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Added value of SPECT/CT in addition to whole-body scintigraphy augmented with prone lateral views in patients with well-differentiated thyroid carcinoma

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Added value of SPECT/CT in addition to whole-body scintigraphy augmented with prone lateral views in patients with well-differentiated thyroid carcinoma

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ABSTRACT:

Purpose: We aimed to determine the impact of SPECT/CT performed in addition to whole-body scintigraphy augmented with prone lateral views in patients with well-differentiated thyroid carcinoma.

Methods and Materials: This retrospective study included 141 patients (87 female, 54 male, mean age 47 years) with well-differentiated thyroid carcinoma (105 papillary, 31 follicular, 1 Hürthle cell and 4 poorly differentiated) treated with radioiodine therapy (1000–7400 MBq). Patients were referred for either first postsurgical therapy (n=76) or further treatment (n=65). Two nuclear medicine physicians interpreted the scans in consensus (first whole-body scintigraphy with prone lateral view, then SPECT/CT) reporting abnormal iodine uptake in the thyroid bed, lymph nodes and distant metastasis. The corresponding ATA risk score was calculated for each patient before and after SPECT/CT, as well as change in disease extension

Results: The analysis showed a difference between scintigraphy and SPECT/CT in n=17 lesions in 14 patients (9.9%): 12 were described as suspicious on scintigraphy and could be considered as benign on SPECT/CT (3 corresponded to local iodine uptake, 6 to lymph nodes metastases and 3 to distant metastases). The others 5 corresponded to metastases (4 lymph nodes and 1 distant) that were not seen on whole-body scintigraphy augmented with prone lateral views. In 10 of 141 (7.1%) patients, we observed a change in ATA risk stratification, with a risk increase in 4 of them (2.8%).

Conclusion: SPECT/CT allowed detecting 5 focal lesions missed on planar scintigraphy, and to precise benignity of 12 suspicious lesions on planar scintigraphy. Moreover, SPECT/CT improved the risk stratification in 10 patients with a significant change in the patient management

Key Words: differentiated thyroid cancer, radioiodine scintigraphy, SPECT/CT, risk classification

INTRODUCTION:

Well differentiated thyroid cancer accounts for nearly 1% of all cancer cases, with an increasing incidence (1,2). Thanks to a right therapy, this type of cancer has a favorable prognosis and good survival rates (3). The standard treatment includes surgical resection (near-total or total thyroidectomy) and ^{131}I radio-ablation (4,5) to remove any physiological and pathologic remnant post-surgery.

To help to better plan further treatments for the patients, guidelines for thyroid cancer management were published by the American Thyroid Association (ATA) to define risk stratification. Many parameters are included, i.e. tumor histology, surgical resection, local or distant metastasis and post-therapy scan results (4). These criteria allow grouping patients in 3 different risk categories. No local or distant metastases, complete surgical resection, no invasion of locoregional structures, no vascular invasion are the criteria for a low-risk patient. Patients are classified as intermediate-risk patients if they have aggressive histology or vascular invasion, microscopic invasion into perithyroidal soft tissues at initial surgery or cervical lymph nodes metastases. High-risk patient are characterized by macroscopic tumor invasion, incomplete resection or distant metastases (4). This risk stratification allows to determine the patient management: further treatment, frequency and intensity of follow-up (6,7).

Imaging is important to determine the risk for the patient. The whole-body planar scintigraphy is a good tool to detect iodine uptakes in post-thyroidectomy patients. However, scintigraphy images don't allow to precise the anatomical localization and the nature of iodine uptake, whether normal or abnormal. Moreover, it has a low resolution. SPECT/CT has been a useful tool to fill this gap of scintigraphy: not only it permits to precise the anatomical localization, but also the nature of radioactive foci (benign or malignant), improving the interpretation of radioiodine scintigraphy (7).

In our center, we perform additional prone lateral views to the planar scintigraphy, which give a more detailed and precise stage than the whole-body scintigraphy alone, but the combination of both techniques still results in a lack of anatomical details. For this reason, the SPECT/CT completes the imaging.

The objective of this study is to determine retrospectively the impact of SPECT/CT performed in addition to whole-body scintigraphy with prone lateral views in patients with well-differentiated thyroid carcinoma in our institution, to see how often the ATA risk stratification changes.

