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Particles deposition induced by the magnetic field in the coronary bypass graft model

Sandor I. Bernad [a,*], Alin F. Totorean [b], Ladislau Vekas [a,*]

[a] Centre of Advanced Research in Engineering Sciences, Romanian Academy, Timisoara Branch, 300223 Timisoara, Romania
[b] Department of Mechanical Machines, Equipment and Transportation, Politehnica University of Timisoara, RO-300222 Timisoara, Romania

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ABSTRACT

Bypass graft failures is a complex process starting with intimal hyperplasia development which involve many hemodynamic and biological factors. This work presents experimental results regarding the possibility to use magnetic drug delivery to prevent the development of the intimal hyperplasia using a simplified but intuitive model. The primary goal is to understand the magnetic particle deposition in the anastomosis region of the bypass graft taking into account the complex flow field created in this area which involves recirculation region, flow mixing and presence of particles with high residence time. The three-dimensional geometry model was used to simulate the motion and accumulation of the particles under the magnetic field influence in anastomotic region of the coronary bypass graft. The flow patterns are evaluated both numerically and experimentally and show a good correlation in term of flow parameters like vortex length and flow stagnation point positions. Particle depositions are strongly dependent on the magnet position and consequently of the magnetic field intensity and field gradient. Increased magnetic field controlled by the magnet position induces increased particle depositions in the bypass graft anastomosis. The result shows that particle depositions depend on the bypass graft angle, and the deposition shape and particle accumulation respectively, depend by the flow pattern in the anastomosis region.

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1. Introduction

After surgical intervention, a coronary by-pass graft supports two kinds of stresses: the blood flow induced stresses [1] and non-flow induced stresses (suture line wall stress) [2]. In the anastomotic region hemodynamic type of stresses regulate the function and dynamic remodeling, and also contribute to the development of pathological conditions [3,4]. Blood flow in these regions is complex and is characterized by flow separation, stagnation, recirculation, turbulent flow, low shear stress in different areas [5,6].

Artery bypass graft present conduit for severe artery stenosis diseases. Clinical statistics indicated that 10 years mortality rate of coronary artery bypass grafts (CABG) is 15÷30% due to intimal hyperplasia (IH) resulting in post-operation restenosis and obstruction at distal anastomosis [7].

IH develops commonly in the distal anastomosis [8]. In a region where flow velocity and shear stress are reduced, and flow departs from unidirectional patterns respectively constitute a favorable site to potentiates atherogenesis. In this region, fluid force induces a vascular response of the endothelium to produce factors to promote inflammatory events. This section creates a favorable zone for prolonged contact with the vessel wall with components that influence atherogenesis (platelets, granulocytes and metabolites).

To identify the relationships between particular blood flow patterns and pathological events, knowledge of detailed hemodynamics data in realistic vessel geometries becomes relevant.

The objective of the present paper is to report on the results obtained from an in vitro experimental study of a bypass graft model, and then to use these results to highlight the possibility and advantage of the particle targeting to reduce the incidence of the bypass graft failure.

To achieve the above mentioned objectives, in this paper we proposes a simplified geometrical model, and an quasi-equivalent working environment and conditions to put in evidence the particularity and challenges of the particle targeting in the bypass anastomosis.

1.1. Coronary bypass graft

Atherosclerosis is the leading cause of the coronary arterial disease. It is a disease process that affects medium to large-sized

* Corresponding authors.
E-mail addresses: sandor.bernad@upt.ro (S.I. Bernad), vekas.ladislau@gmail.com (L. Vekas).

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arteries and results in the deposition of fibrous plaques in the intima that cause a thickening that encroaches on the vessel lumen.

Coronary artery bypass graft surgery is the standard care in the treatment of advanced coronary artery disease.

The bypass procedure creates a two type of anastomosis namely side-to-end anastomosis proximal and an end-to-side distal of the diseased segment to reestablish blood flow in the artery [9].

A vascular anastomosis represents a surgical connection between two vessels in which blood can flow. Depending on the surgical objective, the anastomosis can be a created in an end-to-end or end-to-side configuration [9]. During to the surgical intervention, graft diameter can vary between 3 mm and 8 mm; it is to be similar to or slightly larger than the host vessel.

1.2. Bypass graft disease

Bypass graft remodeling is a complex process involving many biological and hemodynamic factors. Following CABG surgery, bypass graft failures are classified either as early (usually within 1 month after CABG surgery, common cause of graft failure is thrombosis) or late (cause of failure is graft starts to undergo neointimal hyperplasia that induce graft stenosis and in final stage occlusion).

