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Radio-guided Surgery for Lymph Node Recurrences of Differentiated Thyroid Cancer

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Abstract. The objectives of this study were to assess the reliability of radioiodine (^{131}I) and a gamma probe for radio-guided surgery (RGS) to detect and then radically dissect lymph node recurrences (LNRs) in 10 patients with differentiated thyroid cancer (DTC). The major inclusion criterion was the presence of an iodine-positive LNR after previous total thyroidectomy and at least two ineffective ^{131}I treatments. The protocol was designed as follows. Day 0: all patients were hospitalized and received 3.7 GBq of ^{131}I in the hypothyroid condition. Day 3: presurgery whole-body scan with a therapeutic dose (TxWBS). Day 5: neck surgery using a gamma probe (Navigator GPS, AutoSuture, Italy), recording the absolute counts and the lesion/background (L/B) counts ratio. Day 7: post-surgery TxWBS performed using the remaining radioactivity. The presurgery TxWBS was positive in all patients, and the post-surgery TxWBS showed a negative pattern in 7 of 10 patients, suggesting the efficacy of the surgical procedure in most of the patients. After RGS the mean decrease in the absolute counts and the L/B counts ratio were 77.6% (52.7% minimum, 94.6% maximum) and 77.4% (52.3% minimum, 94.8% maximum), respectively. After operation the surgeon judged the procedure to be decisive in two patients, favorable in six, and irrelevant in two. The final histologic examination showed the presence of 78 lymph node metastases (mean of 8 per patient). There were 33 neoplastic lesions found by both TxWBS and gamma probe evaluations; 41 were shown only by gamma probe, and 4 were negative by both TxWBS and gamma probe evaluations. This protocol permitted us to look for neoplastic foci with high sensitivity and specificity, and we were able to remove lymph node metastases resistant to radioiodine therapy at a single session. The protocol also allowed detection of some additional tumoral foci in sclerotic areas or behind vascular structures that are difficult to identify and were not seen at the presurgery TxWBS evaluation. However, because of the possible false-negative results, complete excision must be undertaken in high risk patients with a local recurrence to eradicate the largest number of lymph nodes, independent of the counts measured by the gamma probe.

Intraoperative tumor detection and radio-guided surgery (RGS) using a scintillation gamma probe are currently employed for different tumor types using various tumor-seeking radiopharmaceuticals [1]. So far, the gamma probe has been used to identify the sentinel lymph node in the management of patients with melanoma and breast cancer, but new clinical applications for various tumors are becoming widespread [2, 3]. For the last 2 years we have used therapeutic doses of radioiodine (^{131}I) and an intraoperative probe for RGS to detect and then radically dissect lymph node recurrences (LNRs) of differentiated thyroid cancer (DTC), as previously reported by Travagli et al. [4]. The aims of the present study were to (1) assess the contribution of the above-mentioned protocol to radical dissection in patients with LNRs and (2) evaluate its utility for demonstrating the completeness of the excision after node removal.

Methods

Patients

The study included 10 patients treated between January 1, 2000 and December 31, 2001 (Table 1). There were three women and seven men, ranging in age from 25 to 66 years (mean 46.2 years) at the time of the initial thyroidectomy. All 10 patients had undergone total thyroidectomy, and in 7 cases cervical lymph node dissection was performed as well at the same surgery.Tumors were staged according to the UICC pTNM classification [5]; among our patients the stages were pT1N1 in one case, pT2N1 in two cases, pT3N1in two cases, and pT4N1 in five cases. Lymph node metastases were found in all patients at the initial surgery or during the first whole-body scan with therapeutic doses of ^{131}I (TxWBS); in addition to lymph node involvement, three patients (nos. 1, 3, 5) presented with lung metastases as well. The histopathology of the tumors was papillary in nine patients and poorly differentiated follicular in one.

