

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
18 May 2006 (18.05.2006)

PCT

(10) International Publication Number
WO 2006/053132 A2

(51) International Patent Classification:
A61F 2/28 (2006.01) *A61L 27/56* (2006.01)

(21) International Application Number:
PCT/US2005/040751

(22) International Filing Date:
10 November 2005 (10.11.2005)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/626,725 10 November 2004 (10.11.2004) US
60/628,479 16 November 2004 (16.11.2004) US

(71) Applicant (for all designated States except US): **OHIO UNIVERSITY** [US/US]; 340 West State Street, Unit 14, Athens, OH 45701 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **MEHTA, Bhavin, V.** [US/US]; 8 Kent Drive, Athens, OH 45701 (US). **SET-LOCK, Robert, J., Jr.** [US/US]; 10 Mohler Lane, Athens, OH 45701 (US). **SINDELAR, Betty** [US/US]; 333 Carroll Rd., Athens, OH 45701 (US). **BANTLE, John, A.** [US/US]; 7920 Country Club Rd., Athens, Ohio 45701 (US).

(74) Agents: **HULL, Mark** et al.; Calfee, Halter & Griswold LLP, 800 Superior Avenue, Suite 1400, Cleveland, OH 44114 (US).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Declaration under Rule 4.17:

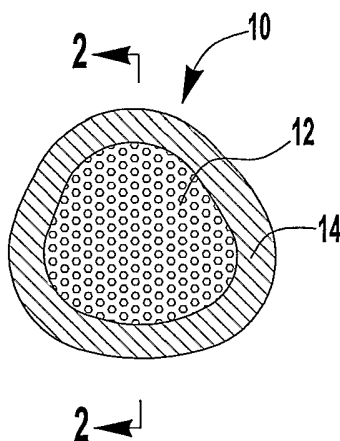
— of inventorship (Rule 4.17(iv))

Published:

— without international search report and to be republished upon receipt of that report

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: PROSTHETIC BONE IMPLANTS



(57) Abstract: The present application relates to prosthetic bone implants that include a solid outer shell and a porous interior core. The prosthetic bone implant may be used to replace bone that has been damaged by trauma or disease. The prosthetic bone implant may be configured to match characteristics that the bone to be replaced would have if the bone to be replaced were healthy.

WO 2006/053132 A2

Prosthetic Bone Implants

Related Applications

[0001] This application claims the benefit of United States provisional patent applications serial nos. 60/626,725 for IMPROVED PROSTHETIC BONE IMPLANTS filed November 10, 2004, and 60/628,479 for IMPROVED PROSTHETIC BONE IMPLANTS filed November 15, 2004, the entire disclosures of which are fully incorporated herein by reference.

Background of the Invention

[0002] Bone is a natural composite material composed of hard, compact osseous tissue surrounding spongy cancellous tissue. Damage or loss of natural bone tissue can result from trauma, congenital deformities, pathologic conditions, and surgical procedures. In some instances, as a result of the bone damage or loss, and as an alternative to amputation, a person may undergo prosthetic operations to replace the missing bone tissue.

[0003] Prosthetic operations can be used to replace missing or diseased portions of bone with solid artificial implants, such as metal rods. These implants, however, do not have the same material and structural properties as natural bone. The material and structural differences of these solid implants can cause unnatural secondary wear patterns on surrounding bone and joints.

Summary

[0004] The present application relates to prosthetic bone implants suitable for mammalian implantation. In one embodiment, a prosthetic bone implant includes an interior region and a peripheral region, which has a relatively greater density than the interior region. The prosthetic bone implant may be used to replace bone that has been damaged by trauma or disease. The prosthetic bone implant may be configured to match the characteristics of the bone to be replaced if that bone were healthy. For example, the peripheral region may approximate the morphologic traits of the cortical layer of a similar healthy bone. The peripheral region and the interior region may be configured such that a density of the prosthetic bone implant and the size and shape of the peripheral region substantially matches a density, size, and shape that healthy bone in the area of bone to be replaced should have.

[0005] In one embodiment, the implant comprises a biodegradable scaffold material. An osteoinductive agent and/or osteointegration agent may be disposed in the implant. In an exemplary embodiment, stem cells, such as for example bone marrow stem cells, are imbedded in a biodegradable scaffold material and eventually grow and replace the biodegradable scaffold material.

[0006] One aspect of the present disclosure relates to a method of making prosthetic bone implants. In one embodiment of the method, a foamable implant precursor, comprising a scaffold material and a foaming agent, is formed. The foamable implant precursor is placed in a mold which is configured based on a region of bone to be replaced by the implant. The foamable precursor is then activated to cause it to expand into engagement with the mold to form a prosthetic bone implant having a peripheral region and an interior region. The resulting bone implant will have a peripheral region with a relatively greater density than the interior region. In one embodiment, the method includes creating a three dimensional model of human bone. A mold is fabricated based on the three dimensional model and the foamable implant precursor is formed based on the three dimensional model.

[0007] Further advantages and benefits will become apparent to those skilled in the art after considering the following description and appended claims in conjunction with the accompanying drawings.

Brief Description of the Drawings

[0008] Figure 1 is a schematic cross-sectional view of an exemplary embodiment of a prosthetic bone implant;

[0009] Figure 2 is a cross-sectional view taken along lines 2--2 of the prosthetic bone implant in Figure 1;

[0010] Figure 3 is a schematic cross-sectional view of the prosthetic bone implant of Figure 1, enriched with living bone tissue;

[0011] Figure 4 is a sectional view taken along lines 4--4 of the exemplary prosthetic bone implant in Figure 3;

[0012] Figure 5 is a graphical representation of an exemplary embodiment of a method of forming the prosthetic bone implant of Figure 1.

[0013] Figure 6 is an image of bone to be replaced by a prosthetic bone implant;

[0014] Figure 7 is an illustration of a solid model of bone to be replaced by a prosthetic bone implant;

[0015] Figure 8 is an illustration of a 3D rendering of a prototype of a bone to be replaced by a prosthetic bone implant;

[0016] Figure 9 illustrates use of a prototype of a bone to create a prosthetic bone implant mold;

[0017] Figure 10 is a schematic illustration of a foamable implant precursor placed in a mold;

[0018] Figure 11 is a schematic illustration of a formed prosthetic bone implant in a mold;

[0019] Figure 12 is a cross-sectional schematic illustration of the prosthetic bone implant of Figure 1, including living bone tissue plugs; and

[0020] Figure 13 is a sectional view taken along lines 13--13 of the prosthetic bone implant of Figure 12.

