Hot-spot Selection and Evaluation Methods for Whole Slice Images of Meningiomas and Oligodendrogliomas

Z. Swiderska*, T. Markiewicz*,†, B. Grala†, J. Slodkowska†

†Department of Pathomorphology , Military Institute of Medicine, Warsaw, Poland

*Warsaw University of Technology, Warsaw, Poland

Corresponding address: Warsaw University of Technology, Dept. of Electrical Eng, Pl. Politechniki 1, 00-661Warsaw, Poland, Tel.+48 22 234-72-17, e-mail: swidersz@ee.pw.edu.pl

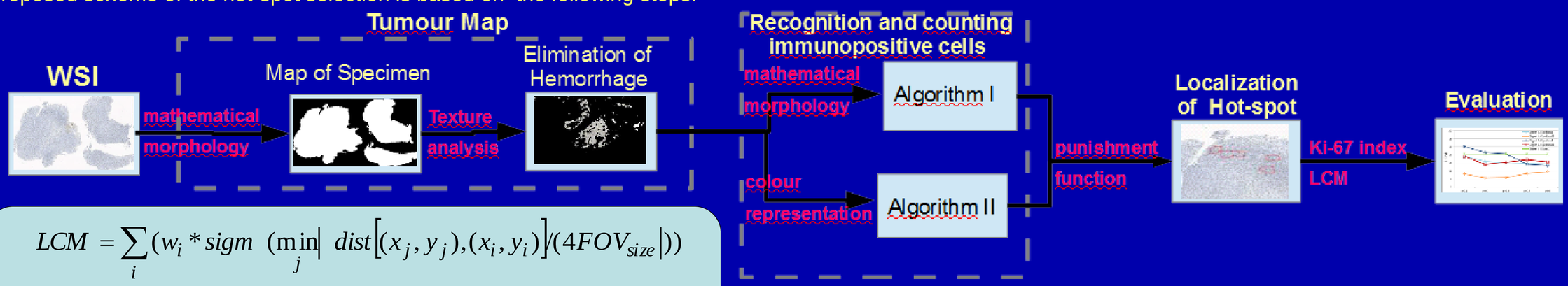
Background

The quantitative examination of histological tissues subject to immunostain tests is a basic method of tumuor recognition, of the optimal therapy choice, and of the prognostic indicators definition. One of the most important marker is the proliferation marker Ki-67/MIB-1 in central nervous system tumours. The quantitative evaluation of tumor proliferation is based on the selection of a set of high power fields of view. For each of them, the immunopositive cell nuclei marked with a brown color and immunonegative cell nuclei marked blue have to be counted to establish the Ki-67 index.

In routine diagnostic practice, representative hot-spot areas are manually selected by histopathologists. The selected fields should represent the areas of the high Ki-67 index, but also different tumor localizations. In this paper we propose and apply the mathematical morphology-based algorithms to estimate the number of immunopositive cells and the selection of high Ki- 67 fields. The additional problem in the whole slide examination is also the occurrence of areas of hemorrhages. Therefore, there is a need to differentiate them from the areas of tumor proliferation. Based on the texture analysis and classification, we eliminate hemorrhages from the specimen map. Finally, to diversify the selected localizations we propose the artificial model of this process with a penalty function to increase spatial distribution of the hot spots. The measure of concordance between the manually and automatically selected hot spot fields was also proposed.

Methods

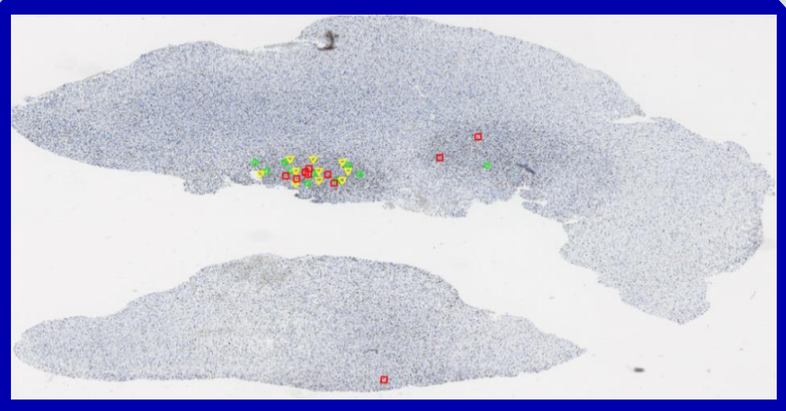
The fifteen cases of meningiomas and oligodendrogliomas subject to Ki-67/MIB-1 immunohistochemical staining were obtained from the archives of Department of Pathomorphology, Military Institute of Medicine in Warsaw, Poland. Acquisition of the whole slide images (WSI) was performed on the Aperio ScanScope scanner. Due to very large size of images, we have chosen eightfold reduction of the resolution to enable the evaluation performed both manually and by computer. The proposed scheme of the hot-spot selection is based on the following steps:

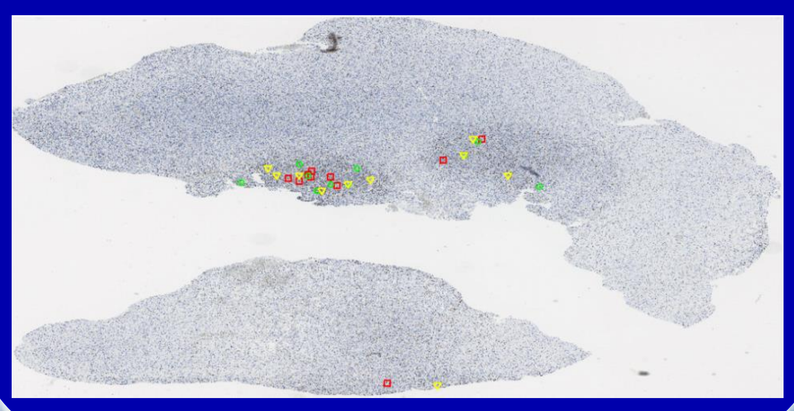


$$LCM = \sum_i (w_i * sigm\ (\min_j |\ dist[(x_j, y_j),(x_i, y_i)]/(4FOV_{size}|))$$

$$where: \quad w_i = \frac{L_{E_i}}{\bar{L}_E}$$

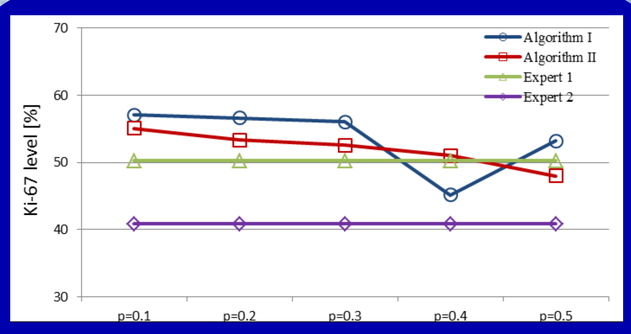
For the purpose of hot-spot selection localization evaluation of by the algorithms in respect to the expert's results, the localization concordance measure (LCM) was proposed. The LCM allows for the evaluation of the correctness of hot spot fields choice. Low value of the LCM testifies to similar hot-spots localization selected by algorithm to expert's result, e.g. represents this same tumour area.

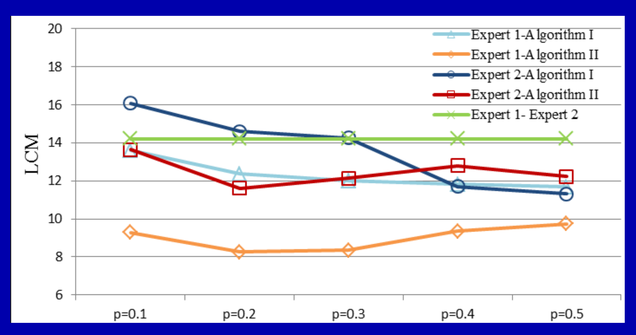




◄ Fig.1. Virtual slide presenting the exemplary hot-spot selection marked by the Expert 1 (□), and hot-spots designated by the algorithms (Algorithm I-○,Algorithm II-Δ) for different values of penalty factor.

▼Fig.2. The results of a penalty factor influence analysis, to the Ki-67 level (A) and LCM (A) for one case.





ID	Ki-67 %			LCM	
	Expert	*Algorithm I*	*Algorithm II*	*Expert-Algorithm I*	*Expert-Algorithm II*
1	15.79	19.67	20.72	9.70	12.12
2	50.24	56.60	53.35	12.36	8.27
3	41.09	50.37	42.32	5.41	7.36
4	25.82	35.01	33.24	9.00	6.89
5	17.52	21.74	21.94	3.23	3.26
6	26.45	24.86	27.25	4.77	4.27
7	11.16	12.25	12.81	5.92	8.26
8	22.36	22.48	26.24	9.76	6.71
9	69.72	71.48	70.62	4.00	3.40
10	22.87	22.05	24.85	3.87	2.95
11	48.96	44.86	48.02	8.29	6.18
12	18.93	20.81	22.65	7.61	8.52
13	32.58	33.23	33.19	3.17	3.84
14	11.53	11.24	13.38	6.48	6.73
15	3.06	3.85	4.94	7.29	7.66
Mean:	27.87	30.03	30.37	6.72	6.43

▲Table 1. The results of quantitative analysis of Ki-67 index and LCM in the designated fields of view for the hot-spot areas selected by the expert and by the developed algorithms (algorithm I and algorithm II).

Results

Studies were conducted for fifteen cases of meningiomas and oligodendrogliomas. By the presented algorithms, we have determined twenty hot-spot fields in each scan and made their diagnostic evaluation by the quantitative analysis. The exemplary hot spot selection are presented in the Fig. 1 with respect to an expert's result.

The analysis of a penalty factor influence on the Ki-67 level and variability, and LCM for one case is presented in Fig.2. The analysis of the selection of 20 hot-spot fields in fifteen investigated cases was performed (Table 1). Both developed algorithms give higher Ki-67 result than expert's result. The LCM comparison shows that fields selected by algorithm I and algorithm II reflect the tumour area selected by the expert. Our results have confirm the advantage of automatic evaluation over the manual assessment.

Conclusion

We have presented the effective method for an automatic localization of the hot-spot areas based on penalty factor in meningioma and oligodendrogliomas tumours. Two different approaches have been suggested.

Fields selected by both developed algorithms had higher Ki-67 level than fields selected by the expert, but the localization was similar. In the case of manual selection of hot-spot areas by an expert, the considerable variability can be observed. The algorithm II has shown the advantage over the algorithm I in accurate detection of hot-spot areas. We conclude, that the algorithm II is more independent of colour intensity of immunohistochemical staining. The use of presented algorithms allows for hot-spot fields selection with high Ki-67 index from miscellaneous localizations. Thanks to this, we can evaluate different tumour areas.

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