A Biomimetic Artificial Disc with Improved Mechanical Properties Compared to Biological Intervertebral Discs**

By *Yasuo Shikinami*,* *Yoshihisa Kotani*, *Bryan W. Cunningham*, *Kuniyoshi Abumi*, and *Kiyoshi Kaneda*

Patients with serious spinal disc disorders will benefit from a novel artificial disc system that is suitable for clinical use in replacement arthroplasty. The disc is composed of a biomimetic three-dimensional (3D) fabric with a triaxial fiber alignment that has superior mechanical properties when compared to conventional implants. This disc improves on the constitutional imperfections of biological intervertebral discs by eliminating the risk of rupture and delamination. The fabric bonds firmly to disc bodies, and functions in combination with bioactive bioresorbable pins and scaffolds as a stand-alone system that maintains the position of the disc and promotes bone growth at the interface. The disc has high biocompatibility and can maintain biomimetic "J-shaped" stress–strain behavior for up to sixty-three million alternating stresses, which is the equivalent of natural biological movements for a period of more than 30 years. This technology exemplifies how, in the best biomaterials, biological flexibility may occasionally overcome artificial rigidity.

1. Introduction

At present, over one million patients per year suffer from spinal disorders affecting the cervical (C) intervertebral disc at the C3–C4 level or the lumbar (L) intervertebral disc at the L4–L5 level. A total of twenty four vertebrae—seven cervical, twelve thoracic, and five lumbar—comprise the human spinal column. The existing surgical instruments and techniques used to repair degenerative disc disorders may be divided into two categories.[1] The first group contains prosthetic discs for interbody fusion, including metal and carbon cages, metal plates and screws, and allo- or autograft bone devices, which have been in use for more than 15 years. These methods provide solid fusion across the vertebral column following disc removal, without pathological effects on the neighboring spinal elements. However, they do not restore the original movement. The second category encompasses disc-augmentation techniques and instruments for disc-replacement arthroplasty that have been under development since the first primate studies more than 35 years ago, and are now clinically approved (even though they still hold hard issues). These methods can be subdivided into four groups: artificial discs, vertebroplasty, gene therapy, and tissue engineering, all of which aim to restore dynamic physiological motion at a similar level to that of an undamaged disc. The artificial discs described here belong to this category, and are suitable for clinical use in disc-replacement arthroplasty, a breakthrough awaited since the first basic biomechanical studies[2] and unsuccessful human implantation tests almost 50 years ago.[3]

Multidisciplinary biomaterials technologies have been used in the quest for clinically functional artificial discs that can maintain biological movement as a segmental unit under alternating stresses. It has been estimated that the spine undergoes approximately one hundred million movements during an average lifetime.[4] Previous studies have shown that the optimal life span of existing implants is only thirty million movements, and ten million movements is the recommended minimum.[5] Up until now, artificial discs have shown insufficient physical dynamic mobility, durability, and pathological protection of the adjacent segments, despite a few clinical trials undertaken for artificially short periods of time.[6,7] Even those synthetic discs that have been shown to maintain unrestricted biological mobility and to have high biocompatibility with the surrounding tissues—such as the unconstrained mobile-bearing SB CharitÈ III[8] and the constrained third-generation AcroFlex[9]—have not overcome all of these general problems. Prostheses composed of biologically foreign substances, with a structure that involves the superposition of solid plates (metallic endplate/plastic core/metallic endplate), have a pseudo-biological mobility that leads to immobilization or dislocation of the structure. This generates wear debris and minor defects through friction at the interfaces and can cause dangerous complications over prolonged periods.[10] In combination, these requirements place excessive demands on the biomechanical and biochemical properties of metallic and elastomer components.

[*] Dr. Y. Shikinami
Takiron Co., Ltd, Medical Div. 2-3-13 Azuchimachi
Chuo-ku, Osaka 541-0052 (Japan)
E-mail: sikinami@takiron.co.jp
Dr. Y. Kotani, Prof. K. Abumi, Prof. K. Kaneda
Department of Orthopaedic Surgery
Hokkaido University Graduate School of Medicine
Kita-15, Nishi-7, Kitaku, Sapporo 060-8638 (Japan)
B. W. Cunningham
Orthopaedic Biomechanics Laboratory
Union Memorial Hospital
201 East University Pkwy
Baltimore, MD 21218 (USA)

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Artificial discs for clinical use in humans must be carefully designed to meet the following minimum criteria, whilst maintaining excellent biocompatibility. First, biological discs do not move spontaneously in vivo, but flex passively in response to the adjacent musculoskeletal movements, acting as a form of damping device, so biomimetic artificial discs should possess these essential properties. Second, a stand-alone system, similar to that available for surgical approaches such as discectomy, should be devised to maintain the proper position of the intervertebral disc without the need for supplemental fixation. Third, delamination between the plates, wear debris, reduced fatigue resistance, and subsidence into the disc bodies should not occur, even under varied alternating loadings, for a minimum of 10 years. Fourth, the invasion of fibrous tissues into the disc substance, and bridging ossification to the adjacent living disc bodies, should be restricted to preserve the original segmental disc movement.

