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

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Statement of Originality

I hereby certify that the work embodied in the thesis is my own work, conducted under normal supervision. The thesis contains no material which has been accepted, or is being examined, for the award of any other degree or diploma in any university or other tertiary institution and, to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference has been made. I give consent to the final version of my thesis being made available worldwide when deposited in the University's Digital Repository, subject to the provisions of the Copyright Act 1968 and any approved embargo.

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 ($\mathrm{TI_{TCD}}$) shows a significant correlation with age. Furthermore, compared to the existing transcranial Doppler augmentation index ($\mathrm{AI_{TCD}}$) and transcranial Doppler pulsatility index ($\mathrm{PI_{TCD}}$), the $\mathrm{TI_{TCD}}$ show stronger correlations with cardiorespiratory fitness and the magnetic resonance imaging pulsatility index ($\mathrm{PI_{MRI}}$).

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 ($\mathrm{TI_{NiRS}}$)

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

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

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

Symbols

Symbol	*Definition*	*Units*
C	Compliance	m^3/Pa
P	Pressure	Pa (1 Pa $\approx$ 1/133 mmHg, or N/m^2)
Q	Flow	m^3/s ($1m^3/s = 10^3 l/s$)
R	Resistance	Pa/m^3
V	Velocity	m/s
$\mathcal{V}$	Volume	m^3 ($1m^3 = 10^3 l$)
Z	Impedance	Pa/m^3
β	Phase Constant	rad/m
Γ	Reflection Coefficient	unitless
γ	Propagation Constant	rad/m
ω	Angular Velocity	rad/s