

DOI: 10.38173/RST.2022.23.1.17:149-154

Title:	<i>LOCAL FOREIGN BODY RESPONSE TO ORTHOPAEDIC BIOMATERIAL IMPLANTS</i>
Authors:	Nicolae Marian CIUREA Razvan ENE Marius OZUN Alexandru Lisias DIMITRIU

Section: MEDICINE

Issue: 1(23)/2022

Received: 4 January 2022	Revised: 22 February 2022
Accepted: 2 March 2022	Available Online: 15 March 2022

Paper available online [HERE](#)

LOCAL FOREIGN BODY RESPONSE TO ORTHOPAEDIC BIOMATERIAL IMPLANTS

Nicolae Marian CIUREA¹
Razvan ENE²
Marius OZUN³
Alexandru Lisias DIMITRIU⁴

ABSTRACT:

THE SURGICAL MANAGEMENT OF BONE LESIONS OFTEN INVOLVES IMPLANTATION OF SURGICAL DEVICES SUCH AS JOINT PROSTHESIS, PLATES, NAILS AND / OR SCREWS IN ORDER TO TREAT DEGENERATIVE PATHOLOGIES OR POSTTRAUMATIC LESIONS.

IN MOST CASES THE SURGICAL TREATMENT IS A SUCCESS WHEN BONE HEALING OR PAIN MANAGEMENT IS ACHIEVED, BUT IN SOME CASES THE INFLAMMATORY RESPONSE SECONDARY TO BIOMATERIALS IMPLANTATION CAN LEAD TO CHRONIC PAIN, FUNCTIONAL IMPAIRMENT AND LOCAL INFECTION.

THESE LOCAL COMPLICATIONS CAN HAVE IMPORTANT SIDE EFFECTS, SOMETIMES THE ONLY REMEDY BEING THE EXTRACTION OF THE BIOMATERIAL.

OF COURSE, IF BONE HEALING IS ACHIEVED THE EXTRACTION OF THE BIOMATERIAL IS NOT A BIG PROBLEM BUT, IN SOME CASES, THE LOCAL INFLAMMATORY RESPONSE AND CLINICAL MANIFESTATIONS CAN REQUIRE EARLY SURGICAL MANAGEMENT WITH THE EXTRACTION OF THE DEVICE; IN THESE CASES, SURGICAL MANAGEMENT WITH FURTHER OSTEOSYNTHESIS TECHNIQUES IS NECESSARY, WITH A GREAT IMPACT IN THE SOCIAL REINTEGRATION OF THE PATIENT BY PROLONGED INFIRMITY.

IN THE PRESENT STUDY WE TRIED TO FIND THE MAIN CHARACTERISTICS THAT CAN LEAD TO INCREASED LOCAL INFLAMMATORY RESPONSE TO BIOMATERIALS IN ORDER TO LIMIT THE NEED FOR SURGICAL REINTERVENTIONS..

KEY WORDS: BIOMATERIALS, FOREIGN BODY RESPONSE, INFECTION, OSTEITIS, OSTEOSYNTHESIS COMPLICATIONS

INTRODUCTION

We already know that the biomaterial surface properties can influence the host response (the material composition, the different coatings of the biomaterial that interact with

¹ MD, Clinical Emergency Hospital, Bucharest, Romania

² Assoc. Prof. PhD. Clinical Emergency Hospital, Bucharest, Romania; “Carol Davila” University of Medicine and Pharmacy, Bucharest, Romania

³ MD, Clinical Emergency Hospital, Bucharest, Romania

⁴ Corresponding author, Assist. Prof., Clinical Emergency Hospital, Bucharest, Romania; “Carol Davila” University of Medicine and Pharmacy, Bucharest, Romania

the host)⁵; the host inflammatory response in reaction with the biomaterial can affect the biocompatibility of the medical device. In order to achieve this, we first must shortly describe the main cellular mechanisms that lead to the activation of local inflammatory mechanism.

We know from the literature that the host reactions following the implantation of the material are tissue injury, blood-material interactions, provisional matrix formation, acute inflammation that leads to certain amount of chronic inflammation, granulation tissue, foreign body response and development of fibrosis⁶.

The first step is the interaction between blood and material with protein adsorption at the material surface and development of the provisional matrix around the material. This is the initial thrombus that develops concomitant with activation of complement system, fibrinolytic system and platelet activation⁷.

The provisional matrix furnishes structural, biochemical and cellular components to the process of wound healing and foreign body reaction by its containers, mitogens, chemoattractants, cytokines, growth factors and they control the subsequent phases of wound healing⁸.

