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(54) **Radiolucent bone graft**

Röntgendurchlässiges Knochentransplantat

Greffe d'os translucide aux rayons x

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Description

BACKGROUND OF THE INVENTION

[0001] This invention relates generally to improvements in bone grafts such as spinal fusion cages of the type designed for human implantation between adjacent spinal vertebrae, to maintain the vertebrae in substantially fixed spaced relation while promoting interbody bone ingrowth and fusion therebetween. More particularly, this invention relates to an implantable bone graft such as a spinal fusion cage having an improved combination of enhanced mechanical strength together with osteoinductive and osteoconductive properties, in a ceramic-based device that additionally and beneficially provides radiolucency for facilitated post-operative monitoring.

[0002] The document US-A-6,149,688 represents closest prior art.

[0003] Implantable interbody bone grafts such as spinal fusion devices are known in the art and are routinely used by spine surgeons to keep adjacent vertebrae in a desired spaced-apart relation while interbody bone ingrowth and fusion takes place. Such spinal fusion devices are also used to provide weight bearing support between adjacent vertebral bodies and thus correct clinical problems. Such spinal fusion devices are indicated for medical treatment of degenerative disc disease, discogenic low back pain and spondylolisthesis. These conditions have been treated by using constructs, typically made from metals such as titanium or cobalt chrome alloys such as used in orthopedic implants, and allograft (donor) or autograft (patient) bone to promote bone ingrowth and fusion.

[0004] Typical interbody spinal fusion devices, such as plugs for example, have hollow or open spaces that are usually filled with bone graft material, either autogenous bone material provided by the patient or allogenous bone material provided by a third party donor. These devices also have lateral slots or openings which are primarily used to promote ingrowth of blood supply and grow active and live bone. These implants may also have a patterned exterior surface such as a ribbed or serrated surface or a screw thread to achieve enhanced mechanical interlock between adjacent vertebrae, with minimal risk of implant dislodgement from the site. See, for example, U.S. Patents 5,785,710; and 5,702,453. Typical materials of construction for such interbody spinal fusion devices include bio-compatible carbon fiber reinforced polymers , cobalt chrome alloys, and stainless steels or titanium alloys. See, for example, U.S. Patent 5,425,772.

[0005] Most state-of-the-art spinal fusion implants are made from titanium alloy and allograft (donor) bone, and have enjoyed clinical success as well as rapid and widespread use due to improved patient outcomes. However, titanium-based implant devices exhibit poor radiolucency characteristics, presenting difficulties in post-operative monitoring and evaluation of the fusion process due to the radio-shadow produced by the non-lucent metal. There is also clinical evidence of bone subsidence and collapse which is believed to be attributable to mechanical incompatibility between natural bone and the metal implant material. Moreover, titanium-based implant devices are primarily load bearing but are not osteoconductive, i.e., not conducive to direct and strong mechanical attachment to patient bone tissue, leading to potential graft necrosis, poor fusion and stability. By contrast, allograft bone implants exhibit good osteoconductive properties, but can subside over time as they assimilate into natural bone. Further, they suffer from poor pull out strength resulting in poor stability, primarily due to the limited options in machining the contact surfaces. Allograft bone implants also have variable materials properties and, perhaps most important of all, are in very limited supply. A small but finite risk of disease transmission with allograft bone is a factor as well. In response to these problems some developers are attempting to use porous tantalum-based metal constructs, but these have met with limited success owing to the poor elastic modulii of porous metals.

[0006] A typical titanium alloy spinal fusion device is constructed from a hollow cylindrical and externally threaded metal cage-like construct with fenestrations that allow communication of the cancellous host tissue with the hollow core, which is packed with morselized bone graft material. This design, constrained by the materials properties of titanium alloys, relies on bony ingrowth into the fenestrations induced by the bone graft material. However, the titanium-based structure can form a thin fibrous layer at the bone/metal interface, which degrades bone attachment to the metal. In addition, the hollow core into which the graft material is packed may have sub-optimal stress transmission and vascularization, thus eventually leading to failure to incorporate the graft. Mechanical stability, transmission of fluid stress, and the presence of osteoinductive agents are required to stimulate the ingrowth of vascular buds and proliferate mesenchymal cells from the cancellous host tissue into the graft material. However, most titanium-based spinal fusion devices in use today have end caps or lateral solid walls to prevent egress of the graft outwardly from the core and ingress of remnant disc tissue and fibroblasts into the core.

[0007] Autologous (patient) bone fusion has been used in the past and has a theoretically ideal mix of osteoconductive and osteoinductive properties. However, supply of autologlous bone material is limited and significant complications are known to occur from bone harvesting. Moreover, the costs associated with harvesting autograft bone material are high, requiring two separate incisions, with the patient having to undergo more pain and recuperation due to the harvesting and implantation processes. Additionally, autologous cancellous bone material has inadequate mechanical strength to support intervertebral forces by itself, whereby the bone material is normally incorporated with a metal-based construct.

[0008] Ceramic materials provide potential alternative structures for use in spinal fusion implant devices and prosthetics, see for example U.S. Patent 5,871,517 which describes a hip joint prosthesis having a zirconia head and a ceramic cup and U.S. Patent 4,000,525 which describes a ceramic prosthesis of high density aluminum oxide. In this regard, monolithic ceramic constructs have been proposed, formed from conventional materials such as hydroxyapatitie (HAP) and/or tricalcium phosphate (TCP). See, for example, U.S. Patent 6,037,519. However, while these ceramic materials may provide satisfactory osteoconductive and osteoinductive properties, they have not provided the mechanical strength necessary for the implant.

[0009] Thus, a significant need exists for further improvements in and to the design of bone grafts such as spinal fusion implant devices, particularly to provide a high strength implant having high bone ingrowth and fusion characteristics, together with substantial radiolucency for effective facilitated post-operative monitoring.

[0010] Hence, it is an object of the present invention to provide an improved bone graft such as an interbody spinal fusion implant or cage made from a bio-compatible open pore structure, which has a radiolucency similar to that of the surrounding bone. It is also an object of the present invention to provide a substrate of high bio-mechanical strength for carrying biological agents which promote intervertaebral bone ingrowth, healing and fusion. It is a further objective of the present invention to provide an interbody fusion device which has mechanical properties that substantially match that of natural bone, by using ceramic construct materials rather than metal.

SUMMARY OF THE INVENTION

[0011] The features of the invention are defined in claim 1. According to claims therefore there is provided a bone graft comprising a ceramic substrate block formed from a material with a flexural strength greater than about 500 mega-Pascals and a fracture toughness greater than about five mega-Pascals root meter.

[0012] Said bone graft may comprise a spinal fusion cage. The bone graft, as embodied in the form of such a spinal fusion cage, may comprise a porous or open-cell substrate block formed from a ceramic composition having a relatively high bio-mechanical strength and load bearing capacity.

