neurogastroenterology & motility

Neurogastroenterol Motil (2009) **21,** 1264–e119 doi: 10.1111/j.1365-2982.2009.01363.x

Intestinal motor activity, endoluminal motion and transit

F. DE IORIO,[*,†,‡] C. MALAGELADA,[*,†,‡] F. AZPIROZ,[*,†,‡] M. MALUENDA,[*,†,‡] C. VIOLANTI,[*,†,‡] L. IGUAL,[§] J. VITRIÀ[§] & J.-R. MALAGELADA[*,†,‡]

[*]Digestive System Research Unit, University Hospital Vall d'Hebron, Barcelona, Spain
[†]Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (Ciberehd), Barcelona, Spain
[‡]Department of Medicine, Autonomous University of Barcelona, Barcelona, Spain
[§]Computer Vision Center, Bellaterra, Spain

Abstract *A programme for evaluation of intestinal motility has been recently developed based on endoluminal image analysis using computer vision methodology and machine learning techniques. Our aim was to determine the effect of intestinal muscle inhibition on wall motion, dynamics of luminal content and transit in the small bowel. Fourteen healthy subjects ingested the endoscopic capsule (Pillcam, Given Imaging) in fasting conditions. Seven of them received glucagon (4.8 $\mu g\ kg^{-1}$ bolus followed by a 9.6 $\mu g\ kg^{-1}\ h^{-1}$ infusion during 1 h) and in the other seven, fasting activity was recorded, as controls. This dose of glucagon has previously shown to inhibit both tonic and phasic intestinal motor activity. Endoluminal image and displacement was analyzed by means of a computer vision programme specifically developed for the evaluation of muscular activity (contractile and non-contractile patterns), intestinal contents, endoluminal motion and transit. Thirty-minute periods before, during and after glucagon infusion were analyzed and compared with equivalent periods in controls. No differences were found in the parameters measured during the baseline (pretest) periods when comparing glucagon and control experiments. During glucagon infusion, there was a significant reduction in contractile activity (0.2 ± 0.1 vs 4.2 ± 0.9 luminal closures per min, $P < 0.05$; 0.4 ± 0.1 vs 3.4 ± 1.2% of images with radial wrinkles, $P < 0.05$) and a significant reduction of endoluminal motion (82 ± 9 vs 21 ± 10% of static images, $P < 0.05$). Endoluminal image analysis, by means of computer vision and machine learning techniques, can reliably detect reduced intestinal muscle activity and motion.*

Keywords *capsule endoscopy, computer vision analysis, endoluminal image analysis, glucagon, intestinal motor inhibition, machine learning techniques, small bowel motility, small bowel transit.*

INTRODUCTION

Intestinal motor function is accomplished by the interplay of action-reaction sequences between the intestinal walls and the luminal content. Understanding gut motor function would require simultaneous measurement and correlation of multiple variables, which is technically complex. The technology of capsule endoscopy provides continuous visualization of the intestinal lumen and wall movement,[1] but simple observation of video images cannot provide a quantitative estimate of motor activity. We have applied computer vision techniques to analyze endoluminal images. These techniques permit detection of wall activity, both contractile (luminal occlusions and radial wrinkles), and non-contractile patterns (open tunnel and smooth wall patterns), wall motion, dynamics of contents and transit (axial displacement of the capsule along the tract). Furthermore, we have incorporated to our system automatic learning programmes to identify patterns, and an algorithm for evaluation of intestinal motility has been developed. This method has been validated against manometry in the diagnosis of severe intestinal motor disorders.[2] However, the heterogeneity of abnormal motor patterns inherent to the various etiological and clinical presentations of patients with severe dysmotility causes difficulties in correlating the various motor events that take place in the small bowel. Thus, to help clarify relations among muscular action, wall motion, dynamics of luminal contents and transit, we have

---

Address for correspondence
Fernando Azpiroz, MD, Digestive System Research Unit, Hospital General Vall d'Hebron, 08035-Barcelona, Spain.
Tel: (34) 93 274 62 22; fax: (34) 93 489 44 56;
e-mail: azpiroz.fernando @gmail.com
Received: 20 March 2009
Accepted for publication: 12 June 2009

used an experimental model of intestinal muscle inhibition in healthy subjects by glucagon administration.

