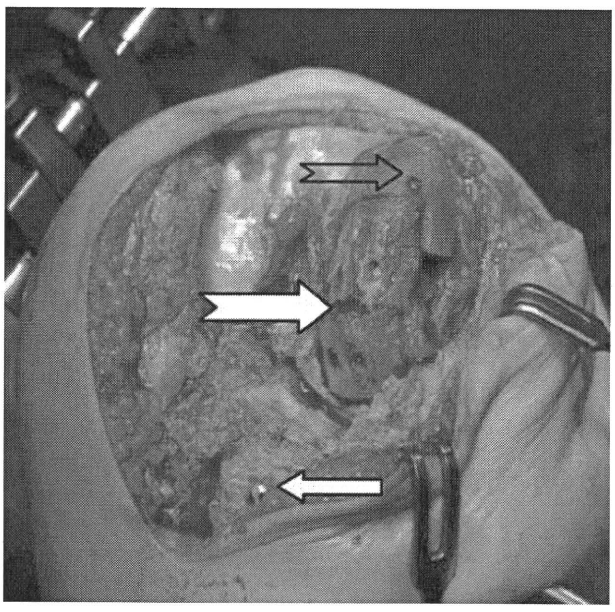

Fig. 4 Artificial bone (NEO BONE) graft fixed by absorbable pins (*transparent arrow*). Autologous iliac bone graft fixed by Herbert screw (*white arrow*). Reconstruction of the tibial condyle by the reformed bone from free bone fragment fixed by cancellous screw (*yellow arrow*)

The patient was completely satisfied having a painless stable knee joint with a pain-free range of motion of 0–150° (Fig. 10).

Discussion

The biological reconstruction of a large osteochondral defect in the weight-bearing area of the knee joint has been a challenge to orthopedic surgeons. This comprises reconstruction of the bony portion and restoration of the original shape of the reconstructed condyles, and the restoration of the hyaline articular cartilage to preserve the joint function and prevent or halt the likely progression towards osteoarthritis. The fragile repair tissue induced from the bone marrow is thought to be damaged by overloading; moreover, a defect of the cartilage in the weight-bearing area eventually progresses to osteoarthritis by causing friction and overload to the opposing articular surface. [13–16].

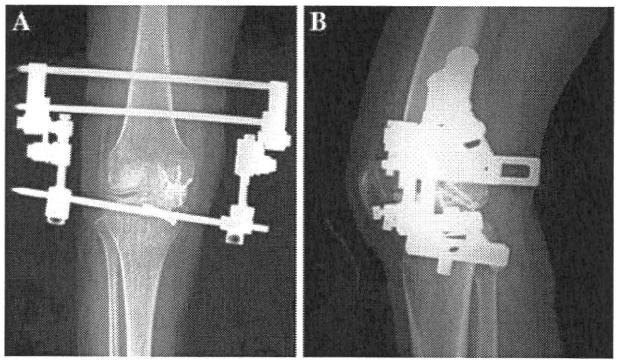

Fig. 5 Postoperative plain X-ray **a** frontal, and **b** lateral views

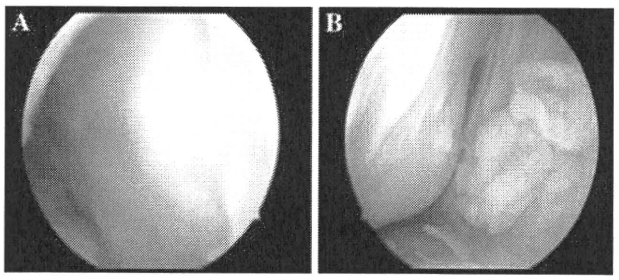

Fig. 6 **a**, **b** Postoperative arthroscopic findings showing resurfacing of the reconstructed bony surface. **a** Represents the reconstructed central weight bearing area of the medial femoral condyle (MFC), while **b** represents the adjacent area of the MFC, as well as the medial gutter as illustrated in MRI Fig. 7

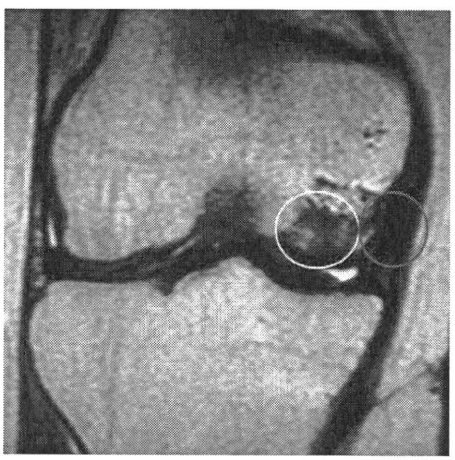

Fig. 7 Two and a half years postoperative coronal MRI showing the reconstructed bony defects, the cartilage layer showing mild residual irregularities [the *yellow circle* represents the arthroscopic view (**a**), while the *red circle* represents the arthroscopic view (**b**)]

The effective role of distraction arthroplasty in cartilage repair was demonstrated in a lot of studies; whereby joint distraction widens the joint space and decreases of the load to regenerated fibrocartilage. [11, 14, 17–19]

It is also well known that joint motion promotes repair of osteochondral defects in the joint [20–22]. Moreover, Kajiwara et al. [4] demonstrated that articulated joint

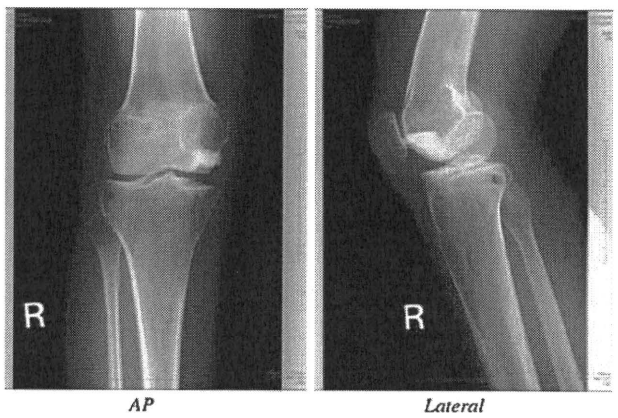

Fig. 8 Shows the latest follow-up X-rays taken about 4.5 years postoperative

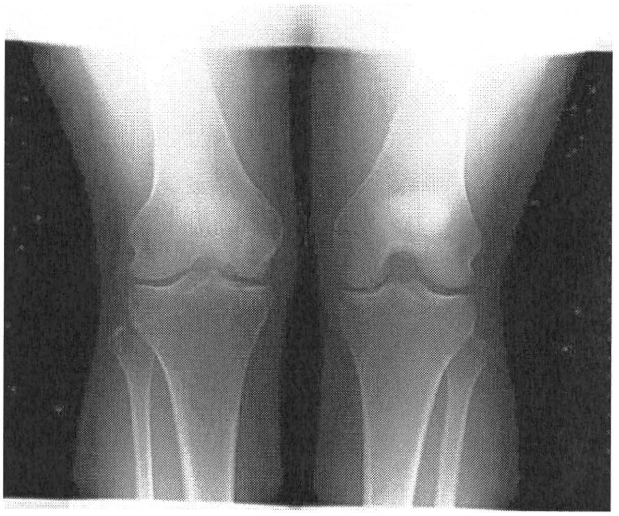

Fig. 9 AP weight-bearing X-ray of both knees taken in the latest follow-up about 4.5 years postoperative showing reconstruction of the bony defects with preservation of the joint space

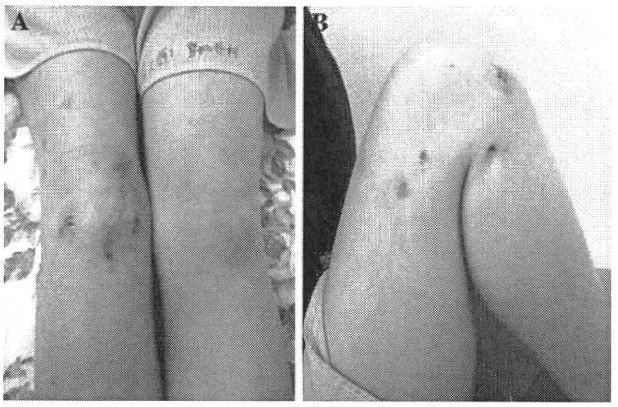

Fig. 10 Shows the postoperative range of movement from 0° (**a**) to 140° flexion (**b**)

distraction added to subchondral drilling is effective for repairing an osteochondral defect in contrast to drilling alone in an animal model. In addition, they determined that distraction for 4 weeks was not of sufficient duration for repair of the defect whereas distraction for 8–12 weeks resulted in a good outcome. They also hypothesized that differentiation of mesenchymal progenitor cells from the bone marrow may be promoted by appropriate shearing and compression stresses acting through the joint fluid exerted by joint motion and loading without excessive compression.

