THE INCREMENTAL CLINICAL VALUE OF SPECT-CT IN NECK REGION IN THE TREATMENT OF DIFFERENTIATED THYROID CANCER WITH LOW DOSE RADIOIODINE-131 FOR THE FIRST THERAPY

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THE INCREMENTAL CLINICAL VALUE OF SPECT-CT IN NECK REGION IN THE TREATMENT OF DIFFERENTIATED THYROID CANCER WITH LOW DOSE RADIOIODINE-131 FOR THE FIRST THERAPY

By

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CERTIFICATE

This to certify that the dissertation entitled

THE INCREMENTAL CLINICAL VALUE OF SPECT-CT IN NECK REGION IN THE TREATMENT OF DIFFERENTIATED THYROID CANCER WITH LOW DOSE RADIOIODINE-131 FOR THE FIRST THERAPY

is the bona fide record of research work done by

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DECLARATION

I hereby declare that this dissertation is the result of my own investigations, except where otherwise stated and duly acknowledged. I also declare that it has not been previously or concurrently submitted as a whole for any other degrees at Universiti Sains Malaysia or other institutions. I grant Universiti Sains Malaysia the right to use the dissertation for teaching, research and promotional purposes.

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Date: 9th August 2020

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List of abbreviations

DTC	differentiated thyroid carcinoma
FTC	follicular thyroid carcinoma
HTC	hurtle thyroid carcinoma
HUSM	Hospital Universiti Sains Malaysia
PTC	papillary thyroid carcinoma
RxWBS	post therapy scintigraphy whole body scan
SPECT-CT	Single-photon emission computed tomography-computed tomography
TNM	Tumour Node Metastasis
WBS	whole-body scan
CT	computed tomography
MRI	magnetic resonance imaging

List of symbols

I^{131}	Iodine 131

ABSTRAK

Latarbelakang Iodin-131 (I-131) imbasan planar seluruh badan (WBS) dianggap sebagai amalan rutin untuk tahap awal, pemulihan dan jangka masa panjang setelah terapi ablasi radioiodin untuk pengurusan pesakit dengan DTC. Walau bagaimanapun, gambar WBS planar mempunyai kekurangan dari segi penandaan anatomi yang akan menjadikan penafsiran gambar lebih sukar. SPECT-CT membolehkan gambar lesion oleh pengimejan planar dikaitkan dengan stuktur anatomi. Penambahan info anatomi meningkatkan sensitiviti dan spesifikasi keputusan sintigrafi. Spesifik dan lokasi tepat dan properti pengambilan radioiodine dalam situasi patologi dan fisiologi menunjukkan kekangan atau masalah daripada pengimejan planar diatasi selepas menggunakan SPECT-CT. Tujuan pengkajian ini dilakukan bagi mengetahui nilai peningkatan SPECT-CT dalam pengurusan pesakit DTC yang menerima I-131 dos rendah berbanding pengimejan planar WBS di Hospital USM. **Kaedah**, pesakit yang menjalani thyrodectomi keseluruhan atau hampir keseluruhan dan dikenalpasti sejarah penyakit DTC dan mempunyai perancangan untuk menjalani ablasi radioiodine I-131 untuk kali pertama akan dipilih untuk kajian ini. Kriteria yang perlu adalah daripada sintigrafi WBS mestilah menunjukkan pengumpulan radioiodin di kawasan leher dan tidak mempunyai fosi yang tidak normal di kawasan lain. Pesakit yang dipilih akan menjalani prosedur SPECT-CT. gambar dari planar WBS dan SPECT-CT kawasan leher akan dinilai oleh doktor dan jumlah foci, jenis kanser tiroid dan tahap TNM akan direkodkan. **Keputusan**, pesakit yang terpilih untuk kajian ini 80% papillary, 10% follicular dan 10% Hurtle tiroid kanser. Faedah diagnosis hasil daripada SPECT-CT pada Kawasan leher untuk melihat lesion adalah 76%. SPECT-CT menjadikan 3 daripada 10 pesakit yang hanya melibatkan pesakit berumur 45 dan keatas dikaji semula. Mereka ini dikelaskan sebagai kelas IV. Analisis untuk tahap TNM adalah 0.508 menggunakan kappa weighted coefficientuntuk dua kaedah yang menunjukkan WBS dan SPECT-CT mempunyai perkaitan sederhana. **Kesimpulan**, perbandingan antara I-131 planar WBS tanpa