Total or partial disc-replacement arthroplasty is at the forefront of techniques for the surgical management of intervertebral disc pathology. However, without the development of new instrumentation and methodology, artificial discs are unlikely to meet these minimum criteria during the next decade. Biomimetic techniques provide great potential for the creation of new biomaterials with structures and properties that mimic those of biological materials. This article describes the first biomimetic products that have overcome those difficulties and are suitable for clinical use in human disc-replacement arthroplasty.

2. Results and Discussion

Biological intervertebral discs have a monolithic structure comprised of three components: the external annulus fibrosus, the central nucleus pulposus (Fig. 1A), and the upper and lower cartilaginous endplates.[11] A biomimetic artificial disc composed of a biomaterial that both imitates this collagenous fiber structure and improves on the constitutional imperfections in biological discs would possess crucial biological properties. Therefore, we designed a cubic three-dimensional fabric (3DF) disc (Fig. 1B) that stands alone and can attach firmly to the endplates and disc bodies (Tables 1,2). This fabric has a structure unique from existing solid artificial discs.

The stress–strain curves of high-strength artificial materials generally have "S-shaped" profiles, in which the slope has a high tangent at low strain levels (Fig. 2a). By contrast, the stress–strain curves of biological tissues, including articular fibrocartilage and intervertebral discs, generally have a downward convex "J-shaped" profile with a low-tangent slope (Fig. 2b) indicating relatively high flexibility (low strength) at low strain levels, and a loading–unloading cyclic hysteresis-loss curve (Fig. 2c). In other words, soft biological tissues are pseudo-elastic within a physiological stress range and their stress–strain curves under either loaded or unloaded conditions are not identical in order to absorb a part of the loading energy.

The destruction of a material occurs through two processes: stress destruction, which is seen when the stress exceeds the strength of the material, and destruction that occurs when the strain caused by deformation exceeds a threshold value. Unlike most artificial materials, soft biological tissues can suffer relatively large amounts of deformation before they are destroyed. Therefore, the evaluation of biomechanical compatibility in flexible biomaterials should take into account the compliance (the elastic coefficient), which is the inverse of strength and strain destruction, rather than the absolute strength. Artificial biomaterials have previously been designed according to the principle that increasing the absolute strength will increase the physical durability and safety. Attempts to increase the strength generally result in the creation of materials with an increased modulus of elasticity, which show an upward, convex S-shaped curve with a slope with a relatively large tangent at

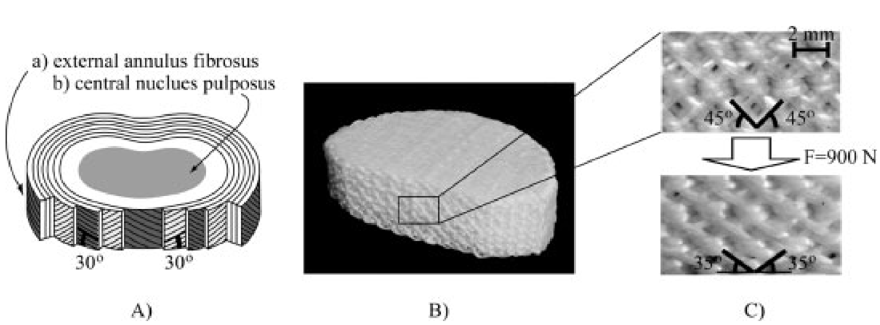
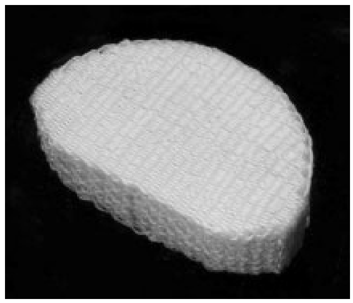
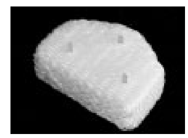
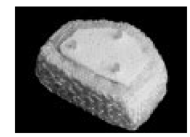
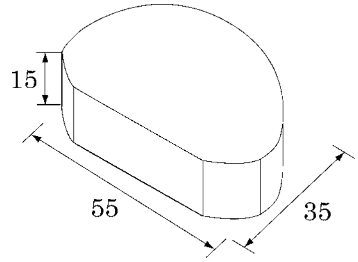
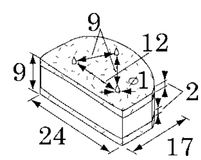
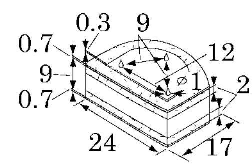


