Time-Resolved NIRS: a Clinical Study on Ischemic Stroke Patients

Marta Zanoletti[a*], Giacomo Giacalone[b], Davide Contini[a], Rebecca Re[a,c], Lorenzo Spinelli[c], Bruno Germinario[b], Luisa Roveri[b], Alessandro Torricelli[a,c]

[a]*Politecnico di Milano, Dipartimento di Fisica, Piazza Leonardo Da Vinci 32, 20133, Milano-Italy*
[b]*San Raffaele Scientific Institute, Via Olgettina 60, 20132, Milano-Italy*
[c]*Istituto di Fotonica e Nanotecnologie, Consiglio Nazionale delle Ricerche, Piazza Leonardo Da Vinci 32, 20133, Milano-Italy*
marta.zanoletti@polimi.it

Abstract: We present a clinical study conducted on 47 ischemic stroke patients to explore the potential of Time Resolved Near Infrared Spectroscopy in the process of neuromonitoring care.

1. INTRODUCTION

Ischemic Stroke (IS) is a global disturbance, which leads to insufficient blood supply to certain regions of the brain. It has been estimated that IS stroke accounts for 70% of the cases (about 820 thousand per year) with a consequent total cost amount of 45 billion €. In this framework, Near Infrared Spectroscopy (NIRS) is an appealing technique for probing different biological tissues non-invasively and in real time, giving a new set of information, which are of clinical relevance and could help clinicians broaden their insight on ischemic stroke in all the steps of ischemic stroke care. NIRS exploits the fact that light in the range 600-1100 nm can penetrate biological tissues for few centimeters due to the low of absorption of their main components (hemoglobin, lipids, water, etc..). In particular, in a Time-Resolved (TR-NIRS) approach, pulses of about 100 ps duration are injected into the medium and recollected at a certain source-detector distance. Information about the properties of the probed tissue are enclosed in the shape of the Distribution of the Time-Of-Flight (DTOF) of the backscattered photons [1]. It is then possible to directly calculate from the absorption coefficient, the absolute values of the concentration of the main constituents of the tissue such as oxygenated hemoglobin, deoxygenated hemoglobin (HbO and HbR, respectively) and thus, total hemoglobin (tHb=HbO+HbR) and tissue oxygen saturation StO_2 (HbO/tHb) in a reproducible way [2].
These parameters can be fundamental in finding a proper biomarker that can help predict the outcome of the ischemic stroke, based on the hemodynamic and metabolism of the area infarcted.

2. MATERIAL AND METHODS

The TR-NIRS based instrument, which was used at the Stroke Unit of San Raffaele hospital, was developed by the Physics Department in Politecnico di Milano. This single-channel device features three pulsed diode lasers at 690, 785 and 830 nm whose output is delivered to the sample by means of a 100 μm core fiber bundle. Backscattered photons are harvested by three 1 mm core POF fibers, which are coupled with three independent hybrid photomultipliers, each dedicated to a specific wavelength thanks to interferential filters. The DTOF is then reconstructed by three Time Correlated Single Photon Counting Boards hosted in an industrial PC. The final temporal resolution of the whole system is less than 200 ps at each wavelength, which is stable for several hours of operation. The characterization of this medical device was carried out following the well-established protocols for the performance assessment of TRS-based systems [3,4]. In collaboration with San Raffaele Hospital measurements on 88 controls and 47 ischemic stroke affected patients were carried out. Patients with Large Vessel Occlusion (LVO) were admitted to the study within 24 hours from symptoms onset. IS patients were grouped in TACS/PACS (Total or Partial Anterior Circulation Syndrome, N=36) and LACS (Lacunar Anterior Circulation Syndrome, N=5). The first group was further divided in recanalized (N=18) and non-recanalized (N=18) patients, according to their recanalization status (i.e. restoration of blood flow). All the subjects were measured on 6 standard positions covering the frontal (F3-F5, F4-F6), central (C3-C1, C4-C2) and parietal (P3-P5, P4-P6) regions of both left and right hemispheres according to the 10-10 international system. Furthermore, IS patients were measured on ad-hoc positions covering the stroke and non-stroke areas of both hemispheres as depicted from CT or MRI scan. The Ethical committee of the San Raffaele Hospital approved the present study.

3. RESULTS

As shown in Fig. 1, regardless of their recanalization status, significant differences have been found in the ischemic area between IS patients and controls for HbR. On the other hand, while not being significantly different from controls' values, HbO shows different values in the ischemic area with respect to the ipsilateral and contralateral

hemisphere for recanalized patients. These results reflect on the tHb, which is significantly higher from controls' values in the ischemic area but also with respect to contralateral and ipsilateral hemisphere of the recanalized patients. Finally, StO_2 is globally lower in recanalized patients with respect to non-recanalized patients. Results obtained for non-recanalized patients could reflect a lower metabolic activity accompanied by a residual blood flow originating from collateral networks or residual blood stagnating in the infarcted area. On the other hand, only recanalized patients showed significant lower StO2, indicating a global hemodynamic activation and metabolic compensation after restoration of blood flow in the affected area. Further details can be found in Giacalone et al. [5]. Finally, LACS patients did not show significant differences highlighting a possible limitation of the instrument in probing deeper tissues where a lacunar stroke occurred.

