DE NOVO CLASSIFICATION REQUEST FOR NAVICAM PROSCAN

REGULATORY INFORMATION

FDA identifies this generic type of device as:

> **Gastrointestinal capsule endoscopy analysis software device**. A gastrointestinal capsule endoscopy analysis software device is used to analyze pre-recorded capsule endoscopy videos of the gastrointestinal tract that are suspected of containing lesions. This device uses software algorithms to identify images and areas of interest as outputs to aid the clinician in analyzing suspected lesions, for clinician review of device outputs. The device may include hardware to support interfacing with a capsule imaging system.

NEW REGULATION NUMBER: 21 CFR 876.1540

CLASSIFICATION: Class II

PRODUCT CODE: QZF

BACKGROUND

DEVICE NAME: NaviCam ProScan

SUBMISSION NUMBER: DEN230027

DATE DE NOVO RECEIVED: April 14, 2023

SPONSOR INFORMATION:

Ankon Technologies Co., Ltd
B3-2, B3-3, D3-4 Biolake, No.666, Hi-Tech Road
East Lake New Technology Development Zone
Wuhan, 430075 Hubei, China

INDICATIONS FOR USE

The NaviCam ProScan is indicated as follows:

> NaviCam ProScan is an artificial intelligence (AI) assisted reading tool designed to aid small bowel capsule endoscopy reviewers in decreasing the time to review capsule endoscopy images for adult patients in whom the capsule endoscopy images were obtained for suspected small bowel bleeding. The clinician is responsible for conducting their own assessment of the findings of the AI-assisted reading through review of the entire video, as clinically appropriate. ProScan also assists small bowel capsule endoscopy reviewers in identifying the digestive tract location (oral cavity and beyond,

esophagus, stomach, small bowel) of the image in adults. This tool is not intended to replace clinical decision making.

LIMITATIONS

The sale, distribution, and use of NaviCam ProScan are restricted to prescription use in accordance with 21 CFR 801.109.

The device is not intended to be used as a stand-alone diagnostic device or replace clinical decision making.

ProScan should only be used with NaviCam Small Bowel Capsule Endoscopy System.

In the clinical study of the device, performance (sensitivity and specificity) of the device in the absence of clinician input was not evaluated. Therefore, the AI standalone performance in the clinical study of NaviCam ProScan has not been established. The clinician is responsible for making the final clinical diagnosis.

Negative or normal result, as determined by ProScan alone, does not exclude the presence of small bowel disease (false negative). Similarly, positive or abnormal result, as determined by ProScan alone, does not automatically confirm the presence of small bowel disease (false positive). The clinician should always carefully review the entire video. If symptoms persist, further evaluation should be performed.

ProScan is not intended to characterize lesions in a manner that would potentially replace biopsy sampling or other characterization tools.

PLEASE REFER TO THE LABELING FOR A COMPLETE LIST OF WARNINGS, PRECAUTIONS AND CONTRAINDICATIONS.

DEVICE DESCRIPTION

The NaviCam ProScan is artificial intelligence software that has been trained to process capsule endoscopy images of the small bowel acquired by the NaviCam Small Bowel Capsule Endoscopy System to recognize the various sections of the digestive tract and to recognize and mark images containing suspected abnormal lesions.

NaviCam ProScan is intended to be used as an adjunct to the ESView software of the NaviCam Small Bowel Capsule Endoscopy System (both cleared in K221590) and is not intended to replace gastroenterologist assessment or histopathological sampling.

NaviCam ProScan does not make any modification or alteration to the original capsule endoscopy video. It only overlays graphical markers and includes an option to only display these identified images. The whole small bowel capsule endoscopy video and highlighted regions still must be independently assessed by the clinician and appropriate actions taken according to standard clinical practice.

The NaviCam ProScan software includes two main algorithms, as illustrated in Figure 1 below:

- Digestive tract site recognition, which includes an image analysis algorithm and site segmentation algorithm to determine: oral and beyond, esophagus, stomach, and small bowel. Tract site is displayed as a color code on the video timeline with descriptions on the indicators at the bottom of the software user interface.
- Small bowel lesion recognition, which includes the small bowel lesion image analysis algorithm with lesion region localization. Potential lesions are marked with a bounding box as illustrated in Figure 2 below, with the active video played at the top section of the figure, and ProScan-identified images in the lower section, which includes images with suspected lesions and individual images marking the transition in the digestive tract. The algorithm is functional only on those sections of the GI tract that were identified as "small bowel" by the digestive tract site recognition software function.

