VALIDATION OF OSCILLOMETRIC BLOOD PRESSURE MEASURING DEVICES; A CASE STUDY OF THE BpTRU™

by

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ABSTRACT

Hypertension is one of the most common reasons why North Americans visit a physician's office and its measurement technique has been reasonably standard since the earliest accepted description of an indirect method of measuring blood pressure by Riva Rocci in 1896. Korotkoff later modified the traditional sphygmomanometer in 1905. However, since then the mercury sphygmomanometer has become not only the gold standard, but also an essential diagnostic tool in everyday medical care.

Recently however, there has been growing concern over the accuracy of the measurements obtained and the potential biohazard with standard mercury sphygmomanometers. Many cities and countries in Europe and North America, are in the process of phasing them out. Newer instruments such as the auscultatory aneroid, and the automated electronic devices of which the majority are of the oscillometric type, are beginning to appear. All new devices have the option of undergoing a validation process to assess the accuracy according to the relevant governing bodies.

The BpTRU™ is an automated oscillometric electronic blood pressure device developed by VSM Medtech Ltd of Vancouver. Connected in parallel by means of a T-tube, to the current gold standard mercury sphygmomanometer, allowed blood pressures to be measured simultaneously. Two observers blinded from each other and the device, recorded blood pressures individually. The mean observer average was compared to the device mean blood pressures for agreement. This was done according to the American National Standard for Electronic or Automated Sphygmomanometers-1992 and the British Hypertension Society protocol-1993.

The validation process was initially conducted in adults and agreement was within the above standards. However the device tended to underestimate at higher systolic blood pressures, so the algorithm was modified and the device re-validated using embedded raw data. After running the validation study in children, which again satisfied the above criteria, the raw data was combined in a final study.

The BpTRU™ is the only automated blood pressure measuring device that has been *independently* validated and has attained a high level of accuracy over this broad age and blood pressure range.

TABLE OF CONTENTS

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A special thank you to my supportive and understanding family,
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CHAPTER I

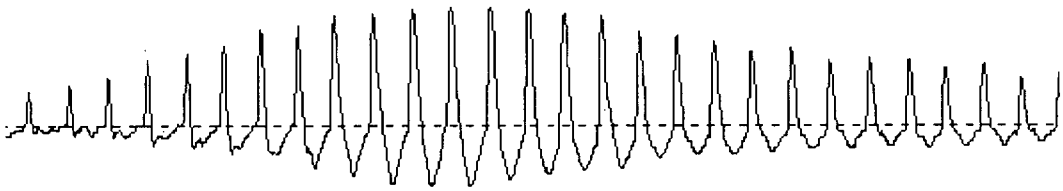
OVERALL INTRODUCTION

Measurement of blood pressure accurately is crucial; as based on these measurements, patients are labelled and non-drug and drug therapies recommended [1][2]. It is therefore essential that the method of measuring blood pressure is accurate and reproducible. The current standard for blood pressure measurement is the auscultatory method using the mercury sphygmomanometer. However, there are pressures to replace that standard with other methods. One of the concerns is about mercury poisoning. As a result of this many States in the US, other cities in North America and some European countries have banned or are preparing to ban mercury in both thermometers and blood pressure sphygmomanometers [3][4]. It is predicted by some that it is only a matter of time before alternatives to the 100-year-old mercury sphygmomanometer are required [5]. Another pressure on the mercury sphygmomanometer is that it is subject to unacceptable inter and intra-observer variability. This is a setting in which a computer, which uses a reproducible and repetitive method has obvious advantages. Another pressure on the mercury sphygmomanometer comes from the requirements of clinical trials. Despite these requirements, bias can be demonstrated to commonly occur during the selection procedure. In the clinical trial setting it is critical to minimize bias at all stages of the trial. During a systematic review of a large number of trials it was found that diastolic blood pressure variability at baseline was substantially less than systolic variability at baseline and substantially less than diastolic variability at the end of the study [6]. The most likely explanation for this decreased variability at baseline is that many subjects must have had a diastolic blood pressure equal to or just above the entry criteria. This reflects observer bias in order to enhance recruitment of patients into the study. The use of an objective blood pressure measuring device to identify patients at baseline would prevent this bias.

Another reason for developing new blood pressure measuring devices are the practicalities of most physician's offices or clinics, the place where most of our blood pressure measurements take place. Most physicians do not have the time, knowledge or skill to carefully measure blood pressure in the same manner that they were measured in the clinical trials [7]. Thus if they cannot reproduce the setting that the evidence is based upon they cannot make decisions for their patients based on the best available evidence. A method that would replace the mercury sphygmomanometer must deal with the practical time constraints in a physician's office and mimic the blood pressure measurements achieved in a clinical trial setting as much as possible.

Most of the new methods for measuring blood pressure at the present time use the oscillometric technique. This method refers to the measurement of the oscillations, caused by the arterial pulse pressure. These oscillations are the result of the cuff causing the occlusion of the artery (usually the brachial), that it overlies. The method does not use sound so microphones are not needed and external noise is not a problem. However, the method is sensitive to patient movement. The cuff, wrapped around the patient's upper arm is automatically inflated with air to occlude the brachial pulse. On deflation, pressure data is recorded by the device in waveform (as shown in figure 1).

Fig 1: pulse waveform against time



The maximum amplitude of the pulse wave is taken as the mean arterial pressure (MAP) and the systolic and diastolic blood pressures are calculated from this plus the pattern of the waveforms. The software algorithms used by the many manufacturers of blood pressure measuring devices are proprietary and therefore not published information.

When a local company, VSM MedTech Ltd. of Vancouver, Canada approached The UBC High Blood Pressure Clinic with a new and novel approach to measuring and recording blood pressure in the office, it was of considerable interest to me. I was interested in learning how such new devices were validated and was therefore enthusiastic to be involved in the design, modification, execution and analysis of clinical trials for that purpose. This involved learning the rigorous uniform criteria as set by the American National Standard for Electronic or Automated Sphygmomanometers, ANSI / AAMI SP10-1992 and the British Hypertension Society protocol, the standard setting bodies for these types of devices [8,9].

The process of participation in 2 clinical validation trials of the BpTRU™, manufactured by VSM Medtech Limited plus re-validation using stored electronic data permitted me to learn a lot about the validation process and standards. As a result of this learning process I have been able to make recommendations

as to how the validation process and standards can be improved and how the BpTRU™ should be further tested in the future.

The results of this thesis are described in four chapters. Chapter two represents a published paper that summarizes the validation trial in adults [10]. Chapter three describes how the computer algorithm was modified using stored electronic data from the trial outlined in Chapter two [11].

Chapter four describes a second trial to determine the accuracy of the device in children (age range 3 to 18 years). The Chapter is ready to be submitted for publication. Finally, to summarize the overall accuracy of the BpTRU™ the raw data for each subject in the adult and paediatric trials was combined and presented in Chapter five. This study is also now ready to be submitted for publication.

Chapter six represents the overall discussion. It includes recommendations to the regulatory bodies as to how to improve the validation process and recommendations to the company that makes the BpTRU™ as to future trials to further demonstrate the usefulness of the device.

Objectives:

- To compare the BpTRU™ oscillometric blood pressure-measuring device with the auscultatory mercury sphygmomanometer in adults.
- To compare the blood pressure device against the standard auscultatory mercury sphygmomanometer in the paediatric population.
- To combine the adult and paediatric data in the form of an individual data meta-analysis, to assess the overall accuracy of the device.
- To critique the regulatory requirements for blood pressure-measuring devices and make suggestions for improvement.
- To recommend and develop new clinical trials to demonstrate the usefulness in the primary care setting.

CHAPTER II

COMPARISION of the OSCILLOMETRIC BLOOD PRESSURE MONITOR (BPM-100$_{Beta}$) WITH THE AUSCULATORY MERCURY SPHYGMOMANOMETER

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Short Title: Validation of the BPM-100$_{Beta}$ monitor.

ABSTRACT

Background:

To compare directly the accuracy of the BPM-100_{Beta} monitor (an automated oscillometric blood pressure device) with standard auscultatory mercury sphygmomanometry.

Design:

The BPM-100_{Beta} was connected in parallel via a T-tube to a mercury sphygmomanometer. The BPM-100_{Beta} and two trained observers (blinded from each other, and the BPM-100_{Beta}) measured the sitting blood pressures (BP) simultaneously.

Methods:

Means, standard deviation and range were calculated for all demographic data: age, arm size, heart rate and BP. Agreement between the BPM-100_{Beta} and the mean of 2 observers (reference) was determined and expressed as the mean ± SD, plus the % of differences within 5, 10 and 15 mmHg.

Results:

Of 92 recruited subjects, 85 (92.4%) met the inclusion criteria, and 391 sets of sitting BP and heart rate measurements were available for analysis. The mean difference between the BPM-100_{Beta} monitor and the reference was –0.62 ± 6.96 mmHg for systolic BP, –1.48 ± 4.80 mmHg for diastolic BP and 0.14 ± 1.86 bpm for heart rate. The only limitation of the device was a tendency for the device to underestimate higher systolic blood pressures. This limitation has been addressed by a minor change in the algorithm (see following companion publication). [8]

Conclusion:

The BPM-100_{Beta} is an accurate BP monitor for the office setting, which meets all requirements of the Association for the Advancement of Medical Instrumentation and achieves an "A" grade according to the British Hypertension Society standard.

Key Words: blood pressure, measurement, monitor, oscillometric, validation, automatic.

INTRODUCTION

Sir George Pickering described blood pressure as a dynamic process, such that a single blood pressure reading in the physician's office is like watching a single frame of a movie [1]. To practice rational evidence-based medicine when managing elevated blood pressure, one should document blood pressures in a manner at least as good as that employed in the large randomized controlled trials (RCTs). The latter generally require that the patient rest comfortably for at least 5 minutes before a technician or nurse measures the blood pressure repeatedly (at least 3 times) following approved standards.[2] This may be achievable in some specialty clinics, but is seldom followed in the family physician setting, where most patients with high blood pressure are managed.

It is a practical reality that accurate reproducible documentation of resting blood pressure is difficult for the average outpatient physician or nurse to achieve. Common errors in blood pressure readings include: insufficient or no time for the patient to rest, unsupported arm, unsupported back, arm not at heart level, talking at the time of the measurement, distracting background noise, inappropriate cuff and bladder size, failure to record measurement immediately, rounding of numbers to nearest 5 or 10 instead of to 2 mmHg, too rapid deflation of cuff pressure, and using a non-calibrated instrument [3].

Any method that might improve blood pressure measurement must satisfy economic and practical realities of office practice. It must generate measurements that are an accurate reflection of the present standard (auscultatory measurements with a mercury sphygmomanometer) from a technique that is equal to or better than usual practice. In addition it should reduce or not add to physician/nurse effort and time.

The BPM-100_{Beta}, produced by VSM MedTech Ltd. of Vancouver, Canada, is an automated, non-invasive blood pressure monitor designed to generate repeated measures of the blood pressure and pulse rate of patients without requiring the presence of a physician or nurse. The device uses standard blood pressure cuffs to measure the blood pressure in the upper arm using the oscillometric technique. The purpose of this study was to directly compare the accuracy of the BPM-100_{Beta} monitor with standard auscultatory measurements using a mercury sphygmomanometer in accordance with guidelines provided by the

Association for the Advancement of Medical Instrumentation (AAMI) SP10:1992, the standard setting body for both these devices.[4]

METHODS

Subject Enrolment

Subjects were recruited using public notices in a University setting, through the Blood Pressure Clinic at the University of British Columbia, and through family physician practices associated with the University. Screening was designed to enrol at least 85 subjects with a minimum of 3 acceptable pairs of blood pressure measurements and meeting the required target population objectives defined below.

Ethical Approval

Ethical approval of the study and consent form was obtained from the Clinical Screening Committee for Human Experimentation of the University of British Columbia prior to initiation of any of the study procedures.

Inclusion criteria

All subjects had to be hemodynamically stable and at least 18 years old. Subjects with rhythm irregularities such as atrial fibrillation or with an auscultatory gap were eligible. All subjects signed the consent form prior to enrolment. To be included screening measurement criteria had to be met, and a minimum of 3 valid pairs of measurements obtained.

Exclusion criteria

Subjects with unstable, accelerated or malignant hypertension were excluded, as were patients with severe peripheral vascular disease or other existing condition that the investigators felt would not allow for safe or accurate non-invasive blood pressure measurements. There were also pre-specified measurement exclusion criteria for both subjects and individual measurements: 1) Subjects in whom the inter-observer agreement was greater than 10 mmHg in either the systolic or diastolic blood pressure measurements at screening. 2) Subjects who had less than 3 valid pairs of readings. 3) Subjects who had such weak Korotkoff sounds, that either of the observers deemed acceptable auscultation impossible. 4) Any measurement in which the inter-observer agreement was greater than 10 mmHg for either the systolic or diastolic reading. 5) Any measurement in which the BPM-100_{Beta} did not record or recorded an error.

Target population objectives:

1) An equal number of males and female subjects.

2) Range of arm sizes (measured at mid-biceps).

- At least 10% greater than 35 cm circumference (large arm cuff).
- At least 10% less than 25 cm circumference (small arm cuff).

3) Range of systolic blood pressures (mean of 2 observers).

- At least 10% greater 180 mmHg systolic.
- At least 10% less than 100 mmHg systolic.

4) Range of diastolic blood pressures (mean of 2 observers).

- At least 10% greater 100 mmHg diastolic.
- At least 10% less than 60mmHg diastolic.

Study design

Subjects were recruited during September and October 1999. All subjects provided signed informed consent prior to enrolment. A signed copy of the consent form was provided to each subject. All subjects were entered into the subject log and assigned a subject code. Basic demographic data were collected on each subject enrolled into the trial including age, sex, pre-existing health conditions and medications, and arm circumferences (measured at mid-biceps on the arm of blood pressure recordings).

Subjects were then seated in a quiet but well illuminated room on a chair with comfortable back support. The arm from which blood pressure measurements were recorded was placed in a comfortable position on an adjustable table at heart level. The appropriate-sized cuff (based on cuff markings) was selected from four sizes provided with the BPM-100_{Beta} and applied to the subject's bare upper arm with the indicator over the brachial artery.

