# Assessment of Cerebral Autoregulation Dynamics in Diabetics Using Time-Domain Cross-Correlation Analysis

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**Abstract**

The main purpose of this paper is to apply time-domain cross-correlation analysis to assess the cerebral autoregulation (CA) dynamics in diabetics with autonomic neuropathy. Continuous and spontaneous arterial blood pressure (ABP) and cerebral blood flow velocity (CBFV) were acquired from 10 normal subjects, 10 diabetics without autonomic neuropathy and 10 diabetics with autonomic neuropathy (sex and age matched) with the Finapres device and the transcranial Doppler ultrasound (TCD) for periods of approximately 5 minutes in both supine and tilting positions. Cross-correlation function (CCF) was calculated through a 64-beat wide moving window. Mean CCF patterns were received for each subject and for the whole group. Mean arterial blood pressure (MABP) and mean cerebral blood flow velocity (MCBFV) signals were bandpass filtered in three different frequency ranges, the very low-frequency range (VLF, 0.015-0.04 Hz), low-frequency range (LF, 0.04-0.15 Hz) and high-frequency range (HF, 0.15-0.40 Hz), before applying CCF for the purpose of studying the effect of different bandwidths on the resulting mean CCFs. Results indicated that the CCF values fluctuated seriously in VLF range of each group. It might show that relation between MABP and MCBFV is uncertain in VLF range. On the other hand, maximum CCF indices in HF range were closer to origin and it indicates that CA is less efficient in this range. Cross-correlation analysis revealed that correlation between MABP and MCBFV in LF range for the group of normal subjects in supine position is the highest among these three groups. It might indicate that CA operates more effectively in normal subjects than diabetics in LF range. Hence, cross-correlation analysis could be a useful method to evaluate the CA dynamics in clinical practice.

***Keywords***: Cerebral autoregulation, Mean arterial blood pressure, Mean cerebral blood flow velocity, Cross-correlation analysis

## Introduction

Diabetes has been one of leading causes of mortality in the world. Complications of both vascular and nervous systems are the major risk factors for mortality of diabetics. According to previous researches, about 70% of diabetics have autonomic nervous dysfunctions. Moreover, it is about 2~4 times risks for a diabetic patient to have a stroke than an age-matched subject. The crucial factor of cerebrovascular diseases is cerebral autoregulation (CA). The cerebral autoregulation mechanism refers to the capacity of cerebral blood flow (CBF) to remain relatively constant despite variations in perfusion pressure (the difference between mean arterial pressure and intracranial pressure) [1]. Before advanced equipments developed, arterial blood pressure (ABP) drops through the release of thigh blood pressure cuffs rapidly were used as an autoregulatory stimulus in clinical practice. However, numbers of measurement techniques in progress have been developed for the safety and accessibility on noninvasive apparatus in last decade. A medical instrument with transcranial Doppler ultrasound (TCD) was adopted to evaluate the dynamic response of CA in normal humans [2]. The characteristic of outstanding temporal resolutions of TCD has allowed studies of the dynamic response of autoregulation. On the other hand, ABP signals can be acquired non-invasively by way of using a finger cuff implement. (eg., Finapres BP monitor).

Though the autoregulatory curve in the brain is created by two parameters, ABP and CBFV, to assess if CA is normal or not in humans, CA is more a concept rather than a physically measurable entity [3]. Assessment of non-invasive approaches have been developed and adopted to study static or dynamic CA [4]. Some investigators used autoregulatory index (ARI) generated by CBFV and ABP values to assess CA and it provided important clinical information [4-7]. Nevertheless, most experiments demand the introduction of variations in ABP via physiological or pharmacological manipulations. It is not easy to find proper approaches to assess CA non-invasively and reliably by simple and acceptable measurements. Recent

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investigations have shown that the autoregulatory dynamic response can be identified from spontaneous fluctuations in mean ABP (MABP) and CBFV [8] and assessed the dynamic relationship between spontaneous MABP and CBFV using transfer function analysis in either normal subjects [9-10] or autonomic failure patients [11]. Spectral and transfer function analyses of CBFV and ABP were performed by fast Fourier transform (FFT) in their studies. However, the stationary property and time resolution are two crucial issues for spectral analysis.

