



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

<p>(51) International Patent Classification⁴ : A61F 2/28, 2/38</p>	<p>A1</p>	<p>(11) International Publication Number: WO 89/ 00413 (43) International Publication Date: 26 January 1989 (26.01.89)</p>
<p>(21) International Application Number: PCT/US88/02447 (22) International Filing Date: 20 July 1988 (20.07.88) (31) Priority Application Number: 075,352 (32) Priority Date: 20 July 1987 (20.07.87) (33) Priority Country: US</p> <p>(71)(72) Applicant and Inventor: STONE, Kevin, R. [US/US]; 325 Twin Peaks Boulevard, San Francisco, CA 94114 (US). (74) Agents: LAPPIN, Mark, G. et al.; Lahive & Cockfield, 60 State Street, Boston, MA 02109 (US). (81) Designated States: AT (European patent), AU, BE (European patent), CH (European patent), DE (European patent), FR (European patent), GB (European patent), IT (European patent), JP, LU (European patent), NL (European patent),</p>		<p>SE (European patent).</p> <p>Published <i>With international search report. Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i></p>
<p>(54) Title: PROSTHETIC MENISCUS</p>		
<p>(57) Abstract</p> <p>A prosthetic meniscus is disclosed which can be implanted in a humanoid knee, and which can act as a scaffold for regrowth of native meniscal tissues. The meniscus comprises a three dimensional array of collagen fibers interspersed with glycosaminoglycan molecules. The collagen fibers are present at a concentration of about 65 to 98 percent by dry weight, and the glycosaminoglycan molecules are present at a concentration of about 1 to 25 percent by dry weight. Crosslinks are provided by at least a portion of the glycosaminoglycan molecules, and may consist of at least one of the group comprising chondroitin 4-sulfate, chondroitin 6-sulfate, keratan sulfate, dermatan sulfate, heparin sulfate, and hyaluronic acid.</p>		

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AT	Austria	FR	France	ML	Mali
AU	Australia	GA	Gabon	MR	Mauritania
BB	Barbados	GB	United Kingdom	MW	Malawi
BE	Belgium	HU	Hungary	NL	Netherlands
BG	Bulgaria	IT	Italy	NO	Norway
BJ	Benin	JP	Japan	RO	Romania
BR	Brazil	KP	Democratic People's Republic of Korea	SD	Sudan
CF	Central African Republic	KR	Republic of Korea	SE	Sweden
CG	Congo	LI	Liechtenstein	SN	Senegal
CH	Switzerland	LK	Sri Lanka	SU	Soviet Union
CM	Cameroon	LU	Luxembourg	TD	Chad
DE	Germany, Federal Republic of	MC	Monaco	TG	Togo
DK	Denmark	MG	Madagascar	US	United States of America
FI	Finland				

PROSTHETIC MENISCUS

BACKGROUND OF THE DISCLOSURE

The present invention is in the field of implantable medical devices, and more particularly, is directed to devices useful as prosthetic menisci.

The meniscus acts in the knee joint as a crucial stabilizer, a mechanism for force distribution, and a lubricant in the area of contact between the tibia and femur. Without the meniscus, stress concentration occurs in the knee in conjunction with abnormal joint mechanics, and premature development of arthritic changes from collagen stress occurs.

In the prior art, treatment of injured or diseased menisci has generally been both by surgical repair and by excision. With excision, regeneration of meniscal tissue may occur. Additionally, it is known that meniscal fibrochondrocytes have the ability to migrate into a defect filled with a fibrin clot and form tissue apparently similar to normal meniscal fibrocartilage. When an adequate matrix scaffold is present within a meniscal defect, such meniscal fibrocartilage may be formed. Meniscal tissue is also capable of self-repair when exposed to bleeding tissues, and additionally, it is also known in the prior art that meniscal cells in tissue culture are capable of cell division and matrix synthesis. Replacement of an injured meniscus in an otherwise healthy joint may prevent arthritic changes and may stabilize the joint. In diseased joints, replacement of the meniscus may reduce the progression of the disease process, and may provide pain relief. Allografting or meniscal transplantation, is one method of replacement which

-2-

has been executed both in dogs and in humans. However, this approach has been only partially successful over the long term due to the host's immunologic response to the graft, to failures in the cryopreservation process, and to failures of the attachment sites.

In alternative prior art replacement approaches, menisci have been replaced with prostheses composed of artificial materials. Such prostheses have been constructed of purely artificial materials in order to minimize the possibility of an immunological response. In addition, the use of such materials is believed to be advantageous because it permits construction of a structure which can withstand the high and repeated loads which are encountered in the knee joint, and because it can alter the joint mechanics in beneficial ways that biological materials would not tolerate. For example, a Teflon net has been used to replace the resected meniscus of a dog upon which fibrous ingrowth or regeneration was observed, although accompanied by significant chondral abrasion. A prosthetic meniscus has also been constructed from resilient materials such as silicone rubber or Teflon with reinforcing materials of stainless steel or nylon strands (U.S. Patent No 4,502,161). In addition, a meniscal component has been made from resilient plastic materials as disclosed in U.S. Patent No. 4,085,466. Reconstruction of meniscal lesions have been attempted with carbon-fiber-polyurethane-poly (L-lactide) with minimal success.

