Iodine Total Body Scintigraphy

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1. Introduction

Radioactive iodine (^{131}I or ^{123}I) is administered to the patient. Usually, the administration is oral.The amount to be administered depends on the clinical indication and can vary from a low, diagnostic dose to a high therapeutic dose. Scintigraphic images of the whole body are made one day post administration (preablation scintigram for evaluation of residual thyroid tissue in the thyroid bed after total thyroidectomy), a few days post administration (diagnostics in the follow-up after ablation with ^{131}I) or about 1 week post administration (post-therapy scintigram).

Inorganic iodide, such as ^{131}I or ^{123}I, is taken up in thyroid cells and organically sythesised into iodotyrosine residues (precursors of thyroid hormones) in thyroglobulin. Thyroglobulin is stored in the colloid of the thyroid follicles. Differentiated thyroid carcinoma cells also possess this uptake and organification mechanism, but to a lesser extent than normal thyroid tissue.The uptake of (radioactive) iodine in thyroid cells and thyroid carcinoma cells is stimulated by thyroid-stimulating hormone (TSH). A high TSH level is achieved by the withdrawal of thyroidhormones. An alternative to this is the intramuscular administration of recombinant human TSH(rhTSH), which is registered as a preparation for the determination of thyroglobulin, whether or not combined with a total-body scintigram in follow-up after ablation and in preparation for the ablation itself. The dose of rhTSH for stimulating radioiodine uptake in benign disorders is lower than in malignancy.

2. Methodology

This guideline is based on available scientific literature on the subject, the previous guideline (Aanbevelingen Nucleaire Geneeskunde 2007), international guidelines from EANM and/or SNMMI if available and applicable to the Dutch situation.

3. Indications

Differentiated thyroid carcinoma (papillary/follicular)

a. Pre-ablation scintigram after thyroidectomy, prior to ablation with ^{131}I in order to asses and measure locoregional uptake.
b. Post-therapy scintigram after ablation or treatment with ^{131}I.
c. Follow-up in patients who do not meet the criteria for low risk of thyroid cancer recurrence (see ^{131}I therapy in patients with thyroid carcinoma) in which Thyroglobulin (Tg) measurements are not reliable. This may occur in dedifferentiation of thyroid cancer or in the presence of Tg-antibodies.

4. Relation to other diagnostic procedures

Although the literature provides limited evidence for the usefulness of conducting a pre-ablation scintigram (since almost all patients are treated with ^{131}I after the scintigram), the

pre-ablationscintigram offers the possibility of adapting the treatment to the findings on the scintigram (the level of the therapeutic dose of ^{131}I; possibly revision operation in the presence of high uptake and/oruptake in multiple lymph nodes). In this respect, uptake measurements should be done with either a low dose ^{131}I or ^{123}I to avoid possible stunning effect.
The role of total-body scintigraphy with diagnostic quantities of ^{131}I in the follow-up after ablation of patients with differentiated thyroid carcinoma is limited. In patients with a low risk of recurrent thyroid carcinoma, the follow-up consists of the determination of Tg, supplemented by an ultrasound of the neck. For this category of patients, the additional value of the total-body scintigraphy is very limited due to a low sensitivity. In the follow-up of patients who do not meet the criteria for a low recurrence risk, there is still a role for the diagnostic total body scintigraphy. If an elevated Tg-level is found during thyroid hormone replacement, a "blind" therapeutic dose of ^{131}I may be decided upon. This may also be decided if an elevated Tg-level is found after TSHstimulation in combination with a negative diagnostic total body scintigram.The post-therapy scintigram is important for further therapeutic management. To increase sensitivity and localization of uptake, SPECT/CT should be added to this diagnostic procedure.

5. Medical information necessary for planning

a. Type of tumour.
b. Date and extent of thyroidectomy and/or lymph node dissection.
c. Findings at surgery and pathological anatomy: tumour size, extension beyond the thyroid capsule, angioinvasion, lymph node metastases, radicality of the resection.
d. Information on any other treatment in connection with the thyroid carcinoma.
e. Use of thyroid hormone medication.
f. Possibility of large iodine load in the past 6 months: iodinated at surgery, iodinated contrast medium and/or medication (including any homoeopathic remedies).
g. Thyroid function tests: TSH, fT3, fT4.
h. Tumour markers: thyroglobulin; thyroglobulin antibodies in serum.
i. Pregnancy and/or breastfeeding.

6. Radiopharmaceutical

Tracer:	^{131}I-sodium iodide (pre-ablative or possibly ^{123}I-sodium iodide)
Nuclide:	Iodine-131 (pre-ablative or possibly Iodine -123
Activity:	Pre-ablation scintigram 40-80 MBq ^{131}I (185-370 MBq ^{123}I) Post-ablation follow-up 80-185 MBq ^{131}I Post-therapy scintigram after ablation 1100-3700 MBq ^{131}I, in locoregional metastases or non-radical resection of primary tumour 3700-7400 MBq ^{131}I, in remote metastases 5550-7400 MBq ^{131}I
Administration:	Usually orally as a capsule, sometimes as an oral or intravenous solution
Adverse effects:	acute adverse effects occuronly with higher doses. These include nausea, vomiting, fatigue, headache, sialadenitis, painful swelling of metastases, thyroid storm, bone marrow depression. Longer term side-effects may include impaired salivarygland function, haematological effects, pneumonitis/pulmonary fibrosis,transformation/dedifferentiation of the tumour, fertility disorders, inductionof leukaemia and solid tumours.

7. Radiation safety

Absolute contraindications: pregnancy and breastfeeding. Breast feeding should be interrupted for at least 3 weeks according to ICRP 106.

