

# NOL MONITORING IN COLORECTAL SURGERY

## Clinical Experience Paper

### Introduction

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Pain after surgery is a major concern for patients, especially when it is undermanaged (Apfelbaum JL. 2003). Postoperative pain delays mobilization and oral intake after surgery, as well as increasing the risk of chronic pain after surgery (Kehlet H 2006). Colorectal cancer is the third most common cancer, with 1.2 million new cases a year, the majority of which undergo surgery (Karsa LV. 2010).

Colorectal surgery using a laparoscopic approach has gained wide acceptance because it is associated with reduced pain and/or analgesic consumption, lower morbidity including reduced wound infection, a faster recovery and a shorter hospital stay, without compromising surgical outcome (Lloyd GM. 2010). Interestingly, a recent study (Franklin 2020) assessed the levels of postoperative pain in 434 patients undergoing elective colorectal surgery. Half the patients experienced moderate to severe pain (NRS >4) on the day of surgery, followed by 64%

on postoperative day 1, 59% on day 2, and 51% on day 3. The interindividual pain response to surgery was large. Postoperative pain ranged from 0 to 10 (NRS) after both minimally invasive and open colon and rectal surgery, despite adherence to the same pain management protocol within an ERAS protocol. The authors concluded that the majority, and young patients in particular, experience moderate to severe pain after open and minimally invasive colorectal surgery, despite following the ERAS perioperative program for analgesia, including epidural analgesia after open surgery, and local anaesthesia and opioids after minimally invasive surgery. The authors note that there is a need for effective and individualized analgesia after colorectal surgery, since the individual pain response to surgery is difficult to predict. In this paper we will outline the potential contribution of intraoperative nociception monitoring to improving patient recovery.

## ERAS Recommendations for Perioperative Anaesthetic Care

The 2018 guidelines for ERAS in colorectal surgery (Gustafsson U. 2019) recommend the avoidance of benzodiazepines and use of short-acting general anaesthesia (GA) agents in an opioid-sparing ERAS pathway allow rapid awakening with minimal residual effects. Propofol for induction of anaesthesia, combined with short-acting opioids such as fentanyl, alfentanil, sufentanil or remifentanil infusions, if opioids are required, minimizes residual effects at the end of anaesthesia. There is no strong data to support the recommendation of either anaesthetic gases or total intravenous anaesthesia (TIVA) using propofol infusions to maintain anaesthesia. The use of propofol TIVA may reduce post-operative nausea and vomiting

(PONV) in certain patients and there is data from a large retrospective study suggesting a beneficial effect of propofol on cancer outcomes, but no definitive recommendation can be made for this currently (Wigmore TJ. 2016).

Depth of anaesthesia monitoring using bi-spectral index (BIS) and maintaining a target between 40 and 60 can reduce the risk of awareness in high-risk patients (Punjasawadwong Y. 2014). The use of BIS with burst suppression monitoring to avoid overdose of anaesthesia in the elderly may have a role in reducing the risk of postoperative delirium and postoperative cognitive dysfunction in this patient population (Chan MT. 2013). Neuromuscular monitoring should be a standard of care and complete reversal of neuromuscular block is recommended.

## Anaesthetic Technique, Neuraxial Blockade, the Use of Epidural Anaesthesia/Analgesia and Multimodal Regimens

The response to surgical stress/nociception occurs through several pathways, the most important being the afferent nervous stimulation of the hypothalamus and anterior pituitary gland leading to the production of catecholamines and glucocorticoids (Wilmore DW. 2002). Neuraxial blockade has been shown in several studies to reduce the surgical stress/nociception response. It is well established that epidural blockade with local anaesthetics, initiated before and continued during and after surgery, is a successful modality to minimize the neuro-endocrine and catabolic response to colorectal surgery (Carli F. 2011). In addition to providing superior pain control, epidural analgesia has been shown to reduce ileus. The use of epidural catheters remains the gold standard in open colorectal surgery (Gustafsson 2019). However, in the last few years, the majority of colorectal surgeries are performed using a minimally invasive approach.

