Neurology monitoring (Entropy) for depth of anaesthesia

April 2009

This technology summary is based on information available at the time of research and a limited literature search. It is not intended to be a definitive statement on the safety, efficacy or effectiveness of the health technology covered and should not be used for commercial purposes.

The National Horizon Scanning Centre Research Programme is part of the National Institute for Health Research
Neurology monitoring (Entropy) for depth of anaesthesia

Target group
Patients receiving general anaesthesia – may be particularly useful in total intravenous anaesthesia (TIVA) and for high risk patients such as those in obstetrics, cardiac surgery, and emergency care.

Technology description
The Entropy module has been designed to be used alongside current haemodynamic and neuromuscular monitoring parameters to monitor the delivery and associated effects of anaesthesia (the adequacy of anaesthesia). Three sensors attached to the patient’s head provide electroencephalography (EEG) and frontal electromyogram (FEMG) readings which are analysed to produce a score of 0-100 for response entropy (RE: response to stimuli), a score of 0-91 for state entropy (SE: depth of anaesthesia) and 0-100% for burst suppression indication (an isoelectric state). This analysis notes the irregularity, complexity, or unpredictability characteristics of a signal. A regular signal where the wavelength and amplitude are constant over time, would have a low entropy value and a signal with an irregular wavelength and amplitude, a higher entropy value. The lower the patient’s entropy value the more sedated they are. In clinical practice the Entropy module has the capacity to produce continuous data which can be stored and printed off.

Innovation and/or advantages
Use of the entropy module provides the anaesthetist with a method of directly monitoring neural activity in sedated patients that may reduce the amount of anaesthetic delivered and may also reduce recovery time.

Developer
GE Healthcare.

Availability, launch or marketing dates, and licensing plans:
The Entropy module is CE marked and is currently used widely throughout Europe with a 60% increase in its use in Europe in 2008. The device has also received FDA approval and is widely used in Australia.

NHS or Government priority area
No NHS or government priority area was identified.

Relevant guidance
- The Royal College of Anaesthetists. Risks associated with your anaesthetic section 8: Awareness during general anaesthesia. 2008^1.

Clinical need and burden of disease
The company estimate that about 6,000,000 patients received anaesthesia in 2007 with an estimated 360,000 patients undergoing a procedure that requires a general anaesthetic.
estimated 1 in 500 patients experience an awareness or recall event during general anaesthesia, equating to around 720 patients a year\textsuperscript{5}.

**Existing comparators and treatments**

Depth and adequacy of anaesthesia is monitored by clinical observations including heart rate, variability and response to stimuli, supplemented by pulse oximetry, EEG, airway-gas composition and nerve stimulation.

Where available and judged to be appropriate an anaesthetist can utilise other methods such as Bispectral analyses (BIS: an EEG based method) and auditory evoked potentials.

**Efficacy and safety**

There are a significant number of non-randomised, non-controlled clinical trials of entropy in both adults and children. There are also a number of clinical trials investigating the effect of different anaesthetic drug concentrations on entropy values.