SPECT-CT berdasarkan bilangan foci, SPECT-CT menunjukkan impak diagnosis yang ketara bagi terapi kali pertama untuk dos rendah. Imej yang dihasilkan melalui penambahan SPECT-CT meningkatkan kebolehan bagi doktor untuk menilai imej yang terhasil dengan penilaian yang lebih baik. Namun nilai p menunjukkan SPECT-CT tiada impak ketara dan weighted kappa coefficient menunjukkan perkaitan yang sederhana antara SPECT dan planar WBS dalam penentuan tahap kelas TNM dan risiko statifikasi pengulangan penyakit. Impak dalam diagnosis telah memberi kesan terhadap pengurusan klinikal pesakit DTC. Berdasarkan keputusan yang diperolehi adalah disarankan untuk menggunakan SPECT-CT bagi pengurusan pesakit DTC.

ABSTRACT

Backgrounds Iodine-131 (I-131) whole-body planar scan (WBS) is considered as a routine practice for initial staging, restaging and long term follow up following radioiodine ablation therapy for management of patients with DTC. However, the planar WBS images produce lack of anatomical landmark that will be challenging for image interpretation. SPECT-CT allows to correlate lesions pictured by functional planar imaging with anatomical structures. The adding of anatomical info increases both the sensitivity and the specificity of the scintigraphy results. The specific and precise location and properties of radioiodine uptake in pathological or physiological situations demonstrated that the restriction or pitfall of planar imaging has been removed using SPECT-CT. The purpose of this study is to evaluate the incremental value of SPECT-CT in the management of DTC patients who received low dose I-131 in Hospital USM over planar WBS imaging. **Methods** Patients who undergo total/near-total thyroidectomy with histopathology confirmed DTC and planned for low dose radioiodine ablation I-131 for first time were recruited into this study. The inclusion criteria were the post-therapy scintigraphy WBS demonstrated sensitive radioiodine uptake in the neck and no other distant irregular foci elsewhere. The selected patient undergone SPECT-CT procedure during same setting. The image for planar WBS imaging and SPECT-CT of the neck was compared by the doctor and the number of foci, type of thyroid carcinoma, TNM staging were recorded. **Results** Patients recruited in the study are 80% papillary, 10% follicular and 10% Hurtle thyroid carcinoma. The average diagnostic benefit of SPECT-CT in the neck for the lesion is 76%. As a result, SPECT-CT resulted in the revision of 3 out of 10 patients (30 %), which only contributed by the 45 years or older (n=5), each of which was stage IV. This results in 3 out of 10 patients (30 %). A relationship analysis for TNM staging resulted in a 0.508 kappa weighted coefficient for the two methods which indicates that the WBS and SPECT-CT planar have a moderate agreement. **Conclusion** In comparison to I-131 planar WBS without the SPECT-CT base on

the basis of the foci number, SPECT-CT of the neck showed a major diagnostic effect for low-dose radioiodine-131 for the first therapy. The image produces by adding SPECT-CT increased the ability for the doctor to interpret the resulting image for better interpretation. Although the p-value suggesting SPECT-CT has no significant impact and the weighted kappa coefficient signifying a moderate agreement between the planar WBS and SPECT-CT in clinical staging based on the TNM classification and risk stratification for disease recurrence. The significant diagnostic effect has directed to substantial impact on the clinical management of DTC patients. Consequently, according to the result, it is suggested that SPECT-CT should be optional when possible.

CHAPTER 1: INTRODUCTION

1.0 Background of study

The most common endocrine malignancy is thyroid cancer and accounting for 2% of all cancers (Goodarzi, 2019). Papillary thyroid carcinoma (PTC) and follicular thyroid carcinoma (FTC) are referred to as well-differentiated thyroid cancers (DTC) (Hakala, 2016). Patients with DTC will undergo ablation that will utilize I-131. Different stage of DTC will receive different activity of I-131. The I-131 has traditionally been carried out in the form of a complete whole-body scan (WBS). This procedure is used in the identification of the remnant thyroid tissue for initial stages following total/near-total thyroidectomy, restaging and long-term follow-up after radioiodine ablation therapy. Though, the image produce lack in anatomical landmark which will be challenging for the image interpretation. Since a decade ago, integrated SPECT-CT scanners were introduced and used to assist in diagnosis. With SPECT-CT, anatomical structures may be aligned with the lesions visualized by functional planar imaging. Adding anatomical details increases the sensitivity and characteristics of scintigraphy results. I-131 SPECT-CT has been confirmed to resolve the restriction or pitfall of planar imaging by correct and precise localisation and characteristic of pathological and physiological sites of radioiodide uptake (Back, 2019). This study is carried out for the intention to find out the necessity of SPECT-CT in neck region in the treatment of differentiated thyroid cancer with low dose radioiodine-131 for the first therapy with no other distant metastasis.

