US009078756B2

(12) **United States Patent**
Gatt et al.

(10) **Patent No.: US 9,078,756 B2**
(45) **Date of Patent: *Jul. 14, 2015**

(54) **IMPLANTABLE DEVICE AND METHOD TO REPLACE THE MENISCUS OF THE KNEE AND OTHER BODY STRUCTURES**

(71) Applicant: **RUTGERS, THE STATE UNIVERSITY OF NEW JERSEY**, New Brunswick, NJ (US)

(72) Inventors: **Charles J. Gatt**, Skillman, NJ (US); **Aaron R. Merriam**, Milltown, NJ (US); **Michael G. Dunn**, Manalapan, NJ (US)

(73) Assignee: **Rutgers, the State University of New Jersey**, New Brunswick, NJ (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

This patent is subject to a terminal disclaimer.

(21) Appl. No.: **13/836,607**

(22) Filed: **Mar. 15, 2013**

(65) **Prior Publication Data**

US 2014/0031933 A1 Jan. 30, 2014

Related U.S. Application Data

(63) Continuation-in-part of application No. 12/995,930, filed as application No. PCT/US2009/045985 on Jun. 2, 2009, now Pat. No. 8,623,085.

(60) Provisional application No. 61/130,791, filed on Jun. 2, 2008.

(51) **Int. Cl.**

A61F 2/38	(2006.01)
A61F 2/30	(2006.01)
A61F 2/44	(2006.01)

(52) **U.S. Cl.**

CPC ***A61F 2/3872*** (2013.01); *A61F 2/30756* (2013.01); *A61F 2/38* (2013.01); *A61F 2002/30062* (2013.01); *A61F 2002/30112* (2013.01); *A61F 2002/30116* (2013.01); *A61F 2002/4495* (2013.01)

(58) **Field of Classification Search**

CPC A61F 2/38; A61F 2/3872; A61F 2/30756; A61F 2002/30062; A61F 2002/30112; A61F 2002/30116

USPC 623/13.12, 14.12, 23.74, 23.76

See application file for complete search history.

(56) **References Cited**

U.S. PATENT DOCUMENTS

5,158,574	A *	10/1992	Stone	264/108
2002/0022884	A1 *	2/2002	Mansmann	623/14.12

FOREIGN PATENT DOCUMENTS

EP	0372811	A1	6/1990
JP	2003-210499	A	7/2003
WO	2006/064025	A2	6/2006

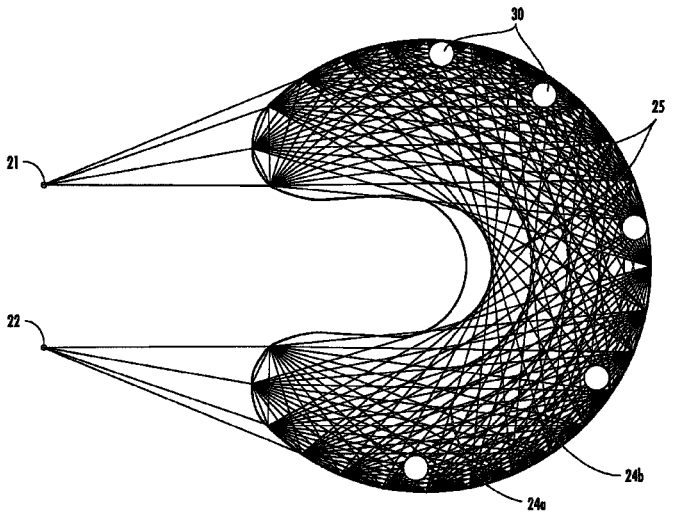
* cited by examiner

Primary Examiner — Randy Shay
Assistant Examiner — Rokhaya Diop
(74) *Attorney, Agent, or Firm* — Fox Rothschild LLP

(57) **ABSTRACT**

A meniscus implant including a c-shaped scaffold having an arcuate middle section extending between an anterior end and a posterior end. A reinforcing network of fibers independent from the scaffold is embedded therein. Fibers of said network fibers exit each end of the scaffold to form respective anterior and posterior attachment segments which extend parallel to a central axis of the scaffold. The network of fibers is configured to convert an axial compressive force on said scaffold to tensile loads on said attachment points.

22 Claims, 32 Drawing Sheets



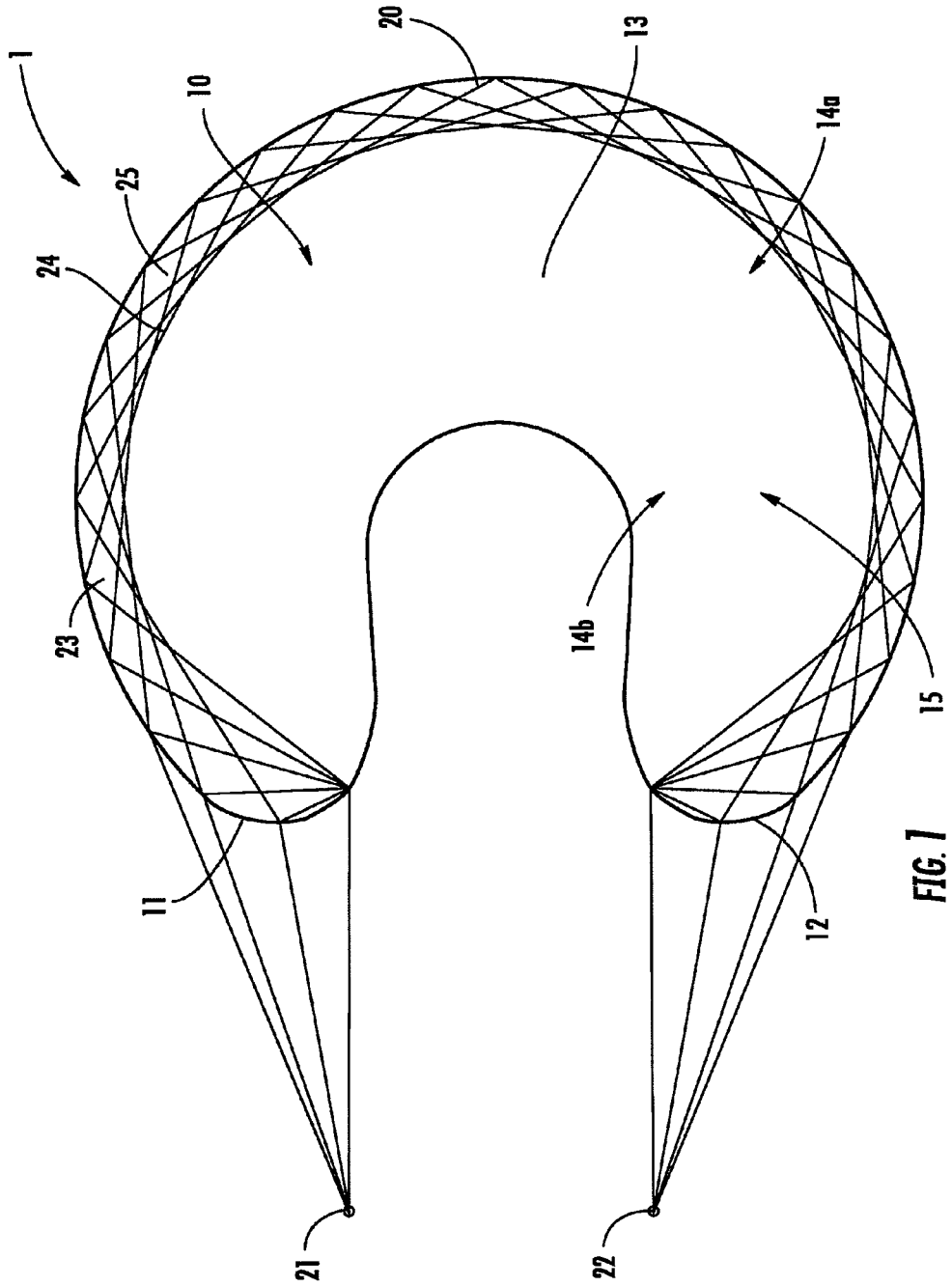


FIG. 1

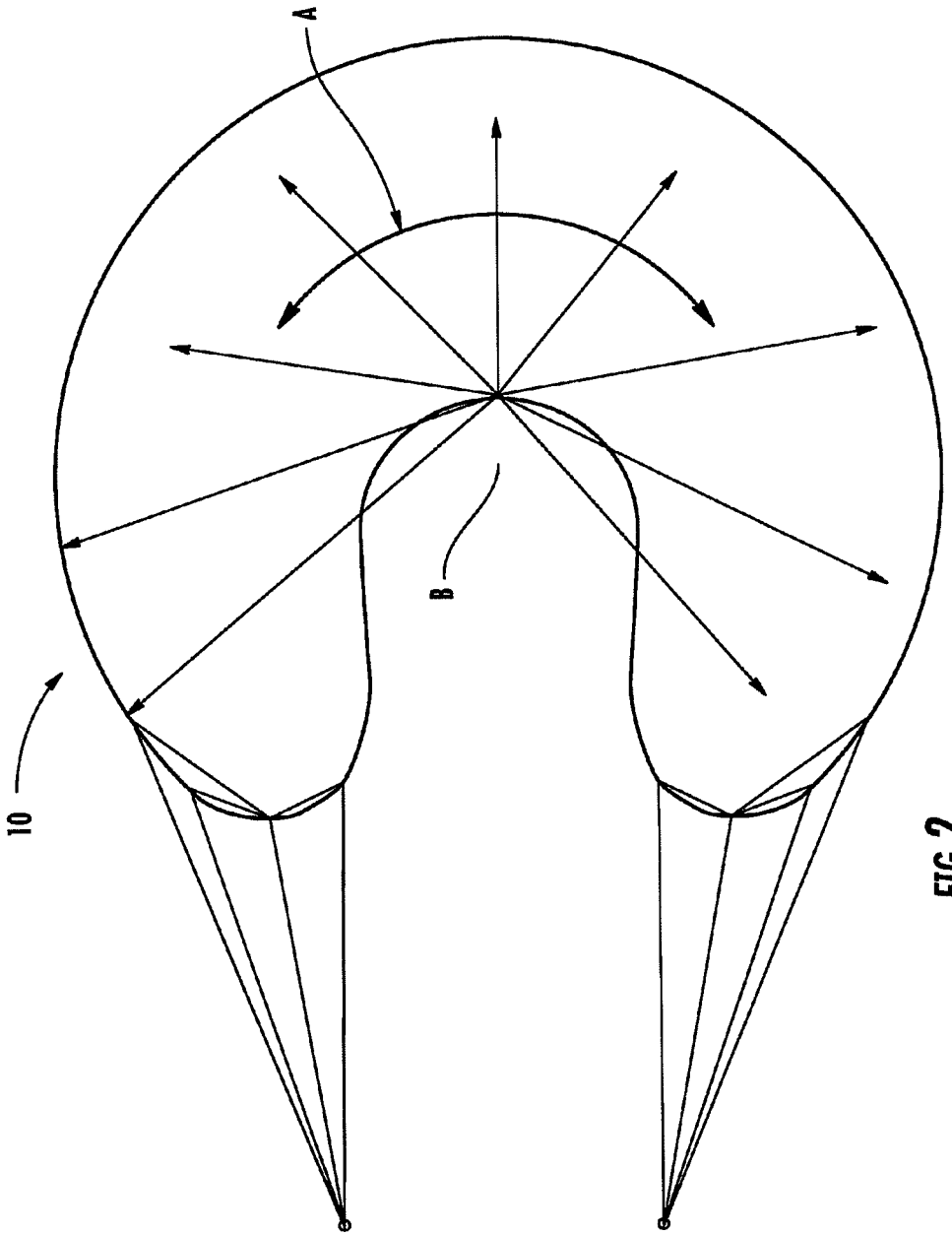


FIG. 2

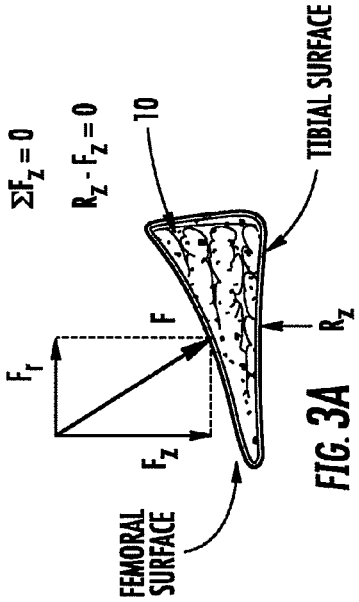

$\Sigma F_Z = 0$
$R_Z - F_Z = 0$
10
TIBIAL SURFACE
F
F_r
F_Z
R_Z
FEMORAL SURFACE

FIG. 3A

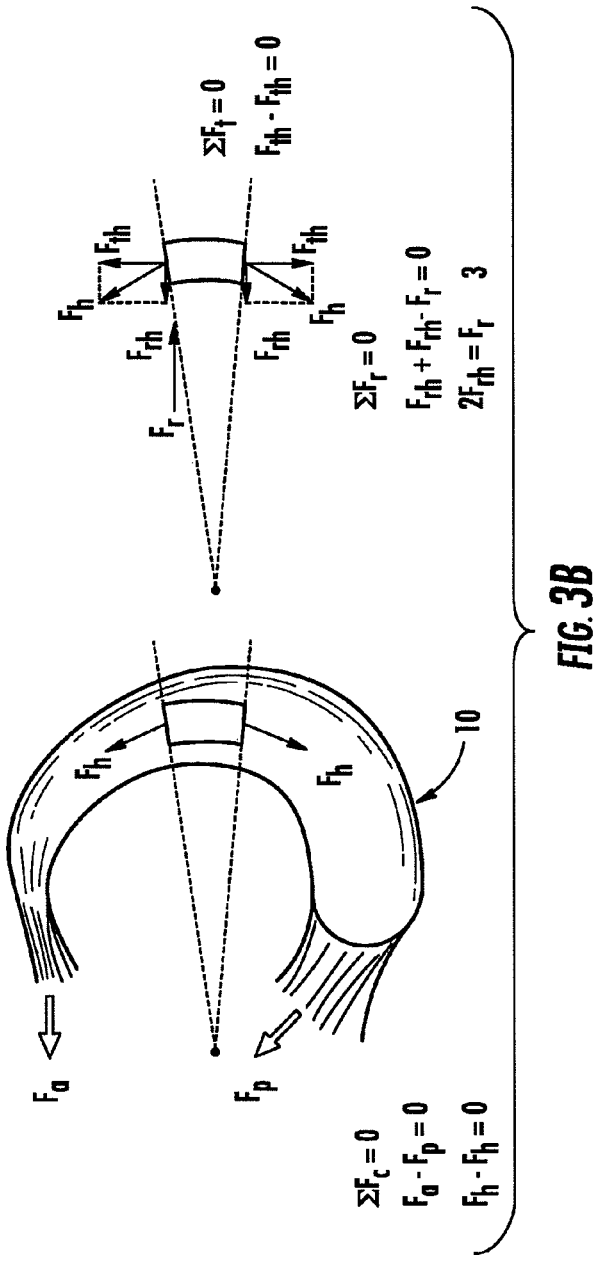

$\Sigma F_r = 0$
$F_{rh} - F_{rh} = 0$
F_{rh}
F_h
F_r
$\Sigma F_r = 0$
$F_{rh} + F_{rh} - F_r = 0$
$2F_{rh} = F_r$ 3
10
F_a
F_p
$\Sigma F_c = 0$
$F_a - F_p = 0$
$F_h - F_h = 0$

