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Declarations under Rule 4.17:

— *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))*

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[Continued on next page]

(54) **Title**: PROSTHESIS FOR CRANIOPLASTY AND METHOD OF MAKING THE SAME

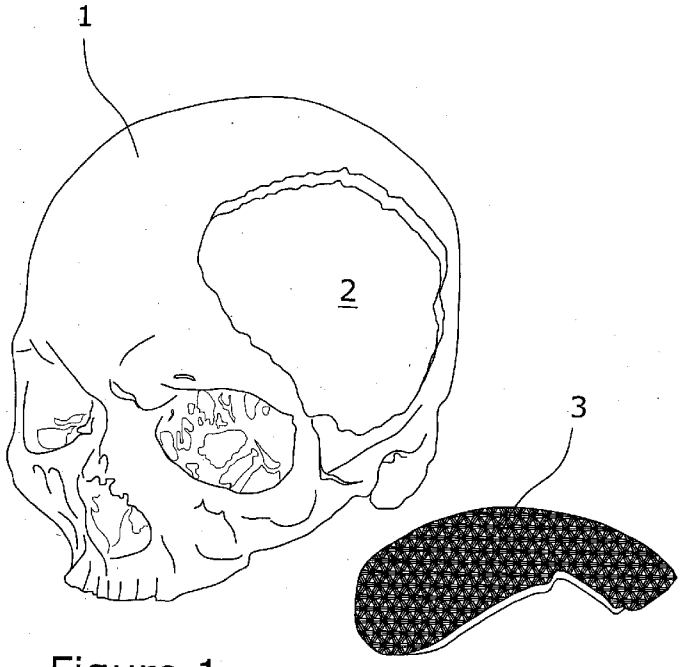

Figure 1

(57) **Abstract**: The present application relates to a prosthesis for cranioplasty made of biocompatible material, which is designed to be implanted to replace part of the missing bone of the skull, and the method for the construction for its embodiment. Said cranial prosthesis (3) made of biocompatible material, is of the type designed to be implanted permanently into a cavity (2) made in the skull (1), precisely imitating its contours and substantially reproducing the geometry of the original bone replaced by said prosthesis (3) and is characterised in that it comprises first means designed o position said prosthesis (3) correctly in said cavity (2) and second means designed to fix said prosthesis (3) permanently to the bone of skull (1), which said fixing, immediately protects the underlying brain tissue, without any additional means.

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PROSTHESIS FOR CRANIOPLASTY AND METHOD OF MAKING THE SAME

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The present invention relates to a prosthesis for cranioplasty made of biocompatible material, which is designed to be implanted to replace part of the missing bone of the skull, and the method for its embodiment.

The three most frequent events requiring cranioplasty are post-traumatic craniectomy, radical craniectomy and bone gaps secondary to malformation syndromes. Like all materials implanted in the human body, a skull prosthesis must be biocompatible. Moreover, it must faithfully reconstruct the original bone contours and be suitable to perform a protective function. The surgical procedure must be simple, and it must not alter the results of any instrumental tests which may be required, such as NMR, angiography, EEG, etc..

The prior art discloses the use of a customised cranioplasty prosthesis made of porous hydroxyapatite. Said prostheses, as well as meeting these requirements, provide an additional benefit, because in addition to biocompatibility they offer the osteoinductive capacity of porous hydroxyapatite, which is a biomimetic material.

In practice, cranioplasty wherein the craniectomy margins are juxtaposed with those of the porous hydroxyapatite implant according to the state of the art allows excellent reconstruction of the missing bone.

However, this method presents some drawbacks.

A first drawback is the initial fragility, which lasts for several months. This obliges patients to wear a protective helmet and pay particular attention to all their actions, because a trauma could cause the prosthesis to break.

A second drawback is the significant cost of manufacture.