MATERIALS AND METHODS:

This retrospective study included 141 patients (87 female and 54 male) with well-differentiated thyroid carcinoma treated with ^{131}I between November 2008 (first date when the SPECT/CT was used for thyroid images regarding this type of cancer at our Nuclear Medicine Department) and June 2013. The mean age of the patients was 47 years ± 14 and the range was from 17 to 82 years. The subjects

were referred to our center either for first postsurgical treatment (n=76) or for recurrent disease, so further treatment (n=65). Every patient needed to have well-differentiated thyroid cancer: 105 of them had papillary type, 31 of them had follicular one, 4 of them a poor differentiated one, and only one had Hürthle cell cancer. They all underwent radioiodine therapy after near-total or total thyroidectomy.

After having received a mean activity of 3403 MBq ± 1034 and a range from 1000 to 7400 MBq, post therapy imaging was performed between 2 and 8 days after ^{131}I capsule administration. For each patient were performed anterior and posterior whole body planar scintigraphy, at least one prone lateral static view and SPECT/CT. Every scan included head and neck region and at least the thorax. All patients underwent scintigraphy imaging and SPECT/CT on the same day. Initially, the scintigraphy with prone lateral views was performed by using a dual head gamma-camera (Biad, Trionix; Infinia Hawkeye IV, GE Healthcare; Discovery NM670, GE Healthcare). Thereafter the SPECT/CT was performed (Infinia Hawkeye IV, GE Healthcare; Discovery NM670, GE Healthcare).

To compare scintigraphy and SPECT/CT findings at our institution, two experienced nuclear medicine physicians interpreted the different scans for each patient. They could have information regarding the type of cancer, the thyroglobulin level or prior treatment results. Their task was to evaluate the iodine uptake and categorize it, by reporting every abnormal uptake. For each scan review, they had to agree with each other. If discordances between the two physicians occurred, a discussion had to be made to reach a consensus. At the beginning they interpreted the scans separately, but we decided that a discussion together and immediate was more productive, so we changed method during the review process. They started at first with the scintigraphy images (both whole body and prone lateral static views together). If the uptake was localized on the medial portion of the neck, they categorized it as positive for tumoral or physiological remnant. If it was located laterally in the neck or in the mediastinal region and obviously not in the thyroid bed, it was considered as positive for lymph nodes metastases. Radioactive foci located outside the neck or the mediastinum were categorized as positive for distant metastasis, when they clearly were not physiologic accumulation (nose, salivary glands, stomach, intestines, etc.) Once the iodine uptake was categorized for the scintigraphy, they could analyze the SPECT/CT scans. Likely for the first part, SPECT/CT findings were described to categorize the iodine uptake as local residue, lymph nodes metastasis or distant metastasis. It's important to underline that the two nuclear medicine physicians could only characterize the findings as benign or malignant. Even if a lesion was equivocal for them, they always had to categorize the uptake as local residue, lymph node or distant metastasis.

Then the ATA risk score was calculated for each patient to know how often SPECT/CT changes the initial risk stratification. Presence of only tumoral or physiological residue determines a low risk. Iodine uptake in lymph nodes means intermediate risk. Patients with distant metastasis are categorized as high-risk patients. So if new distant metastases were identified on the SPECT/CT, the risk would elevate the risk from low or intermediate to high. Iodine uptake in neck lymph nodes would change a low risk patient to an intermediate one and vice versa. According to the guidelines by Cooper et al. (4), the risk attribution considered also the tumor histology, invasion at initial surgery and the resection. Once we have one score for the scintigraphy and one for the SPECT/CT, we compare them and see if there is an improvement of the risk or not, considering planar and SPECT/CT findings.

A statistical analysis is then done to determine the different percentages and to see the contribution of the SPECT/CT on the risk stratification.

