INITIAL BIOCOMPATIBILITY ASSESSMENT OF CERAMIC MATERIAL INTENDED FOR APPLICATION IN IMPLANTABLE HEART ASSIST DEVICE

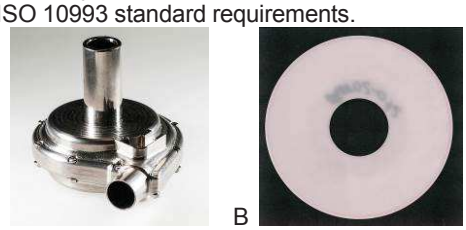
KAROLINA JANICZAK, BARBARA ZAWIDLAK-WĘGRZYŃSKA, MACIEJ GAWLIKOWSKI*, MAŁGORZATA GONSIOR, ROMAN KUSTOSZ

PROFESSOR ZBIGNIEW RELIGA FOUNDATION OF CARDIAC SURGERY DEVELOPMENT, POLAND
*E-MAIL: MGAWLIK@FRK.PL

[ENGINEERING OF BIOMATERIALS 143 (2017) 67]

Introduction

Construction of an implantable continuous flow ventricular heart assist devices (VADs) requires detailed material selection in the aspects of long-term contact with blood under high shear stress conditions. Materials for VADs application should characterise high mechanical resistance and biocompatibility in order to reduce platelet activation on blood contacting pump elements and avoid blood clothing inside the pump. The centrifugal continuous flow blood pump ReligaHeart ROT (RH ROT), with contactless magnetically and hydro-dynamically suspended rotor has been developed as an implantable VAD for advanced heart failure treatment support (FIG. 1A) [1]. The blood pump dielectric elements made of zirconia stabilized with yttrium ZrO_2-Y_2O_3 [2] were evaluated in the aspect of long-term blood contact application in RH ROT elements (FIG.1B). The initial biocompatibility assessment of zirconia included biodegradation, haemolysis, cytotoxicity and thrombogenic properties analysis were performed in accordance with PN EN ISO 10993 standard requirements.



A B

FIG. 1. ReligaHeart ROT implantable clinical version prototype (A), dielectric ceramic elements (B).

Materials and Methods

Zirconia samples were prepared in a representative manner for the medical device.

Degradation evaluation

Degradation analysis was performed according to ISO 10993-14 standard at temperature of 37°C for period of 120 ±1h, in vitro in Tris-HCl buffer. Biodegradation tests were performed in SBF. Incubation was carried out for 30 and 60 days. After degradation process the medium was analysed by Inductively Coupled Plasma (ICP) for zirconia migration evaluation. Morphological surface changes after degradation process were investigated with SEM and SEM-EDX utilization.

Cytotoxicity evaluation

Cytotoxicity test was performed in accordance with PN EN ISO 10933-5 by qualitative method with utilization of normal mouse fibroblasts - NCTC clone 929.

Haemolysis evaluation

Haemolysis assessment was performed on whole human blood, CPDA-1 preserved, in direct contact and static conditions. The blood was diluted with PBS to haemoglobin concentration of 10 g/L. Before examination, initial blood count and free haemoglobin level (fHGB) in blood plasma were assessed. The investigated material was incubated with blood in temperature of 37°C for 3h. Additionally, a blank test was performed under conditions given in test procedure. The free haemoglobin level was assessed and haemolytic index was calculated for blood, after incubation.

Thrombogenicity evaluation

Thrombogenicity assessment was carried out in static as well as in dynamic conditions. Static thrombogenesis evaluation was performed by incubation of the investigated material in platelet rich plasma in temperature of 37°C for 1h. After incubation the investigated material was washed and fixed with formaldehyde. Presence of adhered blood elements was investigated using SEM. Evaluation of thrombogenic properties in dynamic conditions was performed utilizing Impact-R analyser and fresh human blood. The test consist of generating physiological blood flow above the investigated surface. Afterwards platelets activation and platelet-leukocyte aggregates formation was determinate utilizing flow cytometry. Analysis of adhered cells to the biomaterial surface with active receptors (CD62P, CD45) utilizing fluorescent microscopy was performed. Bionate (DSM) polyurethane was investigated as it has a low thrombogenicity potential and polystyrene as a reference material.

Results and Discussion

The results of the degradation tests of ZrO_2-Y_2O_3 showed material stability during degradation process.

Cytotoxicity analysis revealed no adverse effects of zirconia on fibroblasts. Cells characterized normal viability and proliferation.

The haemolysis index of the blood after contact with the investigated material was below 2% (classification of non-haemolytic material according to ASTM F756-00 standard).

The microscopic analysis of surface, after contact with blood in static conditions, revealed proper athrombogenic material properties (low both: platelets adhesion and activation). The number of activated platelets (CD62P) and aggregates platelet-leukocyte (CD62P-CD45) in blood circulating above the biomaterials surface was similar in all tested groups. The number of platelets (CD62P) and platelet-leukocyte aggregates (CD62P-CD45) adhered to investigated biomaterial surface were slightly lower than the number of activated elements on polystyrene surface. The number of adhered platelets (CD62) and aggregates in other test groups was comparable.

Conclusions

Primary investigation's results revealed high biocompatibility properties of zirconia stabilized with yttrium. The investigated material can be classified as non-degradable, non-cytotoxic, no-haemolytic and low thrombogenic.

The research will be continued in order to perform in vivo biocompatibility evaluation of ZrO_2-Y_2O_3 in the aspect of long-term contact with human body in RH ROT device implementation.

Acknowledgments

This work has been financially supported by the Polish Artificial Heart project and by the National Centre of Research and Development - Project no. RH-ROT/266798/STRATEGMED-II.

References

[1] R. Kustosz *et al*., Archives of metallurgy and materials, V.60, 3/2015: 2253–2260
[2] Piconi C. *et al*. (1999) V.20 I.1 :1-25
[3] R. C. Garvie *et al*. (1984) Journal of Material Science 19:3224-3228
[4] J. Li *et al*. (199) Clinical materials;12(4):197-201