



Thyroid

Does intraoperative neuromonitoring of recurrent nerves have an impact on the postoperative palsy rate? Results of a prospective multicenter study



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Background. The impact of intraoperative neuromonitoring on recurrent laryngeal nerve palsy remains debated. Our aim was to evaluate the potential protective effect of intraoperative neuromonitoring on recurrent laryngeal nerve during total thyroidectomy.

Methods. This was a prospective, multicenter French national study. The use of intraoperative neuromonitoring was left at the surgeons' choice. Postoperative laryngoscopy was performed systematically at day 1 to 2 after operation and at 6 months in case of postoperative recurrent laryngeal nerve palsy. Univariate and multivariate analyses and propensity score (sensitivity analysis) were performed to compare recurrent laryngeal nerve palsy rates between patients operated with or without intraoperative neuromonitoring.

Results. Among 1,328 patients included (females 79.9%, median age 51.2 years, median body mass index 25.6 kg/m²), 807 (60.8%) underwent intraoperative neuromonitoring. Postoperative abnormal vocal cord mobility was diagnosed in 131 patients (9.92%), including 69 (8.6%) and 62 (12.1%) in the intraoperative neuromonitoring and nonintraoperative neuromonitoring groups, respectively. Intraoperative neuromonitoring was associated with a lesser rate of recurrent laryngeal nerve palsy in univariate analysis (odds ratio = 0.68, 95% confidence interval, 0.47; 0.98, P = .04) but not in multivariate analysis (odds

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ratio = 0.74, 95% confidence interval, 0.47; 1.17, $P = .19$), or when using a propensity score (odds ratio = 0.76, 95% confidence interval, 0.53; 1.07, $P = .11$). There was no difference in the rates of definitive recurrent laryngeal nerve palsy (0.8% and 1.3% in intraoperative neuromonitoring and non-intraoperative neuromonitoring groups respectively, $P = .39$). The sensitivity, specificity, and positive and negative predictive values of intraoperative neuromonitoring for detecting abnormal postoperative vocal cord mobility were 29%, 98%, 61%, and 94%, respectively.

Conclusion. The use of intraoperative neuromonitoring does not decrease postoperative recurrent laryngeal nerve palsy rate. Due to its high specificity, however, intraoperative neuromonitoring is useful to predict normal vocal cord mobility.

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Thyroidectomy is a relatively common operative procedure. Although considered very safe, it remains associated with a risk of hypoparathyroidism, injury to the recurrent laryngeal nerve (RLN), and compressive hematomas. The following rates of thyroidectomy-related complications have been reported in large case series studies: hematoma, 1.2–2.1%¹⁻⁴; transient hypoparathyroidism, 6.4–35.2%^{1,2,4-6}; permanent hypoparathyroidism, 0.9–6.3%^{1-3,5,6}; transient RLN injury, 0.36–20%^{1-5,7}; and permanent RLN injury, 0.7–1.4%.^{1-3,5} Voice impairment diminishes quality of life and may lead to litigation.⁷ Because many RLN palsies are asymptomatic, the objective evaluation of vocal cord function requires systematic postoperative laryngoscopy.⁸ A vocal cord examination should be performed at least at 6 months postoperatively to diagnose a definitive RLN palsy. While the postoperative laryngoscopy is usually accepted, some patients refuse the 6-month evaluation because they consider that it would provide them no benefit, whatever the status of their voice. In a series of 3,605 patients who underwent total thyroidectomy, Lifante et al showed recently a fairly good correlation between the rates of immediate and permanent RLN palsy ($r = 0.70$, $P = .004$).⁹ Therefore, the rate of postoperative RLN palsy is predictive of the definitive rate and should be considered as a criterion of quality in thyroidectomy. Postoperative RLN palsy rate depends on surgical experience, identification of the nerve and type of thyroid disease (Hashimoto or Grave's disease).⁸⁻¹⁰ Intraoperative neuromonitoring (IONM) of the RLN has been used widely in thyroid surgery for many years. Although IONM tends to become a standard of care, its impact on nerve protection remains debated. The aim of this study was to evaluate the protective effect of IONM on RLN during total thyroidectomy.

