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# Proceedings

## SY08.06 | **Image Analysis II**

# Micrometastasis Detection Guidance by Whole-Slide Image Texture Analysis in Colorectal Lymph Nodes

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### *Introduction/ Background*

Cancer is a disease that affects millions worldwide and accurate determination of whether lymph nodes (LNs) near the primary tumor contain metastatic foci is of critical importance for proper patient management. Histopathological evaluation is the only accepted method to make that determination. However, the current standard of care only examines a single central histological section per LN and yields an unacceptable false-negative rate.

### *Aims*

To help pathologists in their examination we propose a method that extracts textural features from histopathological LN whole slide images (WSI) and then applies support vector machines (SVMs) to automatically identify regions suspicious for metastatic foci.

### *Methods*

The database consisted of WSI from 44 LNs. Sections were stained with hematoxylin-eosin and examined at 20x (0.45µm resolution). Twenty-eight of the LNs were identified by an expert pathologist as positive for cancer (P), and the remaining sixteen were negative (N). This database was divided into two groups. Group 1 (15P and 5N) was used for training and Group 2 (13P and 11N) was used for testing the classification technique. For all analysis each WSI was divided into non-overlapping 1000 x 1000 pixel sub-images that will be referred to as high-power fields (HPFs). For each LN in Group 1, at least one WSI was annotated by a pathologist to identify rectangular, HPF-scale regions as locally cancerous or locally non-cancerous. From these annotated slides, 924 HPFs (462 P and 462 N) were obtained. For each of these HPFs, statistical features based on gray-level co-occurrence matrices [1] and Law's texture energy measures [2, 3] were extracted from 9 derived images [4]. The extracted features were submitted to a sequential forward selection (SFS) method [5] to select few non-redundant features providing best class separation (cancerous vs. non-cancerous region). Combinations of the selected features were tested on the 924 HPFs using k-fold cross-validation to find those that produced the best results and consequently to train our SVM-based classifier. In Group 2, WSI were not annotated for cancerous and non-cancerous zones on a HPF scale. Each LN, however, had been labeled by a pathologist as positive or negative for cancer. For each WSI, each section was divided into contiguous HPFs, and those which mainly contain fatty tissue, background, and tears were automatically excluded. Each selected HPFs was classified as cancerous or non-cancerous using the previously trained classifier to obtain the total number of cancer-classified per LN. A receiver operating characteristics (ROC) curve was traced by changing the discriminator threshold (T) used to label the LN as P for cancer as a function of the total number of cancer-classified HPFs.

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## Results

During training, 5 Laws features were selected by SFS. Highly satisfactory k-fold cross-validation with a F-score of 0.996 ± 0.005 was obtained using only 2 statistical features computed at different scales. The ROC curve obtained by applying the SVM-classifier to the test set is shown in the next figure. Two valuable operating points can be identified which both guaranteed no false-negative. At T=11 we got 2 false-positives and an optimal F-score of 0.917, and with a more conservative approach, T=1, we got 7 false-positives and a F-score of 0.759. The top-left part of the slide displayed in next figure would have been proposed to the pathologist as the most suspicious region of the cancerous LN.

