

In vivo optical spectroscopy monitoring in a new model of muscular compartment syndrome

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Editor's key points

- Muscular compartment syndrome is a rare but serious postoperative complication that lacks proven non-invasive monitoring techniques.
- An *in vivo* optical spectroscopy monitor of regional oxygen saturation was tested in healthy volunteer subjects.
- This non-invasive monitor was as effective as invasive intracompartmental pressure measurements in predicting reversible nerve conduction block.
- Further studies are necessary to confirm clinical efficacy.

Background. Muscular compartment syndrome (MCS) is a rare but serious postoperative complication. *In vivo* optical spectroscopy (INVOS) monitors continuously and non-invasively regional oxygen saturation (rSO_2), and could predict the development of MCS.

Methods. In 10 healthy volunteers, we inflated a tourniquet to the mean arterial pressure to produce slight venous congestion and arterial hypoperfusion. Comparisons were made between the relative reduction in rSO_2 with baseline ($\Delta INVOS$) and the time to observe motor nerve block (with non-invasive electromyography). Neurological symptoms, pain, and invasive intracompartmental pressure (ICP) were assessed.

Results. In the eight volunteers completing the protocol, we observed a profound motor nerve conduction block, immediately reversible. Baseline values were: [mean (sd)] INVOS: 73.3 (8.9)% and ICP: 16.9 (8.6) mm Hg. At the time of the block, values were: INVOS: 46.4 (10.9)%, $\Delta INVOS$: 28.7 (10.6)%, and ICP: 70.0 (5.5) mm Hg. The time to reach the block was 33.0 (10.9) min, and to a $\Delta INVOS > 10\%$: 27.4 (10.4) min. Receiver-operating characteristic curves demonstrated a similar accuracy of ICP and INVOS to predict the occurrence of the block. Twenty minutes with a $\Delta INVOS > 10\%$ or ICP > 30 mm Hg were associated with a sensitivity and a specificity of 95% and 70%; or 91% and 65%, respectively.

Conclusions. We have developed a model of acute immediately reversible MCS. Monitoring using the INVOS technology is as accurate as measurement of ICP, and could be a useful tool to prevent development of intraoperative MCS.

Keywords: compartment syndrome; near-infrared spectroscopy

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Muscular compartment syndrome (MCS) is a rare but dramatic postoperative complication. Although there are many reported cases of acute lower limb compartment syndrome after abdominal surgery, the real incidence is unknown. It appears more frequent during lengthy procedures (especially in excess of 4 h duration) and is particularly associated with the lithotomy position.^{1–3} Possible mechanisms include reduced arterial inflow, obstructed venous/lymphatic outflow, and local increase in pressure (e.g. due to improper placement or external pressure). However, MCS can be seen even after careful positioning.⁴ MCS is also associated with other conditions, including swelling, external compression, and vascular aetiologies. These factors contribute to a cascade of ischaemic injuries. Below a critical level of tissue perfusion pressure, there is a capillary occlusion with tissue hypoxia. Early signs and symptoms, linked to hypoxia, are pain and neurological

deficits, which are absent in anaesthetized or comatose subjects. Objective symptoms, such as oedema, are late and often reflect peripheral tissue damage and muscle necrosis. In this stage, fasciotomy is often needed, and there is a great risk of subsequent permanent functional impairment.¹ There is a clear need for a monitoring technique able to detect early the risk of MCS in anaesthetized or comatose patients.¹

We investigated whether *in vivo* optical spectroscopy (INVOS) can be an accurate tool for the detection of MCS. INVOS provides non-invasive continuous monitoring of regional oxygen saturation (rSO_2). The detection of temporal changes in rSO_2 from baseline and correction of reductions are the basic principles of this type of monitoring. The depth of sensitivity is 1.5–3 cm, which allows analysis of the anterior tibial compartment, which is one at the site of greatest risk of developing MCS.

We hypothesized that a change in rSO_2 predicts the time to onset of nerve block, an early sign of MCS, and invasive intracompartmental pressure (ICP). Since MCS is rare and unethically provoked, we reproduced the pathophysiology seen in MCS occurring during abdominal surgery (i.e. reduced arterial inflow, obstructed venous/lymphatic outflow, and external pressure) in an immediately reversible model in healthy volunteers.

