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(71) **Applicant** *(for all designated States except US)*: **DEPUY INTERNATIONAL LIMITED** [GB/GB]; St Anthony's Road, Beeston, Leeds LS11 8DT (GB).

(72) **Inventors; and**
(75) **Inventors/Applicants** *(for US only)*: **BIRBECK, Alec, Paul** [GB/GB]; DePuy International Limited, St Anthony's Road, Beeston, Leeds LS11 8DT (GB). **COLLINS, Ryan** [GB/GB]; DePuy International Limited, St Anthony's Road, Beeston, Leeds LS11 8DT (GB).

(74) **Agent**: **GOVER, Richard, Paul**; Urquhart-Dykes & Lord LLP, Tower North Central, Merrion Way, Leeds LS2 8PA (GB).

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— *with international search report (Art. 21(3))*

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(54) **Title**: SURGICAL PROSTHESES

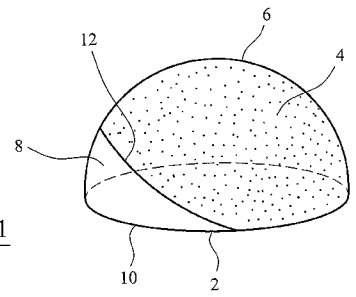


FIG. 1

(57) **Abstract**: A prosthesis arranged to be coupled to a bone. The prosthesis comprises a substrate (2) having a surface (6). The surface (6) of the substrate (2) has a first area and a second area, the first area being treated such that osteointegration is promoted more than in the second area. The interface (12) between the first and second areas forms an alignment mark to assist alignment of the prosthesis relative to a bone. The prosthesis is arranged to be at least partially inserted into a bone cavity such that the position of the alignment mark relative to the bone cavity is indicative of the angle of insertion of the prosthesis or the alignment mark provides a position reference for determining the implanted position of the prosthesis in the cavity. A method of manufacturing the prosthesis and a method of implanting the prosthesis are also provided.

Surgical Prostheses

The present invention relates to surgical prostheses. The present invention is particular suited to a rotationally symmetrical surgical prosthesis such as an acetabular cup.

It is well known to repair bone joints damaged through disease or injury by implanting prosthetic components to replace part or all of the natural bone joint. For example, surgical reconstruction of a hip joint may require a femoral prosthetic component implanted at the end of the femur to replace the natural femoral head with a prosthetic bearing head and a prosthetic acetabular cup implanted within a reamed acetabular cavity or the natural acetabulum to receive the prosthetic bearing head.

There are a range of different fixation techniques known for securing prostheses to the surface of bones, or within bone cavities. Furthermore, these fixation techniques may be used in combination. Commonly, mechanical fixation is provided by securing the prosthesis with screws, pegs, wires or similar fasteners extending from the prosthesis into the bone. It is also known to provide a coating to a surface of a prosthesis which when implanted is in contact with the bone, or in close proximity to the bone, where the coating is chosen to promote osseointegration. Osseointegration is the direct structural and functional connection between living bone and the surface of a prosthesis. Osseointegration may either result from mechanical retention whereby bone ingrowth into surface features of a prosthesis, in particular a metal prosthesis, secures the prosthesis to the bone, or bioactive retention whereby the implant is coated with a bioactive material which stimulates bone formation leading to a chemical bond in which the implant is ankylosed with the bone.

Osseointegration by mechanical fixation occurs for a number of metals commonly used within implantable prostheses, such as titanium and titanium alloys. It can be encouraged by the provision of topological features like vents, slots and dimples upon the surface of the prosthesis in contact with the bone. There is no chemical retention of the prosthesis and the retention is dependent upon the surface area of the prosthesis.

Osseointegration by mechanical fixation may be encouraged by treating a surface portion of a prosthesis to increase its surface area, for example etching the surface. Alternatively, it is known to apply a porous coating to the metallic substrate such that bone ingrowth into the pores forms a firm bond between the prosthesis and the bone. The porous coating may consist of a plurality of small discrete particles of a metallic material bonded together at their points of contact to define a plurality of connected interstitial pores in the coating. Such a coating material, and a method of forming the coating, is described in US-3855638. Preferably, the particles are of the same metallic material as the substrate. The coating may be formed by applying an adhesive to the portions of the substrate to be coated and applying the particles to the adhesive. Alternatively, a slurry of metallic powder suspended in an aqueous solution may be formed and applied to the substrate. The prosthesis is then sintered to remove the adhesive or aqueous solution and to fuse the particles together and to the substrate. Such a porous coating is commercially available from DePuy Orthopaedics, Inc under the name Porocoat.

