NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of intraoperative nerve monitoring during thyroid surgery

The thyroid gland lies close to the vocal cords and the nerves that control movement of the vocal cords (recurrent laryngeal nerves). When surgery is performed on the thyroid gland, a nerve monitor is sometimes used during the operation with the aim of helping to prevent potential damage to the nerves.

Introduction

This overview has been prepared to assist members of the Interventional Procedures Advisory Committee (IPAC) in making recommendations about the safety and efficacy of an interventional procedure. It is based on a rapid review of the medical literature and specialist opinion. It should not be regarded as a definitive assessment of the procedure.

Date prepared

This overview was prepared in August 2007.

Procedure name

- Intraoperative recurrent laryngeal nerve monitoring during thyroid surgery

Specialty societies

The following societies were approached to nominate Specialist Advisers:

- Association of British Neurologists
- British Association of Head and Neck Oncologists
- British Association of Oral and Maxillofacial Surgeons
- British Association of Otorhinolaryngologists, Head and Neck Surgeons
- British Association of Thyroid and Endocrine Surgeons

Description

Indications

Thyroid disease requiring surgery

The thyroid gland is an H-shaped gland that lies just in front of the trachea in the neck. Thyroid hormones have a major role in regulating metabolism. If the gland is overactive or enlarged, or if thyroid cancer is suspected, surgery may be necessary. Surgery may involve removal of the whole thyroid gland (total thyroidectomy) or part of the gland (subtotal thyroidectomy, hemithyroidectomy or lobectomy). The thyroid gland lies close to the voice box (vocal cords in the larynx) and its nerves (the right and left recurrent laryngeal nerves [RLN]). Occasionally, these nerves are damaged during thyroid surgery (through traction, diathermy injury, or ligation and division). Injury to the RLN can result in temporary or permanent paralysis of the vocal cords. Unilateral nerve damage may cause voice changes including hoarseness. Bilateral nerve damage may result in breathing difficulties and an inability to speak. The external branch of the superior laryngeal nerve is also at risk of injury during thyroid surgery. Damage to this nerve may cause a slight deterioration in vocal quality.

Current treatment and alternatives

Conventional thyroid surgery is done without the aid of continuous intraoperative nerve monitoring (IONM). Under general anaesthesia, an incision is made in the front of the neck. The underlying muscles are opened to expose the thyroid gland, some or all of which is removed. Care is taken to avoid injury of nearby nerves, usually by visual identification alone. A hand-held nerve stimulator can also be used, in combination with palpation of the posterior surface of the larynx. A finger is placed behind the larynx to feel the contraction of the vocal cord muscles and the arytenoid cartilages on nerve stimulation.

What the procedure involves

Several techniques and devices can be used for intraoperative electrophysiological nerve monitoring, including specially designed endotracheal tubes, laryngeal surface electrodes attached to the standard endotracheal tube, or intramuscular vocal cord electrodes that are placed through the cricothyroid ligament during surgery, before dissection of the thyroid gland. General anaesthesia is used and a short-acting muscle relaxant is typically administered while the trachea is being intubated. Muscle relaxant drugs are not used during the procedure itself as they can interfere with the nerve monitoring process. The patient is intubated and depending on the exact technique and device being used, this may involve the use of a standard endotracheal tube, with or without surface electrodes, or a specially designed endotracheal tube with integral electrodes. If the endotracheal tube has either integral electrodes or surface electrodes attached to it, these are positioned close to the vocal cords. An incision is made in the front of the neck and the underlying muscles are dissected to expose the thyroid gland. If

intramuscular vocal cord electrodes are used, they are placed through the cricothyroid ligament into the ipsilateral vocal muscle at this point. The electrodes are connected to the neuromonitoring device, which uses sound and graphics on the monitor screen to alert the surgeon when a surgical instrument comes close to one of the RLNs. A hand-held probe can also be used to confirm the location of the nerve at any time during the operation. Postoperative laryngoscopy is used to assess RLN function. The aim of IONM may be to help prevent damage to the RLN during the operation or to diagnose that the nerve has been damaged.

Efficacy

A non-randomised controlled trial of 29,998 nerves at risk that compared no RLN identification, visual RLN identification only, and visual RLN identification with IONM reported no statistically significant difference between IONM and visual RLN identification only with regard to permanent paralysis: 0.80% (95% confidence interval, 0.67 to 0.93) of nerves in the IONM group had permanent paralysis, compared with 0.89% (95% confidence interval, 0.64 to 1.14) in the visual RLN identification group and 0.93% (95% confidence interval, 0.70 to 1.16) in the group where the RLN was not routinely identified.[1]

Three other non-randomised controlled trials (n = 1000, 1043 and 190 nerves at risk) reported permanent rates of RLN paralysis as 0.8%, 0.3% and 2.4% in the IONM groups, compared with 1.2%, 0.3% and 0.9%, respectively, in the control groups (routine RLN identification). Rates of transient RLN palsy were 3.4%, 3.3% and 4.8% in the IONM groups, compared with 4.0%, 4.3% and 2.8%, respectively, in the control groups. None of these differences was reported to be statistically significant.[2,3,4] An additional non-randomised controlled trial reported rates of transient RLN palsy as 3.5% (4/116) nerves at risk in the IONM group and 4.2% (5/120) in the control group (p = 0.89).[5]

Three case series reported rates of transient RLN palsy as 8.6% (43/502), 8.7% (37/429) and 4.8% (13/271).[6,7,8] Rates of permanent RLN paralysis were 3% (15/502), 1.4% (6/429) and 0.7% (2/271), respectively.

The non-randomised controlled trial of 1000 nerves at risk, comparing IONM with visual identification only, reported an overall sensitivity and specificity of 52% and 94%, respectively, for accurate prediction of the postoperative vocal cord outcome (assessed by laryngoscopy). The positive predictive value was 29% and the negative predictive value was 98%.[2]

Safety

No adverse events resulting from IONM were reported in the studies.

Literature review

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to IONM during thyroid surgery. Searches of Medline, PreMedline, EMBASE, Cochrane Library and other databases were made, covering the period from their start to 23/08/2007. Trial registries and the Internet were also searched. No language restriction was applied to the searches. (See appendix B for details of search strategy.)

The following selection criteria (Table 1) were applied to the abstracts identified by the literature search. Where these criteria could not be determined from the abstracts the full paper was retrieved.

