



# Effects of High-dose Radioactive Iodine Therapy on Hormonal Profiles and Sperm Quality in Thyroidectomy Patients

*Tiroidektomi Hastalarında Yüksek Doz Radyoaktif İyot Tedavisinin Hormonal Profiller ve Sperm Kalitesi Üzerine Etkileri*

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## Abstract

**Objectives:** This study investigates the effects of high-dose radioactive iodine therapy on gonadotropin and sex hormone levels, and on sperm parameters in male patients with differentiated thyroid carcinoma following thyroidectomy.

**Methods:** Twenty-five male patients (aged 20-60 years) with differentiated thyroid carcinoma underwent thyroidectomy and iodine therapy. The therapeutic dose was 150 mCi of oral sodium iodide solution. Levels of gonadotropins, sex hormones, and anti-Müllerian hormone (AMH) were measured before and two weeks after radioiodine therapy (RT). Semen analysis included liquefaction, odor, color, viscosity, agglutination, and aggregation. The main parameters evaluated were semen volume, pH, sperm count, percentages of motile and progressively motile sperm, round cells, and sperm morphology. Sperm motility, including progressive, non-progressive, and immotile types, and DNA fragmentation were analyzed according to World Health Organization guidelines.

**Results:** The Wilcoxon signed-rank test was used with a significance level of  $p \leq 0.05$ . Follicle-stimulating hormone levels in patients' sera were significantly higher than pre-RIT measurements ( $p=0.002$ ), whereas luteinizing hormone, dihydrotestosterone, dehydroepiandrosterone sulfate, testosterone, and AMH levels were not significantly different from pre-RT measurements. Total sperm count, volume, motility, and rapid progressive motility increased significantly compared to pre-radioiodine ablation measurements, while other parameters remained unchanged.

**Conclusion:** Male patients who received 150 mCi of radioactive iodine showed no impairment in fertility. Long-term follow-up studies with larger sample sizes are crucial to investigate the physiological roles of gonadal hormones, sperm DNA fragmentation, and AMH in the testes after RIT.

**Keywords:** Radioiodine therapy, sperm DNA fragmentation, thyroid

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## Öz

**Amaç:** Bu çalışma, diferansiye tiroid karsinomlu erkek hastalarda tiroidektomi sonrası yüksek doz radyoaktif iyot tedavisinin gonadotropin, seks hormonu seviyeleri ve sperm parametrelerini nasıl etkilediğini araştırmaktadır.

**Yöntem:** Diferansiye tiroid karsinomlu yirmi beş erkek hastaya (20-60 yaş arası) tiroidektomi ve iyot tedavisi uygulandı. Terapötik doz 150 mCi sodyum iyodür oral solüsyonuydu. Gonadotropin, seks hormonu ve anti-Müllerian hormon (AMH) seviyeleri, radyoiyot tedavisinden (RT) önce ve iki hafta sonra ölçüldü. Semen analizi sıvılaşma, koku, renk, viskozite, aglütinasyon ve agregasyonu içeriyordu. Değerlendirilen başlıca parametreler semen hacmi, pH, sperm sayısı, hareketli ve progresif hareketli sperm yüzdeleri, yuvarlak hücreler ve morfolojydi. Progresif, non-progresif ve immotil tipler dahil olmak üzere sperm motilitesi ve DNA parçalanması, Dünya Sağlık Örgütü kılavuzlarına göre analiz edildi.

**Bulgular:** Wilcoxon işaretli sıralamalar testi,  $p \leq 0,05$  anlamlılık eşiği ile kullanıldı. Hastaların serumlarındaki folikül uyarıcı hormon seviyeleri, RIT öncesi ölçümlere göre anlamlı derecede yüksek bulundu ( $p=0,002$ ), ancak luteinize edici hormon, dihidrotestosteron, dehidroepiandrosteron sülfat, testosteron ve AMH seviyelerinde anlamlı bir fark görülmüdü. Toplam sperm sayısı, hacmi, motilitesi ve hızlı progresif motilite, radyoiyot ablasyonu öncesi ölçümlere kıyasla anlamlı şekilde artarken, diğer parametreler değişmeden kaldı.