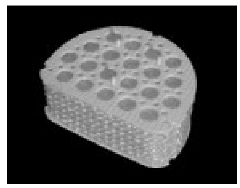
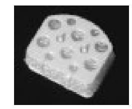
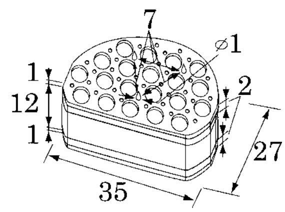
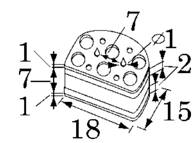
Figure 1. Fiber alignment of a biological disc and an artificial 3DF disc (Fabricube). A) Illustration of a human disc. a) The external annulus fibrosus, showing the characteristic fiber construction, in which distinct thin concentric cylindrical layers pile up to form between 15 and 20 successive lamellae, with slanted collagen fibers arranged at alternating angles (which might enhance the resistance to twisting). The collagenous fibers are aligned with gradually increasing angles of slant (20–55°; average, 30° to the sagittal plane) towards the upper endplate (which might affect the strength under different degrees of compressive forces). b) The central nucleus pulposus incorporates hydrogelatinous proteoglycans that absorb and emit body fluid, thereby maintaining the shock-absorbing capability of the disc. B) 3DF disc woven from triaxial 3D fabrics, the fiber arrangement of which is shown in Table 1, which is comparable in fiber structure to the human disc and has been tested for long-term physical stability, as shown in Figure 4. C) The magnified intersecting fiber structure of the external annulus fibrosus. The upper panel shows the off-angle fiber alignment before loading, which has obliquely intersecting angles (45°) of warps (ν-axis) and wefts (z-axis) with respect to the basis x-axis (y-axis). The lower panel shows the fiber structure after compressive loading of 900 N, which corresponds to the load applied in the axial compression test described in Figure 4, in which the angles have decreased to 35°.

Table 1. Dimensions and fiber arrangements of 3DF total lumbar discs that have been physically characterized (a) and pre-clinically evaluated in sheep (b) and baboons (b,c).

Sample number	a	b	c
Subject	Human (total)	Baboon (total)	Baboon (total)
Type	(Lumbar, monolithic)	(Lumbar, stand-alone with pin)	(Lumbar, stand-alone with pins and porous scaffolds)
Appearance			
Dimension [mm]			
Arrangement [number]			
Warp × layer	28 × 84	11 × 54	11 × 54
Weft × layer	28 × 84	11 × 54	11 × 54
Vertical filament × folding [times]	224 × 4	44 × 4	44 × 4
x y plane	42	27	27
Pitch of *x y* plane [mm]	2.0	2.0	2.0
Alignment ratio (*v*/*w*/*z*)	5:5:3	3:3:2	3:3:2
Intersecting angle [°]	(*v*, *w* ±45)	(*v*, *w* ± 45)	(*v*, *w* ± 45)
Size [mm]	(57 × 35 × 16)	(24 × 17 × 9)	(24 × 17 × 9)
Filament length [m]	136	18	18
Porosity [%]	57	52	52
Weight [g]	12.2	1.6	1.6

low strains. In general, solid metals, ceramics, and plastics that have relatively high strengths are used as biomaterials. However, soft biological tissues are flexible yet tough, and have high breakage strengths in contrast to their low modulus of elasticity (high compliance)—that is, they have a J-shaped stress–strain curve. Therefore, it is inevitable that mechanical incompatibility (mismatch) will exist between conventional implant devices, which are made of solid artificial products, and soft biological tissues. The need for high strength combined with a low modulus of elasticity places conflicting demands on materials with a single structural arrangement. It is necessary to design materials with compositions and arrangements of constituent elements that can satisfy both of these criteria; a combination of solid materials is not sufficient. The strength and deformation characteristics of a material are strongly influenced by its chemical and physical properties, but are also affected by structural factors such as the design, composition, constructional morphology and arrangement of its constituents. Therefore, to achieve physical equivalence between biological and artificial materials it is necessary to biomimetically simulate, or even improve upon, the structural traits relevant to movement in biological tissues. It is important to note that soft biological tissues, including articular cartilages, intervertebral discs, menisci, ligaments, tendons, and bone matrices, contain numerous collagenous fibers in three-dimensional (3D) arrangements.[12] These 3D structures show different strengths and physical behaviors when tested in different directions; that is, they are anisotropic materials in which direction is relevant to their biomechanical properties.[13] Intervertebral discs have a laminate structure in which biaxial (2A) 3D reinforcing plane materials are piled on top of one another.[14] However, excessively high loading of biological discs causes swelling that can lead to rupture and delamination between the concentric cylindrical lamellae, resulting in serious disc disorders. This property can be considered a biological imperfection.[15] An alternative strategy in the design of artificial materials is to construct a 3DF architecture that consists of fibers arranged along the x-, y-, and z-axes (3A) in multilayers with alignment-ratios in 3D.[16]