In literature, intimal hyperplasia are defined as the accumulation of the extracellular matrix in the vessel intimal compartment, and it represent the significant disease process in venous bypass grafts between one month and one year after implantation.

Many investigations and data from the literature suggest that bypass remodeling was initiated by changes in hemodynamic conditions like flow patterns and wall shear stress, and biochemical factors (cytokines, vasoactive substances).

In vivo observations indicate [10–12] that the anastomotic configuration IH occurs preferentially around the suture line, the toe, the middle, and the heel regions (as shown in Fig. 1).

1.3. Bypass graft disease treatment

Different methods have been explored for perivascular delivery of anti-proliferative drugs to reconstructed arteries or veins using a variety of polymers as a vehicle, including drug-releasing polymer gel [13]/depots [14], microspheres [15,16], cuffs [17], wraps/films [18,19], or meshes [20]. While each method has its advantages, none has advanced to clinical trials, likely due to various limitations revealed in animal studies, such as moderate efficacy, lack of biodegradation, or mechanical stress to the blood vessel. Thus, there remains an unsolved clinical need for a vascular delivery system that is durable yet biodegradable, non-disruptive to the vessel, can release drug in a controlled and sustained manner, and ultimately, is highly effective in preventing intimal hyperplasia [14–19].

Local hemodynamics at the anastomoses is essential for the success of bypass graft surgery.

The aim of this study was to determine the three-dimensional flow behaviors that occur at the anastomosis under steady flow conditions, to investigate the changes that resulted from variations in the anastomosis angle and flow division.

The objectives of the study were:

- To examine the flow features in the straight graft model over a range of Reynolds numbers for steady flow conditions.
- To locate the flow features in the model under steady flow conditions for comparison with the known locations of intimal hyperplasia in vivo.
- To estimate the likely physical effects of the flow on the walls of the graft model and from them the impact of blood flow on the walls of the blood vessels.

To solve the above mentioned features, this paper proposes a simplified but efficient experimental and numerical model which put in evidence the crucial aspects of the flow field from the point of view of the particles accumulation in the targeted region.

2. Experimetal setup

A steady-state flow in an in vitro model of arterial bypass graft was used to examine the effects of the different geometry configuration on the flow patterns and the particle depositions in the distal bypass anastomosis model.

A schematic of this system is shown in Fig. 2. The flow system consisted of a constant storage head tank; test section; flow-meter; collecting tank; and variable speed centrifugal pump. The mean flow rate was measured by a metric size ten rotameter with a stainless steel float. A blood analog fluid was prepared to have dynamic viscosity (μ) of 0.00408 Pa s and density (ρ) of 1060 kg/m^3 (a glycerin–water mixture of 60% glycerin and 40% water).

The geometric shape of the aorto-coronary bypass is shown in Fig. 3, and the geometric dimensions of the aorto-coronary bypass models are given in Table 1.

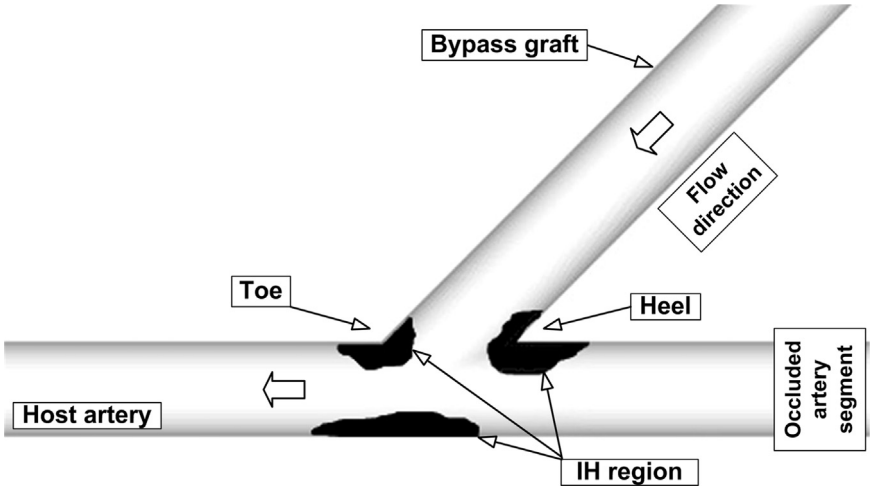

Fig. 1. The region where intimal hyperplasia (IH) occur in the coronary bypass anastomosis.

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