The BPM-100_{Beta} was connected in parallel with a mercury sphygmomanometer by means of a T-tube with arms of equal length. A Trimline precision mercury sphygmomanometer (range 0 to 300 mmHg,

gradations of 1 mmHg, accuracy ± 0.5 mmHg) was used as the standard sphygmomanometer to provide the auscultatory reference readings.

A heart rate monitor, the Nonin finger pulse oximeter, was connected to the subject's other arm or alternate body location as appropriate; this device has a range of 18 to 300 beats per minute and accuracy of ± 3%.

One of the two observers located the diaphragm of the stethoscope over the brachial artery and determined optimal position for adequate auscultation. Auscultation for blood pressures was performed with a dual-headed teaching stethoscope. The observers were seated on adjustable seats opposite the subject so that they could read the standard mercury sphygmomanometer without introducing parallax errors. An interposed curtain blinded observers from each other. The two observers were experienced registered nurses whose blood pressure recording skills were confirmed by the investigators prior to any trial subject enrolment.

The BPM-100_{Beta} device automatically inflates and deflates the cuff, and then uses the oscillometric technique to calculate systolic and diastolic blood pressure. In this technique, the mean arterial pressure (MAP) is measured directly from the cuff pressure during deflation, and the systolic and diastolic BP points are calculated as ratios of the MAP pulse amplitude. The BPM-100_{Beta} automatically inflates the cuff after initiation to preset pressures, and automatically adjusts to higher pressures if necessary to ensure complete capture of the pulse waves. The cuff slowly deflates automatically at a rate of 4 mmHg/second in a true linear fashion.

The BPM-100_{Beta} was set to cycle every 2 minutes and the observers (blinded from each other, and the BPM-100_{Beta}) simultaneously visually recorded the systolic and diastolic blood pressures by listening to the Korotkoff sounds and watching the standard mercury sphygmomanometer. Korotkoff sound phase I (the beginning of the compression sound) was taken as the systolic blood pressure; and phase V (the point of complete disappearance of the sound) was taken as the diastolic blood pressure. These measurements were independently recorded by each of the observers. The BPM-100_{Beta} readings and

pulse rate were recorded by one of us (GSM) independently and blinded from the two observers. A total of six measurements were recorded by this method. The first measurement was considered the screening measurement and was not used further in the validation study (the first reading was used to establish observer agreement and satisfactory auscultation technique).

One of us (GSM) also recorded the heart rate reference value via the standard Nonin finger pulse oximeter at approximately the mid-point of automatic deflation, without knowledge of the BPM-100_{Beta} estimate. After six measurements when all readings and recordings were properly documented the cuff was removed from the subjects' arm, and the subject was allowed to leave.

Data Analysis

Mean, standard deviation and range were calculated for all the demographic data: age, arm size, heart rate and blood pressures. The first blood pressure measurement was a screening measurement only and was not used in the analysis. Each subsequent measurement was reviewed for the exclusion criteria outlined above for both the BPM-100_{Beta} and the observers.

For each included systolic and diastolic blood pressure measurement the mean of the 2 observer values was calculated and defined as the reference standard. Differences between the 2 observers were expressed as the mean difference ± standard deviation, and as the % ≤ 5 mmHg. Differences between the BPM-100_{Beta} and the reference standard were also determined for each systolic and diastolic blood pressure measurement and expressed as the mean difference ± standard deviation according to the AAMI standard [4], as well as the % of inter-technique differences within 5 mmHg, 10 mmHg and 15 mmHg according to the BHS standard [5]. Inter-technique differences between the BPM-100_{Beta} heart rates and the reference heart rates obtained from the Nonin pulse oximeter were also calculated similarly.

To assess how the differences related to the absolute blood pressure value the BPM-100 minus reference standard difference was plotted against the average of the 2 BP values using a Bland Altman display for both systolic and diastolic BP [6].

RESULTS

Enrolled subjects

Of the 92 subjects enrolled, 85 (92.4%) were included and 7 (7.6%) were excluded. Reasons for exclusion are detailed below. Pre-existing medical conditions of enrolled subjects included some with hypertension, renal disease (including subjects on dialysis), obesity, stroke, angina and Crohn's disease. Subjects were also taking various anti-hypertensive and other medications. No adverse side effects were reported during or for up to 30 days after the trial. Three individuals who had elevated blood pressures and possibly unrecognized hypertension were advised to follow up with their regular physician.

Excluded Subjects

The first 3 of the 92 volunteers were excluded because of the inability to obtain at least 3 satisfactory sets of BP readings. This was found to be due to a technical problem with the BPM-100_{Beta} monitor deflation mechanism, which was rectified prior to any further subjects being studied. Two subjects were excluded because of a screening BP inter-observer difference of greater than 10 mmHg, and 2 because of inability to record accurately the diastolic blood pressures.

Target population and demographic data

All target population objectives were met. Of the 85 included subjects 44 (51.8%) were male. The mean age was 43.1 ± 15.6 years (range of 18 - 83 years). There were 10 subjects (11.8%) with arm circumference exceeding 35 cm, and 9 subjects (10.6%) subjects with arm circumference less than 25 cm.

Included blood pressure measurements

Included data totalled 391 sets of simultaneously recorded measurements. In 41 (10.5%) systolic BP exceeded 180 mmHg, and in 53 (13.6%) systolic was less than 100 mmHg. In 43 (11.0%) diastolic BP exceeded 100 mmHg, and in 54 (13.8%) diastolic was less than 60 mmHg.

Excluded blood pressure measurements

Thirty-four (8.0%) systolic and diastolic BP measurements were excluded. Four (0.9%) were due to a BPM-100_{Beta} technical error; the BPM-100_{Beta} either recorded an error or did not display the reading. Four were excluded because one observer forgot the number before recording the mercury sphygmomanometer reading. Twenty-one were excluded because one of the observers did not feel that a satisfactory auscultation could be obtained (15 systolic, 6 diastolic). Five (1.3%) were excluded because the observers did not agree within 10 mmHg for the systolic or diastolic BP.

Sphygmomanometer readings

Mean difference between the observers (observer 1 – observer 2) for the 391 systolic measurements was –0.64 ± 1.94 mmHg. The majority of the differences, 97.7%, were ≤ 5 mmHg. All were ≤ 10 mmHg as the protocol prescribed exclusion of differences exceeding 10 mmHg. Mean difference between the 2 observers for diastolic BP was –1.08 ± 2.46 mmHg. Most (95.7%) were ≤ 5 mmHg and all were ≤ 10 mmHg.

Range and distribution of reference standard measurements

The mean systolic BP for the 391 systolic reference standard measurements (average of the two observers) was 128.7 ± 30.7 mmHg (range 81.5 to 223.5 mmHg). The mean reference standard diastolic BP was 77.4 ± 16.7 mmHg (range 45.5 to 120.5 mmHg). Mean heart rate using the Nonin finger pulse oximeter was 70.2 ± 12.3 beats per minute (range 42 to 104 beats per minute).

Accuracy of BPM-100_{Beta} as compared with the reference standard measurements

The mean difference between the BPM-100_{Beta} and the reference standard systolic and diastolic BP (BPM-100_{Beta} - reference) is well within the AAMI standard [4] and is shown in Table 1. Table 2 shows the proportion of systolic and diastolic differences within 5, 10, and 15 mmHg and how this conforms to the BHS standard [5].

The BPM-100 device is designed to determine the average of up to five blood pressure readings in individual subjects. We therefore calculated the subject mean BPM-100_{Beta} minus the subject mean reference standard systolic and diastolic BP measurements as a measure of accuracy in the practical

clinical setting. This gave a slightly different mean difference and a lower standard deviation for the 85 subjects as shown in Table 1. It was also associated with a slight improvement in the proportion of systolic and diastolic differences within 5, 10 and 15 mmHg (Table 2).

In Fig 1 the Bland Altman display of measurements for systolic BP shows the difference of each BPM-100_{Beta} and reference standard systolic BP plotted against the average of the BPM-100_{Beta} and the reference standard systolic BP. This figure demonstrates that the BPM-100_{Beta} tends to underestimate the systolic BP (negative values) for systolic measurements >150 mmHg. In Fig 2 the Bland Altman display of measurements for diastolic blood pressure shows the difference of each reference and BPM diastolic blood pressure plotted against the average of the BPM-100_{Beta} and reference standard diastolic blood pressure. In this case the differences are clustered around a difference of 0 over the whole range of pressures.

The mean difference of the BPM-100_{Beta} and the reference heart rate was 0.14 ± 1.86 beats per minute.

DISCUSSION

The most common reason for patient office visits to a physician in Canada and the United States is hypertension.[6] For diagnosis and treatment to be consistent, it is important that blood pressure measurements in the physician's office be as standardized and accurate as possible. An accurate, convenient and affordable automatic blood pressure measuring device would improve consistency and accuracy of measurements in different practice settings.

The Association for the Advancement of Medical Instrumentation (AAMI), is the standard setting body for blood pressure measurement devices. Its guidelines require that the mean difference of blood pressure measurements between a new device and the mercury standard must be within ± 5 mmHg with a standard deviation of <8 mmHg. It can be seen that in this study the BPM-100_{Beta} monitor easily met this standard. It can also be seen that the mean difference between the BPM-100_{Beta} and the reference measurements was similar to that for the inter-observer measurements. The standard deviation of the difference between the BPM-100_{Beta} measurements and the reference standard exceeded that of the inter-observer measurements, but was well within the AAMI requirement of a standard deviation of less than 8 mmHg. The low variability of the inter-observer measurements in this study is not an accurate reflection of this measure, as the protocol dictated that inter-observer differences exceeding 10 mmHg be excluded (N = 5 in this study).

The major potential limitation of the BPM-100_{Beta} detected in this study is the underestimation of systolic measurements > 150 mmHg as demonstrated by the Bland Altman display (Fig 1). It is known that the oscillometric technique, when compared with standard auscultatory methods tends to both underestimate systolic BP and to yield high standard deviations for higher systolic pressures.[7] As a result of this potential limitation the manufacturer undertook a further developmental study using the stored raw electronic data and the auscultated blood pressure data obtained during this study. The methods and result of this subsequent study are presented in the following companion paper [8].

Another potential limitation is the relatively high variability of the differences between the BPM device and the reference standard individual measurements. However, the reference standard is an indirect estimate of the true intra-arterial pressure and studies comparing auscultation and intra-arterial pressures are associated with a higher degree of variability than that seen here.[9-12] In other words when a large difference between 2 measurements is seen one cannot be certain which of the measurements is the best estimate of intra-arterial blood pressure.

The BPM-100_{Beta} uses the oscillometric method, which is the one used by most ambulatory and home blood pressure measuring devices. The BPM-100_{Beta} is designed to measure 6 blood pressures and discard the first. The first is discarded, as it is normally done with the physician or nurse present in the room with the patient. The device is designed to measure and save the last 5 measurements plus the average of these 5 measurements automatically while the physician/nurse is involved in other activities. The mean BP as well as the individual measurements can be recorded in the patient's chart.

The mean BP is the best estimate of the resting pressure of the patient for that visit. There is therefore some value in calculating the differences between the mean values for all individual subjects as measured by the BPM-100_{Beta} and by auscultation. This data probably better reflects the clinical reliability of this monitor in a practice setting. As can be seen in Table 1 and 2 this analysis is associated with either no change or an improvement in the performance of the BPM-100_{Beta} monitor.

The importance of measuring blood pressure properly cannot be underestimated.[11-13] Diagnosing hypertension in patients who are truly normotensive and vice versa has potential far reaching consequences for the patient involved. Blood pressure measurements therefore should not only be accurate and consistent but reproducible [13,14]. Our study suggests this is possible using the BPM-100_{Beta} monitor.

Langlois [3], describes common errors in measuring and recording blood pressure measurements. Using a well validated automatic blood pressure monitor could rectify many of these errors. 'No waiting times' can be prevented by setting the time between measurements from 1 to 5 minutes (cycle time), depending

on how long the patient has been seated at rest. Since the first measurement is not used in calculating the mean blood pressure, it gives time for patients to relax and get accustomed to the method. 'Distracting noise or talking' is not an issue because patients can be left alone in a quiet room. 'Rounding off numbers' is avoided because the BPM-100_{Beta} monitor records measurements to the nearest 1 mmHg without any bias. 'Fast deflation' is not a factor because deflation is uniform and preset at 4 mmHg/second.

Asmar and Zanchetti state "as we approach the end of the 20^{th} century, we are assisting the birth of a new era in blood pressure measurement."[15] By utilizing a good automatic BP monitor, one can eliminate the "human error" associated with both mercury and aneroid devices, while performing multiple, accurate BP readings which are in accordance with current clinical guidelines.

In conclusion, this study demonstrates that the BPM-100_{Beta} oscillometric device provides an accurate measure of blood pressure that closely approximates that achieved by the indirect auscultatory method using a mercury sphygmomanometer. This validation study satisfies the AAMI and BHS standards for new devices. We believe that the BPM-100_{Beta} offers practical potential advantages to improve the accuracy, reproducibility and efficiency of blood pressure measurement by physicians or nurses.

