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THYROID PATHOLOGIES IN NUCLEAR MEDICINE

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ABSTRACT

The presented work describes the thyroid pathologies and the nuclear-medical diagnostic approach, in order to obtain a differential diagnosis and the monitoring of various neoplasms; specifically, it describes the importance of radiometabolic treatment with iodine 131, after thyroidectomy surgery.
Through a study conducted in patients suffering from thyroid disease, undergoing metabolic radiotherapy, it is shown that, with equal distribution of radioiodine, uptake with at least 3700 MBq of therapeutic dose is obtained. All this can be seen through the whole body scintigraphic framework, obtained through the use of the double-headed gamma camera with collimators for high emission energies.
Radiometabolic treatment is effective in patients with a high risk of relapse, while radioiodine treatment is not recommended in low-risk patients.

1. ANATOMY OF THE THYROID

The word thyroid derives from the Greek thireos, "oblong shield".
It is an endocrine gland (ie with internal secretion) which is located in the subhyoid region of the neck, in front of the trachea and consists of two lateral lobes joined by an isthmus. The gland assumes lateral relations with the sternocleidomastoid muscle and with the carotids, posteriorly with the laryngeal-recurrent nerve, with the trachea and with the esophagus. Its relationship with the nerve is important for the possible compression actions that it can exert on it (dysphonia).
The thyroid is vascularized by 2 upper thyroid arteries, branches of the internal carotid. From the anatomical-microscopic point of view, the fundamental unit is the "follicle", about 300 microns in diameter, cubic in shape that delimit the follicular cavity, filled with colloid substance, consisting of thyroglobulin, which includes iodinated tyrosine residues and represents the storage form of thyroid hormones.
The thyroid gland is developed in various ways according to sex, age and even the locality of belonging. At birth it weighs about 2 g; in the adult the average weight is about 20 g, but it can undergo considerable variations. The thyroid has a width of about 7 cm, a height of 3 cm in correspondence with the lobes, a variable thickness from 0.5 cm to about 2 cm passing from the isthmus to the lobes.

Thyroid hormones consist of thyroxine T4, triodothyronine, T3. They are made up of iodine for 65%. The daily iodine intake, which is therefore essential for the constitution of hormones, varies from 20 to 600-1000micrograms / day; in areas where iodine is insufficient we will therefore have pathological conditions that go under the name of endemic goiter due to hypertrophy of the gland due to iodine deficiency and TSH stimulation. The thyroid is, in fact, greedy for iodine and captures all the iodine available in the circulation. The uptake of iodine depends on

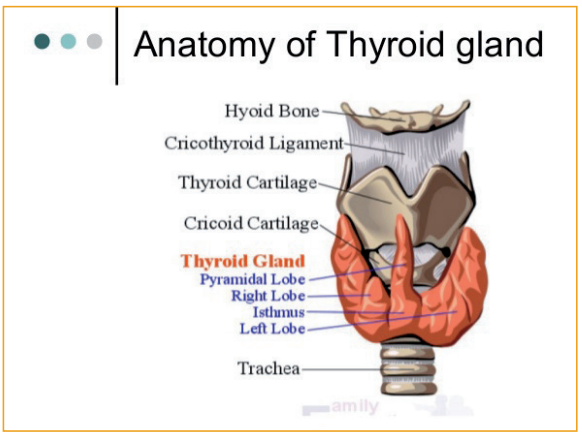

Fig. 1 - thyroid anatomy.

the hormone of the hypothalamus, the TSH. The captured iodine is in turn incorporated into the tyrosine radicals of thyroglobulin, through an oxidation process catalyzed by a peroxidase system and this stage is also under the stimulus of TSH. Iodine is deposited as T4 or T3 within the thyroglobulin molecule. The release of thyroid hormones occurs through the proteolysis of thyroglobulin by proteases and peptidases, with free T3 and T4. T3 is the true active hormone. Two serum proteins, TbG and TbPA are responsible for delivery. The main metabolic transformation of thyroid hormones takes place through the consecutive removal of single atoms which ultimately lead to the total loss of the iodine content and biological activity of the molecule. The regulation of thyroid activity is aimed at maintaining adequate circulating levels of T3 and T4 and is entrusted to three control systems: the first consists of the pituitary release of TSH; the second intrathyroid consists in the possibility of self-regulation of the release of T3 and T4 as a function of intracellular organic iodine levels; the third, peripheral, is represented by the activity of microsomal monodeiodinases and the consequent transformation

of T4 into T3, which is biologically more active. The longest known action is increased oxygen consumption and heat production. These effects depend on the fact that T3 and T4 activate cellular respiration and metabolism. At metabolic level, thyroid hormones stimulate glycogenolysis, neoglucogenesis and have a hyperglycemic action, on lipid metabolism they have a lipolytic action, through the activity of catecholamines. At low doses they have a protidoanabolic action. On the heart T3 and T4 exert a tachycarding and pump increase action; on the digestive tract, an increase in motility but a reduction in absorption. On the skeletal system there is activation of the osteoblasts and therefore bone resorption. It would therefore seem that the thyroid hormones rather than a single site of action have multiple and coordinated sites of attachment.

2. PHYSIOLOGY OF THE THYROID

Thyroid function is regulated by extra- and intrathyroidal mechanisms. The mediator of extrathyroid regulation is TSH, a glycoprotein secreted by the basophilic (thyrotrophic) cells of the adenohypophysis. TSH promotes hypertrophy and hyperplasia of the thyroid gland, accelerates most aspects of intermediate thyroid metabolism, increases the synthesis of nucleic acids and proteins (including thyroglobulin), and ultimately stimulates the synthesis and secretion of thyroid hormones. In turn, TSH is regulated by two opposite mechanisms at the level of the thyrotropic cell. TRH, a tripeptide of hypothalamic origin, stimulates the secretion and synthesis of TSH, while thyroid hormones directly inhibit the mechanism of TSH secretion and antagonize the action of TRH. Then, homeostatic control of TSH secretion is exerted by a negative feedback mechanism by thyroid hormones and the threshold for retroinhibition is apparently established by TRH. TRH reaches the pituitary through the pituitary portal system and binds to specific high-affinity receptors located on the plasma membranes of thyrotropic cells. Activation of the adenyl cyclase system or a simultaneous transfer of extracellular calcium into the cell initiates the secretion of TSH. In addition to promoting the secretion of stored TSH, TRH stimulates TSH synthesis by activating both transcription and translation of the subunit gene. TRH is also important at the post-translational level, as suggested by the fact that patients with hypothalamic hypothyroidism have a TSH characterized by a reduced biological activity. The negative feedback of thyroid hormones appears to take place entirely at the level of the thyrotropic cell. Thyroid hormones have been experimentally shown to inhibit both TRH mRNA levels and pro-TRH, as well as the number of TRH receptors on thyrotropic cells, thus altering TRH sensitivity. The main negative feedback action of thyroid hormones is at the pituitary level and is induced by the binding of the hormones located in the nucleus of the thyrotropic cell, with consequent reduction of the expression of the beta subunit and TSH genes. The key element in the action of thyroid hormones within the pituitary is T3, both that generated locally by T4 and that deriving from the plasma pool. It is not clear to what extent T4 itself acts within the pituitary; however, there are other factors that modify TSH secretion and its response to TRH. Both somatostatin and dopamine appear to be physiological inhibitors of TRH secretion. Estrogen increases sensitivity to TRH, while glucocorticoids inhibit it. The catecholamines, in turn, are able to inhibit (by means of the alpha 1-adrenergic receptors) and to stimulate (by means of the alpha 2-adrenergic receptors) the secretion of TSH. Experimentally, tumor necrosis factor (TNF) and interleukin inhibit TSH secretion and may play a role in entyroid sick syndrome. It is not clear to what extent T4 itself acts within the pituitary; however, there are other factors that modify TSH secretion and its response to TRH. Both somatostatin and dopamine appear to be physiological inhibitors of TRH secretion. Estrogen increases sensitivity to TRH, while glucocorticoids inhibit it. Catecholamines, in turn, are able to inhibit (by means of the alpha 1-adrenergic receptors) and to stimulate (by means of the alpha 2-adrenergic receptors) the secretion of TSH. Experimentally, tumor necrosis factor (TNF) and interleukin inhibit TSH secretion and may play a role in entyroid sick syndrome. It is not clear to what extent T4 itself acts within the pituitary; however, there are other factors that modify TSH secretion and its response to TRH. Both somatostatin and dopamine appear to be physiological inhibitors of TRH secretion. 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The thyroid is a gland that includes two endocrine systems: the first produces thyroid hormones (T3 and T4), the second calcitonin. The thyroid is a follicular gland that is made up of millions of vesicles (follicles) within which thyroid hormones are stored. Calcitonin, on the other hand, is produced by cells located outside the follicles (C or parafollicular cells); it represents

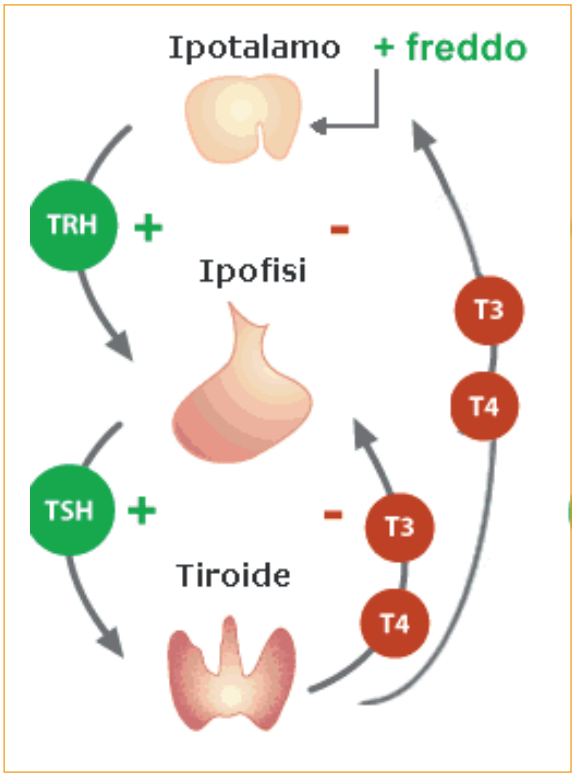

Fig. 2 - physiology of the thyroid gland.

the only case of an endocrine gland that possesses the ability to accumulate the secretion, before it is poured into the bloodstream, in the extracellular area as the hormones, linked to an iodinated glycoprotein (thyroglobulin), accumulate in the follicular lumen under colloid shape.

3. PATHOLOGY OF THYROID NEOPLASIES

Follicular adenoma is a benign capsulated thyroid neoplasm with evidence of follicular cell differentiation. It is the most frequent thyroid neoplasm and can be detected in a variable percentage between 4% and 20% of the thyroid glands examined during an autopsy. The tumor is usually solitary and has a fibrotic capsule which is microscopically complete, with an evident difference between the tumor structure and the surrounding parenchyma which is compressed by the neoplasm. The diameter of the lesion is variable but included, on average, between 10 and 30 mm. at the time of excision. The phenomena of intranodular degeneration are relatively frequent, but less than in hyperplastic and colloid-cystic goiter nodules, and may include hemorrhages, edema, fibrosis, calcifications and cystic degeneration.

Trabecular adenoma has a high cellularity and consists of columns of cells organized in compact cords. Detectable follicular formations are small in size and rarely contain colloidal material. Hyalinizing trabecular adenoma represents a variant and is characterized by the hyaline appearance both at the cytoplasmic level and in the extracellular spaces: it can recall the structure of papillary and medullary carcinoma but is invariably benign. Micro-, normo- and macrofollicular adenomas owe their name to the size of the follicular structures compared with the follicles of the healthy glandular tissue surrounding the tumor. The histological differences between these subtypes are of no clinical significance: however, it must be remembered that the greater the cellularity of an adenoma, the more accurate the search for any signs of malignancy must be. The most important cytological variant of follicular adenoma is represented by oxyphilic cell adenoma which is predominantly composed of large cells with eosinophilic and granular cytoplasm. The ultrastructure of these cells demonstrates numerous mitochondria and exhibits nuclear pleomorphism with the presence of distinct nucleoli. These neoplasms are all potentially malignant even if the clinical course is closely correlated with the initial histological appearance and the absence of invasiveness predicts a benign course Some normofollicular adenomas contain pseudo-papillary structures that can cause confusion with papillary carcinoma: these structures are probably the morphological expression of a localized metabolic hyperactivity as evidenced by their preferential expression in nodules endowed with functional autonomy. These tumors produce excess thyroid hormones independent of TSH and exhibit high uptake of thyrotropic radiopharmaceuticals compared to the remaining glandular parenchyma. When these neoplasms are associated with hyperthyroidism they are defined as "toxic" adenomas: generally these neoplasms are micro- or normofollicular adenomas and the cells grouped in pseudo-papillae tend to assume secretory morphology, similar to that observed in Graves-Basedow's disease . Atypical adenomas are hypercellulated lesions with histological features suggestive of malignant evolution but which do not show signs of invasiveness.

Papillary thyroid carcinoma

Papillary thyroid carcinoma (PTC) represents the most common malignant neoplasm of the thyroid gland, constitutes 50-90% of differentiated thyroid malignancies and has been defined as "a malignant epithelial tumor that demonstrates evidence of follicular cell diffusion and is characterized by papillae formation and / or a variety of nuclear alterations ". The nuclei of PTC cells have a characteristic appearance whose diagnostic significance has the same power as the presence of papillary structures. The PTC can be localized anywhere in the thyroid gland and generally appears as a nodular lesion with a diameter greater than 15 mm., Adhering to the glandular structure, not encapsulated or partially encapsulated. In its context, intra-nodular calcifications or cystic degenerations may be detected and occasionally papillary structures may be macroscopically highlighted. It is also possible to detect areas of hemorrhage or cholesterol collections while necrotic processes are infrequent and, if present, are generally attributable to previous FNAB.

