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Radioguided surgery with combined use of gamma probe and hand-held gamma camera for treatment of papillary thyroid cancer locoregional recurrences: a preliminary study

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Abstract. – BACKGROUND: Persistent differentiated papillary thyroid cancer (PTC) with metastasis followed by radical locoregional surgery is an indication for limited reoperation. Despite excellent prognosis the major challenge is controlling locoregional recurrences.

AIM: To evaluate the efficacy of radioguided excision with combined use of gamma probe and an hand-held gamma camera.

PATIENTS AND METHODS: From June 2009 to January 2012, we enrolled twenty-two patients with locoregional PTC recurrences, previously undergone to central and/or lateral neck dissection for PTC. The diagnosis of recurrent PTC was based on thyroglobulin (TG) evaluation [basal and after thyroid stimulating hormone (TSH) stimulation], ultrasound (US), iodine-131 (^{131}I) whole body scan (WBS) and fine needle aspiration cytology (FNAC). In the morning of surgery, radiotracer was injected directly into the lesions by US guide. Careful dissection was carried out using gamma probe and hand held gamma camera. Metastatic lymph nodes were indentified and excised.

RESULTS: In all the patients recruited, 39 pathologic nodes were injected and 61 nodes were removed. Among the removed nodes, 22 (36.1%) were additional nodes (not injected by radiotracer). Of the additional lymph nodes, 7 (31.8%) were metastatic. Mean radioactive count of the lesion (28.633±9.218 counts/s) was higher than tumor bed (385.73±192.23 counts/s) ($p < 0.0001$). No complications were observed during radioguided excision, neither on post-operative period.

CONCLUSIONS: The use of hand-held gamma camera in addition to gamma probe in our preliminary study allows a minimally invasive procedure and safer identifications of the lesions and ensures the completeness of the excision in a difficult surgical field.

Key Words:
Radioguided surgery, Papillary thyroid cancer, Locoregional recurrences, Gamma camera, Endocrinology.

Introduction

Papillary Thyroid Cancer (PTC) is the most common tumor of thyroid gland. Despite excellent prognosis, 40% of patients with locoregional lymphnode metastasis develop recurrences located in the laterocervical compartments in 53% of cases and in the central neck in 28% of cases[1,2]. Recurrences treatment is actually surgical[3,4]. The prevalence of recurrent laryngeal nerve (RLN) lesion in the reoperation ranges from 1% to 12%, while that of definitive hypoparathyroidism from 1 to 13%[5,6]. In this cases radioguided approach is a new alternative that helps the surgeons for dissection in a difficult operative field, because of the presence of important structures in a scar tissue[7]. These difficulties have encouraged, in the last years, the development of localization and excision radioguided techniques for lateral neck dissection, based on the experience of the breast cancer[8-10], that allowed a minimally invasive procedure directly on the site of the metastasis. In this study we report our preliminary case load about radioguided surgery for the treatment of PTC locoregional lymph node recurrences.

Patients and Methods

From June 2009 to January 2012 twenty two patients with locoregional PTC recurrences were enrolled, having them previously undergone to central and/or lateral neck dissection for PTC. The diagnosis of recurrent PTC was based on thyroglobulin (TG) evaluation (basal and after thyroid stimulating hormone (TSH) stimulation), ultrasound (US), iodine-131 (^{131}I) whole body scan (WBS) and fine needle aspiration cytology (FNAC). One patient came to our attention after a failed operation for one

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mediastinal recidive. Once cytopathological diagnosis was performed for recurrence, patients were prepared for surgery. In the morning of surgery, a 22 gauge standard needle was placed into the center of lesion, and 20 MBq activity of ^{99m}Tc labeled macroaggregate albumin in 0.2 mL was injected. The injections were US-guided. A unilateral or bilateral thyroid bed exploration was based on the location of biopsy proven lesion with the guidance of intraoperative gamma probe (Neoprobe) (Figure 1). Intraoperative radioactivity was detected also with imaging probe (IP, Li Tech Srl, Lauzacco-Pavia di Udine, Italy, FOV 2.6 × 2.6 cm, spatial resolution 2 mm) for the spatial localization of the lesions and the confirm of a radical excision (Figure 2). Count rate for injected lesions and lesions bed after excision were recorded. The complete excision of injected lesions was assessed and confirmed with gamma probe and hand-held gamma camera (imaging probe) before the end of surgery. Subsequent follow up was performed with the measurement of TG, US and ^{131}I WBS. The following data were investigate: age, gender, TNM classification of malignant tumors (TNM), previous surgical procedures, previous ^{131}I treatments, operating time, time to recurrence, number of tracked nodes, number of removed nodes, number of metastatic tracked nodes removed, mean radioactive count of tumor bed and lesion, morbidity.

