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A multiscale 0-D/3-D approach to patient-specific adaptation of a cerebral autoregulation model for computational fluid dynamics studies of cardiopulmonary bypass

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ABSTRACT

Neurological complication often occurs during cardiopulmonary bypass (CPB). One of the main causes is hypoperfusion of the cerebral tissue affected by the position of the cannula tip and diminished cerebral autoregulation (CA). Recently, a lumped parameter approach could describe the baroreflex, one of the main mechanisms of cerebral autoregulation, in a computational fluid dynamics (CFD) study of CPB. However, the cerebral blood flow (CBF) was overestimated and the physiological meaning of the variables and their impact on the model was unknown. In this study, we use a 0-D control circuit representation of the Baroreflex mechanism, to assess the parameters with respect to their physiological meaning and their influence on CBF. Afterwards the parameters are transferred to 3D-CFD and the static and dynamic behavior of cerebral autoregulation is investigated.

The parameters of the baroreflex mechanism can reproduce normotensive, hypertensive and impaired autoregulation behavior. Further on, the proposed model can mimic the effects of anesthetic agents and other factors controlling dynamic CA. The CFD simulations deliver similar results of static and dynamic CBF as the 0-D control circuit. This study shows the feasibility of a multiscale 0-D/3-D approach to include patient-specific cerebral autoregulation into CFD studies.

1. Introduction

One of the most common problems during cardiopulmonary bypass (CPB) is neurological malfunction, which may lead to co-morbidities and increased hospitalization. A proper perfusion and a constant oxygen supply are necessary to minimize the risks of perioperative stroke and improve the success rate of open heart surgery (Schell et al., 1993; Kapetanakis et al., 2004; Scarborough et al., 2003). The brain's ability to maintain a stable cerebral blood flow (CBF) over a wide range of different cerebral perfusion pressures (CPP) is called cerebral autoregulation (CA) (Paulson et al., 1990). A combination of myogenic, neurogenic and metabolic mechanisms assures the necessary nutritional flow (van Beek et al., 2008). During CPB, impaired cerebral autoregulation occurs in approximately 20% of patients (Ono et al., 2012). The consequences are risks of perioperative stroke leading to a 10-fold higher mortality ratio (Ono et al., 2012; Sanders and Grocott, 2012). Especially the elderly often suffer from impaired autoregulation (van Beek et al., 2008). Therefore, cardiac surgeons face the challenge to decrease the risks of neurological complications during CPB in a constantly ageing population. In the past, computational fluid dynamic (CFD) studies have been used to gain insight into the pathological blood flow conditions during CPB (Fukuda et al., 2009; Tokuda et al., 2008; Kaufmann et al., 2009a, 2009b). The impact of the outflow cannula position on cerebral blood flow has been pointed out in Kaufmann et al. (2009a, 2009b). Further on, the imposed outlet boundary conditions have a direct influence on cerebral perfusion (Kaufmann et al., 2014). Pressure based outlet boundary conditions combined with peripheral resistances (Kaufmann et al., 2012; Benim et al., 2011) have been used recently but still do not consider the dynamical regulative behavior. On the other hand there are extensive mathematical models of cerebral autoregulation (Banaji et al., 2005; Ursino, 1998), which consider the biophysics of the circulatory system, the brain biochemistry and the functioning of vascular smooth muscle (Banaji et al., 2005). Such models can be used to properly understand the interaction in the regulatory mechanisms, but are too complex to be included in CFD calculations. One way to include autoregulation is the coupling of a lumped parameter model with a CFD framework. The vascular network is reduced to a three element Windkessel model and connected as an outlet boundary condition to the fluid domain. The work presented by Kim et al. (2009, 2010) laid the foundation of such lumped parameter approach. In Kaufmann et al. (2014) we transferred the work of Kim et al. (2009, 2010) to a CFD description of CPB and included a baroreflex model based on

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Ottesen et al. (2004). However, several limitations had to be accepted. First, the CBF was restored up to the native level during a perfusion pressure of 50–60 mmHg. In general a value of 80–90% is more appropriate (Kaufmann et al., 2012; van Beek et al., 2008). Second, the parameters of the baroreflex model were selected from Ottesen et al. (2004) without an adaptation to a patient-specific representation. In this study we focus on a parameter analysis of the baroreflex model presented in perfusion (Kaufmann et al., 2014) and an application to different autoregulation states as well as the consideration of anesthetic agents. A control circuit was used to describe the baroreflex model. The parameters were investigated concerning their influence on the CBF and the relevant factors were connected to physiological and pathological descriptions of CA. Furthermore, the chosen values were implemented into a CFD model for CPB to prove the transferability from a 0-D control circuit to 3-D CFD.

2. Materials and methods

2.1. Cerebral autoregulation

Description of cerebral autoregulation can be divided into two categories. The first one is the response of the CBF, averaged over a longer period of time, to long-term changes in blood pressure (van Beek et al., 2008). This mechanism is referred to as static cerebral autoregulation (sCA) and it is characterized by a "plateau phase" – the constancy of CBF over a range of blood pressure changes (van Beek et al., 2008). Cerebral autoregulation typically operates between 60 mmHg and 150 mmHg (Paulson et al., 1990) for a normotensive patient, however acute hypertension shifts these values to the right [110–160 mmHg (Strandgaard, 1976)] and impairment of CBF autoregulation decreases the overall regulation interval [80–100 mmHg (Kaufmann et al., 2012)]. Fig. 1 presents the different static autoregulation curves taken from the computational model in Kaufmann et al. (2012).

