different approaches are being discussed. For one, it is attempted to slow the degradation on the part of the implant material by developing appropriate alloys. In addition, coatings are to bring about a temporary inhibition of the degradation. While the existing approaches are promising, none of them has so far been implemented in a commercially available product. Regardless of the efforts made so far, there is rather a continuing need for solutions that make it possible to at least temporarily reduce the in vivo corrosion of magnesium alloys.

SUMMARY

One or more of the disadvantages of the prior art mentioned above are solved, or at least mitigated, by the implant according to the invention. The implant according to the invention comprises a base body made of a biocorrodible magnesium alloy. The magnesium alloy contains a plurality of statistically distributed particles, comprising one or more of the elements Y, ZR, Mn, Sc, Fe, Ni, Co, W, Pt and noble earths with the atomic numbers 57 to 71, or alloys, or compounds containing one or more of these elements. The mean distance of the particles from each other is smaller than the hundredfold mean particle diameter.

In the development of magnesium materials so far, the corrosion resistance has always been improved by increasing the purity of the magnesium material. Iron, nickel, chromium, and cobalt are considered to be critical elements in this context. Particles comprising intermetallic compounds, particles of a different chemical nature (oxides, hydrides) or segregations (Al12Mg17) in magnesium materials result in microgalvanic corrosion due to the different electrochemical potential. This results in local corrosive processes, which massively accelerate the corrosion rate of the material. For this reason, previously attempts have been made to minimize the concentration of the particles to the extent possible.

The solution according to the invention, however, takes exactly the opposite approach. In magnesium materials, in general, the corrosion that is observed attacks the material locally very inhomogeneously. In the process, cathodic processes occur, which are

accompanied by the release of hydroxide ions and the development of hydrogen, more specifically at defined centers, namely the above-mentioned particles. The anodic dissolution process of the magnesium material takes place in the surroundings of the cathodic center. The process can be divided into the following partial reactions:

Anodic: $Mg \rightarrow Mg^{2+} + 2\ e^-$

Cathodic: $2\ H_2O + 2\ e^- \rightarrow 2\ OH^- + H_2$

The anodic press is highly dependent on the pH value. For example, the Mg corrosion is massively accelerated at pH < 5, while it is massively decelerated at pH > 10 and basically completely disrupted. Given this behavior, the release of hydroxide ions on the cathodic center leads to the protection of the direct surroundings.

The invention is based on the realization that the corrosion of implants made of biocorrodible magnesium alloys can be delayed by adding a plurality of homogenously distributed particles to the material volume, a near-surface region, or the surface. The particles act as cathodic centers within the above-mentioned meaning, which is to say, the hydrogen overvoltage is sufficiently low and the reaction can take place at a high rate. The particles comprise one or more of the elements Y, ZR, Mn, Sc, Fe, Ni, Co, W, Pt and nobles earths with the atomic numbers 57 to 71, or alloys, or compounds containing one or more of these elements. In the present invention, the term 'alloy' shall cover metallic compositions of the elements, and also compositions in which covalent bonds exist between the elements. The alloys preferably contain magnesium. Compounds comprise in particular hydrides and carbides of the above-mentioned elements.

Biocorrodible as defined by the invention denotes alloys in the physiological environment of which degradation or remodeling takes place, so that the part of the implant made of the material is no longer present in its entirety, or at least predominantly.

A magnesium alloy in the present case shall be understood as a metal structure, the main constituent of which is magnesium. The main constituent is the alloying constituent having the highest weight proportion in the alloy. The proportion of the main constituent is

preferably more than 50% by weight, particularly more than 70% by weight. The alloy is to be selected in the composition thereof such that it is biocorrodible. A possible test medium for testing the corrosion behavior of a potential alloy is synthetic plasma, as that which is required according to EN ISO 10993-15:2000 for biocorrosion analyses (composition NaCl 6.8 g/l, $CaCl_2$ 0.2 g/l, KCl 0.4 g/l, $MgSO_4$ 0.1 g/l, $NaHCO_3$ 2.2 g/l, Na_2HPO_4 0.126 g/l, NaH_2PO_4 0.026 g/l). For this purpose, a sample of the alloy to be analyzed is stored in a closed sample container with a defined quantity of the test medium at 37ºC and pH 7.38. The samples are removed at intervals – which are adapted to the anticipated corrosion behavior – ranging from a few hours to several months and analyzed for traces of corrosion in the known manner. The synthetic plasma according to EN ISO 10993-15:2000 corresponds to a blood-like medium and thus is a possible medium to reproducibly simulate a physiological environment as defined by the invention.