Statistical Analysis

The Student's *t* test was used to compare the mean radioactive count of tumor bed and lesion. A *p*-value les than 0.05 was considered significant. Results are shown as mean value ± standard deviation.

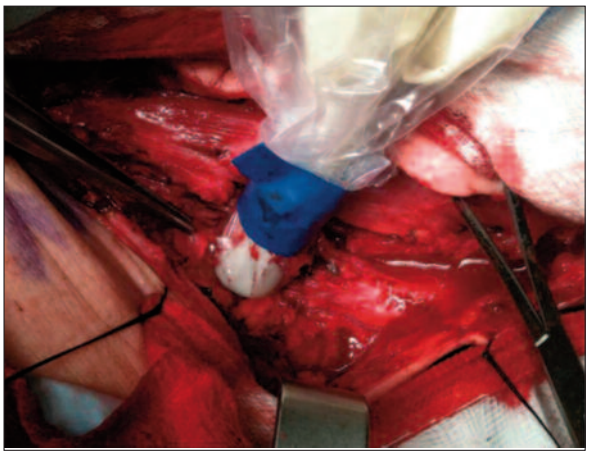

Figure 1. Tyroid bed exploration with gamma probe (ima 1).

The study was approved by the Ethical Committee of the II School of Medicine and Surgery, Sapienza University, Rome, Italy.

Results

The mean age of patients recruited was 43.27±14.8 years. Of them, 14 patients (63.3%) were females. Demographic features of the population under study are shown in Table I. In 41% of patients, previous surgical procedures were total thyroidectomy and sixth level lymphoadenectomy while in the remaining 59% were total thyroidectomy, sixth level lymphoadenctomy and functional monolateral lymphoadenectomy. The mean surgical time was 30±10.82 minutes. All patients underwent to ^{131}I therapy. The mean time between surgery and the first locoregional lymph nodal

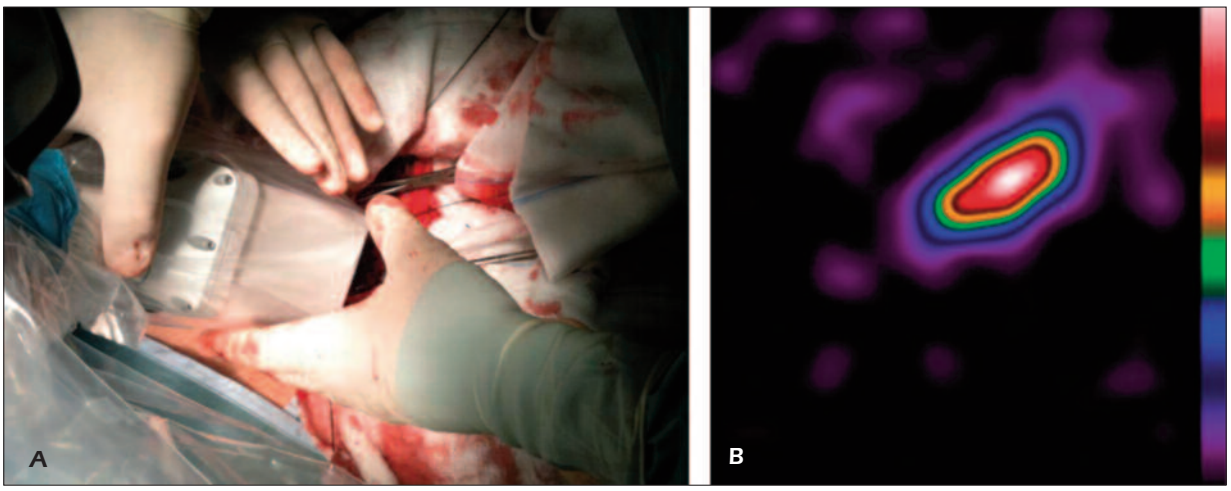

Figure 2. Lesion spatial localization with imaging probe (ima 2 + ima 3).

