AMJ Australasian Medical Journal [AMJ 2017;10(9):759-764]

Protocol for differentiated thyroid cancer management at Dr George Mukhari Academic Hospital

Nyebe Phineas Mahlangu[1,2], Mpumelelo Nyathi[2]

1. Dr George Mukhari Academic Hospital, South Africa
2. Sefako Makgatho Health Sciences University, South Africa

RESEARCH

Please cite this paper as: Mahlangu NP, Nyathi M. Protocol for differentiated thyroid cancer management at Dr George Mukhari Academic Hospital. AMJ 2017;10(9):759–764. https://doi.org/10.21767/AMJ.2017.3076

Corresponding Author:
Mpumelelo Nyathi
Department of Medical Physics, Sefako Makgatho Health Sciences University, South Africa.
Email: mpumelelo.nyathi@smu.ac.za

ABSTRACT

Background

Effective screening procedures and advances in medical imaging technologies have seen increased detection of the differentiated thyroid cancers (DTC). However, management of DTC patients still remains controversial owing to differences in opinion on the extent of surgery (thyroid lobectomy or total thyroidectomy) and the need of radioiodine ablation (RIA) post-surgery.

Aim

This study was aimed to establish a local protocol for DTC management at Dr George Mukhari Academic Hospital (DGMAH). The protocol emphasizes on multidisciplinary management whereby, the nuclear medicine physicians, endocrinologists and surgeons decide on the extent of thyroid resection. The protocol emphasizes on total thyroidectomy for all DTC patients since it reduces morbidity and also optimizes the management of patients for further radioiodine treatment.

Methods

A search of scholar articles for various protocols on management of DTC was conducted using Google search engine, Science Direct and Medline. Abstracts and full texts were reviewed.

Results

The proposed local protocol for DGMAH emphasizes on a multidisciplinary management approach for DTC patients. Furthermore, only patients who have undergone total thyroidectomy should be managed with radioiodine.

Conclusion

Total thyroidectomy reduces morbidity and also optimizes the management of patient for further radioiodine treatment.

Key Words

Differentiated thyroid cancers, total thyroidectomy, thyroid lobectomy

What this study adds:

1. What is known about this subject?

The first line of treatment of DTC patients is surgery. However, controversy rages on the extent of thyroid resection.

2. What new information is offered in this study?

A multidisciplinary management team comprising of endocrinologists, the nuclear medicine physicians and surgeons should decide on the extent of thyroid resection. A correctly selected procedure (total thyroidectomy) reduces morbidity, optimizes the patient for further radioiodine treatment.

3. What are the implications for research, policy, or practice?

Only DTC patients who have undergone total thyroidectomy should be referred for radioiodine ablation. Total thyroidectomy reduces patient morbidity and optimizes patients for radioiodine treatment.

Background

The majority of thyroid cancers are the well differentiated thyroid carcinomas (DTC).[1,2] The DTC account for between 90–95 per cent of all thyroid cancers.[3] They have a high prevalence due to good diagnosis. The survival rates are 90 per cent owing to effective management with radioiodine post-surgery.[1-4] The DTC malignancies can be classified into the following subtypes: papillary thyroid carcinoma (85 per cent prevalence), follicular carcinoma (10 per cent prevalence),[1,2] Hürthle cell carcinoma (HCC), (3 per cent).[5,6] The poorly differentiated insular carcinoma, a rare subtype has also been reported.[7]

The papillary thyroid carcinomas are the most common type of thyroid cancer. They occur in predominantly iodine rich regions whereas the follicular carcinomas are commonly found in low iodine endemic goiter areas.[8] The Hürthle cells can either be of benign or malignant nature. Petric et al.,[6] classified HCC as a rare disease which is more aggressive when compared to thyroid follicular carcinoma. Previously, the World Health Organization (WHO) described HCC as a variant of the follicular carcinoma.[9] However, it was later proved by Ganly et al.,[10] that HCC are different from the follicular carcinomas.

