ORIGINAL ARTICLE

Usefulness of Neuromonitoring in Thyroid Surgery

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KEYWORDS
Thyroid; Thyroidectomy; Surgery; Recurrent laryngeal nerve; Intraoperative nerve monitoring; Complications; Vocal cord; Harmonic

Abstract
Introduction: Identifying the recurrent laryngeal nerve is the gold standard for reducing injury in thyroidectomy.
Objective: To evaluate the usefulness of neuromonitoring in identifying the recurrent laryngeal nerve.
Methods: This was a study of 259 recurrent laryngeal nerves at risk during thyroidectomy performed with neuromonitoring (group A: 129 nerves) and without neuromonitoring (control group B: 130 nerves).
Results: The percentage of visually unidentified nerves was 18% in group A and 20% in group B, with no statistical difference. From the moment of non-identification, identification with neuromonitoring was achieved in group A in 100% of cases. The difference was statistically significant. The positive and negative predictive values of neuromonitoring were 100%.
Conclusions: Neuromonitoring helps to identify the recurrent laryngeal nerve and increases the security of the surgeon in the technique. It is advisable to perform neuromonitoring routinely in thyroid surgery.

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PALABRAS CLAVE
Tiroideos; Tiroidectomía; Cirugía; Nervio laringeo recurrente; Neuromonitorización intraoperatoria; Complicaciones; Cuerda vocal; Armónico

Utilidad de la neuromonitorización en cirugía tiroidea

Resumen
Introducción: La identificación del nervio laringeo recurrente es el patrón de referencia para reducir su lesión en la tiroidectomía.
Objetivo: Evaluar la utilidad de la neuromonitorización en la identificación del nervio laringeo recurrente.
Métodos: Estudio de 259 nervios laringeos recurrentes en riesgo durante la tiroidectomía realizada con neuromonitorización (grupo A: 129 nervios), y sin neuromonitorización (grupo B de control: 130 nervios).
Resultados: El porcentaje de nervios no identificados visualmente es del 18% en el grupo A y del 20% en el grupo B, sin diferencia estadística. A partir del momento de no identificación, en el grupo A, con neuromonitorización se consigue la identificación en el 100% de los casos. La diferencia es estadísticamente significativa. El valor predictivo positivo y negativo de la neuromonitorización es del 100%.

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Conclusiones: La neuromonitoreación ayuda en la identificación del nervio laringeo recurrente, incrementa la seguridad del cirujano en la técnica y es recomendable realizarla sistemáticamente en la cirugía tiroides. © 2011 Elsevier España, S.L. Todos los derechos reservados.

Introduction

The incidence of recurrent laryngeal nerve (RLN) palsy in thyroid surgery is low, but it has a considerable impact on quality of life for patients, potentially severe consequences (dysphonia, cough, dysphagia, pulmonary aspiration or airway obstruction which may require tracheostomy) and represents the most common cause of litigation after thyroidectomy.1-4

The reported incidence of persistent RLN paralysis varies between 0% and 18.6%.5 In the meta-analysis published by Higgins et al.6 it was between 0.59% and 0.75%, increasing to 2.81%-3.72% in the case of reoperations and 1.91%-2.22% in the case of malignant tumours. In general, the mean incidence of persistent paralysis reported by series studies is below 1%,7-9 increasing in reoperations (3.8%-20%) compared to primary surgery (0.3%-1%).10 Extensive substernal goitre with anatomical distortion, previous neck irradiation, re-exploration due to haemorrhage and anatomical variations increase the risk of paralysis.1,11-13

The factor most commonly associated with RLN lesion is an initial error in its identification,8,14,15 facilitated by intraoperative bleeding.16,17 This may increase the incidence of paralysis up to 25%10 through inadvertent damage caused by traction or electrothermal mechanisms, ligation, ischemia, section or suction.1,9,14,15,18

Visual identification of the RLN and its dissection are the gold standard for reducing damage,1,3,15,16,18-21 as confirmed by multicentre studies.22 Thus, its non-identification can increase the risk of lesion or, at least, its dissection does not increase this risk.23-25 The systematic use of neuromonitoring (NM) can reduce damage by facilitating location and dissection of the nerve.24