Methods

After approval of the Ethical Committee of St-Luc Hospital (EC N°B40320107753) provided by the CEBH of the Université catholique de Louvain (Brussels, Belgium), and obtaining written informed consent, we included 10 healthy male volunteers, over 18 yr. Exclusion criteria were arterial hypertension, peripheral neuropathy, peripheral vascular disease (arterial or venous), chronic pain, use of analgesics and anti-thrombotics/anti-coagulants, or history of right tibial or fibular fracture. The goal was to detect possible correlation between the time of rSO_2 reduction, measured by INVOS, and the time of ICP increase leading to functional neurological abnormalities (nerve conduction block more than 30%).⁵ No data permitted sample size calculation, and power analysis was therefore not performed. Pain, paraesthesias, and sensory and motor neurological deficits were assessed clinically.

Oximeter skin stickers (INVOS Somanetics 5100C) were placed 1–2 cm below the tourniquet (see below) between and parallel to the fibula and the tibia. Absolute and relative decreases in rSO_2 were recorded. Other monitoring included pulse oximetry, heart rate, and non-invasive arterial pressure (NIAP). Subjective occurrence of pain, paraesthesia (as described by the subject), or both was also recorded. The presence of nerve conduction block was assessed by motor conduction of the peroneal nerve along the leg segment, stimulated just below the head of the fibula (Select, Viasys Nicolet, San Diego, California, USA). The compound motor action potential (CMAP) was detected on the extensor

digitorum brevis muscle with surface electrodes, before inflation and every 5 min during the inflation. A 30% decrease in CMAP amplitude was considered significant motor conduction block.⁵ Continuous invasive measurement of ICP was made using a 30 mm 20 G needle connected to a Datex S/5 multiparameter monitor (Datex Ohmeda, GE Healthcare) (Fig. 1). Using aseptic technique, the needle was completely inserted strictly perpendicular to the skin, 1–2 cm below the distal end of the tourniquet on the line joining the proximal and the distal ends of the fibula. A soft large (20 cm wide) tourniquet, similar to that used for manual non-invasive pressure measurement, was used to induce intracompartmental compression. The proximal end of the tourniquet was placed 3 cm below the proximal end of the fibula to avoid direct nerve compression. Tourniquet pressure corresponded to mean arterial pressure (MAP) determined by an automatic calculation by the multiparametric monitor from the first measurement of NIAP. This value was chosen as tourniquet pressure, to mimic the pathophysiology of intraoperative MCS. Indeed, MCS is a consequence of increased capillary hydrostatic pressure, increased venous pressure, decreased blood flow, and direct pressure on the calf leading to muscle ischaemia and hypoxia.^{1 2 4 6} Subsequent features, occurring in patients but not in our reversible model, include reperfusion, tissue oedema, raised compartment pressure, and cellular damage/necrosis.² This model rapid simulation of all the diagnostic criteria of compartment syndrome in terms of pressure: >30–45 mm Hg of ICP with a diastolic arterial pressure/ICP pressure difference of 15–30 mm Hg, MAP/ICP pressure difference of 40 mm Hg without complete vascular occlusion.^{1 2 4 6} For safety reasons, inflation was limited up to the occurrence of nerve block, moderate pain (if any), or a maximum of 60 min, even in the absence of block. This period is classically not associated with tourniquet-induced lesions and has widespread use in lower limb orthopaedic surgery.⁶ Since small reductions in INVOS can reflect early consequences of ischaemia, a sensitive threshold was chosen, with a relative reduction of 10% considered significant.^{7 8}

