Multicomponent Coatings Improve The Biocompatibility of Load-bearing Implants

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ABSTRACT

New implants with nanomodified surfaces are studied in vivo under the conditions, when the replaced defect is located on the bone, which accomplishes motions with the large amplitude and with the large load.

Three types of implants were placed into rats femur.

An osteotomy was performed, and a 3 mm length of femur was removed. The implant was placed into the animal's tissue. The animals were allowed full weight bearing without any mobility restrictions immediately postoperatively.

The effectiveness of implants considered in comparison with a control group of implants without nanostructured modification was proved by experimental models not only for stable, but also for moving with the large amplitude load-bearing implants.

Keywords: nanostructured, coatings, implants, biocompatibility

1 AIMS AND INNOVATION

The aim of this work was to estimate the influence of new multicomponent nanostructured coatings on the implant's osseointegration process and osteogenesis around implant.

Titanium implants commonly used in orthopedics and dentistry integrate into host bone by a complex and coordinated process. The results of their application are completely satisfactory in many instances; however, are encountered the cases of the complications, which can be treated as the consequences of the insufficient biocompatibility of pure titanium. Figure 1 shows the inflammatory reaction, which was developed 6 months after operation on the reconstruction of the lower wall of orbital cavity by titanium implant, shown in figure 2. The signs of inflammation, thinning the skin, threat of the formation of sore and even fistulae can be seen. The danger of the similar complications development makes it necessary the search for titanium implants coatings, which would improve their biocompatibility and osseointegration. Osseointegration is a direct connection between living bone and the titanium implant at the level of the light microscope.

Comparing with the previous studies [1] new implants are studied in vivo under the conditions, when the replaced defect is located on the bone, which accomplishes motions with the large amplitude and with the large load.

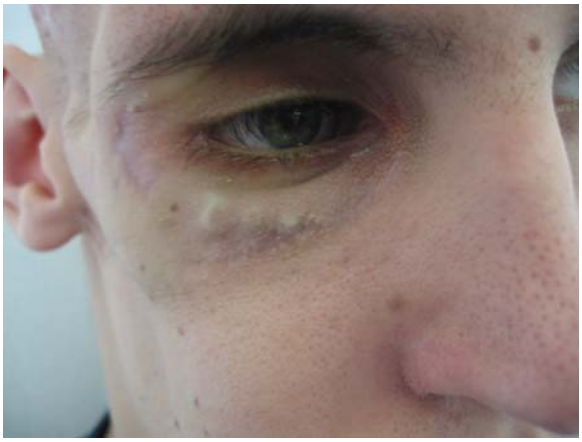

Figure 1: Clinical example: Inflammatory reaction around the pure titanium implant.

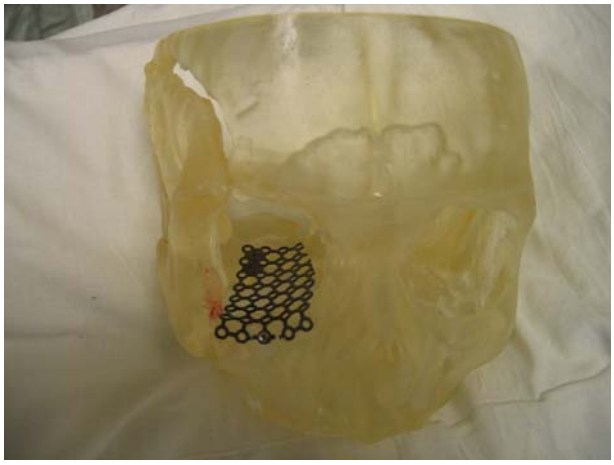

Figure 2: The same implant before the surgery

2 MODEL

2.1 Animals and implants

In this study we used the rat femur model. For the purpose of this investigation 48 rats (250–300 g)were used.

Experimental implants were manufactured from commercially available pure titanium and coated at the Moscow State Institute of Steel and Alloys.