FIG. 3B

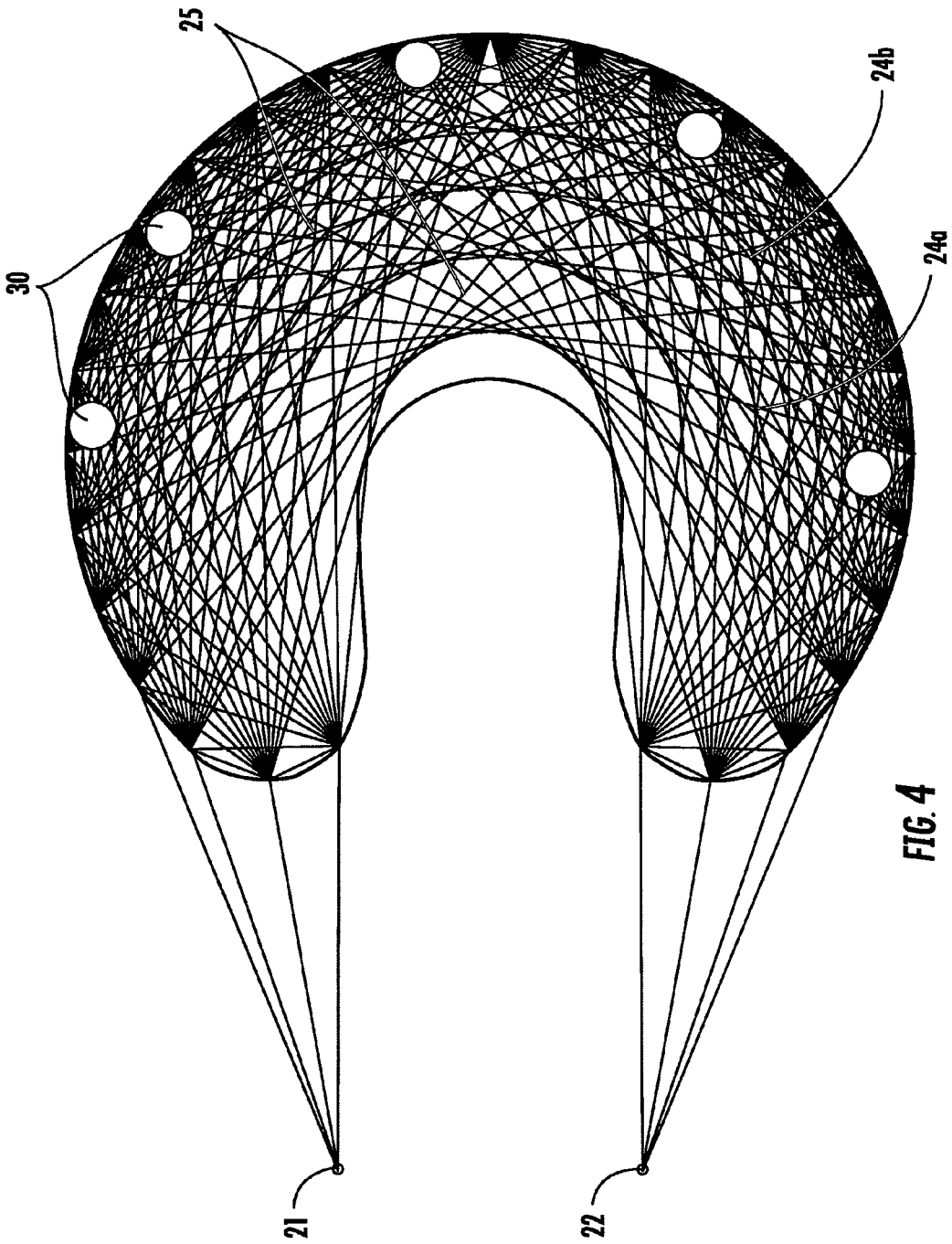


FIG. 4

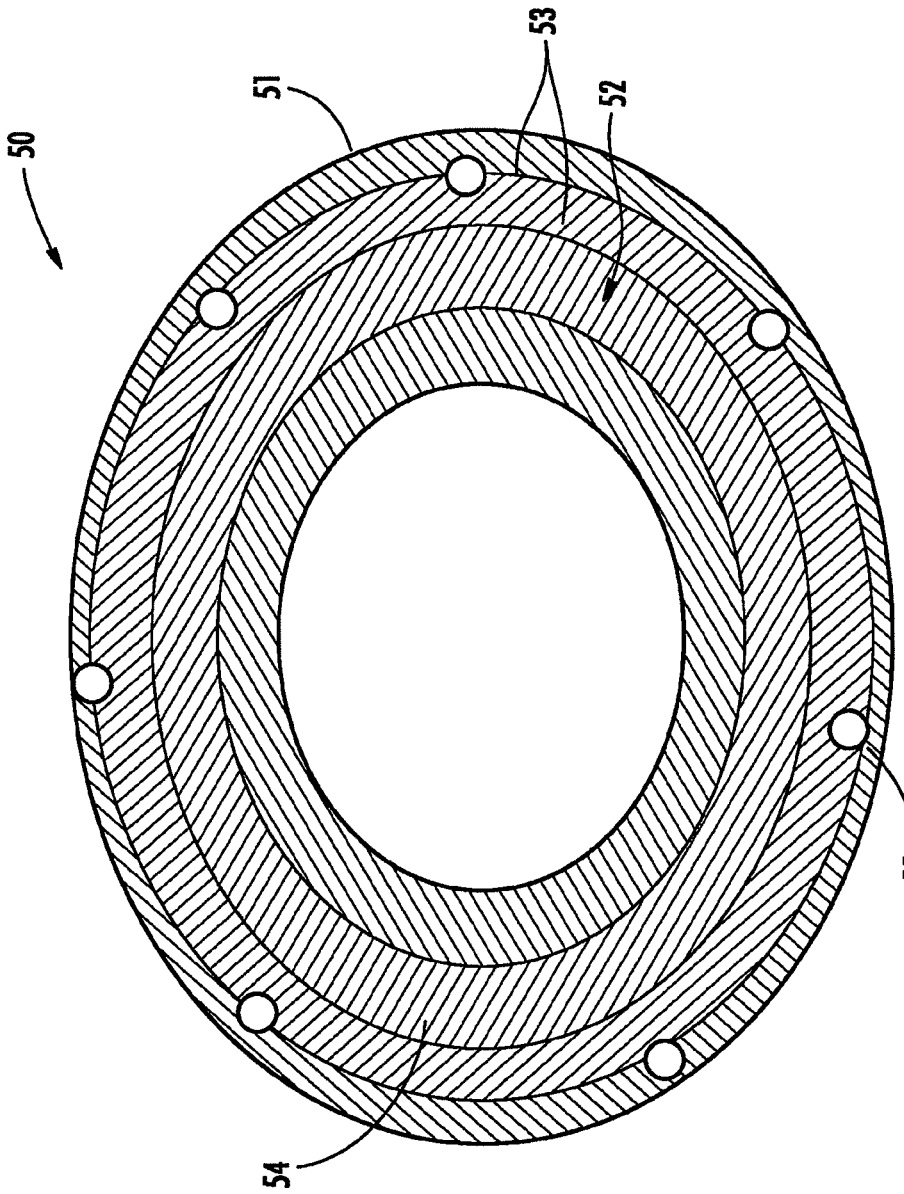


FIG. 5A

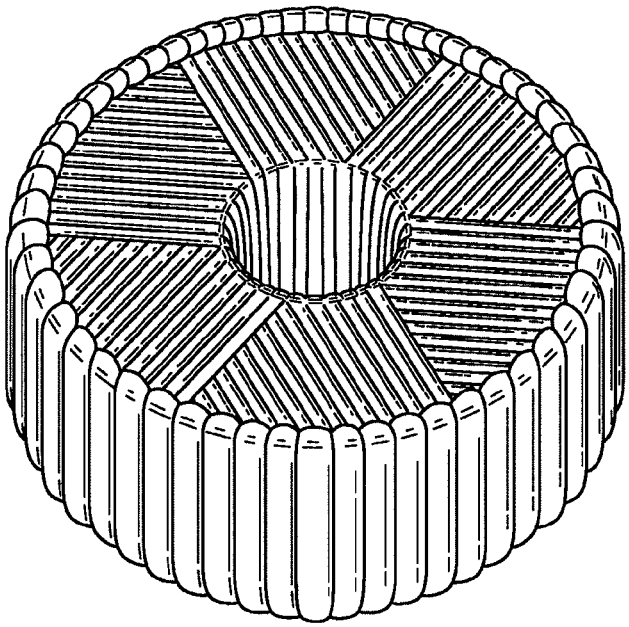


FIG. 5B

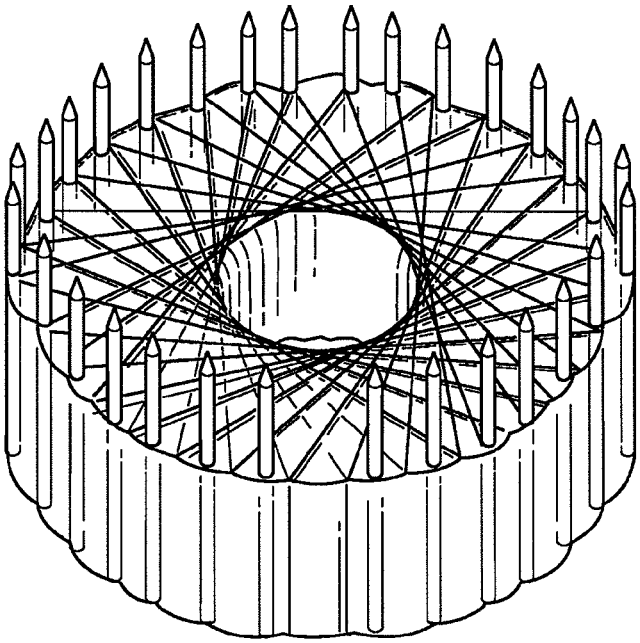


FIG. 5C

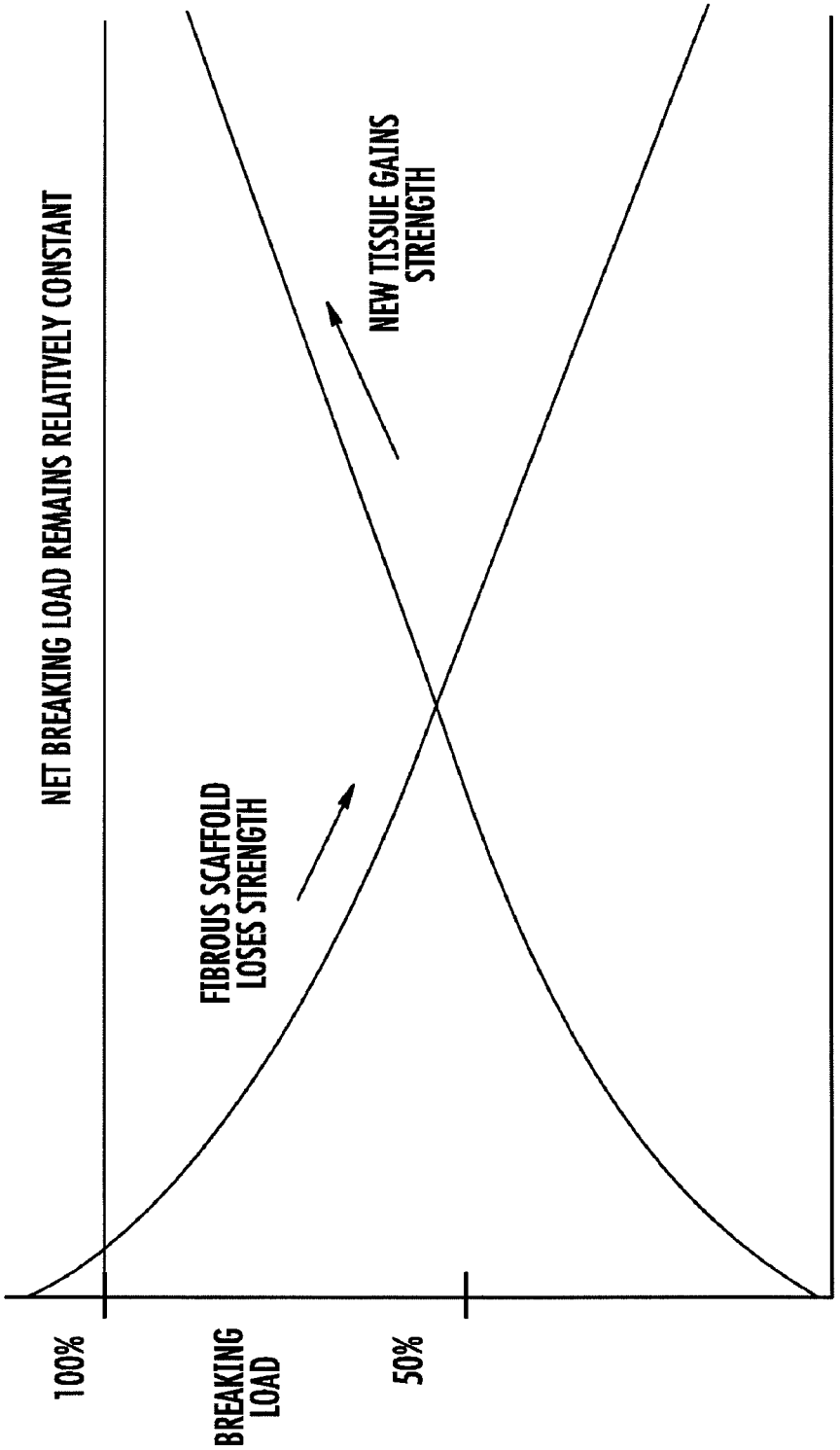

NET BREAKING LOAD REMAINS RELATIVELY CONSTANT
NEW TISSUE GAINS STRENGTH
FIBROUS SCAFFOLD LOSES STRENGTH
TIME POST-IMPLANTATION
100%
BREAKING LOAD
50%

FIG. 6

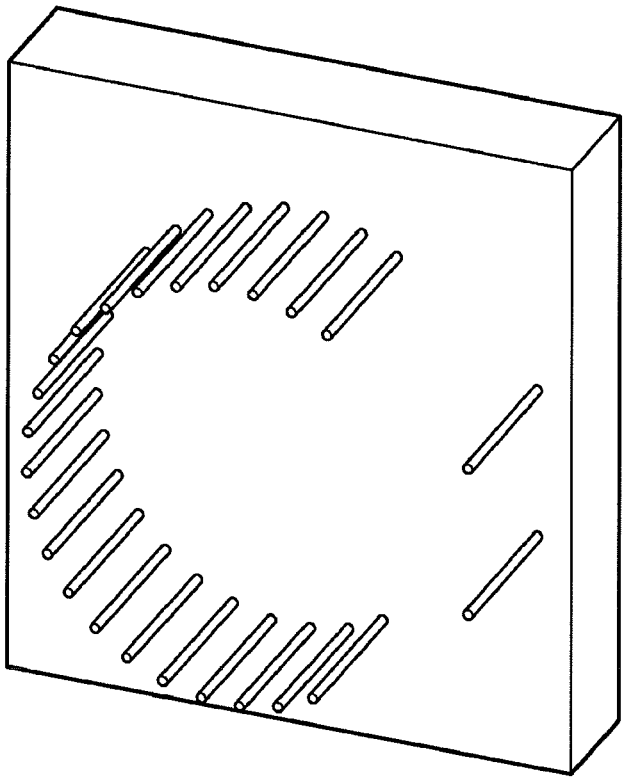


FIG. 7B

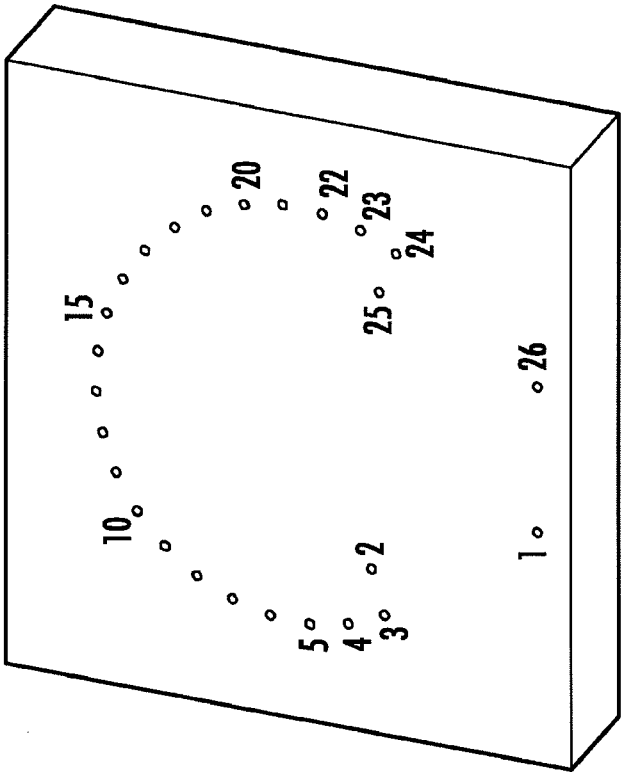


FIG. 7A

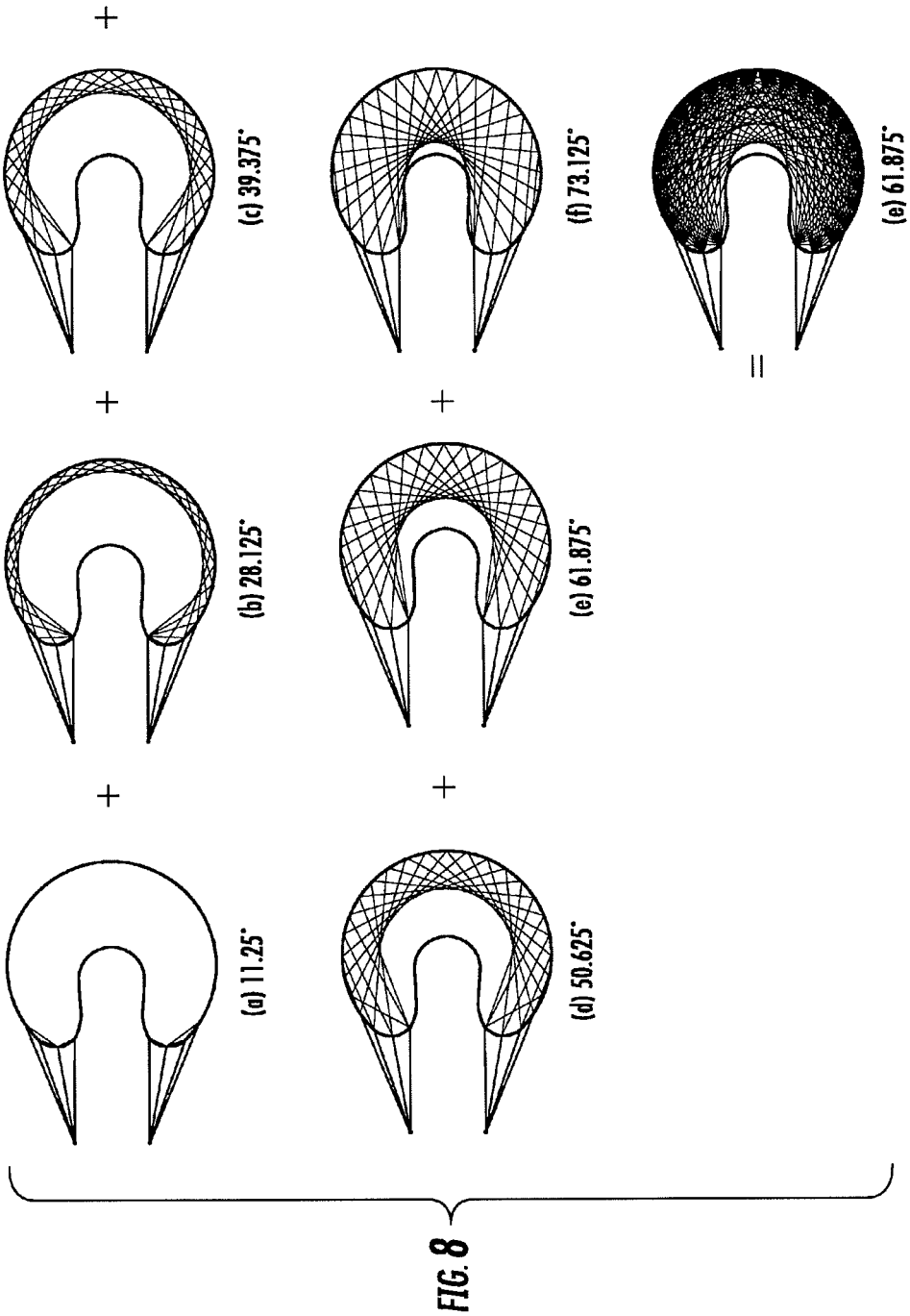


FIG. 8

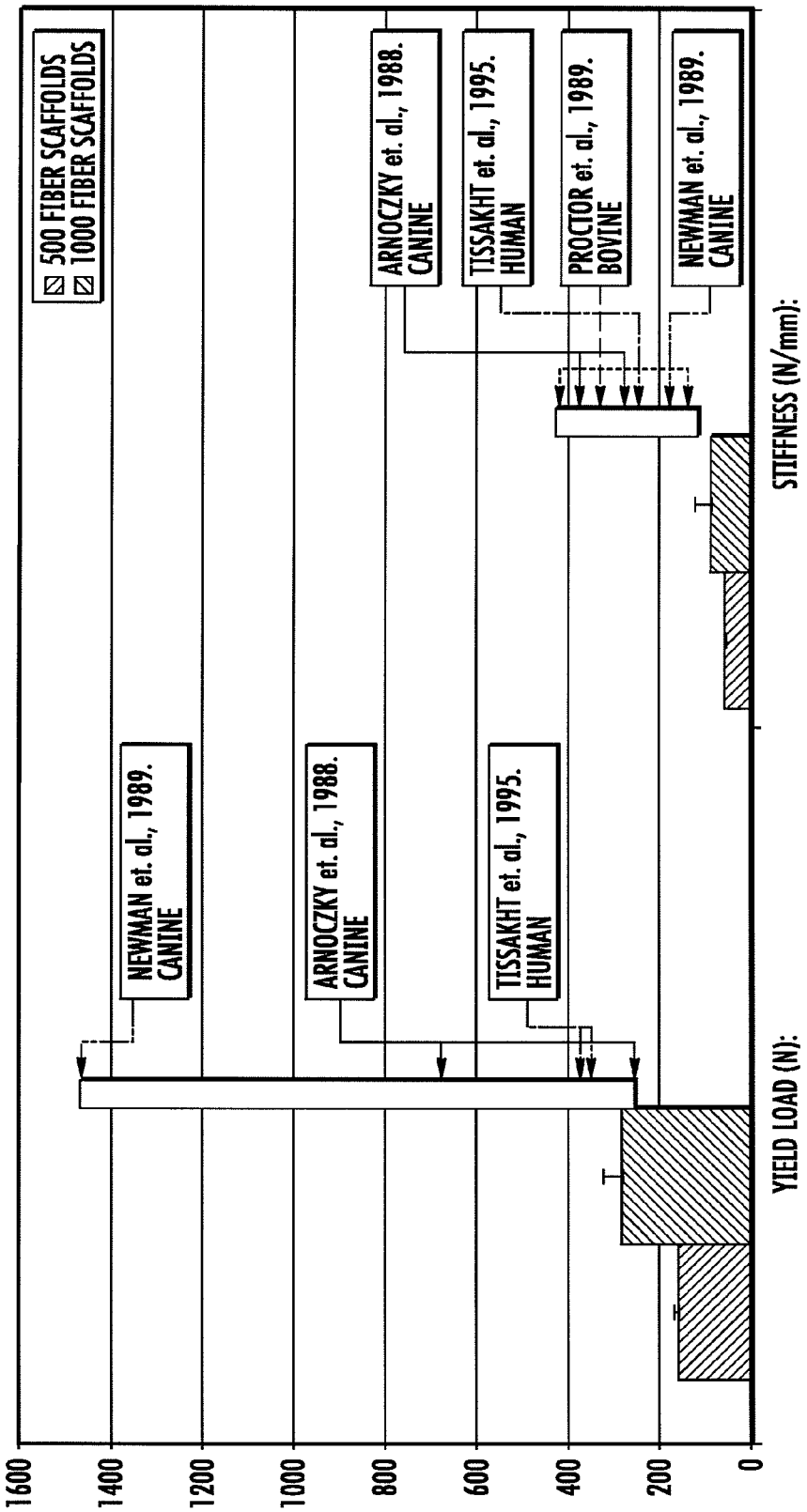

500 FIBER SCAFFOLDS
1000 FIBER SCAFFOLDS
NEWMAN et. al., 1989. CANINE
ARNOCZKY et. al., 1988. CANINE
TISSAKHT et. al., 1995. HUMAN
ARNOCZKY et. al., 1988. CANINE
TISSAKHT et. al., 1995. HUMAN
PROCTOR et. al., 1989. BOVINE
NEWMAN et. al., 1989. CANINE
YIELD LOAD (N):
STIFFNESS (N/mm):
1600
1400
1200
1000
800
600
400
200
0

