

Cardiovascular Research 38 (1998) 605-616

Cardiovascular Research

# Review

# Fifteen years experience with finger arterial pressure monitoring: assessment of the technology

Ben P.M. Imholz<sup>a,\*</sup>, Wouter Wieling<sup>a</sup>, Gert A. van Montfrans<sup>a</sup>, Karel H. Wesseling<sup>b</sup>

<sup>a</sup> Department of Internal Medicine, F4-222, Academic Medical Center, Meibergdreef 9, 1105 AZ Amsterdam, Netherlands <sup>b</sup> TNO-Biomedical Instrumentation, Academic Medical Center, Amsterdam, Netherlands

Received 27 June 1997; accepted 3 March 1998

#### Abstract

We review the Finapres technology, embodied in several TNO-prototypes and in the Ohmeda 2300 and 2300e Finapres NIBP. Finapres is an acronym for FINger Arterial PRESsure, the device delivers a continuous finger arterial pressure waveform. Many papers report on the accuracy of the device in comparison with intra-arterial or with noninvasive but intermittent blood pressure measurements. We compiled the results of 43 such papers and found systolic, diastolic and mean accuracies, in this order, ranging from -48 to 30 mmHg, from -20 to 18 mmHg, and from -13 to 25 mmHg. Weighted for the number of subjects included pooled accuracies were -0.8 (SD 11.9), -1.6 (8.3) and -1.6 (7.6) mmHg respectively. Subdividing the pooled group according to criteria such as reference blood pressure, place of application, and prototype or commercial device we found no significant differences in mean differences or SD. Measurement at the finger allows uninterrupted recordings of long duration. The transmission of the pressure pulse along the arm arteries, however, causes distortion of the pulse waveform and depression of the mean blood pressure level. These effects can be reduced by appropriate filtering, and upper arm 'return-to-flow' calibration to bring accuracy and precision within AAMI limits. For the assessment of beat-to-beat changes in blood pressure and assessment of blood pressure variability Finapres proved a reliable alternative for invasive measurements when mean and diastolic pressures are concerned. Differences in systolic pressure are larger and reach statistical significance but are not of clinical relevance. Finger arteries are affected by contraction and dilatation in relation to psychological and physical (heat, cold, blood loss, orthostasis) stress. Effects of these phenomena are reduced by the built-in Physiocal algorithm. However, full smooth muscle contraction should be avoided in the awake patient by comforting the patient, and covering the hand. Arterial state can be monitored by observing the behaviour of the Physiocal algorithm. We conclude that Finapres accuracy and precision usually suffice for reliable tracking of changes in blood pressure. Diagnostic accuracy may be achieved with future application of corrective measures. © 1998 Elsevier Science B.V. All rights reserved.

Keywords: Finapres; Technology assessment; Accuracy; Precision; Tracking ability

# 1. Introduction

The measurement of the arterial pressure waveform at the finger with Finapres<sup>™</sup> (for FINger Arterial PRESsure) was introduced in the early 1980s. Because the method enabled for the first time a reliable measurement of the beat-to-beat blood pressure signal in a noninvasive manner, it was welcomed as a long-awaited step forward in the measurement of blood pressure [1]. With the increasing acceptance of the technique, a substantial number of comparative and methodological studies was published mainly dealing with accuracy (average discrepancy with the reference pressure) and precision (standard deviation of the average discrepancy).

In this review we will focus on the place finger arterial pressure measurement has achieved in clinical practice and the cardiovascular laboratory. First, the principles of operation of Finapres are discussed, then the data of the various comparative studies are summarised. Third, specific problems in relation to the peripheral site of the measurement

<sup>&</sup>lt;sup>\*</sup> Corresponding author. Present address: Department of Internal Medicine, TweeSteden Ziekenhuis, Locatie Waalwijk, P.O. Box 90107, 5000 LA Tilburg, Netherlands. Tel.: +31 (416) 682222; fax: +31 (416) 342220.

<sup>0008-6363/98/\$19.00 © 1998</sup> Elsevier Science B.V. All rights reserved.

Time for primary review 25 days.

of blood pressure are discussed, and finally we consider the future place of finger arterial pressure measurement.

#### 2. Finapres principles of operation

The method is based on the development of the dynamic (pulsatile) unloading of the finger arterial walls using an inflatable finger cuff with built-in photo-electric plethysmograph. A fast pneumatic servo system and a dynamic servo setpoint adjuster assure arterial unloading at zero transmural pressure and consequent full transmission of arterial blood pressure to cuff air pressure [2-4]. The principle of unloading has been described in detail [5-7], and will not be addressed here. From the finger pressure waveform, heart beats are detected and systolic, diastolic and mean pressure and pulse rate are output in a beat-tobeat mode.

The original apparatus of Peñáz needed personal expertise to establish the unloaded state of the finger arteries and therefore the technique was not easily transferable. Wesseling and coworkers of TNO-Biomedical Instrumentation converted the volume clamp method of Peñáz into

'Finapres', enabling the measurement of continuous finger arterial pressure in clinical settings [8-10]. They contributed numerous technical adjustments and improvements with respect to the finger cuff, the use of a stabilised infrared light-emitting diode (LED), of a fast bi-directional proportional valve and a high speed servo system of at least 30 Hz bandwidth [4,7,9]. Most important was the development of the dynamic servo setpoint adjuster, i.e. the search procedure and criterion for the automated determination and periodic adjustment of the arterial unloaded volume (Physiocal procedure) [10]. The start-up procedure is shown in Fig. 1. With standardised increments in cuff pressure (Fig. 1, trace I) pulsations in the plethysmogram (DC) increase to reach a maximum and subsequently decrease again (Fig. 1, trace II). The cuff pressure at maximal pulsations together with criteria to avoid the locking on to venous pulsations produces the best estimate of the unloaded state of the finger arteries assumed to reflect mean arterial pressure [3,7]. Once this state is established the Physiocal procedure is applied (Fig. 1) [10]. At regular time intervals of up to 70 beats (or approximately 1 min) the set-point is checked during the brief interruptions of the blood pressure recordings. If needed, the set-point is adjusted (Fig. 1, trace III, c).