Takami et al.,[11] reported that the western countries (European and United States) consider HCC as having the worst prognosis compared to conventional follicular carcinoma, a view contrary to findings by two studies conducted in Japan. Furthermore, unlike the western countries, in Japan use of radioiodine is not encouraged except for selected cases. This study was aimed to establish a local protocol for DTC management at Dr George Mukhari Academic Hospital (DGMAH), a protocol meant to optimize management of DTC patients.

Differentiated thyroid cancer treatment

Management of DTC requires a multidisciplinary approach,[3] hence the need for a close cooperation between surgeons, endocrinologists and nuclear medicine physicians.[8] Surgery represents the first line of treatment followed by radioiodine therapy.[1-4,8] However, the extent of thyroid surgery remains controversial with one school advocating total thyroidectomy whilst the other advocates for lobectomy.[8,12-14] With the exception of Japanese strategies on DTC management,[11] most countries opt for radioiodine ablation (RIA) post-surgery.[1-3,8,9,12] However, the American Thyroid Association guidelines do not recommend it for low risks patients.[15]

Basically, RIA is intended for the total destruction of the remaining thyroid tissue after total thyroidectomy,[2,16] and the remaining occult carcinoma in the thyroid bed thus reducing chances of recurrence.[2,4] In addition to improving the local control rate, RIA has also been found to increase the chances of disease free-rate particularly among high risks patients who have undergone total thyroidectomy.[11] Destruction of any remnant thyroid tissue improves the sensitivity of subsequent Iodine-131 whole body scanning and the specificity of serum thyroglobulin (Tg) values, which is required for the detection of any persistent or recurring disease.[2]

The success of RIA is attributed to the ability of the thyroid tissue to take up iodine from the blood. Thyroid follicular cells concentrate radioiodine because they express a sodium-iodide transporter on their surface. Radioiodine I-131 emits beta particles with the range between 1 and 2cm causing acute or delayed death of thyroid cells.[15]

The management of DTC patients with RIA is done at the Nuclear Medicine Department at Dr George Mukhari Academic Hospital by a team of nuclear medicine physicians and medical physicists. In order to guarantee effective management of DTC patients at our centre, a comprehensive DTC management protocol is hereby proposed. The protocol emphasizes on a multi-disciplinary approach in DTC management.

A multidisciplinary management team should consist of the nuclear medicine physicians, endocrinologists and surgeons who should all be given the opportunity to decide on the extent of thyroid resection. A correctly selected procedure (total thyroidectomy) reduces morbidity and also optimizes DTC patients for further radioiodine treatment.

