DE GRUYTER
Current Directions in Biomedical Engineering 2019;5(1):529-532

Rosa Daschner*, Lorena Krames, Yannick Lutz, Axel Loewe, Olaf Dössel and Giorgio Cattaneo

Generation of a Simplified Brain Geometry for the Calculation of Local Cerebral Temperature using a 1D Hemodynamic Model

Abstract: In Western countries, stroke is the third-most cause of death; 35–55% of the survivors experience permanent disability. Mild therapeutic hypothermia (TH) showed neuroprotective effect in patients returning from cardiac arrest and is therefore assumed to decrease stroke induced cerebral damage. Recently, an intracarotid cooling sheath was developed to induce local TH in the penumbra using the cooling effect of cerebral blood flow via collaterals. Computational modeling provides unique opportunities to predict the resulting cerebral temperature without invasive procedures. In this work, we generated a simplified brain model to establish a cerebral temperature calculation using Pennes' bio-heat equation and a 1D hemodynamics model of the cranial artery tree. In this context, we performed an extensive literature research to assign the terminal segments of the latter to the corresponding perfused tissue. Using the intracarotid cooling method, we simulated the treatment with TH for different degrees of stenosis in the middle cerebral artery (MCA) and analyzed the resulting temperature spatial-temporal distributions of the brain and the systemic body considering the influence of the collaterals on the effect of cooling.

Keywords: local therapeutic hypothermia, collaterals, intracarotid cooling, targeted temperature management, computational temperature modeling, ischemic stroke

https://doi.org/10.1515/cdbme-2019-0133

1 Introduction

One method of mitigating the effects of stroke is mild therapeutic hypothermia (TH). It aims at a neuroprotective effect by lowering the patient's body temperature. The current standard method is superficial cooling, which involves a high risk of cardiac arrhythmia, pneumonia and edema. In this context, it has been shown, that it is safe and more effective to perform local hypothermia invasively. [1] Toward this end, a novel intracarotid cooling catheter was developed to induce local TH in the penumbra using the cooling effect of cranial blood flow via ipsilateral collaterals [2]. An emerging problem concerns the possibility of monitoring and thus regulating the novel cooling system. In this work, we established a computational model to predict the cerebral temperatures induced by local TH in ischemic stroke patients without invasive procedures. Our temperature calculation is based on the coupling of a 1D hemodynamics model of the complex cerebral vascular system with a simplified brain geometry via Pennes' bio-heat equation.

2 Methods

Cerebral temperature is mainly affected by the blood perfusion rate v_{bl}, which is defined as the blood flow q_{bl} per perfused tissue volume V and is part of Pennes' bio-heat equation [3]:

$$v_{bl} = \frac{q_{bl}}{V}. \quad (1)$$

q_{bl} is calculated by a 1D hemodynamics model, which contains the cranial arterial system for the most common occurrences (~64% [4]) of the cerebral arteries, including 14 ipsilateral collaterals [5]. The hemodynamics model establishes 58 terminal supply areas to be coupled with a brain geometry. The use of the hemodynamics model requires values of the mean flows $q_{term,i}$ for the individual terminal segment i in the physiological state. In our work, we determined them using eq. (1):

$$q_{term,i} = v_{GM} \cdot V_{term,iGM} + v_{WM} \cdot V_{term,iWM}, \quad (2)$$

with v_{GM} and v_{WM} being the perfusion rates of grey (GM) and white matter (WM) by Parkes et al. [6] and $V_{term,i} = V_{term,iGM} + V_{term,iWM}$ being the volume of the supply area of the terminal segment i. The tissue volumes and composition, as well as perfusion rates depend on age and gender. All parameters used in this work consider a 60-year-old man.

Tissue Distribution

To determine the size and the tissue distribution for the

*Corresponding author: Rosa Daschner: Institute of Biomedical Engineering, Karlsruhe Institute of Technology (KIT), Fritz-Haber-Weg 1, 76131 Karlsruhe, Germany, publications@ibt.kit.edu
Lorena Krames, Yannick Lutz, Axel Loewe, Olaf Dössel: Institute of Biomedical Engineering, Karlsruhe Institute of Technology (KIT), Fritz-Haber-Weg 1, 76131 Karlsruhe, Germany
Giorgio Cattaneo: Adceris GmbH & Co KG, Pforzheim Germany

