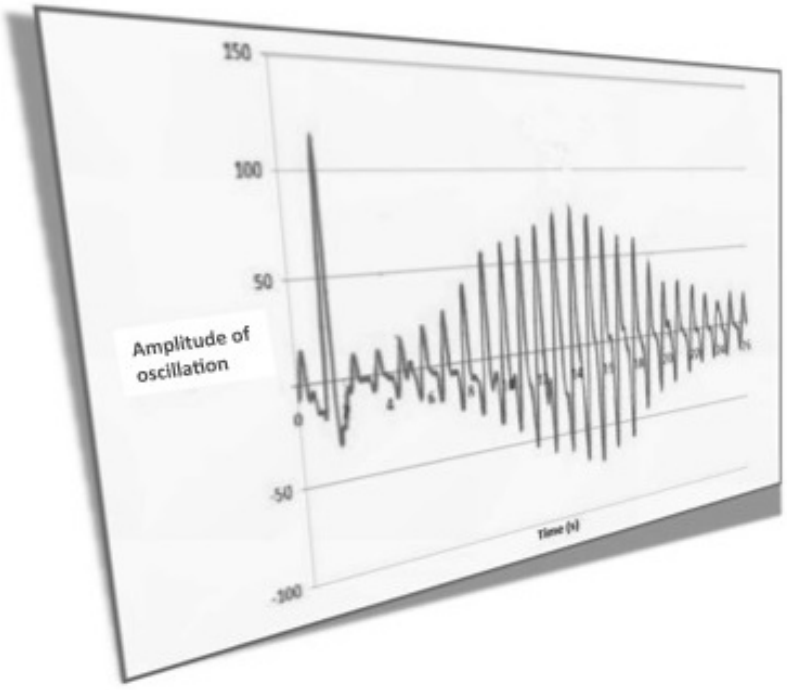
Validity study of oscillometric blood pressure measurement devices using an oscillometric waveform simulator

MSc Thesis in Clinical Science and Technology



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Abstract:

Blood pressure measurement is the most common measurement that is made in clinical practice. There is a large market for commercially available blood pressure devices, and in Germany alone, approximately 1.2 million blood pressure devices are sold annually for personal use. However, there are claims that a majority of blood pressure devices available on the European Union market have not been validated.

Objectives: The purpose of this study was to examine differences between external and internal cuffs when using an oscillometric waveform simulator; to investigate blood pressure device validity and differences within models; and to examine how a simulator could be used in the acquisition of blood pressure devices, before these devices are implemented in the clinical domain.

Methods: Two different models of blood pressure devices, 10 devices per model, were utilized. A simulator was used to generate 8 physiological oscillometric waveforms.

Results: Differences between cuffs did not exceed acceptable measurement limits of ± 3 mmHg, however, many devices were excluded when using the internal simulator cuff. Neither model was able to produce valid measurements within ± 3 mmHg for all 8 simulations. Measurement errors ranged from -3 to 4 mmHg (Model 1), and -8 to 6 mmHg (Model 2).

Differences within models showed significant differences for both Model 1 and Model 2.

Conclusions: Many factors may have had an influence on the validity of the measurements obtained with both models, including: simulator and blood pressure device employment of differing proprietary algorithms, and measurement variability caused by a lack of pressure transducer calibration. Further studies are needed to increase the understanding of the oscillometric method and oscillometric waveforms, so that improved blood pressure devices and oscillometric waveform simulators can be designed.

Picture on front page: Hard&Soft ways - Integrated Circuit Programming Technics, http://hsways.blogspot.dk/

Preface

This document is the main report for my master's thesis for the Master of Science in Clinical Science and Technology, at the Department of Health Science and Technology, Aalborg University, Denmark. This main report is written in article form with appendices. This thesis is aimed at other university students as well as others with an interest in clinical engineering, but it is my hope that it will be of interest to the Danish biomedical and clinical engineering community, as well.

The progression of healthcare technological innovation and it's ability to reshape and merge the fields of medicine and engineering, are of great interest to me. It was my interest in clinical engineering, and my natural curiosity, which were the primary driving forces behind this work.

The work described in this report was carried out during the period February -June 2013, and was under the theme "Clinical Science and Technology". The work described in this report was completed at the Department of Procurement and Clinical Engineering, Aarhus University Hospital, and at the Department of Health Science and Technology, Aalborg University.

I am grateful to Jørn Enggaard for inspiration and support, and for giving me the opportunity to write my thesis in collaboration with the Department of Procurement and Clinical Engineering.

I am also indebted to Steven Brantlov for his support and encouragement. Regardless of the growing responsibility in connection with his own project, he was always willing to take time to contribute with ideas to my project, and for theoretical and slightly philosophical discussions.

Lastly, I would like to thank all the staff at the Department of Procurement and Clinical Engineering for creating a welcoming, friendly and supportive environment.

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List of Abbreviations

A_d	Oscillation amplitude corresponding with diastolic pressure
A_m	Maximum oscillation amplitude
A_s	Oscillation amplitude corresponding with systolic pressure
M_E	Measurement error
P_d	Diastolic pressure
P_s	Systolic pressure
bpm	Beats per minute
Ec	External manufacturer supplied cuff
Ic	Internal simulator cuff
MAP	Mean arterial pressure
mmHg	Millimetre of mercury
Sim	Simulator

Validity study of oscillometric blood pressure measurement devices using an oscillometric waveform simulator

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Abstract

Blood pressure measurement is the most common measurement that is made in clinical practice. There is a large market for commercially available blood pressure devices, and in Germany alone, approximately 1.2 million blood pressure devices are sold annually for personal use. However, there are claims that a majority of blood pressure devices available on the European Union market have not been validated. Objectives: The purpose of this study was to examine differences between external and internal cuffs when using an oscillometric waveform simulator; to investigate blood pressure device validity and differences within models; and to examine how a simulator could be used in the acquisition of blood pressure devices, before these devices are implemented in the clinical domain. Methods: Two different models of blood pressure devices, 10 devices per model, were utilized. A simulator was used to generate 8 physiological oscillometric waveforms. Results: Differences between cuffs did not exceed acceptable measurement limits of ± 3 mmHg, however, many devices were excluded when using the internal simulator cuff. Neither model was able to produce valid measurements within ± 3 mmHg for all 8 simulations. Measurement errors ranged from -3 to 4 mmHg (Model 1), and -8 to 6 mmHg (Model 2). Differences within models showed significant differences for both Model 1 and Model 2. Conclusions: Many factors may have had an influence on the validity of the measurements obtained with both models, including: simulator and blood pressure device employment of differing proprietary algorithms, and measurement variability caused by a lack of pressure transducer calibration. Further studies are needed to increase the understanding of the oscillometric method and oscillometric waveforms, so that improved blood pressure devices and oscillometric waveform simulators can be designed.

1 Introduction

1.1 Background and problem definition

Blood pressure measurement is the most common measurement that is made in clinical practice, and it is the basis for the diagnosis, management, treatment and research of hypertension [15, 14].

The mercury sphygmomanometer has been used to measure blood pressure for over a century, and is still the golden standard method of non-invasive blood pressure measurement [26]. However, as a result of environmental and service considerations, several countries have banned mercury devices [12, 26]. It is therefore not unlikely that mercury sphygmanometers will one day only be available to designated institutions such as validation laboratories [26]. As a consequence of this, mercury sphygmomanometers are being replaced by alternate blood pressure devices [12, 26]. The demand for self measurement of blood pressure is rapidly growing, and there is a large market for these commercially available blood pressure measuring devices [17]. In Germany alone, approximately 1.2 million blood pressure devices are sold annually for personal use [22]. These devices can be advertised outside the pharmacy without medical constraint, and can be purchased by patients without consulting a physician [14]. These factors as well as a growing public interest in health awareness, have resulted in the manufacture of a wide variety of these devices [14]. However, it is reported that not all blood pressure devices are suitable for all patient groups, and that certain blood pressure devices are incapable of accurately determining blood pressure for patients suffering from diabetes or preeclampsia [3].

Detailed requirements for such devices are laid down in harmonized standards, where a harmonized European Standard (EN 1060) was developed in the 1990s [13]. This standard specifies performance including environmental performance, device construction, as well as safety requirements including accuracy (maximum mean error of measurement of $\pm$ 5mmHg compared with manual mercury measurements) [13]. A requirement of European standard EN 1060 (part 3) is that manufacturers need to be able to provide evidence, on demand, that their devices are in accordance with system accuracy limits [22]. However, a study by Sims et al. showed that a majority of blood pressure measurement devices available on the European Union market have not been validated [22]. This claim is supported by the European Society of Hypertension, which states that few blood pressure measurement devices are evaluated according to validation guidelines [14].

These commercially available blood pressure measurement devices are comprised of many individual elements, which together are used to estimate blood pressure. (Figure 1). The technique which is widely used for these devices is the oscillometric technique [2]. This technique relies on analyzing the relationship between arterial pulses (oscillations) which are detected by a cuff placed around a subjects upper arm, as cuff pressure is deflated from above systolic pressure to below diastolic pressure. (Figure 1). The oscillometric waveform describes this relationship between cuff pressure and arterial oscillations [2]. Proprietary algorithmic methods are used by manufacturers to determine the systolic and diastolic pressures from the oscillometric waveform [2]. (Figure 2). The employed algorithms are derived empirically from clinical studies and vary between manufacturers [20].

As a consequence of this, it is strongly recommended that blood pressure devices are validated clinically [2]. However, clinical validation involves use of clinical validation trials, which are associated with logistical difficulties, time-consuming processes, and high costs [1]. This has led to the development of commercial simulators which generate artificial oscillometric waveforms. (Figure 3) These oscillometric blood pressure simulators have the potential to replace clinical validation trials, and to verify oscillometric blood pressure device validity claims [2, 11, 1]. (Figure 4).

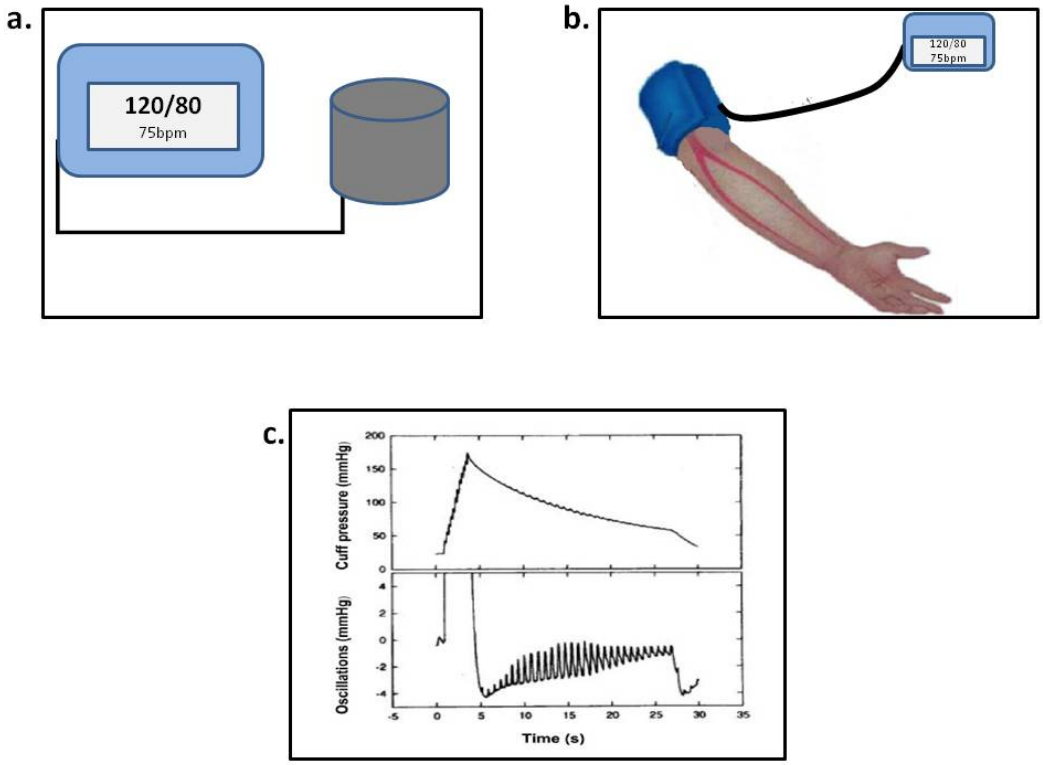


Figure 1: a.) An oscillometric blood pressure device consists of an inflatable cuff, a pneumatic hose connecting the cuff to a device monitor, and a digital display. These devices measure blood pressure using a pressure transducer, and electronic components built into the device monitor. Oscillometric devices do not measure systolic and diastolic pressures directly, but estimate them from the mean arterial pressure using algorithmic methods. b.) The cuff is placed smoothly and snugly around the upper arm and above the brachial artery, at the same height as the heart, while the subject or patient is seated with the arm supported. c.) Top: Cuff pressure (in millimeters of mercury, mmHg) as the cuff is inflated to a pressure exceeding systolic arterial pressure and then reduced to below diastolic pressure. Bottom: Arterial pulses (oscillations) which are caused by bloodflow though the artery, are detected by the blood pressure measurement device, as the cuff is inflated and gradually deflated [2].

Validation of commercially available blood pressure measurement devices using oscillometric waveform simulators, has been dealt with in other studies [2, 1, 4, 20]. However, many questions remain open with regards to the validity of a wide variety of commercially available blood pressure devices [22]. It is the purpose of this study, to evaluate and study

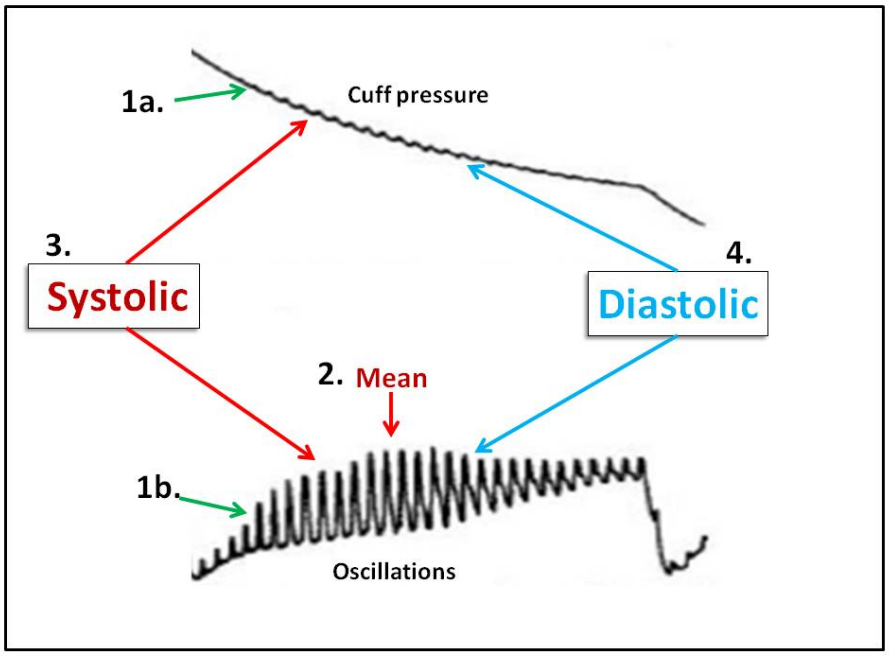


Figure 2: The above illustration is an enlarged and modified version of figure 1c. This illustration shows how cuff pressure decreases as the cuff is gradually deflated. Not pictured is how the blood again begins to flow through the artery, as the pressure in the cuff decreases. 1a) The increased blood flow from the deflation of the cuff, 1b) causes the amplitude of the oscillations detected by the cuff to increase. 2) As the pressure in the cuff further decreases, oscillations reach a maximum. Oscillometric blood pressure devices estimate systolic and diastolic pressures using algorithmic methods. These methods estimate systolic and diastolic pressures based on fixed percentages of mean maximum oscillations. 3) Systolic pressure is estimated based on a fixed percentage of mean maximum oscillations, which corresponds to pressure in mmHg in the cuff. 4) Diastolic pressure is estimated based on a fixed percentage of mean maximum oscillations, which corresponds to pressure in mmHg in the cuff [2].

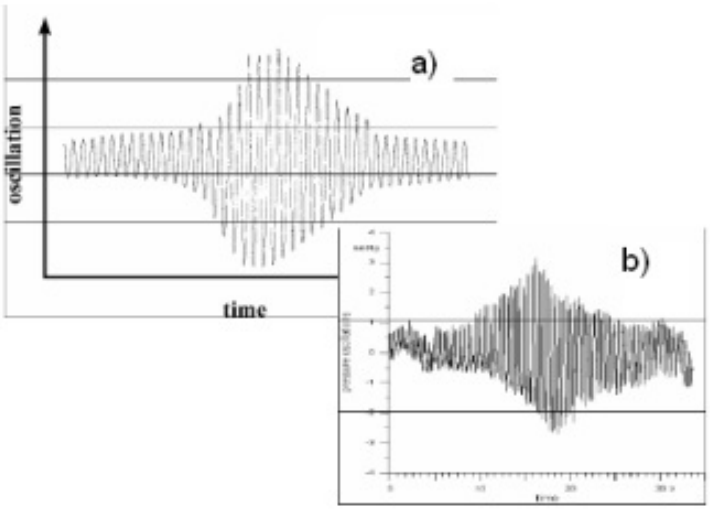


Figure 3: a.) Artifical waveforms as generated by an oscillometric waveform simulator b.) Physiological oscillations as measured from a human upper arm [4].

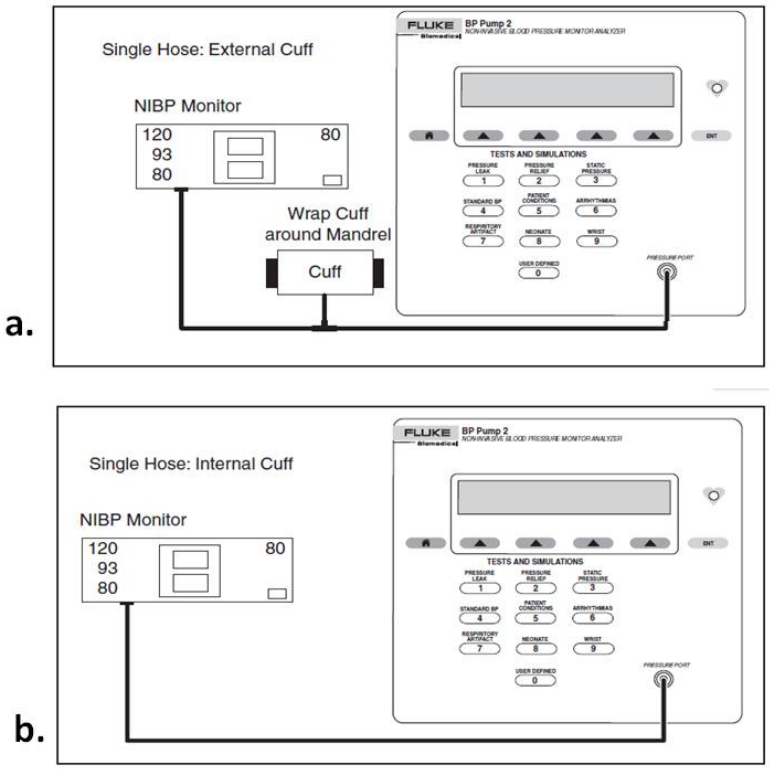


Figure 4: Oscillometric waveform simulators reproduce the physiological and pathological waveforms of human subjects, during a blood pressure measurement sequence [1]. These simulators include a database with oscillometric waveforms from human subjects. a.)Simulators can be used with the external cuff supplied by the blood pressure device manufacturer or b.) they can be used with the internal simulator cuff.

the validity of the measurements provided by two models of commercially available oscillometric blood pressure devices, using an oscillometric waveform simulator. This work was confined to testing commercially available devices, which were acquired by the Department of Procurement and Clinical Engineering, Aarhus University Hospital, in Denmark. The two models of blood pressure measurement devices which were included in this study, were acquired for the purpose of clinical implementation in 2013-2014.

The approach taken was to study how external and internal cuffs could be used to test devices using an oscillomeric waveform simulator, and how differences between measured and simulated pressure could be used to evaluate model validity. Additionally, this work investigated differences within models.

This approach aims at exploring how an oscillometric waveform simulator can be used to assess blood pressure device validity and performance. Furthermore, it is an overall aim of this study to examine how a simulator can be used in the acquisition of blood pressure measurement devices, before these devices are implemented in the clinical domain.

2 Methods

All testing procedures were completed in order to investigate differences between measurements obtained with external and internal cuffs when using an oscillometric waveform simulator, and to study the validity of two different models of blood pressure measurement devices, by simulating 8 physiological conditions. In addition, blood pressure device testing was completed in order to examine differences within models. This study consisted of a total of six testing sessions, which were completed within a time span of 6-7 hours per session. For the theoretical background which is necessary to understand the defined problem, and the work that was completed, see appendix A. For the literature search strategy which was used with this study, see appendix B.

2.1 Instruments

An oscillometric waveform simulator and twenty oscillometric blood pressure measurement devices were utilized. Two different models of oscillometric blood pressure measurement devices were used, ten devices per model, twenty devices in total. All devices were purchased new and unused from the device distributor. All the employed instruments are described below.

The BP Pump 2L Non-invasive Blood Pressure Simulator (Fluke Biomedical, Fluke Corporation USA) is an oscillometric waveform simulator. (Figure 5). This test instrument is a multi-purpose test instrument for use with oscillometric non-invasive blood pressure devices. The simulator is equipped with an internal pump that can generate pressures up to 400 mmHg, and can simulate oscillometric waveforms including adult, neonate, arrhythmias and respiratory artifacts. The BP Pump 2L simulator contains 19 pre-programmed healthy and patient condition simulations. It is also possible to manually program different levels of blood pressure. (Fluke BP Pump 2, Operators Manual). The simulator was calibrated according to the manufacturers instructions. (See certificate of calibration in appendix C).

Figure 5: The Fluke Biomedical BP Pump 2L Non-invasive Blood Pressure Simulator

Model 1 is a fully automated non-invasive blood pressure measurement device. This device inflates automatically using an electric pumping system and takes measurements using the oscillometric method. Measurement is started automatically by having pressed and released the power button. This device has a measurement range of (0-299 mmHg) and a specified measurement accuracy of ± 3 mmHg. This device weighs approximately 380 g, including external cuff and excluding batteries, and can store 28 measurements in its internal memory. Ten Model 1 devices were utilized in this study. (Instruction manual available on request).

Model 2 is a fully automatic non-invasive blood pressure measurement device. This device takes measurements using the oscillometric method and inflation is done automatically using a micropump. Measurement starts automatically after having pressed and released the power button. This device has a measurement range of (20-280 mmHg) and a specified measurement accuracy of ± 3 mmHg. The device weighs approximately 300 g including external cuff and excluding batteries. Ten Model 2 devices were utilized in this study. (Instruction manual, available on request).

2.2 Testing procedures

Device testing was carried out under strictly controlled laboratory conditions. The test laboratory was only used in conjunction with blood pressure device testing during the duration of this study, and the same investigator executed all testing procedures. All instruments were set up in the laboratory before testing commenced, and were not removed from the

Patient Condition	Blood Pressure (mmHg) (MAP)	Heart Rate (bpm)	Pulse volume (cc)
Healthy Heart	120/80 (93)	75	0.68
Weak Pulse	110/80 (90)	95	0.50
Mild Exercise #1	140/90 (106)	120	1.00
Strenuous Exercise #2	140/90 (106)	162	1.40
Obese Subject	120/80 (93)	90	0.50
Geriatric Subject	150/110 (123)	95	0.40
Tachycardia	120/105 (110)	130	0.40
Bradycardia	120/60 (80)	45	1.10

Table 1: Patient condition simulations, using The BP Pump 2L Non-invasive Blood Pressure Simulator.

laboratory or used by others until after completion of all testing sessions.

Blood pressure devices were manually inspected for hose, cuff and device body defects before device testing began. All T-pieces and their associated hoses were manually inspected for leaks. Devices were individually marked with numbers 1-10 for each blood pressure measurement device model.

Devices were tested using the external cuff supplied by the device manufacturer, as well as the internal cuff within the simulator itself. One manufacturer supplied external cuff was used while testing all 10 Model 1 devices (length 125 cm). Accordingly, one manufacturer supplied external cuff was used while testing all 10 Model 2 devices (length 62 cm). Using the internal simulator cuff, the same hose (length 30 cm) was used for testing all Model 1 devices. Accordingly the same hose (length 28,5 cm) was used while testing all Model 2 devices, when using the internal simulator cuff. When testing devices using the external cuff, the cuff was wrapped around the simulator mandrel, and a space of 1 cm was measured between the cuff and the mandrel. The simulator was used to generate physiological and pathological oscillometric waveforms (8 in total), thereby simulating various physiological conditions. (Table 1). Systolic and diastolic pressures were measured simultaneously for each simulation. Devices were tested six times per condition simulation using the external cuff, and six times per simulation using the internal cuff. (Figure 6 and appendix D).

The experimental set-up for device testing consisted of connecting the device to the simulator, and manually registering data into an Excel database. (Excel 2011 Microsoft Office^{TM}). (Figure 6).

2.3 Data analysis

A pilot study was completed to estimate the required sample size, for testing devices using external and internal cuffs. A single Model 1 blood pressure device was used to take 6 measurements during simulations $Healthy$ and $High$. These measurements were taken using both external and internal cuffs. Sample size calculations for two sample means

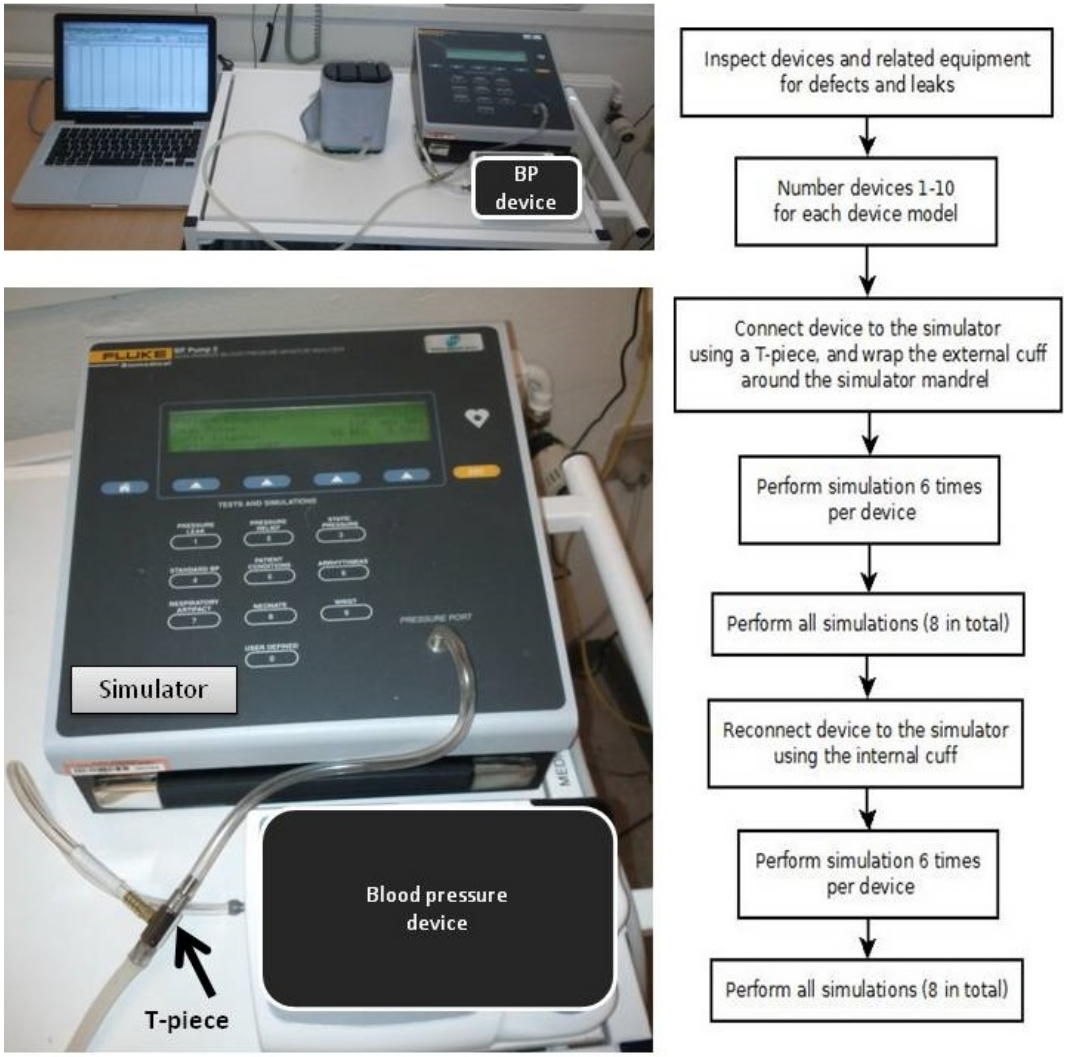


Figure 6: Top: Blood pressure measurement devices were connected to the simulator using an external cuff (pictured) and using the internal simulator cuff (not pictured), and data was registered manually using a laptop computer. Bottom: The simulator was connected to blood pressure measurement devices using a T-piece. Far right: A block diagram for the device testing workflow.

were utilized, to estimate the required sample size for investigating differences between measurements obtained with external and internal cuffs.

A second pilot study was completed to estimate the required sample size, for testing device validity. Measurements acquired using Model 1 and the external cuff during simulations *Healthy* and *High* as described above, were also used for this second pilot test. A single Model 2 blood pressure device was added to this pilot study, and was used to acquire 6 measurements using the external cuff during simulations *Healthy* and *High*. Measurements acquired using both Models 1 and 2 were utilized. Sample size calculations for one sample means were used to estimate the required sample size for investigating blood pressure device validity. The difference to detect was set at 3 mmHg. Power was set at 0,8.

Blood pressure measurement devices were excluded if they were unable to measure pressure three times during the waveform simulation in question. Devices which were unable to successfully measure pressure using both the external and the internal cuff, were excluded solely from the investigation of differences between external and internal cuffs. Devices which were successfully able to measure pressure using only the external cuff, were therefore included in all other investigations carried out in this study.

Statistical analysis was completed using JMP statistical discovery software (SAS^{TM}) and MedCalc statistical software (MedCalc®). Data was tested for normality using the Shapiro -Wilk test. Normally distributed data was described by mean and standard deviation, and non-normally distributed data was described by median, minimum and maximum.

All measurements obtained with the external and the internal cuff, were tested for normality. To investigate differences between measurements obtained with external and internal cuffs, means or medians for the 6 measurements per device were calculated and tested for normality for each simulation, as illustrated in figure 7. Differences between external and internal cuffs were tested for statistical significance using the Wilcoxon Rank Sum test or the Students paired t-test. (Figure 7). Dependant on normality test results, the mean or the median (of the means or medians for the 6 measurements per device), were used to calculate differences between external and internal cuffs. (Differences between cuffs were calculated as: external cuff - internal cuff).

Blood pressure device validity was evaluated by using the Wilcoxon Rank Sum test and by calculating measurement error. Differences between blood pressure device measurements, and the pressure generated by the simulator, were tested for statistical significance using the Wilcoxon Rank Sum test. Medians for the 6 measurements per device for each simulation (external cuff), and pressure (in mmHg) as generated by the simulator, were used for this test. Medians for the 6 measurements per device for each simulation (internal cuff) were tested in the same manner. Measurement error was calculated to determine the degree of closeness between the pressure measured by the blood pressure device (mmHg) and the pressure that was generated by the simulator (mmHg). The mean or the median which was calculated from all measurements for each model that was being tested, and obtained with the external cuff for each simulation, was utilized to determine measurement error. (Figure 7). The same procedure was followed for all measurements obtained with the internal cuff for each model.

Measurement error was determined using the following equation:

$$M_E = m - \mu$$

M_E is measurement error

m is the mean or the median of all measurements obtained by the blood pressure device for the simulation in question

μ is the measurement reference source as generated by the simulator

Graphical representations of calculated measurement errors for the blood pressure devices, and the manufacturer specification accuracy, were constructed for both models for all simulations. The specification accuracy is accuracy as specified in technical specifications provided by the manufacturer. Acceptable measurement error limits were set at $\pm$ 3mmHg [20]. Absolute values for measurement error, values without their sign, were utilized for this graphical comparison.

Differences within models were investigated using the Kruskal -Wallis test. All measurements obtained with the external cuff for each simulation were utilized. Statistical significance was determined at < 0.05.

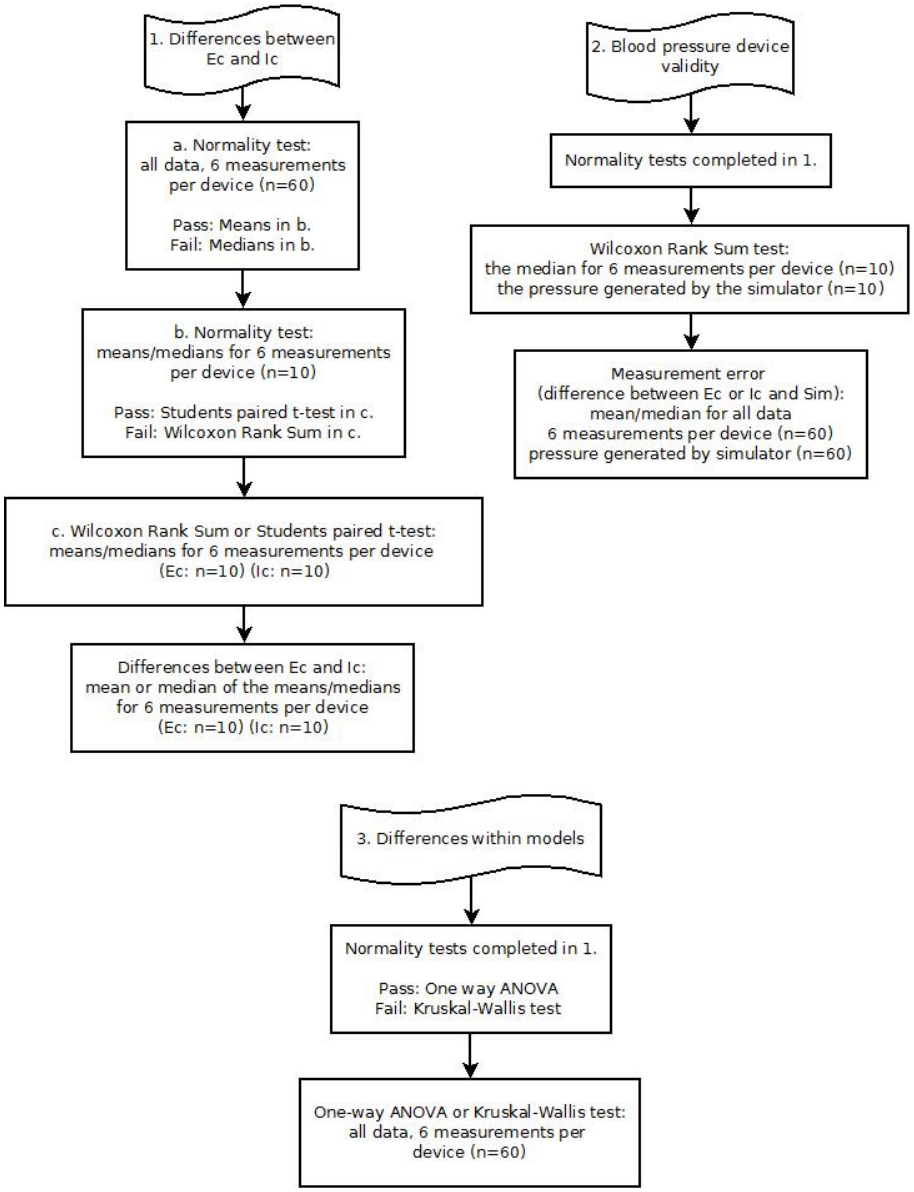


Figure 7: A block diagram of the data analysis procedures used in this study. Iterations are for 10 devices for one simulation. 1) Data analysis procedures for examining differences between measurements obtained with external and internal cuffs. 2) Data analysis procedures for testing blood pressure device validity. 3) Data analysis procedures for investigating differences within models.

3 Results

The following section contains results for all testing procedures. Results are presented for sample size calculations and for differences between measurements obtained with external and internal cuffs. Furthermore, results for the validity of two different models of blood pressure measurement devices, as well as differences within models are shown.

3.1 Sample size determination

Results for sample size calculations are shown in table 2. Sample sizes ranged from 4 to 78 devices in conjunction with examining differences between measurements obtained with external and internal cuffs. Sample sizes were equal to 3 devices in conjunction with testing for measurement validity, for both Model 1 and Model 2.

	External and Internal cuffs		Validity testing (Model 1)		Validity testing (Model 2)	
Simulation	P_s	P_d	P_s	P_d	P_s	P_d
Healthy	78	12	3	3	3	3
High	6	4	3	3	3	3

Table 2: The above table shows results for sample size testing for differences between external and internal cuffs, and validity testing for both blood pressure device models.

3.2 Differences between measurements obtained with external and internal cuffs

Uneven samples sizes were used in connection with Model 1 for a total of three simulations, since individual devices of this model were excluded when using the internal cuff. Not applicable (N/A) was used where relevant. All Model 1 devices were excluded during *Tachycardia* simulations for both external and internal cuffs. Furthermore, 9 devices of this model were excluded during *Obese* simulations using the internal cuff. This model was therefore excluded entirely from this part of the study, for the *Obese* simulation.

All measurements obtained with Model 1 devices using the manufacturer supplied external cuff and the simulators internal cuff were non-normally distributed ($P \leq 0,001$). Therefore the median of the 6 individual measurements per device was calculated. Medians for this model, for the 6 measurements per device employing both cuffs, were both normally and non-normally distributed. (Appendix F).

Results for differences between cuffs ranged from -1 to $2,91$ mmHg. Medians for the 6 measurements per device were used to investigate if there was a significant difference between measurements obtained with the external and internal cuffs. For two simulations it was not possible to calculate a P-value, since too many devices were excluded during these simulations. There was a significant difference between cuffs for all simulations for both P_s and P_d, with the exception of one P_s (one simulation), $P < 0,03$ and $P = 0,8$ respectively. (Table 3). Box plots for medians for measurements obtained with Model 1 devices using external and internal cuffs, can be seen in appendix G.

All measurements obtained with Model 2 devices using the manufacturer supplied external cuff and the simulators internal cuff were non-normally distributed ($P < 0,02$). Therefore the median of the 6 individual measurements per device was calculated. (Appendix F). Medians for this model, for the 6 measurements per device employing both cuffs, were both normally and non-normally distributed. (Appendix F).

Results for differences between cuffs ranged from -1 to 3 mmHg. Medians for 6 measurements per device were used to investigate if there was a significant difference between measurements obtained with the external and internal cuffs. There was a significant difference between cuffs for P_s (5 simulations), and for P_d (4 simulations), ($P \leq 0,02$). (Table 4).

Simulation	P_s External cuff	Min.	Max.	Internal cuff	Min.	Max.	Difference (Ec-Ic)	P-value
Healthy	118 (n=5)	117	119	118 (n=5)	116	118	0	N/A
Weak pulse	108,8 (n=10)	107	117	109 (n=10)	107	110	-0,2	0,8
Mild exercise	142 (n=10)	140	143	140 (n=10)	139	142	2	0,002
Strenuous exercise	144 (n=10)	143	144	143 (n=10)	142	144	1	0,002
Obese	N/A (excluded)			N/A (excluded)				
Geriatric	149,66 (n=6)	145	160	146,75 (6)	145	153	2,91	0,01
Tachycardia	N/A (excluded)			N/A (excluded)				
Bradycardia	123 (n=9)	121	126	121 (n=9)	120	122	2	0,004

Simulation	P_d External cuff	Min.	Max.	Internal cuff	Min.	Max.	Difference (Ec-Ic)	P-value
Healthy	81,2 (n=5)	80	83	81 (n=5)	80	82	0,2	N/A
Weak pulse	82,75 (n=10)	81	84	82 (n=10)	80	83	0,75	0,002
Mild exercise	91,75 (n=10)	90	93	91 (n=10)	89	92	0,75	0,03
Strenuous exercise	90 (n=10)	89	94	91 (n=10)	89	93	-1	0,03
Obese	N/A (excluded)			N/A (excluded)				
Geriatric	114 (n=6)	111	116	113,83 (n=6)	113	115	0,17	N/A
Tachycardia	N/A (excluded)			N/A (excluded)				
Bradycardia	62,5 (n=9)	61	64	60,11 (n=9)	59	61	2,39	0,004

Table 3: The above table shows results for Model 1. The median, minimum and maximum for each simulation as well as number of devices included per simulation, are presented. Results for the Wilcoxon Rank Sum test and the Students paired t-test, as well as results for differences between cuffs are shown. N/A is used where too many devices were excluded during the simulation in question, to be able to calculate a P value. (Statistically significant differences and differences between cuffs exceeding ± 3mmHg are marked in red. Non-significant differences and differences between cuffs within ± 3mmHg, are marked in green.)

