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Quantitative measurements in capsule endoscopy

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ABSTRACT

This review summarizes several approaches for quantitative measurement in capsule endoscopy. Video capsule endoscopy (VCE) typically provides wireless imaging of small bowel. Currently, a variety of quantitative measurements are implemented in commercially available hardware/software. The majority is proprietary and hence undisclosed algorithms. Measurement of amount of luminal contamination allows calculating scores from whole VCE studies. Other scores express the severity of small bowel lesions in Crohn's disease or the degree of villous atrophy in celiac disease. Image processing with numerous algorithms of textural and color feature extraction is further in the research focuses for automated image analysis. These tools aim to select single images with relevant lesions as blood, ulcers, polyps and tumors or to omit images showing only luminal contamination. Analysis of motility pattern, size measurement and determination of capsule localization are additional topics.

Non-visual wireless capsules transmitting data acquired with specific sensors from the gastrointestinal (GI) tract are available for clinical routine. This includes pH measurement in the esophagus for the diagnosis of acid gastro-esophageal reflux. A wireless motility capsule provides GI motility analysis on the basis of pH, pressure, and temperature measurement. Electromagnetically tracking of another motility capsule allows visualization of motility. However, measurement of substances by GI capsules is of great interest but still at an early stage of development.

1. Introduction

Video capsule endoscopy (VCE) has revolutionized imaging of the small bowel. Its exponential clinical use, together with that of the device-assisted enteroscopy, advanced sonographic and other imaging techniques, has led to the accumulation of a broad base of evidence.

Nowadays, the real black box for the majority of clinicians is the computer software used to generate and present capsule videos by selecting relevant images, deriving information from the original images as well as modifying them. The algorithms described in relevant information technology (IT) publications are hardly understandable by medics. To complicate matters further, the majority of proprietary algorithms remain undisclosed. Moreover, many of these approaches have been developed on the basis of few selected video sequences and proof of robustness is often lacking [1]. Nevertheless, several promising approaches for computer based automated image analysis have been developed based on multiple extraction methods, modifiers, and classifiers allowing quantitative measurements and machine learning [2].

VCE has further been transformed from small bowel visualization tool to a panenteric one able to examine esophagus, stomach and colon. Furthermore, non-visual capsules allow measurement of pH, pressure, and temperature. Relevant clinical indications are mainly gastro-esophageal reflux disease and gut motility disorders. Capsules capable of measuring substances in the GI tract are under development.

This review summarizes different approaches for quantitative measurements in capsule endoscopy. The first part focuses on quantitative scores derived from entire wireless capsule endoscopy videos. Such scores are aiming to characterize the cleanliness of the bowel lumen, the severity of small bowel inflammation in Crohn's disease (CD) and the amount of villous atrophy in celiac disease (CeD).

In the second part measurements during processing of capsule endoscopy images are summarized. By abstracting textural and color features from single images, classifiers can be measured and algorithms may help to facilitate cumbersome reading of VCE. Algorithms described aim to omit uninformative obscured images or to select relevant images showing lesions like tumor, polyp, ulcer or blood. Furthermore, size measurement, localization of the

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capsule with the gastrointestinal (GI) tract and motility studies are discussed.

The third part describes non-imaging, wireless capsules with sensors for direct measurements. These capsules include Bravo pH capsule for diagnosis of acid gastro-esophageal reflux, a wireless motility capsule providing combined information of pH, pressure and temperature for diagnosis of gastroparesis, small bowel dysmotility, and delayed colonic transit in constipation, as well as electromagnetic 3 dimensional (3D) capsule tracking system. Approaches for direct measurement of substances in GI tract are finally addressed.

2. Quantitative measurement related to entire capsule endoscopy videos

2.1. Cleansing levels

Luminal cleanliness remains a prerequisite for reliable diagnosis with VCE; capsules have no rinsing or suction capability as in flexible endoscopy. Documentation of the cleanliness is an important factor for assessment of reliability of a VCE diagnosis. Overall, subjective assessment uses a qualitative four-point scale (excellent, good, poor, fair) or a simplified two-point scale (adequate, inadequate) for standardized description [3]. A quantitative Index (QI), based on investigators' visual perception, applies a score for optimal cleanliness with a maximum of 10. Items used are brightness, percentage of visualized mucosa, and presence of bubbles, fluid, and debris. A strong correlation ($p<0.001$) with a 4- or 2-grades visual scale was found, but no correlation with diagnostic yield [4].

Van Weyenberg et al. suggested a method for objective computerized analysis of luminal cleanliness at VCE [5]. The investigators used the color bar of the Rapid software (Medtronic, Dublin, Ireland), displaying mean color of capsule images over time (Fig. 1) by cropping images into a photo editing program. Intensity ratio of red color (thought to represent mucosa) and green color (presumably representing debris) was used to calculate a Computed Assessment of Cleansing (CAC) score. In small bowel segments with adequate cleansing the CAC Score was 6.4 *vs.* 5.0 in segments with inadequate cleansing (first reader, $p<0.001$) and 6.3 *vs.* 4.0 (second reader, $p<0.005$), respectively. Furthermore, good correlation with the subjective QI was demonstrated [5]. Using the CAC score in colon capsule endoscopy (CCE) was feasible as well. A mean score of 5.9 was calculated for segment with excellent cleanliness and of 2.3 for segments judged as poorly clean, resulting in a good inter class correlation coefficient of 0.715 ($p<0.0001$) [6].

