

PhD THESIS DEFENSE: Comprehensive monitoring of the injured brain by hybrid diffuse optics: towards brain-oriented theranostics

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In the intensive care, the multimodal monitoring of the patient is crucial. The systemic physiology is routinely and comprehensively monitored but the practical monitoring of the brain is lacking.

Hybrid diffuse optics (DO) has a potential to fill this gap by combining diffuse correlation spectroscopy (DCS) and near-infrared spectroscopy (NIRS). DO measures local, microvascular cerebral perfusion/blood flow, oxygen extraction fraction and cerebral metabolic rate of oxygen.

Therefore, the overarching purpose of this work was to boost the use of hybrid DO by

validating its utility in clinical applications on the human brain, especially in critically ill populations.
To achieve this goal, new hybrid DO devices were constructed to enhance the data-rate and the quantification of the intracerebral signals while synchronously acquiring data from clinical monitors. In particular, a new platform combining time-resolved NIRS (TRS) and fast (~40 Hz) DCS was constructed.
These were used in the fruitful collaborations with the Vall d'Hebron hospital on different patient cohorts. In a population of patients undergoing surgeries the relationship with electrophysiological assessment of cerebral metabolism, the proprietary bispectral index, and the optically-derived parameters were investigated during propofol-induced anesthesia. This has shown that DO estimates of the oxygen metabolism correlate with this index. The additional DO information could be investigated to evaluate if it can help prevent brain damage due to anesthesia.
A cohort of children diagnosed with benign external hydrocephalus undergoing invasive intracranial pressure (ICP) monitoring were monitored during night sleep. This allowed the quantification of the cerebral hemodynamics and metabolism during ICP waves that are indicative of future morbidity in them. This has revealed that ICP waves are associated with hemodynamic and metabolic oscillations. Furthermore, these results have shown that the presence of ICP waves, in particular B-waves, can be observed by DO monitoring which could, in the future, allow their noninvasive assessment in wider populations.
An important shortcoming for the routine clinical use of DO has been that the results from commercial NIRS devices on clinical population are not reproducible, often give physiologically invalid results and differ between systems. Apart from the limitations due to the use of continuous-wave light, one major culprit is brain heterogeneity and underlying morphological and functional abnormalities. A comprehensive analysis was carried out using data from different cohorts of brain-injured patients to provide a set of examples and suggestions to establish quality control routines.
? Hyperventilation is a relatively common therapy, where a decrease in blood carbon-dioxide s induced to cause vasoconstriction in order to lower ICP. Since high ICP often leads o hypoperfusion and hypoxia, this treatment is meant to be beneficial but the findings fr m clinical practice and large trials provide mixed results. It is hypothesized that this is due o some patients suffering from misery perfusion (MP). Hybrid DO can evaluate whether t e therapy causes MP. This was tested in a cohort of patients using advanced statistic l methods. The findings indicate that MP is common in these patients and DO can character ze its frequency and magnitude. This paves the way for future clinical-trials to validate he findings and evaluate the effica
y. Other protocols were also carried out as small pilot studies such as during blood transfusi n. The results are reported and their potential significance is elucidat
d. Overall, the versatility of the hybrid DO was demonstrated and new biomarkers w

re proposed to develop indices that are relevant to the clinicians. These proof-of-princ ple studies will serve as a backbone for clinical trials and, hopefully in the close future, to the exploitation of this technology in all intensive care un

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