Methods

In this study, we performed a preplanned analysis of data collected in the FOThyr trial, which is being submitted elsewhere for potential publication. Briefly, FOThyr is a prospective, randomized, multicenter, single blind study comparing a single-use device to conventional hemostasis in total thyroidectomy (TT). All patients aged 18 to 80 years scheduled to undergo TT were eligible if they had Graves' disease, toxic or nontoxic thyroid goiter, or any thyroid nodule requiring TT via a transcervical approach. The exclusion criteria were thyroid cancer, known or suspected preoperatively based on

ultrasonography or cytologic assessment (to avoid lymph node dissections associated with the TT); a calcitonin level >30 pg/mL; a planned partial thyroidectomy; abnormal motility of the vocal cords (based on abnormal voice); substernal goiter (>3 cm below the sternal notch); a minimal access videoscopic TT; and a prior history of cervical surgery. Preoperative serum levels of calcium, phosphorus, calcitonin, Thyroid Stimulating Hormone, and albumin were measured for all patients. Preoperative vocal cord examination was only performed in case of any abnormality in the voice.

All TTs were performed according to the same protocol, except for the utilization of IONM, which was left to the surgeon's choice. Therefore, our population was divided into 2 groups: IONM and non-IONM. The operation started with intubation of patients using an IONM-specific tracheal tube (Medtronic, Jacksonville, FL) for the IONM group and a usual tracheal tube for the non-IONM group. Anesthesiologists were instructed to restrain the use of long-acting muscle relaxants in case of IONM. After a cervical Kocher incision, the infrahyoid muscles were opened along the midline and muscles were divided as necessary. Vessels of the upper pole were controlled, preserving the superior laryngeal nerve (whenever possible). Then, the parathyroid glands (whenever possible) and the RLN (mandatory) were visualized. Postoperative drainage was left at the surgeon's discretion. In the IONM group, after resection of the first lobe and before closure, the RLN was stimulated. All surgeons were experienced in thyroid surgery (>30 thyroidectomies a year) and had used IONM for at least 1 year. For all patients operated with IONM, RLN was tested systematically via a sterile, single-use, pulse-generated, monopolar stimulator probe with the stimulation level set at 1.0 mA. In 6 centers, both RLN and vagal nerves were tested. The nerve function was confirmed by acoustic signals in all patients within the IONM group. Thyroid hormone replacement was begun on postoperative day 1.

Postoperative RLN function was evaluated systematically by vocal cord examination with transnasal fiberoptic laryngoscopy carried out before hospital discharge and 6 months postoperatively in case of postoperative abnormal motility. Serum calcium and albumin levels were performed in the laboratories of local hospitals. Immediate hypocalcemia was defined by a serum calcium level <2 mmol/mL corrected for albumin level at postoperative day 2. Postoperative bleeding was defined as the occurrence of a compressive hematoma requiring revisional surgery. Permanent hypocalcemia was

defined as serum calcium level <2 mmol/mL (corrected for albumin level) at 6 months. Clinical examination was performed by the surgeon during hospitalization to detect hematomas.

Statistical analysis

The primary endpoint of the study was the percentage of patients with a postoperative RLN palsy in each group. Categorical variables were expressed as counts and percentages. Quantitative variables were expressed as means, standard deviations, and when appropriate as medians and ranges. Baseline characteristics of patients in the non-IONM and IONM groups were compared with Fisher test, χ^2 test, Student test, or Wilcoxon test depending of the type and distribution of variables. Postoperative rates of RLN palsy and definitive rate of RLN palsy were compared between non-IONM and IONM groups with χ^2 test and Fisher test. A multivariate, generalized linear mixed model was used to determine the effect of predefined parameters, namely age, body mass index, cancer, euthyroidism or hyperthyroidism, weight of the thyroid, sex, procedures (TT only versus TT + lymph node dissection), presence of thyroiditis, and center (center was considered as random effect). A sensitivity analysis was performed using inverse probability of treatment weighting using the propensity score; the propensity score was constructed by logistic regression analyses for IONM including factors cited previously. Sensitivity, specificity, negative predictive value (NPV), and positive predictive value (PPV) of IONM to predict abnormal vocal cord function and complete RLN palsy were estimated with their 95% confidence intervals. Statistical analyses were performed using the software SAS 9.4 (SAS Institute, Cary, North Carolina, USA).

