Examination of necrotizing enterocolitis in preterm infants using diffuse optical tomography

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Abstract

Necrotizing enterocolitis (NEC) is a common gastrointestinal medical/surgical emergency in preterm neonates. Despite advances in identifying factors predisposing infants to NEC, noninvasive diagnosis remains challenging [1]. Since diseased bowel in NEC is ischemic, diffuse optical tomography (DOT) can be used to spatially and functionally quantify the oxygenation state of hemoglobin (Hb) in the affected areas [2]. A DOT imaging device, using interdigitating sixteen-optode illumination and detection arrays and two illumination wavelengths (760, 850 nm), was used to measure the dynamic Hb oxygenation state in the abdomen and simultaneously in the cranium as control. DOT measurements of local tissue oxygenation were performed on six infants, two of whom presented with clinically confirmed NEC (Bell stage II [1]). Results showed an elevated 850nm/760nm ratio in the abdomens, but not crania, of NEC-positive infants, implying less oxygenated Hb in these regions. DOT reconstructions provided localization of the ischemic bowel as well as other measures of altered dynamics of the Hb signal. DOT measurements taken on infants with confirmed NEC display quantitative findings consistent with the known pathophysiology of NEC.

Objectives

The objective of our project was to establish a fast and reliable metric for detecting confirmed NEC using DOT.

Methods

Instrumentation: A DOT imager (NIRScout; NIRx Medical Technologies, LLC.), emitting light at wavelengths of 760nm and 850 nm was used to gather tomographic data of hemoglobin oxygenation state (Fig. 2).

Subjects: Six preterm infants, four being NEC(-) and two being NEC(+). This includes a pair of fraternal twins, one of whom was NEC(+), while the other was NEC(-).

Measurements: Dual identical arrays of 8 x 8 alternating source and detector optodes were utilized to simultaneously measure the amount of light absorbed by the tissue of interest in the cranium and abdomen simultaneously (Fig. 3).

Analysis: The difference in absorption of oxygenated Hb at the different wavelengths used in the experiment (Fig. 1) was used to establish a temporal mean ratio that is indicative of necrotic bowel in NEC (Fig. 6). By computing a ratio of the two raw data files (the light transmitted through the tissue and received for each source - detector channel pair), the relative Hb oxygenation level of tissues becomes apparent.

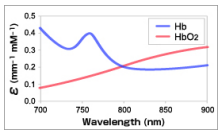

Figure 1: Hb absorption spectra [www.hamamatsu.com]

Figure 2: NIRScout DOT imaging device

Results and Discussion

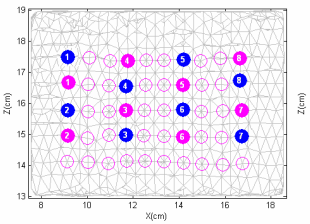

Figure 3: Source (pink) detector (blue) geometry

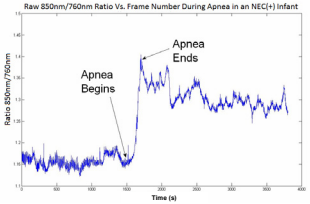

Figure 5: Single Channel 850nm/760nm of the NEC(+) twin during a period of spontaneous apnea

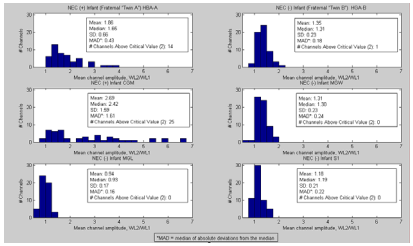

Figure 4: Temporal mean WL2/WL1 data for each subject, showing differences in relative tissue oxygen saturation

Time (s)

Time (s)

Group	Number of channels	Mean	Standard Deviation	P.Value
NEC Positive (n=2)	97	2.28	1.29	p < .0001
NEC Negative (n=4)	231	1.21	.26	

Figure 6: Mann-Whitney U Test

Results and Discussion (Continued)

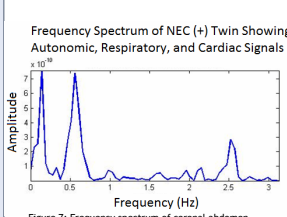

Figure 7: Frequency spectrum of coronal abdomen slice, showing respiratory and cardiac rhythms

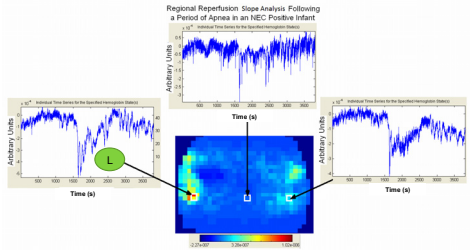

Figure 9: Slope Analysis of Abdomen Showing Delayed Reperfusion Response to Apnea in Lower Right Quadrant (L = Known Site of NEC Lesion)

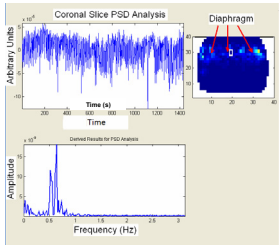

Figure 8: PSD Analysis Showing Diaphragm Location in Abdomen at Respiratory Frequency

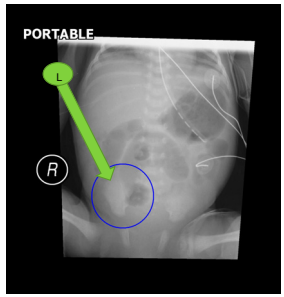

Figure 10: X Ray Showing Known NEC Lesion Site

The temporal mean of the 850nm/760nm data gathered from each subject showed characteristic differences in the number of channels with an elevated ratio (Fig. 4). Analysis shows a statistically significant difference between NEC (+) infants and NEC (-) infants with this simple method of comparison (Fig. 6). Following a spontaneous period of apnea in an NEC(+) infant, it was noted that the oxygen saturation dropped following this period, and showed delayed recovery. The response of the 850nm/760nm ratio to this period was noted across the abdomen of the infant (Fig. 5). By applying Fourier analysis to this raw 850nm/760nm data, known characteristic physiologic frequencies (cardiac, respiratory, and autonomic) are found throughout the time sample (Fig. 7). By reconstructing an image based on this 850nm/760nm ratio data and performing a power spectral density (PSD) analysis, the diaphragm can be visualized at the known respiratory frequency (Fig. 8). The infant that presented with the episode of apnea required surgery to resect necrotic bowel after the completion of the study; the lesion was found localized to the lower right quadrant (LRQ) of the abdomen (Fig. 10). By performing a slope analysis of the reperfusion time period, the variation of the tissue's local response can be seen to vary dramatically (Fig. 9). Specifically, the area known to bear the lesion was found to respond sluggishly to the drop in oxygen saturation in comparison to the midline abdomen and the lower left quadrant, both areas of the gut known to be lesion-free (Fig. 9).

Conclusions

DOT can be used to quickly assess the gross level of bowel tissue oxygenation in neonates with confirmed NEC, and to localize the general area of the lesion. These results suggest that DOT could also have diagnostic utility. Our future goal is to screen a large number of infants in order to determine the point at which the presence NEC is able to be visualized using DOT.

References

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Acknowledgements

This research was support in part by the National Institutes of Health (NIH) under Grants nos. R21NS067278, R42NS050007, 5R44NS049734, the New York State Department of Health, and the Alumni Association of SUNY Downstate Medical Center.