[0013] Suitably, said ceramic substrate block may be porous having a relatively high strength corresponding substantially with natural cortical and cancellous bone. The porosity of the substrate block may be about 10% to about 50% by volume with open pores distributed throughout and a pore size range from about 5 to about 500 μ. Said ceramic substrate block may have a porosity ranging from about 2% to about 80% by volume , and the pore size may range from about 5 μ to about 1500 μ. Suitably, said porosity may range from about 10% to about 50% by volume, and the pore sizes may range from about 100 μ to about 500 μ. Preferably, the pores formed within the substrate block are in substantially open fluid communication sufficient to transmit fluid pressure therebetween.

[0014] Said a porous ceramic substrate block may comprise a ceramic structure form from alumina, zirconia or composition thereof. A preferred composition for the ceramic substrate block comprises a two phase alumina-zirconia composition having a suitable size and shape for seated implantation into the inter-vertebral space, with generally planar or appropriately shaped faces seated respectively upon the end plates of the adjacent vertebrae. In a preferred form, the substrate block may comprise an alumina-zirconia composition with an alumina to zirconia ratio ranging from about 100% (i.e., 2:1) to about 25% (i.e., 1:4). More preferably, the substrate block composition may comprise about 10% to about 20% or 25% by volume zirconia in alumina. Either yttria stabilised zirconia (about 2.5 to about 5 mol% yttria in zirconia) or ceria stabilised zirconia (about 2.5 to about 15 mol% ceria in zirconia) is preferably used for the zirconia phase.

[0015] According to the invention, the ceramic block has a variable porosity gradient substantially mimicking natural cortical and cancellous bone. Thus said ceramic substrate block may have a first region of relatively low porosity substantially mimicking natural cortical bone and a second region of relatively high porosity substantially mimicking cancellous patient bone.

[0016] Said ceramic substrate block may have a first, lower porosity region and a second, higher porosity region, wherein said second, higher porosity region is configured to facilitate bone ingrowth and fusion attachment with adjacent patient bone. In a preferred form, the porosity of the substrate block may be gradated from a first relatively low porosity region emulating or mimicking the porosity of cortical bone to a second relatively higher porosity region emulating or mimicking the porosity of cancellous bone.

[0017] Said first region may have a porosity of less than about 5%. Said second region may have a porosity ranging from about 30% to about 80%. Said second region may have a porosity of greater than about 40%, preferably greater than about 45% and more preferably greater than about 50%.

[0018] In some embodiments, said bone graft may further comprise a surface coating applied to the substrate block, said surface coating having osteo-conductive and osteoinductive properties to promote inter-body bone ingrowth and fusion attachment with adjacent patient bone. Said surface coating may be internally and externally applied to the porous ceramic substrate block. Typically, said surface coating may comprise a bioactive and resorbable surface coating. The porous substrate block may accordingly be internally and externally coated with a bioactive surface coating material selected for relatively high osteo-conductive and osteo-inductive properties, such as hydroxyapatite or calcium phosphate material.

[0019] In some embodiments, said surface coating

may comprise a partially or fully amorphous osteo-inductive material, including a glass and osteo-inductive calcium compound. In some embodiments, said surface coating may comprise an organic coating material. Said organic coating material may be selected from autologous bone marrow aspirates, bone morphogenic proteins, growth factors and progenitor cells and mixtures thereof. Said progenitor cells may include mesenchymal stem cells, haematopoietic cells and embryonic stem cells. Suitably, said progenitor cells comprise non-embryonic cells or cells obtained by methods that that do not involve the destruction of embryos.

[0020] Suitably, said bone graft may include one or more therapeutic agents carried by said substrate block. Said one or more therapeutic agents may be adapted for achieving further enhanced bone fusion and ingrowth. Such therapeutic agents may include natural or synthetic therapeutic agents such as bone morphogenic proteins (BMPs), growth factors, bone marrow aspirate, stem cells, progenitor cells, antibiotics or other osteo-conductive, osteo-inductive, osteogenic or any other fusion enhancing material or beneficial therapeutic agent. In some embodiments, said therapeutic agent may comprise a natural or synthetic osteo-conductive or osteo-inductive agent.

[0021] The method may therefore further include the steps of extracting said therapeutic agent from a patient, and culturing the therapeutic agent *in vitro* using the bone graft implant as a culture medium and substrate prior to said implanting step. Suitably, said method may comprise the steps of:

forming a porous ceramic bone graft implant;
extracting from a patient a therapeutic agent selected from autologous bone marrow aspirates, bone morphogenic proteins, growth factors and progenitor cells and mixtures thereof; culturing the therapeutic agent *in vitro* using the bone graft implant as a culture medium and substrate prior to said implanting step; and
surgically implanting the bone graft implant within a patient at a selected bone regeneration/ingrowth site.

[0022] The bone graft of the invention can be made in a variety of shapes and sizes to suit different specific implantation requirements. Preferred shapes include cylindrical or partly cylindrical with substantially flat opposite ends and a tapered or lordotic cross-section to suit the required curvature of the intervertebral space, in the case of a spinal fusion device. The exterior surface of the cylindrical body may include threads or ribs for facilitated and secure screw-in placement, for example, between adjacent vertebrae. Alternative preferred shapes include a generally rectangular block which may also include serrations or the like on one or more exterior faces thereof, and/or may have a tapered or lordotic cross-section for improved fit in the intervertebral space. Said substrate block may have a rough exterior surface. Suitably, said substrate block may have a ribbed exterior surface.

[0023] Typically, said substrate block may further include means for facilitated grasping and manipulation with a surgical instrument for implantation. The bone graft may desirably include a posterior end having engagement means such as a threaded socket for releasable engagement with a suitable insertion tool. In addition, the bone graft may also include one or more laterally open recesses or bores for receiving and supporting osteoconductive bone graft material, such as allograft (donor) or auto-graft (patient) material.

[0024] Further alternative bone graft configurations may include controlled porosity gradations to define a relatively low porosity first region or regions substantially emulating cortical bone, to define a high-strength loading bearing zone or strut for absorbing impaction and insertion load, in combination with one or more relatively high porosity second regions substantially emulating cancellous bone for contacting adjacent patient bone for enhanced bone ingrowth and fusion. In some embodiments, said first region may comprise at least one structural load-bearing strut extending through the substrate block. Said at least one strut may substantially mimic the structural characteristics of natural bone; said at least one strut may be formed from a porous ceramic material.

[0025] Preferably, said first, lower porosity region may be generally disposed on anterior and posterior surfaces of the substrate block and may further define at least one structural load-bearing strut extending through said substrate block between said anterior and posterior surfaces.

[0026] Said second region may include an extended exposed surface area for contacting the adjacent bone. In some embodiments, said second region may be substantially exposed on medial and lateral surfaces of the substrate block.

[0027] Said first region may circumferentially surround and support the second region.

[0028] In some embodiments, the substrate body of the bone graft may have a bore formed therein. Suitably, the substrate body may have a laterally open bore formed therein, and an osteo-conductive material may be supported within said bore. Said osteo-conductive material may comprise morselised bone graft material.