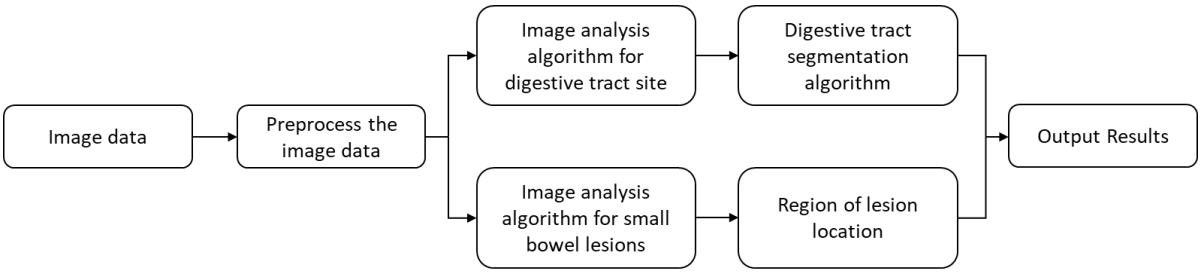

Figure 1: Working Principle of NaviCam ProScan

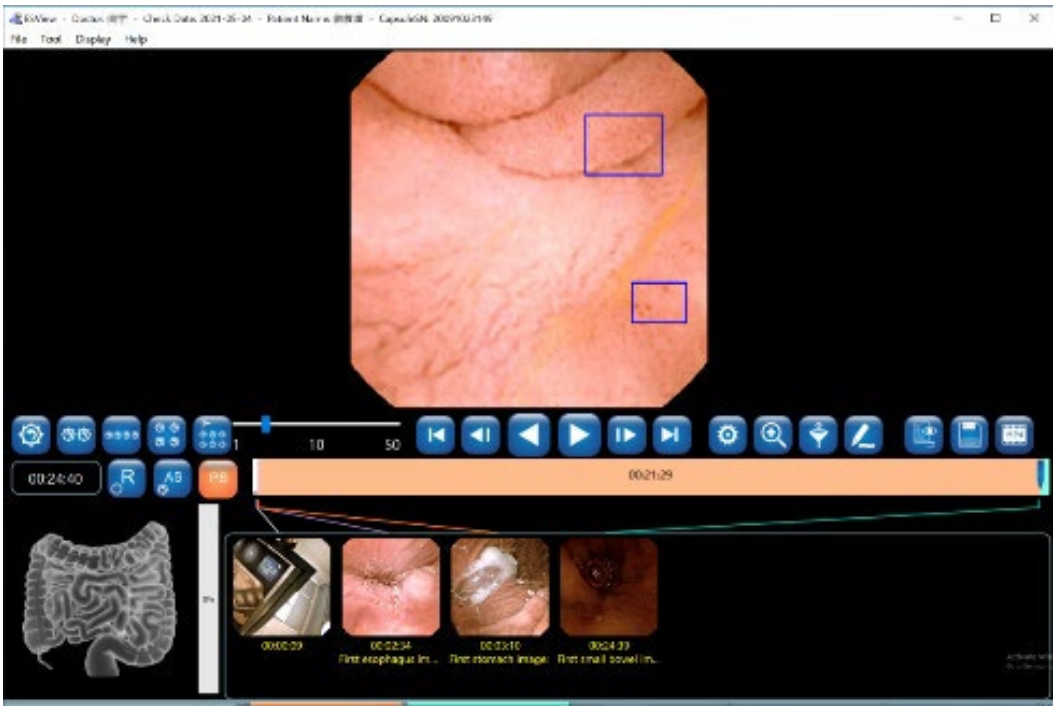

Figure 2: Lesion Recognition

Both software algorithms are based on convolutional neural networks using different deep learning models.

SUMMARY OF NONCLINICAL/BENCH STUDIES

SOFTWARE/CYBERSECURITY

NaviCam ProScan was identified as having a moderate level of concern as defined in the FDA guidance document "Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices." The software documentation included:

1. Software/Firmware Description
2. Device Hazard Analysis
3. Software Requirement Specifications
4. Architecture Design Chart
5. Software Design Specifications
6. Traceability
7. Software Development Environment Description
8. Verification and Validation Documentation
9. Revision Level History
10. Unresolved Anomalies

Risk analysis was provided for the software with a description of the hazards, their causes and severity as well as acceptable methods for control of the identified risks. NaviCam ProScan provided a description, with test protocols including pass/fail criteria and report of results, of acceptable verification and validation activities at the unit, integration and system level. These evaluations include performance, functional, UI, security, installation, compatibility, and regression testing associated with the software implementation into the primary ESView application. All testing met design specifications and passed successfully. This testing is not part of the AI performance evaluation.

