Sonographic Characteristics of the Components of Thyroid Nodules with Histopathologic Correlation

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Most of the thyroid nodules are heterogeneous and have various internal components, which make many radiologists and physicians confused with the various echo patterns of thyroid nodules. In the study, we want to explore the characteristic echogenicities representing the major histopathologic components of the thyroid nodules to provide information for diagnosis.

From Jan. 2005 to Feb. 2006, 49 patients with 75 thyroid nodular lesions were studied. The location and size of the nodules were recorded. Sonographic images best describing the nodule were obtained before operation. After surgical removal of the nodules, the gross specimen was examined, and slices of the targeted nodule according to the corresponding imaging plane were made. The histopathologic specimens of these thyroid nodules were reviewed by an experienced pathologist.

The major components of various thyroid nodules are calcifications, colloid with lining follicular cells (enlarged follicle), follicular cells, papillary cells, fibrosis, cysts, and hemorrhage. Most thyroid nodules have mixed components. Colloid with lining follicular cells (enlarged follicle) shows the highest echogenicity except for calcifications. Fibrosis shows the lowest echogenicity except for cyst and hemorrhage. Pure papillary or follicular cells show the echogenicity in between. Areas with intermediate and lower echo should address the possibility of follicular or papillary neoplasm. Our findings provide information for ultrasound guided aspiration.

Nodular lesions of the thyroid are very common among general populations. The incidence of palpable thyroid nodule in the adult population is about 4% to 7% [1]. Because of non-invasiveness and convenience, sonography is the modality of choice for imaging the thyroid. Most of the thyroid nodules tend to have various internal echogenicities, which make the specific diagnosis of them difficult. If the characteristic echogenicities for the major components of the thyroid nodule can be specialized, the interpretation of thyroid sonography would be more diagnostic; the misdiagnosis of thyroid cancer would be decreased and hence facilitating following management.

Sonographic findings of nodular lesions, such as nodular goiter and thyroid tumors are well documented in textbooks and many articles [1, 2, 3]. In nodular goiter, the sonographic patterns are usually heterogeneous. In follicular adenoma, the echopatterns are either isoechoic or hyperechoic. In carcinoma, the echogenicities vary [4]. However, few reports have been found about correlation between their histopathology and echogenicities. Many physicians are confused about the nature of various echo patterns of thyroid nodules, or even about the target selection of multiple thyroid nodules during ultrasound guided fine needle aspiration.

In this study, we reviewed sonographic images of thyroid nodules with their corresponding pathological findings. The echogenicities of the major histopathologic components of thyroid nodule were
characterized. The results will be very helpful in interpretation of thyroid ultrasound and in target selection during ultrasound guided needle aspiration.

**MATERIAL AND METHOD**

From Jan. 2005 to Feb. 2006, 49 patients (39 females, 10 males, mean age: 43.6 years) with 75 thyroid nodular lesions were studied (63 nodular goiters, 3 follicular adenomas, and 9 papillary carcinomas). Sonographic images of these nodular lesions were obtained before operation with a commercially available sonographic system [GE LOGIQ 700 ultrasound system (Milwaukee, Wisconsin U.S.A.)]. The probe was a B-mode linear array with an operation frequency range of 5 to 10 MHz. The parameters affecting image acquisition were kept the same, including the time-gain compensation and focal zone (7 focal zones and within a 2-cm depth range). Other parameters were set as follows: dynamic range, 78 dB; gain, 34; edge enhance, E2; gray map, MC; frame Average settings, A2 [6]. One image best describing the thyroid nodule was selected. The location and size of the nodules were recorded. After

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**Figure 1.** Sonographic follicles and its 12.5x magnified histopathology. The hyperechoic thyroid nodule a. is composed of abundant colloids with lining follicular cells (enlarged follicles)b.

**Figure 2.** Sonographic follicular cells with follicles and their 100x magnified histopathology. They are also hyperechoic as figure 1. The histopathologic feature of the rectangle region of interest (ROI) in figure a. is follicular cells mixed with follicles b.
surgical removal of the nodules, the gross specimen was examined and pathological slices were made according to the corresponding scanning plane. Through routine paraffin embedding and hematoxylin-eosin (H&E) staining, the histopathologic findings corresponding to sonogram were reviewed via light microscopy by a pathologist.

After thorough correlation of the sonogram and the corresponding pathologic slice, the largest rectangle of interest (ROI) containing the solid portions of the thyroid nodule were marked in the original images (Fig. 1) and classified according to their pathologic findings. There may be several ROIs for one thyroid nodule for evaluation of every solid portion with exclusion of the cystic area, calcifications, and areas containing artifact. One experienced radiologist blindly reviewed the sonographic images with ROIs and rated them according to the 4-level scoring scale (1-4, from high to low echogenicity).

**RESULT**

According to our observation, the major components of thyroid nodules are calcifications, colloid with lining follicular cells (enlarged follicle), follicular cells, papillary cells, fibrosis, cysts, and hemorrhage. The echogenicities of them are different. Except for calcifications, colloid with lining follicular cells (enlarged follicle) shows the highest echogenicity (Fig. 1, 2). If anechoic cyst and hemorrhage are excluded, fibrosis shows the lowest echogenicity (Fig. 3). The papillary or follicular cells show the echogenicity in between (Fig. 4).

