



## Transmission of slow waves in Masimo O<sub>3</sub> near infrared spectroscopy measures

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### ABSTRACT

**Introduction:** Cerebral autoregulation (CA) dysfunction is a key complication following brain injury. CA assessment using near-infrared spectroscopy (NIRS) offers a promising alternative to the current non-invasive standard, cerebral blood flow velocity (CBFV) measured with transcranial Doppler.

**Research question:** Can autoregulatory slow waves (frequency range 0.005–0.05 Hz) associated with spontaneous and induced changes in ABP in healthy volunteers be detected by parameters measured with the Masimo O<sub>3</sub> NIRS device?

**Methods:** ABP, CBFV and Masimo O<sub>3</sub> parameters were measured in 10 healthy volunteers at baseline and during ABP oscillations induced by squat/stand manoeuvres. Transmission of slow waves was assessed with power spectral density and coherence analysis in NIRS signals and compared to that of CBFV.

**Results:** At baseline, slow waves were detected with sufficient power that substantially exceeded the signals' measurement resolution in all parameters except cerebral oxygen saturation. During ABP oscillations in the 0.033 Hz range (induced by squat/stand), the power of slow waves increased in all parameters in a similar pattern, with total (cHb) and oxygenated (O<sub>2</sub>Hb) haemoglobin concentrations most closely mirroring CBFV (median standardised power [first-third quartile], baseline vs squat/stand: CBFV 0.35 [0.28–0.42] vs 0.50 [0.45–0.62], O<sub>2</sub>Hb 0.47 [0.33–0.68] vs 0.61 [0.59–0.69]). Coherence with ABP increased for both CBFV and NIRS measures from low at baseline (<0.4) to high during induced changes (>0.8).

**Conclusion:** Spontaneous fluctuations in ABP can be observed in analysed Masimo O<sub>3</sub> metrics to a varying degree. The clinical utility of Masimo O<sub>3</sub> signals in CA assessment requires further investigation in brain injury patients.

### 1. Introduction

Cerebral autoregulation (CA) is the homeostatic mechanism responsible for maintaining adequate and approximately stable cerebral blood flow (CBF) over a range of systemic blood pressures (Panerai, 1998a). Disturbed CA has been shown to correlate with unfavourable outcome in conditions such as traumatic brain injury (TBI) (Czosnyka et al., 1996) and subarachnoid haemorrhage (Soehle et al., 2004), and its utility in neurocritical care is increasingly recognized (Carney et al., 2017). Continuous assessment of CA primarily relies on observation of changes in CBF surrogates in response to spontaneous fluctuations in cerebral perfusion pressure (CPP) or arterial blood pressure (ABP) in the

'slow wave' frequency range (0.005–0.05 Hz) (Czosnyka et al., 2009). CA operates through changes in the resistance of small cerebral vessels (Panerai, 1998b), and these natural slow oscillations in blood pressure have time periods long enough to trigger the autoregulatory response (in contrast to, for example, the faster respiratory and cardiac-related components) (Zweifel et al., 2014a). If CA is intact, there is little association between fluctuations in blood pressure and CBF. In a non-autoregulating system, these slow waves are transmitted passively to CBF (Czosnyka et al., 2001). Therefore, slow wave activity, and the analysis thereof, provides information regarding CBF control and CA.

Cerebral blood flow velocity (CBFV) monitored using transcranial Doppler (TCD) ultrasonography in large cerebral arteries is one of the

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surrogate measures of CBF used in the assessment of CA (Aaslid et al., 1982). Several different approaches based on TCD-based CBFV measurement have been proposed. For instance, the Mx index is a time-domain measure calculated as the moving correlation coefficient between slow changes in CBFV and CPP (Czosnyka et al., 1996). In the frequency domain, CA may be assessed using transfer function analysis. This analysis assesses the transmission of oscillations from ABP to CBFV (Zhang et al., 1998). However, TCD measurement relies on the operator's ability to locate the temporal bone window for probe placement (which may not be possible in up to 10–20% of patients (Baumgartner, 2006)). Moreover, long-term measurements are susceptible to signal loss and movement artefacts. Recently introduced robotic probes may help to alleviate the latter issue (Zeiler and Smielewski, 2018), but they are still somewhat problematic and are not yet widely used.