The term corrosion refers in the present example to the reaction of a metallic material with the environment thereof, wherein a measurable change of the material is caused, which – when using the material in a component – results in an impairment of the function of the component. The corrosion process can be quantified by the provision of a corrosion rate. Swift degradation is associated with a high corrosion rate, and vice versa. Relative to the degradation of the entire base body, an implant that is modified as defined by the invention will result in a decrease of the corrosion rate.

The particles preferably have a mean diameter of 1 nanometer to 10 micrometers, particularly preferred 500 nanometers to 3 micrometers, and more particularly 1 to 2 micrometers.

In the surroundings of the cathodic center, protected regions develop as a result of the release of hydroxide ions. The majority of the protected region around an individual cathodic center depends on the size and composition of the particles and the surrounding matrix of the magnesium material. The size of the protected area per particle should be at least 1 square micrometer, preferably up to 100 square micrometers, with up to 10000 square micrometers being particularly preferred.

A further concept of the invention is to provide two methods for producing an implant comprising a main body made of a biocorrodible magnesium alloy, wherein the magnesium alloy contains a plurality of statistically distributed particles having the above-mentioned composition, and the mean distance of the particles from each other is smaller than the hundredfold mean particle diameter, and the particles are incorporated in the surface or in a near-surface region of the base body.

According to a first variant, the method comprises the following steps:

(i) providing a blank made of the biocorrodible magnesium alloy;
(ii) applying a non-aqueous suspension of particles having the above-mentioned composition to the blank; and
(iii) rolling the particles into the surface or into the near-surface region of the blank.

Accordingly, an oily suspension containing the particles to incorporated is applied to the blank, from which the base body is to be shaped, and incorporated by rolling. This suspension can be used as a lubricant both during cold rolling and during hot rolling. By optimizing the volume flow of the suspension, temperature, contact pressure and speed, the incorporation of the particles in the surface of the rolled magnesium material can be optimized. The variant is suited in particular for magnesium alloys based on WE43.

According to a second variant, the method comprises the following steps:

(i) providing a blank made of the biocorrodible magnesium alloy;
(ii) applying particles having the above-mentioned composition to the blank; and
(iii) melting the magnesium alloy onto the near-surface region of the blank.

According to this variant, the particles to be incorporated are applied directly onto the blank, which later forms the base body. After that, the magnesium alloy is locally melted on the surface, for example by laser treatment. After cooling, the particles are then embedded in the near-surface region of the blank.

DETAILED DESCRITPION

fragment of the implant can be achieved by locally influencing the degradation rate, for example by providing the surfaces of the segment rings of a stent structure, but not the longitudinal connecting struts of the segment rings, with cathodic centers according to the invention, whereby the struts degrade more quickly than the segment rings. Because the connecting struts dissolve more quickly, high longitudinal flexibility is achieved quickly, wherein the load-bearing capacity of the segment rings is still maintained.

The particles provide not only corrosion protection, but also increase the wear resistance against abrasion by increasing the hardness. In addition, by suitably selecting the particles and the composition thereof, polymeric substances can be effectively bonded to the surface. These polymeric substances can have a corrosion-inhibiting effect on the one hand, and on the other hand, they may contain one or more pharmacological active ingredients, or exhibit a pharmacological effect themselves.

The additional coating with a polymer can be technically implemented, for example, as follows. PLLA L214S (Boehringer Ingelheim) is dissolved in a concentration of 1.6% (w/v) in chloroform and rapamycin is added as the active substance. The active ingredient content preferably ranges between 15% and 20%, in relation to the solid matter content. The implant made of the modified magnesium alloy is immersed for 1 second into the solution using an underwater robot, pulled out, and air containing nitrogen is blown on so as to evaporate the solvent. This process is repeated until a sufficient layer thickness of approximately 5 µm has been reached.

The embodiments also apply analogously to other biocorrodible magnesium alloys and particle compositions.

It will be apparent to those skilled in the art that numerous modifications and variations of the described examples and embodiments are possible in light of the above teaching. The disclosed examples and embodiments are presented for purposes of illustration only. Other alternate embodiments may include some or all of the features disclosed herein. Therefore, it is the intent to cover all such modifications and alternate embodiments as may come within the true scope of this invention.

different approaches are being discussed. For one, it is attempted to slow the degradation on the part of the implant material by developing appropriate alloys. In addition, coatings are to bring about a temporary inhibition of the degradation. While the existing approaches are promising, none of them has so far been implemented in a commercially available product. Regardless of the efforts made so far, there is rather a continuing need for solutions that make it possible to at least temporarily reduce the in vivo corrosion of magnesium alloys.

