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Abstract

In many thyroid diseases the administration of therapeutic dose of ^{131}I as radiopharmaceutical is a well assessed clinical practice. The ^{131}I dose choice and optimization can be achieved in various ways, depending on the type of treatment, of dosimetric methods available and of the clinical context. The use of a modeling dosimetry is the best way to optimize the dose; any assessment procedure for dosimetry requires the measurement of target mass, activity in the target, time course of the activity in the target. The quantitative approach is labor intensive, and a number of intrinsic factors must be measured with good accuracy. Thus, in the clinical practice, the dosimetric approach is not employed frequently, due to the lack of easily manageable clinical diagnostic tools.The aim of the proposed experimental procedure is the extraction of all the ^{131}I uptake quantitative information and of thyroid mass evaluation only from the scintigraphic image. A new experimental protocol, including hardware modifications of the gamma camera and a new data treatment software package were tested in a number of clinical cases, and are here described.

Keywords: *^{131}I – Thyroid - Gamma camera - Dosimetry*

Riassunto

In molte patologie della tiroide la somministrazione di dosi terapeutiche di ^{131}I come radiofarmaco è una pratica clinica ben consolidata. La scelta e ottimizzazione della dose di ^{131}I possono essere realizzate in vari modi, a seconda del tipo di trattamento, dei metodi dosimetrici disponibili e del contesto clinico. L'uso di una valutazione modellistica dosimetrica è il modo migliore per ottimizzare la dose; qualsiasi procedura di valutazione per dosimetria richiede la misurazione della massa di riferimento, l'attività nel target, andamento temporale delle attività nel target. L'approccio quantitativo è però laborioso, e un certo numero di fattori intrinseci deve essere misurata con buona precisione. Così, nella pratica clinica, l'approccio dosimetrico non viene utilizzato di frequente, a causa della mancanza di strumenti di diagnostica clinica facilmente utilizzabili. Lo scopo della presente procedura sperimentale proposta è l'estrazione di tutte le informazioni quantitative dell' uptake di ^{131}I e della valutazione della massa tiroidea solamente dalle immagini scintigrafiche. Un nuovo protocollo sperimentale, comprese le modifiche hardware della gamma camera e un nuovo pacchetto software di trattamento dati sono stati testati in un certo numero di casi clinici, e vengono qui descritti.

Parole chiave: ^{131}I – Tiroide - Gamma camera - Dosimetria.

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Introduction

In the last 40 years a growing role has been acquired by the Nuclear Medicine in the management of thyroid diagnosis, therapy and follow-up of both hyperthyroidism and thyroid carcinoma. The currently used scintigraphic techniques in thyroid diagnosis include ^{99m}Tc (marker of uptake), ^{131}I and ^{123}I (marker of uptake and of thyroid hormone anabolic activity),^{99m}Tc-MIBI (marker of mitochondrial activity), ^{201}Tl (marker of activity of the sodium-potassium pump membrane), ^{99m}Tc(V)-DMSA (marker of thyroid medullary carcinoma), PET-TC with ^{18}F-FDG (marker of glycolytic activity); besides, more than one million patients around the world have received a therapy with ^{131}I.

Different pathologies can affect the thyroid gland.When the thyroid produces too much hormones thyroxine (T_4) and triiodothyronine (T_3), this is defined as hyperthyroidism. The most common cause of hyperthyroidism is the autoimmune disorder called Basedow, or Graves' disease. In this disorder an antibody, called thyroid-stimulating immunoglobulin (TSI), is produced, that causes the thyroid gland to produce too much thyroid hormones. Graves' disease runs in families and is more commonly found in women.

Hyperthyroidism also may be caused by a toxic nodular or multinodular goiter, which are lumps or nodules in the thyroid gland that cause the thyroid to produce excessive amounts of thyroid hormones. Inflammation of the thyroid gland (thyroiditis), resulting from a virus or a problem with the immune system, may cause symptoms of hyperthyroidism. Patients who regularly use drugs containing iodine (such as amiodarone) may have a thyroid gland overproducing thyroid hormones. Hyperthyroidism can be treated with antithyroid medications that interfere with the production of thyroid hormones, or by administration of ^{131}I therapy to "damage" the

cells that produce too much thyroid hormones. In rare cases in which patients do not respond or have side effects from these therapies, surgery to remove, partially or totally, the thyroid may be necessary. The choice of treatment will depend on the severity and underlying cause of symptoms, age, potential side effects of the cure.

When the thyroid gland produces too little amount of hormones thyroxine (T_4) and triiodothyronine (T_3), this is defined as hypothyroidism. This is generally a widespread problem, that is often present for a number of years before it is recognized and treated. There are several common causes, and hypothyroidism can even be associated with pregnancy. Treatment for all types of hypothyroidism is usually straightforward; thyroid hormone is administered to supplement or replace endogenous production, and the disease can be adequately treated with a constant daily dose of levothyroxine (LT_4). Surgery is rarely needed in patients with hypothyroidism, and is indicated mainly for large goiters that compromise tracheoesophageal function.

Thyroid nodules are lumps that commonly arise within an otherwise normal thyroid gland. Often these abnormal growths of thyroid tissue are located at the edge of the thyroid gland, and can be felt as a lump in the throat. When they are large or when they occur in very thin individuals, can sometimes be seen as a lump in the front of the neck. One in fifteen young women and one in forty young men has a thyroid nodule, but more than 95% of all thyroid nodules are benign (non-cancerous growth). The incidence of thyroid nodules increases with age; 70% of 70 year old persons have at least one thyroid nodule. Occasionally, thyroid nodules can take on characteristics of malignancy, and require either a needle biopsy or surgical excision.

The scintigraphic diagnosis of thyroid nodule may range from underactive or "cold", to hyperfunctioning, or "hot spot" . The majority of patients presenting single

palpable nodules are actually multi-nodular, as also demonstrated by gland palpation or ultrasound examination.