	All	First treatment	Further treatment
Patients	141	76 (54)	65 (46)
Sex			
Male	54 (38.3)	25 (32.9)	29 (44.6)
Female	87 (61.7)	51 (67.9)	36 (55.4)
Age (year)			
Mean ± SD	47 ± 16	47 ± 14	48 ± 18
Range	17 - 82	17 - 78	17 - 82
Histology			
Papillary	105 (74.5)	57 (75)	48 (73.8)
Follicular	31 (22)	18 (23.7)	13 (20)
Poorly differentiated	4 (2.8)	1 (1.3)	3 (4.6)
Hürthle cell	1 (0.8)	0 (0)	1 (1.5)
^{131}I Activity (MBq)			
Mean ± SD	3403 ± 1034	2933 ± 919	3952 ± 883
Range	1000 - 7400	1000 - 3859	2000 - 7400

Data in parentheses are percentages.

Table 1: Patient demographics

RESULTS

The analysis showed a difference between scintigraphy and SPECT/CT in n=17 lesions in 14 patients (9.9%): n=8 in 6 patients referred for a first treatment and n=9 in 8 patients with further treatment. In n=12 lesions in 10 patients (7.1%) were suspicious on scintigraphy, but they could be considered as benign on SPECT/CT (n=3 corresponded to local iodine uptake, n=6 to lymph nodes metastases and n=3 to distant metastases). The others n=5 found in 5 patients (3.5%) lesions corresponded to metastasis that weren't seen on whole-body scintigraphy augmented with prone lateral views: n=4 lymph nodes metastases and n=1 distant metastasis.

Thyroid bed

During the scintigraphy scans review, iodine uptakes in the thyroid bed (tumoral or physiological residue) were found in 131 patients, which means in 92.2% of the patients. On the SPECT/CT scans,

128 patients (90.8%) had positive uptake in this region. In 3 patients (2.1%) uptake was present in the scintigraphy and not observed on the SPECT/CT scan. In the first treatment cohort, the findings on scintigraphy correlated with the findings on SPECT/CT. In patients with further treatment, disagreement was observed in 3 of 65 patients.

Lymph nodes metastases

Twenty-two patients (15.6%) were described with lymph nodes metastases on the scintigraphy (n=11 for each first and further treatment). On the contrary, n=20 lymph nodes metastases (n=8 for first vs. n=12 for further treatment) were found on SPECT/CT (14.2%). A certain number of patients had a change in the localization of the pathological lymph nodes. The analysis showed a difference between scintigraphy and SPECT/CT in n=10 lymph nodes lesions in 10 patients (7.1%): n=6 (4.3%) were described as suspicious on scintigraphy and could be considered as benign on SPECT/CT. The others 4 (2.8%) corresponded to lymph nodes metastasis found on SPECT/CT that weren't seen on whole-body scintigraphy with prone lateral views. In the patients who underwent a first therapy, n=4 lymph nodes metastases have been described on the scintigraphy but not on SPECT/CT and n=1 patient had a lymph node metastasis on SPECT/CT that wasn't seen on scintigraphy. On the contrary regarding the patients with a further treatment, n=2 lesions were found only on scintigraphy and n=3 lymph nodes metastases were discovered on SPECT/CT and not seen on the scintigraphy.

