Accuracy of the PetTrust, a non-invasive arterial blood pressure monitor, at three different measurement sites in comparison to direct blood pressure measurement in dogs anaesthetized for clinical procedures.

Prefatory note

Within the training of Veterinary Medicine at Utrecht University, all students have to fulfil a research project. This paper is the final report of the research project carried out at the University's Department of Small Animal Anaesthesia by final year student Katharina Imhäuser. Both coordinator and Research Committee of the University have given their prior approval for the actions required in this research project. Since neither additional invasive procedures, nor additional costs or prolongation of the duration of the procedure were anticipated, it was decided together with the supervisor that an owners declaration of consent was not deemed necessary. All patients participating in this study were dogs that needed to be monitored with an arterial line due to the nature of their surgical procedure or their risk of anaesthesia. These patients were monitored simultaneously with a non-invasive blood pressure measurement method (PetTrust). At our institution, it is routine procedure to equip every patient undergoing anaesthesia with a non-invasive blood pressure monitor, also when blood pressure is eventually measured directly.

Abstract

Objective

To test the accuracy of the oscillometer "PetTrust" and its algorithm, and to determine at which of three standard test sites (forelimb, tail base, and hindlimb, respectively) this device reproduces arterial blood pressure measurements most accurately and reliably compared to the golden standard of invasive blood pressure measurement in dogs anaesthetized for clinical procedures. The non-invasive blood pressure measurement device PetTrust, is validated according to the recommendations of the American College of Veterinary Internal Medicine for the systolic, diastolic and mean arterial blood pressure measured at the three different body sites.

Study design

A prospective clinical study.

Animals

Thirty-three client-owned dogs, American Society of Anesthesiologists (ASA) grade 1 - 3 and anaesthetized for various surgical procedures, in which arterial blood pressure measurement was required.

Methods

Direct arterial blood pressure measurements were obtained from the dorsal pedal artery, while indirect blood pressure was measured at the forelimb, tail base and hindlimb, respectively, using the PetTrust oscillometer. Various anaesthetic protocols tailored to the patients' individual needs were used. Bland Altman plots were used for statistical analysis of the parameters obtained.

Results

Systolic arterial blood pressure values were overestimated at both the forelimb and hindlimb with a mean difference of 4.3 mmHg and 9.1 mmHg, respectively, whereas values at the tail were underestimated with a mean difference of -4.3 mmHg. The diastolic blood pressure values were overestimated at the forelimb and tail with a mean difference of 4.3 mmHg and 3.3 mmHg, respectively, but at the hindlimb values almost equal to those of the invasive method were found (mean difference of 0.1 mmHg). An overestimation of the mean arterial blood pressure value was found for all three body parts tested, in which the forelimb with a mean difference of 7.6 mmHg was the highest. The diastolic blood pressure measured on the tail was read correctly in 82% of all measurements and therefore had the highest accuracy compared to the other body parts used and other values measured, whereas the systolic blood pressure measured on the hindlimb with an accuracy of 51% only just corresponded to the recommendations of the American College of Veterinary Internal Medicine. The highest correlation coefficient of 0.74 was measured on the forelimb for the MAP, but still does not reach the American College of Veterinary Internal Medicine recommendations of ≥0.9.

Conclusions and clinical relevance

The results suggest that arterial blood pressure measured non-invasively by the PetTrust is dependent on the anatomical location of the dog chosen for the cuff. This should be considered when developing future studies to validate non-invasive arterial blood pressure measurement devices. With the exception of the correlation coefficient, the PetTrust handheld blood pressure monitor complies to the American College of Veterinary Internal Medicine recommendations. The PetTrust monitor can therefore, and because of numerous other advantages, be recommended in veterinary practice. The best results, and therefore the highest accuracy, were achieved on the tail.

Keywords

Dog, arterial blood pressure, blood pressure measurement, non-invasive, invasive, oscillometric, PetTrust, measurement sites

Introduction

Arterial blood pressure

In both humans and animals, the pressure (defined as force across a certain area) within the arterial blood vessels is defined as arterial blood pressure (ABP) and is expressed in mmHg. Above all, a mean ABP (MAP) of 60 to 70 mmHg ensures the perfusion of organs and tissues and thus the supply of oxygen to the cells. In addition, the delivery and removal of metabolic products is guaranteed when normal MAP and perfusion are maintained (Wagner et al., 1997). ABP is determined by both cardiac output and peripheral vascular resistance. In addition, the pump function of the heart during the contraction phase (systole) generates an amplitude-shaped fluctuation of the ABP. The highest value reached during systole is called the systolic ABP (SAP), while diastolic ABP (DAP) describes the lowest value reached during the phase of relaxation (diastole). The dicrotic notch marks the closing of the aortic valve in an ABP curve and thus the end of the systolic ejection phase (See Figure 1). The blood collides with the closed aortic valve and is ricocheted off, which causes a transient increase in ABP, resulting in the dicrotic notch. The MAP is the mean value of ABP during a complete cardiac cycle. It should be noted that MAP does not exactly correspond to the arithmetic mean between SAP and DAP. To determine the precise value of MAP, the area under a single blood pressure curve must be determined. Since the systolic part of the ABP curve is slightly higher and narrower in the periphery compared to the aorta, and the DAP in the periphery is hardly or only slightly lower compared to the aortic value, consequently MAP in the periphery is not equal to the MAP measured near the heart, but is slightly lower. For invasive ABP measurement, it is possible to calculate the peripheral MAP using the values of SAP and DAP ($MAP_{periphery} \approx DAP + \frac{1}{3} \times (SAP - DAP)$). Like SAP, the blood pressure amplitude, which is described as the difference between the measured SAP and DAP, is increased in the periphery compared to the aorta, due to changes in the vascular tree from heart to periphery (Wetterer et al., 1985; Haverkamp et al., 2008; Chambers et al., 2019).

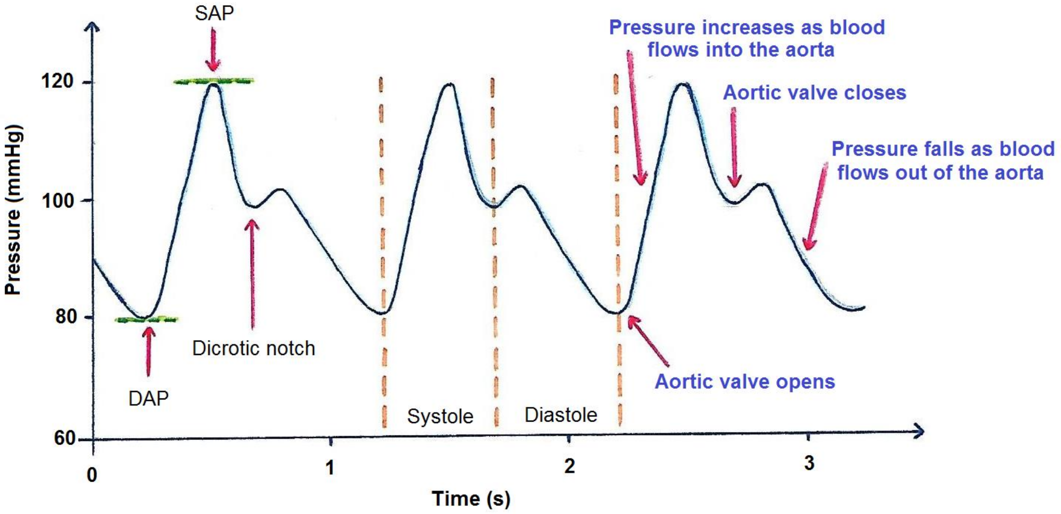

Figure 1 Blood pressure waveform (Drawn based on the example of Chambers et al., 2019)

Blood pressure is not a constant force in both humans and animals but is influenced by a variety of factors. For example, blood pressure waves of different orders are described: 1st order waves describe blood pressure fluctuations that occur during the cardiac cycle, i.e. during systole and diastole; 2nd order waves arise synchronously with breathing and are also described as respiratory fluctuations; and 3rd order waves are described as fluctuations caused by the body's own blood pressure regulation mechanisms (Behrends et al., 2010).

In addition, physiological increases in SAP are seen with advancing age in both humans and dogs (Bodey et al., 1996). Physical activity and psychological stress can also influence ABP. External influences such as time of day, climate, posture or medication will also exert an effect (Wetterer et al., 1985). Normal ABP values differ according to dog breed; and male dogs have slightly higher values compared to intact female dogs (Bodey et al., 1996; Brown et al., 2007; Behrends et al., 2010).

The reference values for normal ABP in healthy, awake dogs vary between different studies: for instance, the upper limit for SAP, i.e. the limit for hypertension, has been described in the range from 150 - 180 mmHg (McCubbin et al., 1953; Littman et al., 1988; Cowgill, 1991; Littman et al., 1995). However, it must be taken into account that different measurement techniques, and a variation in dog breed, sex, age and numbers of dogs studied were used in the individual studies.

Indications for blood pressure measurement in dogs

The measurement of ABP has long been considered an important component for monitoring and assessing critically ill animals, as well as patients undergoing general anaesthesia, especially considering that their cardiovascular status is often compromised by the various drugs used. Ketamine, for example, may increase ABP; while α2-adrenoceptor agonists such as (dex-) medetomidine are also known for their profound hypertensive effects. In contrast to this, agents such as acepromazine, propofol and isoflurane have exactly opposite effects: their administration results in vasodilation, which can lead to hypotension. Hypotension in anaesthetized dogs is defined as MAP and SAP below 60 mmHg and 80 mmHg, respectively (Littman et al., 1995; Erhardt et al., 2004; Wagner et al., 2006; Flecknell, 2009; Shih et al., 2010; Acierno, 2014; CBG MEB accessed on 15.12.19).