The TNM system classification is widely used for PTC, however post-operative staging and prognostic stratification depend not only on the TNM but also on the patient's age (less than or greater than 45 years). Most patients with PTC have stage I (60%) or stage II (22%) disease. Patients over 45 years old with lymph node metastases or extra-thyroidal extension of the disease (stage III) represent just under 20% of cases while only 1-3% of patients have distant metastases and are in stage IV (age> 45 years with each T and N, M1). In pediatric age, the neoplasm generally presents significant dimensions and an extra-thyroid extension at diagnosis, with extracapsular extension, lymph node involvement and possible pulmonary metastasis. Finally,

Relapses and mortality PTC can present three types of disease recurrence after primary surgery:
a) local recovery b) lymph node metastases c) distant metastasis
Local recurrence is defined as "histologically confirmed tumor disease detected at the level of the thyroid lodge, any residual thyroid tissue or other adjacent cervical tissues, excluding lymph nodes" after complete excision of the primary tumor. Lymph node and distant metastases are considered postoperative if detected 30 days and 180 days after surgery, respectively. Ideally, the diagnosis of disease recurrence can only be made if found in patients without metastases at the time of diagnosis who have received complete resection of the primary disease. The incidence of local recurrence, lymph node metastases and distant metastases is, respectively, 6%, 9% and 5%. Compared to follicular thyroid cancer,
Follicular carcinoma
Thyroid follicular carcinoma (FTC) is defined as "an epithelial neoplasm that presents evidence of follicular cell differentiation but for diagnostic characteristics typical of PTC". This definition excludes the follicular variant of PTC as well as islet carcinoma and the mixed follicular-medullary form from the definition of follicular carcinoma. Finally, the correct classification of carcinomas with a predominant oncocyte component (Hurtle cell carcinoma) still remains controversial, even if many authors include these tumors in the context of follicular carcinoma: the WHO committee, in fact, defined this neoplasm as "variant a oxyphilic cells of follicular carcinoma "while the AFIP emphasizes that" this neoplasm has cytogenetic and structural characteristics, microscopic and macroscopic, so different from other differentiated thyroid carcinomas, as to justify a separate treatment and classification. The FTC has an incidence dependent on iodine intake: in fact its incidence is 2-5% in geographical areas where iodine intake is sufficient while in iodine-deficient areas the FTC represents up to 25-30% of thyroid neoplasms.
Insular carcinoma
This histotype is defined as "tumor of follicular origin with biological and morphological characteristics intermediate between differentiated carcinomas and anaplastic thyroid carcinoma". The peculiar histological characteristic of this neoplasm is represented by the presence of rounded or oval-shaped tissue islands composed of small cells with a round nucleus. The predominant growth pattern is solid but micro-follicular structures are also evident, some of which may contain dense colloidal material. Proliferation occurs in an infiltrative manner and angio-invasion phenomena are extremely common. In many cases the neoplasm is larger than 50 mm. at diagnosis and intra-tumor necrotic phenomena are present, with exceeding of the margins and extra-thyroid invasion on macroscopic examination. The average age at diagnosis is about 55 years and the female: male ratio is about 2: 1. Insular carcinoma is aggressive and often lethal: metastases are common both at the regional and distant lymph node level, with bone, pulmonary and skeletal involvement and an overall mortality of 56% at 8 years from diagnosis. Probably some thyroid neoplasms formally defined as undifferentiated compact small cell carcinomas actually belong to this histotype.
Anaplastic thyroid cancer
Anaplastic thyroid carcinoma constitutes about 5-10% of malignant thyroid neoplasms and generally occurs around the 6th decade of life with a slight prevalence in women (1.3-1.5: 1). The neoplasm is characterized by a high degree of malignancy, a rapid invasion of adjacent structures and a frequent diffuse distant matastatisation. Anaplastic carcinoma presents as a non-capsulated and diffusely extended tumor in the context of the thyroid gland, whose macroscopic morphological characters appear completely distorted by the neoplasm. The glandular consistency varies from extreme hardness (stone-like) to the presence of soft or friable areas and it is common to notice invasion of vascular, nervous, laryngeal, esophageal and tracheal, muscle and skin structures. The histopathological structure demonstrates how the neoplasm is composed of atypical cells with numerous mitotic figures that determine a polymorphic growth pattern. Spindle-shaped cells and multinucleated giant cells constitute the predominant cellular component but a squamous histotype is described in which undifferentiated cells predominate which, however, retain epithelial characteristics. Necrotic areas and polymorphonuclear infiltration are common and the coexistence of PTC or FTC type histological features suggests that these histotypes may be the precursors of the development of anaplastic carcinoma. The recognition of normal thyroid tissue may require meticulous and accurate sampling within the gland, almost entirely subverted by the neoplasm: It is interesting to note that mutations in the p53 gene are frequently detectable in anaplastic carcinoma but have never been detected in residual normal tissue. This finding seems to indicate that mutations in the p53 gene arise after the development of the original tumor and may play a crucial role in the anaplastic transformation of the tumor and in tumor progression. The prevailing clinical picture is represented by a rapid and painless development of a cervical mass or by the rapid dimensional increase of a thyroid nodule already present for some years. The neoplasm rapidly invades extra-thyroid structures causing related symptoms such as dysphagia, dyspnoea and inspiratory stridor. Often the skin overlying the neoplasm is discolored and hot. Palpation maneuvers demonstrate hardness, the irregularity and fixity of the neoplastic mass. Regional lymph nodes are almost constantly palpable and there may be evidence of distant metastasis. Anaplastic carcinoma generally does not pick up RAI and widespread neoplastic thyroid infiltration can cause associated hypothyroidism. The prognosis is poor and the patient generally dies within a few months after diagnosis.

Medullary thyroid carcinoma
Medullary thyroid cancer (MTC) accounts for about 10% of malignant thyroid neoplasms and generally occurs over the age of 40, with a slight prevalence in women. This neoplasm easily invades the intra-glandular lymphatic vessels, spreading within the thyroid itself, the capsular region and the loco-regional lymph nodes. This behavior is similar to that of PTC but, just as often, TCM spreads by hematogenous route with metastasization in the skeleton, liver and lungs. The neoplasm appears as a mass of increased consistency and is usually not encapsulated. The salient histopathological characteristic is represented by the presence of cells of polyhedral morphology, with an extremely variable structural architecture, which never cause papillary or follicular growth. Neoplastic

cells may have an undifferentiated appearance and exhibit mitotic figures but typical features of anaplastic carcinoma such as necrosis and polymorphonuclear infiltration are typically absent. Characteristically there is the presence of abundant hyaline connective stroma positive to Congo red staining for the amyloid substance. Macro- or microscopic foci of carcinomatous infiltration can be seen in other regions of the gland in addition to the primary site and vascular infiltration can be detected. The histopathological aspect of the metastases resumes that of the primary tumor. Clinically, TCM presents as a thyroid nodule of increased consistency but, sometimes, the first sign of the neoplasm is constituted by the relief of cervical lymphadenopathies and occasionally by the relief of distant metastases. Neoplastic lesions can be bilateral and usually involve the upper 2/3 of the gland, in accordance with the normal topography of C-parafollicular cells. In fact, TCM derives from C-parafollicular cells and secretes high concentrations of the typical hormone produced by these cells, calcitonin, and is often associated with one or more endocrine manifestations. The possibility of having an early biohumoral signal (calcitonin hypersecretion) is a useful diagnostic tool as well as an important parameter for monitoring therapy. TCM can occur sporadically and, in about 20% of cases, in familial form (FMTC). The FMTC variant occurs at a young age, often with bilateral involvement while it is less frequently associated with cervical lymph node metastases at diagnosis and has a better prognosis than the sporadic form. In particular, it should be emphasized that the FMTC variant is preceded by a phase of pre-malignant C-cell hyperplasia (CCH) which can be treated by prophylactic total thyroidectomy. The extent of MTC was first described in 1959 and the first group of cases included sporadic MTC with TNM stage II or III in about 80% of patients. In particular, it should be emphasized that the FMTC variant is preceded by a phase of pre-malignant C-cell hyperplasia (CCH) which can be treated by prophylactic total thyroidectomy. The extent of MTC was first described in 1959 and the first group of cases included sporadic MTC with TNM stage II or III in about 80% of patients. In particular, it should be emphasized that the FMTC variant is preceded by a phase of pre-malignant C-cell hyperplasia (CCH) which can be treated by prophylactic total thyroidectomy. The extent of MTC was first described in 1959 and the first group of cases included sporadic MTC with TNM stage II or III in about 80% of patients.

Lymphoma-Malignant It is a rare thyroid cancer, characterized by a neoplastic proliferation of B lymphocytes that form large follicles that replace the entire thyroid gland. Depending on the degree of differentiation of the neoplastic lymphoid cells, the lymphoma will be large B cells; follicular type; MALT-lymphoma.

Mesenchymal tumors

Tumors that arise from mesenchymal cells (cells that produce blood and lymphatic vessels, bone tissue, adipose tissue, muscle, collagen tissue and fibrous tissue) may rarely develop in the thyroid gland. These tumors can be benign and malignant. So we have leiomyoma, angiolipoma, the*thyrolipoma, lymphangioma, schwannoma* and the malignant counterpart: leiomyosarcoma, angiosarcoma, liposarcoma, osteosarcoma.

Thyroiditis

Thyroiditis includes inflammatory diseases of various etiology that can be distinguished, from both a temporal and anatomo-pathological point of view, in acute, subacute and chronic. Acute thyroiditis are rare diseases, mainly caused by bacterial infection (a real intrathyroid abscess), sustained in most cases by pyogenic streptococcus, staphylococcus aureus and pneumococcus pneumoniae, and characterized by painful symptoms in the anterior region of the neck, dysphagia, dysphonia and fever. Transient thyrotoxicosis is rarely observed, in relation to'increased release of thyroid hormones into the circulation caused by rupture of the follicles due to'inflammation. Subacute thyroiditis includes the granulomatous (or De Quervain) and silent forms. The first, with a viral etiology (frequently supported by Coxsackie virus, Epstein-Barr virus,'influenza, adenovirus), and the most frequent cause of pain in the anterior neck region. In the first 4-6 weeks there is an increase in circulating thyroid hormones (sometimes followed by transient hypothyroidism), but in general with restoration of normal thyroid function. Silent thyroiditis (also called painless thyroiditis) is characterized by transient hyperthyroidism and is divided into sporadic and postpartum forms. L'etiology is unknown, however in both forms attributed to autoimmune pathogenesis. Chronic forms include, finally, chronic lymphocytic thyroiditis (Hashimoto's thyroiditis) and ligneous (or Riedel's) thyroiditis. Hashimoto's thyroiditis (also called lymphomatous struma, due to anatomo-pathological alterations), mainly affects the female sex (80% of cases) and is the first cause of hypothyroidism in non-iodo-deficient areas. Recognizes an autoimmune pathogenesis linked to the production of antithyroid autoantibodies; in fact, in 95% of cases, high levels of anti-TPO antibodies and, to a lesser extent, of anti-thyrooglobulin (anti-Tg) antibodies are found. Although the events leading up to the autoimmune process are not fully understood, genetic predisposition plays a certain role (frequent association with HLADR5 and DR3 haplotypes). In patients with chronic lymphocytic thyroiditis it is more frequent than in the general population'onset of non-Hodgkin's thyroid lymphomas. Riedel's thyroiditis is a rare pathology characterized by a fibrosclerotic process of unknown etiology that replaces the normal glandular parenchyma, being able to determine a final picture of hypothyroidism.

4. NODULAR PATHOLOGY OF THE THYROID

Nodular thyroid disease is extremely common and includes, from a semeiotic point of view, both single or multiple clinically detectable nodular lesions and non-palpable nodular lesions occasionally detected during diagnostic imaging. The prevalence of clinically detected thyroid nodular lesions in the United States ranges from 4% to 7%, with an annual incidence of 0.1%. The overall lifetime risk of developing clinically detectable nodular thyroid disease is 10%. Estimating an annual survey of approximately 275,000 thyroid nodules, however, only 14,000 will result in carcinomas. Therefore a minimal percentage of clinically palpable thyroid nodules is represented by malignant neoplasms: approximately only 1 in 20 nodules (5%) is neoplastic, with an annual incidence of thyroid carcinomas of

0.004%. Also considering the non-palpable nodules, the percentages increase significantly: autopsy and ultrasound studies estimate that 40-50% of the US population is carriers of 1 or more thyroid nodules. The prevalence of nodular disease increases linearly in correlation with age, exposure to ionizing radiation and iodine deficiency. In this regard, it must be emphasized that many geographical areas still present a deficit in the dietary iodine supply: in these areas the nodular pathology is widely represented and, in particular, the evolution of uni or multinodular forms towards functional autonomy and hyperthyroidism. In all geographical areas and in all groups of patients, the incidence of nodular disease is significantly higher in women than in men. Since most clinically detected nodules are benign in nature, the goal of diagnostic procedures should be to select malignant nodules for aggressive treatment and to avoid unnecessary surgery in most benign disease. A correct diagnostic procedure of the nodular pathology cannot be separated from a careful clinical evaluation based on the knowledge of the epidemiological data and on the basic semantic definitions in which to place the clinical picture detected. Since most clinically detected nodules are benign in nature, the goal of diagnostic procedures should be to select malignant nodules for aggressive treatment and to avoid unnecessary surgery in most benign disease. A correct diagnostic procedure of the nodular pathology cannot be separated from a careful clinical evaluation based on the knowledge of the epidemiological data and on the basic semantic definitions in which to place the clinical picture detected. Since most clinically detected nodules are benign in nature, the goal of diagnostic procedures should be to select malignant nodules for aggressive treatment and to avoid unnecessary surgery in most benign disease. A correct diagnostic procedure of the nodular pathology cannot be separated from a careful clinical evaluation based on the knowledge of the epidemiological data and on the basic semantic definitions in which to place the detected clinical picture.

- Goiter is defined as any increase in the thyroid gland volume of a diffuse (diffuse goiter) or regional (uni- or multinodular goiter) character.
- In particular, a palpable thyroid nodular alteration is identified as a single thyroid nodule or uninodular goiter. Many palpable nodules remain relatively dimensionally stable over time while others may increase or decrease in size and occasionally the disappearance of previously objectivable nodular formations may be observed.
- Multinodular goiter is defined as an increase in thyroid size with more than one clinically objective nodular formation.

In relation to the functional structure, many nodules are hypofunctional compared to the normal thyroid parenchyma but others maintain normal activity and some develop an autonomous function, not subjected to the physiological regulation of the hypothalamus-pituitary-thyroid axis. Autonomous nodules can, particularly with increasing age, increase their volume and secrete an excessive amount of thyroid hormones. The initial picture of euthyroidism can therefore turn towards a sub-clinical hyperthyroidism and, finally, towards a picture of overt thyroid hyperfunction. Although the evolution towards a form of overt hyperthyroidism is rare in the case of an initially compensated hyperfunctioning nodule (about 2-3%), the presence of an autonomous nodule and TSH inhibition even in the presence of normal circulating levels of thyroid hormones, they are important risk factors for hyperkinetic arrhythmias and, in particular, for atrial fibrillation. In relation to the extremely frequent finding of nodular thyroid pathology but to an overall low incidence of malignant thyroid neoplasms, it is clear that the main objective of the diagnosis of thyroid nodules must be the exclusion of malignant pathologies, in order to avoid surgical interventions that, in the vast majority of cases, they would be inappropriate.