Detailed Description

[0021] As compared with prior known artificial implants, the disclosed prosthetic bone implants more closely duplicate the morphology of biological bone to more closely mimic the overall material and structural properties of natural bone. The size, shape, strength, density, density profile, weight, and/or weight distribution of the disclosed prosthetic bone implants more closely matches healthy natural bone than prior known prosthetic bone implants. By fabricating prosthetic bones that duplicate the material and structural properties of natural bone, implants may operate as precision replacements, feeling and functioning like natural bone. In addition to improving patient comfort, the new prosthetic bone implants may reduce the occurrence of unnatural secondary wear patterns caused by current prosthetic bone implants that function in unnatural fashions due to material and structural properties that do not match natural bone. The disclosed prosthetic bone implants can be applied to bone conditions, such as complex fractures or malunions, related to trauma or disease processes and may reduce the number of amputation surgeries. The disclosed prosthetic bone implant can be used in a wide variety of different applications. The prosthetic bone implants can be used to replace bone that has been damaged by trauma, such as trauma that results from automobile accidents or gunfire and can be used to replace bone that has been degraded by disease, such as for example osteocarcinoma and osteoporosis.

[0022] While various aspects and concepts of the invention are described and illustrated herein as embodied in combination in the exemplary embodiments, these various aspects and concepts may be realized in many alternative embodiments, either individually or in various combinations and sub-combinations thereof. Unless expressly excluded herein all such combinations and sub-combinations are intended to be within the scope of the present invention. Still further, while various alternative embodiments as to the various aspects and features of the invention, such as alternative materials, structures, configurations, methods, devices, software, hardware, control logic and so on may be described herein, such descriptions are not intended to be a complete or exhaustive list of available alternative embodiments, whether presently known or later developed. Those skilled in the art may readily adopt one or more of the aspects, concepts or features of the invention into additional embodiments within the scope of the present invention even if such embodiments are not

expressly disclosed herein. Additionally, even though some features, concepts or aspects of the invention may be described herein as being a preferred arrangement or method, such description is not intended to suggest that such feature is required or necessary unless expressly so stated. Still further, exemplary or representative values and ranges may be included to assist in understanding the present invention however, such values and ranges are not to be construed in a limiting sense and are intended to be critical values or ranges only if so expressly stated.

[0023] Figures 1 and 2 schematically illustrate an example of a prosthetic bone implant 10. In the exemplary embodiment, the prosthetic bone implant 10 includes an interior region 12 disposed in a peripheral region 14. The bone implant 10 can be configured to have the same morphology and characteristics of natural, healthy bone in the region of bone being replaced. In the exemplary embodiment, the bone implant 10 can be configured to have substantially the same size, shape, strength, density, density profile, weight, and/or weight distribution of healthy bone in an area of bone to be replaced should have. In one embodiment, the bone implant includes a peripheral region having substantially a shape that healthy bone in an area of bone to be replaced should have. The peripheral region has a peripheral region thickness that corresponds to a cortical bone thickness that healthy bone in the area of bone to be replaced should have. The implant further includes an interior region disposed in the peripheral region, wherein the peripheral region and the interior region are configured such that a density of the prosthetic bone implant substantially matches a density that healthy cortical and trabecular bone in the area of bone to be replaced should have.

[0024] The bone implant 10 may be made from a variety of different materials. Examples of acceptable implant materials include, but are not limited to, polymers, metals, composites, and biodegradable scaffold materials. In one embodiment, the bone implant 10 can be made from one or more non-biodegradable materials that are compatible with biomedical applications. An example of an acceptable non-biodegradable material for use in the bone implant is short-glass-fiber-reinforced (SGFR) epoxy. Other non-biodegradable materials that are compatible with biomedical applications, however, can be used.

[0025] Referring to Figures 3 and 4, in an exemplary embodiment of the prosthetic bone implant 10, the implant can be configured to provide a platform for bone tissue regeneration, such as for example, the eventual, complete regeneration of living bone tissue. For example,

the use of a biodegradable scaffold material may allow eventual bone regeneration within and throughout the prosthesis. In one embodiment, the bone implant 10 can be made from a biodegradable scaffold material, such as one or more biodegradable materials that are compatible with biomedical applications and with regeneration of living bone tissue. An example of an acceptable biodegradable material for use in the bone implant could be a biodegradable ceramic material, such as calcium hydroxyapatite. Other biodegradable materials that are compatible with biomedical applications, however, can be used.

[0026] To promote the regeneration of living bone tissue within the prosthetic bone implant 10, some embodiments of the invention contain osteoinductive agents or osteointegration agents, which could be biological or non-biological. The use of these agents is well known in the art. In one embodiment, living bone tissue 16 may be disposed in the interior region 12. For example, living bone tissue 16 comprising bone marrow stem cells can be disposed in the interior region 12. Any stem cells and suitable agents, however, which promote living bone tissue regenerations can be used.

[0027] In this embodiment, the interior region 12 is a biodegradable scaffold material. As the stem cells grow, regenerated bone tissue will replace the biodegradable scaffold material. Methods that can be used to dispose living bone cells in the interior region 12 to promote bone tissue regeneration are disclosed in U.S. Patent Nos. 5,824,084 and 6,049,026 to Muschler, which are incorporated herein by reference in their entirety.

[0028] Figure 5 illustrates an example of a method for making the prosthetic bone implant 10. Referring to Figure 5, the method includes the steps of creating a three dimensional model 18 (Figure 7) of human bone; fabricating a mold 20 (Figure 9) based on the three dimensional model 18; forming a foamable implant precursor 22 (Figure 10) based on the three dimensional model 18; placing the implant precursor 22 in the mold 20; and activating the foamable implant precursor 22 to cause the precursor to expand into engagement with the mold 20 to form a prosthetic bone implant 10 having a peripheral region 14 and a porous interior region 12 (Figure 1-2). Figure 5 should not be read to imply a specific order to the steps of the example. For example, the step of forming the precursor does not necessarily follow the step of fabricating the mold. In addition, there are many foaming technologies that could be used for making the prosthetic bone implant disclosed in this application. While the method of using the foamable implant precursor 22, disclosed herein, is one possible

approach, other methods can also be used. Some examples of alternative foaming technologies that could be used include, but are not limited to, those disclosed in U.S. Patent Nos. 6,905,516, 6,692,532, 6,607,302, and 6,364,909, the disclosures of which are fully incorporated herein by reference.

