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Sensitivity of Nuclear-Cytoplasmic Index and Nuclear-Cytoplasmic Relation in Computer Aided Cytoscreening Diagnosis

Abstract. *Analysis of cytological images stained with the use of Papanicolaou process is important for women health diagnosis. Computer Aided Diagnosis allows fast detection of atypical cells using analysis of area of cell nuclei and corresponding cytoplasm area. Two techniques based on Nucleus-Cytoplasmic Index (NCI), and Nucleus-Cytoplasmic Relation (NCR) are compared. Sensitivity analysis of these methods is provided.*

Streszczenie. *Analiza obrazów cytologicznych wybarwianych metodą Papanicolaou jest istotna w diagnostyce zdrowia kobiet. Komputerowo wspomagana diagnostyka umożliwia szybką detekcję atypowych komórek wykorzystując pole jądra komórki i cytoplazmy. Porównano dwie techniki bazujące na indeksie jądrowo-cytoplazmatycznym (NCI) oraz relacji jądrowo-cytoplazmatycznej (NCR). Przedstawiono analizę wrażliwości metod.* (***Wrażliwość indeksu jądrowo-cytoplazmatycznego i relacji jądrowo-cytoplazmatycznej w komputerowo wspomaganej diagnostyce cytologicznej***)

Keywords: Image Analysis, Cytoscreening, Sensitivity Analysis.
Słowa kluczowe: Analiza obrazów, Diagostyka cytologiczna, Analiza wrażliwości.

Introduction

The pre-classification could be important tool for improving of cell screening process in computer assisted diagnosis. The identification of cervical intraepithelial lesions in a Papanicolaou screening test (Pap test) [1,2,3] is important, especially in women of reproduction age. The cytoscreening is a standard procedure for preliminary detection of precancerous conditions, that could be effectively treated. The examples of cell nuclei are shown in Fig.1 and the cell nuclei have different sizes [4].

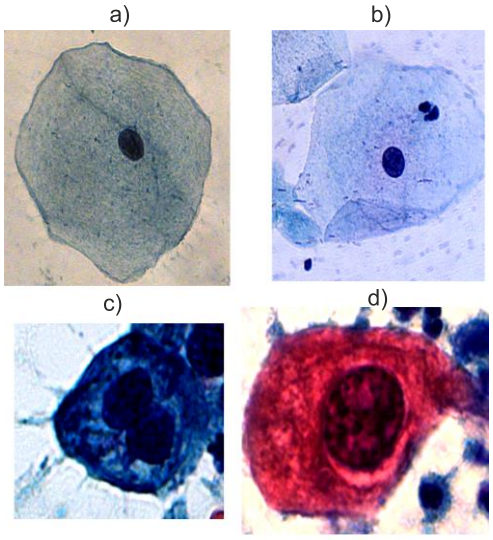

Fig.1. Example images of cell nuclei (a,b - correct; c,d - atypical)

The most important indicator is the Nuclear Cytoplasmic Index [2], that is defined as a following ratio:

(1) $$NCI = \frac{A_{CellNucleus}}{A_{Cytoplasm}}$$

or

(2) $$NCI^{*} = \frac{A_{CellNucleus}}{A_{Cell}}$$

where:

(3) $$A_{Cell} = A_{CellNucleus} + A_{Cytoplasm}$$

The difference is related to the inclusion of the cell area to denominator. Both variants are used in the quantitative analysis. Alternative approach based on the cell Nucleus to Cytoplasm area Relation (NCR) is introduced in [5] that is $A_{Cytoplasm} = f(A_{CelNucleus})$ diagram.

Related Works

There are many approaches for the analysis of cells. Cells nuclei could be analyzed using shape descriptors and texture descriptors. Color images could be obtained depending on staining method and color data could be also used.

The cytoscreening process provided by human specialist is not based on a small number of well recognized rules. There are many years of learning necessary for the achieving of proper diagnosis quality, because Papanicolaou images are the most complex microscopic images. Some rules are simple and are related to the area of cell nucleus and area of cytoplasm. Both of them are used in NCI.

Alternative approaches based on the analysis of texture of cell nuclei using fractal estimators are considered also [6,7,8]. Some approaches are based on the classification using large set of object descriptors and neural networks - it is expected that rules could be obtained by neural network.

The segmentation of biological objects, especially in cytological images is difficult [9,10,11,12]. Texture related techniques allows the consideration of cell nucleus inner part only, so precised segmentation is not necessary.

Content and Contribution of the Paper

In this paper the sensitivity of two techniques for the analysis of Papanicolaou stained cytological images is provided. The first technique is the NCI (Nuclear-Cytoplasmic Index) that is known in literature and is considered in next section. The second technique is the recently proposed NCR (Nuclear-Cytoplasmic Relation) [5] that is analyzed in this paper. The discussion and final conclusions are formulated at the end of paper.

