



## THYROID NODULES

### The ThyroSeq V2.1 multi-gene next-generation sequencing panel is effective at predicting a diagnosis of thyroid cancer in nodules with indeterminate cytology.

#### BACKGROUND

Thyroid nodules are very common and raise the possibility of thyroid cancer. The general recommendation is that nodules larger than 1 cm should be evaluated with a thyroid biopsy. While a thyroid biopsy gives a diagnosis in most cases, up to 10-20% of biopsies are indeterminate, meaning that a diagnosis of cancer vs benign cannot be made on the basis of examining the cells alone. This usually leads to surgery despite the fact that most indeterminate nodules are benign. In recent years, the use of molecular marker testing on thyroid biopsy specimens has helped identify benign indeterminate nodules and avoid surgery. The molecular marker test discussed in this study called ThyroSeqV2.1 detects gene mutations in the DNA and RNA of the nodule that might increase the risk for cancer in the nodule. If certain cancer-associated gene mutations such as BRAF, RAS, RET/PTC, p53, etc. are found to be present in the thyroid nodule, there is a high risk that the nodule is cancerous. Conversely, if these gene mutations are absent, the nodule is most likely benign. The goal of this study was to determine how good the ThyroSeqV2.1 test is at predicting whether a nodule with indeterminate cytology is benign or cancerous.

#### THE FULL ARTICLE TITLE

Nikiforov YE et al. Impact of the multi-gene ThyroSeq next-generation sequencing assay on cancer diagnosis in thyroid nodules with atypia of undetermined significance/follicular lesion of undetermined significance cytology. *Thyroid*. Nov;25(11):1217-23.

#### SUMMARY OF THE STUDY

From March 2014 to March 2015, 465 thyroid biopsy samples in 441 patients were diagnosed as indeterminate (AUS/FLUS) at the University of Pittsburgh Medical

Center and all had the ThyroSeqV2.1 test performed on biopsy specimen. The test found 3 parathyroid nodules and 462 thyroid lesions. ThyroSeqV2.1 did not show a gene mutation in 431 (93%) of AUS/FLUS nodules. ThyroSeqV2.1 did detect a gene mutation in 31 (7%) nodules and 26 patients had thyroidectomy revealing 20 (77%) thyroid cancers. The majority (18) of these cancers were follicular variant of papillary thyroid cancer. Of the 431 patients with a negative ThyroSeqV2.1, 69 patients still had surgery and 2 nodules (3%) were cancer. The most common gene mutations were NRAS and HRAS.

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

The important finding of this study is that the ThyroSeq2.1 molecular test can be valuable in the evaluation of indeterminate nodules with AUS/FLUS cytology. The data suggest that if the ThyroSeq2.1 molecular test is negative (no gene mutations), there is 97% likelihood that the nodule is benign and surgery can be avoided. If the ThyroSeq2.1 molecular test is positive for a gene mutation, there is a 77% change that the nodule is cancerous, so surgery is indicated. The results of this study are important to patients with indeterminate thyroid nodules to help determine which patients have a high or low risk for cancer, and thereby tailor management of either surgery or continued monitoring accordingly.

— Wendy Sacks, MD

#### ATA THYROID BROCHURE LINKS

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

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

#### ABBREVIATIONS & DEFINITIONS

**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.

**THYROID NODULES**, continued

**Indeterminate Thyroid Biopsy:** this happens when a diagnosis of benign or cancerous cannot be made with certainty by looking at the cells. This results in cytology readings of atypia of unknown significance (AUS), follicular lesion of unknown significance (FLUS) and follicular or hurthle cell lesions. 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.

**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.

**Mutation:** A permanent change in one of the genes that can lead to cancer.

**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.

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

