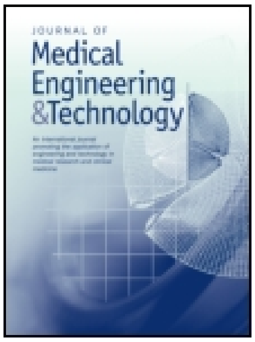

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# Reliability assessment for pulse wave measurement using artificial pulse generator

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**Abstract**

This study aimed to assess intrinsic reliabilities of devices for pulse wave measurement (PWM). An artificial pulse generator system was constructed to create a periodic pulse wave. The stability of the periodic output was tested by the DP103 pressure transducer. The pulse generator system was then used to evaluate the TD01C system. Test–re-test and inter-device reliability assessments were conducted on the TD01C system. First, 11 harmonic components of the pulse wave were calculated using Fourier series analysis. For each harmonic component, coefficient of variation (CV), intra-class correlation coefficient (ICC) and Bland-Altman plot were used to determine the degree of reliability of the TD01C system. In addition, device exclusion criteria were pre-specified to improve consistency of devices. The artificial pulse generator system was stable to evaluate intrinsic reliabilities of devices for PWM (ICCs $> 0.95$, $p < 0.001$). TD01C was reliable for repeated measurements (ICCs of test–re-test reliability $> 0.95$, $p < 0.001$; CVs all $< 3\%$). Device exclusion criteria successfully excluded the device with defect; therefore, the criteria reduced inter-device CVs of harmonics and improved consistency of the selected devices for all harmonic components. This study confirmed the feasibility of intrinsic reliability assessment of devices for PWM using an artificial pulse generator system. Moreover, potential novel findings on the assessment combined with device exclusion criteria could be a useful method to select the measuring devices and to evaluate the qualities of them in PWM.

**Keywords**

Blood pressure, harmonic analysis, radial pulse wave, reproducibility

**History**

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## 1. Introduction

Pulse wave measurement (PWM) has drawn much attention due to its informative value to evaluate the cardiovascular system. The generalized transfer function (GTF), pulse wave velocity (PWV), augmentation index (AI) and harmonic analysis (HA) have been used to assess central aortic pressure [1], arterial stiffness [2] and other cardiovascular diseases [3].

Validation of function or markers mentioned above highly depends on a reliable contour record of pulse wave. Sensors with less reliability could induce errors into the measuring system and increase the variability of the markers. For example, the GTF, scaling function of harmonic components of pulse pressure wave in terms of amplitude and phase, was used to transfer pressure wave from the limb artery to the aortic artery [4]. This method has been validated using radial applanation tonometry [5] and applied in recent decades [6]. However, Shih et al. [7] proved that the input error from the sensor will mostly transfer to the GTF-derived central aortic blood pressure. Therefore, the reliability qualification of sensor is essential for validation of GTF.

Measurement of PWV and AI also rely on high fidelity measurement of pulse wave. The PWV, a marker of arterial stiffness, is the velocity of the pressure pulse wave propagating through the aorta or through the arterial vessel. The critical step in PWV measurement is identification of wavefront of the pulse. There were several methods to detect the wavefront such as measuring the minimum of pulse wave, maximum of pulse wave or calculating the maximum of first derivative of the pulse [8]. However, the change in high frequency content of the pulse may interfere with the wavefront identification process [9,10]. The AI, a representative surrogate of wave reflection, is defined as augmented pressure divided by pulse pressure [11]. AI has also been regarded as a marker of arterial stiffness [12], although that has some arguments among studies [13,14]. Calculation of augmented pressure used the fourth derivative of the pulse wave [15] and also depended on high frequency content of the pulse [5]. Hence, the accurate and reliable reading of PWV and AI based on the high reliability of pulse measuring system with less interference from frequency bias or noise.

Another way of PWM is to analyse the spectrum of blood pressure pulse. The pulse was decomposed into harmonic components (harmonics) by Nichols et al., [16] using Fourier

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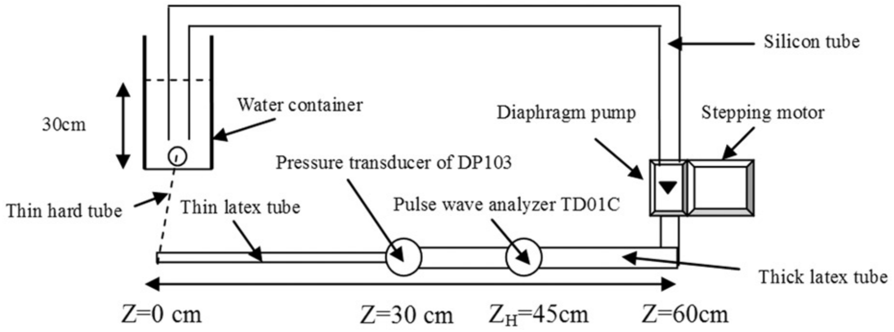

Figure 1. The artificial pulse generator system was outfitted with one Pulse wave analyser TD01C (from TD01C-1 to TD01C-6) at $Z_H = 45$ cm to record the pressure wave in the instrument reliability assessment. In the validation test, the pressure transducer DP103was fixed at $Z_H = 30$ cm. The stepping motor drove the pump to inject the water into the Latex tube periodically with fixed frequency in each measurement.

analysis. Milnor [17] investigated Fourier analysis and described it as one of the most satisfactory approaches to obtain a complete quantitative expression of the pressure wave. Motivated by traditional Chinese medicine, Wang [18] proposed that harmonic components could reveal information about the circulation system in terms of different meridians. To give a further explanation, Lin Wang et al. [19–21] built up a PR wave model to elaborate the meaning of HA in cardiovascular physiology.