Method

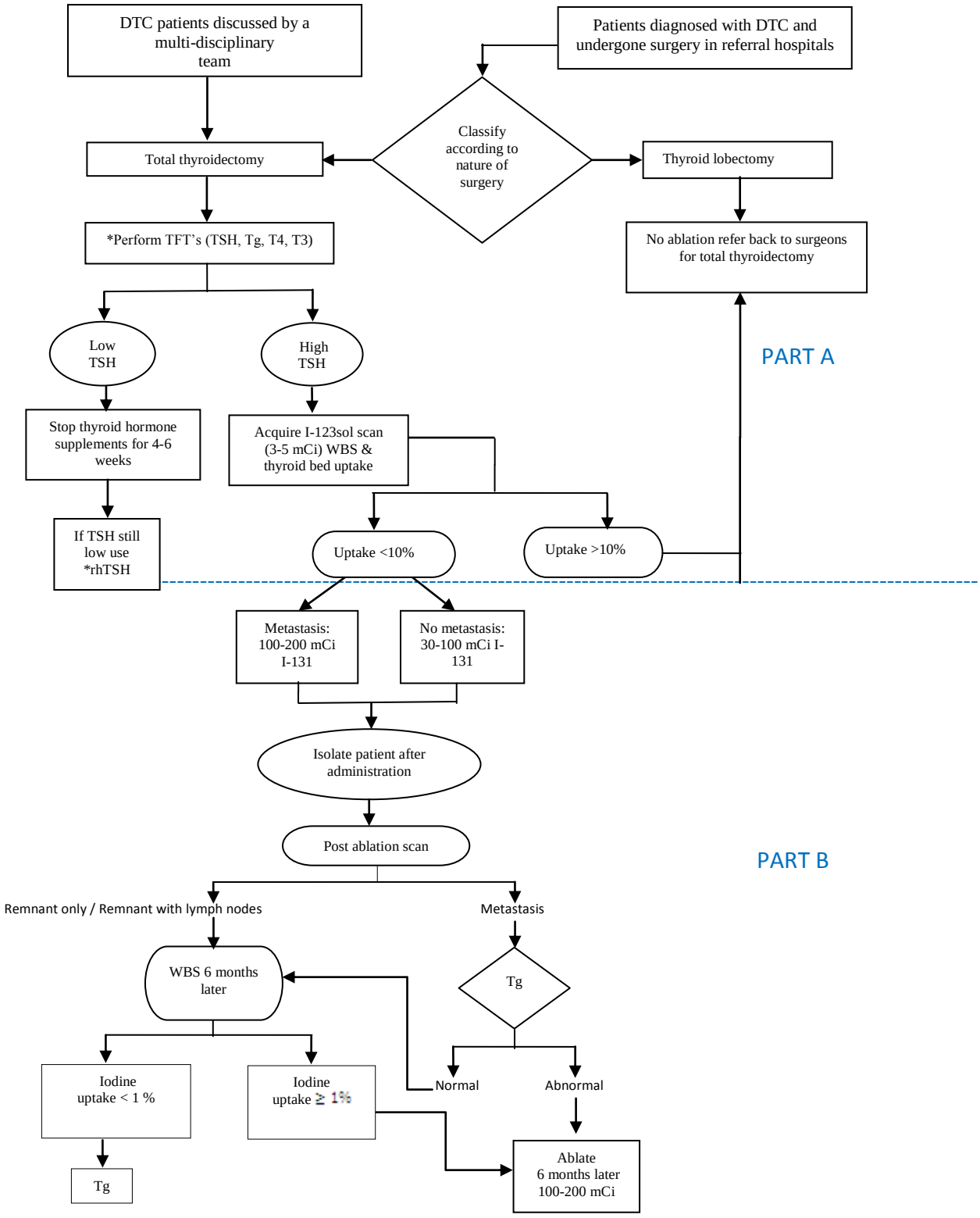
A search of scholar articles on various protocols on management of DTC was conducted using Google search engine, Science Direct and Medline. Furthermore, a discharge rates between total thyroidectomy and thyroid lobectomy patients were compared retrospectively from 2007–2017 culminating with proposal of a local protocol for management of DTC patients.

Discussion

Local DTC protocols have previously been developed.[16,17] The objective of such development is to optimize management of DTC patients. At DGMAH's Department of Nuclear Medicine we also proposed a local protocol which is yet to be implemented for the management of DTC

patients. The proposed protocol emphasizes on a multidisciplinary approach in DTC management form the initial stage of detection. The protocol emphasizes on management of only total thyroidectomy patients. If thyroid lobectomy patients are referred from district hospital to the Department of Nuclear Medicine for management, the newly established protocol proposes that they be sent back for the completion of thyroid resection.

Figure 1: Flow chart showing step by step proposed procedures for managing DTC patients



*TFT';- Thyroid functioning tests; TSH- thyroid stimulating hormones, Tg- serum thyroglobulin, T4 - thyroxine, T3- tri-idothyronine, WBS whole body scans, rhTSH- recombinant human THS

Currently, our Centre manages both categories of DTC patients (total thyroidectomy and thyroid lobectomy patients) with I-131 post-surgery. Management of thyroid total thyroidectomy patients with I-131 destroys the remaining thyroid tissue post total thyroidectomy,[2,16] and the remaining occult carcinoma in the thyroid bed thus reducing chances of reccurrence.[2,4]

This proposed protocol also addresses the radioiodine ablation doses. Several ablation doses ranging from 25mCi – 250mCi have been reported,[18] contrary to a single high dose previously recommended by Beierwaltes for the ablation of normal residual thyroid tissue and destruction of recurrent metastases.[19]

