Visualization of Thyroid Cancer Signs by Atomic Force Microscopy

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ABSTRACT

This work is the continuation of the early publications of our group [1] and is dedicated to the detailed study of morphology and partly the functioning of the thyroid cancer cells in the comparison with the benign diseases. All investigation have been conducted at sub cellular level with extensive use of nanotechnology instrument – Atomic Force Microscopy (AFM).
Keywords: Atomic force microscopy, thyroid cancer, benign diseases, sub cellular level.

1 AIM

Search for the AFM signs of the thyroid cancer. Search for the morphological characteristics of cancer cells, which have prognostic importance.

2 MATERIALS AND METHODS

AFM-system NTEGRA Prima, NT-MDT Co., Zelenograd, Russia. Cytological specimens prepared identically to those used in traditional cytological studies [1].

We have measured the following chatacteristics: the height of nucleus, the height of cytoplasm, the ratio of the height of nucleus to the height of cytoplasm, the sizes of cells in the maximum measurement, the intensity of thyroglobulin production.

The cells of papillary thyroid cancer (figure 1), colloidal goiter (figure 2), follicular adenoma (figure 3) have been investigated.

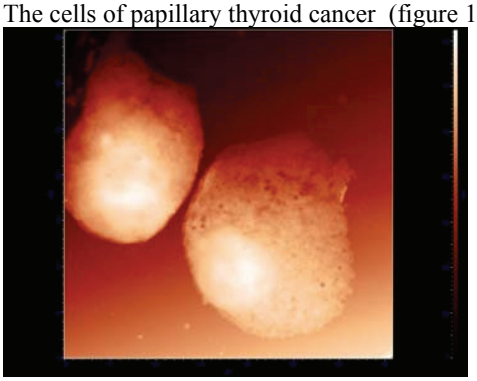

Figure 1: Papillary thyroid Cancer cells.

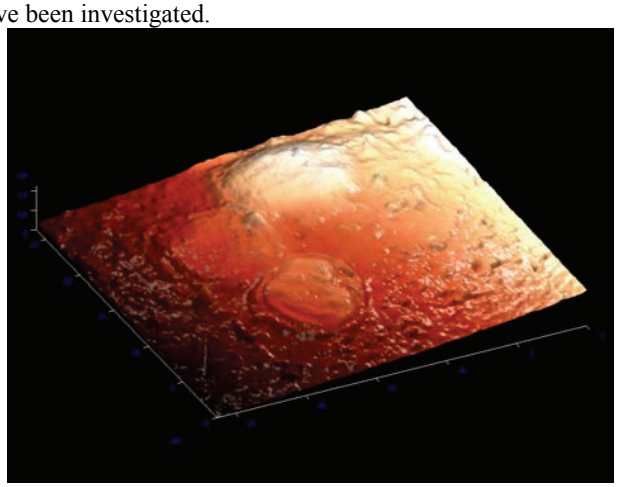

Figure 2: Colloidal goiter cells

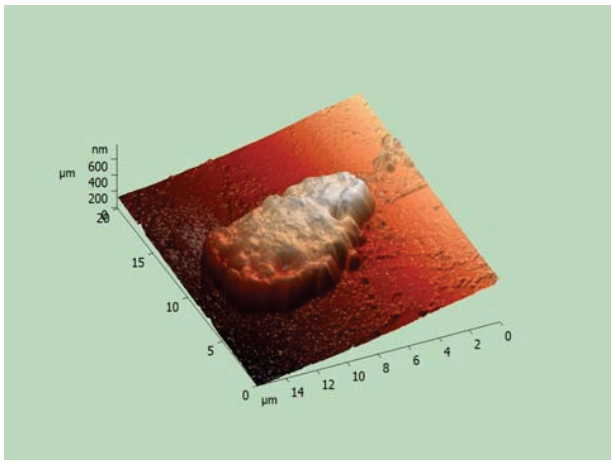

Figure 3: Follicular adenoma cell.

The rough microrelief of the nuclei surface is visualized when studying the cells by AFM. Nucleoli are revealed in the form of local elevations. The measurements of the morphometric parameters by AFM in the follicular adenoma cells showed that the values of the ratio of the height of nucleoli to the height of nucleus differ in cancer

cells and follicular adenoma cells and can be used as the objective criteria of differential diagnostics between these pathologic processes. These ratios for cancer cells are 0.63+0.43 and for follicular adenoma cells - 0.34+0.21, $p<0.05$.

Our measurements showed that the cells of colloidal goiter and cancer cells can be distinguished ($p<0.05$) according to following parameters: the height of cytoplasm, the height of nucleus, the relationship of the heights of nucleus and cytoplasm (1.9±0.6 for colloidal goiter cells and 2.5±1.2 for cancer).

3 RESULTS

Our measurements and statistical calculations showed:

1. Reliable differences between the cells of thyroid cancer and colloidal goiter in parameters: the height of nucleus, the height of cytoplasm, the ratio of the height of nucleus to the height of cytoplasm.
2. Reliable differences between the cells of thyroid cancer and follicular adenoma in cells size.
3. Intranuclear Cytoplasmic Inclusions (INCI) were visualized (figure 4). We managed to measure those inclusions – the depth is 290±82 nm.