Table 1 Inclusion criteria for identification of relevant studies

Characteristic	Criteria
Publication type	Clinical studies were included. Emphasis was placed on identifying good quality studies. Abstracts were excluded where no clinical outcomes were reported, or where the paper was a review, editorial, or laboratory or animal study. Conference abstracts were also excluded because of the difficulty of appraising methodology.
Patient	Patients undergoing thyroid surgery.
Intervention/test	Intraoperative nerve monitoring.
Outcome	Articles were retrieved if the abstract contained information relevant to safety and/or efficacy.
Language	Non-English-language articles were excluded unless they were thought to add substantively to the English-language evidence base.

List of studies included in the overview

This overview is based on five non-randomised comparative studies[1-5] and three case series.[6–8]

Other studies that were considered to be relevant to the procedure but were not included in the main extraction table (table 2) have been listed in appendix A.

Existing reviews on this procedure

There were no published systematic reviews with meta-analysis or evidence based guidelines identified at the time of the literature search.

Related NICE guidance

No NICE guidance related to this procedure was identified.

Table 2 Summary of key efficacy and safety findings on intraoperative nerve monitoring during thyroid surgery

Abbreviations used: CI, confidence interval; IONM, intraoperative nerve monitoring; OR, odds ratio; RLN, recurrent laryngeal nerve; RR, relative risk.

Study details	Key efficacy findings	Key safety findings	Comments
Dralle H (2004)[1] **Non-randomised controlled study (prospective)** Germany (multicentre) Study period: 1998–2001 **n = 16,448 operations (29,998 nerves at risk)** Population: patients undergoing thyroid surgical procedures under general anaesthesia • No RLN identification = 22% (6649/29,998) nerves • Visual RLN identification = 18% (5517/29,998) nerves • Visual nerve identification with electromyographic monitoring = 59% (17832 nerves/29998) Median age: 54 years (range 3–99) Male = 30% (6833/22973) Indications: no inclusion and exclusion criteria were described. Thyroid disease: • Benign multinodular goitre = 82% (24,693/29,998) • Immunogenic goitre = 6% (1868/29,998) • Benign recurrent goitre = 5% (1480/29,998) • Thyroid malignancy = 6% (1833/29,998) • Recurrent thyroid malignancy = <1% (124/29,998)	RLN paralysis persisting 6 months after the operation was defined as being permanent. Overall rate of permanent RLN paralysis (univariate analysis): • No RLN identification = 0.93% (95% CI 0.70 to 1.16) • Visual RLN identification = 0.89% (95% CI 0.64 to 1.14) • IONM = 0.80% (95% CI 0.67 to 0.93) Major significant risk factors for postoperative permanent RLN paralysis identified on multivariate analysis were: • Recurrent malignant goitre (OR = 6.66, p < 0.0001) • Recurrent benign goitre (OR = 4.67, p < 0.0001) • Primary surgery in thyroid malignancy (OR = 2.04, p = 0.0002) • Lobectomy (OR = 1.8, p < 0.0001) Minor significant risk factors for postoperative permanent RLN paralysis identified on multivariate analysis were: • Interventions without any type of nerve identification (OR = 1.37, p < 0.05) • Medium hospital volume (OR = 1.34, p < 0.05) • Low volume surgeon (OR = 1.2, p = 0.12) The study indicates that there is no significant benefit of IONM overall compared with visual nerve identification with regard to functional outcome of the RLN.	No safety outcomes were reported.	Consecutive operations – IONM was done according to the individual surgeon's intraoperative decision and availability of RLN monitoring device. The sample sizes in the three groups were quite different, which affected the subgroup calculations of RLN paralysis frequency between the groups. The authors state that the study was underpowered to detect a significant difference between visual RLN identification and IONM. The number of thyroid operations performed in each participating centre ranged from <20 to >1000. In patients with thyroid malignancy, significantly more patients underwent either visual nerve identification or IONM as compared with no nerve identification (p < 0.0001). A significantly higher proportion of subtotal resections were done with no nerve identification, compared with lobectomy (28% versus 5%, p < 0.001).

Abbreviations used: CI, confidence interval; IONM, intraoperative nerve monitoring; OR, odds ratio; RLN, recurrent laryngeal nerve; RR, relative risk.

Study details	Key efficacy findings	Key safety findings	Comments
Dralle H (2004) continued. Technique: nerve monitor – Neurosign 100 machine (Inomed GmbH, Teningen, Germany). Standard endotracheal tubes were used for intubation and intramuscular vocal cord electrodes were inserted through the cricothyroid ligament into the ipsilateral vocal muscle before dissection of the thyroid gland. All patients were investigated by pre- and postoperative laryngoscopy to assess RLN function. **Follow-up: 6 months** Potential conflict of interest: The paper states that 'logistic support for the study was provided by Henning Berlin GmbH & Co KG, Berlin, Germany and by Inomed GmbH, Teningen, Germany.'			The relative proportion of thyroid malignancy and lobectomy were significantly higher in the group of surgeons with higher number of operated sites per year (≥ 45 sites, $p < 0.001$). At end of study, follow-up for patients with postoperative RLN paralysis was 83% (736/884 nerves at risk). Patients with postoperative RLN paralysis who were unavailable for follow-up were defined as missing values and interpolated for the statistical analysis. The authors conclude that visual identification is the gold standard of RLN treatment in thyroid surgery but that IONM is a promising tool for nerve identification and protection in extended thyroid resection procedures.

Abbreviations used: CI, confidence interval; IONM, intraoperative nerve monitoring; OR, odds ratio; RLN, recurrent laryngeal nerve; RR, relative risk.

<table>
<tr><th>Study details</th><th>Key efficacy findings</th><th>Key safety findings</th><th>Comments</th></tr>
<tr>
<td>Chan WF (2006)[2]

Non-randomised controlled study (prospective)

China

Study period: 2002–2005

n = 639 patients (1000 RLNs at risk of injury)

Population: patients undergoing thyroidectomy

• IONM = 49% (316/639) of patients, 501 nerves at risk
• Routine visual identification of RLN (controls) = 51% (323/639) of patients, 499 nerves at risk

Mean age: 49 years (range 8–93)

Male = 21% (133/639)

• Total or near-total thyroidectomy = 56% (358/639)
• Unilateral lobectomy = 38% (241/639)
• Completion total thyroidectomy = 6% (36/639)
• Subtotal thyroidectomy = <1% (4/639)

Unilateral procedure = 43% (277/639)

Indications: inclusion criteria not stated. Patients with intraoperative finding of tumour involvement of RLN were excluded.</td>
<td>Rates of postoperative (within 2 weeks of surgery) RLN palsy after thyroidectomy:
• IONM = 4.2% (21/501)
• Controls = 5.2% (26/499), p > 0.05