The validations of GTF, PWV, AI and HA are based on a fundamental assumption: a pulse measuring system with qualified reliability. However, only few studies have been conducted on the intrinsic reliability of the instrument for PWM. The intrinsic reliability assesses the degree of variability caused by the instrument, where the effects of patient and observer are excluded. Without the intrinsic reliability assessment before the clinical trial, there is no reference to distinguish the source of variation. Therefore, the purpose of this paper is to establish a standard protocol and a pulse generator system to assess the intrinsic reliability of instrument for PWM. The result of this survey may help clinical practitioner to evaluate an instrument or technology appropriate for PWM and validate its reliability in clinical use.

## 2. Materials and methods

### 2.1. Pulse wave analyser TD01C

TD01C (MII-ANN Technology, Taiwan) is a non-invasive system that detects the blood pressure pulse of the radial artery and analyses the pressure pulse with HA. TD01C has an effective and continuous sensing surface ($>2.0\,\text{cm}^2$). TD01C has architectures of dynamic range adjustment and of automatic pulse-sensing such that it can analyse pressure data within minutes and reach resolution of the 11 harmonic waves. TD01C records 12-s data for each measurement. TD01C should operate within working condition: $0 \sim 2.5$ PSI (peak to peak pressure), 23–35 °C and 15–85% Relative humidity. In this paper, six pulse wave analyser TD01Cs were used and labelled TD01C-1, TD01C-2, TD01C-3, TD01C-4, TD01C-5 and TD01C-6, respectively.

### 2.2. Artificial pulse generator system

An artificial pulse generator system was comprised of two parts. The first part was composed of the ASM46AA stepping motor (Oriental Motor, Tokyo, Japan), a diaphragm pump and a computer. The computer controlled the stepping motor through the actuator control circuit to drive the diaphragm pump. The first part was designed to pump the water to generate the periodic pressure pulse, where the period and duration of the pulse can be controlled precisely.

The second part consisted of a latex tube with 60 cm length and a water container with a water level of 30 cm (30 cm length thin tube from $Z = 0$–30 cm with 2.5 mm inner diameter and 4.5 mm outer diameter; 30 cm length thick tube from $Z = 30$–60 cm with 9.2 mm inner diameter and 9.5 mm outer diameter). The latex tube filled with water was a medium of the pressure wave and was connected to the diaphragm pump. The water container, which was connected to a latex tube and diaphragm pump, respectively, by two hard silicon tubes, maintained a mean pressure of 30 cm-$H_2O$ (22.1 mmHg) in the whole system (Figure 1).

### 2.3. Study protocol

In each measurement, the periodic water input was pumped into the latex tube with a fixed frequency, $f_0$. When the whole artificial pulse generator system reached steady state, then the measurement started. In the validation test, the pressure transducer DP103 (Validyne, CA, USA) was fixed on the latex tube at $Z_H = 30$ cm. In the instrument reliability assessment, the pressure transducer TD01C was strapped at $Z_H = 45$ cm to measure the pressure pulse. Then the 12-s data were recorded from a pressure transducer at a sampling rate of 400 Hz. Each pulse was transformed into Fourier series coefficients. The harmonic components $C_{n,i}$ were defined by the following equation, where *i* indicated the *i*th pulse in 12-s data and *n* indicated the *n*th harmonic component of the pulse.

$$C_{n,i} = \frac{A_{n,i}}{A_{0,i}}$$

In this study, we focused on the first 11 harmonic components ($n = 1 \sim 11$), where $A_{0,i}$ was the mean value of the *i*th pressure pulse and $A_{n,i}$ was *n*th coefficient of Fourier series of the *i*th pressure pulse.

For each harmonic component, the within-measurement mean($\mu_{cn}$) and coefficient of variation ($\text{WCV}_{cn}$) were calculated by the following equation, where *N* is the total number of pulses within the 12-s measurement.

$$\mu_{cn} = \frac{1}{N}\sum_{i} C_{n,i}$$

$$\sigma_{cn} = \sqrt{\frac{\sum_{i=1}^{N} (C_{n,i} - \mu_{cn})^2}{N-1}}$$

$$\mathrm{WCV}_{cn} = \frac{\sigma_{cn}}{\mu_{cn}}$$

Where $\mu_{c1} \sim \mu_{c11}$ were representative parameters that described the sequential pulses and $\mathrm{WCV}_{c1} \sim \mathrm{WCV}_{c11}$ represented the degree of variation within the measurement.

## 2.4. Stability validation of artificial pulse generator system

The DP103 pressure transducer was used to assess the stability of periodic output of the artificial pulse generator system and to confirm the spectrum of the periodic output. The 12-s signals were measured by a DP103 pressure transducer at $Z_H = 30$ cm and then were digitized by a PCI-9111 A/D converter (ADLINK) with a sampling rate of 400 Hz.