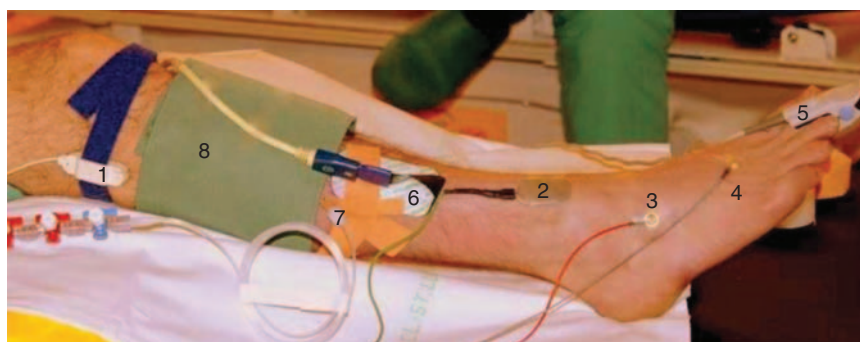


Fig 1 Experimental model of MCS. 1–4, EMG electrodes (Select, Viasys Nicolet); 5, pulse oximeter probe (Datex Ohmeda, GE Healthcare); 6, INVOS skin sticker (INVOS Somanetics 5100C); 7, needle (30 mm 20 G) connected to the pressure line; 8, tourniquet connected to a manometer. For more details, see text.

Statistical analysis

Data are presented as mean (sd). Comparisons are made between the time after a reduction in INVOS value $>10\%$ and the time of ICP elevation using linear regression. Receiver-operating characteristic (ROC) curves were constructed to determine the accuracy of both parameters to predict a nerve block. A P -value of <0.05 was considered statistically significant. NCSS 2004 (Hintze J, 2004, NCSS and PASS, Number Cruncher Statistical Systems, Kaysville, UT, USA) was used for all analyses.

Results

Inadvertent vascular puncture or haematoma due to the needle inserted to monitor ICP invasively was not observed. No complications (persistent pain, neurological deficit) occurred. Baseline characteristics are detailed in Table 1. Baseline values were for INVOS 73.3 (8.9)%, and for ICP 17 (9) mm Hg.

Two volunteers dropped out. One asked to stop the procedure, 20 min after inflation of the tourniquet due to spontaneous paraesthesias without pain or nerve block and without modification to the INVOS. Another was excluded for the absence of a nerve block despite 60 min of elevated ICP. In the eight volunteers completing the protocol, we observed a significant motor nerve conduction block of the peroneal nerve ($>30\%$ decrease in CMAP amplitude), which was immediately reversible. The ICP increased immediately after inflation of the tourniquet (Fig. 2); clinically, the pressure was transmitted to the whole calf. The time of ICP >30 mm Hg needed to observe a nerve block was 33 (11) min. Hypesthesia was present in all but one volunteer. Paraesthesias were described by all but two volunteers. All nerve blocks disappeared immediately (<30 s). Pain, when present (mild, and only in two volunteers), disappeared immediately (<10 s). ICP normalized in <5 min in all volunteers [ICP 5 min after deflation: 14 (5) mm Hg].

At the time of the block, INVOS values were 46.4 (10.9)% (Fig. 3). The relative reduction, compared with baseline (deltaINVOS), was 28.7 (10.6)%. The ICP was 70.0 (5.5) mm Hg. The time to reach nerve block from the beginning of the procedure was 33.0 (10.9) min, and from a deltaINVOS $>10\%$ was 27.4 (10.4) min. ROC curves demonstrated a similar accuracy of the time of ICP >30 mm Hg as the time after

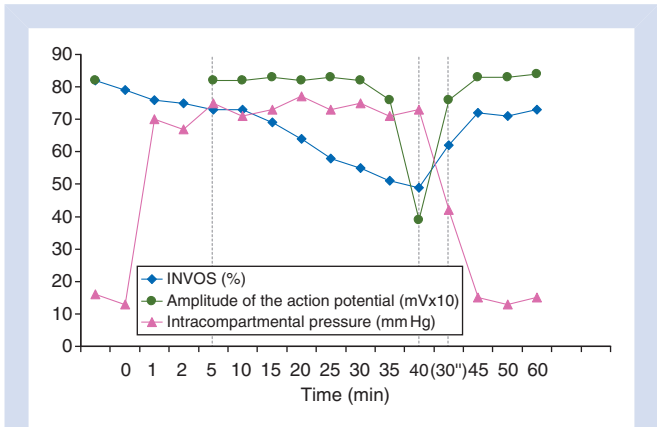


Fig 2 Representative pattern of measurements during the procedure in one volunteer. The tourniquet was inflated at time 0, and deflated at time 40 min. Nerve conduction normalized in 30 s after deflation, INVOS value in 5 min, and ICP in 10 min. Time is expressed in minutes (and seconds: "). Vertical lines in the graph show changes in the time scale.

