

Progress on the development of the MediWatch ambulatory blood pressure monitor and related devices

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The MediWatch™ is a wrist-mounted noninvasive blood pressure monitor designed to capture the radial pulse waveform using arterial tonometry and yield blood pressure measurements when the waveform is calibrated. An early prototype of this monitor uses a pulse-sensing system with a cylindrical plunger to applanate the radial artery. This prototype was evaluated against simulated blood pressure generated by a pneumatic pressure-pulse generator. The simulation-based results show that the prototype gave accurate pressure measurements when the MediWatch waveforms were calibrated against the simulator's pressure, indicating that the pulse-sensing system was able to measure force accurately. The prototype was clinically evaluated against intra-arterial pressure on post-open heart surgery patients. The results show that, under stationary conditions, for short periods of time and when the MediWatch waveforms were calibrated against the intra-arterial pressure, the prototype gave measurements that satisfy some of the statistical criteria of the 1993 Association for the Advancement of Medical Instrumentation standard, the 1993 British Hypertension Society protocol and the 2002 European Society of Hypertension protocol. These clinical results indicate that, under the stated test conditions, the prototype was able to accurately track changes in the patients' systolic and diastolic pressures. The MediWatch is being developed into an ambulatory device that provides a macroscopic view of the patient's blood pressure through measurement at preprogrammed intervals over 24 h, as well as a microscopic view of the patient's pressure through the pulse waveform captured during each measurement cycle. The design features of the MediWatch are being adapted

for other applications that require the arterial pulse waveform, calibrated beat-to-beat blood pressure or both. An improved MediWatch prototype has been developed that provides memory storage for measurement data and functions as an integral part of a Web-based system that allows measurement data to be accessed over the Internet. A pulse-wave analyser has been developed that allows the radial pulse waveform to be captured, calibrated and viewed in real time on a personal computer. A continuous noninvasive blood pressure monitoring system based on arterial tonometry is being developed for use as an alternative to the arterial line in invasive blood pressure monitoring. *Blood Press Monit* 9:149–165 © 2004 Lippincott Williams & Wilkins.

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Introduction

Noninvasive blood pressure (NIBP) monitors are commonly used for home, bedside and ambulatory monitoring [1–4]. In recent years, home blood pressure monitoring and, in particular, ambulatory blood pressure monitoring (ABPM) have increasingly been recognized as useful tools in the diagnosis, treatment and management of hypertension and other cardiovascular disorders [5–15]. Bedside monitoring of NIBP is usually used in critical care as an alternative to invasive blood pressure (IBP) monitoring. It is sometimes used to provide an additional measure of blood pressure in case of problems with IBP monitoring. Most NIBP monitors for home and ambulatory monitor-

ing use the oscillometric method, auscultatory method or both, whereas most NIBP monitors for bedside monitoring use the oscillometric method only [1–4]. These methods require the inflation of a cuff to completely occlude an artery at preprogrammed intervals over an extended period of time, which can cause patients bruises and discomfort and disturb them during sleep. In addition, they determine only one set of point pressures – namely, systolic pressure, diastolic pressure and mean arterial pressure (MAP) – over a period of time encompassing more than one heartbeat, and therefore cannot provide continuous beat-to-beat measurement, which is essential for critically ill patients under intensive care.

Arterial tonometry, also known as applanation tonometry, is a noninvasive method of measuring blood pressure that is less intrusive than cuff-based methods because it does not require the complete occlusion of an artery [1–3, 16–18]. With calibration, it can provide continuous beat-to-beat blood pressure measurement but without the risk of complications that is associated with IBP monitoring. It can be used as an alternative to IBP monitoring in situations that do not justify the use of invasive means, especially for patients who do not already have an arterial line (A-line) in place and who also do not require arterial blood sampling. It can potentially be used in any application that requires the arterial pulse waveform, calibrated beat-to-beat blood pressure or both.

Two models of commercial tonometric blood pressure monitors, manufactured by Colin (Komaki, Aichi, Japan), are currently available. The CBM-7000 (called Jentow-7700 in Japan) provides for tonometric and oscillometric blood pressure monitoring, whereas the Pilot (called BP-508 in Japan) [1,2] is a multiparameter monitor that provides for the monitoring of tonometric and oscillometric blood pressures, IBP, the electrocardiogram (ECG), temperature and, as an optional parameter, oxygen saturation. Both monitors use the same tonometric blood pressure module. These two monitors are, however, relatively expensive. In addition, both are designed for bedside monitoring and are not practical for home or ambulatory monitoring.

Against the foregoing background, HealthSTATS International in Singapore embarked on the development of a low-cost ambulatory blood pressure monitor – the MediWatch™ – which provides a macroscopic view of the patient's blood pressure through measurement at preprogrammed intervals over 24h, as well as a microscopic view of the patient's pressure through the pulse waveform captured during each measurement cycle. This paper first presents an evaluation of an early prototype of the MediWatch against simulated blood pressure and another evaluation against intra-arterial pressure. It then describes further developments of the MediWatch and the development of related devices.

Evaluation methods

Details of the MediWatch prototype and associated computer interface

The MediWatch is designed to be worn like a wristwatch and to function as both a blood pressure monitor and a wristwatch. The prototype that was used for the evaluation, the MW-1, consists of a dummy watch head, a pulse-sensing module and straps (Fig. 1). The device is mounted by positioning the pulse-sensing module over a palpable area of the radial artery and strapping the whole device to the wrist. It runs on a 3V coin-cell battery.

Fig. 1

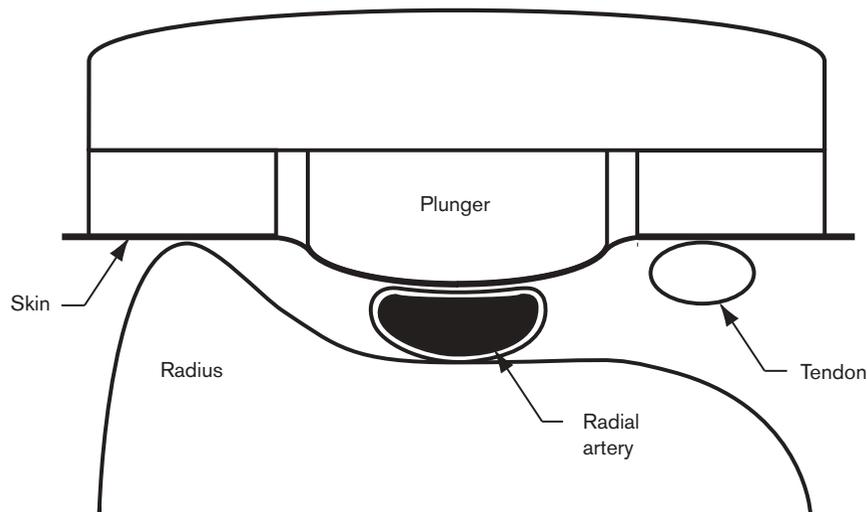


MediWatch prototype (MW-1) used in the evaluations. The light-emitting diode (LED) near the end of the protruding wire flashes when pulses are detected.

The pulse-sensing module uses a force sensor comprising a detachable cylindrical plunger 9 mm in diameter mechanically interfaced to the diaphragm of a pressure transducer, the plunger surface being slightly rounded spherically. The output of the transducer is proportional to the force acting on the transducer diaphragm, and the transducer detects all forces acting on the plunger in the direction of the plunger axis. When in use, the plunger presses against the artery to applanate the arterial wall (Fig. 2). The pulse-sensing module connects to the parallel port of a PC through an interface board that has a 12-bit analog-to-digital converter (ADC). A software program written in Visual Basic® and featuring a graphical user interface is used to initiate continuous beat-to-beat measurement, receive the ADC readings and stop the measurement. The software enables the user to view the beat-to-beat radial pulse waveform in real time on the PC and to store the waveform for further analysis. It accepts reference systolic and diastolic pressures from the user through the graphical interface and uses these pressures to calibrate the ADC readings and derive the beat-to-beat systolic pressure, diastolic pressure and time-weighted MAP; the time-weighted MAP is determined as the area under the time-pressure curve for one full wave, divided by the period of the wave. The pulse rate is determined using a proprietary algorithm.

