The X ISNVD Annual Meeting

Measuring respiratory and cardiac influences on blood and cerebrospinal fluid flow with real-time MRI

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Declaration of Financial Interests or Relationships

- Maria Marcella Laganà: I have no financial interests or relationships to disclose with regard to the subject matter of this presentation.
- Ning Jin works for MR R&D Collaborations, Siemens Medical Solutions USA, Inc., Cleveland, Ohio, USA
- Domenico Zacà works for Siemens Healthcare, Milano, Italy

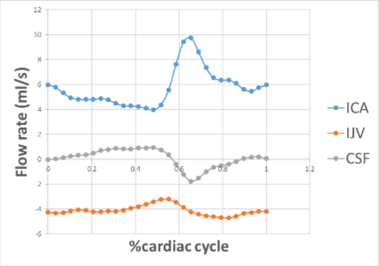
Introduction

- Venous and CSF flow alterations have been described in various neurological conditions[1]
- Cerebrospinal fluid (CSF) flow: crucial role in the brain waste clearance (glymphatic system)[2]

↕

Conventional flow quantification: cine cardiac-gated Phase Contrast (PC) MRI

BUT:
1) heart rate variability
2) respiration modulates venous return and CSF flow[3]
[thoracic pump]



1. Zivadinov et al., BMC Med 2013; Attier-Zmudka et al., Front Aging Neurosci 2019; Jakimovski et al., Fluids and Barriers of the CNS 2020
2. Iliff et al., Sci Transl Med 2012
3. Zamboni et al., J Appl Physiol 2012;
Laganà et al., Ultrasound in Medicine and Biology, 2017

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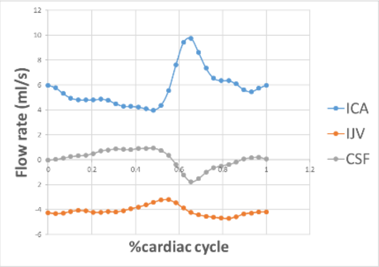

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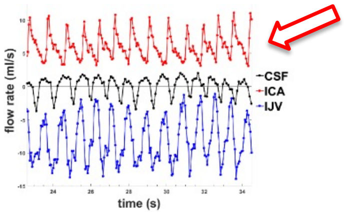
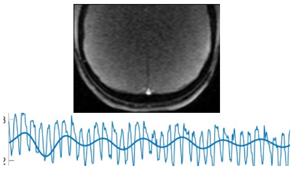
4. Ohno et al., Diagnostics 2020; Yildiz et al., JMRI 2017

↓

Real-time (RT) PC MRI[4] for assessing flow rate respiratory modulations





Aims

Study 1 – Beat-by-beat variability

Aim 1 - Assess the blood and CSF beat-by-beat variability
Aim 2 - Compare the flow rate obtained using the RT-PC and the clinical cardiac-gated cine PC sequence

Real-Time Phase-Contrast MRI to Monitor Cervical Blood and Cerebrospinal Fluid Flow Beat-by-Beat Variability. Baselli et al., Biosensors 2022, 12(6), 417

Study 2 – Blood and CSF flow drivers

Aim 1 - Testing the presence of the cardiac and respiratory drivers
Aim 2 - Assessing how different breathing modes affect the:
(A) mean flow rate
(B) respiratory and cardiac modulations to the flow rate

Blood and cerebrospinal fluid flow oscillations measured with real-time phase-contrast MRI: breathing mode matters. Laganà et al., FBCNS. Preprint at Research Square [https://doi.org/10.21203/rs.3.rs-1722506/v1]

Study 3 – Intra and extracranial venous flow

Aim - Assessing cardiac and respiratory modulations on intracranial (sup sagittal sinus) and neck venous flow

Cardiac and Respiratory influences on intracranial and neck venous flow measured with Real-Time Phase-Contrast MRI. Laganà et al., Biosensors 2022.

Materials and Methods

Subjects
Healthy volunteers
N=30 (21 females)
age: 26[19-57] years

MRI Scanner
3T Siemens Prisma
64-channel head-neck coil

MRI acquisition protocol

- Prototype RT-PC (acquired for 60 s)
- Respiration:
  - normal free breathing (F)
  - paced normal (PN)
  - paced deep breathing (PD)

Measuring	RT-PC Positioning	Venc (cm/s)	Temporal resolution (ms)	#time points
A) blood	Perpendicular to neck vessels	70	58.5	1021
B) CSF	Perpendicular to spinal cord	6	94	637
C) SSS	Perpendicular to the sup sag sinus	40	58.5	1021

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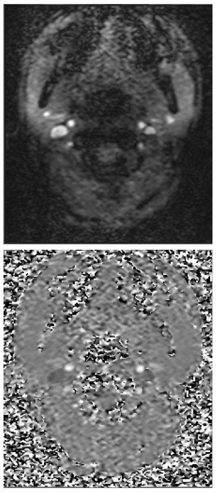
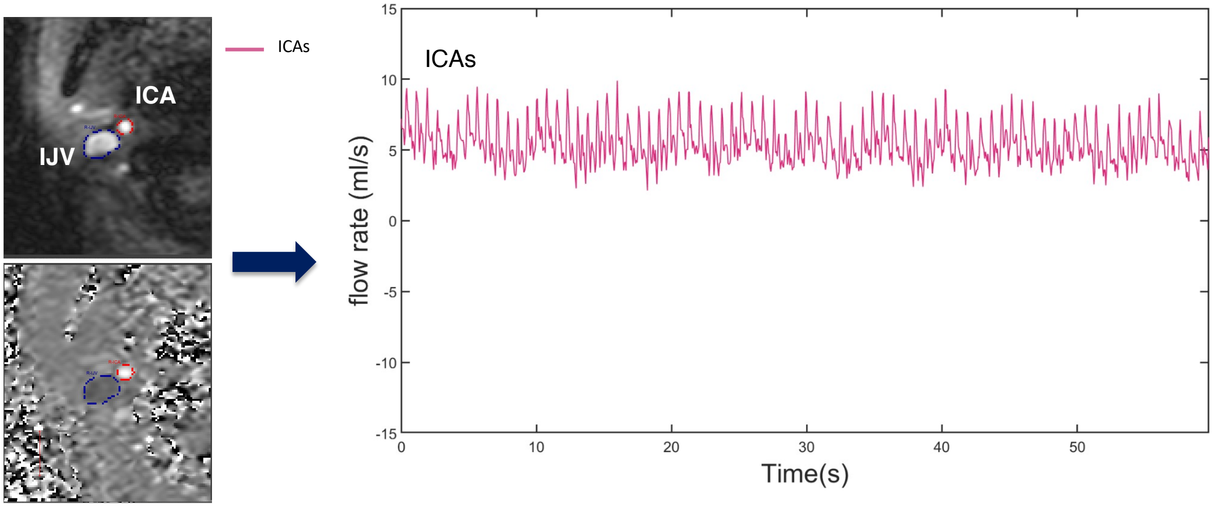
Flow rate and its drivers

Magnitude and Phase images: neck blood



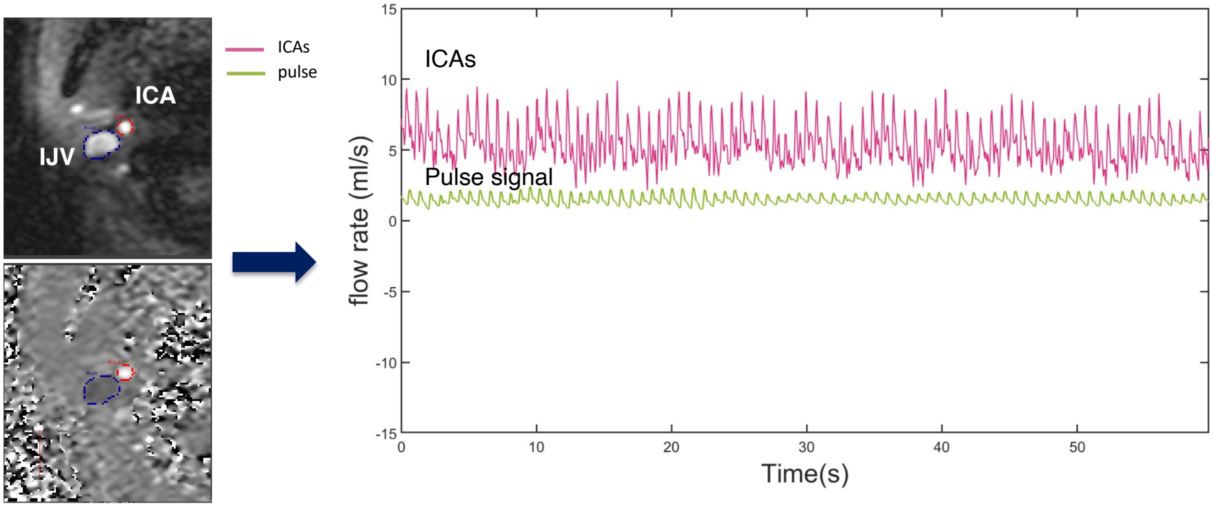
Flow rate and its drivers

Flow rate estimate using SPIN version 1.1.151211 (SpinTech MRI)



