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Dosimetric Evidences in Radioiodine Customized Hyperthyroidism Treatments

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Abstract

The radioiodine therapy is considered an almost definitive and successful hyperthyroidism treatment, alternative to surgery. Unlike a standardized activity approach is still adopted, a customized dosimetric study offers the significant advantage to take into account the individual variabilities in the structures to be treated. In the present work, some of the current issues relating to customized radioiodine treatment are discussed. The experience acquired during several years of customized hyperthyroidism radioiodine treatments performed at the S. Anna Hospital in Como (Italy) is presented, together with the main results of an extensive follow up analysis.

Introduction

Hyperthyroidism and Graves' disease treatments require the administration of important ^{131}I activities [1-4] to achieve a nonhyperthyroidism status (i.e. euthyroidism or hypothyroidism) and cause significant patient residuals over the days following the radiopharmaceutical administration [5-9].

The prescription of standard therapeutic activities is still a common clinical practice. The standardized radioiodine activities range normally between 300 and 600 MBq/patient, depending only on the thyroid volume, and they can exceed 1 GBq for serious illnesses.

Otherwise, the customized treatments, based on *in vivo* kinetic studies, represent a valid choice, allowing the optimization of the administrated activity [10-16]. This approach offers an overall reduction of both the patient dose and the consequent radiation protection concern, maintaining the same level of therapeutic effectiveness. The actual Italian guidelines [6,17] suggest that, at the discharge, the patient residual activity should be less than 0.030 mSv/h (in terms of ambient dose equivalent rate), corresponding to a residual activity less than 600 MBq.

In this context, the evaluation of the optimization process, in terms of clinical outcome and radiation protection impact, is of great significance.

The present communication is devoted to these important topics and describes the main physical aspects in the activity assessment, involving pre-therapeutic uptake measurements and functional volume evaluations. The radioiodine treatment procedure adopted at the Sant'Anna Hospital is described and the experimental evidences supporting its clinical effectiveness are also summarized. Since the residual internal activities may be significant, a short consideration regarding the patient radiation protection is also discussed and an innovative method to estimated the radioiodine residual activity is proposed.

Materials and Methods

According to the AIMN-AIFM (Associazione Italiana di Medicina Nucleare - Associazione Italiana di Fisica in Medicina) guidelines [17], the patient-specific bio-kinetic is studied by administering a ^{131}I sodium-iodide track activity (about 2 MBq) in the pre-treatment phase. The radioiodine kinetic is described by the uptake curve: the experimental data are acquired at 2, 24, 96 hours from the administration time, with an adjunctive point at 6 hours for Graves' diseases. The data were fitted by a bi-exponential mathematical function, according to the two compartment model pharmacokinetics of ^{131}I, by means of a home-made automatic software (PROFit) [18].

The extrapolated functional parameters are: the uptake percentage maximum value U_{max} and the radiopharmaceutical effective half-life $T_{1/2\text{-}eff}$.

To calculate the activity to be administered, two additional parameters must be defined: the functional thyroid volume and the target prescribed dose.

The functional thyroid volume was evaluated by both tomographic SPECT (using ^{99m}Tc-pertecnetate) and CT images, acquired by a SIEMENS SYMBIA T integrated diagnostic system. Both images were combined by means of a 3-D fusion software, working independently from the acquisition modalities. An additional estimation of the functional volume was provided by a home-made software developed with MATLAB 2010b and based on the Recovering Iterative Thresholding Method (RIThM) [19].

The prescribed dose was assessed according to specific clinical protocols.

The customized activity is finally computed by applying the following equations [12,17]:

$$A = 5,829 \cdot \frac{D \cdot m}{U_{max} \cdot T_{1/2\,eff}}$$

(Basedow-Graves' disease).

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(multinodular and uninodular pre-toxic and toxic goiter).

where D is the prescribed dose, m is the functional mass, $T_{1/2\text{-}eff}$ the radiopharmaceutical effective half-life and U_{max} the uptake percentage maximum value.

