Autofluorescence imaging in colonoscopy

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Summary

Contemporary colonoscopy faces the challenge of quite significant adenoma miss rates with serious impact on potential appearance of interval colorectal cancer. The meticulous withdrawal technique is met by new technologies – especially the concept of trimodality imaging – a combination of wide-angle, high resolution white light endoscopy, narrow band imaging and autofluorescence imaging. The latter technique is described and a literature review on this topic and first hands-on experience are presented. In routine practice autofluorescence imaging can be effectively used for proper identification of neoplastic lesions, especially of flat/diminutive ones.

Key words: *autofluorescence imaging, colonoscopy, narrow band imaging, trimodality imaging, light induced fluorescence endoscopy imaging*

Souhrn

Autofluorescenční zobrazení v koloskopii

Současná koloskopie se potýká s významným počtem přehlédnutých lézí s vážným dopadem v možném výskytu karcinomů v krátkém intervalu po vyšetření. Pečlivé prohlížecí technice jdou vstříc nové technologie – zvláště koncept trimodálního zobrazení - kombinace širokoúhlé endoskopie v bílém světle s vysokým rozlišením, zobrazení typu „narrow band" a autofluorescenční zobrazení. Popisujeme poslední jmenovanou techniku, poskytujeme literální přehled a první vlastní zkušenosti. V rutinní praxi může být autofluorescenční zobrazování použito pro správnou identifikaci neoplastických lézí, především plochých a malých.

Klíčová slova: *autofluorescenční zobrazení, koloskopie, narrow band imaging, trimodality imaging, light induced fluorescence endoscopy imaging*

Despite the fact that the story of endoscopy dates back to the middle of the 20th century we are still witness to incredible progress in this field. The spread of endoscopy to all parts of gastrointestinal tube (double balloon endoscopy, [6]) goes arm in arm with focusing on tiny mucosa details (confocal laser endomicroscopy, [7]).

There is no doubt that colorectal carcinoma is the main enemy on the colonoscopy front – relatively slow progression from precursors and early malignant lesions gives us an opportunity for cancer prevention and early diagnosis [18]. Our diagnostic efforts are aimed at better detection, identification and staging of lesions. The adenoma and carcinoma detection rate is limited either by the proportion of mucosa visualised during endoscopy or by the low visibility of flat, isochromatic and small lesions [10]. The endoscopist is able to overcome these limitations by means of a meticulous withdrawal technique and by using chromo-endoscopy. His efforts are met by endoscopy improvement – either high-resolution wide-angle endoscopes with magnifying, or techniques of "virtual chromo-endoscopy" (NBI – narrow band imaging Olympus or FICE – Fujinon intelligent chromo-endoscopy). And there are another motives for progression: "Classic" colonoscopy is driven to focus on tiny mucosal details also by means of "competitive" methods, e.g. virtual colonoscopy. Furthermore every new function of the endoscope advances the value of the instrument and is thus important in competition between endoscopic instrument manufacturers. There are several new technologies in addition to that mentioned above [2]: Raman spectroscopy, light-scattering spectroscopy, optical coherence tomography and among them autofluorescence endoscopy is reaching past the borders of clinical practice. The concept of so-called trimodality imaging (endoscopic trimodality imaging – ETMI) is at stake: wide angle high-resolution white light imaging (high resolution endoscopy – HRE), narrow band imaging (NBI) and autofluorescence imaging (AFI) in one endoscope.

AUTOFLUORESCENCE

The impact of excitatory radiation (e.g. illuminate light) generates radiation of a longer wavelength than the excitatory one in the substance (e.g. bowel mucosa). This phenomenon is named fluorescence. In the case of human tissue, it can be induced by some extrinsic substance (e.g. 5-aminolevulinic acid) or it is spontaneous property of tissue – we then call it autofluorescence. This natural tissue fluorescence is caused by endogenous fluorophores (collagen; flavins – riboflavin, flavin mononucleotide, flavin dinucleotide; reduced nicotinamide adenin dinucleotide, and dinucleotide phosphate; porphyrins etc.) while illuminated by ultraviolet or short-wavelength visible light (blue light). Patho-