Valburg et al. [18] also in a study of OA of the canine knee joint found that joint distraction with motion via an external fixator resulted in a significant improvement in cartilage metabolism.

Therefore, to minimize damage to the repaired tissue, long-term unloading and joint motion with continuous passive motion was applied in this case with a large osteochondral defect in the weight-bearing area of the knee after reconstruction of the bony defect using a combination of autograft and artificial bone.

Articulated joint distraction affords widening of the joint space and reduction of pressure on the regenerating fibrocartilage during weight bearing. Meanwhile allowing functional joint movement, which is one of the most important factors contributing to repair in hyaline-like cartilage [11].

A new articulated distraction devise was used in a previous clinical study by Deie et al. [11]. This new articulated distraction arthroplasty device was developed for the human knee joint and allowed the joint to be smoothly exercised through the functional range of motion during fixation. In accordance with the fact that knee motion is one of the most important factors contributing to repair in hyaline-like cartilage [11].

This device allowed widening of the joint spaces and the continuation of ROM exercises, at the same time, reduction of pressure on the regenerating fibrocartilage during weight bearing, This devise was specially designed not to damage intra-articular structures such as the anterior cruciate ligament, posterior cruciate ligament, and cartilage, with no pin being inserted at the femoral center of knee motion In contrast, in the animal model used by Kajiwara et al. [4], a Kirschner wire was inserted at the femoral center of knee motion to allow full range of motion with articular distraction [4, 11].

An alternative method of treatment of large osteochondral defects is the use of tissue-engineered osteochondral composites. Ochi et al. [24, 25] introduced a new concept for the transplantation of tissue-engineered cartilage, which was made ex vivo by the tissue-engineering technique for the treatment of osteochondral defects of the knee, and demonstrated successful results [23–29].

However, the use of tissue-engineered osteochondral composites require extensive lab work, and has not yet been applied in clinical practice for reconstruction of a large osteochondral defect in the weight-bearing area of human joints. Mosaicplasty, autologous osteochondral grafting, can be used for biological resurfacing of focal osteochondral defects; however, in this technique, the limited amount of autologous tissue and donor site morbidity, as well as the congruency of the reconstructed articular surface are major problems, Tissue-engineered osteochondral composites theoretically have the potential to overcome the limitations associated with autologous osteochondral mosaicplasty [30, 31].

The use of articulated distraction arthroplasty device in this case stimulated biological resurfacing of the reconstructed bony defect with hyaline-like cartilage. This approach constitutes a feasible, easily applied method for the repair of the large osteochondral defect allowing resumption of a functional knee joint. However, the long-term durability, and the biomechanical sufficiency of the reconstructed articular surface is not guaranteed to stand the test of time, and the patient may in the future require arthroplasty.

Conclusion

We experienced a case of large posttraumatic osteochondral defect of the knee joint treated with a novel distraction arthroplasty (DA) device combined with reconstruction of the bony defect using both autologous and artificial bone graft substitute resulting in satisfactory short- and mid-term result, with a painless, stable knee joint with a good functional range of motion.

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Knee Articulated Distraction Arthroplasty for the Middle-aged Osteoarthritic Knee Joint

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Objective: We developed a knee distraction arthroplasty device that allows continuous joint movement. The objective of this article is to show the surgical procedure of knee distraction arthroplasty with a bone marrow-stimulating technique, for treatment of osteoarthritis of the knee and to evaluate the clinical results.

Methods: As we showed in Arthroscopy in 2007, we performed this distraction arthroplasty to 6 knees (in 6 patients, aged 42 to 63 y). Then we compared preoperative findings with postoperative ones. The fixation period for the distraction device ranged from 7 to 12 weeks and the follow-up period ranged from 24 months to 53 months (average 36 mo).

Results: The Japan Orthopaedic Association knee score, range of motion, and the values of the joint spaces were significantly improved in all cases at the latest follow-up ($P<0.05$). Visual analog pain scales were also significantly improved ($P<0.05$).

Conclusions: We conclude that treatment using this arthroplasty device in combination with a bone marrow stimulating method is effective for osteoarthritic knees in middle-aged patients.

Key Words: middle-aged osteoarthritic knee, distraction arthroplasty, articulated distraction device

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Osteoarthritis (OA) of the knee joint is a very prevalent degenerative joint disorder.[1,2] Recent strategies for relatively wide cartilage damage, high tibial osteotomy, or unicomponent knee arthroplasty have been the usual treatments for significantcartilage damage that is limited to one compartment of the knee joint. For older patients, when the osteoarthritic defect has spread over more than 1 compartment of the knee, thus becoming severe, total knee arthroplasty is the appropriate treatment.[3] However, in middle-aged patients, the indications for total knee arthroplasty and unicompartment arthroplasty need to be carefully considered, because of the risk of infection and the limited life span of implants. For this reason, bone marrow-stimulating techniques, which involve drilling and microfracture of the lesions, have become widely accepted for knees with diffuse OA.[4,5] However, there has been some controversy about the clinical outcomes of these procedures.[6–9] The fragile repair tissue induced from the bone marrow may be vulnerable to damage by overloading, whereas reduction of overloading promotes cartilage regeneration. These ideas are supported by findings that new cartilage tissue is formed in the medial tibiofemoral joint after high tibial osteotomy, where overload to the medial condyle has been reduced.[10,11]

Distraction arthroplasty is a technique that has been used mostly at the elbow, hip, and ankle joints to preserve joint space and decrease the weight-bearing load. It delays the need for arthrodesis or joint replacement surgery.[12–14] Ideally, allowance should be made for continuous joint movement, because movement is essential for cartilage repair.[15,16] For this reason, Ochi, who was senior author, developed an articulated arthroplasty device for the knee joint (MEIRA Co, Nagoya, Japan). In addition to the merits of previous devices, which include preservation of the joint surface and protection against overload of the regenerating fibrocartilage during weight bearing, this articulated device permits smooth exercising of the joint during fixation. Before this clinical study, success of a similar device for treating cartilage damage in an animal model was published.[17] Furthermore, we produced a preliminary report of the clinical results of this knee device in 2007.[18] In this report, we show our detailed surgical procedure involved in distraction arthroplasty.

DISTRACTION ARTHROPLASTY

Preparation Before Surgery

All patients were hospitalized. The distraction arthroplasty was performed under lumbar anesthesia or general anesthesia. Before surgery, the patients' physical findings were

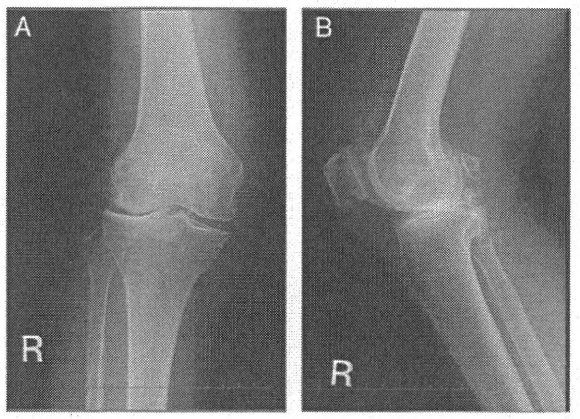

FIGURE 1. A 59-year-old female: (A) anteroposterior view and (B) lateral view.

