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(71) Applicant: **AMEDICA CORPORATION** [US/US]; 1885 West 2100 South, Salt Lake City, Utah 84119 (US).

(72) Inventors: **MCENTIRE, Bryan J.**; 7982 English Oaks Cove, Sandy, Utah 84093 (US). **LAKSHMINARAYANAN, Ramaswamy**; 6891 Bateman Field Road, West Jordan, Utah 84084 (US). **BOCK, Ryan M.**; 914 South 1100 East, Salt Lake City, Utah 84105 (US). **DAVIS, Kevin**; 2947 W. Durham Woods Way, Riverton, Utah 84065 (US). **GRIMALDI, Dr. Nicholas**; 1647 Talon Court, Talbott, Tennessee 37877 (US).

(74) Agent: **THAYNE, Matthew D.**; 124 South 600 East, Salt Lake City, Utah 84102 (US).

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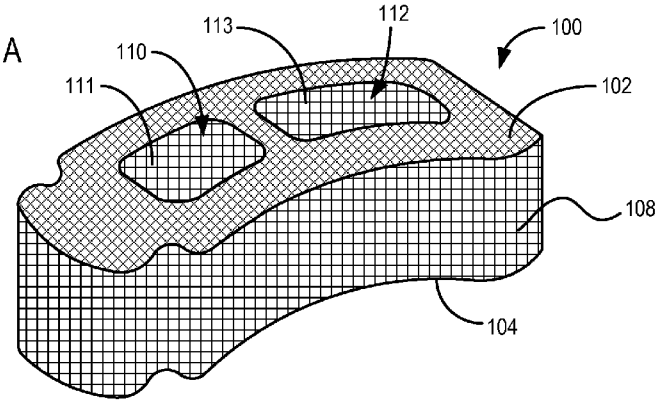
FIG. 1A



(57) Abstract: Methods for improving the antibacterial characteristics of a biomedical implant. In some implementations, the method may comprise providing a biomedical implant material block. The biomedical implant material block may comprise a silicon nitride ceramic material. The surface chemistry of the biomedical implant material block may be altered to improve the antibacterial characteristics of the biomedical implant material block. In some implementations, the surface chemistry may be altered by firing the biomedical implant material block in a nitrogen-rich environment or otherwise increasing the nitrogen content in the transitional oxide layer of at least a portion of the biomedical implant material block. The surface of the biomedical implant material block may also, or alternatively, be roughened to improve antibacterial characteristics of the implant.

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METHODS FOR ALTERING THE SURFACE CHEMISTRY OF BIOMEDICAL IMPLANTS AND RELATED APPARATUS

[0001] This application claims the benefit under 35 U.S.C. § 119(e) of U.S. Provisional Patent Application No. 61/644,906 filed May 9, 2012 and titled "ANTIBACTERIAL BIOMEDICAL IMPLANTS AND ASSOCIATED MATERIALS, APPARATUS, AND METHODS," which application is incorporated herein by reference in its entirety.

BRIEF DESCRIPTION OF THE DRAWINGS

[0002] The written disclosure herein describes illustrative embodiments that are non-limiting and non-exhaustive. Reference is made to certain of such illustrative embodiments that are depicted in the figures, in which:

[0003] FIG. 1A is a perspective view of one embodiment of a spinal implant;

[0004] FIG. 1B is a perspective view of the spinal implant of FIG. 1A after a surface roughening process has been applied to the implant;

[0005] FIG. 1C is a perspective view of the spinal implant of FIG. 1B with surface features for minimizing implant migration;

[0006] FIG. 2A is a perspective view of another embodiment of a spinal implant having a coating applied thereto;

[0007] FIG. 2B is a perspective view of the embodiment of FIG. 2A after a surface roughening process has been applied to the coating of the implant;

[0008] FIG. 3A is a perspective view of an embodiment of a hip stem

implant having a coating applied to a portion of the implant;

[0009] FIG. 3B is a perspective view of the embodiment of FIG. 3A after a surface roughening process has been applied to the coating of the implant;

[0010] FIG. 4A is a cross-sectional view taken along line 4A-4A in FIG. 3A;

[0011] FIG. 4B is a cross-sectional view taken along line 4B-4B in FIG. 3B;

[0012] FIG. 5A is a perspective view of an embodiment of a bone screw implant; and

[0013] FIG. 5B is a perspective view of the embodiment of FIG. 5A after a surface roughening process has been applied to the implant.

[0014] FIG. 6 is a flow chart depicting an example of an implementation of a method for improving the antibacterial characteristics of a biomedical implant.

DETAILED DESCRIPTION

[0015] Embodiments described herein may be best understood by reference to the drawings, wherein like parts are designated by like numerals throughout. It will be readily understood that the components of the present disclosure, as generally described and illustrated in the drawings herein, could be arranged and designed in a wide variety of different configurations. Thus, the following more detailed description of the embodiments of the apparatus is not intended to limit the scope of the disclosure, but is merely representative of possible embodiments of the disclosure. In some cases, well-known structures, materials, or

operations are not shown or described in detail.

[0016] Various embodiments of apparatus, methods, and systems are disclosed herein that relate to biomedical implants having antibacterial characteristics and materials and methods for improving the antibacterial function and/or characteristics of such implants. In preferred embodiments, silicon nitride ceramic implants are provided that may be, in some embodiments, treated so as to improve upon their antibacterial characteristics and/or other desirable characteristics. For example, embodiments and implementations disclosed herein may result in improved inhibition of bacteria adsorption and biofilm formation, improved protein adsorption, and/or enhanced osteoconductive and osteointegration characteristics. Such embodiments may comprise a silicon nitride ceramic or doped silicon nitride ceramic substrate. Alternatively, such embodiments may comprise a silicon nitride or doped silicon nitride coating on a substrate of a different material. In other embodiments, the implant and the coating may be made up of a silicon nitride material. In still other embodiments, one or more portions or regions of an implant may include a silicon nitride material and/or a silicon nitride coating, and other portions or regions may include other biomedical materials.

[0017] In alternative embodiments and implementations, the surface chemistry of silicon nitride implants, silicon nitride coated implants, or other implantable biomedical implants may be altered to improve the antibacterial characteristics of such implants. For example, in some implementations, the chemistry of the surface of a monolithic device or

coating on such a device may be modified to improve antibacterial characteristics. These methods for altering the surface chemistry may be employed as an alternative to, or in addition to, other methods described herein, such as methods for changing the surface roughness of an implant and/or applying a suitable coating to a biomedical implant. These methods for altering the surface chemistry may also be accomplished in several ways, as further described below.

[0018] As another alternative, silicon nitride or other similar ceramic materials may be incorporated into other materials used to form biomedical implants. For example, silicon nitride may be used as a filler or otherwise incorporated into polymers, such as poly-ether-ether-ketone (PEEK), poly(methyl methacrylate), poly(ethylene terephthalate), poly(dimethylsiloxane), poly(tetrafluoroethylene), polyethylene, and/or polyurethane. Silicon nitride may also be used as a filler otherwise incorporated into other materials used to form other biomedical implants, such as metals, including titanium, silver, nitinol, platinum, copper, cobalt/chromium, and related alloys, for example. As still another alternative, silicon nitride may be used as a filler or otherwise incorporated into other materials, such as ceramics and cermets.

[0019] In embodiments including one or more coatings, the coating(s) can be applied by any number of methods such as chemical vapor deposition (CVD), physical vapor deposition (PVD), plasma spraying, electro-deposition or electrophoretic deposition, slurry coating and high-temperature diffusion, or any other application method known by those skilled in the art. In some embodiments, the coating thickness can range

from between about 5 nanometers up to about 5 millimeters. In some such embodiments, the coating thickness may be between about 1 micrometer and about 125 micrometers. The coating may adhere to the surface of the implant, but need not necessarily be hermetic.

[0020] Silicon nitride ceramics have tremendous flexural strength and fracture toughness. In some embodiments, such ceramics have been found to have a flexural strength greater than about 700 Mega-Pascal (MPa). Indeed, in some embodiments, the flexural strength of such ceramics have been measured at greater than about 800 MPa, greater than about 900 MPa, or about 1,000 MPa. The fracture toughness of silicon nitride ceramics in some embodiments exceeds about 7 Mega-Pascal root meter ($MPa \cdot m^{1/2}$). Indeed, the fracture toughness of such materials in some embodiments is about 7-10 $MPa \cdot m^{1/2}$.

[0021] Examples of suitable silicon nitride materials are described in, for example, U.S. Patent No. 6,881,229, titled "Metal-Ceramic Composite Articulation," which is incorporated by reference herein. In some embodiments, dopants such as alumina (Al_2O_3), yttria (Y_2O_3), magnesium oxide (MgO), and strontium oxide (SrO), can be processed to form a doped composition of silicon nitride. In embodiments comprising a doped silicon nitride or another similar ceramic material, the dopant amount may be optimized to achieve the highest density, mechanical, and/or antibacterial properties. In further embodiments, the biocompatible ceramic may have a flexural strength greater than about 900 MPa, and a toughness greater than about 9 $MPa \cdot m^{1/2}$. Flexural strength can be measured on standard 3-point bend specimens per

American Society for Testing of Metals (ASTM) protocol method C-1161, and fracture toughness can be measured using single edge notched beam specimens per ASTM protocol method E399. In some embodiments, powders of silicon nitride may be used to form the ceramic implants, either alone or in combination with one or more of the dopants referenced above.

[0022] Other examples of suitable silicon nitride materials are described in U.S. Patent No. 7,666,229 titled "Ceramic-Ceramic Articulation Surface Implants," which is hereby incorporated by reference. Still other examples of suitable silicon nitride materials are described in U.S. Patent No. 7,695,521 titled "Hip Prosthesis with Monoblock Ceramic Acetabular Cup," which is also hereby incorporated by reference.

[0023] Silicon nitride has been discovered to have unexpected antibacterial properties and increased bone formation properties. Indeed, as discussed in greater detail below, it has been recently demonstrated that the adhesion and growth of bacteria on silicon nitride materials is substantially reduced with respect to other common spinal implant materials, such as titanium and poly-ether-ether-ketone (PEEK). As discussed in greater detail below, compared to medical grade titanium and PEEK, silicon nitride significantly inhibits *in vitro* and *in vivo* bacteria colonization, and bio-film formation. Silicon nitride also exhibits a much lower live count and live to dead ratio for bacteria during studies.

[0024] It has also been demonstrated that silicon nitride materials provide significantly greater adsorption of vitronectin and fibronectin, which proteins are known to decrease bacteria function, than titanium

and PEEK. It is thought that these properties will be very useful in biomedical implants of all types by significantly reducing the possibility of infection. This may be accomplished by, for example, preventing or disrupting bacterial formation on/in the implant and/or killing bacteria that have been transferred to the implant.