METHODS

Participants

Eighteen healthy subjects (nine men, nine women; age range 20–36 years) without gastrointestinal symptoms were included in the study. The protocol for the study was approved by the Ethics Committee of the University Hospital Vall d'Hebron, and all participants gave their prior written informed consent.

Endoluminal imaging and capsule displacement

The Pillcam capsule (Pillcam SB1 video capsule, Given Imaging, Yokneam, Israel) was used to visualize the intestinal lumen at a twice-per-second rate. Eight external antennae were fixed to the anterior abdominal wall to detect the UHF-band signal that is emitted by the capsule. The position of the capsule on a bidimensional plane of the abdomen is estimated depending on the signal strength received by each antenna (Fig. 1). Units of displacement correspond to a fraction of the interantennae distance (the lateral diameter of the abdomen is equivalent to 1800 units). The battery in the capsule allows a total recording time of 8 h.

Experimental procedure

The capsule was ingested after overnight fast, and recording was continued for a total time of 8 h with the subjects lying comfortably on a hospital bed and the trunk 30° above the horizontal. Arrival of the capsule into the jejunum was monitored by endoluminal visualization (jejunal mucosa pattern) at 10-min intervals;[3] when pertinent (see Experimental design below), i.v. glucagon (4.8 μg kg^{-1} in bolus followed by 9.6 μg kg^{-1} h^{-1} infusion for 1 h) was administered 30 min later. This dose of glucagon has been previously shown to inhibit both tonic and phasic intestinal motor activity.[4–8]

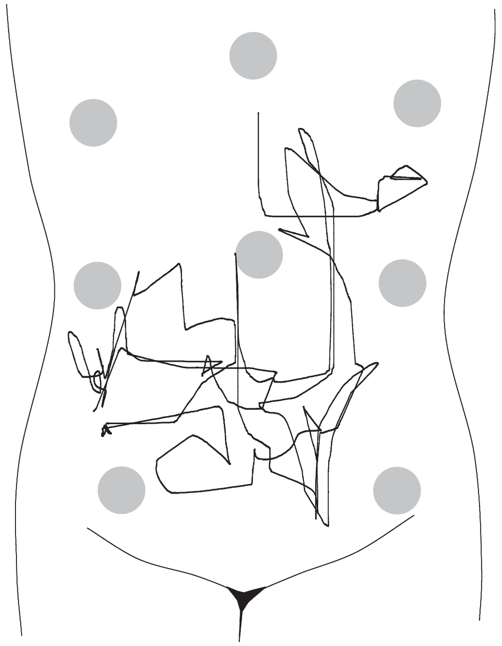

Figure 1 Example of capsule transit through the small bowel registered by the antennae fixed to the abdominal wall.

Experimental design

Main experiments Fourteen healthy subjects were studied: in seven (four men, three women; 20–36 years age range) glucagon was administered 30 min after arrival of the capsule into the jejunum, and in the other seven (three men, four women; 24–29 years age range) fasting activity was recorded, as control. As the main objective was to examine the effect of intestinal muscle inhibition on endoluminal motion and transit, the experiments were not placebo-controlled and randomized.

Ancillary study Recordings in the main experiments were performed with the subjects at rest lying on bed; to determine the potential influence of body motion on capsule recordings, particularly on endoluminal motion and capsule displacement, four additional subjects (two men, two women; 23–24 years age range) were studied twice on separate days in random order, once during rest and another day intercalating 5 min periods of ambulation every 30 min.

Data analysis

Gastric exit of the capsule and arrival in the cecum were visually detected, and small bowel images were analyzed. Endoluminal image and displacement was analyzed blindly by means of a computer vision programme specifically developed for the automatic evaluation of muscular activity (contractile and non-contractile patterns), intestinal contents, endoluminal motion and transit.[2]

Non-contractile patterns tunnel and wall In each image, the intensity of light of the different pixels was analyzed using a Laplacian of Gaussian model, which defines the three-dimensional curve reflecting the relationship between the bright walls close to the light of the capsule and the dark lumen.[9] A tunnel pattern (open lumen) was visualized as a band of bright peripheral wall and a central lumen characterized by a large dark area. Conversely, a wall pattern, reflecting a transverse endoluminal view, was characterized by an image directly focusing on a smooth bright wall without a view of the lumen.

