Technology Brief

Near-infrared spectroscopy (NIRS) for monitoring of paediatric patients at risk of low perfusion following cardiac surgery

February 2012
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**TECHNOLOGY BRIEF**

**REGISTER ID**
WP095

**NAME OF TECHNOLOGY**
NEAR-INFRARED SPECTROSCOPY (NIRS)

**PURPOSE AND TARGET GROUP**
INTRA-OPERATIVE AND POSTOPERATIVE MONITORING OF OXYGENATED HEMOGLOBIN IN THE SPLANCHNIC AND/OR RENAL VASCULAR BEDS OF NEONATES AND SMALL INFANTS UNDERGOING CARDIAC SURGERY

**STAGE OF DEVELOPMENT IN AUSTRALIA**
- □ Yet to emerge
- □ Experimental
- ✓ Investigational
- □ Nearly established
- □ Established
- □ Established but changed indication or modification of technique
- □ Should be taken out of use

**AUSTRALIAN THERAPEUTIC GOODS ADMINISTRATION APPROVAL**
- □ Yes
- ✗ No
- □ Not applicable

**INTERNATIONAL UTILISATION**

<table>
<thead>
<tr>
<th>COUNTRY</th>
<th>Trials underway or completed</th>
<th>Limited use</th>
<th>Widely diffused</th>
</tr>
</thead>
<tbody>
<tr>
<td>United States</td>
<td>✓</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Canada</td>
<td></td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Europe, Middle East, Japan, South Africa</td>
<td></td>
<td>✓ (likely)</td>
<td></td>
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</tbody>
</table>

**IMPACT SUMMARY**

During and immediately following major cardiac surgery in neonates and small children, the assessment of cardiac output is important, both to the brain and to other vital organs such as the gut and kidneys. Ideally, this monitoring should be non-invasive, accurately reflect cardiac performance, be easy to perform, and be reproducible. Near-infrared spectroscopy (NIRS) is a non-invasive technology that, via sensors placed on the skin, is able to continuously assess the degree of tissue perfusion and oxygenation in organs within about 2 cm of each sensor. Initially used to assess cerebral perfusion, clinical applications related to

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1 The website for Somanetics, manufacturer of the industry leader 'INVOS cerebral/somatic oximeter,' states that the system is in use at 700+ hospitals in the USA, including 80% of centres performing paediatric cardiac surgery, and that there are 1,200+ installs internationally (Somanetics 2011a). Further information on utilisation was not located.
the splanchnic and renal circulations are now being explored as an alternative to complex and invasive technologies that obtain intermittent readings.

**BACKGROUND**

During states of low cardiac output, cerebral blood flow becomes a priority for the body and may be better preserved than blood flow to other vital organs. As a result, sites other than the brain have been investigated for a possible correlation with invasive measures of systemic perfusion and oxygenation (e.g. abdomen, flank, and muscle) (Mittnacht 2010). Cardiac output is reflected in tissue perfusion and oxygenation and impacts on important outcomes such as survival, end organ function, and intensive care unit (ICU) length of stay (Bohn 2011).

Real-time, non-invasive detection of tissue oxygen saturation has been possible since 1985, with reports of the first human cerebral oximetry studies using NIRS. After United States (USA) Food and Drug Administration (FDA) approval in 1993, the first commercial cerebral oximetry device, INVOS, was marketed and three similar products have followed (Kaufman et al 2008). Cerebral NIRS monitoring for somatic saturation (rSO$_2$) was followed by two-site (cerebral and somatic) rSO$_2$ monitoring to capture data on perfusion and oxygenation in non-cerebral areas, particularly the kidneys and gut. However, validation of non-cerebral NIRS monitoring is still ongoing (Kaufman et al 2008).

