Contour analysis of the photoplethysmographic pulse measured at the finger

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Analysis of the contour of the peripheral pulse to assess arterial properties was first described in the nineteenth century. With the recognition of the importance of arterial stiffness there has been a resurgence of interest in pulse wave analysis, particularly the analysis of the radial pressure pulse acquired using a tonometer. An alternative technique utilizes a volume pulse. This may conveniently be acquired optically from a finger (digital volume pulse). Although less widely used, this technique deserves further consideration because of its simplicity and ease of use. As with the pressure pulse, the contour of the digital volume pulse is sensitive to changes in arterial tone induced by vasoactive drugs and is influenced by ageing and large artery stiffness. Measurements taken directly from the digital volume pulse or from its second derivative can be used to assess these properties. This review describes the background to digital volume pulse contour analysis, how the technique relates to contour analysis of the pressure pulse, and current and future applications. *J Hypertens* **24:1449–1456 © 2006 Lippincott Williams & Wilkins.**

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Background

Palpation of the pulse has been used since ancient times to assess physical health. In 1860 Etienne-Jules Marey produced a mechanical device that recorded the contour of the radial pulse, and, a few years later, Frederick Mahomed used this to investigate conditions that we now know to be secondary to hypertension [1]. This device was the forerunner of electronic tonometric systems that record the contour of the radial pressure pulse [2] and that are facilitating the current explosion of activity in pulse wave analysis. Another approach to derive information about cardiovascular properties from the pulse wave is based on analysis of an optically derived finger or digital volume pulse (DVP). Although less widely used, this approach deserves further consideration, not least because of its simplicity and ease of use. The technique has the potential to provide an estimate of large artery stiffness. Stiffening of large arteries is an inevitable consequence of ageing, and the ability to identify premature vascular stiffening may be of considerable value in the prevention of cardiovascular disease. This review describes the background to DVP contour analysis, how the technique relates to contour analysis of the pressure pulse, and current and future applications.

Measurement of the digital volume pulse

Alrick Hertzman [3,4] in 1937 produced a 'photoelectric plethysmograph', which he described as a device that 'takes advantage of the fact that the absorption of light by a transilluminated tissue varies with its blood contents' (Fig. 1). This is a consequence of the Lambert–Beer law, which relates light absorption to optical density. Hertzman's device illuminated the skin and measured back-scattered light with a photocell. Robert Goetz [5] described a related device measuring light transmitted through the finger. There is still uncertainty about what the photoplethysmographic pulse actually represents at different body sites, but the continuous component is attributed to light absorption by tissue and fixed blood volume, and the pulsatile component to change in blood volume during the cardiac cycle [6]. Light absorption, measured at wavelengths absorbed by reduced and oxygenated haemoglobin, is used to measure oxygen saturation in pulse oximetry [7]. The photoplethysmographic technique has also been used to provide information relating to low-frequency variations in the signal [8–14], the relative timing of the pulse [15–19] and, in conjunction with a finger pressure cuff, to provide continuous finger blood pressure [20,21].

Contour analysis of the digital volume pulse

The amplitude of the pulsatile component of the DVP is influenced by respiration, sympathetic nervous system activity and other factors that influence local perfusion [8,12–14]. The shape or contour of the pulse, however, remains approximately constant. Henry Lax and

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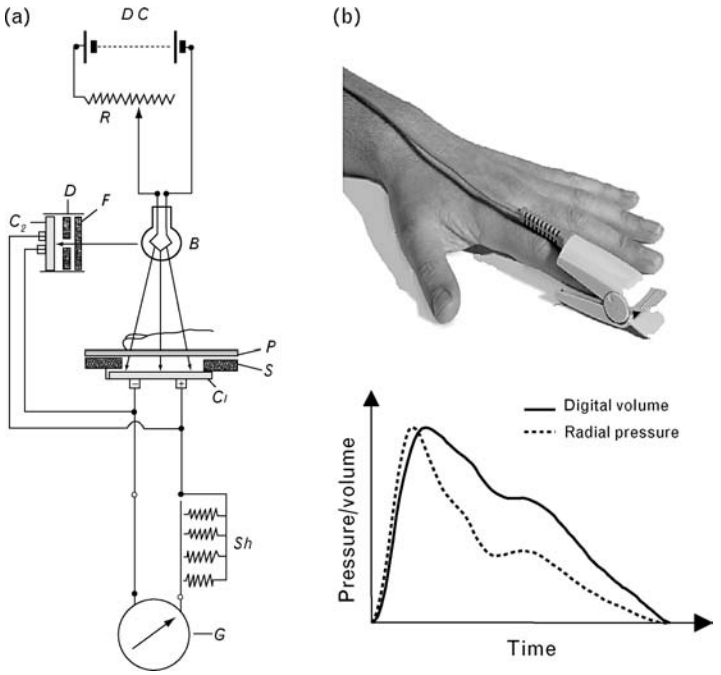
Fig. 1



