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Basic and applied researches in microgravity/Recherches fondamentales et appliquées en microgravité

Blood flow and microgravity

Écoulement sanguin et microgravité

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A B S T R A C T

The absence of gravity during space flight can alter cardio-vascular functions partially due to reduced physical activity. This affects the overall hemodynamics, and in particular the level of shear stresses to which blood vessels are submitted. Long-term exposure to space environment is thus susceptible to induce vascular remodeling through a mechanotransduction cascade that couples vessel shape and function with the mechanical cues exerted by the circulating cells on the vessel walls. Central to such processes, the glycocalyx – *i.e.* the micron-thick layer of biomacromolecules that lines the lumen of blood vessels and is directly exposed to blood flow – is a major actor in the regulation of biochemical and mechanical interactions. We discuss in this article several experiments performed under microgravity, such as the determination of lift force and collective motion in blood flow, and some preliminary results obtained in artificial microfluidic circuits functionalized with endothelium that offer interesting perspectives for the study of the interactions between blood and endothelium in healthy condition as well as by mimicking the degradation of glycocalyx caused by long space missions. A direct comparison between experiments and simulations is discussed.

R É S U M É

L'absence de gravité lors de longues missions spatiales peut altérer le fonctionnement cardiovasculaire à cause, en partie, de l'absence d'activité physique. Ceci a des répercussions sur l'hémodynamique, et en particulier sur le niveau de contraintes de cisaillement auxquelles sont soumis les vaisseaux sanguins. Un séjour de longue durée dans l'espace peut conduire à un processus de remodelage vasculaire via une cascade complexe de mécanotransduction qui couple la morphologie des vaisseaux et leur fonction aux signaux mécaniques dus au passage des corpuscules sanguins le long des parois vasculaires. Dans

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ces processus, le glycocalyx – brosse de biopolymères épaisse d'environ un micromètre, tapissant la paroi endothéliale et directement exposée au flux sanguin – joue un rôle central dans la régulation des interactions mécano-biochimiques. Dans cet article, nous présentons des résultats expérimentaux obtenus en microgravité concernant la force de portance s'exerçant sur les globules rouges et sur les vésicules ainsi que les mouvements collectifs, puis quelques résultats préliminaires portant sur la fonctionnalisation de circuits artificiels par des brosses de polymères et par des cellules endothéliales. Ceci offre des perspectives intéressantes pour étudier l'interaction entre écoulement sanguin et endothélium, sain ou altéré à la suite d'une dégradation du glycocalyx mimant les effets de longues missions spatiales. Une comparaison directe entre expériences et simulations sera présentée.

1. Introduction

Blood represents a very challenging fluid medium in terms of theoretical description because of the scale-dependent changes of its properties and its complex mechanical and biochemical structure. Pathologies associated with blood flow and cardiovascular functions are the primary cause of mortality in Europe and the USA. Intense multi-disciplinary research is therefore essential to develop innovative approaches to identify the key elements that promote cardiovascular disorders.

A major factor that affects cardiovascular dysfunctions is the absence of gravity during stays in space. It is well known that a long-term mission in space is associated with cardiovascular dysfunctions. For example, heart rhythm disturbances have been seen among astronauts. It is documented that long space missions lead to reduction of plasma volume, as well as left ventricular mass decrease. To give a simple estimate that the absence of gravity should have a clear consequence on blood flow, let us evaluate the pressure due to gravity at the level of the heart and compare it to that of the internal body blood pressure. The first is given typically by $\rho g h$. Taking density ρ to be that of water and g earth gravity and considering that the heart height in the upright position is of about $h = 1$ m, we obtain 10^4 Pa $= 0.1$ bar. An average blood pressure is, in terms of medical common usage, 14/8, which means an extra pressure (in comparison to atmospheric pressure) of 140 mm of mercury in the systolic regime and 80 mm in the diastolic regime. Given the fact that the atmospheric pressure corresponds to 760 mm of mercury, a blood pressure of 14/8 thus corresponds to the range of 0.1–0.18 bar. Interestingly the pressure related to earth gravity is very close to the body internal extra pressure. One expects thus that a long term mission in microgravity should impact physiological functions, that can potentially lead to cardiovascular anomalies.

Besides myriads of macroscopic studies (heart rhythm, plasma volume, blood vessel remodeling), other measures performed on astronauts after long missions in space reported several microscopic disturbances. For example it has been reported that space missions are accompanied with anemia, hemolysis and with an increase of amylase activity [1] as well as with variations in Red Blood Cell (RBC) membrane phospholipid composition [2]. Amylase is an enzyme that is known to digest sugar molecules, which are abundant on the glycocalyx as well as on the RBC surface. It is thus an essential goal for studies on blood flow to analyze the far reaching consequences of the impact of microgravity on blood flow, which is our long-term objective.

For many years we have been involved in trying to extract the basic elementary blocks that govern the blood flow properties, ranging from the study of single cell dynamics up to collective motions. Other studies consist in functionalizing artificial circuits with polymer brushes and more recently with endothelial cells in order to mimic real blood vessels. In particular an objective is to alter the endothelium, thanks to enzymatic digestion (mimicking the amylase activity in space), and to study the related consequences. In what follows, we shall briefly describe the main achievements of our studies and the various microgravity experiments that have allowed us to extract this information. In particular we shall discuss the lift force on vesicles and on RBCs, experiments performed in parabolic flights where lipid vesicles are simplified models for RBCs. It will be seen that microgravity has offered a unique opportunity to analyze this question and that an analytical theory as well as full numerical simulations provide a very good agreement with experimental observations. We shall discuss the dynamics of suspensions obtained from experiments in sounding rockets, and explain the inhomogeneous distribution of the suspension in the channel by referring to the knowledge gained from the study of lift force. Also it will be shown that a bidisperse (two vesicle sizes) suspension exhibits a segregation triggered by lift force and shear-induced diffusion: small vesicles are pushed towards the periphery, while large ones have the tendency to migrate towards the center. This is reminiscent of the margination effect known in blood flow, where platelets (small size cells as compared to RBC) are marginalized toward the walls of the blood vessels. Regarding endothelium, we have first clarified the role of a polymer brush (mimicking the glycocalyx) on solvent flow and RBC dynamics, and have found quite significant and striking effects. Those effects were also revealed in our recent simulations. We shall briefly discuss the achievement of artificial microfluidic circuits coated with endothelial cells, with which we have performed the first successful preliminary experiments on blood flow in these functionalized circuits.