We use the database of separated cells nuclei classified as correct and atypical (there are many types of atypical cell

nuclei types). There are 87 of correct and 38 of atypical cells nuclei from single pathomorphology laboratory in our database. Images have been acquired using AxioCamMRc5 color camera, that supports 2584x1936 resolution (5M pixels). The segmentation is provided manually, but the computer aided segmentation is possible. The most important problem is the quality of segmentation that is dependent on the cytological image quality. In classical Papanicolaou smears many artefacts occurs and some of them are important for diagnosis and some of them are real artefacts.

NCI and NCI*

The cytoscreening process should be sensitive on atypical cells, but the number of correct cells examined as atypical should be low even using computer aided cytoscreening systems.

NCI could be examined using histogram, that shows the number of cases for classes. The histogram is shown in Fig.2 and both classes have common NCI value for *NCI<0.1* - there are cases of atypical cells nuclei that cannot be distinguished from correct (9 cases). Similar histogram is obtained for NCI* that is depicted in Fig.3 (4 cases). This example shows the problem of NCI for diagnostic purposes because the detection of all atypical cells is necessary, but some correct cells are marked for further examination by cytoscreener.

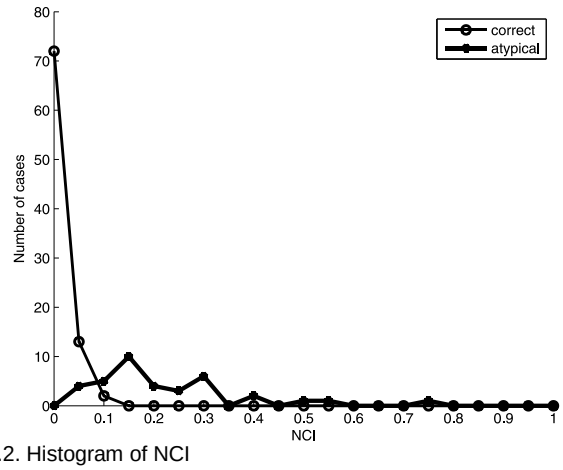

Fig.2. Histogram of NCI

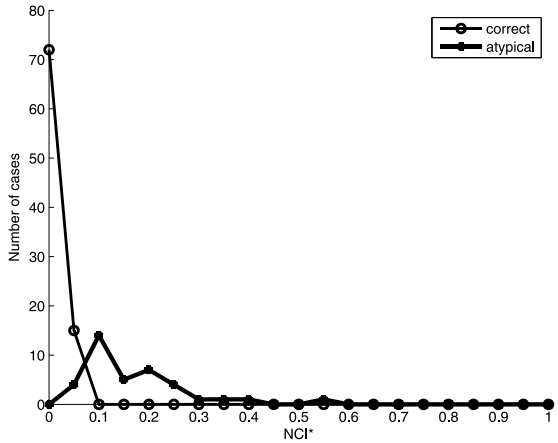

Fig.3. Histogram of NCI*

Sensitivity of NCR

Another approach based on the cell nucleus and cell cytoplasm areas is necessary, because both values are used during cytoscreening process provided by human. The Nuclear-Cytoplasmic Relation is based on the diagram (show in Fig. 4) where the cell nucleus and cell cytoplasm area defines point in 2D space. In the case of NCI they are transformed to the single value so valuable information for classification purposes is lost. Both populations (atypical and correct) of cell nuclei are well separated, that is visible in Fig. 4.

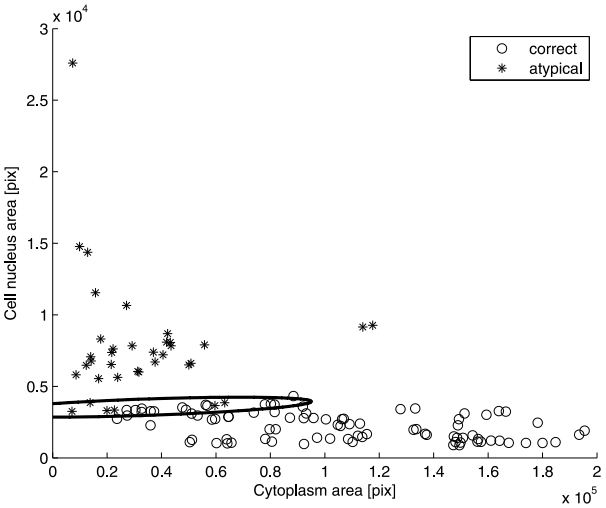

Fig.4. Nuclear-Cytoplasmic Relation and 95% elliptic confidence region for atypical cells from boundary region

The consideration of changes in the cell and cytoplasm areas, allows the simulation of effect related to non-ideal segmentation of cytoplasm and cell nucleus. There are many possible approaches and basing on the observations (Fig. 4) the following modifications are applied:

$$A_{CellNucleus} \leftarrow (1-v)A_{CellNucleus} \tag{4}$$

$$A_{Cytoplasm} \leftarrow (1+v)A_{Cytoplasm} \tag{5}$$

for atypical cells nuclei, and:

$$A_{CellNucleus} \leftarrow (1+v)A_{CellNucleus} \tag{6}$$

$$A_{Cytoplasm} \leftarrow (1-v)A_{Cytoplasm} \tag{7}$$

for correct cell nuclei. The movement vector v is 0.05 for 5% sensitivity and 0.10 for 10% sensitivity. Such deterministic values and rules add significant movement of all population for the testing of segmentation influence.

