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(54) Title: COMPOSITE IMPLANT MATERIAL

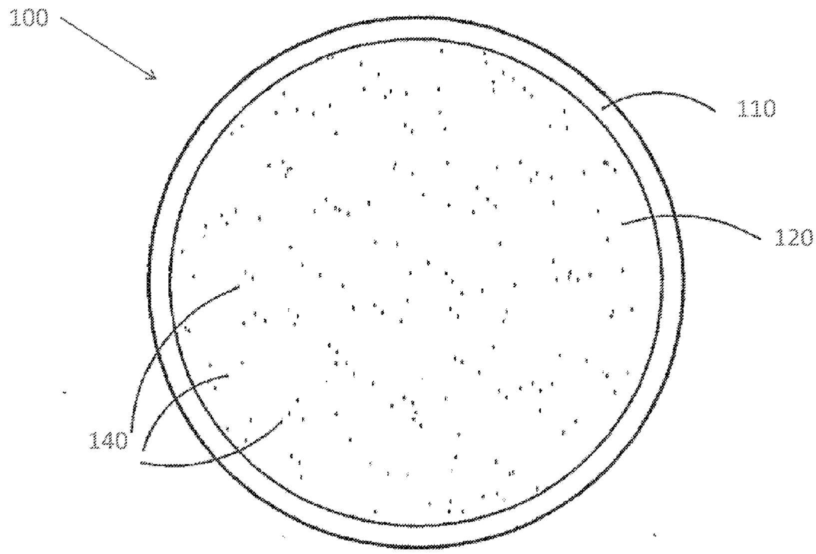

Fig. 1

(57) Abstract: A prosthetic implant with improved properties, suitable for implantation to the human body, comprising a composite comprising a base material and a plurality of additives, wherein the additives are selected from radiolucent additives and/or hyperechoic additives; or wherein the additives are selected to reduce the solvent concentration by between 5%-95%; or wherein the additives are selected to increase the elastic modulus by more than 20%; or wherein the additives are selected for combining these effects.

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COMPOSITE IMPLANT MATERIAL

FIELD OF THE INVENTION

The present invention relates generally to implantable prosthetic devices and specifically to implantable prosthetic devices featuring a composite of a base material and an additive material.

BACKGROUND OF THE INVENTION

In the last century reconstructive and cosmetic surgery has become a common practice. Specifically reconstructive breast surgery has been developed to allow reconstruction of a woman's breast that was affected by procedures such as mastectomy. Cosmetic breast surgery has also become available to amend the appearance of a woman's breast, for example by adding an implant to increase the size of the breast, to correct asymmetries, change shape and fix deformities.

The material chosen for the implant must have the appropriate resilience, elasticity and pliability, which provides it with a specific feeling when being sensed. Generally it is desirable to provide an implant which provides a specific shape and mimics the feel of real human tissue at the position of the implant. It is important that the implant maintain its form and feel for extended periods, to prevent the need for additional surgery.

Prior art implants used today for breast implant surgery for example comprise an outer shell typically formed from vulcanized silicone rubber (elastomer) which can be single or multi layered, smooth or textured, with or without barrier layer/s, or covered with polyurethane foam; and an inner content typically composed of silicone gel or saline. There are also double lumen implants that are combinations of both silicone and saline such as the Becker implant from Mentor Corp.

Prior art implants present challenges in several areas which are described in more detail below including: imaging, such as mammograms; gel bleed from the implant; and mechanical and chemical issues.

Imaging studies are carried out on the augmented breast for two primary reasons: 1) To evaluate the breast tissues (e.g. for lesions); 2) To evaluate the breast implants for complications – for example it is important to be able to clearly identify the integrity of the implant's shell. When evaluating breast tissues it is desirable that the implants do not obscure the tissues under examination or interfere with the chosen imaging technique. Further, it is desirable to be able to clearly identify the integrity of the implant's shell.

Three main imaging modalities are used in breast examination:

- Ultrasonography;
- Mammography (X-Ray); and
- MRI (Magnetic resonance imaging).

Silicone gel as used in standard implants is radiopaque. Therefore, in mammography the typical representation of an implant will be white with no further details of the tissue in front of or behind the implant. This is illustrated in figure 3A which is a mammogram of a breast with a prior art implant. As shown in the mammogram 300, the implant 302 appears completely white (opaque to x-ray) showing no detail of the tissue in front of it or behind it. Breast tissue 304 not obscured by the implant is visible in the mammogram 300.

Accordingly, mammograms for women with breast implants are typically performed twice; once in the normal fashion as for a breast without implants and then again in an oblique position with the implant pushed back as much as possible out of the frame of the mammogram (known as the Eklund implant displacement technique). Typically, 30% of breast tissue can still be obscured by the implant.

When used with ultrasonography, silicone gel is anechoic. Since the silicone gel has a density similar to liquid, the speed of sound in the implant is slightly slower but similar to that of water (and the surrounding tissues) and therefore ultrasonography will usually detect an echo or reverberation of the shell with additional reverberation artifacts from the gel itself. Reverberations from the gel create visual noise on the picture which interferes with the ability of the radiologist to detect abnormalities.

Soft tissues have a conduction speed of 1540 m/sec. Water, which has a conduction speed of 1492 m/sec will appear as dark and the more echoic the material, the more white the image will appear. Silicone has a conduction speed of approximately 997 m/sec and the slowing of the sound waves in the implant is what causes many of the reverberations and artifacts seen.

This is illustrated in figures 5A and 5C which are ultrasound images of the edges of prior art breast implants in situ. As shown in figure 5A, the shell 502 of a prior art implant is visible in an ultrasound image 500 captured with a 12MHz probe.

The top of image 500 is the interface of the probe with the skin. Then there is a representation of tissue 502 comprising skin, fat, glands and other tissue, followed by the shell of the silicone implant 504. The gel 508 is seen as the black area. Reverberations seen as visual noise 506 caused by the implant are also visible in image 500 in the area which should be black (the gel 508). This noise is seen extending 1.5 cm into the area of the image 500. The noise also extends above the shell creating a cloud like snow over the tissue area 502 of the image which is intended for diagnosis. Similarly, figure 5C shows an ultrasound image 520 captured with a 17MHz probe where both the implant shell 522 and the visual noise caused by the implant 524 are visible.

When there is a rupture in the implant, the extravasated gel may migrate to other areas in the body. However, due to its anechoic nature and high resemblance to water, free silicone gel can often be mistaken for a pathology such as a cyst.

The background art therefore does not teach or suggest a prosthetic implant material that does not obscure the tissues under examination or interfere with the chosen imaging technique. Further, as shown, prior art implants cause visual noise that interferes with the ability of the radiologist to detect abnormalities. Finally it would be preferable, in case of a rupture of the shell, for the silicone material to remain cohesive and prevent migration to other parts of the body or for the silicone material to be easily identifiable so as to be able to differentiate it from tissue.

A further problem with prior art implants is gel bleed from an intact implant. Gel bleed is a common term describing a diffusion based phenomena where the solvent (silicone oil) as a part of silicone gel diffuses/bleeds through the shell. Diffusion is a phenomenon where a substance flows from a region of high concentration to a region of low concentration due to chemical potential. The diffusive flux is negatively proportional to the concentration gradient and the coefficient of proportionality is the diffusion coefficient. The flux goes from regions of high concentration to regions of low concentration. Reducing the concentration gradient would therefore reduce the gel bleed.

It is undesirable to have silicone bleed into bodily tissues as the free silicone can elicit a foreign body response resulting in granulomas and calcifications in the breast which can be misinterpreted in radiological screenings as breast tissue abnormalities. Free silicone can also easily migrate into the lymphatic system and accumulate in the lymph nodes (usually in the axilla) resulting in lumps and lymphadenopathy. Gel bleed has also been tagged as one of the causes for capsular contracture. Research in animal models has concluded that "There is a dose-dependent relationship between silicone gel bleed and capsule compliance that is independent of the cohesivity of the silicone" (Moyer HR1, Ghazi BH, Losken A. Plast Reconstr Surg. 2012 Oct;130(4):793-800).

Efforts to reduce gel bleed have focused on two directions:

- Adding and improving the barrier layer/s in the shells;
- Changing the composition of the solvent to reduce the amount of low molecular silicone moieties that may easily diffuse through the elastomeric shell and replacing them with higher molecular weight silicone moieties.

While these efforts have resulted in 4th and 5th generation breast implants which have somewhat reduced gel bleed, they have not solved the problem completely. Furthermore, these solutions are only somewhat effective while the implant shell is intact. When the implant shell is compromised due to rupture or degradation, these solutions provide significantly reduced effectiveness allowing elevated rates of solvent migration into the body. It would therefore be desirable to enhance the implants to reduce solvent bleed from intact as well as ruptured implants.

Finally, it has been show in recent years that it is desirable to use more cohesive gels for several reasons:

- Imitate more closely the surrounding breast tissue for a breast that feels more natural;
- To reduce gel bleed as described above;
- To improve the dynamic mechanical interface with the breast by serving as a scaffold to support the shape of the augmented breast;
- To prevent flow and dispersion of gel in the body in the case of rupture or shell degradation;

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- Prevent breakage of the gel during insertion or use in the body;
- To better maintain the form of the implant during normal use. This is especially important in shaped or anatomical implants; and
- To prevent or reduce wrinkling. Often implants suffer from visible folds and wrinkles (especially in women with thin tissue coverage).

Current silicone gels come in varying degrees of cohesiveness. Silicone gel cohesion can be increased by increasing the degree of crosslinking resulting in a mesh of higher crosslinking density. The average distance between two adjacent crosslinks is thus reduced.

Thus increased crosslinking has advantages, however, excessive increases in crosslinking may result in the gel breaking even without externally applied forces because of internal residual stresses. For example, when taking a gel such as NUSIL Med 3-6300, the mixing ratio specified is 3: 1 part A to part B. Part A contains the catalyst and part B contains the crosslinker and therefore changing the mixing ration results in different crosslinking densities and different cohesions. However, increasing the crosslinker component excessively results in the gel breaking. In this case, mixing at a ratio of 3:2 results in a highly cohesive gel that breaks and fractures without any applied load.

Therefore, for the reasons stated above, a more cohesive gel is desired but simply increasing the crosslinking causes the gel to fracture and therefore another mechanism to make the gel more cohesive is required.

SUMMARY OF THE INVENTION

The present invention aims to address the deficiencies of the background art by providing a prosthetic implant comprising a composite implant material further comprising a base material and additives. The term base material as used herein refers to a polymer network further comprising a free molecule which may be either a solvent or free polymer chain. The free molecule therefore defines whether the polymer network has a gel or elastomer form. The composite material of the presently described invention may herein be alternatively referred to as implant material, composite implant material, or composite material. The addition of additives to the base material provides several improvements.

The implant material has improved radiology characteristics such as improved radiolucency and decreased associated visual noise in ultrasound images. Further, the composite material is uniquely identifiable using imaging modalities and can be easily differentiated from tissue or other materials.

