Pain Evaluation During Colonoscopy by the Erythema Index of the Facial Image

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ABSTRACT

Background Endoscopy of the digestive tract is useful but is associated with significant pain to the patient. Its safety and tolerability could be improved by an immediate and objective method to evaluate the pain level and give feedback to the examiner. However, under the current circumstances, it is difficult to measure and assess the pain level objectively.

Methods We previously developed a discomfort assessment device that measures the changes in brain activity caused by changes in the pain level by extracting the changes in the erythema index from facial color data. In this study, to evaluate the usefulness of this discomfort assessment device, the association between the changes in the erythema index of facial images during colonoscopy and the subjective pain level during the examination were evaluated. For the recording of the subjective pain level during the examination, a subjective pain level recording device that we developed to measure grip strength over time was used. The subjective pain level, facial image, and percutaneous venous oxygen saturation during the examination were recorded in 30 patients who underwent colonoscopy at our hospital.

Results The duration of colonoscopy was divided into the insertion section and the removal section. The subjective pain level was found to be significantly greater during the insertion section than during the removal section, and the changes in the erythema index of the facial images were significantly different between the two groups.

Conclusion These findings indicate that the erythema index changes on facial images determined by the discomfort assessment device may facilitate objective evaluation of the pain level during colonoscopy.

Key words autonomic nerve, brain wave, colonoscopy, erythema, pain measurement

The prevalence of malignant gastrointestinal tumors is increasing as the population ages. To detect and treat such tumors at an early stage, the necessity of examination and treatment using gastrointestinal endoscopy (hereinafter referred to as “endoscopy”) continues to rise. However, significant physical and mental pain is associated with endoscopy, and this significant pain is one of the reasons why colonoscopy in particular is often evaded. In this manuscript, “pain level” refers to the degree of pain that alters brain activity and includes both physical and mental pain.

In preventive screening for colorectal cancer, an immunochemical fecal occult blood test is used as the primary test. This test is the non-invasive and convenient portion of the screening. The secondary test, however, involves significant pain because a comprehensive examination with colonoscopy is performed. According to a survey by the Japan Cancer Society, the rate of undergoing comprehensive screening in FY2015 was 91.0% for breast cancer, 83.9% for cervical cancer, 80.7% for gastric cancer, 79.8% for lung cancer, and 70.8%, the lowest, for colorectal cancer.1

The plausible factors for this include the physical pain associated with the pre-treatment for endoscopy, as well as during the endoscopy, and the mental pain caused by shame. Although the pain level during endoscopy is dependent on the examiner’s technique, there are no devices or methods that can give instantaneous feedback on the pain level during the examination. The pain level is expressed as the subjective pain level or the objective pain level depending on the person in charge of its evaluation. In this article, the subjective pain level is the pain level expressed by the participants themselves. The objective pain level is defined as the pain level that
can be acquired from the participants’ external signs without depending on them to express it.

There are several methods for evaluating physical pain through the measurement of substances that change with the physical stress response. These include measuring salivary amylase and plasma catecholamine, vasopressin, and adrenaline concentrations, as well as urine cortisol excretion. However, these methods are cumbersome and cannot provide instantaneous results. Moreover, although a visual analog scale is used as a scale to evaluate subjective pain, it is also not an immediate or an objective approach. The method that evaluates the autonomic function state from temporal fluctuations in the pulse is convenient and gives immediate results, but it does not directly assess the pain level.4

Since pain affects brain activity, the evaluation of the objective pain level would be possible by objectively ascertaining the differences in brain activity at time points in which there is significant pain and minimal pain. Although electroencephalography, Near-Infrared Spectroscopy, and Functional Magnetic Resonance Imaging may be able to measure brain activity, they all involve the use of a sensor probe, as well as large-scale instruments, and they are not suitable for evaluating the objective pain level during endoscopy.

As a device that is capable of measuring brain activity in a noncontact fashion, there is one that estimates brain activity based on facial skin temperature data from thermography. However, thermography is typically expensive and is difficult to market if it is incorporated into a medical instrument. Previous reports have shown the association of brain activity with cerebral blood flow and with facial blood flow caused by cerebral blood flow. Based on these reports, we developed an algorithm for a noncontact brain activity sensing system that estimates the changes in brain activity from changes in the erythema index on facial images. We then developed a discomfort assessment device to investigate the validity of the sensing technique for evaluating the objective pain level. The discomfort assessment device is composed of a color video camera with a complementary metal-oxide-semiconductor sensor and software for the noncontact brain activity sensing system, which estimates brain activity from facial images.