Generally, the replacement of meniscal tissue with structures consisting of artificial

materials has been unsuccessful, principally because the opposing articular cartilage of human and animal joints is fragile. The articular cartilage in the knee will not withstand abrasive interfaces, nor compliance variances from normal, which eventually results from the implantation of prior art artificial menisci. Additionally, joint forces are multiples of body weight which, in the case of the knee and hip, are typically encountered over a million cycles per year. Thus far, prior art artificial menisci have not been soft, durable, or lubricative enough, nor have they been able to be positioned securely enough to withstand such routine forces.

Prostheses, in general, have been devised out of at least some of the constituents of the structures which they are replacing, or out of materials not considered to be immunogenic to the body. For example, Yannas et al., fashioned endodermal implants, synthetic epidermis (U.S. Patent No. 4,060,081), and sciatic nerve guides out of collagen and glycosaminoglycans, which are biochemical constituents of many body organs. By adjusting the pore size and axes of the pores and fibers comprising these structures, regrowth could be stimulated, and was, indeed, observed. Further regrowth has been advanced by seeding of the nerve guide with Schwann cells prior to implantation. However, even with the foregoing technologies which have been applied to the reconstruction of anatomical structures other than knee joints, a structure suitable as a prosthetic meniscus and constructed from natural materials has not been developed in the prior art.

-4-

Accordingly, it is an object of this invention to provide a meniscal replacement or prosthesis.

Another object is to provide a meniscal replacement, or prosthesis, which does not interfere with normal joint motion, which would lead to either a reduced range of motion, or focal concentration of force at other sites within the joint and therefore progressive cartilage destruction.

Yet another object is to provide a meniscal replacement or prosthesis which is biomechanically able to withstand normal joint forces and is able to function at those loads to protect the cartilage and stabilize the joint.

Still another object is to provide a meniscal replacement or prosthesis which acts as a scaffold for meniscal fibrochondrocyte infiltration, and which is subsequently replaced.

A further object is to provide a meniscal replacement or prosthesis which is composed of biocompatible materials having an organization equivalent to that of the normal meniscus; thereby not evoking an immunologic reaction, nor aggravating other joint structures.

Still a further object is to provide a meniscal replacement or prosthesis which is adapted for implantation by standard operative techniques, preferably transarthroscopically.

SUMMARY OF THE INVENTION

The present invention provides a structure for implantation into the knee joint which assumes

the form and role of a meniscus. This prosthetic meniscus may also promote regrowth of meniscal tissue and may provide a scaffold for the regenerating tissue.

The prosthetic meniscus is generally a three dimensional array of collagen fibers interspersed and crosslinked with glycosaminoglycan molecules. The array may have a simple crescent-shaped wedge, cylindrical pad, or other shape. The structure comprises about 65-95% Type I collagen and about 1-25% glycosaminoglycans by dry weight, the proportions of which may be constant throughout the structure or may be variable.

In the structure, the collagen fibers may be randomly orientated throughout the structure, or ordered at specified regions. Alternatively, the fibers may assume substantially circumferential and radial orientations at specified regions of the structure or may be found uniformly throughout the prosthetic meniscus.

The glycosaminoglycans (GAGs) consist of at least one of the group of molecules comprising chondroitin 4-sulfate; chondroitin 6-sulfate; keratin sulfate; dermatan sulfate; heparin sulfate; and hyaluronic acid. These GAGs may be uniformly dispersed throughout the prosthetic meniscus as individual molecules, or may be present in differing amounts in different regions of the structure.

However, at least a portion of the GAG molecules comprising the prosthetic meniscus are constituents of chemical crosslinks which bridge neighboring collagen fibers. These crosslinks are composed of at least one polymerized GAG molecule, and have a molecular weight in the range 800-60,000 daltons.

-6-

In various forms of the invention, GAG crosslinks may be uniformly dispersed throughout the prosthetic meniscus at a density of less than about 0.9 but greater than about 0.5, as expressed by the 3-hydroxypyridium crosslink/collagen molar ratio, thereby permitting the ingrowth of regenerating meniscal tissue, and eventually providing a fluidic impedance

similar to that of normal meniscus of about $1/8.13 \times 10^{-16} \text{ m}^4/\text{N.s.}$. In other forms of the invention, the density of these crosslinks may be greater than about 0.9, providing a fluidic impedance of greater than about $1/8.13 \times 10^{-16} \text{ m}^4/\text{N.s.}$, and thereby being dense enough to act as a protective and lubricating barrier between the femur and tibia. These crosslinks may also be located with varying densities at specified regions of the prosthetic meniscus, permitting greater physical strength at anticipated high stress points.