individual terminal supply areas, we followed a top-down approach based on literature. The fluxes $q_{term,_j}$ through the individual cerebral main artery (CA) j known from the literature [7] were used as boundary conditions:

$$\sum q_{term,_{ACA}} \overset{!}{;=} 1.4\frac{ml}{s},$$
$$\sum q_{term,_{MCA}} \overset{!}{;=} 2.6\frac{ml}{s}, \qquad \sum q_{term,_{PCA}} \overset{!}{;=} 1.0\frac{ml}{s}, \quad (3)$$

with ACA and PCA being the anterior and posterior cerebral artery. In a first step, we determined the volumes $V_{total_{GM}}$ and $V_{total_{WM}}$ of the total cerebral GM and WM using a mean value of the entire cerebral volume $V_{brain} = 1355\,cm^3$ [8] and its relative tissue composition investigated by Ge et al. [9] and Taki et al. [10]. We distinguished GM belonging to the cortex and subcortical GM. Secondly, we divided $V_{total_{GM}}$ and $V_{total_{WM}}$ into V_j using the known cerebral artery portion of the brain's total supply [11]. Thus, the volumes V_j represents the supply area of the respective CA. Taking eq. (3) into account, the division of V_j into volumes of GM and WM was possible:

$$V_{j,_{GM}} = \frac{q_{term,_j} - V_j \cdot v_{WM}}{v_{GM} - v_{WM}},\ V_{j,_{WM}} = V_j - V_{j,_{GM}}.$$

In the last step, we studied the courses and locations of the terminal segments and their supply areas to divide $V_{j,_{GM}}$ and $V_{j,_{WM}}$ into $V_{term,_{i\,GM}}$ and $V_{term,_{i\,WM}}$ in an extensive literature research. We assumed that V_j is evenly distributed among all terminal segments of the respective CA. Our approach led to terminal supply areas consisting

- exclusively of cortical grey matter,
- exclusively of subcortical grey matter or
- of grey and white matter.

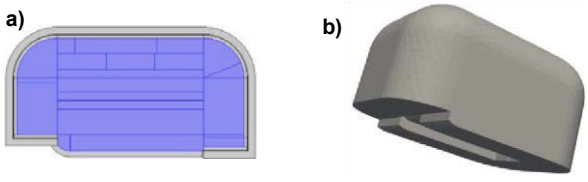

Fig. 1: Left: sagittal view into the right hemisphere: cerebral tissue in blue, outer layers in grey. Right: overview of the simplified geometry.

Simplified Geometry

The head geometry illustrated in Fig. 1 b) consists of the cerebrum including the ventricles and an outer shell. We considered V_{brain} as well as an average brain length, width and depth of 17 cm, 11 cm and 13 cm according to Berry [12]. The geometry was constructed considering the volumes of the terminal supply areas and the anatomical locations. We incorporated an even cortex thickness and the insula for both hemispheres. The brain geometry was covered by layers representing the subarachnoidal space, the dura mater, the skull and the derma with an average thickness of 2.40 mm [13], 0.55 mm [14], 5.36 mm [15] and 3.46 mm [16-17] respectively. A sagittal view of the geometry and its layers is shown in Fig. 1 a).

Temperature Calculation

For the calculation of the cerebral temperature T, Pennes' bio-heat equation was used. It considers the heat exchange between blood and tissue, heat conduction in tissue and heat generation by metabolism:

$$\rho_T c_T \frac{\partial T}{\partial t} = \nabla(\lambda_T \nabla \mathrm{T}) - \rho_{bl} c_{bl} v_{bl}(T - T_a) + P_{met}, \quad (4)$$

where ρ_T is the density ($\frac{kg}{m^3}$), c_T the specific heat ($\frac{J}{kg \cdot K}$) and λ_T the thermal conductivity of the tissue ($\frac{W}{m \cdot K}$), c_{bl} the specific heat and ρ_{bl} the density of blood, v_{bl} the volumetric perfusion rate of the tissue ($\frac{1}{s}$), T_a the arterial blood temperature (K) and P_{met} the metabolic heat of the tissue ($\frac{W}{m^3}$). According to the IT'IS Foundation database, 1049.75 $\frac{kg}{m^3}$ was assumed for ρ_{bl} and 3617 $\frac{J}{kg \cdot K}$ for c_{bl}. The tissue parameters were taken from Pliskow et al. [18].