Table I.

Patient n.	Sex	Age	Operation	Tumor stage	Histology	I^{131}	OT (min)	Time to recurrence (months)	Lesions, number	Localizations	Removed lymphnodes, n	Metastatic lymphnodes	Lesions radioactivity	Bed radioactivity
1	M	32	TT+CND	T4 N1a M0	Papillar	2	35	21	2	VI	3	2	1-23000 2-18500	1-320 2-125
2	F	39	TT+CND+LND	T4 N1b M0	Papillar	2	20	24	1	III	2	2	1-32600	1-430
3	M	36	TT+CND+LND	T1b N1b M0	Papillar	2	26	32	1	III	1	1	1-21000	1-420
4	M	39	TT+CND+LND	T3 N1b M0	Papillar	3	50	43	3	VI/IV	4	4	1-44000 2-26000 3-18000	1-120 2-210 3-450
5	F	41	TT+CND	T2b N1a M0	Papillar	3	52	44	2	LTB/VI	3	2	1-31500 2-24000	1-260 2-128
6	F	53	TT+CND+LND	T4 N1b M1	Papillar	3	32	36	2	IV/III	2	2	1-43000 2-26500	1-560 2-310
7	F	28	TT+CND+LND	T4 N1a M0	Papillar	2	28	26	1	VI	3	2	1-45000	1-320
8	F	45	TT+CND	T2b N1a M0	Papillar	3	24	60	1	RTB	2	2	1-19000	1-230
9	M	28	TT+CND	T3 N1b M0	Papillar	2	34	30	3	IV/III	3	3	1-32000 2-18000 3-21500	1-90 2-330 3-380
10	F	67	TT+CND+LND	T1b N1b M0	Papillar	3	38	42	2	VI/III	3	2	1-18000 2-24000	1-610 2-172
11	F	32	TT+CND+LND	T4 N1a M0	Papillar	1	32	21	2	VI	3	2	1-26000 2-42500	1-320 2-420
12	F	26	TT+CND	T4 N1a M0	Papillar	2	21	28	1	VI	2	1	1-41000	1-1020
13	M	57	TT+CND	T3 N1b M0	Papillar	3	34	22	3	VI/III	4	3	1-22000 2-30500 3-18000	1-980 1-450 3-320
14	F	35	TT+CND+LND	T1b N1b M0	Papillar	2	41	14	2	III/II	3	2	1-28000 2-19000	1-150 2-240
15	F	72	TT+CND	T4 N1a M0	Papillar	2	15	16	1	VI	3	1	1-23000	1-420
16	M	45	TT+CND	T2b N1a M0	Papillar	1	18	12	2	VI	2	2	1-40000 2-23000	1-220 2-110
17	M	45	TT+CND+LND	T4 N1b M0	Papillar	3	24	21	2	III	2	2	1-18000 2-21000	1-240 2-80
18	F	22	TT+CND+LND	T2b N1b M0	Papillar	2	32	11	3	IV/III	3	3	1-24000 2-16000 3-29000	1-720 2-310 3-200
19	F	63	TT+CND+LND	T3 N1b M0	Papillar	2	22	30	2	IV/III	3	2	1-32000 2-21000	1-560 2-230
20	F	68	TT+CND	T1b N1a M0	Papillar	2	46	16	3	VI	4	3	1-19000 2-18000 3-26000	1-1200 2-320 3-250
21	F	27	TT+CND	T4 N1a M0	Papillar	3	12	24	1	VI	2	1	1-52000	1-540
22	M	52	TT+CND+LND	T3 N1b M0	Papillar	1	24	42	2	IV/III	4	2	1-48000 2-31000	1-620 2-320
									42		61	46		

Table II. Comparison between mean lesion radioactivity count and mean bed radioactivity count.

	Value = 0				
				95% CI for difference	
	t	df	Differene of means	Lower	Upper
Lesions radioactivity	14.568	21	28633.273	24545.92	32720.63
Bed radioactivity	9.388	21	385.727	300.29	471.17

PTC recurrence was 27.9±12.4 months. In all patients, 39 pathologic nodes were injected and 61 nodes were removed. Among the removed nodes, 22 (36.1%) were additional nodes (not injected by radiotracer). Among the additional lymph nodes, 7 (31.8%) were metastatic. A mean of 2.0 ± 0.7 of pathologic nodes were removed as well as a mean of 0.6±0.5 of normal nodes. The mean radioactive count of the lesion (28.633±9.218 counts/s) was higher than tumor bed (385.73±192.23 counts/s) ($p < 0.0001$) (Table II). No complications were observed during radioguided excision, neither on post-operative period. All patients underwent to 3 and 6 months follow-up visits, where TG test and ultrasound examination were performed.

