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Mathies(10) **Pub. No.: US 2010/0136082 A1**(43) **Pub. Date: Jun. 3, 2010**(54) **IN SITU SYSTEM FOR INTRA-ARTICULAR
CHONDRAL AND OSSEOUS TISSUE REPAIR**(75) Inventor: **Burkhard Mathies, Givrins (CH)**

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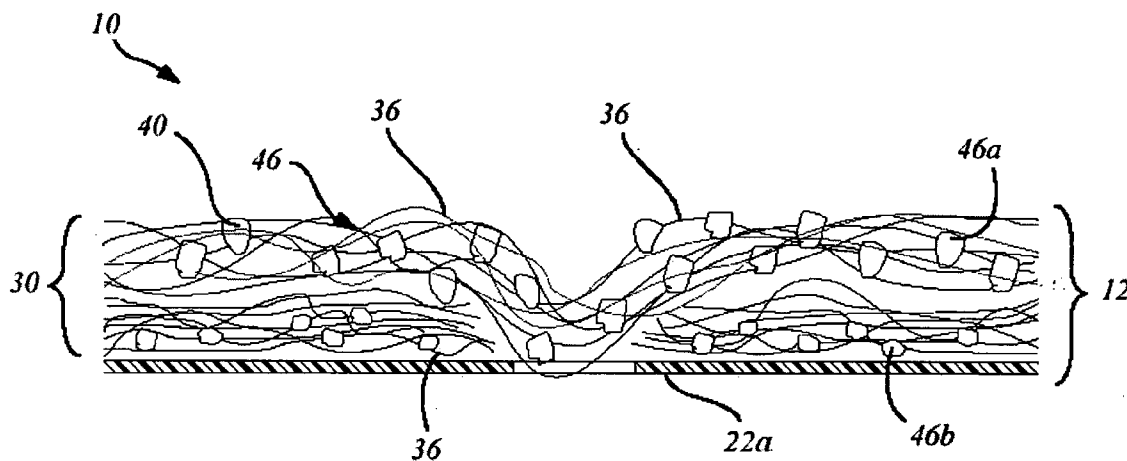
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(57)

ABSTRACT

Disclosed is a device and method which provide a surgical therapy for in situ treatment and repair of intra-articular cartilage lesions and/or defects. The device is an implantable laminate cartilage repair patch which is bio-compatible and physiologically absorbable. The cartilage repair patch has a first outer cell occlusive layer; a second outer, cell porous layer adapted to be disposed proximate a subchondral bone wound site; and a cartilagenic matrix disposed between the first and second layers. The cartilagenic matrix is a sink for diffusion of autologous stem cells and includes chemical components promoting generation of hyaline-like cartilage in the presence of the autologous stem cells. The method of the present invention provides the autologous compositions, which when used in combination with the repair patch provides a therapeutic system to regenerate replacement hyaline-like intraarticular cartilage.