In this study, 151 patients treated at the Department of Nuclear Medicine of the S. Anna Hospital have been considered. The specific thyroid pathologies were: the Graves' disease (50.9%), the multinodular (16.6%) and the uninodular (32.5%) pre-toxic and toxic goiter. The statistical analysis was carried out by both dosimetric and the clinical response data and performed by the SPSS.20 Statistics software (SPSS inc. Chicago, IL, USA).

The mathematical model to evaluate the residual activity is based on the relationship between the activity, the ambient dose equivalent rate $H^*(10)$, the gamma constant Γ and the source-detector distance (d) [4]. To consider both the iodine distribution and the tissue uptake, an effective distance d_{eff} was introduced, where $d_{eff}=d+d_x$, where d_x is virtual distance accounting for both the radiation source geometry and the body tissues attenuation. In this way, both the mean depth of the ^{131}I 3D body distribution and the photon-tissues interaction are evaluated. For this aim, two measurements at known distances (d_1 and d_2) are required. Applying the inverse square law to the H*(10) rates and assuming that:

$$C = \sqrt{\frac{\dot{H}^*_2 (10)}{\dot{H}^*_1 (10)}}$$

the mathematical relation between these variables becomes $d_{1+}d_{x=}C$ ($d_{2+}d_x$) and the activity can be calculated as:

$$A = F^2 \frac{\dot{H}^*(10)d^2}{\tilde{A}}$$

Where F is expressed by the following relationship:

$$F=(d+d_x)/d$$

This algorithm was validated by a clinical trial including 40 patients, comparing the administered activities with the calculated ones. All these cases referred to customized radioiodine therapy: Graves' disease (19), uninodular (15) and multinodular toxic goiter (6). The external measurements were taken immediately after the radioiodine administration and before patient voiding (i.e. with the whole activity inside his/her body), at the hospital discharge (4 hours later) and during the follow-up (4 days later).

Results

The main outcome evidenced by the retrospective analysis of the pretherapeutic dosimetry clinical results is the mean reduction in the administered activities (435 ± 150 MBq/patient) compared to the standard one. These values represent a significant dose savings, given the consolidated tendency to use activities close to 500-600 MBq, which are approximately 20-25% higher than the customized ones.

The clinical response analysis pointed out that all uninodular and multinodular goiters recovered in a single treatment, while Graves' disease account for a 85.1% remission percentage. The low frequencies of Graves' disease re-treatments and the total remission of nodular goiters indicate that the customized radioiodine hyperthyroidism approach is very effective.

The proposed method to evaluate the residual activity provides an effective tool to check the radioiodine remainder at the patient discharge. The mean difference between administered and measured activities was about 0.5% and the standard deviation was 5.4%. The mean percentage excreted activity was 11.3% ± 12.7% at 3-4 hours after the radioiodine administration, and 43.0% ± 14.8%, about 4 days later.

It seems evident that the absolute values of the excreted activity would be significantly higher in the case of standardized activity administration. The same clinical results confirm a significant dose reduction. As regard to the d_{eff} extent, the mean reduction measured in the d_x value (from 82 ± 40 mm after the administration to 34 ± 36 mm 4 day later) can be attributable to the progressive iodine uptake by the thyroid gland, which reduces both the tissues thickness crossed by the photons and the related attenuation.

Discussion

This study pointed out the excellent outcome of the treatment customization and the concomitant reduction of the administered activity, when compared to the standardized procedures.

On the basis of the theoretical-experimental model, a good procedure to estimate the residual activity and an effective radiation protection tool is offered, which significantly reduces the error margins within an approximate range of ±11%.

These results are more than enough to justify the efforts required to improve the procedures to customize the hyperthyroidism radioiodine treatments and to develop a check program to evaluate the residual activity of treated patients.

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