4.1 Clinical framework - objective and laboratory

The data detectable from the personal history of a patient with nodular thyroid disease can be of considerable help in the diagnostic process of ascertaining the benign or malignant nature of the lesion itself. Exposure to ionizing radiation in the neck region represents one of the most important risk factors for thyroid cancer, so much so that previous external irradiation on the neck in childhood is a central aspect of the anamnestic collection. A higher incidence of papillary histotype thyroid carcinoma was in fact observed in pediatric subjects undergoing radiotherapy of the neck or upper mediastinum for hyperplasia of the thymus, tonsils, adenoids or Hodgkin's lymphoma. The age of irradiation and the radiation dose are particularly critical factors, while sex seems to be of lesser importance, although a greater susceptibility of female than male sex is reported. In particular, the risk of developing thyroid cancer decreases with the advancing age in which the irradiation took place, with a latency period estimated in about ten to twenty years. The latter, on the other hand, appears to be just six or seven years in the case of direct or indirect exposure (ingestion of contaminated food) to radioactive isotopes of iodine with a very short half-life (I123), as occurred after the Chernobyl nuclear disaster in 1986, in which there was a significant increase in the incidence of cancer in pediatric age of at least five times compared to that normally encountered. The anamnestic history of medullary thyroid carcinoma (CMT) must lead to the exclusion of those rare familial forms, which can be classified in the context of Multiple Endocrine Neoplasms (MEN) 2A, 2B or Isolated Family Medullary Carcinoma (FMTC). Of less epidemiological impact, but of considerable clinical relevance, is the anamnestic finding of rare family diseases, such as multiple colon polyposis, Gardner's syndrome, Cowden's disease, and Carney's syndrome, which may be associated with a high degree of prevalence of thyroid nodules and thyroid cancer, especially papillary type. Gender and age of onset of a thyroid nodule are not considered important risk factors for malignancy, although some epidemiological studies show that the probability that a thyroid nodule is malignant increases when this is found in a male subject aged> 60 or <25 years. The clinical evolution of the nodule over time is also important for a correct diagnosis: rapid growth over weeks or months must be suspected, particularly if treated with levothyroxine (L-T4). The fact that the node appears as a single lesion or in the context of a multinodular goiter is of little influence. Any compressive symptoms that may express themselves with dyspnea, dysphagia and / or dysphonia, the latter particularly suspected for malignancy if associated with ipsilateral paresis of

the vocal cord, must also be carefully evaluated. With regard to the relationship between thyroid carcinoma and autoimmune thyroid diseases, it should be borne in mind that in Hashimoto's thyroiditis the risk of malignancy does not appear to be increased, while the detection of "pseudo-nodules" that require careful ultrasound evaluation is frequent. A slight increase in malignant disease was instead reported in the cold nodules inserted in the context of Basedow's disease.

4.2 Objective review

The objective examination of the thyroid is of fundamental importance in the diagnosis of benign and malignant neoformations of the thyroid, providing a first impression of the pathology in question, also taking into account the ease of access to the region. In fact, it is possible to appreciate in the first instance the general characteristics of the thyroid region and in particular the apparently single or multiple nodular character, the tumor character (as a differential diagnosis with simple goiters), or on the contrary, in some cases, the massive invasion of the gland. The inspection of the neck should be performed in profile, making the patient extend the head and then inviting him to swallow the saliva, or, preferably, making him drink a glass of water in small sips: the observation of the upward displacement of a mass of the anterior region of the neck is a characteristic element to believe that it is of a thyroid nature, this is because during swallowing the thyroid rises together with the larynx. Therefore it is necessary to consider the characteristics of the skin: appearance, color, evaluate the temperature and other characteristics such as any pulsations and dermographism as an expression of vasodilation; in case of acute thyroiditis, for example, the skin has the characteristics of inflammation. Palpation under normal conditions does not reveal the thyroid gland. The palpatory relief of the gland is usually an expression of pathology. Palpation must be careful, with the patient seated, and with the help of swallowing movements. The examiner is generally placed at the side of the patient or behind in the case of bimanual palpation; in this second way, however, the complete relaxation of the pretyroid muscles is often not obtained: to make the neck muscles relax, the left hand is placed on the patient's head and its passive flexion is determined; the right hand is used for palpation. If the thyroid has increased in volume, palpation is performed by passively flexing the head. To make a nodule palpable in a lateral position, below the sternocleidomastoid muscle, the trachea can be moved by pressing it on the side opposite the lobe to be explored: the nodule can thus slide laterally to the sternocleidomastoid muscle and become palpable. With palpation, the motility of the overlying skin and the motility of the gland on the deep planes, in block with the larynx, are first assessed. Then we appreciate the consistency of the mass, its size, tenderness on palpation and pain. On palpation, the thyroid mass may have a smooth surface (parenchymatous goiter) or lumpy (multinodular goiter). As for the consistency, it should be remembered that the thyroid, when hyperplastic, as in goiter, has a parenchymatous consistency; calcific nodules are an exception; a malignant nodule may appear more consistent and sometimes woody. However, this last figure does not have general characteristics for diagnosing cancer. A thyroid mass may also have a tense-elastic consistency (thyroid cyst). Cervical lymph nodes should be looked for. Then we move on to the evaluation of the vocal cords; it is always advisable to evaluate the motility of the vocal cords, for diagnostic purposes (if there is paralysis of one or both vocal cords, a sign of recurrent nerve infiltration, it will probably be an aggressive and locally advanced malignant neoformation), and for medical purposes legal before surgery, to exclude a pre-existing paralysis of a vocal cord, even more so if it is a reoperation. At the end of the physical examination, a first classification can be made that allows to distinguish the various types of neoplasia: for diagnostic purposes (if there is paralysis of one or both vocal cords, a sign of recurrent nerve infiltration, it will most likely be an aggressive and locally advanced malignant neoformation), and for forensic purposes before surgery, to exclude a pre-existing paralysis of a vocal cord, even more so if it is a reoperation. At the end of the physical examination, a first classification can be made that allows to distinguish the various types of neoplasia: for diagnostic purposes (if there is paralysis of one or both vocal cords, a sign of recurrent nerve infiltration, it will most likely be an aggressive and locally advanced malignant neoformation), and for forensic purposes before surgery, to exclude a pre-existing paralysis of a vocal cord, even more so if it is a reoperation. At the end of the physical examination, a first classification can be made that allows to distinguish the various types of neoplasia: even more so if it is a re-operation. At the end of the physical examination, a first classification can be made that allows to distinguish the various types of neoplasia: even more so if it is a re-operation. At the end of the physical examination, a first classification can be made that allows to distinguish the various types of neoplasia:

1. Benign tumors

They occur under various clinical aspects: isolated node, simple goiter, multinodular, etc. Simple goiter: it is defined by its homogeneous character more or less elastic on palpation. Isolated nodes: details on size, location, consistency (a very hard lump is particularly suspect) and sensitivity. They allow to distinguish:

- Cysts: in typical cases they have a hard consistency or more or less elastic on palpation; however, this impression can be masked by the thickness of the nearby parenchyma. The evolution can be characterized by a sudden growth, often in connection with an intracystic hemorrhage capable, at least in theory, of causing a compression, which is actually very rare.
- Adenomas: tendency to increase in volume slowly; a sudden increase in volume most often corresponds to a hematocele.
- Hot nodule (defined by its hyperfixing character on scintigraphy) is a nodule that does not present any particularities. There appears to be a correlation between the size of the nodule and its functional activity. Toxic nodules are usually 4 cm or more.
- Toxic node: from the first physical examination it is possible to diagnose a toxic nodule on the basis of clinical signs of hyperthyroidism, or hyperthyroid multinodular goiter, which is the most frequent cause of thyrotoxicosis after Graves' disease.
- Multinodular goiter: it can be voluminous with palpable nodules of heterogeneous consistency which happens, in a certain number of cases, to a simple goiter already present for some time.
- Immersed goiters whose lower pole cannot be hooked with the fingers in a position of

extreme extension of the head; the instrumental examinations will allow to distinguish the true immersed goiters from those that touch the cervicothoracic strait. In case of endothoracic development there may be signs of compression.

2. Malignant tumors

They come in different clinical forms. Some clinical elements allow us to think about this possibility: rapid growth of the nodule, irregularity, paralysis of a vocal cord, fixation to adjacent structures, an isolated nodule in a man, the presence of cervical adenopathies, and also anamnestic characters such as the age of the patient (most thyroid cancers occur between 40 and 60 years, but the risk is highest for patients under the age of 20), exposure, especially in childhood, to radiation ionizing, family history of thyroid cancer.
They are distinguished:

- Differentiated carcinoma:
  - Papillary carcinoma: the typical clinical appearance is an isolated node in the thyroid lobe. Laterocervical adenopathy is sometimes found mostly supraclavicular.
  - Follicular carcinoma: classically occurs as an isolated lump greater than 1 cm in diameter
- Medullary carcinoma: Diagnosis starts with the presence of a mono or bilateral goiter, sometimes accompanied by a characteristic symptomatology that includes diarrhea and flushing. In the familial form, it can be discovered in a subclinical stage, during a family investigation or evaluation of a pheochromocytoma, in the presence of a pseudo-Hirschprung (linked to a hyperplasia of the nerve plexuses of the colon), a Cushing-type paraneoplastic syndrome , or in the presence of clinical signs that suggest Gorlin syndrome. This is mostly formed progressively and becomes typical during growth, with the appearance of skeletal dimorphism: large lips, enlarged nose root, thick and inverted eyelids, hypertrophic gums, pointed palate; the subject has a long-limbed, marfanoid morphology, with hyperlaxity of the ligaments, hollow feet, valgus knee, lordosis, scoliosis, funnel chest, underdeveloped musculature. Neuromatosis is widespread with labial, lingual and eyelid involvement in the form of bubbles of varying sizes; in the familiar forms there may also be skin lesions, pigment spots or lichen.
- Undifferentiated carcinoma: the most frequent clinical manifestation is the appearance of a rapidly evolving cervical mass, accompanied by dysphonia, dysphagia, or even dyspnoea. Cervical pain is reported in one third of cases. At the initial examination the node is often hard, fixed, bilateral, measuring more than 5 cm and accompanied by adenomegaly. Locoregional and metastatic invasion was found in 60% of patients.
- Primary lymphoma of the thyroid: it is a rapidly evolving tumor, more often nodular than diffuse, often painful, and responsible for a compression syndrome. In 20% of cases, satellite cervical adenopathies are found during the first examination.

4.3 Diagnostic protocol

The diagnostic process of the thyroid nodule has undergone an evolution over time, correlated with scientific progress, knowledge of pathophysiology (immunohistochemistry with biological markers: thyroglobulin, calcitonin, galectin 3 and drugs: recombinant human TSH) and also technological innovations: ultrasound-guided cytoaspirate (the method has significantly improved thanks to the support adapted to the ultrasound probe for aiming) and PET. In the 1990s the first choice investigation was scintigraphy, followed by function tests and / or ultrasound and subsequently by FNAB (Fine Needle Aspiration Biopsy). Currently, in the presence of a clinically manifest thyroid nodule, the first choice examination is ultrasound together with function tests. Ultrasound has become an indispensable element for diagnostics and can also be used during needle biopsy. The diagnostic protocols proposed by the Italian authors, or cited in the national and international guidelines (CNR / MIUR, NCCN) for the diagnosis of clinically manifest thyroid nodules, highlight an overlapping path that favors ultrasound and functional tests. First of all, an anamnestic and clinical evaluation is carried out, then the ultrasound and the dosage of thyroid hormones, of the TSH of antithyroid antibodies and of calcitonin. Based on the results, it was decided to carry out the scintigraphy which allows us to distinguish hot or cold nodes. If the lump is warm on scintigraphy, the presence of tumor pathology is generally excluded and the subsequent procedure depends on the presence of clinical or biochemical signs of thyrotoxicosis and on the size of the nodule; if the node is scintigraphically cold and cystic, a diagnostic FNAB will be carried out by cytology on the sediment of the centrifuged liquid and therapeutic (thanks to evacuation). Whether the lump is cold and solid, or only partially cystic, treatment decisions will depend on the result of the cytology. Cytology, now recommended in all major centers, is of fundamental importance as ultimately the diagnostic evaluation of a thyroid nodule is mainly based on the result of the cytology. This must be performed systematically in all thyroid nodules greater than one centimeter in diameter and must be interpreted by an experienced cytologist. Based on the result of the cytology, a possible surgical indication will be made. Only in selected cases will CT and MRI be performed. The measurement of circulating anti-thyroid antibodies, calcitonin and calcium is advisable only at the first evaluation of the patient. We underline the importance of calcitonin as a specific tumor marker of medullary carcinoma, not recommended by the American authors who consider this practice uneconomical. The execution of other tests depends on the habits of each center and the practical possibility of performing them, this factor often determines the differences in behavior between different centers. Based on the result of the cytology, any surgical indication will be made. Only in selected cases will CT and MRI be performed. The measurement of circulating anti-thyroid antibodies, calcitonin and calcium is advisable only on the occasion of the first evaluation of the patient. We underline the importance of calcitonin as a specific tumor marker of medullary carcinoma, not recommended by the American authors who consider this practice uneconomical. The execution of other tests depends on the habits of each center and the practical possibility of performing them, this factor often determines the differences in behavior between different centers. Based on the result of the cytology,

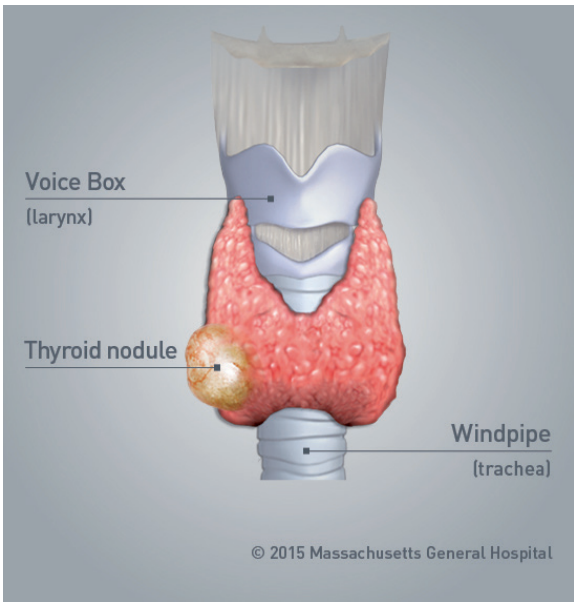

Fig. 3 - thyroid nodule.