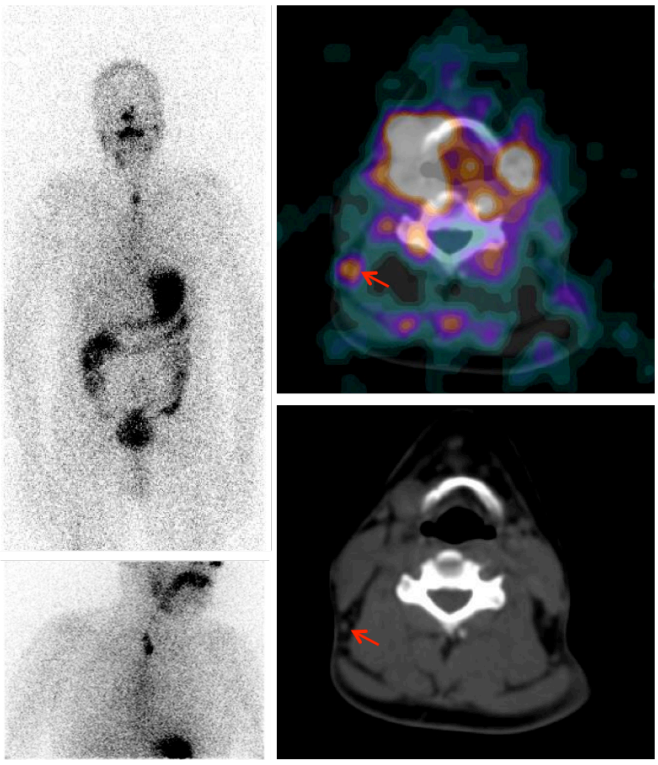

Figure 1. A 34 year-old man with papillary thyroid cancer, second radioiodine therapy, 3 days after administration of 3700 Mbq ^{131}I. On the whole-body scintigraphy (on the left) an asymetrical uptake can be seen on the right side of the neck. With the help of the lateral view, this uptake was considered as benign because of its location (it can be a submandibular gland). For this reason, the patient was classified with a low ATA risk score. On the SPECT/CT (on the right) this uptake is located in a neck lymph node (see the arrow). This proves the malignant characteristic of the uptake, so this patient went from a low to an intermediate risk.

Distant metastases

A total of 6 patients (4.3%) had distant metastases on the whole body scintigraphy with prone lateral views: n=2 of them during the first radiotherapy and n=4 during a further treatment. On SPECT/CT, n=4 lesions (2.8%) were described as positive for distant metastases: n=1 in patients with first therapy, n=3 in those with further treatment. Changes between scintigraphy and SPECT/CT occurred

in n=4 lesions in 4 patients (2.8%). 3 of them (2.1%) were described M1 on scintigraphy, but M0 on SPECT/CT (n=2 first vs. n=1 further treatment). SPECT/CT helped discovering a distant metastasis not seen on scintigraphy in 1 patient during his first radioiodine therapy (0.7%).

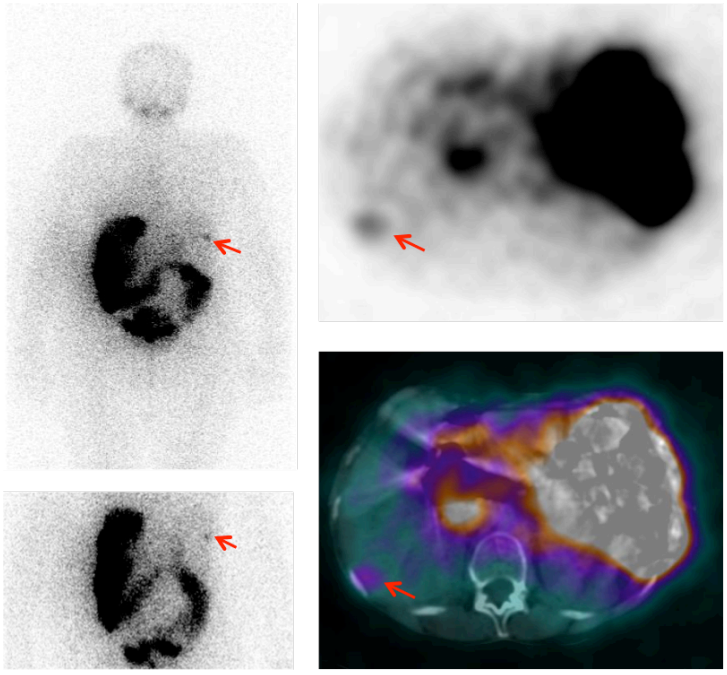

Figure 2. A 65-year-old woman with papillary thyroid cancer, second radioiodine therapy, 3 days after administration of 3700 Mbq ^{131}I. The whole-body scintigraphy (on the left) shows an isolated iodine uptake (see the arrow), which can suggest a bone metastasis. So the patient was classified with a high ATA risk score. The SPECT/CT (on the right) shows its hepatic location, which is not a usual metastasis location for this cancer. In fact, it corresponds to a hemangioma. This patient went from a high to a low risk