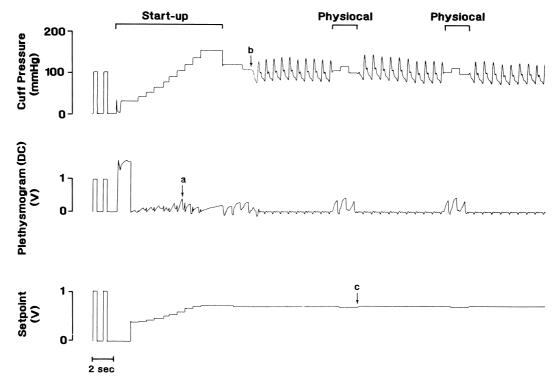


Fig. 1. Finapres start-up and physiocal adjustments. The three simultaneous traces show from above, finger cuff pressure, infrared plethysmogram (more transmitted light plotted upwards), and total amount of infrared light passing through the finger. The initial square wave has a 1 volt or 100 mmHg calibration. Next, the cuff pressure is increased stepwise and held constant until one beat is detected per step level. The plethysmographic amplitude and the total infrared increase with increasing cuff pressure since blood is pressed out from under the cuff with consequent reduced absorption of incident infrared and greater tissue transmission. At (a) the largest plethysmogram is detected and its corresponding pressure level is set upon completion of the up staircase. At this pressure, several further plethysmograms are analyzed for wave shape and the servo setpoint adjusted accordingly at (b). The servo loop is then closed and finger pressure is measured. After ten beats the loop is opened and cuff pressure is set at a level half way between systolic and diastolic and further plethysmograms examined for waveform. At (c) the loop is closed at a slightly higher setpoint, corresponding to a further reduction of blood under the cuff and increased transmission. Intervals between Physiocal interruptions are gradually increased until 70 beats elapse, or about 1 min.

The practical design of the Peñáz-method as implemented in the Finapres<sup>TM</sup> and the ambulant version the Portapres<sup>TM</sup> devices, includes an inflatable finger cuff which comprises an infrared plethysmograph and a small box attached to the wrist enclosing a fast servo-controlled pressurising system for the continuous adjustment of cuff pressure according to changes in the plethysmographic output [10–12]. The cuff and wrist-box are connected to a main unit which holds the air pump, electronics and a computer.

The performance of Finapres by comparing finger arterial pressures with intra-radial, intra-brachial and indirect oscillometric or Riva–Rocci–Korotkoff as reference techniques has been reported in a large number of studies [8,11–53]. We address two questions in the following section; how well do finger arterial pressure values correspond with reference values in terms of average discrepancy (accuracy) and their standard deviations (precision), and how well does the device follow changes in these reference blood pressures during a certain period of time or a manoeuvre that perturbs circulatory stability.

#### 3. Finapres for measurement of blood pressure levels

#### 3.1. Physiological background

Arterial waveforms in the finger and more central arteries differ, since the shape of the pressure wave on its way to the periphery is changed by reflection and by a pressure gradient along the arterial tree [54]. Peripheral reflection results in amplification of the pressure wave and increases systolic pressure; the amplification is frequency- and thus heart rate-dependent [20]. The pressure gradient causes mean and diastolic pressure to be lower [12]. Nevertheless, finger and more central blood pressures are by and large similar in appearance as shown in Fig. 2.

We review all 43 selected evaluation studies published until March 1997. For each study average accuracies between finger and the reference techniques [Finger-Reference] are taken. When averages are not reported we calculated them from the individual data. From these data the accuracy of finger blood pressure among studies was calculated as weighted mean with the total number of patients as weights [55]. Possible influences of confounding factors on the accuracy were identified.

The weighted accuracy of finger arterial pressure measurement among these studies comprising a total of 1031 subjects was  $-0.8 \pm 11.7$  mmHg [range -48 to 30 mmHg] for systolic pressure,  $-1.6 \pm 8.5$  mmHg [range -20.1 to 18.5 mmHg] for mean pressure and  $-1.6 \pm 7.7$  mmHg [range -13.4 to 25 mmHg] for diastolic pressure (Fig. 3A, left panels).

Several factors can influence the outcome of comparison studies.

#### 3.2. Physiological conditions

Fig. 3A shows average values per study in the operating theatre (O.Th; middle panels) versus the cardiovascular laboratory (CVL; right panels). Overall similar discrepancies are seen (Table 1). If from all data only resting —steady state— values are selected similar scatters are seen in the operating room and in laboratory conditions (Fig. 3B, Table 1).

The effect of age as an independent variable for the difference between finger and invasive pressure was investigated in an earlier report [56]. The main finding was that correlations between differences in finger and invasive pressures versus age were not significant (r = -0.24, -0.27 and -0.14 for systolic, mean and diastolic pressure

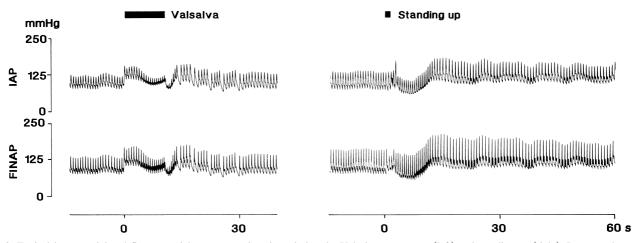


Fig. 2. Typical intra-arterial and finger arterial pressure registrations during the Valsalva manoeuvre (left) and standing-up (right). Pressure changes in intraarterial pressure are followed closely but finger pulse pressures are systematically greater in this subject. (Figure is a composition of original tracings published elsewhere [25,27]).

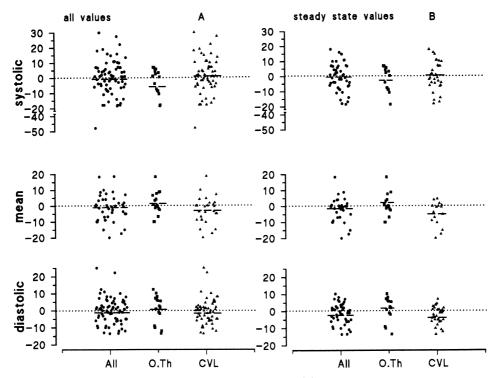


Fig. 3. Average differences between finger and reference blood pressure: The left panels (A) show all differences documented in 43 studies (N = 998) and differences obtained in the operation theatre (O.Th; N = 699) and laboratory conditions (CVL; N = 299) separately. The right panels (B) show a similar break-down with all data from resting steady-state conditions (N = 924) and differences obtained in the operation theatre (O.Th; N = 277) and laboratory conditions (CVL; N = 647) separately.

differences, respectively) (Fig. 4, left panel). In the present review, the 43 studies cover an age range of 5 to 76 years. In this group, correlations of the average finger-to-invasive pressure differences with average age also were not significant with values of -0.15, -0.24 and 0.09 for systolic, mean and diastolic pressure differences, respectively (Fig. 4, right panels).