[0029] Referring to Figures 6-7, the step of creating a three dimensional model 18 of human bone may include creating a digital three dimensional model (Figure 7), which may be based on a variety of approaches and/or information sources. For example, the three dimensional model 18 can be based on, but not limited to, images 24 (Figure 6) of the bone to be replaced; parametric modeling techniques; and/or images of a bone corresponding to the bone being replaced, such as for example, if a person's right tibia is being replaced, images of the person's left tibia might be used or images of another person's right tibia might be used if it is sufficiently similar to the bone being replaced. Various combinations of these or other approaches can be used.

[0030] In one embodiment, the three dimensional model 18 of the bone to be replaced is created using computed tomography (CT) images, Magnetic Resonance Imaging (MRI) images and/or ultrasound images along with solid modeling software, as is known in the art. An example of a method for creating three dimensional models from these images is disclosed in Mehta B.V. and Hussain, T., Modeling of Human Vocal Tract Using MR Imaging and Acoustic Pharyngometer, *Proceedings of IMECE 2004, IMECE2004-59662*, ASME Winter Annual Meeting, Anaheim, November 2004, which are incorporated herein by reference in their entirety. By using these images 24 and software, a model 18 representing bone in the area of bone to be replaced can be generated. The model 18 of the bone to be replaced, however, may need to be adjusted to represent healthy bone. It may be, that the reason underlying the need to replace bone is or causes an undesirable characteristic of the bone. For example, the model 18 of a bone having a degenerative condition, such as for example, osteoporosis, may have to be adjusted to represent healthy bone.

[0031] In the exemplary embodiment, a finite element analysis of the three dimensional solid model 18 may be performed to evaluate stresses that will be applied to the bone implant 10 under a variety of static and dynamic loads to study the effect of varying material properties of the implant 10 on these stresses. The images and/or the finite element analysis can also be used to determine the density profile and/or the weight distribution of the bone to be replaced,

as is known in the art. An example of a method of utilizing finite element analysis to determine a density profile are disclosed in Fening, S. and Mehta, B. V., Finite Element Analysis of the Knee with the Menisci, *Proceedings of the International Symposium on Computer Simulation in Biomechanics*, Aug. 2005, Cleveland, OH, pp. 39-40, which are incorporated herein by reference in their entirety.

[0032] If the density profile and/or weight distribution of the bone to be replaced differs from the density profile and/or weight distribution expected in healthy bone, the model 18 can be adjusted to represent the density profile and/or weight distribution expected in healthy bone. Based on the results of the finite element analysis, an appropriate material for use in the prosthetic bone implant can be selected. Thus, the finite element analysis can be used to determine, for example, the appropriate implant material, the appropriate density profile of the implant including the relative density for the porous interior region 12, the appropriate thickness and thickness profile for the peripheral region 14, an appropriate foaming agent, and/or an appropriate binder.

[0033] In one embodiment, parametric modeling techniques are used to determine the appropriate structural properties of the prosthetic bone implant. An example of a method for utilizing parametric modeling techniques to develop a three dimensional model are disclosed in Fening, S., Gilders, N. and Mehta, B. V., Creating Fast Patient Specific Three Dimensional Models of Human Bones Using a Novel Parametric Approach, *Proceedings of the World Congress on Medical Physics and Biomedical Engineering*, Sydney, Aug. 2003, which are incorporated herein by reference in their entirety.

[0034] Referring to Figures 8, the step of fabricating a mold based on the three dimensional model 18 may include fabricating a full-scale physical model 26 of the prosthetic bone implant 10. The physical model 26 may be produced in a variety of different ways. One acceptable way to produce the physical model 26 is by using rapid prototype technology, as is known in the art. One acceptable rapid prototyping machine is the model Dimension, available from Stratasys. Once fabricated, the physical model 26 may be used as a blank to produce the final casting mold 20 (Figure 9) that is used to fabricate the prosthetic bone implant 10.

[0035] In the example illustrated by Figure 9, the mold 20 can be made by covering the physical model 26 with a mold forming material 28, such as for example, plaster or other

suitable mold forming material. The mold forming material 28 is then allowed to harden. In the exemplary embodiment, the final casting mold 20 is composed of a material 28 that is compatible with temperatures associated with the molding process of the implant 10. For example, in the step of activating the foamable implant precursor 22 (Figure 10) to cause the precursor to expand into engagement with the mold 20 to form a prosthetic bone implant 10, if the precursor is activated by elevated temperature, the mold material 28 used to fabricate the mold 20 would be selected to be able to withstand the elevated temperature.

[0036] Depending on the molding process employed, when the mold 20 has hardened, the physical model 26 may need to be removed from the mold. In the example shown in Figure 9, the mold 20 is bisected, allowing the physical model 26 to be removed by pulling each half of the physical model out of each half of the mold. In alternative embodiments of the molding process, the physical model 26 may be dissolved, melted or burned out of the mold 20.

[0037] The step of forming a foamable implant precursor 22 may include combining the bone implant material with a suitable foaming agent. In the exemplary embodiment, the materials that make up the foamable precursor 22 are selected based on the results of the finite element analysis. In one embodiment, the density of healthy bone in an area of the bone to be replaced is determined and the foamable implant precursor materials are selected based on the density. Other suitable methods, however, may be used for selecting the appropriate materials.

[0038] An appropriate quantity of the material for the prosthetic bone implant 10 is mixed in powdered form with a powdered foaming agent. A variety of foaming agents may be used. An example of an acceptable foaming agent for use with SGFR epoxy and calcium hydroxypatite might be a low temperature sulfonylhydrazine foaming agent that is compatibility for use with thermoset materials including epoxies. Celogen TSH-C[®], available from Crompton Corporation, is an example of such a foaming agent. Other foaming agents which are compatible with the material selected for the prosthetic bone implant 10 may be used.

