AMERICAN THYROID ASSOCIATION
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Clinical Thyroidology® for the Public

VOLUME 11 | ISSUE 5 | MAY 2018

Salivary gland damage is a known complication of radioactive iodine therapy. Unfortunately, we still not have an effective treatment to protect salivary glands from the radiation. Selenium is a known antioxidant that has shown to decrease side effects of radiation therapy in other cancers. In this study the authors explore the role of selenium in preservation of salivary glands function after radioactive iodine therapy.

Son H et al Effect of selenium supplementation for protection of salivary glands from iodine-131 radiation damage in patients with differentiated thyroid cancer. Hell J Nucl Med. 2017 Jan-Apr;20(1):62-70.

In women, radioactive iodine therapy has been associated with irregular menstrual cycles, earlier menopause, and problems with future fertility and delayed pregnancy. In women, one way of measuring ovarian reserve (i.e. the ability to achieve a pregnancy) are blood levels of anti-Mullerian hormone (AMH). This study was done to examine the changes in blood AMH levels among women with thyroid cancer who receive radioactive iodine therapy.

Yaish I et al. A single radioactive iodine treatment has a deleterious effect on ovarian reserve in women with thyroid cancer: Results of a prospective pilot study. Thyroid. 2018 Feb 21. doi: 10.1089/thy.2017.0442. [Epub ahead of print]

The most common cause of hypoparathyroidism is damage to the glands during thyroid surgery. While rare, permanent hypoparathyroidism continues to be a real, clinical problem after thyroid surgery. Only a few studies have tried to report the risks of hypoparathyroidism. The first paper reports on post-surgical hypoparathyroidism in children, while the second paper focuses on adults.

Nordenström E et al 2018 Permanent hypoparathyroidism after total thyroidectomy in children: results from a national registry. World J Surg. Epub 2018 Feb 22. PMID: 29470698.

Gschwandtner E et al Hermann M 2018 How many parathyroid glands can be identified during thyroidectomy? Evidence-based data for medical experts. Eur Surg 50:14–21. Epub 2017 Dec 13. PMID: 29445392

One of the most important ultrasound features of cancer is the presence of calcifications, especially microcalcifications, in a thyroid nodule. The presence of microcalcifications on an ultrasound is felt to be highly suggestive of thyroid cancer. Since calcifications can also be seen in benign thyroid nodules, the aim of the current study was to examine whether ultrasound calcifications truly predict a) calcifications in thyroid tissue itself and b) the diagnosis of papillary thyroid cancer.

Bilici S et al Histopathological investigation of intranodular echogenic foci detected by thyroid ultrasonography. Am J Otolaryngol 2017;38:608-13. Epub July 5, 2017.

Papillary thyroid cancer is the most common type of thyroid cancer and overall has an excellent prognosis. Previous studies showed conflicting evidence regarding the impact of the extent of surgery on overall survival and the risk of death in patients with low risk thyroid cancer. The goal of this study was to examine whether overall survival is affected by extent of surgery for papillary thyroid cancer when categorized by cancer size.

Rajjoub SR et al 2018 Thyroid lobectomy is not sufficient for T2 papillary thyroid cancers. Surgery. Epub 2018 Feb 13.

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EDITOR'S COMMENTS

Welcome to another issue of *Clinical Thyroidology for the Public*. In this journal, we will bring to you the most up-to-date, cutting edge thyroid research. We also provide even faster updates of late-breaking thyroid news through Twitter at @thyroidfriends and on Facebook. Our goal is to provide patients with the tools to be the most informed thyroid patient in the waiting room. Also check out our friends in the **Alliance for Thyroid Patient Education**. The **Alliance** member groups consist of: the *American Thyroid Association, Bite Me Cancer, the Graves' Disease and Thyroid Foundation, the Light of Life Foundation, ThyCa: Thyroid Cancer Survivors' Association, Thyroid Cancer Canada, Thyroid Cancer Alliance* and *Thyroid Federation International.*

We invite all of you to join our **Friends of the ATA** community. It is for you that the American Thyroid Association (ATA) is dedicated to carrying out our mission of providing reliable thyroid information and resources, clinical practice guidelines for thyroid detection and treatments, resources for connecting you with other patients affected by thyroid conditions, and cutting edge thyroid research as we search for better diagnoses and treatment outcomes for thyroid disease and thyroid cancer. We thank all of the Friends of the ATA who support our mission and work throughout the year to support us. We invite you to help keep the ATA mission strong by choosing to make a donation that suits you – it takes just one moment to give online at: www.thyroid.org/donate and all donations are put to good work. The ATA is a 501(c)3 nonprofit organization and your gift is tax deductible.

May is International Thyroid Awareness month. May 25 is World Thyroid Awareness Day.

In this issue, the studies ask the following questions:

- Does selenium help preserve salivary gland problems after radioactive iodine therapy?
- What are the effects of radioactive iodine therapy on fertility in women?
- What is the risk of hypoparathyroidism after total thyroidectomy?
- Do calcifications in thyroid nodules on ultrasound always indicate thyroid cancer?
- Does the extent of initial surgery affect overall survival in low risk thyroid cancers?

We welcome your feedback and suggestions. Let us know what you want to see in this publication. I hope you find these summaries interesting and informative.

— Alan P. Farwell, MD, FACE

THYROID CANCER

Selenium may protect salivary glands from radioactive iodine therapy for thyroid cancer

BACKGROUND

Radioactive iodine therapy is an important part of the treatment of advanced thyroid cancer. It works because the radioactive iodine is taken up and concentrated in thyroid cells, both normal and cancerous, and destroys these cells. Radioactive iodine is also taken up in the salivary glands but is not concentrated in the cells, minimizing any damage. However, inflammation of salivary glands, dryness in the mouth and consequently dental problems are known complications of radioactive iodine therapy that are seen in at least 10% of thyroid cancer patients treated with high dose radioactive iodine. Many agents have been studied in the past (lemon drops, sour candy, vitamin E and C, chewing gum, etc.) in order to preserve salivary gland function. Unfortunately, we still not have an effective treatment to protect salivary glands from the radiation. Selenium is a known antioxidant that has shown to decrease side effects of radiation therapy in other cancers. In this study the authors explore the role of selenium in preservation of salivary glands function after radioactive iodine therapy.

