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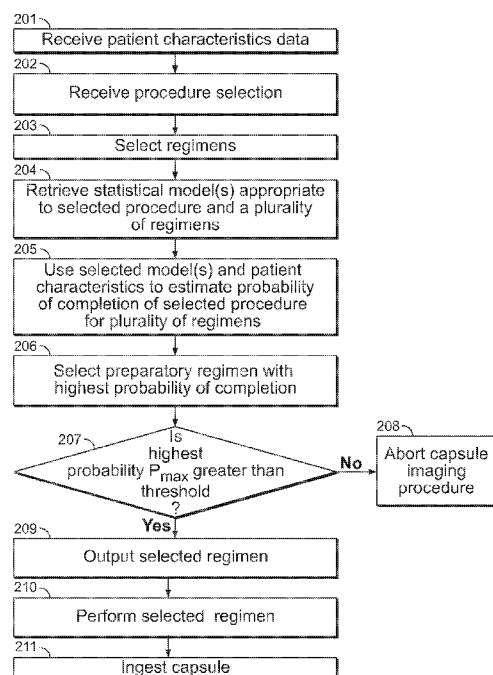


FIG. 2

(57) Abstract: A system and method for capsule imaging system uses an ingestible capsule, a receiver, a data input-output device, data processor and a memory. The receiver sends to the data processor image information received from the capsule. The memory stores a plurality of capsule imaging regimens and one or more statistical models relating patient characteristics to the probability of completion of an imaging procedure for each regimen. The data processor receives input data relating to characteristics of a particular patient, and use the statistical models to estimate, based on the received input data, for each of said plurality of capsule imaging regimens, the probability that the imaging procedure would be completed in the particular patient. The regimen is selected based on the probability estimates, and the patient manages the imaging procedure according to the selected regimen.



CAPSULE IMAGING SYSTEM AND METHOD

FIELD OF THE INVENTION

The present invention relates to methods and systems for in vivo imaging. More specifically, the present invention relates to systems and methods for in vivo imaging using ingestible capsules equipped to image body lumens.

BACKGROUND OF THE INVENTION

In-vivo imaging methods, such as performed by an in-vivo imaging system including a swallowable capsule, may be used to image body lumens within a human or animal patient, such as the gastrointestinal (“GI”) tract. The imaging system may capture and transmit, for example, images of the GI tract to an external recording device, while the capsule passes through the GI lumen. The capsule may capture images in fixed or variable frame rates which may be performed in a duration of for example one to eight hours, and the images may be viewed and/or processed in real time. The images may be combined in sequence, and an image stream or movie of, for example, 30 – 120 minutes in length, may be presented to a user such as the patient or a physician.

The GI tract consists of a series of organs including the esophagus, stomach, small intestine and colon or large intestine. Each organ has a different function. For example the small intestine (also called small bowel) is a part of the GI tract, connecting the stomach with the large intestine. The length of the small intestine in an adult is variable, and, depending on the conditions, can measure from 3 to 8 meters. The main function of the small intestine is the digestion and absorption of nutrients and minerals found in food. In order to do so, the small intestine pushes and mixes ingested food through the lumen by means of a physiological mechanism. Some of the other organs in the GI tract also operate to push food or other ingested material from one end of the GI tract to the other.

The physiological mechanism can be divided into two categories of movement: peristalsis, e.g. synchronized movement of the intestinal wall responsible for moving the food in one direction; and independent contractions, e.g. unsynchronized movement of the intestinal wall where the muscles squeeze substantially independently of each other, which may have the effect of mixing the contents rather than moving them along the GI tract.

The ability of an organ to transport material through the GI tract is called motility. Motility may vary from one part of the GI tract to another and from one patient to another. Various parameters may be measured which relate to motility including but not limited to time taken for a capsule to move from one location in the GI tract to another, absolute time at which the capsule arrives at a location in the GI tract, and velocity of the capsule. These and other parameters indicative of motility are referred to herein as “capsule motility parameters”.

A capsule imaging procedure performed on a patient, also called capsule endoscopy, may include some preparatory operations performed prior to insertion of the capsule, e.g. by swallowing the capsule. These may include operations performed by the patient, for example (but not limited to) fasting or ingesting a drug or other preparation material, e.g. a pharmaceutical preparation, for example in order to obtain optimal images. The drug or preparation material may have one or more functions or effects including (but not limited to) colon cleansing, sometimes called washing, and laxative. The term “capsule imaging procedure”, as used herein, generally refers to a process that may include preparatory operations, insertion (e.g., ingestion) of the capsule and, optionally, operations performed after insertion of the capsule, and it may further include removal of the capsule, e.g. by excreting it from the body. The capsule imaging procedure may also include preparation of a procedure report, either automatically or by a physician.

The term “regimen” is generally used in the art to describe a predetermined operation or sequence of operations which may, for example, be part of a capsule imaging procedure. A regimen may begin with preparatory operations, may include insertion of the capsule (e.g. by swallowing), may include operations performed after insertion of the capsule, and may include the removal of the capsule (e.g. by excretion from the body).

The terms “preparatory operation” and “preparatory regimen” are used herein to refer to a predetermined operation or sequence of operations that are performed prior to insertion of the capsule.

The term “post-insertion regimen” is used herein to refer to a predetermined operation or sequence of operations performed after insertion of the capsule (but typically while the capsule is in the body). A regimen may also be regarded as a kind of procedure.

The capsule imaging system may be powered by a battery which has a limited capacity, or limited total energy. The battery’s capacity may be measured in watt-hours or ampere-hours and is a measure of the charge or energy stored by the battery. A challenge for the successful conduct of a capsule imaging procedure is to ensure that a sufficient number of images are obtained to effectively monitor and diagnose one or more organs in, or sections of, the GI tract

while the battery still has sufficient charge. Capsule imaging procedures may be considered as “incomplete” when image acquisition, or video recording, stops due to the battery having insufficient capacity before the capsule has passed through an organ or a GI location or section to be monitored. For example, in the case of colon examination, a procedure would be incomplete if the capsule was not excreted from the body during image acquisition video recording. In the case of small bowel examination, a procedure would be incomplete if image acquisition and video recording stopped before the capsule passed to the large intestine. Up to 20% of capsule colon imaging procedures are incomplete. Conversely, a procedure may be deemed “complete” if image acquisition (and video recording) continues for as long as the capsule remains in the organ or GI part or section which the procedure is intended to examine.

Incompletion of a capsule imaging procedure (‘procedure’, for short) is one problem associated with conventional capsule endoscopy. Another problem of conventional capsule endoscopy is that, due to the procedure being not patient-specific, the capsule may move in the GI tract slower than expected, resulting in the patient having to ingest boosting materials. Besides the inconvenience involved in ingestion of such materials, these materials may have undesirable effects. Therefore, identifying cases where boosting materials are not required at all, or otherwise limiting consumption of such materials to the minimum level required to ensure completion of a capsule imaging procedure, would be beneficial.

SUMMARY OF THE INVENTION

Some embodiments of the invention provide a method of performing a capsule imaging procedure on a patient using an ingestible capsule. The capsule may comprise one or more imagers to capture images captured in a body lumen, one or more illumination sources for illuminating the body lumen, one or more transmitters for transmitting image data to a receiver, and a battery (which is a power source having a predetermined capacity). Embodiments of the method may comprise receiving data relating to (e.g., representative of) characteristics of (characterizing) a particular patient and, using a data processor, determining or estimating the probability of an imaging procedure being completed for the particular patient. The probability estimation may be carried out for a plurality of capsule imaging regimens or procedures. The estimating may be performed using one or more models, (e.g. statistical models) stored in a memory and relating patient characteristics to a probability of completion of imaging procedure for a plurality of regimens. Thus one probability estimate for each regimen may be obtained. One regimen for the particular patient may then be selected based on the probability estimates. The

selected regimen may then be performed, and then the capsule may be inserted (e.g., by the patient swallowing the capsule) into the GI tract.

Some embodiments of the invention provide a method in which an estimate of probability of completion is obtained after the capsule has been inserted, for example after a regimen has been selected. In such a method, data relating to characteristics of a particular patient may be received and the capsule may be inserted into the GI tract. A data processor may use the data relating to (e.g., representing) the characteristics of the particular patient to estimate the probability that an imaging procedure would be completed for the particular patient for the selected, e.g. ongoing, capsule imaging regimen or capsule imaging procedure. The estimate may use, or include using, a statistical model which additionally uses data received from the capsule. The probability estimate may be used to verify that the ongoing regimen, or procedure, is appropriate, or to modify the ongoing regimen or procedure.

According to embodiments of the invention, a regimen, or procedure, may be chosen based on patient characteristics including but not limited to any of demographic, behavioral, physiological and historical (e.g. clinical history) characteristics.

A system according to some embodiments of the invention may be configured to implement some or all of these methods. Thus some embodiments of the invention may provide a capsule imaging system having an ingestible capsule, a receiver, a data input-output device, data processor and a memory. The capsule may include one or more imagers, one or more illumination sources for illuminating a body lumen, one or more transmitters for transmitting image information to the receiver, and a power source (e.g., battery). The receiver may be configured to transfer, to the data processor, image information that is transmitted from the capsule. The memory may store a plurality of capsule imaging regimens and one or more statistical models that relate patient characteristics to the probability of completion of an imaging procedure for each one of the plurality of capsule imaging regimens. The capsule imaging regimens may include any of preparatory (e.g., pre-insertion) regimens, post-insertion regimens and regimens which include both pre-insertion and post-insertion operations. The data processor may be configured to receive input data relating to characteristics of a particular patient, and use the one or more statistical models to estimate, based on the received input data, for each of the plurality of capsule imaging regimens, the probability that the imaging procedure would be completed for the particular patient. Thus a plurality of probability estimates can respectively be obtained for a plurality of regimens, from which one regimen may be selected.