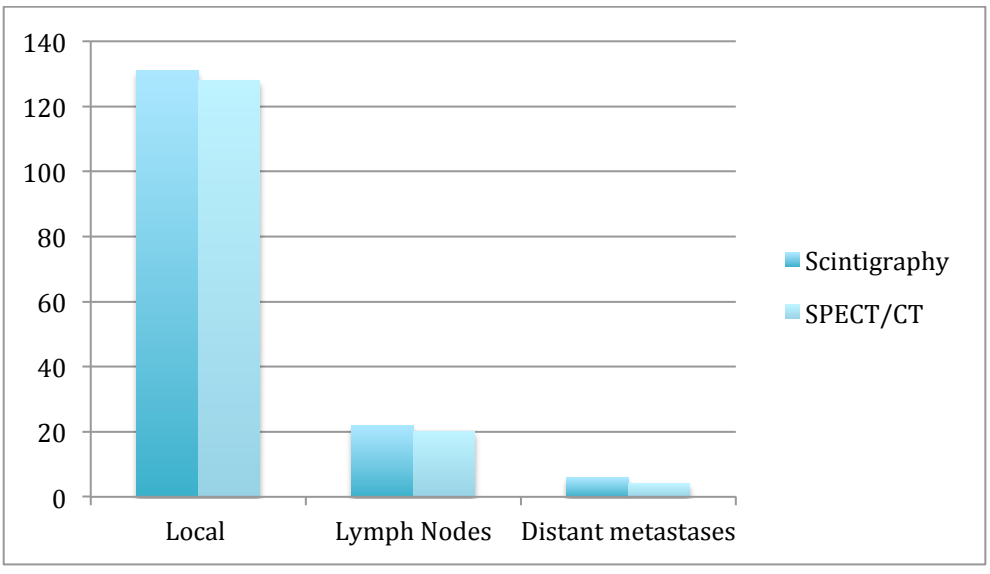

Figure 3. Difference in patient positive findings between SPECT/CT and scintigraphy

ATA risk

On scintigraphy, n=97 patients (68,8%) were classified as low risk patients, n=34 patients (24.1%) as intermediate risk one and n=10 (7.1%) patients as high risk ones. On the contrary, on the SPECT/CT the low risk patients were n=100 (70.9%), the intermediate risk ones n=33 (23.4%) and finally the

high-risk ones n=8 (5.7%). A change in ATA risk stratification between whole body scintigraphy with prone lateral views and SPECT/CT is observed in 10 patients (7.1%). In n=4 patients (2.8%) the ATA risk increased: n=3 of them (2.1%) from a low risk to an intermediate one and n=1 post-surgical patient (0.7%) from an intermediate risk to a high one. On the contrary, n=6 patients (4.3%) showed a decreased ATA risk score after SPECT/CT: n=4 (2.8%) from a high to a low risk, n=2 (1.4%) from an intermediate to a low risk. Others details are showed on table 2.