THE FULL ARTICLE TITLE

Son H et al Effect of selenium supplementation for protection of salivary glands from iodine-131 radiation damage in patients with differentiated thyroid cancer. Hell J Nucl Med. 2017 Jan-Apr;20(1):62-70.

SUMMARY

A total of 16 patients with thyroid cancer undergoing their first radioactive iodine therapy were enrolled in the study. They were divided into two groups: 8 patients in the selenium group received selenium for 10 days, 3 days before and 6 days after radioactive iodine therapy, the other 8 patients in control group received a placebo. Patients were treated with 100-150 mCi of radioactive iodine. The authors measured amylase, a protein produced by salivary glands before, 2 days and 6 months after radioactive iodine therapy. Also salivary gland scintigraphy, a study measuring salivary gland ability to produce saliva, was done before and 6 months after radioactive iodine therapy. A questionnaire evaluating symptoms of salivary gland dysfunction were given before and 6 months after radioactive iodine therapy.

Results of the study showed significantly higher increase of serum amylase 2 days after radioactive iodine therapy in control group compared to selenium group that reflects more injury to salivary glands in the placebo group. Moreover, the results of salivary scintigraphy and scores on the questionnaire 6 months after radioactive iodine therapy were significantly different in the selenium and placebo groups reflecting that the long term damage of salivary glands was higher in control group.

IMPLICATIONS

This study suggests that selenium supplementation during radioactive iodine therapy may be protective to salivary glands. Studies with larger number of patients are needed to further evaluate the clinical significance of changes in laboratory work up and imaging studies.

—Valentina Tarasova, MD

ATA WEB BROCHURE LINKS

Thyroid Cancer (Papillary and Follicular): https://www.thyroid.org/thyroid-cancer/

Radioactive Iodine: https://www.thyroid.org/radioactive-iodine/

THYROID CANCER, continued

ABBREVIATIONS AND DEFINITIONS:

Radioactive iodine (RAI): this plays a valuable role in diagnosing and treating thyroid problems since it is taken up only by the thyroid gland. I-131 is the destructive form used to destroy thyroid tissue in the treatment of thyroid cancer and with an overactive thyroid.

mCi: millicurie, the units used for I-131.

Salivary glands: glands in the neck that produce saliva to keep the mouth lubricated. Between 0.5 and 1.5 liters of saliva are produced every day. Damage to these glands can produce dryness in the mouth and consequently dental problems

Selenium: a mineral found naturally in various foods that is important for making thyroid hormones and for normal thyroid function. It is needed in small amounts by the body. It also has antioxidant properties

Antioxidants: substances that prevent cell damage caused by oxidation in the body which has been linked to cancer and aging.

THYROID CANCER

Radioactive iodine therapy and pregnancy in women

BACKGROUND

Radioactive iodine therapy is an important part of the treatment of advanced thyroid cancer. It works because the radioactive iodine is taken up and concentrated in thyroid cells, both normal and cancerous, and destroys these cells. However, the radiation from the radioactive iodine circulating in the blood after the treatment may affect other tissues in the body. In particular, the ovaries may be particularly sensitive to the radiation from radioactive iodine and this may lead to future problems with fertility. In women, radioactive iodine therapy has been associated with irregular menstrual cycles, earlier menopause, and delayed pregnancy. Women who receive radioactive iodine therapy are generally advised to avoid pregnancy in the 6-12 months after treatment, due to the risks of radiation to the eggs within the ovaries.

In women, one way of measuring ovarian reserve (i.e. the ability to achieve a pregnancy) are blood levels of anti-Mullerian hormone (AMH). This study was done to examine the changes in blood AMH levels among women with thyroid cancer who receive radioactive iodine therapy.

THE FULL ARTICLE TITLE

Yaish I et al. A single radioactive iodine treatment has a deleterious effect on ovarian reserve in women with thyroid cancer: Results of a prospective pilot study. Thyroid. 2018 Feb 21. doi: 10.1089/thy.2017.0442. [Epub ahead of print]

SUMMARY OF THE STUDY

This study evaluated 24 premenopausal women who received radioactive iodine following thyroid cancer surgery. The researchers measured blood levels of AMH before radioactive iodine was given and 3, 6, 9, and 12 months after the treatment. After three months, blood levels of AMH were lower than before the RAI treatment. At the end of one year, average AMH blood levels remained low at approximately 32% less than initial levels. The dose of radioactive iodine therapy was not related to the blood AMH levels. However, there were more women age 35 years who had lower AMH levels, compared to those younger than age 35.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

The findings of this study are relevant to women who receive thyroid cancer treatment. Thyroid cancer occurs over three times more commonly in women than men, and at least a third of women are diagnosed during their childbearing years. The results show that women who receive radioactive iodine therapy for their thyroid cancer have lower blood levels of AMH in the first few months after treatment. Further research is needed to confirm these findings, to see how good of a marker AMH levels are for future fertility, and to evaluate how long the lower AMH levels persist in individuals.

— Angela M. Leung, MD, MSc

ATA THYROID BROCHURE LINKS

Radioactive Iodine: https://www.thyroid.org/radioactive-iodine/

Pregnancy and Thyroid Disease: https://www.thyroid.org/thyroid-disease-pregnancy/

ABBREVIATIONS & DEFINITIONS

Radioactive iodine (RAI): This plays a valuable role in diagnosing and treating thyroid problems since it is taken up only by the thyroid gland. I-131 is the destructive form used to destroy thyroid tissue in the treatment of thyroid cancer and with an overactive thyroid. I-123 is the non-destructive form that does not damage the thyroid and is used in scans to take pictures of the thyroid (*Thyroid Scan*) or to take pictures of the whole body to look for thyroid cancer (*Whole Body Scan*).

THYROID CANCER

Risk of hypoparathyroidism after total thyroidectomy

BACKGROUND

Parathyroid hormone (PTH) is produced by the parathyroid glands and is responsible for directly regulating calcium levels in the blood. If PTH levels are high, calcium levels are high and the disorder is called hyperparathyroidism, which is fairly common. If PTH levels are low, calcium levels are low and the disorder is called hypoparathyroidism, which is relatively rare. Hypoparathyroidism is a chronic illness that greatly impairs patient's quality of life and ongoing treatment can be challenging.