Regarding the cybersecurity, documentation included all the recommended information from the FDA guidance document "Content of Premarket Submissions for Management of Cybersecurity in Medical Devices." This includes a threat model, cybersecurity mitigation information, a malware-free shipping plan, an upgrade plan, and other information for safeguarding the algorithms.

PERFORMANCE TESTING – BENCH – STANDALONE PERFORMANCE

The optimization, training, and validation of the NaviCam ProScan was performed in several phases, as summarized below.

Algorithm Training

In the training phase, the NaviCam ProScan was trained to recognize abnormal small bowel images and to recognize the digestive tract site. A dataset of 2,642 patients that underwent small bowel capsule endoscopy with NaviCam Small Bowel Capsule Endoscopy System, obtained from 8 clinical institutions in China, was collected.

Of those 2,642 patients, the dataset was split so that 1,476 patients were used for training the lesion detection function, and 218 patients were used in internal testing for the lesion detection function (see Standalone Algorithm Testing section, below), with full demographics information shown in Table 1 below. For tract site recognition, the 2,642 patient dataset was split so that 1,386 patients were used for training the tract site recognition function, and 424 patients were used in internal testing of the tract site recognition function (see Standalone Algorithm Testing section, below), with full demographics information shown in Table 2 below. Please note that patients used for training do not overlap with patients used for corresponding testing of that software function. However there may be overlap in selection of patients for training for lesion detection function and training/testing of the tract site recognition function, and overlap in selection of patients for training of the tract site recognition function and training/testing of the lesion detection function.

Table 1: Lesion Detection Function

	Training (No. of subjects = 1,476)	Testing (No. of subjects = 218)
Age (years):		
Mean Age (SD)	47.7 (9.8)	48.4 (9.8)
Age range	12~91	15~91
Sex:		
Male	977	151
Female	478	62
Unknown	21	5
Race/Ethnicity:		
White or Caucasian	0	0
Black or African American	0	0
Hispanic or Latino	0	0
Asian	1476	218
Native Hawaiian or other Pacific Islander	0	0

Table 2: Tract Site Recognition Function

	Training (No. of subjects = 1,386	Testing (No. of subjects =424)
Age (years):		
Mean Age (SD)	48.1(12.6)	47.3(11.6)
Age range	15~97	11~84
Sex:		
Male	898	342
Female	488	82
Unknown	0	0
Race/Ethnicity:		
White or Caucasian	0	0
Black or African American	0	0

Hispanic or Latino	0	0
Asian	1386	424
Native Hawaiian or other Pacific Islander	0	0

Images for the dataset were labelled as follows:

Lesion Detection Function

Pre-Annotation (Initial Labeling) Process:

Full videos were randomly assigned to three gastroenterologists for the annotation of small bowel images. The doctors annotate one or multiple positive lesion image segments and one or multiple negative image segments for each video. These positive lesion image segments and negative image segments constitute the full video of the small bowel for objects. All positive lesion image segments are independently numbered and randomly sampled. Similarly, all negative image segments are independently numbered and randomly sampled. These two parts, obtained through sampling, form the annotated image dataset of the small bowel.

Annotation (Truthing) Process:

The image dataset obtained from the pre-annotation process is annotated by the three gastroenterologists using annotation software in a back-to-back manner. The computer automatically determines consistency and merges the classification results while preserving differing opinions. When the cutoff value for consistency is less than 3, two arbitration experts independently review and modify the classification results, correcting any missed diagnoses, misdiagnoses, or misjudgments. If difficult questions arise, the arbitration experts engage in collective discussion and confirmation.

Tract Site Recognition Function

Pre-Annotation (Initial Labeling) Process:

Full video data is randomly assigned to three experts. The experts mark the boundary positions of each site (including Oral Cavity and beyond, Esophagus, Stomach, and Small Bowel) within each video. For example, the boundary position where the first image enters the esophagus, the first image enters the stomach, and the first image enters the small bowel. These four sets of images form a complete video. Each set of images is individually labeled and randomly sampled. The site annotation data is generated by randomly sampling all site data.

Annotation (Truthing) Process:

The image dataset obtained from the pre-annotation process is annotated by three gastroenterologists using annotation software in a blinded manner. They annotate the classification labels for the four sites (including Oral Cavity and beyond, Esophagus, Stomach, and Small Bowel). The computer automatically determines the consistency and merges the classification results while preserving differing opinions. When the consistency cutoff value is less than 3, two adjudication experts independently review and modify the classification results, correcting any missed diagnoses, misdiagnoses, or misjudgments. In case of difficult cases, collective discussions and confirmations are conducted by the adjudication experts.