Time-domain cross-correlation function (CCF) has been recently utilized by previous investigators as a means to assess the dynamics of CA [12-16]. In addition, cross-correlation analysis of blood pressure and heart rate variability has been applied to investigate the relationship between pulse interval and systolic arterial blood pressure [17]. Previous study showed that CCF would be a useful tool to assess CA in normal subjects [16]. The main purpose of this research is to use time-domain cross-correlation analysis of pre-filtered MABP and mean CBFV (MCBFV) to assess the cerebral autoregulation in normal subjects, diabetics without autonomic neuropathy and diabetics with autonomic neuropathy.

## Materials and methods

*2.1 Subjects and measurements*

There were 3 groups of subjects (sex and age matched) being recruited in this study, i.e., 10 healthy adults for normal subjects (group 1), 10 diabetics without autonomic neuropathy (group 2) and 10 diabetics with autonomic neuropathy (group 3). The subjects in group 1 were included only if they had no history of vascular disease, heart problems, hypertension, migraine, epilepsy, cerebral aneurysm, intracerebral bleeding or other pre-existing neurological conditions. None of the subjects were receiving any medication during the time of the study. CBFV was measured in the right middle cerebral artery using TCD (Transcranial Doppler ultrasound, EME TC2020) in conjunction with a 5-MHz transducer fixed over the temporal bones by an elastic headband. Continuous ABP recordings were obtained through the Finapres (Ohmeda 2300) device with the cuff attached to the middle finger of the right hand. Subjects were investigated on a tilt-table that enabled a motor-driven change from a supine to an upright position within 10 seconds. Data acquisition was started after a 10-min relaxation in supine position. Spontaneous ABP and CBFV were recorded simultaneously to PC for off-line analysis. The acquisition periods were approximately 5 minutes in both the supine and $75^{\circ}$ tilt-up positions by a self-developed data acquisition system as shown in Figure 1. The personal computer combined with a general-purpose data acquisition board and LabVIEW environment for acquiring signals correctly was developed in our previous study [18]. The sampling rate to acquire the analog data from TCD and Finapres was adjustable in this system. In our experiments, the sampling rate is set to 60 Hz. The MABP and MCBFV signals

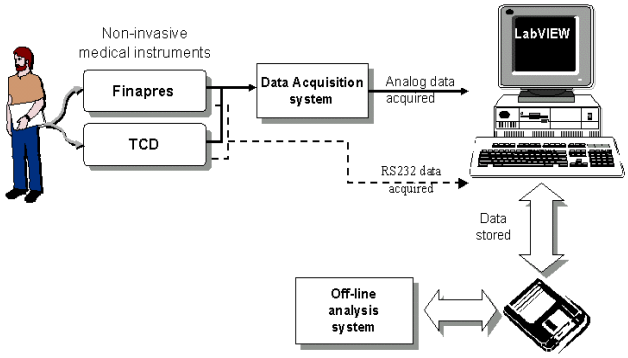


Figure 1 A self-developed data acquisition system for acquiring ABP and CBFV signals.

are bandpass filtered in the very low-frequency (VLF, 0.015-0.04 Hz), low-frequency range (LF, 0.04-0.15 Hz) and high-frequency range (HF, 0.15-0.40 Hz) before applying CCF for the purpose of studying the effect of different bandwidths on the resulting mean CCFs.

