Passamonti S. (Editor)
The Partners and the Objectives of Trans2Care, an Italy-Slovenia cross-border network of science and healthcare institutions
pp. 111-115 / ISBN 978-88-8303-512-8

Nanocoatings for preventing orthopaedic implant–associated bacterial infections

Franja Šulek, Ingrid Milošev

PP11-Valdoltra Orthopaedic Hospital, Ankaran

Abstract — The Research department of the Valdoltra Orthopaedic Hospital is determined to conduct more extensive research studies on modification of materials for orthopaedic implants. The starting research in the newly founded Research laboratory shall include basic and applied studies which results shall be potentially considered and eventually implemented in daily clinical practice of Valdoltra Orthopaedic Hospital. With an accurate inspection of the emerging medical needs in the field of orthopaedics we envisaged the urgent need to provide a long-term protection for orthopaedic prostheses. By means of using nano-engineering approaches for the functionalization of orthopaedic implant surfaces with suitable antimicrobial agents, it is possible to protect orthopaedic implants against harmful bacteria, which trigger the initiation of implant-associated bacterial infection. As the implant-associated bacterial infection can affect the longevity of the prosthesis, thus, the scientific and financial efforts, with the help of the project Trans2care, will be focused substantially on the design and fabrication of protective antibacterial coatings for orthopaedic implants.

Index Terms — research activity, bacterial infections, prevention, orthopaedic implant surface

---

1 RESEARCH LABORATORY

The Research Department takes an important role in the scientific activities of Valdoltra Orthopaedic hospital. The build-up of the new Research laboratory will be financially covered in great part by the hospital itself, whilst, the basic equipment and some necessary apparatus for research activities will be co-financed by the cross-border project Trans2care. Additionally, the laboratory will be equipped in a modern fashion to provide all the comforts and ideal working environment to perform scientific research in the field of new biocompatible materials for orthopaedics. The financial plan shall include the acquisition of the following laboratory equipment and some apparatus, divided into two segments. Within the preparatory activities we will provide:

- Basic laboratory furniture, as benches and stools;
- Fume cupboard with safety storage cabinets for liquids and other reagents;
- Precision and Laboratory weights;
- Laboratory fridge and waste containers;
- General labware and consumables;
- Complete system for vacuum filtration;
- Magnetic stirrer with digital hotplate and vortex mixer;
- Shakers and ultra-sound bath;
- Centrifuges.

Within the analytical activities we plan to purchase:

- Laboratory microscope and
- Spectrophotometer with integrated measurement modes for absorbance, fluorescence and luminescence.

Till now, the majority of the research work at the Research department has been dedicated to the measurement and analysis of wear of implants surface and wear particles, histological analysis, as well as the analysis of periprosthetic tissue [1]. The wear of orthopaedic implants leads to loosening of the prosthesis, classified as »aseptic« and »septic« loosening. The septic loosening is always combined with the contamination of implant surface with bacteria (Figure 1).

2 ACTIVITIES AND ROLES IN TRANS2CARE PROJECT

2.1 Infections associated with orthopaedic implants

Implant-associated infections are the result of bacteria attachment to an implant surface and subsequent biofilm formation at the implantation site. Biofilm formation usually takes place in several phases, starting with rapid bacteria surface adherence, followed by multilayered cellular growth and intercellular adhesion in an extracellular polysaccharide matrix [2,3]. If bacteria adhesion occurs before tissue regeneration takes place, host defenses often cannot prevent surface colonization for certain bacterial species that are capable of forming a protective biofilm layer. Therefore, inhibiting bacterial adhesion is necessary to prevent implant-associated infection, because biofilm are extremely resistant to both the immune system and antibiotics [3]. The ability of the biofilm of detaching some individual bacteria into surrounding tissues and the circulatory system, it might lead to unavoidable spread of the inflammation thorough the body of the host [4]. Pathogenic bacteria,

