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Radioactive Iodine Therapy Dosimetry for a Case of Functioning Follicular Thyroid Carcinoma Metastases

Christopher James Kleimeyer

chriskleimeyer@gmail.com

RBWH: Royal Brisbane and Women's Hospital https://orcid.org/0009-0001-7947-7092

Sarah Ong

RBWH: Royal Brisbane and Women's Hospital

Shaun Patford

RBWH: Royal Brisbane and Women's Hospital

Matthew Griffiths

RBWH: Royal Brisbane and Women's Hospital

Lauren Burrage

RBWH: Royal Brisbane and Women's Hospital

Samuel Kyle

RBWH: Royal Brisbane and Women's Hospital

David Pattison

RBWH: Royal Brisbane and Women's Hospital

Tahleesa Cuda

RBWH: Royal Brisbane and Women's Hospital

Roslyn Francis

RBWH: Royal Brisbane and Women's Hospital

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Title Page

Radioactive Iodine Therapy Dosimetry for a Case of Functioning Follicular Thyroid Carcinoma Metastases

Kleimeyer C[1], Ong S[1], Patford S[1], Griffiths M[1], Burrage L[2], Kyle S[1,3], Pattison DA[1,3], Cuda T[1], Francis RJ[1].

1. Department of Nuclear Medicine, PET & Theranostics, Royal Brisbane and Women's Hospital, Brisbane, Australia
2. Department of Endocrinology, Royal Brisbane and Women's Hospital, Brisbane, Australia
3. School of Medicine, University of Queensland, Brisbane, Australia

Corresponding Author:
Chris Kleimeyer
ORCID - 0009-0001-7947-7092
Email - chriskleimeyer@gmail.com

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Researchers are eligible to request access to de-identified individual participant data, reviewed on a case-by-case basis.

Ethics Approval
This Short Communication is a retrospective case report and discussion that complied with ethical standards.

Consent
Informed patient consent to participate was obtained, and the authors affirm that the patient provided informed consent for the publication of the Figure 1, 2 and 3 images.

Keywords
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Radioactive Iodine Therapy Dosimetry for a Case of Functioning Follicular Thyroid Carcinoma Metastases

Abstract

Purpose

Metastatic differentiated follicular thyroid cancer with functioning metastases is an uncommon and challenging clinical presentation. Radioactive iodine (RAI) is an effective therapy for treatment of metastatic disease and for management of hyperthyroidism resulting from functioning disease. Determining the optimal iodine-131 (^{131}I) administered activity is challenging, as there may be unpredictable and prolonged whole-body retention of activity, due to ^{131}I metabolism and recirculation. Most RAI therapy is performed using a fixed or empiric approach. However, there are advantages to adopting dosimetry approaches and determining the maximum tolerable activity (MTA). Iodine-124 (^{124}I) positron emission tomography/computed tomography (PET/CT) dosimetry prior to ^{131}I RAI therapy aims to ensure the maximum radiation absorbed dose to tumour lesions is safely delivered while minimising off-target effects and toxicity.

Methods

A 74-year-old female with functioning follicular thyroid carcinoma (FTC) metastases underwent ^{124}I PET/CT dosimetry prior to ^{131}I RAI administration. The ^{124}I PET/CT estimated that the MTA was 3100 MBq of ^{131}I which would deliver an estimated 217 Gy to a right lung metastasis index lesion. Based on this estimation, an activity of 3000 MBq ^{131}I was subsequently administered to safely achieve a target lesion dose of 200 Gy.

Results

The patient's serum thyroglobulin decreased from 21,148 µg/L pre-therapy to 4,610 µg/L six months post-therapy, indicating a good response. Her regular carbimazole was discontinued one month post ^{131}I RAI treatment, and she was commenced on thyroxine with a thyroid-stimulating hormone (TSH) target of less than 0.1. Apart from mild left hip pain, she is now asymptomatic.

Conclusion

Using ^{124}I PET/CT for dosimetry calculations, as in this case, is a useful approach in RAI therapy for metastatic differentiated thyroid cancer (DTC), with the aim to ensure the maximum radiation absorbed dose to tumour lesions is safely delivered while minimising off-target effects and toxicity.