*2.2 Data analysis*

In this research, the MABP value was calculated by each heartbeat as follows.

$$MABP_i = \frac{1}{V_i - V_{i-1}} \sum_{k=V_{i-1}}^{V_i-1} x(k) \tag{1}$$

where $x(\cdot)$ is the ABP pulse signal continuously acquired from the analog output port of Finapres. $V_{i-1}$ is the wave-trough time index in the ($i$-1)th pulse beat, and $V_i$ is the time index of the wave-trough in the $i$th pulse beat. Therefore, $MABP_i$ is the calculated mean ABP value for the $i$th pulse beat. Similarly, the mean CBFV value was calculated by each heart beat as follows.

$$MCBFV_i = \frac{1}{D_i - D_{i-1}} \sum_{k=D_{i-1}}^{D_i-1} y(k) \tag{2}$$

where $y(\cdot)$ is the CBFV signal continuously acquired from the analog output port of the TCD. $D_{i-1}$ is the time index of the wave-trough in the CBFV signal corresponding to the ($i$-1)th pulse beat and $D_i$ is the time index of the wave-trough in the CBFV signal corresponding to the $i$th pulse beat. $MCBFV_i$ is the mean value of CBFV for the $i$th pulse beat. Afterward, the MABP and MCBFV time series calculated by Equations (1) and (2) are placed at regular intervals equal to their mean heart period. Before calculating the CCF between MABP and MCBFV time series, MABP and MCBFV were normalized by using their mean values. Assume that the normalized MABP and MCBFV time series are $f(n)$ and $g(n)$ respectively. The normalized MABP and MCBFV time series can be calculated as follows:

$$f(n) = \frac{MABP - \overline{MABP}}{s_{MABP}} \tag{3}$$

where MABP is mean arterial blood pressure, $\overline{MABP}$ is mean MABP and $s_{MABP}$ is standard deviation of MABP.

$$g(n) = \frac{MCBFV - \overline{MCBFV}}{s_{MCBFV}} \quad (4)$$

where MCBFV is mean cerebral blood flow velocity, $\overline{MCBFV}$ is mean MCBFV and $s_{MCBFV}$ is standard deviation of MCBFV.

$f(n)$ and $g(n)$ signals were bandpass filtered used a third-order digital bandpass Chebyshev filter in the VLF, LF and HF ranges before applying the CCF. Assume that the bandpass filtered $f(n)$ and $g(n)$ time series are $\hat{f}(n)$ and $\hat{g}(n)$ respectively. The CCF between $\hat{f}(n)$ and $\hat{g}(n)$ is calculated as follows.

$$CCF_i(k) = \frac{R^i_{\hat{f}\hat{g}}(k)}{\left[R^i_{\hat{f}\hat{f}}(0)R^i_{\hat{g}\hat{g}}(0)\right]^{\frac{1}{2}}}, \quad (5)$$

$$k = 0, \pm 1, \pm 2, \cdots, \quad i=1 \text{ to } N\text{-}W\text{+}1$$

where $R^i_{\hat{f}\hat{g}}(k)$ is an estimate of the cross-covariance in *i*th time window and defined as

$$R^i_{\hat{f}\hat{g}}(k) = \begin{cases} \frac{1}{W}\sum_{j=i}^{i+W} \hat{f}(j)\hat{g}(j+k), k = 0, 1, 2, \cdots \\ \frac{1}{W}\sum_{j=i}^{i+W} \hat{f}(j-k)\hat{g}(j), k = 0, -1, -2, \cdots \end{cases} \quad (6)$$

Also, $R^i_{\hat{f}\hat{f}}(0) = \frac{1}{W}\sum_{j=i}^{i+W}[\hat{f}(j)]^2$, and $R^i_{\hat{g}\hat{g}}(0) = \frac{1}{W}\sum_{j=i}^{i+W}[\hat{g}(j)]^2$. *N* is the total number of cardiac cycles, *W* is the window width and *k* is the time lag. $CCF_i(\cdot)$ is the result of the CCF between $\hat{f}(n)$ and $\hat{g}(n)$ in the *i*th time window. Mean CCF patterns were obtained for each subject and entire population.

*2.3 Statistical analysis*

All resultant and parametric data were presented as mean±SD. The two-sided paired t-test was performed to test supine versus tilt differences in both MABP and MCBFV. The t-test also was applied to test all measurement values of group1, group 2 and group 3 in each group. The statistical significance was defined as $p<0.05$.

