Comparative Analysis of Tissue Reactions during Implantation of Endoprostheses made of Polytetrafluoroethylene in the Anterior Abdominal Wall

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ABSTRACT

Objectives: The objective of this research was a comparative study of the reaction of the tissues of the anterior abdominal wall to the PTFE-endoprosthesis with a DLC-coating at long-term experimental stages.

Material and Methods: The study was performed on 110 white laboratory rats divided into two experimental groups. In the first group, a 1.0–1.0 cm PTFE-endoprosthesis fragment was implanted under the skin of the anterior abdominal wall in animals. In the second group, a DLC-coated PTFE-endoprosthesis fragment was implanted into animals. A morphological study of the preparations was carried out after 180 days of the experiment.

Results: A morphological study revealed significant differences in tissue reactions to two types of PTFE-endoprosthesis after 180 days of the experiment. Both groups showed no acute inflammatory changes, and the differences were related to the delimiting tissue reactions. The giant cell reaction was observed to a greater extent when uncoated PTFE-endoprostheses were used, and type IV collagen fibronectin was accumulated in them. The presence of a DLC coating significantly reduced the degree of this reaction. Also, a significant difference is that the initial PTFE endoprosthesis with micropores is impregnated with plasma and matrix proteins and subsequently grows with collagen fibers. DLC-coating reduces the absorption of proteins in the thickness of the endoprosthesis.

Conclusion: The study found that this surface modification of PTFE-endoprostheses significantly affects the nature of the inflammatory and restrictive reactions that determine the bio-integration of the endoprosthesis.

Keywords: polytetrafluoroethylene, tissue reactions, diamond-like carbon

INTRODUCTION

Endoprostheses made of various polymeric materials have long been widely used in various fields of medicine, and their list is constantly expanding, primarily in connection with the optimization of properties for use in a specific situation. The response of an organism to an implant is determined mainly by its surface properties: chemical composition, structure, and morphology (Brody 2015; Kiradzhiyska & Mantcheva 2019; Yarosh et al. 2011). In this regard, the existing methods for regulating the biological properties of medical devices are aimed at changing the physicochemical properties of the surface using physical, chemical, and physicochemical modification methods. Of particular interest are modification methods that change the physicochemical, structural, and functional properties of a surface without affecting the bulk characteristics of the product, its strength, elasticity, electrophysical parameters, etc (Fattal 2017; Keselowsky 2007; Kim 2011; Kiradzhiyska & Mantcheva 2019). Intriguing in these terms is the original diamond-like carbon coating (diamond-like carbon - DLC), developed at the Belgorod State University (Yarosh et al. 2011). In this regard, the objective of this research was a comparative study of the reaction of the tissue of the anterior abdominal wall on DLC-coated PTFE-endoprostheses (polytetrafluoroethylene - PTFE) in a long-term experiment.

MATERIAL AND METHODS

The study was performed on 110 white laboratory rats divided into two experimental groups. In the first group, a 1.0–1.0 cm PTFE-endoprosthesis fragment was implanted under the skin of the anterior abdominal wall in animals. In the second group, a DLC-coated PTFE-endoprosthesis fragment was implanted into animals. A morphological study of the preparations was carried out after 180 days of the experiment. The biomaterial was excised together with the surrounding tissues and fixed in a 10% formalin solution. The material was paraffin-embedded according to a standard procedure. Histological sections were stained with hematoxylin and eosin, according to Mallory and van Gieson, and Fenaf stain was used to identify elastic fibers. The immunohistochemical method, according to standard protocols, was used to detect type I, III, and IV collagens, fibronectin and laminin, monocyte/macrophage antigen NAM56, myelopeoxidase polymorphonuclear leukocytes. The manufactured micropreparations were scanned using the MiraxDesk image scanning and archiving system.

Qualitative analysis, morphometry, and microphotographs were performed on computer images.

RESULTS

A morphological study revealed significant differences in tissue reactions to two types of PTFE-endoprostheses of different configurations in the long term. Both series of the experiment showed no acute inflammatory changes on day 180, and the differences were related to delimiting tissue reactions.