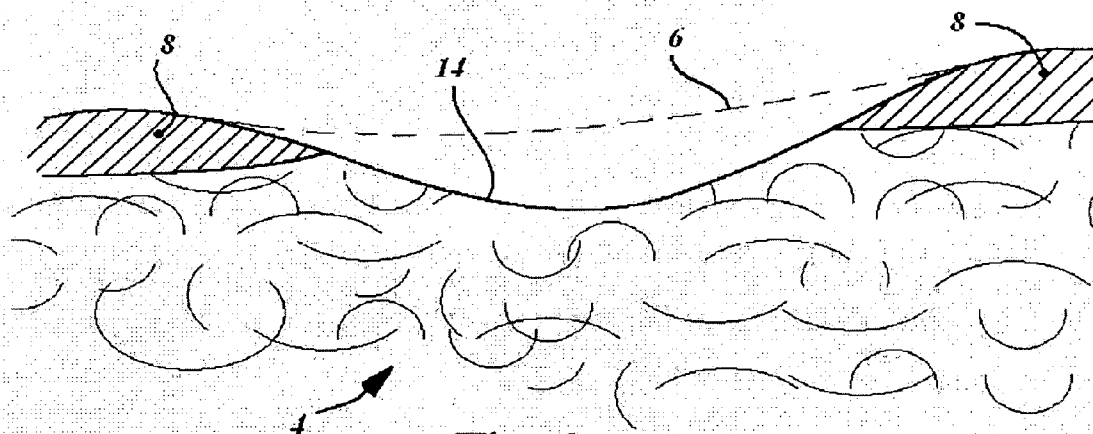


Fig. 1

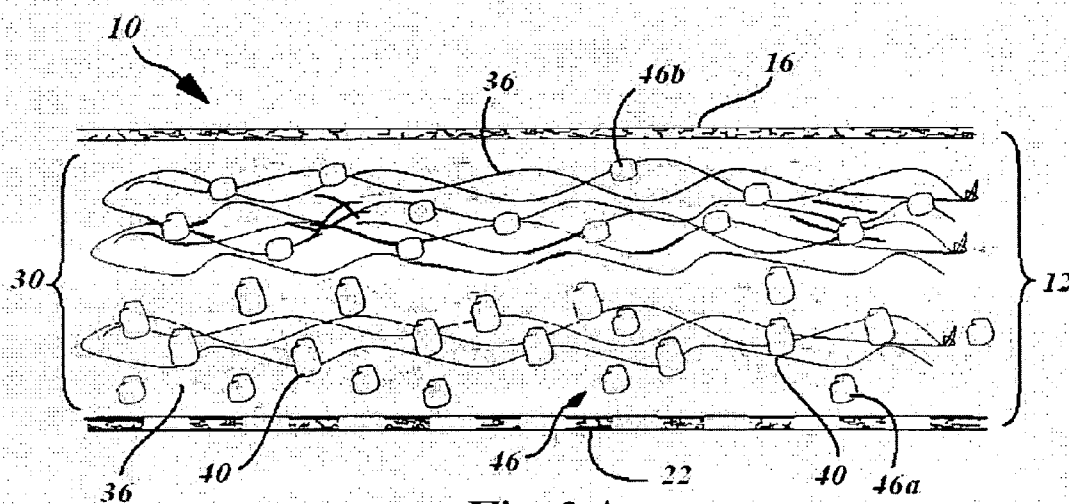


Fig. 2A

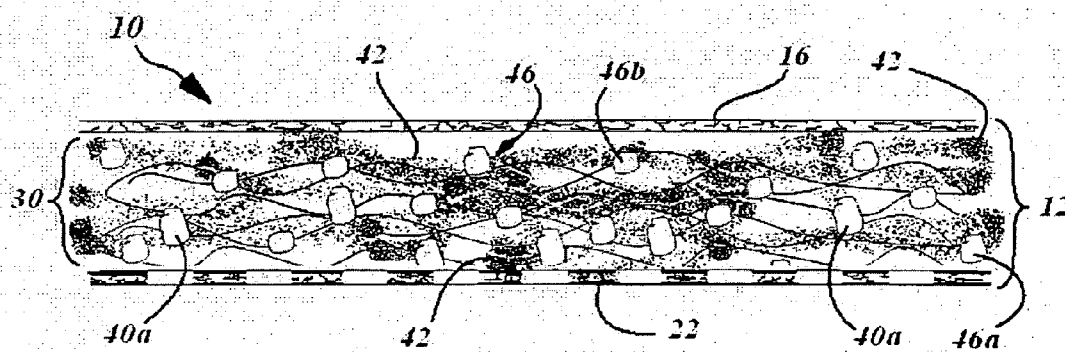


Fig. 2B

