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Hemodynamics in the Circle of Willis with Internal Carotid Artery Stenosis under Cervical Rotatory Manipulation: A Finite Element Analysis

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Data Interpretation D
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Background: The circle of Willis (CoW) plays an important role in cerebral collateral circulation. The hemodynamics changes in the CoW have usually been associated with the internal carotid artery (ICA) stenosis, but whether rotatory manipulation will affect it remains unknown.





Material/Methods: In this study we attempted to analyze the influence of rotatory manipulation on the hemodynamics in the CoW in models with or without ICA stenosis by means of finite element analysis. For this purpose, the CoW was reasonably simplified and a fluid-solid coupling 3D finite element model was created by using MIMICS10.0 and ANSYS14.5. The healthy (without stenosis) and the diseased (ratios of stenosis include 15%, 30%, 45%, 60%, 70%, 80%, and 90%) situations were simulated. A remote displacement of 60° was applied at a distal ICA (the right ICA was chosen here) to imitate the rotatory manipulation. Blood flow was then monitored at the anterior communicating artery (ACoA) and posterior communicating arteries (PCoA).

Results: Before the conduction of rotatory manipulation, blood flow changed significantly only when the stenosis ratio was increased to more than 70%, and the situation did not have significant difference after the application of remote displacement except the model with stenosis ration of 90%.

Conclusions: The result suggests that the rotatory manipulation does not have an obvious influence on the blood flow in the CoW when the stenosis of ICA is less than 90%, and this kind of manipulation is suggested to be a safe technique in most of the clinical applications.

MeSH Keywords: **Carotid Stenosis • Circle of Willis • Finite Element Analysis • Manipulation, Spinal**

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Background

The CoW is a heptagonal vascular circle with the function of auto-regulation when the inflow of the CoW fluctuates or decreases [1]. It consists of the anterior communicating artery (ACoA), bilateral posterior communicating artery (PCoA), A1 segment of anterior cerebral artery, P1 segment of posterior cerebral artery, bifurcation of internal carotid artery, and top of basilar artery. Both sides of the carotid artery system and the vertebrobasilar system are connected by the CoW. As the primary collateral pathway, it was considered as a safeguard mechanism against cerebral arterial stenosis or occlusion [2]. Disease or vibration of the CoW was considered to be closely connected with ischemic cerebral disease. Detailed knowledge of the cerebral hemodynamics inside the CoW is important for clinical application.

Blood is delivered to the brain through the 2 ICAs and the basilar artery (BA). As an important pathway for cerebral blood supply, the internal carotid artery is a popular site for stenosis worldwide [3]. Stenosis of the ICA is closely associated with stroke, transient ischemia attack [4], and cognition impairment [5]. The synergistic effect of cerebral artery stenosis and other arteries, such as the intracranial arteries and carotid artery system, might increase the risk of ischemic stroke [6]. Anatomical variation of the CoW also plays a significant role in the mechanism of stroke [7]. The compensatory ability of the normal CoW could maintain the required efferent flow rates in case of occlusion of an ICA [2]. Several cohort studies showed that compensatory capability of the CoW could maintain the required efferent flow rates in case of occlusion of an ICA. However, the process of blood redistribution in the CoW was not fully revealed in the development of ICA stenosis [8].

Rotatory manipulation is a frequently applied therapy in treating cervical pain, stiff neck, dizziness, and visual impairment, generally known as a safe and effective therapy [9]. Following its wide application, some serious complications were presented, primarily in case reports [10]. The most frequently reported complications are vertebrobasilar accidents (VBAs), which mostly appear as stroke or TIA. There is a controversy about whether a strong association between neck manipulation and stroke exists. It is popularly accepted that conclusive evidence is lacking for a strong association between neck manipulation and stroke, but is also absent for no association. Ultrasonic Doppler, DSA, and MRA are sensitive in detecting the hemodynamics in the CoW, but there is no data in the literature about the association between rotatory manipulation and cerebral blood flow [11].