The structure of the uncoated implants at this time of the experiment was moderately loose and had an edematous appearance. The surfaces of the fragments of endoprostheses were tightly adjacent to the surrounding connective tissue, in which there was no neutrophilic or eosinophilic infiltration, the mast cells were without manifestations of degranulation, which indicates the absence of the allergenic effect of the implants. At the same time, clusters of giant cells of foreign bodies were present on the surface of the implants and, to a greater extent, in the marginal region, and there were foci of basophilia in the intercellular substance, most likely indicating calcification. With additional impregnation according to Kos, it was revealed that large calcifications are contained in the places of accumulation of these cells (Figure 1-3).

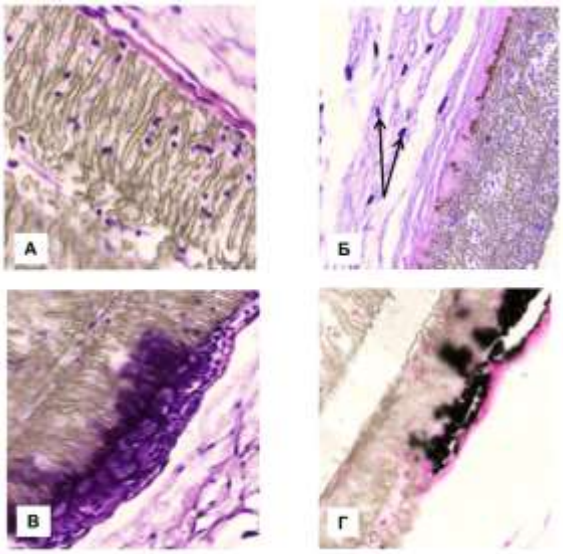


Figure 1: 180 days after implantation of a fragment of an uncoated (A, B, D) and DLC-coated (B) PTFE-endoprostheses.

Note: A - the structure of the endoprosthesis is moderately loosened, with single loose collagen fibers of the connective tissue of the anterior abdominal wall outside, B - firm adherence of the endoprosthesis to the connective tissue, the coating layer is preserved as a narrow strip of brown color, the arrows have intact mast cells, C - a layer of giant cells of foreign bodies, D - a calcification site in the area of accumulation of cells of foreign bodies. Stained with hematoxylin and eosin (A, B), Fenaf stain (B), Kos-impregnation. Microphoto x 100.

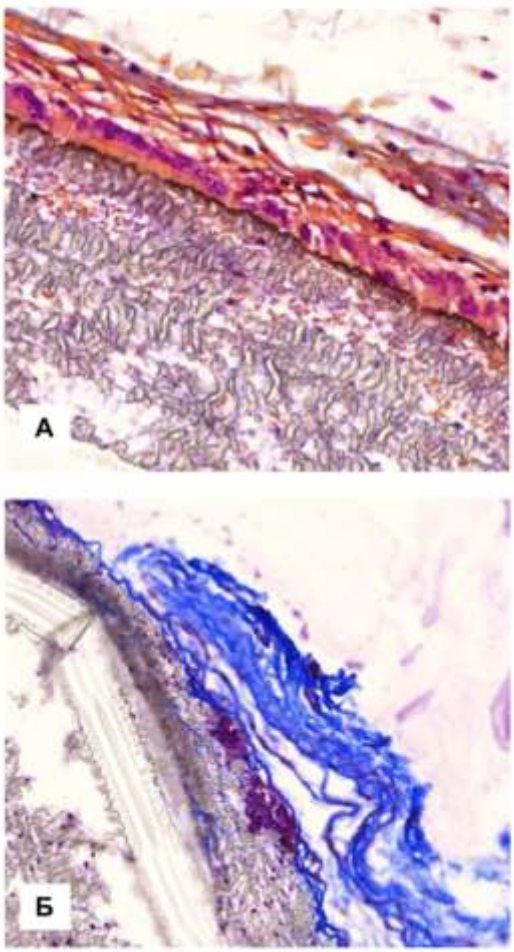
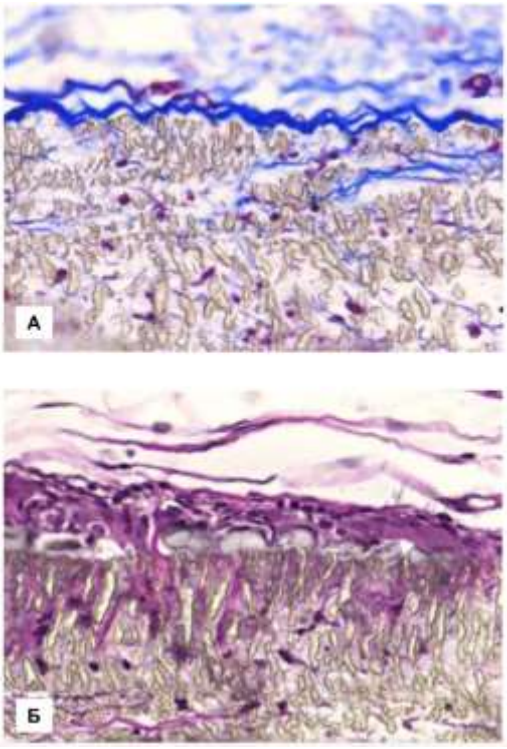