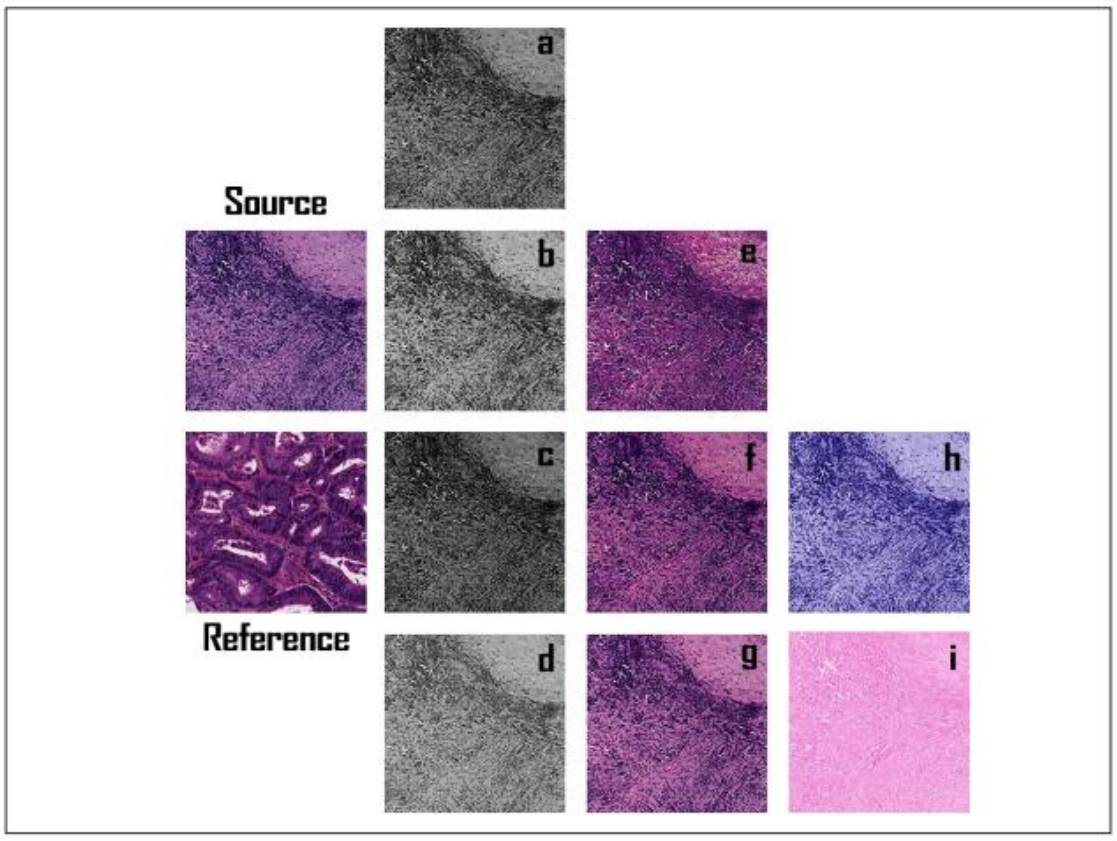


*Figure 1: Derived images obtained from the source. Reference image is used in color normalization methods. a) Intensity; b-d) RGB Channels; e-g) Color normalization methods (RGBHist, Reinhard and Macenko); h-i) Color Deconvolution Stains (Hematoxylin & Eosin).*

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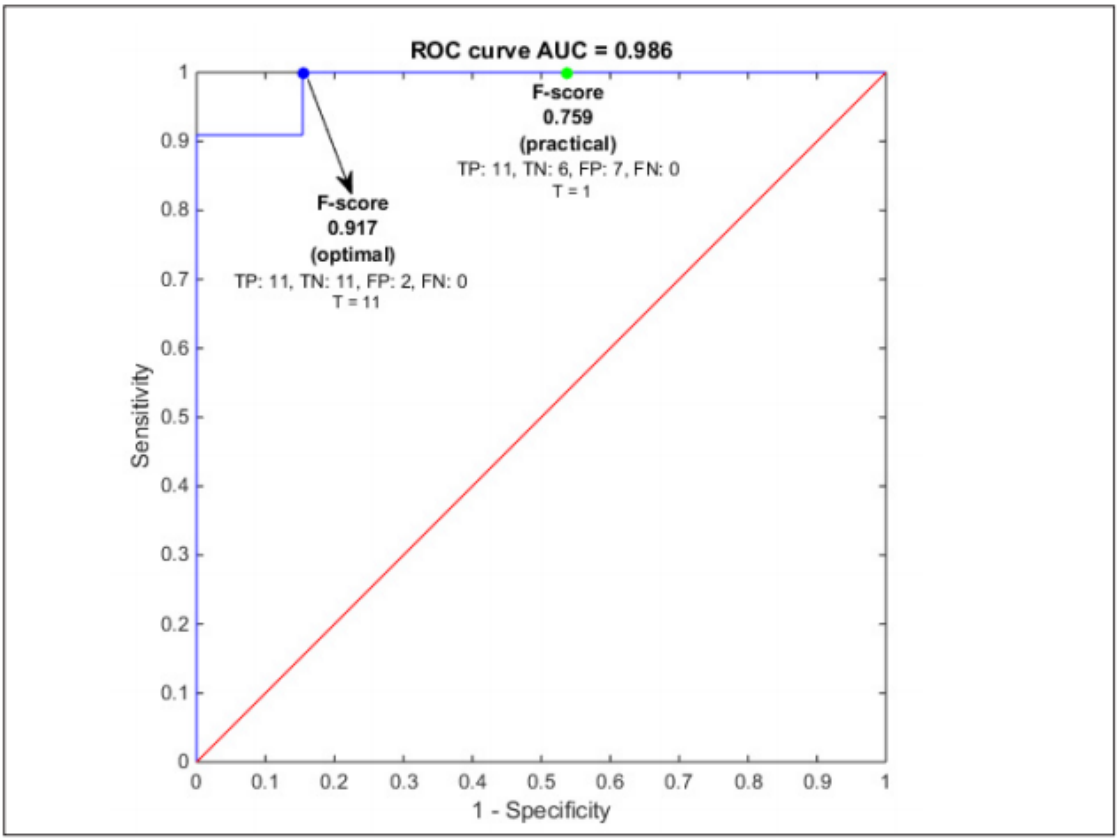