## Results

The MABP and MCBFV time series signals were derived from Equations (1) and (2) respectively. Results of mean and standard deviation analysis are listed in Table 1.

In Table 1, $\overline{MABP}$ represents the average values of MABP time series in both supine and tilt-up positions for whole population. Similarly, $\overline{MCBFV}$ represents the average values of MCBFV time series in both supine and tilt-up positions for whole population. It is depicted in Table 1 that group 1 and group 2 had larger mean value of MABP in tilting position than that of group 3 (group 1: 93.97±11.39mmHg, group 2: 100.43±19.12mmHg, group 3: 74.12±13.35mmHg). It also showed that the values of $\overline{MABP}$ between supine and tilt-up position in the group 3 existed significant difference,

Table 1 Results of mean and standard deviation analysis.

| Normal subjects (Group 1) | | |
|---|---|---|
| | $\overline{MABP}$ (mmHg) | $\overline{MCBFV}$ (cm/sec) |
| Supine | 88.83±9.17 | 40.95±12.05 |
| Tilt-up | 93.97±11.39∗ | 38.92±11.88 |
| Tilt-up/Supine | 1.06±1.24 | 0.95±0.99 |
| Diabetics without autonomic neuropathy (Group 2) | | |
| | $\overline{MABP}$ (mmHg) | $\overline{MCBFV}$ (cm/sec) |
| Supine | 97.35±12.19 | 51.10±15.20 |
| Tilt-up | 100.43±19.12† | 45.30±15.79 |
| Tilt-up/Supine | 1.03±1.57 | 0.89±1.04 |
| Diabetics with autonomic neuropathy (Group 3) | | |
| | $\overline{MABP}$ (mmHg) | $\overline{MCBFV}$ (cm/sec) |
| Supine | 91.55±14.85§ | 41.75±20.76 |
| Tilt-up | 74.12±13.35∗†§ | 35.01±17.52 |
| Tilt-up/Supine | 0.81±0.90 | 0.84±0.84 |

∗ denotes that exists statistical significance ($p<0.05$) between normal subjects and diabetics with autonomic neuropathy. † denotes that exists statistical significance ($p<0.05$) between diabetics without autonomic neuropathy and diabetics with autonomic neuropathy. § denotes that exists statistical significance ($p<0.05$) between supine and tilt-up positions.

however, no significant difference exists in both group 1 and group 2. On the other hand, the mean value of MCBFV in Table 1 revealed no significant change between supine and tilt-up positions in the three groups. The tilt-up/supine ratio in $\overline{MABP}$ with the group 3 is smaller than 1 contrast to the other two groups. The tilt-up/supine ratio in $\overline{MCBFV}$ with the group 3 also is smaller than the other groups. It might be the effect of autonomic neuropathy.

The total number of cardiac cycles for both MABP and MCBFV to compute the CCF was 256 beats. Cross-correlation functions were derived from Equations (5) and (6) and CCF was estimated by using a 64-beat wide moving window. One may notice that higher value of CCF denotes the higher correlation. The signals were bandpass filtered in VLF, LF and HF ranges but the main features were presented in the LF and HF ranges. Representative figures of the effect of the filtered MABP and MCBFV signals in LF in supine position for group 1, group 2 and group 3 are shown in (a) of Figure 2, Figure 3 and Figure 4, respectively. In addition, representative figures of 3D and 2D for CCF in LF in supine position for group 1, group 2 and group 3 are shown in (b) and (c) of Figure 2, Figure 3 and Figure 4. 3D representative figures showed the results of CCF(k) in each beat and all of the 2D representative figures give the mean and standard deviation of the CCF for the representative subjects. As we can observe that the peak of CCF values in LF in supine position for group 1 (Table 2) is more obvious than that for group 2 and group 3 (group 1: 0.52±0.15, group 2: 0.42±0.17, group 3: 0.32±0.14). On the other