A third drawback is that a resin model of the implant deriving from a 3D reconstruction of the skull is used to perform the craniectomy and form the craniectomy edge. In practice, the surgeon must find the best possible location for the test implant, and once it is resting on the skull, will design its perimeter and then remove bone to prepare the edges of the bone crater to receive the final implant. This procedure is particularly delicate, because movements of a few millimetres are very difficult to control when working with soft tissues and with organ positionings which are certainly not comparable to those which would be possible in a mechanical workshop. Positioning errors can therefore be made which, though having no influence on the removal of the lesion, can seriously affect the final appearance, especially if they are located on the parietal or frontal bossings and those areas are not covered by the hair.

To eliminate this drawback, an opening smaller than the implant to be received is made, and the edges are then shaped with a cutter. However, this operation increases the surgery time and, above all, is particularly critical because it is performed freehand, and any inaccuracies in the juxtaposition of the

craniectomy margins with those of the hydroxyapatite implant affect whether the prosthesis takes, and its colonisation by the osteoblasts and osteoclasts.

Finally, in some rare cases the prosthesis moves, and new surgery is required to reposition it.

According to patent application MI 2004 A 001464, the drawbacks deriving from the use of a hydroxyapatite prosthesis have been largely overcome.

According to the teaching of said patent application, a cavity is first made in the skull, then the shape of the skull and the craniectomy perimeter are measured by non-invasive methodologies such as a CAT scan; CAD-CAM techniques are then used to reconstruct the geometry of the prosthesis, and an *ad hoc* mould is made. Finally, a polymethylmethacrylate (PMMA) prosthesis is made and implanted into its seating by means of metal shape-memory clips.

This technique produces a prosthesis that perfectly fits with the edges of the opening in the skull, because said edges are first made by hand and then, measuring their geometry, the precision prosthesis is made. Moreover, working with a compact polymer overcomes the fragility problems presented by a porous hydroxyapatite prosthesis.

The metal alloy shape-memory clips are made in such a way as to tighten both the prosthesis and the cranial bone onto which said prosthesis is implanted. The wings of said clip are straightened cold so as to insert the implant into its seating. The body heat will then eliminate the deformation imposed, and the wings of said clip will tighten against the inner surface of

the bone, thus locking the prosthesis.

The locked prosthesis is sufficiently stable to perform its function effectively.

However, two fairly significant drawbacks still remain.

Firstly, unlike the hydroxyapatite prosthesis, colonisation by osteoblasts and osteoclasts does not take place, so the PMMA prosthesis does not bond with the bone of the skull; its stability, even long after surgery, is therefore based solely on the metal clips which, due to their shape, provide a barely acceptable level of strength.

Secondly, the implant is difficult to position because, even if it is made with great precision, faithfully copying the edges of the opening in the skull, in the objective situation wherein positioning takes place, it is difficult to effectively counteract the thrust of the underlying brain mass without using devices which can be harmful to the patient. If the edges of the opening in the skull are inclined, the situation improves, but the low thickness of the bone significantly limits this improvement.

The present invention at least partly eliminates said drawbacks, offering a prosthesis made of biocompatible material and a method for the construction of said prosthesis as claimed in claims 1 and 9 respectively.

The cranial prosthesis according to the invention is the type designed to be implanted permanently into a cavity made in the skull, precisely imitating its contours and substantially reproducing the geometry of

the original bone replaced by said prosthesis, characterised in that it comprises first means designed to position said prosthesis correctly in said cavity and second means designed to fix said prosthesis permanently to the bone of the skull, which said fixing immediately protects the underlying brain tissue, without any additional means.

Said first means designed to position the prosthesis correctly in the cavity in the skull comprise a projecting edge along the contour of said prosthesis, which said projecting edge abuts against the outer surface of the skull and is secured to it with screws.

A prosthesis of said shape can easily be positioned correctly in its seating because, as well as faithfully reproducing the edges of the seating, it can be pressed strongly against the skull without any risk of damaging the underlying brain tissue. In fact, the projecting edge of the prosthesis abuts against the surrounding cranial bones, against which it stops, and therefore does not enter the space occupied by the brain tissue. According to a preferred form of embodiment, the prosthesis is made of a composite material, in particular carbon fibres impregnated with biocompatible thermosetting resins.

