



## THYROID NODULES

# How accurate is an updated molecular test in diagnosing cancer in indeterminate thyroid biopsies?

### BACKGROUND

Thyroid nodules are very common, occurring in up to 50% of patients. The concern about a thyroid nodule is whether this represents a thyroid cancer, which occurs in 5–6% of thyroid nodules. Depending upon the size and appearance of the nodule on ultrasound, the next step to evaluate a nodule is a thyroid biopsy. Indeterminate biopsy results can occur in 15–20% of biopsies. This happens when a few atypical cells are seen but not enough to be called cancer (atypia of unknown significance (AUS) or follicular lesion of unknown significance (FLUS)) or when the diagnosis is a follicular or hurthle cell lesion. The majority of indeterminate nodules are not cancerous (although cancer rates may vary among institutions). Yet more than 1/3rd of patients with indeterminate thyroid nodule biopsies undergo thyroid surgery to establish a definitive diagnosis and in about half of these cases, thyroid cancer is diagnosed.

There has been great interest in developing molecular tests to determine, without surgery, whether nodules with indeterminate biopsy are cancerous or not. Molecular markers are genes that are expressed in benign or cancerous cells and the presence or absence of these markers in thyroid biopsy specimens can be used to diagnose cancer or to determine that the nodule is benign. The two most common molecular marker tests are the Afirma™ Genomic Sequence Classifier (GSC) and Thyroseq™. Recently, the GSC has been updated.

In this study, the authors report on the diagnostic accuracy of the GSC in diagnosing cancer in indeterminate thyroid biopsies.

### THE FULL ARTICLE TITLE

Patel KN et al 2018 Performance of a genomic sequencing classifier for the preoperative diagnosis of cytologically indeterminate thyroid nodules. *JAMA Surg*. Epub 2018 May 23.

### SUMMARY OF THE STUDY

In this study, stored thyroid tissue from thyroid biopsies was subject to the GSC test. Tissue was obtained from 210 thyroid nodules from 199 patients in 49 institutions in the United States. All of the patients underwent thyroid surgery, without knowledge of the GSC test prior to surgery. The individuals performing the GSC test had no knowledge of the results of the final pathologic diagnosis and the pathologists examining the surgical thyroid tissue did not know the GSC result.

Of the 210 thyroid nodule specimens included in the study, there was too little molecular material available to perform the GSC test in 19 cases (9%). Thus, the final analysis was planned on the GSC test results in 191 indeterminate cytology thyroid nodules from 183 patients. Approximately one in four nodules in the study was ultimately found to be cancerous at surgery (46/191, 24%), however one of these was excluded from the final analysis. Overall, 41/45 (91%) cancers were correctly detected by the GSC test and 99/145 (68%) of benign nodules that were correctly identified by the GSC test.

### WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study shows that the GSC is very good at identifying cancer in indeterminate thyroid biopsies. Further, the current GSC was found to be more specific and results in fewer false positive results as compared to an earlier version of the test. Thus, based on the assumptions that a positive molecular test is an indication for thyroid surgery and a negative test is an indication not to do surgery, the authors concluded that the updated molecular test would be associated with a reduced rate of thyroidectomies for patients with indeterminate cytology thyroid nodules. More research is needed to determine the impact of GSC test utilization on surgical decision-making and long-term health outcomes of patients.

— Anna M. Sawka, MD, PhD





## THYROID NODULES, continued

### ATA THYROID BROCHURE LINKS

Fine Needle Aspiration Biopsy of Thyroid Nodules: <https://www.thyroid.org/fna-thyroid-nodules/>

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

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

### 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 a few atypical cells are seen but not enough to be abnormal (atypia of unknown significance (AUS) or follicular lesion of unknown significance (FLUS)) or 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.

**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. The two most common molecular marker tests are the Afirma™ Gene Expression Classifier and Thyroseq™

**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.

