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Enhancing coronary Wave Intensity Analysis robustness by high order central finite differences

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Abstract *Background:* Coronary Wave Intensity Analysis (cWIA) is a technique capable of separating the effects of proximal arterial haemodynamics from cardiac mechanics. Studies have identified WIA-derived indices that are closely correlated with several disease processes and predictive of functional recovery following myocardial infarction. The cWIA clinical application has, however, been limited by technical challenges including a lack of standardization across different studies and the derived indices' sensitivity to the processing parameters. Specifically, a critical step in WIA is the noise removal for evaluation of derivatives of the acquired signals, typically performed by applying a Savitzky–Golay filter, to reduce the high frequency acquisition noise.
Methods: The impact of the filter parameter selection on cWIA output, and on the derived clinical metrics (integral areas and peaks of the major waves), is first analysed. The sensitivity

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analysis is performed either by using the filter as a differentiator to calculate the signals' time derivative or by applying the filter to smooth the ensemble-averaged waveforms.

Furthermore, the power-spectrum of the ensemble-averaged waveforms contains little high-frequency components, which motivated us to propose an alternative approach to compute the time derivatives of the acquired waveforms using a central finite difference scheme.

Results and Conclusion: The cWIA output and consequently the derived clinical metrics are significantly affected by the filter parameters, irrespective of its use as a smoothing filter or a differentiator. The proposed approach is parameter-free and, when applied to the 10 in-vivo human datasets and the 50 in-vivo animal datasets, enhances the cWIA robustness by significantly reducing the outcome variability (by 60%).

Introduction

Two decades following its introduction, Wave Intensity Analysis has become an established technique to examine arterial dynamics.[1,2] Improvements in catheters[3,4] in the past decades have enabled the application of Wave Intensity Analysis in the coronary arteries,[5–8] which is the focus of this paper. The goal of recent investigations was aimed at exploiting the capacity of coronary Wave Intensity Analysis (cWIA) to distinguish between the proximal haemodynamics and the impact of cardiac mechanics on the microcirculation, for clinical translation. More specifically, the Backward Expansion Wave (BEW) has been primarily studied in order to elucidate the link between myocardial relaxation and the sharp diastolic rise of coronary inflow.

However, application of WIA to the coronary vessels has been considered with skepticism from some investigators[9] mainly due to the lack of evidence that the cWIA-derived indices can have prognostic value. Moreover, the high dependency of the cWIA outcome on the practitioners, mainly due to the unknown dependency on the noise introduced by the acquisition process and the pre-processing filtering step, has been considered a notable weakness. While the first point has been recently addressed since the clinical usefulness of cWIA and the prognostic value of the cWIA derived metrics have been consistently demonstrated,[10–12] the second one remains still unknown. This is a major motivation to undertake the current study in order to enhance the robustness of the cWIA outcome.

In a recent study Kyriacou et al.[10] used cWIA to identify the optimal atrioventricular delay in biventricular pacing in order to improve ventricular contractility and relaxation thereby increasing the cardiac output. Lockie et al.[11] found that a cWIA-derived index was central in the commonly seen but poorly understood phenomenon of 'warm-up' angina. Most recently, De Silva et al.[12] have shown for the first time that a real-time derived BEW peak can predict functional myocardial recovery following myocardial infarction. Given these successes it is becoming increasingly relevant to assess the robustness of cWIA outcomes independently of clinical context through each of the steps involved in the analysis.

In general, measured arterial pressure and velocity waveforms contain appreciable levels of noise. In the coronary vessels this situation is further exacerbated by cardiac motion. For this reason, in the literature, pressure and velocity signals are typically ensemble-averaged and subsequently smoothed most often by using the Savitzky–Golay (S–G) filter.[1,5,11–14] This filter is applied because it is believed to preserve the peaks of the waveforms, which are a principal feature in performing a reliable cWIA.

However, note that the quantities involved in the cWIA are exclusively the first order time derivatives of the signals, on which the relative impact of smoothing is greater than on the signals themselves. Surprisingly, the influence that the S–G filter parameters have on the signals' time derivative and in turn on the cWIA profile has not been investigated to date. Furthermore, the values of the filter parameters used in the different studies are almost never included in the publications.[1,5,11,12,14]

Therefore, the purpose of this paper is firstly to qualitatively and quantitatively characterize the impact that the S–G filter parameters have on the cWIA outcome and the derived clinical metrics.

The S–G filter is applied as a differentiator to calculate the signals' time derivative, input of the cWIA, directly from the ensemble-averaged waveforms. However, there is an alternative approach employed in the literature,[5,11] which is to compute the signals' time derivative after smoothing the ensemble-averaged signals. Due to the lack of a preferred or standardized approach in the literature, we performed the sensitivity analysis for both approaches.

In addition, with the purpose of introducing a straightforward standardized parameter-free approach, we propose a new procedure that applies a finite difference scheme to estimate the time derivatives directly from ensemble-averaged data. We then compare the S–G approaches with the proposed procedure in terms of the variability exhibited with respect to the cWIA metrics (Pulse Wave Speed, area and peak of the main waves and the total energy carried by the forward and backward travelling waves).

Methods

Study protocol and data acquisition

Retrospective human data: method development

The proposed method for cWIA was developed using 20 recordings from 10 human subjects scheduled for coronary