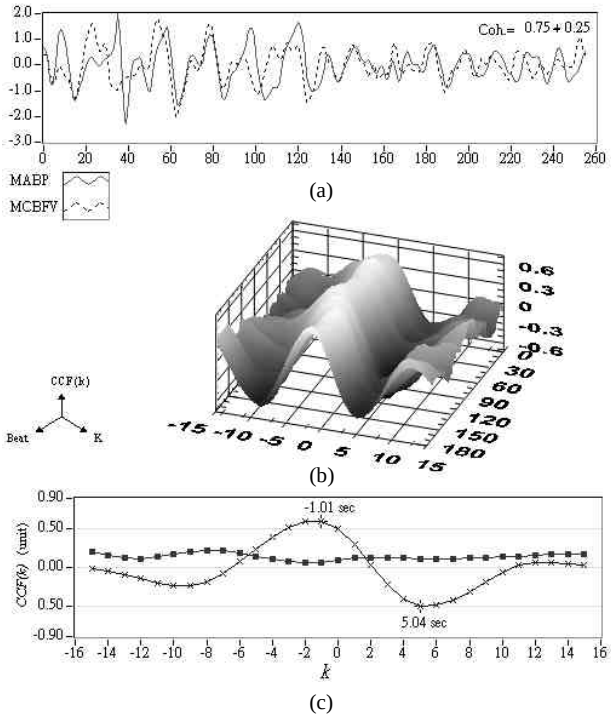


Figure 2 (a) A simultaneously acquired MABP and MCBFV time series which were bandpass filtered in LF range. "coh." is coherence between MABP and MCBFV. (b) 3D representative figures of CCF. (c) 2D representative figures of CCF with mean (×) and SD (■) in LF in supine position for a normal subject.

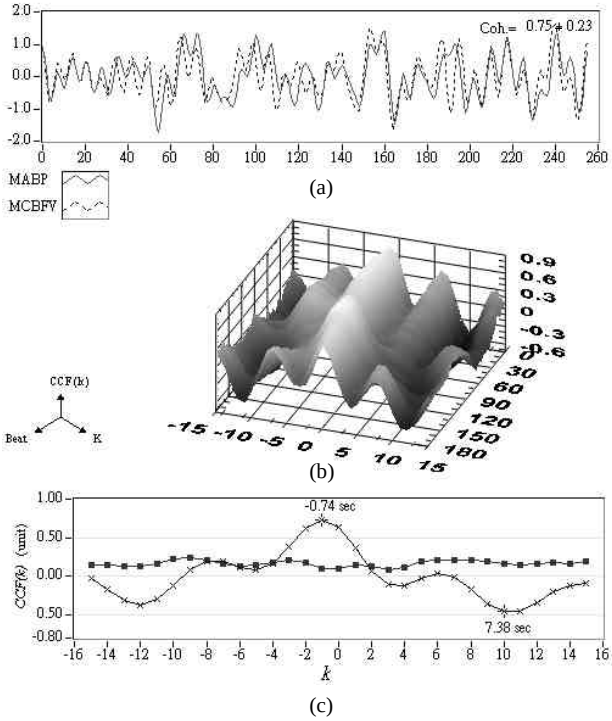


Figure 3 (a) A simultaneously acquired MABP and MCBFV time series which were bandpass filtered in LF range. "coh." is coherence between MABP and MCBFV. (b) 3D representative figures of CCF. (c) 2D representative figures of CCF with mean (×) and SD (■) in LF in supine position for a diabetic without autonomic neuropathy.