FIG. 9

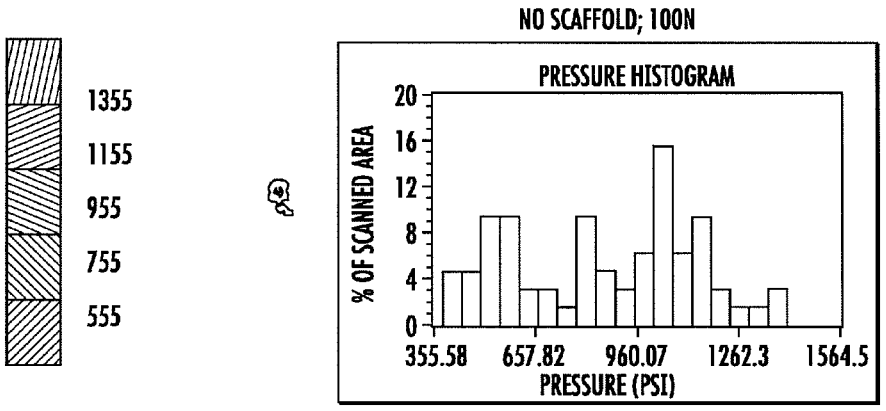


FIG. 10A

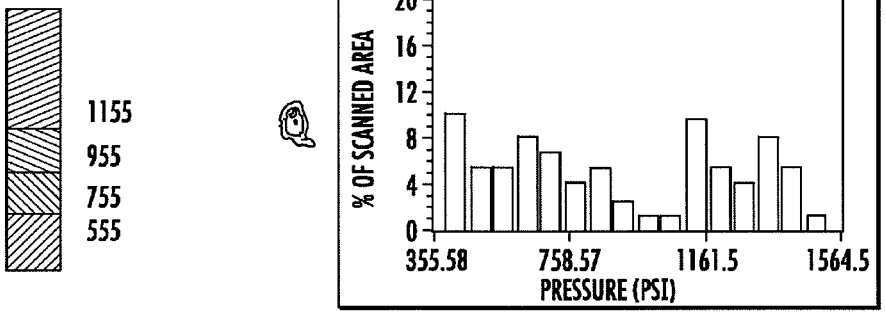


FIG. 10B

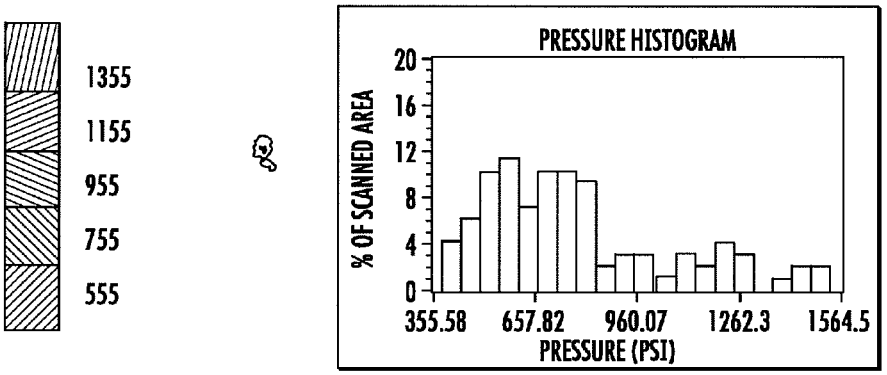


FIG. 11A

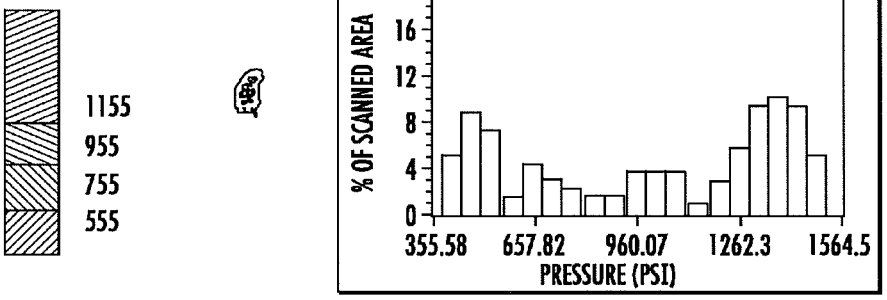
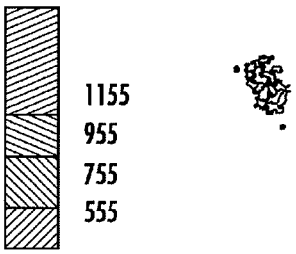


FIG. 11B



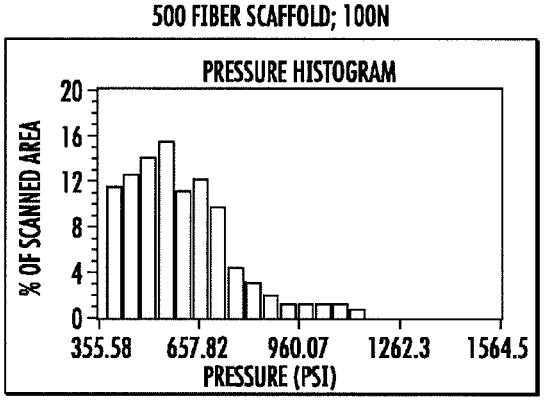
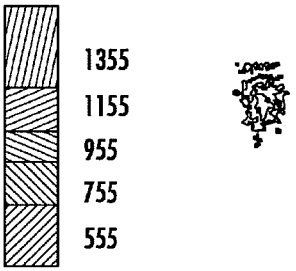


FIG. 12A



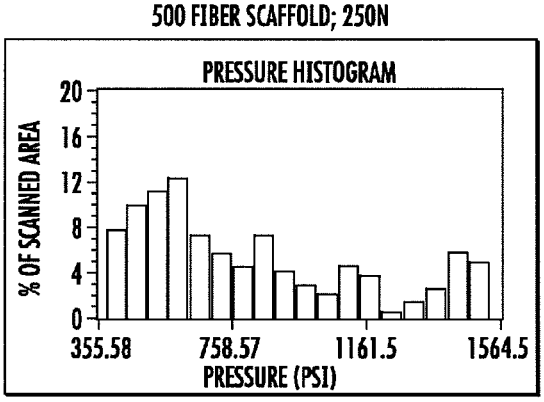


FIG. 12B

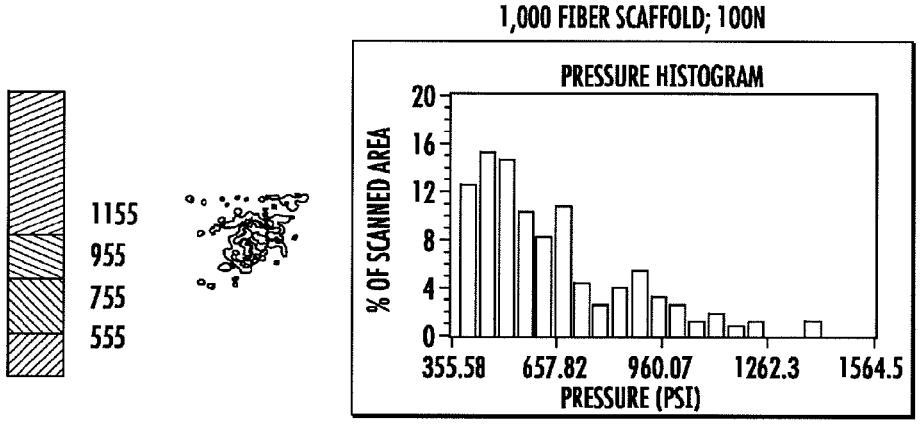


FIG. 13A

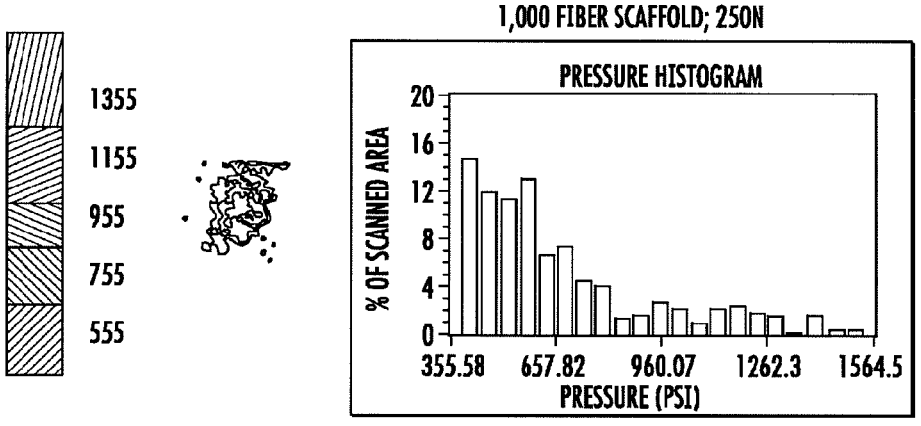


FIG. 13B

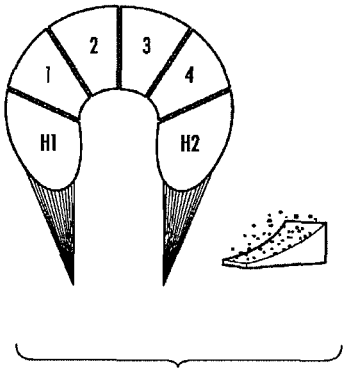


FIG. 14A

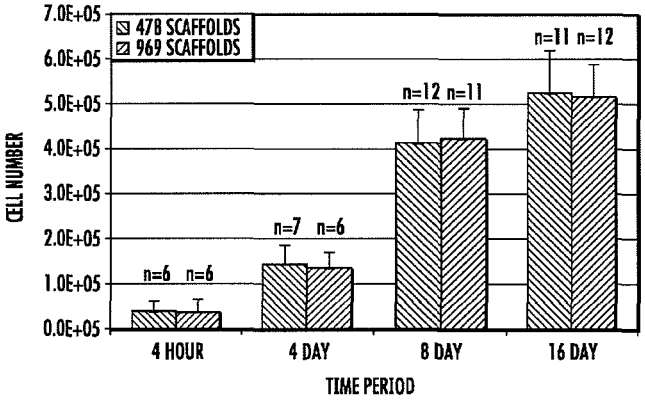


FIG. 14B

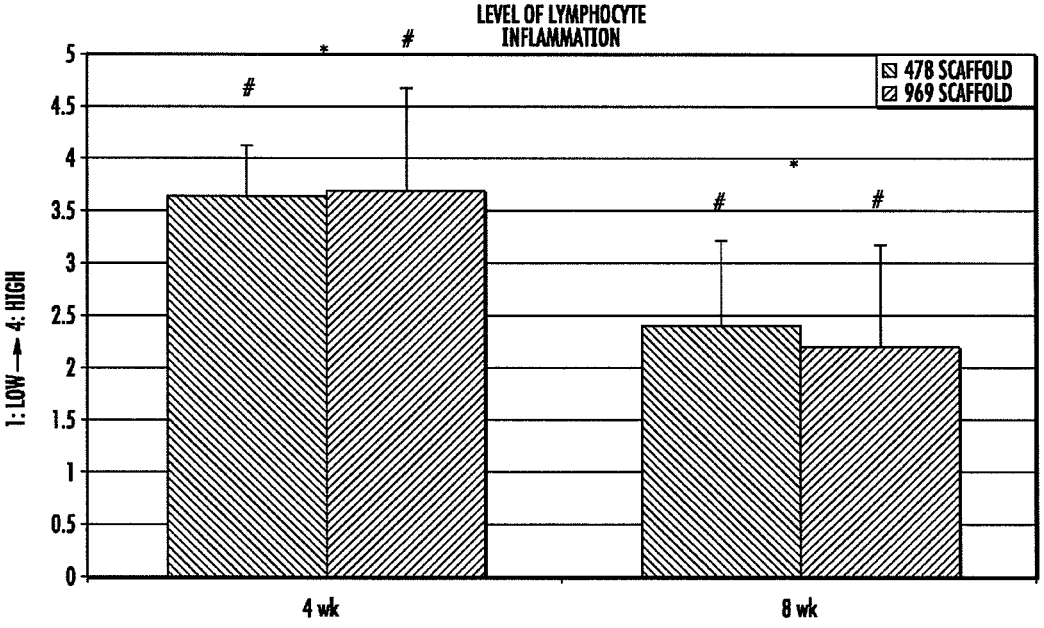

LEVEL OF LYMPHOCYTE INFLAMMATION
478 SCAFFOLD
969 SCAFFOLD
1: LOW → 4: HIGH
5
4.5
4
3.5
3
2.5
2
1.5
1
0.5
0
4 wk
8 wk
*
#

FIG. 15A

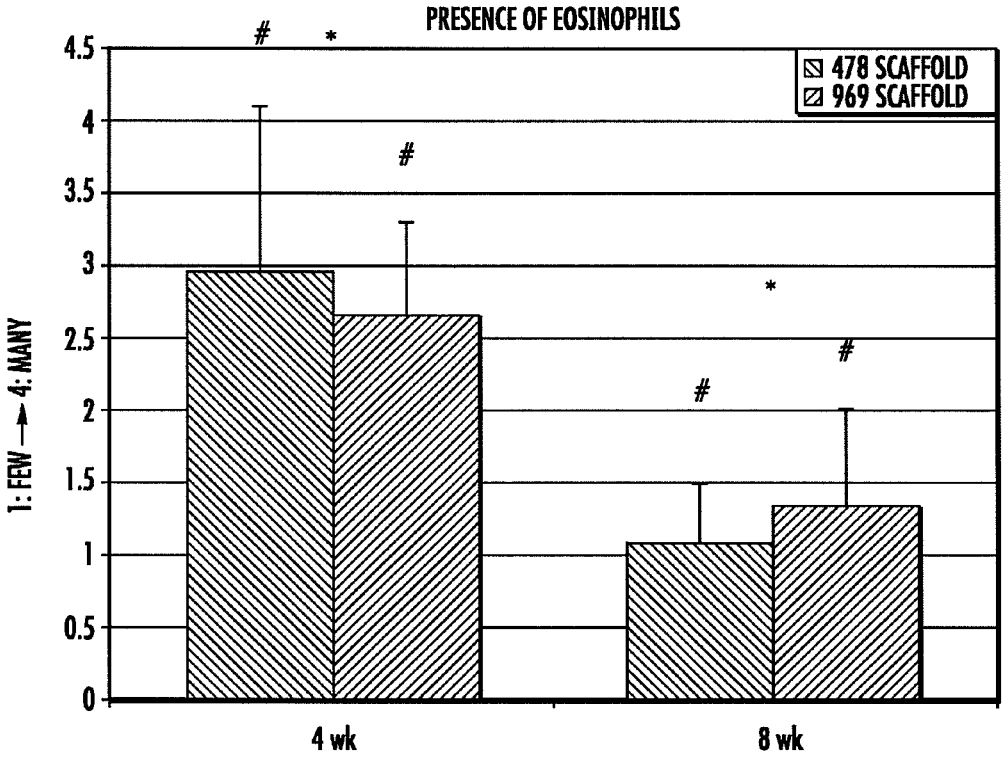

PRESENCE OF EOSINOPHILS
478 SCAFFOLD
969 SCAFFOLD
1: FEW → 4: MANY
4.5
4
3.5
3
2.5
2
1.5
1
0.5
0
#
*
#
*
#
#
4 wk
8 wk

FIG. 15B

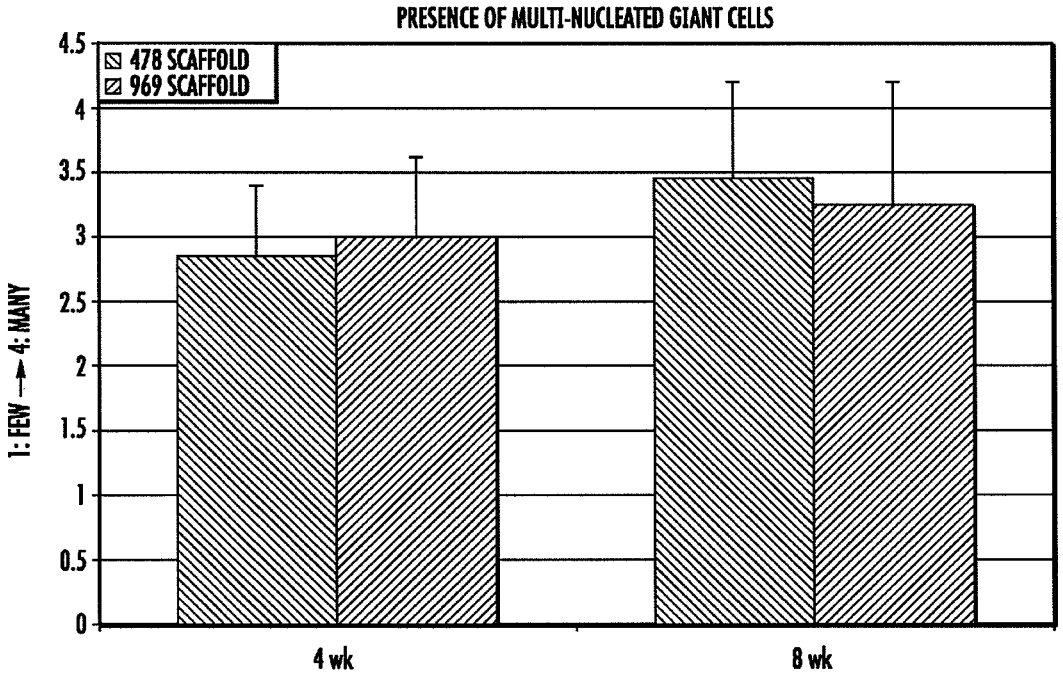

PRESENCE OF MULTI-NUCLEATED GIANT CELLS
478 SCAFFOLD
969 SCAFFOLD
1: FEW → 4: MANY
4.5
4
3.5
3
2.5
2
1.5
1
0.5
0
4 wk
8 wk