After the initial surgery all patients received two or three radioiodine doses (mean 2.4) to ablate any thyroid remnants and to treat any functioning metastases. The mean radioiodine cumulative dose was 11.79 GBq (range 7.4–16.6 GBq).

Radioiodine therapy was performed with the patient in the hypothyroid condition 4 to 5 weeks after thyroidectomy with no replacement therapy during this time or after stopping treatment with levo-thyroxine (L-T_4). To avoid prolonged hypothyroidism, patients were maintained on triiodothyronine (T_3) until 2 weeks prior to administration of the radioiodine.

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Table 1. Patient and tumor characteristics.

Patient no.	Sex	Age at initial surgery	Operation	p Stage[a]	Histology of carcinoma	Dose[b]	Rx times[c]	Time (months)[d]
1	M	43	TT, LN	pT2bN1bM1	Papillary	16.3	3	53
2	F	57	TT	pT1bN1aM0	Papillary	7.4	2	14
3	F	52	TT	pT3N1aM1	Follicular poorly differentiated	9.2	2	60
4	M	49	TT, LN	pT4N1aM0	Papillary	13	2	20
5	M	40	TT, LN	pT4N1bM1	Papillary	11	2	15
6	M	52	TT, LN	pT4N1bM0	Papillary	16.6	3	39
7	M	33	TT, LN	pT4N1bM0	Papillary	7.4	2	16
8	M	45	TT, LN	pT2bN1bM0	Papillary	11.1	3	21
9	F	66	TT	pT3N1aM0	Papillary	14.8	3	32
10	M	25	TT, LN	pT4N1bM0	Papillary	11.1	2	17

TT: total thyroidectomy; LN: lymph node dissection.
[a]UICC pathologic TNM.
[b]Cumulative ^{131}I activity before radio-guided surgery (GBq).
[c]Number of radioiodine treatments.
[d]Time elapsed from TT to radio-guided surgery.

Serum thyrotropin (TSH) levels measured prior to the time of the radioiodine administration were above 30 μUI/ml in all the patients. At the same time serum thyroglobulin (Tg) levels and thyroglobulin autoantibodies (TgAb) were evaluated. Serum Tg levels were measured using a commercial kit, with a sensitivity < 0.1 ng/ml using an electrochemiluminescence immunoassay (ECLIA) kit (Roche Diagnostic, Indianapolis, IN, USA) for Elecsys System 2010. TgAbs were measured by enzyme-linked immunosorbent assay (ELISA) with a lower limit of detection at 2 IU/ml and an interassay coefficient of variation of 14.2%.

To avoid thyroid stunning we did not perform a whole-body scan with diagnostic doses of radioiodine (DxWBS) before radioiodine therapy. The time elapsed from the initial total thyroidectomy to inclusion in the present study ranged from 14 to 60 months (mean 28.7 months).

Criteria for Inclusion and Preoperative Evaluation

The main inclusion criterion in the present study was the presence of persistent or recurrent radioiodine-positive lymph node metastases after at least two radioiodine treatments. Other criteria were clinical evidence of lymph node metastases, positive neck ultrasonography (US) or neck and chest computed tomography (CT) studies, and finally detectable serum Tg values.Before RGS all patients showed focal radioiodine uptake outside the thyroid bed at the last DxWBS or TxWBS. Four patients presented with enlarged lymph nodes at the clinical examination.

Ultrasonography performed using a 7.5-MHz linear probe (Logiq 700 MD; General Electric, Milwaukee, Wisconsin, USA) showed echographic findings suspicious for lymph node involvement in 8 of 10 patients.

Computed tomography performed with injection of contrast medium more than 6 weeks before administration of ^{131}I showed pathologic enlargement of cervical lymph nodes in 6 of 10 patients. Only patients without serum TgAbs were included in the present study, and Tg levels evaluated on L-T_4 suppressive treatment ranged from < 0.1 to 158.0 ng/ml.

The present study was performed with the authorization of the local ethical committee, informed consent of the patients, and permission of the health physics department.