There was no statistically significant difference between cuffs for P_s and P_d (3 simulations each), ($P > 0,1$). (Table 4). Box plots for medians for measurements obtained with Model 2 devices using external and internal cuffs, can be seen in appendix G.

Simulation	P_s External cuff	Min.	Max.	Internal cuff	Min.	Max.	Difference (Ec-Ic)	P-value
Healthy	117 (n=10)	115	119	114 (n=10)	114	116	3	0,002
Weak pulse	106 (n=10)	104	109	105 (n=10)	103	106	1	0,002
Mild exercise	132,5 (n=10)	126	141	133 (n=10)	130	141	-0,5	0,6
Strenuous exercise	133,75 (n=10)	132	142	133 (n=10)	131	141	0,75	0,2
Obese	114 (n=10)	113	117	112 (n=10)	110	114	2	0,002
Geriatric	144,25 (n=10)	142	146	142 (n=10)	140	144	2,25	0,002
Tachycardia	118 (n=10)	110	120	118 (n=10)	117	119	0	0,1
Bradycardia	118 (n=10)	111	124	115,9 (n=10)	110	120	2,1	0,007

Simulation	P_d External cuff	Min.	Max.	Internal cuff	Min.	Max.	Difference (Ec-Ic)	P-value
Healthy	82,75 (n=10)	81	86	83,15 (n=10)	81	86	-0,4	0,4
Weak pulse	82,25 (n=10)	81	85	82,5 (n=10)	81	85	-0,25	0,4
Mild exercise	89 (n=10)	86	90	90 (n=10)	87	91	-1	0,0004
Strenuous exercise	85,9 (n=10)	84	87	86 (n=10)	83	88	-0,1	N/A
Obese	84,2 (n=10)	81	86	84,75 (n=10)	82	86	-0,55	0,02
Geriatric	115,45 (n=10)	114	118	116,4 (n=10)	114	118	-0,95	0,001
Tachycardia	106 (n=10)	102	107	106,25 (n=10)	104	108	-0,25	0,02
Bradycardia	61,8 (n=10)	58	66	62 (n=10)	58	70	-0,2	0,6

Table 4: The above table shows results for Model 2. The median, minimum and maximum for each simulation as well as number of devices included per simulation, are presented. Results for the Wilcoxon Rank Sum test and the Students paired t-test, as well as results for differences between cuffs, are shown. N/A is used where it was not possible to calculate a p-value.

3.3 Blood pressure device validity

3.3.1 Model 1

All Model 1 devices were excluded during *Tachycardia* simulations for both external and internal cuffs. Uneven samples sizes were used in connection with Model 1 for a total of three simulations, since individual devices of this model were excluded when using the internal cuff. Not applicable (N/A) was used where relevant.

Using the external cuff, results for measurement error showed that there was a difference exceeding ± 3mmHg for three simulations, for measurements obtained with Model 1 devices. Measurement errors ranged from -2 to 4 mmHg (7 simulations) using the external cuff. When using Model 1 devices with the internal cuff, results for measurement error showed a difference exceeding ± 3mmHg for only one simulation. Measurement errors ranged from -3 to 4 mmHg (7 simulations) when using the internal cuff. (Table 5).

When using the external cuff, results showed a significant difference between measurements obtained with Model 1 devices and the pressure generated by the simulator for both P_s and for P_d, (for 6 simulations each), $P \leq 0,004$. When using the external cuff, there was no significant difference between measurements obtained with Model 1 and the pressure generated by the simulator, for only one simulation for P_s and one simulation for P_d, ($P = 0,9$ and $P = 0,4$ respectively).

Using the internal cuff, results showed a significant difference between measurements obtained with Model 1 devices and the pressure generated by the simulator, for P_s (three simulations) and for P_d (4 simulations), $P \leq 0,03$. When using the internal cuff, there was no significant difference between measurements obtained with Model 1 and the pressure

generated by the simulator, for P_s (three simulations) and for P_d (two simulations), $P > 0,06$. (Table 5). Box plots for all measurements obtained with Model 1 devices can be seen in appendix H.

3.3.2 Model 2

Using the external cuff, results for measurement error showed that there was a difference exceeding ± 3mmHg for 5 simulations, for measurements obtained with Model 2 devices. Measurement errors ranged from $-7,5$ to 5 mmHg (8 simulations) using the external cuff. When using Model 2 devices with the internal cuff, results for measurement error showed a difference exceeding ± 3mmHg for 7 simulations. Measurement errors ranged from -8 to 6 mmHg (8 simulations) when using the internal cuff. (Table 6).

Using the external cuff, results showed a significant difference between measurements obtained with Model 2 devices and the pressure generated by the simulator, for both P_s (8 simulations) and for P_d (7 simulations), $P \leq 0,01$. When using the external cuff, there was no significant difference between measurements obtained with Model 2 devices and the pressure generated by the simulator, for only one simulation for P_d, $(P = 0,5)$.

When using the internal cuff, results showed a significant difference between measurements obtained with Model 2 devices and the pressure generated by the simulator, for both P_s (8 simulations) and for P_d (7 simulations), $P \leq 0,004$. Using the internal cuff, there was no significant difference between generated pressure and measured P_d pressure, for only one simulation($P = 1$). (Table 6). Box plots for all measurements obtained with Model 1 devices can be seen in appendix H.

Graphical representations of calculated measurement errors for blood pressure devices and the manufacturer specification accuracy, (figure 8), showed that neither Model 1 nor Model 2 were able to measure both systolic and diastolic pressures which were within acceptable accuracy limits of ± 3mmHg, for all 8 simulations. Model 1 was able to measure both systolic and diastolic pressure within acceptable accuracy limits, without outliers, for simulations $Healthy$ and $Mild-exercise$. Model 2 was unable to produce measurements for both pressures that were within the set accuracy limits, without outliers, for any simulation. (Figure 8).

Measurement error (based on absolute values) for Model 1 had a minimum of 0 mmHg and a maximum of 10 mmHg, while measurement error for Model 2 had a minimum of 0 and a maximum of 14 mmHg. (Figure 8).

Simulation	P_s External cuff	Min.	Max.	Simulator (Ps)	Measurement error (Ec-Sim)	P-value
Healthy	118 (n=10)	117	119	120 (75 bpm)	-2	0,002
Weak pulse	109 (n=10)	107	117	110 (95 bpm)	-1	0,004
Mild exercise	142 (n=10)	140	143	140 (120 bpm)	2	0,002
Strenuous exercise	144 (n=10)	143	144	140 (162 bpm)	4	0,002
Obese	118 (n=10)	116	120	120 (90 bpm)	-2	0,002
Geriatric	150 (n=10)	145	160	150 (95 bpm)	0	0,9
Tachycardia	N/A (excluded)			120 (130 bpm)	N/A	
Bradycardia	123 (n=10)	121	126	120 (45 bpm)	3	0,002

Simulation	P_d External cuff	Min.	Max.	Simulator (Pd)	Measurement error (Ec-Sim)	P-value
Healthy	82 (n=10)	80	83	80 (75 bpm)	2	0,004
Weak pulse	83 (n=10)	81	84	80 (95 bpm)	3	0,002
Mild exercise	92 (n=10)	90	93	90 (120 bpm)	2	0,004
Strenuous exercise	90 (n=10)	89	94	90 (162 bpm)	0	0,4
Obese	84 (n=10)	82	85	80 (90 bpm)	4	0,002
Geriatric	114 (n=10)	111	116	110 (95 bpm)	4	0,002
Tachycardia	N/A (excluded)			105 (130 bpm)	N/A	
Bradycardia	62 (n=10)	61	64	60 (45 bpm)	2	0,002

Simulation	P_s Internal cuff	Min.	Max.	Simulator (Ps)	Measurement error (Ic-Sim)	P-value
Healthy	118 (n=5)	116	118	120 (75 bpm)	-2	0,06
Weak pulse	109 (n=10)	107	110	110 (95 bpm)	-1	0,002
Mild exercise	140 (n=10)	139	142	140 (120 bpm)	0	0,1
Strenuous exercise	143 (n=10)	142	144	140 (162 bpm)	3	0,002
Obese	117,2 (n=1)	116	119	120 (90 bpm)	-2,8	N/A
Geriatric	147 (n=6)	145	153	150 (95 bpm)	-3	0,6
Tachycardia	N/A (excluded)			120 (130 bpm)	N/A	
Bradycardia	121 (n=9)	120	122	120 (45 bpm)	1	0,008

Simulation	P_d Internal cuff	Min.	Max.	Simulator (Pd)	Measurement error (Ic-Sim)	P-value
Healthy	81 (n=5)	80	82	80 (75 bpm)	1	0,1
Weak pulse	82 (n=10)	80	83	80 (95 bpm)	2	0,002
Mild exercise	91 (n=10)	89	92	90 (120 bpm)	1	0,004
Strenuous exercise	91 (n=10)	89	93	90 (162 bpm)	1	0,004
Obese	83 (n=1)	82	84	80 (90 bpm)	3	N/A
Geriatric	114 (n=6)	113	115	110 (95 bpm)	4	0,03
Tachycardia	N/A (excluded)			105 (130 bpm)	N/A	
Bradycardia	60 (n=9)	59	61	60 (45 bpm)	0	0,6

Table 5: The above tables show results for the validity of Model 1 devices using external and internal cuffs. The median, minimum and maximum for each simulation as well as the number of devices included in each simulation, are shown. Results for the Wilcoxon Rank Sum test and for measurement error (M_E) are presented. These results show differences between measurements obtained with external and internal cuffs, and the pressure that was simulated by the simulator. (Statistically significant differences and differences exceeding ± 3mmHg are marked in red, and non-significant differences as well as differences within ± 3mmHg are marked in green.)

Simulation	P_s External cuff	Min.	Max.	Simulator (Ps)	Measurement error (Ec-Sim)	P-value
Healthy	117 (n=10)	115	119	120 (75 bpm)	-3	0,002
Weak pulse	106 (n=10)	104	109	110 (95 bpm)	-4	0,002
Mild exercise	132,5 (n=10)	126	141	140 (120 bpm)	-7,5	0,002
Strenuous exercise	134 (n=10)	132	142	140 (162 bpm)	-6	0,002
Obese	114 (n=10)	113	117	120 (90 bpm)	-6	0,002
Geriatric	144 (n=10)	142	146	150 (95 bpm)	-6	0,002
Tachycardia	118 (n=10)	110	120	120 (130 bpm)	-2	0,002
Bradycardia	118 (n=10)	111	124	120 (45 bpm)	-2	0,01

Simulation	P_d External cuff	Min.	Max.	Simulator (Pd)	Measurement error (Ec-Sim)	P-value
Healthy	83 (n=10)	81	86	80 (75 bpm)	3	0,002
Weak pulse	82 (n=10)	81	85	80 (95 bpm)	2	0,002
Mild exercise	89 (n=10)	86	90	90 (120 bpm)	-1	0,008
Strenuous exercise	86 (n=10)	84	87	90 (162 bpm)	-4	0,002
Obese	84 (n=10)	81	86	80 (90 bpm)	4	0,002
Geriatric	115 (n=10)	114	118	110 (95 bpm)	5	0,002
Tachycardia	106 (n=10)	102	107	105 (130 bpm)	1	0,5
Bradycardia	62 (n=10)	58	66	60 (45 bpm)	2	0,004

Simulation	P_s Internal cuff	Min.	Max.	Simulator (Ps)	Measurement error (Ic-Sim)	P-value
Healthy	114 (n=10)	114	116	120 (75 bpm)	-6	0,002
Weak pulse	105 (n=10)	103	106	110 (95 bpm)	-5	0,002
Mild exercise	133 (n=10)	130	141	140 (120 bpm)	-7	0,002
Strenuous exercise	133 (n=10)	131	141	140 (162 bpm)	-7	0,004
Obese	112 (n=10)	110	114	120 (90 bpm)	-8	0,002
Geriatric	142 (n=10)	140	144	150 (95 bpm)	-8	0,002
Tachycardia	118 (n=10)	117	119	120 (130 bpm)	-2	0,002
Bradycardia	116 (n=10)	110	120	120 (45 bpm)	-4	0,002

Simulation	P_d Internal cuff	Min.	Max.	Simulator (Pd)	Measurement error (Ic-Sim)	P-value
Healthy	83 (n=10)	81	86	80 (75 bpm)	3	0,002
Weak pulse	83 (n=10)	81	85	80 (95 bpm)	3	0,002
Mild exercise	90 (n=10)	87	91	90 (120 bpm)	0	1
Strenuous exercise	86 (n=10)	83	88	90 (162 bpm)	-4	0,002
Obese	85 (n=10)	82	86	80 (90 bpm)	5	0,002
Geriatric	116 (n=10)	114	118	110 (95 bpm)	6	0,002
Tachycardia	106 (n=10)	104	108	105 (130 bpm)	1	0,004
Bradycardia	62 (n=10)	58	70	60 (45 bpm)	2	0,002

Table 6: The above tables show results for the validity of Model 2 devices using external and internal cuffs. The median, minimum and maximum for each simulation as well as the number of devices included in each simulation, are shown. Results for the Wilcoxon Rank Sum test and for measurement error (M_E) are presented. These results show differences between measurements obtained with external and internal cuffs, and the pressure that was simulated by the simulator.

3.4 Differences within models

There was a significant difference between measurements produced by Model 1 devices when measuring P_s (5 simulations), $P \leq 0,03$. There was no significant difference between Model 1 devices for P_s (two simulations), $P = 0,09$ and $P = 0,1$ respectively. Using Model 1 devices there was a significant difference between for P_d for all simulations,($P \leq 0,04$). (Table 7).

Using Model 2 devices there was a significant difference between devices when measuring P_s (one simulation), $P = 0,008$. There was no significant difference between devices of this

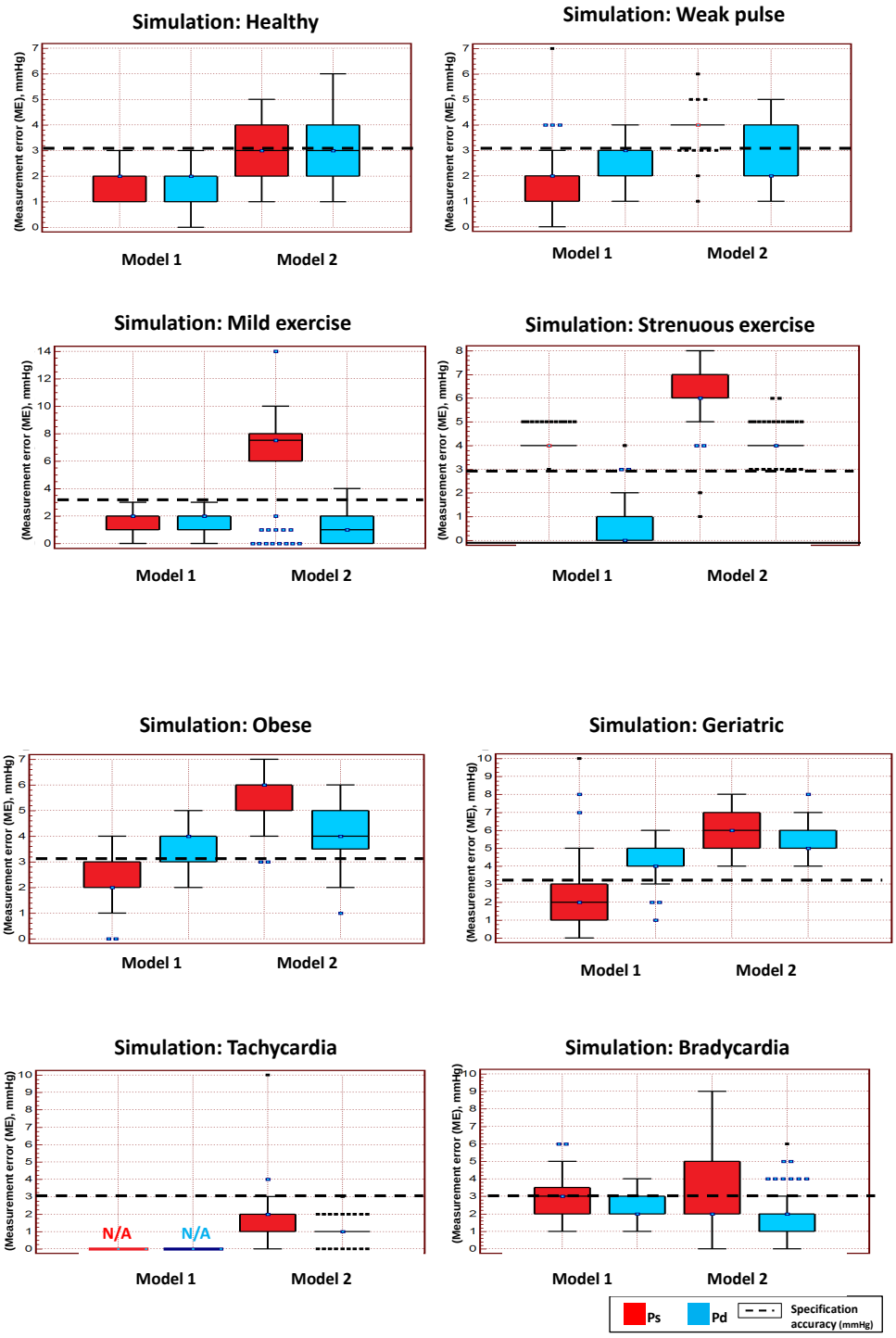


Figure 8: The above figure is a graphical representation of measurement errors (M_E), in absolute values for both models, and the manufacturer specified accuracy (the dotted line), for both models for all simulations.

Simulation	P-value (P_s)		P-value (P_d)	
	Model 1	Model 2	Model 1	Model 2
Healthy	0,0002	0,3	$< 0,0001$	$< 0,0001$
Weak pulse	0,09	0,4	0,005	$< 0,0001$
Mild exercise	0,03	0,2	0,002	0,006
Strenuous exercise	0,02	0,7	0,04	$< 0,0001$
Obese	0,02	0,2	$< 0,0001$	$< 0,0001$
Geriatric	0,1	0,008	0,009	$< 0,0001$
Tachycardia	N/A	0,3	N/A	$< 0,0001$
Bradycardia	0,0003	0,08	0,0001	0,0007

Table 7: The above table shows results for differences within models, for both Model 1 and Model 2. Results from the Kruskal -Wallis test are shown.

model for P_s (7 simulations),$P \geq 0,08$. There was a significant difference between Model 2 devices for P_d for all simulations, $P \leq 0,006$. (Table 7).

4 Discussion

This study explored how external and internal cuffs could be used to test two different models of blood pressure devices using an oscillomeric waveform simulator. Additionally, differences between the measurements produced by blood pressure devices and the pressure generated by the simulator were used to assess model validity, and differences within models were investigated. Lastly, it was an overall aim of this work to evaluate how a simulator could be used in the acquisition of blood pressure measurement devices, before these devices are implemented in the clinical domain.

4.1 Differences between external and internal cuffs

It is reported that it is common practice to use the manufacturer supplied external cuff, when testing devices using an oscillometric waveform simulator [23, 2]. However, various simulators come equipped with an internal cuff, and not all studies specify whether they use the manufacturer supplied external cuff, or the internal simulator cuff [1, 11]. It was therefore an objective of this study, to examine if there were significant differences in measurements obtained with external and internal cuffs.

Significant differences were observed between measurements obtained with external and internal cuffs for both Model 1 and Model 2 devices. However, differences between measurements obtained with both cuffs did not exceed acceptable measurement limits of $\pm$ 3 mmHg, during any of the 8 simulations [20, 14]. (Tables 3 and 4).

It was of interest that out of a total of 480 measurements possible, using the simulator internal cuff, over 90 error readings were generated by Model 1 devices. During *Tachycardia* simulation, devices of this model were unable to produce measurements at all, for far the majority of measurements. In addition, devices of this model sporadically generated measurements during *Tachycardia* simulation, which deviated from simulated pressure to such an extent as to not be viable at all. It has been described elsewhere that the algorithms blood pressure devices employ are cuff specific, and it is therefore not recommended to use cuffs other than the manufacturer supplied cuff when testing blood pressure devices [7, 5]. Based on the many error readings generated by Model 1 devices while using the internal

simulator cuff, algorithmic incompatibility with the internal simulator cuff appears to be a likely explanation for these many error readings. No error readings were generated by Model 2 while using either the external cuff of the internal simulator cuff.

Interestingly the hoses used with external and internal cuffs were of considerably different lengths. The external cuff hose used with Model 1 measured 125 cm, while the hose used with the internal simulator cuff for this model measured 30 cm. The hoses used with Model 2 were also of different lengths, 62 cm (external cuff) and 28,5 cm (internal cuff). The differing lengths of these hoses may have had an affect on the measurements obtained with these blood pressure measurement devices. It is possible that air was lost during cuff inflation and deflation with use of the external cuffs hoses, as a consequence of the extra hose length. Additionally, cuff bladder sizes and the material from which these are made most likely vary between manufacturers [7, 5], (i.e. the bladder is the inflatable bag built into the cuff which is inflated during blood pressure measurement), and there was therefore most likely a difference between the cuff bladder sizes of the cuffs used in this study. If the internal simulator cuff bladder was not the same size as the external cuff bladders, this could have had an influence on the obtained measurements.

Algorithmic methods are used to inflate and deflate both external and internal cuffs, and these algorithms vary between manufacturers [4, 2, 5, 3, 7]. This was most likely a further source of variability and is further discussed in section 4.3.2. These findings for differences between measurements obtained with external and internal cuffs suggest that it isn't suitable to use external and internal cuffs interchangeably, when testing oscillometric blood pressure measurement devices.

4.2 Questionable validity of both models

Technical specifications for both Model 1 and Model 2 specify that devices of these models are capable of producing measurements within accuracy limits of ± 3 mmHg. However, neither model was able to produce meausurements within these accuracy limits for all 8 simulations. Although this suggests unacceptable validity and performance of both models, there are conflicting opinions regarding acceptable accuracy limits [13, 3, 20, 14]. European standard EN 1090 specifies that measurement error may not exceed ± 5 mmHg [13], and a deviation within ± 5 mmHg is described as acceptable in [3]. However, other studies report that a deviation greater than ± 3 mmHg can be deemed a device malfunction [20, 14],

Significant differences were observed between measurements obtained with Model 1 devices, and the pressure generated by the simulator, for the majority of simulations. Likewise, there were significant differences between measurements obtained with Model 2 devices, and pressure generated by the simulator, for the vast majority of simulations. Nevertheless, significant differences did not necessarily correspond with unacceptable measurement error. (Tables 5 and 6).

All measurement errors exceeding ± 3 mmHg for Model 1, were equal to 4 mmHg, whereas measurements errors for Model 2 ranged from -8 to 6 mmHg, thereby deviating considerably from the manufacturer specified measurement accuracy of ± 3 mmHg. The differing measurement errors for both models, as well as the inability of Model 1 to produce

measurements during *Tachycardia* simulations, suggest that these device models employ different blood pressure estimation algorithms.

Interestingly, two out of three simulations in which measurement error for Model 1 exceeded ± 3 mmHg, involved use of pressures which were the highest of all 8 simulations. (Table 1). Sim et al. have previously described that measurement error increased with systolic and diastolic pressures [23]. Three out of five simulations in which measurement errors for Model 2 exceeded ± 3 mmHg, also involved use of pressures which were the highest of all 8 simulations. This would suggest that it is likely that measurement error for both models increased with systolic and diastolic pressures. The further discussion of sources of measurement error can be found in the following section.

4.3 Sources of measurement error

Findings from this work suggest questionable validity of both models, however there are a variety of factors which may have had an influence on the obtained results. Possible sources of measurement error are discussed in this section.

4.3.1 Differing simulator employed algorithms

The simulator which was used for this study has been used in other studies [23, 1] and was calibrated according to the manufacturers instructions [11]. (Appendix C). Additionally, a single Model 1 blood pressure measurement device was tested using both the above-mentioned simulator, as well as a second simulator from another manufacturer. This was completed in order to ensure that differences between simulators did not exceed ± 3 mmHg. The obtained results showed that differences between measurements obtained using both simulators were within accuracy limits of ± 3 mmHg. Nevertheless, differences between simulators ranged from -2,8 mmHg to 1,5 mmHg. It was therefore not possible to reject that the simulator had an influence on the validity of the results obtained with the blood pressure measurement devices. (Appendix I).

Simulator validation is discussed in various other studies, however, there are conflicting opinions with regards to the suitability of using these simulators for blood pressure device validation [1, 23, 2, 4, 5]. It is therefore at present unclear the extent to which simulator validation is suitable, for validating oscillometric blood pressure devices.

Manufacturer specific proprietary algorithms are not limited solely to oscillometric blood pressure devices. Simulators themselves generate manufacture specific proprietary artificial oscillometric waveforms, and there are reports that they are not suitable for testing blood pressure device accuracy [23, 5, 7]. Additionally, it is probable that simulator manufacturers use different patient groups when collecting waveforms for simulator databases, which may contribute to inconsistencies between simulators [4, 5]. A team in Newcastle, UK measured the repeatability of three osillometric waveform simulators and found significant differences between simulators [23]. Furthermore, results from the above-mentioned study showed that different waveform shapes were generated by each simulator for the same blood pressure measurement settings, thereby confirming that there is no standard algorithm for blood pressure measurement [23].

Ideally, simulators should be able to generate waveforms which reproduce human oscillometric waveforms, in a way that is as accurate as possible. However, the physiological waveforms that simulators attempt to reproduce are very complex in nature, and it is therefore very difficult to realistically reproduce these waveforms [4, 1]. The majority of commercially available simulators generate waveforms which are smooth and regular in shape, when in reality, physiological waveforms are more irregular in shape and vary between patient groups. (Appendix A). (Figure 3). It is described that the smoothness of these waveforms affects the ability of a simulator to test for accuracy, since blood pressure device algorithms are developed for use with irregular human waveforms [5, 3]. Be that as it may, studies claim that oscillometric waveform simulators are adequately able to test repeatability and reproducibility [4, 2].

Overall it remains unclear to which extent the simulator may have had an influence on results for device validity, using two different models of blood pressure measurement devices.

4.3.2 Differing blood pressure device employed algorithms

Various studies report that different blood pressure device models, employ different manufacturer specific proprietary algorithms, which consequently result in different blood pressure estimations between models [4, 2, 5, 3, 7].

The wide range of measurement errors which were observed in this study, -3 to 4 mmHg (Model 1), and -8 to 6 mmHg (Model 2), suggest that the different algorithms employed by these devices, were a likely cause of this lack of measurement validity.

Balestieri and Rapuano describe that there are a wide variety of differences in the algorithms which are employed by blood pressure devices [5]. Different methods are used for measuring oscillometric amplitude, and different methods are used for averaging mean oscillation amplitude [5]. Balestieri and Rapuano report that the ratios used to estimate systolic and diastolic pressures (A_s/A_m and A_d/A_m ratios respectively, see appendix A.4.2), vary between studies and vary greatly from textbook definitions of these ratios [5, 3, 6]. A_s/A_m ratios ranging from 0,45-0,64 (textbook A_s/A_m ratio = 0,55), and A_d/A_m ratios ranging from 0,59-0,89 (textbook A_d/A_m ratio = 0,85), have been observed [5, 3, 6]. Amoore et al. state that the characteristics of the ratios used by different manufacturers are unknown, and that it remains unclear whether manufacturers include other factors in their algorithms [3]. Additionally, Amoore et al. describe that slope-based algorithms are employed by some manufactures, where the points of maximum slope of the oscillometric waveform on each side of maximum oscillations, are used to estimate systolic and diastolic pressures [3].

Although it would appear that algorithm standardization is necessary, algorithm standardization is difficult since algorithms are developed for use with the manufacturer supplied cuff [5, 20]. Colak and Isik report that most blood pressure devices employ not only a blood pressure estimation algorithm, but a control algorithm as well [7]. The control algorithm is cuff specific, controls cuff inflation and deflation and also varies between manufacturers [7].

Information about the algorithms which are employed by Model 1 and Model 2 was not available to this investigator. It was therefore not possible to further investigate how these proprietary algorithms may have affected the measurements obtained using these two different blood pressure device models.

4.3.3 Lack of pressure transducer calibration

The importance of blood pressure device pressure transducer calibration, has been described by Balestrieri et al. [4]. It is described that there are two primary uncertainties which affect oscillometric blood pressure devices [4]. Namely, uncertainties surrounding the algorithms which estimate blood pressure as described in the previous section, and lack of calibration of the pressure transducer [4]. Balestrieri et al. propose that a common cause of over and under identification of hypertension, is a lack of pressure transducer calibration [4]. This can have a life altering affect for the individuals, on whom these measurements are taken. Under identification of hypertension can result in an individual not getting necessary drug treatment, whereas over identification of hypertension can result in an individual unnecessarily being commenced on lifelong blood pressure lowering drug treatment [15].

As described in section 4.3.1, it is not unlikely that oscillometric waveform simulators can be used to test blood pressure device repeatability and reproducibility. Because of their ability to repeatedly generate smooth and regular waveforms, it would appear likely that a simulator could be used to calibrate blood pressure device pressure transducers.

Further studies are needed in order to conclude how, and if, a lack of pressure transducer calibration played a role in the observed measurement errors for measurements obtained with Model 1 and Model 2 devices.

4.4 Differences within models

Significant differences were observed between the 10 devices for each model. All Model 1 devices were excluded during *Tachycardia* simulations, and significant differences were examined for the vast majority of simulations for Model 1. No significant differences were observed for all but one simulation (*Geriatric*) for systolic pressures, using Model 2 devices. However, using Model 2 devices there were significant differences for diastolic pressures for all simulations. It was beyond the scope of this study to investigate measurement error within models, and to investigate if significant differences within models corresponded with measurement errors exceeding ± 3 mmHg.

Sims et al. describe that many blood pressure measurement devices perform well with regards to repeatability [24]. Nineteen commercially available blood pressure measurement models were used in the above-mentioned study, and differences within models and between models were investigated [24]. Differences within models were 1,22 mmHg (systolic pressure) and 0,83 mmHg (diastolic pressure), and thereby well within acceptable accuracy limits of ± 3 mmHg [24]. However, differences between models were 4,4 mmHg (systolic pressure) and 3,6 mmHg (diastolic pressure). These results suggest that differences between models are most likely caused by differences in the manufacturer specific algorithms [24].

With regards to the present work, it is unclear whether environmental factors or technological factors of manufacture and assembly, could potentially have had an influence on Model 1 and Model 2 devices. This could include device damage during shipping, inadequate pressure transducer calibration, insufficient performance inspections by the manufacturer, or insufficient device assembly. At present, it remains unclear to which extent these or other factors may have had an influence on these devices. Furthermore, further studies are needed

in order to conclude if significant differences between devices for both models correspond with differences exceeding acceptable accuracy limits.

4.5 Future application of simulator validation

At present clinical validation trials are the only approved method of validating oscillometric blood pressure measurement devices [1]. However, clinical trials are costly and time consuming and there are therefore many commercially available devices that may not have been clinically validated [23]. Blood pressure measurement device validation is imperative, before these devices are implemented in the clinical domain [23, 4]. It is reported that oscillometric blood pressure devices are not suitable for all patient groups, and that blood pressure devices employing the oscillometric technique cannot estimate blood pressure accurately for patients suffering from diabetes or preeclampsia [3]. It is therefore critical that devices are tested for validity before they are put into use [3].

Although it is suggested that oscillometric waveform simulators may be lacking in their ability to test blood pressure device accuracy, there are various claims that they have the potential to replace clinical validation trials [4, 20, 23]. This is likely based in claims of their ability to test blood pressure device repeatability and reproducibility [23, 4]. This is possibly a consequence of a simulators ability to generate waveforms which are stable, unlike human physiological waveforms which can be influenced by movement, coughing or other factors [4].

In theory, the more physiological waveforms a simulator database contains, the more realistically it will be able to simulate various physiological conditions [2, 7, 20]. However, others report that it is debatable whether most simulators contain a physiological database, which is extensive enough to sufficiently test oscillometric blood pressure device accuracy [4, 23]. Balestrieri et al. describe that this has led to the development of an EU database for oscillometric waveforms [4]. It is stated that one of the objectives of the database project is to develop a simulator which is capable of generating realistic oscillometric waveforms based on a library of pre-recorded waveforms from a wide variety of patient groups [4]. This is in contrast to commercially available simulators which generate articial waveforms, which are not based on pre-recorded human physiological waveforms [4]. Riedel et al. claim to have developed a simulator which can test for accuracy more accurately than clinical trials, and report that 4 of these simulator prototypes are currently used for clinical research purposes in hospitals in Europe and in Asia [20]. These simulator prototypes also make use of a database of pre-recorded patient waveforms, and have the advantage of being able to generate unusual or irregular waveforms, repeatedly and reproducibly [20].

The development of simulators which employ pre-recorded human waveforms databases, shows great promise with regards to future simulator evaluation of blood pressure devices.

With regards to simulator use with the present study, it is noteworthy that the simulator was easy to use and that testing procedures were relatively easy to set up. The simulator did not come equipped with a selection of T-pieces and hoses, and it was therefore necessary to acquire the necessary hoses and T-pieces elsewhere. The simulator itself was designed for portability, and could easily be moved from one laboratory to another with use of a

small trolley. The simulator control panel was user-friendly, and it was easy to navigate between pre-installed physiological simulations. Furthermore, the simulator settings were very flexible and additional simulations could be defined manually by the user, with basic assistance from the simulator operator manual. Although testing procedures were very time consuming and involved a great deal of concentration, it was this investigators experience that simulator evaluation involved simple and manageable laboratory procedures.

4.6 Study weaknesses

Although this study was carefully prepared, this work also had its limitations and shortcomings.

One of the major limitations of this study was with regards to time constraints. Consequently, it was not possible to test more than twenty blood pressure measurement devices in total, within the time frame at hand, even though this was not in accordance with results for sample size determinations. Sample size determinations for differences between external and internal cuffs showed that more than 10 models per device should be tested. However, sample size calculations for blood pressure device validity showed that it was necessary to test 3 devices per model. It was therefore determined that 10 devices of each model would be tested for use with this study.

Testing procedures themselves were tedious and it was disadvantageous that manual data entry was necessary. Testing sessions lasted for several hours and required a great deal of concentration. This level of concentration could have had an affect on data entry as a result of human error. The quality of the data entered could have been affected by the length of the testing sessions, and it is possible that data was mistyped or entered in the wrong fields.

With regards to test equipment, it was a study weakness that it was not possible to repeat all test procedures using more than one simulator. The simulator used in this study was used as a measurement reference source, however, it is not possible to conclude that the simulator itself produced accurate simulations. With regards to other test equipment, all T-pieces and hoses were not original simulator accessories and were not provided by the simulator manufacturer. These T-pieces and hoses were purchased aftermarket and it is unclear if this may have had an affect on the obtained measurements. Furthermore, all T-pieces and hoses were manually inspected for leaks, and it is therefore possible that the employed hoses were not entirely air tight.

Much of the literature which this work refers to involves research and development of oscillometric waveform simulators, as well as research regarding how simulators can be used to validate blood pressure devices. Authors of these papers may have an interest in promoting the simulators they themselves develop, or in promoting the simulation evaluation procedures they themselves describe.

4.7 An acquisition and quality assurance model, for simulator evaluation of blood pressure devices

At present blood pressure measurement devices are not tested for validity by the Department of Procurement and Clinical Engineering, Aarhus University Hospital, Denmark, before they

are implemented in the clinical domain. These blood pressure measurement devices are purchased directly from the manufacturer and device suppliers and are delivered "as is" to hospital departments. The Department of Procurement and Clinical Engineering is dependant on information regarding the validity of the measurements produced by these devices, as specified by blood pressure device manufacturers. Information regarding measurement validity is specified as accuracy in ± mmHg.

Findings from this work suggest that there can be discrepancies between manufacturer specified technical specifications and the actual measurements that these devices are able to produce. Furthermore, there is no "one-size fits all" when procuring blood pressure devices, and findings from this study suggest that different blood pressure device models have different weaknesses and strengths.

The testing procedures which were completed in this work were tedious and time consuming, and it is therefore unlikely that these extensive testing procedures could successfully be implemented in Clinical Engineering departments. Alternative acquisition and quality control models are needed, if blood pressure device testing is to be incorporated in device acquisition processes in Clinical Engineering departments.

As illustrated in figure 9, findings from this study could be used to design an acquisition and quality assurance model, for simulator evaluation of blood pressure devices. This model could contribute to minimising the risk of implementing blood pressure devices which are dysfunctional, as well as ensuring that only blood pressure devices which are capable of producing measurements within acceptable measurement limits, are implemented in the clinical domain. The proposed model could be used both before, and after, blood pressure device implementation.

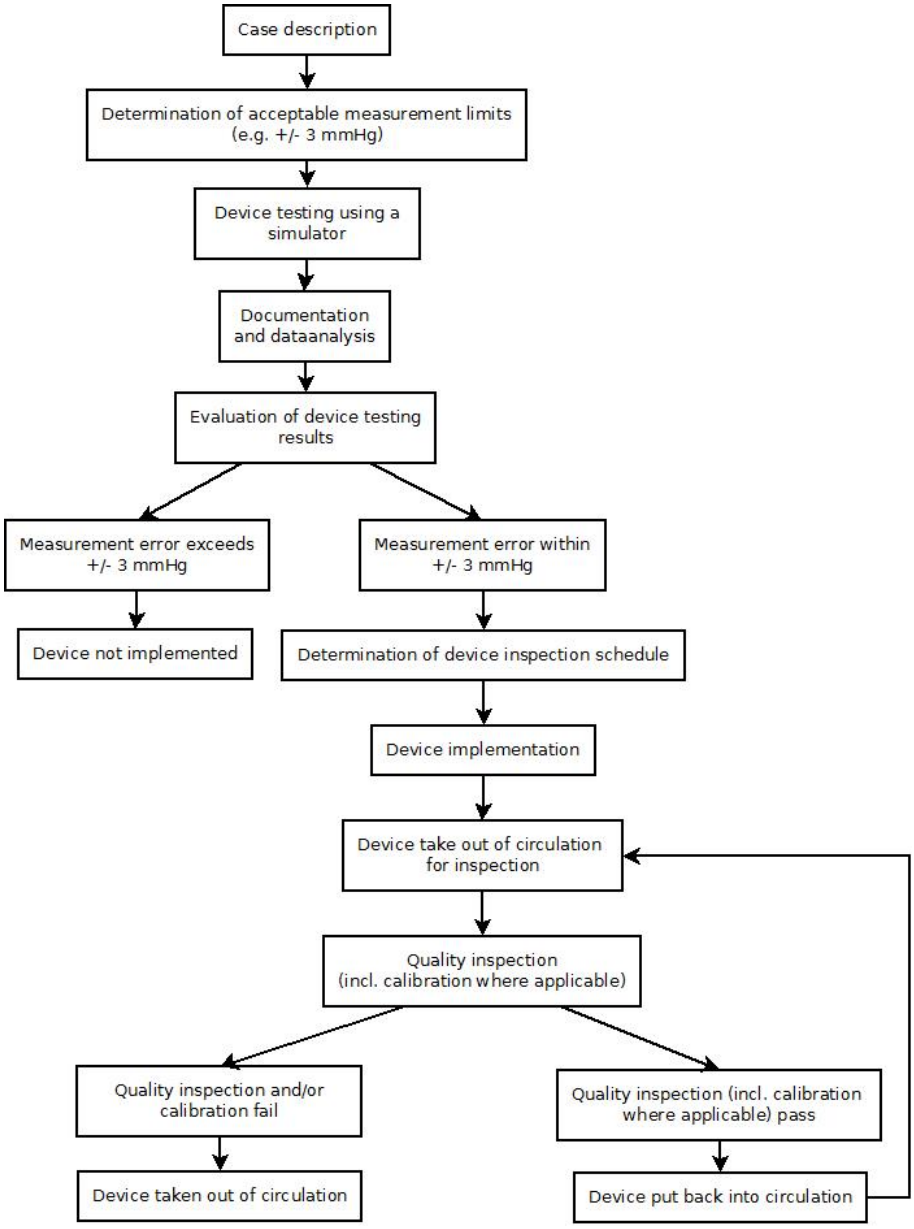


Figure 9: The proposed acquisition and quality assurance model, for use with oscillometric blood pressure measurement devices is shown. This model is intended to be flexible, so that its use corresponds to the individual capacities of Clinical Engineering departments. Use of this model involves device testing procedures, documentation and data analysis of test measurements and evaluation of the generated test results. Devices are implemented or returned to manufacturers based on these evaluations. Devices which are implemented are taken out of circulation for quality inspections at pre-determined intervals, and are inspected for defects and calibrated according to manufacturer specifications. Defective devices are discarded and devices which pass quality control inspections are put back into circulation, until the next quality control inspection is scheduled.

