

# Clinical THYROIDOLOGY FOR THE PUBLIC



AMERICAN  
THYROID  
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McIver B et al An independent study of a gene expression classifier (Afirma™) in the evaluation of cytologically indeterminate thyroid nodules. *J Clin Endocrinol Metab.* April 29, 2014 [Epub ahead of print]. jc20133584. PMID: 24780044

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Jeong SH et al. Outcome of thyroid nodules characterized as atypia of undetermined significance or follicular lesion of undetermined significance and correlation with ultrasound features and BRAF(V600E) mutation analysis. *AJR Am J Roentgenol* 2013;201:W854-60.

**PREGNANCY AND THYROID DISEASE .....7**

**What are the best approaches for diagnosing the etiology of thyrotoxicosis following delivery?** The most common cause of thyrotoxicosis in the postpartum period is postpartum thyroiditis. Graves' disease may also develop after delivery. The management and long term outcomes of these two disorders are quite different. The goal of the current study was to examine the usefulness of other factors in differentiating between the different causes of postpartum thyrotoxicosis

Ide A et al Differentiation of postpartum Graves' thyrotoxicosis from postpartum destructive thyroiditis using antithyrotropin receptor antibodies and thyroid blood flow. *Thyroid* 2014;24:1027-31

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**Subclinical hypothyroidism and thyroid antibodies are risk factors for miscarriage** Thyroid hormone is important for the normal development of a baby during pregnancy. Subclinical hypothyroidism and/or thyroid antibodies during pregnancy can increase the risk of miscarriage at the end of the 1st trimester of pregnancy. This study was done to see if subclinical hypothyroidism and/or autoimmune thyroid disease are associated with miscarriage earlier on in pregnancy.

Liu H et al Maternal subclinical hypothyroidism, thyroid autoimmunity and the risk of miscarriage: a prospective cohort study. *Thyroid.* August 2, 2014 [Epub ahead of print].

**THYROID CANCER .....11**

**Incidentally identified thyroid cancers are not rare and may be advanced at the time of discovery** The frequency of thyroid cancer is rising in the United States, especially among women. One reason this may be the case is the increase in the use of imaging studies (ie CT scans) that include imaging the thyroid (incidental imaging). In this study, the authors determined the method by which thyroid cancers were detected in patients undergoing thyroid surgery for cancer at their institution.

Malone M et al. Thyroid cancers detected by imaging are not necessarily small or early stage. *Thyroid* 2014;24:314-8. Epub September 13, 2013.

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**Exposure to low dose radioactive pre-ablation scanning does not affect long-term outcomes of patients with thyroid cancer** Prior to high dose radioactive iodine therapy for thyroid cancer, a low dose pre-ablation scan can be used to identify if there is any spread of the thyroid cancer outside of the neck. There is some concern that the small dose of radioactive iodine given for these pre-ablation scans will "stun" but not kill thyroid cancer cells, making the high dose of radioactive iodine less effective. This study compared patients who had pre-ablation scans to those who did not to assess whether "stunning" affected long term outcomes in patients with thyroid cancer.

Yap BK, Murby B. No adverse effect in clinical outcome using low pre-ablation diagnostic <sup>131</sup>I activity in differentiated thyroid cancer: refuting thyroid stunning effect. *J Clin Endocrinol Metab* 2014 Apr 24;jc20141405 [Epub ahead of print].

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**Clinical Thyroidology for the Public**

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# CLINICAL THYROIDOLOGY **FOR THE PUBLIC**

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## EDITOR'S COMMENTS

Welcome to *Clinical Thyroidology for the Public*. In this journal, we will bring to you the most up-to-date, cutting edge thyroid research. We will be providing summaries of research studies that were discussed in a recent issue of *Clinical Thyroidology*, a publication of the American Thyroid Association for physicians. These summaries are present in lay language to allow the rapid dissemination of thyroid research to the widest possible audience. This means that you are getting the latest information on thyroid research and treatment almost as soon as your physicians. As always, we are happy to entertain any suggestions to improve *Clinical Thyroidology for the Public* so let us know what you want to see.

We also provide even faster updates of late-breaking thyroid news through **Twitter** at [@thyroidfriends](https://twitter.com/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* and *Thyroid Federation International*.

October is **Thyroid Nodule Awareness month**.

**In this issue, the studies ask the following questions:**

1. How helpful is the Afirma™ gene expression classifier in evaluating indeterminate thyroid nodules?
2. Can ultrasound and more in-depth cytology help in diagnosing cancer in indeterminate thyroid nodules?
3. What are the best approaches for diagnosing the etiology of thyrotoxicosis in the post-partum period?
4. Is autoimmune thyroid disease a risk factor of miscarriage early in pregnancy?
5. Should we care about thyroid nodules found incidentally on imaging studies?
6. Does “stunning” after pre-ablation scanning affect long term outcomes in patients with thyroid cancer?