**Sonuç:** Yüz elli mCi radyoaktif iyot alan erkek hastalarda infertilitede herhangi bir bozulma görülmüdü. RIT sonrası gonadal hormonların, sperm DNA parçalanmasının ve testislerdeki AMH'nin fizyolojik rollerini araştırmak için daha geniş bir örneklem büyüklüğüyle uzun süreli takip çok önemlidir.

**Anahtar kelimeler:** Radyoaktif iyot tedavisi, sperm DNA parçalanması, tiroid

## Introduction

Recently, thyroid cancer has become a common malignancy of the endocrine system, with a threefold higher incidence in females than in males (1). Papillary thyroid carcinoma (PTC) is the most prevalent subtype of differentiated thyroid carcinoma (DTC), accounting for 80% of thyroid cancers. Follicular thyroid carcinoma accounts for a smaller proportion of DTCs (2). PTC usually presents as a thyroid nodule. Treatment for PTC includes surgery (involving the complete removal of the thyroid gland) and radioactive iodine (RAI) therapy (often given after surgery). It is routinely recommended when DTC exceeds 4 cm, demonstrates extrathyroidal or extranodal extension, or presents with distant metastasis (3).

RAI therapy aims to obliterate residual thyroid tissue and any lingering cancer cells remaining after surgery. Additionally, RAI therapy may be employed in cases where DTC has metastasized to distant sites, and thyroid hormone replacement is required after surgery because cessation of endogenous thyroid hormone production necessitates lifelong replacement therapy. These hormones play a crucial role in regulating metabolic processes, growth, and development. Consequently, individuals undergoing thyroidectomy are mandated to receive thyroid hormone replacement therapy lifelong, with careful follow-up to monitor for recurrence (4).

RAI can cause direct damage to gonadal tissues, especially affecting the testes in males and the ovaries in females. This damage may lead to reduced hormone production, impaired spermatogenesis, and dysfunction of oocytes (5). RAI-induced sexual dysfunction in men most commonly presents as erectile dysfunction (ED), which is characterized by the inability to achieve or maintain an erection sufficient

for sexual activity. Studies report a significant increase in ED rates after RAI therapy, with up to 50% of men affected. This treatment adversely affects the patient's quality of life (6). In male patients with DTC, testosterone (T) levels are lower, sperm quality is poorer, and follicle-stimulating hormone (FSH) and luteinizing hormone (LH) levels are higher (7,8). Additionally, other studies have found that transient male infertility is dose-dependent (9,10). As a result, permanent infertility is linked to receiving high or cumulative doses of RAI administered because of metastasis.

RAI therapy using iodine-131 (I-131) effectively destroys thyroid cancer cells by emitting beta particles. This process can be detected through gamma radiation scanning (11).

The primary gap identified is the lack of detailed information regarding the impact of RAI therapy on male fertility following DTC treatment. There is a need for comprehensive findings from relevant studies, a deeper exploration of the effects on reproductive hormones, and insights into personalized approaches to managing DTC. The objective of this study is to assess hormonal alterations and sperm DNA fragmentation following administration of high-dose RAI in individuals with thyroid cancer.

## Materials and Methods

In this study, we identified 25 male patients (20-60 years) who were referred to the clinic for DTC, underwent thyroidectomy, and were selected for iodine therapy. This study excluded patients referred for problems related to environmental pollution, varicocele, excessive heat exposure, infections, non-thyroid cancers, and dietary and lifestyle factors. Those with benign thyroid disease were also excluded. Organic disorders of the reproductive organs, including varicocele, abnormal testicular position,

testicular torsion, and a history of severe genital trauma, were excluded. A limitation of this study is that the sample size is small due to time and cost constraints.