In recent years, the use of Transversus Abdominis Plane (TAP) blocks to reduce post-operative pain whilst minimizing the use of IV opioids and epidural catheters (in open surgeries) has grown. Three studies compared transversus abdominis plane (TAP) blocks with local anaesthesia infiltration into the wounds. Two of those studies showed the superiority of TAP blocks (Elamin G. 2015), (Tolchard

S. 2012), with one showing no difference (Ortiz J. 2012). Some studies (Bhatia N. 2014), (Şahin AS. 2017) have shown that TAP or oblique subcostal TAP (OSTAP) blocks decreased postoperative pain more than placebo or morphine alone. A few studies (El-Dawlatly A. 2009), (Ravichandran T 2017), (Bava EP. 2016), (Sinha S. 2016) showed no difference in pain scores of TAP blocks compared with placebo.

The ERAS guidelines recommend opioid avoiding or sparing techniques for postoperative analgesia in colorectal surgery as these approaches are associated with early mobilization, fast return of bowel function, fewer complications and a reduction in Length of Stay (LOS). Ideally, a multimodal strategy should be included in the intraoperative period already and be a continuum postoperatively (Gustafsson 2019). However, multimodal regimens may include combinations of multiple agents such as non-opioid analgesics (eg paracetamol, lidocaine, magnesium, dexmedetomidine, ketamine, gabapentin, NSAIDs etc), epidural blockade, and peripheral blocks which create challenges in determining the appropriate dosing and overall effectiveness. Therefore, a tool providing objective monitoring of the physiological response to nociception could be of great help in optimizing the multi modal regimen to the patient needs.

## NOL technology overview

The PMD-200 system consists of a proprietary monitoring unit, and a unique sensor platform which consists of a reusable non-invasive finger probe and a single-use sensor.

Using the sensor platform and advanced algorithms, the system processes signals from four signals and analyzes multiple nociception-related physiological parameters and their various derivatives, which correspond with the autonomic nervous system's response to noxious stimuli.

***The finger probe and single-use sensor continuously acquire physiological signals through the following four signals:***

- Photoplethysmograph (PPG)
- Galvanic Skin Response (GSR)
- Peripheral Temperature (Temp)
- Accelerometer (ACC)

From these four sensors the NOL algorithm extracts and analyses the following nociception-related physiological parameters: pulse rate, pulse rate variability, pulse wave amplitude, skin conductance level, skin temperature, movement, and their various derivatives.

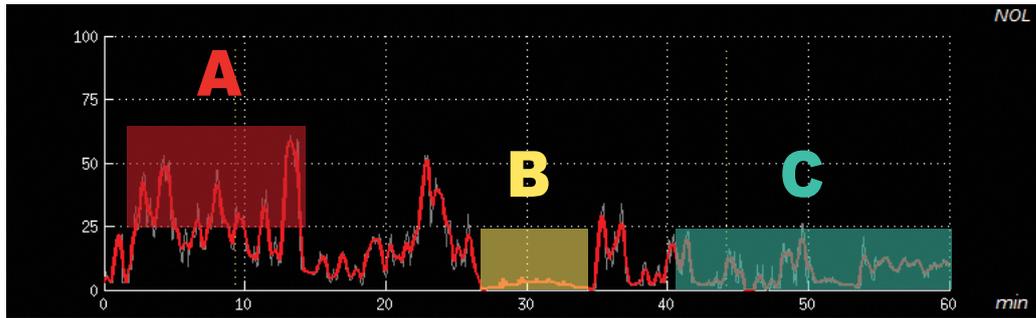


## NOL Index Range & Suggested Thresholds

The NOL index is a relative measure with a range of 0–100, where 0 represents no pain/nociceptive response and 100 represents extreme pain/nociceptive response.

The NOL index and trend are intended to support clinical decisions concerning the administration of analgesic medications.

The NOL index cannot anticipate noxious stimuli and thus a minimal level of analgesics should always be maintained.



- A.** NOL trend above 25 for more than one minute (whether constant or fluctuating) may indicate the patient requires additional analgesic therapy. Higher values indicate a stronger nociceptive response.
- B.** NOL below 10 for more than one minute during a painful stimulation may indicate excessive anti-nociception and reduction of analgesics may be considered. If regional analgesia is used, a low NOL is expected.
- C.** NOL between 0-25 represents an appropriately suppressed physiological response to noxious stimuli and indicates adequate analgesia.