Flow rate and its drivers

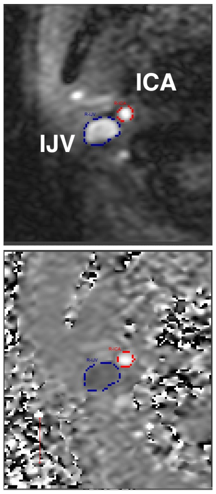
Flow rate estimate

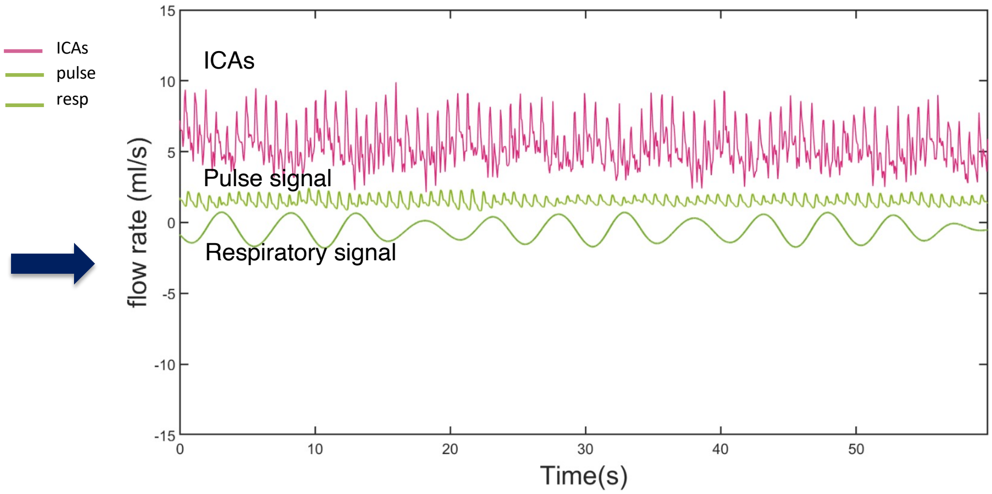


Heart beating influence

Flow rate and its drivers

Flow rate estimate

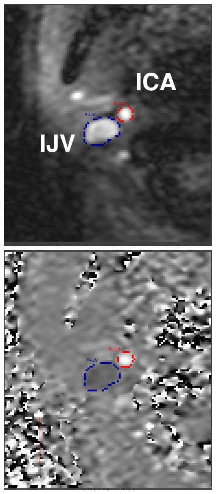


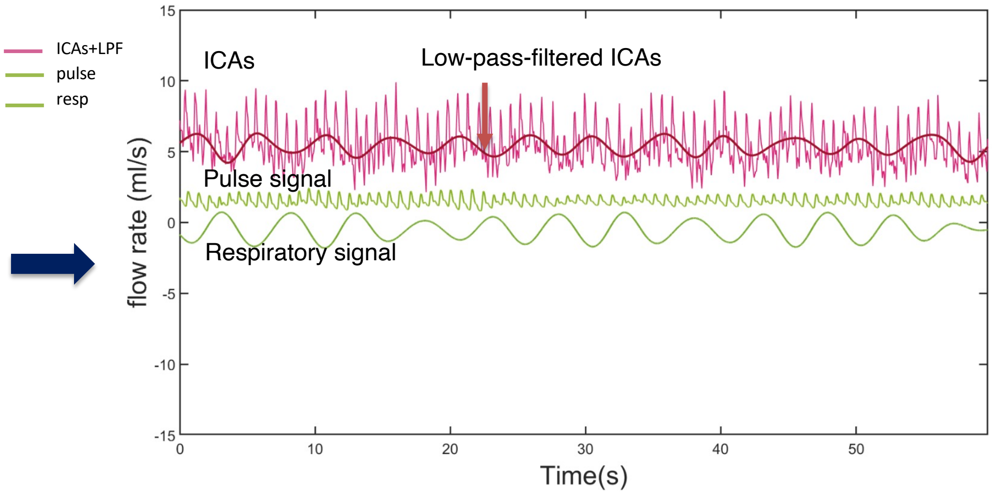


Respiratory pump influence

Flow rate and its drivers

Flow rate estimate

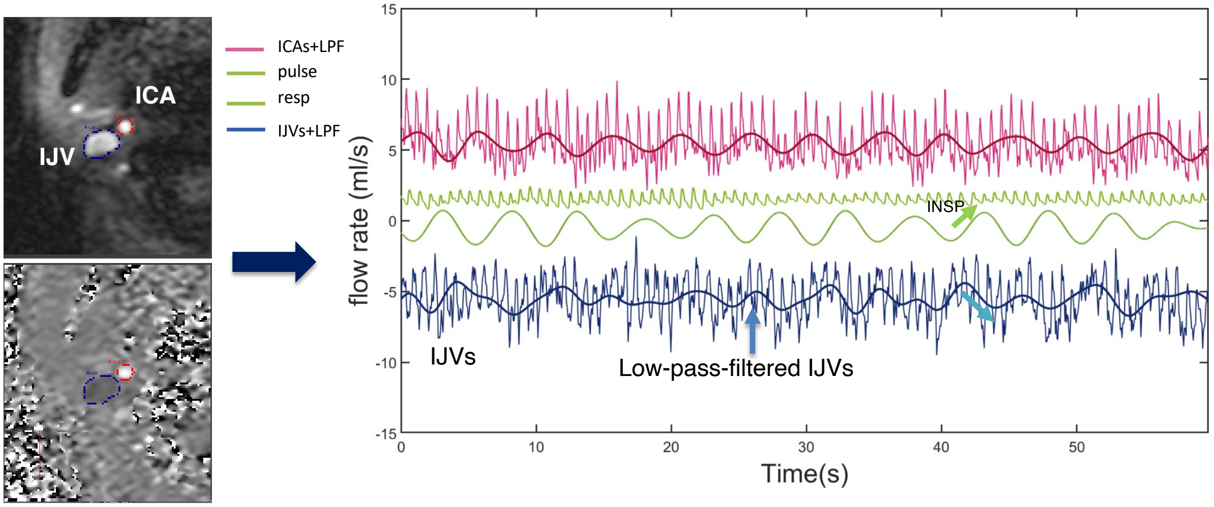




Respiratory pump influence

Flow rate and its drivers

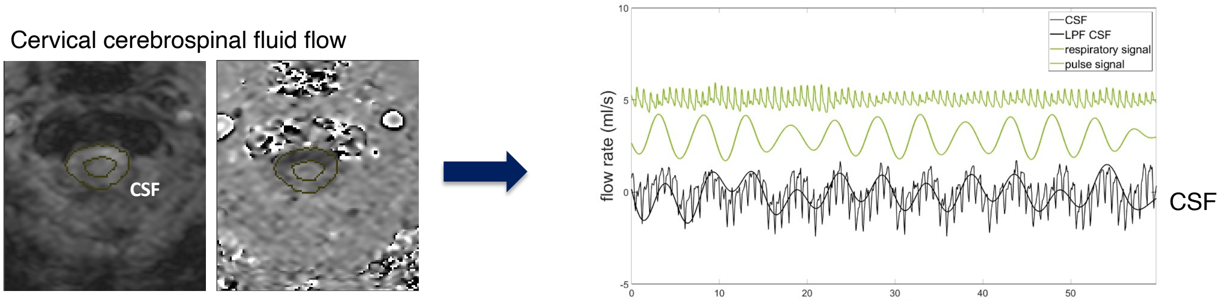
Flow rate estimate



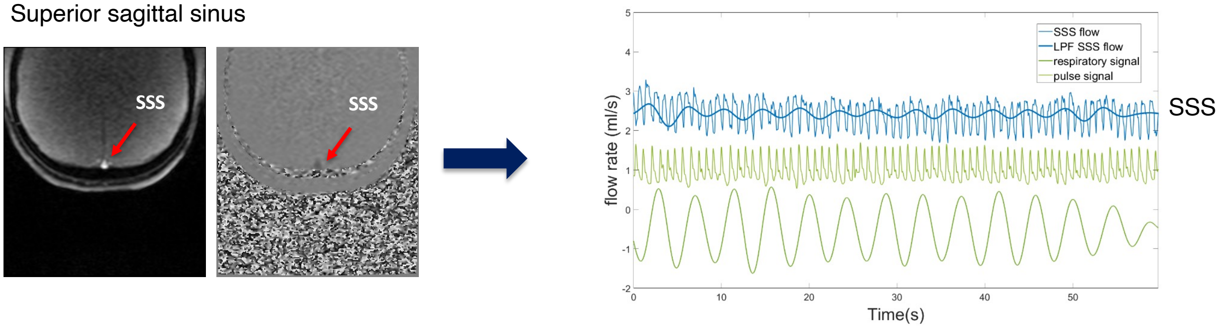
Cardiac and respiratory pump influence

Flow rate and its drivers

Cervical cerebrospinal fluid flow

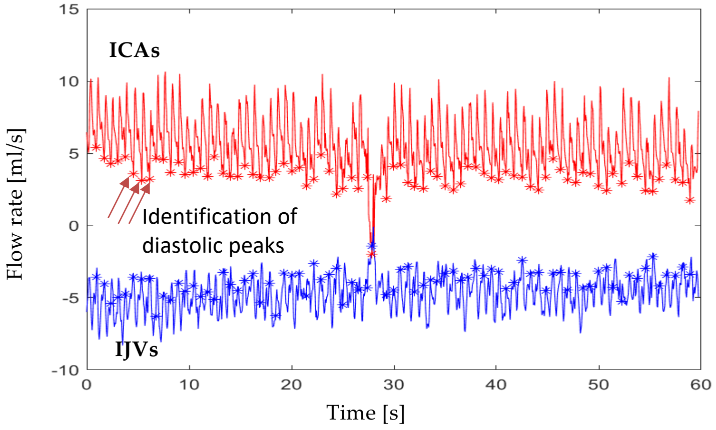


Superior sagittal sinus



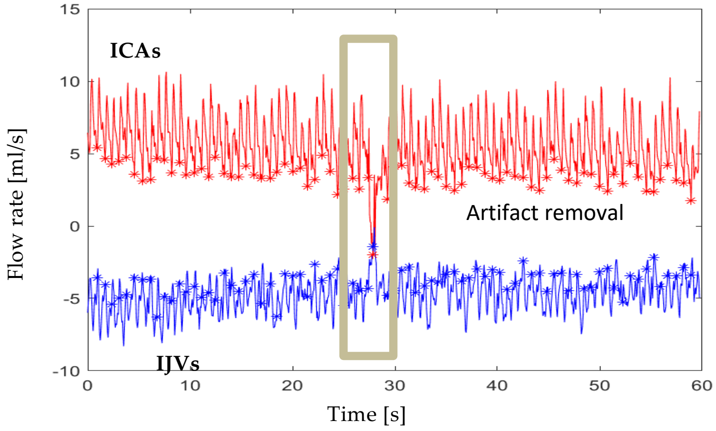
Study 1 – Beat-by-beat variability

- Identification of diastolic peaks

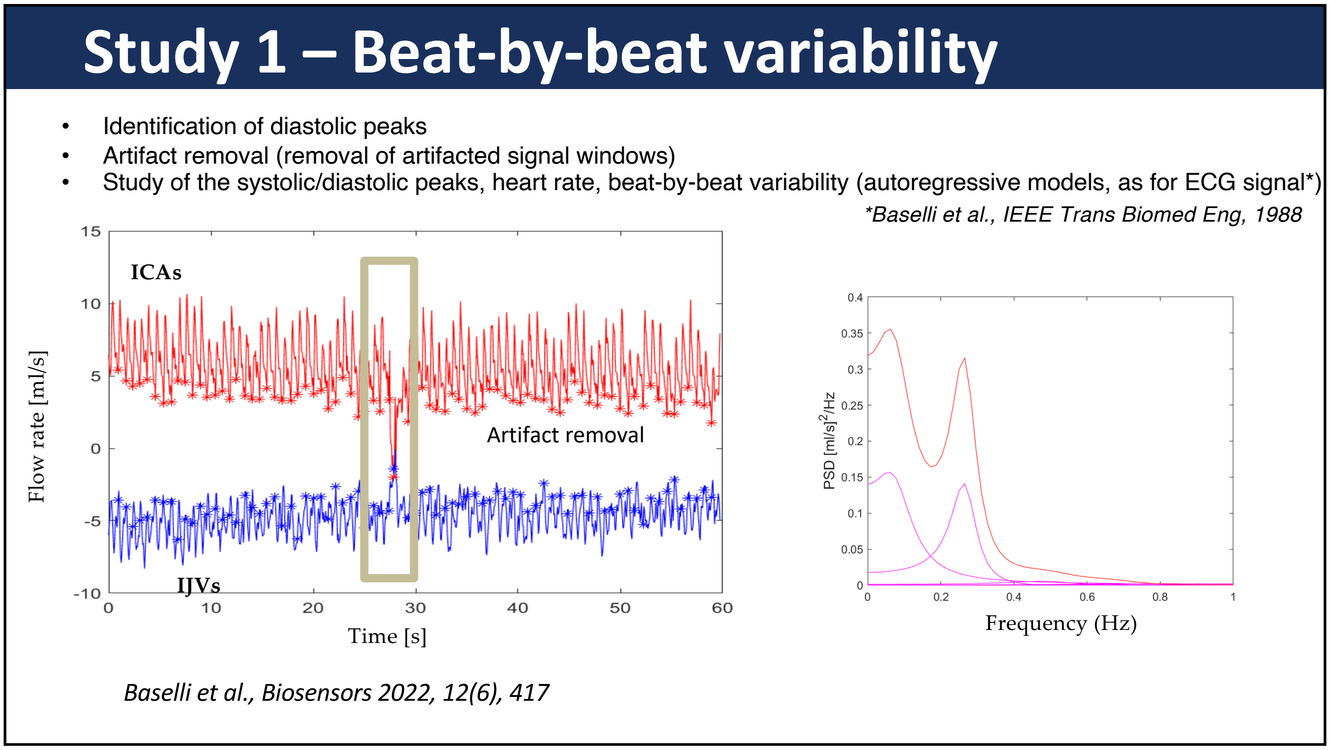


Study 1 – Beat-by-beat variability

- Identification of diastolic peaks
- Artifact removal (removal of artifacted signal windows)



Baselli et al., Biosensors 2022, 12(6), 417