Near-infrared spectroscopy (NIRS) is a different non-invasive technique that offers indirect information on CBF through monitoring of brain oxygenation based on relative absorption of oxygenated (O<sub>2</sub>Hb) and deoxygenated haemoglobin (HHb) (Madsen and Secher, 1999). NIRS measurement offers considerable advantages compared to TCD, as it does not require extensive technical training and involves minimal operator attention once the probes are attached, while still allowing for a continuous monitoring. The tissue oxygenation index (TOI, also called rSO<sub>2</sub>), expressed as the ratio of oxygenated to total haemoglobin concentration, has been used to provide a NIRS-based alternative to Mx called TOx (or COx). It is calculated as the moving correlation coefficient between TOI and CPP (Steiner et al., 2009; Zweifel et al., 2010a). It has been demonstrated that TOx can detect impaired CA and is correlated with Mx (Steiner et al., 2009; Zweifel et al., 2010a; Brady et al., 2010a, 2010b). In addition to CA assessment based on CBF surrogates, NIRS-derived metrics also offer the possibility of non-invasively studying cerebral blood volume (CBV)-related indices. In TBI, CA is commonly evaluated with the pressure reactivity index (PRx) which uses invasively collected intracranial pressure as a surrogate measure of changes in intracranial volume (Czosnyka et al., 1997). As CA operates through vasoconstriction or vasodilation of small cerebral vessels, the response to changes in ABP is reflected in CBV and can therefore be studied by assessing cerebrovascular pressure reactivity. The total haemoglobin index (THI) serves as the basis for the THx index (moving correlation coefficient between THI and ABP), which showed good correlation with PRx and the ability to detect impaired cerebrovascular reactivity in TBI patients (Lee et al., 2009; Zweifel et al., 2010b). Despite the advantages offered by NIRS measurements in the monitoring of CA, it has been suggested that a significant proportion of the monitoring data is not suitable for the assessment of CA due to insufficient power of slow waves in the input signal to ensure robust calculation of CA metrics (Zweifel et al., 2014b).

Masimo Root O<sub>3</sub> Regional Oxymeter (Masimo Corporation, Irvine, California, USA) is a relatively new but increasingly popular NIRS monitor, which in addition to bilateral rSO<sub>2</sub> measurements, also offers O<sub>2</sub>Hb and HHb concentration, along with 4-channel EEG. Therefore, this device could be helpful in implementing continuous monitoring of autoregulation with metrics such as COx or THx at the bedside. To date, the feasibility of such approach in the Masimo O<sub>3</sub> NIRS machine has not yet been established. Hence, we aimed to investigate the feasibility of monitoring slow waves using parameters produced by the Masimo O<sub>3</sub> NIRS device during periods of spontaneous and induced changes in ABP in healthy volunteers. This would inform the use of Masimo O<sub>3</sub> NIRS device for continuous monitoring of CA. Sufficient transmission of ABP variability to NIRS-derived measures would offer the possibility of using the Masimo O<sub>3</sub> device in neurocritical care monitoring of CA.

## 2. Material and methods

### 2.1. Study group

Ten healthy volunteers (6 males, 4 females; median age: 29 years,

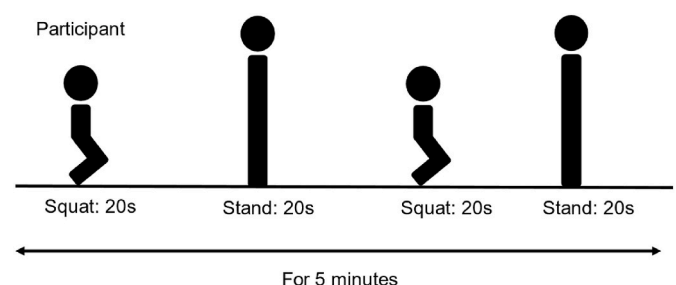
range: 21–55 years) were recruited to this study. The participants had no history of hypertension, neurological disorders, or serious chronic diseases known to influence the cardiovascular, respiratory, and nervous system. One participant had a history of smoking, and two participants were asthmatic. The volunteers were asked to refrain from caffeine for 6 h and drugs and alcohol for 24 h prior to the study to avoid any additional confounders on baseline ABP. Ethical approval was obtained from the local ethics committee (IRAS 266210), and protocols were carried out in accordance with the Declaration of Helsinki. Informed consent was obtained from all participants.

