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(54) **SUPPLEMENTING ENGINEERED ANNULUS  
TISSUES WITH AUTOGRAFT OR  
ALLOGRAFT TENDONS**

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(57) **ABSTRACT**

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**Related U.S. Application Data**

(63) Continuation-in-part of application No. 09/688,716, filed on Oct. 16, 2000, and which is a continuation-in-part of application No. 09/638,726, filed on Aug. 14, 2000, now Pat. No. 6,340,369. Continuation-in-part of application No. 09/415,382, filed on Oct. 8, 1999, now Pat. No. 6,419,704.

(60) Provisional application No. 60/159,488, filed on Oct. 14, 1999. Provisional application No. 60/371,546, filed on Apr. 10, 2002.

Fibrocytes, annulus fibrosis cells, cells that differentiate into annulus fibrosis cells, or cells that function like annulus fibrosis cells are harvested and combined with the extracellular matrix of the annulus fibrosis from a recently deceased human or animal to produce an engineered annulus fibrosis. Autograft tendons are then used to strengthen the annulus fibrosis and to augment or replace the nucleus pulposus. In accordance with a preferred embodiment, tendons such as the palmaris longus are harvested from the patient, a suitable living donor, or a recently deceased human. The tendons are sewn or otherwise attached to the inside of the annulus fibrosis using percutaneous or laparoscopic procedures. The tendons aid the nucleus and/or replace the nucleus by absorbing the compression forces between vertebrae and by transferring the compression forces to the augmented annulus fibrosis. Allograft tendons are preferably treated, with tissue banking techniques well known to those skilled in the art, to prevent disease transmission and graft rejection. The invention can be used to augment discs in the cervical, thoracic, or lumbar spine.

## SUPPLEMENTING ENGINEERED ANNULUS TISSUES WITH AUTOGRAFT OR ALLOGRAFT TENDONS

### REFERENCE TO RELATED APPLICATIONS

[0001] This application is a continuation-in-part of U.S. patent application Ser. No. 09/688,716, filed Oct. 16, 2000, which claims priority from U.S. Provisional Patent Application Serial No. 60/159,488, filed Oct. 14, 1999, and is a continuation-in-part of U.S. patent application Ser. No. 09/638,726, filed Aug. 14, 2000, now U.S. Pat. No. 6,340,369, and Ser. No. 09/415,382, filed Oct. 8, 1999. This application also claims priority from U.S. Provisional Patent Application Serial No. 60/371,546, filed Apr. 10, 2002; the entire content of each application and issued patent being incorporated herein by reference.

### FIELD OF THE INVENTION

[0002] This invention relates generally to the treatment of diseased or traumatized intervertebral discs, and more particularly, to the use of engineered tissues in conjunction with such treatments.

### BACKGROUND OF THE INVENTION

[0003] Intervertebral discs provide mobility and a cushion between the vertebrae. At the center of the disc is the nucleus pulposus. The nucleus pulposus is surrounded by the annulus fibrosis, which is comprised of cells (fibrocyte-like and chondrocyte-like), collagen fibers, and non-fibrillar extracellular matrix. The components of the annulus are arranged in 15-25 lamellae around the nucleus pulposus. The fibers in the lamellae alternate their direction of orientation by 30 degrees between each band.

[0004] The annulus fibrosis has three important functions. First, the annulus contains the nucleus pulposus. Second, the annulus fibrosis, with other ligaments, connects the vertebrae of the spine. Lastly, the annulus fibrosis helps to control movement between the vertebrae.

[0005] The fibers of the annulus can tear causing pain and possible extrusion of the nucleus pulposus. Extrusion of the nucleus pulposus is known as a disc herniation. Disc herniations can compress nerves or the spinal cord resulting in arm or leg pain and dysfunction. Surgery to repair disc herniations leaves a hole in the annulus fibrosis. The hole in the annulus acts as a pathway for additional material to protrude into a nerve, resulting in a recurrence of the herniation. My U.S. Pat. No. 6,245,107 and Patent Cooperation Treaty Application Serial No. PCT/US/14708 describe methods and devices to occlude annular defects.

[0006] To date, the treatment of tears or defects of the annulus fibrosis has relied for the most part on eliminating the defective disc or disc function. This may be accomplished by fusing the vertebra on either side of the disc.

[0007] In terms of replacement, prior-art techniques replace either the nucleus or the nucleus and annulus functions. This may be accomplished using natural or synthetic materials, or a combination of natural and artificial components. Although transplantation of living cells risks rejection by graft host reaction, certain of my previous disclosures, including those in U.S. patent application Ser. Nos. 09/688,716 and 09/638,726 (now U.S. Pat. No. 6,340,369) recog-

nize that transplantation of the extracellular matrix of the annulus fibrosis is unlikely to incite graft host reaction. As such, fibrocytes are harvested, cultured, then added to annulus fibrosis extracellular matrix obtained from recently deceased humans or animals. The combined annulus fibrosis is then introduced into the injured or diseased disc.