BRIEF DESCRIPTION OF THE DRAWINGS

The principles and operation of the system and method according to the present invention may be better understood with reference to the drawings, and the following description, it being understood that these drawings are given for illustrative purposes only and are not meant to be limiting, wherein:

Fig. 1 shows a block diagram of an in-vivo imaging system according to an example embodiment of the present invention;

Fig. 2 is a flow chart showing operations that may be performed in methods according to some embodiments of the present invention;

Fig. 3 is a flow chart showing operations that may be performed in methods according to some embodiments of the present invention; and

Figs. 4 and 5 are screen shots showing example probability estimates obtained using methods according to embodiments of the present invention.

It will be appreciated that for simplicity and clarity of illustration, elements shown in the figures have not necessarily been drawn to scale. For example, the dimensions and/or aspect ratio of some of the elements may be exaggerated relative to other elements for clarity. Further, where considered appropriate, reference numerals may be repeated among the figures to indicate corresponding or analogous elements throughout the serial views.

DETAILED DESCRIPTION OF THE INVENTION

In the following description, various aspects of the present invention will be described. For purposes of explanation, specific configurations and details are set forth in order to provide a thorough understanding of the present invention. However, it will also be apparent to one skilled in the art that the present invention may be practiced without the specific details presented herein. Furthermore, well known features may be omitted or simplified in order not to obscure the present invention.

Unless specifically stated otherwise, as apparent from the following discussions, it is appreciated that throughout the specification discussions utilizing terms such as "processing", "analyzing", "calculating", "computing", "storing", "determining", or the like, refer to the action and/or processes of a computer or computing system, or similar electronic computing device, that manipulate and/or transform data represented as physical, such as electronic, quantities within the computing system's registers and/or memories into other data similarly represented as physical quantities within the computing system's memories, registers or other such information storage, transmission or display devices.

Systems according to embodiments of the present invention, including imaging, receiving, processing, storage and/or display units suitable for use with embodiments of the present invention, may be similar to systems described, for example, in U.S. Patent Application Publication No. 2006/0074275, entitled "System and Method for Editing an Image Stream
5 Captured In-Vivo", U.S. Patent No. 7,009,634 to Iddan et al., entitled "Device for In-Vivo Imaging", and/or U.S. Patent Application Publication No. 2007/0118012, entitled "Method of Assembling an In-Vivo Imaging Device", each assigned to the common assignee of the present application and incorporated herein by reference. Methods for analyzing motility within a GI tract based on comparison of images captured by an in-vivo imaging capsule are disclosed, for
10 example, in U.S. Patent No. 6,944,316 to Glukhovsky et al., entitled "Motility analysis within a gastrointestinal tract" and incorporated herein by reference.

A capsule endoscopy procedure usually commences with the ingestion, e.g. swallowing, of the capsule by the patient. However, for some patients it is preferred to insert the capsule directly into a part of the GI tract, for example using a tool known as a gastroscope. References
15 in the following to "insertion" of the capsule are intended to encompass swallowing the capsule as well as other insertion techniques.

U.S. Patent Application Publication No. 2009/0105537, incorporated herein by reference, entitled "Device, System and Method for In-Vivo Examination" discloses various regimens or procedures, also called protocols, by which a patient may prepare or be prepared for a capsule
20 endoscopy procedure. An imaging regimen may be predetermined and may specify drugs or other preparation materials to be used for cleaning the colon, and the dose and the time frame in which each drug or other preparation material should be administered or implemented, e.g. swallowed.

In general, preparatory regimens may include but are not limited to any of the following:
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- Emptying the colon of content
- Fasting for a predetermined time period prior to insertion (e.g., swallowing) of the capsule
- Ingesting a preparation material, such as but not limited to any one or more of a gut lavage, laxative, stimulant and prokinetic agent.

30 Different preparatory regimens may specify different amounts of preparation material and/or different stages during the preparatory regimen during or at which they (e.g., drugs) should be swallowed or administered.

Additionally or alternatively, a patient may undergo or undertake a post capsule insertion regimen (e.g., while the capsule is still in the patient) including any of:

- Emptying the colon of content
- Fasting for a predetermined time period following insertion or ingestion of the capsule
- Ingesting a preparation material, such as but not limited to any one or more of a gut lavage, laxative, stimulant, prokinetic agent and water.

5

Different post-insertion regimens and different pre-insertion regimens may specify different amounts of preparation material and/or different stages during each regimen, either pre- or post-insertion, at which they should be swallowed or administered or otherwise applied. Preparation materials swallowed or administered prior to swallowing or insertion of the capsule are referred to herein as “preparatory” preparation materials. Preparation materials swallowed or administered after swallowing or insertion of a capsule are generally referred to as “booster” preparation materials. The same, or similar, preparation materials may be used as preparatory and booster preparation materials. Thus for example, a laxative may be ingested to cleanse the colon, and the same laxative may be ingested after the capsule has been swallowed in order to boost capsule excretion.

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The arrival of the capsule at certain landmarks within the GI tract such as esophagus, stomach, duodenum, small bowel, cecum, transverse colon, etc. may be detected, for example, based on automatic analysis of captured images using image processing methods, or other methods, for example as disclosed in U.S. Patent Application Publication Number 2006/0069317, titled “System And Method To Detect Transition In An Image Stream”, which is assigned to the common assignee of the present application and which is incorporated herein by reference.

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U.S. Patent No. 7,215,338 to Horn et al. discloses a system and a method for creating a summarized graphical presentation of a data stream captured in-vivo. The graphical presentation may be in the form of a color bar. Devices and systems as described herein may have other configurations and other sets of components. Devices, systems and methods according to embodiments of the present invention may be similar, for example, to the commercially available PillCam® SB2 or PillCam® Colon capsules and the associated data recorders and RAPID® workstation provided by Given Imaging, Ltd.

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An in-vivo imaging capsule which may be swallowed by a patient, may progress passively along the GI tract, due to peristaltic contractions which move the intestinal tissue walls. The capsule may have an elongate shape so that it maintains a substantially constant orientation with respect to the body lumen, although this is not essential and other shapes such as spherical are possible. During its journey, the capsule passes through different GI organs, such as the esophagus, the

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stomach, the small bowel and the colon. The capsule may capture images at different image capture rates. Due to the relatively narrow tunnel structure of the small bowel tissue walls, while the capsule is traveling in the small bowel and assuming that it has an elongate shape, it may maintain a position which is parallel to the direction of the tunnel. The longitudinal axis of the imaging capsule may generally remain parallel to the direction that the capsule advances in the small bowel. One or more imaging systems of the capsule may be positioned in at least one of the longitudinal ends of the capsule, such that the imaging is performed generally in a forward and/or backward looking position, to capture images of the opening and closing of the lumen quite regularly. Image data capturing the intestinal tissue walls and/or the opening and closing of the lumen hole, in conjunction with the recordation of the time of capturing each image, may permit analysis, display and/or calculation of properties or diagnoses of the patient's GI tract. For example, intestinal motility events, or type and frequency of peristaltic activity, or the amount of intestinal content which may be depicted in images may be analyzed.

Images of movement of intestinal tissue walls may be classified as depicting different categories of intestinal events. In some embodiments, intestinal events may be detected over a sequence of several consecutive image frames. The following categories are non-limiting examples of intestinal events:

- 1) "contraction" - movement of intestinal walls and/or lumen;
- 2) "static closed lumen" - paralyzed or substantially motionless intestine with a closed lumen hole;
- 3) "tunnel" - paralyzed or substantially motionless intestine with open lumen; and
- 4) "turbid lumen" - lumen hole and/or wall occluded by intestinal content.

Other categories of intestinal events and movement are possible.

Obtaining a significant or sufficient number of images and/or a significant or sufficient amount of image data may allow a detailed analysis of physiological condition. However, obtaining a large amount of data may require a long duration of video visualization. Therefore, diagnosis of a study by the physician may take a relatively long time. Detection, characterization and display of specific segments or portions of the image stream which have similar frame properties may be useful for determining diagnosis or assessing condition of a patient by the physician.

Analysis and processing of the image data may be performed automatically by a processing device, without user intervention. The display of summarized graphical data, for example using a color bar, window or display may be performed, e.g., by one or more processors, a workstation, circuitry, a detector or any other computation device. One or more

summarized graphical display windows or bars may be displayed to a health professional for diagnosis.

If a capsule imaging procedure is incomplete, because image acquisition or video recording stopped due to the battery having insufficient capacity before the capsule passed through an organ to be monitored, there may be several adverse effects. At worst, the whole procedure may have to be repeated, which is wasteful of time and energy and may be distressing for the patient and delay diagnosis. With images and possibly other data from only a part of the organ of interest, the remaining part will not be monitored and for example a lesion or other abnormality present in the organ may not be detected. Also, significant events occurring in the organ may be missed because image acquisition stopped too soon. Therefore, if the probability of an incomplete procedure can be reduced, this may contribute to the overall efficiency of the procedure and usefulness of the results.