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



## THYROID NODULES

# Evaluation of the Afirma™ Gene Expression Classifier to determine appropriateness of surgery in patients with indeterminate thyroid nodule biopsy results

### BACKGROUND

Thyroid nodules are very common, occurring in 30-50 % of patients. The absolute risk of thyroid cancer is any one nodule is low (approximately 5%), but the possibility of cancer leads to thorough evaluation and much anxiety in patients and physicians alike. A thyroid biopsy can provide a diagnosis in most cases. The exception is with an indeterminate result, meaning that neither a diagnosis of cancer or benign (noncancerous) is made. Historically, patients with indeterminate biopsy results were sent to thyroid surgery to remove at least half the thyroid for diagnostic reasons. This was done despite a relatively low risk of cancer (15-20%) in these patients.

Recent studies have identified molecular markers in thyroid cells that may be predictive of cancer. These molecular markers are mutations in certain genes that are associated with cancer. While no single molecular marker is that helpful, a group of molecular markers may be useful in predicting cancer. One such panel of molecular markers is the Afirma™ Gene Expression Classifier (GEC) which, when used on thyroid biopsy specimens, has been reported to help make a diagnosis of benign vs cancer in cases of indeterminate cytology. This study was done to evaluate the Afirma™ GEC performance in an academic center (the Mayo clinic).

### THE FULL ARTICLE TITLE

McIver B et al An independent study of a gene expression classifier (Afirma™) in the evaluation of cytologically indeterminate thyroid nodules. *J Clin Endocrinol Metab.* April 29, 2014 [Epub ahead of print]. jc20133584. PMID: 24780044.

### SUMMARY OF THE STUDY

At total of 984 patients with 1207 nodules who underwent FNA at the Mayo Clinic during the study period were evaluated with thyroid biopsy. At the time of the procedure, samples were obtained for the GEC through the same method as the cytology and the samples were reserved. The patients were offered the Afirma™ GEC

test if their cytology results returned in the indeterminate category. If the GEC returned benign, the patients were offered serial ultrasounds and clinical follow-up. If suspicious by GEC, thyroid surgery was recommended.

Of 1207 nodules biopsied, 105 were reported as indeterminate (8.7%). Of these, 18 patients chose surgery, so 72 samples were obtained for analysis by GEC. In 12 samples (17%), there was not enough cellular material to analyze. Of the remainder, 17 (28%) were reported benign on GEC and 43 (72%) were reported as suspicious. A total of 4 patients with a benign GEC result went ahead with surgery anyway, with 1 cancer being found. A total of 32 patients with a suspicious GEC results had surgery with 5 cancers being found.

### WHAT ARE THE IMPLICATIONS OF THIS STUDY?

The use of the Afirma™ GEC at Mayo Clinic showed a lower than expected rate of benign results and a lower than expected rate of cancer at surgery in nodules that were noted to be suspicious on GEC. The authors of the paper suggest that the results of this assay may vary depending upon risk of cancer in the population studied. However, this study also raises questions as to the effectiveness of the GEC in preventing surgery for benign nodules, especially given the high cost of the test.

Cytology alone continues to be the best initial analysis for the evaluation of thyroid nodules. In cases where cytology is unclear (indeterminate cytology), analysis of molecular markers are helpful as another option in the evaluation of thyroid nodules. Further studies of molecular markers are needed to improve the prediction of cancer prior to surgery.

— Julie E. Hallanger Johnson, MD

### ATA THYROID BROCHURE LINKS

Thyroid Nodules: <http://www.thyroid.org/what-are-thyroid-nodules>

Thyroid cancer: <http://www.thyroid.org/cancer-of-the-thyroid-gland>



## THYROID NODULES, continued

### 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 fine needle aspiration biopsy (FNAB):** 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.

**Indeterminate thyroid biopsy:** this happens usually when the diagnosis is a follicular or hurthle cell lesion. Follicular and hurthle cells are normal cells found in the thyroid. Current analysis of thyroid biopsy results cannot differentiate between follicular or hurthle cell cancer from noncancerous adenomas. This occurs in 15-20% of biopsies and often results in the need for surgery to remove the nodule. These cytology results include Atypia of Uncertain Significance, Follicular Lesion of Undetermined Significance, Follicular Neoplasm and Hurthle Cell Neoplasm.

**Cytology:** the results of the review of the cells or tissue removed, often done by Pathologist physicians with special training in this area

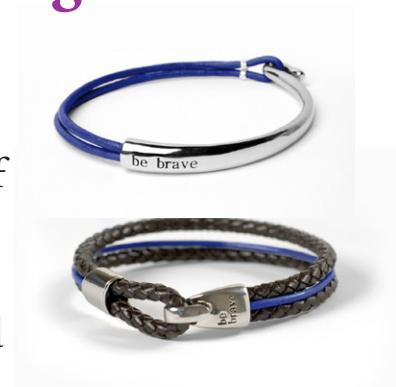
**Genes:** a molecular unit of heredity of a living organism. Living beings depend on genes, as they code for all proteins and RNA chains that have functions in a cell. Genes hold the information to build and maintain an organism's cells and pass genetic traits to offspring.

**Molecular markers:** genes and microRNAs that are expressed in benign or cancerous cells. Molecular markers can be used in thyroid biopsy specimens to either to diagnose cancer or to determine that the nodule is benign.

**Afirma™ Gene Expression Classifier:** a test for a group of molecular markers in thyroid biopsy specimens in order to determine the likelihood that a thyroid nodule is benign or cancerous. This test is performed by the company Veracyte Inc.

