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Curvature Effect on Hemodynamic Conditions at the Inner Bend of the Carotid Siphon and its Relation to Aneurysm Formation

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Abstract

Although high-impact hemodynamic forces are thought to lead to cerebral aneurysmal change, little is known about the aneurysm formation on the inner aspect of vascular bends such as the internal carotid artery (ICA) siphon where wall shear stress (WSS) is expected to be low. This study evaluates the effect of vessel curvature and hemodynamics on aneurysm formation along the inner carotid siphon. Catheter 3D-rotational angiographic volumes of 35 ICA (10 aneurysms, 25 controls) were evaluated in 3D for radius of curvature and peak curvature of the siphon bend, followed by univariate statistical analysis. Computational fluid dynamic (CFD) simulations were performed on patient-derived models after aneurysm removal and on synthetic variants of increasing curvature. Peak focal siphon curvature was significantly higher in aneurysm bearing ICAs (0.36 ± 0.045 vs. 0.30 ± 0.048 mm⁻¹, $p=0.003$), with no difference in global radius of curvature ($p=0.36$). In CFD simulations, increasing parametric curvature tightness (from 5 to 3 mm radius) resulted in dramatic increase of WSS and WSS gradient magnitude (WSSG) on the inner wall of the bend. In patient-derived data, the location of aneurysms coincided with regions of low WSS (<4 Pa) flanked by high WSS and WSSG peaks. WSS peaks correlated with the aneurysm neck. In contrast, control siphon bends displayed low, almost constant, WSS and WSSG profiles with little spatial variation. High bend curvature induces dynamically fluctuating high proximal WSS and WSSG followed by regions of flow stasis and recirculation, leading to local conditions known to induce destructive vessel wall remodeling and aneurysmal initiation.

Keywords

Intracranial aneurysm; aneurysm formation; internal carotid artery; vessel curvature

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INTRODUCTION

Cerebral aneurysmal subarachnoid hemorrhage is often a devastating event, which is still associated with high mortality and morbidity. Patient prognosis is dependent on timely detection and intervention, and consequently, the ability to understand the underlying mechanism of aneurysm formation, especially in high-risk populations, would be of great clinical value.

Clinical and experimental studies strongly suggest that hemodynamic factors play a role in cerebral aneurysm formation, growth, and eventual rupture (Sforza et al., 2009). While there is some controversy over the most indicative hemodynamic markers related to cerebral aneurysm growth and subsequent rupture, there seems to be a consensus that aneurysm initiation is related to the interaction between high-flow hemodynamic forces and the arterial wall (Sforza et al., 2009). Intracranial aneurysms occur predominantly at proximal arterial bifurcations or along the outer curvatures of vessels, locations which are associated with patterns of increased wall shear stress (WSS), as well as flow acceleration and deceleration along the vascular wall quantified by high spatial WSS gradients (Metaxa et al., 2010; Wang et al., 2009). Furthermore, disrupted internal elastic lamina, loss of smooth muscle cells, and interrupted endothelium in acceleration regions of high wall shear stress have been reported in animal experiments (Meng et al., 2007). Autopsies of human and animal cerebral aneurysms suggest these histological events are characteristic of cerebral aneurysm formation, creating favorable conditions which allow the vessel wall to expand outward (Meng et al., 2007).

The purpose of this study is to evaluate the formation of sidewall aneurysms originating off the inner wall of the carotid siphon. Although elevated hemodynamic forces are thought to lead to aneurysmal initiation, little is known about the hemodynamics contributing to aneurysm formation on the inner aspect of vascular bends of the internal carotid artery, where wall shear stress is expected to be low. This study investigates the correlation between aneurysm presence along the inner carotid siphon and the peak focal curvature of the carotid siphon bend. In addition, the hemodynamic environment of the inner wall of the carotid siphon bend is examined in parametric and patient-derived models, and the resultant shear stress and its spatial gradient are explored.

