Flow patterns and wall shear stress distribution in human internal carotid arteries: The geometric effect on the risk for stenoses

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ABSTRACT

It has been widely observed that atherosclerotic stenosis occurs at sites with complex hemodynamics, such as arteries with high curvature or bifurcations. These regions usually have very low or highly oscillatory wall shear stress (WSS). In the present study, 3D sinusoidally pulsatile blood flow through the models of internal carotid artery (ICA) with different geometries was investigated with computational simulation. Three preferred sites of stenoses were found along the carotid siphon with low and highly oscillatory WSS. The risk for stenoses at these sites was scaled with the values of time-averaged WSS and oscillating shear index (OSI). The local risk for stenoses at every preferred site of stenoses was found different between 3 types of ICA, indicating that the geometry of the blood vessel plays significant roles in the atherogenesis. Specifically, the large curvature and planarity of the vessel were found to increase the risk for stenoses, because they tend to lower WSS and elevate OSI. Therefore, the geometric study makes it possible to estimate the stenosis location in the ICA siphon as long as the shape of ICA was measured.

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1. Introduction

The human internal carotid artery (ICA) arises from the common carotid artery, and terminates by branching into the anterior and middle cerebral arteries. Along its complicated course, the section of the ICA that runs inside the cavernous sinus is of particular interest (Meng et al., 2008). As the term ‘cavernous sinus’ is still the subject of debate, we prefer to term it the ‘carotid siphon’, because the S-shaped configuration of these segments resembles a siphon bend (Krivosic, 1987; Weninger and Pramhas, 2000). It has been reported that the carotid siphon is the site most susceptible to atherosclerotic lesions in the human intracranial arteries, directly affecting the cerebral blood supply. The intracranial ICA stenosis has been considered as a dangerous trigger for stroke or transient ischemic attack (TIA) (Craig et al., 1982; Kappelle et al., 1999; Marzewski et al., 1982). In addition to factors like hypertension, hyperglycemia and hyperlipidemia, the geometry of ICA can affect the blood flow pattern through the artery, which in turn, affects the risk of having plaque build-up and atherosclerotic stenosis (Nguyen et al., 2008). Therefore, understanding blood flow patterns in ICAs with different geometries can lead to the identification of people vulnerable to atherosclerosis. Recently, many tools including invasive procedures such as X-ray contrast angiography and non-invasive tools like ultrasonography and magnetic resonance imaging have been applied to detect the arterial geometry in order to investigate its relationship with the progression of atherosclerosis in humans (Acar et al., 2005; Wetzel et al., 2007; Bammer et al., 2007).

In terms of hemodynamics, it has been found that low or oscillatory shear stress contributes to atherogenesis (Thubrikar and Robicsek, 1995; Wada and Karino, 2002; Davies et al., 1986; Deplano and Siouffi, 1999). Atherogenic phenotype was found to be stimulated when the WSS was below 0.4 Pa (Malek et al., 1999). It was also reported that atherogenic phenotype was observed correlated with high oscillating shear index (OSI, an indicator for the oscillation of WSS) in arteries (Rodkiewicz, 1975; Naruse and Tanishita, 1996).

Flow in curved tubes has been investigated computationally by Chang, who modeled sinusoidal and pulsatile flow in curved tubes (Chang and Tarbell, 1985). The flow in ICA was also investigated by abstracting the geometry of ICA into S-shape or Ω-shape (Qiao et al., 2004; Oshima et al., 2005). All these studies suggest that large curvature would cause complex and non-uniform flow pattern, which may affect the function of arterial endothelium.

Investigations on the blood flow in anatomical ICA models were also conducted. Bammer and Wetzel used 4D MR Imaging technology to assess and visualize the blood flow in ICA in vivo, and found very complex flow with helical and twisting patterns in...
carotid siphon (Wetzel et al., 2007; Bammer et al., 2007). WSS in the ICA siphon reconstructed from the original medical images was computationally evaluated by Sforza, and was found relatively low compared to the other cerebral arteries (Sforza et al., 2009). Takeuchi experimentally studied the fluid velocity and WSS in the ICA siphon from human postmortem, and got the similar conclusion (Takeuchi and Karino, 2010). Although Takeuchi firstly pointed out that the atherosclerotic stenosis was found not only in the inner wall of curved segments but also in other regions of the carotid siphon because of the low mean fluid velocity; the preferred sites of ICA stenosis and its relationship with the ICA geometry have not been systematically studied.