#### 3.3. Methodological factors

Choosing a particular reference certainly bears upon these comparative studies that are based on intra-radial, intra-brachial and indirect oscillometric or Riva–Rocci– Korotkoff measurements. These different groups are shown in Fig. 5A. On average, Finapres underestimates mean and

Table 1

Average finger-reference blood pressures 'accuracy' and standard deviation 'precision' (mmHg	Average fin	nger-reference	blood pressures	'accuracy'	and standard	deviation	'precision'	(mmHg)
--	-------------	----------------	-----------------	------------	--------------	-----------	-------------	--------

Condition	Systolic		Mean		Diastolic	
	Accuracy	Precision	Accuracy	Precision	Accuracy	Precision
All [8,11,23–29,31–41,44,45,47,49–51,53]	-0.8	11.9	-1.6	8.3	-1.6	7.6
All-CVL [11,12,14-28,34,35,41,44,45,47,49-51,53]	0.6	12.5	-3.8	8.3	-2.2	7.4
All-O.Th [8,13,29,31–33,36–40,42,43,46,48,52]	- 5.9	8.4	1.3	7.2	0.7	7.9
Rest [8,11,13-29,31-41,44,45,47,49-51,53]	-0.5	8.8	-1.6	7.7	-2.5	6.0
Rest-CVL [11,12,14-28,34,35,41,44,45,47,49,50,53]	0.6	9.3	-5.6	7.2	-4.1	5.0
Rest-O.Th [8,13,29,31–33,36–40,42,43,46,48,52]	-3.0	7.8	2.0	7.3	1.7	6.8
Rest-I.Brach [11,12,14,16,17,20,23-25,27,28,35,44,45]	-0.0	8.9	6.2	7.6	-3.9	5.6
Rest-I. Rad [13,15,26,29,31–34,34,36,37,40,42,43,46–49,52]	-5.3	6.8	0.5	6.4	1.3	5.4
Rest-RRK [8,18,19,21,22,38,39,41,50-52]	0.8	9.4	-1.6	5.6	-4.9	5.0
Rest-F.Proto [8,37,38]	7.0	3.3	-3.7	5.2	-9.5	4.5
Rest-F.P45 [8,11,16,20,21,24–28,40,44]	1.3	8.5	-7.0	10.7	-2.8	7.1
Rest-F.Ohm [17-20,22,23,29,31-34,39,41-43,45-49,52,53]	-1.3	9.0	-0.1	4.1	-2.0	5.1

Values are given as subgroup of the database containing 43 studies, and calculated from average accuracies among studies.

Accuracies are given as weighted means for the number of subjects participating in the study.

CVL = cardiovascular laboratory; O.Th = operating theatre; I.Brach = intra-brachial artery pressure; I.Rad = intra-radial artery pressure; RRK = auscultatory pressure; F.Proto = use of all kinds of TNO-prototypes; F.P45 = use of TNO-prototypes 4 and 5 only; F.Ohm = use of Ohmeda Finapres device

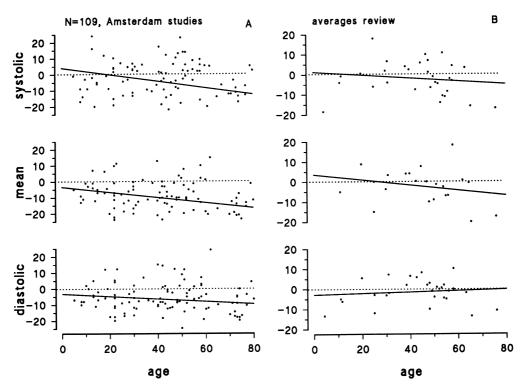


Fig. 4. Finger-to-reference differences related to age: A: Individual systolic, mean and diastolic differences in N = 109 subjects investigated between 1988 and 1995 in Amsterdam. B: Systolic, mean and diastolic differences and average age per study investigated in the review.

diastolic pressures as recorded in the brachial artery, whereas such differences tend to be positive in the radial artery (Table 1; Rest-I.Brach vs. Rest-I.Rad; p = 0.05).

For systolic pressures average differences were not different; no relation between finger-to-reference difference and measurement technique was found.

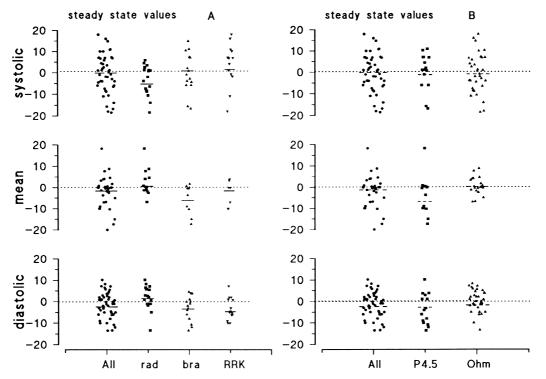


Fig. 5. Panel A: Average differences between finger and reference blood pressure selected per reference technique: Rad refers to intra-radial artery pressure (N = 357); bra refers to intra-brachial artery pressure (N = 202) and RRK refers to indirect auscultatory/oscillometric techniques (N = 404). Panel B: Average differences between finger and reference blood pressure selected per Finapres apparatus: P4.5 refers to TNO-Finapres prototypes 4 and 5 (N = 211), Ohm refers to the use of the commercial Ohmeda 2300 NIBP monitor (N = 787).

Jones et al. investigated the first Ohmeda 2300, a commercially manufactured Finapres device, and the later updated version (2300<sup>e</sup>) and detected a significant improvement of its accuracy [48]. At comparison of the performance of TNO prototypes and commercial devices the TNO prototypes show an underestimation for mean and diastolic pressures (Fig. 5B). This may be largely attributed to the fact that in 8 of the 12 studies intra-brachial artery pressures were used which caused the expected underestimation of brachial mean and diastolic pressures (Table 1).

#### 3.3.1. Conclusions

Although the accuracy of finger blood pressure in our review showed considerable scatter, the weighted accuracy of finger blood pressure among the 43 studies investigated remain within the 5 mmHg limit of the American Association for the Advancement of Medical Instruments [57]. The precision is too low for systolic and mean pressures and does not meet the acceptable limit of the 8 mmHg SD of the AAMI recommendations [12,57]. Although for diastolic pressure the accuracy and precision values are within the AAMI limits the overall performance does not permit finger blood pressure measurements for assessment of absolute blood pressure levels in individual patients.

#### 4. Finapres for tracking of blood pressure responses

The availability of the continuous blood pressure signal enables the device to be used in situations where assessment of sudden transient changes in the circulation is the primary goal [12,58-60]. At the time of introduction, the method was considered a major step in non-invasive cardiovascular monitoring [61] and initial evaluation studies predominantly concerned anaesthetized patients in the operation theatre (Table 1). Although the outcome of this initial work was promising, the use of finger arterial pressure in the operation theatre did not become routine practice [61]. In recent years continuous finger blood pressure has established its place in the field of the investigation of patients suspected to suffer from autonomic dysregulation and syncope [58-60,62,63]. Furthermore, the ability to relate beat-to-beat blood pressure with RR-interval provided an accurate way to investigate blood pressure variabilities [64].

