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Sex-Specific Organ Dose and Cancer Risk Analysis in Thyroid Cancer Patients Treated with I-131: Insights from Dosimetry Modeling and Literature Comparison

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Abstract: ***This study evaluates organ-specific radiation doses and associated cancer risks in thyroid cancer patients treated with 3700 MBq of I-131. Nineteen patients (16 females, 3 males) were retrospectively analyzed using OLINDA/EXM software for dosimetry calculations, with data obtained from post-therapy whole-body scans. The organs analyzed included the liver, kidneys, lungs, spleen, and urinary bladder wall. Results indicated that female patients received higher organ-specific doses and exhibited increased cancer risk probabilities, particularly for the lungs. The findings underscore the importance of integrating sex-specific risk assessment in to radionuclide therapy to enhance patient safety and support personalized treatment planning.***

Keywords: I-131 therapy, organ dosimetry, cancer risk assessment, thyroid cancer, nuclear medicine.

1. Introduction

The use of radioactive isotopes in treatment has become important to complement treatment for some types of cancer. Among these cancers, differentiated thyroid carcinoma (DTC) is a common disease with unique features, and in most cases the patient is given a therapeutic dose of radioiodine (131I) ranging from 30 mCi to 100 mCi. In most patients with DTC, initial therapy consists of (near-) total thyroidectomy followed by ablation with 131I for the thyroid remnants 4 to 6 weeks after surgery. Also, sometimes patients who develop metastases are given higher treatment doses. In such cases, the therapeutic dose may increase to 200 mCi. Patient-specific internal dosimetry with a high accuracy stands as one of the most significant issues in the field of nuclear medicine showing a dramatic change in the different methods for computing the correct organ doses from the ingested radioactivity (Yas¸ar and Tu˘grul,2005) [1], (Daphn´ee Villoing, Simon, Cari and Martha, 2017) [2], (Andersson et al., 2022) [3]. Biokinetic models developed for individual elements and their radioisotopes are used to calculate the total number of transformations occurring within specific tissues, organs, or body regions (source regions) over a specified period. Kolbert et al. (2007) employed PET imaging with Iodine-124 and advanced 3D internal dosimetry software to predict organ-specific absorbed doses in thyroid cancer patients. Their work demonstrated the feasibility of pre-therapy dose estimation and highlighted variability in organ doses across patients, especially the kidneys, liver, and lungs [4]. The MEDIRAD project further expanded this understanding by analyzing a larger patient cohort. It provided harmonized organ dosimetry estimates in patients treated with radioiodine therapy, focusing on standardizing methods across European centers. Importantly, the study emphasized the need for sex-specific risk estimates and personalized approaches to dosimetry [5]. Dewaraja et al. (2019), through the MIRD Pamphlet No. 23, presented guidelines for quantitative SPECT-based 3D dosimetry in clinical radionuclide therapy. Their recommendations established a technical framework for patient-specific dose calculations, yet emphasized the challenges in translating absorbed doses into actual biological effects, such as cancer risk [6]. Despite these advancements, gaps remain—particularly in integrating sex-specific dose and risk estimates into clinical practice. Most studies report average values without stratifying by sex, and risk probability per MBq is rarely emphasized. This study addresses these gaps by presenting absorbed dose, effective dose, and cancer risk probabilities by organ (liver, kidneys, lungs, spleen and wall of urinary bladder) and sex, commonly exposed during systemic iodine therapy. The primary aim of this study is to quantify organ-specific radiation doses and estimate cancer risks in thyroid cancer patients undergoing I-131 therapy, with an emphasis on sex-specific analysis to improve personalized treatment strategies. This study contributes to advancing nuclear medicine by providing sex-specific dosimetric data and cancer risk estimates, which can enhance treatment planning, inform clinical guidelines, and address existing gaps in personalized radionuclide therapy.

2. Materials and Methods

Patient Selection:

This study included 19 patients diagnosed with differentiated thyroid carcinoma (16 females, 3 males). Each patient underwent whole-body planar scans with dual-head gamma camera using the administered activity of 37 MBq of I-131 for imaging purposes, after receiving therapeutic dose of 3700 MBq (100 mCi) of 131I. Images were acquired at 24 and 48

hours post-injection to capture organ-specific kinetics. For the bladder dosimetry patients were instructed to drink plenty of fluids (at least 2-3 liters/day), and they should begin voiding every 4 hours starting from the time of administration.