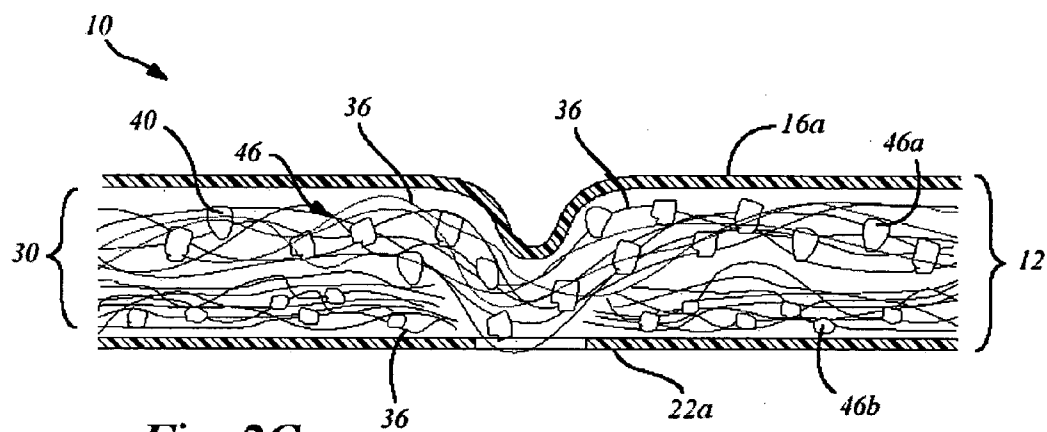


Fig. 2C

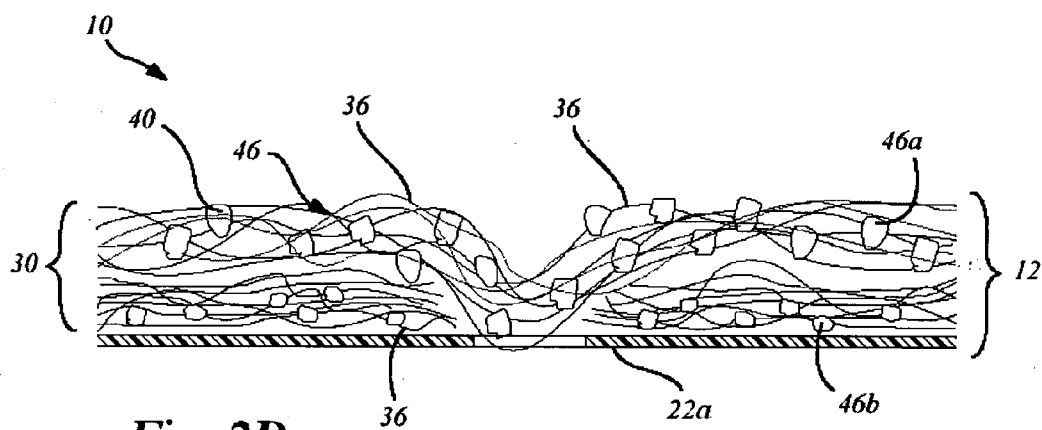


Fig. 2D

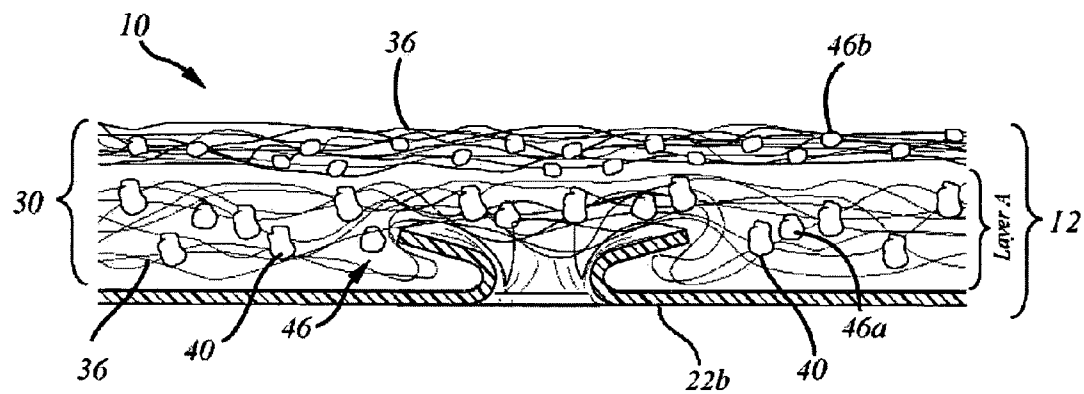
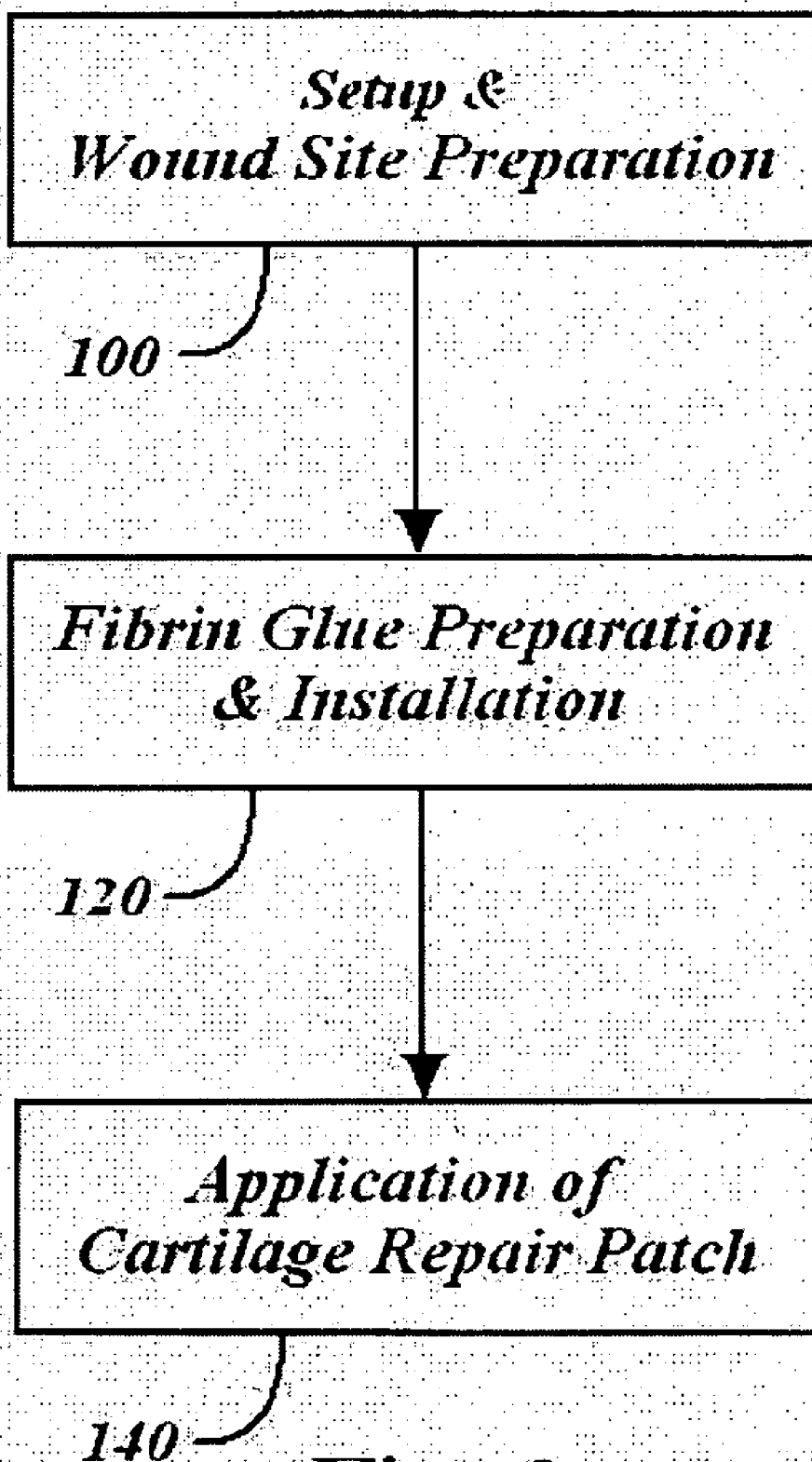