In one aspect, the present invention provides a prosthetic implant when used for implantation to the human body, comprising a composite material which comprises a base material and a plurality of additives, wherein, a) said additives are selected from radiolucent additives and/or hyperechoic additives; b) said additives are selected such that the elastic modulus at 1 Hz of said composite material is greater than the elastic modulus of said base material, and wherein the elastic modulus is greater than the elastic modulus of said base material by at least 20%; c) said additives have a surface roughness of between 0.2 nm and 40 nm $R_{RM}S$; and d) said additives are up to 500 microns in size with at least 20% size difference between them.

In a further aspect, the present invention provides a composite material when used for implantation to the human body, comprising a base material and a plurality of additives, wherein; a) said additives are selected from radiolucent additives and/or hyperechoic additives; b) said additives are selected such that the elastic modulus at 1 Hz of said composite material is greater than the elastic modulus of said base material, and wherein the elastic modulus is greater than the elastic modulus of said base material by at least 20%; c) said additives have a surface roughness of between 0.2 nm and 40 nm $R_{RM}S$; and d) said additives are up to 500 microns in size with at least 20% size difference between them.

The phenomena of gel bleed can be generalized to include bleed of free molecules from a base material. The implant material reduces the total amount of free molecules resulting in the reduction of the concentration gradient and therefore reduction in free molecule bleed. As described above, the concentration gradient is the driving force for free molecule bleed and therefore reducing the free molecule concentration reduces free molecule bleed.

Further, the additives incorporated in the base material limit free molecule bleed based on two additional mechanisms. The first mechanism is physical, where at some point as the composite material shrinks because of the loss of free molecule in the base material, the additives constrain further shrinkage because of their physical size and their contact with each other. The second mechanism is based on the large cumulative surface area of the additives. The free molecule in the base material wets the additive surface due to surface

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interactions and does not tend to be removed (unless there is drying, desorption or replacement with another liquid that has higher affinity to the surface). By contrast, prior art implants are not constrained and can theoretically lose all their solvent to diffusion;

The additives in the implant material increase the crosslinking density/cohesion of the base material, thus strengthening (reinforcing) the base material while maintaining its integrity. The implant material with a reinforced base material provides several advantages when used in a breast implant:

- More closely imitates the surrounding breast tissue for a breast that feels more natural;
- The reinforced implant presents a desirable smooth contour because of the cohesive form-stable nature;
- Prevents or reduces wrinkling;
- Reduces solvent bleed from an intact implant;
- Maintains the form and shape of the implant;
- Prevents breakage during implantation or use;

[Text continued on page 7]

- Improves the dynamic mechanical interface with the breast by serving as a scaffold to support the shape of the augmented breast;
- Prevents the flow and dispersion of base material in the body in the case of rupture or shell degradation, and reduces free solvent that can be absorbed by the body in such cases.

The additives are added to the base material as a volume substitution element creating a two phased system with a continuous phase and a dispersed phase or bi-continuous system. As an example, 30% of the implant's base materialvolume can be replaced by the additives. Optionally, the additives comprise up to 60% by volume of the composite material. Optionally, the additives comprise up to 90% by volume of the composite material.

The implant material is suitable for use in an encapsulated implant according to at least some embodiments of the present invention, in which the implant features a shell and the implant material, such that the implant material is contained within the shell.

Further, the present invention conforms to the requirements of an implantable prosthesis such as being able to provide a specific three-dimensional shape and maintain the shape for many years, preferably for the lifetime of the patient in which the implant is installed; having a specific feel, preferably imitating the feel of human or animal tissue, such as the feel of a real breast; being bio-durable such that it is not ruined by interaction with the human or animal body; being bio-compatible so that the patient's health is not detrimentally affected by the implant even under extreme circumstances: for example the filler (base material with additives) is required to be non-toxic in case of leakage from the implant.

According to preferred embodiments of the present invention, the implant is adapted for use as a breast implant.

According to at least some embodiments of the present invention, the implant material comprises a base material, such as for example silicone gel, and a lower density material. Silicone gel density is ~1gr/cm^3 in the order of densities of other liquids, such as water and organic solvents. The lower density material therefore has a density lower than ~1gr/cm^3. Optionally and preferably, the lower density material comprises a gas.

In an exemplary embodiment of the invention, the implant may be provided in various sizes, for example extending from 50cc to 1500cc or larger or smaller. Optionally, the implant may be implanted in other areas of the body other than the breast, for example to replace or augment testicles, pectorals, a chin, cheeks, a calf, buttocks or other parts of the human or an animal body, while exhibiting tactile properties similar to natural tissue.

According to a preferred embodiment of the present invention a prosthetic implant, suitable for implantation to the human body comprises a composite material comprising a base material and a plurality of additives, wherein the additives are selected from radiolucent additives and/or hyperechoic additives. Preferably the additives are selected from the group consisting of: additives comprising at least one of glass, ceramic, metal, polymers, PMMA, polyacrylonitrile, polybutadiene, PEEK, natural rubber, synthetic rubber, amorphous polymer or semi-crystalline polymer; additives between 1nm and 1mm in diameter; additives comprising a three-dimensional shape comprising spherical, fibrous, platelet, flakes, amorphous, crystalline, semi-sphere, rod, disk or combinations of these shapes or irregular versions of these shapes; hollow additives; porous additives; solid additives; additives comprising at least 2 materials; additives with surface roughness of between 0.2nm and 40nm RRMS; additives comprising a gas; additives comprising a non-solvent liquid; additives comprising a non-silicone gel; additives formed as a micro-lumen; and a combination of the above.

Optionally the base material comprises a silicone gel. Optionally, the implant comprises a plurality of shells, including at least one inner shell and at least one outer shell; wherein the at least one inner shell is at least partially surrounded by the outer shell; wherein the outer shell is filled with the base material and a plurality of hyperechoic additives, and wherein the inner shell is filled with the base material and a plurality of radiolucent additives.

According to another preferred embodiment of the present invention a composite material suitable for implantation to the human body, comprises a base material and a plurality of additives, wherein the additives are selected from radiolucent additives and/or hyperechoic additives. Preferably the additives comprise up to 60% by volume of the composite material. Preferably, the additives comprise up to 90% by volume of the composite material. Optionally, the base material is silicone gel.

According to another preferred embodiment of the present invention a prosthetic implant, suitable for implantation to the human body, comprises a composite material comprising a base material and a plurality of additives, wherein the additives are selected such that the solvent concentration of the composite material is between 5%-95% of the solvent concentration of the base material.

Optionally the additives reduce the solvent concentration of the base material by 20% to 80%. Optionally the additives reduce the solvent concentration of the base material by 40% to 60%. Optionally the additives reduce the solvent concentration of the base material by up to 50%.

Preferably the additives are selected from the group consisting of: additives comprising at least one of glass, ceramic, metal, polymers, PMMA, polyacrylonitrile, polybutadiene, PEEK, natural rubber, synthetic rubber, amorphous polymer or semi-crystalline polymer; additives between 1nm and 1mm in diameter; additives comprising a three-dimensional shape comprising spherical, fibrous, platelet, flakes, amorphous, crystalline, semi-sphere, rod, disk or combinations of these shapes or irregular versions of these shapes; hollow additives; porous additives; solid additives; additives comprising at least 2 materials; additives with surface roughness of between 0.2nm and 40nm RRMS; additives comprising a gas; additives comprising a non-solvent liquid; additives comprising a non-silicone gel; additives formed as a micro-lumen; and a combination of the above.

Optionally the base material comprises a silicone gel. Optionally, the implant comprises a plurality of shells, including at least one inner shell and at least one outer shell; wherein the at least one inner shell is at least partially surrounded by the outer shell; wherein the outer shell is filled with the base material and a higher concentration of additives closer to the outer shell, and wherein the inner shell is filled with the base material and an increasing concentration of additives relative to the distance from the inner shell.

According to another preferred embodiment of the present invention a composite material suitable for implantation to the human body, comprises a base material and a plurality of additives, wherein the additives are selected such that the solvent concentration of the composite material is 5%-95% of the solvent concentration of the base material. Preferably the additives comprise up to 60% by volume of the composite material. Preferably, the additives comprise up to 90% by volume of the composite material. Optionally, the base material is silicone gel.

According to another preferred embodiment of the present invention a prosthetic implant, suitable for implantation to the human body, comprises a composite material comprising a base material and a plurality of reinforcing additives, wherein the additives are selected such that the elastic modulus of the composite material is greater than the elastic modulus of the base material by at least 20%. Preferably, the elastic modulus is between 100% and 1000% greater. Preferably the elastic modulus is between 100% and 500% greater.

Preferably, the additives are chosen such that the cohesiveness of the composite material increases as measured by a penetration test the result of which is 5%-99.5% shorter than that of the base material, wherein the penetration is measured after 5 seconds using a Lab-Line (Melrose, IL, USA) penetrometer with a 12 gram shaft and a foot of 1 inch diameter.

Preferably the additives are selected from the group consisting of: additives comprising at least one of glass, ceramic, metal, polymers, PMMA, polyacrylonitrile, polybutadiene, PEEK, natural rubber, synthetic rubber, amorphous polymer or semi-crystalline polymer; additives between 1nm and 1mm in diameter; additives comprising a three-dimensional shape comprising spherical, fibrous, platelet, flakes, amorphous, crystalline, semi-sphere, rod, disk or combinations of these shapes or irregular versions of these shapes; hollow additives; porous additives; solid additives; additives comprising at least 2 materials; additives with surface roughness of between 0.2nm and 40nm RRMS; additives comprising a gas; additives comprising a non-solvent liquid; additives comprising a non-silicone gel; additives formed as a micro-lumen; and a combination of the above. Optionally, the base material is silicone gel.

Optionally, the implant comprises a plurality of shells, including at least one inner shell and at least one outer shell; wherein the at least one inner shell is at least partially surrounded by the outer shell; wherein the outer shell is filled with the base material and a low concentration of additives, and wherein the inner shell is filled with the base material and a high concentration of additives.

According to another preferred embodiment of the present invention a composite material suitable for implantation to the human body, comprises a base material and a plurality of additives, wherein the additives are selected such that the elastic modulus at 1 Hz of the composite material is 20%-5000% greater than the elastic modulus of the base material. Preferably, the additives are chosen such that the cohesiveness of the composite material increases as measured by a penetration test the result of which is 5%-99.5% shorter than that of the base material, wherein the penetration is measured after 5 seconds using a Lab-Line (Melrose, IL, USA) penetrometer with a 12 gram shaft and a foot of 1 inch diameter.

Preferably the additives comprise up to 60% by volume of the composite material. Preferably, the additives comprise up to 90% by volume of the composite material. Optionally, the base material is silicone gel.