The cold nodule indicates a substrate with high anatomic and pathological variability, in which a scintigraphic alteration in the uptake of an isotope is suggestive of an altered production of thyroid hormones triiodothyronine (T_3) and tetraiodothyronine (T_4). A "cold" nodule may be hypoactive when the fixing of the indicator is less than the remaining parenchyma or when inactive in its capability of hormone production. The incidence of neoplasia in a cold thyroid nodule, suspected of having cell differentiation, is about 20-25% in gland of normal volume, while the incidence drops to 5-10% if the gland has an increased volume (goiter).

A "hot" nodule indicates a scintigraphic region of thyroid tissue with an higher uptake than the surrounding parenchyma, and can be classified in three groups: hot nodule not inhibiting, partially inhibiting and totally inhibiting the remaining thyroid tissue, which, in turn, clinically correspond to thyrotoxic syndrome (marked clinical signs of hyperthyroidism with significant increase of thyroid hormones and very low TSH), complete with hyperthyroid symptoms of moderate intensity, oligosymptomatic and asymptomatic.

From the histopathologic point of view, a hot nodule is almost always an adenoma, which can cause an accelerated catabolism of the protein matrix thyroglobulin , with consequent increase of circulating thyroid hormones, and can be treated with thyroid-inhibiting drugs (thionamides), ^{131}I radiomethabolic therapy, or surgery.

Usually a confirmation diagnosis by fine needle aspiration biopsy is able to discriminate if the nodule is cancerous or benign; fewer than 1% of all thyroid nodules are malignant.

The most common types of thyroid cancer (papillary and follicular thyroid cancer) are the most curable; in younger patients, both papillary and follicular cancers have a more than 97% cure rate, if treated appropriately. Both papillary and follicular thyroid cancers are typically treated with complete removal of the lobe of the thyroid that harbors the cancer, in addition to the removal of most or all of the other side.

Medullary thyroid cancer is significantly less common but has a worse prognosis. Medullary cancers tend to spread to large numbers of lymph nodes very early, and therefore require a much more aggressive surgery than the more localized thyroid cancers, such as papillary and follicular thyroid cancer, with complete thyroid removal plus a dissection to remove the lymph nodes of the front and sides of the neck.

The least common type of thyroid cancer is anaplastic thyroid cancer, which has a very poor prognosis. Anaplastic thyroid cancer tends to be found after the tumor has spread, and it is incurable in most cases.

Thyroid cancer in its more common forms (papillary and follicular cancer) is unique among tumors, as thyroid cells are the only cells that have the ability to absorb iodine, required for thyroid cells to produce thyroid hormone, so they absorb it out of the bloodstream and concentrate it inside the cell. Most thyroid cancer cells retain this ability to absorb and concentrate iodine, amd this provides a perfect "radio-chemotherapy" strategy. Radioactive iodine (^{131}I) is given to the patient with thyroid cancer after their cancer has been removed. If there are any normal thyroid cells or any remaining thyroid cancer cells in the patient's body (and any thyroid cancer cells retaining this ability to absorb iodine), then these cells will absorb and concentrate the radioactive iodine. Since all other cells of our bodies cannot absorb the toxic iodine, they are unharmed. The thyroid cancer cells, however, will concentrate the

element within themselves and the beta radioactivity associated with ^{131}I destroys the cell from within.

Most of the patients with thyroid cancer need radioactive iodine treatments after their surgery. Patients with medullary thyroid cancer usually do not need iodine therapy because medullary cancers almost never absorb the radioactive iodine, and also some small papillary thyroid cancers treated with a total thyroidectomy may not need iodine therapy as well.

Indications for ^{131}I therapy

In patients affected with Basedow's disease, in which hyperthyroidism is supported by high levels of antibodies directed against the stimulating TSH receptor and with poor prognosis on the long-term efficacy of the treatment with thionamides, the treatment by radioactive ^{131}I is considered clinically indicate. The therapy is also indicated for patients who can not receive the drug therapy (allergy, poor compliance or side effects) or surgery (for high risk of comorbidities or patient refusal), with the target nominal dose of 80-120 Gy. In addition, the frequent association of this disease with ophthalmopathy (exophthalmos) is an indication to the definitive treatment of hyperthyroidism with radioiodine ablative doses, that ensure complete destruction of thyroid tissue, and is associated with beneficial long-term effects on eye diseases, due to the subsequent removal of the antigens that are shared by thyroid and orbital tissue, and which are the cause of the pathogenetic Basedow ophthalmopathy (nominal dose 150-200 Gy). Currently it is possible to cure with ^{131}I approximately 80% of patients with a single therapeutic administration, the remaining 20% requiring administration after 6-12 months from the first dose administration.In the case of Basedow's disease

the presence of nodules with suspected malignancy cytology is a contraindication to direct treatment with radioiodine.

In toxic multinodular goiter and in toxic adenoma, therapy with ^{131}I and thyroidectomy is the first choice treatment. This therapy is also indicated in cases of persistent hyperthyroidism after partial thyroidectomy, with reduction of hyperfunctioning nodules activity.

The hyperthyroidism with goitre of large size hardly heals after a single administration of ^{131}I, so in these cases the primary indication is surgery, reserving the use of radioactive iodine to patients unresectable or who refuse surgery.

In patients with toxic adenoma with size < 5 cm, treatment with ^{131}I should be proposed when the adenoma inhibits the surrounding parenchyma or in the conditions of obvious thyrotoxicosis (suppressed TSH and FT_3 and FT_4 high); the aim of the therapy is to obtain by the radiation therapy an euthyroidism (nominal dose 150- 300 Gy), while in the case of subclinical hyperthyroidism (suppressed TSH hormones), the indication is given after evaluation of the clinical picture and individual risk factors.

