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## (54) Title: WEAR RESISTANT POLYMER COMPOSITION

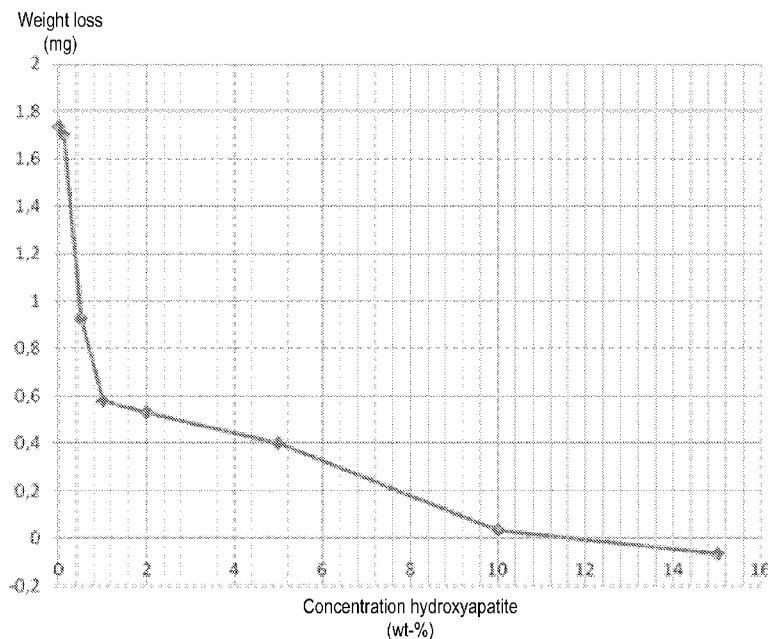


Fig. 1

(57) **Abstract:** A polymer composition with improved abrasion resistance is obtained by adding hydroxyapatite particles to a polymer material selected from silicone, polyurethane and combinations thereof at a concentration of from 0.5 up to 10 % by weight of the polymer composition. The polymer composition is suitable for manufacture of insulating articles to be employed in implantable medical devices.

**WEAR RESISTANT POLYMER COMPOSITION****TECHNICAL FIELD**

The present invention generally relates to polymer compositions and the use thereof, and in particular  
5 to such polymer compositions having improved wear resistance.

**BACKGROUND**

Implantable medical leads and catheters come in various models and for various purposes. For instance, the implantable medical leads and catheters can be used to apply therapy to a subject in the  
10 form of delivering pacing pulses and/or defibrillation shocks generated by an implantable medical device, such as pacemaker, defibrillator or cardioverter, and transferred to the target tissue in the subject by an implantable medical lead or catheter. A further variant is an implantable medical lead and catheter capable of delivering medicaments to a subject, such as in the form of a so-called slow-release device.

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The implantable medical leads and catheters can alternatively or in addition be employed for diagnostic purposes, for instance by sensing or monitoring various characteristics in the subject's body. The implantable medical lead or catheter can then be equipped with electrodes in order to sense electrical activity from the target tissue and/or be equipped with dedicated sensors that monitor various  
20 characteristics, such as blood pressure, blood flow, oxygen concentration, blood glucose concentration, etc.

The implantable medical leads and catheters generally have an elongated lead or catheter body that is typically made of an insulating polymer material. The polymer material of the lead or catheter body  
25 must have certain properties in order to be used inside an animal or human body. For instance, the polymer material should of course be non-toxic and preferably be as biocompatible as possible to not cause any deleterious reactions when introduced into the animal or human body. Also mechanical properties of the polymer material of the lead or catheter body are important, such as flexibility, mechanical strengths, etc.

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Today common polymer materials employed in implantable medical leads and catheters include silicone rubber, polyurethanes and variants thereof. Silicone rubber, such as polydimethylsiloxane (PDMS), is a commonly used polymer. Silicone rubber has a very low glass transition temperature and is therefore less temperature sensitive than other rubbers. It exhibits low surface energy and has good

resistance to hydrolytic and enzymatic degradation in animal and human bodies. Silicone rubber has, additionally, good compatibility with blood. Because of the excellent flexibility, elasticity, bio-inertness, biocompatibility, low surface tension, stability and lack of toxicity, silicone rubber is used in numerous implantable medical leads and catheters on the market. A limitation with this polymer material is, 5 however, its poor mechanical strength.

Polyurethanes are block copolymers with alternating hard and soft blocks. The hard blocks have glass transition temperature above room temperature and impart glassy properties to the material. The soft blocks have glass transition temperature below room temperature and hence impart rubbery 10 characteristics to the material. The soft blocks are therefore responsible for the flexibility of the material, whereas the hard blocks are responsible for the mechanical strength. Polyurethanes additionally have good fatigue and blood-compatibility properties.

Recently copolymers of silicone rubber and polyurethane have been developed and are available on 15 the market under the tradename of Optim®. The copolymers have the mechanical strength and abrasion resistance of polyurethanes but the rubbery flexibility of silicone. A lead body made of Optim® will be almost as soft and flexible like silicone rubber but has a lower surface friction. It is also the most biostable material currently known of all polyurethane materials.

20 There is, however, still a need to improve the polymer materials of implantable medical leads and catheters and in particular with regard to enhancing the wear resistance of the material. When the implantable medical lead or catheter is implanted in the animal or human body it can be exposed to wearing between the lead or catheter and the implantable medical device, to which the lead or catheter is connected. The implantable medical device typically has a housing made of metal, such as titanium, 25 that can wear against the insulating polymer material of the lead or catheter. Additionally, some subjects have multiple implantable medical leads or catheters. In such a case, also lead/catheter against lead/catheter wearing can occur.

In the worst case, the insulating polymer material of the implantable medical lead or catheter can be 30 worn off on some parts of the implantable medical lead or catheter. The lead or catheter must then typically be replaced with a new lead or catheter and possibly explanted from the animal or human body. This implies a new surgical procedure for the subject. Thus, the implantable medical leads and catheters would benefit from having insulating polymer materials with improved wear resistance.

Materials Letters (2008) 62:3307-3309 discloses the usage of a nanocomposite comprising n-hydroxyapatite and silicone rubber. The ratio of n-hydroxyapatite in the nanocomposite is 30, 40, 50 or 60 %. Inclusion of n-hydroxyapatite improves the mechanical properties of the silicone rubber as is seen by the increased strength for n-hydroxyapatite concentrations of 40 and 50 %.

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Journal of Materials Science Letters (2003) 22:343-344 discloses the usage of hydroxyapatite for improving the blood compatibility of silicone rubber. A hydroxyapatite content of 30-70 % was evaluated and the tensile and tear strength improved in particular for 50-60 % hydroxyapatite. The blood compatibility also improved with 50-60 % hydroxyapatite.

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### SUMMARY

It is a general objective to improve wear resistance of polymer materials.

It is a particular objective to provide a polymer composition with improved wear resistance for use in  
15 implantable medical devices.

These and other objectives are met by embodiments disclosed herein.

An aspect of the embodiments relates to a polymer composition comprising a polymer material  
20 selected from silicone, polyurethane and combinations thereof, optionally including other polymers and constituents. The polymer composition comprises hydroxyapatite particles at a concentration of from 0.5 up to 10 % by weight of the polymer composition.

