SURFACE MODIFICATIONS FOR INFLOW CANNULAS OF VENTRICULAR ASSIST DEVICES – COMPARISON OF LATEST SOLUTIONS

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Abstract

Nowadays, the Mechanical Circulatory Support (MCS) within the Ventricular Assist Devices (VAD) appears to be a reliable and effective solution for patients with advanced heart failure (HF). After many years of work, extracorporeal pulsatile VADs have been replaced by new generations of implantable continuous flow (CF) pumps. Clinical experience has shown that present-day pump constructions still need to be improved to minimize the risk of complications during heart assistance.

One of the complications is the pump inflow obstruction caused by the ingrowth of tissue into the blood inflow path and pump thrombosis. The main goal is to develop a coating for the external surface of the inflow cannula to provide controlled tissue ingrowth. The smooth surface of the cannula external wall results in the tissue overgrowth into the pump inflow orifice, and may be a source of emboli. The paper presents external surface modifications of the inflow cannula performed by different VAD manufacturers within the topography characterization.

The inflow cannulas used in CF VADs are mainly made of titanium alloy due to its mechanical properties and high biocompatibility. In general, the discussed surface coatings were characterized by the roughness of about ≈ Ra = 15 μm, high porosity and good wettability Φ ≈ 60°. The surface was covered with titanium microspheres or titanium mesh.

The developed surfaces and clinical experience confirm the ability to control the tissue ingrowth along the external surfaces of the inflow cannula at the tissue-implant interface.

Keywords: *surface modification, VAD inflow cannula, tissue-implant interface, porous surface*

[Engineering of Biomaterials 151 (2019) 17-23]

Introduction

Surface modifications of medical implants provide many possibilities to control the processes occurring after implantation in peri-implant tissues. The healing process of orthopaedic implants and the processes occurring in bone tissues after implantation have already been well described in the literature and the provided knowledge is successfully used in the clinic. An example is the modification of surfaces in cementless endoprostheses where the surface coating increases the potential for biomechanical bonding at the implant-bone interface and affects the rate of protein adsorption [1-5]. A close correlation between pore size and bone ingrowth is also noticeable [5-7]. Unfortunately, there is still no data concerning issues of cardiac surgical implants healing, despite the widespread use of mechanical circulatory support systems. Therefore, it is necessary to provide clinical data which will determine the morphological parameters of the surface coating providing a permanent and stable connection of cardiac implants with myocardial tissue.

Nowadays, the Mechanical Circulatory Support (MCS) is becoming a viable alternative to heart transplantation for non-effective pharmacological and minimally invasive treatment of advanced heart failure (HF). The actual degree of heart failure is determined with the New York Heart Association (NYHA) functional scale and referred on the Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) profiles, which provide important prognostic information for HF patients with MCS. The HF is a complex set of clinical symptoms that are characterized by an insufficient blood supply in accordance with the body's metabolic needs. The number of patients suffering from heart insufficiency increases every year. Meanwhile, the number of successful heart transplants has remained stable. The number of organ donors, including the heart, is limited, while the MCS systems often give patients time to wait for transplantation. In the case of long-term MCS the Continuous Flow Ventricular Assist Devices (CFVAD) (FIG. 1) are the most commonly used.

The implantation of the blood pump stops the expanding ischemia zone, provides the relief of the weakened heart and increases coronary perfusion, but - above all - it improves the cardiovascular hemodynamic. The fast development of technology brought about a variety of MCS solutions on the market, including LVAD (Left Ventricular Assist Device) for left ventricular support, RVAD (Right Ventricular Device) for right ventricular support and BIVAD (Biventricular Assist Device) for the assistance of both ventricles.

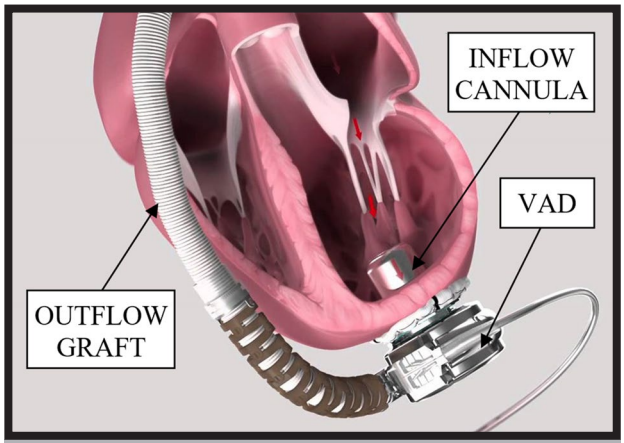

FIG. 1. The position of the implanted VAD on the example of MEDTRONIC HEARTWARE® pump [8].

