

# Development of a non-invasive lung oximeter

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## Research note

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# Abstract

**Objective:** Monitoring of regional lung ventilation and perfusion in critically ill patients may assist in detection and management of lung injury. We developed a non-invasive oximeter that uses the principles of pulse oximetry to measure lung microvascular oxygen levels and a lung pulse waveform. The oximeter was tested in a healthy volunteer. Lung oxygen levels and the pulse waveforms were assessed in 2 lung regions; the apex (matched ventilation and perfusion) and the base (low ventilation relative to perfusion). Simultaneous conventional skin pulse oximetry was also recorded.

**Results:** At the lung apex, oxygen saturation fell markedly during systole to ~60%, but rapidly recovered and peaked at 100% by the end of diastole. The lung pulse waveform was similar in shape and timing to a pulmonary artery pressure trace. At the lung base, oxygen saturation remained low ~ 80% throughout systole and diastole. The lung pulse was similar in shape and timing to a left atrial pressure trace. Skin oxygen levels remained at 100% throughout the pulse. The lung oximeter recordings were consistent with the expected regional changes in ventilation and perfusion at the apex and base. The lung oximeter could assist clinicians in the management of critically ill patients.

## Introduction

Critically ill patients that require prolonged mechanical ventilation are at risk of developing diffuse alveolar damage that may result in the clinical features of the acute respiratory distress syndrome (ARDS). Patients that develop ARDS have a mortality of 25–40% and are at high risk of long-term disability (1, 2). Monitoring of the lungs to assess regional ventilation perfusion distributions could provide earlier detection of diffuse alveolar damage and assist in determining the optimal mechanical ventilation settings, to limit further lung injury.(3–6)

Currently, available forms of non-invasive lung monitoring have significant limitations. Electrical impedance tomography, which only assesses ventilation, has not been shown to improve patient outcomes.(5, 7) Computerised tomography, magnetic resonance imaging and positron emission tomography scans provide detailed information, but these approaches require the patient to be transported out of the critical care unit and continuous monitoring is not possible.(3, 8)

To address, these limitations we developed a non-invasive lung oximeter that uses the principles of pulse oximetry to continuously measure lung microvascular oxygen levels and the lung pulse (which provides a measure of relative pulmonary blood flow).

The aims of study were to monitor ventilation and perfusion at the lung apex and the lung base in a healthy individual to determine if the changes were consistent with those expected. The ventilation to perfusion ratio is typically higher at the lung apex than at the base and lung blood oxygen levels are higher at the apex.(9) In addition, the possible contamination of the signal by skin blood flow was also assessed.

## Methods

The data was routinely collected as part of the technical development phase of the monitor build and not as part of a clinical trial. The light sources used are safe and emit less power than a conventional skin pulse oximeter.(10) The first author was both the experimenter and the single subject. Approval by an ethics committee was not sort.

The oximeter is relatively simple to use and small in size and suitable for continuous monitoring of multiple lung regions. The lung oximeter utilizes wavelengths in the near infra-red (NIR) range 660 and 895 nm, and uses the principles of pulse oximetry to detect the pulsatile changes in the optical signal arising from blood volume changes in the lungs.(10) To minimize skin blood flow influencing the signal the sensor has a number of new elements. As with conventional pulse oximetry the lung pulse oximeter calculates a ratio of ratio's (RR) to estimate blood oxygen saturation. As the optical pulsatile signal from the lung pulse oximeter is unlike that of conventional skin pulse oximetry, a novel signal processing algorithm was developed, which we denote as a modified ratio of ratio's ( $RR_m$ ). We used the known relationship between RR and blood oxygen saturation ( $SO_2$ ), where  $SO_2 = 110 - 25(RR)$  to estimate blood oxygen saturations, as the exact correlation of  $RR_m$  with blood oxygen levels is yet to be established. Unlike conventional pulse oximetry the monitor also assesses oxygen levels throughout the entire cardiac cycle, during both systole and diastole.