[0029] The bone graft may exhibit relatively high mechanical strength for load-bearing support, for example, between adjacent vertebrae in the case of a spinal fusion cage, while additionally and desirably providing high osteo-conductive and osteo-inductive properties to achieve enhanced bone ingrowth and interbody fusion. Importantly, these desirable characteristics maybe achieved in a structure that is substantially radiolucent so that the implant does not interfere with post-operative radiographic monitoring of the fusion process. As such, the ceramic block may be substantially radiolucent.

[0030] Other features and advantages of the invention will become more apparent from the following detailed description, taken in conjunction with the accompanying

drawings which illustrate, by way of example, the principles of the invention.

BRIEF DESCRIPTION OF THE DRAWINGS

[0031] The accompanying drawings illustrate the invention. In such drawings:

FIGURE 1 is a perspective view illustrating an externally threaded radiolucent bone graft such as a spinal fusion cage having an externally threaded and generally cylindrical shape in accordance with one preferred for of the invention;

FIGURE 2 is a perspective view showing the spinal fusion cage of FIG. 1 in exploded relation with a tip end of an associated insertion tool for use in implanting the spinal fusion cage into the inter-vertebral space between a pair of adjacent vertebrae in a patient;

FIGURE 3 is a perspective view showing implantation of the spinal fusion cage into the inter-vertebral space;

FIGURE 4 is a perspective view depicting one alternative preferred and generally cylindrical bone graft such as a spinal fusion cage;

FIGURE 5 is a perspective view depicting a further alternative preferred form of the invention, comprising a generally rectangular bone graft such as a spinal fusion cage having at least one serrated external surface;

FIGURE 6 is a perspective view showing still another alternative preferred form of the invention, comprising a generally rectangular bone graft such as a spinal fusion cage;

FIGURE 7 is a perspective view showing a further alternative preferred form of the invention, comprising a generally rectangular bone graft such as a spinal fusion cage with localized regions of varying porosity;

FIGURE 8 is a transverse sectional view taken generally on the line 8-8 of FIG. 7;

FIGURE 9 is another perspective view showing a modified preferred form of the invention, comprising a generally rectangular bone graft such as a spinal fusion cage with alternative localized regions of varying porosity; and

FIGURE 10 is a transverse sectional view taken generally on the line 10-10 of FIG. 9.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

[0032] As shown in the exemplary drawings, a radiolucent bone graft such as a spinal fusion cage referred to generally in FIGURES 1-3 by the reference numeral 10 is provided for seated implantation between a pair of adjacent patient bones such as spinal vertebrae 12 (FIG. 3) to maintain the vertebrae in spaced relation while promoting interbody bone ingrowth and fusion. In general, the improved bone graft 10 comprises a bio-compatible ceramic substrate having a porous construction to define an open lattice conducive to interbody bone ingrowth and fusion, while providing a strong mechanical load bearing structure analogous to the load bearing properties of cortical and cancellous bone. This open-celled ceramic substrate is coated internally and externally with a bio-active surface coating selected for relatively strong osteoconductive and osteoinductive properties, whereby the coated ceramic substrate provides a scaffold conducive to cell attachment and proliferation to promote interbody bone ingrowth and fusion attachment. The ceramic substrate may also carry one or more selected therapeutic agents suitable for bone repair, augmentation and other orthopedic uses.

[0033] FIGS. 1-3 illustrate the improved bone graft in the form of an improved spinal fusion cage 10 in accordance with one preferred embodiment, in the shape of a generally cylindrical body having external ribs formed thereon in the shape of a screw thread 14. The opposite ends of this cylindrical body are generally flat, with a posterior end 16 shown to include a shallow diametrically extending notch 18 in combination with an axially centered and rearwardly open threaded socket 20 for releasible engagement with an insertion tool 22 (FIGS. 2-3), as will be described in more detail. The cylindrical body is shown further to include a laterally open recess or bore 24 for receiving and supporting morselized bone graft material 26 (FIG. 2), such as allograft bone material from a third party donor, or autograft bone material from the patient.

[0034] The preferred ceramic substrate composition comprises a relatively high strength ceramic substrate block. In accordance with one preferred form of the invention, this substrate block comprises a two phase alumina-zirconia composition having a controlled porosity and having a suitable size and shape for seated implantation, such as into the inter-vertebral space in the case of the spinal fusion cage 10. In a preferred form, the composition comprises an alumina-zirconia composition with an alumina to zirconia ratio ranging from about 100% (i.e., 2:1) to about 25% *(i.e.,* 1:4). More preferably, the substrate composition comprises about 10% to about 20% by volume zirconia in alumina. Either yttria stabilized zirconia (about 2.5 to about 5 mol% yttria in zirconia) or ceria stabilized zirconia (about 2.5 to about 15 mol% ceria in zirconia) are preferably used for the zirconia phase.

[0035] The alumina-zirconia composition is processed to provide a homogeneous distribution of the two phases, and sintering temperatures are controlled to provide a particle size of about 0.5 micron or less in the sintered state. The resultant ceramic substrate block has a porosity ranging from about 2% to about 80% by volume, and preferably from about 10% to about 50% by volume, with pore sizes ranging from about 5 microns to about to about 1,500 microns, and preferably from about 100 to about 500 microns. In the preferred form, the pores are

arranged for fluid continuity therebetween, and with a rough porous outer surface of large or extended surface area. Moreover, in the preferred form, the pores are arranged with a variable porosity gradient to define a first region of relatively low or reduced porosity (less than about 5%) mimicking cortical bone structure and a second region of relatively large or increased porosity (ranging from about 30% to about 80%) mimicking cancellous bone structure. In one preferred configuration, the outer or external surfaces of the reticulated substrate block comprise the first or low porosity region for improved load bearing capacity, while the interior surfaces of the substrate block comprises the second or high porosity region mimicking cancellous bone for enhance bone ingrowth and fusion. This material used to form the substrate block exhibits a substantially optimal combination of flexural strength (greater than about 500 MPa [mega-Pascals]) and fracture toughness (greater than about 5 $Mpam^{0.5}$ [mega-Pascal root meter]). These strengths are as measured for standard bend bars and single edge notched beam (SENB) specimens, per ASTM E-1304 and C-1162 procedures.

[0036] This high strength ceramic substrate block is surface-coated internally and externally with a bio-active organic or inorganic surface coating material selected for relatively strong osteoconductive and osteoinductive properties to provide a nutrient rich environment for cellular activity to promote interbody bone ingrowth and fusion attachment. Preferred surface coating materials comprise a resorbable material such as hydroxyapatite or a calcium phosphate ceramic. Alternative glassy (amorphous) materials having a relatively rich calcium and phosphate composition may also be used, particularly wherein such materials incorporate calcium and phosphate in a ratio similar to natural bone or hydroxyapatite. Such glassy compositions may comprise a partially or fully amorphous osteoinductive material comprising a composite of a glass and osteoinductive calcium compound, with a composition varying from about 100% glass to 100% osteoinductive calcium compound. The surface coating may also comprise autologous bone marrow aspirates.