In this study, the association between the output data from this discomfort assessment device and the patient’s subjective pain level during colonoscopy was examined to investigate the usefulness of the noncontact brain activity sensing system and discomfort assessment device.

**MATERIALS AND METHODS**

**Ethics**

This study was conducted at the Advanced Medicine, Innovation and Clinical Research Center, Tottori University Hospital, Yonago, Japan. The study was approved by the Tottori University Ethics Committee (no. 1610B057) and registered in UMIN-CTR (no. UMIN000035052).

**Study participants**

This study included men and women, ≥ 20 years old, who were outpatients or inpatients at the Gastroenterology Department of Tottori University Hospital between December 2016 and September 2018 and were scheduled to undergo medically-indicated colonoscopy. Patients who were deemed unsuitable to participate in the study by the attending physician or principal investigator were excluded.

**Equipment and instruments**

Subjective pain level recording device: Temporal gripping strength measurement device (Tottori University Hospital).

Discomfort assessment device (Fig. 1): Analysis software (noncontact brain activity sensing system) and Color video camera (HX-A1H-K, Panasonic, Osaka, Japan).

Pulse oximeter: Percutaneous oxygen saturation measurement device (Pulsfit MP-1000, Japan Precision Instruments, Shibukawa, Japan).

**Measurement of the subjective pain level during colonoscopy**

To evaluate the subjective pain level of the study participants, a subjective pain level recording device was used. This device records the changes in the participant’s grip strength throughout the colonoscopy and is composed of a gripping device and a computer that records the grip strength over time.

The maximum grip strength of the study participants was recorded in the internal memory of the device. The change in grip strength from the initial state to maximum grip strength was designated as the recording range of the subjective pain level for each study participant, and its percentage was shown on the number display. Participants were instructed to hold the device throughout the examination and to change the grip in accordance with the pain level when they felt pain. The number was defined as the subjective pain level and was recorded in the internal memory of the device over time. The device was positioned such that the examiner could not view the numerical display.

The maximum value of the subjective pain level was
set prior to the endoscopy based on the measurements obtained from the subjective pain level recording device.

When the subjective pain level obtained during the examination exceeded the pre-set maximum value, the recording range was corrected with the exceeded value as the new maximum, and the data obtained in all sections was normalized accordingly.

The point when the tip of the endoscope enters the cecum was specified as the time point of reaching the deep area, and from the start of the examination to this point was defined as the “insertion section,” and from this point to the conclusion of the examination was defined as the “removal section.” Formulas for determining subjective pain level are as follows: the section average value for subjective pain level $X_A$ is $X_A = \frac{\sum_{i=1}^{E} X_i}{f_E-j_S}$, where $i =$ the total number of recorded values, $j_S =$ the number of recorded values at the beginning of the section, and $j_E =$ the number of recorded values at the end of the section; the section variation value for subjective pain level $X_{SD}$ is $X_{SD} = \sqrt{\frac{\sum (X_i-X_A)^2}{f_E-j_S-1}}$.

**Facial image acquisition and erythema index calculation using the discomfort assessment device**

The face of the study participant during the colonoscopy was captured with a color video camera and recorded as a video file. To eliminate the effects of ambient light, ring-shaped white LED lighting was placed around the color video camera and fixed to each study participant’s head with the head mount. Conditions were specified such that the positional relationship between the light source, color video camera, and facial area of the study participant remained constant. Measurement recording conditions were: frame rate, 30 frames per second; resolution, 1920 × 1080 pixels; compression format, H.264 (MPEG-4 AVC); and bit rate, approximately 15 Mbps.

Endoscope operation and changes in the participant's state, such as body movement or shift in body position during the examination, were recorded on audio.