5 Conclusions

The reported findings showed that it was not possible to use external and internal cuffs interchangeably for both blood pressure measurement device models. A lack of consistency between manufacturer supplied technical specifications, and the measurements produced by blood pressure devices, showed that neither Model 1 or Model 2 performed well enough to justify implementing solely one or the other in the clinical domain. However, a variety of factors may have had an influence on the validity of the measurements obtained with Model 1 and Model 2 devices. This may include, but is not limited to, simulator and blood pressure device employment of proprietary and differing algorithms, and measurement variability caused by a lack of pressure transducer calibration. Furthermore, this work illustrated significant differences within models, however, it was beyond the scope of this study to investigate this any further.

In conclusion this study highlights the importance of validating blood pressure measurement devices before they are implemented and taken into use at hospital departments. It was proposed that findings from this study could be used to design an acquisition and quality assurance model, for the evaluation of blood pressure devices. Although research shows great promise with regards to simulator evaluation of blood pressure devices, there is still a lack of clarity regarding the extent to which this can be used to test device accuracy. Lastly, further studies are needed to increase the understanding of the oscillometric method and oscillometric waveforms, so that improved blood pressure devices and oscillometric waveform simulators can be designed.

6 Future perspectives

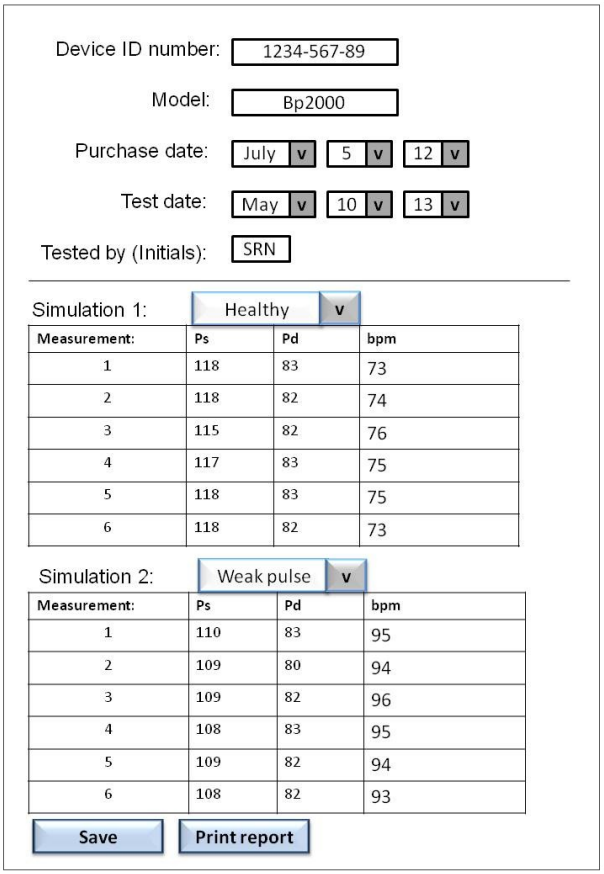
Findings from this work illustrate the importance of conducting oscillometric blood pressure device validation, before these devices are taken into use. Furthermore, these findings suggest that it is advisable that blood pressure devices are tested for validity by Clinical Engineering departments, before these devices are implemented in the clinical domain. Various simulator prototypes are under development, some of which have the potential to emulate clinical trials even more closely than is possible with existing simulators [4, 20]. These simulators offer promising prospects of simulator validation, in particular if they are integrated with more extensive physiological waveform databases. The present study has provided at least as many new questions, as it has supplied answers for existing ones. The many sources of measurement error and the complexity of the oscillometric technique, show promise as areas of interest for future studies.

The significance of measurement validity is not limited to blood pressure measurement devices alone, but is likely also of great importance with regards to medical equipment in general. Future development of quality assurance guidelines could contribute to improving the quality of the medical equipment that is implemented in hospital departments, as well as improving cost-effectiveness. Such quality assurance guidelines could be beneficial for Clinical Engineering departments in Denmark, as well as Clinical Engineering departments abroad. As illustrated in figure 10, aspects of the statistical and experimental design of this

study could be used to develop a computer program for validity testing. This could be used as a tool in the acquisition and quality assurance model, previously described in this work. A computer program for validity testing could take the form of a computer program where experimental data from device testing is input, and is saved as a data output file. This data output file could then be used to generate a validity report printout. The validity report printout could be used by biomedical technicians to document and evaluate device validity before devices are used in clinical settings.

The medical equipment procurement process is complex and Clinical Engineering departments are at present, primarily dependant on information regarding equipment validity and performance, as provided by equipment manufacturers. Quality assurance procedures are not intended as a means of replacing the necessary cooperation between Clinical Engineering departments and equipment manufacturers. To the contrary, open communication and the sharing of equipment performance experiences could strengthen this cooperation.

Finally, quality assurance guidelines could contribute to safeguarding the development and implementation of high-quality medical equipment, thereby contributing to improving patient treatment and care.



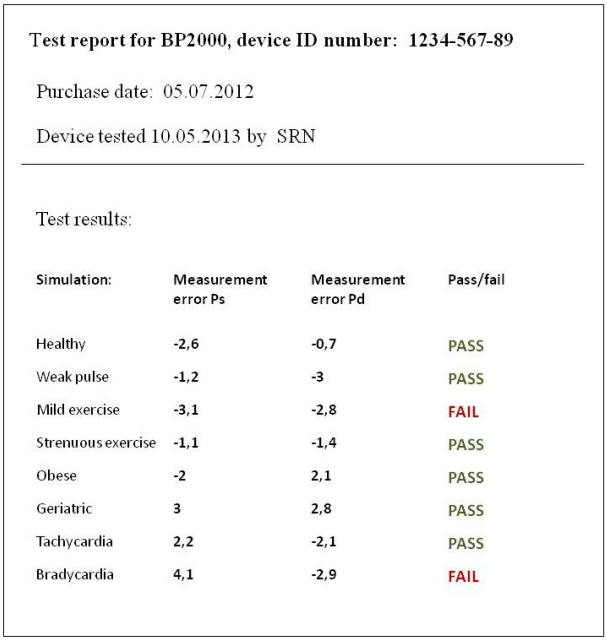


Figure 10: Top: Example of the data input design, for a quality assurance system for blood pressure devices. Bottom: Example of the design for data output, which would give biomedical technicians a clear overview over testing results, before devices are implemented in clinical settings.

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A Theoretical background

This appendix contains the theoretical background that is necessary to understand the defined problem, and the work that was completed. This appendix gives a general picture of blood pressure physiology, blood pressure meaurement techniques, and oscillometric blood pressure device testing using a simulator.

A.1 The pulmonary circulatory system

As illustrated in figure 11, the heart is divided into two pumping sytems. These two systems consist of the right and left side of the heart. The right side of the heart pumps blood into the pulmonary system where oxygen is absorbed, and carbon dioxide is released from the blood [21, 27]. The now oxygenated blood flows from the pulmonary system into the left side of the heart [27]. Blood is then pumped from the left side of the heart, through the aorta and to the rest of the body. This cycle, also known as the cardiac cycle, consists of two primary phases: a contraction and ejection phase, known as the systole, and a relaxing and filling phase, known as the diastole [21].

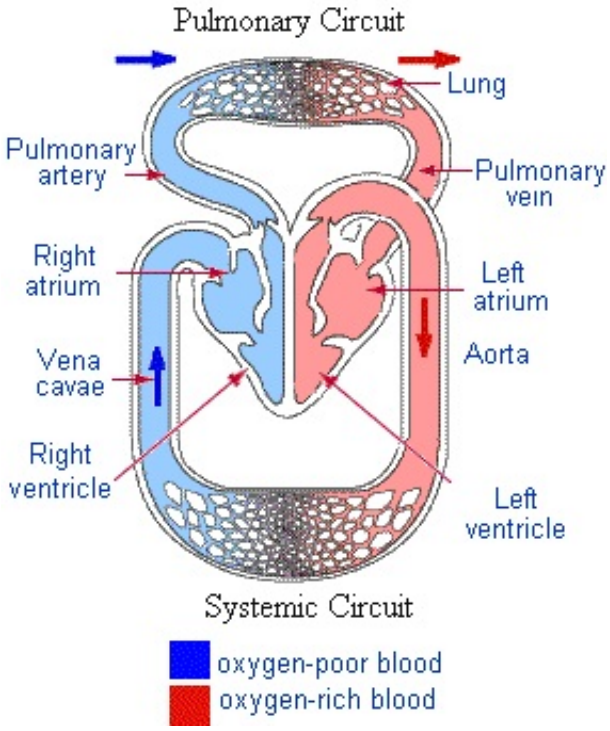


Figure 11: The figure illustrates how the right side of the heart ejects blood into the pulmonary system, and how the left side of the heart ejects blood into the aorta and to the rest of the body [18].

A.2 Definition of blood pressure

Blood pressure is a standard clinical measurement, and values from these measurements help physicians to determine the functional condition of the cardiovascular system of a patient [27]. Abnormally high arterial pressure is referred to as hypertension, while abnormally low blood pressure is referred to as hypotension. Blood pressure varies between individuals and some of factors that can have an affect on blood pressure are the following: stress, age, nutritional factors, drugs, disease, exercise, obesity and genetic predisposition for elevated blood pressure. Blood pressure measurement is the most common measurement that is made in clinical practice [15], and the term blood pressure refers to the arterial blood pressure in the circulatory system.

With each contraction of the heart, blood is pumped from the heart to the larger arteries. Arterial blood pressure will vary during the cardiac cycle, and the maximum pressure in the arteries during a cardiac cycle is known as the systolic pressure. The systolic blood pressure (P_s) is the pressure that occurs when the heart contracts and ejects blood to the rest of the body. The lowest pressure in the arteries during a cardiac cycle is known as the diastolic pressure. The diastolic blood pressure (P_d) is the pressure that occurs when the heart is relaxed and the ventricles fill with blood from the atria. (Figure 12). The amount of pressure of the arterial blood pressure is dependant on various factors some of which are:

- Cardiac output: this is the volume of blood that is pumped by the heart. An elevated cardiac output will result in elevated blood pressure.
- Arterial elasticity: this means how easily the arterial walls yield to increased pressure. If arterial elasticity is poor this will result in an increased workload for the heart, in order for blood to be pumped through these arteries, which will result in elevated blood pressure.
- Resistance: the resistance blood meets as it flows through the blood vessels. Increased resistance with result in elevated blood pressure. (Figure 13)
- Blood volume: is the volume of blood in the circulatory system of any individual. Blood volume affects blood pressure since it affects cardiac output. (Figure 13).
- Psychological state, metabolic state and physical activity.

Blood pressure is measured in millimeters of mercury (mmHg) and is routinely measured externally according to the Riva-Rocci method by sphygmomanometer [21]. (Section A.4.1). The normal arterial blood pressure range is typically defined as 60-80 mmHg diastolic and 100-120 mmHg systolic for an individual at rest. (Table 8).

A.3 Blood pressure measurement

Blood pressure is one of the vital signs that is most routinely monitored by clinicians and other healthcare providers[15, 14]. Blood pressure measurement interpretation has a wide range of implications for the individual on whom the technique is performed. Measurement interpretation and the decisions that are made as a result of this, can be influenced for better

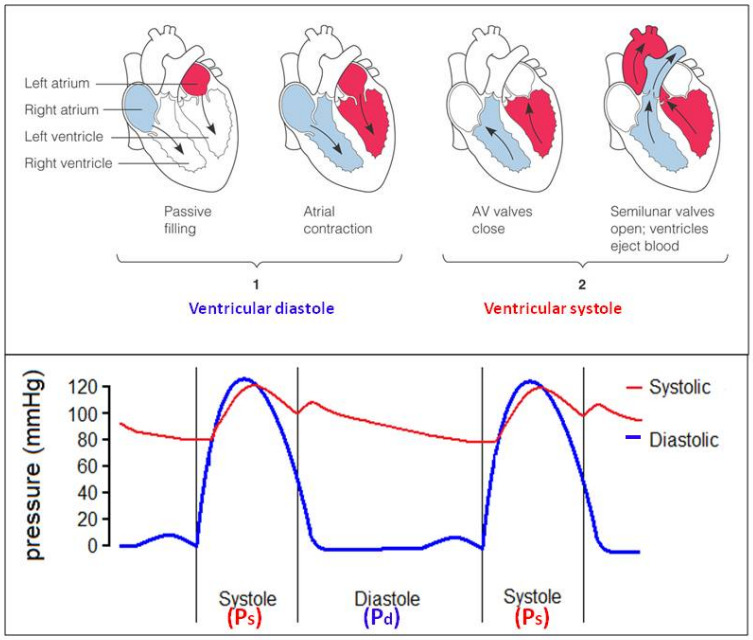


Figure 12: The above figures illustrates how systolic and diastolic pressures change during cardiac cycles. Top: The filling of the ventricles when the heart is relaxed (diastole), and the ejection of the blood from the ventricles to the rest of the body (systole) [19]. Bottom: Systolic pressures (P_s) and diastolic pressures (P_d) during two cardiac cycles, are shown [9].

Categories	**Systolic BP, mmHg**	**Diastolic BP, mmHg**
Normal	< 120	< 80
High-normal	130 – 139	85 – 89
Grade 1 hypertension (mild)	140 – 159	90 – 99
Grade 2 hypertension (moderate)	160 – 179	100 – 109
Grade 3 hypertension (severe)	≥ 180	≥ 110
Isolated systolic hypertension (grade 1)	140 – 159	< 90
Isolated systolic hypertension (grade 2)	≥ 160	< 90

Table 8: The above table shows the classification of normal blood pressure as well as the different degrees of hypertention as defined by the British Hypertension Society [8].

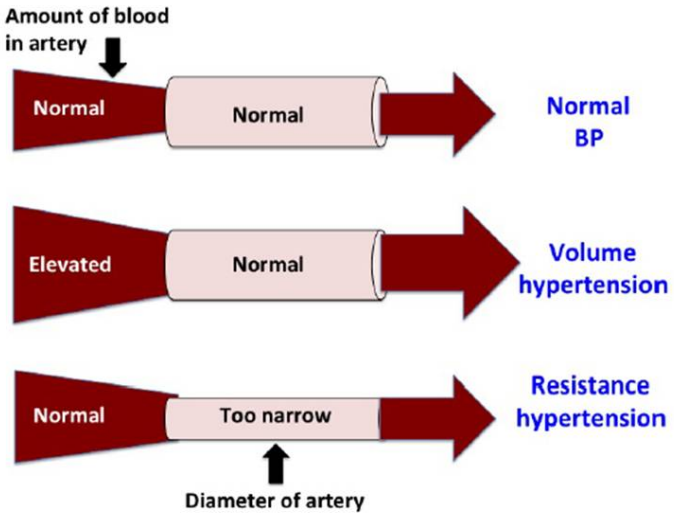


Figure 13: The figure illustrates how changes in blood volume and artery resistance can increase blood pressure.

or for worse by the accuracy of the measurement [14]. Measurements that are falsely low, for example, can result in hypertensive patients being denied drug treatment that would prevent future occurrences of stroke and heart attack [15]. Conversely, measurements that are falsely high could result in lifelong blood pressure lowering treatment, of an individual with normal blood pressure [14]. It is therefore imperative that blood pressure measurement devices are validated independently in the clinical setting, before they are commercially available [16, 15].

A.4 Techniques for measuring blood pressure

There are various techniques that can be used to measure blood pressure, and this can be done either directly (invasive) or indirectly (noninvasive). Direct measurement is an invasive procedure and is done by measuring blood pressure directly in the artery. Indirect measurement is completed in an attempt to measure intraarterial pressure noninvasively, and is typically done using the large artery in the upper arm (arteria brachialis) [27].

There are various techniques that can be used to measure blood pressure indirectly. This document is confined to indirect measurements which consist of the following: the auscultatory technique and the oscillometric technique. Both techniques consist of blocking the blood flow with an inflatable cuff, which makes it possible to measure the amount of external pressure that is required in order to block blood flow through the artery [21]. The fundamental difference between these two techniques is the manner in which the systolic and the diastolic pressures are determined.

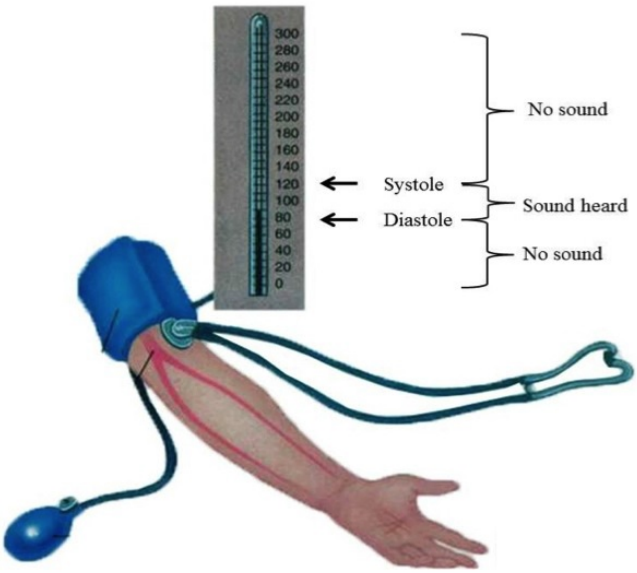


Figure 14: Illustration of blood pressure measurement with sphygmomanometer [10].

A.4.1 Auscultatory technique

The auscultatory method makes use of a sphygmomanometer which consists of an inflatable cuff, a rubber bulb for inflating the cuff and either a mercury or an aneroid manometer which is used to detect pressure. The mercury sphygmomanometer is the golden standard method of non-invasive blood pressure measurement [26]. When measuring blood pressure using this technique the inflatable cuff is placed snuggly around the upper arm, and a stethoscope is placed over the brachial artery. The cuff is inflated until the pressure is above the expected P_s, and the air in the cuff is then slowly released (2-4 mmHg/s) [27, 21]. Audible sounds known as Korotkoff sounds can be heard through the stethoscope. These sounds are generated by the blood flow and vibrations of the vessel under the cuff. When first heard these sounds indicate that the cuff pressure has fallen below the P_s. This value is then read from the manometer and indicates the systolic pressure [27, 21]. The Korotkoff sounds become increasingly louder, then decrease to muffled and then eventually disappear when the cuff pressure falls below the P_d [6, 27]. The Korotkoff sounds can no longer be heard when the cuff pressure falls below the P_d, since the cuff no longer provides any restriction to blood flow, blood flow stabilizes and thus produces no further audible sound [6, 27]. This value is then read from the manometer and indicates the diastolic pressure. (Figure 14).

A.4.2 Oscillometric technique

The oscillometric method is an indirect technique, and estimates blood pressure by measuring the changes in pressure that are caused by the expansion of the arterial wall. (Figure 15). This method is generally not completed manually but is measured with an automatic blood pressure measurement device [6]. (Figure 16). As with the auscultatory method, the cuff around the upper arm is inflated to a pressure that completely occludes the underlying

artery [27]. The cuff is then slowly deflated, and as the pressure in the cuff decreases, blood again begins to flow through the artery. Oscillometric devices measure the amplitude of oscillations which are detected by the pressure transducer in the cuff, as changes in arterial pulses (oscillations) occur by restricted blood flow through the occluded artery [27, 6].

As illustrated in figure 17, a device cuff is fully inflated and then gradually deflated. The blood again begins to flow through the artery, as the pressure in the cuff decreases. The increased blood flow from the deflation of the cuff, (figure 17, 1a), causes the amplitude of the oscillations detected by the cuff to increase (figure 17, 1b). As the pressure in the cuff further decreases, oscillations detected by the cuff reach a maximum (A_m). (Figure 17, 2). As illustrated in figure 17, 2, maximum oscillations (A_m) correspond with cuff pressure equal to mean arterial pressure (MAP) [27, 6]. Further cuff deflation causes the pressure in the cuff to decrease even further, and it is at this point that oscillations begin to decrease in amplitude. It is this rising and falling of the amplitude of the oscillations which is used to estimate systolic and diastolic blood pressure.

Algorithmic methods are used to estimate systolic (P_s) and diastolic (P_d) blood pressure. These methods estimate P_s and P_d based on fixed percentages of mean maximum oscillations. As illustrated in figure 17, 3, A_s is the amplitude of oscillations corresponding with P_s. A_s is calculated using the A_s/A_m ratio. The textbook definition of this ratio is 0,55, but this varies between oscillometric device manufacturers [6]. The cuff pressure in mmHg which corresponds to A_s, is used to determine P_s [2]. (Figure 17, 3). Correspondingly, A_d is the amplitude of oscillations corresponding with P_d. (Figure 17, 4). A_d is calculated using the A_d/A_m ratio, and the textbook definition of this ratio is 0,85, which also varies between manufacturers [6]. The cuff pressure in mmHg which corresponds to A_d, is used to determine P_d [2]. (Figure 17, 4).

It is the above described A_s/A_m and A_d/A_m ratios, which form the basis for the algorithms device manufactures use to estimate systolic and diastolic blood pressure [6].

A.5 Oscillometric blood pressure device testing

There are currently two methods which are used to test oscillometric blood pressure measurement devices [4]. The first involves validating the device comparing oscillometric blood pressure device measurements with manual reference blood pressure measurements, which are performed using the auscultatory technique and a mercury sphygmomanometer [4]. Guidelines for this type of testing requires recruitment of a large number of human subjects, an extensive range of blood pressures, as well as an extensive range of arm circumferences [4]. The second test method involves simulating oscillometric waveforms. Simulators generate oscillometric waveforms, and they include a wide variety of physiological and pathological oscillometric waveforms [4]. (Figure 3). This test method has the potential to replace test methods that require the use of human subjects, since it is more a cost-effective and less time consuming alternative to clinical validation trials [4, 23, 2]. The following subsection describes the concept of oscillometric waveform simulation.

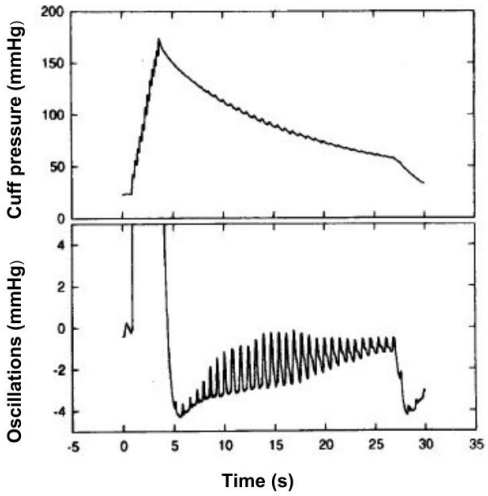


Figure 15: The top panel illustrates cuff pressure during oscillometric blood pressure measurement. The bottom panel shows the changes in oscillation amplitudes during oscillometric blood pressure measurement of the upper arm [6].

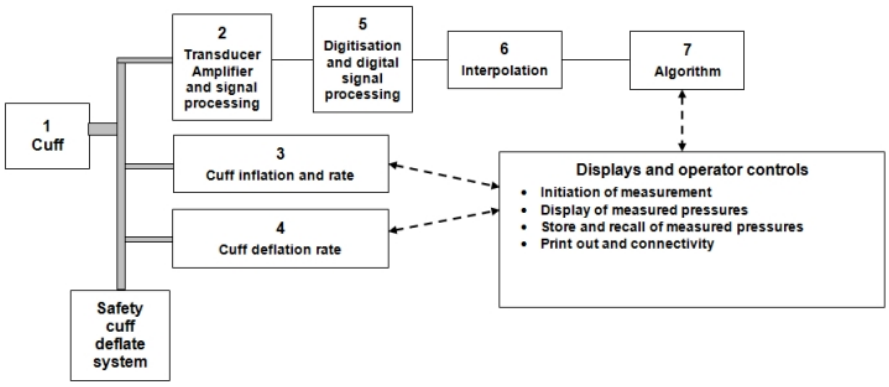


Figure 16: The above figure is a simplified block diagram of an oscillometric blood pressure measurement device [25].

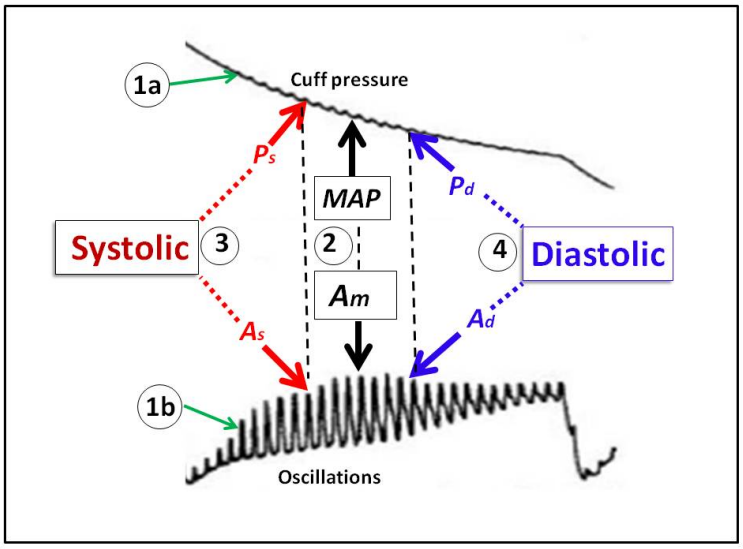


Figure 17: The above figure is an enlarged and modified illustration of figure 15. This figure illustrates how oscillometric blood pressure measurement devices estimate systolic pressure (P_s) and diastolic (P_d) pressure from mean maximum amplitude (A_m). For a detailed description of this measurement technique, see section A.4.2.

A.5.1 Simulator concept

Oscillometric blood pressure simulators were developed to assist oscillometric blood pressure device maintenance, and to verify validity claims of these devices [1, 11]. They allow the user to execute blood pressure simulations, automated leak testing, and pressure relief valve testing. The oscillometric waveform describes the relationship between cuff pressure and arterial pulses (oscillations) [4]. The main function of waveform simulators is to reproduce the physiological and pathological oscillometric waveforms of human subjects, during a blood pressure measurement sequence [1]. Simulators include a database with oscillometric waveforms from human subjects. The number and type of waveforms included in simulator databases vary between simulators [2].

Commercially available oscillometric waveform simulators are used to inject pressure pulses to the blood pressure measurement device cuff [23]. It is pulsation frequency and volume which simulates heart rate, in beats per minute (bpm) [11]. Simulators inject these pressure pulses through a pneumatic hose connected through a T-piece to the device that is being tested, and the cuff which is firmly wrapped around a mandrel. (Figure 18).

Different simulators have different means of creating pressure pulses [4]. One way of creating pressure pulses, involves use of a step motor. The step motor and a lead screw move a piston into the simulator manifold in order to decrease manifold volume [11]. This creates pressure pulses in order to simulate human subject blood pressure. A rolling diaphragm seal is used to maintain a seal around the piston, and the amplitude of the pressure pulsations is controlled by the microprocessor driving the step motor [11]. (Figure 19).

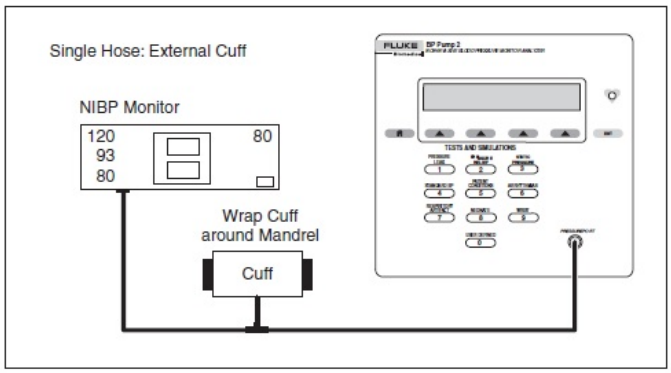


Figure 18: Typical setup for testing an oscillometric blood pressure device, using an oscillometric waveform simulator [11].

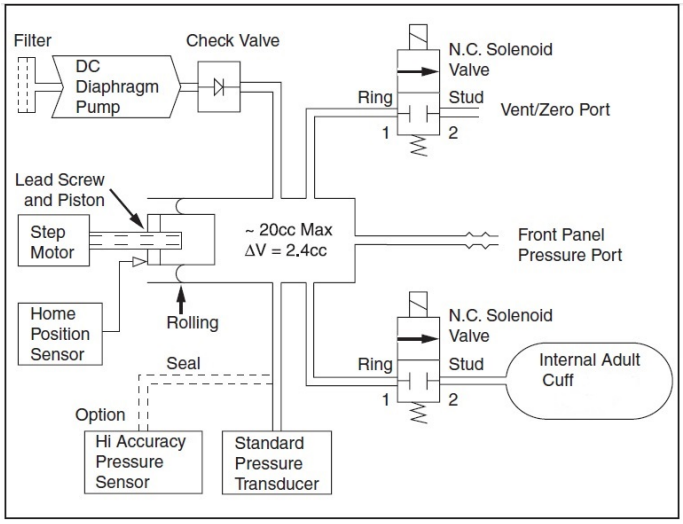


Figure 19: A block digram of an oscillometric waveform simulator [11].

B Literature search strategy

This appendix includes the literature search strategy which was utilized for this study. The databases used were the Pubmed database (using MESH) and the IEEE Xplore Digital Library. Additional databases were not utilized due to the time constraints of this study.

Pubmed (MESH database)

Search	Add to builder	Query	Items found
#8	Add	Search ("Blood Pressure Determination"[Mesh]) AND "Validation Studies" [Publication Type]	302
#12	Add	Search (("Blood Pressure Determination"[Mesh]) AND "Validation Studies as Topic"[Mesh]) AND "Guidelines as Topic"[Mesh]	1

Search	Add to builder	Query	Items found
#27	Add	Search (waveform[All Fields] AND simulator[All Fields] AND ("blood pressure"[MeSH Terms] OR ("blood"[All Fields] AND "pressure"[All Fields]) OR "blood pressure"[All Fields] OR ("blood"[All Fields] AND "pressure"[All Fields] AND "determination"[All Fields]) OR "blood pressure determination"[All Fields])	15
#26	Add	Search ((oscillometric[All Fields] AND waveform[All Fields] AND simulator[All Fields]AND ("Simulation"[Journal])	0
#25	Add	Search ((oscillometric[All Fields] AND waveform[All Fields] AND simulator[All Fields]AND ("Simulation"[Journal]))	0
#24	Add	Search (((oscillometric[All Fields] AND waveform[All Fields] AND ("Simulation"[Journal] OR "simulation"[All Fields]))))	1

Search	Add to builder	Query	Items found
#21	Add	Search oscillometric blood pressure validity	28
#20	Add	Search ((("Oscillometry/instrumentation"[Mesh] OR "Oscillometry/methods"[Mesh])) AND "Patient Simulation"[Majr]) AND ("Blood Pressure Determination/instrumentation"[Mesh] OR "Blood Pressure Determination/methods"[Mesh])	0
#19	Add	Search ((("Oscillometry/instrumentation"[Mesh] OR "Oscillometry/methods"[Mesh])) AND "Patient Simulation"[Majr]) AND ("Blood Pressure Determination/instrumentation"[Mesh] OR "Blood Pressure Determination/methods"[Mesh])	0
#11	Add	Search (Blood Pressure "[Majr]) AND "Reproducibility of Results"[Majr]	0
#10	Add	Search (Blood Pressure "[Majr]) AND "Reproducibility of Results"[Majr]	0
#9	Add	Search (Blood Pressure Monitors"[Majr]) AND "Reproducibility of Results"[Majr]	0
#8	Add	Search (Blood Pressure Monitors"[Majr]) AND "Reproducibility of Results"[Majr]	0
#6	Add	Search (("Oscillometry/methods"[Mesh]) AND "Blood Pressure Monitors"[Majr]) AND "Reproducibility of Results"[Majr]	0
#5	Add	Search (("Oscillometry/methods"[Mesh]) AND "Blood Pressure Monitors"[Majr]) AND "Reproducibility of Results"[Majr]	0
#3	Add	Search ("Oscillometry/methods"[Mesh]) AND "Blood Pressure Monitors"[Mesh]	26

IEEE, Xplore Digital Library

Search results:

(((oscillometric) AND waveform) AND simulator)	2 Results returned
(((oscillometric) AND blood pressure) AND simulation)	12 Results returned
(((blood pressure) AND device) AND validity)	8 Results returned
(((oscillometry) AND waveform) AND blood pressure) And simulator)	2 Results returned
(((oscillometry) AND blood pressure monitor) AND reproducibility)	4 Results returned

C Simulator certificate of calibration

This appendix contains the certificate of calibration for the BP Pump 2L Non-invasive Blood Pressure Simulator (Fluke Biomedical, Fluke Corporation USA). This simulator was calibrated on September 12th 2012 by Ultramedic Ltd, Liverpool, England.

ULTRAMEDIC LTD

4 Wavertree Boulevard South
Wavertree Technology Park,
Liverpool L7 9PF
Tel: 44 (0)151 228 0354
Fax: 44 (0)151 252 1673
e-mail: service@ultramedic.com
Web Site: http://www.ultramedic.com/

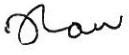
CERTIFICATE OF CALIBRATION

INSTRUMENT:	Fluke NIBP Monitor Analyzer
MODEL:	BP PUMP 2L
CERTIFICATE NO:	43443
SERIAL NO:	9443024
DATE:	12 September 2012
CALIBRATION DUE:	11 September 2013

This notification serves to certify that the unit mentioned above has been inspected and tested in accordance with the manufactures published specifications.

The accuracy and calibration of the test instruments utilised are directly or indirectly traceable to recognised National Standards through calibration at planned intervals.

The calibration will be valid for the period of one year, provided the instrument is used strictly according to the manual.

AUTHORISED: 

ULTRAMEDIC LTD

4 Wavertree Boulevard South
Wavertree Technology Park,
Liverpool L7 9PF
Tel: 44 (0)151 228 0354
Fax: 44 (0)151 252 1673
e-mail: service@ultramedic.com
Web Site: http://ultramedic.com/

Calibration And Quality Control Equipment Utilised And Environment Conditions

Product:	BP PUMP 2L	**Serial Number:**	9443024
Calibration Date:	12/09/2012	**Customer:**	Nordic Service Group
Work Order Number:	43443	**Engineer:**	D J Law

ISO 9001 Registration Number: 40213

Temperature:	24 °C	**Relative Humidity:**	47 %

Calibration And Quality Control Equipment Utilised

Manufacturer / Model	Equipment Number	Calibration Date	Recalibration Due
Testo 6010 Hygrometer	50529	02/04/2012	01/04/2013
Keithly 2000 Multimeter	50589	11/11/2011	10/11/2012
Druck DPI 601 Digital Pressure Meter	50520	26/09/2011	25/09/2012
Biotek 601Pro Electrical Safety Tester	50524	04/10/2011	03/10/2012

The instrument(s) above were calibrated and inspected against the standards of the laboratory which are traceable, directly or indirectly to National Standards.

Certified by: _____ **Title:** Service Engineer

Date: 12 September 2012

ULTRAMEDIC LTD

4 Wavertree Boulevard South
Wavertree Technology Park,
Liverpool L7 9PF
Tel: 44 (0)151 228 0354
Fax: 44 (0)151 252 1673
E-mail: service@ultramedic.com
Web Site: http://ultramedic.com/

BP Pump 2L Calibration Data Sheet

Work Order Number: 43443	**Serial Number:** 9443024
Customer: Nordic Service Group	**Engineer:** D J Law

				Tolerance	Pass/Fail
1.0	**Gross Leak Test:**				
	Start Pressure:	**400.0**	**mmHg**		
	End Pressure:	**399.3**	**mmHg**		
	Leak Rate:	**0.7**	**mmHg**	< 3mmHg/min	Pass

2.0	**Grounding Test:**	
	Pressure port barbed fitting: <1Ω	Pass
	Serial Port Connector Shroud: <1Ω	Pass
3.3	**Single Beep Audible:**	Pass
3.5	**Firmware Version Initial**	2.01
	Firmware Version Final	2.01
3.6	**System Configuration:**	
	Units:	**mmHg**
	Language:	**English**
4.1	**Communication Test:**	**Pass**
4.2	**Pressure Calibration:**	
	Offset A/D Counts:	
	Actual Applied Pressure per Std:	**mmHg**
	Returned Value A/D Counts:	

	Static Pressure Test:			Tolerance mmHg	Pass/Fail
5.1	0.0	**0.0**	**mmHg**	-1 ~ +1	Pass
	50.0	**50.0**	**mmHg**	49 ~ 51	Pass
	100.0	**100.0**	**mmHg**	98 ~ 102	Pass
	150.0	**150.0**	**mmHg**	148 ~ 152	Pass
	200.0	**200.0**	**mmHg**	198 ~ 202	Pass
	250.0	**250.0**	**mmHg**	248 ~ 252	Pass
	300.0	**300.0**	**mmHg**	297 ~ 303	Pass
	350.0	**350.0**	**mmHg**	343 ~ 357	Pass
	395.0	**395.0**	**mmHg**	387 ~ 403	Pass
	50.0	**50.0**	**mmHg**	49 ~ 51	Pass
	0.0	**0.0**	**mmHg**	-1 ~ +1	Pass

				Tolerance	Pass/Fail
6.1	**DC Pump Circuit & Vent Test:**				
	Pressure Time:	**14.3**	**S**	< 44s	Pass
	Vent Time:	**3.7**	**S**	> 2.5s	Pass
7.1	**Bottle Test:**			Tolerance	Pass/Fail
	VentTime:	**0.2**	**S**	< = 0.5s	Pass
8.1	**Pressure Leakage Test:** *Internal Cuff (400mmHg)*			Tolerance mmHg	Pass/Fail
	Ambient Pressure:	**0**	**mmHg**	0 ~ 1	Pass
	Leak Rate:	**0.7**	**mmHg**	< 2.0	Pass
9.1	**Pressure Leakage Test:** *External Cuff (400mmHg)*	**0.0**	**mmHg**	< 3.0 mmHg/min	Pass

BP Pump 2L Calibration Data Sheet

Work Order Number: 43443	Serial Number: 9443024

10.1	**Pressure Leakage Test:** *External Cuff (50mmHg)*	0.0 mmHg	< 3.0 mmHg/min	Pass

	Pressure Source Test:	Reading	Tolerance mmHg	Pass/Fail
11.1	Set Point 200mmHg	204.5	190-210	Pass
	Set Point 400mmHg	405.1	390-410	Pass

12.1	**Pulse Pump Test:**			
	Start Pressure:	400.0 mmHg		
	End Pressure:	409.7 mmHg	Tolerance	Pass/Fail
	Step Pressure:	9.7 mmHg	7 – 11 mmHg	Pass

13.1	**BP Simulation Test:**	
	Preset Reads 120/80 (93):	**Pass**
	Pulse Pump Heard:	**Pass**
	Heartbeat LED synchronised:	**Pass**

14.1	**Printer Test:**	**Pass**
15.1	**Parameters Restored:**	**Pass**

Comments:

No adjustments required

Signature: _____ **Date:** 12 September 2012

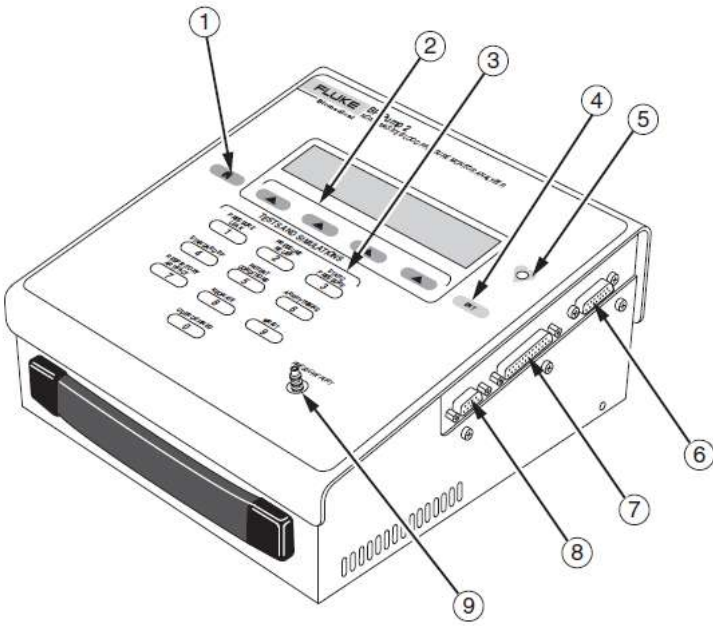
D Test protocols

The following appendix includes the test protocol for oscillometric blood pressure measurement device testing procedures. Test procedures were strictly followed according to the manufacturer instructions, for both the simulator and for blood pressure devices. The simulator operator manual contains 82 pages of instructions, and was therefore modified by this author to make a test protocol that was both user-friendly, and study design specific.