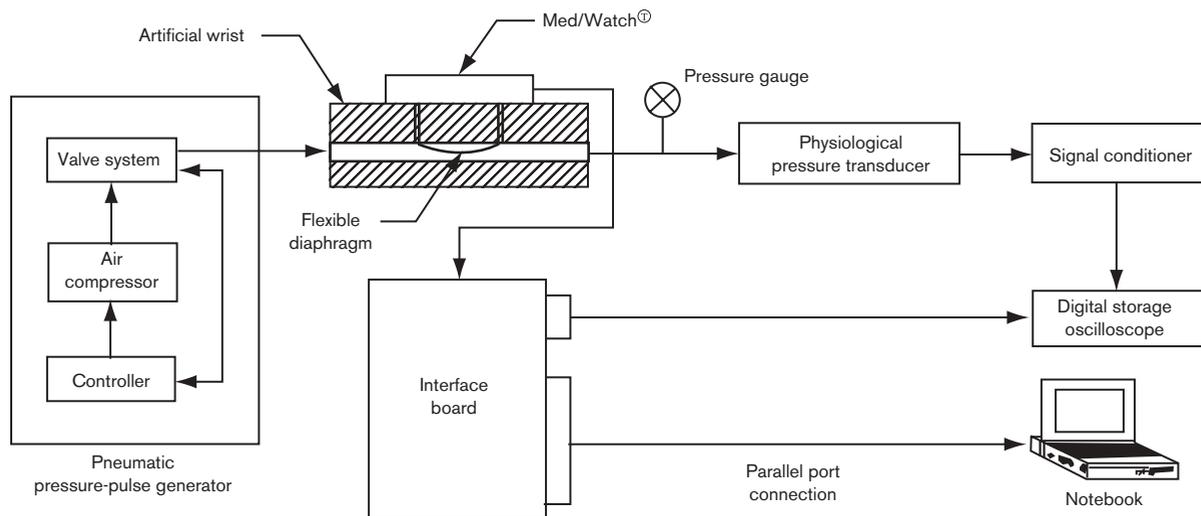
At this writing, new features of the MediWatch are protected by a US patent [19], a Singapore patent [20] and a Malaysia patent [21].

Fig. 2



Plunger-artery contact configuration for MediWatch prototype.

Fig. 3



Setup for evaluation of the MediWatch prototype against simulated pressure waveforms.

Evaluation against simulated blood pressure

To assess the accuracy of the pulse-sensing system, or tonometer, of the MW-1 prototype in measuring force, the prototype was evaluated against the simulated blood pressure generated by a pneumatic pressure-pulse generator that had an artificial wrist (Fig. 3). This evaluation was performed at the Cardiovascular Dynamics Laboratory in Singapore's Nanyang Technological University.

The MW-1 was mounted on the artificial wrist, and the simulated blood pressure was transmitted to the plunger through a thin latex diaphragm that came into contact with the full area of the plunger surface. The artificial wrist was designed such that pressure was always transmitted to the full and same area of the plunger, and the latex diaphragm was constrained from bending at the edge of the plunger so that minimal circumferential forces were generated as the applied pressure increased.

(Fig. 3). In this way, the force sensed by the force sensor varied linearly with the applied pressure, enabling the pressure to be easily determined by calibrating the sensor signal (in mV) against reference pressure measurements (in mmHg) using only two points.

Waveforms with various combinations of peak and trough were generated. The MediWatch signal was acquired by continuous polling using a software program written in Visual Basic and running under the Windows® Me operating system on a notebook PC powered by a Mobile Intel® Pentium® III 700E processor. The sampling rates, determined in a separate study, ranged from 17.8 to 18.2 data points per second (mean 18.1 ± 0.1 SD); these sampling rates were limited largely by the software timer used in the program. The MediWatch signal was also displayed on a digital storage oscilloscope (DSO) for visual inspection.

The peaks and troughs of the simulated blood pressure waveforms were measured using a pressure gauge that had been calibrated against a mercury manometer. The simulated pressure was also measured by a physiological pressure transducer (model PT43-604, sensitivity of $5 \mu\text{V}/\text{V}/\text{mmHg}$, operating range of -50 to $+300$ mmHg; Vivitro Systems, Victoria, British Columbia, Canada), the transducer output signal being amplified by a signal conditioner (Tri-Pack pressure measuring system TP8891, Vivitro Systems). The amplified signal was calibrated against the same mercury manometer and interfaced to the DSO. Waveforms that were intended for analysis were captured by the DSO at a sampling rate of 200 data points per second and stored on diskette. The recorded waveforms were digitally filtered using a 10-point median filter implemented through the MATLAB® software (The MathWorks, Natick, MA, USA). The filtered data were then converted into mmHg.

Data for 110 different peak–trough combinations representing a wide range of pressure were recorded and used for analysis. The pressure pertaining to the MediWatch signal was determined by first calibrating the ADC readings for the first set of peak and trough of the signal against the corresponding peak and trough pressure measurements made using the pressure gauge. The MediWatch pressures for the remaining sets of peak and trough were then computed using the resulting calibration curve (relationship between ADC reading and mmHg) and used with the corresponding simulated pressures for analysis ($n = 109$). Difference statistics were used to characterise the simulated and MediWatch pressures.

Evaluation against intra-arterial pressure

To assess the ability of the MW-1 prototype to faithfully capture the radial pulse waveform under stationary

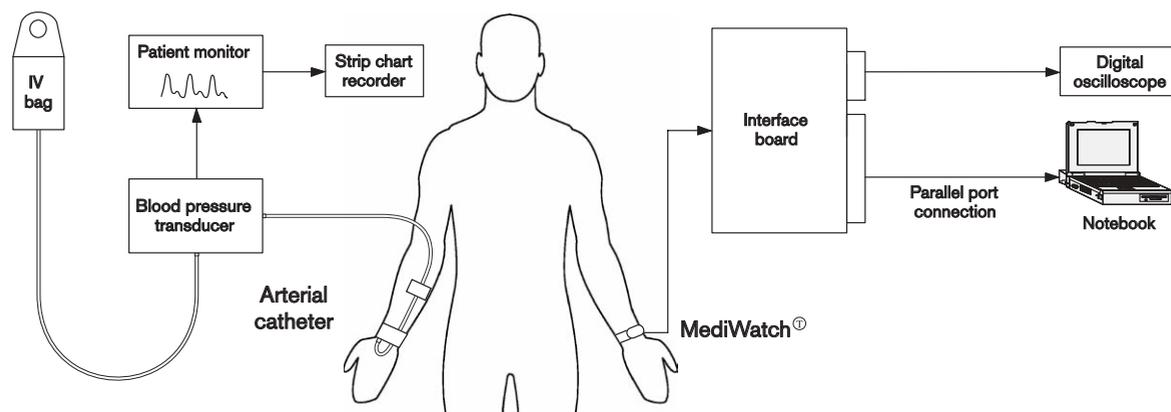
conditions, the prototype was evaluated against intra-arterial pressure on 23 patients from the Cardiothoracic Intensive Care Unit of the National University Hospital, Singapore. These were 1-day post-open heart surgery patients whose medical conditions included coronary heart disease, diabetes mellitus and hypertension. Most of the patients had more than one condition. All of them already had an indwelling arterial catheter in place. In compliance with the Declaration of Helsinki [22,23], the clinical protocol was approved by the hospital's Research and Ethics Committee (now Institutional Review Board), and informed consent was obtained from all the patients.

Intra-arterial pressure was measured using a semi-disposable blood pressure transducer (model BIO-TRANS™ I, Biosensors International, Singapore) with 84 inches of tubing, and the transducer output was connected to an M1006B IBP module (formerly under Agilent Technologies, Palo Alto, California, USA; now under Philips Medical Systems, Best, The Netherlands); this IBP module forms part of a Philips CMS patient monitoring system. The MW-1 was mounted on the opposite wrist for patients with a radial arterial line and on the same limb for one patient with a brachial arterial line (Fig. 4). The wrist with the MW-1 was always adjusted to as close to the neutral position as possible. The MW-1 plunger was always centered over the area where the radial pulse was most strongly felt and was adjusted until the maximum possible pulse amplitude was obtained on the oscilloscope, and both the pulse amplitude and baseline appeared stable over time.

The MW-1 and intra-arterial measurement sites were always kept at about the same level. As with the simulation-based evaluation, the MediWatch signal was acquired by continuous polling, using the same notebook PC and software program. It was also displayed on a digital oscilloscope to help ensure that the MW-1 had been properly mounted on the wrist. The intra-arterial waveforms were printed on strip charts.