Bioactive osseointegration occurs when the coating stimulates bone formation. A suitable coating material is hydroxyapatite (HA, also known as hydroxylapatite). Hydroxyapatite is a naturally occurring mineral form of calcium apatite which forms up to seventy percent of natural bone. Hydroxyapatite is commonly used as a filler to replace amputated bone or as a prosthesis coating to promote osseointegration.

Correct alignment of an implanted prosthesis relative to the natural bone, and in particular to any reamed cavity within the bone arranged to receive the prosthesis, is essential to ensure a strong bond to the bone and to achieve correct mobility of the reassembled joint. For instance, for an acetabular cup, a cavity is formed in the acetabulum (or if appropriate the natural acetabular cavity may be used) shaped to receive the cup (which generally has a hemispherical outer surface). The cup is intended to be positioned eccentrically within the cavity such that a portion of the cup protrudes above the rim of the cavity. However, inexperienced surgeons may mistakenly believe that the cup is intended to be seated and secured in position flush with the acetabulum rim in order to replicate the cups natural orientation. This is incorrect and can restrict the movement of the hip.

A second problem with conventional acetabular cup placement results from difficulty in positioning the cup owing to the surgeons viewing angle. To position an acetabular cup, typically the cup is inserted at an inclination of 40° relative to the patient's longitudinal axis. It is then typically necessary to apply 20° of anteversion (rotation about the patient's longitudinal axis) to assume a correct anatomic position. However, if the surgeon is viewing the patient on an anterior-posterior plane then when the operative anteversion is applied the inclination angle appears to increase. This compound angle effect could cause an inexperienced surgeon to compensate by reducing the inclination. However, this results in incorrect cup implantation, which increases the wear rate of the cup.

A third problem is that for conventional acetabular cups, when correctly placed in the cavity portions of the cup protruding from the cavity may comprise rough surfaces due to surface treatment of the substrate to promote osseointegration. The rough surfaces may abrade surrounding soft tissues.

It is an object of embodiments of the present invention to obviate or mitigate one or more of the problems associated with the prior art, whether identified herein or elsewhere. In particular it is an object of embodiments of the present invention to provide a prosthesis which aids the surgeon in correctly positioning the implanted prosthesis by reference to local bone landmarks.

According to a first aspect of the present invention there is provided a prosthesis arranged to be coupled to a bone, the prosthesis comprising a substrate having a surface: wherein the surface of the substrate has a first area and a second area, the first area being treated such that osseointegration is promoted more than in the second area; wherein the interface between the first and second areas forms an alignment mark to assist alignment of the prosthesis relative to a bone; and wherein the prosthesis is arranged to be at least partially inserted into a bone cavity such that the position of the alignment mark relative to the bone cavity is indicative of the angle of insertion of the prosthesis or the alignment mark provides a position reference for determining the implanted position of the prosthesis in the cavity.

An advantage of the first aspect of the present invention is that the alignment mark assists a surgeon in aligning the prosthesis relative to local bone landmarks. For instance, for embodiments of the present invention relating to acetabular cups, the alignment mark may indicate a correct alignment of the cup relative to the acetabular cavity. More specifically, the alignment mark may advantageously identify to the surgeon the correct proportion of the cup to protrude from the bone cavity. This reduces the risk of a cup incorrectly being inserted flush with the acetabular rim or the inclination angle being set incorrectly due to the effect of compound angles from the surgeon's viewing angle. The surface treatment may comprise applying a coating to the substrate to promote osseointegration. Alternatively, the surface treatment may comprise grit blasting the surface or otherwise treating the surface to remove material to increase the porosity or surface area of the substrate. The surface treatment may only be applied to the first area. Alternatively, the first area and the second area may both be treated, but the amount of treatment or the type of treatment may vary between the two areas. For instance, the depth of a coating material may be greater in the first area.

