Problems and pitfalls in thyroid uptake measurements with iodine-131

To the Editor: We consider of use to remind possible errors in the measurement of radioiodine uptake (RAIU) because in articles published in HJNM in the past these errors have not been mentioned [1]. Measurement of RAIU by the thyroid introduced in 1930s, remained an essential test for several years to confirm the diagnosis of hyperthyroidism, to distinguish other causes of thyrotoxicosis and to provide data for calculation of the therapeutic ^{131}I dosage [2]. Today RAIU test is used only in some centres for the calculation of the therapeutic dose of ^{131}I in hyperthyroid patients. Nevertheless, differences in neck phantom characteristics, high voltage fluctuations on phantom count rates, problems of attenuation and unpredictable scatter characteristics, among other causes, have been shown to induce significant errors in RAIU measurements [3]. We describe 4 cases of incorrect RAIU due to error. As a standard procedure all patients before the RAIU study, refrained from taking T_4 for 6 weeks, antithyroid drugs for 1 week and iodinated drugs for 4-6 weeks [4]. All patients had an iodine free diet the last week before the RAIU study. After fasted for 4-6 h, all patients received 185 kBq ^{131}I orally in liquid form. An accurately measured aliquot was used as standard, placed in the thyroid uptake phantom. The dose was counted with the same scintillation detector from a distance of 25 cm from the crystal. Counts were obtained for 2 min with the same detector-to-skin distance, from the neck and from the thigh, for background correction. Calculation was performed with the formula described below [4]:

$$RAIU = \frac{\text{Neck counts (cpm) - Thigh counts (cpm) x 100}}{\text{Administered counts (cpm) - Background counts (cpm)}}$$

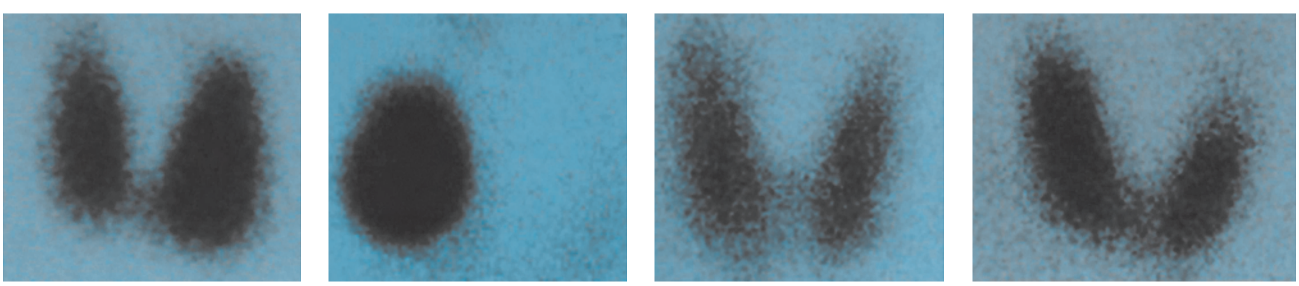
The reference values for RAIU in our centre range from 6% to 18% for 4h and 10% to 35% for the 24h.

In the first case, a 32 years old female patient with hyperthyroidism, underwent RAIU study and thyroid scintigraphy. Free triiodothyronine (FT3), free thyroxin (FT4) and thyroid-stimulating hormone (TSH) levels were measured as; TSH: 0.025 μIU/mL (N: 0.27-4.2 μIU/mL), FT3: 5.69 pmol/L (N: 3.95-6.8 pmol/L) and FT4: 21.42 pmol/L (N: 12-22 pmol/L). Thyroid scintigraphy with $^{99m}TcO_4^-$ showed a diffusely by hyperplasic thyroid gland (Fig. 1A). RAIU values were 1% and 1.8%, for 4h and 24h, respectively discordant with thyroid scintigraphy and thyroid function tests. RAIU study repeated 2 weeks later, showed values of 24% and 46%, respectively. Re-evaluation of the medical history revealed that the patient had undergone hystero-salphingography 6 weeks prior her first RAIU measurement.

A second male patient 70 years old with subclinical hyperthyroidism (TSH: 0,05 μUI/mL) underwent RAIU and thyroid scintigraphy to identify the nature of an hyperechoic nodule in the right thyroid lobe, and if hyperactive, to determine the therapeutic ^{131}I dose. The lobe was hyperactive causing suppression of the gland (Fig. 1B) while the RAIU was 2.6% at 4h and 9.7% at 24h. The discrepancy between the two studies led us to repeat the 24 h measurement, considering possible inproper location of the probe [5-9]. The second measurement was 26% at 24 h.

A third male 36 years old patient treated for leukaemia was referred for RAIU study and thyrotoxicosis was diagnosed by thyroid hormone levels (TSH<0.005 μUI/mL, FT_4: <100 pmol/L and FT3 was 20.75 pmol/L). A diffuse hyperplasic gland was seen on the thyroid scan (Fig. 1C). Four and 24h ^{131}I uptake values were 3.6% and 6.3%, respectively. The discordance between scintigraphy and RAIU study was due to interferon ttreatment during the RAIU study. Low iodine uptake values can also be attributed to the downregulation of TSH stimulated by Na^+/I^- symporter (NIS) mRNA expression caused by interferon as well as cytokine [10-12].