Standalone Algorithm Testing

1. Lesion detection function

Following the training phase, the performance of the NaviCam ProScan to correctly recognize abnormal small bowel images was tested. For this purpose, 218 patients from the dataset described above were selected for testing, with results provided in Table 3 below. From that same dataset, normal and abnormal small bowel capsule endoscopy images were used to test the algorithm, with results provided in Table 4 below.

A. Patient-level analysis

Table 3: Patient-level Analysis Results

		Expert Reading	
		Normal	Abnormal
ProScan Prediction	Normal	33	2
	Abnormal	56	127

Patient-level sensitivity and specificity were determined to be 98% (95% CI: 93.95%-99.71%) and 37% (95%CI: 27.27%-48.02%), respectively. Subgroup analyses for patient-level sensitivity and specificity did not identify major differences when analyzed by gender, age, or lesion type.

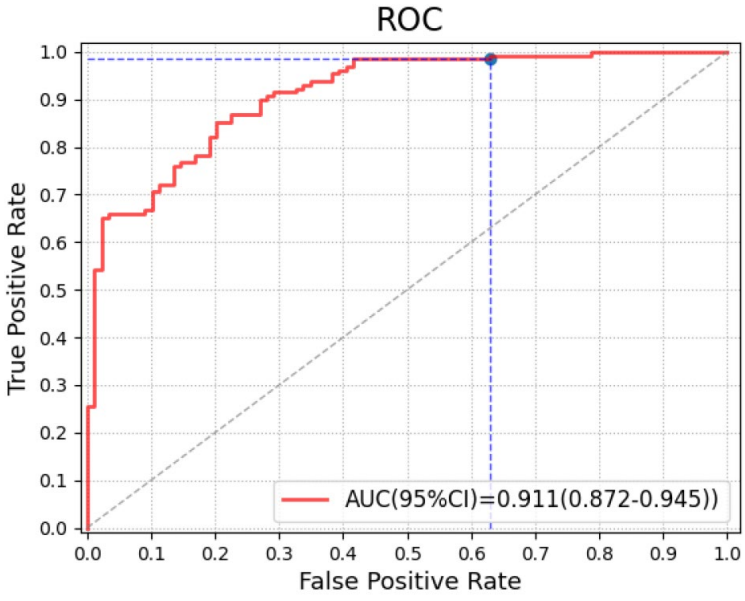

Figure 3: Patient-Level ROC and AUC Analysis

The patient-level ROC analysis, shown in Figure 3 above, is based on the assumption of worst-case device failure analysis, where the AI algorithm identifies a case as positive if it detects at least one positive image.

B. Image-level analysis

Table 4: Image-level Analysis Results

		Expert Reading	
		Normal	Abnormal
ProScan Prediction	Normal	14743	179
	Abnormal	372	3439

Image level analysis refers to the analysis of the dataset consisting of normal (no lesion present) and abnormal (lesion present) images. This dataset may include multiple images of the same lesion from different angles. Image level sensitivity and specificity were determined to be 95.05% (95% CI: 94.28%-95.72%) and 97.54% (95% CI: 97.28%-97.78%), respectively. ROC and AUC analysis is shown below in Figure 4.

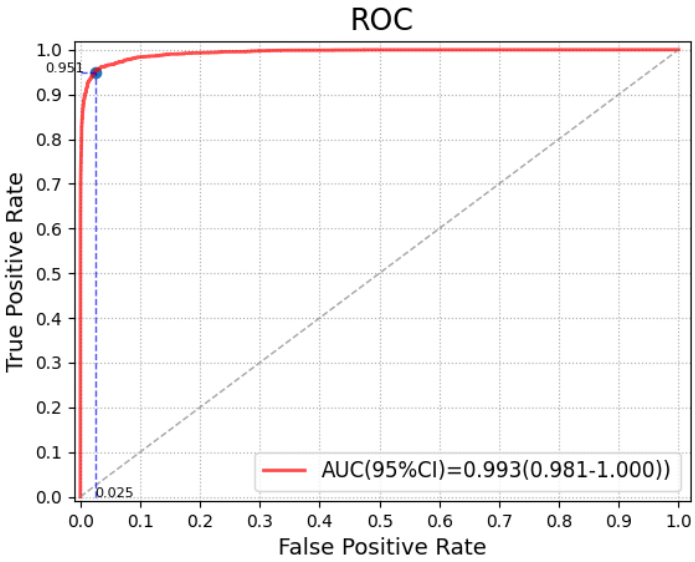

Figure 4: Image-Level ROC and AUC Analysis

Conclusions from Lesion Detection Testing

Patient-level sensitivity was high, at 98%, demonstrating that the lesion detection function resulted in few false negatives for patients. Patient level specificity was 37%, suggesting that clinicians will need to carefully review ProScan findings to identify false positive predictions. Lesion-level (or object-level) sensitivity and specificity are unknown. Patients may have multiple true positive lesions. The lack of lesion-level data introduces uncertainty regarding the ability of the device to detect individual lesions. At the image-level, results demonstrate sensitivity of 95.05% and specificity of 97.54%.