### 2.2. Experimental protocol

The squat/stand manoeuvre was used to induce periodic changes in the ABP signal with different oscillation frequencies. This method was previously proposed to improve assessment of CA by increasing the signals' coherence and the signal-to-noise ratio compared to spontaneous ABP analysis (Claassen et al., 2009). The measurement started with 5 minutes of baseline recording with the participant in the standing position. Next, the participant was asked to alternate between squatting and standing for 5 minutes (Fig. 1). The squat/stand manoeuvre was performed with three different time periods, referred to as 'cycles': 40 seconds (s) (20 s of squatting followed by 20 s of standing), 30 s (15 s squatting, 15 s standing), and 20 s (10 s squatting, 10 s standing), corresponding to oscillation frequencies of 0.025 Hz, 0.033 Hz, and 0.05 Hz, respectively. These periods were selected based on an initial pilot study (unpublished data) showing the feasibility of inducing ABP oscillations of different frequencies with these squat/stand manoeuvres. Between each of the 5-min squat/stand stages the participant rested for at least 5 minutes until the physiological parameters (specifically end-tidal carbon dioxide, respiratory rate, heart rate, systemic oxygenation) returned to baseline.

### 2.3. Data acquisition

Non-invasive beat-to-beat ABP was measured using a photoplethysmographic system (Finometer Pro, Finapres Medical Systems B. V., Enschede, the Netherlands) with a cuff placed on the middle finger of the subject's left hand. The hand was kept at the level of the heart throughout the measurement. CBFV in the middle cerebral artery (MCA) was recorded using a TCD unit (Delica EMS-9PB Robotic TCD, Shenzhen Delica Medical Equipment Company, Shenzhen, P.R. China) with a 2-MHz probe placed over the subject's temporal window. CBFV was collected as the current non-invasive 'gold standard' to compare the ABP to NIRS transmission of slow waves with ABP to CBFV. Two NIRS probes (Masimo O<sub>3</sub><sup>TM</sup> Regional Oxymeter, Masimo Corporation, Irvine, California, USA) were placed symmetrically on the participant's forehead according to the operator's manual provided by the manufacturer. The following NIRS parameters were recorded: concentration of



**Fig. 1.** Schematic representation of the experimental protocol for the squat/stand manoeuvre in the 40-s cycle. The participant was asked to alternate between squatting and standing with each position assumed for 20 s. The cycle was repeated for 5 min. The same procedure was performed in the 30 and 20-s squat/stand cycles.

deoxygenated (HHb), oxygenated (O<sub>2</sub>Hb), and total haemoglobin (cHb; equivalent to HHb + O<sub>2</sub>Hb), and total oxygen saturation (rSO<sub>2</sub>). Importantly, the inherent 60 s smoothing function of Masimo O<sub>3</sub> applied by default to HHb and O<sub>2</sub>Hb signals was disabled to achieve higher temporal resolution. Bilateral measurements of both CBFV and NIRS parameters were collected where possible, with the robotic TCD probes secured in position using Delica's own fixation system. The participant's respiratory rate and end-tidal carbon dioxide were measured continuously through a respiratory mask connected to a Carescape monitor with a capnograph unit (Carescape B125M, GE Healthcare, Chicago, Illinois, USA). Heart rate and systemic oxygenation were measured using a finger pulse oximeter provided with Carescape monitor. These measures were monitored to ensure that the volunteer's physiological state returned to baseline between each squat/stand cycle. The signals were recorded using ICM+ software (<https://icmplus.neurosurg.cam.ac.uk>, Cambridge Enterprise Ltd, Cambridge, UK) (Smielewski et al., 2005) with sampling frequency of 125 Hz for CBFV, 1 Hz for the NIRS parameters, and 100 Hz for ABP. During the data acquisition process, all variables were resampled to a uniform sampling frequency of 300 Hz via the "sample and hold" approach of ICM+ software. The signal resolution (i.e. the minimum distinguishable difference in signal value between two data points) was determined individually for each signal and device by consulting the manufacturer's documentation provided with the device. The resolutions were as follows: 0.03 mm Hg for ABP, 0.93 cm/s for CBFV, 1% for rSO<sub>2</sub> and 0.1 μmol/l for haemoglobin concentration measures. The signal resolution of each machine is also specified in Table 1.

#### 2.4. Data processing and calculated indices

ICM+ software was used to process the recorded signals. Prior to analysis, artefacts were manually identified and removed from raw data. This primarily included sharp drops or spikes and non-physiological values resulting from movement beyond the squat/stand changes, particularly accidental cable or probe displacement during position changes. The pulsatile signals ABP and CBFV were additionally inspected to identify any segments with distorted waveforms. The artifact removal process was performed jointly by two authors (CAS and AK) using the artifact selection tool in ICM+ software.

To reduce short-term disturbances with frequencies outside the analysed range of slow waves, both ABP and CBFV were filtered using a moving average filter (window length: 2 s). In participants with bilateral TCD and NIRS recordings, the side with better quality of the signals was selected by experienced researchers (initial selection by author AK, confirmed by PS), and final analysis included only unilateral CBFV and NIRS parameters. The baseline and three squat/stand stages were manually extracted from each recording and treated as separate analysis periods. An illustrative example of recorded signals is presented in Fig. 2.