The position of the alignment mark relative to the bone cavity may be indicative of the portion of the prosthesis extending from the cavity.

The prosthesis may comprise a coating applied to the surface of the substrate in at least the first area to promote osseointegration, the second area comprising an interruption in the coating to form the alignment mark

According to an embodiment of the present invention there is provided a prosthesis arranged to be coupled to a bone, the prosthesis comprising a substrate and a coating applied to a surface of the substrate to promote osseointegration; wherein at least one interruption in the coating is provided forming an alignment mark to assist alignment of the prosthesis relative to a bone; and wherein the prosthesis is arranged to be at least partially inserted into a bone cavity such that the position of the interruption in the coating relative to the bone cavity is indicative of the angle of insertion of the prosthesis or the portion of the prosthesis extending from the cavity.

At least a portion of the coating may be arranged in use to be in contact with bone tissue. The coating may comprise a porous coating having a greater surface area than the underlying substrate. Alternatively, the coating may comprise a bioactive material to promote bone growth. The interruption in the coating may be detectable as a difference in roughness of the prosthesis surface and / or a step discontinuity in the prosthesis surface.

The prosthesis may be rotationally symmetrical about a first axis extending into the cavity. In particular, the prosthesis may comprise a cup arranged to be inserted into a bone cavity to form a socket component of a prosthetic ball and socket joint. The interruption in the coating may extend across a portion of a convex surface of the cup from a rim of the cup to a dividing line extending across the convex cup surface, the dividing line extending relative to the rim of the cup at a predetermined angle such that the interruption in the coating corresponds to a portion of the cup which is intended to protrude from a bone cavity when the cup is tilted within the bone cavity. Alternatively, the interruption in the coating may be formed along at least one line across the convex surface of the cup extending relative to the rim of the cup at a predetermined angle.

According to a second aspect of the present invention there is provided a method of manufacturing a prosthesis comprising: providing a substrate; identifying a first area and a second area; and treating the first area such that osseointegration is promoted more than in the second area, the interface between the first and second areas forming an alignment mark to assist alignment of the prosthesis relative to a bone; wherein the prosthesis is arranged to be at least partially inserted into a bone cavity such that the position of the alignment mark relative to the bone cavity is indicative of the angle of insertion of the prosthesis or the alignment mark provides a position reference for determining the implanted position of the prosthesis in the cavity.

Said step of treating the first area may comprise: masking the second area of the surface of the substrate; and applying a coating to promote osseointegration to the surface of the substrate in the first area such that the coating adheres to the non-masked first area of the substrate and the masked second area of the substrate comprises an interruption in the coating forming the alignment mark.

According to an embodiment of the present invention there is provided a method of manufacturing a prosthesis comprising: providing a substrate; masking a portion of a surface of a substrate; and applying a coating to promote osseointegration to the surface of the substrate such that the coating adheres to the non-masked portions of the substrate and the masked portion comprises an interruption in the coating forming an alignment mark to assist alignment of the prosthesis relative to a bone; wherein the prosthesis is arranged to be at least partially inserted into a bone cavity such that the position of the interruption in the coating relative to the bone cavity is indicative of the angle of insertion of the prosthesis or the portion of the prosthesis extending from the cavity.

According to a third aspect of the present invention there is provided a method of implanting a prosthesis comprising: inserting a prosthesis into a bone cavity, the prosthesis comprising a substrate having a surface, wherein the surface of the substrate has a first area and a second area, the first area being treated such that osseointegration is promoted more than in the second area, and wherein the interface between the first and second areas forms an alignment mark to assist alignment of the prosthesis relative to a bone; and aligning the alignment mark relative to a local bone feature by rotating the prosthesis within the bone cavity such that the position of the alignment mark relative to the bone cavity is indicative of the angle of insertion of the prosthesis or the alignment mark provides a position reference for determining the implanted position of the prosthesis in the cavity.

According to an embodiment of the present invention there is provided a method of implanting a prosthesis comprising: inserting a prosthesis into a bone cavity, the prosthesis comprising a substrate and a coating applied to a surface of the substrate to promote osseointegration, the coating having at least one interruption forming an alignment mark; and aligning the interruption in the coating with a local bone feature by rotating the prosthesis within the bone cavity such that the position of the interruption in the coating relative to the bone cavity is indicative of the angle of insertion of the prosthesis or the portion of the prosthesis extending from the cavity.

