A new imaging tool for real-time measurement of flow velocity in intracranial aneurysms

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Abstract

With modern imaging modalities of the brain a significant number of unruptured aneurysms are detected. However, not every aneurysm is prone to rupture. Because treatment morbidity is about 10% it is crucial to identify unstable aneurysms for which treatment should be discussed. Recently, new imaging tools allow analysis of flow dynamics and wall stability have become available. It seems that they might provide additional data for better risk profiling. In this study we present a new imaging tool for analysis of flow dynamics, which calculates fluid velocity in an aneurysm (Phillips Electronics, N.V.). It may identify regions with high flow and calculate flow reduction after stenting of aneurysms. Contrast is injected with a stable injection speed of 2 mL/sec for 3 sec. Two clinical cases are illustrated. Velocity in aneurysms and areas of instability can be identified and calculated during angiography in real-time. After stenting and flow diverter deployment flow reduction in the internal carotid aneurysm was reduced by 60% and there was a reduction of about 65% in the posterior cerebral artery in the second case we are reporting. The dynamic flow software calculates the flow profile in the aneurysm immediately after contrast injection. It is a real-time, patient specific tool taking into account systole, diastole and flexibility of the vasculature. These factors are an improvement as compared to current models of computational flow dynamics. We think it is a highly efficient, user friendly tool. Further clinical studies are on their way.

Introduction

Flow dynamics in aneurysms are of great interest as they may model how blood flow and wall shear stress determine aneurysm stability and its risk of rupture. On the other side when endovascular stenting has been used for aneurysm treatment the aneurysm is not excluded from the vascular system immediately but the blood flow in it is significantly reduced and leads to coagulation in the aneurysm lumen.[1] The success of flow diversion is not assured since recanalization, occlusion failure and delayed subarachnoid haemorrhage are reported.[2,3] Another application of flow dynamic analysis is during aneurysm stenting. As a matter of fact, for successful aneurysm treatment by a flow diverter, the velocity in the aneurysm has to be reduced to about one third of the pre-stent velocity.[4] At present, velocity is modelled by complex computational fluid dynamics analyses. The short-comings are: they are time-consuming, not readily available and based on a number of physical assumptions like pulsatile laminar flow, newtonian fluid dynamics and rigid vessel walls with nonslip conditions.[4,5] Analogous methods are used to determine the presence of high-pressure areas in unruptured aneurysm in order to estimate the risk of rupture.[5] In the present study, we used a real-time imaging tool, which calculates semi-quantitatively intra-aneurysmal flow during angiography. It allowed determination of areas of high- and low-flow and calculation of flow reduction after deployment of a flow-diverting stent.

Materials and Methods

This study is introducing a real-time method of calculating intra-aneurysmal flow during digital subtraction angiography. The vector analysis is calculated by a so-called *flow tool* software developed by Phillips Electronics N.V. Contrast medium is given 7 cm proximal to the aneurysm with a flow rate of 2 mL/sec for 3 sec (Figure 1). Based on high-speed image acquisition the flow tool allows reconstruction of flow vectors, which are calculated by the theoretical movement of contrast particles in the vessel and the aneurysm by density changes due to the injection of this small amount of contrast.

The description of the *flow tool invention* (Phillips Electronics, N.V.) is given under patent: US6442235 B2. The invention is based on the recognition of a two-dimensional or a three-dimensional image data set containing information concerning the course of the blood vessels in the object to be examined, and can be encoded in time in a manner that it also contains information concerning the blood flow as a function of time. The image data set is compared with a series of X-ray projection images, which are formed successively in time and contain the information concerning the distribution of an injected contrast medium in the blood vessels at each time at different instant. Because each image value of the image data set is compared with the image values of the individual X-ray projection images, it is checked which parts of the vascular system contained in the image data set are filled with the contrast medium at the individual instants associated with the respective X-ray projection images. The image data set encoded in time can be converted into one or more images, which show the blood flow as a function of time.