For each patient, attempts were made to collect data for three different time periods, each ranging from 3 to 5 min. Before collecting data for each time period, the MW-1 was always checked to ensure that it was properly mounted on the wrist. If necessary, the position of the MW-1 was adjusted until the oscilloscope signal showed that it had been properly mounted. For most of the patients, however, data were collected for fewer than three time periods and for periods shorter than 3 min for one or more of the following reasons. First, it was difficult to obtain an acceptable signal for some of the patients because they could not rest their wrist in an optimum

Fig. 4



Setup for evaluation of the MediWatch prototype against intra-arterial pressure.

position and the investigators did not wish to disturb them for too long in trying to adjust their wrist position. Second, some of the patients had a thick layer of tissue at the radial artery, and it turned out that more time was required to obtain a signal with adequate pulse amplitude from these patients, but the investigators also did not wish to disturb them for too long. Third, it was in some instances difficult to obtain a stable signal because the patient was unable to keep his or her wrist stationary. Last but not least, the evaluation was discontinued on some of these patients before all the desired data had been collected because the patients expressed tiredness or a desire to sleep, or they directly or indirectly indicated that they would like the evaluation to stop.

For 2 of the 23 patients, an artefact was introduced into the intra-arterial and MediWatch signals by pressing the brachial artery of both arms simultaneously for about 1 s. This artefact was intended for use in matching the waveforms later on.

The strip charts were scanned and the intra-arterial waveforms digitised. For each patient, the MediWatch and intra-arterial waveforms were superimposed by matching the timing of their peaks. It was observed that the time interval between successive peaks varied, and this characteristic was used to help ensure that the two waveforms were correctly matched. For each set of MediWatch and intra-arterial waveforms, 11 consecutive beats of stable and correctly matching waveforms were identified. Intra-arterial systolic and diastolic measurements from the first beat were then used to calibrate the first beat of the MediWatch waveform. The MediWatch blood pressures for the remaining 10 beats were then computed and used with the corresponding intra-arterial blood pressures for analysis. Measurements from the first beat were excluded from the analysis because they were

calibration measurements, the differences between the MediWatch and corresponding intra-arterial blood pressures being zero for this beat.

The data were analysed according to the statistical and graphical methods of the 1993 ANSI/AAMI SP10–1992 standard [24,25], the main validation phase of the 1993 British Hypertension Society (BHS) protocol [26], and phases 2.1 and 2.2 of the 2002 European Society of Hypertension (ESH) International Protocol [27]. These methods were intended to be used to provide quantitative indications of the ability of the MW-1 to track changes in blood pressure.

Evaluation results

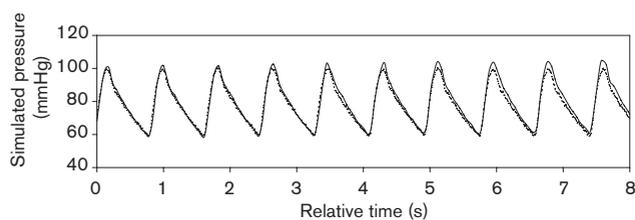
Evaluation against simulated blood pressure

For the simulation-based evaluation, the simulated blood pressure ranged from 90 to 182 mmHg (mean 137.6 ± 23.2) for the peaks and from 60 to 140 mmHg (101.0 ± 20.0) for the troughs. The MediWatch waveforms closely resembled the corresponding simulated pressure waveforms (Fig. 5). The MediWatch–simulator (MediWatch minus simulator) differences were 0.1 ± 1.5 mmHg (mean \pm SD) for the peaks and 0.1 ± 1.3 mmHg for the troughs.

Evaluation against intra-arterial pressure

For the clinical evaluation, data for 8 of the 23 patients were excluded from the analysis for one or more of the following reasons. First, the MediWatch-mounted wrist of the patient moved too much, to the extent that it was not possible to identify a sufficiently long segment of stable waveform for analysis; some of these patients actually exhibited an involuntary tremor of the arm during the data collection. Second, the pulse amplitude of the MediWatch signal for the stable segments turned out to be too small, probably because the plunger had been

Fig. 5



Sample segments of MediWatch and simulated waveforms: solid line, MediWatch; dotted line, simulated.

shifted at some point during the data collection, this shift probably being caused by wrist motion. Third, the intra-arterial waveform was distorted or suspected of being distorted because of improper placement of the catheter, kinking of the tubing or excessive movement of the cannulated arm; in these instances, the distortion was normally first noticed on the screen of the patient monitor. Last but not least, it was impossible to ascertain whether the MediWatch and intra-arterial waveforms were correctly matched because of, for example, artefacts caused by wrist motion. For some of these eight patients, evaluation was performed during the earlier part of the evaluation period, which was also a time when the evaluation team was still acquiring experience with the evaluation process.

Analysis was performed on data from the remaining 15 patients ($n=150$). These patients comprised 11 male and four female patients who exhibited a wide range of medical conditions, which are listed in Table 1. Their ages ranged from 45.7 to 74.7 years (mean 60.0 ± 10.1 years). Their intra-arterial pressure for the 10 beats used for analysis ranged from 96 to 166 mmHg (mean 130.2 ± 17.4 mmHg) for systolic pressure and 43 to 76 mmHg (mean 58.6 ± 8.2 mmHg) for diastolic pressure. The average intra-arterial pressures for each patient for the 10 beats are given in Table 1. The MediWatch waveforms of all 15 patients resembled the corresponding intra-arterial waveforms (Fig. 6). Among them was one patient, patient 15, who had an artefact introduced into his MediWatch and intra-arterial waveforms (Fig. 6). The artefact manifested itself as an almost obliterated beat on the waveforms; this can be explained by the fact that pressing the brachial artery prevented blood from flowing through it, and this in turn prevented the pressure pulse from being transmitted to the radial artery. This artefact proved to be useful in ensuring that the intra-arterial and MediWatch waveforms for that patient were correctly matched.

The MediWatch–intra-arterial differences (MediWatch minus intra-arterial values) were 0.1 ± 4.1 mmHg

(mean \pm SD) for systolic pressure and 0.5 ± 3.8 mmHg for diastolic pressure. These results satisfy the accuracy criteria of the ANSI/AAMI SP10–1992 standard, namely a mean difference within ± 5 mmHg and a standard deviation within 8 mmHg [24,25].

For systolic pressure, 78.0%, 99.3% and 100% of the differences lie within ± 5 , ± 10 and ± 15 mmHg respectively. For diastolic pressure, the percentages are 80.0%, 99.3% and 100%, respectively. Both sets of percentages correspond to grade A of the 1993 BHS protocol [26]; this grade requires the following respective percentages: $\geq 60\%$, $\geq 85\%$ and $\geq 95\%$. For clinical use of the monitor, the protocol stipulates a grade of A or B for systolic and diastolic pressures; grade B requires the following respective percentages: $\geq 50\%$, $\geq 75\%$ and $\geq 90\%$.

The above percentages also satisfy the criteria of phase 2.1 of the ESH protocol, if the percentage of readings instead of number of readings is used for the criteria. This phase effectively requires at least two of the following respective percentages to be satisfied: $\geq 66\%$, $\geq 81\%$ and $\geq 96\%$. It also effectively requires all of the following respective percentages to be satisfied: $\geq 61\%$, $\geq 76\%$ and $\geq 91\%$.

For systolic pressure, 12 of the 15 test subjects (patients) or, equivalently, 80% of the subjects, have two-thirds of their differences lying within ± 5 mmHg. For diastolic pressure, 13 of the 15 subjects or, equivalently, 86% of the subjects, have two-thirds of their differences within ± 5 mmHg. None of the subjects has all 10 differences exceeding ± 5 mmHg. If the criteria of phase 2.2 of the ESH protocol [27] were modified to use the percentage of subjects rather than the number of subjects, these percentages would meet the modified criteria; the original criteria require at least 22 of 33 subjects (67%) to have 2 of their 3 differences within ± 5 mmHg and at most 3 of the 33 subjects (9%) to have all 3 differences (100% of the differences) exceeding ± 5 mmHg.

Bland–Altman scatterplots [28,29] for systolic and diastolic pressures are shown in Fig. 7. For both plots, only one difference out of 150 exceeds ± 10 mmHg.

