Australian Government

Department of Health and Ageing

Australia and New Zealand Horizon Scanning Network

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Horizon Scanning Technology Prioritising Summary

Nerve stimulation in thyroid surgery

February 2008

ASERNIP-S

Australian Safety and Efficacy Register of New Interventional Procedures - Surgical

Royal Australasian College of Surgeons

ISBN
Publications Approval Number:

Electronic copies can be obtained from http://www.horizonscanning.gov.au

Enquiries about the content of the report should be directed to:

HealthPACT Secretariat
Department of Health and Ageing
MDP 106
GPO Box 9848
Canberra ACT 2606
AUSTRALIA

The production of this Horizon scanning prioritising summary was overseen by the Health Policy Advisory Committee on Technology (HealthPACT), a sub-committee of the Medical Services Advisory Committee (MSAC). HealthPACT comprises representatives from departments in all states and territories, the Australia and New Zealand governments; and ASERNIP-S. The Australian Health Ministers' Advisory Council (AHMAC) supports HealthPACT through funding.

This Horizon scanning prioritising summary was prepared by Miss Deanne Leopardi from the Australian Safety and Efficacy Register of New Interventional Procedures – Surgical (ASERNIP-S).

PRIORITISING SUMMARY

REGISTER ID **S000068**

NAME OF TECHNOLOGY **NERVE STIMULATION IN THYROID SURGERY**

PURPOSE AND TARGET GROUP **TO DECREASE RECURRENT LARYNGEAL NERVE DAMAGE IN PATIENTS UNDERGOING THYROIDECTOMY**

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 — ARTG number **NA**
- ☐ No
- ☑ Not applicable

INTERNATIONAL UTILISATION

COUNTRY	LEVEL OF USE		
	Trials Underway or Completed	Limited Use	Widely Diffused
Australia	✓		
China	✓		
Germany	✓		
Hungary	✓		
Italy	✓		
Japan	✓		
Poland	✓		
United States	✓		

IMPACT SUMMARY

Discontinuous nerve stimulation and digital palpation during thyroidectomy is a potential alternative to dissection for the intraoperative identification of laryngeal nerves and the prediction of their postoperative integrity. This technique is currently in the investigational stage in Australia.

BACKGROUND

The thyroid, located at the front of the neck, is responsible for regulating metabolic activities and supporting various other functions such as heart rate and blood flow (Medline Plus 2007). Surgical removal of part or all of the thyroid (thyroidectomy) is required to treat a number of conditions, including thyroid tumours (both malignant and benign), hyperthyroidism, hypothyroidism and thyroid nodules. Damage of the nerves attached to the larynx during thyroid surgery, in particular the recurrent laryngeal nerve (RLN) and the external branch of the superior laryngeal nerve (EBSLN), is the most significant complication of thyroidectomy (Loch-Wilkinson et al. 2007). Unilateral damage of the laryngeal nerves may result in temporary or permanent verbal hoarseness (dysphonia), or difficulty speaking (including trouble producing higher vocal frequencies and projection of the voice) or swallowing (dysphagia) (Loch-Wilkinson et al. 2007). Bilateral damage of these nerves is a more urgent situation as it may lead to difficulty breathing and permanent vocal damage (Tomoda et al. 2006).

Although laryngeal nerve damage during the first thyroidectomy is relatively uncommon (1% to 2%), the likelihood increases significantly with subsequent thyroid surgery (12.5%) (Otto et al. 2002; Loch-Wilkinson et al. 2007). The incidence of permanent and transient dysphonia and dysphagia after thyroidectomy ranges from 3.4% to 7.2% and 0.2% to 0.9%, respectively (Tomoda et al. 2006). Thus, it is imperative that surgeons take measures to avoid damaging the laryngeal nerves (Loch-Wilkinson et al. 2007).

