

**THYROID NODULES****Cytology, ultrasound features and the BRAF mutation predicts cancer in thyroid nodules classified as AUS/FLUS****BACKGROUND**

Although thyroid nodules are very common, only 5-10% of them are cancerous. Thyroid biopsy is the most accurate method to differentiate between benign and cancerous thyroid nodules. While a diagnosis of cancer or benign can usually be made, indeterminate results can be seen in anywhere from 3-18% of biopsies meaning that a definitive diagnosis cannot be made. Atypia of undetermined significance (AUS) and follicular lesion of undetermined significance (FLUS) are a major part of the indeterminate category. Most of these patients undergo a repeat biopsy and a large number of patients undergo surgical removal of their thyroid nodules for a definitive diagnosis. The recent use of molecular markers has been helpful in sorting out the presence of cancer, especially the presence of the BRAF V600E mutation. The aim of this study was to determine whether several features (cytology features, ultrasound appearance of the thyroid nodules and the presence of the BRAF V600E mutation) are helpful to predict cancer in thyroid nodules with initial indeterminate cytology with 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 thyroid nodules were biopsied at a hospital in Korea between January 2010 and June 2012 with 411(6.7%) nodules having AUS/FLUS cytology. Of these 165 nodules were included in this study and divided

according to 9 AUS/FLUS cytologic subcategories. A total of 91 nodules (55.2%) with AUS/FLUS cytology were confirmed to be cancer by surgery or repeat biopsy. Of these, 13 were in the subcategory of mild follicular-cell atypia (76.2% cancer) and 59 were in the subcategory of focal features of papillary carcinoma in an otherwise predominantly benign-appearing specimen (83.1% cancer). The cancer rate of nodules with at least one suspicious ultrasound feature was 79.3% (73 of 92) and the cancer rate of AUS/FLUS cytology and the BRAF V600E mutation was 97.5% (39 of 40). The cancer rate without this mutation was 39.7% (25 of 63).

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

In this study, a much higher percentage of AUS/FLUS thyroid nodules were determined to be cancerous than previously reported. In particular, 2 categories of AUS/FLUS had the highest cancer rate. Thyroid nodules with suspicious ultrasound features and those with the BRAF V600E mutation also had a high cancer rate. Thus, indeterminate nodules in the AUS/FLUS nodules should be managed according to their cancer risk. Surgery rather than a repeat biopsy might be a better option for those with the highest cancer risk.

— Alina Gavrila, MD, MMSC

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

**ABBREVIATIONS & DEFINITIONS**

**Cytology:** the study of cells from a biopsy specimen.

**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 (malignant).

**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

**Atypical thyroid biopsy (atypia of undetermined significance or follicular lesion of undetermined significance, AUS/FLUS):** this happens when there are some abnormal/atypical cells in the biopsy sample but not enough to diagnose a cancer. However, because there are abnormal cells in the biopsy sample, the specimen cannot be called benign. Sometimes a repeat biopsy may be helpful but often surgery is recommended to remove the nodule.

**Indeterminate thyroid biopsy (follicular neoplasm/suspicious for follicular neoplasm):** this happens usually when the diagnosis is a follicular or Hürthle cell lesion. Follicular and Hürthle cells are normal cells found in the thyroid. Current analysis of thyroid biopsy results cannot differentiate between follicular or Hürthle cell cancer from noncancerous adenomas. This occurs in 15-20% of biopsies and often results in the need for surgery to remove the nodule.

**Thyroid ultrasound:** a common imaging test used to evaluate the structure of the thyroid gland. Ultrasound uses sound waves 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.

**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.

**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.