[0037] The resultant bone graft 10 thus comprises the substrate block formed from the high strength ceramic material having bio-mimetic properties and which is non-resorbable, or slowly or infinitely slowly resorbable when implanted into the patient, in combination with the bio-active surface coating which is comparatively rapidly resorbable to promote rapid and vigorous bone ingrowth activity.

[0038] The substrate block may also advantageously be coated or impregnated with one or more selected therapeutic agents, for example, such as autologous, synthetic or stem cell derived growth factors or proteins and growth factors such as bone morphogenic protein (BMP) or a precursor thereto, which further promotes healing, fusion and growth. Alternative therapeutic agents may also include an antibiotic, or natural therapeutic agents such as bone marrow aspirates, and growth factors or progenitor cells such as mesenchymal stem cells, hematopoietic cells, or embryonic stem cells, either alone or as a combination of different beneficial agents.

[0039] More particularly, such therapeutic agent or agents can be applied to the bone graft 10 substantially at the time of or in the course of an implant surgical procedure, as by soaking the bone graft in the therapeutic agent or a liquid-based solution containing the therapeutic agent and then implanting the bone graft into the patient. In an alternative procedure, progenitor cells or the like can be taken from a specific patient and then cultured in vitro using the bone graft as a culture medium and substrate to produce a high and therapeutically effective concentration of the selected cells carried on and within the bone graft. Thereafter, the bone graft carrying the cultured cells can be surgically implanted. In one convenient configuration, the bone graft implant can be formed in the size and shape of a small pellet for suitable packing of multiple implants into a bone regeneration/ingrowth site.

[0040] The resultant bone graft such as the illustrative spinal fusion cage 10 exhibits relatively high bio-mechanical strength similar to the load bearing characteristics of natural bone. In addition, the spinal fusion cage 10 exhibits relatively strong osteoconductive and osteoinductive characteristics attributable primarily to the surface coating, again similar to natural bone. Importantly, the fusion cage 10 is also substantially radiolucent, so that the fusion cage does not interfere with post-operative radiological analysis of interbody bone ingrowth and fusion.

[0041] FIG. 2 illustrates the spinal fusion cage 10 with the bone graft material 26 carried within the laterally open bore 24, to achieve further enhanced bone ingrowth and fusion when the device is implanted into the inter-vertebral space. The insertion tool 22 includes a threaded tip 28 at a forward or nose end thereof for threaded engagement into the threaded socket 20 at the posterior end of the fusion cage 10. A locking abutment 30 is also provided at the forward end of the insertion tool 22 for seated engagement into the shallow notch 18 on the fusion cage. Thus assembled, the insertion tool 22 is used by a surgeon as viewed in FIG. 3 to seat the spinal fusion cage 10 into the space between a selected adjacent pair of vertebrae 12, with the fusion cage bearing against a substantial portion of the end plates of the two vertebrae on opposite sides of the inter-vertebral space. This insertion process may be accompanied by appropriate rotation of the insertion tool 22 so that the abutment 30 thereon rotatably drives the fusion cage 10 to the desired and securely seated implanted position. Then, the abutment 30 can be retracted from the fusion cage 10 followed by back-rotation of the threaded tip 28 for release from the fusion cage.

[0042] FIGS. 4-6 illustrate alternative configurations for improved bone grafts such as spinal fusion cages constructed in accordance with the present invention, it

being recognized and understood that the bone graft can be constructed in a wide range of different geometric sizes and shapes. FIG. 4 shows a spinal fusion cage 110 having a generally cylindrical shape similar to the fusion cage 10 shown and described in FIGS. 1-3, but wherein the external screw thread 14 is omitted. As shown, the spinal fusion cage 110 (FIG. 4) has an open-celled structure defined by a high strength porous ceramic substrate block (as previously described) coated with the bio-active surface coating material, but wherein the cylindrical exterior surface is defined by the relatively rough open-lattice substrate structure having sufficient surface discontinuity and high surface area for optimized contact with cancellous bone to achieve substantially optimized bone ingrowth. FIG. 5 shows another alternative spinal fusion cage 210 comprising a surface-coated high strength porous ceramic substrate block (formed as previously described) with a generally rectangular block configuration to include at least one exterior surface to include a plurality of serrations 214 for securely mechanical locking with adjacent patient bones such as adjacent vertebrae 12 at opposite sides of the inter-vertebral space. FIG. 6 depicts an alternative rectangular block-shaped spinal fusion cage 310 comprising another surface-coated high strength porous ceramic substrate block (formed as previously described) having a narrower cross sectional dimension and an exterior surface defined by the relatively rough-textured open-lattice substrate (similar to FIG. 4). Each of the embodiments depicted in FIGS. 1-3 and FIGS. 4-6 has a height dimension and may be tapered or lordotic in shape (as shown in FIG. 6) for enhanced anatomical fit, for example, into the inter-vertebral space or the like.

[0043] FIGS. 7-10 depict further alternative preferred forms of the invention, wherein the porosity gradient within the high strength porous ceramic substrate block is controllably varied to provide desirable load bearing benefits consistent with bone ingrowth and fusion. More particularly, FIGS. 7-8 show a generally rectangular bone graft such as a spinal fusion cage 410 having a tapered height dimension in the anterior-posterior direction. The substrate block is formed with the first region 40 of relatively low porosity substantially mimicking cortical bone to extend across the anterior and posterior faces and further to include at least one interconnecting load bearing strut 42 shown in the illustrative drawings to extend centrally in an anterior-posterior direction within the body of the substrate block. The remainder of the substrate block comprises the second portion 44 of relatively high porosity substantially mimicking cancellous bone. The harder first region 40 including the central strut 42 beneficially provides a hard and strong load bearing structure capable of withstanding impaction and insertion forces in the anterior-posterior direction without damage to the implant, while the softer second region 44 presents an exposed and large surface area for substantially optimized interknitting ingrowth and fusion with adjacent patient bone. In a spinal fusion cage application, the medial-lateral faces of the implant are advantageously defined by the softer second region 44, wherein these regions are thus exposed to traditional medial-lateral X-ray imaging for post-operative radiological analysis of the implant/bone interface. Persons skilled in the art will recognize and appreciate that alternative configurations for the load bearing strut or struts 42 may be used, such as an X-shaped strut configuration extending in a cranial-caudial direction, in combination with or in lieu of the exterior faces 40 and/or the anterior-posterior central strut as shown.

[0044] FIGS. 9-10 show another generally rectangular bone graft such as a spinal fusion cage 510 having the tapered height dimension in the anterior-posterior direction. The substrate block is formed with the first region 40 of relatively low porosity substantially mimicking cortical bone to extend circumferentially about the substrate block in surrounding relation to the second portion 44 of relatively high porosity substantially mimicking cancellous bone. The harder first region 40 once again beneficially provides a hard and strong load bearing structure capable of withstanding impaction and insertion forces in the anterior-posterior direction without damage to the implant, and additionally provided high strength vertical load carrying capacity. By contrast, the softer second region 44 is vertically exposed to present a large surface area for substantially optimized interknitting ingrowth and fusion with adjacent patient bone. The external corners of the substrate block may incorporate laterally open slots 46 (FIG. 9) for convenient engagement by and manipulation with a suitable surgical tool (not shown).