It may also be useful to measure ABP in awake animals, as this may aid in early detection of diseases associated with high blood pressure in certain patients. Regular ABP checks should also be carried out in those patients whose medication is expected to cause fluctuations in ABP. Illness-related hypertension is more common than illness-related hypotension. Hypertension can be divided into three categories: idiopathic or primary hypertension, which is described when all possible causative diseases and stress have been excluded. Secondary hypertension is associated with clinical disease, which is either triggered or promoted by high ABP, or the disease itself triggers high ABP. The most important causative conditions are heart- or kidney insufficiency, diabetes mellitus, hyperthyroidism, and Cushing’s disease. In addition, iatrogenic hypertension, i.e. hypertension caused by medication, also belongs to this second category. The last category is stress-related hypertension and is also known as the ‘white coat effect’ and is a reversible, short-term increase in ABP which is triggered by anxiety or excitement.

Prolonged hypertension may cause injuries to tissues and organs exposed to it. In such cases, the term ‘target organ damage’ (TOD) is often used. Organs most often damaged by long-term hypertension are the kidneys, eyes, brain, heart and blood vessels (Brown et al., 2007). According to the American College of Veterinary Internal Medicine (ACVIM) (Brown et al., 2007), normal values for ABP and the transition to hypertension in dogs is classified based on the risk of TOD:

- Normotensive (minimal risk) SAP <140 mmHg
- Prehypertensive (low risk) SBP 140 - 159 mmHg
- Hypertensive (moderate risk) SBP 160 - 179 mmHg
- Severely hypertensive (high risk) SAP ≥180 mmHg

Invasive versus non-invasive blood pressure measurement techniques

For ABP measurement, the direct invasive technique is considered the "golden standard". In most cases the dorsal pedal artery is preferred in dogs because of its relatively easy access, ease of observation of the cannula in situ, and reduced risk of haematoma formation compared to for instance the much larger femoral artery. To begin with, the area around the arterial puncture site is clipped and disinfected, after which a temporarily cannula is aseptically inserted into the artery. The cannula is connected to an electronic transducer via an extension line filled with sterile saline solution (0.9% NaCl); the transducer is connected to the monitor via a wire. In addition, the transducer is coupled to a pressurized (300 mm Hg) infusor bag, which is equipped with a 500mL 0.9% saline solution bag, to prevent back flow through the cannula, and to maintain its patency. A small diaphragm serves as interface between the fluid-filled tubing and the transducer, which vibrates when the arterial pulse wave is transmitted via the saline solution. These vibrations trigger changes in resistance of the transducer, which are processed and digitized by the monitor, and consequently result in calculations of SAP, DAP and MAP. It is important that the whole system is flushed beforehand in order to remove all air bubbles present within the fluid-filled line as these will result in damping of the signal and therefore in inadequate measurements (Ward et al., 2007).

For the most accurate reproduction of ABP values, the transducer should be positioned at the level of the right atrium. If the level of the transducer is raised or lowered compared to the level of the heart, the measured blood pressure values will decrease or increase, respectively, due to the effect of hydrostatic pressure (He et al., 2015; Jacq et al., 2015).

Invasive ABP measurements should only be carried out by experienced veterinarians or anaesthetists, because of the risk of complications. Possible complications include high volume bleeding in case of accidental disconnection, haematoma formation after dislodging at the placement site, local or systemic infections, aneurysms, embolism of thrombus or air, and nerve damage during cannula placement (Al-Shaikh et al., 2007; Ward et al., 2007; Easby et al., 2008).

There are a variety of non-invasive measurement methods available; the ones mentioned below are used most frequently in both human and veterinary medicine. As the name implies, it is a non-invasive process, with the actions confined to the patient's exterior only. In contrast to invasive ABP measurement, in which data is determined from heartbeat to heartbeat, continuous blood pressure values cannot be measured with the non-invasive techniques, which renders them less detailed.

Palpation and auscultation

This includes the Riva-Rocci method (developed 1896 by Scipione Riva-Rocci), a palpation technique that can be used to determine SAP only, and which is still used today in human medicine. Riva-Rocci was an Italian medical professional who was the first to indirectly measure ABP using an inflatable cuff combined with a mercury manometer. The cuff is used to apply circular compression to the upper arm until the pulse cannot longer be felt on the patient’s wrist. Afterwards, the air is slowly released from the cuff until the first pulse beat is perceptible again at which moment the value for SAP is read on the mercury manometer. In 1905, the Russian doctor Korotkoff succeeded in improving the Riva-Rocci method by making the blood pressure audible with the aid of a stethoscope placed over an artery distal of the blood pressure cuff. This auscultatory method describes the five Korotkoff tones, the first being defined as SAP, with the fifth sound representing DAP (Geddes et al., 1976; Wetterer et al., 1985; Ward et al., 2007).

Doppler ultrasonography

When measuring blood pressure using Doppler ultrasound, two variants in techniques are distinguished: the first one measures the blood flow in an artery (Doppler flowmetry); and the second one focuses on the arterial wall movement (Doppler kinetoarteriography). Both techniques imply the Doppler principle which is based on the frequency change of ultrasonic waves after reflection of moving objects or fluids (Binns, 1995; Ward et al., 2007; Garofalo, 2012).

Oscillometry

The values determined by an oscillometric sphygmomanometer are based on proprietary algorithms. These algorithms are developed by the manufacturers of the individual devices and thus differ for each oscillometer. In most cases, MAP is determined first, with SAP and DAP consequently calculated from this value. An oscillometer therefore enables an objective and automated measurement of ABP, whereby the calculation of the individual data differs from the invasive ABP measurement, since here SAP and DAP are measured first and used to calculate the MAP (da Cunha et al., 2017).

The oscillometer device and cuff are connected to each other via an extension hose, which is used to inflate and deflate the cuff. A transducer and a microprocessor are located within the device; the latter controls inflation and deflation. The transducer transmits the detected oscillations of blood pressure to the microprocessor, which converts them and displays them as SAP, DAP and MAP. The width of the cuff should be more or less half the circumference of the limb being measured, with a recommendation of approximately 40 - 60% of the circumference in dogs (Geddes et al., 1980; Sawyer et al., 1991). The cuff should be neither too small nor too large; a cuff too small results in ABP over-read; a cuff too wide will result in ABP values under-read (Geddes et al., 1980; Al-Shaikh et al., 2007). Oscillometric sphygmomanometers are used in many veterinary practices since they are technically easier to apply than both the invasive and the Doppler measurement methods; it takes only a small effort and little time to attach the cuff of an oscillometer to a patient to obtain ABP values, and the technique can also be used in more uncooperative patients without sedation. In addition, oscillometric ABP measurement is less costly than the invasive technique due to the fast process and the few materials needed for the measurement; no extra monitor is needed and oscillometers can be used under almost every circumstance (“bedside-technique”). The afore mentioned risks of invasive blood pressure measurement are also bypassed with the non-invasive techniques (Murray, 1981; Al-Shaikh et al., 2007).

Measurement location

The composition and size of the blood vessels located in the periphery are different from that of the central vessels. While the peripheral blood vessels are narrower and of the fibrous type, the central blood vessels are wider and can be described as a more elastic type. In addition, the vessel volume in the periphery decreases. These anatomical deviations result in a phenomenon called *distal pulse wave amplification* which is characterized by a higher SAP but a relatively constant DAP and MAP. This can lead to impairments of ABP measurements when various parts of the body are used for measurement (Tomlinson et al., 2012; Acierno, 2014). Also, the thickness of the tissue or the circumference of the limbs could interfere with the transmission of the pulse waves to the cuff. Thus, size and body condition score also play a role in choosing the appropriate body site to measure ABP non-invasively (Geddes et al., 1980). Therefore, it is important to know at which body site ABP is measured most accurately when using a non-invasive device.

The already published studies on blood pressure measurement in dogs are difficult to compare. This is not only caused by differences in individual dog breeds, but also by the variations in the way ABP was measured in these studies. Within the different studies, not only invasive but also non-invasive blood pressure measurement techniques were used, as well as different oscillometers. As already mentioned, oscillometers may use different algorithms to determine the blood pressure values. Another factor limiting comparison between studies is the fact that measurements were also performed on different body parts. All these aspects result in a relatively large discrepancy between the individual studies (Acierno, 2014).

In this study, the PetTrust handheld non-invasive blood pressure monitor, an oscillometric blood pressure monitor device, is used. The PetTrust consists of the actual electronic oscillometer with LED screen and seven colored measurement cuffs corresponding to seven different sizes, which can be attached to the oscillometer. For each individual patient the cuff size is determined with a measuring tape which is enclosed with the PetTrust device. On this tape seven sections are shown with different colors, which coincide with the different colored cuffs. The measuring tape is wrapped around the desired part of the body of the patient to obtain the color of the cuff suitable for the patient after which the particular cuff is attached to the patient at that particular location. In order to obtain a patient's blood pressure value, the PetTrust must go through a cycle that consists of a single inflation and deflation of the cuff, which takes about 30 - 40 seconds. The measured blood pressure values are then displayed on its screen.

Aim of this study was to test the accuracy of the oscillometer "PetTrust" and its algorithm and to examine at which of the three tested sites (tail base, foreleg and hind leg, respectively) this device reproduces ABP values most accurately and reliably compared to the invasive ABP technique as golden standard in dogs anaesthetized for clinical procedures.

Materials and Methods

Thirty-three client-owned dogs were used to obtain the required data. Dogs included were those patients of which the dedicated anaesthetist deemed it necessary to place an arterial catheter to measure ABP directly, either because the patient's clinical condition or the planned surgical procedure were anticipated to increase anaesthetic risk. Dogs excluded were those with a missing extremity (limb or tail) or with pre-existing heart rhythm disturbances (arrythmias).

All measurements required for the study were taken during the surgical procedure, and no invasive procedures related to the study (i.e. placement of the arterial catheter) were carried out in the conscious patient. This means that the study caused no additional harm or pain to the patients and no delay in the actual surgical procedure; therefore, no additional owner consent was deemed necessary. All anaesthetic protocols were tailored to the individual patients to ensure optimal patient safety; set drug protocols were not used. In case needed, drugs for cardiovascular support were administered during the surgical procedure.