VADs were developed to improve the failing heart function without replacing the biological organ. The methods of MCS can be described according to the diagnosis and prognosis of assistance goal and duration as: Bridge To Decision (BTD), Bridge To Recovery (BTR), Bridge To Transplant (BTT) and the Destination Therapy (DT) [9].

After many years of work, extracorporeal pulsatile VADs were replaced by new generations of implantable continuous flow (CF) devices in long term assistance [10]. So far, the clinical experience has shown that present-day pump constructions still need to be improved to minimize the risk of complications during heart assistance. In comparison to older constructions, there is a huge improvement thanks to the most modern biocompatible materials and surface engineering, along with the VAD miniaturization, limitation of its complexity and removal of mechanical bearings systems. Despite many new solutions, patients still experience high morbidity, many side effects and mortality. Actual VAD constructions consist of many components that may fail. As the pump is fully implantable, the procedure is difficult, invasive and requires the use of systemic anticoagulation. Moreover, the patients themselves become more complex and undergo VAD implantation in an increasingly critical form, causing many postoperative and direct support complications. One of the most important complications is embolization of the pump which may be caused by thrombus formation resulting from the thrombocyte activation. The thrombus may form in any part of the pump on the surfaces which stay in direct contact with blood. Bleeding and thrombotic complications are strongly related with haemostasis affected by antithrombotic and/or antiplatelet treatment. So the optimal balance is sometimes a challenge. However, there is still room to improve the pump construction to minimize blood clotting. One way is to change the design of the inflow cannula, its tissue attachment, as well as the length, location, and orientation of its introduction into the heart left ventricle. There is still no perfect solution and each device utilizes its own cannula design.

Materials and Methods

The main goal of the project is to develop coating for the external surface of the inflow cannula of the Polish CF-VAD RELIGA HEART ROT [11] (FIG. 2) to provide the controlled myocardial tissue ingrowth around the cannula external wall. The clinical records exhibit the high importance of this phenomenon. The smooth external surface of the inflow cannula in the CF pump may cause the growth of tissue upwards the cannula inflow orifice, which may result in adverse flow turbulences or suction events disrupting the proper work of the inflow cannula.

The pump inflow obstruction is one of complications which are directly connected to the external surface of the inflow cannula design. It is caused by the tissue ingrowth into the flow passage, resulting in the pump flow collapse and possible pump thrombosis. According to the literature, the surface of the confluent cells monolayer may prevent thrombogenicity and develop an ideal blood-contacting surface eliminating the platelet deposition. The key role is played here by the surface topography including the presence of grooves, ridges, hills or pores. The textured topography represents the three-dimensional morphology, therefore it cannot be sufficiently characterized by only the linear profile. It requires additional measurement methods, such as Scanning Electron Microscopy (SEM), Energy-dispersive X-ray spectroscopy (EDS), atomic force microscope (AFM) and optical profilometer.

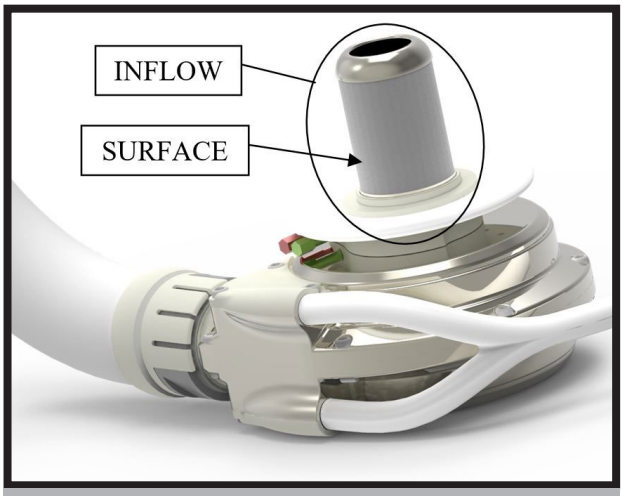

FIG. 2. The 3D visualization of the RELIGA HEART ROT pump under development in the Foundation of Cardiac Surgery Development in Zabrze, Poland.