[0045] In both of the embodiments of FIGS. 7-10, the substrate block comprises a high strength porous ceramic as previously described, and is coated with the bio-active surface coating material, again as previously described, to enhance bone ingrowth and fusion. The substrate block may also include one or more therapeutic agents. Persons skilled in the art will recognize and appreciate that the relatively low and high porosity regions 40 and 44 shown in FIGS. 7-10 will be integrally joined by a suitable albeit relatively narrow gradient region wherein the porosity transitions therebetween.

[0046] The improved bone graft such as the illustrative spinal fusion cage of the present invention thus comprises an open-celled substrate block structure which is coated with a bio-active surface coating, and has the strength required for the weight bearing capacity required of a fusion device. The capability of being infused with the appropriate biologic coating agent imparts desirable osteoconductive and osteoinductive properties to the device for enhanced interbody bone ingrowth and fusion, without detracting from essential load bearing characteristics. The radiolucent characteristics of the improved device beneficially accommodate post-operative radiological examination to monitor the bone ingrowth and fusion progress, substantially without undesirable radio-shadowing attributable to the fusion cage. The external serrations or threads formed on the fusion cage may have

a variable depth to enable the base of the device to contact the cortical bone for optimal weight bearing capacity. In addition to these benefits, the present invention is easy to manufacture in a cost competitive manner. The invention thus provides a substantial improvement in addressing clinical problems indicated for medical treatment of degenerative disc disease, discogenic low back pain and spondylolisthesis.

[0047] The bone graft of the present invention provides at least the following benefits over the prior art:

[a] a porous osteoconductive scaffold for enhanced fusion rates;
[b] a bio-mimetic load bearing superstructure providing appropriate stress transmission without fatigue failure;
[c] a pore structure and size suitable for ingrowth and vascularization,
[d] the ability to absorb and retain an osteoinductive agent such as autologous bone marrow aspirate or BMPs;
[e] bio-inert and bio-compatible with adjacent tissue and selected for ease of resorption;
[f] fabricatable and machinable into various shapes;
[g] sterilizable; and
[h] low manufacturing cost. A variety of further modifications and improvements in and to the spinal fusion cage of the present invention will be apparent to those persons skilled in the art. Accordingly, no limitation on the invention is intended by way of the foregoing description and accompanying drawings, except as set forth in the appended claims.

Claims

1. A bone graft, comprising:

   a ceramic substrate block comprising a first, lower porosity region (40) and a second, higher porosity region (44), wherein said second, higher porosity region is configured to facilitate bone ingrowth and fusion attachment with adjacent patient bone.

   characterised in that said ceramic substrate block (410) is formed from a material with a flexural strength greater than about 500 mega-Pascals, and a fracture toughness greater than about 5 mega-Pascal root meter..

2. The bone graft of claim 1, wherein said first region (40) has a porosity of less than about 5%.

3. The bone graft of claim 1 or claim 2, wherein said second region (44) has a porosity ranging from about 30% to about 80%.

4. The bone graft of any of claims 1-3, wherein said second region has a porosity of greater than about 40%.

5. The bone graft of any of claims 1-4, wherein the pore sizes range from about 5 microns to about 1,500 microns.

6. The bone graft of any of claims 1-5, wherein the pores formed within said substrate block are in substantially open fluid communication sufficient to transmit fluid pressure therebetween.

7. The bone graft of any of claims 1-6, wherein said first region (40) is generally disposed on anterior and posterior surfaces of said substrate block (410) and further defines at least once structural load bearing strut (42) extending through said substrate block between said anterior and posterior surfaces.

8. The bone graft of any of claims 1-7, wherein said first region (40) circumferentially surrounds and supports said second region (44).

9. The bone graft of any of the preceding claims further comprising a surface coating applied to said substrate block, said surface coating having osteoconductive and osteoinductive properties to promote bone ingrowth and fusion attachment with adjacent patient bone.

10. The bone graft of any of the preceding claims, wherein said porous ceramic substrate block is substantially radiolucent being visible under X-ray imaging, but having a density allowing for passage of X-rays through the ceramic material of the body under medial-lateral X-ray imaging thus facilitating post-operative assessment of bone ingrowth into the higher porosity region of the ceramic substrate block.

11. The bone graft of any of the preceding claims, wherein said substrate body has a bore (24) formed therein.

12. The bone graft of any of the preceding claims, wherein said bone graft comprises a spinal fusion cage (10) for implantation between and fusion with adjacent vertebrae.

13. The bone graft of claim 9, wherein said surface coating is internally and externally applied to said porous ceramic substrate block.

14. The bone graft of either of claims 9 or 13, wherein said surface coating is selected from hydroxyapatite and calcium compounds.

15. The bone graft of either of claims 9 or 13, wherein said surface coating comprises a partially or fully

amorphous osteoinductive material including a glass and osteoinductive calcium compound.

16. The bone graft of either of claims 9 or 13, wherein said surface coating comprises an organic coating material.

17. The bone graft of claim 16, wherein said organic coating material is selected from the group consisting of autologous bone marrow aspirates, bone morphogenic proteins, growth factors and progenitor cells, and mixture thereof.

18. The bone graft of claim 17, wherein said progenitor cells include mesenchymal stem cells, hematopoietic cells, and embryonic stem cells,

19. The bone graft of any of the proceeding claims, further including a therapeutic agent carried by said substrate bock,

20. The bone graft of claims 19, wherein said therapeutic agent comprises a natural or synthetic osteoconductive or osteoinductive agent.

Patentansprüche

1. Knochentransplantat mit:

einem keramischen Substratblock mit einem ersten niedrigen Porositätsbereich (40) und einem zweiten höheren Porositätsbereich (44), bei dem der zweite höhere Porositätsbereich dazu ausgebildet ist, den Knocheneinwuchs und die Verschmelzungsbefestigung mit einem benachbarten Knochen des Patienten zu vereinfachen,

dadurch gekennzeichnet, dass der keramische Substratblock (410) aus einem Material mit einer Biegefestigkeit größer als ungefähr 500 MPa und einer Bruchzähigkeit größer als ungefähr 5 MPa $\sqrt{m}$ gebildet ist.

2. Knochentransplantat nach Anspruch 1, bei dem der erste Bereich (40) eine Porosität von weniger als ungefähr 5 % aufweist.

3. Knochentransplantat nach Anspruch 1 oder Anspruch 2, bei dem der zweite Bereich (44) eine Porosität aufweist, die sich von ungefähr 30 % bis ungefähr 80 % erstreckt.

4. ochentransplantat nach einem der Ansprüche 1 bis 3, bei dem der zweite Bereich eine Porosität von größer als ungefähr 40 % aufweist.