Power spectral density (PSD) analysis (Kay, 2001) was performed to assess the power of slow waves in the recorded signals. PSD analysis is a

signal processing technique that allows for estimation of the energy distribution of the signal over frequency. Here, it was used to obtain a measure of variability of the signals in the frequency range corresponding to slow-wave activity as proposed in a previous study on slow waves in the ICP signal (Beqiri et al., 2020). PSD spectra for each signal were obtained using the periodogram method with Hanning window and the power of slow waves was calculated as the integral of the signal's spectrum in the range 0.005–0.05 Hz.

Then, two different operations were performed. First, to compare estimated power of slow waves in each signal to the measurement resolution of that signal, square root was applied to power estimates obtained at baseline and during the 30-s squat/stand cycle which was identified as producing the largest oscillations. This operation can be interpreted as providing an 'effective amplitude' of a pure sinusoidal wave carrying the same amount of energy as the analysed signal and representing the amplitude of slow waves expressed in the units of measurement of a given signal. This measure is hereafter referred to as 'amplitude'. Secondly, to compare power of slow waves between measurement stages (i.e., baseline and squat/stands with different oscillation frequencies), power estimates obtained from each stage were standardised by dividing them by the total power of the signal (expressed as its variance) in a given analysis period. The standardised power obtained via this operation is unitless and within the 0–1 range, thus enabling comparison between experiment stages.

Furthermore, the representative value of coherence between ABP, CBFV, and each of the NIRS measures was defined as the maximum value of coherence observed in the slow wave frequency range of 0.005–0.05 Hz. In general, coherence assesses the degree of coupling between oscillations of a given frequency, with values close to 1 indicating strong linear relationship between the signals and values close to 0 suggesting lack of linear relationship or poor signal-to-noise ratio. The maximum values were selected instead of the mean as it is the metric better suited to analysis of the spectral components induced by the squat/stand manoeuvre.

### 3. Results

10 healthy participants underwent the study protocol. 5 volunteers had bilateral TCD signal, and hence the better-quality signal was used for further analyses. The standing baseline and 40-s squat/stand manoeuvre were successful in all 10 participants. The 30 and 20-s cycles were unsuccessful in one participant. The maximum number of recordings available was used in each individual case.