According to the anatomic classification of the siphon, the ICA shape could be classified into 4 types: U-shape, V-shape, C-shape and S-shape (Fig. 1) (Zhong et al., 1985). The U-shaped ICA was characterized by a U-shaped vessel at the siphon bend with 2 obvious bends, B1 and B2. The V-shaped ICA was characterized by a much less curved B2. In the former mentioned two types of ICA, B1 and B2 are approximately in the same plane. But in the C-shaped ICA, B1 that is approximately horizontal nearly bends into a right angle to B2. The S-shaped ICA has one more bend above the siphon, which forms into another S-shape above the siphon. Because of the complex shape of the ICA, a large number of ICA subjects need to be studied. Consequently, the numerical simulation was used in our study to investigate the association between the ICA shape and its stenosis from a great amount of subjects. Sinusoidal, 3D blood flow in the ICA was simulated, using a finite volume numerical method for a great amount of ICA models, which were reconstructed from the clinical MRA images.

2. Methods

2.1. Data source

The study population consisted of the inpatients at Peking University First Hospital in the past three years, who met the following inclusion criteria: (1) over 40 years old, (2) anterior cerebral arteries, middle cerebral arteries and basilar artery remained patent, (3) systemic vascular diseases like vasculitis were not found clinically and (4) no evidence of ICA stenosis or common carotid artery on transcranial Doppler (TCD), carotid duplex ultrasound or MRA was found. Accordingly, 31 subjects namely 62 ICA branches were chosen for the study. They were anatomically classified by an experienced radiologist blinded to the following hemodynamic simulation. The numbers of all types of ICA are shown in Table 1.

Because the population of S-shaped ICA was too low, it was not considered in the study. Consequently, 61 ICA branches were reconstructed and simulated for the hemodynamic study. The study was approved by the Ethics Committees of both Heihang University and Peking University First Hospital.

2.2. 3D geometric reconstructions

All the MRA images were acquired on a 1.5T MR scanner (GE HD, Milwaukee) with an 8-channel head coil in the cross-sectional direction. A 3D TOF sequence was used for the image acquisition. The settings were as follows: TR/TE 22/6.9 ms, flip angle 20°, Field of View 220 × 180 mm², matrix 288 × 192 and slice thickness 1.4 mm. The raw data of MRA was reconstructed with the technique of maximal intensity projection.

The 3D reconstruction of the ICA was performed with the Mimics (Materialise, Belgium) (Lorensen and Cline, 1987; Lin et al., 1988). The ICA lumen images were segmented with the threshold method and reconstructed into the 3D models. The pixel effect on the image contour was removed using the smoothing algorithm with volume compensation. Because the viscoelasticity of the blood vessel wall of the models was not considered in the hemodynamic simulation, the taper of the ICA was omitted. The cross-section of the models was modified to be a circle to overcome the effect of slight stenoses in the ICA on the local hemodynamic factors.

### Table 1

<table>
<thead>
<tr>
<th>Shape</th>
<th>Number</th>
<th>Proportion</th>
</tr>
</thead>
<tbody>
<tr>
<td>U shape</td>
<td>34</td>
<td>54.8%</td>
</tr>
<tr>
<td>V shape</td>
<td>17</td>
<td>27.4%</td>
</tr>
<tr>
<td>C shape</td>
<td>10</td>
<td>16.1%</td>
</tr>
<tr>
<td>S shape</td>
<td>1</td>
<td>1.6%</td>
</tr>
</tbody>
</table>

2.3. Hemodynamic study

The CFD simulation was performed for all the ICA branches from the beginning of siphon to the end of the ICA. The ophthalmic artery and posterior communicating artery bifurcating from the ICA was removed from the model, because the maximum diameter of the daughter branches was less than 1 mm, much less than that of the ICA. The models were meshed in Gambit software. The tetrahedral meshes were used for the interior of the blood vessel, while more detailed hexahedral meshes were used near the wall of the blood vessel, in order to acquire precise results of WSS. The maximum volume of computational cell was $2.4 \times 10^{-3} \text{ m}^3$. Every model was separated into about 100,000 cells for the finite element analysis.

The inlet and outlet were set perpendicular to the centerline for ICA models. The outlet surface was far away from the siphon to minimize the computational error caused by the boundary conditions. To simulate the unsteady flow, the blood flow velocity at the inlet was expressed as $v = 0.15 - 0.15 \cos(2.5\pi t) \text{ m/s}$.