After induction of anaesthesia, monitoring equipment consisting of capnography, in- and expired concentration of volatile agent, pulse-oximetry, electrocardiography (ECG), body temperature and ABP measurement, were applied. For the latter, both the non-invasive (PetTrust) and invasive techniques were used. For direct ABP measurement the dorsal pedal artery was aseptically inserted with a, for that patient's size suitable, catheter *(ABBOcath 22G or 24G Hospira Inc Venisystems, Illinois, USA, or BD Arterial Cannula with flow switch 20G Becton Dickinson Infusion Therapy Systems Inc, Utah, USA, respectively)* which was connected to a short T-connector *(Discofix C, 10cm length, B. Braun Melsungen AG, Germany)* pre-flushed with sterile saline *(0.9% NaCl, B. Braun Melsungen AG, Germany)*. Catheter size depended on patient size and ease of palpation of the artery. The arterial catheter was secured to the patient with tape and intermittently flushed with sterile saline solution to reduce the risk of clot formation. After instrumentation and clipping as required for the surgical procedure, patients were then transported into theatre and positioned on the operating table. All parameters monitored were displayed on a Datex Ohmeda S/5 monitor *(Datex Ohmeda Inc., Wisconsin, USA)*.

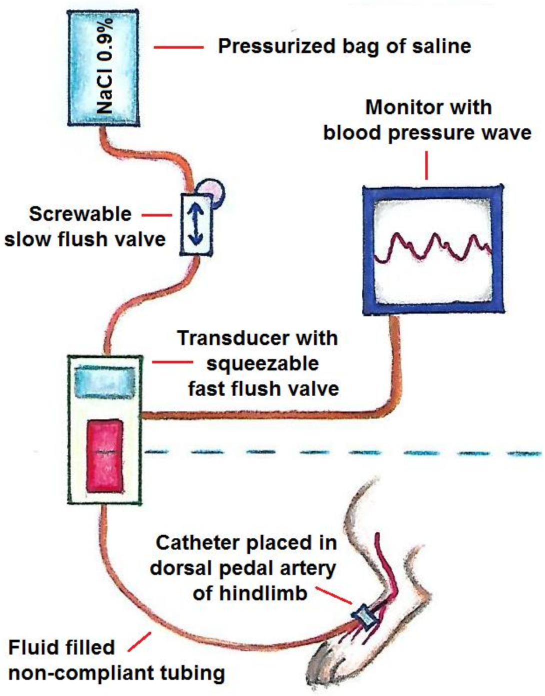

Figure 2 Schematic arrangement of the direct ABP measurement system (Modelled and drawn based on the example of Bloom, 2019).

Invasive blood pressure measurement:
A new customized ABP measurement system was used for each individual patient and prepared as described above. Before connecting to the patient, the transducer was adjusted at the level of the right atrium of the patient and calibrated with atmospheric pressure as reference standard pressure.

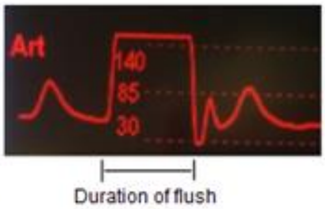

Figure 3 Fast flush test performed in one of the patients of the study

Prior to the first measurement, the square wave test, also called fast-flush test, was performed, which consists of flushing the fluid-filled tubing with the saline out of the high-pressure bag by opening the valve incorporated in the fluid system for a very brief period. This flushing causes under- and overshooting, respectively, of the on the monitor displayed arterial waveforms, which resonates at the natural frequency of the system. Each invasive ABP measurement system has its own damping coefficient, which describes the speed at which the oscillations induced by the fast-flush test, disappear, and the graph has its normal appearance again. The fast-flush test has been executed to ensure that the degree of damping of the system was acceptable. The square-wave test can lead to three possible scenarios: adequate damping, which is characterized by the fact that no more than two post-test oscillations occur before baseline is resumed and subsequent oscillations should not exceed one third of the height of the previous oscillation. If this is the case, and if subsequent blood pressure waves have a distinct dicrotic notch, the displayed values can be considered as accurate. Another possible scenario is overdamping of the signal, which is characterized by only one or even an absence of oscillations after the fast-flush test. Overdamping implies that the response speed is too slow and will result in underestimating of SAP and overestimating of DAP, respectively. Lastly, there is also the possibility of an underdamped result, which is detected by the occurrence of multiple oscillations after flushing before baseline is returned again. In this case, SAP values are overestimated, and DAP values underestimated, respectively (Warburg, 1950; Kleinman et al., 1996).

Non-invasive blood pressure measurement:
The non-invasive blood pressure measurement was taken with the oscillometer PetTrust (PetTrust, BioCARE, Taiwan). In each dog, three different body sites were used for comparison with the direct measurement technique: (a) just above the carpal bones, (b) at the tail base, and (c) just below the tarsus of the hindlimb not used for direct measurement. The cuff size was determined with a measuring tape which is enclosed with the PetTrust. The available sizes of the cuffs are 2.05, 2.55, 3.05, 3.55, 4.05, 4.55 and 5.55 cm, respectively, with either a long (203cm) or short (63cm) line used for in- and deflating the cuff.
During the observation period, MAP, SAP and DAP were measured repeatedly with an interval of approximately 10 minutes, and for as long as surgical procedure lasted. The measurements for the non-invasive values were carried out successively on all three parts of the body with the same "PetTrust" device in order to rule out deviations that could result from the use of several devices. The sequence of measurements was kept the same for each patient; starting with the invasive measurement, followed by the non-invasive measurements. The sequence of non-invasive measurements was the front leg, the base of the tail and the hind leg, chronologically from the point closest to the heart to the periphery. The peripheral pulse frequency of the "PetTrust" was compared with that of the invasive line. In some patients, the surgical procedures caused changes in cardiovascular status, and therefore rapid fluctuations in blood

pressure. Since the PetTrust does not allow for continuous blood pressure measurement, it was decided to wait with obtaining results until ABP had stabilized again to prevent false comparisons.
At the end of the surgical procedure the arterial catheter was removed, and the puncture site was compressed with elastic bandage for at least 20 minutes to prevent bleeding or haematoma formation; all other monitoring equipment was removed at appropriate times.

Statistical analysis:
To compare the non-invasive ABP measurement method to the invasive technique, Bland Altman difference plots were used (Altman et al., 1986). In these diagrams, the difference between both the invasive and non-invasive measurements is shown as the distance between the invasive and the non-invasive method. The mean value of all invasive measurements (X-axis) is displayed as a horizontal zero line, and the difference with respect to the non-invasive measurements is plotted with dots around this zero line. The difference (Y-axis) is calculated as the sum of the invasive and non-invasive measurements divided by two. The difference between the means of all invasive and non-invasive pressure values is also drawn as a horizontal line. The position of this line indicates whether the average blood pressure value of the non-invasive blood pressure monitor over- or underestimates the invasive blood pressure method. If it is above the zero line, the non-invasive method on average overestimates the values of the invasive method; if it is below, the values are underestimated on average. The 95% Limits of Agreement (LoA) can also be read in the Bland Altman plot. These are represented in the plot as error bars which reflect the 95% confidence interval for both the upper and lower limits of agreement. These limits are defined as the mean difference ± 1.96 * standard deviation (SD). The described Bland Altman plots are presented as figures 4 to 12 in the appendix. All statistical analysis and calculations were performed using IBM SPSS Statistics version 20.

For the validation of the non-invasive blood pressure monitor "PetTrust", recommendations of the ACVIM for veterinary medicine were used (Brown et al., 2007). These recommendations are:

- The mean difference of paired measurements for systolic and diastolic pressures treated separately is ±10 mmHg or less, with a SD of 15 mmHg or less;
- The correlation between paired measures for systolic and diastolic pressures treated separately is ≥0.9 across the range of measured values of blood pressure;
- 50% of all measurements for systolic and diastolic pressure treated separately lie within 10 mmHg of the reference method;
- 80% of all measurements for systolic and diastolic pressure treated separately lie within 20 mmHg of the reference method;
- The subject database contains no fewer than eight animals for comparison with an intra-arterial method.

Results

Thirty-three client-owned dogs of various breeds (Table 1) weighing between 6.2 and 43.2 kg (mean 25.7 kg, SD 12.0 kg) and age between 1 and 13 years (mean 7.4 years, SD 3.3 years), anaesthetised for a variety of surgical procedures, were included. Due to the wide range in bodyweight and -size, all of the seven available cuff sizes were used. In those few patients where the measured size of the extremity was exactly between two cuff sizes in, the smaller cuff was always used.

Various anaesthetic protocols customized for the individual patient were used to ensure optimal patient safety. Pre-anaesthetic medication consisted of acepromazine, alfaxalon, butorphanol, (dex-)medetomidine, methadone, midazolam and ketamine. For induction of anaesthesia, propofol, alfaxalon or the combination of ketamine with midazolam, was used, and anaesthesia was maintained with isoflurane or sevoflurane vaporized in a mixture of oxygen with air. To provide additional analgesia, or cardiovascular support, some patients also received (through a constant rate infusion pump) lidocaine, ketamine, sufentanyl, methadone, (dex-)medetomidine, dobutamine or dopamine.

The duration of the surgical treatments, and thus the time during which the measurements were obtained, was between 50 and 260 minutes (mean 116.4 minutes, SD 60.2 minutes). Several factors including patient repositioning, temporary loss of the arterial line trace, and irregularities in pulse rate, resulted in prolonged measurement intervals in several patients.

Due to the loss of the arterial line because of likely clogging of the arterial canula, in three cases the recording of data was stopped early, although the duration of the surgical procedure would have allowed the collection of further data.

In two cases, the surgeon accidentally leaned against the cuff and/or its extension line, causing the PetTrust to emit incorrect values or show an error message on the display. These sporadic incorrect values were not included in the data analysis. Successively obtained values were deemed accurate and therefore were included in the analysis.

Furthermore, the pulse rate was counted incorrectly in 5 cases by the PetTrust, whereby an almost doubled value was indicated. In all these cases, the patient had a transient irregular pulse rate, which was also reflected in the arterial wave form, that was displayed on the monitor. After the pulse rate normalized again, the pulse rate was measured correctly again by the PetTrust monitor. In all other patients the PetTrust monitoring device worked without obvious problems.