Measurement of tissue oxygen saturation and tissue haemoglobin content is determined by the difference in intensity between transmitted and received light delivered at specific wavelengths (Murkin and Arango 2009). Most published studies have compared NIRS with some other measure of tissue oxygenation such as systemic venous oxygen saturation (SvO$_2$), serum lactate, and gastric tonometry (allows calculation of pH); however, the latter procedures can be complex and invasive.

According to Bohn (2011), some centres now use NIRS (cerebral and regional) as a routine part of both pre- and postoperative monitoring; however, ‘*although there are strong believers both for and against the usefulness of NIRS monitoring in improving the outcome in infants undergoing heart surgery, there is as yet no conclusive evidence to support it being adopted as a standard of care’.*

**CLINICAL NEED AND BURDEN OF DISEASE**

Congenital heart defects$^2,3$ are a major killer of infants aged <1-year. Overall, the incidence of their moderate and severe forms has been estimated (at least in the USA) at 6/1,000 live births.

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$^2$ Congenital heart defects are defined by the Australian Institute of Health & Welfare (AIHW) as ‘disorders of the heart or central (main) blood vessels present at birth, such as abnormalities of the heart or heart valves, defects of vessels such as the aorta and pulmonary artery or combinations of defects. Most children with congenital heart defects are treated with surgery or catheter-based techniques, usually in infancy or early childhood.’ (AIHW 2011)

$^3$ Although NIRS has a number of current and potential applications in monitoring oxygenation and perfusion, this report focuses on its use in young children post-surgery for congenital heart defects.
births (Hoffman and Kaplan 2002). As shown in Table 1, the most common congenital heart defects in Australia are transposition of great vessels, coarctation of the aorta, tetralogy of Fallot and hypoplastic left heart syndrome (AIHW 2011).

<table>
<thead>
<tr>
<th>Congenital heart defect</th>
<th>New cases, 2003</th>
<th>Deaths, 2005</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transposition of great vessels</td>
<td>103</td>
<td>8</td>
</tr>
<tr>
<td>Coarctation of the aorta</td>
<td>92</td>
<td>3</td>
</tr>
<tr>
<td>Tetralogy of Fallot</td>
<td>82</td>
<td>6</td>
</tr>
<tr>
<td>Hypoplastic left heart syndrome</td>
<td>37</td>
<td>25</td>
</tr>
</tbody>
</table>

Australian data for 1995 reported 1,648 operations for congenital heart defects with a mortality rate of 2.5 per cent. Operations by defect are shown in Figure 1 (Senes and Davies 1999).

DIFFUSION OF TECHNOLOGY

Four oximetry devices/manufacturers were mentioned in the retrieved literature (Murkin and Arango 2009, Mittnacht 2010), with Somanetics products dominating. The first three devices have received marketing approval in the USA with the Somanetics products being the first in 1993 and all four products are listed on the ARTG:

1. INVOS oximeter for cerebral ± somatic monitoring of site-specific regional oxygen saturation. ARTG number 186881 (26/07/2011). Manufactured by Somanetics Corporation (Troy, MI), sponsor Covidien Pty Ltd.

Searches can be conducted at: [http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm](http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm)
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- FORE-SIGHT cerebral oximeter, Manufactured by CAS Medical Systems (Branford, CN), sponsor Ecomed Pty Ltd. ARTG number 169394 (26/02/2010).
- Nonin oximeter used for the measurement of haemoglobin oxygen saturation for which a portion of the signal pathway is by means of radio transmission. Manufactured by Nonin Medical Inc (Minneapolis, MN), sponsor Device Technologies Australia Pty Ltd. ARTG number 194060 (23/01/2012).
- NIRO oximeter for monitoring the change of oxygenated and deoxygenated haemoglobin and the tissue oxygenation and tissue haemoglobin indices in human tissues such as brain and muscle in acute care and sports medicine situations. Manufactured by Hamamatsu Photonics (Hamamatsu City, Japan), sponsor SDR Scientific Pty Ltd. ARTG number 127674 (9/05/2006).