[0025] Without being limited by theory, it is thought that the higher adsorption of proteins that characterizes silicon nitride may facilitate the inhibition of bacteria growth and promote stem cell differentiation to osteoblasts. This preferential adsorption may be a cause for silicon nitride's ability to decrease bacteria function. Again, without being limited by theory, the mechanisms for the enhanced antibacterial characteristics of silicon nitride may be a combination of its features. For example, its hydrophilic surface may lead to preferential adsorption of proteins that are responsible for reduced bacteria function. This effect may be enhanced by increasing the surface texture or roughness of a silicon nitride based implant or silicon nitride based coating on an implant made up of a different material. Because of these characteristics, silicon nitride also exhibits enhanced *in vivo* osteoconduction and osteointegration when compared with titanium or PEEK.

[0026] As discussed above, using a silicon nitride coating on one or more regions of an implant's surface may be used, in some embodiments and implementations, to inhibit bacterial adhesion, while increasing/fostering adsorption of proteins necessary for healing and bone reformation. This same effect may, in other embodiments, be accomplished using monolithic silicon nitride as an implant.

[0027] In such embodiments, the surface of the ceramic implant may be engineered to provide for an increased degree of micro-roughness and surface texture to enhance these desirable properties. For example, in some embodiments, the micro-roughness—i.e., the texture of the surface in between the peaks and valleys typically measured by Ra values—may also, or alternatively, be increased by suitable texturing. In some implementations, the micro-roughness of the implant and/or coating may be increased by micromachining, grinding, polishing, laser etching or texturing, sand- or other abrasive-blasting, chemical, thermal or plasma etching, and the like. Micro-roughness may be measured by measuring the height of surface asperities using cut-off limits on a profilometer. This method may be used to selectively assess the roughness of a surface between the peaks and valleys. Alternatively, or additionally, the skewness and/or kurtosis could be measured. These measurements consider the deviation of the surface from what might be expected of a normal Gaussian distribution of surface roughness. Such surface engineering may also be performed on a silicon nitride coating, rather than on a monolithic silicon nitride or silicon nitride composite implant.

[0028] In some embodiments, the density of the silicon nitride material, or doped silicon nitride material, may vary throughout the implant, or throughout the portion of the implant made up of silicon nitride. For example, in spinal implant embodiments, the outermost layer, or a portion of the outermost layer, may be more porous, or less dense, than the core or center of the implant. This may allow for bone to

grow into or otherwise fuse with a less dense portion of the implant, and the denser portion of the implant can be wear-resistant, and may have a higher strength and/or toughness, for example.

[0029] In certain embodiments, one or more inner portions of the implant may have a relatively low porosity ceramic, and thus exhibit high density and high structural integrity generally consistent with, and generally mimicking the characteristics of, natural cortical bone. And, by contrast, one or more of the surface coatings, layers, or linings formed at an outer surface of the implant can exhibit a comparatively greater or higher porosity that is generally consistent with and generally mimics the characteristics of natural cancellous bone. As a result, the higher porosity surface region(s), coating(s), or lining(s) can provide an effective bone ingrowth surface for achieving secure and stable bone ingrowth affixation of the ceramic portion of the implant (which, in some embodiments, comprises the entire implant) between a patient's vertebrae or another suitable location within the human body.

[0030] In some embodiments, the antibacterial behavior of other implant materials, such as polymeric, metallic, or ceramics, may be improved through the application of silicon nitride as an adherent coating. This coating may, in some implementations, be roughened or textured to provide for increased surface area of the silicon nitride material/coating. In other embodiments, monolithic silicon nitride implantable devices may be provided which may be subjected to similar surface engineering.

[0031] The surface roughness values disclosed herein may be calculated using the arithmetic average of the roughness profile (Ra).

Polished silicon nitride surfaces may have a roughness of 20 nm Ra or less. However, as discussed in greater detail below, counterintuitively, the antibacterial properties of certain embodiments may be improved by roughening, rather than polishing, all or one or more portions of the surface of a silicon nitride ceramic or another similar ceramic implant. In some embodiments, a relatively rough surface may be created as part of the process of creating the material, such as during a firing stage, without further roughening or other surface engineering. However, in other embodiments, as discussed in greater detail below, the surface may be roughened to further increase the roughness beyond what would occur as a result of standard firing/curing alone. Thus, in some embodiments, the surface roughness may be greater than about 1,250 nm Ra. In some such embodiments, the surface roughness may be greater than about 1,500 nm Ra. In some such embodiments, the surface roughness may be greater than about 2,000 nm Ra. In some such embodiments, the surface roughness may be greater than about 3,000 nm Ra. In other embodiments, the surface roughness may be between about 500 nm Ra and about 5,000 nm Ra. In some such embodiments, the surface roughness may be between about 1,500 nm Ra and about 5,000 nm Ra. In some such embodiments, the surface roughness may be between about 2,000 nm Ra and about 5,000 nm Ra. In some such embodiments, the surface roughness may be between about 3,000 nm Ra and about 5,000 nm Ra.

[0032] In some embodiments, metallic, polymeric, or ceramic substrates may be pre-engineered with a surface texture onto which a

silicon nitride coating may be applied. This texture can range from as low as about 5 nanometers up to about 5,000 nanometers or more in average surface roughness (Ra). Alternatively, as another embodiment, the surface texture of the silicon nitride coating itself can be increased, exclusive of the surface roughness of the substrate, to obtain a similar Ra range and resulting antibacterial effect. Some of the methods disclosed herein may therefore provide for engineering of the surface roughness of monolithic silicon nitride ceramic implants in order to improve their antibacterial performance, and other methods disclosed herein may provide for engineering the surface roughness of layers or coatings applied to substrates made up of any other suitable material available for use in biomedical implants. Of course, in some implementations, surface engineering may be applied to both the substrate and the coating.

[0033] Increasing the surface roughness of the ceramic can be accomplished using any number of known methods by those skilled in the art, including micromachining, grinding, polishing, laser etching or texturing, sand or other abrasive blasting, chemical etching, thermal etching, plasma etching, and the like.

[0034] The inventive techniques disclosed herein, including but not limited to the silicon nitride coatings and roughened surface finishes, may be applied to any number and type of biomedical components including, without limitation, spinal cages, orthopedic screws, plates, wires, and other fixation devices, articulation devices in the spine, hip, knee, shoulder, ankle and phalanges, catheters, artificial blood vessels and

shunts, implants for facial or other reconstructive plastic surgery, middle ear implants, dental devices, and the like.

[0035] As illustrated in the Examples presented below, in comparison with titanium and poly-ether-ether-ketone (PEEK), silicon nitride significantly inhibits *in vitro* and *in vivo* bio-film formation and bacterial colonization, and shows much lower bacteria live/dead ratios for bacteria, including but not limited to *Staphylococcus epidermidis* (*Staph. Epi.*), *Staphylococcus aureus* (*Staph. aureus*), *Enterococcus*, *Pseudomonas aeruginosa* (*Pseudo. aeruginosa*), and *Escherichia Coli* (E. Coli). Silicon nitride also demonstrates significantly higher *in vitro* adsorption of three proteins (Fibronectin, Vitronectin, and Laminin) which can displace or inhibit bacteria growth and promote stem cell differentiation to osteoblasts.

[0036] In a clinical setting, bacteria are an ever present menace, particularly when associated with surgical intervention and the introduction of foreign material into the human body, such as orthopedic, cardiac or dental endoprostheses. Microorganisms introduced during surgery tend to initially populate the sterile surfaces of implants. Bacterial adhesion to the biomaterial surface is the essential step in the development of an infection. The human body's defensive mechanisms are triggered if the implant is excessively colonized by bacteria. Chronic infections arise when the bacterial colony reaches a critical size and overcomes the local host defenses. When this occurs, the body tends to encapsulate the infection and reject the implant. Consequently, patients typically must undergo re-operation, removal of the implant, treatment of

the infection, and replacement of the implant. Deep wound infections associated with common orthopedic surgeries can be as high as 4% and cost up to $100,000 or more for corrective treatment. The reduction in quality of life and the associated cost of treating infections represents a significant burden for present day medical care.

[0037] Various embodiments and implementations disclosed herein will therefore provide materials and methods that resist bacterial adhesion, colonization, and growth, which, as discussed above, often lead to chronic infections. The embodiments and implementations disclosed herein may also provide for enhanced *in vivo* osteointegration and increased bone growth in comparison to other common implants, such as those made up of titanium and PEEK.

[0038] Factors influencing bacteria adhesion to biomaterial surfaces may include chemical composition, surface charge, hydrophobicity, and surface roughness or physical characteristics of the surface and/or coating of an implant. There are marked differences in the surface chemistry of metallic, polymeric, and ceramic implants. Metals typically have a thin protective oxide layer on their surfaces (typically less than about 25 nm in thickness). Polymers may also have oxide surfaces, but the oxides are typically part of longer chain carboxyl or hydroxyl groups. Both metallic and polymeric surfaces are often low in hardness, and therefore are easily abraded and highly sensitive to chemical attack and dissolution. Ceramics, such as silicon nitride ceramics, may also have oxide surfaces. However, unlike their metal counterparts, they are highly resistant to chemical and abrasive action.

[0039] Metallic and polymeric devices are also typically hydrophobic. Consequently, bacteria do not have to displace aqueous bodily fluids in order to adhere to the implant's surface. By contrast, ceramics, and silicon nitride in particular, are known to be hydrophilic. For instance, sessile water drop studies demonstrate that silicon nitride has higher wettability than either medical grade titanium or PEEK. This higher wettability is thought to be directly attributable to the hydrophilic surface of silicon nitride based ceramics.

[0040] In order for bacteria to adhere to a hydrophilic surface, it must first displace the water that is present on the surface. Therefore, hydrophilic surfaces typically inhibit bacterial adhesion more effectively than do hydrophobic surfaces. It has also been shown that implant surface finish and texture play important roles in bacteria colonization and growth. Irregularities on the surface of typical polymeric or metallic implants tend to promote bacterial adhesion, whereas smooth surfaces tend to inhibit attachment and bio-film formation. This is true because rough surfaces have greater surface area and include depressions that provide favorable sites for colonization.

[0041] Counterintuitively, however, certain ceramic materials, including in particular silicon nitride-based ceramic materials, have been demonstrated to not only provide desirable antibacterial properties, but have also been demonstrated to provide further enhanced antibacterial properties with increased, rather than decreased, surface roughness. In other words, silicon nitride surfaces of higher roughness appear to be more resistant to bacterial adhesion than smooth surfaces. This is

precisely the opposite of what is observed for many other implant materials, such as titanium and PEEK. As referenced above and as discussed in greater detail below, compared to medical grade titanium and PEEK, silicon nitride has been shown to significantly inhibit *in vitro* bacteria colonization and bio-film formation, and show a much lower live count and live to dead ratio for bacteria during studies. However, in studies between different types of silicon nitride, rough silicon nitride surfaces have been shown to be *more effective* in inhibiting bacterial colonization (rather than less effective as with most common implant materials) than polished silicon nitride (although both were much more effective in doing so than either titanium or PEEK).