## 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 October is **Thyroid Nodule Awareness Month** and a bracelet is available through the [ATA Marketplace](#) to support thyroid cancer awareness and education related to thyroid disease.





## THYROID NODULES

# Adding ultrasound features and more in-depth cytology can improve our ability to diagnose cancer in patients with indeterminate thyroid nodules

### BACKGROUND

Thyroid nodules are very common, affecting up to 50% of the population. The concern about any thyroid nodule is whether the nodule is cancerous or not. Fine needle aspiration biopsy is an important part of the workup of thyroid nodules and the only way outside of surgery to determine if a nodule is cancerous. The problem is that a significant number of patients are found to have an “indeterminate” result, meaning that neither a diagnosis of cancer or benign (noncancerous) is made. Specifically the diagnosis of atypia of uncertain significance/follicular lesion of undetermined significance (AUS/FLUS) fits into the indeterminate category. Many of these patients undergo surgical removal of their thyroid gland in order to make the definitive diagnosis of whether they have thyroid cancer or not. This study was performed in order to determine if one of three additional approaches could help predict whether the nodule was benign or cancerous without the need for surgery. These three additional approaches were 1) testing for the cancer molecular marker BRAF V600E on the cells removed during a biopsy, 2) characterizing the ultrasound features of the nodule and 3) reporting the biopsy specimen using one of the 9 subcategories of AUS/FLUS.

### THE FULL ARTICLE TITLE

Jeong SH et al. Outcome of thyroid nodules characterized as atypia of undetermined significance or follicular lesion of undetermined significance and correlation with ultrasound features and BRAF(V600E) mutation analysis. *AJR Am J Roentgenol* 2013;201:W854-60.

### SUMMARY OF THE STUDY

A total of 6118 biopsy specimens from patients with thyroid nodules were evaluated for inclusion in this study. A total of 411 of these biopsy specimens were

diagnosed as AUS/FLUS and 165 of these ultimately were included in this study. Thyroid cancer was found in 91 of these 165 (55.2%) either based on the patient undergoing surgery or repeat thyroid biopsy. The rate of cancer was highest if there were abnormal follicular cells (76.5%) or with focal papillary cancer cells in the midst of otherwise benign cells. Importantly, biopsies reported as belonging to 6/9 subcategories were 100% benign. The cancer rate of nodules with suspicious ultrasound features was higher (79.3%) than nodules with indeterminate features (24.7%). Nodules that had a mutation in the BRAF V600E gene had a higher rate of cancer (97.5%) compared to those that were BRAF V600E gene mutation negative (39.7%).

### WHAT ARE THE IMPLICATIONS OF THIS STUDY?

The authors concluded that the cancer rate in patients with AUS/FLUS was higher than previously reported (55.2%, 91/165). Nodules that have suspicious features on ultrasound, have an atypical category of cytology or express the BRAF gene mutation are significantly more likely to have a thyroid cancer than those whose nodules and biopsies do not follow into these categories. Using these criteria may spare some patients from undergoing surgery for the purpose of diagnosis alone and allow for a better more comprehensive operation for patients who do have thyroid cancer.

— Jennifer E. Rosen MD FACS

### ATA THYROID BROCHURE LINKS

Thyroid Nodules: <http://www.thyroid.org/what-are-thyroid-nodules>

Thyroid cancer: <http://www.thyroid.org/cancer-of-the-thyroid-gland>





## THYROID NODULES, continued

### 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 fine needle aspiration biopsy (FNAB):** 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.

**Molecular markers:** genes and microRNAs that are expressed in benign or cancerous cells. Molecular markers can be used in thyroid biopsy specimens to

either to diagnose cancer or to determine that the nodule is benign.

**Cancer-associated genes:** these are genes that are normally expressed in cells. Cancer cells frequently have mutations in these genes. It is unclear whether mutations in these genes cause the cancer or are just associated with the cancer cells. The cancer-associated genes important in thyroid cancer are BRAF, RET/PTC and RAS.

**BRAF gene:** this is gene that codes for a protein that is involved in a signaling pathway and is important for cell growth. Mutations in the BRAF gene in adults appear to cause cancer.



## PREGNANCY AND THYROID DISEASE

# What are the best approaches for diagnosing the etiology of thyrotoxicosis following delivery?

### BACKGROUND

Approximately 5-10% of women will develop thyroid dysfunction during the first year after delivery of a baby. This includes both an increase in thyroid hormone levels (thyrotoxicosis) as well as hypothyroidism. The most common cause of thyrotoxicosis in the postpartum period is postpartum thyroiditis, which is an autoimmune process characterized by inflammation of the thyroid gland by antibodies that attach and try to destroy the thyroid gland. This can lead to “leaking” of thyroid hormone from the damaged thyroid gland, causing transient thyrotoxicosis which resolves on its’ own in a few months without specific thyroid therapy. Indeed, as the gland is depleted of thyroid hormone, many women with postpartum thyroiditis develop hypothyroidism. While the majority of cases of postpartum thyrotoxicosis are from thyroiditis, Graves’ disease may also develop after delivery. In Graves’ disease, also an autoimmune disease, antibodies attack and stimulate the thyroid gland. Graves’ disease does require specific thyroid therapy.