Table 2. Dimensions and fiber arrangements of 3DF total lumbar (d) and cervical (e) discs. These are suitable for use as biomimetic artificial discs in humans. Disc d at the L4-L5 level is relatively small in comparison with disc a, as implantation into the intervertebral space requires the preservation of as much of the intact circumferential disc as is possible, and is a smaller size to other solid artificial discs. Similarly the e at the C3-C4 level is relatively small.

Sample number	d	e
Subject	Human (total)	Human (total)
Type	(Lumbar, stand-alone with pins & hard perforated sheets)	(Cervical, stand-alone with pins)
Appearance		
Dimension [mm]		
Arrangement [number]		
Warp × layer	18 × 76	9 × 42
Weft × layer	18 × 76	9 × 42
Vertical filament × folding [times]	126 × 4	27 × 4
x y plane	38	21
Pitch of *x y* plane [mm]	2.0	2.0
Alignment ratio (*v*/*w*/*z*)	4:4:3	6:6:5
Intersecting angle [°]	(*v*, *w* ± 30)	(*v*, *w* ± 30)
Size [mm]	(35 × 27 × 12)	(18 × 15 × 7)
Filament length [m]	60	9
Porosity [%]	46	43
Weight [g]	5.4	0.8

Intervertebral discs are exposed in vivo to extensive, flexile, compressive, shearing, bending, and twisting forces, which lead to breakage and destruction. These forces are applied at various loading strengths and rates, continuously and intermittently, statically and dynamically, and for short and prolonged periods of time. Therefore, for 3DFs to be used in artificial discs they must be able to cope with a variety of loading conditions and to match the mechanical behavior of the surrounding biological tissues. The 3DF discs described here are the first to fulfill these requirements.

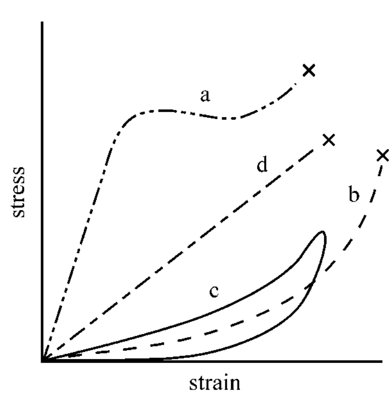


Figure 2. Shape comparison of stress–strain curves. a) The general S-shaped curve of artificial materials. b) The J-shaped curve of 3DFs, soft biological tissues (such as skin and muscle) and fibrocartilaginous tissues. c) Hysteresis-loss curve for biological materials. d) The linear elasticity of artificial materials that obey Hooke's law and Newton's law. X is the break point.

3DFs have been reported to show similar J-shaped profiles in their stress–strain and hysteresis curves to those of biological discs, and to have good biocompatibility, bonding, and anchoring capabilities with both bone and articular cartilage tissues.[17] Surface modifications of the 3DF described enhanced the bonding strength and osteoconductivity. Bio-inert and ultrahigh strength ultrahigh molecular weight polyethylene (UHMWPE) biomaterials have been used in vivo for over 20 years as part of artificial hip and knee joints. 3DFs avoid the general problems associated with UHMWPE block devices—in which wear debris that arises from mutual friction with metallic parts can cause a destructive osteolytic reaction in the long term—because their flexible construction and J-shaped yielding behavior alleviate the loading forces. No wear debris has been observed in the 3DF discs[18] in contrast to the collision and friction that has been reported between the hard surfaces in artificial hip and knee joints.[19]

The fiber arrangement of 3DF discs that were physically characterized and pre-clinically evaluated in sheep and baboons are shown in Table 1. Type a was tested in vitro to assess its long-term dynamic mechanical properties in humans. Types b,c were tested in vivo in baboons, after pre-clinical experiments of type b in sheep.[20,21] Types d,e, as shown in Table 2, are clinically suitable for total-lumbar and cervical-disc-replacement arthroplasty, respectively, in humans.

The stand-alone 3DF discs described incorporate bioactive bioresorbable pins (type b) or both pins and porous or perforated scaffolds (types c–e). The original mobility of the 3DF implants is maintained as a result of the gradual loss in mechanical strength of the pins and scaffolds through biodegradation after strong bonding has occurred with the disc bodies.