1.1 Objective of the study

1.1.1 Main objective

To evaluate the incremental value of SPECT-CT over planar WBS imaging in the management of DTC patients receiving low dose I-131.

1.1.2 Specific objective

1) To determine the number of lesions in planar imaging in the first low dose I-131 ablation of DTC patients.
2) To identify the changes in the TNM staging between planar WBS and SPECT-CT imaging.
3) To determine number of lesions in SPECT-CT imaging in the first low dose I-131 ablation of DTC patients.
4) To determine the agreement between planar and SPECT-CT imaging in the first low dose I-131 ablation of DTC patients.

1.2 Problem statement

The I-131 has largely been carried out in the form of planar WBS and is still considered as a routine in management of DT patients in Malaysian. This procedure is used in the identification of the remnant thyroid tissue for initial stages following total/near-total thyroidectomy, restaging and long-term follow-up after radioiodine ablation therapy. Nevertheless, the image produce lack in anatomical landmark which will be challenging for the image interpretation.

Since a decade ago, integrated SPECT-CT scanners were introduced and used to assist in diagnosis. It allows functional planar imaging to represent lesions that can be associated with anatomical structures in SPECT-CT. Adding anatomical details increases the sensitivity and characteristics of scintigraphy tests. The planar imaging and SPECT-CT are the two different type of imaging approach that can be used to diagnose the patient with DTC. There are some differences in the result from both imaging approach. A deficiency of anatomical specificity in the imaging of planar gamma cameras and the superposition of radioiodine absorption areas which can challenge a precise diagnosis and location of metastatic radioiodine avid. So with the intent to investigate is there a necessity to add SPECT-CT imaging for the treatment of DTC with low dose radioiodine I-131 for the first therapy at neck area. It is by evaluating the incremental clinical value of SPECT-CT in neck region in the treatment of DTC with low dose radioiodine-131 for the first therapy.

1.3 Significant of study

Lesions showed by functional imaging can be associated with anatomic structures by adding SPECT-CT images and the addition of anatomic information surges the sensitivity as well as the specificity of the scintigraphy results (Ritt, 2014). I-131 SPECT-CT has been confirmed to resolve the restriction or pitfall of planar imaging by correct and precise localisation and characteristic of pathological and physiological sites of radioiodide uptake (Back, 2019). The resulting image of the patients can be interpreted more accurately and precisely compare to planar imaging alone. Furthermore, patient management, treatment planning and follow up will significantly improve.

Other than that, by using SPECT-CT for treatment imaging, it definitely can avoid unnecessary or any additional imaging using others modalities such as CT or MRI scanner, which those modalities have their own disadvantages such as for CT scan can increase dose receive by the patient because CT scan is still a leading cause of radiation exposure for the patient (Mattsson, 2011). Or MRI that will take a longer time for imaging (Donohue, 2017).

Chapter 2: Literature review

2.1 Planar imaging

Planar imaging use principles of Gamma Camera to operate. The basic principles of how a Gamma Camera operate are, In the scintillation crystal, a collimator shall produce an imaging of the distribution of the ingest gamma-ray-emitting radiopharmaceutical. The invisible gamma rays are converted by the scintillation crystal into light. The light is converted by a series of photomultiplier (PMT) tubes the view the back side of the crystal into electronic signals. Upon processing, the PMT outputs are converted into three signals, (X and Y) which give the spatial location of the scintillation, (Z) is the energy of the gamma ray deposited in the crystal. Such signals pass through correction circuits in order to enhance their efficiency. The Z signal is used to measure the energy of the gamma ray within the predicted range of values for the particular radionuclide being imaged. The Pulse Height Analyzing (PHA) measures If an appropriate value is given for the Z signal, a signal is sent to indicate that the display has detected a gamma ray and that the location is determined by the X and Y signals. (Shackett, 2009) (Johansson, 2015)

2.2 SPECT-CT

The SPECT is a tomographic scintigraphic tool by detecting single-photon emissions of radionuclides from local tissue radioactive tracers. In this technique a computer-generated image is generated. Single photon emission computed tomography (SPECT) is a technique of tomographic imaging in nuclear medicine that involves placing the camera head at various angles across the body, for example 180° or 360° of data at different angular intervals, typically 2–6 degrees depending on the structure. Iterative methods were used to reconstruct SPECT which including photon attenuation correction based on the x-ray transmission map and scatter correction. While CT is a technique of tomographic imaging using an external radiation source

that is x-ray source, transmit through the patient body and detected by the CT detector to produce anatomic image data. The image data can be reconstructed to 2-D or 3-D image.

