論 文 の 内 容 の 要 旨

論文題目　Development of computational method for investigation of cerebral hyperperfusion syndrome initiation using patient-specific 1D-0D simulation （過灌流症候群の検討のための1D-0Dシミュレーション手法の開発）

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Background:

According to the report of the World Health Organization (WHO), cardiovascular diseases (CVDs) are the leading causes of death worldwide. In 2012, an estimated of 17.5 million people died from CVDs, representing 31% of all global deaths. Of these deaths, an estimated of 6.7 million (11.9%) were due to stroke. The ischemic stroke is the more common type of stroke (accounts for more than 87% of all stroke cases) and is mainly caused by a stenosis. For example, stenosis in the carotid arteries will prevent blood from flowing to the brain hence causing an ischemic stroke.

Invasive treatment (surgeries) are considered for symptomatic patients with stenosis ratio greater than 50%. Carotid endarterectomy (CEA) is the criterion standard for invasive treatment of carotid stenosis. CAS has been proposed as an alternative to CEA in the last decades.

Cerebral hyperperfusion syndrome (CHS) is one of the main risks after CEA and CAS. It is characterized by throbbing ipsilateral frontotemporal or a periorbital headache, face and eye pain, macular edema, vomiting, and visual disturbances, focal motor seizures with frequent secondary generalization, focal neurological deficits, and intracerebral or subarachnoid haemorrhage.

CHS usually occurs within several hours to several days after the surgery. Almost all reports detected the immediate postoperative hyperperfusion (most commonly defined as >100% increase in cerebral blood flow over baseline) before the initiation of CHS.

Since the hemodynamics play an important role in the initiation of CHS, the detailed information of blood flow in the cerebrovascular system would significantly benefit the understanding and treatment of CHS. Due to the limitation of medical imaging technologies in the spatial and temporal resolution, the obtainable blood flow information in the CoW is quite limited. A numerical method combining with medical imaging data were considered to be a promising way to solve this difficulty.

Objectives:

Due to the limitation of medical imaging techniques, measurable hemodynamics in the cerebral circulation is limited. The treatment strategy is largely based on the doctors' experience and statistical reports. A method that can provide detailed and reliable hemodynamics for an individual will greatly improve the treatment of carotid stenosis.

This research aimed at developing a numerical method for investigation of the CHS initiation. The prediction of the postoperative flow rate is the main difficulty for the prediction of the CHS initiation. Since the flow rate is dominantly affected by the local peripheral resistance, the estimation of the postoperative peripheral resistance is significantly important. We assume the vessel remodeling does not happen immediately after the surgery, therefore the postoperative peripheral resistance is considered to be the same with the preoperative one.

The objectives of this research are:

1. To develop a numerical method by incorporating the medical data into the 1D-0D simulation for estimation of the peripheral resistance.
2. To investigate the effects of the uncertainties in the medical imaging data on the simulation results.
3. To explore the possibility of our method for investigation of CHS initiation.

Results and conclusion:

<u>Development of patient-specific 1D-0D simulation system</u>

We investigated the two different ways to estimate the peripheral resistance using SPECT data: SPECT data only (Sim_SPECT); SPECT data combined with PC-MRA data (Sim_PS).

- ✧ The method of adjusting the peripheral cerebral resistance was developed to match the calculated efferent flow rates with the reference flow rates (measurement data).
- ✧ Using only SPECT data as the reference flow rates (Sim_SPECT), the patient-specific flow distribution in the CoW can be obtained with our simulation system. However, the absolute value of calculated flow rates in the CoW showed differences from the PC-MRA measurement data.

- ✧ Combining SPECT with PC-MRA data as the reference flow rates (Sim_PS), the magnitude of flow rate in each artery of the CoW can be obtained from our simulation.

Quantification of uncertainty and sensitivity analysis

The effects of uncertainties in the medical imaging data on simulation results were investigated:

As for the vessel diameter, we discussed the effects of model uncertainty and segmentation uncertainty respectively.

- ✧ As for the model uncertainty, the detailed vessel geometry (DVG) model can capture some important details of the vessel geometry that are missing in the simplified vessel geometry (SVG) model. This difference led to the different vessel resistance in the communicating arteries that sensitively affected the flow distribution in the CoW.
- ✧ Sensitivity analysis showed that the segmentation uncertainties in the communicating arteries displayed much more impact on the flow distribution in the CoW than those in the other arteries.
- ✧ We developed a method to optimize the diameters extracted from the medical imaging data. The communicating arteries' diameters were adjusted to match the calculated afferent flow rates with the measurement data (Ultrasound data). A case study showed the blood flow in the CoW was significantly affected by this adjustment.

As for the effects of uncertainties on the prediction results, we discussed the uncertainties in stenosis ratio (CT and DSA data), inflow rate (ultrasound data) and *CBF* (SPECT data) respectively.

- ✧ Uncertain in the measurement of stenosis ratio due to segmentation uncertainty was quantified. Sensitivity analysis showed this uncertainty dominantly affected the prediction of the increase in postoperative flow rate from preoperative one.
- ✧ Sensitivity analysis showed that prediction of an increase in postoperative flow rate from preoperative one was moderately affected by the uncertainty in the flow rate measurement in the stenotic artery.

Sensitivity analysis showed that prediction of an increase in postoperative flow rate from preoperative one was not obviously affected by the uncertainties in flow rate measurement in the normal artery and the uncertainties in *CBF*.

Estimation of CHS initiation

We developed a method to predict the postoperative flow rates using the peripheral resistances estimated from the patient-specific 1D-0D simulation of pre-surgery. We applied this method to a patient who received the staged CAS surgery.

- According to the SPECT measurement data, the patient in this study showed a high risk of CHS. If the measurement uncertainties in the medical imaging data were considered, the simulation showed the regular CAS surgery could lead to significant increase in postoperative flow rate from preoperative one comparing to the staged CAS surgery.