Case Report

We present the case of a 74-year-old female with functioning metastatic follicular thyroid carcinoma, who underwent ^{124}I PET/CT dosimetry to determine the RAI ^{131}I treatment dose. She was diagnosed after presenting with symptomatic thyrotoxicosis, with initial bloods showing an elevated FT3 level of >30.7 pmol/L (2.7-5.7 pmol/L), an FT4 level of 25.6 pmol/L (9.0-20.0 pmol/L), a TSH of <0.01 mIU/L (0.3-5.0 mIU/L) and a Thyroid Stimulating Immunoglobulins level of 23 IU/L (<0.55 IU/L). A fluorodeoxyglucose (FDG) PET/CT (Figure 1) demonstrated an occipital scalp, extensive lung, left adrenal, right 8th rib and left sacroiliac metastases. Biopsy of the left sacroiliac lesion confirmed metastatic FTC.

Histology post total thyroidectomy demonstrated a high-grade differentiated follicular carcinoma of the left thyroid lobe, measuring a maximal dimension of 44 mm with extensive vascular and capsular invasion, clear margins and no extrathyroidal extension. Due to the functional metastases, the hyperthyroidism persisted post-thyroidectomy, requiring the continuation of carbimazole. The left sacroiliac metastasis was treated with external beam radiotherapy (30 Gy in 5 fractions).

Following the oral administration of 28 MBq of ^{124}I, early and delayed timepoint PET/CT imaging at 6 (Figure 2), 24, 48, 72 and 144 hours was performed for dosimetry of the functioning metastases. MTA was defined as the administered activity that will deliver a radiation absorbed dose of 2 Gy to the blood and was determined by blood sampling and whole body gamma counting as described by Jentzen, Bockisch and Ruhlmann in 2015 (1). Due to continuous ^{124}I circulation from functional disease, radioactivity concentration remained elevated in blood sampling. Curve fitting was by piecewise trapezoidal integration up to 168 hours and physically decayed to infinity. Estimated MTA was 3100 MBq of ^{131}I which would deliver an estimated 217 Gy to a right lung metastasis index lesion.

Following ^{124}I dosimetry, the patient was admitted for radioiodine therapy. Her regular carbimazole was withheld for three days prior to RAI therapy. Her TSH level was 0.01 mIU/L on the day of therapy. An activity of 3000 MBq ^{131}I was administered, with post-treatment scintigraphy performed 3 and 7 days later (Figure 3) demonstrating mild to moderate radioiodine avidity within remnant thyroid tissue and intense radioiodine avidity within the pulmonary, left adrenal, osseous and subcutaneous metastases.

She remained an inpatient for three days post administration until her external dose rate was within discharge limits, and she was advised to follow radiation precautions for two weeks post discharge, due to radioiodine retention and recirculation from the functioning thyroid cancer metastases. Carbimazole was re-commenced on discharge from hospital following her radioiodine therapy.

Carbimazole was discontinued one month post treatment, at which time the patient required the commencement of thyroxine. Her pre-treatment thyroglobulin of 21,148 µg/L reduced to 4,610 µg/L six months post-treatment, consistent with a good partial response, and her thyroglobulin antibody levels remained undetectable. Her TSH target is <0.1 mIU/L. Apart from mild left hip pain, she is now asymptomatic. A second dose of RAI will be administered in six months.

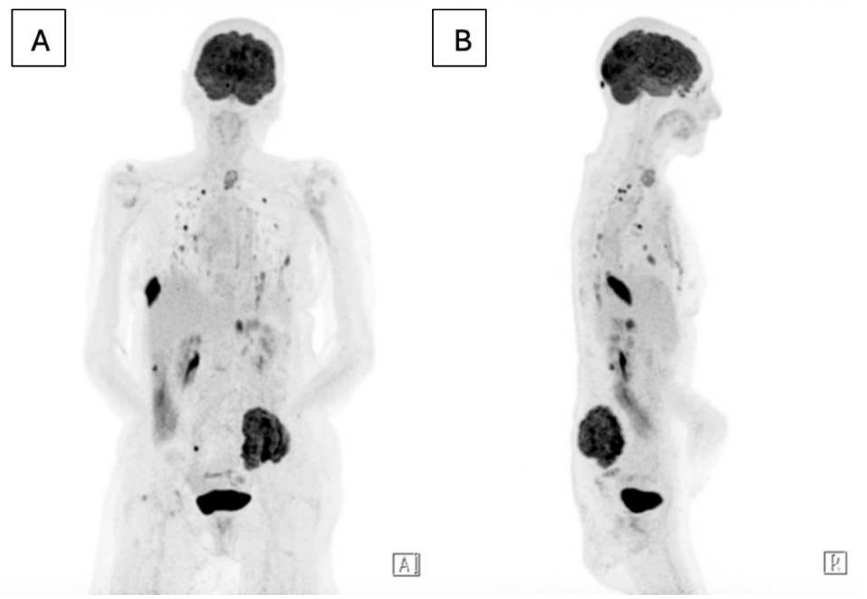


Figure 1. Anterior (A) and right anterior (B) maximum intensity projection (MIP) images of the pretreatment FDG PET demonstrating a moderately FDG avid nodule in the left thyroid surgical bed and intensely FDG avid occipital scalp, pulmonary, left adrenal, right 8th rib and left pelvic metastases, with the left posterior pelvis lesion centred on the sacroiliac joint and extending to involve the adjacent gluteal and piriformis muscles.

