

# Indexing Cerebrovascular Health Using Near-Infrared Spectroscopy: A Multi-Model Analysis

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*Statement of Originality*

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Rashid Ghorbani Afkhami

# *Abstract*

Cerebrovascular health is of great concern, especially in the ageing population, as stiff vessels are linked with diseases such as stroke, dementia, and age-related disabilities. Data from brain imaging techniques, including magnetic resonance imaging (MRI) and transcranial Doppler ultrasound (TCD), can be used to infer information regarding the health of underlying arteries. Such health assessments are commonly based on an index that is dependent on the properties of the device and can be related to known vascular health factors by a mathematical model.

The contribution of this thesis to the field of cerebrovascular health and brain imaging is twofold: First, we develop a timing index (TI) as a measure of cerebrovascular health. The relationship between TI and vascular health factors is derived in the context of pressure waveforms using transmission line theory and Windkessel model models. The proposed formula for TI matches data reported in the literature and helps to understand the flattening behaviour observed in the arrival time of reflected waves in aged subjects. Using similar mathematical modelling we also derive an expression for the relationship between the existing augmentation index (AI) and the same vascular health factors. Together with existing pulsatility index (PI) results, we show mathematically that TI is potentially more strongly related to vessel stiffness than either of the two indices currently used to index cerebrovascular health i.e., PI and AI. This is particularly so in younger to middle-aged subjects where interventions are best applied. We then show that TI can be applied to TCD measurements of blood flow velocity. To our knowledge, this is the first use of wave reflection time to measure vascular health in the brain. Transcranial Doppler Ultrasound Timing Index ( $TI_{TCD}$ ) shows a significant correlation with age. Furthermore, compared to the existing transcranial Doppler augmentation index ( $AI_{TCD}$ ) and transcranial Doppler pulsatility index ( $PI_{TCD}$ ), the  $TI_{TCD}$  show stronger correlations with cardiorespiratory fitness and the magnetic resonance imaging pulsatility index ( $PI_{MRI}$ ).

The second contribution of this thesis is in its application of near-infrared spectroscopy (NiRS). Firstly, we propose a NiRS signal model capable of producing synthetic NiRS signals comprising low-frequency components, arterial pulsation signals, reflected waves, Mayer and respiratory waves and a haemodynamic response function. The model outputs are compared with measured NiRS signals, and it is shown that the modelled signal is equivalent to the recorded signal as a later set of recordings on the same channel. Then, as an emerging tool for measuring cerebrovascular health, we propose a novel algorithm for locating systolic and reflected peaks on an averaged NiRS signal, thereby applying the TI to NiRS. The new near-infrared spectroscopy timing index ( $TI_{NiRS}$ )

shows stronger correlations with age, cardiorespiratory fitness (CRF) and  $PI_{MRI}$  than the pulse relaxation function (PReFx) which is an existing NiRS-based vascular health index.

Compared with existing brain imaging techniques, NiRS offers several advantages, such as being inexpensive, portable and easy-to-use. The NiRS-related contributions of this thesis are the development of a NiRS signal model and a NiRS-based cerebrovascular health measure. These will help in the development of a technique for the routine clinical measurement of cerebrovascular health. Such a technique would facilitate early intervention in the progression of vascular stiffness with age and, potentially, vascular-related diseases such as stroke and dementia.