The ability of Finapres to follow sudden changes in blood pressure is summarised in Table 2. The table shows the deviations of finger blood pressure responses from simultaneously measured intra-arterial pressure responses during various cardiovascular reflex tests. Several conclusions can be drawn: First, second-to-second changes in the reference blood pressure were reliably followed in the finger; although occasionally statistically significant differences were obtained (Table 2; Standing up [27], Valsalva [25,26]). These differences were usually small as compared to the magnitude of the responses (Table 2) and therefore not of clinical relevance [12,25,27]. As such, the specific information that is contained within these blood pressure responses [65] is always secured [12]. Second, minute-tominute changes in some conditions (Table 2, head-up tilting (HUT) [14-16,28]) show increases in differences for all pressures, i.e. systolic, mean and diastolic. Although the true origin of these differences is unknown, it has been attributed to changes in local tissue turgidity [66,67]. Third, in addition to changes of pulse wave amplification -as a result of modification of heart rate and left-ventricular ejection time [20]— different responses in systolic reference and finger measurement can occur, such as during the continuous infusion of phenylephrine and exercise. In such circumstances changes in mean finger pressure are reliable [17].

For the investigation of blood pressure variability Omboni et al. reported comparisons of finger and intra-arterial brachial variabilities in terms of standard deviations and specific time-domain and frequency-domain components [64]. As far as the standard deviations were concerned similar values were obtained from finger and invasive recordings for mean and diastolic pressures. Systolic standard deviations were larger in the finger. For assessment of power spectral analysis the comparison in low frequency (LF; 0.025–0.07 Hz), midfrequency (MF; 0.07–0.14 Hz) and high frequency (HF; 0.14-0.35 Hz) identified similar LF, MF and HF powers of diastolic and mean finger and brachial arterial pressures. For systolic pressures similar values in finger and brachial powers were found for the HF band, and significant overestimation intra-arterial systolic MF and LF powers in the finger trace [64,68].

# 4.1. Conclusion

For the assessment of beat-to-beat changes in blood pressure and assessment of blood pressure variability Finapres proved a reliable alternative for invasive measurements when mean and diastolic pressures are concerned. Differences in systolic pressure are larger and reach statistical significance but are not of clinical relevance. As such, the ability of the technique for tracking blood pressure responses is established in clinical practice for the assessment of syncopal attacks, the investigation of disabling orthostatic hypotension. Furthermore the device is crucial in the routine cardiovascular laboratory for assessment of blood pressure regulation investigated by standard reflex tests and variability measures.

# 5. Operational aspects of finger arterial pressure measurement

In our database of 43 studies, in seven studies it was reported that in a total of 33 subjects out of the overall

Table 2	
Tracking ability of finger arterial pressure	

Ref	Author	Test		Response			Deviation from ref. resp.		
				Sys (mmHg)	Mean (mmHg)	Dia (mmHg)	Sys (mmHg)	Mean (mmHg)	Dia (mmHg)
23]	Imholz	Bicycle ergometry 300 Watts supine		67	35	13	18*	1	5
27]	Imholz	Standing up							
			Trough	-30	-28	-20	3	1	2
			Overshoot	29	17	21	2	$-6^{*}$	-5*
			30 s	18	9	13	1	-3*	-3*
			120 s	14	13	17	-7 *	-3*	-4*
		Head-up Tilt 70° 2 min							
			Time trough	4.6	2.6	3	$6.4^{\dagger}$	1.7	1
			Time overshoot	8.1	6	8	5.8 *	0.4	-1
			30 s	11.3	9.6	10.8	1.3	-1.4	-1.9*
			120 s	11	10	13	-4*	$-2^{*}$	-2*
7]	Imholz	Phenylephrine 5 min infusi	on						
			1.6 µg/kg/min	47		15	-13*		-33*
5]	Imholz	Valsalva Hypertensives							
			instant a	24	20	17	2	2 *	3*
			instant b	-17	6	-9	-9	0	-1
			instant c	-10	18	-1	-7	2 *	0
			instant d	- 39	3	-20	2	0	0
			instant e	38	12	14	-8*	7 *	7*
6]	Jellema	Head-up Tilt 70° 30 min							
			last min of tilt	-	_	-	7†	7†	$6^{\dagger}$
6]	Parati	Valsalva							
			phase I	-		-	4		0
			phase II	-		-	4		0
			phase III	-		_	1		0
5]	Petersen	Head-up Tilt 60° 45 min		_	_	_	7.5	_	7.4
4]	Friedman	Head-up Tilt 60° 60 min		-57	_	-21	-1	_	-2
8]	Rongen	Head-up Tilt 60° 15 min							
•	c	*	30 s	-3.5	-2	0.9	1.4	-2.8*	-2.5
			10 min	0	2.2	8.2	7 *	4.4 *	=

\* Indicates p < 0.05, <sup>†</sup> indicates p < 0.01 (Student's t-test).

total of 1031 it was impossible to obtain finger pressure [18,35,40,41,43,51,52]. These were associated with technical problems in early prototype devices (N = 7) [35], with the inability to apply appropriate cuff sizes in the very young (N = 5) [18,51], with perioperative cold temperature (N = 11) [40,41], or were unexplained (N = 10) [43,52]. Sometimes the impossibility to measure the plethysmogram in the finger was due to the combination of vascular disease and ambient cold temperature (N = 3) [41].

Arteriolar vasoconstriction can interfere with measurement of the plethysmogram [8,17,20,50]. Vasoconstriction was initiated experimentally by vasoactive agents [17,20] or ambient cold temperature in patients known with spastic problems of the arteries [8,41,51]. If graded vasoconstriction with phenylephrine is performed measurement continues to be possible [17,20]. Cold fingers during initiation of the measurement can interfere with proper measurement of the plethysmogram and even result in no outcome [41]. However, the induction of cold temperature, as in open heart surgery [40], with finger pressure measurement operative can cause the plethysmogram signal to decrease substantially but it remains possible to perform measurement [8], even in Raynaud patients [50]. It is only upon reaching a state of full arterial constriction that physiocal is no longer able to establish a setpoint and measurements stop [10].

# 5.1. Cuff application

According to the user manual the correct selection of cuff size and application of cuffs is crucial. Just as with the auscultatory technique, the proper application of finger cuffs can affect outcome; Jones et al. found a decrease in accuracy when cuffs were applied too loose [49]. His study does not mention specific alterations of the finger waveform, but in our experience oscillations are more frequent in case of loose cuffs.

#### 5.2. Selection of fingers

According to the Ohmeda users manual middle or annular fingers are preferred. The basis for this is experimental rather than anatomical or physiological. From the time early prototypes were developed studies in the operation theatre described the use of the thumb using prototype thumb cuffs; however this proposal was never fully developed to reach success [29,39,40].