*Figure 2 : ROC curve and its Area Under the Curve (AUC). The blue and green points are respectively the optimal operating point (0.917 F-Score, 2 False Positive) and a more conservative choice (0.759 F-Score, 7 False-Positive). T is the discriminant threshold.*

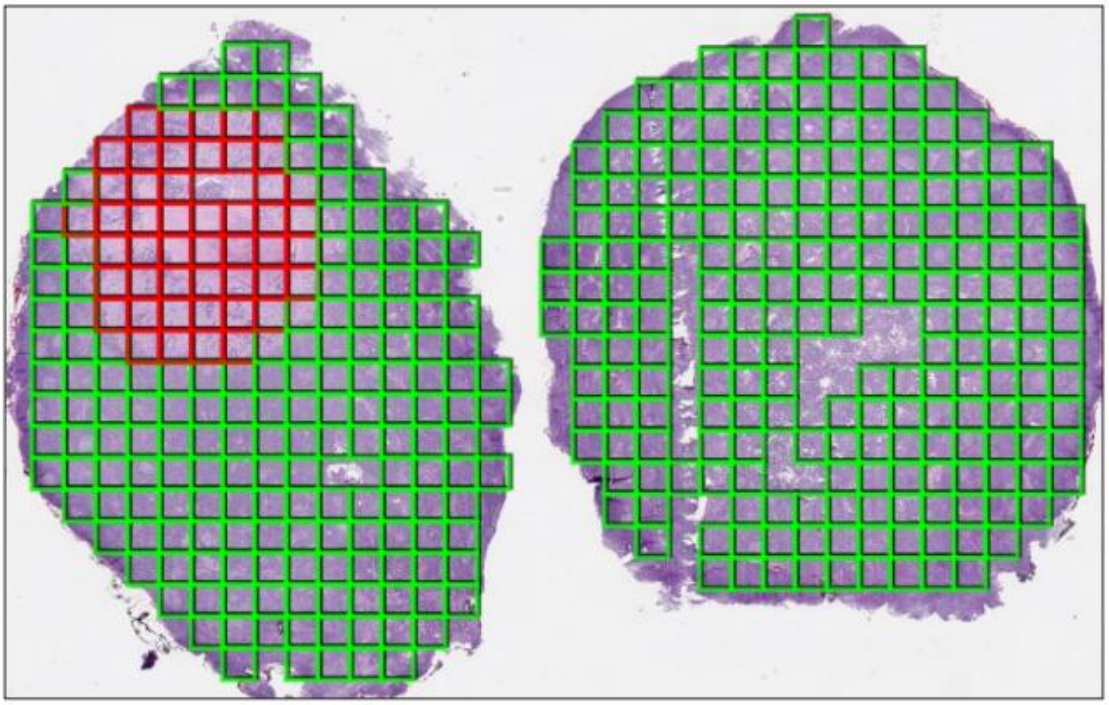

*Figure 3: Example of a test positive LN which was classified as positive and the classification at the HPF level.*

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