The goal of RAI therapy is to destroy both remaining thyroid cells and cancer cells after surgery. Based on thyroid radionuclide results, the therapeutic dose was 150 mCi of oral sodium iodide solution. The RAI dose is typically selected based on an assessment of tumor recurrence risk and other factors (12), as there is no definitive agreement on the optimal dose (13).

Consequently, 10-mL blood samples were collected from all patients undergoing thyroidectomy to assess the levels of gonadotropins and sex hormones. Serum concentrations of FSH, LH, dihydrotestosterone (DHT), dehydroepiandrosterone (DHEA), T, and anti-Müllerian hormone (AMH) were measured using immunoassay techniques, specifically by ELISA (enzyme-linked immunosorbent assay) or chemiluminescence (CL), both before and at two weeks after radioiodine therapy. Semen samples were collected from patients twice—once before iodine treatment and again two weeks after treatment—to evaluate semen parameters and sperm DNA fragmentation. We asked the patients to abstain from sexual intercourse for 3-5 days prior to semen collection. Each participant was asked to complete a comprehensive health questionnaire covering age, weight, height, reproductive characteristics, pregnancies and outcomes, medical history, intoxications, and medication use. Additionally, all patients provided their signed informed consent before undergoing surgery and iodine treatment.

Semen analysis was conducted in accordance with the additional guidelines outlined by Björndahl et al. (14) the observational evaluation stage for semen parameters is classified as A-. This evaluation encompasses several elements, including volume (the total count of spermatozoa and non-sperm cells present in the ejaculate, which must be calculated) and concentration, often referred to as sperm count. Number of sperm count x dilution factor/volume x 1000 = sperm/mL. Stickiness: Semen is typically a semisolid, coagulated mass. At room temperature, semen usually begins to liquefy within a few minutes to approximately 15 minutes, becoming thinner and changing color. A standard liquefied semen sample has a homogeneous, grey-opalescent appearance (15).

Semen analysis should begin with a basic inspection shortly after liquefaction, ideally within 30 minutes but no later than 1 hour post-ejaculation. The microscopic evaluation of semen parameters involves examining sperm shape, motility, and count using light microscopy on slides. A comprehensive analysis includes assessment of motility (total and progressive), morphology (sperm shape), and

concentration. Determining sperm concentration, along with evaluating motility and morphology, is essential for assessing fertility (16). The next step involves molecular evaluation of semen parameters to assess DNA integrity. This includes using the halo sperm method with the sperm chromatin structure assay (SCSA) kit to analyze sperm DNA. SCSA is a flow cytometric test that detects high levels of DNA fragmentation in sperm samples, a condition characterized by small breaks in DNA. Sperm DNA breaks are assessed indirectly by measuring DNA denaturability. SCSA is the most extensively studied method for determining DNA integrity. In this assay, sperm are exposed to a dye that highlights damaged DNA. The assay measures the susceptibility of sperm DNA to acid-induced denaturation *in situ*, followed by staining with the fluorescent dye acridine orange (17,18).

These observations were used to calculate the DNA fragmentation index (DFI), with a DFI of less than 25% was considered within the normal range. Normal sperm DNA exhibited radiating halos, whereas damaged sperm DNA exhibited either no halos or only minor halos. Fragmented sperm were defined as those having a small or absent halo (19). The DFI was calculated using the following formula:

$$\text{DFI (\%)} = 100 \times (\text{number of spermatozoa with fragmented DNA} / \text{total number of spermatozoa}) \text{ (20).}$$

Sperm DNA fragmentation was measured using the SDFA kit (DNA Fragmentation Assay Kit; Ideh Varzan Farda, Tehran, Iran). This kit facilitates the detection of DNA fragmentation through a halo assay, where stained sperm are examined under bright-field microscopy. Following the manufacturer's protocol, sperm samples were processed, stained, and observed. The extent of DNA fragmentation was determined by assessing the halo size and contrast, with larger halos indicating intact DNA and smaller or absent halos indicating fragmentation.