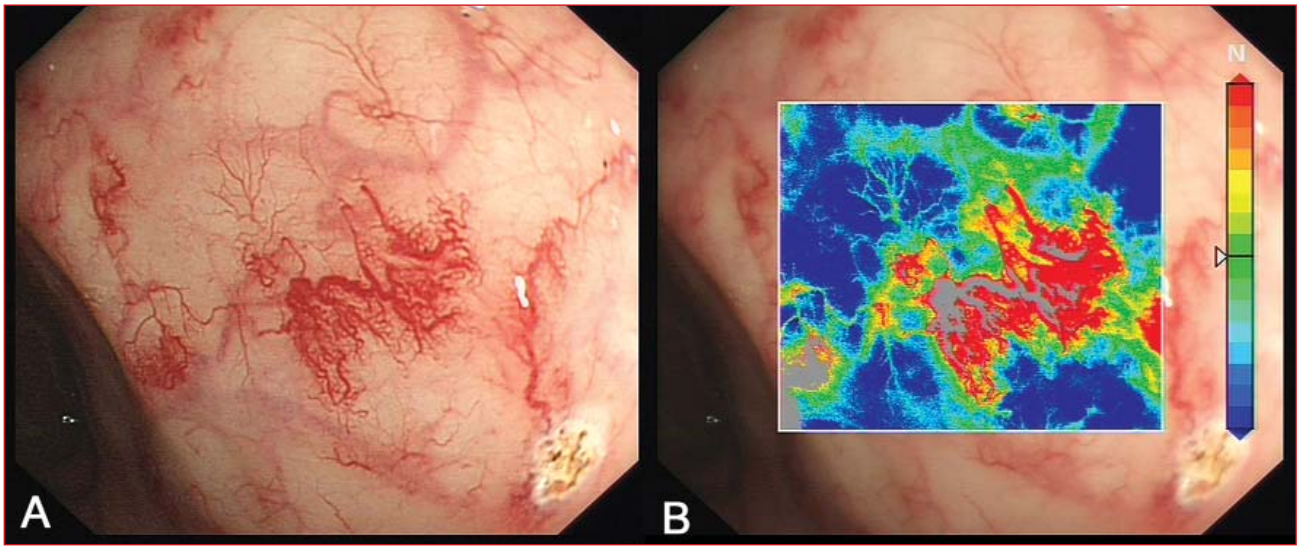

Fig. 1.
Postradiation proctitis in a 70-year old man with prostate cancer (A). Enhanced pathologic vascularisation using the indices of haemoglobin colour chart function (B).

logic mucosal tissue is probably specified not only by different concentration and distribution of these fluorophores but also by changed tissue architecture and blood perfusion (haemoglobin has absorption capability for green light) [2,11]. All these factors lead to decreased autofluorescence in adenomatous tissue – masking of submucosal collagen by mucosa thickening and replacement of submucosa by cancer cells seems to be the major mechanism [5]. This principal results in various medical implications: identification of atherosclerotic arteries, carious teeth and neoplastic tissue in the respiratory and gastrointestinal tract.

SYSTEM OF AUTOFLUORESCENCE IMAGING

The principle described above came into practice named LIFE imaging system (light-induced fluorescence endoscopic imaging) characterised by blue-light excitation with dual-channel (green and red) detection of tissue autofluorescence in real time. From 3 main commercial prototypes - LIFE-GI, Xillix Technologies Corporation, Canada; D-Light system, Karl Storz, Germany and Auto-Fluorescence Imaging (AFI), Olympus Optical Corporation, Japan – only the last one has been developed to be used in videoendoscopes.

The AFI system consists of a light source, processor (Olympus EVIS LUCERA), videomonitor and videoendoscope (Olympus CF type FH260AZL/I). The endoscope is equipped with 2 charged coupled devices (CCDs) – one for white-light imaging (140° wide angle optics equipped with mechanical 100× magnifying facility), the other with special filters for the autofluorescence mode. Insertion of this particular endoscope can be facilitated by using the variable stiffness function and by integration with the endoscope position detection system (UPD – ScopeQuide). The final AFI picture is a pseudocoloured composition of autofluorescence and green reflection images – magenta (purple-blue) indicates neoplasia on green non-neoplastic background. Blood and vessels are dark green or black, ulcerations and erosions are purple (due to the damaged submucosal layer). A quite weak autofluorescence signal has to be captured for a longer time and electronically amplified – this causes limited resolution, longer refresh rate and thus lower overall quality of the image as compared with standard white light endoscopy. Real-time white-light (WL), narrow band (NBI) and autofluorescence (AFI) modes can be changed between each other by simply pushing a switch on the endoscope control section, processor or keyboard, the change itself lasts approximately 3 seconds, during which the image is frozen.

