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Technical note

# How measurement artifacts affect cerebral autoregulation outcomes: A technical note on transfer function analysis

Aisha S.S. Meel-van den Abeelen[a,1], Daan L.K. de Jong[a,c,1], Joep Lagro[a], Ronney B. Panerai[b], Jurgen A.H.R. Claassen[a,*]

[a] Radboud University Medical Centre, Donders institute for Brain Cognition and Behaviour, Radboud Alzheimer Centre, and Department of Geriatric Medicine, Reinier Postlaan 4, 6525 GC, Nijmegen, the Netherlands
[b] Leicester Royal Infirmary, NIHR Biomedical Research Unit in Cardiovascular Sciences, Glenfield Hospital, Leicester LE2 7LX, UK
[c] University of Twente, MIRA institute for Biomedical Technology and Technical Medicine, Enschede, the Netherlands

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ABSTRACT

Cerebral autoregulation (CA) is the mechanism that aims to maintain adequate cerebral perfusion during changes in blood pressure (BP). Transfer function analysis (TFA), the most reported method in literature to quantify CA, shows large between-study variability in outcomes. The aim of this study is to investigate the role of measurement artifacts in this variation. Specifically, the role of distortion in the BP and/or CBFV measurement on TFA outcomes was investigated. The influence of three types of artifacts on TFA outcomes was studied: loss of signal, motion artifacts, and baseline drifts. TFA metrics of signals without the simulated artifacts were compared with those of signals with artifacts. TFA outcomes scattered highly when more than 10% of BP signal or over 8% of the CBFV signal was lost, or when measurements contained one or more artifacts resulting from head movement. Furthermore, baseline drift affected interpretation of TFA outcomes when the power in the BP signal was 5 times the power in the LF band. In conclusion, loss of signal in BP and loss in CBFV, affects interpretation of TFA outcomes. Therefore, it is vital to validate signal quality to the defined standards before interpreting TFA outcomes.



## 1. Introduction

Cerebral autoregulation (CA) is the mechanism that aims to maintain adequate cerebral perfusion during changes in blood pressure (BP). Its clinical importance lies in the protection of the brain from hypo- and hyperperfusion. The quantification of CA can be helpful in understanding pathophysiology and in monitoring and management of different diseases, for example stroke or traumatic brain diseases [1,2].

Currently, transfer function analysis (TFA) is the most used method in the literature to quantify dynamic CA from spontaneous oscillations in BP and cerebral blood flow velocity (CBFV). In these publications, a large variability in TFA outcomes is observed between different studies [3]. A possible explanation is the lack of a standard signal processing method for TFA. Meel-van den Abeelen et al. showed that it is possible to reduce the variability in TFA outcomes by standardizing signal processing methods [4].

Another possible cause of the large variations in TFA outcomes lies in the quality of measurement of BP and CBFV. Very few studies [5–7] have investigated the effect of the measurement quality on the CA transfer function outcomes. Lorenz et al. studied the consequences of poor insonation conditions on TFA parameters for CA and found that poor bone windows can cause considerable bias in TFA outcomes [7]. Furthermore, Deegan et al. [5] studied the effect of signal loss in BP or CBFV measurements and found detrimental changes in TFA outcomes when using time series waveforms as input signal. However, when the raw data was transformed to beat-to-beat data and that data was used as input data for TFA the changes in TFA outcomes were, although still significant, much smaller [5]. Whether these significant changes also change the interpretation of the TFA outcomes between normal cerebral autoregulation and impaired cerebral autoregulation has not been explored.

At this moment, no standard quality requirements for the transcranial Doppler (TCD) measurements are available, except for some qualitative descriptions on signal depth, velocity, and wave characteristics, which are not suitable to quantify quality

* Corresponding author. Tel.: +31 24 3616772; fax: +31 24 3617408.
*E-mail address:* Jurgen.Claassen@radboudumc.nl, j.claassen@ger.umcn.nl (J.A.H.R. Claassen).
[1] Aisha S.S. Meel-van den Abeelen and Daan L.K. de Jong contributed equally to this article.

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of placement [8]. Next to CBFV, BP measurements may also be subjected to external artifacts. External noise decreases signal quality, which may influence TFA outcomes. The aim of this study was to investigate whether different types of distortion in both the BP and/or CBFV measurements change the interpretation of the transfer function outcome metrics between good and impaired cerebral autoregulatory functioning.

## 2. Methods

### 2.1. Blood pressure and cerebral blood flow velocity measurement

Fifteen young healthy subjects participated in this study. The study was approved by the local Medical Ethics Committee and all participants gave written informed consent. BP was measured noninvasively at the middle finger of the right hand using Finapres (Finapres Medical Systems, Amsterdam, the Netherlands). It has been shown that BP measured indirectly in a finger by arterial volume clamping is similar to auscultatory measurements [9]. It also closely corresponds to intra-arterial recordings [10]. The subjects underwent several minutes of acclimatization and the servo-adjust mechanism was turned off prior to each recording.

CBFV was obtained in the left middle cerebral artery (MCA) by TCD (Multi-Dop, Compumedics DWL, Germany). The TCD probe was placed on the left temporal window. After identification of the MCA according to signal depth, velocity, and wave characteristics [8] the signal was further optimized by adjusting place, insonation angle, and depth. During data collection, the probe was locked at a constant angle and position with a customized headband (Spencer technologies, Seattle, WA., USA). Both BP as CBFV were recorded at 200 Hz.