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No potential conflict of interest declared.

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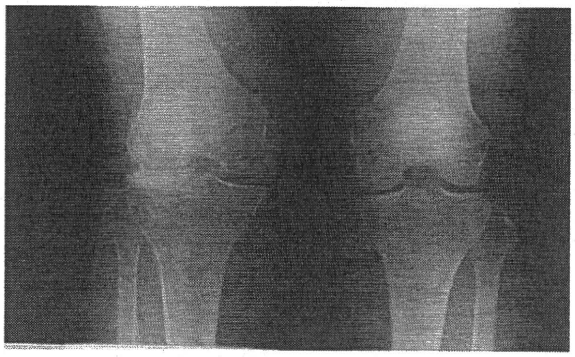

FIGURE 2. A 59-year-old female: Rosenberg's view: lateral joint space was closed.

examined: anterior-posterior view x-ray, lateral view x-ray (Figs. 1A, B), Ronsenberg view x-ray[19] (Fig. 2), and magnetic resonance imaging (Figs. 3A, B).

SURGICAL PROCEDURE

Bone Marrow Stimulation Under Arthroscopy

Arthroscopy was used to examine the cartilage surfaces, menisci, and ligaments in all of the cases. For arthroscopy, we used infrapatellar medial and lateral portals, and a pump inflow pressure of 80 mm Hg/m. When meniscal tears were found, we additionally performed partial menisectomy of the menisci. Bone marrow stimulation was then performed under arthroscopy. The OA lesions were drilled with 1.5-mm Kirschner wire or microfractured with an ice pick at 4 to 5 points/cm^2 (Fig. 4).

Fixation of Distraction Arthroplasty Device

After drilling and microfracture, the external device was fixed. At the proximal tibia, the 2-mm guide pin was passed parallel with the joint line. The position was checked using fluoroscopy (Fig. 5), and two 6-mm pins were drilled into the proximal tibia at 2 cm below the tibial plateau surface (Fig. 6) to fix the external device. These pins indicated the optimum location of the external fixation device. Next, two 2-mm guide pins were inserted into the apexes of the medial and lateral epicondyles, which are at the center of rotational motion of the knee. These guide pins did not penetrate the intercondylar space and did not damage the intra-articular ligaments. Then, according to the original guide frame (Fig. 7A), 2-mm guide pins were inserted, followed by two 6-mm pins, which were passed through the femur bone (Fig. 7B). The external device was fixed and the distractive tension applied (Fig. 8). We checked the range of motion (ROM) (Figs. 9A, B) and used arthroscopy to determine how much to increase the tibio-femoral joint space. The postdistraction and predistraction tibio-femoral joint spaces were measured using the length of a probe, with the knee at 10 degrees of flexion and without any valgus or varus stress. Finally, we examined the x-ray to check the change in the joint space (Fig. 10).

Postoperative Rehabilitation

A soft knee brace was fixed for 2 weeks. Continuous passive motion exercise commenced 2 weeks after the external device was fixed, and was continued for approximately 2 weeks. Patients were allowed to walk with partial weight bearing from 3 weeks after surgery. One month after surgery, patients were allowed to walk with full weight bearing.

Removal of the Device and Follow-up Arthroscopy

The external fixation device was removed 2 to 3 months after fixation. After the external device was removed, follow-up arthroscopy was performed in all cases to observe the articular surface that had been treated by the bone marrow stimulation procedure.

CLINICAL RESULTS

The detailed clinical results were shown our earlier report in 2007.[18] From April 2002 to September 2005, we performed this distraction arthroplasty and bone marrow-stimulating method on 7 knees (in 7 patients). In these knees, the OA had spread to both medial and lateral tibio-femoral joints. The indication for the procedure was grade 3 or greater using the Kellgren-Lawrence classification, at 1 or 2 compartments of the tibio-femoral joint. All of the patients provided consent for treatment with this therapy. One patient was excluded from the analysis, because he was found to have rheumatoid arthritis after the surgery. The remaining subjects comprised 2 men and 4 women, aged 42 to 63 years (mean: 49 y). According to the Kellgren-Lawrence grading scale, 1 case was grade 3 and

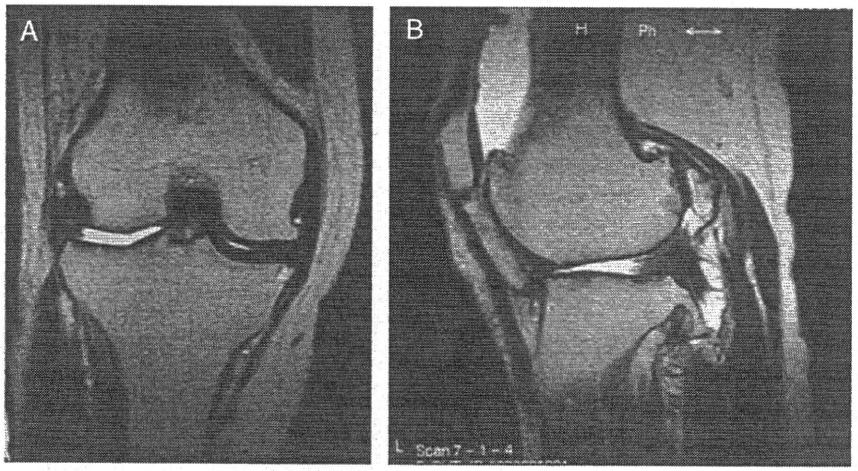

FIGURE 3. A 59-year-old female: magnetic resonance imaging T2 views: (A) coronal view and (B) sagittal view. The articular cartilage on both the femur and tibia side disappeared.

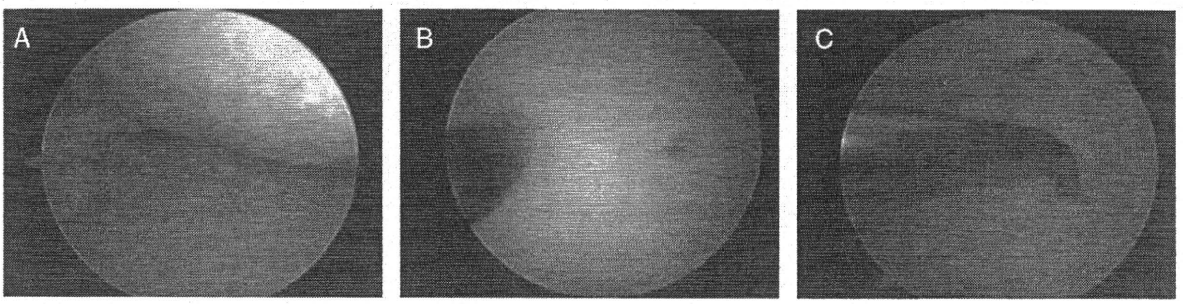

FIGURE 4. Arthroscopic view of lateral compartment of tibio-femoral joint (A). B, Microfracture performed on the femoral condyle. C, Microfracture performed on the tibial plateau.

