LONG TERM LOCAL EFFECT AFTER IMPLANTATION AND TOXICITY OF MODIFIED Ti6Al7Nb ALLOY SURFACE

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Introduction

A further long-term biological study of ReligaHeart® ROT [1] device material construction was performed in order to allow the device for clinical utilisation in long-term heart support. Modification of the well-known glow discharge assisted nitriding process called as active screen plasma nitriding has been used to produce of TiN+Ti_2N+αTi(N) diffusive surface layers, improving the mechanical as well as short-term biocompatible properties of the titanium alloy [2,3].

As the final biological material evaluation, the long term local effect after implantation of the modified TiN surface as well as ceramic composite ZrO_2-Y_2O_3 was tested in vivo using small animal model, to complete the complex biocompatibility assessment required by ISO 10993 standard.

Materials and Methods

The athrombogenic diffusive nitrided surface layers TiN+Ti_2N+αTi(N)- type have been produced on Ti6Al7Nb titanium alloy surface, with the roughness of Ra=80nm, using plasma nitriding process with active screen. Biomaterial flat samples of titanium (TiAl67Nb) and titanium with nitrid layer (TiN+Ti_2N+αTi(N)) were in form of discs,14mm diameter and ZrO_2-Y_2O_3 8mm diameter and 1,5mm thickness were sterilized with ETO as the final device RH ROT sterilization method (EOGas 4, H.W.Andersen Products Ltd.).

The in vivo investigation was performed according to biocompatibility standard for medical devices, including tests for local effects after implantation (ISO 10993-6) and systemic toxicity (ISO 10993-11).

Local effects after implantation and systemic toxicity tests were carried out with the utilization of New Zealand white rabbits (n=40), both sexes, weighing over 2kg. 10 animals were used for each biomaterial subcutaneous implantation (4 implants for the titanium alloy and titanium alloy with TiN surface layer group, 2 implants in the group with zirconia implants) and 10 animals as control group (only surgical procedure, no biomaterial implanted).

Biomaterials dosage were calculated in order to select the proper sample mass comparing to animal mass, to simulate number of biomaterial kg used in blood pump recalculated for 1 kg of human body. After 4 and 12 weeks, the final observation period was 26 weeks. Every day the post-operative scar macroscopic evaluation was carried out (healing level, tissue status around the implant location). General animal behavior and condition were observed. Before the implantation as well as before euthanasia the blood was collected for hematological and biochemical evaluation and the animals were weight. The macroscopic evaluation of post-operative scar and tissues around biomaterial implants were done. After the experiment vitals samples (heart, thymus, liver, spleen, kidneys and lungs) were collected for histopathological examination.

Results and Discussion

Standardized tests to local tissue reaction and systemic toxicity, demonstrated the safety and biocompatibility of evaluated materials: titanium, titanium with nitride layer and zirconium, after 26 weeks post-implantation. Blood samples assessment did not revelled a negative impact of the investigated materials on tested animals. The testes parameters remained at a constant level. Clinical observation of animals showed no abnormal behaviour. The post-operative wound healed without complication. Finally the histopathological evaluation of the implantation area (FIG. 1) and internal organs reveled no normal healing process around the implants and changes in the internal organ structure.

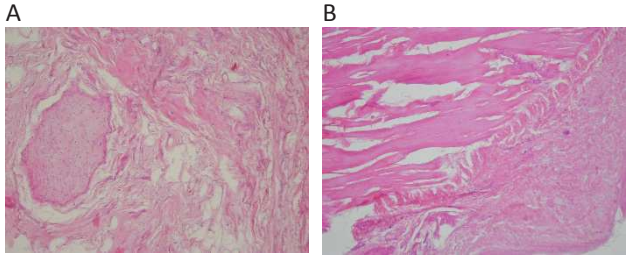

FIG. 1. Histopathological analysis of the implantation area. (A) titanium group (b) titanium with nitride layer group. No changes were found.

Conclusions

The performed studies showed in the long-term evaluation proper local effects and no syndromes of systemic toxicity of the nitrided layers TiN+Ti_2N+αTi(N)-type produced on Ti6Al7Nb titanium alloy surface, using plasma nitriding process with active screen. The results together with in-vitro biocompatibility evaluation as well as short term in-vivo studies carried out before, confirmed that the biomaterial can be safety used in the construction of implant having contact with blood, especially the Polish implantable rotary blood pump.

Acknowledgments

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