Figure 2: 180 days after implantation of a fragment of an uncoated PTFE-endoprostheses.

Note: A - loose structure of the endoprosthesis, with the layers of immature collagen fibers of the forming capsule outside, B - bundles of mature collagen fibers in the adjacent dermis, on the surface of the endoproteosplast from cells of foreign bodies. Mallory stain. Microphoto x 100.



Note: A - migration of leukocytes into the pores of the material, the ingrowth of single thin collagen fibers, B - the site of a more pronounced ingrowth of collagen fibers. Mallory (A) and Van Gieson (B) stain. Microphoto x 200.

Figure 3: 180 days after implantation of a fragment of an uncoated PTFE-endoprostheses.

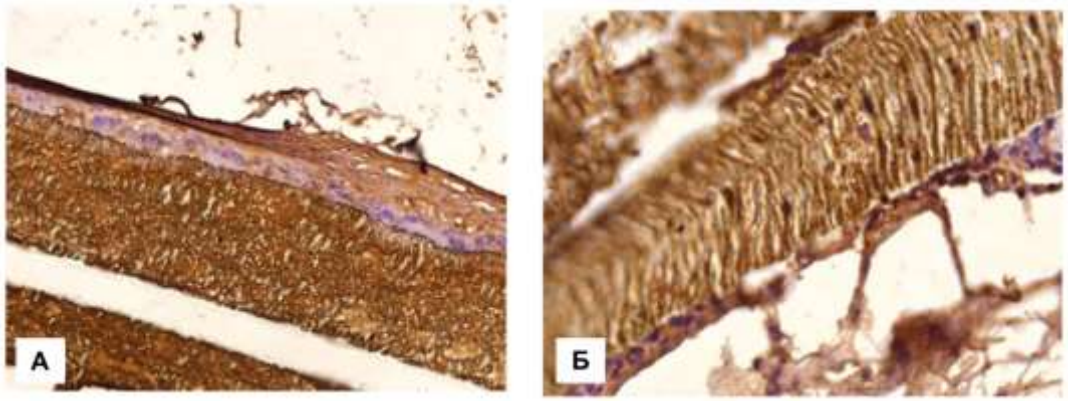


Figure 4: Deposition of fibronectin (A) and type I collagen (B) in the thickness and on the surface of an uncoated PTFE-endoprosthesis.

