Osseointegration of titanium implants into compact bone in female rabbits

(SUMMARY OF THE PhD THESIS)

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INTRODUCTION

Millions of people and animals around the world experience bone or joint conditions, either degenerative or inflammatory. Such problems appear mainly in the second half of life and unfortunately their frequency, instead of decreasing, is constantly increasing. Very often, such ailments cannot be solved only by drug therapy, hydrotherapy, physical therapy, etc., being necessary quite frequently, surgical interventions either to correct some modified structures or even to replace some compromised structures. Such interventions are necessary in many situations such as bone fractures, arthropathy, lumbar pain, osteoporosis, scoliosis or various musculoskeletal conditions. To solve them, different devices are used that can be permanent, temporary or biodegradable.

These devices are made of special materials that must have mechanical strength, not be corrosive or toxic and be very well tolerated by the body. Materials that possess such qualities are called orthopedic materials. They are used either alone or in various combinations in the manufacture of devices used to replace or support the repair of various tissues such as bone, cartilage or ligaments and tendons.

For a long time (most of the 20th century), some materials used for industrial applications have been used as orthopedic biomaterials. In other words, the surgeons used the available materials used in various fields of chemical, mechanical, energy, aeronautical, etc. The major problem they faced was that the internal environment of the human and animal body is extremely corrosive. This aspect imposed very strict requirements regarding the properties of candidate materials to be used in orthopedics.

Under these conditions, materials for industrial use that are easily accessible and as inert as possible were sought to reduce the risk of corrosion and the release of ions and particles at the implantation site. These materials had to have appropriate mechanical properties that would allow taking over to a large extent the stresses exerted on the prosthetic structures. **Osteointegrarea implanturilor de titan în os compact la femelele de iepure**

THE STRUCTURE AND CONTENT OF THE THESIS

The PhD thesis entitled "Ossointegration of titanium implants in compact bone in female rabbits" spans X pages. The content of the thesis is argued by a rich imagery represented by 73 figures, respectively 10 macroscopic and 63 microscopic. It also contains 2 tables. The thesis respects the methodology of writing doctoral theses regarding the relationship between the components and the way of writing, it being structured in two parts: Current state of knowledge and Personal contribution.

The current state of knowledge extends over X pages and is structured into 2 chapters that include information from the specialized literature directly related to the chosen topic

Chapter I, entitled "***Orthopedic implants***" contains information about permanent and temporary orthopedic implants, the properties of orthopedic implants, the types of biomaterials used in the manufacture of orthopedic implants, the advantages and disadvantages of their use.

Chapter II, entitled "***The behavior of orthopedic implants in tissues and their response to the presence of implants***" contains information about the qualities of orthopedic implants necessary for their acceptance by the body and their persistence in the tissues for a longer period of time. Also presented are the adverse reactions that can be triggered in the body due to the presence of implants which, although tolerated by the body, still represent foreign bodies.

The personal contribution is presented on X pages and is structured in 8 chapters in which information is presented about the objectives of the welding, the materials and working methods, histological investigations about the process of osseointegration of the screws inserted in different variants, the compensatory reactions that appeared in response to the operative trauma and the events that accompany this process, the general conclusions drawn from the results obtained, the originality and innovative aspects and finally the bibliography used.

THE OBJECTIVES OF THE WORK

- self-drilling insertion of titanium screws with a diameter of 2 mm into the femur of female rabbits, after drilling a hole with a diameter of 1.8 mm;

- self-drilling insertion of titanium screws with a diameter of 2 mm into the femur of female rabbits, after drilling a hole with a diameter of 1 mm;

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- evaluation of the osseointegration process after 6 weeks from the insertion of the screws.

MATERIALS AND METHODS

Materials taken in the study were titanium self-tapping screws, with a length of 5 mm and a diameter of 2 mm.
The animals used in the study were 10 female common breed rabbits, 11 months old and clinically healthy, the animals were euthanized and samples were collected for histological investigations.

