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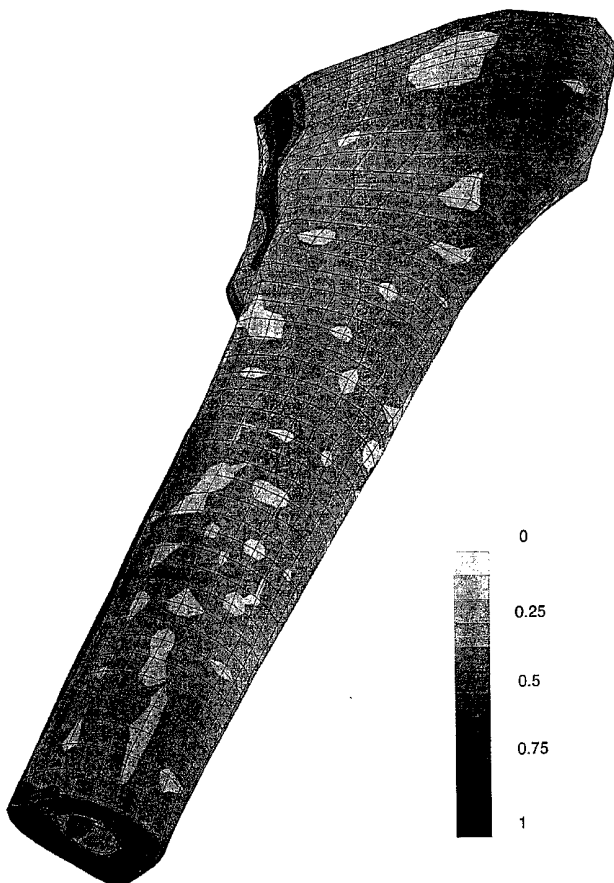
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- (71) **Applicants (for all designated States except US): HOPI-TAL ORTHOPEDIQUE DE LA SUISSE ROMANDE** [CH/CH]; 4, av. Pierre Decker, CH-1005 Lausanne (CH). **ECOLE POLYTECHNIQUE FEDERALE DE LAUSANNE (EPFL)** [CH/CH]; Service Des Relations Industrielles, Ecublens, CH-1015 Lausanne (CH). (84) **Designated States (regional):** European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).
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(54) Title: ACTIVE BIOCOATING FOR BONE IMPLANT



(57) **Abstract:** This invention relates to a bone implant coated with a layer which releases an active agent in order to control the bone remodeling.



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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

Active biocoating for bone implant

The present invention relates to bone implant.

- 5 More specifically, this invention relates to a bone implant coated with a layer which releases an active agent controlling the bone remodeling.

This kind of implant can be used for a total joint replacement, where it is observed following the procedure a marked phenomena of osteolysis in the
10 peri-implant zone. This bone tissue resorption can considerably decrease the efficiency of the implant necessitating generally to proceed a revision surgery.

In the United States of America, it is estimated that such revision surgery costs more than two billions dollars per year.

15

US patent No. 5 972 913 discloses an implant coated which a layer delivering progressively a dose of bisphosphonate in order to control the bone resorption in the peri-implant zone.

- 20 It is indeed known that bisphosphonates act as inhibitors of the bone resorption. Their progressive release at the implant surface enables to slow the bone resorption in the peri-implant zone.

Prior art bone implants such as the ones described in US patent No.
25 5 972 913, present however several drawbacks.

During their carrying out, it is not taken into account that the bone resorption in the peri- implant zone is not uniform. Some zones present a marked bone resorption while others, where the mechanical stress is important, present an
30 important bone formation. This means that a uniform coating of the active agent on the implant will considerably reduce its efficiency. In some situations,

the controlling of bone resorption with an active agent biocoating can be as much or even more detrimental as in situations where the implant is not coated with an active agent.

- 5 The present invention aims to remedy among others, the previously described problems.

