Abstract: An implantable medical device can be made more durable and long-lasting by providing a passivating layer or film on at least a portion of a metal or metal alloy outer surface of an electrically conductive device, upon which passivating layer or film is placed an insulating layer. The passivation is suitably a chemical passivation, preferably an acid treatment.
Title of the Invention
Passivated metal conductors for use in cardiac leads and method of preparing the same

Field of the Invention
The invention relates generally to the field of passivation of metal surfaces. More specifically, the invention relates to passivation of metal surfaces on conductors used in cardiac leads which shelter polymeric electrical insulation adjacent thereto from metal and metal ions in the lead.

Background of the Invention
Medical devices and components thereof often comprise significant amounts of metal or metal alloys. While metals are typically selected based on their biocompatibility, it is often the case that structural demands on the device require that materials which are not entirely biocompatible or which are not entirely compatible with other components of the device, particularly non-metal components, are employed. One example of this is in the field of cardiac pacemakers, where electrically conductive leads extend from the pacemaker to the heart of the recipient and comprise metal conductors with electrical insulation along their length.

In cardiac pacemaker lead bodies, the metals used are chosen based on a number of factors. Among these is fatigue-resistance; cobalt is known to improve the fatigue-resistance to an acceptable degree. The insulating materials are also carefully chosen and flexible polymer compositions, for example, polyether-based polyurethane are commonly used. One problem which can arise from this combination, though, is that the polymer insulation rapidly degrades if it is in direct contact with metal, particularly cobalt, and/or reactive species produced in the lead body. This catalytic degradation of the polymer insulation can lead to device failure or injury to the patient, both of which should be avoided whenever possible.

The degradation phenomenon is referred to as metal ion-induced oxidation or MIO. Some solutions to the problem of improving compatibility between metal-containing devices and insulating layers, i.e., ways to prevent or reduce MIO, have been disclosed. For example, a barrier formed of a material such as polytetrafluoroethylene (PTFE, a.k.a. TEFLON) or ethylene tetrafluoroethylene (ETFE) can be placed over the conductor or along the inside of
the insulating layer to shield the insulation from the metal or metal alloys of the device. This process does have drawbacks; the addition of a third component in the device increases its size and makes the manufacturing process more complex and costly. Furthermore, creating bonds and joints in the resultant three-layer component is more complex.

With particular regard to cardiac pacemaker leads, researchers face intense pressure to maintain or even reduce the small diameter of present cardiac leads, meaning solutions that increase size are avoided whenever possible.

One way to reduce MIO without making drastic increases in final product dimensions is to provide a layer of conductive metal on the conductor, which metal is tolerated by the insulator. An example is platinum. This increases the overall dimensions by a lesser degree and typically does not present new issues during joining and bonding. However, the additional complex process steps to provide the layer and the materials themselves tend to be prohibitively expensive for many applications.

To meet the strict size demands and minimize manufacturing costs, other solutions have been proposed. For example, a voltage stabilizing additive (VSA) can be added to a polymeric insulating layer as taught in US 6,879,861. However, such polymers can be difficult and expensive to produce and the VSAs incorporated therein can leak into the patient, causing injury.

Alternatively, two layers of polymers with different characteristics can be used, the layer closest the metal being selected from those which are particularly resistant to MIO, while the outer layer is chosen based on qualities such as insulating ability and glidability. US 5,375,609, among others, provides examples of this configuration. While this might provide improved MIO-resistance in the outer insulating layer, the product cannot be optimized as the first layer must be considered, which may make the overall device less flexible, thicker, etc.

To help addressing the issues of flexibility, the inner layer of insulation can be a silicone layer, see US 5,628,774. However, this results in a device which still has undesirably large dimensions.
Thus, despite the advances described above, there remains a need in the art to improve known techniques and optimally provide improved devices which reduce the stress on the insulators without compromising device dimensions or other beneficial properties such as flexibility.

Summary of the Invention

It is therefore an object of the present invention to provide improved implantable devices which comprise an electrically conductive metal or metal alloy having an outer surface.

This object is achieved with a device as claimed in claim 1, namely by an implantable medical device, comprising an electrically conductive metal or metal alloy having an outer surface; a passivated area on at least a portion of the metal or metal alloy outer surface; and an insulating layer having an inner surface configured to fit over at least part of said passivated area.

The electrically conductive metal or metal alloy can comprise cobalt, and/or the insulating layer can be polymer-based, such as polyurethane. The improvement resides in providing the metal or metal alloy with a passivated surface, such that metal ion-induced oxidation (MIO) will be reduced.