2. Tract Site Testing

Following the training phase, the performance of the NaviCam ProScan to recognize the tract site (oral cavity and beyond, esophagus, stomach, or small bowel) was tested. For this purpose, 424 patients from the dataset described above were selected for testing. The performance of the site recognition model at the image level was tested using four categories of digestive tract sites: Oral Cavity and beyond, Esophagus, Stomach, and

Small Bowel. The digestive tract images captured by capsule endoscopy exhibit a sequential relationship. Based on this sequential relationship and the results of image site classification, all digestive tract images were divided into four groups. Subsequently, the boundaries between different digestive tract sites, namely esophagus, stomach, or small bowel, were determined based on these groups, with results shown in Table 5 below.

Table 5: Tract Recognition – Image-level Analysis Results

		Expert Reading			
		Oral Cavity and beyond	Esophagus	Stomach	Small bowel
ProScan Prediction	Oral Cavity and beyond	3216	25	39	50
	Esophagus	11	704	5	24
	Stomach	5	10	17215	306
	Small Bowel	2	1	48	2986

Sensitivity and specificity were calculated for each category of anatomical site recognition (including Oral Cavity and beyond, Esophagus, Stomach, and Small Bowel) using a binary classification approach, with results shown in Table 6 below. The current category being evaluated is considered as positive, while the other categories are considered as negative. The Youden index is used to determine the optimal threshold, and sensitivity and specificity values are calculated accordingly. The prediction result of ProScan based on the confusion matrix are obtained by selecting the maximum probability value among the four anatomical site classifications for each image, and these predictions are used for statistical analysis and the final threshold setting for the device.

Table 6: Sensitivity and Specificity for Tract Site Recognition

	Sensitivity (95% CI)	Specificity (95% CI)
Oral cavity and beyond	99.47% (99.14%-99.68%)	99.50% (99.39%-99.58%)
Esophagus	98.92% (97.79%-99.50%)	99.10% (98.98%-99.22%)
Stomach	99.60% (99.49%-98.69%)	99.06% (98.80%-99.26%)
Small Bowel	99.26% (98.89%-99.51%)	98.36% (98.18%-98.52%)

Conclusions from Tract Site Recognition Testing

Based on the actual test results, the site recognition sensitivity and specificity values for each site (including Oral Cavity and beyond, Esophagus, Stomach, and Small Bowel) are all above 98%.

SUMMARY OF CLINICAL INFORMATION

Retrospective Evaluation

In a retrospective evaluation, two independent reviewers in China read capsule endoscopy images from 87 patients. The image review time of NaviCam reading with and without the ProScan feature on was assessed. The NaviCam SB System with ProScan feature on significantly

reduced the physician's reading time compared to the reading time of the NaviCam SB System without the ProScan on (21.47±8.05 vs. 58.10±45.28, p<0.0001).

Role of Artificial intelligence in Capsule Endoscopy for the identification of small bowel lesions in patients with small intestinal bleeding: the first prospective, multicenter trial (ARTIC Study).

Primary aim of this study was to assess the non-inferiority of the diagnostic yield (DY) for detection of significant small bowel (SB) pathology from three different readings of the small bowel capsule videos: clinicians reading videos with AI assistance from ProScan (described as AI+Physician below), conventional/standard video reading without AI assistance, and an expert board reading and adjudication of videos. Diagnostic yield is defined as the number of positive patients (as determined by interpretation of capsule images for significant small bowel pathology) divided by the total number of patients. Secondary aim was to compare mean reading time of the AI-assisted and standard reading modalities.

From February 2021 to January 2022, 137 patients were prospectively enrolled in 7 European centers to perform small bowel capsule endoscopy with the NaviCam SB system, which is provided with a convolutional neural network (CNN)-based function (ProScan software) for analysis of images for lesions. 22 clinician readers from 7 different European countries participated in the study. All readers had capsule endoscopy experience of over 500 readings.