The prosthesis according to the invention can therefore be implanted easily in the correct position and can be secured with screws that guarantee a connection with high mechanical strength. In this way the convalescence period is considerably shortened, and above all, there are no risks of damage.

The method according to the invention involves the following operations after removal of part of the skull:

- measurement by non-invasive methods of the geometry of said skull and the craniectomy edge, namely the edge of the cavity resulting from said removal;
- generation of the geometry of the prosthesis by CAD techniques;
- construction of the mould with a numerical-control machine tool, using CAM techniques;
- construction of the prosthesis using the mould made by numerical control.

The projecting edge that abuts against the skull allows the prosthesis to be positioned in its seating with great precision and speed, with obvious advantages involving shorter surgery times and improved results, especially in terms of appearance. Fixing with screws means maximum strength right from the outset, with a drastic reduction in recovery times.

The invention will now be described in detail according to a preferred embodiment thereof, by way of example but not of limitation, with reference to the annexed figures, wherein:

- figure 1 shows a skull, part of which has been removed, and a prosthesis according to the invention;
- figures 2 (a, b) show the prosthesis according to the invention implanted in the skull, and a detail of said prosthesis.

In fig. 1, no. (1) denotes a skull which has undergone craniectomy with removal of a large part of

said skull, said removal leaving a large cavity (2) in which a prosthesis (3) can be housed.

According to a preferred embodiment of the invention, prosthesis (3) is made of a composite material, in particular based on carbon fibres impregnated with biocompatible thermosetting resins, such as a BADGE (bis-phenol A diglycidyl ether) epoxy resin hardened with an amide hardener.

Fig. 2 shows prosthesis (3) implanted into the skull.

As shown in cross-section A-A, prosthesis (3) is characterised in that it presents a projecting edge (4) along the entire contour of prosthesis (3), which abuts against the outer surface of skull (1) in such a way that when fixed against the bone with screws (5), prosthesis (3) is already operational. In this way prosthesis (3) immediately has the strength required to perform a protective function. The width and thickness of edge (4) can have values of 3÷5 millimetres and 3÷4 tenths of a millimetre respectively.

Subsequent integration with the bone tissue seals the bone-prosthesis joint, but adds practically nothing to the strength of the prosthesis.

To facilitate precise positioning of prosthesis (3) in cavity (2), and to promote said integration with the bone tissue, it is advisable to make prosthesis (3) in such a way that it is inserted into cavity (2) with a clearance of about a millimetre.

The manufacturing process of said prosthesis involves measuring the geometry of cavity (2) and constructing a mould which will be used to make

prosthesis (3).

In practice, after the craniectomy, as the craniectomy edge is made in such a way that it is generally regular and substantially devoid of undercuts, the geometry of said craniectomy edge is measured by non-invasive methods, such as a CAT scan, which can be performed at the end of the surgical operation.

The skull cannot be closed immediately after surgery, because the swelling of the brain tissue and membranes caused by the operation must be resorbed. A helmet that protects the brain tissue against possible trauma is therefore worn by the patient for a few days. There is consequently time to measure the geometry of the skull and the craniectomy edge, construct a mould and manufacture prosthesis (3).

This procedure primarily prevents all contact with cavity (2), and also, with the use of CAD techniques, enables the complete geometry of the surface of said prosthesis to be determined, depending on the geometry of the intact part of the skull.

The geometry measured by said non-invasive techniques is used to make a mould with a numerical-control machine tool using CAM techniques, said mould being used to construct a prosthesis (3) to be implanted in cavity (2).

The presence of projecting edge (4), which abuts precisely against the surrounding bone surface of the craniectomy edge, also reproducing any irregularities in it, and the insertion of the prosthesis into cavity (2) with a suitable tolerance, allows prosthesis (3) to

be positioned very quickly in complete safety, thus reducing the length of the surgical operation.