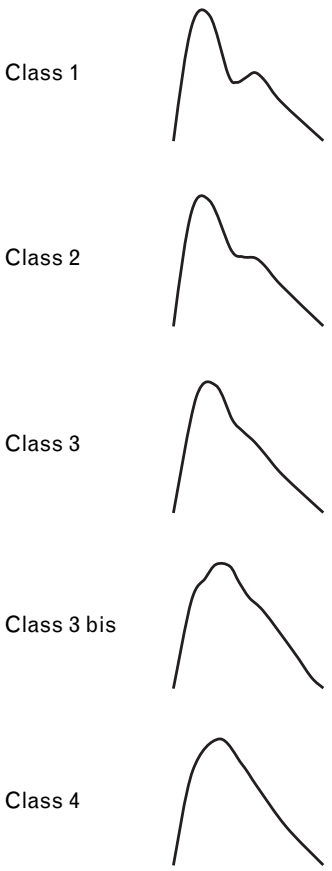
(a) An early photoplethysmograph device for measuring light transmission through the finger [4]. (b) A modern photoplethysmograph incorporating a light-emitting diode and sensor within a finger clip. A typical waveform (solid line) is shown, together with a radial pressure waveform (obtained using a tonometer) in the same individual.

colleagues [22] noted that when individuals had cold fingers, this 'reduces the over-all amplitude but does not affect the configuration of the pulse wave'. Hertzman and Spealman [3,4] noted that 'local cold diminished the pulse without significant effect on the form of the curve; heat has the opposite effect'. More recently, we infused vasodilator drugs into the brachial artery to produce pharmacologically active concentrations in the distal forearm but low – subthreshold for pharmacological effect – concentrations in the systemic circulation. This increased forearm blood flow and the amplitude of the DVP but had little effect on its contour, which remained similar to that recorded from a finger in the contralateral non-infused arm [23]. This observation suggests that the contour of the DVP is primarily influenced by characteristics of the systemic circulation, as is the contour of the radial pressure pulse.

Contour analysis of the DVP was initiated by John Dillon and Alrick Hertzman [24]. They described the shape of the DVP in terms of 'crest time, the duration of the ascent of the primary wave' and 'height of the incisura on the catacrotic limb'. They observed a tendency of the incisura to rise with generalized systemic vasoconstriction (caused by immersing the opposite hand in water at 4°C) and to decrease after inhalation of amyl nitrite [24]. They also reported 'an increase in the crest time, loss of the rebound wave and triangulation of the DVP' in individuals with hypertension [4,24] and arteriosclerosis [24]. Morikawa subsequently used a 'reflection photoelectric plethysmograph' to detect the effect of organic nitrates and alcohol on the pulse wave, producing a 'depression of the dicrotic notch' [25]. Morikawa *et al.* suggested that the change in 'dicrotism' was due to vasodilator effects of nitrates and alcohol [26]. A 'dicrotic index' has subsequently been used as a sensitive indicator of the vasomotor effects of drugs including nitrates [27–34], isoprenaline and nifedipine [33,35].