The artificial pulse generator pumped with a fixed frequency of 1 Hz and then five repeated measurements were carried out using the DP103. There was at least a 5-min interval between measurements. In each measurement, the $\mu_{cn}$ and $\mathrm{WCV}_{cn}$ were calculated and recorded. Furthermore, the pumping frequency was changed from 1 Hz to 2 Hz with a step of 0.2 Hz to simulate the population variation of the heart rate. Five measurements were performed in each pumping frequency with DP103. In total, 30 measurements were performed.

## 2.5. Assessment of test–re-test reliability

At first, an artificial pulse generator pumped with a fixed frequency of 1 Hz. Second, five measurements were carried out using the same device, TD01C-1, following the study protocol. The transducer of TD01C-1 was detached and retied with at least a 5 min interval between measurements. In each measurement, the $\mu_{cn}$ and $\mathrm{WCV}_{cn}$ were calculated and recorded. Furthermore, the pumping frequency was changed from 1 Hz to 2 Hz with a step of 0.2 Hz to simulate the population variation of the heart rate. Five measurements were performed in each pumping frequency with TD01C-1. In total, 30 measurements were performed.

In each pumping frequency, between-measurement coefficient of variation (BCV) was calculated as below, where *j* indicated the *j*th measurement and *n* indicated the *n*th harmonic component.

$$\mathrm{B}\mu_{cn} = \frac{1}{5}\sum_{j=1}^{5} \mu_{cn,j}$$

$$\mathrm{B}\sigma_{cn} = \sqrt{\frac{\sum_{j=1}^{5} (\mu_{cn,j} - \mathrm{B}\mu_{cn})^2}{5-1}}$$

$$\mathrm{BCV}_{cn} = \frac{\mathrm{B}\sigma_{cn}}{\mathrm{B}\mu_{cn}}$$

Where $\mathrm{B}\mu_{cn}$ and $\mathrm{B}\sigma_{cn}$ and were, respectively, mean and standard deviation of $\mu_{cn}$s of the five measurements in the same pumping frequency. $\mathrm{BCV}_{c1} \sim \mathrm{BCV}_{c11}$ represented the degree of variation between the measurements.

## 2.6. Assessment of inter-device reliability

Initially, the artificial pulse generator pumped with a fixed frequency of 1 Hz. Six measurements were carried out on six different devices (TD01C-1 to TD01C-6) following the study protocol. The transducer of TD01C was detached and retied with at least a 1 min interval between measurements. In each measurement, the $\mu_{cn}$ and $\mathrm{WCV}_{cn}$ were calculated and recorded.

Second, the pumping frequency was changed from 1 Hz to 2 Hz, with a step of 0.2 Hz to simulate the population variation of the heart rate. In each pumping frequency, six measurements were performed from TD01C-1 to TD01C-6. In total, 36 measurements were performed.

In each pumping frequency, inter-device coefficient of variation (IDCV) was calculated as below, where *k* indicated the measurement from the *k*th device and *n* indicated the *n*th harmonic component. The quantity of devices was denoted by *M*.

$$\mathrm{ID}\mu_{cn} = \frac{1}{M}\sum_{k=1}^{M} \mu_{cn,k}$$

$$\mathrm{ID}\sigma_{cn} = \sqrt{\frac{\sum_{k=1}^{M} (\mu_{cn,k} - \mathrm{ID}\mu_{cn})^2}{M-1}}$$

$$\mathrm{IDCV}_{cn} = \frac{\mathrm{ID}\sigma_{cn}}{\mathrm{ID}\mu_{cn}}$$

where $\mathrm{ID}\mu_{cn}$ and $\mathrm{ID}\sigma_{cn}$ were, respectively, mean and standard deviation of $\mu_{cn}$s of the six measurements from TD01C-1 to TD01C-6 in the same pumping frequency. $\mathrm{IDCV}_{c1} \sim \mathrm{IDCV}_{c11}$ represented the degree of variation between the measurements from difference devices.

## 2.7. Device exclusion criteria

In the assessment of inter-device reliability, the *k*th device (TD01C-j) was excluded if $\mu_{cn,k}$ beyond the range $\mathrm{ID}\mu_{cn}(1 \pm 10\%)$ for all *n*. This process excluded the devices whose spectrum response of transducers was obviously inconsistent with the others. Both data before and after device exclusion calculated the $\mathrm{IDCV}_{cn}$s and Intra-class correlation coefficients to assess the effect of device exclusion.