Contractile patterns Phasic luminal closure Phasic intestinal contractions are visualized as reversible changes in lumen size (closure/opening) within a 9-frame sequence (4.5 s). These events were detected using a cascade of sequential steps,[10] first filtering out turbid and static sequences, and then using an automatic classifier (support vector machine),[11] as follows. From the Laplacian analysis of each image described above, 54 parameters were measured in each 9-frame sequence. Based on a series of examples of contraction sequences and non-contraction sequences selected by visual analysis, the programme found the best discriminatory function to identify contractions. Discrimination between occlusive and non-occlusive contractions (complete *vs* partial luminal closure) was performed by a second classifier based also on a training set of both types of contractions.

Radial wrinkles. Contraction of the circular intestinal muscle produces wrinkles in the intestinal wall radial to the shrinking intestinal lumen. In each image, the amount of intestinal wrinkles was measured by structural tensor analysis,[12,13] as follows. The image was treated as a topographic map in which the crests and valleys were identified and their direction towards the central lumen was measured. The degree of wrinkles was measured from 0 to 1 using a radial Gaussian basis function kernel, and a threshold of 0.9 was used to define wrinkles.

Turbid intestinal content Each image was defined by two parameters representing the mean value (chromacity) of the blue–yellow *vs* the red–green component.[14] Using these parameters, an automatic classifier was trained to detect the turbid frames in each video.

Endoluminal motion Endoluminal motion was measured by analysis of colour differences (red–green–blue composition) in consecutive images using the Earth Mover's Distance method,[15]. The method measures the amount of work (Euclidian distance) necessary to transform the colour plot of one frame into the following one, and static images are defined using a pre-established threshold. This method was used to measure wall motion in clear frames, and the dynamics of contents in turbid frames (Fig. 2).

Capsule transit Displacement of the capsule was estimated by the change in the location of the capsule on a bidimensional plane of the abdomen over time (Fig. 1). Cumulative displacement during transit through the small bowel was calculated (Fig. 3).

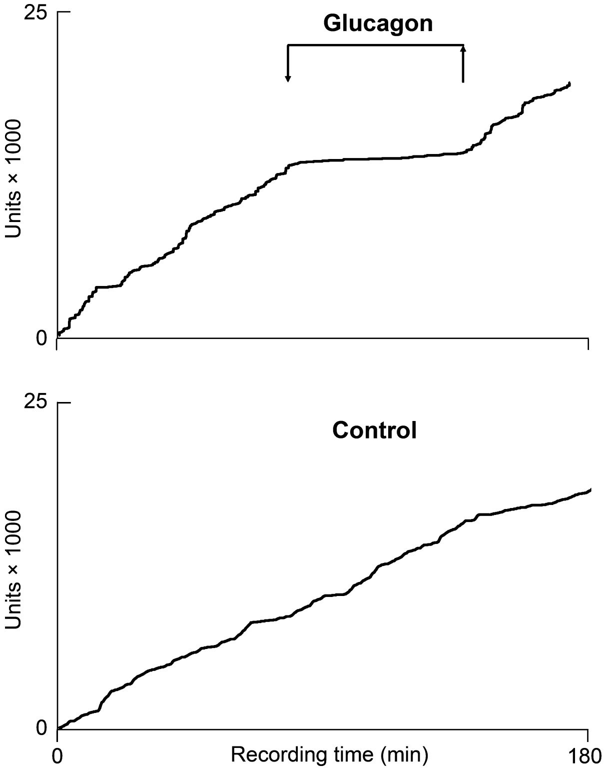

Figure 3 Displacement of the capsule. Examples of abdominal projection and cumulative displacement over time.