SUMMARY

The invention is defined in the independent claims. Some optional features of the invention are defined in the dependent claims.

One or more of the disadvantages of the prior art mentioned above may be solved, or at least mitigated, by the techniques as disclosed herein. One implant comprises a base body made of a biocorrodible magnesium alloy. The magnesium alloy contains a plurality of statistically distributed particles, comprising one or more of the elements Y, ZR, Mn, Sc, Fe, Ni, Co, W, Pt and noble earths with the atomic numbers 57 to 71, or alloys, or compounds containing one or more of these elements. The mean distance of the particles from each other is smaller than the hundredfold mean particle diameter.

In the development of magnesium materials so far, the corrosion resistance has always been improved by increasing the purity of the magnesium material. Iron, nickel, chromium, and cobalt are considered to be critical elements in this context. Particles comprising intermetallic compounds, particles of a different chemical nature (oxides, hydrides) or segregations (Al12Mg17) in magnesium materials result in microgalvanic corrosion due to the different electrochemical potential. This results in local corrosive processes, which massively accelerate the corrosion rate of the material. For this reason, previously attempts have been made to minimize the concentration of the particles to the extent possible.

The solution as disclosed herein, however, takes exactly the opposite approach. In magnesium materials, in general, the corrosion that is observed attacks the material locally very inhomogeneously. In the process, cathodic processes occur, which are

accompanied by the release of hydroxide ions and the development of hydrogen, more specifically at defined centers, namely the above-mentioned particles. The anodic dissolution process of the magnesium material takes place in the surroundings of the cathodic center. The process can be divided into the following partial reactions:

Anodic: $Mg \rightarrow Mg^{2+} + 2\ e^-$

Cathodic: $2\ H_2O + 2\ e^- \rightarrow 2\ OH^- + H_2$

The anodic press is highly dependent on the pH value. For example, the Mg corrosion is massively accelerated at pH < 5, while it is massively decelerated at pH > 10 and basically completely disrupted. Given this behavior, the release of hydroxide ions on the cathodic center leads to the protection of the direct surroundings.

The techniques disclosed herein are based on the realization that the corrosion of implants made of biocorrodible magnesium alloys can be delayed by adding a plurality of homogenously distributed particles to the material volume, a near-surface region, or the surface. The particles act as cathodic centers within the above-mentioned meaning, which is to say, the hydrogen overvoltage is sufficiently low and the reaction can take place at a high rate. The particles comprise one or more of the elements Y, ZR, Mn, Sc, Fe, Ni, Co, W, Pt and nobles earths with the atomic numbers 57 to 71, or alloys, or compounds containing one or more of these elements. In the present invention, the term 'alloy' shall cover metallic compositions of the elements, and also compositions in which covalent bonds exist between the elements. The alloys preferably contain magnesium. Compounds comprise in particular hydrides and carbides of the above-mentioned elements.

Biocorrodible as defined by the invention denotes alloys in the physiological environment of which degradation or remodeling takes place, so that the part of the implant made of the material is no longer present in its entirety, or at least predominantly.

A magnesium alloy in the present case shall be understood as a metal structure, the main constituent of which is magnesium. The main constituent is the alloying constituent having the highest weight proportion in the alloy. The proportion of the main constituent is

preferably more than 50% by weight, particularly more than 70% by weight. The alloy is to be selected in the composition thereof such that it is biocorrodible. A possible test medium for testing the corrosion behavior of a potential alloy is synthetic plasma, as that which is required according to EN ISO 10993-15:2000 for biocorrosion analyses (composition NaCl 6.8 g/l, $CaCl_2$ 0.2 g/l, KCl 0.4 g/l, $MgSO_4$ 0.1 g/l, $NaHCO_3$ 2.2 g/l, Na_2HPO_4 0.126 g/l, NaH_2PO_4 0.026 g/l). For this purpose, a sample of the alloy to be analyzed is stored in a closed sample container with a defined quantity of the test medium at 37ºC and pH 7.38. The samples are removed at intervals – which are adapted to the anticipated corrosion behavior – ranging from a few hours to several months and analyzed for traces of corrosion in the known manner. The synthetic plasma according to EN ISO 10993-15:2000 corresponds to a blood-like medium and thus is a possible medium to reproducibly simulate a physiological environment.

