Holographic Pulse Wave Technology

Technical White Paper

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Introduction

With the aging population and changes in lifestyle in China, the incidence of cardiovascular diseases continues to rise. Currently, cardiovascular diseases have become the leading cause of death among urban and rural residents, accounting for 43.81% in urban areas and 46.66% in rural areas [1]. Among various cardiovascular diseases, atherosclerosis is the main cause of disability and mortality [2, 3].

The process of arteriosclerosis is shown in Figure 1. In the early stage of arteriosclerosis, the elastic fibers and collagen fibers in the arterial vessel wall undergo fatigue and damage under long-term blood pressure impact, resulting in a gradual loss of elasticity [4], leading to functional changes. At this stage, the vascular wall does not show structural abnormalities, but is usually accompanied by increased blood pressure. With the exacerbation of blood pressure and abnormal arterial wall elasticity, structural changes occur in the vascular wall, and the intima at certain locations may be damaged, leading to the accumulation of substances such as blood cells and lipids, forming plaques. Thickening of the plaques can cause arterial stenosis and block blood flow. If the plaques rupture, it may lead to serious problems such as stroke.

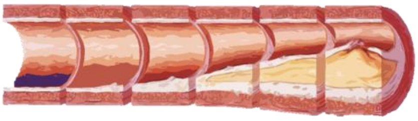


Figure 1: Illustration of the process of arteriosclerosis

The clinical diagnosis of arteriosclerosis often focuses on the stage after significant changes occur in the vascular wall structure, typically when the intima-media thickness (IMT) of the carotid artery exceeds 1 mm, while the early changes in elasticity are not given enough attention. Studies have found that arteriosclerosis can lead to a decrease in vascular compliance, which, on the one hand, increases blood pressure in end organs during systole, causing penetrating injuries to the organs [5, 6], and on the other hand, decreases the ability to maintain blood supply during diastole, leading to long-term ischemia during the diastolic phase. At the same time, it is believed that functional changes in the arterial wall occur earlier than structural changes, and early intervention can help slow down or even reverse the progression of the disease, fundamentally reducing the mortality rate of cardiovascular diseases. Therefore, early assessment of arteriosclerosis is of great significance for the prevention and control of cardiovascular diseases. Some diseases and surgeries can also have a significant impact on the cardiovascular system. For example, diabetes can easily induce atherosclerotic lesions, especially in the lower extremities [7, 8], while certain genetic diseases can cause arterial damage [9], and arteriovenous fistula surgery can lead to calcification problems in the related blood vessels [10, 11]. Early detection of arterial wall elasticity can promptly identify abnormalities in the cardiovascular system and guide doctors to intervene, thus reducing the likelihood of cardiovascular diseases caused by these factors.

Pulse wave velocity (PWV) serves as the gold standard for measuring arterial elasticity [12] and can be independently used to predict cardiovascular events [13]. Studies have found that changes in PWV occur even earlier than traditional indicators such as IMT in patients with cardiovascular diseases. Thanks to these advantages, the research interest in PWV has been increasing year by year, and PWV has become one of the important indicators in cardiovascular research. However, traditional PWV measurement solutions are complex to operate, which limits their clinical application [14]. Mindray's Resona A20 has introduced the Holo-PWV function to address this situation. The expected uses of this product include:

- Early warning of cardiovascular risks, improving existing prevention and treatment system for cardiovascular diseases.
- Monitoring of arterial status, assessing the impact of various factors on the cardiovascular system.

With the outstanding hardware performance and advanced post-processing algorithms of the platform, the Holo-PWV function achieves fully automated non-invasive measurement of PWV based on raw radio frequency (RF) signals and provides multi-index multi-dimensional analysis. Compared to other solutions, it has the following advantages:

- Accuracy: It achieves accurate measurement of pulse wave propagation time-distance information, providing accurate and reliable local arterial PWV results.
- Multi-dimensionality: The results cover various aspects of information such as arterial wall elasticity and structure, assisting doctors in comprehensive assessment of vascular health.
- Simplicity: The data acquisition and analysis process can be completed with a single button press, without the need for additional operations.