Radio-guided Surgery

Our protocol for RGS of persistent or recurrent lymph node metastases from a DTC was first reported by Travagli et al. [4]. We summarize protocol used here.

Day 0. All patients were hospitalized and received 3.7 GBq of ^{131}I in the hypothyroid condition obtained as previously reported. Patients were not placed on a low-iodine diet but were asked to avoid iodine-containing drugs. We did not routinely measure urinary iodine prior to ^{131}I administration, but patients were carefully screened by history for pharmacologic or environmental iodine intake.

Day 3. Patients were discharged from the isolated room 3 days later when the radiation emission was < 30 μSv/hr at 1 m. At the same time a presurgery TxWBS with a neck spot view was performed using a rectilinear scanner that had a double head equipped with a high-energy collimator (Fig. 1).

Day 5. Two days later neck surgery using a handheld gamma detection probe (Navigator GPS; AutoSuture, Milan, Italy) was performed. With guidance of the ^{131}I neck scan obtained on day 0, the patient's neck was scanned with the probe to localize the cutaneous projection of the radioiodine focal uptake sites. Before surgically removing the tumoral tissue, the probe was placed in direct contact with any pathologic sites, and the counts per second were recorded. The activities in normal adjacent soft tissues were counted as well and were used as the background value. The lesion/background (L/B) ratios of these measurements were then obtained. After the nodes were removed, radioactivity was measured in the lesion bed to confirm the success of the dissection. At the end of the procedure a scan of the operative field with the handheld gamma detection probe was repeated, looking for any residual activity of the tracer. The radiation doses to the surgeon's hands during surgery and the contamination of surfaces and surgical tools were measured by thermoluminescent dosimeters and a portable dedicated device, respectively. The amount of operator time necessary to perform the complete surgical procedure was recorded in each case. At the end of the operation the surgeon made the following judgments on the usefulness of the gamma probe: It was a "decisive" procedure if it showed tumoral foci that had not otherwise been detected; a "favorable" procedure in cases where assisted intraoperative detection of tumoral foci had already been demonstrated by preoperative diagnostic methods; an "irrelevant" procedure if it had made

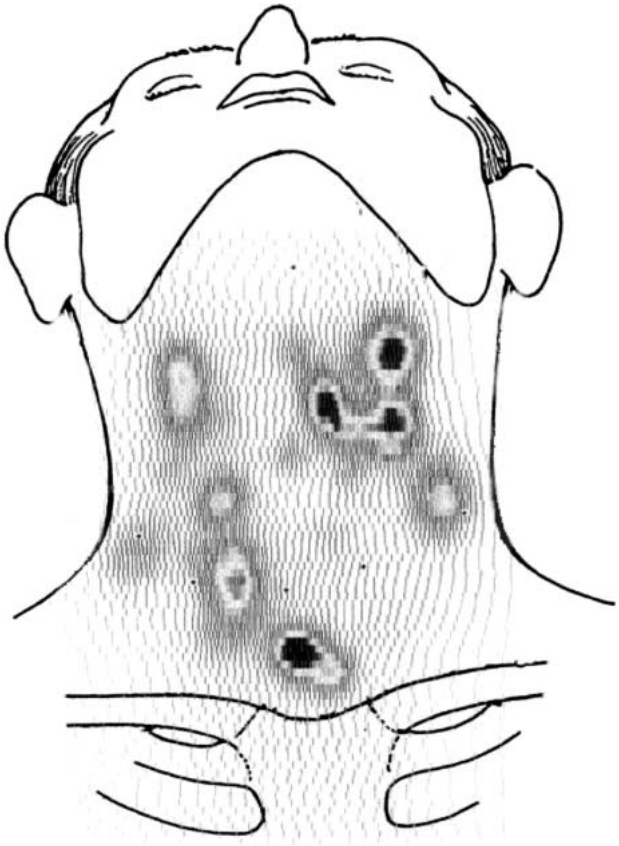

Fig. 1. Presurgery neck scan of patient 7. Preoperative scintigraphy shows numerous sites of ^{131}I focal uptake due to lymph node metastases.