The majors on the market are currently MEDTRONIC® with HEARTWARE (HW) ventricular assist system (VAS) and ABBOTT® with HEARTMATE III (HM3) VAS. However, there are many other VAD devised used in the clinical practice or during preclinical trials. The titanium alloy is the most common material used for the inflow cannulas and as the pump of most systems. Below there are presented VADs with modified inflow cannulas – FIG. 3. Every VAD is characterized by the different design of the inflow cannula, although many similarities can also be observed.

It is also worth noting that the surface modification was performed only on the external side of the inflow cannula in the case of HeartWare, Evaheart and Jarvik. This surface mainly contacts the heart muscle tissue and a small volume of flowing blood. However, the HeartMate II and HeartMate III have both external and internal surfaces subjected to spherical modifications. Similarly to other constructions, the external surface of the inflow cannula interfaces with the heart muscle tissue, whereas the internal porous surface is subjected to dynamic blood flows, which requires shear stress limitation and simultaneous stimulation of the protein film formation.

The clinical experience has confirmed positive effects of applying surface coating on the inflow cannula. Samer S. Najjar et al. performed the analysis of 382 patients who underwent the HVAD implantation to evaluate the statistics on the pump thrombus and treatment outcomes. One of the analyzed issues was the application of the inflow cannula coating. The original design of HVAD included highly polished titanium alloy on internal and external surfaces of the inflow cannula. However, the examinations of the explanted heart showed the tissue ingrowth encircling the external surface, which may be a source of emboli – FIG. 4a. Therefore, the modification of the inflow cannula was performed. To create a matrix enhancing the tissue ingrowth, the external surface was covered with the titanium microspheres via sintering. Thus, the tissue surrounding the well-polished inflow cannula did not adhere to the pump surface and may continue to grow upwards the orifice of the inflow cannula. The microspherical coating on the HVAD inflow cannula allowed the controlled growth of tissue in the coated area and limitated the tissue overgrowth upwards the cannula. Yet, the paper did not show the direct impact of surface modifications on the thrombus events limitation, as the longer observation period was required to conclude [17].