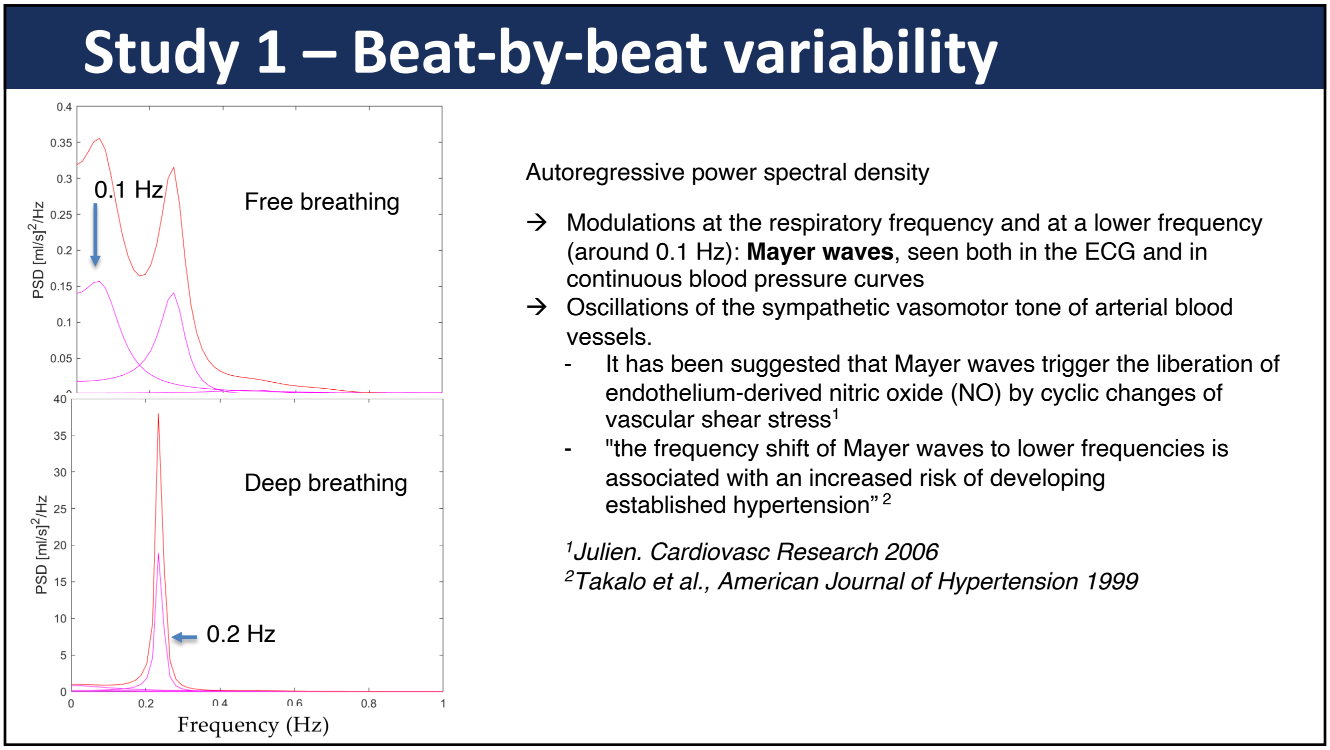


Study 1 – Beat-by-beat variability

- Identification of diastolic peaks
- Artifact removal (removal of artifacted signal windows)
- Study of the systolic/diastolic peaks, heart rate, beat-by-beat variability (autoregressive models, as for ECG signal*)

**Baselli et al., IEEE Trans Biomed Eng, 1988*

Baselli et al., Biosensors 2022, 12(6), 417



Study 1 – Beat-by-beat variability

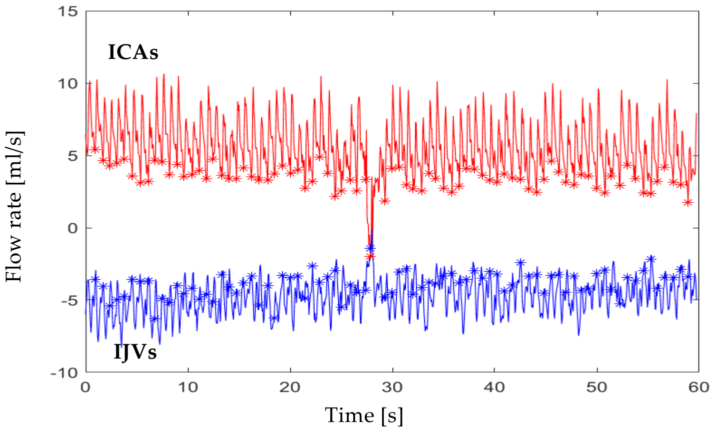
Autoregressive power spectral density

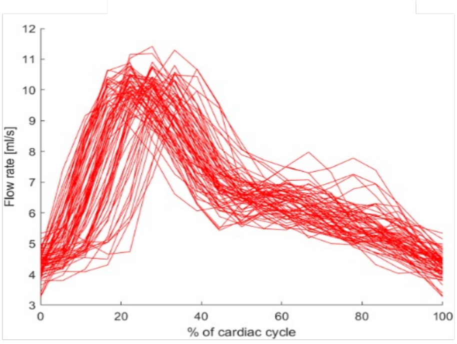
- → Modulations at the respiratory frequency and at a lower frequency (around 0.1 Hz): **Mayer waves**, seen both in the ECG and in continuous blood pressure curves
- → Oscillations of the sympathetic vasomotor tone of arterial blood vessels.
  - It has been suggested that Mayer waves trigger the liberation of endothelium-derived nitric oxide (NO) by cyclic changes of vascular shear stress[1]
  - "the frequency shift of Mayer waves to lower frequencies is associated with an increased risk of developing established hypertension" [2]