Optionally, the implant of any of the above embodiments comprises a plurality of shells, including at least one inner shell and at least one outer shell; wherein the at least one inner shell is at least partially surrounded by the outer shell; wherein the outer shell is filled with the base material and a first concentration of additives, and wherein the inner shell is filled with the base material and a second concentration of additives. Preferably the first concentration is lower than the second concentration. Alternatively the first concentration is higher than the second concentration.

Optionally, the implant comprises multiple areas or compartments. Optionally, the implant material is only present in selected areas or compartments of the implant. Optionally, the implant comprises different concentrations of base material and/or additives in different areas. Optionally, a single additive is used or alternatively multiple additives are used. Optionally, different concentrations of base material are provided with different combinations of additives in different areas of the implant.

Unless otherwise defined, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this invention belongs. The materials, methods, and examples provided herein are illustrative only and not intended to be limiting.

Implementation of the method and system of the present invention involves performing or completing certain selected tasks or steps manually, automatically, or a combination thereof.

BRIEF DESCRIPTION OF THE DRAWINGS

The invention is herein described, by way of example only, with reference to the accompanying drawings. With specific reference now to the drawings in detail, it is stressed that the particulars shown are by way of example and for purposes of illustrative discussion of the preferred embodiments of the present invention only, and are presented in order to provide what is believed to be the most useful and readily understood description of the principles and conceptual aspects of the invention. In this regard, no attempt is made to show structural details of the invention in more detail than is necessary for a fundamental understanding of the invention, the description taken with the drawings making apparent to those skilled in the art how the several forms of the invention may be embodied in practice.

In the drawings:

FIG. 1 shows a non-limiting example of an illustrative prosthetic implant according to at least some embodiments of the present invention;

FIG. 2 shows another non-limiting example of an illustrative prosthetic implant according to at least some embodiments of the present invention;

FIGS. 3A and 3B show mammography images of respectively a breast with a prior art implant and a breast with the implant of the presently claimed invention;

FIGS. 4A and 4B show mammography images of a prior art implant and the implant of the presently claimed invention placed on top of a marked localization paddle and a turkey breast;

FIGS. 5A-5D show ultrasound images of breasts with prior art implants (5A, 5C) and implants of the presently claimed invention (5B, 5D).

FIGS. 6A and 6B are photographs and a graph showing comparative diffusion of a prior art implant gel and the composite material of the presently claimed invention; and

FIG. 7 is an exemplary rheology graph showing comparative elastic modulus of a prior art implant gel and three alternative composite materials as per the presently claimed invention.

DESCRIPTION OF THE PREFERRED EMBODIMENTS

The present invention provides a composite implant material comprising a base material mixed with additives. The implant material has improved radiology characteristics such as improved radiolucency and decreased associated visual noise from ultrasonography. The definition of the implant shell, when imaged using ultrasound, is preferably improved through use of a composite material immediately adjacent to the shell that is hyperechoic. As echoes are created by the differences in conduction speed of sound waves, hyperechoic implant material is created through the maximum reduction in the speed of sound. The implant therefore preferably comprises low density additives such as hollow additives or additives that include gas. Preferably, the additives have a partial or complete vacuum, making the echo even stronger, as there are less sound conducting molecules.

The material of the present invention is more radiolucent than pure silicone gel, when viewed for example in a mammogram, improving the visibility of tissue in front of or behind the implant and therefore improving the diagnostic capability of the physician or radiologist. The material preferably comprises additives suited for radiology such as those that are radiolucent such as less dense elements which are hollow, porous or gaseous. Optionally, additive materials are used that are relatively transparent to x-rays where the x-ray settings (voltage and milliamps) used are those commonly used in imaging studies. A non-limiting example of x-ray voltages are those typically used in mammography of between 24kV-32kV.

A non-limiting example of a radiolucent material optionally used as an additive is polyether ether ketone (PEEK) as in Kurtz SM, Devine JN. (PEEK Biomaterials in Trauma, Orthopedic, and Spinal Implants. Biomaterials. 2007;28(32):4845-4869. doi:10.1016/j.biomaterials.2007.07.013.) “PEEK is now broadly accepted as a radiolucent alternative to metallic biomaterials in the spine community.”

The composite material of the current invention preferably includes additives such that, in case of rupture, the extravasated composite material of the present invention is easily identifiable using imaging technology and distinguishable from physiologic aberrations such as cysts, whether intracapsular or extracapsular due to the presence of the additives.

For a base material comprising a solvent, the additives in the implant material reduce the total amount of free molecules resulting in the reduction of the concentration gradient and therefore in free molecule bleed. As described above, the concentration gradient is the driving force for free molecule bleed and therefore reducing the free molecule concentration reduces gel bleed. Preferably the additives reduce the free molecule concentration in the base material by between 5%-95%. The reduced free molecule concentration is measured by comparing the free molecule concentration of the base material with no additives compared to the free molecule concentration of the composite material. A non-limiting example of the improvement is shown in the pictures and graphs presented in figures 6A and 6B.

Further, if there is bleed from the implant, the remaining additives limit the total amount of liquid that can be removed using the two mechanisms as described above. By contrast, prior art implants are not constrained and can theoretically lose all their liquid to diffusion.

The additives in the implant material increase the crosslinking density/cohesion of the base material, thus strengthening the base material while maintaining its integrity. Preferably the additives are selected to enhance the mechanical properties such as increasing the Elastic Modulus (G') by 20%-1000% or 5000% or more. A non-limiting example of the improvement is shown in the graphs presented in figure 7. Alternatively, the increase in cohesiveness is measured by a penetration test, comprising placing a weighted shaft with a plate on the surface of the tested material and measuring how deeply it has sunk after a certain amount of time. Preferably, the additives increase the cohesiveness as measured by a penetration test such that the penetration into the composite material is 5%-99.5% shorter than into the base material.

These improvement and others are preferably provided by the addition of additives to base material as a volume substitution element creating a two phased system with a continuous phase and a dispersed phase or bi-continuous system.

The implant material is preferably contained within a shell to form an encapsulated prosthetic implant. A non-limiting example of a suitable shell material is a silicone elastomer, optionally with a material such as polyurethane foam overlaid on the shell. At least the shell, but preferably all of the materials of the implant, is biologically compatible and safe for therapeutic and/or cosmetic use internally to the human body.

The above described base material is preferably a silicone gel as is known in the art, such as PDMS and derivatives thereof for example. Alternatively, the base material is a polyurethane network. Alternatively the base material is any other suitable biocompatible base material or combination of base materials.

Optionally the base material is chosen such that it may form covalent bonds with the chosen additive which may be any one of the additives described herein.

The additive or combination of additives is preferably chosen based on factors including but not limited to biocompatibility, durability, price, and other factors.

The additive optionally comprises one or more materials such as glass, ceramic, metal, polymers, such as PMMA (polymethyl methacrylate), polyacrylonitrile, polybutadiene, polyether ether ketone (PEEK) (or any other natural or synthetic rubber or similar materials) for example, or any other amorphous or semi-crystalline polymer. The materials may optionally be determined according to their relative flexibility. For example, for PMMA, the tensile strength at yield is preferably from 52 to 71 mega-Pascal and the tensile modulus is preferably from 2.2 to 3.1 giga-Pascal. As a further example, for Borosilicate glass (Pyrex®) with 80% silica, 13% Boron and salts, the tensile strength at yield is preferably between 35 to 100 mega-Pascal and the tensile modulus is 64*10^3 mega-Pascal.

Optionally the additive comprises rubber. Non-limiting examples of suitable rubber include: Ethylene-acrylate Rubber, Polyester Urethane, Bromo Isobutylene Isoprene, Polybutadiene, Chloro Isobutylene Isoprene, Polychloroprene, Chlorosulphonated Polyethylene, Epichlorohydrin, Ethylene Propylene, Ethylene Propylene Diene Monomer, Polyether Urethane, Perfluorocarbon Rubber, Fluoronated Hydrocarbon, Fluoro Silicone, Fluorocarbon Rubber, Hydrogenated Nitrile Butadiene, Polyisoprene, Isobutylene Isoprene Butyl, Acrylonitrile Butadiene, Polyurethane, Styrene Butadiene, Styrene Ethylene Butylene Styrene Copolymer, Polysiloxane, Vinyl Methyl Silicone, Acrylonitrile Butadiene Carboxy Monomer, Styrene Butadiene Carboxy Monomer, Thermoplastic Polyether-ester, Styrene Butadiene Block Copolymer, Styrene Butadiene Carboxy Block Copolymer.

The additive may optionally be of any suitable size. Each additive is optionally between 1 nm (nanometer) and 1mm. Preferably, the additive is no bigger than 500 microns. Preferably, the packing factor of the additives may be increased by using polydispersity of additive sizes. Preferably, the additives comprise particles of a plurality of different sizes, optionally of at least 20% difference between them.

The additive may optionally comprise any three-dimensional shape. Non limiting examples of additive shapes optionally include spherical, fibrous, platelet, flake, amorphous, crystalline, semi-sphere, rod, disk or combinations of these shapes or irregular versions of these shapes. Each additive may optionally have an internal or external structural element(s), or a combination thereof, for maintaining the three-dimensional shape of the additive, including but not limited to a beehive, etc.

The additives may optionally be hollow or may be completely solid. Hollow additives preferably comprise a shell that ranges in thickness from a monolayer of atoms to 95% of the radius of the additive. Hollow additives may optionally be filled with a gas. Optionally, the additives may be porous, having holes or pores with varying tortuosity within the additive that can be filled with the base material or other material. Porous additives preferably comprise a solid component that ranges in thickness from a monolayer of atoms to 95% by radius of the additive.

The additive may optionally be a composite of several materials. These materials may optionally be arranged in multiple layers where subsequent layers enclose inner layers or alternatively may be arranged such that the separate layers are in contact with the surrounding base material. The additives may optionally comprise a plurality of stacked layers, whether flat or with curvature; in the latter case, the curvature is preferably determined according to the implant shape. Non-limiting examples of materials that may be combined include glass, ceramics, metals, plastics, and rubbers. For example a glass micro-sphere may be covered with a layer of rubber. More preferably, a blend of polymers is used, for example a blend of a polymer such as PMMA and a rubbery material such as polybutadiene for example.

The additive optionally has varying surface roughness. Optionally, the RMS roughness varies between 0.2nm and 40nm.

Optionally, the additive is a non-solvent liquid such as an oil that forms bubbles inside the base material. Non-solvent liquids of varying viscosities may optionally be used. Optionally, the additive is a non-silicone gel such as a hydrogel.

Optionally, the additive is a gas. Preferably the gas is inert such as nitrogen. Optionally, the gas may comprise oxygen or carbon dioxide. Optionally, the gas is formed as micro-lumens, which may optionally comprise rigid materials, including but not limited to glass, ceramic, etc. Optionally, the micro-lumens are enclosed by a rigid material such as rigid plastic. A non-limiting example of a rigid plastic is Polyether ether ketone (PEEK).