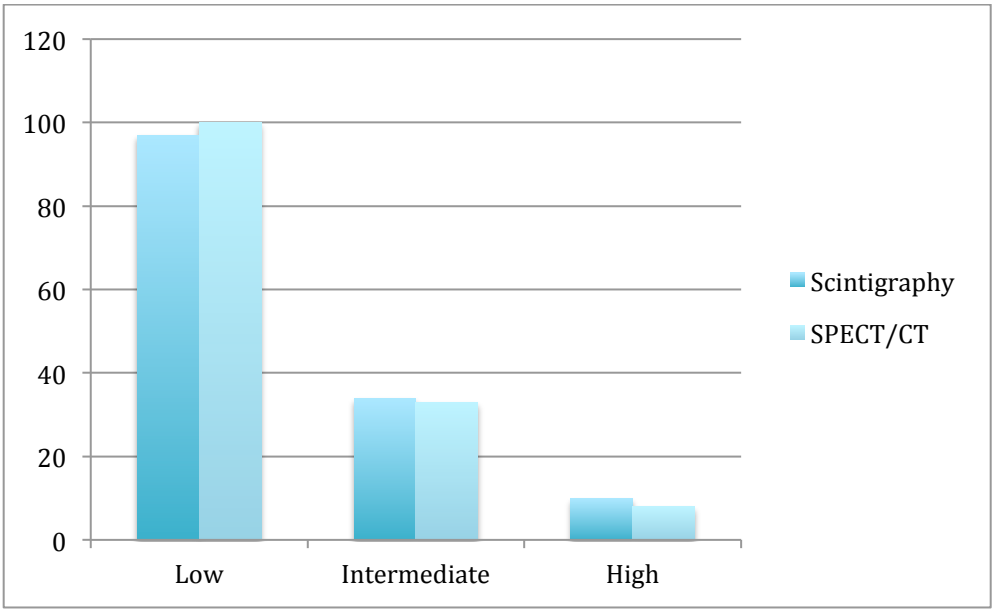

Figure 4. Difference in patient ATA risk score between SPECT/CT and scintigraphy

Patient	Age	Sex	Therapy	Histology	ATA Risk for Scintigraphy	ATA Risk for SPECT	Diagnostic
1	32	F	2nd	papillary	low	intermediate	
2	34	M	2nd	papillary	low	intermediate	
3	42	F	1st	papillary	low	intermediate	
4	52	F	1st	follicular (oncocytic type)	intermediate	high	Poor iodophile pulmonary mass
5	51	M	1st	papillary	intermediate	low	
6	48	M	2nd	papillary	intermediate	low	
7	58	F	2nd	papillary (follicular type)	intermediate	low	
8	37	F	1st	papillary (follicular type)	high	low	degenerative pathology, physiological residue
9	30	F	1st	follicular	high	low	contamination
10	65	F	2nd	papillary	high	low	Liver hemangioma

Table 2. Change in ATA risk score between scintigraphy and SPECT/CT

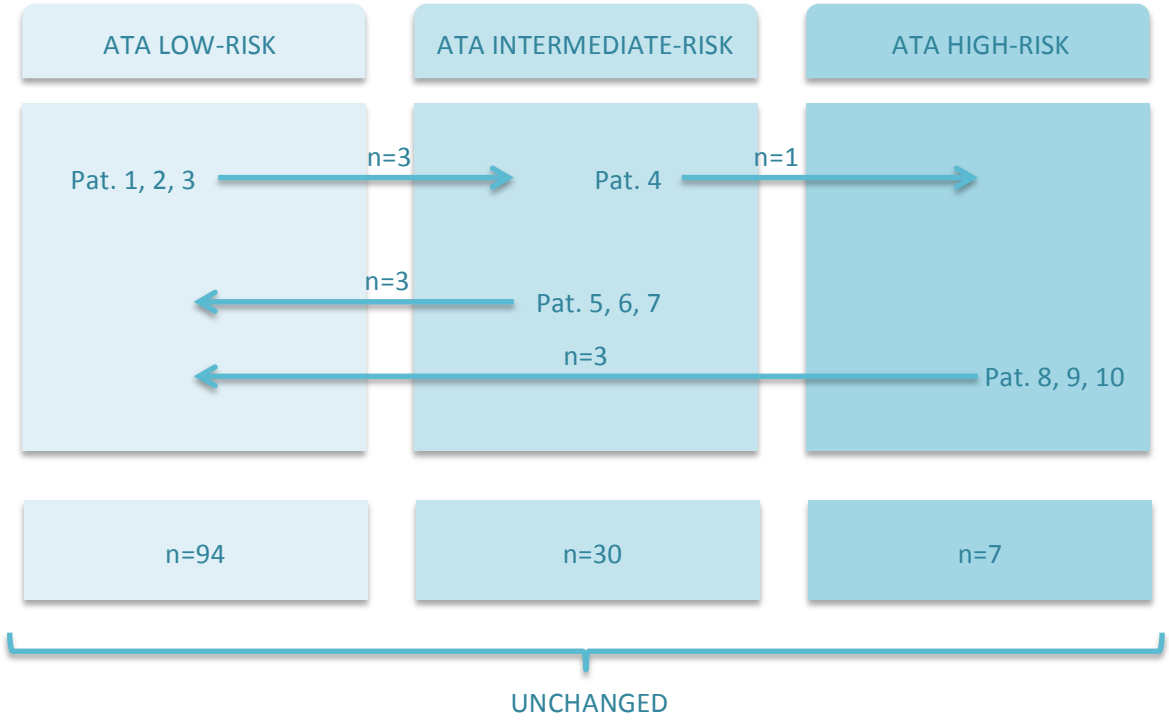

Figure 5. Patients ATA risk stratification after SPECT/CT

DISCUSSION:

^{131}Iodine scintigraphy is an important initial and primary tool for the detection of this disease in post surgery patients with well-differentiated thyroid carcinoma. With the introduction of new technique, it was proved that SPECT/CT provides additional information to the scintigraphy (6–18), with a benefit on the patient management, linked to the more accurate localization and characterization of nature of the iodine uptake.