Some embodiments of the invention use one or more statistical models, which may be compiled from experimental data, relating patient characteristics to probability of procedure being completed. These patient data or characteristics may be obtained prior to an imaging procedure being performed. The patient data or characteristics may include demographic and physiological characteristics such as but not limited to age, gender, and body mass index. The patient data or characteristics may include physiological characteristics. The patient data or characteristics may include characteristics which are based on, or derived from, the patient's clinical history including medications regularly taken by the patient, or existence of medical conditions such as inflammatory bowel disorder. The patient data or characteristics may include characteristics obtained in a previous imaging procedure. The patient characteristics may include behavioral characteristics such as but not limited to alcohol consumption (e.g., average weekly alcohol consumption). Any combination of kinds of patient characteristics may be taken into account in the statistical models, which may then be used to determine or estimate the probability of procedure completion for a patient with particular characteristics.

The term "statistical model", as used herein, may be any relationship from a simple linear equation, such as might be generated between, using, or based on two parameters which vary in proportion to each other, to a complex (e.g., multivariate) mathematical expression including many variables. It should be noted also that a set of equations is sometimes referred to in the art as a single "model" and a set of models as described herein may also be referred to in the art as a model (singular). A single model as described herein may also be considered to be a part of one larger model.

A model that relates one thing to another such as patient characteristic to probability may include each thing as a variable. Thus for example patient characteristics may be independent variables in a model, and probabilities may be dependent variables.

Some embodiments of the invention may use, or include using, different statistical models for different regimens. These statistical models may then be used to determine the probability of a procedure being completed for several different regimens for a particular patient with particular characteristics. The procedure with the highest (completion) probability may then be selected for, and applied to, that patient.

Some embodiments of the invention may use, or include using, different statistical models for different capsule imaging procedures. Thus some imaging regimens; e.g., preparatory (pre-insertion) regimens or post insertion regimens, may have, or result in, a higher probability of completion for one procedure, e.g. small intestine examination, than for another procedure, e.g. colon examination.

Using prior art capsule endoscopy, a relatively high proportion of capsule imaging procedures is incomplete and may not therefore provide conclusive information. Incomplete procedures occur for many currently used preparatory and post insertion regimens. Therefore, it is not currently possible to choose one imaging regimen over another with a higher expectation of completion of procedure.

A study was carried out, retrospectively analyzing the capsule excretion status and clinical history of around 1,100 patients who had undergone capsule colon imaging procedures, for which a requirement for completion was that the capsule was excreted before imaging stopped. Other definitions of "completion" of an imaging procedure may be used; for example, an imaging procedure lasting until or through a particular anatomical landmark, such as the colon, or the small intestine. The study identified statistically significant parameters that affected procedure incompleteness (i.e. capsule not excreted before imaging stopped). Various parameters were considered including patient behavioral characteristics, such as whether patients were smokers, clinical history parameters such as drugs they were taking and whether they had undergone surgery, whether they were prone to anxiety or depression, and more.

The following parameters were identified as significant for assessing capsule excretion:

- Age
- Body mass index ("BMI")
- Gender
- Average gastric and small bowel transit time
- Bowel preparatory protocol

It will be noted that certain behavioral and clinical parameters were not identified as being statistically significant in this study. The prevalence of some variables in the sample was very small. For example, it was not possible to examine “smoking” as a risk factor for “capsule not excreted before imaging stopped” since there were only 4 smokers (0.36% of the sample).
5 However it may be that larger studies in the future may identify these or other parameters as being statistically significant for the prediction of completion of an imaging procedure, so other or additional parameters may be used in the future in order to enhance the imaging regimen(s) selection methods. Therefore, some embodiments of the invention may use one or more patient characteristics to estimate probability of completion other than those found in the study to be
10 significant.

In the study, significant parameters were identified in a univariate logistic regression model, i.e. each parameter, when taken alone, was found to have an effect on the probability of capsule excretion while the capsule video was still running. Following identification of the statistically significant parameters, a multivariate logistic regression model was obtained for the
15 calculation of the predictive probability of colon study completion (e.g. capsule excreted before imaging ceased).

Methods of creating final multivariate model from univariate models will be familiar to those skilled in the art and will not be described in detail herein. Logistic regression was used and found to be suitable, but other regression techniques, familiar to those skilled in the art, may
20 be used including, but not limited to, linear, non-linear, parametric, polynomial and ordinary least squares. Such models, multivariate or univariate, may be used to define a relationship between dependent variables, such as procedure completion probability, and one or more independent variables (or 'predictors') such as the parameters identified in the study. The relationship may then be used to estimate the procedure completion probability for a new set of
25 values of independent variables.

Thus according to some embodiments of the invention, one or more multivariate statistical models, which may have been derived from results of previous capsule imaging procedures, are used to estimate the probability of a capsule imaging procedure being completed.

It should be noted that the available parameters for identification were limited by the
30 available study data, and it may be that in the future different patient parameters may be recorded by physicians, and these may be found in to be significant predictors of likelihood of procedure completion.

A multivariate model may be regarded as a set of models. For example a multivariate model that takes account of gender may also be regarded as two models, one for male and one for female.

A multivariate statistical model equation, for example derived from univariate models, may be of the following form:

Consider Y to be the outcome scenario, where,

$$Y = \begin{cases} 0 & \text{procedure incompleteness} \\ 1 & \text{procedure completion} \end{cases}$$

The model equation could be written:

$$\begin{aligned} \text{Logit}(P\{Y = 1\}) &= \log \left(\frac{P\{Y = 1\}}{1 - P\{Y = 1\}} \right) = \\ &= \beta_0 + (\beta_1 \cdot \text{Age}) + (\beta_2 \cdot \text{BMI}) + (\beta_3 \cdot \text{Gender}\{\text{Male} = 1; \text{Female} = 0\}) \\ &+ (\beta_4 \cdot \text{Average gastric and small bowel transit time}) \\ &+ (\beta_5 \cdot \text{Bowel preparation protocol: bp1}\{\text{Yes} = 1; \text{No} = 0\}) \\ &+ (\beta_6 \cdot \text{Bowel preparation protocol: bp2}\{\text{Yes} = 1; \text{No} = 0\}) \\ &+ (\beta_7 \cdot \text{Bowel preparation protocol: bp3}\{\text{Yes} = 1; \text{No} = 0\}) \end{aligned}$$

Where β_0 is a constant (e.g. the intercept with an axis if the data was plotted) and the rest of the parameters ($\beta_1, \beta_2, \beta_3 \dots$) are the predictors regression coefficients for different independent variables Male=1, BMI etc. Thus, for example, in case of a male patient that received bowel preparation #2 (i.e. "bp2"), the predictive probability for procedure completion will be:

$$\begin{aligned} \text{Logit}(P\{Y = 1\}) &= \\ &= \beta_0 + (\beta_1 \cdot \text{Age}) + (\beta_2 \cdot \text{BMI}) + (\beta_3 \cdot 1) \\ &+ (\beta_4 \cdot \text{Average gastric and small bowel transit time}) + (\beta_6 \cdot 1) \end{aligned}$$

If the patient was a female, the prediction probability for procedure completion would have been:

$$\begin{aligned} \text{Logit}(P\{Y = 1\}) &= \\ &= \beta_0 + (\beta_1 \cdot \text{Age}) + (\beta_2 \cdot \text{BMI}) + (\beta_3 \cdot 0) \\ &+ (\beta_4 \cdot \text{Average gastric and small bowel transit time}) + (\beta_6 \cdot 1) \end{aligned}$$

Generally, the predictive probability may be extracted using:

$$P\{\widehat{Y} = 1\} = \frac{e^{\beta_0 + (\beta_1 \cdot \text{Age}) + \dots}}{1 + e^{\beta_0 + (\beta_1 \cdot \text{Age}) + \dots}}$$

A model in which transit time does not appear might be used, for example, in the selection of an imaging regimen (e.g., preparatory regimen) prior to insertion at which time the gastric and small bowel transit times are not yet known.

5 A simple set of models for a system or method according to embodiments of the invention may operate using a simple application or program such as Microsoft Excel. Some examples of probability estimations or determinations obtained using the logistic multivariate models derived from the study of around 1,100 patients are described with reference to **Figs. 4** and **5**.

10 Reference is now made to FIG. 1, which illustrates an example block diagram of an in-vivo imaging system according to an embodiment of the present invention. In an exemplary embodiment, the system includes an ingestible capsule **40** having one or more imagers **46**, for capturing images (e.g., in a body lumen), one or more illumination sources **42**, for illuminating the body lumen, and one or more transmitters **41**, for transmitting image and possibly other
15 information to a receiving device, and a battery **43**. Illumination source(s) **42** may include, for example, one or more light emitting diodes ("LEDs"). Battery **43** may have a predetermined or pre-set, or finite, capacity, e.g., total amount of energy that can be used by components in capsule **40**. Typically, the image capture device may correspond to embodiments described in in U.S. Patent No. 7,009,634 to Iddan et al., and/or in U.S. Patent Application Publication No.
20 2007/0118012 to Gilad, incorporated herein by reference, but in alternate embodiments may be other sorts of image capture devices. The images captured by the imager system may be of any suitable shape including for example circular, square, rectangular, octagonal, hexagonal, etc.

System components shown in **Fig. 1** other than the capsule are typically located outside the patient's body in one or more locations. These components may include a receiver **12** and a
25 workstation **11**. Receiver **12** may include an antenna or antenna array (not shown in Fig. 1), an image storage unit **16**, a data processor **14**, and a display **15**. Workstation **11** may include a second data processor **25**, a data storage unit **19** associated with processor **25**, and an image monitor or visual display unit **18**, for displaying, inter alia, images recorded/transmitted by (originating from) capsule **40**. Data storage unit **19** may include an image database **21**.