The additives optionally incorporate varying surface interactions from inert to chemical bond interactions with the surrounding base material. Optionally, the additives are free floating, i.e.: not bonded to the base material, and are mechanically constrained by the base material. Optionally, the additives are bonded to the base material with weak bonds such as van der Waals, hydrogen bonds, or ionic interactions. Preferably, the additives are bonded to the base material using chemical bonds. The bonds preferably prevent the base material and the additive(s) from separating into two phases.

The additives are preferably surface treated to enable better bonding with the surrounding base material and prevent slippage or separation into two phases. Also the bonding of additives to the base material causes the base material to surround the additives; in the event of rupture or leakage, without wishing to be limited by a single hypothesis, it is expected that the base material will continue to cover the additives, such that the body would only be exposed to the base material.

Non-limiting examples of surface treatments include: surface anchored long molecular weight chains such as stearic acid, or any other long organic chain, or polymer brushes, hydrophobic or hydrophilic molecules and other such molecules; creation of a charged surface that favors electrostatic attraction for example by the addition of polyelectrolyte to silicone gel; increasing the "roughness" or physical variability of the surface of the additives, such that parts of the surface project out into the base material and hence may interact with the base material; or use of silanes with additives, for example, glass. The organofunctional group of the silane is selected according to the type of interaction that is favorable between the base material and the additive.

Preferably one interface material is used to surface treat the additives. Optionally one or more than one coupling agent is used as a surface treatment with successive coupling agents added on top. Preferably two coupling agents are used. Optionally up to 20 coupling agents may be used. Most cases of surface treatment by organofunctional silanes, zirconates, titanates and other coupling agents result in a polymer-surface interaction. The type of coupling agent is selected according to the surface chemistry of the additive and the chemistry of the base material.

Various other surface treatments and methods for applying these are taught in US Patent Application No. 13/520,356, filed on July 3 2012, hereby incorporated by reference as if fully set forth herein, which is co-owned in common with the present application and which has at least one inventor in common, may also optionally be used, additionally or alternatively.

Optionally, the additives are provided in different concentrations in different areas of the implant. As a non-limiting example, additives adapted for use in ultrasound can have a higher concentration just adjacent to the shell to create a strong echo as described above. As a further non-limiting example, additives adapted for use in mammography can have a higher concentration in the internal parts of the implant in order to create a high degree of radiolucency in the implant.

As a further non-limiting example, additives can have a higher concentration in internal parts of the implant in order to create a diffusion gradient aimed inwards. As a further non-limiting example, additives can also have higher concentration close to the shell in order to serve as a barrier/buffer for diffusion.

As a further non-limiting example, additives can have a higher concentration in internal parts of the implant in order to create a less rigid implant material closer to the surface.

Optionally, additives have the same density as the base material or alternatively, they have a greater density. Additives preferably have a lower density than the surrounding base material.

Preferably, the additives combine any of the characteristics from those listed above to allow a range of embodiments of the present invention encompassing additives of combined and varied sizes, shapes, densities, materials, and structures, with a chosen bonding mechanism to the base material.

The principles and operation of the present invention may be better understood with reference to the drawings and the accompanying description.

Reference is now made to figures 1 and 2 which show non-limiting exemplary embodiments of implants according to the present invention. Any of the above described characteristics of shell material, base material and additives or combinations thereof may optionally be used with the below described structures.

Figure 1 shows a non-limiting example of an illustrative encapsulated prosthetic implant according to at least some embodiments of the present invention. As shown, an implantable prosthesis 100 comprises a low penetratable shell 110 that optionally comprises a biocompatible silicone, polyurethane or other material as is commonly used for implants. Shell 110 may comprise a single layer or multiple layers, wherein some layers may be from one material and others from another. Additionally, shell 110 may be smooth or textured, with various patterns. Shell 110 can have areas of varying elasticity. Shell 110 can have a different thickness in different areas. Optionally, the material of shell 110 may be a combination of several materials. Generally, shell 110 serves as an enclosure for preventing part or all of the content of prosthesis 100 from leaking out. Optionally, shell 110 may be provided in various shapes, for example round, oval, anatomical, custom or other.

Shell 110 contains a base material 120 and at least one additive 140. In this non-limiting example, shell 110 contains a plurality of additives 140, which may optionally comprise any of the characteristics described above. Optionally, the additives are distributed uniformly throughout the base material 120. Optionally, the additives are provided in different concentrations in different parts of the base material 120.

Reference is now made to figure 2 which shows a partially cut-away view of another non-limiting example of an illustrative encapsulated prosthetic implant 200 according to at least some embodiments of the present invention. In this example, an outer shell 202 contains an outer composite material 204, while an inner shell 206 contains an inner composite material 208. Each of outer shell 202 and inner shell 206 may optionally be constructed from a silicone elastomeric material as described herein, optionally with a plurality of layers and also optionally with a barrier layer. Outer shell 202 may optionally feature any of a smooth, non-textured surface; a textured surface; or a micro polyurethane foam coated surface. Surface texturing has been shown to reduce the incidence and severity of capsular contraction. Inner shell 206 is preferably smooth but may also optionally be textured.

Outer composite material 204 preferably features additives adapted for use in ultrasound which have a higher concentration to create a strong echo as described above. Inner composite material 208 preferably features additives adapted for use in mammography with a high degree of radiolucency as described above.

Alternatively, outer composite material 204 preferably features additives having a higher concentration close to the shell in order to serve as a barrier/buffer for diffusion as described above. Inner composite material 208 preferably features a higher concentration of additives as the distance from inner shell 206 increases in order to create a diffusion gradient aimed inwards as described above.

Alternatively, outer composite material 204 preferably features a lower concentration of reinforcing additives to create a less rigid implant material closer to the surface. Inner composite material 208 preferably features a higher concentration of additives and therefore greater reinforcement. Alternatively, inner composite material 208 features a higher concentration of additives as the distance from inner shell 206 increases

Optionally, each of outer shell 202 and inner shell 206 is closed with a patch made of the same silicone elastomers as the respective shell 202 and 206, and glued using an adhesion component, with small silicone cap 210 on the inner side of the posterior patch 212, used for filling the implant with the composite material. Optionally. Inner shell 206 is situated concentrically within outer shell 202 and glued to it at a base 214.

Various other arrangements of the shell and/or other components which are taught in US Patent Application No. 20090299473, filed on April 24 2006, hereby incorporated by reference as if fully set forth herein, which is co-owned in common with the present application and which has at least one inventor in common, may also optionally be used, additionally or alternatively.

Reference is now made to figures 3A and 3B which are mammography images of respectively a breast with a prior art implant and a breast with the implant of the presently claimed invention. As shown in the mammogram 300, the prior art implant 302 appears completely white (opaque to x-ray) showing no detail of the tissue in front of it or behind it. Breast tissue 304 not obscured by the implant is visible in the mammogram 300.

By contrast, in the mammogram 310 of the breast 314 with the implant 312 of the presently claimed invention, tissue 316 of the breast is visible through the implant 312 due to the presence of radiolucent additives as described above.

Reference is now made to figures 4A and 4B which are mammography images of breast implants on top of a marked localization paddle and a turkey breast. Figure 4A shows a prior art implant and figure 4B shows an implant according to the presently claimed invention. Both mammograms were performed under the same thickness and exposure parameters.

As shown in figure 4A, in mammogram 400, prior art implant 402 almost completely obscures localization paddle 404. By contrast, in figure 4B, mammogram 410 shows the implant 412 of the presently claimed invention, where the lettering on localization paddle 414 is visible through the implant 412. This is due to the radiolucency of the additives in implant 412 as described above.

Reference is now made to figures 5A-5D which are ultrasound images of breasts with prior art implants (5A, 5C) and implants of the presently claimed invention (5B, 5D). As shown in figure 5A, the shell 502 of a prior art implant is visible in an ultrasound image 500 captured with a 12MHz probe.

The top of image 500 is the interface of the probe with the skin. Then there is a representation of tissue 502 comprising skin, fat, glands and other tissue, followed by the shell of the silicone implant 504. The gel 508 is seen as the black area. Reverberations seen as visual noise 506 caused by the implant are also visible in image 500 in the area which should be black (the gel 508). This noise is seen extending 1.5 cm into the area of the image 500. The noise also extends above the shell creating a cloud like snow over the tissue area 502 of the image which is intended for diagnosis.

By contrast, the 12 MHz ultrasound 510 of the breast with the implant of the presently claimed invention, shows very little visual noise 516, and the tissue 512, shell 514, and implant material 518 are not obscured by noise as found in ultrasound 500.

Similarly, figure 5C shows an ultrasound image 520 captured with a 17MHz probe where both the implant shell 522 and the visual noise caused by the implant 524 are visible. The echoic borders at the interface of shell 522 appear thick, presenting a shell that is thicker than it actually is to the radiologist. By contrast, the 17 MHz ultrasound 530 of the breast with the implant of the presently claimed invention, shows far less visual noise 534, and the tissue 532, shell 534, and implant material 538 are not obscured or distorted by noise as found in ultrasound 520.

Reference is now made to figures 6A-6B which are photographs and a graph showing comparative solvent diffusion of a prior art implant gel and the composite implant material of the presently claimed invention. Figure 6A shows a table 600 with rows as follows: time elapsed row 602, prior art gel row 604 and composite implant material row 606. Each of rows 604 and 606 show progressive photographs of equal sized samples of gel/composite material laid on absorbent paper 610. Gel 612 is from a prior art implant and composite material 614 is the composite implant material of the presently claimed invention comprising additives to reduce diffusion.

Column 622 shows photographs taken at time = 0, i.e.: immediately after setting the gel/material in place; Column 623 shows the same materials photographed after 2 day and 7.5 hours; Column 624 shows the same materials photographed after 5 days and 4 hours; Column 625 shows the same materials photographed after 17 days and 10 hours; Column 626 shows the same materials photographed after 33 days and 17 hours; and Column 627 shows the same materials photographed after 82 days and 19 hours.

Figure 6B shows a graph 650 that plots the elapsed time 602 (in hours) against the calculated wetted area 652 (in mm^2) of the absorbent paper 610 as shown in the photographs of figure 6A.

As shown in column 623 after 2 days and 7.5 hours, solvent from prior art gel 612 has diffused significantly more than solvent from the composite material 614 of the presently claimed invention. The difference is evident from the greater diameter of diffused prior art solvent 616 compared to the diameter of diffused solvent 618 from the presently claimed invention. Similarly, in columns 624-627 solvent from prior art gel 612 has diffused significantly more than solvent from the composite material 614 of the presently claimed invention. Graph 650 shows the greater diffusion of prior art gel solvent (line 654) compared to the solvent in the composite material of the presently claimed invention (line 656).