Table 1: The performance of the BPM-100_{Beta} compared to the AAMI Standard.[4]

		SYSTOLIC		DIASTOLIC	
	N	mean difference (mmHg)	standard deviation (mmHg)	mean difference (mmHg)	standard deviation (mmHg)
AAMI SP10 - 1992		± 5.0	< 8.0	± 5.0	< 8.0
BPM-100_{Beta} minus Reference	391	- 0.62	6.96	- 1.48	4.80
Subject mean BPM-100_{Beta} minus Ref	85	- 0.63	6.23	-1.41	4.22

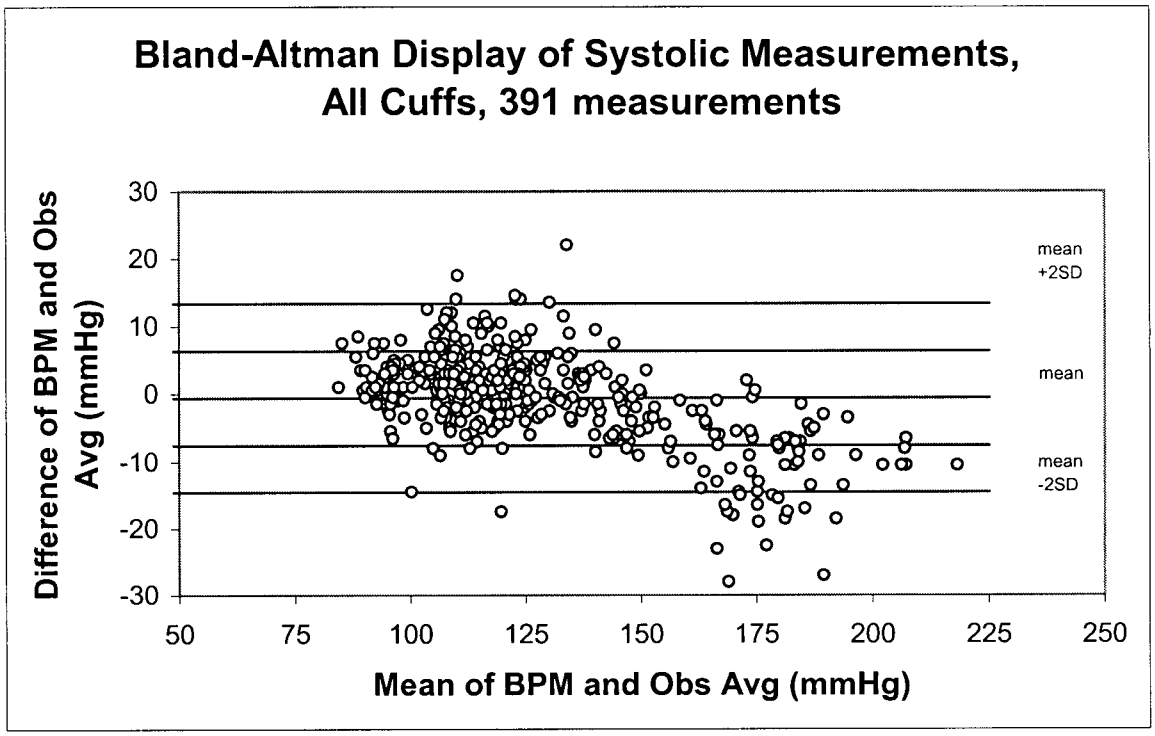
AAMI - Association for the Advancement of Medical Instrumentation.

Table 2: Performance of the BPM-100_{Beta} compared to BHS Grade 'A' standard.[5]

	N	≤ 5 mmHg	≤ 10 mmHg	≤ 15 mmHg
Grade " A " BHS standard		≥ 60 %	≥ 85 %	≥ 95 %
BPM-100_{Beta} minus Reference systolic BP	391	61.6	87.0	95.7
BPM-100_{Beta} minus Reference diastolic BP	391	78.5	92.6	98.5
Subject mean BPM-100_{Beta} minus Ref syst BP	85	61.2	91.8	95.0
Subject mean BPM-100_{Beta} minus Ref diast BP	85	82.4	95.3	98.0

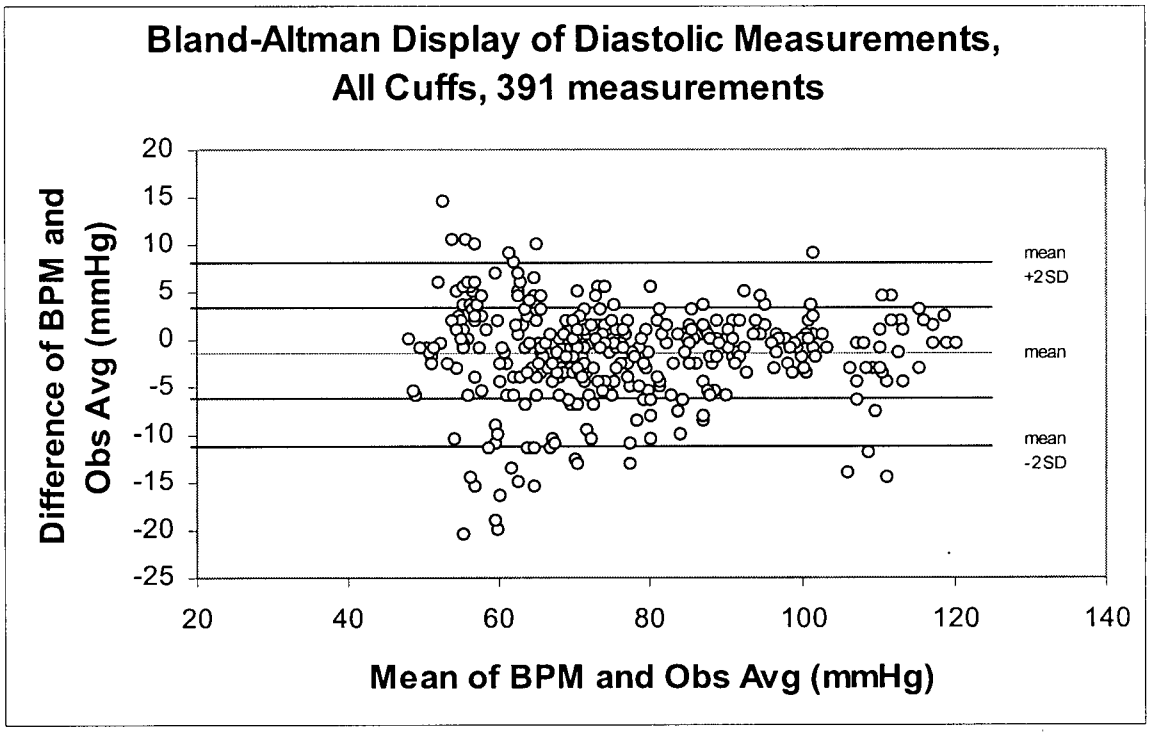
BHS – British Hypertension Society

Fig 1



Bland-Altman display of all systolic measurements for all cuffs (n = 391).
BPM, BPM-100_{Beta} monitor; Obs Avg, observer average.

Fig 2



Bland-Altman display of all diastolic measurements for all cuffs (n = 391).
BPM, BPM-100_{Beta} monitor; Obs Avg, observer average.

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CHAPTER III

Validation of a New Algorithm for the BPM-100 Electronic Oscillometric Office Blood Pressure Monitor

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Source of Funding: VSM – MedTech

Short Title: BPM-100 algorithm validation.

ABSTRACT

Background:

To test the accuracy of a new algorithm for the BPM-100, an automated oscillometric blood pressure (BP) monitor, using stored data from an independently conducted validation trial comparing the BPM-100_{Beta} with a mercury sphygmomanometer.

Design:

Raw pulse wave and cuff pressure data were stored electronically using embedded software in the BPM-$100_{Beta,}$ during the validation trial. The 391 sets of measurements were separated objectively into two subsets. A subset of 136 measurements was used to develop a new algorithm to enhance the accuracy of the device when reading higher systolic pressures. The larger subset of 255 measurements (3 readings for 85 subjects) was used as test data to validate the accuracy of the new algorithm.

Methods:

Differences between the new algorithm BPM-100 and the reference (mean of two observers) were determined and expressed as the mean difference ± SD, plus the % of measurements within 5 mmHg, 10 mmHg, and 15 mmHg.

Results:

The mean difference between the BPM-100 and reference systolic BP was –0.16 ± 5.13 mmHg, with 73.7% ≤ 5 mmHg, 94.9% ≤ 10 mmHg and 98.8% ≤ 15 mmHg. The mean difference between the BPM-100 and reference diastolic BP was –1.41 ± 4.67 mmHg, with 78.4% ≤ 5 mmHg, 92.5% ≤ 10 mmHg, and 99.2% ≤ 15 mmHg. These data improve upon that of the BPM-100_{Beta} and pass the AAMI standard, and "A" grade BHS protocol.

Conclusion:

This study illustrates a new method for developing and testing a change in an algorithm for an oscillometric BP monitor utilizing collected and stored electronic data and demonstrates that the new algorithm meets the AAMI standard and BHS protocol.

Key Words: blood pressure, measurement, monitor, algorithm, oscillometric

INTRODUCTION

The use of electronic blood pressure measuring instruments in diagnosing hypertension and monitoring blood pressure (BP) has increased dramatically over the past several years. There have been many articles written supporting the use of such devices, especially in the home setting (self) [1] and for ambulatory use (24 hour) [2]. Most of these devices use the oscillometric technique, which measures the mean arterial BP directly from cuff pressure, then calculates the systolic and diastolic BP's according to an algorithm that is unique to each device or manufacturer. These instruments can be validated by testing them against auscultatory measurement using a mercury sphygmomanometer, according to established protocols set by either the Association for the Advancement of Medical Instrumentation (AAMI) [3] or the British Hypertension Society (BHS) [4]. It is known that most oscillometric monitors, though accurate, tend to underestimate and give a higher standard of deviation for higher systolic pressures when compared with standard auscultatory methods [5].

The BPM-100 is an oscillometric blood pressure measuring instrument that has been developed and manufactured by VSM MedTech Ltd. of Vancouver, Canada. This device was designed specifically for the primary care setting, to aid the clinician in diagnosing hypertension and in monitoring the patient's course. It was tested in an independently conducted validation study according to the AAMI standard; the details of this study are reported separately in the previous article [6]. The device performed well, passing both the AAMI standard and BHS protocol, but tended to underestimate the higher systolic blood pressures as detected with the Bland-Altman plot. In this article, we report a method for the development and testing of a modification to the algorithm for estimating systolic BP using stored electronic data.

METHODS

Subjects were recruited and tested at the Blood Pressure Clinic of the University of British Columbia according to the method reported in the companion paper and included ethical approval, explicit inclusion and exclusion criteria, target population objectives, study design, data analysis and results [6].

In the original BPM-100_{Beta} clinical trial [6], 85 patients were tested and accepted for statistical analysis. Each patient was measured a total of six times. The first reading was used for subject screening purposes, and not used further in the analysis. The remaining five readings were further screened for exclusion according to pre-determined criteria, resulting in a minimum of three and maximum of five readings for each subject. The total number of readings included for statistical analysis was 391, 136 readings more than the minimum AAMI requirement of 255 readings (85 subjects times 3 readings for each subject).

During the original study, the oscillometric algorithm of the BPM-100_{Beta} collected the cuff pressure and pulse information from the blood pressure cuff during deflation and calculated the systolic and diastolic blood pressures as well as the pulse rate. The embedded software in the BPM-100_{Beta} performed the data collection and BP calculations. After each measurement, the cuff pressure and pulse information was exported to another computer to archive the raw data and allow for analysis of the algorithm.

The original BPM-100 clinical trial data set of 391 measurements was objectively separated into two data subsets as described below. The first subset included a total of 255 measurements, which included 3 measurements from each of the 85 subjects, and represented the minimum requirements for AAMI criteria. The second subset of 136 measurements was available to assist in the development of a modification to the BPM-100_{Beta} algorithm. Once the new algorithm was developed the first subset of 255 measurements was used to objectively evaluate the performance of the algorithm on "new" data.

To avoid bias towards early, middle or late data points in the sequence of up to five measurements collected from each subject in the original clinical data [6], the first subset was selected using a rotating

selection pointer. The procedure involved selecting the first three available measurements from the first subject and then the second, third, and fourth measurement from the second subject and so on. Some subjects had only three or four measurements, as some were excluded in the original clinical trial data collection, but the pointer skipped to the next available measurement until each subject had exactly 3 measurements. When the end of the measurements was reached for any subject without selecting 3 measurements, the selection pointer rotated back to the start of the measurements for that subject.

The smaller subset was used to develop a new algorithm that gave a better estimate for higher systolic measurements. This did not require changing the algorithm for the diastolic BP. After the algorithm modification was successfully developed using the smaller data subset, it was then ready for validation. The external algorithm was formally tested on the first subset of 255 measurements from the original clinical trial population (85 subjects times 3 measurements per subject). The performance results of the new algorithm were analyzed according to the AAMI standard for all population, observer, and accuracy requirements.

The new algorithm was then incorporated into the embedded software to create the BPM-100.

An NIBP simulator (BP Pump, Bio-Tek Instruments, Inc., Winooski, Vermont) was used to provide oscillometric input data to the BPM-100 device. The BPM-100 displayed the results and exported the cuff pressure and oscillometric data to the PC. The new algorithm developed and tested in the PC now used the new data from the simulator via the BPM-100, and calculated and displayed the results. A regression test compared the 2 sets of data over a wide range of parameters (BP 80-220/50-130 mmHg and heart rate 50 to 130 bpm); acceptance criteria were that the difference between each reading must be within +/- 1 mmHg. This test ensured that the algorithms implemented in the 2 different software platforms operated identically and validated the implementation of the algorithm in the embedded software.

RESULTS

Enrolled subjects

See companion publication for details of enrolled, included and excluded subjects [6].

All target population objectives and requirements of the AAMI protocol were met in this study as they included the same 85 subjects included in the companion study [6].

Included blood pressure measurements

The total number of included measurements amounted to 255. Twenty-seven blood pressure measurements (10.6%) had a systolic of greater than 180 mmHg, and 37 measurements (14.5%) had a systolic of less than 100 mmHg. The remaining 191 systolic measurements (74.9%) were between these extremes. Twenty-five blood pressure measurements (9.8%) had a diastolic of greater than 100 mmHg, and 39 measurements (15.3%) had a diastolic of less than 60 mmHg. The remaining 191 diastolic measurements (74.9 %) were between these extremes.

Excluded blood pressure measurements

For details of the 34 excluded blood pressure measurements see companion study [6].

In addition, a second subset of 136 measurements used to develop the new algorithm was excluded as described in the methods section.

Reference standard measurements (Inter-observer)

Overall mean difference between the observers (observer 1 – observer 2) for the 255 systolic blood pressure measurements was –0.65 ± 1.99 mmHg, (range –10 to +9 mmHg). Most of the systolic measurement differences, 98.0%, were within 5 mmHg. All were within 10 mmHg as any outside this range were excluded as one of the exclusion criteria. The overall mean difference between the 2 observers for diastolic blood pressure was –1.05 ± 2.46 mmHg, (range, –8 mmHg to +7mmHg). Most (95.3%) were within 5 mmHg and all were within 10 mmHg as described above.

Range and distribution of reference measurements

The overall mean systolic blood pressure for the 255 systolic blood pressure measurements recorded (average of the two observers) was 128.5 ± 30.9 mmHg (range 81.5 to 223.5 mmHg). The overall mean diastolic blood pressure was 77.3 ± 16.6 mmHg (range 48 to 119.5 mmHg). The mean heart rate using the Nonin finger pulse oximeter (Onyx, Nonin Medical Inc., Plymouth, Minnesota) was 70.1 ± 12.4 beats per minute (range 42 to 104 beats per minute).