Both SPECT and CT image are attained with exact and matching subject position to make sure accurate image registration. SPECT-CT combination is the combined SPECT and CT sets view. The SPECT information colour coded to CT data in the gray scaling which usually display superimposed data. (Agency, 2008) (Ljungberg, 2018)

2.3 I ^{131}

Radiodine I-131 is known as radioactive iodine or radioiodide, also known as sodium iodide NaI. The I-131 is an artificial iodine isotope, coming from Uranium fission products or Tellurium-130 neutron irradiation in a nuclear reactor in form of sodium iodide (NaI). I-131 has an exceptionally low half-life which about 8 days, emitting beta and gamma radiation. Radioioiodine is readily absorbed from the gastrointestinal tract and dispersed in the extracellular fluid as it is orally administered as an iodide ion. This is contained in salivary, thyroid and gastric mucous membranes. RAI not concentrated in the thyroid and other organs is excluded from the body urine and sweat. (michigan, 2018) and (Aljubeh, 2012)

2.1 restaging cases

Restaging cases, there are high percentage of restaging cases after patient undergo SPECT-CT scanning. There were 36.4% of restaging cases as reported by S. Kohlfuerst (Kohlfuerst, 2009). It also supported by Daniela Schmidt who reported there is about 25% cases that were restage after SPECT-CT imaging (Schmidt, 2009). SPECT-CT helps to conclude staging in thyroid cancer patients through improved N and M characterisation. (Avram, 2014). It is also supported by Xue *et al.* that does systematic review, conclude that "current information shows that I-131 SPECT-CT is a precious device not just for diagnostic

resolutions but also for the staging and monitoring of DTC patients post-thyroidectomy".(Xue *et al.*, 2013)

2.2 anatomical landmark and diagnostic value

The interpretation of I-131 images may be difficult when using planar WBS because of the nonappearance of anatomic landmarks. Consequently, it is still not possible to identify hot spots precisely. In addition, physiologic uptake of I-131 may cause false-positive findings. Integrated SPECT-CT potentially enables the physiological, artificial and pathological uptake of I-131 to be differentiated. Xue *et al.* found that "In 44 % cases, SPECT-CT enhanced localization, making I-131 SPECT-CT a valuable way for an accurate evaluation of area or distant foci" (Xue *et al.*, 2013). "Avram *et al* state that SPECT-CT is a versatile device that can be used to diagnose the precise anatomical location and characterisation of radioiodine foci and the description of classical radioiodine scintigraphy have been greatly improved". (Avram, 2014). "SPECT-CT is a powerful diagnostic tool that allows an exact anatomical positioning and characterization of radioiodine foci. The diagnosis, proper staging, restaging and treatment planning technique will benefit patients and physicians alike".(Zilioli, 2016). For equivocal cases, there is high number of equivocal lesions for patient who undergo planar imaging. After undergo SPECT-CT imaging it allow precise characterization of equivocal lesions of about 82% patient (Back, 2019). "In 47.6–88 percent of the cases, integrated I-131 SPECT-CT imaging had an incremental diagnostic benefit relative to I-131 WBS" (Xue *et al.*, 2013). "The sensitivity, specificity, and diagnostic accuracy of each imaging modality were 65, 55, and 59%, respectively, for 131I WBS; 65, 95, and 85% for 131I SPECT/CT, respectively" (Oh *et al.,* 2011). This is showing that I-131 have same sensitivity with SPECT-CT. SPECT-CT have higher specificity which is 95% compare to I-131 WBS that only 55%. SPECT-CT also showing greater diagnostic accuracy compare to WBS.

2.3 Patient management

SPECT-CT have the ability provide incremental data, thus providing significant impact on patient management (Fig, 2013). This also supported by (Avram, 2014), which stating that SPECT-CT has been reported to improve clinical management both in daily use in all consecutive patients as well as in selected patients with unresolved planar images. “Therapeutic strategy modification in 23.5%–25% of patients in DTC” (Xue *et al.*, 2013).

Chapter 3: Material and Method

3.1: Material

3.1.1 SPECT-CT machine (Discovery NM/CT 670 Pro) in Figure 1, were used for the imaging purpose both for planar imaging and SPECT-CT imaging.