It should be noted that the absorbent paper 610 is not comparable to the human body since the solvent (on the paper) is not removed and therefore the rate of diffusion (on the paper) is actually slowed. In the human body, a large portion of the solvent is removed or spreads through various biological mechanisms and the diffusion gradient remains high. Nevertheless, the absorbent paper 610 illustrates the significant difference between the prior art and the composite material of the current invention.

Over a longer time therefore, there are significant differences in the amount of total solvent that can be potentially released into the body. The composite material of the presently claimed invention has a slower rate of diffusion and a significantly smaller overall amount of solvent to release. This could potentially show up as less likelihood of lymphadenopathy, even in case of a rupture.

Reference is now made to figure 7 which is a set of rheology graphs showing comparative elastic modulus of a prior art implant gel and three alternative composite materials as per the presently claimed invention. Rheological characterization provides a measure of storage modulus (G') as a function of shear rate (frequency measured in Hz or rad/s). The graph shows rheological characteristics for four different materials where 702 is a rheology graph for a prior art implant gel and 704, 706 and 708 are rheology graphs for implant materials of the presently claimed invention – each comprising different additives in different concentrations.

As shown, the implant materials of the presently claimed invention display increasing elastic modulus compared to the prior art implant gel (graph 702), with the composite material of graph 708 showing the most increased elastic modulus.

While the invention has been described with respect to a limited number of embodiments, it is to be realized that the optimum dimensional relationships for the parts of the invention, to include variations in size, materials, shape, form, function and manner of operation, assembly and use, are deemed readily apparent and obvious to one skilled in the art, and all equivalent relationships to those illustrated in the drawings and described in the specification are intended to be encompassed by the present invention.

Therefore, the foregoing is considered as illustrative only of the principles of the invention. Further, since numerous modifications and changes will readily occur to those skilled in the art, it is not described to limit the invention to the exact construction and operation shown and described and accordingly, all suitable modifications and equivalents may be resorted to, falling within the scope of the invention.

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Having described a specific preferred embodiment of the invention with reference to the accompanying drawings, it will be appreciated that the present invention is not limited to that precise embodiment and that various changes and modifications can be effected therein by one of ordinary skill in the art without departing from the scope or spirit of the invention defined by the appended claims.

Further modifications of the invention will also occur to persons skilled in the art and all such are deemed to fall within the spirit and scope of the invention as defined by the appended claims.

While the invention has been described with respect to a limited number of embodiments, it will be appreciated that many variations, modifications and other applications of the invention may be made.

Throughout the specification and claims, unless the context requires otherwise, the word “comprise” or variations such as “comprises” or “comprising”, will be understood to imply the inclusion of a stated integer or group of integers but not the exclusion of any other integer or group of integers.

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What is claimed is:

1. A prosthetic implant when used for implantation to the human body, comprising a composite material which comprises a base material and a plurality of additives, wherein,

a) said additives are selected from radiolucent additives and/or hyperechoic additives;

b) said additives are selected such that the elastic modulus at 1 Hz of said composite material is greater than the elastic modulus of said base material, and wherein the elastic modulus is greater than the elastic modulus of said base material by at least 20%;

c) said additives have a surface roughness of between 0.2 nm and 40 nm $R_{RM}S$; and

d) said additives are up to 500 microns in size with at least 20% size difference between them.

2. The implant of claim 1, wherein said additives are selected from the group consisting of:

a) additives comprising at least one of glass, ceramic, metal, polymers, PMMA, poly aery lonitrile, polybutadiene, PEEK, natural rubber, synthetic rubber, amorphous polymer or semi-crystalline polymer;

b) additives comprising a three-dimensional shape comprising spherical, fibrous, platelet, flakes, amorphous, crystalline, semi-sphere, rod, disk or combinations of these shapes or irregular versions of these shapes;

c) hollow additives;

d) porous additives;

e) solid additives;

f) additives comprising at least 2 materials;

g) additives comprising a gas;

h) additives comprising a non-solvent liquid;

i) additives comprising a non-silicone gel;

j) additives formed as a micro -lumen; and

k) a combination of the above.

3. The implant of claim 1 or claim 2, wherein said base material comprises a silicone gel.

4. The implant of any one of claims 1-3, comprising a plurality of shells, including at least one inner shell and at least one outer shell; wherein said at least one inner shell is at least

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partially surrounded by said outer shell; wherein said outer shell is filled with said base material and a plurality of hyperechoic additives, and wherein said inner shell is filled with said base material and a plurality of radiolucent additives.

5. A composite material when used for implantation to the human body, comprising a base material and a plurality of additives, wherein;

a) said additives are selected from radiolucent additives and/or hyperechoic additives;

b) said additives are selected such that the elastic modulus at 1 Hz of said composite material is greater than the elastic modulus of said base material, and wherein the elastic modulus is greater than the elastic modulus of said base material by at least 20%;

c) said additives have a surface roughness of between 0.2 nm and 40 nm $R_{RM}S$; and

d) said additives are up to 500 microns in size with at least 20% size difference between them.

6. The composite material of claim 5, wherein said additives comprise up to 60% by volume of the composite material.

7. The composite material of claim 5, wherein said additives comprise up to 90% by volume of the composite material.

8. The composite material of claim 5, wherein said base material is silicone gel.

9. The implant of any one of claims 1-4, wherein said additives are selected such that the solvent concentration of said composite material is between 5%-95% of the solvent concentration of said base material.

10. The implant of claim 9, wherein said base material comprises a silicone gel.

11. The implant of claim 9, comprising a plurality of shells, including at least one inner shell and at least one outer shell; wherein said at least one inner shell is at least partially surrounded by said outer shell; wherein said outer shell is filled with said base material and a higher concentration of additives closer to said outer shell, and wherein said inner shell is

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filled with said base material and an increasing concentration of additives relative to the distance from said inner shell.

12. The composite material of claim 5, wherein said additives are selected such that the solvent concentration of said composite material is 5%-95% of the solvent concentration of said base material.

13. The composite material of claim 12, wherein said additives comprise up to 60% by volume of the composite material.

14. The composite material of claim 12, wherein said additives comprise up to 90% by volume of the composite material.

15. The composite material of claim 12, wherein said base material is silicone gel.

16. The implant of any one of claims 1-4 or claims 9-11, wherein said additive are selected such that the elastic modulus at 1 Hz of said composite material is between 20%-5000% greater than the elastic modulus of said base material.

17. The implant of any one of claims 1-4 or claims 9-11, wherein the elastic modulus is between 100% and 1000% greater than the elastic modulus of said base material.

18. The implant of any one of claims 1-4 or claims 9-11, wherein the elastic modulus is between 100% and 500% greater than the elastic modulus of said base material.

19. The implant of any one of claims 1-4, claims 9-11 or claims 16-18, comprising a plurality of shells, including at least one inner shell and at least one outer shell; wherein said at least one inner shell is at least partially surrounded by said outer shell; wherein said outer shell is filled with said base material and a low concentration of additives, and wherein said inner shell is filled with said base material and a high concentration of additives.

20. The composite material of claim 5, wherein said additives are selected such that the elastic modulus at 1 Hz of said composite material is 20%-5000% greater than the elastic modulus of said base material.

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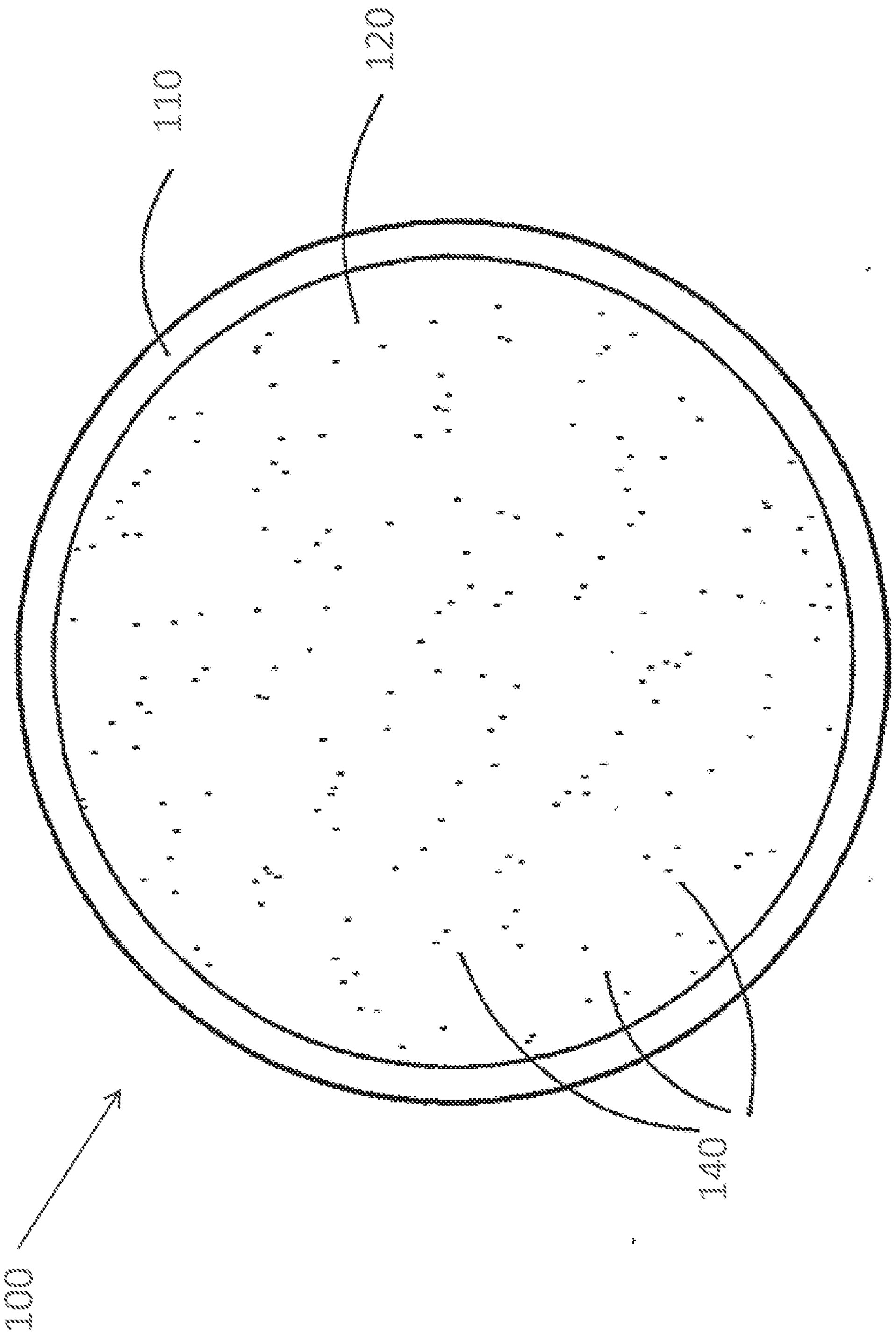