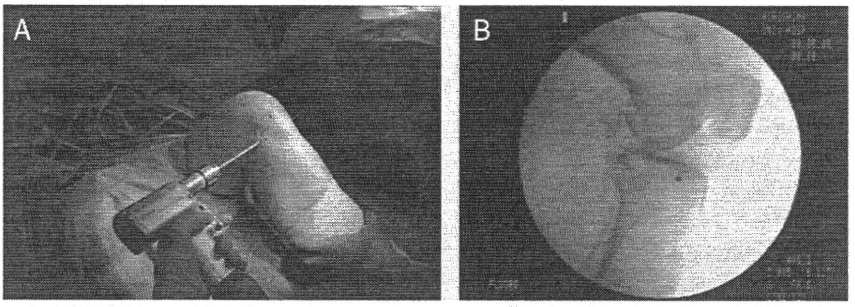

FIGURE 5. Before passing the 6 mm pins, we checked the position of the insertion site using 2 mm guide pins (A) with fluoroscopy (B).

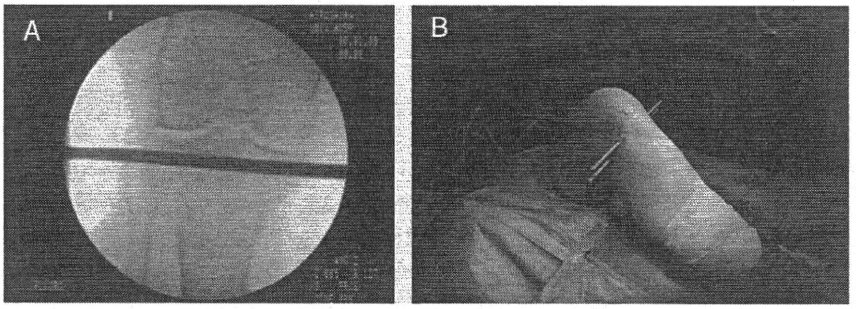

FIGURE 6. After checking the position of the guide pins with anteroposterior and lateral views of fluoroscopy, two 6 mm pins were inserted at the tibial proximal site (A, B).

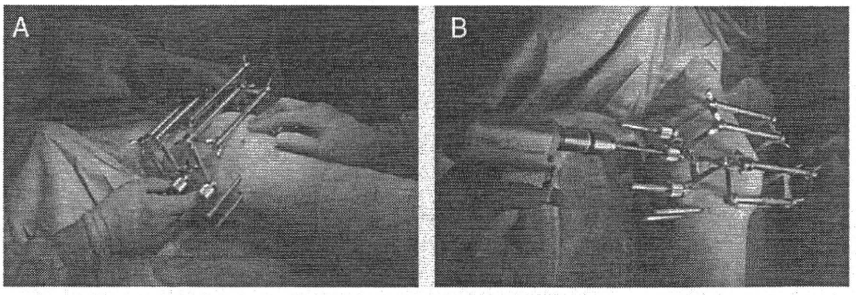

FIGURE 7. According to the original guide frame (A), 2-mm guide pins were inserted, followed by two 6-mm pins, which were passed through the femur bone (B).

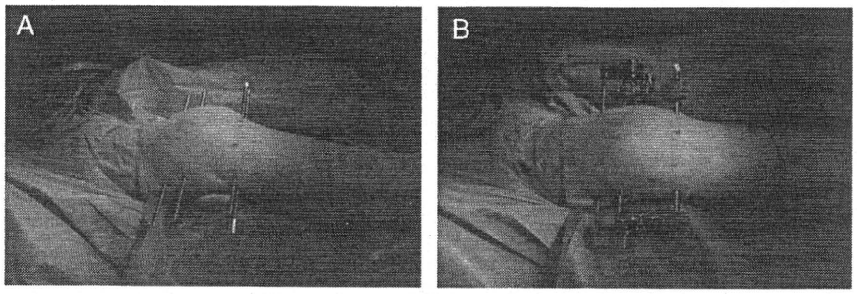

FIGURE 8. The two 6 mm pins were inserted into the femur bone (A), then the external device was fixed and the distractive tension applied (B).

5 cases were grade 4. The fixation period of the distraction device ranged from 7 to 13 weeks (mean: 9 wk). The follow-up period ranged from 2 to 4 years and 5 months (mean: 3 y).

COMPLICATIONS

Although 2 cases had suffered a superficial skin infection around the insertion of the pin at the tibia and the femur, none had experienced any major complications such as nerve palsy or deep infection.

EVALUATION

We compared preoperative and postoperative assessments of the Japan Orthopaedic Association score, the ROM, the joint space by the Rosenberg x-ray view,[19] and the visual analog pain scale. The Rosenberg x-ray view was carefully taken as a posteroanterior view. The patient stood with the knees flexed to 45 degrees, and with the anterior aspect of the knee touching the radiographic cassette. The x-ray beam was centered at the joint line, parallel to the tibial plateau.[19] The narrowest joint space on the preoperative and postoperative Rosenberg x-ray views was measured for every patient by one of the co-authors. Preoperative and postoperative data were analyzed using the paired t test. P value less than 0.05 was considered significant.

RESULTS

After the external devices were removed, the follow-up arthroscopies revealed that in all cases the regions treated with the bone marrow-stimulation procedure were covered with newly formed tissues.

The Japan Orthopaedic Association score significantly improved from a mean of 56 points (range: 55 to 60 points) before treatment to a mean of 81 points (range: 70 to 85 points) after treatment ($P<0.001$). The ROM (mean ± SD) was -5 ± 4 to 111 ± 5 degrees before surgery. During the external fixation, the ROM decreased, but at the final follow-up, the mean ROM increased to become -5 ± 3 to 122 ± 5 degrees. The joint space, as measured by the Rosenberg x-ray view, increased from a preoperative mean of 0.4 mm (range: 0 to 1.0 mm) to a mean of 1.6 mm (range: 0 to 3.0 mm) at external fixation. At the final follow-up, the joint space remained at a mean of 1.6 mm (range: 0 to 3.0 mm). Visual analog pain scales significantly improved from a mean of 9 points (range: 8 to 10 points) before treatment to a mean of 4 points (range: 1 to 7 points) ($P=0.001$).

DISCUSSION

We have been performing the articulated distraction arthroplasty procedure since 2002, and we reported a preliminary clinical result in 2007.[18] We used an articulated distraction arthroplasty device that was developed for the human knee joint by Ochi, and that allowed the joint to be smoothly exercised during fixation. This device allowed widening of the joint spaces and the continuation of ROM exercises. It was specially designed not to damage intra-articular structures such as the anterior cruciate ligament, the posterior cruciate ligament, and cartilage, with no pin being inserted at the femoral center of knee motion. Another feature of our procedure was that distraction of the joint space elongated the contractured ligaments of the knee joint. In this study, we found not only enlargement of the joint space and improvement of pain, but also an increase in the ROM. From these findings, we expect joint contracture to be reduced even after the patient's external fixation device is removed.

Former distraction arthroplasty procedures satisfied only 2 factors in the repair of a damaged joint surface: (1) widening of the joint space and (2) reduction of pressure on the regenerating fibrocartilage during weight bearing.[13,14] These procedures did not enable functional joint movement, even though knee motion is one of the most important factors contributing to repair in hyaline-like cartilage. In one clinical study, a hinge-distractor apparatus was used to provide some movement of the knee and elbow joint, but it did not allow continuous active movement.[20]

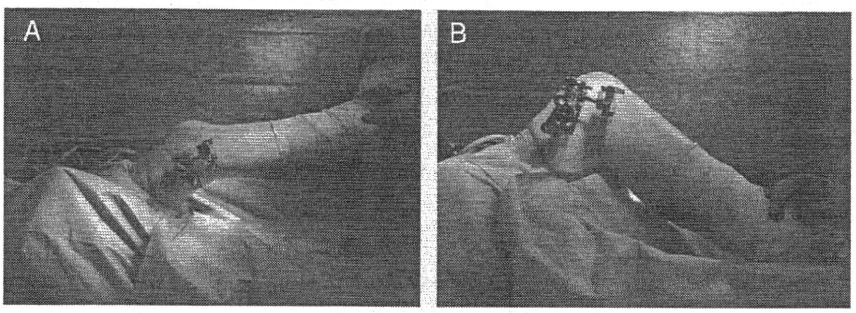

FIGURE 9. After fixing the device, range of motion was checked. A, Extension and (B) flexion.

