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## ▶ To cite this version:

Pan Liu, Kimi Owashi, Heimiri Monnier, Serge Metanbou, Cyrille Capel, et al.. Cerebral arterial venous blood flow dynamics under the influence of free and deep breathing. ISMRM 2024, International Society for Magnetic Resonance in Medicine, May 2024, Singapore, Singapore. hal-04628748

# HAL Id: hal-04628748 https://hal.science/hal-04628748

Submitted on 28 Jun2024

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# Cerebral arterial venous blood flow dynamics under the influence of free and deep breathing

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# Synopsis

#### Motivation

The hydrodynamic characteristics of arterial venous cerebral blood flow (AVCBF) in different breathing patterns remain insufficiently understood.

#### Goal

Quantifying the effects of free and deep breathing on multiple parameters of CBF using real-time phase contrast MRI.

#### Approach

We applied RT-PC on 14 healthy volunteers to continuously quantify AVCBF dynamics in the main cerebral vessels during free and deep breathing. A time-domain analysis investigated the influence of breathing change on the AVCBF parameters: mean flow, stroke volume, cardiac period.

#### Results

Deep-breathing decreased global AVCBF dynamics. Mean flows, stroke volumes and cardiac periods decreased but their percentage change between inspiratory and expiratory periods increased.

## Impact

This study quantified the effects of free- and deep-breathing on cerebral blood flow dynamics. It should contribute to a better understanding of cerebral hemodynamics and its relation with breathing, providing a valuable reference for clinical applications and physiological studies.

#### Introduction

Cerebral blood flow (CBF) is the main driver of brain metabolic activity and CSF oscillations<sup>1,2</sup>. Using real-time phase-contrast (RT-PC) MRI, it has been shown that breathing can significantly affect CBF<sup>3-6</sup>. However, systematic studies of the effects of free- versus deep-breathing on various parameters of CBF remain limited. This study aimed to analyze the specific effects of different breathing patterns on CBF parameters, including cerebral blood inflow and outflow.

#### Methods

#### - Image acquisition

Due to the higher compliance and significant variability in internal jugular veins morphology, we selected the intracranial level to quantify the arterial and venous CBF (AVCBF).

Fourteen healthy volunteers (age: 20~34) were examined using a clinical 3T scanner and a 32-channel head coil. Pulse and breathing signals were recorded simultaneously using a finger plethysmograph and a chest sensor during two acquisitions: under free-breathing and deep-breathing conditions.

The RT-PC used in this study was a multi-shot, gradient-recalled echo-planar imaging sequence with parallel acquisition technology. Parameters were as follows: SENSE=2.5, EPI-factor=7, spatial resolution=2\*2mm<sup>2</sup>, and temporal resolution=75ms/image (Fig.1-A).

#### - Image processing

All image and signal processing were performed using in-house software – Flow 2.0<sup>7,8</sup>. Inflow and outflow were extracted through post-processing steps, including image segmentation, background field correction, and de-aliasing.

The sum of flows from the left/right internal carotid arteries and the basilar artery was considered the intracranial inflow. Similarly, the sum of flows from the superior sagittal sinus and the straight sinus was considered as the intracranial outflow.

The venous outflow curve was adjusted by multiplying the measured venous flow curve by a factor  $\lambda$  to account for unconsidered peripheral venous drainage. Then  $\lambda$  = mean arterial flow divided by mean measured venous flow. The AVCBF curve was calculated by subtracting the venous outflow curve from the arterial inflow curve (Fig.1-B&C). The oscillating positive and negative segments of the AVCBF curve represent the increase and decrease in intracranial blood volume during the cardiac cycle.

#### - Effect of breathing conditions on cerebral blood flow

Time-domain analysis was used to individually segment cardiac cycle on RT-PC to quantify the effects of breathing on measured flows<sup>9</sup> (Fig.2):

A) The software segmented each flow signal into multiple independent cardiac cycle flow curves (CCFCs).

