TECHNICAL NOTE

The Role of Computer-Aided Detection and Diagnosis System in the Differential Diagnosis of Thyroid Lesions in Ultrasonography

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Abstract To avoid abuse of fine-needle aspiration cytology (FNAC) and to save the time of a learning curve, a computer-aided detection and diagnosis (CAD) system to detect suspicious lesions for FNAC from thyroid ultrasonography has been developed by the Department of Industrial Engineering, cooperative with the Department of Surgery at the National Taiwan University, Taipei, Taiwan. The purposes of this article are to introduce how to utilize the CAD system in thyroid ultrasonography, and to outline the real role of the CAD system. After marking the apparently transverse (extending across) axis and longitudinal axis of the nodule appearing by ultrasonography, four parameters are calculated and displayed by the computer system automatically, which include microcalcifications, hypoechoic lesion, heterogeneity, and indistinct margin. The results are displayed by the pointers in the semilunar figures. The necessity of FNAC is dependent on the size and numbers of positive findings (pointers displayed in the right side). This CAD system is objective and easy to use. It may supply an easy method to determine the necessity for FNAC, but what we must keep in mind is that this method can reduce the necessity of FNAC, not replace FNAC for the diagnosis of thyroid cancer.

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Introduction

The number of cases of thyroid cancer have the trend of increasing gradually in many countries, including the United States [1] and Taiwan [2,3], although the increase in mortality is not noted. The dramatic increase in the number of thyroid cancer cases is considered to be related to many factors, but increased screening by ultrasonography may be the most important factor [1]. However, the increased incidence across all tumor sizes suggests that increased diagnostic scrutiny is not the only reason [1].

Although it is cheap to carry out fine-needle aspiration cytology (FNAC) in Taiwan, especially under the coverage of health insurance, the work-load would delay the further work-up and management of patients if every case suspected to have thyroid nodule was to be aspirated and read after staining to judge whether it is malignant or not.

In the study reported by Bonavita et al [4], there are several patterns shown by thyroid ultrasonography which are indicative of benignancy, and further FNAC is not necessary. These include spongiform configuration, cysts with colloid clots, giraffe pattern, and diffuse hyper-echogenicity. The specificity is 100%. They estimated 60% of FNAC procedures could be saved. Different patterns on thyroid ultrasonograms between benign and malignant lesions have also been stressed [5].

Figure 1  (A) Locate the first point in the left border of the thyroid lesion with the largest diameter. (B) Draw to extend across to the right border with the largest diameter of the lesion. Locate the second point of the middle part in the upper border of the thyroid nodule, then draw to the middle part in the lower border of the thyroid nodule.

Figure 2  For the longitudinal axis, locate the second point at the middle part in the upper border of the thyroid nodule, then draw to the middle part in the lower border of the thyroid nodule.

Figure 3  As soon as the two axes are defined, the contour is automatically generated by the computer-aided detection and diagnosis system.
Learning curves

It is not easy to read ultrasonography accurately for the beginner, and the diagnosis by cytology is even more difficult. Both of them need a so-called learning curve. Accumulation of experience can conquer this problem. However, at the initial stage, this problem can be solved by the coverage of senior doctors. Although this is a formal way of learning medical knowledge, it is better to have a faster and objective way to solve this problem in the image system.

Computer-aided detection or computer-aided diagnosis

According to the recently published Food and Drug Administration (FDA) guidance [6], computer-aided detection (CADe) devices are computerized systems intended to identify, mark, highlight, or in any other manner direct attention to portions of an image, or aspects of radiology device data, that may reveal specific abnormalities during interpretation of patient radiology images or patient radiology device data by the clinician, while the computer-aided diagnosis (CADx) devices include those that are intended to provide an assessment of disease or other conditions in terms of the likelihood of the presence or absence of disease, or are intended to specify disease type (i.e., specific diagnosis or differential diagnosis), severity, stage, or intervention recommended. The method mentioned in this article therefore includes both CADe and CADx (CAD).

To differentiate benign from malignant thyroid lesions automatically in order to avoid the need of a learning curve and to save working time, a review of CAD of thyroid nodule in thyroid ultrasonography was published [7]. The authors showed that the features can be categorized into (1) the sonographic features from the ultrasound images, and (2) the nonclinical features extracted from the ultrasound images using statistical and data mining techniques.
CAD in Taiwan

With the cooperation of experts from the Department of Industrial Engineering and the Department of Surgery, National Taiwan University, Taipei, Taiwan, a CAD for thyroid nodule was developed successfully, and obtained the patents from the FDA of the United States [8,9], Taiwan [10–12], China [13], Malaysia [14], and Singapore [15,16]. They proved that the new CAD method is more sensitive and more objective than traditional observation of ultrasonography in the detection and quantification of microcalcifications [17]. This method is also correlated with conventional ultrasonic heterogeneity assessment, but can be a better aid in the diagnosis of thyroid malignancy [18].