The performance of these discs in total disc-replacement arthroplasty was investigated in a non-human primate model—the baboon[22] (Figs. 3a,b)—after initial investigations in sheep. Histopathological and histomorphometric analyses of the undecalcified tissue in the paraffin-embedded systemic reticuloendothelial tissues showed no significant pathological changes after six months. The high biocompatibility and osteological integrity of the implants was confirmed by macroscopic,

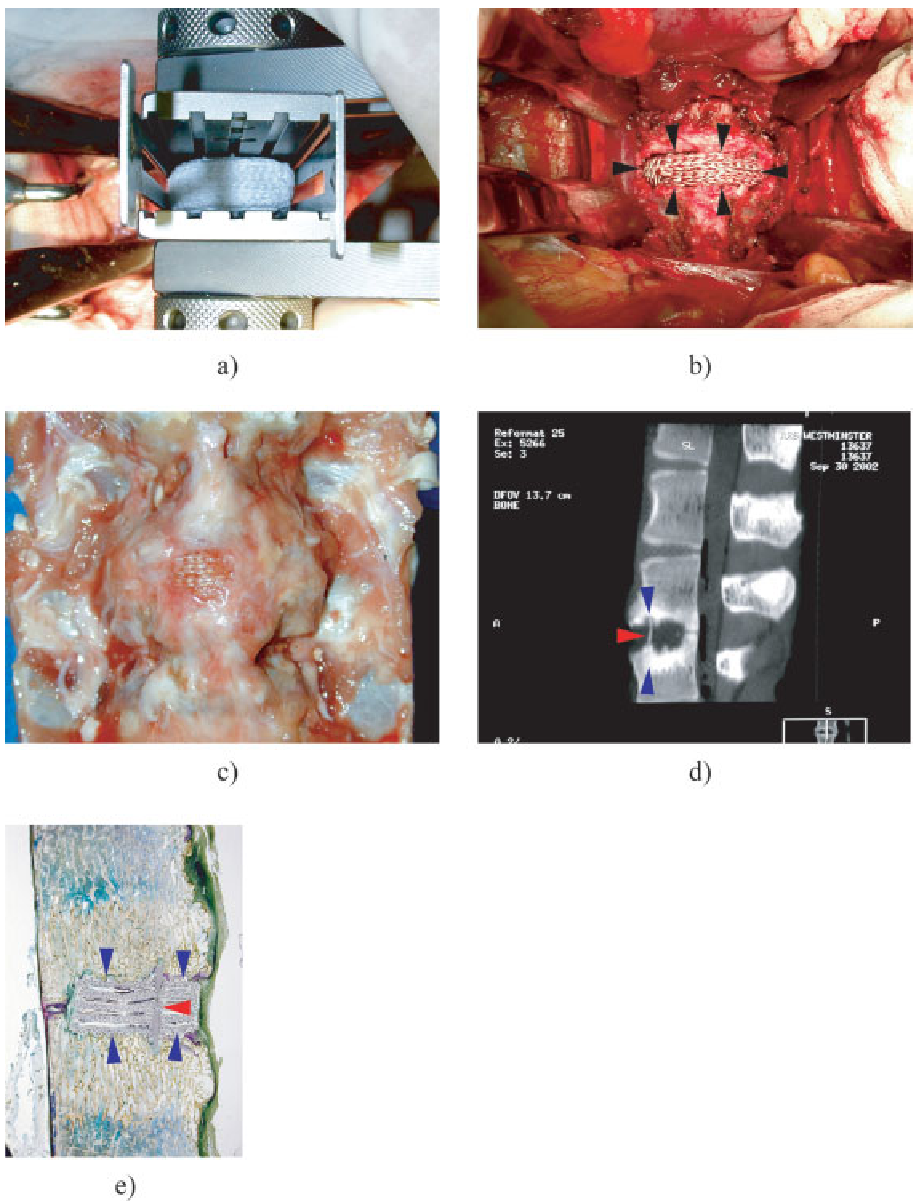


Figure 3. Surgical approach and implantation. a) The anterior transperitoneal surgical approach for total disc-replacement arthroplasty in the baboon spine at level L5–L6, using appropriate instrumentation. b) A 3DF disc embedded in the vertebral space, which has made firm contact with the remaining partial endplates and the external annulus fibrosus. c) A macroscopic view of 3DF disc c in Table 1 after six months: the systemic histopathology shows no significant pathological changes, and all of the tissues appear normal. d) A radiographic view at the L5–L6 level after six months shows connected new bone growth around the upper and lower surfaces of the 3DF disc body. e) A light microscopic view of 3DF disc b in Table 1 after six months shows no significant histopathological changes; good bonding (blue arrows) has been achieved on the resected surfaces of the disc body. A red arrow shows a bioactive, bioresorbable pin for standing alone.

microradiographic, and light microscopic observations after six months (Figs. 3c–e). There was no evidence of substantial cellular reactions, inflammatory responses, or other significant histopathological changes. The range of motions (ROMs) of the 3DF discs (types b,c in Table 1) were equivalent to those of AcroFlex discs, and were inferior to intact discs only in bilateral bending motion. At present, we are investigating more flexible discs with improved bilateral bending motion in trials with non-human primates.