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5. MORPHO-FUNCTIONAL EXPLORATION OF THE THYROID

5.1 Ultrasound

Thyroid ultrasound has become an extremely widespread investigation due to its simplicity and non-invasiveness and is today the most requested imaging investigation, in the first instance, in the face of nodular thyroid pathology. The use of high frequency "small parts" probes (7.5 - 10 MHz and above) allows to obtain an excellent anatomical representation of the thyroid and surrounding structures and to identify very small thyroid lesions (2-3 mm.). Unfortunately, precisely because of the very high sensitivity in identifying lesions but also of minimal eco-structural alterations devoid of any clinical significance, thyroid ultrasound demonstrates extremely low tissue specificity and also cannot be used for definitive discrimination between benign and malignant nodules. Finally, although the search for thyroid nodules remains a common indication for the request for thyroid ultrasound, scientific evidence has recently reduced the role of this diagnostic method, based on some general considerations:
1) thyroid nodules are very frequent but malignant nodular pathology is relatively infrequent; 2) clinically non-palpable ultrasound nodular changes are extremely common: undergoing thyroid ultrasound; 3) the finding of small non-palpable nodules associated with a clinically dominant nodule does not change the risk of thyroid malignancy or the incidence of thyroid malignancy does not significant modification in uni and multinodular goiter; 4) in the case of a clinically significant nodule associated with small ultrasound nodules, the cytological investigations must in any case be directed to the dominant nodule; 5) the assumption that ultrasonographically cystic nodules are benign is unfounded. A higher than expected incidence of malignancy has also been described in cystic nodules. Palpation and ultrasound revealed 24% and 43%, respectively, of the nodules identified by the pathologist. In any case, it must be emphasized that the average diameter of these nodules was 3 mm. and that the identification of nodules of this size has no definite clinical significance;
The main indications for performing a thyroid ultrasound can be summarized as follows:
1) difficulty in cervical palpation maneuvers (eg. "Squat" neck) 2) targeted assessment of non-palpable nodules highlighted scintigraphically 3) screening of thyroid nodules in patients at risk (eg previous external irradiation of the neck) 4) determination of volume of thyroid and thyroid nodules, if clinically useful and with the limitations exposed 5) execution of ultrasound-guided FNAB on small nodules or nodules difficult to access directly (e.g. retro-sternoclavicular nodules) 6) pre-operative study, morphological and topographical, of the thyroid and cervical region.
An absolutely fundamental role of thyroid ultrasound, thanks to its high sensitivity, is instead reserved for the study of the thyroid lodge and cervical lymph nodes and for the screening of small recurrences of thyroid cancer after thyroidectomy and possible radiometabolic treatment. With ultrasound you can: Measure the exact size of the gland, calculate its volume and evaluate the response of an enlarged thyroid to treatment (fig. 4)

- Check for the presence of a nodule, measure it in three dimensions, examine its characteristics (solid, liquid, mixed), margins, relationships with other structures.
- Evaluate the response to therapy of a single nodule.
- Follow up a tumor-operated patient to evaluate a possible relapse.
- Perform a guided biopsy when the lump is small or near delicate structures such as arteries.
- With the Doppler technique associated with ultrasound it is possible to study the

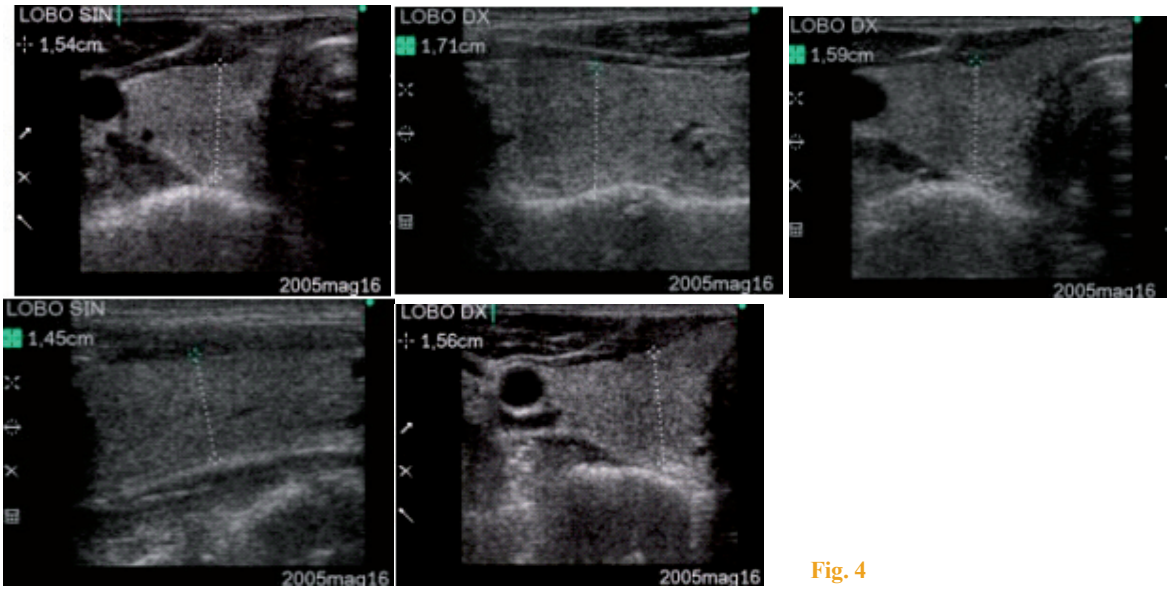

Fig. 4

vascularization of the thyroid or of a single nodule and obtain important information about its functionality and metabolic activity.

There are no ultrasound semeiological elements that identify with certainty each histotype of differentiated thyroid tumors, but signs that guide us towards a selection of the nodules to be entrusted to cytology. The isoechogenicity of the nodules is an ultrasound element that can orient us towards a benignity of the nodule, especially if associated with anechoic micro-areas that are suggestive of hyperplastic nodules with cystic colloid involution.
Uniformly isoechoic nodules with peripheral vascular ring and internal vascular response orient towards a cytological diagnosis of follicular proliferation to be clinically framed with scintigraphy and TSH and possibly sent to histology. The hypoechogenicity of the nodules was the first ultrasound sign of possible malignancy reported by ultrasound in 80-90% of TDT (thyroid tumors).
The sensitivity in selecting suspicious nodules increases reaching almost 100% with two other ultrasound diagnostic elements which are internal vascularization (Fig. 5) and micro calcifications (Fig. 6).

Micro calcifications are semiological elements suggestive of malignancy even if they are not very sensitive evaluated individually as they are present only in about 60% of TDTs.

5.2 Citoagoaspirazione

The main clinical problem in the management of the thyroid nodule is represented by the need to highlight the minority of malignant nodules in the context of the frequent finding of thyroid nodules, in order to initiate the former to an adequate treatment and avoid, for the latter, unsuccessful surgical interventions. necessary. Fine needle aspiration biopsy-FNAB is the most accurate procedure to determine if a nodule has enough risk elements to justify surgical resection or if the probability of benignity is so high that simple clinical observation is recommended. The selection of nodules based on clinical and laboratory criteria in fact determines surgical excision in at least 50% of patients: among these, however, 75% of the operations are unnecessary and the absolute benignity of the nodular formations is histologically detected. The advent of FNAB has radically changed the situation: in fact, the

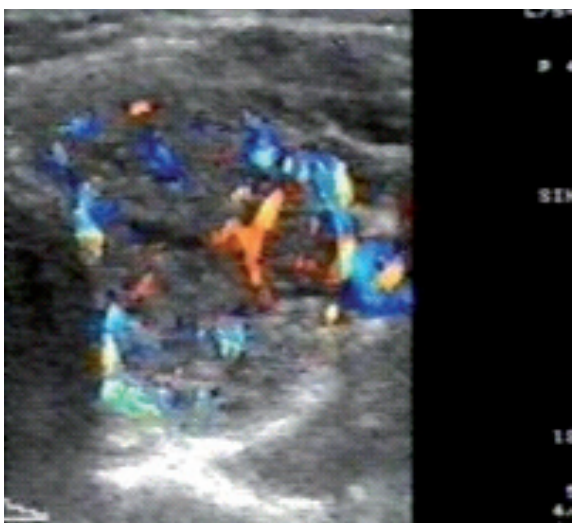

Fig. 5

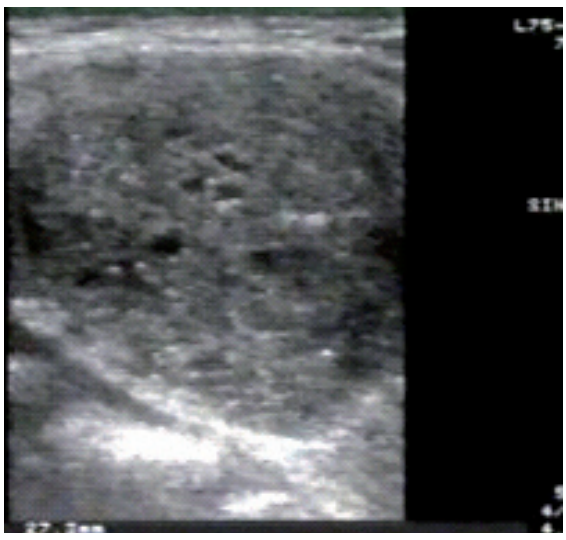

Fig. 6

surgical pre-selection based on FNAB reduces the need for surgery to less than 20% of nodular lesions and over 50% of these are malignant on definitive histological examination. The only palpable thyroid nodules that do not require cytoagoaspiration are those that present an increased uptake of radioiodine compared to the surrounding glandular parenchyma: these formations are autonomously functioning adenomas or functioning hyperplastic nodules which present an extremely low risk of malignancy but which may, at the same time, produce dubious or suspicious cytological pictures if subjected to FNAB. Since the probability of malignancy of nodules with a cystic component or of clinically significant nodules in the context of a multinodular goiter does not change substantially compared to single solid nodules and ultrasound does not provide discriminating information about the nature of the nodule, these lesions must also be subjected. a FNAB. The execution involves the participation of two operators. The patient is placed in the supine position with a thin pillow under the shoulders and the neck slightly extended. The second operator, seated behind the patient's head, identifies the nodular formation and, after disinfecting the skin plane, blocks it using both hands after having the patient perform a swallow. The first operator performs the cytoagoaspiration maneuver using a 20 cc syringe. connected with a 21 or 23G needle. After inserting the needle into the nodular formation, a moderate suction is exerted simultaneously with the execution of a delicate "back and forth" movement along the direction of the needle possibly associated with the rotation of the needle on its axis. These maneuvers end when material appears in the cone connecting the needle which is then extracted from the nodule. The needle is momentarily deconected and a few cc. of air are introduced into the syringe: at this point the needle is connected to the syringe and the air is blown with good pressure in order to spread the contents of the needle and the cone on the specially prepared slide. A second slide is affixed to the first in order to obtain two slides with the material coming from the sampling: the first is sent without fixation while the cytological fixator preferred by the cytopathologist is applied to the second slide. Generally at least 3 samples are performed for each nodular formation: the number of samples necessary to obtain a sufficient representation of the nodular cytology obviously increases in relation to the size of the nodule. In the presence of voluminous nodules, the frequent occurrence of colloid-cystic or colliquative intra-nodular degeneration must be remembered, generally more evident in the centronodular area: it is therefore necessary to proceed with sampling in the peripheral regions of the nodule where it is easier to find vital tissue. cytological diagnosis of malignancy is extremely accurate if carried out by an expert thyroid cytopathologist (2-5% of false positives) and, consequently, surgical excision is definitely recommended. A cytological diagnosis of benignity is equally reliable, if the sampling of the nodule has been adequate, and justifies a conservative attitude. However, there are particular conditions in which surgical excision may be indicated despite negative cytology such as, for example, a scintigraphic study demonstrating uptake of 99mTc-pertechnetate or radioiodine in the cervical lymph nodes or a family history of medullary thyroid carcinoma. A cytological diagnosis of suspected malignancy is less specific, indicating a probability of malignancy between 25% and 75%, but it is common opinion that surgical excision is necessary. The finding of follicular type lesions represents an important problem: the detection of cytological characters compatible with follicular adenoma or Hurtle cell adenoma (oxyphilic cells) in the absence of clear cytological atypia of malignancy (eg nuclear atypia) indicate a probability of neoplasia between 5% and 10%. However, many of these neoplasms will have a low degree of malignancy, with minimal capsular and / or vascular invasion and a consequent low probability of significant related morbidity or mortality. Unfortunately, if left "in situ" for years, such lesions can become aggressive and there are no definitive data on the safety of long-term observation of such lesions. The finding of follicular and oxyphilic lesions therefore requires the exeresis of the nodule and its histological examination for a definitive diagnosis of benignity (follicular adenoma, Hurtle cell adenoma) or malignancy (follicular carcinoma, Hurtle cell carcinoma). An FNAB with a non-diagnostic result requires repetition of the procedure: in about 50% of cases the second FNAB allows the diagnosis to be obtained. In case of further inadequacy of the sample, the procedure can be repeated under ultrasound guidance. In case of non-conclusive cytology, the use of oncotropic tracers and radiopharmaceuticals may be useful. In the presence of inconclusive cytology, however, the clinical decision relating to the exeresis or a conservative attitude (observation with or without treatment with l-thyroxine) must be taken on the basis of the epidemiological, clinical and instrumental data available but always informing and discussing with the patient the limits, risks and advantages of the various possible solutions. Hurtle cell carcinoma). An FNAB with a non-diagnostic result requires repetition of the procedure: in about 50% of cases the second FNAB allows the diagnosis to be obtained. In case of further inadequacy of the sample, the procedure can be repeated under ultrasound guidance. In case of non-conclusive cytology, the use of oncotropic tracers and radiopharmaceuticals may be useful. 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6. MEDICAL-NUCLEAR DIAGNOSTIC TECHNIQUES

Nuclear Medicine is a discipline based on in vivo and in vitro techniques, for diagnosis and therapy using radionuclides. The form of energy used in nuclear medicine is that emitted by the nuclei of unstable (radioactive) atoms during their transformation (decay) to stable forms. Nuclear medicine techniques can be classified into three categories:

1) Diagnostic imaging techniques
2) In vitro diagnostic techniques
3) Therapeutic techniques