Fig. 2E

*Fig. 3*

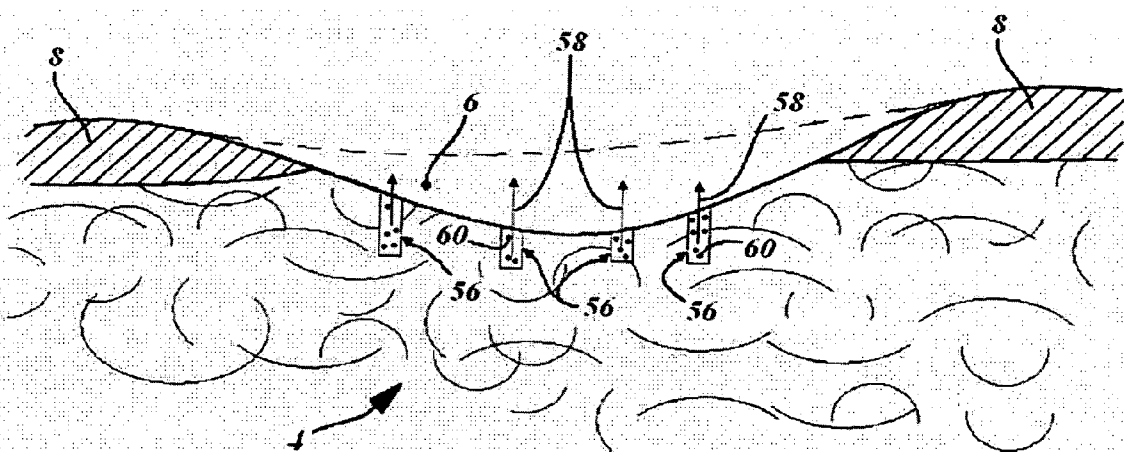


Fig. 4A

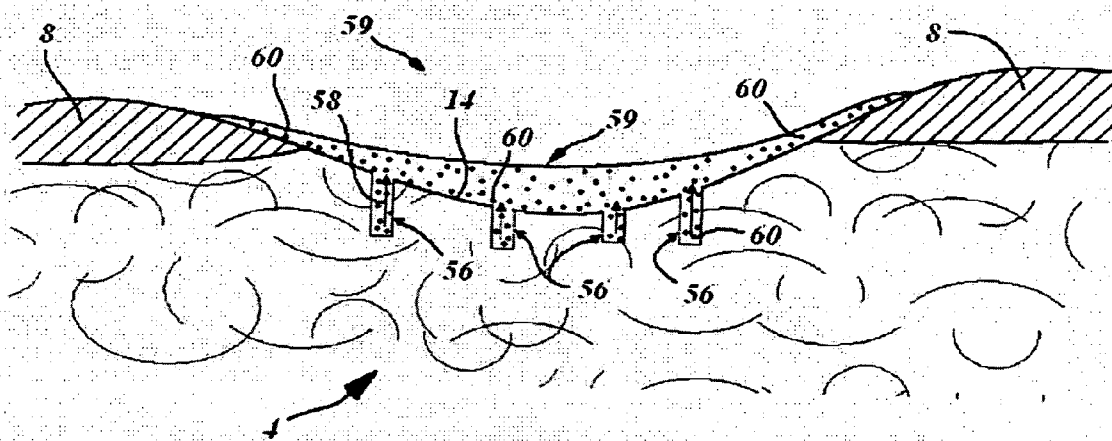
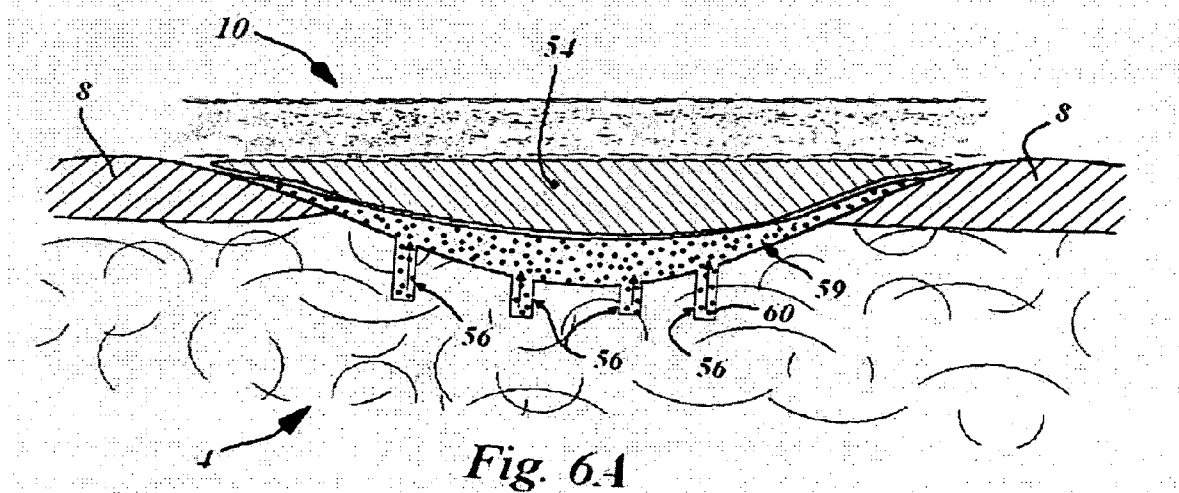
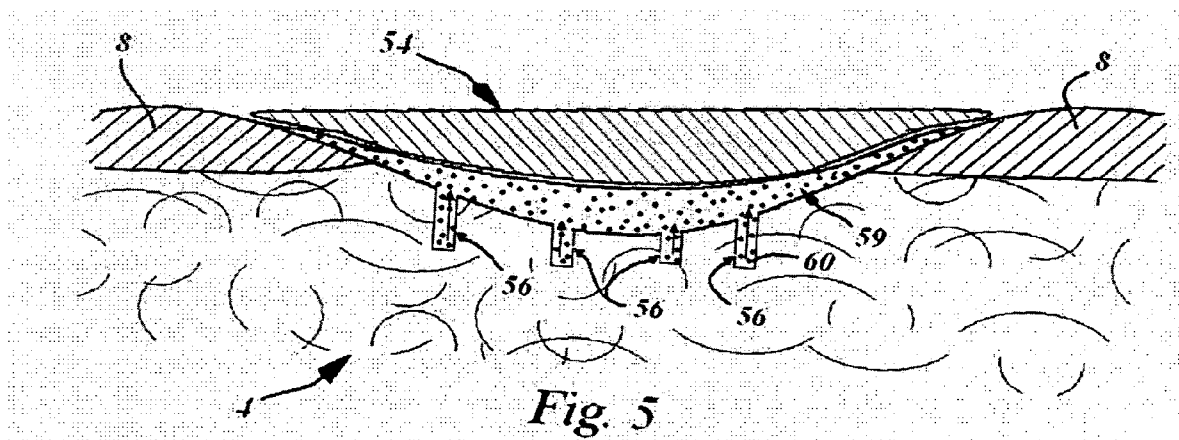