[0008] The cells or engineered tissues may be introduced using any surgical technique, including percutaneous or laparoscopic approaches. As one delivery mechanism, a passageway may be formed through the annulus fibrosis, with the cells or engineered disc tissue being introduced into the disc through the passageway. In particular, the engineered disc tissue may be sewn or otherwise adhered to the inside or outside of the existing annulus fibrosis using a surgical procedure performed from the posterior or anterior portion of the body.

### SUMMARY OF THE INVENTION

[0009] Certain of my co-pending patent applications and issued patents referenced above disclose the step of adding one or more substances to disc-related cells or annular tissue prior to transplantation. Such substances could include culture media, growth factors, differentiation factors, hydrogels, polymers, antibiotics, anti-inflammatory medications, immuno-suppressive medications, or any useful combination thereof. These previous disclosures further teach that such substances and materials may be combined with any compatible nucleus replacement procedure, including the embodiments described in co-pending U.S. Pat. No. 6,371,990 and the continuations thereof, all of which are incorporated herein by reference.

[0010] According to this invention, autograft or allograft tendons are used to strengthen the annulus fibrosis and to augment or replace the nucleus pulposus. In accordance with the method, tendons such as the palmaris longus are harvested from the patient, a suitable living donor, or a recently deceased human. The tendons are sewn or otherwise attached to the inside of the annulus fibrosis, through a hole in the annulus fibrosis, for example.

[0011] The tendons aid the nucleus and/or replace the nucleus by absorbing the compression forces between vertebrae and by transferring the compression forces to the augmented annulus fibrosis. Allograft tendons are preferably treated, with tissue banking techniques well known to those skilled in the art, to prevent disease transmission and graft rejection. The invention can be used to augment discs in the cervical, thoracic, or lumbar spine.

### DETAILED DESCRIPTION OF THE INVENTION

[0012] Broadly according to the inventions disclosed in U.S. patent application Ser. Nos. 09/688,716 and 09/638,726 (now U.S. Pat. No. 6,340,369), fibrocytes are harvested, cultured, added to annulus fibrosis extracellular matrix material, then sewn or otherwise placed relative to an injured or diseased disc. The annulus fibrosis cells and extracellular matrix are preferably harvested from a live human, though recently deceased human or animal donors may alternatively be used. Depending upon the extent of the harvest, the recipient may function at least in part as a donor, or the tissues from others, including fetal or embryo sources, may be used.

[0013] The fibrocytes may be obtained from a tendon of the patient; for example, a palmaris longus tendon may be removed from one arm. The harvested fibrocytes are isolated and cultured using standard techniques. Precursor cells of the annulus fibrosis, annulus fibrosis cells, chondrocytes, or other living cells that could function like annulus fibrosis cells or that could differentiate into cells to build a functional annulus fibrosis may also be used. The cells from the culture are then implanted into the donor extracellular matrix to form a living annulus fibrosis. In the preferred embodiment, the cells are injected into small holes drilled into the donor extracellular matrix. In an alternative embodiment, living cells are not added to the harvested annulus fibrosis. The harvested annulus fibrosis is processed as described above to kill the living host annulus cells.

[0014] The engineered tissue may be added to the inside or the outside of the patient's annulus. Surgical procedures to access the inner or outer surface of the annulus fibrosis are well known to those skilled in the art. For example, the engineered annulus could be sutured, placed against, or "glued" to the patient's annulus. Platelet rich plasma combined with calcium and thrombin or "fibrin glue" could be used to glue the annular tissues together.

[0015] Additional substances may also be added to the transplanted annulus. For example, resorbable culture medium, tissue growth or differentiation factors (recombinant generated morphogenetic proteins, PDGF, TGF- $\beta$ , EGF/TGF- $\alpha$ , IGF-I,  $\beta$ FGF), hydrogels, absorbable or non-resorbable synthetic or natural polymers (collagen, fibrin, polyglycolic acid, polylactic acid, polytetrafluoroethylene, etc.), antibiotics, antiinflammatory medication, immunosuppressive medications, etc. may be used.

[0016] As part of a further alternative embodiment, autograft or allograft tendons are used to strengthen the annulus fibrosis and to augment or replace the nucleus pulposus. In accordance with this method, tendons such as the palmaris longus are harvested from the patient, a suitable living donor, or a recently deceased human. The tendons are sewn or otherwise attached to the inside of the annulus fibrosis, through a hole in the annulus fibrosis, for example.

[0017] The tendons aid the nucleus and/or replace the nucleus by absorbing the compression forces between vertebrae and by transferring the compression forces to the augmented annulus fibrosis. Allograft tendons are preferably treated, with tissue banking techniques well known to those skilled in the art, to prevent disease transmission and graft rejection. The invention can be used to augment discs in the cervical, thoracic, or lumbar spine.

