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DOSIMETRIC AND RISK IMPACT OF CLINICAL I-131 DOSE SCHEDULING IN THYROID CANCER: SINGLE VS. FRACTIONATED THERAPY

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ABSTRACT

This study compares organ doses, effective doses, and cancer risk in thyroid cancer patients treated with either a single 3700 MBq (100 mCi) or three times of 1110 MBq (30 mCi)) I-131 doses 15 days apart. Nineteen patients (16 females, 3 males) underwent whole-body scans at 24 and 48 hours post-administration after one month using 37 MBq of I-131. Organ dosimetry was calculated with OLINDA/EXM and cancer risks estimated using ICRP 103. Fractionation lowered organ doses and cancer risk by ~10% in both sexes. Females patients' consistently experienced higher absorbed doses and risks. The lungs and bladder wall were the largest contributors to overall risk.. Fractionated I-131 therapy modestly reduces exposure and supports sex-specific planning.

INTRODUCTION

Radioiodine therapy with Iodine-131 (^{131}I) remains a cornerstone in the management of differentiated thyroid cancer (DTC), particularly after thyroidectomy for remnant ablation or treatment of distant metastases. Its selective uptake by thyroid tissue allows for targeted therapy with relatively low systemic toxicity. Typically, therapeutic activities range from 3.7 to 7.4 GBq depending on the patient's risk stratification and disease extent [1,2]. Despite its efficacy, single high-activity administrations pose a substantial radiation burden to non-target organs such as the liver, lungs, kidneys, and bladder, potentially increasing the risk of long-term radiation-induced effects [3]. To mitigate these concerns, fractionated radioiodine therapy—dividing the total intended activity into multiple smaller doses—has been proposed. This approach allows for biological clearance of radioactive material between cycles and may reduce cumulative organ dose and late toxicity [4,5]. Fractionation has been studied in other forms of radionuclide therapy, including peptide receptor radionuclide therapy (PRRT) and radioimmunotherapy, where improved therapeutic indices and reduced toxicity have been observed [6,7]. Although limited, available evidence suggests fractionated I-131 therapy may be beneficial, particularly in patients at higher risk for radiation-related complications. Our assumption that each fractionated dose clears fully before the next administration is supported by Zhang et al. [8], who demonstrated that most patients exhibited rapid bi-exponential clearance of I-131, with retained activity significantly reduced within 72 hours. This supports the validity of modeling fractionated doses as independent exposures. This study compares the dosimetric and cancer risk profiles of two I-131 therapy regimens a single 3700 MBq administration versus a fractionated protocol of three 1110 MBq doses to evaluate their potential clinical impact on radiation protection and treatment optimization.

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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 I-131. 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. B 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, after patients receiving a therapeutic activity 3700 of I-131 (100 mCi). 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.

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.

RESULTS

Table 1 summarizes the demographic and physical characteristics of the study population. Female patients (n=16) had a mean age of 55.4 years, while male patients (n=3) averaged 61.3 years. Weight, height, and BMI values also differed slightly between sexes.

Table 1: Patient Demographics and Physical Characteristics.

Sex	Age (years)	Weight (kg)	Height (cm)	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)

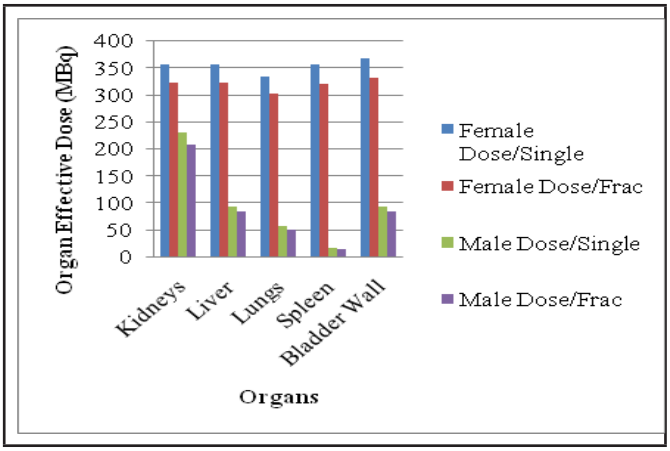

Chart 1 demonstrates a consistent reduction in organ doses in the fractionated group, with the largest decreases observed in the bladder wall and lungs.

Chart 1 illustrates organ-specific absorbed dose comparisons between the two therapy schedules. Across all organs, the fractionated group consistently exhibited approximately 10% lower doses compared to the single 3700 MBq administration. The greatest absolute dose reductions were seen in the bladder wall and lungs, which not only receive some of the highest baseline absorbed doses but also play key roles in I-131 clearance. Because these organs contribute disproportionately to the total effective dose and cancer risk, even a uniform 10% reduction represents a meaningful decrease in absolute radiation burden and potential long-term risk.

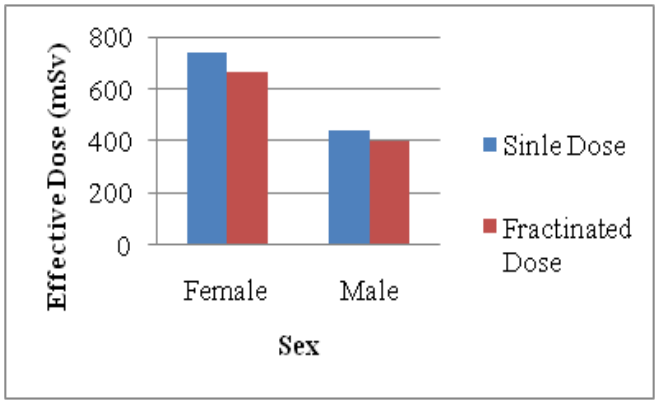

Chart 2: Effective Dose per , Sex, and Therapy Schedule for I-131 Therapy (Single and Fractionated).

