LEAST SIGNIFICANT CHANGES AND REPRODUCIBILITY OF 131I UPTAKE TEST

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INTRODUCTION

- Radioiodine I-131 plays an important role in the management of patients with thyroid disorders, including well-differentiated thyroid cancer and hyperthyroidism.

- A standard quantification of RAIU using a formulation with constant-variable is consider to reflect thyroid hormonogenesis depending on the degree of trapping and organification of radioiodine in the thyroid gland.

INTRODUCTION

- RAIU level by the thyroid gland at 4th and 24th hours has been used for several purposes, such as differential diagnosis, stratification, randomization and especially treatment dose calculation (Leslie, 2003; Bahn, 2011).

- Some authors showed that 24 hour value of the RAIU is very important to calculate the radioiodine dose proposal in the treatment of hyperthyroidism (Kung, 1990; de Bruin, 1994).

INTRODUCTION

- In most clinics, both the RAIU values and the estimated thyroid gland weight are taking into account in the calculation of the treatment dose. So, administered dose of radioiodine 131I for hyperthyroidism treatment is calculated by the formula indicated in the brackets [Dose (MBq) = K (MBq g-1) x thyroid weight (g) / 24-h RAIU (1)], with K typically ranging from 3.0 to 8.1 MBq g-1 (Bahn, 2011; Silberstein, 2012; Özdoğan, 2015; Pelletier-Galarneau, 2018).
- Because RAIU test is a guideline for the differential diagnosis of hyperthyroid-causing diseases and dose calculation of patients the accuracy and reproducibility of these measurements are very important in terms of reliability of the test.

INTRODUCTION

- Interpretation of the reproducibility and low-meaningful change values of the measurements made for this reason may closely concern in the management of the patients. Taking all this into consideration, it can be said that the reliability of the RAIU test applied to the patient and the accuracy of the device are essential for good medical practices.
- Aim of this study is to determine the compliance and reproducibility level of RAIU test and to make a check whether a meaningful difference between measurements pairs for favorable two periods of time.

MATERIALS AND METHODS

- This study was carried out in the Ministry of Health, Dışkapı Yıldırım Beyazıt Training and Research Hospital, Nuclear Medicine Department, Ankara, Turkey. This study was approved by the Local Ethical Committee. The informed consent was obtained from the patients.
- The study was performed consecutively on one hundred nineteen patients (65 females, 54 males, age ranging; 55 ± 12 years, TSH level; 2.07 ± 6.74 uIU mL-1). All patients were put on low iodine diet 2 weeks before RAIU test. In the test day patients took orally a 185 - 370 kBq dose of 131I NaI in liquid form.

MATERIALS AND METHODS

- In all patients we measured the RAIU by same commercial thyroid uptake system that is consisting of a 2" NaI crystal, photomultiplier tube, and multichannel analyzer (Biodex Medical Systems, ATOMLAB 930, New York, USA).

- Each measurement of all participants was repeated twice consecutively under equal geometry and stable counting conditions to examine the reproducibility of the test. We followed a standard procedure in accordance with following guidelines (de Bruin, 1994, Özdoğan, 2015) to measure RAIU at 4 h and 24 h after radiopharmaceutical administration.

MATERIALS AND METHODS

- Measurements were obtained on the patient's neck to detect the RAIU in thyroid gland and on thigh to make a correction according to background activity, using 1-min acquisitions, a 10% photopeak energy window centered at 364 keV. As a result, the device generates an automatic RAIU value using counts coming from the probe.
- The quality control of the thyroid uptake system is routinely performed by an authorized company. Quality control consists of three stages; daily calibration using 137Cs, monthly testing of sensitivity of the probe and finally yearly examination of the energy spectrum of multiple channel analyzer.

MATERIALS AND METHODS

- We evaluated final data statistically by SPSS software (IBM SPSS Statistics, version 23.0, New York, USA). We evaluated the difference between the averages of repeated measurements with the Mann-Whitney U test. We assessed the averages versus differences of repeated measurements using Bland-Altman analysis.
- The Pearson correlation coefficient was used to evaluate the correlation between the difference and averages of repeated measurements. We used one of the commonly preferred methods to find the reproducibility coefficient between the two same time measurements that is twice the standard deviation of the differences between the measurements (Bland, 1986).