The finite element method has recently been used to validate the behavior of material under different circumstances, without the need for physical models [12]. Over the years, numerous

idealized finite element models of cerebral circulation have been developed and used for further researches, but few of them focus on the CoW. Anatomical variability among individuals is large, and the normal structure of the CoW is relatively uncommon. Only 40% of the population has a complete, well-balanced circle like the ones shown in anatomy textbooks [13]. Realistic patient-specific models which can provide new insight into the cerebral hemodynamics have recently been attempted. The first blood-flow 3-D model of the CoW from MRI data was created by Cebra [14]. Although computational fluid dynamics has recently been developed, credible finite element solid-fluid coupling models which consist of vessel and blood-flow are still absent. A solid-fluid coupling model based on MRI data was created first in the current study and then several different hypotheses were tested in this study:

1. There is no obvious blood flow in ACoA and PCoA in the healthy model.
2. Accompany increased degree of stenosis, the mass flow that passes the CoW increases as well.
3. There is no significant change in blood flow whether the rotatory manipulation is applied or not.

Material and Methods

Medical image data

In order to construct a patient-specific model of the CoW, a series of magnetic resonance angiography (MRA) images were adapted. Those images come from a 23-year-old female volunteer, whose former MRI scan showed no obvious cerebral vessel disease or stenosis of ICA. The MRA images typically consist of a stack of 2D slices of constant width covering the volume of interest. Most of the arteries appear whiter than the surrounding tissue, causing a contrasting grey signal. Typical image sizes are approximately 150 slices of 464×284 pixels. These images were stored in DICOM format [14].

Patient-specific model

We processed the DICOM MRA images using Mimics v. 10 (Materialise, Leuven, Belgium) according to the following steps:

1. Analyze the threshold and select the region of interest. The area of the CoW can be distinguished in green.
2. Each slice of these images should be checked and edited to fill the holes and interrupt the vessel, eliminate secondary branches, and leave the CoW only.
3. Region growing and calculate 3D, a rough 3D model can be obtained; although this model contains only surface instead of body, it is enough for the next step [15].
4. Vessel centerline was extracted and processed to another software, the Space Claim Direct Modeler, by which the centerline can be divided into many points.

Table 1. Internal diameters and thickness of all the branches of CoW.

| Date | Vessels | | | | | | |
|-----------|---------|------|-----|------|------|------|------|
| | ICA | BA | ACA | MCA | PCA | ACoA | PCoA |
| ID (mm) | 3.6 | 3.24 | 2.4 | 2.86 | 2.14 | 1.48 | 1.46 |
| Thickness | 0.5 | 0.4 | 0.3 | 0.36 | 0.27 | 0.19 | 0.18 |

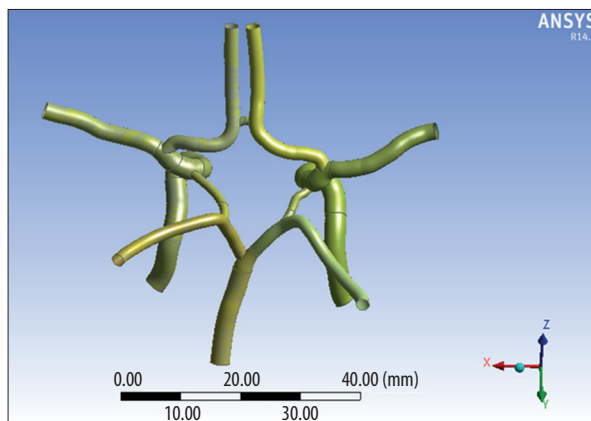
SDCM is the preprocessor module of ANSYS v. 14.5 (ANSYS Inc., Pittsburgh, USA), mostly focusing on 3D modeling.

1. The CoW consists of 12 vessels: 3 inlets (2 ICAs and a BA), 6 outlets (2PCAs, 2MCAs and 2ACAs), and 3 communicating arteries (1 ACoA and 2 PCoAs). Centerlines of each vessel were formed by ligaturing the points, leaving the joint of vessels unconnected.
2. A circle was dragged with the distal point as its center to form the distal transverse section. The internal diameters (ID) and thickness are shown [7] in the Table 1.
3. Drag the transverse section face along each centerline to form those vessels.
4. All of the 12 vessels were joined to form a new body named "blood", the blood was considered as the fluid part of the basic healthy model. The model was processed to Workbench.

The ANSYS Workbench platform is the framework with bidirectional CAD connectivity, meshing, parameter management, and optimization tools [16].

1. To form the solid part of a complete model in the Design Modeler (DM) module, the vessel was created by endowing the blood with a shell unit (surface from face), and the shell thickness of each vessel section is shown in Table 1. A healthy fluid-solid geometry model of the CoW was constructed (Figure 1).
2. Models of different degrees of stenosis were constructed. The right ICA was chosen as the stenosis place. Nine points in the centerline of ICA were nearly in a row and were picked out without linking to other points. Drag a circle as the healthy model to act at each of the 9 points. Diameter of center point circle faces was coherent with different degrees of stenosis. The degree of stenosis is the ratio of the minimal cross-sectional luminal area at the apex of the stenosis to the cross-sectional luminal area in a section upstream from the apex without any narrowing.