[1] *Julien. Cardiovasc Research 2006*
[2] *Takalo et al., American Journal of Hypertension 1999*

Study 1 – Beat-by-beat variability

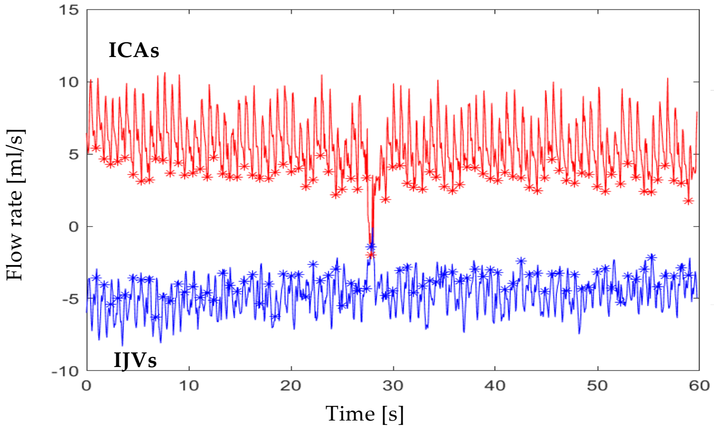
- Identification of diastolic peaks
- Artifact removal (removal of artifacted signal windows)
- Alignment of cardiac cycles, beginning from diastolic peak

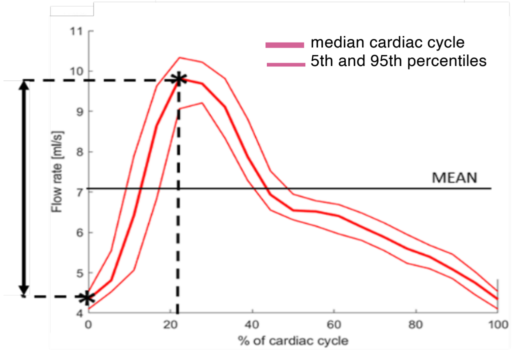




Study 1 – Beat-by-beat variability

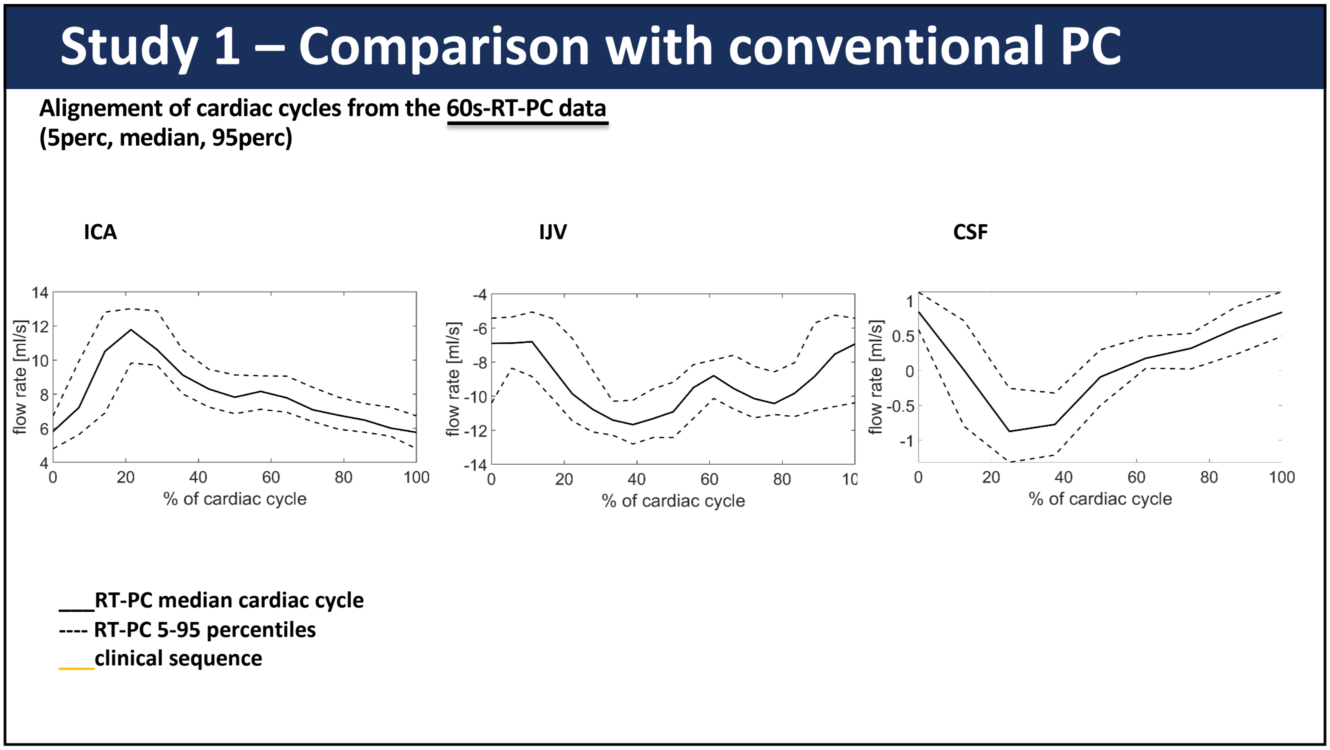
- Identification of diastolic peaks
- Artifact removal (removal of artifacted signal windows)
- Alignment of cardiac cycles, beginning from diastolic peak → median curve for each subject





Median curve, 5th and 95th percentiles

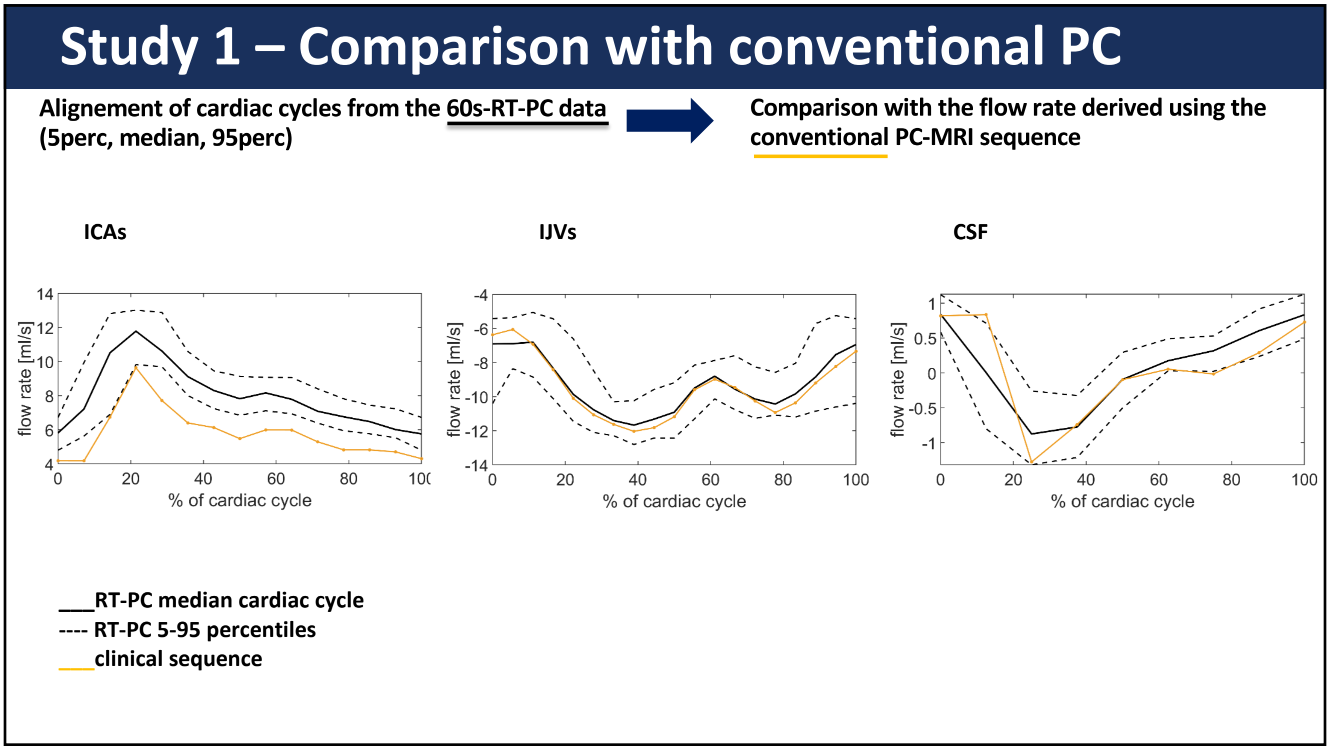
Baselli et al., Biosensors 2022, 12(6), 417