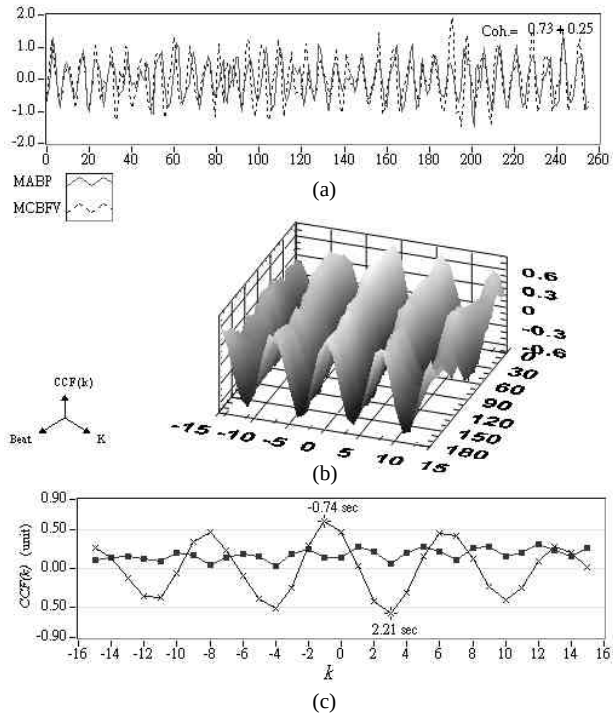


Figure 4 (a) A simultaneously acquired MABP and MCBFV time series which were bandpass filtered in LF range. "coh." is coherence between MABP and MCBFV. (b) 3D representative figures of CCF. (c) 2D representative figures of CCF with mean (×) and SD (■) in LF in supine position for a diabetic autonomic neuropathy.

hand, the fluctuations of standard deviation in LF in supine position for group 1 are smaller than that for group 2 and group 3 (Maximum CCF SD of group 1: 0.17±0.08, maximum CCF SD of group 2: 0.22±0.12, maximum CCF SD of group 3: 0.21 ±0.10). A detailed list of the CCF results for group 1, group 2 and group 3 are shown in Table 2. In VLF range, there was no significant difference for the maximum CCF values in each group as shown in Table 2. Moreover, the maximum CCF standard deviations are large. Hence, the relation between MABP and MCBFV is uncertain. According to previous study results for VLF range, it also showed that the correlation between MABP and MCBFV is low, the results are agreed with the previous results [16,19]. On the other hand, the results indicate that averages of (maximum CCF SD)/(maximum CCF value) in LF for supine position for group 1 are smaller than that for group 3 and exists significant difference. It depicts that the fluctuations of normal subjects in LF for supine position are smaller than that of group 3. The low fluctuations indicate high correlation and the results can be observed from the maximum CCF values as shown in Table 2. In (a) of Figure 2, Figure 3 and Figure 4, "coh." indicates the coherence between MABP and MCBFV, which were presented as mean±SD. The curves estimated by equation (3) and (4) shown in the figure are normalized MABP and MCBFV time series and the vertical axis stands for the normalized value. The normalization of time series translates and scales the axis so that features have zero mean and unit variance. In (c) of Figure 2 to Figure 4 the value shown in second is the corresponding time of maximum CCF

Table 2 Results of cross-correlation analysis.

