Photoacoustic Imaging of Valves in Superficial Veins

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Background and Objectives: In intravenous access to veins there is a risk of puncturing venous valves or blocking of the catheter by the valves. Therefore, we have investigated whether and how photoacoustic imaging (PAI), which visualizes the lumen of blood vessels, can be used to detect these valves.
Study Design/Materials and Methods: Venous valves in superficial veins on the dorsal side of the hand of human volunteers were located by palpation and visual inspection. Next, this location was imaged using PAI.
Results: In 16 of 21 human volunteers venous valves that were found by palpation could be observed by PAI as local discontinuities in the imaged vessel. From these images, four characteristic features by which venous valves can be recognized in photoacoustic images were identified.
Conclusions: PAI has the potential to be applied in the detection of venous valves. Lasers Surg. Med. 38:740–744, 2006. © 2006 Wiley-Liss, Inc.

Key words: blood vessel; optoacoustic; ultrasound; vascular

INTRODUCTION

Intravenous access is among the most basic and frequently applied procedures in the medical profession. Puncturing these vessels can be hampered by the presence of valves, which are present to prevent backflow of blood, by blocking the lumen of the catheter when it abuts a valve. Furthermore, these valves can be punctured when inserting a needle in the vessel, causing these valves to become incompetent [1].

In this proof of principle study we applied photoacoustic imaging (PAI) to detect venous valves. PAI is a hybrid-imaging tool that combines high optical contrast with high ultrasound resolution. PAI is based on the generation of acoustic waves by pulsed light being absorbed by tissue chromophores such as hemoglobin in blood. Whereas in classical ultrasound imaging a blood vessel can be identified by reflection and scattering of ultrasound, in PAI the blood vessel is visualized by absorption of light by blood inside the vessel. The induced temperature rise generates a thermoelastic pressure transient, which amplitude is dependent on the amount of absorbed light, being determined by the local energy fluence [J/m^2] and the optical absorption coefficient of the target. From the time of flight of this pressure wave to reach the tissue surface (detector position), the position of the photoacoustic source can be calculated using knowledge about the speed of sound in tissue. Measurement of this pressure transient in PAI is most commonly performed with piezoelectric probes which are in acoustic contact with the tissue. However, also some optical methods have been developed [2,3] which allow for fully non-contact PAI.

Next to this qualitative approach, the amplitude and the shape of the photoacoustic signal can also be analyzed quantitatively. First, in the case that the condition of stress confinement is fulfilled, the initial pressure rise will be proportional to the absorbed energy. This condition requires that there is insignificant relaxation of pressure in the region of light absorption during the laser pulse, which means that the pulse duration t_p has to be smaller than the propagation time of the pressure transient through the region (size d) with speed of sound c: $t_p < d/c$. The size of region d is determined by its smallest dimension or by the optical penetration depth that is equal to $1/\mu_{eff}$, with μ_{eff} being the effective optical attenuation coefficient. Second, the temporal profile of the pressure transient will be dependent on the source geometry [4]. For spherical and cylindrical sources this temporal profile will have a typical bipolar shape, in which the distance between the two peaks is dependent on the size of the source [5].

Due to the increased light absorption by blood compared to the surrounding tissue, PAI has successfully been applied to in vivo imaging of the lumen of blood vessels in small animals [6–10] and humans [11–14].

Recently, we showed that the diameter of the vessel can be estimated from the peak-to-peak time (Fig. 1) of the bipolar laser-induced pressure transient. The maximum vessel diameter for which this method is valid is determined by the effective size of the photoacoustic source, which is determined by the penetration depth of light into the vessel [5].