While both Graves’ disease and postpartum thyroiditis lead to thyrotoxicosis, their management and long term outcomes are quite different. Consequently, differentiating the etiologies of postpartum thyroid dysfunction is a priority. Unfortunately, this is not an easy task as a radioactive iodine uptake, a key test used to differentiate between thyroiditis and Graves’ disease, cannot be performed while patients are breastfeeding. The goal of the current study was to examine the usefulness of other factors in differentiating between the different causes of postpartum thyrotoxicosis such as: 1) levels of thyroid stimulating antibodies, 2) thyroid blood flow on neck ultrasound and 3) the time of onset of hyperthyroidism after delivery.

### THE FULL ARTICLE TITLE

Ide A et al Differentiation of postpartum Graves’ thyrotoxicosis from postpartum destructive thyroiditis using

antithyrotropin receptor antibodies and thyroid blood flow. *Thyroid* 2014;24:1027-31.

### SUMMARY OF THE STUDY

The authors reviewed the charts of 42 patients who developed thyrotoxicosis within 1 year of delivery from January 2010 to July 2012. They found that all of the patients with postpartum Graves but none of the patients with postpartum thyroiditis tested positive for thyroid stimulating antibodies. Similarly, most patients with Graves (83.3%) had high thyroid blood flow on neck ultrasound, whereas all of the patients with postpartum thyroiditis had low thyroid blood flow. Finally, 12 of 14 patients (85.7%) in whom thyrotoxicosis developed at 3 months postpartum or earlier had thyroiditis and all 11 patients (100%) in whom thyrotoxicosis developed at 6.5 months or later had Graves’ disease.

### WHAT ARE THE IMPLICATIONS OF THIS STUDY?

These results demonstrate that early onset of thyrotoxicosis within 3 months after delivery of a baby is usually the result of thyroiditis, whereas later onset after 6.5 months is almost certainly from Graves’ disease. Between 3 and 6.5 months the etiology of postpartum thyrotoxicosis could be either Graves’ or thyroiditis. In this situation measuring thyroid stimulating antibody levels and thyroid blood flow on neck ultrasound can help differentiate the two.

— Phillip Segal, MD

### ATA THYROID BROCHURE LINKS

Thyroid and Pregnancy: <http://www.thyroid.org/thyroid-disease-and-pregnancy>

Postpartum Thyroiditis: <http://www.thyroid.org/postpartum-thyroiditis>



## PREGNANCY AND THYROID DISEASE, continued

### ABBREVIATIONS & DEFINITIONS

**Thyrotoxicosis:** the clinic syndrome resulting from elevated levels of circulating  $T_3$  and/or  $T_4$ . Hyperthyroidism is the cause of most cases of thyrotoxicosis, with the remainder caused by thyroiditis or overdosing on thyroid medication.

**Hyperthyroidism:** a condition where the thyroid gland is overactive and produces too much thyroid hormone. Hyperthyroidism may be treated with antithyroid meds (Methimazole, Propylthiouracil), radioactive iodine or surgery.

**Postpartum thyroiditis:** an inflammation of the thyroid in women who have just delivered a baby. The inflammation first causes mild hyperthyroidism for 1-3 months after delivery. This is followed by hypothyroidism starting 4-6 months after delivery. The hypothyroidism resolves and normal thyroid function returns 12–18 months after delivery in most women. While many women have both the hyperthyroid and the hypothyroid phase, some women may only have one or the other.

**Graves' disease:** the most common cause of hyperthyroidism in the United States. It is caused by antibodies (thyroid stimulating antibodies) that attack the thyroid and turn it on.

**Thyroid stimulating antibodies:** antibodies present in the blood of patients with Graves' disease that are directed against the TSH receptor, often causing stimulation of this receptor with resulting hyperthyroidism.

**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.





## THYROID AND PREGNANCY

### Subclinical hypothyroidism and thyroid antibodies are risk factors for miscarriage

#### BACKGROUND

Thyroid hormone is important for the normal development of a baby during pregnancy. Some studies have shown that even a mildly underactive thyroid (subclinical hypothyroidism) in pregnant women between 11-13 weeks of pregnancy is a risk factor for miscarriage. Other studies have shown that having high levels of thyroid antibodies in the blood, which are associated with one form of hypothyroidism, during pregnancy can also increase the risk of miscarriage. This study was done to see if subclinical hypothyroidism and/or autoimmune thyroid disease in pregnant women during an earlier period of pregnancy, from 4-8 weeks of pregnancy, are similarly associated with higher rates of miscarriage.

#### THE FULL ARTICLE TITLE

Liu H et al Maternal subclinical hypothyroidism, thyroid autoimmunity and the risk of miscarriage: a prospective cohort study. *Thyroid*. August 2, 2014 [Epub ahead of print].

#### SUMMARY OF THE STUDY

The authors studied over 3300 pregnant women beginning in early pregnancy (4-8 weeks of pregnancy) from multiple hospitals and clinics in China starting in 2012. The women were grouped according to the severity of subclinical hypothyroidism and/or whether autoimmune thyroid disease was present and followed to see if there was a difference in the rates of miscarriage (defined by loss of the fetus before 20 weeks gestation). From blood tests, women were considered as having normal thyroid function, subclinical hypothyroidism, autoimmune thyroid disease, or both subclinical hypothyroidism and autoimmune thyroid disease.