Study 1 – Comparison with conventional PC

Alignement of cardiac cycles from the 60s-RT-PC data
(5perc, median, 95perc)

____RT-PC median cardiac cycle
---- RT-PC 5-95 percentiles
____clinical sequence



Study 1 – Comparison with conventional PC

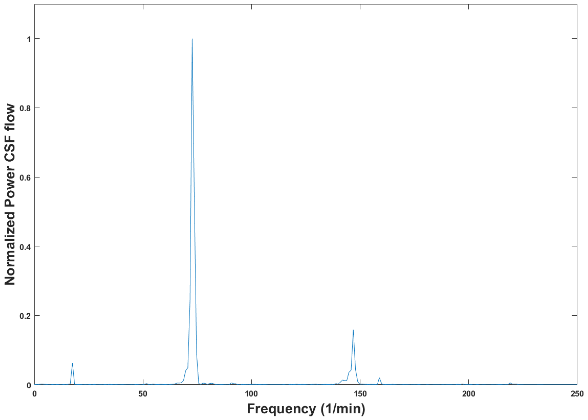
Alignement of cardiac cycles from the 60s-RT-PC data
(5perc, median, 95perc)

Comparison with the flow rate derived using the conventional PC-MRI sequence

____RT-PC median cardiac cycle
---- RT-PC 5-95 percentiles
____clinical sequence

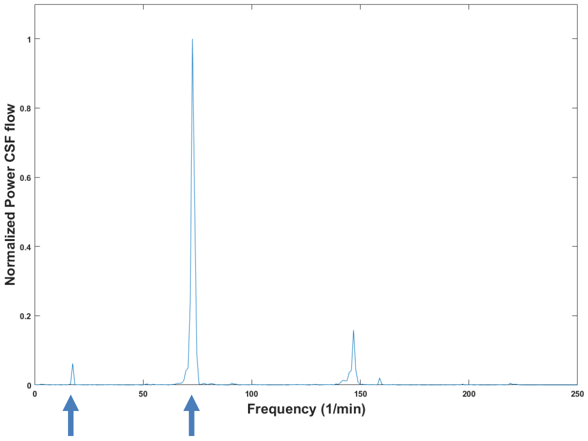
Study 2 – Blood and CSF flow drivers

- Power Spectral Density of the flow rate



Study 2 – Blood and CSF flow drivers

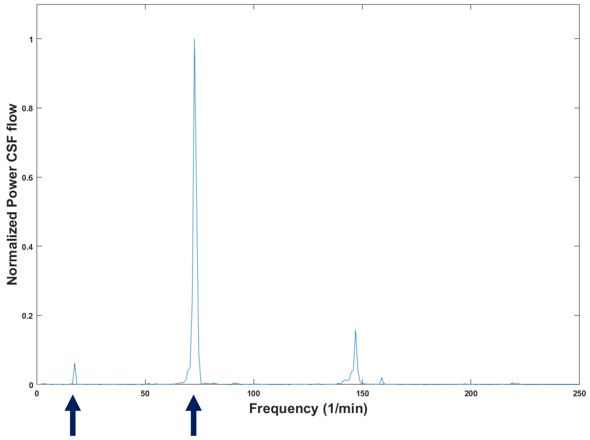
- Power Spectral Density of the flow rate
- Identification of main peaks



Main peaks

Study 2 – Blood and CSF flow drivers

- Power Spectral Density of the flow rate
- Identification of main peaks
- Breathing rate and heart rate computed from physiologic signals



Main peaks

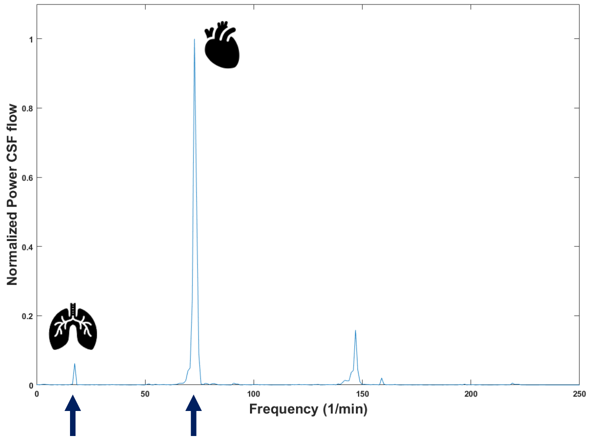
Breathing rate (BR) from thoracic band

Heart rate (HR) from pulse oximeter

Frequencies comparison

Study 2 – Blood and CSF flow drivers

- Power Density Spectrum of the flow rate
- Identification of main peaks
- Breathing rate and heart rate computed from physiologic signals
- Peak frequencies compared to breathing rate and heart rate

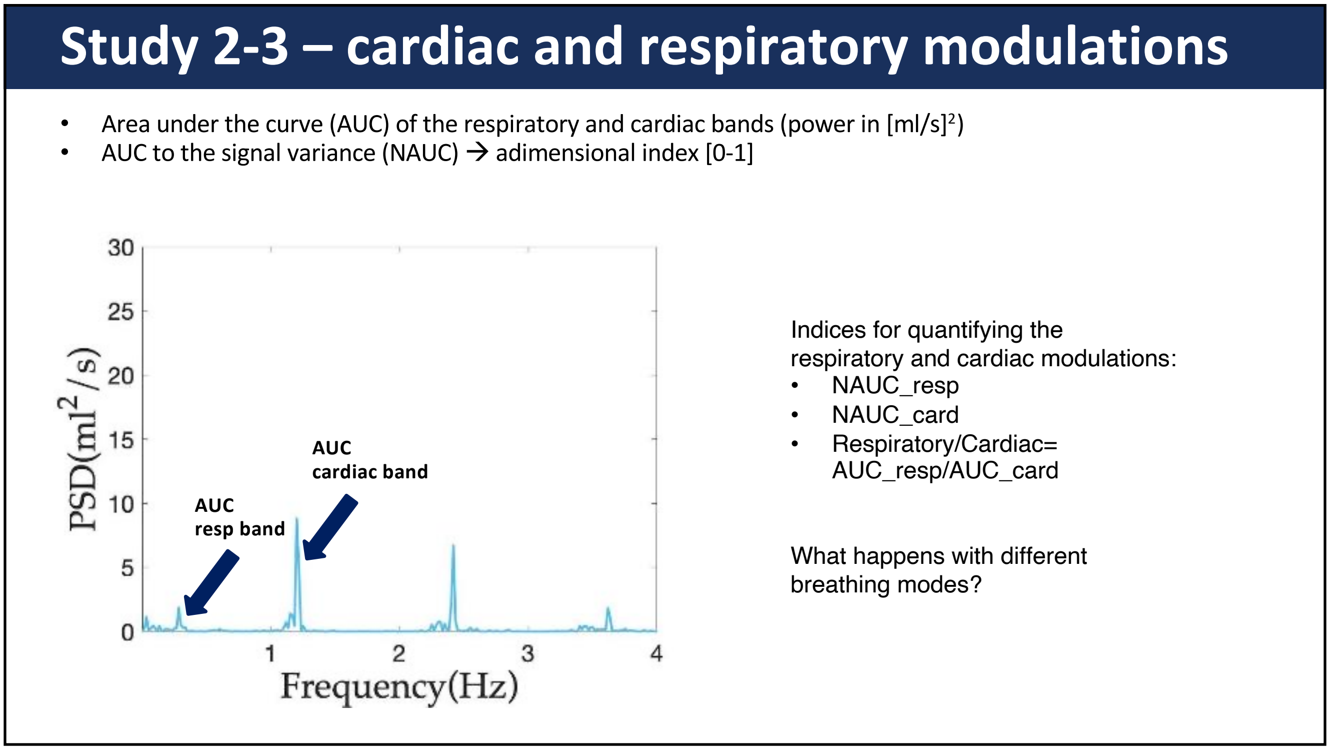


Main peaks

Breathing rate (BR) from thoracic band

Heart rate (HR) from pulse oximeter

Frequencies comparison:
- First peak: not significantly different compared to the BR
- Second peak: not different compared to the HR