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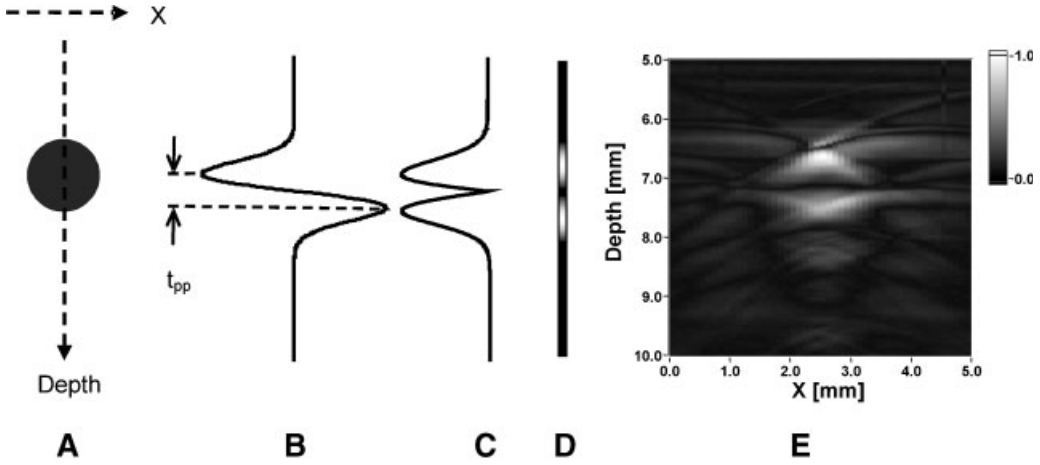

Fig. 1. Photoacoustic imaging: (**A**) sensor is scanned over blood vessel; (**B**) photoacoustic pressure transient (peak-to-peak time t_{pp}) at position above vessel (A-scan), time is converted to depth by multiplying time with speed of sound; (**C**) rectified time trace; (**D**) conversion to grayscale; (**E**) repeating (A–D) as a function of x-position results in a photoacoustic image.

In this article, we investigated whether PAI is able to visualize the venous valves and we determined characteristic features by which those valves can be recognized.

MATERIALS AND METHODS

Photoacoustic Imaging

To perform PAI, light pulses were guided to the tissue by a glass fiber (ø 600 μm, NA = 0.22) that was integrated in a home-built double-ring photoacoustic sensor, which has been extensively described elsewhere [11,12]. In short, this double-ring sensor consisted of two concentric ring-shaped electrodes with equal areas. The pressure transients were detected by 25-μm thick PVdF (Piezotech SA, Saint-Louis, France), biaxially stretched, electrically polarized, with one side Au/Pt metallized, which was glued to the electrodes. The photoacoustic signals were amplified by amplifiers with a high pass cut off frequency at about 1 MHz. This sensor had an angular aperture of 1.5–10° (−6 dB of directivity pattern) for acoustic signals with a peak-to-peak time of 67–350 nanoseconds, respectively. The time traces detected by this sensor were digitized by a dual channel oscilloscope-card (NI PCI-5112, 100 M sample/second, simultaneous sampling, 100 MHz bandwidth, National Instruments, Austin, TX) and the acquisition was synchronized on the Q-switch trigger generated by the laser. As the sensor had a narrow angular aperture, the measured time traces could be regarded as one-dimensional depth images (amplitude (A)-scans) of photoacoustic sources inside the measurement volume. The sensor was mounted on a translation stage to enable scanning, which allowed us to obtain a 2D dataset (scan direction vs. depth) of photoacoustic signals.

We plotted the absolute value of the time traces (A-scans) in a 2D imaging plane. As the peak-to-peak time of the laser-induced pressure transient is dependent on the diameter [5], the contour of the lumen of the blood vessels is visualized in this way. This procedure is schematically shown in Figure 1.

In Vivo Measurements

Measurements were performed on superficial dorsal veins in the hands of 21 healthy volunteers aging from 10 to 40 years (7 women, 14 men). Acoustic coupling between the skin and the photoacoustic sensor was obtained by using an optically transparent ultrasound contact gel (Sonogel®, Bad Camberg, Germany). Laser light from an Nd:YAG laser (DiNY pQ, IB Laser AG, Berlin, Germany) with a pulse energy of 1.25 mJ was applied at a wavelength of 1,064 nm, a repetition rate of 100 Hz and a pulse duration of 8 nanoseconds. The radiant exposure was in all cases less than 20 mJ/cm^2. A schematic overview of the setup is shown in Figure 2.

