Near-infrared spectroscopy study of tourniquet-induced forearm ischaemia in patients with coronary artery disease

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ABSTRACT

Near-Infrared Spectroscopy (NIRS) can be employed to monitor local changes in haemodynamics and oxygenation of human tissues. A preliminary study has been performed in order to evaluate the NIRS transmittance response to induced forearm ischaemia in patients with coronary artery disease (CAD). The population consists in 40 patients with cardiovascular risk factors and angiographically documented CAD, compared to a group of 13 normal subjects. By inflating and subsequently deflating a cuff placed around the patient arm, an ischaemia has been induced and released, and the patients have been observed until recovery of the basal conditions. A custom NIRS spectrometer (IRIS) has been used to collect the backscattered light intensities from the patient forearm throughout the ischaemic and the recovery phase. The time dependence of the near-infrared transmittance on the control group is consistent with the available literature. On the contrary, the magnitude and dynamics of the NIRS signal on the CAD patients show deviations from the documented normal behavior, which can be tentatively attributed to abnormal vessel stiffness. These preliminary results, while validating the performance of the IRIS spectrometer, are strongly conducive towards the applicability of the NIRS technique to ischaemia analysis and to endothelial dysfunction characterization in CAD patients with cardiovascular risk factors.

Keywords: NIRS, near-infrared spectroscopy, cardiovascular risk, CAD

1. INTRODUCTION

In the last few years the interaction between endothelial dysfunction and coronary risk factors has attracted growing interest, as an opportunity of assessing the possibility of interventions in the long preclinical phase of cardiovascular disease. Actually, a correlation between the impairment of endothelium-dependent vasodilation (such as of reactive hyperemia) and cardiovascular risk factors has been observed[1]. Moreover, it is also clear that endothelial function in the coronary arteries and peripheral circulation is closely correlated[2], and therefore an assessment performed on a peripheral district is significant to the purpose.

To this respect, near-infrared spectroscopy (NIRS) offers a simple, non-invasive method for the measurement of local perfusion and of oxygen saturation of tissue. Moreover, NIRS instrumentation offers broad scope for dedicated low-cost implementations. The purpose of the present study has therefore been to perform a preliminary evaluation of NIRS as an indicator of anomalies in the peripheral response to induced ischaemia and subsequent reactive hyperemia in patients with cardiovascular risk factors and coronary artery disease (CAD). Because of the simplicity in setup, control and repeatability, the ischaemia has been induced by inflating a tourniquet around the arm of the subjects under examination, and the response has been observed on a large forearm muscle.

2. MATERIALS AND METHODS

The ischaemia has been induced by occluding the blood flow with a pressure-controlled fast-inflating cuff (AG 101, Hokanson, U.S.A) connected to a suitable clean air source (E 20, Hokanson, U.S.A.). The cuff has been applied around the patient left arm.

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The patient systolic and diastolic pressure and heart rate have been measured using a portable oscillometric system (Visomat Comfort, Roche Diagnostics, Italy). The measurement cuff has been applied on the right arm, symmetrically with respect to the occlusion cuff. Between the measurements, the cuff has been kept loosely wrapped in position.

The NIRS measurements have been performed with IRIS, a research-grade apparatus developed in the framework of the activities of The National Institute for Physics of Matter - Italy (INFM) and of the Clinical Engineering Division of IRCCS Policlinico S.Matteo, Pavia, Italy. As the instrument structure is described elsewhere[3], it will be only briefly recalled.

IRIS is composed by a modular computer-based acquisition system, dedicated to NIRS acquisition. For the measurements described in this paper, the acquisition system has been equipped with a digital front-end module[4], which is capable of measuring the continuous-wave NIRS backscattering of the tissue under examination at 4 wavelengths on a single measurement site, through the connection to a suitable probe head. The backscattered light intensities at the four measurement wavelengths are sampled at a rate of 1 sample/s and stored on a hard disk for postanalysis.

The probe head carries four plastic-case LED sources with nominal peak wavelengths of 880, 850, 700 and 660 nm and a transimpedence-amplified plastic-case photodiode. The sources and the detector are shielded and encapsulated in a potting compound. A metal retainer ring ensures sufficient mechanical robustness. The source-to-detector separation is 15 mm.

The probe has been applied to a large muscle on the patient forearm by interposing a layer of a refractive index matching gel in order to minimize artifacts due to patient movement. It has been held into position by an adhesive strip and an elastic retaining cuff, which acts also as a shield from the ambient light.

pO_2-pCO_2 measurements have been performed transcutaneously with an electrochemical transcutaneous oximeter (TCM3, Radiometer, Copenhagen) equipped with a combination electrode. The instrument has been connected to a personal computer for data acquisition at a sample rate of 1 sample/s. The electrode, held a temperature of 43°C has been applied, after the required calibration with a standard gas mixture, as near as possible to the NIRS probe. The electrode response time is 7 s for pCO_2 and 20 s for pO_2.

