Recent treatments for spinal disorders have rapidly progressed, and new motion preservation technologies such as AID replacement or flexible spinal stabilization have evolved.3–5,7,8,10,13–21,24,37,38,41 The AID technology includes several different designs and surgery-related concepts. To date, some devices are undergoing multicenter clinical trials for clinical approval;17,19 however, a paucity of information exists regarding appropriate design concepts of unconstrained or constrained interface material and its modification, and their in vivo alterations. There have been some in vivo studies involving several animal models, in which investigators have described the short-term biomechanical and histological effects of devices.18,20,21,24 When considering the ultimate goals of an artificial disc in preserving mobility and stability function during a long-term period, however, basic studies to investigate long-term biological and biomechanical effects are essential.

Our AID is based on the concept of a durable, constrained, and single-component design with surface modification that enables a biological bonding to the VB. It consists of a triaxial 3D polymer fabric woven with an UHMWPE fiber, and spray-coated bioactive ceramics on the disc surface.18,21,28,31 In previous studies members of our group have demonstrated that its biocompatibility, endurance, and biomechanical properties were similar to those of the normal disc.18,21,28,31 In an in vivo study in which we used a sheep model we demonstrated the excellent interface bonding and preservation of segmental spinal mobility at 6 months postoperatively.21

To investigate further the long-term biological and bio-
mechanical effects of AID replacement, this 2-year study was conducted using a sheep lumbar spine model. We also focused on the use of bioresorbable spinal stabilization combined with the AID, providing both initial spinal stabilization and late mobilization after degradation of material.

Materials and Methods

Design and Biomechanical Properties of the AID

The triaxial 3D fabric disc was a semieliptically shaped near-net woven with an UHMWPE fiber bundle, which was coated by linear low-density polyethylene (Fig. 1).18,21,28,31 The 3D fabric disc consisted of a number of fibers in the x, y, and z axes and their respective multilayers with some alignment ratios in three dimensions. Importantly, this prosthesis was uniform without any nucleus portion and was composed of a single material. The bioactive ceramic granules were spray coated to the designed depth either by sintered HA or apatite–wollastonite glass ceramic granules. The mean diameter of the two ceramic granules was 2.88 and 4 μm, respectively.

Several human 3D fabric prototypes were woven with orthogonal or off-angle fiber alignment and underwent cyclic tensile-compressive and torsional testing. Finally, the off-angle 45° model was selected based on the superior torsional property of the orthogonal and off-angle 30° models.18,21,28,31 The arrangement of layer numbers and alignment ratio among three weaving axes resulted in balanced mechanical properties.

Animal Model and AID Replacement Procedure

In 36 sheep, the L2–3 and L4–5 intervertebral discs were totally replaced with scaled-down 3D fabric discs (20 × 17 × 10 mm) in a procedure performed via a retroperitoneal approach. After a circumferential removal of the intervertebral disc, the upper and lower endplates, as well as the anterior wall of spinal canal were resected. Two types of 3D fabric discs coated with either sintered HA or apatite–wollastonite glass ceramic granules were randomly assigned. The animals were divided into the following three groups: Group I, 13 with no initial fixation; Group II, 13 with temporary Kaneda SR screws (Takiron Co., Ltd., Osaka, Japan) (Fig. 2). The bioresorbable rod was made of 40% bioresorbable rod spanning two Kaneda SR screws (Takiron Co., Ltd., Osaka, Japan); and Group III, 10 with the augmented PLLA with an ultra-high strength bioresorbable rod spanning two Kaneda SR screws (Takiron Co., Ltd., Osaka, Japan). In a previous basic study by Furukawa, et al.,12 the authors reported that the bending strength of the HA/PLLA composites implanted in the subcutaneous tissue of rabbit was maintained at more than 200 MPa for 25 weeks. At 6, 15, and 24 months postoperatively, the animals were killed, and DBUs were obtained and the spinal instrumentation removed.

Biomechanical and Histological Analyses

The L2–3 and L4–5 DBUs were mounted using a polyester resin; motion was allowed only at the disc space. The biomechanical tests were conducted using pure moment application of 0 to 5 Nm to the DBUs in flexion–extension and axial rotation with loading increments of three stages. The 3D motion values of the spinal segment were analyzed using the stereophotogrammetry method.21,28,31 The possible error of this stereophotogrammetry system was 0.1° including the digitization procedure. Ten normal DBUs harvested from nonsurgically treated sheep served as the control. The ROM and NZ were calculated from torque–angle curves.26 The NZ was defined as total (positive and negative) ROM at the moment of 0-Nm application.

