CEREBRAL BLOOD VOLUME CHANGES DURING BRAIN ACTIVATION

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Intoduction: FMRI studies have begun to utilize changes in cerebral blood volume (CBV) as well as BOLD contrast methods [1,2]. CBV changes may provide better localization of neural activity changes [3]. Among important contributors to volume changes are the capillary vessels [4], entailing changes of their mean diameter [5], as confirmed by microscopic studies, which quantify the average capillary diameter change during elevated cerebral blood flow (CBF) to be 5 – 10% [6]. However, the finding that capillaries expand during increases of CBF is still poorly recognized in the literature [7] and the concept of CBV itself has received little analysis. According to the Monro-Kellie doctrine, the sum of cerebral blood volume, cerebrospinal fluid (CSF) volume and brain tissue volume must remain constant over time to minimize changes of intracranial pressure (ICP) [8], due to the inextensibility of the skull and spinal canal. An increase of one compartment can only occur at the expense of another [6,9]. The question becomes: how can cerebral capillaries expand inside the rigid cranium, keeping brain tissue and CSF volume constant, without dangerously increasing the ICP? Modelling of the BOLD response and its physiological origins usually fails to address this conceptual issue [10,11]. We propose that changes in CBV are largely facilitated by exchange of water between capillaries and surrounding tissue via the plentiful aquaporin channels [12]. To explore this idea, we developed a novel hemodynamic boundary value model and found approximate solutions using a numerical algorithm. We constructed a macroscopic experimental model of a single capillary to provide biophysical insight. The experimental and theoretical approaches respect the Monro-Kellie doctrine as well as the elastic and permeable properties of capillaries.

Methods: Activation and hypercapnia-based changes in CBV were modelled via the Navier-Stokes and continuity equations in radial coordinates. Additionally, a non-linear differential equation modelled the motion of the capillary wall and its elastic properties. Matching boundary conditions for wall permeability and the geometry of the capillary were used. Solutions were found using a numerical algorithm, in which the capillary length was split into a finite number of compartments. The results of CBF, static pressure and capillary radius for each compartment were used to feed the next compartment. Simulations were performed with different realistic physiological parameters. Capillary volume, time courses of radius changes, and pressure distributions were compared, for two levels of input pressure change ("stage1" and "stage2").

In the experimental approach, a thin elastic balloon made of rubber was used to simulate a single capillary. The balloon, running between two rigid nozzles, was mounted inside a rigid cylindrical cavity constructed of Perpex (representing the cranium) which was filled with water to simulate the Monro-Kellie situation. Recordings were made by video camera. The effects of capillary wall permeability were studied using a perforated balloon. Diameter changes of the balloons and pressure changes within the cavity were observed when inlet pressure was increased. The connection of one of the nozzles to a water reservoir allowed a precisely defined input pressure. Water exchange through the permeable balloon wall was monitored by putting ink as a marker into the water reservoir (see fig. 1).

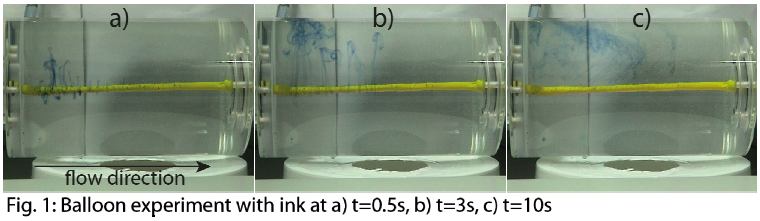

Fig. 1: Balloon experiment with ink at a) t=0.5s, b) t=3s, c) t=10s

Results: The numerical model gave capillary CBV changes of about 17% for realistic initial flow parameters and arterial pressure changes. Typically, capillary CBV changes took place over a few seconds (see fig. 2b). The capillary radius change decreased along the z-axis, with a continuous pressure drop from the arterial to the venous end in equilibrium (see fig. 2a).

Vascular response to neuronal activation was simulated in the experiment by increasing the arterial input pressure and inflow into the balloon. When the balloon was impermeable, negligible volume changes were observed, even with highly increased cavity pressures. With the permeable balloon, an average volume increase of 21% was seen (see fig. 3a and b) without significant changes in cavity pressure. Using ink as a perfusion marker, water exchange through the balloon wall was observable. The ink moved radially out of the balloon along its first half, gained a slow axial velocity component and moved to the venous end. There, some of the ink permeated back into the balloon.

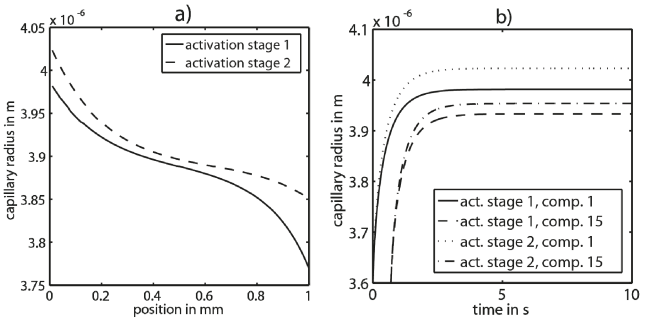

Fig. 2: Compartment model. a) balloon radius, b) radius time courses

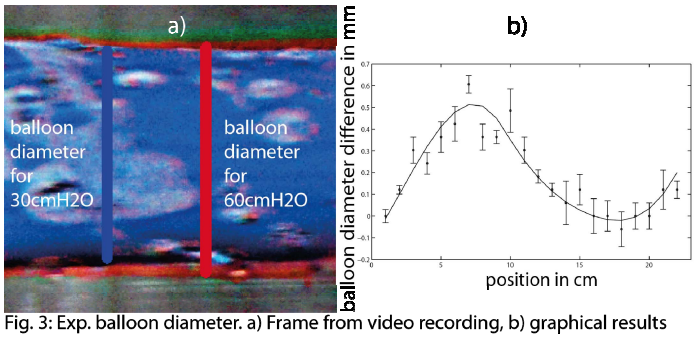

Fig. 3: Exp. balloon diameter. a) Frame from video recording, b) graphical results

Discussion: The time constants calculated using the numerical model are comparable with those measured in-vivo with fMRI [2] and in-vitro with optical techniques [4,13]. The negative pressure gradient along the flow axis is consistent with Starling's hypothesis [14]. Regarding radius changes, note that in the experiment the radius of the balloon at each end is fixed due to the nozzle mounting. In equilibrium, along the middle section of the balloon, the radius decreases roughly in accordance with the numerical simulation. This additional boundary condition was absent from the theoretical model. Volume changes of 17% derived by the compartment model and 21% observed in the experiment are comparable to those measured in vivo, for instance with VASO [2]. When the balloon was impermeable, a large ensuing pressure increase within the cavity was observed, demonstrating the importance of capillary permeability during neuronal activation processes. Both theoretical and experimental models suggest that capillary wall permeability to water is a crucial factor in preventing intolerable intracranial pressure changes during vasodilation. BBB permeability to water may need to be taken into account for quantitative modeling of the fMRI BOLD signal.

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