

Original Research Article**THE ROLE OF RADIOACTIVE IODINE IN
THYROTOXICOSIS PATIENTS****ABSTRACT**

Aims: The primary objective is to investigate the role of I-131 in the treatment of GD and to measure the sensitivity of thyroid uptake in investigating thyroid disease.

Study design: A comparison done and some factors examined such as age and most common symptoms in hyperthyroidism

Place and Duration of Study: Department of Nuclear Medicine (KAUH) and Department of Diagnostic Radiology (KAU), Jeddah, KSA, between Nov. 2012 and May 2013.

Methodology: Data of 39 patients collected before radioactive iodine dose is giving. Thyroid scans applied and had TFT test before and after radio-iodine therapy. Patients evaluated within TFT, thyroid survey test to illustrate the demographic feature and response to treatment.

Results: The most common symptoms presented are tachycardia, weight loss, excessive sweating and tremors. 90% of patients were on anti-thyroid medication before taking iodine therapy while 10% were not. 95% had abnormalities result of TFT. Except excessive sweating, there was no significant association between age and symptoms. After radio-iodine therapy, there is a significant changing within a three-month period of increase TSH and decrease of T3 and T4. Within more than six months, 60% of patients' data became hypothyroidism, 30% being standard and only 10% did not respond to treatment.

Conclusion: Radioactive iodine provides excellent and definitive treatment of choice among Graves' disease patients to therapy with less complication in reverse of taking anti-thyroid medication or performing surgery.

Keywords: Hyperthyroidism, Graves' disease, Thyroid hormone, radioactive iodine.

1. INTRODUCTION

Hyperthyroidism is a type of thyrotoxicosis. If there are elevating serum levels of T3, T4, or both a hypermetabolic clinical syndrome occurred.^[1]

The most common cause of hyperthyroidism is Graves' disease. It recognized and characterized by the immune system attacking the thyroid gland with overproduction of thyroxin hormone and increased the metabolic rate. So it leads to a host of health problems of most of the vital body organs such as the heart, CNS, reproductive system and GIT system. The variety of very alarming physical and mental effects caused by this activity.^[2]

Graves' disease followed by toxic multi-nodular goiter considered the most common cause of thyrotoxicosis.^[3] The most frequent signs of thyrotoxicosis are heat intolerance, nervousness, palpitations, fatigue and weight loss. The standard examination findings include sinus tachycardia, tremor, hyperreflexia and agitation.^[3] There is some correlation between the degree of thyroid hormone excess and the clinical severity.^[4]

The exquisitely sensitive indicator of thyroid status in patients with an intact hypothalamic-pituitary axis is called the TSH serum. It is rare that the patient is thyrotoxic when the TSH is considered normal. The TSH suppression with elevated free T3, but normal free T4 described thyrotoxicosis. Subclinical hyperthyroidism is defining by suppressed TSH or weak in the presence of normal free thyroid hormone concentrations.^[5]

Serologic data, combined with thyroid imaging and radiotracer thyroid uptake measurements enable accurate diagnosis and appropriate patient treatment.^[6]

Diagnostic imaging plain films not routinely ordered, but these films may show: Pulmonary metastasis, Tracheal deviation and Calcifications (suggest papillary or modularly carcinoma)^[7].

Thyroid scintigraphy remains an important tool for guiding clinical decisions in thyroid diseases. Thyroid scintigraphy is so used in the diagnosis of the cause of a patient's hyperthyroidism. Pregnancy, and breastfeeding are contraindications to the thyroid scintigraphy.^[8]

Beside radioiodine, there are many treatment options of GD as anti-thyroid medication, surgery and radioactive iodine (RAI) therapy. Some patients treated surgically with uncomplicated GD with many choices of treatment that depend on the countries and locations.^[9]

The primary purpose of this study is to investigate the treatment effect of radioactive iodine upon those patients who suffer from Graves' disease as it has the first line of therapy recommended by American Thyroid Association.^[10]

Another goal is to measure the sensitivity of thyroid uptake in investigate the condition while giving reasons of hyperthyroidism. Using the static's works, a comparison done and some factors examined such as gender, age and most common symptoms in hyperthyroidism.

2. MATERIAL AND METHODS

This study conducted on nonrandomized, observational clinical case series. The records of patients diagnosed that they had Thyrotoxicosis and registered in the nuclear medicine department, academic year 2012/2013 to perform thyroid scanned retrospectively analyzed.