The oximeter assessed ventilation perfusion matching in 2 regions of the lungs, the apex and the base. The sensor was placed in the supra-sternal notch over the lung apex with the subject lying at an angle of  $30^0$  from the horizontal (head higher than feet). The base of the lung was assessed with the sensor placed on the back between the 10<sup>th</sup> and 11<sup>th</sup> ribs, ~8 cm lateral to the midline with the subject lying supine and horizontal. The sensors were moved until the appropriate lung waveform was obtained. A skin pulse oximeter sensor (Max-Fast, Covidien, MA, USA) was placed on the forehead to simultaneously record a conventional skin pulse oximeter signal.

*Figures:* The figures demonstrating light intensity are presented, by convention, with the Y axis (light-intensity) inverted. The figures represent recordings during a breath hold. Systole and diastolic periods were determined by the pulse waveform changes in the lung and skin.

## Results

The single subject was a healthy adult Caucasian male.

### Lung Apex:

*Pulse Waveform:* The pulse changes for both wavelengths are demonstrated in *Fig. 1*. The lung pulse for 660 nm was similar in shape and timing to a pulmonary artery pressure trace, with a steep rise during systole, an inflection point, a dicrotic notch and a second peak during early diastole. The waveform also

demonstrated a small wave just before systole consistent with an A wave, as seen in central venous pressure traces. The start of the lung pulse commenced ~100 msec before the start of the simultaneous forehead skin conventional pulse oximetry pulse. The lung pulse waveform for 895 nm was different to 660 nm. It peaked in early systole, then fell rapidly to reach a trough in late systole, a waveform consistent with a high amplitude A wave was also present. Simultaneous conventional skin pulse oximetry was different and demonstrated a waveform similar in shape and timing to an arterial pressure trace for both wavelengths.

*Oxygen levels:* During the early systolic phase of the cardiac cycle the estimated oxygen saturations rapidly from 100% to <60%. Oxygen levels rapidly recovered during early diastole and peaked at the end of diastole at 100%. The skin oxygen levels remained relatively constant at 100%, throughout the cardiac cycle. *Fig. 2a.*

## Lung Base:

*Pulse Waveform:* The pulsatile changes for both wavelengths are demonstrated in *Fig. 3*. The lung pulse waveform for both 660 nm and 895 nm were similar in shape and timing to a left atrial pressure waveform, with A, X, V and Y waves. The V wave amplitude was greater than the A wave and no C wave was obvious. The conventional skin pulse oximetry waveform demonstrated a waveform similar in shape and timing to an arterial pressure trace for both wavelengths.

*Oxygen levels:* Oxygen saturation levels remained relatively constant and low (~ 80%), throughout the cardiac cycle. The skin oxygen levels were relatively constant at 100% *Fig. 2b.*

## Discussion

The recordings of the lung oximeter at the lung apex and base were consistent with the expected regional changes in ventilation and perfusion with higher oxygen levels and blood flow at the apex than at the base. These findings provide evidence that the lung oximeter could be used to assess regional distributions of lung ventilation and perfusion and could assist clinicians in management of critically ill patients.

## Lung apex:

At the apex the lung oximeter pulse waveform for 660 nm demonstrated a shape and timing consistent with a pulmonary artery pressure trace, with a steep rise during systole, an inflection point, a dicrotic notch and a second peak during early diastole.<sup>(11)</sup> The pulse waveform or optical signal is predominately influenced by pulsatile changes in lung blood volume associated with pulmonary blood flow. The distribution of blood in the lung vascular compartments is as follows, ~ 30% of the blood volume resides in the pulmonary arteries, 40% in the capillary beds and the remaining 30% in the

pulmonary veins.(12–14) Consequently, a relative high proportion (70%) of the blood volume resides in the pulmonary arteries and capillaries. Changes in pulmonary artery blood flow will therefore have a strong influence on blood volume in these compartments and therefore the optical signal. As the blood returning to the lungs via the pulmonary artery is deoxygenated these pulsatile changes in blood volume will have a greater influence on the 660 nm wavelength, which is intensely absorbed by deoxygenated blood. The second wavelength 895 nm, is more intensely absorbed by oxygenated blood.