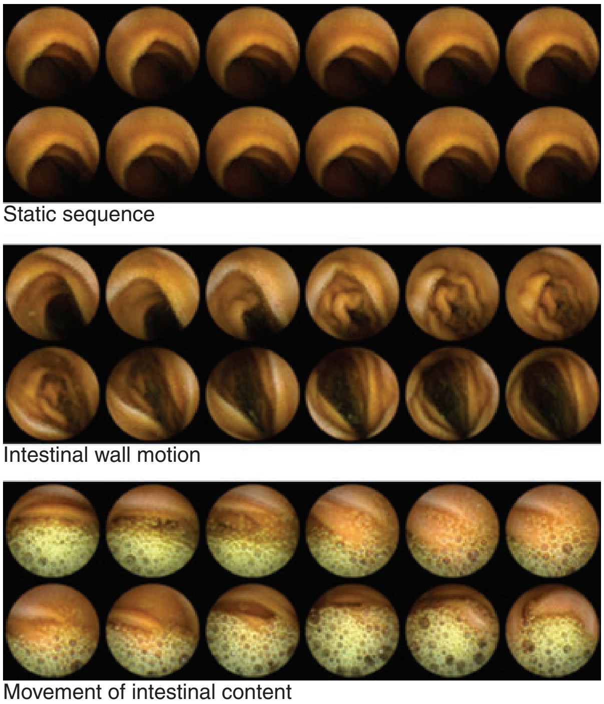

Figure 2 Examples of consecutive image sequences.

Periods analyzed Once the capsule entered the jejunum (by mucosal appearance on an on-line viewer) a 30-minute pretest period began. Following this period, glucagon infusion was initiated. Ten minutes after, the test period began, also lasting 30 min. The post-test period corresponded to the 30 min that followed cessation of the glucagon infusion. Equivalent periods were tested in controls.

Statistical analysis

The sample size was calculated based on the percentage of static images in previous studies (24% mean, 14% standard deviation),[2] anticipating a 25% difference in static images between the two groups (with *vs* without glucagon) with a power of 80% and a significance level of 5% (two-sided).

Fasting activity was characterized in the 11 subjects who did not receive glucagon, to determine the general pattern of activity. Mean values (±SE) of the parameters measured were calculated in each group of subjects. Within each group normality was tested by the Shapiro–Wilk test. Analysis of variance was performed by ANOVA. *Post hoc* comparisons of parametric, normally-distributed data were made by the Student's *t*-test, paired tests for intragroup comparisons and unpaired tests for intergroup comparisons; otherwise, the Wilcoxon signed rank test was used for paired data between groups, and the Mann–Whitney *U* test for unpaired data between groups.

RESULTS

Fasting activity

In eight of the 11 subjects not receiving glucagon (seven in the main experiments and four in the ancillary study), the capsule had reached the colon by the end of the study, and in them, mean transit time from the duodenum to the cecum was 235 ± 40 min. During the studies, 944 ± 157 events of phasic luminal closure were detected (5.2 ± 0.4 events per min), in 4.9 ± 1.4% of which luminal closure was incomplete (non-occlusive contractions). Wrinkles were detected in 2.9 ± 0.8% of frames. Non-contractile patterns consisted in a smooth wall image, recorded 26 ± 5% of the time, and an open tunnel view, recorded 7 ± 2% of the time. A tunnel pattern appeared in 36 ± 8 s sequences. Turbid intestinal content was detected 31 ± 6% of the time. In the videos, 15 ± 3% of the images were static, i.e. corresponded to static sequences. The mean duration of static sequences was 44 ± 15 s. The image was static in 12 ± 4% of frames showing turbid intestinal content, and in 15 ± 4% of nitid images (6 ± 3% of tunnel images, and 25 ± 7% of wall images). In subjects in whom the capsule arrived to the cecum, the location diagram of the capsule showed a displacement over the abdomen from an upper region corresponding to the epigastrium down to the right iliac fossa. During intestinal transit, total displacement of the capsule was 28660 ± 3449 units (115 ± 5 units per minute).

Effect of glucagon

As compared with the baseline period, glucagon significantly inhibited contractile patterns, specifically, reduced the number of luminal closures by 93 ± 2% (0.2 ± 0.1 *vs* 4.2 ± 0.9 events per min, $P = 0.018$) and the presence of wrinkles by 85 ± 7% (0.4 ± 0.1 *vs* 3.4 ± 1.2% of frames with wrinkles, $P = 0.028$). Inhibition of motor activity was associated with a 63 ± 5% reduction of endoluminal motion (average EMD 0.006 ± 0.001 *vs* 0.017 ± 0.002, $P = 0.001$) and a 61 ± 11% increase of static images (82 ± 9 *vs* 21 ± 10%, $P = 0.018$). Reduced motion affected both the intestinal walls seen in the clear images (82 ± 8 *vs* 22 ± 9% during baseline, $P = 0.018$), and intestinal content in turbid images (78 ± 11 *vs* 13 ± 9% during baseline, $P = 0.018$).