In accordance with another aspect of the invention, the prosthetic meniscus may further comprise a mesh composed of a dissolvable, nonimmunogenic material which is attached to portions of the outer surface of the prosthetic meniscus. The mesh, which may be in the form of suture material, aids in the successful implantation of the prosthetic meniscus into the knee joint by providing a temporary anchoring mechanism.

BRIEF DESCRIPTION OF THE DRAWING

The foregoing and other objects of this invention, the various features thereof, as well as the invention, itself, may be more fully understood

-7-

from the following description, when read together with the accompanying drawings:

Fig. 1 shows a simplified diagrammatic representation of a humanoid knee joint, with menisci in native positioning;

Fig. 2 shows a perspective view of an exemplary prosthetic meniscus in accordance with the present invention;

Fig. 3 shows a perspective radial section of the prosthetic meniscus of Fig. 2;

Fig. 4 shows a perspective view of an alternative embodiment of the present invention;

Fig. 5 shows a sectional view along line 5-5 of the prosthetic meniscus of Fig. 4.

DESCRIPTION OF THE PREFERRED EMBODIMENT

Fig. 1 shows a diagrammatic representation of the normal positioning of medial meniscus 7 and collateral meniscus 8 in the human knee joint 3 between the femur 2 and tibia 4.

Figs. 2 and 3 show an exemplary prosthetic meniscus 10 embodying the present invention. The prosthetic meniscus 10 is adapted for implantation in the normal location in the knee joint.

Generally, the prosthetic meniscus 10 has the shape of a crescent-shaped wedge comprising a relatively wide central region 12 between two narrow distal regions 14 and 16. In the preferred form, the wedge has height A at its peripheral edge of approximately 0.4 inches, a height D at its central point of approximately 0.2 inches, and a radius C of approximately 1.0 inches. The crescent shaped wedge subtends an angle B substantially in the range of

about 25 to about 45 degrees, and preferably of about 30 degrees.

The prosthetic meniscus is composed essentially of collagen and glycosaminoglycans (GAGs), and more particularly, of a three-dimensional array of collagen type I fibers interconnected via crosslinks consisting of polymerized GAG molecules. In other embodiments, additional GAG molecules may be present outside of the crosslinked GAGs.

In the preferred embodiment, the collagen fibers in the array are ordered in substantially circumferentially-extending and substantially radially-extending orientations, with the density of fibers being substantially uniform throughout the array. However, in other embodiments, the array of collagen fibers may be unordered. In either configuration, ordered or unordered, the density of said fibers may be non-uniform, particularly having high densities at points in the prosthetic meniscus at which high stress levels are anticipated, such as at the distal regions 14 and 16.

The GAG crosslinks have a molecular weight in the range of 600 to 80,000 daltons, and are composed typically of at least one of the group of GAG molecules consisting of chondroitin 4-sulfate; chondroitin 6-sulfate; keratin sulfate; dermatan sulfate; heparin sulfate; and hyaluronic acid. The dispersion of GAG crosslinks is preferably uniform, but may be more concentrated at anticipated points of high stress, typically at the distal regions 14 and 16, and less concentrated in the central region 12. In such configurations, the GAG concentration may be in the range of about 3-25% in the distal regions 14 and 16, and in the range of about 1-10% in the central region 12. However, when uniform, the

dispersion of GAG crosslinks throughout the prosthetic meniscus may be, for example, in the range of about 1-15%.

In the preferred embodiment, the density of the crosslinks is relatively low (for example, on the order of about 0.7 crosslink/collagen molar ratio) in the array to permit ingrowth of regenerated meniscal tissue. In other embodiments, the density of said crosslinks may be relatively high (for example, on the order of 0.9 crosslink/collagen ratio) to provide cushioning, lubrication and support for the knee joint and to slow vascular ingrowth, thereby diminishing the rate of scaffold resorption.

In the embodiment illustrated in Fig. 2, the prosthetic meniscus 10 includes a mesh member 20 extending from its peripheral edge. The mesh member 20 is composed of a nonantigenic, dissolvable suture material, and provides a readily used means for anchoring the meniscus 10 in place. The mesh member 20 may function in this capacity until sufficient tissue ingrowth occurs to then provide that function. By way of an example, the mesh member 20 may be a # 1 mesh screen composed of absorbable suture materials such as polyglyconate, Dexon or polydioxane (PDS) woven into a mesh. Nonabsorbable suture materials such as Gore-tex may also be used.