Dosimetry and Protocol:
Whole-body nuclear medicine scans (gamma camera GE-670) were acquired according to the protocol: Collimators: HEGP. Energy windows: 364 Kev, 20 %. HIGH RES (512 x 512). Orientation: 180. Gantry movement: Continuous. Scan speed: 8-10 cm/min. Scan Limits: According to the area of interest. Detector mask: Zoom (1.0 x Full field). Patient position: Supine. Orientation: Feet first. Flood: Tc-99m – INTR. At two time points after being injected 37 MBq (1 mCi) of I-131 and whole body exam were performed after 24 Hours and 48 Hours. Regions of interest (ROIs) were manually delineated using the Hermes processing station for whole body images (Anterior AND posterior). Organ-specific absorbed doses and effective doses (ED) were calculated using the OLINDA/EXM software in HERMES SOFTWARE, which follows ICRP dose conversion models.

Image Analysis and Organ ROI Definition
Regions of interest (ROIs) anterior- posterior views were manually drawn for the whole body images, and target organs (kidneys, liver, lungs, spleen, urinary bladder, gall bladder) were selected for OLINDA/EXAM report. The geometric mean method was applied to anterior and posterior counts to improve accuracy. Organ residence times were calculated using mono-exponential fitting of time-activity curves.

Dosimetry Calculation Using OLINDA/EXM
Absorbed doses were computed using OLINDA/EXM software. Residence times were entered into the software using the standard adult male and female phantom models depending on patient sex. Organ doses were reported in mGy, and then converted to mSv/MBq by dividing by the injected activity of 37 MBq.

Effective Dose and Risk Estimation
Effective dose (ED) was calculated by multiplying organ absorbed doses (mSv/MBq) by the corresponding ICRP 103 tissue weighting factors. The total effective dose was calculated as the sum of individual weighted organ doses.

Cancer risk probability was estimated using ICRP nominal risk coefficients per Sv for each organ. Risk per organ was calculated using the formula:

$$Risk\ Probability = \left(\frac{Organ\ Dose\ \left(\frac{mSv}{MBq}\right)\ x\ 3700MBq}{1000} \right) x\ Risk\ Coefficient(/Sv)$$

Data Collection and Analysis
Patient demographic data—including age, height, weight and BMI—were recorded table (1). Statistical analysis was performed using SPSS software (version 25). Mean, Standard Deviation, Min and Max were calculated for all quantitative variables. Cancer risk probabilities were estimated using ICRP Publication 103 risk coefficients, based on organ-specific dose data.

3. Results

A total of 19 patients (16 females and 3 males) were included in the dosimetric analysis. The following results summarize the organ absorbed doses, effective doses, and cancer risk probabilities derived from post-therapeutic I-131 imaging.

Table 1: Patient Demographics and Physical Characteristics.

Sex	Age	Weight	Height	BMI
Female	55.44±17.72 (29-85)	74.69±16.88 (49-106)	156.38±5.03 (148-165)	30.64±6.93 (20-44)
Male	61.33±11.85 (54-75)	95.33±5.77 (92-102)	171.33±6.51 (165-178)	32.48±0.97 (31.46-33.79)

Organ Absorbed Dose (mSv/MBq)
The mean organ absorbed doses per MBq of administered activity, along with standard deviation (SD) and range, are summarized in table (2). Female patients consistently exhibited higher absorbed doses across all organs compared to males.

Table 2: Mean organ absorbed doses mSv/MBq of administered activity

Organ	Mean ± SD (mSv/MBq)	Range (mSv/MBq)
Kidneys	0.0908 ± 0.0654	0.0376 – 0.3270
Liver	0.0908 ± 0.0654	0.0378 – 0.3270
Lungs	0.0851 ± 0.0620	0.0354 – 0.3054
Spleen	0.0908 ± 0.0654	0.0378 – 0.3270
Urinary Bladder Wall	0.0937 ± 0.0691	0.0284 – 0.3432
Total Body	0.0832 ± 0.0604	0.0295 – 0.3027