RESULTS AND CONCLUSIONS

In chapter 1 entitled "***Histological evaluation of the osseointegration of some titanium screws 6 weeks after insertion in the femur of female rabbits***"**,** the impact of the method of inserting the screws on the osseointegration process of the titanium screws was followed and for this purpose we set the following objectives:
- inserting screws with a diameter of 2 mm in a hole of 1.8 mm and in a hole of 1 mm;
-verification by histological study of the osseointegration process in the case of the two work variants, after 6 weeks from the insertion of the screws.
Based on the results obtained from this investigation, the following conclusions were drawn:
At 6 weeks after the insertion of the titanium screws, the supraperiosteal soft tissues are regenerated with well-vascularized loose connective tissue and young muscle cells in both experimental variants.
The stage reached by the reparative processes at the level of the supraperiosteal soft tissues being comparable, shows that the insertion of the screws in the hole with the different diameter did not influence the repair of these tissues.
Quantitatively, the most newly proliferated bone is found in the periosteal and endosteal areas of the interface, which has spread across the interface giving it a fan- like appearance, so the body has tolerated the titanium implant very well.
As a remodeling stage, the proliferated bone in the periosteal area is only in the primary bone stage, while that in the endosteal area is somewhat more advanced, so the proliferation of new bone in the endosteal area preceded the proliferation in the periosteal area. **Osteointegrarea implanturilor de titan în os compact la femelele de iepure**

If we compare the newly proliferated bone in the periosteal and endosteal areas of the interface in the two experimental variants, we find that both in terms of quantity and structural organization, the situation is comparable.
On the interface next to the bone wall, that is, between the periosteum and the endosteum, there are significant differences between the two experimental variants regarding the bone deposited through contact osteogenesis
In the version with a 1.8mm hole, the newly proliferated bone is present as a thick continuous layer in the grooves between the implant coils and significantly thinner over the tip of the coils, and in the one with a 1mm hole it is in a thin layer uniform in thickness.
If we compare the situation of the bone from the depth of the interface in the two experimental variants, we find that there are lesions represented by polymorphic cracks in shape and size, alongside empty osteoplasts, in both variants.
However, there are some differences regarding the depth to which such lesions are present, in the sense that in the version with a 1mm hole, they are somewhat deeper, but here they are not very deep either.
The connection between the proliferated bone on the interface and that in the depth of the interface is good in the periosteal and endosteal areas, but very modest in the central portion of the interface, in both experimental variants.
If we refer to the destination of the implants, we can say that the version with a 1.8 mm hole is indicated in the case of permanent implants, while for temporary ones, either of the two versions can be used.
In chapter 2 entitled "***The histomorphometric evaluation of contact osteogenesis in relation to the diameter of the insertion hole***" the way contact osteogenesis unfolds on the bone-implant interface was followed according to the space that remains between the surface of the experimental bone defect and the surface of the screw, at the moment of its insertion. To pursue this goal, we set the following goals:
- the histomorphometric evaluation of newly proliferated bone on the bone- implant interface in the case of implant insertion in a 1.8mm hole;

- the histomorphometric evaluation of newly proliferated bone on the bone- implant interface in the case of implant insertion in a 1mm hole;

-statistical interpretation of the differences between the two experimental variants.
Following this investigation, the following conclusions were drawn:
There must be a favorable ratio between the diameter of the insertion hole and the diameter of the screw thread so that contact osteogenesis can take place in the best conditions;
Between the two experimental variants there are great differences in terms of contact osteogenesis, the amount of newly formed bone being clearly superior in the case of insertion in a hole larger than the diameter of the screw shaft;
If the insertion hole is smaller than the screw shank, self-tapping insertion exerts additional pressure on the bone wall, with significant repercussions on contact osteogenesis; Ioan Sabou
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In this method of insertion, there is not enough space left between the surface of the screw and the surface of the bone wall, which does not allow the organization of the fibrino-leukocyte network at optimal thickness;
This narrow space does not allow the easy migration of cells with osteogenic potential through the fibrino-leukocyte network, but also the expansion of newly proliferated bone, which significantly limits contact osteogenesis.
The statistical analysis of the results obtained by histomorphometric methods showed that the differences between the two experimental variants are statistically significant in favor of the variant with an orifice of 1.8 mm.