The pressure at the outlet was expressed as $p = 12000 - 2667.5 \cos(2.5\pi t) \text{ Pa}$.

The blood was considered as incompressible Newtonian fluid, with the density $\rho = 1056 \text{ kg/m}^3$ and the dynamic viscosity $\mu = 4 \times 10^{-3} \text{ kg/(m \cdot s)}$ (Lee et al., 2008). The effect of gravity ($9.81 \text{ kg/m}^3$) was considered in the study. The wall of the blood vessel was considered as a rigid wall without viscoelasticity under non-slip condition. According to the inside diameter $D$ arranged from 3.4 to 5.2 mm at the inlet of ICA measured from the simulation models, the Peak Re number $Re = \rho D \mu$ changed from 364 to 428. The motion of blood in ICA was assumed as unsteady laminar flow in the study. Considering the previous hypotheses, the governing equations of blood flow can be expressed as follows:

1. Continuity equation
   \[ \nabla \cdot \mathbf{v} = 0 \] (3)

2. Navier–Stokes equation
   \[ \frac{\partial \mathbf{v}}{\partial t} + (\mathbf{v} \cdot \nabla) \mathbf{v} = -\frac{1}{\rho} \nabla p + \frac{\mu}{\rho} \nabla^2 \mathbf{v} \] (4)

where $\mathbf{v}$ is the blood flow velocity; $\rho$ and $\mu$ denote the density and dynamical viscosity of blood, respectively; $p$ is the pressure.

Flow in the ICA was simulated with the finite volume-based software Fluent (ANSYS, US) and using a second-order unsteady solver. As the cycle of the pulsatile flow was 0.8 s, the time step was set to 0.001 s to get time-step independence results. The calculation was performed for 6 cycles, and the data of the sixth cycle were considered as the simulation results to make sure the convergence of the solution.

2.4. The risk quantification

The risk for stenoses is directly related to the local WSS and OSI near the vascular wall (Markl et al., 2010). The local lowest time-average WSS and highest OSI at three sites along the ICA siphon were recorded for all the subjects, because the three sites were most susceptible to stenoses according to the clinical data.
which consisted of 47 inpatients with ICA stenoses in Beijing University First Hospital in the last 3 years. They were all examined by MRA and transcranial Doppler (TCD) and diagnosed with over 50% decrease of the vessel diameter in the ICA siphon. Either systematic cardiovascular diseases or other vascular lesions were not found in all the patients. The quantification results were compared with the incidence of stenoses, which was summarized from the clinical data. For every simulation case, the risk for stenoses was quantified by two formulas:

\[
RWSS_i = \frac{WSS_i^{-1}}{WSS_{B2} + WSS_{B1} + WSS_{C2}} \quad (i = B2, B1 \text{ or } C2)
\]

\[
ROSI_i = \frac{OSI_i}{OSI_{B2} + OSI_{B1} + OSI_{C2}} \quad (i = B2, B1 \text{ or } C2)
\]

where RWSS, denotes the risk of stenoses at the outer of B2, the outer of B1 or the inner of C2, which is quantified with WSS, while OSI, is quantified with OSI. WSS, and OSI, are the lowest time-average WSS and highest OSI at one of the three regions. Accordingly, the regions with the lowest WSS and the highest OSI are assumed to have the highest risk for stenoses among the three preferred sites for atherosclerosis.

3. Results

Five locations along the ICA siphon were chosen as representative measuring stations. The locations were the 5 planes that ran across the ICA siphon and were perpendicular to the axis of vessel, as shown in Fig. 2. The planes 1, 2, 3, 4 and 5 were located at the beginning of B2, the middle of B2, the beginning of B1, the middle of B1 and the end of B1, respectively. The lines from the outer to the inner of the bend in planes 2, 4 and 5 were, respectively, defined as line A, B and C. Below, we present simulation results on these planes and lines.