The data of 39 patients subjected to nuclear medicine who was complaining of signs and symptoms of thyroid disorder that diagnosed with grave's disease collected. Those numbers, of patients, had a TFT test before and after radioiodine therapy. The exclusion criteria examined in the case of patients who had previous radioiodine treatment dose. The studied samples contained both gender (females and males) with a wide range of age ranging from 15 to 65 years. Before radioactive iodine treatment dose given, the thyroid scan applied to confirm the type of thyroid disorder. The conducted scan clarified the importance and role of radiography scintigraphy in the detection of disease. The patients evaluated within TFT, thyroid survey test to illustrate the demographic feature and response to treatment.

Thyroid Scintigraphy was performed using radioactive material that is either Tc-99m injected or Iodine 123 swallowed in the form of capsules or liquid.

After all investigations of patient status and Graves' disease were confirmed by thyroid scan, the treatment dose given. So, the patient should perform a blood test before and within two to four months later in assisting the response of the thyroid gland to therapy by measuring TSH, FT3 and FT4.

The patient had given the dose of radioactive iodine orally either in liquid or capsule form where the range of dose was 15 - 25 mCi. The images produced were evaluated using PACS workstations. The collected TFT data of each patient in the study before and after the treatment dose given that helped to evaluate the rate of treatment by using iodine 131. The collected data is statistically analyzed using SPSS program to investigate the role of radioactive iodine 131 in the treatment of Graves' disease.

3. RESULTS AND DISCUSSION

3.1 Results

A total number of 39 patients collected in KAU hospital. Only 11 patients who have TFT and thyroid survey results while 28 patients did not have both of result where 18 patients have only TFT data and another ten patients have only thyroid survey data.

The 21 patients suffered of Thyrotoxicosis. Data tested with demographic variables. The majority of ages of the sample were ranged from 25 to 35 by 42.9 %, and most of the

84 samples were females by 61.9 % as shown in Table 1.

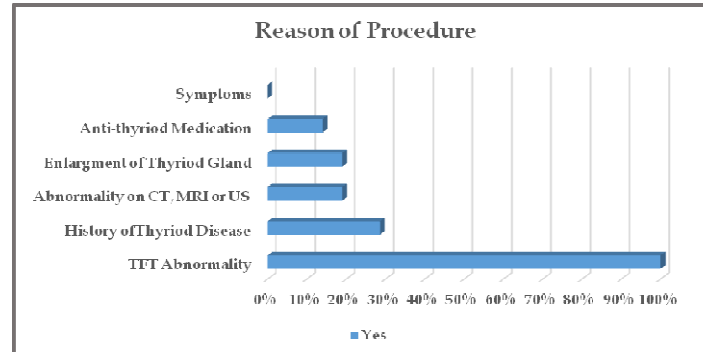
85
86

Table 1. Descriptive Statistics of collected data

Variable		Number %
Age N (%)	15 – 25	5 (23.8 %)
	25 – 35	9 (42.9 %)
	35 – 45	4 (19.0 %)
	45 – 55	2 (9.50 %)
	55 – 65	1 (4.80 %)
	Above 65	0
Gender N (%)	Male	8 (38.1 %)
	Female	13 (61.9 %)

87
88
89
90
91
92
93
94
95
96
97
98

By the assessment of thyroid survey, 90 % of patients were on antithyroid medication before taking radioiodine therapy while 10 % were not. According to the thyroid survey analysis, 95 % of patients have an abnormality result of thyroid function test due to thyroid scan while 29 % have a history of thyroid disease. However, 19 % of them had an abnormality on CT, MRI and US. In fact, 19 % were complaining of the enlarged thyroid gland while 14 % of them were on antithyroid medication as it seen from Figure 1. The most common type of medication was Carbimazole. The patients presented with tachycardia, weight loss, excessive sweating and tremors. Heat intolerance was more in female while other symptoms were equal in both groups (female and male) as shown in Table 2.



99
100
101

Figure 1. illustration of reason referred of thyroid scan

Table 2. the correlation between gender and each symptoms respectively.