Discussion of the evaluations

Simulation-based evaluation

The results of the simulation-based evaluation show that the MW-1 prototype gave accurate pressure measurements when the captured waveforms were calibrated against the simulator's pressure. They also show that the MediWatch waveforms closely resembled the simulated pressure waveforms. By virtue of the design of the artificial wrist, as described above, these results effectively

Table 1 Patient data pertaining to the evaluation of the MediWatch prototype against intra-arterial pressure

Patient #	Sex	Age (years)	MediWatch measurement site (artery)	Intra-arterial measurement site (artery)	Intra-arterial systolic pressure for the 10 beats (mean \pm SD, mmHg)	Intra-arterial diastolic pressure for the 10 beats (mean \pm SD, mmHg)	Medical conditions and procedures*
1	Female	47.14	Radial, right	Radial, left	137.3 \pm 2.0	55.0 \pm 1.8	Asthma, CAD, DM, hypertension
2	Female	71.83	Radial, right	Radial, left	127.9 \pm 4.3	52.4 \pm 2.3	CAD, DM, hypertension
3	Female	60.93	Radial, left	Radial, right	103.7 \pm 2.1	53.3 \pm 1.3	CAD
4	Male	45.67	Radial, right	Radial, left	160.0 \pm 3.4	66.4 \pm 1.3	CAD, DM
5	Male	68.23	Radial, right	Radial, left	141.0 \pm 1.6	44.2 \pm 0.7	CAD, DM, high lipids, hypertension
6	Male	71.93	Radial, left	Radial, right	157.1 \pm 3.6	67.7 \pm 1.7	IHD, TVD
7	Male	65.87	Radial, right	Radial, left	143.8 \pm 2.7	54.1 \pm 0.6	Heart valve replacement
8	Male	68.04	Radial, right	Radial, left	139.0 \pm 9.1	64.1 \pm 5.1	CAD, DM, hypertension, IHD
9	Male	60.62	Radial, right	Radial, left	140.8 \pm 2.3	73.1 \pm 2.1	CAD
10	Male	48.18	Radial, right	Radial, left	110.5 \pm 2.1	56.6 \pm 1.3	CAD, DM
11	Female	48.27	Radial, right	Radial, left	101.9 \pm 4.5	50.0 \pm 1.6	Mitral stenosis with left aortic thrombus
12	Male	55.20	Radial, left	Brachial, left	122.4 \pm 3.1	70.9 \pm 1.8	CAD, hypertension
13	Male	50.52	Radial, left	Radial, right	119.1 \pm 2.4	61.3 \pm 1.7	CAD
14	Male	74.69	Radial, left	Radial, right	123.6 \pm 3.9	53.5 \pm 2.6	CAD
15	Male	62.15	Radial, left	Radial, right	125.5 \pm 2.9	56.9 \pm 1.5	CAD, DM, hypertension, PVD
Mean \pm SD		59.95 \pm 10.11			130.2 \pm 17.4	58.6 \pm 8.2	
Range		45.67 to 74.69			96 to 166	43 to 76	

*CAD, coronary artery disease; DM, diabetes mellitus; IHD, ischemic heart disease; PVD, peripheral vascular disease; TVD, triple vessel disease.

indicate that the pulse-sensing system was able to measure force accurately. This ability will ultimately facilitate accurate blood pressure measurement.

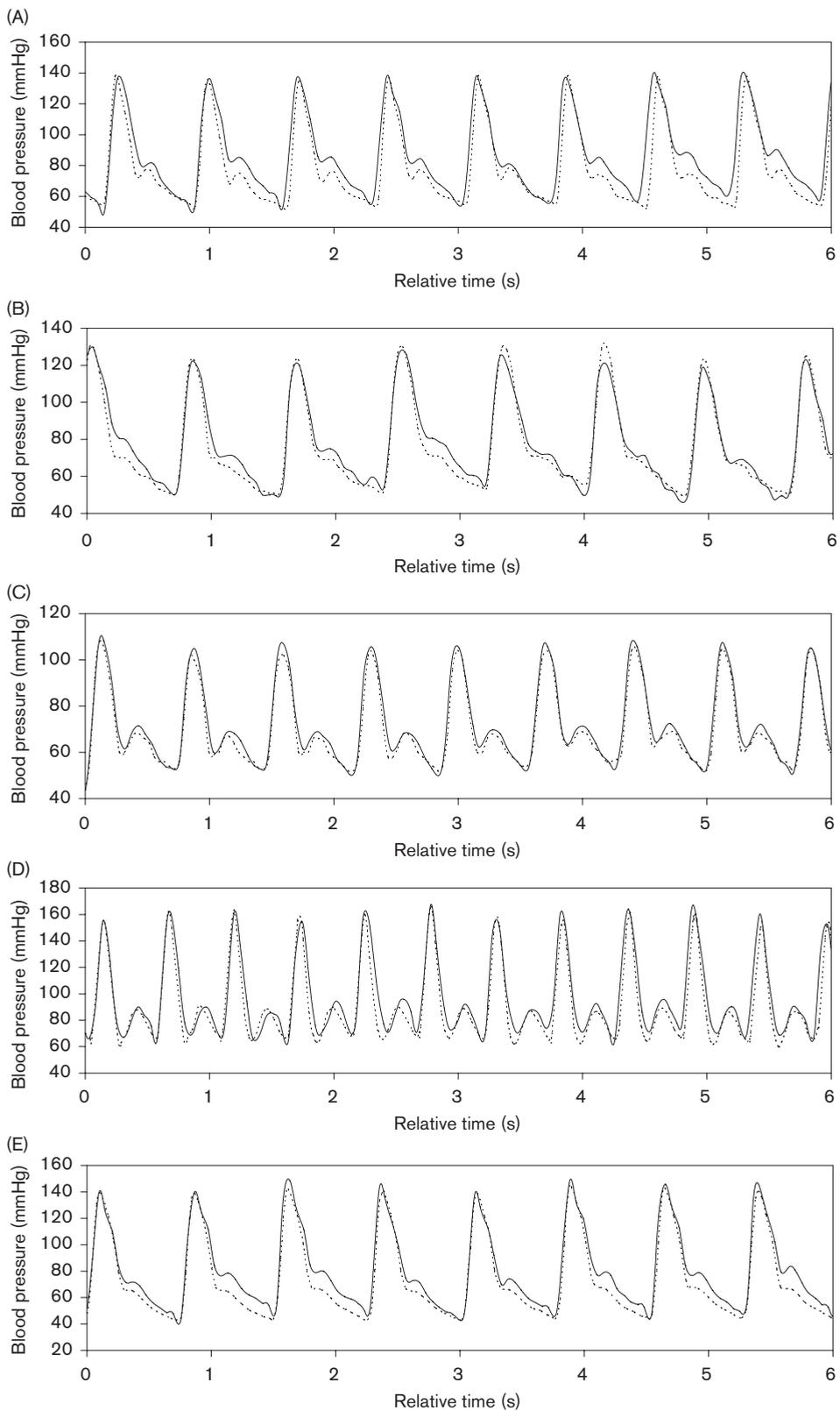
It should be noted that the plunger–diaphragm contact configuration for the simulation-based evaluation did not closely simulate the actual plunger–artery contact configuration using the MW-1. In the plunger–diaphragm contact configuration (see Fig. 3 above), the pressure transmission area is equal to the plunger area and does not change with pressure, as the latex diaphragm comes into contact with the full area of the plunger surface. In addition, the plunger area is subjected to minimal circumferential forces. As a result, the force as sensed by the force sensor varies linearly with applied pressure.

The actual artery–plunger contact configuration and the way in which forces are generated for this configuration are, however, quite complex. In the actual artery–plunger contact configuration, the appanated area of the artery or, equivalently, the pressure transmission area, always lies within the plunger's sensing area, which is also the plunger's surface area (9 mm in diameter). The force sensor senses not only all the forces acting on the plunger's surface, but also circumferential forces that act along the edge of the plunger. These circumferential forces generally increase with appanation force or, equivalently, appanation depth.

For any given appanation depth, the pressure transmission area for the appanated part of the artery increases

and decreases as the artery, being distensible, expands and contracts with changes in the arterial pressure, even when the device and wrist are kept stationary. This change in area is expected to increase with pulse pressure and decrease with arterial stiffness at the measurement site; arterial stiffness is known to increase with age and the presence of certain diseases, among other factors [30–32]. For any given appanation depth and for any increase in arterial pressure, the force as detected by the sensor will consist of three components. The first component is due to the increase in arterial pressure acting on the original area. The second component results from the arterial pressure acting on the additional pressure transmission area. The third component is due to extraneous forces that are generated on the surrounding tissue by the arterial pulsations and that act on the non-artery part of the plunger surface. A combined effect of the second and third components is that the force as detected by the sensor, and hence the sensor signal (in mV, for example), will no longer vary linearly with arterial pressure. In other words, the relationship between the sensor signal (mV) and the arterial pressure (mmHg) becomes non-linear, so that the shape of the MediWatch waveform will deviate from that of the corresponding intra-arterial waveforms if a linear two-point calibration method is used. The nature of this non-linearity will depend on pulse pressure, arterial stiffness, appanation depth, arterial pressure and the mechanical properties of tissue around the artery. This non-linearity is expected to increase the further the pressure is from the calibrated points.