The early observations by Hertzman and Dillon were confirmed in a substudy of the Framingham cohort. Lax *et al.* [22] introduced a device they called a 'vasculograph'. This measured pressure in a sensitive rubber cuff inside an inelastic backing applied around the finger, producing a signal almost identical to that obtained by measuring light transmission. They observed the presence of a 'well-defined dicrotic wave' in healthy volunteers, whereas 98% of patients with overt arteriosclerosis had a 'diminution or disappearance of the dicrotic wave' [22]. Using this technique, Dawber *et al.* [36] obtained the DVP in 1778 individuals from the Framingham cohort recruited in 1965 and 1966. They proposed that the DVP be classified into one of the following classes [36] (see Fig. 2): class 1, a distinct notch is seen on the downward slope of the pulse wave; class 2, no notch develops but the line of descent becomes horizontal; class 3, no notch develops but there is a well-defined

Fig. 2

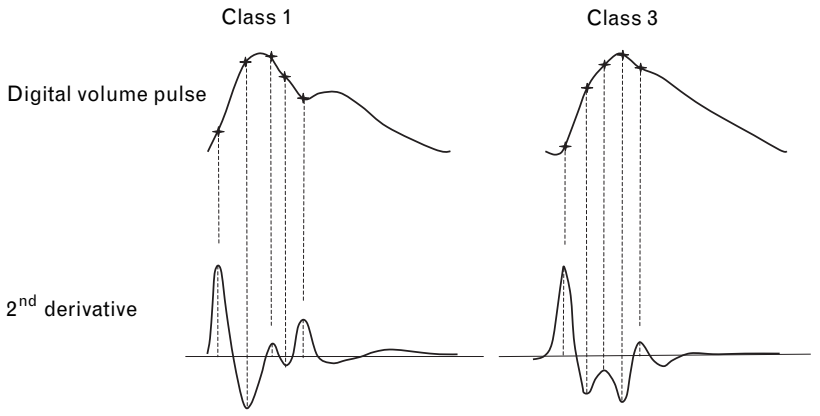


Classification of the digital volume pulse (DVP) waveform according to Dawber *et al.* [36]. With increasing age and/or presence of vascular disease, the waveform changes from class 1 to class 4. The change in contour can be interpreted in terms of earlier arrival of a pressure wave reflected from the peripheral circulation (see Fig. 4). With increasing stiffness of the conduit arteries, the reflected wave arrives early and its contribution moves from the diastolic to the systolic component of the DVP. bis, bisferiens.

change in the angle of the descent; or class 4, no notch develops or no change in angle of descent occurs. They found class 1 to be prevalent in younger individuals and class 4 present in older participants and in individuals with established coronary artery disease [36]. In men aged 65–74, the prevalence of myocardial infarction was approximately fourfold greater in participants with a class 4 waveform compared with a class 1 waveform.

A sophisticated approach to contour analysis of the DVP has been developed by investigators in Japan. Takazawa *et al.* [37], Takada *et al.* [38] and Imanaga *et al.* [39] have proposed using the second derivative of the DVP (d^2DVP/dt^2, sometimes referred to as the 'acceleration photoplethysmograph'). This facilitates the distinction of five sequential waves called a, b, c, d and e waves (Fig. 3). The relative heights of these waves (b/a, c/a, d/a and e/a ratios), particularly the d/a ratio, have been related to age [37,38,40], arterial blood pressure [38,40], large artery stiffness [41] and effects of vasoactive drugs [42]. The b/a ratio has been related to ageing and carotid distensibility [39]. Following analysis of the correlation of the b/a, c/a, d/a and e/a ratios with age, a more complex 'ageing index' was defined as (b–c–d–e)/a [37]. In a study to assess arterial distensibility in adolescents, the d/a ratio identified individuals at increased risk of developing atherosclerosis [43]. The second-derivative approach has recently been applied to the study of the peripheral pressure pulse [44]. Other mathematical approaches to analysis of the DVP include artificial neural networks [45–47], the extraction of periodic components using frequency analysis [48] or nonlinear dynamical analysis [49]. The physiological and clinical characteristics relating to the derived mathematical parameters, however, have not been clearly identified.

Fig. 3



The digital volume pulse (DVP) (upper panel) and its second derivative (d^2DVP/dt^2, lower panel) showing the definition of the a, b, c, d and e waves for waveforms of class 1 and class 3 according to Dawber *et al.* (see Fig. 2) [36].