FIG. 15C

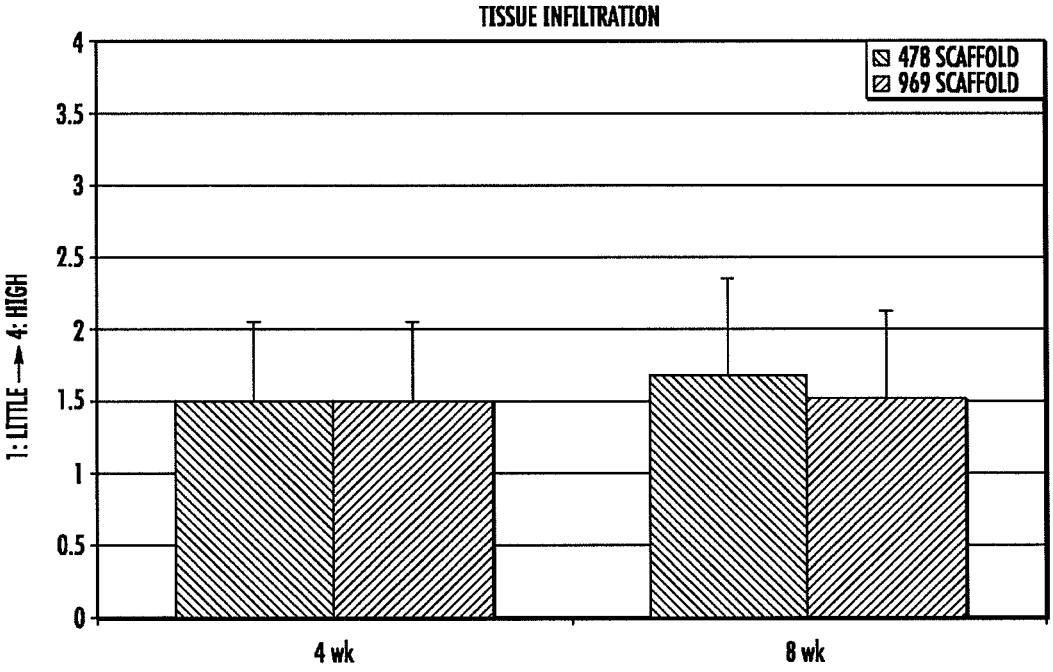

TISSUE INFILTRATION
478 SCAFFOLD
969 SCAFFOLD
1: LITTLE → 4: HIGH
4
3.5
3
2.5
2
1.5
1
0.5
0
4 wk
8 wk

FIG. 15D

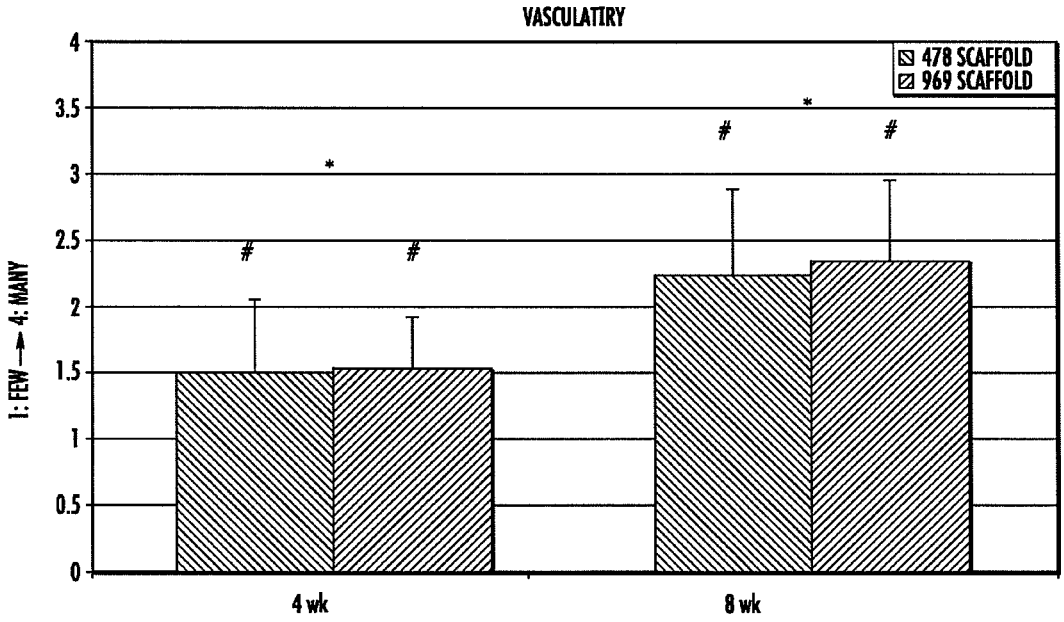

VASCULATIRY
478 SCAFFOLD
969 SCAFFOLD
1: FEW → 4: MANY
4
3.5
3
2.5
2
1.5
1
0.5
0
4 wk
8 wk
#
*

FIG. 15E

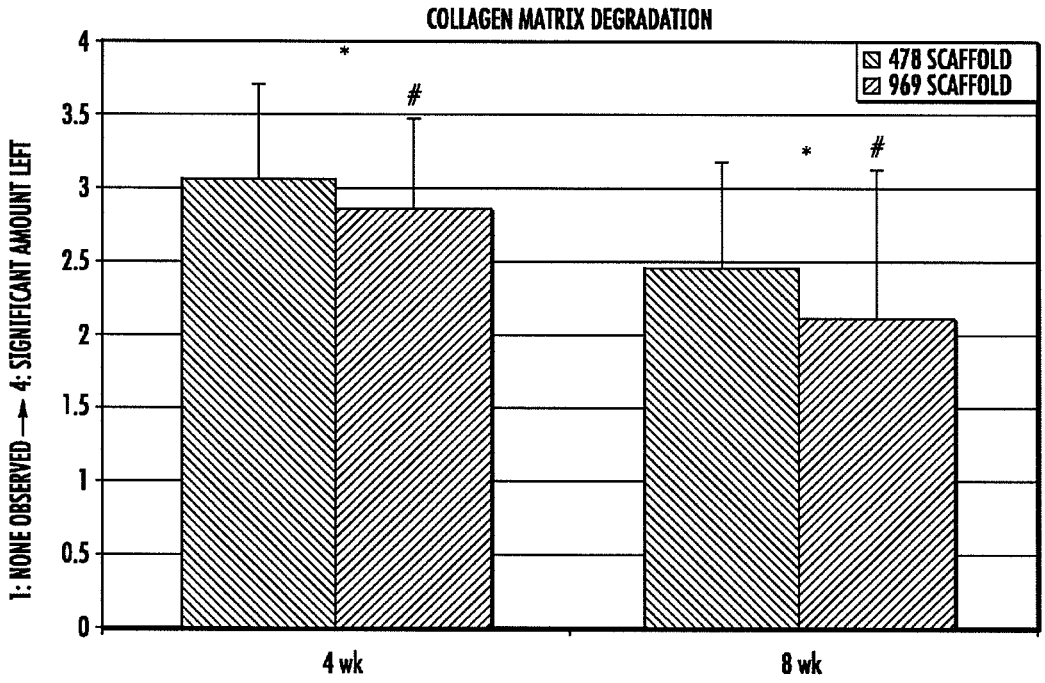

COLLAGEN MATRIX DEGRADATION
478 SCAFFOLD
969 SCAFFOLD
1: NONE OBSERVED → 4: SIGNIFICANT AMOUNT LEFT
4
3.5
3
2.5
2
1.5
1
0.5
0
*
#
*
#
4 wk
8 wk