The term corrosion refers in the present example to the reaction of a metallic material with the environment thereof, wherein a measurable change of the material is caused, which – when using the material in a component – results in an impairment of the function of the component. The corrosion process can be quantified by the provision of a corrosion rate. Swift degradation is associated with a high corrosion rate, and vice versa. Relative to the degradation of the entire base body, an implant that is modified as defined herein may result in a decrease of the corrosion rate.

The particles preferably have a mean diameter of 1 nanometer to 10 micrometers, particularly preferred 500 nanometers to 3 micrometers, and more particularly 1 to 2 micrometers.

In the surroundings of the cathodic center, protected regions develop as a result of the release of hydroxide ions. The majority of the protected region around an individual cathodic center depends on the size and composition of the particles and the surrounding matrix of the magnesium material. The size of the protected area per particle should be at least 1 square micrometer, preferably up to 100 square micrometers, with up to 10000 square micrometers being particularly preferred.

Also disclosed are two methods for producing an implant comprising a main body made of a biocorrodible magnesium alloy, wherein the magnesium alloy contains a plurality of statistically distributed particles having the above-mentioned composition, and the mean distance of the particles from each other is smaller than the hundredfold mean particle diameter, and the particles are incorporated in the surface or in a near-surface region of the base body.

According to a first variant, the method comprises the following steps:

(i) providing a blank made of the biocorrodible magnesium alloy;
(ii) applying a non-aqueous suspension of particles having the above-mentioned composition to the blank; and
(iii) rolling the particles into the surface or into the near-surface region of the blank.

Accordingly, an oily suspension containing the particles to incorporated is applied to the blank, from which the base body is to be shaped, and incorporated by rolling. This suspension can be used as a lubricant both during cold rolling and during hot rolling. By optimizing the volume flow of the suspension, temperature, contact pressure and speed, the incorporation of the particles in the surface of the rolled magnesium material can be optimized. The variant is suited in particular for magnesium alloys based on WE43.

According to a second variant, the method comprises the following steps:

(i) providing a blank made of the biocorrodible magnesium alloy;
(ii) applying particles having the above-mentioned composition to the blank; and
(iii) melting the magnesium alloy onto the near-surface region of the blank.

According to this variant, the particles to be incorporated are applied directly onto the blank, which later forms the base body. After that, the magnesium alloy is locally melted on the surface, for example by laser treatment. After cooling, the particles are then embedded in the near-surface region of the blank.

DETAILED DESCRIPTION

fragment of the implant can be achieved by locally influencing the degradation rate, for example by providing the surfaces of the segment rings of a stent structure, but not the longitudinal connecting struts of the segment rings, with cathodic centers according to the exemplary techniques disclosed herein, whereby the struts degrade more quickly than the segment rings. Because the connecting struts dissolve more quickly, high longitudinal flexibility is achieved quickly, wherein the load-bearing capacity of the segment rings is still maintained.

The particles provide not only corrosion protection, but also increase the wear resistance against abrasion by increasing the hardness. In addition, by suitably selecting the particles and the composition thereof, polymeric substances can be effectively bonded to the surface. These polymeric substances can have a corrosion-inhibiting effect on the one hand, and on the other hand, they may contain one or more pharmacological active ingredients, or exhibit a pharmacological effect themselves.

The additional coating with a polymer can be technically implemented, for example, as follows. PLLA L214S (Boehringer Ingelheim) is dissolved in a concentration of 1.6% (w/v) in chloroform and rapamycin is added as the active substance. The active ingredient content preferably ranges between 15% and 20%, in relation to the solid matter content. The implant made of the modified magnesium alloy is immersed for 1 second into the solution using an underwater robot, pulled out, and air containing nitrogen is blown on so as to evaporate the solvent. This process is repeated until a sufficient layer thickness of approximately 5 µm has been reached.

The embodiments also apply analogously to other biocorrodible magnesium alloys and particle compositions.

It will be apparent to those skilled in the art that numerous modifications and variations of the described examples and embodiments are possible in light of the above teaching. The disclosed examples and embodiments are presented for purposes of illustration only. Other alternate embodiments may include some or all of the features disclosed herein. Therefore, it is the intent to cover all such modifications and alternate embodiments as may come within the true scope of the claims.