MATERIALS AND METHODS

- In addition, as another method for testing the reproducibility of repeated measurement results; the root-mean-square standard deviation ($SDM_{RMS} = \sqrt{\sum_{i=1}^{m} SDi/m}$), SDi; standard deviation of the repeated measures of the ith subject, m; the number of subjects) and the lowest significant change (LSC= Z* $\sqrt{2}$ SDM_{RMS}, Z*; a chosen value as 1.28, 1.65, 1.96, and 2.58 according to the level of statistical confidence of 80%, 90%, 95%, and 99%, respectively) values were calculated empirically by using the formulas specified in parentheses (Gluer, 1995, Bonnick, 2001, Pelletier-Galarneau, 2018).

MATERIALS AND METHODS

- We expressed the data as mean ± standard deviation for continuous variables, and as number or percentage for categorical variables. A p value of less than 0.05 was considered statistically significant.

RESULTS

- In 119 patients referred to our nuclear medicine department to examine thyroid gland function in Graves' disease (60/119), toxic multinodular goiter (29/119), thyroiditis (10/119), thyroid cancer (6/119) and unknown etiology (14/119), the RAIU measured at 4 and 24 hours twice.
- Averages values for first and second measurements of RAIU were 23.71 ± 16.52 and 23.94 ± 16.64 at 4th hour ($p>0.05$), and 35.33 ± 19.22 and 35.49 ± 19.19 at 24th hour ($p>0.05$), respectively (Table 1).

RESULTS

Measurements	Mean ± Standard deviation	P value
First vs. second measurements; 4 h (%)	23.71 ± 16.52 vs. 23.94 ± 16.64	>0.05
First vs. second measurement; 24 h (%)	35.33 ± 19.22 vs. 35.49 ± 19.19	>0.05

Table 1. Mean values of RAIU measurements at 4th and 24th hours.

RESULTS

- RAIU level in the thyroid gland is a good indicator to estimate the tolerance of the diseased gland to the treatment dose to be administered. Therefore, it is important to know the compliance and reproducibility of the measurement.
- In order to assess the compliance and limits of agreement of repeated measurement pairs, scatter plots of the differences versus averages were used. It is observed that the differences in the graphs do not show a systematic distribution around zero and there is no clear relationship between the differences and the averages. This finding indicates that the compliance can be examined via the differences and the limits of agreement (Figures 1).