Fig. 6



Sample segments of MediWatch and intra-arterial waveforms: solid line, MediWatch; dotted line, intra-arterial. (A) Patient 1. (B) Patient 2. (C) Patient 3. (D) Patient 4 (tachycardia). (E) Patient 5. (F) Patient 6. (G) Patient 7. (H) Patient 8. (I) Patient 9. (J) Patient 10. (K) Patient 11 (irregular heart rate). (L) Patient 12. (M) Patient 13. (N) Patient 14 (bradycardia). (O) Patient 15 (with artefact).

Fig. 6 (Continued)

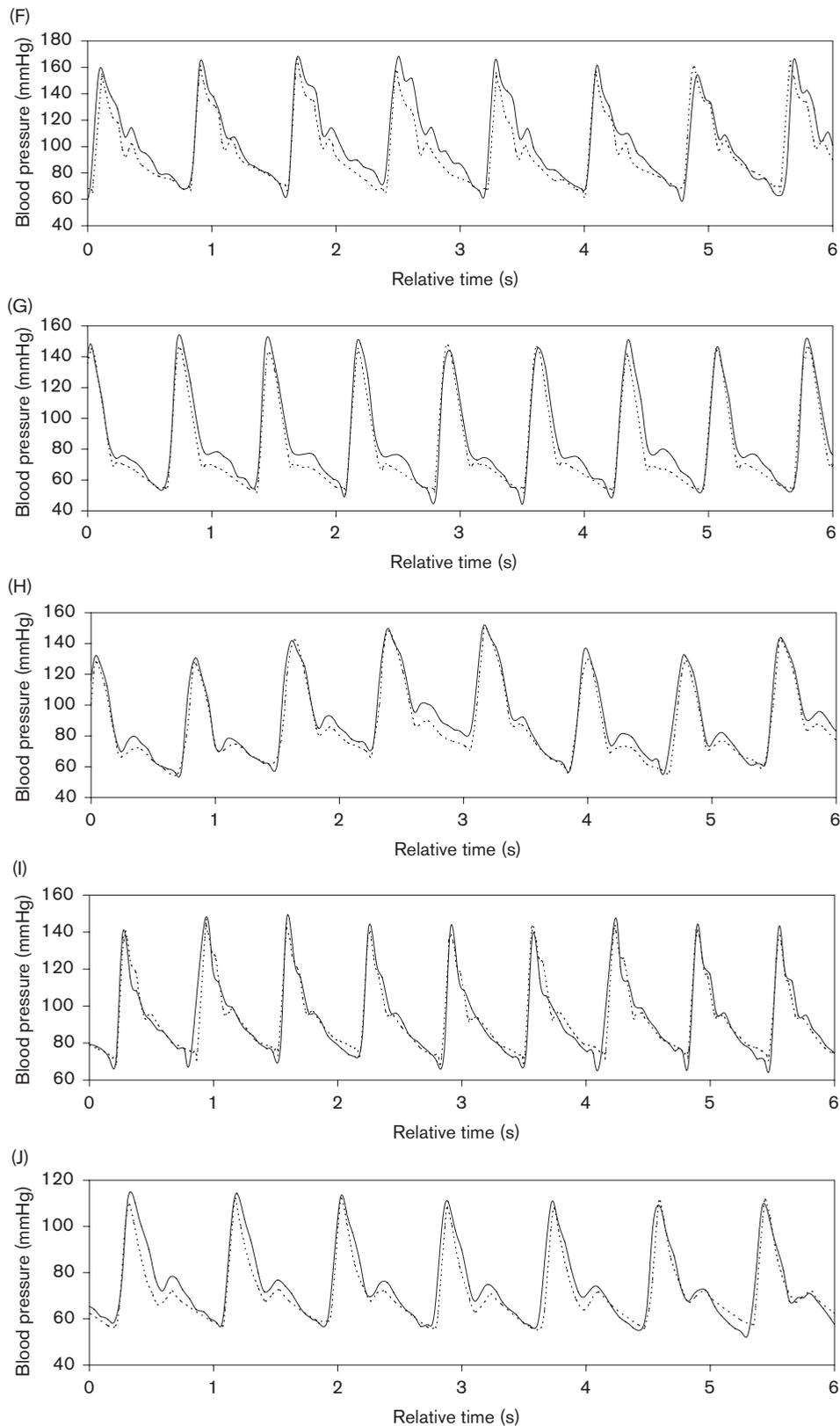


Fig. 6 (Continued)

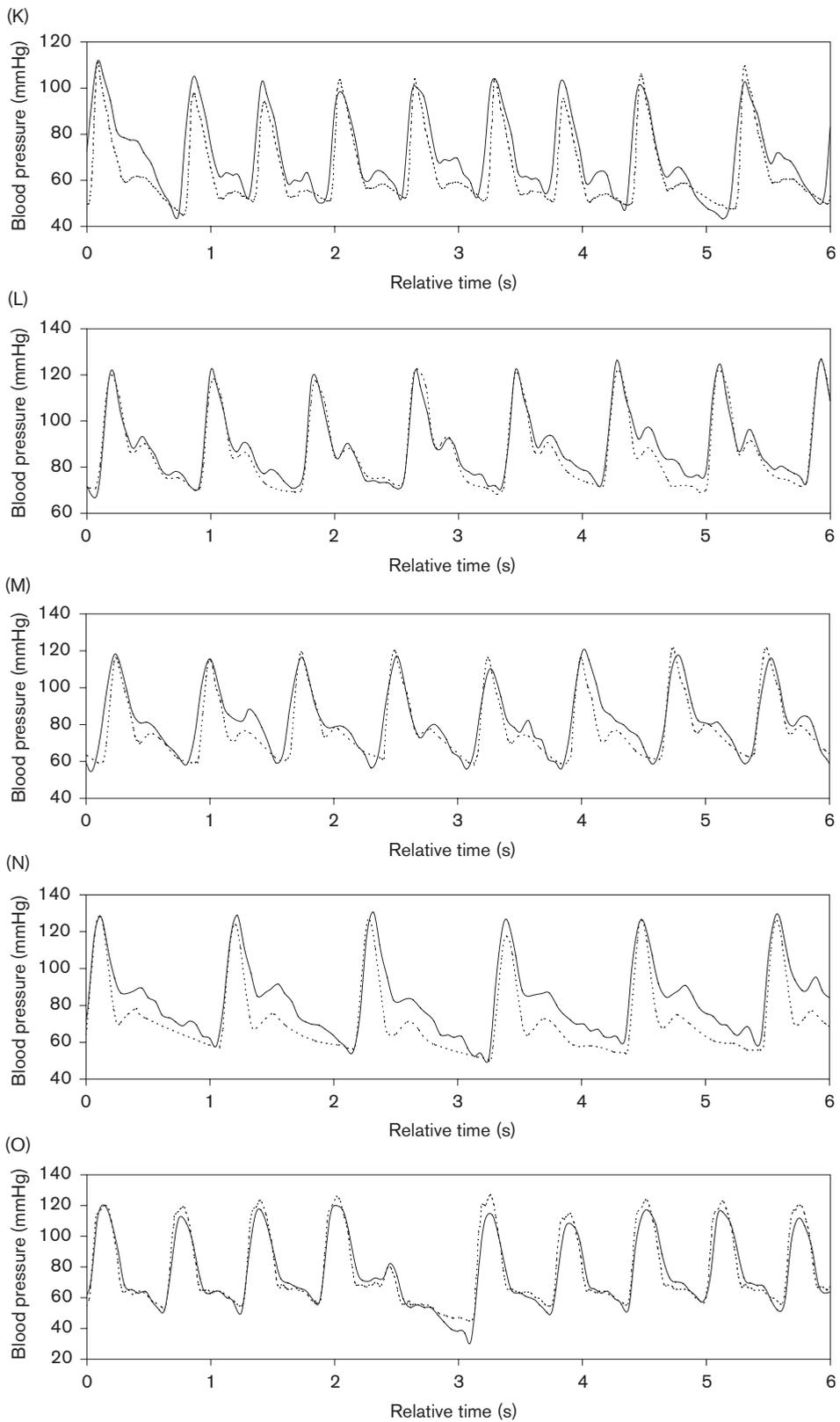
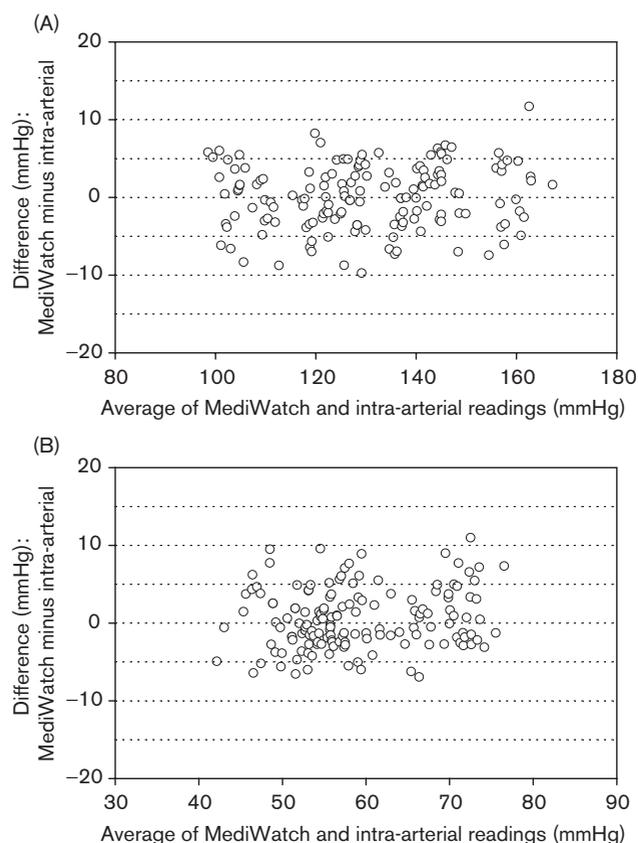