## 2.8. Statistics

### *2.8.1. Bland-Altman analysis*

The test–re-test reliability assessment was evaluated using the Bland-Altman analysis [22], which provides a good framework for reliability validation. For each $\mu_{cn}$, the difference between first measurement and second measurement was plotted against their mean value. Then the mean ($\bar{d}$) and the standard deviation (SD) of differences for all participants

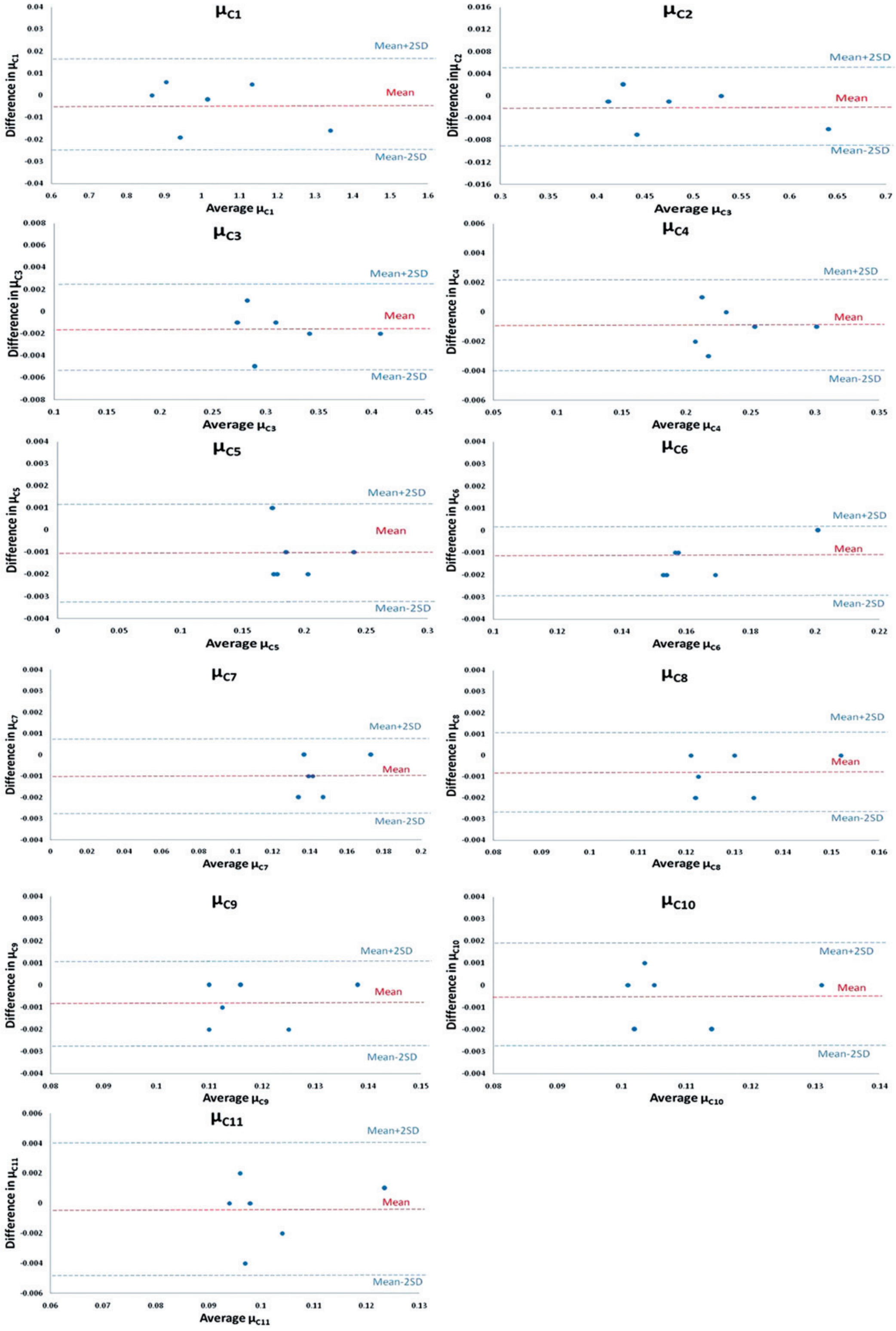

Figure 2. The Bland-Altman plots of the first 11 mean harmonic components ($\mu_{C1} \sim \mu_{C11}$) of the arterial pulse wave in the test–re-test assessment.

were calculated. Limits of agreement ($\bar{d} \pm 2$ SD) were marked by dashes lines (Figure 2).

### 2.8.2. *Intra-class correlation coefficient*

For the stability validation, the test–re-test and inter-device reliability assessment, two-way random single-measure intra-class correlation coefficients, ICC (2, 1) = $\rho$, were calculated for each mean harmonic ($\mu_{C1} \sim \mu_{C11}$) with Matlab 2008 (USA); 95% confidence intervals and $p$ values of ICC (2, 1)s were reported. According to the suggestion of Fleiss [23], the value $\rho > 0.75$ was deemed as excellent reliability. Furthermore, Portney and Watkins [24] recommend that $\rho > 0.9$ is appropriate for clinical application to ensure valid interpretation.