The electrically conductive metal or metal alloy can be the conductor in an elongated lead, such as a cardiac pacemaker lead.

Preferably the metal conductor surface is depleted of Co atoms, and more preferably it is also enriched in Cr atoms.

The passivated metal surface can be provided by chemical treatment, such as acid treatment.

The insulation layer can be provided around the entire passivated surface of the conductor.
According to a further aspect of the invention, a method of preparing an implantable medical device comprising an insulated conductor is provided, the method comprising providing an elongated metal or metal alloy conductor having an outer surface, treating the conductor with a suitable acid, such as HNO₃, and providing an insulation layer around at least a portion of the metal alloy conductor.

According to a further aspect of the invention, a method of protecting electrical insulation, suitably polymeric insulation, from metal ion-induced oxidation is provided, which comprises providing an electrically conductive metal or metal alloy having an outer surface, passivation treatment of at least a portion of the conductive metal or metal alloy outer surface, and positioning the polymeric electrical insulation on the passivated surface.

According to a further aspect of the invention, a kit for preparing an implantable medical device is provided, which comprises an electrically conductive metal or metal alloy, a means to provide the metal or metal alloy with a passivated area in the form of a layer or a film, and an insulating layer configured to fit on the electrically conductive metal or metal alloy.

**Detailed Description**

For the purposes of this invention the term "passivation" shall be taken to mean a chemical treatment rendering the surface less prone to cause or contribute to metal ion-induced oxidation (MIO). Consequently a "passivated surface" or "passivated metal" shall be taken to mean a surface or metal that has been treated to exhibit a reduced degree of MIO in any application, preferably medical applications.

As noted above, the present invention provides a new configuration for implantable medical devices which allows for a slim profile while protecting insulating layers from MIO. This is achieved by providing a passivated surface on the medical device, suitably as a passivated layer or film, on at least part of the metal or metal alloy-containing device. This passivated surface layer or film shields the overlying insulating layer from MIO while having a negligible effect on the dimensions and mechanical properties of the device. The
thickness of this film or layer is 1 nm - 20 nm, preferably 2 nm - 5 nm. In particular the passivated layer is depleted of Co and suitably enriched in Cr.

Acid treatments of metal surfaces for passivation purposes are known in the art. For example treatment of stainless steel by subjecting it to HNO$_3$ is a commonly used procedure to enhance corrosion resistance. Other known chemical treatments are e.g.

a) submersion in a chromic acid bath for 30 minutes at 46 °C,
b) submersion in a chromic acid bath for 60 minutes at 56 °C,
c) submersion in a tricresyl phosphate (TCP) bath for 2 days at 107 °C,
d) exposing the steel to citric acid solution, typically 4-10% by weight.

In a presently preferred embodiment HNO$_3$ is used as the acid for the chemical treatment. Suitably an aqueous solution of HNO$_3$ is used, the concentration of which is 5 — 30 % by weight. More preferably the concentration is 8-20% by weight, most preferred 10-15 % by weight.

The resultant passivated metal conductor has a layer of a modified alloy which is extremely thin, in the area of 1 nm to 20 nm. This allows the present invention to provide a device which does not measurably exceed current product dimensions. Furthermore, the passivated metal conductor maintains the advantageous properties of the underlying material, whether those are strength, flexibility, or other.

The devices and methods of the present invention are particularly effective at shielding polyether-based polyurethane insulations from cobalt present in conductors in cardiac pacemaker leads. This is both because the passivated layer effectively depletes the surface of Co, but also because the passivated layer does not have a significant effect on product dimensions and mechanical properties, two factors that are exceedingly important with cardiac pacemaker leads.

EXAMPLES

Example 1 (passivation using HNO$_3$)
A passivation treatment of pacemaker lead coils was performed using 10.5% HNO₃ (aq) in order to improve the corrosion resistance as described below.

A cardiac pacemaker lead conductor was formed according to known methods from the fatigue-resistant electrical conducting material 35N LT (a non-magnetic, nickel-cobalt-chromium-molybdenum alloy available from FWM (Fort Wayne Metals, Indiana, USA); composition: approx 35% Co, 35% Ni, 20% Cr and 10% Mo by weight).

Sample lead coils (both inner and outer coils) were immersed in a 10.5% (by weight) HNO₃ (aq) bath at a temperature of 35°C for a time of 150 minutes. Stirring could be beneficial.