[0039] The mixture is homogenously blended and heated to a temperature that is lower than the melting temperature of the mixture. The powdered foaming agent decomposes near the melting temperature of the implant material. In one embodiment, if the selected bone implant

material does not have a compatible melting temperature, a powdered binder with an appropriate melting temperature may be included in the mixture. For example, the biodegradable ceramic material calcium hydroxyapatite can be used with a biodegradable thermoplastic such as polycaprolactone which would act as a binder. Other suitable binders that are compatible with the selected implant material may be used. In one embodiment, one or more additional components can be added to strengthen the prosthetic bone implant. For example, carbon fibers may be added to the mixture to add strength.

[0040] The composition of the foamable precursor mixture may vary, depending on the exact application. For a non-biodegradable implant, an example of a mixture used to make the foamable precursor can include 0.5% to 5.0% of a foaming agent and 99.5% to 95.0% of SGFR epoxy (by weight). For a biodegradable implant, an example of a mixture used to make the foamable precursor can include 0.5% to 45.0% of a foaming agent and 80.0% to 20.0% of calcium hydroxyapatite, and 90.0% to 10.0% polycaprolactone (by weight).

[0041] After heating, the mixture is pressed to form the foamable precursor 22 of predetermined size and shape for use in molding the prosthetic bone implant. The predetermined size, shape, and composition of the precursor 22 are selected to ultimately result in a bone implant with the desired characteristics, as will be discussed in more detail herein.

[0042] Referring to Figure 9, the step of placing the implant precursor in the mold 20 may include bisecting the mold or creating an opening in the mold to allow the insertion of the foamable precursor 22. Once properly positioned inside the mold 20, the precursor 22 can be activated

[0043] Referring to Figure 10-11, the step of activating the foamable implant precursor 22 may include applying heat 30. The foamable precursor 22, however, could be activated in other ways, such as for example, by a chemical reaction or by application of pressure. In one embodiment, the mold 20 is heated in a furnace to bring the foamable precursor 22 to a temperature that activates the foaming agent and melts the implant material and/or the binder. For example, in one embodiment, the mold is heated to about 140 degrees Celsius, the activation temperature for the foaming agent, Celogen TSH-C®.

[0044] The foaming agent decomposes as the powdered material and/or binder melts together. As the foaming agent decomposes, the foaming agent causes small bubbles to form throughout the foamable precursor 22, which causes the foamable precursor 22 to expand into engagement with a mold wall 32. As the foamable precursor 22 expands, more material of the foamable precursor will be pressed against the walls 32 of the mold 20 than will remain in the inner core 12. As a result, peripheral region 14 of the implant 10 will be denser than the interior region 12 resulting in the peripheral region 14 surrounding the interior region 12.

[0045] The predetermined size, shape, and composition of the precursor 22 impacts the resulting characteristics of the bone implant 10. The foam core porosity and peripheral region thickness, density, and distribution of thickness and density can be controlled by the proper sizing, shaping, and material selection of the pre-foamed precursor 22. For example, peripheral region thickness of the prosthetic bone implant 10 is dependent on the ratio of an amount of implant material to an amount of foaming agent in the precursor 22. More foaming agent will result in thicker walls, since more of the prosthetic bone implant material is displaced to walls 32 of the mold 20 by the foaming agent. Thus, the overall density of the prosthetic bone implant is dependent on the total amount of implant material used, and the magnitude of the distribution of that material from the porous core to the outer surface is dependent on a ratio of an amount of implant material to an amount of foaming agent.

[0046] Furthermore, different portions of the foamable precursor 22 can be configured to have different implant material to foaming agent ratios. This could be achieved, for example, by forming the precursor material in batches, in which one portion of the precursor is formed from a first batch and a second portion of the precursor is formed from the second batch. As a result, the prosthetic bone implant can have regions with varying densities and varying peripheral region thickness to provide a density profile that substantially matches the density profile of the healthy bone in the area of bone replacement. Multiple foamable precursor could also be used with the same mold to provide a prosthetic bone implant with regions having varying densities and/or varying peripheral region thickness. In one embodiment, the foamable precursor 22 is formed such that a first portion of the prosthetic bone implant 10 approximates the density of the first bone region and a second portion of the prosthetic bone implant approximates the density of the second bone region. For example, the prosthetic bone implant 10 can have a density profile that varies along a length of the implant.

[0047] The three dimensional model 18 can be configured to provide a representation of a density of a first bone region and a representation of a density of a second bone region. Thus, the three dimensional model 18 can include a representation of bone density and bone thickness and the foamable precursor is formed such that the peripheral region of the prosthetic bone implant approximates the model's representation of bone density or and thickness.

[0048] Once the foamable precursor 22 has been activated and has expanded within the mold 20, the formed prosthetic bone implant 10 is cooled and removed from the mold.

[0049] Referring to Figures 12 and 13, in one embodiment, plugs 50 of living bone cells 16 are placed in the interior region 12. The plugs 50 of living bone cells can be taken from healthy bone and implanted into the biodegradable scaffold material. The inclusion of living bone plugs 50 in the prosthetic bone implant may reduce the number of occurrences of rejection of the bone implant by the patient's body. The living bone plugs 50 grow and eventually replace the biodegradable scaffold material, resulting in a fully living regenerated bone capable of remodeling to loading. This ability could help ensure the longevity of the bone replacement in the system. The inclusion of stem cells in the bone plugs 50 stimulates the regeneration of living bone tissue.

[0050] While the invention has been described with reference to specific embodiments, it will be apparent to those skilled in the art that many alternatives, modifications, and variations may be made. Accordingly, the present invention is intended to embrace all such alternatives, modifications, and variations that may fall within the spirit and scope of the appended claims.

Claims

1. A method of making a prosthetic bone implant, comprising:

forming a foamable implant precursor comprising a scaffold material;

placing the foamable implant precursor into a mold, wherein the mold configuration is based on a region of bone to be replaced by the implant; and

activating the foamable implant precursor to cause the foamable precursor to expand within the mold to form a prosthetic bone implant having a peripheral region the substantially conforms to the configuration of the mold and an interior region, the peripheral region having a relatively greater density of scaffold material as compared to the density of scaffold material in the interior region.