The added hydroxyapatite particles will improve the wear and abrasion resistance of the polymer  
25 material. This improvement in abrasion resistance comes without any negative effects in terms of water absorption by the polymer composition, which occurs at hydroxyapatite particle concentrations above 10 % by weight.

The polymer composition is advantageously employed to manufacture articles and devices to be used  
30 in implantable medical devices that are implanted in animal or human bodies. The polymer composition is particularly suitable for manufacturing insulating articles, such as insulating tubes of implantable medical leads.

## BRIEF DESCRIPTION OF THE DRAWINGS

The invention, together with further objects and advantages thereof, may best be understood by making reference to the following description taken together with the accompanying drawings, in which:

5

Fig. 1 is a diagram illustrating abrasion resistance for a co-polymer of silicone and polyurethane at varied concentrations of hydroxyapatite;

Figs. 2A and 2B are 1000× magnifications of hydroxyapatite microparticles (Fig. 2A) or nanoparticles  
10 (Fig. 2B) employed according to the embodiments;

Figs. 3A and 3B are 1000× magnifications of a polymer composition of a co-polymer of silicone and polyurethane doped with 5 % by weight of hydroxyapatite microparticles (Fig. 3A) or nanoparticles (Fig. 3B);

15

Fig. 4 schematically illustrates an insulating tube according to an embodiment;

Fig. 5 is a schematic overview of an implantable medical lead according to an embodiment connectable to an implantable medical device; and

20

Fig. 6 is a cross-sectional view of a distal portion of an implantable medical lead according to an embodiment.

## DETAILED DESCRIPTION

25 Throughout the drawings, the same reference numbers are used for similar or corresponding elements.

The present embodiments generally relate to polymer compositions having improved abrasion and wear resistance and the use of such polymer compositions in manufacturing articles of implantable medical devices, including implantable medical leads and catheters.

30

The present embodiments utilize hydroxyapatite (HA), also denoted as hydroxylapatite, which is a calcium apatite with the formula  $\text{Ca}_5(\text{PO}_4)_3\text{OH}$  but is usually written as  $\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2$ . Hydroxyapatite is, according to the embodiments, added to various polymer compositions, similar to a dopant, to achieve desired material properties in terms of improved abrasion or wear resistance.

The embodiments are based on the discovery that small amounts of hydroxyapatite added to polymer compositions will have positive effects. This was highly surprising since the prior art utilizes addition of very high concentrations of hydroxyapatite, i.e. 40-60 %, to impart target effects on the polymer material. The inventors have discovered that sub-percentage up to a few percents of hydroxyapatite is indeed sufficient to achieve improved abrasion or wear resistance but without negative effects that the high concentration of hydroxyapatite according to the prior art impart on the polymer material.

An aspect of the embodiments therefore relates to a polymer composition comprising a polymer material and having hydroxyapatite particles at a concentration of from 0.5 up to 10 % by weight of the polymer composition. Experimental results as presented herein illustrate that 0.5 % by weight is a lower limit in order to achieve any significant improvement of the abrasion or wear resistance of the polymer composition. The upper limit of 10 % by weight is defined by unexpected negative effects that the hydroxyapatite doping causes to the polymer composition. Thus, at concentrations of more than 10 % by weight the hydroxyapatite particles in the polymer composition cause the polymer composition to absorb water and medium from the surrounding. This was very surprising in the light of the prior art uses of hydroxyapatite at concentrations 4 to 6 times higher than this upper limit of 10 % by weight. The water absorption caused by too high concentrations of hydroxyapatite particles in the polymer composition, i.e. above 10 % by weight, could alter the electrical and mechanical characteristics of the polymer composition, and may additionally affect the biostability of the polymer composition.

The polymer compositions according to the embodiments are electrically insulating and are advantageously employed as electrical insulators in implantable medical devices. It is therefore important that the polymer composition does not become electrically conducting due to water and ion absorption caused by addition of hydroxyapatite particles. Up to the upper limit of 10 % by weight there is no significant uptake of any water or medium in the polymer composition or any significant effect in the electrically insulating properties of the polymer composition.

Water uptake in the polymer composition may additionally affect various mechanical properties of the polymer composition and in particular cause a gradual change in such mechanical properties over time as more and more water is taken up by the polymer composition. Such a gradual change in mechanical properties during the use of the polymer composition in a water-containing environment, such as implanted in an animal or human body, will make it hard to predict how the polymer composition will perform over time.

A further disadvantage of increased water or medium uptake, in particular for implantation applications, is that increased water content can alter the physical characteristics of the polymer composition and articles and devices made of the polymer composition. For instance, water molecules taken up in the polymer composition can promote binding of proteins to the polymeric articles or devices. Depending on the interaction between the surface of the polymeric articles and devices and the proteins the adsorption often causes conformational change of the proteins. This is of importance since the conformation change can expose hidden epitopes, which may be responsible for initiating reactions such as inflammation, coagulation and foreign body response that eventually may lead to fibrous encapsulation. Also various cells will be recruited and adhere to the surface of the polymeric articles or devices, possibly via the adsorbed proteins. As a consequence, a thrombus will be formed due to the accumulation of blood components including proteins and cells. The thrombus will over time start to fibrose and calcify into a tough fibrous capsule. This process causes the polymeric article or device to adhere to the tissue, as for example the vascular wall. The tissue adherence will increase the risk of damaging the tissue when extracting the polymeric article or device.

The present embodiments are, however, not marred by these water-absorption related problems by limiting the upper concentration of hydroxyapatite particles to 10 % by weight.

Hydroxyapatite particles included in the polymer composition may, however, affect physical properties of the polymer composition even at concentrations that do not exceed 10 % by weight. It is particularly optical properties of the polymer compositions that become affected in terms of reduced transparency for higher hydroxyapatite concentrations. Thus, the experiments conducted herein confirm that the transparency of polymer compositions doped with hydroxyapatite concentrations of more than 5 % by weight will be reduced and the polymer compositions become opaque, typically white, for hydroxyapatite concentrations in the interval 5 to 10 % by weight. Polymer compositions with a concentration of hydroxyapatite below 5 % and in particular below 2.5 % or 2 % basically have the same transparency as the undoped polymer material.

A particular embodiment therefore relates to a polymer composition with hydroxyapatite particles provided at a concentration from 0.5 up to 5 % by weight of the polymer composition. The hydroxyapatite particles are more preferably provided at a concentration of from 0.5 up to 2.5 % by weight of the polymer composition, such as from 0.5 up to 2 % by weight of the polymer composition. In these embodiments, the transparency of the doped polymer composition will basically be defined and

limited by the transparency and optical characteristics of the polymer material. The hydroxyapatite particles will therefore have no or at least very low effect on the transparency of the polymer composition.