The blood perfusing the brain circulates via the venous system through the bloodstream of the remaining body, which affects T_a and the systemic temperature of the remaining body T_{sys}. To model these influences, we adapted Pennes' bio-heat equation neglecting the heat conduction and heat generation:

$$M_{sys} c_{sys} \frac{\partial T}{\partial t} = \rho_{bl} c_{bl} q_{bl}(T_{sys} - T_{br}), \quad (5)$$

assuming an average systemic heat capacity c_{sys} of 3470 $\frac{J}{kg \cdot K}$ and a body mass M_{sys} of 75 kg. T_{br} represents the mean temperature of the brain and q_{bl} the sum of all 58 terminal flow rates $q_{term,i}$. Concerning the outer most layer, we considered convection and radiation, assuming an ambient temperature of 20 °C and an emission coefficient of an ideal black radiator ($\epsilon = 1$).

Modeling TH: Our computational model aims to predict the cerebral temperatures during the treatment of ischemic stroke patients with selective TH, induced by an intra-carotid cooling catheter. In vitro experiments revealed a mean temperature drop between the catheter inlet and outlet of approximately 2.17 °C and 1.55 °C for flow rates of 250 $\frac{ml}{min}$ and 400 $\frac{ml}{min}$ [2]. In this work, we assumed a temperature drop of 2 °C.

Influence of collaterals: The brain regions are not only perfused by the respective cerebral arteries. In our approach, we considered the effect of flow mixing for blood coming from the communicating arteries and from ipsilateral collaterals [19]. Therefore, a temperature mixing was realized:

$$T_{x,y} = \frac{T_x \cdot q_x + T_y \cdot q_y}{q_x + q_y}, \quad (6)$$

with $T_{x,y}$ being the resulting temperature after the mixing of the flows q_x with temperature T_x and q_y with temperature T_y.

For the influence of the ipsilateral collaterals, the mean temperatures in the respective areas were considered.

3 Results

Treatment with selective TH by the intracarotid catheter system was simulated for 60 minutes for the physiological case and the case of a 75 % and a 100 % stenosis in the right MCA. As initial temperatures for the calculation, the steady state values without cooling were used.

The initial cerebral temperature, especially for the MCA supply area, was elevated for the ischemic cases (+ 0.2 °C). Fig. 2 a) shows the average temperature of the entire brain (red) and the MCA supply area (blue) for the physiological case (dotted), the case of the 75 % stenosis (dashed) and the case of the 100 % stenosis (solid). In all cases, the cerebral temperature experienced the strongest decrease in the first 5 minutes. In the MCA supply area, a cooling of 1.5 °C could be achieved in the physiological case, a cooling of 0.9 °C in case of the 75 % stenosis and of 0.1 °C in case of the 100 % stenosis. Afterwards, the decrease diminished, and the cerebral temperature followed the systemic temperature (compare Fig. 2 b)).

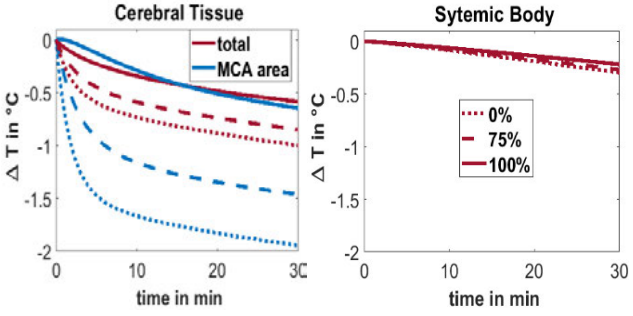

Fig. 2: Temperature decrease for selective TH in the physiological case (dotted), in case of the 75 % stenosis (dashed) and 100 % stenosis (solid). Left: brain: total cerebral tissue (red) and tissue of the MCA supply area (blue). Right: Systemic body.

The systemic temperature showed a nearly linear decrease of approximately 0.01 $\frac{°C}{min}$ for all cases over the whole cooling period. In contrast to the other cases, the temperature in the MCA supply area in case of the 100 % stenosis was higher than that of the entire brain over the whole cooling period. After one hour of cooling, the temperature of the MCA supply area decreased to 34.8 °C in the physiological case, to 35.4 °C in case of the 75 % stenosis and to 36.5 °C in case of the 100 % stenosis. The resulting temperature changes in 10 minutes intervals are listed in Table 1. Fig. 3 shows the spatial cerebral temperatures for the physiological case (top) and the pathological case of a 100 % stenosis (bottom).