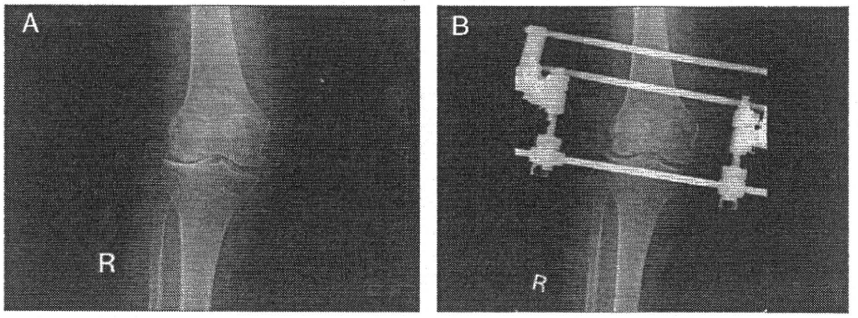

FIGURE 10. After distraction, the joint space was wider (B) than before surgery (A).

In an animal model, Kajiwara et al[17] evaluated damaged rabbit knees treated with an articulated distraction arthroplasty device or with the drilling method. They described that the distraction device in combination with subchondral drilling was more effective for repairing an osteochondral defect than drilling alone. Furthermore, they determined that distraction for 4 weeks was not of sufficient duration for repair of the defect, whereas distraction for between 8 and 12 weeks resulted in a good outcome.

We believe that good clinical results were achieved because the device enhanced joint space and joint movement. This would have favored the unloading and protection from damage of the newly formed fibrocartilage that was produced after bone marrow stimulation.

However, it is necessary to continue the clinical and basic studies to resolve some uncertainties of this arthroplasty. Firstly, the appropriate distraction force and the optimal loading are still unclear. The measurement of load pressure in the joint of a living human is difficult. Therefore, we checked the joint space after fixing the device and compared the postfixation and prefixation spaces using arthroscopy and Rosenberg x-ray views. Secondly, it was necessary to estimate the appropriate fixation period. We removed the articulated distraction device after 7 to 12 weeks. There were 2 reasons for choosing this duration of fixation: (1) the patients' lifestyles were restricted by the device, and (2) we took into account the findings of Kajiwara et al,[17] that distraction for 8 to 12 weeks results in a good outcome. Thirdly, the number of cases included in this study was small, and the follow-up period was limited.

In conclusion, we described that the distraction arthroplasty using the knee distraction arthroplasty device is effective for OA of middle-aged knees.

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3T-MRIにおける関節軟骨変性の定性的、定量的評価
－病理組織像との比較

久保晴司[1)]、黒田良祐[1)]、岩間祐基[2)]、松下雄彦[1)]、松本知之[1)]、藤井雅彦[2)]、杉村和朗[2)]、黒坂昌弘[1)]

3T-MRIでは、高いsignal noise ratio(SNR)を活用することで軟骨病変のより詳細な評価が可能となり、関節変性疾患に対する応用が期待されている。本研究の目的は、3T-MRIの画像所見が関節軟骨の病理所見をどの程度まで反映しているのかを定量的に評価することである。関節軟骨の定量的な評価に有用なMRI撮影法としてdGEMRIC、T1roh, T2 mappingが諸家により報告されているが[1)-3)]、本研究では、コントラストに優れた脂肪抑制プロトン強調像(FS-PDWI)を用いてまず定性的性評価を行い、造影剤を使用すること無く、比較的簡便に撮影できるT2 mappingによるT2値を用いて関節軟骨変性の定量的評価を行った。

【対象と方法】

対象は内反型変形性膝関節症に対し全人工膝関節置換術を行った10例（女性9例、男性1例、年齢58から78才、平均年齢71才）の大腿骨外顆荷重面である。まず術前に、3T-MRI(Philips社製Achiva 3T)を用いて、矢状断での脂肪抑制Ｔ２強調像、T2 mapping, 脂肪抑制プロトン密度強調像を撮影した。

次いで、病理学的評価として、手術にて切除した大腿骨外顆を脱灰病理標本とし、HE染色、safraninO染色した。まずＨＥ染色で形態の評価を行い、サフラニンＯ染色で、関節軟骨の変性、軟骨基質の染色性の低下などを評価した。定性的な検討項目としてMRI所見と、病理のマクロ像がどの程度一致しているか、関節軟骨の全層欠損、軟骨の層構造の一部破壊、広範な軟骨の変性菲薄化、につきに評価した。軟骨変性の定量的評価としてはそれぞれの標本で4カ所のregion of interest(ROI)を設定し、その染色性を3段階（normal, moderate, poor）にgradingし、各gradeにおけるROIの術前矢状断MRI（1．脂肪抑制プロトン密度強調画像：FS-PDWI, 2．T2 mapping）各撮像法での信号強度を比較した。

【結果】定性的評価においては、軟骨全層欠損、軟骨の層構造の一部破壊ないし軟骨表面のみの変性、関節軟骨の変性と菲薄化いずれについてもFS-PDWIにおいて優れたコントラストを示し、形態的評価においても有用であった（図1）。

Quantitive evaluation of degenerative change of articular cartilage using 3T-MRI

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Key Words: articular cartilage, MRI, histology

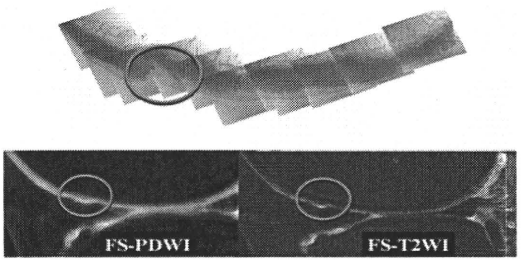

図１．肉眼的には軟骨の層構造の一部破壊も FS-PDWI においてより鮮明に描出されている

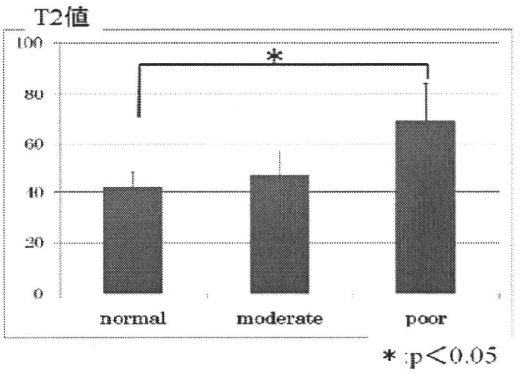

図２．safraninO 染色性の違いによる T2 値の変化

一方、safraninO 染色性の grade による定量的評価においては FS-PDWI 信号強度は normal 群(1349±244), moderate 群(1386±292) poor 群(1528±199)といずれの群間にも信号強度に有意差を認めなかったのに対し、T2 mapping による T2 値では normal 群（42.1±6.4）, moderate 群（47.1±10.1）,poor 群 (69.7±14.6) であり、safraninO 染色性 normal 群は safraninO 染色性 poor 群に比べ有意に低い T2 値を示していた。 ($p<0.05$)。moderate 群では他の群との統計学的有意差を認めなかった（図２）。

【考察】

FS-PDWI では関節軟骨と軟骨下骨、半月板のコントラストが明瞭で関節軟骨の全体像や形態をとらえるにはもっとも適していると考えられたが、定量的評価においてはsafraninO染色性によって信号強度に有意な差が無かった。一方、T2 mapping では形態的評価におけるコントラストには劣るものの、高度軟骨変性によって T2 値は有意に延長し、軟骨変性の定量的評価に適していることが示された。今後、関節軟骨への様々な治療に対する評価にも有用である可能性が示唆された。