## Meet the Expert



**Dan Longrois**  
MD PhD

Dan Longrois MD PhD is Professor of Anaesthesia and Intensive Care in Bichat-Claude Bernard and Louis Mourier Hospitals (both affiliated with the University of Paris), Assistance Publique-Hôpitaux de Paris, France. His research interests include cardiovascular and thoracic anaesthesia and intensive care, extracorporeal life support, pharmacology of anaesthetic drugs and monitoring of their effects.

Prof. Longrois, has been using NOL in regular practice for over 24 months.

## Using NOL in Clinical Practice - Expert Insights

### Clinical Challenges for the Anaesthetist in Colorectal surgery

Patients undergoing colorectal surgery have varying intraoperative analgesia needs as many patients suffer from chronic pain or have been receiving chemotherapy. Preventing opioid overdose is critical to promote fast recovery and prevent complications associated with opioid overdose such as ileus, post-operative nausea & vomiting (PONV). Therefore, the use of multimodal analgesia approaches including regional anaesthesia is a mainstay of ERAS and fast track programs. If spinal anaesthesia is used (typically epidural as a complement to general anaesthesia), there is a risk of anaesthetic drugs overdose that is difficult to recognize in the absence of BIS/NOL monitoring.

### Potential benefits of NOL monitoring

Personalized monitoring helps enable opioid sparing approaches that are achieved using multimodal techniques such as the use of regional blocks and non-opioid analgesia in combination with IV opioids (Coeckelenbergh S. 2021). In a recent controlled study in patients undergoing major abdominal surgery, NOL guided analgesia resulted in a 30% reduction in remifentanyl dosing with an 80% reduction in hypotensive events (Meijer 2019).

In colorectal surgery, NOL and BIS monitoring (particularly with the latest DSA display that enables deeper personalization of anaesthesia) complement each other, enabling the clinician to deliver smooth, balanced anaesthesia with patients experiencing a fast and more comfortable recovery with less pain and opioid related complications. A recently published controlled study (Meijer 2020) comparing NOL guided intraoperative analgesia to standard of care analgesia reported a reduction of 1.6 in NRS pain scores in patients undergoing major abdominal surgery in the NOL guided

group. We see that with NOL monitoring we are able to provide analgesia according to patient needs and be confident that regional blocks are working well. This then translates into patient benefits in the form of less postoperative pain and faster recovery.

### NOL monitoring during laparoscopic Colorectal surgery

Beyond choosing a general anaesthesia regimen (conventional, opioid-sparing, opioid-free) with or without epidural or a block (TAP) and after integrating the results of publications (that apply to a cohort of patients), anaesthesiologists must ask themselves some key questions when managing a single patient:

1. Is my regimen effective in controlling the response to surgery-induced nociception during the GA procedure?
2. Will my regimen avoid delayed extubation?
3. Will my regimen result into adequate immediate postoperative analgesia without side effects (respiratory depression, somnolence, nausea/vomiting)?
4. How will I estimate the effectiveness of the selected regimen for this specific patient? (knowing that heart rate and blood pressure values are not sufficiently sensitive and specific for indicating inadequate antinociception)
5. In case of arterial hypertension/hypotension, is there a contribution of insufficient/excessive antinociception?

When we combine EEG-based depth of anaesthesia monitoring (in this case using the BIS tracing) and monitors of the nociception-anti nociception balance (NOL being the monitor with the most impressive diagnostic performance), there is clear evidence that each monitor is providing different information that is valuable to clinical reasoning.

## Case Report

### NOL Supports Multimodal Anaesthesia in Colorectal Surgery

*Type Of Surgery:* Right colectomy with anastomosis, under laparoscopy

*Anaesthesia Regimen:* Continuous intravenous lidocaine with intermittent bolus injections of low doses of ketamine, propofol and sufentanil

*Patient Medical Background:* Hypertension, Peripheral vascular disease, previous stroke and paroxysmal atrial fibrillation.