A total of 110 (3.5%) of the women had a miscarriage, with the women who had subclinical hypothyroidism,

autoimmune thyroid disease, or both subclinical hypothyroidism and autoimmune thyroid disease having the highest risks, compared to women with normal thyroid function. In addition, women with subclinical hypothyroidism and autoimmune thyroid disease tended to have miscarriages earlier during their pregnancies, compared to women with normal thyroid function.

#### WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study shows that subclinical hypothyroidism and autoimmune thyroid disease during early pregnancy are both risk factors for having a miscarriage. It confirms several previous studies in which these are also important risk factors for pregnant women during later pregnancy. The findings suggest that trying to achieve and maintain normal thyroid hormone levels as early on in pregnancy may lessen the risk of miscarriage. Guidelines by several medical societies recommend prescribing thyroid hormone in pregnant women with hypothyroidism in order to target normal thyroid function blood tests.

Although one study has shown that thyroid hormone given to pregnant women with normal thyroid function but with autoimmune thyroid disease may decrease the odds of having a miscarriage, additional studies (one of which is underway in the United Kingdom) are needed to confirm this. Thus, at present, thyroid hormone is not routinely prescribed in pregnant women with normal thyroid function who have autoimmune thyroid disease.

— Angela Leung, MD

#### ATA THYROID BROCHURE LINKS

Thyroid and Pregnancy: <http://www.thyroid.org/thyroid-disease-and-pregnancy>

Thyroid Function Tests: <http://www.thyroid.org/blood-test-for-thyroid>

#### ABBREVIATIONS & DEFINITIONS

**Subclinical Hypothyroidism:** a mild form of hypothyroidism where the only abnormal hormone

level is an increased TSH. There is controversy as to whether this should be treated or not.



## **THYROID AND PREGNANCY, continued**

**Autoimmune thyroid disease:** a group of disorders that are caused by antibodies that get confused and attack the thyroid. These antibodies can either turn on the thyroid (Graves' disease, hyperthyroidism) or turn it off (Hashimoto's thyroiditis, hypothyroidism).

**Miscarriage:** this occurs when a baby dies in the first few months of a pregnancy, usually before 22 weeks of pregnancy.



## THYROID CANCER

### Incidentally identified thyroid cancers are not rare and may be advanced at the time of discovery

#### BACKGROUND

The frequency of thyroid cancer is rising in the United States, especially among women. One reason this may be the case is the increase in the use of imaging studies (ie CT scans) that include imaging the thyroid (incidental imaging). Consistent with this idea is that small papillary thyroid cancers make up a large percentage of newly diagnosed thyroid cancers and are the fastest growing type of thyroid cancer. However, studies have also demonstrated an increase in larger or more advanced thyroid cancers. Screening and incidental imaging are now thought to be responsible for finding approximately half of all thyroid cancers. In this study, the authors determined the method by which thyroid cancers were detected in patients undergoing thyroid surgery for cancer at their institution.

#### THE FULL ARTICLE TITLE

Malone M et al. Thyroid cancers detected by imaging are not necessarily small or early stage. *Thyroid* 2014;24:314-8. Epub September 13, 2013.

#### SUMMARY OF THE STUDY

The authors reviewed the charts of the 473 patients who underwent thyroidectomy at a single center between January 2007 and August 2010 and were found to have cancer on the final pathology review. Patients were separated into three groups based on how the cancer was found. Imaging detected 184 cancers (39%), physical exam detected 218 cancers (46%) and final pathology after the thyroid was removed for a benign process found cancer in 71 patients (15%).

Only 77% of patients in the physical exam group had the mass first felt by their health-care provider. Early-

stage, smaller cancers without lymph node involvement were more likely to be found in the specimen only or by imaging. A total of 38% of cancers larger than 4 cm were found on imaging. Nearly half (47%) of advanced cancers were found in the imaging group; 39% of cancers with lymph node involvement were also found in this group.

#### WHAT ARE THE IMPLICATIONS OF THIS STUDY?

Over one third of the thyroid cancers in this study were initially found through an imaging study and not through examination. Interestingly, nearly half of those cancers could be felt on examination at the time of surgery, even though they were not originally detected on physical exam. This is a worrisome finding that calls into question the effectiveness of physical exam in screening for thyroid malignancy. The fact that many (46%) of these “occult” cancers were actually palpable at the time of surgery underscores the fact that clinicians often have difficulty detecting thyroid disease and lymph node enlargement on physical exam. Inability to detect thyroid cancer by palpation offers a possible explanation for why the increasing frequency of thyroid cancer is not limited to small early-stage cancers.