Ethical clearance for this research was obtained from the Fasa University of Medical Sciences Ethics Committee on May 22, 2022, and the study was conducted in accordance with the approved protocol. This committee reviewed and endorsed the study's ethical considerations (ethical code: REC.1401.020, date: 11.05.2025).

### Statistical Analysis

The data were analyzed using SPSS version 23, presenting the results as the median, 25<sup>th</sup> percentile (P25), and 75<sup>th</sup> percentile. The Wilcoxon signed-rank test, a non-parametric test, was used when the assumptions of the dependent t-test were violated. The significance level was set at  $p \leq 0.05$ .

## Results

### Study Population Characteristics

We identified 25 male patients (20-60 years) who were referred to the clinic for DTC, who underwent thyroidectomy, and who were selected for iodine therapy.

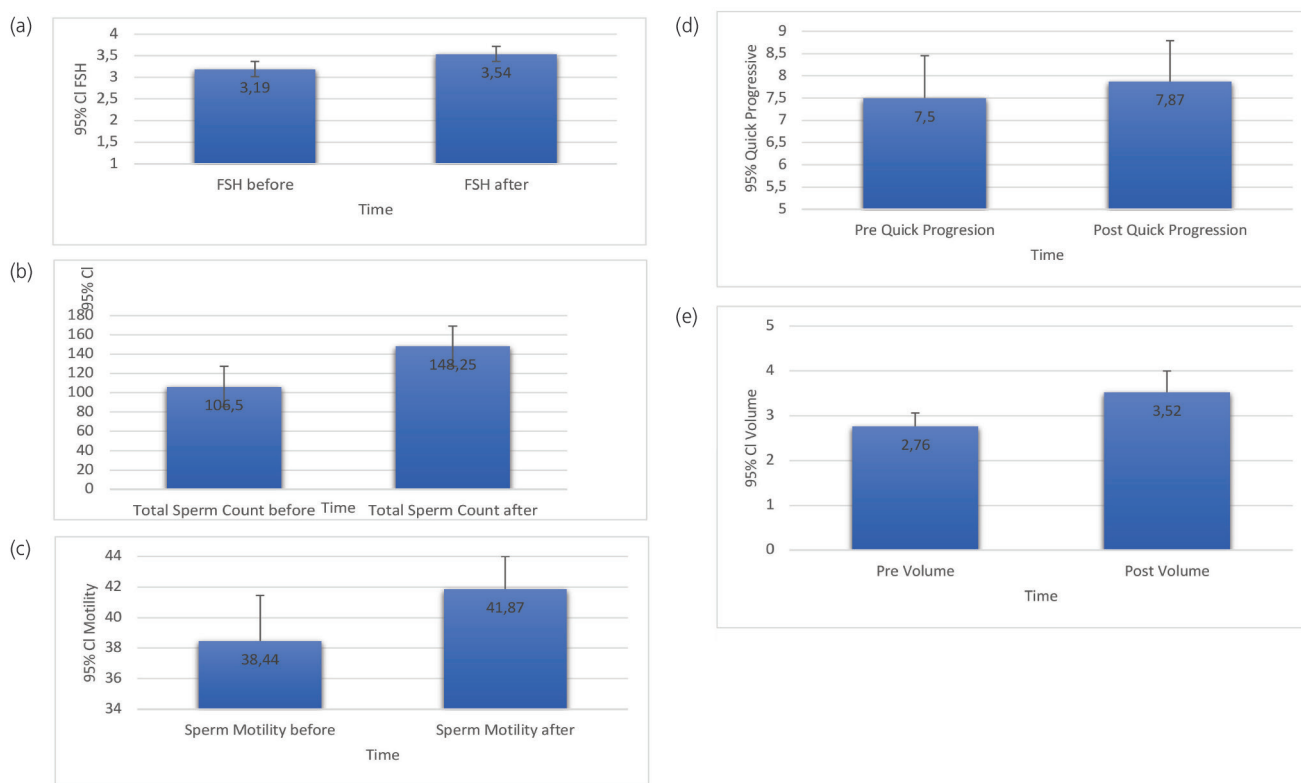
### Hormonal Assessment Via Immunoassay

The median serum FSH level in patients increased significantly compared with levels before RAI therapy (RIT) ( $p=0.002$ ;  $p<0.05$  Wilcoxon test). However, values for LH, DHT, DHEA-SO<sub>4</sub> (DHEA sulfate), T, and AMH did not change significantly before and after RIT (Figure 1 and Table 1).