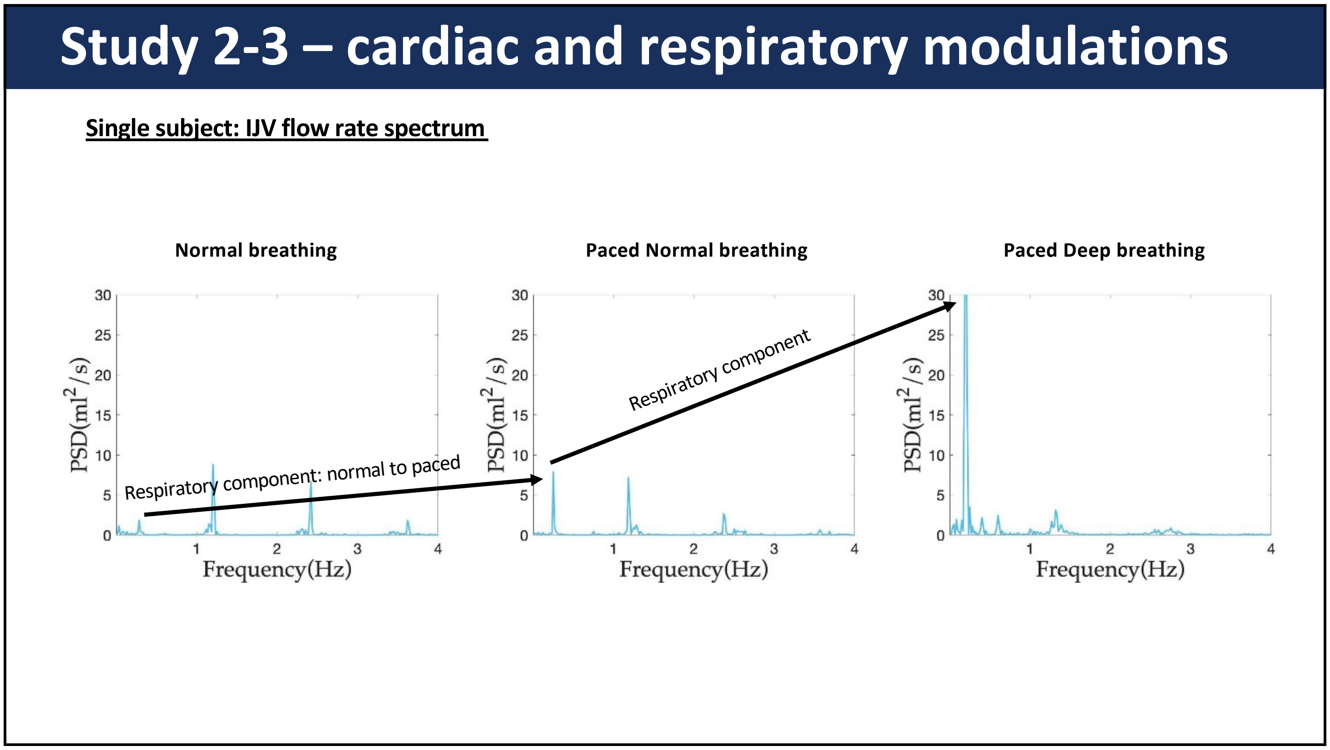
Study 2-3 – cardiac and respiratory modulations

- Area under the curve (AUC) of the respiratory and cardiac bands (power in [ml/s]^2)
- AUC to the signal variance (NAUC) → adimensional index [0-1]

Indices for quantifying the respiratory and cardiac modulations:

- NAUC_resp
- NAUC_card
- Respiratory/Cardiac= AUC_resp/AUC_card

What happens with different breathing modes?



Study 2-3 – cardiac and respiratory modulations

Single subject: IJV flow rate spectrum

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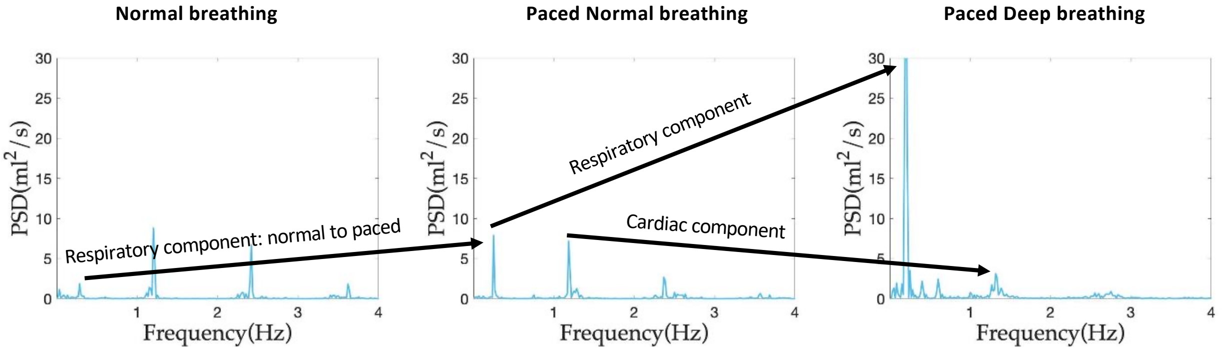


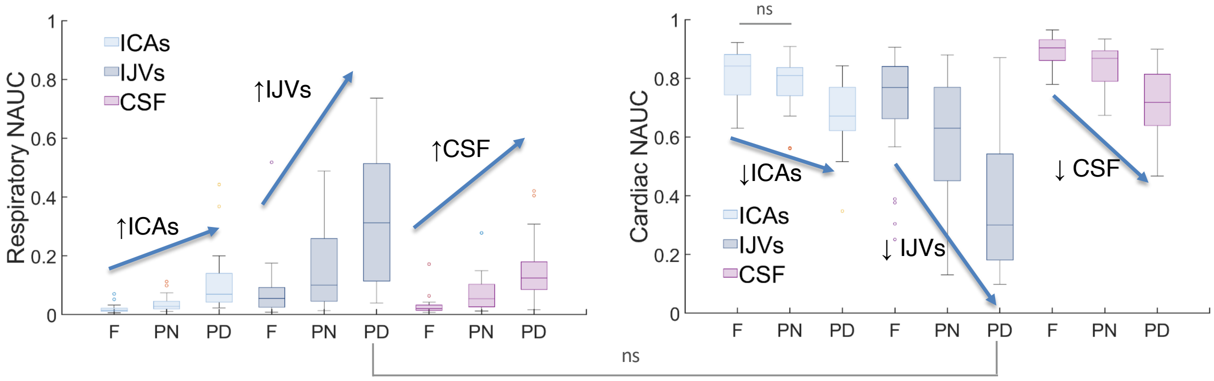
Study 2 – cervical flow rate modulations

Group analysis: respiratory and cardiac components

What happens from free (F) to paced normal (PN) to paced deep (PD) breathing?

- Respiratory component ↑ ($p<0.001$)
- Cardiac component ↓ ($p<0.001$)
- Cardiac > respiratory component ($p<0.001$)

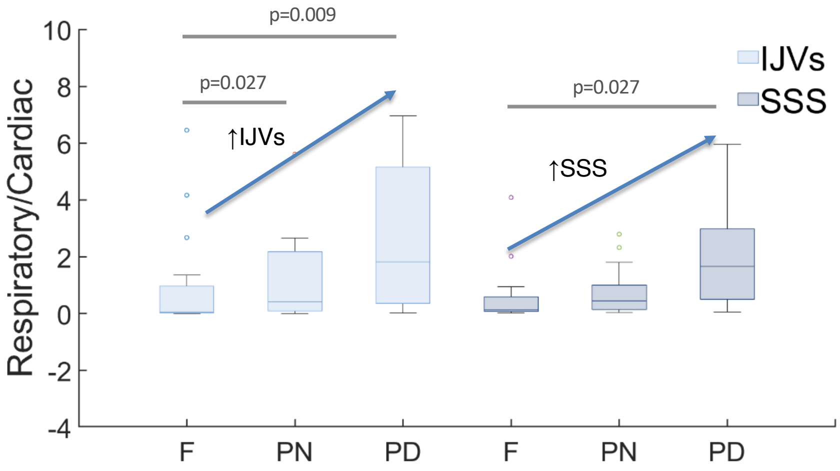
With the exception of non-significant comparisons written in the graph



Study 3 – intracranial vein flow rate modulations

Group analysis: respiratory and cardiac modulation changes

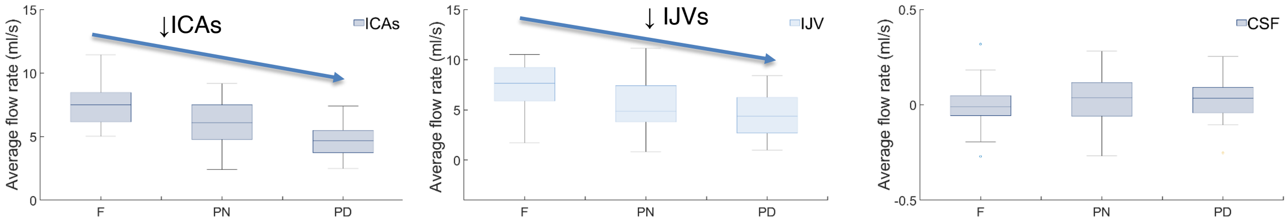
- Respiratory/cardiac component increment from free (F) to paced normal (PN) to paced deep (PD) breathing



Study 2 – average cervical flow rate

Group analysis: flow rate and area changes

- Blood average flow rate decrement (p<0.001 for all the paired comparisons)



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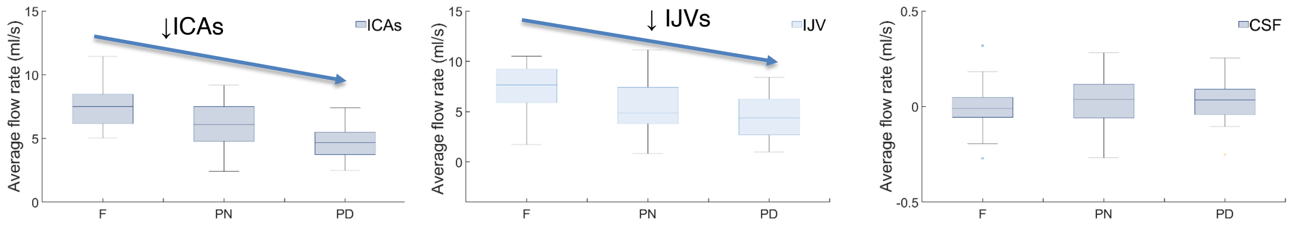
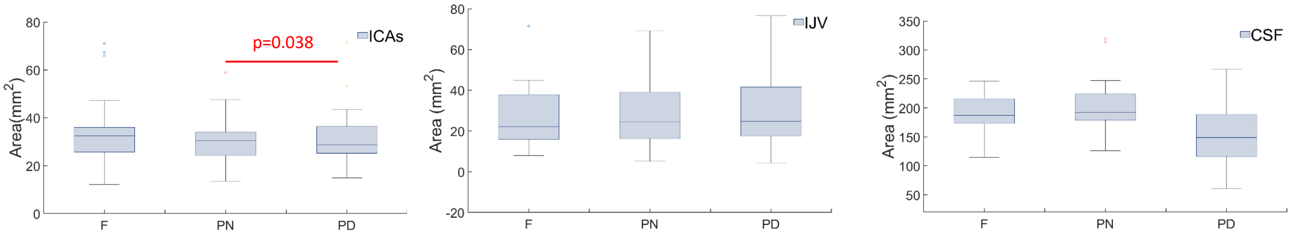


