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- (71) **Applicant:** OXFORD UNIVERSITY INNOVATION LIMITED [GB/GB]; Buxton Court, 3 West Way, Botley, Oxford OX2 0SZ (GB).
- (72) **Inventor:** PEGG, Elise; University of Oxford, Nuffield Department of Orthopaedics, Rheumatology & Musculoskeletal Sciences, Nuffield Orthopaedic Centre, Windmill Road, Headington Oxford OX3 7HE (GB).
- (74) **Agent:** FRESH IP; St John's Innovation Centre, Cowley Road, Cambridge CB4 0WS (GB).
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(54) **Title:** A METHOD OF PROVIDING A RADIO-OPAQUE POLYMER ELEMENT

(57) **Abstract:** A method of providing a polymer element with enhanced radio-opacity, comprising providing a treatment fluid comprising an oil-based fluid having a contrast agent, and bringing the polymer element and treatment fluid into contact such that the contrast element passes from the treatment fluid into the polymer element.

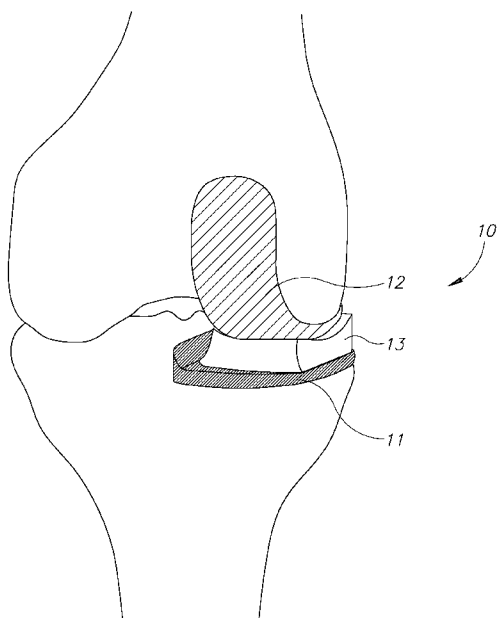


FIG.1



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Title: A Method of Providing a Radio-Opaque Polymer Element

[0001] The present invention relates to a method of providing a radio-opaque polymer element, particularly but not exclusively for providing a component for a surgical implant.

Background to the Invention

[0002] It is known to use polymers to provide components or bearing materials in surgical implants. A particular example is polyethylene, and in particular ultra-high molecular weight polyethylene (UHMWPE), which is used as a bearing material in replacement joint devices. A problem with polymer components of surgical implants is that they are not visible on a radiograph, as the material is radiolucent. This means that if the polymer component breaks, moves out of place or wears significantly, a surgeon may only become aware of this as result of an operation, or an MRI scan, and hence it can take a long time for such issues to be diagnosed.

[0003] A number of methods are known for making polymer components radio-opaque, in particular for use in medical devices. A conventional method involves introducing metal powders or other radio-opacifiers into a polymer powder, before the polymer powder is processed to form a component. It is also known to include more substantial pieces of metal embedded in a polymer implant as markers, such that the position of the implant can be inferred from the appearance of the metal pieces on a radiograph.

[0004] These solutions however have disadvantages, particularly with reference to the durability and lifetime of the polymer implant. Including pieces of metal as markers can increase the risk of the implant or component fracturing. The introduction of metallic powders or other radio-opacifiers into a polymer powder before processing can lead to the component having mechanical characteristics which are not suitable for use in long-term implantation. Polymeric materials fabricated using metal powders are usually used for temporary implantable devices such as catheters where long-term mechanical robustness and durability are not significant.

[0005] However, many polymer components and especially UHMWPE components used in joint replacements have very high requirements because they will be included in the body for many years, under high load. The material must be resistant to fatigue loading, must be bio-inert, have high wear resistance, high fracture toughness and very low friction. Such materials can be sensitive to changes in the manufacturing process and small changes can undesirably influence its performance.

Summary of the Invention

[0006] According to the present invention there is provided a method of providing a polymer element with enhanced radio-opacity, comprising providing a treatment fluid comprising an oil-based fluid having a contrast agent, and bringing the polymer element and treatment fluid into contact such that the contrast element passes from the treatment fluid into the polymer element.

[0007] The polymer element may comprise polyethylene, and preferably ultra-high molecular weight polyethylene (UHMWPE).