PATIENTS AND METHODS

Patient Selection and Demographics

Consecutive high-resolution 3D angiographic datasets of patients with intradural intracranial aneurysms located on the ICA were collected over a period of 4 years and reviewed for this study. Fusiform, mycotic, and extradural aneurysms were excluded, the latter because of their known different natural history and low risk of subarachnoid hemorrhage (Kupersmith et al., 2002). Similar to other studies (Dhar et al., 2008), only cases in which the rotational angiographic images were of sufficient quality for accurate segmentation and reconstruction were considered. A total of 72 aneurysms met these technical criteria. From these, 10 aneurysms met the location criteria of originating off the inner bend of the carotid siphon

(Figure 1). The temporal aneurysm shape evolution and clinical symptomatology were not followed clinically over a period of time, and were not available prior to aneurysm formation. All aneurysmal patients were women; we therefore restricted non-aneurysmal control data to women. Consequently, 25 angiographic datasets representing control ICAs were available for analysis. Regarding the female gender predominance in this study, from the total of 72 initial ICA aneurysms, 80% were women (Lauric et al., 2013). This is consistent with previous reports showing that not only are women more prone to cerebral aneurysms formation in general, but among women most aneurysms are located on the ICA, whereas for men most aneurysms are located on the anterior communication artery (Ghods et al., 2012). Clinical information regarding hypertension, hypercholesterolemia, and smoking status were extracted from a prospectively maintained patient database.

Cerebral Angiography

All patients underwent catheter-based cerebral angiograms by one interventional neurosurgeon. 3D-rotational angiography (3DRA) imaging was performed on the Siemens Axiom-Artis system, using 3 ml/sec of contrast medium for 5 seconds with a 1.5-second pre-injection delay. All raw 3D acquisition data were reconstructed using the Leonardo/Syngo workstation software (Siemens AG, Munich Germany).

Morphological Feature Extraction

Vessel segmentation was performed using an in-house level-set algorithm based on the open-source Insight Segmentation and Registration Toolkit (ITK, version 3.20, Kitware Inc., Clifton Park, NY). The centerline of the vasculature was determined using the algorithm proposed by Bouix et al. (2005). The ICA branch was isolated from the centerline, and curvature statistics were automatically computed from the discrete curve representing the ICA (An et al., 2011). The curvature of a curve at a point is defined geometrically as the inverse of the radius of the osculating circle at that point. Here this value is estimated analytically by employing discrete derivatives (Figure 2). For each model, the peak focal curvature in the carotid siphon was estimated from the curvature histograms along the ICA curve.

The radius of curvature of the carotid siphon bend was estimated manually, as previously described (Heller and Malek, 2011), in 3D using multiplanar reconstruction (MPR) of the volumetric dataset, by employing OsiriX software (Version 3.8, Pixmeo, Bernex, Switzerland) (Figure 3).

Computational Fluid Dynamics Analysis

Synthetic models of the proximal carotid siphon were constructed using SolidWorks (Concord, MA). The models were created by extrusion of a circle (5 mm diameter) perpendicular over a centerline path (Figure 4). The initial model consisted of a proximal horizontal arm of 25 mm, followed by a bend over a curve representing a semicircle with a radius of curvature of 5 mm (curvature along the bend equals 0.20 mm^{-1}) and ending with a distal horizontal arm of 25 mm. Three additional models were created by decreasing the radius of curvature from 5 to 3 mm in increments of 1 mm. This created three different models with radius of curvature of 5 mm, 4 mm, and 3 mm which we labeled R5, R4, and

R3, respectively. In order to model vessel bends in which the peak curvature of the bend is higher compared to the global radius of curvature of the bend, an additional model was created with an overall radius of curvature of 5 mm, but with a proximal peak curvature corresponding to a radius of 3 mm (labeled R5/R3) (Figure 4).

In addition to synthetic models, patient-derived models of the ICA (both control and aneurysmal) were also evaluated by CFD analysis. Aneurysms were digitally removed by local Laplacian smoothing (Cebal et al., 2010) (Figure 5), and the parent vessels were reconstructed in MeshLab version 1.3.1 (ISTI-CNR, Pisa, Italy). Laplacian smoothing tends to shrink the surface being smoothed. High number of smoothing iterations was applied on an area constrained to the aneurysm neck, which resulted in the removal of the aneurysm while preserving the surrounding vasculature (Supplementary Material).