Another additional function of the Olympus EVIS LUCERA system is the indices of haemoglobin (IHb) colour chart function, enhancing the vascular pattern (see Fig. 1) [4].

CLINICAL IMPACT OF AUTOFLUORESCENCE IMAGING IN COLONOSCOPY

A Netherlands research group proposed the term ETMI (endoscopic trimodality imaging) as a combination of HRE (high resolution white light imaging), AFI (autofluorescence imaging) and NBI (narrow band imaging). These authors found no difference in a prospective study of 100 patients between autofluorescence and white light imaging in detection of adenomas. Not surprisingly sequential use of both methods gained 30 % of detected adenomas. Adding of AFI to the NBI pit pattern identification improved sensitivity for identification of adenomas as compared with histology [15]. In contrast, 2 Japanese

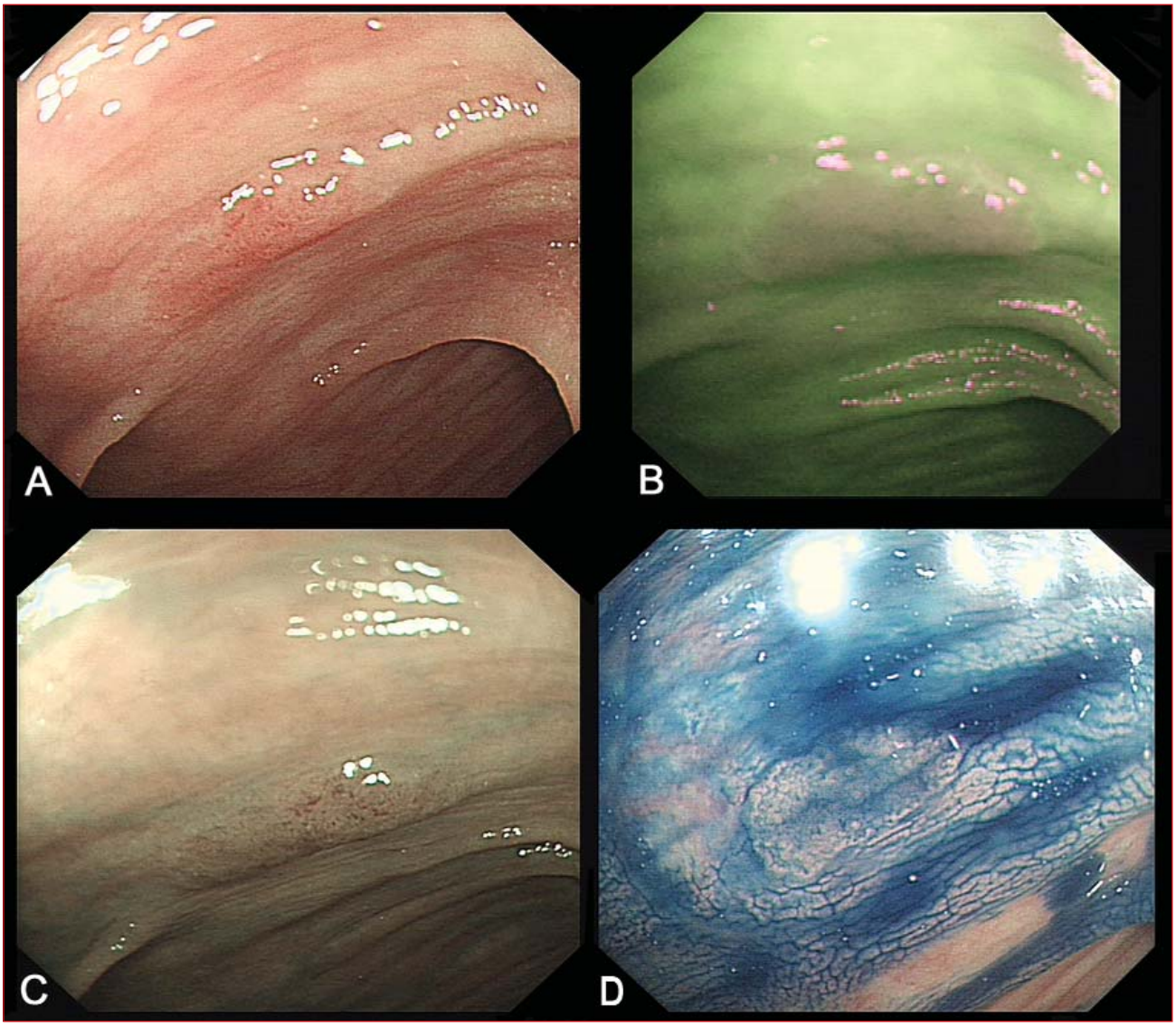

Fig. 2.
Flat neoplastic lesion type 0-IIa in a 75-year old women, histology: tubular adenoma with low grade dysplasia. A – white-light, B – autofluorescence, C – narrow band imaging, D – indigo carmine chromo-endoscopy.

groups of authors found autofluorescence imaging potentially superior to white light imaging in prospective studies (167 patients [8] and 64 patients [12] examined by modified back-to-back technique) especially for flat and/or diminutive lesions. The Netherlands group also studied the additive value of AFI to NBI pit pattern analysis for accurate diagnosis of neoplastic vs. non-neoplastic lesions. The