In differentiated thyroid carcinoma, the therapy with ^{131}I is indicated in the elimination of residual thyroid after surgery, except in cases of papillary carcinoma with a diameter < 1 cm with no evidence of metastasis, of capsular invasion, or multifocality. Thyroid cancer may metastasize to the lymph nodes, lungs, bone and occasionally brain, that often take up iodine at first. Therefore ^{131}I high-dose therapy may still be a useful treatment for patients with metastases, particularly for small lung metastases that may not be visible by CT scan, but are only seen on a radioactive iodine scan. Metastatic thyroid cancer, that is large enough and visible on ultrasound

or CT scan, should be surgically removed. This is a common treatment for lymph node metastases in the neck. A significant survival advantage was observed among patients who underwent radioactive iodine therapy, and better prognosis seemed generally to be obtained with greater doses of radioactive iodine [1].
Diffusion of bone and brain metastases are much less frequent, but a complete cure is relatively rare [2,3]

After total thyroidectomy for thyroid carcinoma, excision of the gland is seldom complete, but the volume of residual thyroid is often not measurable because too small. The ablative treatment with ^{131}I is performed to "reset" the thyroglobulin levels, with doses aimed to exclude distant metastases, by the use of doses empirical "calibrated" according to the clinical stage; in these cases the values of the iodine test uptake after 24 h from administration and thyroglobulin blood concentration also allow some form of empirical optimization.

Likewise, in the follow up of a patient with thyroid cancer, in the presence of high thyroglobulin levels and with negative ^{131}I whole body scan, a therapeutic activity of 3.7 GBq (100 mCi) of ^{131}I typically prove often justified on a clinical basis.

The most common protocols in clinical paractice are:

1.) High, fixed administered activity: 75–200 mCi of ^{131}I. This protocol tends to be followed by many practitioners, as statistics are quoted as achieving 85% success in eliminating all functioning thyroid activity. The advantages include obviating most need for reablation, fewer laboratory visits and tests, less hospitalization, but higher activities of radioiodine are administered, with radiation protection complications, and an increased radiation dose to critical organs with the potential for complications.

2.) Low, fixed administered activity: 30 mCi of ^{131}I. The advantages include avoidance of hospitalization and reduced radiation dose to the whole body and critical organs. The disadvantage lies in the failure to achieve complete ablation in 17 to 40% of patients, and the possibility that micrometastases may receive inadequate radiation or that residual thyroid tissue after low dose treatment may be more radioresistant.

3.) Administered activity calculated according to a predetermined radiation dose. In this protocol, the activity to be administered is determined according to a formula involving the desired radiation dose, residual tissue mass, effective half-time, 6 and 24-hour uptake.This approach can be considered patient specific, if the individual parameters are known. A dose value of 50,000 to 100,000 rad (cGy) was used in first therapies, but 30,000 rad (cGy) is actually generally considered sufficient.

4.) Quantitative Diagnostic. In this protocol, a tracer dose of ^{131}I is administered to the patient and quantitative imaging techniques are employed to establish patient specific biokinetics. From this diagnostic data, utilizing appropriate calculational algorithms (typically following the MIRD schema involving residence time), the radiation dose to the residual tissue is estimated. The radiation dose that would be delivered by a given therapeutic administration of ^{131}I is extrapolated from the results of this tracer study. A tracer activity commonly used is 2 mCi (74 MBq) Through this protocol, the administered activity may be tailored to provide the desired radiation dose for ablation (generally 30,000 rad (cGy)) while minimizing the radiation dose to other organs by not administering more activity than required.

In the presence of distant metastases the most recent dosimetric ptotocols suggest a maximization of administered dose, by keeping limiting toxicity to red marrow

within safety limit, as a low-rate irradiation allows the repair of sublethal cellular damage and the selection of radioresistant cell clones.

^{131}I dose choice and optimization

When necessary, the ^{131}I dose choice and optimization can be achieved in various ways, depending on the type of treatment, of dosimetric methods available and of the clinical context. When technically possible and clinically convenient, the use of a modeling dosimetry is the best way to optimize the dose; any assessment procedure for dosimetry requires the measurement of three physical parameters:

- target mass (usually considering a density equal to 1 g/ml)
- the activity in the target (with determination of maximum uptake rate)
- time course of the activity in the target (determination of biological half-life, with measures of radioisotope activity during the accumulation and elimination phases).

The estimation of dose to the target must still be supplemented by a dose assessment to critical organs (blood / marrow, but also lungs or other organs). The main aim, in non-oncological patients, should be ideally that of ensuring the conservation of the right amount of healthy tissue, which is essential for a theoretical therapeutic success (euthyroidism).

The optimal outcome after ^{131}I therapy for hyperthyroidism is obviously euthyroidism without postablative hypothyroidism and the consequent need for thyroid hormone replacement. Unfortunately this aim can be hardly realized, as the number of variables affecting the outcome, like severity and duration of the autoimmune thyroid

disease, fractional ^{131}I uptake, dose distribution. Apparently, the higher the prescribed dose, the higher the fractions of patients who are cured and who develop postablative hypothyroidism [4-6].

Optimal doses of ^{131}I could be determined with dosimetry based on the absorbed thyroid radiation dose required, the mass of the thyroid gland, the effective ^{131}I uptake, and the distribution of radioiodine within the gland, as shown by scintigraphy. All these data allow the calculation of the precise quantity of ^{131}I required to deliver a specific absorbed radiation dose to the thyroid.

Although several authors claim to have defined the required absorbed dose, their reports recommend a wide range of absorbed doses from 60 Gy to 300 Gy [7-9].

In a clinical report hyperthyroidism was eliminayed in in all patients at 1 year with an absorbed dose of 300 Gy, but 93% of their patients became hypothyroid [10].

This relatively broad range of recommended absorbed doses makes it apparent that a more quantitative approach is necessary, that could be of benefit in the standardization of the absorbed dose to successfully treats hyperthyroidism, and reduce the incidence of treatment failures and/or subsequent hypothyroidism.
In differentiated thyroid carcinoma, the therapy with ^{131}I aimed to the elimination of residual thyroid after surgery, offers significant survival advantage and better prognosis. A number of retrospective studies have shown conclusively that postsurgical treatment with ^{131}I and thyroid hormone therapy reduces tumor recurrence and mortality [11-13].

Through this quantitative protocol, the administered activity may be tailored to provide the desired radiation dose for ablation (e.g., 30,000 rad (cGy)) while

minimizing the radiation dose to other organs by not administering more activity than required.