Regardless of the model origin (patient or synthetic data), high-resolution tetrahedral meshes with prismatic boundary layer enrichment were generated with Harpoon version 4.4 (Sharco Ltd, Manchester, UK) at a count of approximately 300,000 to 4,000,000 cells. The meshes were subsequently converted to polyhedral domain using Fluent version 12.0 (Ansys, Lebanon, NH). Computational fluid dynamic (CFD) simulation were performed using Ansys Fluent 12.0, by modeling laminar transient flow with a Carreau non-Newtonian profile to better approximate the viscosity and flow of blood (Schirmer and Malek, 2007). In order to account for variability in the size, shape and length of the parent vessel, flow scaling factors were determined for each model to insure ideal parent vessel WSS conditions of approximately 1.5 Pa at the proximity of the aneurysm neck (Malek et al., 1999). Subsequently, scaled pulsatile flow was applied at the inlet for three complete cardiac cycles to allow flow to develop adequately and the third cycle was used for analysis. Each cycle period was $T=1$ sec and had a time step of $t=0.002$ sec with the peak-systole at $t=0.16$ sec. At the outlets, gauge pressure was set to zero Pascal (Bowker et al., 2010). Post-processing was performed using EnSight Version 9 (CEI, Apex, NC).

For all models (synthetic and patient-derived), a 2D curve cut was obtained longitudinally on the inner wall of the bend, aligned with the middle of the bend. In the case of aneurysmal ICAs, the cut was overlapping the site of the aneurysm location (Figure 5C). The length of the curve covers the region of interest of the bend and depends on its approximate global radius of curvature. The curve is used to visualize the change in the WSS and magnitude of the spatial WSS gradient (WSSG) over the entire cardiac cycle along the inner curve of the proximal bend of the carotid siphon. The product of $WSS \cdot WSSG$ (Kadasi et al., 2013) was analyzed at peak systole.

Statistical Analysis

Mean and standard variation (SD) values were computed for peak curvature and radius of curvature, and reported as mean $\pm$ SD. JMP Version 10.0 (SAS Institute, Cary, NC) was used to analyze the data. Statistical significance was assumed for $p < 0.05$. The analysis was performed retrospectively and data was labeled as aneurysmal ICA and non-aneurysmal control ICA. The curvature variables were tested independently using the Student's t-test followed by statistical power analysis. Whole model multivariate statistics were used to determine the relative dependence of the peak curvature on other clinical features.

RESULTS

Demographics and Presentation

A total of 35 ICA angiographic 3DRA volumetric data were available for analysis. The dataset contains 10 aneurysmal ICA originating from the inner proximal bend of the carotid siphon (mean age 57.1 ± 22.6 years; range 20–91) and 25 non-aneurysmal control ICA data (mean age 46.22 ± 10.3 years; range 28–75). There was no statistical age difference between aneurysmal and control subsets. All aneurysms analyzed were unruptured.

Synthetic models: Hemodynamic Results

CFD simulations on synthetic models demonstrated that flow patterns along curves were highly dependent on the curvature of the bend (Figure 6). In all synthetic models the presence of the bend induced an area of flow stagnation as well as a sharp decrease in WSS values within the inner bend. The location and size of this area depended on the curvature of the bend. For low curvature (R5 and R4), the area of flow stagnation was located on the inner wall of the outflow arm (distal from the bend). Subsequent increase in bend curvature (R3) resulted in a widening of the stagnation area, as well as a shift towards the inner wall of the bend.

Figure 7 shows plots of WSS and WSSG values along the inner bend of all models, evaluated over the entire cardiac cycle. With increasing curvature, WSS values at peak systole increased from 5.6 Pa (model R5) to 18.5 Pa (model R3). Even more dramatic, the WSSG increased from -3 Pa/mm (model R5) to 320 Pa/mm (model R3). It is apparent from figures 6 and 7, that bends of high curvature are characterized by high proximal WSS and regions of flow stasis flanked by high WSSG.

Adding a proximal region of higher peak curvature to the R5 model resulted in an increase of WSS values at the site of the peak curvature from 5.6 Pa (model R5) to 14 Pa (model R5/R3). Compared to R4 and R5 models, the inner wall of the R5/R3 model showed high WSSG, which reached up to 40 Pa/mm at peak systole.