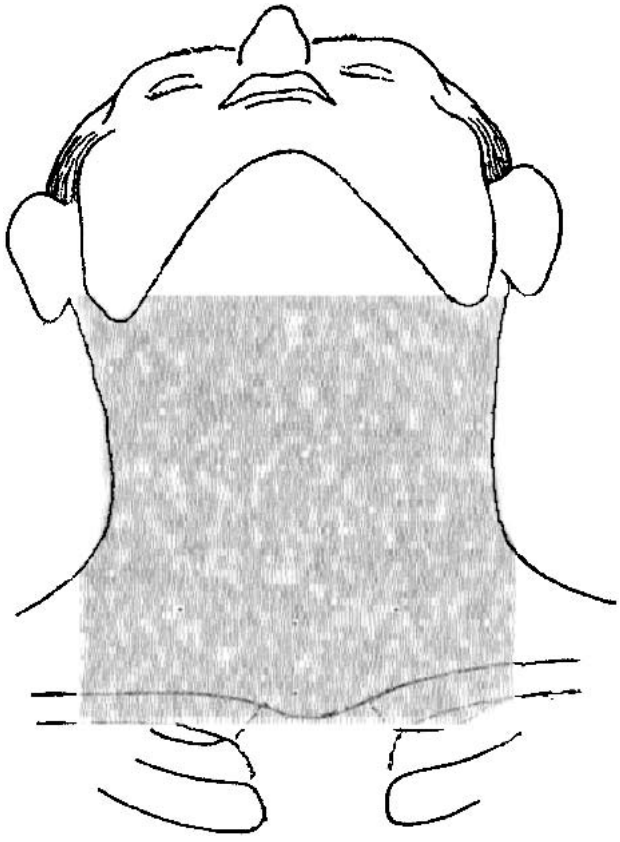

Fig. 2. Postsurgery neck scan of patient 7. Postoperative scintigraphy (day 7) shows complete disappearance of all foci of radioiodine uptake.

only an unimportant contribution to the operation. All surgical specimens were sent separately to the pathologist for a detailed histologic examination. The recorded lymph node counts and the pathologist's reports were then compared.

Day 7. Seven days later a postoperative neck scan was performed using the remaining radioactivity to evaluate the success of the surgery (Fig. 2). Patients were then followed up with periodic TSH and Tg measurements (every 3–6 months) on L-T_4 therapy and with clinical and US evaluation; a DxWBS and off L-T_4 serum Tg evaluation 1 year later were planned for all patients.

Results

Table 2 shows the results of TxWBS performed before and after surgery, the Tg level on and off L-T_4, the counts of the most radioactive lymph nodes recorded during RGS, the pathology examination results and the surgeons' judgments about the usefulness of the gamma probe.TxWBS performed before RGS was positive in all patients, with a total of 33 scintigraphic sites of radioiodine focal uptake (3.3 mean sites per patient). Focal radioiodine uptake was present in the laterocervical compartments in all 10 patients, in the central compartment in 3 patients, and in the supraclavicular compartments in 2 patients.

Preoperative US and CT studies have been positive in eight and six patients, respectively. Both of these diagnostic procedures showed fewer abnormalities and gave more equivocal results than TxWBS.

Before RGS, Tg on L-T_4 was detectable in seven patients, with a mean level of 28.67 ng/ml (range 2.5–158.0 ng/ml). Tg off L-T_4 increased in eight patients and remained undetectable in two.

The preexcision absolute counts obtained by placing the probe in direct contact with all the pathologic sites (evident or not evident at TxWBS) showed a mean count of 145.48 counts per second (cps; 18 cps minimum, 553 cps maximum). The mean L/B ratio was 10.43 (2.75 minimum, 27.6 maximum).