FIG. 15F

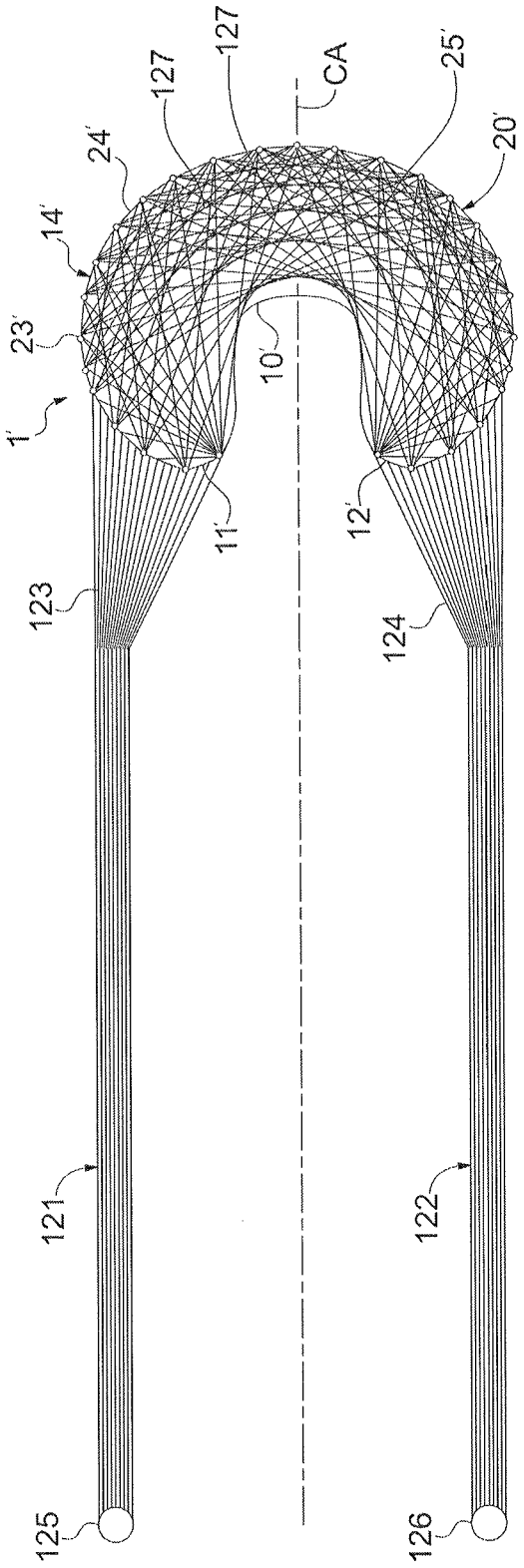


FIG. 16

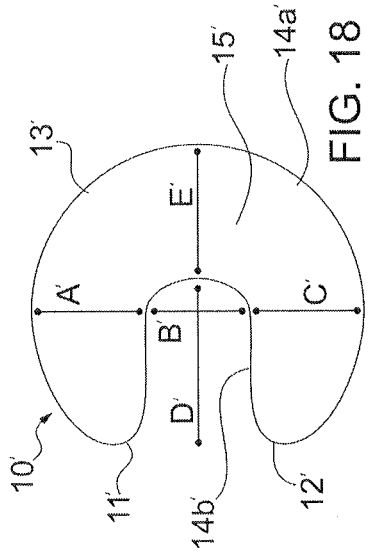


FIG. 18

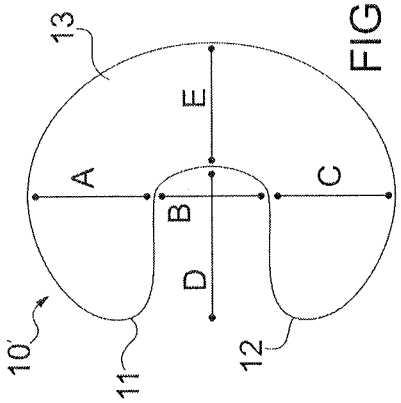


FIG. 17

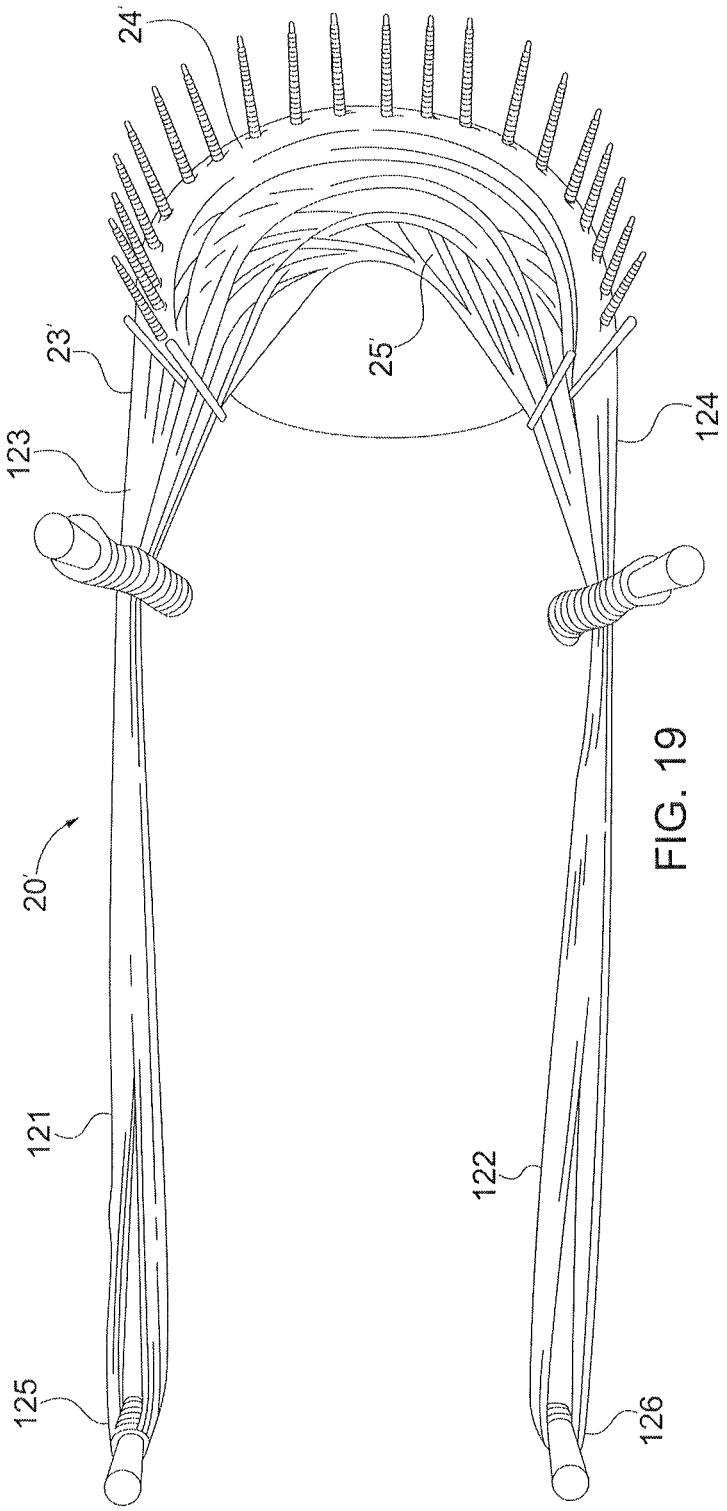


FIG. 19

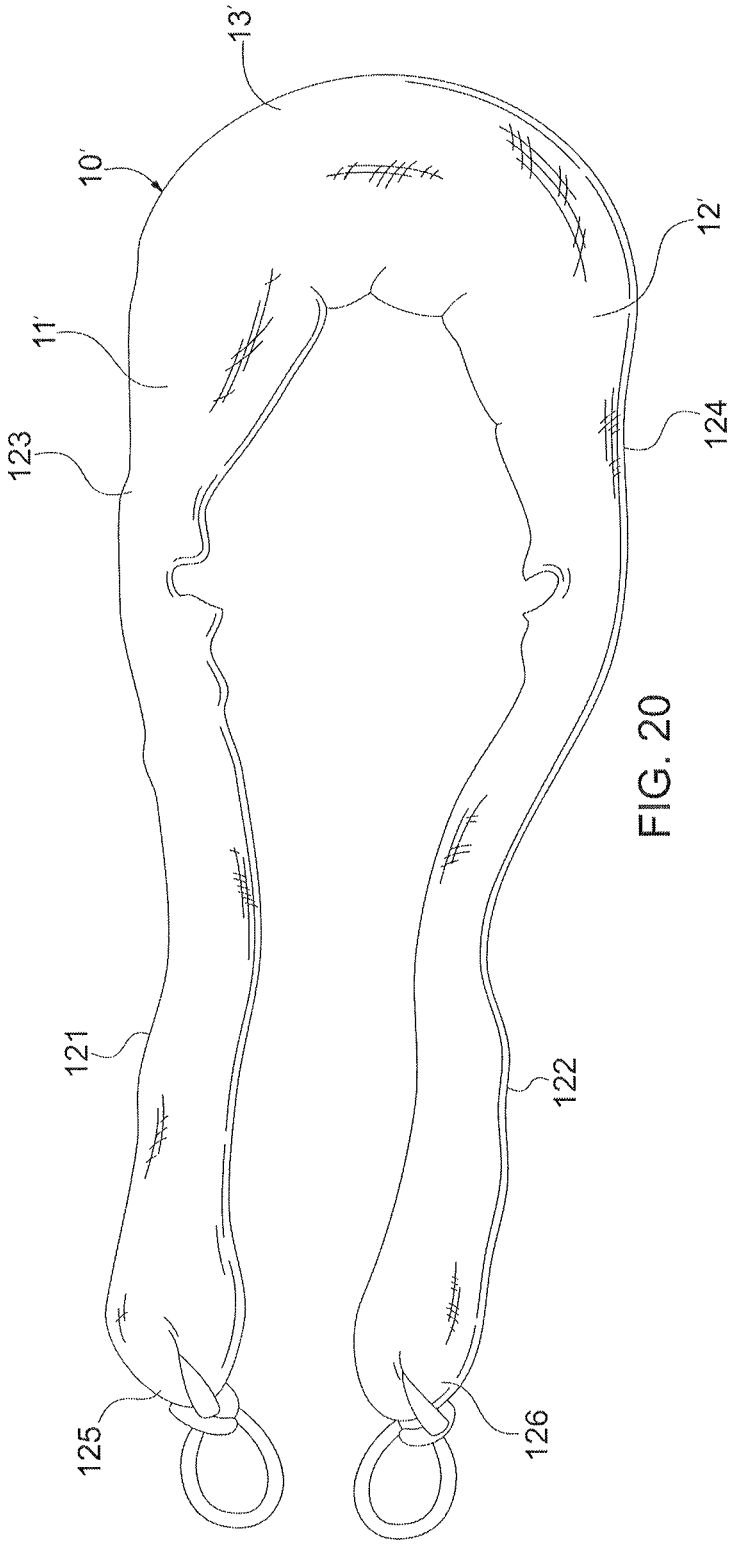


FIG. 20

Fig. 21A

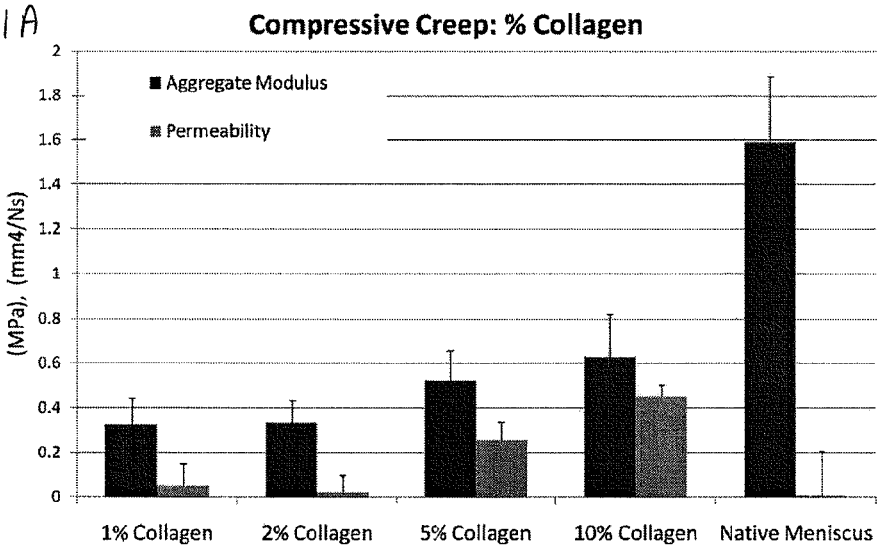


Fig. 21B

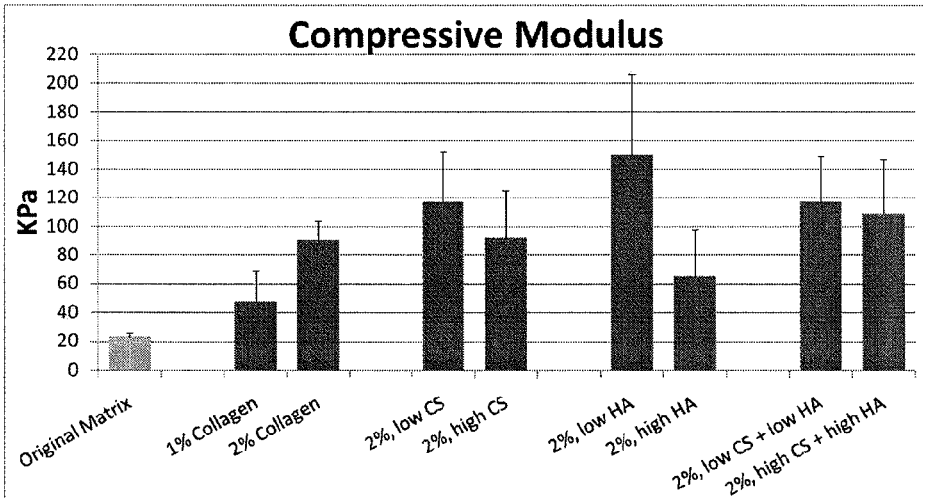


Fig. 21C

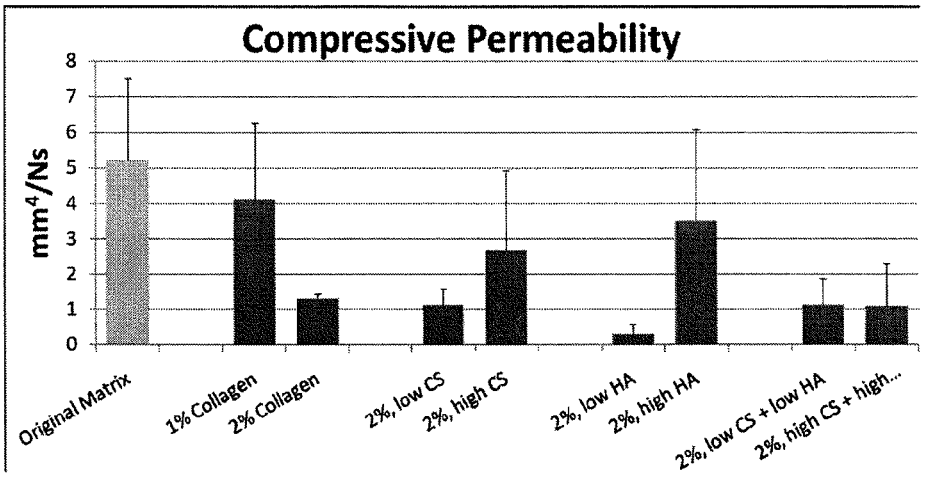


Fig. 22A

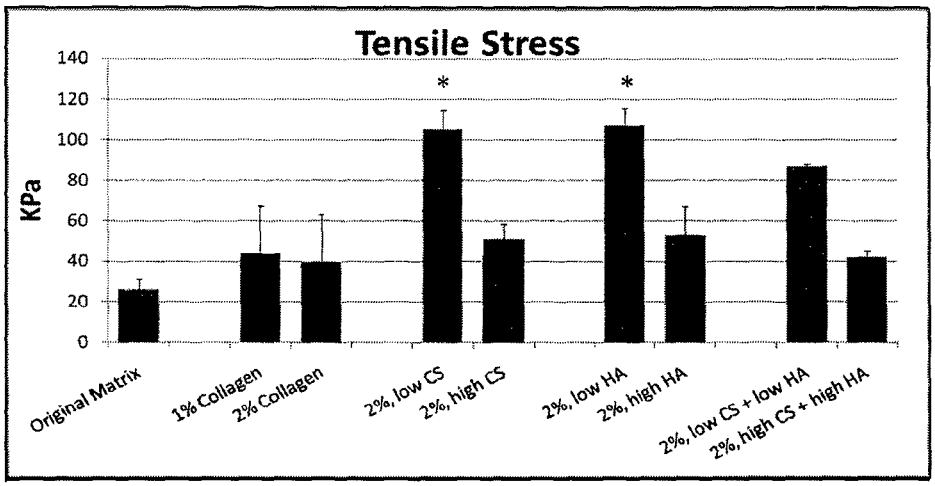


Fig. 22B

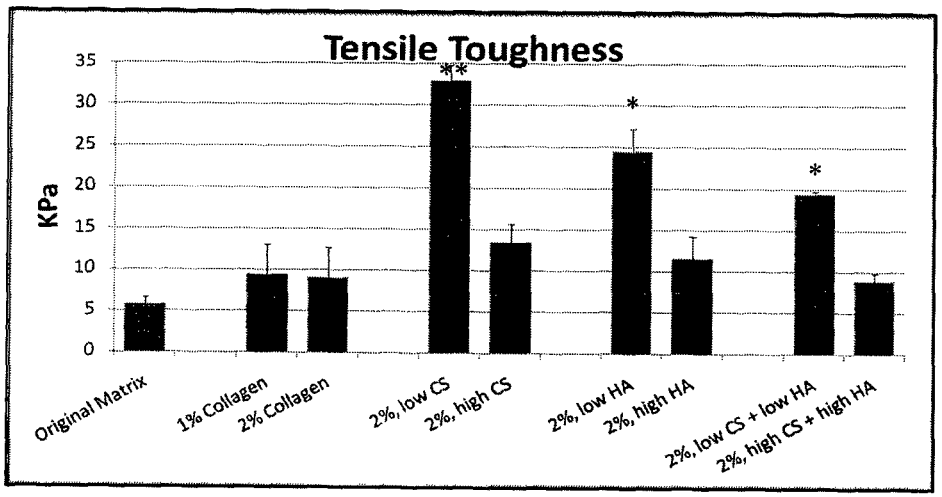


Fig. 23A

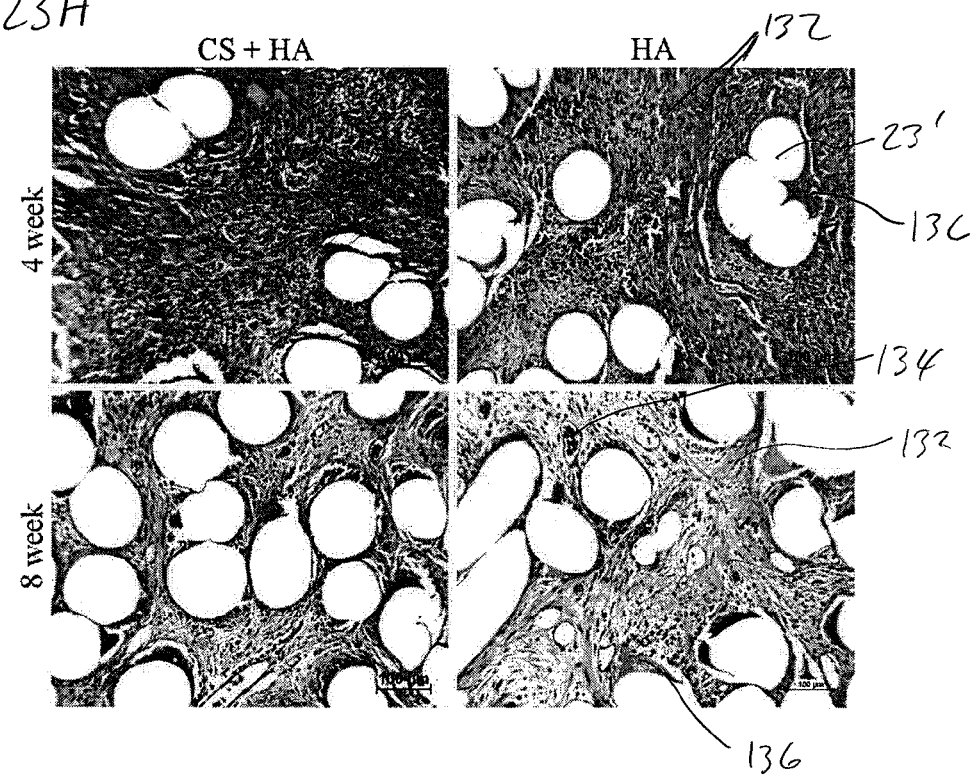
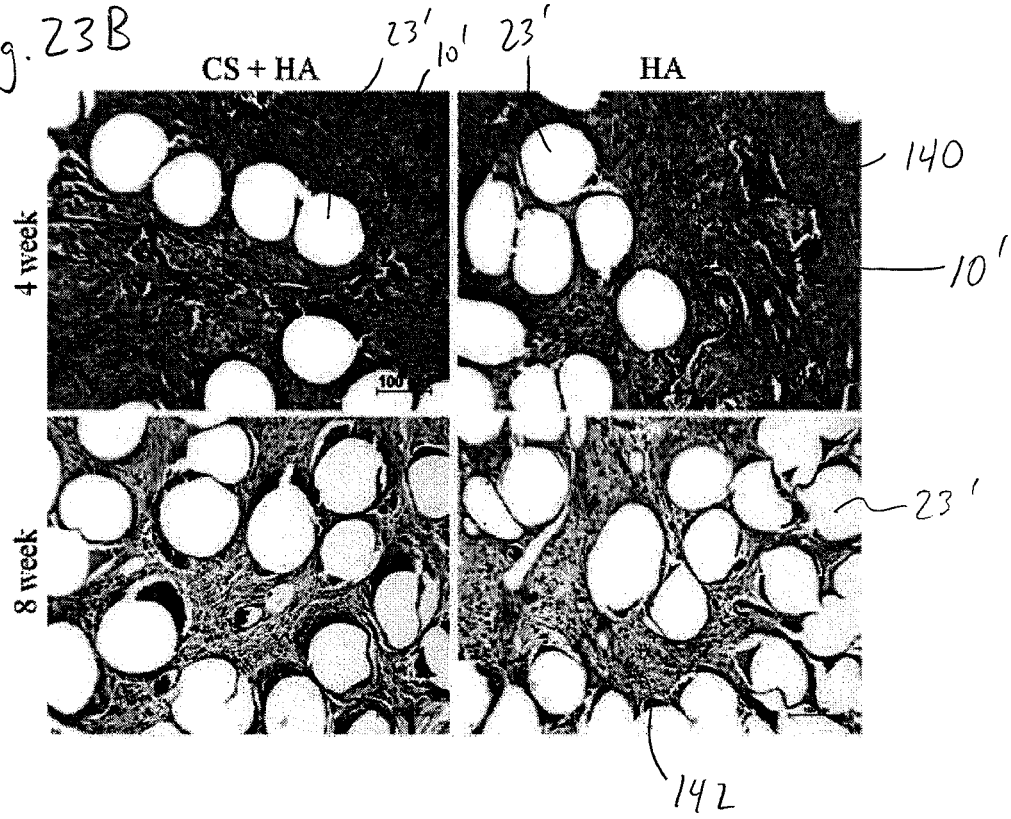


Fig. 23B



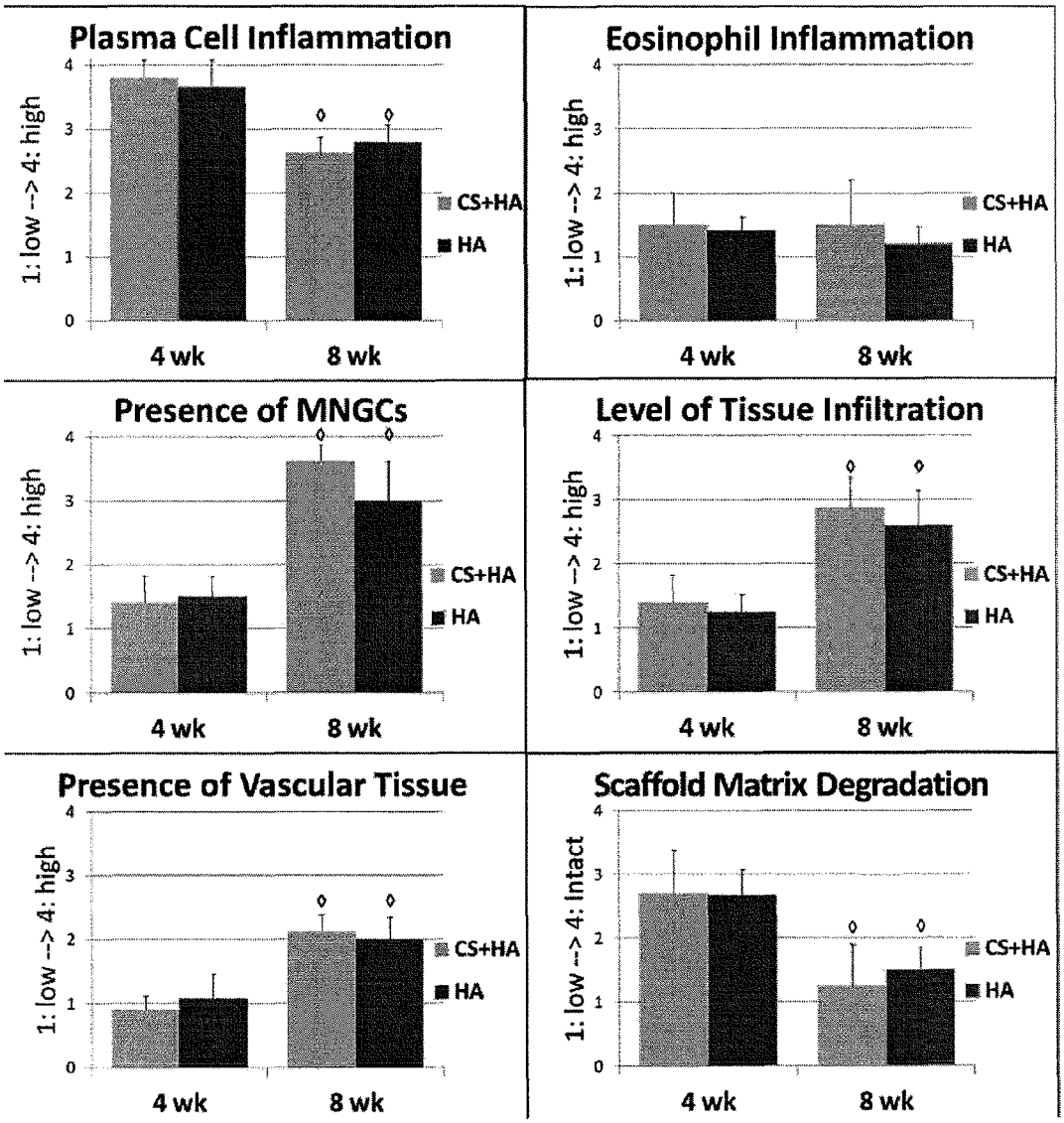

Plasma Cell Inflammation
1: low --> 4: high
CS+HA
HA
4 wk
8 wk
Eosinophil Inflammation
1: low --> 4: high
CS+HA
HA
4 wk
8 wk
Presence of MNGCs
1: low --> 4: high
CS+HA
HA
4 wk
8 wk
Level of Tissue Infiltration
1: low --> 4: high
CS+HA
HA
4 wk
8 wk
Presence of Vascular Tissue
1: low --> 4: high
CS+HA
HA
4 wk
8 wk
Scaffold Matrix Degradation
1: low --> 4: Intact
CS+HA
HA
4 wk
8 wk