Fig. 1

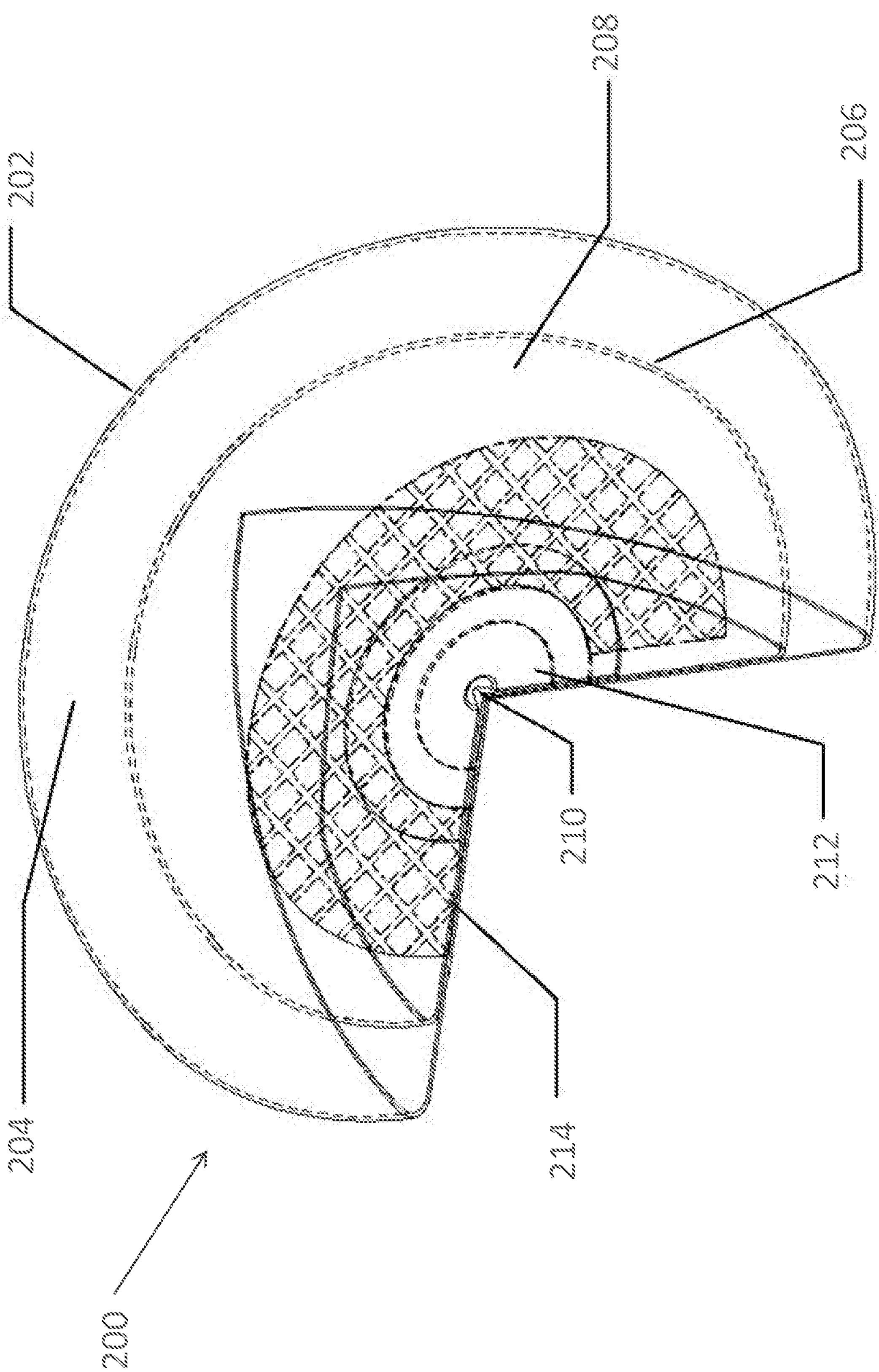

Fig. 2

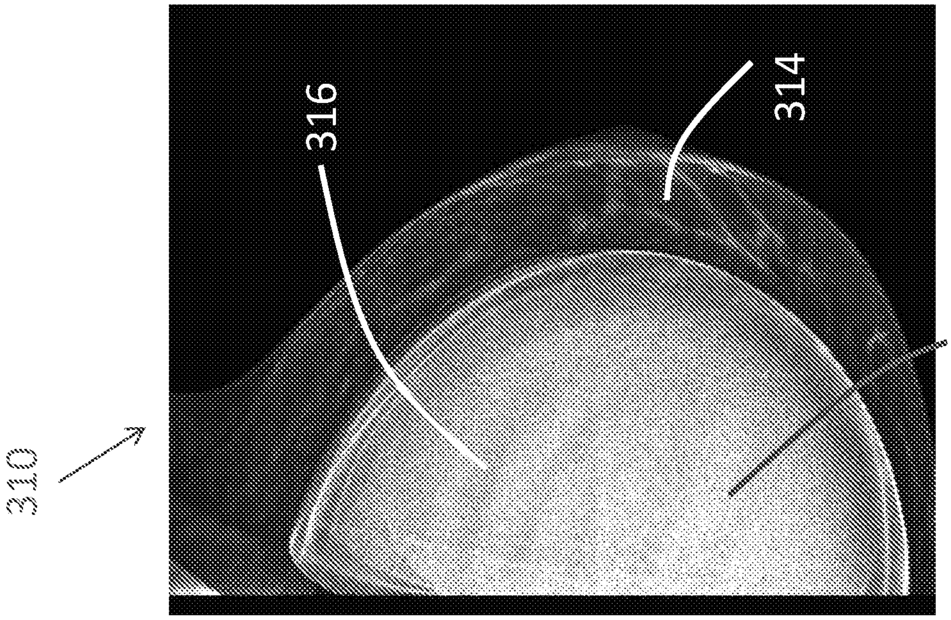

Fig. 3B

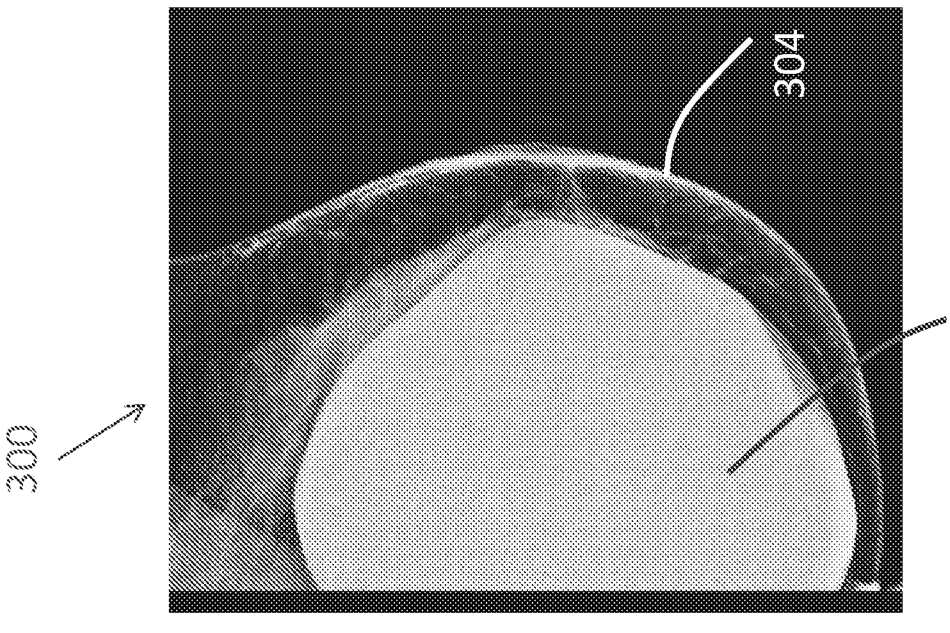

Fig. 3A
Prior Art

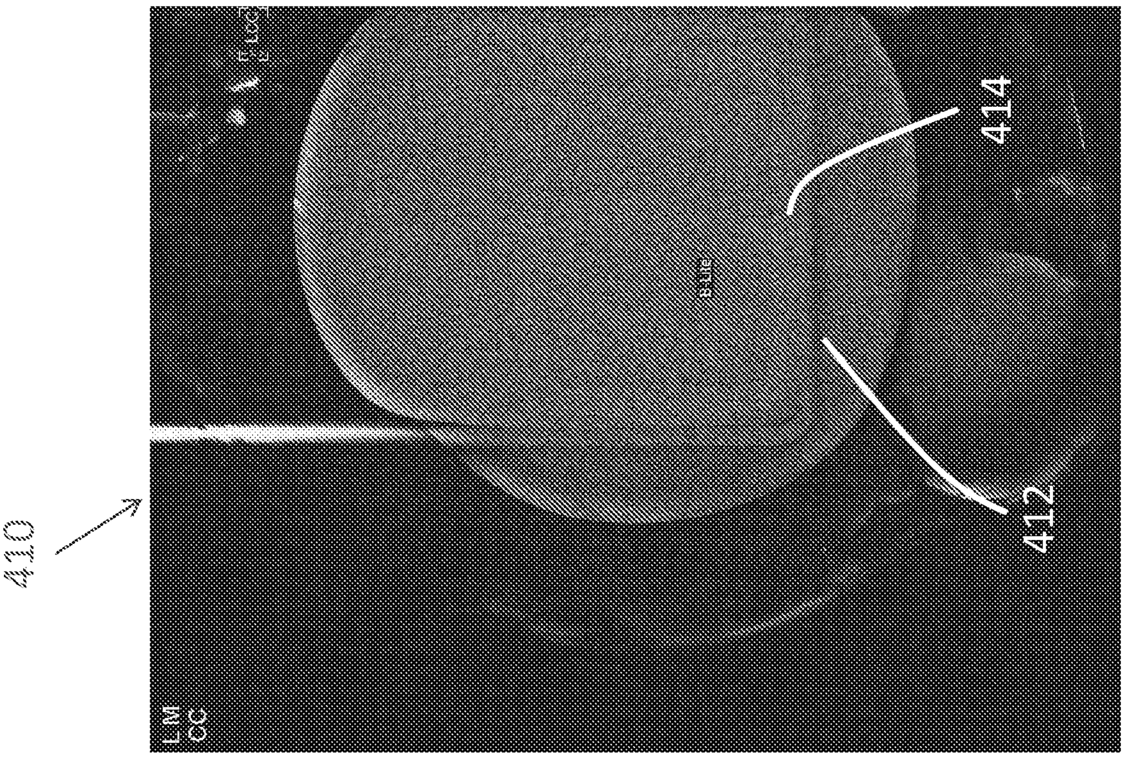

Fig. 4B

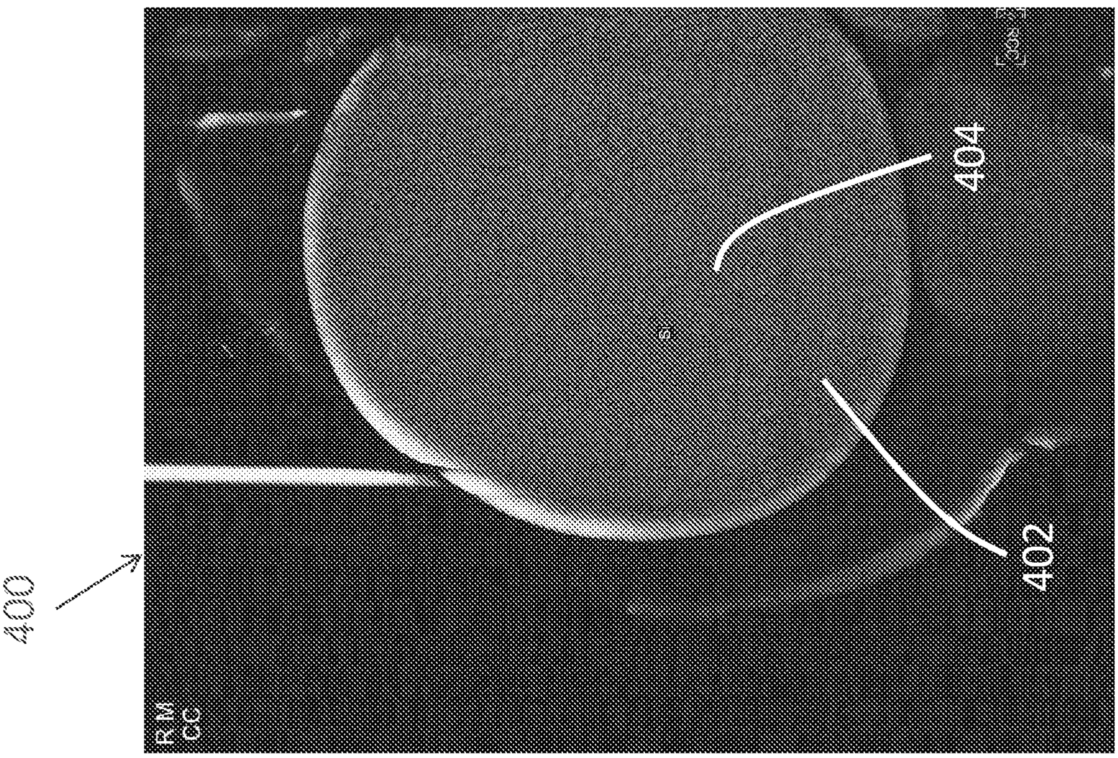

Fig. 4A
Prior Art