Finapres users sometimes switch the site of finger measurement until finger pressure values correspond close enough to auscultatory reference values [51,69]. This suggests that finger pressures differ between fingers of one hand. With Portapres during 24-h recordings using middle and annular fingers in alternation at 30 min interval, nearly similar finger pressures were seen in 8 subjects but due to differences in 16 subjects overall differences between fingers were 1.1 mmHg for systolic, 2.4 mmHg for mean and 3.3 mmHg for diastolic pressure [11]. In contrast in studies investigating two-finger differences from simultaneous measurements large differences were unusual [17,22,51]. Whether or not differences in cuff application are involved may need further clarification.

#### 5.3. Warming of the hand

The beneficial effect of heating on finger pressure measurement was investigated systematically by Hildebrandt et al. [22] and Tanaka and Thulesius [50]. Hildebrandt showed that during isometric exercise the systolic overestimation as compared to RRK decreased by 10 mmHg, by applying 44°C temperature to the fingertip distal to the cuffed finger [22], and suggested that vasodilatation had lowered the pressure pulse amplification, leading to lower systolic pressures in the finger. Tanaka reported the effects of cooling and the disparate effects of local (finger) versus central (truncal) heating [50]. Finger cooling showed a tendency towards higher systolic and diastolic finger pressures with lower temperature [8]. Local heating returned these trends towards pre-cooling values, but only after truncal heating these values were actually reached. It appears that feeling cold is worse than only 'cold hands'.

### 5.4. Assessment of the Finapres signal output

Barras in 1973 used a micropuncture technique to actually measure intra-arterial digital pressure. He found a waveform similar to the radial waveform; having a steep systolic pressure increase and deep dicrotic notch [70]. Another study compared finger artery aplanation tonometry with Finapres at adjacent fingers [4]. The waveforms appeared similar, suggesting an adequate pneumatic servo system bandwidth [4,10].

Low gave practical advice for obtaining adequate finger blood pressures in the AAN newsletter [71]. If the cuff is snugly applied, Finapres signals were considered acceptable when the signal was (a) large in size, (b) sharp in shape having a distinct dicrotic notch, and (c) within reasonable agreement with brachial (RRK) recordings. In addition the patient had to feel warm, and a temperature controlled muff is used in order to warm actively the fingers at 42°C. These suggestions largely agree with our own experiences [72]. However, the major criteria for accepting the Finapres output should be that it is considered stable. This is the case when the periods between servo self adjusts (Physiocals) are above 30 beats magnitude (Table 3). As a second criterion the fall in steepness of the pressure wave in case of increasing vasomotor tone can be used [72].

Table 3 Optimal measurement conditions for finger arterial blood pressure measurement

Surrounding:		
	Clinic	ambient temperature $> 22^{\circ}C$
	Outclinic/ambulant	hand covered with clothing
Subject:		
	Children	no specific guidelines
	Elderly	
	Vascular disease	
Measurement:		
Site:	Temperature hands	warm hands if cold
	Position of hand	always at heart level
Cuff:	Type finger	digit III en IV, do not use thumb
Signal:	Stable	measurement beyond 5 min, interval between $physiocal > 30$ beats
•	Physiocal on/off	minute-to-minute measurement: ON
Reproducibility:		
Within measurement		do not re-applicate finger-cuff
Between measurements		use same finger and cuff

#### 5.5. Hydrostatic errors

The relative level of the finger to the heart affects the mean blood pressure value at the finger. Therefore the finger must be kept at heart level. This can be achieved using a fixed position in the anterior axillary line [60], and when subjects are supine [HUT] by abduction of the arm so that the finger cuff is 10 cm below the cardiac apex [71]. If not, a near linear relation is observed between the hydrostatic level and the error [73]. This relation is used in the height correction system of Portapres [11]. Although mean pressures are adjusted correctly when finger pressures are still higher with the arm and hand below heart level. Correct systolic and diastolic pressures are not guaranteed due to the change in pressure waveform, and the finger is best kept at heart level [11,60].

#### 5.6. Reproducibility of finger blood pressures

Finapres enables measurement of continuous blood pressure tracings fairly unrestricted, and thus repeated measurements can be performed on different occasions or within one recording session by switching fingers each 30 min as currently advocated with the Portapres device [11].

Switching the measurement on/off in one finger during a measurement session gives highly reproducible measures; In our study with Portapres, average differences between finger and brachial artery pressures were constant in one finger [11].

The data concerning the reproducibility of Finapres with reapplication of finger cuffs are limited to the study of Lal who investigated different fingers at one time [51]. In a recent study the reproducibility of the 24-h Portapres BP profile is reported to be less than 10% [74]. This figure is similar to the reproducibility of conventional techniques

[75]. Additional, unpublished, observations were made in pregnancy. Using a TNO-Finapres as reference, variations of finger pressures with repeated cuff applications remained within 5 mmHg.

#### 5.6.1. Conclusions

Finger blood pressures can be obtained in almost all subjects; even in vasospastic or severe artherosclerotic disease [28]. Since conditions of peripheral vasoconstriction limit the use of Finapres, 'feeling' or subjective cold is best avoided and ambient temperature should be above 22°C. In outclinic conditions the hand should be protected [11]. Clinical practice suggests the benefit of active heating of the hand. Cuffs are best applied to the middle and annular fingers. If a height corrections system is used the hand should still be held near heart level (Table 3).

For accepting Finapres output, measurements must be without obvious artifacts and considered stable; guidelines are indicated in Table 3. Reproducibility of finger blood pressure also depends on cuff reapplication; if measurements are continued without reapplication finger blood pressures are highly reproducible [11,74]. With proper reapplication of cuffs reproducibility appears similar to invasive techniques, but definite studies are lacking thus far.

# 6. Recent developments

We have reviewed fifteen years of experience with finger arterial pressure monitoring, including age groups not easily subjected to invasive recordings [76,77]. For measurement of continuous blood pressure responses the technique is now an established alternative for invasive techniques as evidenced by many papers in various leading journals [78–80]. Diagnostic accuracy is achieved only after application of corrective measures.

#### 6.1. Adjustments of finger blood pressure levels

#### 6.1.1. Conventional adjustments

The incidental large differences between finger and reference blood pressures have convinced clinicians to try to correct finger with conventional measurements. For this reason finger pressures were tuned towards conventional brachial pressures by varying cuff application until differences between finger and RRK or oscillometric pressures were acceptable; Epstein in 1991 suggested the use of oscillometric thumb pressures to correct finger pressures [31]. Although simple guidelines are mentioned based on clinical experience, no systematic study has evaluated the value of such guidelines.