The postexcision absolute counts obtained by placing the probe in the bed of the removed lesion showed a mean count of 27.39 cps (4 cps minimum, 49 cps maximum). The mean L/B ratio was 1.62 (0.8 minimum, 4.1 maximum).

The mean decrease in absolute counts was 77.57% (52.7% minimum, 94.6% maximum). The mean decrease in the L/B ratio was 77.4% (52.3% minimum, 94.8% maximum).

After RGS, the TxWBS performed on day 7 showed a negative pattern in seven patients, suggesting the efficacy of the surgical procedure; three patients (nos. 3, 5, 10) showed reduced radioiodine uptake owing to persistent residual neoplastic disease. Adjuvant external radiotherapy was planned for two patients (nos. 5 and 10) owing to their pathologic stage (pT4N1b).

After the operation surgeons judged the procedure "decisive" in two patients, "favorable" in six patients, and "irrelevant" in two patients.

The final histologic examination showed the presence of 78 lymph node metastases, with a mean of 7.8 per patient (4 minimum, 12 maximum); among them, 33 were evident by both TxWBS and gamma probe evaluation, 41 were demonstrated only by gamma

Table 2. Results of radio-guided surgery.

	TxWBS	Tg	Counts[a]	L/B ratio[a]						
Patient no.	Day 3	Day 7	On L-T_4	Off L-T_4	Pre	Post	Pre	Post	Histology[b]	Surgeon's opinion
1	3	0	3.2	51	73	20	2.75	0.8	PTC	Decisive
2	2	0	< 0.1	3.1	55	9	6.8	1.1	PTC	Favorable
3	2	1	158	804	250	25	17.8	1.7	FTC	Irrelevant
4	2	0	< 0.1	< 0.1	18	4	4.5	1.0	PTC	Irrelevant
5	4	1	15	302	79	11	9.8	1.3	PTC	Decisive
6	1	0	< 0.1	< 0.1	88	14	11	1.75	PTC	Favorable
7	9	0	7	106	231	26	13.5	1.5	PTC	Favorable
8	3	0	2.5	30	75	20	12.5	3.3	PTC	Favorable
9	2	0	5	70	122	25	20.3	4.1	PTC	Favorable
10	5	2	10	150	553	49	27.6	2.4	PTC	Favorable

Tg: thyroglobulin; TxWBS, number of ^{131}I-positive lesions at initial (day 3) and final (day 7) whole body scans; L/B: lesion/background ratio; PTC: papillary thyroid cancer lymph node metastases; FTC: follicular thyroid cancer lymph node metastases.

[a]Counts andL/B ratio: absolute counts and lesion/background counts ratio before and after excision, reported only for the most radioactive lymph node.

[b]Final histologic examination.

probe, and 4 were negative by both TxWBS and gamma probe evaluation.

The mean operating time necessary to perform the RGS was 102 minutes (range 60–180 minutes). No morbidity or complications were observed during surgery, and there were no transient or permanent injuries to the recurrent laryngeal nerve. There also were no cases of permanent hypoparathyroidism during the postoperative period.The dosimetric and radioactivity measurements in all cases revealed extremely low levels of radiation exposure for the surgeon's hands (< 40 μSv) and no radioactive contamination of surfaces or surgical tools.

During the subsequent follow-up, DxWBS, Tg off L-T_4, and US showed cured locoregional disease in 9 of the 10 patients. Further radioiodine treatments have been planned for patients with distant functioning metastases.

Despite the high cure rate for these patients, the brief period of inclusion and the short follow-up highlight the need to obtain definitive long-term clinical data.

Discussion

Local recurrences in patients with previous thyroidectomy and ^{131}I ablative therapy for DTC indicate disease progression in the thyroid bed, regional lymph nodes, or soft tissues of the neck [6]. They appear in 5% to 20% of patients, being more frequent in those with high risk prognostic factors. Frequently they are the result of incomplete initial treatment or a particularly aggressive tumor. They usually appear during the early years of follow-up, although some are detected later [6].