To start with, in each volunteer the valve was located by a method that uses palpation and inspection of veins that were visible through the skin [15]. A finger was placed on the superficial vein and some pressure was applied. Then the finger was moved over the vessel distally against the blood flow direction, while the pressure on the vein was maintained. By moving the finger in this direction, the blood was forced out of the vein. As there was still an amount of blood upstream, this blood tended to flow back and refilled the vein. When this blood reached a valve, the valve stopped the backflow and the position of the valve appeared as the separation between the empty part of the vessel and the part of the vessel filled with blood. In a few cases the valve could be observed as a local increase of blood vessel diameter *before* the finger crossed the valve, caused by accumulation of blood in front of the closed valve.

After localization of the valve first a scan perpendicular (transverse scan; step size 100 μm) to the superficial vein was made to localize the vessel. Next, the photoacoustic sensor was positioned above the center of the vessel. A longitudinal scan, parallel to the vein was made consisting

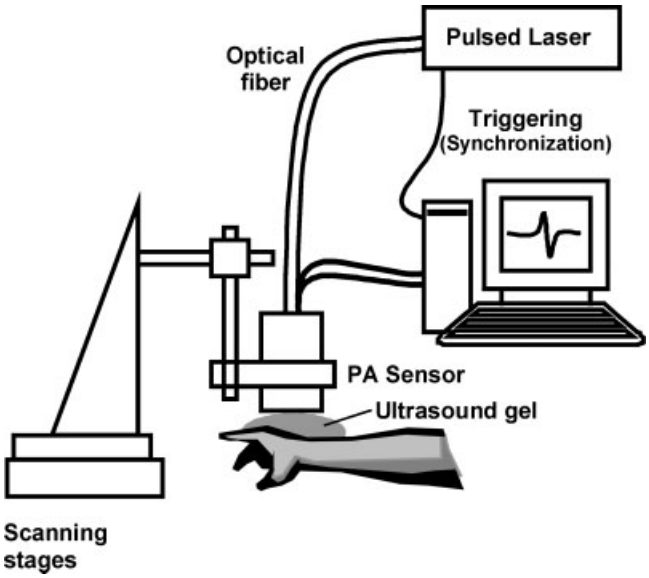

Fig. 2. Setup for photoacoustic imaging of venous valves at the dorsal side of the hand of a volunteer.

of 201 subsequent A-scans, equidistantly positioned with 50-μm spacing, resulting in a scan time of 2.5 minutes. For each A-scan 16 time traces were averaged.

RESULTS

A selection of six photoacoustic images of longitudinal scans of superficial veins with palpated valves on the dorsum of the hand is shown in Figure 3. The contour (upper part and lower part) of the lumen of the vessel is visualized in the image. In these images the skin is visible as a thin white line 1–2 mm above the vessel. It has to be noted that a thin white line precedes the blood vessel in the images. This is originating from a high pass filter in our photoacoustic sensor that causes an additional (negative) peak in the detected pressure transient which precedes the actual pressure transient.

In 16 cases (7 female, 9 male), out of in total 21 human volunteers, venous valves could be clearly identified with photoacoustic imaging. In five cases (one female, four male) the position of the valve could not be indicated in the photoacoustic images.

The valves appear in the longitudinal scans by several features:

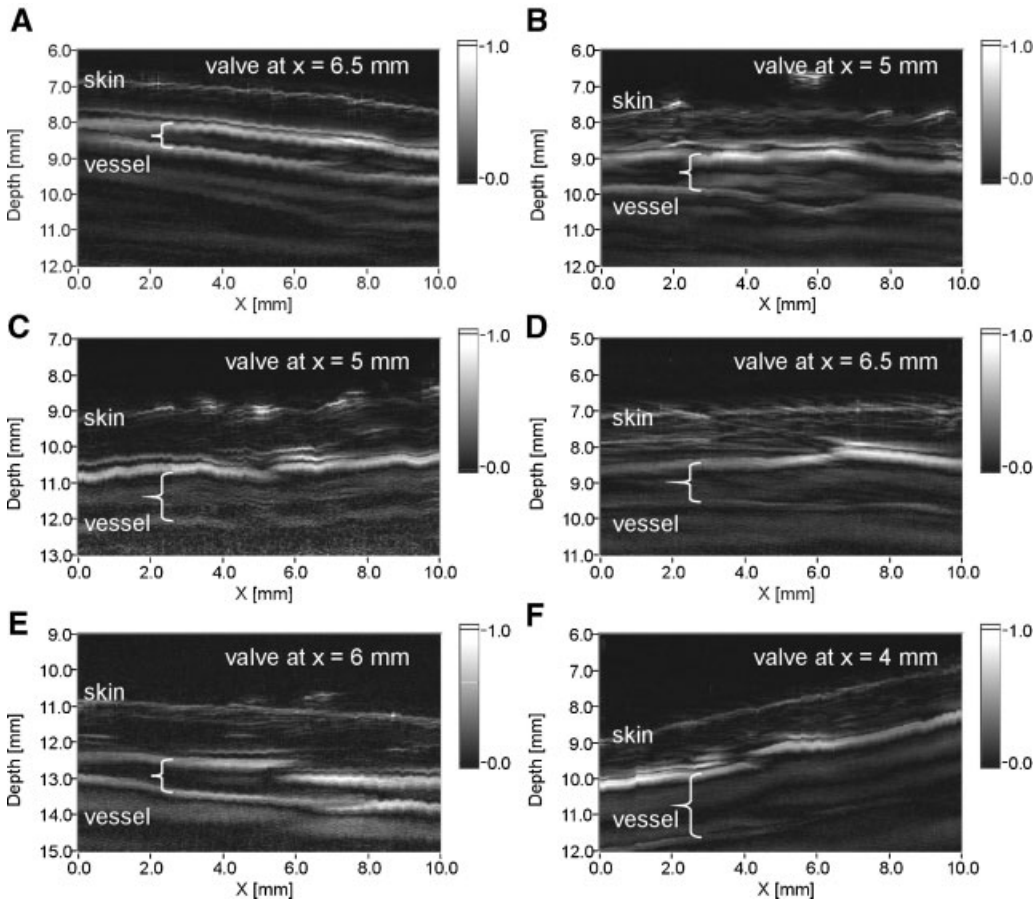

Fig. 3. Longitudinal scan of superficial veins in the dorsal side of the hand of human volunteers at positions where valves were expected based on palpation. In these images, the x-position of the valve is indicated. The direction of blood flow was from left to right in all images.

Feature 1. A discontinuity in the contour of the lumen in either the upper part of the vessel (Fig. 3C–F) or the lower part of the vessel (Fig. 3B). The discontinuity in the contour of the lumen manifests itself as a PA signal-lucent (dark) zone that appears diagonally from the upper left to the lower right of the broad intense (white) zone, which indicates the PA signals generated by the blood in the upper part of the vessel. In some cases the dark stripe also appears diagonally from the upper right to the lower left, which can be seen in Figure 3E.

Feature 2. An increase in lumen diameter at the proximal side of the valve, as is visible in Figure 3A,B,D,F.

Feature 3. An increase in intensity of the PA signal, visualized as an increase in brightness of the contour of the vessel at the proximal side of the valve in the upper part of the vessel, visible in Figure 3A,B,D,E.

Feature 4. An additional flap-like contour in the lower part of the vessel, as shown in Figure 3A.

A transverse scan of a vessel at the position where a valve is expected (position $x = 6.5$ mm of image A in Figure 3) is shown in Figure 4. Although the lumen could be visualized, we were not able to identify valves in a single transverse scan of a vessel.

DISCUSSION

In this article the use of PAI to visualize venous valves was demonstrated. The presence of venous valves appeared in the photoacoustic images in various ways as local discontinuities and increase in the lumen.

It has been shown earlier that the contribution of the vessel wall to the laser-induced pressure transient can be neglected [5]. Therefore, it is expected that the valves will not directly contribute to the generated pressure transient.