結論として、3T-MRI による 脂肪抑制プロトン強調像と T2 mapping 撮影法の組み合わせは変性軟骨の定性的、定量的評価に有用であると考えられた

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MRIによる関節軟骨の画像診断の新たな展開

渡辺淳也[1]　吉岡　大[2]

核磁気共鳴撮像(magnetic resonance imaging；MRI)は関節軟骨の直接的な評価が可能であり，軟骨の損傷や変性の診断にきわめて有用な非侵襲的評価法である。近年，3T MRIの普及や，RFコイル，パルスシーケンスの改良などに伴い，より高い空間分解能での撮像が可能となってきた。また関節軟骨中の分子構造変化を鋭敏に捉えることが可能な新しいMRI撮像法が臨床応用されつつあり，従来困難であった変形性関節症(OA)の早期診断に有用な方法として期待される。本稿では，これらの最新のMRI撮像法などについて解説する。

3T MRIを用いた関節軟骨のルーチンMRI撮像法

3T MRIでは1.5T MRIと比較し，RFコイルなどを含めた撮像条件が同一であれば理論上2倍の信号雑音比(signal to noise ratio；SNR)が得られる[1]。SNRの向上は，空間分解能の向上や撮像時間の短縮に有効であり，骨軟部領域の撮像においても静磁場強度の上昇による多くの恩恵を受けることが可能となる。特に病変が比較的小さく，また薄く複雑な立体構造をとる関節軟骨では，SNRの向上が診断精度に大きく寄与するため，3T MRIを用いたイメージングはきわめて有用性が高い(**図1**)。一方，3T MRIでは1.5T MRIと比較し，緩和時間，磁化率効果，化学シフト効果などが異なるため，撮像プロトコルの作成にあたってはパラメータの設定に注意が必要である。また静磁場強度の上昇に伴う比吸収率(specific absorption rate；SAR)の上昇や磁場不均一性の増加など解決すべき問題も多く存在する。

われわれは3T MRIを用いた関節軟骨や半月板，靱帯などを主な対象としたルーチン撮像では，fast spin echo(FSE)法を用いた少し長めのエコー時間(echo time；TE)のプロトン密度(proton density；PD)強調像("intermediate weighted image"ともよばれる)を中心に用いている(**図2**)。PD強調像では，T1強調像とT2強調像の中間的な像が得られ，軟骨と関節液，軟骨下骨との間に比較的良好なコントラストが得られる。また脂肪抑制法を用いたPD強調像では，関節液は強い高信号に，正常海綿骨は低信号に描出されるため，損傷軟骨部にある関節液や，剥離した骨軟骨片と骨髄との間に介在する関節液を鋭敏に捉えることが可能であり，軟骨損傷の評価に有用である。また比較的短いバンド幅や大きなピクセルサイズを用いた撮像では，化学シフトアーチファクトによる骨髄脂肪像の軟骨像への重なりにより，軟骨の評価が困難となることがあるが，脂肪抑制法を併用すると骨髄脂肪像を抑制することが可能である。

3D Isotropic MRI

膝関節のMRIの撮像には，現在さまざまなシーケンスが使われているが，そのほとんどはanisotorpic(非等方性または異方性)なボクセルでの撮像法であり，オリジナルの撮像断面，例えば矢状断から冠状断または横断へのリフォーマット

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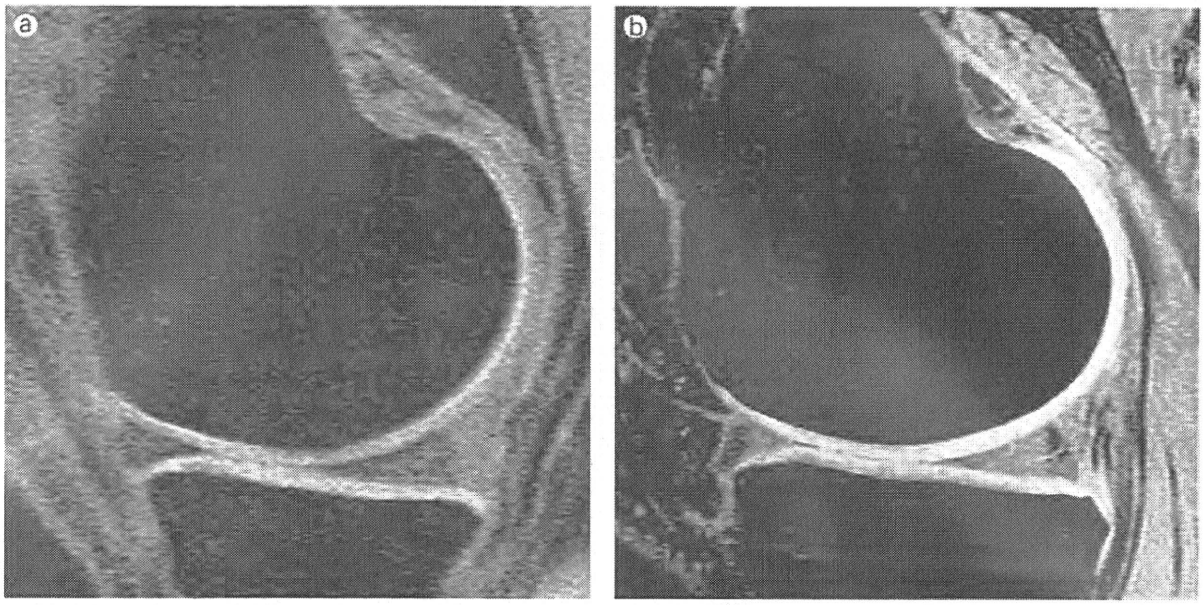
図1　1.5Tと3.0T MRIによる膝関節軟骨描出能の比較



a：1.5T脂肪抑制PD強調矢状断像，b：3.0T脂肪抑制PD強調矢状断像

像は，画像の劣化により診断には役に立たない場合が多い。

それを解決する方法として，3D isotropic(等方性)MRIが近年試みられている。通常の膝関節MRIは，FOV：14～16cm，マトリックスサイズが最低でも256×256以上で撮像すると仮定すると，撮像面内のピクセルサイズは最大でも0.625mmということになり，スライス厚を同じく0.625mmに設定しなければisotropicな画像にはならない。オリジナルの撮像断面を矢状断とし，撮像に必要な膝の左右の幅が12.5cmとするとちょうどスライス枚数は200枚となる。スライス枚数だけでも膨大な数であるが，0.625mmのスライス厚で十分なSNRが得られるかどうか，十分なSNRのためには撮像時間がどのくらい必要なのかなどが実際に臨床応用するには問題となる。

SNRを稼ぐ手っ取り早い方法は，3Tなどの高磁場MRIを用い，マルチチャンネルの膝コイルを使うことである。しかし，十分なSNRの画像が得られても，関節軟骨とその周囲の良好なコントラストが得られる撮像シーケンス(TR，TE，FAなど)を使わなければ軟骨病変の診断はできない。