Moreover, interest in improving techniques for RLN location is due to anatomical reasons:

- In 60%-75% of cases, the RLN is divided into ascending extralaryngeal branches which are vulnerable during identification and dissection, with connections to other systems (sympathetic plexus, trachea, oesophagus and superior laryngeal nerve).4,9,26 Therefore, these connections represent a common finding, so laryngeal innervation could be considered as a plexus with important implications in the interpretation of clinical and functional results in laryngeal nerve incidents or lesions, and may also explain the variability in laryngeal functional recovery.26

- The right inferior laryngeal nerve may not be recurrent in between 0.4% and 1% of cases. Instead, it exits directly from the trunk of the vagus nerve, associated to an aberrant retrooesophageal or intertracheoesophageal subclavian vessel.22,27

- The relationship of the RLN with the inferior thyroid artery (ITA) is highly variable.27

The relationship of the RLN with the ligament of Berry is highly constant, but at this point the nerve is very vulnerable and easily damaged. In addition, this is a bleeding site, since it is vascularised by branches of the ITA, hindering a clean dissection and making it the most dangerous site.18

Various procedures for identifying the RLN have been described1,19:

1 Caudally, from the origin of the RLN at the mediastinum, in the triangle formed by the trachea, common carotid and inferior thyroid pole. The fatty tissue at this location is very loose, making it difficult to dissect, but the nerve is thicker and more resilient. Dissection must be performed in a cranial direction on the superficial side, whilst maintaining the fatty tissue.9,19,28 Some authors advise against this technique, due to the increased risk of devascularisation of the inferior parathyroids.27

2 Laterally in relation to the ITA. This point is the safest and recommended by many authors.9,15,16,27-29 Ligation of the ITA branches must be extracapsular and as peripheral as possible.4,9,30

3 At the entry of the RLN into the larynx in relation to the ligament of Berry19 and the inferior horn of the thyroid cartilage.11 Initial visual identification at this point should be avoided.

4 By electrical stimulation and registration of laryngeal motility.

Several techniques to identify laryngeal motility after electrical stimulation of the RLN or vagus nerve in thyroidectomy have been published since the mid-twentieth century1,6,7,14,18,31-35:

- Registry of pressure changes in the ball of an endotracheal tube (ETT) due to vocal cord movement following the stimulus.36

- Palpation of the arytenoids in the retrocricoid area (twitch).2,26,31,34,37,38 The validity of this technique is similar to electromygographic recording and its cost is less,2 but it should not be performed with small incisions, in large thyroids or with cervical fibrosis. In addition, it may cause damage to the RLN due to stretching and traction of the larynx. At present, this technique can be used in case of signal loss during NM.

- Observation of the movement of the vocal cords with direct laryngoscopy or fibroscopy through a laryngeal mask.39

- Through electromyo graphic registration of the vocal muscles:
  - With surface electrodes placed in the retrocricoid area.40
  - With surface electrodes attached to the ETT, in contact with the vocal cords.1,13,41
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- With monopolar needle electrodes inserted directly into the vocal cords through direct laryngoscopy.\textsuperscript{13,41}
- With monopolar or bipolar needle electrodes inserted into the thyroarytenoid muscles, by puncture through the cricothyroid membrane.\textsuperscript{1,14,15,32,35,41,42}
- With fixed electrodes in the vagus nerve in the ETT surface and with needle electrodes inserted into the vocalis muscle through the cricothyroid membrane, with real-time registration.\textsuperscript{43}

Of these, the techniques that have generated most publications are NM through transcricothyroid puncture and surface electrodes in the ETT.

In summary, we emphasise that the improvement in safety during thyroid surgery is multifactorial.