In our study, there is a difference between whole-body scintigraphy with prone lateral views and SPECT/CT in 17 lesions (12.1%). It's a lower rate of changed findings from scintigraphy to SPECT/CT compared with others studies, which vary from 20% (6) to 74% (3). The results diverge especially in relation to different methodology.

One of the reasons of the difference in the results between the studies can be the timing of the scans: SPECT/CT before radioiodine therapy (9,12,14), post-therapy (5,9,10, 14,18,19) or a mixture of both (13). More radioiodine foci can be detected in the post-therapy scans, because target-to-background ratio is more important, in reason of the higher radioiodine activity and the longer interval between activity administration and imaging (20–23).

In this study the SPECT/CT was obtained in all patients independently on the findings in the planar imaging, so every subject had a SPECT/CT scan that included head and neck region and at least the thorax. In the contrary, in some others articles (9,11,13,3,19), the SPECT/CT was performed only in

the contest of equivocal scintigraphy. Not only it's a source of selection bias, but it can also result in missing some lesions that were hidden in clear scintigraphy with no uptake. In fact, some of our patients had a planar scintigraphy that wasn't equivocal for malignant lesions that were then seen on the SPECT/CT.

Another reason of the difference with others results is the consideration of the prone lateral views in our institution. The anterior and posterior projections of the whole-body scintigraphy don't always allow clearly identifying the thyroid bed residues or the localization of lymph nodes metastases. In our institution, we also performed the prone lateral views, with the conviction that they give additional information thanks to a projection of the uptakes in a sagittal plane view. In many patients, these lateral views allowed to make the difference between a more probable lymph node uptake and a physiological remnant. However, even if the lateral views helped to better identify the status and they were carefully analyzed, the uptakes were often equivocal and the anatomic field was not defined. In fact, it wasn't always clear to distinguish a physiological from pathologic uptake on scintigraphy A confirmation with the SPECT/CT was necessary to better characterize this lesion related to better anatomic precision and the higher resolution. Moreover, It can confirm the benign nature of lesions seen as pathologic to the whole body scintigraphy.

In our study, 12 lesions in 10 patients (7.1%) were described as suspicious on the whole body scintigraphy with the prone lateral views and could be considered as benign on SPECT/CT: 3 corresponded to local iodine uptakes, 6 to lymph nodes metastases and 3 to distant metastases. On the opposite 5 lesions in 5 patients (3.5%) corresponded to pathological uptakes that weren't seen on the scintigraphy: 4 to lymph nodes metastases and 1 to distant metastasis. The SPECT/CT changed the nodal status in 10 lymph nodes lesions (7.1%) and distant metastasis status in 4 lesions (2.8%) in our study. That can be explained for many reasons. SPECT/CT gave a more precise anatomic localization, which allowed a more correct image interpretation. In fact, it distinguished more efficiently the malignant lesions from sites of physiologic (salivary glands, esophagus, thyreoglossal duct) or remnant uptake, which can interfere with the proper reading of the scintigraphy images, not always conclusive. Despite the more accurate diagnosis and stage with the addition of SPECT/CT, the results in our study have a lower rate compared with other article. Schmidt et al. (10) studied the incremental value of SPECT/CT on the nodal stage: the N status was changed in 20 (35%) of 57 patients. Similar lymph nodes results (36.4%) are found by Kohlfuerst et al. (11), which also reported 36.4% of changes in the distant metastasis status. Grewal et al. (6) noted an alteration of lymph nodes status in 15% of the subjects.