Relation to the pressure pulse: physiological determinants of the digital volume pulse

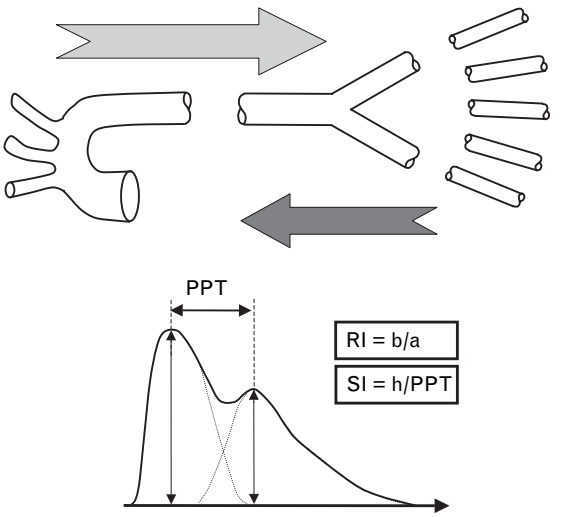
The early observations on the contour of the DVP and the more complex second-derivative approach have been pursued largely in terms of an empirical comparison with physiological and clinical characteristics. Surprisingly, the fundamental question of what determines the contour of the DVP has been neglected. We and other workers recently addressed the related question of how the DVP relates to the pressure pulse [50,51]. If the mechanical properties of vessels in the finger remain constant over the cardiac cycle, a change in vessel diameter and hence a change in volume can be expected to bear a complex but consistent relationship to the change in arterial pressure. We demonstrated that the relationship between the DVP and the radial pressure pulse (or the digital pressure pulse, which is almost identical to the radial pulse) can be represented by a single mathematical transfer function [50]. This implies that the information in the DVP is similar to that contained in the radial pressure pulse and that the physiological determinants of the DVP are similar to those of the radial pressure pulse.

Haemodynamic mechanisms determining the contour of the radial and aortic pressure waveform have been widely studied. It is generally accepted that the aortic pulse is influenced by the cushioning or Windkessel effects of the aorta and large conduit artery pressure and by wave reflection in the systemic circulation [52]. When pressure increases in the aorta during systole, the increase in pressure is not transmitted instantaneously to the peripheral circulation but travels as a forward-going pressure wave travelling at a speed known as the 'pulse wave velocity' (PWV). The PWV is closely related to the distensibility of the aorta and large arteries (and hence to the magnitude of the Windkessel effect) [53,54]. At various points along the arterial tree a proportion of this forward travelling pressure wave is reflected backwards (travelling towards the heart at approximately the same PWV as the forward wave). Although reflection occurs from many points in the arterial tree, the arterial system behaves, to a first approximation, as if a single wave is reflected back from the lower body [52] (see Fig. 4). The pressure wave at the aortic root is determined by the summation of the forward (direct) and backward (reflected) waves, and depends on the size and time of arrival of the reflected wave. The size of the reflected wave is determined mainly by arterial tone of small muscular arteries distal to conduit arteries but proximal to the resistance arteries that determine blood pressure. The time of arrival of the reflected wave relative to the direct wave is determined by PWV and the length from the aortic root to the point of reflection.

The radial pulse is further influenced by transmission along the upper limb. Changes in the contour of the pulse due to transmission along the upper limb are, however, predictable and relatively constant from individual to individual [52,55–57]. Indeed, the relatively small inter-individual variation in effects of transmission is illustrated by the much used but controversial transfer function used for estimating aortic pressure from radial pressure [58–66]. Even though the absolute accuracy of this approach may be debated [58–61,63], it is clear that determinants of the radial pulse include those of the aortic pulse; namely, PWV in large arteries and wave reflection in the systemic circulation. In addition, the early part of the waveform is influenced by the characteristics of ventricular ejection [52]. As a single transfer function relates the DVP to the pressure wave [50], we have proposed that similar properties determine the contour of the DVP.