2. The method of claim 1 further comprising creating a three dimensional model of human bone.

3. The method of claim 2 further comprising fabricating a mold based on the three dimensional model.

4. The method of claim 2 wherein the three dimensional model is based on images of bone to be replaced.

5. The method of claim 4 wherein the images are magnetic resonance images.

6. The method of claim 4 wherein the images are computed tomography images.

7. The method of claim 2 wherein the three dimensional model includes a representation of bone density and the foamable precursor is formed such that the prosthetic bone implant approximates the representation of bone density.

8. The method of claim 2 wherein the three dimensional model includes a representation of cortical bone thickness and the foamable precursor is formed such that the peripheral region of the prosthetic bone implant approximates the representation of cortical bone thickness.

9. The method of claim 2 wherein the three dimensional model includes a representation of a density of a first bone region and includes a representation of a density of a second bone region; wherein the foamable precursor is formed such that a first portion of the prosthetic bone implant approximates the density of the first bone region and a second portion of the prosthetic bone implant approximates the density of the second bone region.
10. The method of claim 1 wherein the foamable precursor further comprises a foaming agent and wherein the overall density of the prosthetic bone implant depends on the total amount of scaffold material used, and the magnitude of the distribution of that material from the interior region to the peripheral region depends on a ratio of an amount of scaffold material to an amount of foaming agent.
11. The method of claim 1 wherein the foamable precursor is formed such that different portions of the foamable precursor have varying concentrations of scaffold material to form a prosthetic bone implant with varying densities.
12. The method of claim 1 wherein the foamable precursor further comprises a foaming agent and wherein the peripheral region thickness of the prosthetic bone implant is dependent on a ratio of an amount of scaffold material to an amount of foaming agent.
13. The method of claim 12 wherein the foamable precursor is formed such that different portions of the foamable precursor have different scaffold material to foaming agent ratios to form a prosthetic bone implant with a varying peripheral region thickness.
14. The method of claim 1 wherein the scaffold material is biodegradable.
15. The method of claim 14 wherein the foamable implant precursor further comprises a foaming agent.
16. The method of claim 14 further comprising the step of inserting an osteoinductive agent into the prosthetic bone implant.
17. The method of claim 14 further comprising the step of inserting bone marrow stem cells into the prosthetic bone implant.

18. The method of claim 1 further comprising the step of determining a density of healthy bone in an area of the bone to be replaced and selecting a foamable implant precursor composition based on the density.

19. A prosthetic bone implant, suitable for mammalian implantation, the implant comprising:

a peripheral region; and

an interior region, wherein the peripheral region has a relatively greater density than the interior region,

wherein the implant is formed from substantially the same material throughout.

20. The prosthetic bone implant of claim 19 wherein the interior region comprises a biodegradable scaffold material.

21. The prosthetic bone implant of claim 19 wherein living bone tissue is disposed in the interior region.

22. The prosthetic bone implant of claim 19 wherein an osteoinductive agent is disposed in the interior region.

23. The prosthetic bone implant of claim 19 wherein an osteointegration agent is disposed in the interior region.

24. The prosthetic bone implant of claim 19 wherein bone marrow stem cells are disposed in the biodegradable scaffold material.

25. The prosthetic bone implant of claim 19 wherein the prosthetic bone implant is made by:

forming a foamable implant precursor comprising a scaffold material;

placing the implant precursor into a mold, wherein the mold configuration is based on a region of bone to be replaced by the implant; and

activating the foamable precursor to cause the foamable precursor to expand into engagement with the mold to form a prosthetic bone implant having a peripheral region and

an interior region, the peripheral region having a relatively greater density than the interior region.

26. The prosthetic bone implant of claim 19 wherein the prosthetic bone implant has a density profile that varies along a length of the prosthetic bone implant.

27. The prosthetic bone implant of claim 19 wherein the density profile of the prosthetic bone implant substantially matches a density profile that healthy bone in the area of bone to be replaced should have.

28. The prosthetic bone implant of claim 19 wherein the peripheral region has substantially a shape that healthy bone in an area of bone to be replaced should have, wherein the thickness of the peripheral region corresponds to the desired thickness of the region of bone intended to receive the implant.

29. A prosthetic bone implant, made from a biodegradable scaffold material comprising:

a) a peripheral region having substantially a shape that healthy bone in an area of bone to be replaced should have;

b) interior region, wherein the peripheral region and the interior region are configured such that a density of the prosthetic bone implant substantially matches a density that healthy bone in the area of a bone to be replaced should have; and

c) an osteoinductive agent disposed in the interior region.

30. The prosthetic bone implant of claim 29 wherein the osteoinductive agent comprises bone marrow stem cells.

31. A method of making a prosthetic bone implant, comprising:

a) creating a three dimensional model of human bone;

b) fabricating a mold based on the three dimensional model;

c) positioning a foamable material into the mold;

d) forcing a portion of the foamable material into contact with the mold to form a prosthetic bone implant having a peripheral region and a

32. The method of claim 31 wherein the foamable material is formed based on the three dimensional model.

33. A method of making a prosthetic bone implant, comprising:

forming a first foamable implant precursor comprising a first scaffold material;

placing the first foamable implant precursor into a mold, wherein the mold configuration is based on a region of bone to be replaced by the implant; and

activating the first foamable implant precursor to cause the foamable precursor to expand within the mold to form a prosthetic bone implant having a peripheral region that substantially conforms to the configuration of the mold and a hollow interior region

forming a second foamable implant precursor comprising a second scaffold material;

placing the second foamable implant precursor into the interior region;

activating the second foamable implant precursor to cause the second foamable precursor to expand into engagement with the peripheral region to form an interior region; wherein the peripheral region has a relatively greater density of first scaffold material as compared to the density of second scaffold material in the interior region.