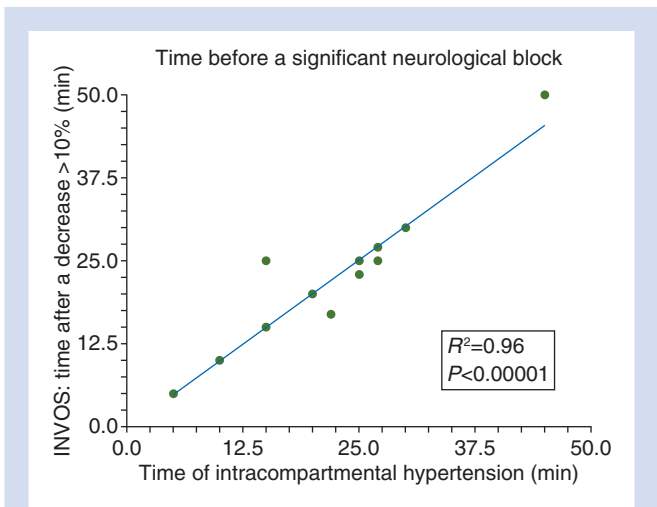


Fig 3 Correlation between time of ICP (>30 mm Hg) observed before occurrence of nerve block ($>30\%$), and time after reduction in the INVOS value of $>10\%$ (compared with baseline).

Table 1 Baseline characteristics of healthy volunteers (eight males) before the inflation of a tourniquet on the right leg. Values are expressed as mean (sd). INVOS, *in vivo* optical spectrometry

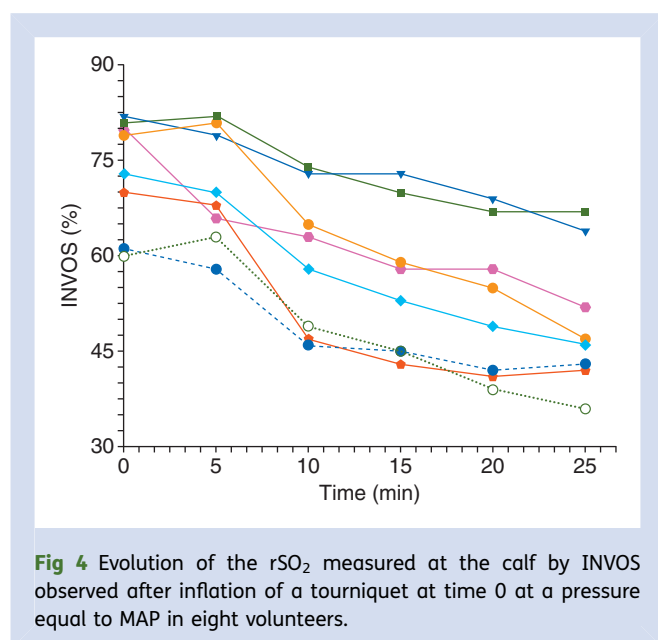
Age	33 (25–39)
Weight (kg)	68 (11)
Height (cm)	174 (7)
BMI (kg m^{-2})	22.2 (2)
Heart rate (beats min^{-1})	75 (10)
Mean arterial pressure (mm Hg)	94 (6)
INVOS (%)	73 (9)
Intracompartmental pressure (mm Hg)	17 (9)
Calf perimeter (cm)	36.3 (1.3)

deltaINVOS $>10\%$ to predict the occurrence of nerve block (Figs 4 and 5) ($P>0.05$ between the two methods, and $P<0.001$ compared with 0.5). The time of deltaINVOS $>10\%$ during 20 min predicted the presence of nerve block with a sensitivity and a specificity, respectively, of 95% and 70% compared with, 91% and 65%, respectively, for ICP >30 mm Hg during 20 min (Table 2).

Arterial pressure, heart rate, and pulse oximetry did not change significantly during the procedure (data not shown).