The protocol of the FOThr trial was reviewed and approved by a regional ethics committee (Comité de Protection des Personnes Ouest IV N°58/2012) and by the CNIL (Commission Nationale de l'Informatique et des Libertés N°1170319). The study was performed in accordance with the Good Clinical Practice Guidelines and the Declaration of Helsinki. All patients provided written informed consent before inclusion. This study was supported by a grant from the French Ministry of Health and was registered with ClinicalTrials.gov number NCT01551914.

Results

From March 2012 to June 2014, 1,350 patients were enrolled at 13 sites, and of those, 1,328 could be analyzed. IONM was used in 807 patients (60.8%), while 521 were in the non-IONM group. The percentage of patients operated using IONM ranged from 0% to 100% across the 13 study sites (Fig). The main characteristics of the patient groups are summarized in Table I. Statistically significant differences were observed between the 2 groups: in patients who underwent IONM, the percentage of females was greater, median body mass index and median thyroid weight were less, thyroiditis was more frequent, and thyroid cancer was less frequent. Cancers were diagnosed incidentally in 290 patients. The median size was 6 mm (6 mm in IONM group and 7 mm in non-IONM group). An unplanned, central lymph-node dissection was performed in 29 patients, including 13 in the IONM group and 16 in the non-IONM group. Both RLN and vagal nerves were tested systematically by IONM in 316 patients from the IONM group (39%). In 5 patients (all in the IONM group), the planned TT was changed to a lobectomy, because no acoustic response at IONM was obtained after resection of the first lobe. Postoperative laryngoscopy was performed after a mean time of 1.4 ± 1.4 days. Postoperative abnormal vocal cord motility was diagnosed in 131 patients (9.9%), including 69 (8.6%) in the IONM group and 62 (12.1%) in the non-IONM group. The rates of partial, complete, and bilateral RLN palsies in each group are shown in Table II. The global rates of transient RNL palsies by site, whether IONM was used or not, are shown in the Figure. They vary between 4.1% and 17.4%. In univariate analysis, only IONM (odds ratio [OR] = 0.68; 95% confidence interval [CI], 0.47; 0.98, $P = .035$) and the operative procedure (TT with central lymph node dissection versus TT alone (OR = 2.59, 95% CI, 1.03; 6.50, $P = .04$) were associated with a lesser rate of transient RLN palsy. In multivariate analysis, no predefined factor was associated with the rate of RLN palsy (Table III). For IONM, the OR was 0.74, 95% CI, 0.47; 1.17, $P = .197$. Using a propensity score, IONM had no impact on the rate of postoperative RLN palsy rate (OR = 0.76, 95% CI, 0.53; 1.07, $P = .113$). Among the 131 patients with postoperative RLN palsy, only 64 underwent