— Ronald B. Kuppersmith, MD, FACS

#### ATA THYROID BROCHURE LINKS

Thyroid cancer: <http://www.thyroid.org/cancer-of-the-thyroid-gland>

Thyroid Surgery: <http://thyroid.org/patients/patient-brochures/surgery.html>

#### DEFINITIONS

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

**Papillary thyroid cancer:** the most common type of thyroid cancer.



## THYROID CANCER

### Exposure to low dose radioactive pre-ablation scanning does not affect long-term outcomes of patients with thyroid cancer

#### BACKGROUND

Radioactive iodine (I-131) is a very effective adjunctive treatment for thyroid cancer after a patient undergoes thyroid surgery. Since only thyroid cells take up and concentrate iodine, radioactive iodine serves as a “magic bullet” to destroy thyroid cancer cells as well as normal thyroid cells. Prior to the high dose radioactive iodine therapy, a low dose of radioactive iodine is often used to identify if there is any spread of the thyroid cancer outside of the neck (pre-ablation scans). Some physicians believe that the small dose of radioactive iodine given for these pre-ablation scans will “stun” but not kill thyroid cancer cells, making the high dose of radioactive iodine less effective. An alternative to the I-131 pre-ablation scans is the use of a different isotope of radioactive iodine (I-123) which does not cause thyroid cell damage and will not result in stunning. However, I-123 scans are much more expensive. This study compared patients who had pre-ablation scans to those who did not to assess whether the “stunning” after I-131 radioactive iodine pre-ablation scans affected long-term outcomes in patients with thyroid cancer.

#### THE FULL ARTICLE TITLE

Yap BK, Murby B. No adverse affect in clinical outcome using low pre-ablation diagnostic <sup>131</sup>I activity in differentiated thyroid cancer: refuting thyroid stunning effect. *J Clin Endocrinol Metab* 2014 Apr 24;jc20141405 [Epub ahead of print].

#### SUMMARY OF THE STUDY

In Manchester, England, between 2004 to 2008, patients routinely got a low dose (1.1 mCi) pre-ablation radioactive iodine scan 24 hours before being treated

with high dose (95mCi) radioactive iodine therapy 6 days later. Between 2009 to 2011, most patients did not get the pre-ablation scan prior to receiving the high dose radioactive iodine therapy. A total of 305 patients that received the pre-ablation scan were compared with 237 patients that did not receive the pre-ablation scan. The patients were tested at various times to look for recurrence of their thyroid cancer by blood tests for the thyroid cell marker thyroglobulin as well as stimulation testing with recombinant human TSH (Thyrogen™). There was no difference between the groups in either thyroglobulin levels or stimulation testing. Recurrence of thyroid cancer was found in 4.3% of the patients that received the pre-ablation scans and 3.4% in patients that did not receive the scans.

#### WHAT ARE THE IMPLICATIONS OF THIS STUDY?

The findings of this study suggest that doing a diagnostic pre-ablation scan 6 days prior to high dose radioactive iodine does not result in “stunning” or decrease the effectiveness of the radioactive iodine treatment. While the practice of performing pre-ablation scans is less common recently in many institutions, it is reassuring that this study has shown that such scanning does not affect the thyroid cancer recurrence rates at 3 years of follow up.

— Wendy Sacks, MD

#### ATA THYROID BROCHURE LINKS

Thyroid cancer: <http://www.thyroid.org/cancer-of-the-thyroid-gland>

Radioactive Iodine Therapy: <http://www.thyroid.org/radioactive-iodine>

#### 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



## **THYROID CANCER**, continued

whole body to look for thyroid cancer (Whole Body Scan).

**Pre-ablation scans:** a low dose of radioactive iodine used to identify if there is any spread of the thyroid cancer outside of the neck prior to high dose radioactive iodine therapy.

**Thyroglobulin:** a protein made only by thyroid cells, both normal and cancerous. When all normal thyroid tissue is destroyed after radioactive iodine therapy in patients with thyroid cancer, thyroglobulin can be used as a thyroid cancer marker in patients that do not have thyroglobulin antibodies.

**Stimulation testing:** measuring thyroglobulin levels and/or performing radioactive iodine scans under TSH stimulation, either after thyroid hormone withdrawal or after injections of recombinant human TSH (Thyrogen™).

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

**“Stunning” effect of I-131:** the idea that a small dose of I-131 radioactive iodine given prior to a large dose of I-131, will result in “stunning” but not killing of thyroid cancer cells, making the high dose of radioactive iodine less effective.





## 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 towards the improvement of thyroid education and resources for patients.

### WHO WE ARE (in alphabetical order)

- **American Thyroid Association**
- **Bite Me Cancer**
- **Graves' Disease and Thyroid Foundation**
- **Light of Life Foundation**
- **ThyCa: Thyroid Cancer Survivors' Association, Inc.**
- **Thyroid Cancer Canada**
- **Thyroid Federation International**

### AMERICAN THYROID ASSOCIATION

[www.thyroid.org](http://www.thyroid.org)

ATA Patient Resources: <http://www.thyroid.org/patients/>

Find a Thyroid Specialist: [www.thyroid.org](http://www.thyroid.org)

Phone (toll-free): 1-800-THYROID

e-mail: [thyroid@thyroid.org](mailto:thyroid@thyroid.org)

**ATA Mission:** The ATA leads in promoting thyroid health and understanding thyroid biology.

**ATA Vision:** The ATA is the leading organization focused on thyroid biology and the prevention and treatment of thyroid disorders through excellence and innovation in research, clinical care, education, and public health.

**ATA Values:** The ATA values scientific inquiry, clinical excellence, public service, education, collaboration, and collegiality.