Three types of implants (Figures 3, 4) were placed:

Figure 3. Implants shape

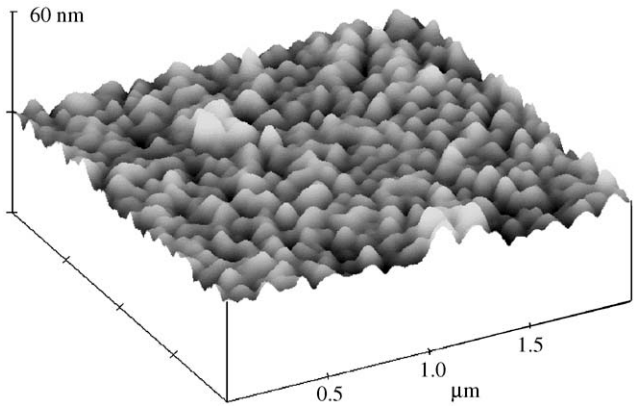

Figure 4. ATM image of implants surface [2]

One type had pure titanium core (Ti medical nets) with $TiC_{0.5}$+10%($Ca_{10}(PO_4)_6(OH)_2$) composition coated on the surface. The average grain size is 10 – 40 nm.

Another tpe had pure titanium core with TiC0.5+CaO composition coated on the surface. The average grain size is 10 – 40 nm as well.

The control was a pure titanium implant.

2.2 Surgical procedures

Surgical procedures were conducted in compliance with ethical principles for animal research, as approved by MROI and European (European Convention for the protection of vertebrate animals used for experimental and other scientific purposes) guidelines.

An anesthetic solution containing phentanili and droperidoli was injected intraperitoneally. Surgery was performed on the front of the lower limb, unilaterally under sterile conditions.

An osteotomy was performed, and a 3 mm length of femur was removed under general anesthesia. The implant was placed into the animal's tissue. Four screws fasten the implant to the femur's fragments fixing them (Figure 5). The animals were allowed full weight bearing without any mobility restrictions immediately postoperatively.

Standard plain radiographs of the dissected bones were taken in lateral projections (Figure 6) to ensure implant's stability.

2.3 Tissue processing

The rats were sacrificed and tissues investigated 5, 10, 15 and 30 days postoperatively.

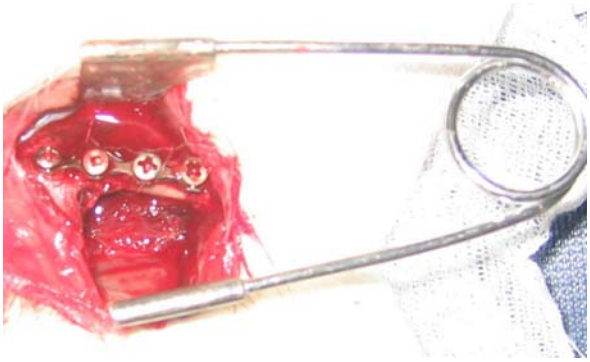

Figure 5. Intraoperational view

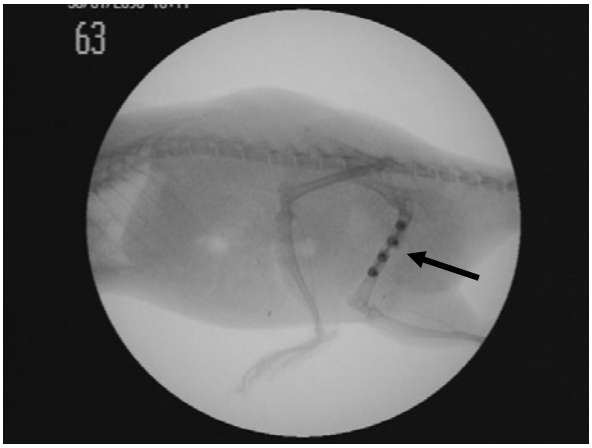

Figure 6. A radiograph 5 days after the implantation showing (arrow) the location of the implant

The degree of osseointegration correlates with the presence of osteocalcine (evaluated with indirect immunofluorescence), a differentiation marker of mature bone cells. The more rapidly increases osteocalcine concentration on the boundary between the bone and the implant, the more biocompatible implant appears.