The method includes the following steps: i) acquisition of a series of X-ray projection images during administration of a contrast medium to the blood vessels of interest; ii) acquisition of an image data set containing the course of the blood vessels; iii) segmentation of the regions of the blood vessels in the individual X-ray projection images filled with contrast medium; iv) encoding the image data in time by comparing it with the segmented X-ray projection images; v) displaying one or more images formed from the time-encoded image data set based on the one or more pixel sub-sets and representing the blood flow as a function of time.

The rate of flow reduction after stenting is calculated in percentages. The pulsatility in the aneurysm before and after stenting is also calculated (in mL/sec).

We demonstrate the clinical applicability of this flow- tool in two patients with fusiforme aneurysms of the internal carotid artery that were treated by flow diverter stents (3 stents, Derivo, Acandis Inc. and

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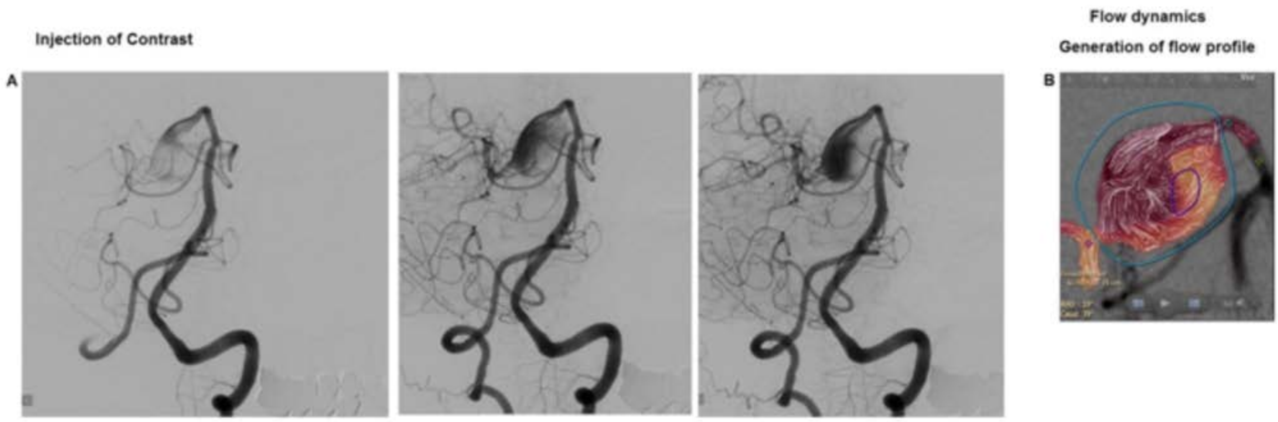

Figure 1. Methodology of the *flow tool*: A) Contrast is injected in a speed of 2 mL/sec for 3 sec in order to create a stream of contrast so that the flow dynamics can be calculated by the software. B) Flow dynamics analysis calculated by the *flow tool* software, which shows the vector of the flow velocity. The red-colored area indicates regions of high flow.

Koaxial Silk, Balt Inc., USA). The flow dynamics before and after treatment are shown immediatelly after stenting in the patient with the internal carotid aneurysm and 7 months after treatment in the patient with the posterior cerebral artery aneurysm.

Results

Injection of contrast medium with a speed of 2 mL/sec during 3 sec allowed calculation of flow vectors in the aneurysm (Figure 1). The red color-coded areas showed regions of high velocity, in which a high wall shear stress was expected. The length of the vectors indicated the speed of flow.

Figure 2 illustrates the case of an unruptured fusiform aneurysm of the posterior cerebral artery in a 67 y.o. female patient. The aneurysm was treated with a stent (Koaxial Silk, Balt Inc., USA) and coiling. The 7 months follow-up angiography showed a good result. Flow vector analysis showed a significant reduction of intra-aneurysmal flow as indicated by significant reduction of the red areas. Also flow speed was diminished as translated by shorter vector lengths. There is a complete remodelling of flow in the aneurysm after stent-coiling treatment.