Technical Principles

Pulse wave is a mechanical wave generated by the pumping action of the heart, which vibrates along the short axis of the artery and propagates from the proximal end to the distal end along the long axis of the artery. The waveform is shown in Figure 2, which exhibits significant differences among individuals and different locations. The vibration amplitude is usually around 1 mm, and the propagation velocity is generally between 3 and 20 m/s in the carotid artery. During one cardiac cycle, multiple pulse waves are generated, with the two main ones being: 1) at the beginning of systole when the aortic valve opens, marked as the Begin of Ejection (BE); 2) at the end of systole when the left ventricular blood pressure decreases and the aortic valve closes, collision occurs between the blood flow and the aortic valve, producing a pulse wave, marked as the End of Ejection (EE). PWV-BE approximately represents the elasticity of the arterial wall during the systolic phase, while PWV-EE approximately represents the elasticity of the arterial wall during the transition from diastole to systole. Generally, PWV-EE is slightly higher than PWV-BE, and it also has slightly higher sensitivity to arteriosclerosis.

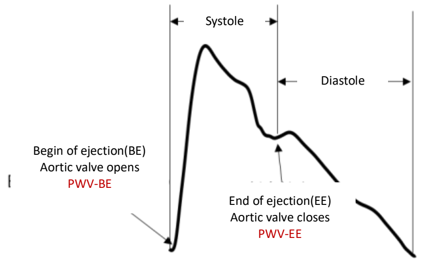


Figure 2: Illustration of the waveform of carotid artery pulse wave

Assuming that the blood vessels are uniform, purely elastic tubular structures filled with fluid, according to the Moens-Korteweg equation, PWV is related to arterial elasticity (E) as follows:

$$PWV = \sqrt{E \cdot \frac{h}{\rho \cdot D}}$$

where h is the vessel wall thickness, D is the vessel wall diameter, and ρ is the vessel wall density. According to this formula, arterial elasticity is positively correlated with PWV. When the arteries become hardened, PWV increases. In addition, there is a correlation between PWV and vessel wall thickness and diameter, but this is generally ignored in clinical research.

The traditional measurement methods usually use specialized measurement devices, and doctors need to input patient information such as height and weight. Several probes are placed on the patient's body surface (usually from neck to groin or arm to ankle). The instruments automatically record the time it takes for the pulse wave to reach various locations based on pressure, photoacoustic, and other signals, and estimate the propagation distance of the pulse wave based on the patient's height to obtain the corresponding PWV. This method was introduced earlier and has a higher degree of clinical acceptance. It mainly reflects the overall degree of arteriosclerosis in the body and lacks the ability to measure locally. It only identifies the pulse wave at the BE moment. The measurement process is complex [14], and the estimation based on height introduces significant errors.

Ultrasound, as the preferred imaging modality for cardiovascular disease screening, has also introduced a PWV measurement method combining blood pressure and conventional ultrasound grayscale images. During the measurement, doctors need to input the patient's blood pressure information and perform continuous scanning in the long-axis view of the carotid artery to obtain the results. Due to the limitation of the probe width, the propagation time of the pulse wave within the probe's acoustic window is only in the millisecond range, and the conventional ultrasound frame rate is insufficient to image its propagation process. Therefore, the PWV is estimated by calculating the change in vessel diameter during the cardiac cycle and combining it with the blood pressure, according to the following formula:

$$v = 0.36 * \sqrt{\frac{dP}{dD^2/D^2}}$$

where dP is the change in blood pressure, D is the vessel diameter, and dD is the change in vessel diameter during one cardiac cycle. This type of measurement solution cannot directly measure PWV, and the results differ significantly from the true values. In practice, doctors are required to provide the patient's current blood pressure information, which not only makes the operation process cumbersome but also introduces further errors.

Thanks to Mindray's wide-beam tracking imaging technology (as shown in Figure 3), the Holo-PWV function captures the details of pulse wave propagation within a local region by performing full-field imaging at an extremely high frame rate. The Holo-PWV function of Resona A20 can achieve nearly 20,000 frames per second of full-field imaging with a width of approximately 3-5 cm in each emission.

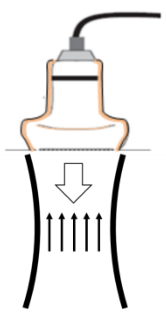


Figure 3: Illustration of wide-beam tracking imaging technology

Since the pulse wave is a signal spontaneously generated by the human body, the exact time it reaches the probe position cannot be predicted. Therefore, the function requires continuous scanning of the carotid artery, and the RF signals of the arterial wall at various horizontal positions are analyzed to extract the pulse wave information. By combining the time information of the pulse wave reaching various horizontal positions, the average propagation speed of the pulse wave within the probe's acoustic window is calculated, as shown in Figure 4. Compared to previous generations of technology, Mindray's Holo-PWV achieves accurate measurement of pulse wave propagation time-space information, thereby obtaining accurate and reliable PWV results.