Figs. 4 and 5 show additional embodiments of the present invention which are similar in composition to the prosthetic meniscus depicted in Fig. 2. More particularly, Fig. 4 depicts a right circular cylinder-shaped meniscus 22. Fig. 5 shows a sectional view along line 5-5 of the meniscus shown in Fig. 4.

In other forms of the invention, still other shapes may be used, particularly with varying densities of collagen fibers and dispersions of GAG molecules and crosslinks, permitting accommodation of

-10-

differing stress levels, rates of ingrowth, and resiliency.

Exemplary menisci may be constructed in the following manner:

EXAMPLE I

(A) Type I collagen from bovine Achilles tendon is mechanically processed to disintegrated tissue, soaked in 0.1% N HCl, and mechanically compressed under high pressure while methodically narrowing the gap between metal rollers. Swollen collagen fibers are dehydrated in 20% NaCl for 3 days, and the mechanical separation repeated. Final mechanical separation is repeated at pH 3.0-3.5 in the presence of 0.7% NaCl. The deswollen fibers produce 20 to 30 centimeter long fibers at pH 3.0-3.5. These fibers are ground into a dispersion and further washed in 0.7% NaCl and neutralized in the presence of 0.1% HCl as described above. They are then suspended in a 20% NaCl solution. Ethanol may be added to decrease the isoelectric point and further increase the concentration of collagen fibers in the dispersion.

(B) The fiber dispersion is then subjected to dehydrothermal crosslinking conditions: heating to from about 100 to 135 degrees C for about 24 to 72 hours, and then further crosslinked by exposure for 1-15 hours to 0.1-0.5% glutaraldehyde at room temperature.

(C) Further neutralization and washes with a balanced electrolyte solution containing 20% NaCl and 25% acetone in 0.5 M phosphate buffer, pH 5.5 are carried out. Multiple washes in the buffered

-11-

salt-acetone solution also containing 0.5 M EDTA are also performed. The final rinse step includes 0.15 M phosphate buffer, 7.2, with drying in preformed meniscal molds.

EXAMPLE II

(A) - (C) same as steps (A) - (C) described in EXAMPLE I.

(D) While in dispersion form, selected glycosaminoglycans are added which may include chondroitin 6-sulfate, chondroitin 4-sulfate, hyaluronate, dermatan sulfate, heparin sulfate, and keratin sulfate to a concentration of about 0.5-25 weight %, preferably to about 2.5 weight %. The GAGs are allowed to diffuse freely in the solution, creating a porous matrix with properties defined by the pore sizes of 30-60 microns, the purity of the collagen at 99.9%, the density of the structure, and the quantity of GAGS.

EXAMPLE III

(A) - (D) same as steps (A) - (D) as described in Example II.

(E) For attachment purposes, a mesh of absorbable polyglyconate suture material, matched to the size of the mold, is laid in the dispersed collagen such that it protrudes from the structure's periphery to form a skirt which may extend over the tibial plateau. This mesh provides both immediate attachment sites and long term fibrous ingrowth.

-12-

EXAMPLE IV

(A)-(C) same as steps (A) - (C) as described in EXAMPLES I and II.

(D*) While in dispersion form, selected glycosaminoglycans are added. The dispersion is then subjected to pressurization to 20,000 lbs compressing the structure to reduce the pore sizes to 10-50 microns.

(E) same as step (E) as described in EXAMPLE II.

EXAMPLE V

(A) same as step (A) as described in EXAMPLES I - IV.

(B) The fiber dispersion is then crosslinked by exposure for 1 - 15 hours to 0.05 M 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide-HCl in a balanced electrolyte solution at pH 5.0 at room temperature.

(C) same as step (C) as described in EXAMPLES I - IV.

(D) same as step (D) as described in EXAMPLES II and III.

EXAMPLE VI

(A) same as step (A) as described in

-13-

EXAMPLES I - V.

(B) The fiber dispersion is then subjected to dehydrothermal crosslinking conditions: heating to from about 100 to 135 degrees C for about 24 to 72 hours, and then further crosslinked by exposure for 1-15 hours to 0.05 M 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide-HCl in a balanced electrolyte solution, pH 5.0 at room temperature.

Other chemical crosslinking reagents known to those skilled in the art (such as hexamethylene diisocyanate) may be substituted for glutaraldehyde or carbodiimide in the above EXAMPLES.

With the processes described in the above examples, a prosthetic meniscus of the form shown in Figs. 2 and 3 may be constructed having the following dimensions:

height A = 0.20 - 0.40 inches
angle B = 25° - 45° degrees
radius C = 0.5 - 2.0 inches
height D = 0.05 - 0.1 inches

Generally, that exemplary meniscus has substantially uniform GAG concentration of approximately 50 mg/ml of tissue, and crosslink density as expressed by the 3-hydroxy pyridinium crosslink/collagen molar ratio of 0.86 when the collagen has a content of >85% by dry weight. In the preferred form, the functional characteristics of the exemplary meniscus after repopulation with host meniscal fibrochondrocytes are as set forth in Table 1.