[0042] Various embodiments and implementations will be further understood by the following Examples:

EXAMPLE 1

[0043] In a first working example, the abilities of biomedical implant materials to inhibit bacterial colonization were tested. The study included silicon nitride materials, Biomedical grade 4 titanium, and PEEK. Four types of bacteria were included in the study: *Staphylococcus epidermidis*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Escherichia coli*, and *Enterococcus*.

[0044] Implant samples in the study were sterilized by UV light exposure for 24 hours and surface roughness was characterized using scanning electron microscopy. Bacteria were then inoculated on the surfaces of the samples and incubated for 4, 24, 48, and 72 hours.

[0045] Two methods were used to determine bacteria function at the

end of each time period: (1) Crystal violet staining; and (2) Live/dead assay. Bacteria were also visually counted using a fluorescence microscope with image analysis software. The experiments were completed in triplicate and repeated three times. Appropriate statistical analyses were then completed using Student t-tests.

[0046] For all bacteria, and all incubation times, the silicon nitride samples demonstrated lower bio-film formation, fewer live bacteria, and smaller live to dead bacteria ratios when compared with medical grade titanium and PEEK. Rough silicon nitride surfaces were even more effective in inhibiting bacterial colonization than polished surfaces. In addition, silicon nitride implants with polished or rough surfaces were both significantly better in inhibition of bacterial colonization than either titanium or PEEK.

[0047] Bio-film formation was also much higher for titanium and PEEK than for silicon nitride. For example, bio-film formation for *Staphylococcus aureus* on titanium was three times higher than polished silicon nitride after 72 hours of incubation and more than eight times higher than PEEK after 72 hours of incubation. And the results were even better using relatively rough silicon nitride having a surface roughness of about 1,250 nm Ra. Bio-film formation for *Staphylococcus aureus* on this rougher silicon nitride was less than half of that for the polished silicon nitride after 72 hours.

[0048] Live bacteria counts followed similar patterns. Live bacteria counts after 72 hours of incubation were between 1.5x and 30x higher for titanium and PEEK when compared with silicon nitride. And, again,

rough silicon nitride outperformed polished silicon nitride. For example, for *Pseudomonas aeruginosa*, live bacteria count after 72 hours for rough silicon nitride (again, about 1,250 nm Ra) was about one-fifth of that for polished silicon nitride.

[0049] Live/dead bacteria ratios were similarly lowest for silicon nitride, and generally lower for rough silicon nitride than for polished silicon nitride. For example, live/dead ratios after 72 hours of incubation for *E. coli* on polished silicon nitride were over three times as high as titanium and about twice as high as PEEK. For rough silicon nitride, live/dead ratios were about six times as high for titanium and nearly three times as high for PEEK.

Example 2

[0050] In this study, the ability of biomedical implant materials to adsorb common bone-forming proteins was tested. As with Example 1, rough silicon nitride, polished silicon nitride, medical grade titanium, and PEEK were tested. The proteins tested were fibronectin, vitronectin, and laminin. Enzyme-linked immunosorbent assays (ELISA) were performed for 20 minutes, 1 hour, and 4 hours. Fibronectin, vitronectin, or laminin were directly linked with primary rabbit anti-bovine fibronectin, anti-vitronectin, and anti-laminin, respectively. The amount of each protein adsorbed to the surfaces was measured with an ABTS substrate kit. Light absorbance at 405 nm on a spectro-photometer was analyzed with computer software. ELISA was performed in duplicate and repeated

three different times per substrate.

[0051] For all incubation times, silicon nitride exhibited significantly greater adsorption of fibronectin and vitronectin when compared with titanium and PEEK. Silicon nitride also showed greater adsorption of laminin at 1 and 4 hours incubation in comparison to titanium and PEEK. Rough silicon nitride surfaces (approximately 1,250 nm Ra) were more effective in adsorption of proteins than polished silicon nitride surfaces. However, both silicon nitride surfaces were generally better than either titanium or PEEK, particularly for fibronectin and vitronectin. Without being limited by theory, it is thought that preferred adsorption of these proteins onto silicon nitride is a probable explanation for its improved bacterial resistance.

Example 3

[0052] In this study, *in vivo* bone formation, inflammation, and infection of various implant materials were studied using a Wistar rat calvaria model. The study considered the strength of bone attachment to these materials. Rough silicon nitride, medical grade titanium, and PEEK were used in the study.

[0053] The study was conducted by implanting sterilized samples into the calvaria of two-year old Wistar rats using standard techniques. Another group of samples was inoculated *apriori* with *Staphylococcus epidermidis* and implanted into a second group of similar Wistar rats.

[0054] The animals were sacrificed at 3, 7, 14, and 90 days. Histology was quantified for the number of macrophages, bacteria, and bio-film proteins surrounding each of the implant materials. In addition,

push-out tests were performed to determine bone attachment results and performance.

[0055] After 3 days using the non-inoculated samples, the titanium and PEEK implants were unstable, and thus no histology was able to be performed. The silicon nitride implants (surface roughness of approximately 1,250 nm Ra) exhibited about 3-5% bone-implant interface, as measured using microscopic linear analysis, and about 16-19% new bone growth in the surgical area, as measured using microscopic areal analysis, after 3 days.

[0056] After 7 days using the non-inoculated samples, the titanium and PEEK implants were unstable, and thus no histology was able to be performed. The silicon nitride implants, by contrast, exhibited about 19-21% bone-implant interface and about 28-32% new bone growth in the surgical area after 7 days.

[0057] After 14 days using the non-inoculated samples, the titanium implant exhibited about 7% bone-implant interface and about 11% new bone growth in the surgical area. The PEEK implant exhibited about 2% bone-implant interface and about 14% new bone growth in the surgical area. The silicon nitride implants, by contrast, exhibited about 23-38% bone-implant interface and about 49-51% new bone growth in the surgical area after 14 days.

[0058] After 90 days without inoculation, the titanium and PEEK implants exhibited about 19% and 8% bone-implant interface, respectively, and about 36% and 24% new bone growth, respectively. The silicon nitride implants again performed much better. These

implants exhibited a bone-implant interface of about 52-65% and new bone growth of about 66-71%.

[0059] With the inoculated samples, all implants were too unstable to perform histology at 3 and 7 days. After 14 days, the titanium implant exhibited only about 1% bone-implant interface, 75% bacteria-implant interface (measured using microscopic linear analysis), about 9% new bone growth in the surgical area, and about 45% bacterial growth in the surgical area. PEEK exhibited essentially no bone-implant interface, about 2% new bone growth, and about 25% bacterial growth. The bacteria-implant interface with PEEK was unclear. The inoculated silicon nitride implants exhibited a bone-implant interface of about 3-13% after 14 days. New bone growth with the silicon nitride implants was about 25-28%, and bacterial growth was about 11-15%.

[0060] After 90 days, the inoculated titanium implant exhibited about 9% bone-implant interface, about 67% bacteria-implant interface, about 26% new bone growth, and about 21% bacterial growth. The PEEK implant exhibited about 5% bone-implant interface, about 95% bacteria-implant interface, about 21% new bone growth, and about 88% bacterial growth. The inoculated silicon nitride implants exhibited a bone-implant interface of about 21-25% after 90 days. New bone growth with the silicon nitride implants was about 39-42%, and there was no measurable bacterial-implant interface or bacterial growth after 90 days. In fact, there were no bacteria detected on the silicon nitride implants after 90 days.

[0061] Push-out strengths were also substantially better with the silicon nitride implants than with either the titanium or PEEK implants

after all implantation times were measured, both with and without inoculation. After 90 days implantation without inoculation, push-out strengths for the silicon nitride implants were more than twice as high as titanium and more than two-and-a-half times as high as PEEK. With innoculation, silicon nitride push-out strengths were even better compared to titanium and PEEK for all implantation times. Silicon nitride push-out strengths were more than five times those of either titanium or PEEK. These results demonstrate substantial bone attachment for silicon nitride when compared to titanium and PEEK.

[0062] Push out strengths were measured by taking a sectioned portion of the calvaria including the implant and cementing the calvaria to wood blocks over a support plate. A load was then applied to the implant and the force required to dislodge the implant from the calvaria was measured.

[0063] The histology results further confirm the tested push-out strengths. As discussed above, significantly greater new bone growth was observed in the calvaria defect area for silicon nitride when compared with titanium and PEEK at all implantation times and under all inoculation conditions.

[0064] The results in each of the Examples discussed above suggest that, compared to medical grade titanium and PEEK, silicon nitride results in a substantially better inhibition of *in vitro* bacterial colonization and bio-film formation, and results in a much lower live to dead ratio for all studied bacteria at all incubation periods. Silicon nitride also demonstrates significantly higher *in vitro* adsorption of three proteins

which may inhibit bacteria growth and promote stem cell differentiation to osteoblasts. This preferential adsorption correlates with, and may be a causative factor in, silicon nitride's ability to decrease bacterial function. Silicon nitride also exhibits enhanced *in vivo* osteogenesis and osteointegration and demonstrates significant resistance to bacteria compared to titanium and PEEK.

[0065] The studies discussed in the Examples also tend to suggest that roughened silicon nitride implants generally outperform polished silicon nitride in terms of antibacterial function and/or bone growth and integration. These results suggest not only that monolithic silicon nitride implants and/or or other similar ceramic implants may be surface roughened in order to improve antibacterial function, but also that silicon nitride coatings may be applied to other implants (both silicon nitride and non-silicon nitride, such as metals, polymers, and/or other ceramics). Such coatings may be surface roughened to further improve antibacterial function and provide other desirable characteristics, as discussed above. Preliminary research also tends to indicate that increasing the surface roughness beyond the levels used in the Examples—i.e. about 1,250 nm Ra—may further increase the antibacterial function of the material. For example, in some such embodiments, the surface roughness may be greater than about 1,500 nm Ra. In some such embodiments, the surface roughness may be greater than about 2,000 nm Ra. In some such embodiments, the surface roughness may be greater than about 3,000 nm Ra. In other embodiments, the surface roughness may be between about 500 nm Ra and about 5,000 nm Ra. In some such

embodiments, the surface roughness may be between about 1,500 nm Ra and about 5,000 nm Ra. In some such embodiments, the surface roughness may be between about 2,000 nm Ra and about 5,000 nm Ra. In some such embodiments, the surface roughness may be between about 3,000 nm Ra and about 5,000 nm Ra.