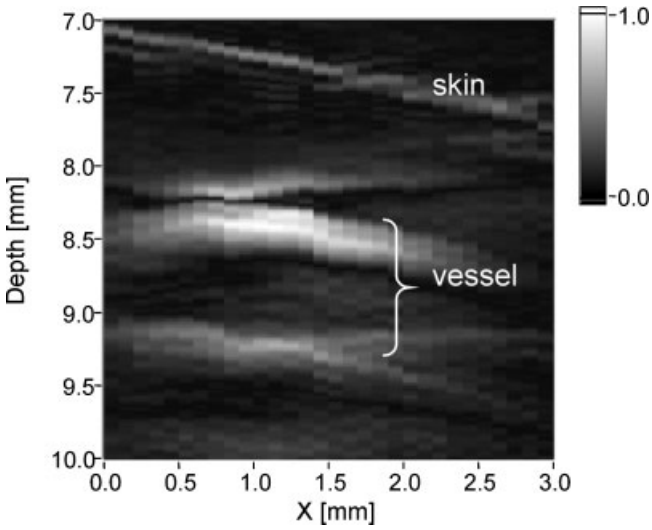

Fig. 4. Transverse scan of a superficial vein in the dorsal side of the hand of a human volunteer, at the location where a valve is expected: position $x = 6.5$ mm of image A in Figure 3.

Consequently, the presence of a valve inside the vessel will result in a discontinuity in the photoacoustic images (Feature 1) as blood at that position is replaced by the much less absorbing valve in either or both the upper and lower part of the vessel. Whether this feature is observed may be dependent on the orientation of the valves in the blood vessel. Venous valves usually have two cusps; occasionally they have three and sometimes only one [16–18]. We hypothesize that the orientation of the cusps in the vessel determines whether these valves will be detected in the photoacoustic scan. If the orientation, for example, is such that in the imaged area no cusp is attached to the vessel wall, then Feature 1 will not be observed, which may explain why in five cases we were not able to identify the valves.

An increase in diameter of the vein observed at the position of a valve, Feature 2, is a known phenomenon [16]. Besides an anatomical larger diameter, the observed increase in diameter can also be caused by an occasional closure of the valves. When the valves are closed, blood trying to flow back will accumulate at the closed valve, resulting in an increase in diameter at the proximal side of the valve. In addition, an increased diameter of the vein implies that at this position a larger volume of blood is present, which means that more light will be absorbed resulting in a larger amplitude of the photoacoustic signal. The increased amplitude is reflected in an increase in brightness (intensity) in the resulting photoacoustic images (Feature 3).

In Figure 3A, a flap-like structure is visible which should be interpreted as a narrowing of the diameter of the vessel. This can be explained by a valve being present in the vein that causes the vessel to narrow at that position. In between the valve and the vessel wall also blood is present that generates a photoacoustic signal, showing the outer contour of the vessel. This feature will only be observed when the valve is in a stationary position during the scan. As the typical time needed for a scan was about 2.5 minutes it is very likely that the valves are moving during the scan. This may explain why this feature is not always observed. The time needed for a scan is mainly determined by mechanically scanning the sensor. Using a multi-element sensor like, for example, a linear array will significantly reduce measurement time and it will enable imaging of these moving valves.

However, without a faster imaging method available at this moment, it is difficult to make a statement about the loss of information. Anyway, movement artifacts did not severely impede a proper localization of the valves.

In the transverse scans we have not been able to identify valves in the cross-sections of the vessels. The features we have observed in the longitudinal scans will result in changes in the appearance of the cross-section of the vessel. To identify a valve in such a cross-sectional image, multiple cross-sectional images at various positions around the valve have to be compared. As this requires scanning in longitudinal direction as well, it is with the present setup favorable to make a single longitudinal scan instead of multiple transverse scans. In addition, movement of the

valve during the measurement will make it more difficult to identify a valve in such a cross-sectional image unless the time needed to obtain an image is reduced.

In this study, we selected superficial veins as this allowed us to use visual inspection and palpation as a reference method to localize valves. This method can only be applied to superficial veins. As we now have shown the potential of PAI in the detection of valves in veins, this can also be applied to deeper veins. This allows for screening for valves during intravenous access. Finally, this study was performed on young and healthy volunteers. For further research it will be necessary to include people where intravenous access problems occur often such as elderly people, oncology patients, neonates, and obese people.

CONCLUSION

In this proof of principle study, the potential of PAI of valves in superficial veins has been explored. Four different features were identified by which valves can be identified in longitudinal scans. In measurements on healthy human volunteers, venous valves that were identified by palpation were detected in 16 of 21 cases.

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