- Cross-sectional area decrement for ICA only (smallest in deep breathing)



Study 3 – intracranial average flow rate

Group analysis: flow rate and cross-sectional area changes

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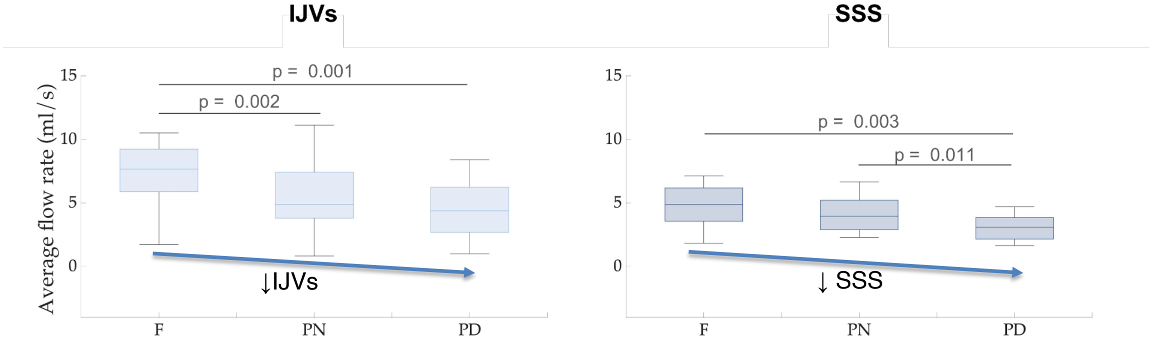

- Cross-sectional areas do not change

Conclusions

Prototype RT-PC for measuring blood and CSF flow rates with **high temporal resolution allows to quantify** not only the cardiac but also the respiratory influence and the low-frequency modulations.

- The beat-to-beat changes with HR variability can be studied

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Prototype RT-PC for measuring blood and CSF flow rates with **high temporal resolution allows to quantify** not only the cardiac but also the respiratory influence and the low-frequency modulations.

- The beat-to-beat changes with HR variability can be studied

- From normal to deep breathing:
  mean flow ↓ (vasoreactive response, ↓ CO2 blood concentration?)
- From normal to deep breathing:
  respiratory modulation ↑ (greater effect of the thoracic pump) and cardiac modulation ↓ for cervical CSF, arterial and venous flow, but also for the superior sagittal sinus

Conclusions

Limitations:
- Only supine position
- Separate acquisitions of blood and CSF flows
- Limited spatial resolution
- Image movement artifacts during deep breathing
- CO2 blood concentration was not measured

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Clinical studies: RT-PC MRI used in pathological cases might allow to investigate how the flows in/out the brain are modulated by breathing patterns.
- Various pathologies might change respiration during sleep → effects on CSF circulation?
- Arterial-venous-CSF flows are linked (Monro-Kellie): might venous alterations change CSF flow?
- Impact of respiration type for drug delivery through CSF

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SIEMENS Healthineers

Ning Jin

Domenico Zacà

POLITECNICO MILANO 1863

Giuseppe Baselli

Students: Ferrari, Fasani, Caglioni, Cavallini, Giudetti, Giudici

backup

RT-PC prototype

- Developed for cardiovascular applications
- Echo planar imaging readout module
- Parallel acceleration in the temporal direction (T-PAT).
- Novel reconstruction algorithm, shared velocity encoding (SVE)* to improve temporal resolution →

2-sided velocity encoding: also called symmetric or bipolar encoding. It acquires a positive (k +) velocity encoded and a negative velocity encoded (k -) acquisition for each cardiac phase to produce the phase difference image.

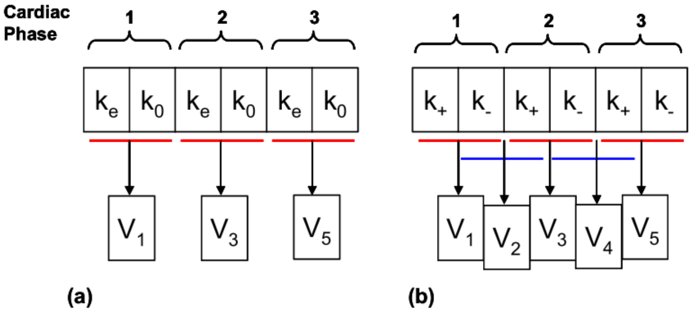
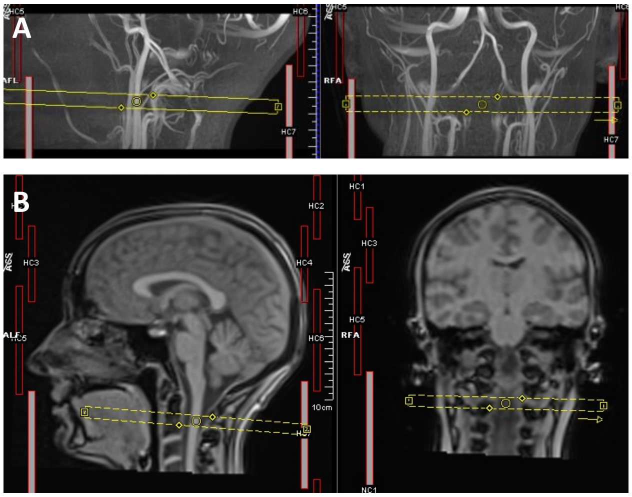


Figure 4. *(**a**) The conventional PC with 1-sided velocity encoding. Velocity information was extracted using the flow encoded (k_e) and flow compensated (k_0) data within the same cardiac phase. (**b**) SVE with 2-sided velocity encoding. Additional velocity frames (V_2 and V_4) are reconstructed by sharing the flow encoded data across cardiac phases to double the effective frame rate by a factor of 2.*

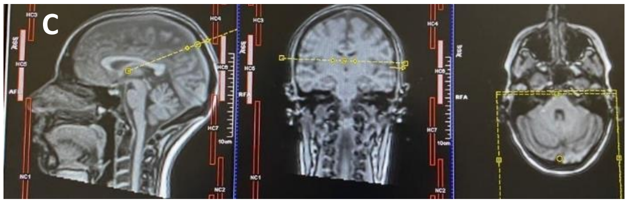
*Lin H et al. Magn Reson Med. 2011

Methods: positioning

Extracranial acquisitions



Intracranial acquisition



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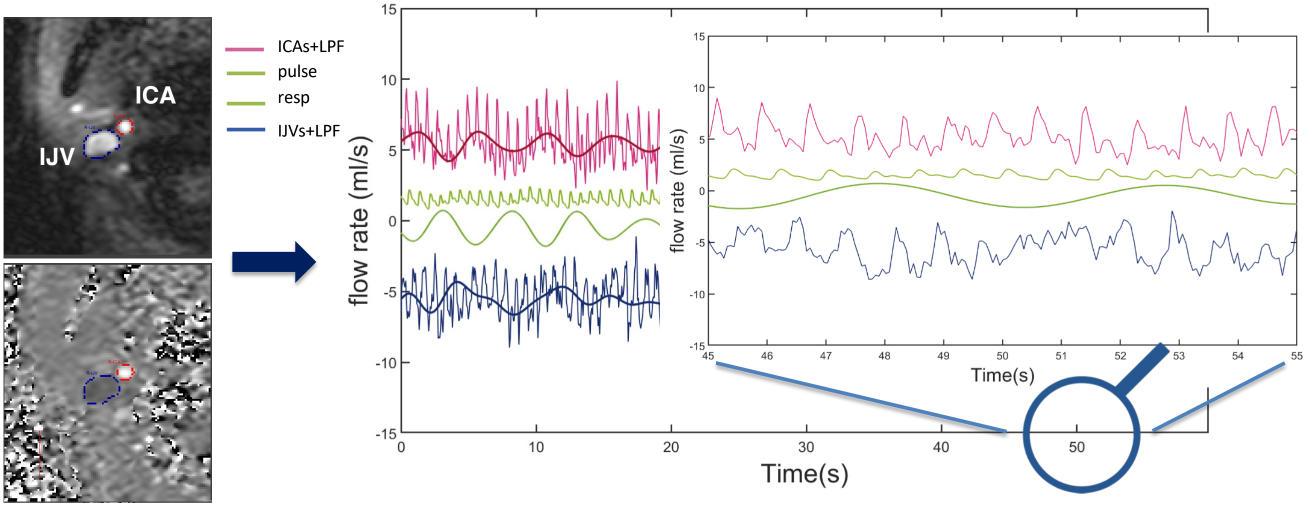
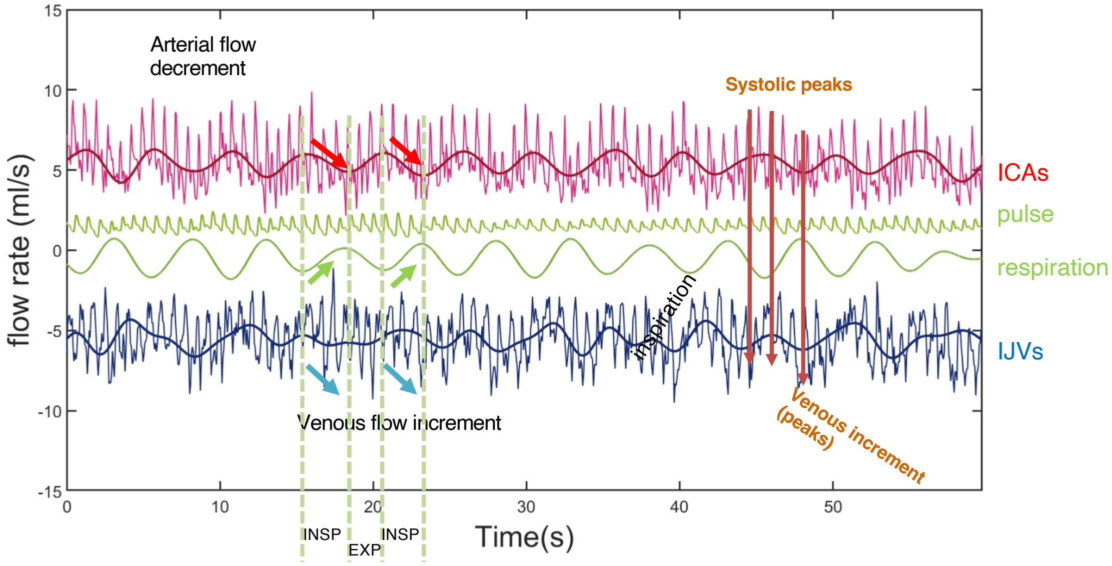
Flow rate and its drivers