The most common cause of hypoparathyroidism is damage to the glands during thyroid surgery. There are usually 4 parathyroid glands in the neck and they located next to the thyroid, with 2 glands on each side. These glands frequently get bruised during surgery and mild hypoparathyroidism is rather common after surgery but usually resolves after a few days to weeks. While rare, permanent hypoparathyroidism continues to be a real, clinical problem after thyroid surgery. If it appears that the parathyroid gland(s) will not be able to recover, surgeons may autotransplant one or more parathyroid glands into the muscles of the neck during surgery. However, there remains considerable controversy and uncertainty among surgeons as to the best approach to reduce the risk of hypoparathyroidism when performing thyroidectomy.

In the hands of an experienced surgeon that does a lot of thyroid surgeries (high volume thyroid surgeon), the risk of permanent hypoparathyroidism should be <5%. The incidence in children is higher than in adults, possibly related to the decreased incidence of thyroid surgery and therefore decreased experience among many pediatric thyroid surgeons. However, even in experienced surgical hands in adult patients, the risk of temporary hypoparathyroidism is high. Only a few studies have tried to report the risks of hypoparathyroidism. The first paper reports on post-surgical hypoparathyroidism in children, while the second paper focuses on adults.

THE FULL ARTICLE TITLE

Nordenström E et al 2018 Permanent hypoparathyroidism after total thyroidectomy in children: results from a national registry. World J Surg. Epub 2018 Feb 22. PMID: 29470698.

Gschwandtner E et al Hermann M 2018 How many parathyroid glands can be identified during thyroidectomy? Evidence-based data for medical experts. Eur Surg 50:14–21. Epub 2017 Dec 13. PMID: 29445392.

SUMMARY OF THE STUDY

In the first paper, three Swedish national databases were combined and reviewed for patients < 18 years of age that had a total thyroidectomy over a 10 year period. The end point studied was the incidence of permanent hypoparathyroidism at 6 months after total thyroidectomy. Of 275 patients ages 10–17, the majority of total thyroidectomy operations were for Graves' disease (78%) while 12% were for thyroid cancer and 10% were for other benign disease. Of these patients, 7.3% (20 patients) had permanent hypoparathyroidism, with the only significant predictor being operative time > 3 hours. There was no significant association between hypoparathyroidism and patient age, type of thyroid disease, performance of autotransplantation of parathyroid glands during surgery, lymph node surgery, weight of thyroid gland specimens, length of hospital stay, or hospital thyroidectomy volume.

In the second study, 350 adult patients > 18 years of age had a near-total, subtotal, or total thyroidectomy over an 8 year period by a single surgeon, mainly for benign disease (only 14% were for Graves' disease). Almost 1/3 of patients developed temporary hypoparathyroidism, but only 4% had permanent hypoparathyroidism, all but one of which was not severe. An average of 2.28 parathyroid glands were identified by the surgeon at the time of thyroid surgery. No parathyroid glands were found in 20 patients, 1 in 16 patients, 2 in 126 patients, 3 in 114 patients, and 4 in 41 patients. Central node dissection for cancer and parathyroid autotransplantation increased the risk of temporary and permanent hypoparathyroidism.

THYROID CANCER, continued

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

These papers show that mild temporary hypoparathyroidism after surgery is common in both children and adults. While permanent hypoparathyroidism is rare, it appears to be more common in children and teens than initially reported and is more common after longer, more extensive surgery. Even though it is recommended that the parathyroid glands be identified during surgery, not all parathyroid glands can be identified if the search for them is confined to those that are in the usual locations. Hypoparathyroidism is a chronic illness that greatly impairs quality of life and research should to done to prevent as well as improve treatment of the disease.

— Melanie Goldfarb, MD

ATA THYROID BROCHURE LINKS

Thyroid Surgery: https://www.thyroid.org/thyroid-surgery/

ABBREVIATIONS & DEFINITIONS

Thyroidectomy: surgery to remove the entire thyroid gland. When the entire thyroid is removed it is termed a *total thyroidectomy*. When less is removed, such as in removal of a lobe, it is termed a partial thyroidectomy.

Hypoparathyroidism — low calcium levels due to decreased secretion of parathyroid hormone (PTH) from the parathyroid glands next to the thyroid. This can occur as a result of damage to the glands during thyroid surgery and usually resolves. This may also occur as a result of autoimmune destruction of the glands, in which case it is usually permanent.

Hypocalcemia: low calcium levels in the blood, a complication from thyroid surgery that is usually short-term and relatively easily treated with calcium pills. If left untreated, low calcium may be associated with muscle twitching or cramping and, if severe, can cause seizures and/or heart problems.

Parathyroid glands: usually four small glands located around the thyroid that secrete parathyroid hormone (PTH) which regulates the body's calcium levels.

Central neck compartment: the central portion of the neck between the hyoid bone above, and the sternum and collar bones below and laterally limited by the carotid arteries.

Central neck dissection: careful removal of lymph nodes in the central compartment of the neck during surgery for thyroid cancer.

Parathyroid autotransplantation: removal of a parathyroid gland that appears damaged during thyroid surgery and transplanting it into the muscles in the neck to avoid hypoparathyroidism.

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THYROID NODULES

Calcifications on thyroid ultrasound do not necessarily represent thyroid cancer

BACKGROUND

Thyroid nodules are a very common that can be detected in up to 2/3rds of people, often on a physical examination or a test done for other reasons. While most thyroid nodules are not cancer (benign), ~5% are cancerous. Thus, clinicians are often faced with the task of deciding which nodules require further investigation for thyroid cancer with a biopsy, and which nodules can be followed by just observation. In this respect, thyroid ultrasound is the best imaging test to evaluate thyroid nodules, because it can detect features that are felt to predict cancer.

One of the most important ultrasound features of cancer is the presence of calcifications, especially microcalcifications, in a thyroid nodule. Microcalcifications within a nodule are small flecks of calcification 1 mm or less in size that appear bright on an ultrasound image. In contrast, macrocalcifications are more coarse areas of calcification that are greater than 1 mm in size. The presence of microcalcifications (and not macrocalcifications) on an ultrasound is felt to be highly suggestive of thyroid cancer because they are assumed to correlate with the round, calcified *Psammoma* bodies of papillary thyroid cancer that a pathologist sees when examining thyroid tissue under a microscope after surgery. Thus, it is commonly accepted that, when present on an ultrasound, microcalcifications represent areas of papillary thyroid cancer. Since calcifications can also be seen in benign thyroid nodules, the aim of the current study was to examine whether ultrasound calcifications truly predict a) calcifications in thyroid tissue itself and b) the diagnosis of papillary thyroid cancer.