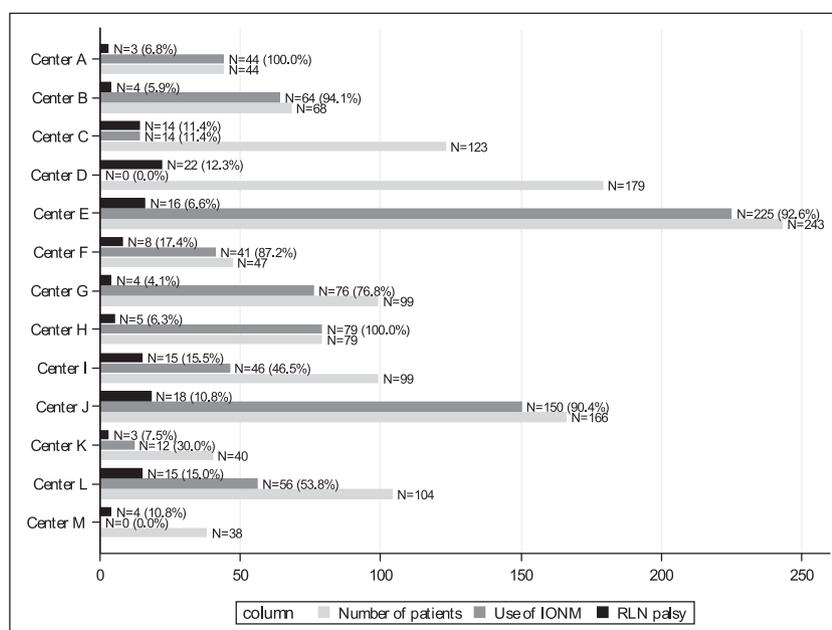


Fig. Number (%) of patients included (green), number (%) of patients operated with IONM (red), and number (%) of transient RLN palsies (blue) in each center.

Table I
Characteristics of patients in each group.

	IONM n = 807	Non-IONM n = 521	Total n = 1,328	P value
Age (y) median (range)	51.8 (18–80)	50.7 (18–79)	51.2 (18–80)	.121
Female	663 (82.2%)	398 (76.4%)	1061 (79.9%)	.015
BMI, kg/m ² median (range)	25.2 (16.7–49.1) MD: 7	26.5 (16.6–56.4) MD: 12	25.6 (16.4–56.4) MD: 19	.003
BMI ≥30	164 (20.5%)	126 (24.8%)	290 (22.2%)	.070
Thyroid weight (g) median (range)	32.0 (4–578) MD: 33	39.0 (4–500) MD: 14	35.0 (4–578) MD: 47	.003
Thyroiditis	153 (19.4%) MD: 17	64 (12.7%) MD: 17	217 (16.8%) MD: 34	.001
Procedure	TT: 789 (97.8%) TT + CLND: 13 (1.6%) Lobectomy: 5 (0.6%)	TT: 505 (96.9%) TT + CLND: 16 (3.0%)	TT: 1296 (97.8%) TT + CLND: 29 (2.19%)	.077
Hyperthyroidism	151 (19.8%) MD: 43	104 (21.4%) MD: 36	255 (20.4%) MD: 79	.473
Cancer	152 (18.8%)	138 (26.5%) MD: 1	290 (21.9%) MD: 1	<.001

BMI, body mass index; CLND, central lymph node dissection; MD, missing data.

the 6-month evaluation, among whom a definitive RLN palsy was diagnosed in 12 patients. The remaining 67 patients refused the 6-month evaluation. There was no difference in the rates of definitive RLN palsy between the IONM and the non-IONM groups: 0.8% and 1.2% respectively, $P = .391$. We assessed the ability of IONM to predict RLN palsy. The test was considered as positive when no acoustic signal could be detected with IONM. Sensitivity, specificity, PPV and NPV values of IONM for detecting abnormal postoperative vocal cord motility were respectively (29%, 98%, 61%, and 94%; Table IV). Because the clinical impact of a partial RLN palsy is much less clinically than that of a complete RLN palsy, we calculated sensitivity, specificity, PPV, and NPV for detecting complete RLN palsy; the results were similar with high specificity and NPV associated with modest sensitivity and PPV (Table IV). Five patients had bilateral abnormal mobility in the IONM group. All but one had a normal acoustic response at IONM. The only patient with a bilateral absence of intraoperative acoustic response had a bilateral partial RLN palsy. Among other complications, postoperative hypocalcemia was diagnosed in 266 patients (20.0%) and 26

(2.0%) had definitive hypocalcemia. Sixteen patients had a postoperative hematoma requiring reoperation for control (1.2%) occurring after a median time of 2 hours (range: 0.2–4).

