Computer-assisted Thyroid Fine Needle Aspiration Interpretation Method for Thyroid Nodules with FNA Indeterminate Results

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Introduction

Fine needle aspiration (FNA) of the thyroid gland is an invaluable method to evaluate the patient with thyroid nodule, but morphologic interpretation of the smear is subjective with a significant number of benign cases misidentified in the indeterminate categories (AUS/FLUS, FN/SFN, SUSP). The objective of this study is to develop the computer-assisted thyroid FNA interpretation method (CATFNAIM) for further detection of benign cases from the FNA indeterminate cases.

Methods

There were 309 cases, including 118 cases with benign thyroid disease (Group 0) and 191 cases with primary thyroid neoplasm (Group 1), recruited for the database collection, all with surgical pathology results as the evaluation gold standard. For each case, we took at least 3 digital images of various field views of pre-operative thyroid FNA smear by Riu's stain, a type of Romanowsky stain. The nuclei and cytoplasm were identified by computer algorithm automatically to compute 22 quantified cytological features, including 16 morphologic and 6 chromatic features. We established a logistic regression model based on the 247 cases to differentiate cases with benign thyroid disease using 4 significant quantified features, including nuclear to cytoplasmic ratio, NC saturation ratio, NC value ratio, and interaction of mean of nuclear size and mean of nuclear elongation. The model was then validated with another independently collected 62 indeterminate cases, with 16 cases proven benign thyroid disease.

Table 1. The cytological classification for benign thyroid disease and primary thyroid neoplasm between 247 cases for model construction and 62 cases for model validation.

Diagnostic Category (Bethesda system for reporting thyroid cytopathology)	Group 0 (NG, NH, AG, AH/ Thyroiditis, Graves' disease)	Group 1 (PTC/ MTC/ Follicular carcinoma/ adenoma)
Training (N=247)	N=102 (58.7%)	N=145 (41.3%)
Benign	70 (68/2)	19 (10/0/1/8)
Atypia (AUS/FLUS)	13 (11/2)	29 (19/0/4/6)
Follicular Neoplasm (FN/SFN)	16 (16/0)	16 (5/0/5/6)
Suspicious for Malignancy (SUSP)	3 (3/0)	50 (50/0/0/0)
Malignancy	0 (0/0)	31 (25/6/0/0)
Validation (N=62)	N=16 (25.8%)	N=46 (74.2%)
Atypia (AUS/FLUS)	13 (12/1)	24 (21/0/0/3)
Follicular Neoplasm (FN/SFN)	2 (2/0)	6 (1/0/3/2)
Suspicious for Malignancy (SUSP)	1 (1/0)	16 (16/0/0/0)

Results

Table 1 shows the demographic information of cases for model training and validation, respectively. The area under the receiver operating characteristic (AUROC) curve was 0.850 ($p < 0.001$) for the logistic model (Figure 1 and Table 2). Based on a cut-off value of 0.35, the CATFNAIM was applied to 62 cases (Figure 3). The sensitivity, specificity, positive and negative predictive values, and accuracy of the CATFNAIM were 100.0%, 31.25%, 80.7%, 100.0% and 82.2%, respectively.

Table 2. Multivariate logistic regression analysis using pathological diagnosis as the dependent variable and four cytological parameters as independent variables. Each parameter showed statistically significant.

Variable	Coefficient	Std. Error	Wald	P
NCR	0.93302	0.31933	8.5367	0.0035
NCSR	-1.46471	0.31448	21.6925	<0.0001
NCVR	-12.19695	3.29711	13.6847	0.0002
MNSize x MNElon	0.14190	0.019747	51.6366	<0.0001
Constant	7.38786	2.92568	6.3765	0.0116

*NCR: Nuclear to cytoplasmic ratio, NCSR: Nuclear to cytoplasmic saturation ratio, NCVR: Nuclear to cytoplasmic value ratio, MNSize: Mean of Nuclear Size, MNElon: Mean of Nuclear Elongation

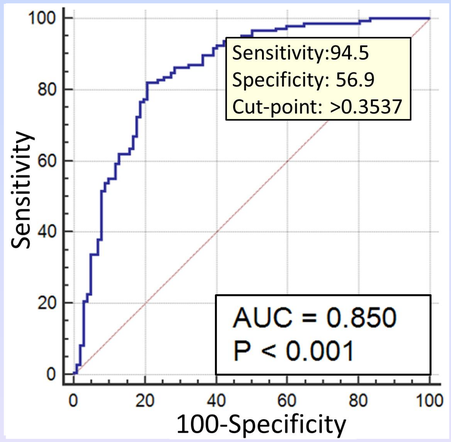

Figure 1. The probability value of 0.35 is chosen as cut-off value based on ROC curve analysis; the AUC was 0.850 showed statistically significant.