THE FULL ARTICLE TITLE

Bilici S et al Histopathological investigation of intranodular echogenic foci detected by thyroid ultrasonography. Am J Otolaryngol 2017;38:608-13. Epub July 5, 2017.

SUMMARY OF THE STUDY

This study included 81 thyroid nodules from 81 patients who underwent thyroidectomy at a single center in Turkey between January 2013 and March 2014. Patients were included if the same ultrasound features were observed by two different radiologists. The presence of calcifications in both the ultrasound image and the surgical tissue was noted and the relationship between cancer and calcification patterns was determined.

Of the 81 patients, 63% were female and the average age was 50 years. Ultrasound calcifications were detected in 42 (51.9%) of all nodules, although only 22 of those (27%) were true microcalcifications and the other 20 (24.7%) were macrocalcifications. Of the 42 nodules with any type of ultrasound calcification, 28 of them (66.7%) actually had calcifications in the tissues examined after surgery. However, only 11 of the 22 nodules (50%) with ultrasound microcalcifications contained calcifications in the thyroid tissue. In fact, 5 (12.8%) nodules without ultrasound calcifications were found to have calcifications on in the thyroid tissue.

Overall 23 of the 42 (54%) nodules with any type of ultrasound calcification were cancer, but 13 of the 29 nodules (45%) without ultrasound calcifications were also found to be cancer. Consequently, the rate of cancer was not different between nodules with or without ultrasound calcifications. Finally, only 12 of the 22 nodules (54%) with microcalcifications on ultrasound were found to be cancer and there was no difference in the rate of thyroid cancer between nodules with ultrasound microcalcifications and macrocalcifications.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

Overall patterns of microcalcifications and macrocalcifications seen on ultrasound were only loosely correlated with calcification in thyroid tissue. Furthermore, the presence of either of these types of calcifications did not reliably predict cancer. These results highlight the importance of evaluating multiple criteria for thyroid cancer, including those obtained through clinical history, physical examination and diagnostic imaging, and not relying on the presence or absence of a single finding.

— Phillip Segal MD FRCPC

THYROID NODULES, continued

ATA THYROID BROCHURE LINKS

Thyroid Cancer (Papillary and Follicular): https://www.thyroid.org/thyroid-cancer/
Thyroid Nodules: https://www.thyroid.org/thyroid-nodules/

ABBREVIATIONS & DEFINITIONS

Thyroid nodule: an abnormal growth of thyroid cells that forms a lump within the thyroid. While most thyroid nodules are non-cancerous (Benign), ~5% are cancerous.

Thyroid Ultrasound: a common imaging test used to evaluate the structure of the thyroid gland. Ultrasound uses soundwaves to create a picture of the structure of the thyroid gland and accurately identify and characterize nodules within the thyroid. Ultrasound is also frequently used to guide the needle into a nodule during a thyroid nodule biopsy.

Papillary thyroid cancer: the most common type of thyroid cancer. There are 4 variants of papillary thyroid cancer: classic, follicular, tall-cell and noninvasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP).

Microcalcifications: Small flecks of calcium within a thyroid nodule, usually seen as small bright spots on ultrasonography. These are frequently seen in nodules containing papillary thyroid cancer.

Macrocalcifications: Large flecks of calcium that can be seen either inside a thyroid nodule or in the periphery (so called egg-shell/rim calcifications), usually seen as large bright spots on ultrasonography.

Thyroidectomy: surgery to remove the entire thyroid gland. When the entire thyroid is removed it is termed a *total thyroidectomy*. When less is removed, such as in removal of a lobe, it is termed a *partial thyroidectomy*.

Thyroid biopsy: a simple procedure that is done in the doctor's office to determine if a thyroid nodule is benign (non-cancerous) or cancer. The doctor uses a very thin needle to withdraw cells from the thyroid nodule. Patients usually return home or to work after the biopsy without any ill effects

Thyroid Awareness Monthly Campaigns

The ATA will be highlighting a distinct thyroid disorder each month and a portion of the sales for Bravelets™ will be donated to the ATA. The month of **May** is **International Thyroid Awareness Month** and a bracelet is available through the **ATA Marketplace** to support thyroid cancer awareness and education related to thyroid disease.

THYROID CANCER

Extent of initial surgery may impact overall survival, even in low-risk papillary thyroid cancers

BACKGROUND

Papillary thyroid cancer is the most common type of thyroid cancer, making up to 80% of all thyroid cancers. In 2015, the American Thyroid Association issued updated guidelines for the management of differentiated thyroid cancer. These guidelines propose that thyroid lobectomy, which involves removing only the thyroid lobe involved with cancer, may be adequate for patients with low-risk papillary thyroid cancer. Low-risk papillary thyroid cancers were defined as cancers larger than 1 cm but smaller than 4 cm in size, with no evidence of extension of the cancer beyond the thyroid or spread to the lymph nodes of the neck.

The risk assessments recommended in the ATA guidelines refer to risk of cancer recurrence as opposed to the risk of death. Previous studies showed conflicting evidence regarding the impact of the extent of surgery on overall survival and the risk of death in these patients. The goal of this study was to examine whether overall survival is affected by extent of surgery for the two most common variants of papillary thyroid cancer (classical and follicular-variant) when categorized by cancer size.

THE FULL ARTICLE TITLE

Rajjoub SR et al 2018 Thyroid lobectomy is not sufficient for T2 papillary thyroid cancers. Surgery. Epub 2018 Feb 13.

SUMMARY OF THE STUDY

The authors of this study used patient data from the National Cancer Database (NCDB), which contains information from approximately 70% of newly diagnosed cancer patients in the United States. A total of 33,816 patients who underwent a lobectomy or total thyroidectomy for low-risk papillary thyroid cancer (classical or follicular variants) between 2004 and 2008 were included in the study. Of the 22,899 patients with classical papillary thyroid cancer, 21,589 (94.3%) had a total thyroidectomy and 1310 (5.7%) had a lobectomy. Of the 10,917 patients with follicular-variant papillary thyroid cancer, 9392 (86.0%) patients underwent a total thyroidectomy and 1310 (14.0%) a thyroid lobectomy. Patients who were younger than 18 years of age, had a cancer size ≥4 cm and/or had lymph node involvement were excluded. Overall survival was analyzed based on cancer size, categorized as 1.0-1.9 cm, 2.0-2.9 cm and 3.0-3.9 cm.