Symptoms		Gender		Uncertainty Coefficient			Test
		Male	Female	Symmetric	Gender	Symptom	
Heat Intolerance	Yes	2	6	0.391	0.383	0.400	Fisher's Exact
	No	12	1				Sig. (0.003*)

102

Nervousness	Yes	5	11	0.051	0.047	0.057	Fisher's Exact
	No	3	2				Sig. (0.325)
Rapid heart rate	Yes	8	0	0.055	0.035	0.123	Fisher's Exact
	No	12	1				Sig. (1.000)
Weight Loss	Yes	8	0	0.055	0.035	0.123	Fisher's Exact
	No	12	1				Sig. (1.000)
Eyes Changing	Yes	3	5	0.041	0.041	0.040	Chi-Square
	No	8	5				Sig. (0.284)
Excessive sweating	Yes	7	12	0.006	0.005	0.010	Fisher's Exact
	No	1	1				Sig. (1.000)
Tremors	Yes	7	1	0.006	0.005	0.010	Fisher's Exact
	No	12	1				Sig. (1.000)

* 0.0 = No Association, 0.0 < r ≤ 0.2 Very weak, 0.2 < r ≤ 0.4 Weak, 0.4 < r ≤ 0.6 Moderate, 0.6 < r ≤ 0.8 Strong, 0.8 < r ≤ 1.0 Very Strong.

Fisher Exact test shows how there is a strong the correlation between gender and symptoms presenting, there were an active relationship, and it is significant (0.003). However, regarding male's age, most of the young patients had excessive sweating with significant association of (0.033). Also, here are no significant associations between age groups and symptom factors except excessive sweating. In excessive sweating, there is a significant relationship between it (0.604), and it is a moderate association as it seen in Table 3. The most common symptoms that were significant in our collected patients include tremors, tachycardia, excessive sweating and weight loss which correspond with universal joint symptoms.

Table 3. the correlation between Age and each symptoms.

Symptoms		Age					Contingency Coefficient	Test
		15 - 25	25 - 35	35 - 45	45 - 55	55 - 65		
Excessive sweating	Yes	5	9	3	2	0	0.608	Fisher's Exact
	No	0	0	1	0	1		Sig. (0.033*)

Nervousness	Yes	4	6	4	2	0	0.458	Fisher's Exact
	No	1	3	0	0	1		Sig. (0.346)
Rapid heart rate	Yes	4	9	4	2	1	0.371	Fisher's Exact
	No	1	0	0	0	0		Sig. (0.571)
Weight Loss	Yes	5	9	3	2	1	0.419	Fisher's Exact
	No	0	0	1	0	0		Sig. (0.333)
Eyes Changing	Yes	3	3	4	1	0	0.476	Fisher's Exact
	No	2	6	0	1	1		Sig. (0.173)
Heat Intolerance	Yes	3	7	4	0	0	0.539	Fisher's Exact
	No	2	2	0	2	1		Sig. (0.073)
Tremors	Yes	4	9	4	1	1	0.469	Fisher's Exact
	No	1	0	0	1	0		Sig. (0.262)

* 0.0 = No Association, 0.0 < r ≤ 0.2 Very weak, 0.2 < r ≤ 0.4 Weak, 0.4 < r ≤ 0.6 Moderate, 0.6 < r ≤ 0.8 Strong, 0.8 < r ≤ 1.0 Very Strong.

Thyroid Function Test (TFT)

Thyroid gland absorbs the radioactive material within 15-30 minutes in case of using Tc-99m or 4-6 hours using of I-123. Those results collected for 29 patients before and after they took a dose. There is a significant changing within three months after receiving I-131 treatment. There's a gradual drop of T4, which is very clear after three months, inconsistent with responses to therapy. It should note that TSH gets increased within normal range with decreasing in both T4 and T3. There is a substantial variation among all parameters, which means that the radioactive iodine impacted was very high (Table 4 and Figure 2). The relation between TFT results before and after treatment seen in Table 5. There is a significant relation between T4 before and after taking radioactive iodine, and it is increasing but it is not significant between TSH and T3 before and after treatment.

The relation was not significant between test result before and after which means that the relation between TSH before and after. That means; the change in TSH before and after randomly has no trend. However, at the same time, doesn't mean there is no difference between TSH before and after treatment.