30 Image receiver **12** may be designed to be carried by or worn by a user, for example it may be attached to a belt.

Typically, data processor **25**, storage unit **19** (e.g., a memory) and monitor **18** are part of a personal computer or workstation **11**, which may include standard components such as a

memory, a disk drive, and input-output devices such as a mouse **22** and keyboard (not shown in Fig. 1), although alternate configurations are possible. Data processors **14** and **25** may be or include any standard data processor, such as a microprocessor, multiprocessor, accelerator board, or any other serial or parallel high performance data processor. Data processor **25**, as part of its functionality, may act as a controller controlling the display of the images (e.g., which images, the location of the images among various windows, the timing or duration of display of images, etc.). Image monitor **18** is typically a conventional video display, but may, in addition, be any other device capable of providing image or other data. The image monitor **18** presents image data, typically in the form of still and moving pictures, motility data and in addition may present other information. In an exemplary embodiment, the various categories of information are displayed in windows. A window may be for example a section or area (possibly delineated or bordered) on a display or monitor; other windows may be used. Multiple monitors may be used to display images, motility properties, motility events and other data, for example an image monitor may also be included in image receiver **12**. When used in the context of a sequence of frames, a window of a set or sequence (e.g., ordered by time of capture or receipt, or another ordering) of frames may be a sequential subset of image frames within a stream of image frames.

In operation, imager **46** captures images and may transfer data representing the images (e.g., image data) to transmitter **41**, which transmits images to image receiver **12** (e.g., as image frames) using, for example, electromagnetic radio frequency (RF) waves. Image receiver **12** transfers the image data to image receiver storage unit **16**. After a certain period of time of data collection, the image data stored in storage unit **16** may be sent to the data processor **25** or the data processor storage unit **19**. For example, receiver **12** or only storage unit **16** may be taken off the patient's body and connected to the personal computer or workstation which includes the data processor **25** and data processor storage unit **19** via a standard data link, e.g., a serial, parallel, USB, or wireless interface of known construction.

The image data is then transferred from storage unit **16** to image database **21** within data storage unit **19**. Typically, the image stream is stored as a series of images in the image database **21**, which may be implemented in a variety of known manners. Data processor **25** may analyze the data and provide the analyzed data to image monitor **18**, where a user may view the image data. For example, data processor **25**, or data processor **14** in receiver **12**, may process images and create a motility bar according to embodiments of the present invention. Data processors **14** and **25** may execute software that, in conjunction with basic operating software such as an operating system and device drivers, controls the operation of data processors **14** and **25**.

Typically, the software controlling data processors **14** and **25** includes code written, for example, in the C++ language, and may be implemented using various development platforms such as Microsoft's .NET platform, but may be implemented in a variety of known methods.

5 Either of data processors **14** and **25** may also operate or execute other software for use in estimating the probability of an imaging procedure being completed for a particular patient, such as Microsoft Excel. Operations according to embodiments of the invention may be distributed between processors **14** and **25** and some or all may be performed by a remote processor that may be, for example, part of a server. Patient data, for example data relating to characteristics of the patient, may be input using input device **22**, and processors **14** or **25** may use the software to
10 perform the probability estimation, and the result of the probability estimation may be displayed on monitor **18**. The result may be an estimated probability, or, according to some embodiments of the invention, a particular regimen may be automatically selected, in which case monitor **18** may display details of (e.g., instructions to the patient which are related to, or in connection with) the selected regimen.

15 Receiver **12** may be or include any kind of mobile communication device and may for example comprise a hand held device such as a smart phone or personal digital assistant ("PDA"). Therefore, software for use in implementing methods according to embodiments of the invention may also operate on processor **14** within image receiver **12**, instead of or in addition to processor **25** at workstation **11**.

20 The image data recorded and transmitted by the capsule **40** may be digital color image data, although in alternate embodiments other image formats may be used.

Data processor storage unit **19** may store a series of images recorded by a capsule **40**. The images the capsule **40** records, for example as it moves through a patient's GI tract, may be combined consecutively to form a series of images displayable as an image stream.

25 Data processor **25** may include, or may be operationally connected to, a segment display generator **24**. Segment display generator **24** may process images from the captured set of images, and may calculate a set of pixel-based properties of the images to determine points of segmentation of the image stream. The segmented presentation may be generated and displayed in a predetermined section of the graphical user interface (GUI). Segment display generator **24**
30 may produce a segment display, e.g. a segment color bar or other graphical presentation, calculated based on pixel-based properties of at least a portion of frames from the image stream.

In one example, a subset of images used for generating a segment bar may include images captured between certain anatomical landmarks which may be identified in the image

stream, e.g. the duodenum, the cecal valve, the Z-line (indicating entrance to the stomach), etc. Two anatomical landmarks may be selected (e.g. may be predetermined in the system, or selected by a user), and all, or some, images captured during the time the capsule traveled from a selected anatomical landmark which was captured first to the selected anatomical landmark which was captured later, may be included in the generation of a segment bar. In another example, images may be selected according to color parameters, image quality parameters, number of detected pathology candidates in the image, etc. The segment bar may be generated for selected organs (esophagus, small bowel, colon, stomach, etc.), or for a specified duration of time selected from the complete imaging procedure (for example, the first 2 hours). In yet another example, images may be merged or fused, e.g. based on similarity between adjacent images, and a segment bar may be generated based on the subset of fused or merged images. Other image selection methods may be used for determining or selecting the subset of images. Different image selection methods may be combined for producing the subset of images which may be used in the generation of a segment bar.

A method of performing a capsule imaging procedure according to some embodiments of the invention will now be described with reference to **Fig. 2**. **Fig. 2** shows operations that may be performed prior to insertion of a capsule into the GI tract. Some of the operations described in **Fig. 2** may be implemented in a receiver such as receiver **12** of **Fig. 1** or in a workstation such as workstation **11** of **Fig. 1**. Alternatively, some operations may be distributed between a receiver and a workstation. In some embodiments, data processing operations may be carried out by a remote device in a distributed system, not shown in **Fig. 1**.

The methods illustrated in **Figs. 2** and **3** may be implemented using any kind of computing device such as a smart phone or desktop computer in which a set of statistical models for determining probability of imaging procedure completion are stored in memory. In the example apparatus of **Fig. 1**, the methods may be implemented in workstation **11**, or in image receiver **12**, or various tasks associated with the methods may be distributed between workstation **11** and image receiver **12**. Methods according to embodiments of the invention may be performed using a dedicated application running on the computing device, and it is assumed that the application is running and the operator has been presented with a graphical user interface (“GUI”) into which data may be input.

The method illustrated in **Fig. 2** commences at operation **201** with the reception of data, for example data input via a GUI, relating to (e.g., representative of) characteristics of a particular patient about to undergo a procedure. This data may be input by a physician (e.g., in a clinic) or by the patient (e.g., at home). The characteristics may include, for example, any of

demographic characteristics such as age, physiological characteristics such as body mass index, clinical characteristics such as medication currently used by the patient or existing medical conditions, and behavioral characteristics. The GUI may present the user with a field (e.g., text field or text entry box) for each of a number of possible characteristics to be input.

5 Some systems or methods according to embodiments of the invention may be configured to perform procedure completion probability estimations for multiple types of imaging procedures. For example, some procedures may be directed to examination of the small intestine whereas others may be directed to examination of the colon only. For such embodiments, at operation **202** a selection of a procedure such as for colon examination or for small bowel
10 examination may be input by, for example, a user. In other embodiments of the invention, for example intended for one procedure only, this operation may be omitted or skipped. For “single procedure” embodiments of the invention, a selection may, thus, not be necessary, and probability may be estimated for all procedures for which a model is stored.

 At operation **203** a selection of imaging regimens, protocols or procedures may be made
15 for which probability of completion is to be estimated and from which one will be selected for implementation.

 The selection may be automatic, for example based on one or more received patient characteristics. For example, the use of laxatives may be ruled out for patients with particular clinical characteristics, and this (ruling out use of laxative(s)) can be done automatically. The
20 regimens may include regimens that differ from each other only in terms of amount or concentration of a preparation material to be ingested. Amounts larger than a threshold amount may automatically be ruled out for certain groups of patients.

 Alternatively, selection of a regimen may be done by the user, e.g. physician. In some embodiments of the invention the user may be presented with a plurality of capsule imaging
25 preparatory regimens, for example in the form of a drop down list, from which the user may select regimens, at operation **203**, either as a group or one at a time. According to some embodiments of the invention the selection at operation **203** may be omitted. For example, probabilities may be determined for all of the regimens available, e.g. stored in memory, for a particular procedure, in which case there would be no selection; that is, operation **203** may be
30 skipped.

 At operation **204**, statistical models appropriate to the (selected) procedure and/or (selected) regimen may be retrieved, for example from memory, in order for the corresponding completion probabilities to be estimated. The models may relate patient characteristics to probability of completion of imaging procedure for a plurality of regimens or for particular

regimens. For example, the patient characteristics and the probabilities may be different variables in the models.

At operation **205**, for each of the plurality of regimens, optionally for those selected at operation **203** and optionally for a procedure selected at operation **202**, the models retrieved at operation **204** are used, at operation **205**, to estimate or determine the probability of completion of the procedure for a particular patient, using patient characteristics, for example as received at operation **201**.