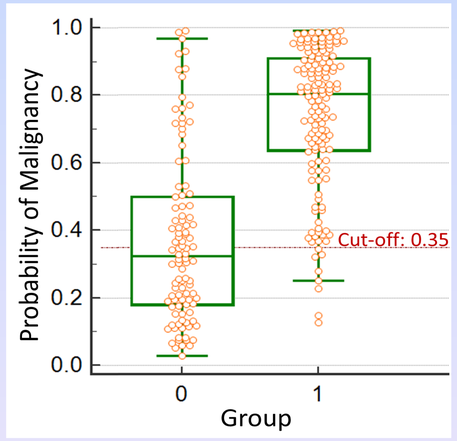

Figure 2. The comparison graph of malignancy probability between model training cases. The Mann–Whitney U test showed statistically significant difference between two groups ($p < 0.001$).

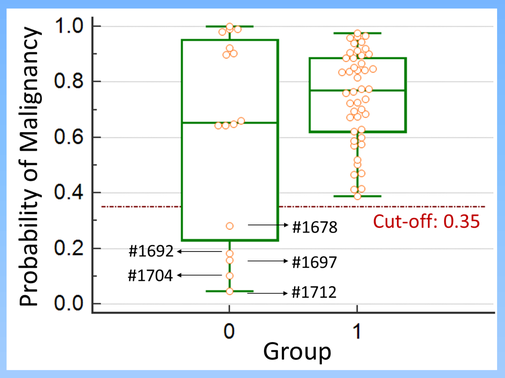

Figure 3. Comparison graph of malignancy probability between model validation cases. The Mann–Whitney U test showed statistically significant difference between two groups ($p < 0.001$).

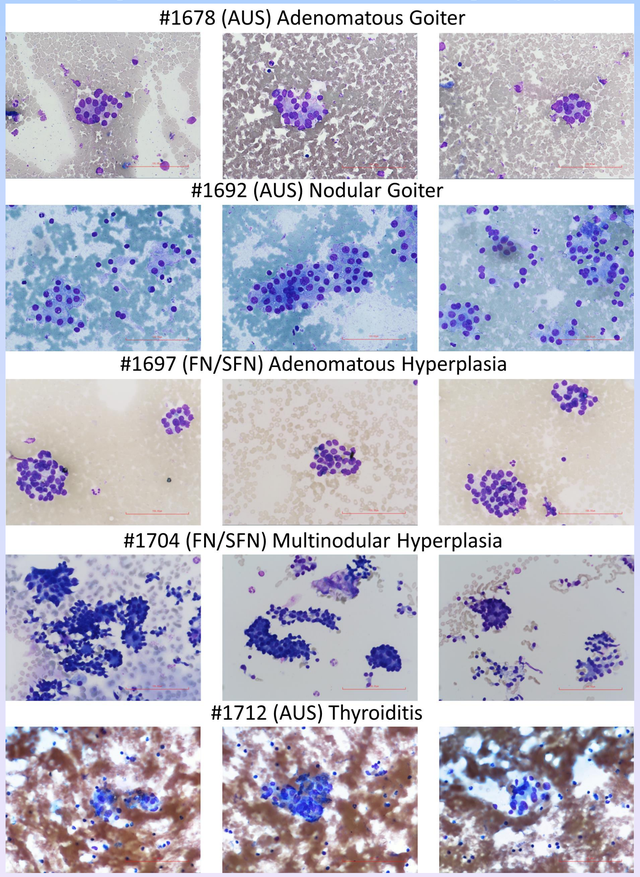

Figure 4. Cytological images acquired from the thyroid FNA smears of five true negative cases mentioned in Figure 3 (Riu's stain, 400x).

Discussion/Conclusion

We have used the CATFNAIM to quantify not only morphological but also chromatic features. Five of 16 pathological benign cases were successfully found out by the CATFNAIM (Figure 4). In this study, the results showed the potential of the computer-assisted tool for further screening of benign cases out of the indeterminate FNA cases.

Conflict of interest disclosures

ISJ, SRS, and TCC received research grant support from AmCad BioMed. WYC and HMW are employed by AmCad BioMed. AC was previously employed by and is now a consultant for AmCad BioMed.