**Health outcome trials:**

<table>
<thead>
<tr>
<th>Trial</th>
<th>Elective surgery of 45-150 minutes; Entropy vs standard practice.</th>
<th>Elective surgery of at least 1 hour; Entropy vs BIS vs standard practice.</th>
<th>Upper or lower extremity surgery; clinical parameters vs Entropy vs BIS.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sponsor</td>
<td>Datex-Ohmeda GE Healthcare.</td>
<td>Datex-Ohmeda GE Healthcare.</td>
<td>-</td>
</tr>
<tr>
<td>Status</td>
<td>Published\textsuperscript{6}.</td>
<td>Published\textsuperscript{7}.</td>
<td>Published\textsuperscript{8}.</td>
</tr>
<tr>
<td>Location</td>
<td>Finland, Norway, Sweden.</td>
<td>France.</td>
<td>Germany.</td>
</tr>
<tr>
<td>Participants and schedule</td>
<td>n=368; adults; elective surgery of 45-150 minutes duration. Randomised to alfentanil and propofol bolus of 1.0-2.5mg/kg maintained with continuous infusion of alfentanil (max dose 30µg /kg/h) and propofol (max dose 9mg/kg/h) adjusted using Entropy or clinical parameters.</td>
<td>n=140; adults; elective surgery. Randomised to propofol, sufentanil and atracurium with sevoflurane in nitrous oxide adjusted using Entropy, BIS or clinical parameters.</td>
<td>n=80; adults; surgery to upper or lower extremity; regional anaesthesia for post and intraoperative pain control. Randomised to anaesthesia by propofol and remifentanil infusion adjusted using clinical parameters or Entropy or BIS.</td>
</tr>
<tr>
<td>Primary outcomes</td>
<td>Anaesthetic response and recovery time.</td>
<td>Reduction in sevoflurane consumption.</td>
<td>Drug consumption and recovery times</td>
</tr>
<tr>
<td>Secondary outcomes</td>
<td>Postoperative nausea, vomiting or pain.</td>
<td>Intraoperative recall.</td>
<td>-</td>
</tr>
<tr>
<td>Key results</td>
<td>Entropy assisted titration of propofol, decreased consumption of propofol and reduced recovery times: orientation to time and space average 15 mins for control vs 10 mins for entropy (p&lt;0.001). No difference in postoperative nausea and vomiting or pain.</td>
<td>Both BIS and entropy reduced consumption of sevoflurane by 29% compared to the standard practice. Recovery times were similar in all groups.</td>
<td>Neither BIS nor entropy when compared to clinical parameters resulted in a reduction in drug consumption or recovery time.</td>
</tr>
</tbody>
</table>
Diagnostic efficacy trials:

<table>
<thead>
<tr>
<th>Trial</th>
<th>Sponsor</th>
<th>Status</th>
<th>Location</th>
<th>Design</th>
<th>Participants and schedule</th>
<th>Primary outcomes</th>
<th>Key results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elective surgery; Entropy and BIS.</td>
<td>Datex-Ohmeda GE Healthcare.</td>
<td>Published</td>
<td>Finland</td>
<td>Randomised</td>
<td>n=70; adults; elective surgery. Randomised to anaesthesia with sevoflurane, propofol or thiopental adjusted using BIS, Entropy and clinical parameters.</td>
<td>Loss of consciousness (LOC), recovery of consciousness (ROC).</td>
<td>Both Entropy and BIS distinguished between conscious and unconscious states. Entropy and BIS were equal over the range of 41-44 on the RE and BIS scores. Predictive performance of entropy and AAI to correctly differentiate between states of consciousness depended on the anaesthetic agent used.</td>
</tr>
<tr>
<td>Laparoscopic banding; Entropy and BIS.</td>
<td>-</td>
<td>Published</td>
<td>USA</td>
<td>Randomised</td>
<td>n=40; adults; laparoscopic gastric banding. Randomised to anaesthesia with propofol and desflurane adjusted using Entropy and BIS.</td>
<td>Steady state anaesthesia. LOC and ROC.</td>
<td></td>
</tr>
<tr>
<td>Minor orthopaedic surgery.</td>
<td>-</td>
<td>Published</td>
<td>Germany</td>
<td>Randomised</td>
<td>n=40; adults; minor orthopaedic surgery. Randomised to anaesthesia with sevoflurane and remifentanil or propofol and remifentanil adjusted using Entropy and A-line autoregressive index (AAI) observer’s assessment of alertness/sedation scale (OAA/S).</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Estimated cost and cost impact**

The module may be purchased as capital equipment or with an agreement about annual consumption. The company estimate a cost of £8-10 per patient.

**Potential or intended impact – speculative**

**Patients**

- Reduced morbidity
- Reduced mortality or increased length of survival
- Improved quality of life for patients and/or carers
- Other: May reduce anaesthetic dose and recovery time
- None identified
- Quicker, earlier or more accurate diagnosis or identification of disease

**Services**

- Increased use
- Service reorganisation required
- Staff or training required
- Decreased use: may reduce recovery time
- Other:
- None identified

**Costs**

- Increased unit cost compared to alternative
- Increased costs: more patients coming for treatment
- Increased costs: capital investment needed
References