5. Knochentransplantat nach einem der Ansprüche 1 bis 4, bei dem sich die Porengrößen von ungefähr 5 µm bis ungefähr 1500 µm erstrecken.

6. ochentransplantat nach einem der Ansprüche 1 bis 5, bei dem die innerhalb des Substratblocks gebildeten Poren in einer im Wesentlichen offenen Fluidverbindung sind, die eine Übertragung von Fluiddruck dazwischen ausreichend ist.

7. Knochentransplantat nach einem der Ansprüche 1 bis 6, bei dem der erste Bereich (40) im Allgemeinen Vorder- und Hinterflächen des Substratblocks (410) angeordnet ist und ferner wenigstens eine strukturelle Belastungsstrebe (42) definiert, die sich durch den Substratblock zwischen der Vorder- und Hinterfläche erstreckt.

8. Knochentransplantat nach einem der Ansprüche 1 bis 7, bei dem der erste Bereich (40) den zweiten Bereich (44) umlaufend umgibt und abstützt.

9. Knochentransplantat nach einem der vorangehenden Ansprüche, ferner mit einer auf dem Substratblock aufgebrachten Oberflächenbeschichtung, wobei die Oberflächenbeschichtung osteokonduktive und osteoinduktive Eigenschaften zum Fördern des Knocheneinwuchses und der Verschmelzungsbefestigung mit einem benachbarten Knochen des Patienten aufweist.

10. Knochentransplantat nach einem der vorangehenden Ansprüche, bei dem der poröse keramische Substratblock im Wesentlichen strahlungsdurchlässig und sichtbar unter Röntgenbildgebung ist, aber eine Dichte aufweist, die das Durchgelangen der Röntgenstrahlen durch das keramische Material des Körpers unter edial-lateraler Röntgenbildgebung ermöglicht und deshalb eine postoperative Bewertung des Knocheneinwuchses in den höheren Porositätsbereich des keramischen Substratblocks vereinfacht.

11. ochentransplantat nach einem der vorangehenden Ansprüche, bei dem der Substratkörper eine darin gebildete Bohrung (24) aufweist.

12. Knochentransplantat nach einem der vorangehenden Ansprüche, bei dem das Knochentransplantat einen Wirbelkörperkäfig (10) zum Einpflanzen zwischen und Verschmelzung mit benachbarten Wirbeln aufweist.

13. Knochentransplantat nach Anspruch 9, bei dem die Oberflächenbeschichtung intern und extern auf den porösen, keramischen Substratblock aufgebracht ist.

14. Knochentransplantat nach Anspruch 9 oder 13, bei dem die Oberflächenbeschichtung aus Hydroxyapatit- und Kalziumverbindungen ausgewählt ist.

15. Knochentransplantat nach Anspruch 9 oder 13, wobei die Oberflächenbeschichtung ein teilweises oder vollständig amorphes osteoinduktives Material aufweist, das eine glas- und osteoinduktive Kalziumverbindung aufweist.

16. Knochentransplantat nach Anspruch 9 oder 13, bei dem die Oberflächenbeschichtung ein organisches Beschichtungsmaterial aufweist.

17. Knochentransplantat nach Anspruch 16, bei dem das organisches Beschichtungsmaterial aus der Gruppe auswählt ist, die aus autologen Knochenmarkaspiraten, knochenmorphogenen Proteinen, Wachstumsfaktoren und Vorläuferzellen und Gemischen von diesen besteht.

18. Knochentransplantat nach Anspruch 17, bei dem die Vorläuferzellen mesenchymale Stammzellen, hämatopoetische Zellen und embryonische Stammzellen enthalten.

19. Knochentransplantat nach einem der vorhergehenden Ansprüche, ferner mit einem von dem Substratblock getragenen Therapeutikum.

20. Knochentransplantat nach Anspruch 19, bei dem das Therapeutikum ein natürliches oder synthetisches osteokonduktives oder osteoinduktives Mittel aufweist.

Revendications

1. Greffon osseux comprenant :

   un bloc de substrat en céramique comprenant une première région de moindre porosité (40) et une deuxième région de plus forte porosité (44), ladite deuxième région de plus forte porosité étant configurée de manière à faciliter la croissance d'os et l'attachement par fusion à un os adjacent du patient,

   caractérisé en ce que ledit bloc de substrat en céramique (410) est formé d'un matériau présentant une résistance à la flexion supérieure à environ 500 MPa, et une ténacité à la rupture supérieure à environ 5 $MPa \cdot m^{1/2}$.

2. Greffon osseux selon la revendication 1, dans lequel ladite première région (40) présente une porosité inférieure à environ 5 %.

3. Greffon osseux selon la revendication 1 ou 2, dans lequel ladite deuxième région (44) présente une porosité située dans la plage allant d'environ 30 % à environ 80 %.

4. Greffon osseux selon l'une quelconque des revendications 1 à 3, dans lequel ladite deuxième région présente une porosité supérieure à environ 40 %.

5. Greffon osseux selon l'une quelconque des revendications 1 à 4, dans lequel les tailles de pores sont situées dans la plage allant d'environ 5 micromètres à environ 1500 micromètres.

6. Greffon osseux selon l'une quelconque des revendications 1 à 5, dans lequel les pores formés à l'intérieur dudit bloc de substrat sont en communication de fluide sensiblement ouverte, suffisante pour transmettre la pression de fluide entre eux.

7. Greffon osseux selon l'une quelconque des revendications 1 à 6, dans lequel ladite première région (40) est globalement disposée sur les surfaces antérieure et postérieure dudit bloc de substrat (410) et en outre définit au moins un montant de support de charge structurel (42) s'étendant à travers ledit bloc de substrat entre lesdites surfaces antérieure et postérieure.

8. Greffon osseux selon l'une quelconque des revendications 1 à 7, dans lequel ladite première région (40) entoure circonférentiellement et supporte ladite deuxième région (44).

9. Greffon osseux selon l'une quelconque des revendications précédentes, comprenant en outre un revêtement de surface appliqué audit bloc de substrat, ledit revêtement de surface présentant des propriétés ostéo-conductrices et ostéo-inductives pour favoriser la croissance d'os et l'attachement par fusion à un os adjacent du patient.

10. Greffon osseux selon l'une quelconque des revendications précédentes, dans lequel ledit bloc de substrat en céramique poreux est pratiquement radiotransparent en étant visible par imagerie aux rayons X, mais présente une densité permettant le passage des rayons X à travers le matériau céramique du corps lors d'une imagerie aux rayons X médiale-latérale, en facilitant ainsi la détermination postopératoire de la croissance d'os dans la région de plus forte porosité du bloc de substrat en céramique.

11. Greffon osseux selon l'une quelconque des revendications précédentes, dans lequel ledit corps de substrat présente un trou (24) formé dans celui-ci.

