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공학박사 학위논문

A NOVEL SUMMARY REPORT OF
COLONOSCOPY: TIMELINE VISUALIZATION
PROVIDING MEANINGFUL COLONOSCOPY
VIDEO INFORMATION

대장내시경 영상에서 유의미한
정보를 제공하는 새로운 형태의
시각화된 대장내시경 요약 보고서

2019 년 8 월

서울대학교 대학원
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Ph. D. Dissertation

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BY

MINWOO CHO

AUGUST 2019

INTERDISCIPLINARY PROGRAM IN BIOENGINEERING
THE GRADUATE SCHOOL
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Abstract

A NOVEL SUMMARY REPORT OF COLONOSCOPY: TIMELINE VISUALIZATION PROVIDING MEANINGFUL COLONOSCOPY VIDEO INFORMATION

By

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Colorectal cancer is one of the most important diseases in which early diagnosis can make a significant difference. Colonoscopy is the most commonly used method for early diagnosis of colorectal cancer. Recently, studies have been actively conducted to obtain more information from colonoscopy images by applying image processing methods, where polyp detection is an important factor for the early diagnosis of colorectal cancer. Since the size and shape of the polyps are variable, it is not easy to find them with human eye due to the nature of the colon wall that continues to move.

So, this study intends to develop a system that could automatically detect polyps by applying image processing and machine learning methods to

colonoscopy images.

In addition, it is also anticipated to provide various useful information to clinicians performing colonoscopy. In this study, 7 meaningful information that can be useful for clinicians are defined and extracted with respect to time information. This information is classified as bleeding, instruments, polypectomy, residue, inflated, non-inflated, and no-fold.

Next, the directions of the colonoscopy scope are also classified. It is extremely important to determine the time-location of the cecum, i.e., the cecal intubation time, since the reaching the appendix orifice is a major factor in determining whether a colonoscopy has been successfully performed. If the direction of the colonoscopy scope is classified, the cecal intubation time can be calculated as the insertion movement phase. Also, the withdrawal movement phase can be automatically calculated.

All the results from the above processes are visualized for efficient delivery and organized as a summary report. The proposed novel summary report of colonoscopy with timeline visualization provides meaningful and formulated colonoscopy video information

Under the Institutional Review Board (IRB) approval of Seoul National University Hospital, 113 colonoscopy video were collected. Support Vector Machine (SVM) model was used to classify colonoscopy images into 7 types. The mean, variance, skewness, correlation, contrast, Laplacian energy, energy of gradient, and scale invariant feature transform values were used as feature of SVM and performed with 5-cross validation.

Inflated, non-inflated, and no-fold frames were applied to polygon detection algorithms learned by SVM. Here, the same features as above are used, and gray-level co-occurrence matrix values are used.

Moreover, the motion vector was calculated by the Horn-Schunk algorithm in order to detect the direction of the colonoscopy scope. Based on this value, the convolutional neural network deep learning technique was used to classify the insertion and withdrawal phases.

Finally, all of the above information was quantified as time information and visualized as a summary report of colonoscopy video (SRCV).

For 113 colonoscopy images, the mean accuracy and sensitivity of the seven categories were 93.7% and 87.4%, respectively. The accuracy in polyp detection was 82.1% and the positive predicted value was 39.3%.

The classification of the direction of the colonoscopy scope was trained and evaluated by convolutional neural network (CNN) using a total of 328,927 image frames with an overall average accuracy of 95.6%. The recall and precision for the entry movement were 95.8% and 97.6%, respectively and the recall rate and precision for the recall movement were 94.6% and 96.9%, respectively. At the value $t = 30$ sec obtained from the study, the position of the cecum was detected with an accuracy of 96.7%.

In this study, image processing methods and machine learning methods have been applied to colonoscopy images to quantify and visualize the direction of the scope and 7 meaningful information as type of timeline. Through the results of this study, it is expected to contribute to the improvement of quality of medical service by assisting in the detection of polyps and re-observing colonoscopy images or sharing information with other clinicians and other hospitals.

Keywords: Colonoscopy, Colorectal cancer, Polyp, Informative frame, Metadata, Structuring, Image processing, Machine learning, Deep learning, Visualization, Medical chart.

Student number: 2014-30269

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1. Introduction

1.1. Colonoscopy Diagnosis and Colorectal Cancer

Colorectal cancer (CRC) is the fourth leading cause of cancer deaths worldwide [1]. Conventional white light colonoscopy is considered the gold standard screening test for CRC, as several prospective studies with a large number of cases have demonstrated that conventional colonoscopy with polypectomy reduces CRC's incidence by 40~90%. Because of this, the demand for colonoscopy continues to increase [2].

It is well known that adenomas develop into high grade dysplasia and carcinomas, that eventually lead to the development of CRC, thus, the adenoma detection rate (ADR) has become increasingly important as an index of the quality of screening and surveillance colonoscopy [3]. However, colonoscopy is not perfect. The miss rate of colonoscopy for polyps has been reported to be up to 22%, and the rate of interval cancer is between 3% and 6% [4, 5]. Furthermore, ADR, which represents the effectiveness of colonoscopy, relies heavily on the physician's experience and skill [6, 7]. A polyp is an abnormal

growth of tissue and is one of the most common diseases in the intestine [1]. Since all colon and rectal cancers originate from them, it is crucial to detect polyps at an early stage and treat them before they develop into cancer cells (Fig. 1.1) [8]. Colonoscopy is the most commonly used method to detect polyps and most available method [9]. For this reason, the demand for colonoscopy continues to increase.

Figure 1.1. Progression of polyps into colorectal cancer [10].

Colonoscopy is a test consisting on the insertion of a special camera called a colonoscope into the rectum, in order to observe the distal part of the small intestine and colon adjacent to the inner and large intestine. Most modern colonoscopes are 1.3~1.7 m long, with a camera attached to the end of a flexible tube with a fiber optic cable. Colonoscopy is a particularly important test for the diagnosis of colorectal cancer and inflammatory bowel disease. If there is sudden abnormality in the stool of a patient, a colonoscopy is recommended [11]. It also has a therapeutic purpose of directly diagnosing the eye by looking at the mucous membrane of the large intestine, hemostasis as needed, histological examination or removing a suspicious lesion (Fig. 1.2). In recent years, various instruments and techniques have been used to treat the hemorrhage at the bleeding site or to remove the polyps and tumors in the mucosa.

Figure1.2. Polyp resection using electric snare mounted on a scope [12].

Colonoscopy is performed by inserting a colonoscope through the anus and observing the inside of the large intestine by capturing images (Fig. 1.3). The large intestine is in the form of a corrugated tube with an average length of about 1.5~1.6 m, with contraction and peristalsis. During the examination, the colonoscope moves in the opposite direction to the direction of the intestinal tract. The air is appropriately insufflated into the large intestine, and the fluid and fecal remnant are aspirated.

Figure 1.3. Insertion and progress of colonoscope [13].

The detection rate of polyps or lesions may vary according to the degree of clearance of the large intestine, or the size and location of the lesions. In the case of the expert, the cecal intubation rate does not reach 100% [14]. In the case of the polyp, the quality of the colonoscopy is evaluated by the detection rate of the polyp in the general population and the insertion rate of the cecum [15, 16].

1.2. Colonoscopy Video Structuring

1.2.1. Video Storage Process

As IT and digital technology develops, colorectal colonoscopy video can be easily stored as digital files [17]. Images from the colonoscope's special cameras are displayed in real-time on an observation monitor and are simultaneously compressed and stored as video files. During the course of the colonoscopy, the doctor can press the pedal to store the still images separately if there is an area of interest to be recorded. Colonoscopy video shows simple patient and time information, so it is easy to check these in the stored images. In addition to checking the stored video files, it is also easy to transfer or share the files between the colonoscopy dedicated equipment and the computer.

Olympus Endoscopic Video Imaging System (EVIS) the most commonly used colonoscopy equipment. In this study, Olympus CV260 (Olympus, Tokyo, Japan) equipment was used. The information for that device is shown in Figure 1.4. A Xenon lamp with a color temperature of 5,900K & Luminous emittance of 5,000lm was used as the light source of the colonoscope.

EVIS LUCERA SPECTRUM is launched, endoscopic video imaging system for observation using specific light spectra

EVIS LUCERA SPECTRUM
Endoscopic Video Imaging System

EVIS LUCERA VIDEO SYSTEM CENTER OLYMPUS CV260

Video signal output	HDTV (RGB: 1 or YPrPb: 1) SDTV (RGB: 3, Y/C: 2, NTSC: 2)	
Main functions	Observation using specific light (Narrow Band Imaging: NBI, Auto Fluorescence Imaging: AFI, and Infra Red Imaging: IRI), HDTV output, adaptive IHB color enhancement, IHB pseudo-color display, structure enhancement, electronic zoom, color drift correction for live images, flash release, automatic iris control, pre-freeze image capture, automatic white balance)	
Optical System	Field of view	140°
	Direction of view	0° Forward viewing
	Depth of field	3 to 100 mm
Distal End	Outer diameter	9.8 mm
Insertion Tube	Outer diameter	9.5 mm
Bending Section	Angulation range	Up 210°, Down 90°, Right 100, Left 100°
Working Length	1330mm	
Total Length	1655mm	
Xenon Lamp	Power consumption	14V 300W
	Color temperature	5,900K
	Luminous emittance	5,000lm

Figure 1.4. Olympus equipment used for colonoscopy video storage in this study.

This study recorded colonoscopy video from the Department of Internal Medicine, Seoul National University Hospital, SNUH (Seoul, Korea). In the case of SNUH, all medical data obtained is stored through the picture archiving and communication system (PACS). Colonoscopy images are also acquired through the Olympus equipment and then stored in the PACS computer.

1.2.2. Video Type Classification

The sequence of adenoma, followed by high-grade dysplasia, and carcinoma eventually leads to CRC development. Thus, the adenoma detection rate (ADR) is an important index of the quality of screening and surveillance colonoscopy [2]. However, ADR is largely determined by the subjective judgment of the physician and relies heavily on the technique and expertise of the colonoscopists [6, 7]. Overlooked colorectal adenomas due to a low ADR during colonoscopy can lead to the development of interval cancer [4, 11]. The miss rate of colonoscopy for polyps has been reported to be as high as 22%, and the rate of interval cancer is between 3% and 6% [5]. Hence, endoscopy centers or clinics with inexperienced medical staff in rural areas could benefit from using image processing software to detect polyps [18-20]. Additionally, experienced colonoscopists may also miss polyps because of various factors such as fatigue, patient status, equipment quality, preparation quality, start time, and other circumstances [21-25].

Polyps and observation of polypectomy sites and bleeding regions are important findings on colonoscopy [26]. Given that the purpose of colonoscopy itself is to detect polyps, it would be meaningful to find them in colonoscopy videos through image processing techniques [27]. In particular, assistance by image processing techniques can be of great help, since the detection of polyps in the colonoscopy process can vary due to many factors such as physician

condition, surroundings conditions, concentration, and intestinal clearance [18-20, 25]. Observation of the polypectomy site is necessary to confirm whether ablation and clipping are done well and whether bleeding is present [28]. In addition, identifying where the polypectomy has been performed in the large intestine is also helpful for future follow-ups. Before and after polypectomy, injecting materials or ablating polyps requires high proficiency. The physician's instruments skill during colonoscopy and polypectomy can be checked by reviewing the video [29].