Fig. 24

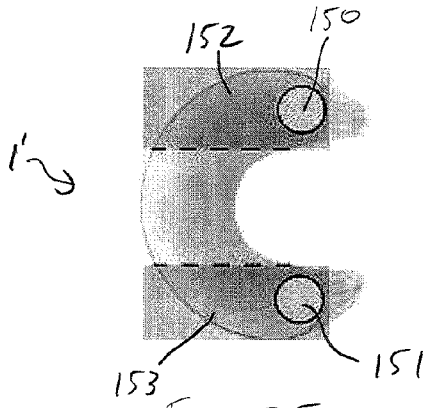


Fig. 25

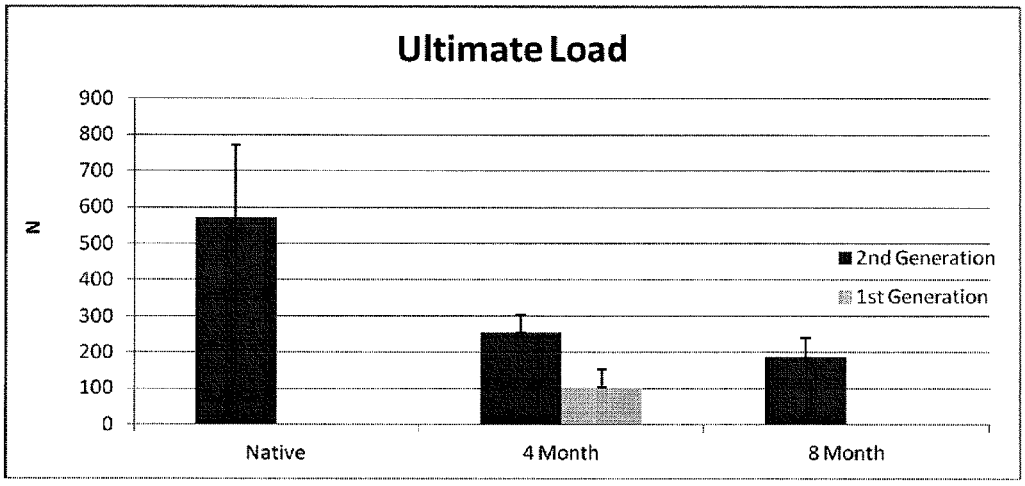


Fig. 26A

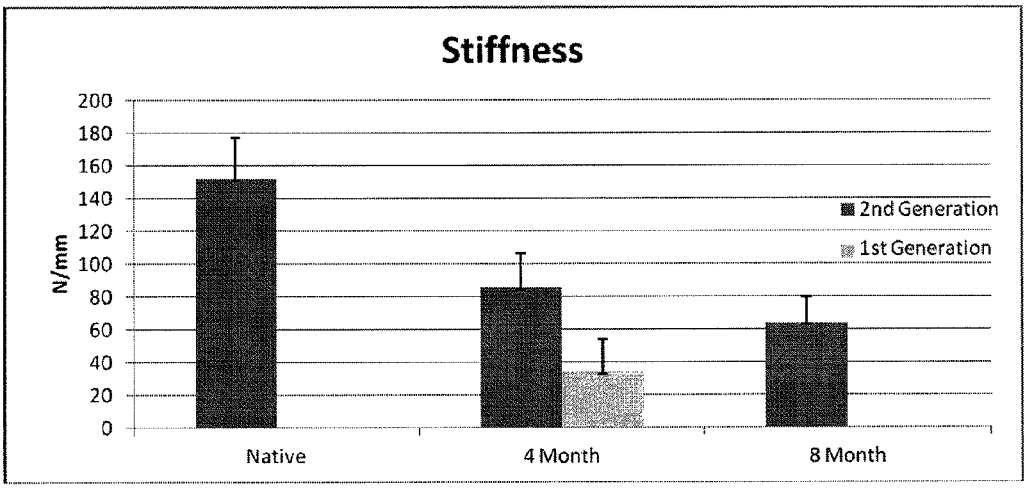


Fig. 26B

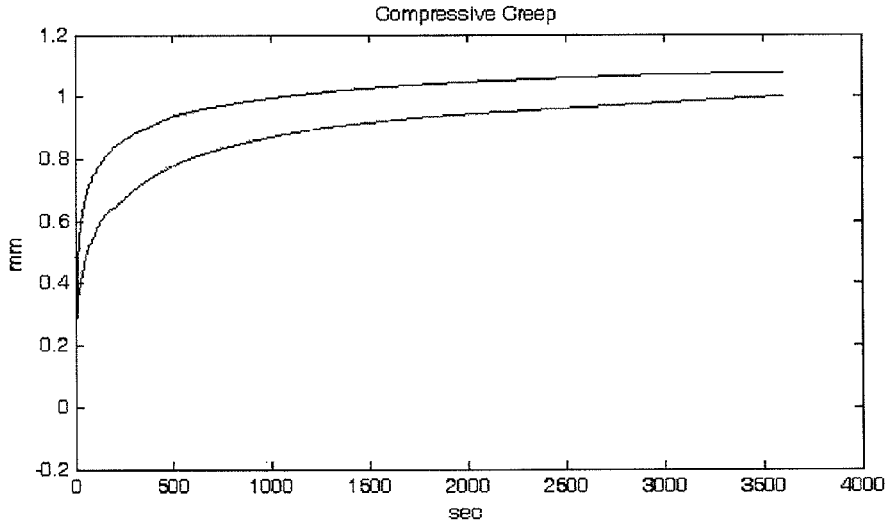


Fig. 27

Fig. 28A

Fig. 28B

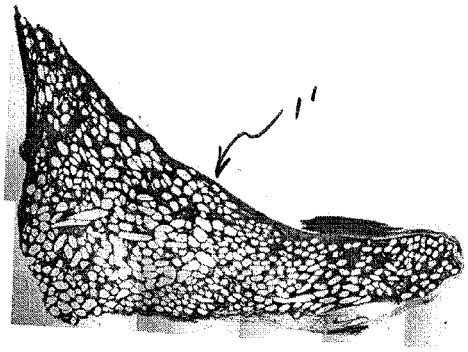


Fig. 29A

Fig. 29B

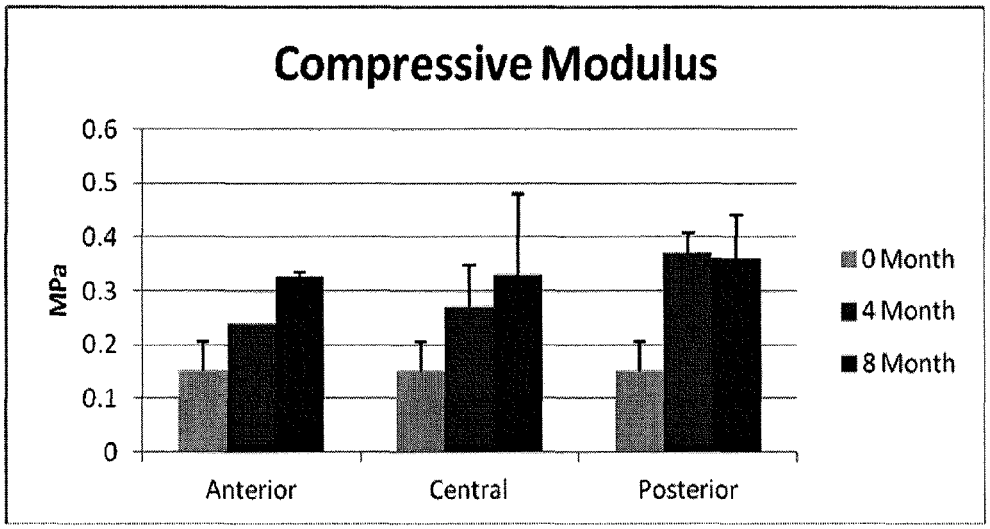

Compressive Modulus
MPa
0.6
0.5
0.4
0.3
0.2
0.1
0
Anterior
Central
Posterior
0 Month
4 Month
8 Month

Fig. 30

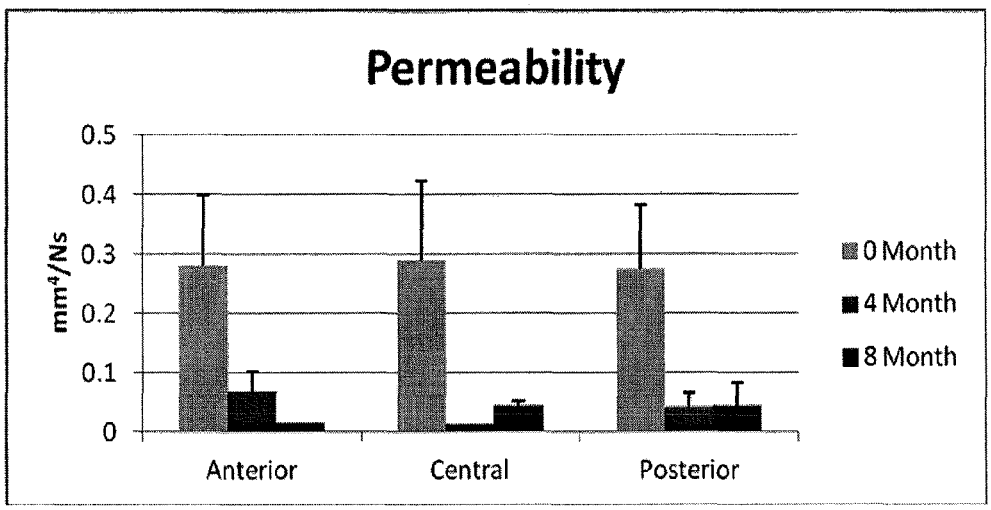

Permeability
mm⁴/Ns
0.5
0.4
0.3
0.2
0.1
0
Anterior
Central
Posterior
0 Month
4 Month
8 Month

Fig. 31

IMPLANTABLE DEVICE AND METHOD TO REPLACE THE MENISCUS OF THE KNEE AND OTHER BODY STRUCTURES

CROSS-REFERENCE TO RELATED APPLICATIONS

This application is a continuation-in-part of U.S. application Ser. No. 12/995,930 filed Dec. 6, 2010, which is a National Stage entry of International Application Ser. No. PCT/US09/45985 filed Jun. 2, 2009, which, in turn, claims 35 U.S.C. 119(e) priority benefit of U.S. Provisional Application Ser. No. 61/130,791, filed Jun. 2, 2008. The disclosure of all three applications are incorporated herein by reference in their entirety.

FIELD OF THE INVENTION

This invention relates to methods and devices for replacement of severely damaged fibrocartilage tissue and, in particular, to the replacement of the lateral or medial meniscus of the knee and other body structures.

BACKGROUND

The menisci are two C-shaped discs of fibrocartilage found between the condyles of the femur and the tibial plateau which play a critical role in the load transmission, load distribution, shock absorption, joint stability, and lubrication of the knee. Despite the recognized importance of the tissue, arthroscopic removal of a torn meniscus is one of the most common orthopedic procedures performed in the United States. Because the tissue has limited healing potential, the clinical outcomes of subtotal meniscectomies are generally poor. At this time, a reliable surgical procedure to replace significant loss of meniscal tissue does not exist. There is no autologous procedure to replace the meniscus and the results of allograft replacement are unreliable.

Another approach is that of tissue engineering. Current approaches include synthetic polymer scaffolds and collagen meniscus implants. With synthetic polymer scaffolds, polyurethane sponges are used to replace the meniscus. This approach has led to inconsistent results. Fibrocartilage growth is seen in some studies using this technology while in others fibrous tissue did not remodel into fibrocartilage. The underlying cartilage was protected in some studies but not protected in others.

Another type of meniscus implant uses a sponge containing collagen, hyaluronic acid and chondroitin sulfate. There is promising preliminary data for this implant, but it is not widely accepted by the orthopedic community because of issues with cytotoxic byproducts of cross-linking and scaffold shrinkage.

Both of these approaches generate an amorphous structure, the mechanical properties of which may not be appropriate for a device designed to replace the meniscus. Thus, while scaffold technology holds promise, no methods have met with the clinical success necessary for acceptance by the orthopedic community. There remains a need for a tissue engineered scaffold with the necessary mechanical properties and biocompatibility for treatment of significant meniscal damage.

SUMMARY

This need is met by the present invention. The present invention incorporates the discovery that the shortcomings of prior art implants can be overcome by reinforcement of the scaffold with a fiber matrix extending in a circumferential direction along the scaffold, the fibers of which are in turn held together by scaffold matrix fibers embedded orthogonally to the circumferential fibers. The resulting configuration behaves like natural fibrocartilage that translates an axial compressive load into a circumferential tensile load. When the implant is an artificial knee meniscus, the implant translates the axial compressive load exerted by the femur on the implant into a tensile load propagated in the circumferential direction of the scaffold, like a natural meniscus.

In one aspect, the present invention thus provides a fiber reinforced implant for use as a replacement for significantly damaged fibrocartilage tissue, such as meniscal tissue of the knee, jaw or wrist, or an intervertebral disc. The inventive implant is constructed of resorbable natural or synthetic biomaterials which allow for infiltration, attachment and proliferation of cells from the surrounding tissues. The implant of the present invention is a natural or synthetic scaffold having the shape and geometry of the original undamaged fibrocartilage with a reinforcing matrix embedded therein.

Therefore, according to one embodiment of the present invention, an artificial fibrocartilage implant is provided in which an arcuate or torroidal scaffold has a circumferential fiber network embedded therein and an orthogonal fiber network embedded in the scaffold to prevent separation of the circumferential fiber network, wherein the fiber networks convert an axial compressive force on the scaffold to tensile loads along the circumferential fiber network.

According to arcuate embodiments of the present invention, the arcuate scaffold has an anterior end, a posterior end and a middle section therebetween defining a curved path between the anterior and posterior ends. The circumferential fiber network extends between the anterior and posterior ends along the path of the curve and exits the anterior and posterior ends of the scaffold to form respective anterior and posterior attachment points.

According to a more specific arcuate embodiment of the present invention, the arcuate implant is fabricated in the shape of a knee meniscus. Another embodiment of this aspect of the present invention therefore provides an artificial knee meniscus implant with a c-shaped scaffold having an arcuate middle section extending between an anterior end and a posterior end and a reinforcing fiber network embedded in the scaffold, wherein the fibers of the network exit each end of the scaffold to form respective anterior and posterior attachment points and the fiber network converts an axial compressive force on the scaffold to tensile loads on the attachment points.

According to a more specific embodiment of the knee meniscus of the present invention, at least a portion the fiber network extends along the arcuate middle section in a substantially circumferential direction. According to an even more specific embodiment, the fiber network further includes an orthogonal fiber network embedded within the scaffold to prevent separation of the circumferential fiber network. In a preferred embodiment the artificial knee meniscus has a wedge-shaped cross-section substantially equivalent to a human knee meniscus.

According to another embodiment of the meniscus implant of the present invention, the implant comprises a c-shaped scaffold having an arcuate middle section extending between an anterior end and a posterior end. A reinforcing network of fibers independent from the scaffold is embedded therein. Fibers of said network fibers exit each end of the scaffold to form respective anterior and posterior attachment segments which extend parallel to a central axis of the scaffold. The

network of fibers is configured to convert an axial compressive force on said scaffold to tensile loads on said attachment points.

According to another more specific embodiment of the arcuate and torroidal menisci of the present invention, the inventive implants have at least one peripheral attachment point. In a preferred embodiment, at least one peripheral attachment point coincides with a point at which the circumferential fiber network intersects with the orthogonal fiber network. In another preferred embodiment, the fiber network(s) extend throughout the wedge-shaped cross section of the arcuate middle section.

According to one torroidal embodiment of the invention, the inventive implant is a torroidal-shaped scaffold having the circumferential and orthogonal fiber networks of the present invention. Such a device is particularly useful for replacement of intervertebral discs or temporomandibular joint discs. Artificial implants according to this embodiment of the present invention are fabricated in the shape of a vertebral disc or an articular disc for a joint.

More specific torroidal embodiments have at least one peripheral attachment point. In preferred versions of this embodiment, at least one peripheral attachment point coincides with a point at which the circumferential fiber network intersects with the orthogonal fiber network.

According to one torroidal embodiment torroidal implants are fabricated in the shape of a vertebral disc, wherein the torroidal-shaped scaffold defines an interior cavity filled with a biocompatible material with physical properties equivalent to the properties of the nucleus pulposus of a human vertebral disc. According to another torroidal embodiment, torroidal implants are fabricated in the shape of articular disc, for example, in the shape of the meniscus of the temporomandibular joint or the wrist.

In any of the inventive embodiments at least one of the scaffold, the circumferential fiber network or the orthogonal fiber network may be formed from a material selected from proteins, proteoglycans, biocompatible synthetic polymers and combinations thereof. In some embodiments the material is bioresorbable. In other embodiments the proteins comprise collagen, and in certain of these embodiments the collagen is cross-linked.

In any of the inventive embodiments at least one of the scaffold, the circumferential fiber network or orthogonal fiber network is formed from a biocompatible synthetic polymeric material. In some embodiments the polymeric material is bioresorbable.

According to another aspect of the present invention, a method is provided for replacement of a damaged knee meniscus. Methods according to this aspect of the present invention include the steps of:

replacing a damaged meniscus with a knee meniscus implant according to the present invention by inserting a knee meniscus implant according to the present invention, having anterior and posterior attachment points, between the tibial plateau characterized by having anterior and posterior anchor plugs inserted therein, and the corresponding femur condyle; and

securing the anterior and posterior attachment points of the implant to the corresponding anterior and posterior anchor plugs.

According to yet another aspect of the present invention, a method is provided for fabricating a soft tissue repair implant such as a meniscus implant. Methods according to this aspect of the present invention include the steps of:

forming a reinforcement matrix with at least one fiber; and

embedding the reinforcement matrix into a scaffold, wherein the scaffold has an arcuate middle section extending between an anterior end and a posterior end; and wherein the at least one fiber exits each end of the scaffold.

By creating an implant that has the same geometry as that of the normal tissue, along with a network of embedded, reinforcing fibers, the mechanics of the natural tissue can be replicated. As cells infiltrate this implant, they will experience the same mechanical environment of that of a normal tissue, thus promoting the formation of neofibrocartilaginous tissue which has the biological and mechanical properties to function as a load-bearing structure.

BRIEF DESCRIPTION OF THE FIGURES

FIGS. **1** and **2** are top views of a first exemplary embodiment of the instant device;

FIGS. **3**A and **3**B present diagrams of forces on the instant device when the device is implanted;

FIG. **4** is a top view of the device in FIGS. **1** and **2** with another embodiment of the reinforcing matrix;

FIG. **5**A is a top view of a torroidal embodiment of the instant device; and FIGS. **5**B and **5***c* are elapsed time perspective views of a torroidal embodiment as it is being wound;

FIG. **6** presents a desirable degradation profiles for polymers suitable for use in instant devices;

FIGS. **7**A-**7**B show a base plate pattern for fabrication of meniscus scaffolds;

FIGS. **8**A-**8**G show the organization of embedded fibers;

FIG. **9** presents the results from a primary mechanical evaluation of the tensile strength of the scaffold of the device of FIGS. **1** and **2**;

FIGS. **10**A-**10**B present the results of an advanced mechanical evaluation for the "No Scaffold" group;

FIGS. **11**A-**11**B present the results of an advanced mechanical evaluation for the "100% Collagen Scaffold" group;

FIGS. **12**A-**12**B present the results of an advanced mechanical evaluation for the "500 Fiber Scaffold" group;

FIGS. **13**A-**13**B present the results of an advanced mechanical evaluation for the "1000 Fiber Scaffold" group;

FIGS. **14**A-**14**B present the results of an in vitro evaluation of the scaffold of the device of FIGS. **1** and **2**;

FIGS. **15**A-**15**F present the results of an in vivo evaluation of the scaffold of the device of FIGS. **1** and **2**;

FIG. **16** is a top view of another exemplary embodiment of a device of the present invention;

FIG. **17** is a top view of the scaffold of the device of FIGS. **1** and **2**;

FIG. **18** is a top view of the scaffold of the device of FIG. **16**;

FIG. **19** is a top view illustrating the weaving pattern of the fiber network of the device of FIG. **16**;

FIG. **20** is a top view similar to FIG. **19** illustrating the fiber network embedded in scaffold material;

FIGS. **21**A-**21**C present the results of testing of devices having varying material properties;

FIGS. **22**A-**22**B present the results from a primary mechanical evaluation of the tensile strength of the scaffold of the device of FIG. **16**;

FIG. **23**A present haematoxylin and eosin stained micrographs showing cellular inflammation including plasma cells, eosinophils, and MNGCs;

FIG. **23**B present trichrome stained micrographs showing scaffold degradation and tissue formation including polymer fibers, blood vessels, scaffold matrix, and newly synthesized collagen;

FIG. **24** presents results of blinded grading of histological micrographs;

FIG. **25** depicts an exemplary mechanical testing set-up;

FIGS. **26**A and **26**B present tensile strength and stiffness test results versus a natural meniscus;

FIG. **27** presents a time-deformation graph of a device of the instant invention versus that of a native meniscus;

FIG. **28**A is a top plan view of an exemplary recovered implant 4-months post-implantation in a sheep total meniscus replacement model and FIG. **28**B is a similar view of an exemplary normal native meniscus;

FIG. **29**A is a cross-sectional histological view of an exemplary recovered implant 8-months post-implantation in a sheep total meniscus replacement model and FIG. **29**B is a similar view of an exemplary normal native meniscus; and

FIGS. **30** and **31** present improvements in compressive modulus and permeability test results after implantation (0, 4, and 8 months) in a sheep total meniscus replacement model.

DETAILED DESCRIPTION

The instant implants improve upon current meniscus scaffolding approaches in conjunction with current tendon/ligament scaffolding approaches. With regard to tissue-type, the meniscus can be viewed as a combination of organized fibrous connective tissue predominant at its outer portion (i.e. tendon/ligament) and cartilaginous tissue at its inner portion. This extracellular matrix (ECM) organization occurs because of the way the meniscus is loaded under normal conditions.

For the meniscus of the knee, during static or dynamic weight-bearing the tissue is compressed by the femur. Because of the geometry of the meniscus (C-shaped with wedge-shaped cross-section), this axial load extrudes the tissue from the joint capsule. This extrusion is resisted by the anterior and posterior attachments to the tibial plateau, resulting in the generation of tensile hoop stresses directed along the circumferentially arranged collagen fibers within the tissue.

The hoop stresses are predominantly developed near the periphery of the tissue, where the ECM is more tendon-like. Near the inner margin, the tissue primarily undergoes standard compression, meaning the ECM organization is closer to that of cartilage.

Although the instant implants are described in relation to making and using a knee meniscus replacement device, the teachings of the instant disclosure may also be applied to make and use implants for replacing other tissues similar in nature as the articular cartilage of the knee, intervertebral discs, temporomandibular discs, wrist menisci, the rotator cuff of the shoulder, hernia repair, soft tissue repair and augmentation (nose, ear, soft tissue defects), skeletal muscle repair and function to the meniscus, such the like. These tissues are similar to the knee meniscus in that they are composed of ECM and function as load transmitters and distributors in the connective tissue or musculoskeletal system. It will also be understood that the instant teachings may be applied to make and use implants for both human and animal patients.

Accordingly, one aspect of the invention provides an implant **1** comprising a scaffold **10** and reinforcing matrix **14** embedded in the scaffold **10** as shown in FIG. **1**. The shape and geometry of the scaffold, and consequently the implant, is based on the shape and geometry of the soft tissue in need of replacement. Thus, in the case of a meniscus implant, the scaffold may be constructed as a c-shaped disc with a wedge-like cross-section, similarly to a knee meniscus. Furthermore, it may be shaped concave on the top, which would come in contact with femur, and flat on the bottom, which would rest on the tibial plateau. Although not necessary, the reinforcing matrix may also have the same general shape and geometry as the scaffold.

The scaffold **10** includes an anterior end **11**, a posterior end **12** and a middle section **13** defining a path between the anterior end **11** and the posterior end **12**. In a meniscus replacement device, the middle section is essentially arc-shaped and defines a curved path between said anterior and posterior ends. The scaffold also has peripheral regions **14***a* and **14***b* and an inner region **15** between the peripheral regions **14***a* and **14***b*. Referring to FIGS. **1-2**, for the purposes of the instant disclosure, the circumferential direction of the scaffold is indicated by arrow A and generally extends along the middle section of the scaffold.