Table 4. Descriptive statistics of changing the value of TSH, T3 and T4 before and after the treatment

Variables		Descriptive Statistics		
		Mean	Std. Deviation	Skewness
Before	TSH	0.038	0.172	5.35
	T4	39.69	28.21	1.06
	T3	16.54	14.44	1.39
After	TSH	16.02	26.61	1.97

T4	15.89	17.17	4.43
T3	5.857	8.567	3.97

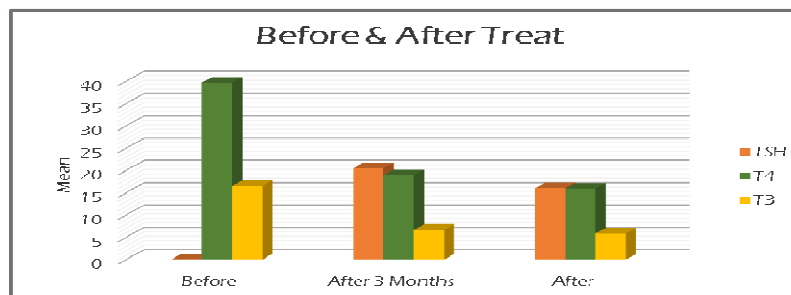


Figure 2. Histogram graph of TSH , T3 and T4 values before and after the treatment

Table 5. paired correlation of TSH , T3 and T4 before and after the treatment

Variables	Paired Correlation	
	Correlation	P-Value
TSH_B & TSH_A	-0.088	0.651
T4_B & T4_A	0.357	0.057
T3_B & T3_A	0.486	0.008*

*0.0 = No Association, 0.0 < r ≤ 0.2 Very weak, 0.2 < r ≤ 0.4 Weak, 0.4 < r ≤ 0.6 Moderate, 0.6 < r ≤ 0.8 Strong, 0.8 < r ≤ 1.0 Very Strong.

It seen in Table 5 that there are significant differences before and after the treatment of TSH, T4 & T3, which means that the treatment has a high impact on the disease. TSH increases after treatment, but T4 & T3 decrease after treatment.

However, it noted that 60 % of patients were on Thyroxin; this is an indication of good response to treatment. On the other hand, 30 % being normal after treatment and 10 % of them were encountered failure of therapy by the retaking of Carbimazole.

3.2. Discussion

Graves' disease defined as an autoimmune disorder characterized by the presence of thyroid-stimulating hormone (TSH) receptor antibodies. GD clusters in families and genetic relations found, but there no single gene is known to be necessary or sufficient to cause Graves' disease.^[11, 12] In the present study, the majority ages of the sample ranged from 25 to 35 by 42.9 % and most of the samples were females by 61.9 %. By the assessment of thyroid survey, 90 % of patients were on antithyroid medication before taking radioiodine therapy while 10 % were not.^[4] The prevalence of thyrotoxicosis increases with age.^[13, 14] Patients who suffer from Graves' disease and were on course of radioactive iodine therapy responded highly significantly to treatment. 60% of patients' data become hypothyroidism, 30 % being standard and only 10 % did not respond to treatment. This conclusion comes with the recommendation of ATA regarding the treatment decision among this category of patients and shows the importance of performing thyroid scan and TFT in order to diagnose the disease of a thyroid more accurately.

Treatment of GD seeks to suppress thyroid function. With treatment options include antithyroid medication, surgery or radioactive iodine (I-131). Radioiodine is considered a safe and effective material in achieving high cure rates, although there are differences in the

treatment of thyrotoxicosis with radioactive iodine with proper patient selection and regular follow-up.^[15]

Radioactive Iodine (I-131) for Graves' hyperthyroidism has no opposite effects on the health of the offspring of treated patients. There are no ultimate data that provide evidence for increased rates of leukemia, thyroid cancer, infertility or neonatal abnormality for patients treated with radioiodine.

The purpose of therapy is to destroy sufficient thyroid tissue to help the patient either euthyroid or hypothyroid. It remains the radionuclide the choice for treatment because of the long half-life of just over eight days.^[15] In the present study, radioactive material will be absorbed by the thyroid gland within 15-30 minutes in case of using Tc-99m or 4-6 hours using of I-123. Those results collected for 29 patients before and after they took a dose. There is a significant changing within three months after taking I-131 treatment. There's a gradual drop of T4, which is very clear after three months, inconsistent with responses to treatment. It noted that TSH gets increased within normal range with decreasing in both T4 and T3. There is a considerable variation among all parameters, which means that the radioactive iodine impacted was very high.