#### 3.1. Amplitude of slow waves at baseline

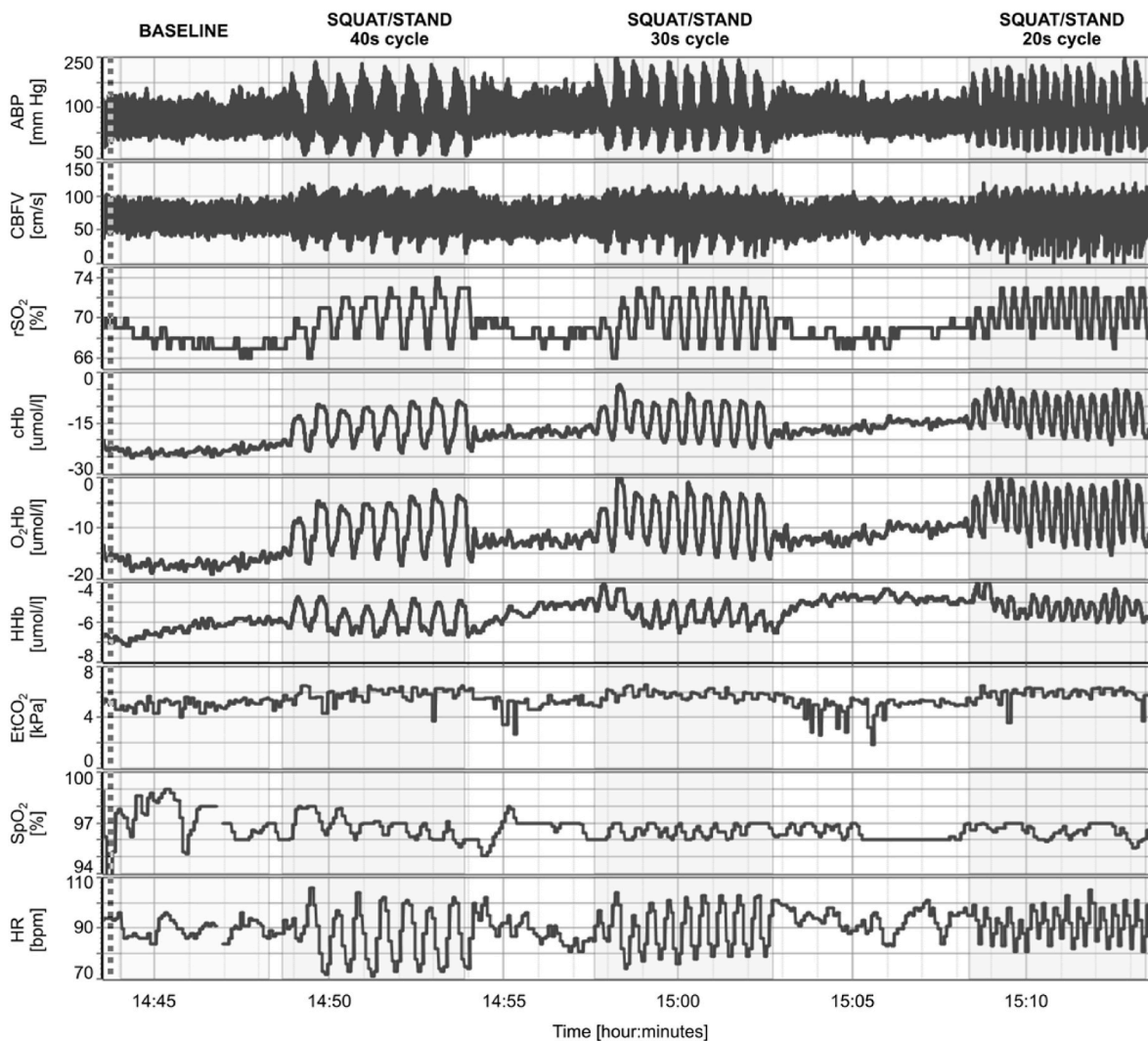
Table 1 presents the amplitude of the slow wave component of each signal averaged over the whole study group in relation to the signal's measurement resolution for the 30-s squat/stand cycle. At baseline, the amplitudes of the ABP and CBFV signals exceeded the machine resolution (last column) by two orders of magnitude and over three times,

**Table 1**

Amplitude of slow waves (calculated as the square root of slow wave power) in each of the analysed signals at baseline and during the 30-s cycle of the squat/stand manoeuvre compared to the signal's measurement resolution. The resolution (defined as the minimum distinguishable difference in signal value between two data points) was determined from the manufacturer's specification individually for each signal or device. Results are presented as group-averaged values from all 10 participants as presented as median (first–third quartile). n = number of participants in the group.

Signal	Amplitude of slow waves at baseline (n = 10)	Amplitude of slow waves during the 30-s squat/stand cycle (n = 9)	Signal resolution
ABP (mmHg)	5.61 (4.83–6.08)	13.26 (8.87–16.76)	0.03
CBFV (cm/sec)	3.25 (2.79–5.70)	8.15 (6.27–8.93)	0.93
rSO <sub>2</sub> (%)	0.85 (0.70–1.34)	1.24 (0.67–1.48)	1.00
cHb (μmol/l)	1.22 (0.67–1.94)	1.59 (0.98–2.06)	0.10
HHb (μmol/l)	0.47 (0.35–0.80)	0.51 (0.40–0.66)	0.10
O <sub>2</sub> Hb (μmol/l)	1.33 (0.85–1.73)	1.53 (1.23–1.96)	0.10

ABP—arterial blood pressure, CBFV—cerebral blood flow velocity, rSO<sub>2</sub>—total oxygen saturation, cHb—total haemoglobin concentration, HHb—deoxygenated haemoglobin concentration, O<sub>2</sub>Hb—oxygenated haemoglobin concentration.



**Fig. 2.** Illustrative example of signals recorded at baseline and during the squat/stand manoeuvres with increasing frequency of induced oscillations (periods marked by grey background) for a single volunteer. From top to bottom: ABP—arterial blood pressure, CBFV—cerebral blood flow velocity,  $rSO_2$ —total oxygen saturation, cHb—total haemoglobin concentration, HHb—deoxygenated haemoglobin concentration,  $O_2Hb$ —oxygenated haemoglobin concentration.

respectively. For NIRS-derived measures at baseline, the effective amplitude was also approximately ten times higher than the machine resolution for  $O_2Hb$  and cHb, and nearly five times higher than machine resolution for HHb. However, for  $rSO_2$ , the two values were similar, with slow wave amplitude lower than machine resolution by more than 10%.