The Ligasure and Harmonic haemostasis systems enable techniques with less intraoperative bleeding, less traction manoeuvres and less thermal damage, although no statistically significant reduction in the incidence of RLN paralysis has been shown.\textsuperscript{4,8} Moreover, the literature is unanimous in considering that NM aids in the identification of the RLN, especially in cases with difficulties (carcinoma, reinterventions), thus facilitating its dissection by reducing its manipulation. Furthermore, it also helps to document the functional status of the RLN at the end of the intervention, although it has not been shown to significantly reduce the incidence of paralysis.\textsuperscript{1,3} NM has other advantages, such as helping in decision-making in case of signal loss,\textsuperscript{31} for training\textsuperscript{8} and as documentary support in case of litigation.\textsuperscript{1,4}

Given the low initial incidence, it is difficult to demonstrate that a reduction in the incidence of paralysis is due to a particular factor.\textsuperscript{3} Several studies have shown that observation of statistically significant changes would require costly, prospective, multicentre studies involving thousands of patients. These studies would need to avoid bias such as variability in the complexity of the surgical technique, technology used, random assignment of cases and different levels of surgical training and experience.\textsuperscript{2,3,12,18,32}

The aim of this work was to evaluate the usefulness of NM in the identification of the RLN during thyroid surgery.

Material and Methods

This was a prospective, descriptive, non-randomised study which was designed to calculate the probability of identifying the RLN in 2 groups of patients undergoing thyroidectomy with the Harmonic Ultracision Focus system, with NM (study group: group A) and without NM (control group: group B). NM was conducted with a Medtronic Xomed Inc. device and a NM-Response\textsuperscript{6} 2.0 monitor, connection box, 2-channel paired needle electrode, 2 single-channel ground-electrodes and a standard, monopolar stimulation probe.

Table 1 shows the characteristics of the sample.

We included 132 consecutive patients operated by the same surgeon between May 2010 and December 2011 (67 patients in group A and 65 in group B).

We assessed 259 RLN at risk (129 patients in group A and 130 in group B).

Both groups underwent pre- and postoperative laryngoscopy with a rhinofibrolaryngoscope and mirror (at 1–3 days and 3–6 weeks), with registration of pre- and postoperative voice problems. Patients with voice or motility abnormalities were re-evaluated by another specialist.

In both groups we attempted visual, extracapsular identification of the RLN in relation to the ITA.\textsuperscript{4,16,28} If the RLN was not located, it was classified as non-identified. At this point, group A used NM mapping as support. No other location manoeuvres were attempted in either group.

Once the posterior edge of the thyroid gland was released and the cricothyroid space was identified, we inserted the paired needle electrode in the thyroarytenoid muscles, through the cricothyroid membrane with an inclination of 20–30° and a depth of 3–5 mm.\textsuperscript{7} The ground-electrodes were placed in the sternoclavicular area, outside the surgical field.

We programmed stimulation at 0.5–1 mA and an event threshold of 70–100 \(\mu\)V.\textsuperscript{29,31} The system was checked by stimulation of the midline of the cricothyroid space, obtaining registration of a potential and a distinctive audible warning (low tone).

We followed the 4-step technique (V1 initial vagal stimulation and V2 after completion and R1 initial RLN stimulation and R2 after completion) in a sequential order V1–R1–R2–V2.\textsuperscript{29,31,44} We located the vagus nerve by opening a small sac 1 cm above the common carotid and stimulating at 1 mA. This was increased to 2–3 mA in case of non-identification.\textsuperscript{37}

RLN monitoring was performed in a cranial direction, with Harmonic until its entry into the larynx, attempting to maintain the perineural area, avoiding traction and with short, quick movements of the active branch in the direction of the nerve until the ligament of Berry was sectioned.

In group A we followed the path with the help of NM by intermittent stimuli without exerting traction or rotation manoeuvres. After lobectomy, we confirmed function by stimulating the RLN (R2) and the vagus nerve (V2).

The twitch test was not performed routinely.

We noted the visual identification of the RLN in both groups, signal incidences during the NM in group A and the outcome of postoperative laryngoscopy (normal motility or paralysis).