Figure 2 shows the designated area for analysis on the study participants’ facial images. The area is enclosed by the outer corners of the eyes, immediately under the lower lid, and immediately above the upper lip. The red, green, and blue values (8-bit color depth) contained in each pixel in the designated area of all image frames. The equation and formulas for determining the erythema index, its section average value and variations are as follows: for determining erythema index $a^*$, a conversion equation from the RGB value to the erythema index is done (CIE-L*a*b* color system): $a^* = 500 \left( \frac{X}{X_m} \right)^2 - \left( \frac{Y}{Y_m} \right)^2$, $X = 0.4124 \times R + 0.3576 \times G + 0.1805 \times B, Y = 0.2126 \times R + 0.7152 \times G + 0.0722 \times B, X_m = 98.071, Y_m = 100.0, RGB$ value (range is 0-255; R, red; G, green; B, blue); the section average value of erythema index $a_{SA}^*$ is $a_{SA}^* = \frac{\sum_{i=1}^{E} a_{if}^*}{f_E-f_S+1}$, where $f =$ the total number of frames, $f_S =$ the number of frames at the beginning of the section, $f_E =$ the number of frames at the end of the section, and $n =$ the number of pixels contained in ROI of one frame; the average value of erythema index per frame $a_{SA}'^*$ is $a_{SA}'^* = \frac{\sum_{i=1}^{n} a_{i}'^*}{n}$; and the section variation value of erythema index $a_{SD}^*$ is $a_{SD}^* = \sqrt{\frac{\sum (a_{SA}' - a_{SA}^*)^2}{f-1}}$. 
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The mean erythema index of each pixel for each frame within the designated area was determined to generate a time series waveform of the changes.

The present investigation showed that there are individual differences in the changes in erythema index from heart rate fluctuations, even in the resting state. This was thought to reflect the individual difference in skin tone and variations in ambient light. For this reason, the erythema index was corrected for each participant using the range of the erythema index caused by heart rate fluctuations. The data processing flow chart is shown below (Fig. 3).

Recording of percutaneous oxygen saturation over time
Percutaneous oxygen saturation was measured using a pulse oximeter (MP-1000, Japan Precision Instruments). The device was worn on the right index finger, and the recording frequency was 25 Hz.

Collected data
This study investigated patients who gave their written consent to participate in the study after receiving a thorough explanation using a consent form approved by the Tottori University Ethical Review Board.

None of the 30 study participants were excluded by the attending physician or by the study participant.

The subjective pain level could be recorded in 11 of 30 participants. Excluded participants were those with data recording failure from failure to operate the device correctly or to set the time.

Facial images from the discomfort assessment device could be acquired in 25 of 30 participants. Those who were excluded had data that were not suitable for analysis due to body movement or poor camera stabilization. Furthermore, one case was excluded because the time point of reaching the deep area was unknown due to device battery depletion. Two participants whose analysis sections could not be set up due to body movement noise around the point of reaching the deep area were excluded, and 22 of 24 participants were investigated.

Percutaneous oxygen saturation could be obtained in 12 of 30 participants. Excluded participants were those who failed to wear the sensor or those with device battery depletion. Analysis was conducted with the data of 10 of 12 participants. One participant was excluded due to missing facial image data for analysis, and another was excluded because the time point of reaching the deep area could not be determined.

Statistical analysis
References for subjective pain level and erythema index between the insertion section and removal section during colonoscopy used a paired t test for continuous variables. We used the R 3.5.0 (R Development Core Team, Auckland, New Zealand) to perform all the statistical analyses.
RESULTS
The erythema index was a numerical value having no unit. Therefore, it was difficult to directly compare with the subjective pain level expressed in percentage. We compared the erythema index and the subjective pain level in the insertion section and in the removal section during colonoscopy, respectively.

Comparison of the subjective pain level in the insertion section and in the removal section during colonoscopy
A time series waveform for changes in the subjective pain level was generated for every participant.

Figure 4a shows an example of the measurement of the subjective pain level. During the insertion section of colonoscopy, intermittent gripping was prominent. Compared to the removal section, both the number of grips and grip strength were greater, indicating that the subjective pain level was greater during the insertion section compared to the removal section.

The mean subjective pain level and amount of variation (also defined as standard deviation) were compared between the insertion section and removal section; both were significantly greater in the insertion section compared to the removal section (Figs. 4b and c).