Nuclear medicine is first of all a methodology for the in vivo investigation of biochemical, physiological and pathological processes. Nuclear medicine techniques allow to obtain results that in the process of diagnosis, prognostic evaluation and follow-up are integrated with information deriving from morphological investigations (X-ray, CT, MRI, Echo, endoscopies, etc.), laboratory and histopathological investigations. Nuclear medicine investigations allow to detect pathological processes at their onset (high sensitivity) even before the morphological damage is evident, and to characterize the nature of the lesions on the basis of biochemical aspects (high specificity) without having to resort to many cases to invasive techniques (biopsy and / or endoscopic). Nuclear medicine images are obtained following the in vivo administration of compounds labeled with radioactive atoms. These compounds, called radiopharmaceuticals, are distributed in the body according to the rules of pharmacokinetics. Nuclear medicine images therefore derive from the examination of the distribution in space and time of a radiopharmaceutical consisting of a vector and a source of radiant energy.
At the base of in vivo nuclear medicine procedures there is the vitality of the organism examined as a fundamental requirement, necessary so that the radiocompounds used can be distributed in tissues, organs and systems, on the basis of normal and pathological physiological processes and biochemical reactions. The image therefore derives from the revelation of an energy source internal to the subject under examination. The radionuclides used for in vivo diagnostic purposes must decay with the emission of electromagnetic radiation (X, γ) detectable by instruments placed outside the body of the subject studied because they are very penetrating. The γ emission, characterized by low linear energy transferred (LET), must be exclusive or largely prevalent over the emission of corpuscular radiation (α, β-) since the latter are not useful for the formation of diagnostic images and can produce undesirable biological effects if present in high quantities. Through the use of specific radiopharmaceuticals, nuclear-medical imaging allows to evaluate functional aspects and / or biochemical-metabolic processes that occur at the organ, tissue, and even cellular level; a radiopharmaceutical is generally constituted by the combination of a radionuclide (responsible for the signal detectable from the outside of the body) with a compound that determines the biological properties of the molecule. In addition to

their chemical structure, localization mechanism and possible therapeutic action, Radiopharmaceuticals are sometimes classified according to the type of "positive" or "negative" visualization they can produce in the specific diagnostic application. In particular, a positive indicator radiopharmaceutical accumulates electively where the pathological process takes place, directly highlighting the site of the specific metabolic alteration; on the contrary, a negative indicator radiopharmaceutical accumulates in the normal and functioning parenchyma of an organ and, therefore, the pathological process is highlighted as an uptake defect. However, this is not a rigidly fixed distinction since, depending on the different applications, some radiopharmaceuticals can behave as both positive and negative indicators. Eg, in the thyroid field, radioiodine or 99mTc-Pertechnetate are negative indicators in the case of non-functioning nodular pathology (so-called "cold" nodules), but become positive in the case of thyroid hyperfunction (nodular or diffuse type). Most of the radionuclides used in nuclear medicine are gamma-emitting and their use allows the production of planar or tomographic images by single photon emission (Single Photon Emission Computed Tomography, SPECT). However, in most of the radiopharmaceuticals currently in use, the radionuclide simply has the function of allowing (through its γ or β + emission) the scintigraphic localization of the distribution of the radiopharmaceutical itself inside the body or the spread of a certain therapeutic action (via its β- o emission, more rarely, α particles), while the characteristics of distribution and localization in certain districts depend on being incorporated into a more complex molecular structure with its own pharmacokinetics and pharmacodynamics (biological fate). The chemical reaction by which a radionuclide is inserted into the structure of a more complex radiopharmaceutical is the so-called "tagging reaction". Such marking can occur by direct replacement of a native atom of the original molecule with a radioactive isotope; for example, by replacing a native iodine atom (Iodine-127) of L-Thyroxine (thyroid hormone which normally contains four iodine atoms) with an Iodine-131 atom, we obtain a radioactive tracer identical to the original L-Thyroxine, whose distribution and metabolic fate within the body are therefore identical to those of the same L-Thyroxine produced by the thyroid. The radiopharmaceuticals obtained after radiolabelling with 99mTc cover 85% of the diagnostic investigations of a nuclear medicine department. This radionuclide is widely used because: (a) although its short half-life (6 hours) would theoretically limit its use, it is produced locally by a commercially available generator (Molybdenum / Technetium generator, 99Mo / 99mTc) which any nuclear medicine service can easily manage in the radiopharmacy laboratory because the physical half-life of the progenitor (99Mo) is 66 hours; (b) it is characterized by a fairly standardized chemistry that allows a fast and stable labeling of many drugs over time; (c) it has an optimal emission for gamma camera detection (whose NaI (Tl) crystals, in the thickness used for this instrumentation, have an optimal detection efficiency for γ energies between 100 and 200 KeV). The diagnostic information provided by the scintigraphic images derives from the characteristic distribution within the body of a radiopharmaceutical, generally injected intravenously (more rarely, the administration takes place by the oral or interstitial route). The main parameters that determine the scintigraphic information are the speed of disappearance from the circulation, the accumulation, the retention, and the clearance (or washout) at the level of a specific tissue of interest. Alterations of the state of physiological function in certain parts of the body are reflected in variations of these parameters (especially the retention and / or the disposal of the radiopharmaceutical in the tissue / organ under examination). For example, the increased accumulation of radioiodine in a thyroid nodule indicates an increased production of thyroid hormones by the nodule itself. The 99mTc-Pertechnetate ($99mTcO_4^-$), which is obtained in physiological solution directly by eluting the 99Mo / 99mTc generator, can be used as a real radiopharmaceutical. In fact, after iv administration the pertechnetate ions remain in equilibrium in the blood, partly free and partly bound to plasma proteins; thanks to their small size, the free ions easily leave the vascular compartment and, migrating towards the interstitial fluids, lower the blood concentration of pertechnetate, facilitating the release of the 99TcO share$_4^-$ bound to proteins (the visualization of vascular structures observed in early scintigraphic acquisitions is thus gradually reduced over time). From interstitial liquids, pertechnetate ions accumulate in the stomach, thyroid, salivary glands, intestines, choroid plexuses, mucous membranes in general (especially if equipped with exocrine secretion glands), and in the kidney (main physiological site of excretion). The accumulation of $99TcO_4^-$ in the thyroid parenchyma is mediated by the sodium-iodine cotransporter (Sodium-Iodide Symportero NIS) a transmembrane protein consisting of 643 amino acids arranged in 13 domains (with extracellular amino-terminal and in-tracellular carboxy-terminal), with a weight that, in depending on the degree of glycosylation, it can vary from approximately 79kDa to 90kDa. NIS, which is located on the basolateral membrane of thyroid cells, is capable of simultaneously transporting sodium and iodides from the extracellular space into thyroid cells with a stoichiometric ratio of 2: 1. This protein (whose expression is regulated by the level of thyrotropic hormone, by the amount of iodide in extracellular fluids, by thyroglobulin, and by some cytokines) is encoded by a gene on chromosome 19p12-13.2; a mutation of this gene resulting in reduced NIS function can cause congenital hypothyroidism. The extraction of iodine from the plasma and its concentration in the thyroid cells is an active and saturable process; since this concentration occurs against an electrochemical gradient (the intra-cellular iodine concentration is 20 to 40 times higher than that in the plasma), the process requires energy which is ensured by the Na / K-dependent ATPase system. The 99mTcO the process requires energy which is provided by the Na / K-dependent ATPase system. The 99mTcO the process requires energy which is provided by the Na / K-dependent ATPase system. The $99mTcO_4^-$ is transported by the NIS from the extracellular to the intracellular compartment because it simulates the behavior of the iodide ion, to which it is analogous in mass, size and charge density; however, once 99mTcO is transported into the thyroid cell$_4^-$-does not undergo the subsequent stages of iodine metabolism (organization and subsequent incorporation into thyroid hormones), and finally tends to leave this intracellular compartment. The $99mTcO_4^-$ circulating is excreted, in the form of pertechnic acid, in the gastric mucosa; the

pertechnetate ion is in fact exchanged with the carbonate ion present on the gastric mucosa and normally secreted by the gastric cells. The pertechnetate ion present in the gastric lumen can in turn be reabsorbed by diffusion, if its blood concentration is lower than that present in the gastric contents. However, a part of pertechnetate present in the stomach passes into the intestine, in whose proximal portions it is partly reabsorbed (with various transport mechanisms). The elective concentration of the pertechnetate ion by the cells of the gastric mucosa is the basis of its use for scintigraphic research of ectopic gastric tissue, for example in Meckel's diverticulum. Due to its chemical-physical analogy with the anionic compounds physiologically present in saliva, the pertechnetate ion is also excreted by the salivary glands. Due to this property, it is the radiopharmaceutical of choice also for the scintigraphic study of the salivary glands. The 99mTcO ion$_4^-$ does not cross the whole blood-brain barrier, normally accumulating only at the level of the choroid plexuses. On the other hand, it can spread to the brain in case of lesion of the blood-brain barrier (caused, for example, by tumors or other pathological processes); this property has in the past been exploited for the scintigraphic evaluation of the integrity of the blood-brain barrier, a survey currently completely abandoned.

Radiopharmaceuticals used as tracers must have three well-defined properties:

- First of all, the mass of the tracer must not exceed 1% of the mass of the substrate traced, so that the processes examined are not disturbed.
- To be detectable at base concentrations, tracers must have a high specific activity, i.e. high concentration of activity per unit mass of the tracer. The specific activity is different from the specific concentration which instead defines the activity per unit volume of the vehicle used for the administration of the radiopharmaceutical.
- The tracers must behave in an identical way to the substances whose behavior they trace in vivo, or at least exhibit predictable behavior differences, so that from the examination of their distribution it is possible to obtain measures of the processes under study.

It is important to note that the replacement of a stable atom with its radioisotope can alter the molecular structure by producing a variation in the chemical-physical characteristics of the labeled molecule and its biodistribution characteristics in vivo, this effect is called isotopic effect. The optimal characteristics of a radiopharmaceutical for diagnostic use are: constant availability, easy synthesis, short half-life, γ emission, exclusive localization in the organ under examination, low dosimetry. Radiopharmaceuticals can be prepared in solid form, liquid or gaseous, to be administered according to the oral, inhaled, intravascular and rarely intrathecal or intraperitoneal formulation. Radiopharmaceuticals can be classified with respect to the substrates and processes whose behavior they follow in: homogeneous, with heterogeneous equivalence and indicators. Radionuclides that have a behavior substantially identical to that of a normal constituent of the organism are considered homogeneous radiopharmaceuticals. The homogeneous radiopharmaceuticals include radioactive iodine, used in place of stable iodine, and all the normal constituents of the organism labeled with radionuclides so that their structure is not altered, (e.g .: glucose labeled with one or more atoms of radioactive carbon instead of stable carbon atoms). The use of homogeneous tracers is necessary for the study of very specific chemical processes, in which variables such as optical polarity, the angle of an interatomic bond, the molecular conformation, can determine relevant differences between the substrate whose behavior and the tracer used for this purpose. The homogeneous tracers include many compounds that contain carbon, nitrogen and oxygen atoms, all elements that are normally present in the molecules of living organisms and that are easily replaceable with the respective radioactive isotopes: carbon-11, nitrogen-13, oxygen-15 . Heterogeneous equivalence tracers are considered to be radionuclides that have, by chemical analogies, a behavior similar but not identical to that of a substance normally present in the body (e.g .: strontium compared to calcium), or similarities in metabolic behavior even though they belong to different chemical groups (eg: thallium compared to potassium). Among the tracers with heterogeneous equivalence there are also radiopharmaceuticals that are very similar to the normal constituents of the organism, and behave in a similar way to a constituent of the organism, (e.g. deoxyglucose labeled with a radioactive fluorine atom instead of a hydroxyl group, and which is transported and partly metabolized as glucose). Most of these tracers have differences from the element or compound whose behavior they follow, which can be exploited to examine specific steps in a metabolic sequence. Compounds that are not normal constituents of the organism are classified as indicators, but which allow to trace a physiological or biochemical process in the organism (renal function tracers, cardiac or cerebral perfusion, excretion, intravascular, etc.). Indicators are frequently labeled with relatively high mass atoms, such as iodine-123 (atomic number 53) or technetium-99m (atomic number 43), and therefore behave differently from that of any other molecule normally present in the body.

Radionuclides used in nuclear medicine must have different physicochemical characteristics according to the diagnostic or therapeutic purpose for which they are used. The radionuclides must have a sufficiently long half-life to allow their use for the labeling of radiopharmaceuticals, high chemical reactivity and stability of the chemical bonds formed with the carrier molecules, low or preferably no toxicity. Radionuclides intended for diagnostic use must also have a minimum emission of corpuscular radiation and a high flux of very penetrating photons in the tissues, therefore with energy detectable by the equipment, between 50 and 500 KeV; radionuclides intended for therapeutic use must decay with the emission of radiation with a high ionization density. Of element 43, technetium, 21 isotopes are known, with a mass number ranging between 90 and 110. Metastable technetium-99 is the most widely used radionuclide in nuclear medicine and is used only for diagnostic purposes: it is an emitter of monoenergetic γ radiation with an energy of 140 KeV, it has a half-life of 6 hours; it is produced by a generator from the decay of Molybdenum-99 (T½ = 67 hours). In the metastable Technetium-99 generator there are three radionuclides at the same time: the parent radionuclide, Molybdenum-99, the child radionuclide, Technetium-99 metastable, and the decay product of the latter, Technetium-99. The maximum activity due

to the metastable technetium-99, and therefore the maximum yield of the generator, is reached in about 23 hours from the previous elution. Simultaneously with the formation of metastable Technetium-99 its decay with the formation of Technetium-99 (T½ = 2.1 x 105 years), which has chemical characteristics identical to those of the metastable Technetium-99. Technetium-99 therefore constitutes an undesirable element of contamination, and is present in greater quantities in the eluted doses after a prolonged period without elutions. 99mTc is the most used isotope in nuclear medicine due to the following characteristics: pure γ emitter, energy of 140 KeV, half-life of 6 hours, production from generator, possibility of binding to a large number of drugs. The quality controls carried out on the radiopharmaceutical make it possible to ascertain that the final product corresponds in qualitative terms to the desired tracer. A good quality tracer reduces the absorbed dose to the patient and provides better quality images. In particular, at least three types of impurities can be defined:

- a) radionuclide, due to the presence of radionuclides other than the marking one;
- b) radiochemistry, when part of the radionuclide is not bound to the desired molecule;
- c) chemistry, due to the presence of non-radioactive contaminants.