Each length of the minimal distal between the apexes of stenosis (A) is shown in Table 2. As there are 9 separated points and 8 segments of surface, the shell unit (surface from face) thicknesses differ according to degree of stenosis, as shown in Table 2.

**Figure 1.** The healthy fluid-solid geometry model of the CoW.

Meshing

The solid and the fluid parts of the models were meshed. The blood was meshed mostly by hexahedron element, with the method of patch confirming independently, and a restriction in body sizing. No inflation or swapping method was applied in fluid parts of the model. The healthy model was meshed into 298574 elements and 61592 nodes.

All the contact was clear. Vessel and plaque were considered to be integrated. The vessel and plaque were meshed mostly by hexahedron elements, with the method of patch confirmed independently, and a restriction in body sizing (minimal element size decreased from 0.26 mm to 0.2 mm). The shell unit element size in the stenosis area was restricted to 0.1 mm in another body sizing. The healthy model was meshed into 67382 elements and 67417 nodes. The composite joint of different vessels has co-nodes to ensure a smooth transition between different diameters.

After the meshing, a sensitivity test was performed to ensure sufficient meshing refinement. Skewness was <70%, with an average of 0.23. The element quality of solid mesh was about 0.85.

Material properties and boundary condition

Blood was considered as a viscous, elastic, incompressible, Newtonian fluid. Arteries and plaques used in FEM are usually simplified as homogeneous, isotropic, and linearly elastic

Table 2. Shell unit (surface from face) thicknesses according with different degree of stenosis.

| R of stenosis | 15% | 30% | 45% | 60% | 70% | 80% | 90% |
|----------------|------|------|------|------|-------|------|-------|
| A (mm) | 3.06 | 2.52 | 1.98 | 1.44 | 1.08 | 0.72 | 0.36 |
| Segment 1 (mm) | 0.57 | 0.64 | 0.7 | 0.77 | 0.815 | 0.86 | 0.905 |
| Segment 2 | 0.63 | 0.77 | 0.9 | 1.04 | 1.13 | 1.22 | 1.31 |
| Segment 3 | 0.7 | 0.9 | 1.11 | 1.31 | 1.445 | 1.58 | 1.715 |
| Segment 4 | 0.77 | 1.04 | 1.31 | 1.58 | 1.76 | 1.94 | 2.12 |
| Segment 5 | 0.77 | 1.04 | 1.31 | 1.58 | 1.76 | 1.94 | 2.12 |
| Segment 6 | 0.7 | 0.9 | 1.11 | 1.31 | 1.445 | 1.58 | 1.715 |
| Segment 7 | 0.63 | 0.77 | 0.9 | 1.04 | 1.13 | 1.22 | 1.31 |
| Segment 8 | 0.57 | 0.64 | 0.7 | 0.77 | 0.815 | 0.86 | 0.905 |

Table 3. Mass flow rate in each outlet and its proportion.

| Position | Proportion in literature (%) | Proportion used (%) | Mass flow-rate (g/s) |
|----------|------------------------------|---------------------|----------------------|
| ACA | 15–20% | 18% | 1,188 |
| MCA | 55–60% | 58% | 3,828 |
| PCA | 20–25% | 24% | 1,584 |

incompressible material. As the Reynolds number is less than 200, the blood can be assumed as laminar flow instead of turbulence, without conduction of heat. The material properties were defined as below [17]:

For the blood, ρ (Density) = 1056 Kg/m³, η (Viscosity Coefficient) = 0.0035 Pa·s.

For the vessels, ρ = 1150 Kg/m³, E (Modulus of Elasticity) = 1.6 × 10⁶ Pa, ν (Poisson's ratio) = 0.42.

The boundary conditions were configured in fluent, transient, and coupling modules.

In the mechanic module:

1. Fixed support. Considering that all the intracranial vessels barely have movement or degree of freedom, a fixed support was inserted into each inlet and outlet except the right ICA.
2. Remote displacement. Direction of remote displacement was set to be counter-clockwise, for about 60°, loading on the far end of the right ICA.
3. Intracranial pressure was imposed upon outer faces of vessels, accounting for about 1596 Pa.
4. The outer face of blood was appointed as a fluid solid interface, which was the conducting surface in the next coupling computation.