Rates of transient (< 12 months) RLN palsy after thyroidectomy:
• IONM = 3.4% (17/501)
• Controls = 4.0% (20/499), p > 0.05

Rates of permanent (defined as > 12 months) RLN palsy after thyroidectomy:
• IONM = 0.8% (4/501)
• Controls = 1.2% (6/499), p > 0.05

Correlation of neuromonitoring results with postoperative outcome:
<table>
<tr><td></td><td colspan="3">Postoperative outcome (laryngoscopy within 2 weeks)</td></tr>
<tr><td>IONM</td><td>Paralysis</td><td>No paralysis</td><td>Total (n)</td></tr>
<tr><td>No signal</td><td>11</td><td>27</td><td>38</td></tr>
<tr><td>Intact signal</td><td>10</td><td>453</td><td>463</td></tr>
<tr><td>Total</td><td>21</td><td>480</td><td>501</td></tr>
</table>
Sensitivity = 52%
Specificity = 94%
Positive predictive value = 29%
Negative predictive value = 98%

Multivariate analysis showed that malignant disease, reoperation and operative time were all independent risk factors for adverse postoperative outcome.</td>
<td>No safety outcomes were reported.</td>
<td>Consecutive patients - intraoperative nerve monitoring was performed on the basis of availability of equipment and choice of operating surgeon.

There were no significant differences between the groups in terms of age, gender, type of thyroidectomy, proportion of bilateral procedures, concomitant neck dissections and pathological condition.

The weight of resected specimens was significantly heavier in the IONM group than the control group (p < 0.008).

A greater proportion of nerves at risk that were undergoing reoperation and thyroidectomy for non-toxic goitre had IONM (p = 0.024 and 0.012 respectively).

The authors note that an impractically large number of patients would be needed for a prospective RCT because of the rarity of RLN injury achieved in specialised centres.

The authors state that there was some selection bias, favouring the use of IONM in patients of certain high-risk subgroups, particularly in reoperation.</td>
</tr>
</table>

Abbreviations used: CI, confidence interval; IONM, intraoperative nerve monitoring; OR, odds ratio; RLN, recurrent laryngeal nerve; RR, relative risk.

Study details	Key efficacy findings	Key safety findings	Comments
Chan WF (2006)[2] continued. Final pathological condition: • Benign nodular goitre = 56% (357/639) • Thyroid malignancy = 22% (141/639) • Graves disease = 13% (86/639) • Follicular adenoma = 8% (50/639) • Thyroiditis = 1% (5/639) Technique: Nerve monitor –Neurosign 100 machine (Magstim Clarify Company, Whitland, UK) consisting of laryngeal surface electrode attached to endotracheal tube. Routine postoperative vocal cord examination was done using an indirect or flexible laryngoscope. Any reduction in the movement of the cord was recorded as postoperative cord paralysis. **Median follow-up = 6 months (range 1–12 months) for patients with postoperative cord palsy.** Potential conflict of interest: none stated	Rates of transient RLN palsy after secondary thyroidectomy: • IONM = 5.2% (2/38) • Controls = 14.2% (3/21), p > 0.05 Rates of permanent RLN palsy after secondary thyroidectomy: • IONM = 2.6% (1/38) • Controls = 4.8% (1/21), p > 0.05 Rates of transient RLN palsy in patients with carcinoma: • IONM = 6.3% (9/142) • Controls = 6.1% (7/115), p > 0.05 Rates of permanent RLN palsy in patients with carcinoma: • IONM = 0.7% (1/142) • Controls = 1.7% (2/115), p > 0.05 Rates of transient RLN palsy in patients with retrosternal goitre: • IONM = 1.7% (1/59) • Controls = 7.7% (4/52), p > 0.05 Rates of permanent RLN palsy in patients with retrosternal goitre: • IONM = 1.7% (1/59) • Controls = 0% (0/52), p > 0.05 Rates of transient RLN palsy in patients with toxic goitre: • IONM = 4.3% (4/92) • Controls = 1.6% (2/124), p > 0.05 Rates of permanent RLN palsy in patients with toxic goitre: • IONM = 0% (0/92) • Controls = 0.8% (1/124), p > 0.05		

Abbreviations used: CI, confidence interval; IONM, intraoperative nerve monitoring; OR, odds ratio; RLN, recurrent laryngeal nerve; RR, relative risk.

Study details	Key efficacy findings	Key safety findings	Comments
Shindo M (2007)[3] **Non-randomised controlled study (retrospective)** USA Study period: 1998–2005 **n = 684 patients (1043 nerves at risk)** Population: patients undergoing thyroid surgery under general anaesthesia • IONM = 62% (427/684) of patients, 64% (671/1043) nerves at risk • Routine identification of RLN (controls) = 38% (257/684) of patients, 36% (372/1043) nerves at risk Indications: inclusion and exclusion criteria not stated. Patients undergoing only a paratracheal node dissection were excluded. Total thyroidectomy = 52% (359/684) Technique: nerve integrity monitoring EMG endotracheal tube (Medtronic Xomed, Jacksonville). The tube was positioned so that the electrodes were situated at the level of the true vocal folds. A standard endotracheal tube was used when IONM was not done. All patients underwent pre- and postoperative laryngoscopy. **Follow-up: not stated** Conflict of interest: none reported	Impairment of postoperative vocal fold mobility (paresis or paralysis): • IONM = 5.8% (25/427) of patients • Controls = 6.6% (17/257) of patients None of the patients experienced bilateral vocal cord paralysis. Unexpected postoperative vocal fold paresis: • IONM = 3.3% (14/427) of patients • Controls = 4.3% (11/257) of patients Vocal cord function returned to all 9 patients in the IONM group and all 7 patients in the control group available for long-term follow-up (period not stated). Unexpected postoperative vocal cord paralysis: • IONM = 1.6% (11/427) of patients • Controls = 1.6% (6/257) of patients In 2 of the paralysis cases, the vocal cord did not regain full function and the paralysis was considered to be permanent. In both cases, the injury was because of inadvertent transection that was recognised intraoperatively (the paper does not state whether these were monitored or control patients). Rate of permanent paralysis: • IONM = 0.3% (2/671) of patients • Controls = 0.3% (1/372) of patients There was no significant difference in the rates of postoperative vocal cord paresis or complete paralysis between the 2 groups.	'No patients experienced a complication from the intubation of either type of tube.'	The unmonitored cases were those performed when the nerve monitoring system was not available for use, primarily in the earlier years of the study. All procedures were done by a single senior surgeon. 5 of the 14 monitored patients with paresis were lost to follow-up. 4 of the 11 control patients with paresis were lost to follow-up. 2 of the 11 monitored patients with paralysis were lost to follow-up. 3 of the 6 control patients with paralysis were lost to follow-up. Follow-up is described as 'long-term' but not specified.