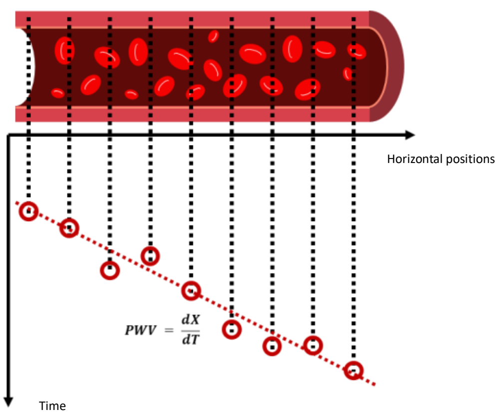


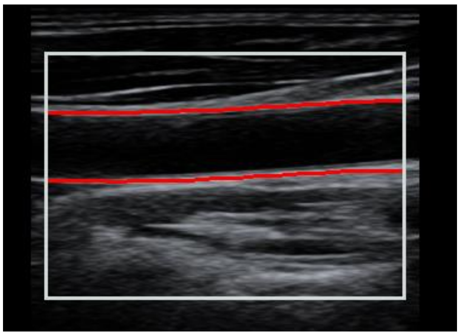
Figure 4: Principle schematic of Holo-PWV based on wide-beam tracking imaging technology: red circles represent time-position information of pulse wave propagation

Operation Process

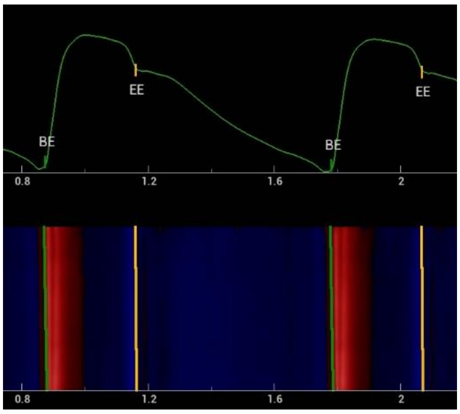
The acquisition conditions for the Holo-PWV function are similar to routine ultrasound examination of the carotid artery. During the acquisition, the patient should be in a supine position at rest, and the doctor should hold the probe to scan the long-axis view of the carotid artery. The specific position is 1-2 cm below the bifurcation, in the straight segment of the carotid artery, ensuring clear visualization of the intima-media. The scanning position should avoid vascular curvature, blurred vessel walls, veins, or other factors that may interfere with pulse wave conduction. After the start of the acquisition, continuous data acquisition is performed for 1-4 seconds according to the user's setting. During the acquisition process, the probe should be held steadily, and the patient should avoid swallowing or other movements. After the acquisition is completed, the data enters the post-processing stage. The progress is displayed in the lower right corner of the user interface. At this time, the user and the patient can relax, and the measurement results will be automatically returned after the processing is completed. The data on one side of the carotid artery needs to be continuously acquired at the same position for 3-5 times, and the median value is taken as the final result.

In the current medical environment, doctors often face a large number of patients who need routine carotid artery ultrasound examinations. Therefore, complex operation procedures and numerous measurement items can seriously interfere with the daily work of doctors. In response to this situation, the Holo-PWV function has optimized the operation process and measurement items. The entire process only requires a single button press, and the scanning, post-processing, and result indicators are all automatically completed by the system, greatly simplifying the work of doctors and minimizing interference with daily work, while ensuring that doctors can quickly adapt to it with simple training. According to the actual situation, the time required for a single measurement and post-processing is only about 8 seconds, and the complete measurement process of one side of the carotid artery takes about one minute. With the improvement of user proficiency, the time required can be further reduced.

The Holo-PWV function includes multiple information windows, as shown in Figure 5:



(a)



(b)

Figure 5: Schematic representation of Holo-PWV function windows: long-axis section of the vessel and vessel wall

identification results (a) and vessel diameter curve and vessel wall motion spatiotemporal map (b)

The long-axis section of the vessel and vessel wall identification result display the initial section image and the corresponding wall identification result (highlighted in red) at the start of the acquisition. The vessel diameter curve represents the change in vessel diameter during the scanning time, and the vessel wall motion spatiotemporal map represents the change in diameter in the spatial-temporal two-dimensional plane. The X-axis corresponds to time, and the Y-axis corresponds to space. In Figure 5(b), the X-axis at -0s corresponds to the start of the acquisition, and the Y-axis at -0 mm corresponds to the leftmost part of the region of interest (ROI). Red indicates a positive change in diameter, meaning an increase in vessel diameter, while blue indicates a negative change in diameter, meaning a decrease in vessel diameter. The pulse waves detected during the scanning period are marked on the vessel diameter curve and the vessel wall motion spatiotemporal map, as shown in Figure 5(b). The pulse wave at the beginning of ejection is labeled as BE and marked in green, while the pulse wave at the end of ejection is labeled as EE and marked in yellow. Ideally, the vessel identification result should match the vessel wall in the section, the vessel diameter curve and the spatiotemporal map should be smooth and stable without abnormal fluctuations or noise, and PWV-BE and PWV-EE should appear alternately at the moments corresponding to each cardiac cycle.