The first radiopharmaceutical that used for thyroid scanning was iodine-1-131. The requirement of high energy collimators results in a reduced spatial resolution. Combined with the fact that the radiation dose delivered is high, this explains why I-131 is unfavorable for thyroid imaging. The two commonly used radiopharmaceuticals for imaging are iodine-123 and technetium-99m pertechnetate as TcO₄⁻.^[7, 8]

On the other hand, Table 6 indicates the relation between TFT results before and after. It is seeing that there is a significant relation between T4 before and after taking radioactive iodine, and it is increasing but it is not significant between TSH and T3 before and after treatment. The physiological role of the radioactive iodine (RAI) describing the mechanism of RAI. The RAI is taken up by iodide transporter of the thyroid as the same way that the natural iodine process. Then, the follicular cell destroyed by beta particle and gradually volume decreased and thyrotoxicosis will be controlled.^[15]

Table 6. paired T-test shows the difference before and after the treatment of TSH, T3 and T4

Variables	Paired T-test				
	Mean Differ	95% CI		t	P-Value
TSH_B - TSH_A	-15.98	-26.1	-5.85	-3.23	0.003*
T4_B - T4_A	23.80	13.41	34.18	4.69	0.000*
T3_B - T3_A	10.69	5.851	15.52	4.53	0.000*

* 0.0 = No Association, 0.0 < r ≤ 0.2 Very weak, 0.2 < r ≤ 0.4 Weak, 0.4 < r ≤ 0.6 Moderate, 0.6 < r ≤ 0.8 Strong, 0.8 < r ≤ 1.0 Very Strong.

The relation between test result before and after wasn't significant which means that the relation between TSH before and after. That means; the change in TSH before and after randomly has no trend, but, at the same time, doesn't mean there is no difference between TSH before and after treatment. There are significant differences before and after the treatment of TSH, T4 & T3, which means that the treatment has a high impact on the disease. TSH is increasing after treatment, but T4 & T3 decrease after treatment. However, it noted from Figure 3 that 60 % of patients were on Thyroxin, and this is an indication of good response to therapy. On the other hand, 30 % being normal after treatment and 10 % of them, were encountered failure of therapy by the retaking of Carbimazole.

Iodine-131 used for the measurement of thyroid uptake, which requires only small amounts of radiotracer. It no longer used for routine imaging of the thyroid gland because of a high absorbed radiation dose related to the long physical half-life of eight days and beta emissions. I-131, however, continues to be valuable for the detection of metastases and recurrences in differentiated thyroid cancer.^[16, 17, 18]

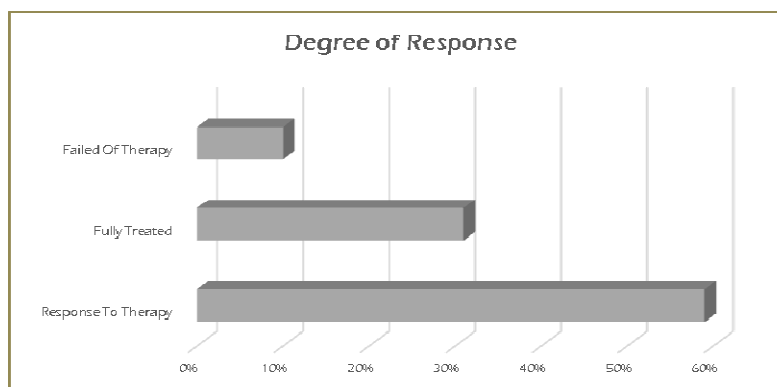


Figure 3. illustrated the response to therapy of collected data during the treatment duration.

According to the thyroid survey analysis, 95 % of patients have an abnormality result of thyroid function test due to thyroid scan while 29 % have a history of thyroid disease. However, 19 % of them had an abnormality on CT, MRI and US, 19 % complaining of the enlarged thyroid gland while 14 % of them were on antithyroid medication. The most common type of medication was Carbimazole. On the other hand, it can be noted that most of the patients presented with tachycardia, weight loss, excessive sweating and tremors.^[17, 18, 19]

According to the symptoms presented, the heat intolerance was more in female while other symptoms were equal in both groups (female and male). Though the disease can have a serious effect on someone's life if not properly treated, it is not typically life menacing. It found that 5-10 times more common in women than in men.^[15]

4. CONCLUSION

The present study indicated that radioactive iodine provides excellent and definitive treatment of choice among Graves' disease patients. Keeping in view of the safety, convenience, low cost, and effectiveness in hyperthyroid patients with less complication in contrast to antithyroid medication or performing surgery.