Table 1. The stability validation of the periodic output of an artificial pulse generator system using the mean harmonic components ($\mu_{cn}$) and intra-class correlation coefficient, ICC (2,1).

| | ICC (2, 1) | 95% CI | $p$ Value |
|---|---|---|---|
| $\mu_{c1}$ | 0.998 | 0.993–1.000 | <0.001 |
| $\mu_{c2}$ | 0.996 | 0.988–0.999 | <0.001 |
| $\mu_{c3}$ | 0.996 | 0.986–0.999 | <0.001 |
| $\mu_{c4}$ | 0.995 | 0.985–0.999 | <0.001 |
| $\mu_{c5}$ | 0.993 | 0.979–0.999 | <0.001 |
| $\mu_{c6}$ | 0.991 | 0.973–0.999 | <0.001 |
| $\mu_{c7}$ | 0.990 | 0.968–0.998 | <0.001 |
| $\mu_{c8}$ | 0.990 | 0.968–0.998 | <0.001 |
| $\mu_{c9}$ | 0.987 | 0.960–0.998 | <0.001 |
| $\mu_{c10}$ | 0.985 | 0.953–0.998 | <0.001 |
| $\mu_{c11}$ | 0.973 | 0.918–0.996 | <0.001 |

The $p$-value assesses the statistical significance of the null hypothesis that there is no correlation between five measurements ($H_0$: $ICC(2,1) = 0$); CI, confidence internal.

## 3. Results

### 3.1. Result of stability validation of artificial pulse generator system

In the validation test, we used intra-class correlation coefficients to evaluate the stability of periodic output for each mean harmonic ($\mu_{C1} \sim \mu_{C11}$). All the intra-class correlation coefficients of the mean harmonics exceeded 0.95, with $p$ value less than 0.001 (Table 1). The time domain and frequency domain of the periodic outputs were drawn for all pumping frequency. The periodic output with pumping frequency of 1.4 Hz was shown in Figure 3.

### 3.2. Result of test–re-test assessment

Test–re-test reliability was statistically analysed using coefficient of variation, Bland-Altman plot and intra-class correlation coefficient. Table 2 revealed that all $WCV_{cn}$s were less than 2% from $n = 1$ to $n = 11$ and from $f_0 = 1.0$ Hz to $f_0 = 2.0$ Hz. $BCV_{cn}$s were less than 3% for all harmonics at all pumping frequencies. Bland-Altman plots for first and second measurements were constructed for all mean harmonics ($\mu_{C1} \sim \mu_{C11}$) of test–re-test assessment. The differences of $\mu_{Cn}$ between two measurements were plotted against the mean for each harmonic ($n = 1 \sim 11$). The first 11 examples ($\mu_{C1} \sim \mu_{C11}$) of the plots are shown in Figure 2. For all harmonics the mean differences were near to zero (deviations were $\sim 1\%$ of the average $\mu_{Cn}$s from the zero). All reading differences were within 95% confidence intervals ($\bar{d} \pm 2SD$). Intra-class correlation coefficient for test–re-test reliability assessment, ICC (2, 1), are reported in Table 3, which presents that all the ICCs exceeded 0.97 for all harmonics.

### 3.3. Result of inter-device assessment

Statistical analysis of test–re-test reliability assessment utilized coefficient of variation and intra-class correlation coefficient. $IDCV_{cn}$s (Table 2) and intra-class correlation coefficients (Table 4) were reported both with and without device exclusion.

Without device exclusion, the $IDCV_{cn}$s of six devices (TD01C-1, TD01C-2, TD01C-3, TD01C-4, TD01C-5 and TD01C-6) ranged from 4–16% and was dependent on pumping frequency and order of harmonic. Inter-device reliability assessment revealed that all the ICC (2, 1)s were less than 0.75 for all harmonics.

With device exclusion, the $IDCV_{cn}$s of five devices (TD01C-1, TD01C-2, TD01C-3, TD01C-5 and TD01C-6) ranged from 4–9%. ICC (2, 1)s exceeded 0.75 for the first five harmonics ($\mu_{c1} \sim \mu_{c5}$). ICC (2, 1)s of other harmonics ranged from 0.65–0.70.

## 4. Discussion

Our primary effort was to construct an artificial pulse generator system to evaluate intrinsic reliability of the instrument for PWM. We proved that the system could create a stable and periodic pressure output (Table 1). The main energy of the output was dissipated in fundamental frequency (pumping frequency) and its harmonics, which is similar to the arterial pulse wave *in vivo*.

The non-invasive measuring technology has evolved from a traditional cuff sphygmomanometer to alternative techniques such as applanation tonometry [25], ultrasound [26] and photoplethysmography [27,28]. The evolution of non-invasive measuring techniques makes the PWM more convenient to perform and more applicable in a variety of clinical trials. Several studies have been performed on reliabilities assessment in clinical test [29,30]. Nonetheless, little work has been carried out on intrinsic reliability assessment of the instrument. If one instrument has poor reliability, the variation could be within subject, among subjects, from an observer or from the instrument. Therefore, accessing the intrinsic reliability is a fundamental step to identify the source of variation and to give a valid interpretation in PWM.

Scolletta et al. [31] proposed that PWM-derived variables provided relevant information on cardiac contractility and performance in critically ill patients. Kuo et al. [32] found that within-subject variation of the harmonics reflected the stage of severity in terminally ill patients. If we can measure instrument uncertainty for PWM precisely, we will be able to distinguish the within-subject variation from variation of others; thus, the stages of illness can be investigated to improve the hospice and palliative care service.

