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A model of blood supply to the brain via the carotid arteries: Effects of obstructive vs. sclerotic changes

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ABSTRACT

The carotid artery is one of the major supply routes of blood to the brain and a common site of vascular disease. Obstructive and sclerotic disorders within the carotid artery impact local blood flow patterns as well as overall impedance and blood supply to the brain. A lumped parameter model and an experimental in-vitro flow loop were used to study the effects of local stenosis and stiffness in the carotid artery based on a family of phantoms with different degrees of stenosis and compliance. The model also allows independent examination of the effects of downstream resistance and compliance. Mild to moderate stenosis was found to lead to minimal (~1%) reduction in blood supply to the brain. Reduction in mean internal carotid artery (ICA) flow was statistically significant ($p < 0.01$) only above 70% stenosis. On the other hand, a three-fold increase in stiffness of the carotid artery, as might occur in aging, was found to lead to a modest yet statistically significant reduction ($p < 0.01$) in mean ICA flow. Effects of changing downstream resistance and compliance were examined. For a given pressure waveform, reduction in downstream compliance led to altered waveform shape and reduction in peak systolic flow rates where the mean flow rates were not altered. Increased downstream resistance resulted in drastic reduction in mean flow rates.

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1. Introduction

Stroke resulting from ischemic episodes or thrombotic events within the brain remains a leading cause of death in North America [1]. The common carotid artery (CCA), carotid sinus, and internal carotid artery (ICA), which form a major supply route for blood to the brain [2], are therefore the subject of much clinical concern [3,4]. Both carotid atherosclerosis and arterial compliance are related to risk factors associated with the occurrence of stroke [5–7]. A considerable body of theoretical and experimental work has been aimed at studying the nature of hemodynamic disruptions that may occur as a result of disease within the carotid artery or sinus [8–17]. However, the major focus of these studies has been on local hemodynamic changes, or in the case of clinical studies, on the local pathology (e.g. plaque composition). The present study focuses on the global effects of relative changes in vascular resistance

and compliance in terms of blood flow to the brain and the relationship of pressure and flow rate waveforms (overall impedance).

We consider two types of changes within the carotid arteries that may lead to hemodynamic disruptions: obstructive changes [18–22] – leading to a direct reduction in the physical space available to the flow, and sclerotic changes [18–22] – affecting the mechanical properties of the arterial wall. Both are important clinically in terms of the different pathologies that may lead to these changes, and hemodynamically for the different resulting consequences for blood supply to the brain. More specifically, obstructive changes may result from atherosclerotic plaques [2,18–22] and may lead to an increase in resistance to flow, while sclerotic changes (either local or global) may result from arteriosclerosis associated with disease or aging [18–23] and may lead to a disruption in the pulsatile dynamics of the flow.

Local disruptions within the carotid arteries are used to extrapolate some of the global consequences to the system specifically in terms of blood supply to the brain using two parallel avenues: an experimental setup, with a physiologically based phantom of the carotid arteries and sinus coupled with physiologically based resistance and compliance components downstream [17,24], and a

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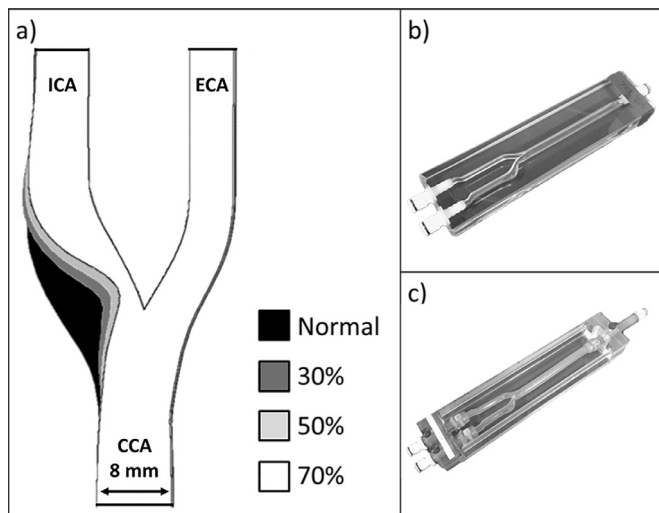


Fig. 1. (a) Family of carotid-bifurcation phantom geometries with increasing plaque progression (stenosis severity) overlaid on the normal (plaque-free) geometry. CCA, ICA, and ECA inner diameters are 8, 5.5, and 4.6 mm, respectively. (b) Rigid phantom (50% stenosis severity) consisting of a hollow flow channel in a PDMS block. (c) Compliant phantom (50% stenosis severity) consisting of PDMS vessel with 1-mm thick walls mounted inside an acrylic box.

theoretical lumped parameter (LP) model [25–28] that allowed us to match to experimental data and extend the experimental results beyond the parameter values available in the experiment as a prediction tool [29,30]. LP models are helpful in demonstrating the relationship between pressure and flow rate waveforms, and thus aid in understanding the shapes of the resulting waveforms. They can give meaning to the impedance of the system [31]. The LP model was used for this study as an efficient means to characterize the impedance of the experimental system, specifically the vascular compliance and resistance. The accuracy of the LP model is dependent upon its design and must be validated. Traditionally, LP models have been used extensively to calculate compliance. However, an LP model is a simplification of the overall system, and therefore will tend to be less accurate than numerical simulations. Only limited work on blood flow to the brain via the carotid arteries has been done in the past using this methodology [32]. The aim of our study was to evaluate and quantify the effects of local disturbances within the carotid as well as global disturbances, such as changes in overall vascular resistance and compliance, and what effect these ultimately have on blood supply to the brain and the pressure-flow relationship between the pressure and flow-rate waveforms. This study helps to develop a framework for understanding and quantifying global changes that are sometimes not reflected in the local ICA hemodynamics that have previously been studied [17,24,33–35]. It also offers the opportunity to continuously improve experimental setups to be more reflective of the physiological system.