All capsule videos were first evaluated in the enrollment center without AI assistance (standard reading). Anonymized videos were then randomly assigned to another center for a second blinded reading that was performed with the AI. In the AI+Physician arm, the clinicians were presented with the AI output, but made their own determination of SB pathology, and may have overruled the output from the AI. Finally, main diagnoses (small bowel lesions with high -P2- to moderate -P1- bleeding potential according to Saurin classification) and mean reading time reported by readers in the AI+Physician arm and Standard reading arm were compared by an expert board, who was used also to adjudicate the findings in case of disagreement. The participants on the expert board consisted of 5 of the original 22 readers. Expert board readings were used as the ground truth to measure the diagnostic performance of the readers and the software.

RESULTS: 133 patients from Italy, France, Germany, Hungary, Spain, Sweden, and UK were included in the final analysis (demographics in Table 7 below). Race/ethnicity of study participants was not collected. Four patients were excluded (2 due to missing documentation, 1 unable to swallow, and 1 due to device technical failure). The completion rate, defined as having the capsule reach the cecum, was 84.2%.

Table 7: ARTIC Study Patient Demographics

	Overall (No. of subjects = 133)
Age (years):	
Mean (SD)	66.5 (± 14.4)
Age range	24-101
Sex:	
Male	60

	Overall (No. of subjects = 133)
Female	73

The expert board reading identified P1+P2 lesions in 105 patients out of 133 patients (DY 78.2% [95% CI: 71.0% - 85.5%]). Standard readings and AI+Physician readings were compared to the expert board readings and discordant cases were re-evaluated and eventually reclassified during the adjudication phase. To note, all lesions missed in the standard reading arm were detected in the AI+Physician reading arm. At per-patient analysis, diagnostic yields for P1+P2 lesions were 62.4% (95% CI: 53.6% - 70.7%) and 73.7% (95% CI: 65.3% - 80.9%), for standard readings and AI+Physician readings, respectively (p=0.015). AI+Physician reading did not identify 7 patients in whom a small bowel pathology was identified by the expert board reading (i.e., there were 7 false negatives). Physician analysis of images resulted in no false positive patients, in both the standard reading arm as well as the AI+Physician reading arm, demonstrating the ability of physicians to correctly rule out false positives. The results are presented in Table 8 below. The number of false positive predictions from the AI software (in the absence of physician input) is unknown. Mean SB reading time was 33 minutes and 42 seconds (± 22 minutes and 51 seconds) in standard reading and 3 minutes and 50 seconds (± 3 minutes and 20 seconds) in AI-assisted reading ($p < 0.001$).

Table 8: ARTIC Study Reading Results

Comparison of Identification of significant SB pathology to Expert Board Reading		Expert Board Reading Identification of SB Pathology		Total	Diagnostic Yield (95% CI)
		Yes	No		
Expert Board Reading		105	28	N/A	78.2% (71.0%, 85.5%)
Standard reading mode (physician alone)	Yes	83	0	83	62.4% (53.6%, 70.7%)
	No	22	28	50	
AI+Physician reading mode (physician + ProScan)	Yes	98	0	98	73.7% (65.3%,80.9%)
	No	7	28	35	

CONCLUSION: AI+Physician reading resulted in non-inferior diagnostic yield compared to the expert board reading and the standard reading mode, demonstrating that the use of ProScan does not negatively impact identification of patients with small bowel pathology. However, the mean reading time was significantly decreased with the AI+Physician reading, as compared to the standard reading.

Pediatric Extrapolation

In this De Novo request, existing clinical data were not leveraged to support the use of the device in a pediatric patient population.

POSTMARKET SURVEILLANCE

In order to satisfy special control (1) below, NaviCam must collect and report postmarket surveillance data acquired under anticipated conditions of use to demonstrate that the device performs as intended when used to analyze data from the intended patient population. Specifically, the sponsor must conduct postmarket clinical validation performance testing to demonstrate the performance of the NaviCam ProScan lesion detection feature with physician input in the intended patient population, at the lesion-level, image-level, and patient-level, and demonstrate the performance of the NaviCam ProScan anatomic tract site recognition function at the object-level.

FDA expects that the postmarket clinical validation performance testing will address the performance of NaviCam ProScan (with physician input), as compared to a standard unassisted read using a clinically justified ground truth, on:

- Lesion-level, image-level, and patient-level analysis for lesion detection feature, including relevant FROC (free response receiver operating characteristic) analysis, ROC (receiver operating characteristic) analysis, sensitivity, specificity, and confusion matrices, as applicable and provide additional analysis for these endpoints for ProScan outputs (before physician input); and

- Object-level ROC analysis for anatomic tract site recognition function, including sensitivity, specificity, and confusion matrices, as applicable.