Abbreviations used: CI, confidence interval; IONM, intraoperative nerve monitoring; OR, odds ratio; RLN, recurrent laryngeal nerve; RR, relative risk.

Study details	Key efficacy findings	Key safety findings	Comments
Witt RL (2005)[4] **Non randomised controlled study (retrospective)** USA Study period: 1998–2003 **n = 136 patients (190 nerves at risk)** Population: patients undergoing thyroidectomy • IONM = 44% (83/190) nerves at risk • Routine identification of RLN (controls) = 56% (107/190) of nerves at risk Indications: inclusion and exclusion criteria not stated. Technique: Nerve Integrity Monitor (Medtronic, Minneapolis) was used, consisting of an endotracheal tube integrated with surface electromyography electrodes. Vocal fold mobility was evaluated pre- and postoperatively for all patients (method not described in paper). **Follow-up: not stated** Conflict of interest: none stated	Permanent vocal fold immobility was defined as lasting more than 1 year. None of the RLNs were severed. Rate of transient vocal fold immobility: • IONM = 4.8% (4/83) nerves at risk • Controls = 2.8% (3/107) nerves at risk, p > 0.05 Rate of permanent vocal fold immobility: • IONM = 2.4% (2/83) nerves at risk • Controls = 0.9% (1/107) nerves at risk, p > 0.05 Both cases of permanent vocal fold immobility that were monitored had a positive electrophysiological stimulation of the RLN at the conclusion of the RLN dissection, before wound closure, suggesting electrophysiological integrity.	No safety outcomes were reported.	Retrospective survey of consecutive patients. All operations were performed by one surgeon.

Abbreviations used: CI, confidence interval; IONM, intraoperative nerve monitoring; OR, odds ratio; RLN, recurrent laryngeal nerve; RR, relative risk.

<table>
<tr><th>Study details</th><th>Key efficacy findings</th><th>Key safety findings</th><th>Comments</th></tr>
<tr>
<td>Robertson ML (2004)[5]

Non-randomised controlled study (retrospective)

USA

Study period: 1999–2002

n = 165 patients (236 nerves at risk)

Population: patients undergoing total or partial thyroidectomy
• IONM = 50% (82/165) of patients, 49% (116/236) nerves at risk
• Routine identification of RLN (controls) = 50% (83/165) of patients, 51% (120/236) nerves at risk

<table>
<tr><th></th><th>IONM (n = 116 nerves)</th><th>Controls (n = 120 nerves)</th><th>p value</th></tr>
<tr><td>Age (years)</td><td>42.8</td><td>46.4</td><td>0.06</td></tr>
<tr><td>Female</td><td>85%</td><td>69%</td><td>0.003</td></tr>
<tr><td>Revision</td><td>4.3%</td><td>1.7%</td><td>0.3</td></tr>
<tr><td>History of neck irradiation</td><td>0%</td><td>5.1%</td><td>0.03</td></tr>
<tr><td>History of radioiodine ablation</td><td>9.6%</td><td>0%</td><td>0.0003</td></tr>
<tr><td>Substernal goitre</td><td>6.9%</td><td>7.0%</td><td>1.0</td></tr>
<tr><td>Malignancy</td><td>32.8%</td><td>34.8%</td><td>0.7</td></tr>
<tr><td>Lateral neck dissection</td><td>2.6%</td><td>9.2%</td><td>0.05</td></tr>
</table>
</td>
<td>Postoperative RLN paralysis (not further defined):
• IONM = 0.86% (1/116) nerves at risk
• Controls = 2.54% (3/120) nerves at risk
RR = 0.34, 95% CI = 0.04 to 3.27, p = 0.62

Postoperative RLN paresis (described as temporary):
• IONM = 3.45% (4/116) nerves at risk
• Controls = 4.24% (5/120) nerves at risk
RR = 0.90, 95% CI = 0.23 to 3.55, p = 0.89

Total RLN injury:
• IONM = 4.31% (5/116) nerves at risk
• Controls = 6.78% (8/120) nerves at risk
RR = 0.66, 95% CI = 0.21 to 2.09, p = 0.48

Among patients with thyroid malignancy, T-stage was a significant predictor of RLN paresis (p = 0.006) but not paralysis (p = 1.0). Preoperatively functional RLN with T4 malignant tumours were associated with 8-fold RR increase of RLN paresis following thyroidectomy when compared with all other nerves at risk.

No other baseline characteristic (other than tumour stage) was significant for RLN paralysis, paresis or total injury (age, sex, substernal goitre, history of irradiation or radioiodine ablation, central or lateral neck dissection, or revision surgery).

RLN paresis in nerves at risk with advanced stage tumours (T4):
• IONM = 16.7% (1/6) nerves at risk
• Controls = 33.3% (2/6) nerves at risk
RR = 0.5, 95% CI = 0.06 to 4.15, p = 1.0

RLN paresis in nerves at risk with advanced stage tumours (T 3 and T4):
• IONM = 10.0% (1/10) nerves at risk
• Controls = 30.0% (3/10) nerves at risk
RR = 0.36, 95% CI = 0.04 to 3.0, p = 0.59

Univariate analysis did not show a significant association between attending surgeon and RLN paralysis.</td>
<td>No safety outcomes were reported.</td>
<td>Surgery was performed by 5 different surgeons at a single centre.

Patients with preoperative RLN injuries were included in the study but the nerves were excluded from the analyses of nerves at risk.

There was a statistically significant difference between groups with respect to sex, history of irradiation, history of radioiodine ablation and concurrent lateral neck dissection.

Sample size was calculated assuming a control rate of RLN paralysis of 3% and setting an absolute risk difference of 2% as clinically relevant. The sample size was calculated at 121 nerves at risk in each group for 80% power.

As the control rate of RLN paralysis was lower than assumed when calculating sample size, the study was under powered to detect a significant difference.

Multiple surgeons were involved with different rates of IONM usage.</td>
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</table>

Abbreviations used: CI, confidence interval; IONM, intraoperative nerve monitoring; OR, odds ratio; RLN, recurrent laryngeal nerve; RR, relative risk.