In three cases the patient's position was changed from the Trendelenburg to the reverse Trendelenburg position during the surgical procedure. In all these patients, the MAP measured by the invasive technique decreased by approximately 10 mmHg. This also occurred in the non-invasive measurement of the forelimb, whereas the MAP measured at both the tail and hind limb increased by approximately 10 mmHg.

When comparing the mean differences of all values, the mean SAP values were overestimated when measured at both the forelimb and hindlimb with values of 4.3 mmHg and 9.1 mmHg, respectively, whereas the values measured at the tail were underestimated with a value if -4.3 mmHg. The mean DAP values were overestimated at the forelimb and tail with values of 4.3 mmHg and 3.3 mmHg, respectively, but at the hindlimb they were almost equal to those of the invasive method with a mean difference of just 0.1 mmHg. Overestimation of the mean MAP value was found in each of the three body parts tested, in which the forelimb with a mean difference value of 7.6 mmHg was the highest.

The values of the SD ranged from 7.6 mmHg for the DAP value of the forelimb to 15.1 mmHg for the SAP value of the tail.

The smallest LoA with a range of 29.8 mmHg, was found for the DAP values measured at the forelimb, whilst largest LoA with a range of 63.7 mmHg, was found for SAP values measured at the tail. Looking at the SAP measured at the tail, 59% of the measurements differed less than ±10 mmHg from the invasive ABP measurements, compared to 77% for the DAP measured at the forelimb. So, even with a wider range for the 95% LoA, most of the measurements still deviated less than 10 mmHg from the invasive measurements and therefore comply with the recommendations of the ACVIM.

If the values of the invasive and non-invasive blood pressure measurements correspond correctly, a correlation coefficient of 1.0 is obtained. The highest correlation in this study was found for the MAP on the forelimb, which was 0.74, and the lowest correlation for the DAP on the hindlimb, which was 0.47. The remaining values were in this range.

Most fast-flush tests showed only a single or even no oscillations, which could indicate that the arterial line system may have been overdamped, resulting in slightly too low SAP and to high DAP values of the invasive ABP measurement system, while MAP remains relatively stable.

Discussion

During routine anaesthesia the PetTrust monitor appeared to work adequately, with a fail attempt in only a few cases, due to surgeons leaning against the line of the cuff or because of an irregular pulse rate, while successive readings taken after the trouble shooting, seemed appropriate.

Analyzing the various Bland Altman plots, the mean difference between the invasive and non-invasive method was smallest at the tail, or in other words, measured values at this part of the body had the highest accuracy. The SAP, DAP and MAP values, on all the tested body sites, fulfilled the recommendations of the ACVIM, except for the correlation coefficient, which in all cases was too low and did not reach the ACVIM limit of ≥ 0.9.

It is not quite clear why the pulse rate was almost doubled in some measurements of the PetTrust. In addition, the PetTrust monitor was verified and complies with the ACVIM recommendations, except for the correlation coefficient. However, reading the article by Hartnack (2014), it is clarified that the correlation coefficient is used to measure the strength of a linear relationship between two methods, but not the agreement. Accordingly, it should only be used when comparing different invasive blood pressure measurement materials or different non-invasive blood pressure devices, respectively, but not when comparing two different methods, such as invasive and non-invasive one (Hartnack, 2014).

Comparing the results, it becomes clear that when only the correlation coefficient is considered, the measurements at the forelimb gave the best results. If, however, attention is paid to how many percent of the measurements are within the range of ±10 mmHg, the tail would have to be preferred in the future to obtain the most accurate blood pressure values.

Since both short and long line cuffs were used during the study, one point of concern could be that this variation in length might have an impact on the results. Therefore, Table 3 shows the percentage of SAP, DAP and MAP values of non-invasive blood pressure measurement, that are in the range of ± 10 mmHg of invasive measurements, obtained with either a short or long line. The results demonstrate that for both for the measurements carried out with the short cuff line and for the measurements with the long cuff line the most accurate measuring point for non-invasive ABP measurement in dogs, is the tail with an accuracy of 85.7% for the MAP and 80.8% for the DAP, respectively, while the hindlimb is the least-suited with an accuracy of 45.7% for the SAP and 53.2% for the SAP, respectively. This implies that this study, as well as the study by Bodey et al. (1994) and similar studies, came to the same conclusion, namely that for the non-invasive measurement of ABP in dogs, the tail provides the most accurate results.

With all measurements, it should be kept in mind that even the invasive blood pressure measurement (and especially the SAP) is not infallible and is also susceptible to artifacts (Kittleson et al., 1983). The non-invasive blood pressure measurement does not necessarily have to be the cause of a higher difference and SD when found, as this can also be explained by errors in the direct measurement. As already mentioned, through distal pulse wave amplification, a higher SAP but a relatively constant DAP and MAP are found in the periphery. The invasive SAP values can therefore be influenced more by the catheter placed in the dorsal pedal artery and thus could show a greater deviation from the non-invasive blood pressure SAP values of the forelimb and tail. This assumption is supported by the fact that, compared to the DAP and MAP values, the measured values of the SAP in this study, are less frequently within the range of ±10 mmHg difference to the invasive value. That means, if the catheter for the invasive ABP measurement would be placed more centrally, the found values could show a different result to the present study. The greater distance to the heart could explain a higher invasive measurement of the SAP from the dorsal pedal artery compared to the non-invasive measurement of the SAP from the forelimb or tail. This could explain the large bias between invasive and non-invasive SAP for the forelimb and tail, but not the greater bias between the invasive and non-invasive SAP if both are measured on the hindlimb. Therefore, the disparities observed in the present study cannot be fully explained by the use of different arteries for the ABP measurements (Drynan et al., 2016).
The PetTrust uses the cuff deflation method, which could affect the accuracy of ABP measurement, especially SAP (Grosenbaugh et al., 1998). Due to the gradual pressure drop in the cuff, the peak systolic pressure may be missed if the duration of each step is greater than the duration of the peak pressure (Drynan et al., 2016). If this would apply to the PetTrust monitor, it could be one of the possible causes for the disagreement between invasive and non-invasive measurement of SAP.

When considering the precision, it should be recognized that the PetTrust monitor needs a time span of about 30 - 40 seconds to perform its measurement. The accuracy depends on whether the blood pressure values for SAP, DAP and MAP are relatively stable in the required time span. Cardiovascular changes can even occur within 60 seconds, i.e. while the measurement is running. An invasive measurement, on the other hand, takes place from heartbeat to heartbeat or during a cardiac cycle and is therefore more accurate (Bodey et al., 1994).

If only the time, required for a routine measurement of blood pressure performed with the invasive and non-invasive method (set-up, performance and removal), is compared, it was shown that the non-invasive blood pressure measurement can be completed much faster with approximately five minutes; whereas the process for an invasive blood pressure measurement was much more time consuming with approximately 20 minutes.

There are several limitations in this study. Catheters of different sizes and diameters were used for the invasive blood pressure measurement. As a result, the smaller catheters were more frequently occluded and failed more often to transmit pressure values, compared to the larger catheters and therefore had to be flushed more often. In three patients this resulted in loss of arterial line data and thus in an early stop of the data recording. Furthermore, the values of the larger catheters are in most cases likely to be overestimated: by increasing the inner radius of the catheter, the damping coefficient decreases significantly, which means that the system is underdamped (Romagnoli et al., 2014). Furthermore, in several cases failed attempts at catheter placement resulted in formation of a haematoma in one of the hindlimbs, which was consequently used for the PetTrust measurements, which may have affected the readings. A further study could clarify whether haematoma formation could significantly influence the results.

Furthermore, the position of the operating table was changed in three cases. If the position of the patient was changed to the reverse Trendelenburg position, the blood pressure value, measured with the PetTrust device, dropped at the front leg and rose in the back leg and tail and vice versa. McCann et al. (2001) and Jaqc et al. (2015) mentioned similar findings in their studies. According to these studies the accuracy of the measurement results can be affected due to changes in patients' position. These positional changes, however, occurred in only three of 33 patients tested and therefore have only a minor impact on the results of this study.

The fast-flush test showed an over-damping of the arterial line system. There may be several reasons for this condition, such as an excessively long high-pressure tubing system, additional connector pieces, loose connections through which air could enter or fluid could escape, and air bubbles still present in the system. In addition, non-isotonic fluids such as blood entering the tubing system could cause a pressure difference, as well as clot formation at the catheter (McGhee et al., 2002). Since the tubing system is flushed and checked properly beforehand, remaining air bubbles or loose connections can be nearly excluded. As per routine in our clinic, a short T-connector was placed between the arterial catheter and the line connected to the pressure transducer. Here again, the diameter and degree of rigidity of the connecting piece could have a negative impact on the damping coefficient and thus lead to a higher damping of the system and affect the measured values.

As mentioned earlier, the body condition could potentially also influence the non-invasively measured ABP values, which may lead to the possibility that obese patients could obtain different results than those obtained by using slim patients exclusively for the measurement (Geddes et al., 1980).

Another shortcoming of the present study is that no distinction was made between hypo-, normo- and hypertensive blood pressure values, because most blood pressure values were in the normotensive range and only relatively few blood pressure measurements were in the hyper- (SAP >150 mmHg) and hypotensive (SAP <80 mmHg or MAP <60 - 70 mmHg) range (McCubbin et al,. 1953; Littman et al., 1988; Cowgill, 1991; Littman et al., 1995; Gaynor et al.,1999; Shih et al., 2010). A wide range of blood pressure values was nonetheless examined. Since these were client-owned animals, blood pressure was not pharmacologically manipulated to obtain more blood pressure values in the hyper- or hypotensive range.

Averaging several measurements to minimize errors is recommended by many investigators. (Geddes et al., 1980; Bodey et al., 1994 and 1996; Meurs et al., 1996; Bodey, 1997). This could explain why this study showed slightly larger measurement differences than other known studies, as they worked with the median of several blood pressure values. In contrast to the arithmetic mean, the median is hardly influenced by outlier values.