[0066] Some alternative ceramic materials, such as alumina and zirconia (ZrO_2), for example, have certain properties that are similar to those of silicon nitride. As such, it is thought that these ceramic materials, or other similar materials, may exhibit similar antibacterial and osteogenic effects. It is thought that those of ordinary skill in the art, after having had the benefit of this disclosure, may be able to identify such alternative materials. It is also thought that these ceramic materials, or other similar materials, may exhibit improvement in antibacterial function with increased surface roughness, as is the case with silicon nitride ceramics.

[0067] Additional embodiments and implementations will be further understood by the following drawings.

[0068] Figure 1A depicts a spinal implant 100. Spinal implant 100 has relatively smooth top, bottom, and side surfaces (102, 104, and 108, respectively). Spinal implant 100 may comprise a silicon nitride ceramic material or another similar ceramic material. Spinal implant 100 also comprises two openings 110 and 112 extending through the top and bottom surfaces of the implant. In some embodiments, spinal implant 100 may comprise a doped silicon nitride material, as described in greater detail above. One or more of the surfaces of spinal implant 100

may be roughened or textured to provide for increased surface area of the silicon nitride material making up the surface(s). For example, one or more surfaces of spinal implant 100 may be roughened or textured by micromachining, grinding, laser etching or texturing, sand or other abrasive blasting, chemical etching, thermal etching, plasma etching, and the like.

[0069] Figure 1B depicts spinal implant 100 after each of the exterior surfaces 102, 104 (surface not visible in the figure), and 108 has been roughened. As explained above, this surface roughening improves the antibacterial function and characteristics of the implant. One or more interior surfaces may also be roughened. For example, interior surfaces 111 and 113 that define openings 110 and 112, respectively, may also be roughened. The extent of roughening of the interior surfaces may be identical to, greater than, or less than, the roughening of exterior surfaces 102, 104, and 108, as desired.

[0070] Figure 1C depicts spinal implant 100 having a plurality of surface features or teeth 114 on the top and bottom surfaces. Surface features 114 may help prevent or at least minimize migration of the implant once positioned within a patient's intervertebral space. Surface features 114 may be formed from the implant 100 before or after the surface roughening has taken place. Similarly, surface features 114 may, alternatively, comprise another material that is attached to the implant 100, again before or after surface roughening.

[0071] Figure 2A depicts an alternative embodiment of a spinal implant 200. Spinal implant 200 may comprise any suitable material or

materials, such as metals, polymers, and/or ceramics. Spinal implant 200 also comprises a coating 220. Coating 220 preferably comprises a silicon nitride or doped silicon nitride ceramic material, although it is contemplated that other ceramic materials having certain properties similar to silicon nitride may alternatively be used as a coating. Coating 220 may be applied to any surface exposed or potentially exposed to biological material or activity. For example, in the depicted embodiment, coating 220 is applied to top surface 202, bottom surface 204, side surface 208, and to interior surfaces 211 and 213 that define openings 210 and 212, respectively. Coating 220 may be applied to take advantage of the unique antibacterial properties and characteristics of silicon nitride discussed elsewhere herein. In some embodiments, the coating thickness can range from between about 5 nanometers up to about 5 millimeters. In some preferred embodiments, the coating thickness may be between about 1 micrometer and about 125 micrometers.

[0072] For example, because PEEK, which is very common in spinal implants, performs very poorly in a bacterial environment, silicon nitride ceramic coatings or layers (or another similar material) may be applied to a PEEK spinal implant to improve the antibacterial function of the implant and/or to provide other advantages as discussed in greater detail above. The coating(s) may be applied by any suitable methodology known to those of ordinary skill in the art, such as chemical vapor deposition (CVD), physical vapor deposition (PVD), plasma spraying, electro-deposition or electrophoretic deposition, slurry coating and/or high-

temperature diffusion.

[0073] To further enhance the antibacterial characteristics of the implant, the coating 220, or one or more portions of the coating 220, may be surface roughened, as illustrated in Figure 2B. The coating surface roughening may be applied to any and all portions of the implant that are or could be exposed to biological activity or material. For example, in the embodiment depicted in Figure 2B, each of surfaces 202, 204, 208, 211, and 213 have been roughened or textured as described above. In some embodiments, the surface of the implant may be roughened or textured before the coating is applied, either in lieu of, or in addition to surface roughening or texturing on the coating.

[0074] The principles, materials, and methods described herein may also be applied to other biomedical implants. For example, Figures 3A-3B and 4A-4B illustrate a hip implant 300 comprising a femoral stem 330 that is configured to be received within a patient's femur, a neck 340, and a modular acetabular head 350 configured to receive a ball joint (not shown) that will ultimately be positioned in an acetabular cup, or within a patient's natural acetabulum.

[0075] One or more coatings 320 may be applied to the femoral stem 330 of hip implant 300, as shown in Figure 3A. In preferred embodiments, coating 320 comprises a silicon nitride ceramic material. In alternative embodiments, other portions of the implant may also be coated with a silicon nitride ceramic or another similar material. For example, coating 320 may also be applied to femoral stem 330, neck 340, and/or modular acetabular head 350, as desired.

[0076] In order to further enhance the antibacterial properties of the implant 300, one or more surfaces/portions of the implant 300 may be roughened and/or textured. For example, as shown in Figure 3B, femoral stem 330, which comprises coating 320, may be roughened and/or textured after coating 320 has been applied. Alternatively, femoral stem 330 and/or any other desired region of implant 300 (or any of the other implants discussed herein) may be roughened and/or textured before coating 320 has been applied. As yet another alternative, one or more surfaces of the implant may be textured and/or roughened both before and after the antibacterial coating has been applied.

[0077] Figure 4A is a cross-sectional view taken along line 4A-4A in Figure 3A. As shown in this figure, coating 320 extends only along the femoral stem 330 portion of implant 300. However, as discussed above, in alternative embodiments, coating 320 may be applied to other portions of the implant as well (in some embodiments, the coating may be applied to the entire implant).

[0078] Figure 4B is a cross-sectional view taken along line 4B-4B in Figure 3B. This figure illustrates the surface of the femoral stem 330 of implant 300 after the roughening/texturing process has been completed.

[0079] Still other alternative embodiments are depicted in Figures 5A and 5B. These figures illustrate a bone screw 500. Bone screw 500 may comprise a pedicle screw, for example. Bone screw 500 comprises a spherical head 510 and a threaded shaft 520. Bone screw 500, or one or more portions of bone screw 500, may comprise a silicon nitride ceramic

material. One or more portions or surfaces of bone screw 500 may also be roughened or textured to improve antibacterial or other characteristics of the implant. For example, as shown in Figure 5B, threaded shaft 520 has been roughened. Head 510 of screw 500 may remain smooth, or may be polished smooth, to provide for desired articulation within a spinal fixation system connector. However, for other embodiments, it may be desirable to roughen the surface of head 510 as well. This may provide for not only the improved antibacterial characteristics discussed herein, but may also provide a desirable friction interface with another component of a spinal fixation system.

[0080] In other embodiments, bone screw 500, or any of the other embodiments disclosed herein, may comprise another suitable material, such as titanium. In such embodiments, a silicon nitride coating may be applied to the implant rather than forming the entire implant from a silicon nitride material. As disclosed above, the coating and/or the undersurface of the coating (i.e., the surface of the original implant itself) may be roughened or textured to further improve antibacterial and other characteristics.

[0081] In still other embodiments, bone screw 500, or any of the other embodiments disclosed herein, may comprise a biomedical material, such as a metal, ceramic, or polymer that includes a silicon nitride filler, or that otherwise incorporate a silicon nitride material into the material used to form the implant. For example, silicon nitride may be used as a filler or otherwise incorporated into polymers, such as poly-ether-ether-ketone (PEEK), poly(methylmethacrylate), poly(ethyleneterephthalate),

poly(dimethylsiloxane), poly(tetrafluoroethylene), polyethylene, and/or polyurethane. Silicon nitride may also be used as a filler otherwise incorporated into other materials used to form other biomedical implants, such as metals, including titanium, silver, nitinol, platinum, copper, and related alloys, for example. As still another alternative, silicon nitride may be used as a filler or otherwise incorporated into other materials, such as ceramics and cermets. By incorporating silicon nitride into other materials, it is expected that some of the antibacterial advantages and/or other advantageous properties described herein may be realized. Silicon nitride may also be incorporated into another materials used as part of one or more of the coatings described herein to increase antibacterial function.

[0082] In alternative embodiments and implementations, the surface chemistry of silicon nitride implants, silicon nitride coated implants, or other implantable biomedical implants may be altered to improve the antibacterial characteristics of such implants. Such methods may be employed in addition to, or in lieu of, the surface roughening and/or coating steps described above. Such methods for altering the surface chemistry of biomedical implants to improve antibacterial characteristics may be accomplished using several different implementations, as described herein.

[0083] For example, silicon nitride implants, including both monolithic silicon nitride implants and implants comprising silicon nitride coatings, often have a thin transitional oxide layer on their surface. This transitional oxide layer typically comprises a gradient wherein higher concentrations

of nitrogen are positioned near the silicon nitride grains, and higher concentrations of oxygen are positioned at relatively greater distances from the silicon nitride grains.

[0084] The overall surface charge for silicon nitride can be markedly affected by the amount of either nitrogen or oxygen which is present in this transitional oxide layer. If more nitrogen is present in the form of amine groups ($SiNH_3^+$), then the surface tends to have a positive charge. Conversely, if higher concentrations of hydroxyl groups (SiOH) are present, then the surface charge can become negative. Furthermore, the presence of amine groups (particularly quaternary amines) and a positive surface charge can prevent biofilm formation for certain types of bacteria. Therefore, the antibacterial characteristics of silicon nitride biomedical implants and other implantable devices may be improved by changing the surface chemistry and, in some implementations, the surface charge, of such implants.

[0085] To use silicon nitride implants as an example, changes in surface chemistry may result from reactions with the environment in accordance with, for example, the following chemical equations:

$$Si_3N_4 + H_2O \rightarrow Si_2NH + SiOH$$

$$Si_2NH + H_2O \rightarrow SiNH_2 + SiOH$$

[0086] Hydrogen can also be absorbed or desorbed from the surface depending upon the pH of the surrounding environment via, for example, the following reactions:

$$SiNH_2 + H^+ \rightarrow SiNH_3^+$$

$$SiOH + H^+ \rightarrow SiOH_2^+$$

$$SiOH \leftrightarrow SiO^- + H^+$$

[0087] Desirable results of one or more of these reactions on biomedical implants may be obtained, for example, by employing methods designed to increase the amount of nitrogen in the transitional oxide layer of, for example, a silicon nitride implant or an implant having a silicon nitride coating. Additionally, or alternatively, some implementations may comprise one or more chemical treatment steps.