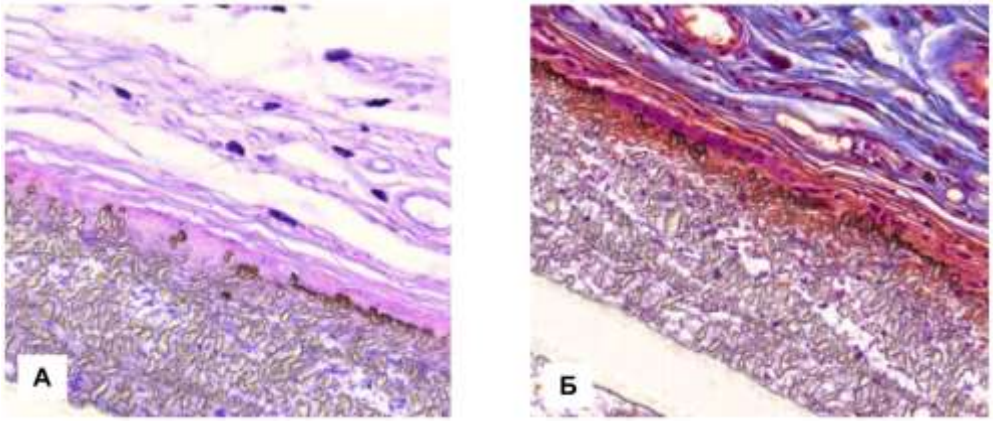


Figure 5: 180 days after implantation of a fragment of a DLC-coated PTFE-endoprostheses.

Note: A - the structure of the endoprosthesis is weakly loosened, single leukocytes are thicker, the coating particles (brown layer) cover the surface, dense unformed connective tissue, intact mast cells, without giant cell reaction; B - endoprosthesis site with the presence on the surface of layers of immature collagen fibers of the forming capsule and the surrounding tissues of the abdominal wall with bundles of mature collagen fibers (blue); the endoprosthesis connecting tissue does not grow in the thickness, between the fibers of the capsule and its surface are small cells of foreign bodies. Fenaf (A) and Mallory (B) stain. Microphoto x 100.

The obtained data indicate that the DLC-coating modifies the properties of PTFE-endoprostheses without reducing the initial biocompatibility of the material (Figure 5). A significant difference is that the initially microporous PTFE-endoprosthesis is impregnated with plasma and matrix proteins and subsequently overgrown with collagen fibers, which can cause rigid fixation of the endoprosthesis in the tissues of the anterior abdominal wall. A negative consequence may be the mechanical effect of the edges of the endoprosthesis on the tissue, a manifestation of which we observed in the form of calcification foci in these areas with a giant cell reaction. The DLC-coating reduces the absorption of proteins in the thickness of the endoprosthesis. Its influence extends to tissue reactions only in close proximity to the surface of the endoprosthesis, since, regardless of the presence of a coating, a connective tissue capsule is formed around the endoprosthesis, the severity of which depends on the previous inflammation, mainly due to surgical trauma and the degree of infection of the implantation area.

DISCUSSION

According to the literature, one of the indicators of the surface properties of endoprostheses that affect their biocompatibility is the reaction of monocytes / macrophages and the formation of giant cells of foreign bodies (giant foreign body cells – GFBC). However, the data on the dependence of the giant cell reaction on the properties of the substrate at its development sites are ambiguous. It has been found that monocyte adsorption to the fibronectin surface inhibits the formation of GFBC (Shen et al. 2007). Materials that do not promote adhesion cause a loss of primary adhesion of monocytes/macrophages and their death through apoptosis. On the other hand, a mechanism for avoiding apoptotic death is cell fusion with the formation of GFBC (Brodbeck et al. 2001). Experiments on knockout mice for the synthesis of plasma fibronectin provided mixed results from studying tissue reactions to subcutaneous implantation of polyethylene terephthalate discs (Mc Nally et al. 2007). In knockout mice, the thickness of the fibrous capsule was paradoxically twice as large as in intact mice; the amount of GFBC was three times higher. Surfaces that promote the accumulation of another adhesive protein, vitronectin, also contribute to the formation of GFBC (Yarosh et al. 2011). The effect of the surface of biomaterials on the adhesive properties of cells and apoptosis is significant for providing a bactericidal environment. Induction of apoptosis of inflammatory cells and monocytes / macrophages, depending on the surface of the endoprosthesis, may be a factor in the persistence of infection, which is observed, in particular, in cardiac implants (Ferraris et al. 2011; Kim et al. 2018).