A 12-derivation electrocardiogram (ECG) has been recorded using a standard electrocardiograph (ECT WS2000, Remco, Italy), which stores the ECG on a personal computer. As the induced ischaemia, even if not presenting any specific risk, can be quite painful in patients with impairment of peripheral circulation, the main purpose of the ECG monitoring was to ensure real-time on-line assessment of the patient conditions throughout the whole procedure.

For the occlusion checks, we employed a Spectradop 2 ultrasonic Doppler flowmeter (D.M.S., France), operating at a frequency of 8 MHz.

No automatic synchronization facility is provided between the instruments. The acquisition has therefore been manually started by the operator with a known timing, and the acquired data have been temporally aligned during postanalysis.

The measurements have been performed on a control group of 13 healthy subjects and on 40 patients with cardiovascular risk factors, who udergone regular diagnostics tests and agreed to the study. Of these, the cardiac risks present were: hypertension (57%), dyslipidemia (70%), cigarette smoking (67%). 85% of the patients presented angiographically documented CAD. The mean number of risk factors is 1.9, with a standard deviation of 0.9.

During the test, the patients have been kept supine, at rest up to full stabilization of the blood pressure and heart rate. The instrumentation has been applied to the patient after all appropriate calibrations, and the measurement have been started only after all the signals reached a stationary value. Basal values of the NIRS transmittance signals have then been measured and averaged for 30 s, and used as reference for signal stability evaluation. Let $t = 0$ be the acquisition start time. At $t = 60$ s the tourniquet has been inflated at a pressure 50 mmHg higher than the systolic pressure, verifying the occlusion on the radial artery using the Doppler flowmeter. At $t = 240$ s (i.e. after 3 minutes from the occlusion) the tourniquet pressure has been released. The recovery has been recorded up to $t = 720$ s.

As shown in the following paragraphs, most of the analysis has been performed on the raw NIRS data. The reconstruction of perfusion and saturation variations from the continuous-wave NIRS data has been performed using a simple Lambert-Beer model, as extensively treated in the literature[5]. As only the morphology of the signal has been analyzed, no significant variations to the results has been seen after the correction of the model to account for the wavelength dependence of the optical pathlength, again derived from the literature[6].

3. RESULTS AND DISCUSSION

An example of the NIRS transmittance fractional deviations from the basal values (BRDs, baseline-referenced deviations), acquired on a healthy voluntary at the four measurement wavelengths, is reported in Figure 1.

In particular, the BRDs will be defined as

$$BRD = I / I_b - 1$$

where I is the backscattered light intensity and I_b its basal value. Its morphology is fully consistent with the literature[7]. On a number of patients, however, we observe the anomalous signal reported in Figure 2.

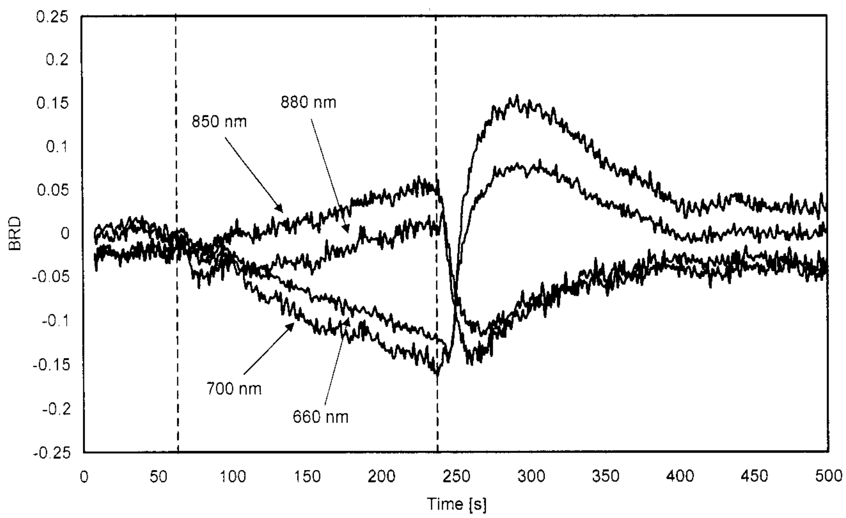

Figure 1: Baseline-referenced deviations of the NIRS transmittance during forearm ischaemia. The dotted lines indicate onset and release of the occlusion.