Table 1: Temperature decrease of cerebral tissue in °C over the time for different degrees of stenosis.

time in min	physiological		75% stenosis		100% stenosis	
	total	MCA	total	MCA	total	MCA
10	- 0.74	- 1.66	- 0.59	- 1.16	- 0.34	- 0.29
20	- 0.88	- 1.83	- 0.74	- 1.35	- 0.48	- 0.51
30	- 1.00	- 1.95	- 0.85	- 1.46	- 0.59	- 0.64
60	- 1.32	- 2.27	- 1.14	- 1.76	- 0.84	- 0.91

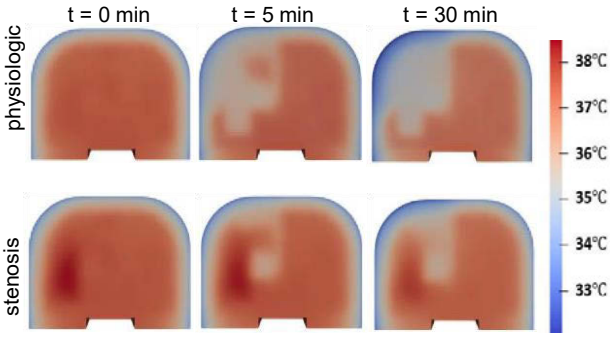

Fig. 3: Spatial cerebral temperature for the physiological (top) and the pathological case of a 100% stenosis (bottom) in the initial case (left), after 5 (middle) and after 30 minutes (right).

4 Discussion

A quick decrease in temperature in the area of the penumbra is of major importance for the treatment of ischemic stroke patients. In our model, a temperature difference of almost 2 °C was predicted in the physiological case within 30 minutes of cooling. In the pathological cases, the decrease in temperature was significantly lower due to the reduced perfusion rates. Moreover, the blood temperature of the collateral flow affected the resulting temperatures. In case of the 100 % stenosis, the MCA supply area was only perfused by collaterals, in fact mostly by the blood originating from the PCA. The cooling catheter only affects directly the blood temperature in the right common carotid artery which branches into the ACA and the MCA, but not into the PCA. Unfortunately, a direct comparison of the resulting temperatures with human clinical studies is not possible as the catheter is still under development and the temperature measurements of cerebral tissue require invasive procedures. However, our results show a comparable course to measured data in sheep [20]. As in our studies, the cerebral temperature of the animals dropped strongly in the first few minutes, followed by a smaller approximately linear decrease. The temperature gradient in the animal studies was noticeably greater. However, it should be remembered that cerebral blood flows are greater in sheep than in humans.

Limitations

$V_{term,iGM}$ and $V_{term,iWM}$ were narrowed down by studies of Ge et al. [9], Taki et al. [10], and Mut et al. [11]. The resulting supply areas of the CA's correspond to the expectations emerging from anatomical literature: The MCA as the largest CA supplies the largest area, followed by the ACA and the PCA as the smallest CA. Furthermore, the suitability of the determined regions was confirmed by the resulting flow rates, which corresponded to the literature [7]. However, the cerebral tissue and terminal supply distribution could be improved using segmented MRI data sets.

For the determination of v_{GM} and v_{WM}, the investigation results of Parkes et al. [6] were used. Their ratio is approximately 2.2, which is within the range of the values found in the literature [21-22].

5 Conclusion

In this work, a temperature model of the brain was created by means of a simplified head geometry. In interaction with a 1D hemodynamics model, the local cerebral tissue and blood temperatures were calculated for the treatment with selective TH using an intracarotid cooling catheter. In the pathological case, the cooling effect within one hour was significantly lower than in the physiological case. In this context, a significant influence of the ipsilateral collaterals on the temperature in the penumbra could be determined.

The structure of the cerebral arteries and especially of the collaterals vary greatly between individuals. Our results underline the influence of collaterals on the effect of intravascular cooling. In this context, a larger simulation study regarding the degree of collateralization is needed to further analyze the respective influences.

Author Statement

This study was supported by the German Federal Ministry of Economic Affairs and Energy (ZF4363901AK6). Authors state no conflict of interest.