Capsule displacement was reduced during glucagon administration by 65 ± 9% (46 ± 10 *vs* 142 ± 14 units min^{-1} during baseline, $P = 0.002$) (Fig. 3). Interrupting glucagon administration, the effect rapidly faded, and no statistically significant differences were found between postglucagon *vs* baseline.

Comparing glucagon and control experiments, no differences were found in the parameters measured during the baseline (pretest) periods. By contrast, the same differences found when comparing glucagon *vs* baseline in the glucagon experiments were also found when comparing the test periods during glucagon *vs* control experiments. The delta values (test minus baseline) in the glucagon experiments were significantly different than in the control experiments (Figs 4 and 5).

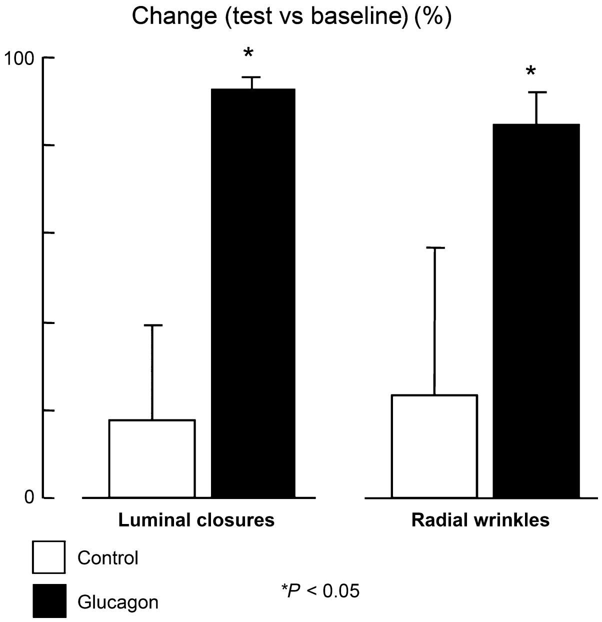

Figure 4 Effect of muscular inhibition on intestinal contractile activity.

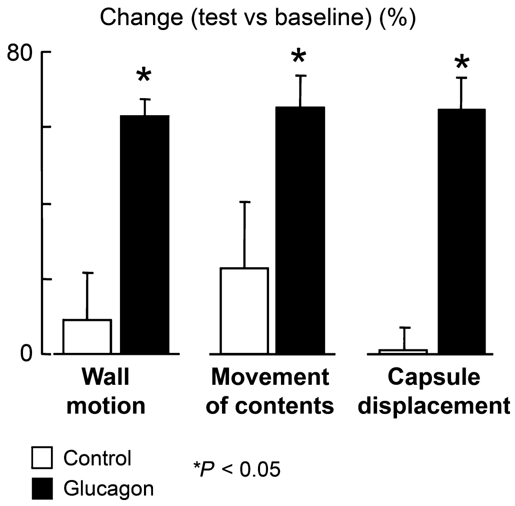

Figure 5 Effect of muscular inhibition on endoluminal motion and capsule propulsion.

Effect of body motion

In the ancillary experiments, periodic ambulation did not influence endoluminal motion of the walls (average EMD of nitid images 0.024 ± 0.003 with ambulation and 0.023 ± 0.003 without ambulation) or the motion of content (average EMD of turbid images 0.028 ± 0.003 with ambulation and 0.023 ± 0.004 without ambulation). Capsule displacement with ambulation was 30570 ± 5628 units (n.s. *vs* 26734 ± 4799 units without ambulation), and the speed of transit was 118 ± 8 units $\min^{-1}$ (n.s. *vs* 116 ± 10 units $\min^{-1}$ without ambulation). No differences between both sets of experiments were found in any of the other parameters measured, i.e. contractile patterns (luminal closures, wrinkles), non-contractile patterns (wall and tunnel pattern) and intestinal content (percentage of turbid images).

DISCUSSION

Using a new technological approach we have established the relation between muscular contraction, wall motion, dynamics of intraluminal contents and axial displacement along the small bowel, under two different contractile states: quiescence and activity.