Figure 1: SPECT-CT machine (Discovery NM/CT 670 Pro)

3.1.2 Iodine-131 in Figure 2 that were taken by patient on the first day of the ablation therapy

Figure 2: Iodine-131

3.1.3 Control panel and monitor for controlling and viewing in Figure 3

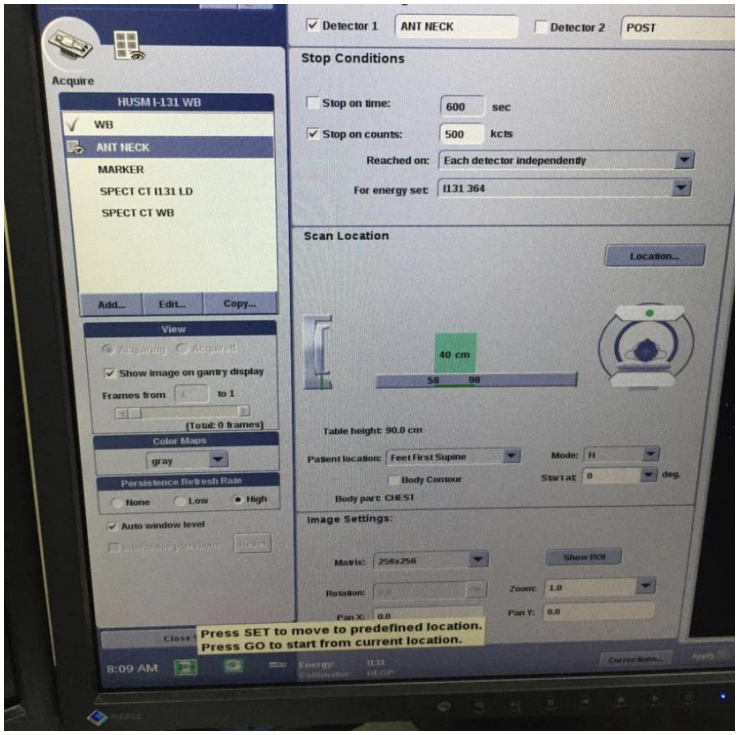

Figure 3: monitor

3.2 Methods

3.2.1 Ethical Board

This study was approved by the Jawatankuasa Etika Penyelidikan (Manusia), JEPeM Universiti Sains Malaysia (USM). Approval letter on appendix D and E

3.2.2 Inclusion criteria

i) Histopathologically confirmed diagnosis of DTC

ii) Undergo first low dose ^{131}I radioiodine ablation therapy

iii) uptake in the neck with no other abnormal distant foci uptake elsewhere in post therapy planar scintigraphy.

3.2.3 Exclusion criteria

i) Patient who does not give consent to this study.

ii) Patient who received high dose I-131 radioiodine ablation therapy.

3.2.4 Patient recruitment

This study was conducted in the Department of Nuclear Medicine, Radiotherapy and Oncology, Hospital Universiti Sains Malaysia (Hospital USM). The study participants included patients who confirmed diagnosis of DTC and had undergone total/near-total thyroidectomy. The inclusion criteria for the study are newly diagnosed DTC patients who planned for low dose radioiodine ablation I-131 for first time. They were referred to Nuclear Medicine Department, Hospital Universiti Sains Malaysia (HUSM) for radioiodine ablation therapy.

The patient had been described regarding the study details earlier prior to the tentative date for low dose I-131 radioiodine ablation therapy and informed consent had been signed. Patients received radioiodine I-131 ablation therapy and underwent planar imaging WBS on day 3. The images were evaluated by the doctors to view the radioiodine sensitive foci. After the post

therapy WBS, patients that presented with radioiodine sensitive foci in the neck only with no other atypical distant foci elsewhere were selected in to the study.

3.2.5 SPECT-CT Procedure

The selected patients that showed radioiodine sensitive foci in the neck only with no other irregular distant foci were underwent SPECT-CT procedure immediately after the post therapy WBS.

3.2.6 Image comparison

The image for planar imaging and SPECT-CT were compared by the doctor and the patient's data, histology cancer type, stage and risk stratification and number of foci detected were recorded. Figure 4 showed the example of planar imaging WBS and Figure 5 showed example of SPECT-CT neck imaging.