This invention refers to an implant releasing an active agent which influences the bone remodeling, the implant being partially coated with a layer
10 comprising the active agent. The coated zones are located in peri-implant zones where the bone remodeling has to be controlled. The inventors of the present invention have surprisingly noted that a partial coating of the implant with an active agent that influences the bone remodeling, in particular with a bisphosphonate, can result in a significant decrease of the bone resorption in
15 the peri-implant zones. In all cases, the decrease of bone resorption with a partial coating of the implant was more marked than the bone resorption observed with an implant completely coated with the active agent.

In accordance with a preferred embodiment, the zones coated with the active
20 agent are determined by means of a model representing the bone remodeling in the peri-implant environment.

As example of model which may be used for the present invention, we can cite the model described in the article of A. Terrier, L. Rakotomanana, N.
25 Ramaniraka, and P.F. Leyvraz "Adaptation models of anisotropic bone", Computer Methods in Biomechanics and Biomedical Engineering, vol. 1, pp. 47-59, 1997.

In a variant of the invention, the model uses constant values experimentally
30 determined, which define the rate of bone resorption and formation.

The active agent used can be chosen among all substances acting on the bone remodeling.

Preferably, the active agent is a bisphosphonate.

5

By way of example of bisphosphonate, it can be cited the one described in US patent No. 5 972 913 or the Zolendronate™ from the company Novartis.

10 In another embodiment the implant is partially coated with an hydroxyapatite layer on which the active agent is superposed.

A particularly advantageous configuration of the invention is the coating of the implant with hydroxyapatite on which a bisphosphonate layer is superposed.

15 In the following text, the invention will be described by means of illustrated examples on the following figures:

Figure 1 illustrates the bone density distribution of a femur at the time of implantation of a hip prosthesis.

20

Figure 2 illustrates the bone density distribution of the femur of figure 1 following the bone adaptation corresponding to two years post-operatively.

25 Figure 3 illustrates the bone density distribution of the femur of figure 1 following the bone adaptation corresponding to two years post-operatively when the implant is completely coated with the active agent.

30 Figure 4 illustrates the bone density distribution of the femur of figure 1 following the bone adaptation corresponding to two years post-operatively when the implant is partially coated with the active agent.

On each figure, a low bone density is represented by a color tending to white, while a high bone density is represented by a color tending to black.

The color gray indicates zones where bone density has slightly changed with respect to the initial bone density measured at the time of prosthesis
5 implantation.

The femur shown on figure 1 together with its bone density have been reconstructed from CT-scan images. The inserted prosthesis is neither shown in this figure nor in the others.

10

A numerical simulation was then performed taking into account loading conditions simulating a loading on one leg (weight and muscles forces) and using the model of A. Terrier, L. Rakotomanana, N. Ramaniraka, and P.F. Leyvraz described in the previously cited article.

15

The figures 2 to 4 represent each time the bone remodeling of the same femur of figure 1 two years after the insertion of the prosthesis.

The figure 2 represents the bone density of the femur whose implant had no
20 bioactive coating. We note in this case a marked bone resorption in the proximal part of the femur, which can lead to an aseptic loosening of the implant.

A similar situation can be observed on figure 3 where the prosthesis had been
25 completely coated on its surface with a bisphosphonate. We note more precisely that the biocoating decreases only slightly the proximal bone resorption and has therefore no significant effect in comparison with the situation of an implant without an active agent coating.

30 The figure 4 illustrates the situation in accordance with the invention where the prosthesis has been coated only in its proximal portion. It clearly emerges that the partial coating enables to strongly decrease the bone resorption.

In examples not illustrated in the present text, an optimal bone remodeling has been observed by coating the prosthesis on zones of bone resorption observed on the figure 2.

5

Of course, the invention is not limited to the coating of the prosthesis at a precise position. It should be understood that the invention relates to a partial coating of a prosthesis by an active agent to control notably the bone remodeling in the peri-implant environment.