Referring to FIG. **3**A, in operation, a compressive force F would normally be applied on the scaffold **10** in axial direction, which is indicated by an arrow F. Referring to FIG. **3**B, the design of the implant is such that the compressive force F on the scaffold **10** is translated into tensile hoop stresses in circumferential direction, as shown by arrows F_h. For consistency, the same terminology is also applied in reference to the reinforcing matrix and the implant as a whole.

Referring back to FIG. **1**, the reinforcing matrix **20** may be formed by at least one fiber **23** extending between the anterior end **11** and posterior end **12** of the scaffold **10** and exiting each end to form an anterior attachment point **21** and a posterior attachment point **22**. As used herein, the term "fiber" refers to any generally elongated member consisting of a single component, e.g. monofilament suture, or multiple components, e.g. multifilament suture. The fibers may be formed by any suitable method for forming the biocompatible materials from which they are made into a fiber or filament. The fibers may be drawn, extruded, cast, etc. The physical property of the fiber, such as tensile strength, cross-sectional area, diameter, flexibility, etc, may vary over the length of the fiber. In some embodiments, multiple fibers may be used to form the reinforcing matrix. The fibers may be made of the same or different materials and may follow the same or different paths.

Preferably, at least a portion of the fiber **21** forming the reinforcing matrix **20** is positioned substantially in circumferential direction **24**. In some embodiments, the fiber **23** forming the reinforcing matrix **20** may be arranged in two different arrangements: the circumferential arrangement **24** and an orthogonal arrangement **25**. As used herein, the terms "orthogonal arrangement," or "arranged orthogonally," means an arrangement of fibers extending in directions substantially parallel to arrows B in FIG. **2** at various angles in relation to the scaffold.

In reference to FIG. **4**, the reinforcing matrix **20** comprises one or more circumferential fibers **24** and one or more orthogonal fibers **25**. The term "circumferential fiber" refers to fiber that extends between the anterior end and posterior end of the scaffold along the middle section of the scaffold and is positioned at least in part substantially parallel to the circumferential axis. The term "orthogonal fiber" refers to fibers that cross the circumferential fibers at various angles to keep them from separating. Keeping the circumferential fibers from separating increases the durability and longevity of the implant. For convenience, terms "circumferential fiber network" and "orthogonal fiber network" may be used herein to refer to multiple circumferential fibers or multiple orthogonal fibers, respectively.

As noted above, in operation the compressive force on the device in the axial direction is translated into tensile hoop stresses in the circumferential direction. The hoop stresses propagate along the circumferential fibers. In vivo, as meniscal tissue grows into the implant and cells attach to the fiber networks, cells on or about the circumferential fibers experience the same mechanical environment as in a normal meniscus, resulting in the formation of tissue with the essentially the same organization and directionality of collagen fibers as the original meniscus.

The reinforcing matrix may be formed with one single continuous fiber arranged both circumferentially and orthogonally, or, the matrix may be formed using multiple fibers. In such embodiments, the circumferential fibers as well as orthogonal fibers may be formed by the same or different strands of fiber or a combination thereof.

The instant implant includes an anterior attachment point **21** and a posterior attachment point **22** for attaching the implant to tissue adjacent to the implantation site. These attachment points are formed by fiber exiting from the anterior and posterior end of the scaffold, respectively. Referring to FIGS. **3**A-**3**B, attaching the implant in place by these attachment points converts axial compressive force F on the scaffold **10** and reinforcing matrix **20** into tensile loads along the circumferential fibers and on the anterior and posterior attachment points. The forces on the anterior and posterior attachment points are presented as force F_a and force F_p, respectively.

Moreover, in some embodiments, the implant may comprise one or more additional attachment points **30** formed in the middle section of the scaffold, preferably on the exterior periphery of the middle section. Such attachment points are referred to as peripheral attachment points. In suitable embodiments, peripheral attachment points preferably coincide with points at which orthogonal fibers cross circumferential fibers.

As noted above, intervertebral discs or temporomandibular joint discs function as load transmitters and distributors to prevent high-stress bone-on-bone contact. For example an intervertebral disc comprises the annulus fibrosus and the nucleus pulposus. The nucleus pulposus is the inner gelatinous material surrounded by the annulus fibrosus. It distributes mechanical loads placed upon the disc, while the annulus fibrosus provides structural integrity and constrains the nucleus pulposus to a specific spinal region.

The annulus fibrosus has an internal structure which is very similar to the internal structure of meniscal tissue. Accordingly, torroidal concepts herein described may be utilized to construct implants for full or partial replacement of annulus fibrosus.

Referring to FIG. **5**A, in one embodiment the instant implant **50** may comprise a torroidal-shaped scaffold **51** and a reinforcing matrix **52**. The reinforcing matrix **52** may be constructed as is described above in reference to meniscus implants. In preferred embodiments, the reinforcing matrix comprises circumferential fibers **53** and orthogonal fibers **54** that cross the circumferential fibers to prevent separation of the circumferential fibers. However, in contrast to embodiments described above, the fibers forming the reinforcing matrix do not exit the scaffold and the implant may be secured by attaching the implant to the healthy tissues at peripheral attachment points **55**. A device in the process of being wound is depicted in FIGS. **5**B and **5**C.

According to one torroidal embodiment, torroidal implants may be fabricated in the shape of a vertebral disc, wherein the torroidal-shaped scaffold defines an interior cavity filled with a biocompatible material with physical properties equivalent to the properties of the nucleus pulposus of a patient's vertebral disc. Materials suitable for use as nucleus pulposus are known and are disclosed, for example, in U.S. Pat. Nos. 5,976,186; 7,004,971 and 7,214,245, all of which are incorporated herein by reference in their entirety. Alternatively, the implant is configured to replace only the annulus fibrosus or a part of the annulus fibrosus.

Referring to FIGS. **16** and **18**-**20**, another exemplary implant device **1'** of the instant invention will be described. As in the previous meniscus implant, the instant implant **1'** comprises a scaffold **10'** and a reinforcing matrix **14'** embedded in the scaffold **10'**. The scaffold **10'** includes an anterior end **11'**, a posterior end **12'** and a middle section **13'** defining a path between the anterior end **11'** and the posterior end **12'**. In a meniscus replacement device, the middle section is essentially arc-shaped and defines a curved path between said anterior and posterior ends. The scaffold also has peripheral regions **14***a'* and **14***b'* and an inner region **15'** between the peripheral regions **14***a'* and **14***b'*.

Again, the shape and geometry of the scaffold, and consequently the implant, is based on the shape and geometry of the soft tissue in need of replacement. Thus, in the case of a meniscus implant **1'**, the scaffold **10'** may be constructed as a c-shaped disc with a wedge-like cross-section, similarly to a knee meniscus.

FIGS. **17** and **18** illustrate exemplary shapes of the scaffolds **10** and **10'** of the implant **1** and l', respectively. The scaffold **10** of the implant **1** has a slightly elongated circular configuration, with the dimension A+B+C being slightly greater than the dimension D+E, for example, by about 15%. Additionally, the width A toward the anterior end **11** and the width C toward the posterior end **12** are generally equal and only slightly larger than the open area width B, for example, by about 15%. Illustrative dimensions for the scaffold **10** are A=7 mm, B=6 mm, C=7 mm, D=9.5 mm and E=8 mm. The scaffold **10'** of the implant **1'** has a more elliptical shape, with the dimension A'+B'+C' being greater than the dimension D'+E', for example, by about 30%. With this configuration, the width A' toward the anterior end **11'** and the width C' toward the posterior end **12'** are still generally equal to one another, but are larger than the open area width B', for example, by about 40%. Illustrative dimensions for the scaffold **10'** are A'=8.5 mm, B=6 mm, C=8.5 mm, D=9.5 mm and E=8 mm.

Referring back to FIGS. **16** and **19**, the reinforcing matrix **20'** may be formed by at least one fiber **23'** extending between the anterior end **11'** and posterior end **12'** of the scaffold **10'** and extending to form an anterior attachment segment **121** and a posterior attachment segment **122**. The attachment segments **121**, **122** extend generally parallel to a central axis CA of the implant **1'**. The attachment segment **121** is formed by fibers **23'** extending from the anterior end **11'** through a tapering horn section **123** to an extended end **125**. Similarly, the attachment segment **122** is formed by fibers **23'** extending from the posterior end **12'** through a tapering horn section **124** to an extended end **126**. Comparing FIG. **16** to FIG. **1**, the horn sections **123**, **124** of the present embodiment are wider than the corresponding horn sections of the implant **1**. The widened horns **123**, **124** accommodate placement of the attachment segments **121**, **122** through bone tunnels and also prevent joint impingent on the scaffold **10'**. The elongated attachment segments **121**, **122** are configured to traverse the entire length of a bone tunnel (not shown). This allows for a fixation method wherein the segments **121**, **122** extend through the bone tunnel and then are fixed to the tibia using interference screws (not shown) or the like. This provides a more rigid attachment.

As in the previous embodiments, the reinforcing matrix **20'** comprises one or more circumferential fibers **24'** and one or more orthogonal fibers **25'**. The term "circumferential fiber" refers to fiber that extends between the anterior end and posterior end of the scaffold along the middle section of the scaffold and is positioned at least in part substantially parallel to the circumferential axis. The term "orthogonal fiber" refers to fibers that cross the circumferential fibers at various angles to keep them from separating. Keeping the circumferential fibers from separating increases the durability and longevity of the implant. For convenience, terms "circumferential fiber network" and "orthogonal fiber network" may be used herein to refer to multiple circumferential fibers or multiple orthogonal fibers, respectively. In addition to the circumferential fibers **24'** and orthogonal fibers **25'** the reinforcing matrix **20'** further comprises radial tie fibers **127** are now woven thru the circumferentially oriented patterns to provide addition stability and support to the structure. Referring to FIG. **19**, it is seen than the weaving pattern is configured such the fibers **23'** circumferentially surround all nodes along the outer perimeter of the implant **1'**.

For both the arcuate and torroidal constructs, both the scaffold and the reinforcing circumferential and orthogonal matrix fibers may be constructed of naturally-occurring or synthetic biocompatible materials or a combination thereof so to enable infiltration, attachment and proliferation of cells from surrounding tissues once the implant is in place. The naturally-occurring or synthetic biocompatible materials may also be bioresorbable. The scaffold and the reinforcing matrix fibers may be constructed from the same material or different materials and may be fully or partially biodegradable and may have the same or different rate of degradation.

As used herein the term "synthetic polymer" refers to polymers that are not found in nature, even if the polymers are made from naturally occurring biomaterials. The term "natural polymer" refers to polymers that are naturally occurring. The term "biocompatible" refers to materials that, in the amounts employed, do not elicit a detrimental response in the host. This term is intended to include materials that may cause some inflammation, tissue necrosis or other immune responses when introduced into the host, provided that these effects do not rise to the level of pathogenesis. The term "bioresorbable" refers to those materials that when placed in a living body at standard physiological conditions are degraded through either enzymatic, hydrolytic or other chemical reactions or cellular processes into by-products that are either integrated into or expelled from the body. It is recognized that in the literature, the terms "bioresorbable," "resorbable", "absorbable", "bioabsorbable" and "biodegradable" are frequently used interchangeably and such interchangeable meaning is intended for the present application.

In preferred embodiments, the implant is formed from biodegradable material or materials. The polymers for the instant implant are selected so the implant possesses mechanical properties which are the same or substantially similar to the mechanical properties of the native tissue being replaced. Moreover, as shown in FIG. **6**, it is desirable for the mechanical properties of the implant to remain consistent as the implant is being remodeled. Accordingly, the polymers are selected so their degradation profile closely matches neotissue formation and remodeling, so the new tissue is afforded sufficient time to gain enough strength to compensate for the decrease in strength of the polymers. As shown in FIG. **6**, this ensures that at all times the implant-tissue combination possesses mechanical properties resembling those of native tissue, which allows the implant to assume loads experienced in the joint at all times without failure.

Examples of suitable natural polymers include, but are not limited to, collagen, hyaluronic acid, fibrin glue, bone marrow, chitosan, alginates, celluloses, starches, silk, elastin, and other animal- or plant-derived proteins or polysaccharides. Suitable synthetic polymers include, but are not limited to, poly(alpha-hydroxy acids), poly(lactide-co-glycolide) (PLGA), poly(L-lactides) (PLLA), polylactides (PLA), polyglycolides (PGA); polyethylene, polypropylene, polyvinyl alcohol (PVA), polyethylene oxide (PEO); poly-p-dioxanone (PDO); polyarylates, polyacrylates, polycarbonates, polyesters, polycaprolactone (PCL) and combinations thereof. Suitable polyarylates and polycarbonates include, but are not limited to the tyrosine-derived polyarylates and polycarbonates disclosed by U.S. Pat. Nos. 5,099,060; 5,198,507; 5,216,115; 5,587,507; 5,658,995 and 6,048,521, the disclosures of all of which are incorporated herein by reference.

In preferred embodiments, the scaffold is an amorphous structure composed primarily of Type I collagen. The collagen may be from animal (for example, including BNLT bovine, porcine, equine), human, or recombinant sources. In addition to collagen, other types of materials may be added to alter the scaffold's properties as necessary or desired. For example, other proteins or proteoglycans may be used, including, but not limited to, glycosaminoglycans such as chondroitin sulfate, keratan sulfate, dermatan sulfate, heparin, heparin sulfate and hyaluronic acid. The percentage of these materials in the scaffold may range between 0 and about 20% of the dry weight of the scaffold. The fiber for the reinforcing matrix may preferably be made from a bioresorbable synthetic polymer, such as a polyarylate, or a non-synthetic material, such as collagen.

The physical characteristics of the implant may be modified by using different materials for the scaffold and/or forming the reinforcing matrix from fibers of different diameter, mechanical strength, stiffness, or durability. Moreover, the physical characteristics of the implant may be modified by cross-linking the scaffold, the reinforcing matrix or both. Cross-linking may be achieved by employing a variety of known methods, including, but not limited to, chemical reaction with a carbodiimide, glutaraldehyde or formaldehyde among others; the application of energy such as radiant energy, which includes irradiation by UV light or microwave energy; dehydrothermal treatment in which water is slowly removed while the implant is subjected to a vacuum; and, enzymatic treatment.

More specifically, it has been found that altering the source and concentration of the type I collagen along with the addition of glycosaminoglycans (GAGs) has had the greatest improvement on its compressive and viscoelastic properties. Sponge materials which may be used to form the scaffolds **10**, **10'** were mechanically evaluated using several methods: swelling potential, confined compressive creep, and tension to failure. The sponges varied in the source of collagen (dermis or Achilles tendon), amount of Chondroitin Sulfate (CS), and the amount of Hyaluronic Acid (HA). These alterations make the scaffold more closely resemble the properties of the native meniscus and improve the protective attributes of the scaffold on the articular cartilage.

Perhaps the most important in vitro evaluation of the sponge is its mechanical response to compressive load. The sponge should reproduce the viscoelastic properties of the normal meniscus. In order to evaluate this, a confined compressive creep test was performed. The first variable analyzed was the amount of collagen used to create the matrix. It was hypothesized that higher concentrations of collagen would create a stiffer matrix more akin to the native meniscus.

Increasing the amount of collagen in the sponge did improve its aggregate modulus making it stiffer, but also increased its permeability allowing fluid to flow through it too easily (FIG. **21**A). In addition, the dispersions made with higher concentrations of collagen were initially too thick and did not swell properly. This resulted in sponges that were weakly held together and easily damaged. Since the 1% and 2% collagen sponges had the best balance of stiffness, permeability, and handleability, all further testing was limited to these concentrations.

The source of the collagen used in the matrix of the meniscus scaffold was next evaluated. Sponges fabricated with bovine Achilles tendon were shown to be mechanically superior to that used bovine dermis collagen. The addition of glycosaminoglycans (GAGs) to the Achilles tendon collagen further improved the mechanics of the sponges, but only when added in small concentrations (0.025% dry weight/volume) (See FIGS. **21**B, **21**C, **22**A, **22**B). In these figures, the original matrix consisted of 1% Bovine Dermis Collagen while all others consisted of Bovine Tendon Collagen with 0.025%/0.05% Chondroitin Sulfate C, 0.025%/0.05% Hyaluronic Acid.

Larger concentrations (0.05%) did not significantly alter the mechanics. Perhaps the larger concentration of sodium associated with more GAG powder prevents the collagen from fully swelling forming an inferior matrix. Lower concentrations (0.025%) of GAGs increased the compressive modulus (FIG. **21**B) and decreased the permeability (FIG. **21**C) of the matrix giving them characteristics closer to the native meniscus. These sponges also had significantly higher UTS (FIG. **22**A) and toughness (FIG. **22**B), when pulled in tension to failure, compared to all other sponge matrixes. Higher concentrations of GAGs had little effect. Based on the results of these evaluations, a preferred scaffold will be made from Bovine Achilles Tendon collagen with a collagen concentration of approximately 2% dry weight/volume. Addition of Hyaluronic Acid at low concentrations will provide beneficial properties to the scaffold. Furthermore, altered dispersion processing, for example, high speed mini blender with ground collagen, may also be utilized.

The instant implant may act as a carrier for various medical agents such as therapeutic agents and biologic factors that promote the in-growth and repair of fibrocartilage tissues and vasculature networks, and the attachment of bone tissue, where needed, including various growth factors. Suitable therapeutic agents may be selected from anti-inflammatory agents, antibiotic agents, immunosuppressive or immunomodulator agents, analgesics, anti-apoptotic agents, or combinations thereof. Small molecule therapeutics may form part of the polymer backbone of synthetic scaffold polymers, one example of which is polyaspirin, or the small molecule therapeutics may be supplied as covalent pendant polymer attachments.

The biologic factors or therapeutic agents may elute or be released from the implant as the implant degrades in the event of a bioabsorbable or a partially bioresorbable implant. Prior to elution or release by degradation, and in some embodiments that do not degrade, the biological factor or therapeutic agent is expressed on a device at the polymer surface without release. Alternatively, the implant may include additional components, such as coating or embedded bioresorbable matrices loaded with the biologic factors or therapeutic agents.

In addition, instant implants may be populated with cells of the type typically found in the type of tissue to be replaced or that can differentiate into such type of cells. By way of a non-limiting example, the instant implants may be seeded with fibroblasts, chondrocytes or mesenchymal stem cells. The mesenchymal stem cells may be derived from essentially any stem cell source, including, but not limited to bone marrow, umbilical cord blood, muscle tissue, skeletal tissue, embryonic tissue, etc. The cells may be added to the implant immediately prior to insertion of the implant into the patient's body or may be grown on the implant in the days or weeks prior to implantation. Alternatively, cells may be delivered to the implant after implantation. Techniques for preparing implants populated with cells are known in the art and are disclosed for example in U.S. Pat. No. 6,103,255, the disclosure of which are incorporated herein by reference.

Moreover, the instant implant may include radio-opaque, echogenic materials and magnetic resonance imaging (MRI) responsive materials (i.e., MRI contrast agents) to aid in visualization of the implant under ultrasound, fluoroscopy and/or MRI. For example, a device may be made with or coated with a composition which is echogenic or radiopaque (e.g., made with echogenic or radiopaque with materials) or, by the addition of microspheres or bubbles which present an acoustic interface). For visualization under MRI, contrast agents may be incorporated into or onto the implant. In some embodiments, the instant implant may include radio-opaque or MRI visible markers.

The instant implants may, alternatively, or in addition, be visualized under visible light, using fluorescence, or by other spectroscopic means. Visualization agents that can be included for this purpose include dyes, pigments, and other colored agents. In one aspect, the instant implant may further include a colorant to improve visualization of the implant in vivo and/or ex vivo. Frequently, implants can be difficult to visualize upon insertion, especially at the margins of implant. A coloring agent can be incorporated into the instant implant to reduce or eliminate the incidence or severity of this problem. The coloring agent provides a unique color, increased contrast, or unique fluorescence characteristics to the implant so it is readily visible (under visible light or using a fluorescence technique) and easily differentiated from its implant site.