REFERENCES

1. Kittisupamongkol W. Hyperthyroidism or thyrotoxicosis? Cleveland Clinic. Journal of Medicine 2009; 76 (3): 152.
2. Spinass GA, Ott P, Stoeckli, SJ. Disorders of the Head and Neck. In: Siegenthaler W Differential Diagnosis in Internal Medicine: From Symptom to Diagnosis, 1st edn München, Verlag CH Beck, 2007: 474-491.
3. Cooper DS. Hyperthyroidism. Lancet 2003; 362: 459–68.
4. Boelaert K, Newby PR, Simmonds MJ, Holder RL, Carr-Smith JD, Heward JM et al. Prevalence and relative risk of other autoimmune diseases in subjects with autoimmune thyroid disease. Am J Med 2010; 123 (183e): 1–9.
5. Bahn Chair RS, Burch HB, Cooper DS, Garber JR, Greenlee MC, Klein I, et al. Hyperthyroidism and other causes of thyrotoxicosis: management guidelines of the

- 262 American Thyroid Association and American Association of Clinical Endocrinologists.
263 Thyroid 2011; 21: 1– 54.
- 264 6. Pittas AG, Lee SL. Evaluation of Thyroid Function. In: Hall JE, Nieman LK. Handbook
265 of Diagnostic Endocrinology. 1st ed. New Jersey; Humana Press, 2003: 107-130.
- 266 7. Piciu D. The Thyroid Gland. In: Piciu D. Nuclear Endocrinology. 1st edn Berlin;
267 Springer-Verlag (2012): 53-163.
- 268 8. Hindle E, Calzada-Naucaudie M, Keller I, Askienazy S. The Endocrine System. In:
269 Biersack HJ, Freeman LM. Clinical Nuclear Medicine. Berlin; Springer-Verlag, 2007:
270 287-306.
- 271 9. Solomon B, Glinoe D, Lagasse R, Wartofsky LN. Current trends in the management
272 of Graves' Disease. J Clin Endocrinol Metab. 1990; 70: 1518–1524.
- 273 10. American thyroid association. Hyperthyroidism Management Guidelines, Endocrine
274 Practice 2011; 173: 2-65.
- 275 11. Weetman AP. Graves' disease. N Engl J Med 2000; 343: 1236–1248.
- 276 12. Weetman AP. Diseases associated with thyroid autoimmunity: explanations for the
277 expanding spectrum. Clin Endo (Oxf) 2011; 74: 411–418.
- 278 13. O'Leary PC, Feddema PH, Michelangeli VP, Leedman PJ, Chew GT, Knuiman M, et
279 al. Investigations of thyroid hormones and antibodies based on a community health
280 survey: the Busselton thyroid study. Clin Endo (Oxf) 2006; 64: 97–104.
- 281 14. Gopinath B, Wang JJ, Kifley A, Wall JR, Eastman CJ, Leeder SR, Mitchell P. Five-
282 year incidence and progression of thyroid dysfunction in an older population. Int
283 Med J 2010; 40: 642–9.
- 284 15. Mumtaz M, Lin LS, Hui KC, Mohd Khir AS. Radioiodine I-131 for the Therapy of
285 Graves ' disease, Malays J Med Sci. Jan-Mar 2009; 16 (1): 25–33.
- 286 16. Sarkar SD, Becker DV. Thyroid uptake and imaging. In: Becker KL (3ed) Principles
287 and practice of endocrinology and metabolism. Lippincott, Philadelphia, 1995: 307–
288 313.
- 289 17. Sarkar SD, Kalapparambath T, Palestro CJ. Comparison of I-123 and I-131 for whole
290 body imaging in thyroid cancer. J Nucl Med 2002; 43: 632–634.
- 291 18. Sarkar, SD, Savitch I. Management of thyroid cancer. Applied Radiol 2004; 34–45.
- 292 19. Ward LS, Santarosa PL, Granja F, da Assumpção LV, Savoldi M, Goldman GH. Low
293 expression of sodium iodide symporter identifies aggressive thyroid tumors. Cancer
294 Lett. 2003; 200: 85–91.