Comparison of the facial erythema index obtained from the discomfort assessment device between the insertion section and the removal section during colonoscopy
Figure 5a shows an example of the time series waveform for the changes in the facial erythema index. A significant change in the numerical value is observed when there is a shift in body position during colonoscopy.
Significant difference was observed between the insertion section and the removal section. The data acquired in both gray areas were used for analysis, while the patient’s posture was supine. The analysis was conducted only in the sections in which the participant was in a supine position.

Fig. 5. (a) Change in color tone of face measured by discomfort assessment device during the colonoscopy operation. Dotted line indicates the time point of reaching the deep area, and from this point to the conclusion of the examination was defined as the “removal section (light gray area).” The area from the start of the examination to this point was defined as the “insertion section (dark gray area),” and from this point to the conclusion of the examination was defined as the “removal section (light gray area).” The shaded areas indicate the analyzed sections. The sections were defined as a period from the time point of reaching the deep area until, both forward and backward, the time point in which there appeared a clear external factor due to changes in lighting caused by a shift in body position. The analysis was conducted only in the sections in which the participant was in a supine position.

For the facial erythema index acquired from the discomfort assessment device, the mean and amount of variation (standard deviation) were calculated for each section (insertion and removal) to determine statistical significance (Figs. 5b and c).

The mean was not significantly different between the two groups, and the trend for an increase or decrease was unknown. The standard deviation was significantly greater for the insertion section than the removal section. Significance (Figs. 5b and c).

Comparison of heart rate obtained from the facial image and from the percutaneous oxygen saturation waveform

The changes in the facial erythema index represent the changes in facial blood flow. Using the technique developed by McDuff et al. that estimates the heart rate from facial images, a band-pass filter (0.75-3 Hz) was applied to the erythema index waveform, and the peaks were determined from the resulting waveform. The estimated heart rate was determined using the peak per 10 seconds. Table 1 shows the comparison of heart rate measured by pulse oximetry and by the facial erythema index waveform. These data were obtained simultaneously. The formulas for determining the concordance rate of the mean heart rate of each section between the two measurement methods are as follows: the concordance rate $Y_C$ is $Y_C = \frac{Y_F}{Y_P} \times 100$ where $Y_F$ = the section
average value of the heart rate (bpm) by facial erythema
index, and \( Y_P \) = the section average value of the heart
rate (bpm) by pulse oximetry.

The average concordance rate (%) was 95.4% for
the insertion section and 97.4% for the removal section.
Based on these results, the heart rate obtained from the
changes in the facial erythema index was used in the
evaluation.

**DISCUSSION**

In this study, the subjective pain level was shown ex-
perimentally to be significantly greater in the insertion
section than in the removal section during colonoscopy
(Figs. 4a–c).

The facial erythema index standardized by the
changes in the erythema index from changes in the heart
rate in the insertion section and the removal section
was investigated. For the average value \( a^*_A \) of the erythema
index for each section, we set the average value of the
erythema index in the insertion section to \( a^*_A_i \) and the
average value of the erythema index in the removal sec-
tion to \( a^*_A_r \). When \( "a^*_A_r - a^*_A_i > 0" \), we called it “increased
group”; \( "a^*_A_r - a^*_A_i < 0" \) was called “decreased group”; and
\( "a^*_A_r - a^*_A_i = 0" \) was “invariant group.” Of these, “invariant
group” was not recognized. It was found that
there were cases in which the erythema index increased
with decreased pain, and there were also cases that
showed the opposite trend. It was difficult to directly
compare the erythema index and the subjective pain
level because the erythema index varies in properties de-
pendent on the subject and measurement conditions. The
amount of change of the erythema index was very small
compared to the absolute value. This was the reason
why there was no significant difference in the average
value. For this reason, a significant difference in the
mean value was not observed between the two sections;
however, differences in the size of the amplitude and
in the number of fluctuations in the waveform were ob-
served. Therefore, the standard deviation was calculated
as the amount of variation, and it was found that the
fluctuations were significantly greater in the insertion
section than in the removal section (Fig. 5c). These find-
ings indicated that the facial erythema index from pain
can be used as an indicator of the objective pain level
by using the standard deviation within the section. This
study is a preliminary study investigating an evaluation
method for an erythema index. Further experiments and
studies are necessary to understand the mechanisms that
alter variability of the erythema index.