However, the treatment can be performed at different temperatures. The temperature could be as low as 0°C but suitably not exceeding boiling temperature for the solution, i.e. approx. 100°C. A suitable interval is room temperature (20°C) up to 75°C, suitably 30 to 60°C, ideally 30 to 50°C.

The treatment period could vary between 1 min and up to 24 hours, preferably 30 minutes up to 6 hours, most preferred 2 hours to 4 hours.

The release rates of metal from the alloy during the passivation treatment was followed by measuring the concentration of the metals in question in the bath liquid using ICP-AES (Inductive Coupled Plasma - Atomic Emission Spectroscopy). Data from the experiment are shown in Table 1

<table>
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<tr>
<th>Metal</th>
<th>Metal release (µg/cm²/h)</th>
<th>SD</th>
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<tbody>
<tr>
<td>Co</td>
<td>0.13</td>
<td>0.008</td>
</tr>
<tr>
<td>Cr</td>
<td>0.03</td>
<td>0.005</td>
</tr>
<tr>
<td>Mo</td>
<td>0.02</td>
<td>0.000</td>
</tr>
<tr>
<td>Ni</td>
<td>0.12</td>
<td>0.036</td>
</tr>
</tbody>
</table>

As can be seen, the release rate is considerably higher for Co and Ni (the largest alloy constituents) than for Cr and Mo. Of the total amount of metal released, Co accounts for 43%,
Ni 40%, Cr 10% and Mo 7%. Thus, these results show preferential dissolution of Co and Ni during the passivation in the strong acidic solution. Relatively lower release rates of Cr and Mo may be a result of formation of stable oxides of these elements. When stainless steel is passivated in an acidic solution, the passive surface film becomes enriched in Cr, as a consequence of selective dissolution of Fe. Similarly, preferential dissolution of Co and Ni leads to a Cr enriched passive oxide film on the Co-base alloy.

Example 2 (release of metal in synthetic biological media)

The release of Co, Ni, Cr and Mo from non-passivated and passivated 35N LT, respectively, was investigated by immersing lead coils in PBS (phosphate buffer saline) with 100 mM H₂O₂, a synthetic biological media. Total immersion time was 3 hours (180 minutes). The addition of H₂O₂ is done to take into account accelerated corrosion due to generation of aggressive species in the biological system during inflammatory response. The metal release rates are shown in Table 2, which compares passivated and non-passivated lead coils made of alloy 35N LT.

<table>
<thead>
<tr>
<th>Metal</th>
<th>Metal release (µg/cm²/h)</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Co, pass.</td>
<td>0.12</td>
<td>0.02</td>
</tr>
<tr>
<td>Co, non-pass.</td>
<td>0.23</td>
<td>0.04</td>
</tr>
<tr>
<td>Cr, pass.</td>
<td>0.17</td>
<td>0.01</td>
</tr>
<tr>
<td>Cr, non-pass.</td>
<td>0.19</td>
<td>0.06</td>
</tr>
<tr>
<td>Mo, pass.</td>
<td>0.09</td>
<td>0.00</td>
</tr>
<tr>
<td>Mo, non-pass.</td>
<td>0.13</td>
<td>0.01</td>
</tr>
<tr>
<td>Ni, pass</td>
<td>0.55</td>
<td>0.19</td>
</tr>
<tr>
<td>Ni, non-pass.</td>
<td>0.76</td>
<td>0.07</td>
</tr>
</tbody>
</table>

The table clearly shows that the passivation treatment resulted in a decrease in metal release, in particular of Co, from the alloy 35N LT in PBS + 100mM H₂O₂. This can be explained by the enrichment of Cr and depletion of Co in the passive oxide film provided by the passivation treatment.

Since MIO is believed to be caused by metal (notably Co) ions originating from the alloy, the results show that chemical passivation treatment according to the present invention is
beneficial in reducing MIO in applications were metals are exposed to corrosive environments.

Example 3

A lead coil as in Example 1 is submersed in a chromic acid bath for 30 minutes at 46 °C. A passivated surface is obtained.

Example 4

A lead coil as in Example 1 is submersed in a chromic acid bath for 60 minutes at 56 °C. A passivated surface is obtained.

Example 5

A lead coil as in Example 1 is submersed in a tricresyl phosphate (TCP) bath for 2 days at 107 °C. A passivated surface is obtained.

Example 6

A lead coil as in Example 1 is exposed to citric acid solution typically 4-10% by weight. A passivated surface is obtained.

The resultant passivated, insulated lead can be connected to a cardiac pacemaker at a proximal end, inserted into a patient and connected to the patient's heart at a distal end.