#### 6.1.2. Re-transmission filtering

The propagation of a central pressure waveform towards the periphery causes considerable changes in its shape. Recently, the distortion between brachial artery and finger was described in terms of a transfer function [72,81,82]. Based on the characteristics of this function, inverse filtering yields the 'brachial-alike' pressure waveform using any finger pressure as input [81,82]. To correct for any differences in pressure, the filtered waveform is tuned towards brachial artery pressure using a simultaneously performed RRK measurement applying an alternative criterion to assess Korotkoff-I, the return-to-flow technique [81]. Whether or not we will see finger blood pressure measurement to be used in absolute values in the near future will depend on the introduction and acceptance of these inverse modelling and calibration techniques.

# 6.2. Finger blood pressure as input for non-invasive assessment of circulatory control

The availability of the full pressure wave form enables the application of analytical methods to investigate cardiovascular function. The calculation of pulsatile systolic area has been related to relative changes in stroke volume by applying pulse contour formulae [83,84]. More recently, a different approach was introduced, the modelflow method. This method in contrast to pulse contour derives an aortic flow pulse by using a nonlinear, time-dependent model of aortic input impedance [85].

# 6.3. Future perspective of finger arterial pressure monitoring

Besides the availability of Portapres for more precise measures of variability in daily life [64], the development of a so-called Cardiapres in which 24-hour EKG-holtering and finger blood pressure recording are combined has great potential to correlate symptoms such as syncope with the underlying blood pressure changes [86]. In addition, the above mentioned measures of cardiac output applied on the non-invasive finger pressure waveform supports its potential as a key-hole to the circulation.

#### References

- Sleight P. Ambulatory blood pressure monitoring. Hypertens 1985;7:163–164.
- [2] Peñáz J. Photoelectric measurement of blood pressure, volume and flow in the finger. Digest 10th Int Conf Med Biol Engp 104, Dresden, Germany, 1973.
- [3] Wesseling KH, van Bemmel R, van Dieren A, Hyndman B, Snoeck B, Weha H, de Wit B, Zwart A. Two methods for the assessment of hemodynamic parameters for epidemiology. Acta Cardiol 1978;33:84–87.
- [4] Wesseling KH, de Wit B, Settels JJ, Klawer WH. On the indirect registration of finger blood pressure after Peñáz. Funkt Biol Med 1982;1:245–250.
- [5] Wesseling KH. A century of noninvasive arterial pressure measurement: from Marey to Peñáz and Finapres. Homeostasis 1995;36:50– 66.
- [6] Imholz BPM. Non-invasive finger arterial pressure recording: evaluation of Finapres and Portapres. 1991, Thesis, Amsterdam.
- [7] Boehmer RD. Continuous real-time, non-invasive monitor of blood pressure: Peñáz methodology applied to the finger. J Clin Monit 1997;3:282–287.
- [8] Wesseling KH, Settels JJ, van der Hoeven GMA, Nijboer JA, Butijn MWT, Dorlas JC. Effects of peripheral vasoconstriction on the measurement of bloodpressure in the finger. Cardiovasc Res 1985;19:139–145.
- [9] Wesseling KH, Settels JJ, de Wit B. The measurement of continuous finger arterial pressure noninvasively in stationary subjects. In: Schmidt TH, Dembroski TM, Bluemchen G, editors. Biological and Psychological Factors in Cardiovascular Disease, Berlin: Springer-Verlag, 1986:355–75.
- [10] Wesseling KH, de Wit B, van der Hoeven GMA, van Goudoever J, Settels JJ. Physiocal, calibrating finger vascular physiology for Finapres. Homeostasis 1995;36:76–82.
- [11] Imholz BPM, Langewouters GJ, van Montfrans GA, Parati G, van Goudoever J, Wesseling KH, Wieling W, Mancia G. Feasibility of ambulatory, continuous, 24-hour finger arterial pressure recording. Hypertension 1993;21:65–73.
- [12] Imholz BPM, Wieling W, Langewouters GJL, van Montfrans GA. Continuous finger arterial pressure; utility in the cardiovascular laboratory. Clin Auton Res 1991;1:43–53.
- [13] Epstein RH, Huffnagle S, Bartkowski RR. Comparative accuracies of a finger blood pressure monitor and an oscillometric blood pressure monitor. J Clin Monit 1991;7:161–167.
- [14] Friedman DB, Jensen FB, Matzen S, Secher NH. Non-invasive blood pressure monitoring during head-up tilt using the Penaz principle. Acta Anaesthesiol Scand 1990;34:519–522.
- [15] Petersen MEV, Williams TR, Sutton R. A comparison of non-invasive continuous finger blood pressure measurement (Finapres) with intra-arterial pressure during prolonged head-up tilt. Eur Heart J 1995;16:1647–1654.
- [16] Jellema WT, Imholz BPM, van Goudoever J, Wesseling KH, van Lieshout JJ. Finger arterial versus intra-brachial pressure and continuous cardiac output during head-up tilt testing in healthy subjects. Clin Sci 1996;91:193–200.
- [17] Imholz BPM, Parati G, Mancia G, Wesseling KH. Effects of graded vasoconstriction on the measurement of arterial pressure. J Hypertens 1992;10:979–984.