Protocol for oscillometric waveform simulation using the Fluke BP Pump 2 Simulator and tester

(Bio-tek Instruments*. Non-invasive blood pressure simulator and tester: Operator's Manual, BP Pump 2.* Bio-tek Instruments, 2003.)

The following describes how oscillometric blood pressure measurement devices were tested using the Fluke BP Pump 2 Simulator.

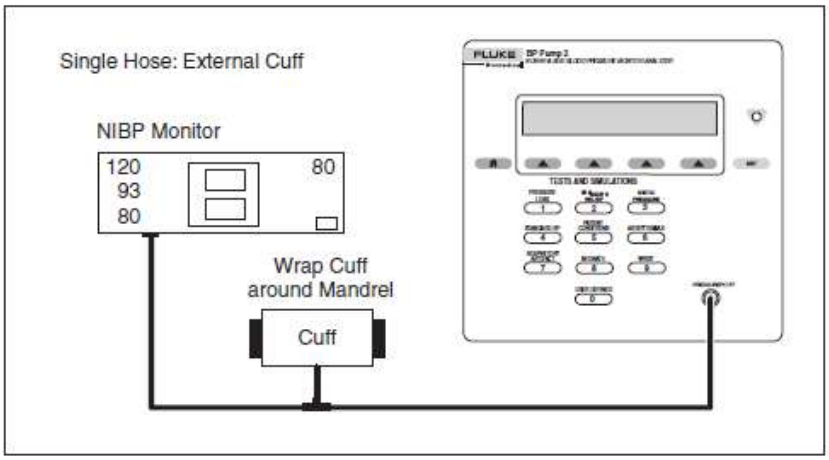


Label	Name	Function
1	Home Key	Returns the operator to the Main Menu.
2	Soft Keys 1 - 4	Makes dynamic assignments based on the current screen.
3	Number (Test and Simulations) Keys	Allows the operator to perform auto sequences and simulations using numeric keys.
4	Enter Key	Advances to the next menu or saves/selects options.
5	Pulse Indicator	LED blinks in synchronization with beeper, indicating that the pump is generating a simulated blood pressure pulse.
6	ECG Interface Port	Allows connection of optional ECG accessory (refer to Appendix, ECG Option).
7	Printer Port	Provides D-25 female connector for external parallel printer.
8	RS-232 Serial Port	Provides serial D-9 female connector for bi-directional computer control.
9	Pressure Port	Connects to the Non-Invasive Blood Pressure Monitor for all pressure simulations and tests.

Figure 1: Components of the Fluke BP Pump 2 NIBP simulator and tester

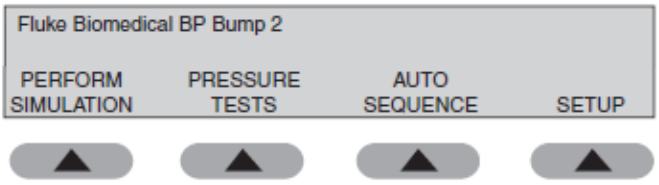
1. Power on the simulator.

2. Connect the blood pressure measurement device to the simulator using a T-piece, as illustrated below. Use the external cuff that is supplied by the blood pressure measurement device manufacturer. Ensure that there is 1cm of space between the cuff and the mandrel.

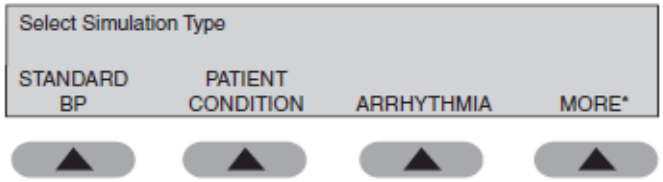


3. Power on the simulator.

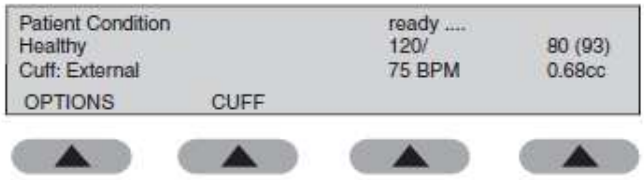
4. Press the "Perform Simulation" key. This accesses the "Select Simulation Type" menu.



5. Press the "Patient Condition" key.



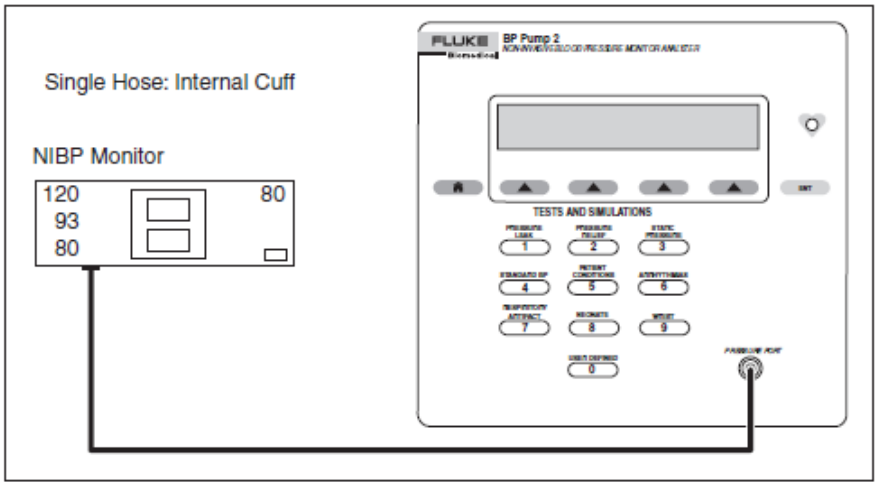
6. Patient conditions are selected by pressing the "Options" key.
Parameters for patient simulations are shown in Table 1.



Patient Condition	Blood Pressure (mmHg) (MAP)	Heart Rate (bpm)	Pulse volume (cc)
Healthy Heart	120/80 (93)	75	0.68
Weak Pulse	110/80 (90)	95	0.50
Mild Exercise #1	140/90 (106)	120	1.00
Strenuous Exercise #2	140/90 (106)	162	1.40
Obese Subject	120/80 (93)	90	0.50
Geriatric Subject	150/110 (123)	95	0.40
Tachycardia	120/105 (110)	130	0.40
Bradycardia	120/60 (80)	45	1.10

Table 1: Patient condition simulations

7. Press the "Cuff" key to select "External Adult" cuff.
8. Press "Start" on the oscillometric blood pressure measurement device.
9. Repeat step 7, five times (six times in total) per blood pressure measurement device.
10. Repeat steps 5, 7 and 8, until having simulated all patient conditions for the test device.
11. Reconnect the blood pressure measurement device to the simulators internal cuff, as illustrated below:



12. Repeat steps 5 and 6, selecting "Internal Adult" cuff instead of "External Adult".
13. Repeat steps 7-9.
14. Repeat steps 2-12 until all test devices have been tested.

E Sample size calculations

The following appendix contains results for sample size calculations. These sample size calculations were completed for:

- Differences between measurements obtained using external and internal cuffs. 6 measurements obtained with Model 1 using both the external and the internal cuff, for simulations Healthy (120/80 mmHg) and High (150/110). (Sample size calculations for two sample means was utilized). Sample 1 = measurements obtained with the external cuff, sample 2 = measurements obtained with the internal cuff.
- Blood pressure device validity. 6 measurements obtained with Model 1 using the external cuff, for simulations Healthy (120/80 mmHg) and High (150/110). (Sample size for one sample mean was utilized). The difference to detect was set at 3 mmHg.
- Blood pressure device validity. 6 measurements obtained with Model 2 using the external cuff, for simulations Healthy (120/80 mmHg) and High (150/110). (Sample size for one sample mean was utilized). The difference to detect was set at 3 mmHg.

Sample size calculations for two sample means (External /internal cuff (Model 1))

Ps, Simulation: Healthy

Sample Size

Two Means

Testing if two means are different from each other.

Alpha	0,05
Std Dev	0,516398
Extra Parameters	0

Supply two values to determine the third.
Enter one value to see a plot of the other two.

Difference to detect	0,3333
Sample Size	78
Power	0,8

Sample Size is the total sample size; per group would be n/2

Continue

Back

Pd, Simulation: Healthy

Sample Size

Two Means

Testing if two means are different from each other.

Alpha	0,05
Std Dev	1,169045
Extra Parameters	0

Supply two values to determine the third.
Enter one value to see a plot of the other two.

Difference to detect	2,16666
Sample Size	12
Power	0,8

Sample Size is the total sample size; per group would be n/2

Continue

Back

Ps, Simulation: High

Sample Size

Two Means

Testing if two means are different from each other.

Alpha	0,05
Std Dev	0,816497
Extra Parameters	0

Supply two values to determine the third.
Enter one value to see a plot of the other two.

Difference to detect	2,66666
Sample Size	6
Power	0,8

Sample Size is the total sample size; per group would be n/2

Continue

Back

Pd, Simulation : High

Sample Size

Two Means

Testing if two means are different from each other.

Alpha	0,05
Std Dev	0,516398
Extra Parameters	0

Supply two values to determine the third.
Enter one value to see a plot of the other two.

Difference to detect	6,3333
Sample Size	4
Power	0,8

Sample Size is the total sample size; per group would be n/2

Continue

Back

Sample size calculations for one sample mean (Model 1, external cuff)

Ps, Simulation: Healthy

Sample Size

One Mean

Testing if one mean is different from the hypothesized value.

Alpha	0,05
Std Dev	0,632456
Extra Parameters	0

Supply two values to determine the third.
Enter one value to see a plot of the other two.

Difference to detect	3
Sample Size	3
Power	0,8

Continue

Back

Animation Script

Pd, Simulation: Healthy

Sample Size

One Mean

Testing if one mean is different from the hypothesized value.

Alpha	0,05
Std Dev	0,816497
Extra Parameters	0

Supply two values to determine the third.
Enter one value to see a plot of the other two.

Difference to detect	3
Sample Size	3
Power	0,8

Continue

Back

Animation Script

Ps, Simulation: High

Sample Size

One Mean

Testing if one mean is different from the hypothesized value.

Alpha	0,05
Std Dev	0,547723
Extra Parameters	0

Supply two values to determine the third.
Enter one value to see a plot of the other two.

Difference to detect	3
Sample Size	3
Power	0,8

Continue

Back

Animation Script

Pd, Simulation : High

Sample Size

One Mean

Testing if one mean is different from the hypothesized value.

Alpha	0,05
Std Dev	0,408248
Extra Parameters	0

Supply two values to determine the third.
Enter one value to see a plot of the other two.

Difference to detect	3
Sample Size	3
Power	0,8

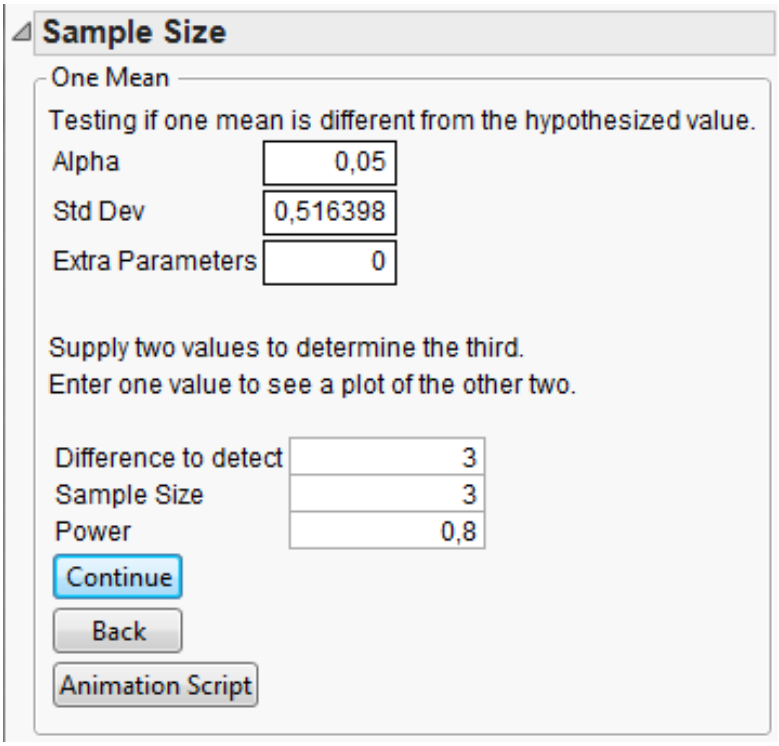
Continue

Back

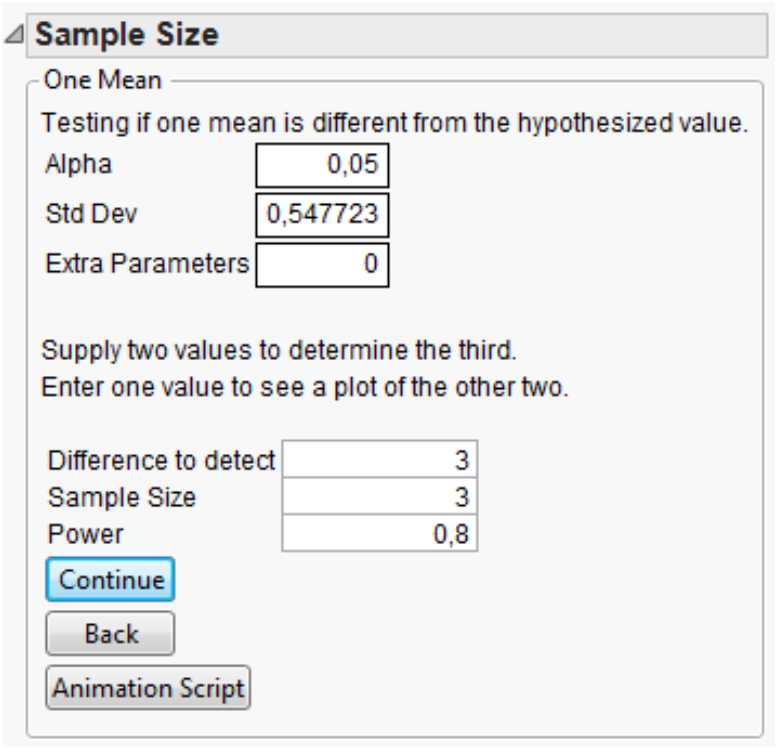
Animation Script

Sample size calculations for one sample mean (Model 2, external cuff)

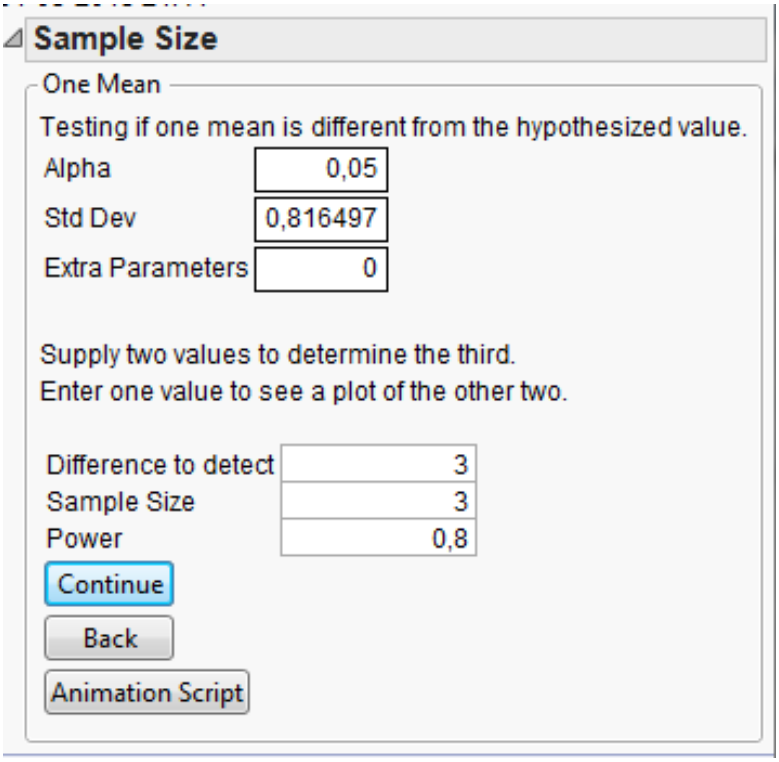
Ps, Simulation: Healthy



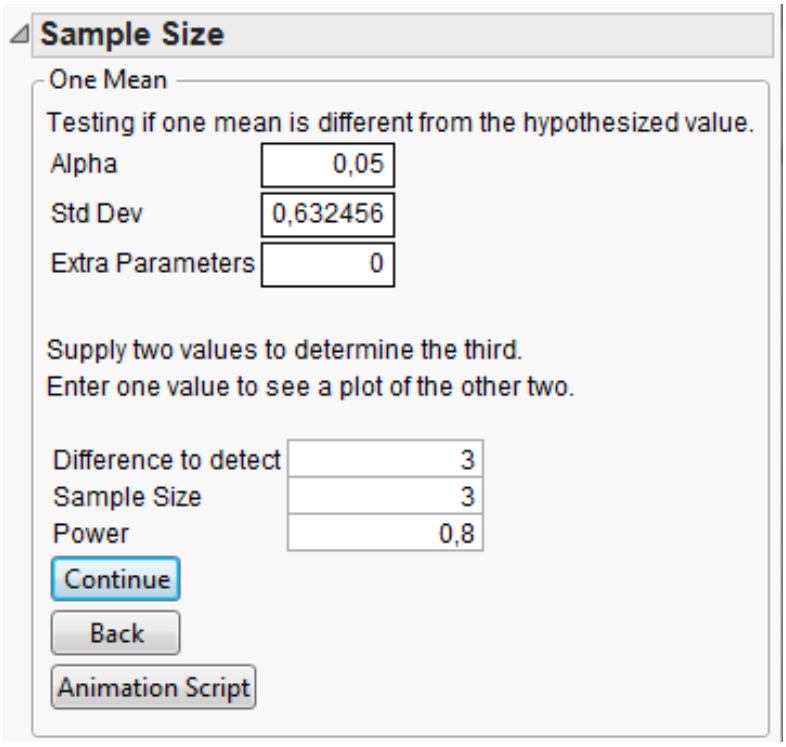
Pd, Simulation: Healthy



Ps, Simulation: High



Pd, Simulation : High



F Tests for normality

The following appendix shows findings for all tests for normality including the following:

- all measurements obtained with Model 1, using external and internal cuffs
- all measurements obtained with Model 2, using external and internal cuffs
- medians for the 6 measurements for each device, obtained with Model 1, using external and internal cuffs
- medians for the 6 measurements for each device, obtained with Model 2, using external and internal cuffs

Tests for normality, Model 1 , external and internal cuff. (All measurements)

Model	Simulation	Cuff	Nr of devices	Measurements pr device	Pressure	Pass/fail	P value	Pressure	Pass/fail	P value
Model 1	Healthy	External	10	6	Ps	F	< 0,0001	Pd	F	< 0,0001
Model 1	Healthy	Internal	5	6	Ps	F	< 0,0001	Pd	F	< 0,0001
Model 1	Weak pulse	External	10	6	Ps	F	< 0,0001	Pd	F	< 0,0001
Model 1	Weak pulse	Internal	10	6	Ps	F	< 0,0001	Pd	F	< 0,0001
Model 1	Mild exercise	External	10	6	Ps	F	< 0,0001	Pd	F	< 0,0001
Model 1	Mild exercise	Internal	10	6	Ps	F	< 0,0001	Pd	F	< 0,0001
Model 1	Strenuous exercise	External	10	6	Ps	F	< 0,0001	Pd	F	< 0,0001
Model 1	Strenuous exercise	Internal	10	6	Ps	F	< 0,0001	Pd	F	< 0,0001
Model 1	Obese	External	10	6	Ps	F	< 0,0001	Pd	F	< 0,0001
Model 1	Obese	Internal	1	6	Ps	N/A	N/A	Pd	N/A	N/A
Model 1	Geriatric	External	10	6	Ps	F	0,001	Pd	F	< 0,0001
Model 1	Geriatric	Internal	6	6	Ps	F	< 0,0001	Pd	F	< 0,0001
Model 1	Tachycardia	External	0	6	Ps	N/A	N/A	Pd	N/A	N/A
Model 1	Tachycardia	Internal	0	6	Ps	N/A	N/A	Pd	N/A	N/A
Model 1	Bradycardia	External	10	6	Ps	F	< 0,0001	Pd	F	< 0,0001
Model 1	Bradycardia	Internal	9	6	Ps	F	< 0,0001	Pd	F	< 0,0001

Tests for normality, Model 2, external and internal cuff. (All measurements)

Model	Simulation	Cuff	Nr of devices	Measurements pr device	Pressure	Pass/fail	P value	Pressure	Pass/fail	P value
Model 2	Healthy	External	10	6	Ps	F	0,0002	Pd	F	< 0,0001
Model 2	Healthy	Internal	10	6	Ps	F	< 0,0001	Pd	F	0,0008
Model 2	Weak pulse	External	10	6	Ps	F	< 0,0001	Pd	F	< 0,0001
Model 2	Weak pulse	Internal	10	6	Ps	F	< 0,0001	Pd	F	< 0,0001
Model 2	Mild exercise	External	10	6	Ps	F	< 0,0001	Pd	F	< 0,0001
Model 2	Mild exercise	Internal	10	6	Ps	F	< 0,0001	Pd	F	< 0,0001
Model 2	Strenuous exercise	External	10	6	Ps	F	< 0,0001	Pd	F	< 0,0001
Model 2	Strenuous exercise	Internal	10	6	Ps	F	< 0,0001	Pd	F	< 0,0001
Model 2	Obese	External	10	6	Ps	F	< 0,0001	Pd	F	<0,0005
Model 2	Obese	Internal	10	6	Ps	F	< 0,0001	Pd	F	< 0,0001
Model 2	Geriatric	External	10	6	Ps	F	0,0002	Pd	F	< 0,0001
Model 2	Geriatric	Internal	10	6	Ps	F	< 0,0001	Pd	F	0,0002
Model 2	Tachycardia	External	10	6	Ps	F	< 0,0001	Pd	F	< 0,0001
Model 2	Tachycardia	Internal	10	6	Ps	F	< 0,0001	Pd	F	< 0,0001
Model 2	Bradycardia	External	10	6	Ps	F	0,015	Pd	F	0,0063
Model 2	Bradycardia	Internal	10	6	Ps	F	< 0,0001	Pd	F	< 0,0001

Tests for normality, Model 1 , paired external and internal cuff. (Medians for 6 measurements for each device)

Model	Simulation	Measurements pr device	Nr of devices	Cuff	Pressure	Pass/ fail	P value	Cuff	Pressure	Pass/ fail	P value
Model 1	Healthy	1 (median)	5	External	Ps	P	0,3254	Internal	Ps	F	< 0,0001
Model 1	Healthy	1 (median)	5	External	Pd	P	0,314	Internal	Pd	F	< 0,0001
Model 1	Weak pulse	1 (median)	10	External	Ps	P	0,2619	Internal	Ps	F	0,0085
Model 1	Weak pulse	1 (median)	10	External	Pd	F	0,0114	Internal	Pd	F	0,0009
Model 1	Mild exercise	1 (median)	10	External	Ps	F	0,0002	Internal	Ps	F	0,0021
Model 1	Mild exercise	1 (median)	10	External	Pd	F	0,0096	Internal	Pd	F	0,0005
Model 1	Strenuous exercise	1 (median)	10	External	Ps	F	< 0,0001	Internal	Ps	F	< 0,0001
Model 1	Strenuous exercise	1 (median)	10	External	Pd	F	0,0311	Internal	Pd	P	0,1052
Model 1	Obese	1 (median)	N/A (excluded)	External	Ps	10 devices	N/A (excluded)	Internal	Ps	1 device	N/A (excluded)
Model 1	Obese	1 (median)	N/A (excluded)	External	Pd	10 devices	N/A (excluded)	Internal	Pd	1 device	N/A (excluded)
Model 1	Geriatric	1 (median)	6	External	Ps	P	0,2479	Internal	Ps	P	0,8201
Model 1	Geriatric	1 (median)	6	External	Pd	F	0,0309	Internal	Pd	P	0,4733
Model 1	Tachycardia	1 (median)	N/A (excluded)	External	Ps		N/A (excluded)	Internal	Ps		N/A (excluded)
Model 1	Tachycardia	1 (median)	N/A (excluded)	External	Pd		N/A (excluded)	Internal	Pd		N/A (excluded)
Model 1	Bradycardia	1 (median)	9	External	Ps	F	0,0122	Internal	Ps	F	< 0,0001
Model 1	Bradycardia	1 (median)	9	External	Pd	F	0,0309	Internal	Pd	P	0,1121

Tests for normality, Model 2, paired external and internal cuff. (Medians for 6 measurements for each device)

Model	Simulation	Measurements pr device	Nr of devices	Cuff	Pressure	Pass/fail	P value	Cuff	Pressure	Pass/fail	P value
Model 2	Healthy	1 (median)	10	External	Ps	P	0,5496	Internal	Ps	F	< 0,0001
Model 2	Healthy	1 (median)	10	External	Pd	F	0,049	Internal	Pd	P	0,2668
Model 2	Weak pulse	1 (median)	10	External	Ps	F	N/A (All measurements the same)	Internal	Ps	F	0,0359
Model 2	Weak pulse	1 (median)	10	External	Pd	F	0,0084	Internal	Pd	F	0,0269
Model 2	Mild exercise	1 (median)	10	External	Ps	F	0,0032	Internal	Ps	P	0,5189
Model 2	Mild exercise	1 (median)	10	External	Pd	P	0,1085	Internal	Pd	P	0,1052
Model 2	Strenuous exercise	1 (median)	10	External	Ps	F	0,0085	Internal	Ps	F	< 0,0001
Model 2	Strenuous exercise	1 (median)	10	External	Pd	P	0,2122	Internal	Pd	F	0,0079
Model 2	Obese	1 (median)	10	External	Ps	F	0,0014	Internal	Ps	F	0,0006
Model 2	Obese	1 (median)	10	External	Pd	P	0,3108	Internal	Pd	P	0,3654
Model 2	Geriatric	1 (median)	10	External	Ps	P	0,6377	Internal	Ps	F	< 0,0001
Model 2	Geriatric	1 (median)	10	External	Pd	P	0,8834	Internal	Pd	P	0,7986
Model 2	Tachycardia	1 (median)	10	External	Ps	F	0,0021	Internal	Ps	F	< 0,0001
Model 2	Tachycardia	1 (median)	10	External	Pd	F	0,0021	Internal	Pd	P	0,0515
Model 2	Bradycardia	1 (median)	10	External	Ps	P	0,8312	Internal	Ps	P	0,1488
Model 2	Bradycardia	1 (median)	10	External	Pd	P	0,3351	Internal	Pd	F	0,0077

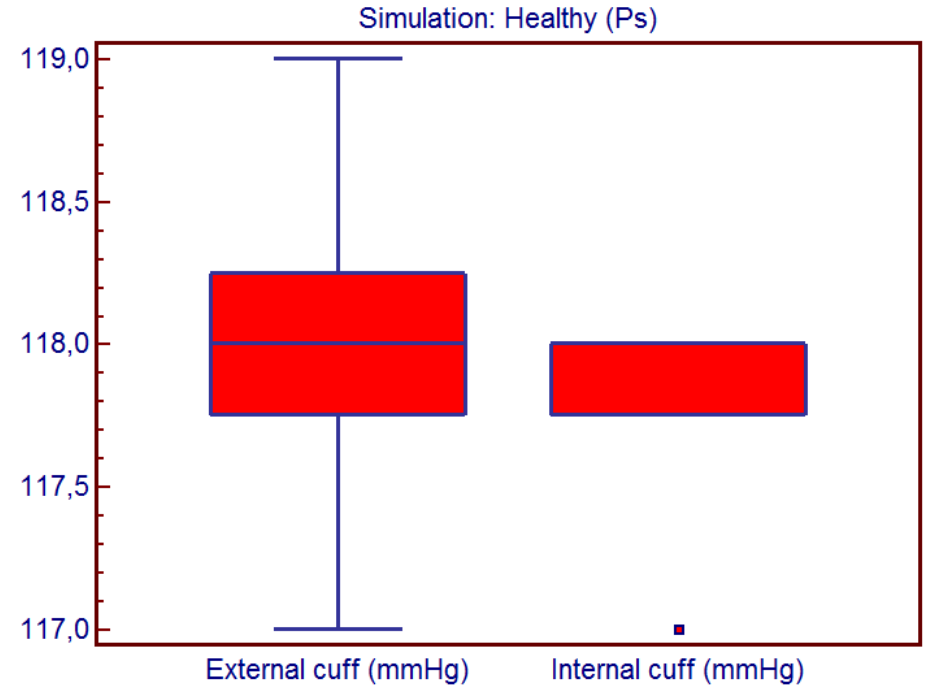
G Differences between external and internal cuffs

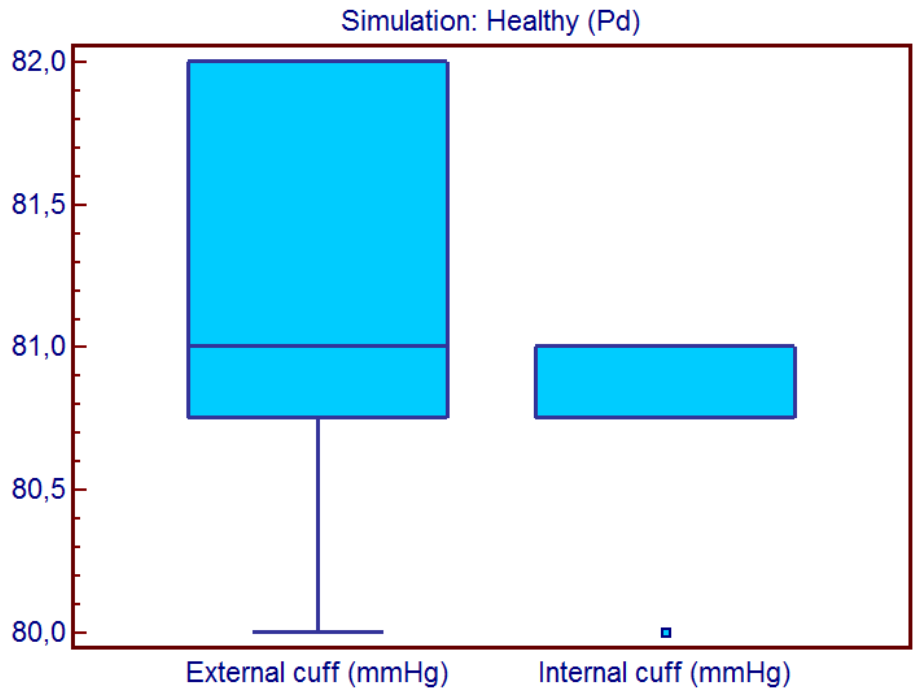
The following appendix contains boxplots for measurements obtained with external and internal cuffs, for each waveform simulation, using Model 1 and Model 2 blood pressure devices. Boxplots were generated from medians, for the 6 measurements for each device. See the table below, for the systolic and diastolic pressures generated by the simulator, for each of the 8 simulations.

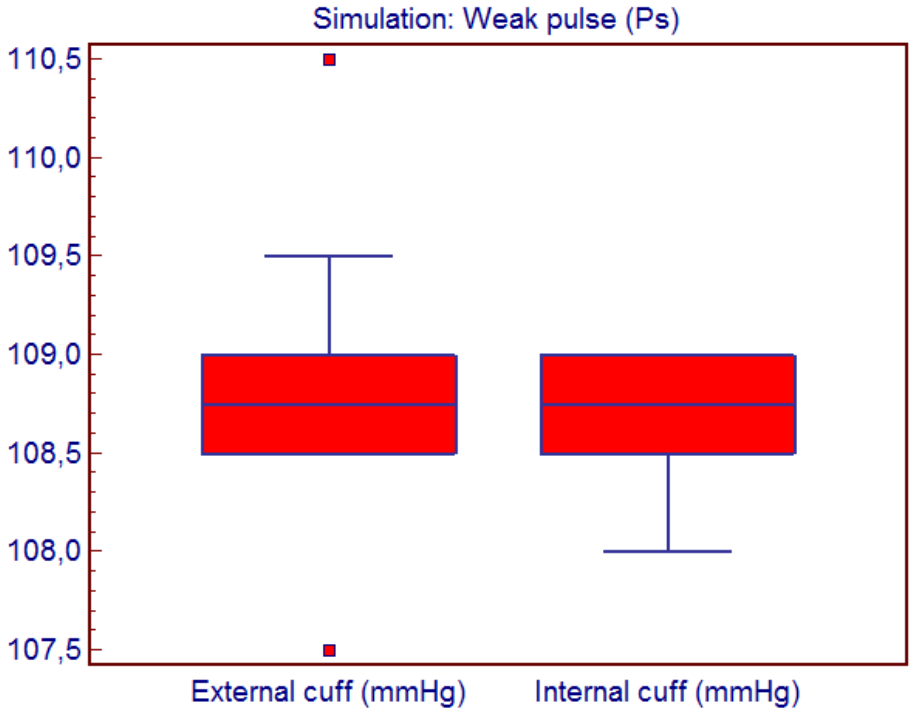
Systolic pressures are marked in red, and diastolic pressures are marked in blue.