LABELING

The labeling includes a detailed description of the device, description of the patient population for which the device is indicated for use, and instructions for use. The labeling also includes summary information, including patient demographics, on the algorithm training, the non-clinical standalone performance testing and the clinical performance testing of the device in the ARTIC study.

The labeling includes limitations and warnings that prohibit the device from diagnosis or characterization of the lesions, and that the images and data acquired using the device are to be interpreted only by qualified medical professionals. There is a warning that the device should not replace clinician decision-making. There is also a warning regarding overreliance on the device.

Labeling will be updated in accordance with data collected via postmarket surveillance to provide updated clinical performance data and effectiveness data of the device.

RISKS TO HEALTH

The table below identifies the risks to health that may be associated with use of a gastrointestinal capsule endoscopy analysis software device and the measures necessary to mitigate these risks.

Risks to Health	Mitigation Measures
Algorithm failure leading to: • False positive resulting in unnecessary patient treatment; or • False negatives resulting in delayed or lack of patient treatment; or • Missed analysis due to misclassification of tract site resulting in delayed treatment	Clinical performance testing Postmarket surveillance Standalone algorithm performance testing Software verification, validation, and hazard analysis Electromagnetic compatibility (EMC) testing Electrical safety, thermal safety, and mechanical safety testing Labeling
False positive or false negative due to user overreliance on the device	Clinical performance testing Postmarket surveillance Labeling

SPECIAL CONTROLS

In combination with the general controls of the FD&C Act, the gastrointestinal capsule endoscopy analysis software device is subject to the following special controls:

(1) Data obtained from premarket clinical performance validation testing and postmarket surveillance acquired under anticipated conditions of use must demonstrate that the device performs as intended when used to analyze data from the intended patient population, unless FDA determines based on the totality of the information provided for premarket review that data from postmarket surveillance is not required. The following must be met:
   (i) Validation must use a clinical test dataset acquired from a representative patient population. Data must be representative of the range of data sources and data quality likely to be encountered in the intended use population and relevant use conditions in the intended use environment. Establishment of ground truth must be clinically justified. Study protocols must include a description of the process(es) for determining ground truth of training and test datasets;
   (ii) Objective performance measures (e.g., patient-level, lesion-level, and image-level data) with corresponding confusion matrices and statistical analyses must be reported with relevant descriptive or developmental performance measures. Summary level demographic information for study subjects and clinicians and sub-group analyses must be provided for each study site, relevant demographic sub-groups, and acquisition systems;
   (iii) The test dataset must be from sites that are different from sites used in training or development of the model; and
   (iv) Adverse events must be reported.

(2) Performance testing of the algorithm (i.e., standalone performance of the device itself, in the absence of any interaction with a clinician) must be provided.

(3) Software verification, validation, and hazard analysis must be provided. Software description must include a detailed, technical description including the impact of any software and hardware on the device's functions, the associated capabilities and

limitations of each part, the associated inputs and outputs, and mapping of the software architecture.

(4) Performance data must demonstrate electromagnetic compatibility, electrical safety, mechanical safety, and thermal safety for any hardware components of the device.

(5) Labeling must include:

(i) Warnings to avoid overreliance on the device, including that findings, or the lack thereof, should be reviewed by the clinician; that the device is not intended to be used as a standalone diagnostic device; and that the device does not replace clinical decision-making; and

(ii) A summary of the performance testing methods, including tested hardware, tested/supported patient population, results of the performance testing for tested performance measures/metrics with statistical analysis, summary-level descriptions of patient and clinician demographics and associated subgroup analyses for training and test datasets;

(iii) According to the timeframe specified in any postmarket surveillance protocol approved by FDA to satisfy the requirements in paragraph (1) of this section, a detailed summary of the postmarket surveillance data must be provided, including updates to the labeling to accurately reflect device performance based upon data collected during the postmarket surveillance experience.

BENEFIT-RISK DETERMINATION

Risks and Other Factors

The risks of the device are based on data collected in the ARTIC clinical study and standalone performance testing described above.

The use of NaviCam ProScan in conjunction with clinician reading demonstrated non-inferiority to standard reading. There remains risk of overreliance on the device, which may result in a missed diagnosis or improper diagnosis. The device is only intended to support the clinician without making clinical decisions. The clinical study results show that the AI+Physician reading resulted in 7 false negatives, meaning that the software with physician did not identify those patients as having suspected lesions despite presenting the condition. To compare, standard reading without AI resulted in 22 false negatives. This result indicates that the AI+physician use of the device is no worse than traditional capsule reading but remains imperfect. Without careful evaluation, suspected small bowel lesions may still be missed.