Analysis of WSS*WSSG product showed that only models R3 and R5/R3 had WSS*WSSG larger than 50 Pa²/mm (Figure 8A). WSS*WSSG reached values of 5000 Pa²/mm on the inner wall of R3 model, and values of 410 Pa²/mm on the inner wall of the R5/R3 model.

Patient-derived models: Univariate Analysis

The peak curvature of the proximal bend of the carotid siphon was significant higher in aneurysmal bends (0.36 ± 0.045 vs. 0.30 ± 0.048 mm⁻¹, $p=0.003$) compared to control siphon bends. This analysis resulted in a power value of 0.83 (significance assumed for $p > 0.05$). In contrast, the radius of curvature of the proximal bend of the carotid siphon was not statistically different between controls and aneurysmal ICAs (3.71 ± 0.64 vs. 3.93 ± 0.70 mm, $p=0.36$).

In addition to the peak curvature, the 95th percentile of the curvature distribution in the siphon bend was also considered. Aneurysmal ICAs had significantly higher 95th percentile

curvature compared to non-aneurysmal ICAs (0.34 ± 0.02 vs. 0.29 ± 0.01 mm⁻¹, $p=0.02$). This analysis resulted in a power value of 0.70 (significance assumed for $p > 0.05$).

Multivariate Analysis

Whole model analysis of the peak curvature was evaluated in order to determine the relative correlation of curvature to aneurysm presence, age, hypertension, hypercholesterolemia, and smoking status. Peak curvature was highly associated with the aneurysm presence (Table 1), but not with age, hypertension, hypercholesterolemia, and smoking status.

Patient-derived models: Hemodynamic Results

Figure 9 shows two patient aneurysmal carotid siphon bends evaluated using CFD simulations. Similar to the synthetic models, high fluctuating WSS values were found in the inner wall of the aneurysmal siphon bend, followed by an area of slow flow. For the first aneurysmal model (top panel, Figure 9), the WSS at peak systole decreased from 14.2 to 0.1 Pa, whereas for the second aneurysmal model (bottom panel, Figure 9) the WSS decreased from 7 to 0.6 Pa. Overall, for the 10 aneurysms, the inner wall of siphon reached peak WSS values between 4.6 and 14.2 Pa (mean 8.1 ± 2.9 Pa) and peak WSSG values between 2.9 and 25.2 Pa/mm (mean 11.9 ± 8.5 Pa/mm). The inner walls of the aneurysmal bends were characterized by high WSS and WSSG values, with a pattern of slow flow flanked by dynamically fluctuating high WSS and WSSG peaks.

In contrast to aneurysmal siphon bends, control patient carotid bends displayed low, almost constant, WSS and WSSG profiles with little variation. For the first control ICA (top panel, Figure 10), the WSS at peak systole decreased from only 4.6 to 2.7 Pa, whereas for the second control (bottom panel, Figure 10) the WSS decreased from 3.4 to 0.5 Pa. The inner walls of control bends were characterized by constant low WSSG values.

Analysis of WSS*WSSG product showed that aneurysmal patient carotid models were characterized by significantly higher WSS*WSSG compared to control patient-based models (Figure 8B). Whereas in the aneurysmal patient models WSS*WSSG reached values of 130 Pa²/mm, control patient models had consistently low WSS*WSSG product of less than 10 Pa²/mm.

Patient derived-models: Correlation with Aneurysm Location

The width of the aneurysm neck was statistically correlated to the distance between the WSS peaks on the inner wall of the carotid siphon. The correlation was statistically significant for both WSS at peak-systole ($p = 0.007$, $R^2 = 0.61$) and for time-average WSS evaluated over the entire cardiac cycle ($p = 0.008$, $R^2 = 0.61$). The relative location of the proximal and distal ends of the aneurysm neck were recorded and correlated with the locations of the proximal and distal peaks of the WSS, WSSG and WSS*WSSG. The results suggest a strong correlation between the aneurysm location and high WSS and WSSG values (Table 2).