Fig. 7



Bland-Altman scatterplots pertaining to the evaluation of the MediWatch prototype against intra-arterial pressure. (A) Systolic pressure. (B) Diastolic pressure.

The simulation-based results can therefore be used only to indicate how well the pulse-sensing system can measure force.

Clinical evaluation

The results of the clinical evaluation show that, under stationary conditions and for short periods of time, the MW-1 prototype gave blood pressure measurements that satisfy some of the statistical criteria of the Association for the Advancement of Medical Instrumentation (AAMI) standard, BHS protocol and ESH protocol when the captured waveforms were calibrated against the intra-arterial pressure. These results effectively indicate that, under the stated test conditions, the prototype was able to accurately track changes in the patients' systolic and diastolic pressures. Such an ability is a prerequisite for accurate blood pressure measurement.

It should be noted, however, that the clinical results cannot be interpreted to mean that the prototype met the accuracy requirements of the AAMI standard, BHS protocol or ESH protocol, for at least two reasons. First,

the evaluation did not comply with all the requirements of the standard or protocols. For example, the BHS and ESH protocols stipulate only manual auscultatory measurements as the reference, whereas the evaluation used intra-arterial measurements as the reference. In addition, the evaluation was not performed according to the various phases stipulated in the BHS and ESH protocols.

Second, the blood pressure corresponding to the captured waveforms was obtained by calibrating the waveforms against the intra-arterial pressure, the very reference against which the prototype was evaluated. For a monitor that requires calibration, the overall measurement accuracy of the monitor must necessarily refer to the accuracy of the monitor's measurements when they are calibrated against the calibration device that is intended for use with the monitor. The intra-arterial method cannot be used as the calibration device because it is generally neither practical nor justifiable to cannulate a patient for the sole purpose of calibrating an NIBP monitor. The accuracy of the MediWatch or, for that matter, any blood pressure monitor that requires external calibration, will therefore ultimately depend on the accuracy of the calibration device that is used with the monitor, and the accuracy of the MediWatch can only be as good as that of the calibration device. Nevertheless, the approach of calibrating the MediWatch waveforms against intra-arterial pressure makes it possible to evaluate the ability of the device to track changes in blood pressure, as opposed to its ability to measure blood pressure.

It can be observed from Fig. above 6 that although the MediWatch waveforms did resemble the corresponding intra-arterial waveforms, the shape of the MediWatch waveforms from some of the patients did not quite match the shape of the corresponding intra-arterial waveforms, even after allowing for some loss of fidelity in reconstructing the analogue waveforms from digital data. In particular, the dicrotic notch and the following dicrotic wave of the MediWatch waveforms appeared noticeably higher than the corresponding dicrotic notch and dicrotic wave of the intra-arterial waveforms for patients 1, 5, 7, 10, 11, 12, 13 and 14 (see Fig. 6 above). This discrepancy could be due in part to differences between the frequency response of the fluid-filled system of the arterial line and the frequency response of the measurement system comprising the pulse-sensing system (tonometer) in contact with the radial artery; the latter frequency response is expected to vary from patient to patient because the mechanical properties of the arterial wall and surrounding tissue through which arterial pressure is transmitted to the plunger are likely to vary from patient to patient. The discrepancy could also be partly related to actual site-to-site differences between the waveforms as the intra-arterial and MediWatch

waveforms were not obtained from the same measurement site. More significantly, it could be due to the non-linearity in the relationship between the sensor signal and arterial pressure, as already explained above. It is noteworthy, however, that the MediWatch waveforms for patients 3 and 4 matched the corresponding intra-arterial waveforms well.

Despite the significant deviations of the shape of the MediWatch waveforms from that of the intra-arterial waveforms for a number of the patients, the clinical results indicate that such deviations did not, in general, adversely affect the prototype's ability to track changes in the systolic (maximum) and diastolic (minimum) pressures of the tested patients when a linear two-point calibration method was used. It is recognised that this ability to track changes is valid for the relatively small variations in the systolic and diastolic pressures of each subject during the 10 beats used for the analysis (see Table 1 above), and that studies are required to determine the effects of larger pressure variations on this tracking ability. It is also recognised that such deviations can introduce error into any characteristic that depends on the area under the waveform, such as the time-weighted MAP, as well as any characteristic that depends on the shape of the waveform, such as the frequency spectrum of the waveform.

Developments of the MediWatch and related devices

It is the primary intent of the development team at HealthSTATS to develop the MediWatch into a device that can be used for 24-h ABPM and that can also provide the arterial pulse waveform at the same time. It is also the intent of the team to adapt the design features of the MediWatch for other applications that require the arterial pulse waveform, calibrated beat-to-beat blood pressure or both. Since the completion of the above evaluations, a number of significant developments have taken place, are in progress or are being considered. These developments are described as follows.

Artefacts and the design of pulse-sensing system

The MW-1 prototype uses a single sensor in the pulse-sensing system and a sensing area (9 mm in diameter) that is larger than the appanated area of the radial artery. The Colin CBM-7000 and BP-508 monitors, on the other hand, use a pulse-sensing system comprising a linear array of 30 piezoresistive sensors spaced 0.2 mm from each other, this array being similar to the 15-sensor array used in earlier models [33–49]. The use of an array of sensors was intended to increase the chances that at least one of the sensors would be positioned over the appanated part of the artery; this sensor is identified as the sensor that gives the maximum pulse amplitude. The sensing area for this sensor is constant, is always flat, always lies within

the appanated part of the artery and is not subjected to circumferential forces, so that the force as detected by the sensor changes linearly with applied pressure. This sensor array is integrated with a microprocessor-controlled system that automatically moves the array up and down and across the wrist over a range of about 17 mm to locate an optimum position that gives an acceptable signal level when the pulse-sensing system is first mounted on the wrist and whenever it has shifted during monitoring [50,51]. This automated positioning system is used with a wrist brace to partially immobilise the wrist in order to reduce motion artefacts. The MW-1 prototype does not use any automated positioning system or wrist brace.

The use of a single sensor and the lack of an automated positioning system make for a simple pulse-sensing system design for the MW-1 prototype. The use of a larger sensing area gives the advantage that less precision is required in positioning the pulse-sensing system to obtain a pulse waveform than if a smaller sensing area is used. This design does, however, require the plunger to be correctly positioned the first time it is mounted on the wrist and to remain in the same position throughout the monitoring period. The lack of a wrist brace makes not only for greater patient comfort, as the hand can move more freely without a wrist brace, but also for a more compact device. However, it leaves the artery-plunger contact configuration more susceptible to motion artefacts since the wrist is easily subjected to motion during regular activities.