In addition, intestinal clearance can be evaluated by examining the stool and other residues [30]. Intestinal clearance is a very important index in order to perform colonoscopy and has a great effect on the cecal intubation rate and adenoma detection rate [31]. The quality assessment of colonoscopy may be affected by intestinal clearance. Related research is being conducted in the capsule endoscopy field, but we demonstrated that these observations can be utilized, not only for capsule endoscopy, but also for colonoscopy [32, 33].

Images obtained on colonoscopy can be easily stored as digital video files, allowing re-observation by a physician as needed. Re-observation is necessary in many cases, such reviewing a performed colonoscopy, finding a missed polyp, changing hospital or doctor, or conducting clinical studies [17, 20]. However, re-observing video files is burdensome due to the time and concentration it requires [34]. To alleviate this problem, a method for analyzing and summarizing the colonoscopy videos using image processing technique is needed [35].

Taken together, there is a need for a system to automatically detect significant information, including polyps, and make it accessible to the physician.

1.2.3. Colonoscope Direction Classification

Cecal intubation time (CIT) provides various data, which may be important indicators [15, 16]. In addition, when performing colonoscopy, the cecum is the turning point that determines the insertion phase and withdrawal phase of the colonoscope, that is, the colonoscopist inserts the colonoscope close to the appendix orifice and withdraws it from the cecum [14]. However, there are individual (i.e., patient and colonoscopist) differences in the sequence and process of advancing the colonoscopy [36-38]. Thus, obtaining information about the time-location of the cecum in the colonoscopy procedure is very useful.

Information about the time-location of the cecum can also be helpful when checking colonoscopy videos [39]. Because analyzing a video requires much time and concentration, it places a great burden on the physician, especially when the doctor re-watches the video or shares the video due to change of doctor or hospital [34]. Knowing the time-location of the cecum can help physicians distinguish the insertion phase and the withdrawal phase—where most detailed examination is undertaken—of the colonoscope, which can help reduce the burden on video observation [40, 41]. Furthermore, the CIT and withdrawal phase can also be useful as metadata [42, 43]. The location of other anatomic sites such as the T-colon and S-colon can be inferred on the assumption that the location of the cecum is known (Fig. 1.5) [44].

Figure 1.5. Anatomical structure of the large intestine [45].

Moreover, the movement data of the colonoscope can be utilized for proficiency assessment [46]. Since insertion and withdrawal are technically different movements, the pattern, combination, and repetition of insertion/withdrawal/stop can be utilized to express individual features of the colonoscopist and to assess proficiency [47-49]. Thus, it is necessary to detect the direction of the scope's movement and time-location information of the cecum.

Recently, with advances in computer technology and equipment, colonoscopists do not need to record these data anymore [50]. In various medical fields, systems that automatically record medical reports are being developed [51, 52].

Horn-Schunk algorithms are the most popular differential algorithms that have been used for many applications and have been referenced for many performance evaluation models [53]. The Horn-Schunk algorithm is a technique used to identify the image velocity or motion vector based on spatial temporal gradient technique that computes the image velocity from spatiotemporal derivatives of the image intensity [54, 55]. Through this algorithm, we can compute the pixels' motion change between consecutive frames [56]. In other words, it is possible to know the direction of movement of the pixels in the current frame relative to the previous frame, allowing to determine the direction in which the current frame is moving. Therefore, we aimed to provide more useful information to physicians by recording the direction of the scope's movement and time-location of the cecum using Horn-Schunk algorithm by applying convolutional neural network (CNN).

1.3. Objectives and Scope

Recently, studies have been actively conducted to acquire more meaningful information from colonoscopy images by applying image processing methods and deep learning method. Because polyps are highly likely to develop into colorectal cancer, colonoscopies provide very useful and important information. The polyps are not easy to detect because their size and shape differs and the intestinal mucosa continues to move irregularly. In addition, the discovery of polyps is influenced by many factors, including environmental conditions, physician's condition, concentration, patient's intestinal clearance. Even with the doctor's subjective judgment, the results may vary.

For this reason, the first goal of our study is to detect the polyps. In order to assist the discovery of polyps, we will develop a system that can automatically detect polyps by applying image processing methods and machine learning methods to colonoscopy images. In addition, we intended to extract meaningful information that can be useful for clinicians in colonoscopy. The purpose of this study is to define seven types of meaningful information that can be helpful for clinicians in colonoscopy and to classify and quantify them. The definition of meaningful information was obtained through a focus group interview with Gastroenterology fellow from Seoul National University Hospital. These 7 data items are classified as bleeding, polypectomy, instruments, residue, inflated,

non-inflated, and no-fold. Polyps are extracted from inflated, non-inflated, and no-fold frames. With the results, it will be easy to see how the colonoscopy images are distributed by type.

In the second step, we want to classify the direction of the colonoscopy scope. It is of great clinical importance to determine the time-location of the cecum, i.e., the cecal intubation time, since reaching the cecum is a major factor in determining whether a colonoscopy has been successfully performed. Therefore, if the direction of the colonoscopy scope is classified, the cecal intubation time can be automatically calculated as the insertion movement phase. Also, the withdrawal movement phase can be automatically calculated too.

All the results from the above processes will be visualized for efficient delivery and organized into a summary report. The proposed novel summary report of colonoscopy with timeline visualization will provide meaningful and structured colonoscopy video information.

Figure1.6. Overall research flow.

2. Materials and Methods

2.1. Colonoscopy Video Acquisition

2.1.1. Study Design and Population

This prospective, single-center study enrolled patients aged 19 to 75 years who underwent colonoscopy for screening, surveillance, or therapy such as polypectomy at Seoul National University Hospital, a tertiary referral center in Korea, from August 2016 to December 2016. Potential participants were excluded if they had a previous history of colorectal resection, severe constipation, idiopathic pseudo-obstruction, acute exacerbation of inflammatory bowel disease, impaired renal function (glomerular filtration rate <30 mL/min/1.73 m²), other serious medical illnesses (major cardiac, metabolic, or psychiatric illness), or if they were pregnant or lactating. This study was approved by the institutional review board of the Seoul National University Hospital (IRB No. 1509-062-703, approval date July 13, 2016), and

it was conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from all participants.

2.1.2. Colonoscopy Procedure

All patients received standard bowel preparation including 4 L of polyethylene glycol solution. All colonoscopies were performed by two experienced colonoscopists, who have performed >10,000 colonoscopies and are certified by the Korean Society of Gastrointestinal Endoscopy. Colonoscopies were performed with a high-resolution endoscopy device CV260. The size, location, morphology (Yamada type), and histology of all polyps detected during the procedure were reported. Bowel preparation quality was assessed using the Boston bowel preparation scale [31]. Adequate bowel preparation was defined as a score of ≥ 2 for each location [57]. The ADR, defined as the number of colonoscopies with at least one adenoma detected, divided by the total number of colonoscopies was calculated.

2.1.3. Acquisition of Colonoscopy Video File

In this study, colonoscopy was performed using a high-resolution colonoscopy device CV260. Colonoscopy videos were acquired using a video capture card (SkyCaputre U6T, Skydigital, Seoul, Korea), after signal branching from the CV260.

The video was converted to an Mpeg4 format to avoid alteration of the resolution, and the resolution was 1920×1080 , 30fps. Videos were acquired from 113 patients, and the play time was about 20~40 min. The colonoscopy video was decomposed into frames. A frame was extracted as a PNG file per 0.5 s using Virtualdub software. All frames were cropped to 850×750 pixels to extract only the colonoscopy area, excluding patient information and the settings.

2.1.4. Sample Size Calculation and Statistical Analysis

Statistical analyses were performed using SPSS 18.0 software (SPSS version 18.0 for Windows, SPSS, Chicago, Ill., USA). Assuming that the accuracy of the system in detecting polyps was 80% and that of colonoscopy performed by a professional colonoscopist was 90%, a sample size of 180 polyps was required to detect this difference with 80% power and an α of 0.05. According to several previous studies, about 72 polyps were detected with conventional colonoscopy in 40 patients. Therefore, we assumed that a sample size of 100 patients would be sufficient to detect 180 polyps.

The actual polyps detected by colonoscopists during colonoscopy and the proposed polyps detected by the system were compared to determine the sensitivity. Continuous variables were calculated as the mean $\pm$ standard deviation and categorical variables as the number (%). Student's t-test was used to compare continuous variables, and the χ^2 test was used to compare categorical variables between the 2 groups. The relative risk and 95% confidence interval of the significant factors were calculated. A *p-value* <0.05 was considered statistically significant.

Figure 2.1. Acquisition of Colonoscopy Video File.

2.2. Informative Frame Classification

Due to the colonoscopy video's play time is long and have much noise, it is inefficient to use the whole video [58]. It is more efficient to extract the frame which is necessary to re-observe or applied to image processing, in the whole video [59]. In the colonoscopy video, the frames that have meaningful information is called as informative frame, and the other is called as non-informative frame [60]. In this study, only informative frame were used for image processing. The criteria for classification of informative frame and non-informative frame were as follows: presence of noise such as color separation phenomenon, blur caused by motion, and non-observable screen such as excessive dark, brightness, enlargement screen. Difficult to analyze or meaningless frames that had color separation, blurring caused by motion, excessive darkness, brightness, or enlargement of the screen were classified as non-informative frames. These frames were recorded in the summary report, but they were not used for image processing.

Figure 2.2. Informative frame classification.

The colonoscopy video is decomposed into frames. A frame is extracted as PNG file per 0.3 sec by using Virtualdub software. And all frame were cropped to 850×750 in order to extract only colonoscopy area with excluding patient's information and settings.

Figure 2.3. Colonoscopy frame pre-processing.

To classify the informative frame and non-informative frame, the support vector machine (SVM) of matlab were utilized [61]. The SVM of matlab is suitable for image classification, because SVM of matlab is commonly used to classify the data with finding the hyperplane by using the various features [62]. The mean, variance, skewness, correlation, contrast, energy of laplacian, energy of gradient values were acquired from the decomposed frames, and these values were used as features of SVM model to classify the informative frame and non-informative frame.

SVM model were performed with method of 5-cross validation [61]. Before training the SVM model with training data set, dividing all frames to informative frame and non-informative frame manually is preceded to get the training data set. SVM model could set up the optimized parameter and frame image's information which can classify the images most efficiently by performing the 5-cross validation [62]. Informative frame and non-informative frame were classified through applying the trained SVM model to frame images.

Figure 2.4. Five-fold cross-validation for SVM. In the five-fold cross validation process, the test data, which guarantee generalizability, is obtained.

2.3. Type classification

2.3.1. Overview

The informative frames were classified into 7 types: bleeding, polypectomy, instruments, residue, inflated, non-inflated, and no-fold (Fig. 2.5).

“Bleeding” refers to a frame containing bleeding regions, and it can be used to check internal bleeding or other lesions and monitor for bleeding caused by the scope during colonoscopy.

“Polypectomy” refers to a frame containing polypectomy or injection regions; it can be used to confirm whether ablation and clipping have been performed and whether bleeding is present at the resected area after polyp ablation.

“Instruments” refers to a frame containing instruments for biopsy, polypectomy, injection, or others. These frames can be used to monitor details of the physician's actions during colonoscopy.

“Residue” refers to a frame containing stool or other material remaining inside the large intestine and disturbing observation, which can be used to evaluate intestinal clearance.

Other frame types were as follows: inflated, non-inflated, and no-fold, meaning frames containing inflated, many non-inflateds, and flat intestinal wall with no wrinkles, respectively. After classification, these frame were applied to the polyp detection algorithm to optimize image processing and machine learning.

Figure 2.5. (A) Classification of non-informative frames and informative frames (B) The classification of informative frames into 7 types: bleeding, instruments, polypectomy, residue, no-fold, inflated, and non-inflated.

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Figure. 2.6. Overview and process of the proposed system.