The control of the radionuclide purity of Technetium-99m must be performed at each elution of the generator, in order to determine the amount of Molybdenum-99 present. The procedure involves measuring the activity contained in the elution bottle, before and after shielding with a lead screen of such thickness as to absorb the photons of technetium, but not the more energetic ones of molybdenum. This procedure allows to determine the relationship between activity due to metastable Technetium-99 and activity due to metastable Molybdenum-99. An eluate in which the molybdenum activity is less than 0.15 mCi for each mCi is considered acceptable. The half-life of metastable Technetium-99 is about 1/10 of that of Molybdenum, therefore the radiochemical purity of the eluate decreases over time after elution. Radiochemical purity is evaluated in percentage terms and is defined as the amount of total radioactivity that is related to the desired chemical form. For example, if 5% of the activity of Technetium-99m remains in the form of pertechnetate during a labeling procedure, the radiochemical purity of the labeled product is 95%. For most radiopharmaceuticals, the presence of radiochemical impurity can be recognized by an altered biodistribution of the product, however the presence of impurities can be detected prior to administering the tracer to the patient using thin layer chromatography, for which Numerous commercial products are available to be used in combination with specific solvents for the quality control of each radiopharmaceutical. The most common chemical contaminant of technetium-labeled radiopharmaceuticals is aluminum (Al3 +), which can render technetium insoluble, causing unwanted colloid formation that can concentrate in the endothelial reticulum system and lung. Quality control is carried out using colorimetric systems.

6.1 Radioiodine and thyroid uptake

Radioiodine in its various radioisotopic forms is one of the earliest introduced radionuclides in nuclear medicine practice. In fact, in addition to its direct use in the chemical form of iodide (for all applications involving thyroid diseases), this radiohalogen has been and still is used to mark a series of more complex molecules, thus assuming the biodistribution characteristics of radiopharmaceuticals. thus obtained. The availability of radioisotopes with variable characteristics, each suitable for different uses, also contributed to this broad spectrum of applications of radioiodine. In particular, Iodine-131 (historically the first available for medical applications) can be used both for therapeutic purposes (thanks to its emission of β- particles of suitable energy) and for diagnostic purposes (by virtue of its emission of γ rays, even if of energy not optimal for gamma-camera detection); on the other hand, Iodine-123 involves a lower dosimetric load on the patient (both for its short half-life and for its β- emission with very low energy, the so-called Auger electrons); moreover, the energy of its emission γ is optimal for gamma-camera visualization. Finally, the availability of Iodine-124 (which decays by emitting positrons) has opened the possibility of applying to the most modern PET method all the biochemical knowledge acquired in recent decades with conventional iodine radioisotopes. As a final note, Iodine-125, which emits γ-rays of too weak energy (35 keV) for gamma-camera visualization, at least in humans, has been widely used for in vitro investigations (for example, for measurements of analysis by radio-immunological techniques) and in this field it still finds important applications, as well as for biodistribution studies in animal models of disease, in an early phase of radiopharmaceutical testing. The medical-nuclear methods for the study of the thyroid are based, from a kinetic and physiological point of view, both on the detection of the accumulation (thyroid uptake) and glandular dismissal of a suitable radiopharmaceutical, and on the intraglandular distribution of the same (thyroid scintigraphy) . As mentioned above, the first radioisotope tracer introduced in clinical practice and used for the morpho-functional study of the thyroid was Iodine-131, in the form of iodide. The use of this radioisotope has progressively decreased over time, due to non-optimal physical and radiobiological characteristics, so much so that, although widely used in the past for the nuclear-medical study of thyroid pathology, iodine-131 today has a limited role for the diagnosis of benign thyroid disease (evaluation of thyroid radioiodine uptake), while it appears irreplaceable for the radio-metabolic therapy of differentiated thyroid neoplasms. Iodine-123 is a pure gamma-emitter tracer with optimal physical and radiobiological characteristics (half-life 13.3 hours, gamma emission energy 159 keV), but it has some limitations related to low availability and above all to the high cost of production. The use of Iodine-123 is recommended in particular conditions (suspicion of retrosternal goiter or lingual thyroid) and, more generally, in the evaluation of agenesis-ectopias of the thyroid. The distribution of a radiopharmaceutical precursor of hormone synthesis, or analogue of native iodine in the uptake phase (such as 99mTc-pertechnetate), can provide important information on the location, extent and morpho-functional characteristics of the thyroid tissue. In fact, the 99mTc-pertechnetate ion has important biodistribution characteristics in the thyroid area, very similar to those of iodine; however, it differs from this in that, once it has entered the intracellular district (with

a transport mechanism mediated by the NIS), it is not organized and is instead rapidly cleared by the thyroid cells. These physical and kinetic characteristics allow the acquisition of early images which, despite having a relatively high background activity, are nevertheless considered to be of good quality, making this indicator an acceptable alternative to radioiodine in the diagnostic field. In addition to the low cost and the reduced radiodosimetric load for both the thyroid and the patient, favorable elements for its clinical use are the high availability, the shorter half-life (6 hours) compared to Iodine-123 (13, 3 hours) and the lowest gamma emission energy (140 keV). Iodine uptake is one of the basic functions of the thyroid gland, a fundamental metabolic stage for the formation of thyroid hormones. From a strictly molecular point of view, iodine uptake is proportional to NIS expression. Thyroid clearance of iodine is defined as the volume of plasma (generally expressed in mL) purified of iodine over a certain time by thyroid uptake; the normal range is between 5 and 40 mL / min in regions with adequate dietary iodine intake. However, clearance may increase to 800 mL / min or more in the presence of iodine deficiency or glandular hyperfunction. Iodine clearance can be estimated by measuring that of 123I, the gold standard tracer in the evaluation of iodine entrapment function. The calculation of this parameter therefore represents the most accurate method for the quantification of thyroid iodine uptake, although the technique requires relatively long measurement and processing times. Therefore, the percentage uptake values of 123I and 99mTc-pertechnetate at predetermined times (each suitably standardized and referred to a population of control subjects with normal thyroid function) can be considered reliable, albeit indirect, indices of the thyroid clearance of iodine. The evaluation of thyroid uptake on the basis of gamma-camera scintigraphic acquisitions is performed using the so-called regions of interest (ROI) technique. The background activity in the cervical region is however relatively high and in constant dynamic transformation, due to the accumulation and excretion of the radiopharmaceutical also by the salivary glands.

Adopting these necessary indications, the value of radioiodine uptake correlates with the value of the thyroid clearance of iodine. Early uptake values (1-2 hours after tracer injection) are generally more reliable than late determinations (24 hours). Early after its administration, a linear correlation is also observed between thyroid uptake of 99mTc-pertechnetate (TcTU) and thyroid clearance of Iodine-123; the TcTU values (calculated with the same formula used for the calculation of the 123I uptake) reflect with some accuracy those of iodine thyroid clearance, especially if measured with an early scintigraphic acquisition (5-15 minutes after the administration of 99mTc -pertecnetate); however, early detection of TcTU requires a careful protocol with well-defined acquisition times, often difficult to follow in daily clinical practice. Furthermore, even in the early phase of uptake there are some differences between thyroid accumulation of 123I-iodide and 99mTc-pertechnetate. The evaluation of TcTU as a single datum of thyroid function does not generally allow to draw sufficient diagnostic conclusions, since the result depends on many additional factors: among all, in particular, the glandular volume, the iodine supply before the examination, and the patient's age. Sometimes overlapping values of thyroid uptake are observed both in patients with normal-functioning endemic goiter and in the presence of glandular functional autonomy or primary hyperthyroidism. It follows that only particularly high or low uptake values can be diagnostic, respectively for Graves-Basedow disease (TcTU> 15%) or for iodine contamination (TcTU <0.3%). The most common cause of reduced thyroid uptake is therefore iodine overload, typically secondary to an excessive dietary intake of iodine, but more often on a pharmacological basis (for example during amiodarone therapy). In common clinical practice this high iodine content drug is administered at a maintenance dose of 200 mg / day; with this dosage 75 mg of organic iodine are introduced into the body, with a percentage equal to 10% of inorganic iodine. Considering that the average daily requirement of iodine ranges from 150 to 300 μg, it can be deduced that this situation determines a daily overload of iodine intake equal to at least 25-50 times. Radiological investigations involving the use of iodinated contrast medium also involve a high load of iodine for the body; although the latest generation (non-ionic) contrast media have a decidedly lower percentage of inorganic iodine released, these quantities remain in absolute value even if they are still excessive for the thyroid economy. Synthetic thyroid hormones, when used in a suppressive dosage, are able to decrease the endogenous secretion of TSH, and with it the expression of NIS on thyrocytes; consequently, the uptake of radioiodine or 99mTc-pertechnetate is reduced for a more or less long period in relation to said therapy. A suspension of any compound containing synthetic thyroid hormones is therefore recommended for at least 4-6 weeks before performing a thyroid scan. Potassium perchlorate also interacts with NIS, competing with radioiodine or 99mTc-pertechnetate; therefore, this compound reduces the measured thyroid uptake values and it is recommended to suspend it for at least 7 days before performing a thyroid scan. The most common cause of an increase in glandular uptake of radioiodine or 99mTc-pertechnetate, in the absence of a real thyroid disease, is the dietary deficiency of iodine. Thyroid iodine uptake is evaluated after oral administration of 131I-iodide in the patient fasted for 12 hours (in capsule or liquid form, with activity generally of 1850 KBq), using a scintillation probe equipped with a diverging collimator positioned at about 30-40 cm from the anterior surface of the neck, with acquisitions of about 2 minutes at predetermined intervals (typically 2nd and / or 6th and 24th hours, less frequently at 48th and 72nd hours hour) from the administration of the radiopharmaceutical. On the occasion of each detection of radioactivity in the thyroid gland, a count of the general background activity is also carried out (generally at the distal third of the thigh), to be subtracted from the total measured uptake value. In the normal subject, thyroid uptake progressively increases until it reaches the maximum value at 24 hours, and then decreases without ever exceeding 45% of the administered activity; combining the three classic points of determination (2ª, 6th and 24th hour) we obtain the thyroid radioiodine uptake curve (Fig. 6). This curve is proportional to the kinetics of radioiodine uptake as iodide in the first 2 hours and, subsequently, to the kinetics of tracer organization and

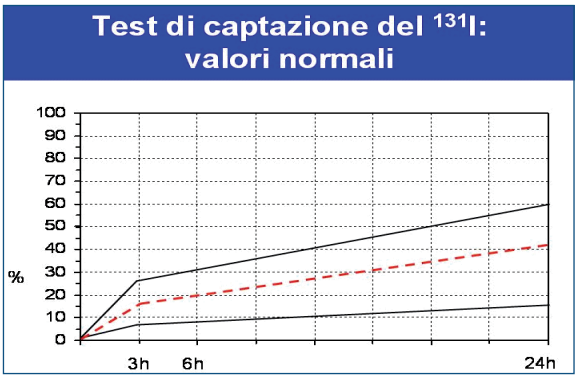


Fig. 7 - Normal picture (dashed red line); hyperthyroidism (black line above the red line); hypothyroidism (black line below the dashed red line).

glandular disposal. The second part of the curve in progressive decrease (from the 24th to the 72nd hour), is a function of the speed of hormonal secretion and is used to calculate the effective half-life ($T_{1/2eff}$) of thyroid radioactivity, which in the normal subject is 6-7 days. In diffuse non-toxic goiter, characterized by an increase in the intrathyroid iodine pool, a rapid intraglandular radioiodine transfer curve is observed, not followed by an equally rapid process of decommissioning. In the presence of an expansion of the circulating iodine pool, however generated, both a low percentage of radioiodine extraction from the blood compartment and a low intrathyroid entrapment are observed, with extremely low percentage values of uptake. On the contrary, in hyperthyroidism there is a rapidly rising curve that reaches maximum values within the 2-3rd hour (usually greater than 60% of the administered activity), with a subsequent rapid descent which at the 24th hour may be slightly less than 40%, with a 4 day T1 / 2eff. Hypothyroidism, on the other hand, is characterized by a very slow accumulation kinetics, with a maximum percentage value of less than 20-25% of the administered activity. The uptake test is currently used mainly as a preliminary measure to a subsequent radioiodine therapy (in hyperthyroidism), for which it is necessary to establish the percentage of radiopharmaceutical captured by the gland to calculate the activity of the radiopharmaceutical to be used for the therapy according to formulas pre-established (for example, Marinelli's formula).

6.2 Thyroid scintigraphy

Thyroid scintigraphy can be performed with different radiopharmaceuticals: the most commonly used are the radioactive isotopes of iodine (radioiodine) and technetium-99m pertechnetate (99mTc-pertechnetate). Both isotopes are actively taken up by the thyroid follicular cell through the active sodium / iodine co-transport system (Na / I symporter). Subsequently, only the iodine isotopes are organized: therefore 99mTc-pertechnetate traces only the glandular "trapping" phase of the anions while radioiodine allows the evaluation of the entire thyroid hormone biosynthesis. As a first approximation, however, 99mTc-pertechnetate can be considered, due to its physical and dosimetric characteristics, the first-line radiopharmaceutical while iodine isotopes are used for functional studies (for example in anticipation of metabolic radiotherapy) or in selected cases in which it is necessary to integrate the information provided by 99mTcpertecnetate (for example in suspected "trapping only" nodules) . It has been known for over 60 years that malignant thyroid neoplasms are characterized by a low uptake of radioiodine (and 99mTc-pertechnetate) compared to normal thyroid tissue. A variable percentage between 80 and 85% of thyroid nodules are hypocaptive ("cold" nodules) on scintigraphy but only 10-20% of "cold" nodules are malignant. The potential for malignancy of a "cold" nodule is directly related to the patient's age (higher risk for age below 30 years or above 60 years), to sex (relative risk of 4.2% in women and 8.2% in men), to iodine intake (relative risk of 2.7% in iodine-deficient areas and 5.3% in iodine-deficient areas) as well as to the history of previous irradiation of the cervical region (30-50% increase in risk). The nodules with a hyperfunctioning attitude ("hot" nodules) represent about 5% of the thyroid nodules, with different representation in regions with different iodine intake, and present an extremely low risk (<1%) of malignancy. The isocaptive nodules ("warm" nodules) represent the remaining 10-15% of the nodules with an intrinsic risk of malignancy of about 10%. Generally

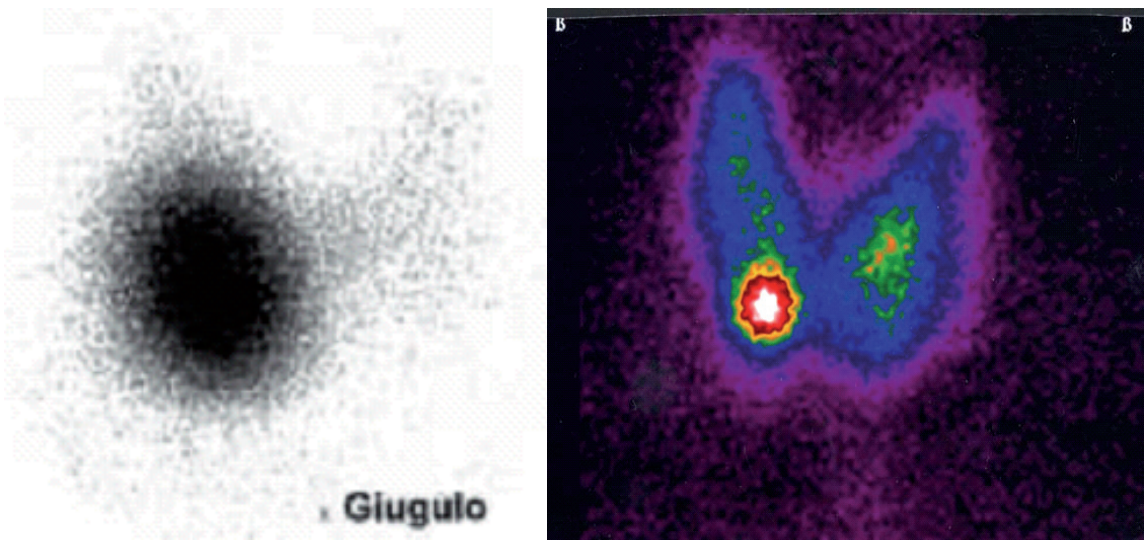


Fig. 8, 9 - Thyroid scintigraphy performed with 99mTcO4−. The area of intense accumulation of the radioisotope at the base of the right lobe is evident, in correspondence with the clinically palpable nodule, with reduced uptake on the remaining glandular parenchyma which is poorly evident.