- [18] Tanaka H, Thulesius O, Yamaguchi H, Mino M, Konishi K. Continuous non-invasive finger blood pressure monitoring in children. Acta Paediatr 1994;83:57–73.
- [19] De Mey C, Schroeter VM, Butzer R, Roll S, Belz GG. Method specificity of non-invasive blood pressure measurement: oscillometry and finger pulse pressure vs. acoustic methods. Br J Clin Pharmacol 1995;40:291–297.
- [20] Bos WJW, van den Meiracker AH, Wesseling KH, Schalekamp MADH. Effect of regional and systemic changes in vasomotor tone on finger pressure amplification. Hypertension 1995;26:315–320.
- [21] Nijboer JA, Dorlas JC, Lubbers J. The difference in blood pressure between upper arm and finger during physical exercise. Clin Physiol 1988;8(5):501–510.
- [22] Hildebrandt W, Schutze H, Stegemann J. On the reliability of the Penaz cuff during systemic and local fingertip vasodilatation at rest and in exercise. Eur J Appl Physiol 1991;62(3):175–179.
- [23] Silke B, Spiers JP, Boyd S, Graham G, McParland G, Scott ME. Evaluation of non-invasive blood pressure measurement by the Finapres method at rest and during dynamic exercise in subjects with cardiovascular insufficiency. Clin Auton Res 1994;4:49–56.
- [24] Imholz BPM. Automated blood pressure measurement during ergometric stress testing: Possibilities of Finapres. Z Kardiol 1996;85(S3):76–80.
- [25] Imholz BPM, van Montfrans GA, Settels JJ, van der Hoeven GMA, Karemaker JM, Wieling W. Continuous noninvasive blood pressure monitoring: Reliability of Finapres device during the Valsalva manoeuvre. Cardiovasc Res 1988;22:390–397.
- [26] Parati G, Casadei R, Groppeli A, Di Rienzo M, Mancia G. Comparison of finger and intra-arterial blood pressure monitoring at rest and during laboratory testing. Hypertension 1989;13:647–655.
- [27] Imholz BPM, Settels JJ, van den Meiracker AH, Wesseling KH, Wieling W. Non-invasive continuous blood pressure measurement during orthostatic stress compared to intra-arterial pressure. Cardiovasc Res 1990;24:214–221.
- [28] Rongen GA, Bos WJW, Lenders JWM, van Montfrans GA, van Lier HJJ, van Goudoever J, Wesseling KH, Thien T. Comparison of intra-brachial and finger blood pressure in healthy elderly volunteers. Am J Hypertens 1995;8:237–248.
- [29] Kermode JL, Davis NJ, Thompson WR. Comparison of the Finapres blood pressure monitor with intra-arterial manometry during induction of anaesthesia. Anaesth Intensive Care 1989;17:470–486.
- [30] Aitken HA, Todd JG, Kenny NC. Comparison of Finapres and direct arterial pressure monitoring during profound hypotensive anaesthesia. Br J Anaesth 1991;67:36–40.
- [31] Epstein RH, Bartkowski RR, Huffnagle S. Continuous noninvasive finger blood pressure during controlled hypotension. A comparison with intra-arterial pressure. Anesthesiology 1991;75:796–803.
- [32] Gibbs NH, Larach DR, Derr JA. The accuracy of Finapres non invasive mean arterial pressure measurement in anesthetized patients. Anesthesiology 1991;74:647–652.
- [33] Stokes DN, Clutton-Brock T, Patil C, Thompson JH, Hutton P. Comparison of invasive and non-invasive measurement of continuous arterial pressure using the Finapres. Br J Anaesth 1991;67:26–35.
- [34] Lindqvist A. Beat-to-beat agreement of non-invasive finger artery and invasive radial artery blood pressure in hypertensive patients taking cardiovascular medication. Clin Physiol 1995;15:219–229.
- [35] Molhoek GP, Wesseling KH, Arntzenius AC, Settels JJ, van Vollenhoven E, Weeda HWH. Initial results of non-invasive measurement of finger blood pressure according to Penaz. Automedica 1983;4:241–246.
- [36] van Egmond J, Hasenbos M, Crul JF. Invasive versus non-invasive measurement of arterial pressure. Br J Anaesth 1985;57:434–444.
- [37] Smith NT, Wesseling KH, de Wit B. Evaluation of two prototype devices producing noninvasive, pulsatile, calibrated blood pressure measurement from a finger. J Clin Monit 1985;1:17–29.
- [38] Dorlas JC, Nijboer JA, van der Hoeven GMA, Settels JJ, Wesseling KH. Effects of peripheral vasoconstriction on the blood pressure in

the finger, measured continuously by a new method (the Finapres). Anesthesiology 1985;62:342–345.

- [39] Epstein RH, Kaplan S, Leighton BL, Norris MC, DeSimone CA. Evaluation of a continuous noninvasive blood pressure monitor in obstetric patients undergoing spinal anesthesia. J Clin Monit 1989;5(3):157–163.
- [40] Kurki TS, Smith NT, Sanford TJ Jr., Head N. Pulse oximetry and finger blood pressure measurement during open-heart surgery. J Clin Monit 1989;5:221–228.
- [41] Kurki TS, Piirainen HI, Kurki PT. Non-invasive monitoring of finger arterial pressure in patients with Raynaud phenomenon: effects of exposure to cold. Br J Anaesth 1990;65:558–563.
- [42] Farquhar IK. Continuous direct and indirect blood pressure measurement (Finapres) in the critically ill. Anaesthesia 1991;46(12):1050– 1055.
- [43] Pace NL, East TD. Simultaneous comparison of intra-arterial, oscillometric and Finapres monitoring during anesthesia. Anesth Analg 1991;73:213–220.
- [44] Bos WJW, Imholz BPM, van Goudoever J, Wesseling KH, van Montfrans GA. The reliability of noninvasive continuous finger blood pressure measurement in patients with both hypertension and vascular disease. Am J of Hypertens 1992;5:529–535.
- [45] Poncelet P, Durand P, Lechantre R, Mounier-Vehier C, Fouquoire B, Petetin N, Carre A. Measurement of blood pressure in obese persons: Comparison of intra-arterial and finger arterial blood pressure (Finapres). Arch Mal Coeur 1992;85:1165–1168.
- [46] Bardoczky GI, Levarlet M, Engelman E, d'Hollander A, Schmartz D. Continuous noninvasive blood pressure monitoring during thoracic surgery. J Cardiothorac Vasc Anesth 1992;6(1):51–54.
- [47] Gabriel A, Lindblad LE, Angleryd C. Non-invasive vs. invasive beat-to-beat monitoring of blood pressure. Clin Physiol 1992;12(2):229–235.
- [48] Jones RD, Brown AG, Roulson CJ, Smith ID, Chan SC. The upgraded Finapres 2300E. A clinical evaluation of a continuous noninvasive blood pressure monitor. Anaesthesia 1992;47(8):701– 705.
- [49] Jones RD, Kornberg JP, Roulson CJ, Visram AR, Irwin MG. The Finapres 2300E finger cuff. The influence of cuff application on the accuracy of blood pressure measurement. Anaesthesia 1993;48(7):611–615.
- [50] Tanaka H, Thulesius O. Effect of temperature on finger artery pressure evaluated by volume clamp technique. Clin Physiol 1993;13:535–545.
- [51] Lal SKL, Mihailidou AS, Cejnar M, Henderson RJ, Jones M, Hunyor SN. Continuous, non-invasive volume-clamp blood pressure: determinants of performance. J Hypertens 1993;11:1413–1422.
- [52] Triedman JK, Saul JP. Comparison of intra-arterial with continuous noninvasive blood pressure measurement in postoperative pediatric patients. J Clin Monit 1994;10(1):11–20.
- [53] de Jong-de Vos van Steenwijk CCE, Imholz BPM, Settels JJ, Wesseling KH. The usefulness of finger arterial pressure measurement with Finapres in Paediatric medicine. The Role of the Autonomic Nervous System in Juvenile Chronic Arthritis, Thesis, Utrecht, 1996.
- [54] Smith JJ, Kampine JP. Circulatory Physiology, The Essentials, 3rd ed. Baltimore, London, Williams and Wilkins, 1990.
- [55] Armitage P. Statistical Methods in Medical Research. 2nd ed. London, Blackwell Scientific 1991;312:194–196.
- [56] Imholz BPM. The brachial to finger pressure difference: are effects of modifiers of pulse wave distortion detectable among subjects? In Proceedings to Satellite Symposium: Continuous Finger Arterial Blood Pressure Measurement to the Seventh Meeting of the European Society of Hypertension. Chap. 15. 1995;109–112.
- [57] Association for the Advancement of Medical Instrumentation: Electronic or Automated Sphygmomanometers. ANSI/AAMI SP 10-1992. Arlington, VA: AAMI; 1992.
- [58] Mathias CJ, Armstrong E, Browse N, Chaudhuri KR, Enevoldson P,

Ross Russell RW. Value of non-invasive continuous blood pressure monitoring in the detection of carotid sinus hypersensitivity. Clin Auton Res 1991;1:157–159.