[0088] For example, in some implementations, the implant, or at least a portion of the implant, may be cleaned in, for example, a highly caustic or acidic solution, such as hydrofluoric acid (HF). These solutions can strip the surface of its native oxide, leaving behind a nitrogen rich surface, which may be beneficial for preventing biofilm formation for at least some types of bacteria.

[0089] For example, a solution having a pH of greater than about 10 should be considered highly caustic and a solution having a pH of less than about 4 should be considered highly acidic. Examples of caustic solutions that may be used in some implementations include solutions comprising sodium hydroxide (NaOH) and/or potassium hydroxide (KOH). In some such implementations, the solution may comprise a molarity or molar concentration of sodium hydroxide and/or potassium hydroxide of at least about 1.0.

[0090] Examples of acidic solutions that may be used in some implementations include solutions comprising hydrofluoric acid, as mentioned above, as well as sulfuric acid (H_2SO_4), nitric acid (HNO_3), and hydrochloric acid (HCl). In some such implementations, the solution

may comprise a molarity or molar concentration of hydrofluoric acid, sulfuric acid, nitric acid, and/or hydrochloric acid of at least about 1.0. In some implementations, the solution, whether caustic or acidic, may be heated to further enhance the ability of the solution to remove the transitional oxide layer. In some such implementations, the solution may be heated to a boil before applying the solution to the implant/implant material.

[0091] In still other implementations, the nitrogen content of the transitional oxide surface layer may be increased by firing the implant in a high nitrogen environment. In some implementations, the implant may be fired in an environment that combines nitrogen and hydrogen, or nitrogen and carbon monoxide. In some implementations comprising a firing step in a nitrogen rich environment, a ceramic material may be fired in an environment comprising at least essentially 100% nitrogen gas. In such implementations, the environment may be at approximately atmospheric pressure and may be at temperatures above about 1500°C for extended time periods, typically greater than about 1 hour, and preferably greater than about 2 hours.

[0092] With respect to silicon nitride ceramic materials, such firing environments may result in preferential evaporation of silicon monoxide (SiO) gas from the ceramic. Since evaporation occurs at the surface of the ceramic material, this process may result in removal of this species from the transitional oxide layer, leaving behind a nitrogen enhanced layer.

[0093] In various implementations, nitrogen gas pressure can be

applied in the form of hot-isostatic pressing at temperatures of at least about 1500°C and pressures of at least about 35 MPa to further enhance removal of the transitional oxide layer. This may be performed, for example, inside a furnace comprising graphite elements and/or supports. In such implementations, there may be small amounts (ppm levels) of carbon-monoxide gas present in the equipment, which may further aid in removing the oxide layer and thereby further enhance the antibacterial properties of the resulting implant material.

[0094] In some implementations, one or more steps may be taken subsequent to firing in order to eliminate, or at least minimize, exposure of the implant to the natural environment. This may be accomplished, for example, using suitable packaging to reduce or eliminate exposure to air and/or the natural environment. In addition, or alternatively, handling steps involving nitrogen and/or nitrogen desiccation, such as, for example, use of nitrogen glove boxes. In some implementations, gas impermeable packaging may be used, into which the fired implants may be placed and sealed prior to removing them from a suitable glove box.

[0095] In still other implementations, the nitrogen content of the transitional oxide surface layer may be increased to improve antibacterial characteristics by subjecting the implant to high energy nitrogen implantation using, for example, an ion gun. In some such implementations, nitrogen ions may be sub-planted into the surface of the transitional oxide layer, thereby resulting in a significant increase in nitrogen content, particularly with respect to silicon nitride coated implants. In some implementations involving such implants, the same or

similar equipment used to deposit an adherent silicon nitride coating may also be used to increase the nitrogen content of the surface of this coating through ion implantation.

[0096] After having received the benefit of this disclosure, it will be apparent to those knowledgeable in the art that there may be numerous other ways of increasing the nitrogen content within the transitional oxide layer of a biomedical implant. Any number of such techniques may therefore be used that prove effective in improving the antibacterial characteristics of biomedical implants, including but not limited to monolithic silicon nitride implants and/or implants comprising silicon nitride coatings.

[0097] In some embodiments and implementations, the antibacterial characteristics of an implant may be further improved by adding any number of antibacterial metals, including but not limited to silver (Ag), copper (Au), selenium (Se), and the like. For example, in some implementations involving high energy ion implantation, a relatively small amount of silver or another such antibacterial metal ion may be included in the ion source used during the implantation process. In some implementations, such metal ions may comprise about 5 to about 15% atomic percent of silver and/or other such metal ions relative to all of the ions added to the transitional oxide layer of the material. The addition of such ions to the transitional oxide layer of, for example, a monolithic silicon nitride ceramic implant material block, is likely to result in further improvements to the antibacterial characteristics of the resulting implant. In some embodiments and implementations, silver and/or other such

antibacterial metal ions may be added to silicon nitride or other biomedical implant materials by ion implantation, as described elsewhere herein.

[0098] However, it should be understood that other embodiments and implementations are contemplated that are not restricted solely to silicon nitride ceramics, but may be more broadly applicable to a wide variety of other biomaterials, including metals and plastics. Such materials may also, or alternatively, be implanted with nitrogen ions into their native surface oxides to increase their nitrogen content and accompanying resistance to bacteria, as discussed above.

[0099] With respect to certain implementations and embodiments involving biomedical implants comprising silicon nitride coatings, antibacterial metals and silicon nitride may be co-deposited, either simultaneously or sequentially. In some such implementations, the deposition process may utilize a dual magnetron sputtering process and/or a combination reactive PVD deposition of silicon nitride concurrent with PVD application of silver. Again, it is expected that only a few atomic percent of an antibacterial metal may be useful for imparting significant antibacterial improvements.

[00100] Figure 6 is a flow chart depicting an example of an implementation of a method 600 for improving the antibacterial characteristics of a biomedical implant. At step 602, a biomedical implant material block is provided. In some implementations, the biomedical implant material block may comprise a finished biomedical implant, such as an intervertebral spacer or other spinal implant, orthopedic screw,

orthopedic plate, spinal articulation device, hip implant, knee implant, shoulder implant, ankle implant, shunt, stent, facial or other reconstructive plastic surgery implant, dental device, etc.

[00101] In other implementations, the biomedical implant material block may comprise an unfinished piece of material that will ultimately be shaped, machined, or otherwise formed into a suitable shape and/or configuration to serve as one of the above-referenced finished biomedical implants. In some such implementations, the unfinished piece of may require one or more additional processing steps—other than shaping and other than the steps involved in process 600—before it can be considered completed and ready for implantation. For example, in some implementations, the biomedical implant block may comprise only a part or portion of what will eventually become a finished biomedical implant.

[00102] Following step 602, one or more steps may be performed to improve the antibacterial characteristics of the biomedical implant material block. For example, in process 600, at step 604 the surface chemistry of the biomedical implant material block may be altered in order to improve the antibacterial characteristics of the biomedical implant material block. In some implementations, step 604 may comprise a step that alters the surface charge of the biomedical implant material block.

[00103] Step 604 may comprise, for example, increasing the amount of nitrogen in the transitional oxide layer of the biomedical implant material block. This may be particularly useful in connection with implementations

comprising a silicon nitride biomedical implant material block or a biomedical implant material block comprising a silicon nitride coating. In some implementations, the nitrogen content of the transitional oxide surface layer may be increased at step 604 by firing the implant in a high nitrogen environment. In some implementations, the implant may be fired in an environment that combines nitrogen and hydrogen, or nitrogen and carbon monoxide, in order to increase the amount of nitrogen in the transitional oxide layer of the biomedical implant material block.

[00104] In alternative implementations, step 604 may comprise altering the surface chemistry of the biomedical implant material block using one or more chemical treatment steps. For example, in some implementations, the biomedical implant material block, or at least a portion of the biomedical implant material block, may be cleaned in, for example, a highly caustic or highly acidic solution, such as sodium hydroxide (NaOH) or hydrofluoric acid (HF). Such solutions may be used to strip the surface of its native oxide, leaving behind a nitrogen rich surface in order to enhance the block's antibacterial characteristics.

[00105] In some implementations, one or more steps may be taken subsequent to step 604 in order to eliminate, or at least minimize, exposure of the implant to the natural environment. This may be accomplished, for example, using suitable packaging and/or handling steps involving nitrogen and/or nitrogen desiccation.

[00106] In still other implementations, step 604 may comprise increasing the nitrogen content of the transitional oxide surface layer by subjecting the biomedical implant material block to high energy nitrogen

implantation using, for example, an ion gun. In some such implementations, the high energy nitrogen implantation may be sufficient to implant nitrogen ions into the surface of the transitional oxide layer of the biomedical implant material block.

[00107] At step 606, an antibacterial metal, such as silver (Ag), may be added to the biomedical implant material block by high energy ion implantation. In some implementations, about 5 to about 15% atomic percent of silver may be added to the transitional oxide layer of the biomedical implant material block to further enhance the antibacterial characteristics of the implant. In some implementations, particularly implementations in which silicon nitride coatings are employed, the antibacterial metal and silicon nitride may be co-deposited, either simultaneously or sequentially, as part of step 606. In some such implementations, the deposition process may utilize a dual magnetron sputtering process and/or a combination reactive PVD deposition of silicon nitride concurrent with PVD application of silver ions.

[00108] Step 608 may comprise machining or otherwise forming the biomedical implant material block into a suitable shape/form for a desired biomedical implant. As mentioned above, in some implementations, the biomedical implant material block may comprise a pre-formed block already in a desired shape. In such implementations, step 606 would, of course, be omitted.

[00109] At step 610, an antibacterial coating, such as a silicon nitride coating, may be applied to at least a portion of the formed biomedical implant material block. In some implementations, such a coating may be

applied to the entire exposed surface of the formed biomedical implant material block. Such coating or coatings may also comprise antibacterial metal ions, such as silver ions, which may be deposited simultaneously with deposition of the coating(s) or, alternatively, may be deposited onto the coating after the coating has been applied

[00110] Various methods may be used in order to apply the antibacterial coating(s). For example, coatings may be applied by way of a variety of processes, such as physical vapor deposition (PVD) or chemical vapor deposition (CVD) processes. More specifically, antibacterial coatings can be applied via low or high-temperature reactive CVD (i.e., LT-CVD, HT-CVD), DC or RF plasma-assisted CVD, DC or RF assisted PVD, balanced or unbalanced magnetron sputtering, ion-beam assisted deposition (IBAD), filtered cathodic arc deposition (FCAD), pulsed laser ablation and deposition (PLAD), electron cyclotron resonance CVD (ECR-CVD), or any other appropriate physical vapor deposition (PVD) or chemical vapor deposition (CVD) processes.