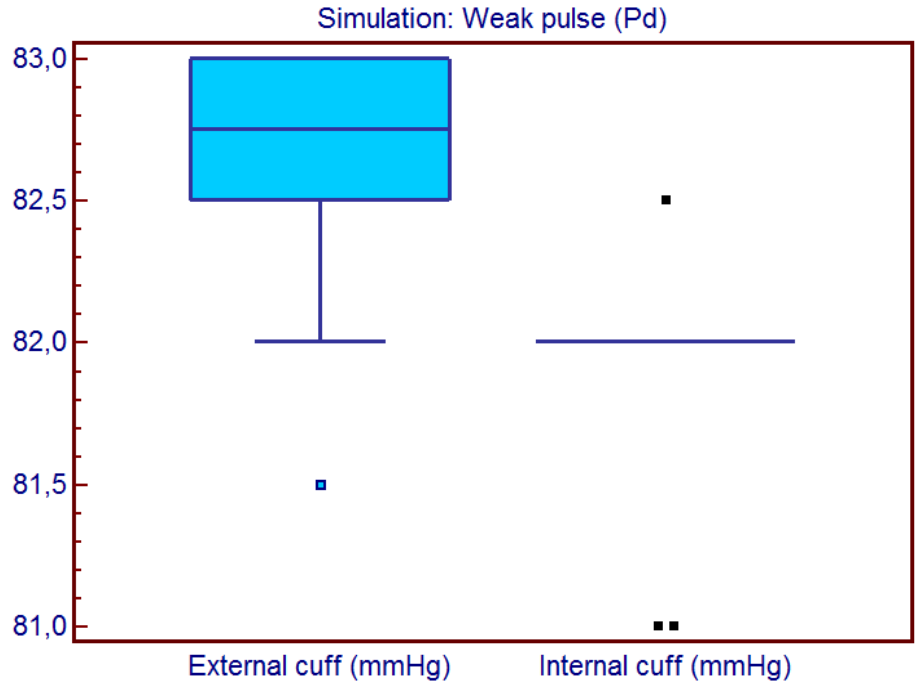
Patient Condition	Blood Pressure (mmHg) (MAP)	Heart Rate (bpm)	Pulse volume (cc)
Healthy Heart	120/80 (93)	75	0.68
Weak Pulse	110/80 (90)	95	0.50
Mild Exercise #1	140/90 (106)	120	1.00
Strenuous Exercise #2	140/90 (106)	162	1.40
Obese Subject	120/80 (93)	90	0.50
Geriatric Subject	150/110 (123)	95	0.40
Tachycardia	120/105 (110)	130	0.40
Bradycardia	120/60 (80)	45	1.10

Model 1

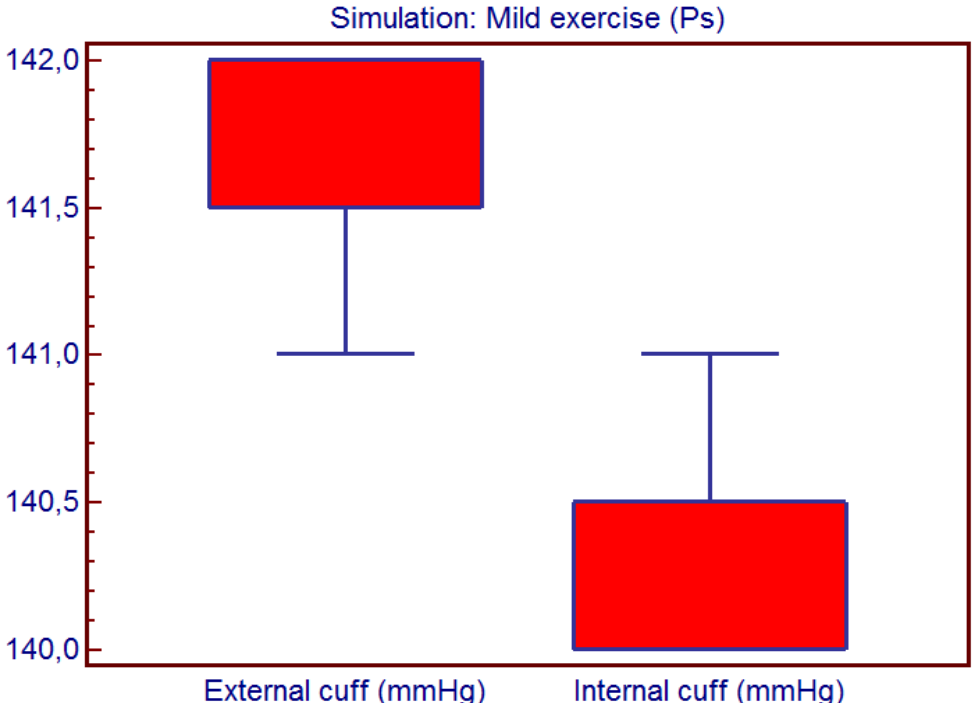

Simulation: Healthy (Ps)
119,0
118,5
118,0
117,5
117,0
External cuff (mmHg)
Internal cuff (mmHg)

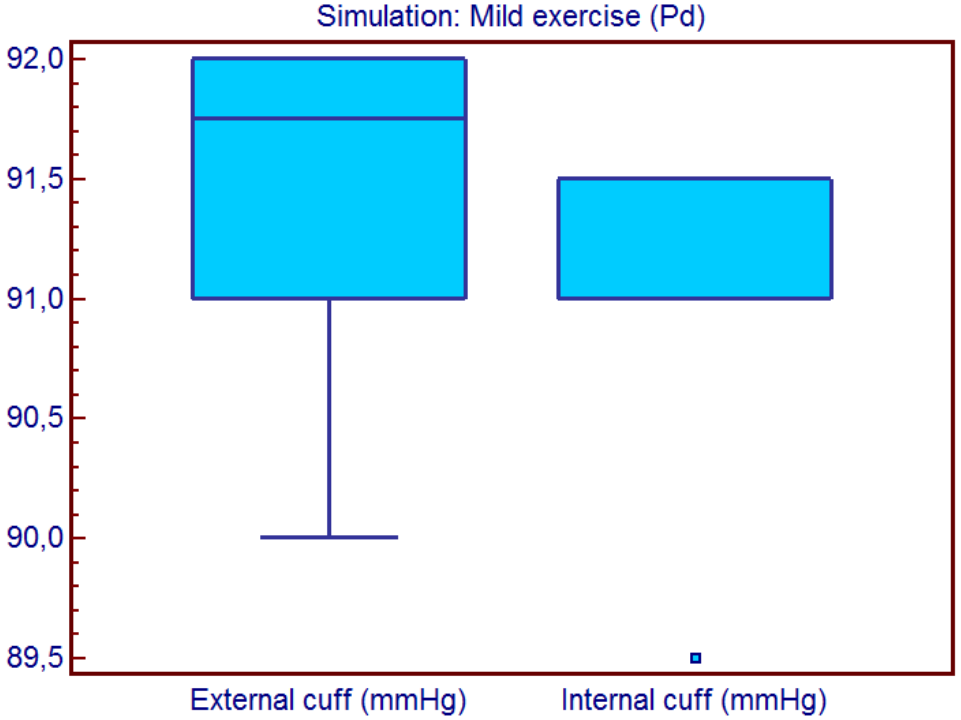

Simulation: Healthy (Pd)
82,0
81,5
81,0
80,5
80,0
External cuff (mmHg)
Internal cuff (mmHg)

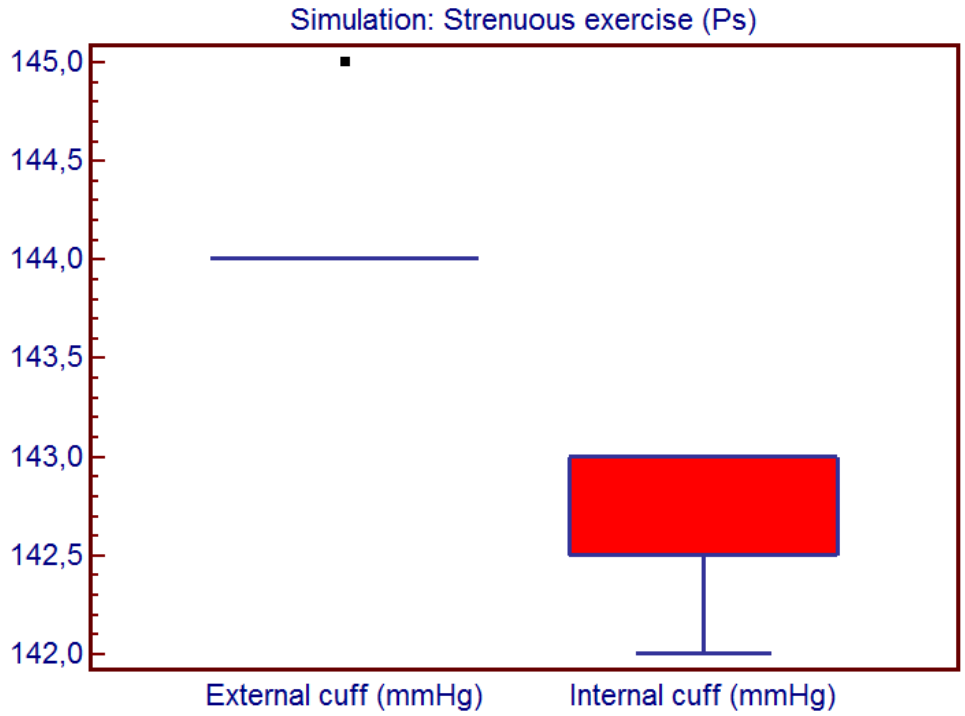

Simulation: Weak pulse (Ps)
110,5
110,0
109,5
109,0
108,5
108,0
107,5
External cuff (mmHg)
Internal cuff (mmHg)

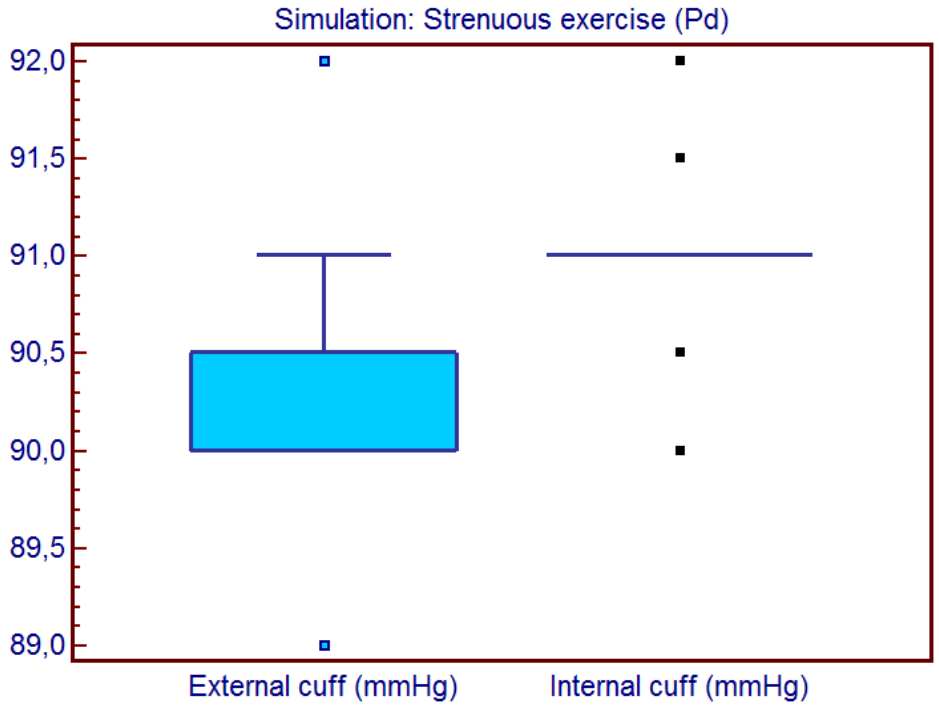

Simulation: Weak pulse (Pd)
83,0
82,5
82,0
81,5
81,0
External cuff (mmHg)
Internal cuff (mmHg)

Model 1


Simulation: Mild exercise (Ps)
142,0
141,5
141,0
140,5
140,0
External cuff (mmHg)
Internal cuff (mmHg)

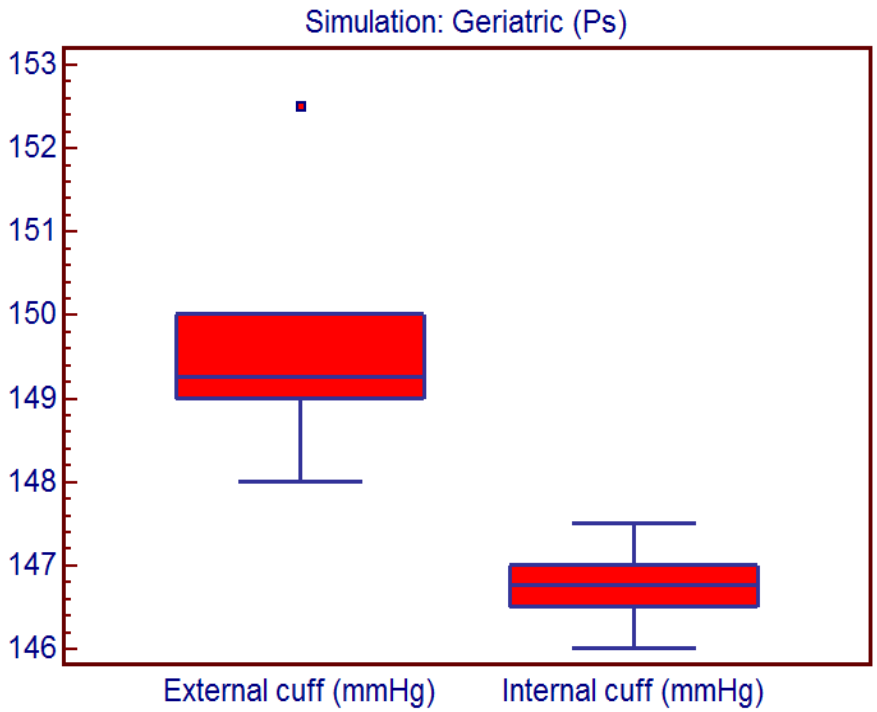

Simulation: Mild exercise (Pd)
92,0
91,5
91,0
90,5
90,0
89,5
External cuff (mmHg)
Internal cuff (mmHg)

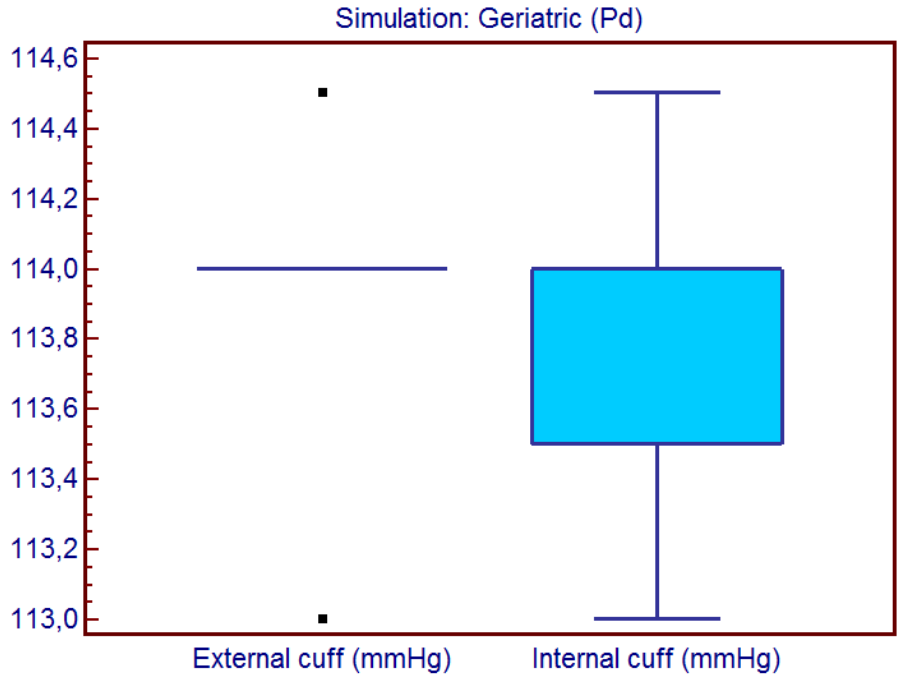

Simulation: Strenuous exercise (Ps)
145,0
144,5
144,0
143,5
143,0
142,5
142,0
External cuff (mmHg)
Internal cuff (mmHg)


Simulation: Strenuous exercise (Pd)
92,0
91,5
91,0
90,5
90,0
89,5
89,0
External cuff (mmHg)
Internal cuff (mmHg)

Model 1

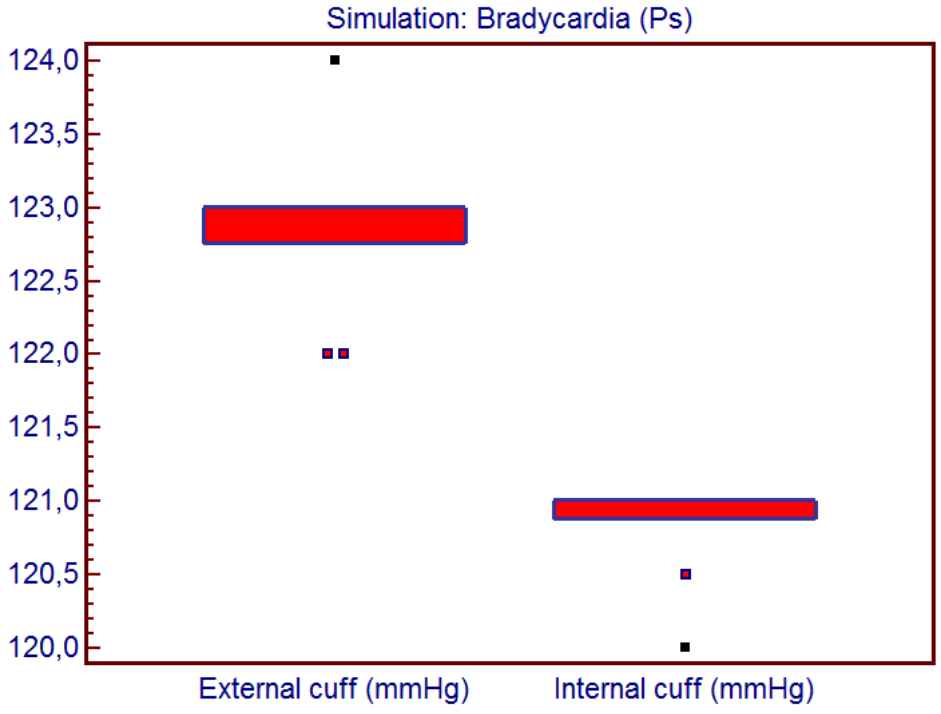
Simulation: Obese
N/A (all devices excluded)

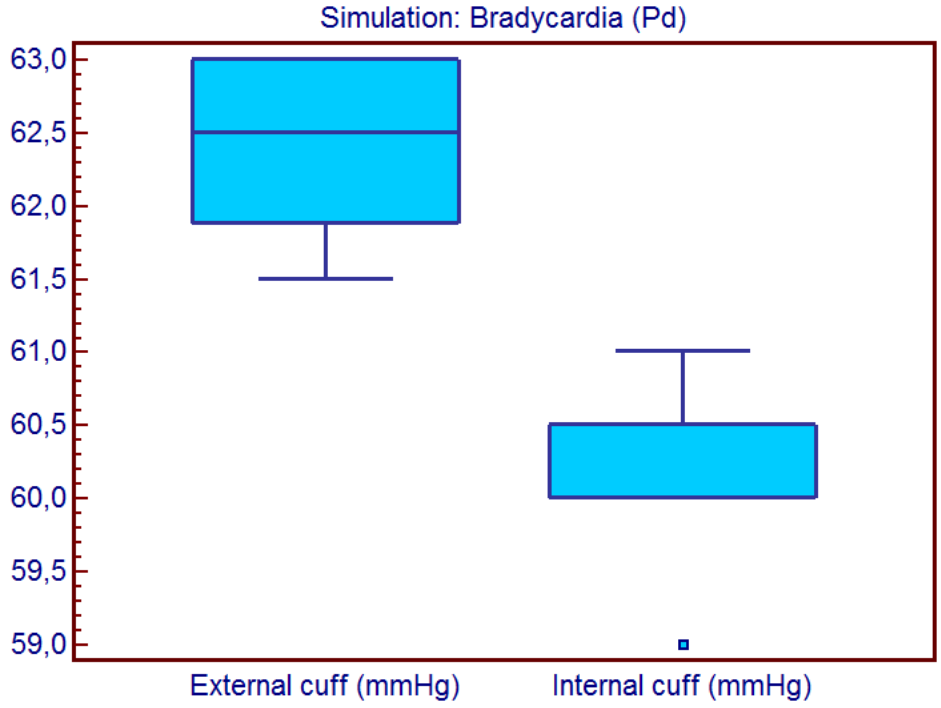




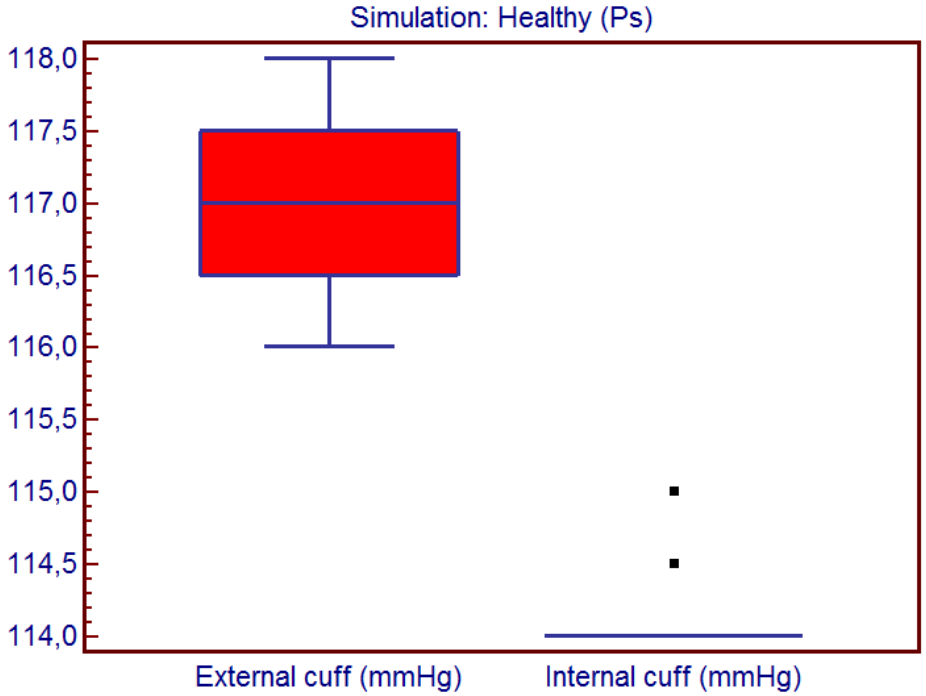
Model 1

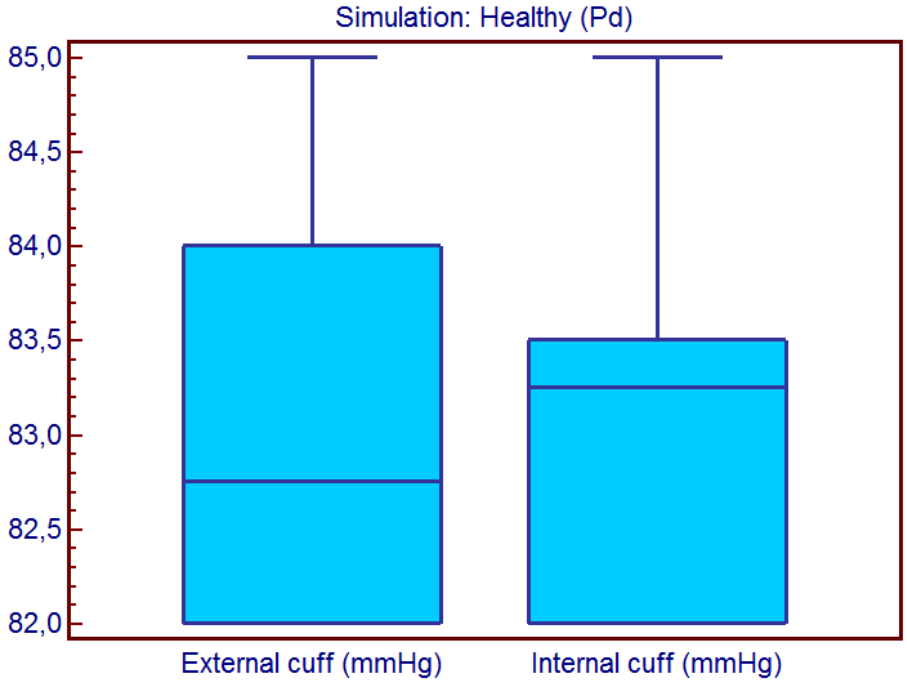
Simulation: Tachycardia
N/A (all devices excluded)

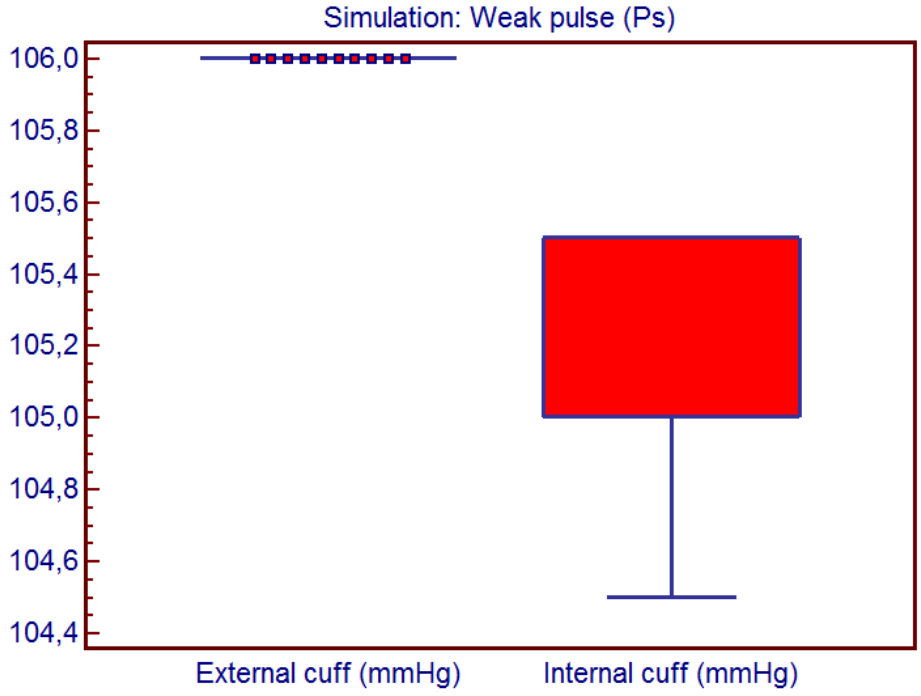


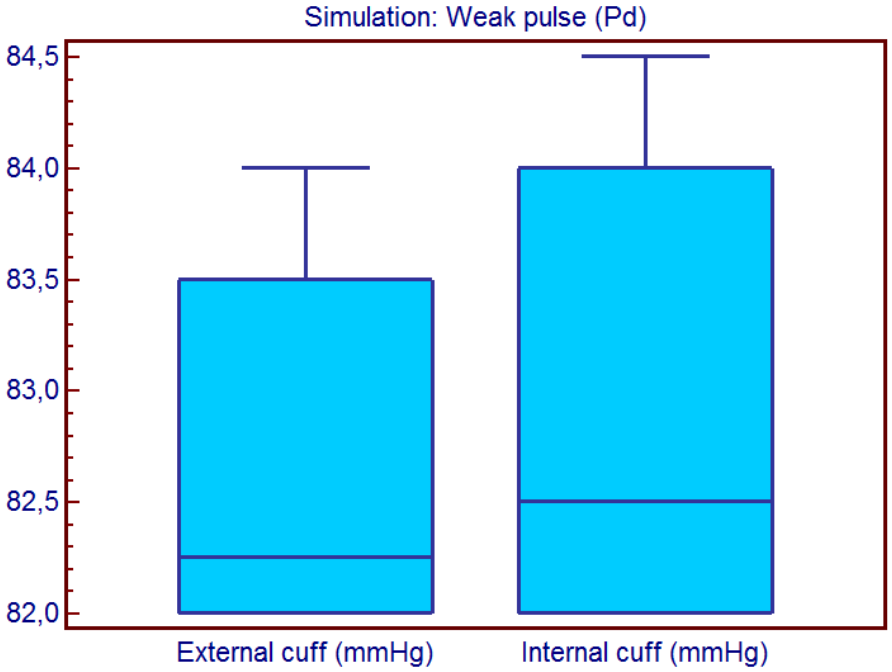


Model 2

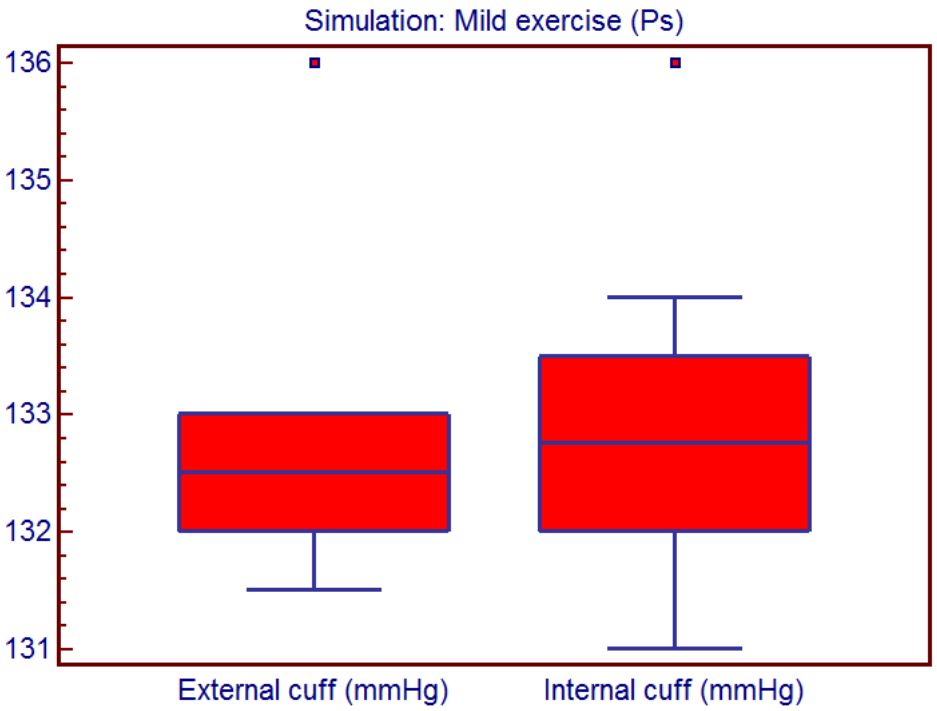

Simulation: Healthy (Ps)
118,0
117,5
117,0
116,5
116,0
115,5
115,0
114,5
114,0
External cuff (mmHg)
Internal cuff (mmHg)

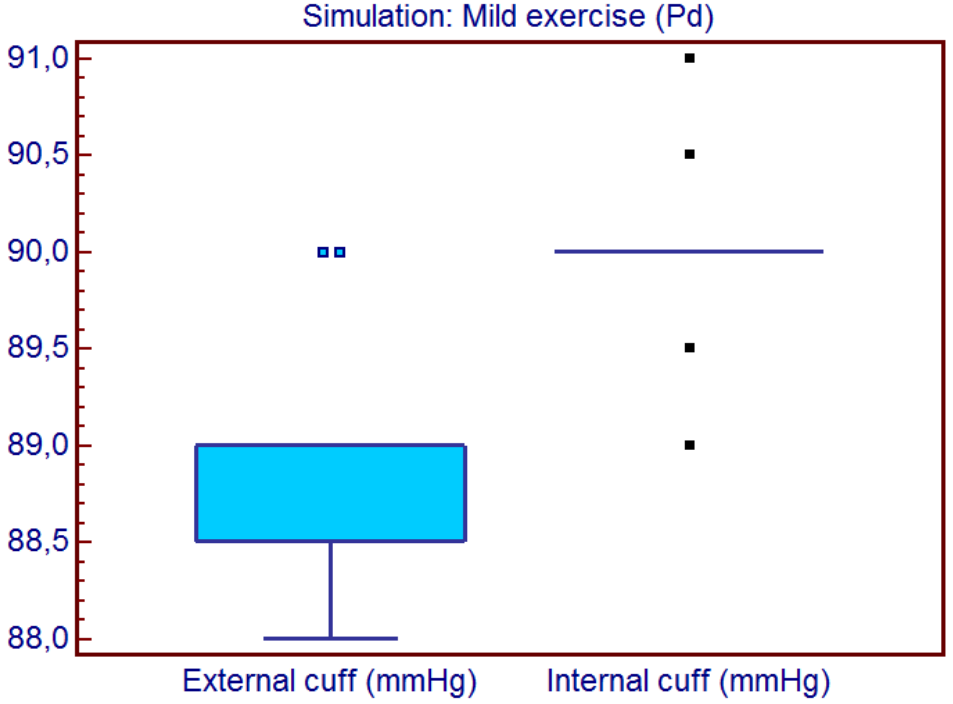

Simulation: Healthy (Pd)
85,0
84,5
84,0
83,5
83,0
82,5
82,0
External cuff (mmHg)
Internal cuff (mmHg)

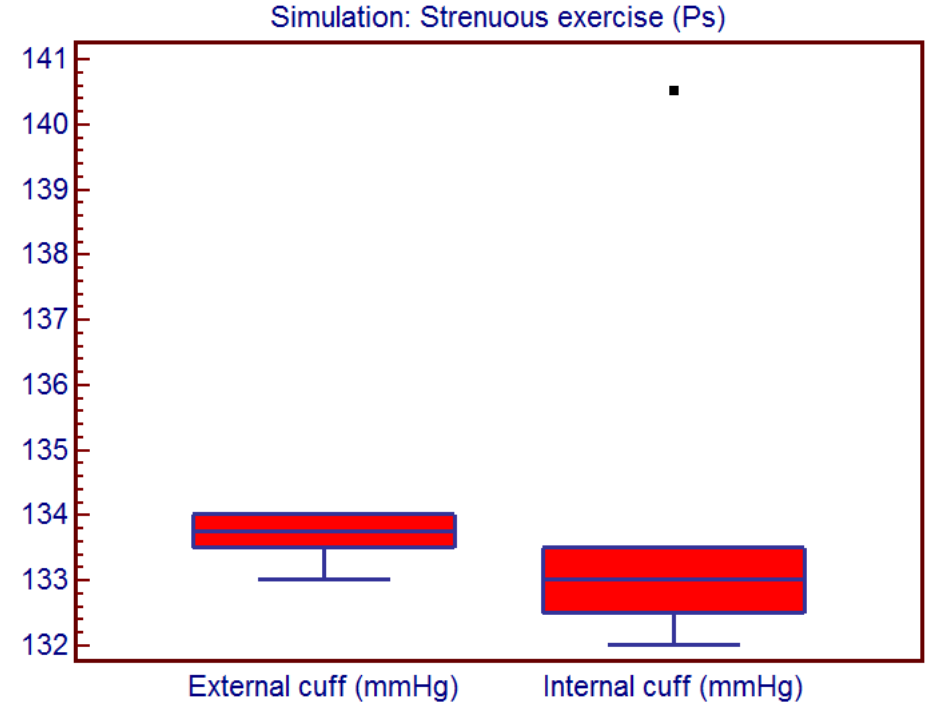

Simulation: Weak pulse (Ps)
106,0
105,8
105,6
105,4
105,2
105,0
104,8
104,6
104,4
External cuff (mmHg)
Internal cuff (mmHg)

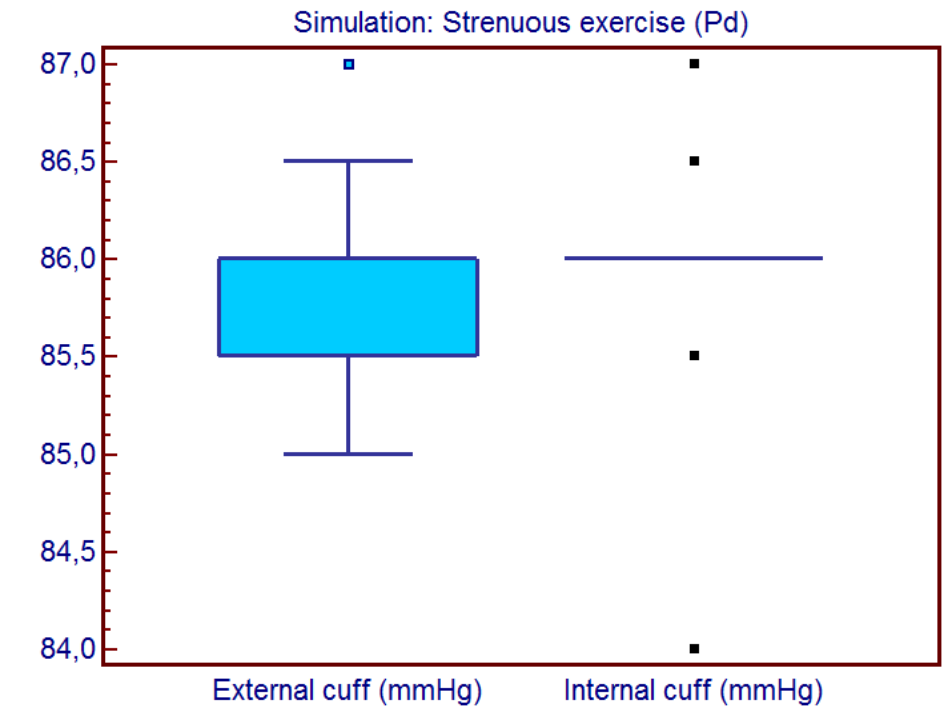

Simulation: Weak pulse (Pd)
84,5
84,0
83,5
83,0
82,5
82,0
External cuff (mmHg)
Internal cuff (mmHg)

Model 2

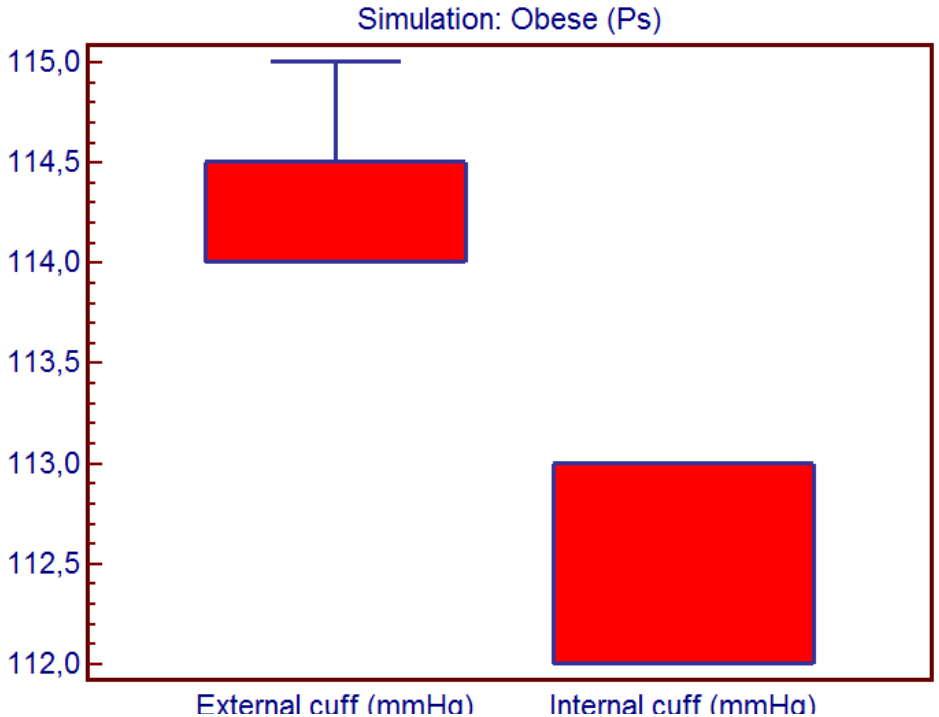

Simulation: Mild exercise (Ps)
136
135
134
133
132
131
External cuff (mmHg)
Internal cuff (mmHg)

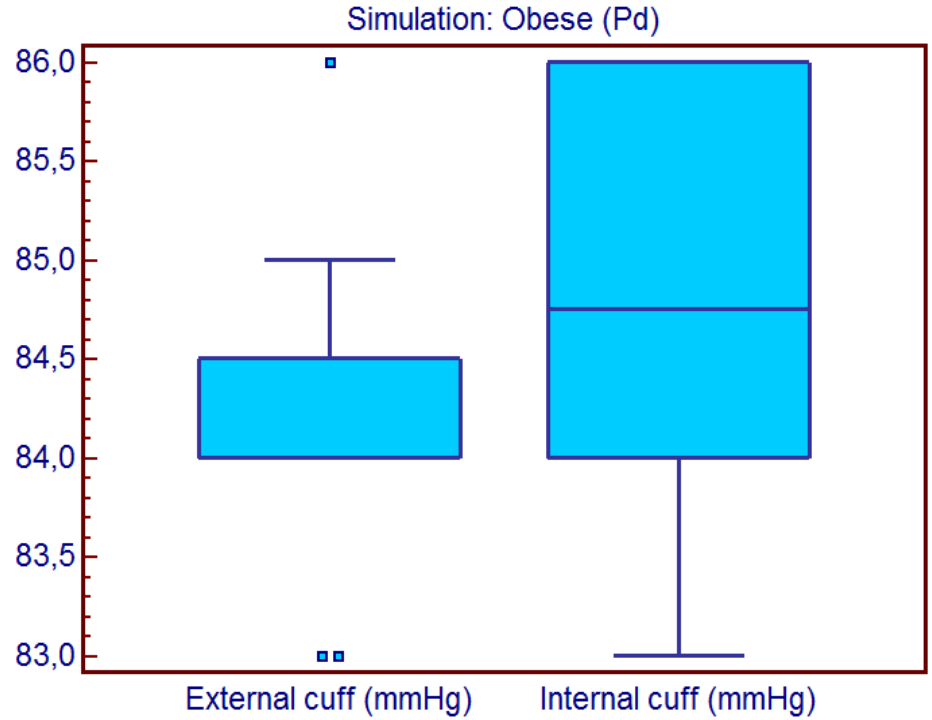

Simulation: Mild exercise (Pd)
91,0
90,5
90,0
89,5
89,0
88,5
88,0
External cuff (mmHg)
Internal cuff (mmHg)

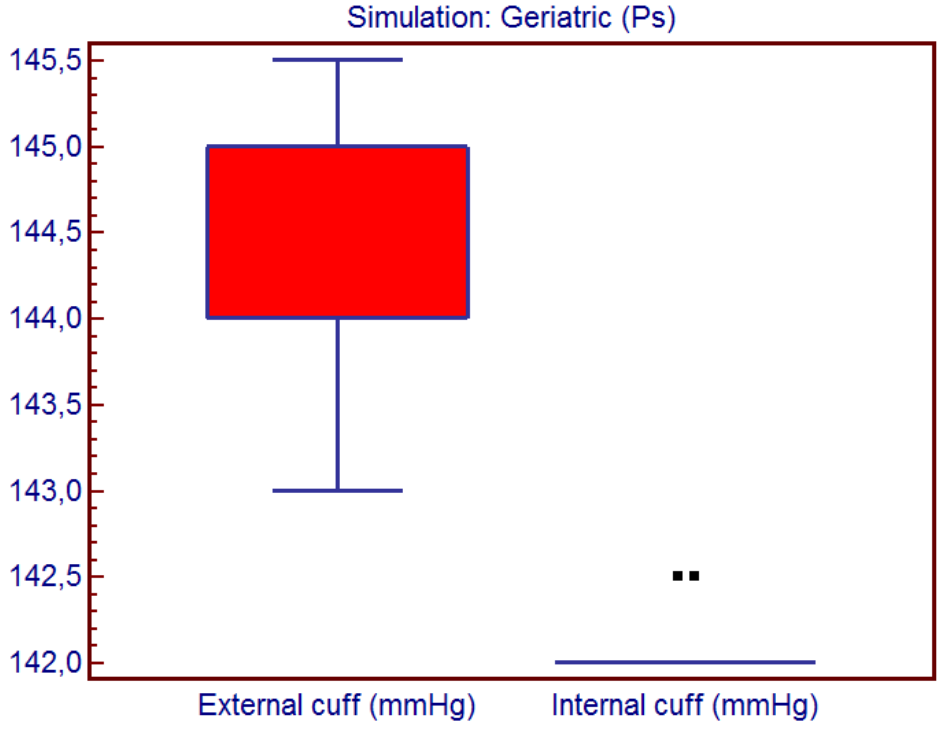

Simulation: Strenuous exercise (Ps)
141
140
139
138
137
136
135
134
133
132
External cuff (mmHg)
Internal cuff (mmHg)