After this phase, acute and chronic inflammation follows, with their extent being in direct relation with the extent of the tissue injury. So, the implantation procedure is an important factor that can limit or extend the inflammation process (conventional procedures vs minimally invasive procedures, also plates vs. nails).

The presence of neutrophils characterizes the acute inflammation process; also, interleukin 4 and interleukin 13 plays an important role in determining the extent and degree of the foreign body reaction⁹.

The acute phase of the inflammation usually resolves in less than one week, in direct relation with the extent of tissue injury¹⁰.

The chronic inflammation phase that follows, is characterized by the presence of mononuclear cells, like monocytes, lymphocytes and plasma cells. In the case of high biocompatible material, the chronic inflammation process lasts no more than 2 weeks¹¹.

The persistence of the chronic inflammation phase more than 3 weeks, usually indicates a local infection.

After this phase is over, granulation tissue can be identified, that relates to the presence of macrophages, fibroblasts and neoformation blood vessels. Granulation tissue appears prior to the formation of the fibrous capsule, and is separated by the implant surface by a thin layer of cells formed by monocytes, macrophages and foreign body giant cells¹².

⁵ Anderson JM, Rodriguez A, Chang DT. Foreign body reaction to biomaterials. *Semin Immunol.* 2008;20(2):86-100

⁶ Gretzer C, Emanuelsson L, Liljensten E, Thomsen P. The inflammatory cell influx and cytokines changes during transition from acute inflammation to fibrous repair around implanted materials. *J Biomater Sci Polym Ed.* 2006;17(6):669-87

⁷ Luttkhuizen DT, Harmsen MC, Van Luyn MJ. Cellular and molecular dynamics in the foreign body reaction. *Tissue Eng.* 2006;12(7):1955-70

⁸ Klopffleisch R, Jung F. The pathology of the foreign body reaction against biomaterials. *J Biomed Mater Res A.* 2017;105(3):927-40

⁹ Braune S, Grunze M, Straub A, Jung F. Are there sufficient standards for the in vitro hemocompatibility testing of biomaterials? *Biointerphases.* 2013;8(1):33

¹⁰ Nilsson B, Ekdahl KN, Mollnes TE, Lambris JD. The role of complement in biomaterial-induced inflammation. *Mol Immunol.* 2007;44(1-3):82-94

¹¹ Nilsson B, Ekdahl KN, Mollnes TE, Lambris JD. The role of complement in biomaterial-induced inflammation. *Mol Immunol.* 2007;44(1-3):82-94

¹² Love RJ, Jones KS. The recognition of biomaterials: pattern recognition of medical polymers and their adsorbed biomolecules. *J Biomed Mater Res A.* 2013;101(9):2740-52

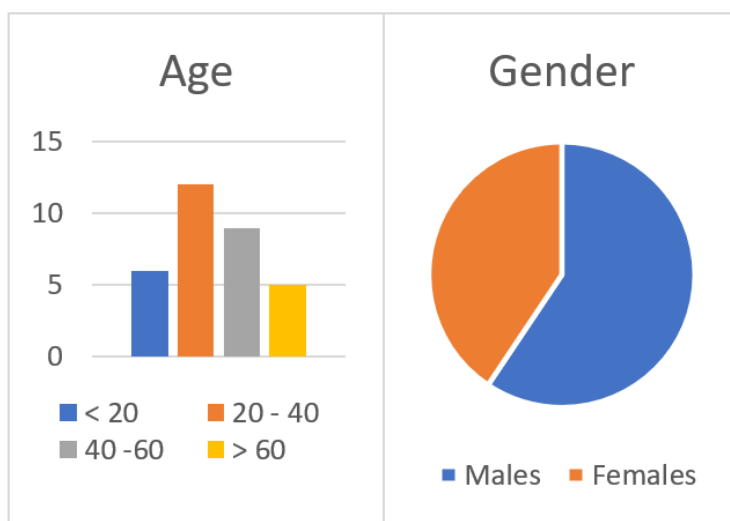
MATERIAL AND METHOD

In order to find the factors that can lead to local complications and to limit the need for surgical reintervention in patients with bone lesions that require biomaterials, we conducted a study in our clinic for a period of two years.