Efforts are under way to develop this single-sensor system further by incorporating a feedback method to help to ensure proper placement of the plunger over the artery and to provide for repositioning of the plunger during monitoring. A comprehensive system of straps and pads is being developed to help minimise the movement of the pulse-sensing system relative to the wrist in order to reduce motion artefacts. Intelligent software algorithms based on waveform characteristics are being developed to correct for artefacts caused by motion or by the time-dependent or viscoelastic properties of the compressed tissue under and around the plunger; the effects of the viscoelastic properties are particularly significant if the device is used for continuous, long-term monitoring of the blood pressure because the compressed tissue will gradually lose its elasticity over time and this will alter the artery-plunger contact configuration and, as a result, the MediWatch signal. In addition, changes to the mechanical design of the pulse-sensing system are being considered with a view to (1) reducing non-linearity in the relationship between the sensor signal and arterial pressure, so that the MediWatch waveform (in mV) can correctly represent the corresponding intra-arterial waveform; and (2) reducing the effect of wrist motion on the artery-plunger contact configuration.

Calibration of tonometric waveforms

As with Colin's tonometric blood pressure monitors, uncalibrated tonometric waveforms must be calibrated against reference measurements made by a separate calibration device in order to obtain the blood pressure level associated with the waveforms. An oscillometric monitor is being developed for use as the calibration device for the MediWatch. At least two other approaches to address this need for a calibration device are being considered. The first involves developing a calibration measurement method that does not require complete occlusion of an artery at all times. Such a method will be more comfortable for the patient than the oscillometric method because the oscillometric method requires the artery under the cuff to be completely occluded when determining the systolic pressure. The second approach involves developing a pulse-sensing system that is capable of measuring the absolute level of the arterial pressure and is also noninvasive. Such a system will eliminate the need for a separate calibration device.

For an uncalibrated tonometric waveform whose signal level (in mV) is proportional to the arterial pressure being measured, a two-point linear calibration curve (relationship between mV and mmHg) based on systolic and diastolic pressures can be used for calibration, and the calibrated waveform (in mmHg) will correctly represent the arterial pressure waveform. If the signal level is not proportional to the arterial pressure being measured but a two-point linear calibration curve is used, the calibrated waveform (in mmHg) will not correctly represent the arterial pressure waveform. One way to resolve this problem is to use a non-linear calibration curve that is based on three points: systolic pressure, diastolic pressure and time-weighted MAP. The third point, i.e. the MAP, must necessarily be available from the calibration device, and it is usually available if an oscillometric monitor is used as the calibration device because the oscillometric method does measure MAP, albeit indirectly, and this MAP is not calculated from a fixed mathematical relationship between the three pressures [1–3]. The use of this three-point calibration method is being considered for the MediWatch and devices that use the same or a similar pulse-sensing system to that of the MediWatch.

Improved MediWatch prototype, the Internet and Bluetooth

Following the simulation-based and clinical evaluations, an improved prototype of the MediWatch, the MW-2, has been developed (Fig. 8). This prototype consists of a functional watch head, the same pulse-sensing module as that used in the MW-1 except that the plunger has a mushroom head, and a system of straps and pads. The mushroom shape of the plunger head increases both patient comfort and ease of detecting the radial pulse. The watch head and the pulse-sensing module are

Fig. 8



An improved prototype of the MediWatch (MW-2). This prototype uses a functional watch head, a comprehensive system of straps and pads, and a mushroom-head plunger. The connector on the prototype is used for connecting to a PC.

electrically connected. The watch head serves as the data acquisition unit for the sensor signal and provides regular timekeeping, stopwatch and alarm functions. It houses an interface board containing signal conditioning circuitry, a microcontroller, a 12 bit ADC, data acquisition firmware and data storage memory. As with the MW-1, the MW-2 runs on a 3 V coin cell battery.

The MW-2 provides two modes of operation. The first mode, called the continuous mode, provides for the

continuous beat-to-beat pulse waveform to be captured and viewed in real time on a PC and stored on the PC for further analysis. The device is connected to the PC by means of an RS-232 interface cable. ADC readings are sent to the PC by pressing a button on the watch head, and pressing the same button again will stop transmission of the readings. A PC software program written in Visual Basic and featuring a graphical user interface is used to accept and process the ADC readings. As with the MW-1, the software accepts reference blood pressures from the user and uses these pressures to calibrate the ADC readings and derive the beat-to-beat blood pressures, and the pulse rate is determined using a proprietary algorithm.

The second mode, called the programmable mode, provides for measurement data to be acquired at preprogrammed intervals and stored without needing to connect the device to a PC during the measurement period. It allows the following parameters to be preset on the watch head: measurement interval, from 1 to 60 min; sampling time for each measurement cycle, from 1 to 30 s; and sampling rate, from 1 to 30 data points per second. A measurement cycle refers to the series of events required by the device to complete a measurement. The stored data can be downloaded to a PC through an RS-232 serial interface by means of the same software program. The software is used to process the downloaded data, accept reference blood pressures provided by the user, calibrate the data and derive the systolic pressure, diastolic pressure, time-weighted MAP, pulse pressure and pulse rate for each measurement cycle. As an example, for a data acquisition period of 7 s and a sampling rate of 30 data points per second, the device is capable of storing 77 sets of data, each set comprising all the data points for the 7 s of the continuous waveform. This second mode of operation is intended to prepare the device for ambulatory monitoring.

The MW-2 prototype has been designed as an integral part of a Web-based system that involves access to measurement data over the Internet to facilitate speedy data interpretation and therapeutic intervention. The intent is for this system to work in such a way that once the measurement data have been downloaded from the device to the PC, the data are uploaded to the company's secured Web server. The Web server then creates an electronic medical file containing graphical profiles and statistical summaries of the patient's systolic pressure, diastolic pressure, time-weighted MAP and pulse rate; the levels of nocturnal dip for systolic and diastolic pressures are also included in the summaries. By password access, this medical file is accessible not only to the user, but also to the examining physician and to whomever the patient authorizes. Confidential messages can be posted on the patient's medical file. At this

writing, the development of this Web-based system is in progress.

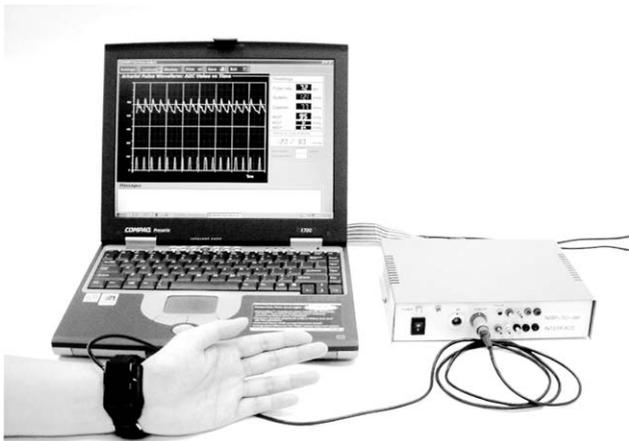
The MW-2 is being enhanced with Bluetooth® technology to enable wireless transmission of measurement data to the company's Web server through a Bluetooth-enabled mobile phone or similar device. Its memory capacity is being substantially expanded to store several days of measurement data, including the blood pressure readings, pulse rate reading and pulse waveform for each measurement cycle. The memory will also be used to store statistical summaries such as the average daytime and night-time systolic and diastolic pressures and the levels of nocturnal dip. As mentioned earlier, intelligent software algorithms based on waveform characteristics are being developed to correct for artefacts; preliminary studies have suggested that it is to some extent possible to correlate changes in pulse rate and changes in certain waveform characteristics to changes in blood pressure for subjects whose waveforms consistently exhibit a discernible dicrotic notch throughout the monitoring period. Software is being developed to generate and display graphical profiles and statistical summaries on a PC. In preparation for a more advanced version of the MediWatch, considerations are under way to enable a sampling rate higher than 30 data points per second, the display of selected pulse waveforms on the device itself, the downloading of measurement data to most personal digital assistants and processing of the data on the personal digital assistants.

Pulse-wave analyser

Along with the development of the MW-2 prototype, a pulse-wave analyser, model N8000, has been developed that also allows the radial pulse waveform to be captured and viewed in real time on a PC (Fig. 9). Incorporating the design features of the MediWatch, this analyser uses the same pulse-sensing module as that used for the MW-1 and MW-2, but the data acquisition electronics comes as a separate interface that connects between the pulse-sensing module and a PC. The analyser uses a software program written in Visual Basic.