Discussion

Using a human model of MCS, we have shown that use of the non-invasive optical spectroscopy monitor INVOS (time after



deltaINVOS >10%) is as accurate as the time of elevated ICP to predict profound nerve block. This is potentially clinically useful since nerve block is an early sign of MCS.

MCS is the consequence of elevated tissue pressure on nerves and muscles, leading to ischaemia, pain, damage, and necrosis. The hypoxic damage causes release of vasoactive substances that increase endothelial permeability, which in turn increases further the pressure and tissue damage. At neurological examination, a sensory deficit is present early.^{1 4 5} Reduced CMAP amplitude and slower nerve conduction velocity is observed, with early involvement of sensory and motor nerves. Some nerves are more sensitive to conduction block, such as the peroneal nerve in the tibialis anterior compartment, resulting in a loss of sensitivity in the first interdigital space. The early appearance at this level and the ease in monitoring it led us to study this non-invasive sign of neurological dysfunction. CMAPs were preferred to sensory potentials. The amplitude of sensory nerves is much lower than that of motor nerves, and this amplitude decreases much more than motor responses as a function of the distance between stimulation and detection points. In clinical practice, conduction block is usually determined from motor nerve conduction studies, particularly in peroneal neuropathies.⁵

Several methods have been described to help in the diagnosis and monitoring of MCS. The gold standard is invasive measurement of ICP. Magnetic resonance imaging can demonstrate tissue oedema and changes in tissue density, but only when neurological symptoms are already present. Scintigraphy and perfusion studies are used in the study of chronic MCS more than a diagnostic tool in acute situations. Arterial Doppler is not often used since disappearance of blood flow is a very late sign. In summary, all these methods are inaccurate in the early diagnosis of acute MCS, and lack sensitivity, specificity, or both in this setting.⁶

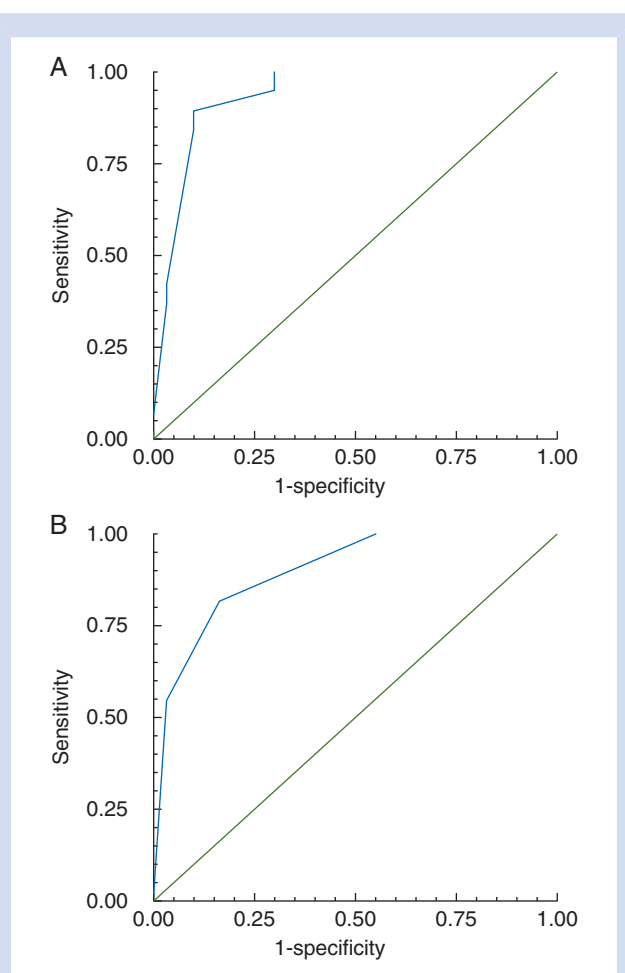


Fig 5 Sensitivity and specificity of different durations of ICP >30 mm Hg (A), or reduction in INVOS value >10% (B) to predict occurrence of nerve block. (A) AUC=0.93. (B) AUC=0.90. $P < 0.001$ compared with 0.5. $P > 0.05$ between A and B curves.