12. Greffon osseux selon l'une quelconque des reven-

dications précédentes, lequel greffon osseux comprend une cage de spondylodèse (10) pour une implantation entre des vertèbres adjacentes et une fusion avec ces dernières.

13. Greffon osseux selon la revendication 9, dans lequel ledit revêtement de surface est appliqué en interne et en externe audit bloc de substrat en céramique poreux.

14. Greffon osseux selon l'une ou l'autre des revendications 9 et 13, dans lequel ledit revêtement de surface est choisi parmi l'hydroxyapatite et les composés du calcium.

15. Greffon osseux selon l'une ou l'autre des revendications 9 et 13, dans lequel ledit revêtement de surface comprend un matériau ostéo-inductif partiellement ou complètement amorphe comprenant un verre et un composé du calcium ostéo-inductif.

16. Greffon osseux selon l'une ou l'autre des revendications 9 et 13, dans lequel ledit revêtement de surface comprend un matériau de revêtement organique.

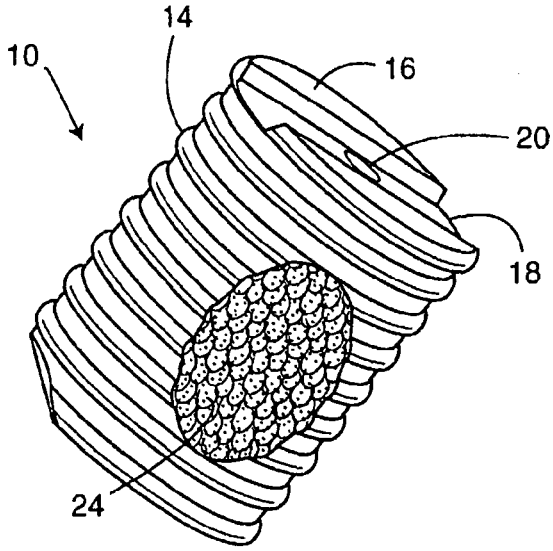
17. Greffon osseux selon la revendication 16, dans lequel ledit matériau de revêtement organique est choisi dans l'ensemble constitué par les aspirats de moelle osseuse autologues, les protéines morphogéniques osseuses, les facteurs de croissance et les cellules progénitrices, ainsi que leurs mélanges.

18. Greffon osseux selon la revendication 17, dans lequel lesdites cellules progénitrices comprennent les cellules souches mésenchymateuses, les cellules hématopoïétiques, et les cellules souches embryonnaires.

19. Greffon osseux selon l'une quelconque des revendications précédentes, comprenant en outre un agent thérapeutique supporté par ledit bloc de substrat.

20. Greffon osseux selon la revendication 19, dans lequel ledit agent thérapeutique comprend un agent ostéo-conducteur ou ostéo-inductif naturel ou synthétique.