Velocity profiles have been calculated throughout the whole pulsatile cycle. It was observed that the axial velocity is generally low within the siphon, which was considered as the reason for the low WSS along the siphon. But the difference between the velocity contours in three types of ICA is obvious. Fig. 2 shows axial velocity contours over different cross-sections of the siphon at time 0.2 s (i.e., the time when the instant velocity equals the average velocity at the inlet) for the cases of U-, V- and C-shaped ICA. For the U- and C-shaped cases, regions of flow recirculation formed near the wall of bends, due to the large curvature of the bends. Within such recirculation regions indicated by the negative velocity (blue color), blood moves in the direction opposite to the mean flow, increasing the probability of stenoses. Velocity skewing is observed (the maximum velocity does not occur at the center, as was also observed by Ku) in almost all the planes along the siphon (Ku, 1997). The skewing caused by the tremendous curvature of the siphon bends, dramatically decreases the WSS at one side of the bend. The skewing is more significant in the U- and C-shaped ICA, because they have larger curvatures than the V-shaped, indicating that the curvature of the bend influences the intensity of velocity skewing.

The profile of the axial velocity \(V_{ax}\) is shown in Fig. 3 from time \(t=0.2–0.8\) s along the line A, B and C, which cross the middle of B2, the middle of B1 and the end of B1, respectively. At the beginning of the cycle, the blood flow rate starts rising and reaches the peak at 0.4 s and then decreases gradually to the lowest level at the end of the cycle \(t=0.8\) s). The velocity gradients near the inner side of lines A and B are much higher than those near the outer side. The situation is reversed on line C. In the U- and C-shaped ICA, the negative axial velocity appears at B2 and B1, respectively, indicating negative WSS and flow recirculation near the outer wall of the bends.

Fig. 4 shows contours of the WSS magnitude as a function of time. The region indicated by dark blue color has low WSS (lower than the critical point of 0.4 Pa). Throughout the pulsatile cycle, the WSS at all regions along the siphon changes tremendously as the velocity fluctuates. But the WSS at some special regions, such as the outer wall of B2, the outer wall of B1 and the inner wall of the end of B1, stays at a low level. The WSS in some regions even oscillates around zero. The oscillating shear index (OSI) indicates the intensity of the oscillation around zero throughout the cycle, which can be expressed as

\[
OSI = 0.5 \left[ 1 - \frac{1}{T} \int_0^T |\tau_w| \, dt \right]
\]

where \(T\) is the cardiac cycle, \(\tau_w\) is the temporal WSS vector. There are studies suggesting the intensively oscillating WSS causes the fatigue lesions of the arterial intima and further the atherosclerosis and arterial stenoses (Ku et al., 1985; Deplano and Siouffi, 1999). The average WSS and oscillating shear index (OSI) are also shown in Fig. 4(e) and (f), respectively.

The risk for stenoses at 3 locations in all the cases was calculated with WSS and OSI. The incidences of stenoses at these
3 locations were summarized from 47 patients with ICA stenoses (24 patients with unilateral stenoses, 23 with bilateral). The statistics of the ICA shape and the stenosis locations were shown in Table 2. The results for the risk quantification and the clinical statistics were shown in Fig. 5.

A good correlation was found between the quantified risk for stenoses and the statistical results for the incidence of stenoses in the ICA siphon, indicating the availability of the risk quantification methods. The risk quantified with OSI seems more effective than that scaled with WSS, because the bar diagram of OSI is more similar to the graph of the incidence of stenoses. The quantified risk shows that the local risk for stenoses is different between 3 types of ICA siphon that the stenosis is less likely to occur at the outer of B2 in the V-shaped ICA or the outer of B1 in the C-shaped ICA. It indicates that the geometry of ICA, especially the curvature and planarity, plays a significant role in the hemodynamic mechanism of stenoses.

4. Discussion

The hemodynamic factors in ICA siphons were investigated according to the anatomic classification. The simulation results showed that the velocity profiles and WSS distributions in ICAs with different shapes were different.

4.1. Fluid velocity, wall shear stress and preferred sites of stenoses

It has been reported that the siphon bend of the ICA is the site most susceptible to the atherosclerotic lesions in the human intracranial arteries (Sakata and Takebayashi, 1988; Samuel, 1956). In Asia, the lesions of ICA siphon are quite common, increasing the risk for stroke and TIA (Huang et al., 1997). The correlation between WSS, OSI and the preferred sites of atherogenesis has been confirmed by previous studies (Shojima et al., 2004; Liu et al., 2002; Garanich et al., 2005; Jiang et al., 1999). In the carotid siphon, WSS was generally low, resulting in that wall thickenings and stenoses were found in not only the inner but also the outer wall of bends.