Finally a 84 years old male patient with chronic renal failure underwent a RAIU study and thyroid scintigraphy. Thyrotoxicosis was detected on routine hormone measurements (TSH: 0.005 μUI/mL, FT_4 28.74 pmol/L and FT3 4.67 pmol/L). Thyroid scan showed a diffuse hyperplasic thyroid gland (Fig. 1D). The RAIU study, performed before haemodialysis, showed 4h uptake of 0.7% and 24h uptake of 0.8%. Two weeks later the study was repeated after haemodialysis and the uptake values were 4.6% and 11.2%, respectively. The patient had an ex-



(A) (B) (C) (D)

Figure 1. A-D. All patients had a thyroid scintiscan with $^{99m}TcO_4^-$ 20 min after the i.v. injection of 105 MBq. A, C and D: Diffusely hyperplastic gland. B: Hyperactive thyroid nodule on the right thyroid lobe. The left lobe is suppressed.

panded iodine pool due to renal failure. Haemodialysis may have a lessening effect on serum iodine levels, which may have increased RAIU [13].

Other factors that may induce low RAIU values are: a) When capsules were used instead of the liquid form of ^{131}I [6]. Although the mechanism for this effect is not clear it may take longer for the capsule to dissolve in the intense and thus measurements of RAIU at 15-45 min may be low. b) The presence of non-absorbable ^{131}I in the capsule [7]. It has been suggested that the United States Pharmacopeia (USP) dissolution test could be applied to radioiodide capsules as a quality assurance procedure [7]. c) The depth of the thyroid gland, its mass and lobe separation (distance between the centre points of each simulated lobe where the maximum value is 6.5 cm). [8]. Phantom studies showed that the depth of the thyroid gland caused a variation of a factor of two in the uptake of ^{99m}Tc and ^{131}I, and of a factor of 4 for ^{125}I. Gland mass and lobe separation cause only small errors for medium energy isotopes [8]. d) High voltage power supply stability, selection of energy window and attenuation characteristics of neck phantoms [3]. Recent administration of another radionuclide is a source of error, but with 20% windowing, it was unlikely that the 140 keV photons of ^{99m}Tc would interfere with the 364 keV photopeak of ^{131}I. e) Dead time losses for commercial probe systems in thyroid RAIU with ^{123}I, underlined the role of linearity studies.

To avoid many of the above errors in measuring RAIU, Quality control consists of: daily calibration using Cs-137, monthly testing of absolute sensitivity of the probe and yearly examination of the energy spectrum of multiple channel analyzer.

Bibliography

1. Sekulic V, Rajic M, Vlajkovic M et al. Thyroid blood flow and uptake of technetium-99m pertechnetate in Graves' disease. *Hell J Nucl Med* 2006; 9: 173-176.
2. Cavalieri RR, McDougall IR. In Vivo Isotopic Tests and Imaging. In: Werner and Ingbar's *The Thyroid*. A fundamental and Clinical Text. 7th edn, Braverman LE, Utiger RD eds. Lippincott-Raven, 1996; 352-376.
3. Chervu S, Chervu LR, Goodwin PN, Blaufox MD. Thyroid uptake measurements with I-123: Problems with I -123: Problems and pitfalls: Concise communication. *J Nucl Med* 1982; 23: 667-670.
4. Park HM. The thyroid gland. In: *Nuclear Medicine*. Henkin RE, Boles MA, Dillehay GL et al. Mosby, St Louis, Missouri, 1996; 830-854.
5. Becker D, Charkes D, Dworkin H et al. Procedure guideline for thyroid uptake measurement. *J Nucl Med* 1996; 37: 1266-1268.
6. Halpern S, Alazraki N, Littenberg R et al. ^{131}I thyroid uptakes: capsules versus liquid. *J Nucl Med* 1973; 14: 507-510.
7. Yu MD, Huang WS, Cherng CC, Shaw SM. The effect of formulation on reduced radioiodine thyroid uptake. *J Nucl Med* 2002; 43: 56-60.
8. O'Connor MK, Malone JF. Thyroid uptake measurements: the influence of gland depth, gland mass and lobe separation. *Brit J Radiol* 1978; 51: 454-459.
9. Robenson W, Margouleff D. Discrepancies in thyroid uptake values, use of commercial probe systems versus scintillation cameras. *Clin Nucl Med* 1996; 21: 268-269.
10. Ajjan RA, Watson PF, Findlay C et al . The sodium iodide symporter gene and its regulation by cytokines found in autoimmunity. *J Endocrinol* 1998; 158: 351-358.
11. Spitzweg C, Joba W, Morris JC, Heufelder AE. Regulation of sodium iodide symporter gene expression in FRTL-5 rat thyroid cells. *Thyroid* 1999; 9: 821-830.
12. Misaki T, Miyamoto S, Alam MS et al. Tumoricidal cytokines enhance radioiodine uptake in cultured thyroid cancer cells. *J Nucl Med* 1996; 37: 646-648.
13. Pahlka RB, Sonnad JR. The effects of dialysis on ^{131}I kinetics and dosimetry in thyroid cancer patients-a pharmacokinetic model. *Health Phys.* 2006; 91: 227-237.

Pinar Ozgen Kiratli, M.D, Gonca Kara Gedik, M.D.

Hacettepe University Medical Faculty Department of Nuclear Medicine Ankara-Turkey

Pinar Ozgen Kiratli, M.D.

Hacettepe University Medical Faculty
Dept of Nuclear Medicine, 06100, Sihhiye
Ankara, Turkey. E-mail: pkiratli@hacettepe.edu.tr
Fax: 00903123093508