| | | Max CCF index (sec) | Max CCF value | Max CCF sd. | Max CCF sd./Max CCF value |
|---|---|---|---|---|---|
| Normal subjects (Group 1) | VLF(0.015~0.04Hz) | | | | |
| | Supine | -2.5±6.43 | 0.36±0.23 | 0.43±0.11 | 0.35±7.98 |
| | Tilt-up | -2.5±7.41 | 0.37±0.24 | 0.47±0.17 | 2.11±1.63 |
| | LF(0.04~0.15Hz) | | | | |
| | Supine | -1.01±1.17∗ | 0.52±0.15∗† | 0.17±0.08 | 0.39±0.27† |
| | Tilt-up | -0.59±0.89 | 0.45±0.17 | 0.20±0.07 | 0.50±0.25 |
| | HF(0.15~0.4Hz) | | | | |
| | Supine | -0.08±0.25∗ | 0.35±0.16∗ | 0.12±0.05 | 0.47±0.34 |
| | Tilt-up | -0.22±0.48 | 0.37±0.19 | 0.15±0.09 | 0.52±0.38 |
| Diabetic without autonomic neuropathy (Group 2) | VLF(0.015~0.04Hz) | | | | |
| | Supine | -4.1±8.20 @ | 0.33±0.22 | 0.43±0.14 | 2.84±3.11 |
| | Tilt-up | 3.2±6.37 @ | 0.40±0.18 | 0.42±0.07 | 1.53±1.33 |
| | LF(0.04~0.15Hz) | | | | |
| | Supine | -0.37±0.93 | 0.42±0.17 | 0.22±0.12 | 0.72±0.60 |
| | Tilt-up | -0.58±0.92∗ | 0.49±0.22 | 0.19±0.07∗ | 0.55±0.45 |
| | HF(0.15~0.4Hz) | | | | |
| | Supine | -0.21±0.33# | 0.36±0.19 | 0.17±0.11 | 1.06±1.56 |
| | Tilt-up | 0.07±0.21∗# | 0.44±0.26 | 0.11±0.05∗ | 0.47±0.58 |
| Diabetic with autonomic neuropathy (Group 3) | VLF(0.015~0.04Hz) | | | | |
| | Supine | -3.25±9.57 | 0.33±0.21 | 0.51±0.17 | 2.56±2.54 |
| | Tilt-up | -1.58±8.98 | 0.35±0.21 | 0.47±0.17 | 2.17±1.94 |
| | LF(0.04~0.15Hz) | | | | |
| | Supine | -0.35±1.36 | 0.32±0.14† | 0.21±0.10 | 0.75±0.44∗† |
| | Tilt-up | -0.35±0.86 | 0.41±0.24 | 0.24±0.11∗ | 0.98±0.97 |
| | HF(0.15~0.4Hz) | | | | |
| | Supine | -0.07±0.22 | 0.42±0.14 | 0.14±0.09 | 0.38±0.28∗ |
| | Tilt-up | -0.09±0.28 | 0.40±0.29 | 0.14±0.07∗ | 0.75±0.72 |

∗ denotes that exists statistical significance ($p<0.05$) between LF and HF. @denotes that exists statistical significance ($p<0.05$) in VLF range between supine and tilt-up. † denotes that the result of LF in supine exists statistical significance ($p<0.05$) between normal subjects and diabetic autonomic neuropathy. # denotes that the result of diabetic without autonomic neuropathy exists statistical significance ($p<0.05$) between supine and tilt-up.

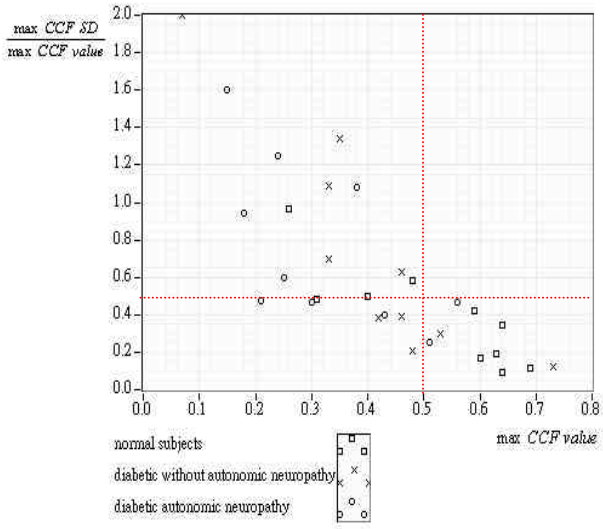


Figure 5 The plot of max CCF value vs. (max CCF SD)／(max CCF value) for normal subjects, diabetic without autonomic neuropathy and diabetic autonomic neuropathy.

index for the value of "k" based on average period. Furthermore, the values of maximum CCF index in HF range are smaller than that in LF range. It showed significant difference in group 1 with supine position and group 2 with tilt-up position.

A distributive plot of (maximum CCF SD)/(maximum CCF value) for three groups of subjects is shown in Figure 5. The values of maximum CCF and the ratios of maximum CCF SD to maximum CCF values indicate that correlation of MABP and MCBFV in supine position for group 1 is higher than that for group 2 and group 3. Contrary to group 1, most distributions for group 3 are lower than 0.5 for maximum CCF value, and being higher than 0.5 for (maximum CCF SD)/(maximum CCF value). Moreover, the distribution plot for group 2 is between group 1 and group 3. This trend indicates that correlations of both MABP and MCBFV for group 1 are higher and variations are lower comparing to group 3.

