



THYROID NODULES

The Afirma™ gene sequencing classifier (GSC) performs better in indeterminate thyroid nodules than the Afirma™ gene expression classifier (GEC)

BACKGROUND

Thyroid nodules are very common, occurring in up to 50% of individuals. Thyroid cancer is found in ~5% of thyroid nodules, so the vast majority are benign (non-cancerous). A thyroid nodule biopsy can be benign (normal), malignant (cancer) or indeterminate. Indeterminate means the pathologist cannot tell if the nodule is benign or malignant with certainty. Historically, most patients with indeterminate thyroid nodule biopsies were referred for surgery though most would ultimately not have thyroid cancer (around 75% or more would have an “unnecessary surgery”). Currently, gene tests can provide more information as to whether an indeterminate nodule is a cancer or not. One such test is the Afirma gene test.

The original Afirma gene test was a gene expression classifier (GEC) that used a technology called a microarray that results in a pattern of gene expression. These gene patterns are better at ruling out thyroid cancer in an indeterminate nodule than confirming cancer. Therefore, a new version of the Afirma test was created called a gene sequencing classifier (GSC) to better predict thyroid cancers in indeterminate nodule while still being able to rule out cancer in benign nodules. The GSC incorporates nuclear and mitochondrial RNA transcriptome gene expression, RNA sequencing, and genomic copy number analysis.

The aim of this study was to determine the clinical performance of the GSC as compared with the GEC at one academic medical center.

THE FULL ARTICLE TITLE

Endo M et al 2019 Afirma Gene Sequencing Classifier compared with Gene Expression Classifier in indeterminate thyroid nodules. *Thyroid* 29:1115–1124.

SUMMARY OF THE STUDY

Patients with thyroid nodule biopsies with indeterminate cytology results were chosen for additional genetic testing; the Afirma GEC (during the period February 2, 2011–

July 11, 2017) or the Afirma GSC (during the period July 11, 2017–December 19, 2018).

Of the 343 nodules that underwent the GEC test, 178 cases (51.9%) were considered suspicious for cancer. The rest were called benign by the GEC. If all nonsurgical GEC benign cases were actually benign, when evaluating the cases that had surgery, the chance that a GEC suspicious nodule was actually cancer was 33.3% and the chance that a GEC benign nodule was actually benign at surgery was 98.2%. A total of 27 patients with GEC benign nodules had surgery for nodule growth or patient preference and 3 had a papillary thyroid microcarcinoma discovered at final pathology while the rest were benign.

Of the 164 nodules included in the study with the GSC test, suspicious nodules were found in 39 of the 164 nodules (23.7%). The benign call rate for GSC was 76.2%. Of the 164 GSC nodules, 29 (17.6%) underwent thyroid surgery. If all nonsurgical GSC benign cases were truly benign, the chance a suspicious nodule was truly a thyroid cancer was 60% and a benign nodule was benign was 100%.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

These results show an improved accuracy for the GSC as compared with the GEC. Additionally, there is an increase in the benign call rate with GSC, which in this study decreased surgical interventions by 68%. This study indicates that the newer Afirma GSC test is superior to the Afirma GEC test by better predicting which indeterminate nodules are more likely to be cancers and should be removed while maintaining the same or better performance of predicting which indeterminate nodules are benign and can be monitored without surgery. With these genetic tests, patients and physicians have more information to feel confident about avoiding surgery or pursuing it based on the test results.

— Joshua Klopper, MD





THYROID NODULES, continued

ATA THYROID BROCHURE LINKS

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), ~5-10% are cancerous.

Thyroid fine needle aspiration 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.

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.

microRNA: a short RNA molecule that has specific actions within a cell to affect the expression of certain genes.

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™