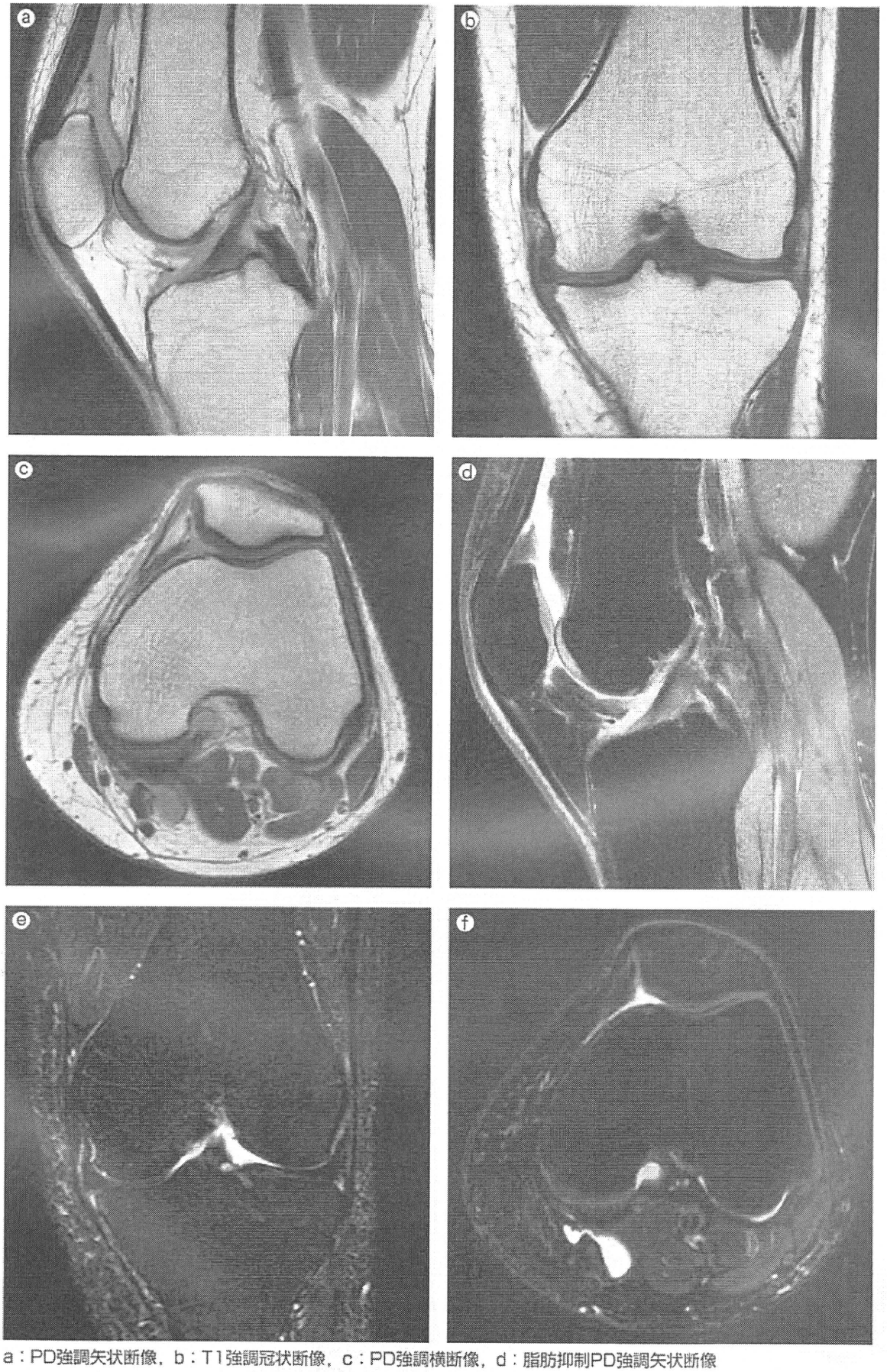
したがって，3D isotropic MRIの実用化には撮像シーケンスの改良も不可欠である。FSE法ではエコートレイン数を増やさざるをえず，画像のぼけ(blurring)につながる。そのため，3D isotropic MRIには，撮像時間を半減させ，またエコートレイン数も調整しやすいパラレルイメージングは非常に有用な技術である。また，少し姑息ではあるが，スライス厚を0.625mmではなく0.7mmに設定し，near-isotropic MRIでもリフォーマット像に画像の劣化がなければ，スライス厚の少しの違いが，撮像時間の短縮にはかなり影響してくる。

Goldら[2]は，3D-FSE with extended echo-train acquisition(XETA)法を2D-FSE 法と比較し，非常に有用な方法だとしている。

その他の3D isotropic MRIの撮像方法として，double-echo steady state(DESS)法があげられる。DESS 法は，高速gradient echo(GRE)法で，1つのパルス間隔の間にsteady state precession(FISP)法とreversed FISP(PSIF)法を組み合わせた撮像法である。DESS法では，関節液を高信号，関節軟骨は中間信号に描出される。脂肪抑制法の代わりに水励起(water-excitation)法を加えることで，TRを短く保ったまま，軟骨-軟骨下骨，骨髄間のコントラストも良好となる。

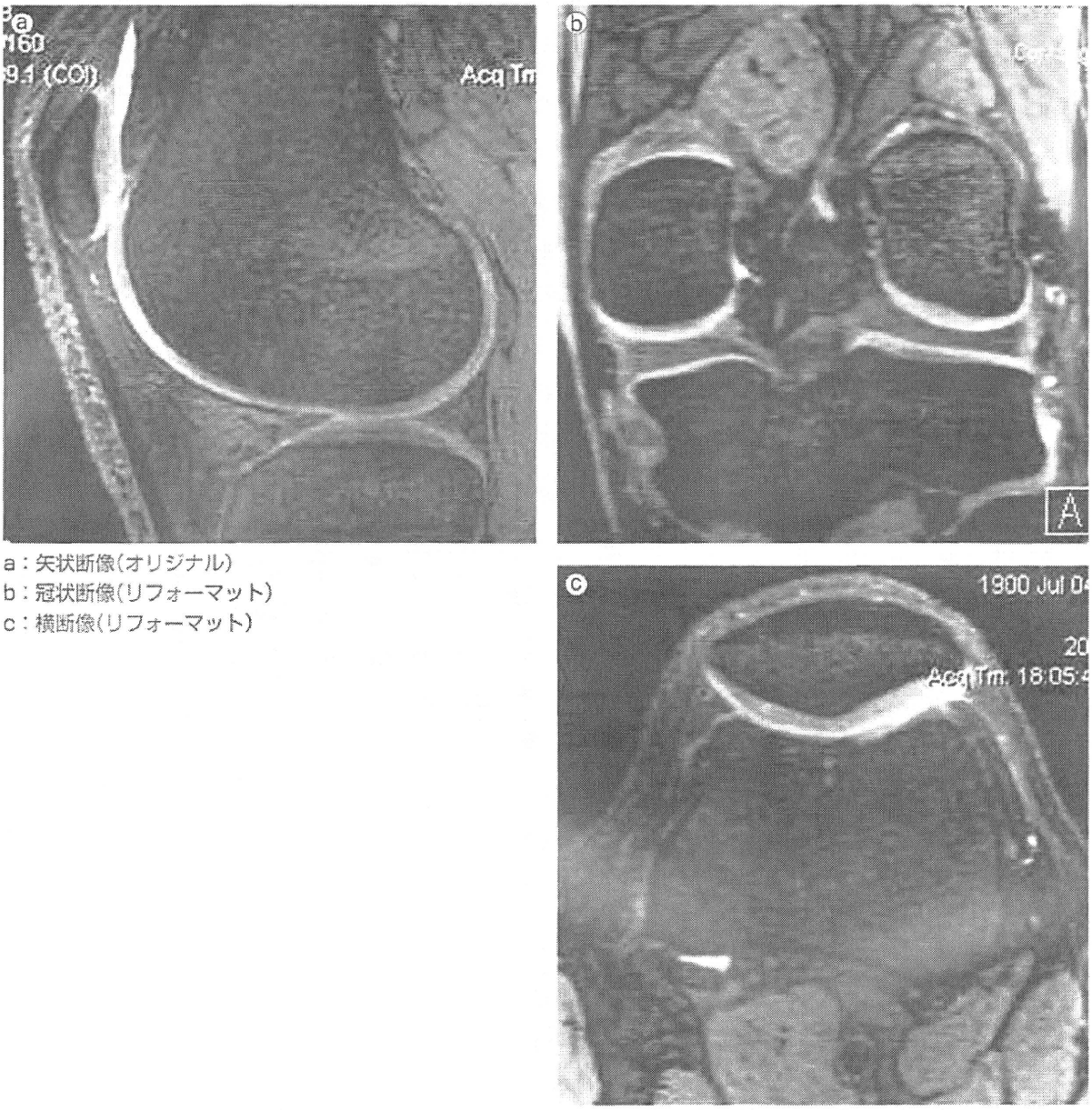
さまざまなコントラストの3D isotropic knee MRIがルーチンの撮像時間内で行えることが理想であるが，現実的には，関節軟骨に限っていえば，PD強調像またはそれに類似の画像(DESSやinter-