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2.3.2. Hierarchical Classification

In this paper, we applied the SVM model hierarchically according to the optimized order. With this method, 7 frame types were classified and were used to optimize the polyp detection algorithm.

First, the “bleeding” frames were extracted from the other frame types. These could be classified easily because of their distinctly red color [63-65]. Next, “polypectomy” frames were extracted. These were easily identified by their unique blue color, which is rare in the large intestine [66, 67]. Third, “instruments” frames were extracted by identifying the color of metal, which is heterogeneous in the large intestine [68]. Fourth, yellow, brown or green frames were classified as stool or residue [69]. In the above 4 steps, the SVM models used the following red, green, blue channel values: mean, variance, median, correlation, contrast, percentage of all pixels with values of 0-63, percentage of all pixels with values of 64-127, percentage of all pixels with values of 128-191, and percentage of all pixels with values of 192-255. After extraction, all frames labeled “bleeding,” “polypectomy,” “instruments,” and “residue” were recorded into the summary report and were not used in the next step.

Next, the frame types “inflated,” “non-inflated,” and “no-fold” were identified to train the polyp detection algorithm. Because the specificity of the 3 types of

frames differed, it was inefficient to apply one polyp detection algorithm to 3 type frames uniformly. Since the performance of the SVM model used in the polyp detection algorithm was based on the training dataset, the training of the polyp detection algorithm was performed differently according to each type to increase the accuracy of the SVM model. For this reason, it was necessary to classify these 3 frame types separately to optimally train the polyp detection algorithm.

Fifth, “inflated” frames were extracted by using the linear feature. The scale-invariant feature transform (SIFT) value was utilized to check linearity [70]. The SIFT was used as the standard to express pixel direction and gradient distribution. Finally, the “non-inflated” and “no-fold” frames were separated. These were classified based on the curvature via SIFT value and texture value. A gray-level co-occurrence matrix (GLCM) was used as the texture parameter [71].

Figure 2.7. Overall structure of hierarchical support vector machine and application of the summary report of the colonoscopy video.

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2.3.3. Polyp Detection

In this research, we applied the SVM model hierarchically according to the optimized order (Fig. 2.7). With this method, 7 frame types were classified and were used to optimize the polyp detection algorithm. The frame image applied to the polyp detection algorithm was inefficiently large. The polyp detection algorithm had difficulty detecting polyps at the original frame size because most polyps were less than a quarter of the frame image. To resolve this problem, the 3 types of frames were divided into smaller sizes before being analyzed. To avoid missing polyps during division, a sliding window method was used (Fig. 2.8) [72]. Although this increased the amount of data to process, it prevented loss of polyps. The size of the image was 850×750 pixels, and the size of the sliding window was set at 350×350 pixels with a 100 pixel interval, considering the polyp's size. Finally, 30 divided window images were acquired from a single frame. The polyp detection algorithm was applied to the divided window images, and the frame number of the window image was recorded when the algorithm detected a polyp. Because the time information of the frame can be calculated with the frame number, the time when polyps were found could be confirmed in the summary report.

Figure 2.8. Sliding window method was used to apply the polyp detection algorithm efficiently.

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For the 3 types of frames, the SVM model was used as the polyp detection algorithm to classify the polyp and non-polyp window images with various classifiers [73-77]. The polyp detection algorithm was trained using 5-fold cross-validation with the polyp dataset that was selected for each type by fellow doctors and a professor in the Department of Gastroenterology.

2.4. Colonoscopy Direction Classification

2.4.1. Overview

In order to analysis the direction of scope's movement, the Horn-Schunck algorithm was used to compute the pixel's motion change between consecutive frames. Horn-Schunck-algorithm applied images were trained and tested through convolutional neural network deep learning methods, and classified to the insertion, withdrawal and stop movements. Based on the scope's movement, the graph was drawn with a value of +1 for insertion, -1 for withdrawal, and 0 for stop. We regarded the turning point as a cecum candidate point when the total graph area sum in a certain section recorded the lowest.

Figure 2.9. Overview and process of scope's movement classification [117].

2.4.2. Motion Vector Calculation

Horn-Schunk algorithms are the most popular differential algorithms that have been used for many applications and have been referenced for many performance evaluation models [53]. The Horn-Schunk algorithm is a technique used to identify the image velocity or motion vector based on spatial temporal gradient technique that computes the image velocity from spatiotemporal derivatives of the image intensity [54, 55]. Through this algorithm, we can compute the pixel's motion change between consecutive frames [56]. In other words, it is possible to know the movement direction of the pixels in the current frame relative to the previous frame; thus, it is possible to determine the direction in which the current frame is moving.

The equation for calculating the optical flow is as follows [78]:

$$\frac{\partial E}{\partial x} \frac{dx}{dt} + \frac{\partial E}{\partial y} \frac{dy}{dt} + \frac{dE}{dt} = 0 \quad (1)$$

The equation (1) is acquired by numerical procedure for error function minimization. The error function E is defined in terms of spatial and time gradients of optical flow vector field. Correlation of two terms are shown in equation (2)-(6).

$$E = \iint (\alpha^2 E_c^2 + E_b^2) dx dy \quad (2)$$

$$E_b = E_x u + E_y v + E_t \quad (3)$$

$$E_c^2 = \left(\frac{\partial u}{\partial x}\right)^2 + \left(\frac{\partial u}{\partial y}\right)^2 + \left(\frac{\partial v}{\partial x}\right)^2 + \left(\frac{\partial v}{\partial y}\right)^2 \quad (4)$$

$$E_x = \frac{\partial E}{\partial x} \quad E_y = \frac{\partial E}{\partial y} \quad E_t = \frac{\partial E}{\partial t} \quad (5)$$

$$u = \frac{dx}{dt} \quad v = \frac{dy}{dt} \quad (6)$$

$E(x, y, t)$ means luminance if the image in point (x, y) at time moment t . In order to solve the minimization problem, a steepest descent method is used which is based on computation of gradient to determine the direction of search for the minimum. First step, gradient coefficients E_x, E_y, E_t are computed from input images. As shown in equation (5), the coefficients represent predicted value of the image gradients in space & time. Second step, the optical flow vector u and v defined by equation (6) are computed. Depending on image content, the number of iteration steps must be chosen.

As the Horn-Schunk algorithm can only estimate small motions and compares the current frame with the previous frame to calculate the motion vector, the time interval between the two frames has a significant effect on the outcome. If the interval is too large, the calculation error will increase beyond the small motion, and if the interval is too small, the movement of the scope will not be considered sufficiently. Considering this limitation, we extracted the frame per 0.5 seconds.

Figure 2.10. Horn-Schunck algorithm application [117].
 (A) Original image frame, (B) Horn-Schunck algorithm applied image, (C) motion vector and its color expression

Because the image inside the large intestine had varied shapes and colors depending on the conditions of position, health status, and patient's condition, it is advantageous to remove other information from the frame image for training, leaving only information about the position using Horn-Schunck algorithm. After Horn-Schunck algorithm application, we acquired the image shown in Figure. 2.10 by expressing the direction change of the pixels inside the frame in color. Since all elements inside the frame do not move in the same direction consistently, various colors appear mixed, as shown in Fig. 2.10. To understand the pattern of colors according to these positions, we used CNN deep learning in the next step.

2.4.3. Scope's Movement Classification

In this paper, Horn-Schunck algorithm-applied color images were classified into three types: insertion, withdrawal, and stop. Among 113 patients with visual 1case failed to reach the cecum were excluded. Therefore, frames from colonoscopy images of 112 patients were classified as insert, withdrawal, and stop as the standard for deep training set. To make a standard setting, a colonoscopy video was reproduced at a speed of 0.7 times, and a user observing it pressed the direction key of the keyboard in real time. The up, down, and space buttons were matched to insert, withdrawal, and stop, respectively, and the frames were classified based on the input keyboard values. Five colonoscopist with more than 5 years experienced participated in this work, and the values selected by more than three were used as the standard [79, 80]. An overview of the entire process is shown in Figure 2.9.

CNN deep learning was applied based on the standard created above. Horn-Schunck algorithm-applied color images were used as training data and test data. Unlike previous research using SVM, we used CNN, a deep learning technique, because it was difficult to select features from the Horn-Schunck algorithm-applied color image [81].

The CNN structure and training procedure are described in Figure 2.11. The network architecture consisted of an input stage, a feature extraction stage with

three convolutional layers, and an output classification stage (82). The input stage received the Horn-Schunck algorithm applied color image which was converted to 170*150 pixels. The feature extraction stage that followed a triple ternary convolution block structure was composed of convolution, pooling, and activation functions. The rectified linear unit (ReLU) activation function and max pooling layer were placed after each convolutional layer (83). The classification stage included fully connected layers and a dropout function (drop rate of 0.5) and provided an output from a Softmax function. Fully connected layer were classified into three classes using the Softmax function.

Figure 2.11. Overall architecture of the convolutional neural network (CNN) deep learning model [117]. All image were reduced to 170×150 and were input into the model. Next, it was passed through all convolution layers and the entire binding layer, and it was classified into three classes

The learning was carried out with batch size 128 (set by experimental trials) images. The model is optimized for hyper-parameters by a randomized grid search method (84). We initialized search ranges to be $[1.0 \times 10^{-7} \ 1.0 \times 10^{-2}]$, $[0.8 \ 0.99]$, and $[1.0 \times 10^{-10} \ 1.0 \times 10^{-2}]$ for the learning rate, SGD, and L2-regularization parameters, respectively.

Finally, the trained network was validated using the 5-fold cross-validation method (85). Five groups of data were established such that four groups were used for training and the remaining groups were used for validation (86). Each group was designed to participate in validation in turn. The performance was measured using the mean of the validation results for each group (87).

The model was trained and tested on a Windows 10 Pro system with Intel i9-9900K CPU 3.6GHz processor, 2TB SSD, 64 GB RAM, GeForce RTX 2070 Gaming OC D6 8GB.

2.4.4. Cecum Time-location Detection

To determine the location of the cecum, we analyzed the direction of the scope's movement. Based on the results of the analysis, the graph was drawn with a value of +1 for insertion, -1 for withdrawal, and 0 for stop. Because the cecum is a large turning point that distinguishes the insertion phase from the withdrawal phase, the turning point of transition from insertion to withdrawal is the candidate for the cecum. However, some scopic insertion-withdrawal repeat movements often occur during colonoscopy, and turning points can be found very often. Therefore, in this study, the scope movement for a certain range was analyzed to find the real turning point. All points that transitioned from insertion to withdrawal were recorded. These turning points were referred to as a cecum candidate point.

Figure 2.12. The movement of the scope [117].

(A) Original curve graph of insertion and withdrawal movement, (B) graph area calculation for cecal position prediction, (C) cecum candidate point.

We set a certain range “ t ” and calculated the sum of the graph area $\pm \frac{t}{2}$ around the turning points. Since the value is +1 during insertion, the area of the graph will be positive, and when the value is -1 during withdrawal, the area of the graph will be negative. At the turning point with a certain range “ t ,” when the total sum of the graph areas is the minimum value, that turning point is regarded as the cecum (Fig. 2.12). If the value “ t ” is too small, light repetitive movements of insertion-withdrawal may have a minimum area value, so “ t ” is set to a sufficiently large value. For several candidate points, the graph area was calculated based on range “ t .” The range “ t ” was set to 10, 20, and 30 sec.