At operation **206**, the regimen, regimens, protocol or procedure is selected on the basis of the probability estimates obtained at operation **205**. The regimen with the highest probability of completion may be selected. The selection may be automatic, or the selection may be performed by the physician or another user. More than one regimen may be selected automatically (for example more than one regimen for which the completion probability estimate is above a predetermined threshold), from which the physician may then select one to be implemented.

For some patients, the highest probability of completion may still be too low. For such patients, a decision may be made not to perform capsule endoscopy at all. Therefore, according to some embodiments of the invention, at operation **207** the highest probability, $P_{\max}$, is compared to a predetermined threshold value. If the highest probability, $P_{\max}$, is lower than the threshold value (this condition is shown as “No” at operation **207**), it may be recommended not to proceed with capsule endoscopy. The procedure may, therefore, be aborted or canceled at operation **208**, and this may be notified to the user via monitor **18** or a display screen of image receiver **12**, for example as a message, for example “Do not proceed with capsule procedure!”. However, if the highest probability, $P_{\max}$, is greater than the predetermined threshold value (this condition is shown as “Yes” at operation **207**), the process continues to operation **209** at which a selected regimen or procedure may be output (e.g., notified to the user undergoing the capsule procedure).

Some systems and methods according to embodiments of the invention may be designed such that the user can perform the selected regimen, and the imaging procedure may be conducted without further assistance from the physician. Indeed, all of operations **201-208** may be performed without the assistance of the physician.

Thus according to some embodiments of the invention, the regimen selected in operation **206** is output at operation **209**, for example in the form of an identification of the regimen displayed to the user. The regimen (e.g., preparatory regimen) may comprise a series of operations, or steps, including but not limited to ingesting preparation materials in specified dosages at specified times and fasting for a minimum period prior to insertion of the capsule. The

selected regimen or procedure may be visually, or otherwise, presented to the user for execution in the form of, for example, instructions displayed on a display of the image receiver **12**, a list and set of times for ingestion of drugs or compounds, or reference to a standard regimen among a number of regimens. The series of operations may be displayed to the user on the screen of the image receiver **12** and/or displayed on monitor **18**, and may be printed and provided to the patient.

Operation **210** indicates the performance of the selected regimen by the patient. The regimen may be a purely preparatory regimen and include no post-capsule insertion operations. Alternatively, the regimen may include post-insertion operations. This performance of the regimen may involve, for example, the physician administering a preparation material to the patient, or the patient independently performing the regimen, for example by ingesting a preparation material. Following performance of the regimen, or those steps of the regimen required to be performed pre-insertion, at operation **211** the capsule is inserted into the GI tract, for example by the patient swallowing the capsule, or a physician administering the capsule.

Some embodiments of the invention may be implemented only for the selection of a pre-insertion or preparatory regimen, in which case a method according to the invention may end with the insertion of the capsule into the GI tract. Some embodiments of the invention may be implemented only for the selection of post-insertion regimens. Some embodiments of the invention may relate to the selection of preparatory (or pre-insertion) regimens and to the selection of post-insertion regimens.

Fig. 3 illustrates a method of performing a capsule imaging procedure according to some embodiments of the invention, which may be performed as a stand-alone process after the receipt of patient characteristics data in operation **201** or in addition to operations **202-211** of **Fig. 2**.

After insertion of the capsule into the GI tract, data processor **14** or data processor **25** may receive, via image receiver **12**, image and other data that may be output from capsule **40**. The image and/or the other data may be analyzed to derive parameters (e.g., intestine motility related parameter(s)) that may include, among other things, the position of the capsule within the GI tract (e.g., positions at selected times elapsing from the ingestion time of the capsule), the amount of time travelled by the capsule in the gastric region (e.g., from throat to stomach) and the amount of time the capsule was in the small bowel. Such parameters are collectively referred to herein as “capsule motility parameters” and relate to a current journey of the capsule in the GI tract during which motility information may be collected ‘on-the-fly’ or in real time (as the capsule moves in the GI tract), as opposed to parameters that might have been derived from a previous capsule imaging procedure for the same patient. Capsule motility parameters may be

useful for obtaining a new, or for updating a previously obtained (e.g. in operation **205**), estimate of the probability that the procedure will be completed. In other words, while parameters other than capsule motility parameters may be factored in prior to ingestion of a capsule in order to estimate an initial probability that a procedure will be completed, capsule motility parameters may be used to 'fine tune' the estimated probability while the capsule already moves in the GI tract. A particularly useful capsule motility parameter is the mean of the transit times of the capsule in the gastric region and in the small bowel. Determining a probability of an imaging procedure being completed for a capsule imaging regimen may include using a model stored in a memory (e.g., data storage **16** or data storage **19**, Fig. 1) and relating patient characteristics and one or more capsule motility parameters to a probability of completion.

The first operation **301** shown in **Fig. 3** may include receipt of one or more capsule motility parameters, such as may have been derived already by processor **14** or any other processor in a system according to embodiments of the invention.

The next operation **302** is the retrieval from memory of a model (e.g. statistical model) appropriate to the ongoing procedure, for the ongoing regimen(s) or for the ongoing protocol, for example a procedure, regimen or protocol chosen according to the operations of **Fig. 2**. The model may relate patient characteristics and the one or more capsule motility parameters received at operation **301** to the completion probability of the procedure now in progress. For example, the patient characteristics and the probabilities as well as the capsule motility parameter(s) may be different variables in the models. It should be noted that the ongoing regimen may not include any ingestion operations post-insertion whereas a regimen would usually include some pre-insertion ingestion operations to cleanse the organ to be examined.

In operation **303**, the retrieved model is used to obtain a new estimate of the probability, P_{new} , that the procedure will be completed for the chosen regimen. This new estimate, P_{new} , may be more accurate since it is based on one or more capsule motility parameters which may have been obtained in real time. This new estimate, P_{new} , may then be used to determine whether to modify the chosen regimen, for example by the addition of an operation, or to select (continue with) an alternative regimen. Regimens may continue to change as more capsule motility information is obtained, or as capsule motility parameters are updated, while the capsule procedure continues.

Regimens used in conventional capsule endoscopy usually include at least one post-insertion operation involving the ingestion of a preparation material such as a booster material. It is desired to reduce use of boosting materials to as minimal amount as possible in order to disburden the patient of the inconvenience and possible undesired side effects involved in

ingesting such materials. Some embodiments may include as an advantage of that the regimen selected prior to insertion may include no, or fewer than would normally be expected, ingestions of post-insertion preparation materials. Some embodiments of the invention may be used to determine whether one or more post-insertion operations, such as ingestion of a booster preparation material, should be added to the selected regimen.

At operation **304**, the new probability estimate, P_{new} , is compared to a high probability threshold and to a low probability threshold in order to determine whether the selected regimen should be modified. Three possibilities are contemplated: (1) the new probability estimate, P_{new} , is below a low threshold, for example below 30%, in which case an operation such as ingestion of a booster preparation material may be added to the regimen, (2) the new probability estimate, P_{new} , is higher than a high threshold, for example higher than 70%, in which case it may be deemed that no additional operations are required, and (3) the probability estimate, P_{new} , is between the two thresholds, in which case it may be deemed that the probability estimate, P_{new} , is not a sufficient basis for a decision as to whether to add an operation to the regimen.

These three possibilities are shown in Fig. 3 as three possible paths after operation **304**. If the probability P_{new} is higher than or equal to the high threshold, the flow continues to operation **309** where the selected regimen continues without modification (without intervention). If the probability P_{new} is below the low threshold, the flow continues to operation **311** where the selected regimen is modified by adding an operation such as the addition of one or more ingestion operations.

If the probability is between the two thresholds, it may be deemed that no determination can be made, at this stage, regarding whether an intervention (e.g., administering a boosting material) is required, or if an intervention would ultimately result in the completion of the imaging procedure. Therefore, a second level of decision making, indicated by operation **306** may then be used to determine whether the chosen regimen should be modified. In that case, a decision, as to whether to modify the regimen, may be based on a subset of the one or more of the patient characteristics and capsule motility parameter(s) that provides the strongest indicator(s) of likelihood of completion (for example because the subset of patient characteristics and capsule motility parameter(s) are strongly correlated to actual completion). The subset of characteristics or parameters may be found by using, or from previous, experimental results. The subset of characteristics or parameters may comprise a single parameter or characteristic, for example gastric transit time, small bowel transit time, mean gastric and small bowel transit time, etc.

Thus in the example embodiment of the invention shown in **Fig. 3**, the modification of the regimen depends on the value of a particular capsule motility parameter. The flow of Fig. 3 is appropriate to the mean gastric and small bowel transit time for which the larger the value of the transit time, the lower the probability of procedure completion. At operation **306**, the motility parameter is compared to a motility threshold. If it is greater than or equal to the motility threshold, the flow continues to operation **311** where the selected regimen is modified by adding an operation to the regimen such as the addition of one or more ingestion operations. If the motility parameter is lower than the motility threshold, the flow continues to operation **309** where the selected regimen continues without modification (without intervention). Following completion of the regimen, the procedure ends at operation **310**, for example with the excretion of the capsule.

In the examples described with reference to **Figs. 4** and **5**, at operation **306** a single parameter was used, namely the mean of the transit times of the capsule in the gastric region and in the small bowel.

Thus, according to some embodiments of the invention, instead of the patient having to follow a conventional predetermined post-insertion regimen, which might be determined, for example, according to the location of the capsule in the GI tract, a patient-specific regimen may be selected for the particular patient. The selection may be based on one or more patient characteristics, and these may include, or be used in addition to, or in combination with one or more capsule motility parameters (e.g., travel time of the in-vivo device from one landmark in the GI tract to another; e.g., from the stomach to the small intestine's entrance and/or from the entrance to the small intestine to the entrance of the colon, etc.).