How to perform CAD

It is simple to perform the CAD invented in Taiwan. The first point in the left border of the thyroid lesion with the largest diameter (Figure 1) is located, then drawn to extend across the lesion to the right border with the largest diameter of the lesion. For the longitudinal axis, the second point at the middle part in the upper border of the thyroid nodule is located, and then drawn to the middle part in the lower border of the thyroid nodule (Figure 2). Then the margin is shaped automatically (Figure 3). If users are not satisfied with the initial contour generated automatically, the selected marker that the observer wants to move can be selected and dragged to a new location. Release of the mouse button sets the contour shape. Therefore, users can fine-tune the contour by adding additional markers to the

Figure 7 The thyroid lesion is < 1 cm in diameter; follow-up only is required.

Figure 8 The thyroid lesion from Figure 7. Parameter 1 (microcalcification) and Parameter 2 (hypoechogenicity) detected by the computer-aided detection and diagnosis system are both negative.

Figure 9 Thyroid lesions 1–1.5 cm in diameter, for which fine-needle aspiration cytology needs to be performed.
contour and moving their position (Figure 4). Then the severity of the parameters are calculated and displayed by the computer system automatically, which include microcalcification, hypoechoic lesion, heterogeneity, and indistinct margin. The results are displayed by the pointers in the semilunar figures. The necessity of FNAC is dependent on the size and number of positive findings (pointers displayed on the right hand side) according to the guideline of the American Thyroid Association for differentiated thyroid cancer [19].

Figures 5 and 6 represent the example of thyroid lesions < 1 cm in diameter, for which FNAC needed to be performed because Parameter 1 (microcalcification) and Parameter 2 (hypoechogeticity) detected by the CAD were both positive.

Figures 7 and 8 represent the example of thyroid lesions < 1 cm in diameter which needed follow-up only because Parameter 1 and Parameter 2 detected by the CAD were both negative.

Figure 10 The thyroid lesion from Figure 9. Either Parameter 1 (microcalcification) or Parameter 2 (hypoechogenicity) detected by the computer-aided detection and diagnosis system is positive.

Figure 11 Thyroid lesions 1–1.5 cm in diameter which need follow-up only.

Figure 12 Thyroid lesion from Figure 11. Both Parameter 1 (microcalcification) and Parameter 2 (hypoechogenicity) detected by the computer-aided detection and diagnosis system are negative.
Figures 9 and 10 represent the example of thyroid lesions 1–1.5 cm in diameter, for which FNAC needed to be performed because either Parameter 1 or Parameter 2 detected by the CAD is positive.

Figures 11 and 12 represent the example of thyroid lesions 1–1.5 cm in diameter which needed follow-up only because both Parameter 1 and Parameter 2 detected by the CAD are negative.

Figures 13 and 14 represent the example of thyroid lesions >1.5 cm in diameter which need FNAC because of the presence of any one of Parameters 1–4 found by the CAD.

Figures 15 and 16 represent the example of thyroid lesions >1.5 cm in diameter, which need follow-up only because Parameters 1–4 detected by the CAD are all negative.

These examples show that for small lesions (<1 cm in diameter), both Parameter 1 (microcalcification) and Parameter 2 (hypoechogenicity) need to be positive, and then FNAC is required. If there is a lesion with diameter from 1 cm to 1.5 cm, either microcalcification or hypoechogenicity need to be positive. However, if the lesion detected by thyroid ultrasonography is >1.5 cm in diameter, then any one of four parameters (microcalcification, hypoechogenic lesion, heterogeneity, and indistinct margin) being positive is enough for the necessity of FNAC. Therefore, the necessity of FNAC depends on size and items of positive finding. Microcalcification and hypoechoic lesion are more important than heterogeneity and indistinct margin in this system for small thyroid lesion (<1 cm in diameter).

**CAD cannot replace FNAC**

This CAD system is objective and easy to use. It may supply an easy method to determine the necessity for FNAC, but what we must keep in mind is that while this method can reduce the necessity of FNAC, it cannot replace FNAC in the diagnosis of thyroid cancer as many people believe.
When to perform FNAC and how to perform FNAC at the time with CAD

Using the CAD system, the necessity for performing FNAC can be determined. If the lesion is not easily located, it is better under ultrasonography-guidance [20]. The method of further management may be further planned with the help of cytomorphology [21] or molecular determination [22].

Conclusion

CAD is an objective way to determine which thyroid nodules need to have FNAC. It saves workload, and there is no interobserver variation. However, no examination is perfect, which also includes CAD of the thyroid nodule. Therefore, follow-up is necessary if the thyroid lesions are considered not to require FNAC by CAD. It is important to follow this rule to avoid the legal problems which may occur if CAD predicts the lesion does not require FNAC, but the lesion ultimately is malignant.

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References