Moreover, it should be said that the circumstances for measuring blood pressure during anaesthesia and surgery are different from those of an awake animal in a medical practice.

Conclusion and clinical Relevance

Except for the correlation coefficient, the PetTrust handheld blood pressure monitor fulfills the recommendations of the ACVIM.

The most accurate measuring point for non-invasive ABP measurement in dogs is the tail, whereas the hindlimb is the least-suited measuring point, but still fulfills the recommendations of the ACVIM. In all body parts tested, the DAP value is the most accurate in all of them.

Despite good agreement, there are clear differences between invasive and non-invasive blood pressure measurements in individual animals, so that several measurements should be averaged to avoid misdiagnoses, and diseases and clinical symptoms of the animals should be included into the value of the obtained measurements.

Using non-invasive ABP measurement devices, like the PetTrust, in veterinary practice saves considerable costs and time, and the risks associated with the use of an invasive blood pressure measurement method are avoided.

All in all, it can be concluded that the PetTrust monitor fulfills the ACVIM recommendations and is therefore suitable for veterinary practice, although it is not clear whether these recommendations are strict enough to conclude that the PetTrust can replace the invasive measurement method as a clinically applicable alternative in the future. In addition, the circumstances under which the non-invasive blood pressure readings were obtained are completely different from those in normal everyday practice, which is why a similar study in awake animals should be considered.

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Appendix

Table 1
Dog breeds and surgical procedures evaluated in the study.

Breed	Sex*	Age (years)	Weight (kg)	Surgical procedure
Cockerspaniel	F	9	16.9	Partial hepatectomy
Cockerspaniel	MN	11	17.8	Laparoscopic splenectomy
Labrador	FN	4	35.8	Liver biopsy
Labrador	MN	7	41.1	Thoracotomy
Labrador	MN	5	36	Stick trauma throat
Labrador	M	10	41.5	Tumor removal
Labrador	FN	10	37.5	Laparoscopic tumor removal
Labrador	FN	9	27.3	Ventral decompression
Labrador	MN	10	30.7	Craniotomy brain tumor
Collie	M	12	24	Amputation of left forelimb
Dutch Sheepdog	F	2	14.3	OVE
German shepherd dog	M	7	36.6	Thoracoscopy
Golden Retriever	M	1	27.3	Castration
Golden Retriever	MN	9	40.7	Mandibulectomy
Golden Retriever	M	12	36.4	Maxillectomy
Maltese	FN	9	9.2	Adrenalectomy left
Mixed-breed dog	MN	4	35.7	Maxillectomy
Mixed-breed dog	FN	4	17.1	Parathyroidectomy
Mixed-breed dog	MN	9	29.6	Tumor removal
Mixed-breed dog	MN	10	16.4	Cataract surgery
Rottweiler	FN	6	43.2	Tumor removal
Bernese Mountain Dog	MN	5	40.7	Thoracoscopy
E. Springer Spaniel	F	2	15.5	Exploratory laparotomy
Boxer	F	8	34.3	Reposition of tracheal ring
Boxer	MN	7	32	Mandibulectomy
Norfolk Terrier	M	10	8.2	Cataract surgery
Dutch Partridge Dog	M	13	28	Tooth root abscess
Kooikerhondje	FN	2	12.2	Portosystemic shunt ligation
Norwich Terrier	M	9	6.2	Ventral decompression
Ridgeback	FN	5	31	Exploratory laparotomy
Pug	M	11	10.2	Adrenalectomy
Jack Russel	F	3	6.3	Portosystemic shunt ligation
Jack Russel	FN	9	8	Insulinoma removal

F = Female, FN = Female neutered, M = Male, MN = Male neutered
OVE = Ovariectomy

Table 2

Comparison of the non-invasive measurements at each cuff site with invasive measurements of ABP.

Absolute	Mean difference	SD	95% LoA	Correlation coefficient	Between 20 mmHg	Between 10 mmHg
SAP Forelimb	4.3	13.2	-21.7 - 30.2	0.69	87%	59%
DAP Forelimb	4.3	7.6	-10.7 - 19.1	0.73	98%	77%
MAP Forelimb	7.6	8.5	-9.1 - 24.2	0.74	94%	66%
SAP Tail	-4.3	15.1	-34.0 - 29.7	0.53	81%	59%
DAP Tail	3.3	8.4	-13.3 - 19.8	0.66	98%	82%
MAP Tail	3.2	8.5	-13.4 - 19.8	0.70	97%	79%
SAP Hindlimb	9.1	14.2	-18.8 - 37.0	0.60	81%	51%
DAP Hindlimb	0.1	10.6	-20.5 - 20.8	0.47	93%	76%
MAP Hindlimb	6.8	9.9	-12.7 - 26.3	0.59	88%	68%

SD = Standard deviation;
SAP = systolic arterial pressure; DAP = diastolic arterial pressure; MAP = mean arterial pressure;
95% LoA = 95% Limits of Agreement;
Between 20 mmHg/10mmHg = percentage of values of non-invasive blood pressure measurement, lying in the range of ±20/±10 mmHg of invasive measurements.

Table 3

Comparison of the non-invasive blood pressure measurements with short and long cuff line. Percentage of values that differ less than ± 10 mmHg of invasive blood pressure.

	SAP short line	DAP short line	MAP short line	SAP long line	DAP long line	MAP long line
Forelimb	67.2%	73.9%	60.4%	54.0%	78.8%	69.9%
Tail	73.5%	84.4%	85.7%	48.8%	80.8%	74.6%
Hindlimb	45.7%	73.6%	55.8%	53.2%	76.6%	75.3%

For all Bland Altman plots:

Invasive measurements are displayed as a horizontal dashed zero line. The differences of the invasive and the non-invasive ABP measuring methods (y-axis) are plotted against the mean value (x-axis) of the invasive one (as golden standard). The green line constitutes mean difference, and the red lines constitute 95% limits of agreement (mean difference ± 1,96 * SD).

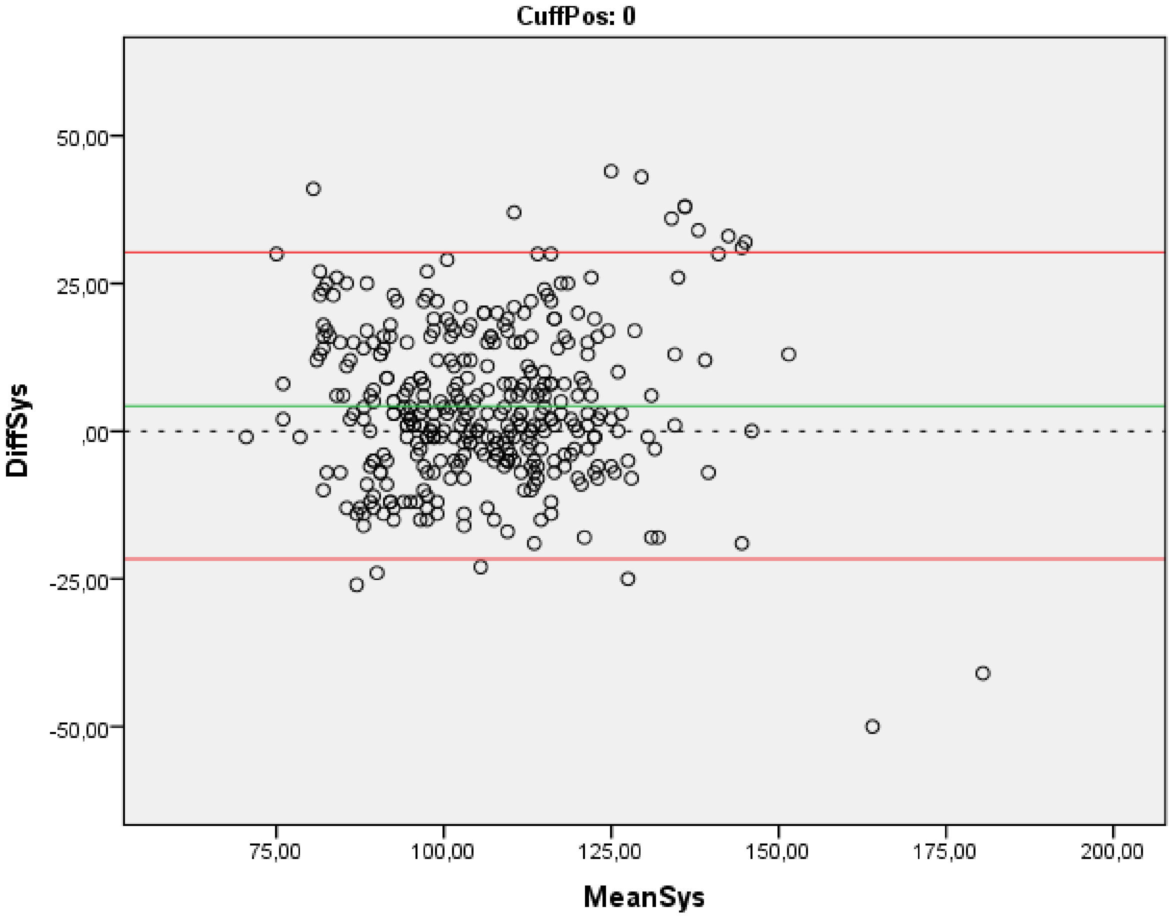

Figure 4 - Bland Altman difference plot of agreement between the PetTrust oscillometer on the forelimb and the invasive ABP measurement for systolic arterial pressure.