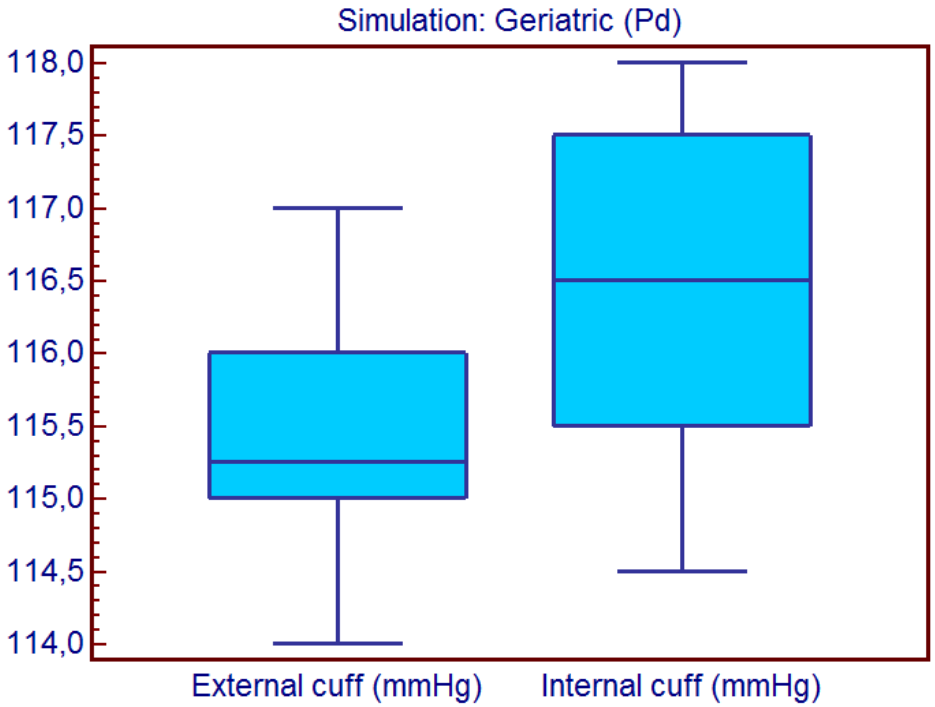

Simulation: Strenuous exercise (Pd)
87,0
86,5
86,0
85,5
85,0
84,5
84,0
External cuff (mmHg)
Internal cuff (mmHg)

Model 2

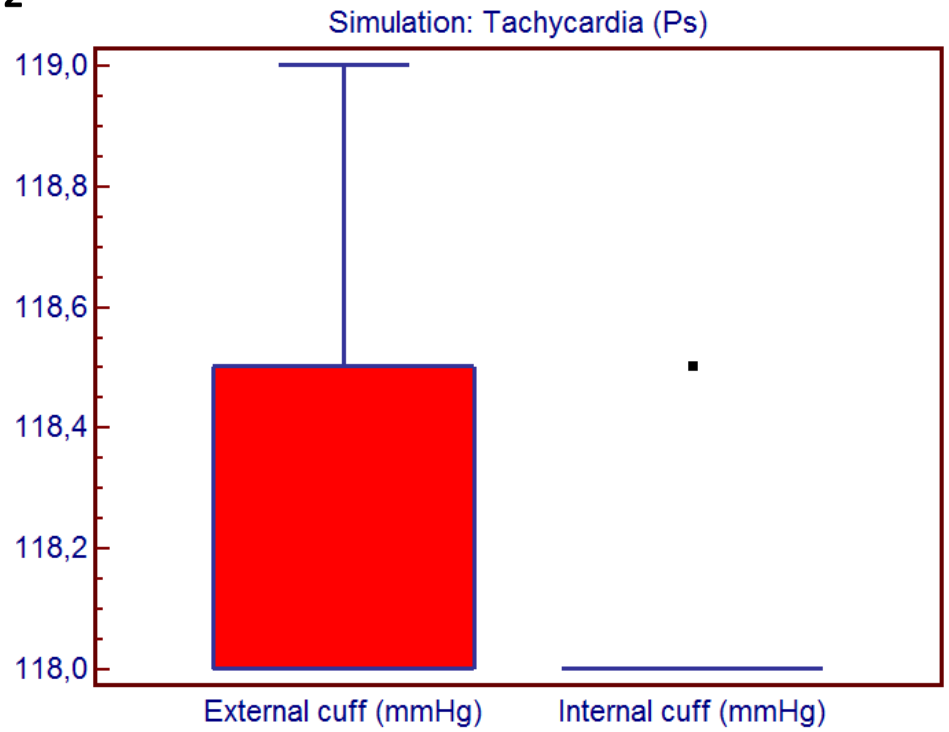

Simulation: Obese (Ps)
115,0
114,5
114,0
113,5
113,0
112,5
112,0
External cuff (mmHg)
Internal cuff (mmHg)

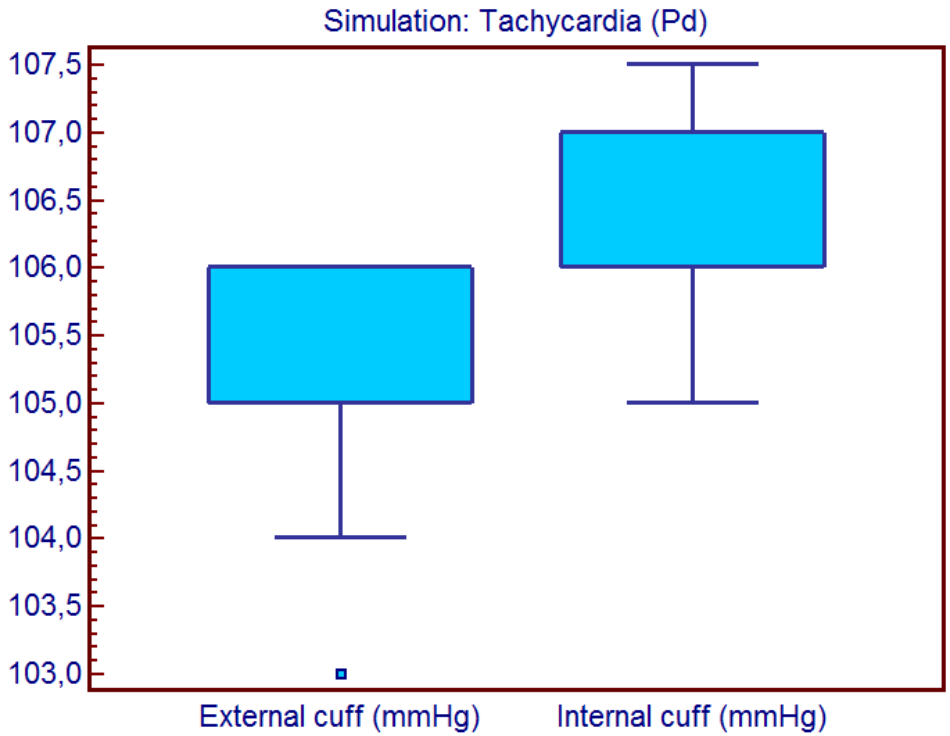

Simulation: Obese (Pd)
86,0
85,5
85,0
84,5
84,0
83,5
83,0
External cuff (mmHg)
Internal cuff (mmHg)

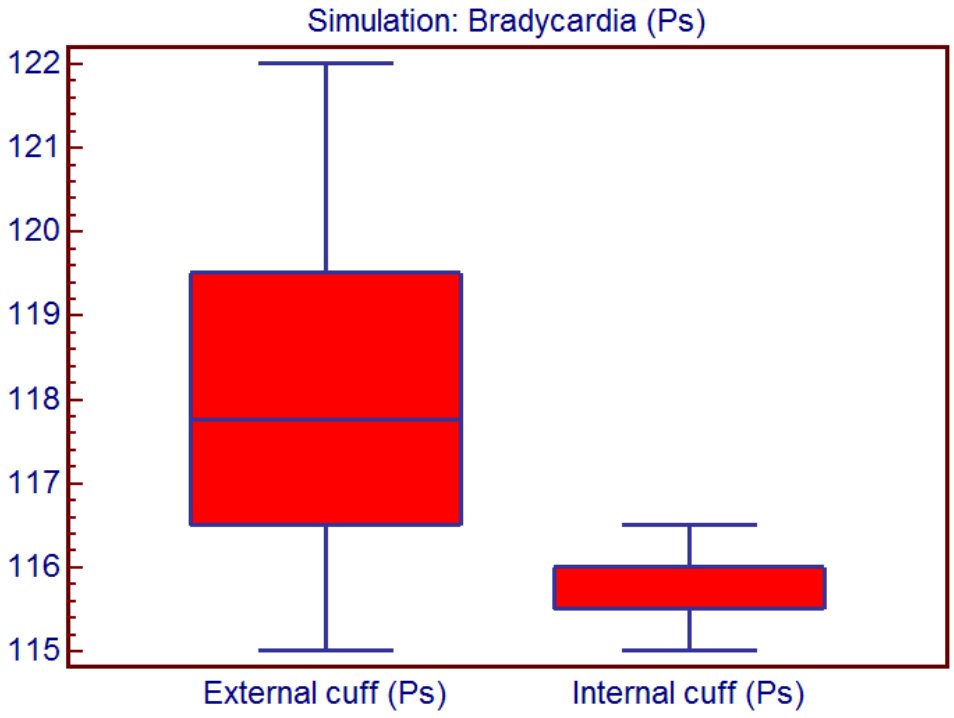

Simulation: Geriatric (Ps)
145,5
145,0
144,5
144,0
143,5
143,0
142,5
142,0
External cuff (mmHg)
Internal cuff (mmHg)

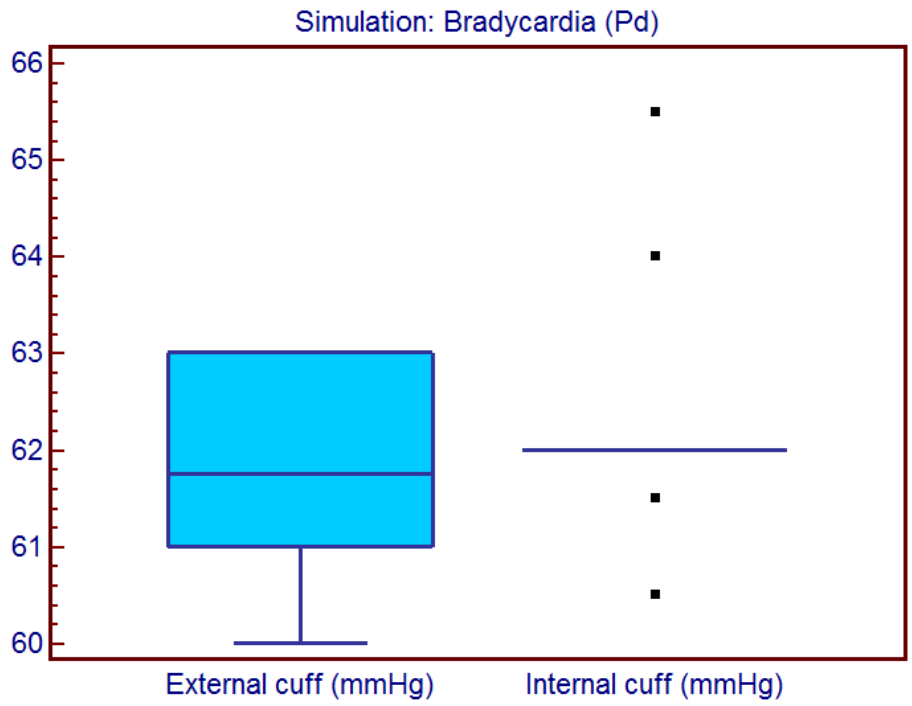

Simulation: Geriatric (Pd)
118,0
117,5
117,0
116,5
116,0
115,5
115,0
114,5
114,0
External cuff (mmHg)
Internal cuff (mmHg)

Model 2


Simulation: Tachycardia (Ps)
119,0
118,8
118,6
118,4
118,2
118,0
External cuff (mmHg)
Internal cuff (mmHg)


Simulation: Tachycardia (Pd)
107,5
107,0
106,5
106,0
105,5
105,0
104,5
104,0
103,5
103,0
External cuff (mmHg)
Internal cuff (mmHg)


Simulation: Bradycardia (Ps)
122
121
120
119
118
117
116
115
External cuff (Ps)
Internal cuff (Ps)


Simulation: Bradycardia (Pd)
66
65
64
63
62
61
60
External cuff (mmHg)
Internal cuff (mmHg)

nn

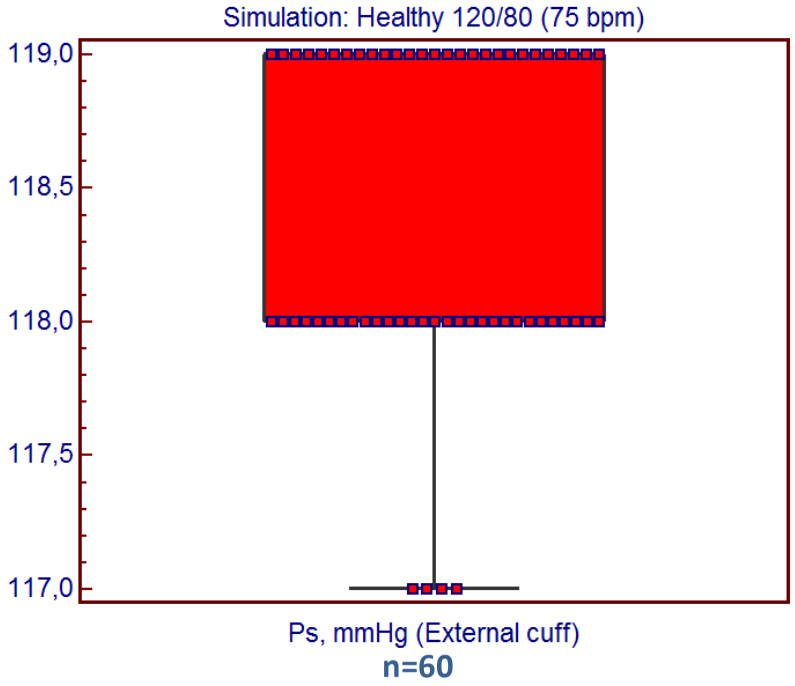
H Blood pressure measurement device validity

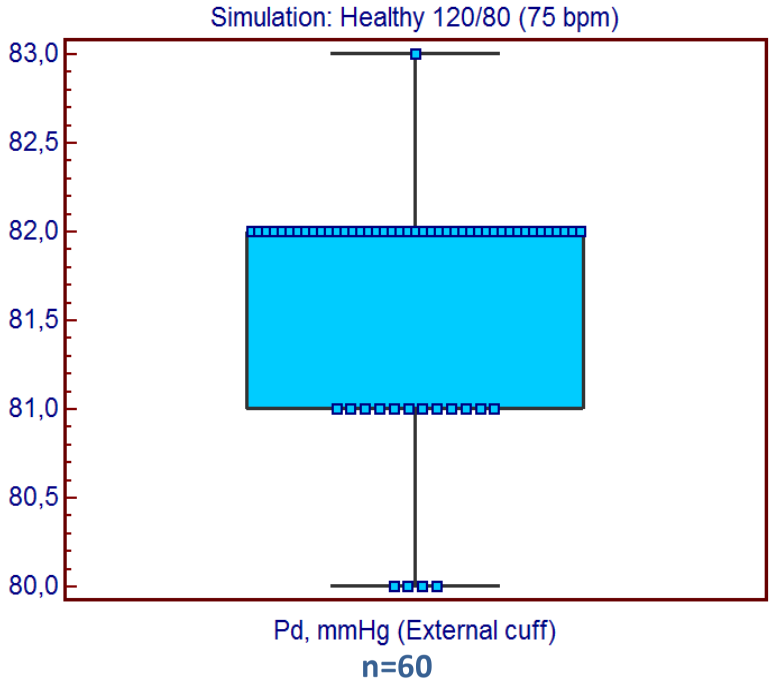
The following appendix contains boxplots for measurements obtained with external and internal cuffs, for each waveform simulation, using Model 1 and Model 2. The title of each of the following pages shows the simulation in question, simulated pressures in mmHg, and simulated pulse in bpm. Box plots are for all P_s and P_d measurements produced by the blood pressure measurement devices. Systolic pressures are marked in red, and diastolic pressures are marked in blue. See the table below, for systolic and diastolic pressures for each simulation.

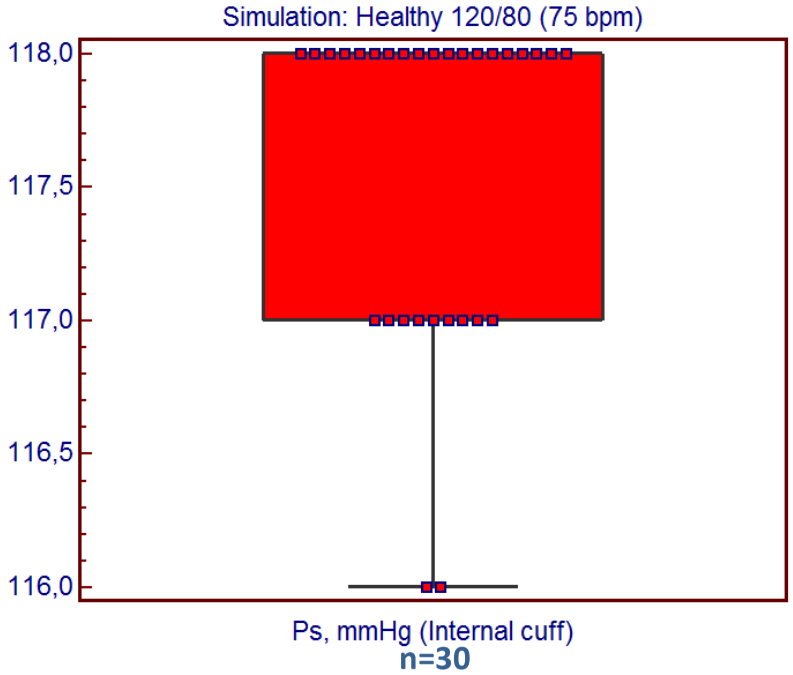
Patient Condition	Blood Pressure (mmHg) (MAP)	Heart Rate (bpm)	Pulse volume (cc)
Healthy Heart	120/80 (93)	75	0.68
Weak Pulse	110/80 (90)	95	0.50
Mild Exercise #1	140/90 (106)	120	1.00
Strenuous Exercise #2	140/90 (106)	162	1.40
Obese Subject	120/80 (93)	90	0.50
Geriatric Subject	150/110 (123)	95	0.40
Tachycardia	120/105 (110)	130	0.40
Bradycardia	120/60 (80)	45	1.10

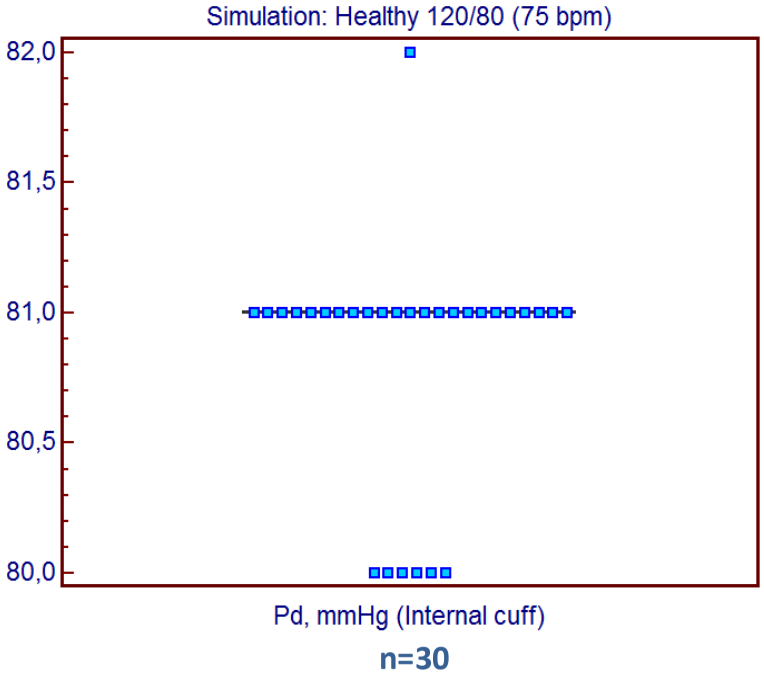
Model 1

Simulation: Healthy 120/80 (75 bpm)



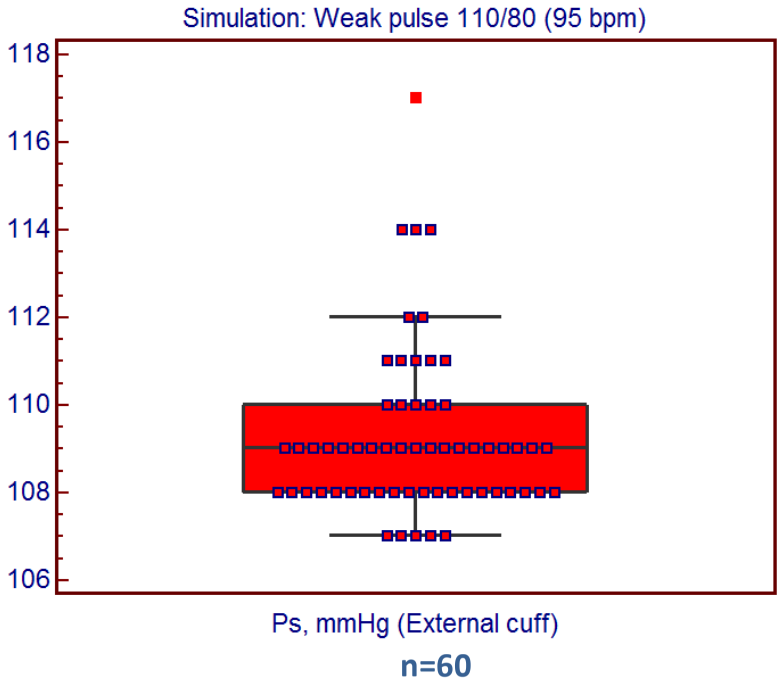


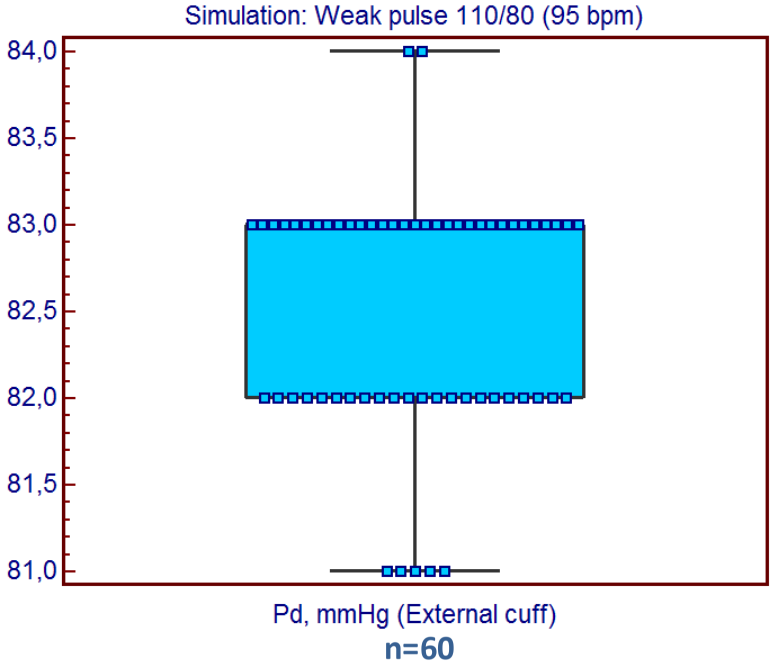


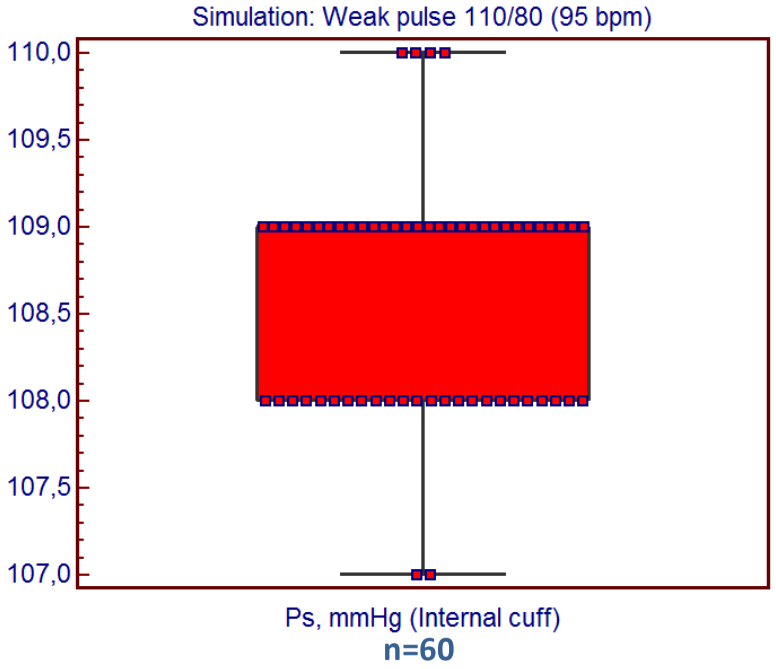


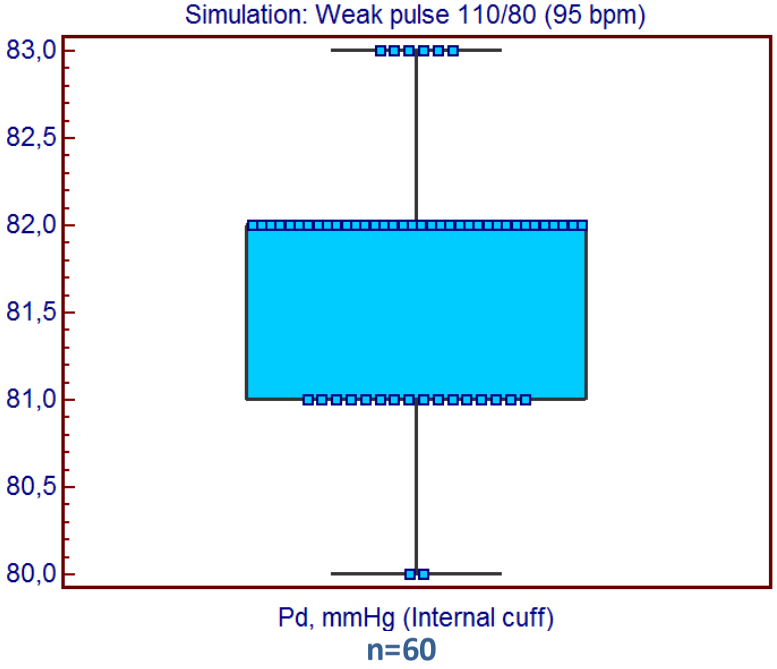
Model 1

Simulation: Weak pulse 110/80 (95 bpm)



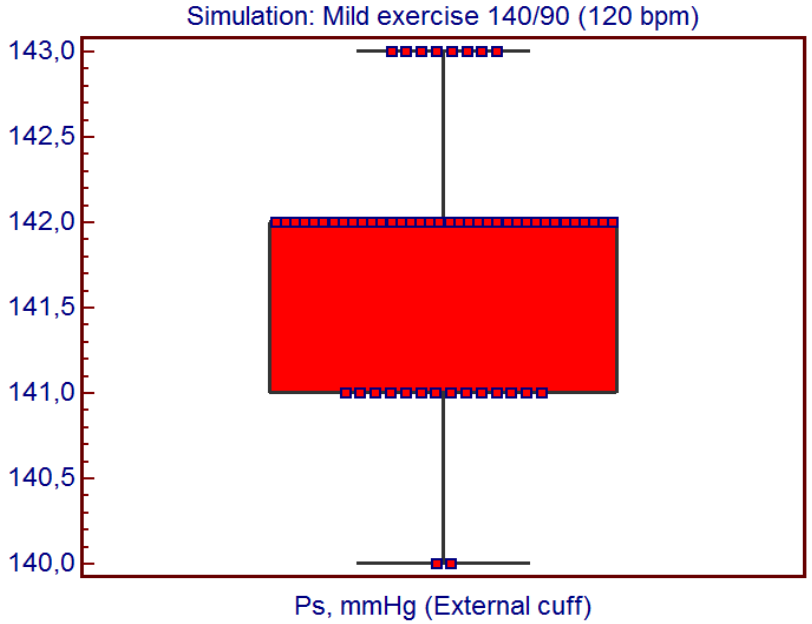


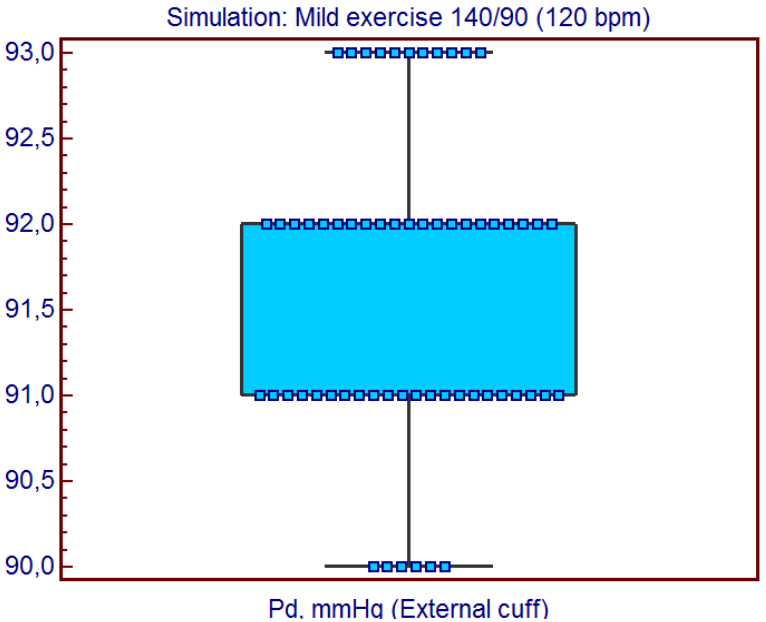


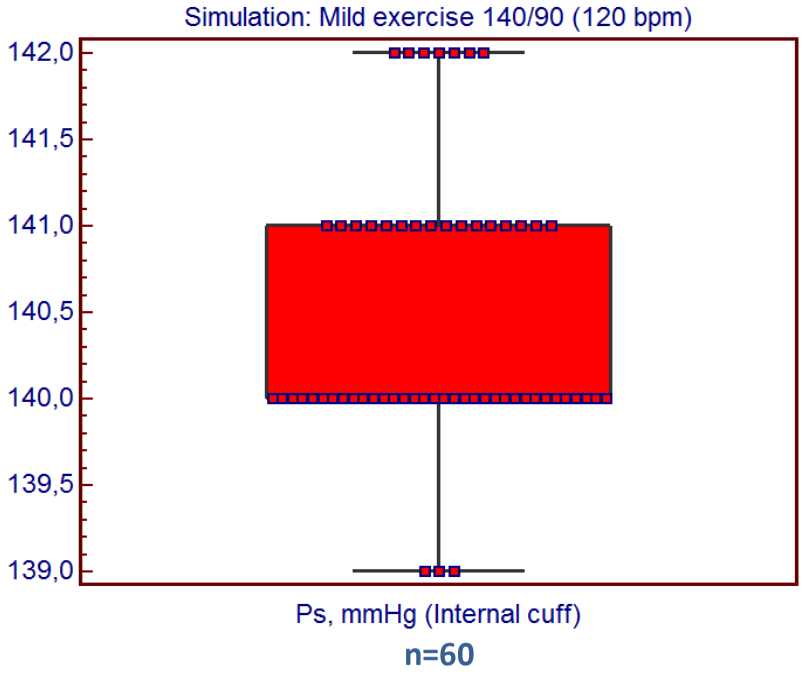


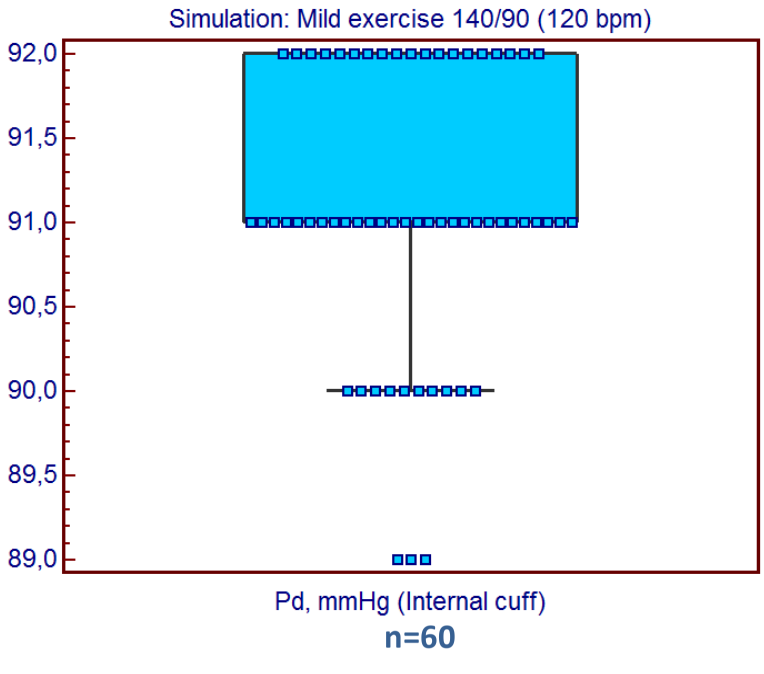
Model 1

Simulation: Mild exercise 140/90 (120 bpm)



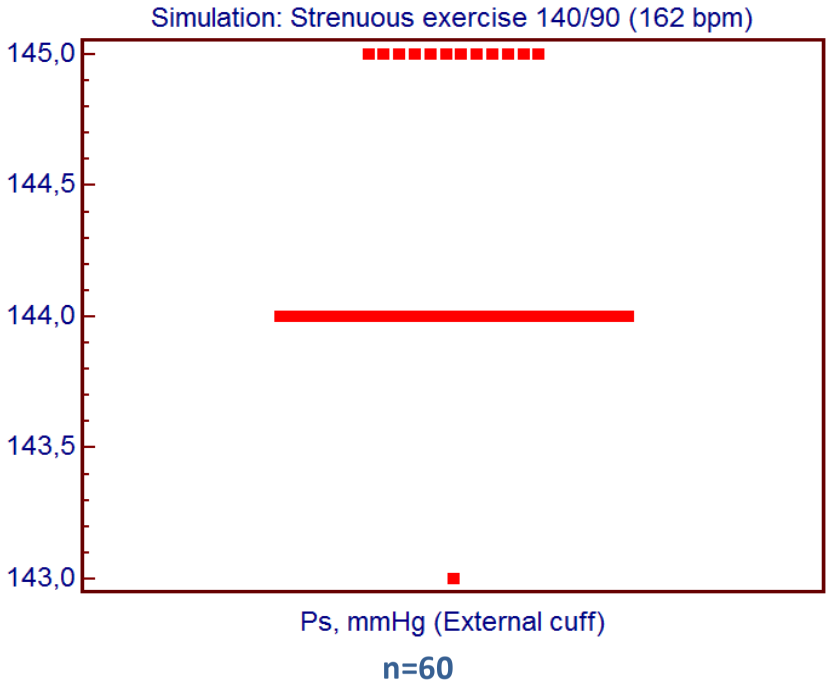


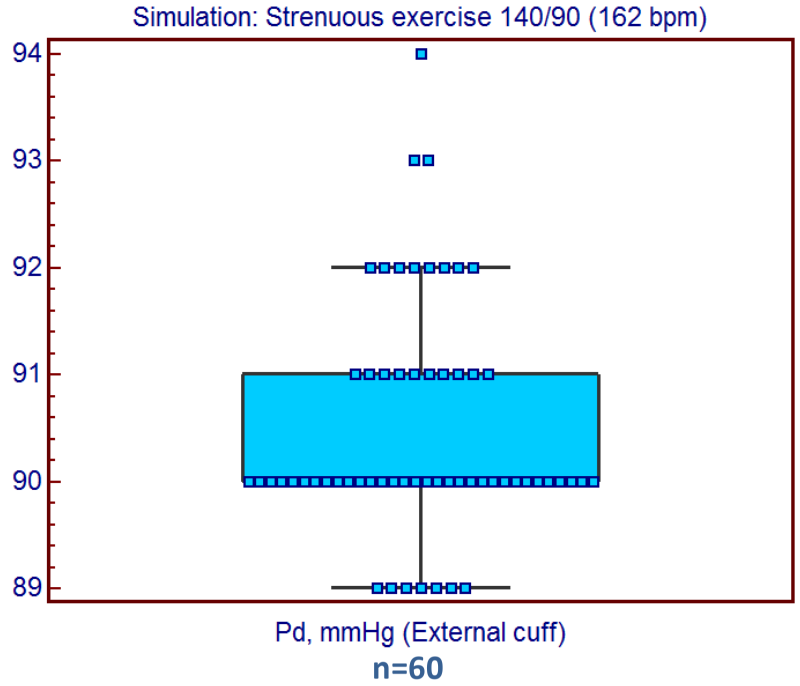


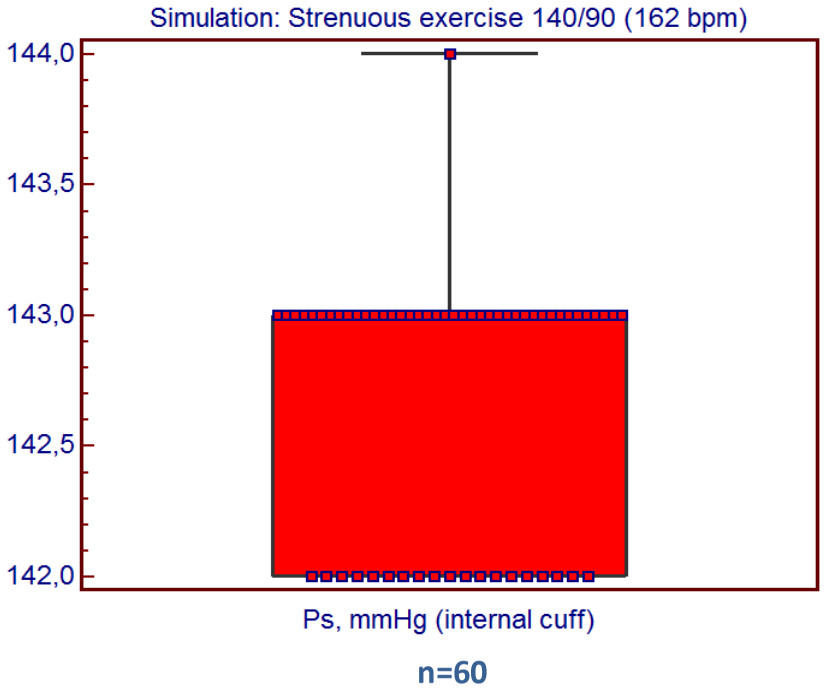


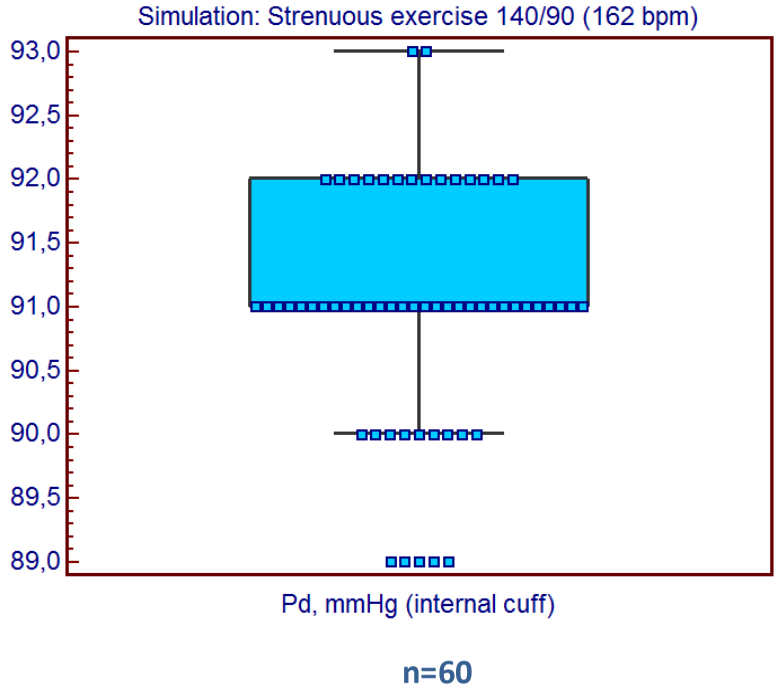
Model 1

Simulation: Strenuous exercise 140/90 (162 bpm)