2. Methods

2.1. Experimental setup

The study incorporates a family of carotid artery bifurcation phantoms (Fig. 1a) starting with normal (plaque-free or stenosis-free) geometry and progressing to eccentric 30%, 50%, and 70% stenosis of the ICA, based on diameter reduction relative to the downstream ICA (i.e. NASCET criteria: [36,37]). Realistic, vascular phantoms that have been previously fabricated were used [17,24,33–35]. They are based on idealized geometries obtained through a quantitative analysis of diseased carotid bifurcations

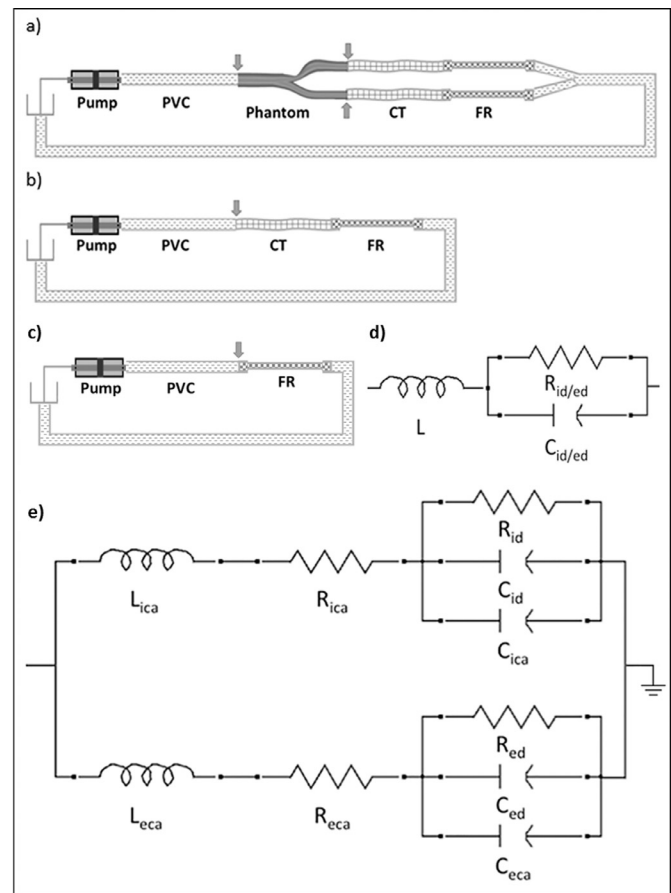


Fig. 2. (a) Schematic of in vitro flow loop incorporating a carotid bifurcation phantom with downstream compliant tubing (CT: 30 cm) and flow resistors (FR: ICA 15 cm, ECA 30 cm) to mimic downstream vasculature. Pressure and flow-rate waveforms were measured at locations indicated by arrows. (b) A reduced flow loop used to determine parameter values for the downstream elements containing both CT and FR. (c) The most simplified flow loop containing only FR. (d) The simplified LP model used to determine the downstream parameters. (e) The LP model used as an analogue of the in vitro flow loop. Resistance (R), compliance (C), and inductance (L) were placed as shown representing different parts of the flow loop, with subscripts 'ica', 'eca' referring to ICA and ECA branches of the phantom and 'id', 'ed' referring to downstream elements from the ICA and ECA, respectively.

[38] with geometries extrapolated from 62 patients with ICA stenosis. They provide a more realistic approximation of stenosis shape than simpler pinched-tube or Y-bifurcation models previously used, and thus more representative of human physiology. Different geometries have been constructed with either a normal (stenosis-free) bifurcation or varying degrees of stenosis in the ICA based on the NASCET criteria [36,37]. The study concentrated on eccentric stenosis because it has been found to have increased risk of cerebrovascular events [39]. Phantoms were manufactured from polydimethylsiloxane (PDMS) (Sylgard 184, Dow Corning) [35] using a lost-material method to create a low-compliance (effectively rigid) version with hollow flow channel in a block of PDMS (Fig. 1b), and for the 50%-stenosed geometry, an additional, more compliant phantom [34] – consisting of a vessel with 1-mm thick PDMS wall mounted in a box (Fig. 1c). For simplicity, these have been dubbed 'rigid' and 'compliant', respectively.

The in vitro flow loop (Fig. 2a), as previously described [17,33], consisted of life-size carotid bifurcation phantoms of varying geometry and compliance (Fig. 1), downstream resistance and compliance components, a programmable volumetric-displacement pump [40] (CompuFlow 1000, Shelley Medical Imaging, London CAN), and suitable blood-mimicking-fluid (viscosity

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