18. THYROID CANCER IMAGING

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INTRODUCTION

Molecular imaging in thyroid cancer using nuclear medicine methods is based on specific cellular characteristics. These characteristics can be derived from common cell features, but can also be based on specific properties of thyroid cancer cells. While in the diagnosis of thyroid cancer these methods have not found great potential, many applications can be found in treatment and follow up of the papillary, follicular and medullary thyroid carcinoma patients. In anaplastic thyroid carcinoma the experience with nuclear imaging is scarce, but the clinical relevance in this aggressive tumor is low.

The broad spectrum of radioactive tracer methods is associated with a great variety in sensitivity and specificity. This variation is partly based on cellular or tumor cell characteristics but also can be explained by the different technical factors and techniques. For example, where radioiodine imaging is among the cornerstones of thyroid cancer treatment, this tracer is of limited value in medullary thyroid cancer. This difference illustrates the importance of the specific cell characteristics that governs uptake of radiotracers. C-cells do not take up radioiodine, while follicular thyroid cells do. Another example can be found in the uptake of the tracer 18 FluoroDeoxyGlucose (FDG), which can be used in conjunction with the Positron Emission Tomography (PET) technique. Uptake of this tracer is based on the glucose metabolism that is present in benign and malignant cells. However, the demand for glucose is considerably higher in malignant cells, which results in higher tracer uptake and adequate

imaging of thyroid cancer lesions. Also other nuclear imaging techniques have their additional value in the diagnosis and sometimes treatment of thyroid cancer. For some tracers the discovery of its value in the diagnosis of thyroid cancer is a matter of serendipity and the mechanisms of action are not always fully understood.

In this chapter nuclear medicine tracers methods, commonly used in thyroid cancer patients, will be reviewed, with a special emphasis on the general uptake mechanism, followed by the method of scanning and the clinical applications.

IODINE

General mechanism

The synthesis of thyroid hormone depends on the supply and metabolism of iodine in the thyroid gland and on the synthesis of thyroglobulin (a receptor protein for iodine). Iodine is taken up by the thyroid follicular cells as inorganic iodide and is transformed through a sequence of metabolic process into thyroid hormones (thyroxine (T4) and triiodothyronine (T3)).

The recommendations of the World Health Organization (WHO) for the iodine intake is 90–200 μg/day (90 μg/day for the newborn, 200 μg/day for the pregnant and lactating women) to maintain growth, development and normal thyroid function (1). The average daily dietary intake of iodide varies greatly per area or country. An average of 190–300 μg iodide per person is ingested daily in the United States. In Europe the average daily intake varies greatly from 50 μg (Belgium) to 430 μg (Great Britain) (2,3). About 60 to 80 μg of iodide is taken up daily by the thyroid from the circulating pool that ranges from 250 to 750 μg. If this extrathyroidal iodide pool is labeled with radioactive iodine (^{131}I or ^{123}I), the percentage of uptake of this tracer in 24 hours (8 to 35%) gives a dynamic index of the thyroid gland activity. The total iodide content of the thyroid gland averages 7500 μg, virtually all of which is in the form of iodothyronines (secretory products of the thyroid gland). In a steady state condition 60 to 80 μg (approximately 1% of the total) iodide is released from the thyroid gland daily. Of this amount 75% is secreted as thyroid hormones, and the remainder is free iodide. The large ratio of iodide stored in the form of hormone to the amount of tuned over daily, can protect the individual from the effects of iodide deficiency for about 2 months (4).

Iodide is actively transported into the thyroid follicular cells against chemical and electrical gradients, the iodide trapping. The site of active iodide transport in thyroid follicular cells is the basolateral membrane. The transport of iodide across this membrane is linked to the transport of sodium (Na+/I symporter (NIS)), generated by Na+/K+-ATPase as the driving force. Iodide trapping is stimulated by the thyroid-stimulating hormone (TSH).

Once in the thyroid follicular cell, iodide moves to the apical surface of the cell and seems to be translocated across the apical membrane by the chloride/iodide transporter molecule pendrin (encoded by PDS-gene) into the lumen (colloid) of the follicle cell (5,6,7). The function of pendrin in the thyroid is currently not precisely determined (5,6,8). Once in the follicular lumen, iodide is immediately incorporated into tyrosine