In young individuals, the DVP exhibits a clearly defined first and second peak (Fig. 2, class 1). The first peak probably corresponds to a direct forward-travelling pressure wave from the heart to the finger (where it produces a change in arterial diameter and hence volume), and the second to the backward-travelling 'reflected' pressure wave. The amplitude of the reflected wave depends on the amount of reflection and hence on muscular tone

Fig. 4



The systolic component of the digital volume pulse (DVP) waveform arises mainly from a forward-going pressure wave transmitted along a direct path from left ventricle to the finger. The diastolic component arises mainly from pressure waves transmitted along the aorta to small arteries in the lower body, where they are then reflected back along the aorta as a reflected wave that then travels to the finger. The upper limb provides a common conduit for both the directly transmitted pressure wave and the reflected wave. The reflection index (RI) provides a measure of the amount of reflection. The time delay (PPT) between the systolic and diastolic peaks (or, in the absence of a second peak, the point of inflection) is related to the transit time of pressure waves from the root of the subclavian artery to the apparent site of reflection and back to the subclavian artery. This path length can be assumed proportional to height (h) and an index of large artery stiffness (SI) can be formulated as: SI = h / PPT.

in small arteries, the sites of impedance mismatch from which wave reflections arise [23,25,26]. The timing of the reflected wave relative to the first peak is determined by the PWV in the aorta and conduit arteries [23,67]. A 'reflection index' can be defined as the ratio of the reflected wave to the first peak (Fig. 4), an index closely related to the 'dicrotic index' described by Morikawa [25]. The time between the first peak and second peak ('peak to peak time') has been proposed as a surrogate measure of pulse wave velocity and arterial stiffness (see Fig. 4) [23,67]. The variation of path length with height can be addressed by means of a 'stiffness index' defined as height (metres) divided by peak to peak time. The stiffness index thus has units of metres per second, as does the PWV, and is numerically similar to, but not identical to, the PWV measured over the carotid to femoral path [67].

In older individuals, the second peak of the DVP is attenuated and replaced by a point of inflection in the downslope of the waveform. This inflection point can still be used to determine the reflection index and the stiffness index. In individuals with multiple risk factors for and/or established cardiovascular disease, however – in whom the large arteries are already very stiff – the DVP can exhibit a class 4 waveform (Fig. 2) [36]. In these cases, the reflected wave arrives so early during systole that it becomes difficult to distinguish between the direct and reflected waves.

Irrespective of the method of analysis of the photoplethysmograph signal, it is important to employ the correct signalling conditioning since inappropriate filtering can distort the signal. This is particularly important when using second-derivative analysis [68]. In addition, measurements need to be made under standardized conditions: usually after the participant has been resting supine for at least 15 min and in a quiet temperature-controlled environment [23].

Applications

Vasomotor responsiveness and endothelial function

The reflection index or a closely related index has been used by several authors to quantify effects of vasoactive drugs including organic [25,27–34] and inorganic nitrates [69,70] and nifedipine [33,35]. Second-derivative indices are also sensitive to effects of vasoactive drugs [37,71]. Changes in the reflection index in response to vasoactive drugs closely follow changes in the radial or aortic augmentation index obtained by contour analysis of the pressure pulse. The reflection index is sensitive to vasodilator effects of nitrates (as is the augmentation index) possibly because of the relatively selective effects of these drugs on the small to medium-sized arteries that determine pulse wave reflection [72,73]. Effects of nitrates on the reflection index can thus be detected before other changes in systemic haemodynamics, such as changes in heart rate or blood pressure. The sensitivity of reflection index to exogenously administered nitric oxide donors suggests that, given a suitable stimulus to the release of nitric oxide from the endothelium of the systemic vasculature, the reflection index could be used to assess endothelial function. One suitable stimulus is the β-adrenergic agonist salbutamol, which activates β_2 receptors on endothelial cells and produces vasodilation partially through the release of nitric oxide by the endothelium [74–77]. Salbutamol may be safely administered either by inhalation or intravenously at doses that have minimal effects on the heart rate and blood pressure but that produce similar changes in the reflection index as do low doses of nitrates. A number of investigators have used this method (or the response of the closely related pressure pulse to salbutamol) to study endothelial function (Table 1). Sackner *et al.* [78] recently used the DVP and an index directly related to the reflection index with whole body periodic acceleration to increase pulsatile shear stress and measure endothelial function.