-14-

TABLE 1

Physiologic Loading Rate:	70 - 100 kg/cm ² /sec
Strain Rate:	1.7 - 9 %/sec
Breaking Strain:	15 - 25%
Modulus of Elasticity: (of hydrated tissue after creep)	0.412 mPa
Modulus of Superficial (200um) Isotropic Fibers:	45 - 65 mPa
Modulus of Deep Anisotropic Fibers:	
Circumferential Fibers:	
Superficial	35 - 55 mPa
Middle	185 - 205 mPa
Deep	130 - 150 mPa
Radial Fibers:	
Superficial	65 - 80 mPa
Middle	1 - 4 mPa
Deep	3 - 6 mPa
Average Permeability Density Coefficient:	8.13 x 10 ⁻¹⁶ m ⁴ /N.s.
Coefficient of Friction	0.001 when covered in synovial fluid

The invention may be embodied with other specific forms without departing from the spirit or essential characteristics thereof. The present embodiments are therefore to be considered in all respects as illustrative and not restrictive, the scope of the invention being indicated by the appended claims rather than by the foregoing

description, and all changes which come within the meaning and range of equivalency of the claims are therefore intended to be embraced therein.

What is claimed is:

-16-

CLAIMS

1. A prosthetic meniscus comprising a three-dimensional array of collagen fibers interspersed with glycosaminoglycan molecules, wherein said collagen fibers are present at a concentration of about 65%-98% by dry weight, wherein said glycosaminoglycan molecules are present at a concentration of about 1%-25% by dry weight, and wherein at least a portion of said molecules provide glycosaminoglycan crosslinks between said collagen fibers.

2. The prosthetic meniscus of claim 1, wherein said array is substantially wedge-shaped.

3. The prosthetic meniscus of claim 2, wherein said wedge-shaped array is crescent-shaped, having a wide central region between two narrow distal tip regions.

4. The prosthetic meniscus of claim 3, wherein said glycosaminoglycan molecules consist of at least one of the group comprising: chondroitin 4-sulfate; chondroitin 6-sulfate; keratin sulfate; dermatan sulfate; heparin sulfate; and hyaluronic acid.

5. The prosthetic meniscus of claim 3, wherein said crosslinks consists of at least one of the group of glycosaminoglycan molecules comprising: chondroitin 4-sulfate; chondroitin 6-sulfate; keratin sulfate; dermatan sulfate; heparin sulfate; and hyaluronic acid, and wherein the molecular weight of said molecular crosslinks is within the range of

800-60,000 daltons.

6. The prosthetic meniscus of claim 3, wherein the orientation of said collagen fibers is substantially random throughout said meniscus.

7. The prosthetic meniscus of claim 5, wherein the orientation of said collagen fibers is ordered substantially throughout said array, said array comprising substantially circumferentially extending and radially extending fibers.

8. The prosthetic meniscus of claim 5 wherein the density of said collagen fibers is substantially uniform throughout said array.

9. The prosthetic meniscus of claim 4, wherein the dispersion of said glycosaminoglycan molecules is substantially uniform throughout said array.

10. The prosthetic meniscus of claim 5, wherein the dispersion of said glycosaminoglycan crosslinks is substantially uniform throughout said array.

11. The prosthetic meniscus of claim 3, wherein the density of said collagen fibers is substantially non-uniform throughout said array.

12. The prosthetic meniscus of claim 4, wherein the dispersion of said glycosaminoglycan molecules is substantially non-uniform throughout said array.

13. The prosthetic meniscus of claim 5, wherein the dispersion of said glycosaminoglycan crosslinks

is substantially non-uniform throughout said array, said crosslinks having relatively high density at the tip regions of said array, and relatively low density at the central region.

14. The prosthetic meniscus of claim 3, further comprising a mesh extending from portions of the outer surface of said array, said mesh being dissolvable and nonimmunogenic.

15. The prosthetic meniscus of claim 1, wherein said array is substantially in the shape of a cylindrical pad.

16. The prosthetic meniscus of claim 1, wherein said glycosaminoglycan crosslinks comprises at least one of the group of glycosaminoglycan molecules consisting of: chondroitin 4-sulfate; chondroitin 6-sulfate; keratin sulfate; dermatan sulfate; heparin sulfate; and hyaluronic acid, and wherein the molecular weight of said molecular crosslinks is within the range of about 800-60,000 daltons.

17. The prosthetic meniscus of claim 16, wherein said glycosaminoglycan crosslinks are present at a density less than about 0.95 and greater than about 0.50 crosslink/collagen ratio, thereby permitting ingrowth of, and providing support for regenerated meniscal tissue.