A waveform consistent with a central venous pressure A wave was also present just prior to systole for both wavelengths. The pulmonary circulation is a low-pressure system and left atrial contraction may also give rise a relative increase in the blood volume in the lungs through a retrograde pressure wave. The high amplitude of the A wave for 895 nm is likely to represent well oxygenated blood in the lungs at this time point at the end of diastole.

The onset of the pulse for 660 nm was ~100 msec before the forehead skin pulse. This is consistent with the right ventricular systole preceding the left ventricle systole and also the lag time required for blood to travel to the forehead.

Oxygen levels at the apex of the lung dropped markedly to <60% within 200–300 msec of systole onset. Thereafter, oxygen levels rapidly increased and peaked back at 100% by the end of diastole. These rapid changes in oxygen levels are consistent with those expected in the normal lung microcirculation with matched ventilation and perfusion.(9) Equilibration between alveolar and blood oxygen levels is typically reached within 250 msec.(15, 16) The temporal changes in oxygen levels in the skin were different and remained constant at around 100% throughout the pulse.

## Lung base:

At the base of the lung the pulse waveform for both 660 nm and 895 nm were similar in shape and timing to a typical left atrial pressure waveform, with A, X, V and Y waves. The V wave was higher in amplitude than the A wave and no C wave was apparent.(17) This finding may represent pulsatile changes in lung blood volume predominately driven by left atrial pressure rather than pulmonary artery pressure. At the base of the lungs, in the supine position, the weight of the dorsal lungs may cause basal atelectasis, which in turn triggers pulmonary arterial vasoconstriction to minimize blood flow to poorly ventilated regions.(18) In a low pressure system, such as the pulmonary circulation, left atrial pressure may then become the predominate influence on pulsatile changes in lung blood volume.

Oxygen levels in the lung base remained low at ~ 80% throughout the cardiac cycle phases. This finding is potentially consistent with shunting of mixed venous blood oxygen through the atelectatic lung bases. (18)

The oximeter's lung pulsatile waveform appears to reflect the regional changes in lung blood volume. At the apex, the lung pulse waveform was similar to a pulmonary artery pressure waveform suggesting high

levels of pulmonary blood flow, while at the base the lung pulse waveform was similar to a left atrial pressure waveform suggesting low levels of pulmonary blood flow. In addition, the changes in blood oxygen levels over the phases of the cardiac cycle provided a potential indicator of regional ventilation. At the apex an initial fall in blood oxygen levels occurred during the early systolic phase followed by a rapid increase in oxygen levels during the diastolic phase, suggesting good ventilation and perfusion with rapid equilibrium of blood and alveolar oxygen levels. At the base, however, blood oxygen levels remained at mixed venous levels throughout the cardiac cycle suggesting low ventilation.

The simultaneous lung and skin pulse waveforms and oxygen levels were quite distinct at both the apex and the base, suggesting the lung oximeter signal was not influenced by skin oxygen levels or skin blood flow.

Monitoring of the lungs to assess regional ventilation perfusion distributions could enable earlier detection and diagnosis of disorders resulting in lung injury, such as atelectasis, pneumonia and ARDS, and could be used to determine the optimal mechanical ventilation settings to reduce tidal volumes while maintaining adequate oxygen levels.(3–6, 19)

## Conclusion

The recordings of the non-invasive lung oximeter were consistent with the expected regional changes in ventilation and perfusion. The lung oximeter could assist clinicians in the management of critically ill patients at risk of lung injury.

**Limitations** – The association between the  $RR_m$  value derived by the lung monitor and blood oxygen levels has not as yet been established. To estimate lung blood oxygen levels, we therefore used the known relationship between RR and blood oxygen levels, of conventional pulse oximetry. At low oxygen saturations (< 75%), the accuracy of the known relationship between RR and blood oxygen levels deteriorates, which adds uncertainty to the oxygen estimates.(20) Further work is required to accurately determine the relationship between  $RR_m$  and blood oxygen levels. The data was from a single subject. Further research is required comparing with invasively measured lung blood oxygen levels to confirm the current findings in the setting of a large clinical study.