FIG. 1



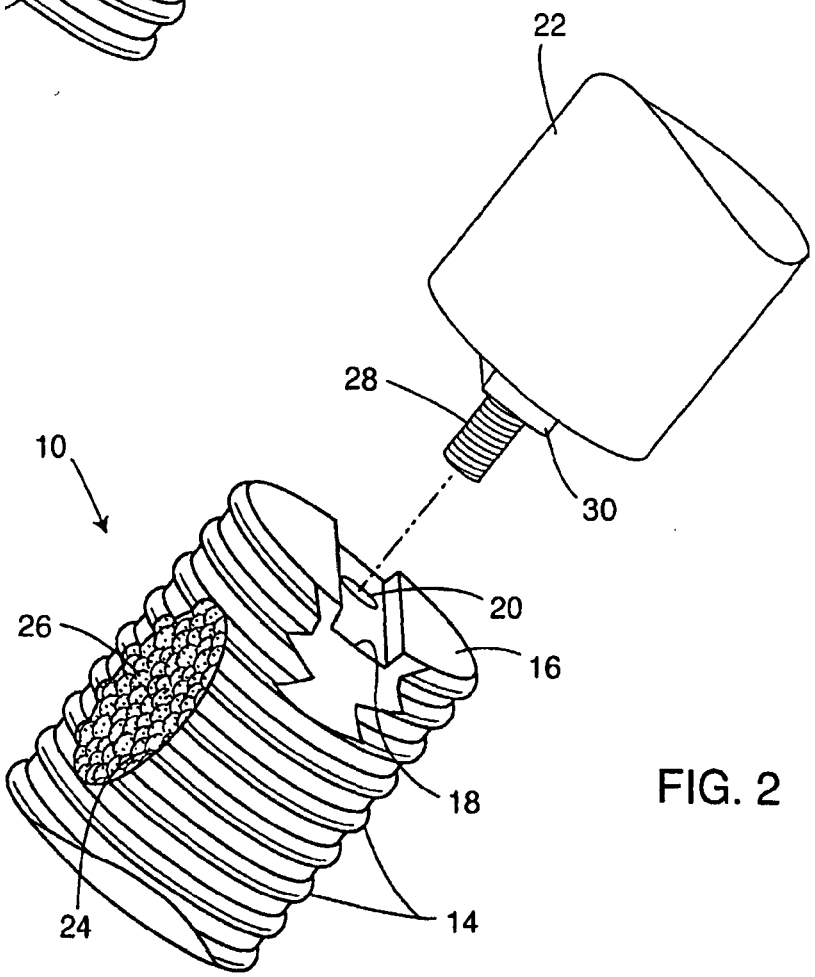


FIG. 2

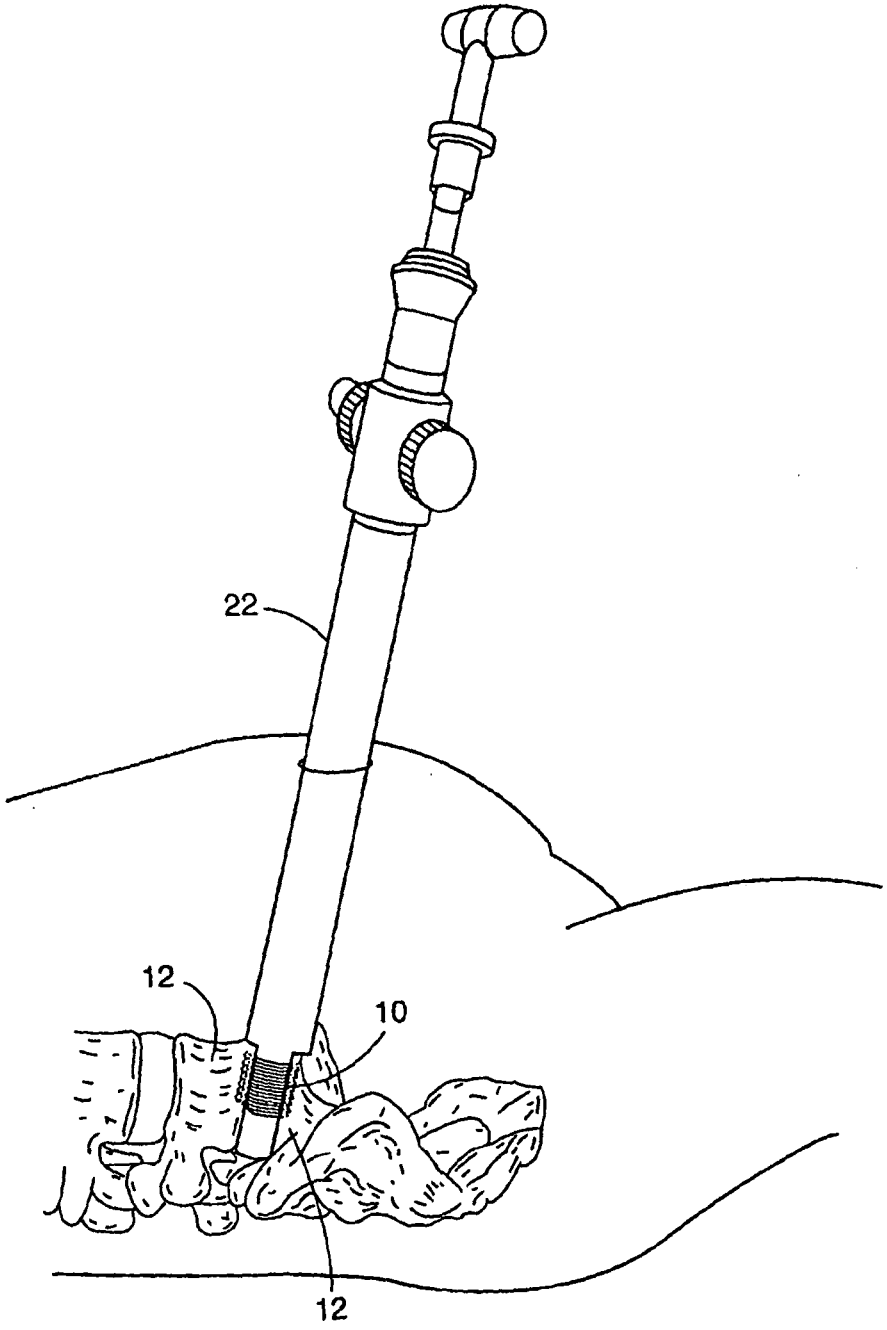
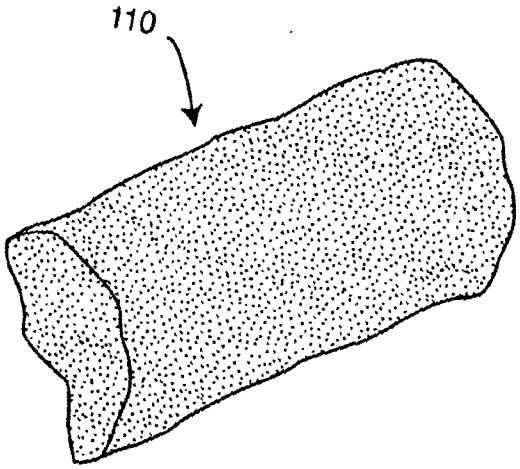


FIG. 3

FIG. 4



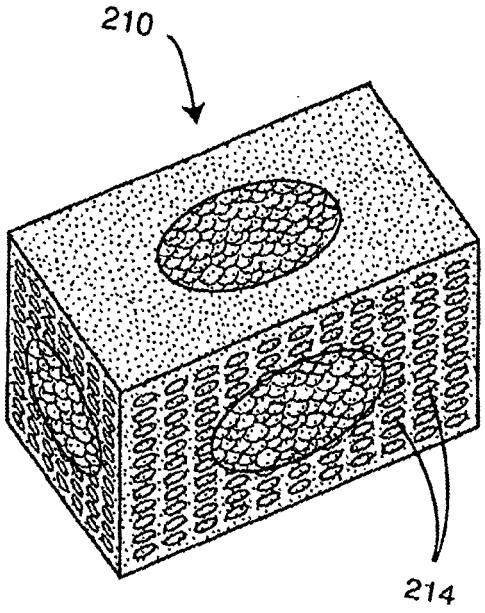


FIG. 5

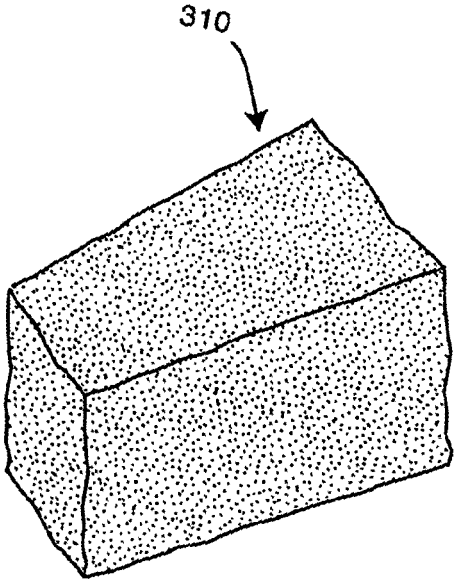


FIG. 6

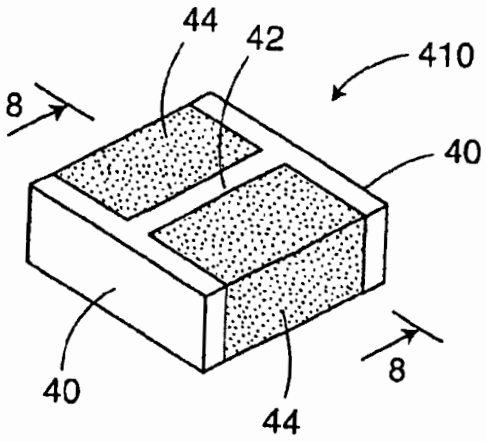


FIG. 7

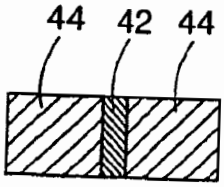


FIG. 8

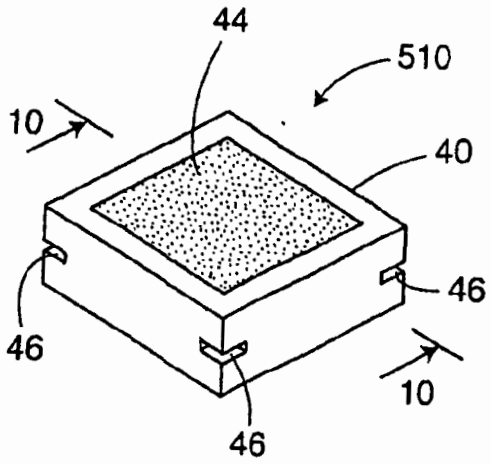


FIG. 9

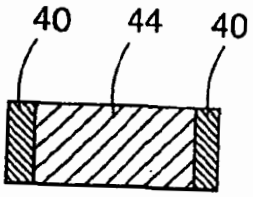


FIG. 10

REFERENCES CITED IN THE DESCRIPTION

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