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COMMENT

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Evolution of gas in scattering media absorption spectroscopy as a neonatal pulmonary monitoring device

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This is a commentary on the review article: "Gas in scattering media absorption spectroscopy (GASMAS) as a potential tool in neonatal respiratory care."

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Monitoring of respiratory status and function in neonates and infants has evolved with advances in healthcare technology over the past few decades since the unmonitored and unrestricted use of oxygen prior to 1950s.[1] Continuous use of pulse oximetry to guide oxygen administration, intermittent blood gases, and/or non-invasive measurement of partial pressure of carbon dioxide via transcutaneous or end tidal route to determine adequate ventilation and chest radiographs to assess pulmonary status have now become the standard of care in neonatal intensive care units (NICUs).[2] Additionally, near-infrared spectroscopy (NIRS) provides the ability to measure regional tissue oxygen saturations and has been increasingly used in preterm infants for cardio-respiratory monitoring and management.[3] However, we do not yet have a reliable way to measure oxygenation status and content directly and within the lungs itself. The recent review by Panaviene et al. has highlighted a technology named gas in scattering media absorption spectroscopy (GASMAS) that has been in development over the past two decades as a potential device to measure oxygen content and concentration within the lung directly. The authors in their review describe the physics, current evidence, and possible clinical applicability over different neonatal lung pathologies and scenarios.[4] Table 1 summarizes information about devices used for measures of oxygenation and ventilation status in the NICU.

GASMAS is based on absorbance of light by oxygen and water in the gas phase, which occurs in the window of 650–950 nm (the tissue optical window) in which the absorbance by the tissue is comparatively low. As the background from non-gaseous components in the body is low, this allows the specific identification of water vapor and oxygen concentrations by choosing wavelengths that will be absorbed by them. The extent of absorbance is directly proportional to the concentration as per the Beer–Lambert Law, allowing for quantitative determination of their concentrations. Two laser light sources are used to transmit light at 760 nm and at 820 or 935 nm, the wavelengths absorbed by oxygen and water vapor, respectively. Essentially, the GASMAS instrumentation is a very small spectrophotometer consisting of a light source emitting these two wavelengths and a detector that measures how much of the incident light is absorbed. Pulse oximetry as well as NIRS also make use of the low background absorbance in the tissue optical window but are based on the shift in hemoglobin's absorbance in the aqueous environment of the tissues when oxygen binds to it. While they can be used to quantify oxygenation levels indirectly through binding of oxygen to hemoglobin, they do not detect oxygen directly.[4,5]

GASMAS was studied in the food industry as a potential tool to assess fruit maturity, where oxygen is a major contributor to the ripening process, and for the fertilization of egg where the fertilized egg shows an increased water vapor signal and decreased oxygen signal over time in comparison with the unfertilized egg.[6] In the pharmaceutical industry, it was used for external spectroscopic analysis of ingredients as a quality control measure.[6]

The potential role of GASMAS in the clinical setting was recognized early by the researchers at Lund University, Sweden. GASMAS has been reported to detect oxygen and water vapor signals in phantom model cavities simulating sinuses and the middle ear with reduced and abnormal signal patterns detected in conditions simulating sinusitis and middle ear effusions.[6] In adult volunteers, GASMAS was reported to detect signal abnormalities in subjects with recurrent sinus problems and mastoid cavity opacities on imaging and has been proposed as a potential diagnostic tool in sinusitis and otitis media.[7,8] GASMAS has also been shown to differentiate absorption signals between post-operative samples of heads of femur affected with osteonecrosis by detecting water vapor signals when compared to normal femur head specimens.[9]

Much of the work in neonates and infants has come from the same group of researchers from Lund University in Sweden who originally described GASMAS in 2001. This group has been methodically and systematically studying and improving the ability of GASMAS to detect air and water vapor with both in vivo

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Table 1. Measures of oxygenation and ventilation status in the NICU.