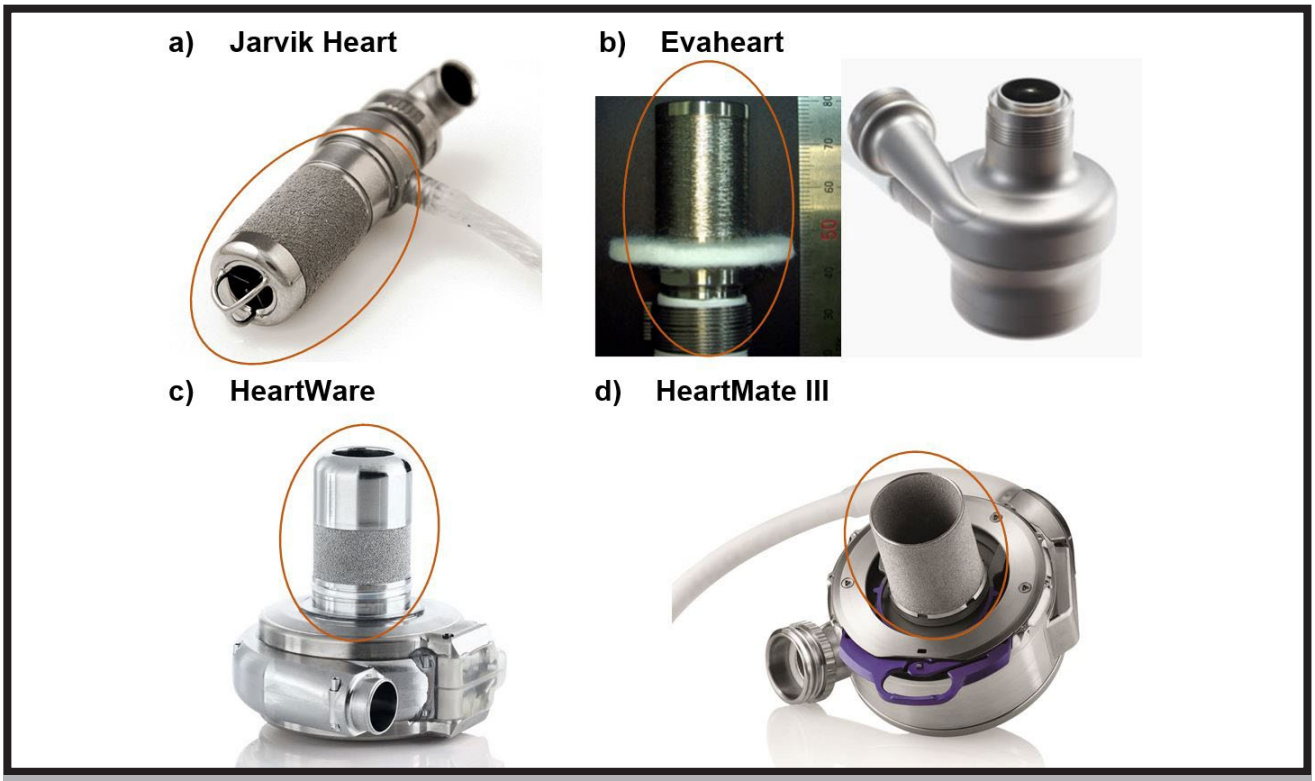

FIG. 3. Four VAD construction with presented inflow cannulas: a) Jarvik Heart [12], b) Evaheart [13,14], c) HeartWare [15], d) HeartMate III [16].