2.5. Focus Group Interview

In this study, we proposed the system that can analyze the colonoscopy video and provide meaningful direction information of endoscope's movement and time-location information of the cecum via visualized summary report. To ask for comments on the system and reflect colonoscopists' requirements, we had implemented a FGI. Seven colonoscopists with more than 5 years experienced participated in this FGI, and it was conducted in the face-to-face meeting. The comments on necessity referred in this research were selected by FGI, and ideas about visualization were also recruited and validated. This FGI simply asked positive and negative opinions, and the results are as follows. All seven doctors determined that this system would positively benefit physicians and patients. Six doctors agreed that a visualized Summary report based on this system would be helpful for medical records management and data sharing. Five doctors agreed that the results could be used for proficiency testing.

3. Results

3.1. Clinical Analysis

3.1.1. Characteristics of Patients and Colonoscopy Quality Assessment

A total of 113 patients were enrolled prospectively from August 1, 2016, to December 31, 2016. To increase the reliability of the colonoscopies performed in this study, we recruited mostly patients receiving repeat colonoscopy (90.5%) within 2 years. The patients' baseline characteristics and the results of the colonoscopy quality assessment are shown in Table 3.1. The patients' mean age was 60.4 years (range, 47~73), and 62 patients (54.8%) were men. The indications for colonoscopy were referral for treatment of polyps or further evaluation of symptoms from our hospital or outside hospitals (72.6%) and screening or polyp surveillance (27.4%). Cecal intubation succeeded in 112 patients; The mean withdrawal time was 19.7 min, and bowel preparation using the Boston Bowel Preparation Scale was adequate in 92.9% of the patients.

Table 3.1. Characteristics of study patients and colonoscopy quality assessment

Characteristic	N=113
Age (years), mean (SD)	60.4 (12.5)
Male sex, <i>n</i> (%)	62 (54.8)
Previous colonoscopy history within 2 years, <i>n</i> (%)	102 (90.5)
Indication for colonoscopy, <i>n</i> (%)	
Screening and surveillance of CRN	31 (27.4)
Referral from our hospital or outside hospitals	82 (72.6)
Treatment (polypectomy)	50 (44.2)
Further evaluation for symptom	32 (28.3)
Cecal intubation, <i>n</i> (%)	112 (99.1)
Withdrawal time(min), mean (SD)	19.7 (6.0)
BBPS, mean (SD)	8.1 (1.7)
Adequate bowel preparation, <i>n</i> (%)	105 (92.9)
ADR, %	61.9

CRN, Colorectal neoplasm; BBPS, Boston bowel preparation scale; ADR,

Adenoma detection rate.

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3.1.2. Polyp Characteristics

The baseline characteristics of the polyps detected by the colonoscopists are summarized in Table 3.2. The colonoscopists detected a total of 351 polyps during the colonoscopy. The mean polyp size was 6.0 mm (range 2~60 mm), and the most common locations where polyps were found were the ascending colon (32.7%) and the transverse colon (31.0%). Yamada type I (47.0%) and type II (42.5%) were the most common morphologies of polyps detected on colonoscopy [88], and tubular adenoma (56.4%) was the most common histologically

Table 3.2. Characteristics of the polyps detected during colonoscopy

Characteristic	Detected polyps (n=351)
Size (mm), mean (SD)	6.0±5.9
Location, <i>n</i> (%)	
Cecum	21 (6.0)
Ascending colon	115 (32.7)
Transverse colon	109 (31.0)
Descending colon	31 (8.6)
Sigmoid colon	23 (6.6)
Rectum	52 (14.9)
Morphology (Yamada type), <i>n</i> (%)	
I	165 (47.0)
II	149 (42.5)
III	29 (8.3)
IV	8 (2.3)
Histology, <i>n</i> (%)	
Hyperplastic polyp	40 (11.4)
Tubular adenoma	198 (56.4)
Serrated polyp [†]	14 (4.0)
Cancer	7 (2.0)
Others [‡]	92 (26.2)

[†]Serrated polyp include sessile serrated adenomas/polyps and traditional serrated adenomas. [‡]Others include nonspecific, inflammatory polyps.

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3.2. Informative Frame Classification

As the play time of the colonoscopy videos was long and had much noise, it was inefficient to use the whole video. Thus, frames were extracted to select only meaningful information or applied to image processing. In the colonoscopy video, the frame that has meaningful information is called informative frame, and the other is called non-informative frame. Since non-informative frames are frames that do not have meaningful information in the image itself, they have had a negative effect on training. In this study, only informative frames were used. The classification accuracy of the informative frame used in this study was 97.7%.

3.3. Type Classification

3.3.1. Hierarchical Classification

The SVM was applied hierarchically to optimize classification, in the following order: “bleeding,” “instruments,” “polypectomy,” “residue,” “inflated,” and “non-inflated.” After classification, false positive and false negative extracted frames were confirmed manually. The accuracy and sensitivity of each frame type were averaged (Table 3.3)

Table 3.3. Mean accuracy and sensitivity of classification according to type

	Mean accuracy (%)	Mean sensitivity (%)
Informative	97.77	93.05
Type: bleeding	99.75	93.33
Type: instruments	98.56	92.01
Type: polypectomy	98.86	96.77
Type: residue	99.50	87.23

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3.3.2. Polyp Detection

The window images of suspected polyps were detected through a polyp detection algorithm. The sensitivity of polyp detection was validated differently than type classification. Because one polyp appeared in several frames, a frame-by-frame comparison was inefficient. Thus, the system counted the number of polyps present in the video, not in every frame where the polyp appeared. Based on clinical judgments, true positive (TP), true negative (TN), and false positive (FP) values were calculated by matching the polyps detected from the system and doctors' clinical judgments [89]. Among the 351 polyps found on colonoscopy, 288 polyps were detected by the system, and the average sensitivity of the system for polyp detection was 82.1%. In contrast, specificity was calculated using frame-by-frame comparison for each patient because the number of non-polyp parts can be counted only in frame units. The average specificity of the system for polyp detection was 89.1% with a standard deviation of 4.6%. Likewise, the positive predictive value (PPV) was also calculated in frame units. PPV was defined as follows, where TP represent polyps classified as polyps. The average PPV was 39.3% with a standard deviation of 4.1%. We compared the polyps detected and missed by the system (Table 3.4).

Table 3.4. Performance of detecting polyp

Variable	Systemic detection		p-value
	Detected polyps (n=288)	Missed polyps (n=63)	
Size (mm), mean (SD)	6.3 ± 6.4	4.9 ± 2.5	0.003
Mean size, <i>n</i> (%)			0.479
<10 mm	251 (87.2)	57 (90.5)	
≥10 mm	37 (12.8)	6 (9.5)	
Distribution, <i>n</i> (%)			0.167
Right-sided	197 (68.4)	48 (76.2)	
Left-sided	91 (31.6)	15 (23.8)	
Morphology (Yamada type) , <i>n</i> (%)			0.000
I	111 (38.9)	54 (81.5)	
II	137 (48.1)	12 (18.5)	
III	29 (10.2)	0 (0)	
IV	8 (2.8)	0 (0)	
Histology, <i>n</i> (%)			0.420
Hyperplastic polyp	33 (11.5)	7 (11.1)	
Tubular adenoma	165 (57.3)	33 (52.3)	

Serrated polyp [†]	11 (3.8)	3 (4.8)
Cancer	6 (2.1)	1 (1.6)
Others [‡]	73 (25.3)	19 (30.2)

Values are presented as mean±SD or number (%). [†]Serrated polyp included sessile serrated adenomas/polyps and traditional serrated adenomas.[‡]Others included nonspecific, inflammatory polyps.

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Figure 3.1. False positive and negative result of polyp detection.

The mean size of the detected polyps was greater than that of the missed polyps (6.3 mm vs. 4.9 mm, $p=0.003$). Most polyps missed by the system were Yamada type I (81.5%). Yamada type IV polyps were not missed by the system. However, regarding the distribution and histology of the polyps, there were no statistically significant differences between the 2 groups.

3.3.3. Type Classification Visualization and Summary Report

Through the proposed system, the position information of “bleeding,” “instruments,” “polypectomy,” “residue,” and “polyp” frames were checked in the colonoscopy video. These results were displayed to effectively deliver the information to physicians. In the process of making and displaying the summary report of the colonoscopy video (SRCV), advice and comments were received from the focus group. The SRCV is shown in Figure 3.2. The white gaps in the timeline represent the three types of frames in which polyps were not found: “non-inflated,” “inflated,” and “no-fold.” The SRCV is linked with the colonoscopy video frame by frame. If the user clicks or double-clicks a certain point on the SRCV, the frame of that point is shown, or the video plays from that point.

Figure 3.2. Summary report of the colonoscopy video (SRCV). The SRCV matches the colonoscopy video frame by frame.

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3.4. Colonoscopy Direction Classification

3.4.1. Scope's Movement Classification

Since the features of Horn-Schunk-algorithm applied images were difficult to specify, we applied the CNN deep learning method to the images for high accuracy. The overall accuracy, drawn from 5-fold cross-validation, was 95.6%.

Table 3.5 shows the classification results in confusion matrix form.

Table 3.5. The confusion matrix of classification results using the 5-fold cross-validation of the CNN algorithm

		Target class		Sum by row
		Insertion	Withdrawal	Stop
Output class	Insertion	116,437	1,533	119,349
	Withdrawal	1,586	107,336	110,679
	Stop	3,484	4,603	98,899
Sum by column		121,507	113,472	328,927

Each cell in the table 3.5 represents the number of samples classified by the trained CNN algorithm. The vertical title indicates the actual class (input class of the algorithm), whereas the horizontal title indicates the classified results (output class of the algorithm). Performance comparisons according to the indicators of recall, precision, and f1 score for each class are presented in Table 3.6. These numbers can be used for alternative algorithm assessments [90].

Table 3.6. Performance indicators of the CNN and other algorithms for the three individual classes

Class/Indicators		Insertion	Withdrawal	Stop
CNN	Recall	0.958	0.946	0.967
	Precision	0.976	0.969	0.918
	F1 score	0.967	0.958	0.942
VGG-16	Recall	0.95	0.916	0.964
	Precision	0.953	0.959	0.911
	F1 score	0.952	0.937	0.937
LeNET	Recall	0.907	0.833	0.872
	Precision	0.874	0.909	0.83
	F1 score	0.89	0.87	0.85
SVM	Recall	0.844	0.775	0.799
	Precision	0.804	0.832	0.785
	F1 score	0.823	0.802	0.792

3.4.2. Cecum Time-location Detection

We regarded the turning point as a cecum candidate point when the total area sum in a certain section recorded the lowest. We checked the existence of the actual cecum within a certain interval $\pm \frac{t}{2}$ around the cecum candidate point. The accuracy according to “ t ” values is shown in Figure 5 and Table 3.7. The position of the cecum recorded by three clinicians was compared with the results of the proposed system.

Figure 3.3. Accuracy according to “ t ” values ranging from 10 sec to 30 sec [117].

Table 3.7. Accuracy of cecum discovery according to the set certain range “ t ”

	$t = 10$ sec	$t = 20$ sec	$t = 30$ sec
Accuracy	83.9%	94.6%	96.4%

3.4.3. Colonoscope Direction Visualization and Summary Report

The movement of the scope, shown in Figure 2.12 as a graph, was changed to a color code to increase visibility. Insertion, withdrawal, and stop were mapped to each color and expressed in 1 sec, as shown in Figure 3.4 (A). Again, the scale was changed to a 10 sec scale, 30 sec scale to increase visibility (Figure 3.4 (B,C)). One 10 sec square represents 10 seconds. One 30 sec square represents 30 seconds.