2.2. Overall assessment of severity in small bowel Crohn's disease

CD is a chronic inflammatory bowel disease often affecting the small bowel. Lesions detectable by VCE are edema, hyperemia, aphthae, ulcers and stenosis. Besides clinical parameters endoscopic scores aim to reproducibly measure disease activity.

The simplest way to assess the severity of small bowel inflammation by VCE is to count the number of ulcers in the small bowel. Historically, an arbitrary cut off of three or more ulcers has been used as being suggestive of CD in a compatible clinical setting [7].

A **Lewis Score (LS)** has been developed to provide a common language to quantify small bowel inflammatory changes visualized by VCE. Based on an initial overall endoscopic impression of severity, several factors have been weighted [8]. Presence of ulcers is weighted by number (single: 3; few: 5; multiple: 10). Ulcers and edema are both weighted by extent of affected segments (short: 8; long: 12; whole: 20), circular extent ($<\frac{1}{4}$: 9; $\frac{1}{4}-\frac{1}{2}$: 12; $>\frac{1}{2}$: 18), distribution (single: 1; patchy: 12; diffuse: 17). Luminal stenosis is weighted by number (single: 14; multiple: 20), ulceration (no: 2; yes: 20), and traversibility (yes: 7; no: 10). The final Lewis Score is the sum of the maximum tertile score plus the stenosis score. Calculation and visual display of the tertiles in the time bar is provided by the Rapid software, based on manual entry of start and end point of the small bowel. The score can be calculated from a toggle bar of the selection menu (Fig. 2).

A cut off for normal score has been set at <135. Values between ≥ 135 and <790 are suggested to correlate with mild inflammation and ≥ 790 with severe disease. These cut-off levels had been derived from overall assessment of severity in the entire video with a 'significant overlap' [8]. In 30 patients with suspected or established diagnosis of CD and inflammatory lesions, LS correlated well with fecal calprotectin (FC) concentration (surrogate gold standard marker for mucosal inflammation) at inclusion ($p=0.003$) and at follow-up VCE after 9 month ($p<0.001$). C-reactive protein (CRP) correlated only at the initial VCE investigation with the LS ($p=0.006$), but not at follow-up. Symptoms, assessed by the Harvey–Bradshaw index showed no correlation with the LS [9] (Table 1).

Another study found a correlation between LS and FC in the group with low FC levels (<100 μg/g), but not in the groups with higher values [10]. Correlation between FC levels and the LS for quantification of VCE findings was not better, if a blue light filter was used instead of white light for LS calculation of the Score [11]. Comparison of systemic (CRP) or intestinal (FC) inflammatory markers showed no significant correlation with degree of inflammation at VCE assessed by the LS in 187 patients with established CD [12]. Furthermore, in another study it was found that in multivariate analysis, the only positive predictor for FC was the higher tertile ulcer subscore (only with descriptors of ulcer size and number) of LS [13].

The **Capsule Endoscopy Crohn's Disease Activity Index (CECDAI or Niv Score**) is calculated on the basis of three sub-scores (inflammation, extent and stenosis) and separately assessed for proximal and distal small bowel [14]. The inflammatory subscore (normal: 0; mild to moderate edema/hyperemia/denudation: 1; severe edema/hyperemia/denudation: 2; bleeding, exudate, aphthae, erosion, small ulcer [<0.5 cm]: 3; moderate ulcer [0.5–2 cm], pseudopolyp: 4; large [>2 cm] ulcer: 5). A second subscore with weights for the

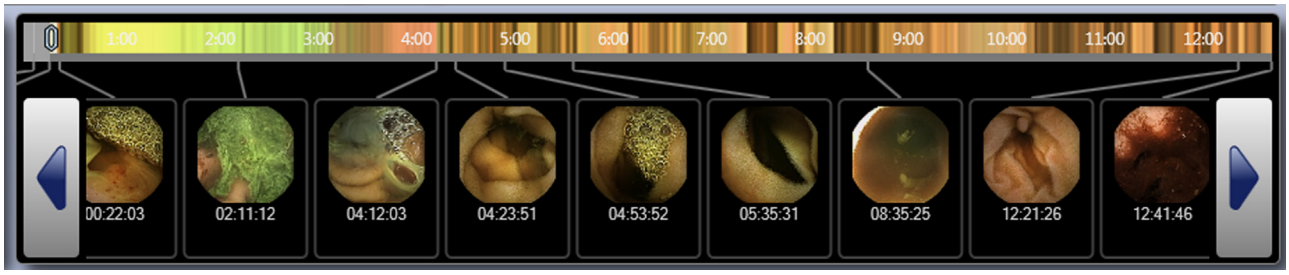

Fig. 1. Rapid 8 software time line with mean color bar (top row) showing yellow and green areas with large amounts of debris, orange and light brown regions with visible mucosa, dark brown segments with dark bile and blood. Below manual marked thumbnails are displayed. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)