Dynamic autoregulation (dCA) is used to describe the pressure-flow relationship over a short period of time. (Tiecks et al., 1995) introduced the autoregulatory index (ARI) to quantify the different regulation velocities, by assuming a step change in BP and indicating an ARI of 0 to no autoregulation and an ARI of 9 to a very fast autoregulation. The curves were calculated using a computational model characterized by a 2nd order lag element (Tiecks et al., 1995) and are shown in Fig. 2.

Both, static and dynamic autoregulation, can be furthermore affected by the use of inhalation anesthetics (Strebel et al., 1995; Summors et al., 1999). Classification of the autoregulation influence for several agents can be found in Strebel et al. (1995), Summors et al. (1999) and is summarized in Table 1.

2.2. Baroreflex model and Windkessel effect

The baroreflex plays a leading role in cerebral autoregulation (Ottesen et al., 2004) and describes the change of cerebrovascular resistance, R, and cerebrovascular compliance, C, dependent on the perfusion pressure. In this control mechanism the sympathetic and parasympathetic nervous system starts to change R and C, if the actual cycle averaged pressure $\bar{p}$ differs from the target pressure p_t. The underlying equations have been presented in Kim et al. (2010) and Ottesen et al. (2004). The application of this model in a CFD study combined with an experimental validation of the calculations can be found in Kaufmann et al. (2014).

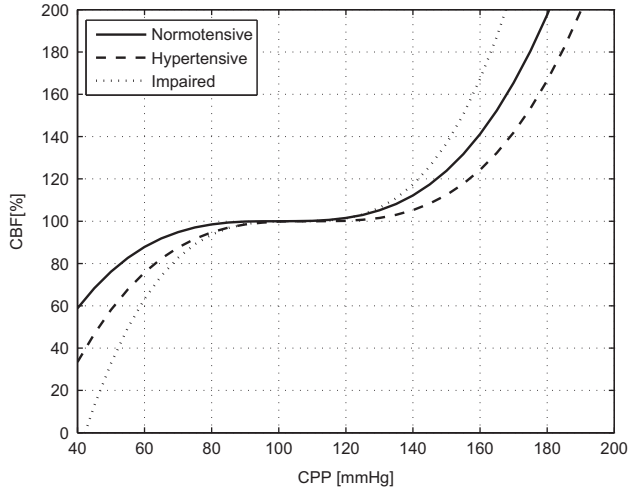

Fig. 1. Relationship between CBF and CPP for normotensive, impaired and hypertensive patients.

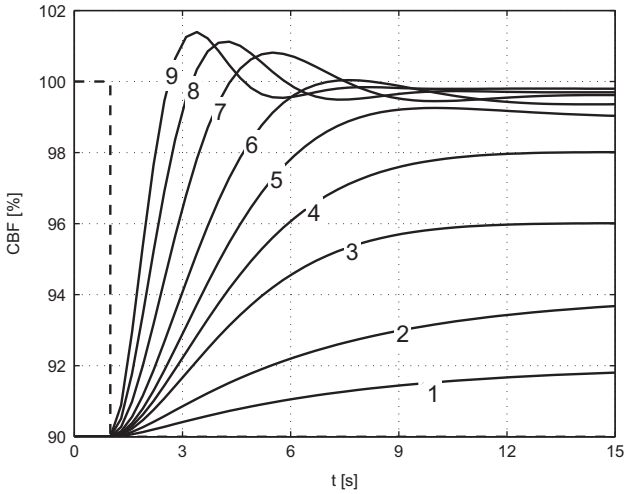

Fig. 2. Responses of a cerebral autoregulation model to a step change in blood pressure.

Table 1
Impact of different anesthetic agents on cerebral autoregulation.

Anesthetic	Reaction
Low-dose isoflurane	dCA decreases, sCA stays the same
Low-dose desflurane	dCA decreases, sCA decreases
High-dose Isoflurane and high-dose desflurane	Impairment of dCA and sCA
Low- and high-dose propofol	No change in sCA and dCA
Sevoflurane	Slight decrease in dCA

Table 2
Variable values for baroreflex model.

Parameter	Value
γ_R	1 mmHg s/ml
α_R	4 mmHg s/ml
β_R	4 mmHg s/ml
τ_R	60 s
γ_C	1.4 ml/mmHg
α_C	2 ml/mmHg
β_C	2 ml/mmHg
τ_C	60 s
ν	5

The sympathetic activity n_s and the parasympathetic activity n_p are governed by the following equation:

$$n_s = \frac{1}{1+(\bar{p}/p_t)^{\nu}} \tag{1a}$$

$$n_p = \frac{1}{1+(\bar{p}/p_t)^{-\nu}} \tag{1b}$$

The changes in resistance and compliance are described by the ODEs (2a) and (2b) and can be determined after the calculation of n_s and n_p:

$$\tau_R \frac{dR}{dt} + R = \alpha_R n_s - \beta_R n_p + \gamma_R \tag{2a}$$