Discussion

The claimed advantages of IONM during thyroid surgery are (1) the detection of the exact location of the nerve, (2) a decrease in the rate of RLN palsy, and (3) the prediction of postoperative vocal cord function.¹⁰ In our study, no surgeon used IONM to localize the RLN. The procedure was standardized with a systematic dissection. We suggest that a systematic visualization of the nerve should be performed to decrease nerve damages.^{11,12} Using only IONM for localizing the nerve exposes the RLNs to injury at areas of the non-recognized part of the nerve.

With regard to the decrease in rates of postoperative RLN, our study showed that the rate with IONM compared with a simple identification of the nerve was not statistically significant (8.6% vs 12.1%). Our findings are in accordance with the literature. Many studies evaluated the impact of IONM on RLN palsy, and most found no statistical difference between IONM and non-IONM groups.^{7,10,12–14} In a review, Malik and Linos reported data from 12 studies including 44,575 nerves at risk.¹⁰ Among these, 25,843 (58.0%) were operated with IONM and 18,732 (42.0%) without IONM. The rates of RLN palsy were 3.2% in the IONM group and 3.8% in the non-IONM group. There were no differences for either transient or definitive palsy rates. The only study that reported a difference is a retrospective analysis of 152 patients (76 in each group) who underwent thyroidectomy for thyroid cancer.¹⁵ In this study, 32% (non-IONM) and 38% (IONM patients) had a central neck dissection.¹⁵ Nevertheless, it is not clear whether the operation consisted of a bilateral central neck dissection in all cases. The authors reported a RLN palsy rate of 3.9% with IONM vs 9.2% without IONM ($P < .05$).¹⁵ Chan et al reported that the

Table II
Rates of partial, complete, and bilateral RLN palsies in each group.

	IONM, n = 807	Non IONM, n = 512*
RLN palsy	69 (8.6%)	62 (12.1%)
Partial RLN palsy	38 (4.7%)	38 (7.4%)
Complete RLN palsy	31 (3.8%)	24 (4.7%)
Bilateral RLN palsy	5 (0.6%)	3 (0.6%)
Complete bilateral RLN palsy	1	1

* Missing data for 9 patients.

Table III
Multivariate analysis of risk factors for RLN palsy tested in univariate analysis.

	OR	CI 95%	P value
IONM use	0.74	0.47–1.17	.196
Thyroid weight (g)	0.99	0.99–1.00	.522
BMI	1.01	0.98–1.05	.603
Age	0.99	0.98–1.00	.189
Cancer	1.06	0.66–1.70	.815
Female	0.83	0.50–1.35	.443
Thyroiditis	0.17	0.70–1.93	.553
Hyperthyroidism	1.07	0.67–1.72	.782
TT + CLND	1.90	0.59–6.11	.284

BMI, body mass index; CLND, central lymph node dissection.

Table IV
Sensitivity, specificity and NPV and PPV of IONM to predict RLN palsy.

Complete or partial RLN palsy	Sensitivity	29% (95 CI, 18–40)
	Specificity	98% (95 CI, 97–99)
	NPV	94% (95 CI, 92–95)
	PPV	61% (95 CI, 44–77)
Complete RLN palsy	Sensitivity	52% (95 CI, 34–69)
	Specificity	98% (95 CI, 97–99)
	NPV	98% (95 CI, 97–99)
	PPV	48% (95 CI, 31–66)

rate of RLN palsy was greater after reoperative thyroidectomy (19.0% vs 4.6%) in the non-IONM group but not in the IONM group (7.8% vs 3.8%).¹⁶ Thus, one may consider IONM to be helpful primarily in “difficult thyroidectomies” such as reoperation and associated lymph node dissection.

In our study, there was no difference in the rates of RLN palsy between patients operated with or without IONM within the same center (data not shown). Indeed, the use of IONM may have indirect positive effects in inducing changes in surgical practice. Duclos et al showed that the introduction of IONM in a university hospital referral center decreased the rate of RLN palsy.¹¹ The authors noted a variation in the outcomes of thyroid surgery that was mostly attributable to the implementation of IONM. Surgeons declared that IONM improved their sense of safety during thyroidectomy and provided more comfort for the dissection and control of RLN.¹¹ In contrast, IONM may increase the surgeon’s awareness of the potential fragility and localization of the motor branch of the RLN.^{13–17} This knowledge of nerve fragility during traction may have helped surgeons to improve the quality of the thyroidectomy, even without the use of IONM.