DISCUSSION

The effect of arterial geometry on cerebral aneurysm formation and growth has been evaluated before, with several studies demonstrating the effect of parent vessel morphology on aneurysm hemodynamics (Hassan et al., 2005; Xiang et al., 2011). In particular, the curvature of the parent vessel has been shown to play a role in aneurysm formation, as well as aneurysm growth and possible progression to rupture. Experiments on animal models showed that increased vessel tortuosity preceded aneurysm formation following bilateral carotid ligation in rabbit models (Tutino et al., 2014). Following analysis on 3D synthetic models of curved arteries, Foutrakis et al. (1999) and Hoi et al. (2004) theorized that high hemodynamic stress is responsible for the formation of aneurysms on the lateral outer wall of the curved bends. Previous studies showed that aneurysmal ICAs had significantly higher curvature compared to non-aneurysmal ICAs (Lauric et al., 2013) and that ICA segments hosting aneurysms have significantly higher curvature compared to non-aneurysmal segments (Piccinelli et al., 2011). In addition, Piccinelli et al. (2011) showed that aneurysms form predominantly along the outer wall of the parent vessel, close to the site of peak of curvature.

To the best of our knowledge, aneurysm formation along the inner wall of curved vessels has not been thoroughly investigated. Our current report demonstrates that the inner wall of the proximal carotid siphons harboring aneurysms have higher peak curvatures compared with non-aneurysmal bends. While in clinical practice the curvature of a bend was previously quantified by evaluating the overall radius of curvature of the bend (Hoi et al., 2004), our results suggest that the peak focal curvature of the bend may be a more reliable measure compared to the global radius of curvature in distinguishing between control and aneurysmal bends.

We hypothesized that aneurysmal bends fall in one of two categories: (1) smooth bends with small overall radius of curvature, corresponding to constant high curvature and (2) bends with higher overall radius of curvature, but also with a region of high peak curvature located at the proximal elbow of the bend. Hemodynamic implications were evaluated for both of these categories using synthetic 3D models of the carotid siphon bend. For bends with constant curvature, increasing the curvature resulted in a dramatic increase of WSS and WSSG, with fluctuating high WSSG peaks flanking regions of flow stasis and recirculation. Importantly, increasing the curvature of the bend resulted in a shift of the slow flow area from the distal region of the bend towards the center of the bend (Figure 6).

Adding a region of high peak curvature (a sharp proximal turn) to a bend of otherwise low overall radius of curvature induced an area of high WSS and high WSSG, which was not previously seen in the absence of the sharp turn (Figure 6). This area was close to the site of peak curvature, in the distal orientation. Importantly, this area was completely enclosed in the area of the bend and did not extend to the distal horizontal arm. The effect of the peak focal curvature may explain aneurysmal presence in bends of otherwise high overall radius of curvature.

In this population, the overall global radius of curvature was similar between aneurysmal bends and controls. However, there was a significant difference in the peak focal curvature of the bend. This suggests that the R5/R3 synthetic model, in which the bend is characterized by a region of higher peak curvature proximal to an otherwise wider bend, offers the best parametric approximation of the proximal bend of the carotid siphon. Indeed CFD simulations on models representing aneurysmal patients yielded WSS and WSSG values similar to those reported for the R5/R3 model.

The interplay between WSS and WSSG has been reported in animal models (Meng et al., 2007; Metaxa et al., 2010; Wang et al., 2009) showing that aneurysm formation occurs in regions exposed to accelerating flow with high WSS and positive WSSG. Wang et al. (2009) reported that vessel bifurcations characterized by elevated WSS and large WSSG were associated with molecular changes implicated in intracranial aneurysmal formation. Metaxa et al. (2010) showed that vascular bifurcations subject to hemodynamic impact were characterized by prominent internal elastic lamina loss and medial thinning and displacement of the vessel wall, consistent with aneurysmal initiation in areas of simultaneous high values of both WSS and its spatial gradient, WSSG.