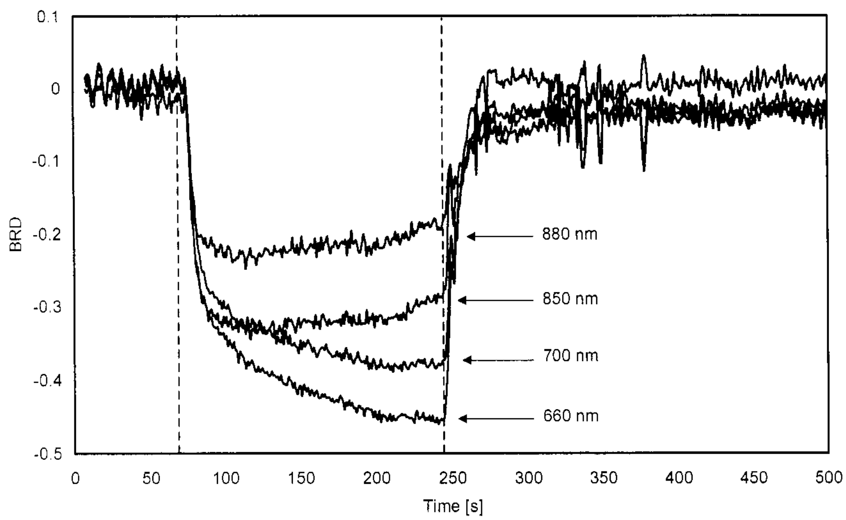

Figure 2: Anomalous baseline-referenced deviations of the NIRS transmittance. Again, the dotted lines indicate onset and release of the occlusion.

A consistency check on the pO_2-pCO_2 measurements confirm an occlusion with constant oxygen consupmption from the tissue, as it can be expected for so short ischaemia times. No significant pressure or heart rate variations are induced by the occlusion in any of the patients.

It can be noted that the anomalous signal is quite consistent with the literature in the case of a venous occlusion. This should not be however our situation, as the Doppler flowmeter confirms the absence of flow on the radial artery. As the absence of flow could be objectionable, since it can be difficult to monitor blood flow directly other than in large arteries, we turned our attention to the blood volume and saturation overshoot (reactive hyperemia) after the ischaemia release. In fact, if we look at saturation and blood volume variations, as derived from the NIRS data, (Figures 3 and 4), we see that to the anomalous signals correspond significant reductions of such overshoot.

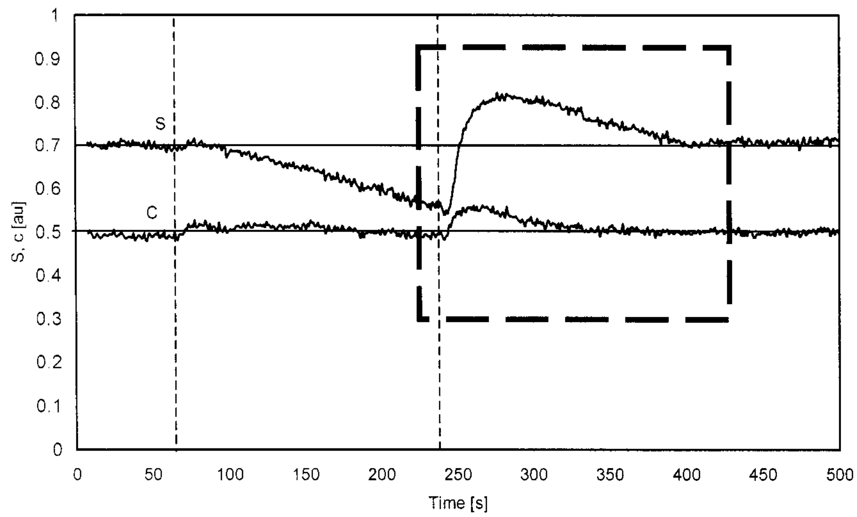

Fig. 3: Saturation (S) and concentration (c) derived from the transmittances in Figure 1. The full lines indicates the baseline values. The reactive ischaemia phase (overshoot) is highlighted.