In fact, prosthesis (3) can be pressed against its seating (2) perfectly safely, because the presence of edge (4) prevents the prosthesis from pressing on the brain tissue. Subsequent locking with screws (5) will secure prosthesis (3) to skull (1) in a stable manner, the mechanical strength of said joint being amply sufficient to maintain the prosthesis in its seating.

Moreover, any accidental trauma which the patient may suffer will be effectively withstood by the prosthesis, due to the high strength of the material from which it is made and to the fact that it uniformly distributes the load caused by trauma to the surrounding bones, due to projecting edge (4), which rests effectively on a relatively large surface that surrounds the craniectomy edge.

The thickness of the edge, namely 3÷4 tenths of a millimetre, is small enough not to be visible through the skin, said thickness being made possible by the high mechanical strength of the material from which prosthesis (3) is made.

This invention has been described by way of example but not of limitation according to a preferred form of embodiment thereof. The skilled person could devise numerous other embodiments and variations thereof, all of which fall into the ambit of protection of the following claims.

CLAIMS

1. Cranial prosthesis (3) made of biocompatible material, of the type designed to be implanted permanently into a cavity (2) made in the skull (1), precisely imitating its contours and substantially reproducing the geometry of the original bone replaced by said prosthesis (3), characterised in that it comprises first means designed to position said prosthesis (3) correctly in said cavity (2) and second means designed to fix said prosthesis (3) permanently to the bone of skull (1), which said fixing immediately protects the underlying brain tissue, without any additional means.

2. Cranial prosthesis (3), as claimed in claim 1, characterised in that said first means designed to position said prosthesis (3) correctly in said cavity (2) comprise a projecting edge (4) along the contour of said prosthesis (3), which said projecting edge abuts against the outer surface of said skull (1).

3. Cranial prosthesis (3), as claimed in claim 1, characterised in that said second means designed to fix said prosthesis (3) permanently to the bone of skull (1), which said fixing immediately protects the brain tissue without any additional means, comprise screws (5) which are inserted in said projecting edge (4) of said prosthesis (3), and are screwed into the bone against which said projecting edge (4) abuts, to position said prosthesis (3) in said cavity (2).

4. Cranial prosthesis (3), as claimed in claims 2 and 3, characterised in that said projecting edge (4) of said prosthesis (3) is 3÷4 tenths of a millimetre

thick.

5. Cranial prosthesis (3), as claimed in claims 2 to 4, characterised in that said projecting edge (4) of said prosthesis (3) is 3÷5 millimetres wide.

6. Cranial prosthesis (3), as claimed in claims 1 to 5, characterised in that the clearance between said prosthesis and the cranial bone is approximately one millimetre.

7. Cranial prosthesis (3), as claimed in claims 1 to 6, characterised in that it is made of a composite material.

8. Cranial prosthesis (3), as claimed in claim 6, characterised in that said composite material comprises carbon fibres impregnated with biocompatible thermosetting resins.

9. Cranial prosthesis (3), as claimed in claim 8, characterised in that said biocompatible thermosetting resins comprise a BADGE (bis-phenol A diglycidyl ether) epoxy resin hardened with an amide hardener.

10. Method for the construction of a cranial prosthesis (3), as claimed in claims 1 to 8, characterised in that it comprises the following stages after removal of part of the skull, said removal being performed in such a way that the shape of the edge is generally regular and substantially devoid of undercuts:

- measurement of the geometry of said skull (1) and the craniectomy edge by non-invasive methods;
- generation of the geometry of prosthesis (3) by CAD techniques;

- manufacture of a mould with a numerical-control machine tool using CAM techniques;
- manufacture of prosthesis (3) using said mould made with said numerical-control machine tool.