## Discussion

It is important to ensure safety and harmlessness for patients by non-invasive treatment, especially for diabetics. Therefore, we must look more carefully into that how to treat patients in an appropriate process to keep from secondly injury. The advances in TCD and computerized acquisition techniques have allowed simultaneous recording and analysis of velocity signals from the intracranial arteries with other physiological parameters. This study focused mainly on using the time-domain cross-correlation approach to test the effects of changes in MABP on MCBFV. The MABP and MCBFV signals were bandpass filtered before applying cross-correlation analysis for the purpose of studying the effect of different bandwidths on the resulting mean CCF. Cross-correlation analysis can provide correlation and phase relationship between MABP and MCBFV. The mean and standard deviation analysis results listed in Table 1 showed that the changes in MABP resulted in an insignificant change in MCBFV. The mean MABP value changed more than that of MCBFV from the supine to tilt-up positions in group 3. In this research, we found that the mean values of MABP dropped significantly in tilt-up position for group 3 compare with group 1 and group 2.

The effect of spontaneous MABP changes to MCBFV was evaluated by the cross-correlation analysis in time-domain and the results were shown in Table 2. According to the results of previous study that applied time-domain cross-correlation analysis in normal subjects [16], it showed that correspond time lag is –1.20±0.91 seconds in LF range and is –0.07±0.42 seconds in HF range. Compare to previous study, the results in this study (time lag is –1.01±1.17 seconds in LF range and is –0.08±0.25 seconds in HF range) are close to the results obtained in the previous study. We may say that CCF could be an appropriate method to assess CA. We also adopted maximum CCF value and (maximum CCF SD)/(maximum CCF value) to be critical indices to correct CCF lag time. The parameters of maximum CCF value and (maximum CCF SD)/(maximum CCF value) indicate that correlation in supine position for normal subjects is higher than that for diabetics without autonomic neuropathy and diabetics with autonomic neuropathy. Figure 5 reveals this trend as mentioned above. On the other hand, the phase relationship between MABP and MCBFV can be established easily by computing the correlation for a number of different lags and taking the significant value as the correct value. The phase shift analysis between MABP and MCBFV demonstrated its usefulness as a test of dynamic autoregulation [20]. In our study, the results of cross-correlation analysis in Table 2 revealed that a good relation between MCBFV and MABP in the LF range in normal subjects with supine position. In contrast to group 1, the relationship is poor in the LF range in supine position for group 2 and group 3. It also means that the CA mechanism of the group 1 is better than the other two groups. The negative lag of the CCF peak between MABP and MCBFV is a result of the phase-lead property and it also indicates that CA is a highpass filter. The increasing time lag of the CCF peak might be a good evidence to show the disturbance of autoregulatory effect. The cross-correlation analysis indicated that the MCBFV preceded MABP in LF range. In LF range, time lag in group 1 with supine position is more than 1 second but the values in the other two group are smaller than 0.5. It might mean that the CA mechanism in group 1 works better than diabetics. Generally, the maximum CCF values in VLF range are smaller than that in LF range of both group 1 and group 2. However, its standard deviation is the largest among the three groups. Therefore, it indicates that the relation of MABP and MCBFV is uncertain in VLF range. As to the results in the HF range, the time lags between MABP and MCBFV were closer to the origin. It implies that CA is less efficient in the HF range. Some investigators presumed that a failure to autoregulate manifests as a zero or nearly zero time delay [14]. Therefore, we conclude that the CA operates efficiently in the LF range rather than in HF range. According to the results, cross-correlation analysis and non-invasive method has been shown a useful tool in estimating the dynamic response of CA. Our future work involves reproducing our findings in a larger population that might show absence or impairment of cerebral autoregulation and might be helpful in clinical practice.

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