CuffPos 0 = Forelimb; DiffSys = difference of non-invasive and invasive SAP values (non-invasive - invasive); MeanSys = mean of all SAP values ((non-invasive + invasive) / 2)

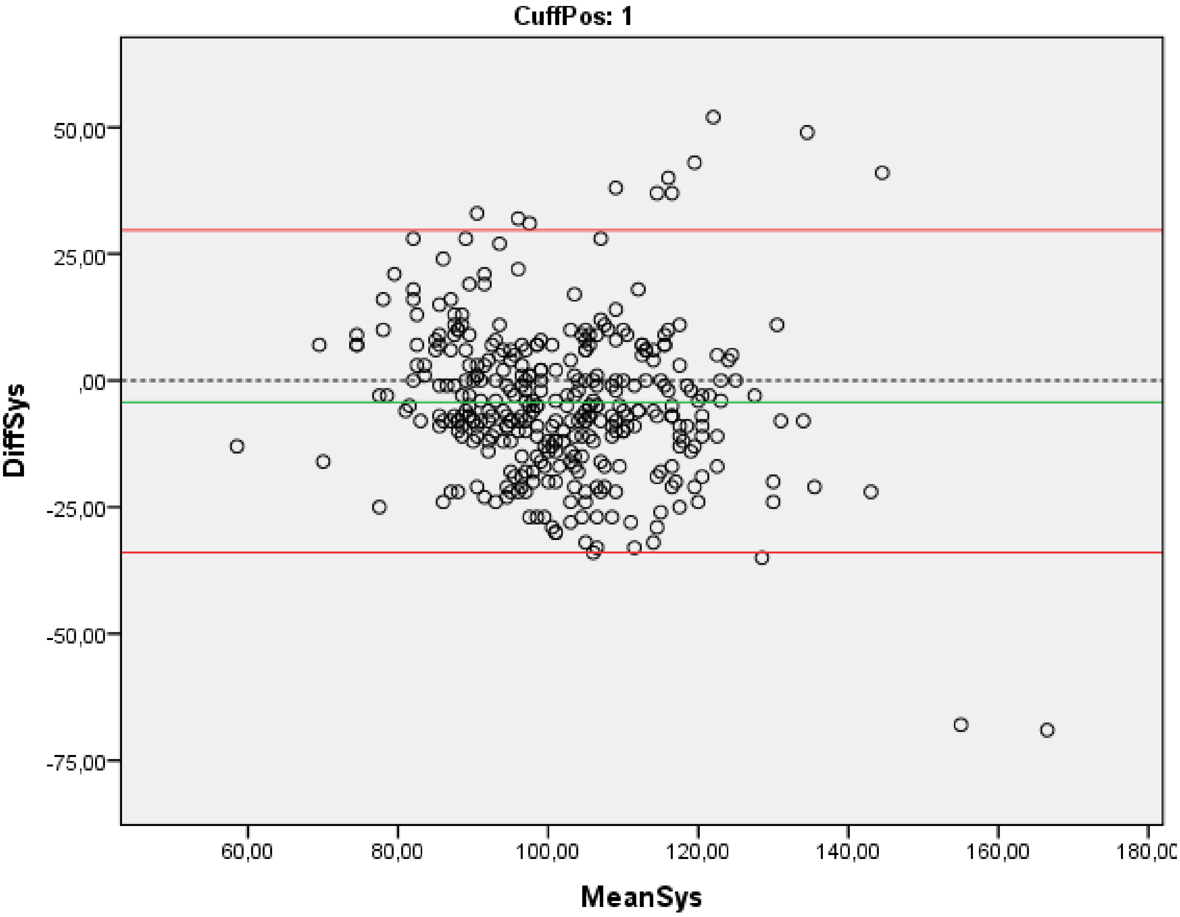

Figure 5 - Bland Altman difference plot of agreement between the PetTrust oscillometer on the tail and the invasive ABP measurement for systolic arterial pressure.
CuffPos 1 = tail; DiffSys = difference of non-invasive and invasive SAP values (non-invasive - invasive); MeanSys = mean of all SAP values ((non-invasive + invasive) / 2)

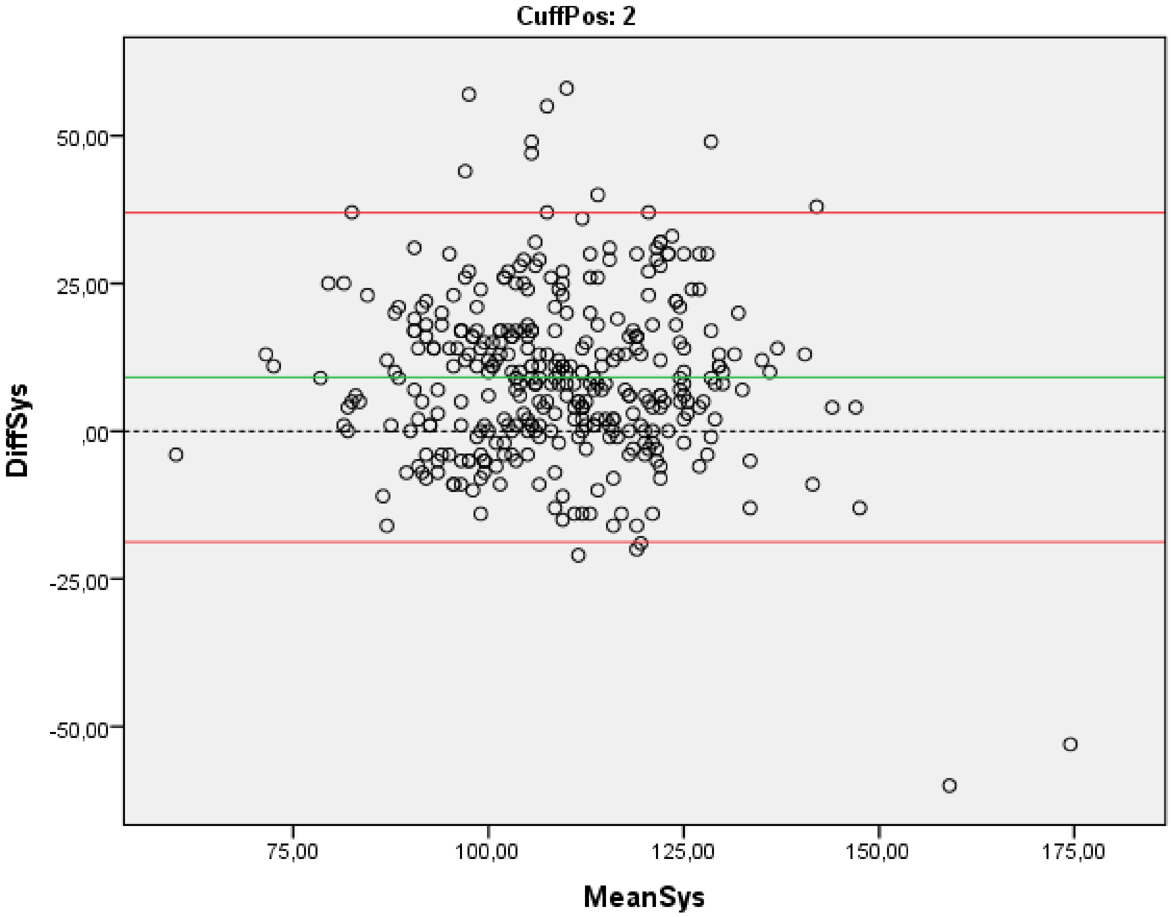

Figure 6 - Bland Altman difference plot of agreement between the PetTrust oscillometer on the hindlimb and the invasive ABP measurement for systolic arterial pressure.
CuffPos 2 = hindlimb; DiffSys = difference of non-invasive and invasive SAP values (non-invasive - invasive); MeanSys = mean of all SAP values ((non-invasive + invasive) / 2)

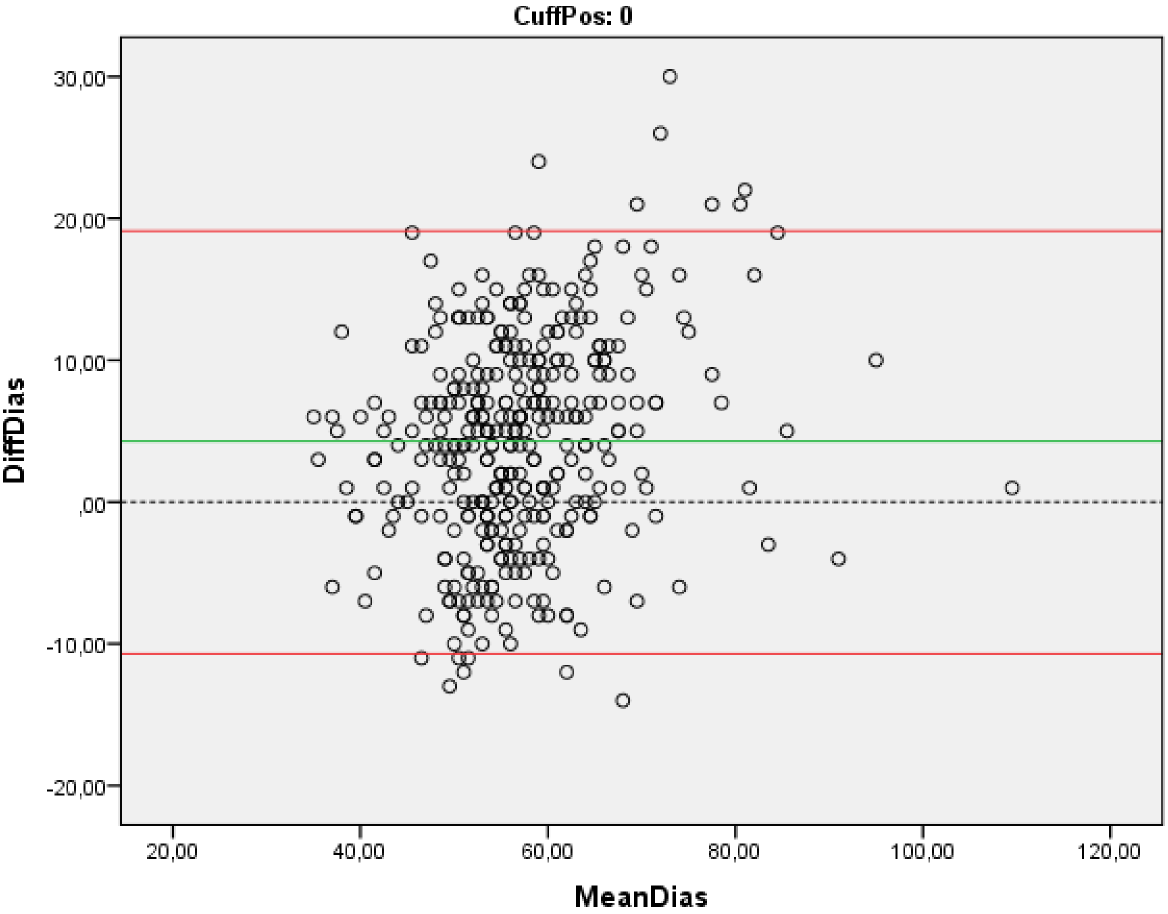

Figure 7 - Bland Altman difference plot of agreement between the PetTrust oscillometer on the forelimb and the invasive ABP measurement for diastolic arterial pressure.