At present, proponents of the patient specific quantitative diagnostic preliminar analysis for ^{131}I ablation of thyroid remnants are in the minority of practitioners. The primary reasons are that the quantitative approach is labor intensive (and thus expensive, with commitment of both staff and patient extended over a period of days) and that a number of intrinsic factors introduce inaccuracies (e.g., mass estimation) that mitigate significance of the result in spite of the effort.

Thus, in the clinical practice, the dosimetric approach is not employed frequently, due to the lack of easily manageable clinical diagnostic tools.The dosimetric approach is highly useful for the treatment of loco-regional and/or distant metastases. Dosimetry is particularly indispensable in the case of a pediatric patient, or in patients with lung and/or bone metastases, where standard activities can lead to a radiation dose imparted to the lesions lower than necessary.

A successive change in the biokinetics of pulmonary metastases after several therapies has been observed. In these studies it has been demonstrated that dosimetric parameters such as radioiodine uptake as a percentage of therapeutic activity, effective halflife and radiation dose delivered to the lungs which were evaluated with each therapy, showed a progressive decline in each of these parameters with successive therapies.

Their data also suggest that the repetition of treatment of a lesion drastically reduces its uptake, with a loss of therapeutic efficacy along the sequence of fixed activity administrations [14,15].

^{131}I uptake test

Thyroid uptake determination is the measurement of the fraction of an administered amount of radioactive iodine that accumulates in the thyroid at selected times following ingestion. The radioactive iodine uptake test is a type of scan used in the diagnosis of thyroid problems, particularly hyperthyroidism. The test is also used as a follow up to ^{131}I therapy, to verify that no thyroid cells survived, which could still be cancerous.

The patient swallows radioactive iodine in the form of capsule or fluid, and its absorption by the thyroid is studied after 4–6 hours and after 24 hours with the aid of a scintillation counter. The ingested activity is typically 0.15–0.37 MBq (4–10 μCi) of ^{131}I sodium iodide, or 3.7–7.4 MBq (100–200 μCi) of ^{123}I sodium iodide [16].

The normal uptake at 24h is between 15% and 25%, but this may be forced down if, in the meantime, the patient has eaten foods high in iodine, such as dairy products and seafood [17].

As a matter of fact, in the literature,the customary normal range of values is usually given as between 10% and 35% for 24-hr uptake, and between 6% and 18% for 4-hr uptake. These values must be interpreted loosely, since they were determined with a variety of equipment, standards, uptake phantoms, and in individuals from populations with different iodine intakes, which may not be directly comparable to the patients under study. Low uptake suggests thyroiditis, high uptake suggests Graves' disease, and unevenness in uptake suggests the presence of a nodule.

Usually a probe with a 2-inch thick sodium iodide crystal at least 2 inches in diameter with suitable shielding and a flat-field collimator, providing a field 10 cm in diameter at the surface of the patient’s neck, is used for uptake determinations, usually 6 and

24 hr after administration of the radioiodine. The measurement is usually performed with 25–30 cm between the face of the crystal and the anterior neck or phantom. Neck counts, lower thigh counts and counts of a calibrated standard in a neck phantom and background counts are preferably obtained at each counting session. The radioiodine uptake (RIU) is calculated as :

$$\frac{\textit{Neck Counts (cpm)} - \textit{Thigh Counts (cpm)}}{\textit{Administered Counts (cpm)} - \textit{Background Counts (cpm)}}$$

The Thigh Counts is subtracted from the Neck Counts in order to empiricaly account for the blood pool ^{131}I activity. This subtraction is sometimes misleading, as the background can be different from the one calculated in this way. As four different countings are necessary in this procedure, a great care should be taken in the reproducibility of the position of the patient during the countings. Source of errors are caused by the variations in neck to detector distance, inappropriate neck phantom for administered activity counts, improper centering of the probe over the patient's neck [18-27].

New proposed experimental protocol for the measurement of ^{131}I uptake and thyroid volume evaluation

Measurement of the gland mass (or volume) is an important source of inaccuracy that is inherent in both simple and sophisticated dose calculations. The dimension of the thyroid are usually extracted by ultrasonographic measurements.

Unfortunately, the total mass is not of the thyroid is not always coincident with the ^{131}I uptaking tissue, and radiotracers obtains information not only on thyroid size but also on its functional morphological function.

Although the fractional thyroid uptake of radioiodine is a precise measurement, determinations at only one time point provide limited information about isotope residence in the gland over time (*i.e.* area under the curve). The effective half-life (T_{eff}) has to be at least determined from a 4 to 6 h, and a 24-hour uptake measurement.

The radioactive iodine uptake test is usually associated in time with scintigraphy of the thyroid. In the same session the patient usually undergoes scintigraphy by a planar gamma camera, and uptake measurements by using the sodium iodide crystal scintillator device. In this way five different measurements each time are necessary (scintigraphy, neck measurements, thigh measurements for patient blood background, administered activity, room background).

In line of principle, however, all the necessary qualitative and quantitative informations on thyroid dimensions, uptake and distribution could be extracted only from the recorded scintigraphy. The aim of the proposed experimental procedure is the extraction of all the ^{131}I uptake quantitative information and of thyroid mass evaluation only from the scintigraphic image; in order to do this it is, first of all, necessary the warrant of an accurate positioning of the patient or neck phantom respect to the gamma camera.

To accomplish this all geometrical variations should be minimized as much as possible; in the present work a gamma camera model MONOGAMMA (L'ACN, Milan, Italy) was slightly modified.

In this gamma camera a lead collimator is present, which reduces the detection of background radiation of the camera head, and furnish a focusing of a readable image. The collimator can be a parallel multi-hole collimator, composed of lead septa that absorb photons that are not normal to the plane of imaging, or a pinhole collimator,

that consist of a single small circular aperture at the end of a conical shape lead shield.

After the collimator, the detector assembly is contained, basically consisting in a scintillator array (e.g., sodium iodide scintillator, activated with a trace of thallium), to convert the photons into visible light. The scintillator is coupled through light guides to multiple photomultiplier tubes, or other light sensors, that convert the light coming from the scintillator into an electric signal. The obtained electric signals can be easily transferred, converted, and processed by electronic modules in a data acquisition system, to facilitate viewing and image manipulation. In all present experiments the apparatus was always used in pinhole configuration.