In the fluent module:

1. All of the 3 inlets were appointed as pressure inlet, with the pressure of 12265.6 Pa, which is the average blood pressure.
2. All of the 6 outlets were assigned as mass flow-rate outlet. The total mass flow-rate was known as 13.2 g/s, and proportion of each outlet had already been found in previous studies [18], shown in Table 3.
3. Monitor surface. Three monitor surfaces were selected to supervise mass flow-rate in the 3 communicating arteries.
4. Dynamic mesh was activated, with the method of smoothing and remeshing, and the meshing zones consisted of deforming in blood and right ICA.

In the system coupling module:

1. Solving in the fluent was scheduled to be prior to the transient in the coupling sequence, enabling the vessel filled with blood before the couple.
2. Before updating the coupling program, both transient and fluent were allowed to run independently to assure the convergence of each module.
3. Before the trial operation of transient, a modal analysis should be carried out to ensure the structural stability (Figure 2).

Model validation and solution

The model was validated before solution. We compared the mass flow obtained from the monitor surfaces of 3

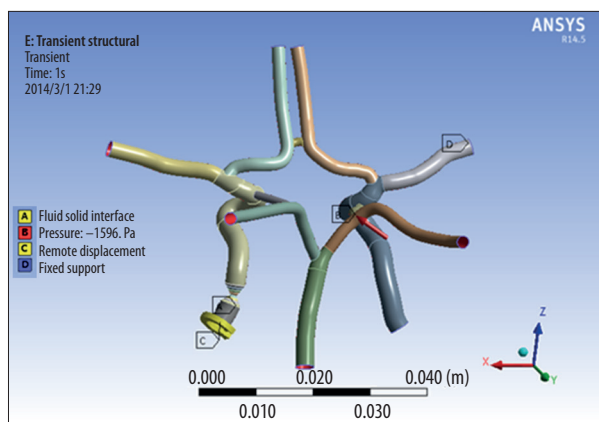


Figure 2. Boundary condition of models.

communicating arteries to the corresponding data we found in previous studies [15]. The flux passing through ACoA and PCoA were 0.14, 0.11, and 0.10 in the healthy model, respectively, which was negligible compared with the total mass flow, and the flow could hardly be seen in a dynamic graph. A linear increase of the flux in all of the 3 arteries could be found as the degree of stenosis increased. The flow in BA accounted for nearly 20% of total inlet quantity, 1/4 of which is in bilateral ICA, matching reality.

We evaluated the mutual impact between blood flow change and vessels by the following aspects:

1. Comparison of mass flow-rate in the 3 communicating arteries monitor surface in all of the pre- and post-manipulation models as a measure of rotatory manipulation influence.
2. Von Mises stress distribution and total deformation in the vessel (especially in the right ICA) in the models during and after the loading of 60°'s remote displacement, as a measure of potential injury induced by the rotatory manipulation.
3. Von Mises stress distribution and total deformation in the vessel (especially in the right ICA) in the post-stenosis models as a measure of potential injury induced by the stenosis to the vessel wall.

The hemodynamics in both inlets and outlets can also be observed, but it is not the main focus of this article.

Results

A model of a normal CoW was constructed from MRA imaging data, and other models that included different degrees of stenosis were built based on it. The mass flow rates were measured in ACoAs and PCoAs of all the models, including the healthy model and every degree of stenosis models. Figure 1 shows that the initial flow (g/s) before the implementation of manipulation were 0.14, 0.11, and 0.10 in ACoA, right PCoA, and left PCoA, respectively. With the increase of stenosis rate in the

right ICA, the flux increased obviously in ACoA and right PCoA, up to 2.8 and 2.3, and the augmentation in the left PCoA was 0.29, which was not as distinct as those in the other 2 communicating arteries. Once the stenosis rate was up to 70%, obvious ischemia appeared in the ICA section of the right ACA, to maintain the outflow of ACA, and the flow in the 3 communicating arteries kept rising gradually. We noticed that the flux to ACA was mainly from ACoA. The direction of blood in the CoW all went from posterior to anterior, from left side to right side, which meant it flowed to the ischemia area.