Accuracy of BPM-100 as compared to the reference standard measurements.

The overall mean difference between the reference standard systolic and diastolic blood pressure and the BPM-100 (reference – BPM-100) is well within the AAMI standard and is shown in Table 1 [3]. Table 2 shows the proportion of systolic and diastolic differences within 5, 10, and 15 mmHg and how this conforms to the BHS protocol. [4]

The BPM-100 device is designed to determine the average of up to five blood pressure readings in individual subjects. We therefore compared the mean of the 3 reference standard systolic blood pressure measurements with the mean of the 3 BPM-100 measurements for individual subjects so as to observe the accuracy in the practical clinical setting. This gave the same mean difference and a lower standard deviation as can be seen in Table 1. It also led to an improvement in the proportion of systolic and diastolic differences within 5, 10 and 15 mmHg according to the BHS protocol (Table 2).

In Fig 1 the Bland-Altman display [7] of individual measurements for systolic blood pressure (N = 255) shows that the differences of the reference standard and BPM-100 blood pressures are clustered around 0 over the whole range of systolic readings. In Fig 2 the Bland-Altman display of individual measurements for diastolic blood pressure (N = 255) shows that the differences of the reference standard and BPM-100 blood pressures gives the same picture as for the 391 measurements in the previous paper. [6]

The mean difference between the reference and measured heart rate (measured minus reference) was 0.16 ± 2.02 bpm, with a range of –16 to +6 bpm.

DISCUSSION

The BPM-100 electronic office blood pressure instrument with the new algorithm meets the protocol and standard of the Association for the Advancement of Medical Instrumentation for accuracy when compared to traditional mercury BP measurement performed by trained nurses using a research-grade precision mercury sphygmomanometer. As well, it earned an "A" grade for both systolic and diastolic readings, according to the British Hypertension Society protocol. It improves on the accuracy of estimation of higher systolic blood pressures as compared to the previous version ($BPM\text{-}100_{Beta}$) [6]; the BPM-100 is the only version that is available for sale in North America.

The methods used in this study demonstrate the unique characteristics of using the oscillometric method for detecting blood pressure. The readings were obtained and recorded using standard validation methods. However, because the oscillometric technique utilizes electronic analysis of the pulse waves of each blood pressure measurement, we were able to utilize the previously recorded test readings to develop a new algorithm to improve upon the estimate of systolic blood pressure and subsequently to validate the new algorithm using recognized protocols and standards.

The use of oscillometric devices for measuring blood pressure is rapidly increasing, and O'Brien and others have written about the need for better methods to test and validate these devices, [8] [9]. They are aware that many manufacturers change the algorithm in their devices and do not always report or re-validate the devices because the cost of re-testing is prohibitive. Presumably, as in the case of the BPM-100, the changes in the algorithm are to improve the accuracy of the device. The method we describe is one way in which companies can validate and report these changes, while saving the time and money associated with repeating the entire validation process. The original clinical data is collected in the prescribed manner, and is recorded and stored both manually and electronically. This data is then available to "re-test" any changes in the algorithms used to estimate the systolic and diastolic blood pressures.

We believe that the method presented could represent a precedent for improving the efficiency of validation of changes to the embedded software of oscillometric blood pressure measuring devices. In

this particular case the method created an algorithm that improved the accuracy of the BPM-100 oscillometric device for higher systolic measurements. When this algorithm was tested, it readily satisfied the AAMI standard and BHS "A" protocol.

Table 1: The performance of the BPM-100 compared to the AAMI Standard.[3]

		SYSTOLIC		DIASTOLIC	
	N	mean difference (mmHg)	standard deviation (mmHg)	mean difference (mmHg)	standard deviation (mmHg)
AAMI SP10 - 1992		$\leq \pm 5.0$	< 8.0	$\leq \pm 5.0$	< 8.0
BPM-100 minus Reference*	255	- 0.16	5.13	- 1.41	4.67
Subject mean (BPM-100 minus Ref.)	85	- 0.16	4.31	-1.41	4.21

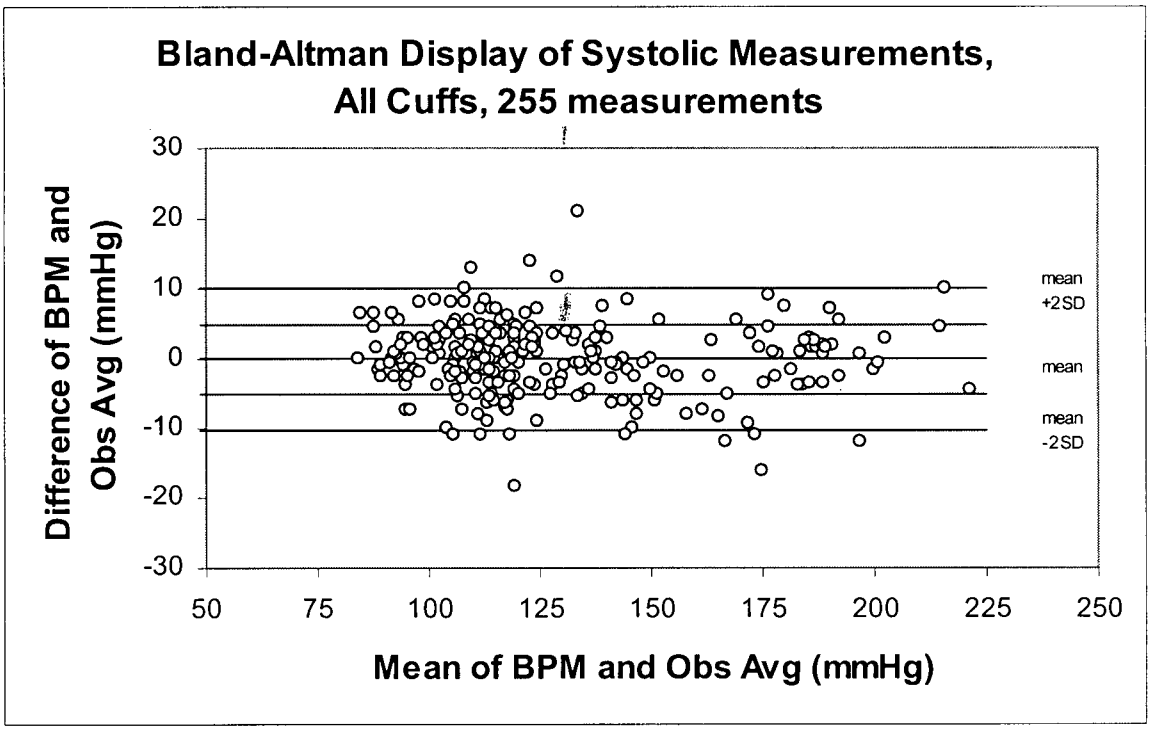
AAMI - Association for the Advancement of Medical Instrumentation.
* includes all individual measurements as stipulated in the AAMI protocol.

Table 2: Performance of the BPM-100 compared to BHS Grade 'A' protocol.[4]

	N	≤ 5 mmHg	≤ 10 mmHg	≤ 15 mmHg
Grade " A " BHS protocol		≥ 60 %	≥ 85 %	≥ 95 %
BPM-100 minus Reference systolic BP*	255	73.7	94.9	98.8
BPM-100 minus Reference diastolic BP*	255	78.4	92.5	99.2
Subject mean (BPM-100 minus Ref syst BP)	85	77.6	98.8	100.0
Subject mean (BPM-100 minus Ref diast BP)	85	80.0	95.3	100.0

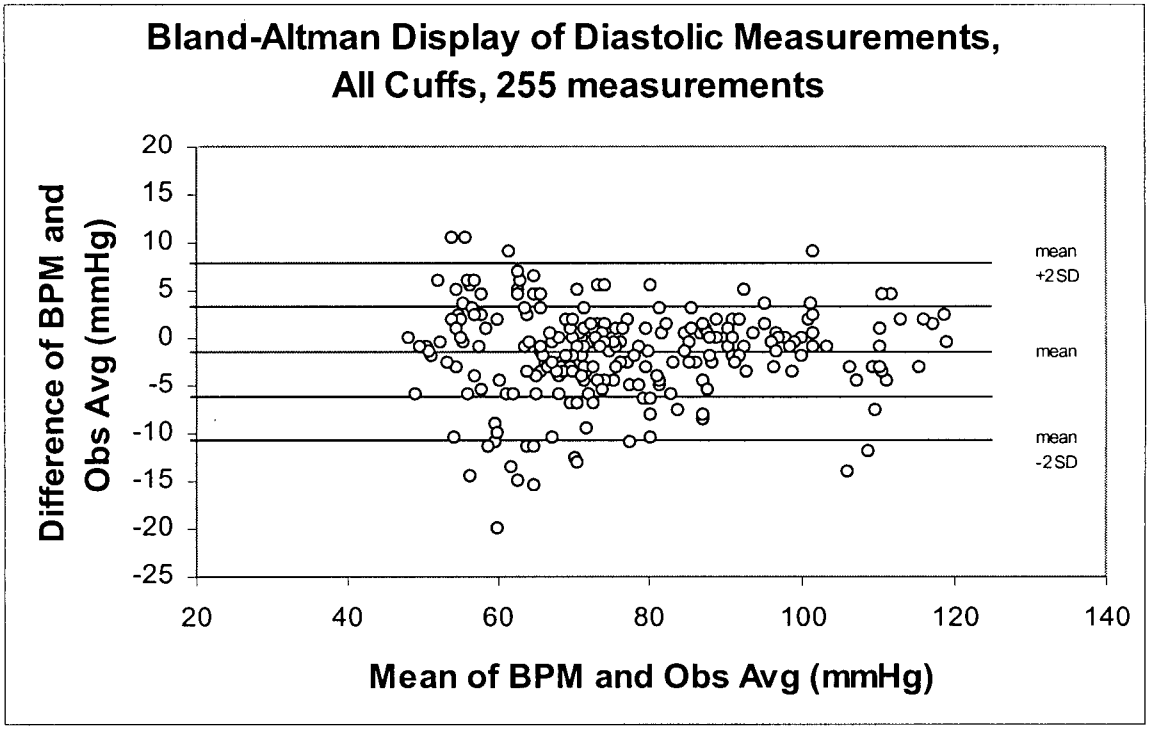
BHS - British Hypertension Society.
* includes all individual measurements as stipulated in the BHS protocol.

Fig 1



Bland-Altman display of systolic measurements, all cuffs, 255 measurements.
BPM, BPM-100 electronic oscillometric monitor; Obs Avg, observer average.

Fig 2



Bland-Altman display of diastolic measurements, all cuffs, 255 measurements.
BPM, BPM-100 electronic oscillometric monitor; Obs Avg, observer average.

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CHAPTER IV

COMPARISON OF THE AUTOMATED NON-INVASIVE OSCILLOMETRIC BLOOD PRESSURE MONITOR (BpTRU™) WITH THE AUSCULTATORY MERCURY SPHYGMOMANOMETER IN THE PAEDIATRIC POPULATION

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Short Title: Validation of the BpTRU™ in Paediatrics.

ABSTRACT

Background

To compare directly the accuracy of the BPM-100 monitor (an automated oscillometric blood pressure device) with standard auscultatory mercury sphygmomanometry in a paediatric population.

Design

The BPM-100 was connected in parallel with a standard mercury sphygmomanometer. Two observers measured the blood pressures simultaneously with the BPM-100. The observers and the BPM-100 were all triple-blinded from each other.

Methods

For each of the demographic data - subject age, sex and arm sizes, - the mean, standard deviation (SD) and range was calculated. The difference between the mean BPM-100 and the standard reference measurements (observer average) was calculated with SD and ranges. The percentage of measurements within 5, 10 and 15 mmHg agreement was expressed.

Results

From the 36 subjects recruited aged 3-18 years, 162 pairs of sitting blood pressures were included. The difference between the mean BPM-100 readings and the reference standard measurements (as determined by the observers) was 1.45 ± 5.67 mmHg for systolic blood pressures, and -3.24 ± 7.39 mmHg for diastolic pressure and 0.20 ± 2.47 bpm for heart rate.

Conclusion

The BPM-100 is as accurate in measuring blood pressure in children as it is in the adult population. It meets all requirements of the Association of Advancement of Medical Instrumentation and achieved a grade 'B' in the modified BHS protocol.

Introduction

Until the publication of the first Task Force Report on blood pressure control in children just over 25 years ago, the measurement of blood pressure was infrequently performed [1]. Currently the American Heart Association recommends all children have annual blood pressures recorded. Although the prevalence of hypertension in the paediatric population is very low, accurate diagnosis and management of it can have far-reaching consequences in the prevention of end-organ damage.

Since the earliest accepted description of an indirect method of measuring blood pressures described by Riva Rocci in 1896, it has become increasingly apparent that this technique is highly subjective. If not properly practised, measuring blood pressure with a mercury sphygmomanometer and stethoscope can be highly inaccurate with grave consequences for patients. In addition it is time-consuming when done properly and thus does not fit well into a busy physician's schedule.

With mercury being banned by several European countries and many US cities, due to the concern of mercury poisoning, potentially causing learning disabilities, impairing kidney and immune function, and in extreme cases the loss of sight and hearing. Accurate automatic oscillometric devices are increasingly desirable. This may be the end of the era of mercury sphygmomanometer, and herald the beginning of new standard of blood pressure measurement.

The BPM-100 was previously validated in a study with 85 adult subjects (aged 18 years and older). It met the AAMI requirements and achieved an 'A' grade according to the BHS protocol [2]. It subsequently improved its algorithm to correct for underestimation of higher systolic blood pressures. [3].

The purpose of this study is to determine the accuracy and reproducibility of the automated non-invasive oscillometric blood pressure monitor, BpTRU™ (model BPM-100) as compared to the gold standard mercury sphygmomanometer in the paediatric population (ages 3 to 18 years). To achieve this, the study was performed in accordance with the standard guidelines and protocols AAMI SP10-1992 provided by the Association for the Advancement of Medical Instrumentation (AAMI) as well as the recently released

draft AAMI / CDV-1 SP-10 Manual, Electronic or Automated Sphygmomanometers; the regulating bodies for validating these types of monitors.

Methods

Ethical Approval

Ethical approval of the study, the consent and assent forms was obtained from a sovereign body, the Independent Review Consulting group from California prior to initiation of any study procedures.