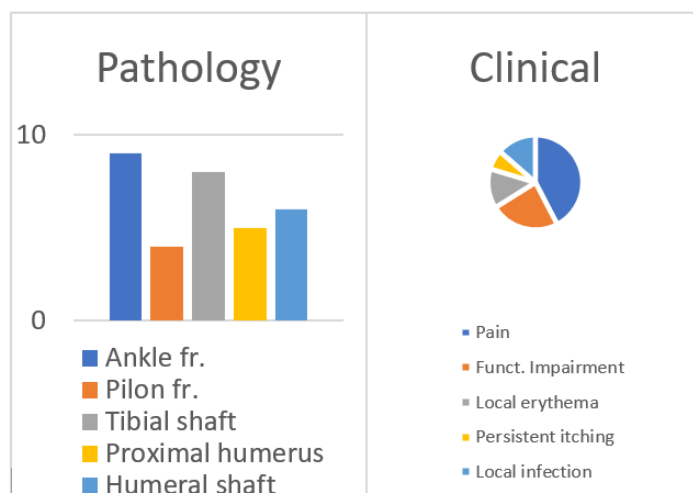
We included only posttraumatic patients with bone fractures that required surgical stabilization with osteosynthesis biomaterials (plates, nails and/or screws).

We included 32 patients with posttraumatic injuries that were operated in our clinic. Most of the patients were young, < 40 years old, mostly males with no other associated pathologies.

RESULTS

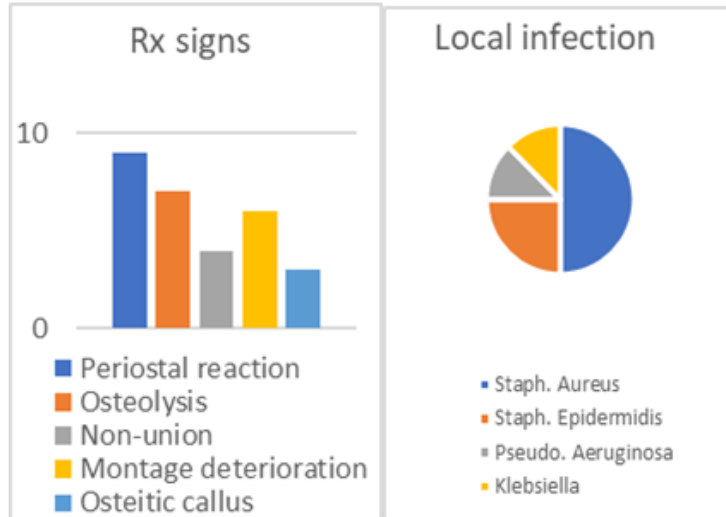


The main pathologies for which the patients were operated included: ankle fractures, pilon fractures, tibial shaft fractures, proximal humerus fractures and humeral shaft fractures.



The main clinical manifestations that required surgical management were local pain, functional impairment, local erythema, persistent itching and local signs of infection with pathological secretions.

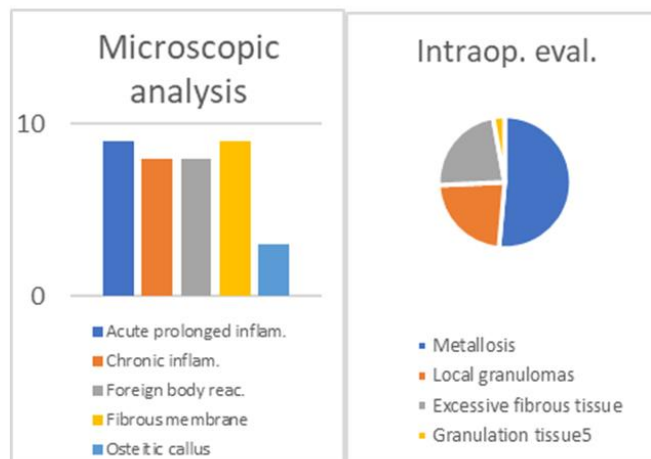
Radiological signs that were discovered were periosteal reaction, osteolysis, non-union and osteitic callus formation.



The most frequent germs identified in bacteriological tissue analysis in local septic complication were Staphylococcus aureus, followed by Staphylococcus epidermidis.

