Ocean Optics

# Application Note

**Keywords**

- Blood bilirubin
- Neonate (newborn)
- Diffusion theory

**Techniques**

- Optical spectroscopy
- Low coherence spectroscopy
- Reflection

**Applications**

- Blood analysis
- Bilirubin concentration
- Hemoglobin concentration

# Blood Analysis without Pain for Neonates

Application material and images were provided by Nienke Bosschaart, then-doctorate student at the department of Biomedical Engineering and Physics of the Academic Medical Center (AMC), Amsterdam, The Netherlands. In October 2013, Dr. Bosschaart was recognized by The Netherlands' prestigious Technology Foundation STW (Stichting Technologie en Wetenschap) for her work described here.

## Introduction

Jaundice is a common and often harmless condition in neonates. However, especially preterm neonates have an increased risk for developing jaundice related brain damage, which is the reason for close monitoring of the blood bilirubin concentration (the indicator of jaundice) in these patients. The bilirubin concentration is determined from a blood sample obtained by a heel stick, often up to three times a day. Naturally, this is a very painful and harmful procedure for the child. In addition, this diagnosis creates an unwanted delay in the treatment of the patient, since it may last more than one hour.

Figure 1. Optical spectroscopy is a less painful and faster technique for bilirubin concentration measurement in newborns.

At the AMC we investigate the possibility to measure the bilirubin concentration faster and non-invasively, by using optical spectroscopy. The absorption peak of bilirubin around 455 nm allows for spectroscopic assessment of its presence in the blood vessels of the skin. Although bilirubinometers based on this principle have been developed since 1980, no device has been found accurate enough to completely replace the heel stick[1]. The focus of this study is therefore 1) to investigate the reasons for the inaccuracy of current bilirubinometers and 2) to develop a bilirubinometer that can replace the painful heel stick.

## Experiment Details

To investigate the reasons for the inaccuracy of current bilirubinometers, a special bilirubinometer was developed at the AMC, based on a multidistant fiber optic probe that was fabricated by Ocean Optics[2] (Figure 1). Using diffusion theory, we obtained not only the bilirubin concentration from the skin reflection spectrum (430-600 nm), but we also determined the blood volume fraction in the investigated tissue volume (Figure 2). In an explorative patient study at the neonatal intensive care of the AMC, we found that the measured bilirubin concentration consists primarily of bilirubin in the tissue surrounding the blood vessels in the skin, instead of bilirubin inside the blood vessels themselves. Since the bilirubin concentration in the surrounding tissue is difficult to relate to the concentration in blood, this introduces an inevitable inaccuracy in the comparison of existing bilirubinometers to the heel stick determination[1].

## Low Coherence Spectroscopy (LCS)

The only possibility to improve the accuracy of the existing bilirubinometers is by confining the measurement volume to the inner lumen of a blood vessel. Current spectroscopic techniques are unable to do such a determination, since light scattering from the surrounding tissue always contributes to the measured value. Therefore, we developed a new spectroscopic technique – low coherence spectroscopy (LCS) – which, based on low coherence interferometry, allows for very careful control over the size and location of the investigated tissue volume[3]. To validate our LCS measurements, the USB4000 spectrometer was used repeatedly for measuring reference spectra[2-5] (Figure 3). Currently, LCS is the only spectroscopic technique that can be used for the measurement of blood values inside a single blood vessel, without any influence from the surrounding tissue. The first in vivo measurements with this technique are very promising[4].

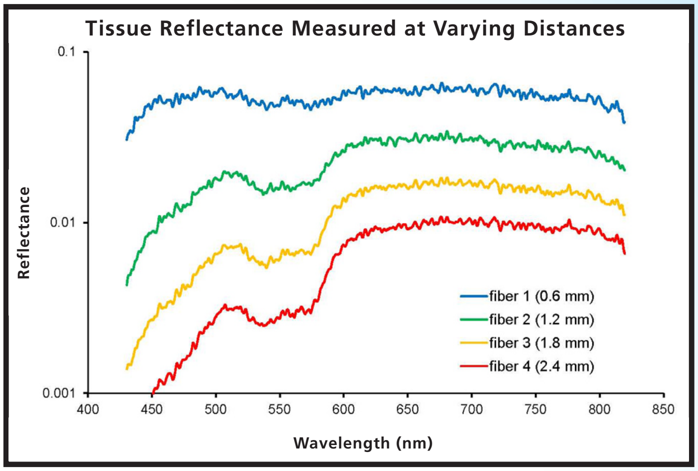


Figure 2. Reflection spectra of neonatal skin help to determine blood volume fraction in the tissue.

## Spectroscopic Detection in LCS with the Ocean Optics USB4000

The relatively slow acquisition time of our LCS system limits the current clinical utility of the technique. Therefore, we investigated the possibility to replace the detecting photodiode in the LCS system by a spectrograph. The USB4000 proved to be very suitable for this purpose, resulting in an almost 4 times faster acquisition time[5].

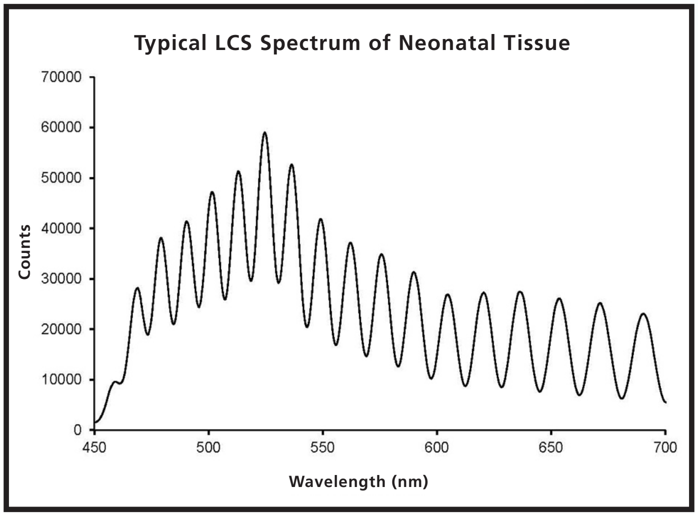


Figure 3. Low coherence spectroscopy techniques show promise as an alternative to traditional bilirubin monitoring methods.

## Conclusion

Besides the applications described above, we also used the Ocean Optics probe for the determination of the optical properties of neonatal skin in the investigated patient population[2]. This information is of great value for both this research and other studies involving optics and neonatal skin.

For further improvement of the clinical utility of LCS, it is necessary to implement a spectrograph that has a higher acquisition rate than the USB4000. Since a spectrograph with the required specifications is not commercially available, such a spectrograph needs to be designed and developed. Furthermore, a fiber optic probe for clinical LCS measurements needs to be developed as well.

The future development of LCS offers additional opportunities for clinical applications. The technique may not only be used for bilirubin concentration measurements, but also for the determination of other blood values, such as hemoglobin concentrations and oxygen saturation. Also for the determination of these blood values, a localized measurement in a single blood vessel implies a very valuable improvement compared to existing spectroscopic determinations. The expected clinical utility of the technique is extensive, since it may be applied not only on neonates, but also on older children and adults. Furthermore, we found that LCS is also sensitive to the changes in tissue scattering that are related to the morphology and organization of cells[6]. The latter offers new opportunities for the diagnosis of cancer.

## References

This research resulted in the following publications:

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