The Integral Flow Chart

The proposed protocol (Figure 1) is divided into two parts: Part A and B. Part A deals with the patient's histology and clinical examination whilst Part B reflects on the administered treatment and follow-up. Patient's history is essential to establish the type of thyroid carcinoma. It has previously been established that papillary, follicular and Hürtle cell carcinomas have the ability to accumulate I-131. However, the Hürthle cell carcinoma has been found to have less vigorous uptake of I-131.[20]

Part A: Classification of the referred patients

In part A, patients are grouped in accordance to the nature of their surgery (total thyroidectomy or thyroid lobectomy). If patients underwent thyroid lobectomy at the referral hospitals, they are sent back to the surgeons with a recommendation for total thyroidectomy. Management of these patients is not recommended since morbidity rates are high. Furthermore, they would require use of high doses of I-131 resulting in high cumulative doses which will tend to be toxic to critical organs such as the salivary glands and lacrimal glands. In case patients have undergone total thyroidectomy, they can be managed with RIA. Management of these patients with radioiodine bears successful outcomes.[3] The rationale behind this treatment procedure is to destroy any postoperative microscopic disease and ablate residual thyroid tissue with the hope of decreasing the recurrence rates.[21,22]

Pre-ablation diagnostic assessment

Once the patient has been categorized as having undergone total thyroidectomy, thyroid function tests (TFTs) are done with the measurement of thyroid stimulating hormone (TSH), triiodothyronine (T3) and thyroxine (T4) levels. If TSH levels are below 30µIU/mL thyroid hormone supplements should be stopped for a period of 4-6 weeks. However, if TSH levels do not improve, the recombinant human Thyroid Stimulating Hormones (rhTHS) should be prescribed.

In case of TSH ≥30µIU/mL, a pre-ablation diagnostic scan should be performed. In this case 3–5mCi of I-123 sodium solution should be injected intravenously. This is followed by acquisition of diagnostic scans, one after four hours (ant-neck) and others after 24 hours (whole body scan and ant-neck). If the thyroid bed uptake is less than 10 per cent, then therapy should be administered, otherwise, the patient should be referred back for total thyroidectomy.

Traditionally, TSH elevation is achieved by thyroid hormone withdrawal. In some cases, rhTSH has been recommended for patients whose TSH level cannot be elevated to the set value of 30µIU/mL due to symptoms of clinically relevant-hypothyroidism, large thyroid hormone producing metastases and pituitary or hypothalamic insufficiency.[21.22] A patient is administered 0.9mg rhTSH intramuscularly on two consecutive days and should receive radioiodine 24 hours after the second injection.[20,23]

The possibility of thyroid stunning effect still remains controversial and may affect the amount of activity of radioiodine for diagnostic studies. There are diverse views among the authors with some believing that I-123 or low activity (3–5 mCi) of I-131 should be used in reducing stunning effect. Even though it is believed that stunning may be dominant on high dose, no significant outcomes were observed in patient who received higher doses. However, I-123 is ideal for imaging since it has photon energy of 159keV and provides high quality images compared to lower resolution images of I-131.[20,21,23] In this protocol, I-123 is recommended for pre-therapy scanning and essentially for follow-up studies when metastases are suspected. However, Tc-99m may also be used to estimate an amount of remaining normal tissue although not referred in the proposed protocol.

Recommended Patient Dose on the basis of uptake during pre-ablation scanning

This protocol recommends that patients should be given radioiodine treatment based on pre-ablation neck uptake. The evidence of metastases will be determined through the whole body scans. It is essential that neck uptake of <0.1 per cent coupled with undetectable Tg level should be declared as a disease free.[24] The neck uptake of >0.1 per cent but <10 per cent should be ablated with evidence of remnant thyroid tissue and metastases. The patients presenting with thyroid lobectomy or and neck uptake of >10 per cent should not be given radioiodine therapy but

should be referred back to surgeons for completion of thyroid resection.