The present invention will now be described, by way of example only, with reference to the accompanying drawings, in which:

Figure 1 illustrates an acetabular cup in accordance with a first embodiment of the present invention;

Figure 2 illustrates in partial cross section the acetabular cup of figure 1 implanted into a reamed bone cavity; and

Figure 3 illustrates an acetabular cup in accordance with a second embodiment of the present invention.

Referring first to figure 1, this illustrates an acetabular cup comprising a hollow, generally hemispherical metal substrate 2 and a coating 4 over a portion of the convex surface 6, which when implanted is at least partially in contact with the bone. The coating 4 is intended to promote osseointegration and may be a porous coating such as Porocoat or a bioactive coating such as hydroxyapatite or any other similar coating material applicable to a surface of a prosthesis. The cup may have additional bone fixation means, for instance a screw hole (not shown) generally positioned at the pole of the hemisphere. The coating 4 extends over the majority of the convex surface 6, but is interrupted by an uncoated portion 8 which extends from one edge of the cup rim 10. The uncoated portion 8 is separated from the coating along a dividing line 12 which extends along an arc across the convex surface 6. The arc may begin and end at discrete points about the rim 10, or may extend to and from a single point on the rim 10. Alternatively, the dividing line 12 may generally comprise a circle extending about the cup.

Referring now to figure 2, this illustrates in partial cross section the cup of figure 1 during insertion into a bone cavity 14 formed within a patient's acetabulum. It can be seen that the dividing line 12 extends across the convex surface 6 at approximately 20° to the rim 10. The cup is positioned such that the dividing line 12 is approximately aligned with the acetabular rim 16 such that the uncoated portion 8 of the cup protrudes from the reamed acetabular cavity or the natural acetabulum 14. The angle of the dividing line 12 relative

to the rim 10 is chosen to allow the surgeon to clearly identify the proportion of the cup which should protrude from the cavity 14. It will be appreciated that in other embodiments of the invention the angle between the dividing line 12 and the rim 10 may vary.

The difference between the coating 4 and the uncoated portion 8 is clearly identifiable by the surgeon as both a difference in surface roughness and a step change in the surface of the cup (equal to the thickness of the coating 4). Consequently the uncoated portion 8 which serves as an alignment mark for positioning the cup relative to local bone landmarks (that is, the acetabular rim 16) is clearly identifiable even if obscured by blood or other fluids. Clear identification of the alignment marks is important in ensuring that they are readily identifiable during surgery. As such, forming alignment marks using differential coating techniques is preferable to alignment marks formed by laser marking or applying colours to the prosthesis surface, which may be more easily obscured.

The cup may be readily inserted into a prepared cavity by firstly rotating the cup about its polar axis such that the uncoated portion points to the edge of the cavity from which the cup is intended to protrude and then tilting the cup until the dividing line is parallel to the acetabular rim. As the uncoated portion of the cup is not in contact with the bone, there is no loss of strength due to the reduction in the area of the coating.

Referring now to figure 3, this illustrates an acetabular cup in accordance with a second embodiment of the present invention. Features that are common to figures 1 and 2 are referred to using the same reference numbers. While figures 1 and 2 illustrate a cup intended to be inserted into a bone cavity such that a fixed portion of the cup protrudes from the cavity at a fixed angle, it may be desirable for the angle of protrusion to be chosen by the surgeon intraoperatively. In place of a single uncoated portion of the convex surface 6, figure 3 illustrates a series of lines 20 within the coating 4 formed from regions where the coating is absent from the cup. Lines 20 comprise elongate gaps within the coating such that the coating is present between the lines 20. There may be four lines 20 as illustrated spaced apart from the rim 10 by 5°, 10°, 15° and 20°, however the number of lines and their spacing may vary, for instance there may only be a single line at the same angular position relative to the rim as the dividing line 12 illustrated in figure 1. The lines

may extend to the rim of the cup as shown in figure 3, however they may alternatively stop short of the rim or not intersect the rim.