Changes in the hysteresis-loss curves during a cycle of compulsory movement consisting of seven different stresses, with a 0.3 s recovery interval between each load, were investigated (Fig. 4).[23,24] We confirmed that the 3DF model of the human artificial disc surpassed expectations of its mechanical properties by showing bioanalogous, J-shaped stress–strain and hysteresis-loss behaviors. It also maintained dynamic mobility for the equivalent of 30 years.

The 3DF disc remained intact for approximately 8×10^5 cycles of simulated stress (about 5 600 000 stresses). All hysteresis loss decreased slightly after approximately 8×10^5 cycles as a result of the dissolution of strains that arose during the reaction to the periodic stresses. This phenomenon resembles the relaxation behavior of soft biological tissues and might be unique to flexible 3DF fabrics among artificial biomaterials. Subsequently, there was no significant change in the relationship between strains and stresses, and J-shaped hysteresis-loss curves resembling those of biological discs were maintained for 9×10^6 cycles (6.3×10^7 stresses, equivalent to natural biological movements for 30 years). The test is ongoing, and will continue until it reaches 1.0×10^8 stresses (equivalent to in-vivo stresses for about 50 years) in order to determine the limit of the response to long-term (to approximately one hundred million movements during the supposing longest lifetime after operation) periodic loadings. A slight modification to the fiber arrangement of the 3DF disc, as shown in parts d,e of Table 2, aims to improve the ROM values. Discs with a range of sizes and scaffold arrangements are necessary for use in total-lumbar (L4–L5 level) and cervical (C3–C4 level) disc-replacement arthroplasty for humans, to allow variation in the fixation method used and the synchronization of movement with the remaining intact disc portion.

The addition of growth factors, including cytokines such as bone morphogenetic protein (BMP) and basic fibroblast growth factor (b-FGF), in bioactive and bioresorbable porous