Table 2 shows the elements which may help to interpret the validity of NM.\textsuperscript{3,11–13,29,31}

We conducted a descriptive statistical study of the distribution of the sample. The confidence interval for the comparison of the mean was 95%. We used the Pearson \(\chi^2\) test for discrete variables.

Results

The results obtained are shown in Tables 3–5.

The groups were homogeneous with respect to age, gender, type of condition and degree of technical difficulty.

Around 7.5%–9.2% of patients suffered previous voice condition (Table 1).

There were no cases of temporary or permanent paralysis.

The initial visual identification of the RLN was possible in over 80% of cases in both groups (no significant difference).
Table 1  Neuromonitoring in Thyroid Surgery. Sample Distribution.

<table>
<thead>
<tr>
<th></th>
<th>Study Group</th>
<th>Control Group</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Number of patients</strong></td>
<td>67</td>
<td>65</td>
</tr>
<tr>
<td><strong>Age (mean, years±2SD)</strong></td>
<td>57±7.55</td>
<td>54±7.35</td>
</tr>
<tr>
<td><strong>Females, %</strong></td>
<td>48 (72)</td>
<td>54 (83)</td>
</tr>
<tr>
<td><strong>Males, %</strong></td>
<td>19 (28)</td>
<td>11 (17)</td>
</tr>
<tr>
<td><strong>Preoperative laryngeal motility</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RLN at risk</td>
<td>129</td>
<td>130</td>
</tr>
<tr>
<td>Normal laryngeal motility</td>
<td>128</td>
<td>130</td>
</tr>
<tr>
<td>Preoperative RLN paralysis</td>
<td>1 (left)</td>
<td>0</td>
</tr>
<tr>
<td><strong>Preoperative voice evaluation</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients with normal voice</td>
<td>62</td>
<td>59</td>
</tr>
<tr>
<td>Patients with preoperative voice involvement, %</td>
<td>5 (7.5)</td>
<td>6 (9.2)</td>
</tr>
<tr>
<td>Functional dysphonia</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Laryngeal nodules</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Laryngeal polyp and submucosal oedema</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Prior RLN paralysis</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td><strong>Preoperative evaluation of local risk factors</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Without local risk factors (first intervention, benign goitre, without anatomical distortion – small volume, non-compressive –), %</td>
<td>37 (57)</td>
<td>38 (58)</td>
</tr>
<tr>
<td>With one or more local risk factors (reintervention on the same side, malignant tumour, anatomical distortion – large volume, compressive–, mediastinal extension, difficult airway, Graves-Basedow, irradiated neck, cervical rigidity), %</td>
<td>28 (43)</td>
<td>27 (42)</td>
</tr>
<tr>
<td><strong>Techniques employed</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total thyroidectomy, %</td>
<td>62 (92.5)</td>
<td>65 (100)</td>
</tr>
<tr>
<td>Hemithyroidectomy, %</td>
<td>5 (7.5)</td>
<td>0</td>
</tr>
<tr>
<td>Associated to parathyroidectomy</td>
<td>7</td>
<td>6</td>
</tr>
<tr>
<td>With total thyroidectomy</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>With hemithyroidectomy</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Functional lymph node dissection</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Primary surgery</td>
<td>64</td>
<td>65</td>
</tr>
<tr>
<td>Reinterventions (previous surgery 30 years earlier)</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Totalisations</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td><strong>Involvement</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Benign involvement, %</td>
<td>55 (82)</td>
<td>52 (80)</td>
</tr>
<tr>
<td>Malignant involvement (papillary/follicular), %</td>
<td>12 (18)</td>
<td>13 (20)</td>
</tr>
</tbody>
</table>

RLN, recurrent laryngeal nerve; SD, standard deviation.

Visual identification reached 98% in group A with NM. The RLN was not visualised in 2 cases (1.6%), although an electromyographic signal was obtained, so final identification reached 100%.

We observed a statistically significant difference in the final location of the RLN in group A (100%) compared to group B (80%) (Table 4 and Fig. 1).

Signal losses observed were due to disinsertion of the electrode, connection loss, fault in the connection box and programming errors in the monitor settings. All were easily resolved.