The prescribed dose is also a subject of debate, however a dose range of 30–200mCi will be recommended based on extent of the disease.[25,26] Quantitative dosimetric approach should be implemented instead of standard doses.[23]

Part B: Management and monitoring of patients during treatment

Patients diagnosed with metastasis should be managed with radioiodine doses between 100–200mCi. Patients without metastasis should be managed with doses ranging from 30–100mCi.

During hospitalization it is essential that the patient is isolated in the ward with fitted en-suite facilities, non-absorbent floor and elbow operated tabs. This will ensure that the patient does not impose radiation hazard to the family members and other patients as well as to control radiation contamination. The patient should be given a set of cutlery, crockery and extra linens to keep him in the room. The patient should be advised to use hospital gowns instead of personal clothes in order to contain radiation contamination. The patient must be encouraged to consume lots of water and sucked lemon sweets in order to reduce radiation dose to the bladder and salivary glands respectively. Furthermore, to minimize radiation levels in bathroom the patient should be encouraged to flush twice after using a toilet and to preferably use a shower for bathing.

Family visiting times should be restricted to a short stay once a day at maximum distance. Pregnant women and children must be prohibited to visit at all cost. The nursing care should be minimized and be monitored with pen dosimeters; no pregnant radiation worker is to be allowed to look after the patient.

Prior to administration of the prescribed dose, the patient details should be verified. The nuclear medicine physician should ensure that the patient was starved for at least 2 hours before therapy and after therapy to avoid vomiting. Post dose administration, the medical physicist should measure the exposure rate at 1 meter from the thyroid position. Subsequent daily measurements should be performed until the exposure rate is below 25μSv/h at a distance of 1 m from the patient's neck. When the value is attained then the patient can be discharged from the isolation ward. Following discharge, the medical physicist should monitor the ward for possible contamination before any cleaning takes place and they should also survey the linen for contamination before they are sent to the laundry.

Post ablation scan

Immediately after discharge, patients should be referred for post ablation scan. Two views, the static view of the extended neck including the skull above the lacrimal glands and the whole body scan should be taken.

Scan interpretation

a) Remnant only or with lymph nodes

These are characterized by a high uptake of I-131 in the affected tissue. Affected patients' TFTs should be monitored monthly. After six months, patient is required to undergo I-123 pre-ablation scan. If the iodine uptake is less than 1 per cent, a thyroglobulin antibodies test is recommended. In this case the patient should be followed up for six months before administration of another radioiodine dose. If the iodine uptake is greater or equal to 1 per cent, I-131 ablation should be administered.

b) Metastases

Metastases are followed by the assessment of Tg levels. If normal, a whole body scan is done after six months. The same procedure for patients described in a) should be followed. In case of abnormal Tg levels, the ablation should be performed immediately.

Conclusion

A local protocol for the management of DTC patients at DGMAH has been successfully presented. This protocol optimizes management of DTC patients with radioiodine. It stimulates ablation of only total thyroidectomy patients.

References

1. Padma S, Sundaram PS, Radioiodine as an adjuvant therapy and its role in follow-up of differentiated thyroid cancer. J Can Res Ther. 2016;12:1109–13.
2. Carballo M, Quiros RM. To treat or not to treat: the role of adjuvant radioiodine therapy in thyroid cancer patients. J Oncol. 2012;2012:1–11.
3. To K, Nixon IJ. The surgical approach of managing differentiated thyroid cancer. Indian J Med Research. 2016;143(6):689–695.
4. Ejeh JE, Adepapo KS. Relationship between THS level and effective half-life of I-131 in differentiated thyroid cancer patients. J Cell Sci Ther. 2011:S2:006. doi: 10.4172/2157-7013.S2-006.
5. Ahmadi S, Stang M, Jiang XS, et al. Hürthle cell carcinoma: current perspectives. Onco Targets and Therapy. 2016:9;6873–6884.