B) The inspiration and expiration phases were determined by the respiratory signal. The corresponding CCFCs for inspiration and expiration were labeled as CCFC\_In and CCFC\_Ex, respectively.

C) Average of the CCFC\_ In and CCFC\_Ex was then reconstructed to calculate their mean flow, amplitude, cardiac period and stroke volume (SV).

D) Diff\_InEx% was calculated to quantify the percentage of change between inspiration and expiration period for all the flow parameters.

E) By shifting the respiratory signal with RT-PC signal, the maximum change of Diff-InEx% was determined. For example, in Figure 2-C, the highest Diff-InEx%, for the mean flow, occurred when the respiratory phase window was shifted 26%. This indicates a 10% increase in mean flow from mid-inspiration to mid-expiration.

#### Results

The changes of AVCBF, inflow, and outflow signals between inspiration and expiration periods during free- and deep-breathing acquisitions are presented in Fig.3.

During inspiration (free&deep), SV and cardiac periods of AVCBF increased.

Deep-breathing significantly reduces AVCBF SV and cardiac period by 42% and 16%, respectively, compared to free-breathing. Furthermore, deep-breathing increases Diff-InEx of mean flow by 49% and Diff-InEx% of SV by 69% in CBF, with no significant impact on Diff-InEx of SV.

Fig.4 illustrates the distribution of the effect of free- and deep-breathing on each parameter.

Fig.5-A demonstrates the correlation, specifically regarding mean flow, between the Diff-InEx in CBF and the Diff-InEx% in inflow during free-breathing. Fig.5-B shows that during free-breathing, compared to inflow, the shift% of mean flow in outflow is closer to the shift% of cardiac period.

#### Discussion

The mean CBF (669±97 ml/min) measured by RT-PC in young healthy population is in agreement with previous studies using conventional PC-MRI with higher spatial resolution<sup>10</sup>.

During free- and deep-inspiration, the cardiac period increases while mean inflow decreases, somewhat reducing the SV variation (Fig.5-B).

The Diff-InEx% of all the parameters increased significantly during deep-breathing. Conversely, the cardiac period and mean values of inflow and outflow decreased, which, to some extent, counteracted

the effect of the increase in Diff-InEx. For example, the SV in CBF increased significantly in Diff-InEx% during deep-breathing, but not in Diff-InEx.

#### Conclusion

Deep-breathing decreased global AVCBF dynamics. Mean flows, SV and cardiac periods decreased but their percentage change between inspiratory and expiratory periods increased. This study can enhance our comprehension of fluid dynamics associated with CBF and CSF oscillations.



Figure 1: A) RT-PC acquisition plane and image processing. The inflow contains three arteries and the outflow contains two sinuses. B) and C) show the respective blood flow signals during free breathing and deep breathing. The outflow curve is multiplied by  $\lambda$  to ensure a mean outflow equal to the mean inflow. CBF is obtained by subtracting outflow from inflow.

## Figures (5/5) (500 characters each)



Figure 2: A) Segmentation of flow curve into multiple CCFCs using the pulse signal, reconstructed into an average CCFC. B) CCFC-In and CCFC-Ex for inspiratory and expiratory phases. Quantification of the percentage difference (Diff-InEx%) between these two CCFCs for each parameter. Process repeated to find the extremes of Diff-InEx% by shifting the respiratory phase (shift%). C) Mean blood flow difference between CCFC-In and CCFC-Ex was maximal (10%) at 26% rightward respiratory phase shift.