A series of additional lead pinhole collimators have been manufactured and assembled in our laboratory, with hole diameter from 2 to 5 mm in diameter, in order to find the the best compromise between sensitivity and resolution for clinical imaging.

Furthermore, a new positioning device, located in front of the pinhole of the gamma camera, was assembled, aimed to keep a contant distance of the pinhole from the neck of the patient during the measurements.

The positioning device with fiduciary marks was made using only soft neoprene and nylon wire, in order to ensure an accurate positioning, avoiding the patient discomfort, and any collision of hard, potentially dangerous material against the reegion of the neck of the patient during the movement of the gamma camera (see Figure 1).

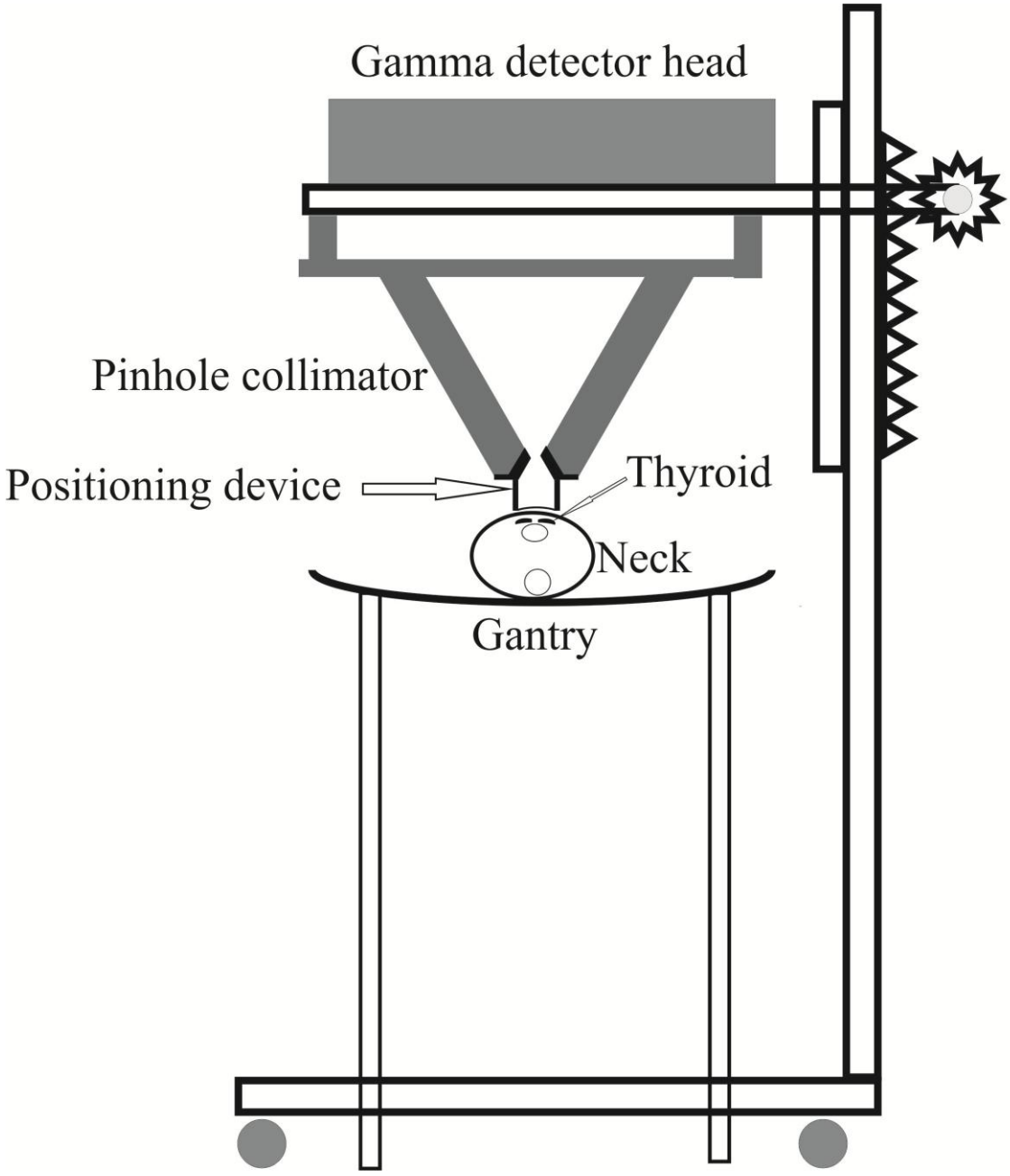

Figure 1

The reproducibility of the movements of the positioning device has been measured in neck phantom and in 30 different patients; a standard deviation in spatial position of about 1 mm was found.

The optimization of the resolution of the gamma camera and the additional positioning device allowed the possibility of a quantitative measurements of the absolute activity of the ^{131}I, as the geometric uncertainty of the counting due to misalignement of the patient or to distance variations between the detector and the thyroid is virtually eliminated. The same device is also used for the accurate positioning of the capsule of ^{131}I , in order to obtain the absolute value of the administered activity for each patient.

After the accurate positioning of the patient under the gamma camera, and the acquisition of the scintigraphic image, the data treatment is started. In order to perform all the necessary calculation, an original program in JAVA language has been written, by working with the software package Image-J, an open source product, distributed by National Institute of Health, widespread used for data imaging analysis in the biology and medical fields. After the acquisition of the scintigraphies, usually 6 and 24 h after the ^{131}I ingestion, the following operations are sequentially and automatically performed by the new software:

- Convert stored files from proprietary format to general use DICOM
- Measurement decay of ^{131}I capsule
- Measurement of background
- Measurement activities of the of ^{131}I certified source, to calculate the efficiency factor of the detector
- For each scintigraphy and each patient:

  - ✓ Automatic measurement of the thyroid ROI (Region Of Interest)
  - ✓ Automatic measurement of backgrond ROI
  - ✓ Approvation of the operator of the correctness of chosen ROI
  - ✓ Scaling for decay

- ✓ Conversion of thyroid counting to absolute activity
- ✓ Calculation of uptake for each scintigraphy

- Printing of the final uptake curve graph.