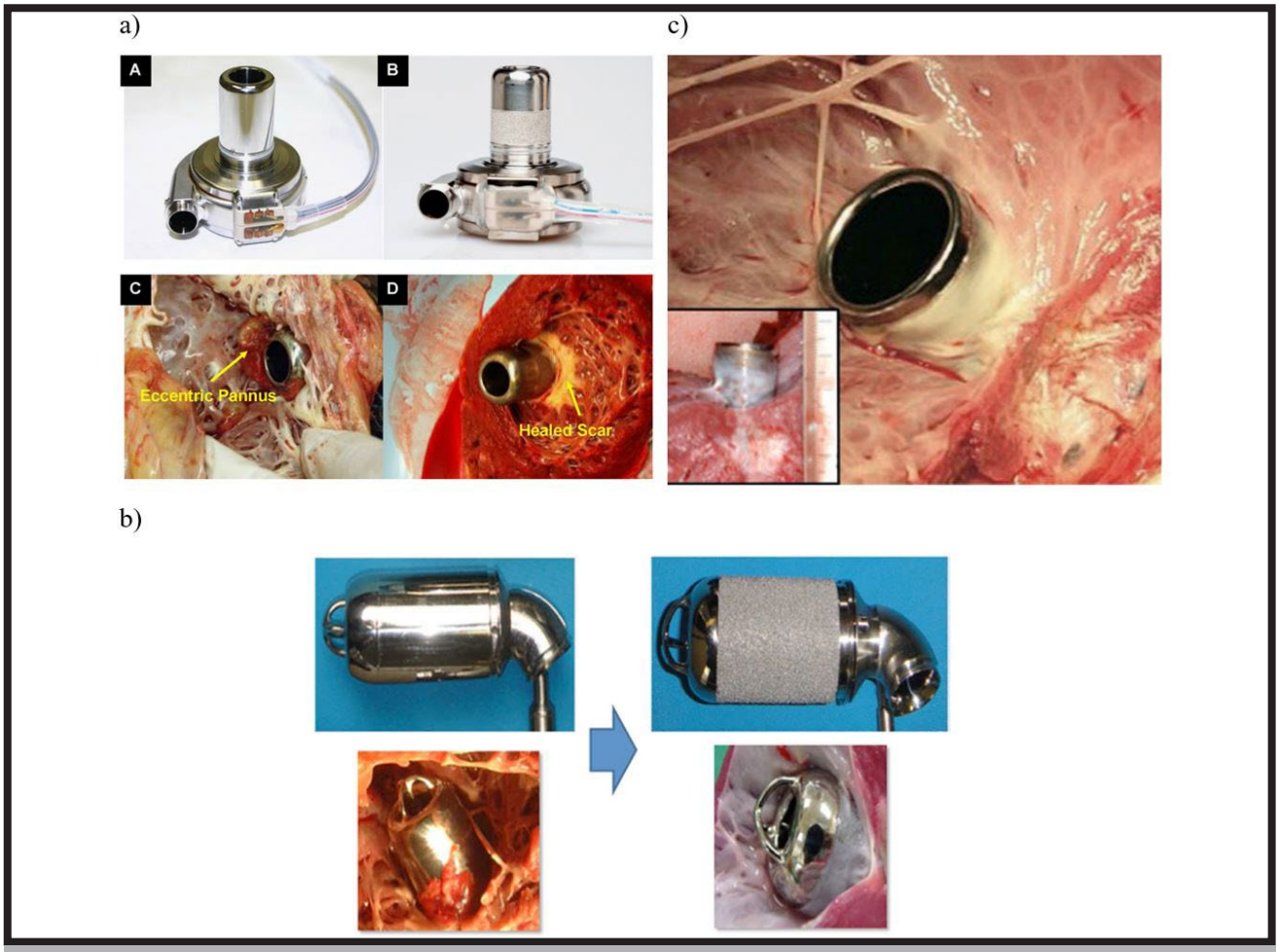

FIG. 4. Tissue ingrowth after surface modifications on the inflow cannulas of: a) Heartware [17], b) Jarvik 2000 [18], c) Evaheart [13].

Craig H. Selzman et al. presented a paper on Jarvik 2000 improvements to eliminate adverse events related to the pump thrombus and embolic events. One of the solutions was a modification of the inflow cannula design and the use of microsphere coating. The angle between the pump and the surrounding ventricular endocardium may result in the blood stasis and formation of thrombus. The external surface of the inflow cannula was modified within titanium microspheres to improve tissue adherence, provide better healing and reduce the risk of wedge thrombus formation – FIG. 4b [18].

Yukiko Yamada et al. hypothesized that the titanium mesh scaffold commonly used for cell culture could promote the growth of neointima, which would suppress the thrombus formation. The titanium wire of a diameter 85 μm was wrapped around the inflow cannula creating a textured external surface characterized by the volumetric porosity of 40-70%. The mesh was then treated with high temperature to bond titanium fibers to the substrate. The wire structure was developed on the external surface of the inflow cannula on the section of <20 mm in length. To prevent the tissue overgrowth, an area of unmodified surface was left between the mesh tip and the cannula. The animal trials were performed on four healthy calves weighing 81-98 kg that were sacrificed humanely after 2 months. The analysis after the ex-plantation revealed white neointimal tissue on the titanium mesh structure without any wedge thrombus formation around the tip of the inflow cannula – FIG. 4c. A single layer of endothelial-like cells and mature connective tissue was detected during histological studies. The surface coating, which induces the ingrowth of autologous neointima, may result in limitation of thromboembolic events related to wedge thrombus, but also may allow the clinical introduction of less stringent anticoagulation procedures [13].

The presented studies confirm the necessity of surface modifications to enhance tissue ingrowth to the inflow cannula, which will minimize the risk of thrombus formation and pump embolization. This paper focuses on the physicochemical analysis of the porous surfaces developed in HeartMate III and HeartWare. The study includes the use of MarSurf XR for roughness measurements – FIG. 5, the Scanning Electron Microscopy (SEM) for morphology analysis with the dimensions measurements, the Energy-dispersive X-ray spectroscopy (EDS) for the surface composition study and the contact angle test using goniometric method.

The roughness measurements were performed in the axial direction of the inflow cannula. In order to preserve statistics, 5 measurements were taken for each sample. The roughness results are presented in TABLE 1, however parameters are very similar for both HM3 and HW. Additionally, the microcontour function was used to assess the step between the polished and porous surface of the HeartWare inflow cannula, which equals ~200 μm. In the case of HeartMate III the modified surface covers the whole inflow cannula – no step is observed.

The SEM analysis revealed the microspherical morphology of the surface in the inflow cannulas of both the HeartMate III and HeartWare VADs – FIG. 6ab. The surfaces were probably subjected to the sintering process and most of the microspheres partially melted to each other. In the case of HM3 the surface consists of microspheres of 130 μm mean diameter and includes 3 spherical layers. The actual thickness of coating is ~300 μm. The surface morphology is characterized by high porosity with inhomogeneous pore sizes in the range of 1-200 μm. Such porosity allows migration and penetration of cells deep into the coating, enhancing tissue adhesion to the substrate. In the case of HW the surface is covered with microspheres of 115 μm mean diameter. The thickness of the coating is ~200 μm and consists mainly of 2 spherical layers. Similarly to HM3, the surface of HW is characterized by high porosity and loose packing of the spheres on the cannula surface with inhomogeneous pore sizes in the range of 1-250 μm. The pore sizes were estimated by means of microscopic observations using SEM. It is necessary to use a more precise test method to obtain more reliable data regarding the degree of porosity and average pore sizes. For both devices, the magnification in the 860-1,3k range revealed the mechanical deformations of spheres, a result of thermal stresses during the sintering process – FIG. 6cd.