The lymph node is the most frequent site of local recurrence, and the prognostic significance of this occurrence is highly controversial. Although it does not appear to be an independent prognostic factor, the tumor-specific mortality rate after LNR is increased in most series, especially for patients over 45 years of age [7].

The therapeutic tools for lymph node metastases include radioiodine therapy, surgery, and external irradiation (with the choice conditioned by the lesion's size, the radioiodine uptake, and the clinical characteristics of the disease). The efficacy of radioiodine therapy is conditioned essentially by the size, the radioiodine uptake, and the radiation dose absorbed by residual or recurrent thyroid tissue. For macroscopic tumor deposits and absorbed radiation doses below 3500 cGy, the therapeutic response is poor [8]. External adjuvant radiotherapy can improve the recurrence-free survival in patients older than 45 years who have invasive papillary thyroid cancer and lymph node involvement, but only after surgery [9]. Therefore surgery represents the main form of treatment for lymph node metastases together with total thyroidectomy and for local recurrences that appear during long-term follow-up. There is great difficulty when tumoral foci are present inside an area of sclerosis due to previous surgery, at unusual sites such as behind vascular structures, or in the mediastinum. Surgery should be performed at a single session, thereby precluding the need for subsequent surgical procedures. To avoid these difficulties we used the advantages of high radioiodine activity and a gamma probe to perform the radical surgery at a single session. Our results confirmed that TxWBS and Tg off L-T_4 are the best presurgery diagnostic procedures for identifying lymph node metastases from DTCs. They are more sensitive and specific than US or CT, even though they underestimated the metastatic nodal involvement in three patients.

The gamma probe permitted us to look for neoplastic foci with high sensitivity and specificity and to remove metastatic lymph nodes resistant to radioiodine therapy. It allowed removal of pathologic areas of uptake in the neck in most patients; moreover, it allowed detection of some difficult to identify additional tumoral foci inside areas of sclerosis or behind vascular structures that were not seen during the presurgical evaluation. In confirmation of these results, in most cases the surgeons expressed a positive opinion about the procedure, describing it as "decisive" or "favorable."

Histologic examination confirmed the presence of lymph node metastases in tissue specimens with radioactivity counts higher than those found in background tissues, even if (unlike Travagli et al. [4] and Lippi et al. [10]) we did not find any definitive cutoff point that suggested the presence of lymph node metastases. In addition, the histologic evidence of 45 lymph node metastases undetected by TxWBS and with low radioactivity counts during the gamma probe evaluation confirms that sometimes lymph node metastatic involvement displays insufficient or absent radioiodine uptake.

An additional advantage of this protocol is the possibility of clearly evaluating the efficacy of the surgery. In fact, the rapid decrease in radioactivity count shown by the gamma probe and the

negative qualitative evaluation of the TxWBS at day 7 allowed us to evaluate the completeness of the tumoral excision at an early stage.

We did not observe significant lengthening of the normal operating times needed to perform a radical lymph node dissection, nor was there an increase in morbidity, particular risks, or surgical complications. Although we administered a high radioiodine dose 4 days before surgery, we always observed low levels of radioactive exposure to the surgeon's hands and no radioactive contamination of surfaces or surgical tools.

Together with the reported advantages, however, some limitations must be noted. First, as already observed by Wartofsky et al. [11], the patient has been exposed to a high radiation dose not for therapeutic purposes but for diagnostic reasons alone. Second, owing to the physical properties of ^{131}I the gamma probe gives a suboptimal performance with this radiopharmaceutical; a better performance has been obtained using a gamma probe after injection of ^{99m}Tc-MIBI or ^{123}I [12–14]. Third, in most countries radioprotection regulations do not permit the use of large ^{131}I doses in outpatients. Hence the dose used for the present study (i.e., 3.7 GBq) requires that the patient be hospitalized, with its consequent costs and patient discomfort.