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# Abbreviations

<b>AHA</b>	American Heart Association
<b>AI</b>	Augmentation Index
<b>AI<sub>TCD</sub></b>	Transcranial Doppler Augmentation Index
<b>AI*</b>	Augmentation Index, Alternative Definition
<b>AP</b>	Arterial Pulsation
<b>ASL</b>	Arterial Spin Labelling
<b>ba-PWV</b>	Brachial-ankle Pulse Wave Velocity
<b>bf-PWV</b>	Brachial-femoral Pulse Wave Velocity
<b>BOLD</b>	Blood-oxygenation Level Dependent
<b>bpm</b>	Beats Per Minute
<b>BR</b>	Breathing Rate
<b>CBF</b>	Cerebral Blood Flow
<b>cf-PWV</b>	Carotid-femoral Pulse Wave Velocity
<b>CFEn</b>	Cross-fuzzy Entropy
<b>CPP</b>	Cerebral Perfusion Pressure
<b>CRF</b>	Cardiorespiratory Fitness
<b>CSF</b>	Cerebrospinal Fluid
<b>CVR</b>	Cerebrovascular Resistance
<b>DC</b>	Direct Current
<b>DCS</b>	Diffuse Correlation Spectroscopy
<b>ECG</b>	Electrocardiography
<b>EEG</b>	Electroencephalography
<b>fMRI</b>	Functional Magnetic Resonance Imaging
<b>HR</b>	Heart Rate
<b>HRF</b>	Haemodynamic Response Function
<b>ICP</b>	Intracranial Pressure
<b>IIR</b>	Infinite Impulse Response
<b>LF</b>	Low-frequency
<b>MAP</b>	Mean Arterial Pressure
<b>MBP</b>	Mean Blood Pressure
<b>MCA</b>	Middle Cerebral Artery

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<b>MRI</b>	Magnetic Resonance Imaging
<b>NiR</b>	Near-infrared
<b>NiRS</b>	Near-infrared Spectroscopy
<b>PC</b>	Phase Contrast
<b>PI</b>	Pulsatility Index
<b>PI<sub>MRI</sub></b>	Magnetic Resonance Imaging Pulsatility Index
<b>PI<sub>TCD</sub></b>	Transcranial Doppler Pulsatility Index
<b>PI<sup>*</sup><sub>TCD</sub></b>	Transcranial Doppler Pulsatility Index, Alternative Definition
<b>PP</b>	Pulse Pressure
<b>PReFx</b>	Pulse Relaxation Function
<b>PWV</b>	Pulse Wave Velocity
<b>SNR</b>	Signal-to-noise Ratio
<b>std</b>	Standard Deviation
<b>SVD</b>	Small Vessel Disease
<b>T<sub>refl</sub></b>	Reflection Time
<b>TCD</b>	Transcranial Doppler Ultrasound
<b>TI</b>	Timing Index
<b>TI<sub>NiRS</sub></b>	Near-infrared Spectroscopy Timing Index
<b>TI<sub>TCD</sub></b>	Transcranial Doppler Ultrasound Timing Index
<b>TL</b>	Transmission Line
<b>TOST</b>	Two One-sided T-tests
<b>TPR</b>	Total Peripheral Resistance
<b>VLF</b>	Very Low Frequency
<b>WGN</b>	White Gaussian Noise
<b>WK</b>	Windkessel Model
<b>WK2</b>	Two-element Windkessel Model
<b>WK3</b>	Three-element Windkessel Model
<b>WK4</b>	Four-element Windkessel Model

# Symbols

<i>Symbol</i>	<i>Definition</i>	<i>Units</i>
$C$	Compliance	$\text{m}^3/\text{Pa}$
$P$	Pressure	$\text{Pa}$ ( $1 \text{ Pa} \approx 1/133 \text{ mmHg}$ , or $\text{N}/\text{m}^2$ )
$Q$	Flow	$\text{m}^3/\text{s}$ ( $1\text{m}^3/\text{s} = 10^3\text{l}/\text{s}$ )
$R$	Resistance	$\text{Pa}/\text{m}^3$
$V$	Velocity	$\text{m}/\text{s}$
$\mathcal{V}$	Volume	$\text{m}^3$ ( $1\text{m}^3 = 10^3\text{l}$ )
$Z$	Impedance	$\text{Pa}/\text{m}^3$
$\beta$	Phase Constant	$\text{rad}/\text{m}$
$\Gamma$	Reflection Coefficient	unitless
$\gamma$	Propagation Constant	$\text{rad}/\text{m}$
$\omega$	Angular Velocity	$\text{rad}/\text{s}$