Subject enrolment

Subjects were recruited from notices in Primary Care practices and the B.C.'s Children's Hospital, University of British Columbia, which included hypertension and renal clinics to meet some of the hypertensive criteria listed below. Recruitment into the study was without bias. Screening was established in order to meet the target requirements for the study of 34 subjects. At the end of the study subjects were enrolled, in order to meet the deficiencies in the target population requirements.

Inclusion criteria

Either a parent or guardian, who signed the consent form, accompanied all subjects. Subjects who were able, were given the assent form and instructed to read and sign prior to any study procedures being performed. Subjects were between the ages of 3 years to 18 years, and were all hemodynamically stable. To be included in the study, screening measurement criteria to evaluate observer agreement for the subject had to be met.

Exclusion criteria

Pre-measurement screening criteria allowed for subjects with significant arrhythmias or any other existing condition, who the investigators felt would not allow for safe and accurate blood pressure measurements, to be excluded.

As with the study with adults there were five post-measurement but pre-specified exclusion criteria for both subjects and individual measurements [2]:

1. subjects in whom the first (screening) measurements had an inter-observer agreement for either systolic or diastolic blood pressures greater than 10 mmHg (this precludes all other post-measurement criteria down the list);

2. subjects who had less than three systolic and diastolic pairs of readings (this precludes all other post-measurement criteria down the list);

3. any measurements in which the inter-observer agreement for either systolic or diastolic blood pressures was greater than 10 mmHg

4. subjects who had sufficiently weak pulses and consequently weak Korotkoff sounds such that the observers felt that satisfactory auscultation was not possible;

5. measurements by the BPM-100 that did not record for technical reasons.

Target population objectives

1. An equal number of male and female subjects.
2. A range of ages (all aged 3 to 18 years of age)
   - at least 6 subjects aged 3 to 5 years
   - at least 6 subjects aged 6 to 8 years
   - at least 4 subjects aged 9 to 11 years
   - at least 4 subjects aged 12 to 14 years
   - at least 4 subjects aged 15 to 18 years

   with at least 20 of these subjects being aged 3 to 12 years.
3. At least 6 subjects previously identified as hypertensive by their Primary Care Physician.
4. At least 7 subjects with arm sizes (measured at mid-biceps with the infant cuff) between 13 and 18cm circumference - (infant sized blood pressure cuff).

Study design

Subjects were recruited from June to August 2001. All subjects below 16 years of age had accompanying parents or guardians and were explained study procedures. Consent forms (signed by parents and children 16 to 18 years of age) and where applicable assent forms (signed by subjects) were obtained prior to any study procedures. All were given copies of these. They were then entered into the subject log and assigned a subject code. Demographic data including age, sex, height, arm circumference

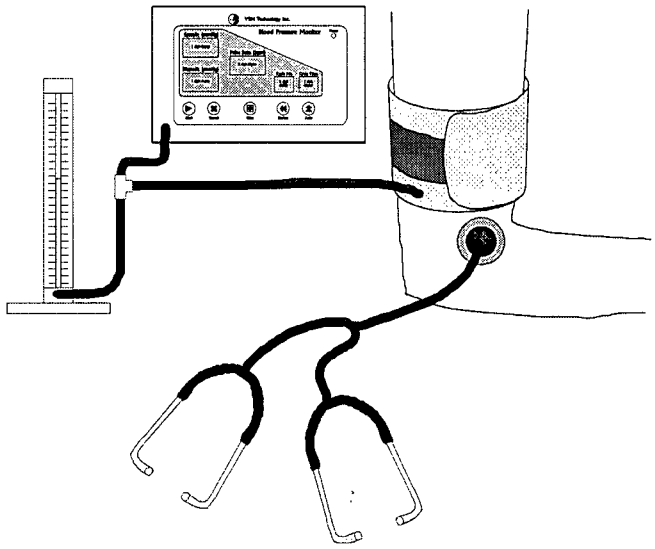
(measured at mid-biceps) and pre-existing health conditions and current medications were all recorded by GSM (investigator).

The subjects were then seated in a quiet room, with the back well supported and feet flat on the ground. For the smaller subjects an additional footstool was provided to aid the achievement of this posture. Also, subjects in the younger age ranges were allowed to be seated in the laps of their parents or guardian, but were still standardised by the above criteria. An appropriately sized cuff (based on the arm size markings on the cuffs provided) was applied to the subject's left arm, which was placed on a comfortable surface at heart level.

As in the original study in adults, the BPM-100 was connected in parallel with a Trimline mercury sphygmomanometer by means of a T-tube to the cuff, and was used to provide the auscultatory reference readings [2]. A Nonin heart rate monitor was connected to the subject's right hand or other body part. The Trimline mercury sphygmomanometer (Trimline Medical Products, Branchburg, New Jersey, USA) has range of 0-300 mmHg with gradations of 1mmHg, accuracy ±0.5 mmHg. The Nonin finger pulse oximeter (Onyx, Nonin Medical Inc., Plymouth, Minnesota, USA) has a range of 18-300 beats / min (bpm) with an accuracy of ± 3%. The BPM-100 was also connected to a Toshiba data collection laptop computer, to store all cuff pressure and pulse information from the blood pressure cuff.

One of the observers palpated the brachial pulse of the left arm and placed the diaphragm of a dual-headed teaching stethoscope over this point. The observers were seated opposite the subject on adjustable seating so that they were able to read the mercury sphygmomanometer at eye-level without introducing parallax errors. A curtain separated the observers but did not interfere with the ability to read the sphygmomanometer. The observers were experienced paediatric nurses whose blood pressure reading skills were tested prior to the initiation of the study by the means of validating readings with the one of the investigators (GSM), figure 1.

Fig 1: Set-up of the validation process



The BPM-100 is an automated oscillometric device that measures the mean arterial pressure (MAP) directly from the cuff pressure; and then uses this MAP to calculate the systolic and diastolic pressures. It has a linear deflation rate of 4mmHg / second and can be set at cycle interval times of 1 to 5 minutes. It records six readings, at the end of its reading period, it also generates the average of the systolic and diastolic readings 2 to 6 (maximum of 5). The first reading is not used in determining the overall average and is used here to establish observer agreement (screening measurement) and determine if satisfactory auscultation could be obtained.

GSM checked the data collection computer and entered a subject code to record all cuff pressure and pulse information. The BPM-100, blinded to the observers, was started by GSM when the dual headed stethoscope was placed over the brachial artery by one of the observers. The observers auscultated for systolic blood pressure (Korotkoff sounds phase I - the first sound heard) and then diastolic pressure (Korotkoff sound phase V - the disappearance of all sounds).

At the end of each measurement the observers independently recorded the systolic and diastolic blood pressures. The BPM-100 blood pressure measurements, blinded from the observers, and the heart rate from the Nonin finger pulse oximeter was recorded by GSM when the BPM-100 had deflated to

approximately 90mmHg. All measurements were independently recorded onto separate data sheets, and triple-blinded between the observers and the investigator.

In this manner a maximum of six measurements were recorded. The first blood pressure measurement was used to determine inter-observer agreement and to determine that satisfactory auscultation was possible; it was not used in any subsequent analysis. A minimum of 3 subsequent satisfactory readings were required to be included the study. After all measurements were completed the cuff was removed, the arm checked, and the subjects were allowed to leave.

Data Analysis

For all included subjects age, sex and arm size was recorded. The mean, standard deviation and ranges were calculated for each of these. The first or screening blood pressures was used to determine the primary determinant in our hierarchy of inclusion and exclusion criteria, and was not included in any subsequent breakdown. All other data was put through our remaining hierarchy of inclusion and exclusion criteria, and the resulting information was used in the analysis.

As in our study in adults, means were calculated from the included systolic and diastolic measurements recorded by the observers, and was known as the reference systolic or diastolic blood pressure [2]. For each measurement the observer agreement, difference between the observers (observer 1 – observer 2), the mean difference ± standard deviation was calculated. The percentage less than 5 mmHg and 10 mmHg was also expressed.

The percentages of systolic blood pressures as measured by the observers was expressed for those <100 mmHg, those >100 mmHg but <180 mmHg and those >180 mmHg. These percentages were also expressed for diastolic measurements, <60 mmHg, >60 mmHg but <100 mmHg and those >100 mmHg. The mean difference ± standard deviation (difference between the BPM-100 and the observer reference) was also determined for both the systolic and diastolic measurements. The agreement between the two techniques was also expressed as the percentage agreement within 5 mmHg, 10 mmHg and 15 mmHg for each of the systolic and diastolic blood pressure measurements. The mean difference ± standard

deviation was also determined for the difference between the Nonin finger pulse oximeter and the observer reference values.

We also calculated the individual subject means ± standard deviation (difference between the BPM-100 and the observer reference) for both systolic and diastolic blood pressure measurements and expressed the agreement as percentages within 5, 10 and 15 mmHg as above. This gave us a better estimate of individual subject measurements as opposed to total measurements in the group.

For all excluded subjects the age, sex and arm size was also recorded. The reason for exclusion was also listed and all subjects were ultimately accounted for.

The magnitude of difference in blood pressure measurements by the BPM-100 and the auscultatory reference values by the observers, was plotted against, the means of blood pressure measurements by the two methods for each of the systolic and diastolic measurements. This is an accepted method as suggested by Bland and Altman [4].

Results

Enrolled subjects

There were 46 subjects enrolled. Of these, 36 (78.3%) subjects were included and 10 (21.7%) subjects were excluded. Of the included subjects average age was 9.4 years with a standard deviation of 4.2. Enrolled subjects included those with hypertension, renal artery stenosis, kidney failure and congenital co-arctation of the heart. Some of these subjects were taking many different medications including anti-hypertensives, steroids and immunosuppressants.

Excluded subjects

Ten (21.7%) subjects were excluded; all were post-measurement exclusions. The average age was 6.9 with a standard deviation of 4.2 years. The age range of this group was between 3 and 15 years. There were 3 (30.0%) male subjects and 7 (70.0%) female subjects among those excluded. Six (60%) of those excluded were because observer agreement on the first or screening measurement did not meet the pre-specified criteria. Of these, one was because one of the observers did not hear the screening measurement. Three subjects were excluded because of technical errors produced by the BPM-100 that did not allow three satisfactory blood pressure measurements to be achieved. One subject had readings that because of technical reasons and observer agreement on individual data points did not allow for three satisfactory measurements to be collected.

Target population results

All of the target population objectives were met, except for the hypertensive subjects. There were 23 (63.9%) male subjects and 13 (36.1%) female subjects included. The ages ranged from 3 to 18 years. There were 6 subjects aged 3 to 5 years, 10 subjects aged 6 to 8 years, 9 subjects aged 9 to 11 years, 5 subjects aged 12 to 14 years and 6 subjects aged 15 to 18 years. Of these 28 (60.9%) subjects were between the ages of 3 and 12 years, this met all age requirements specified in the methods section and fulfilled the AAMI Draft SP 10 criteria [d]. There were 5 hypertensive subjects that enrolled and all were included. This did not meet the enrolment criteria specified in the methods section and will be discussed later. Seven (15.2%) of the enrolled subjects, all of whom were included, were tested with the infant cuff (13 to 18 cm circumference at mid-biceps with the cuff, as specified in the target population section) and

met the AAMI Draft SP 10 criteria [5]. There were 16 (44.4%) subjects with arm sizes less than or equal to 18 cm, and the remaining 20 (55.6%) had arm sizes greater than 18 cm measured at mid-biceps. The mean population arm size was 20.8 ± 5.2 cm with a range from 15 - 33.5 cm.

Included blood pressure measurements

Of the included 162 sets of readings; 62 (38.3%) measurements were less than 100 mmHg for systolic blood pressure, 100 (61.7%) measurements were greater than or equal to 100mmHg but less than 180 mmHg. There were no readings greater than 180 mmHg for the systolic blood pressures. For diastolic blood pressure 13 (8.0%) measurements were below 60 mmHg, 149 (92.0%) of measurements were greater than or equal to 60 mmHg with no readings greater than 100 mmHg.

In the included population 5 or 13.9% subjects were previously diagnosed as having hypertension by their Primary Care Physicians. This did not meet the target criteria of 6 subjects as specified in the methods section. This pre-specified target criteria was intended to reflect the AAMI SP 10-1992 standard [6], which requires 10% of the systolic measurements to be greater than 180 mmHg (or stage 3 hypertension), and 10% of the diastolic measurements should be greater than 100 mmHg (or stage 2 hypertension) [7]. It should be noted that the determination of hypertension in children is based on the child's height, and therefore a range of blood pressures are considered hypertensive [1]. However regardless of age or height of the child a systolic blood pressure greater than 140 mmHg for boys or 132 mmHg for girls, or diastolic pressures greater than 89 mmHg for boys or 86 mmHg for girls would be considered hypertensive [8]. The 23 measurements collected from these subjects accounted for 14.2% of the total 162; although of these only 9 (5.6%) systolic measurements exceeded the 140 mmHg for boys or 132 mmHg for girls and 1 (0.6%) diastolic measurements exceeded the 89 mmHg for boys or 86 mmHg for girls.

Excluded blood pressure measurements

From the 10 subjects excluded, thirty-five measurements were recorded that were not used in the data analysis for the study. Their mean reference systolic and diastolic blood pressures were 98.6 ± 9.5 mmHg (range 82.5 - 118.5 mmHg) and 63.5 ± 7.0 mmHg (range 48.5 - 76.0 mmHg) respectively, with heart rates from the Nonin finger pulse oximeter of 85.3 ± 20.2 bpm (range 54 - 113 bpm). There were 22

(62.9%) systolic blood pressure measurements less than 100 mmHg and 13 (37.1%) were greater than or equal to 100 mmHg but less than 180 mmHg. There were no systolic measurements greater than 180 mmHg. There were 8 (22.9%) diastolic pressure measurements less than 60 mmHg and 28 (77.1%) were greater than or equal to 60 mmHg but less than 100 mmHg, with no measurements greater than 100 mmHg.

Reference standard blood pressure readings

The reference standard (mean of the two observer's measurements) included 162 sets of readings. The mean systolic blood pressure (average of the two observers) was 100.9 with a standard deviation of 15.3. The measurements ranged from 78.0 to 151.5 mmHg. The mean reference standard diastolic blood pressure measurement was 62.3 ± 9.3 mmHg with a range of 45.0 to 89.5 mmHg. Similarly the mean reference heart rate using the finger pulse oximeter was 88.2 ± 13.0 bpm with a range of pulse rates from 59 to 116 bpm.