Advantageously, if only a limited angular protrusion from the cavity is required, the reduction of coating area represented by the lines 20 that are positioned within the bone cavity is minimal. Conversely, for the cup of figures 1 and 2, if the surgeon decides to implant the cup at a smaller angular protrusion than that indicated by the full extent of the uncoated portion then there may be a significant reduction in coating in contact with the bone compared with a cup according to the prior art for which the whole of the convex surface is coated.

It will be appreciated that in alternative embodiments of the present invention differing sizes and shapes of the convex surface may be left uncoated to serve as alignment markings. For instance, the uncoated lines may be replaced by dashed lines, short lines not extending fully to the rim or only a single small circular interruption in the coating. More generally, any interruption in the coating capable of conveying alignment information for a prosthesis relative to local bone landmarks is within the scope of the present invention.

The interruptions in the coating may be provided by masking off portions of the prosthesis surface prior to applying the coating, as will be well known to the skilled person according to the particular coating material.

Although the present invention has been described above primarily with reference to a prosthetic acetabular cup, the invention is not limited to this application. For instance, the present invention may be applied to a cup arranged to be couple to a glenoid of a shoulder joint. More generally, the present invention is applicable to any prosthetic component and is particular suited to applications where the prosthetic component may be implanted at a variable angle relative to the bone, or with a varying proportion of the prosthesis protruding from a bone cavity, such that the interruptions in the coating assist in correctly aligning the prosthetic component. In particular, the coating interruptions assist in determining the proportion of the prosthetic component which is intended to protrude from a bone cavity.

The interruptions in the coating have been described above as a difference between a portion of the prosthesis surface where the coating is applied and a portion of the prosthesis surface where the coating is absent. However, in alternative embodiments of the present invention the interruptions may comprise a difference in coating thickness or the presence or absence of an additional layer of coating material. In further embodiments of the present invention there may be no coating material applied to the surface of the substrate. Instead, selected portions of the substrate may be treated to promote osseointegration, for instance by increasing the porosity or surface area of the material. For instance, selected portions may be grit blasted or otherwise treated to increase their roughness. The alignment mark comprises the interface between adjacent surface areas which have been differently treated to promote osseointegration to different extents. For instance, one area may not be treated at all, or treated to a lower extent or treated differently.

Further modifications to, and applications of, the present invention will be readily apparent to the appropriately skilled person without departing from the scope of the appended claims.

CLAIMS:

1. A prosthesis arranged to be coupled to a bone, the prosthesis comprising a substrate having a surface:

wherein the surface of the substrate has a first area and a second area, the first area being treated such that osseointegration is promoted more than in the second area;

wherein the interface between the first and second areas forms an alignment mark to assist alignment of the prosthesis relative to a bone; and

wherein the prosthesis is arranged to be at least partially inserted into a bone cavity such that the position of the alignment mark relative to the bone cavity is indicative of the angle of insertion of the prosthesis or the alignment mark provides a position reference for determining the implanted position of the prosthesis in the cavity.

2. A prosthesis according to claim 1, wherein the position of the alignment mark relative to the bone cavity is indicative of the portion of the prosthesis extending from the cavity.

3. A prosthesis according to claim 1 or claim 2, wherein the prosthesis comprises a coating applied to the surface of the substrate in at least the first area to promote osseointegration, the second area comprising an interruption in the coating to form the alignment mark

4. A prosthesis according to claim 3, wherein at least a portion of the coating is arranged in use to be in contact with bone tissue.

5. A prosthesis according to claim 3 or claim 4, wherein the coating comprises a porous coating having a greater surface area than the underlying substrate.

6. A prosthesis according to claim 3 or claim 4, wherein the coating comprises a bioactive material to promote bone growth.

7. A prosthesis according to any one of claims 3 to 6, wherein the interruption in the coating is detectable as a difference in roughness of the prosthesis surface and / or a step discontinuity in the prosthesis surface.

8. A prosthesis according to any preceding claim, wherein the prosthesis is rotationally symmetrical about a first axis.

9. A prosthesis according to any preceding claim, wherein the prosthesis comprises a cup arranged to be inserted into a bone cavity to form a socket component of a prosthetic ball and socket joint.

10. A prosthesis according to claim 9 when dependent upon claim 3, wherein the interruption in the coating extends across a portion of a convex surface of the cup from a rim of the cup to a dividing line extending across the convex cup surface, the dividing line extending relative to the rim of the cup at a predetermined angle such that the interruption in the coating corresponds to a portion of the cup which is intended to protrude from a bone cavity when the cup is tilted within the bone cavity.

