

# Follicular thyroid cancer avid on C-11 Methionine PET/CT

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## Summary

A case of follicular thyroid cancer with intense focal Methionine uptake on 11C-Methionine PET/CT is reported here. The use of 11C-Methionine PET in differentiated thyroid cancer is currently being investigated as a surrogate tracer compared to the more widely used 18F-FDG PET. This case illustrates the potential incremental value of this modality, not only in the localizing of parathyroid adenoma, but also indicating that 11C-Methionine PET might have a potential of increasing the pretest likelihood of thyroid malignancy in a cold nodule with highly increased Sestamibi uptake.

## Learning points:

- 11C-Methionine PET/CT and 18F-Fluorocholine PET/CT often visualizes the parathyroid adenoma in case of negative Tc-99m-MIBI SPECT/CT.
- A cold nodule in Tc-99m Perchnetat thyroid scintigraphy with a negative Sestamibi scintigraphy has a very low probability of being malignant.
- However, the pretest likelihood of thyroid cancer in a cold nodule with increased Sestamibi uptake is low.
- 11C-Methionine PET might have a potential incremental value in increasing the pretest likelihood of thyroid malignancy in a cold nodule with highly increased Sestamibi uptake.

## Background

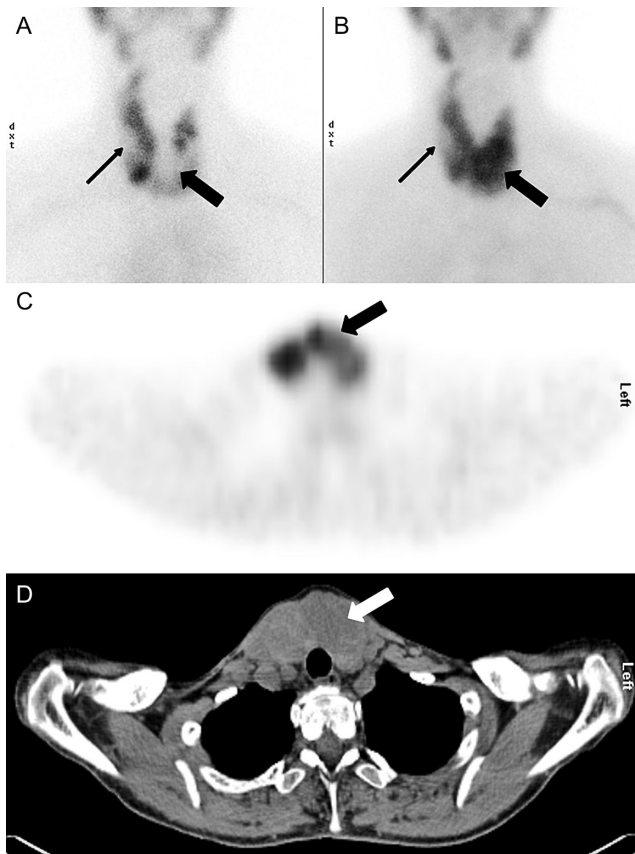
This case is interesting as it illustrates how the relatively new scan modality 11C-Met PET, which is used for the detection of parathyroid adenomas, can have extremely important coincidental findings such as an aggressive thyroid cancer. 11C-Met PET might have a role as a novel diagnostic procedure in thyroid cancer and in qualifying whether cold thyroid nodules with Sestamibi uptake are suspicious of malignancy or not.

## Case presentation

A 66-year-old woman with a known history of osteoporosis was suspected for primary hyperparathyroidism due to persistent elevated mean parathyroid blood hormone level of 11.4 pmol/L and hypercalcemia. She was referred for a state of the art combined Tc-99m pertechnetate

thyroid scintigraphy and Tc-99m Sestamibi parathyroid scintigraphy with visual simple image subtraction technique. The thyroid scintigraphy showed two cold nodules in the thyroid gland (Fig. 1A), a large nodule in the lower third of the left thyroid lobe involving the isthmus area, and another nodule laterally in the middle third of the right thyroid lobe. The cold nodule in the left thyroid lobe had intense Sestamibi uptake, with a corresponding low attenuating process on low-dose CT scan (Fig. 1B, C and D), while the nodule in the right thyroid lobe had no Sestamibi uptake (Fig. 1B). No pathological parathyroid tissue was identified, and the patient was referred for an 11C-Methionine PET/CT in order to optimize the pre-surgical localization of the parathyroid adenoma.

