The Role of PET/CT in Assessment of Post Thyriodectomy Recurrence in Differntiated Thyroid Carcinoma With negative iodine isotope scan andElevated Thyroglobulin

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ABSTRACT

In the last decade, combined PET/CT has been introduced into the field of oncology imaging representing a unique imaging modality that scans the whole body integrating functional information from a PET scan with anatomical information from a CT scan. Combined PET/CT is considered a major breakthrough in oncology imaging with valuable applications in thyroid cancer, especially during post-operative follow up in differentiated thyroid cancer patients. It is very efficient with least possible pitfalls and false results compared to either of its components alone and to side by side reading of separately acquired PET and CT. It can be a standard modality for the new vision in management and treatment plan. The future of Combined PET/CT seems bright with new applications are awaited with great interest.

Key words

Thyroid cancer -recurrence - PET- Combined PET/CT

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Introduction

INTRODUCTION

Thyroid cancer is the 6th common cancer in women and accounts for approximately 1% of all cancer cases (Lin et al, 2010)

Differentiated thyroid cancer is generally characterized by long term survival, good prognosis and low aggressiveness. Its prognosis is related to the age at diagnosis, tumor dimension, extra capsular extension and presence of distant metastases. Distant metastases is relatively rare with incidence ranging from 4-27%. (Bertagna et al, 2010).

Most people diagnosed with thyroid cancer have a total thyroidectomy followed by radio-active iodine ablation. After treatment has finished patients will have regular check ups. At some visits, patients may have blood tests, US, CT, MRI and scans. (Razfar et al, 2011)

The thyroglobulin (Tg) is primarily used as a tumor marker to evaluate the effectiveness of treatment for thyroid cancer and to monitor for recurrence. Not every thyroid cancer will produce thyroglobulin, but the most common types, papillary and follicular thyroid cancer, frequently do, resulting in increased levels of thyroglobulin in the blood. The magnitude of Tg levels may be related to tumor mass, degree of differentiation & location of metastasis. Low level of Tg(1ng/ml or less); provide a sensitive test, whereas higher cut-off levels result in a greater specificity at the expense of decreasing sensitivity in detection of recurrent cancer. Thyroid suppression & withdrawal of suppression influence the serum Tg levels. Tg surveillance is the sole screening test for recurrent thyroid cancer patients who have low risk & no evidence of recurrence on prior I-131 scan (Aygun, 2008).

I-131 whole body scan (WBS) had been at the center of recurrent thyroid cancer detection; it detects iodine-avid cancers & is ineffective in undifferentiated

tumors. One distinct advantage of I-131 WBS over other imaging modalities is its ability to identify distant metastasis. Similar to Tg, I-131 becomes more sensitive after thyroid suppression withdrawal & thyrotropin stimulation (Aygun, 2008)

The differentiated thyroid cancer cells after total thyroidectomy & radioiodine ablation may undergo a process of transformation thus losing some or all their ability to take up & retain 131-iodine, but they still retain the ability to absorb FDG (Agyun, 2008).

Recently reported that the loss of I-131 uptake in recurrences depends not only on a decrease in energy-dependent transport mediated by the Na+/I-symporter (NIS) gene but possibly on a reduction in the molecules regulating its intracellular metabolism. Moreover, high glucose transporter type1 (GLUT-1) gene expression supports the use of PET with specific tracers in clinical management of such cancers (Bertagna et al, 2010).

The role of F-18 FDG PET/CT in differentiated thyroid cancer (DTC) is well established, particularly in patients presenting with elevated thyroglobulin (Tg) levels and negative radioactive iodine whole body scan (WBS). It has been demonstrated that F-18 FDG uptake represents less differentiated thyroid cancer cells or dedifferentiated cells and PET positive lesions are more likely to be resistant to 131-Iodine treatment. The uptake of F-18 FDG is related to tumor size, thyroid capsule invasion and histological variants with a poor prognosis (Mosci et al, 2011).

Combination between positron emission tomography (PET) and computed tomography (CT) allow anatomic, functional & molecular information. The advantages of this combined technique over PET alone have become obvious. There is increasing evidence to suggest that PET/CT adds complementary

information in staging, re-staging and follow-up in post-thyroidectomy patients, leading to changes in management plans (Kim et al, 2010)

The sensitivity of using FDG PET/CT in the detection of cancer thyroid is very high and more accurate than the other imaging modalities as it is capable of differentiating among tumors, scars, fibrosis and necrosis (Leboullex et al, 2007)

Also PET/CT images from survey of the body could reveal abnormal areas of uptake indicating the spread of the thyroid cancer to lymph nodes, lungs, bones or central nervous system (Muresan et al, 2008).

AIM OF WORK

The focus of this study is to detect the sensitivity & specificity of 18F-FDG PET/CT in comparison to CT detection of post-thyroidectomy recurrence in de-differentiated thyroid cancer patients with negative iodine (I-131 Whole Body Scan) & elevated serum thyroglobulin.

Anatomy of the Thyroid Gland

Anatomy

The thyroid gland (from Greek "Thyroeides", meaning shield-like) is a brownish-red, highly-vascular, ductless gland situated anteriorly in the visceral compartment of the neck at the level of the fifth, sixth, seventh cervical and first thoracic vertebrae. The normal adult gland weighting 20 to 25 gm and is slightly larger in woman. It enlarges further during puberty, menstruation and pregnancy **(Hendrix, 2003).**

Development of the Thyroid Gland:

The thyroid gland is the first of the body's endocrine glands to develop, on approximately the 24Th day of gestation as an endodermal thickening in the midline of the floor of the pharynx between the tuberculum impar and the copula. Later, this thickening becomes a diverticulum that grows inferiorly into the underlying mesenchyme and is called the thyroglossal duct. As development continues, the duct elongates, and its distal end becomes bilobed. Soon, the duct becomes a solid cord of cells, and as a result of epithelial proliferation, the bilobed terminal swellings expand to form the thyroid gland **(Kratzsch & Pulzer, 2008).**

The thyroid gland then migrates inferiorly in the neck and passes either anterior to, posterior, or through the developing body of the hyoid bone. By the 7Th week, it reaches its final position in relation to the larynx and trachea. Meanwhile, the solid cord connecting the thyroid gland to the tongue fragments and disappears. The site of origin of the

thyroglossal duct on the tongue remains as a pit called the foramen cecum. The thyroid gland may now be divided into a small median isthmus and two large lateral lobes **(Kratzsch & Pulzer, 2008).**

In the earliest stages, the thyroid gland consists of a solid mass of cells. Later, as a result of invasion by surrounding vascular mesenchymal tissue, the mass becomes broken up into plates and cords and finally into small clusters of cells. By the 3rd month, colloid starts to accumulate in the center of each cluster so that follicles are formed (see Fig.). The fibrous capsule and connective tissue develop from the surrounding mesenchyme (**Bifulco &Cavallo, 2007).**

The thyroid also has a neural crest origin from the ultimobranchial body, which is derived from the fifth pharyngeal pouch (which in turn is usually considered to be a part of the fourth pharyngeal pouch). The ultimobranchial body becomes incorporated into the lateral portion of the thyroid, which can persist as a small nodule on the lateral aspect of the thyroid lobe (the tubercle of Zuckerkandl). The ultimobranchial body gives rise to the parafollicular cells, which secrete calcitonin. Hence, the thyroid gland is derived from both the primitive pharynx (the follicular cells) and the neural crest (the parafollicular cells) **(Gravante et. al, 2007).**