While most of the corrections are trivial, the automatic measurements of thyroid and background ROI's had to be accurately tested and validated with a series of thyroid neck phantoms.

Different image data algorithms (Triangle algorithm, Huang method, Max Enthropy method, Otsu's Clustering algorithm, Li's Minimum Cross Entropy Thresholding method) for automatic ROI definition have been tested, with different clinical thyroid images.

At last, an iterative procedure based on the Isodata Algorithm [28] was developed, that has proved to be able to discriminate the thyroid region in a wide range of uptake values, and in different thyroid pathologies and morphologies of the organ.

The procedure divides the image into object and background by taking an initial threshold, then the averages of the pixels at or below the threshold and pixels above are computed. The averages of those two values are computed, the threshold is incremented and the process is repeated until the threshold is larger than the composite average.

After all the corrections, the value of absolute activity residing in the thyroid is easily and reliably obtained from a single scintigraphic measurement.

The volume of the thyroid can be otained from a simple planar image of the thyroid, by using the Himanka and Larson expression [29]

$$V=0.33 \cdot A^{3/2}$$

where ***A*** is the planar area of the thyroid extracted from the ROI, or, if a SPECT is obtained, from the formula of the ellypsoid method [30]

$$L \times AP \times T \times 0{,}523$$

where ***AP*** is the anteroposterior , ***L*** the lateral and ***T*** the transversal diameter of each thyroid lobe .

It has been demonstrated [31] that from a simple planar scintigraphy the thyroid volume otained differ from about 5% from the sonography extimation, so the planar method has been adopted in the present work s for all volume measurements.

The Figure from 2 to 6 show some example of the images obtained with the modified apparatus.
In Figure 2 a normal thyroid is shown.
The Figure 3 shows a thyroid in which the right lobe has an higher ^{131}I uptake than the left one.
The Figure 4 shows a thyroid in which the uptake of one lobe is strongly predominant.
In the following Figure 5 and Figure 6 are shown the thyroid residues after surgery. It can be seen that the pictures have an excellent spatial resolution, and a virtual absence of background from the neck of the patients.