	Flow rate (ml/s)					Stroke volume (ml/CC)				Cardiac Period (s)			Amplitude (ml/s)		Surface (mm <sup>2</sup> )
	Mean	λ	Diff-InEx	Diff-InEx (%)	Shit (%)	Mean	Diff-InEx	Diff-InEx (%)	Shit (%)	Mean	Diff-InEx (%)	) Shit (%)	Mean	pulsatility	Mean
<b>Free-Breathing</b> (Period = $3.7s \pm 0.4s$ )															
Inflow	12.4 ± 1.8		-0.49 ± 0.26	$-4.0 \pm 2.0$	$10\pm13$	11.4 ± 3.2	$0.58 \pm 0.24$	$5.0 \pm 1.7$	$-5 \pm 21$				10.2 ± 1.2	0.83 ± 0.11	$60\pm8$
Outflow	$7.8 \pm 2.0$	1.7 ± 0.4	$0.31 \pm 0.14$	$2.6\pm1.3$	$-7 \pm 22$	$7.1 \pm 2.3$	$0.76\pm0.40$	$\textbf{6.6} \pm 3.2$	$-1 \pm 12$	0.90 ± 0.2	$5.4 \pm 2.8$	$-2 \pm 8$	$2.9\pm0.6$	0.39 ± 0.12	$55 \pm 8$
AVCBF	0		-0.49 ± 0.33		$9\pm 8$	$1.5 \pm 0.4$	$0.16\pm0.08$	11.2 ± 5.9	$2 \pm 15$				$9.3\pm1.3$		115 ± 7
<b>Deep-Breathing</b> (Period = $6.2s \pm 2.2s$ )															
Inflow	$8.8\pm1.6$		-0.90 ± 0.35	$-10.8 \pm 5.2$	-8 ± 20	6.9 ± 1.9	$-0.61 \pm 0.32$	$-9.3 \pm 4.8$	$16 \pm 21$				$8.9 \pm 1.4$	$1.00 \pm 0.10$	59 ± 7
Outflow	$5.2 \pm 0.8$	$1.7 \pm 0.3$	$-0.80 \pm 0.47$	-9.9 ± 6.5	-14 ± 14	$4.1 \pm 0.9$	$0.65 \pm 0.29$	$9.9 \pm 4.2$	-1 ± 26	0.76 ± 0.2	9.2 ± 5.7	-16 ± 15	$2.3 \pm 0.5$	$0.45 \pm 0.13$	51 ± 7
AVCBF	0		-0.73 ± 0.35		$6 \pm 24$	$1.0\pm0.3$	$0.17 \pm 0.08$	$18.9\pm8.9$	-13 ± 25				$7.9 \pm 1.1$		$110\pm9$
Difference Deep-Free															
Inflow	-29% **		84% **	170% **		-39% **	5% **	86% **					-13% *	20% **	<u>n.s</u> .
Outflow	33% **	<u>n.s</u> .	158% **	281% **		-42% **	<u>n.s</u> .	50% *		-16% **	70%**		-21% **	n.s.	-7% *
AVCBF			49% **			-42% **	<u>n.s</u> .	69% *					-15% **		<u>n.s</u> .

Figure 3: Inflow, outflow and CBF parameters during free and deep breathing, including mean and breathing effects (Diff-InEx% & Shift%). Data expressed as mean $\pm$ SD. At the bottom the percentage change between the two breathing patterns are presented. Analysis was done using t-test or Wilcoxon. \* indicates p<0.05, \*\* p<0.01. Pulsatility is the ratio of amplitude to mean flow. CBF stroke volume is calculated as the sum of volume to skull and volume to extracranial.



Figure 4: Comparison of effects of free and deep breathing on inflow, outflow and AVCBF parameters (Mean value & Diff-InEx%). B) Diff-InEx%, where mean AVCBF flow uses Diff-InEx(ml) to represent breathing effect.



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Figure 5: A) Distribution of free breathing effect on each cerebral blood flow, AVCBF Diff-InEx shows correlation with inflow Diff-InEx. A') An example of the red pentagram, the InOutflow- $\Delta$ Diff% indicates the difference between the Diff-InEx% of inflow and outflow, and  $\Delta$ Shift% indicates the difference between the two Shift%. B) Shift% distributions of inflow, outflow and cardiac period under free breathing.

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#### Acknowledgements

This research was supported by EquipEX FIGURES (Facing Faces Institute Guilding Research), Hanuman ANR-18-CE45-0014 and Region Haut de France.

Thanks to the staff members at the Facing Faces Institute (Amiens, France) for technical assistance.

Thanks to David Chechin from Phillips industry for his scientific support.