On average, the 30-s squat/stand manoeuvre resulted in an increase in the amplitude of slow waves in both ABP and CBFV by a factor of approximately 2.5 compared to baseline. The ABP oscillations induced via the 30-s squat/stand also led to a small rise in the amplitudes of cHb (approx. 30%),  $O_2Hb$  (approx. 15%), and HHb (approx. 8%) slow waves compared to baseline. Although the amplitude of slow waves in  $rSO_2$  increased by nearly 50%, even during induced changes in ABP, the variability of the signal only slightly exceeded the machine resolution.

### 3.2. Effect of induced oscillations on power of slow waves

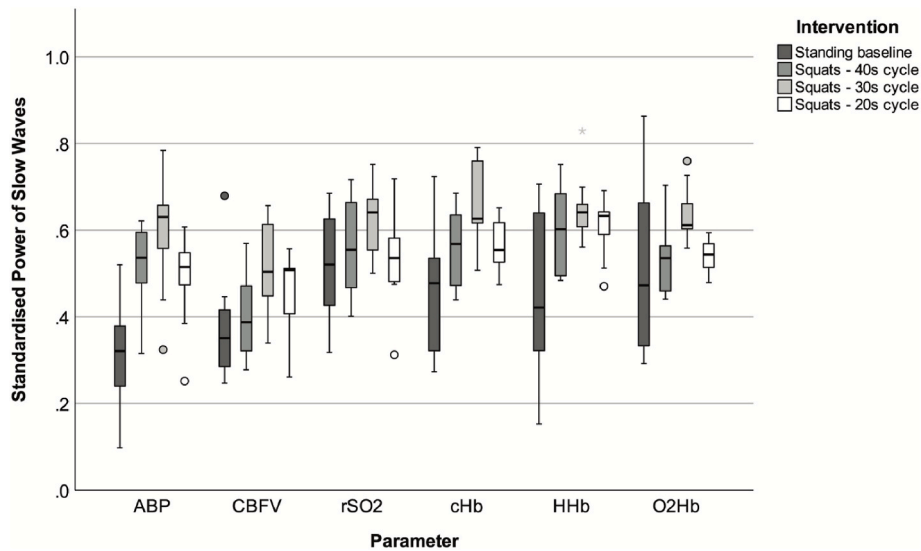
Comparison of standardised power of slow waves between different measurement stages is presented in Fig. 3. The squat/stand manoeuvres generally led to an increase in the power of slow waves with a similar pattern of changes in all the analysed signals. In all cases the slow oscillations were weakest at baseline, then increased gradually during the 40 and 30-s squat/stand cycles and decreased again in the last measurement period. However, the signals exhibited a varying degree of

relative changes. In the ABP signal, the 30-s squat/stand cycle produced an almost two-fold increase in the median power of slow waves compared to baseline (0.63 vs 0.32). In the CBFV signal, the baseline level was similar to ABP, but the 30-s squat cycle median power was still low at 0.50. Baseline power of slow waves for all NIRS measures was higher than for ABP and CBFV, and the squat/stands resulted in an increase in the median power. Moreover, the dispersion of results at baseline was visibly larger for the NIRS measures but mostly comparable during induced oscillations.

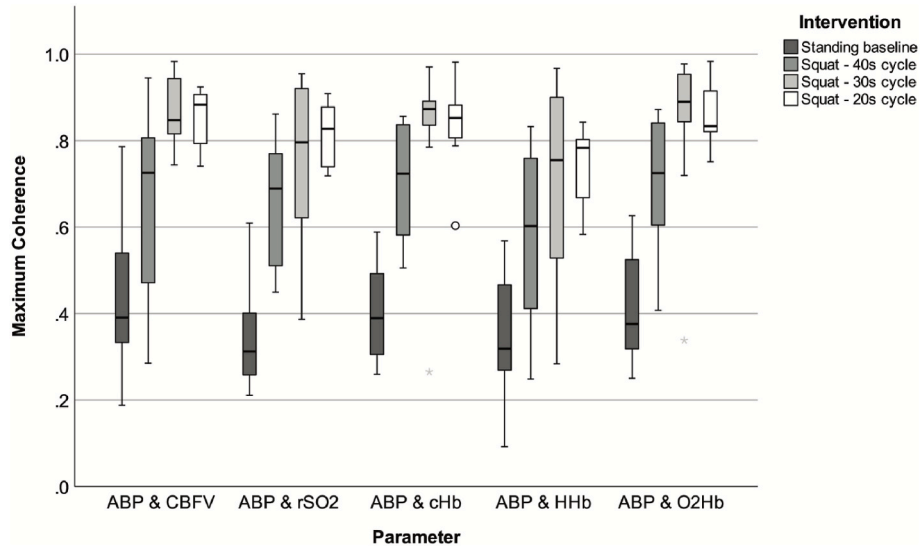
Changes in maximum coherence (Fig. 4) also followed a similar pattern in all of the analysed signals. At baseline, coherence in the slow wave frequency range was relatively low (below 0.4). During the 40-s squat/stands coherence increased to approx. 0.8 (with the exception of the ABP–HHb pair where it only reached approx. 0.6), and the higher frequency manoeuvres increased it further, up to nearly 0.9 for CBFV,  $O_2Hb$ , and cHb.