The result indicators of the Holo-PWV within the acquisition time are shown in Figure 6, from top to bottom: PWV-BE, PWV-EE, maximum diameter (Max), minimum diameter (Min), diameter change value (Delta), and diameter change ratio (Delta/Diam). In addition to describing the arterial wall elasticity with pulse wave indicators, Holo-PWV provides structural indicators of the vessel to assist doctors in evaluating arterial status from multiple perspectives. Ideally, the fluctuation range of PWV results should be less than 20%.

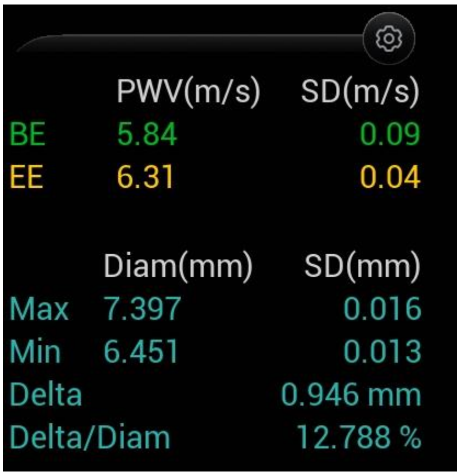


Figure 6: Illustrative diagram of Holo-PWV results in a healthy individual

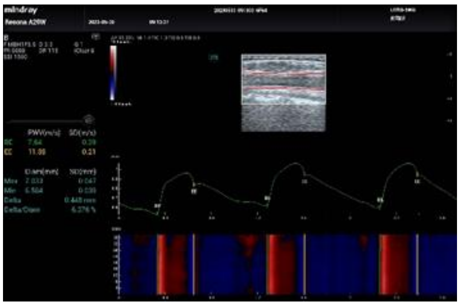
Case Studies

In healthy individuals, the vessels are elastic and have strong compliance, typically showing lower PWV-BE and PWV-EE values. The vessel diameter changes significantly under the periodic action of blood pressure, indicating good compliance, as shown in Figure 6. When patients have symptoms of arteriosclerosis, the arterial elasticity is lost, and compliance decreases, resulting in an increase in PWV-BE or PWV-EE and a decrease in diameter change value and ratio. Table 1 summarizes the possible changes in indicators that may occur in patients with arteriosclerosis compared to healthy individuals:

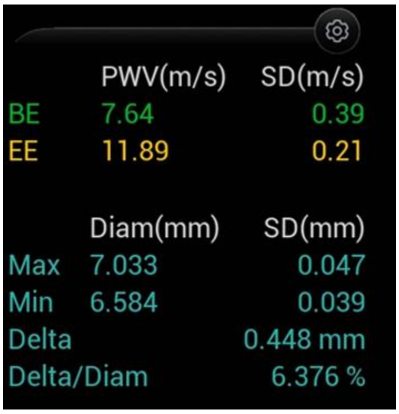
Table 1: Possible changes in indicators in patients with cardiovascular functional abnormalities compared to healthy individuals

	Indicator	**Meaning**	**Change**
Arterial Elasticity PWW	BE	Pulse wave velocity at the beginning of ejection	↑
	EE	Pulse wave velocity at the end of ejection	↑
Arterial Structure DIAM	Max	Maximum vessel diameter	~
	Min	Minimum vessel diameter	~
	Delta	Diameter change value	↓
	Delta/Diam	Diameter change value divided by maximum vessel diameter	↓

The actual measurement results of a hyperlipidemia patient (Patient A) are shown in Figure 7. Compared to healthy individuals, both PWV-BE and PWV-EE are significantly increased, indicating loss of arterial elasticity. The value of Delta/Diam is significantly decreased, indicating declined arterial compliance.