18. The prosthesis meniscus of claim 16 which permits ingrowth of and providing support for regenerated meniscal tissue.

-19-

19. The prosthetic meniscus of claim 16, further comprising a mesh extending from portions of the outer surface of said array, said mesh being absorbable and nonimmunogenic.

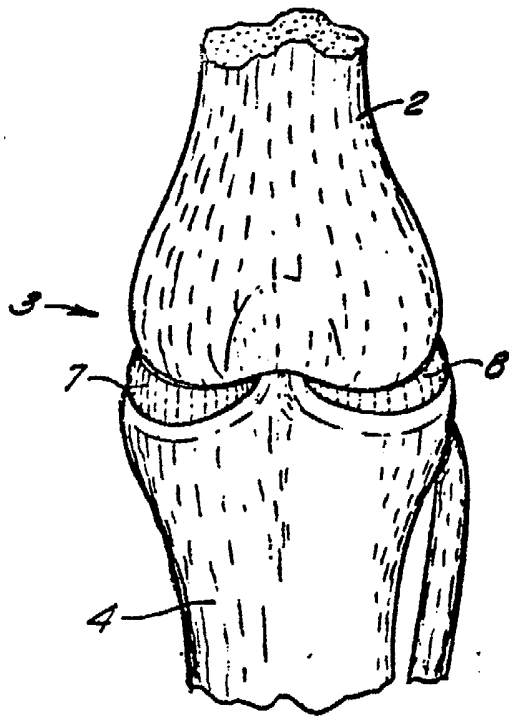


FIG. 1

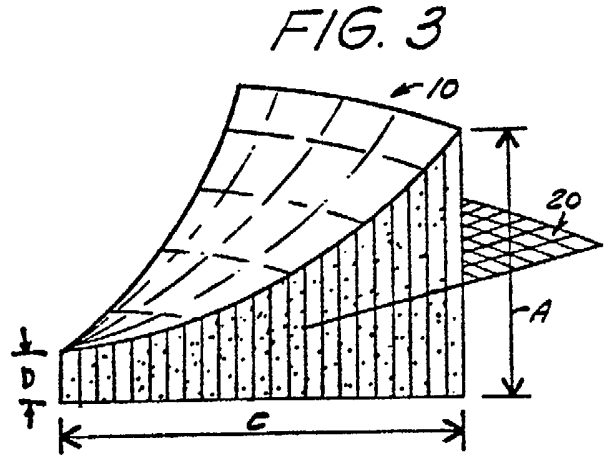


FIG. 3

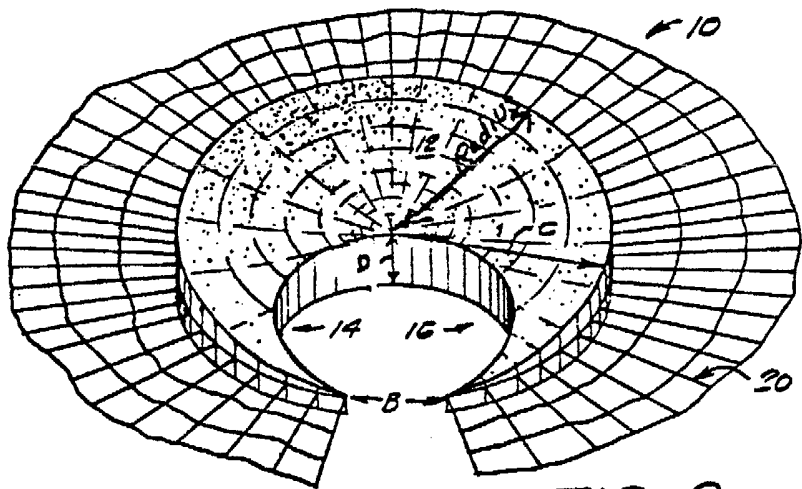


FIG. 2

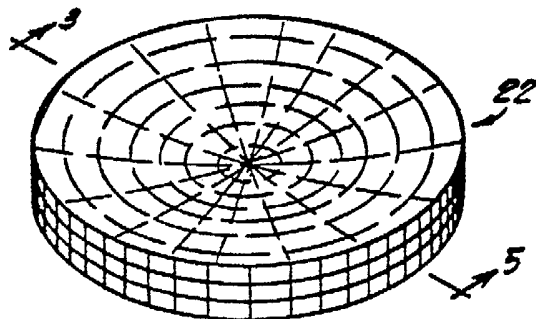


FIG. 4

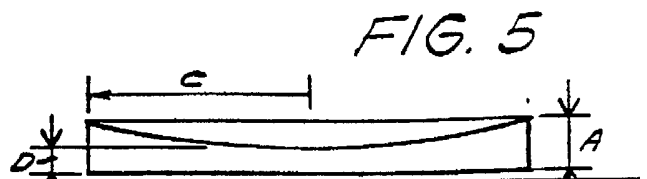


FIG. 5

INTERNATIONAL SEARCH REPORT

International Application No. PCT/US88/02447

I. CLASSIFICATION OF SUBJECT MATTER (if several classification symbols apply, indicate all) ⁶ According to International Patent Classification (IPC) or to both National Classification and IPC <p style="text-align: center;">IPC (4): A61F 2/28, 2/38 US. CL: 623/16; 128/DIG 8; 530/356</p>																				
II. FIELDS SEARCHED <p style="text-align: center;">Minimum Documentation Searched ⁷</p> <table border="1" style="width: 100%; border-collapse: collapse;"> <tr> <td style="width: 30%; padding: 5px;">Classification System</td> <td style="padding: 5px;">Classification Symbols</td> </tr> <tr> <td style="padding: 5px;">US</td> <td style="padding: 5px;">623/16, 20 128/ 1R, DIG8 530/356</td> </tr> </table> <p style="text-align: center;">Documentation Searched other than Minimum Documentation to the Extent that such Documents are Included in the Fields Searched ⁸</p>			Classification System	Classification Symbols	US	623/16, 20 128/ 1R, DIG8 530/356														
Classification System	Classification Symbols																			
US	623/16, 20 128/ 1R, DIG8 530/356																			
III. DOCUMENTS CONSIDERED TO BE RELEVANT ⁹ <table border="1" style="width: 100%; border-collapse: collapse;"> <thead> <tr> <th style="width: 10%; padding: 5px;">Category ⁹</th> <th style="width: 70%; padding: 5px;">Citation of Document, ¹¹ with indication, where appropriate, of the relevant passages ¹²</th> <th style="width: 20%; padding: 5px;">Relevant to Claim No. ¹³</th> </tr> </thead> <tbody> <tr> <td style="text-align: center; vertical-align: top; padding: 5px;">Y</td> <td style="padding: 5px;">GB,A,1,515,963 (MASSACHUSETTS INSTITUTE of TECHNOLOGY) 28 June 1978; see page 1, lines 10-13; page 2, lines 7-32; page 4, lines 45-47.</td> <td style="text-align: center; vertical-align: top; padding: 5px;">1-19</td> </tr> <tr> <td style="text-align: center; vertical-align: top; padding: 5px;">Y</td> <td style="padding: 5px;">US,A,4,614,794 (EASTON ET AL) 30 September 1986; see column 1, lines 7-14 and 43-46.</td> <td style="text-align: center; vertical-align: top; padding: 5px;">1-19</td> </tr> <tr> <td style="text-align: center; vertical-align: top; padding: 5px;">Y</td> <td style="padding: 5px;">US,A,4,627,853 (CAMPBELL ET AL) 09 December 1986; see column 1, lines 33-35; column 1, line 67 to column 2, line 7; column 4, lines 33-48; column 5, lines 35-40 and 53-56; column 6, lines 20-26.</td> <td style="text-align: center; vertical-align: top; padding: 5px;">1-19</td> </tr> <tr> <td style="text-align: center; vertical-align: top; padding: 5px;">Y</td> <td style="padding: 5px;">US,A,4,000,525 (KLAWITTER ET AL) 04 January 1977; see figure</td> <td style="text-align: center; vertical-align: top; padding: 5px;">2,15</td> </tr> <tr> <td style="text-align: center; vertical-align: top; padding: 5px;">Y</td> <td style="padding: 5px;">US,A,4,344,193 (KENNY) 17 August 1982; see column 3, lines 7-19</td> <td style="text-align: center; vertical-align: top; padding: 5px;">3,14,19</td> </tr> </tbody> </table>			Category ⁹	Citation of Document, ¹¹ with indication, where appropriate, of the relevant passages ¹²	Relevant to Claim No. ¹³	Y	GB,A,1,515,963 (MASSACHUSETTS INSTITUTE of TECHNOLOGY) 28 June 1978; see page 1, lines 10-13; page 2, lines 7-32; page 4, lines 45-47.	