



Proceedings

PS02.11 | ePoster Session II

Semi-Automatic And Automatic Ki-67 Index Examination In Whole Slide Images Of Meningiomas

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Introduction/ Background

Histological examination of tissue subjects by immunohistochemical staining is the basic method of recognizing types of cancer and it provides valuable indicators concerning choice of optimal therapy or defining the prognosis. One of a most important markers is the mitotic receptor Ki-67, among others, in meningiomas [1]. According to examination guidelines, ROI's (Region of interest) whose fields correspond with the high positive receptors' reaction should be selected.

Aims

The aim of this paper is a compare of Ki-67 index examination in meningioma specimens performed on the whole slide images(WSI) in two ways: with selection of hot-spot regions by the experts, and with automatic selection of hot-spots. Using both ways we have analyzed variability of results between two experts and between the experts and the automatic procedure, also in respect of Ki-67 level.

Methods

The fifty cases of meningiomas were stained with the ready-to-use FLEX Ki-67 antigen (Dako, code IR626) in Dako Autostainer Link. Acquisition of WSIs was carried out by the 3DHistech Panoramic 250 Flash II scanner under the 20x magnification of lens. The selection of hot-spots was done manually by two experts and automatically with the proposed method of automatic hot-spot detection. The suggested WSI processing scheme was based on the following steps:

- defining the map of specimen using the thresholding procedure and morphological filtering,
- eliminating the areas containing blood cells (hemorrhages) by the texture analysis (Unser features) and classification,
- eliminating the specimen folds by the texture analysis (Unser and Local Binary Patterns) and classification,
- selecting sequential fields of the hot-spots based on cells segmentation and the punishment function to avoid excessive proximity, and it is the extension of idea presented in paper [2]. The final analysis of Ki-67 index was performed on the full resolution images with the same procedure of image analysis.

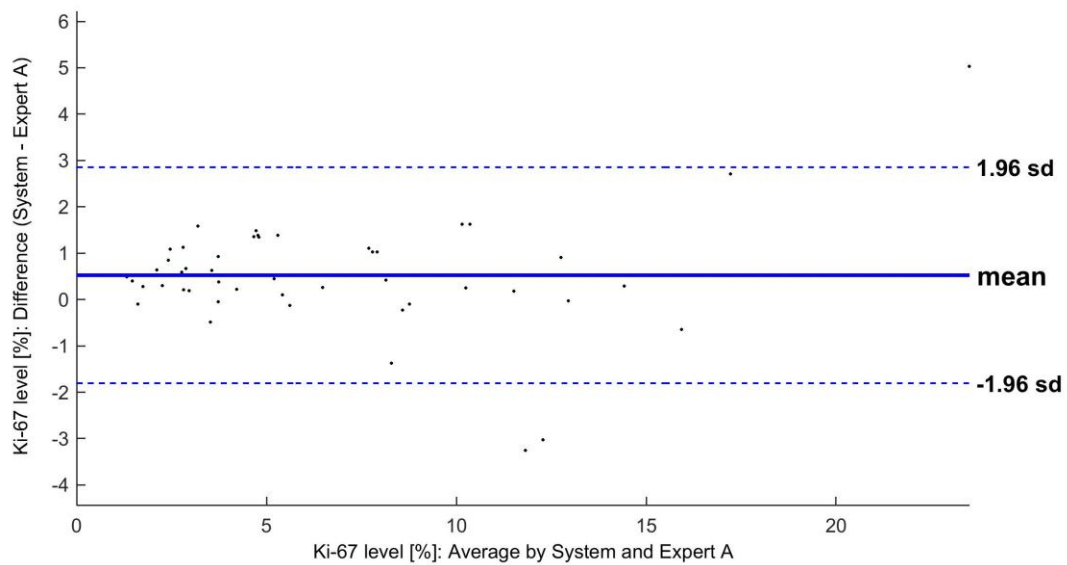
Results

The results indicated that the mean difference between the Ki-67 index of Expert A and Expert B was -0.6065% (SD \pm 1.27%). Comparison between the results of Automatic system and Expert A gives mean difference 0.5207% (SD 1.18%) whereas in relation to the Expert B, it was -0.0858% (SD 1.21%). No significant skewness was observed in any of Bland-Altman plots.



The determination analysis gives R^2 equals 0.947 (Expert A to Expert B), 0.947 (System to Expert A), and 0.944 (System to Expert B), all $p < 0.000001$. The automatic procedure for the hot-spot detection in meningioma WSI gives the high concordance of results with the expert's examinations. The differences between the automatic and both experts' results are included in the range of variability of experts' results. The presented results confirm that the proposed automatic procedure can be introduced to the multicenter verification process for practical applicability in histopathological diagnosis in the near future.

This work has been supported by the National Centre for Research and Development (PBS2/ A9/21/2013 grant), Poland.



References:

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