10

Claims

1. Bone implant releasing an active agent which influences the bone remodeling, **characterized** by the fact that it is partially coated with a layer
5 containing the said active agent, said layer being situated in peri-implant zones where the bone remodeling has to be controlled.
2. Implant according to claim 1, **characterized** by the fact that the position of said layer is determined by means of a model which represents the bone
10 remodeling in a peri-implant environment.
3. Implant according to claim 2, **characterized** by the fact that the model uses constant values, determined experimentally, which define the rate of bone resorption and formation.
15
4. Implant according to any of the previous claim, **characterized** by the fact that active agent is a bisphosphonate.
5. Implant according to any of the previous claim, **characterized** by the fact
20 that it is coated with a layer of hydroxyapatite on which the active agent is superposed.
6. Implant according to claim 5, **characterized** by the fact that the active agent is a bisphosphonate.
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Fig. 1

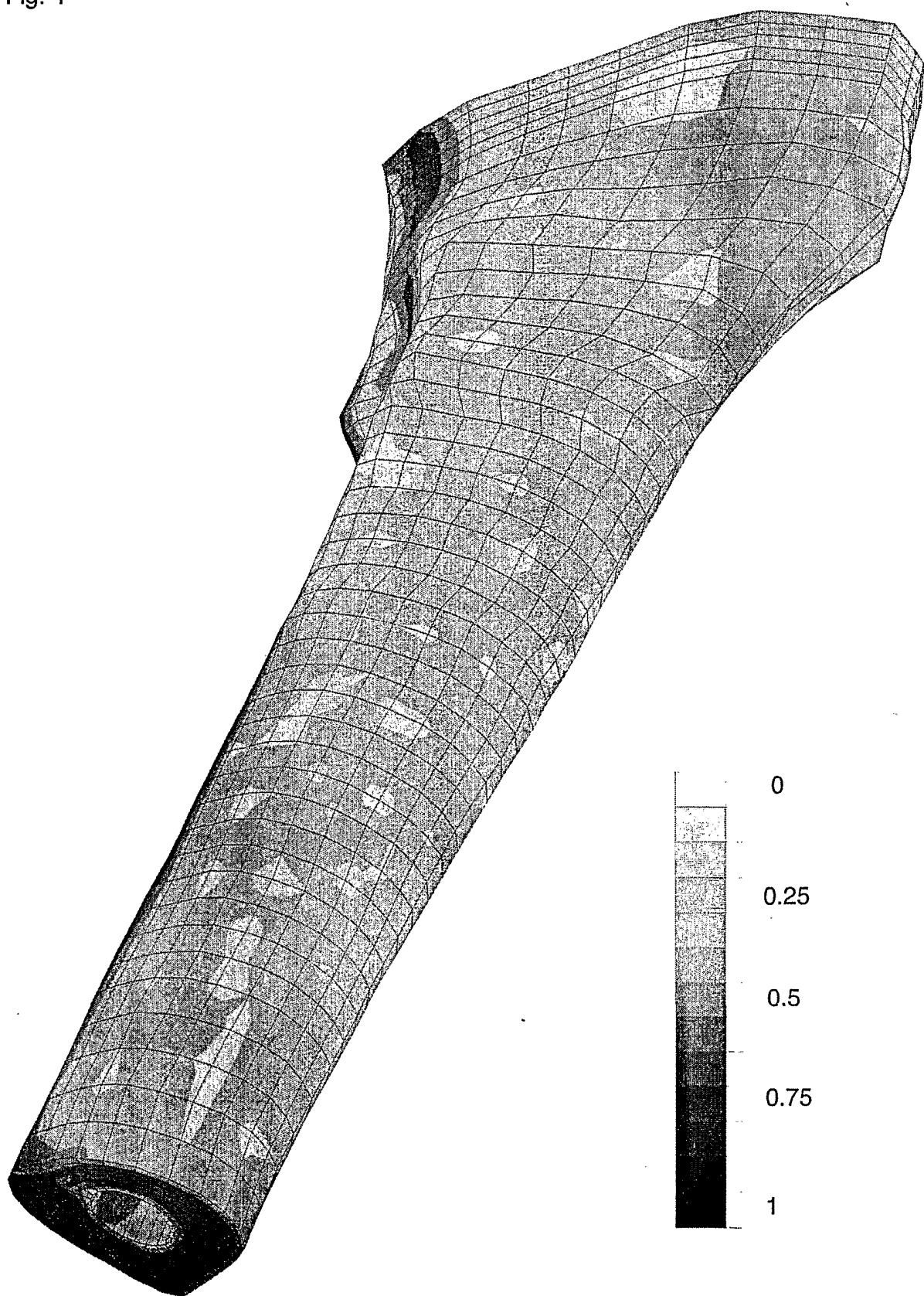
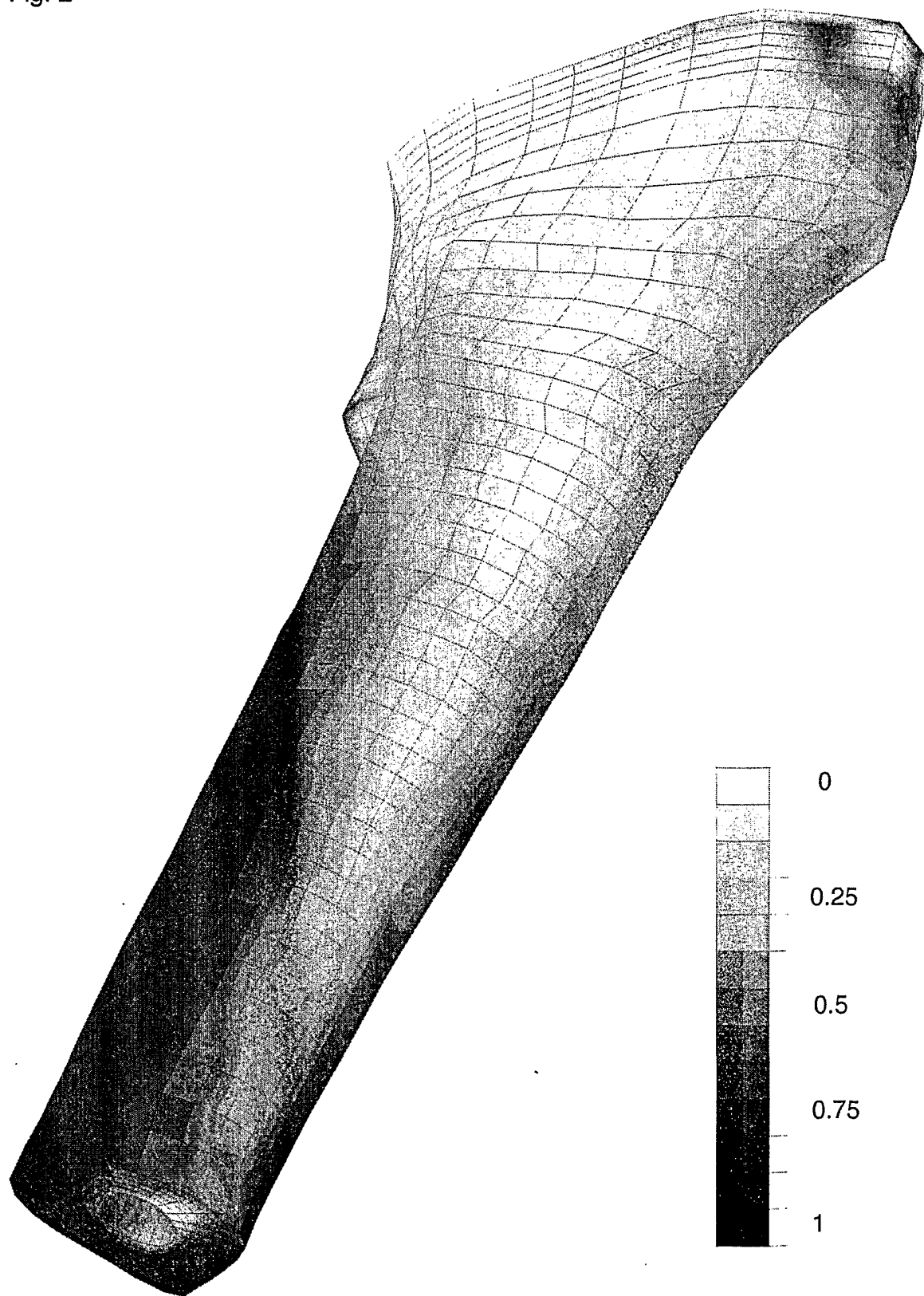
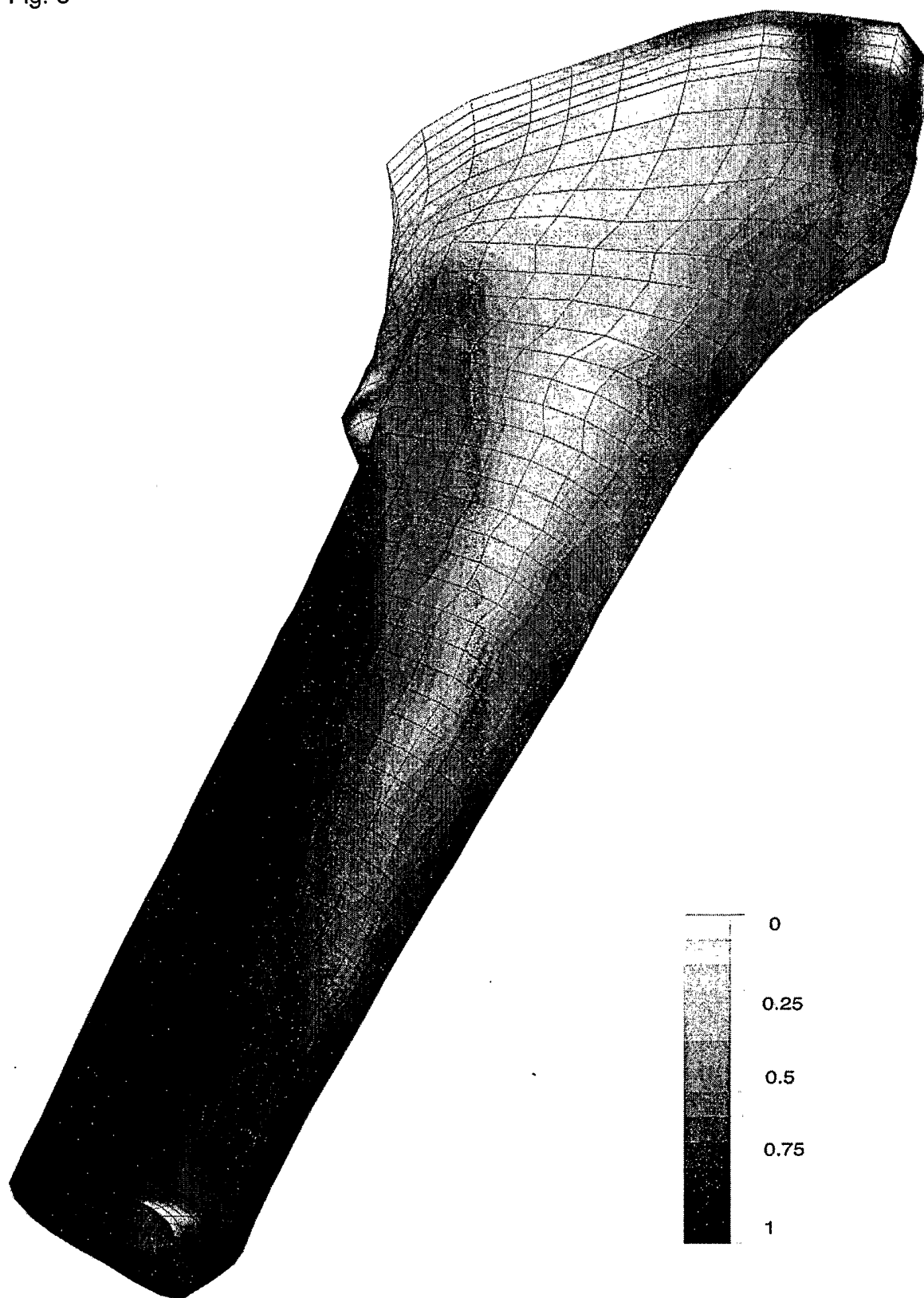