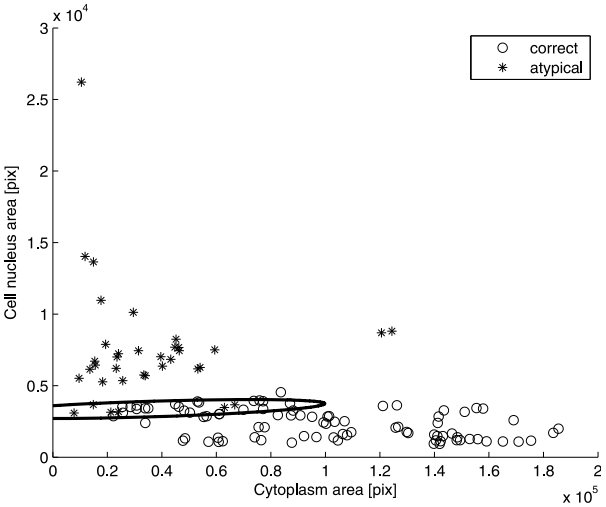

Fig.5. Nuclear-Cytoplasmic Relation and 95% elliptic confidence region for atypical cells from boundary region - 5% movement of areas

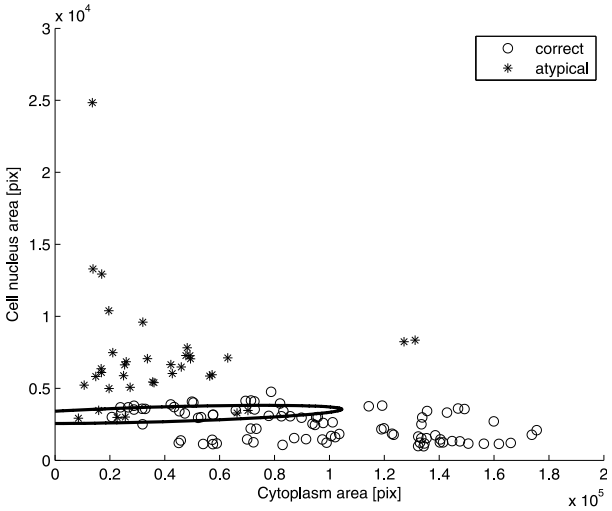

Fig.6. Nuclear-Cytoplasmic Relation and 95% elliptic confidence region for atypical cells from boundary region - 10% movement of areas

Discussion

Correct cell nuclei are not correlated with cytoplasm area. Atypical cell nuclei have correlation between cell nucleus and cytoplasm area, but the relation cannot be reliably inferred, because the number of cases is rather low.

There are two subpopulations of atypical cell nuclei. The first population is characterized by the large cell nucleus area (>5000 pixels) and is not overlapped with correct cell nuclei population. This is very important result that could be used for the formulation of the inferring rule. There are 6 cases of atypical cells that have medium cell nucleus area (<5000 pixels). This subpopulation is located on the border of the correct cells population and should be considered separately. The area of the subpopulation could be marked using elliptic confidence region and the 95% value is assumed. There are 16 correct cells that are inside this region and should be examined carefully as atypical cells.

The results for 5% and 10% movements of areas are shown in Fig.5 and Fig.6 respectively. There are 21 and 16 of correct cells nuclei inside the region. The number of tested cases for the second test should be extended by 11 cases that are over this region, so there is 27 finally.

Changes of areas for NCI gives 16 and 18 cases of atypical cells nuclei is common area with correct cells nuclei (5% and 10% movement respectively). The first case corresponds to necessary testing of 17 and all correct cells nuclei. The second cases are important especially because for selected bins of histogram with 0.05 resolution NCI cannot be applied.

Conclusions

Analysis of Papaniocolaou smears is possible using NCI and NCR, but the sensitivity of the segmentation algorithm is very important. The particular segmentation algorithm is not considered in this paper, but the tests of sensitivity is provided for manually segmented images. Conventional techniques of analysis (NCI) could be applied, but for well segmented images only. Poor quality images will influence the segmentation, so the number of correct cells considered for the analysis by cytoscreener will be highly increased.

NCR has lower sensitivity on the segmentation problems that was shown in this paper and is recommended, but both techniques have problem of the cytoplasm segmentation that is very difficult due to cells overlapping in clusters. Modern techniques based on the analysis of the texture of nonrectangular objects (cell nuclei) are very important [13,14,15] due to higher contrast between cell nucleus and cytoplasm (contrast between cytoplasm and background is rather low). Such estimators are related to the single cells, but cell structures analysis is possible using computer analysis of images [16].

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