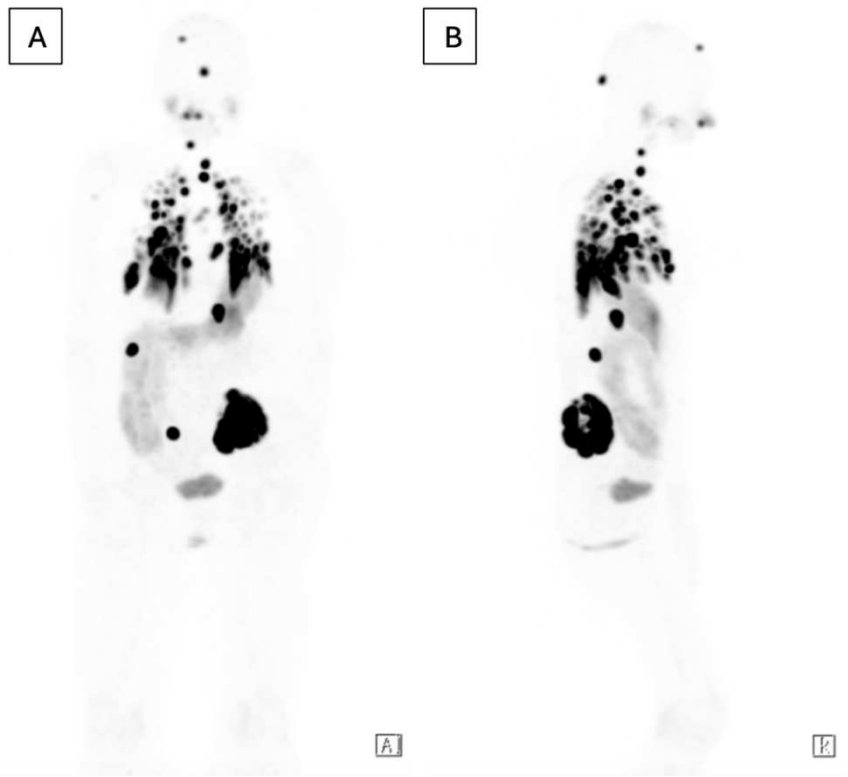


Figure 2. Anterior (A) and right anterior (B) MIP images of the 6 hour post administration ^{124}I PET demonstrating radioiodine avid lesions in the thyroid surgical bed bilaterally in keeping with remnant thyroid tissue, along with innumerable lung, a left adrenal, occipital scalp and osseous disease.