図2　3T MRIを用いた膝関節のルーチン撮像



a：PD強調矢状断像，b：T1強調冠状断像，c：PD強調横断像，d：脂肪抑制PD強調矢状断像
e：STIR冠状断像，f：脂肪抑制T2強調横断像

図3　DESS法を用いた膝関節3D isotropic MRI像(0.7×0.7×0.7mm)



a：矢状断像(オリジナル)
b：冠状断像(リフォーマット)
c：横断像(リフォーマット)

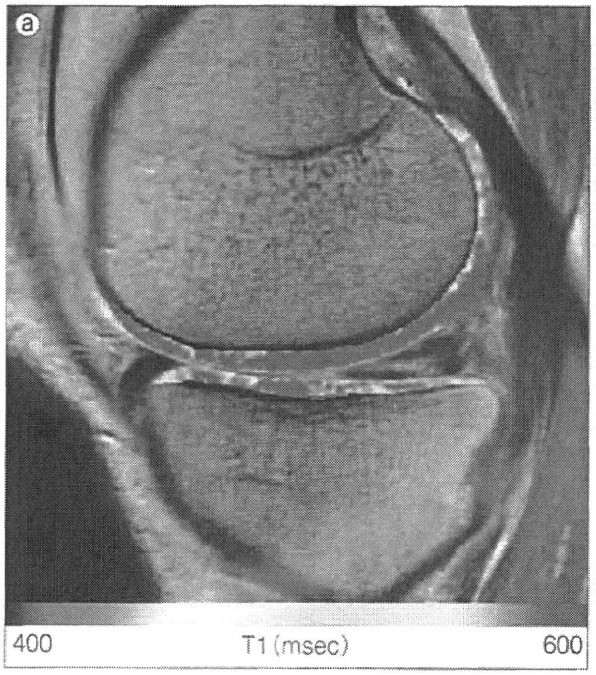
mediate TE画像も含む)が脂肪抑制の有無(または通常画像と水励起画像)で，一種類ずつあれば十分である。

isotropic MRIの最大の利点は，ただ単に細かい高分解能画像が得られるというだけでなく，いったんオリジナルの画像を撮像すれば，それから任意の断面に画像の劣化なくリフォーマットできる点である(**図3**)。通常の矢状断，冠状断，横断像に加え，滑車部の軟骨評価のために，斜冠状断像が必要になったとしても，すべてオリジナルの矢状断像からリフォーマットすることができ，余分な撮像を必要としない。2Dの3つの撮像面(矢状断，冠状断，横断像)がルーチンのプロトコルであるなら，3D isotropic MRIが3つの合計撮像時間より短ければ，スループットに関しても利点があることになる。

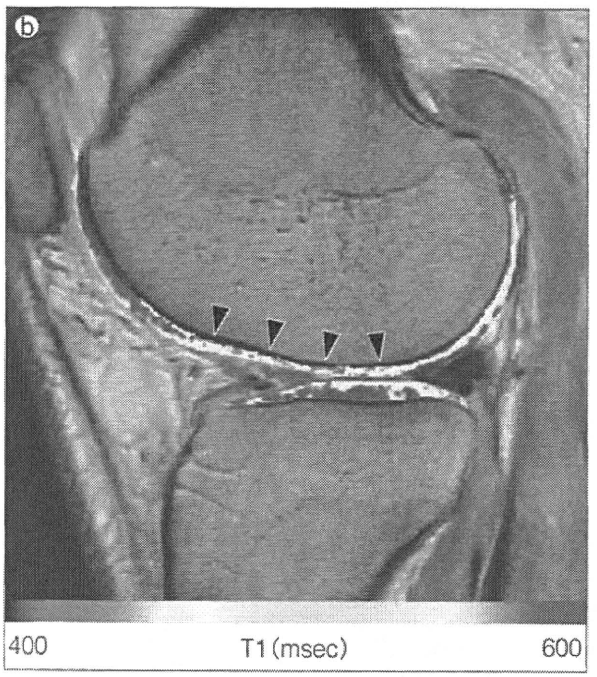
また，isotropic MRIでは，細かな病変の確認を複数の撮像断面から行うときも，現在のデジタル画像(ワークステーション)で簡単に位置ずれなくクロスリンクさせることができる。

ただ，最大の問題は，軟骨の3D isotropic MRIで膝関節のほかの病変，たとえば半月板損傷，靱帯損傷の診断も現在使用されている2D-FSEのプロトコルと同程度の感度，特異度であるかという点である。Jungら[3]は，内側半月板，外側半月板，前十字靱帯，および後十字靱帯の損傷に関して

図4　dGEMRICによる膝関節軟骨変性の評価
カラーバーの青色はT1の長い健常部位を，赤色はT1の短い変性部位を示している。



a：健常症例のdGEMRIC矢状断像
健常症例のdGEMRIC像では，関節軟骨は均一で比較的長いT1で示される。



b：外側半月板損傷症例のdGEMRIC矢状断像
20歳代，男性。大腿骨外側顆および脛骨外側顆の軟骨のT1短縮が認められ(▲)，GAG濃度の低下を伴う軟骨変性が示唆される。

0.5×0.5×0.5mmの3D isotropic MRIと2D-FSE MRIを用いて比較したところ，感度，特異度，正確度に関して2つの撮像法間で統計的な有意差はないと報告している。しかし，実際に膝関節MRIのルーチンプロトコルをすべて3D isotropic MRIに置き換えられるかどうかについては，もう少しデータの蓄積が必要であると思われる。

最新の関節軟骨のMRI評価方法

一般的なルーチンMRIは，関節軟骨の形態異常の検出は比較的鋭敏であるものの，軟骨内の信号強度異常の検出に関しては，信号強度自体に定量性がないこともあり，必ずしも鋭敏ではない。このため形態異常や明らかな信号強度異常が出現する以前の，変形性関節症の早期に発生する軟骨変性を詳細に評価することは困難であった。これに対し最近，軟骨の組成や構造の変化などを定量的に評価可能な新しいMRI撮像法が臨床応用されつつあり，軟骨の質的評価に有用な方法として期待されている。ここでは軟骨中の主要構成成分であるグリコサミノグリカン(glycosaminoglycan；GAG)，コラーゲン，水分などの質的評価可能なMRI撮像法について述べる。

dGEMRIC(図4)

dGEMRIC(delayed gadolinium enhanced magnetic resonance imaging of cartilage)[4]は，軟骨中のGAG濃度が評価可能なMRI撮像法であり，早期軟骨変性の検知や軟骨変性度の定量的評価に有用とされる。GAGは陰性荷電を有する極性分子であり，正常軟骨中に豊富に含まれるが軟骨変性に伴って減少する。dGEMRICでは同じく陰性荷電を有するMRI用造影剤(gadopentetate dimeglumine；Gd-DTPA^{2-})を経静脈投与すると，電気的反発力のためGd-DTPA^{2-}が軟骨内のGAG濃度と反比例して浸透することを原理としている。すなわち，GAG濃度が低い変性軟骨ほどGd-DTPA^{2-}濃度が高くなり，より強いT1短縮が認められる。dGEMRICでは，撮像の約90～120分前にGd-DTPA^{2-}を0.2mmol/kgの用量で経静脈投与する。

また，Gd-DTPA^{2-}の安定した軟骨内浸透を目的として，投与後に約10分間の荷重歩行を行わせる[5]。Gd-DTPA^{2-}は投与後主に関節液を介して軟骨内に