[0008] The polymer may alternatively comprise one of polytetrafluoroethylene (PTFE), polyurethane, and polyether ether ketone (PEEK)

[0009] The oil-based fluid may comprise poppyseed oil or a derivative of poppyseed oil.

[0010] The oil-based fluid may comprise rapeseed oil or a derivative of rapeseed oil.

[0011] The oil-based fluid may comprise peanut oil a derivative of peanut oil.

[0012] The contrast agent may comprise iodine.

[0013] The oil-based fluid may comprise iodized poppyseed oil.

[0014] The method may comprise bringing the polymer element and treatment fluid into contact for at least 24 hours.

[0015] The method may comprise bringing the polymer element and treatment fluid into contact for at least 48 hours.

[0016] The method may comprise heating the treatment fluid such that the treatment fluid has a temperature of at least 100° C.

[0017] The polymer element may comprise a component for a surgical implant

[0018] The polymer element may alternatively comprise a blank, the method further comprising subsequently forming the blank into a component for a surgical implant.

[0019] Alternatively the polymer element may comprise a powder, the method further comprising subsequently comprising forming the powder into a component for a surgical implant or a blank for component for a surgical implant.

[0020] According to a second aspect of the invention there is provided a polymer material comprising ultra-high molecular weight polyethylene and up to 1 wt% oil-based fluid having a contrast agent.

[0021] The oil-based fluid having a contrast agent may comprise an iodised oil, preferably wherein the iodised oil may comprise poppyseed oil.

[0022] The ultra-high molecular weight polyethylene may comprise a medical grade material.

[0023] The polymer material may have enhanced radio-opacity.

Brief Description of the Drawings

[0024] An embodiment of the invention is described by way of example only with reference to the accompanying drawings, wherein;

[0025] Figure 1 is a diagrammatic illustration of a known surgical joint as an example showing a UHMWPE polymer element,

[0026] Figure 2 is a diagram showing treated and untreated samples of a treatment fluid and of UHMWPE blocks treated with treatment fluid,

[0027] Figure 3 is a radiograph of the samples of Figure 2,

[0028] Figure 4 is a box plot illustrating the variation in radiographic intensity for each of the images UHMWPE samples of Figure 3, and

[0029] Figure 5 is a box plot illustrating the variation in radiographic intensity for each of the images of the treatment fluid samples of Figure 3.

Detailed Description of the Preferred Embodiments

[0030] With specific reference now to the drawings in detail, it is stressed that the particulars shown are by way of example and for purposes of illustrative discussion of the preferred embodiments of the present invention only, and are presented in the cause of providing what is believed to be the most useful and readily understood description of the principles and conceptual aspects of the invention. In this regard, no attempt is made to show structural details of the invention in more detail than is necessary for a fundamental understanding of the invention, the

description taken with the drawings making apparent to those skilled in the art how the several forms of the invention may be embodied in practice.

[0031] Before explaining at least one embodiment of the invention in detail, it is to be understood that the invention is not limited in its application to the details of construction and the arrangement of the components set forth in the following description or illustrated in the drawings. The invention is applicable to other embodiments or of being practiced or carried out in various ways. Also, it is to be understood that the phraseology and terminology employed herein is for the purpose of description and should not be regarded as limiting.

[0032] With reference to figure 1, an example of a conventional surgical joint is shown, in this case a partial knee replacement joint. The replacement joint generally shown at 10 has first and second components 11, 12 which partially replace and are connected to the tibia and femur, and an ultra-high molecular weight polyethylene (UHMWPE) liner 13, to provide a low friction bearing between the components 11, 12. As discussed above, while the components 11 and 12 are radiopaque, the liner 13 is radiolucent and it is desirable that this be made radiopaque such that it is visible on radiograph. The UHMWPE comprises a suitable medical grade material, such as GUR 1020 or GUR 1050.

[0033] In accordance with an embodiment of the present invention, a polymer component such as liner 13 is treated by bringing the polymer component into contact with a treatment fluid. The treatment fluid is preferably oil-based, and includes a contrast agent. By bringing the treatment fluid and polymer component into contact, the contrast agent diffuses into the polymer component and provides such that the polymer component is at least partially radio-opaque, that is that it has an enhanced radio-opacity compared to the untreated polymer, and will appear on radiograph images.

[0034] The resulting component would be predominantly UHMWPE and comprise up to 1 wt % iodised oil. The use of an iodised oil enables the iodine to suitably mix with the UHMWPE. It is believed that the iodised oil sits between, not within, the crystalline phases of the polymer, and the UHMWPE-iodised oil composite would have a slightly lower crystallinity than normal UHMWPE.