NIRS has been used as a research tool for nearly 20 years, particularly as a means of measuring cerebral oxygenation and perfusion during the intraoperative and postoperative period in neonates and infants. More recently however, this technology has begun to make the transition from research tool to bedside tool in clinical practice. This has already happened in North America. It is anticipated that NIRS will soon be marketed heavily in Australia, principally for anaesthesia and intensive care applications, and it is likely that there will be a great deal of enthusiasm for this technology amongst Australian clinicians.

**Comparators**

The accurate assessment of global tissue perfusion is crucial in the management of critically ill children in the ICU, and/or following major surgery. Typically, blood lactate levels and SvO₂ are used to assess adequate tissue perfusion, but both involve invasive procedures via central venous and/or arterial catheter access. Also, data are acquired intermittently rather than continuously, and may present a delayed picture of oxygen delivery and consumption. In contrast, NIRS is a non-invasive tool for continuously measuring tissue oximetry; the issue is whether it is accurate enough to replace currently employed invasive tools (Mittnacht 2010).

**Safety and Effectiveness Issues**

**Study description**

A total of three small studies assessing the use of NIRS for renal (Owens et al 2011, Ortmann et al 2011) and splanchnic oximetry (Kaufman et al 2008) were included in this brief (Table 2). All studies were conducted in the USA and enrolled neonates, infants and/or children with congenital heart defects who were undergoing either cardiac surgery (Kaufman et al 2008, Owens et al 2011), or cardiac catheterisation before surgery (Ortmann et al 2011). Information about the three included studies, including study design and size, level of evidence, inclusion criteria, outcomes assessed, and characteristics of enrolled patients are outlined in Table 2.
Table 2  Overview of studies included in this report

<table>
<thead>
<tr>
<th>Authors (Year); Location</th>
<th>Study Type &amp; Level of Evidence (See Appendix)</th>
<th>Patient Enrolment</th>
<th>Outcomes Assessed</th>
<th>Inclusion Criteria (Exclusion criteria)</th>
<th>Patient Characteristics</th>
</tr>
</thead>
</table>
| Kaufman et al (2008); USA (Colorado) | Prospective observational ‘data gathering’ study, diagnostic accuracy level III-2 evidence | n=20 neonates & infants, age ≤9 months, w/in 48 hours post-cardiac surgery at a single centre | Intervention: Monitored rSO2 of splanchnic bed & renal bed  
- Splanchnic rSO2 values vs a reference standard, intramucosal gastric pH  
- Splanchnic & renal rSO2 values vs reference standards:  
  - Serum lactate  
  - Svo2 | Patients who required surgery or catheter intervention for congenital heart defects: univentricular palliation (n=8) or biventricular repair (n=12) |  
- Median age, 6 days (range 4-220); 15 (75%) were age ≤30 days  
- Median weight, 3.3 kg (range 2-7); 15 (75%) were ≤3.7 kg  
- Wide range of cardiac conditions, e.g. HLHS, TA, TGA, TOF |
| Ortmann et al (2011); USA (Little Rock, Arkansas) | Prospective observational study, diagnostic accuracy level III-2 evidence | n=37 children, age <18 years, undergoing cardiac catheterization at a single centre | Intervention: Renal rSO2 compared w/ blood samples from renal vein and IVC  
Data further analysed for 2 weight groups: ≤10 kg & >10 kg | Children age <18 years undergoing medically indicated cardiac catheterisation |  
- ≤10 kg:  
  - Mean age, 4.8 months (range 3 days to 20 months)  
  - Mean weight, 6.2 kg (range 2.2-10)  
- >10 kg:  
  - Mean age, 83 months (range 18-163)  
  - Mean weight, 18.8 kg (range 10.4-67)  
- Wide range of cardiac conditions & procedures including heart transplant |
| Owens et al (2011); USA (Ann Arbour, Michigan) | Prospective observational study, prognosis level III-1 evidence | n=40 neonates & infants, age <12 months, w/in 48 hours post- cardiac surgery at a single centre | Intervention: Renal oximetry data collected & compared between two patient groups: subjects w/ low oximetry values (<50% for >2 hrs) vs those w/ normal oximetry values re:  
- Occurrence of AKI  
- Peak creatinine by 48 hours  
- Various aspects of post-op course | Biventricular repair w/ CPB (Excluded: prematurity, chromosomal disorder, single-ventricle anatomy, abnormal renal US or function) |  
- Median age, 81 days (range 5-330); 65% male  
- Median weight, 4.8 kg (range 2.4-8.8)  
- Wide range of cardiac conditions, e.g. TGA, TOF, double chamber or double outlet right ventricle, VSD |