In chapter 3 entitled "***Evaluation of proliferated compensatory structures around the intervention area***" the response of the bone in the immediate vicinity of the interface, but also of the one far from the intervention area, to the aggression given by the surgical intervention and the other phenomena that accompany the insertion of implants was followed. To pursue this goal, we set the following objectives:

- the histomorphometric evaluation of the proliferated bone on the bone- implant interface and in its immediate vicinity;

- evaluation of the proliferated bone structures at a distance from the interface, to restore the total strength of the bone.

The conclusions reached at the end of this investigation were:
The newly proliferated bone forms in the periosteal and endosteal areas a thick layer that extends laterally from the interface for a long distance, the greatest thickness being at the level of the interface, after which it gradually thins.
The result is significant thickening of the bone wall up to a large distance from the interface, and thus the bone wall largely recovers the strength lost by drilling the insertion hole and the events that accompany this process.
The significant thickening of the bone wall over a long distance represents a compensatory reaction due to the weakening of the mechanical strength of the bone following the operative trauma, to bring it back at least to the level that existed before the surgical intervention.
In addition to this thickening, in the case of the 1-mm orifice variant, newly proliferated bone with an endosteal starting point extends into the medullary cavity in the form of polymorphous trabeculae and bony protrusions of various shapes and sizes, which project into the medullary cavity.
According to their appearance and structure, they leave the impression that they have an obvious tendency to expand further, tending to form a kind of trabecular scaffold anchored to the internal wall of the bone, to increase the mechanical resistance of the bone around the intervention area.
Restoring the strength of the bone is also done through processes of bone remodeling with the appearance of numerous, large and dense osteons, most of them **Osteointegrarea implanturilor de titan în os compact la femelele de iepure**

being arranged in the wall opposite the intervention area, where they occupy approximately 2/3 of the internal part of the bone wall.

The thickening of the bone wall at a great distance from the intervention area and the remodeling of the bone towards Haversian bone, make the resistance of the wall in those areas to be significantly higher than the mechanical resistance of the area before the surgical intervention.

In Chapter 4, entitled "***General conclusions***", the conclusions that emerged from the general assessment of the results obtained from the investigations carried out are presented in a synthetic way, as follows:

After 6 weeks after the insertion of titanium screws, the supraperiosteal soft tissues are restored with well-vascularized loose connective tissue and young muscle cells, with small and insignificant differences between the two experimental variants.

The most new bone proliferated in the periosteal and endosteal areas of the interface and expanded on the interface giving it a fan appearance, the situation being comparable in the two experimental variants, so the diameter of the insertion hole did not influence the osseointegration here.

In the osteal area of the interface there are significant differences, in the version with a 1.8mm hole the bone deposited by contact osteogenesis is thick in the grooves between the turns and thin over the top of the turns, and in the one with a 1mm hole it is in a thin layer and uniform in thickness.

Histomorphometry revealed the fact that between the two experimental variants there are large differences in terms of contact osteogenesis, these being statistically significant in favor of the variant with a 1.8 mm orifice.

The newly proliferated bone forms in the periosteal and endosteal areas a thick layer that extends laterally from the interface to a great distance, resulting in significant thickening of the bone wall to a great distance from the interface.

In response to the weakening of the mechanical strength of the bone following the operative trauma, a compensatory reaction materialized by the significant thickening of the bone wall over a long distance was triggered, to bring it back to the level that existed before the surgical intervention.

In the case of the 1-mm orifice variant, the newly proliferated bone with an endosteal starting point extends into the medullary cavity in the form of polymorphous trabeculae and bony protrusions of various shapes and sizes, which project into the medullary cavity.