Finally, our study confirmed that IONM can predict accurately normal postoperative vocal cord mobility. The specificity (98%) and the NPV (94%) were very high, allowing a prediction of normal RLN function in almost all patients. The results of NPV are in accordance with the literature.¹⁰ The sensitivity and PPV, however, were low. The sensitivity for the detection of both partial and complete RLN palsies was 29%, while in other studies it ranges from 52% to 93%.¹⁰ When considering only complete RLN palsies, the sensitivity was 52%. In our study, IONM failed to detect 15 of the 31 complete RLN palsies and 37 of the 42 partial RLN palsies. It might be because many surgeons did not stimulate the vagal nerve, but only the RLN. An abnormal acoustic response of IONM was predictive of a complete RLN palsy in 48% of the patients and predictive of an abnormal motility (complete/partial palsy) in 61% of the patients. This low PPV may be due to the time between the TT and the vocal cord examination (mean: 1.0 day \pm 1.4): some patients may have recovered spontaneously normal RLN function. Our RLN palsy rates are greater than those reported in many studies,^{1,4,7,10,18–21} although the rate of other complications is in line with previously reported results, showing that our patients are representative of those undergoing TT for noncancer diseases.

We offer several potential explanations. First, postoperative vocal cord examination was systematic for all patients in our study and was built into the protocol because many RLN palsies are asymptomatic. In other studies, postoperative RLN palsy rates vary from 1.9% to 12.5% and depend on whether or not laryngoscopy was systematic.¹⁰ Second, we reported all cases of abnormal vocal cord motility (i.e., partial and complete RLN palsies). Only 4.2% of patients had a complete postoperative RLN palsy. Third, our study included patients operated in 13 centers by surgeons with experience with thyroidectomy, but still with various experience and skills. Dionigi et al reported that a complete recovery of vocal cord function was documented in 91% of patients with RLN injuries.²⁰ It should be noted, however, that some patients refused the 6-month examination. They may have refused either because their voice had recovered to normal level or because, despite hoarseness, they did not expect any benefit from a second laryngoscopy. In addition, laryngoscopy can be uncomfortable and even painful. Transcutaneous ultrasonography of the vocal cords could be useful in these patients for a late evaluation of vocal cord function.²² Of note, in our study, no surgeon used continuous vagal nerve monitoring. The main objective of continuous monitoring is to allow an early detection of a reversible damage of the RLN. Indeed, an extensive dissection with traction of the RLN can be responsible for RLN palsy. Intermittent IONM may fail to detect any injury to the nerve before it is complete.¹⁸ In contrast, continuous IONM

may reveal an imminent lesion timely enough to stop excessive traction on the nerve.^{18–20} This theoretic benefit of continuous monitoring should still be demonstrated and one should keep in mind that vagal lesions (due to the electrode) have been described with this procedure.¹⁸

We acknowledge the limitations of our study. Our conclusions cannot apply to patients with invasive cancers or substernal goiters, who were excluded from the present study. Currently, for thyroid cancers and substernal goiters, most surgeons use IONM systematically. Approximately half of the patients with postoperative RLN palsy refused the 6-month laryngoscopy, resulting in a possible underestimation of the rate of definitive palsy. The use of IONM was highly variable across centers. Lastly, although anesthesiologists were asked to refrain from the use of short-acting muscles relaxants before intubation, we did not evaluate the depth of neuromuscular block depth at the time of IONM.²³ Therefore, we cannot absolutely exclude that neuromuscular block medications could have been responsible in part for the false positive results of the IONM. Despite these limitations, we can conclude that the rate of transient RLN palsy was not statistically less in the IONM group, but we confirm that IONM can predict a normal vocal cord function in almost 100% of cases.