Current practice uses anatomical dissection to identify and preserve the RLN during thyroid surgery, but nerve stimulation has been suggested as a more effective alternative (Loch-Wilkinson et al. 2007). Discontinuous nerve stimulation in conjunction with digital palpation involves stimulating the RLN at its proximal exposed site. The surgeon then determines nerve function by inserting a finger into the postcricoid region of the larynx to feel for contraction of the posterior crioartenoid (PCA) muscle in response to RLN stimulation (Loch-Wilkinson et al. 2007). In a similar fashion, the integrity of the EBLSN can be determined by stimulating the nerve and eliciting a cricothyroid muscle twitch (Loch-Wilkinson et al. 2007).

CLINICAL NEED AND BURDEN OF DISEASE

Thyroid diseases are extremely common in Australia, with one in seven people being affected (Australian Thyroid Foundation 2007). Of these a significant number would undergo thyroidectomy as a treatment.

Thyroid cancer is relatively uncommon; 298 and 822 new thyroid cancer cases were diagnosed in Australian men and women in 2001. The survival rate is significantly higher than for other types of cancer, with the 5-year survival rate being 87.9% in men and 95.6% in women (AIHW 2007). During 2004, a total of 97 Australians died from thyroid cancer (ABS 2007).

DIFFUSION

The FDA approved the use of disposable hand-held nerve stimulators in 2006 (FDA Database 2006). Manufacturers of the device include; Medtronic and Aaron Medical. None of these devices were available on the TGA database.

The use of discontinuous nerve stimulation and palpation to identify the RLN during thyroid surgery appears to be in various stages of investigation throughout Australia, the United States, China, Japan, and Europe.

COMPARATORS

Anatomical dissection for the identification of the RLN is the current standard of care for preserving nerve integrity during thyroid surgery, and is the main comparator for discontinuous nerve stimulation with palpation for RLN identification (Loch-Wilkinson et al. 2007).

However, continuous nerve stimulation is another form of nerve stimulation that uses electrodes placed on the endotracheal tube or inserted into muscles innervated by the RLN to continuously stimulate the laryngeal nerves (Loch-Wilkinson et al. 2007).

SAFETY AND EFFECTIVENESS ISSUES

No randomised controlled trials were found. One non-randomised comparative study and two prospective case series studies were identified that examined the efficacy of nerve stimulation and palpation in thyroidectomy for the location and prediction of postoperative laryngeal nerve deficits.

The non-randomised comparative study by Loch-Wilkinson et al. (2007) compared the outcomes of total thyroidectomy using discontinuous nerve stimulation with palpation and total thyroidectomy using anatomical dissection. Fifty consecutive patients were recruited for the study group (with nerve stimulation) and 20 patients were enrolled from another hospital for the control group (without nerve stimulation). Both the study and control groups were comparable in terms of mean age, gender ratio and pathological makeup (Loch-Wilkinson et al. 2007).

Total thyroidectomy was carried out by the standard technique of capsular dissection with attempted visualization of the RLN and EBLSN. For the study group, if anatomical recognition was not possible, nerve stimulation was used to identify their position.

Stimulation (1 to 2 mAmps) of all four nerves was carried out following dissection; a twitch response (felt by palpation technique) confirmed the nerves location and functionality. The vocal cords and voice of both patient groups were assessed before and after surgery by an independent ear, nose and throat surgeon, and patients completed dysphagia score sheets (scores ranged from 0 = 'no symptoms' to 10 = 'real difficulty swallowing') (Loch-Wilkinson et al. 2007).

Tomoda et al. (2006) conducted a prospective case series study of 1376 patients (2197 nerves at risk), and included patients with malignant or benign tumours, as well as those undergoing primary or secondary thyroid surgery. Complete RLN identification and dissection was carried out in all patients followed by neural stimulation (1.0 mAmp) at the end of each surgery. Palpation for contraction of the PCA muscle was performed to confirm the location and function of the RLN (Tomoda et al. 2006).