In the evaluation of the TD01C system, harmonic components of the pulse were used to assess test–re-test reliability and inter-device reliability. All harmonics were statistically analysed using coefficient of variation, Bland-Altman plot and intra-class correlation coefficient. $WCV_{cn}$s revealed the stability of the whole measuring system, including a pulse generator system and transducer of TD01C-1. $BCV_{cn}$s and $WCV_{cn}$s provided the degree of uncertainty using TD01C-1. The difference between $BCV_{cn}$s and $WCV_{cn}$s pointed out the effect of re-strapping of the transducer. Moreover, the ICC of test–re-test assessment exceeded 0.9, with $p$ value less than 0.001 for each mean harmonics (Table 3). The above results showed that the instrument reliability of TD01C-1 reached criterion suggested by Portney and Watkins [24]. Therefore, we concluded that TD01C-1 was reliable to perform studies of PWM.

$IDCV_{cn}$ showed the consistency of each harmonic among devices (TD01C-1 ~ TD01C-6). Lack of consistency among

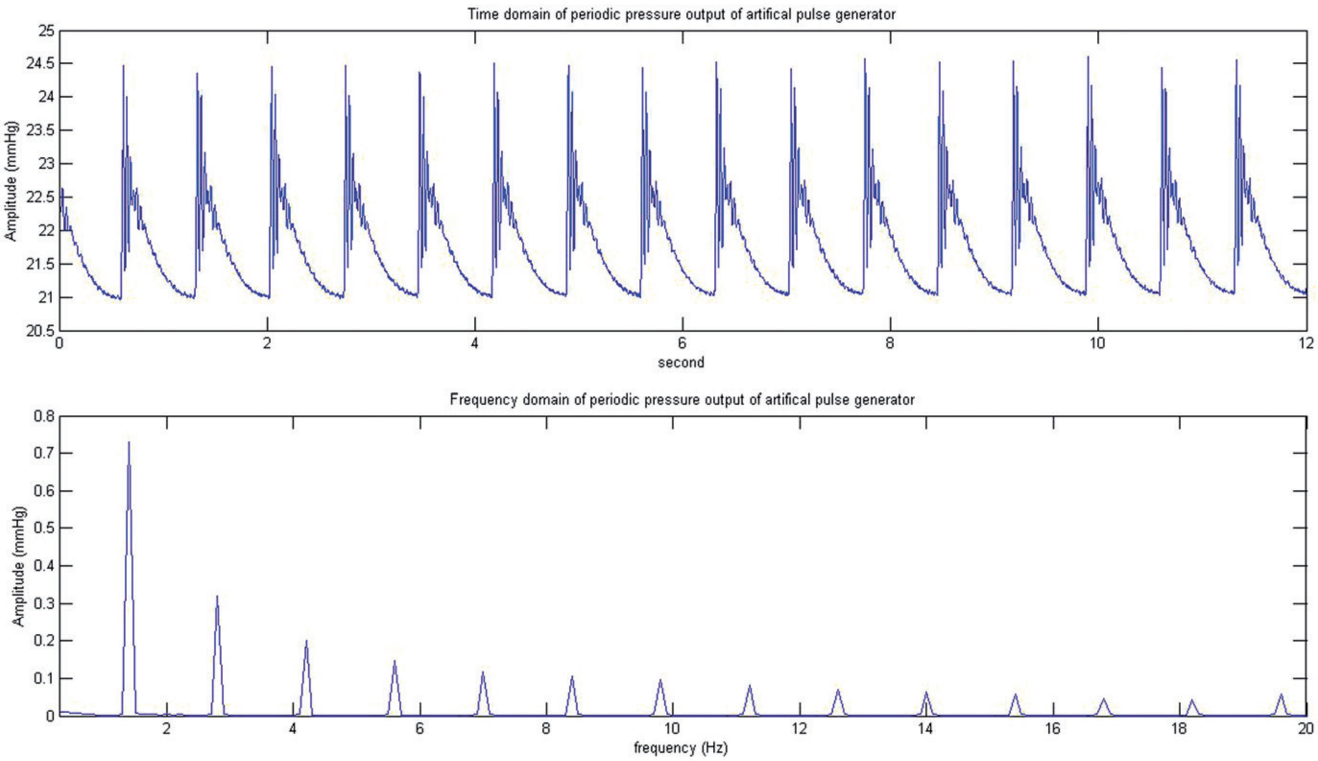

Figure 3. The time domain and frequency domain of the periodic pressure of an artificial pulse generator system with a pumping frequency of 1.4 Hz.

Table 2. Three types of CVs: Within-measurement coefficient of variation (WCV), between-measurement coefficient of variation (BCV) to access test–re-test reliability and inter-device coefficient of variation (IDCV) to access inter-device reliability.