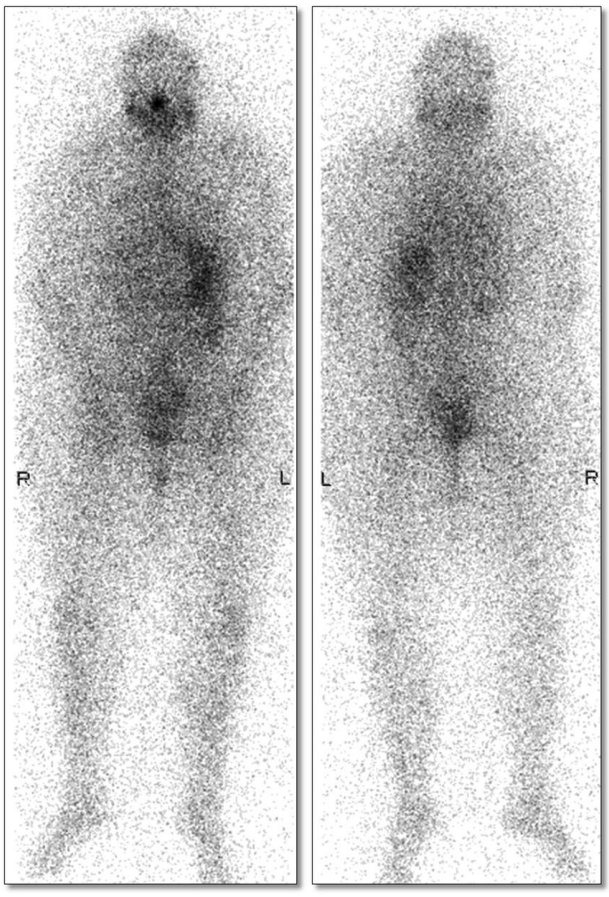

Figure 4: Planar imaging WBS.

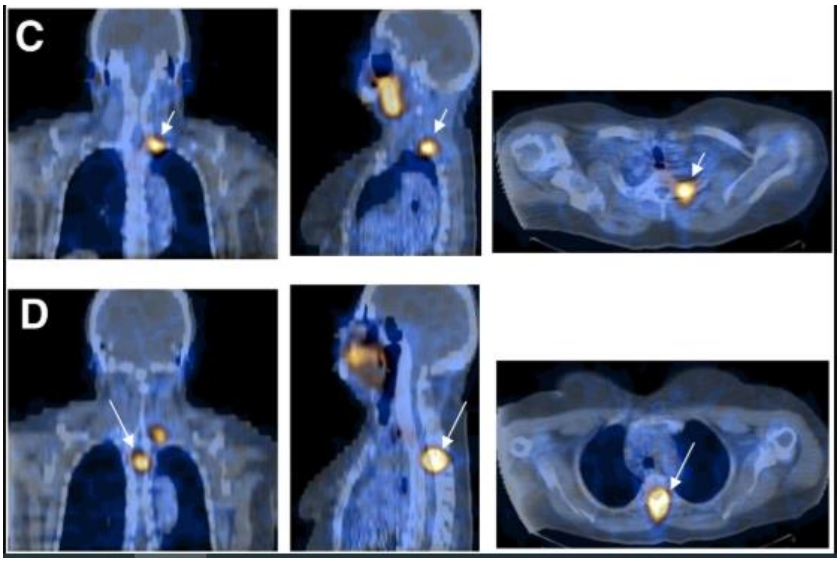

Figure 5: SPECT-CT image fusion (C and D) in coronal, sagittal and transverse slices

Chapter 4: Result

4.1. Data Collection tool and data management.

For the purpose of data collection, a data collection form Appendix A was developed. It consists of population data, clinical characteristics, I-131 planar imaging WBS results and SPECT-CT interpretations and analyses of the patient image. Data were stored in the MS excel spreadsheet and then transferred for data analysis to SPSS Statistics 26.

4.2 Statistical analysis

The McNemar or Stuart – Maxwell test generalized or paired T test was applied to determine whether necks area of planar imaging WBS and SPECT-CT were of the same distribution for assigning the scan results, TNM staging, risk stratification and management plan. In addition, the concordance / accuracy of the two methods with respect to TNM staging and risk stratification was determined with a weighted kappa statistic. Table 1 shows the guidelines for interpreting kappa statistics as proposed by Landis and Koch (Hartling, 2012).

Table 1: Interpretation of kappa statistic

Kappa	Agreement
<0	poor agreement
0.01–0.20	slight agreement
0.21–0.40	fair agreement
0.41–0.60	moderate agreement
0.61–0.80	substantial agreement
0.81–1.00	almost perfect agreement

A total of 10 patients that histologically confirmed with DTC were involved in this study. I-131 planar imaging WBS and static view of neck area were done and if the patient suited all the inclusion criteria that needed for study, they were selected into the study. Added SPECT-CT were immediately performed after planar imaging. For the study, 3 patients (30%) were male and 7 patients (70%) were female.