[0035] In the present example, it has been found that a suitable treatment fluid comprises poppyseed oil, or a derivative thereof, with a contrast agent comprising iodine, generally referred to as iodised poppyseed oil. As an example of the iodising process, the pure poppyseed oil is first converted to ethyl esters of the polyunsaturated fats. The ethyl esters are then reacted with hydroiodic acid, which results in the iodine being attached to the esters of the fatty acids by double

bonds. A commercially available example of iodised poppyseed oil is sold under the trade name Lipidol Ultra (R) which includes 478 mg of iodine per millilitre.

[0036] Other derivatives of poppyseed oil may be used as appropriate, or other oil based fluids may be suitable, in particular rapeseed oil, or a derivative of rapeseed oil, or peanut oil or a derivative of peanut oil. An appropriate oil may be selected bearing in mind the oil's biocompatibility and the patient's possible response, including possible allergic responses. Other contrast agents may be used as desired, such as bromine, for example through bromination, providing the contrast agent will form appropriate bonds with the treatment fluid or otherwise be carried by it, and the treatment fluid will diffuse appropriately into the polymer element being treated. Using iodized poppyseed oil in this manner is advantageous in that such oil is known to be biologically inert.

Example

[0037] A set of sample polymer elements were tested for a variety of infusion times, and the results are illustrated with reference to figures 2 to 5. As seen in figure 2, polymer elements comprising UHMWPE blocks 20 were provided. In this example, the blocks were cut from a sheet moulded specimen using a CNC machine and comprised 1 cm³ cubes.

[0038] The sample blocks 20 were separated into four groups A, B, C, D which were treated as summarised in table 1. In groups A to C, the blocks were immersed in the treatment fluid, where the treatment fluid was raised to 100° C. Groups A and B were immersed for 24 hours in the treatment fluid, and group A was prepared 24 hours before testing. Group C was immersed for 48 hours, and group D remained untreated as negative control. For each test condition, six UHMWPE blocks were immersed. After the testing was complete, samples were removed from the oil, wiped clean and placed in a well plate 21. The oil which corresponded to each test was also removed, and 2ml of each fluid transferred to a separate well plate 22. Untreated control samples were also used for the oil which acted as a positive control and the untreated UHMWPE cubes were a negative control. An image of the polymer samples and oil samples is shown in Figure 2 and the groups A, B, C, D are labelled.

[0039] The samples were then imaged using a standard X-ray machine. A fine focus was used, with a voltage of 60 kV and a current of 1.25 mA. The resulting radiograph is shown in Figure 3. The radiolucency, or radiographic intensity, of the samples within the radiograph of Figure 3 were quantified using a custom program which identified region for each sample and then calculated the mean value of the image greyscale for each sample. A one-way analysis of variance (ANOVA) was

used to assess whether there were any statistical significant differences between the groups with a Tukey post-test.

Group	Immersion Time (h)	Time before testing (h)	Temperature (°C)
A	24	24	100
B	24	0	100
C	48	0	100
D	0	0	100

Table 1: treatment parameters

[0040] Figure 4 is a boxplot illustrating the variation in average radiographic intensity for each of the sample polymer element groups and figure 5 is a boxplot illustrating the variation in average radiographic intensity for each of the iodised oil sample groups. The line in the middle of each box represents the median, the box the interquartile range and the lines the total range. It is apparent that groups A to C of the sample polymer elements exhibit enhanced, or increased, radio-opacity compared to the sample polymer element blocks of group D. This effect was significant ($p < 0.00001$). Immersion time was also found to have a significant effect ($p = 0.023$), the sample immersed for 48 h was significantly brighter than the ones immersed for 24 h. The 24 h resting time prior to testing did not significantly affect the test result. It can be clearly seen from the immersed samples that the outer surface of the UHMWPE cubes had absorbed a greater amount of the contrast agent, because the intensity at the surface is greater. This is a feature of the diffusion process. However, more uniform absorption could be possible with optimised diffusion temperatures and times. Fewer differences were observed between the oil samples, however, significant differences were identified between the untreated sample and the treated samples ($p < 0.007$). The temperature increased the effectivity of the contrast agent.