In another aspect, a method for implantation of the instant implant in place of a damaged tissue is provided. The instant devices may be implanted by surgical or arthroscopic techniques. In general, to implant the instant device the tissue in need of replacement is removed, the implant is inserted to replace the removed tissue and is fixed in place to tissue adjacent the implantation site, for example, by suturing. When a compressive force is applied to the instant implant after implantation, the force is converted into tensile loads along circumferential fibers in the reinforcing matrix.

By way of non-limiting example, the instant implant is particularly useful for treatment of anatomical variances in meniscus, such as tears or discoid meniscus. The instant implant may be used in partial, sub-total, or total meniscectomy. The damaged meniscal tissue, representing a total or part of a meniscus, is removed and the instant implant, tailored to have the same size and shape as the removed tissue, is placed in its place.

In total or subtotal meniscectomy, the implant is secured in place by attaching the anterior and posterior attachment points of the implant to the tibial plateau. One or more holes may be drilled in the tibial plateau, preferably, at the site of the anterior and posterior attachments of the original meniscus. The anterior and posterior attachment points may be inserted into these holes and secured in place by any known techniques, such as using metal or polymeric interference screws, pressure fitting, stapling, suturing, and so forth. Such tibial attachments enable generation of hoop stresses in the implant.

In addition, the implant may be further secured in place by suturing it to healthy tissue adjacent to the implantation site, namely the joint capsule, bone, periosteum, cartilage, or remaining meniscal tissue, at one or more peripheral attachment points in the middle section of the scaffold. In a partial meniscectomy, the meniscus may be secured in place exclusively at one or more peripheral attachment points in addition to being sutured to the remaining meniscus tissue.

In yet another aspect, a method for fabrication of the instant device is provided. First, the reinforcing matrix is formed from one or more fibers, preferably in a shape of the soft tissue the implant is designed to replace. The matrix may be formed by any method known and used in the art for physically interlacing fibers, such as, without limitation, weaving, braiding, knitting, or combination thereof. Alternatively, the fibers may be attached using chemical means such as gluing or cross-linking the fibers together. Moreover, a polymer may be molded into the shape of a three-dimensional matrix.

Second, the reinforcing matrix is inserted into a mold assembly or a mold assembly is formed around the matrix. The mold preferably has the same shape as the soft tissue in need of replacement. In some embodiments, the ends of the fiber forming the reinforcing matrix extend outside each end of the mold assembly to form the attachment points. Third the polymer is injected into the mold assembly to form the scaffold body, which is then solidified.

The process for solidifying the scaffold depends on the polymer used to form the scaffold. For example, if collagen is used, the implant assembly may be lyophilized. In some embodiments, the implant may be cross-linked to alter its physical characteristics. Moreover, additives such as cells, growth factors, medical agents, and/or labels, etc., may be added to the implant at any point during the fabrication of the device according to standard techniques known and used in the field.

As noted above, in some embodiments both the fiber network matrix and the scaffold have same the shape and geometry as the soft tissue they are made to replace. For example, in embodiments for the knee, the reinforcing matrix and the mold assembly may be constructed as a c-shaped disc with a wedge-like cross-section, similar to a knee meniscus.

EXAMPLES

Example I

Fabrication of Meniscus Implant

The mold for the scaffold was made up of a plastic base plate, outer glass tube, inner sphere, and 24 clothing pins. Twenty-four holes (0.05 mm) were drilled through the large face of the plate as shown in FIG. **7**A. Twenty-two holes were at equal intervals forming a semi-circle with the remaining two holes opposite the center of the semi-circle. Twenty-four pins were pushed through the holes forming the pattern shown in FIG. **7**B. For purposes of explanation, each hole of the base plate was assigned a number from 1 through 26. Holes **2** through **25** define the actual dimensions of the meniscus scaffold, while holes **1** and **26** define the anchor points for the scaffold.

Referring to FIGS. **8**A-**8**G, a continuous length of polymer fiber was wrapped around the pins in a quasi-circumferential pattern. Starting from point **1**, fibers were wrapped and pivoted at one of six different off-tangent angles from the pins: (a) 11.25°, (b) 28.125°, (c) 39.375°, (d) 50.625°, (e) 61.875°, and (f) 73.125°. This continued until point **26**, at which time the fiber was wrapped in reverse. For pins **2** through **5** and **22** through **25**, fibers were wrapped back to point **1** or **26** for formation of anchor bundles. This process was repeated for each angle to produce a complete pattern shown in FIG. **8**G. Depending on the amount of fiber desired for reinforcing, this pattern was repeated several times.

The pin pattern allows for a semi-lunar shape to be formed along with two bundles of fibers at each horn for formation of the anchor plugs. After wrapping was complete, the fibers were teased up to form a wedge shape (cross-section). The fiber wrapped assembly was then stored in a low humidity chamber until the collagen dispersion was ready for the molding step.

A collagen dispersion was made by swelling lyophilized type I bovine collagen in an acid solution (pH .≈2.4). The appropriate amount of collagen was added to a volume of acid (e.g. for 1% dispersion, 1.0 g collagen added to 100 ml acid). As noted above, in different embodiments, other materials may be added to alter the properties of the matrix portion and dispersion concentrations may be modified. The collagen/acid mixture was then homogenized using a high speed blender (pulse blending to reduce possible heat denaturation effects on collagen). After about five minutes of pulse blending (mix≈5 seconds, wait for ≈1 minute), the mixture was de-aerated under vacuum for about five minutes. About 8 ml of the dispersion was drawn up into a syringe using a 20 gauge needle to prevent large, non-homogenized chunks of collagen from entering scaffold.

The outer glass tube and inner sphere were placed in position around the base plate to complete the mold assembly. The collagen dispersion was injected into the mold, ensuring no air bubbles were introduced into the scaffold body. The assembly was wrapped in a thin plastic bag and submerged in an ethanol-dry ice bath (≈−30° C.) for about 10 minutes. The resultant solid was then transferred to a standard freezer for about an hour to ensure complete freezing. After the entire assembly was frozen completely, it was lyophilized.

After lyophilization, the pins were pulled from the base plate, resulting in a fiber reinforced collagen sponge with a semi-lunar shape, a wedge-shaped cross-section, and a series of small holes around it periphery. The extra lengths of fibers from the ends of the scaffold were used to form anchor plugs which can be implanted into the tibial plateau.

After construction, the scaffolds were crosslinked to increase the durability of the collagen matrix. The implant was stored dry until use.

Example 2

Mechanical Evaluation

A preliminary mechanical evaluation was carried out using standard tensile testing. The following groups were tested: collagen scaffold with a reinforcing fibers consisting of 500 fibers ("500 Fiber Scaffold"), and collagen scaffold with a reinforcing fibers consisting of 1000 fibers ("1000 Fiber Scaffold). In this evaluation the anterior and posterior fiber ends were soaked in poly-urethane glue to enhance gripping in the test machine and dried overnight. They were then loaded into an Instron Mechanical Tester (model 4202) and pulled in tension until failure at a speed of 10 mm/min. The structural properties were calculated from recorded data. The results are set forth in FIG. **9**.

An advanced mechanical evaluation of the meniscus replacement of the invention measured pressure distribution on the tibial plateau but did not measure circumferential hoop stresses developed from axial compressive loads using "indirect" measurement. The results are shown in FIGS. **10**-**13**. With regard to the contact area, no significant difference was seen between the "No Scaffold" and "100% Coll. Scaffold"

groups while there were significant differences between "No Scaffold" and "100% Coll. Scaffold" groups and "500 Fiber Scaffold" and "1000 Fiber Scaffold" groups.

Example 3

Biological Evaluation

The scaffold was evaluated by characterizing the in vitro biological response to the scaffold as well as preliminary in vivo evaluations in rabbit models.

In an in vitro evaluation a fibrochondrocyte cell line was harvested from NZW rabbits and cultured until 2nd/3rd passage. Scaffolds were sectioned into 6 wedges as shown in FIG. **14**A. 1×10^5 cells were seeded onto the anterior surface of each section and the cell-seeded scaffolds were incubated in complete cell media for 4 hrs, 4 days, 8 days, or 16 days. The scaffolds were then analyzed with either MTS assay or standard H&E histology. A normal growth curve was observed with a significant difference between all time points, as seen in FIG. **14**B. There was no significant difference between the two scaffold types of the invention.

In a non-functional in vivo evaluation in rabbits, two sections were cut from each scaffold for 4 and 8 week time points. Two scaffold designs were studied (500 fiber and 1,000 fiber scaffolds). A medial parapatellar arthrotomy created a pocket for an implant between medial joint capsule and medial femoral condyle and the scaffold was inserted. The scaffold therefore was exposed to harsh synovial environments but was under no significant load and did not interfere with joint function. Both knees of each rabbit were used with the 500 fiber scaffold on one side and the 1000 fiber scaffold in the other. At sacrifice the scaffolds were excised along with 2-3 mm of surrounding tissue. The samples were preserved in buffered formalin and then processed histologically with H&E stain. The results are shown in FIGS. **15**A-**15**F.

Example 4

Biocompatibility Implantation Study

The objective of the biocompatibility study was to observe the in vivo response to the scaffold and determine its ability to initiate cellular infiltration, proliferation, and protein deposition within the construct. The Orthopaedic Research Laboratory at Robert Wood Johnson Medical School has demonstrated that the implantation site has strong implications on both the degradation rate of the material as well as cellular infiltration. Thus, implanting the scaffold within its functional location will divulge a more representative response than cell studies alone.

The biological incorporation of fiber-reinforced scaffolds was evaluated in an in vivo rabbit model. Sections of meniscus scaffolds were implanted in synovial pockets of 10 New Zealand white rabbits (one per knee, 20 implants). Scaffolds were positioned such that they were exposed to the harsh enzymatic environment of the knee, while carrying no mechanical load, or interfering with joint function. Animals were sacrificed at either 4 or 8 weeks post-implantation. The excised scaffolds were fixed in formalin and then processed for standard histological analysis with H&E and Masson's Trichrome. Slides were analyzed and graded in a random, blinded fashion by a pathologist for inflammation, vascularization, neo-tissue formation, and scaffold degradation. All surgeries were performed using an IACUC approved protocol.

All results were statistically analyzed using a two-way ANOVA with pair wise comparisons by the Student-Newman-Keuls method.

Gross observations of the excised scaffolds showed no negative host response to the implants. The implants were firm and showed signs of good tissue in-growth. As previously seen with these types of implants, a considerable inflammatory response was observed in all implants consisting of plasma cells **132**, eosinophils **134**, and multi-nucleated giant cells (MNGCs) **136**. Inflammation due to plasma cells **132** was found predominantly around the matrix portion of the scaffold and significantly decreased from 4 to 8 weeks (FIG. **23**A, **24**). Eosinophils **134** were found sporadically among the plasma cells **132** and their levels remained moderately low for both time points. MNGCs **136** were found next to or around the reinforcing polymer fibers **23'**. At 4 weeks, the level of MNGC inflammation was relatively low but significantly increased by 8 weeks (FIG. **23**A, **24**). No significant differences were noted between different scaffold types.

Scaffold resorption and tissue formation proceeded in a predictable progression. Partial degradation of the collagen matrix **140** was observed at the four week time point and nearly all original matrix was degraded by eight weeks ($p<0.05$). The polymer fibers **23'** remained intact during both time points. Minor vascularization was observed at the four week time point which significantly increased by eight weeks ($p<0.05$). Tissue **142** infiltration was noted throughout the samples for both time points with a significant increase in amount and organization by eight weeks (FIG. **23**B, **24**). No differences were noted between scaffolds with HA alone or both HA and CS.

Results from the in vivo study suggest that the scaffold with HA or HA and CS elicits a biological response conducive to its incorporation, degradation, and eventual replacement with native tissue. While the collagen portion of the scaffold is almost completely replaced by cells and amorphous tissue at 8 weeks, the continued presence of the polymer fibers shows that, despite the harsh synovial environment of the joint, the primary load-bearing portion of the scaffold will persist thru the early remodeling phase. This is important for a meniscus scaffold, which needs to provide mechanical function for a relatively extended period of time as new collagen is deposited and organized into a structurally sound tissue. It is yet unclear what long term role CS or HA will have on the biological incorporation of the scaffold in a long term functional model. Similar results were seen when compared to the 1st Generation Scaffold.

Example 5

Functional Implantation Study—Total Meniscus Replacement in Sheep

The implant **1'** was evaluated in a functional sheep model to determine its ability to promote neo-fibrocartilaginous tissue growth and minimize degenerative changes to the articular surfaces of the knee joint. Based on the collective data obtained from the mechanical testing and the non-functional rabbit model, the scaffold design containing Bovine Tendon Collagen with Hyaluronic Acid and poly(DTD DD) fibers was chosen as the optimal Meniscus Implant to be used in this functional sheep evaluation.

The medial menisci of 20 sheep were removed and 16 were replaced with a polymer fiber/collagen/GAG implant **1'**. Four were left as meniscectomy controls. Scaffold horn attachments **121**, **122** were fed into bone tunnels located at the anterior/posterior horn attachments of the normal meniscus and secured with interference screws. The periphery of the scaffold was secured to the synovial lining with suture. The animals were allowed recovery times of either 16 or 32 weeks post-operatively.

At sacrifice, all scaffolds were fully intact and firmly adhered to the surrounding tissue. Scaffold anchor attachments to the tibial plateau were structurally sound. Even at a gross level, the tissue integration and ingrowth into the scaffolds was obvious.

The following table shows the attachment stability of the attachment segments utilized in the implants 1'.

Device/Time	No. Implanted	Fully Intact/Secured	Ruptured	Pulled out of bone tunnel
Implant 1' 8 weeks	8	8	0	0
Implant 1' 16 weeks	8	8	0	0

There were no gross degenerative changes in the articular cartilage surfaces in knees with the implants **1'**. In sharp contrast, the cartilage was severely damaged in the control total meniscectomy knees with no implant.

The recovered implants were mechanically evaluated to assess both their strength retention as well as the strength of the new tissue being deposited within the construct. Each implant that was recovered for mechanical testing was soaked in saline prior to testing and then had a posterior and anterior 4 mm biopsy sample **150**, **151** removed as shown in FIG. **25**. The 4 mm samples **150**, **151** were then tested in confined creep to determine the aggregate modulus and permeability of the tissue. The remaining tissue was then used in a circumferential tensile testing to failure by gripping the posterior and anterior sections **152**, **153** as depicted by the shaded regions in FIG. **25**.

Based on the samples that have been tested, so far there are no statistical differences between 4 and 8 month implants in either breaking load or stiffness as shown in FIGS. **26**A and **26**B, respectively. All of the implants **1'** that were recovered were at about half of the native medial menisci tensile properties which was a positive, somewhat unexpected result in view of some of the recovered implants **1'** having an extruded and thinned central section which in itself could lead to a weaker circumferential strength. Thus, these higher than expected values show the resilience of the scaffold design.

Confined compressive creep experiments have been run and the compressive properties (aggregate modulus, permeability) of the new tissue ingrowth analyzed to date, using constant permeability biphasic theory in a custom Matlab program, have shown a slightly higher deformation under compressive creep but the values are nearing that of the native medial meniscus as shown in FIG. **27**.

Furthermore, FIG. **28**A shows the gross appearance of an exemplary recovered implant **1'** with neo-meniscus tissue formation at 4 months post-implantation in the sheep total meniscus replacement model. The recovered implant **1'** is of similar size and shaped compared to a normal native meniscus as shown in FIG. **28**B. Similarly, FIG. **29**A shows a cross-sectional histological view of the wedge-shaped recovered implant **1'** at 8 months post-implantation. Again, the recovered implant **1'** is of similar size and shape compared to normal native meniscus as shown in FIG. **29**B.

FIGS. **30** and **31** further illustrate the positive results of the study, showing compressive properties of the implant prior to implantation (0 month) and at 4 and 8 months post-implantation in the sheep total meniscus replacement model. As illustrated, there is a general increase in the compressive modulus and decrease in permeability with time as the neo-meniscus tissue remodels and becomes more similar to the normal native meniscus.

Although the invention herein has been described with reference to particular embodiments, it is to be understood that these embodiments are merely illustrative of the principles and applications of the present invention. It is therefore to be understood that numerous modifications may be made to the illustrative embodiments and that other arrangements may be devised without departing from the spirit and scope of the present invention which is defined by the following claims.

What is claimed:

1. An artificial knee meniscus implant comprising:

a c-shaped scaffold having an arcuate middle section extending between an anterior end and a posterior end with a central axis extending through a center of the arcuate middle section and evenly spaced between the anterior and posterior ends ; and

a reinforcing network of fibers independent from and embedded in the scaffold, the reinforcing network of fibers defining a matrix having a three-dimensional shape and geometry which is substantially the same as a three-dimensional shape and geometry of the c-shaped scaffold;

wherein fibers of said network fibers exit each end of the scaffold to form respective anterior and posterior attachment segments which extend parallel to the central axis of the scaffold; and said network of fibers is configured to convert an axial compressive force on said scaffold to tensile loads on said attachment points.

2. The artificial meniscus of claim **1**, wherein at least a portion said network of fibers extends along said arcuate middle section in a substantially circumferential direction.

3. The artificial meniscus of claim **2**, wherein said network of fibers further comprises an orthogonal fiber network embedded within said scaffold to prevent separation of said circumferential fiber network.

4. The artificial meniscus of claim **3**, wherein said network of fibers further comprises radial tie fibers woven through the circumferentially oriented fibers.

5. The artificial implant of claim **1**, wherein the scaffold has a wedge-shaped cross-section.

6. The artificial implant of claim **5**, further comprising at least one peripheral attachment point.

7. The artificial implant of claim **6**, wherein the at least one peripheral attachment point coincides with a point at which said fibers extending in a substantially circumferential direction intersect with said orthogonal fiber network.

8. The artificial implant of claim **3**, wherein the reinforcing network extends throughout said wedge-shaped cross section of said arcuate middle section.

9. The artificial implant of claim **1**, wherein the scaffold is formed from a material selected from the group consisting of proteins, proteoglycans, biocompatible synthetic polymers and combinations thereof.

10. The implant of claim **1**, wherein the scaffold is formed from proteins comprising collagen.

11. The implant of claim **10**, wherein the collagen is cross-linked.

12. The implant of claim **1**, wherein the scaffold is made from bovine Achilles tendon collagen.

13. The implant of claim **12**, wherein the collagen concentration is approximately 2% dry weight/ volume.

14. The implant of claim **12**, wherein the scaffold further includes Hyaluronic Acid at low concentrations.

15. The implant of claim **12**, wherein the collagen undergoes a dispersion processing including high speed mini blender with ground collagen.

16. The artificial implant of claim 1, wherein at least one of the scaffold and the reinforcing network comprises a biocompatible synthetic polymeric material.

17. The artificial implant of claim 1, wherein at least one of the scaffold and the reinforcing network comprises a bioresorbable material.

18. The artificial implant of claim 17, wherein the reinforcing network of fibers are manufactured from a bioresorbable material selected such that a rate of degradation of the bioresorbable material is sufficiently long so as to allow for tissue ingrowth to occur within the biomaterial.

19. A method for replacement of a damaged meniscus comprising replacing a damaged portion of said meniscus with an implant according to claim 1 corresponding to the damaged portion being replaced by inserting said implant between a tibial plateau and a corresponding femur condyle.

20. The method of claim 19, wherein said method comprises a total or sub-total meniscectomy and said method further includes a step of extending the anterior and posterior attachment segments through a bone tunnel and securing the attachment segments to the tibial plateau.

21. The method of claim 20, wherein said implant further comprises at least one attachment point on an exterior periphery of said arcuate middle section and said method further comprises a step of attaching the implant to a surrounding tissue wall through at least one of said attachment points.

22. The method of claim 21, wherein at least one of said attachment points coincides with a point at which a fiber extending circumferentially along said arcuate middle section contacts said exterior periphery of said arcuate middle section.

* * * * *