Is it practical and cost effective to detect differentiated thyroid carcinoma metastases by $^{18}$F-FDG PET/CT, by $^{18}$F-FDG SPET/CT or by $^{131}$I SPET/CT?

Fluorine-18-labeled 2-fluoro-2-deoxy-D-glucose positron emission tomography/computerized tomography ($^{18}$F-FDG PET/CT) plays an important role in detecting differentiated thyroid carcinoma (DTC) metastases with elevated thyroglobulin (Tg) and negative radioiodine ($^{131}$I) uptake. On the other hand, $^{18}$F-FDG single photon emission tomography/CT ($^{18}$F-FDG SPET/CT) is also effective and has a comparatively lower expense and possible reimbursement paid by the government as is the case in China. The efficiency of the above-mentioned scanning techniques is compared with the whole body $^{131}$I SPET/CT scan in detecting DTC metastases. It seems that both $^{18}$F-FDG SPET/CT and $^{131}$I SPET/CT are practical and cost effective to detect DTC metastases instead of $^{18}$F-FDG PET but $^{131}$I SPET/CT is cheaper and has a lower radiation burden, compared to $^{18}$F-FDG SPET/CT. Therefore, $^{131}$I SPET/CT may be preferred and is at present recommended and reimbursed in China as the first choice modality for diagnosing DTC metastatic disease. The overall usual protocol now is $^{131}$I imaging, SPET/CT and Tg measurements. Future studies may address the choice of $^{131}$I SPET/CT with more patients studied and be related to the actual mechanism of uptake of the radionuclide to DTC metastases.

Bone metastases from DTC occur in 2%-13% of the patients, mainly in the spine [1]. Nearly half of patients with bone metastases from thyroid cancer develop vertebral metastases. Spinal metastases are associated with significantly reduced quality of life due to pain, neurological deficit, and increased mortality [2]. For the detection of bone metastases in patients with DTC, it has been reported that the sensitivity of $^{18}$F-FDG PET/CT is significantly lower than that of $^{18}$F-fluoride PET/CT [1]. A recent study showed that a significant part of DTC patients has a solitary spinal involvement at the time of presentation and may be considered for aggressive treatment with the intention to improve quality of life and survival [2, 3].

Diagnostic surveillance for DTC metastases includes a $^{131}$I whole body scan ($^{131}$I WBS) and measurement of serum Tg levels after endogenous or exogenous TSH stimulation. These metastases are usually positive for $^{131}$I uptake and negative for $^{18}$F-FDG PET uptake, whereas poorly differentiated thyroid carcinomas are negative for $^{131}$I uptake and positive for $^{18}$F-FDG uptake [4, 5]. On the other hand, DTC metastases with elevated Tg and negative $^{131}$I uptake may be detected by $^{18}$F-FDG PET/CT or SPET/CT scan [4-6]. The discrepancies between the uptakes of $^{18}$F-FDG and $^{131}$I in detecting metastases of DTC, which were called flip-flop phenomena have been observed and reviewed by us previously [5-7]. The uptake of $^{18}$F-FDG in DTC metastases indicates the dedifferentiation of the carcinoma. Fluorine-18-FDG SPET/CT is useful in DTC patients with elevated Tg and negative $^{131}$I uptake but for $^{18}$F-FDG PET uptake, whereas poorly differentiated thyroid carcinomas are negative for $^{131}$I uptake and positive for $^{18}$F-FDG uptake [4, 5]. On the other hand, DTC metastases with elevated Tg and negative $^{131}$I uptake may be detected by $^{18}$F-FDG PET/CT or SPET/CT scan [4-6]. The cost of the $^{18}$F-FDG PET/CT scan in China is 1132$ while for the $^{18}$F-FDG SPET/CT scan is 461$. The $^{18}$F-FDG PET/CT scan is commonly used in China since 2001 not only because of its lower expense but also because of its possible reimbursement by the government for detecting malignant disease. It is also simpler to detect DTC metastases by $^{18}$F-FDG SPET/CT. The cost of the equally effective $^{131}$I SPET/CT scan is 200$. The $^{18}$F-FDG PET/CT scan after $^{131}$I treatment causes no additional radiation burden as compared to $^{18}$F-FDG PET/CT or $^{18}$F-FDG PET/CT who emit radiation by $^{18}$F and CT. The effective dose of $^{18}$F-FDG PET/CT to an adult is...
~0.019 mSv/MBq [10]. All these advantages make 131I SPET/CT scan an important diagnostic tool for thyroid cancer staging and risk stratification [11] better than 18F-FDG SPET/CT. Iodine-131 SPET/CT is often used post-therapy in DTC patients with suspicious cervical lymph nodes, 4-5 days after the 131I WBS, while 18F-FDG SPET/CT is commonly used for stage T3 or T4 DTC patients at regular follow-up.

We refer here to a recent case of ours of detecting DTC metastases in a 43 years old man, who had been treated 8 times with 5.5 GBq by 131I for having lung metastases. His Tg was 1321.59 ng/mL and TSH 129 μIU/mL. Post-therapy 131I WBS showed multiple functioning metastases in the left parotid gland and the left mandible, in both lungs and the thoracic vertebrae (Figure 1A). The pre-therapy 18F-FDG SPET/CT was performed. The post-therapy transverse images of 131I SPET/CT (Figure 1B) and of 18F-FDG SPET/CT also showed the same metastases (Figure 2). Histopathology confirmed the above (Figure 3A and B). Of the three mentioned modalities both 131I SPET/CT and 18F-FDG SPET/CT better showed these metastases and also lung metastases. It is worth mentioning that for the above case, DTC metastases were diagnosed both by 131I and 18F-FDG SPET/CT scans which have been reported for the first time.

In conclusion, 18F-FDG PET/CT may fail to detect all DTC metastases, while 131I WBS combined with 131I SPET/CT may be a better cheaper diagnostic tool as suggested by the case we presented here. Positive metastases in both 131I and 18F-FDG SPET/CT may indicate worse prognosis. Future research may add more evidence as to which is the best diagnostic imaging modality and relate it to the molecular mechanism of the uptake of the radionuclide used.

The authors declare that they have no conflicts of interest.

Bibliography

Editorial

19. Moon SH, Oh YL, Choi JY. Comparison of 18F-Fluorodeoxyglucose uptake with the expressions of glucose transporter type 1 and Na+/I- symporter in patients with Untreated Papillary Thyroid Carcinoma. Endocr Res 2013; 38(2): 77-84.