To further our mission, vision and values the ATA sponsors "Friends of the ATA" online to advance the information provided to patients and the public such as this publication, *Clinical Thyroidology for the Public*. We welcome your support.

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ASSOCIATION  
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ThyCa: Thyroid Cancer  
Survivors' Association, Inc.<sup>SM</sup>  
[www.thyca.org](http://www.thyca.org)





## ATA Alliance for Thyroid Patient Education

Continued...

### BITE ME CANCER

<http://www.bitemecancer.org>

Bite Me Cancer was formed as a nonprofit foundation in September, 2010, by Nikki Ferraro, who was 17-years old at the time. Nikki was diagnosed with a rare form of thyroid cancer in April 2010 when she was a junior at Chantilly HS in Virginia. Nikki was determined to lead a Relay for Life team just two weeks after her diagnosis. She named the team Bite Me Cancer and experienced immediate success. When Nikki decided to create a foundation a few months later, she wanted to continue the legacy of her team name and thus her foundation became the Bite Me Cancer Foundation.

e-mail: [info@bitemecancer.org](mailto:info@bitemecancer.org)

### GRAVES' DISEASE AND THYROID FOUNDATION

[www.gdatf.org](http://www.gdatf.org)

Phone (toll-free): 1-877-NGDF-123 or 643-3123

e-mail: [Gravesdiseasefd@gmail.com](mailto:Gravesdiseasefd@gmail.com)

Founded in 1990, the Graves' Disease Foundation offers support and resources to Graves' disease patients, their families, and health care professionals. Their mission is to find the cause of and the cure for Graves' thyroid disease through research, to improve the quality of life for persons with Graves' disease and their caregivers and to educate persons with Graves' disease, their caregivers, healthcare professionals, and the general public about Graves' disease and its treatment. The web site features a monitored bulletin board.

### LIGHT OF LIFE FOUNDATION

[www.checkyourneck.com](http://www.checkyourneck.com)

email: [info@checkyourneck.com](mailto:info@checkyourneck.com)

The Light of Life Foundation, founded in 1997, is a nonprofit organization that strives to improve the quality of life for thyroid cancer patients, educate the public and professionals about thyroid cancer, and promote research and development to improve thyroid cancer care.

### THYCA: THYROID CANCER SURVIVORS' ASSOCIATION, INC.

*continued on next page*



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ThyCa: Thyroid Cancer  
Survivors' Association, Inc.<sup>SM</sup>  
[www.thyca.org](http://www.thyca.org)





## ATA Alliance for Thyroid Patient Education

Continued...

### [www.thyca.org](http://www.thyca.org)

Phone (toll-free): 877 588-7904

e-mail: [thyca@thyca.org](mailto:thyca@thyca.org)

ThyCa: Thyroid Cancer Survivors' Association, Inc., founded in 1995, is an international nonprofit organization, guided by a medical advisory council of renowned thyroid cancer specialists, offering support and information to thyroid cancer survivors, families, and health care professionals worldwide.

### THYROID CANCER CANADA

[www.thyroidcancercanada.org](http://www.thyroidcancercanada.org)

Phone: 416-487-8267

Fax: 416-487-0601

e-mail: [info@thyroidcancercanada.org](mailto:info@thyroidcancercanada.org)

Thyroid Cancer Canada is a non-profit organization founded in 2000. The organization works towards creating an environment in which people who are dealing with thyroid cancer, especially the newly diagnosed, are met with support and information. Their goals & objectives include facilitating communication among thyroid cancer patients, providing credible information about the disease, providing emotional support, and assisting thyroid cancer patients with voicing their needs to health care professionals and those who are responsible for health care policy.

### THYROID FEDERATION INTERNATIONAL

<http://www.thyroid-fed.org/>

e-mail: [tfi@thyroid-fed.org](mailto:tfi@thyroid-fed.org)

Thyroid Federation International (TFI) was established in Toronto in 1995. Thyroid Federation International aims to work for the benefit of those affected by thyroid disorders throughout the world by providing a network of patient support organizations.

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[www.thyca.org](http://www.thyca.org)





## ATA Alliance for Thyroid Patient Education

### CALENDAR

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#### **FREE PUBLIC HEALTH FORUM** **Thyroid Disease and You**

**Saturday, November 1, 2014, 1:00 pm – 3:00 pm**  
**Coronado/San Diego, California**

Thyroid Experts from the American Thyroid Association and thyroid patients join together to inform the general public, other thyroid patients, and their friends and families about: **Thyroid Disease and You**

Concerned about low energy?...Memory loss?...Fatigue?...Depression? ...Rapid heartbeat?...Restlessness?... Infertility?...Weight or hair changes?... A lump on your neck?... Could it be your thyroid?

Physician experts will discuss thyroid disorders. This program is free and all are welcome, including walk-in-attendees. Reservations are encouraged to ensure we have enough seating.

For more information and to register, please e-mail ThyCa at [thyca@thyca.org](mailto:thyca@thyca.org)

Phone: 1-619-435-6611

[See flier on page 18.](#)

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#### **THYCA ANNUAL MEETING** **17th International Thyroid Cancer Survivors' Conference**

**October 17-19, 2014, Denver, Colorado**

- The latest research, advances in treatment and follow-up, plus issues for survivors and caregivers, and coping skills for well-being
- More than 100 sessions. For everyone whose life has been touched by thyroid cancer—people being tested, those newly diagnosed, long-term survivors, people with advanced disease, caregivers, and friends
- Featuring leading physicians plus other specialists—more than 50 speakers
- Meet and learn from experts. Share experiences with others with thyroid cancer.