- 5 The abrasion or wear resistance of the polymer composition is, as is further disclosed herein, doubled with 0.5 % hydroxyapatite as compared to no hydroxyapatite at all or smaller concentrations of hydroxyapatite, i.e. 0.1 % by weight of the polymer composition. Increasing the hydroxyapatite concentration further leads to a further significant improvement of abrasion or wear resistance at 1 % by weight of the polymer composition. Further increase in hydroxyapatite concentration in the interval  
10 of from 1 % up to 5 % improves the abrasion or wear resistance even further but the improvement is not as large as compared to going from 0.5 % to 1 % hydroxyapatite. A particular embodiment therefore relates to polymer compositions comprising hydroxyapatite particles at a concentration from 1 up to 10 % by weight of the polymer composition, preferably from 1 % up to 5 %, more preferably from 1 % up to 2.5 % and in particular from 1 % up to 2 % by weight of the polymer composition. At these  
15 latter preferred concentration intervals, significant improvements are achieved in terms of abrasion or wear resistance but without any negative water uptake in the polymer composition or any significant impact to the transparency of the polymer material due to the hydroxyapatite particles.

The hydroxyapatite particles can have an average size in the nanometer range or in the micrometer  
20 range. It is generally preferred to have smaller hydroxyapatite particles, i.e. in the nanometer range, since larger hydroxyapatite particles seem more prone to cause water uptake by the polymer composition and larger optical effect, i.e. affect the transparency of the polymer material, as compared to smaller hydroxyapatite particles. Thus, an upper preferred limit of the largest dimension of the hydroxyapatite particles is preferably one or a few 100  $\mu\text{m}$ . However, in particular embodiments, even  
25 smaller hydroxyapatite particles are preferably employed, such as having a largest dimension equal to or smaller than 500 nm, preferably equal to or smaller than 250 nm and more preferably equal to or smaller than 200 nm. The hydroxyapatite particles are advantageously so-called nanoparticles, i.e. having an average size in the range of 1-100 nm.

- 30 The hydroxyapatite particles can be in the form of fairly spherical particles having a diameter as defining their size and the largest dimension of the particle. However, also other particle forms, such as cylindrical particles, can be used according to the embodiments. In such a case, the largest dimension as defined above is then the particle dimension, such as particle diameter, particle height, particle length, etc., that is, on average, largest for the particles. The above presented preferred size ranges

relate to the average size of the hydroxyapatite particles. It is anticipated by the embodiments that individual particles may in fact have a size that is larger or smaller than the preferred ranges. However, the average size of the particles is preferably within the disclosed preferred ranges.

5 The polymer composition according to the embodiments comprises a polymer material selected from the group of silicone, polyurethane and combinations thereof. These polymer materials are electrically insulating and are commonly employed among implantable medical devices and have favorable properties in terms of being non-toxic, flexible, electrically insulating, etc. There are, however, still a need to improve the abrasion or wear resistance of these polymer materials and thereby improve their  
10 durability against abrasion and wear caused during the use of polymer materials, in particular as implanted in an animal, preferably a mammalian and more preferably a human body. In such an environment, articles or devices made of the polymer material can be exposed to wear from other implanted devices. For instance, the outer insulating tube of an implantable medical lead can wear against other implantable medical leads and/or against the implantable medical device, to which the  
15 implantable medical lead is connected. It is then desired to have a polymer material of the insulating tube that has improved abrasion and wear resistance and durability.

Combinations of silicone and polyurethane include any combinations of the two materials, possibly including other polymers or materials, in any desired proportions. Particular preferred such  
20 combinations are co-polymers of polyurethane and silicone. Such co-polymers of polyurethane and silicone are available on the market under various trade names, such as Optim® and Elast-Eon™. Optim® is a methylene diisocyanate (MDI) based silicone-polyurethane copolymer containing about 60 % of a silicone-rich macrodiol blend and chain-extended with 1,4-butanediol. The macrodiol consists of about 80 % bis-hydroxy-ethoxy-propyl-polydimethylsiloxane and about 20 % polyhexamethylene  
25 oxide. The resulting co-polymer of polyurethane and silicone has mechanical strength and abrasion resistance of polyurethane and the rubbery flexibility of silicone. The co-polymer is highly biostable, soft and flexible and also has low surface friction. The co-polymer of polyurethane and silicone may additionally comprise other components, such as components to compatibilize the polyurethane and silicone precursors. A non-limiting example of a particular resulting co-polymer of polyurethane and  
30 silicone consists of 45 to 50 %, preferably about 48 %, silicone rubber; 37.5 to 42.5 %, preferably about 40 %, of polyurethane and 9.5 to 14.5 %, preferably about 12 %, of polyhexamethylene oxide (PHMO). The percentages presented above are weight percentages unless otherwise indicated. Other ratios of these components are possible to achieve a broad range of mechanical properties.

Other preferred co-polymers of polyurethane and silicone that can be used as polymer material according to the embodiments include co-polymers of silicone, polyurethane and polycarbonate. Such co-polymers are available on the market under the trade name ECSil™. ECSil™ polymer materials are available at various relative concentrations of their including polymers resulting in different tear  
5 strength, tensile strength and modulus of elasticity of the polymer material. A particular suitable co-polymer of silicone, polyurethane and polycarbonate is ECSil™ 75A. ECSil™ 75A is a polycarbonate urethane copolymer with silicone rubber. It contains 60 % silicone-carbonate soft segment and the silicone content is about 50 %. Co-polymers of silicone, polyurethane and polycarbonate that can be used according to the embodiments are further disclosed in WO 98/54242.

10

The polymer compositions of the embodiments are preferably employed to manufacture electrically insulating articles and devices and in particular such articles and devices to be used in implantable medical devices. Fig. 4 is a schematic illustration of such an article and device in the form of an insulating tube 40 having a lumen 48. The lumen 48 is preferably designed and dimensioned to house  
15 at least one electrical conductor so that the insulating tube 40 will be used as an insulator for the at least one electrical conductor. The insulating tube 40 of Fig. 4 is then made of a polymer composition according to the embodiments.

The polymer article or device made of the polymer composition according to the embodiments, such as  
20 the insulating tube 40 of Fig. 4, can be manufactured according to well-known prior art techniques that are selected based on the particular design and form of the article or device and based on the particular polymer material of the polymer composition. Examples of manufacturing methods that can be used include molding, extruding, thermoforming, dip-coating and machining.

25 Fig. 5 is a schematic illustration of an implantable device according to an embodiment, exemplified by an implantable medical lead 1. The implantable medical lead 1 has a so-called distal end 2 adapted to be introduced into a suitable pacing site to enable delivery of pacing pulses and sensing electric activity of the tissue, such as heart, at the particular pacing site. At least one electrode 22, 24, generally denoted pacing and sensing electrode in the art, is arranged in connection with the distal end 2. It is  
30 this electrode 22, 24 that delivers pacing pulses to the tissue and captures electric signals originating from the tissue.

An opposite or proximal end 3 of the implantable medical lead 1 is configured to be mechanically and electrically connected to an implantable medical device (IMD) 5. The IMD 5 can be any implantable

medical device used in the art for generating and applying, through the implantable medical lead 1, electric pulses or shocks to tissues. The IMD 5 is advantageously a pacemaker, defibrillator or cardioverter, such as an implantable cardioverter-defibrillator (ICD), to thereby have the implantable medical lead 1 implanted in or in connection to a ventricle or atrium of the heart.