Conclusions

Our results confirm the previous favorable impressions already reported by others [4, 10] and show that RGS can be of great help when performing radical lymph node dissection in patients with LNR at a single session. In high risk patients with a local recurrence, however, because of the possible false-negative results a complete excision must be undertaken along with eradicating a large number of lymph nodes regardless of the radioactive counts measured by the gamma probe.

Résumé. L'objectif de cette etude était d'établir l'apport d'une sonde de detection per-opératoire de l'Iode 131 dans la recherché et l'élimination des métastases ganglionnaires chez 10 malades ayant une tumeur différentiée de la thyroïde. Les critères d'inclusion étaient la présence de métastases ganglionnaires décelables à la scintigraphie réalisée après thyroïdectomie et après au moins deux traitements inefficacies par l'Iode 131. Le protocole était le suivant: à J0, hospitalisation et traitment par 3.7 GBq d'Iode 131 en condition d' hypothyroïdie, à J3, scintigraphie corps entire (SCE); à J5: chirurgie du cou avec utilization de la sonde de detection per-opératoire pour comptage des structures ganglionnaires et calcul du rapport lésion/bruit de fond; à J7, SCE post-opératoire. La SCE était positive en pré-opératoire chez tous les maladies, et negative en post-opératoire dans 7 cas, ce qui souligne l'efficacité de la CRG chez la plupart des malades. Après CRG, la mesure du comptage et de la valeur du rapport lesion/bruit de fond étaient diminués respectivement de 77,6% (entre 52.7% et 94.6%) et de 77.4% (entre 52.3% et 94.8%). Après l'intervention, le chirurgien a jugé la procédure décisive dans 2 cas, favorable dans 6 cas et inefficace dans 2 cas. L'examen histologique définitif montrait la présence de 78 métastases ganglionnaires (au moins 8 par malade): 33 lésions cancéreuses étaient évidentes à la fois en SCE et en détection per-opératoire, 41 lésions ont été identifiées uniquement avec la sonde per-opératoire et 4 lésions étaient négatives avec les deux procédures. Notre protocole a permis d'une part de montrer les foyers cancéreux avec une grande sensibilité et une grande spécificité, et d'autre part d'éliminer en une seul temps les métastases ganglionnaires résistantes au traitement par l'iode radioactive. Cette étude a permis en outré de détecter des foyers cancéreux difficiles à localiser avec les techniques conventionelles (par exemple dans une zone de sclérose ou en arrière d'une structure vasculaire). Du fait de possibles resultants faux négatifs chez les malades à haut risque de récidive locale, il est important de réaliser une exérèse radicale du plus grand nombre possible de ganglions sans tenir compte de la valeur du comptage revélée par la sonde de detection per-opératoire.

Resumen. Los objetivos del presente estudio son establecer la fiabilidad del radioyodo (^{131}I) y de una sonda detectora de rayos gamma (GP) para cirugía radio-guiada (RSG), con el fin de detectar y realizar una disseción radical de las recidivas de los ganglio linfáticos (LNR) en 10 pacientes con cancer diferenciado del tiroides. El criterio de inclusión utilizado es la presencia de LNR captantes el radioyodo, después de una tiroidectomia total y al menos dos tratamientos ineficaces con yodo. El protocolo es el siguiente: Día 0: todos los pacientes ingresan y reciben 3.7 GBq de^{131}I en condición de hipotiroidismo. Día 3: se realiza un rastreo corporal pre-quirúrigico con dosis terapeútica (TxWBS). Día 5: se realiza cirugía del cuello usando una GP (Navigator GPS, AutoSuture, Italy), registrando las cuentas de manera absoluta y la relación/fondo. Día 7: (TxWBS) post-quirúrgico, usando la radioactividad restante. El (TxWBS) pre-quirúrgico fué positivo en todos los pacientes, mientras el post-quirúrgico mostraba en 7 de 10 pacientes un patrón negativo, mostrando la eficacia de éste procedimiento quirúrgico en la mayoría de los pacientes. Después de la (RGS), la caída media del contaje absoluto y de la relación lesión/fondo fué del 77.6% (52.7%min-94.6%max) y del 77.4% (52.3%-94.8%) respectivamente. Después de la operación, el cirujano juzgó éste procedimiento como decisvo en 2, favorable en 6 y irrelevante en 2 pacientes. El examen histológico final mostró la presencia de 78 ganglios metastáticos (media de 8 por paciente); 33 lesiones neoplásicas fueron evidentes tanto en el (TxWBS) como con la (GP). Nuestro protocolo nos ha permitido buscar focos neoplásicos con gran sensibilidad y especificidad y extirpar en una única sesión ganglios metastáticos resistentes al tratamiento con radioyodo. Permite detectar algunos focos tumorales difíciles de indentificar dento de areas de esclerosis o detrás de estructuras vasculares, que no se habían visto a la valoración prequirurgica con el (TxWBS). De todas formas, debido a los posibles falsos negativos, en pacientes de alto riesgo con recidiva local es aconsejable una extipación completa del mayor número de ganglios posible, independientemente del contaje medido con la sonda.