This study suggests that the aneurysmal inner wall of the carotid siphon is characterized by sudden WSS changes, from high to low values, and high WSSG peaks. In our simulations, WSS reached values of 14 Pa in parametric models (R5/R3) and 14.3 Pa (mean 8.1 ± 2.9 Pa) in aneurysmal patient-derived models whereas WSSG reached values of 40 Pa/mm in model R5/R3 and as high as 25.2 Pa/mm (mean 11.9 ± 8.5 Pa/mm) in aneurysmal models (consistent with the values reported by (Meng et al., 2007) – peak WSS 13 Pa, and peak WSSG 11 Pa/mm seen in areas of destructive wall remodeling). Regions of proximal high WSS and high WSSG correspond to the site of the peak curvature of the bend. Aneurysms in these regions form distal from the site of peak curvature, in the area of stagnant flow, flanked by high WSS and WSSG peaks. The width of the aneurysm neck correlates strongly with the distance between WSS peaks. The product between WSS and WSSG (Kadasi et al., 2013) was much higher in synthetic models with increased curvature. As shown in Figure 8B, the WSS*WSSG product clearly discriminated between control and aneurysmal models.

Prior to cerebral aneurysm formation, acquired or inherited risk factors such as smoking, hypertension, hypercholesterolemia, alcohol and drug use, and polycystic kidney disease, may have already lowered the threshold for the onset of pathological responses in the vasculature (Meng et al., 2013). Previous animal studies (Aoki et al., 2007; Chalouhi et al., 2012) have demonstrated that hemodynamic insult represents a necessary condition for the formation of intracranial aneurysms and that these aforementioned additional risk factors may compromise the ability of the cerebral vasculature to tolerate and adapt to these hemodynamic forces (Meng et al., 2013). Overall, our data suggests that, in the absence of a vessel bifurcation (a site associated with high WSS, flow separation, and an increased risk for aneurysm initiation) high vessel curvature may represent an additional predisposition favoring the pathological formation of sidewall aneurysms on the inner wall of curved vessels. Future larger studies are required to determine any potential utility and applicability of vessel curvature in cerebral aneurysm risk stratification analysis.

Study Limitations

This analysis is retrospective in nature and thus can only imply prediction of aneurysm formation based on curvature analysis. Larger prospective randomized studies will be required to evaluate the potential usefulness of curvature features for assessment of risk of aneurysm formation. Related to the above limitation, it is unknown the degree to which the presence of aneurysms affects the geometry of the parent vessels. This is an issue that can only be conclusively addressed by prospective studies, in which follow-up data is available prior to aneurysm formation. We are encouraged by the fact that in the particular location of the carotid siphon, the carotid artery is fixed within the bone of the skull base, so it is unlikely to have changed especially in the case of relatively small aneurysms (5.48 ± 4.96 mm). In addition, the results show good correlation between analysis on patient-derived data and synthetic models which suggest that aneurysm presence had a limited effect on vessel curvature. One limitation inherent to the use of synthetic carotid siphon models is that they do not always represent a faithful realistic physiological reconstruction. Nonetheless, thanks to their simplicity, the synthetic models allowed us to explore the effect of well defined alterations. Specifically it enabled us to show the isolated effect of reducing the radius of curvature in a constant fashion, and also uncover the effect of introducing a tighter proximal radius segment just proximal to a wider radius.

CONCLUSION

High peak focal curvature of the carotid siphon is correlated with aneurysm presence. In synthetic and patient-derived models, bends of high curvature are characterized by high WSS and WSSG, which correspond to the site of peak focal curvature. Aneurysms in these regions seem to form distal from the site of peak curvature, in areas of stagnant flow flanked by dynamically fluctuating high WSS and WSSG peaks. The distance between WSS peaks correlates with the size of the aneurysm neck. The peak curvature of the internal carotid siphon has the potential of being a candidate for consideration in future studies for evaluating propensity for aneurysm formation.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.
Volumetric reconstruction of the 10 aneurysmal ICA models. All aneurysm originate from the inner wall of the proximal carotid siphon.

Figure 2.
Centerline curvature computation of aneurysmal (top row) and control (bottom row) ICAs.
The black arrows demonstrate the areas of greatest curvature which are proximal to the
aneurysm in each case.

Figure 3.

