

## Chapter 2

# Breast Cancer Diagnosis Using Relational Discriminant Analysis of Malignancy– Associated Changes

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### ABSTRACT

*The chapter is devoted to description of a novel method of breast cancer diagnostics based on the analysis of the distribution of the DNA concentration in interphase nuclei of epitheliocytes of buccal epithelium with the aid of novel algorithms of statistical machine learning, namely: novel proximity measure between multivariate samples, novel algorithm of construction of tolerance ellipsoids, novel statistical depth and novel method of multivariate ordering. In contrast to common methods of diagnostics used in oncology, this method is a non-invasive and offers a high rate of accuracy and sensitivity.*

### INTRODUCTION

Today, the problem of early diagnosis of breast cancer is one of the most challenging problems. The point of view of authors is based on the premise that a human organism has cytological reactivity and the appearance of a tumor causes the malignancy-associated changes in buccal epithelium. These changes (the nuclei heterogeneity and presence of the numerous Feulgen-negative zones) have sub visual character and to detect the it is necessary to apply novel achievements of machine learning.

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The chapter is devoted to description of a novel method of breast cancer diagnostics based on the analysis of the distribution of the DNA concentration in interphase nuclei of epitheliocytes of buccal epithelium with the aid of novel algorithms of statistical machine learning. In contrast to common methods of diagnostics used in oncology, this method is a non-invasive and offers a high rate of accuracy and sensitivity; these characteristics are considerably greater than the ones of the majority of common methods. Besides, the method has a formal scientific background, since it uses modern achievements of statistical machine learning. We give an accurate and clear description of the method.

## **BACKGROUND**

Today, it is well known that in the presence of malignant tumor in a human organism the malignancy associated changes (MAC) of the distant tissues occur (see, for example, Susnik et al. (1995), Mairinger et al. (1999), Us-Krasovec et al. (2005), Hassanien Aboul Ella, et.al.(2014), Hossam Moftah et.al (2014)). However, these changes have sub visual nature and their quantitative measurement is a difficult problem. That is why till now oncomorphologists studied only qualitative changes characterizing the influence of a tumor on various organs and tissues of an organism distant from the tumor. In the chapter the authors describe the methods of quantitative estimations of these changes to discover significant statistical properties of DNA content distribution in nuclei of epitheliocytes of the buccal epithelium in the presence of pre-tumor processes and cancers of the mammary gland. The aim of the research is to compare the indices characterizing the state of chromatin and DNA content in the epithelial cells of mammary gland among patients suffering from the breast cancer and fibroadenomatosis, and healthy women also

## **MATERIAL AND METHOD**

For investigation the groups of the women suffering from the breast cancer (stages T2 and T3) and fibroadenomatosis from 25 to 53 years old (25 cases of breast cancer and 25 cases of fibroadenomatosis) were taken. The scrapes were taken from the spinous layer of buccal mucous after gargling and taking down of the superficial cell layer. The smears were dried out under the room temperature and fixed during 30 min in the Nikiforov mixture. Then, the Feulgen reaction with the cold hydrolysis in 5 n. HCl during 15 min under the temperature  $t=21-22\text{ }^{\circ}\text{C}$  was made. The optical density of the nuclei was registered by cytospectrophotometer LOMO with the help of the scanning method for the wave length 575 nm and probe diameter 0.05 mkm. We investigated from 10 to 30 nuclei in each preparation. The DNA- fuchsine content in the nuclei of the epitheliocytes was defined as a product of the optical den-

sity on area. Thus, under investigation of the interphase nucleus a rectangular matrix  $\{r_{ij}\}_{i=1, n}^{j=1, m}$ , whose entries characterizes the DNA content in the corresponding grid cell was obtained (mostly,  $n$  and  $m$  were equal to 8 or 9).

On the basis of these cytophotospectrometric indices the following morpho- and densitometric features that characterize structural and textural peculiarities of chromatin were calculated.

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