5

The proximal end 3 comprises at least one matching electrode terminal 32, 34 that provides the electric interface of the implantable medical lead 1 towards the IMD 5. Thus, each electrode terminal 32, 34 is connected to a respective connector terminal in the IMD 5 to thereby provide electric connection between the IMD 5 and the at least one electrode 22, 24 through the at least one electrode terminal 32, 34 and at least one conductor, to be further described herein.

10

The implantable medical lead 1 typically comprises a respective electrode terminal 32, 34 for each electrode 22, 24 in connection with the distal end 2.

15 The implantable medical lead 1 also comprises a lead body 4 running from the proximal end 3 to the distal end 2. This lead body 4 comprises an insulating tube 40 having a lumen or bore and being made of a polymer composition according to the embodiments. This lumen is designed and dimensioned to house the at least one conductor.

20 According to the embodiments, the insulating tube 40 is made of a polymer material selected from silicone, polyurethane or a combination thereof and comprises hydroxyapatite particles at a concentration from 0.5 up to 10 % by weight of the polymer composition.

Fig. 6 illustrates a greatly enlarged cross-sectional view of an embodiment of the distal end 2 of an implantable medical lead of the active fixation type. As seen, the implantable medical lead has an outer flexible insulating tube 40 made of silicone rubber, polyurethane or a combination thereof comprising hydroxyapatite particles according to the embodiments. The outer insulating tube 40 covers a first or outer coiled conductor 44. The conductor 44 extends along through the lead body and terminates in connection with the distal end 2, where it is electrically coupled, for example by spot or laser welding, to a ring electrode 24.

30

Extending along the length of the lead body through the ring electrode 24 is a second or inner coiled conductor 42, which is insulated from the outer coiled conductor 44 by an inner insulating sheath or tube 46. The inner conductor 42 terminates at a substantially cylindrical crimp bus. The crimp bus is

coupled to a fixation helix 22. The fixation helix 22 has the dual function of fixing the implantable medical lead to the myocardium or other target tissue and functions as a sensing/pacing electrode.

In an alternative embodiment of an active fixation lead, the ring electrode 24 is omitted. In other words, the lead is of the unipolar type. The electrode is then the active helix fixation electrode 22 or another type of active fixation electrode.

Fig. 6 also illustrates the lumen 48 of the insulating tube 40, in which the inner and outer coil conductors 42, 44 are running.

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The implantable medical lead must not necessarily be of a so-called active fixation type. An implantable medical lead of passive fixation type could also benefit from having an outer insulating tube according to the embodiments. Such an implantable medical lead does not have any fixation electrode but rather has a tip electrode. Passive fixation of the implantable medical lead at a correct position in a patient body is achievable by a tine assembly or other physical structure at the distal end of the implantable medical lead.

## EXPERIMENTS

The abrasion and wear resistance of various polymer materials was tested for different hydroxyapatite (HA) concentrations and particle types.

### Materials

Optim® pellets (P/N 60000772-001) from AorTech International plc were used for all blending and testing unless otherwise specified. Micro-hydroxyapatite (MicroHA) was obtained as Reagent Grade hydroxyapatite from Sigma-Aldrich (cat. No. 289396), as was the Nano-hydroxyapatite (NanoHA) with particle size  $\leq 200$  nm, (cat. no. 6777418). ECSil™ 75A were obtained from AorTech International plc.

### Methods

Blending of hydroxyapatite powders with Optim® or ECSil™ 75A polymer was carried out using a Brabender internal mixer. Conditions used were 200 °C/ 2 min / 60 rpm. The blends were removed from the mixer and compression-molded into test bars of 2 mm × 10 mm × 150 mm at 200 °C and 250 N/cm<sup>2</sup>, and cooled to room temperature under pressure. The test bars were annealed at 85 °C for 4 hours in a hot air oven. These test bars were used for hardness testing and tensile testing. Test

samples for lead-to-can abrasion (LCTA) testing were cut from the test bars and had a size of 2 mm × 2 mm × 65 mm. Test bars and samples without filler (0 % HA) received same processing procedures.

Shore D hardness of the test bars was measured by Durometer using two test bars, on top of each other, resulting in a total thickness of 4 mm.

Tensile modulus was measured on test bars at 25 mm/min head speed, gauge length 77.2 mm, using a tensile tester. Modulus at 10 mm elongation (12.95 %) was recorded and used for comparison of material stiffness.

10

LTCA testing was conducted by an LTCA Test Apparatus using titanium plates to simulate the titanium can of a pacemaker or ICD. The titanium plates were soda-blasted to have the exact same finish as found on pacemaker cans from St. Jude Medical present on the market, e.g. IDENTITY™, XL DR Model 5376. A freshly soda-blasted plate surface was used at the start of each run. The plate was fixed on an oscillating panel and an abrasion speed of 90 rpm and an abrasion force of 75 grams were employed. Test strips of 2 mm × 2 mm × 65 mm were used with angled corner facing the titanium plate. The test strips were held in a saline tank with 0.9 % saline (0.9 % w/w sodium chloride in deionized water) and the tests were stopped after 1 million cycles. The abrasion testing was carried out at ambient room temperature. The test strips were dried 3 hours in 37 °C forced air oven, and weighed to determine weight loss.

Quality of blending dispersion was verified using scanning electron microscope in low vacuum mode.

### Observations

Optim® with hydroxyapatite in concentrations at 2 % w/w and lower has essentially the same transparent appearance as unfilled Optim®. At 5 % w/w and higher, the Optim® becomes a white, opaque material.

### Durometer Hardness

Durometer Shore D hardness was tested on 4 mm thick samples (2 bars together), using 10 seconds of equilibration time. The results are presented in Table 1 below:

Table 1 - Durometer (Shore D) Hardness of Optim®/HA composites

| Sample (wt % and type of HA) | Durometer (Shore D) |
|------------------------------|---------------------|
| 0 %                          | 43.1                |
| 1 % MicroHA                  | 40.2                |
| 5 % MicroHA                  | 41.9                |
| 15 % MicroHA                 | 42.1                |
| 1 % NanoHA                   | 40.0                |
| 2 % NanoHA                   | 40.0                |
| 5 % NanoHA                   | 38.9                |
| 10 % NanoHA                  | 38.7                |
| 15 % NanoHA                  | 39.5                |

Hardness values are most commonly considered to have an experimental variation of  $\pm 5$  units, and therefore there appears to be no significant difference between the hardness of any of the samples with the employed measurement protocol.