<http://www.thyca.org/support/conferences>

[See flier on page 19.](#)

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#### **GRAVES' DISEASE AND THYROID FOUNDATION** **Kids and Graves' Disease — Special Seminar for Parents**

**November 22, 2014, Childrens Hospital of Philadelphia**

The Foundation's patient & family conferences are designed to help attendees learn more about Graves' Disease, thyroid eye disease, and related disorders. Guest speakers include physicians, researchers, and allied health professionals. Attendees will also be able to share their own experiences and connect with fellow patients and family members.

<http://gdatf.org/conference>

# FREE Public Health Forum

Thyroid Experts from the American Thyroid Association and thyroid patients join together to inform the general public, other thyroid patients, and their friends and families about:

## Thyroid Disease and You



®

AMERICAN  
THYROID  
ASSOCIATION

FOUNDED 1923

Concerned about low energy?...Memory loss?...Fatigue?...  
Depression? ...Rapid heartbeat?...Restlessness?...Infertility?...  
Weight or hair changes?... A lump on your neck?... Could it be your thyroid?

**Saturday, November 1, 2014**

1:00 pm – 3:00 pm

Coronado/San Diego, California

Hotel Del Coronado

1500 Orange Avenue, Coronado, California 92118

Phone: 1-619-435-6611

### **Physician experts will discuss thyroid disorders.**

This program is free and all are welcome, including walk-in-attendees. Reservations are encouraged to ensure we have enough seating. For more information and to register, please e-mail ThyCa at [thyca@thyca.org](mailto:thyca@thyca.org).

### **Who should attend?**

Anyone who has had an overactive or underactive thyroid, thyroiditis, a thyroid nodule, thyroid cancer, or a family history of thyroid problems or related disorders, including rheumatoid arthritis, juvenile diabetes, pernicious anemia, or prematurely gray hair (starting before age 30) Please come if you have questions, symptoms, or concerns about a thyroid problem. Receive free educational materials.

### **Reservations requested. Walk-ins welcome.**

*\$15 one-day, self-parking; \$20 valet parking. Nearby street parking available as well.*

E-mail [thyca@thyca.org](mailto:thyca@thyca.org) to RSVP

(Please indicate in your message the thyroid condition you are most concerned about.)

*Online educational information for patients is provided by all members of the ATA Alliance for Patient Education co-sponsoring this forum: ThyCa: Thyroid Cancer Survivors' Association, Graves' Disease and Thyroid Foundation, Light of Life Foundation, Bite Me Cancer, Thyroid Cancer Canada and Thyroid Federation International. Go online to [www.thyroid.org](http://www.thyroid.org) and click on "Public and Patients" to access the resources you need.*



*You're invited to the  
17th International*

# Thyroid Cancer Survivors' Conference

Sponsored by ThyCa: Thyroid Cancer Survivors' Association, Inc.<sup>SM</sup>

**October 17 - 19, 2014**

**Denver, Colorado**

Doubletree by Hilton Denver Hotel  
3203 Quebec Street  
Denver, CO 80207



- The latest research, advances in treatment and follow-up, plus issues for survivors and caregivers, and coping skills for well-being
- More than 100 sessions. For everyone whose life has been touched by thyroid cancer—people being tested, those newly diagnosed, long-term survivors, people with advanced disease, caregivers, and friends
- Featuring leading physicians plus other specialists—more than 50 speakers
- Meet and learn from experts. Share experiences with others with thyroid cancer.
- Registration information and more details:
  - Individual: •Regular \$50 •Annual members \$40 •Lifetime members \$35 •Added family members/guests \$30
  - Early-bird discount: \$5 off if postmarked or sent online by September 17, 2014.
  - Scholarships are available to cover the registration fee. Use the scholarship line on the registration form.
  - Walk-in attendees are welcome. The conference opens at 8 a.m. Friday. Sessions go from 9:30 a.m. to 5:15 p.m. on Friday; from 8 a.m. to 5:15 p.m. on Saturday; and from 8 a.m. to 3:30 p.m. on Sunday. Each day, there are 5-7 choices of topics and speakers in different rooms at every time period throughout the day.
  - Hotel's Special Room Rate for conference attendees is \$89 for a single or double, plus tax; triple \$99; quad \$109. The hotel is convenient to area attractions. Free parking, plus free shuttle to and from Denver International Airport.

***Save the dates! Please share this flyer with others. For details & registration form:***

Visit .....**www.thyca.org**

E-mail .....conference@thyca.org or thyca@thyca.org

Write.....ThyCa: Thyroid Cancer Survivors' Association, Inc.

P.O. Box 1545, New York, NY 10159-1545

Call toll-free .....1-877-588-7904



ThyCa: Thyroid Cancer Survivors' Association, Inc. is an international non-profit 501(c)(3) organization of thyroid cancer survivors, family members, and health care professionals, dedicated to education, communication, support, awareness for early detection, and thyroid cancer research fundraising and research grants.