This study found that patients with classical papillary thyroid cancer with cancers measuring 2.0-3.9 cm, and who underwent a total thyroidectomy, had improved overall survival compared to patients who underwent lobectomy. In this group of patients, older age, male sex, black race, not having private insurance, positive or unknown lymph node involvement by cancer, extension of the cancer beyond the thyroid, unknown surgical margins, more medical problems and not receiving radioactive iodine therapy were factors associated with worse overall survival.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study has attempted to address the gap in knowledge regarding the effect of extent of surgery on overall survival in patients with papillary thyroid cancer. This is different than most other thyroid cancer studies which focus on risk of cancer recurrence since patients with papillary thyroid cancer overall have an excellent prognosis. The observation that the procedure of choice should be total thyroidectomy in patients with classical papillary thyroid cancer and cancers >2 cm in size is different than the recommendations in the ATA guidelines and needs to be examined more closely. This has implications for both physicians and patients as the risk of a more extensive surgery has to be weighed against its potential benefit on overall survival. This is an important paper in that the general recommendations for less surgery in some low risk thyroid cancers may need to be revised. Further studies are needed to help sort this out.

— Maria Papaleontiou, MD

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THYROID CANCER, continued

ATA THYROID BROCHURE LINKS

Thyroid Cancer (Papillary and Follicular): https://www.thyroid.org/thyroid-cancer/

ABBREVIATIONS & DEFINITIONS

Papillary thyroid cancer: the most common type of thyroid cancer. There are 4 main variants of papillary thyroid cancer: classical, follicular, tall-cell and noninvasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP).

Lobectomy: surgery to remove one lobe of the thyroid.

Total thyroidectomy: surgery to remove the entire thyroid gland.

Extrathyroidal extension: the involvement of the soft tissues surrounding the thyroid gland by thyroid cancer.

Surgical margin: the visible normal tissue or skin margin that is removed with the surgical removal of a tumor or cancer. A negative surgical margin means that the outer edge of the tissue removed is clear of any cancer cells. A positive surgical margin means that cancer cells or tumor extend to the edge of the sample.

Lymph node: bean-shaped organ that plays a role in removing what the body considers harmful, such as infections and cancer cells.

Radioactive iodine (RAI): this plays a valuable role in diagnosing and treating thyroid problems since it is taken up only by the thyroid gland. I-131 is the destructive form used to destroy thyroid tissue in the treatment of thyroid cancer and with an overactive thyroid. I-123 is the non-destructive form that does not damage the thyroid and is used in scans to take pictures of the thyroid (*Thyroid Scan*) or to take pictures of the whole body to look for thyroid cancer (*Whole Body Scan*).

Overall survival: the proportion of people within a group who are expected to be alive after a specified time (usually years). It takes into account death due to any cause, both related and unrelated to the type of cancer in question.

Cancer recurrence: this occurs when the cancer comes back after an initial treatment that was successful in destroying all detectable cancer at some point.

ATA Alliance for Thyroid Patient Education

GOAL

The goal of our organizations is to provide accurate and reliable information for patients about the diagnosis, evaluation and treatment of thyroid diseases.

We look forward to future collaborations and continuing to work together toward the improvement of thyroid education and resources for patients.

WHO WE ARE (in alphabetical order)

AMERICAN THYROID ASSOCIATION
www.thyroid.org
ATA Patient Resources:
http://www.thyroid.org/thyroid-information/
Find a Thyroid Specialist: www.thyroid.org
(Toll-free): 1-800-THYROID
thyroid@thyroid.org

BITE ME CANCER
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info@bitemecancer.org

GRAVES' DISEASE AND THYROID FOUNDATION
www.gdatf.org
(Toll-free): 877-643-3123
info@ngdf.org

LIGHT OF LIFE FOUNDATION
www.checkyourneck.com
info@checkyourneck.com

THYCA: THYROID CANCER SURVIVORS' ASSOCIATION, INC.
www.thyca.org
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THYROID CANCER CANADA
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416-487-8267
info@thyroidcancercanada.org

THYROID FEDERATION INTERNATIONAL
www.thyroid-fed.org
tfi@thyroid-fed.org

Friends of the ATA

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- Updates on the latest patient resources through the ATA website and elsewhere on the world wide web
- Special e-mail alerts about thyroid topics of special interest to you and your family

We will use your email address to send you *Friends of the ATA e-news* and occasional email updates. We won't share your email address with anyone, and you can unsubscribe at any time.

www.thyroid.org

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JOIN US

PLEASE JOIN OUR JOURNEY TO ADVANCED DISCOVERIES AND TREATMENT FOR THYROID DISEASE AND THYROID CANCER

As patients with thyroid disease navigate the challenges to their quality of life and researchers and physicians look for more effective directions, we at the ATA have our own destination– **funding for critical thyroid research, prevention, and treatment.** For 94 years, the ATA has led the way in thyroidology. It's a daily obstacle course to find new drugs, better treatments, advanced surgical methods, and more rapid diagnoses for the 20 million Americans who have some form of thyroid disease.

The ATA has paved the way with management guidelines for clinicians who diagnose and treat thyroid disease. For physicians treating pregnant women diagnosed with thyroid disease, our recent publication presents 97 evidence-based recommendations making sure that best practices are implemented with the latest, most effective treatment.

Through your generous support and donations, research takes the lead and hope is on the horizon. **Will you join us** in our campaign to raise **$1.5 million** for thyroid research, prevention, and treatment? Your compassionate, tax-deductible gift will provide funds for:

- Research grants that pave the way for 1,700 ATA physicians and scientists who have devoted their careers to understanding the biology of and caring for patients affected by thyroid disease.
- Patient education for individuals and families looking for life-changing clinical trials, the best thyroid specialists, and cutting edge treatment and drugs.
- Professional education that offers a wealth of knowledge and leading-edge research for trainees and practitioners.
- A website that is the go-to resource for thyroid information for patients and practitioners alike. In 2016 alone, there were more than 3,700,000 website views of ATA's library of online thyroid information patient brochures.