Fig. 4B



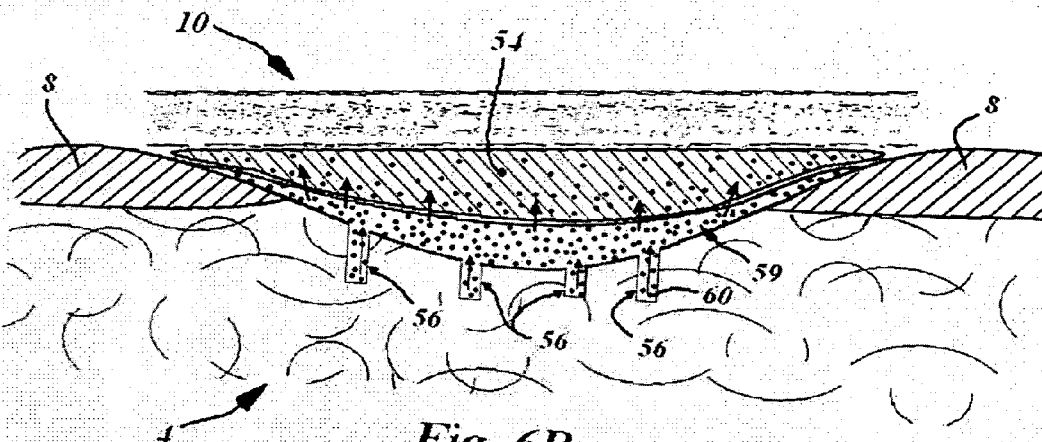


Fig. 6B

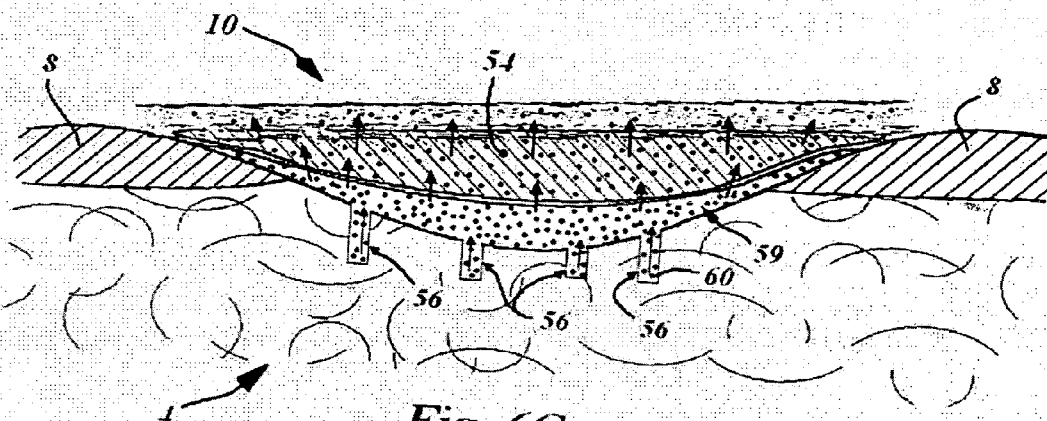


Fig. 6C

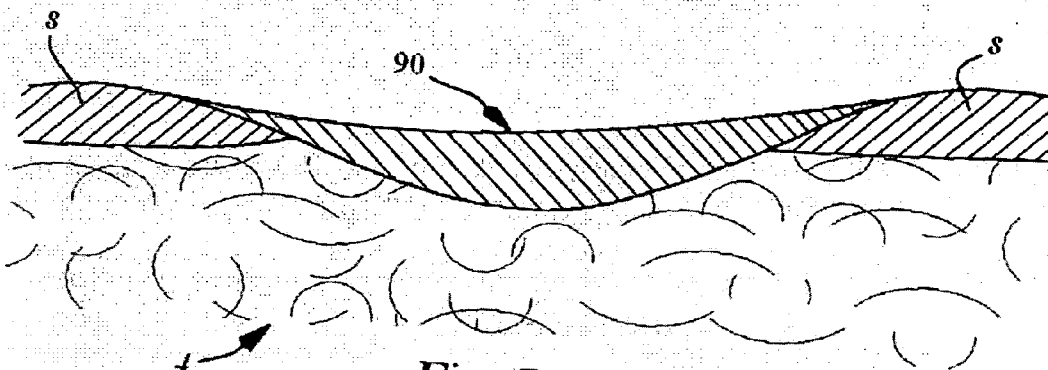


Fig. 7

IN SITU SYSTEM FOR INTRA-ARTICULAR CHONDRAL AND OSSEOUS TISSUE REPAIR

[0001] The present application claims the benefit of prior filed U.S. provisional patent application Ser. No. 60/871,554 filed 22 Dec. 2006, the content of which is incorporated herein by reference.

FIELD OF THE INVENTION

[0002] The present invention is in the field of bioaffecting and body treating compositions having components associated as layers or impregnated matrix (believed to be classified in Class 424/400). Specifically, the present invention relates to compositions in a physical form to adapt for surgical implanting or inserting in the living body (believed to be classified in Class 424/400; 423). More specifically, the present invention relates to such compositions in which the surgical implant or material is errodable, resorbable, or dissolving (believed to be classified in Class 424/400; 423; 426).

BACKGROUND OF THE INVENTION

[0003] One of the goals of medicine, including the surgical arts, is the recovery of health that has been lost, whether the loss occurred as a result of injury or disease. In the surgical arts, ever more effective treatment strategies for addressing cartilage defects are being sought. Such defects in joints (intra-articular) can result from a number of different causes, including trauma and diseases such as osteoarthritis. The hyaline articular cartilage is a specialized connective tissue in the body with weight bearing and shock absorbing properties and functions. Injury to or loss of this specialized connective tissue in a joint leads to pain and impaired joint function.

[0004] Although the hyaline articular cartilage does have some self-repairing capabilities, these are very limited. Therefore, the orthopedic surgical arts field has been motivated to develop therapies which replace or promote regeneration of damaged joint cartilage. This is in response to the large number of joint injuries that occur yearly, and the increasing number of the elderly with joint problems. Typically, these therapies are merely surgical methods which debride and mechanically repair the injury, with or without the addition to the injury site of an active composition to promote healing or to prevent inflammation/infection.

[0005] More recently, the field has tried bio-engineering influenced therapies which added a structural composition to the injury, such as autologous tissue grafts, in order to promote appropriate healing. However, osteochondral injuries, which are a combination lesion of bone and cartilage, represent therapeutic challenges, and fully satisfactory therapeutic compositions and treatment methods are still lacking in many cases. For example, certain surgical procedures for osteochondritis dissecans using autologous chondrocyte transplantation require extensive periods for the cell cultivation and growth aspect and multiple surgeries. Additionally, these therapies often result in the propagation of a fibrocartilaginous replacement tissue, which is a poor substitute for hyaline articular cartilage. See J. Kramer et al., *Cell. Mol. Life Sci.*, 63, 616-626 (2006).

[0006] Therefore, it would be beneficial in the field to have alternative treatment for osteochondral injuries that do not require cell culture, and do not result in propagation of a

fibrocartilaginous replacement tissue at the injury site. It would be even more advantageous if the resultant replacement tissue was appreciably representative of natural hyaline-like articular cartilage.

SUMMARY OF THE INVENTION

[0007] The present invention is an in situ healing/tissue growth promoting system and method, utilizing natural, non-human Hyaluronic Acid and 5 autologous mesenchymal stem cells to regenerate intra-articular cartilage lesions. More specifically, a system and method is provided that can stimulate growth of hyaline-like cartilage in situ to correct intra-articular cartilage defects. To this end, the present system comprises a medical cartilage repair patch consisting of a natural composite 10 Hyaluronic Acid and collagen fiber matrix additionally embedded with growth hormones and/or growth factors, and Diacerein and/or Rhein compositions. The system utilizes autologous mesenchymal stem-cells obtained through micro-fracture of the subchondral bone during installation of the cartilage repair patch as a component of the system to accomplish chondral and osseous tissue engineering in intra-articular defects.

[0008] The implantable laminate cartilage repair patch of the present invention is a surgical device that is bio-compatible and physiologically absorbable for in situ cartilage repair in intra-articular lesions. The cartilage repair patch is a laminate or multi-layered device. The device has a basement or bottom layer which is adapted to be disposed adjacent the bone site to be treated. This layer is "cell-porous" in that it allows the migration of cells from the wound site to pass through the layer. On top of and closely associated with the basement layer is a cartilaginous matrix layer. The cartilaginous matrix is a collagenous layer and is a sink for the diffusion of autologous stem cells and other blood components at the wound site. The matrix layer includes chemical components which promote the generation of hyaline-like cartilage in the presence of the autologous stem cells. Also optionally, the top layer may be occlusive to one degree or another, for example, not allow cells to pass through, but allowing other small things, like water, gas and small molecules to pass through. All of these elements and features in combination provide the flexible, bio-compatible materials which are physiologically absorbable laminate cartilage repair patch of the present invention.