While no false positives were identified in the clinical study, there remains a probable likelihood that a normal image may be incorrectly identified as having lesions. This is evident from the standalone performance testing, which demonstrated a high patient-level false positive rate being output by the device. Clinician input is therefore an important part of device use, and clinical experience will impact the evaluation of these patients.

Benefits

The probable benefits of the device are also based on data collected in the clinical studies as described above.

Both studies evaluated the reading time with and without assistance from NaviCam ProScan. In the retrospective study, NaviCam SB System with ProScan significantly reduced the physician's reading time compared to NaviCam SB System without ProScan (21.47 minutes ± 8.05 vs. 58.10 ± 45.28, $p < 0.0001$). Similarly, in the ARTIC study, mean SB reading time was 33 minutes and 42 seconds (± 22 minutes and 51 seconds) in standard reading and 3 minutes and 50 seconds (± 3 minutes and 20 seconds) in the AI+Physician arm ($p < 0.001$). These results indicate that NaviCam ProScan has demonstrated the ability to reduce reading time while maintaining comparable outcomes to standard of care reading. By reducing read times, patients can receive faster turnaround in receiving a diagnosis from clinicians, allowing for more timely treatments as well.

Uncertainty

There remains uncertainty in the clinical study. The study did not assess device performance without clinician input. A postmarket study will be conducted to address the residual uncertainty regarding the ProScan's contributions to the readings in the clinical study. The postmarket study will characterize the ProScan's performance before clinician input, in a dataset independent from the training dataset. The data will be used to update the labeling describing performance of the ProScan. While the NaviCam ProScan is only intended for use with a clinician, results of the study will enable physicians to have a better understanding of their contributions and the ProScan's contributions when reading small bowel videos, and address the generalizability of device performance in additional patient populations, separate from those used for algorithm development.

All readers in the ARTIC study were highly experienced and well-qualified. The impact of over-reliance on the device may have been less pronounced, given their experience reading these videos. Among clinicians with limited experience in capsule endoscopy, the impact of over-reliance may be more applicable.

The ARTIC study was limited to a European population, while the internal study was limited to an Asian population. While this information supports a basic assessment of algorithm generalizability across different patient populations, we cannot exclude the possibility of unaddressed variables associated with these differences. For example, different lesion types may be more prevalent among certain ethnic groups. Based on the studies provided in this submission, it is unknown how well this variability has been addressed. If the algorithm were initially trained on a more diverse population – and evaluated in a similarly diverse followup study – the impact of this variability may be more properly understood.

In addition, the performance of tract site recognition was not evaluated in this study. While risks associated with this function are minimal, images incorrectly classified as being outside the small bowel carry the possibility of not being evaluated by the device, resulting in no AI reading for the impacted images.

Conclusion

It is a well-known fact that capsule endoscopy is a time-consuming procedure. Successive reads may result in reviewer fatigue, further impacting effectiveness of clinician reading performance. NaviCam ProScan has demonstrated its ability to improve on reading time without being inferior

to standard of care capsule endoscopy. Despite the existence of uncertainty, there is unlikely to be a negative impact on the procedural outcomes.

Based on the information above, the probable benefits of NaviCam ProScan outweigh the probable risks in light of the listed special controls and the general controls.

Patient Perspectives

This submission did not include specific information on patient perspectives for this device.

Benefit/Risk Conclusion

In conclusion, given the available information above, for the following indication statement:

> NaviCam ProScan is an AI assisted reading tool designed to aid small bowel capsule endoscopy reviewers in decreasing the time to review capsule endoscopy images for adult patients in whom the capsule endoscopy images were obtained for suspected small bowel bleeding. The clinician is responsible for conducting their own assessment of the findings of the AI-assisted reading through review of the entire video, as clinically appropriate. ProScan also assists small bowel capsule endoscopy reviewers in identifying the digestive tract location (oral cavity and beyond, esophagus, stomach, small bowel) of the image in adults. This tool is not intended to replace clinical decision making.

The probable benefits outweigh the probable risks for the NaviCam ProScan. The device provides benefits and the risks can be mitigated by the use of general and the identified special controls.

CONCLUSION

The De Novo request for the NaviCam ProScan is granted and the device is classified as follows:

> Product Code: QZF
> Device Type: Gastrointestinal capsule endoscopy analysis software device
> Regulation Number: 21 CFR 876.1540
> Class: II