[00111] Finally, at step 612, at least a portion of the surface of the biomedical implant material block may be roughened to further enhance antibacterial characteristics. In some implementations, this roughening step may comprise applying a texture to the biomedical implant material block. Step 612 may be performed using, for example, micromachining, grinding, polishing, laser etching or texturing, sand or other abrasive blasting, chemical etching, thermal etching, plasma etching, and the like. The surface roughness in some embodiments and implementations may be greater than about 1,200 nm Ra. In some such embodiments, the

surface roughness may be greater than about 1,500 nm Ra. In some such embodiments, the surface roughness may be greater than about 2,000 nm Ra. In some such embodiments, the surface roughness may be greater than about 3,000 nm Ra. In other embodiments, the surface roughness may be between about 500 nm Ra and about 5,000 nm Ra. In some such embodiments, the surface roughness may be between about 1,500 nm Ra and about 5,000 nm Ra. In some such embodiments, the surface roughness may be between about 2,000 nm Ra and about 5,000 nm Ra. In some such embodiments, the surface roughness may be between about 3,000 nm Ra and about 5,000 nm Ra.

[00112] It should be understood that some implementations can be practiced without some or all of the steps disclosed above. In addition, the steps of a method do not necessarily need to be executed in any specific order, or even sequentially, nor need the steps be executed only once, unless otherwise specified. For example, with respect to the method 600 of Figure 6, it is contemplated that some implementations may omit one or more steps, such as step 610 of adding an antibacterial coating. Similarly, in some implementations, step 612 of roughening at least a portion of a surface of the implant may be performed prior to 610 or, alternatively, both before and after step 610. As another example, the forming/machining step 608 may be performed before any of the steps listed in process 600 prior to step 608 if desired. For example, the implant may be fully formed/machined before altering the surface chemistry of the implant according to step 604 in some implementations. In addition, as another example, and as mentioned above, some

implementations may comprise a pre-formed biomedical implant material block, in which case the forming/machining step 608 may be omitted from the process. A wide variety of alternative implementations will be apparent to those of ordinary skill in the art, after having received the benefit of this disclosure.

[00113] Similarly, it will be understood by those having skill in the art that changes may be made to the details of the above-described embodiments without departing from the underlying principles presented herein. For example, any suitable combination of various embodiments, or the features thereof, is contemplated.

[00114] Any methods disclosed herein comprise one or more steps or actions for performing the described method. The method steps and/or actions may be interchanged with one another. In other words, unless a specific order of steps or actions is required for proper operation of the embodiment, the order and/or use of specific steps and/or actions may be modified.

[00115] Throughout this specification, any reference to "one embodiment," "an embodiment," or "the embodiment" means that a particular feature, structure, or characteristic described in connection with that embodiment is included in at least one embodiment. Thus, the quoted phrases, or variations thereof, as recited throughout this specification are not necessarily all referring to the same embodiment.

[00116] Similarly, it should be appreciated that in the above description of embodiments, various features are sometimes grouped together in a single embodiment, figure, or description thereof for the purpose of

streamlining the disclosure. This method of disclosure, however, is not to be interpreted as reflecting an intention that any claim require more features than those expressly recited in that claim. Rather, inventive aspects lie in a combination of fewer than all features of any single foregoing disclosed embodiment. It will be apparent to those having skill in the art that changes may be made to the details of the above-described embodiments without departing from the underlying principles set forth herein. The scope of the present invention should, therefore, be determined only by the following claims.

CLAIMS

1. A method for improving the antibacterial characteristics of a biomedical implant, the method comprising the steps of:

providing a biomedical implant material block, wherein the biomedical implant material block comprises a silicon nitride ceramic material; and

altering the surface chemistry of the biomedical implant material block to improve the antibacterial characteristics of the biomedical implant material block.

2. The method of claim 1, wherein the step of altering the surface chemistry of the biomedical implant material block comprises increasing the nitrogen content in the transitional oxide layer of at least a portion of the biomedical implant material block.

3. The method of claim 2, wherein the step of altering the surface chemistry of the biomedical implant material block comprises subjecting the biomedical implant material block to high energy nitrogen implantation.

4. The method of claim 3, wherein the high energy nitrogen implantation is performed using an ion gun.

5. The method of claim 2, wherein the step of altering the surface chemistry of the biomedical implant material block comprises

cleaning the biomedical implant material block in a solution configured to strip away at least some of a transitional oxide layer of the biomedical implant material block.

6. The method of claim 5, wherein the solution comprises at least one of a highly caustic solution and a highly acidic solution.

7. The method of claim 6, wherein the solution comprises at least one of hydrofluoric acid, sulfuric acid, nitric acid, hydrochloric acid, sodium hydroxide, and potassium hydroxide.

8. The method of claim 7, wherein the solution comprises at least one of hydrofluoric acid, sulfuric acid, nitric acid, hydrochloric acid, sodium hydroxide, and potassium hydroxide in a molarity of at least about 1.0.

9. The method of claim 2, wherein the step of altering the surface chemistry of the biomedical implant material block comprises firing the biomedical implant material block in a nitrogen-rich environment.

10. The method of claim 1, further comprising subjecting the biomedical implant material block to high energy ion implantation of antibacterial metal ions.

11. The method of claim 10, wherein the antibacterial metal ions comprise silver ions.

12. The method of claim 10, wherein the step of altering the surface chemistry of the biomedical implant material block comprises subjecting the biomedical implant material block to high energy nitrogen implantation and high energy silver ion implantation, and wherein the amount of silver ions implanted into the biomedical implant material block comprises about 5 to about 15% by atomic percent of the total ions implanted into the biomedical implant material block.

13. The method of claim 1, further comprising increasing a surface roughness of at least a portion of the biomedical implant material block to further improve the antibacterial characteristics of the biomedical implant material block.

14. The method of claim 13, wherein the step of increasing a surface roughness of at least a portion of the biomedical implant material block comprises increasing the surface roughness to a roughness profile having an arithmetic average of at least about 1,250 nm Ra.

15. The method of claim 14, wherein the step of increasing a surface roughness of at least a portion of the biomedical implant material block comprises increasing the surface roughness to a roughness profile having an arithmetic average of at least about 2,000 nm Ra.

16. The method of claim 1, wherein the biomedical implant comprises an intervertebral spinal implant.

17. A method for improving the antibacterial characteristics of a ceramic biomedical implant, the method comprising the steps of:

providing a biomedical implant material block, wherein the biomedical implant material block comprises a silicon nitride ceramic material in a green state; and

firing the biomedical implant material block in a firing environment comprising a gas, wherein the firing environment is configured to facilitate a chemical reaction between a surface of the biomedical implant material block and the gas so as to result in an increase of a surface charge of the biomedical implant material block.

18. The method of claim 17, wherein the gas comprises nitrogen gas.

19. The method of claim 18, wherein the firing environment comprises at least essentially 100% nitrogen gas.

20. The method of claim 17, further comprising, after the step of firing the biomedical implant material block, increasing a surface roughness of at least a portion of the biomedical implant material block to

enhance the antibacterial properties of the biomedical implant material block.

21. The method of claim 20, wherein the step of increasing a surface roughness of at least a portion of the biomedical implant material block comprises increasing the surface roughness to a roughness profile having an arithmetic average of at least about 1,250 nm Ra.

22. A method for improving the antibacterial characteristics of a biomedical implant, the method comprising the steps of:

providing a biomedical implant material block;

applying a coating to the biomedical implant material block, wherein the coating comprises a silicon nitride material; and

altering the surface chemistry of the biomedical implant material block to improve the antibacterial characteristics of the biomedical implant material block.

23. The method of claim 22, further comprising forming the biomedical implant material block into an orthopedic bone screw.

24. The method of claim 22, wherein the biomedical implant material block comprises a silicon nitride ceramic material.

25. The method of claim 22, further comprising increasing a surface roughness of at least a portion of the biomedical implant material

block to a roughness profile having an arithmetic average of at least about 1,200 nm Ra.

26. The method of claim 22, wherein the step of altering the surface chemistry of the biomedical implant material block comprises depositing antibacterial metal ions into the coating.

27. The method of claim 26, wherein the step of applying a coating to the biomedical implant material block takes place at least substantially simultaneously with the step of depositing antibacterial metal ions.