## 4. Discussion

In this study, we provide evidence for the feasibility of using NIRS-derived measures obtained with the Masimo  $O_3$  device to monitor slow wave activity in healthy volunteers. Our experimental design allowed the evaluation of the transmission of blood pressure variability



**Fig. 3.** Standardised power of slow waves in each of the analysed signals at baseline and during squat/stand manoeuvres with different frequency of induced oscillations (40-s cycle: 0.025 Hz; 30-s cycle: 0.033 Hz; 20-s cycle: 0.05 Hz). Presented results are group-averaged values from all participants who completed a given cycle. Data are presented as median (central line) with interquartile range (box) and whiskers extend to minimum and maximum values, not including outliers (defined as a value outside the quartile  $\pm 1.5 \times$  IQR range) marked as dots and extreme values (outside the quartile  $\pm 3 \times$  IQR range) marked as stars. ABP—arterial blood pressure, CBFV—cerebral blood flow velocity, rSO<sub>2</sub>—total oxygen saturation, cHb—total haemoglobin concentration, HHb—deoxygenated haemoglobin concentration, O<sub>2</sub>Hb—oxygenated haemoglobin concentration, IQR—interquartile range.



**Fig. 4.** Maximum coherence between ABP and other measured signals in the slow wave frequency range at baseline and during squat/stand manoeuvres with different frequency of induced oscillations (40-s cycle: 0.025 Hz; 30-s cycle: 0.033 Hz; 20-s cycle: 0.05 Hz). Presented results are group-averaged values from all 10 participants. Data are presented as median (central line) with interquartile range (box) and whiskers extend to minimum and maximum values, not including outliers (defined as a value outside the quartile  $\pm 1.5 \times$  IQR range) marked as dots. ABP—arterial blood pressure, CBFV—cerebral blood flow velocity, rSO<sub>2</sub>—total oxygen saturation, cHb—total haemoglobin concentration, HHb—deoxygenated haemoglobin concentration, O<sub>2</sub>Hb—oxygenated haemoglobin concentration, IQR—interquartile range.

to NIRS-derived signals. This transmission was compared to the well-established relationship between ABP and CBFV.

A robust transmission of blood pressure variability is necessary for reliable estimation of CA. Our results show that natural variability in blood pressure can be observed in analysed parameters to a varying degree. The amplitude of slow waves in the concentration of both oxygenated (O<sub>2</sub>Hb) and total (cHb) haemoglobin (and to a lesser extent, deoxygenated haemoglobin (HHb)) substantially exceeded the signals' resolution, suggesting that those measures allow for monitoring of changes in the slow wave frequency range. On the other hand, estimated amplitude of slow waves in total oxygen saturation (rSO<sub>2</sub>), was

comparable to its resolution during both spontaneous and induced changes in ABP.

During the squat/stand manoeuvre, both TCD and NIRS-based measures exhibited a similar pattern of changes in the power of slow waves that was comparable to those observed in ABP. As expected, ABP oscillations induced by alternating body position led to a clear increase in the signal's power in analysed frequency range. Although the difference between measurement stages was not as pronounced in NIRS-derived parameters as in ABP, in all cases a clear shift towards higher power was detected, particularly in the 30-s cycle. Observed decrease in the 20-s cycle could be explained by the technical aspects of PSD