In our study, a giant cell reaction was commonly observed with the use of endoprostheses without the original DLC-coating, which accumulated both fibronectin and type IV collagen (Figure 4). The DLC-coating reduced this reaction rate. This difference cannot be unequivocally explained by the above literature data, since calcification of tissues adjacent to the surface of endoprostheses was revealed in the foci of the giant cell reaction.

CONCLUSION

Our studies of tissue reactions of the anterior abdominal wall to traditional polytetrafluoroethylene endoprostheses and DLC-coated endoprostheses showed that this surface modification of PTFE-endoprostheses significantly affects the nature of the inflammatory and restrictive reactions that determine the bio-integration of the endoprosthesis.

The results indicate that the ion-plasma modification of the surface properties of endoprostheses performed at the Belgorod State Research University is promising for obtaining surgical materials with desired properties.

The key is that the DLC-coating developed and proposed by us can control the relationship of the endoprosthesis with the surrounding connective tissue, which can develop in two ways: overgrowth of the endoprosthesis with connective tissue with mechanical integration, or encapsulation in the form of a foreign body without biomechanical integration into the structures of the abdominal wall. Modifications of the implant itself - its biodegradation processes depending on the surface properties - also require further research.

CONFLICT OF INTEREST: Nil

REFERENCES

1. Brodbeck, WG, Shive, MS, Colton, E, Nakayama, Y, Matsuda, T, Anderson, JM. 2001. Influence of biomaterial surface chemistry on the apoptosis of adherent cells. J Biomed. Mater Res., 55 (4): 661 – 668.
2. Brody, H. 2015. Biomaterials. Nature, 519 (7544), S1. PMID: 25806489, DOI: 10.1038/519S1a
3. Fattal, E. 2017. Materials for the Medicine of Tomorrow Editorial Med Sci (Paris). 33 (1):9-10. PMID: 28120749. DOI: 10.1051/medsci/20173301002.
4. Ferraris, S, Spriano, S, Pan, G, Venturello, A, Bianchi, CL, Chiesa, R, Faga, G, Maina, MG, Vernè E. 2011. Surface modification of Ti-6Al-4V alloy forbiomineralization and specific biological response: Part I, inorganic modification. J. Mater. Sci. Mater. Med., 22 (3): 533–545.
5. Keselowsky, BG, Bridges, AW, Burns, KL, Tate, CC, Babensee, JE, LaPlaca, MC, Garcia, AJ. 2007. Role of plasma fibronectin in the foreign body response to biomaterials. Biomaterials, 28 (25): 3626 – 3631.
6. Kim, JH, Shin, JH, Shin, DH, Moon, MW, Park, K, Kim, TH, Shin, KM, Won, YH, Han, DK, Lee KR.

2011. Comparison of diamond-like carbon-coated nitinol stents with or without polyethyleneglycol grafting and uncoated nitinol stents in a canine iliac artery model. Br. J. Radiol., 4 (999): 210–215.

7. Kiradzhiyska, DD, Mantcheva, RD. 2019. Overview of Biocompatible Materials and Their Use in Medicine. FoliaMed (Plovdiv), 61 (1), 34-40.
8. Mc Nally, AK, Jones, JA, Mac Ewan, SR, Colton, E., Anderson, JM. 2007. Vitronectin as a critical protein adhesion substrate for IL-4-induced foreign body giant cell formation. J Biomed. Mater. Res., 86A: 535-543.
9. Shen, M, Garcia, I, Maier, RV, Horbett, TA. 2004. The effects of adsorbed proteins and surface chemistry on foreign body giant cell formation, TNFα release, and procoagulant activity of monocytes. J Biomed. Mater. Res., 70A: 533–541.
10. Yarosh, AL, Dolzhikov, AA., Soloshenko, AV., Kolpakov, AY, Bitenskaya, EP, Molchanova, AS, Gerasimenko, DV. 2011. Biocompatibility investigation of new surgical prosthetic applied in abdominal plastic surgery. Fundamental research, 10(1):186-189. (in Russian).

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