TABLE 1. Roughness measurements obtained for HM3 and HW.

Roughness parameter	HeartMate III		HeartWare	
	Arithmetic mean value	Standard deviation	Arithmetic mean value	Standard deviation
Ra [μm]	14.57	2.07	12.30	1.98
Rq [μm]	17.73	2.74	15.38	2.50
Rz [μm]	72.77	12.05	66.21	10.90
Rt [μm]	90.23	18.83	89.98	14.62

FIG. 5. The MarSurf XR measuring unit and exemplary measurement.

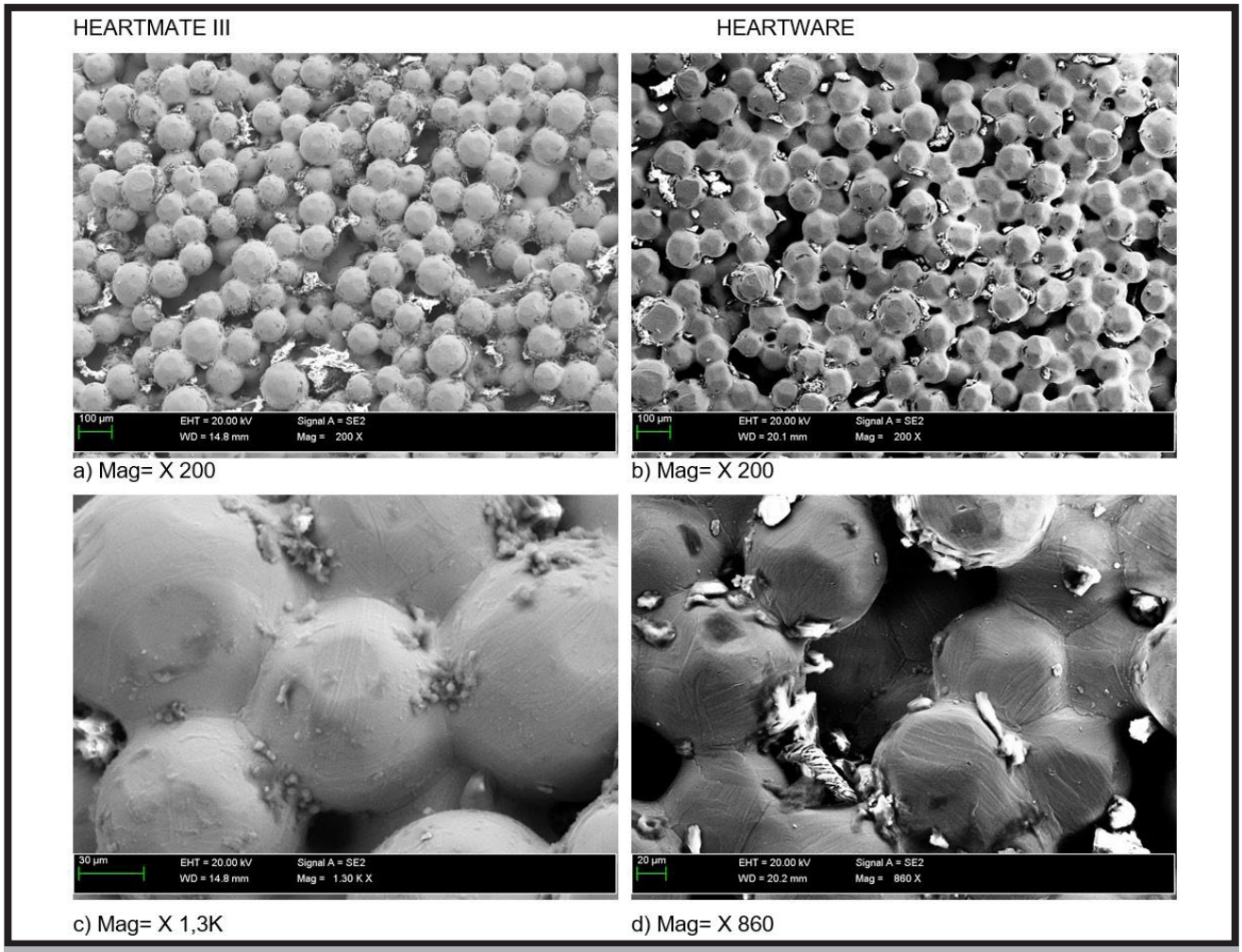

FIG. 6. Morphological analysis of microspherical coatings in HM3 and HW with different magnifications using Scanning Electron Microscopy.

