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## Comparison of a Classification Software based on Image Retrieval with the Off-Line Diagnosis of Expert Endoscopists for probe-based Confocal Laser Endomicroscopy (pCLE) of Colorectal Polyps

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**BACKGROUND AND AIMS** pCLE (Cellvizio, Mauna Kea Technologies) enables *in vivo* microscopic imaging of the epithelium in real-time during ongoing endoscopy. An image retrieval software prototype for automatic classification of pCLE images, recently developed to assist the endoscopists in the *in vivo* pCLE diagnosis of colorectal polyps, has the great potential of decreasing inter-observer agreement while increasing diagnostic performance of endoscopists. This study aims at comparing the performances of the classification software with the performance of pCLE diagnosis established off-line by expert endoscopists. **METHODS** Intravenous fluorescein pCLE imaging of colorectal lesions was performed on patients undergoing surveillance colonoscopies, followed by polypectomies. Histopathology was used as gold standard for the differentiation between neoplastic and non-neoplastic lesions. The pCLE sequences, recorded for each polyp, were analyzed off-line by 2 expert endoscopists, blinded to the endoscopic characteristics and histopathology. These pCLE videos, along with their histopathology diagnosis, were used to train the classification software which is a content-based image retrieval technique followed by *k*-nearest neighbor classification. All evaluations were performed using leave-one-patient-out (LOPO) cross-validation to avoid bias. **RESULTS** 135 colorectal lesions, including 6 serrated adenoma cases, were imaged in 71 patients. Based on histopathology, 93 of these 135 lesions were neoplastic and 42 were non-neoplastic. No statistical significance was found for the difference between the performance of software classification (accuracy 89.6%, sensitivity 92.5%, specificity 83.3%, using LOPO) and the performance of off-line diagnosis of pCLE established by the expert endoscopists (accuracy 89.6%, sensitivity 91.4%, specificity 85.7%). The 95% confidence intervals for equivalence testing ( $-0.073$  to  $0.073$  for accuracy,  $-0.068$  to  $0.089$  for sensitivity,  $-0.18$  to  $0.13$  for specificity) are sufficiently small to suggest statistical equivalence. The  $-0.18$  lower bound for the specificity should be sufficient if the classification software is only taken as a second-reader tool to support pCLE diagnosis. **CONCLUSIONS** The image retrieval software for automatic classification of pCLE sequences of colorectal polyps achieves a high performance which is statistically comparable to that of off-line diagnosis of pCLE sequences established by expert endoscopists. A fortiori, the classification software should be useful, not only to train non-expert endoscopists, but also to assist any endoscopist in *in vivo* pCLE diagnosis. **DISCUSSION** The proposed software is not a “black box” but an informative tool based on the query by example model that produces, as intermediate results, visually similar annotated pCLE videos directly interpretable by the endoscopist.

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**Table 1.** Performance comparison between automatic software classification and off-line expert diagnosis of pCLE sequences, for the differentiation between neoplastic and non-neoplastic colorectal polyps. TP, TN, n, n1 and n2 successively indicate “true positives”, “true negatives”, “number of pCLE sequences”, “number of neoplastic pCLE sequences” and “number of non-neoplastic pCLE sequences”.

	(1) Automatic Software Classification (LOPO)	(2) Off-line Expert Diagnosis of pCLE
Accuracy		
%	89.6	89.6
(TP+TN)/n	121 / 135	121 / 135
Sensitivity		
%	92.5	91.4
TP/n1	86 / 93	85 / 93
Specificity		
%	83.3	85.7
TN/n2	35 / 42	36 / 42
Statistical significance between (1) and (2)		
McNemar's test, alpha=0.05		
Accuracy: ( <i>P</i> , power)		(not significant, 2.5%)
Sensitivity: ( <i>P</i> , power)		(not significant, 6.5%)
Specificity: ( <i>P</i> , power)		(not significant, 5.2%)
Statistical equivalence between (1) and (2)		
Two-sided Z-test		
95% CI for Accuracy		-0.073 to 0.073
95% CI for Sensitivity		-0.068 to 0.089
95% CI for Specificity		-0.18 to 0.13

**Figure 1.** Typical result of automatic retrieval of pCLE video sequences, represented by mosaic images and annotated with their histopathology diagnosis.