Observer agreement (observer 1 - observer 2) for systolic measurements showed a mean difference of 0.4 ± 2.8 mmHg (range -10 to 10 mmHg). Of these 154 (95.1%) measurements were less than or equal to 5 mmHg. For diastolic measurements, observer agreement mean difference was 0.8 ± 4.0 mmHg (range -10 to 10 mmHg) with 135 (83.3%) measurements less than or equal to 5 mmHg. This did not meet the 85% agreement level listed in the AAMI SP10-1992, although this standard was established from studies in adult populations with much higher blood pressures [6].

Measurements of BpTRU™ (model BPM-100)

There were also 162 sets of included measurements collected by the BPM-100. The mean systolic blood pressure measurement was 102.3 with a standard deviation of 14.6 mmHg and a range of 77 to 145 mmHg. Mean diastolic blood pressure measurements were 59.1 ± 8.6 mmHg (range of 40 to 83 mmHg). The pulse rates collected by the BPM-100 had a mean of 88.4 ± 12.8 bpm and showed ranges from 63 to 116 bpm.

Accuracy

The difference between the mean BPM-100 readings and the reference standard measurements, determined by the observers, as displayed in Table 1 for systolic blood pressures was 1.45 ± 5.67 mmHg (range -15 to 22.5mmHg) and for diastolic measurements was -3.24 ± 7.39 mmHg (range -22.5 to 17 mmHg), which met the criteria set by the AAMI standard [c]. The accuracy of the BPM-100 against the heart rate reference showed a mean difference of 0.20 ± 2.47 bpm (range -8 to 7 bpm).

Table 2 shows the proportion of individual and then subject measurements of both systolic and diastolic blood pressure differences within 5, 10 and 15 mmHg and how this compares to the BHS protocol [9].

Also the mean systolic blood pressure between the BPM-100 and the observer reference standards was 101.6 ± 14.7 mmHg and the diastolic blood pressure was 60.7 ± 8.2 mmHg.

Discussion

Most International bodies agree that all automated blood pressure devices should have independent validation performed. However this is not the case for most devices [10]. Recently the working group on blood pressure monitoring of the European Society of Hypertension has come up with a revised BHS protocol that will be known as the 'International Protocol' in order to encourage blood pressure device manufacturers to validate their devices and make the process easier and potentially less costly. However, it is designed for adults greater than 30 years of age and does not make recommendations for special ages or circumstances including children [11].

As discussed above, the hypertensive criterion was intended to reflect the AAMI SP10-1992 standard and ultimately ensure the BPM-100 to be accurate in subjects with elevated blood pressures. Hypertension in children is not a common occurrence and, therefore, despite numerous attempts to locate this population subset, VSM Medtech Ltd. chose to stop enrolment at 5 subjects.

Although this study only included 5 pre-determined hypertensive subjects, elevated blood pressures were tested as part of the main (original) clinical study [2]. The BPM-100 performed well in both original studies [2] [3]. In the companion paper that combines the adult and child data as a meta-analysis it can be seen that all hypertensive criteria are clearly met.

Hypotension was not directly tested in this study because the AAMI standard requests that in adults 10% of systolic measurements to be less than 100 mmHg and 10% of diastolic measurements to be less than 60 mmHg. In our study 61.7% (n = 100) of the systolic readings were <100 mmHg and 42.6% (n = 69) of diastolic readings were <60 mmHg.

The inter-observer agreement required 85% of readings to be within ± 5 mmHg. In our study 83.3% of diastolic readings were within this requirement. This is not totally unexpected as auscultating diastolic blood pressure in children with low blood pressures and rapid heart rates is more difficult than in adults [8] [12].

The 85% agreement described in the AAMI SP10-1992 standard was established based on adult studies for adults in a sample size of 85. This requirement may be unrealistic when looking at a small subset of subjects made up of only children.

Gerin et al described in their paper on, 'How we should be measuring blood pressure in the doctor's office?' that "Routine blood pressure measurement would be more representative of daily ambulatory pressures if an automated device, without doctor or nurse present, were used" [13]. The BpTRU™ (BPM-100 model) is not only a safe and accurate device for determining blood pressure in children in the primary care setting, but also meets the requirements of the ANSI / AAMI SP10-1992 and achieved a 'B' grade according to a modified BHS protocol.

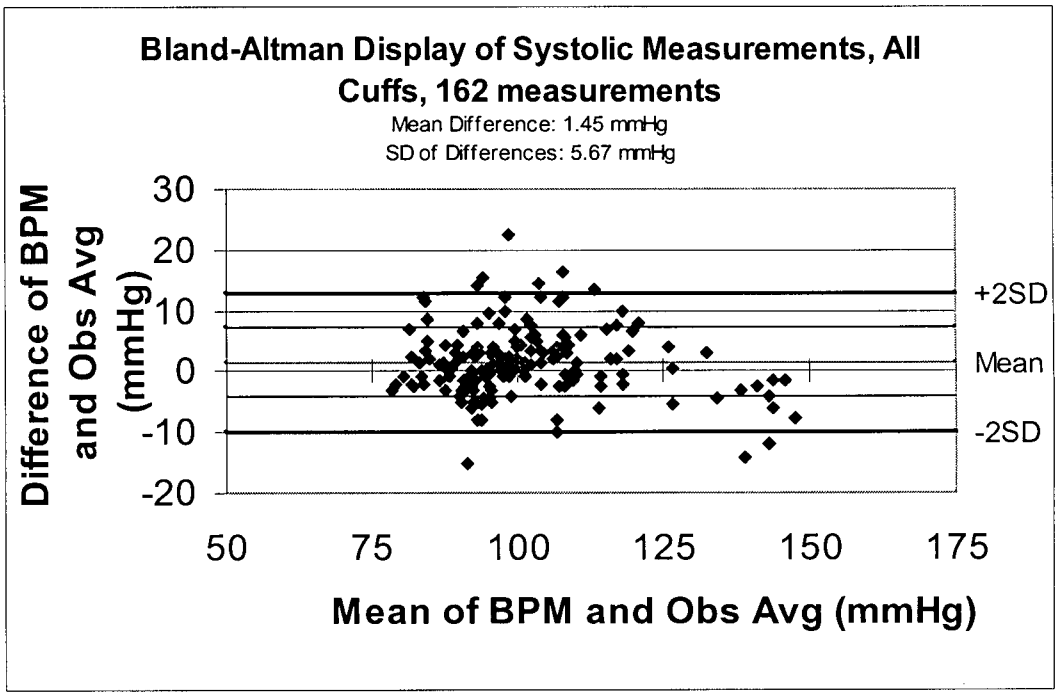
Table 1 Difference between the BPM-100 and the reference standard measurements compared to the American National Standard for Electronic or Automated Sphygmomanometers [c]

		Systolic		Diastolic	
	n	mean difference (mmHg)	standard deviation (mmHg)	mean difference (mmHg)	standard deviation (mmHg)
ANSI / AAMI SP10-1992		± 5.0	< 8.0	± 5.0	< 8.0
BPM-100 minus reference standard	162	1.45	5.67	- 3.24	7.39
Subject mean BPM-100 minus reference standard	36	1.60	4.23	- 3.52	6.70

Table 2 Performance of the BPM-100 compared to the British Hypertension Society (BHS) grade 'B' protocol [e].

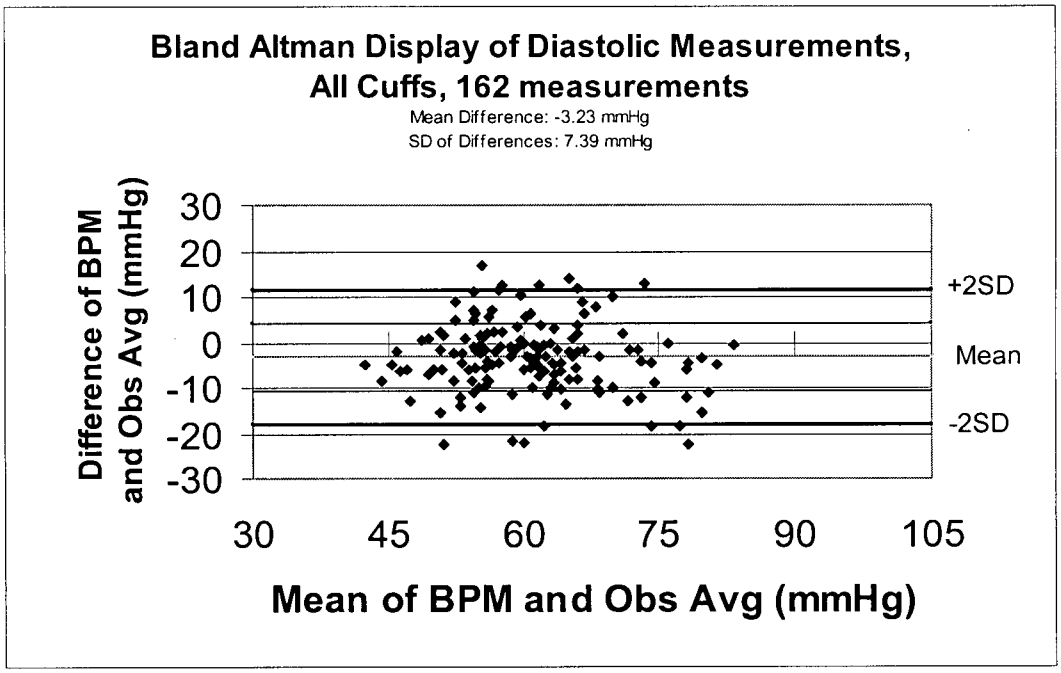
	n	≤ 5 mmHg	≤ 10 mmHg	≤ 15 mmHg
Grade 'B' BHS standard		≥ 50 %	≥ 75 %	≥ 90 %
BPM-100 minus reference systolic blood pressure	162	72.2	90.7	98.1
BPM-100 minus reference diastolic blood pressure	162	51.2	79.6	93.8
Subject mean BPM-100 minus subject mean reference systolic blood pressure	36	69.4	97.2	100.0
Subject mean BPM-100 minus subject mean reference diastolic blood pressure	36	50.0	86.1	94.4

Fig. 2



Bland Altman display of all systolic blood pressure measurements (n = 162).
BPM, BpTRU™ (model BPM-100) monitor; Obs Avg, observer average (reference standard)

Fig. 3



Bland Altman display of all diastolic blood pressure measurements (n = 162).
BPM, BpTRU™ (model BPM-100) monitor; Obs Avg, observer average (reference standard)

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ABSTRACT

Background

To combine the data from an earlier adult study with the data from the subsequent paediatric study using the BpTRU™ (BPM-100 model) in order to determine the overall accuracy against recognised standard auscultatory mercury sphygmomanometer in the general population.

Design

The individual blood pressure points recorded for both adult and paediatric studies was compared directly to its corresponding observer reference measurements from data collected and stored from the two separate studies. There were 255 sets of readings in the adult study and 162 sets from the paediatric study, which were combined to make 417 pairs of blood pressure readings for this study.

Methods

The overall observer standard reference mean for 417 measurements was calculated and the difference between this and the overall mean BPM-100 was calculated with SD and ranges. Measurements within 5, 10 and 15 mmHg agreement were expressed as percentages.

Results

A total of 121 subjects were included for this study (85 from the adult study and 36 from the paediatric study). From these, 417 paired measurements were recorded. The mean difference between the BpTRU™ and the reference standard systolic BP was 0.47 ± 5.40 mmHg with 89.2% measurements within 5 mmHg, 96.4% within 10 mmHg and 99.3% within 15 mmHg. Comparatively we found a mean difference between the BpTRU™ and reference diastolic BP was -2.12 ± 5.93 mmHg with 81.1% within 5 mmHg, 92.1% within 10 mmHg and 97.6% within 15 mmHg agreement.

Conclusion

The BpTRU™ has been shown to be an accurate non-invasive blood pressure monitoring device in the general population from age 3 up to the elderly. This combined study meets all requirements of the Association of Advancement of Medical Instrumentation and achieved a grade 'A' in the BHS protocol.

Introduction

The BpTRU™ (model BPM-100) is a non-invasive automated electronic blood pressure monitor that uses the oscillometric technique to determine the mean arterial pressure and then calculate the systolic and diastolic blood pressures from this. It records six measurements automatically, separated by a time period of 1 to 5 minutes set as required by the operator. It uses the first reading to acclimatise to the patient's pressures and then generates the average of the remaining five readings.

Home blood pressure readings with an automated device has been shown to have greater predictive value than office blood pressures for mortality in a recent population-based observational study [1].

Hypertension has a major impact on our health services; it is the major risk factor for heart disease, stroke and renal disease. Heart disease is the leading cause of death in the US, with cerebrovascular disease being the third leading cause of death [2]. Joffres et al discuss differences in hypertension awareness, treatment and control of hypertension between the US and Canada yet place little importance on the two very different sets of observers taking the blood pressures, saying that these should have minimal impact. In contrast Gerin et al clearly emphasized the differences and concluded that an automated device would be better than both methods [3] [4].

The most accurate techniques for measuring blood pressure (eg: intra-arterial catheterisation) are not practical or functional for the primary care physician who is the frontline for diagnosing, monitoring and managing hypertension. If performed correctly, office blood pressures with a mercury sphygmomanometer may be accurate; however, it has been shown that at least 20% of hypertension is misdiagnosed this way [5]. In addition the difficulties of managing mercury spills is a growing concern to a degree that many European and US cities have already banned mercury and others are set to follow suit [6] [7].

It has been shown many times that blood pressures recorded in the physicians office by the physician can be misleading and readings performed by the office nurse or the patient are more representative. In fact

such measurements would result in less treatment initiation, change in current treatment or escalation of dosage [8].

The importance of correctly diagnosing and managing blood pressure clearly has a potential for impact on mortality, morbidity and health care costs. However, these benefits can only be realized if we have a method of accurately recording blood pressures in a manner similar to that seen in the clinical trial setting.

The purpose of this study was to combine the data for the general population from 3 years of age to the elderly in order to determine the overall accuracy of the automated blood pressure monitor, BpTRU™ against the gold standard mercury sphygmomanometer. To achieve this, the study was assessed in accordance with the standard guidelines of the AAMI SP10-1992 provided by the Association for the Advancement of Medical Instrumentation (AAMI) and in accordance with the British Hypertension Society protocol-1993; the regulating bodies for validating these types of monitors.