These formations leave the impression that they have an obvious tendency to expand further, tending to form a kind of trabecular scaffold anchored to the internal wall of the bone, to increase the mechanical resistance of the bone around the intervention area.

Bone remodeling processes also take part in the restoration of bone strength with the appearance of numerous, large and dense osteons, most of them being Ioan Sabou

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arranged in the wall opposite the intervention area, where they occupy approximately 2/3 of the internal part of the bone wall.
The thickening of the bone wall, the proliferation of trabeculae and spicules in the medullary cavity, together with the remodeling of the bone towards haversian bone, cause the strength of the bone wall to become even greater than it was before surgery.
In chapter 5 entitled "***Originality and innovative contributions of the thesis***" the particular aspects that were caught during the investigations were pointed out, as follows:
The body triggers compensatory reactions to restore the mechanical strength of the weakened area following the operations required to insert the screws.
In both experimental variants, bone proliferates in the periosteal and endosteal areas in the form of a thick layer that extends laterally from the interface to a large distance, causing significant thickening of the bone wall.
In the version with a 1 mm hole, bone trabeculae and spicules are formed that start from the endosteum and project into the medullary cavity, forming a kind of consolidation scaffold.
Bone remodeling processes are present with the appearance of numerous polymorphic osteons that increase the zonal resistance of the bone above that before the intervention.
The insertion of screws in the hole with a smaller diameter than the screw shaft causes the most and most pronounced compensatory reactions up to a long distance from the intervention area, an advantageous aspect in the case of temporary implants.

GENERAL CONCLUSIONS AND RECOMMENDATIONS

The general conclusions that emerge from the studies can be systematized as follows:
1. After 6 weeks after insertion of the titanium screws, the supraperiostal soft tissues are restored with well-vascularized lax connective tissue and young muscle cells, with small and insignificant differences between the two experimental variants.

2. Most of the new bone proliferated in the periosteal and endosteal areas of the interface and extended over the interface giving it a fan-like appearance, the situation being comparable in the two experimental variants, so that the diameter of the insertion orifice did not influence osteintegration here.

3. In the osteal area of the interface there are significant differences, in the

1.8mm orifice variant the bone deposited by contact osteogenesis is thick in

4. the grooves between the coils and thin over the tips of the coils, while in the 1mm orifice variant it is thinly layered and uniform in thickness.

5. Histomorphometry revealed that there were large differences in contact osteogenesis between the two experimental variants, which were statistically significant in favor of the 1.8 mm orifice variant.

6. In response to the weakening of the mechanical strength of the bone following the operative trauma, a compensatory reaction materialized by a significant thickening of the bone wall over a large distance, to bring it back to the level existing before surgery, was triggered.

7. In the 1-mm arygiform variant, the newly proliferated bone with an endosteal starting point extends into the medullary cavity in the form of polymorphous trabeculae and bony prominences of various shapes and sizes, which project into the medullary cavity.

8. These formations give the impression that they have an obvious tendency to extend further, tending to form a kind of trabecular scaffold anchored to the internal wall of the bone, for increasing the mechanical strength of the bone around the area of intervention.

9. The restoration of bone strength also involves processes of bone remodeling with the appearance of numerous, large and dense osteons, most of which are located in the wall opposite the intervention zone, where they occupy about 2/3 of the internal part of the bone wall.

10. The thickening of the bone wall, the proliferation of trabeculae and spicules in the medullary cavity, together with the remodeling of the bone towards haversian bone, make the bone wall strength even greater than it was before surgery.

RECOMMENDATION

When using titanium screws to fix osteosynthesis plates on compact bone, we recommend inserting them in a hole smaller than the screw shank, as this ensures the best mechanical stability.
This modality causes the transmission of most signals up to the distance from the insertion zone, stimulating the processes of bone proliferation and remodeling in the fracture zone.