RESULTS

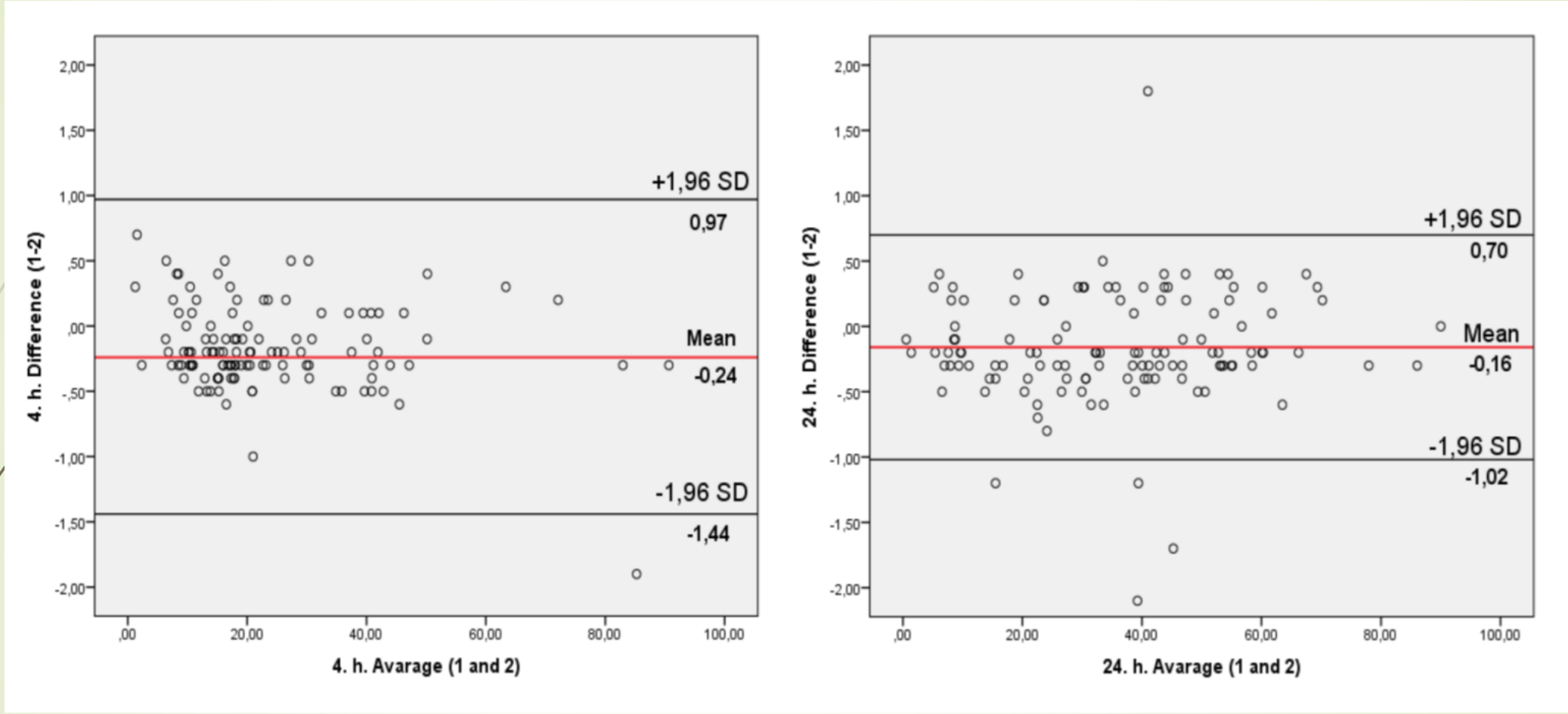

Fig. 1. Bland-Altman scatter plots of differences versus averages belonging to repeated measurements at 4 h and 24 h in 119 patients. The difference and the 95% confidence interval are indicated by red and black lines, respectively.

RESULTS

- Table 2 shows the parameters and their values producing from repeated RAIU measurement both at 4th and 24th hours. Mean values of differences for these measurements were found to be -0.24 ± 0.62 (limits of agreement; -1.44 to 0.97) at 4th hour and -0.16 ± 0.44 (limits of agreement; -1.02 to 0.70) at 24th hour. So, compliance values were within the limits of agreement.
- According to the calculated limits; first measurements of 4th and 24th hours were 0.97 and 0.70 units higher or 1.44 and 1.02 units lower than the repeated one, respectively. When we investigated the correlation between repeated measurement pairs, considering differences and averages; Negative correlation was found for 4th hour measurements ($r = -0.203$, $p < 0.05$), no significant correlation was found for 24th hour measurements ($r = 0.074$, $p > 0.05$).

RESULTS

- Reproducibility coefficients were determined as 1.23 for a 4th hour measurement and 0.88 for a 24th hour measurement pairs. An empiric value of reproducibility (SDM_{RMS}) and the 95% absolute LSC value of measurement pairs were computed as 0.37% and 1.02% for the 4th hour measurements and as 0.40% and 1.11% for the 24 hours measurements, respectively.
- These reproducibility levels of RAIU test determining in our department is not a strong limiting factor for the dose estimation because it is less than 0.1% level. As well known, the change in the level of radioiodine involvement in the thyroid gland changes dynamically over time, and it is mainly affected by physiological and pathological processes.

RESULTS

- We obtained our repeated measurements in a short time period of a few minutes. Therefore, our findings showed that a range of difference between pairs may reflect mainly variations in probe direction and background activity rather than change over time and device-related or measurement-method-related variables.

RESULTS

Parameters	Values	
	4th h (1st vs. 2nd)	24th h (1st vs. 2nd)
Number (n)	119	119
Difference (d)	-0.24	-0.16
Standard deviation (SD)	0.62	0.44
Limits of agreement (d ± 1.96 × SD)	0.97 / -1.44	0.70 / -1.02
Reproducibility coefficient (n)	1.23	0.88
Rootmean-square standard deviation (SDM_{RMS})	0.37	0.40
The lowest significant change (95% absolute LSC)	1.02	1.11

Table 2. The table shows the difference, standard deviation, limits of agreement, reproducibility coefficient, empiric reproducibility and lowest significant change values belonging to RAIU measurement pairs obtained at 4th and 24th hours.

RESULTS

- Our study has some limitations. An important limitation in this study is that it is difficult to provide the same geometric conditions in patients who have been measured. It is difficult for the patients to take same positions for the second measurement and remain stable after the first measurement. Another limitation is that we could only one model device and in this case the measurement results are not compared on a different device.

CONCLUSIONS

- It is important to define the reproducibility of tests in laboratories. We notice two practical methods for reproducibility of probe-based RAIU test that can be used in a typical nuclear medicine department and presented their findings here. Our compliance values were within acceptable limits. Although we found a statistically significant difference in the reproducibility of the measurements, we think that it couldn't cause an apparent effect in the clinical setting.

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Thank you for your attention.