The EDS analysis performed on the microspheres have shown the composition of Ti, Al, V. The HM3 surface consists of Ti = 92.68%, Al = 4.73%, V = 2.59%, however the HW surface includes Ti = 91.48%, Al = 3.66%, V = 4.86%. For both devices, the surface was characterized as the titanium alloy Ti6Al4V, which confirmed the information disclosed by the manufacturer. The Ti6Al4V alloy is the most widely used material to manufacture implants because of its high biocompatibility and corrosion resistance. However, according to literature, vanadium (V) may cause potential cytotoxicity and adverse tissue reactions. Nowadays, the Ti6Al7Nb alloy is becoming more and more often used for long-term medical implants.

The investigation of the contact angle was carried out on the samples at 20°C with the Möller-Wedel Optical apparatus, using the goniometric method – FIG. 7. The distilled water was applied on the sample surface with a volume of the 1.5 µl measuring drop.

In order to preserve statistics, 5 measurements were taken for each sample. The samples were cleaned and dried from the residual water, using compressed air before each measurement. The measurements were performed for the spherical surface of HM3 and HW. In the first case the surface was characterized by the contact angle of $\Phi = 72.4°$. In the case of HW the contact angle was equal to $\Phi = 69.3°$. The obtained results for both devices allowed determining the wettability characteristics of modified surfaces which proved to be highly hydrophilic. The good wettability has a positive effect on the cell migration in the area of surface modification, which results in good tissue ingrowth.

Results and Discussions

Currently surface modifications of medical implants provide enormous opportunities to customize and functionalize implant-tissue connections. The phenomenon of bone tissue growth has already been successfully investigated in the clinical practice. Unfortunately, the issues of cardiac surgical implants have not found such interest so far, despite the widespread use of mechanical circulatory support systems. There is still a lack of detailed data on advanced assessment of the phenomena occurring in the heart muscle at the tissue-inflow cannula interface. There are no data in the literature which determines the morphological parameters of the surface coating that would provide a permanent and stable connection of the cardiac support device with myocardial tissue. The clinical experience has shown the positive influence of surface modifications on the inflow cannula. On the basis of actual literature, the microspherical coating on the inflow cannula of HVAD allowed the controlled growth of tissue and limited the tissue overgrowth upwards the cannula. On the other hand, the surface modification which stimulates the ingrowth of autologous neointima may limit thromboembolic events related to wedge thrombus, possibly allowing the clinical introduction of less stringent anticoagulation procedures. The presented studies confirm the necessity of surface modification to enhance tissue ingrowth to the inflow cannula, which will minimize the risk of the thrombus formation and pump embolization.