#### Tensile modulus at 10 mm elongation

Tensile modulus at 10 mm elongation corresponds to modulus at 12.95 % strain. This value was chosen since it was the most reproducible way to determine the modulus at a fixed point within the elastic region of the materials. Although the choice of strain is somewhat arbitrary, the relative comparison of material stiffness should not be affected by a different choice since the chosen value lies within the elastic region of the materials. The sample thickness and test bar widths varied somewhat due to differences in molding (and that sufficient uncut test bars were not always available at time of measurement). The data is presented below in Table 2:

15

Table 2 – Average tensile modulus at 10 mm elongation for Optim®/HA composites

| Sample (wt % and type of HA) | Average tensile modulus (MPa) |
|------------------------------|-------------------------------|
| 0 %                          | 15.3                          |
| 1 % MicroHA                  | 15.8                          |
| 5 % MicroHA                  | 16.4                          |
| 15 % MicroHA                 | 20.9                          |

Cont. of Table 2:

| Sample (wt % and type of HA) | Average tensile modulus (MPa) |
|------------------------------|-------------------------------|
| 1 % NanoHA                   | 14.2                          |
| 2 % NanoHA                   | 15.6                          |
| 5 % NanoHA                   | 17.4                          |
| 10 % NanoHA                  | 17.9                          |
| 15 % NanoHA                  | 19.9                          |

Taking into account experimental error, it is estimated from Table 2 that both the MicroHA and the NanoHA have the same impact on material stiffness as determined by tensile modulus, and that it is roughly a linear relationship – increasing HA content increases stiffness. In practical applications if the polymer composition is employed to manufacture an insulating tube of an implantable medical lead, a maximum tensile modulus of no more than about 20 MPa is generally preferred.

#### Abrasion resistance as measured by LTCA

The results from the abrasion resistance test conducted with the LTCA test apparatus are presented below in Table 3. Results are presented as an average weight loss calculated for 3 or 4 test samples per polymer material. Lower weight loss is indicative of better abrasion resistance compared to high weight loss.

Table 3 - Lead to Can Abrasion test results for Optim®/HA composites

| Sample (wt % and type of HA) | Average weight loss (mg) |
|------------------------------|--------------------------|
| 0 %                          | 1.73                     |
| 1 % MicroHA                  | 1.33                     |
| 5 % MicroHA                  | 0                        |
| 15 % MicroHA                 | -0.93                    |
| 0.1 % NanoHA                 | 1.70                     |
| 0.5 % NanoHA                 | 0.93                     |
| 1 % NanoHA                   | 0.58                     |
| 2 % NanoHA                   | 0.53                     |
| 5 % NanoHA                   | 0.40                     |
| 10 % NanoHA                  | 0.03                     |
| 15 % NanoHA                  | -0.07                    |

It is seen from Table 3 that the polymer compositions with a hydroxyapatite concentration of more than 10 % by weight actually gained weight during the test. Repeated and more extensive drying before the weighing did not alter this effect. The weight gain was due to the fact that the salt water medium (0.9 % saline) is absorbed by the polymer composition. After extensive drying some of the absorbed water is driven off leaving salt remaining in the dried polymer composition. The NanoHA had less tendency to absorb saline than MicroHA. Furthermore, the MicroHA particles might contain voids and pores in which the salt water medium can enter.

Fig. 1 visually illustrates the results presented in Table 3 for the NanoHA samples by plotting the weight loss for increasing concentrations of hydroxyapatite in Optim®.

In a related experimental setting ECSil™ 75A was employed as polymer material instead of Optim® together with NanoHA particles. ECSil™ 75A inherently has higher abrasion resistance as compared to Optim® but there was still a significant improvement in terms of reduced weight loss with NanoHA as is evident from Table 4 below:

Table 4 - Lead to Can Abrasion test results for ECSil™ 75A/HA composites

| Sample (wt % and type of HA) | Average weight loss (mg) |
|------------------------------|--------------------------|
| 0 %                          | 0.55                     |
| 2 % NanoHA                   | 0.25                     |

### Particle dispersion

One of the difficulties in dealing with nanometer scale particles is that if the material agglomerates and is not well-dispersed in the polymer, it will behave as though it had a much larger primary particle size than intended. Figs. 2A and 2B illustrate the differing morphology of the MicroHA (Fig. 2A) and the NanoHA (Fig. 2B) before blending at 1000× magnification.

After blending with the polymer material, the nanoscale particles are difficult or impossible to detect by scanning electron microscope (SEM), see Fig. 3B. However, it is possible to demonstrate that the blending of NanoHA did not produce macroscopic agglomerates in the blend. In Fig. 3A the MicroHA particles are clearly visible, with one shown half embedded in the lower right hand side of Fig. 3A. It appears much as in Fig. 2A. In Fig. 3A, the smallest hydroxyapatite particles are not visible, but the larger ones which were visible in Fig. 2A are also visibly dispersed in the Optim® polymer material. It is

therefore judged that the blending procedures did not induce any further agglomeration, and that true nanoscale particles are likely well-dispersed in the material.

Both nanometer and micrometer sized hydroxyapatite particles can be used to impart additional abrasion resistance to polymer materials, such as Optim® and ECSil™. Addition of the hydroxyapatite particles increases the stiffness of the polymer material, which is generally considered as a negative effect. The stiffness increases proportionally to the amount of hydroxyapatite added. However, at the hydroxyapatite concentrations of the embodiments, i.e. from 0.5 up to 10 % by weight, the stiffness increase is low and will be well tolerable for the desired application. It is rather the water or medium uptake that dictates the upper concentration limit of 10 % by weight.

The abrasion resistance imparted by addition of hydroxyapatite exhibits a significant dependence on particle size. The smaller sized particles (NanoHA) exhibited a strong anti-abrasion enhancement even as low as 0.5% w/w in Optim®, and it was estimated that the micrometer sized hydroxyapatite requires about three times the concentration in order to achieve the same effect.

The results indicate that a very small amount of hydroxyapatite particles can achieve a significant reduction in abrasive wear of polymer materials, such as Optim® and ECSil™.

The embodiments described above are to be understood as a few illustrative examples of the present invention. It will be understood by those skilled in the art that various modifications, combinations and changes may be made to the embodiments without departing from the scope of the present invention. In particular, different part solutions in the different embodiments can be combined in other configurations, where technically possible. The scope of the present invention is, however, defined by the appended claims.

## CLAIMS

1. A polymer composition comprising a polymer material selected from silicone, polyurethane and combinations thereof, **characterized by** hydroxyapatite particles at a concentration of from 0.5 up to 10 % by weight of said polymer composition.
- 5 2. The polymer composition according to claim 1, **characterized in** that said polymer material is a co-polymer of silicone and polyurethane.
3. The polymer composition according to claim 2, **characterized in** that said co-polymer of silicone  
10 and polyurethane comprises 45 to 50 % by weight, preferably about 48 % by weight, of silicone, 37.5 to 42.5 % by weight, preferably about 40 % by weight, of polyurethane and 9.5 to 14.5 % by weight, preferably about 12 % by weight, of polyhexamethylene oxide.
4. The polymer composition according to claim 2, **characterized in** that said co-polymer of silicone  
15 and polyurethane is a co-polymer of silicone, polyurethane and polycarbonate.
5. The polymer composition according to any of the claims 1 to 4, **characterized in** that said hydroxyapatite particles have a largest dimension equal to or smaller than 500 nm.
- 20 6. The polymer composition according to claim 5, **characterized in** that said hydroxyapatite particles have a largest dimension equal to or smaller than 250 nm, preferably equal to or smaller than 200 nm.
7. The polymer composition according to any of the claims 1 to 6, **characterized in** that said  
25 hydroxyapatite particles are provided at a concentration from 0.5 up to 5 % by weight of said polymer composition.
8. The polymer composition according to claim 7, **characterized in** that said hydroxyapatite particles are provided at a concentration from 0.5 up to 2.5 % by weight of said polymer composition.
- 30 9. The polymer composition according to claim 8, **characterized in** that said hydroxyapatite particles are provided at a concentration from 1 up to 2 % by weight of said polymer composition.