Two aneurysmal ICAs with wide global radius of curvature (4.4 mm and 3.96 mm respectively) describing a wider anterior bend, but with tight local radius of curvature (2.88 mm and 2.74 mm respectively) of the proximal elbow of the bend. Black arrows represent flow direction.

Figure 4.

Synthetic models of the anterior bend of the carotid siphon are represented as tubular structures with a bend of variable radius of curvature. Shown are bends with radius of curvature of 5 mm, 4 mm, and 3 mm. Additional model (R5/R3) has an overall radius of curvature of 5 mm with a proximal peak curvature corresponding to a radius of curvature of 3 mm.

Figure 5.

Digital removal of aneurysms. (A) Initial model with aneurysm in the inner bend of carotid siphon. (B) The aneurysm is digitally removed and (C) the vessel is reconstructed. The one dimensional curve where flow properties are evaluated during fluid dynamics postprocessing is shown in gray.

Figure 6. Hemodynamic results on synthetic models. All values are shown at peak systole ($t = 2.275s$). Black arrows point to the inflow direction. First column: wall shear stress (WSS). Second column: magnitude of WSS gradient (WSSG). Third column: Velocity shown on a longitudinal plane cutting through the middle of the model. Black rectangles highlight regions of flow stasis and recirculation.

Figure 7.

WSS values plotted over a one dimensional (1D) curve cut positioned on the curved inner wall for multiple synthetic models (R5, R4, R3 and R5/R3). The length of the 1D curve is dependent on the radius of curvature of the bend. The cardiac cycle was sampled at 9 time points. The red curve is obtained at peak systole, whereas the gray curve is obtained at end diastole. First column: wall shear stress (WSS). Second column: magnitude of WSS gradient (WSSG).

Figure 8.

The product of the wall shear stress and the magnitude of the wall shear stress gradient (WSS*WSSG). (A) Synthetic models. (B) Patient-derived models for two aneurysmal (red) and two control (black) ICAs.

Figure 9.

Hemodynamic results on two aneurysmal patient-derived models. Red arrows point to the site of the aneurysm. Black arrows point to the site of the maximum peak curvature. First column: for each aneurysm, WSS and WSSG images were captured at peak systole ($t=2.275s$). Second column: for each aneurysm, WSS and WSSG were plotted over a 1 dimensional curve cut positioned on the curved inner wall. The cardiac cycle was sampled at 9 time points. Red curve is obtained at peak systole. Gray curve is obtained at end diastole. The horizontal line represents the width of the aneurysm neck.

Figure 10.

Hemodynamic results on control patient-derived models. Black arrows point to the site of the maximum peak curvature. First column: for each control WSS and WSSG images are captured at peak systole ($t=2.275s$). Second column: for each control, WSS and WSSG were plotted over a one dimensional curve cut positioned on the curved inner wall. The cardiac cycle was sampled at 9 time points. Red curve is obtained at peak systole. Gray curve is obtained at end diastole.

Table 1

Whole model analysis of peak focal curvature of the anterior genu of the carotid siphon, evaluating the relative effect of aneurysm presence, age and known risk factors.

Whole Dataset Model		
Predicted Value	Effect Variable	p
Peak Focal Curvature	Aneurysm?	.003*
	Age	.91
	Hypertension	.58
	High cholesterol	.22
	Smoking	.14

* indicates statistical significance, which is assumed for $p < .05$. Whole model statistics were similar for all curvature features.

Table 2

Statistical correlation between the locations of the proximal and distal ends of the aneurysm neck and the locations of the proximal and distal peaks of the WSS, WSSG and WSS*WSSG recorded at peak-systole. The results, shown in the table below, suggest a strong correlation between the aneurysm location and high WSS and WSSG values. Statistical significance was assumed for $p < .05$. R^2 is the coefficient of determination.

	Proximal neck end	Distal end neck
Proximal WSS peak	$P < .001, R^2 = 0.81$	
Proximal WSSG peak	$p = .002, R^2 = 0.72$	
Proximal WSS*WSSG peak	$p = .002, R^2 = 0.72$	
Distal WSS peak		$p < .001, R^2 = 0.81$
Distal WSSG peak		$p < .001, R^2 = 0.77$
Distal WSS*WSSG peak		$p < .001, R^2 = 0.88$