At the 1 s scale, the result was too microscopic and not suitable for intuitive observation. However, since the outlier belonging to a small number was removed from the 10 sec scale, the movement of the scope and the position of the cecum could be intuitively grasped. In addition, as the scale increased, the distinction between the insertion phase and the withdrawal phase became clearer.

Figure 3.4. Summary report of the colonoscope movement with various scale (10 sec, 30 sec, 1 min) with cecum candidate point marking [117].

Insertion, withdrawal, and stop were mapped to each color and expressed with various scale. (A) 1 second per square, (B) 10 seconds per square, (C) 30 seconds per square

Figure 3.5. Recording the direction of scope's movement and cecum time-location information on SRCV [117].

3.5. System Usability Scale

To evaluate the utility of the SRCV, we adapted the System Usability Scale (SUS) questionnaire. The SUS is a popular, simple, ten-item attitude Likert scale assessing usability [91]. We modified the general questions for the SRCV evaluation. The questionnaire was administered to 30 physicians from the Department of Internal Medicine (gastroenterology, n=15; non-gastroenterology, n=5), Department of Family Medicine (n=5), and the Department of Gastrointestinal Surgery (n=5).

Figure 3.6 shows the answer distribution of the usability questionnaire, grouping the results related to positive and negative questions. Regarding positive questions (questions 1, 3, 5, 7, and 9), 73.3% of participants expressed agreement (scores 4 and 5), and 2.7% gave disagreement scores (scores 1 and 2). Regarding negative questions (questions 2, 4, 6, 8, and 10), 54.7% of answers were in disagreement (scores 1 and 2), and 18.7% gave agreement scores (scores 4 and 5). However, all participants could understand the SRCV without any detailed help. We suppose the necessity for an explanation of “classification by frame unit” affected the result.

Figure 3.6. Usability questionnaire results.

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4. Discussion

4.1. Type Classification and Polyp Detection

In this study, we developed and verified a system that extracts meaningful information from recorded colonoscopy videos by hierarchically applying an SVM. Most recent studies that used machine learning algorithms applied these algorithms to an optimized dataset and evaluated their accuracy [92-94]. However, the present study used all images extracted from real endoscopy videos, analyzing the entire videos. The results containing informative frames and suspected polyps were presented on a timeline. When the utility of the SRCV was evaluated by an SUS questionnaire, a large majority of participants expressed positive opinions.

The mean accuracy and sensitivity of the system for classification according to type was over 90%. We introduced an efficient order by applying the SVM hierarchically. The types of frames were extracted in the order of importance as follows: “bleeding,” “instruments,” “polypectomy,” and then “residue.” To optimize classification and avoid duplicate notation in the SRCV, this order of hierarchical SVM was determined to be the most effective.

Bleeding - Polypectomy

Polypectomy - Instruments

Instruments - Residue

Figure 4.1. The cases belonging to two types.

In order to classify the case that belonging to two types, the proposed order of hierarchical SVM is required.

We tried to convey meaningful information from the colonoscopy video through data visualization. The non-informative frames were included in the SRCV because physicians want to reference which points were non-informative when they conduct colonoscopy again. In this study, one frame was extracted per 0.3 sec. If the frames would be extracted from the video more frequently, the SRCV would become more detailed and omissions would be reduced.

The proposed system that creates a summary report automatically from colonoscopy videos is expected to contribute to the gastroenterology and endoscopy field by enabling physicians to have easier access to important colonoscopy data. The system can summarize meaningful colonoscopy information, provide visualized guidelines, or be utilized for educational purposes. Nowadays, the colonoscopists take a still shot during colonoscopy, so important scene are recorded. However, if the proposed system is used, the summary report can be completed automatically without taking a still shot. It will be more convenient because important information can be provided by summary report more efficient. Moreover, when a physician who did not conduct the colonoscopy reads the medical records, the SRCV can help increase the reliability of the report and the physician's understanding of the results by matching the video with the SRCV [95]. Additionally, if the SRCV is included in the medical records, it will be helpful when medical records and patient information are shared among doctors or hospitals [96-99].

The colonoscopy videos used in this research were reliable for polyp detection

because skilled experienced physicians performed the colonoscopies and most patients enrolled in the study had previously undergone colonoscopy within the past 2 years, a period of time that is shorter than the 3- to 5-year post-polypectomy surveillance period recommended by the American Society for Gastrointestinal Endoscopy and the American Gastroenterological Association [100, 101]. This may have resulted in lowering the false negative results when the system was applied to the video.

The mean sensitivity and specificity of polyp detection were also over 80%, but the PPV was low in the study. In recent years, considerable efforts have been made to develop an efficient approach to automatically detect polyps using colonoscopy videos. However, automated detection of polyps from colonoscopy videos is very challenging because of high variations in polyp size, color, shape, texture, and location [102-104]. Although there have been considerable advancements in automatically detecting polyps, these methods still have low detection accuracy. In several previous studies using datasets, sensitivity ranged from 36.9% to 71.4%, and the PPV ranged from 13.6% to 93.5% [105-108]. In the present study, the polyps detected by the system were larger and had more pedunculated morphology than the polyps missed by the system. The proportion of advanced histologic features gradually increases as the polyp size increases, and it is important not to miss large polyps. Lesions are considered advanced when they are ≥ 1 cm in size [109]. A previous study showed that only 10.7% of adenomas ≤ 1 cm in size had a villous component,

versus 56% of those larger than 1 cm [110]. However, in our study, when the size cutoff was set at 1 cm (<1 cm and ≥ 1 cm), there were no statistically significant differences in the detection rate between the detected polyp group and the missed polyp group by the system. The 6 cases of missed polyps ≥ 1 cm in the system were all non-granular were a pseudo-depressed type of lateral spreading tumors. These lesions are difficult to distinguish visually, and we need to improve the system in the future.

The low PPV of polyp detection in our study was because we preferred “false positive” over “false negative” when the polyp detection algorithm was applied. Although the occurrence of false positive results reduces efficiency by providing unnecessary information to physicians, it is better than missing polyps. Moreover, it has the possibility of identifying polyps missed during colonoscopy by identifying suspicious areas. In this study, we used the SVM to solve a series of processes with one tool, which is simple and efficient. The SVM can be replaced by another classification tool. In future studies, accuracy is expected to improve by using deep learning methods.

4.2. Colonoscope Direction Classification and Cecum Time-location Detection

In this study, we developed and verified a system that can detect the direction of scope's movement from colonoscopy video using Horn-Schunk algorithm by applying CNN deep learning methods. The motion change of the video is extracted through the Horn-Schunk algorithm for calculating optical flow. Through this algorithm, we can compute the pixel's motion change between consecutive frames, and the direction of scope's movement was trained and determined through the CNN. The extracted information about the direction of scope's movement was visualized and added to the summary report of colonoscopy video (SRCV). In addition, the time-location of the cecum was calculated based on the results of direction of the scope's movement and included in the SRCV. This proposed system can assist physician's observation of the colonoscopy video and provide helpful information.

The videos used in this research were favorable for image acquisition and image processing because skilled physician performed the colonoscopy. This may have resulted in lowering the false-negative results when the system was applied to the video. In a previous study, we extracted 1 frame of images in 0.3 s from a colonoscopy video. The higher the extraction frequency, the more

frames can be extracted, so more images can be used in the system. However, in applying the Horn-Schunck algorithm in this study, we extracted one frame at 0.5 sec. Note that the Horn-Schunck algorithm can only calculate motion vectors for small changes [56]. Therefore, if the interval between frames is too large, Horn-Schunck algorithm is not applicable. However, to calculate the motion vector based on the difference between the previous frame and the current frame, there should be a proper change between the two frames. In our colonoscopy video, a 0.5 sec period yielded optimal results. As the standard setting, observing the colonoscopy video at a speed of 0.7 times to avoid misreading directions, participation of five fellow doctors, and selecting values more than three made the accuracy of the gold standard more reliable [79, 80].

We did not consider real-time use in this study. This is because the movement of the scope is meaningful when analyzed with the whole video. When the insertion and withdrawal movements of the scope throughout the video are analyzed, a clear distinction between the insertion phase and the withdrawal phase can be obtained. As a result, the position of the cecum can be accurately calculated.

In the methods section, we used the certain range value “ t ” to find the real cecum point accurately. When analyzing 112 patient images, we found numerous light insertion-withdrawal repeat movements. With the exception of polypectomy, the scopes frequently repeat insertion-withdrawal movements to find the polyps [7]. In addition, withdrawal movement was often accompanied

by smooth insertion [6]. Most repetitive movements did not exceed 10 sec. In other words, if “ t ” is less than 10 sec, light repetitive insertion-withdrawal movements may have a minimum area value, so “ t ” is set to a sufficiently large value. Considering this, we analyzed the results when t values were 10, 20, and 30 sec.

In this study, we used the CNN deep learning method to classify the movement of the scope [111, 112]. The images used for deep learning input were the Horn-Schunck algorithm-applied images, and the motion vector was expressed in color. In the images, the layer did not have to be deep because the directions were classified according to the color distribution only. The CNN architecture used in this study was developed with reference to LeNET and VGG, and the layer structure was experimentally optimized. The trained network was validated using the 5-fold cross-validation method, and overfitting did not occur [113]. As a limitation of this study, we did not test data from outside the hospital. In a future study, we plan to conduct research and testing with independent data from other hospitals.

During colonoscopy, the CIT was recorded by a physician. However, as the technology is under development today, the trend is to automatically store the data generated during the medical procedure, and the information generated during colonoscopy also needs to be automatically analyzed and stored [114]. In our previous study, we have already developed a system that automatically analyzes and records colonoscopy videos, and through the system, the video

was classified by types and visualized as summary report to communicate meaning effectively [115]. In addition to the previous research, it will be possible to provide more useful information to physicians via recording the direction of scope's movement and cecum time-location information (Fig. 3.4). It can also be used to calculate the withdrawal time. The withdrawal time that is used purely for observations can be calculated, since we calculate the time from when the scope comes out of the CIT to the anus with excluding the time allocated to polypectomy.

With the proposed system, we believe that if the current handwritten medical records can be automatically summarized together with more detailed, graphical information, it will be useful for physicians and patients and will improve medical services [95]. The results of this study may contribute to improving the medical record after colonoscopy has finished. We hope that the findings of this study can contribute to the informatics field of medical records so that medical charts can be transmitted graphically and effectively in the field of colonoscopy

4.3. Future Work

In classifying informative frames by type, we were able to extract the residue frames. If we can develop and validate a method to normalize the amount and frequency of residue frames, we can measure the clearance of the large intestine based on the residue frame. Because the clearance of the large intestine is a very important factor that can affect the quality of the colonoscopy, we expect that normalization and quantification of clearance will contribute greatly to the progress of colonoscopy.

With regards to polyp detection, we obtained a polyp detection rate of 82.1%. In this study, only 43 polyps were ≥ 1 cm in diameter among 351 polyps, and 6 polyps were missed. Detection of polyps that are flat and larger than 1 cm have great importance. For this reason, further studies and improved detection rates are needed for finding polyps ≥ 1 cm.

In the scope's movement classification, only the insertion, withdrawal, and stop phases were analyzed and determined. Through Focus Group Interview (FGI), colonoscopists have expressed the need to identify and visualize the anatomical structure of the large intestine. In future studies, if left and right movements can be recognized, the direction of the colonoscope can be recorded in more detail. Based on this, it is expected that the anatomical structure of the

large intestine can be deduced and the anatomical position with time can be indicated.

Information obtained in this study can be utilized as metadata for proficiency assessment and training for colonoscopist. Since insertion and withdrawal are technically different movements, data regarding the scope's movement and phase can be quantified and utilized to express a pattern unique to the colonoscopist and to train proficiency [116]. When viewed with reference to the SRCV, we could estimate colonoscopist's proficiency if there were repetitive insertion-withdrawal movements or no movements at all, which was not related to polyps, bleeding, or polypectomy.