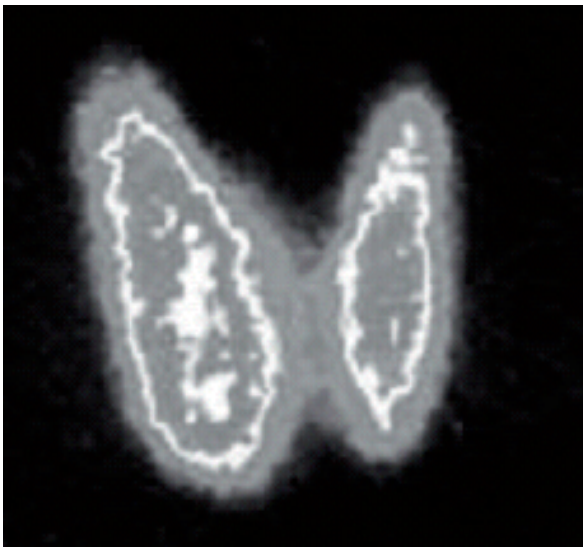
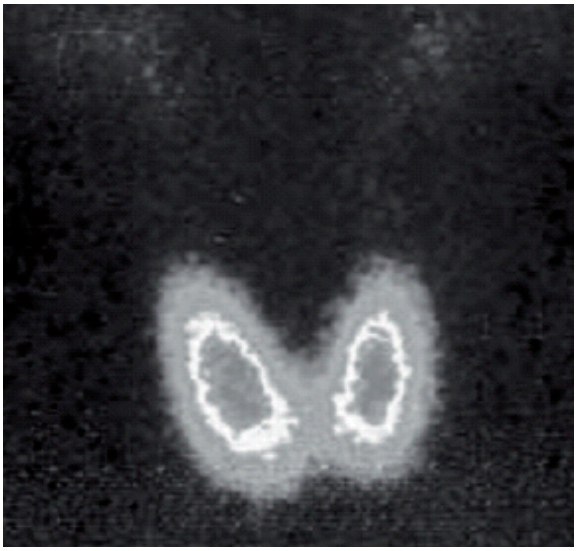


Fig. 10 - Thyroid scintigraphy performed with 99mTcO4− in a patient with Graves' disease. The scintigraphic picture shows a thyroid of modestly increased size, mainly in the right lobe with high and homogeneous uptake of the tracer. It is possible to note the almost absent background activity.



Fig, 11 - Thyroid scan performed with 99mTcO4−. The scintigraphic picture appears normal in appearance either morphological (butterfly image) and dimensional. The tracer uptake is homogeneous over the entire glandular parenchyma.

the "warm" nodules and the "cold" nodules are considered within a single category, in relation to the similar risk of malignancy. Such an approach raises the sensitivity of thyroid scintigraphy towards malignant thyroid neoplasms to almost absolute values but at the price of almost zero specificity (5%). Consequently, the positive predictive value is 10%. The clinical utility of scintigraphy is therefore to highlight "hot" nodules, with a very low risk of malignancy, and to exclude them from further diagnostic tests, while in "non-hot" nodules, it does not provide further indications useful for the differential diagnosis between nodules benign and malignant. Therefore, thyroid scintigraphy allows to discriminate the "hot" nodules and to identify the "non-hot" nodules to be subjected to further diagnostic evaluations.

Scintigraphy with oncotropic tracers

The search for a tracer capable of identifying "cold" nodules with an increased risk of malignancy has been a central topic in nuclear thyroidology for many years. Positive indicators or oncotropic tracers accumulate in tissues as a function of cell proliferation and their use is widespread in nuclear oncology for the diagnosis, differential diagnosis and monitoring of various neoplasms (breast cancer, lung cancer). The first oncotropic tracer used in the study of thyroid nodules was the Thallium-201 chloride (201Tl) subsequently replaced by the 99mTc-sestaMIBI and 99mTc-tetrafosmin technical lipophilic tracers.

Under normal conditions, thyroid scintigraphy appears with the well-known butterfly shape and with a uniform intraparenchymal tracer distribution (Fig. 11).

7. RADIOMETABOLIC THERAPY

Iodine-131 is administered after thyroidectomy surgery for three basic reasons:

- destroy any residual normal thyroid tissue to increase the sensitivity of whole body radioiodine scintigraphy and of the circulating thyroglobulin dosage during the subsequent follow-up to highlight any recurrence of the disease or distant metastases.
- destroy any carcinomatous microfocolai and thus reduce the risk of long-term relapse.
- allow the carrying out of a whole body scintigraphy, using the high activity of iodine-131 administered for therapeutic purposes, which has a higher sensitivity than the scintigraphy with conventional diagnostic activity (<185 MBq of iodine-131) in highlighting persistence of disease.

Dosimetry and biological assumptions Iodine-131 has a half-life of 8.02 days and emits β-type corpuscular radiation (electrons) with an average energy of 191 KeV and γ-photonic radiation with an average energy of 364 KeV. The main advantage of radioiodine treatment consists in the possibility of addressing the radio-induced damage solely on the thyroid tissue, with substantial savings of the surrounding tissues that receive a minimum dose of radiation. The dose delivered to the thyroid tissue is related to both the concentration of the isotope by the tissue and the biological half-life of the isotope. In normal thyroid tissue, the radioiodine concentration is approximately 1% of the administered activity per gram of tissue and the biological half-life is approximately 8 days. In carcinomatous thyroid tissue, the concentration can vary from 0.001% to 0.5% per gram of tissue and the half-life is decidedly shorter, ranging from a few hours to 3 days: as a result, the dose released is often relatively low. Considering, in a well-differentiated thyroid carcinoma tissue, an average concentration per gram of 0.1% of the activity administered to the patient, it can be deduced that an administered activity equal to 100 mCi (3700 MBq) will determine an absorbed dose of about 30 Gy for a half-life of 3 days and 15 Gy for a half-life of 1.5 days. The dose is related to the concentration in the tumor tissue and not to the uptake: considering a half-life of 3 days, a tumor with a mass equal to 5 grams and an uptake of 0.

Although radiometabolic treatment has been practiced with substantial clinical advantages for some decades, the dosimetric aspects still present multiple points of discussion. The heterogeneity of the dose distribution in neoplastic tissue (micro-dosimetry) is caused, as demonstrated by autoradiographic studies, by the

uneven distribution of radioiodine and its geometric emission characteristics. The radio-induced damage is basically determined by β radiations, which have an extremely reduced geometric travel range, around 1 mm. This feature produces two main effects:
a) a tumor volume that has a low radioiodine concentration and a diameter greater than 1 mm. receives a low dose even when surrounded by normal thyroid tissue with high radiodium concentration.
b) the dose received by a small volume of radioiodine concentrating tissue is lower than that expected according to the equations used for thyroid dosimetry, where it is assumed that the tissue mass is much more voluminous than the average travel time of the β particles . In fact, when the mass is small, the energy lost by the particles leaving the tissue is no longer balanced by the energy released by the particles coming from the isotope concentrated in the surrounding normal tissue. The degree of radioiodine accumulation can be assessed in vivo by quantitative scintigraphy: it has been shown that radioiodine accumulation and a higher grade uptake are more frequent in well-differentiated histotypes, in younger patients and in those with small metastatic foci . This seems to suggest an accumulation of metabolic deficits with age and the progression of thyroid cancer. Radioiodine can eradicate small foci of neoplastic tissue, however it may not be sufficient on its own for the permanent eradication of large tumor masses: in this sense the synergy with surgery and any trans-cutaneous radiotherapy treatment can be extremely useful. A fundamental dosimetric problem is represented by the irradiation of extra-thyroid organs and in particular of the blood and bone marrow and gonads. The dose delivered to these structures varies between 0.1 cGy and 1 cGy per 1 mCi (37 MBq) of iodine-131 administered and, in relation to the extremely short distance of the β particles, the irradiation of the structures surrounding the foci of absorbing thyroid tissue is however very limited. It must be considered that, since patients are in a state of hypothyroidism at the time of radioiodine administration, the renal clearance of the radioisotope is decreased with a relative increase in the volume of distribution, in iodine-131 retention and, in essence, in the irradiation of whole body. The dose to each organ depends on the total body retention which, in turn, is variable in the individual patient. On average, the whole body dose in these patients is approximately double that estimated for euthyroid patients. Many biological studies have been conducted in order to be able to increase the uptake of radioiodine in the tumor tissue: a reduced trapping of radioiodine and a low concentration of stable iodine were detected in all differentiated thyroid carcinomas. Radioiodine uptake only weakly correlates with stable iodine concentration while it responds significantly to TSH stimulation especially in tumors with higher iodine content. Various biochemical abnormalities have been highlighted in the tumor thyroid tissue, in particular in the iodine transport mechanism. The iodine organization rate is generally very low especially in less differentiated neoplasms: this can be caused by defects in the enzymatic system associated with oxidation and organization (eg thyro-peroxidase). The concentration of thyroglobulin (hTG) is often reduced in tumor tissue and in many cases can only be demonstrated by immunocytochemical techniques. Many differentiated thyroid neoplasms express the TSH receptor on the membrane of their cells and the receptor number and density vary with histotype; many receptors are detectable in well-differentiated follicular neoplasms while the smaller number of receptors is detectable in less differentiated neoplasms. Stimulation with TSH increases the uptake of radioiodine in all thyroid tissues capable of incorporating iodine-131 and determines the increase of circulating hTG even in neoplasms that cannot receive radioiodine: this data shows that all differentiated thyroid neoplasms are TSH-dependent. TSH also plays a fundamental role in the control of cell proliferation, demonstrated in culture of normal thyroid cells, and TSH-suppressive therapy with l-thyroxine has a favorable effect on proliferation rate, tumor progression and mortality from thyroid cancer. . Stimulation with supra-physiological concentrations of TSH is necessary before each administration of iodine-131 for diagnostic and / or therapeutic purposes but this does not induce, in relation to the short term, any significant proliferation of the neoplasm. demonstrated in normal thyroid cell culture, and TSH-suppressive therapy with l-thyroxine has a favorable effect on proliferation rate, tumor progression and thyroid cancer mortality. Stimulation with supra-physiological concentrations of TSH is necessary before each administration of iodine-131 for diagnostic and / or therapeutic purposes but this does not induce, in relation to the short term, any significant proliferation of the neoplasm. demonstrated in normal thyroid cell culture, and TSH-suppressive therapy with l-thyroxine has a favorable effect on proliferation rate, tumor progression and thyroid cancer mortality. Stimulation with supra-physiological concentrations of TSH is necessary before each administration of iodine-131 for diagnostic and / or therapeutic purposes but this does not induce, in relation to the short term, any significant proliferation of the neoplasm.
The administration of an ablative dose of RAI after surgery depends on prognostic factors and the extent of the surgery performed. In fact, in clinical practice two post-surgical conditions can occur to the nuclear doctor: 1) complete surgical resection and 2) incomplete surgical resection. The routine administration of radioiodine after complete exeresis of the neoplastic tissue can have two theoretical advantages, namely a) the increase in the sensitivity of radioiodine scintigraphy and the dosage of thyroglobulin during the subsequent follow up and b) the destruction of any residual neoplastic tissue not highlighted by conventional diagnostic investigations.
The optimal iodine-131 activity to achieve the therapeutic effect still remains undetermined. The organization of iodine is a specific function of the thyroid cell and iodine-131 is an extremely effective agent for delivering radiation to the thyroid tissue with a minimum "spill-over" to other regions of the body. However, to be effective, the radioiodine must be concentrated by the tumor tissue: this does not happen when the thyroid is present because the tumor is generally hypocaptic compared to normal thyroid tissue. Therefore, RAI administration should occur after thyroidectomy and RA uptake should be stimulated by elevated TSH levels. A whole body radioiodine scan or a cervical iodine uptake scan must be performed 4-6 weeks after surgery, without the patient having in the meantime taken hormone therapy, verifying that the TSH has reached a concentration