Arterial ageing and stiffness

The influence of ageing on the contour of the radial pulse is well recognized [52,79,80], and parallel changes in DVP are also well described [18,24,67,81,82]. Age-related changes in pulse contour are mainly due to an increase in large artery stiffness. Increased stiffness augments the PWV, decreasing the time taken by the reflected wave to arrive at the finger. In healthy individuals, the stiffness index as defined earlier is closely correlated with the carotid–femoral PWV [67]. Second-derivative indices

Table 1 Endothelial function measured using the response of the digital volume pulse (DVP) or the pressure pulse wave to a β_2-adrenergic agonist

Investigators	Condition	DVP/pressure pulse	Comparator method
Chowienczyk *et al.* [23]	Type 2 diabetes	DVP	–
Gopaul *et al.* [89]	Insulin resistance	DVP	–
Laucevicius *et al.* [90]	Coronary artery disease	DVP	–
Hayward *et al.* [91]	Coronary artery disease	Pressure (radial)	–
Wilkinson *et al.* [92]	Hypercholesterolaemia	Pressure (aortic)[a]	ACh
Suh *et al.* [93]	Obesity	Pressure (radial)	–
Lind *et al.* [94]	Elderly individuals	Pressure (radial)	MCh, FMD[b]
Kalra *et al.* [95]	Ethnic variation	DVP	–

ACh, acetylcholine infused into the brachial artery. [a]Aortic pressure estimated from the radial pressure using a transfer function. [b]Pulse wave response to the β_2-adrenergic agonist correlated with the response to metacholine infused into the brachial artery (MCh) but not to flow-mediated dilation of the brachial artery (FMD).

are also closely related to age [37–40]. Both second-derivative indices and the stiffness index may provide a biological measure of arterial age, which may differ usefully from chronological age. Chronological age is a most powerful determinant of cardiovascular risk. Additional information on arterial age may identify individuals with accelerated arterial ageing due to lifestyle and/or to genetic predisposition. The PWV has been established as an important biophysical marker of arterial ageing, which is independently highly predictive of cardiovascular outcome in the groups so far studied [83–87]. It is probable that similar information can be obtained from the DVP either using existing indices or a novel approach to contour analysis. The stiffness index was recently used to study the association of arterial properties with birth weight in young adults (16–26 years old) and found to be independently correlated with birth weight, which accounted for 17% of the variance in stiffness index [88].

Future development of digital volume pulse contour analysis

It is evident from the work to date that DVP contour analysis provides much information relating to arterial structure and function. Because the DVP contour is determined by a complex interaction of ventriculovascular properties, however, it is equally clear that the interpretation of pulse contour indices in terms of the biomechanical properties of arteries is complex. The reflection index and the stiffness index represent an attempt to relate pulse contour indices to arterial tone and stiffness, respectively. These indices, however, are likely to be influenced, to a greater or lesser extent in different participant groups, by other properties. One challenge for the future is to determine under what circumstances these indices provide reliable indices of arterial tone and stiffness, and whether their reliability can be improved in older individuals or in individuals with a waveform that exhibits unusual characteristics.

Another challenge is to define the relationship between indices derived from the DVP and indices derived from the pressure pulse. As already described, the two waveforms are influenced by similar physiological factors. Because current pressure wave and DVP indices are determined from different features of the pulse contour, however, they may not behave identically, and they are not interchangeable. The augmentation index, derived from the pressure pulse, is determined in systole and depends on ventricular ejection characteristics, the PWV and arterial tone.

Perhaps the most exciting application of DVP contour analysis is the possibility of providing a rapid biophysical measure of vascular age. Because of its simplicity, it can be employed in large-scale epidemiological studies and be used to assess effects of interventions on arterial stiffness. Such applications will, however, require prospective evaluation because it is possible that the complex interactions of cardiac and vascular properties that determine the DVP contour will confound this simple concept.

Conclusion

Optical determination of the DVP is a particularly simple method for performing pulse contour analysis. Like the pressure pulse, the DVP is influenced by large artery stiffness and by pressure wave reflection in the systemic vasculature. Contour analysis of the DVP provides a rapid means of assessing vascular tone and arterial stiffness. Applications include the assessment of endothelial function, arterial stiffness and characterization of arterial ageing.

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