5. Conclusion

The proposed study demonstrated the effectiveness that extracts meaningful information from colonoscopy videos and provides a summary report on a color-coded timeline. The accuracy and sensitivity of classification type and polyp detection was verified. Further validation of the system is needed after system improvement, including an increase in the positive predictive value (PPV) for polyp detection by using deep learning methods. If the system improves accuracy and is capable of real-time application, then clinical application of this system can be expected to assist in the detection of polyps and increase ADR in colonoscopy.

Information obtained in this study can be utilized as metadata for proficiency assessment. Since insertion and withdrawal movements are technically different, data of scope's movement and phase can be quantified and utilized to express a pattern unique to the colonoscopist and to assess proficiency. Furthermore, when the utility of the SRCV was evaluated using a System Usability Scale (SUS) questionnaire, 89.3% of participants expressed positive opinions. Thus, the proposed system to analyze colonoscopy videos is expected to have a positive impact.

With the system, it is anticipated that adding more detailed graphical information to the medical records will be useful for clinicians & patients

and will improve medical services. The results of this study could also contribute to improving the medical record after the colonoscopy has concluded. The outcomes of this study can contribute to the informatics field of medical records so that medical charts can be transmitted graphically and effectively in the field of colonoscopy.

References

1. Hagggar FA, Boushey RP. Colorectal cancer epidemiology: incidence, mortality, survival, and risk factors. *Clinics in colon and rectal surgery* 2009;22:191-197.
2. Rex, Douglas K. Rationale for colonoscopy screening and estimated effectiveness in clinical practice. *Gastrointestinal endoscopy clinics of North America*, 2002, 12.1: 65-75.
3. Leslie A, Carey F, Pratt N, et al. The colorectal adenoma–carcinoma sequence. *British Journal of Surgery* 2002;89:845-860.
4. Burggraaf, Jacobus, et al. Detection of colorectal polyps in humans using an intravenously administered fluorescent peptide targeted against c-Met. *Nature medicine*, 2015, 21.8: 955.
5. Hong SN, Sung IK, Kim JH, et al. The effect of the bowel preparation status on the risk of missing polyp and adenoma during screening colonoscopy: a tandem colonoscopic study. *Clinical endoscopy* 2012;45:404-411.
6. Simmons, Dia T., et al. Impact of endoscopist withdrawal speed on polyp yield: implications for optimal colonoscopy withdrawal time. *Alimentary pharmacology & therapeutics*, 2006, 24.6: 965-971.
7. Anderson, Bradley W., et al. Endoscopic overestimation of colorectal polyp size. *Gastrointestinal endoscopy*, 2016, 83.1: 201-208.
8. Leslie, A., Carey, F. A., Pratt, N. R., & Steele, R. J. C. The colorectal adenoma–carcinoma sequence. *British Journal of Surgery*, 2002, 89(7), 845-

860.

9. Quintero E, Hassan C, Senore C, et al. Progress and challenges in colorectal cancer screening. Gastroenterology research and practice 2012.

10. **병원간호사회** “http://www.khna.or.kr/homecare_new/06_diges/gastro09.php”

11. Nishihara, Reiko, et al. Long-term colorectal-cancer incidence and mortality after lower endoscopy. New England Journal of Medicine, 2013, 369.12: 1095-1105.

12. **질병관리본부 국가건강정보포털** “http://health.cdc.go.kr/health/mobileweb/content/group_view.jsp?CID=19FE2F726D”

13. **서울대학교병원 의학정보** “https://terms.naver.com/imageDetail.nhn?docId=927609&imageUrl=https%3A%2F%2Fdbscthumb-phinf.pstatic.net%2F1983_000_3%2F20190318181514651_8ITRCCRSJ.jpg%2F986.jpg%3Ftype%3Dm4500_4500_fst_n%26wm%3DY”

14. Fatima, H., Rex, D. K., Rothstein, R., Rahmani, E., Nehme, O., Dewitt, J., & Bensen, S.. Cecal insertion and withdrawal times with wide-angle versus standard colonoscopes: a randomized controlled trial. Clinical Gastroenterology and Hepatology, 2008, 6(1), 109-114.

15. Marshall, J. B., & Barthel, J. S. The frequency of total colonoscopy and terminal ileal intubation in the 1990s. Gastrointestinal endoscopy, 1993, 39(4), 518-520.

16. Bernstein, C., Thorn, M., Monsees, K., Spell, R., & O'Connor, J. B. A

prospective study of factors that determine cecal intubation time at colonoscopy.

Gastrointestinal endoscopy, 2005, 61(1), 72-75.

17. Terada, Tadashi. Histopathological study using computer database of 10 000 consecutive gastric specimens:(1) benign conditions. Gastroenterology report, 2015, 3.3: 238-242.

18. Kaz, Andrew M.; DOMINITZ, Jason A. The Name Game: Circumventing Quality Metrics by Categorizing Incomplete Colonoscopy as Sigmoidoscopy. The American journal of gastroenterology, 2017, 112: ajg2017258.

19. De Jonge, Vincent, et al. Quality evaluation of colonoscopy reporting and colonoscopy performance in daily clinical practice. Gastrointestinal endoscopy, 2012, 75.1: 98-106.

20. Wolf, Holly J., et al. Colon cancer screening for Colorado's underserved: a community clinic/academic partnership. American journal of preventive medicine, 2015, 48.3: 264-270.

21. Adler, Andreas, et al. Factors determining the quality of screening colonoscopy: a prospective study on adenoma detection rates, from 12 134 examinations (Berlin colonoscopy project 3, BECOP-3). 2013, 62.2: 236-241.

22. Gurudu, Suryakanth R., et al. Adenoma detection rate is not influenced by the timing of colonoscopy when performed in half-day blocks. *The American journal of gastroenterology*, 2011, 106.8: 1466.

23. Serper, Marina, et al. Patient factors that affect quality of colonoscopy preparation. *Clinical Gastroenterology and Hepatology*, 2014, 12.3: 451-457.

24. Sanaka, Madhusudhan R., et al. Adenomas are detected more often in morning than in afternoon colonoscopy. *The American journal of gastroenterology*, 2009, 104.7: 1659-1664.
25. Lee, Thomas JW, et al. Colonoscopic factors associated with adenoma detection in a national colorectal cancer screening program. *Endoscopy*, 2014, 46.03: 203-211.
26. Shang-bo, Z. H. O. U., et al. Bleeding Detection in Wireless Capsule Endoscope Based on Color Feature Vector. *DEStech Transactions on Computer Science and Engineering*, 2016, aice-ncs.
27. Shah-Ghassemzadeh, Nicole K., et al. Training mid-career internists to perform high-quality colonoscopy: a pilot training programme to meet increasing demands for colonoscopy. *Postgraduate medical journal*, 2017, postgradmedj-2016-134578.
28. Brooker, Jim C., et al. Treatment with argon plasma coagulation reduces recurrence after piecemeal resection of large sessile colonic polyps: a randomized trial and recommendations. *Gastrointestinal endoscopy*, 2002, 55.3: 371-375.
29. Gupta, Sachin, et al. Development and validation of a novel method for assessing competency in polypectomy: direct observation of polypectomy skills. *Gastrointestinal endoscopy*, 2011, 73.6: 1232-1239. e2.
30. Kaneoka, Asako S., et al. The Boston residue and clearance scale: preliminary reliability and validity testing. *Folia Phoniatica et Logopaedica*, 2013, 65.6: 312-317.

31. Hong SN, Sung IK, Kim JH, et al. The effect of the bowel preparation status on the risk of missing polyp and adenoma during screening colonoscopy: a tandem colonoscopic study. *Clinical endoscopy* 2012;45:404-411.
32. Münzer, B., Schoeffmann, K., & Böszörményi, L.. Content-based processing and analysis of endoscopic images and videos: A survey. *Multimedia Tools and Applications*, 2017, 1-40.
33. Sudha, N.; SANTHIYAKUMARI, N. MIEEE. Summarizing wireless capsule endoscopy video frame based on inter-frame structural similarity index. *Advances in Natural and Applied Sciences*, 2016, 10.6 SE: 199-208.
34. Hu, Erzong, et al. Bleeding and Tumor Detection for Capsule Endoscopy Images Using Improved Geometric Feature. *Journal of Medical and Biological Engineering*, 2016, 36.3: 344-356.
35. Münzer, B., Schoeffmann, K., & Böszörményi, L. Content-based processing and analysis of endoscopic images and videos: A survey. *Multimedia Tools and Applications*, 2017, 1-40.
36. Spier, B. J., Benson, M., Pfau, P. R., Nelligan, G., Lucey, M. R., & Gaumnitz, E. A. Colonoscopy training in gastroenterology fellowships: determining competence. *Gastrointestinal endoscopy*, 2010, 71(2), 319-324.
37. Rex, D. K. Effect of variable stiffness colonoscopes on cecal intubation times for routine colonoscopy by an experienced examiner in sedated patients. *Endoscopy*, 2001, 33(01), 60-64.
38. Saifuddin, T., Trivedi, M., King, P. D., Madsen, R., & Marshall, J. B. Usefulness of a pediatric colonoscope for colonoscopy in adults.

Gastrointestinal endoscopy, 2000, 51(3), 314-317.

39. Barclay, R. L., Vicari, J. J., Doughty, A. S., Johanson, J. F., & Greenlaw, R. L. Colonoscopic withdrawal times and adenoma detection during screening colonoscopy. *New England Journal of Medicine*, 2006, 355(24), 2533-2541.

40. Barclay, R. L., Vicari, J. J., & Greenlaw, R. L. Effect of a time-dependent colonoscopic withdrawal protocol on adenoma detection during screening colonoscopy. *Clinical Gastroenterology and Hepatology*, 2008, 6(10), 1091-1098.

41. Moritz, V., Bretthauer, M., Ruud, H. K., Glomsaker, T., de Lange, T., Sandvei, P., & Hoff, G. Withdrawal time as a quality indicator for colonoscopy—a nationwide analysis. *Endoscopy*, 2012, 44(05), 476-481.

42. Taber, A., & Romagnuolo, J. Effect of simply recording colonoscopy withdrawal time on polyp and adenoma detection rates. *Gastrointestinal endoscopy*, 2010, 71(4), 782-786.

43. Lee, H. L., Eun, C. S., Lee, O. Y., Jeon, Y. C., Han, D. S., Sohn, J. H., ... & Lee, D. H. Significance of colonoscope length in cecal insertion time. *Gastrointestinal endoscopy*, 2009, 69(3), 503-508.

44. Cherian, S., & Singh, P. Is routine ileoscopy useful? An observational study of procedure times, diagnostic yield, and learning curve. *The American journal of gastroenterology*, 2004, 99(12), 2324.