Methods

Adult subjects were recruited during September and October 1999 at the University of British Columbia using subjects from the Hypertension clinic and affiliated primary care practices. The paediatric subjects were recruited from June to August 2001 at the Research office of VSM MedTech Ltd from B.C.'s Children's Hospital and also family practice offices.

Details of all ethical approval, consent acquired, inclusion, exclusion criteria and target population requirements can be obtained from the companion paper and the two original adult publications [9] [10] [11].

In the adult population two experienced nurses were used whose blood pressure reading skills were tested prior to the initiation of any data collection. Similarly in the paediatric population three experienced nurses rotated as the two observers.

The set up was the same for both studies with the BpTRU™ being connected in parallel with the Trimline precision standard mercury sphygmomanometer and the Nonin finger pulse oximeter being connected to the other arm or alternate body part. The observers, who were seated opposite the standard mercury sphygmomanometer, were blinded by a curtain between them and also blinded to the BpTRU™ device. One of them would palpate the brachial pulse and put the diaphragm of the dual-headed stethoscope over it. The only difference between the two population sub-groups was that the paediatric subjects were allowed to sit on the laps of their accompanying parent or guardian.

All data recorded by the BpTRU™ device was simultaneously saved onto a connected laptop from which subsequent analysis could be performed. From the 121 subjects recruited for this study, 417 data points were obtained, all of which were used in our study having already conformed to the inclusion and exclusion criteria specified in the previous studies.

Data Analysis

After combining the 85 adult subjects (at least 18 years of age) and the 36 paediatric subjects (from 3 to 18 years of age), a total of 121 subjects were included. For these subjects the sex and age distributions were determined.

For each of the included measurements, distribution of blood pressures was determined and expressed as the number and percentages in the ranges 180 mmHg < systolic < 100 mmHg and 100 mmHg < diastolic < 60 mmHg. Included in this was an expression of the mean, standard deviation and range of blood pressures in the population group.

From the 417 measurements the mean, standard deviations and range of blood pressure and heart rate was also determined for observer 1 and observer 2. Subsequently, the mean of the two observers was also calculated and became known as the reference standard measurements. Agreement of readings within 5 and 10 mmHg was also expressed. Similarly, the mean, standard deviation and range of blood pressure were also determined for the BpTRU™ device.

To assess the accuracy of the device, the mean difference and standard deviation, between the BpTRU™ and the reference standard was determined as per the ANSI / AAMI SP10-1992 standard [12]. Subsequently, in order to reflect this accuracy in the clinical setting, the subject mean difference with standard deviation was also determined (subject mean BpTRU™ measurements minus the subject mean reference measurements). The percentage agreement of measurements within 5, 10 and 15 mmHg was also expressed in order to represent the requirements of the British Hypertension Society protocol [13].

Results

Included subjects

There was a total of 121 subjects included from the two studies (85 from the adult study [10] and 36 from the paediatric study [11] - see companion paper). Of these 67 (55.4%) were male subjects and 54 (44.6%) were female subjects. The average age of included subjects was 33.1 years of age, ranging from 3 to 83 years. Details of included and excluded subjects can be seen in the original adult study [10] and the paediatric companion paper [11]. All of the target population requirements for each study were met, except the hypertensive criteria specified in the paediatric study, this was discussed at some length in the paediatric paper.

Included blood pressure measurements

From the 121 subjects included there was a total of 417 sets of readings obtained. Of these, 27 (6.5%) had systolic measurements greater than 180 mmHg and 137 (32.8%) had systolic measurements less than 100 mmHg. The remaining or 253 (60.7%) had blood pressure measurements equal to or greater than 100 mmHg and equal to or less than 180 mmHg as according to the mean reference observer standard measurements. Twenty-five (6.0%) blood pressure readings had diastolic measurements greater than 100 mmHg and 108 (25.9%) had diastolic blood pressures less than 60 mmHg with remaining 284 (68.1%) between these. The overall average systolic blood pressure was 117.7 $\pm$ 29.23 mmHg (range 78 to 223.5 mmHg) and the overall average diastolic blood pressure was 71.5 $\pm$ 15.95 mmHg (range 45 to 119.5 mmHg). The overall mean heart rate was 77.1 $\pm$ 15.41 bpm (range 42 to 116 bpm) using the Nonin finger pulse oximeter. These overall values were determined from the mean observer reference measurements.

Excluded blood pressure measurements

There were six subjects excluded because of technical errors made by the BpTRU™ device that did not allow for a minimum of three blood pressure readings to be recorded. More detailed explanations of all excluded subjects and measurements can be obtained from the previous publications [9] [10] [11].

Reference standard blood pressure readings

Observer agreement (or the mean difference between observer one and two) for the 417 systolic measurements was -0.26 ± 2.38 mmHg (range -10 to 10 mmHg) as recorded using a Trimline mercury sphygmomanometer. Of these 404 (96.9%) readings were within 5 mmHg. Similarly the observer agreement for the 417 diastolic blood pressure readings was -0.35 ± 3.27 mmHg (range -10 to 10 mmHg) with 378 or 90.6% being within 5 mmHg, as seen in Table 1. Although most of the readings were within 5 mmHg agreement (as mean values greater than 10 mmHg were excluded as one of the post-measurement exclusion criteria), the diastolic measurements had a smaller number within this agreement range. This highlights the difficulty of accurately measuring diastolic blood pressure, particularly in the paediatric populations or young female adults when reading values from as low as 45 mmHg.

Measurements of BpTRU™ (model BPM-100)

Table 1 also shows is that the overall mean systolic blood pressure recorded by the BpTRU™ was 118.2 ± 28.47 mmHg with a range of 77 to 221 mmHg, and diastolic blood pressure of 69.4 ± 16.3 mmHg (range 40 to 120 mmHg) for 417 measurements. The overall mean heart rate recorded by the BpTRU™ was 77.3 ± 15.33 bpm with a range of 116 to 417 bpm for the 417 readings.

Accuracy

The accuracy of the BpTRU™, or the mean difference between the BpTRU™ and the observer reference standard systolic blood pressure was 0.47 ± 5.40 mmHg which is well within the ANSI / AAMI SP10-1992 standard. Similarly the mean difference between the BpTRU™ and the reference diastolic blood pressure was 2.12 ± 5.93 mmHg which is also within the ANSI / AAMI SP10-1992 standard, as seen in Table 2. The mean difference of the observer reference and the BpTRU™ for the heart rate was 0.18 ± 2.20 bpm.

In Table 3 it can be seen that from these values 372 (89.2%) systolic measurements were less than or equal to 5 mmHg, 402 (96.4%) were within 10 mmHg and 414 (99.3%) were within 15 mmHg agreement. For the diastolic measurements 338 (81.1%) were within 5 mmHg, 384 (92.1%) were within 10 mmHg and 407 (97.6%) were within 15 mmHg.

These determinants all fall within the British Hypertension Society (BHS) grade 'A' protocol. It can also be seen that the percentage of systolic measurements in agreement was better than that of the diastolic.

As stated previously the BpTRU™ is an automated device that records and calculates the average of five blood pressure measurements. It is intended to be used in the physician's office in this manner. Thus the subject mean difference was determined in order to reflect the accuracy of the device in the clinical setting. The subject mean difference for systolic blood pressures was 0.4 ± 4.3 mmHg, diastolic measurements produced -2.0 ± 5.1 mmHg and the subject mean difference for heart rate was 0.2 ± 1.1 bpm. From these, for systolic blood pressure 91 (75.2%) subjects were within 5 mmHg, 119 (98.3%) were within 10 mmHg and 121 (100%) were within 15 mmHg. For diastolic blood pressure, 86 (71.1%) subjects were within 5 mmHg, 112 (92.6%) were within 10 mmHg and 119 (98.3%) were within 15 mmHg agreement between the BpTRU™ and the mean observer reference standard, as shown in Table 3.

Bland Altman plots were also displayed as the difference of the BPM and the observer average against the mean of the BpTRU™ and the observer average for both systolic and diastolic pressures (see figures 1 and 2) [14].

Discussion

There have been several publications on the importance of taking accurate and reproducible blood pressures. Campbell and McKay have illustrated the potential difficulties with inaccurate readings; demonstrating that consistent overestimation of diastolic blood pressure by 5mmHg would increase the hypertension in a physicians practice by 100% and conversely, underestimating the diastolic blood pressure by just 5mmHg would reduce by 62% the number of patients seen to be hypertensive [15].

Blood pressure should be recorded bearing in mind the following factors: - [4] [16] [17] [18]

- patients should refrain from smoking or ingesting caffeine at least 30 minutes before having their blood pressures recorded
- blood pressure should be recorded in a quiet and calm environment
- patients should be seated with their backs well supported, feet flat on the ground with the mid-point of the bare upper arm supported at heart level
- an appropriate sized cuff (the bladder inside the cuff should be at least 80% of the circumference) should be placed on the upper arm of the patient 2 to 2.5 cm above the antecubital fossa
- blood pressure measurements should only be recorded after at least 5 minutes of rest in this position
- measurements should be taken either with an automated blood pressure device or a regularly calibrated mercury sphygmomanometer
- inflate the cuff to at least 30 mmHg above the disappearance of the radial pulse of the arm from which pressures are being recorded
- allow a linear deflation of 2 mmHg / sec
- Korotkoff V or the disappearance of sounds should be recorded as the diastolic blood pressure
- the average of at least two readings, at least two minutes apart should be taken at each visit
- at least two visits are required to make the diagnosis of hypertension unless there is evidence of end-organ damage with hypertension at one visit

The automated device assessed here saves time and makes it more likely that the above criteria will be followed: -

- patients can be placed in a quiet room by themselves avoiding the effects of white coat or office hypertension
- different cuffs supplied with the device are clearly marked to allow for the most appropriate cuff to be used according to arm size
- the device automatically calibrates to atmospheric pressure and ambient temperature before each measurement reducing errors of calibration
- it inflates to 35 mmHg the level of occlusion of the radial pulse so as not to miss auscultatory gaps
- it has linear deflation to reduce errors of detecting pulse waves
- the device has reproducible smooth inflation and deflation that can only be obtained using standardised computers or a device and not by any observers
- the device is calibrated to agree with Korotkoff V generating accurate diastolic blood pressures
- the first measurement is ignored since the person starting the device may still be in the room
- five measurements can be obtained at 1 to 5 minute intervals with the average calculated at the end giving a more representative recording of their blood pressure status

With the advent of newer blood pressure measuring devices, there has been renewed call for more validation trials and standardisation of the comparisons of these devices. [19]. Recently The European Society of Hypertension Working Group has used published data to devise a new International protocol that is hoped would encourage all device manufacturers to perform and adhere to minimum validation and subsequently approval protocols [20].

The device tested here met the requirements set by the governing bodies mentioned, which are far more rigorous than the new International Protocol. However, it was desirable to see if a study in all age groups would also meet these strict requirements. Dùe to time, and financial constraints it was more appropriate to combine the study data if reasonable to do so. It was felt that because we were combining raw individual data rather than means and imputed standard deviations that this would be appropriate to do. In reality we were doing much the same as if we were combining data for a meta-analysis; however we were better off in that we had original data do all analyses from scratch.

The BpTRU™ is the only non-invasive automated oscillometric blood pressure device currently available that has been tested in a population group aged from 3 years to the elderly; and that has satisfied the criteria set out by the American National Standard for Electronic or Automated Sphygmomanometers, ANSI / AAMI SP10-1992 [12]. Overall it has also achieved a grade 'A' according to the British Hypertension Society protocol for the evaluation of blood pressure measuring devices-1993 [13].

Table 1 Systolic, diastolic blood pressure and heart rate measurements for the two Observers and the BpTRU™

		Systolic			Diastolic			Heart rate		
	n	mean mmHg	± SD mmHg	range mmHg	mean mmHg	±SD mmHg	range mmHg	mean bpm	±SD bpm	range bpm
Observer one [1]	417	117.6	29.13	78-224	71.3	15.82	44-119	77.1	15.41	42-116
Observer two [2]	417	117.9	29.34	76-223	71.6	16.25	43-120	77.1	15.41	42-116
Observer mean (ref)	417	117.7	29.23	78-223.5	71.5	15.95	45-119.5	77.1	15.41	42-116
Obs. agreement [1-2]	417	-0.26	2.38	-10 to 10	-0.35	3.27	-10 to 10	0	0	0
BpTRU™ readings	417	118.2	28.47	77-221	69.3	16.30	40-120	77.3	77.3	42-116
Accuracy (BpTRU™ - ref)	417	0.47	5.40	-18.5-22.5	2.12	5.93	-22.5-17	0.18	2.20	-16-7

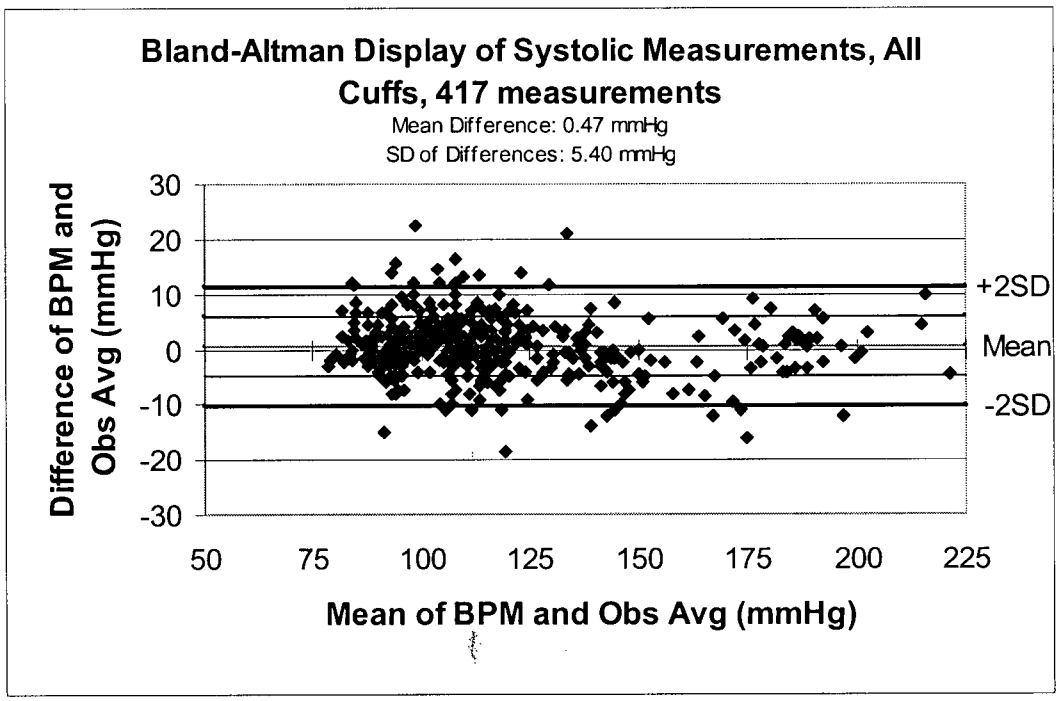
Table 2 Difference between the BpTRU™ and the reference standard measurements compared to the American National Standard for Electronic or Automated Sphygmomanometers [d]

		Systolic		Diastolic	
	n	mean difference (mmHg)	standard deviation (mmHg)	mean difference (mmHg)	standard deviation (mmHg)
ANSI / AAMI SP10-1992		± 5.0	< 8.0	± 5.0	< 8.0
BpTRU™-100 minus reference standard	417	0.47	5.40	- 2.12	5.93
Subject mean BpTRU™ minus reference standard	121	0.40	4.34	- 2.00	5.15

Table 3 Performance of the BpTRU™ compared to the British Hypertension Society (BHS) grade 'A' protocol [d].