Relative contraindications:

a. Bone marrow depression: if administration of high dose of ^{131}I is intended.
b. Pulmonary function restriction: if significant ^{131}I uptake is expected in lung metastases.
c. Salivary gland function restriction.
d. Neurological symptoms which can be worsened by ^{131}I therapy.

Radiation exposure: The effective dose depends on the administered activity and uptake in target tissue, i.e. thyroid remnant and/or thyroid cancer metastases.

8. Patient preparation/essentials for procedure

The following preparations are prerequisites for an optimal procedure:

a. Pregnancy test prior to ^{131}I administration in women of childbearing age.
b. An interval of 4 weeks must be adheredto between thyroidectomy and post-operative ablation. During this interval thyroid hormone treatment should not be commenced.
c. At the time of maximal TSH stimulation, just before administration of ^{131}I therapy, determine Tg and anti-Tg , as well as TSH and fT4.
d. Thyroid hormone medication should be discontinued prior to scintigraphy: 4 weeks for levothyroxine, 2 weeks fortriiodothyronine (Cytomel R).
e. If the patient is to be treated/ assessed under recombinant TSH, 0,9 mg rhTSH is administered intramuscularly at 48 h and 24 h prior to the administration of radioactive iodine. This is an alternative to thyroid hormone withdrawal and can be administered by a general practitioner. Thyroid medication need not be stopped if rhTSH is used.
f. After rhTSH-preparation, a check of the TSH stimulation must take place on at least one occasion, e.g. just before the second injection of rhTSH, and preferably also just prior to the administration of radioactive iodine.
g. If rhTSH is used Tg and anti-Tg should be determined on the day of total-body scintigraphy, i.e. 48 h after administration of the radioactive iodine. Additional measurements of Tg and anti-Tg at other times (e.g. prior to the first administration of rhTSH and 5 days after the administration of iodine) may be of use.
h. Skin iodination, iodinated contrast medium and iodinated medication (including homoeopathic remedies) must be avoided.
i. As of 7 days prior to the administration of radioactive iodine, salt-water fish should be avoided. A diet limited in iodine is recommended as of 4 days prior to radioactive iodine administration.
j. Admission to an isolation ward for the administration of therapeutic doses of ^{131}I.
k. Prior to the scintigraphy allow the patient to urinate and to drink a glass of water. Remove all metal as well as handkerchiefs from pockets.

9. Acquisition and processing

General aspects:

a. Allow patients to urinate shortly before the acquisitions.
b. Views: Supine, whole body anterior, posterior and possibly lateral. Some authors consider SPECT or SPECT/CT to be mandatory for better localization of tumour deposits.

c. Time: depending on the indication between 1 day to approximately 1 week post ^{131}I or ^{123}I administration.
d. Standard for calibration: 10 min recording and/or total body recording of a standard solution in a perspex phantom.
e. Processing of data: For dosimetry purposes, regions of interest and a calibration source are used to determine the absolute uptake (%) in the residual tumour after background correction. (A geometric mean may be used.) By performing this calculation on a series of images, an impression of the effective half-life ($T_{1/2}$ eff) can be obtained.

Gamma camera and computer settings:

Energy:	^{131}I setting, 364 keV (^{123}I setting, 159 keV)
Window:	15-20%
Collimator:	HEAP (LEHR or MEAP if using ^{123}I)
Planar images:	Counting time : Diagnostic 10-15 min, post-therapeutic 5-7 min
Computer:	Matrix size 128×128
Total-body scans:	Running speed 5-10 cm/min (especially with diagnostic quantities of ^{131}I keep to a low speed). Matrix size 128×512

The imaging session may be completed with a SPECT (SPECT/CT) scan of the anatomical regions showing pathological tracer uptake on planarimages. The SPECT images are obtained over a 360°orbit (128×128 word matrix, 6° angle steps, 30-45 sec per stop). Co-registered CT images (100-130 kV, mAs modulation recommended) from SPECT/CT cameras, enable attenuation and facilitate precise localizationof foci of increased activity.

Reconstruction:
SPECT iterative reconstruction or reconstruction using validated protocols to allow accuratevisualization of lesions and CT-based attenuation correction of SPECT, can be performed. Attenuation correction can be done on SPECT images alone based on the constant μ before or after processing (e.g. Sorenson,Chang), but it is not usually done. Scatter correction methods using spectral analysis can be used to improve the accuracy of quantification.

10. Interpretation and pitfalls

To improve the interpretation of an Iodine total body scintigram, all clinical, histological, biochemical and radiological information should be used.

a. Structures that normally show high uptake of ^{131}I include the salivary glands, oral cavity, oesophagus, thyroid tissue, gastrointestinal tract and bladder.
b. Concentrations outside these structures are suspected tumour.
c. False-positive findings are caused by accumulation of activity resulting from contamination (e.g. handkerchief), hydronephrosis, salivary activity in the oesophagus. Furthermore, uptake of ^{131}I is also described in certain conditions, such as pneumonitis, kidney cysts, Meckel's diverticulum, benign and malignant tumours of the lung, stomach and ovaries.
d. False-negative outcomes can result from inadequate preparation, (e.g. insufficient TSH stimulation, iodine intake) or dedifferentiation of the tumour (no iodine uptake).

11. Report

a. The images are evaluated for the presence of pathological activity concentrations corresponding to tumour sites.
b. The uptake (% of the dose) and retention (T eff in days) of iodine in the residual thyroid gland and/or tumour is stated.
c. In the event of unanticipated findings, confirmation by another (anatomical) technique may be indicated.

12. Literature

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