45. WebMD “<https://www.webmd.com/digestive-disorders/picture-of-the-colon#1>”

46. Snyder, C. W., Vandromme, M. J., Tyra, S. L., & Hawn, M. T. Retention of colonoscopy skills after virtual reality simulator training by independent and proctored methods. *The American surgeon*, 2010, 76(7), 743-746.
47. Marshall, J. B. Technical proficiency of trainees performing colonoscopy: a learning curve. *Gastrointestinal endoscopy*, 1995, 42(4), 287-291.
48. Benson, M. E., Reichelderfer, M., Said, A., Gaumnitz, E. A., & Pfau, P. R. Variation in colonoscopic technique and adenoma detection rates at an academic gastroenterology unit. *Digestive diseases and sciences*, 2010, 55(1), 166.
49. Anderson, J. C., Messina, C. R., Cohn, W., Gottfried, E., Ingber, S., Bernstein, G., & Polito, J. Factors predictive of difficult colonoscopy. *Gastrointestinal endoscopy*, 2001, 54(5), 558-562.
50. Terada, Tadashi. Histopathological study using computer database of 10,000 consecutive gastric specimens:(1) benign conditions. *Gastroenterology report*, 2015, 3.3: 238-242.
51. Greenhalgh, T., Stramer, K., Bratan, T., Byrne, E., Russell, J., & Potts, H. W. Adoption and non-adoption of a shared electronic summary record in England: a mixed-method case study. *Bmj*, 2010, 340, c3111.
52. Taira, R. K., Soderland, S. G., & Jakobovits, R. M. Automatic structuring of radiology free-text reports. *Radiographics*, 2001, 21(1), 237-245.
53. Meinhardt-Llopis, E., Pérez, J. S., & Kondermann, D. Horn-schunck

optical flow with a multi-scale strategy. Image Processing on line, 2013, 151-172.

54. Gong, X., & Bansmer, S. Horn–Schunk optical flow applied to deformation measurement of a birdlike airfoil. Chinese Journal of Aeronautics, 2015, 28(5), 1305-1315.

55. Horn, B. K., & Schunck, B. G. Determining optical flow. Artificial intelligence, 1981, 17(1-3), 185-203.

56. Bruhn, A., Weickert, J., & Schnörr, C. Lucas/Kanade meets Horn/Schunck: Combining local and global optic flow methods. International journal of computer vision, 2005, 61(3), 211-231.

57. Ikematsu H, Saito Y, Tanaka S, Uraoka T, Sano Y, Horimatsu T, et al. The impact of narrow band imaging for colon polyp detection: a multicenter randomized controlled trial by tandem colonoscopy. Journal of gastroenterology 2012, 47:1099-1107.

58. Vilarino, Fernando, et al. Automatic labeling of colonoscopy video for cancer detection. Pattern Recognition and Image Analysis, 2007, 290-297.

59. Fallah, Mina; NIAKAN KALHORI, Sharareh R. Systematic Review of Data Mining Applications in Patient-Centered Mobile-Based Information Systems. Healthcare informatics research, 2017, 23.4: 262-270.

60. Hoyos, Jesus. Automatic Classification of Non-informative Frames in Colonoscopy Videos Using Texture Analysis. In: Progress in Pattern Recognition, Image Analysis, Computer Vision, and Applications: 21st Iberoamerican Congress, CIARP 2016, Lima, Peru, November 8–11, 2016,

Proceedings. Springer, 2017. p. 401.

61. Park BE, Jang WS, Yoo SK. Texture Analysis of Supraspinatus Ultrasound Image for Computer Aided Diagnostic System. Healthcare Informatics Research 2016, 22:299-304.

62. Timotius, Ivanna K., et al. Abnormality detection for capsule endoscope images based on support vector machines. Biomedical Engineering: Applications, Basis and Communications, 2012, 24.01: 71-83. .

63. Xiong, Yi, et al. Bleeding detection in wireless capsule endoscopy based on mst clustering and svm. In: Signal Processing Systems (SiPS), 2015 IEEE Workshop on. IEEE, 2015. p. 1-4.

64. Mackiewicz, Michal W.; FISHER, Mark; JAMIESON, Crawford. Bleeding detection in wireless capsule endoscopy using adaptive colour histogram model and support vector classification. In: Medical Imaging. International Society for Optics and Photonics, 2008. p. 69140R-69140R-12.

65. Hwang, Sae, et al. Polyp detection in colonoscopy video using elliptical shape feature. In: Image Processing, 2007. ICIP 2007. IEEE International Conference on. IEEE, 2007. p. II-465-II-468.

66. Nagtegaal, Iris D. Current concepts of colorectal cancer resection pathology. Histopathology, 2015, 66.1: 102-111.

67. Hua, B. O., Fu-Long, M. A., & Li-Cheng, J. Research on computation of GLCM of image texture [J]. Acta Electronica Sinica, 2006, 1(1), 155-158.

68. Williams, J. E., Holub, J. L., & Faigel, D. O. Polypectomy rate is a valid quality measure for colonoscopy: results from a national endoscopy database. *Gastrointestinal endoscopy*, 2012, 75(3), 576-582.
69. Cho, M., et al. Residue detection in the large intestine from colonoscopy video using the support vector machine method. In: 2018 18th International Conference on Control, Automation and Systems (ICCAS). IEEE, 2018. p. 398-401.
70. Sonka, Milan; HLAVAC, Vaclav; BOYLE, Roger. Image processing, analysis, and machine vision. Cengage Learning, 2014.
71. Hua, B. O.; FU-LONG, Ma; LI-CHENG, Jiao. Research on Computation of GLCM of Image Texture [J]. *Acta Electronica Sinica*, 2006, 1.1: 155-158.
72. Iakovidis, Dimitris K.; MAROULIS, Dimitris E.; KARKANIS, Stavros A. An intelligent system for automatic detection of gastrointestinal adenomas in video endoscopy. *Computers in Biology and Medicine*, 2006, 36.10: 1084-1103.
73. Bae, Seung-Hwan; YOON, Kuk-Jin. Polyp detection via imbalanced learning and discriminative feature learning. *IEEE transactions on medical imaging*, 2015, 34.11: 2379-2393.
74. Ionescu, Mihaela, et al. METHODS OF DIAGNOSIS OF INTESTINAL POLYPS WITH SOFTWARE APPLICATIONS IN WIRELESS CAPSULE ENDOSCOPY. *Annals. Computer Science Series*, 2015, 13.1..
75. Valdeavilla, Edreen Bryan; MIAOU, Shaou-Gang. Classification of

Capsule Endoscope Images Using Local Binary Patterns and Support Vector Machines.

76. Rastogi A., Bansal A., Wani S et al. Narrow-band imaging colonoscopy--a pilot feasibility study for the detection of polyps and correlation of surface patterns with polyp histologic diagnosis . *Gastrointest Endosc* 2008, 67: 280 – 6.
77. Hochberger, J., et al. Training simulators and education in gastrointestinal endoscopy: current status and perspectives in 2001. *Endoscopy*, 2001, 33.06: 541-549.
78. GaliC, S., & LonCariC, S. Spatio-temporal image segmentation using optical flow and clustering algorithm. In IWISPA 2000. Proceedings of the First International Workshop on Image and Signal Processing and Analysis. in conjunction with 22nd International Conference on Information Technology Interfaces. 2000, (IEEE (pp. 63-68). IEEE.
79. Cho, M., Lee, D. H., Kim, Y., Koh, W., Chung, J. H., Kim, H. C., & Kim, S. Development and clinical validation of a novel photography-based skin pigmentation evaluation system: a comparison with the calculated consensus of dermatologists. *International journal of cosmetic science*, 2016, 38(4), 399-408.
80. Cho, M., Lee, D. H., Doh, E. J., Kim, Y., Chung, J. H., Kim, H. C., & Kim, S. Development and clinical validation of a novel photography-based skin erythema evaluation system: a comparison with the calculated consensus of dermatologists. *International journal of cosmetic science*, 2017, 39(4), 426-434.
81. Rajaraman, S., Antani, S. K., Poostchi, M., Silamut, K., Hossain, M.

- A., Maude, R. J., & Thoma, G. R. Pre-trained convolutional neural networks as feature extractors toward improved malaria parasite detection in thin blood smear images. *PeerJ*, 2018, 6, e4568.
82. Nagasawa, T., Tabuchi, H., Masumoto, H., Enno, H., Niki, M., Ohsugi, H., & Mitamura, Y. Accuracy of deep learning, a machine learning technology, using ultra-wide-field fundus ophthalmoscopy for detecting idiopathic macular holes. *PeerJ*, 2018, 6, e5696.
83. Jang, Y., Kim, S., Kim, K., & Lee, D. Deep learning-based classification with improved time resolution for physical activities of children. *PeerJ*, 2018, 6, e5764.
84. Bergstra, J., & Bengio, Y. Random search for hyper-parameter optimization. *Journal of Machine Learning Research*, 2012, 13(Feb), 281-305.
85. Ou, Y. Y. Prediction of FAD binding sites in electron transport proteins according to efficient radial basis function networks and significant amino acid pairs. *BMC bioinformatics*, 2016, 17(1), 298.
86. Ou, Y. Y. Identifying the molecular functions of electron transport proteins using radial basis function networks and biochemical properties. *Journal of Molecular Graphics and Modelling*, 2017, 73, 166-178.
87. Le, N. Q. K., Sandag, G. A., & Ou, Y. Y. Incorporating post translational modification information for enhancing the predictive performance of membrane transport proteins. *Computational biology and chemistry*, 2018, 77, 251-260.
88. Oh, Seung Taek. Colorectal polyps: endoscopic diagnosis and

- polypectomy. Journal of the Korean Medical Association, 2003, 46.7: 594-604.
89. Sosna, Jacob, et al. CT colonography of colorectal polyps: a metaanalysis. American journal of roentgenology, 2003, 181.6: 1593-1598.
90. Kainz, P., Pfeiffer, M., & Urschler, M. Segmentation and classification of colon glands with deep convolutional neural networks and total variation regularization. PeerJ, 2017, 5, e3874.
91. Brooke J. SUS-A quick and dirty usability scale. Usability evaluation in industry 1996;189:4-7.
92. Liu, Ding-Yun, et al. Identification of lesion images from gastrointestinal endoscope based on feature extraction of combinational methods with and without learning process. Medical image analysis, 2016, 32: 281-294.
93. Wu, Xiao, et al. Automatic hookworm detection in wireless capsule endoscopy images. IEEE transactions on medical imaging, 2016, 35.7: 1741-1752.
94. Wang, Shuai, et al. Computer-Aided Endoscopic Diagnosis Without Human-Specific Labeling. IEEE Transactions on Biomedical Engineering, 2016, 63.11: 2347-2358.
95. Ahn M, Choi M, Kim Y. Factors associated with the timeliness of electronic nursing documentation. Healthcare Informatics Research. 2016;22:270-276.
96. Salvi, Elisa, et al. Exploring IBM Watson to Extract Meaningful Information from the List of References of a Clinical Practice Guideline.

In: *Conference on Artificial Intelligence in Medicine in Europe*. Springer, Cham, 2017. p. 193-197.

97. Diomaiuta, Crescenzo, et al. A novel system for the automatic extraction of a patient problem summary. In: *Computers and Communications (ISCC), 2017 IEEE Symposium on*. IEEE, 2017. p. 182-186.

98. Hoyt, Robert Eugene, et al. IBM Watson analytics: automating visualization, descriptive, and predictive statistics. *JMIR public health and surveillance*, 2016, 2.2.

99. Cruz, Joseph A.; WISHART, David S. Applications of machine learning in cancer prediction and prognosis. *Cancer informatics*, 2006, 2: 59.

100. Davila RE, Rajan E, Baron TH. ASGE guideline: colorectal cancer screening and surveillance. *Gastrointestinal endoscopy*. 2006;63:546-57.

101. Sanaka MR, Super DM, Feldman ES, Mullen KD, Ferguson D, McCullough AJ. Improving compliance with postpolypectomy surveillance guidelines: an interventional study using a continuous quality improvement initiative. *Gastrointestinal endoscopy*. 2006;63:97-103.

102. Wang Y, Tavanapong W, Wong J, Oh J, De Groen PC. Part-based multiderivative edge cross-sectional profiles for polyp detection in colonoscopy. *IEEE journal of biomedical and health informatics* 2014;18:1379-1389.