Otto et al. (2002) conducted a prospective case series study of 55 patients (81 nerves at risk) who underwent thyroid or parathyroid surgery between January 1998 and February 2000. Each patient underwent pre- and postoperative assessment by an otolaryngology resident proficient in laryngeal examination to evaluate vocal cord mobility. During surgery all RLNs at risk were identified and exposed. At the conclusion of each surgery the RLNs were stimulated using 0.5 mAmp to confirm their integrity. A second 0.5 mAmp stimulus was applied if the first attempt was unsuccessful. Digital palpation was used to detect contraction of the PCA muscle during stimulation. Results were recorded as 'positive' (no contraction) or 'negative' (palpable contraction).

a) Safety

In the study by Loch-Wilkinson et al. (2007) there were no instances of equipment malfunction. The adverse effects associated with the technique included nerve palsy, severe dysphagia and dysphonia. Postoperatively, complete unilateral temporary RLN palsy (predicted intraoperatively) occurred once and there were two cases of mild dysphonia (not predicted) reported. All three patients recovered completely within a short period; the latter two were not considered to be true RLN injuries. The study group displayed no bilateral nerve palsies or permanent vocal cord paralysis. Dysphagia scores were completed by 82% of patients in the stimulation group and 100% in the control group. The average scores were 3.6 (95% confidence interval (CI), 2.99 to 4.20) and 3.4 (95% CI, 2.52 to 4.28), respectively. Therefore, there was no significant difference in rates of dysphagia between the two groups. Other postoperative complications in the study group included four patients with temporary hypocalcaemia and one with haematoma. In the control group two patients reported temporary hypocalcaemia and one required reoperation due to haemorrhage (Loch-Wilkinson et al. 2007).

Tomoda et al. (2006) reported all incidences of temporary and permanent RLN palsy and cases of vocal hoarseness. Overall, 3.6% (80/2197) nerves at risk experienced temporary palsy and 1.0% (21/2197) experienced permanent palsy. Temporary and permanent RLN palsy was more common in patients with cancer and those undergoing a secondary

thyroid surgery. Eleven patients with RLN palsy reported no symptoms. Recovery time for temporary palsy ranged from seven days to 12 months, with 92.1% of patients recovered fully within six months. Thirty patients experienced hoarseness (from one or more causes) but did not have RLN palsy. The cause was attributed to haematoma (n=5), oedema with vocal cord and/or arytenoid involvement (n=8), acute laryngitis (n=7), chronic laryngitis (n=5) or vocal cord polyps (n=2). Eight patients had no identifiable cause for their hoarseness (Tomoda et al. 2006).

Little safety data were reported by Otto et al. (2002). Four patients incurred damage to their RLN, which resolved in three cases by the time of the postoperative examination (follow-up time not specified). The remaining patient did not attend a follow-up appointment but reported no adverse outcomes from surgery.

b) Effectiveness

Positive and negative likelihood ratios (LRs) were reported where possible. A positive LR is the ratio of the true-positive rate to the false-positive rate (sensitivity/(1 - specificity)). A negative LR is the ratio of the false-negative rate to the true-negative rate ((1 - sensitivity)/specificity). A LR > 1 indicates a higher likelihood of having the condition, whereas LRs < 1 indicate a higher likelihood that the condition is absent. LRs above 10 and below 0.1 indicate that the test has a strong ability to detect the presence or absence of the condition, respectively (Deeks et al. 2004).

In the study by Loch-Wilkinson et al. (2007), there were 100 RLNs and 100 EBLSNs at risk for investigation (n=50 patients). Intraoperatively, 100% (100/100) of the RLNs and 86% (86/100) of the EBLSNs were identified without the need for nerve stimulation. A negative twitch result occurred in seven of the 100 RLNs (two bilaterally and 3 unilaterally; n=5 patients). Postoperative assessment found only one RLN palsy, thus six false-positives and one true-positive were found by nerve stimulation. Thirteen EBLSNs could not be identified by dissection and only one was then found with nerve stimulation. Thus, a total of 12 nerves were not found by either method. A negative twitch response occurred in 14% of EBLSNs (eight unilaterally and 3 bilaterally; n=11 patients). Of the eight unilateral negative twitches, there were two negative twitches for the RLN in the same patient. These false-positives may have been due to the residual effect of the neuromuscular blocking agents or a secondary effect of the reversal agent. Overall, the sensitivity and specificity of RLN stimulation was 100% and 94%, with a positive predictive value (PPV) of 14% and negative predictive value (NPV) of 100%. The positive and negative LRs were 16.7 and 0, which indicate that discontinuous nerve stimulation provides convincing or definitive diagnostic evidence (Loch-Wilkinson et al. 2007).