34. The method of claim 33 wherein the first scaffold material is a different than the second scaffold material.

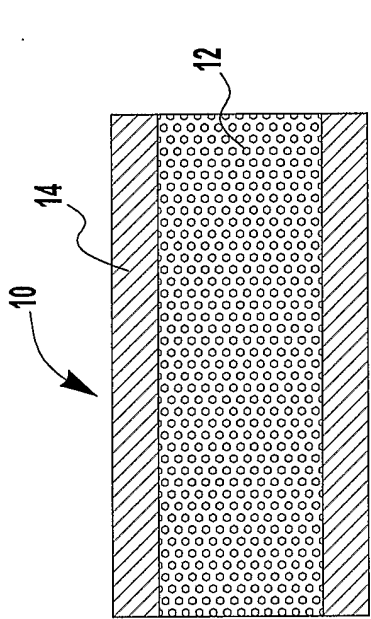


FIG. 2

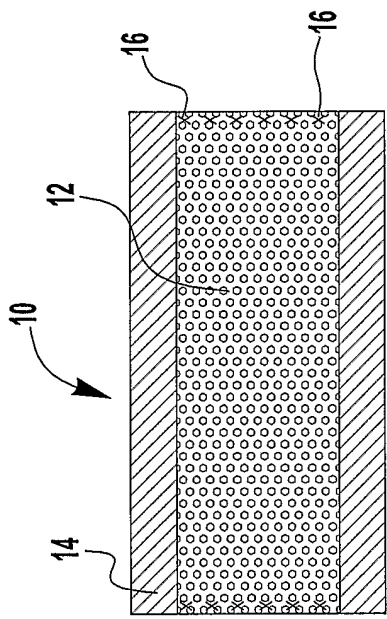


FIG. 4

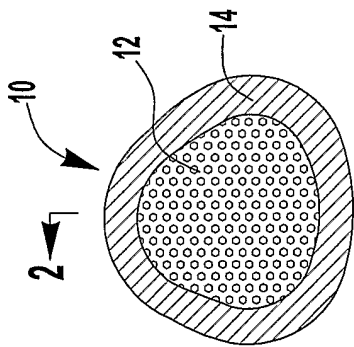


FIG. 1

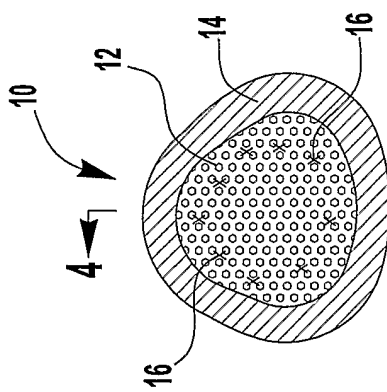
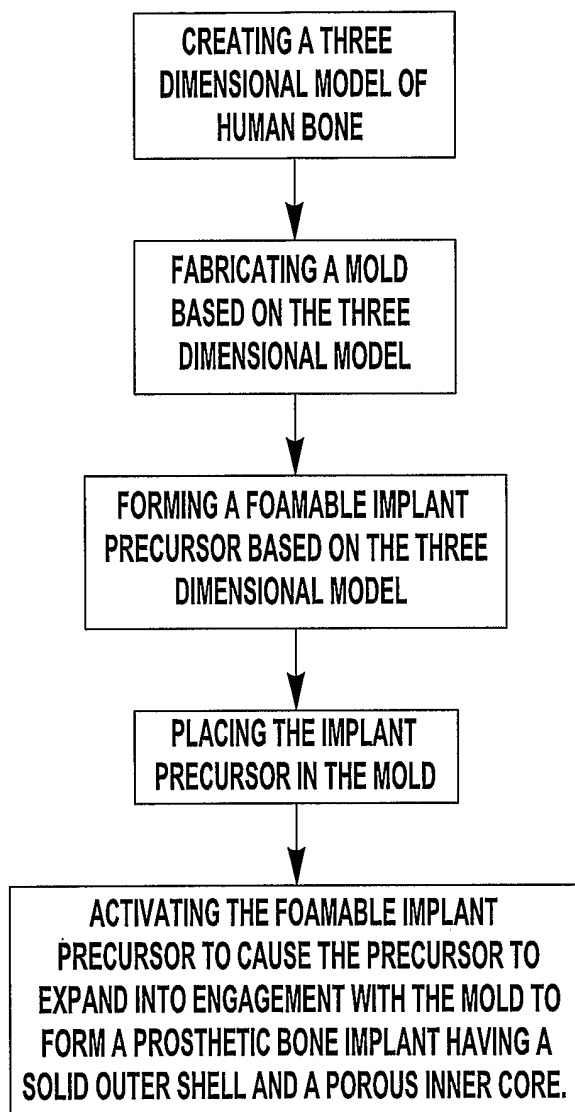