### Sperm Analysis

Through detailed microscopic examinations, essential parameters in patients such as semen volume (mL,  $p=0.02$ ), total sperm count (million/ejaculate,  $p=0.034$ ), sperm motility (%), and rapid progressive motility (%), showed significant changes before and after RAI

therapy. However, we assessed characteristics such as liquefaction, color, odor, viscosity, agglutination, and aggregation during semen analysis; these assessments revealed no significant differences before and after RIT. Additionally, following World Health Organization (WHO) guidelines, we assessed sperm motility to determine the percentages of progressive, non-progressive, and immotile sperm. No significant changes were observed in these parameters before or after RIT. Furthermore, we evaluated semen pH; sperm count (million/mL); motile sperm (%); slow progressive sperm (%); non-motile sperm (%); round cells (million/mL); and normal and abnormal morphology (%), and found no significant differences before and after RIT (Figure 1a-e and Table 2). Figure 2 presents a semen analysis report generated using the High-Frame-rate Tracking-Computer-Assisted Semen Analysis system, following WHO 2010 (6<sup>th</sup>) guidelines.



**Figure 1.** Values of different parameters before and after treatment with radioactive Iodine  
 (a): FSH values in patients before and after treatment with radioactive iodine ( $p$ -value=0.02)  
 (b): Total sperm count values in patients before and after treatment with radioactive iodine ( $p$ -value=0.034)  
 (c): Sperm motility values in patients before and after treatment with radioactive iodine ( $p$ -value=0.017)  
 (d): Quick progressive motility values in patients before and after treatment with radioactive iodine ( $p$ -value=0.031)  
 (e): Semen volume values in patients before and after treatment with radioactive iodine ( $p$ -value=0.020)  
 FSH: Follicle-stimulating hormone

Sperm DNA Fragmentation

Moreover, other WHO-defined dynamic parameters that use standardized terminology for velocity variables were measured using CASA systems. No significant change in sperm DNA fragmentation was observed before and after RIT (p=0.460; Table 2).

Discussion

In DTC patients, RAI has been widely used for postoperative remnant ablation. RAI causes side effects in DTC patients, particularly in male patients. Spermatogonia and the germ-cell-producing of the testis are the tissues most sensitive to radiation. Therefore, low doses of radiation to the

Table 1. Determining the effect of radioactive iodine on men’s sex hormones before and after removing the thyroid gland			
Variables	Mean ± SD before intervention	Mean ± SD after intervention	p-value
Follicle stimulating hormone	3.18±0.45	3.54±0.48 mIU/mL	0.02
Luteinizing hormone	3.70±0.40	3.87±0.39 mIU/mL	0.453
Testosterone	14.37±1.49	13.76±1.58	0.17
DHEA-SO4	348.75±46.24	354.93±49.54 mIU/mL	0.660
Dihydrotestosterone	585.41±49.54	598.64±65.51 Pg/mL	0.717
anti-Müllerian hormone	6.93±0.84	6.44±0.62 ng/mL	0.211
SD: Standard deviation			



**Figure 2.** Semen analysis results including motility and velocity profiles [World Health Organization (WHO) 2010, 6<sup>th</sup> Ed.]. The report includes visual inspection parameters (liquefaction, color, viscosity, agglutination), main semen parameters (volume, pH, sperm count, motility, morphology), motility assessment results (progressive: 36.11%, non-progressive: 4.44%, immotile: 59.44%), and other WHO dynamic parameters (e.g., curvilinear velocity, straight-line velocity, average path velocity). Velocity profiles illustrate the distribution of sperm velocities, using standard terminology for velocity variables measured by CASA systems. Data were analyzed as part of a fertility evaluation study