AKI: acute kidney injury; CPB: cardiopulmonary bypass; HLHS: hypoplastic left heart syndrome; ICU: intensive care unit; IVC: inferior vena cava; rSO2: somatic saturation; Svo2: systemic venous O2 saturation; TGA: transposition of great arteries; TA: tricuspid atresia; TOF: Tetralogy of Fallot; US: ultrasound; VSD: ventricular septal defect; w/ : with; w/in: within,  
* Defined by the study authors as creatinine clearance <35 ml/min or absolute increase in creatinine of 0.4 mg/dl and at least 50% |

Kaufman et al (2008) assessed a non-invasive way to monitor low perfusion states in non-cerebral areas of neonates and infants immediately after cardiac surgery (level III-2 diagnostic accuracy evidence). The authors hypothesised that NIRS over the anterior abdomen would correlate with gastric tonometry, an accepted but more intrusive method of assessing splanchnic perfusion. NIRS over the dorsolateral flank (renal bed) was also explored. The goal was to determine how to best identify impaired splanchnic oxygenation due either to regional hypoperfusion or global low cardiac output.

The study by Ortmann et al (2011) explored the relationship of non-invasive NIRS readings over the renal bed to more intrusive venous oxygenation monitoring of blood obtained from a renal vein and the inferior vena cava (IVC) above the renal vein (level III-2 diagnostic accuracy evidence). A NIRS probe was placed on the skin laterally at the T10-L2 level and
NIRS readings were taken each time blood from the renal vein and IVC was drawn. The study assessed whether NIRS measurements from the renal bed correlated with venous oxygen saturations measured from the renal vein and IVC.

Owens et al (2011) differed in its approach, concentrating on the prognostic value of NIRS readings with respect to acute kidney injury (AKI) (rather than the technology’s diagnostic accuracy). The objective of this level III-1 prognostic study was to evaluate whether persistent low renal oximetry (<50% for >2 hours) was associated with AKI after cardiac surgery in neonates and infants. Renal oximetry was monitored every 20 seconds for 48 hours after cardiac surgery, and the primary caregivers of patients were blinded to the results. Patients were divided into ‘low oximetry’ or ‘normal oximetry’ groups based on the total time (>2 vs ≤2 hours, respectively) each patient spent below an oximetry threshold of 50 per cent. Comparisons at 48 hours after surgery were then made between the groups, including incidence of AKI, serum creatinine levels, serum lactate levels, and post-operative course details (e.g. ventilator days, vasoactive inotropic score peak, and hospital length of stay).

Safety

The most relevant adverse events due to the intervention (splanchnic or renal oximetry systems) would relate to the monitoring itself. The authors of all three included studies noted that no adverse events were attributable to this intervention.

Effectiveness

Table 3 displays the effectiveness results for key outcome measures, which are also briefly described below:

- Kaufman et al (2008): Results showed strong correlations between NIRS rSO₂ readings over the abdomen with the more conventional indices of oxygenation and perfusion (gastric pH, serum lactate and Svo₂). Associations over the flank were weaker. The authors suggested that NIRS is a valid tool for the easy, immediate, and non-invasive measurement of splanchnic rSO₂ in infants following cardiac surgery for congenital heart disease. However, a number study limitations were identified, including a small sample size, shortcomings of the NIRS technology (between-subject variability based on age, sensor probe position, and underlying blood volume), as well as questions regarding applicability to more diverse patient populations (e.g. those with large-volume ascites, pneumoperitoneum, severe abdominal wall oedema, or varying body size).