All the patients were Malays. The mean age of the patients was 49.1 years old. For the purpose of TNM staging for thyroid carcinoma, the patient was separated into two age group. Age group of below 45 years old (<45 years old) which comprised of 5 patients (50%) and age group of 45 years old and above ≥45 years old which comprised of 5 patients (50%) from the total number of patients involved in the study.

Patients involved in the study were 8 patients (80%) diagnosed with PTC and 1 patient (10%) was FTC and another 1 patient (10%) was Hurtle carcinoma thyroid carcinoma.

Table 2: Patients age

PATIENTS AGE					
AGE	N	Range	Minimum	Maximum	Mean
	10	44.00	33.00	77.00	49.10

Table 3: Patients gender

Distribution of Gender					
		Frequency	%	Valid %	Cumulative %
Valid	male	3	30.0	30.0	30.0
	female	7	70.0	70.0	100.0
	Total	10	100.0	100.0	

Table 4: Patients histology type

Histology_type				
	Frequency	%	Valid %	Cumulative %
Papillary thyroid carcinoma (PTC)	8	80.0	80.0	80.0
Follicular thyroid carcinoma (FTC)	1	10.0	10.0	90.0
Hurtle thyroid carcinoma	1	10.0	10.0	100.0
Total	10	100.0	100.0	

From 10 patients involved in this study, there were 25 foci detected on I-131 planar WBS and 44 were detected on SPECT-CT of the neck. The SPECT-CT of the neck were done for all of the patients which I-131 planar WBS showed significant uptake greater than the background count in the neck region. The scan results of I-131 planar WBS and SPECT-CT of the neck area are shown in Table 5

Table 5: Numbers of foci for planar WBS and SPECT-CT

	Numbers	Range	Minimum	Maximum	Sum	Mean	df	p-value
Number of foci for planar	10	4.0	0.0	4.0	25.0	2.5	9	0.012
Number of foci for SPECT-CT	10	6.0	2.0	8.0	44.0	4.4		

The clinical staging based upon the TNM classification has been updated in 3 (30%) out of 10 patients, with additional details collected through added SPECT-CT, provided solely in patients ≥ 45 years of age. Table 6 shows the modifications to the TNM stages from the I-131 planar WBS and SPECT-CT of the neck.

Table 6: Stage altered for the patient after SPECT-CT

Stage altered					
		Frequency	%	Valid %	Cumulative %
Valid	up staging	3	30.0	30.0	30.0
	same staging	7	70.0	70.0	100.0
	Total	10	100.0	100.0	

Table 7: Staging for planar WBS and SPECT-CT

			Staging for SPECT-CT			Total
			Stage I	Stage II	Stage IV	
Staging for planar	Stage I	Count	6	0	0	6
		% within staging_spect	100.0%	0.0%	0.0%	60.0%
	Stage II	count	0	1	2	3
		% within staging_spect	0.0%	100.0%	66.7%	30.0%
	Stage III	count	0	0	1	1
		% within staging_spect	0.0%	0.0%	33.3%	10.0%
Total		count	6	1	3	10
		% within staging_spect	100.0%	100.0%	100.0%	100%
p-value	0.096					
weighted kappa coefficient	0.508					

Subsequently the p=0.096, it is concluded that the I-131 planar WBS stage does not vary significantly from the added SPECT-CT neck. Agreement analyses for TNM stages have resulted in a weighted coefficient of kappa of 0.508 for both approaches and imply a moderate agreement between SPECT-CT and the planar WBS.The changes in the TNM staging from I-131 planar WBS and SPECT-CT of the neck by patient according to the age group on Table 8.

Table 8: stage altered for age group after SPECT-CT

Stage altered for age group					
			stage_altered		Total
			up staging	same staging	
AGE_GROUP	BELOW 45	Count	0	5	5
		% of Total	0.0%	50.0%	50.0%
	45 & ABOVE	Count	3	2	5
		% of Total	30.0%	20.0%	50.0%
Total		Count	3	7	10
		% of Total	30.0%	70.0%	100.0%

Chapter 5: Discussion

DTC is a slow-growing malignancy that ranks 9th and 7th for males and children respectively, among all malignancies in Malaysia. In general, given the limited sample size (N=10), our patients' demography outcome is comparable with the demography trends for thyroid cancer as documented in the *National Cancer Registry Report* for year 2012-2016 mostly for the gender-based incidence rate (Azizah and Hashimah, 2019). In our study, majority of the recruited participants are female with ratio of 7:3 compared with male. And most patients recruited in this study were PTC 80%, followed by FTC 10% and hurtle thyroid carcinoma of 10%. Ethnicity related cases were all Malay, which are substantially different from the national registry data on cancer (Azizah and Hashimah, 2019) that shown Chinese has the highest number of patients.