Effective Dose (mSv/MBq)
Organ-specific effective doses, calculated using ICRP 103 tissue weighting factors, are reported as follows:

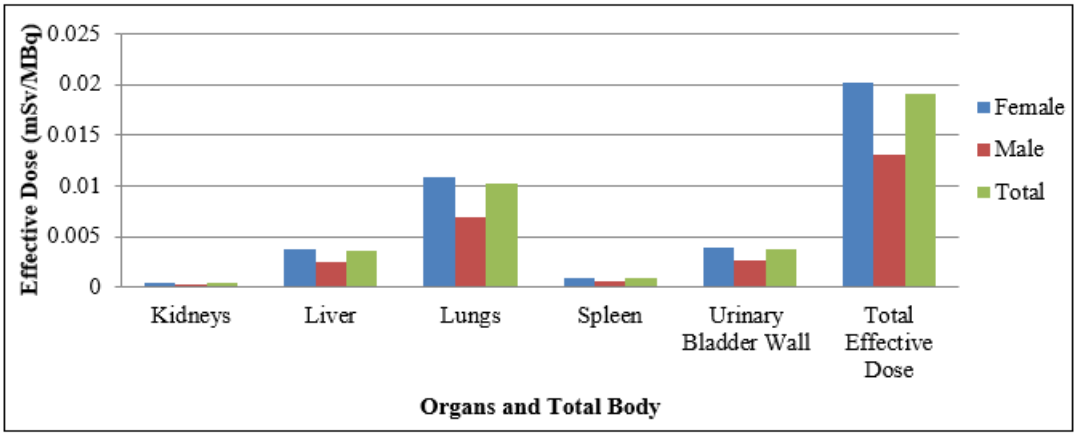

Chart 1: Effective Dose Comparison for male and female per (mSv/MBq).

From the Chart (1), it is observed that the highest effective dose was recorded in the lungs, with a mean of 0.0102 mSv/MBq. The total effective dose for female patients averaged 0.0201 mSv/MBq (range: 0.0079–0.0684), while for male patients it was 0.0130 mSv/MBq (range: 0.0128–0.0132).

Cancer Risk Probability (for 3700 MBq Injection)

Based on ICRP risk coefficients, the estimated organ-specific mean cancer risk probabilities were illustrated in chart 2:

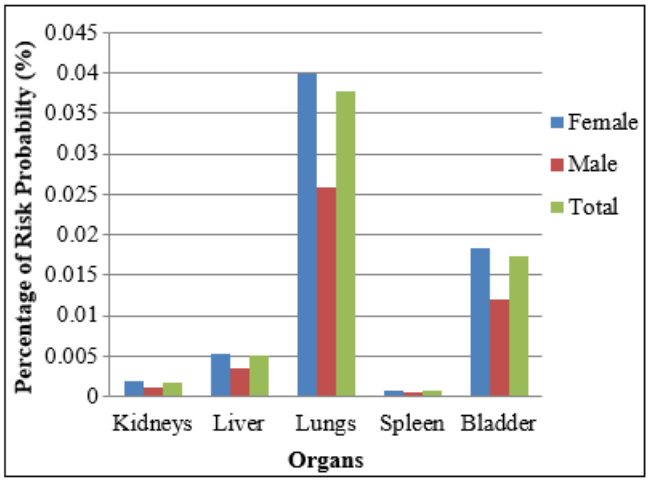

Chart 2: Percentage of Cancer Risk Estimation by Sex.

As is showing in chart (2), the lungs exhibited the highest predicted cancer risk, consistent with their high tissue weighting factor. Female patients showed higher risk estimates across all organs due to higher absorbed doses.