highest sensitivity for a correct diagnosis is obtained by AFI, the highest specificity by the combined use of NBI-AFI. Overall accuracy was highest by combining NBI + AFI [13,14]. In patients with hyperplastic polyposis syndrome (n = 7) trimodality imaging failed to distinguish between hyperplastic polyps and serrated adenomas, though differentiating with an adenoma is highly possible [1]. The same group analysed the potency of trimodality imaging in patients with longstanding ulcerative colitis. The sensitivity of AFI seemed to be better for detection of neoplastic lesion, but not significantly different because of the small sample size (50 patients). Trimodality imaging showed negative predictive value as high as 94 % (lesion green on AFI never revealed neoplasia) [16,17]. German researchers found AFI equivalent to indigo carmine chromo-endoscopy in the detection of neoplastic versus non-neoplastic polyps with the advantage of simplicity for AFI [3]. The same group found AFI to be a promising tool for proper evaluation of lateral resection margin during endoscopic submucosal dissection [9].

OUR INITIAL EXPERIENCE WITH AUTOFLUORESCENCE IMAGING

We hereby present our first experience with the autofluorescence system described above. The first impression in practice is lower quality of the image in white light mode, including a lot of colour artefacts when the distal end of the endoscope is moving rapidly or in immersion. On the other hand, NBI mode in conjunction with