In recent years, some studies have been carried out to examine the practicality of SPECT-CT in the assessment of patients with DTC since the emergence of SPECT-CT hybrid imaging. However, there is still argument about the clinical significance of SPECT-CT in the management of DTC patients.

The improvement in diagnostic value for SPECT-CT, according to previous reports, ranged considerably between 16.3 % (Mareen Menges and Uder, 2012) and 73.9 % (Libo Chen and Luo, 2008). These statistics typically reflect the number of patients with a shift in the scan findings from I-131 planar WBS to SPECT-CT. This diverse pattern of findings may be attributed to different scores such as difference of patient numbers, various standard I-131 doses for example, for therapeutical purpose or diagnostic purpose, the different areas of interests investigated for example, neck-to-neck or thorax-to-body and the form of examination of the sample for example, lesion-based or patient-orientated.

For the lesion-based analysis, the incremental value for SPECT-CT in this study is 76%. The planar WBS imaging is an image taken in the previous and subsequent estimates and the exact position of the focus in certain patients can be difficult to recognize. Several false-positive absorption sources have been reported, including physiological accumulation on I-131 planar WBS, that could lead to misdiagnosis. On I-131 planar WBS images, it is difficult to differentiate between pathological uptakes and physiologic accumulation, even if carefully viewed. For SPECT-CT image it easier for the doctor to differentiates between pathological uptakes and physiologic accumulation. SPECT-CT images are particularly useful in these situations.

The clinical stage of most malignancies is based generally on the primary tumor parameters and regional metastatic disease (TNM) involvement, used to assess the prognosis and estimate the death risk. Age is another important in DTC risk stratification, special among malignancies. The same degree of disease involvement and a markedly different prognosis are likely for patients 45 years of age and older. As a result, SPECT-CT triggers only a revision of the stage in 3 out of 10 patients (30 %) even with 45 years or older (n = 5), all 3 of them in stage IV.

On the other hand, all patients under the age of 45 (n=5) had persistently been classified as stage I according to TNM studies even though the SPECT-CT lymph node findings in the neck are changed. This is because in our study protocol, the possible remote metastasis in patient selection is excluded, so for the age group less than 45 years, TNM stages remain unchanged irrespective of regional lymph node involvement or local disease.

Chapter 6: Conclusion

As conclusion, SPECT-CT of the neck for the low dose radioiodine-131 for the first therapy has shown a significant diagnostic impact as compared to I-131 planar WBS without the SPECT-CT base on the result of the number of foci found after the interpretation of the patient's images. The images produced by adding SPECT-CT have shown a good quality image which great in helping to increase the ability for the doctor to interpret the resulting image for better interpretation and reducing error or false interpretation.

Although the p-value that indicates SPECT-CT has no significant effect and the weighted kappa coefficient indicates a poor agreement in clinical staging between the planar WBS and SPECT-CT according to TNM classification and disease risk stratification, the major diagnostic effect has had a major impact on the clinical management of DTC patients. Hence, based on the result, it is recommended that SPECT-CT should be recommended whenever available.

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Appendices

Appendix A

Data collection sheet

Appendix A: DATA COLLECTION SHEET.

INDEX

DATA COLLECTION SHEET

THE INCREMENTAL CLINICAL VALUE OF SPECT-CT IN NECK REGION IN THE TREATMENT OF DIFFERENTIATED THYROID CANCER WITH LOW DOSE RADIOIODINE-131 FOR THE FIRST THERAPY

Age						
Sex						
Race						
Dose						
Histology type	○ Papillary Thyroid Carcinoma ○ Follicular Thyroid Carcinoma ○ Hurtle Thyroid Carcinoma					
Risk stratification	○ Low risk ○ Intermediate risk ○ High risk					
Serum thyroglobulin level						
Stage	Patient age < 45 years ◯ Stage I ◯ Stage II		Patient age > 45 years ◯ Stage I ◯ Stage II ◯ Stage III			
Procedure	Thyroid remnant	Lymph Nodes	Equivocal	TNM Staging		
				Same	up	down
Planar Imaging						
SPECT-CT						