**Table 2. Determining the effect of radioactive iodine on microscopic observations of sperm analysis before and after removing the thyroid gland**

Variables	Mean $\pm$ SD before intervention	Mean $\pm$ SD after intervention	Unit	p-value
Volume	2.76 $\pm$ 0.30	3.52 $\pm$ 0.48	mL	0.02
Liquefaction	28.12 $\pm$ 1.20	28.12 $\pm$ 1.43	min	0.914
Sperm count	41.31 $\pm$ 7.52	44.12 $\pm$ 5.98	Million/mL	0.98
Total sperm count	106.50 $\pm$ 20.09	148.25 $\pm$ 28.11	Million/ejaculate	0.034
Motility	38.43 $\pm$ 3.01	41.84 $\pm$ 2.13	%	0.017
Quick progressive motility	7.50 $\pm$ 0.94	7.87 $\pm$ 0.92	%	0.031
Slow progressive motility	26.62 $\pm$ 2.60	29.87 $\pm$ 1.90	%	0.48
Non-progressive motility	4.25 $\pm$ 0.77	4.06 $\pm$ 0.80	%	0.97
Non-motile	61.56 $\pm$ 3.01	56.88 $\pm$ 2.41	%	0.079
Normal morphology	4.25 $\pm$ 0.78	4.81 $\pm$ 0.67	%	0.111
Abnormal morphology	95.75 $\pm$ 0.78	95.18 $\pm$ 0.67	%	0.111
Count	20.98 $\pm$ 3.62	24.31 $\pm$ 3.54	Million/mL	0.285
Sperm DNA fragmentation	19.90 $\pm$ 1.33	21.43 $\pm$ 2.00	%	0.460
SD: Standard deviation				

gonads can seriously disrupt their function (21,22). Our research revealed elevated serum FSH levels in a sample of 25 men aged 20-60 years. This outcome aligns with similar observations reported in other studies (23,24). Gonadotropins typically exert a direct influence on sex hormones and on the production of sperm and ova (25). The effects of gonadotropins on testicular cells delineate the precise pathways governing T synthesis, spermatogenesis, and sperm quality (6). The available literature indicates that the risk of permanent gonadal dysfunction may increase in certain patients of either sex following cumulative doses (26). Another study, albeit with a limited sample size, identified a positive correlation between radioiodine dose and FSH levels over a mean follow-up period exceeding seven years. However, their results did not demonstrate a significant impact of radioiodine treatment on infertility rates (27).

In a sample of 12 men with DTC undergoing I-131 therapy, an increase in serum FSH levels and a dose-dependent impairment of spermatogenesis were observed. However, clinically significant effects were mainly seen in individuals receiving multiple doses totaling over 100 mCi (5). Conversely, our results showed that levels of LH, DHT, DHEA, and T did not change significantly from before to after RIT. T secretion and spermatogenesis depend on the hormones FSH and LH, with FSH serving as a key indicator of spermatogenesis and LH playing a vital role in T production. These hormones are produced in the anterior pituitary gland (28). When assessing infertility, measuring

LH and FSH is important because they have an inverse relationship with sperm concentration (29). Additionally, LH levels are linked to sperm motility (30). A meta-analysis found increases in FSH, LH, and T levels, as well as in sperm quality parameters; however, at one-year follow-up these increases were not statistically significant (1). Our findings suggest there were no changes in serum T levels or in the occurrence of oligospermia despite a temporary rise in FSH levels. These results are consistent with a study of testicular function following radioiodine therapy in patients with thyroid cancer (31). The transient increase in FSH generally reverses several months after receiving RAI therapy, indicating that high cumulative I-131 activity does not necessarily cause permanent infertility. Our data suggest that testicular dysfunction caused by I-131 therapy is likely temporary, consistent with another study in which all patients maintained normal T levels (9). T affects the paracrine activity of Sertoli cells, promoting their function and helping the maturation of spermatogonia into spermatocytes (32). Studies have demonstrated that Leydig cells in the testes are more resistant to radiation than the reproductive epithelium and are damaged only by high doses of therapeutic radiation (33). However, this study found no statistically significant differences in LH and T levels before and after RAI treatment, even in subgroup analyses. This indicates that Leydig cell function remains unaffected after RAI, although further research is needed to determine whether higher doses of RAI would produce different results.