analysis employed in this study. As the participants were asked to change position every 10 s, thereby inducing oscillations with the frequency of 0.05 Hz, and given the slight divergence from the metronome rhythm that is observed in real-life experiments, the induced component was not fully contained within the analysed range of 0.005–0.05 Hz and its power may have been underestimated in the calculations. We chose to analyse this part of the experiment alongside the other two as it was selected in the unpublished pilot feasibility study and highlights an important concern in study design, but the results suggest that in order to keep the PSD approach consistent with other studies (i.e., use the 0.005–0.05 Hz analysis range), the 40 and 30-s squat/stand cycles are preferable. Coherence analysis also revealed that NIRS-based parameters show a relatively good level of association with CBFV in terms of their relationship to the ABP signal. At baseline, coherence between ABP and the other signals was generally low (0.3–0.4), but the increasing pattern visible in CBFV across the measurement stages was present in NIRS measures. Particularly, cHb and O<sub>2</sub>Hb showed coherence values comparable to CBFV both at baseline and in the squat/stand cycles. The strong variations in ABP produced by faster changes in body position in the two faster squat/stand cycles were especially well represented as coherence exceeded 0.8 for most of analysed parameters. However, coherence for the 20-s cycle did not increase compared to 30-s cycle, suggesting that further increase in the squat/stand frequency does not improve the slow wave transmission. As TCD-based CBFV measurement is the established non-invasive ‘gold standard’ CBF surrogate, the high degree of similarity in transmission of ABP oscillations between CBFV and NIRS measures suggests that the latter offer the possibility of evaluating the surrogate CBF response to ABP variability and may potentially allow for continuous CA monitoring. However, certain differences remain between the specific signals, and the NIRS measures are likely not equally suitable for this approach. As previously mentioned, rSO<sub>2</sub> changes in the slow wave frequency range at baseline were comparable to the signal’s resolution. Although induced oscillations in ABP appear to be transmitted, this parameter may not have enough resolution to allow for CA assessment based on spontaneous pressure variability. In the context of neurocritical monitoring, this may significantly limit the system’s applicability, as subjecting the severely ill patients to induced changes in ABP may not be an option. Moreover, oxygenated haemoglobin content is related to both arterial and venous flow and considered to represent CBF, whereas the changes in deoxygenated haemoglobin are a marker of changes in CBV (Reinhard et al., 2006). Therefore, theoretically, O<sub>2</sub>Hb should be better suited to analysing the CBF response to spontaneous ABP. The pattern of changes in coherence between ABP and O<sub>2</sub>Hb did in fact resemble the relationship between ABP and CBFV more closely than the trends in HHb. Additionally, the difference in slow wave power during the three squat/stand stages was also more pronounced in the concentration of oxygenated haemoglobin. As cHb appeared to follow the changes in O<sub>2</sub>Hb rather than HHb, monitoring of total haemoglobin and/or oxygenated haemoglobin could prove to be an appropriate surrogate tool for CA assessment.

## 5. Conclusions

A robust transmission of ABP slow waves to measured surrogate CBF signals is necessary for reliable estimation of CA. Masimo O<sub>3</sub> NIRS-derived total haemoglobin and oxygenated haemoglobin concentrations showed the most promise with regard to reliably detecting slow wave transmission from ABP when compared to that of non-invasive ‘gold standard’ CBFV, demonstrating similar power and coherence in the slow wave frequency range. This work acts as a preliminary study on the use of Masimo O<sub>3</sub> parameters in non-invasive CA assessment, and further investigation in brain injury patients is required to assess its clinical utility.

## Limitations and future work

This study was performed in a small group of healthy young volunteers who performed the squat/stand manoeuvre. The results show that ABP oscillations produced by alternating body position are reliably transmitted to NIRS-derived measures obtained with the Masimo O<sub>3</sub> device, with power and coherence similar to that of TCD flow velocity. However, in neurointensive care patients, such induced changes may not be feasible to produce. The feasibility of using Masimo NIRS parameters to monitor CA based on spontaneous ABP oscillations should be investigated in a separate patient cohort to assess their ability to identify diminished CA. Because of the limited number of participants, this investigation was conducted as a preliminary observational study. The results reported in this work should be followed by more precise statistical analysis of the differences between NIRS-based measures during CA challenges.

## Competing interests

Peter Smielewski and Marek Czosnyka receive part of the licensing fees for ICM + software, licensed by Cambridge Enterprise Ltd, University of Cambridge, Cambridge, UK.

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## Author contributions

CAS– data acquisition, analysis, and interpretation, initial writing and drafting of the manuscript. AK– data acquisition, analysis, interpretation, initial writing and drafting of the manuscript. MMP– study design, data acquisition, interpretation, and analysis. EB– study design, data acquisition and interpretation. EK– study design, data acquisition. MC– study design, data interpretation. AH– study design, data interpretation. PS– study design, data acquisition, analysis, and interpretation. All authors edited and finally approved the manuscript.

## Previous presentations

Elements of this work were presented at the International Symposium on Intracranial Pressure and Brain Monitoring (14–18 November 2022, Cape Town, South Africa).

## Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests. Peter Smielewski and Marek Czosnyka have patent with royalties paid to Cambridge Enterprise Ltd, University of Cambridge, Cambridge.

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