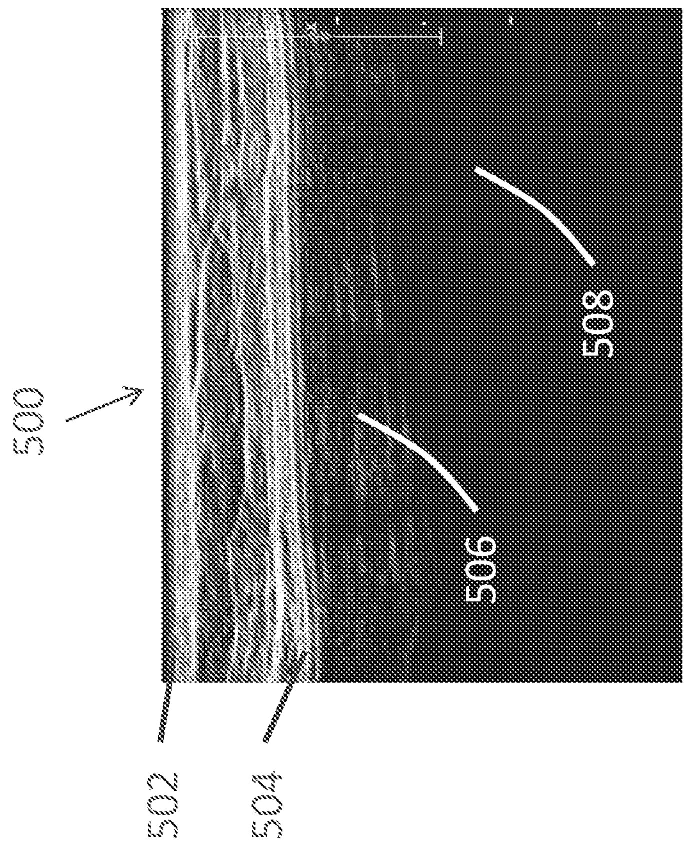

Fig. 5A
Prior Art

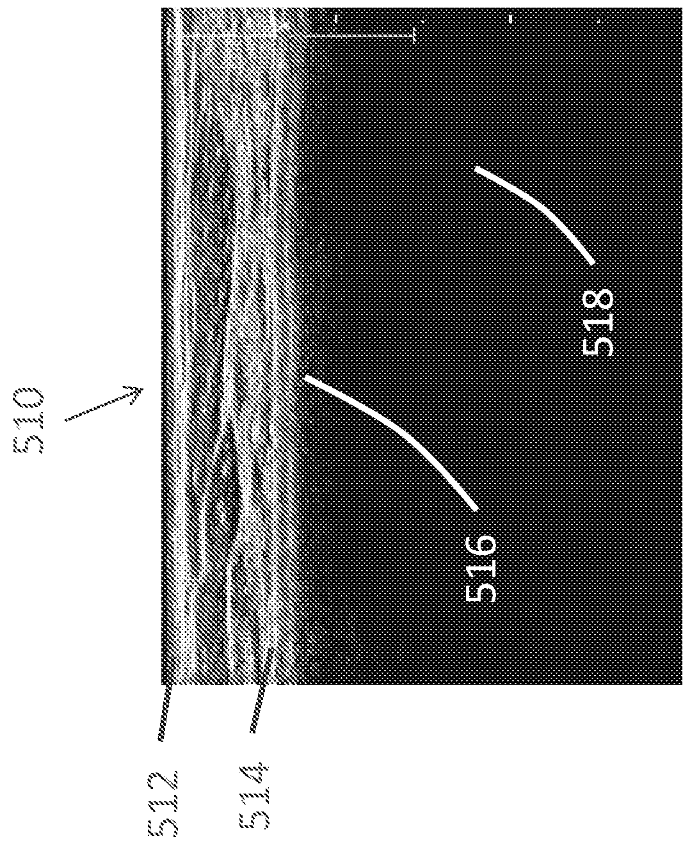

Fig. 5B

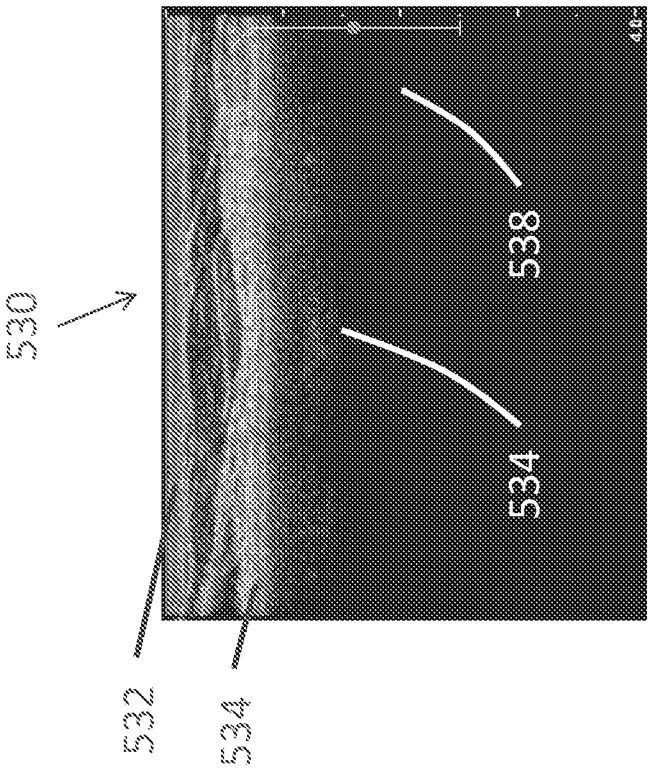

Fig. 5D

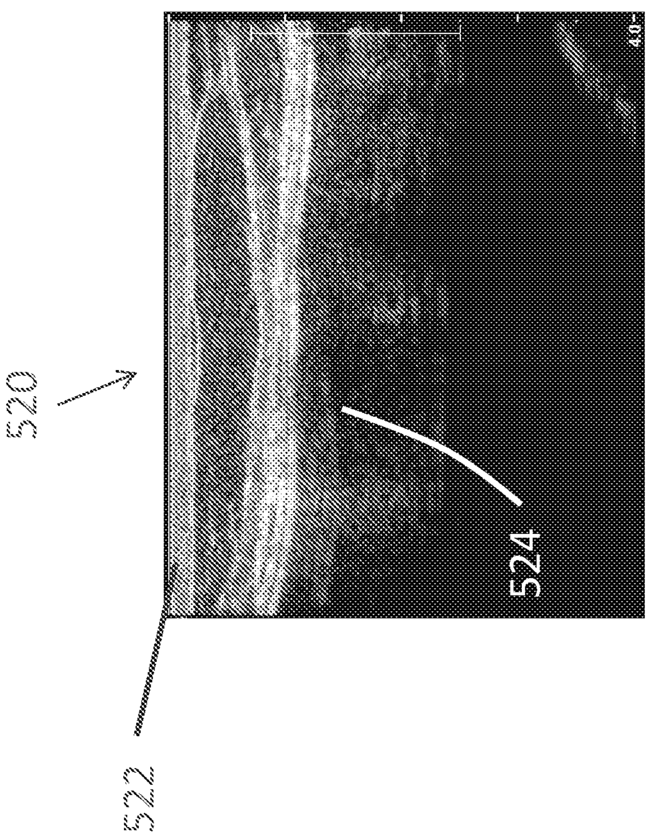

Fig. 5C
Prior Art

600

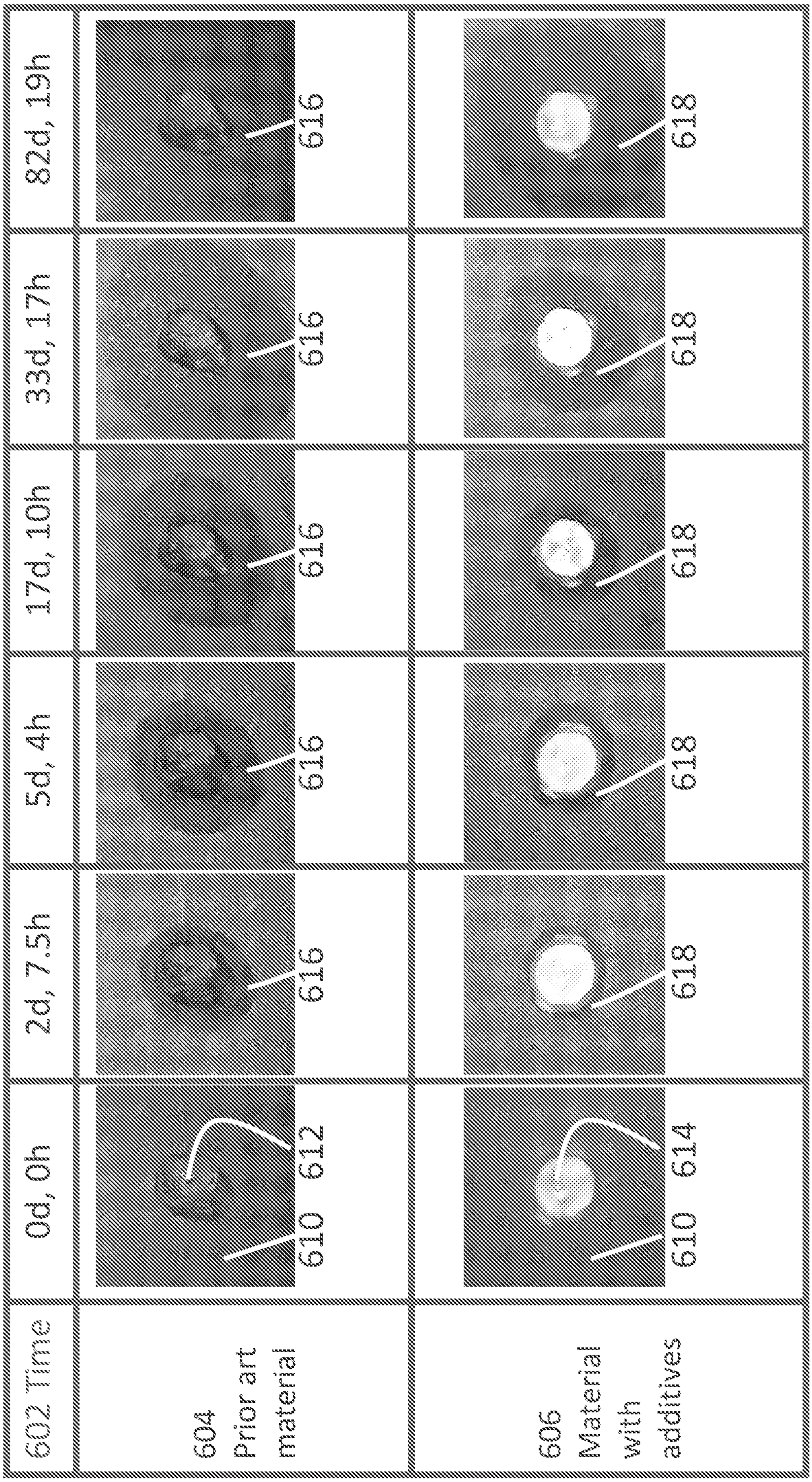
602 Time
604 Prior art material
606 Material with additives