The second case was a 53 y.o. female patient with two internal carotid artery aneurysms in their cavernous segment, respectively. The right aneurysm became symptomatic with a abducent nerve palsy. Three flow diverter stents were implanted end to end (Figure 3). Immediately after application of the flow diverter intraaneurysmal flow was reduced by 59% as

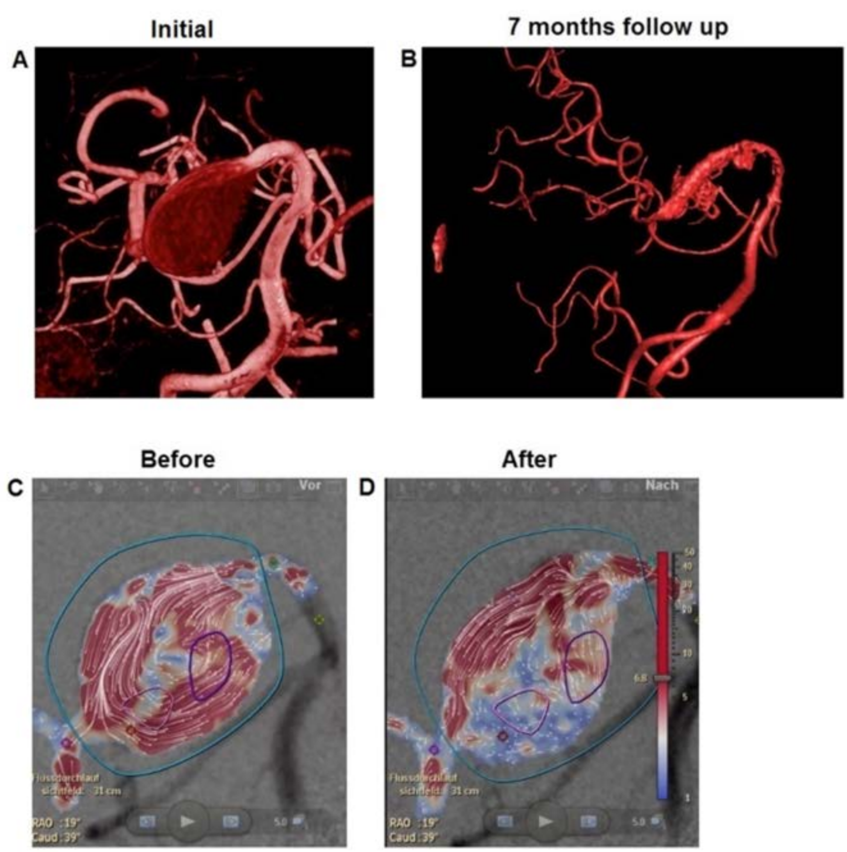

Figure 2. Coil-embolization and stenting of a posterior cerebral aneurysm: A) Initial 3D reconstruction angiography of the posterior cerebral artery fusiform aneurysm; B) Coilembolization and stenting (Koaxial Silk, Balt Inc) of the aneurysm shown in the 3D reconstruction 7 months later. The aneurysm is almost completely occluded; C) Flow analysis of the aneurysm before embolization shows high flow areas in red color and with long vectors; D) 7 months after endovascular therapy the flow through the aneurysm is low (blue color) and the flow through the stent is maintained.

shown in the flow analysis (Figure 4A and B). Also pulsatility in the aneurysm was dramatically reduced after flow diversion (Figure 4C).

Discussion

The flow tool analysis which was developed in cooperation with Phillips (Eindhoven, NL) is promising because of its applicability, which is easy to use as well as fast without any time delays. Even if it cannot generate absolute numbers of flow velocity or wall shear stress it can estimate the relative speed and the stress, which is caused on the aneurysm walls. We also can calculate reduction of flow in the aneurysm and observe the changes it causes on the wall stress. We expect the device to become more precise and to enable us to calculate absolute numbers of velocities and pressures on the aneurysm walls.