References

[1] Song SS, Lyden PD. Overview of therapeutic hypothermia. Curr Treat Options Neurol 2012;14(6):541–548.
[2] Cattaneo G, Schumacher M, Wolfertz J, Jost T, Mecke S: Open access combined selective cerebral hypothermia and mechanical artery recanalization in acute ischemic stroke: In vitro study of cooling performance. Am J Neuroradiol 2015, 36(11):2114-20.
[3] Pennes HH: Analysis of tissue and arterial blood temperatures in the resting human forearm. Appl Physiol 1998, 85(1):5-34.
[4] Umansky F, Juarez SM. Dujovny M, Ausman JI, Diaz FG, Gomes F, Mirchandani HG, Ray WJ. Microsurgical anatomy of the proximal segments of the middle cerebral artery. J Neurosurg 1984, 61(3):458–67.
[5] Van der Eecken HM, Adams RD: The anatomy and functional significance of the meningeal arterial anastomoses of the human brain. J Neuropathol Exp Neurol 1953, 12(2):132-57
[6] Parkes LM, Rashid W, Chard DT, Tofts PS: Normal cerebral perfusion measurements using arterial spin labelling: Reproducibility, stability, and age and gender effects. Magn Reson Med. 2004, 51(4):736-43.
[7] Fahrig R, Nikolov H, Fox AJ, Holdsworth DW: A threedimensional cardiovascular flow phantom. Med Phys 1999, 26(8):1589-99
[8] Allen JS, Damasio H, Grabowski T: Normal neuroanatomical variation in the human brain: An MRI volumetric study. Am J Phys Anthropol 2002, 118(4):341–58.
[9] Ge Y, Grossman RI, Babb JS, Rabin ML, Mannon LJ, Kolson DL: Age-related total gray matter and white matter changes in normal adult brain. Part I: Volumetric MR imaging analysis. Am J Neuroradiol 2002, 23(8):1327-33.
[10] Taki Y, Thyreau B, Kinomura S, Sato K, Goto R, Kawashima R, Fukuda H. Correlations among brain gray matter volumes, age, gender, and hemisphere in healthy individuals. PLoS ONE 2011, 6(7): e22734.
[11] Mut F, Wright S, Ascoli GA, Cebral JR: Morphometric, geographic, and territorial characterization of brain arterial trees. Int J Numer Method Biomed Eng. 2014, 30(7):755–66.
[12] Berry RJA: Brain size and mentality. Br Med J. 1936, 2:62
[13] Frydrychowski A, Szarmach A,Czaplewski B, Winklewski P: Subarachnoid space: New tricks by an old dog. PloS one 2012, 7:e37529.
[14] Bashkatov A, Genina E, Sinichkin YP, Kochubey V, Lakodina NA, Tuchin V: Glucose and mannitol diffusion in human dura mater. Biophysical journal 2003, 85:3310–18.
[15] Li H, Ruan J, Xie Z, Wang H, Liu W. Investigation of the critical geometric characteristics of living human skulls utilising medical image analysis techniques. Int J Veh Saf 2007, 2:345–67.
[16] Hori H, Moretti G, Rebora A, Crovato F: The thickness of human scalp: normal and bald. J Invest Dermatol 1972, 58(6):396-9.
[17] Geerligs M: Skin layer mechanics. PhD thesis, Department of Biomedical Engineering, TU Eindhoven, Eindhoven 2010
[18] Pliskov B, Mitra K, Kaya M: Simulation of scalp cooling by external devices for prevention of chemotherapy-induced alopecia. J Therm Biol 2016, 56:199-205.
[19] Liebeskind DS: Collateral circulation. Stroke 2003, 34:2279–84.
[20] Cattaneo G, Schumacher M, Maurer C, Wolfertz J, Jost T, Büchert M, Keuler A, Boos L, Shah MJ, Foerster K, Niesen WD, Ihorst G, Urbach H, Meckel S: Endovascular Cooling Catheter for Selective Brain Hypothermia: An Animal Feasibility Study of Cooling Performance. Am J Neuroradiol 2016, 37(5):885-91
[21] Koshimoto Y, Yamada H, Kimura H, Maeda M, Tsuchida C, Kawamura Y, Ishii Y: Quantitative analysis of cerebral microvascular hemodynamics with T2-weighted dynamic MR imaging. J Magn Reson Imaging. 1999 Mar;9(3):462-7.
[22] Wu WC, Lin SC, Wang DJ, Chen KL, Li YD: Measurement of cerebral white matter perfusion using pseudocontinuous arterial spin labeling 3T magnetic resonance imaging--an experimental and theoretical investigation of feasibility. PLoS One 2013, 8(12):e82679.