Fig. 2



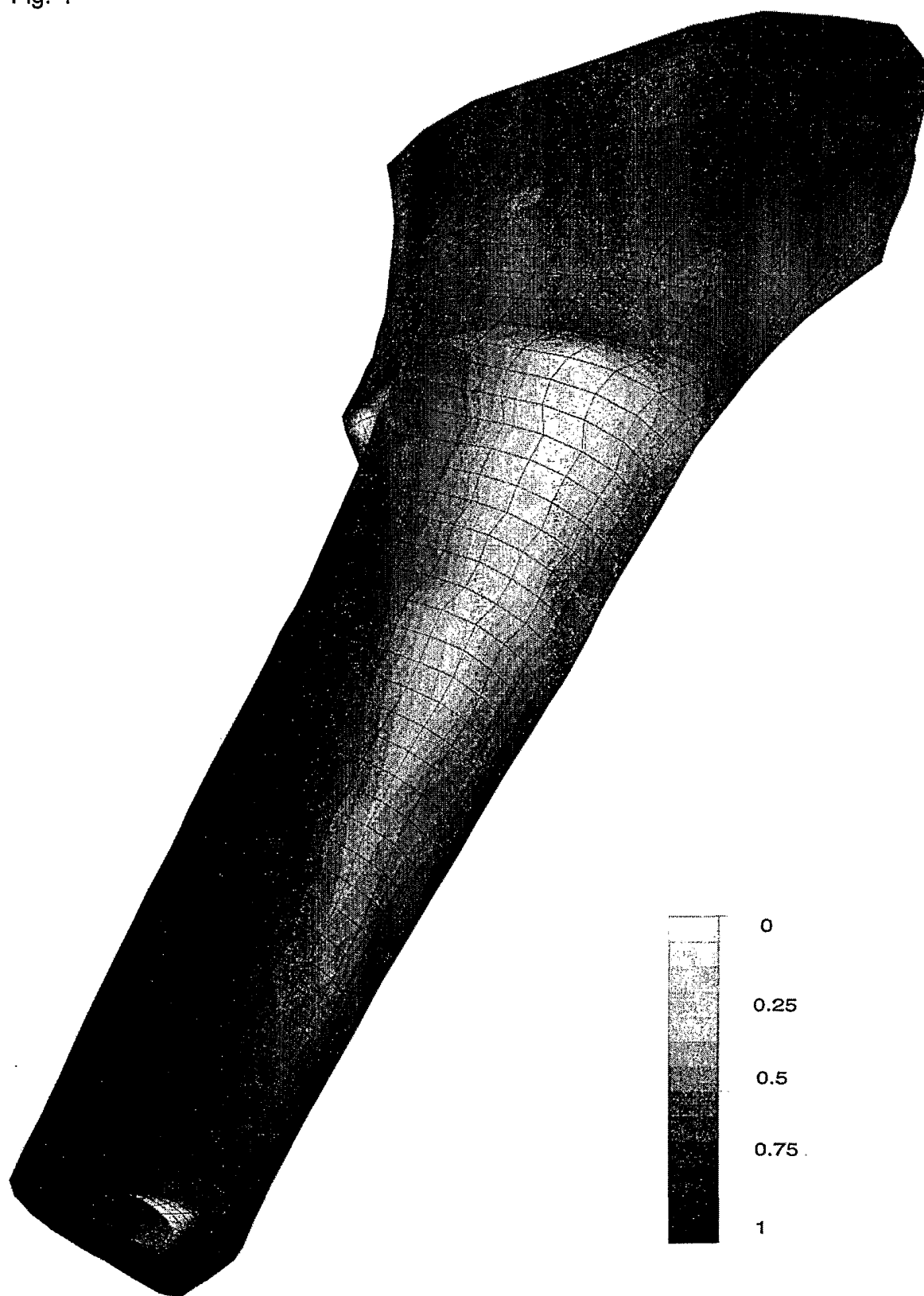
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Fig. 3



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Fig. 4



INTERNATIONAL SEARCH REPORT

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A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61L27/54 A61L27/32

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)
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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, WPI Data, PAJ

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Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

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- *A* document defining the general state of the art which is not considered to be of particular relevance
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- *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
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INTERNATIONAL SEARCH REPORT

In Application No
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