*Chronic medications:* Atenolol, atorvastatin, ramipril.

*Report Date:* 27-Apr-2021

*Hospital Name:* Louis Mourier

*Physician's Name:* Prof. Dan Longrois

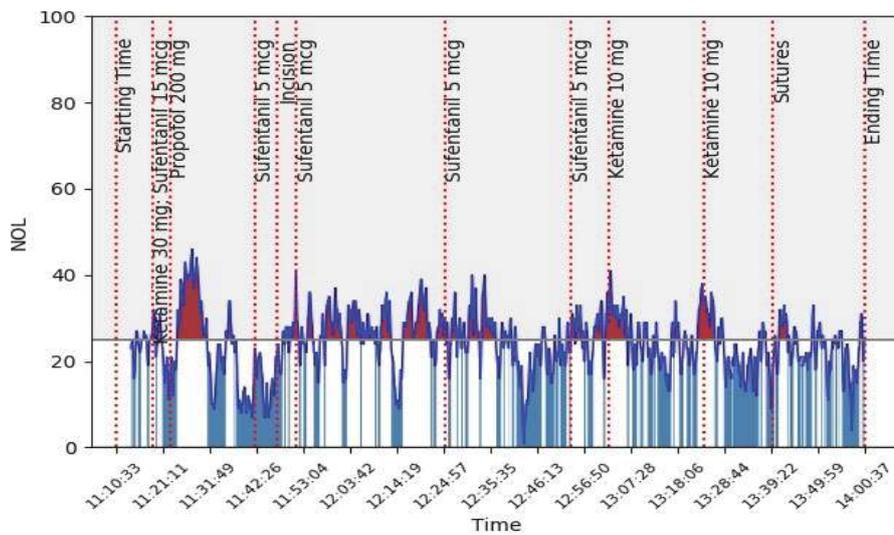
*Patient Weight:* 103 kg

*Patient Gender:* Male

#### Case Highlights

NOL excursions above 25 triggered additional sufentanil boluses. As blood pressure excursions from patient baseline did not exceed 20%, the anaesthesiologist decided not to correct them with vasoactive drugs. BIS values were kept between 40 and 60 using propofol and ketamine.

#### NOL® TREND - SESSION OVERVIEW



#### Conclusion:

Patient awoke with very low pain scores indicating that the analgesia regimen was effective and appropriate,

When using a combination of continuous intravenous lidocaine with/without intermittent bolus injections of low doses of ketamine, the NOL trends present differently from a classic anaesthesia regimen (boluses of opioids and continuous inhalation of sevoflurane for example). With continuous infusion of lidocaine, the NOL values are attenuated with less variance in the trends.

Dosing models for anaesthetic and analgesic drugs (including TIVA TCI) are based on cohort statistics and are not personalized to a particular patient. Using different patient monitors, the clinician can detect and correct for interpatient variability.

In this particular example, the BIS tracing was stable between 40-60, indicating that the hypnotic drugs regimen was effective

but there were moderate changes in the NOL tracing triggering additional sufentanil boluses. As blood pressure excursions from patient baseline did not exceed 20%, the anaesthesiologist decided not to correct them with vasoactive drugs. An interesting observation is the fact that upon CO<sub>2</sub> insufflation, there may be an increase in arterial blood pressure that in this patient, was not associated with an increase in NOL values and therefore no additional sufentanil was injected. An obvious benefit of NOL monitoring is to help to understand the mechanisms/

causes behind changes in arterial blood pressure. In the absence of NOL, an increase in arterial blood pressure may be interpreted as a lack of antinociception.

In the PACU, there was no doubt that the anaesthetic regimen was effective. The patient was comfortable reporting very low pain scores and no side effects such as PONV. No further opioids were required. On the following day, the patient reported no pain, adequate sleep and return of bowel sounds and flatus.

## Conclusion

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*Balanced anaesthesia and analgesia are an important component of colorectal surgery and monitoring both hypnotics and analgesia can help patient recovery whilst minimizing preventable side effects due to over and under opioid dosing.*

*NOL provides an objective monitoring tool that helps personalize opioid dosing to patient requirements.*

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