BRIEF DESCRIPTION OF THE DRAWINGS

[0009] FIG. 1 is a cross-sectional view of subchondral bone showing a chondral/osteo-chondral lesion where a section of cartilage covering the osseous portion of the bone is missing.

[0010] FIG. 2A is a cross-sectional side view of the sterilizable, flexible laminate wound cartilage repair patch of the present invention, detailing the composition of the matrix of the patch wherein the collagen and the Hyaluronic Acid are disposed as fibers.

[0011] FIG. 2B is a cross-sectional side view of the sterilizable, flexible laminate wound cartilage repair patch of the present invention, detailing the composition of the inner matrix of the patch, wherein the collagen is disposed as fibers and the Hyaluronic Acid is disposed as a cream suspension or as a viscoelastic solution.

[0012] FIG. 2C is a cross-sectional side view of the sterilizable, flexible laminate wound cartilage repair patch of the

present invention, showing a lower and an upper layer both having a mechanical stabilizing feature in each layer.

[0013] FIG. 2D is a cross-sectional side view of the sterilizeable, flexible laminate wound cartilage repair patch of the present invention, showing an embodiment having only a lower layer and with a mechanical stabilizing feature.

[0014] FIG. 2E is a cross-sectional side view of the sterilizeable, flexible laminate wound cartilage repair patch of the present invention, showing an embodiment wherein the lower layer has complex mechanical stabilizing features in it.

[0015] FIG. 3 is a generalized flow chart illustrating the main stages of the method of the present inventive system.

[0016] FIGS. 4A and 4B are cross-sectional views of a representative wound site and illustrate a first stage of preparation of the wound site to receive the present flexible laminate cartilage repair patch: (A) causing micro-fractures or perforations into the surface of the subchondral bone, and (B) forming a blood clot from local bleeding initiated by the causing of the micro-fractures.

[0017] FIG. 5 is a cross-sectional view of a representative wound site and illustrates a step of the second stage of the present system: applying the autologous serum enhanced "fibrin glue" at the wound site.

[0018] FIG. 6A is a cross-sectional view of a representative wound site and illustrates the placement of the flexible laminate cartilage repair patch to the wound site over a fibrin glue/blood clot.

[0019] FIG. 6B is a cross-sectional view of a representative wound site and illustrates the migration of Mesenchymal Stem Cells and other injury responsive blood components from the blood clot into the fibrin glue to form a blood clot/fibrin glue composite.

[0020] FIG. 6C is a cross-sectional view of a representative wound site and illustrates the migration of Mesenchymal Stem Cells and other injury responsive blood components from the blood clot/fibrin glue composite further still into the matrix of the cartilage repair patch.

[0021] FIG. 7 is a cross-sectional view of a representative wound site and illustrates the resultant repaired site after the cartilage repair patch has been reabsorbed and the site transformed into bone and/or a hyaline-like cartilage.

DETAILED DESCRIPTION OF THE INVENTION

[0022] Referring now to the drawings, the details of preferred embodiments of the present invention are graphically and schematically illustrated. Like elements in the drawings are represented by like numbers, and any similar elements are represented by like numbers with a different lower case letter suffix.

[0023] As shown in FIG. 1, one of the problems faced in this field is how to promote regeneration of a cartilaginous tissue at the defect or wound site (cartilage lesion) 6 that is as close as possible to the natural cartilage 8 proximate the site, or as otherwise would have covered the subchondral bone 4 at the site 6. This is particularly challenging at wound sites where the lesion involve both cartilage and bone.

[0024] As shown in FIGS. 2A to 2E, the present invention is an implantable cartilage repair patch 10 that is bio-compatible and physiologically absorbable, and that functions in situ to promote the regeneration of cartilage in intra-articular chondral or osteo-chondral lesions 6 (see FIG. 1). The present cartilage repair patch 10 is a sterilizeable, flexible laminate 12 that can be implanted at a wound site 6 and act to promote the generation of hyaline-like cartilage. The objective of the car-

tilage repair patch 10 is to stimulate growth of hyaline-like cartilage in-situ following arthroscopic or open surgical application of the cartilage repair patch 10 in patients with chondral or osteo-chondral damage. An additional object is that the cartilage repair patch 10 is biodegradable through the interaction of its constituents with collagenase and other proteases and will be reabsorbed and disappear over time.

[0025] The laminate 12 of the cartilage repair patch 10 is constructed completely of materials that are both bio-compatible and physiologically absorbable, so that the cartilage repair patch can be implanted indwelling in a patient and disappear from the implantation site over time. In one embodiment, the cartilage repair patch laminate 12 has a first top (optionally occlusive) layer 16, and a second bottom or basement porous layer 22. See FIGS. 2A to 2C. In another preferred embodiment, the cartilage repair patch laminate 12 is only two layers: a basement layer 22 and a matrix layer 30. See FIGS. 2D and 2E. The basement layer is intended to be interfaced with the surface of the bone at the wound site 6. Both of the basement layer 16 and the top layer 22 are made of sheet collagen (see Angele et al., U.S. Pat. No. 6,737,072. The content of which is incorporated herein by reference). An example of a satisfactory commercially available source of sheet collagen is: XENODERM™, Biometica AG, Switzerland. Disposed on the porous basement layer 22 is a cartilaginous matrix layer 30. The cartilaginous matrix layer 30 provides a collagenous substrate in which to entrap mesenchymal stem-cells, and a cell growth support medium on which they will grow and differentiate into chondrocytes in presence of the other natural components of the matrix layer 30.

[0026] In a preferred embodiment, the matrix layer 30 is a sterile or sterilizeable, porous collagenous composite pad, interspersed with non-human collagen fibers 36 and natural Hyaluronic Acid fibers 40. The natural collagen is derived from a non-human source, such as porcine, bovine or vegetal collagen. The natural Hyaluronic Acid (HA) is derived from a natural non-mammalian source, such as via bacterial fermentation and via extraction from rooster combs. Other names for HA include: hyaluronic acid sodium salt, sodium hyaluronate, and hyaluronan. The natural HA can be provided in the matrix 30 in form of natural HA fibers 40 as shown in FIG. 2A, or as HA powder 40a in a gel or cream suspension 42 dispersed into the vacant spaces of the collagen fibers 36 as in FIG. 2B.