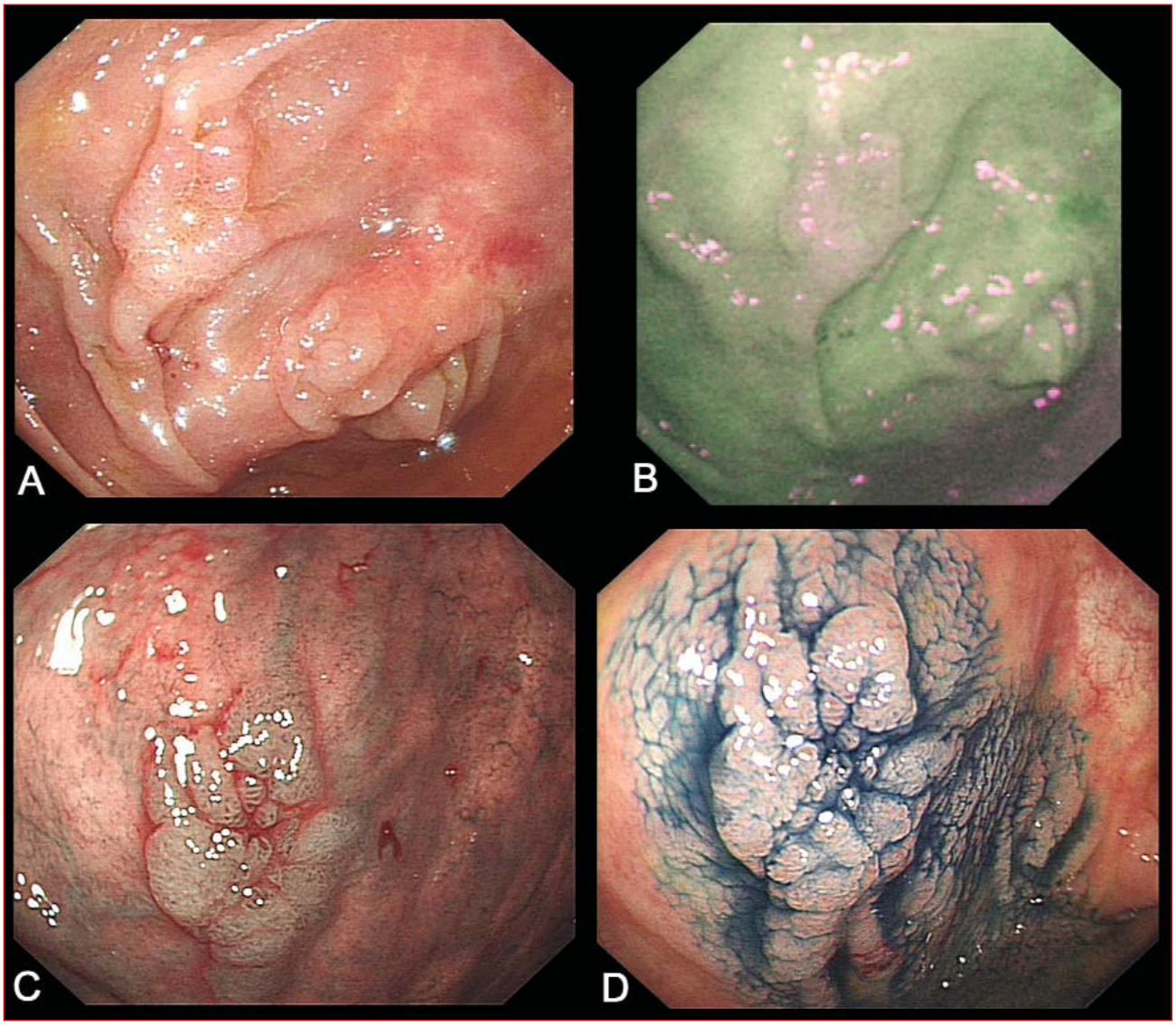

Fig. 3
Flat neoplastic lesion type 0-IIaIIc in a 73-year old man at the dead end of the sigmoid colon after subtotal colectomy for polyposis, histology: tubular adenoma with high grade dysplasia. A – white-light, B – autofluorescence, C – narrow band imaging, D – indigo carmine chromo-endoscopy.

the magnifying function is very effective and allows proper identification of the pit pattern. We used the system during examination of 10 patients and the most interesting images are presented (see Figs. 2,3), including small flat lesions marginally seen in white light imaging, with histologically proven high-grade dysplasia (see Fig. 4).

DISCUSSION

In our opinion increasing the adenoma detection rate by routine use of autofluorescence as a "red flag" method is limited in clinical practice – the back-to-back technique is not feasible for routine use and low resolution autofluorescence imaging cannot replace the gold standard of diligent white light imaging. The above-mentioned literature is also inconsistent in this point.

From our first experience we concluded, that autofluorescence imaging can help in proper identification of lesions, giving quite rapid additional information in case of doubt about the existence or type of a flat lesion (purple neoplastic vs. green non-neoplastic). Sequentially used narrow band imaging with magnification can help proper rating of dysplasia by pit pattern. These observations correspond with contemporary literature. This identification capability is especially important in the case of follow-up endoscopy in patients with longstanding ulcerative colitis.

FUTURE PERSPECTIVES

A significant disadvantage of this particular LUCERA system by Olympus is the lower quality of white light imaging based on black-and-white CCD as compared with the previous EXERA system based on colour CCD. On the other hand, taking into account the speed of progression from AFI fibreoptic endoscopes to much more manageable contemporary AFI videoendoscopes with better image quality, we can await even further improvement. The future lies in improving the resolution of the autofluorescence image,