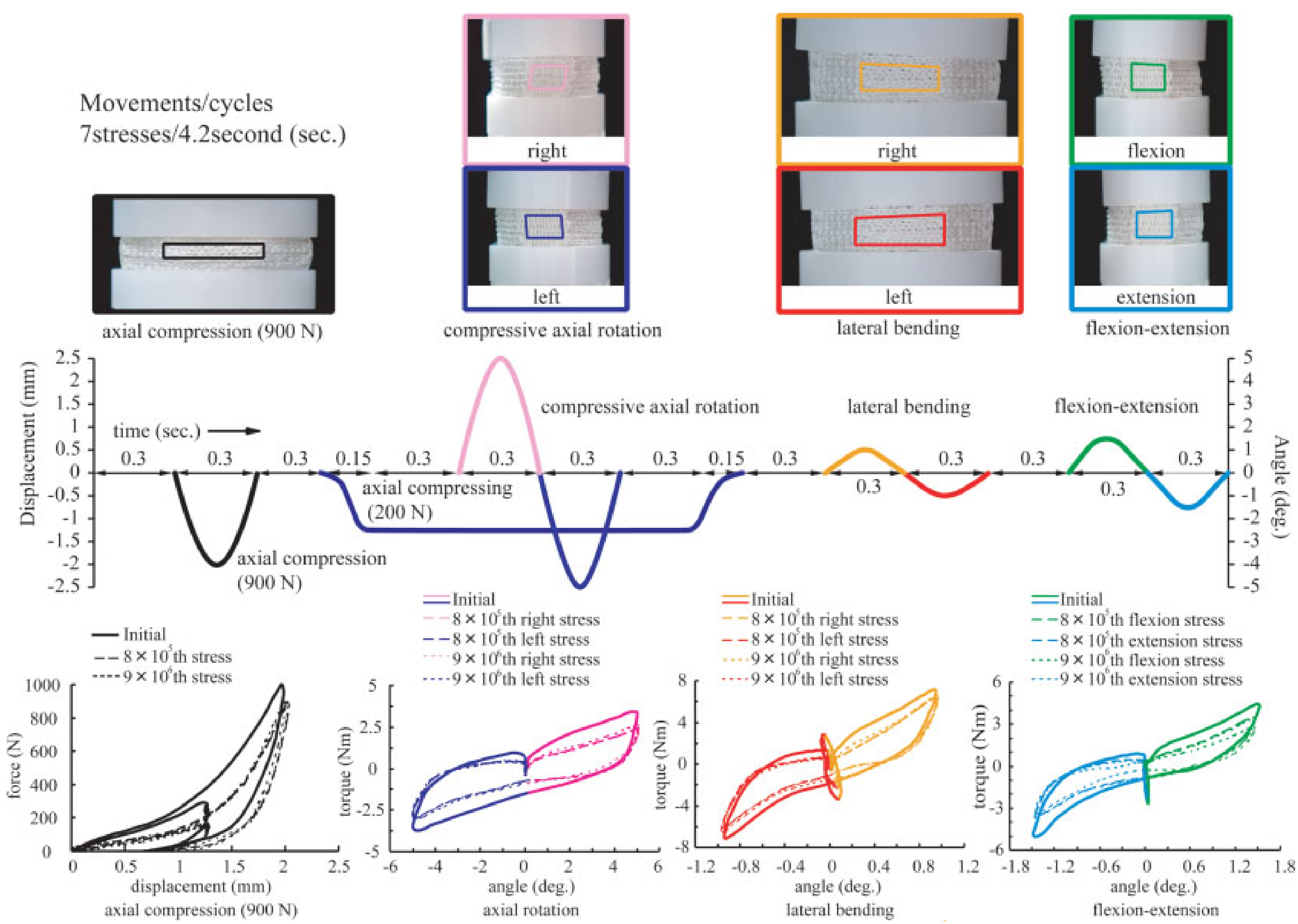


Figure 4. Change in hysteresis loss and the maintenance of dynamic motion in a 3DF disc during a simulated 30 year in vivo period under harsh, dry conditions. The 3-DF disc kept the same profiles as those for 10 and 20 year in-vivo periods. The strain change in each hysteresis-loss curve in response to a given stress is shown as a component of the total cyclical motion that accompanies each distortion of 3DF disc.

scaffold sheets attached to the upper and lower surface of the 3DF disc will be effective in promoting the growth of new bone or cartilage and ensuring a stand-alone system through reliable bonding between the 3DF disc and the endplates and disc bodies.

3. Conclusions

In this paper, we have demonstrated a novel artificial disc system that is suitable for clinical use in replacement arthroplasty. The disc is composed of a three-dimensional fabric with a triaxial fiber alignment that confers high biocompatibility and biomimetic stress–strain behavior. It has superior properties compared with conventional implants and improves on biological intervertebral discs by eliminating the risk of rupture and delamination.

An alternative method for the treatment of spinal disorders is the use of new technologies based on tissue engineering to restore degenerating tissues. However, these techniques are not universally applicable and still have several limitations. For example, tissues that are cultured and proliferate ex vivo cannot always regain the same shape as that of the removed tissue. Also, bioengineered tissues do not always have the physiological and biomechanical qualities necessary for successful transplantation into the defective site. In other words, because normal organs have a life history including cell formation, metabolism, growth, and maturity, and take on specific biomechanical and physiological roles with respect to their surrounding tissues, it is unlikely that newly regenerated tissues will be capable of performing all of the functions of a mature tissue when transplanted. Many serious and complicated issues remain to be solved with respect to the regeneration of flexible articulated fibrocartilages, such as intervertebral discs, that are subjected to complex and dynamic mechanical loadings for long periods of time in vivo. Therefore, the need for high quality artificial implants is likely to continue for the foreseeable future. So, finally, we return to a fundamental principle in the design of flexible biomaterials—"better bend than break".[25] The stand-alone 3DF disc system described here is one of the best examples of this tenet in the field of third-generation biomaterials[26] and will greatly benefit patients suffering from serious disc disorders in the near future.

4. Experimental

3DF Architecture: The 3DFs had off-angle fiber alignments, in which the fibers were intersected obliquely at an angle of 45° in the warps (*v*-axis) and wefts (*w*-axis) with respect to the basis *x*-axis (*y*-axis). They were semi-automatically woven from bioinert ultrahigh molecular weight polyethylene (UHMWPE) multi-filaments. These had a diameter of 12 μm/filament (which is equivalent to the diameter of the fibrillar bundles in the lamellae of biological lumbar vertebral discs)[27], a linear density of 192 filaments/220 dtex (mass in grams per 1×10^4 m of yarn), and a total cross-sectional area of 2.17×10^{-4} cm^2. The UHMWPE multifilaments were coated with a linear low-density polyethylene (LLDPE) (coated thickness 92 μm) to bind them into a flexible monofilament (diameter 350 μm, tensile strength 7.6 kgf, (where 1 kgf = 9.806 N)); this prevented the loosening of the fiber into thin individual filaments, even after prolonged alternate loading with various forces. The properties were controlled by altering the thickness and number of fibers in each of the *x*-, *y*-, and *z*-axes (the size, distribution, and arrangement of filaments in the fabric), and the angles of crossing in the fiber alignment. The bioinert UHMWPE avoided ossification in the 3DF body and mobility was retained; these properties are similar to those of the central annulus pulposus of the human disc. Surface modification of filaments in the upper and lower external layer of the 3DF disc was carried out by corona-discharge oxidation to increase the hydrophilic properties of the disc (the contact angle with water was reduced from 70° to 33°) and by spray treatment with particulate hydroxyapatite (average particle diameter of about 3 μm) to a depth of about 2 mm from the surface (density about 20–30 g cm^{-3}) to enhance the osteological bioactivity.