CuffPos 0 = Forelimb; DiffDias = difference of non-invasive and invasive DAP values (non-invasive - invasive); MeanDias = mean of all DAP values ((non-invasive + invasive) / 2)

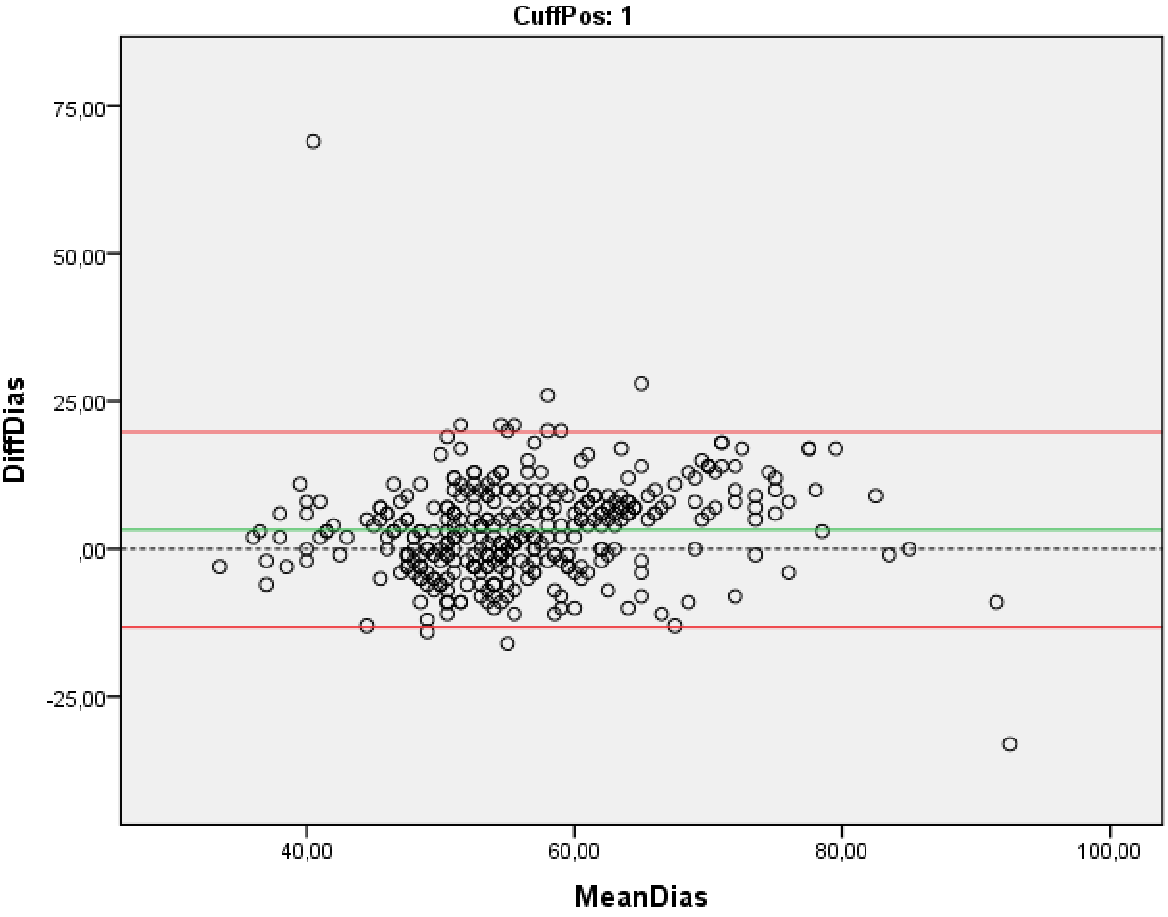

Figure 8 - Bland Altman difference plot of agreement between the PetTrust oscillometer on the tail and the invasive ABP measurement for diastolic arterial pressure.
CuffPos 1 = tail; DiffDias = difference of non-invasive and invasive DAP values (non-invasive - invasive); MeanDias = mean of all DAP values ((non-invasive + invasive) / 2)

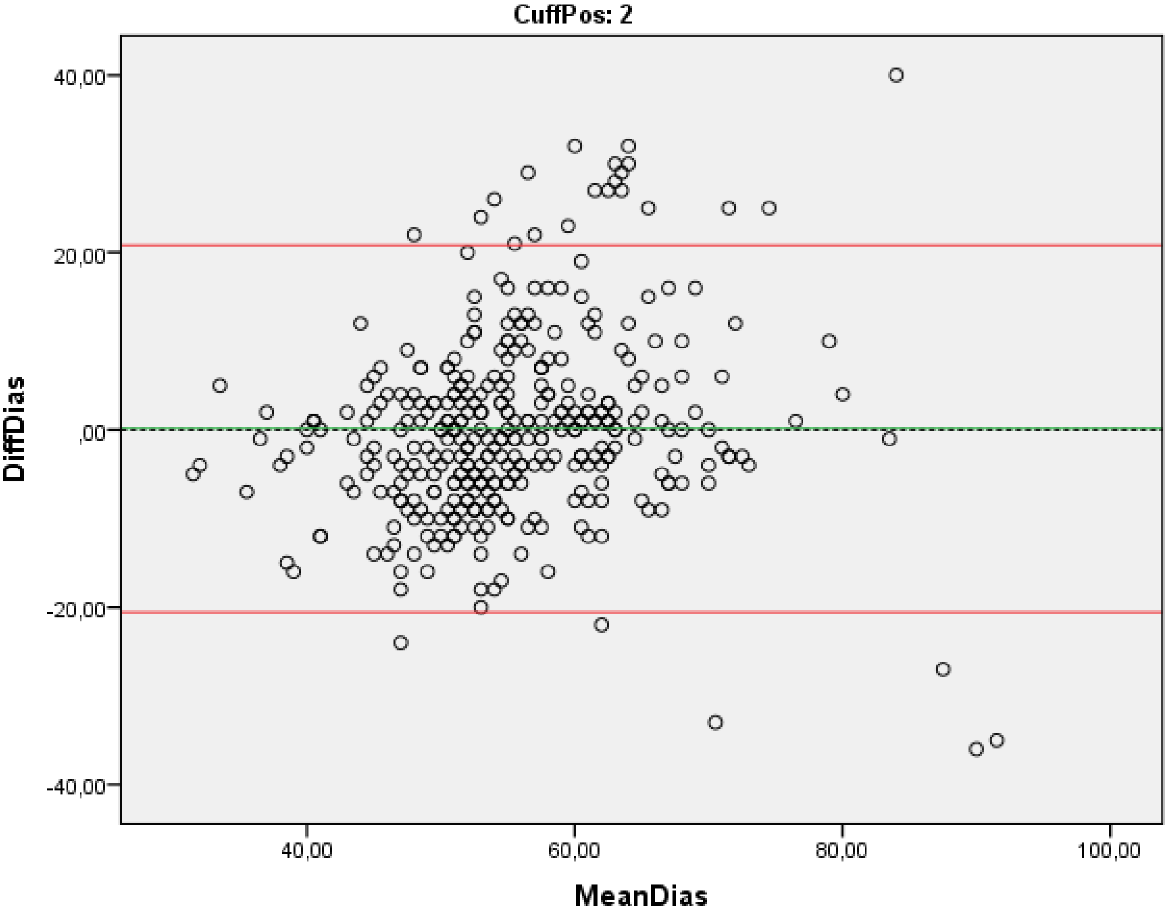

Figure 9 - Bland Altman difference plot of agreement between the PetTrust oscillometer on the hindlimb and the invasive ABP measurement for diastolic arterial pressure.
CuffPos 2 = hindlimb; DiffDias = difference of non-invasive and invasive DAP values (non-invasive - invasive); MeanDias = mean of all DAP values ((non-invasive + invasive) / 2)

