



## 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.