A change in the autonomic function state may also
be a factor that alters the facial erythema index, since
changes in facial blood flow can be induced from dilation/
constriction of facial surface blood vessels, as well as
changes in heart rate. Therefore, the facial erythema
index can be viewed as a mixture of components that
reflect changes in brain activity, as well as the autonomic
function state.

In the current investigation, a decreased pain level
led to an increase in the facial erythema index in some
participants and a decrease in other participants, indicat-
ing the absence of a specific trend. We hypothesized that
these modulations reflected the changes in the autonomic
function state. To test this hypothesis, the changes in
the autonomic function state were analyzed based on the
heart rate and temporal fluctuations in the pulse, albeit
in a limited number of cases.

The heart rate waveform determined from the facial
erythema index was deconstructed by frequency through
spectral analysis, and the size of the fluctuation of each
frequency component was expressed as numerical

<table>
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<tr>
<th>ID</th>
<th>Heart rate (bpm) by pulse oximetry</th>
<th>Heart rate (bpm) by facial erythema index</th>
<th>Concordance rate (%)</th>
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ID, subject identification number.
Pain evaluation during colonoscopy by the facial image

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<th>Table 2. Comparisons of mean heart rates and LF/HF ratios in the group with an increased mean erythema index</th>
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\( t \)-test \( P = 0.41 \) \( P = 0.17 \)
Average \( −2.14 \) \( −0.03 \)

HF, high frequency; ID, subject identification number; LF, low frequency.

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<th>Table 3. Comparisons of mean heart rates and LF/HF ratios in a group with a decreased mean erythema index</th>
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\( t \)-test \( P = 0.24 \) \( P = 0.10 \)
Average \( 2.46 \) \( −0.09 \)

HF, high frequency; ID, subject identification number; LF, low frequency.

values.\(^{18}\) Fluctuation corresponding with the respiratory cycle with a relatively high frequency is designated as high frequency (HF), and fluctuation at a low frequency corresponding to the blood pressure cycle is designated as low frequency (LF). By calculating the LF/HF ratio, the autonomic function state can be assessed.\(^4\) A large LF/HF ratio indicates sympathetic dominance, while a low LF/HF ratio indicates parasympathetic dominance.

The participants were divided into two groups based on the increase or decrease in the facial erythema index. For each group, the increase group and the decrease group, the association between each section was examined for the mean heart rate and LF/HF ratio. The results are shown in Tables 2 and 3. There were no significant differences between any combination of two groups for the mean heart rate and LF/HF ratio of the increase group and the mean heart rate and LF/HF ratio of the decrease group, indicating the absence of a specific trend or association.

Based on the study results, the changes in the autonomic function state, compared to changes in the pain level, have a relatively small effect on the changes in the facial erythema index, suggesting that they can be disregarded, since they do not exhibit a specific trend.
However, the number of analyzed participants was limited, indicating the necessity to accumulate more data and perform further investigations. If the objective pain level could be immediately assessed during endoscopy, it would be possible to provide a safer and more comfortable examination. In particular, colonoscopy is considered to involve multiple pain-increasing factors, such as extension of the sigmoid colon at insertion or bloating from air insufflation. Moreover, because the pain level changes over time, an instantaneous assessment would be especially useful.

This study demonstrated that the standard deviation of the facial erythema index is significantly greater during the insertion section, which involves a greater pain level. The immediate assessment of the objective pain level is clinically significant from the perspective of objectively evaluating the examiner’s technique and from the standpoint of improving the technique to lower the patients’ pain level during endoscopy.

The results of this study suggested that the discomfort assessment device that was developed may be capable of providing an objective assessment of the pain level associated with colonoscopy. This discomfort assessment device evaluates the facial erythema index from images taken with a color video camera and an algorithm using a noncontact brain activity sensing system.

LIMITATIONS
Evaluations in this study were not limited to the conditions used in colonoscopy and did not include other types of endoscopy.

This study also did not take into consideration how butyl scopolamine bromide, given to study participants as an antispasmodic for endoscopy, may affect the autonomic nervous system.

Data on the LF/HF ratio do not include respiratory rate assessment.

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The authors declare no conflict of interest.

REFERENCES