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Papillary and follicular cells can be mixed with fibrosis and/or follicles. If there is component of fibrosis, the echogenicity may decrease (Fig. 5). On the contrary, mixed follicles cause higher echo (Fig. 6). Table 1 summarizes the echogenicity and scores of the common histopathological classifications of thyroid nodules including colloid with lining follicular cells, follicular cells, papillary cells, fibrosis, and their mixture. The lower score means the higher echogenicity. The results show statistically significant difference in echogenicity (two sample T test, p<0.01) between above classifications. From high to low echogenicity, they are enlarged follicles, papillary cells with follicles, follicular cells with fibrosis, and fibrosis. The echogenicity between follicular cells

**Table 1. The number of ROIs on the ultrasound images of each score and mean score for every classification. The lower score means the higher echogenicity.**

3a

3b

**Figure 3.** Sonographic fibrosis and its histopathology. The hypoechoic ROI in a. shows the central reticular fiber in b.
Thyroid nodule sonography with histopathologic correlation

and fibrosis, and the echogenicity between papillary cells and fibrosis is not statistically different (p=0.13).

**DISCUSSION**

Six major histopathologic compositions can be observed from routine thyroid ultrasound examination, including: (1) Calcifications: coarse or eggshell calcifications represent degenerative process of the goitrous nodules while microcalcifications of the papillary carcinoma are resulted from deposition of calcium salt in the psammoma bodies. (2) Follicular cells: They line thyroid follicles and elaborate colloid. (3) Colloid: it is semi-fluid to gel-like and elaborated by the follicle. Thyroid colloid is composed mainly of a glycoprotein (thyroglobulin) of high molecular weight. (4) Papillary cells: they are commonly found in papillary carcinoma. The tumor primarily consists of papillary fronds covered by one or more layers of tall epithelial cells having characteristic “ground-glass” nuclei. Psammoma bodies

Figure 4. Sonographic papillary cell cancer and its histopathology. The ROI in a. shows predominant papillary cells in b.

Figure 5. Sonographic follicular cells with fibrosis and their histopathology. The ROI in a. demonstrates multifocal fibrotic tissue in the follicular cells b. The echogenicity of this case is lower as compared with the fig. 2.
are common in papillary carcinoma and may be seen either within the tumor or in adjacent thyroid tissue. (5) Fibrosis: during embryogenesis, inflammatory process and wound healing, most connective tissues have an abundance of reticular fibers. Most papillary carcinoma shows dense fibrosis within the tumor masses [5]. Fibrosis also increases with the duration of the nodular goiter alteration. (6) Cysts or hemorrhage: they are common in an adenomatous goiter but can also occur in a neoplasm [1, 4].

Besides calcifications, cysts and hemorrhage, colloid with lining follicle cells (enlarged follicles) show the highest echo. Fibrosis shows the lowest echo. In our study, follicular cells and papillary cells, as the most common and important components of thyroid neoplasm, show intermediate echo if there is no other components. However, it is uncommon for a thyroid nodule to have pure follicular cells and papillary cells as the dominant feature. They are usually mixed with other components, such as fol-

**Figure 6.** Sonographic papillary cells mixed with follicles a. and their histopatholgy b. The ROI of a. shows higher echogenicity as compared with fig. 4 and 7. The finding is due to more follicles mixed in the papillary cells as shown in b.

**Figure 7.** Sonographic papillary cancers with dominant fibrosis and its corresponding histology. The hypoechoic ROI in a. is actually fibrosis as shown in b. Papillary cancers are commonly associated with fibrosis.
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Sonographers should carefully scan the thyroid nodule for areas with various echogenicity, rather than focus on its global appearance. Areas with intermediate and lower echo should address the possibility of follicular or papillary neoplasm. They provide more cellular information for ultrasound guided aspiration.

CONCLUSION

In conclusion, our study suggests the different components in thyroid nodules and also provides the rule for prediction of their composition. It should be very helpful in interpretation of thyroid ultrasound.

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6. LOGIQ 700 basic user manual. GE Company 2000
甲狀腺結節之組織成份與其超音波影像特徵

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甲狀腺結節通常包含數種組織成份，所以在超音波影像上結節內部常呈現各種不同的回音。本研究之目的在了解甲狀腺結節內部各組織成份與其超音波影像學特徵，盼能對選擇細針抽吸之區域與區分良性悪性結節有所助益。自2005年一月至2006年二月間，49位病人共75個甲狀腺結節被納入此研究。在外科手術切除前，記錄每個結節的位置、大小、與在最大切面的超音波影像；術後依照影像的切面來做病理標本的切片，並由病理科醫師來判讀。結節的各組織成份包括鈣化、被濾泡包圍的膠質體（大濾泡）、濾泡細胞、乳突狀細胞、纖維化組織、囊泡與出血，這些組織通常是混雜出現。在超音波影像上：除了鈣化，以大濾泡為主的結節具有最高的回音；其次是乳突狀細胞與濾泡細胞為主的結節；除了囊泡與出血外，纖維化組織的回音最低。在甲狀腺結節超音波影像上呈現中到低回音區域通常表示此區域包含有濾泡細胞或甚至乳突狀細胞，針對這些區域做超音波導引的細針抽吸可以得到最多的細胞學資訊。