103. Amber, Aashish, et al. Feature Point Based Polyp Tracking in Endoscopic Videos. In: *Applied Computing and Information Technology/2nd International Conference on Computational Science and Intelligence (ACIT-COI)*, 2015 3rd International Conference on. IEEE, 2015. p. 299-304..

104. Park, Sungheon; LEE, Myunggi; KWAK, Nojun. Polyp detection in colonoscopy videos using deeply-learned hierarchical features. Seoul National University, 2015.
105. Yu L, Chen H, Dou Q, Qin J, Heng PA. Integrating online and offline 3D deep learning for automated polyp detection in colonoscopy videos. *IEEE Journal of Biomedical and Health Informatics*. 2016.
106. J. Bernal, F. J. Sanchez, G. Fernandez-Esparrach, D. Gil, C. Rodriguez, and F. Vilarino, "WM-DOVA maps for accurate polyp highlighting in colonoscopy: Validation vs. saliency maps from physicians," *Comput. Med. Imag. Graph.*, vol. 43, pp. 99–111, 2015.
107. N. Tajbakhsh, S. R. Gurudu, and J. Liang, "Automated polyp detection in colonoscopy videos using shape and context information," *IEEE Trans. Med. Imag.*, vol. 35, no. 2, pp. 630–644, Feb. 2016.
108. N. Tajbakhsh, S. R. Gurudu, and J. Liang, "Automatic polyp detection in colonoscopy videos using an ensemble of convolutional neural networks," in *Proc. 2015 IEEE 12th Int. Symp. Biomed. Imag.*, 2015, pp. 79–83.
109. Sousa AC, Figueiredo P, Lopes S, Gouveia H, Sofia C, Correia LM. A thousand total colonoscopies: what is the relationship between distal and proximal findings? *Acta Medica Portuguesa*. 2007;21:461-6
110. Silva SM, Rosa VF, Santos AC, Almeida RM, Oliveira PG, Sousa JB. Influence of patient age and colorectal polyp size on histopathology findings. *Arquivos Brasileiros de Cirurgia Digestiva (São Paulo)*. 2014;27:109-113.
111. Le, N. Q. K., Ho, Q. T., & Ou, Y. Y. Incorporating deep learning with

convolutional neural networks and position specific scoring matrices for identifying electron transport proteins. *Journal of computational chemistry*, 2017, 38(23), 2000-2006.

112. Ho, Q. T., & Ou, Y. Y. Classifying the molecular functions of Rab GTPases in membrane trafficking using deep convolutional neural networks. *Analytical biochemistry*, 2018, 555, 33-41.

113. Taju, S. W., Nguyen, T. T. D., Le, N. Q. K., Kusuma, R. M. I., & Ou, Y. Y. DeepEfflux: a 2D convolutional neural network model for identifying families of efflux proteins in transporters. *Bioinformatics*, 2018, 34(18), 3111-3117.

114. Yuan, Yixuan; LI, Baopu; MENG, Max Q.-H. Improved bag of feature for automatic polyp detection in wireless capsule endoscopy images. *IEEE Transactions on Automation Science and Engineering*, 2016, 13.2: 529-535.

115. Cho, M., Kim, J. H., Kong, H. J., Hong, K. S., & Kim, S. A novel summary report of colonoscopy: timeline visualization providing meaningful colonoscopy video information. *International journal of colorectal disease*, 2018, 33(5), 549-559.

116. Robertson, Douglas J.; KAMINSKI, Michal F.; BRETTHAUER, Michael. Effectiveness, training and quality assurance of colonoscopy screening for colorectal cancer. *Gut*, 2015, gutjnl-2014-308076.

117. M. Cho, J. H. Kim, et al. Identification of cecum time-location in a colonoscopy video by deep learning analysis of colonoscope movement. Accepted by PeerJ, in progress.

Abstract in Korean

국문초록

대장암은 조기 진단이 매우 중요한 질병 중 하나이며, 대장암을 조기 진단하기 위해 가장 많이 사용되는 대표적인 방법은 대장내시경 이다. 오늘날, 영상 처리 기술을 적용하여 대장내시경 영상에서 더욱 많은 정보들을 획득하고자 하는 연구가 활발히 진행되고 있다. 가장 대표적인 연구로서, 대장암의 조기 진단에 중요한 요소인 용종 검출이 있다. 용종은 크기와 모양이 각기 다르며, 계속해서 움직이는 대장 내벽의 특성상 육안으로 발견하기가 쉽지 않다. 이러한 이유로, 본 연구에서는 용종 발견을 돕기 위하여 대장내시경 영상에 영상처리 기술과 기계학습 기술을 적용하여 자동으로 용종을 검출할 수 있는 시스템을 개발하고자 한다. 뿐만 아니라, 대장내시경 영상에서 임상 의에게 도움이 될 수 있는 유의미한 정보를 다수 추출하여 제공하고자 한다. 본 연구에서는 대장내시경 영상에서 임상 의에게 도움이 될 수 있는 유의미한 정보를 7가지로 정의하고, 이를 추출하여 시간 정보로 정형화 하고자 한다. 7가지 유의미한 정보는 Bleeding, instruments, polypectomy, residue, inflated, non-inflated, no-fold 로 분류된다.

두 번째로, 대장내시경 스코프의 진행 방향을 분류하고자 한다. 맹장 도달 여부는 대장내시경이 성공적으로 수행 되었는지를

판단하기 위한 주요한 요소이기 때문에, 맹장의 위치, 즉 맹장도달시간 (Cecal intubation time)을 파악하는 것은 임상적으로 큰 의미가 있다. 따라서, 대장내시경 스코프의 진행 방향을 분류하고, 이를 바탕으로 진입 단계와 후퇴 단계를 구분함과 동시에 맹장도달시간을 자동으로 계산할 수 있다면, 대장내시경 영상을 시간정보로 자동 정형화하여 제공할 수 있을 것이다.

서울대학교 병원의 의학연구윤리심의위원회 (Institutional Review Board, IRB) 승인 하에, 113명의 대장내시경 영상 데이터를 수집하였다. 대장내시경 영상을 7가지 종류로 분류하기 위해서 Support Vector Machine (SVM) 모델이 사용되었다. Mean, variance, skewness, correlation, contrast, energy of laplacian, energy of gradient, 그리고 scale invariant feature transform 값들이 SVM의 feature로 사용되었으며, 5-cross validation으로 수행되었다.

Inflated, non-inflated, no-fold 프레임들에 대하여, SVM으로 학습된 용종 검출 알고리즘이 각각 적용 되었다. 여기에서도 위와 같은 feature들이 사용되었으며, 추가로 gray-level co-occurrence matrix 값이 사용되었다.

다음으로, 대장내시경 스코프의 진행 방향을 검출하기 위해서 Horn-Schunk 알고리즘으로 모션 벡터를 계산하였고, 이 값을 바탕으로 합성곱 신경망 딥러닝 기법을 통해 진입 운동, 후퇴 단계가 분류 되었다.

마지막으로, 위의 모든 정보들은 시간 정보로 정형화 된 다음,

대장내시경 요약보고서 (Summary report of colonoscopy video, SRCV)로 시각화 되어 평가 되었다.

113명의 대장내시경 영상에 대하여, 7가지 분류에 대한 평균 정확도는 93.7%, 민감도는 87.4% 였으며, 용종의 검출 정확도는 82.1%, 양성예측치는 39.3%를 획득 하였다.

대장내시경 스코프의 진행 방향에 대한 분류는 112명의 환자 영상으로부터 총 328,927개의 이미지 프레임을 사용하여 CNN에 의해 학습, 평가되었으며, 전체 평균 정확도는 95.6% 였다. 진입 운동에 대한 재현율과 정밀도는 각각 95.8%, 97.6% 였으며, 후퇴 운동에 대한 재현율과 정밀도는 각각 94.6%, 96.9% 였다. 연구를 통해 얻어진 값 $t = 30$ 초 에서, 맹장의 위치는 96.7%의 정확도로 검출 되었다.

본 연구에서는 대장내시경 영상에 영상처리 기술 및 머신러닝 기술을 적용하여, 용종, 7가지 유의미한 정보와 스코프의 진행방향에 대한 정보를 시간 정보로 정형화 하고, 의사 및 환자에게 효율적으로 전달 될 수 있도록 시각화하여 제공하였다. 본 연구의 결과물을 통하여, 용종 검출을 보조하고 대장내시경 영상을 재관측 하거나 다른 의료진, 타 의료기관에 공유하는 경우에 정보를 효율적으로 전달하며, 의료 서비스의 품질 향상에 기여하고자 한다.

핵심어: 대장내시경, 대장암, 용종, 메타데이터, 구조화, 영상처리, 기계학습, 시각화, 의료기록
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감사의 글

늘 옆에서 응원해 주고 발전 할 수 있도록 무한한 신뢰를 보내준, 세상에서 가장 사랑하는 나의 반쪽 가림이에게 가장 먼저 이 논문을 바칩니다. 짧지도 쉽지도 않은 여정이었지만, 당신이 있었기에 여기까지 올 수 있었다고 생각합니다. 항상 사랑하고 늘 고맙습니다.

학문의 길에 도전할 수 있도록 지원해 주시고 응원해 주신 사랑하는 가족들에게 깊은 감사의 말씀을 드립니다. 바른 길로 자랄 수 있도록 길러내 주신 아버지, 어머니, 할머니. 늘 믿고 격려해 주신 장인어른, 장모님. 항상 형을 믿고 따르며, 훌륭하게 성장한 동생 봉우. 가족들이 있었기에, 쉽지 않은 고비마다 앞으로 나아갈 힘을 얻을 수 있었습니다.

긴 시간 동안 끝까지 의미 있는 결실을 맺을 수 있도록 지도해 주신 김성완 교수님께 깊은 감사의 말씀을 드립니다. 교수님의 지도 아래 도전적인 연구 과제를 좋은 환경에서 수행할 수 있었다고 생각합니다.

논문을 잘 마무리할 수 있도록 지도해 주신 박광석 교수님, 정승용 교수님, 이정찬 교수님, 공현중 교수님께도 진심으로 감사의 말씀을 올립니다. 가르침 깊이 새기어, 훌륭한 연구자가 되도록 하겠습니다.

마지막으로, 오랜 시간 동안 가족 같은 유대감으로 서로를 지탱해 주고 도와준 BMC 연구원들께 감사의 말씀을 전합니다. 언제까지나 연구실 기둥으로 기억될 치원이, 늘 노력하는 자세를 가르쳐준 가람이, 유익하고 도움되는 조언을 아낌없이 주신 민혁이형, 행동력과 의지력을 보여주신 형우형, 동생이지만 배울게 많은

명준이, 함께 연구하며 물심양면으로 도와준 성우, 힘들 때 격려하고 조언해준 원식이, 인생의 반쪽을 찾아준 석규, 다방면에서 연구동향을 알려준 나영이, 부족한 의학 지식을 여쭙볼 때마다 항상 친절히 알려주신 범재원 선생님, 형석이형, 우형이형, 그리고 마지막까지 함께 동고동락한 윤재와 예은이. 오랜 시간 함께 교류하며 많은 도움을 준 동현이 까지.

많은 분들의 격려와 도움이 있었기에 쉽지만은 않았던 기간을 무사히 마무리 할 수 있었습니다. 앞으로도 정진하고 노력하며, 늘 감사함을 잊지 않도록 하겠습니다. 더욱 발전하고 성공한 모습으로 다시 뵙기를 기원하겠습니다.

2019 년 7 월

조민우 올림