Our results suggest 3 preferred sites of atherogenesis in the siphon, the outer of B2, the outer of B1 and the inner of the B1 downstream (C2, named by Fischer (1938)). In these regions, the WSS is low while the OSI is high. But the situation differs between the three types of ICA. Because the curvature of B2 in the V-shaped ICA is much less than that in the other 2 types, the flow skewing and the low WSS at B2 of the V-shaped are not so remarkable as those of the other 2 types, which suggests that the possibility of the stenosis at the outer of B2 in the V-shaped ICA is relatively low.

Besides the effect of the curvature, the planarity of the siphon also contributes to the velocity profile and WSS distribution. In the C-shaped ICA, B1 is perpendicular to B2, while B1 and B2 are generally in the same plane in the U- and V-shaped ICA. Consequently, the flow velocity and WSS at B1 in the C-shaped ICA are different from those in the U- and V-shaped. Strong helical flow is observed at B1 in the C-shaped ICA (Fig. 6). Because of the helical flow, the blood flow formed into a vortex with relatively low flow velocity in the center but high velocity around. Consequently, WSS at the wall of B1 is relatively high, especially when the inlet velocity reaches the peak and the helical flow is the strongest.
Fig. 4. The magnitude of shear stress on the ICA siphon wall at different instances for (I) U-, (II) V- and (III) C-shaped cases: (a) $t=0.12$ s, (b) $t=32$ s, (c) $t=0.52$ s and (d) $t=0.72$ s. (e) The time-averaged WSS throughout the pulsatile cycle. The color scale is in Pa in these contours. The blue regions in the average WSS contours indicate zones where the average WSS is low (<0.4 Pa). (f) The OSI. The red and yellow regions in the OSI contour indicate the zones with high OSI (for interpretation of the references to color in this figure legend, the reader is referred to the web version of this article).
throughout the pulsatile cycle. Compared to the other two types of ICA, the C-shaped ICA siphon has a higher average WSS and lower OSI at the outer of B1, indicating the lower possibility of stenoses at B1 in the C-shaped ICA.

### 4.2. The risk quantification

The risk quantification of stenoses was first proposed by Nguyen to compare the risk for stenoses between subjects with different arterial geometries (Nguyen et al., 2008). The method was modulated to compare the risk for stenoses at different sites within one subject in the present study. However, the results cannot be compared between cases. Because the same inlet velocity function is used as the boundary condition in the simulation for cases with different vessel diameters, it makes no sense to compare the results of WSS and OSI calculated from different subjects. Besides this limitation, the physiologically pulsatile flow needs to be performed in the simulation for the further study.

In conclusion, the WSS and OSI distribution patterns are found different between the 3 types of ICA, because the curvature and planarity of the blood vessel play significant roles in the flow pattern in the ICA siphon. Indicating that the local risk for stenoses can be estimated with the shape of ICA siphon, these findings make it possible to predict the stenosis location when the ICA shape is measured.

### Conflict of interest statement

This study has no conflict of interest to report.

### Acknowledgment

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### Table 2

Statistical results for the stenosis locations.

<table>
<thead>
<tr>
<th></th>
<th>With stenosis</th>
<th>Without stenosis</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>N with stenosis</td>
<td>C2</td>
</tr>
<tr>
<td>U-shaped</td>
<td>57</td>
<td>42 (73.7%)b</td>
</tr>
<tr>
<td>V-shaped</td>
<td>24</td>
<td>21 (87.5%)</td>
</tr>
<tr>
<td>C-shaped</td>
<td>13</td>
<td>7 (53.8%)</td>
</tr>
</tbody>
</table>

* Number of ICA branches.  
  b Basal level is the number of ICA branches of every type. Because some patients had multiple stenoses along the siphon, the sum of ICA branches with stenoses at 3 locations could be larger than the number of stenosed branches.

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**Fig. 5.** Comparison between the quantified risk for stenoses and the incidence. (a) The average risk is scaled with WSS and OSI in all cases; (b) the incidence of stenoses at the 3 preferred locations of stenoses in every type of ICAs, scaled by the proportion of the number of the subjects with ICA stenoses at one region to the amount of ICAs for every type.

**Fig. 6.** Helical flow in B1 of the C-shaped ICA ($t=0.4$ s). (a) The pathlines of the blood flow. The color denotes the helicity of the flow. The red color indicates the strong helical flow in B1. (b) The vector of the flow in the plane 4 of the C-shaped ICA. The arrow indicates the direction of the flow. The length of the vector and the color denotes the velocity magnitude of the flow.
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