With an adequately fast PC, the analyser is capable of sampling up to 100 data points per second. The desired sampling rate can be selected through the graphical user interface of the software program. As with the MW-1 and MW-2, reference blood pressures can be entered by the user through the graphical interface to calibrate the pulse waveform. For calibrated waveforms, the software provides a host of parameters including systolic pressure, diastolic pressure, time-weighted MAP, pulse rate, time-weighted mean blood pressure during systole, and time-weighted mean blood pressure during diastole. The software provides options for the user to store the raw and processed data on the PC. An oscilloscope can be

Fig. 9



An N8000 pulse-wave analyser shown with the pulse-sensing module mounted on the wrist, the electronics interface and a notebook PC. This particular analyser also functions as a prototype to demonstrate the concept of the N9000 M-Line system (see Fig. 10) because the hardware of the interface and the PC software have been enhanced with the capability to convert a calibrated noninvasive blood pressure (NIBP) signal to an equivalent IBP signal for display on an IBP monitor.

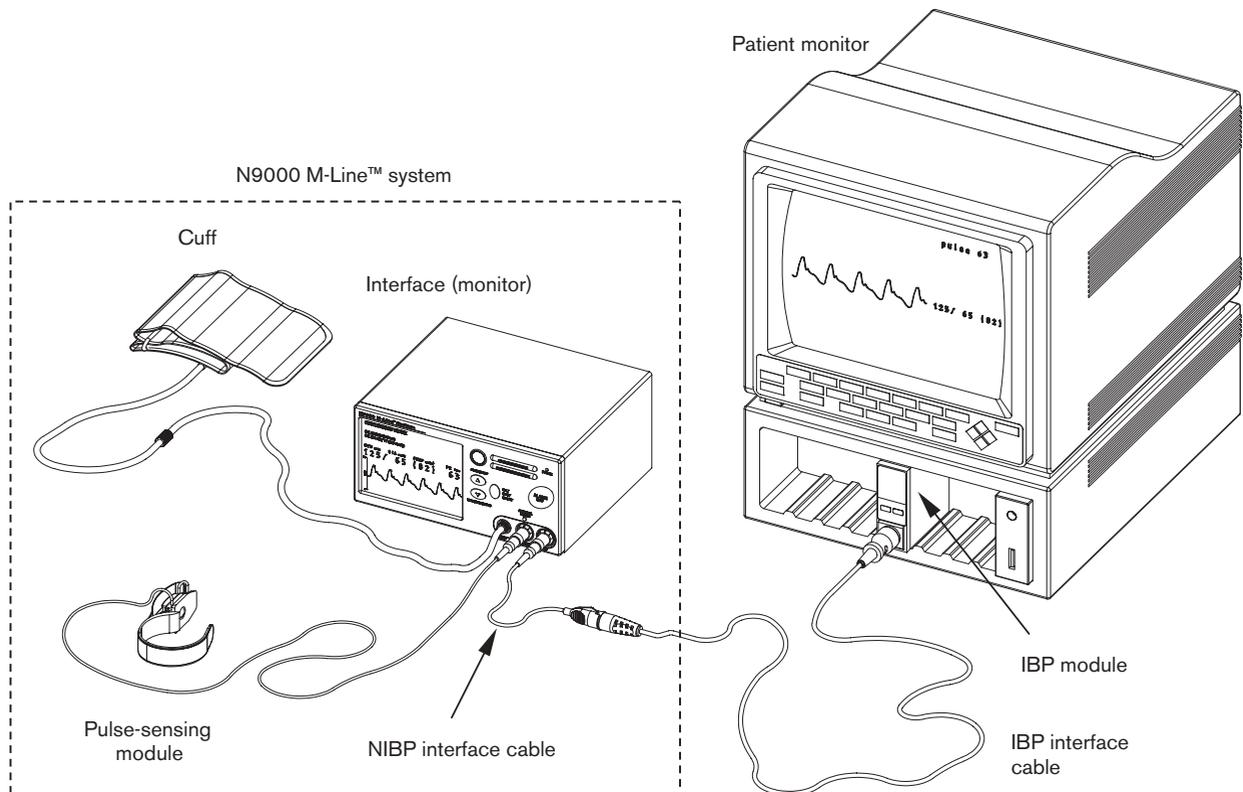
connected to the pulse-sensing module to display the analog waveform. Flexibility is being built into the software to enable users to incorporate their own software code to compute parameters or indices not provided by the software.

This pulse-wave analyser is intended for use by researchers who are involved in the analysis of arterial pulse waveforms.

Noninvasive arterial line for bedside monitoring of blood pressure

In addition to the foregoing developments, a continuous NIBP monitoring system based on arterial tonometry is being developed for use as an alternative to the arterial line in IBP monitoring. Called the N9000 M-Line™ system, this noninvasive system uses the same pulse-sensing module to capture the radial pulse waveform for display on an IBP monitor (Fig. 10). It connects to the IBP monitor using the same IBP interface cable (or transducer interface cable) that is used for the blood pressure transducer of the invasive arterial line. It effectively emulates the blood pressure transducer of the fluid-filled system of an invasive arterial line in such a

Fig. 10



Conceptual design of the N9000 M-Line system shown connected to an invasive blood pressure (IBP) module of a patient monitor. The blood pressure cuff is used for calibrating the radial pulse waveform captured through the pulse-sensing module, and the continuous blood pressure waveform is displayed on both the interface and the patient monitor.

way that the IBP monitor sees the interface as if it were a regular blood pressure transducer from the invasive arterial line. A proof-of-concept prototype is illustrated in Figure 9.

The N9000 M-Line system comprises the pulse-sensing module, an interface or monitor, a blood pressure cuff, and an NIBP interface cable. The proximal end of the NIBP interface cable connects to the M-Line interface and the distal end to the transducer end of the IBP interface cable for the IBP monitor. The connector at the distal end of the NIBP interface cable is the same as the connector of the pressure transducer that is to be used with the IBP interface cable. The interface calibrates the sensor signal using the built-in oscillometric monitor, determines blood pressure from the signal, detects the excitation voltage provided by the IBP monitor and converts the measured blood pressure to an equivalent IBP signal for display on the IBP monitor. It also functions as a display unit for the blood pressure waveform and the blood pressure and pulse rate readings. The interface is also called an NIBP-to-IBP interface since it converts an NIBP signal to an equivalent IBP signal.

The N9000 M-Line system works with all IBP monitors that accept pressure transducers with a sensitivity of $5 \mu\text{V}/\text{V}/\text{mmHg}$, the most widely used sensitivity, although provision for the use of other sensitivities is being considered. Zeroing of this noninvasive system with the IBP monitor can be easily performed in a way that is similar to that for an invasive arterial line. A wrist stabiliser will be provided to help minimise artefacts caused by wrist motion. At least two versions of the pulse-sensing module are being considered: a disposable version and a reusable or semi-disposable version.

The N9000 M-Line system is designed to provide two user-selectable modes of operation: the continuous mode and the oscillometric mode. In the continuous mode, the M-Line functions as a noninvasive arterial line providing blood pressure and pulse rate measurements as well as the continuous blood pressure waveform. Because the waveform is displayed on the interface as well as on the IBP monitor to which the interface is connected, the M-Line can be used as a stand-alone continuous NIBP monitor when the interface is not connected to an IBP monitor. In the oscillometric mode, the interface functions as an oscillometric blood pressure monitor that permits a single (on-demand) measurement (manual mode), measurements at preprogrammed intervals (auto mode) and consecutive measurements for a period of 5 min for critical situations (STAT mode).

In the continuous mode, the M-Line not only enables the continuous beat-to-beat blood pressure waveform to be obtained by noninvasive means, but also allows medical

staff to continue to use existing IBP monitors with which they are already familiar. The medical staff can continue to benefit from multiparameter monitoring offered by patient monitors that provide for the monitoring of multiple vital signs such as the ECG, oxygen saturation, respiration and cardiac output, in addition to IBP. They can also continue to benefit from the use of the central monitoring system to which the IBP or patient monitors are connected. In addition, the interface of the M-Line can be connected to a PC to enable researchers to tap the continuous blood pressure signal for further processing and for analysis.

The design of the interface for the N9000 M-Line system is the subject of a recent patent application. The design in this patent application provides for the use of arterial tonometry as well as other NIBP measurement methods to capture the arterial pulse waveform.

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