For the histological analysis, undecalcified 40-μm sagittal sections were created and stained with Cole H & E and Toluidine blue O. The surface contact between 3D fabric and VB and the insertion of trabeculae into the 3D fabric fiber were examined. A university animal study review board previously approved the animal surgery, handling, and housing protocols. The statistical analysis was performed using a one-way analysis of variance and a post hoc analy-

Results

In Group I, the excised segments at 6 months were shown to be covered with noninfectious tight scar and incomplete osseous bridging. In Group II, however, these changes had completely disappeared and spinal mobility was preserved after removal of spinal instrumentation. There were some implant-related displacements without dislodgment in Group I, whereas in Group II all 3D fabric discs were firmly in place. In Group III, all bioresorbable rods broke secondary to degradation and spinal segments exhibited segmental motion (Fig. 3). The 6-month follow-up biomechanical data have been previously reported.21 In the present study, the 15- and 24-month data are newly presented.

In the control group the overall DBU ROM at a maximum moment of 5 Nm was 11.4° in flexion–extension (Fig. 4). In Group I this significantly decreased to 28% at 6 months. In Group II, 65% of the ROM was preserved compared with that in control animals at 6 months. In Group III, ROM significantly decreased to 49 and 40% of control values at 15 and 24 months, respectively.

In the control group, the overall DBU ROM at maximum moment of 5 Nm was 3.53° in torsion (Fig. 4). The statistically equivalent ROM values of 60 and 90% were
demonstrated in Groups I and II, respectively, at 6 months postoperatively. In Group III, 151% of the ROM value was detected at 15 months, and nearly equivalent ROM of 101% was demonstrated at 24 months postoperatively.

The NZ in the control and all surgical groups demonstrated statistically equivalent subsets both in flexion–extension and torsion (Fig. 5). These data basically showed the same tendency as those for ROM; however, statistical significance was not reached because of the high standard deviations.

Histological examination showed no particulate debris of 3D fabric fiber present in periimplant tissues and no foreign body reaction such as macrophage or giant cell appearance. The histological features at the interface between the 3D fabric disc and the VB were classified into three grades, with features in the dominant grade occupying 70% of combined upper and lower surfaces of the 3D fabric disc. Typically, in Grade 1, continuous trabeculae were observed without soft-tissue membranes inserting into the fabric (Fig. 6). Grade 2 showed a gap of less than 90 μm between the 3D fabric fiber and trabeculae occupied by calcified fibrocartilages. In Grade 3, a soft-tissue membrane occupied the interface. According to this grading system, Grades 1, 2, and 3 were observed in 36, 36, and 28%, respectively, of Group I animals. Of Group II specimens at 6 months, however, 63, 37, and 0% were Grade 1, 2, and 3, respectively. In Group III grades further improved at 24 months: 80% Grade 1 and 20% Grade 2. Macroscopic and scanning electron microscopy clearly demonstrated that 3D fabric fibers were directly surrounded by trabeculae and making direct contact.

**Discussion**

To our knowledge, our group is the first to perform an experimental evaluation of the mid- to long-term biomechanical and histological changes of AID prostheses. Although several artificial discs have been developed and experimentally evaluated in an animal model, the maximum observation periods were mostly within 6 months and only in a few were they extended to 1 year. Vuono-Hawkins, et al.,38 evaluated the results of an elastomeric intervertebral disc spacer with a surface modification of porous HA plate in a canine model through 12 months.38 The interface was occupied with dense fibrous tissues without bone ingrowth, and five of 12 spacers had migrated significantly. Urbaniak, et al.,34 evaluated a silicone–Dacron disc prosthesis in chimpanzee lumbar spines with a follow-up period of 1 year. In the four animals, eight spinal levels were evaluated, and spinal infections occurred in 50%. Useful biomechanical and histological data were not obtained. Kostuik,20 conducted a 6-month follow-up study in sheep in which a metal hinged prosthesis was implanted in the lumbar spine. At 6-month histological examination showed an osseous bridging between consecutive VBs was shown with a tendency toward anterior device subluxation. No quantitative biomechanical data were reported. In the largest baboon study Cunningham, et al.,8 evaluated anterior lumbar disc replacement with an AcroFlex prosthesis. Twelve-month histological examination demonstrated excellent osteointegration at the bone–metal interface; however, segmental
motion was significantly decreased compared with intact spinal segments in axial rotation, flexion–extension, and lateral bending. In a sheep model our short-term results indicated that nearly equivalent ROM was preserved in flexion–extension and axial rotation at 6 months postimplantation when temporary internal fixation was performed. Histological evaluation demonstrated an excellent osteointegration between the artificial disc and vertebral disc.