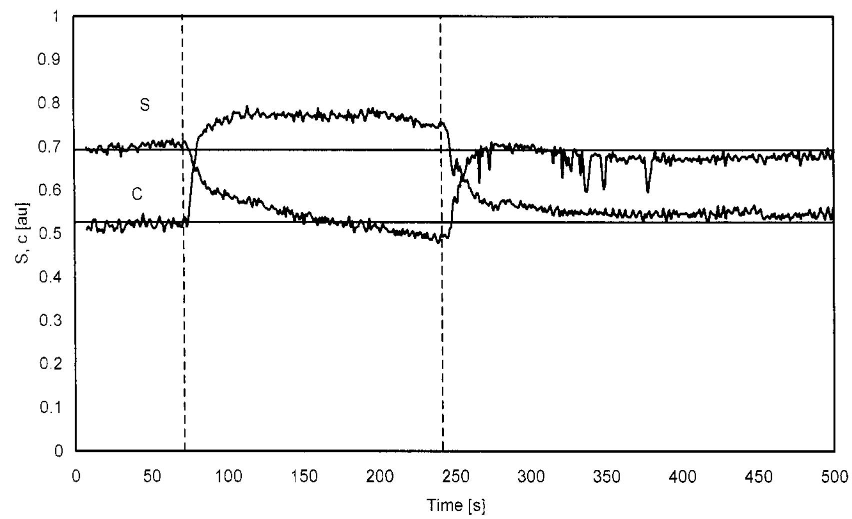

Fig. 4: Saturation (S) and concentration (c) derived from the transmittances in Figure 2. The full lines indicates the baseline values. Note the absence of overshoot.

Of the 40 patients, 6 were not sufficiently compliant to the operator directives to yeld a signal sufficiently clean for analysis. Of all the others, the signals have been classified as 'normal' or 'anomalous', as indicated in the preceeding paragraphs. The monovariate occurrences are reported in Figure 5.

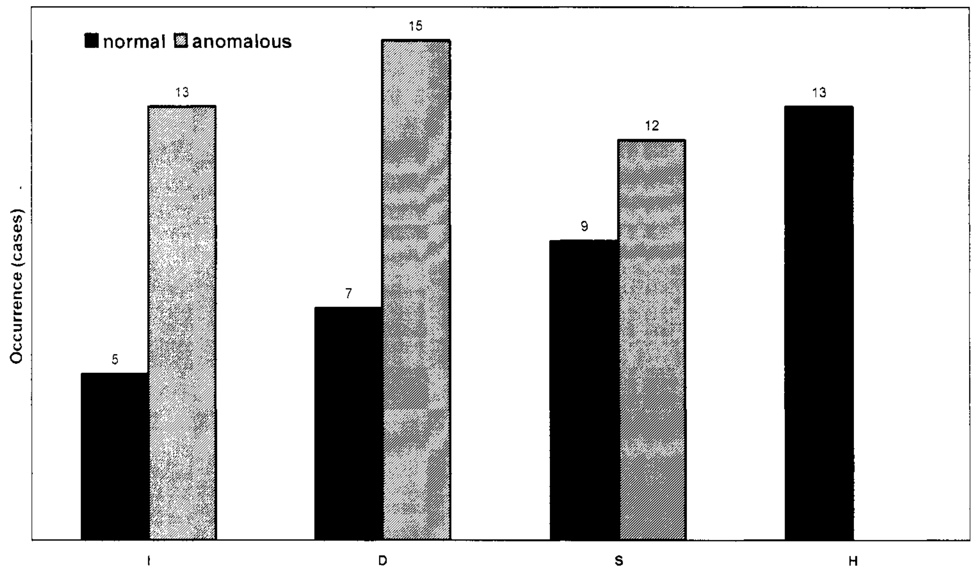

Figure 5: Occurrences of normal and anomalous signals. Risk factors: I – hypertension, D – dyslipidemia, S – cigarette smoking, H – reference group.

As the study has been dedicated to primary evaluation of the NIRS technique for signal contrast, the patient group is, at the present state, too scattered to allow an easy correlation to pathology, and a statistical analisys of the data is under development. We can distinctly note, however, that no healthy subject presents anomalous signals, while anomalies clearly occur with a high rate among the dislipidemic patients, and in the subjects who present a substantial hypertension. A few anomalies are present among the smokers too.

This agrees with the endothelium-dependent vascular relaxation anomalies which have been observed in the last years among subjects with cardiovascular risk factors, such as increased cholesterol levels[8], essential hypertension[9] or cigarette smoking[10]. In particular, the impairment of flow-mediated vasodilation could well accont for the absence of blood volume and saturation overshoot as the ischaemia is released and normal blood flow is restored.

4. CONCLUSIONS

The study, even though very preliminary in scope and sample choice, shows that the NIRS technique and the IRIS spectrometer can yeld clean signals on induced ischaemia on CAD patients. Moreover, the signals fit well in the framework of endothelial function anomalies in subjects with cardiovascular risk factors. This is strongly conducive towards the applicability of NIRS as a potential low-cost technique for endothelial dysfunction characterization in patients who present cardiovascular risk.

ACKNOWLEDGMENTS

We whish to thank L.Nespoli (IRCCS Policlinico S.Matteo, Pavia, Italy) for help in the measurements. We acknowledge funding from IRCCS Policlinico S.Matteo Current Research "Infrared Spectroscopy in a Clinical Environment".

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