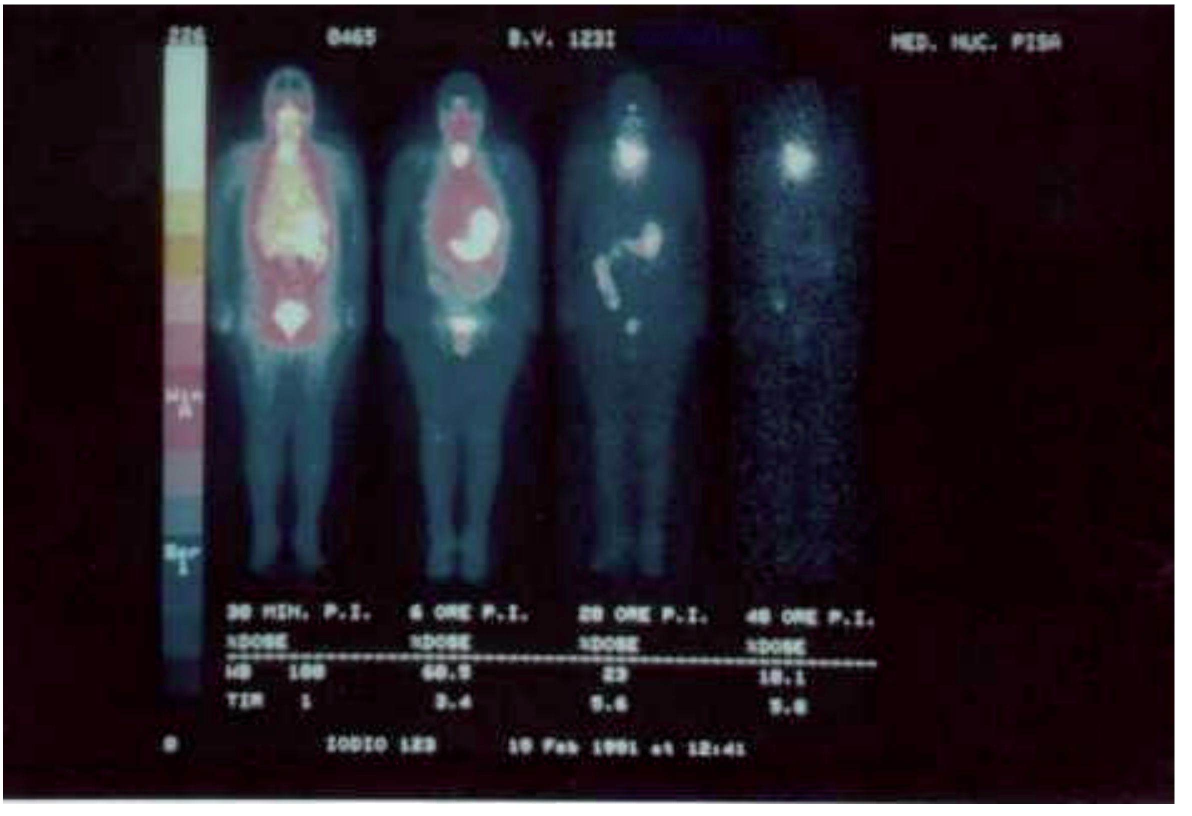


Fig. 12 - whole body radioiodine scintigraphy.

equal to at least 30 µIU / mL. Whole body scintigraphy is performed with activities ranging between 2 mCi (74 MBq) and 5 mCi (185 MBq) of iodine-131 as higher activities can determine the "stunning" of residual thyroid tissue or tumor possibly present and reduce the effectiveness of the therapeutic activity administered subsequently. Cervical scintigraphy is performed by administering tracer activities (3-4 MBq of iodine-131) and presents no problems. verifying that the TSH has reached a concentration equal to at least 30 µUI / mL. Whole body scintigraphy is performed with activities ranging between 2 mCi (74 MBq) and 5 mCi (185 MBq) of iodine-131 as higher activities can determine the "stunning" of residual thyroid tissue or tumor possibly present and reduce the effectiveness of the therapeutic activity administered subsequently. Cervical scintigraphy is performed by administering tracer activities (3-4 MBq of iodine-131) and presents no problems. verifying that the TSH has reached a concentration equal to at least 30 µUI / mL. Whole body scintigraphy is performed with activities ranging between 2 mCi (74 MBq) and 5 mCi (185 MBq) of iodine-131 as higher activities can determine the "stunning" of residual thyroid tissue or tumor possibly present and reduce the effectiveness of the therapeutic activity administered subsequently. Cervical scintigraphy is performed by administering tracer activities (3-4 MBq of iodine-131) and presents no problems. Whole body scintigraphy is performed with activities ranging between 2 mCi (74 MBq) and 5 mCi (185 MBq) of iodine-131 as higher activities can determine the "stunning" of residual thyroid tissue or tumor possibly present and reduce the effectiveness of the therapeutic activity administered subsequently. Cervical scintigraphy is performed by administering tracer activities (3-4 MBq of iodine-131) and presents no problems. Whole body scintigraphy is performed with activities ranging between 2 mCi (74 MBq) and 5 mCi (185 MBq) of iodine-131 as higher activities can determine the "stunning" of residual thyroid tissue or tumor possibly present and reduce the effectiveness of the therapeutic activity administered subsequently. Cervical scintigraphy is performed by administering tracer activities (3-4 MBq of iodine-131) and presents no problems.

The cervical study is generally performed for the assessment of the extent of post-surgical thyroid residue in centers where radioiodine therapy is used extensively and the whole body study is performed after administration of the therapeutic dose. Total ablation of residual thyroid tissue at surgery requires the release of a dose of at least 300 Gy and is achieved with activities ranging from 30 (1110 MBq) to 100 mCi (3700 MBq) of iodine-131 in over 80% of patients undergoing total or "neartotal" thyroidectomy. Therefore a total or "near-total" thyroidectomy is strongly recommended in anticipation of radiometabolic treatment.

7.1 Whole Body Radioiodine Scanning (WBS)

The result of a whole body radioiodine scan depends on the ability of the thyroid tumor tissue to pick up radioiodine in the presence of high concentrations of TSH, obtained by suspension of treatment with l-thyroxine for 4-6 weeks. This procedure involves a state of hypothyroidism which is particularly poorly tolerated in some patients. It is possible to alleviate the disorders related to this condition by using triiodothyronine, which has a faster metabolism, in the form of liothyronine sodium for three weeks instead of thyroxine and then suspending it for two weeks before the investigation or simply reducing the dosage of thyroxine to the 50% without completely stopping the treatment. Serum TSH concentrations must be higher than 30 µIU / mL and in the presence of lower

concentrations the administration of radioiodine should be postponed. In anticipation of the scintigraphic study, the patient must be instructed on the need to avoid foods containing iodine as well as drugs or iodized products and radiological contrast media. In doubtful cases of expansion of the iodine pool, evaluation of ioduria may be useful, if an accurate method is available. In women of childbearing age, the possibility of pregnancy must be excluded by means of an appropriate immunological test. The dose administered for diagnostic purposes can vary between 74 and 185 MBq (2-5 mCi): doses higher than 185 MBq can in fact cause "stunning" phenomena of the iodocaptive tissue and reduce the uptake of a possible subsequent therapeutic dose of radioiodine. Whole body scintigraphy is performed 48-72 hours after administration of the radioiodine diagnostic activity by means of a double-headed range chamber equipped with suitable collimators for high emission energies. The interpretation of radioiodine scintigraphy requires a good knowledge of the pathophysiological mechanisms of radioiodine accumulation and its physiological biodistribution. False-positive results are rare overall. Assuming an equal distribution of radioiodine after administration of a diagnostic and therapeutic activity, it is demonstrated that an excessively low and therefore undetectable uptake with a diagnostic dose of 74-185 MBq (2-5 mCi) can be detected scintigraphically after administration of a therapeutic dose. of 3700 MBq (100 mCi). This evidence forms the rationale for administering a dose of 3700 MBq (100 mCi) and more of iodine-131 in patients with circulating thyroglobulin elevation and negative diagnostic scintigraphy. If the whole body scintigraphy obtained after administration of the post-surgical therapeutic dose of radioiodine does not reveal any areas of uptake outside the thyroid lodge (residual thyroid tissue) the patient begins TSH-suppressive treatment with l-thyroxine and TSH levels Thyroglobulin (with measurement of circulating AbhTG) are checked three months later. Subsequently, 6-12 months after the metabolic radiotherapy, the treatment with l-thyroxine is suspended for 4-6 weeks and the patient performs a whole body scintigraphy with 185 MBq of iodine-131: if this investigation is positive for the presence of iodo-enhancing areas, 3700 MBq (100 mCi) of iodine-131 are administered and, subsequently, the TSH-suppressive treatment is restored.

7.2 Role of trsm in nuclear medicine

In a Nuclear Medicine ward, the medical radiology technician plays a fundamental role. Specialized and in possession of all the necessary knowledge, he works daily under controlled conditions with unsealed radioactive sources. The Nuclear Medicine workflow begins with the booking of a scintigraphic examination (in our case thyroid scintigraphy and / or a thyroid uptake test) in which the use of a specific radiopharmaceutical is required. Once the gamma camera has been warmed up, the TSRM then proceeds to elute the 99Mo / generator.

99mtc and the preparation of the doses of free 99mtc necessary for the execution of thyroid scans, taking into consideration the worklist of the day. Due to its decay characteristics, the radiopharmaceutical must be prepared just before administration. For this reason, when booking the exams, the technician takes into account the availability / activity of the materials useful for the creation of the radiopharmaceutical, in the future forecast of creating it on the requested day. After the waiting time necessary for the distribution of the injected radiopharmaceutical, the technician welcomes the patient into the gamma-camera diagnostic room, provides simple and clear explanations regarding the technical aspect of the examination: average duration, position to be taken during the acquisition, underlining which precautions must be respected in order to obtain a good result in terms of imaging. With communication skills, professionalism and availability, the radiology technician empathizes with the patient, often reassures him about a method, for the most part unknown, positively stimulating him to collaborate: the patient must become an active part of the procedure. At the end of the examination, the technician proceeds with the re-elaboration of the image and its filing. The patient must become an active part of the procedure. At the end of the examination, the technician proceeds with the re-elaboration of the image and its filing. The patient must become an active part of the procedure. At the end of the examination, the technician proceeds with the re-elaboration of the image and its filing.

The professional profile of the TSRM is regulated by DM n.746 / 94:

- art. 1.1. The figure of the medical radiology technician is identified with the following profile: the radiology health technician is the health worker who, in possession of the qualifying university diploma and registration in the professional register, is responsible for the acts of his competence and is authorized to carry out radiological investigations and services.
- art. 1.2. The medical radiology technician is the health worker qualified to carry out, in compliance with the provisions of the law of 31 January 1983, n. 25, independently, or in collaboration with other health professionals, on medical prescription all interventions that require the use of sources of ionizing radiation, both artificial and natural, of thermal, ultrasonic, nuclear magnetic resonance energies as well as interventions for physical protectionism or dosimetry.
- art. 1.3. The medical radiology technician: a) participates in the planning and organization of work within the structure in which he operates in compliance with his own skills; b) plans and manages the provision of multipurpose services within its competence in direct collaboration with the radiodiagnostic doctor, the nuclear doctor, the radiotherapist physicist and the health physicist, according to diagnostic and therapeutic protocols previously defined by the head of the facility; c) is responsible for the acts within his competence, in particular by checking the correct functioning of the equipment entrusted to him, by eliminating minor problems and by implementing verification and control programs to guarantee quality according to predefined indicators and standards;
- art. 1.4. The medical radiology technician contributes to the training of support staff and directly contributes to updating their professional profile and research.

The medical radiology technicians assigned to the Nuclear Medicine services take over the radioactive sources, taking care of their loading and unloading as

well as the disposal of radioactive waste; they report the movement and storage of radioactive material to the person in charge and make the related recordings; carry out the operations necessary for the preparation of the radioactive doses to be administered to patients and to be manipulated in vitro and any other operation concerning the work of the hot room; if necessary, they accept the patient, ascertain the personal data, record and archive the results of the technical operations carried out and treat the photo scintigrams; they check the efficiency of the equipment they prepare for use. They collaborate with the nuclear doctor in carrying out investigations and in the collection and recording of data also through the use of electronic computers; they provide for the decontamination and control of glassware and contaminated objects or environments and carry out all operations related to radiation protection, according to current legislation carry out any other technical operation requested by the nuclear doctor.

The Legislative Decree n.230 and subsequently the Legislative Decree n.187, are decrees that, as we know, have both civil and criminal legal repercussions and the TSRM is also involved in these responsibilities. It is important, however, that as a professional he is certainly attentive to the regulatory aspects of radiation protection but, above all, becomes aware that in the exercise of his profession he can irradiate the patient in an "unjustified" way. These aspects and problems recall the role of TSRM as a health educator towards the person-patient, an educator who must have his utmost skills on radiation protection and must increasingly transform his role with a different conception of professionalism by learning to go beyond the its technical-scientific dimension. The performance of the radiology technician must cease to be understood as a purely technical act but must also contemplate the relationship and be aware that communicating is an integral part of the profession. The radiology technician is the operator who meets the person undergoing radiological investigation and it is on this meeting that the TSRM has built its professional role in all these years. This choice is witnessed in the Code of Ethics which, in addition to contributing to the orientation of professional choices, recognizes the centrality of the person as a starting point for a direct and responsible participation of the TSRM professional in the various relational dynamics, with a certain attention to communication processes and above all the quality of the information provided to the person (before, during and after the specific investigation). At the beginning, the TSRM profession was carried out by simple operators who positioned the patient, subsequently positioned the X-ray machine and pressed a button to activate the irradiation that would have exposed the "plate", finally moving on to the development phase of the same. During this time, all knowledge and procedures were passed on to the technician by the radiologist. In fact the technician is by definition the man of trust of the radiologist, he is the one who practices the radiological technique. Years of cultural and scientific study followed. For many years, after its birth, the TSRM carried out a work coordinated by the radiologist, based on instructions and tasks dictated by the radiologist himself; this is the period in which the TSRM training grew only from the experience acquired in the field, based exclusively on abstract notions perhaps only sufficient to carry out daily practice. The profession of Health Technician of Medical Radiology (TSRM) has evolved considerably over the past 20 years. The technology associated with the radiological technique changes year after year bringing the figure of the TSRM professional to a continuous update. Traditional Radiology, Radiotherapy, Nuclear Medicine, Health Physics, CT, Magnetic Resonance, Interventional Radiology, Senology: these are just some of the ways in which the TSRM professional commits his working hours every day within the hospital walls to achieve good health. . The patient for a few minutes or more, depending on the examination and the diagnostic specialty to which it refers, you come in contact with the radiology technician. This meeting is aimed at the technical execution of all those acts necessary for the correct execution of the examination requested by the doctor; therefore the TSRM is required to operate with scrupulous attention and competence since its professional training has been finalized for this purpose.

CONCLUSIONS

On the basis of these evidences it is possible to conclude that radiometabolic treatment with iodine-131 should be used with selective modalities: in fact, in low-risk patients the long-term prognosis guaranteed by surgical therapy is so favorable that radioiodine treatment is generally not recommended. Conversely, all patients at risk of disease recurrence, with ongoing relapse and / or with distant metastases should be treated with radioiodine as it has been shown to be effective in reducing both the relapse rate and overall mortality.

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