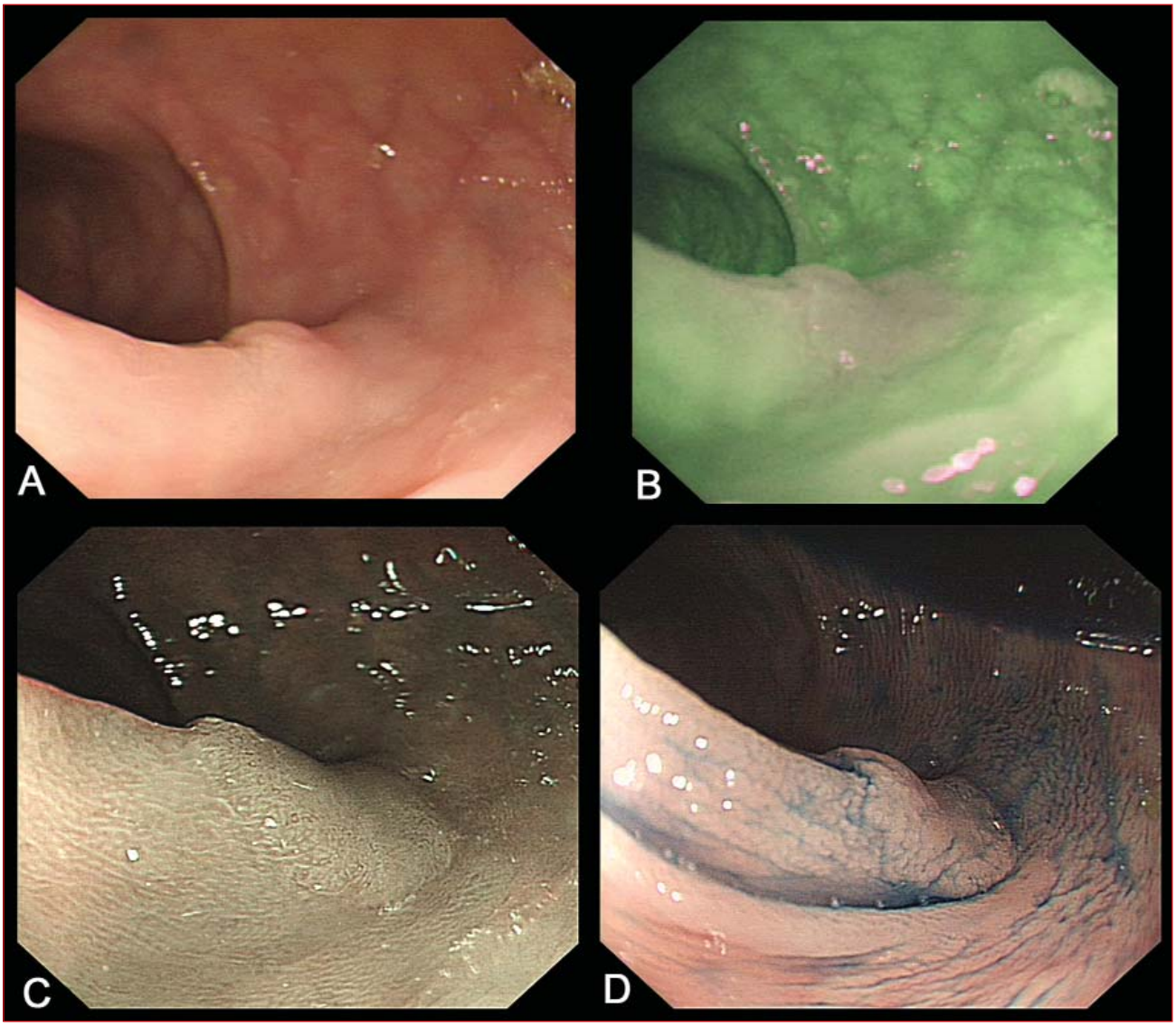

Fig. 4
Flat neoplastic lesion type 0-IIallc in a 59-year old man after resection for colorectal cancer, histology: tubular adenoma with high grade dysplasia.
A – white-light, B – autofluorescence, C – narrow band imaging, D – indigo carmine chromo-endoscopy.

maybe also in the simultaneous processing of white light and autofluorescence imaging. Another step might be infrared imaging, also allowing collection of information from below the mucosal surface.

CONCLUSIONS

Optimal colonoscopy is based on these elements: adequate bowel preparation, white-light wide-angle colonoscope, endoscopist with accurate withdrawal technique (at least 6 minutes, removal of virtually all stool remnants and focusing on proximal sides of folds, flexures and valves, in an optimally distended colon) [10].

Whether some additional techniques, although promising – such as autofluorescence imaging – can add significant value to this basis is still questionable. We found the autofluorescence imaging technique feasible for better identification of neoplastic lesions.

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