1-19	Y	US,A,4,614,794 (EASTON ET AL) 30 September 1986; see column 1, lines 7-14 and 43-46.	1-19	Y	US,A,4,627,853 (CAMPBELL ET AL) 09 December 1986; see column 1, lines 33-35; column 1, line 67 to column 2, line 7; column 4, lines 33-48; column 5, lines 35-40 and 53-56; column 6, lines 20-26.	1-19	Y	US,A,4,000,525 (KLAWITTER ET AL) 04 January 1977; see figure	2,15	Y	US,A,4,344,193 (KENNY) 17 August 1982; see column 3, lines 7-19	3,14,19
Category ⁹	Citation of Document, ¹¹ with indication, where appropriate, of the relevant passages ¹²	Relevant to Claim No. ¹³																		
Y	GB,A,1,515,963 (MASSACHUSETTS INSTITUTE of TECHNOLOGY) 28 June 1978; see page 1, lines 10-13; page 2, lines 7-32; page 4, lines 45-47.	1-19																		
Y	US,A,4,614,794 (EASTON ET AL) 30 September 1986; see column 1, lines 7-14 and 43-46.	1-19																		
Y	US,A,4,627,853 (CAMPBELL ET AL) 09 December 1986; see column 1, lines 33-35; column 1, line 67 to column 2, line 7; column 4, lines 33-48; column 5, lines 35-40 and 53-56; column 6, lines 20-26.	1-19																		
Y	US,A,4,000,525 (KLAWITTER ET AL) 04 January 1977; see figure	2,15																		
Y	US,A,4,344,193 (KENNY) 17 August 1982; see column 3, lines 7-19	3,14,19																		
<table style="width: 100%;"> <tr> <td style="width: 50%; vertical-align: top; padding: 5px;"> ¹⁰ Special categories of cited documents: "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier document but published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed </td> <td style="width: 50%; vertical-align: top; padding: 5px;"> "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art. "&" document member of the same patent family </td> </tr> </table>			¹⁰ Special categories of cited documents: "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier document but published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art. "&" document member of the same patent family																
¹⁰ Special categories of cited documents: "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier document but published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art. "&" document member of the same patent family																			
IV. CERTIFICATION <table style="width: 100%;"> <tr> <td style="width: 50%; padding: 5px;">Date of the Actual Completion of the International Search 18 October 1988</td> <td style="width: 50%; padding: 5px;">Date of Mailing of this International Search Report 20 DEC 1988</td> </tr> <tr> <td style="padding: 5px;">International Searching Authority ISA/US</td> <td style="padding: 5px;">Signature of Authorized Officer <i>David Bender</i> David Bender</td> </tr> </table>			Date of the Actual Completion of the International Search 18 October 1988	Date of Mailing of this International Search Report 20 DEC 1988	International Searching Authority ISA/US	Signature of Authorized Officer <i>David Bender</i> David Bender														
Date of the Actual Completion of the International Search 18 October 1988	Date of Mailing of this International Search Report 20 DEC 1988																			
International Searching Authority ISA/US	Signature of Authorized Officer <i>David Bender</i> David Bender																			