The 11C-Methionine PET showed intense Methionine uptake in the nodule in the lower third of the left thyroid



**Figure 1**

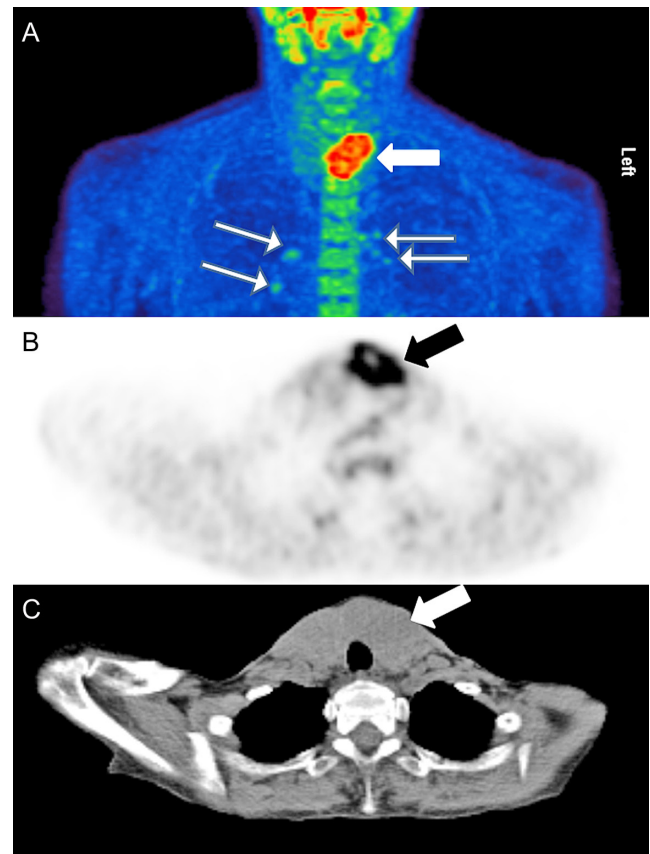
Benign cold nodule (small arrows) and follicular thyroid carcinoma (large arrows) shown on Tc-99m pertechnetate thyroid scintigraphy in anterior projection (A), Tc-99m Sestamibi parathyroid scintigraphy in anterior projection (B), axial Tc-99m sestamibi SPECT image (C) and axial low-dose CT image (D).

lobe, including the isthmus area (Fig. 2A, large arrow in Figs. 2B and C), making the nodule suspicious of malignancy. Noticeably no Methionine uptake was seen in the cold nodule on the right side. Additionally, the 11C-Methionine PET showed slightly increased activity in lymph nodes located near the aorta arch and in both lung hilii, which were considered reactive (Fig. 2A, small arrows).

A pretracheal focus with increased Methionine uptake was identified posterior of the lower pole of the thyroid gland close to the midline (Fig. 3A and B), with a correlate on low-dose CT scan (Fig. 3C), suspicious of a P3-derived parathyroid adenoma located in the left thymus.

## Investigation

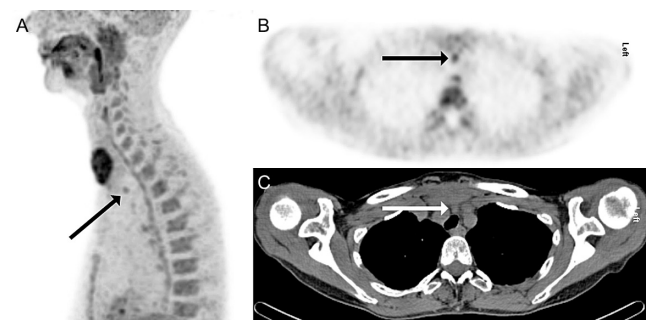
Results of Tc-99m Pertechnetate thyroid scintigraphy, Tc-99m Sestamibi parathyroid scintigraphy, 11C-Methionine PET/CT and follow-up stimulated



**Figure 2**

Slightly increased activity in lymph nodes located near the aorta arch and in both lung hilii, which were considered reactive (A, small arrows). Follicular thyroid carcinoma (large arrows) shown on 11C-Met PET anterior maximum intensity projection (MIP) (A), axial 11C-Met PET image (B) and axial low-dose CT image (C).

thyroglobulin test, cervical ultrasound examination and iodine-131-tracer scintigraphy are described.