11. A prosthesis according to claim 10, wherein the interruption in the coating is formed along at least one line across the convex surface of the cup extending relative to the rim of the cup at a predetermined angle.

12. A method of manufacturing a prosthesis comprising:

providing a substrate;

identifying a first area and a second area; and

treating the first area such that osseointegration is promoted more than in the second area, the interface between the first and second areas forming an alignment mark to assist alignment of the prosthesis relative to a bone;

wherein the prosthesis is arranged to be at least partially inserted into a bone cavity such that the position of the alignment mark relative to the bone cavity is indicative of the angle of insertion of the prosthesis or the alignment mark provides a position reference for determining the implanted position of the prosthesis in the cavity.

13. A method of manufacturing a prosthesis according to claim 12, wherein said step of treating the first area comprises:

masking the second area of the surface of the substrate; and

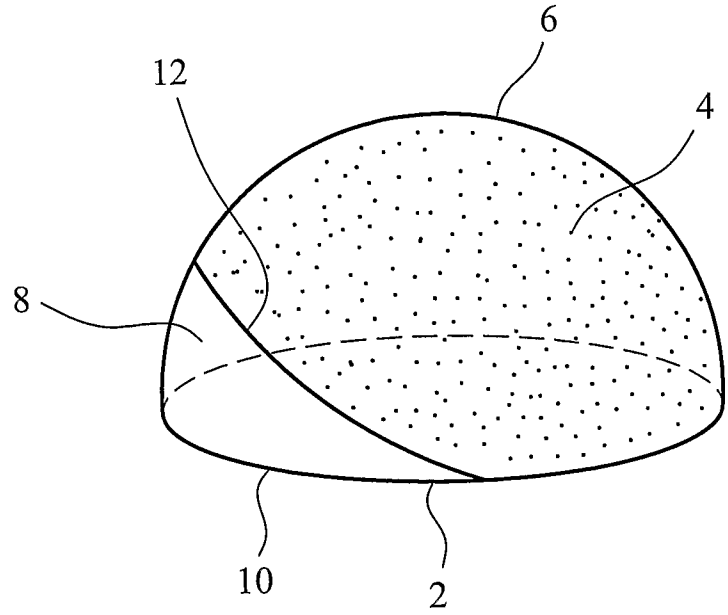
applying a coating to promote osseointegration to the surface of the substrate in the first area such that the coating adheres to the non-masked first area of the substrate and the masked second area of the substrate comprises an interruption in the coating forming the alignment mark.

14. A method of implanting a prosthesis comprising:

inserting a prosthesis into a bone cavity, the prosthesis comprising a substrate having a surface, wherein the surface of the substrate has a first area and a second area, the first area being treated such that osseointegration is promoted more than in the second area, and wherein the interface between the first and second areas forms an alignment mark to assist alignment of the prosthesis relative to a bone; and

aligning the alignment mark relative to a local bone feature by rotating the prosthesis within the bone cavity such that the position of the alignment mark relative to the bone cavity is indicative of the angle of insertion of the prosthesis or the alignment mark provides a position reference for determining the implanted position of the prosthesis in the cavity.