Study details	Key efficacy findings	Key safety findings	Comments
Robertson ML (2004) continued. Indications: patients undergoing thyroidectomy in conjunction with laryngectomy were excluded. Patients who underwent thyroidectomy by surgeons who infrequently perform thyroidectomy (< 10 during the study period) were also excluded. Technique: NIM and NIM2 EMG endotracheal tube (Medtronic Xomed, Jacksonville). The tube was positioned such that the electrodes were situated at the level of the true vocal folds. A standard endotracheal tube was used when IONM was not done. All patients underwent pre- and postoperative laryngoscopy. **Follow-up: not stated** Conflict of interest: none			

Abbreviations used: CI, confidence interval; IONM, intraoperative nerve monitoring; OR, odds ratio; RLN, recurrent laryngeal nerve; RR, relative risk.

<table>
<tr><th>Study details</th><th>Key efficacy findings</th><th>Key safety findings</th><th>Comments</th></tr>
<tr>
<td>Hermann M (2004)[6]

Case series (prospective)

Austria

Study period: not stated

n = 328 patients (502 nerves at risk)

Population: Patients undergoing thyroid surgery for different indications.

Indications: inclusion and exclusion criteria not stated. The paper states that inclusion criteria were changed during the study to subsequently select patients with relapses or malignant disease to obtain reasonably comparable numbers and to test the performance of neuromonitoring in challenging cases.

Technique: nerve monitor – Neurosign 100 machine (Inomed GmbH, Teningen, Germany). Standard endotracheal tubes were used for intubation and intramuscular vocal cord electrodes were inserted through the cricothyroid ligament into the ipsilateral vocal muscle, via the neck incision, before dissection of the thyroid gland. The routine procedure called for dissection of the entire RLN but surgeons were left the option to adapt the dissection procedure according to the extent of resection and to the anatomic situation. All patients were investigated by pre- and postoperative laryngoscopy to assess RLN function.

Follow-up: 12 months

Conflict of interest: none stated</td>
<td>Postoperative injury to RLN
<table>
<tr><th></th><th>Nerves at risk</th><th>RLN paresis</th><th>Permanent RLN palsy</th></tr>
<tr><td>Total</td><td>502</td><td>43 (9%)</td><td>15 (3%)</td></tr>
<tr><td>Benign disease, first operation</td><td>179</td><td>7 (4%)</td><td>0 (0%)</td></tr>
<tr><td>Benign disease, re-operation</td><td>197</td><td>19 (10%)</td><td>8 (4%)</td></tr>
<tr><td>Malignant disease, first operation</td><td>74</td><td>11 (15%)*</td><td>4 (5%)*</td></tr>
<tr><td>Malignant disease, re-operation</td><td>31</td><td>4 (13%)</td><td>1 (3%)</td></tr>
</table>
* 2 additional nerves had to be severed to allow for radical removal of the tumour; these were excluded from subsequent analysis.

Sensitivity and negative predictive value (n = 475 nerves at risk):
• Sensitivity (postop paresis) = 57.1%
• Sensitivity (permanent palsy) = 44.4%
• Negative predictive value (postop paresis) = 96.6%
• Negative predictive value (permanent palsy) = 98.8%

Specificity (permanent palsy) = 97.3% (99.3% if intraoperative technical problems excluded)

Positive predictive value (postop paresis) = 62.5% (87% if technical problems excluded)
Positive predictive value (permanent palsy) = 25% (57.1% if technical problems excluded)</td>
<td>No safety outcomes were reported.</td>
<td>Consecutive patients in a single centre (8 surgeons, 2 surgical trainees).</td>
</tr>
</table>

Abbreviations used: CI, confidence interval; IONM, intraoperative nerve monitoring; OR, odds ratio; RLN, recurrent laryngeal nerve; RR, relative risk.

<table>
<tr><th>Study details</th><th>Key efficacy findings</th><th>Key safety findings</th><th>Comments</th></tr>
<tr>
<td>Beldi G (2004)[7]

Case series (prospective)

Switzerland

Study period: 1996–2002

n = 288 patients (296 operations, 429 nerves at risk)

Population: patients undergoing thyroid surgery

Mean age: 49 years (range 13–82)

Male = 20% (58/288)

Indications: inclusion and exclusion criteria not stated.

Thyroid disease:
• Benign goitre = 59% (176/296)
• Adenoma = 10% (30/296)
• Graves’ disease = 8% (23/296)
• De Quervain’s disease = 2% (7/296)
• Malignancy = 14% (40/296)
• Recurrent benign goitre = 5% (15/296)
• Recurrent malignancy = 2% (5/296)

Technique: nerve monitor - Neurosign 100 machine (Magstim Clarify Company, Whitland, UK), consisting of a laryngeal surface electrode attached to endotracheal tube. All patients were investigated by pre- and postoperative laryngoscopy to assess RLN function. Patients with postoperative palsy had follow-up laryngoscopy (follow-up period not defined).

Follow-up: not stated

Conflict of interest: none stated</td>
<td>The monitoring failed in 39 (13%) procedures because of technical problems.

Transient RLN palsy = 8.7% (37/429)
Permanent RLN palsy = 1.4% (6/429)

<table>
<tr><th></th><th>Number of nerves at risk</th><th>Transient RLN palsy</th><th>Permanent RLN palsy</th></tr>
<tr><td>Benign disease</td><td>333</td><td>7.2%</td><td>0.6%</td></tr>
<tr><td>Malignant disease</td><td>70</td><td>11.4%</td><td>2.9%</td></tr>
<tr><td>Recurrent goitre</td><td>26</td><td>19.2%</td><td>7.7%</td></tr>
</table>

Among 5 patients with permanent postoperative RLN palsy, 2 were correctly assessed during the operation and 3 were falsely negative. False positive results were found in 4 of 252 patients without permanent RLN lesions.

Sensitivity = 40%
Specificity = 98%
Positive predictive value = 33%
Negative predictive value = 99%

Among the patients with transient postoperative paresis, a normal intraoperative signal was found in 81%.

Positive predictive value = 67%
Negative predictive value = 91%.</td>
<td>No safety outcomes were reported.</td>
<td>Patient selection not described.

Operations were performed by 36 surgeons (3 ‘expert’ surgeons with > 65 operations, 15 ‘experienced’ surgeons with 15–65 operations and 18 residents).

Only patients with postoperative palsy were given follow-up laryngoscopy (period not stated).</td>
</tr>
</table>

Abbreviations used: CI, confidence interval; IONM, intraoperative nerve monitoring; OR, odds ratio; RLN, recurrent laryngeal nerve; RR, relative risk.