Any of the operations of **Fig. 3** may be performed by a processor in image receiver **12** such as processor **14**, or by processor **25** in workstation **11** after receipt of image data and other data from image receiver **12**. For a system designed to be used without the aid of a physician, at least the output of the selected regimen at operation **309** may be performed by image receiver **12**, for example by displaying instructions (e.g., directives) relating to the regimen on display **15**.

The statistical models used in embodiments of the invention may be updated or improved on receipt of additional data relating to imaging procedures that are carried out after the initial creation of the models. Thus, for example, a memory at workstation **11**, or another computing device, may be configured as a central repository for data relating to imaging procedures, and may receive such data from other computing devices. The initial dataset, from which the models were created, may be enlarged and the models may be updated, for example, at regular intervals, for example by time period or number of additional procedures added. The updated models may

be distributed among computing devices that may be configured to implement methods according to embodiments of the invention. Alternatively, methods according to embodiments of the invention may be implemented in a client-server architecture, in which case the models may be stored at a server.

5 **Figs. 4 and 5** show examples of results that were obtained using models derived from a study including approximately 1200 patients that were subjected to colon imaging procedures. **Fig. 4** shows that the user entered the age, BMI and gender of a patient and one of a selection of preparatory (“Prep”) regimens or preparatory procedures including the ingestion of polyethylene glycol (PEG) plus Sodium Phosphate, PEG plus SuPrep™, PEG plus Clear Liquid Diet plus
10 sodium phosphate (indicated as NAP), and PEG plus magnesium citrate. For a female aged 65 with regimen unspecified, the probability of procedure completion is 66%, indicating that some kind of preparatory regimen is advisable. The second set of data shows that if a BMI of 24 is also taken into account, the probability is reduced to 65%. While the probability in one example is expressed as a percentage, other measures such as a number from 0 to 1, can be used.

15 **Fig. 5** is an example suitable for the selection of a post-insertion regimen after the capsule has passed through the gastric region and the small bowel (“SB”), and the mean transit time for these two regions can be determined (e.g., based on image analysis). The calculation using variables in rows 3 to 5 shows that with a Prep-PEG + SuPrep™ regimen, for a 70-year old male with a BMI of 35 the probability of procedure (colon examination) completion is only 44%.
20 At this stage there is no option to cancel the procedure. If the probabilities for all regimens are below a predetermined threshold, the result of which is that it is difficult to select a regimen, a second level of decision making may take place. Selection of a regimen may be made on the basis of a limited number of available patient characteristics. As described in connection with **Fig. 3**, the mean transit time (a post-insertion characteristic) was found to be a strong indicator
25 for completing a procedure, and the selection of a post-insertion regimen may be based solely on this transit time. Thus, in a procedure including operations similar to operations **306, 309** and **311**, a decision made by a processor, as to whether to modify a regimen or not, may be based solely on the mean transit time. For example, if the mean transit time is lower than, for example, 90 minutes (or if it is lower than another predetermined threshold), the processor may decide that
30 there is no need for a booster operation, or an additional booster operation. However, if the mean transit time is greater than or equal to 90 minutes, the processor may decide that a booster operation or an additional booster operation is required.

The table below (Table-1) shows the parameters used in the regression model, which are used to generate the results shown in Figs. 4 and 5. A procedure according to embodiments of the invention for colon examination may include three stages as follows:

- 5 1. Calculation of a baseline predictive probability for procedure completion, for example according to **Fig. 2**, operations **201-205**. This stage may help physicians to determine the optimal bowel preparation for a specific individual (for example based on age, gender and BMI).
- 10 2. After capsule intake and obtaining the mean SB and GI transit time – while the capsule is in the patient body (but after passing the stomach and small bowel), the predictive probability for procedure completion may be reevaluated, for example according to **Fig. 3**, operations **301-303**, noting that one of the post-insertion regimens may involve taking no further action. In this case, according to embodiments of the invention the following scenarios may occur:
 - 15 a. The predictive probability for procedure completion with no further action is higher than an upper/high threshold, e.g. higher than ~70%, in which case no further action (e.g., intervention or modification of the selected regimen) is required.
 - 20 b. The predictive probability for procedure completion with no further action (e.g., without intervention of the selected regimen) is lower than a lower threshold, e.g. lower than ~30%, in which case action may be required and post insertion operations may be added.
 - 25 c. The predictive probability for procedure completion is below the upper/high threshold and higher than the low threshold, for example between 30%-70% for the selected regimen. In this case the predictive probabilities are indecisive in the sense that none of them is sufficiently reliable to ensure procedure completion. In this case, therefore, a further level of decision making may be applied, for example as described in connection with operation **306**.
- 30 3. In the scenario c above, reliance may be placed solely on the mean small intestine and GI transit times to determine new probabilities, and a cutoff point may be used to determine whether an action should be taken, or not.

Table-1 below demonstrates stages 1 and 2, and includes adjusted odds ratios (Adj.OR) that represent the direction and the strength of the association ('association' – between two variables), along with the 95% confidence intervals (CI, upper and lower) and P (probability)-values.

5

Effect	Baseline model				Model after capsule intake			
	Adj.OR	95% CI		P-value	Adj.OR	95% CI		P-value
		Low	Up			Low	Up	
Age	0.95	0.92	0.98	0.0004	0.96	0.93	0.99	0.0029
Gender - Male	1.68	1.14	2.49	0.0091	1.62	1.08	2.45	0.0208
BMI	1.03	0.99	1.07	0.1027	1.04	0.997	1.08	0.0726
Bowel preparation				<.0001				<.0001
Prep-PEG+magnesium citrate	1				1			
Other prep	1.81	0.69	4.74	0.2294	1.61	0.58	4.41	0.3586
prep Prep-PEG + Sodium Phosphate	2.92	1.32	6.49	0.0084	2.84	1.23	6.6	0.0149
prep Prep-PEG + SuPrep	4.94	2.57	9.48	<.0001	4.34	2.15	8.73	<.0001
prep Prep-PEGClearLiquidDiet-NAP	1.57	0.66	3.74	0.3036	1.54	0.61	3.89	0.3589
Mean SB and GI transit time	-	-	-	-	0.98	0.98	0.99	<.0001

Table 1

10

A model is useful if it fits the experimental data well. Therefore parameters, e.g. patient characteristics, may be excluded from consideration if they do not contribute to making the model better fit the data. For the parameters shown in the table, the following two indices were obtained:

1) C-statistic*=77%;

15

2) Hosmer and Lemeshow Goodness-of-Fit Test P=0.9763

(*When outcomes are binary, the C-statistic (equivalent to the area under the related Receiver Operating Characteristic curve) is a standard measure of the predictive accuracy of a logistic regression model.)

Different embodiments are disclosed herein. Features of certain embodiments may be combined with features of other embodiments; thus certain embodiments may be combinations of features of multiple embodiments.

Embodiments of the invention may include an article such as a computer or processor
5 readable non-transitory storage medium, such as for example a memory, a disk drive, or a USB
flash memory encoding, including or storing instructions, e.g., computer-executable instructions,
which when executed by a processor or controller, cause the processor or controller to carry out
methods disclosed herein. In some embodiments, a computer processor or computer controller, e.g.,
data processor **14** or **25**, may be configured to carry out embodiments of the invention, for example
10 by executing software or code stored in a memory connected to the processor, and/or by having
dedicated circuitry. Thus some embodiments of the invention may comprise a transitory or non-
transitory computer readable medium which when implemented in the computer or computing
system cause the computer to perform operations of methods according to embodiments of the
invention.

15 Various embodiments have been presented, and elements or operations from one
embodiment may be used with another embodiment. In addition, the specific ordering of operations
may be altered. The foregoing description of the embodiments of the invention has been presented
for the purposes of illustration and description. It is not intended to be exhaustive or to limit the
invention to the precise form disclosed. It should be appreciated by persons skilled in the art that
20 many modifications, variations, substitutions, changes, and equivalents are possible in light of the
above teaching. It is, therefore, to be understood that the appended claims are intended to cover all
such modifications and changes as fall within the true spirit of the invention.

CLAIMS

1. A method of performing a capsule imaging procedure on a patient using an ingestible capsule comprising an imager to capture images in a body lumen during an imaging procedure, an illumination source to illuminate the body lumen, a transmitter to transmit image data to a receiver, and a battery, the method comprising:
 - receiving patient characteristics related to a patient;
 - using a data processor, estimating a probability of completion of an imaging procedure for the patient for each of a plurality of regimens related to the imaging procedure, wherein the estimating comprises using one or more statistical models stored in memory relating patient characteristics to a probability of completing the imaging procedure for a plurality of capsule imaging regimens; and
 - selecting, for effecting the imaging procedure, prior to insertion of the capsule into the patient, a regimen from the plurality of regimens based on the probability estimates.
2. The method of claim 1, in which said selecting comprises selecting the regimen for which the estimated probability of completion of the imaging procedure is the highest.
3. The method of claim 1, further comprising receiving a selection of the plurality of preparatory regimens for which statistical models are stored in the memory, and performing the probability estimation for each selected regimen.
4. The method of claim 1, further comprising selecting a plurality of regimens from the plurality of regimens, wherein the selection is based on data relating to characteristics of the patient.
5. The method of claim 1, wherein at least some of the regimens include steps performed after insertion of the capsule.
6. The method of claim 1, further comprising, after insertion of the capsule:
 - receiving one or more capsule motility parameters; and
 - estimating the probability of an imaging procedure being completed using a statistical model stored in memory relating patient characteristics and the one or more capsule motility

parameters to a probability of completing the imaging procedure, to obtain a new probability estimate for the selected regimen.

