Biophotonics Congress: Biomedical Optics (Translational, Microscopy, OCT, OTS, BRAIN) © Optica Publishing Group 2022

Miniaturized, multi-spectral optics for tissue differentiation

Konstantin Grygoryev, Huihui Lu, Simon Sorensen, Celina L. Li, Rachel Georgel, Daniel O'Hare, Ray Burke and Stefan Andersson-Engels

Tyndall National Institute, Lee Maltings Complex, Dyke parade, Cork, Ireland, T12R5CP

konstantin.grygoryev@tyndall.ie

Abstract: Identification of tumour margins during resection of the brain is critical for improving the post-operative outcomes. Present research aims to develop a miniaturized, optical system for simultaneous measurement of DRS and auto-fluorescence for brain tumour detection.

1. Introduction

Due to the highly infiltrative nature of Glioblastoma multiforme (GBM) and limited intraoperative visualization of the tumour margin, incomplete surgical resection has been observed to occur in up to 80 % of GBM cases, leading to nearly universal tumour recurrence and overall poor prognosis of 14.6 months median survival [1,2]. The current gold standard for tumour delineation is fluorescence guided resection (FGR) which used a surgical microscope in combination with a fluorescent contrast agent, the 5-aminolevulinic acid (5-ALA) [3, 4].Unfortunately even with use of FGR, definitive delineation between tumour infiltration zone and healthy brain tissue remains challenging due to subjectivity of visually identifying the magnitude of fluorescent signal [5, 6].

To address this problem, we have previously investigated a number of multi-spectral, clinical and laboratory based instruments designed to provide simultaneous diffuse reflectance spectroscopy (DRS) and quantitative fluorescence measurements [7, 8]. Our current aim is to miniaturize the detector optics and sensor footprint without sacrificing low-light sensitivity while maintaining the ability of the instrument to account for strong ambient illumination.

2. Materials and methods

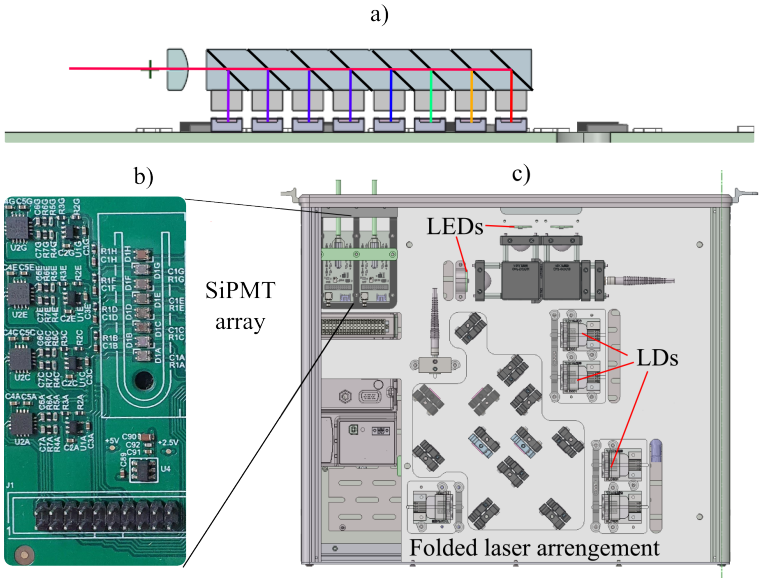

Fig. 1. a) Schematic of of spatial light separation between the SiPMTs. b) PCB with an array of eight SiPMTs. c) The schematic of hybrid light source which consists of 5 laser diodes in a folded arrangement as well as three LEDs.

2.1. *Detectors*

The DRS and auto-fluorescence measurements are performed using eight separate silicon photo-multipliers (SiPMT). Figure 1(a) shows a schematic of wavelengths-dependant spatial separation of light where a custom prism with eight dichroic surfaces is positioned above eight SiPMT. A set of eight bandpass filters, placed between detectors and the dichroics, further define the collection band and reduce channel cross-talk. The SiPMTs in turn are soldered to a compact PCB that houses amplifiers and an analog output for data acquisition (Figure 1(b)).