FIG. 1A

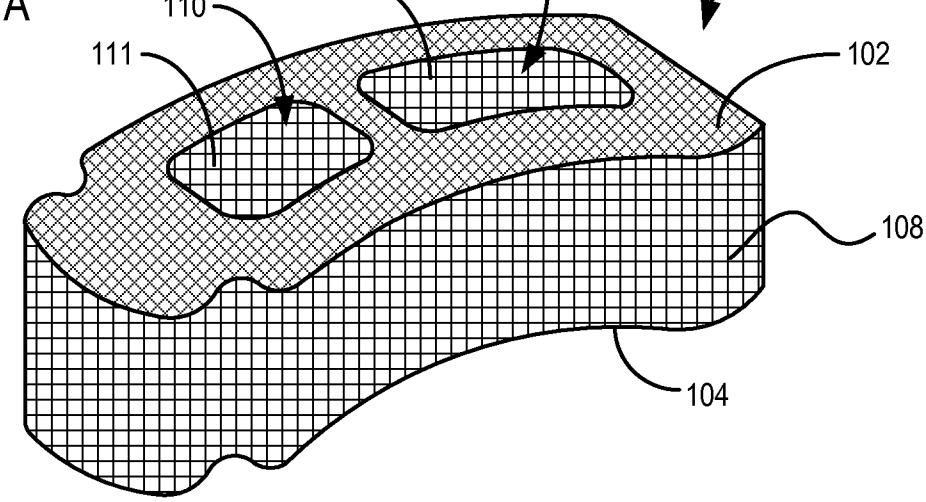


FIG. 1B

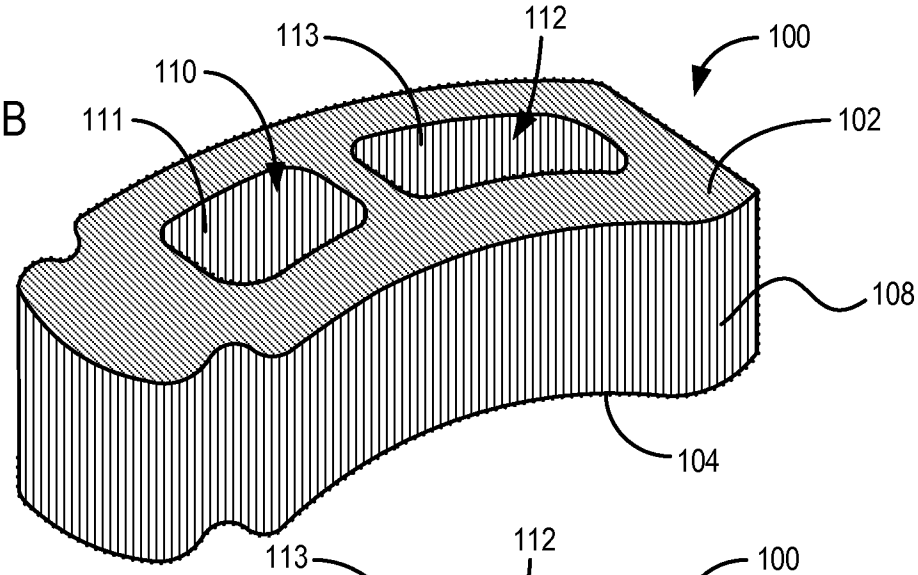


FIG. 1C

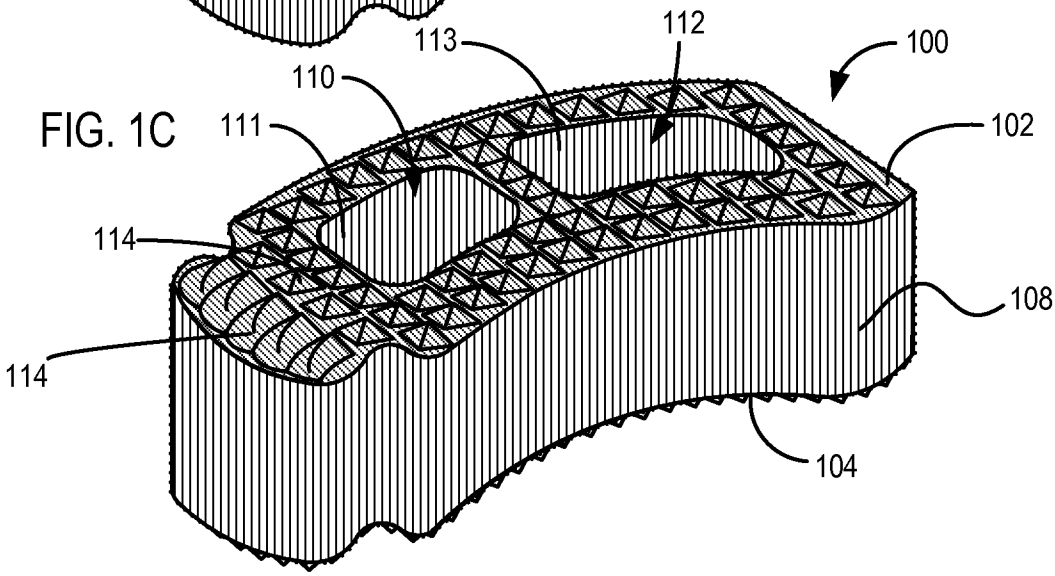
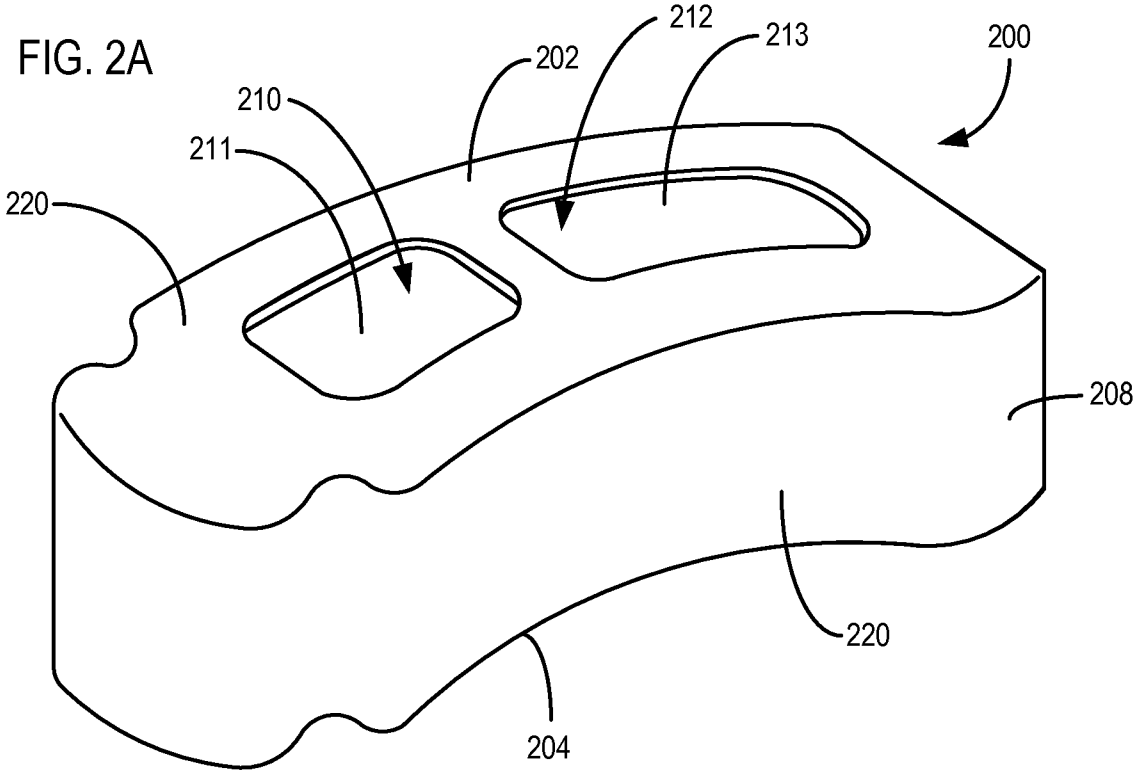


FIG. 2A


212
213
200
202
210
211
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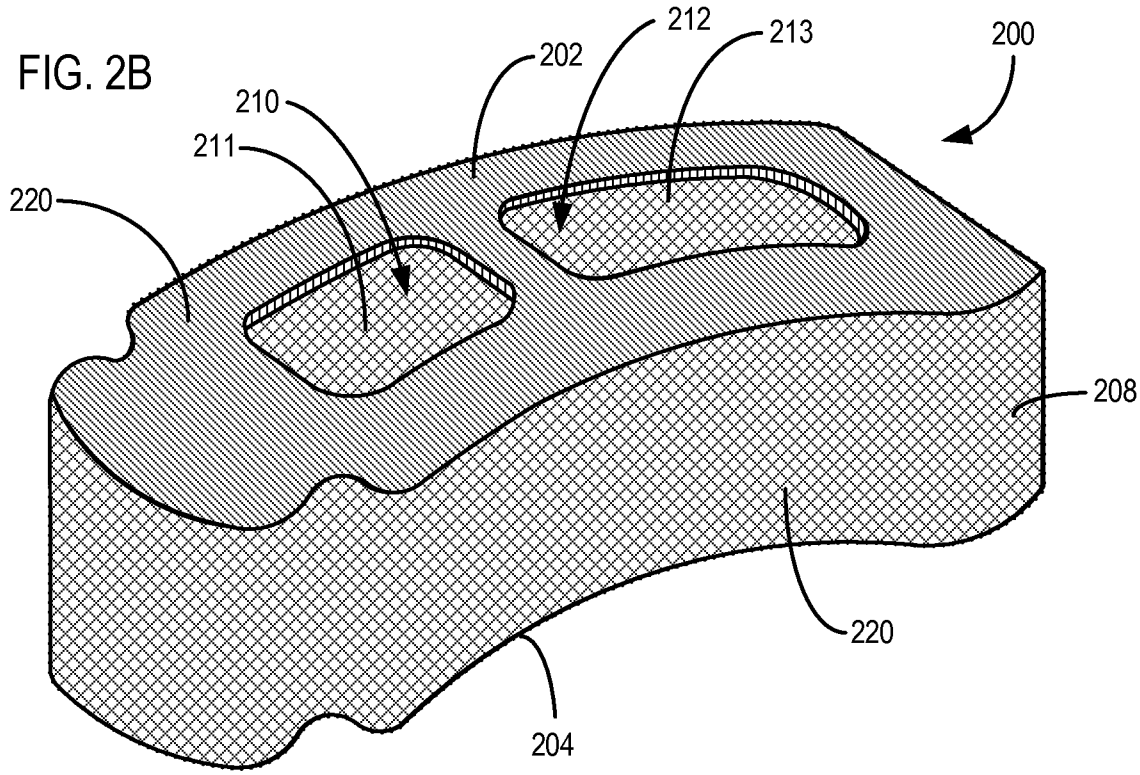
208
220
204

FIG. 2B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213
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211
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204