Donations **of all sizes** will change the future for thyroid patients. You will make a direct impact on patients like Mary Catherine's father as he deals with Anaplastic Thyroid Cancer. You will help scientists like ATA Associate Member Julia Rodiger, Ph.D., a scientist at the National Institutes of Health, as she analyzes thyroid hormones for intestinal stem cell development.

"The ATA was a valuable resource for our family when my dad was diagnosed with Anaplastic Thyroid Cancer. When you're faced with a detrimental diagnosis where even a few days can make the difference in life or death, understanding your options quickly is critical. The ATA website offers a one-stop shop for patients and caregivers to find specialists, current clinical trials, general thyroid cancer information, and links to other patient support groups and information."

Mary Catherine Petermann

- Father who was diagnosed with Anaplastic Thyroid Cancer in 2006
- He was treated at Mayo Clinic
- He has clean scans as of October 2016

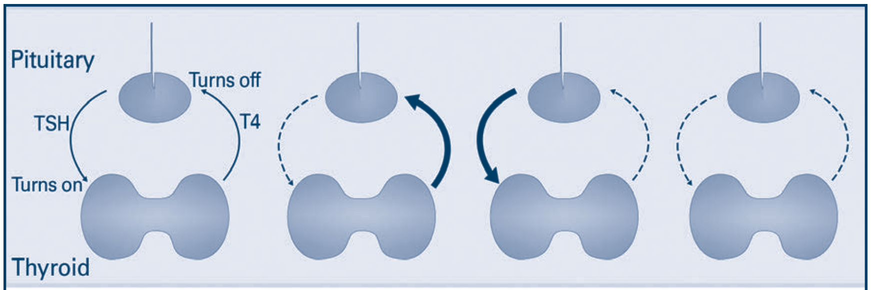
Thyroid Function Tests

WHAT IS THE THYROID GLAND?

The thyroid gland is a butterfly-shaped endocrine gland that is normally located in the lower front of the neck. The thyroid's job is to make thyroid hormones, which are secreted into the blood and then carried to every tissue in the body. Thyroid hormone helps the body use energy, stay warm and keep the brain, heart, muscles, and other organs working as they should.

FUNCTION

HOW DOES THE THYROID GLAND FUNCTION?
The major thyroid hormone secreted by the thyroid gland is thyroxine, also called T4 because it contains four iodine atoms. To exert its effects, T4 is converted to triiodothyronine (T3) by the removal of an iodine atom. This occurs mainly in the liver and in certain tissues where T3 acts, such as in the brain. The amount of T4 produced by the thyroid gland is controlled by another hormone, which is made in the pituitary gland located at the base of the brain, called thyroid stimulating hormone (abbreviated TSH). The amount of TSH that the pituitary sends into the blood stream depends on the amount of T4 that the pituitary sees. If the pituitary sees very little T4, then it produces more TSH to tell the thyroid gland to produce more T4. Once the T4 in the blood stream goes above a certain level, the pituitary's production of TSH is shut off. In fact, the thyroid and pituitary act in many ways like a heater and a thermostat. When the heater is off and it becomes cold, the thermostat reads the temperature and turns on the heater. When the heat rises to an appropriate level, the thermostat senses this and turns off the heater. Thus, the thyroid and the pituitary, like a heater and thermostat, turn on and off. This is illustrated in the figure below:



CONDITION:	Normal	Hyperthyroidism	Hypothyroidism Primary	Hypothyroidism Secondary
TSH	Normal	Low	High	Low
T4	Normal	High	Low	Low

T4 and T3 circulate almost entirely bound to specific transport proteins, and there are some situations which these proteins could change their level in the blood, producing also changes in the T4 and T3 levels (it happens frequently during pregnancy, women who take control birth pills, etc)

Another measurement done to assess the thyroid status of patients is the Free T4 measurement. The Free T4 avoids any change the proteins could have, giving us a more accurate value for the T4 level (see below).

TESTS

Blood tests to measure TSH, T4, T3 and Free T4 are readily available and widely used.

Tests to evaluate thyroid function include the following:

TSH TESTS
The best way to initially test thyroid function is to measure the TSH level in a blood sample. A high TSH level indicates that the thyroid gland is failing because of a problem that is directly affecting the thyroid (primary hypothyroidism). The opposite situation, in which the TSH level is low, usually indicates that the person has an overactive thyroid that is producing too much thyroid hormone (hyperthyroidism). Occasionally, a low TSH may result from an abnormality in the pituitary gland, which prevents it from making enough TSH to stimulate the thyroid (secondary hypothyroidism). In most healthy individuals, a normal TSH value means that the thyroid is functioning normally.

T4 TESTS
T4 circulates in the blood in two forms:

1) T4 bound to proteins that prevent the T4 from entering the various tissues that need thyroid hormone.

2) Free T4, which does enter the various target tissues to exert its effects. The free T4 fraction is the most important to determine how the thyroid is functioning, and tests to measure this are called the Free T4 (FT4) and the Free T4 Index (FT4I or FTI). Individuals who have hyperthyroidism will have an elevated FT4 or FTI, whereas patients with hypothyroidism will have a low level of FT4 or FTI.

Thyroid Function Tests

Combining the TSH test with the FT4 or FTI accurately determines how the thyroid gland is functioning.

The finding of an elevated TSH and low FT4 or FTI indicates primary hypothyroidism due to disease in the thyroid gland. A low TSH and low FT4 or FTI indicates hypothyroidism due to a problem involving the pituitary gland. A low TSH with an elevated FT4 or FTI is found in individuals who have hyperthyroidism.

T3 TESTS

T3 tests are often useful to diagnosis hyperthyroidism or to determine the severity of the hyperthyroidism. Patients who are hyperthyroid will have an elevated T3 level. In some individuals with a low TSH, only the T3 is elevated and the FT4 or FTI is normal. T3 testing rarely is helpful in the hypothyroid patient, since it is the last test to become abnormal. Patients can be severely hypothyroid with a high TSH and low FT4 or FTI, but have a normal T3. In some situations, such as during pregnancy or while taking birth control pills, high levels of total T4 and T3 can exist. This is because the estrogens increase the level of the binding proteins. In these situations, it is better to ask both for TSH and free T4 for thyroid evaluation.