It is of great interest for the prediction of rupture risk to be able to calculate pressures on aneurysm walls. It has been shown that a high-pressure difference in the aneurysm can indicate thin-walled regions in an aneurysm and help the surgeon to avoid such regions during surgery.[5] The authors of the study conducted by Suzuki *et al.*, 2016 compared the maximum pressure (Pmax) area in the aneurysm wall with intraoperative images and came to the conclusion that regions with Pmax were very thin walled.[5] Therefore the results of this computational study could be used to predict stability of aneurysms.

At the moment treatment decision of aneurysms are based on clinical scoring systems which include morphological parameters such as size and lobularity of aneurysms (UIATS and PHASES) as well as a number of clinical factors like, hypertonia and nicotine abuse but they negelct flow dynamics and wall stress.[1,6,7] However, it seems that during the development of an aneurysm there are stages of stability with a low rupture risk and stages of instability with a high rupture risk. Such stages could be determined by analysis of flow and calculation of high and low pressure areas on the aneurysm wall which could cause a local inflammation on the aneurysm wall and lead to a rupture.[1,7-9] This hypothesis is strengthened by histological analyses of aneurysms which showed that aberrant flows cause endothelial dysfunction inducing accumulation of cytotoxic and pro-inflammatory substances leading to reduced structural integrity of aneurysm walls.[8,10] In accordance to these results it could be shown that aneurysms have two subpopulations, one with weak vulnerable walls and

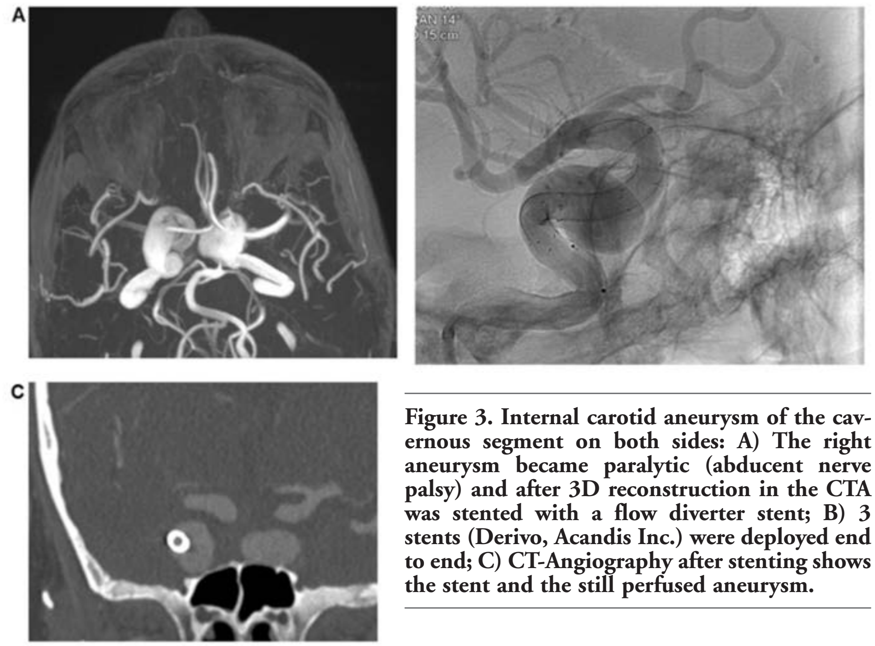

Figure 3. Internal carotid aneurysm of the cavernous segment on both sides: A) The right aneurysm became paralytic (abducent nerve palsy) and after 3D reconstruction in the CTA was stented with a flow diverter stent; B) 3 stents (Derivo, Acandis Inc.) were deployed end to end; C) CT-Angiography after stenting shows the stent and the still perfused aneurysm.