[0027] In the preferred embodiment, the composite cartilaginous matrix 30 also includes one or more tissue growth hormones (e.g., Somatotropine) and/or stimulators of growth factors 46. Growth factor stimulators are chemicals that enhance the expression of a growth factor at a given site. In the embodiment illustrated, the growth factor stimulators are Diacerein 46a and Rhein 46b. In the embodiment illustrated in FIG. 2B, the suspension 42 also contains Rhein 46b and/or Diacerein 46a. The weight range ratio of collagen to HA should be from about 0.1:99.9 to about 50:50 when the natural HA has a molecular weight of between 0.5 to 6 million Dalton. The Diacerein or Rhein concentrations should be in the range of about 10 to 50 micromolar added to the matrix in a powder form or as HA gel or cream containing the Diacerein or Rhein. Other compositions that are anticipated for inclusion in the matrix layer 30 include Chitosan compositions and Poly-Lactic Acid compositions.

[0028] Autologous mesenchymal stem cells 60 derived from a source external to the cartilage repair patch 10 diffuse

into the patch **10** through the porous basement layer **22** and into the matrix layer **30** where they are supported by the fibrous components (collagen fibers **36** and/or HA fibers **40a**) of the matrix **30**. The matrix fibers **40** & **40a** provide a support medium for the stem cells to grow and differentiate into chondrocytes. The exogenous growth factors **46**, such as Diacerein down regulate inflammatory parameters (e.g., cytokines: IL-1, TNF-alpha, alpha, and free radicals) which contribute to inflammation and cartilage breakdown. Diacerein stimulates the production of certain growth factors, like TGF- β that additionally will stimulate production of cartilage components such as HA, collagen type-II, and proteoglycans (including aggrecans). Growth hormone will stimulate the production of cartilage and bone tissue. Further, endogenous growth factors **50** from an autologous serum fraction are added to the fibrin glue composition **54** stimulates differentiation of stem cells **60** in the blood clot/patch interface. The cumulative effect of these interactions leads to growth of hyaline-like cartilage.

[0029] FIG. 3 is a generalized flow chart illustrating the main stages of the method of the present inventive system. In a preferred method of use, the present system comprises three stages: preparation of the wound site **100**; preparation and installation of the fibrin glue **120**; and application of the cartilage repair patch **140**. In the first stage **100**, as part of the set up, a blood sample is taken from the patient and an autologous serum fraction is obtained. The autologous serum fraction is used as a source of wound healing components, such as TGF- β 1, and will be added at implantation within the fibrin glue to the wound site **6**. These endogenous components will enhance mesenchymal stem cell differentiation.

[0030] Also in this stage, micro-fractures/perforations are made at the subchondral bone surface **14** to cause local bleeding **58** which perfuses the wound site **6** with fresh blood. See FIG. 4A. Causing local bleeding **58** at the subchondral bone surface **14** can be accomplished in a number of ways. In the preferred embodiment illustrated in FIG. 4B, the preparation of the existing chondral or osteochondral lesions is accomplished by causing micro-fractures or perforations **56** in the surface **14** of the subchondral bone **4**—often associated with abrasion of sclerotic bone. As shown in the figure, the micro-fractures/perforations/abrasions **56** in the subchondral bone **4** causes bleeding **58** into the wound site **6**. The blood **58** entering the wound site **6** contains autologous mesenchymal stem cells **60** and other healing components released by the subchondral bone **4** in response to the causing of the micro-fractures, perforations or abrasions **56**.

[0031] As shown in FIG. 4B, the blood **58** that perfuses the wound site **6** results in a blood clot **59** that forms at the site. The present system uses the micro-fracture technique to cause bleeding and stimulate release of autologous mesenchymal stem cells (MSCs) and growth factors into the clot **59**. These pluripotential MSCs in the presence of the present cartilage repair patch **10** will differentiate into chondrocytes and produce extracellular hyaline-like cartilage matrix to repair/replace the existing chondral/osteo-chondral lesion **6**.

[0032] After the wound site **6** is prepared, the second stage **120** of the method of the present system is accomplished. This stage **120** is the preparation and application of the fibrin glue **54** to the blood clot **59** at the wound site **6**. As shown in FIG. 5, the fibrin glue **54** mingles with the fresh blood clot to form a blood clot/fibrin glue composite clot **54-59**. However, other means of installing the fibrin glue **54** in place are known to and selectable by one of ordinary skill in the art for practice in

the present system. For example, the cartilage repair patch **10** can be sutured in place (not shown).

[0033] After the fibrin glue **54** is applied in the wound site, the third stage **140** of the present method is then to be accomplished. This third stage **140** is the placement of the flexible laminate repair patch **10** to the wound site over the fibrin glue/blood clot composite **59/54** at the wound site **6**. In FIG. 6A, the flexible laminate cartilage repair patch **10** is applied to the wound site **6**. The fibrin glue **54** also may be freely applied after the repair patch **10** is in place to further accomplish adhering the repair patch **10** to the wound site **6**. Once this step is accomplished, the surgical stages of the present system are completed and the cartilage repair patch **10** continues healing purpose in situ.

[0034] As shown in FIG. 6B, Mesenchymal Stem Cells and other injury responsive blood components from the blood clot **59** migrate into the fibrin glue **54**. FIG. 6C illustrates the further migration of the Mesenchymal Stem Cells and other injury responsive blood components from the fibrin glue/blood clot composite **54/59** continues through the porous outer layer **22** and into the matrix layer **30** of the cartilage repair patch **10**. In the matrix layer **30**, the mesenchymal stem cells and autologous growth factors interact with the constituents of the cartilage repair patch **10**. The presence of these components results from their diffusion from the clot **59** into the cartilaginous matrix **30** of the cartilage repair patch **10**. The occlusive layer **16** of the cartilage repair patch **10** prevents for a time the further diffusion of these different compositions into the joint space. Conversely, the mobile constituents of the matrix layer **30** can migrate out of the cartilage repair patch and into the mass of the fibrin clot **54**, and further, into the blood clot **59** at the surface **14** of the subchondral bone **4**.