Chart 2 presents the effective dose stratified by sex and therapy regimen. In both groups, fractionation led to a measurable decrease in total effective dose:

- Females: 740 mSv (single dose) → 666 mSv (fractionated)
- Males: 444 mSv (single dose) → 399.6 mSv (fractionated)

These reductions reinforce the benefit of fractionation in reducing systemic radiation burden. However, female patients consistently received higher effective doses than male counterparts in both treatment schedules.

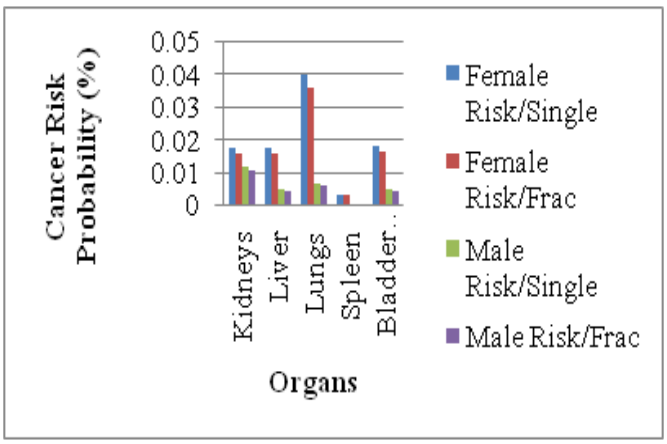

Chart 3 shows that female patients consistently received higher doses and risk values than male patients, confirming a similar

~10% reduction.

Chart 3 shows the cancer risk probability estimates by sex and regimen. Similar to absorbed dose, risk values were uniformly lower (~10%) with the fractionated protocol, yet females exhibited higher risk estimates across all organs. Notably, the lungs and bladder wall contributed the highest share to overall cancer risk, aligning with their dose load and tissue sensitivity.

Table 2 provides a detailed breakdown of organ-specific absorbed doses and corresponding cancer risk probabilities for both sexes, under single and fractionated dosing. The results confirmed:

A consistent ~10% reduction in both dose and risk for all assessed organs with fractionation.

For instance:

Female kidneys: 355.94 mSv (single) → 320.35 mSv (fractionated); Risk: 0.01780 → 0.01602

Male liver: 92.50 mSv (single) → 83.25 mSv (fractionated); Risk: 0.00463 → 0.00416

These findings support the validity of the linear dose scaling model and highlight sex-specific radiation burden, with female patients experiencing greater absorbed dose and risk, even after fractionation.

Table 2. Presents a detailed breakdown by organ and sex, highlighting persistent differences despite fractionationfor the total organ dose and associated risk probability.

Organ	Female Dose (mSv) Single vs. Fractionated	Δ%	Female Risk Single vs. Fractionated	Δ%	Male Dose (mSv) Single vs. Fractionated	Δ%	Male Risk Single vs. Fractionated	Δ%
Kidneys	355.94/ 320.35	10.0%	0.01780/ 0.01602	10.0%	229.40/ 206.46	10.0%	0.01147/ 0.01032	10.0%
Liver	355.94/ 320.35	10.0%	0.01780/ 0.01602	10.0%	92.50/ 83.25	10.0%	0.00463/ 0.00416	10.15%
Lungs	333.37/ 300.03	10.0%	0.04000/ 0.03600	10.0%	55.50/ 49.95	10.0%	0.00666/ 0.00599	10.06%
Spleen	355.57/ 320.01	10.0%	0.00356/ 0.00320	10.11%	14.80/ 13.32	10.0%	0.00015/ 0.00013	13.33%
Bladder Wall	366.30/ 329.67	10.0%	0.01832/ 0.01648	10.04%	92.50/ 83.25	10.0%	0.00463/ 0.00416	10.15%

DISCUSSION

This extended analysis explored the dosimetric and cancer risk implications of two I-131 administration strategies: a single 3700 MBq injection versus three fractionated injections of 1110 MBq each, administered 15 days apart. The findings validate the linear dose-scaling assumption, with organ doses and risk estimates showing a proportional reduction of approximately 10% under the fractionated schedule. Importantly, these reductions were consistent across all organs analyzed. For instance, the female bladder wall dose decreased from 366.3 mSv to 329.7 mSv, and risk decreased from 0.01832 to 0.01648. Notably, female patients exhibited consistently higher absorbed doses and cancer risk probabilities than their male counterparts in both therapy regimens. This sex-based difference underscores the need for sex-specific internal dosimetry and highlights a critical dimension often overlooked in standardized treatment protocols. Fractionated radionuclide therapy has been shown in other contexts to improve the therapeutic index and reduce toxicity by allowing partial repair of sublethal tissue damage [6,7]. Emphasized the potential for individualized and fractionated dosing in optimizing theranostic applications, including I-131. While the dosimetric benefit of fractionation is modest, the clinical relevance becomes significant in high-risk or radiosensitive patients. However, practical considerations such as patient compliance, treatment logistics, and therapeutic efficacy must be balanced against these dosimetric advantages. Future prospective trials are warranted to determine whether these reductions in dose and risk translate into improved long-term outcomes.

CONCLUSION

This study compared the dosimetric and cancer risk profiles of single versus fractionated I-131 therapy in thyroid cancer patients. The fractionated regimen resulted in a consistent ~10% reduction in organ doses and associated risks, while sex-specific disparities in dose and risk remained evident. These findings quantitatively support the consideration of fractionation as a strategy to reduce radiation burden, particularly in high-risk patients, and advocate for personalized and sex-informed treatment planning in nuclear medicine.

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