Table 2 Sensitivity and specificity of duration of reduction in INVOS value (compared with baseline) of >10% (deltaINVOS >10%) and of an ICP of >30 mm Hg (ICP >30) to predict occurrence of nerve block

Time (min)	deltaINVOS >10%		ICP >30 mm Hg	
	Sensitivity (%)	Specificity (%)	Sensitivity (%)	Specificity (%)
5	100	0	100	0
10	100	23	100	23
15	100	47	100	45
20	95	70	91	65
25	84	90	82	84
30	37	97	55	97

INVOS is one application of near-infrared spectroscopy (NIRS). Absorption in the infrared spectrum is produced by various chromophores including haemoglobin,³ which absorbs at different wavelengths depending on its state of

oxidation. The relative reduction in rSO_2 from baseline was used rather than the absolute value. Many physiological factors explain the large range in normal values, which justifies monitoring of tendencies more than absolute values.⁹ A relative reduction of 10% was considered clinically significant, since a sensitive monitor is needed to prevent MCS. It has been shown that early small reductions in rSO_2 can reflect consequences of anaemia and ischaemia linked to neurological symptoms.^{7 8}

This is not the first study to assess the place of NIRS in an acute model of MCS. Gentilello and colleagues¹⁰ described its use in a study involving 15 volunteers using another NIRS device (Biospectrometer NB Oximeter, Hutchinson Technology). The authors found a significant association between perfusion pressure and compartmental rSO_2 with variables such as ischaemic nerve conduction.¹⁰ This study used a model including gradual increase in pressure, leading, in our opinion, to much more venous congestion, at least in the initial phase. This and the different device used are the major differences between the two studies. The study by Gentilello and colleagues does not reflect the same processes involved in our study. Subjects in the lithotomy position probably suffer initially from decreased arterial inflow or venous outflow and direct pressure;^{2 4} and our model reproduces all these factors. In the model used by Gentilello and colleagues, venous congestion is the first event, as in some trauma patients, which is not necessarily the case in the lithotomy position. However, even with a different model and with a different device, the conclusions of the two studies are similar.

Several cases have been reported of the diagnostic use of NIRS in established acute MCS.^{2 6} Our work suggests a place for intraoperative use of NIRS to detect and prevent MCS early. rSO_2 assessed by INVOS or other NIRS devices¹⁰ is sensitive in detecting early signs of MCS, at least in experimental conditions. Our results suggest that a sensitive cut-off is $\Delta INVOS > 10\%$ over 20 min to warn clinicians to check and correct factors linked to MCS, especially position of the legs and calves. Taking into account the relatively low prevalence of postoperative MCS, further studies will probably focus on prospective follow-up of large cohorts to confirm these results.

A limitation of our work is the small number of volunteers involved. A larger number could help limit the impact of the large range of the absolute value. Nevertheless, a pragmatic approach leads us to develop sufficiently sensitive parameters for use in all patients. Another limitation is the depth of analysis, which is limited to 1.5–3 cm. This allows analysis of the anterior tibial compartment, which is at the highest risk of developing MCS, but it does not allow analysis of the deep posterior compartment where the risk of MCS is also present.⁶ Moreover, our results cannot be extrapolated to cases of obesity or massive interstitial oedema. In an animal model, however, NIRS was sensitive when MCS was induced by intramuscular infusion of albumin.¹¹ Finally, the two volunteers dropped from the analysis are not indicators of failure of the model, but more a sign of the careful protocol designed to avoid excessive discomfort.

Conclusion

Compartment syndrome is a serious complication of major surgery, most often observed during long procedures or with extended lithotomy position. Intraoperative detection of compartment syndrome is difficult due to lack of validated and easy-to-use, non-invasive continuous monitoring. We have developed a model of acute MCS, immediately reversible, in healthy volunteers. Our results show that monitoring of rSO_2 with the INVOS device is as accurate as continuous monitoring of ICP, and represents a possible way to prevent development of MCS, intraoperatively.

Declaration of interest

This study was investigator-driven, and the manufacturer (Somanetics) had no role in any part of the experimentation, the results interpretation, or the publication decision.

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