Flow rate estimate



Zoomed signal (signal portion from 45s to 55s)

Flow rate and its drivers



BBV

Signal	All	Insp	Exp	Δ Insp-Exsp	p-value of Δ
Mean AF	7.39±1.72	7.32±1.65	7.26±1.64	0.0607	0.068
Mean VF	-7.28±2.28	-7.35±2.45	-7.25±2.23	-0.0954	0.216
Mean CSFF	0.111±0.134	0.085±0.098	0.093±0.134	-0.0084	0.772
Syst AF	10.29±2.44	10.20±2.42	10.08±2.39	0.1244	0.059
Syst VF	-9.08±3.14	-9.21±3.35	-9.16±3.17	-0.0493	0.524
Syst CSFF	-1.81±0.60	-1.87±0.60	-1.80±0.62	-0.0733	0.062
Dia AF	5.11±1.37	5.02±1.26	5.02±1.26	0.0063	0.875
Dia VF	-5.90±2.05	-5.96±2.13	-5.88±2.08	-0.0830	0.310
Dia CSFF	1.44±0.53	1.38±0.42	1.41±0.42	-0.0267	0.416

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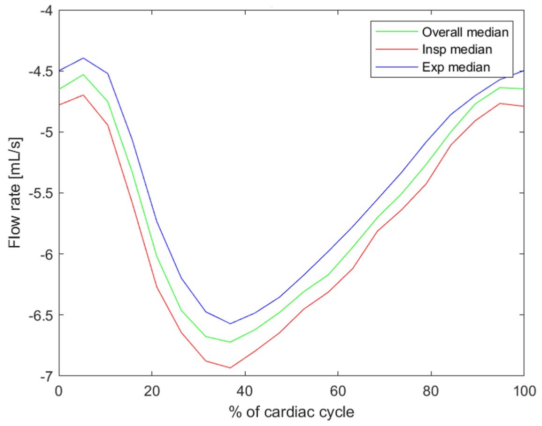
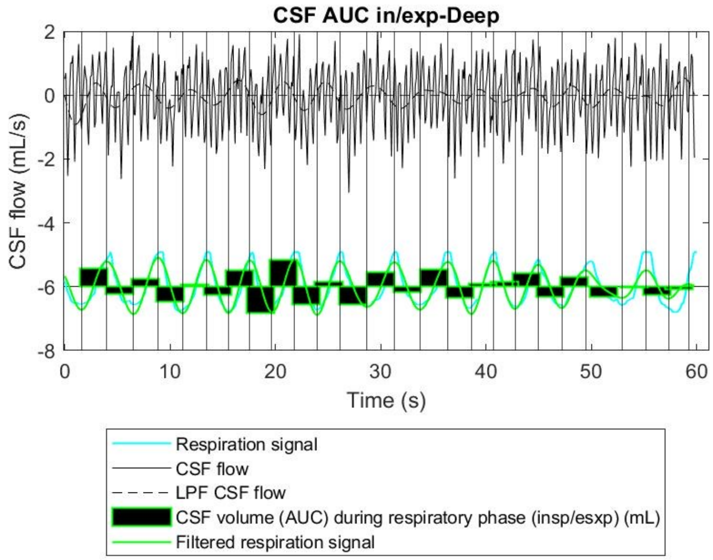
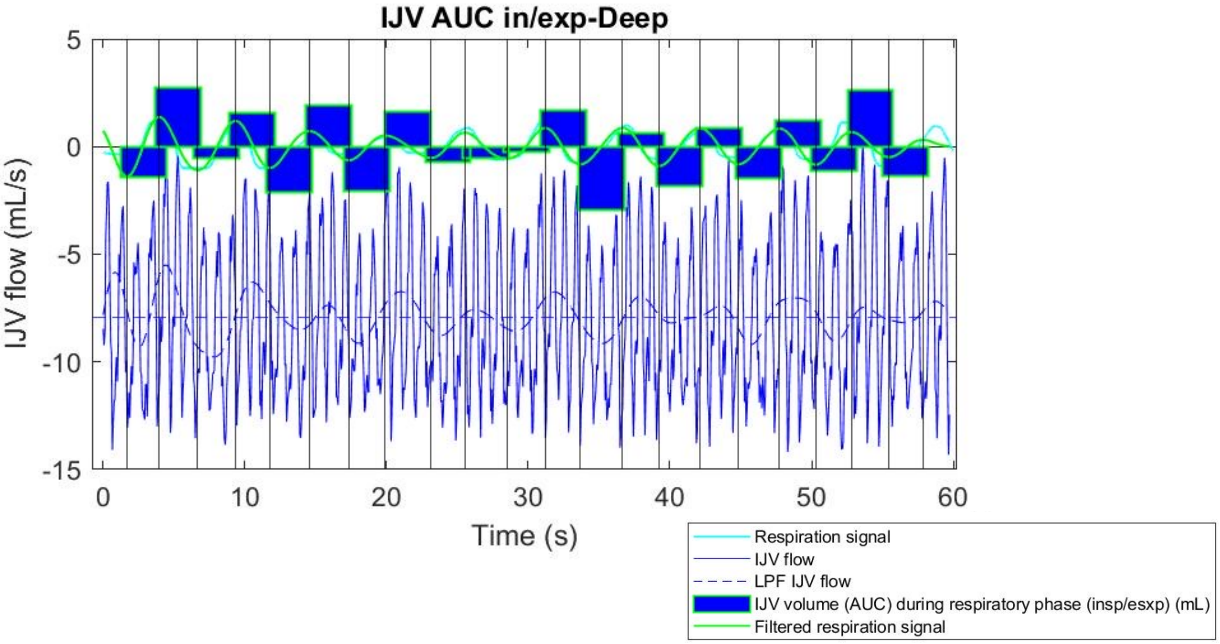
Inspiration and expiration



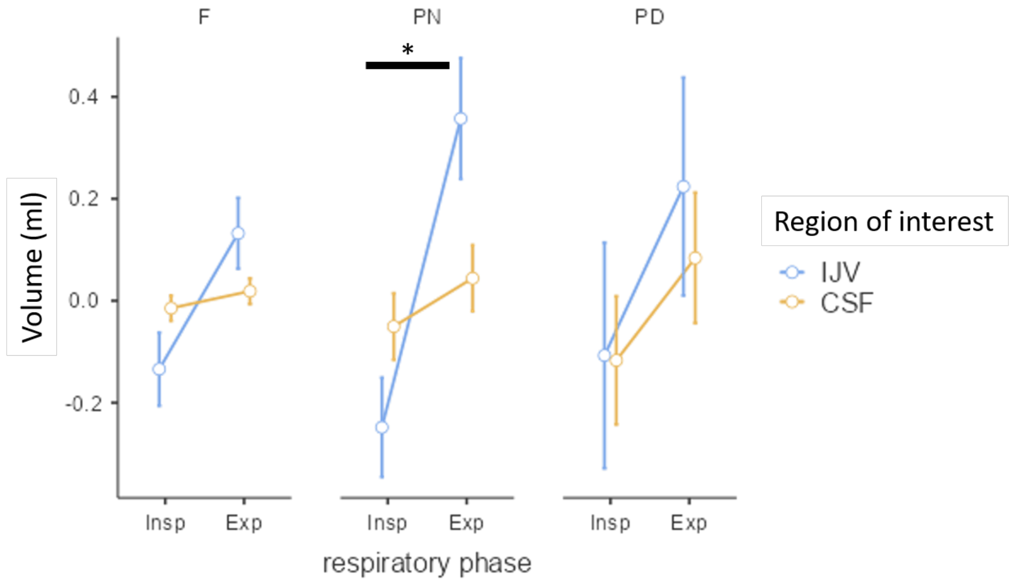
Flow volumes in inspiration and expiration



Flow volumes in inspiration and expiration



Flow volumes in inspiration and expiration



Flow rate: from free to deep breathing