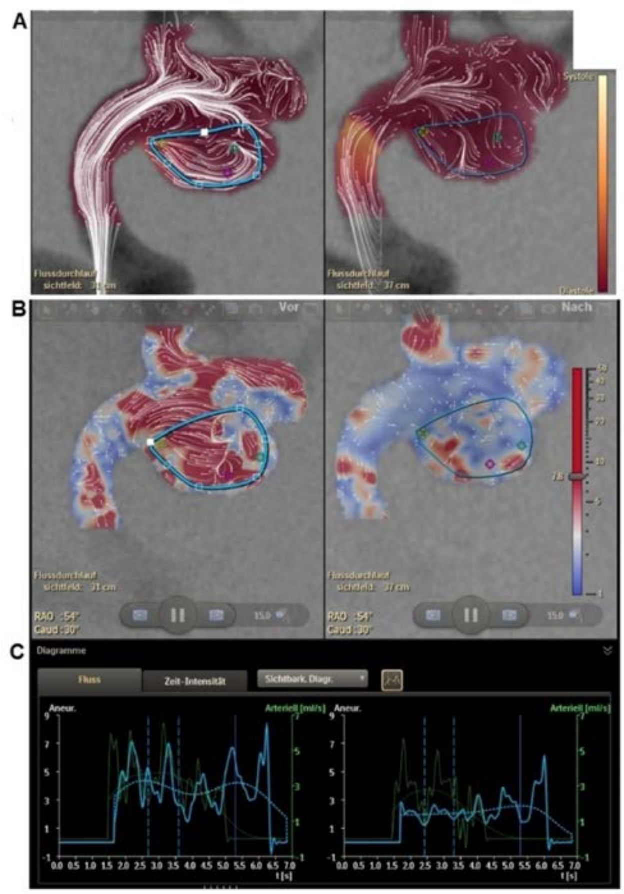

Figure 4. Flow analysis. Aneurysm of Figure 3: A) The *flow tool* analysis gives the vectors in different lengths (longer vectors, higher velocity). The marked region (blue area) is analysed in C for its pulsatility. Left: before treatment with the flow diverter stent; Right: After treatment. The velocities are significantly less (41%) than before treatment; B) Different color-coding: Left: before treatment; Right: After treatment. The high velocity areas which were red before treatment are turned to blue now; C) Pulsatility courves of flow in the aneurysm. The pulsatility in the aneurysm (blue line) is significantly higher compared to the pulsatility of the proximal arterial segment (green line) (right). The pulsatility is reduced after insertion of the flow diverter (blue line) and approximates the value of the proximal artery (green line) (left).

one with stronger walls.[11] Although high wall shear stress seems to be responsible for the creation of aneurysms, low wall shear stress could lead to their rupture.[12] The computational flow dynamics calculations as well as the *flow tool* are methods which will help understanding aneurysm biology and help future predictions of aneurysm rupture by calculating the wall stability. At the moment we do not have the possibility to calculate the wall pressures with the new flow tool.

As stated before, to establish an aneurysm occlusion by flow diversion a reduction of flow after stent application to at least 1/3 of the initial flow has to be reached.[4] For such calculations virtual stenting computational fluid dynamics simulations were built which showed a significant reduction of flow velocity and wall shear stress after stent deployment, indicating a stagnant blood flow.[13] The study showed that an average reduction of flow velocity of 10% leads to a reduction of wall shear stress of about 15%.[13] The wall shear stress is associated with the gradient of velocity,[12] which seems to be dramatically increased after deployment of the flow diverter as shown in the present report by a reduction of pulsatility in the aneurysm after stenting. As stated by Wang *et al.*, 2016[13] it is difficult to monitor changes in patients' intra-aneurysmal pressure after stent procedures, although it seems that the flow tool device allows to observe semi-quantitatively such differences through changes in flow velocity.

Conclusions

Computational flow dynamics have limitations in so far that hemodynamic parameters are set uniformly and blood vessels are assumed to have rigid walls, which can be overcome by our model. Particle image velocimetry is applied in a laboratory manner but did not find its way to clinical applications yet. On the other hand one of the main limitations of the flow tool is that we are not able to quantitatively calculate the wall shear stress at the moment but since the wall shear stress depends on the velocity an algorithm could be soon developed.

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