FIG. 3

2/6

**FIG. 5**

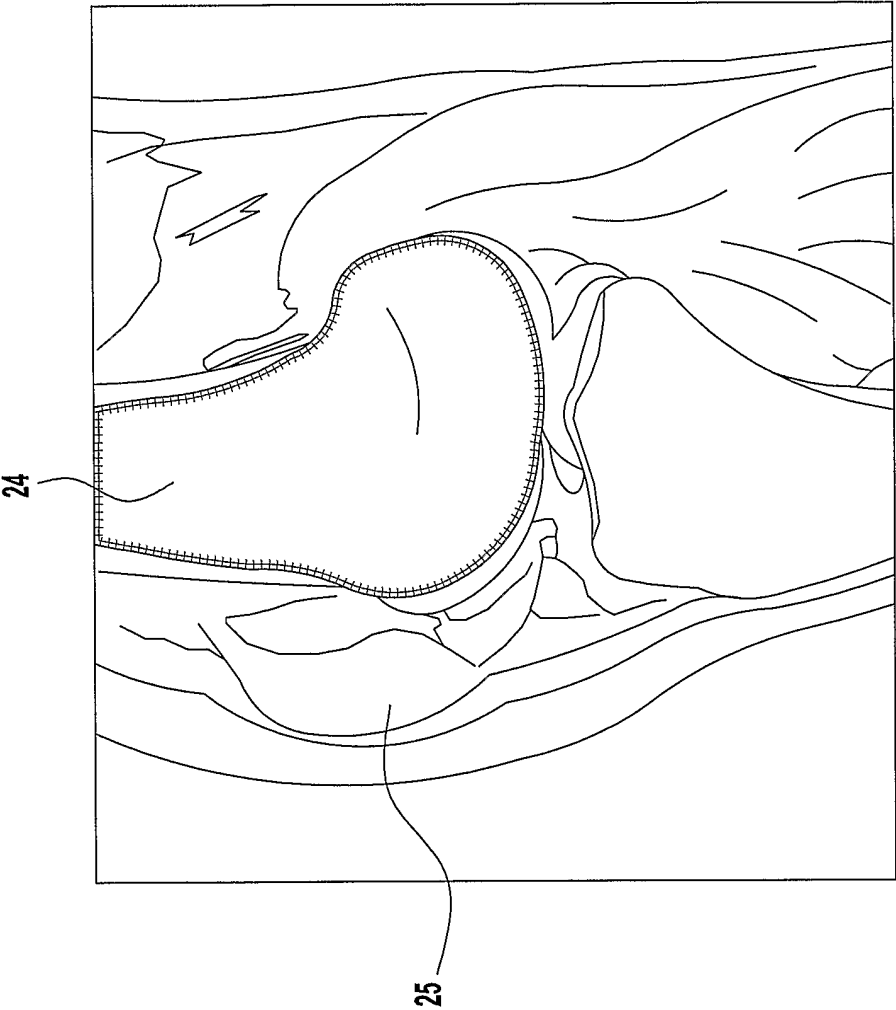


FIG. 6

4/6

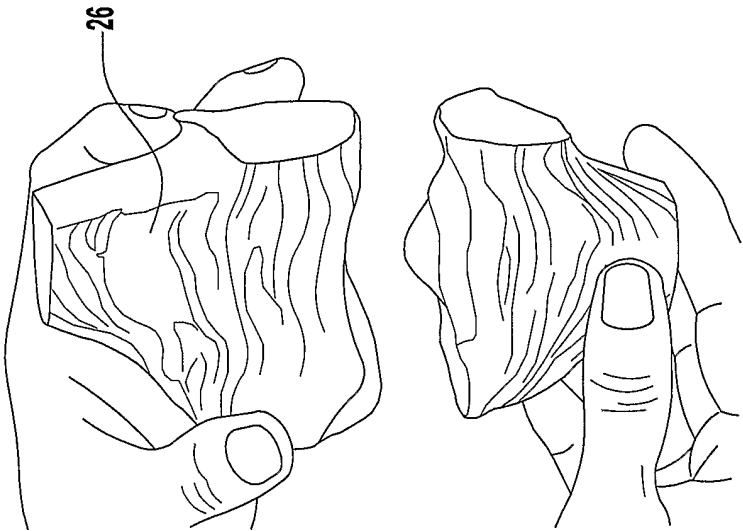


FIG. 8

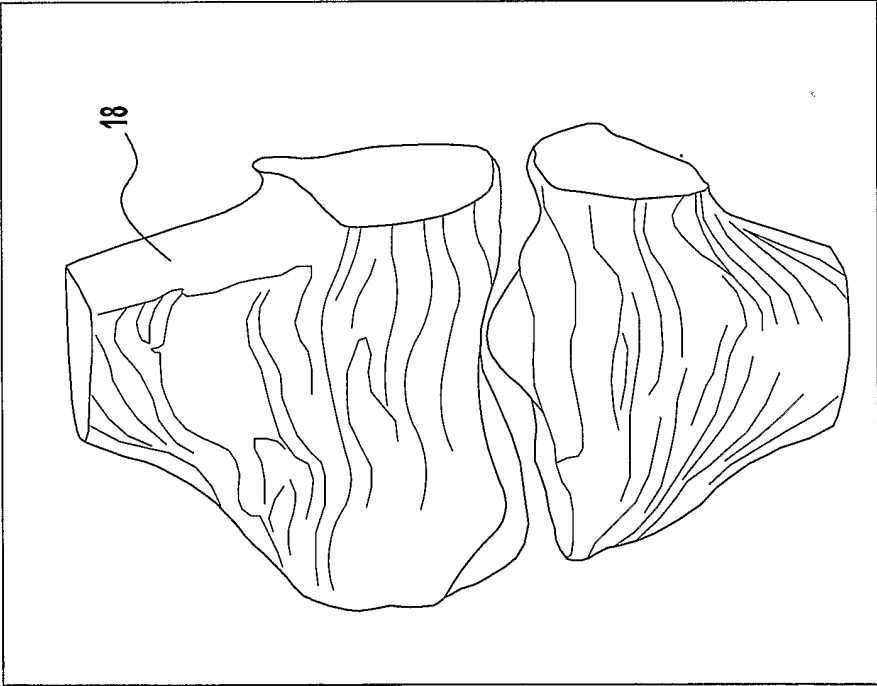


FIG. 7

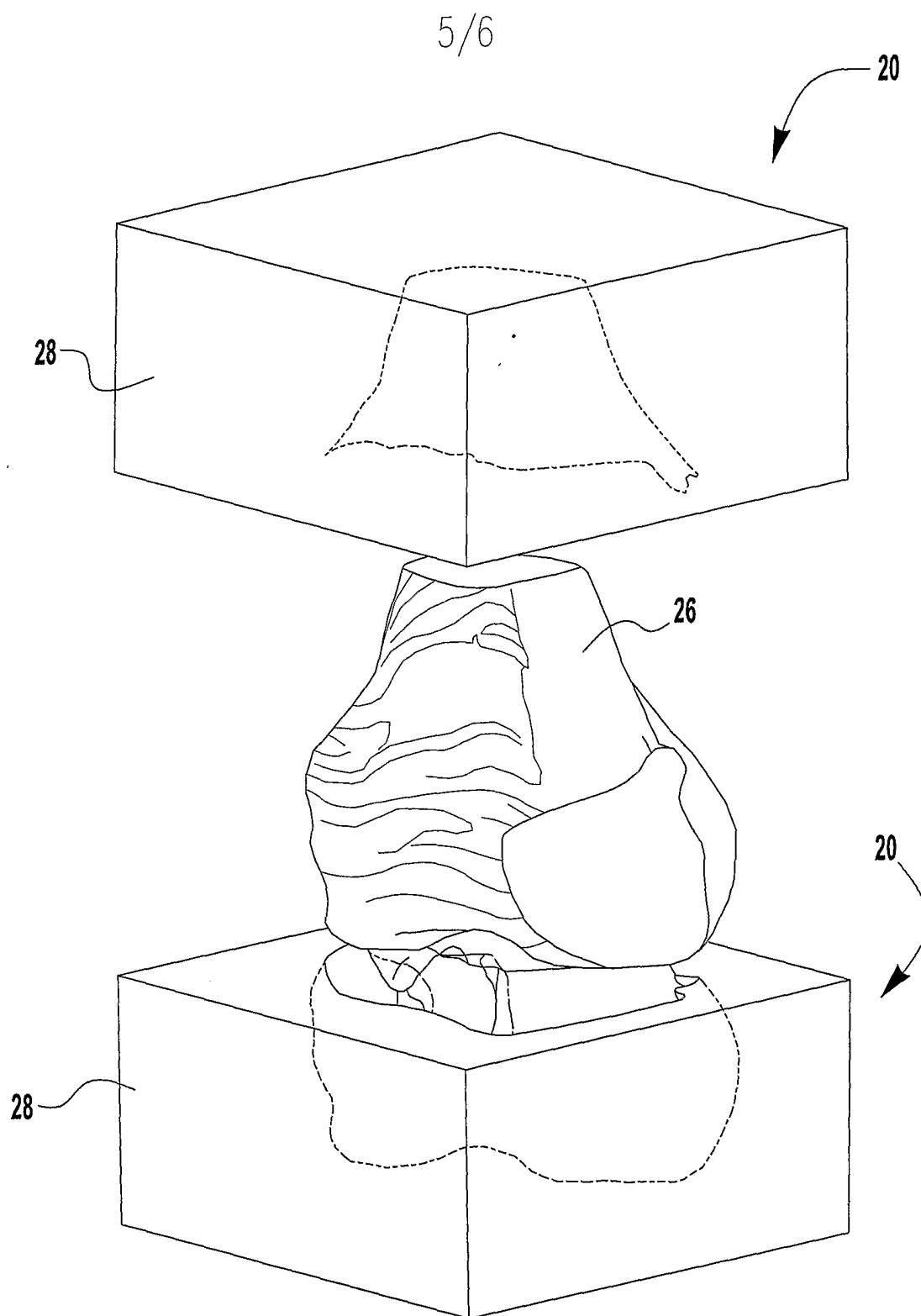