FURTHER INFORMATION CONTINUED FROM THE SECOND SHEET		
Y	US,A, 3,551,560 (THIELE) 29 December 1970; see column 2, lines 53-56; column 3, lines 22-43	7,13
Y	US,A, 4,542,539 (ROWE, JR. ET AL) 24 September 1985; see Abstract, lines 16-21	13
Y	US,A, 4,064,567 (BURSTEIN ET AL) 27 December 1977; see Abstract; column 2, lines 66-68; column 5, lines 19-26	14,19
Y	US,A, 4,400,833 (KURLAND) 30 August 1983; see column 1, lines 52-55; column 4, lines 11-20	14,19
V. <input type="checkbox"/> OBSERVATIONS WHERE CERTAIN CLAIMS WERE FOUND UNSEARCHABLE¹		
This international search report has not been established in respect of certain claims under Article 17(2) (a) for the following reasons:		
1. <input type="checkbox"/> Claim numbers _____, because they relate to subject matter ¹² not required to be searched by this Authority, namely:		
2. <input type="checkbox"/> Claim numbers _____, because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out ¹³ , specifically:		
3. <input type="checkbox"/> Claim numbers _____, because they are dependant claims not drafted in accordance with the second and third sentences of PCT Rule 6.4(a).		
VI. <input type="checkbox"/> OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING²		
This International Searching Authority found multiple inventions in this international application as follows:		
1. <input type="checkbox"/> As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims of the international application.		
2. <input type="checkbox"/> As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims of the international application for which fees were paid, specifically claims:		
3. <input type="checkbox"/> No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claim numbers:		
4. <input type="checkbox"/> As all searchable claims could be searched without effort justifying an additional fee, the International Searching Authority did not invite payment of any additional fee.		
Remark on Protest		
<input type="checkbox"/> The additional search fees were accompanied by applicant's protest.		
<input type="checkbox"/> No protest accompanied the payment of additional search fees.		

III. DOCUMENTS CONSIDERED TO BE RELEVANT (CONTINUED FROM THE SECOND SHEET)

Category *	Citation of Document, with indication, where appropriate, of the relevant passages	Relevant to Claim No
A	US,A, 4,544,516 (HUGHES ET AL) 01 October 1985	6-13
A	US,A, 3,855,638 (PILLIER) 24 December 1974	1-19