### 2.2. Transfer function analysis

TFA assesses the dynamic relationship between BP and CBFV based on spontaneous oscillations in these variables. To obtain beat average BP and CBFV values the raw BP and CBFV data were filtered using a 4th order low-pass Butterworth filter with a cut-off frequency of 0.5 Hz (forward and reverse direction for a zero-phase response). The consecutive series were resampled to 10 Hz, which is the most common signal type for input in TF-analysis on cerebral autoregulation [3]. Transfer function gain, phase, and coherence were estimated using the cross-spectral method which has been described in detail previously [11,12]. The 5 min time series of mean BP and CBFV were subdivided into five segments of 950 samples with 50% overlap for spectral estimation. Fast Fourier transforms were implemented with each Hanning-windowed segment and averaged to quantify the transfer function. The gain, phase, and coherence were quantified as the mean for the following frequency bands: very low frequency (VLF): 0.02–0.07 Hz; low frequency (LF): 0.07–0.15 Hz; high frequency (HF): 0.15–0.4 Hz [11]. In this article we have emphasized the LF results, because this frequency band includes the major frequency range of CA [13,14]. Results for the VLF and HF are presented in the online supplemental material.

### 2.3. Effects of artifacts

Measurements obtained by the Finapres and TCD can be influenced by various types of artifacts which reduce signal quality. We studied the influence of three types of artifacts on transfer function outcomes: (1) loss of signal, (2) motion artifacts, and (3) baseline drift. Of each type of artifact and methods for approximating these artifact types are discussed below.

#### 2.3.1. Loss of signal

TCD measurements are often subject to loss of the CBFV signal due to probe movement and several mechanisms may cause interruptions of BP recordings. Therefore, recordings of both techniques can be subject to periods of unusable data of varying number and duration.

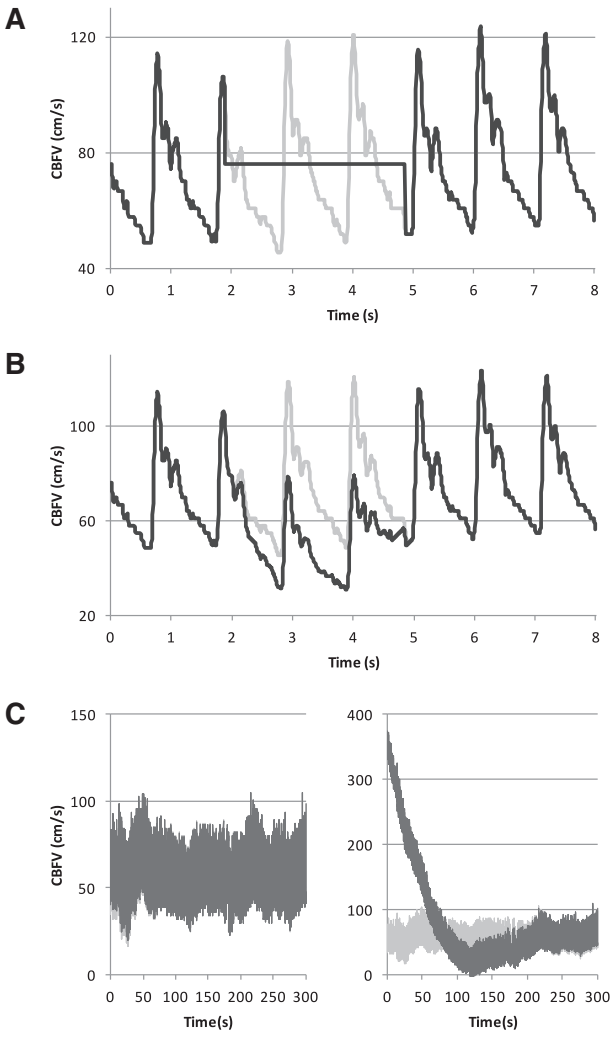


**Fig. 1.** (A): Example of signal loss in CBFV signal. The grey line shows the original CBFV signal and the black line shows the CBFV signal with the signal loss. (B): Example of the artificial generation of head movement in CBFV signal. The graph represents the effect of the motion template on an original CBFV signal. The CBFV signal before (grey line) and after (black line) adding the motion template are shown. (C): Examples of the effect of baseline drift on the CBFV signal. The light grey lines represent the original CBFV and the dark grey lines the CBFV signal with baseline drift with a power of 0.1 (left) and 5 (right) times the power of the power in the LF-band.

To investigate the effects of signal loss on TFA outcomes, random sections of the 5 min BP and/or CBFV signal were removed and replaced by the mean of the previous ten seconds (Fig. 1A). The length and number of missing segments were varied, either in the BP or CBFV signal or in both. For each length of data loss (1, 2, 3, 4, 5, 10, 20, 30, 40, and 50 s) the number of segments was varied over a range of 1 to 5. In the case of loss in both signals, length and number of segments were similar, but the moment in time where data loss occurred differed. To avoid potentially misleading results caused by a specific timing of the data loss, each of the 150 conditions was repeated 10 times and the results were averaged per condition.

#### 2.3.2. Motion artifacts

Motion artifacts may occur, either during movement of the subject or of the TCD probes. Spencer et al. reported these artifacts to be bidirectional and to have a wider frequency spectrum,