## Abbreviations

Acute respiratory distress syndrome (ARDS), blood oxygen saturation ( $SO_2$ ), modified Ratio of Ratios ( $RR_m$ ), near infra-red (NIR), oxygen saturation ( $SO_2$ ), Ratio of Ratios (RR).

## Declarations

## Ethics approval and consent to participate:

The data was routinely collected as part of the technical development phase of the oximeter and not as part of a clinical trial. The first author was both the experimenter and the subject. There were no risks. Ethics approval was not sort.

## **Consent for publication:**

Not applicable

## **Availability of data and materials:**

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

## **Competing interest:**

Dr Dixon and Ms Gibson have a financial interest in Cyban Pty Ltd, that is developing the lung oximeter.

## **Funding:**

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## **Authors' Contributions:**

Protocol/project development was performed by BD; data collection or management was done by BD, EG; data analysis was performed by BD, EG; manuscript writing was done by BD with editing by EG.

## **Acknowledgments;**

None

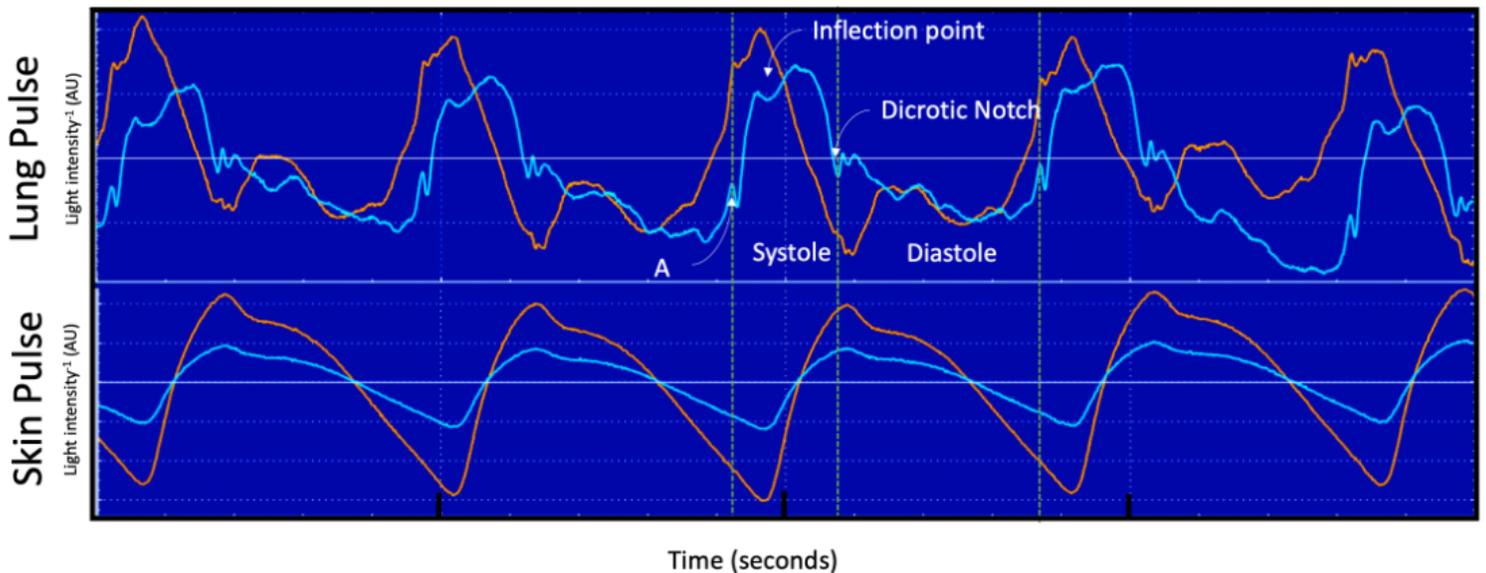
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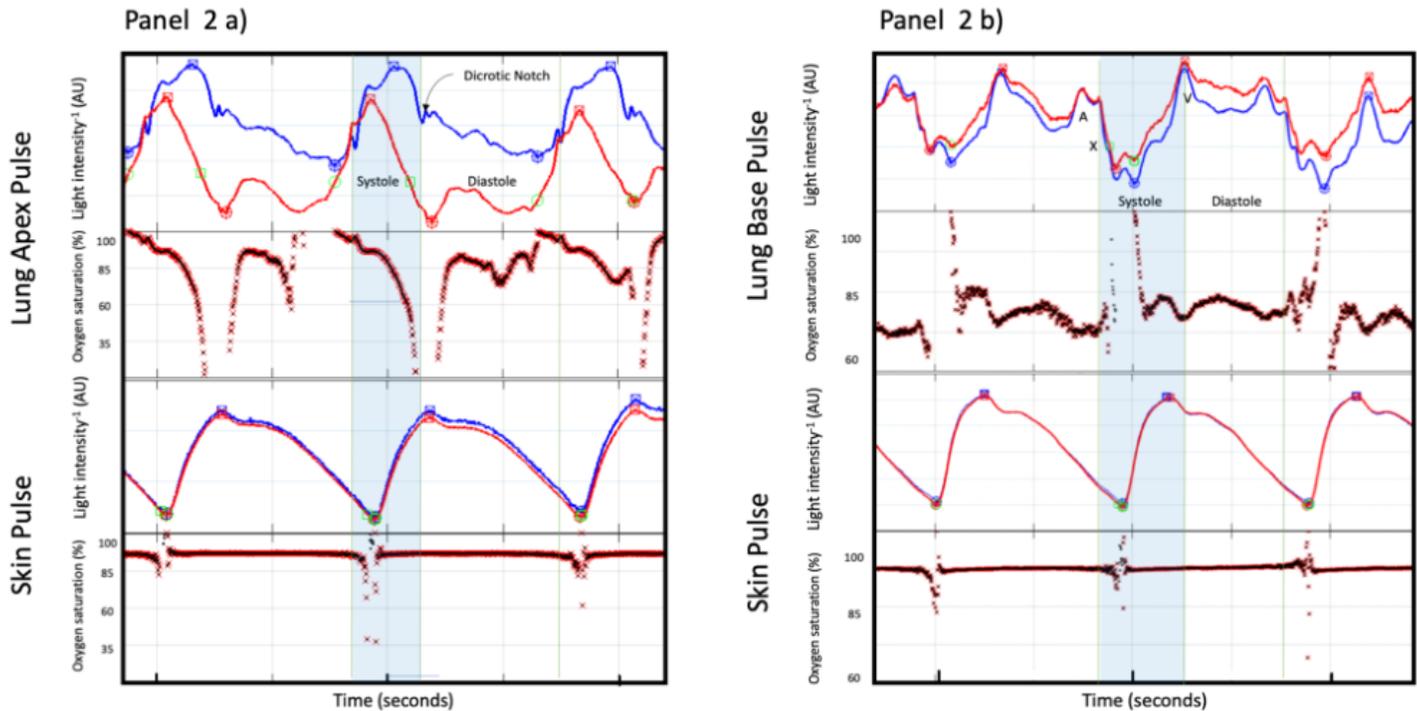
## Figures