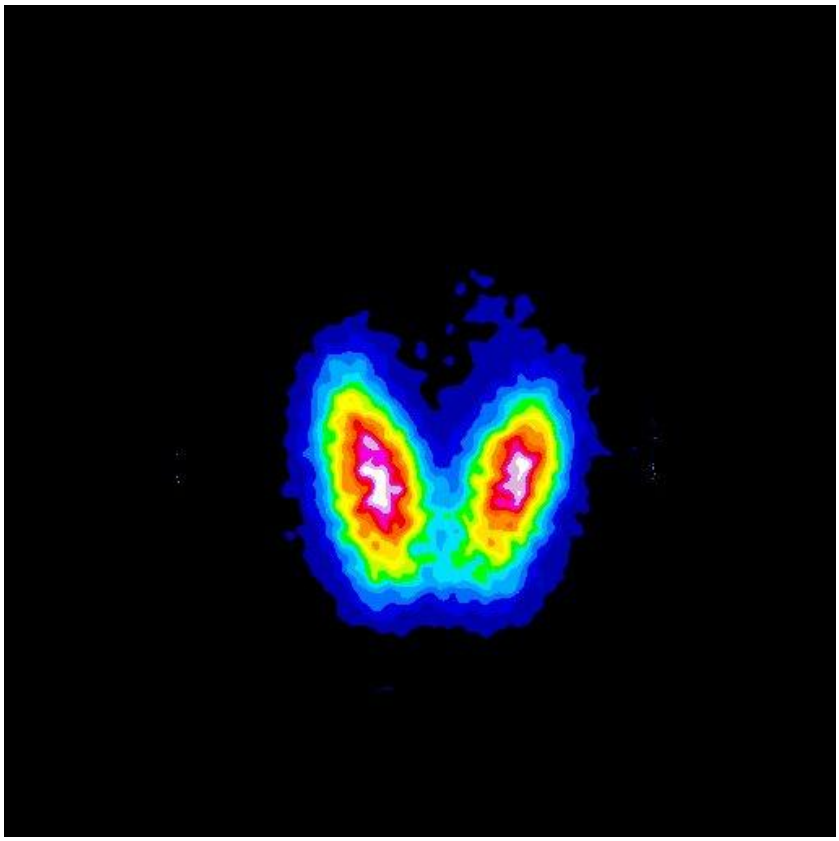

Figure 2

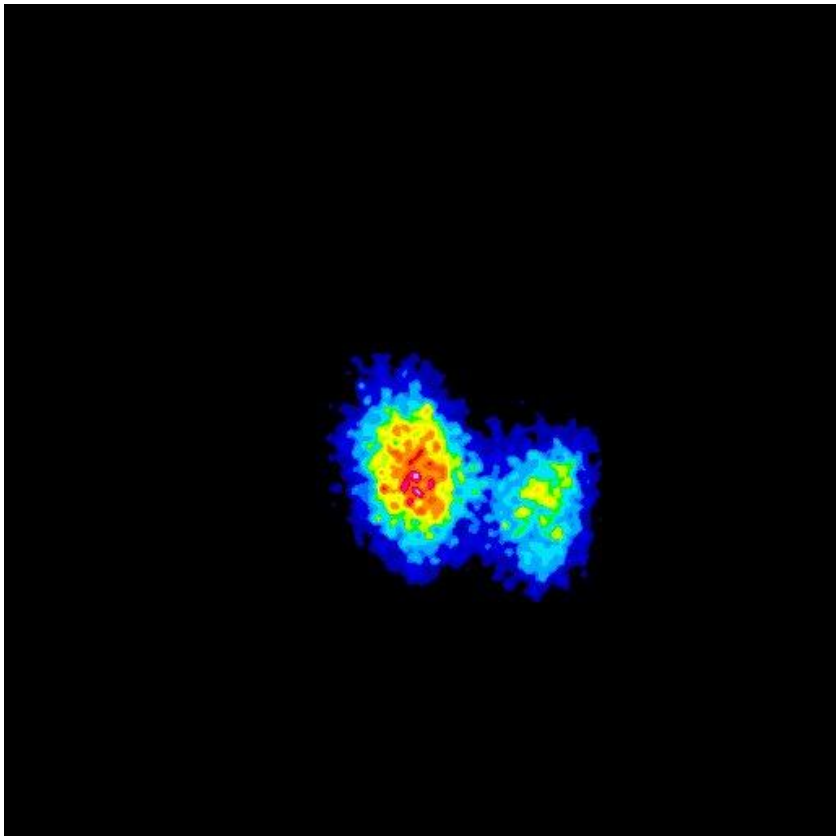

Figure 3

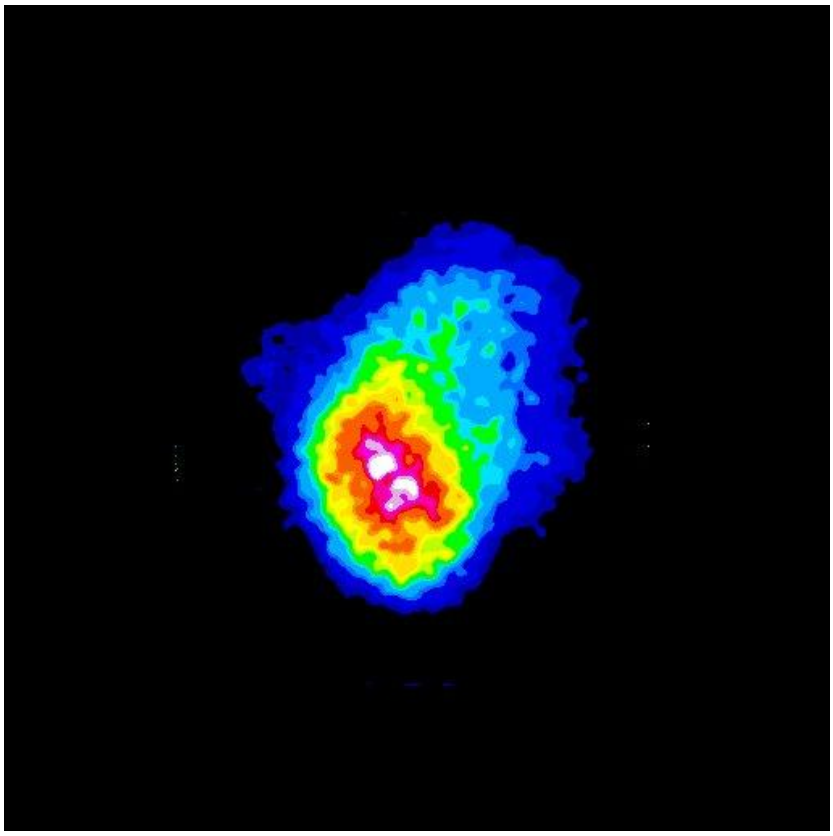

Figure 4

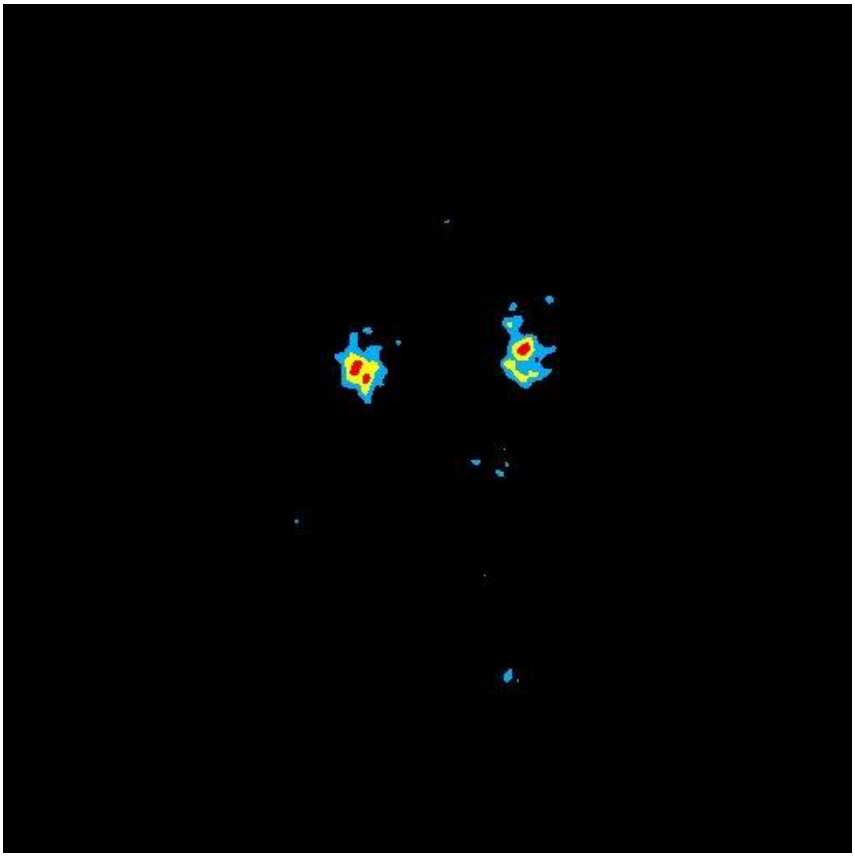

Figure 5

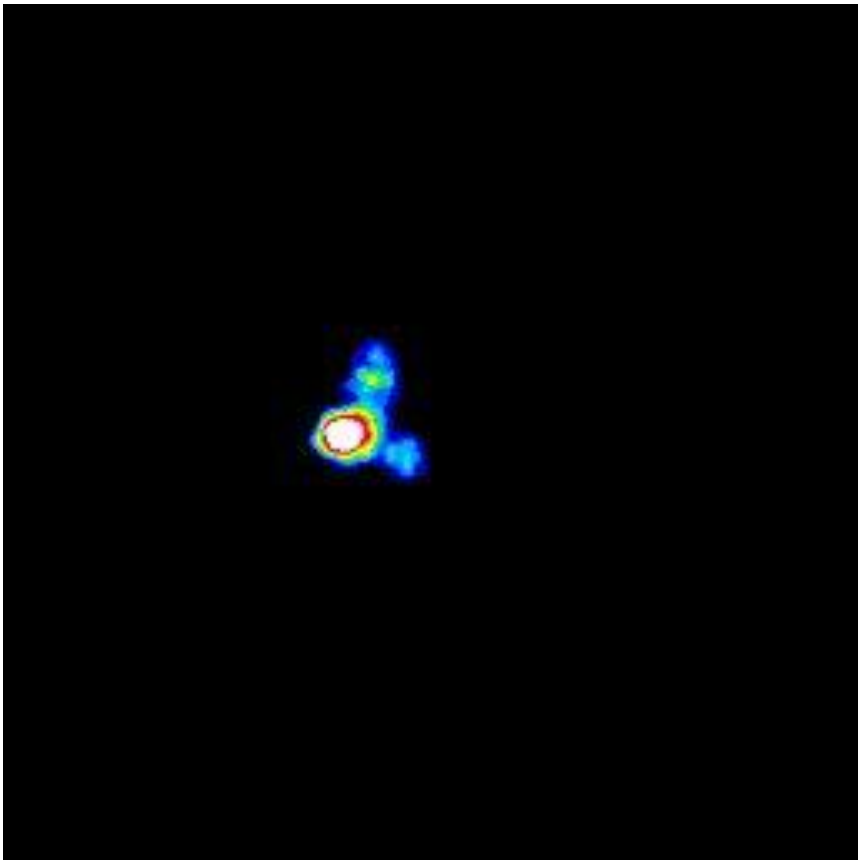

Figure 6

In order to check the quantitative radioactivity determination of the new protocol, on a cohort of patients a double measurement of of ^{131}I uptake has been performed, by using both single scintillation detector, and gamma camera scintigraphy.

The Figure 7 shows the comparison of obtained data; it is clearly visible that a close proportionality was always found between gamma camera and single scintillator tube.

A comparison of absolute radioactivity sources with neck phantoms containing calibrated ^{131}I sources demonstrated for the two methods a closed proportionality, but the gamma camera determination had always greater accuracy; this fact can be fundamental for high or low thyroid activity values, in which relative errors with single detector can be unacceptably high.