[0041] According, it will be apparent that the method described herein can be used to introduce contrast agent into a polymer element, in particular to introduce iodine into an UHMWPE element, in order to increase the radio-opacity of the element. This method may be used to prepare a component for a surgical implant, for example by treating the component as described above after manufacturing, or by treating a blank, that is a solid polymer element ahead of shaping or machining, before the blank is subsequently shaped to provide the implantable surgical component. The method may be used for other polymers where appropriate, such as polytetrafluoroethylene (PTFE), polyurethane, or polyether ether ketone (PEEK). Although a knee joint of known type is shown in figure 1 by way of example, it will be apparent that a polymer component treated by the method described herein may be used in any other suitable device or application. For example,

UHMWPE elements may be used in many surgical implants or replacement devices including hip, knee, ankle, shoulder, elbow, finger and toe devices, spinal replacement devices such as artificial disc replacements, cranial and maxillofacial implants, ligament replacement, cardiovascular implants (including but not limited to sutures), heart valves, abdominal, thoracic, aortic or aneurysm stents, sutures, meshes, and vascular grafts, and as an alternative to metal wires when treating trauma.

[0042] Further, although in the present example a single block was uniformly marked over its surface with a contrast agent, it will be apparent that localised areas or sub-elements of a polymer component may be marked. For example, an elongate component such as a replacement ligament may be marked with radio-opaque stripes using this method, such that changes in the length of the ligament would be apparent from measuring the separation of the radio-opaque stripes on a radiograph image. In other implants or components, other localised marking may be used to improve identification of the location of an element, or indicate wear, on the other function as desired.

[0043] The precise method and parameters by which the polymer element is brought into contact with the treatment fluid may be adjusted as appropriate, in particular as diffusion rates are known to be dependent on the fluid temperature and pressure, and the material forming the polymer component. For example, the elements may be partially or completely immersed in treatment fluid as described above, or contact a continuous stream of treatment fluid. Although treatment times of 24 hours and 48 hours are identified above, the treatment times may be at least 24 hours or at least 48 hours, or less than 24 hours if appropriate, and the treatment fluid temperature may be held constant or varied during treatment.

[0044] As an alternative to allowing the treatment fluid to diffuse into bulk polymer, the method may comprise combining a treatment fluid as described herein with UHMWPE powder, prior to forming the powder into a bulk polymer. The treatment fluid is thus brought into contact with the UHMWPE at an earlier stage in the manufacturing process. The combined UHMWPE powder and treatment fluid would then be combined in a process similar to manufacturing known UHMWPE components. For example, the combined UHMWPE powder and treatment fluid would be placed in a mould and exposed to a raised temperature and pressure for a suitable dwell time, to form a fully consolidated UHMWPE component. For example, a temperature of $\sim 170^{\circ}\text{C}$ and a pressure of $\sim 20\text{MPa}$ for a dwell time of about 2 hours. The percentage of iodised oil mixed with the powder in this example may be from 0.1 to 0.3% by weight. The resulting component may be a component for a surgical implant, or may be a blank or precursor which is subsequently shaped or machined to a component for a surgical implant.

[0045] In the above description, an embodiment is an example or implementation of the invention. The various appearances of “one embodiment”, “an embodiment” or “some embodiments” do not necessarily all refer to the same embodiments.

[0046] Although various features of the invention may be described in the context of a single embodiment, the features may also be provided separately or in any suitable combination. Conversely, although the invention may be described herein in the context of separate embodiments for clarity, the invention may also be implemented in a single embodiment.

[0047] Furthermore, it is to be understood that the invention can be carried out or practiced in various ways and that the invention can be implemented in embodiments other than the ones outlined in the description above.

[0048] Meanings of technical and scientific terms used herein are to be commonly understood as by one of ordinary skill in the art to which the invention belongs, unless otherwise defined.

CLAIMS

1. A method of providing a polymer element with enhanced radio-opacity, comprising;
providing a treatment fluid comprising an oil-based fluid having a contrast agent, and
bringing the polymer element and treatment fluid into contact such that the contrast element passes from the treatment fluid into the polymer element.
2. A method according to claim 1, wherein the polymer element comprises polyethylene, and preferably ultra-high molecular weight polyethylene (UHMWPE).
3. A method according to claim 1 where the polymer comprises one of polytetrafluoroethylene (PTFE), polyurethane, and polyether ether ketone (PEEK)
4. A method according to any one of claims 1 to 3 wherein the oil-based fluid comprises poppyseed oil or a derivative of poppyseed oil.
5. A method according to any one of claims 1 to 3 wherein the oil-based fluid comprises rapeseed oil or a derivative of rapeseed oil.
6. A method according to any one of claims 1 to 3 where in the oil-based fluid comprises peanut oil a derivative of peanut oil.
7. A method according to any one of the preceding claims wherein the contrast agent comprises iodine.
8. A method according to claim 7 where dependent on claim 4 wherein the oil-based fluid comprises iodized poppyseed oil.
9. A method according to any one of the preceding claims comprises bringing the polymer element and treatment fluid into contact for at least 24 hours.
10. A method according to any one of the preceding claims comprising bringing the polymer element and treatment fluid into contact for at least 48 hours.
11. A method according to any one of the preceding claims comprising heating the treatment fluid such that the treatment fluid has a temperature of at least 100° C.
12. A method according to any one of the preceding claims wherein the polymer element comprises a component for a surgical implant