2.2. *Light source*

Figure 1(c) shows the CAD design of the hybrid light source. The source consists of five laser diodes and three LEDs. The wavelengths of each source are matched to one detection band. The laser diodes and LEDs are coupled into 200μm and 600μm fibres, respectively. Both the detector boards and the source are packaged into a compact enclosure of standard size.

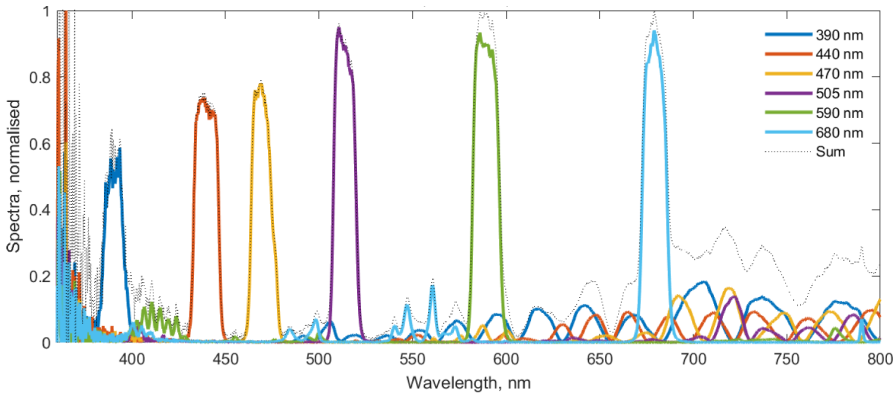

Fig. 2. Measured, normalized spectra of the detector array.

3. Preliminary results

As part of the development, this instrument is currently undergoing characterization of the optical elements. Figure 2 shows the measured spectra of six, longer wavelengths channels intended for measurement of auto-fluorescence intensity. In early 2022, further characterization experiments, such as estimation of dynamic range as well as fluorophore detection limits, will be performed prior to deployment of the instrument in the clinic.

References

1. M. Mischkulnig, B. Kiesel, M. Borkovec, L. I. Wadiura, D. Benner, A. Hosmann, S. Hervey-Jumper, E. Knosp, K. Roessler, M. S. Berger, and G. Widhalm, "High Interobserver Agreement in the Subjective Classification of 5-Aminolevulinic Acid Fluorescence Levels in Newly Diagnosed Glioblastomas," Lasers Surg. Medicine pp. 1–8 (2020).
2. S. W. Cramer and C. C. Chen, "Photodynamic Therapy for the Treatment of Glioblastoma," Front. Surg. **6**, 1–11 (2020).
3. W. Stummer, U. Pichlmeier, T. Meinel, O. D. Wiestler, F. Zanella, H.-J. Reulen, A.-G. S. Group *et al.*, "Fluorescence-guided surgery with 5-aminolevulinic acid for resection of malignant glioma: a randomised controlled multicentre phase iii trial," The lancet oncology **7**, 392–401 (2006).
4. N. Sanai, M.-Y. Polley, M. W. McDermott, A. T. Parsa, and M. S. Berger, "An extent of resection threshold for newly diagnosed glioblastomas," J. neurosurgery **115**, 3–8 (2011).
5. C. G. Hadjipanayis, G. Widhalm, and W. Stummer, "What is the surgical benefit of utilizing 5-aminolevulinic acid for fluorescence-guided surgery of malignant gliomas?" Neurosurgery **77**, 663–673 (2015).
6. J. C. Richter, N. Haj-Hosseini, M. Hallbeck, and K. Wårdell, "Combination of hand-held probe and microscopy for fluorescence guided surgery in the brain tumor marginal zone," Photodiagnosis photodynamic therapy **18**, 185–192 (2017).
7. H. Lu, K. Grygoryev, N. Bermingham, M. Jansen, M. O'Sullivan, G. Nunan, K. Buckley, K. Manley, R. Burke, and S. Andersson-Engels, "Combined autofluorescence and diffuse reflectance for brain tumour surgical guidance: initial ex vivo study results," Biomed. Opt. Express **12**, 2432–2446 (2021).
8. K. Grygoryev, H. Lu, C. L. Li, A. V. Zhdanov, R. Burke, and S. Andersson-Engels, "Multi-spectral clinical prototype for fluorophore detection," Front. Phys. **9**, 476 (2021).