After the application of manipulation, the blood flow direction showed no significant change. The mass flow in all 3 arteries remained almost the same as before or had moderate growth when the stenosis rate of ICA was not more than 80%. As long as the degree of stenosis was at least 90%, the flux decreased sharply from 2.8 to 1.4, 2.3 to 1.2, and 0.29 to 0.21. Taking the right side as an example, the right ICA supplies blood not only to the right MCA and right ACA but also to the left ACA through the ACoA, and it can also be seen that blood flows from the posterior to the anterior part of the CoW through the right PCoA, and then in the opposite direction (Figure 3).

Discussion

In the 1960s the mathematics simulation model of the cerebral arterial circle was created by Clark et al. accompanied with the development of computer-aided technology [19]. The digital model was improved in the following 3 decades, and changed from steady flow to unsteady flow. The material property was changed from linear elastomer to nonlinear viscoelastic body. Due to their over-complexity and neglect of vessels, those models were unpractical. After a reasonable simplification, a lumped parameter model of unilateral ICA system was created by Takashi, exclusive of opposite-side and communicating arteries [20]. A lumped parameter model of the CoW was built by Ding et al. [21]; this model is useful in detecting the cerebrovascular blood flow dynamic indexes but is useless in visually displaying the blood flow inside the vessels. The finite element method was first used in constructing the first 3D finite element model of the CoW by Cebra et al. in 2003 [10]. A 2D model of the CoW was created by Ferrandez and David [22]. Further computational fluid dynamics analysis found that the vascular resistance was consistent with animal experiments, proving the collateral compensative capacity of the CoW [17]. A 3D model of the CoW was simulated by Moore and David at 2006 [3], but blood-vessel interaction was also neglected. The current finite element-simulated research on the CoW assumes that a vessel can be seen as a rigid body, regardless of the hemodynamics induced by vessel deformation, and the interaction between blood and vessel was not taken into account.

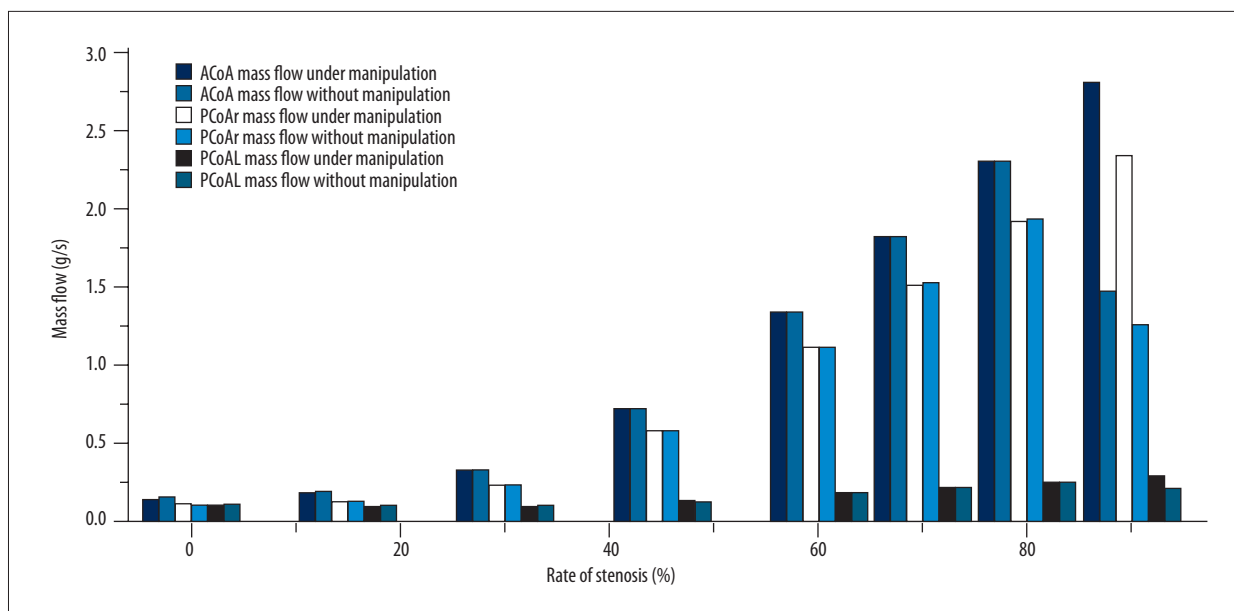


Figure 3. Mass flow rate in the 3 communicating arteries under different conditions.