- Ortmann et al (2011): Results showed a strong correlation between NIRS readings and those obtained from renal and IVC samples in children ≤10 kg but not for those >10 kg. The difference was attributed to the shallow sampling depth of the NIRS probe (1-2 cm), i.e. infrared light likely did not penetrate deeper than subcutaneous tissue in larger children. The authors commented that further research is needed to determine how
measurements of flank NIRS values are correlated with renal function, and whether interventions aimed at improving perfusion and NIRS values results in less kidney injury and improved outcomes.

- Owens et al (2011): Results showed that prolonged low renal oximetry as measured using NIRS, appears to correlate with renal dysfunction, decreased systemic oxygen delivery, and the overall postoperative course in this patient group. The authors suggest that as a non-invasive technology that provides continuous real-time output, regional NIRS oximetry may ultimately prove to be a critical part of postoperative care in the paediatric cardiac ICU. However, the authors acknowledge a number of study limitations, including a small sample size and narrowly defined patient group.

Table 3  Effectiveness results from included studies

<table>
<thead>
<tr>
<th>Authors (Year)</th>
<th>Effectiveness Results</th>
</tr>
</thead>
</table>
| Kaufman et al (2008) | Spearman & Pearson correlation coefficient values:  
  - Splanchnic (abdominal) rSO\textsubscript{2} compared with:  
    - Gastric pH: r = 0.79; \( p < 0.0001 \)  
    - Serum lactate: r = 0.77; \( p < 0.0001 \)  
    - Svo\textsubscript{2}: r = 0.89; \( p < 0.0001 \)  
  - Renal (dorsal lateral) rSO\textsubscript{2} compared with:  
    - Gastric pH: r = 0.47; \( p = 0.22 \)  
    - Serum lactate: r = 0.64; \( p < 0.0001 \)  
    - Svo\textsubscript{2}: r = 0.79; \( p < 0.0001 \)  
  - Bland-Altman plots of difference vs average values for rSO\textsubscript{2} and Svo\textsubscript{2} demonstrated a narrower level of agreement for splanchnic vs renal site NIRS |
| Ortmann et al (2011) | Pearson correlation coefficient values for NIRS SO\textsubscript{2} vs. renal vein saturation & IVC saturation:  
  - Children ≤ 10 kg  
    - NIRS SO\textsubscript{2} vs. renal vein saturation: r = 0.82; \( p = 0.002 \)  
    - NIRS SO\textsubscript{2} vs. IVC saturation: r = 0.64; \( p = 0.004 \)  
  - Children > 10 kg  
    - NIRS SO\textsubscript{2} vs. renal vein saturation: r = 0.16; \( p = 0.57 \)  
    - NIRS SO\textsubscript{2} vs. IVC saturation: r = -0.11; \( p = 0.67 \) |
| Owens et al (2011) | Subjects w/ low oximetry values (<50% for >2 hours; n=8 or 20% of patients) vs those w/ normal oximetry values (n=32 or 80% of patients): *  
  All data presented as low oximetry group vs normal oximetry group  
  - AKI at 48 hours post-op: 50% vs 3%; \( p = 0.003 \)  
  - Peak creatinine levels by 48 hours: 0.8 ± 0.4 vs. 0.5 ± 0.2; \( p = 0.003 \)  
  - Average lactate levels by 48 hours: 3.0 ± 2.5 vs. 1.5 ± 0.7; \( p = 0.004 \)  
  - Post-op course:  
    - Ventilator days: 7.6 ± 3.6 vs. 4.2 ± 2.9; \( p = 0.008 \)  
    - VIS peak: 23.6 ± 17 vs. 13.8 ± 8.8; \( p = 0.03 \)  
    - Hospital LOS: 15.4 ± 5.7 vs. 12.7 ± 11; \( p = 0.51 \) |