| $F_0$ | $WCV_{c1}$ | $WCV_{c2}$ | $WCV_{c3}$ | $WCV_{c4}$ | $WCV_{c5}$ | $WCV_{c6}$ | $WCV_{c7}$ | $WCV_{c8}$ | $WCV_{c9}$ | $WCV_{c10}$ | $WCV_{c11}$ |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 1.0 Hz | 1.7% | 1.7% | 1.7% | 1.7% | 1.7% | 1.6% | 1.6% | 1.5% | 1.6% | 1.5% | 1.4% |
| 1.2 Hz | 1.4% | 1.5% | 1.4% | 1.3% | 1.2% | 1.2% | 1.1% | 0.8% | 1.0% | 0.9% | 0.7% |
| 1.4 Hz | 1.3% | 1.3% | 1.2% | 1.2% | 1.1% | 1.0% | 1.0% | 0.9% | 0.8% | 0.6% | 0.8% |
| 1.6 Hz | 1.5% | 1.6% | 1.5% | 1.4% | 1.4% | 1.4% | 1.4% | 1.3% | 1.2% | 1.3% | 1.2% |
| 1.8 Hz | 1.5% | 1.6% | 1.5% | 1.4% | 1.4% | 1.4% | 1.4% | 1.3% | 1.2% | 1.3% | 1.2% |
| 2.0 Hz | 0.6% | 0.6% | 0.5% | 0.5% | 0.6% | 0.5% | 0.4% | 0.5% | 0.5% | 0.5% | 0.6% |
| | $BCV_{c1}$ | $BCV_{c2}$ | $BCV_{c3}$ | $BCV_{c4}$ | $BCV_{c5}$ | $BCV_{c6}$ | $BCV_{c7}$ | $BCV_{c8}$ | $BCV_{c9}$ | $BCV_{c10}$ | $BCV_{c11}$ |
| 1.0 Hz | 1.4% | 1.5% | 1.5% | 1.5% | 1.5% | 1.5% | 1.5% | 1.4% | 1.5% | 1.6% | 1.5% |
| 1.2 Hz | 0.6% | 0.6% | 0.7% | 0.9% | 1.1% | 1.3% | 1.5% | 1.6% | 1.7% | 2.0% | 2.1% |
| 1.4 Hz | 0.5% | 0.4% | 0.3% | 0.3% | 0.3% | 0.4% | 0.4% | 0.4% | 0.5% | 0.7% | 0.8% |
| 1.6 Hz | 0.9% | 0.9% | 1.0% | 0.9% | 1.0% | 1.0% | 1.1% | 1.2% | 1.1% | 1.3% | 1.4% |
| 1.8 Hz | 0.5% | 0.5% | 0.8% | 0.8% | 1.0% | 1.1% | 1.2% | 1.3% | 1.7% | 1.4% | 1.3% |
| 2.0 Hz | 0.3% | 0.5% | 0.7% | 0.9% | 1.1% | 1.2% | 1.4% | 1.9% | 1.9% | 2.2% | 2.9% |
| | $IDCV_{c1}$ | $IDCV_{c2}$ | $IDCV_{c3}$ | $IDCV_{c4}$ | $IDCV_{c5}$ | $IDCV_{c6}$ | $IDCV_{c7}$ | $IDCV_{c8}$ | $IDCV_{c9}$ | $IDCV_{c10}$ | $IDCV_{c11}$ |
| Without device exclusion (6 devices) | | | | | | | | | | | |
| 1.0 Hz | 4.0% | 7.7% | 8.0% | 8.4% | 8.4% | 8.7% | 8.5% | 8.5% | 8.6% | 8.6% | 8.6% |
| 1.2 Hz | 9.4% | 11.8% | 12.5% | 12.6% | 12.8% | 12.8% | 12.7% | 13.0% | 13.1% | 12.9% | 13.1% |
| 1.4 Hz | 12.8% | 14.7% | 15.3% | 15.4% | 15.3% | 15.4% | 15.7% | 15.6% | 15.4% | 15.5% | 15.2% |
| 1.6 Hz | 13.5% | 15.0% | 15.5% | 15.8% | 15.8% | 15.7% | 15.8% | 15.8% | 15.8% | 15.1% | 14.9% |
| 1.8 Hz | 12.7% | 14.0% | 14.2% | 14.2% | 14.1% | 14.0% | 14.0% | 13.7% | 13.1% | 13.2% | 13.6% |
| 2.0 Hz | 10.9% | 11.9% | 12.0% | 11.9% | 11.9% | 11.7% | 11.4% | 11.0% | 11.0% | 11.3% | 11.4% |
| With device exclusion (5 devices) | | | | | | | | | | | |
| 1.0 Hz | 3.9% | 5.6% | 5.3% | 5.3% | 5.4% | 5.6% | 5.5% | 5.6% | 5.6% | 5.6% | 5.8% |
| 1.2 Hz | 7.3% | 7.7% | 7.7% | 7.9% | 8.0% | 8.0% | 8.0% | 8.3% | 8.3% | 8.2% | 8.0% |
| 1.4 Hz | 8.2% | 8.2% | 8.3% | 8.3% | 8.3% | 8.4% | 8.4% | 8.3% | 8.2% | 8.1% | 8.0% |
| 1.6 Hz | 6.9% | 6.7% | 6.9% | 6.9% | 6.9% | 7.0% | 6.8% | 6.7% | 6.8% | 6.4% | 6.4% |
| 1.8 Hz | 6.0% | 5.8% | 5.8% | 5.9% | 5.9% | 5.6% | 5.5% | 5.4% | 5.2% | 5.1% | 5.6% |
| 2.0 Hz | 5.1% | 5.0% | 5.0% | 5.1% | 5.1% | 4.9% | 4.8% | 4.8% | 4.4% | 4.9% | 5.5% |

$F_0$ was pumping frequency of an artificial pulse generator.