THYROID ANTIBODY TESTS

The immune system of the body normally protects us from foreign invaders such as bacteria and viruses by destroying these invaders with substances called antibodies produced by blood cells known as lymphocytes. In many patients with hypothyroidism or hyperthyroidism, lymphocytes make antibodies against their thyroid that either stimulate or damage the gland. Two common antibodies that cause thyroid problems are directed against thyroid cell proteins: thyroid peroxidase and thyroglobulin. Measuring levels of thyroid antibodies may help diagnose the cause of the thyroid problems. For example, positive anti-thyroid peroxidase and/or anti-thyroglobulin antibodies in a patient with hypothyroidism make a diagnosis of Hashimoto's thyroiditis. If the antibodies are positive in a hyperthyroid patient, the most likely diagnosis is autoimmune thyroid disease.

THYROGLOBULIN

Thyroglobulin (Tg) is a protein produced by normal thyroid cells and also thyroid cancer cells. It is not a measure of thyroid function and it does not diagnose thyroid cancer when the thyroid gland is still present. It is used most often in patients who have had surgery for thyroid cancer in order to monitor them after treatment. Tg is included in this brochure of thyroid function tests to communicate that, although measured frequently in certain scenarios and individuals, Tg is not a primary measure of thyroid hormone function.

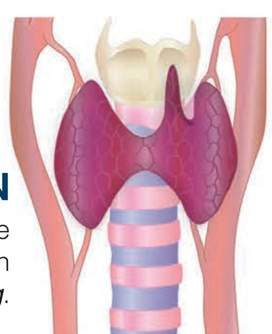
NON-BLOOD TESTS

RADIOACTIVE IODINE UPTAKE

Because T4 contains much iodine, the thyroid gland must pull a large amount of iodine out from the blood stream in order for the gland to make an appropriate amount of T4. The thyroid has developed a very active mechanism for doing this. Therefore, this activity can be measured by having an individual swallow a small amount of iodine, which is radioactive. The radioactivity allows the doctor to track where the iodine molecules go. By measuring the amount of radioactivity that is taken up by the thyroid gland (radioactive iodine uptake, RAIU), doctors may determine whether the gland is functioning normally. A very high RAIU is seen in individuals whose thyroid gland is overactive (hyperthyroidism), while a low RAIU is seen when the thyroid gland is underactive (hypothyroidism). In addition to the radioactive iodine uptake, a thyroid scan may be obtained, which shows a picture of the thyroid gland (see *Thyroid Nodules brochure*).

FURTHER INFORMATION

Further details on this and other thyroid-related topics are available in the patient information section on the American Thyroid Association® website at *www.thyroid.org*.



Pruebas De Función Tiroidea

QUE ES LA GLÁNDULA TIROIDES?

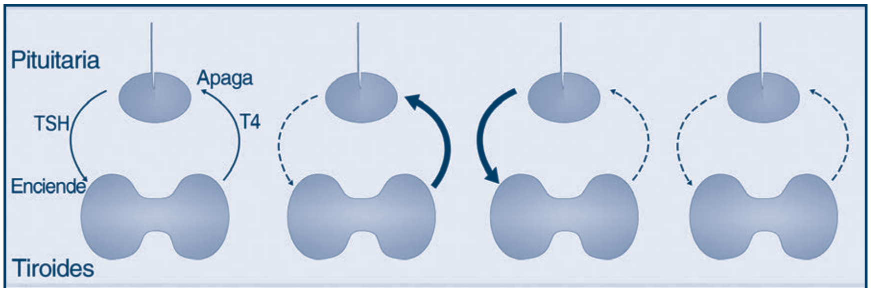
La glándula tiroides tiene forma de mariposa y normalmente se localiza en la parte de adelante del cuello, su trabajo es formar las hormonas tiroideas, volcarlas al torrente sanguíneo y entregarla a todos los tejidos del cuerpo.

Las hormonas tiroideas ayudan al cuerpo a utilizar energía, mantener la temperatura corporal y a que el cerebro, el corazón, los músculos y otros órganos funcionen normalmente.

FUNCION

CÓMO FUNCIONA LA GLÁNDULA TIROIDES?

La principal hormona secretada por la glándula tiroides es la tiroxina, también conocida como T4 porque contiene cuatro átomos de yodo. Para ejercer sus efectos, la T4 se convierte en triiodotironina (T3), eliminando un átomo de yodo. Esto ocurre principalmente en el hígado y en ciertos tejidos como el cerebro donde actúa la T3. La cantidad de T4 producida por la glándula tiroides es regulada por otra hormona que se produce en la glándula pituitaria, la cual está localizada en la base del cerebro, y la hormona se conoce como hormona estimulante de la tiroides (TSH). La cantidad de TSH que la glándula pituitaria envía al torrente sanguíneo, depende de la cantidad de T4 que ve la pituitaria. Si la pituitaria ve poca T4, entonces produce más TSH para indicarle a la glándula tiroides que debe producir más T4. Una vez que la T4 en la sangre sube por encima de cierto nivel, se suspende la producción de TSH por parte de la pituitaria. De hecho, la tiroides y la pituitaria actúan en cierto modo como un calentador y un termostato. Cuando el calentador está apagado y hace frío, el termostato lee la temperatura y enciende el calentador. Cuando la temperatura sube al nivel apropiado, el termostato siente esto y apaga el calentador. De esta manera la tiroides y la pituitaria, al igual que un calentador y un termostato, se encienden y se apagan. Esto se ilustra en la figura anterior.



CONDICIÓN:	Normal	Hipotiroidismo	Hipotiroidismo Primario	Hipotiroidismo Secundario
TSH	Normal	Baja	Alta	Baja
T4	Normal	Alta	Baja	Baja

La T4 y T3 circulan casi completamente unidas a proteínas de transporte específicas, y existen algunas situaciones en las cuales el nivel de estas proteínas en la sangre puede cambiar, lo cual producirá también cambios en los niveles de T4 y T3 (esto sucede con frecuencia durante el embarazo, en mujeres que toman píldoras anticonceptivas, etc.)

Otra medición que se hace para evaluar el estado de la tiroides de los pacientes es la medición de la T4 libre. La T4 libre evita cualquier cambio que pudiera haber en las proteínas, lo cual nos da un valor más exacto del nivel de T4 (véase más abajo).