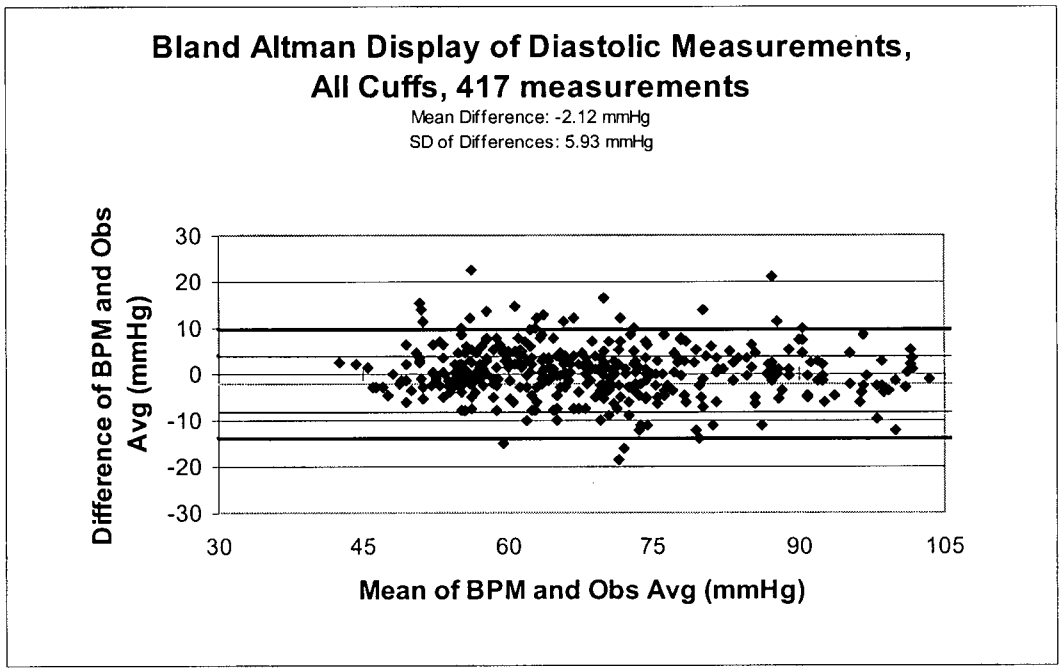
	n	≤ 5 mmHg	≤ 10 mmHg	≤ 15 mmHg
Grade 'A' BHS standard		≥ 60 %	≥ 85 %	≥ 95 %
BpTRU™ minus reference systolic blood pressure	417	89.2	96.4	99.3
BpTRU™ minus reference diastolic blood pressure	417	81.1	92.1	97.6
Subject mean BpTRU™ minus subject mean reference systolic blood pressure	121	75.2	98.3	100.0
Subject mean BpTRU™ minus subject mean reference diastolic blood pressure	121	71.1	92.6	98.3

Fig. 1



Bland Altman display of all systolic blood pressure measurements (n = 417).
BPM, BpTRU™ (model BPM-100) monitor; Obs Avg, observer average (reference standard)

Fig. 2



Bland Altman display of all diastolic blood pressure measurements (n = 417).
BPM, BpTRU™ (model BPM-100) monitor; Obs Avg, observer average (reference standard)

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CHAPTER VI

OVERALL DISCUSSION

In North America the most common reason for patients to visit their physician's offices is hypertension, and one of the commonest diagnostic procedures to be performed is the measurement of blood pressure [14]. The screening, diagnosis and ongoing management of hypertension depend extensively on an accurate and standardised method of blood pressure measurement. In the literature there are numerous examples of the potential difficulties with inaccurate readings. The consequences of inaccuracy have been estimated: the consistent overestimation of diastolic blood pressure by 5 mmHg would increase the diagnosis of hypertension in a physicians practice by 100% and conversely underestimating the diastolic blood pressure by 5mm Hg would reduce by 62% the number of patients diagnosed to be hypertensive. In other words the potential for large numbers of false positive and false negative blood pressure measurements is significant, with possible adverse consequences for the patient [15].

The completion of these two trials has demonstrated the difficulty in enrolling the number of subjects required and having them meet the required parameters such as blood pressure range, arm size and age range. However, after completing these requirements and obtaining the results seen here, it is possible to gain a fair amount of confidence in the accuracy and reproducibility of the device under question. This confidence takes cognizance of the problems associated with the gold standard, the auscultatory mercury sphygmomanometer. This is partly reflected in the somewhat surprising inter-observer variability seen in these trials. If trained research nurses under research standards measuring blood pressure simultaneously get variable results, one can imagine the much larger variability of blood pressures measured in a busy primary care office. The variability in that usual setting is probably so large that most diagnostic and treatment decisions cannot be made with any degree of confidence.

Some examples of the many different circumstances that can affect blood pressure are:

- talking can increase the systolic blood pressure by up to 17 mmHg
- having patients arm 10 cm below the heart level can increase the blood pressure by 8 mmHg
- measuring blood pressure with a cuff that is too small can increase the systolic blood pressure by up to 8 mmHg.

All potential errors have to be recognised and steps put into place to avoid these errors [16]. An automated blood pressure measuring device can be an important step towards avoiding some of these errors.

Modern blood pressure-measuring devices have to be accurate, reproducible, and easy to operate, convenient, time saving and affordable. Many available devices however, do not have the most basic of merits such as accuracy and reproducibility demonstrated in a published report. Devices that have published validation data, and fulfill some of the other criteria specified have significant advantage over those that do not [17].

The BpTRU™ is an electronic automated blood pressure device that has been shown to be of similar accuracy and reproducibility to the current gold standard of auscultatory mercury sphygmomanometry in a wide range of patients. In the original study in adults it was seen that the earlier version of the device the BPM-100_{Beta} was shown to underestimate systolic blood pressures over 150 mmHg. This only became evident when the data was plotted on a Bland-Altman plot. This version of the device met the standards of both regulatory bodies and could have been marketed as such. However, both the investigators and the manufacturers found this limitation unacceptable. As a result a random sample of the data was used to create a modified algorithm, which corrected the problem. The rest of the data was then available to test the modified algorithm and it was clear using the Bland-Altman plot that it had corrected the problem. The methods described could set a precedent allowing manufacturers to re-validate altered algorithms using data already collected by their embedded software. This could save time and resources and allow testing of more devices especially those that have modified algorithms.

I believe the present standards for validation of blood pressure measuring devices are not sufficiently stringent and should be revised in the following ways.

- The regulations should require validation using simultaneous measurements as was done in our protocol. The new International protocol and previous standards allow or recommend the use of sequential blood pressure measurements rather than simultaneous measurements. The sequential measurements are recorded at least 30 seconds apart, but not more than 60 seconds apart. This has the significant disadvantage of adding the variability of blood pressure over time and does not allow enough time between measurements for resolution of venous congestion, which can also affect the measurement.

- The device blood pressure is compared to pressures measured by reference standard observers both before and after. The difference between the observer and the device is determined and the smaller of the two values used. This invariably creates a bias to make the device look more accurate than it is [18].

- The regulations should also require that a device meets both the AAMI standard and the BHS standard. The AAMI standard appears to be the more robust of the two, however the requirement for a standard deviation of the difference of as much as 8 mmHg is relatively lenient.

- The requirement for a Bland Altman plot is essential as demonstrated by the first trial. A device could underestimate blood pressure for high values and overestimate for low values and pass the standard in terms of a mean difference from the mercury measurements. Standards need to be established as to what deviations seen on the Bland Altman plot would be acceptable. [20]. It was clearly seen in the first adult paper that the machine was under-estimating higher systolic blood pressures which was rectified in the revalidation paper with the modified algorithm.

In addition the new International protocol introduces additional problems. It requires that if the inter-observer difference for systolic or diastolic pressures is not within 4 mmHg agreement it must be repeated. This leads to lesser inter-observer variability and could lead to bias. If a Sphygmocorder is used to record the sounds and the observers do not agree, they are required to re-assess until agreement is reached. Again this appears to introduce some bias.

Since the BpTRU™ has met the more stringent requirements set out by the American National Standard for Electronic or Automated Sphygmomanometers and the British Hypertension Society, it can be assumed that it would also meet the more recent and less rigorous International Protocol for validation of blood pressure measuring devices in adults as set out by the Working Group on Blood Pressure Monitoring of the European Society of Hypertension [18]. One of the aims of this International protocol was to encourage more device manufacturers to undergo validation before marketing.

If clinical decisions are going to made based on the best available evidence then blood pressures need to be measured in a manner that is similar to that which was used in the trials. It is clear that single blood pressures measured by a physician in the office represent a significant overestimate of the resting blood pressure measurements by a nurse in a clinical trial. Any new blood pressure measuring methodology must be shown to be a better estimate of the research standard than casual office measurements by a physician.

My recommendation to the manufacturer is that they fund a trial comparing BpTRU™ with the research standard and casual office measurements by a physician. The best design for this trial would be to assess 50 patients in a primary care clinic setting. The best design would be a cross-over design where all measurements are taken on the same day, but the order of measurements is randomized. In the clinic setting where in one room the BpTRU™ machine is set up, the patient follows the standard routine of resting for 5 minutes; the first pressure is taken with the investigator in the room and is discarded, the blood pressure recorded is the mean of the remaining 5 measurements with nobody in the room. The research standard would be resting 5 minutes followed by 3 measurements taken by a nurse in the correct standardised way. The third would be one or two measurements by a physician as part of his or her busy practice day. The challenge in the trial would be to not allow the research design to affect how the pressures are taken by the physician. The trial should answer the question as to whether physician measurements or BpTRU™ measurements most closely mimics blood pressures as taken in the clinical trial setting (ie: those measurements recorded by the nurse reading with research standards).

With the wave of newer devices coming to the market and the end of an era with mercury sphygmomanometers getting closer, we can be confident that the BpTRU™ is one of those devices that has attained the accuracy that is required of it by the current governing bodies on blood pressure measuring instruments. The BpTRU™ can be used with confidence and understanding that patients in the physician's office will have appropriate decisions based on accurate, reproducible and completely objective blood pressure measurements. It can thus not only reduce inappropriate prescribing to those with 'white coat hypertension' and consequently reduce iatrogenic disease elements, but also appropriately identify that 30% of the population unaware of their hypertension and consequently monitor

their blood pressure to help avoid or reduce the huge number of deaths directly related to being uncontrolled [19].

Henceforth when the BpTRU™ was tested in children (aged 3 to 18 years with a mean of 9.4 years) it also met the requirements of the ANSI / AAMI SP10-1992 and achieved a 'B' grade according to a modified BHS protocol. It is one of the few devices to have been validated in children and to have achieved significant levels of accuracy. When the raw paediatric data was combined with the raw adult data, the BpTRU™ met the ANSI / AAMI SP10-1992 criteria and achieved an overall grade 'A' from the British Hypertension Society protocol.

CHAPTER VII

CONCLUSIONS

Regarding the BpTRU™:

- The BpTRU™, an electronic non-invasive automated oscillometric blood pressure device has been shown to be as accurate as the current gold standard of auscultatory mercury sphygmomanometry.

- When tested in adults (ages 18 to elderly - oldest included subject was 83 years old, mean age of 43.1 years) it met all requirements of the Association for the Advancement of Medical Instrumentation and achieved an "A" grade according to the British Hypertension Society standard.

- When tested in children (aged 3 to 18 years with a mean 9.4 years) it also met the requirements of the ANSI / AAMI SP10-1992 and achieved a 'B' grade according to a modified BHS protocol.

- When the raw data from both population groups was combined to determine the overall accuracy of this blood pressure device over an age range of 3 years to 83 years (mean age 33.1 years) it satisfied the criteria set out by the American National Standard for Electronic or Automated Sphygmomanometers, ANSI / AAMI SP10-1992.

- Overall it has also achieved a grade 'A' according to the British Hypertension Society protocol for the evaluation of blood pressure measuring devices-1993.

- The BpTRU™ is the only automated blood pressure measuring device that has been validated and has attained this high level of accuracy over this broad age range.

Regarding the validation process, my opinion is such that:

- All blood pressure devices irrespective of the target audience (home or office use) should undergo validation.

- Device manufacturers should be more transparent about their algorithms.

- The methods and requirements for calibration should be clearly stated.

- In order to validate an automated blood pressure measuring device, simultaneous measurements from the same arm should be directly compared to the reference standard.

- The mean of two observer's measurements should be regarded as the gold or reference standard.

- Devices should be made to clearly demonstrate the accuracy across a full range of blood pressures and cuff sizes using the Bland Altman plot.

- All devices should meet the requirements set forth by both the ANSI / AAMI SP10-1992 and the British Hypertension Society protocol.

- Newer validation guidelines, such as the International Protocol that appear to encourage device manufacturers to undertake the validation process, but have less rigid criteria are unacceptable.

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