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# Does the gravity orientation of saccular aneurysms influence hemodynamics? An experimental study with and without flow diverter stent

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ABSTRACT

Most intracranial aneurysms morphologic studies focused on characterization of size, location, aspect ratio, relationship to the surrounding vasculature and hemodynamics. However, the spatial orientation with respect to the gravity direction has not been taken into account although it could trigger various hemodynamic conditions.

The present work addresses this possibility. It was divided in two parts: 1) the orientations of 18, 3D time-of-flight MRI (3D TOF MRI), scans of saccular aneurysms were analyzed. This investigation suggested that there was no privileged orientation for cerebral aneurysms. The aneurysms were oriented in the brain as follows: 9 – down, 9 – up; 11 – right, 7 – left; 6 – front, 12 – back. 2) Based on these results, subsidiary *in vitro* experiments were performed, analyzing the behavior of red blood cells (RBCs) within a silicone model of aneurysm before and after flow diverter stent (FDS) deployment in the parent vessel. These experiments used a test bench that reproduces physiological pulsatile flow conditions for two orientations: an aneurysm sack pointing either up (opposite to gravitational force) and down (along the gravitational force). The results showed that the orientation of an aneurysm significantly affects the intra-aneurysmal RBCs behavior after stenting, and therefore that gravity can affect the intra-aneurysm behavior of RBCs. This suggests that the patient's aneurysm orientation could impact the outcome of the FDS treatment. The implementation of this effect in patient-specific numerical and preoperative decision support techniques could contribute to better understand the intrasaccular biological and hemodynamic events induced by FDS.



## 1. Introduction

Saccular intracranial aneurysms are focal “sac-like” dilations of the wall of an artery. Aneurysms can be located on the side, top or bottom of the arteries or arterial bifurcations with regards to the gravitational orientation (Fig. 1A and B). However, whether these different spatial orientations induce differential gravity effects on blood components and influence hemodynamic conditions remains an open question.

Nevertheless, it has already been reported that during angiography the density difference between the contrast agent and blood (1404–1060 kg/m$^3$) can lead to an unwanted gravity effect known as contrast settling (Wang et al., 2005) (Fig. 1C). This effect may even be amplified in the case of stented aneurysms due to velocity drop inside the aneurysm sac as a result of the change in the balance between the drag force, the buoyancy force and the gravity force that act on the contrast agent (Wang et al., 2004). By decreasing the drag force in the aneurysm sac, *e.g.* placing a flow diverter stent (FDS), other forces may become dominant. A different

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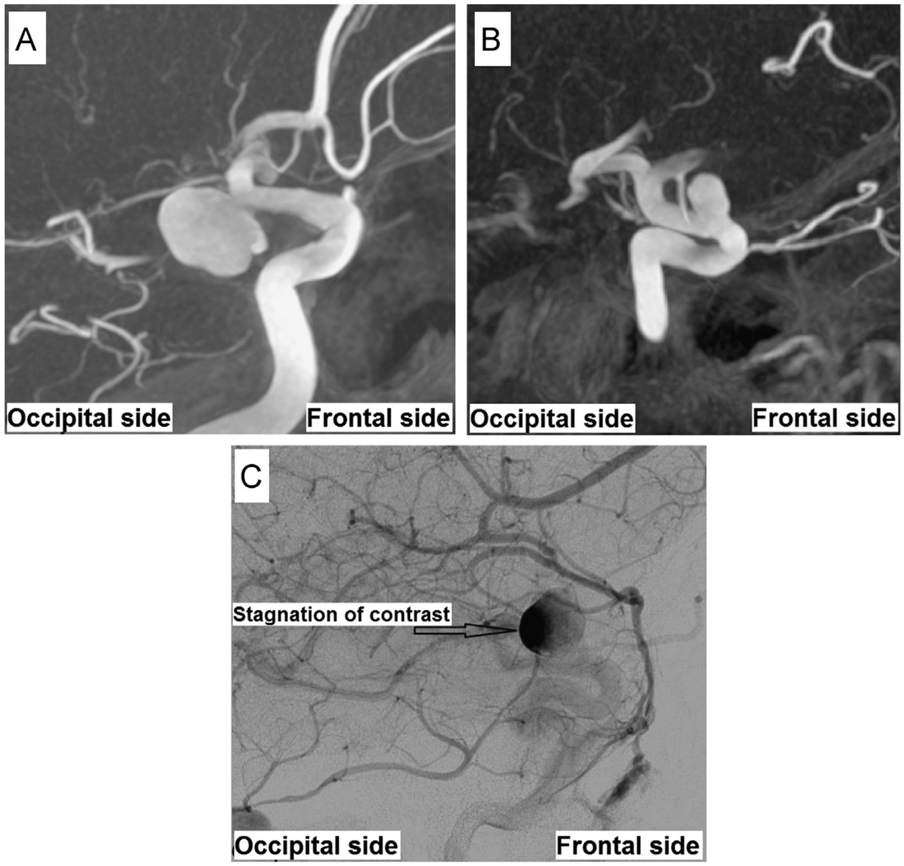