6. Petric R, Gazic B, Goricar K, et al. Expression of miRNA and occurence of distant metastases in patients with Hurtle Cell Carcinoma. Int J Endocrinal. 2016;2016:8945247.
7. Carcangiu ML, Zamp G, Rosai J. Poorly differentiated thyroid carcinoma: A reinterpretation of Langhans "wuchernde Struma". Am J Path. 1984;8(9):655–668.
8. Vini L, Hammer C, Macready VR. Thyroid Cancer: a review of treatment and follow up. Ann Nucl Med. 1996;10(1):1–7.
9. Hedinger C, Williams ED, Sobin LH. The WHO histological classification of thyroid tumours. A complementary of the second edition. 1989;63:908–911.
10. Ganly I, Ricarte J, Eng S, et al. Genomic dissection of Hurtle carcinoma reveals a unit of class of thyroid malignancy. J Clin Endocrinol Metab. 2013;98(5):E-962–E972.
11. Takami H, Ito Y, Okamoto T, et al. Therapeutic strategy for differentiated thyroid carcinoma in Japan based on a newly established guideline managed by Japanese Society of Thyroid Surgeons and Japanese Association of Endocrine Surgeons. World J Surg. 2010;2011(35):111–21.
12. Qin CD, Saha S, Meacham R, et al. Surgical risks after unilateral lobectomy versus total thyroidectomy: A review of 47 patients. Surgery Curr Res. 2008;4(6):1–7.
13. Teoh CM, Rohaiza M, Chan KY, et al. Pre-ablation diagnostic whole-body scan following total thyroidectomy for well-differentiated thyroid cancer: is it necessary? Asian J Surg. 2005;28(2):90–96.
14. Middendorp M, Grunwald F. Update on recent developments in the therapy of differentiated thyroid cancer. Semin Nucl Med. 2010;40:145–152.
15. Haugen BR, Alexander EK, Bible CK, et al. 2015 American thyroid association management guidelines for adult patients with thyroid nodules and differentiated cancer: Thyroid. 2016;26(1):1–133.
16. Vini L, Harmer C. Radioiodine treatment for differentiated thyroid cancer. Clin Oncol. 2000;12:365–372.
17. Kebebew E, Duh QY, Clark OH. Total thyroidectomy or thyroid lobectomy in patients with low-risk differentiated thyroid cancer: Surgical decision analysis of a controversy using a mathematical model. World J Surg. 2000;24:1295–1302.
18. Anand SS, Sood V, Kumar PG, et al., Retrospective analysis of thyroid cancer patients. MJAF. 2008;64:07–10.24.
19. Beierwaltes WH. Radioiodine therapy of thyroid disease. Nucl Med Bio. 1987;14(3):177–181.
20. Goldsmith SJ. To ablate or not to ablate: issue and evidence involved in I-131 ablation of residual thyroid tissue in patients with differentiated thyroid carcinoma. Semin Nucl Med. 2011;41(2):96–104.
21. Schlumberger MJ. Diagnostic follow-up of well-differentiated thyroid carcinoma: historical perspective and current status. J Endocrinol. 1999;22(11):3–7.
22. Intenzo CM, Jabbour S, Dam HQ, et al. Changing concepts in the management of differentiated thyroid cancer. Semin Nucl Med. 2005;35:257–265.
23. Solanki KK, Padhy AK, Dondi M. Nuclear medicine in thyroid cancer management: A practical report. IAEA-TECDOC-1608 2009.
24. Silberstein EB, Alavi A, Clarke S, et al. The SNM practice guideline for therapy of thyroid disease with 131I. J Nucl Med. 2012;53(10):1–19.
25. Luster M, Clarke SE, Dietlein M, et al. Guidelines for radioiodine therapy of differentiated thyroid cancer. Eur J Nucl Med Mol Imaging. 2008;35:1941–1959.
26. Nakada K, Ishibashi T, Takei T, et al. Does lemon candy decrease salivary gland damage after radioiodine therapy for thyroid cancer? J Nucl Med. 2005;46(2):261–266.

PEER REVIEW

Not commissioned. Externally peer reviewed.

CONFLICTS OF INTEREST

The authors declare that they have no competing interests.

FUNDING

None

ETHICS COMMITTEE APPROVAL

This study was approved by the research committees of the Medunsa Campus of the University of Limpopo, now Sefako Makgatho Health Sciences University. The clearance number assigned to the project is: SMUREC/M/68/2014:PG.