Actually none of the patients under study has recurrent nodal disease.

Discussion

PTC is the most frequent tumor found in thyroid gland, and affects women more than men with an average age of 40-50 years. Although the papillary cancer is accompanied by a good prognosis, long-term survival is mainly linked to the control of locoregional recurrences whose prevalence amounted to 40%[1,2]. Surgical treatment of PTC with lymph node metastasis at stage N1a/b is currently based on the total extracapsular thyroidectomy with lymphadenectomy of the central compartment (level VI) and lateral cervical compartments (II/III/IV level)[1,4,11]. Since most of these lesions are not responsive to metabolic radiotherapy, the only therapeutic alternative remains the surgery[12-14]. Re-interventions for the removal of cervical recurrences are often difficult even for skilled surgeons[7]. This is related both to the particular anatomy of the cervical region, characterized by a high density of noble structures in a physical space extremely limited and for the presence of tenacious adhesions caused by previous surgical procedures and radiotherapy-metabolic cycles. As described in the literature, the prevalence of recurrent laryngeal nerve injury ranges from 1 to 12%, that of permanent hypoparathyroidism from 1 to 13%, that of Horner syndrome from 0.8% to 1%, that of injuries to the spinal accessory nerve from 0.7 to 1%, and that of injuries to the thoracic duct from 0.2% to 1%[7]. In this study, all patients was previously subjected to a total thyroidectomy with lymphadenectomy of central compartment and/or laterocervical compartment, and one patient came to our observation after an unsuccessful removal of metastatic lymph node recurrence of the sixth level. All patients underwent to at least two cycles of iodine radiotherapy[15]. Positive lymph nodes were inoculated with 0.2 ml of microaggregates of human albumin labeled with technetium-99m (1 mCi). The tracer used was selected for its characteristics of low spreading to surrounding tissues. At the beginning of the procedure we previously recorded the surgical field using the hand-held gamma camera searching and identifying hot spots. Subsequently the dissection was carried out following the area of maximum radioactivity using the gamma probe until the metastatic lymph nodes were identified and excised. The success of the procedure was confirmed by the hand-held gamma camera before the termination of surgery.

This technique has proven to be feasible, safe and useful in all those cases where also the gamma probe could show difficulties in the localization of the lesions, especially those embedded in the scar tissue. The gamma camera allows, through a minimally invasive approach, a direct visualization of the inoculated lesions leading to an easier and safer route for dissection reducing at the same time the extension of the incision. We found no surgical complications and we removed all the lesions preoperatively identified. Although does not seem rational to assume that such good results, especially in terms of complications, could be ascribed only to the radioguided technique, however, the reduction of the surgical

field, the minimally invasive approach and the precision of a difficult neck dissection, carried out with the gamma camera, lead to a decrease of complications. In our investigation the mean duration of surgery was 33 minutes, ranging from 20 to 52 minutes. These results show that the use of hand-held gamma camera does not increase the surgical time, but allows a direct and fast localization of the lesions.

In almost all patients a greater number of lymph nodes compared to those inoculated with the tracer were removed, in some cases due to the presence of lymph node packages, in others due to the attendance of suspicious lesions based on the macroscopic aspect.

The presence of a nuclear specialist is very useful to guide the surgeon through a correct interpretation of the findings of the gamma camera, and it should be implemented.

Conclusions

The radioguided excision of PTC lymph node recurrences allowed (1) to decrease the rate of new excisions, (2) to reduce the extent of dissection leading to a minimally invasive approach and (3) to avoid surgical complications, assuring the effectiveness of the excision. The use of the hand-held gamma camera in addition to neoprobe in our preliminary case load allows a faster and safer identifications of the lesions and ensures the completeness of the excision in a difficult surgical field. Subsequent studies are needed to assess the real advantages and efficacy of the hand-held gamma camera combined to the gamma probe vs the gamma probe alone, in order to standardized this procedure.

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Conflict of Interest

The Authors declare that there are no conflicts of interest.

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