DHEA, produced by the adrenal glands, is a precursor of T and estrogens, which are crucial for male reproductive health and sperm production (34). Reported DHT levels are likely to influence prostate growth (35). T can also be converted by the enzyme 5 $\alpha$ -reductase 2 into a potent non-aromatizable androgen, 5 $\alpha$ -DHT, which is required for the masculinization of the external genitalia in utero and for many of the changes associated with puberty, including the growth and activity of the prostate gland (36). Additionally, DHEA exhibits anti-inflammatory properties (37), while DHT contributes to improved oocyte quality and increased likelihood of conception. Both DHT and DHEA offer potential benefits for fertility (38). Our findings revealed that levels of DHT, DHEA, and T did not change significantly before and after RIT. Our investigation also assessed another factor: AMH levels before and after RIT did not change significantly. Evidence shows that serum AMH levels are markedly decreased in infertile men (39). In our study, their levels remained unchanged before and after the intervention. AMH (Müllerian inhibiting substance, AMH) and inhibin B (InhB) are produced by the Sertoli cells of the testes. AMH is secreted during testis development and in adulthood, whereas sperm production in adult men is regulated by InhB. These hormones are also recognized as regulators of homeostasis. In a cohort study involving men over 50, InhB levels were inversely associated with age, although no age-related effect was observed in young men (40). Furthermore, these hormones were correlated with each other. The health status of older adults is influenced by the AMH/InhB ratio, although they (AMH and InhB) may be independent (41). In an animal study, AMH and InhB cooperatively inhibited testicular cancer, and AMH also suppressed aromatase activity in FSH-stimulated Sertoli cells, independent of LH. Future research could explore AMH's role after RIT with respect to its physiological function in the testis (42). In infertile men, low serum AMH levels are associated with severely impaired gonadal function, as evidenced by compromised semen quality and a reduced T-to-LH ratio. Additionally, the role of circulating AMH during adulthood is less well understood (39).

Semen analysis currently serves as the benchmark for assessing male fertility status; however, a standard semen analysis does not guarantee fertility (1). Semen analysis was conducted within one hour of collection in accordance with the WHO laboratory manual, supplemented by additional guidelines (15). The assessment evaluated semen parameters, including pH, viscosity, volume, sperm concentration, motility, round cells, and morphology. Poor semen quality, characterized by abnormal physical parameters, low sperm count, reduced motility, and

irregular morphology, is a significant contributor to male infertility. Our study results indicate a significant increase in semen volume, total sperm count, and sperm motility, particularly rapid progressive motility. Total sperm count is the number of spermatozoa in the ejaculate, calculated by multiplying sperm concentration by semen volume (43). The normal sperm concentration is  $\geq 20$  million sperm per milliliter of semen (3), and our study results confirm this.