- [59] Kenny RA, Introduction. In: Kenny RA, editor. Syncope in the Older Patient, -Causes, Investigations and Consequences of Syncope and Falls. Chap. 1. Chapman and Hall Medical, London, 1996;8–10.
- [60] Wieling W, Karemaker JM. Measurement of heart rate and blood pressure to evaluate disturbances in neurocardiovascular control. In: Bannister R, Mathias CJ, editors. Autonomic Failure. A Textbook of Clinical Disorders of the Autonomic Nervous System, 5th ed. Oxford University Press, Oxford, 1997, in press.
- [61] Partridge BL, Sanford TJ Jr.. Finger plethysmography in Anesthesia. Semin Anesth 1989;8(2):102–111.
- [62] Benditt DG, Ferguson DW, Grubb BP, Kapoor WN, Kugler J, Lerman BB, Maloney JD, Raviele A, Ross B, Sutton R, Wolk MJ, Wood DL. Tilt table testing for assessing syncope — ACC expert consensus document. JACC 1996;28(1):263–275.
- [63] Low PA. Assessment: clinical autonomic testing report of the therapeutics and technology assessment subcommittee of the american academy of Neurology. Neurology 1996;46:873–880.
- [64] Omboni S, Parati G, Fratola A, Mutti E, DiRienzo M, Castiglioni P, Mancia G. Spectral and sequence analysis of finger blood pressure variability. Comparison with analysis of intra-arterial recordings. Hypertension 1993;22:26–33.
- [65] Smith ML, Beightol LA, Fritsch-Yelle JM, Ellenbogen KA, Porter TR, Eckberg DL. Valsalva's maneuver revisited: a quantitative method yielding insights into human autonomic control. Am J Physiol 1996;271:H1240–H1249. (Heart Circ Physiol. 40).
- [66] Low PA. Pitfalls in autonomic testing, In: Low PA, editor. Clinical Autonomic Disorders: Evaluation and Management. Chap. 28. Boston: Little Brown, 1993;355–365.
- [67] Ristuccia HL, Grossman P, Watkins LL, Lown B. Oncremental bias in Finapres estimation of baseline blood pressure levels over time. Hypertension 1997;29:1039–1043.
- [68] Veerman DP, Imholz BPM, Wieling W, Karemaker JM, van Montfrans GA. Effects of aging on blood pressure variability in resting conditions. Hypertension 1994;24:120–130.
- [69] Nordin M, Fagius J. Effects of noxious stimulation on sympathetic vasoconstrictor outflow to human muscles. J Physiol 1995;489:885– 894.
- [70] Barras JP. Direct measurement of blood pressure by transcutaneous micropuncture of peripheral arteries — Use of a new developed isovolumetric manometer. Scand J Clin Lab Invest 1973;31:153–157. (Suppl 128).
- [71] Low PA. Laboratory notes -tilt testing for adrenergic failure. AAN Newsletter 1993-8; Autonomic Nervous System:p6.
- [72] Wesseling KH. Finger arterial pressure measurement with Finapres. Z Kardiol 1996;85:38–44. (Suppl 3).

- [73] Gizdulich P, Aschero G, Guerrisi M, Wesseling KH. Effect of hydrostatic pressure of finger pressure measured with Finapres. Homeostasis 1995;36(3):120–129.
- [74] Voogel AJ, van Montfrans GA. Reproducibility of 24-hour finger arterial blood pressure, variability and systemic hemodynamics. J Hypertens 1997; in press.
- [75] Trazzi R, Mutti E, Frattola A, Imholz B, Parati G, Mancia G. Reproducibility of non-invasive and intra-arterial blood pressure monitoring. Implications for studies on antihypertensive treatment. J Hypertens 1991;9:115–119.
- [76] Imholz BPM, Dambrink JHA, Karemaker JM, Wieling W. Orthostatic circulatory control in the elderly evaluated by non-invasive continuous blood pressure measurement. Clin Sci 1990;79:73–79.
- [77] de Jong-de Vos van Steenwijk CCE, Wieling W, Johannes JM, Harms MP, Kuis W, Wesseling KH. Incidence and hemodynamic characteristics of near-fainting in healthy 6- to 16-year old subjects. JACC 1995;25:1615–1621.
- [78] Grassi G, Seravalle G, Cattaneo BM, et al. Sympathetic activation and loss of reflex sympathetic control in mild congestive failure. Circulation 1995;92(11):3206–3211.
- [79] van de Borne P, Beston P, Paiva M, Nguyen H, Linkowski P, Degaute JP. Cardiorespiratory transfer during sleep: a study in healthy young men. Am J Physiol 1995;269(3Pt2):H952–H958.
- [80] Randin D, Vollenweider P, Tappy L, Jéquier E, Nicod P, Scherrer U. Suppression of alcohol-induced hypertension by dexamethosone. New Engl J Med 1995;332:1737–1773.
- [81] Bos WJW, van Goudoever J, van Montfrans GA, van den Meiracker AH, Wesseling KH. Reconstruction of brachial artery pressure from noninvasive finger pressure measurements. Circulation 1996;94:1870–1875.
- [82] Gizdulich P, Prentza A, Wesseling KH. Models of brachial to finger pulse wave distortion and pressure decrement. Cardiovasc Res 1997;33:698–705.
- [83] Jansen JRC, Wesseling KH, Settels JJ, Schreuder JJ. Continuous cardiac output monitoring by pulse contour during cardiac surgery. Eur Heart J 1990;11(S1):26–32.
- [84] Sprangers RLH, Wesseling KH, Imholz ALT, Imholz BPM, Wieling W. The initial blood pressure fall upon stand up and onset to exercise explained by changes in total peripheral resistance. J Appl Physiol 1991;70(2):523–530.
- [85] Wesseling KH, Jansen JR, Settels JJ, Schreuder JJ. Computation of aortic flow from pressure in humans using a nonlinear, three-element model. J Appl Physiol 1993;74:2566–2573.
- [86] Omboni S, Smit AAJ, Wieling W. Twenty four hour continuous non-invasive blood pressure monitoring: a novel approach to the evaluation of treatment in patients with autonomic failure. Br Heart J 1995;73:290–292.