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

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 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.

自动荧光成像在结肠镜检查中的应用

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摘要
当代结肠镜检查面临着显著的腺瘤漏检率，对癌症出现有重大影响。精细的检查技术受到新科技的挑战——尤其是三模态成像的概念——即宽角度、高分辨率白光内镜检查、窄带成像和自动荧光成像。该技术得到了描述，并对其进行了文献回顾，以及初步的临床经验。在常规实践中，自动荧光成像可以有效用于区分恶性病变，尤其是平坦/微小的病变。

关键词：自动荧光成像，结肠镜检查，窄带成像，三模态成像，光诱导荧光内镜成像

尽管结肠镜检查的故事可以追溯到20世纪中期，我们仍然见证着这个领域的令人难以置信的进步。结肠镜检查在结肠镜检查领域中的主要敌人——相对缓慢的进展从前体和早期恶性病变——提供了癌症预防和早期诊断的机会 [18]。我们的诊断努力旨在更好地检测、识别和分期病变。腺瘤和癌的检测率受到在内镜检查过程中可视化的黏膜比例的限制，或者由于平坦、等色性和小病变的低可见性 [10]。内镜检查者能够通过精细的退缩技术以及使用染色内镜检查克服这些限制。他的努力遇到了内镜技术的改进——要么是带有放大功能的高分辨率宽角度内镜，要么是“虚拟染色内镜技术”（NBI —窄带成像 Olympus 或 FICE — Fujinon智能染色内镜）。还有其他动机促使进步：“传统”结肠镜检查被推向关注于微小黏膜细节的“竞争”方法，例如虚拟结肠镜。此外，内镜的每一项新功能都增加了仪器的价值，因此在内镜仪器制造商之间具有重要性。此外，还有其他新技术，例如 [2]：拉曼光谱、光散射光谱、光学共焦成像和其中的自动荧光内镜检查。其中，自动荧光内镜检查正在超越临床实践的边界。三模态成像（即三模态内镜检查——ETMI）的概念正受到挑战：宽角度高分辨率白光成像（高分辨率内镜——HRE）、窄带成像（NBI）和自动荧光成像（AFI）在一根内镜中存在。
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 tri-modality 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
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...
Autofluorescence imaging in colonoscopy

Folia 2007; 5(3-4)

36

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 fiberoptic 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. 3
Flat neoplastic lesion type 0-IIc 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.
Autofluorescence imaging in colonoscopy 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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References

Fig. 4
Flat neoplastic lesion type 0-IIa in a 59-year old man after resection for colorectal cancer, histology: tubular adenoma with high grade dysplasia.


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