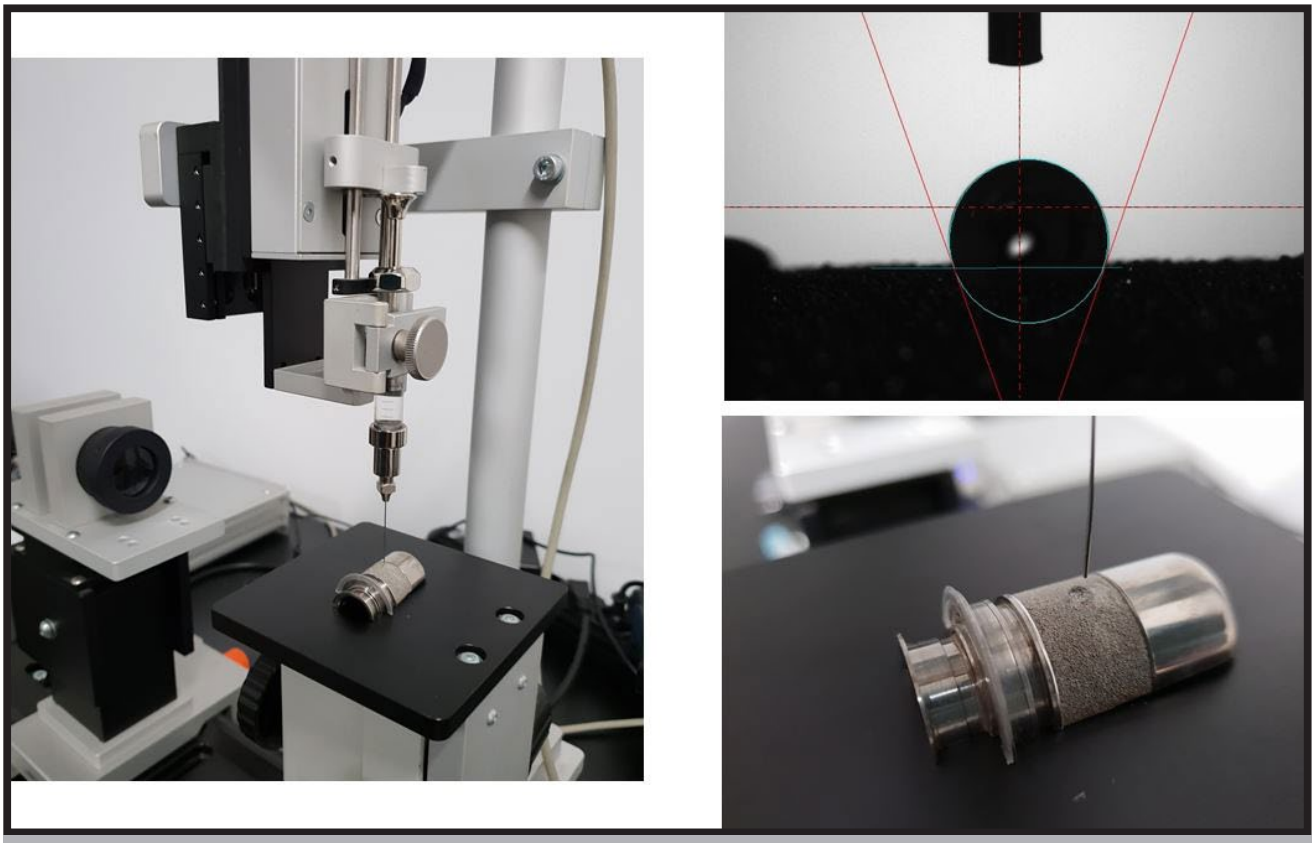

FIG. 7. Wettability measurements performed for HM3 and HW with exemplary result.

The physicochemical analysis of the porous surfaces on the inflow cannulas of the two VADs was performed. The SEM analysis revealed the microspherical morphology of the surface in both cases. The mean diameter of spheres observed in HM3 is 130 μm, however in HW it is 115 μm. Both surfaces are characterized by high porosity and loose packing of spheres on the cannula surface. Pore sizes are inhomogeneous and vary in the range of 1-200 μm for HM3, and 1-250 μm for HW, respectively. The HM3 coating consists of 3 spherical layers, while in HW there are just 2 layers. Consequently, the thickness is ~300 μm for HM3 and ~200 for HW. In both cases, the surface was characterized as the titanium alloy Ti6Al4V. The external surface of the inflow cannula for both VADs was characterized by similar roughness of Ra (12-15 μm) and Rz (66-73 μm) parameters. The contact angle measurement for both devices allowed determining the wettability characteristics of modified surfaces which proved to be highly hydrophilic. Further research is needed to collect data on the cellular profile of tissues in the contact area with the biomaterial.

Conclusions

So far, the clinical research has shown that VAD pumps still need to be improved in order to minimize the risk of complications during heart assistance. In comparison to older systems, there is a huge improvement through the application of modern biocompatible materials and surface engineering, accompanied by the VAD minimalization, the complex limitation of its complexity and removal of mechanical bearings systems. Despite many new solutions, patients still experience many side effects, including high morbidity and even death. One of the complications directly connected to the inflow cannula design is the inflow obstruction, caused by the ingrowth of tissue into the flow passage and pump thrombosis. The solution may be improving the design of the inflow cannula, its attachment, as well as the length, location, and orientation of its introduction or development of the bioactive surface. There is still no perfect solution and each device has its own cannula design with different external surfaces promoting cell adhesion. The clinical experience confirms that thanks to the developed surfaces, it is possible to control the tissue ingrowth on the external surfaces of the inflow cannula at the tissue-implant interface. However, it is still necessary to perform more trials to provide a better understanding of the phenomena occurring at the implant-tissue interface.

Acknowledgments

Project supported by NCBiR within the project RH-ROT/266798/STRATEGMED-II.

Project co-financed by National Science Centre, Poland within the project PRELUDIUM 16 2018/31/N/ST8/01085.

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