The lead discussed herein offers improved resistance to degradation of the polymer insulation without possessing any statistically significant increase in product dimension. Furthermore, the flexibility, fatigue-resistance, glidability and other beneficial properties of the insulated lead are maintained. The passivated layer on the conductor thus provides the additional benefit of extending potential product life. Extending product life in a product such as a pacemaker lead reduces the risk of complications or injury to the patient while also reducing the chance that an additional procedure is required to remove and replace a lead, which also reduces the risk of adverse outcome for the patient while minimizing medical treatment costs.
The complete disclosures of all patents, patent applications, and publications are incorporated herein by reference as if individually incorporated. The preceding specific embodiments are illustrative of the practice of the invention. It is to be understood, therefore, that other materials, methods, and procedures known to those skilled in the art or disclosed herein, may be employed without departing from the invention or the scope of the appended claims.
Claims

1. An implantable medical device, comprising:
   an electrically conductive metal or metal alloy having an outer surface;
   a passivated area on at least a portion of the metal or metal alloy outer surface; and
   an insulating layer having an inner surface configured to fit over at least part of said passivated area.

2. A device according to claim 1, wherein the passivated area is a film having a thickness of 1 nm to 20 nm.

3. A device according to claim 1 or 2, wherein the electrically conductive metal or metal alloy comprises cobalt.

4. A device according to claim 1, 2 or 3, wherein the passivated area of the metal or metal alloy is depleted of Co.

5. A device according to any preceding claim, wherein the passivated area of the metal or metal alloy is enriched in Cr.

6. A device according to any preceding claim, wherein the electrically conductive metal or metal alloy is an elongated conductor.

7. A device according to claim 6, wherein the elongated conductor is a cardiac pacemaker lead.

8. A device according to any preceding claim, wherein the insulating layer is polymer-based.

9. A device according to claim 8, wherein the polymer is polyurethane, preferably polyether-based polyurethane.
10. A method of preparing an insulated conductor, comprising:
providing an elongated metal or metal alloy conductor having an outer surface;
chemically treating at least a portion of said conductor to provide a passivated area thereon;
and providing an insulation layer around at least a portion of said passivated area.

11. A method according to claim 10, wherein said chemical treatment step comprises immersing the conductor in a solution of a compound capable of modifying the metal or metal alloy to render it passivated.

12. A method according to claim 10 or 11, wherein said chemical treatment step comprises immersing in an acidic solution.

13. A method according to claim 12, wherein the acid for the acidic solution is selected from HNO₃, citric acid, chromic acid, tricresyl phosphate (TCP).

14. A method according to claim 13, wherein aqueous HNO₃ is used, the concentration of which is 5—30 % by weight, preferably the concentration is 8-20% by weight, most preferred 10-15 % by weight.

15. The method according to claim 14, wherein the treatment has a duration of 1 min and up to 24 hours, preferably 30 minutes up to 6 hours, most preferred 2 hours to 4 hours.

16. The method according to any of claims 14 - 15, wherein the treatment is carried out at a temperature in the range of room temperature (20°C) up to 75°C, suitably 30 to 60°C, ideally 30 to 50°C.

17. A method according to any of claims 10 - 16, wherein the insulation layer is provided around the entire passivated area.

18. A method of protecting electrical insulation from metal ion-induced oxidation, comprising:
providing an electrically conductive metal or metal alloy having an outer surface;
chemically treating at least a portion of said conductive metal or metal alloy outer surface so as to passivate said portion; and positioning the electrical insulation on the passivated area.

19. The method according to claim 18, wherein the insulation is polymeric.

20. A kit for preparing an implantable medical device, comprising:
   a conductor of an electrically conductive metal or metal alloy;
   a means to passivate at least a portion of the metal or metal alloy conductor;
   and
   an insulating layer configured to fit on the electrically conductive metal or metal alloy conductor.
## A. CLASSIFICATION OF SUBJECT MATTER

**IPC:** see extra sheet

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)

**IPC:** A61N, C23C

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

SE, DK, FI, NO classes as above

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

## EPO-INTERNAL, WPI DATA, PAJ

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

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**Date of the actual completion of the international search:** 16 April 2007

**Date of mailing of the international search report:** 18-04-2007

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International patent classification (IPC)
A61N 1/05 (2006.01)
C23C 22/06 (2006.01)

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Paper copies can be ordered at a cost of 50 SEK per copy from PRV InterPat (telephone number 08-782 28 85).

Cited literature, if any, will be enclosed in paper form.
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