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References

1. Reintgen D, Cruse CW, Wells K. The next revolution in general surgery: radioguided surgery. Ann. Surg. Oncol. 1999;6:125–126
2. Glass EC. Nuclear medicine in the detection of the sentinel node. Ann. Surg. Oncol. 2001;8:5S–8S
3. Mariani G, Moresco L, Viale G, et al. Radioguided sentinel lymph node biopsy in breast cancer surgery. J. Nucl. Med. 2001;42:1198–1215
4. Travagli JP, Cailleux AF, Ricard M, et al. Combination of radioiodine (131I) and probe-guided surgery for persistent or recurrent thyroid carcinoma. J. Clin. Endocrinol. Metab. 1998;83:2675–2860
5. Sobin, LH, Wittekind, CH. UICC: TNM Classification of Malignant Tumours, 5th edition, Wiley-Liss, New York, 1997
6. Schlumberger M, Pacini F, Thyroid Tumors, Paris, Edition Nucleon, 1999
7. Voutilainen PE, Multanen MM, Leppaniemi AK, et al. Prognosis after lymph node recurrence in papillary thyroid carcinoma depends on age. Thyroid 2001;11:953–957
8. Maxon HR, Englaro EE, Thomas SR, et al. Radioiodine-131 therapy for well differentiated thyroid cancer: a quantitative radiation dosimetric approach: outcome and validation in 85 patients. J. Nucl. Med. 1992; 33:1132–1136
9. Tsang RW, Brierley JD, Simpson WJ, et al. The effects of surgery, radioiodine, and external radiation therapy on the clinical outcome of patients with differentiated thyroid carcinoma. Cancer 1998;82:375–388
10. Lippi F, Capezzone M, Miccoli P, et al. Use of surgical gamma probe

for the detection of lymph node metastases in differentiated thyroid cancer. Tumori 2000;86:367–369
11. Wartofsky L, Sherman SI, Gopal J, et al. The use of radioactive iodine in patients with papillary and follicular thyroid cancer. J. Clin. Endocrinol. Metab. 1998;83:4195–4203
12. Boz A, Arici C, Güngör F, et al. Gamma probe-guided resection and scanning with Tc-99m MIBI of a local recurrence of follicular thyroid carcinoma. Clin. Nucl. Med. 2001;26:820–822
13. Rubello D, Piotto A, Pagetta C, et al. 99mTc-MIBI radio-guided surgery for recurrent thyroid carcinoma: technical feasibility and procedure, and preliminary clinical results. Eur. J. Nucl. Med. 2002;29:1201–1205
14. Gallowitsh HJ, Fellinger J, Mikosch P, et al. Gamma probe-guided resection of a lymph node metastasis with I-123 in papillary thyroid carcinoma. Clin. Nucl. Med. 1997;22:591–592