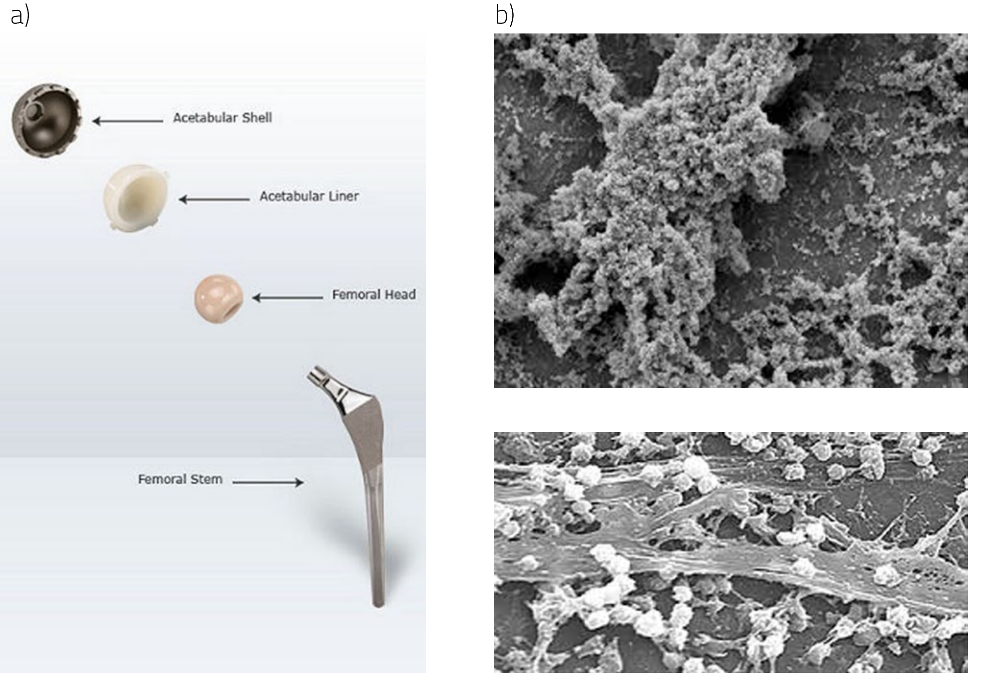

Fig.1. Components of a joint hip replacement: acetabular shell and liner, femoral head and femoral hip stem (a); surface of joint hip replacement infected by bacteria (b).

particularly gram(+) S. aureus and S. epidermidis, are found at the implantation site of approximately 90% of all implants [5]. Gram(-) bacteria, as E. coli and P. aeruginosa, have also been diagnosed in implant-associated infections [6]. The average infection rate has been reported to range between 0,5% and 3% for total hip replacement arthroplasties and the rate of reinfection after revision of infected hip prostheses is stated to be up even to 14% [7,8]. On the basis of these data, it is evident, that orthopaedic implants require better protection to avoid or at least diminish the incidence of prosthetic joint-associated bacterial infections, and consequently, the loosening of the implant with time might be prevented as well. All of these contribute to the extension of the longevity of an orthopedic implant.

2.2 Antimicrobial agents used in coating techniques

New strategies for the design of safer orthopaedic devices have been proposed to control and prevent bacterial contamination of implants. One of the promising approaches is to adjust, at the nano-meter scale, the antimicrobial capabilities of the implant surface [9]. This might be achieved by the utilization of different surface functionalization strategies in use, as the direct impregnation of implant surface with antibiotics or any other antimicrobial agent, as well as the coating technique with antimicrobial metals such as copper and silver. Titanium-oxide coatings deposited on the implant surface have been also successfully examined [10]. However, the usage of certain coatings is still partially restricted to implants, thus, new coatings need to be developed to gain better protection against post-operative infection and provide a barrier to minimize metal ion release into the body.

2.3 Nanostructured coatings for better protection of orthopaedic implants

In comparison to conventional coatings, the advantages of using nanostructured coatings for orthopaedic implants are multiple. In addition to adding antibacterial properties to implants, it is possible, by the nanoengineering approaches, to attain other functionalities such as higher biocompatibility and mechanical stability as well as the ability of the implant to stimulate the process of new bone formation [11,12]. Moreover, due to higher surface area the modified implant surface with nano-scaled topography might provide additional available sites for protein adsorption, thereby enhancing cellular interactions directly at implantation site [12,13]. This is very positive, because even the implant acts against bacteria, at the same time, it influences the bone and the surrounded tissue to heal more rapidly and in a more proper way, respectively.