Design of Bioactive Bioresorbable Pins and Scaffolds: The osteologically bioactive and biodegradable pins were made of a high-strength composite of particulate unsintered hydroxyapatite/poly(L-lactide) (u-HA/PLLA; u-HA, 40 wt.-%; similar devices, such as Super-Fixsorb-30, are clinically available for humans) [28,29] and protruded 1 mm from the upper and lower surfaces of the disc, to ensure full contact and firm attachment to the vertebral bodies. The pins generally lost their strength within 8–12 months, were completely degraded through hydrolysis and absorbed within 4–5 years, and were eventually replaced by new bone [30]. The pins that were used at the L5–L6 level of the baboon lumbar spine (Fig. 3) were positioned at each of the vertices of an isosceles triangle with sides of 12 mm, 9 mm, and 9 mm, to ensure reliable fixation. Comporus sheets (thickness 1 mm) filled the space between the 3DF disc and the uneven resected surfaces of the disc bodies (endplates). The porous scaffold consisted of a u-HA 70 wt.-% fraction of u-HA/PDLLA (L-lactide/D-lactide = 1:1 molar ratio) composite with interconnected pores of about 70 vol.-% fraction and a pore size of between 100 and 400 μm; this range of pore spaces is effective for osteoconductivity and promoted bone growth [31]. The scaffold sheet degrades while conducting new bone growth, and is totally reabsorbed within one year, allowing the 3DF disc to achieve relatively strong bonding with the vertebral bodies and minimizing dislocation and breakage. Subsequently, the 3DF disc completely bonded to the vertebral bodies and recovered its unrestricted mobility. Disc b, which had pins only, also had the ability to bond directly to bone as a result of a spray coating of u-HA particles.

Discs d,e have Super-Fixsorb hard perforated sheets, which leads to stronger and more reliable bonding to the disc bodies as this material has higher mechanical strength and takes fewer years to completely degrade and be replaced with natural bone.

Measurement of Hysteresis Loss and the Maintenance of Dynamic Motion: In the simulation model, the 3DF disc was fixed by UHMWPE filaments to the concave surface (depth, 2 mm) of polyethylene (PE) blocks, which represented the superior and inferior disc bodies and had the same contours as the 3DF disc, the outer surfaces of which had been treated with sticky silicone adhesives. The UHMWPE filaments were retied after every million cycles in order to avoid loosening. A cycle comprising a series of seven stresses including compression with an axial load of 900 N (height change, –2.00 mm/0.3 s), bi-torsional deformation (+5°/2.5 N m/0.3 s; –5°/2.5 N m/0.3 s) under an axial load of 200 N (height change, –1.25 mm/200 N/0.15 s), bilateral bending (+1°/7 N m/0.3 s; –1°/7 N m/0.3 s) and flexion–extension (+1.5°/5 Nm/0.3 s; –1.5°/5 Nm/0.3 s) was repeated for up to sixty-three million stresses, simulating the natural motions of a human spinal disc for approximately 30 years, by using the Model 858 Mini Bionix II Spine Simulator (MTS System Corporation, USA). A 0.3 s period was allowed between each stress, during which time the material could recover from the strain and return to its original state. The strain change in each hysteresis-loss curve in response to a given stress was calculated as a component of the total cyclical motion that accompanied each distortion of the 3DF disc. Throughout the test, textural fraying, fiber loosening in the UHMWPE filaments, and PE wear-debris of the 3DF disc caused by mutual friction were not observed.

In-Vivo Animal Tests: The surgical techniques used were those previously described for the Acroflex lumbar disc (Depuy–Acromed, Inc., Raynham, Massachusetts, USA) [22], which has an unrestricted sandwiched structure of titanium endplates and an olefin rubber core. Each animal underwent an anterior transperitoneal surgical procedure performed at the L5–L6 level of the lumbar spine, with total disc reconstruction. Post mortem analysis including the histopathological assessment of the systemic reticuloendothelial tissues was carried out, in addition to biomechanical, multi-directional flexibility testing to determine the peak range of motions (ROMs)—axial rotation, flexion–extension, and lateral bending—of the operative functional spine units. Quantitative histological analysis of the trabecular bone coverage at the interface between the 3DF disc and the endplates and disc bodies was also performed.

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