[0018] Although annulus fibrosis augmentation and/or transplantation are being described herein in detail, the invention is not limited to treatment of the intervertebral disc. For example, the invention could also be used to treat other tissues of the body such as the meniscus of the knee. In such cases, a meniscus would be removed from recently deceased humans. The harvested meniscus would be processed to kill the cells but preserve the extracellular matrix. Fibrocytes harvested as described above would then be added to the extracellular matrix prior to insertion of the engineered meniscus into a patient's knee. Similarly, chondrocytes could be harvested and added to the meniscus extracellular matrix as described in my pending U.S. patent

application Ser. Nos. 09/639,309; 09/628,727; 09/638,726; and 09/638,242, all of which are incorporated herein by reference.

[0019] Similarly, the process could be used to repair or replace other tissues or organs of the body such as the pancreas, liver, kidney, heart, etc. Healthy live cells would be obtained thorough biopsy and tissue culture. The live cells would be added to the extracellular matrix of tissues or organs harvested to recently deceased human or animals.

I claim:

1. A method of augmenting the annulus fibrosis of an intervertebral disc, comprising the steps of:

harvesting fibrocytes, annulus fibrosis cells, cells that differentiate into annulus fibrosis cells, or cells that function like annulus fibrosis cells;

harvesting the extracellular matrix of the annulus fibrosis from a recently deceased human or animal;

combining the harvested cells with the extracellular matrix to produce an engineered annulus fibrosis;

adding autograft or allograft tendon material to the combined cells and matrix thus forming an engineered annulus fibrosis; and

transplanting the engineered annulus fibrosis into or onto the disc.

2. The method of claim 1, further including the steps of:

forming a passageway through the disc and transplanting the engineered annulus into the disc through the passageway, or placing the engineered annulus onto the disc.

3. The method of claim 1, further including the step of adding one or more therapeutic substances to the engineered annulus fibrosis.

4. The method of claim 3, wherein the therapeutic substances include one or more of the following:

culture media, growth factors, differentiation factors, hydrogels, polymers, antibiotics, anti-inflammatory medications, or immunosuppressive medications.

5. The method of claim 1, further including the step of keeping the harvested cells viable until placed into the disc being treated.

6. The method of claim 1, wherein the tendon material includes palmaris longus tissue harvested from the patient, a suitable living donor, or a recently deceased human.

7. The method of claim 1, further including the steps of treating and/or banking the tendon material to prevent disease transmission and graft rejection.

8. An engineered annulus fibrosis according to the method of claim 1.

9. The engineered annulus fibrosis of claim 8, further including one or more therapeutic substances.

10. The engineered annulus fibrosis of claim 9, wherein the therapeutic substances include one or more of the following:

culture media, growth factors, differentiation factors, hydrogels, polymers, antibiotics, anti-inflammatory medications, or immunosuppressive medications.

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专利名称(译)	用自体移植物或同种异体移植肌腱补充工程化的环状组织		
公开(公告)号	<a href="#">US20020156532A1</a>	公开(公告)日	2002-10-24
申请号	US10/167503	申请日	2002-06-13
[标]申请(专利权)人(译)	FERREE BRET一个		
申请(专利权)人(译)	费里布雷特A.		
当前申请(专利权)人(译)	ANOVA CORP.		
[标]发明人	FERREE BRET A		
发明人	FERREE, BRET A.		
IPC分类号	A61B17/70 A61F2/00 A61F2/30 A61F2/44 A61L27/36 A61L27/38		
CPC分类号	A61B17/7059 Y10S623/908 A61F2/30771 A61F2/30965 A61F2/441 A61F2/442 A61F2002/30092 A61F2002/30133 A61F2002/30331 A61F2002/30383 A61F2002/30462 A61F2002/30584 A61F2002/30677 A61F2002/30828 A61F2002/30841 A61F2002/30879 A61F2002/4435 A61F2002/444 A61F2002/4445 A61F2002/445 A61F2002/448 A61F2210/0014 A61F2220/0025 A61F2220/0033 A61F2220/0075 A61F2230/0015 A61F2310/00017 A61L27/3604 A61L27/3633 A61L27/3658 A61L27/3804 A61L27/3817 A61L27/3856 A61L2430/38 A61B2017/7073		
优先权	60/159488 1999-10-14 US 60/371546 2002-04-10 US		
其他公开文献	US6645247		
外部链接	<a href="#">Espacenet</a> <a href="#">USPTO</a>		

#### 摘要(译)

收获纤维细胞，纤维环纤维细胞，分化成纤维环细胞的细胞，或像纤维环细胞一样起作用的细胞，并与来自最近死亡的人或动物的纤维环的细胞外基质组合，以产生工程化的纤维环。然后使用自体移植肌腱来加强纤维环并增强或替换髓核。根据一个优选的实施方案，从患者，合适的活体供体或最近死亡的人体中收获诸如掌长肌的腱。使用经皮或腹腔镜手术将肌腱缝合或以其他方式附接到纤维环的内部。肌腱通过吸收椎骨之间的压缩力并通过将压缩力传递到增强的环状纤维化来辅助细胞核和/或替换细胞核。同种异体移植肌腱优选用本领域技术人员熟知的组织库技术进行治疗，以预防疾病传播和移植物排斥。本发明可用于增强颈椎，胸椎或腰椎中的椎间盘。