We thank all the surgeons who included patients in the trial.

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Discussion



Dr Martha A. Zieger (Baltimore, MD): Very well-presented paper. Thank you.

I have one quick question, if I may. Did you control for surgeon experience, surgeon age?

Dr Eric Mirallié: No, we did not. We did not look at the specific surgeon. That is one of the problems. I agree.

Dr Ashok R. Shaha (New York, NY): Congratulations on your great study and honest reporting. I think that is what is really important in this study. Because your rate is as far as anybody would have thought in their own mind, rather than what is described in literature.

I have 2 questions. Number 1, did you use vagal nerve monitoring? Because in Germany that seems to be the practice, and at least from the description, that you could prevent or avoid impending nerve injury. I just want to know your thoughts.

And the second question I have, which is a major concern, when you lose the signal on one side and the patient really needs total thyroidectomy, would you avoid operating on the other side at the same time, or you will say, I know the nerve is intact and I will proceed with completion thyroidectomy at the same time?

Dr Eric Mirallié: Thank you for your questions. The first question about vagal nerve stimulation, only 316 patients had vagal nerve stimulation, so about one-third of our patients in the IONM group, and this may be responsible for the low sensitivity. Because when we evaluate results of sensitivity, specificity and predictive value, on the centers which use the vagal nerve stimulation and not on the recurrent nerve, we see that sensitivity is much higher. This was your first question.

The second question was about the loss of signal. In the IONM group we have 5 patients who had only lobectomy because of a loss of signal. And I personally, in my opinion, I recommend stopping the procedure, wait for the nerve to recover normal function, and then after there is, perform completion of the lobectomy.

Dr Jacob Moalem (Rochester, NY): I think you just addressed the question that I was going to ask, which was, in my view, regarding the main utility here, which is avoiding exposure to a bilateral recurrent laryngeal nerve palsy, particularly in the context of benign thyroid disease. So can you please just reiterate or expand on what you just said? How often was a planned total thyroidectomy aborted at a lobectomy stage because of loss of signal on the initial side?

Dr Eric Mirallié: Only 5 times on the table. We have 8 by total; but 5 in the IONM group and 3 in the non-IONM group. Three in the non-IONM group abort. For the 5 signal was lost, only once did the surgeon keep on performing thyroidectomy. I would not have done the same.

Dr Jacob Moalem (Rochester, NY): And that was the case that resulted in a bilateral? Because there was one patient with a bilateral recurrent laryngeal nerve injury in that group.

Dr Eric Mirallié: Yes. The one patient a bilateral complete recurrent nerve palsy, but the signal was not lost on both sides at the end of the procedure.

Dr Quan Yang Duh (San Francisco, CA): Just a quick question regarding the method of the study. This is not a randomized study on nerve monitoring. This is a randomized study on Harmonic scalpel, then you use the data to look at neuromonitoring. So there is obviously some kind of selection process going on if there is some people use it and some people do not.

Have you looked at the data and sorted out those that routinely use it versus routinely not use it and excluded the selective ones? Because the people that use it selectively would, in general, use it for the higher-risk patients and not use it for the lower-risk patients. So that will introduce some bias into your study.

Dr Eric Mirallié: Can I go back on the slide?

You are right on the nerve palsy rate. In our series, most of the centers either use nearly always IONM or never, because they have not the device or they do not believe it is useful. For centers of health, there was no difference of RNP between the group of patients with and without in the same center. But I agree with what you said, most of the centers, of the expert centers, have an IONM, maybe more complicated patients, but we excluded huge cancer, substernal goiter to avoid this kind of program.

So, it may be only because maybe the best surgeon or the best device to operate. We do not know. It is maybe an explanation of the different rate for recurrent nerve palsy rate between centers.

Dr Quan Yang Duh (San Francisco, CA): Because an alternative explanation for your finding is that the surgeons use intraoperative neuromonitoring appropriately to lower the risk to that of the ones that are less risky. Anyway, I think it is a great study.

Dr Eric Mirallié: Thank you very much.