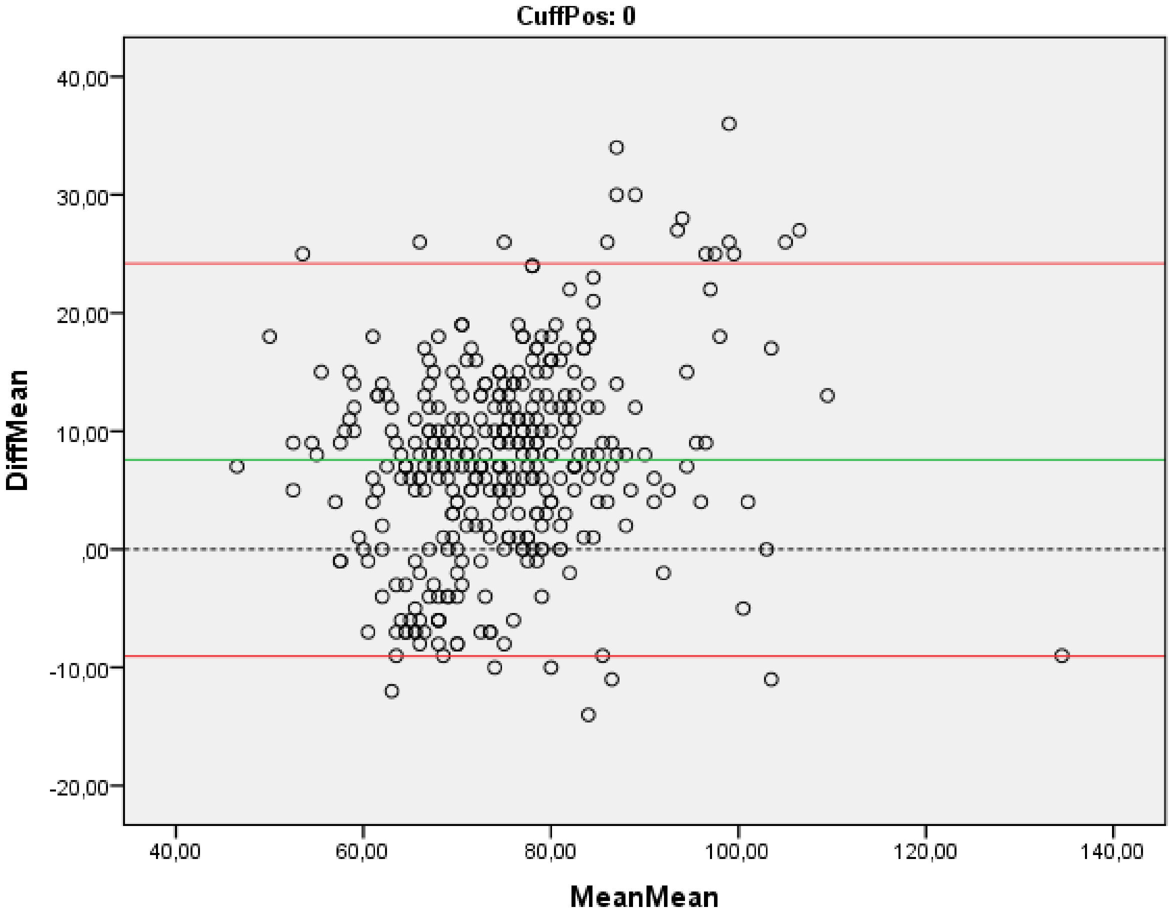

Figure 10 - Bland Altman difference plot of agreement between the PetTrust oscillometer on the forelimb and the invasive ABP measurement for mean arterial pressure.
CuffPos 0 = forelimb; DiffMean = difference of non-invasive and invasive MAP values (non-invasive - invasive); MeanMean = mean of all MAP values ((non-invasive + invasive) / 2)

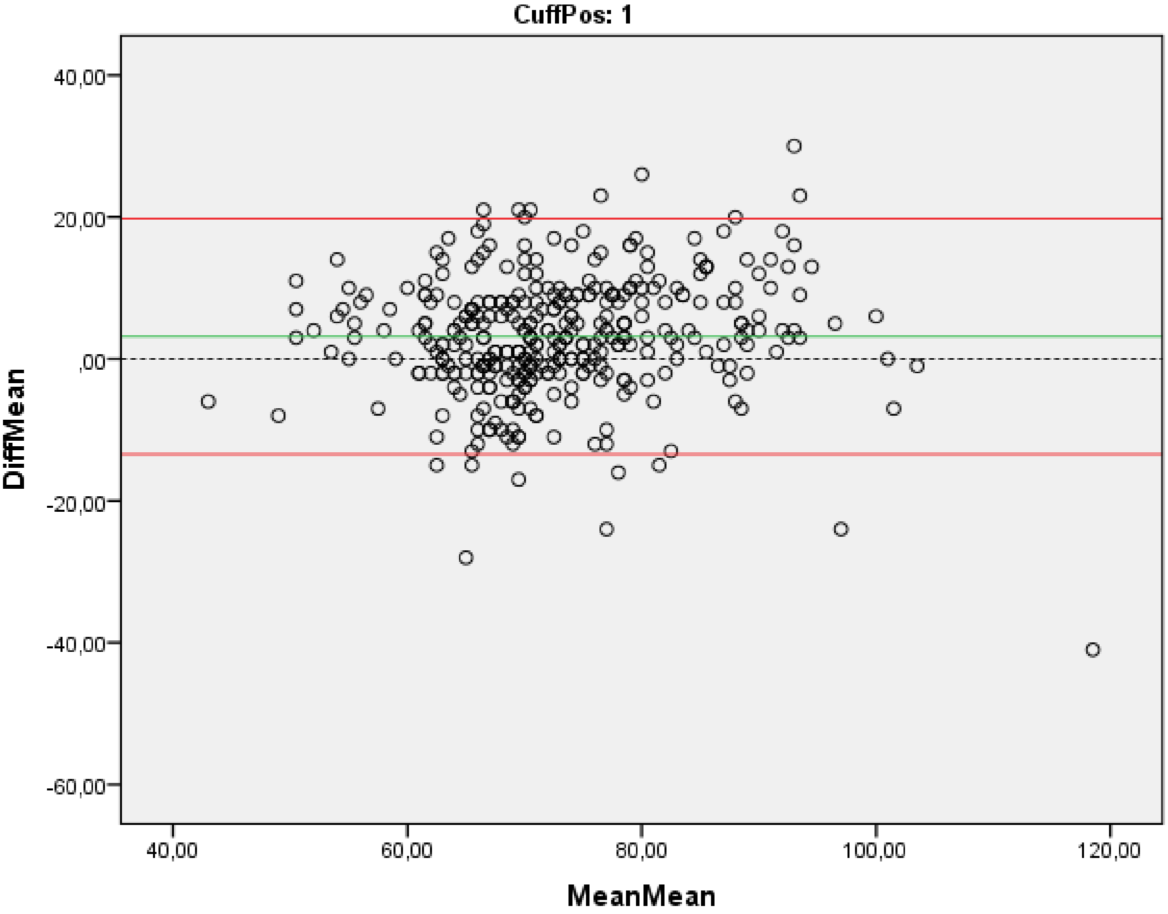

Figure 11 - Bland Altman difference plot of agreement between the PetTrust oscillometer on the tail and the invasive ABP measurement for mean arterial pressure.

CuffPos 1 = tail; DiffMean = difference of non-invasive and invasive MAP values (non-invasive - invasive); MeanMean = mean of all MAP values ((non-invasive + invasive) / 2)

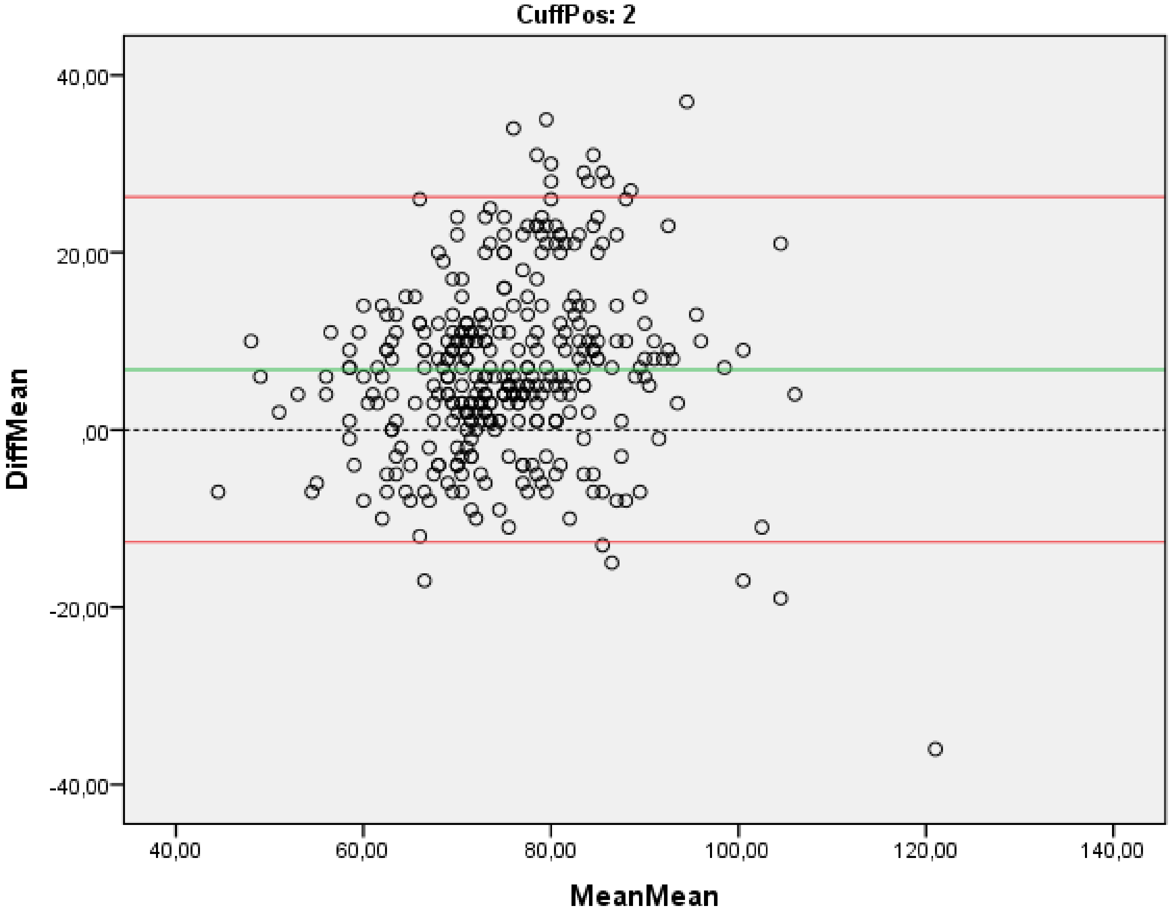

Figure 12 - Bland Altman difference plot of agreement between the PetTrust oscillometer on the hindlimb and the invasive ABP measurement for mean arterial pressure.

CuffPos 2 = hindlimb; DiffMean = difference of non-invasive and invasive MAP values (non-invasive - invasive); MeanMean = mean of all MAP values ((non-invasive + invasive) / 2)