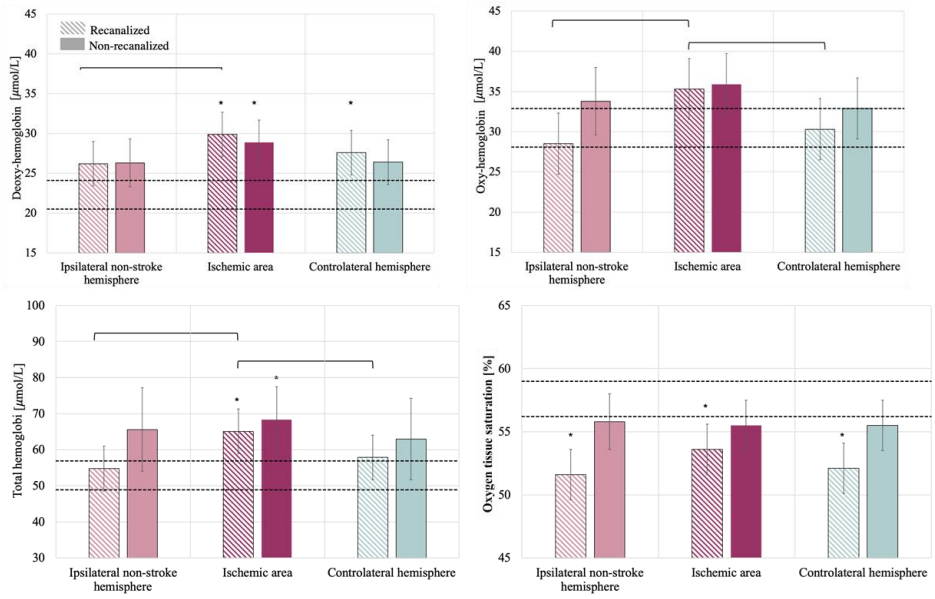

Fig. 1 Deoxygenated hemoglobin, oxygenated hemoglobin and total hemoglobin as well as saturation tissue of oxygen for both recanalized and non recanalized patients in the ischemic, ipsilateral non-stroke and finally, contralateral hemisphere. Hemoglobin species are expressed in µmol/L while StO_2 as a %. Values are compared with the ones obtained for age-matched controls whose 95% IC is here depicted by dashed lines (---). (*) $p<0.001$ while brackets represent statistical differences between different areas among IS patients.

4. CONCLUSION

This study demonstrates the ability of TR-NIRS to detect statically significant differences in hemoglobin species and saturation tissue of oxygen between controls and ischemic stroke affected patients, according to their recanalization status. In fact, StO_2 can be used as a fiducial marker for better understanding brain tissue status. This is a promising step towards the implementation of TR-NIRS device in real-life scenario during bed-side neuromonitoring care.

References

[1] F. Lange and I. Tachtsidis, "Clinical brain monitoring with time domain NIRS: A review and future perspectives," Appl. Sci. (2019).

[2] G. Giacalone, M. Zanoletti, D. Contini, R. Re, L. Spinelli, L. Roveri, and A. Torricelli, "Cerebral time domain-NIRS: Reproducibility analysis, optical properties, hemoglobin species and tissue oxygen saturation in a cohort of adult subjects," Biomed. Opt. Express **8**, (2017).

[3] A. Pifferi, A. Torricelli, A. Bassi, P. Taroni, R. Cubeddu, H. Wabnitz, D. Grosenick, M. Möller, R. Macdonald, J. Swartling, T. Svensson, S. Andersson-Engels, R. L. P. van Veen, H. J. C. M. Sterenborg, J.-M. Tualle, H. L. Nghiem, S. Avrillier, M. Whelan, and H. Stamm, "Performance assessment of photon migration instruments: the MEDPHOT protocol," Appl. Opt. (2005).

[4] H. Wabnitz, D. R. Taubert, M. Mazurenka, O. Steinkellner, A. Jelzow, R. Macdonald, D. Milej, P. Sawosz, M. Kacprzak, A. Liebert, R. Cooper, J. Hebden, A. Pifferi, A. Farina, I. Bargigia, D. Contini, M. Caffini, L. Zucchelli, L. Spinelli, R. Cubeddu, and A. Torricelli, "Performance assessment of time-domain optical brain imagers, part 1: basic instrumental performance protocol," J. Biomed. Opt. **19**, (2014).

[5] G. Giacalone, M. Zanoletti, R. Re, B. Germinario, D. Contini, L. Spinelli, A. Torricelli, and L. Roveri, "Time-domain near-infrared spectroscopy in acute ischemic stroke patients," Neurophotonics **6**, (2019).