<table>
<tr><th>Study details</th><th>Key efficacy findings</th><th>Key safety findings</th><th>Comments</th></tr>
<tr>
<td>Chan WF (2006)[8]

Case series (prospective)

China

Study period: not stated

n = 171 patients (271 nerves at risk)

Population: patients undergoing thyroidectomy

Median age: 46 years (range 8–93)

Male = 24% (41/171)

Indications: inclusion and exclusion criteria not stated.

Final pathological condition:
• Nodular goitre = 48% (83/171)
• Thyroid carcinoma = 25% (43/171)
• Graves disease = 11% (19/171)
• Benign adenoma = 8% (14/171)
• Recurrent nodular goitres = 5% (9/171)
• Thyroiditis = 1% (2/171)
• Recurrent Graves disease = < 1% (1/171)

Technique: nerve monitor - Neurosign 100 machine (Magstim Clarify Company, Whitland, UK), comprising laryngeal surface electrode attached to endotracheal tube. Routine postoperative vocal cord examination was done using an indirect or flexible laryngoscope. Any reduction in the movement of the cord was recorded as postoperative cord paralysis.

Follow-up: 12 months

Conflict of interest: none stated</td>
<td>The presence of vocal cord paralysis for > 12 months was regarded as permanent.

Patients undergoing primary thyroidectomy for benign disease were classified as low risk. High risk patients consisted of those undergoing secondary thyroidectomy for recurrent disease and surgery for malignancy.

Incidence of RLN palsy diagnosed by postoperative laryngoscopy, according to stratified surgical risks
<table>
<tr><th></th><th>Low risk group (n = 179)</th><th>High risk group (n = 92)</th><th>Total (n = 271)</th></tr>
<tr><td>Transient palsy</td><td>8 (4.5%)</td><td>5 (5.4%)</td><td>13 (4.8%)</td></tr>
<tr><td>Permanent palsy</td><td>0 (0%)</td><td>2 (2.2%)</td><td>2 (0.7%)</td></tr>
<tr><td>Overall</td><td>8 (4.5%)</td><td>7 (7.6%)</td><td>15 (5.5%)</td></tr>
</table>
Correlation of neuromonitoring results with postoperative outcome
<table>
<tr><th>IONM</th><th colspan="2">Paresis</th><th colspan="2">No paresis</th></tr>
<tr><th></th><th>Low risk</th><th>High risk</th><th>Low risk</th><th>High risk</th></tr>
<tr><td>No signal</td><td>2</td><td>6</td><td>11</td><td>4</td></tr>
<tr><td>Intact signal</td><td>6</td><td>1</td><td>160</td><td>81</td></tr>
<tr><td>Total</td><td>8</td><td>7</td><td>171</td><td>85</td></tr>
</table>
Validation of performance of IONM for predicting postoperative RLN function
<table>
<tr><th></th><th>Low risk</th><th>High risk</th><th>Overall</th></tr>
<tr><td>Sensitivity</td><td>25%</td><td>86%</td><td>53%</td></tr>
<tr><td>Specificity</td><td>94%</td><td>95%</td><td>94%</td></tr>
<tr><td>Positive predictive value</td><td>15%</td><td>60%</td><td>35%</td></tr>
<tr><td>Negative predictive value</td><td>96%</td><td>99%</td><td>97%</td></tr>
<tr><td>Accuracy</td><td>91%</td><td>95%</td><td>92%</td></tr>
</table>
</td>
<td>No safety outcomes were reported.</td>
<td>There may be some overlap of patients with Chan 2006[2] study also in table 2.

Patient selection not described. Procedures were done by a single endocrine surgical team.

Three patients were excluded from the analysis because of recognised machine failure and two were excluded because of the need for inevitable nerve transection due to tumour invasion.

The authors state that IONM is not a replacement for routine RLN identification and meticulous surgical technique. It is neither sensitive enough nor able to predict accurately the presence of an injured or malfunctioning RLN intraoperatively. Routine application of IONM is not recommended except for selected high risk patients.</td>
</tr>
</table>

Validity and generalisability of the studies

- Although there were five comparative studies, none of them randomly assigned patients to receive either monitoring or no monitoring.
- The rate of RLN injury during thyroid surgery without IONM is low and a large number of patients would be needed to show a statistically significant difference. The authors of the largest study, involving nearly 30,000 nerves at risk, stated that the study was underpowered to detect a statistically significant difference between visual identification of the nerve and IONM.[1]
- The definition of permanent paralysis varied between studies. One study defined it as paralysis persisting at 6 months after surgery[1] and three studies defined it as paralysis persisting at 12 months.[2,4,8] The remaining studies did not report a definition.
- Different methods of electrode placement were used (attached to an endotracheal tube or inserted through the cricothyroid ligament before dissection of the thyroid gland).
- One study excluded patients who were operated on by a surgeon who had performed fewer than 10 thyroidectomies during the study period.[5]
- One non-randomised controlled study and one case series were reported from the same study centre and there may be some patient overlap between these studies.[2,8]

Specialist Advisers' opinions

Specialist advice was sought from consultants who have been nominated or ratified by their Specialist Society or Royal College. The advice received is their individual opinion and does not represent the view of the society.

Mr H Mehanna, Mr M Papesch, Mr M Quraishi, Mr N Tolley (British Association of Otorhinolaryngologists, Head and Neck Surgeons)
Mr P Pracy, Mr F Stafford (British Association of Head and Neck Oncologists)
Mr G Sadler, Mr W James Smellie (British Association of Endocrine and Thyroid Surgeons), Mr B Visavadia (British Association of Oral and Maxillofacial Surgeons)

- Six Specialist Advisers perform the procedure regularly, two have performed it at least once, and one adviser has never performed the procedure.
- Four advisers described the procedure to be definitely novel and of uncertain safety and efficacy, two described it as a minor variation of an established procedure, and three described it as established practice.
- One adviser commented that there are significantly different opinions between surgeons as to whether this technology improves outcomes or whether it gives false reassurance to inexperienced surgeons.
- Two advisers stated that the procedure is useful for teaching. One also commented that a nerve monitor provides hard evidence of nerve function if questions arise in litigation.
- There are several devices available.

