Postograduate student: **Louis Papageorgiou**

Thesis Tiltle:

Computer aided diagnosis of histopathological images in microscopy

Abstract

The objective of the present thesis is the study and development of a system which receives, processes and analyses histopathological microscopical images, to assist/support the diagnosis of endometrial cancer. From the current available literature, no other study has been found with regard to the quantitative analysis of histopathological images related to endometrial cancer. Similar studies, regarding complete systems of histopathological image classification, concern other types of cancer. The structure of the implementation is divided into five basic procedures.

The first one concerns the digitation of available biopsies of endometrial cancer. The biopsies were processed by staining with Hematoxylin-Iosin to assess the grading of the tumor and immunohistochemically for the expression of the oncogene cerb-B. We have digitized 17 biopsy / incidents involving different patients, from which 117 digital histopathologic microscopical images were taken. The histopathological image sample was taken using an optical microscope and an integrated camera.

The second procedure concerns the processing of histopathological microscopical images by segmenting the region of interest (ROI). The ROI is defined as the expressed nuclei that where colored brown. With a combination of techniques, the system is able to predict and distinguish ROIs that conceal two or more adherent nuclei.

The third procedure involves the feature extraction stage. We extract 24 features, of which 18 are textural features and the other 6 are morphological features. Textural features were calculated based on the gray level co-occurrence matrix and the gray level run length matrix.

The fourth procedure concerns the implementation of the pattern recognition system. For the features selection stage, the Kruskal-Wallis statistical test and a linear regression method were employed as non optimal techniques. The exhaustive search method was also utilized as the optimum feature selection technique. For the classification stage, a variety of classifiers were tested such as the Minimum Distance (MDC), the k-Nearest Neighbor (K-NN), the Least Squares Minimum Distance (LSMDC), the 'Linear Bayes (LBC) and the Probabilistic Neural Network (PNN). The classification task was to characterize an image into three grades of endometrial cancer (grade I, II, or III). Apart from the classical implementation of the pattern recognition system of choosing the best classifier, methods of implementation combining classifiers ‘ensemble classification schemes’ were proposed, using combinatorial techniques and decision rules ‘majority rules’.

The last procedure concerns the evaluation of the techniques and algorithms which have been proposed. Comparing the results, the best technique which the system implementation proposes, is selected. For the best estimation of the parameters, methods of iterative

sampling techniques were used, such as ‘leave one out’ and ‘external cross validation’.

Best classification algorithm was found the PNN that gave 94% of correct classification when non optimal feature selection method were employed. The PNN scored around 96% overall accuracy employing the ‘exhaustive search‘ and the ‘leave one out’ methods. The proposed image analysis system proved capable of classifying a ‘new’ image with an average accuracy of 82% employing the ‘external cross validation’ method. Results are promising for the development of such system and with some modest modifications might be suitable for application in a clinical environment.

SUBJECT AREA: Digital image processing , Pattern Recognition

KEYWORDS: Image Processing, Image Segmentation, Texture features, Morphological features , Features selection, Pattern Recognition, Endometrial cancer, Oncogene cerb-B, Optical microscope, Histopathological image

Examining Committee:

Phd. Dionisis Cavouras, Professor, Department of Medical Instruments Technology, TEI-A (thesis advisor)

Phd. Manolis Sangkriotis, Associate Professor, Dept. of Informatics and Telecommunications, UoA

Phd. Spyridon Kostopoulos, postdoctoral researcher