10. An insulating tube (40) having a lumen (48), **characterized in** that said insulating tube (40) is made of a polymer composition according to any of the claims 1 to 9.

11. An implantable medical lead (1) comprising:

5 a proximal lead portion (3) comprising at least one electrode terminal (32, 34) connectable to an implantable medical device (5);

a distal lead portion (2) comprising at least one electrode (22, 24);

a lead body (4) comprising an insulating tube (40) according to claim 10 and at least one conductor (42, 44) running in a lumen (48) of said insulating tube (40), each electrode (22, 24) of said  
10 at least one electrode (22, 24) is electrically connected to an electrode terminal (32, 34) of said at least one electrode terminal (32, 34) through a respective conductor (42, 44) of said at least one conductor (42, 44).

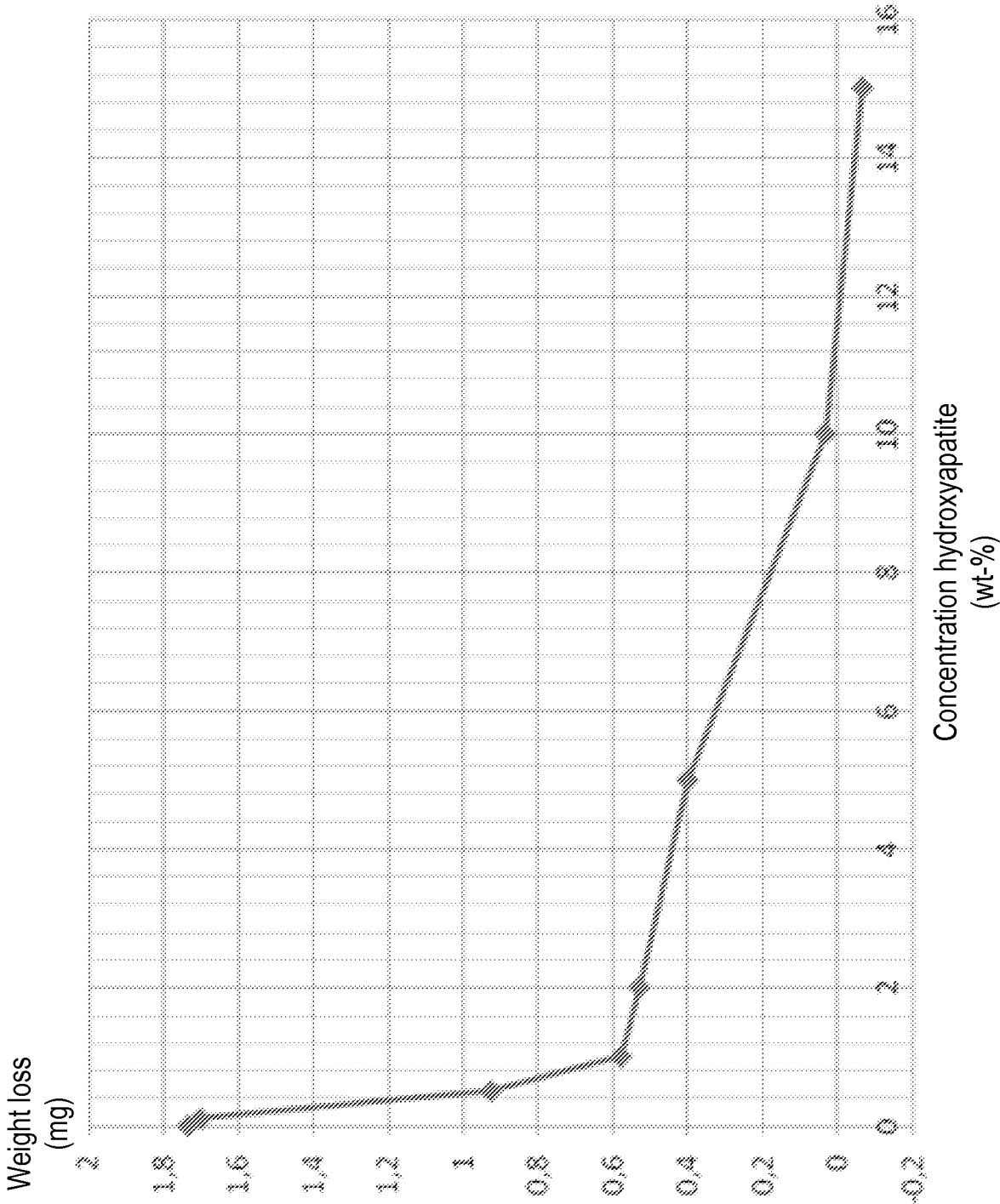


Fig. 1

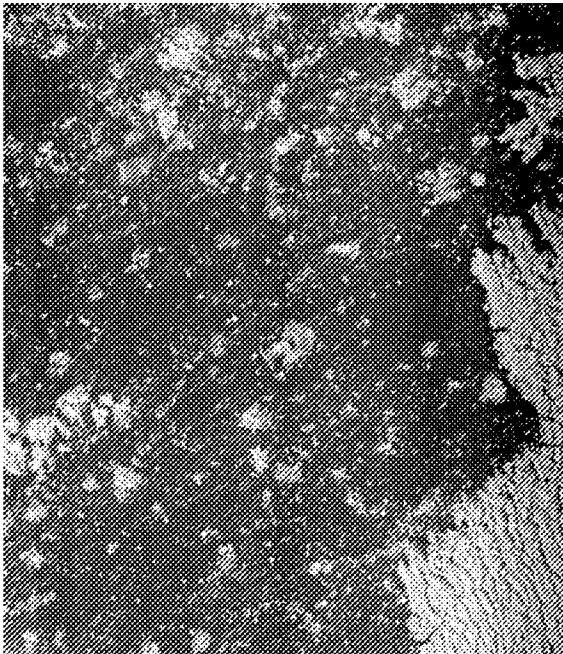


Fig. 2B

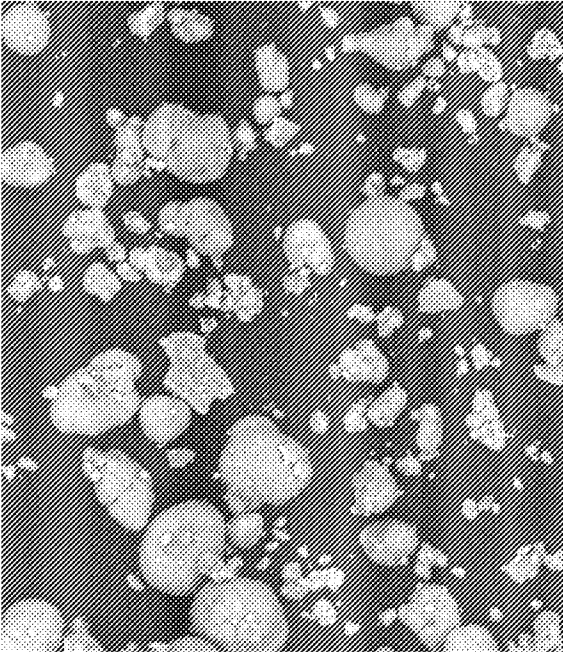


Fig. 2A

3/6

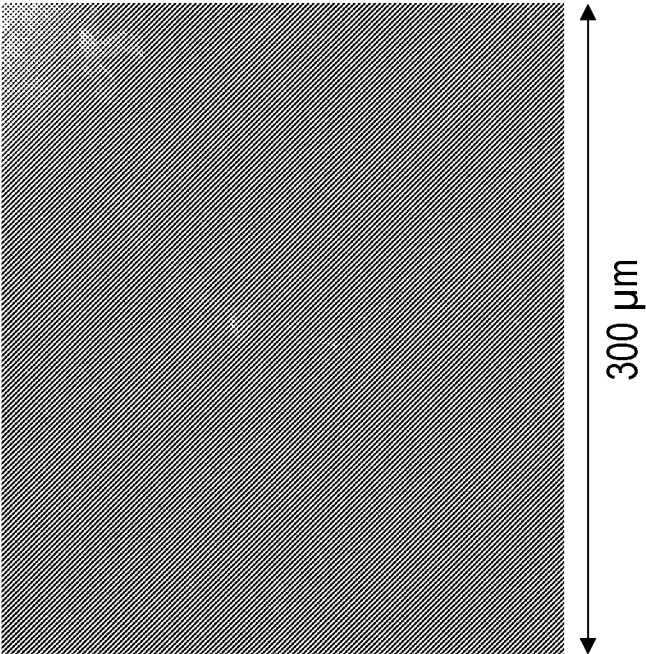


Fig. 3B

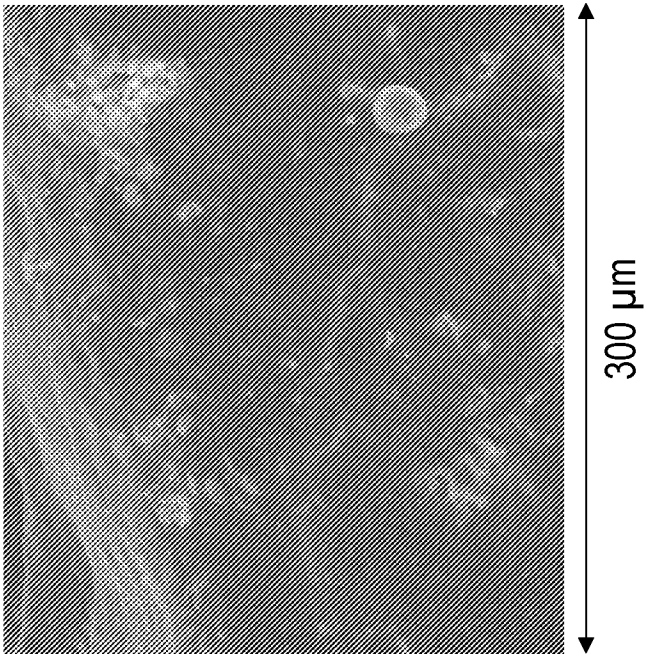


Fig. 3A

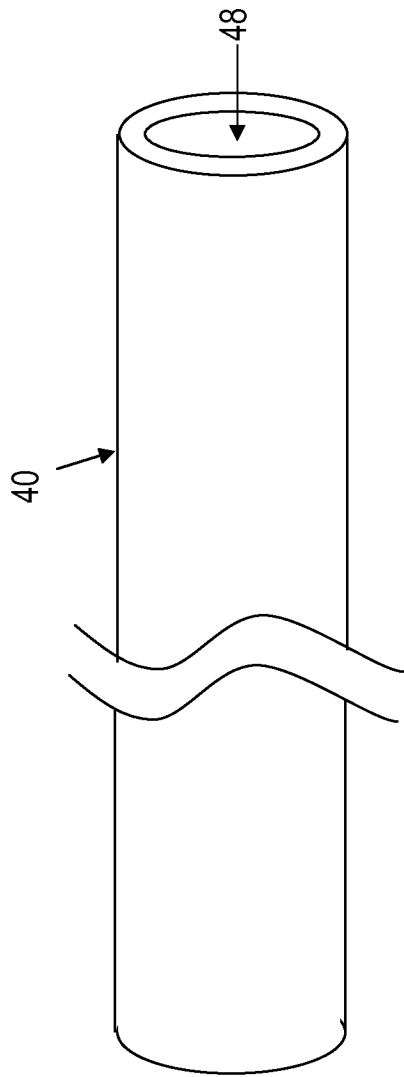
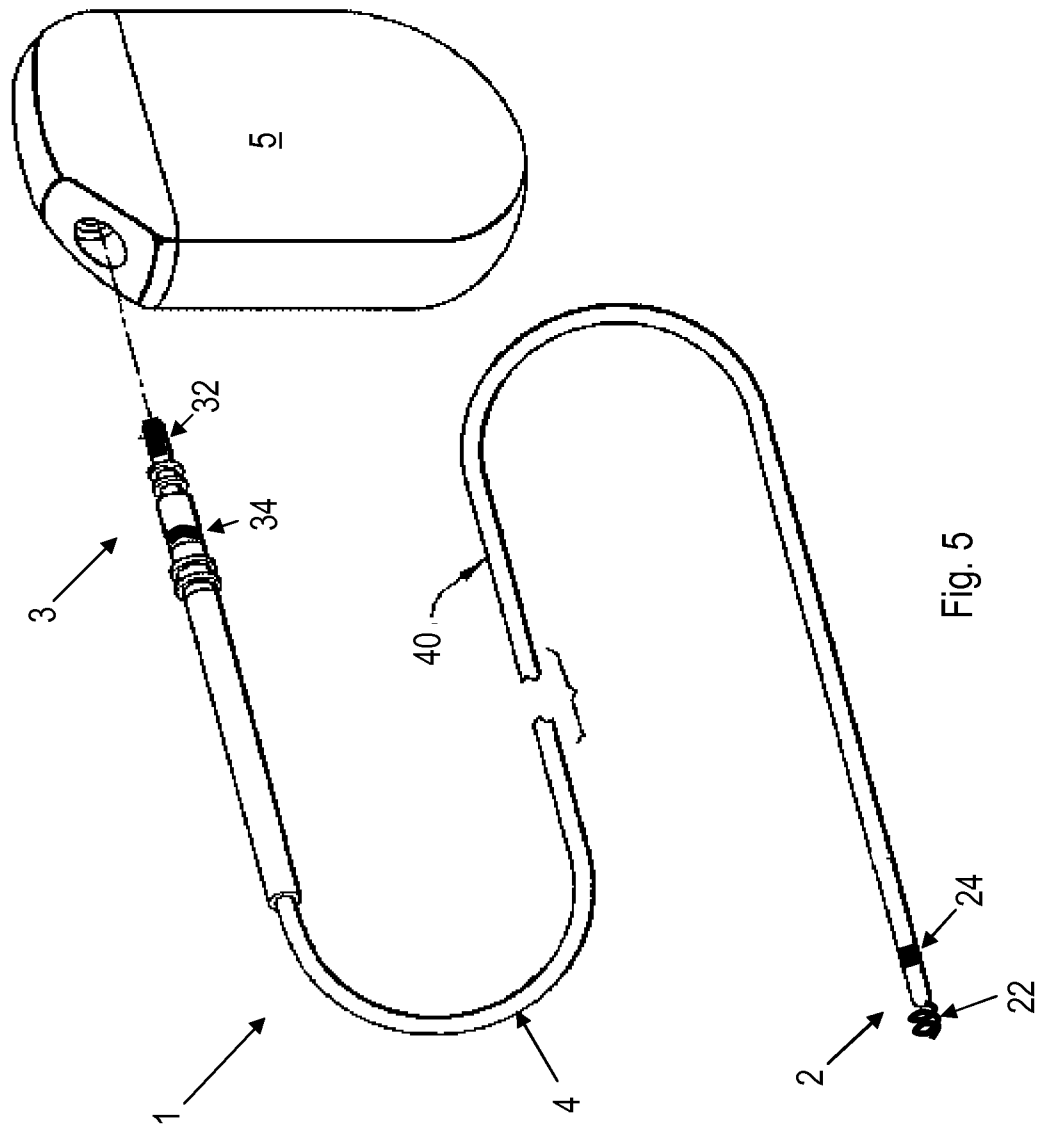