622
0d, 0h
610
612
614
623
2d, 7.5h
624
5d, 4h
625
17d, 10h
626
33d, 17h
627
82d, 19h
616
618

Fig. 6A

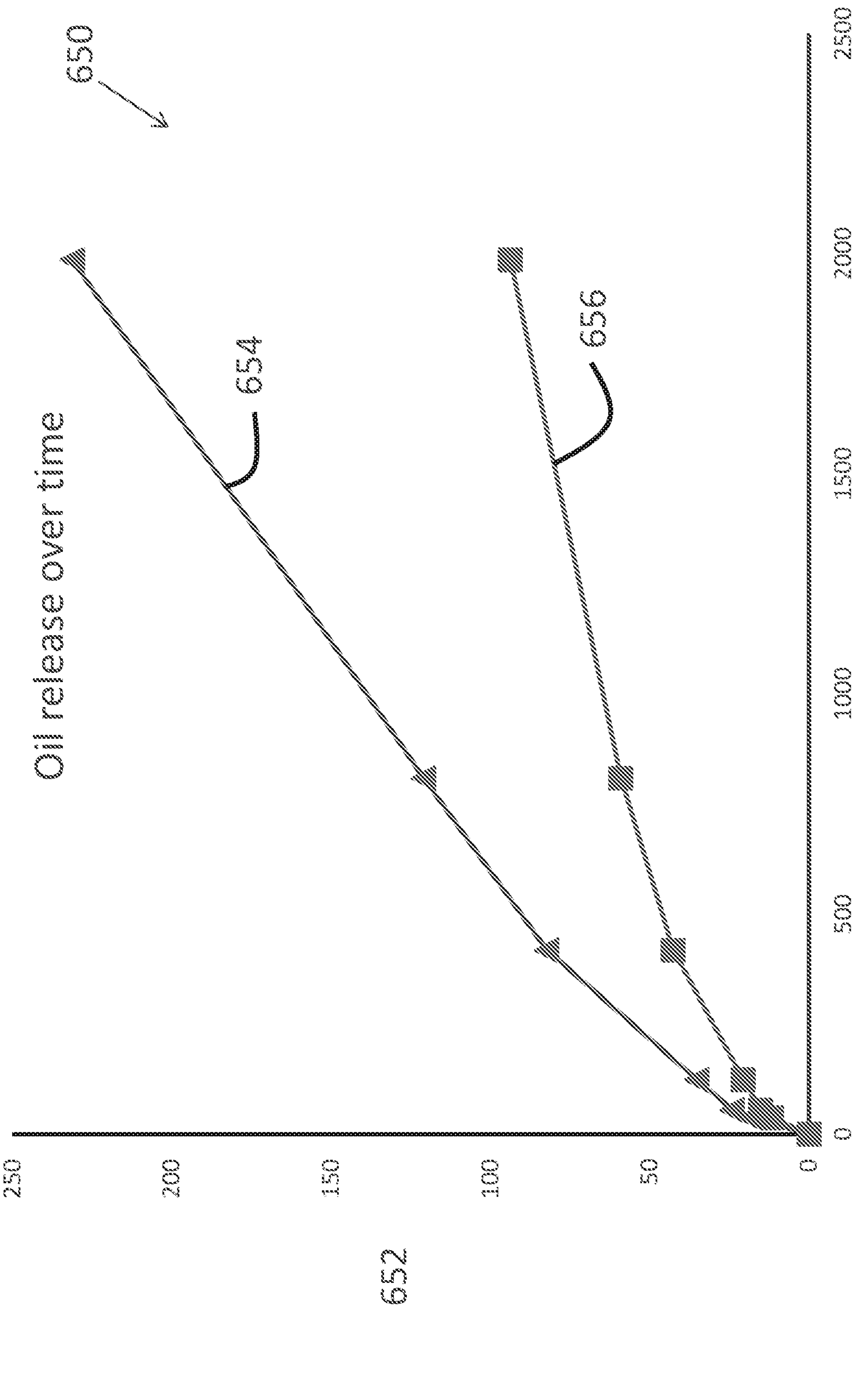
Oil release over time
650
654
656
652
602
0
50
100
150
200
250
0
500
1000
1500
2000
2500

Fig. 6B

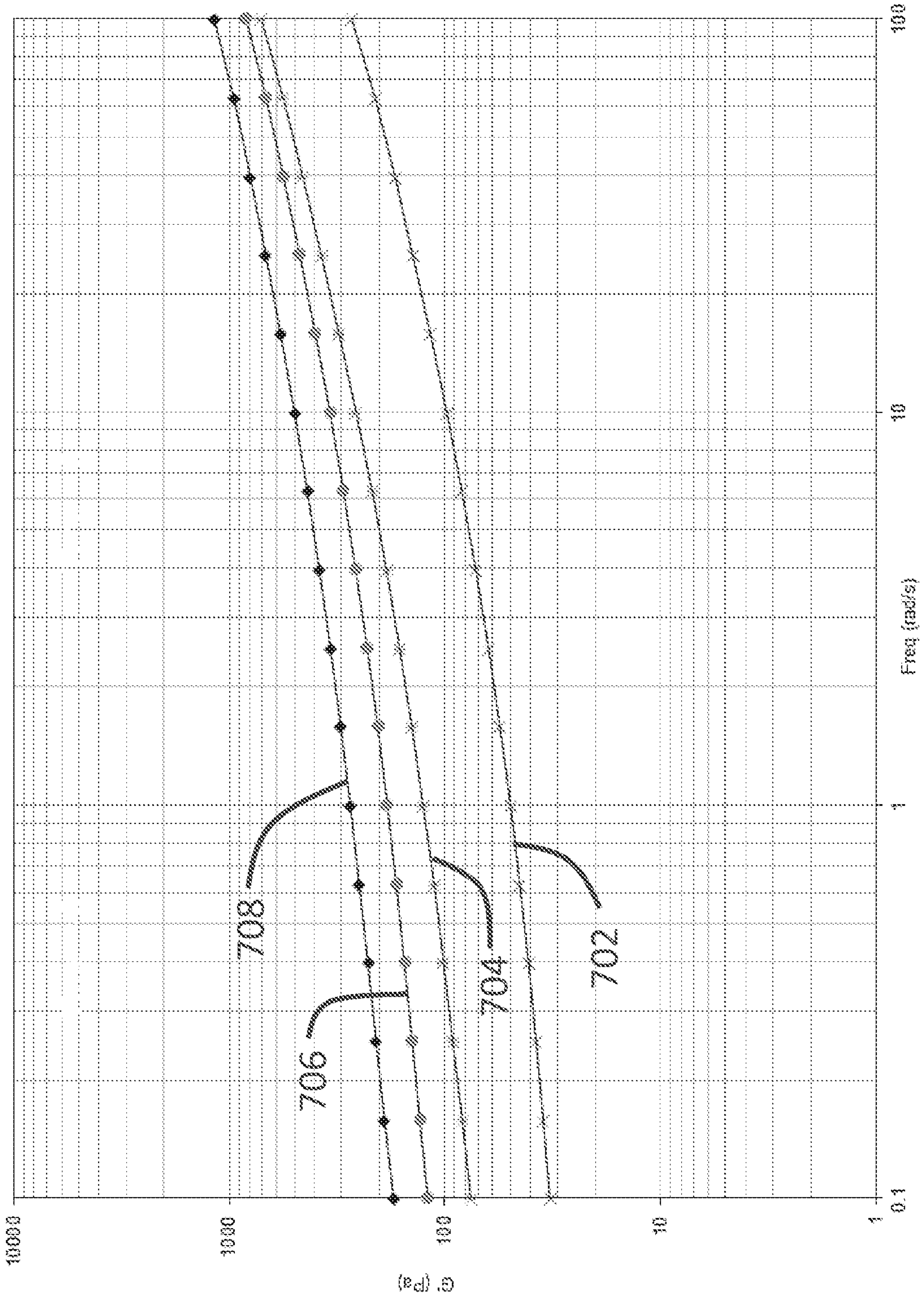

Fig. 7