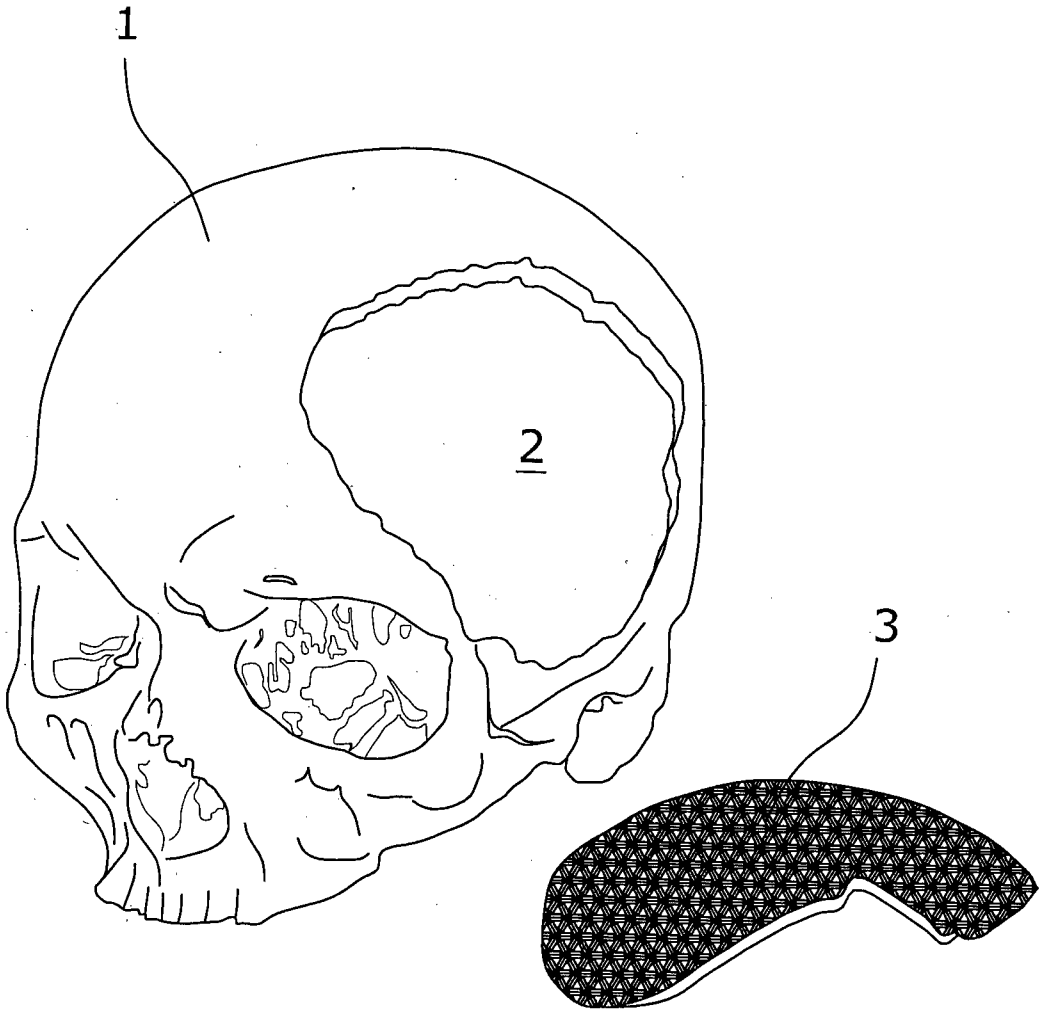

Figure 1

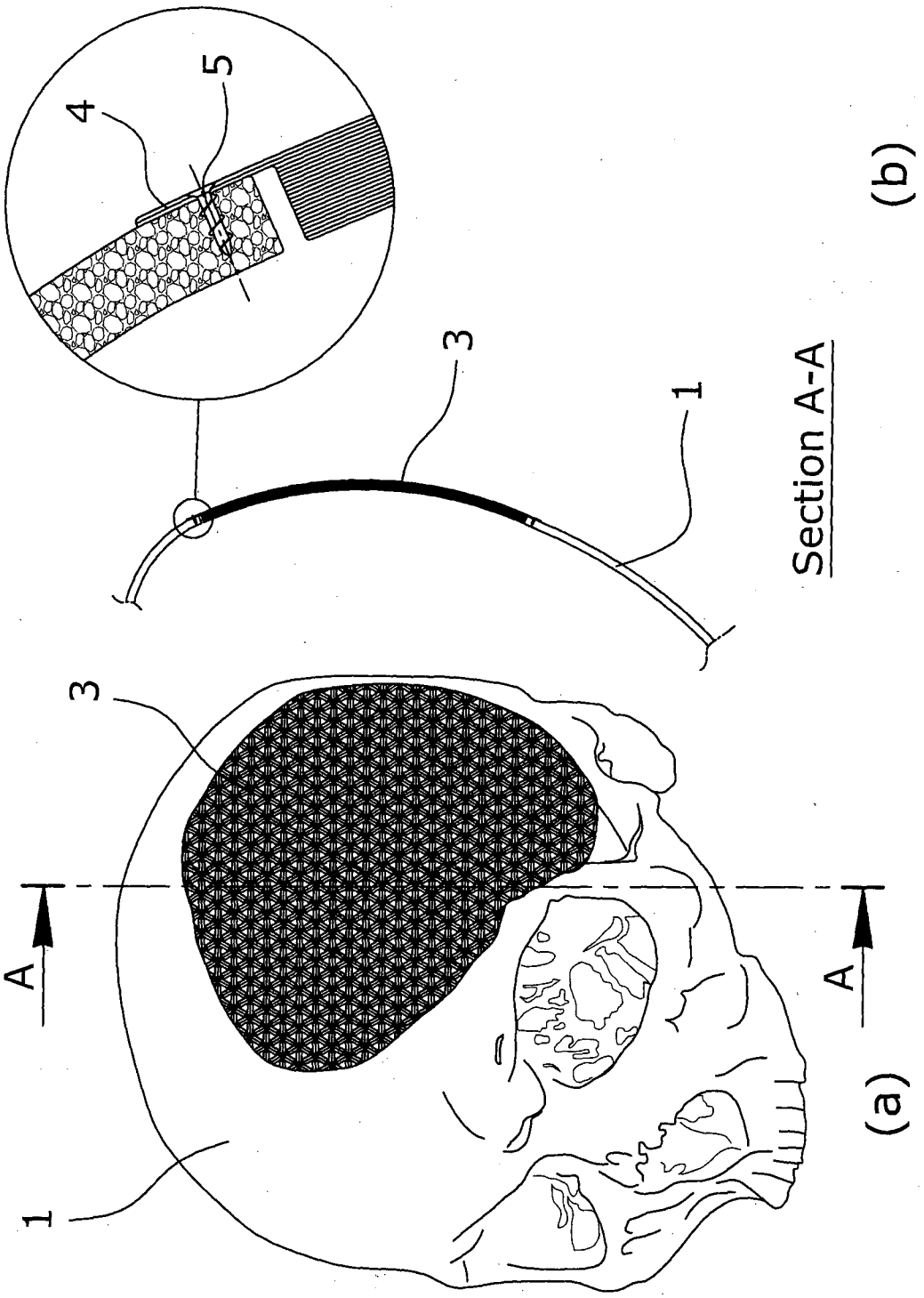

Figure 2

INTERNATIONAL SEARCH REPORT

International application No
PCT/IT2012/000125

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61B17/80
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)
A61B 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 practicable, 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 Y	WO 2010/141935 A2 (LINARES MEDICAL DEVICES LLC [US]; LINARES MIGUEL A [US]) 9 December 2010 (2010-12-09) page 1, paragraphs 2,3 page 2, paragraph 16 - page 5, paragraph 25 figures 3-3B -----	1-3,5,7 4,9,10
X A	EP 2 014 258 A1 (MAASTRICHT INSTR B V [NL]) 14 January 2009 (2009-01-14) column 1, paragraph 1-4 column 2, paragraph 16 - column 3, paragraph 18 figures 1,2 -----	1,2,7,8 10
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[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

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Date of the actual completion of the international search	Date of mailing of the international search report
20 July 2012	30/07/2012

Name and mailing address of the ISA/	Authorized officer
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INTERNATIONAL SEARCH REPORT

International application No
PCT/IT2012/000125

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

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Information on patent family members

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