Table 3. The test–re-test reliability assessment of the mean harmonic components ($\mu_{cn}$) using intra-class correlation coefficient, ICC (2,1).

| | ICC (2, 1) | 95% CI | *p* Value |
|---|---|---|---|
| $\mu_{c1}$ | 0.989 | 0.991–1.000 | <0.001 |
| $\mu_{c2}$ | 0.997 | 0.990–1.000 | <0.001 |
| $\mu_{c3}$ | 0.997 | 0.987–0.999 | <0.001 |
| $\mu_{c4}$ | 0.996 | 0.984–0.999 | <0.001 |
| $\mu_{c5}$ | 0.995 | 0.979–0.999 | <0.001 |
| $\mu_{c6}$ | 0.993 | 0.959–0.998 | <0.001 |
| $\mu_{c7}$ | 0.987 | 0.945–0.997 | <0.001 |
| $\mu_{c8}$ | 0.982 | 0.926–0.996 | <0.001 |
| $\mu_{c9}$ | 0.976 | 0.918–0.996 | <0.001 |
| $\mu_{c10}$ | 0.973 | 0.921–0.996 | <0.001 |
| $\mu_{c11}$ | 0.975 | 0.906–0.995 | <0.001 |

The *p*-value assesses the statistical significance of the null hypothesis that there is no correlation between five measurements ($H_0$: ICC $(2,1) = 0$); CI, confidence internal.

Table 4. The inter-device reliability assessment of the mean harmonic components ($\mu_{cn}$) using intra-class correlation coefficient, ICC (2,1). Both ICCs before and after device exclusion were calculated as below.

| | Before device exclusion (6 devices) | | After device exclusion (5 devices) | |
|---|---|---|---|---|
| | ICC (2, 1) | 95% CI | ICC (2, 1) | 95% CI |
| $\mu_{c1}$ | 0.663 | 0.246–0.932 | 0.868 | 0.454–0.979 |
| $\mu_{c2}$ | 0.621 | 0.197–0.921 | 0.866 | 0.451–0.979 |
| $\mu_{c3}$ | 0.556 | 0.156–0.899 | 0.842 | 0.399–0.975 |
| $\mu_{c4}$ | 0.522 | 0.139–0.886 | 0.824 | 0.367–0.971 |
| $\mu_{c5}$ | 0.445 | 0.104–0.851 | 0.778 | 0.299–0.962 |
| $\mu_{c6}$ | 0.329 | 0.065–0.778 | 0.695 | 0.217–0.943 |
| $\mu_{c7}$ | 0.292 | 0.055–0.747 | 0.657 | 0.188–0.933 |
| $\mu_{c8}$ | 0.287 | 0.054–0.742 | 0.649 | 0.190–0.931 |
| $\mu_{c9}$ | 0.310 | 0.060–0.762 | 0.666 | 0.204–0.935 |
| $\mu_{c10}$ | 0.344 | 0.070–0.789 | 0.701 | 0.226–0.944 |
| $\mu_{c11}$ | 0.337 | 0.068–0.784 | 0.692 | 0.218–0.942 |

The *p*-value assesses the statistical significance of the null hypothesis that there is no correlation between five measurements ($H_0$: ICC $(2,1) = 0$); All *p*-values of data were $< 0.001$; CI, confidence internal.

devices could create artifact of pulse signal and, thus, could lead to wrong conclusion in meta-analysis. Without device exclusion, the maximum of IDCV$_{cn}$s reached 16%, which was large uncertainty compared to WCV$_{cn}$s. The ICCs of inter-device reliability were less than 0.75 (Fleiss criteria) for all mean harmonics ($\mu_{c1} \sim \mu_{c11}$). The result showed a lack of consistency among six devices. We then exclude the TD01C-4 in accordance with the device exclusion criteria. We sent back the TD01C-4 to the MII-ANN Technology and its QC department found that a part of TD01C-4 had defects. It is, therefore, proved that the method is powerful to assure instrument reliability. Without TD01C-4, the maximum of IDCV$_{cn}$s decreased to 9% and ICCs exceed 0.75 for the first five mean harmonics ($\mu_{c1} \sim \mu_{c5}$). Thus, the degree of uncertainty was lower and the consistency was improved. However, there was still room to improve consistency for higher mean harmonics ($\mu_{c6} \sim \mu_{c11}$).

This report focused on the fundamental frequency of the heart and its harmonics, which approximately ranged from 1–20 Hz. However, some activities also affect the peripheral pulse, such as respiration (0.15–0.4 Hz) and sympathetic activity on microcirculation (0.04–0.15 Hz) [33,34]. The reliabilities of TD01C in those frequency ranges are still not validated and need more studies in the future. In addition, TD01C records only 12-s data for each measurement. Thus, TD01C is not suitable for measuring frequencies below roughly 0.1 Hz [8].

This research demonstrated that an artificial pulse generator system could be used to statistically access intrinsic reliability of one device or among devices. A Bland-Altman plot for each mean harmonics showed the limitation of a specific device to measure the index in PWM (Figure 2). Furthermore, the device exclusion criteria could be set to assure consistency of selected devices for PWM. The investigator can choose appropriate device inclusion criteria and validate the intrinsic reliability of selected devices to fit their intended use.

## Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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