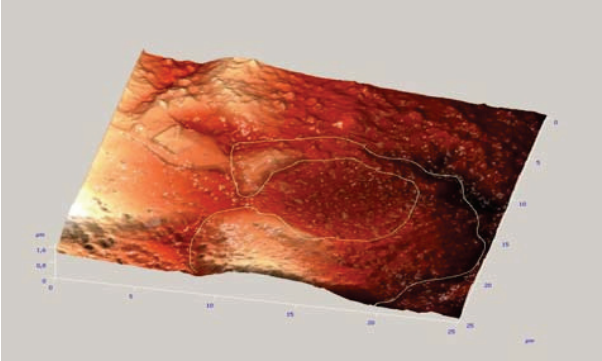

Figure 4: Visualization of INCI.

When studying the specimens, subjected to immunocytochemical processing, correlation between the intensity of thyroglobulin production and the heights of specific subcellular structures was noted. In the figures 2-4 the scale of the intensities of thyroglobulin production is represented: intensive production with the colloidal goiter (figure 5), the moderate production with moderate-differentiated cancer (figure 6) and weak production with poorly-differentiated cancer (figure 7) with the unfavorable prognosis.

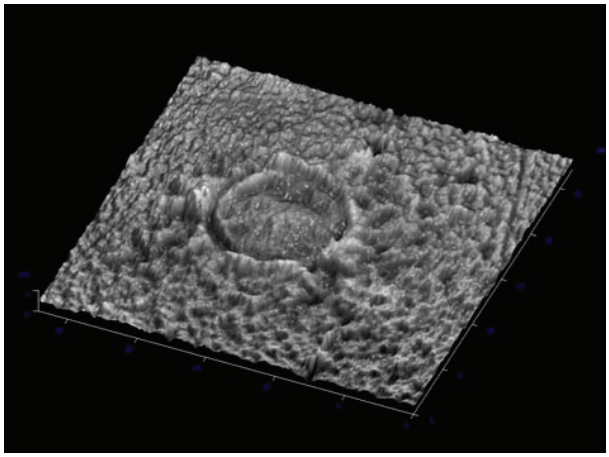

Figure 5: Intensive production of thyroglobulin in colloidal goiter cells.

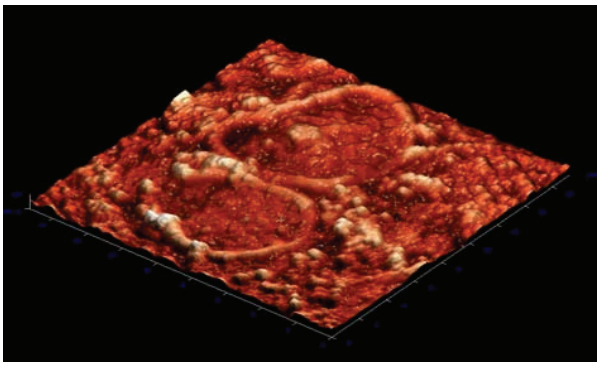

Figure 6: Moderate production of thyroglobulin by moderate-differentiated cancer cells.

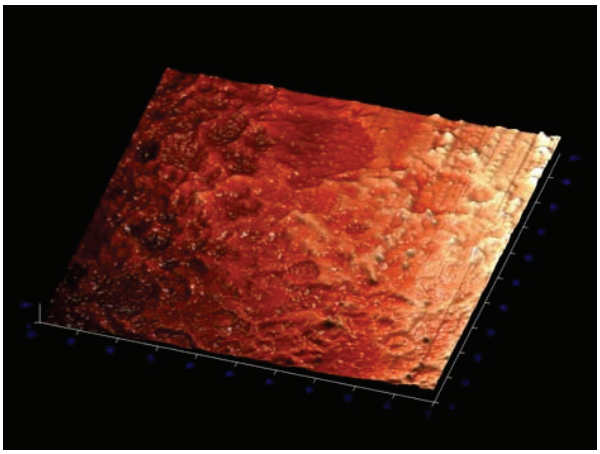

Figure 7: Weak production of thyroglobulin by poorly-differentiated cancer cells.

We succeeded in visualizing cellular pores and measuring the globules of thyroglobulin during evacuation through ones (figure 8).

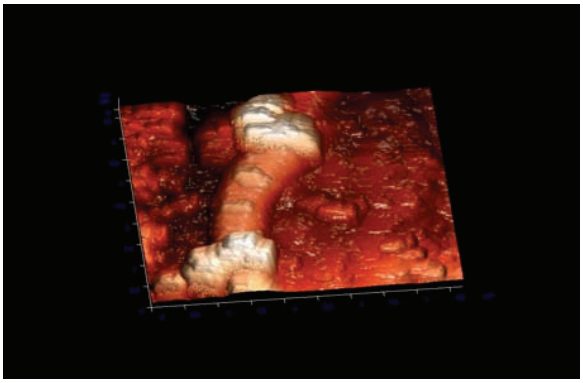

Figure 8: Visualization of cellular pores.

4 CONCLUSIONS

The measurements and investigations conducted with extensive use of nanotechnologies could form the basis for differential diagnosis between malignant and benign deceases of thyroid gland.

REFERENCES

[1] I.V. Reshetov, V.I. Chissov, N.N. Volchenco, V.A.Bykov, S.S. Sukharev, E.N. Slavnova, Yu.S. Ivanov. Atomic Force Microscopy as a Tool for Research in Oncocytology. Technical Proceedings of the 2009 Nanotechnology Conference and Trade Show, Vol.2, pp. 18 – 21