**Figure 1**

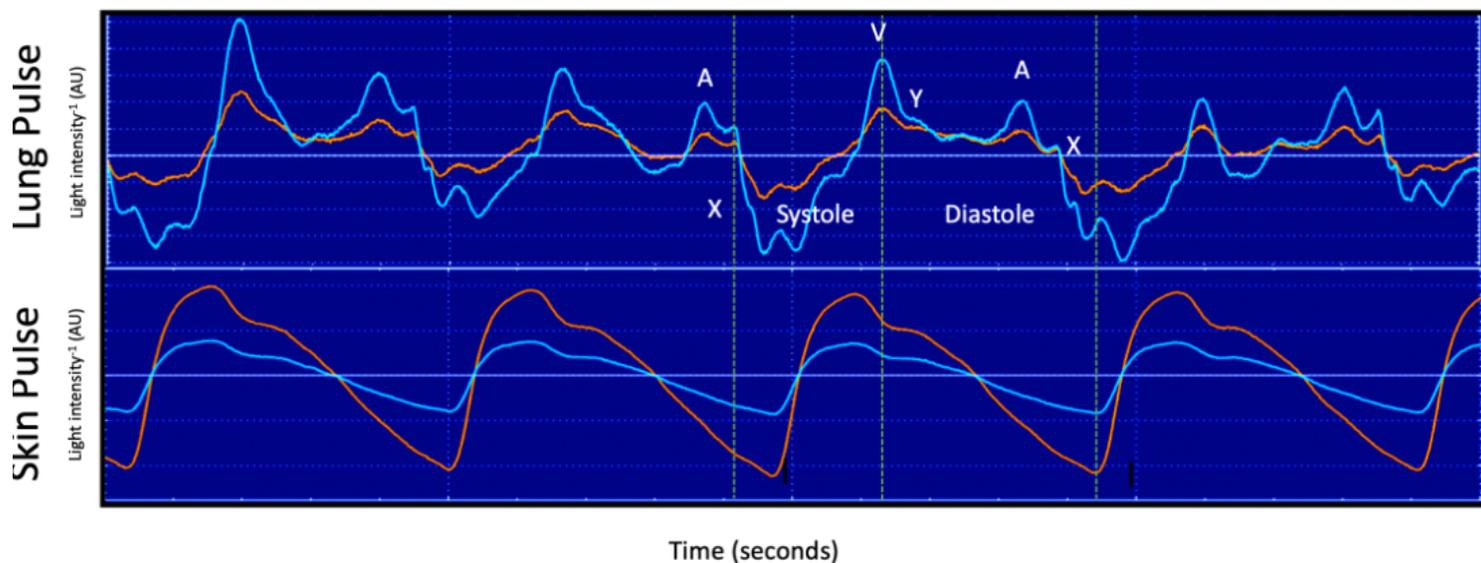
Simultaneous recording over the lung apex and conventional forehead skin pulse oximetry pulse waveforms from a subject. The optical signals for both wavelengths 660nm (blue) and 895 nm (orange) are demonstrated. The dashed lines represent the start of systolic and diastolic phases of the cardiac cycle based on the lung pulsatile waveform changes. The lung pulse for 660 nm demonstrated a waveform similar in shape and timing to a pulmonary artery pressure trace, with a step rise during

systole, an inflection point, a dicrotic notch and a second peak during early diastole. In addition, the start of the pulse was ~ 100 msec before the start of the simultaneous forehead skin pulse. The lung pulse waveform for 895 nm was different. It peaked during early systole, then fell rapidly to a trough during late systole, a waveform consistent with a high amplitude central venous pressure A wave was also present just before the onset of systole. The skin pulse demonstrated a waveform similar in shape and timing to an arterial pressure waveform. Arbitrary units (AU).



**Figure 2**

Simultaneous display of the estimated oxygen saturation and the pulse oximeter waveforms for the lung and forehead skin from a subject. The optical signals for both wavelengths 660nm (blue) and 895 nm (red) are demonstrated. The shaded area represents the systolic phase of the cardiac cycle based on the lung pulsatile waveform changes. Panel a) The lung apex: The lung oxygen levels fell rapidly during systole. During early diastole oxygen levels rapidly recovered and peaked at the end of diastole back at 100%. The skin oxygen levels remained relatively constant at 100%, throughout the cardiac cycle. Panel b) The lung base: The lung oxygen levels remained relatively constant at ~ 80% throughout the cardiac cycle. The skin oxygen levels also remained relatively constant at 100%, throughout the cardiac cycle. Arbitrary units (AU).



**Figure 3**

Simultaneous recording over the lung base and conventional forehead skin pulse oximetry pulse waveforms from a subject. The optical signals for both wavelengths 660nm (blue) and 895 nm (orange) are demonstrated. The dashed lines represent the start of systolic and diastolic phases of the cardiac cycle based on the lung pulsatile waveform changes. The lung pulse for 660 nm and 895 nm demonstrated a waveform similar in shape and timing to a left atrial pressure waveform, with A, X, V and Y wave. The V wave was higher than the A wave and no C wave was apparent. The skin pulse demonstrated a waveform similar in shape and timing to an arterial pressure waveform. Arbitrary units (AU).