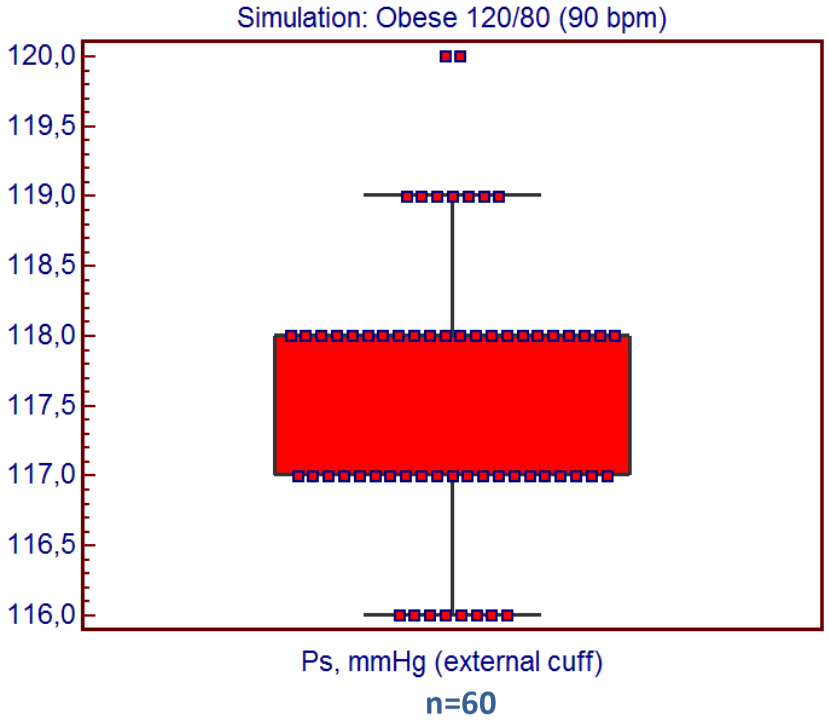


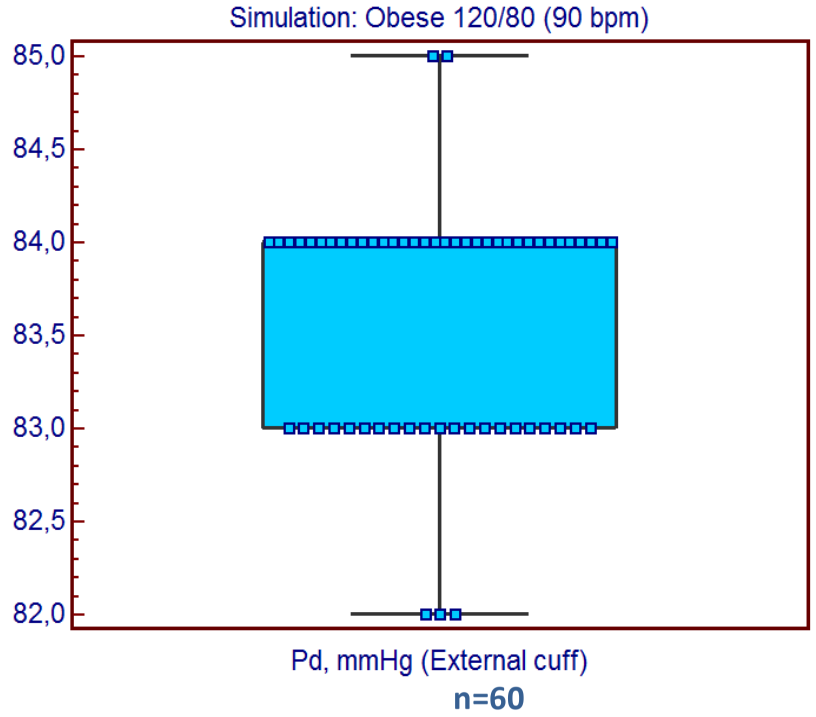






Simulation: Obese 120/80 (90 bpm)

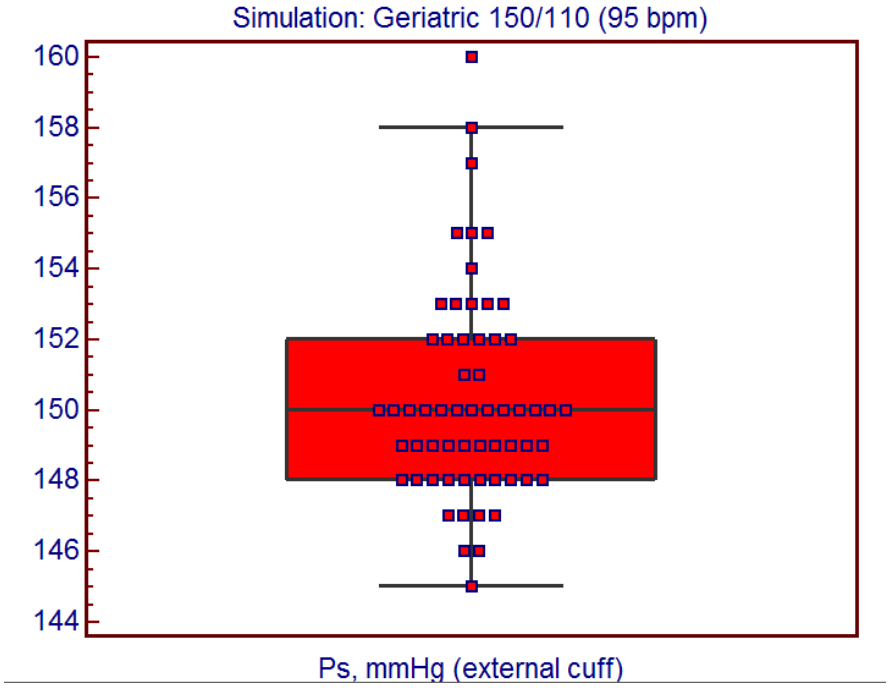


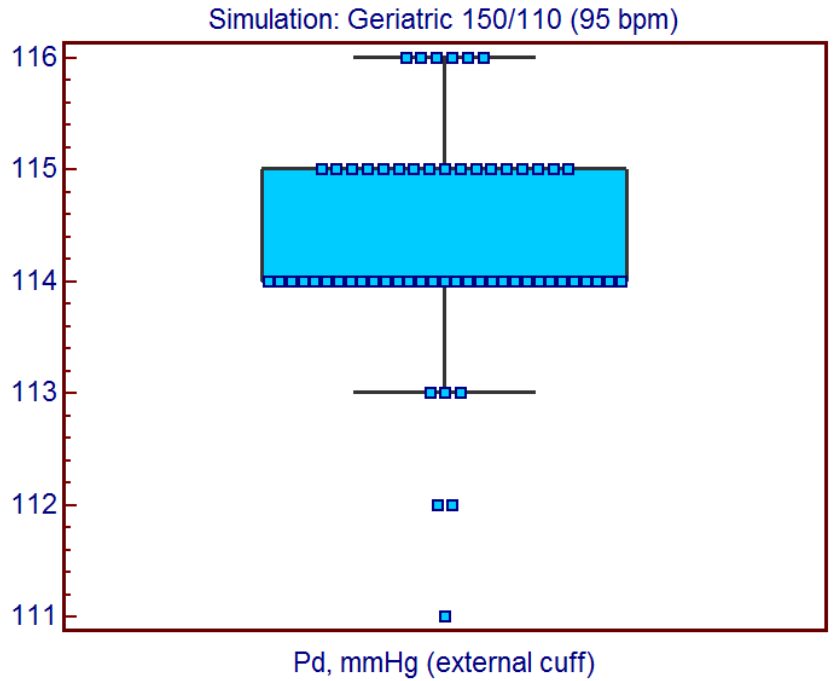


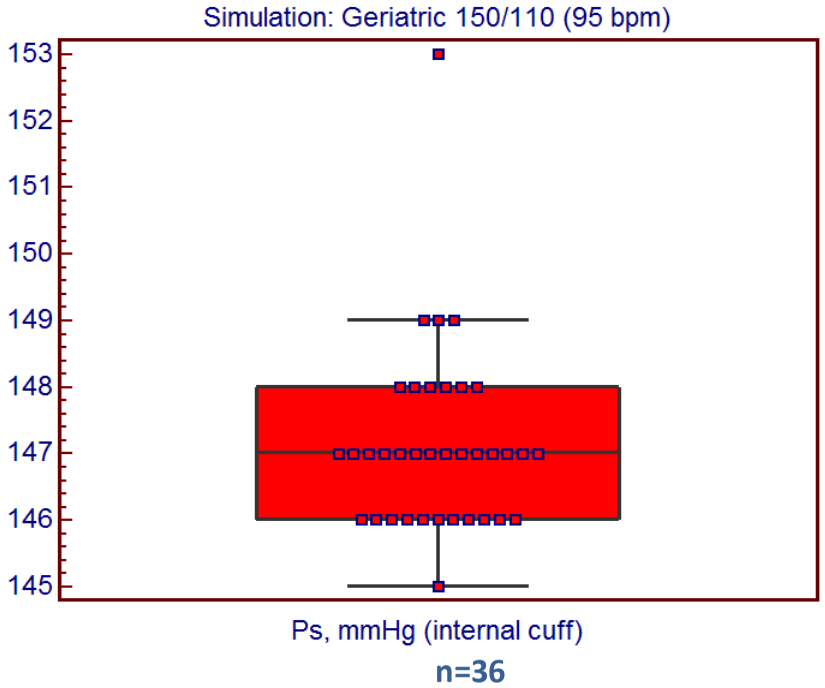
Simulation: Obese 120/80 (90 bpm)
Internal cuff:
N/A (excluded)

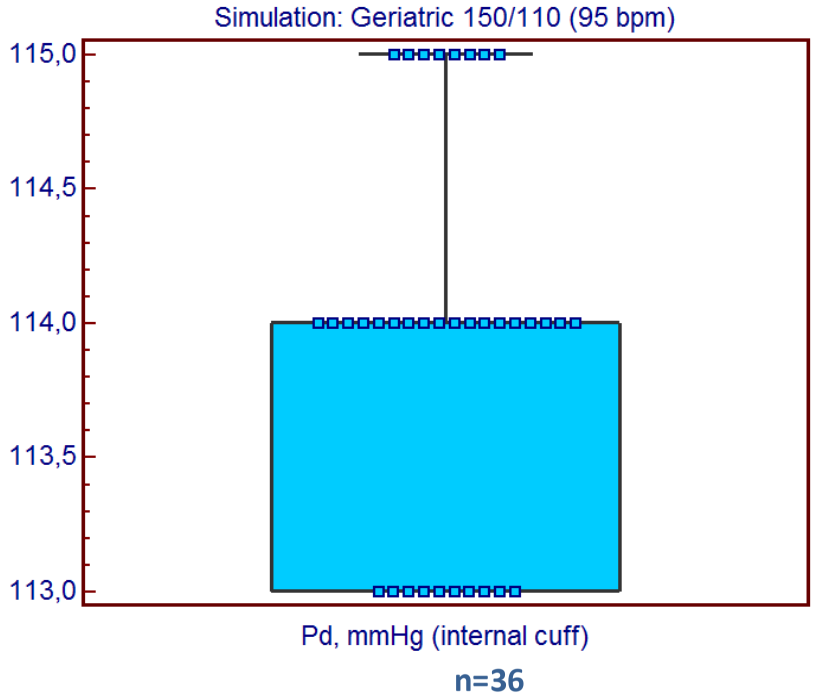
Model 1

Simulation: Geriatric 150/110 (95 bpm)







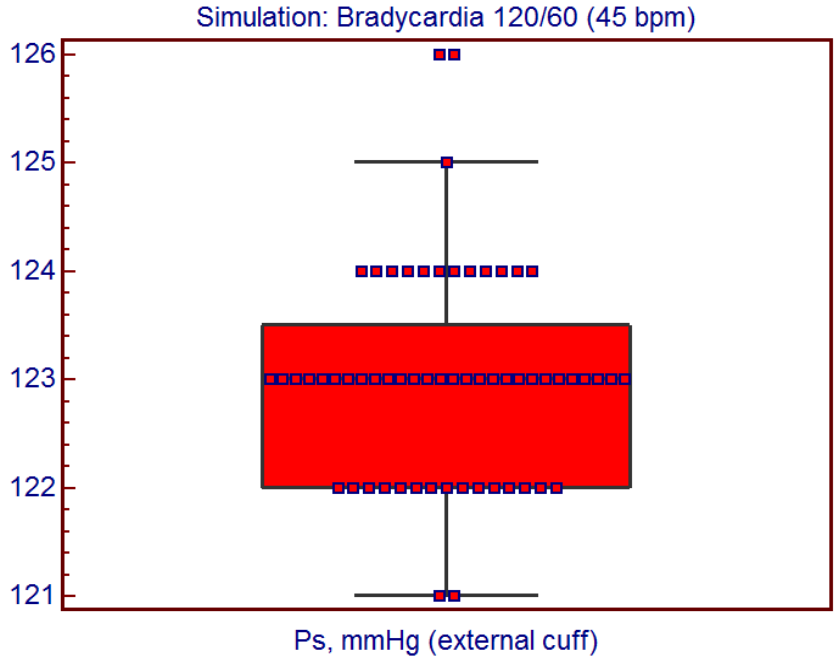


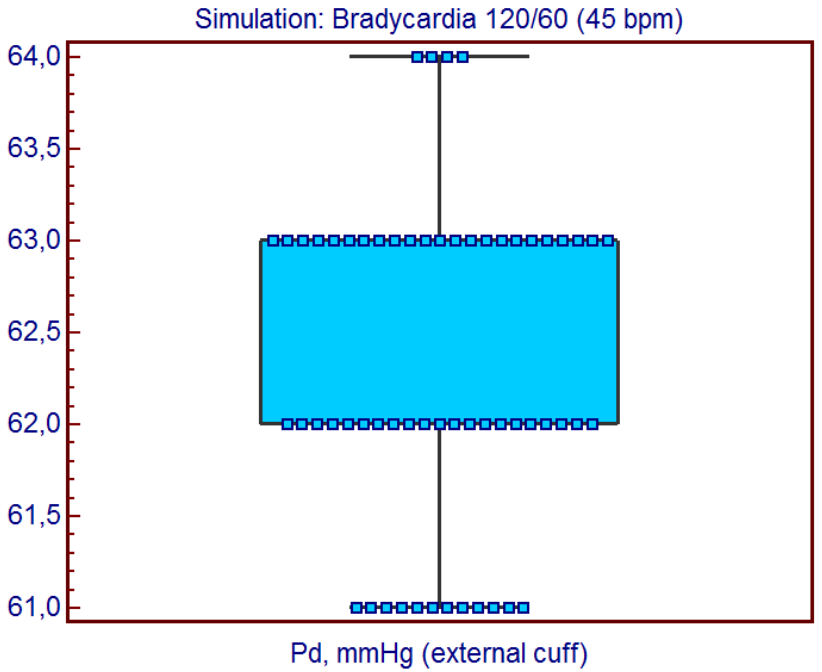
Model 1

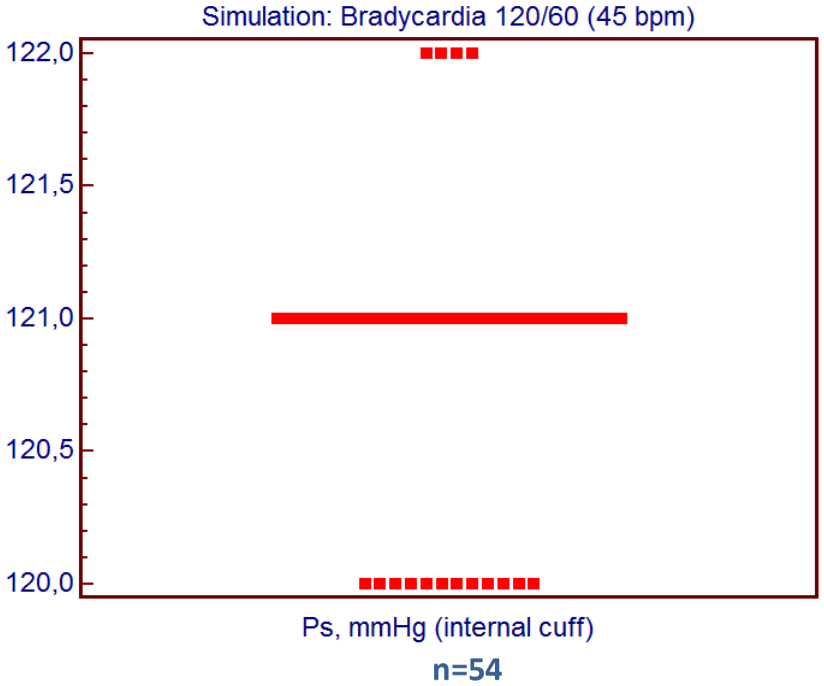
Simulation: Tachycardia 120/105 (130 bpm)
External and Internal cuff:
N/A (excluded)

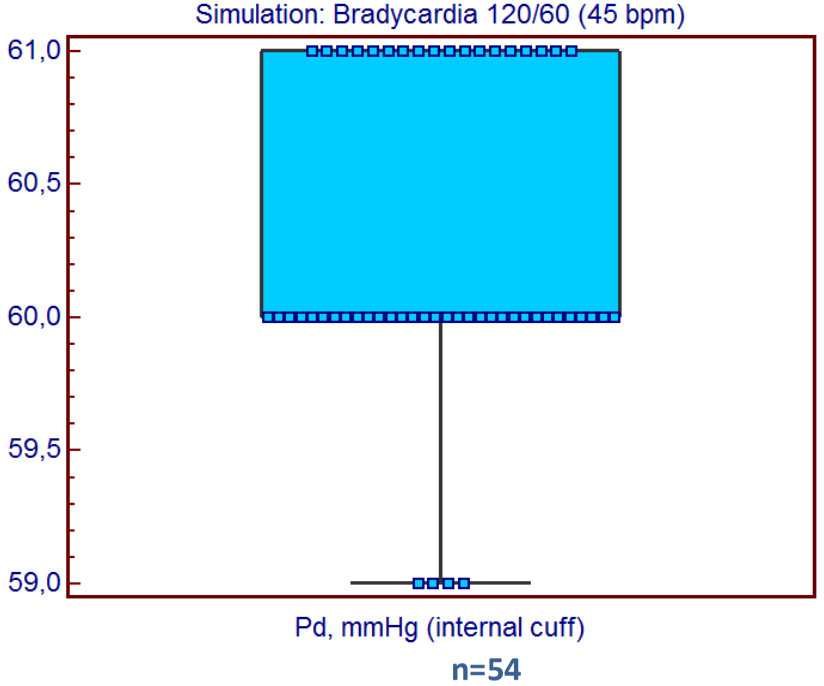
Model 1

Simulation: Bradycardia 120/60 (45 bpm)



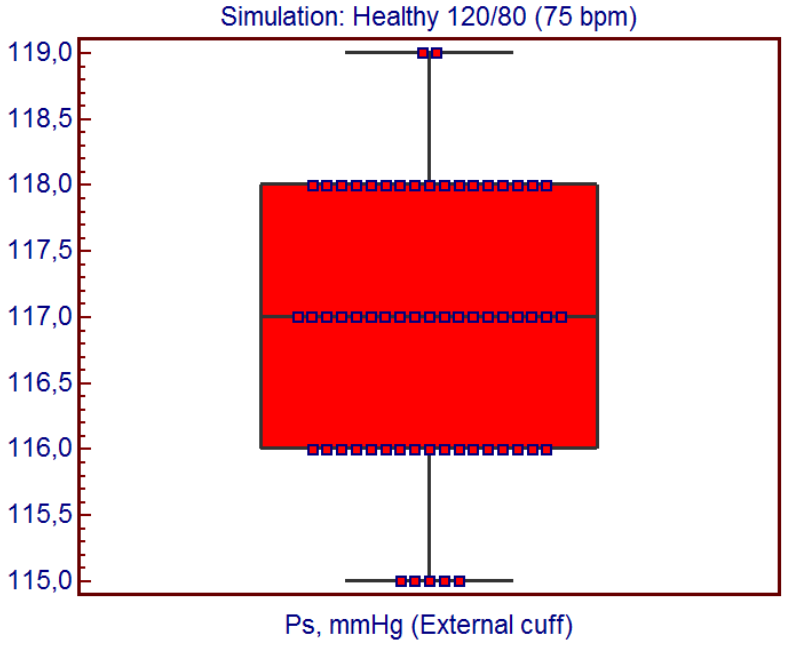


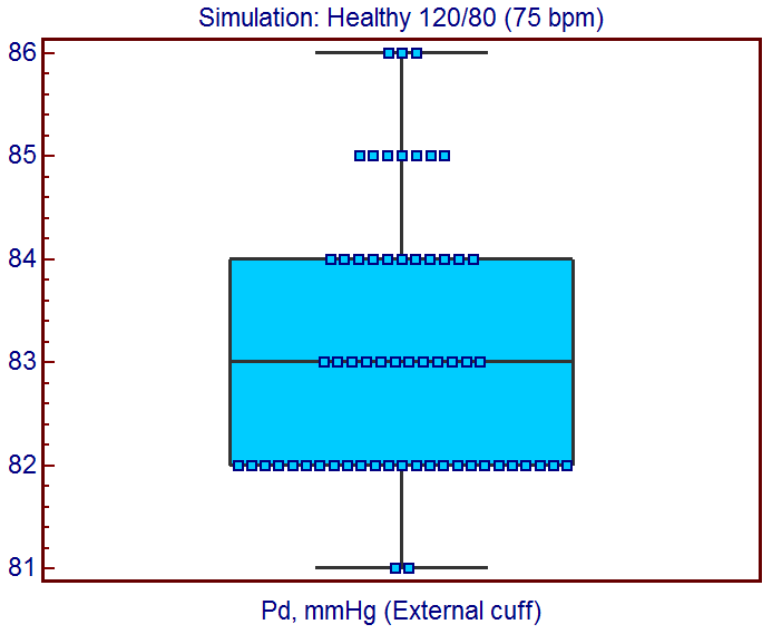


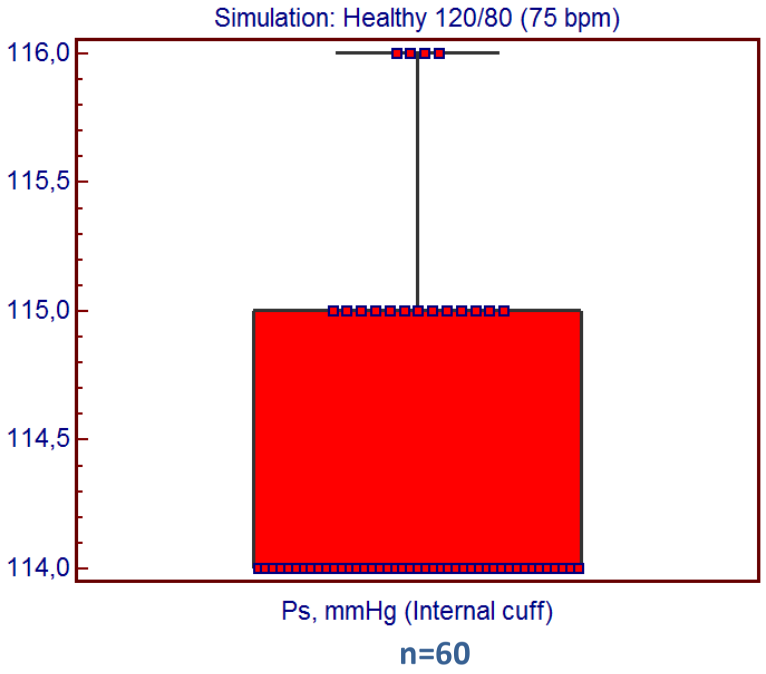


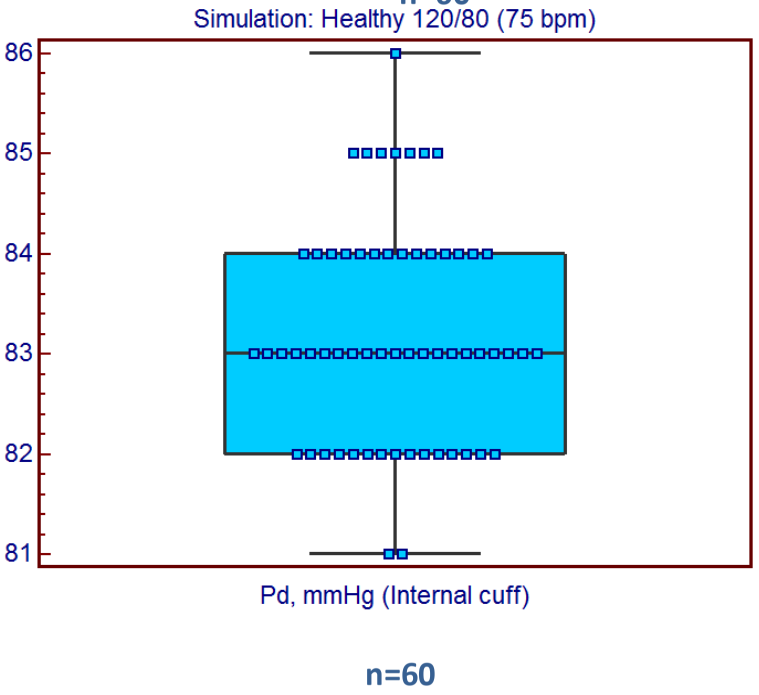
Model 2

Simulation: Healthy 120/80 (75 bpm)



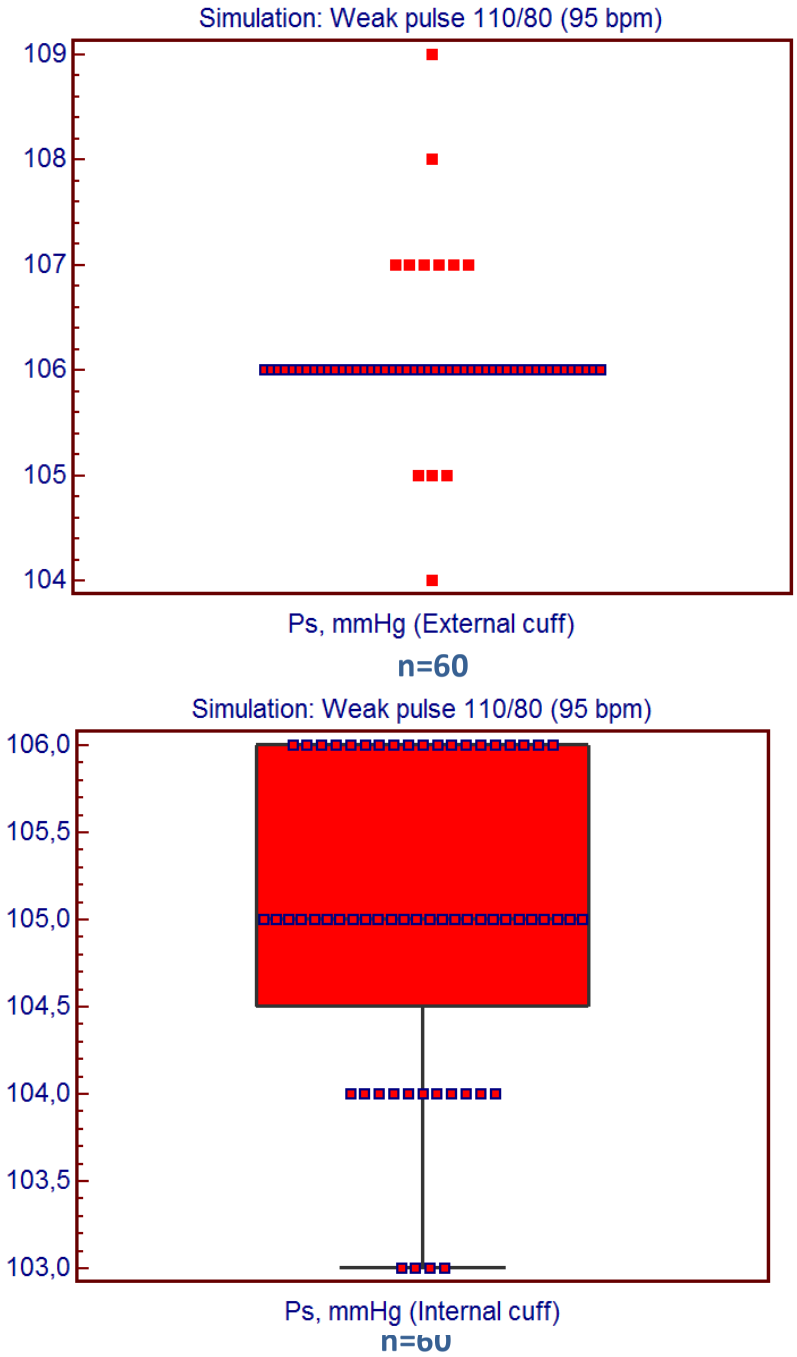


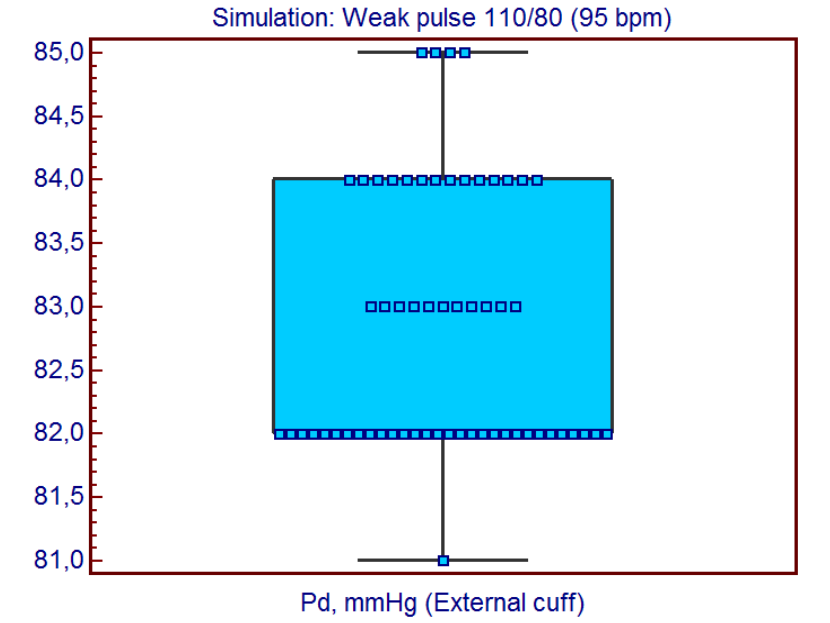


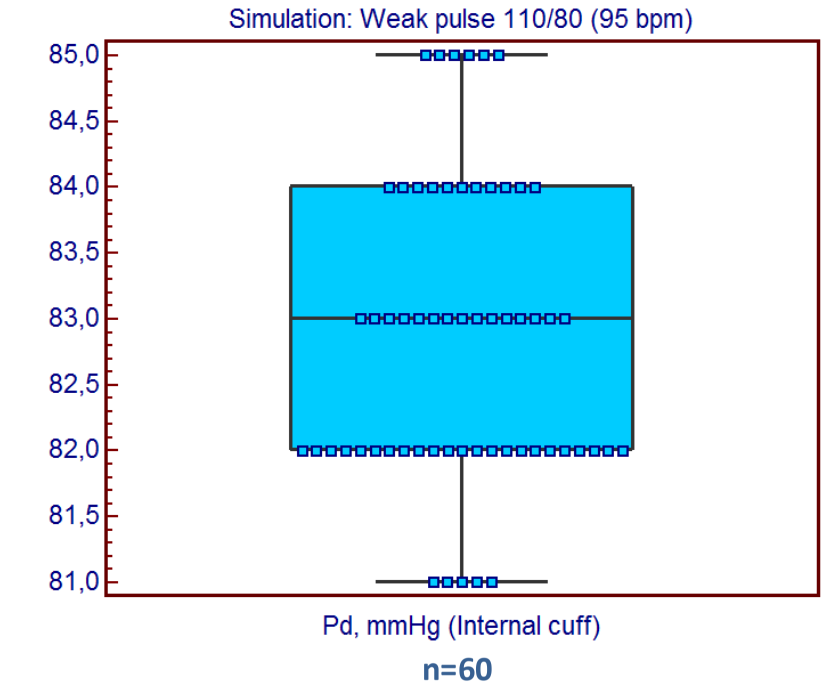


Model 2

Simulation: Weak pulse 110/80 (95 bpm)

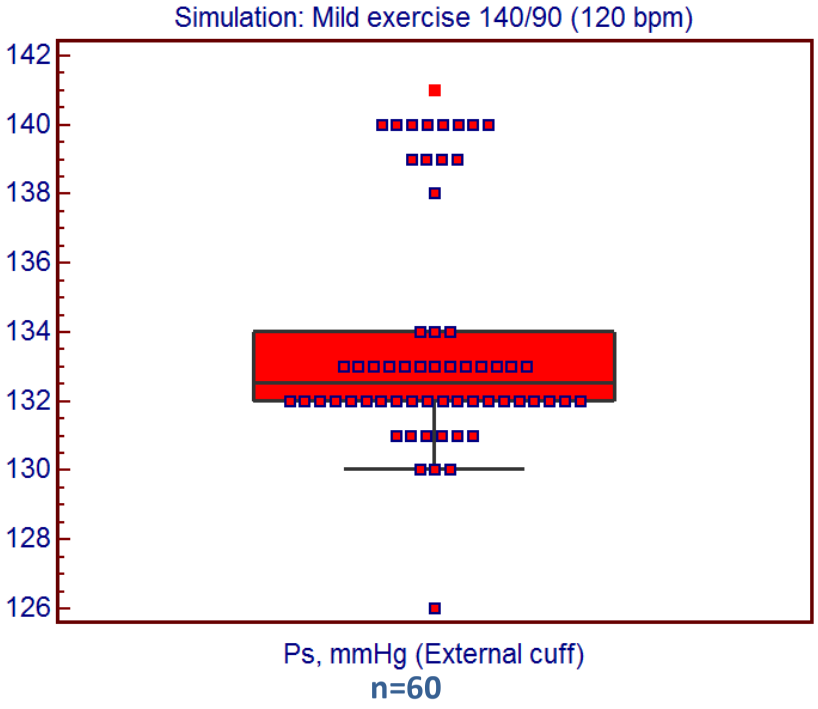


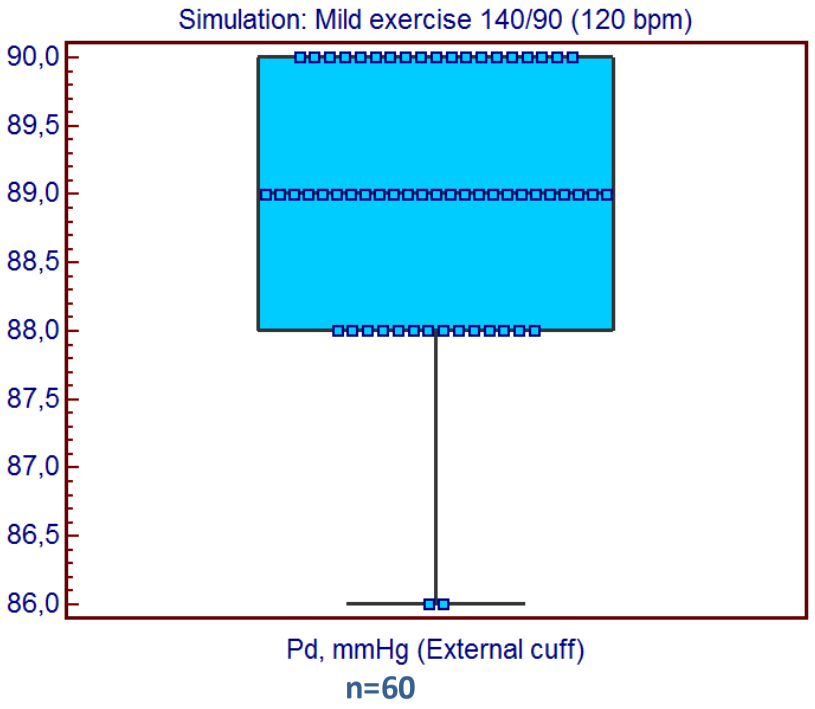


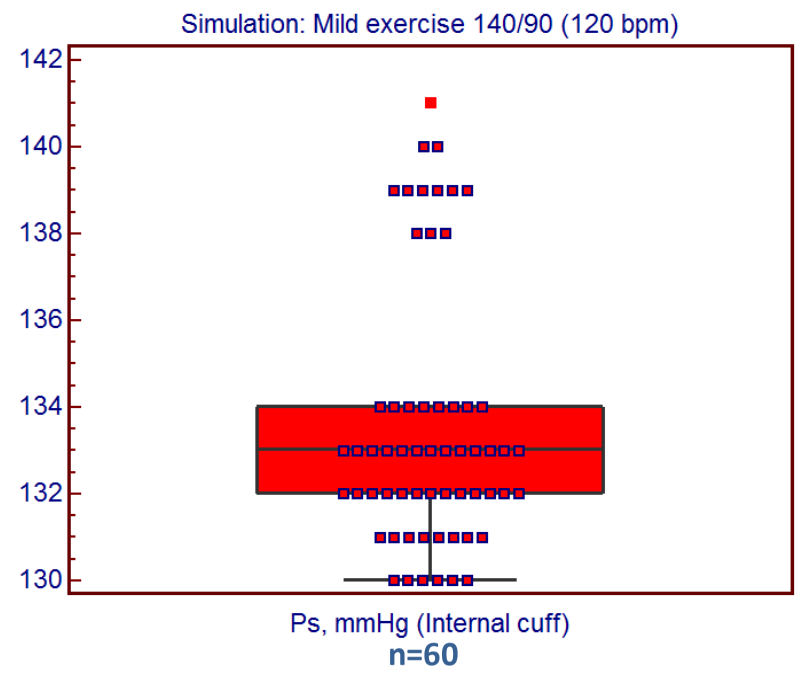


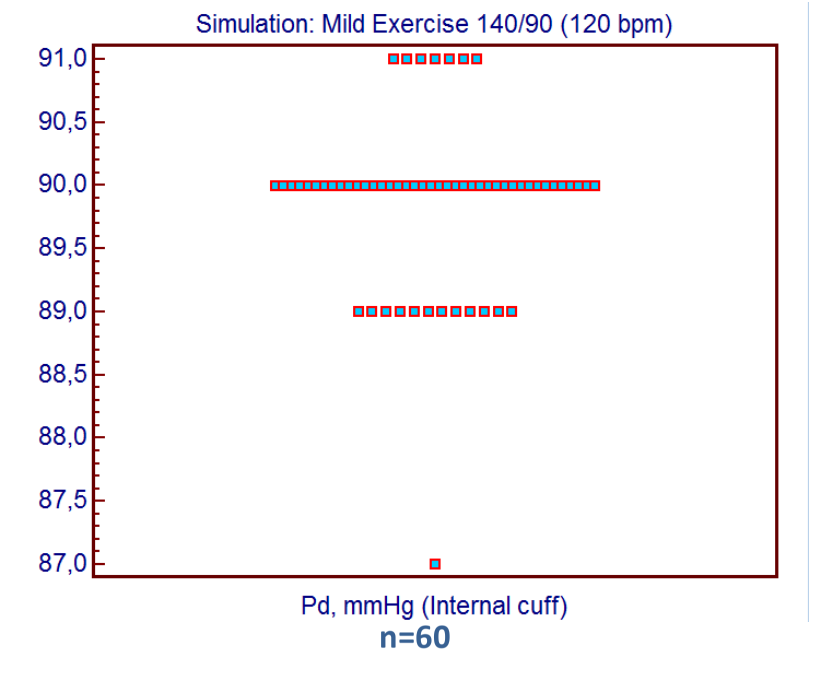
Model 2

Simulation: Mild exercise 140/90 (120 bpm)