Fig. 4



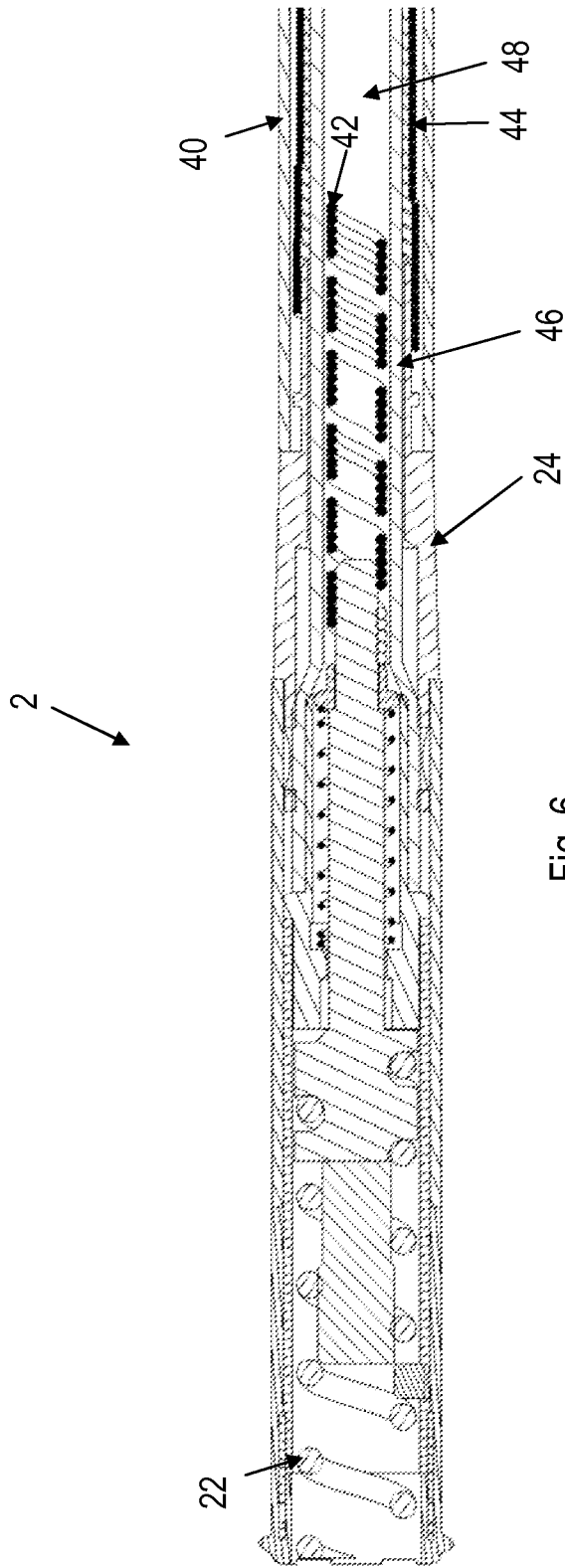


Fig. 6

## INTERNATIONAL SEARCH REPORT

International application No  
PCT/EP2011/056397

## A. CLASSIFICATION OF SUBJECT MATTER

INV. C08L75/04 A61N1/05 C08L83/10  
ADD.

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

C08L A61N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category* | Citation of document, with indication, where appropriate, of the relevant passages                                                                                                                                                                                                                                                                                                                                                                                                        | Relevant to claim No. |
|-----------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------|
| X         | <p>THEIN-HAN W W ET AL: "Superior in vitro biological response and mechanical properties of an implantable nanostructured biomaterial: Nanohydroxyapatite-silicone rubber composite",<br/>ACTA BIOMATERIALIA, ELSEVIER, AMSTERDAM, NL,<br/>vol. 5, no. 7,<br/>1 September 2009 (2009-09-01), pages 2668-2679, XP026500031,<br/>ISSN: 1742-7061, DOI:<br/>10.1016/J.ACTBIO.2009.04.029<br/>[retrieved on 2009-05-03]<br/>abstract<br/>2.1. - 2.2.;<br/>page 2669</p> <p>-----<br/>-/--</p> | 1-11                  |



Further documents are listed in the continuation of Box C.



See patent family annex.

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"&" document member of the same patent family

Date of the actual completion of the international search

16 January 2012

Date of mailing of the international search report

25/01/2012

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Authorized officer

Pouilley, Delphine

## INTERNATIONAL SEARCH REPORT

International application No

PCT/EP2011/056397

| C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT |                                                                                                                                                                                                                                                     |                       |
|------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------|
| Category*                                            | Citation of document, with indication, where appropriate, of the relevant passages                                                                                                                                                                  | Relevant to claim No. |
| A                                                    | MOU SHANSONG ET AL:<br>JOURNAL OF MATERIALS SCIENCE LETTERS,<br>vol. 22, no. 5,<br>1 January 2003 (2003-01-01), pages<br>343-344, XP55015185,<br>ISSN: 0261-8028, DOI:<br>10.1023/A:1022632823906<br>cited in the application<br>the whole document | 1-11                  |
| A                                                    | -----<br>WO 2009/064223 A1 (ST JUDE MEDICAL [SE];<br>OERNBERG ANDREAS [SE]; HILL ROLF [SE];<br>MICKSKI EV) 22 May 2009 (2009-05-22)<br>claims 1-17<br>pages 9-10<br>-----                                                                           | 1-11                  |

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/EP2011/056397

| Patent document<br>cited in search report | Publication<br>date | Patent family<br>member(s) | Publication<br>date |
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| -----                                     |                     |                            |                     |