NM was performed successfully in all patients in group A. There were no postoperative complications related to NM.

We obtained an electromyographic signal in the 128 RLN at risk and we did not obtain it in 1 RLN which presented previous palsy.

The positive and negative predictive values of NM were both 100%. There were no false positives or negatives (Table 5).

Discussion

The principles of Riddell16 are still applicable to the reduction of laryngeal paralysis based on visual identification of the RLN in its relationship with the ITA, functional testing after completion of the intervention by electrical stimulation and pre- and postoperative routine laryngoscopy.17

The validity of NM to locate and evaluate the functional status of the RLN has been sufficiently established in the literature, with very similar results and redundant information. However, its use has not become generalised so far.1,11,31
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Table 2  Neuromonitoring in Thyroid Surgery. Interpretation of the Signal.

<table>
<thead>
<tr>
<th>Present Signal</th>
<th>Absent Signal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Precautions</td>
<td></td>
</tr>
</tbody>
</table>
| Conduct V2 stimulus to reduce the possibility of a false negative | - Verify possible equipment failure  
- Verify V2 stimulus  
- If there is no V2 signal: conduct twitch test  
- If the V2 fails, then:  
  - Contralateral lobectomy must be postponed  
  - If there was previous contralateral paralysis: precautions during extubation must be maximised |

Laryngoscopy

<table>
<thead>
<tr>
<th>Normal motility</th>
<th>False negative</th>
<th>False positive</th>
</tr>
</thead>
</table>
| Normal laryngeal motility | - Normal laryngeal motility  
- Normal function of equipment |
| False negative | - Causes:  
  - Lesion caused after the last R2 test  
  - Incorrect technique: there is a proximal lesion in the RLN and a distal stimulus was conducted |
| True positive | - Causes:  
  - Undetected previous paralysis  
  - Damage during intervention (traction, thermal, section) |

Laryngeal paralysis

<table>
<thead>
<tr>
<th>False positive</th>
<th>True positive</th>
</tr>
</thead>
</table>
| - Normal laryngeal motility  
- No visualisation or location of the RLN:  
  - Absence of the RLN  
  - Extralaryngeal ramifications  
  - Fibrosis  
  - Tumoural invasion  
  - Excessive perineural tissue  
  - Equipment failure (loss of signal):  
    - System failure (electrodes, connection box, error in monitor programming)  
    - Device failure  
    - Device misuse  
    - Pharmacological cause (relaxant)  
    - Muscle fatigue  
    - Transient paralysis due to excessive traction-manipulation |

R2, stimulation of recurrent nerve after the intervention; V1, stimulation of vagus nerve before locating the recurrent nerve; V2, stimulation of vagus nerve after the intervention and after R2.

Figure 1  Cumulative probability of identifying the recurrent laryngeal nerve in the study group (with neuromonitoring) and in the control group (without neuromonitoring). ID, identification of the RLN.
The incidence of laryngeal paralysis may be higher in cases where identification of the RLN is not possible due to several factors including:

- Variants in its relation to the ITA.4,16,27,28
- Intraoperative bleeding, which is the most common risk factor in RLN lesion16,17 and which is related to the haemostasis system employed.8
- The experience of the surgeon.4,13,22
- Knowledge and correct interpretation of the results obtained by NM (especially signal loss and interference).1,3,14,45

Visual identification of the RLN is the gold standard for reducing lesions.1,18 NM increases safety by locating the RLN in both routine and complex situations,3,11,22,45 (absence of RLN, extralaryngeal branches, variants in relation to ITA), facilitates dissection of the trunk and extralaryngeal branches, reducing manipulation and the incidence of transient paralysis,1,3,14,45 and provides information on its functional status at the end of surgery.