The most accurate image data so far is an image-based normal 3D finite element model of the CoW, with an MR slice thickness of 0.1 mm. As mentioned earlier in the section on validation, after a reasonable simplification, the models will not be too complicated, and can be used in further research. Compared with previous models [8], this model is the first fluid-solid coupling model instead of fluid model or solid model, and is the first model that has a 2-way coupling pattern instead of 1-way. Consideration of the interaction between vessel and blood flow would be useful in improving the veracity of simulate calculation; at the same time, large deflection analysis was also taken into account to make it closer to the actual situation.

It is generally accepted that less severe stenosis (<70% diameter narrowing) is not associated with a decrease in the volume flow rate through the ipsilateral artery, and the presence of severe stenosis at the carotid can diminish the flow-related enhancement in the downstream arterial bed [4], which was confirmed in our research by the decrease of flux in the ACA from the ICA. Variation of the CoW is considered to be a major risk factor for strokes [7]. No previous data was found to show change of blood flow in the CoW in patients with stenosis of the ICA. By monitoring blood flow hemodynamic change in the CoW, we noticed that the blood direction and the flow through the right inlet (right ICA) keep steady when the rate of stenosis is lower than 70%, which confirmed here that if the stenosis rate is lower than 70%, it rarely influences the intracranial blood circulation, mostly because 30% of the flow in the ICA is much larger than that in the CoW. But when the degree is higher than 70%, ICA itself is not enough to compensate for minor and transient reductions in blood flow, then

primary collateral circulatory channels, the CoW, would have to radically raise its flow to maintain the flow in the intracranial main artery. As noted in this study, flux in the ACA is mainly from ACoA, and blood flows from left to right side, from posterior to anterior (to the ischemia zone), variation of the CoW would block this process and lead to worse ischemia, and absence of ACoA would lead to low out-flux from the ACA, which creates high risk of stroke.

Whether the cerebral artery hemodynamic conditions would be significantly affected by rotatory manipulation or not remains controversial. Most of the existing research concludes that cervical rotation may not significantly reduce vertebral artery blood flow in healthy individuals [23]. Haynes and Milne (2001) concluded that cervical rotation did not significantly reduce blood flow by involving both the extra-cranial and the intracranial vertebral arteries [24]. Mitchell found reductions in blood flow velocities in 54% of their sample, but the amplitude of variation had no obvious difference [25]. Some other authors found a significant increase of V_{max} of the intracranial artery in patients with atherosclerosis of the ICA [26]. Conclusions from the mean velocity ratio have subsequently been criticized as being an unreliable measure of blood flow [27]. It is currently unknown if the manipulation will affect flow in the CoW. We compared the mass flow rate in the same model with and without remote displacement. Flux through the 3 communicating arteries changes slightly when the stenosis ratio is less than 90%, which confirms that the influence of blood flow rotation in the CoW is insignificant in most patients. The blood flow through the stenosis area would not fluctuate drastically under rotatory manipulation. The diameter itself is big

enough and qualified to compensate the influence from the manipulation. The action time should not be too short, considering that the compensation requires for some time to be completed [28]. In the case of severe stenosis (ratio of stenosis >90%), the flux through the 3 communicating arteries drops sharply and the CoW is not able to compensate for loss of blood in the ischemia zone induced by the manipulation. Manipulation would be dangerous in aggravating the condition of ischemia, leading to severe sequelae, for example, stroke and TIA, as was described in previous reports.

Conclusion

Despite some limitations, we suggest that rotatory manipulation is safe for most patients, but can be dangerous to those who have severe stenosis in ICA. Clinicians should be cautious in recommending cervical rotary manipulation to individuals who potentially have severe (>90%) stenosis of the internal carotid.

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Limitation

Several challenging problems still remain to be solved. The anatomical model is one of them, and the precision of the models can be improved. The image thickness can be as thin as 0.01 mm in the digitized virtual human data [29]. The model has been simplified in several aspects. For example, the ICA here was simplified to a nearly straight vessel, which in fact was divided into 2 parts (extra-cranial and intra-cranial) and 7 segments. The specification of physiologic flow conditions is another challenging problem, and perhaps the most complicated one is blood pressure and mass flow changes according to the heartbeat, but in our analysis, blood was thought to be steady without fluctuation. Because this research was carried out in young volunteers who had a total circle of Willis, it remains unclear if the same situation happens in elderly people if the CoW is incomplete. Due to the tremendous amount of computing required (the working condition file of each project is close to 2G), we propose that project for a later study.