FIG. 9

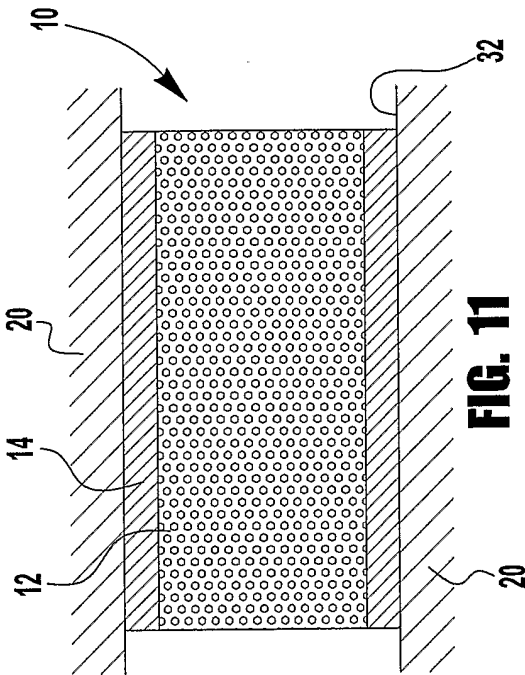


FIG. 10

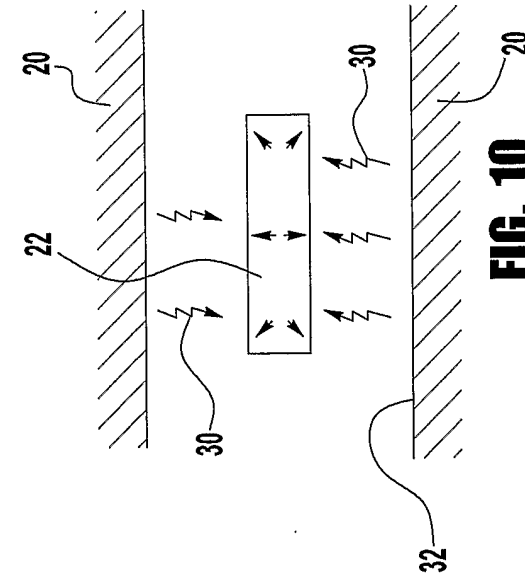


FIG. 11

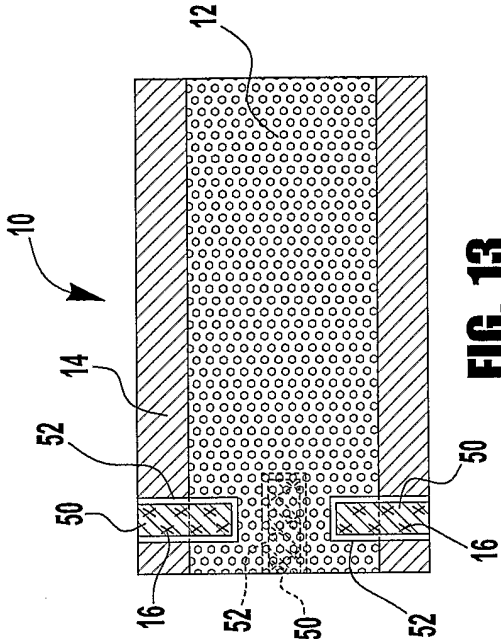


FIG. 12

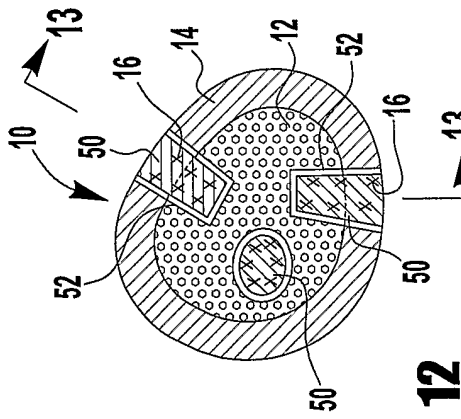


FIG. 13