FIG. 1



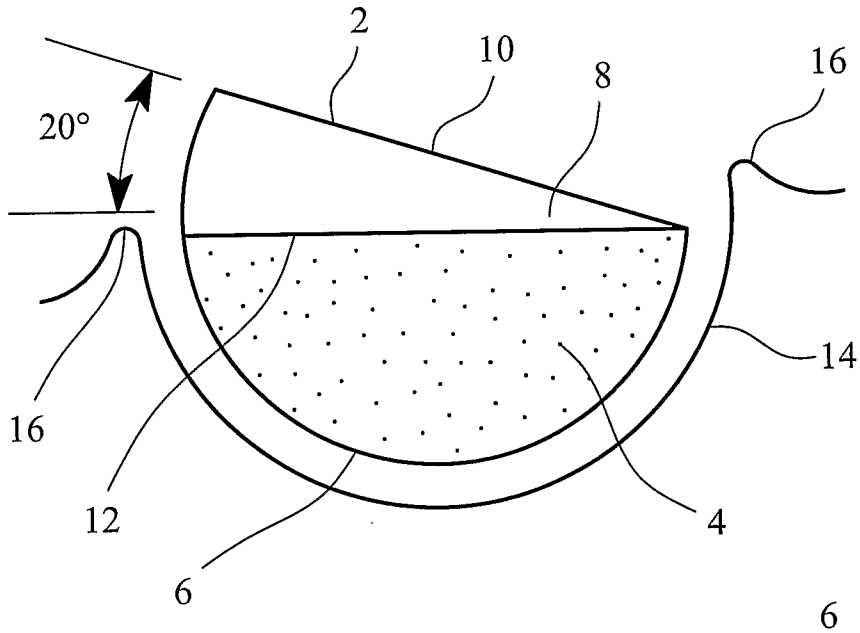


FIG. 2

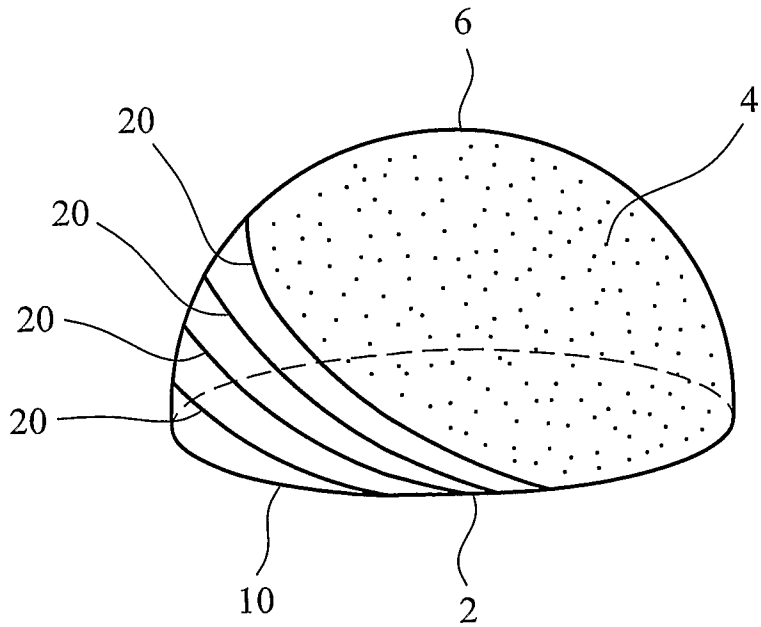


FIG. 3

INTERNATIONAL SEARCH REPORT

International application No
PCT/GB2010/000718

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61F2/34 A61F2/30
ADD. A61F2/00

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)
A61F

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

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 03/005928 A1 (INNOVA CORP [CA]; SHELEMAY AVI [CA]; KEHOE MIKE [CA]) 23 January 2003 (2003-01-23) page 5, paragraph 3 - page 7, paragraph 2; figures 1,2,4,6	1-13
A	US 3 855 638 A (PILLIAR R) 24 December 1974 (1974-12-24) cited in the application the whole document	1-13
A	US 2005/060040 A1 (AUXEPAULES ARNAUD [FR] ET AL) 17 March 2005 (2005-03-17) the whole document	1-13
A	EP 0 612 509 A2 (LENNOX D W [US] LENNOX DENNIS W [US]) 31 August 1994 (1994-08-31) the whole document	1-13

-/--

[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
13 July 2010	26/07/2010

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Cuiper, Ralf

Form PCT/ISA/210 (second sheet) (April 2005)

INTERNATIONAL SEARCH REPORT

International application No
PCT/GB2010/000718

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	FR 2 904 931 A1 (ADVANCED TECHNICAL FABRICATION [FR]) 22 February 2008 (2008-02-22) the whole document -----	1-13

INTERNATIONAL SEARCH REPORT

International application No.
PCT/GB2010/000718

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.: 14
because they relate to subject matter not required to be searched by this Authority, namely:

Rule 39.1(iv) PCT - Method for treatment of the human or animal body by surgery. Inserting a prosthesis into a bone cavity is a surgical treatment.

2. [ ] Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

[ ] The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

[ ] No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/GB2010/000718

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