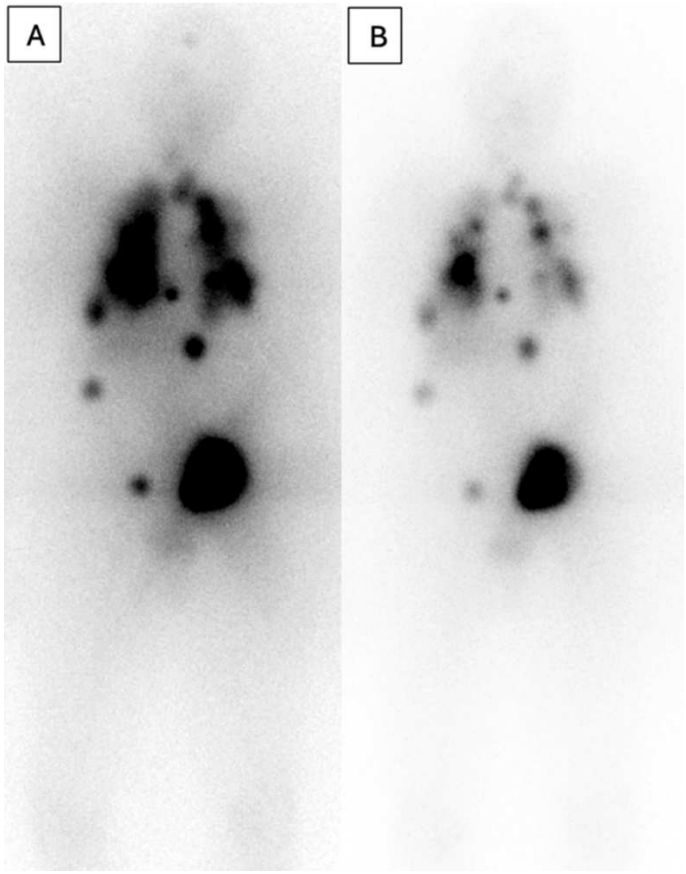


Figure 3. Anterior planar scintigraphy images taken Day 3 (A) and Day 7 (B) after 3000 MBq ^{131}I administration, showing mild to moderate radioiodine accumulation at the thyroid bed and intense accumulation within the known metastases, with persistent retention of ^{131}I at Day 7 post administration.

Discussion

RAI therapy is effective in the treatment of differentiated thyroid cancer (DTC) as circulating radioiodine is taken up by the sodium iodide symporter plasma membrane proteins of thyroid cancer cells (2–4). Effective therapy is dependent on dose delivery to tumour, which is influenced by multiple factors including administered activity and the degree of differentiation of the thyroid cancer cells which determines radioiodine retention at tumour sites. In the absence of an MTA the alternative is multiple administrations of lower fixed activities, which evidence suggests may induce changes in the thyroid cancer biokinetics, with literature suggesting less differentiated cells with lower ^{131}I avidity are more likely to survive when a course of ^{131}I therapy with a non-maximum activity is administered. This subsequently causes a gradual loss of therapeutic efficacy over multiple courses of fixed-activity therapy and can lead to eventual dedifferentiation of the tumour (5–7).

Thyrotoxicosis due to functioning thyroid metastases is extremely rare, and is most often associated with FTC (8,9). Potential mechanisms for thyrotoxicosis include a large total tumour mass and thyroid-stimulating immunoglobulins that can activate TSH receptors (8). The ability of functional thyroid carcinoma to concentrate iodine is thought to result in an improved treatment response with RAI, particularly with lung metastases (9).

It is recommended that oral antithyroid medications are withheld in these patients before RAI treatment to reduce the risk of RAI uptake being affected. RAI dose retention and recirculation with metabolism can occur in patients with functional metastases, and these patients can get greater tumour exposure, but also greater marrow exposure, requiring longer hospital stays. Clinicians also need to be aware of the risk of thyroid storm when treating these patients with RAI, as although the frequency of thyroid storm after RAI treatment is estimated to be 0.34%, it can be associated with a mortality rate as high as 20 to 50% (10–12). Pre-emptive beta blockers and steroid coverage can be considered for patients deemed to be at higher risk, including patients with poorly controlled hyperthyroidism or comorbid patients, particularly those with significant cardiovascular disease including atrial fibrillation or heart failure. (13).

Most RAI activity selections are based on the fixed or empiric activity concept, with ablation and adjuvant activities lower than those for metastatic disease, and activities usually ranging from 1100 MBq to 3700 MBq (14–16). The main alternative is the dosimetric approach, with two key concepts. The first is aiming to determine the maximum tolerable activity with an appropriate margin of safety, to avoid off target effects including bone marrow toxicity, pneumonitis and pulmonary fibrosis (5). Maxon et al. (1983) developed a second dosimetry concept of delivering a desired radiation absorbed dose to tumour lesions, with a proposed radiation dose of 300 Gy to thyroid remnants and 80 Gy to nodal metastases, after exploring the minimum dosimetry thresholds needed to achieve a complete response (17).

^{124}I is a PET isotope suitable for pre-therapeutic dosimetry to calculate the absorbed dose to a lesion and predict the response to radioiodine treatment (18). Sgouros et al. (2004) demonstrated the feasibility of using the ^{124}I PET-based tumour dosimetry method for absorbed dose estimation in patients with metastatic DTC, in which multi-timepoint PET images defined the temporal distribution of radioactivity after administration of 74-158 MBq ^{124}I at approximately 4, 20 and 44 hours, and between 4-6 days (19).

The outcome post-treatment for patients with functional DTC usually involves down-titrating and ultimately ceasing anti-thyroid medications, such as carbimazole. Thyroxine is then commenced with a TSH target of <0.1mlU/L (depending on ongoing dynamic risk stratification) to reduce the risk of progressive metastatic disease.

Conclusion

Using ^{124}I PET/CT for dosimetry calculations, as in this case, is a useful approach in RAI therapy for metastatic DTC, with the aim to ensure the maximum radiation absorbed dose to tumour lesions is safely delivered while minimising off-target effects and toxicity.

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