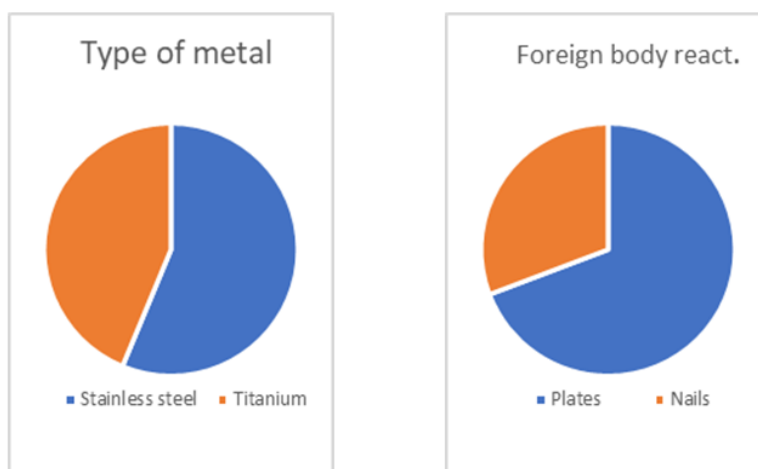
The intraoperative macroscopic evaluation of surrounding tissues found that local signs of metallosis were present in the majority of the cases; other tissue changes that were observed included local granulomas and excessive fibrous tissue formation around the implant.

Local tissue samples were collected for pathological analysis. Acute prolonged inflammation was discovered, followed by chronic inflammation, foreign body reaction with giant foreign body cells and fibrous membranes.



In terms of the main metal from which the material is composed by, we used either stainless steel implants or titanium implants. Metallosis and foreign body cells were observed more often in relation with stainless steel implant rather than titanium.

Also, foreign body reaction was more present and more severe when plates were used rather than nails or screws; when it comes to plates, inflammation was more severe and prolonged when classical large surgical approaches were used rather than minimally invasive techniques.



In our study we tried to find correlations between different factors and the need for surgical reinterventions, by using statistical analysis like chi-square test.

Positive correlations were considered for $p < 0.05$.

Signs of tissue metallic impregnation were found more often in patients operated with stainless steel implants than titanium implants ($p=0.03$). Also, metallic impregnation was more obvious when plates were used, with a lower rate in patients operated with intramedullary nails ($p=0.043$).

More than that, signs of local inflammation were more obvious in relation with stainless steel implant rather than titanium implants ($p=0.038$).

When choosing the surgical approach, we have to bear in mind that extensive approaches can cause extensive tissue damage that can lead to prolonged local inflammation that can cause local infection. This is more likely to happen when using plate osteosynthesis than intramedullary nails.

When the microscopic examination was performed, it discovered that foreign body reaction and persistent inflammatory cells were more present near stainless-steel implants rather than titanium implants ($p=0.031$).

Local septic complications were also more frequent found with stainless steel implants ($p=0.043$), and were more likely to develop when large paracortical implants were used, rather than intramedullary nails ($p=0.034$).

CONCLUSIONS:

When conditions permit, we recommend the use of titanium implants, that tend to be more biocompatible than stainless steel ones. Also, when possible is best to use IM nails because they tend to be less exposed to develop local complications such as infection, and because smaller surgical approaches are used when implanting them. A smaller surgical approach means a smaller tissue injury with a lower rate of local inflammations and a less likely chance to develop infection.

If we must use paracortical osteosynthesis, we recommend using titanium plates, that have a lower rate of developing foreign body reaction with a less chance of needing early material extraction.

Although fibrous tissue does not increase the risk of infection, the excessive fibrous tissue development may cause local functional impairment and joint stiffness (through arthrofibrosis if it develops near a joint site) with the need of material extraction and fibrous tissue ablation.

REFERENCES

1. **Anderson JM, Rodriguez A, Chang DT.** Foreign body reaction to biomaterials. *Semin Immunol.* 2008;20(2):86-100.
2. **Gretzer C, Emanuelsson L, Liljensten E, Thomsen P.** The inflammatory cell influx and cytokines changes during transition from acute inflammation to fibrous repair around implanted materials. *J Biomater Sci Polym Ed.* 2006;17(6):669-87.
3. **Luttikhuisen DT, Harmsen MC, Van Luyn MJ.** Cellular and molecular dynamics in the foreign body reaction. *Tissue Eng.* 2006;12(7):1955-70.
4. **Klopfleisch R, Jung F.** The pathology of the foreign body reaction against biomaterials. *J Biomed Mater Res A.* 2017;105(3):927-40.
5. **Braune S, Grunze M, Straub A, Jung F.** Are there sufficient standards for the in vitro hemocompatibility testing of biomaterials? *Biointerphases.* 2013;8(1):33.
6. **Nilsson B, Ekdahl KN, Mollnes TE, Lambris JD.** The role of complement in biomaterial-induced inflammation. *Mol Immunol.* 2007;44(1-3):82-94.
7. **Love RJ, Jones KS.** The recognition of biomaterials: pattern recognition of medical polymers and their adsorbed biomolecules. *J Biomed Mater Res A.* 2013;101(9):2740-52.