FIG. 3A

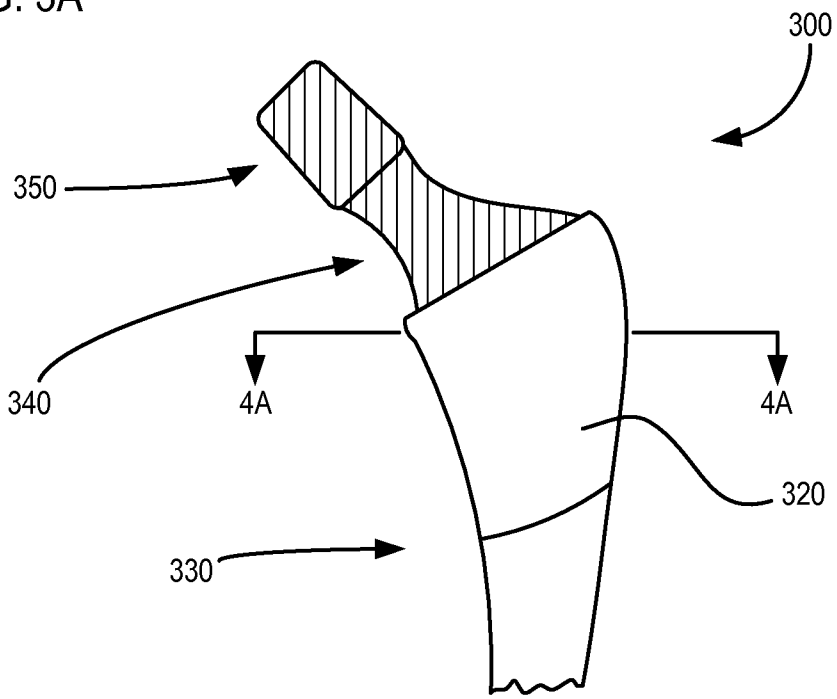


FIG. 3B

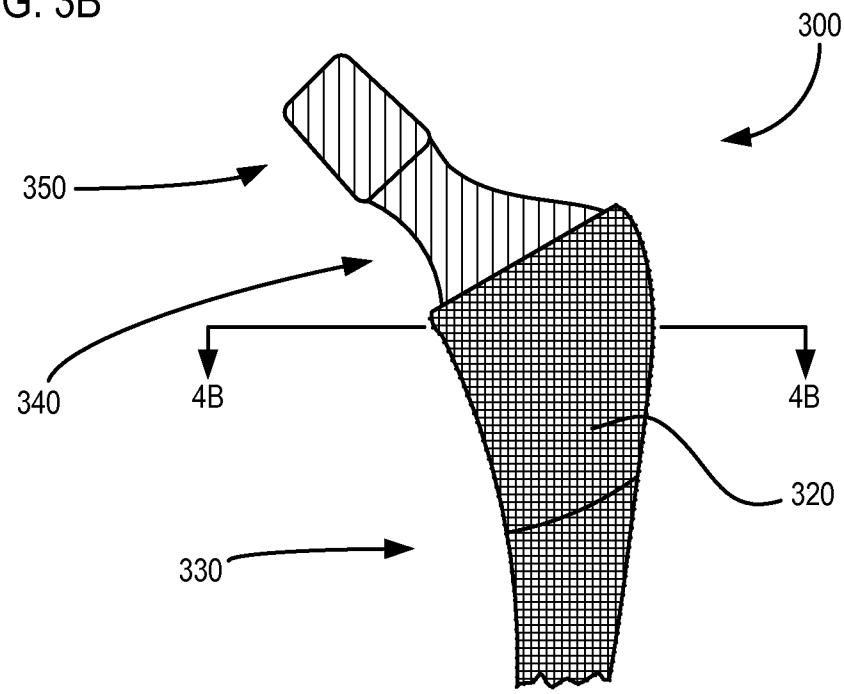


FIG. 4A

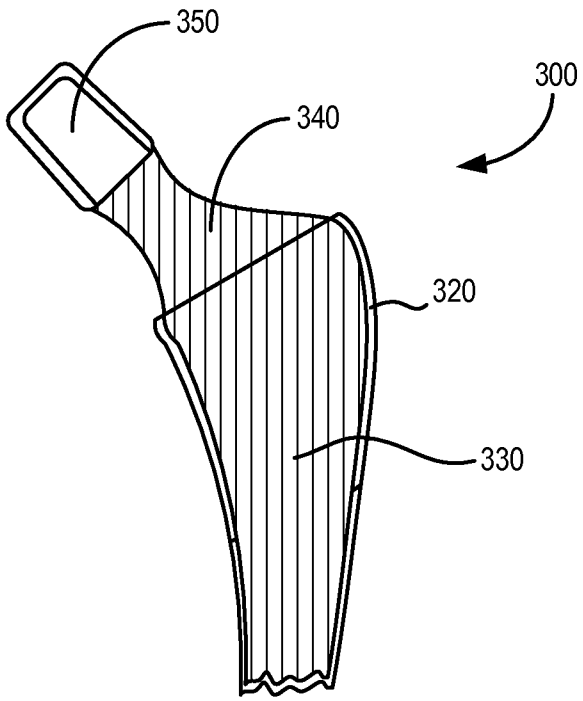


FIG. 4B

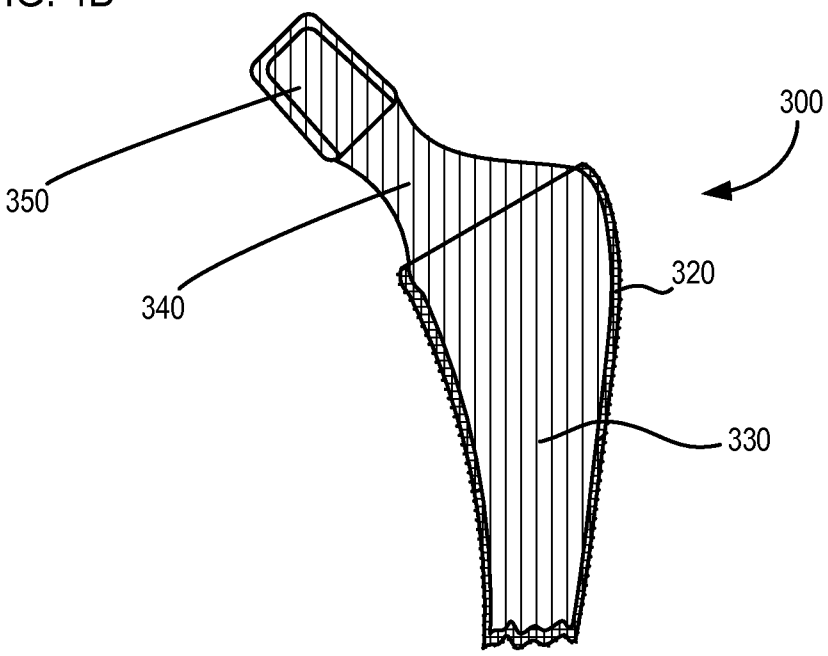


FIG. 5A

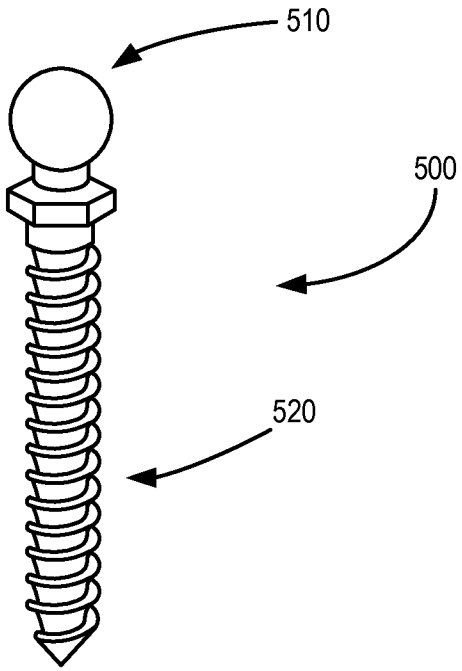
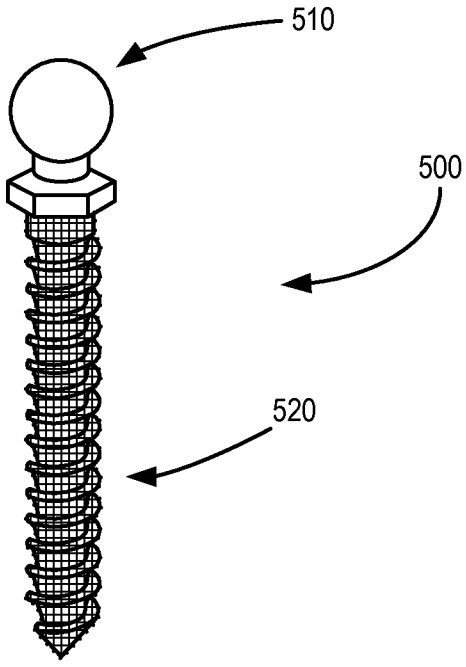


FIG. 5B



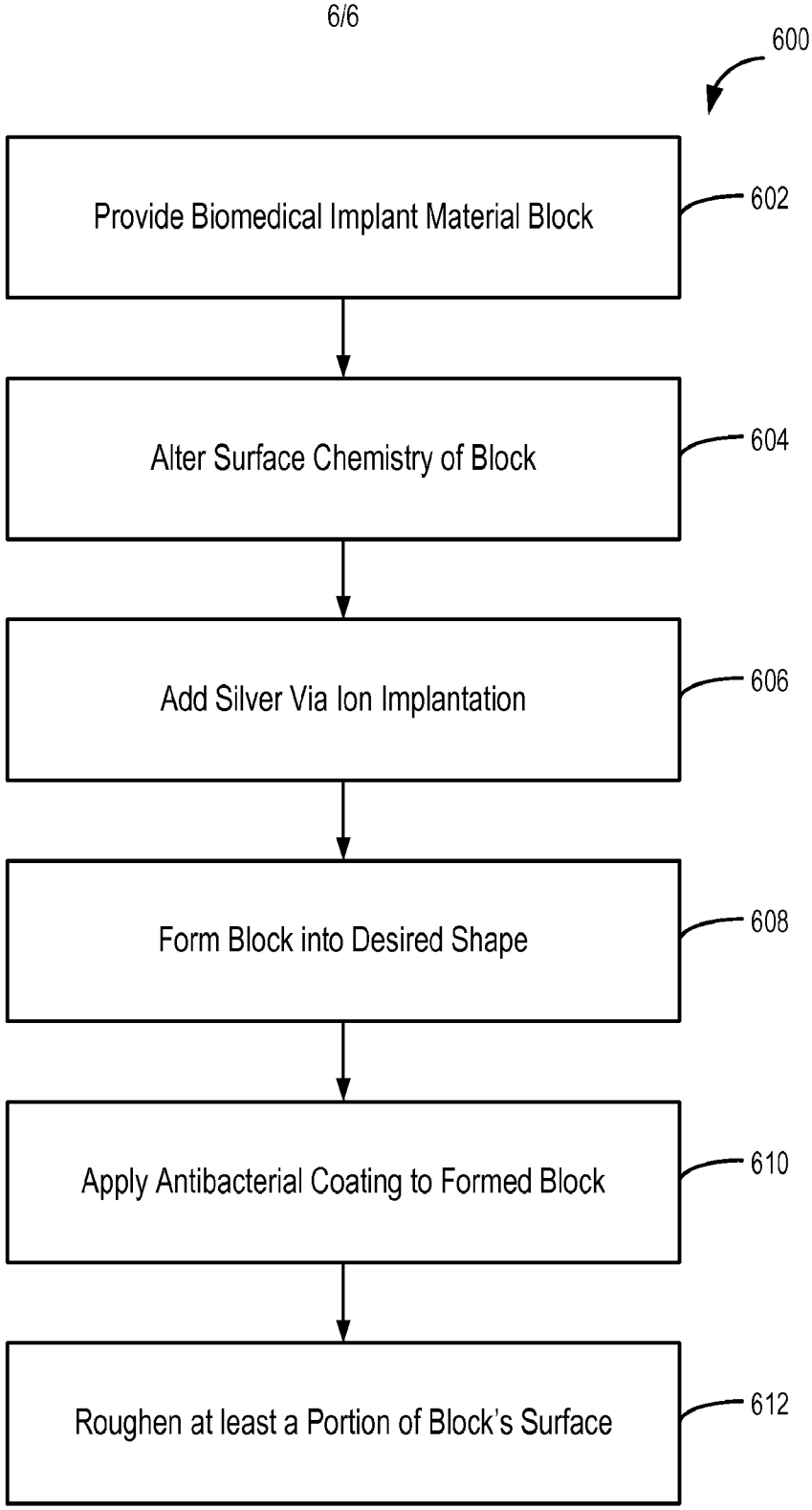

600
Provide Biomedical Implant Material Block
602
Alter Surface Chemistry of Block
604
Add Silver Via Ion Implantation
606
Form Block into Desired Shape
608
Apply Antibacterial Coating to Formed Block
610
Roughen at least a Portion of Block's Surface
612

FIG. 6