- 5 7. The method of claim 6 further comprising using the new probability estimate to modify the selected regimen.
8. The method of claim 7 wherein the modification of the selected regimen comprises addition of one or more steps to be performed after insertion of the capsule.
- 10 9. The method of claim 6 comprising comparing the new probability estimate to a low threshold, determining that the new probability estimate is below the low threshold, and in response to the determination modifying the regimen by adding ingestion of a booster preparation material.
- 15 10. The method of claim 8 comprising:
 comparing the new probability estimate to a high threshold and to a low threshold,
 determining that the new probability estimate is between the high and low thresholds, and
 in response to the determination, determining whether or not to modify the regimen based
 on a selection of the one or more patient characteristics and capsule motility parameters
20 having the greatest statistical significance for completion of the procedure.
11. The method of claim 10 wherein the determination whether or not to modify the regimen is based on a capsule motility parameter and comprises comparing the capsule motility parameter to a motility threshold.
- 25 12. The method of claim 1, wherein performing at least some of the plurality of regimens includes ingestion of a preparation material by a patient.
13. The method of claim 1, wherein the plurality of regimens include regimens which differ
30 from each other by amount of a particular preparation material to be administered to a patient.
14. The method of claim 1 further comprising performing the selected regimen and inserting the capsule into the gastrointestinal tract.

15. A method of performing a capsule imaging procedure on a patient using an ingestible capsule comprising one or more imagers, one or more illumination sources, one or more transmitters, and a battery, the method comprising:
- 5 receiving characteristics of a particular patient, the characteristics comprising one or more of demographic and medical history information;
- inserting the capsule into the gastro-intestinal tract of the patient;
- using a data processor, determining the probability of an imaging procedure being completed for a capsule imaging regimen, wherein said determining uses a model stored in
- 10 memory and relating patient characteristics and one or more capsule motility parameters to probability of completion;
- comparing the probability to a first, low, threshold;
- determining that the probability is below said low threshold; and
- in response to said determination, modifying the capsule imaging regimen.
- 15
16. The method of claim 15 wherein the modification of the capsule imaging regimen depends on the value of one or more of said capsule motility parameters.
17. A capsule imaging system comprising:
- 20 an ingestible capsule, a receiver, a data input-output device, a data processor and a memory; wherein the capsule comprises one or more imagers, an illumination source, a transmitter, and a battery;
- wherein the receiver is configured to send to the data processor image information received from the capsule;
- 25 the memory storing a plurality of capsule imaging regimens and one or more statistical models relating patient characteristics to the probability of completion of an imaging procedure for each of said plurality of capsule imaging regimens,
- the data processor being configured to:
- receive input data relating to characteristics of a particular patient,
- 30 use the one or more statistical models to estimate, based on the received input data, for each of said plurality of capsule imaging regimens, the probability of the imaging procedure being completed for the particular patient,
- select a regimen based on the probability estimates, and
- output the selected regimen.

18. The system of claim 17 wherein the data processor is additionally configured to receive input data identifying a capsule imaging procedure, and wherein the capsule imaging regimens include different regimens for different imaging procedures.

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19. The system of claim 17 wherein the data processor is further configured to receive input data identifying different capsule imaging preparatory regimens for which statistical models are stored in said memory, and to perform said probability estimation for said identified capsule imaging preparatory regimens.

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20. The system of claim 17 wherein the data processor is further configured to receive one or more capsule motility parameters from said capsule, or to derive the one or more motility parameters from data output by said capsule.