Femur bone was harvested and fixed in a formaldehyde fixative for 48 hours at 4 °C.

Then it was rapidly decalcified in Acid Decalcifier at 4 °C for about 72 hours until flexible and cut longitudinally or with a single-edge razor blade. The titanium fixture was carefully removed, and femurs were further rinsed in distilled deionized water for 3 hours. All tissue was embedded in paraffin and cut in 10 µm-thick sections. The material was stained with hematoxylin and eosin.

3 TISSUE INVESTIGATION

3.1 5 days after implantation

Destruction and necrosis of soft tissues adjacent to the bone fragments ends and shaping of the blood clot can be seen in the zone of fracture among a small quantity of bone fragments. In the lumen of medullary channel in the zone adjacenting to the line of fracture the focuses of the necrosis of bone marrow are also revealed. *Signs of healing:* In the preserved part of the periosteum its thickening due to osteogenic cells proliferation with the tendency of their transformation into the chondrocytes is noted. This process is expressed in all the rats to the different degree, but most clearly in rats with TiC0.5+CaO composition coated on the implants surface (Figure 6).

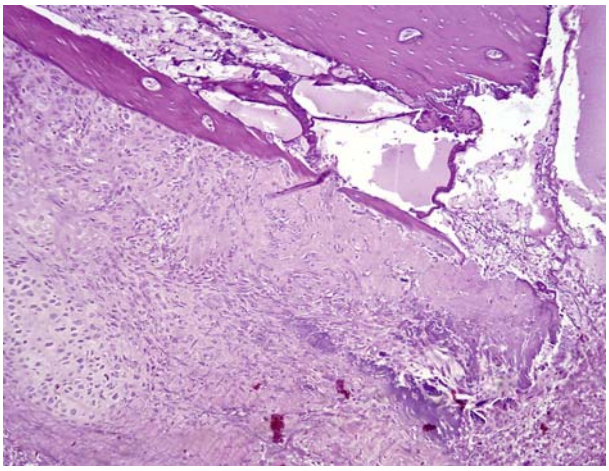

Figure 6. Osteogenic cells proliferation with the tendency of their transformation into the chondrocytes (TiC0.5+CaO composition coated on the implants surface)

3.2 10 days after implantation

The formation of the fibrous tissue is noted in the zone of fracture. The formation of the internal callus, which is manifested in the appearance of the bone trabeculas begins in the lumen of medullary channel.

Signs of healing: Further thickening of periosteum due to the osteogenic cells proliferation continues in the external part of the bone. Since this process occurs in the absence of the blood vessels, whose formation does not manage after the rate of the of osteogenic cells differentiation, then the significant chondroidal differentiation is noted (Figure 7). Cartilaginous callus is formed around the bone fragments.

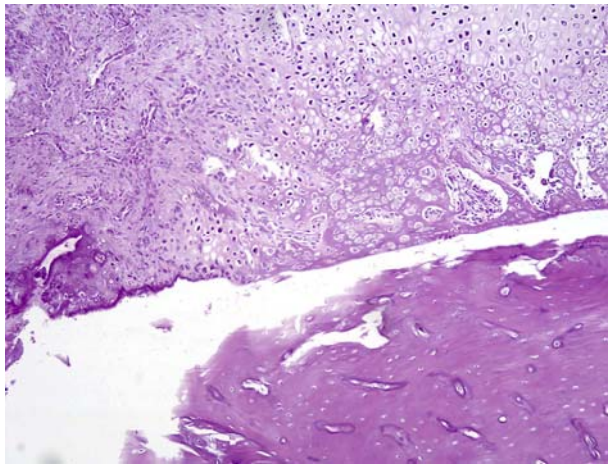

Figure 7. Chondroidal differentiation

The degree of the manifestation of the processes of healing is approximately identical for all implants.