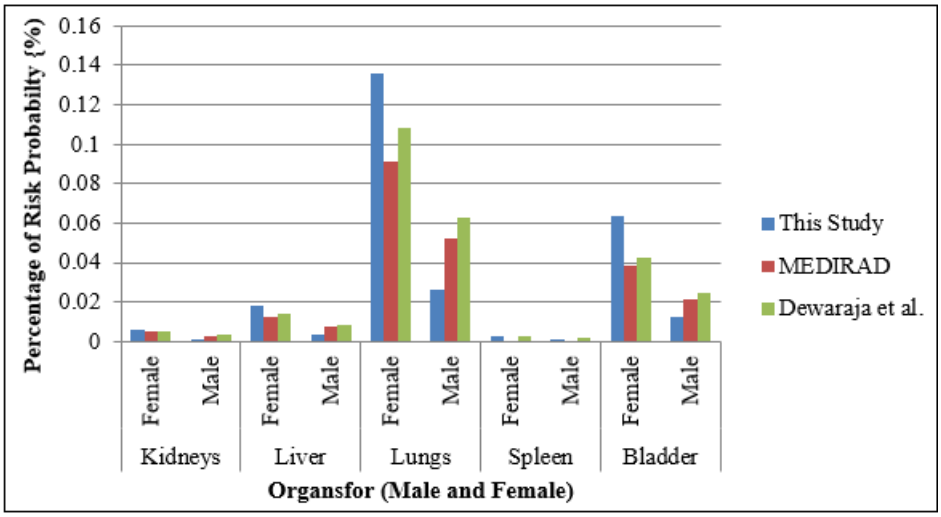

Chart 3: Comparison of Cancer Risk Probability per MBq with some Published Literature

4. Discussion

This study provides a comprehensive sex-specific analysis of organ absorbed dose, effective dose, and associated cancer risk for patients undergoing 131I therapy, with comparisons to major prior studies by Kolbert et al. (2007), MEDIRAD (2023), and Dewaraja et al. (2019). By expressing dose metrics in mSv/MBq and applying a consistent administered activity of 3700 MBq, our findings offer both clinical relevance and methodological clarity. For most organs, our results fall between the ranges reported in the MEDIRAD and Dewaraja studies, with some notable deviations. For example: Kidneys: Our data showed a lower absorbed dose in males (0.0620 mSv/MBq) compared to MEDIRAD (0.103 mSv/MBq) and Dewaraja (0.117 mSv/MBq), while in females (0.0962 mSv/MBq), it was also below Kolbert (0.176 mSv/MBq) but closer to MEDIRAD (0.131 mSv/MBq). This suggests a potential sex-related biokinetic difference or differences in methodology, especially in renal clearance modeling. Liver: Our values (0.0962 mSv/MBq for both sex) exceeded those reported in MEDIRAD and Dewaraja, possibly due to hepatic uptake variability in our cohort or differences in dosimetry software handling liver segmentation and time-integrated activity. Lungs: Our female lung dose (0.0901 mSv/MBq) was considerably higher than Kolbert (0.040 mSv/MBq) and other references. This may reflect either a different patient population or improved temporal resolution in our data collection, leading to more accurate capture of early lung uptake. Spleen: Doses in our study (0.0961 mSv/MBq female, 0.0621 mSv/MBq male) aligned more closely with Dewaraja, suggesting consistency in organ-specific retention patterns. Slight overestimation compared to MEDIRAD might be linked to patient-specific spleen volume assumptions. Bladder wall: Our estimates (0.0990 mSv/MBq female, 0.0650 mSv/MBq male) were consistently higher than all other studies. This may be attributed to our real-time bladder voiding model or longer biological half-life observed in our dataset, warranting further review of urinary kinetics. Total Body Dose: Our results (0.0880 mSv/MBq female, 0.0577 mSv/MBq male) were slightly lower than Dewaraja (0.080 mSv/MBq and 0.071 mSv/MBq) and MEDIRAD (0.054 mSv/MBq and 0.047 mSv/MBq), reinforcing the value of patient-specific dosimetry in optimizing administered activity. For Effective Dose and Risk Estimates Our effective dose per MBq (chart 3) was higher in females, consistent with known ICRP weighting factors and organ sensitivities. The resulting cancer risk per MBq followed a similar trend, with females showing higher probability values, highlighting the importance of sex-stratified risk analysis in therapeutic planning. By integrating organ dose, effective dose, and cancer risk, our model allows for individualized risk assessment (a growing priority in personalized nuclear medicine).

5. Conclusion

This study provides sex-specific organ dose and cancer risk data for thyroid cancer patients undergoing I-131therapy. The findings highlight differences in organ uptake between males and females and propose individualized dosimetric strategies to enhance patient safety. By comparing results to prior studies, this work advances the call for personalized treatment planning in nuclear medicine.

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