- If the electrodes are not placed correctly, there is potential for false signals.
- The main safety concern raised was that false negative or false positive readings may lead to misidentification of the nerve. One Specialist Adviser also mentioned that an anaesthetist inadvertently kept the patient on muscle relaxant during most of the procedure and so the device gave no signal when the nerve was stimulated.
- The endotracheal tube is larger than usual and there is a risk of cord ulceration and temporary hoarseness postoperatively.
- One adviser commented that there has been concern regarding the electrodes on the endotracheal tube being dislodged, and causing direct laryngeal injury. A device warning was sent out about this problem, and it is believed that the matter has since been addressed.
- Anaesthetists need to be trained in the use of unparalysed anaesthesia.
- The procedure is likely to be most useful in more difficult cases such as those with particularly large thyroid glands, malignancy or revision thyroid surgery.
- One adviser commented that IONM should be used regularly so that staff was experienced in its use ready for cases where there is a clinical need for it.
- When thyroid surgery is undertaken by experienced surgeons the rate of vocal cord palsy is very low.
- Key efficacy outcomes are reduction in nerve damage and subsequent vocal cord palsy.
- Patients should be assessed preoperatively and postoperatively by laryngoscopy.
- Suggested audit criteria include postoperative vocal cord weakness (temporary or permanent) with or without normal intraoperative nerve monitoring, false negative rate of monitor, technical problems such as endotracheal tube misplacement and direct laryngeal injury from electrodes, and operative time.
- Two Specialist Advisers commented that published evidence shows that IONM does not improve outcomes and does not decrease complication rates over the direct visualisation technique.
- Four Specialist Advisers thought that the procedure would have a minor impact on the NHS in terms of use of resources and numbers of patients. Three advisers thought the impact would be moderate and one thought it would be major.

Issues for consideration by IPAC

- There is a large evidence base for this procedure, including a number of non-English language papers.
- There are several different types of devices available for intraoperative monitoring of the recurrent laryngeal nerve.
- Evidence has only been presented on intraoperative monitoring of the recurrent laryngeal nerve. The literature also includes a small number of reports on the superior laryngeal nerve.

References

1. Dralle H, Sekulla C, Haerting J et al. (2004) Risk factors of paralysis and functional outcome after recurrent laryngeal nerve monitoring in thyroid surgery. *Surgery* 136: 1310–22.
2. Chan WF, Lang BH, Lo CY (2006) The role of intraoperative neuromonitoring of recurrent laryngeal nerve during thyroidectomy: a comparative study on 1000 nerves at risk. *Surgery* 140: 866–73.
3. Shindo M, Chheda NN (2007) Incidence of vocal cord paralysis with and without recurrent laryngeal nerve monitoring during thyroidectomy. *Archives of Otolaryngology – Head and Neck Surgery* 133: 481–5.
4. Witt RL (2005) Recurrent laryngeal nerve electrophysiologic monitoring in thyroid surgery: the standard of care? *Journal of Voice* 19: 497–500.
5. Robertson ML, Steward DL, Gluckman JL et al. (2004) Continuous laryngeal nerve integrity monitoring during thyroidectomy: does it reduce risk of injury? *Otolaryngology – Head and Neck Surgery* 131: 596–600.
6. Hermann M, Hellebart C, Freissmuth M (2004) Neuromonitoring in thyroid surgery: prospective evaluation of intraoperative electrophysiological responses for the prediction of recurrent laryngeal nerve injury. *Annals of Surgery* 240: 9–17.
7. Beldi G, Kinsbergen T, Schlumpf R (2004) Evaluation of intraoperative recurrent nerve monitoring in thyroid surgery. *World Journal of Surgery* 28: 589–91.
8. Chan WF, Lo CY (2006) Pitfalls of intraoperative neuromonitoring for predicting postoperative recurrent laryngeal nerve function during thyroidectomy. *World Journal of Surgery* 30: 806–12.

Appendix A: Additional papers on intraoperative nerve monitoring during thyroid surgery not included in summary table 2

The following table outlines studies considered potentially relevant to the overview not included in the main data extraction table (table 2). It is by no means an exhaustive list of potentially relevant studies.

Article title	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Bailleux S, Bozec A, Castillo L et al. (2006) Thyroid surgery and recurrent laryngeal nerve monitoring. *Journal of Laryngology and Otology* 566–9.	n = 36	Sensitivity = 98% Specificity = 86%	Small case series.
Brauckhoff M, Gimm O, Thanh PN et al. (2002) First experience in intraoperative neurostimulation of the recurrent laryngeal nerve during thyroid surgery of children and adolescents. *Journal of Paediatric Surgery* 37: 1414–8.	n = 97 children non-randomised comparative study	Temporary RLN palsy: • IONM = 1.9% (1/53) • Controls = 4.6% (2/44) Permanent RLN palsy: • IONM = 0% (0/53) • Controls = 2.3% (1/44) In all cases, results of intraoperative neurostimulation were identical to postoperative function of vocal cords.	Larger non-randomised studies are included.
Brennan J, Moore EJ, Shuler KJ. (2001) Prospective analysis of the efficacy of continuous intraoperative nerve monitoring during thyroidectomy, parathyroidectomy and parotidectomy. *Otolaryngology – Head and Neck Surgery* 124: 537–43.	n = 140 nerves at risk (96 RLN, 44 facial nerves)	Temporary RLN paralysis = 1% (1/96) Permanent RLN paralysis = 0%	Larger case series are included.
Dackiw AP, Rotstein LE, Clark OH (2002) Computer-assisted evoked electromyography with stimulating surgical instruments for recurrent/external laryngeal nerve identification and preservation in thyroid and parathyroid operation. *Surgery* 132: 1100–6.	n = 176 RLN and 152 external branches of the superior laryngeal nerve at risk	91.5% (161/176) RLN were correctly identified.	Larger case series are included.
Eisele DW (1996) Intraoperative electrophysiogic monitoring of the recurrent laryngeal nerve. *Laryngoscope* 106: 443–9.	n = 31 patients	42 RLNs were successfully monitored in 31 patients.	Small case series.
Hemmerling TM, Schmidt J, Bosert C et al. (2003) Intraoperative monitoring of the recurrent laryngeal nerve in 151 consecutive patients undergoing thyroid surgery. *Anesthesia and Analgesia* 93: 396–9.	n = 151 patients (266 nerves at risk)	Temporary paresis = 2%	Larger case series are included.
Horn D, Rotzscher VM (1999) Intraoperative electromyogram monitoring of the recurrent laryngeal nerve: experience with an intralaryngeal surface electrode. A method to reduce the risk of recurrent laryngeal nerve injury during thyroid surgery. *Langenbecks Archives of Surgery* 384: 392–5.	n = 167 nerves at risk	Postoperative transient and permanent nerve palsy = 0.6% of nerves (1% of patients). Rate of failure of method = 7.3%	Larger case series are included.