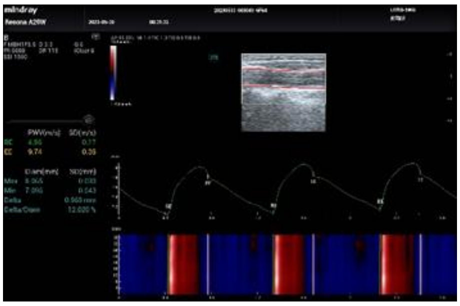
(a)



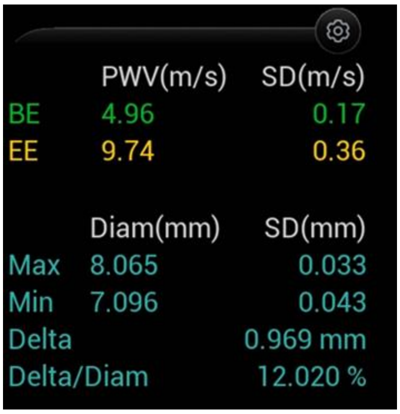
(b)

Figure 7: Holo-PWV results (a) and selected indicators (b) of Patient A with hyperlipidemia

Not all indicators will show differences in patients, and sometimes only one indicator will increase. Another example is the measurement results of another hyperlipidemia patient (Patient B) shown in Figure 8. The results indicate that PWV-BE does not show a significant change, but PWV-EE increases significantly. At the same time, there is no significant decrease in the value of Delta/Diam. This indicates that the collagen fibers in the arteries may be abnormal, leading to a certain degree of hardening under high load, but the elastic fibers still work normally, resulting in good elasticity under low load. The overall compliance of the arteries has not shown a significant change.



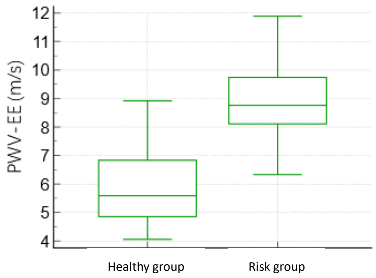
(a)



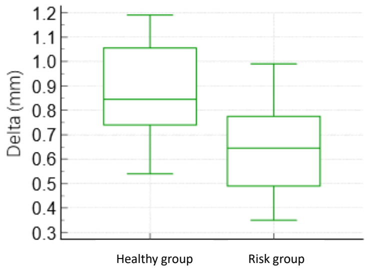
(b)

Figure 8: Holo-PWV results (a) and selected indicators (b) of Patient B with hyperlipidemia

The Holo-PWV function was used in a renowned hospital in Shenzhen to collect data from one side of the carotid artery in 29 subjects, including 15 healthy individuals and 14 risk individuals with at least one cardiovascular disease (hyperlipidemia, hypertension, hyperglycemia, or vessel plaques). The measurement results are shown in Figure 9, and all the listed indicators show significant differences ($p<0.01$). The experimental results demonstrate that the Holo-PWV function effectively distinguishes the differences in arterial status between healthy individuals and those at risk of cardiovascular diseases.



(a)



(b)

Figure 9: Comparison of measurement results between the healthy group and the risk group: PWV-EE (a) and Delta (b)

Various factors can cause arteriosclerosis, including but not limited to age, gender, blood lipids, blood sugar, blood pressure, and smoking. According to existing research, age is one of the main factors affecting arterial elasticity, and there is a positive correlation between age and arterial elasticity. The mechanism may be that long-term periodic impacts under blood pressure lead to fatigue and damage to the elastic structure of the vessel wall, resulting in decreased vascular compliance. After excluding the interference of other factors, PWV in the elderly population is still significantly higher than in middle-aged and young populations. At this stage, due to limitations in the number of subjects and the scope of coverage, there is still no clear conclusion on the threshold of carotid artery PWV based on ultrasound. However, based on experience, users can pay attention to patients with PWV-BE > 7 m/s or PWV-EE > 8 m/s, as they may have a higher risk of cardiovascular diseases.

Conclusion

Mindray's Holo-PWV function, as an analysis tool for arterial elasticity, provides a new tool for clinical doctors to early warn of cardiovascular risks and evaluate arterial health status. It not only achieves accurate measurement of local arterial PWV for the first time but also provides multiple index results to assist doctors in evaluating arterial health status from multiple dimensions. Moreover, a simplified operation process is provided, making it easy for doctors to use in their daily work.

In preliminary clinical trials, the Holo-PWV function can effectively identify the impact of common cardiovascular risk factors such as hypertension, hyperlipidemia, and hyperglycemia on arterial elasticity, demonstrating the clinical value of the function. The Holo-PWV function will play an important role in the prevention, treatment, and assessment of the impact of diseases on arteries in cardiovascular disease research.

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