PRUEBAS

Las pruebas sanguíneas para medir la TSH, T4, T3 y T4 libre están fácilmente disponibles y son usadas ampliamente. Las pruebas para valorar la función tiroidea incluyen las siguientes:

PRUEBA DE TSH

La mejor manera de medir inicialmente la función tiroidea es medir el nivel de TSH en una muestra de sangre. Un nivel de TSH elevado indica que la glándula tiroides está fallando debido a un problema que afecta directamente a la glándula (hipotiroidismo primario). La situación opuesta, en la cual el nivel de TSH está bajo, generalmente indica que la persona tiene una glándula hiperactiva que está produciendo demasiada hormona tiroidea (hipertiroidismo). Ocasionalmente, una TSH baja puede ser el resultado de una anormalidad en la glándula pituitaria, que previene que esta produzca suficiente TSH para estimular a la tiroides (Hipotiroidismo secundario). En la mayoría de los individuos sanos, un valor de TSH normal indica que la tiroides está funcionando normalmente.

Pruebas De Función Tiroidea

PRUEBAS DE T4

La T4 circula en la sangre de dos maneras:

1. T4 unida a proteínas, lo que previene que la T4 entre en los tejidos que necesitan hormona tiroidea
2. T4 libre, la cual entra los tejidos apropiados para ejercer sus funciones. La fracción de T4 libre es la más importante para determinar cómo está funcionando la tiroides, y las pruebas que miden esta fracción se llaman T4 libre (FT4) y el Índice de T4 libre (FT4I o FTI). Las personas con hipertiroidismo tendrán FT4 o FTI elevados, mientras que los pacientes con hipotiroidismo tendrán un nivel bajo de FT4 o FTI.

La combinación de la TSH y la FT4 o FTI ayuda a determinar en forma exacta como está funcionando la glándula tiroides.

El hallazgo de una TSH alta y FT4 o FTI baja indica hipotiroidismo primario debido a enfermedad de la glándula tiroides. Una TSH baja combinada con FT4 or FTI bajas indica hipotiroidismo debido a un problema que afecta la glándula pituitaria. Una TSH baja y FT4 o FTI elevada se encuentra en personas con hipertiroidismo.

PRUEBAS DE T3

Las pruebas de T3 suelen ser útiles para diagnosticar hipertiroidismo o para determinar la severidad del hipertiroidismo. Los pacientes hipertiroideos tendrán niveles elevados de T3. En algunos individuos con TSH baja, sólo la T3 está elevada, y la T4 libre o FTI estarán normales. La prueba de T3 rara vez es útil en pacientes con hipotiroidismo, ya que esta es la última prueba en alterarse. Los pacientes pueden tener hipotiroidismo severo con niveles de TSH elevados y FT4 o FTI bajos, pero tener niveles de T3 en rango normal. En algunas situaciones, como puede ser durante el embarazo o cuando se está tomando píldoras anticonceptivas, pueden existir niveles elevados de T4 y T3 totales. Esto es debido a que el estrógeno aumenta el nivel de proteínas de unión. En estas situaciones es mejor solicitar ambos niveles de TSH y de T4 libre (FT4) para evaluación de la tiroides.

PRUEBAS DE ANTICUERPOS CONTRA LA TIROIDES.

El sistema inmune del cuerpo normalmente nos protege contra invasores extraños como son las bacterias y los virus, destruyendo estos invasores con sustancias conocidas como anticuerpos, los cuales son producidos por las células sanguíneas llamadas linfocitos. En muchos pacientes con hipotiroidismo o hipertiroidismo, los linfocitos producen anticuerpos contra su propia tiroides, que o bien estimulan o dañan la glándula. Dos anticuerpos comunes que causan problemas de tiroides están dirigidos contra proteínas de las células tiroideas: La Tiroperoxidasa (TPO) y la tiroglobulina. La medición de los niveles de anticuerpos contra la tiroides puede ayudar a diagnosticar la causa de los problemas de tiroides. Por ejemplo, la presencia de anticuerpos anti-tiroperoxidasa y/o anti-tiroglobulina en un paciente con hipotiroidismo puede ayudar a establecer el diagnóstico de tiroiditis de Hashimoto. Si los anticuerpos son positivos en un paciente hipertiroideo, el diagnóstico más probable es enfermedad autoinmune de la tiroides.

TIROGLOBULINA.

La tiroglobulina (Tg) es una proteína producida por las células tiroideas normales y también por las células tiroideas cancerosas. No es una medida de la función tiroidea y no ayuda a diagnosticar cáncer de tiroides cuando la glándula tiroides está todavía presente. Se utiliza con más frecuencia en pacientes que han tenido cirugía para tratar el cáncer de tiroides, con el fin de monitorearlos después del tratamiento. La Tg está incluida en este folleto sobre pruebas de función tiroidea para indicar que, aunque se mide con frecuencia en ciertas situaciones e individuos, la Tg no es una medida primaria de la función de la hormona tiroidea.

PRUEBAS NO SANGUÍNEAS

CAPTACIÓN DE YODO RADIACTIVO

Debido a que la T4 contiene mucho yodo, la glándula tiroides debe extraer una gran cantidad de yodo de la sangre para que la glándula pueda producir la cantidad apropiada de T4. La tiroides ha desarrollado un mecanismo muy activo para lograr esto. Por lo tanto, esta actividad se puede medir dándole a tragar a una persona una pequeña cantidad de yodo radiactivo. La radioactividad permite que el médico pueda identificar a donde van las moléculas de yodo. Al medir la cantidad de radioactividad que es captada por la glándula tiroides, (captación de yodo radiactivo, RAIU), los doctores pueden determinar si la glándula está funcionando normalmente. Una RAIU muy alta se puede observar en personas cuyas glándulas tiroideas están hiperactivas (*Hipertiroidismo*), mientras que una RAIU baja se verá en cuando la glándula tiroides está hipoactiva (*Hipotiroidismo*). Además de la captación de yodo radiactivo, se puede obtener un gamagrama tiroideo el cual muestra una foto de la glándula tiroides (véase el folleto de *Nódulos Tiroideos*).

INFORMACIÓN ADICIONAL

Más detalles sobre este y otros temas relacionados se encuentran disponibles en la sección información para pacientes de la web de la American Thyroid Association® *www.thyroid.org*