HEART DISEASES AND STENT TECHNOLOGY IN BRAZIL: PANORAMAS, OUTLOOKS, CHALLENGES. HOW MUCH INTERDISCIPLINARY IS ALL THAT?

Author: Oliveira, G.P.[1] *gustavo.oliveira@uerj.br*

[1] State University of Rio de Janeiro

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Introduction

This paper presents a simple panorama on heart diseases in Brazil over the last years through facts and figures, especially coronary artery disease, summarizes the evolutionary trajectory of the drug-eluting stent (DES) technology and its lawful incorporation into Unique Health System - SUS, the public healthcare system in Brazil. Intended to promote a knowledge exchange between medical and applied sciences, the author singles out a couple of data obtained from health surveys regarding facts and figures that support the relevance of the scientific research for DES optimized design. We will see how a plethora of high-complexity challenges is demanding a wholesome handshake among cardiologists, mathematicians and engineers worldwide. Amid viewpoints and ongoing research issues, we hope to answer the question: after all, how much interdisciplinary is all that?

Cardiovascular diseases in Brazil

Coronary artery disease (CAD) and the acute myocardial infarction are among the main causes of obits in South America and especially in Brazil [3]. Cardiovascular diseases (CVD) as a whole were responsible by 28% of them from 1996 to 2011, being the second most relevant cause (see Fig. 1). From 2000 to 2005, the National Centre of Cardiovascular Interventions (CENIC), an entity of the Brazilian Society of Hemodynamics and Interventional Cardiology (SBHCI) has registered 154,406 angioplasty procedures. DES were used in 10,426 percutaneous coronary interventions, i.e. 7% of total prothesis implemented in the period. From 2008 to 2012, the number of stent-based angioplasties was 543,937, i.e. an increase of 352% in relation to the previous period. The annual cost for cardiovascular treatment in 2004 was R$ 30,8 billion, of which 36,4% were related to direct medical costs. The estimated direct costs associated with acute coronary syndrome (ACS) for 2011, for example, reached R$ 522,286,726 for the SUS (0.77% of the total government healthcare budget), and the amount of R$ 515,138,617 for the Suplementar Health System. Indirect costs reach R$ 2.8 billion from the societal standpoint, with the total direct and indirect costs of ACS in Brazil for 2011 estimated at R$ 3.8 billion [5].[1]

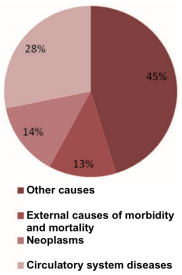

Figure 1: Main causes of deaths in Brazil (1996-2011). Adapted from [4].

According to a recent study published by the International Diabetes Federation, Brazil has the highest number of people with diabetes mellitus in South and Central America (ave. 14.3 million). The Diabetes Atlas shows that in the region as a whole, nearly 30,900 children aged < 15 amidst other 45,100 in the region affected by type 1 diabetes live in Brazil. Such index places the country as the third highest in the rank of children with type 1 diabetes in the world, coming after USA and India. In 2015, 247,500 adults died as a result of diabetes in the region. Over 42.7% of these deaths occurred in people aged < 60 and half of the obits occurred only in Brazil (130,700). This figure explains why the country spent at least US$ 21.8 billion to combat diabetes.

Stents, interventional cardiology and applied sciences

Since 1977, when the first angioplasty procedure was performed, several generations of stents have been being devised in growing levels of complexity. Until 2002,

[1] To the best of the author's knowledge, DATASUS is the main data source about the health status in the country, which was lastly fed after the National Health Survey 2013. Other figures were obtained in literature. References were omitted due to text limitation, but are available under request.

bare-metal stents (BMS) were the main devices used in interventional procedures. On the other hand, they were also known to generate inflammations and injuries over the artery walls. From 2003 and on, drug-eluting stents came up with a solution aiming to reduce the restenosis rate while releasing a drug that inhibits the proliferation of endothelial cells. Nowadays, we are getting to a new generation of DES, which appeals to a biodegradable concept based on polymer-free coatings, being classified as macroporous, microporous, nanoporous or of smooth surface. Figure 2 shows the Scitech Inspiron, a sirolimus eluting stent with abluminal coating and biodegradable polymer in a CoCr platform, the first DES made in Brazil under international standards.

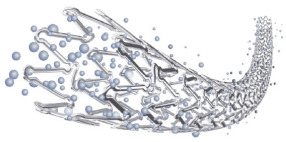

Figure 2: Scitech Inspiron: the first DES made in Brazil under international standards. (Source: http://goo.gl/iavAiO)

Although DESs had already been used in Brazilian patients earlier, its incorporation into SUS budget took place only on 2014. By means of its Report 111, the National Commission for Technology Incorporation (CONITEC), governmental entity liable for advising the Brazilian Health Ministry as to incorporation, exclusion or modification of health technologies and clinical protocols into SUS, decided to recommend the incorporation of DESs for a limited class of people and clinical scenarios. Such incorporation was legally concluded on August 27th through Portaria MS 29/2014.

DES design optimization is by far complex and requires much attention not only from the medical community, but also from mathematicians and engineers in several frontlines (e.g. chemical, materials, mechanical) [2]. Today, the use of *in vitro*, *in vivo*, *ex vivo*, *in silico* and mathematical models has enhanced understanding of DES mechanisms [1]. The challenges, in turn, encompass an interdisciplinary scope that includes, but is not limited to hemodynamics, porous media, fatigue and structural mechanics and CFD. All of them require not only experimental essays, but also theoretical models tailored to a determined situation and validated numerical modelling. In the next section*, we navigate over a sea of opportunities regarding DES research.

Interdisciplinary research issues

Here we briefly list a series of issues that have been being investigated by researchers involved with DES. This broad and rich interdisciplinary scope also highlights the remarkable partaking of mechanical engineering for future community's achievements.

- hemodynamics: arterial wall shear stresses and flow metrics; non-Newtonian blood flow models, luminal protrusion and stent apposition;
- chemistry/materials: polymer-free coating; biocompatible materials and drugs; controlled drug release;
- mechanics: porous media properties (tortuosity); fracture, fatigue and structural integrity of stent struts; fluid-structure interaction stent/vessel; drug transport; pulsatile and disturbed flows CFD;
- mathematics: analytical models of drug release;
- manufacturing: laser technology; nanofabrication; design optimization; image processing and CAD modelling;

Conclusions

We have provided an overview on heart diseases and drug-eluting stent technology in Brazil. We assure that, given the wideness of open challenges, the interdisciplinary nature of this research is paramount and require the contribution of different expertises. The future of drug-eluting stents is promising and we hope that the interested reader be stimulated to find an effluent that may debouches into this vast sea of opportunities.

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