15

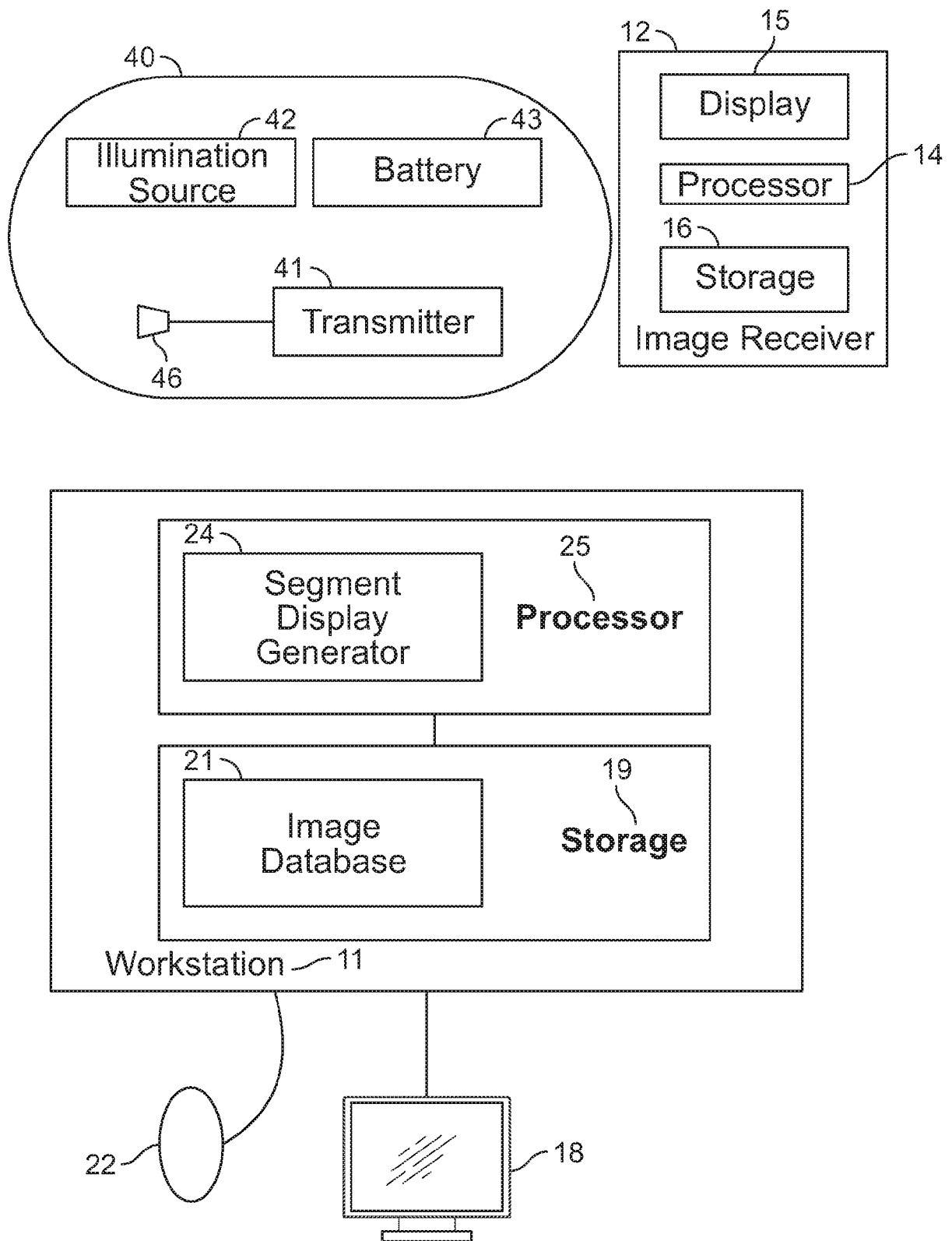


FIG. 1

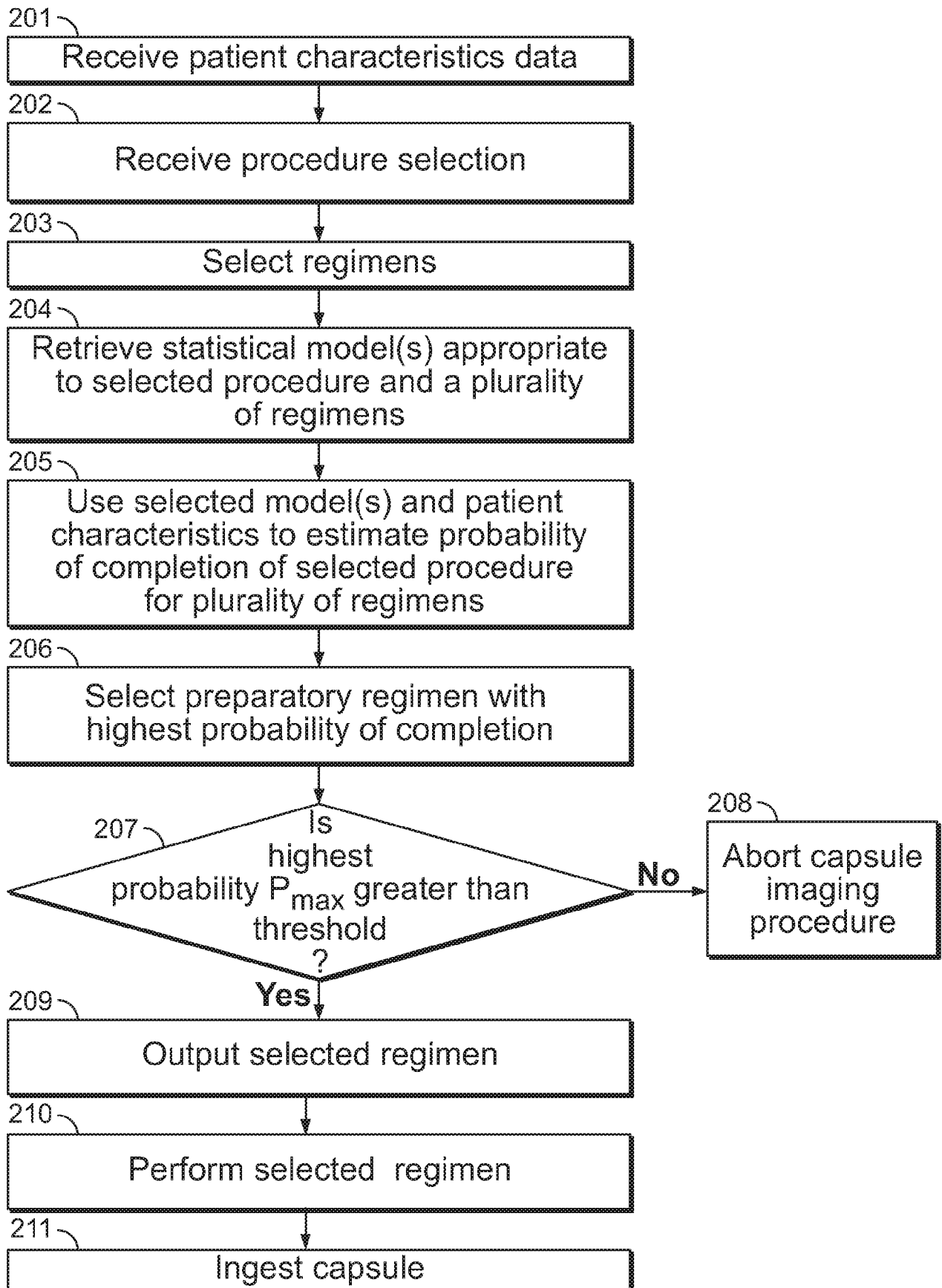


FIG. 2

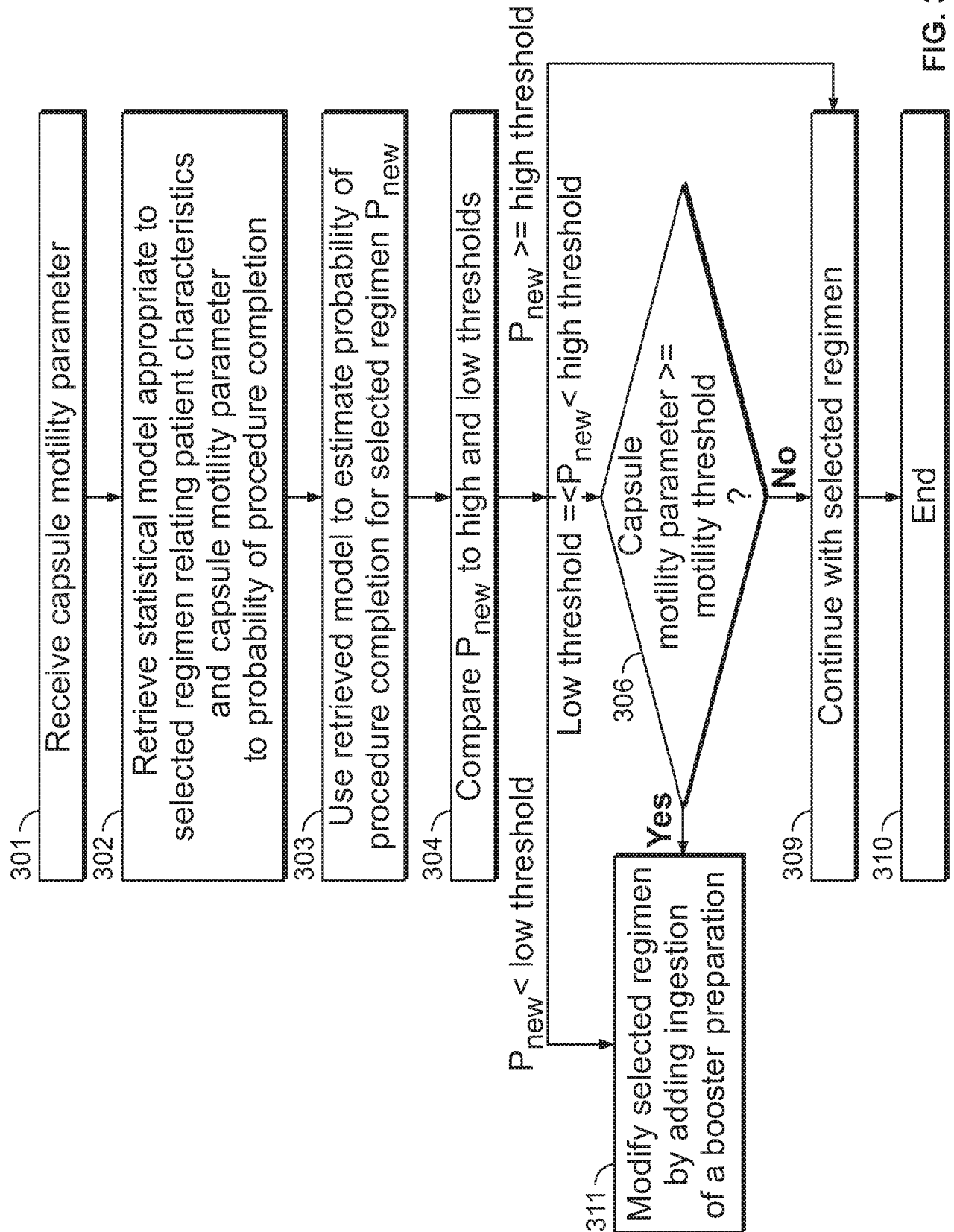


FIG. 3

ID	A		B	C	D	E
	VARIABLE	VALUE				
1	AGE	65				PREDICTIVE PROBABILITY FOR COMPLETE PROCEDURE 66%
2	PREP	OTHER				
3	GENDER	FEMALE				
4						
5						
6						
7	OTHER	MALE				
8	PREP.PEG+SODIUM PHOSPHATE	FEMALE	YES			
9	PREP.PEG+SUPREP		NO			
10	PREP.PEGCLEARLIQUIDDIET-NAP					
11	PREP.PEG+MAGNESIUM CITRATE					
12						
13						
14						
15	VARIABLE	VALUE				PREDICTIVE PROBABILITY FOR COMPLETE PROCEDURE 65%
16	AGE	65				
17	BMI	24				
18	PREP	OTHER				
19	GENDER	FEMALE				
20						
21						
22	OTHER	MALE	YES			
23	PREP.PEG+SODIUM PHOSPHATE	FEMALE	NO			
24	PREP.PEG+SUPREP					
25	PREP.PEGCLEARLIQUIDDIET-NAP					
26	PREP.PEG+MAGNESIUM CITRATE					
27						
28						
BASELINE MODEL (BEFORE)			MODEL AFTER CAPSULE INTAKE		④	

Fig. 4

A		B	C	D	E
VARIABLE		VALUE			
1	AGE	70			PREDICTIVE PROBABILITY FOR COMPLETE PROCEDURE 44%
2	BMI	35			
3	PREP	PREP-PEG+SUPREP			
4	GENDER	MALE			
5	MEAN GASTRIC AND SB TRANSIT TIME (MIN)	200			
6					
7					
8					
9	OTHER	MALE			
10	PREP-PEG+SODIUM PHOSPHATE	FEMALE	YES		
11	PREP-PEG+SUPREP		NO		
12	PREP-PEG+CLEARLIQUID/NAP				
13	PREP-PEG+MAGNESIUM CITRATE				
14					
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28					
BASELINE MODEL (BEFORE)		MODEL AFTER CAPSULE INTAKE			

Fig. 5

INTERNATIONAL SEARCH REPORT

International application No.

PCT/IL17/50521

A. CLASSIFICATION OF SUBJECT MATTER
 IPC - A61R 19/00, 5/05; A61N 2/00 (2017 01)
 CPC - A61B 5/073, 1/00016, 1/00036, 1/00158, 1/041, 5/037, 5/062, 5/065, 5/14539, 5/42; H02N 15/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

See Search History document

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

See Search History document

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

See Search History document

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 2014/0121474 A1 (CIACCIO, E) May 1, 2014; paragraphs [0108]-[0110], [0145], [0148]; claims 12, 17	1-20
A	US 2014/0296666 A1 (GIVEN IMAGING LTD.) October 2, 2014; figures 5, 9; paragraphs [0025], [0041], [0109], [0136], [0148], [0157], [0160]-[0161], [0274], [0307]; claim 1	1-20
A	US 2012/0316421 A1 (KUMAR, R et al.) December 13, 2012; paragraphs [0045], [0187], [0189], [0199], [0211]; claims 1, 18	1-20
A	WO 2016/047190 A1 (OLYMPUS CORPORATION) 31 March, 2016; pages 12-13, 21-23	1-20
A	US 2013/0311472 A1 (COHEN-SOLAL, E et al.) November 21, 2013; abstract; paragraphs [0013], [0015]	1-20

☐ Further documents are listed in the continuation of Box C.

☐ See patent family annex.

* Special categories of cited documents:

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"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search

20 August 2017 (20.08.2017)

Date of mailing of the international search report

15 SEP 2017

Name and mailing address of the ISA/

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