It is helpful in locating the point of injury and in decision making upon suspicion of lesion due to signal loss.28,31

If an initial visualisation of the RLN cannot be obtained, NM helps to locate it through neural mapping, thus avoiding confusion with non-nervous structures.45

No significant reduction in the incidence of persistent RLN paralysis has been demonstrated with the use of NM, since its low incidence would require very large samples to achieve statistical significance.12

However, visual identification of the RLN in relation to the ITA associated with NM achieves 0% incidences of paralysis.28

In our study, the incidence of paralysis was nil in both groups. In order to obtain significance, we would have to conduct studies with over 2000 RLN in each group.

However, a significant reduction has been shown in the number of non-identified RLN, since NM obtained 100%
identified nerves (98% visualised). This increased the speed and safety of surgical procedures.

For some authors, NM should be conducted in all thyroidectomies, not just in those considered as high risk. This should be done in addition to visual identification, rather than as a replacement. Preoperative laryngoscopy should be performed routinely to detect involvement (in our work it reached 9.2%). In case of previous surgery, it can reveal late-onset or unnoticed motility disorders (0.8% in our work). Postoperative laryngoscopy can confirm true and false negatives and positives.

The sensitivity and positive predictive values of NM with surface electrodes in the ETT were variable and relatively low in most studies due to false positives, usually caused by technical errors (between 33.4%–37.8% and 40%–63%). Therefore, dealing with signal loss situations and reducing false positives is the goal of research. In general, the highest rate of false positives takes place at the beginning of the experience, since the NM technique requires a learning period for the programming and interpretation of signals. The overall validity of NM is increased by an initial and final test, both in the RLN and the vagus nerve (4-step technique). Testing the vagus nerve helps to verify true positives and reduce the rate of false negatives and false positives. In cases of non-identification of the RLN, it is sufficient to know its functional status at the end of surgery.

NM with electromyographic registration of the thyroarytenoid muscles via electrodes inserted through the cricothyroid membrane, as performed in this work, was described by Flisberg and published by Alon in 2009. This technique increases sensitivity and offers a positive predictive value approaching 100%. This is explained by electrophysiological reasons (lower impedance, wider electromyographic registration, no change with muscle relaxants), making it the technique of choice for many researchers, ahead of ETT with surface electrodes or monopolar electrodes inserted by laryngoscopy, as well as the most used in the German literature. Furthermore, the technique is simple and only uses 1 electrode for the bilateral monitoring of the RLN and superior laryngeal nerve. These elements are available for NM of the facial nerve in parotid and otological surgery.

The results obtained in our study were similar to those reported by other authors. There were no false positives, incidents were easily resolved and there were no surgical complications related to the technique.

In summary, NM by puncture with translaminageous bipolar needle electrode is a reliable technique because:

- It is not influenced by muscle relaxation even when there is no larynx reflex.
- The electrodes have a higher signal-noise ratio and offer broader records than surface electrodes.
- It is not necessary to use 2 electrodes.
- There are no interferences due to respiratory movements.
- The electrodes are visible and controlled by the surgeon. Verification in case of signal loss is simple, as its only possible causes are the following: disinsertion of the electrodes (in the patient or in the connection box) and errors whilst setting parameters or equipment failure.
- It does not produce laryngeal damage.
- When placed in the cricothyroid muscle, it evaluates the role of the external branch of the superior laryngeal nerve.
- Its cost is less than that of using ETT.
- It can be used in all cases (even with anatomical distortion or fibrosis).

Conclusions

During thyroid surgery, NM helps in the location, identification, visualisation and dissection of the RLN and reports on its functional status after the intervention. It also increases the rate of location and visualisation of the RLN in situations of initial non-identification. Reduced manipulation during dissection may be accompanied by a decrease in RLN paralysis. In case of signal loss, it aids in decision-making and increases safety (differing contralateral lobectomy or maximising care during extubation in cases of contralateral paralysis). The technique must be adequately mastered in order to avoid false positives and false negatives.

Transcricothyroid NM is a simple, safe and reliable technique, which reduces the rate of false positives compared to other techniques.

NM improves information for patients about the prognosis for vocal cord motility.

The routine use of NM is recommended in thyroid surgery.

Conflict of Interests

The authors have no conflict of interests to declare.

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