3.3 15 days after implantation

Remainders of blood clots and insignificant quantity of bone fragments among the formed fibrous cloth are visible in the zone of fracture. In the thickened cortical layer, and also in the cartilaginous callus, formed along the edges of bone fragments, the beginning of the osteoidal differentiation together with the chondroidal differentiation, which displaces the cartilage (Figure 8), is noted.

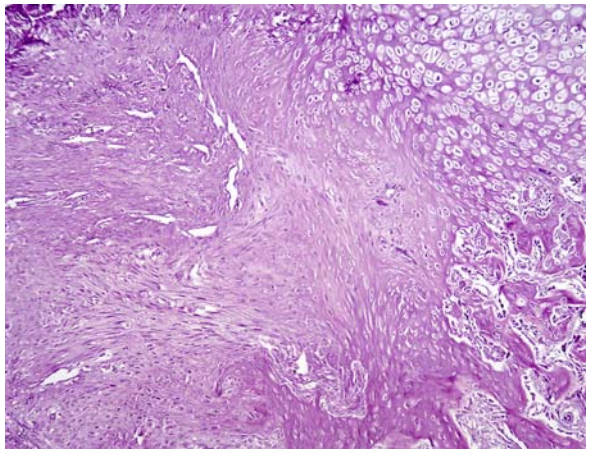

Figure 8. Osteoidal differentiation, which displaces the cartilage

This process is expressed in all the rats, but most clearly in rats with $TiC_{0.5}$+10%($Ca_{10}(PO_4)_6(OH)_2$) composition coated on the implants surface.

3.4 30 days after implantation

Signs of healing: The significant second ossification, which is characterized by the substitution of cartilaginous cloth by bone beams in the osteocartilaginous calluses located on the ends of the bone fragments, is noted (figure 9).

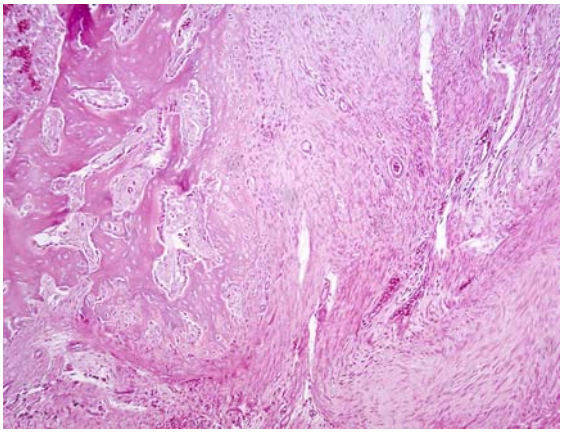

Figure 9. Substitution of cartilaginous cloth by bone beams

However, cartilaginous cap remains on the periphery of calluses, what can be explained both by the mobility of bone fragments because of the insufficient fixation and by the bad trophicity because of the insufficient vascularization of the newly formed bone.

3.5 Clinical observations

Animals were clinically observed and physically examined during entire study. Their basic biological functions were close to normal.

X-ray investigations showed an absence of the patalogical periostal reaction around the implants.

Area of operation exploration allowed to do conclusion, that the wounds were healed by first intension; there were no inflammatory reactions around them at the moment of examination.

4 RESULTS

All the animals are alive. Osteogenesis is stable, which means, that fixation by four screws is sufficient for implants stability.

There were no postoperative complications noted. The protocol of experiment was executed completely.

Biological material in experimental and in control groups was studied by optical microscopy.

The effectiveness of implants considered in comparison with a control group of implants without nanostructured modification was proved by experimental models not only for stable [1], but also for moving with the large amplitude load-bearing implants.

5 CONCLUSIONS

Collectively, these data suggest that

1. Optimal experimental animal model for investigation of mechanism of osseointegration and osteogenesis.
2. Method of nanostructured implants surface coating is realized for standard titanium mesh.
3. Optical microscopy examination showed tendency toward the acceleration of osteogenesis for implants, which have the nanostructured coatings.
4. Electron microscopy and immunohistochemical studies will make it possible to refine the quantitative characteristics of osteogenesis and to strictly prove the advantages of implants, carrying the nanostructured coatings

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