AKI: acute kidney injury; LOS: length of stay; NIRS: near-infrared spectroscopy; rSO\textsubscript{2}: somatic saturation; Svo\textsubscript{2}: systemic venous O\textsubscript{2} saturation; VIS: vasoactive inotropic score; w/: with; w/in: within  
* The two groups were not significantly different with respect to age, weight, RACHS-1 score (risk scoring system for congenital heart disease), cardiopulmonary bypass (CPB) time, aortic cross-clamp time, or use of circulatory arrest.
COST IMPACT
The INVOS System costs US $30,000 and disposable sensors list at $280-$390 per pair, depending on the sensor type (discounted for high volume orders) (Somanetics 2011d). No studies evaluating the cost-effectiveness or cost impact of NIRS devices were identified from the retrieved material.

ETHICAL, CULTURAL OR RELIGIOUS CONSIDERATIONS
No issues were identified from the retrieved material.

OTHER ISSUES
Upcoming clinical trials

- NCT01382758: This planned case-control study (not yet open for participant recruitment) is an expansion of Kaufman et al (2008) that enrolled 20 patients at the University of Colorado. Planned enrolment is 150 children aged <4 years who are undergoing cardiac surgery with the use of cardiopulmonary bypass (CPB), examining the use of NIRS for early detection of AKI. Study completion is estimated to be late 2012.

- NCT01251939: A planned case-control study in Turkey (not yet open for participant recruitment; was due to start in early 2011) will assess NIRS monitoring of splanchnic and renal perfusion in ibuprofen treatment of patent ductus arteriosus in preterm infants. Planned enrolment is 20 children gestational age <32 weeks and <1500 g.

Conflicts of interest of study authors
No studies or study authors appear to have received compensation from industry, with funding generally coming from academic or hospital sources. However, there was no funding or conflict-of-interest information in Owens et al (2011) or Bohn (2011). Devices were supplied by a manufacturer in Kaufman et al (2008).

SUMMARY OF FINDINGS
The use of NIRS for monitoring tissue perfusion and oxygenation in the brain during and after cardiac surgery in small children appears to be established, at least in some institutions. However, in states of low perfusion the body may preserve cerebral blood flow at the expense of perfusion to other vital organs (e.g. gut and kidneys) and a non-invasive method of monitoring this would be ideal. Based on the three small low-quality studies reviewed in this brief, NIRS has potential in this application, and appears to be safe; however, additional research is required, ideally involving larger and more rigorous studies. At least one larger study may soon be underway in Colorado and the results from this study may assist in future decision-making regarding this technology.

Information from www.ClinicalTrials.gov
**HealthPACT Assessment:**

Based on the evidence presented in this brief, NIRS has a low sensitivity and specificity in assessing splanchnic and renal blood flow in neonates following cardiac surgery and consequently should not be relied upon in this clinical situation. Therefore, HealthPACT have recommended that no further assessment of this technology is warranted. In addition, as it is expected that NIRS will soon be marketed to Australian clinicians, HealthPACT have recommended that the findings of this brief be made available to neonatologists and other clinical groups that are likely to use this technology.

**Number of Studies Included**

All evidence included for assessment in this Technology Brief has been assessed according to the revised NHMRC levels of evidence. A document summarising these levels may be accessed via the following link on the HealthPACT website.

- Total number of studies: 3
- Total number of diagnostic accuracy level III-2 studies: 2
- Total number of prognosis level III-1 studies: 1

**References**


**SEARCH CRITERIA TO BE USED**

Near-infrared spectroscopy OR NIRS; Paediatric OR Cardiac OR Intensive care OR Anaesthesia