[0035] The Diacerein **46a** and the Rhein **46b** inhibit the production and activity of inflammatory cytokines such as IL-1 β , nitric oxide (NO), free radicals and matrix metalloproteinases all of which are involved in inflammation and cartilage destruction, particular in osteoarthritic joints. The Diacerein **46a** and the Rhein **46b** also stimulate the production of growth factors such as TGF- β which in turn stimulates expression of cartilage components such as hyaluronic acid, proteoglycans, aggrecans and collagenase II, all of which are important components of cartilage matrix. The growth hormone will also stimulate the growth of cartilage and bone tissue. Over time, as illustrated in FIG. 7, the cartilage repair patch **10** is reabsorbed and the defect site **6** is relatively rapidly transformed into a more physiologically hyaline-like cartilage **90**.

The Collagen Cartilage Repair Patch

Example

[0036] A collagen sheet **22** (Xenoderm—porcine type 1 and 2 collagen) was used for the lower layer **22**. The Lower layer had mechanical properties to resist shear and pull stress and was resorbable in about 6 weeks. The collagen sheet **22** was put into a form, and then loaded with a collagen-HA suspension to which was added either a solution of Diacerein or Diacerein powder to obtain a concentration of 5-50 micromol. in dry-weight in patch after freeze-drying and sterilization. The result is a double layer collagen-pad with the lower layer to be disposed adjacent the bone surface. After manufacturing and before sterilization, the pads are put into a mechanical press to obtain a thickness of 0.5-2 mm. HA-concentration in the dry-frozen end product was in the range

of about 0.1% to 2%. The HA is natural HA, that is, non-chemically modified HA, of fermentation origin.

[0037] In an advantage, a device and therapy is provided which better promotes regeneration of damaged joint cartilage.

[0038] In another advantage, a treatment and device for osteochondral injuries is provided that does not require cell culture.

[0039] In yet another advantage, a treatment and device for such injuries is provided that does not result in propagation of a fibrocartilaginous replacement tissue at the injury site.

[0040] In still another advantage, a treatment and device is provided which better insures that the resultant replacement tissue is appreciably representative of natural hyaline-like articular cartilage.

[0041] While the above description contains many specifics, these should not be construed as limitations on the scope of the invention, but rather as exemplifications of one or another preferred embodiment thereof. Many other variations are possible, which would be obvious to one skilled in the art. Accordingly, the scope of the invention should be determined by the scope of the appended claims and their equivalents, and not just by the embodiments.

What is claimed is:

1. An implantable laminate cartilage repair patch, the cartilage repair patch comprising:

- a first outer cell occlusive layer;
- a second outer, cell porous layer adapted to be disposed proximate a subchondral bone wound site; and
- a cartilagenic matrix disposed between the first and second outer layers, the cartilagenic matrix being a sink for diffusion of autologous stem cells and including chemical components promoting generation of hyaline-like cartilage in the presence of autologous stem cells.

2. The implantable laminate cartilage repair patch of claim 1, wherein the cartilagenic matrix is a biologically compatible and physiologically absorbable composite including natural hyaluronic acid and collagen.

3. The implantable laminate cartilage repair patch of claim 1, wherein the cartilagenic matrix is a biologically compatible and physiologically absorbable composite including natural hyaluronic acid and collagen, wherein the collagen consists essentially of collagen from a non-human source.

4. The implantable laminate cartilage repair patch of claim 1, wherein the cartilagenic matrix is a biologically compatible and physiologically absorbable composite natural hyaluronic acid and collagen, wherein the natural hyaluronic acid of the cartilagenic matrix consists essentially of a natural, non-human hyaluronic acid.

5. The implantable laminate cartilage repair patch of claim 1, wherein the cartilagenic matrix is a biologically compatible and physiologically absorbable composite including natural hyaluronic acid and collagen, wherein the natural hyaluronic acid of the cartilagenic matrix consists essentially of a natural, non-human hyaluronic acid from a bacterial fermentation source.

6. The implantable laminate cartilage repair patch of claim 1, wherein the cartilagenic matrix is embedded with a chemical composition promoting cartilage regeneration.

7. The implantable laminate cartilage repair patch of claim 1, wherein the cartilagenic matrix is embedded with at least one chemical composition promoting cartilage regeneration selected from the group of compositions consisting of: a

growth factor composition, a diacerein composition, a rhein composition, a poly-lactic acid composition, and a natural, non-mammalian hyaluronic acid composition.

8. A method of in situ intra-articular cartilage repair at an intra-articular wound site in a patient, comprising:

providing an implantable laminate cartilage repair patch comprising:

- a first outer cell occlusive layer;
- a second outer, cell porous layer adapted to be disposed proximate a subchondral bone wound site; and
- a cartilagenic matrix disposed between the first and second outer layers, the cartilagenic matrix being a sink for diffusion of autologous stem cells and including chemical components promoting generation of hyaline-like cartilage in the presence of autologous stem cells;

preparing the wound site;

causing a fibrin glue and blood clot layer to be disposed at the wound site; and

applying the cartilage repair patch in proper orientation over the fibrin glue and blood clot layer at the wound site, closing the wound site and allowing the cartilage repair patch to initiate growth of hyaline-like cartilage at the wound site, and the cartilage repair patch over time to be absorbed.

9. The method of claim 8, wherein preparing the wound site comprises:

- taking a blood sample from the patient and obtaining an autologous serum fraction having endogenous wound healing components including components that cause differentiation of mesenchymal stem cells; and
- micro-fracturing a subchondral bone surface at the wound site to cause local bleeding to perfuse the wound site with fresh blood containing autologous mesenchymal stem cells released by the subchondral bone in response to the micro-fracturing.

10. The method of claim 8, wherein preparing the wound site comprises:

- taking a blood sample from the patient and obtaining an autologous serum fraction having endogenous wound healing components including components that cause differentiation of mesenchymal stem cells; and
- micro-fracturing a subchondral bone surface at the wound site to cause local bleeding to perfuse the wound site with fresh blood containing autologous mesenchymal stem cells released by the subchondral bone in response to the micro-fracturing, wherein the autologous mesenchymal stem cells released by the subchondral bone are pluripotent mesenchymal stem cells, which in the presence of the cartilage repair patch will differentiate into chondrocytes and produce an extracellular hyaline-like cartilage at the wound site.

11. The method of claim 8, wherein the causing the fibrin glue and blood clot layer to be disposed at the wound site further comprises suturing the cartilage repair patch in place.

12. The method of further comprises replacing the thrombin fraction of the fibrin glue in a 50/50 proportion with autologous centrifugated serum, mixing it with blood obtained from the microfracture/abrasion site of the wound site, and placing the this fibrin glue/blood clot into the wound bed under the cartilage repair patch to seal and obtain a mechanically stable construct.

* * * * *