A man is considered fertile when total motility is at least 40% and progressive motility is at least 32%. Sperm motility refers to the ability of sperm to move efficiently and is a crucial factor in fertility (44). Our results for motility and rapid progressive motility are consistent with previous reports that demonstrate that sperm motility is regulated by various factors, including intracellular and extracellular pH, the concentrations of calcium ions ( $\text{Ca}^{2+}$ ) and bicarbonate ions ( $\text{HCO}_3^-$ ), and sperm surface proteins. Factors such as radiation, psychological stress, and environmental pollution can impair motility. For example, radiation exposure, mutations in CatSper genes, or psychological stress through hormonal changes and impaired calcium metabolism can impair sperm motility (44). Fertility clinics typically analyze sperm parameters such as density, count, motility, and morphology. Still, sperm DNA fragmentation testing, such as the SCSA, is often overlooked due to limited awareness, cost concerns, or practical considerations. This test, first described by Son in 1980, uses flow cytometry to detect DNA fragmentation through acid- or heat-induced denaturation and identifies poor-quality sperm (45). Healthy and mature sperm nuclei contain abundant disulfide bonds, resulting in their DNA being in the double-stranded form (46).

The SCSA detects sperm DNA fragmentation; rates exceeding 30% are associated with a significant decrease in term pregnancies. Multiple RAI treatments can cause permanent testicular damage, resulting in a 50% reduction in sperm count and a 40% reduction in FSH levels. These effects occur in 20% of patients who undergo multiple treatments and in 10% of those who receive a single treatment. Despite these potential risks, our findings indicate minimal changes in sperm DNA fragmentation measured before and after RIT, suggesting a limited impact on DNA integrity, which is consistent with Anderson's findings (47). The mechanisms underlying DNA damage in sperm may include unrepaired DNA breaks during chromatin remodeling and packaging, as well as abortive apoptosis during spermatogenesis. Other possible causes include the effects of endogenous endonucleases and caspases; exposure to various genotoxic agents for therapeutic purposes or from occupational or environmental sources; infections; certain types of cancer;

and oxidative damage (48). Taken together, these points suggest that administration of RAI is unlikely to impair long-term male fertility in DTC patients receiving doses of 100 mCi (3.7 GBq) or higher (49). Therefore, conflicting findings exist regarding the effect of RAI on semen quality; this relationship may depend on RAI dose and follow-up duration after treatment (1).

### Study Limitations

The study assessed subjects before therapy and again two weeks afterward, thereby potentially overlooking long-term effects on male fertility. Exclusion criteria may limit the applicability of the results to the broader thyroid cancer patient population, as individuals with factors that influence fertility, such as varicocele or lifestyle factors, were excluded. Although the study evaluated sperm DNA fragmentation and semen parameters, the lack of a comprehensive longitudinal follow-up may hinder a thorough assessment of permanent fertility changes. Variations in RAI dosing and the lack of consensus on optimal dosing complicate the interpretation of results. Future research with diverse and extended follow-up periods is necessary to understand the long-term impact of RAI therapy on male fertility.

### Conclusion

Radioiodine therapy for thyroid cancer may temporarily increase serum FSH levels, indicating a transient impact on gonadal function. Other reproductive hormones, such as LH, DHT, DHEA, and T, remain unaffected. Our results did not demonstrate that male patients with DTC experienced infertility after receiving a cumulative RAI dose of 150 mCi. Larger sample sizes and longer follow-up are needed to further assess the possible effects of sex and gonadal hormones on sperm DNA fragmentation. Further investigation into the role of AMH post-RIT in testicular physiological function is recommended.

### Ethics

**Ethics Committee Approval:** Ethical clearance for this research was obtained from the Fasa University of Medical Sciences Ethics Committee on May 22, 2022, and the study was conducted in accordance with the approved protocol. This committee reviewed and endorsed the study's ethical considerations (ethical code: REC.1401.020, date: 11.05.2025).

**Informed Consent:** The authors declare that they have no competing interests.

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### Footnotes

#### Authorship Contributions

Surgical and Medical Practices: M.A., R.H., Concept: M.A., M.S., Design: M.A., M.S., Data Collection or Processing: R.H., M.S., Analysis or Interpretation: R.H., A.T., M.S., Literature Search: R.H., Writing: R.H., A.T., M.S.

**Conflict of Interest:** No conflict of interest was declared by the authors.

**Financial Disclosure:** The authors declared that this study has received no financial.

#### Availability of Data

The dataset analyzed during the current study is available from the corresponding author upon reasonable request.

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