13. A method according to any one of claims 1 to 11 wherein the polymer element comprises a blank, the method further comprising subsequently forming the blank into a component for a surgical implant.
14. A method according to any one of claims 1 to 11 wherein the polymer element comprises a powder, the method further comprising subsequently comprising forming the powder into a component for a surgical implant or a blank for a surgical implant.
15. A polymer material comprising ultra-high molecular weight polyethylene and up to 1 wt% oil-based fluid having a contrast agent.
16. A polymer material according to claim 15 wherein the oil-based fluid having a contrast agent comprises an iodised oil, preferably wherein the iodised oil comprises poppyseed oil.
17. A polymer material according to claim 15 or claim 16 wherein the ultra-high molecular weight polyethylene comprises a medical grade material.
18. A polymer material according to any one of claims 15 to 18 having enhanced radio-opacity.

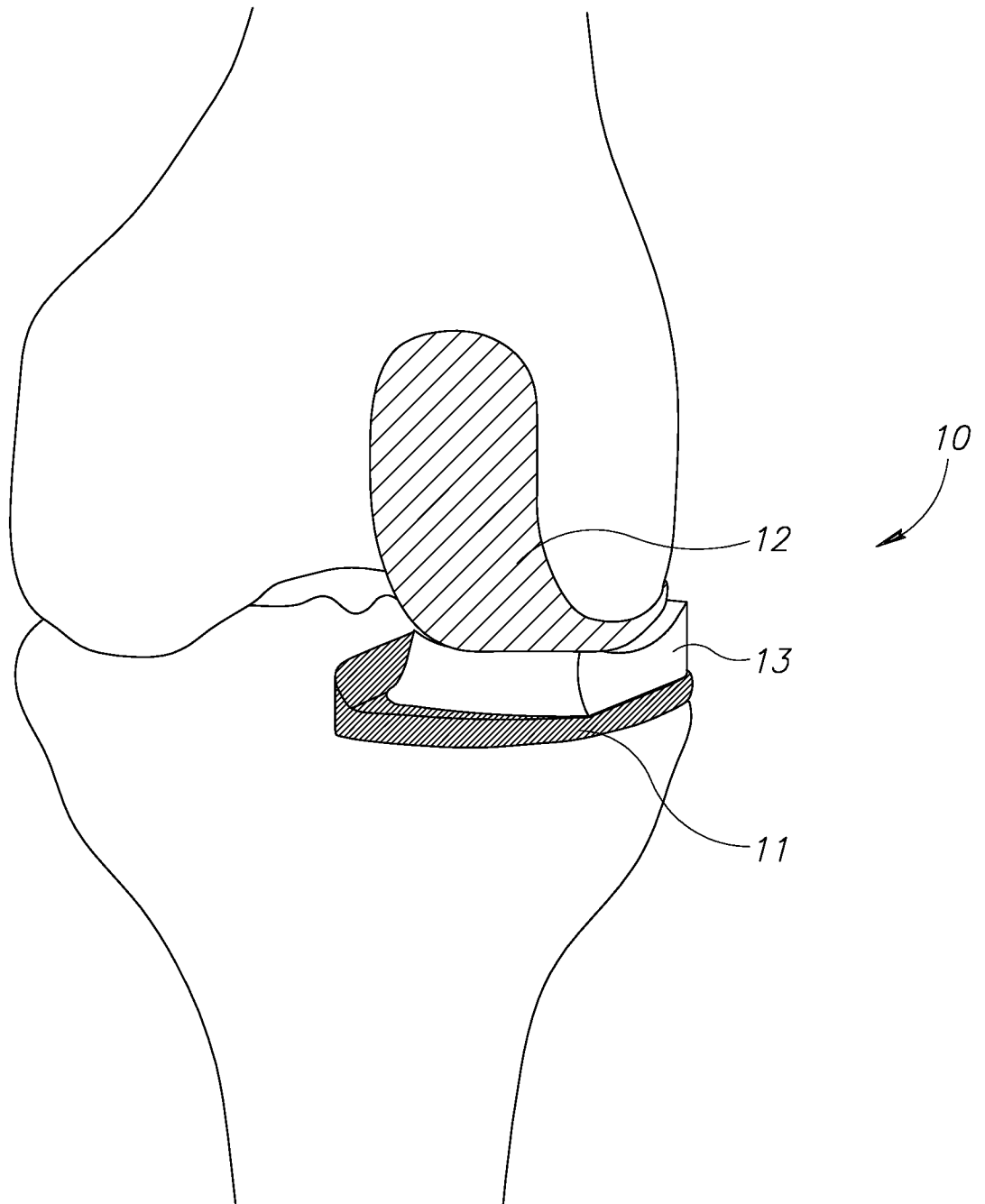


FIG.1

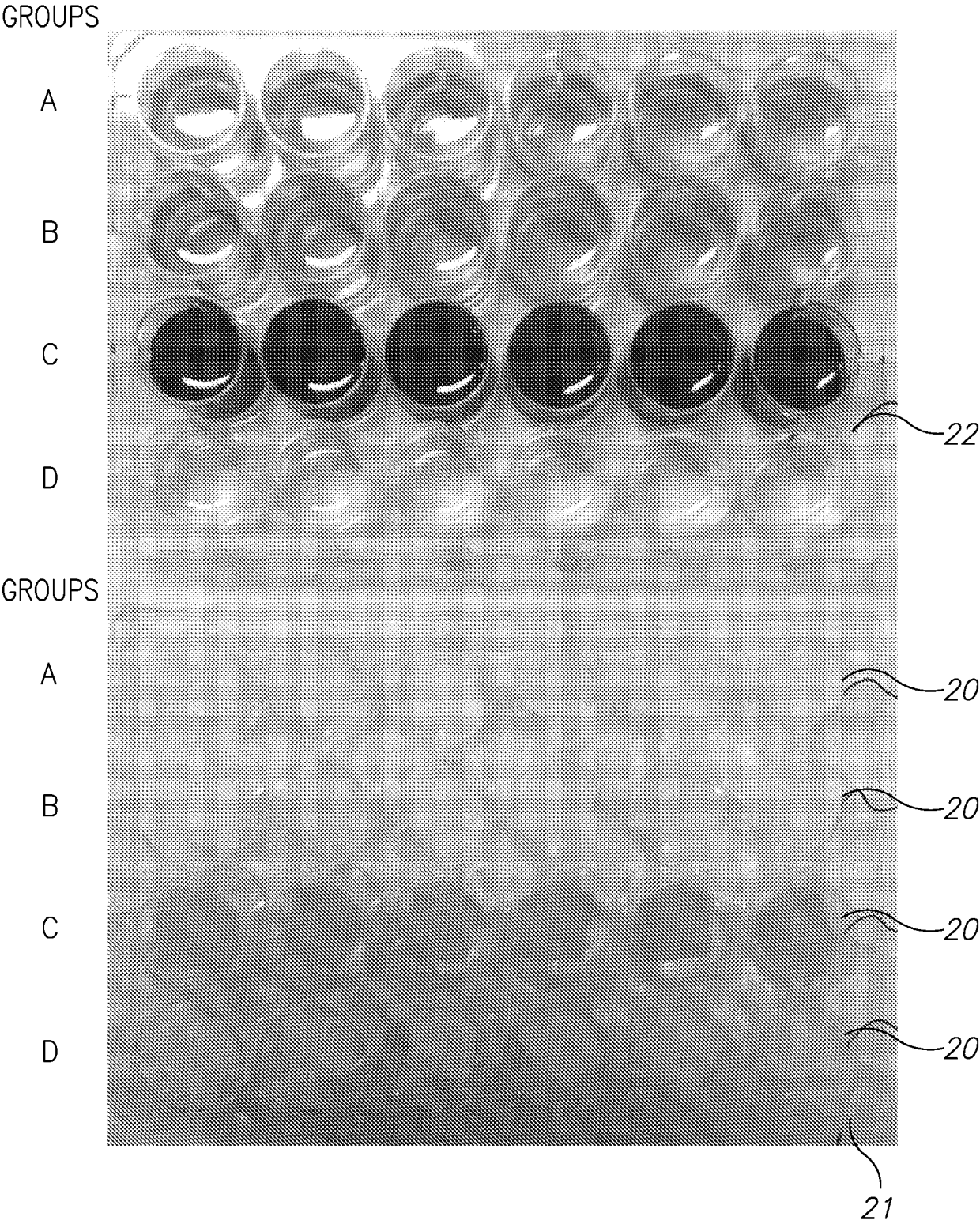


FIG.2

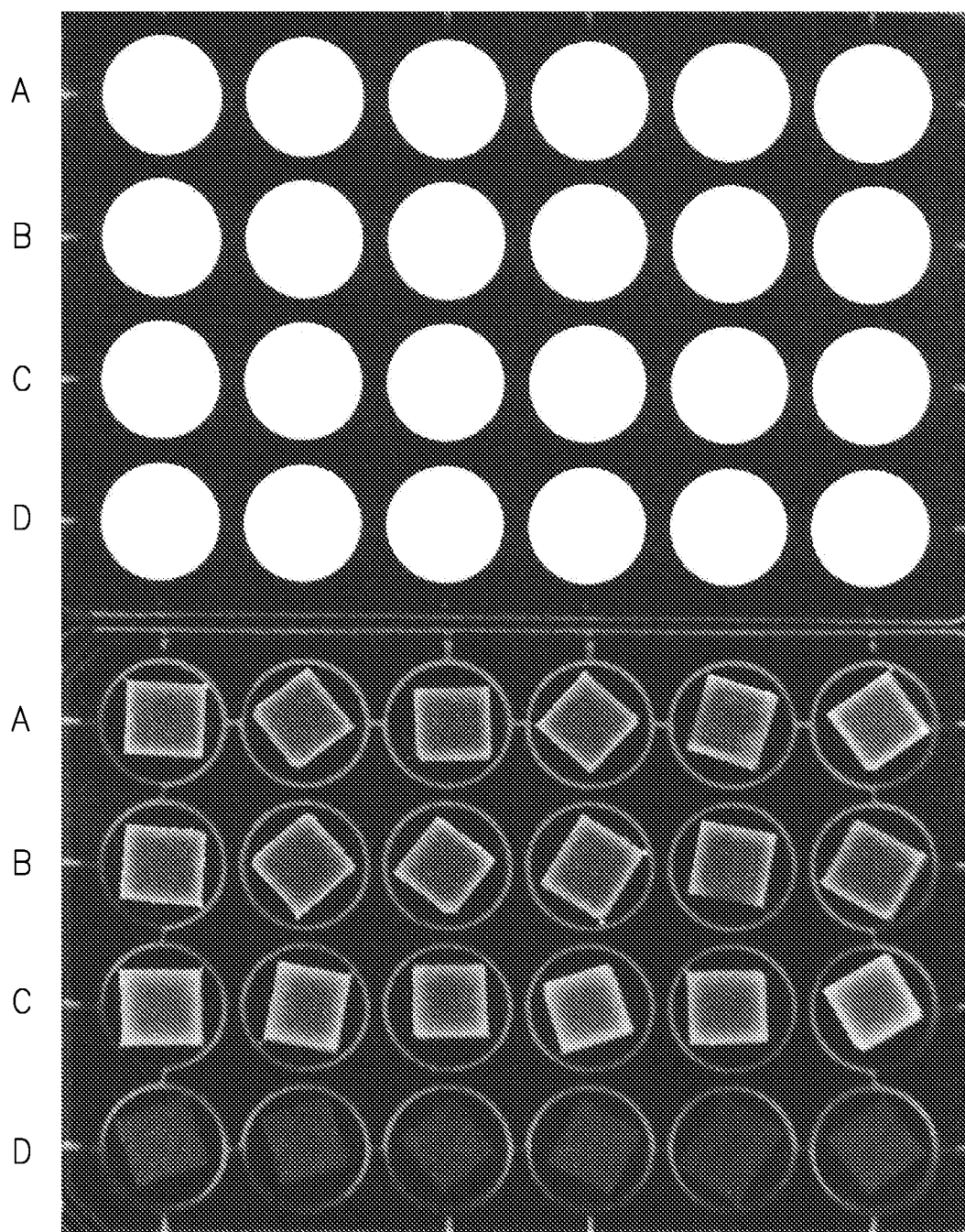


FIG.3

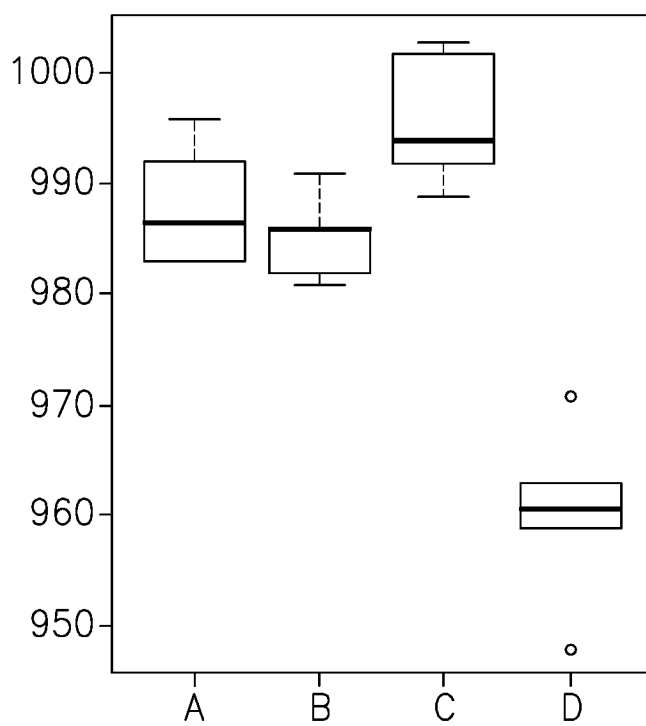


FIG.4

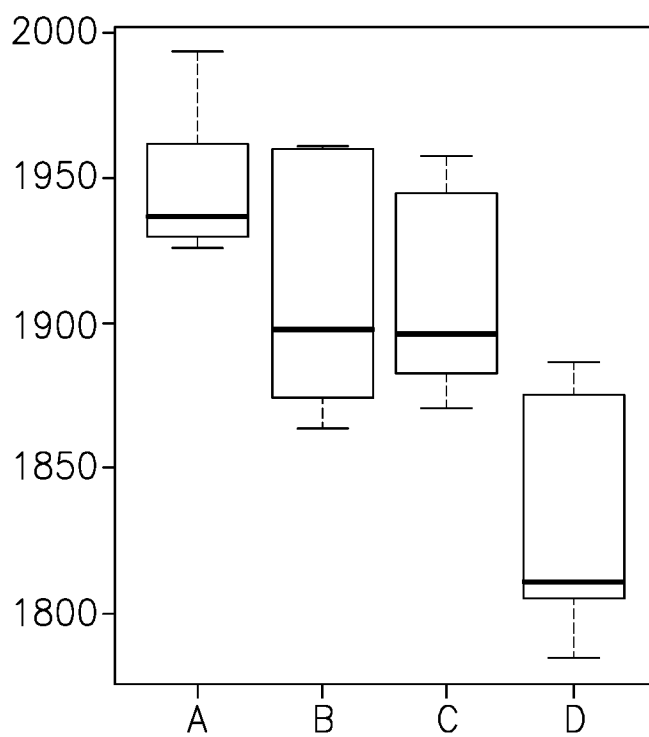


FIG.5

INTERNATIONAL SEARCH REPORT

International application No
PCT/IB2016/051171

A. CLASSIFICATION OF SUBJECT MATTER INV. A61L27/16 A61L27/18 A61L27/50 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) A61L		
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 practicable, search terms used) EPO-Internal, COMPENDEX, EMBASE, 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	US 2003/010939 A1 (DEMEO RONALD [US] ET AL) 16 January 2003 (2003-01-16) paragraph [0002] paragraph [0010] paragraph [0026] paragraph [0035] paragraph [0043] claims 1, 3, 13	1-4,7,8, 15-18
X	----- US 6 599 448 B1 (EHRHARD JR JOSEPH A [US] ET AL) 29 July 2003 (2003-07-29) column 1, lines 49-53 column 1, line 62 - column 2, line 9 column 2, lines 17-28 column 3, lines 10-18 example 3 ----- -/--	1,5-7, 9-12, 14-18
☒ Further documents are listed in the continuation of Box C. ☒ 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 application or patent 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 20 May 2016		Date of mailing of the international search report 31/05/2016
Name and mailing address of the ISA/ European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016		Authorized officer Zalfen, Alina

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