Device	Clinical applicability	Advantages	Disadvantages
Arterial blood gas (ABG)	Measures pH, PaO_2, $PaCO_2$, and SaO_2	Accurate and reliable measures of oxygenation, ventilation and acid–base balance.	Invasive: requires indwelling catheter or painful arterial punctures. Intermittent measurements.
Capillary blood gas (CBG)	Measures pH and PCO_2 reliably for clinical utility	Does not require indwelling arterial catheter. Less expertise required for procedure.	Invasive painful heel stick procedures. Intermittent measurements. Unable to measure PO_2 reliably.
Venous blood gas (VBG)	Measures pH and PCO_2	May be used in infants with central venous access or with routine venous blood draws.	Less accurate and reliable than ABG and CBGs. Unable to measure PO_2 reliably.
Transcutaneous O_2 ($TcPO_2$)	Measures partial pressure of oxygen at skin surface	Non-invasive and continuous measurement. Good agreement of $TcPO_2$ and PaO_2 with optimal electrode temperature, stable infant conditions, and non-extreme PaO_2 values.	Slow response time. Needs frequent repositioning of sites with adequate recovery time in between. Risk of burns and heat-related skin complications. Less reliable when skin is inadequately perfused, hypoxemic ($PaO_2 < 50$ mmHg), or hyperoxemic ($PaO_2 > 80$ mmHg) conditions.
Pulse oximetry	Measures oxygen saturations (SpO_2)	Non-invasive and continuous measurement. Fast response time. Sensitive to short episodes of desaturations.	Prone to motion artifact and ambient light interference. Values affected by decreased skin perfusion, temperature, and pigmentation and type of hemoglobin. Short average time and alarm time delay may to lead to increased alarms and contribute to alarm fatigue.
Transcutaneous CO_2 ($TcPCO_2$)	Measures partial pressure of carbon dioxide at skin surface	Non-invasive and continuous measurement. Can be used in non-invasive ventilated infants or those on high-frequency ventilation.	Needs frequent repositioning of sites and recalibration of electrodes. Risk of burns and heat related skin complications. Sensitivities decreases with hypercapnia. May require intermittent blood gases monitoring for evaluating correlation.
End tidal CO_2 ($ETCO_2$)	Measures partial pressure of carbon dioxide from exhaled gas. Trends may be valuable in long-term ventilated infants or infants with tracheostomy with decreased dead space.	Non-invasive and continuous measurement.	Poor agreement between $ETCO_2$ and $PaCO_2$ in ventilated preterm infants due to higher respiratory rates and smaller tidal volumes precludes its use in high-frequency ventilation. Not reliable in non-invasive ventilated infants via nasal cannula with large air leaks. May require intermittent blood gases monitoring for evaluating correlation.
Near infra-red spectroscopy (NIRS)	Measures the balance between oxygen delivery and consumption and provides information on oxygen uptake in the tissue or regional tissue oxygenation (rSO_2)	Non-invasive and continuous measurement. Fast response time. May be beneficial in hemodynamic monitoring in infants with cardiac anomalies or significant patent ductus arteriosus.	No consensus on normative values for individual organ/tissue in extreme preterm infants. Evolving evidence of NIRS on clinical outcomes in preterm infants.
Gas in scattering media absorption spectroscopy (GASMAS)	Potentially measures oxygen content and concentration directly in the lungs. Potentially beneficial in targeting ventilation strategies and recognizing change in respiratory status.	Non-invasive when using dermal light source and detector. Continuous measurement.	Needs additional data for accuracy, reliability and clinical utility. May be impractical if it requires an internal light source.

Source: Di Fiore.[17]

pH potential of hydrogen, *PaO_2* partial pressure of oxygen in arterial blood, *$PaCO_2$* partial pressure of carbon dioxide in arterial blood, *SaO_2* saturation of oxygen in arterial blood.

and in vitro studies, working towards developing a reliable and clinically applicable device, over the past two decades. In a feasibility study published in 2013 involving 3 term infants, they were able to first detect absorption bands of water vapor in neonatal lungs but were unable to detect oxygen signaling.[10] In a subsequent study published in 2016 involving 29 term infants and a diode laser with increased power output at 760 nm for oxygen-specific detection, the researchers were able to detect oxygen at least once in all the infants.[11] While there have been no published studies involving preterm infants, the group from Lund University and researchers from University College Cork, Ireland have developed three-dimensional computerized and physical lung phantom models using computerized tomography images of preterm infants simulating optical properties of organs and tissues in the thorax for measurements of oxygen to study and understand light transmission and absorption and improve signal detection.[12–14]

Throughout their experimental studies, the researchers have focused on finding optimal placement of light source and detecting probes. In their initial work on term infants, the researchers reported placing the light source in the mid-clavicular line between clavicle and nipple level with the detection probe in the axilla as the most favorable position for detection of signal. Their recent studies have reported improved light transmission and signal strength detection using an internal light source. Internal light source placed via the esophagus has been studied in newborn piglets and reported it to be superior at quantifying the fraction of inspired oxygen (FiO_2) as compared to dermal-placed light sources.[15] The intra-tracheal route for placement of the light source has been evaluated recently to detect oxygen content and volume change during simulated respiration using a computational model of the thorax. The authors reported that the endotracheal light source improved the assessment across the lung as light exhibited less attenuation and distributed evenly in the lung.[16] While the provision of an internal light source via an endotracheal tube in mechanically ventilated infants or via gastric tube in preterm infants is plausible, the development, safety, and practicality of using the light source in routine neonatal care has yet to be determined.

The researchers are to be commended for their methodical work and dedication toward this technology and their efforts toward developing GASMAS into a clinically applicable device. The authors describe the potential for clinical use in neonatal respiratory management in various settings, including delivery room stabilization, endotracheal tube placement, surfactant therapy, lung ventilation, and bronchopulmonary dysplasia (BPD) management strategies.[4]

Based on the current status of this technology and the pilot studies, additional testing of this device in research settings is required to be able to measure oxygen content and concentration in the lungs with precision and consistency. GASMAS appears to be safe, and if shown to be accurate and reliable, it may improve our knowledge of alveolar oxygen concentration and content and its changes during postnatal transition and in diverse neonatal lung conditions, including respiratory distress syndrome, BPD, pneumothorax, pneumonia, atelectasis, and pulmonary edema, among others. Future clinical studies can then determine the cost effectiveness and utility of GASMAS in improving neonatal outcomes.

DATA AVAILABILITY

Data sharing not applicable to this article as no datasets were generated or analyzed during the current study.

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AUTHOR CONTRIBUTIONS

H.K.M. wrote the first draft of the manuscript, edited it for content, and approved the final version of the submitted manuscript. J.K.-S. edited it for content and approved the final version of the submitted manuscript. V.B. provided the concept, design, edited it for content, and approved the final version of the submitted manuscript.

COMPETING INTERESTS

The authors declare no competing interests.

ADDITIONAL INFORMATION

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