In well-differentiated thyroid cancers, risk stratification is used to predict the probability for death from this disease, for local recurrence and for treatment failure (6,24). The ATA risk stratification in our study changed in 10 of 141 patients (7.1%). Grewal et al. (6) also looked for a difference of the risk of recurrence between scintigraphy and SPECT/CT. An altered risk of recurrence in 7 of 109 patients (6.4%) was reported. In contrast with our study, all patients had intermediate or high risks. If we consider only these types of patients, the ATA risk changes in 7 patients (5%) in our cohort. Since our protocols are similar, the slight difference can be attributed to the prone lateral views added to the whole-body scintigraphy, which weren't performed in their institution. It's important to note that the presence of abnormal ^{131}I uptake on the first post ablation scan is just one parameter to calculate the risk: for example one patient had a suspicious lymph node metastasis on the scintigraphy that wasn't seen on the SPECT/CT (intermediate to low risk patient), but because of the invasion into the

perithyroidal soft tissues at initial surgery, the patient continues to have an intermediate risk of recurrence. That leads to a lower percentage, even if there was a radiological change that affected the risk. Schmidt et al. also showed an alteration of the risk, and so the follow-up, in 25% of the patients (10), which is more elevated than our rate, probably for the same reasons.

Sometimes an iodine uptake was classified differently between scintigraphy and SPECT/CT without a change in the ATA risk: it happened for example if distant metastases were already present in both technics, and a lymph node metastasis was reclassified as an uptake to thyroid bed. In this case the patient still has a high risk, but SPECT/CT helped to precise the diagnostic. In many cases, SPECT/CT was useful to find others lesions without changing the stage: for example if another lymph node in a different localization was found in addition to the one already seen on the scintigraphy. The risk remained intermediate, even if SPECT/CT could help to choose a different treatment approach. Others pathological lesions, not related to the thyroid cancer, were occasionally found (liver hemangioma, sinusitis, etc.)

Because of the impossibility for the nuclear medicine physician to consider equivocal an uptake on the whole body scintigraphy with the lateral views; they classified some lesions based of probability according to other information given (histology, thyroglobulin level, etc.). Thyroglobulin level may help to exclude tumor if a suspect uptake was correlated to a low level. The SPECT/CT increased such cases the diagnostic certitude and it was determinant in patients with unclear scintigraphy.

This study had some limitations. First of all it did not allow to consider as equivocal a lesion during the scan review. It results in an absence of rate of the lesion, in which SPECT/CT helped to describe better the nature of the iodine uptake. During the scan interpretation, it often occurred that some lesions were equivocal by the two nuclear medicine physicians, but they had to give an answer, so they gave the most probable. In those cases, the SPECT/CT was useful to categorize the iodine uptake.

To see a better help from the prone lateral views, it should have been better to analyze the anterior and posterior projections separately from the prone lateral views, to see how often the situations on the lateral views allowed to clarify some status. Moreover, some of the patients had only one lateral view. We decided to include these patients because they gave us another point of view compared to whole body scintigraphy. However, having two prone lateral views give a better condition to describe and make the difference between local uptake and lymph nodes metastases.

Most of the high-risk patients are not included, because the whole body scintigraphy was already clear and so a SPECT/CT was directly done without the lateral prone views. That could result in a selection bias.

It’s important to precise also that there is a learning curve of the scans reader: the physicians could improve the analysis during the study.

During the time of the study, another SPECT/CT machine (Discovery NM 670) arrived and so some of the last subjects had this new machine and others had the old one.

CONCLUSION:

This study confirmed the utility of SPECT/CT: in relation to the anatomical landmarks and the high resolution, it improves the findings of ^{131}I scintigraphy. It allows to confirm the diagnostic, reclassify the disease in some cases and provide a more correct prognosis. The additional prone lateral views permitted to clarify the situation by making a first differentiation between thyroid bed remnant and lymph nodes metastases, resulting in a reduced rate of changed finding between the whole-body scintigraphy and the SPECT/CT compared with previews studies.

SPECT/CT allowed detecting 5 focal lesions in 5 patients missed on planar scintigraphy, and to precise benignity of 12 suspicious lesions in 10 patients on planar scintigraphy. Moreover, SPECT/CT improved the risk stratification in 7% of the patients with a significant change in the patient management, leading to an appropriated therapeutic strategy (alteration of the dose administration or further surgical neck dissection) and avoiding unnecessary treatment.

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