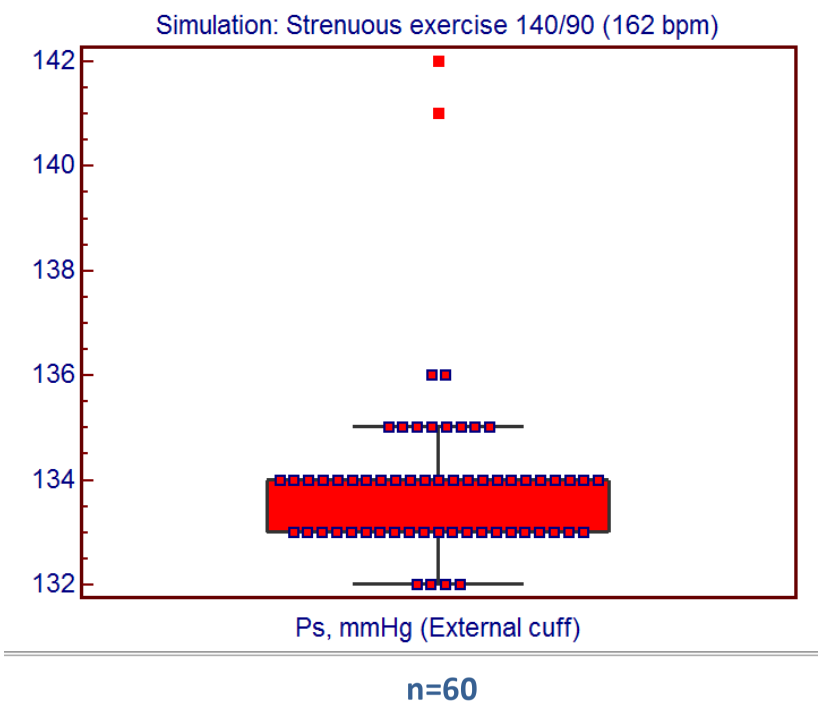


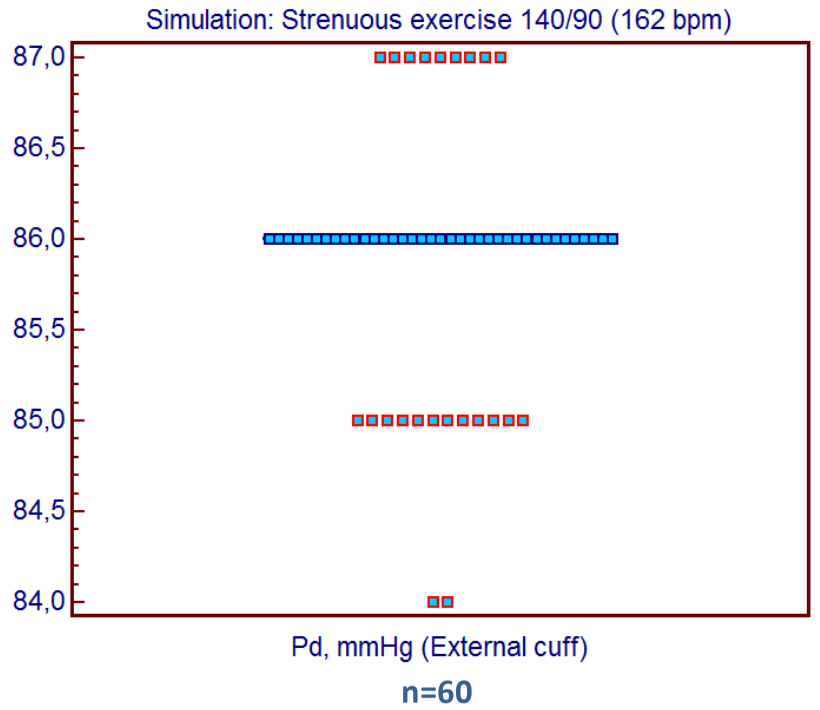


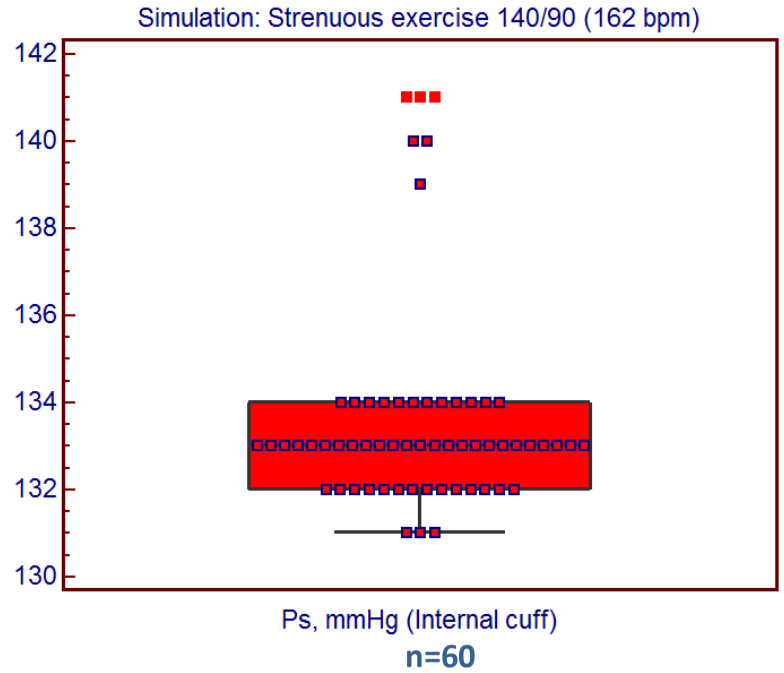


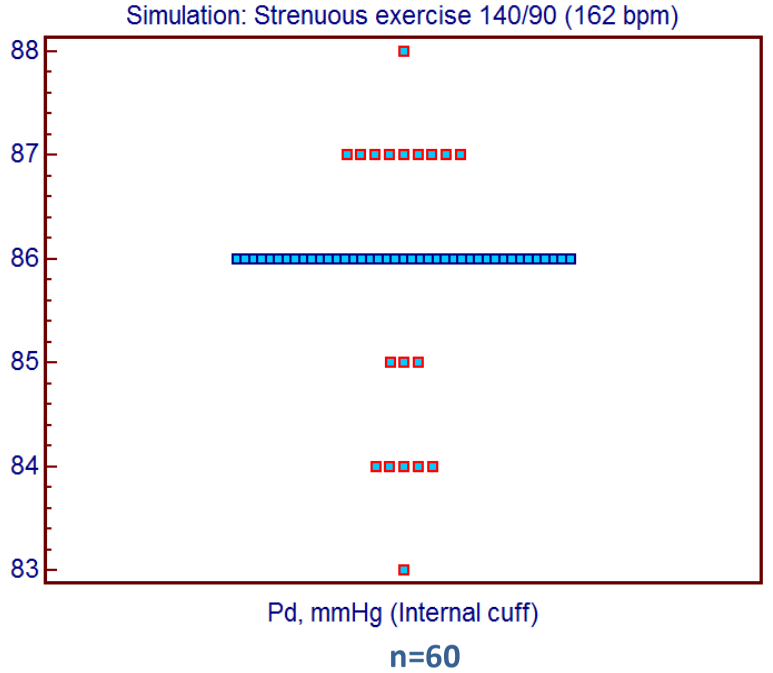
Model 2

Simulation: Strenuous exercise 140/90 (162 bpm)



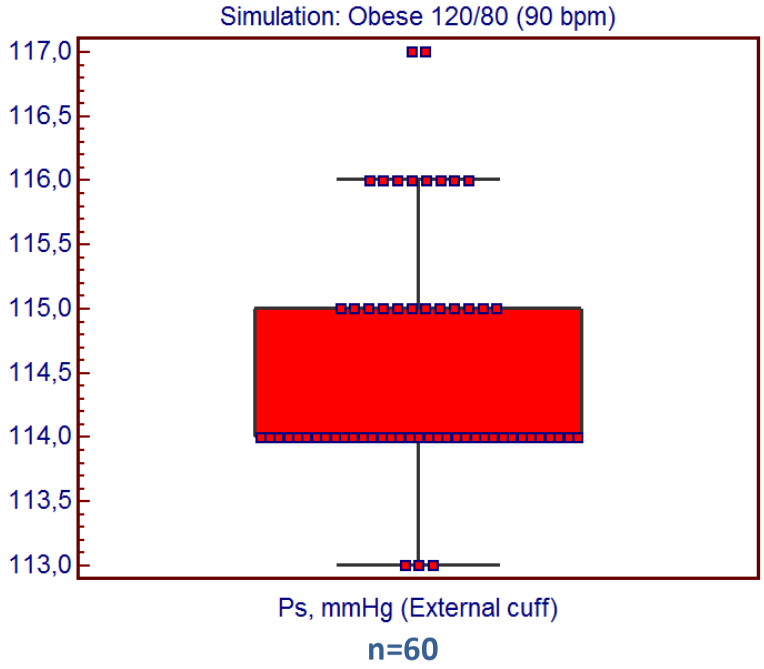


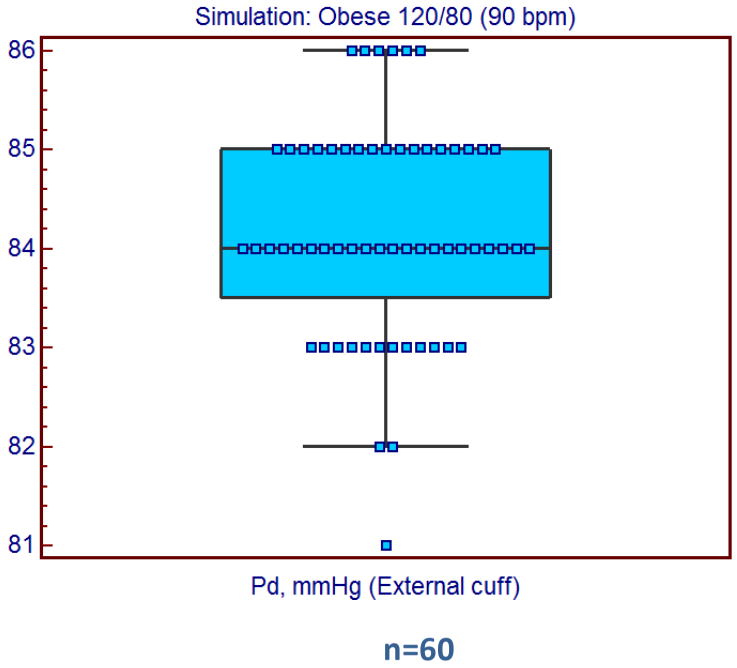


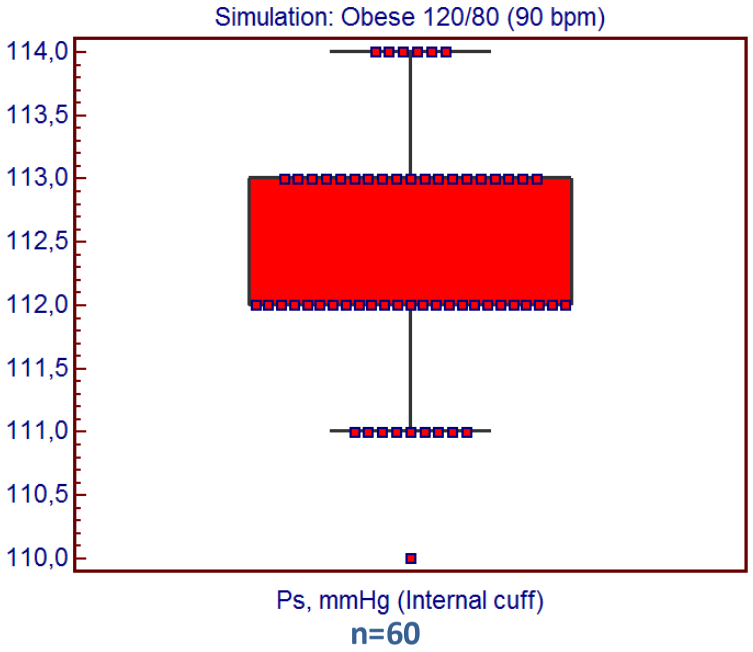


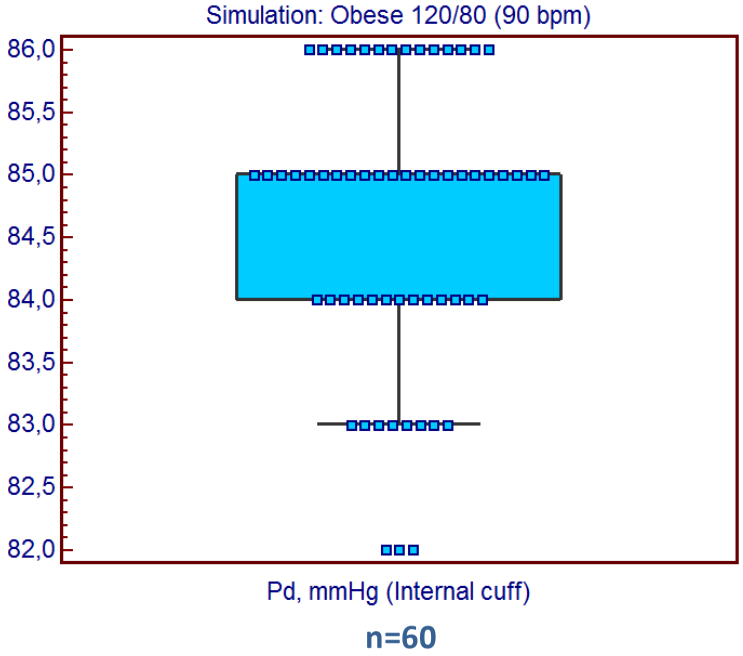
Model 2

Simulation: Obese 120/80 (90 bpm)



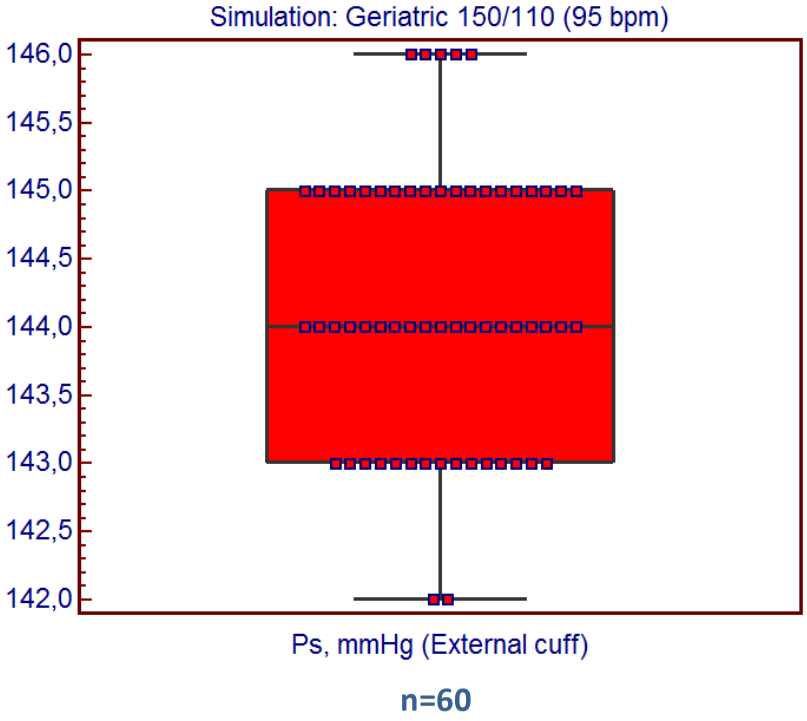


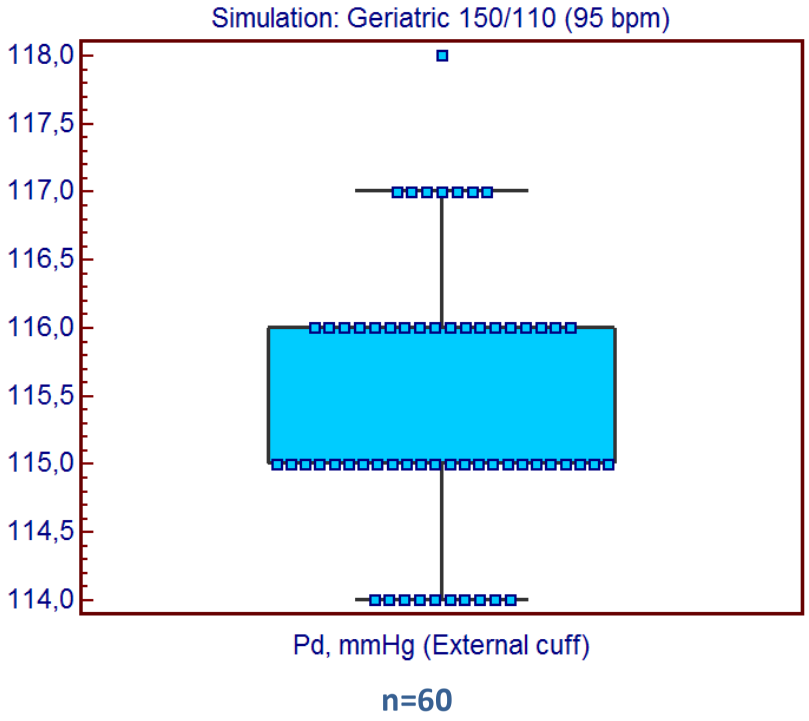


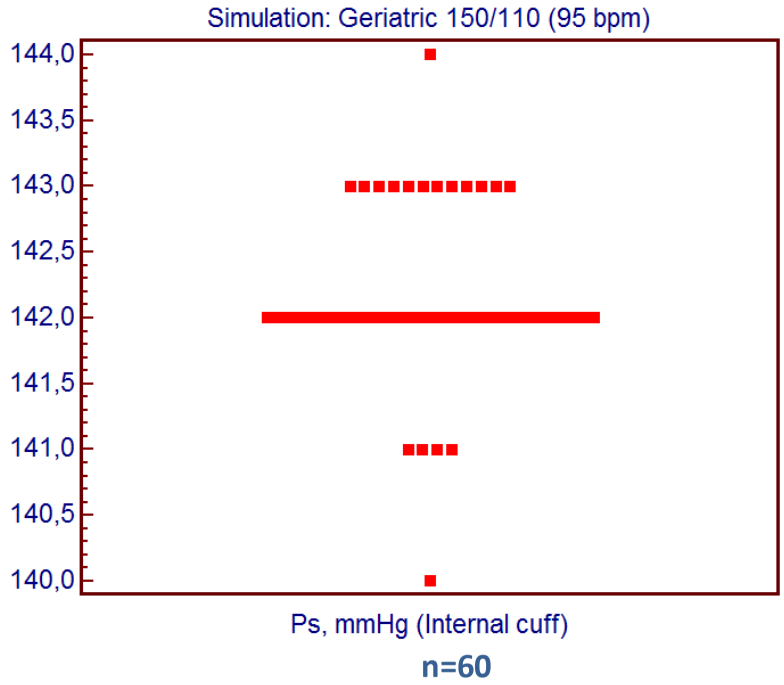


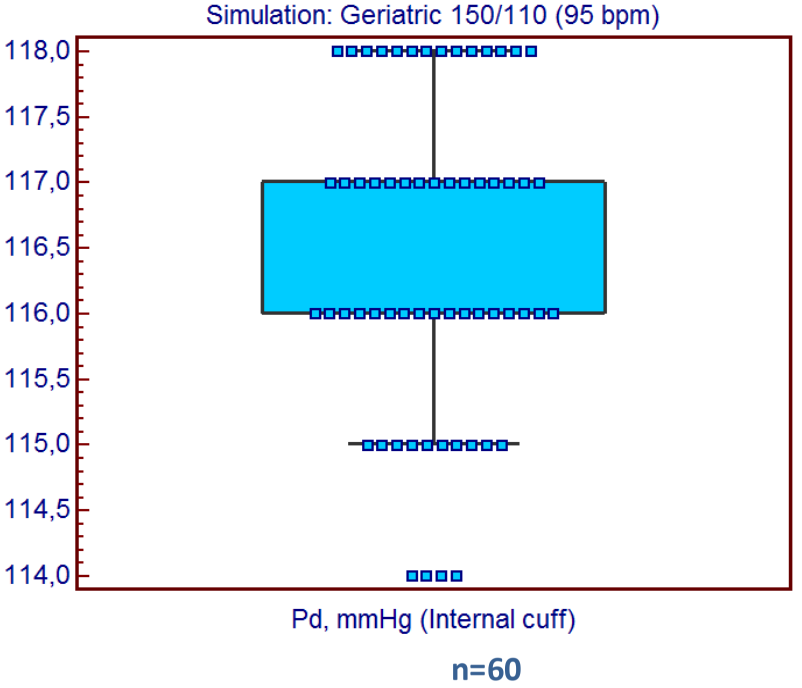
Model 2

Simulation: Geriatric 150/110 (95 bpm)



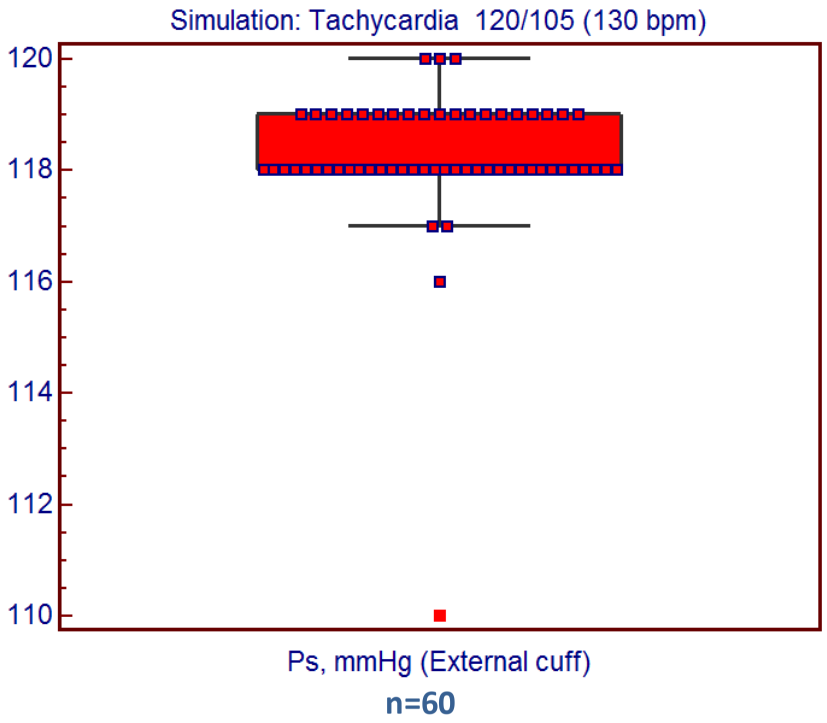


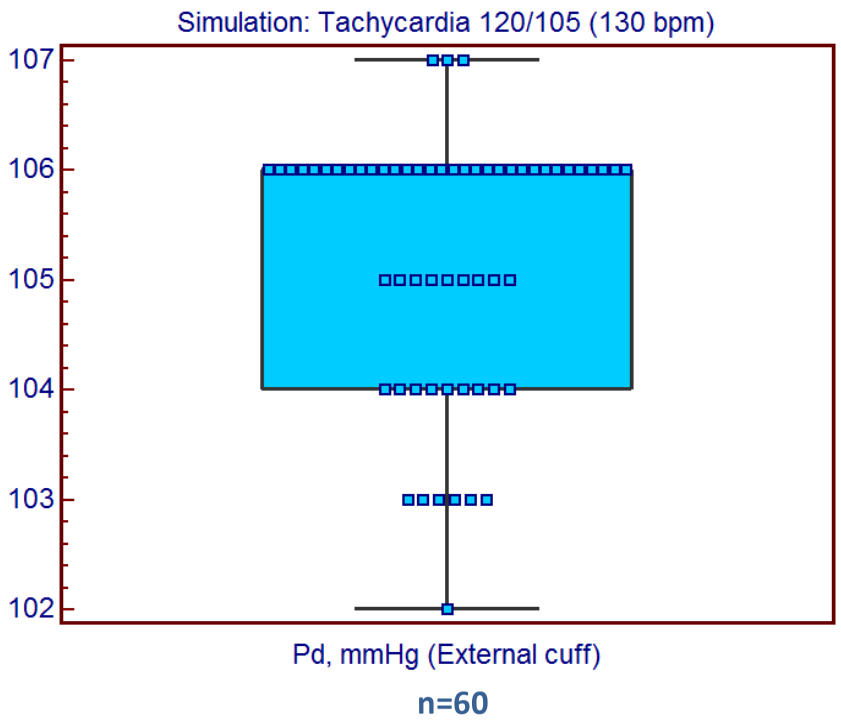


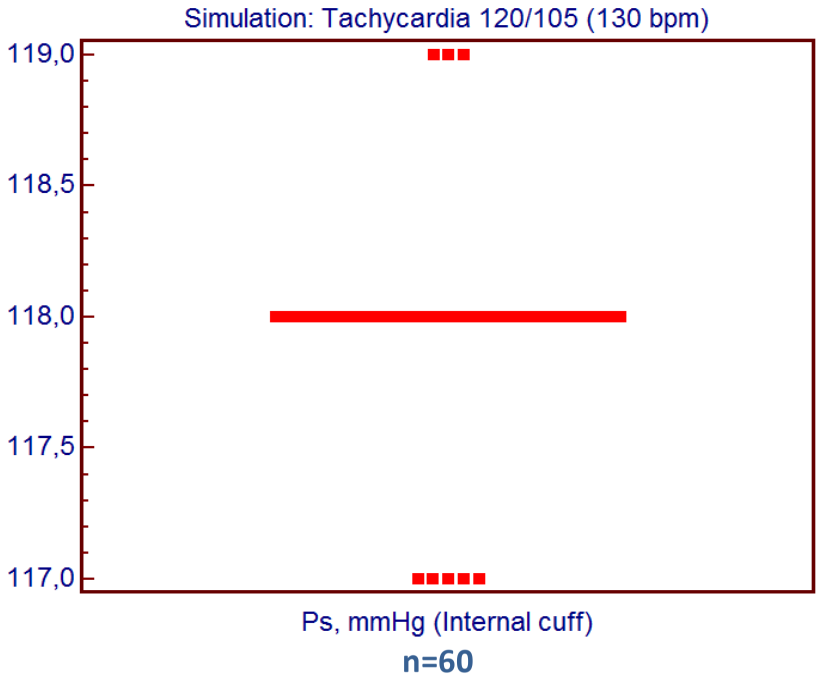


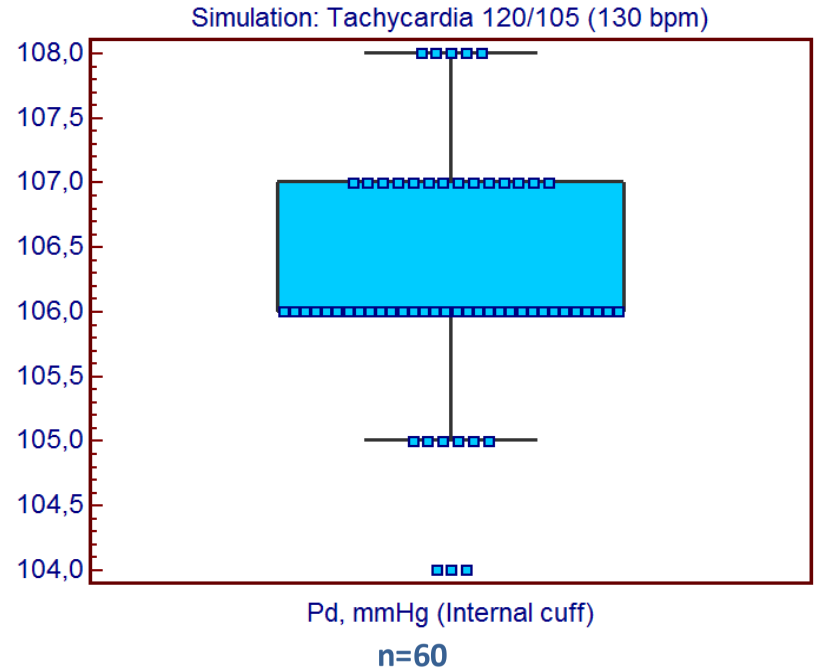
Model 2

Simulation: Tachycardia 120/105 (130 bpm)



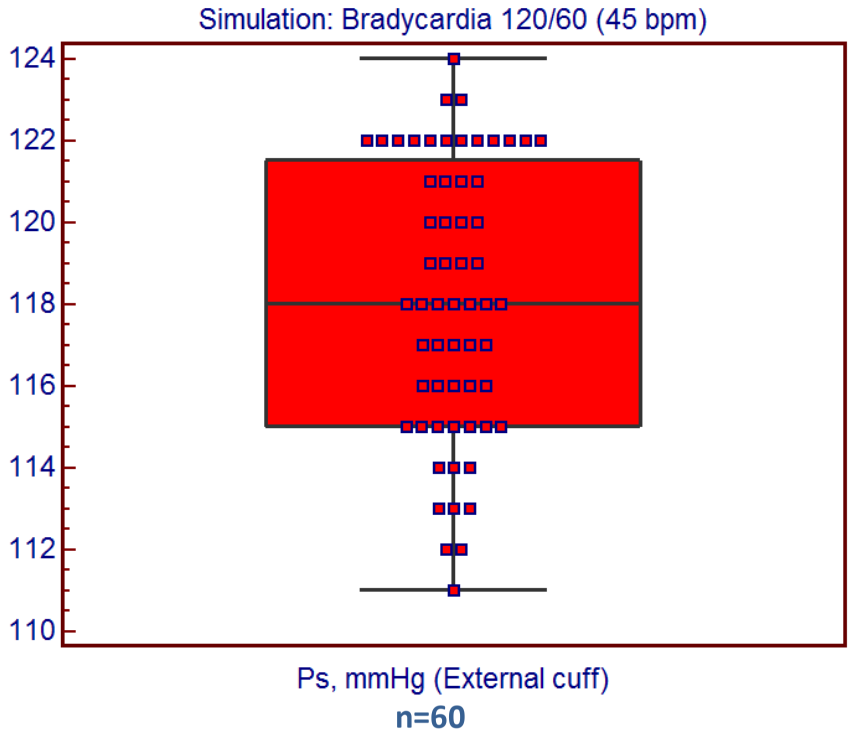


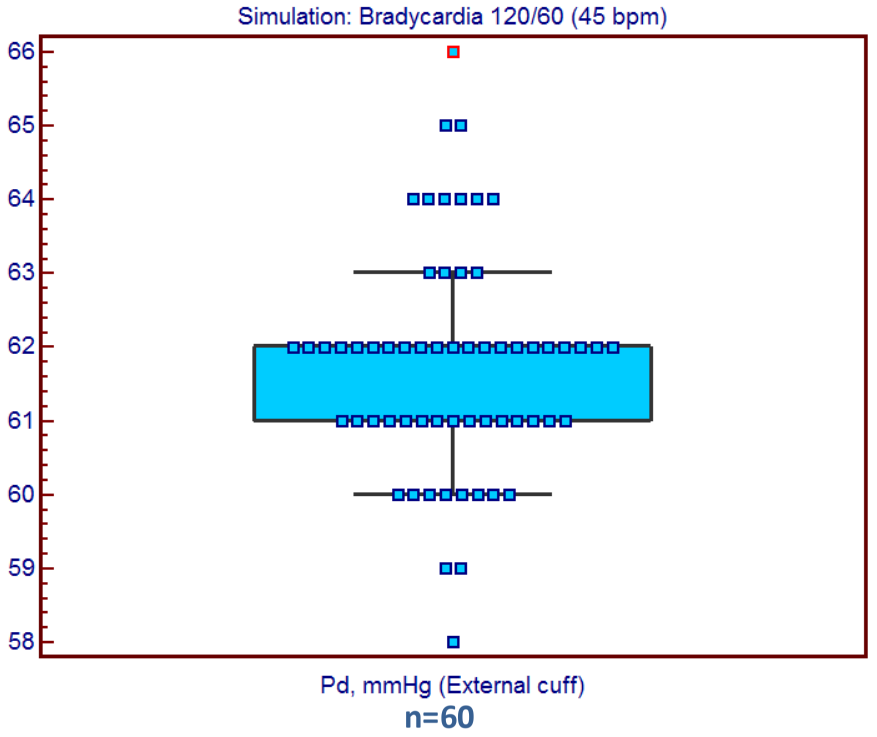


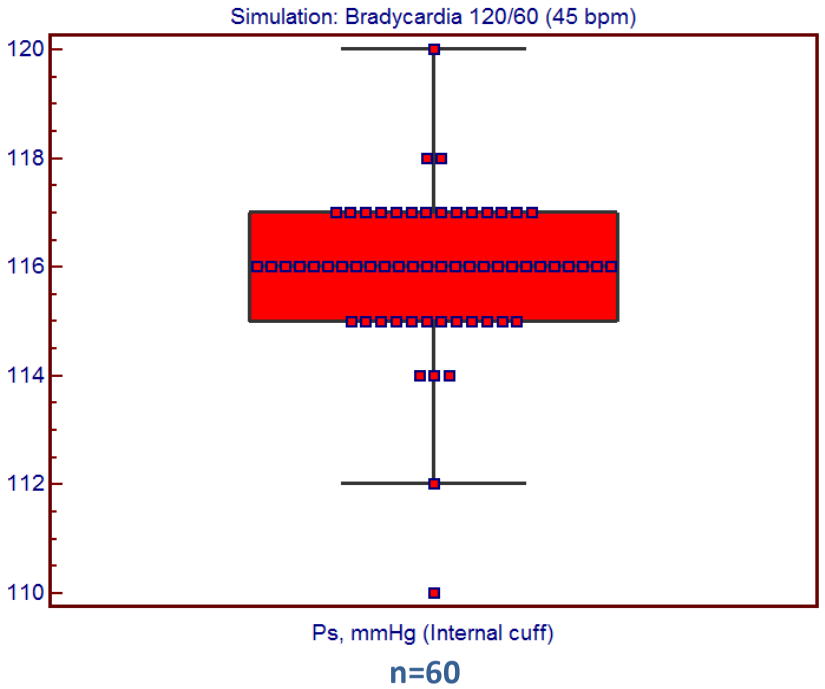


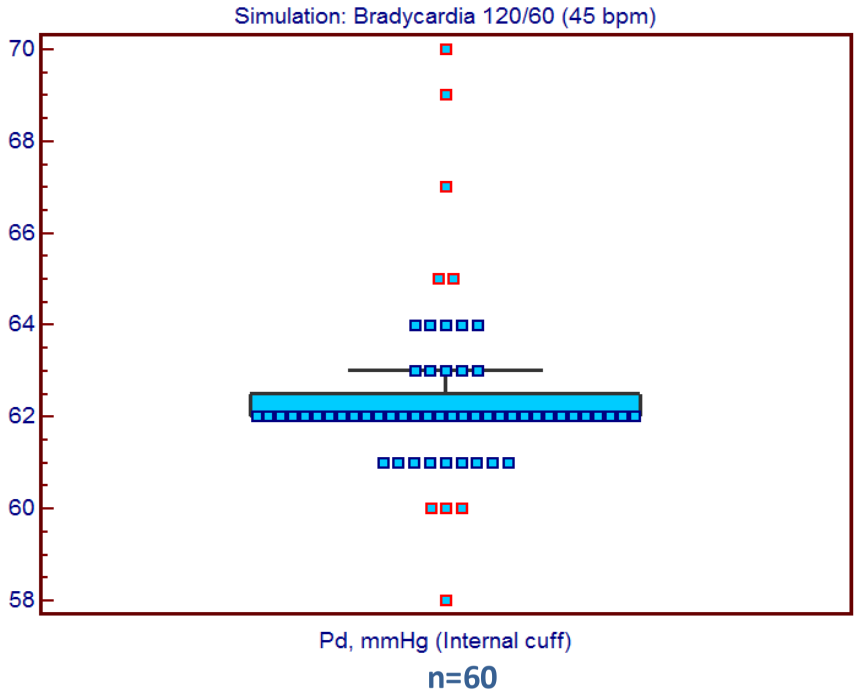
Model 2

Simulation: Bradycardia 120/60 (45 bpm)









I Test for differences between simulators

The following appendix includes results for the testing of two different simulator models. The simulator settings, and the mean differences between pressures and pulse for the two simulators, are shown.

Differences between simulators

Simulatorsetting: Healthy (120/80, 75bpm)		
Difference Ps	Difference Pd	Difference pulse
-1	-2	0
0	-1	0
-1	-1	0
0	-1	0
0	-1	0
0	-1	-1
Mean diff. Ps	Mean diff. Pd	Mean diff. Pulse
-0,333333333	-1,166666667	-0,166666667

Simulatorsetting: (220/180, 90bpm)		
Difference Ps	Difference Pd	Difference pulse
1	1	0
-1	1	0
0	2	-1
-1	2	0
0	1	-1
0	2	0
Mean diff. Ps	Mean diff. Pd	Mean diff. Pulse
-0,166666667	1,5	-0,333333333

Simulatorsetting: (220/180, 90bpm)		
Difference Ps	Difference Pd	Difference pulse
E3	E3	E3

Simulatorsetting: (140/100, 100bpm)		
Difference Ps	Difference Pd	Difference pulse
1	2	-1
2	-1	0
0	0	0
2	-1	-1
1	0	-1
2	0	-1
Mean diff. Ps	Mean diff. Pd	Mean diff. Pulse
1,333333333	0	-0,666666667

Simulatorsetting: (180/140, 80bpm)		
Difference Ps	Difference Pd	Difference pulse
E3	E3	E3

Simulatorsetting: (100/60, 60bpm)		
Difference Ps	Difference Pd	Difference pulse
0	-1	0
-1	-2	0
0	-1	1
-1	-2	0
-1	-1	0
0	-2	0
Mean diff. Ps	Mean diff. Pd	Mean diff. Pulse
-0,5	-1,5	0,166666667

Simulatorsetting: (140/100, 140bpm)		
Difference Ps	Difference Pd	Difference pulse
0	0	0
3	-1	-2
-2	0	-1
1	0	-1
0	0	0
-1	2	-1
Mean diff. Ps	Mean diff. Pd	Mean diff. Pulse
0,166666667	0,166666667	-0,833333333

Simulatorsetting: (120/80, 45bpm)		
Difference Ps	Difference Pd	Difference pulse
1	-4	0
0	-3	0
5	-4	0
-2	-3	0
1	-3	0
2	0	0
Mean diff. Ps	Mean diff. Pd	Mean diff. Pulse
1,166666667	-2,833333333	0

J Raw data

Raw data for all acquired measurements using twenty Model 1 and Model 2 devices, and an oscillometric waveform simulator, can be seen in the included DVD.