**Fig. 1.** Cerebral aneurysm orientation. Images A and B compare two typically different orientations of the cerebral aneurysms. Image C shows an example of contrast product stagnation was captured during intervention.

gravity effect is also well-known between blood components such as red blood cells (RBCs) and plasma due to their density difference (1125–1025 kg/m$^3$), and it is indeed used in the sedimentation rate blood exam. However, the sedimentation rate test is performed under steady-state conditions, distinct from real pulsatile physiological flow conditions. Although contrast settling has been already reported, the effect of orientation, with respect to gravitational force, of non-stented and stented saccular aneurysms on blood hemodynamics has seldom been investigated (Bouillot et al., 2014; Endres et al., 2014; Wang et al., 2005).

Gravity could interfere with the behavior of Red Blood Cells (RBCs) inside the plasma medium that, with an average blood volume fraction of 44%, is responsible for the complex rheological behavior of blood. Complex non-Newtonian flow behavior and dispersion of blood elements occur as a result of RBC properties, attraction and aggregation, their shape, their tendency to orient themselves in the direction of flow, the Brownian motion and the gravitational effect. Furthermore, the presence of RBCs affects the adhesion and aggregation of the platelets and, therefore, eventual thrombus formation by pushing platelets towards the wall (Mountrakis et al., 2013). In addition, similarly to contrast settling, the gravitational force could lead to RBCs stagnation resulting in increased local hematocrit level itself impacting local blood viscosity and shear conditions. These shear conditions are one of the factors triggering the pathways of thrombus formation (Ribeiro de Sousa et al., 2015).

The investigation of the gravity effects on RBCs rheology by the numerical method (CFD) is not well documented. However, Kim et al. (2006) showed that introduction of a gravity term in the incompressible Navier–Stokes equations for flow simulations in carotid bifurcation and brain arteries considerably affects computed and simulated arterial contraction/dilatation and hence changes the resulting flow conditions. Another work reported by Grandchamp et al. (2013) showed that the anisotropic diffusion of RBCs is altered when subjected to microgravity.

In the present study, we used a 3D time-of-flight MRI (3D TOF MRI) to determine the spatial orientation of 18 saccular aneurysms (17 patients) and we highlight the RBCs behavior within the aneurysm before and after placement of a FDS using an *in vitro* test bench (Chodzynski et al., 2014) able to reproduce pulsatile flow conditions in silicone aneurysm models.

## 2. Materials and methods

### 2.1. Subjects

This work has been approved by the Ethical committee of Lyon University Hospital as a part of Thrombus European project no. 269966 and subjects gave their informed consent. Data of 18 saccular aneurysms from 17 patients (4 males, 13 females) are included in this study.

### 2.2. MRI acquisition

All aneurysm assessments were performed by 3D TOF MRI acquisitions using a clinical system operating at 3 T with 32-Channel Array Head-Neck coil (3 T, 45 mT/m, 200 T/m/s, Skyra, SIEMENS, Erlangen, Germany). The 3D TOF MRI acquisition parameters were as follows :149 slices, TR/TE 21/3.4 ms, 18° flip angle, 0.6 mm section thickness, in-plane resolution 0.27 × 0.26 mm$^2$, acquisition time 5 min 29 s.

### 2.3. MRI analysis

All MRI analysis were made using the OsiriX DICOM viewer 6.5.1 (Pixmeo, Geneva, Switzerland° and after post processed using Matlab R2015a software. More details can be found in the Supplementary data – MRI analysis.