In Tomoda et al. (2006) there were 76 negative RLN twitch results, 70 of which were true-positives for RLN palsy. Of these true-positive results, 25.7% (18/70) of nerves experienced permanent palsy. There were 31 false-positive results, of which 90% (28/31) of RLN palsies resolved within a year. For identifying immediate (temporary) postoperative vocal cord palsy, the sensitivity and specificity of nerve stimulation was 69.3% and 99.7%, with a PPV of 92.1% and a NPV of 98.5%. For permanent vocal cord

palsy, the sensitivity and specificity of nerve stimulation was 85.7% and 97.3%, with a PPV of 23.7% and a NPV of 99.8%. The positive and negative LRs for temporary RLN palsy were 231 and 0.31, which indicate that in this case nerve stimulation provides moderate to strong diagnostic evidence as it is very good at detecting a positive result (ruling in nerve palsy) rather than ruling it out. The positive and negative LRs for permanent RLN palsy were 31.7 and 0.15, which indicate that nerve stimulation provides strong diagnostic evidence as its ability to detect both positive and negative results was high.

In the study by Otto et al. (2002) there were a total of 72 palpable contractions (positives) and 9 non-contractions (negatives). Of these, six were false-positives and one was a false-negative. The sensitivity and specificity of intraoperative RLN stimulation for predicting laryngeal damage after thyroid surgery was 75% and 92.2%, respectively. The PPV and NPV were 33.3% and 98.6%. The positive and negative LRs were 9.62 and 0.27, which indicate that nerve stimulation provides moderate to strong diagnostic evidence.

COST IMPACT

For total thyroidectomy, according to the Medicare Benefit Schedule, the maximum benefit paid is $693.40 (MBS 2007). One study described the estimated treatment cost for surgical complications related to vocal cord surgery to repair functionality after RLN damage at $8479.70 (Zanocco et al. 2006).

Continuous nerve stimulation is considered to be the most efficient way to minimise RLN damage during thyroidectomy, but it is not cost-effective when measured by the true cost per nerve injury prevented (Loch-Wilkinson et al. 2007). Initiation and equipment costs for continuous neurostimulation are estimated at AU$40,000, with ongoing costs of AU$500 per operation (Loch-Wilkinson et al. 2007). Discontinuous monitoring is a simpler and potentially cost effective method of RLN identification because it uses hand-held disposable nerve stimulators valued at AU$128 (Loch-Wilkinson et al. 2007).

ETHICAL, CULTURAL OR RELIGIOUS CONSIDERATIONS

No issues were identified from the retrieved material.

OTHER ISSUES

No issues were identified from the retrieved material.

SUMMARY OF FINDINGS

Limited evidence from one non-randomised comparative study and two case series studies suggested that intraoperative RLN stimulation for locating and predicting vocal cord injuries after thyroid surgery is safe and efficient. Nerve stimulation appeared to offer a level of diagnostic evidence in detecting and conserving the integrity of vocal cord

nerves. However, as this is based on very little evidence it is unknown whether this tool could potentially be used in place of the current standard of care.

HealthPACT Action

Based on the available, nerve stimulation in thyroid surgery will be archived.

Number of Studies included

Total number of studies	3
Level III-2 evidence	1
Level IV evidence	2

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SEARCH CRITERIA TO BE USED

Thyroidectomy
(Recurrent laryngeal nerve) OR (RLN)
(External branch superior laryngeal nerve) OR (EBLSN)