Article title	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Horne SK, Gal TJ, Brennan JA (2007) Prevalence and patterns of intraoperative nerve monitoring for thyroidectomy. *Otolaryngology – Head and Neck Surgery* 136: 952–6.	n = 685 question-naires	41% (685/1685) questionnaires received from random selection of otolaryngologists in the US. 28.6% reported using IONM routinely for all thyroidectomy cases. Surgeons currently using IONM during thyroidectomy were 41% less likely to report a history of permanent RLN injury.	Study reports on current usage of IONM in the United States.
Lambert AW, Cosgrove C, Barwell J et al. (2000) Vagus nerve stimulation: quality control in thyroid and parathyroid surgery. *Journal of Laryngology & Otology* 114: 125–7.	n = 59 RLNs, 40 patients	One case of equipment failure (electrode misplacement). 'The use of the Neurosign 100 Nerve Monitor is no substitute for meticulous surgery'.	Small case series.
Meyer T, Hocht B (2006) Recurrent laryngeal nerve monitoring during thyroid surgery in childhood. *European Journal of Pediatric Surgery* 16: 149–54.	n = 16 nerves at risk, 10 children	Clear and reliable identification of RLN in all cases. Partial temporary paralysis in one patient despite constant intraoperative signal of the RLN.	Small case series.
Petro ML, Schweinfurth JM, Petro AB (2006) Transcricothyroid intraoperative monitoring of the vagus nerve. *Archives of* Otolaryngology – *Head and Neck Surgery* 124: 537–43.	n = 31	All RLNs were identified with continuous electromyographic monitoring. Vocal cord paresis or paralysis was not observed. In 70% cases, the technique was given a rating of 1 (most useful) on a 5-point scale.	Small case series.
Snyder SK, Hendricks JC (2005) Intraoperative neurophysiology testing of the recurrent laryngeal nerve: plaudits and pitfalls. *Surgery* 138: 1183–91.	n = 100 patients, 185 RLNs	7.6% (14/185) nonfunction of visually intact RLNs at some point during the operation. Temporary paralysis = 2.2% (4/185) 4.3% (8/185) altered RLN function with no altered vocal cord function postoperatively. Nerve stimulator aided dissection of the RLN in 17 instances (9.2%). There were 7 episodes (3.8%) of equipment dysfunction that hampered surgical dissection.	Larger case series are included.
Thomusch O, Sekulla C, Walls G et al. (2002) Intraoperative neuromonitoring of surgery for benign goiter. *American Journal of Surgery* 183: 673–8.	n = 4382 patients	Transient RLN palsy = 1.4% Permanent RLN palsy = 0.4% Rates of RLN palsy were significantly lower with IONM than for visual identification $p < 0.05$.	Earlier results from a subset of the same study as Dralle et al, 2004 that is summarised in table 2.[1]

Article title	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Thomusch O, Sekulla C, Timmermann W et al. (2003) Intraoperative neuromonitoring in thyroid surgery – results of the German prospective multicentre study. *European Surgery – Acta Chirurgica Austriaca Supplement* 35: 240–5.	n = 8900 patients, 16,148 nerves at risk	The use of IONM significantly decreased the early RLN palsy rate (3.3% vs 4.9%, p = 0.04). The difference for permanent RLN palsy was not statistically significant (0.7% vs 0.9%). Overall, IONM was beneficial in high-risk procedures such as recurrent goitre, thyroid carcinoma and extended resections.	Earlier results from a subset of the same study as Dralle et al, 2004 that is summarised in table 2.[1]
Thomusch O, Sekulla C, Machens A et al. (2004) Validity of intra-operative neuromonitoring signals in thyroid surgery. *Langenbecks Archives of Surgery* 389: 499–503.	n = 8534 patients, 15,403 nerves at risk	Transient RLN palsy = 2.8% Permanent RLN palsy = 0.7% Indirect IONM stimulation via the vagal nerve was more reliable than direct RLN stimulation.	Earlier results from a subset of the same study as Dralle et al, 2004 that is summarised in table 2.[1]
Yarborough DE, Thompson GB, Kasperbauer JL et al. (2004) Intraoperative electromyographic monitoring of the recurrent laryngeal nerve in reoperative thyroid and parathyroid surgery. *Surgery* 136: 1107–15.	n = 52 procedures with IONM, 59 patients with no monitoring	Rate of unintended permanent nerve damage: • IONM = 1.9% (1/52) • Controls = 1.7% (1/59) Seven false-negative and two false-positive findings occurred.	Larger non-randomised comparative studies are included.

Appendix B: Literature search for intraoperative nerve monitoring during thyroid surgery

Database	Date searched	Version searched
Cochrane Library	22/08/2007	Issue 3, 2007
CRD databases (DARE & HTA)	22/08/2007	Issue 3, 2007
Embase	21/08/2007	1980 to 2007 Week 33
Medline	21/08/2007	1950 to August Week 2 2007
Premedline	21/08/2007	August 20, 2007
CINAHL	21/08/2007	1982 to August Week 3 2007
British Library Inside Conferences	23/08/2007	-
NRR	22/08/2007	2007 Issue 3
Controlled Trials Registry	13/08/2007	-

Search strategy used in Medline

The search strategy was adapted for use in the databases above

1	Thyroid Gland/su [Surgery]
2	Thyroid Diseases/su [Surgery]
3	Thyroidectomy/
4	thyroidectomy.tw.
5	Parathyroidectomy/
6	parathyroidectomy.tw.
7	Parathyroid Glands/su [Surgery]
8	(thyroid$ adj3 (surg$ or operat$)).tw.
9	(parathyroid$ adj3 (surg$ or operat$)).tw.
10	or/1-9
11	Monitoring, Intraoperative/
12	Electromyography/
13	(electromyograph$ or EMG).tw.
14	(intraoperative$ adj3 nerve$ adj3 monitor$).tw.
15	(intraoperative$ adj3 monitor$ adj3 nerve$).tw.
16	(intraoperative$ adj3 (neuromonitor$ or neuro-monitors)).tw.

17	IOM.tw.
18	Electrophysiology/
19	(electrophysiologic$ adj3 monitor$).tw.
20	(nerve$ adj3 integrity adj3 monitor$).tw.
21	NIM.tw.
22	Neurosign.tw.
23	(cascade adj3 IOM).tw.
24	EpochXP.tw.
25	(Nicolet adj3 Bravo).tw.
26	or/11-25
27	10 and 26
28	Animals/
29	Humans/
30	28 not (28 and 29)
31	27 not 30