3 CONCLUSION

The working objectives of the new Research laboratory within the project Trans2care are to develop a new, multifunctional nanocoating with desirable properties such as, to be antibacterial and osteoinductive. We believe that the project goals shall be attainable also with the collaboration with other scientific and clinical partners, involved in the project network.

ACKNOWLEDGEMENT

We greatly acknowledge the financial support of the Fondo europeo di sviluppo regionale (Evropski sklad za teritorialni razvoj) for the Trans2care project. The co-financing of research activities in the Research laboratory by the Valdoltra Orthopaedic hospital is fully appreciated.

REFERENCES

[1] V. Pišot, I. Milošev, S. Kovač, R. Trebše, A. Berce, M. Pukl, M. Topolovec, B. Marjanovič, V. Levašič, J. Mohar, R. Mihalič, N. Hero, A. Cör, D. Terčič. V. Beltram, J.A. Hočevar, "Ortopedska bolnišnica Valdoltra", Zdravniški Vestnik – Suplement. Vol. 78, pp. 1-112, 2009.

[2] A. Simchi, E. Tamjid, F. Pishbin, A.R. Boccaccini, "Recent progress in inorganic and composite coatings with bactericidal capability for orthopaedic applications", Nanomedicine. Vol. 9, pp. 22-39, 2011.

[3] A. Trampuz, D. Osmon, R. Douglas, A. Hanssen, J. Steckelberg, R. Patel, "Molecular and antibiofilm approaches to prosthetic joint infection", Clin. Orthop. Relat R. Vol. 414, pp. 69-88.

[4] W. Zimmerli, "Prosthetic-joint-associated infections", Best Pract. Res. Cl. Rh. Vol. 20, pp. 1045-1063, 2006.

[5] D. Davis, "Understanding biofilm resistance to antibacterial agents", Nat. Rev. Drug Discov. Vol. 2, pp. 114-122, 2003.

[6] B.J. Nablo, A.R. Rothrock, M.H. Schoenfisch, "Nitric oxide-releasing sol-gels as antibacterial coatings for orthopaedic implants", Biomaterials. Vol. 26, pp. 917-924, 2005.

[7] Y.H. An, R.J. Friedman, "Prevention of sepsis in total joint arthroplasty", J. Hosp. Infect. Vol. 33, pp. 93-108, 1996.

[8] C.L. Nelson, R.P. Evans, J.D. Blaha, "A comparison of gentamicin impregnated polymethylmethacrylate bead implantation to conventional parenteral antibiotic therapy in infected total hip and knee arthroplasty", Clin. Orthop. Vol. 295, pp. 96-103, 1993.

[9] A.J. Tasman, F. Wallner, R. Neumeier, "Antibiotic impregnation of cartilage implants: diffusion kinetics of fluroquinolones", Laryngo. Rhino. Otol. Vol. 79, pp. 30-33, 2000.

[10] C.J. Chung, h.I. Lin, H.K. Tsou, Z.Y. Shi, J.L. He, "An antibacterial TiO2 coating for reducing hospital-aquired infection", J. Biomed. Mater. Res. B. Vol. 85, pp. 220-224, 2007.

[11] H. Boettcher, "Bioactive sol-gel coatings", J. Prakt. Chem. Vol. 342, pp. 427-436, 2000.

[12] H. Liu, T.J. Webster, "nanomedicine for implants: a review of studies and necessary experimental tools", Biomaterials. Vol. 28, pp. 354-369, 2007.

[13] P. Linez-Bataillon, F. Monchau, M. Bigerelle, H.F. Hildebrand, "In vitro MC3T3 osteoblast adhesion with respect to surface roughness of Ti6Al4V substrate", Biomol. Eng. Vol. 19, pp. 133-141, 2002.

CONTACT INFO

Franja Šulek and Ingrid Milošev are with Valdoltra Orthopaedic Hospital, Ankaran, Jadranska cesta 31, 6280 Ankaran, Slovenia.