Moreover, by using the gamma camera method it is always possible to perform a check of the centering of the thyroid, due to the fact that the clinical scintigraphic image is always registered; the same is not true for the single scintillator determination, for which positioning errors in clinical routine are far more frequent, and often undetectable.

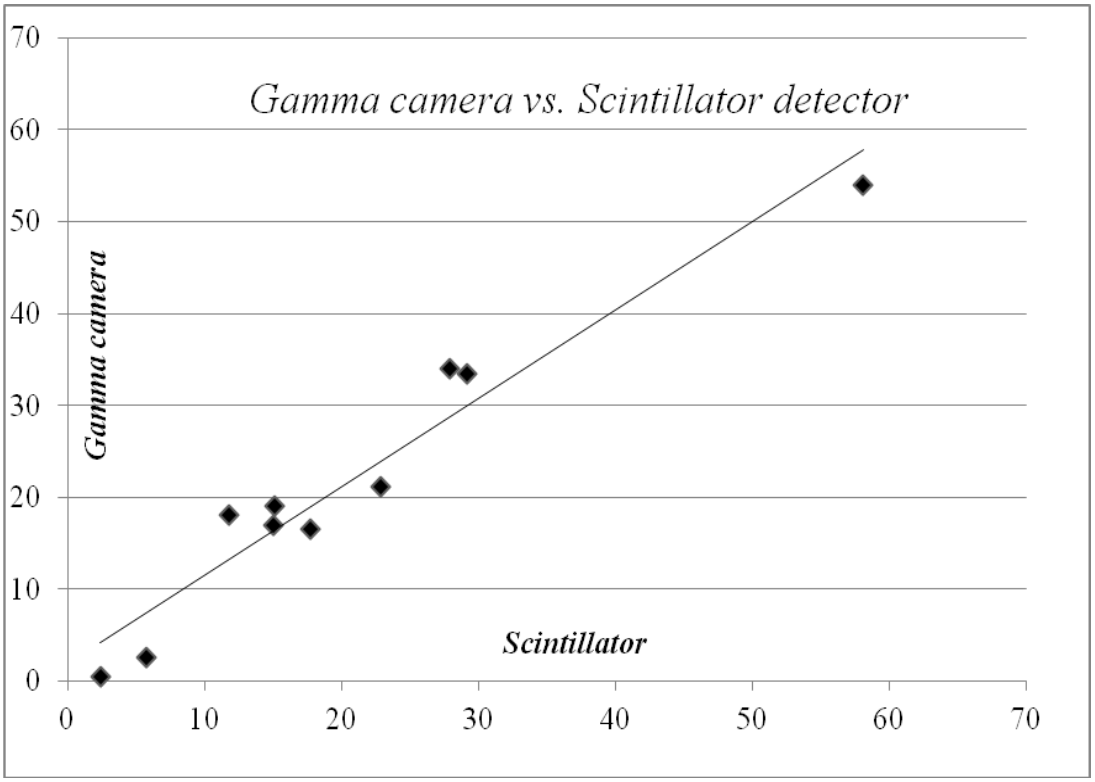

Figure 7

In conclusion, we have demonstrated that by performing small modifications to the gamma camera hardware to increase the repeatability of the measurements, and by using a software that can extract all the informations contained in the scintigraphic image, it is possible to use as a routinary clinical protocol a quantitative dosimetry approach.

From each scintigraphic image the residual or active tissue mass, the effective half-time and the 6 and 24-hour uptake are obtained, and for each patient the activity to be administered is determined according to a formula involving the desired radiation dose.

This approach can be considered really patient specific, so providing a base for the optimization of the desired radiation dose for ablation while minimizing the radiation dose to healthy organs.

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