In this 2-year observation study, we focused on any interface loosening or subsequent osseous ankylosis occurring in the mid- to long-term period; additionally we examined the efficacy of internal fixation involving the use of bioresorbable materials. We found that the bioresorbable HA/PLLA rod broke and replaced segments that exhibited spinal mobility at 15 and 24 months. Although excellent bone fusion occurred at the interface by 24 months, the segmental spinal mobility tended to decrease with time, especially in flexion and extension. This was due to significant scar and bone spur formations including fibrocartilagenous or bone tissues surrounding both end plates. In a separate study by Takahata, et al., however, implant–bone interface strength was maintained between 15 and 24 months postoperatively, and this surpassed the effect of representative bioceramic interface with bone. Importantly, this study provided further critical information regarding the interface histological and biomechanical maturation. First, the osseous fusion of the bone to the fabric disc and trabeculae progressed with time. Second, spinal mobility, when achieved, had no deleterious effect on interface strength and histological characteristics. By 24 months postoperatively, no interface bone resorption, 3D fabric disc loosening, and no adverse biological reactions were observed despite the decreased segmental mobility. The limitation of the present study lies in the decreased mobility at the spinal segment, possibly eliminating the wear-related debris caused by friction between VB and 3D fabric disc. Additional study is underway in nonhuman primates to preserve physiological spinal motion and to assess the long-term device loosening status.

Another focus of this study was to evaluate the bioresorbable spinal instrumentation for the artificial disc augmentation. To date, several spine-related bioresorbable implants have been reported. These have included anterior cervical plates, cervical and lumbar interbody fusion cages, resorbable film acting as an adhesion barrier, and bone graft containment in a posterolateral fusion. The bioresorbable rods used in this study were manufactured from a forged composite of raw particulate HA/PLLA, which demonstrates total bioresorption, osteological bioactivity, and the highest strength found in this kind of composite to date. This highly distinctive and biocompatible qualities of the HA/PLLA composite are also useful for cervical and lumbar interbody fusion cages. In the present study, bioresorbable rods broke after 6 months and successfully allowed segmental spinal mobility. According to previous experimental data, almost 5 years are required until total resorption occurs.

In the present study, the artificial discs were separately
fixed using screws and bioresorbable rods in this animal model. Ideally, the artificial disc should have a standalone design that permits fixation to the vertebral endplate, obviating the need for external augmentation. Additionally, it is difficult to control the degradation process and breakage period when using bioresorbable fixation. Therefore, we have developed several standalone disc types and in vivo investigation in a baboon model is underway.

Finally, recent concepts in artificial disc replacement involve two major principles of either total lumbar disc replacement via an anterior approach or partial lumbar disc replacement via a posterior approach. The former procedure includes SB Charité and Acroflex implants that have been mainly indicated for the discogenic pain involved in isolated disc resorption.\textsuperscript{7,10,14,24,41} Although a multicenter clinical study for anteriorly implanted artificial disc is underway in the US, it remains uncertain whether artificial disc replacement effectively reduces low-back pain in the long term. The artificial disc for total disc replacement anteriorly has several benefits: wide surface area occupation, excellent mechanical endurance, and wide ROM. Surgical indications, however, are extremely limited—that is, to application in cases of degenerative disc disease and postdiscectomy disorders without neurological deficits.\textsuperscript{7,10,14,24,41} The ideal indications for future artificial disc replacement include lumbar degenerative disease associated with neurological deficits and slight segmental instability; postdiscectomy instability; low-grade lumbar spondylolisthesis; and cervical disc disease associated with neurological disturbance. The posterior partial disc replacement procedure has the potential for solving both disc function and neural problems by simultaneously replacing a disc and resolving neural compression. This will effectively expand the pool of candidates for artificial disc replacement and truly surpass spinal fusion as the spinal reconstruction method of choice. Our ultimate goal is that the artificial disc be as unique and flexible as the 3D fabric disc.

Conclusions

A 2-year experimental study was performed to investigate the biomechanical and histological changes associated with an implanted artificial disc, with a goal to undertake a clinical trial. In a sheep model, L2–3 and L4–5 discs were replaced with 3D fabric discs, and the segments were stabilized using two titanium screws and a spanning bioresorbable rod. At 15 and 24 months postoperatively, the spinal segments allowed the segmental mobility with gradually decreased ROM; however, the excellent bone ingrowth was observed at both time periods. The 3D fabric disc has an excellent clinical potential, although further refinements are necessary in terms of device design and surgical strategy.

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References


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