**Figure 3**

Parathyroid adenoma (arrows) shown on sagittal 11C-Met PET image (A), axial 11C-Met PET image (B) and axial low-dose CT image (C).



## Treatment

Fine-needle aspiration cytology (FNAC) showed malignant cells in the nodule in the lower left thyroid lobe and isthmus, and benign cells in the nodule in the right thyroid lobe. The patient had a simultaneous left hemithyroidectomy and extirpation of the parathyroid adenoma. Histology showed a parathyroid adenoma of 0.14g and a follicular thyroid carcinoma with a diameter of 35mm expanding outside its own capsule but not outside the thyroid capsule. Because of the aggressive growth, the patient also underwent a complete right hemithyroidectomy. No further malignancy was found. Subsequently, the patient was ablated with radioiodine (I-131).

## Outcome and follow-up

The patient was followed clinically, biochemically and by imaging after radioiodine treatment. Six months post treatment, the patient was euparathyroid and eucalcemic, stimulated thyroglobulin test was negative, cervical ultrasound examination and iodine-131-tracer scintigraphy showed no sign of residual cancer tissue. Thus, the patient was considered in complete remission regarding both parathyroid adenoma and thyroid cancer.

## Discussion

When a state-of-the-art combined Tc-99m pertechnetate thyroid scintigraphy and Tc-99m sestamibi parathyroid scintigraphy fail to visualize a parathyroid adenoma, a supplementary 11C-Methionine PET/CT often visualizes a parathyroid adenoma, enabling focused parathyroidectomy (1, 2, 3). 18F-Fluorocholine PET/CT is an alternative add-on examination for improvement of preoperative localization of parathyroid adenoma in case of a negative parathyroid scintigraphy (4, 5). It is well known that there is a high negative predictive value of a negative sestamibi scintigraphy in qualifying whether cold nodules in Tc-99m pertechnetate thyroid scintigraphy are benign or malignant. However, the positive predictive value is low (6, 7). Methionine is needed for protein synthesis, as a biological methyl donor for the methylation of DNA, transfer-RNA and other compounds (transmethylation) after formation of 5-adenosylmethionine (SAM). 11C-Methionine PET is in a clinical setting used to evaluate the extent and recurrence of brain tumors, as Methionine accumulates in viable cancer cells (8). Furthermore 11C-Methionine

PET has been suggested as a diagnostic tool in qualifying whether an 18F-FDG PET positive solitary lung nodule is malignant or benign (9). The use of 11C-Methionine PET in differentiated thyroid cancer is currently being investigated as a surrogate tracer compared to the more widely used 18F-FDG PET; however, 11C-Methionine PET has not proven to be superior to 18F-FDG PET in the detection of recurrent disease in differentiated thyroid cancer (10, 11). Methionine uptake in a benign colloid nodule has previously been described (12). It is possible that the tumor would have had a similar uptake of Fluorocholine, as differentiated thyroid cancer previously have shown positive on 18F-Fluorocholine PET/CT (13, 14, 15). This case illustrates the potential incremental value of 11C-Methionine PET/CT, not only in the localizing of parathyroid adenoma, but also indicating that 11C-Methionine PET might have a potential of increasing the pretest likelihood of thyroid malignancy in a cold nodule with highly increased sestamibi uptake. Further studies with larger sample size are needed to determine the performance of 11C-Methionine PET/CT in classification of cold sestamibi-uptaking thyroid nodules into benign and malignant, as well as to determine the cost-effectiveness of such an add-on examination.

### Declaration of interest

The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

### Funding

This research did not receive any specific grant from any funding agency in the public, commercial or not-for-profit sector.

### Patient consent

Written informed consent has been obtained from the patient for the publication of this report.

### Author contribution statement

Mads Ryo Jochumsen: scan analysis and writer of the primary draft; Peter Iversen: scan analysis especially the follow-up scans, proof reading and feedback; Anne Kirstine Arveschoug: supervision, proof reading, feedback.

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Received in final form 29 November 2017

Accepted 13 December 2017