Our method allows direct and continuous measurement of wall motor activity from a luminal observation point. We have identified muscular activity by phasic, i.e. rapid and reversible, luminal occlusions and radial wrinkles. Muscular contraction results in active motion of the intestinal wall that may accomplish various actions upon luminal content, such as accommodation, propulsion, fragmentation/mixing or resistance to flow, that finally determine the dynamics of chime/secretions (flow and turbulences) and transit (displacement) of the capsule itself.

Our experimental design aims at elucidating relations between intestinal contractions, wall movement and intraluminal contents by comparing normal and pharmacologically inhibited muscular activity. Inhibition of motor activity was demonstrated by a significant reduction of contractile patterns, e.g. luminal closures and radial wrinkles. Studying the dynamic behaviour of the sequence of images in the video, our data showed that reduction of contractile patterns is associated with reduced motion of the intestinal walls, presence of static endoluminal content and slow transit of the capsule itself. Glucagon in previous studies was showed to almost completely abolish phasic contractions recorded by manometry.[16,17] A similar effect was observed with endoluminal vision, although still some residual activity could be detected. It has been also shown that glucagon produces a tonic relaxation recorded by an intestinal barostat (117–195% volume increment at a fixed pressure level; [5,6,16]. Studies on intestinal clearance of exogenous gas loads have shown that these relaxatory effects result in impaired gas propulsion and pooling (62% retention with *vs* 18% without glucagon; [7]. All these bits of information obtained with different methodologies fit well with the comprehensive view integrating muscular activity, wall motion, characteristics and dynamics of contents and transit provided by endoluminal vision analysis. Alternatively to intestinal inhibition, these relations could have been explored in a model of intestinal stimulation, but potent prokinetics such as neostigmine,[18] have secondary effects that limit their experimental use in healthy subjects.

Continuous endoluminal measurement of intestinal motility was achieved by a miniaturized camera contained within a capsule with a transparent window. The capsule is swallowed and propelled through the gastrointestinal tract while emitting two images per second, which are received by an array of antennae fixed of the abdominal surface and recorded on a holter system. The capsule is eventually eliminated with faeces. A major advantage of the system is that recordings are taken in the minimally disturbed gut, except for the potential disturbance produced by the capsule itself.

The capsule endoscopy system is a standard commercially available device but quantification of intestinal motility by endoluminal vision analysis is based on newly developed computer vision techniques. A series of features of the images are chosen, such as mean colour, colour distribution and the presence of specific structures. Each one of these features is then quantitatively analyzed by specific mathematical models measuring numerical parameters. The next step consists in identifying whether the parameters that define one feature conform to specific pattern or not. This classification process is performed by automatic learning using machine learning techniques.[11] A series of images of a given pattern are provided to the machine, which then learns to identify them, by developing the mathematical function that best discriminates positive from negative examples.

The method to detect endoluminal motion is based on colour dissimilarity of sequential images. Theoretically, motion (dissimilarity of sequential images) can be due to capsule displacement within the intestinal lumen, as a vehicle driving through a tunnel, or to active movement of the wall or content over the capsule. Previous validation studies with the capsule fixed over an endoluminal tube, showed that active displacement of endoluminal structures, both wall and contents, is a major component of endoluminal motion measurements. Movement of liquids and large solid particles through the gut is distinctively different,[19] and the capsule behaves as a relatively static reference point with respect to the flow of secretions freely moving around the device; capsule displacement cannot be extrapolated to reflect transit of chime.

The experimental model of intestinal inhibition by glucagon mimics in part the pathophysiological conditions observed in patients with severe motor disorders. In a previous study we have shown that quantitation of intestinal motility by endoluminal vision analysis identifies patients with intestinal dysmotility with a similar specificity and higher sensitivity than conventional intestinal manometry.[2] Patients with abnormal motility exhibited some features similar to the present pharmacological model of intestinal motor inhibition in healthy subjects: less contractile activity and reduced wall motion with more static endoluminal content. Furthermore, in separate studies we have shown that patients with intestinal dysmotility have impaired gas transit and develop gas retention, abdominal symptoms and distension in response to exogenous gas loads,[20] and this effect is reproduced by glucagon in healthy subjects.[7]

Endoluminal measurement of intestinal motility provides an integrated and dynamic assessment of various intestinal motor functions. The clear-cut detection of differences between normal motility and pharmacologically manipulated muscular activity provides further evidence of the validity of our technology in the evaluation of intestinal motility. Furthermore, the similarity of artificially induced abnormal motor patterns in healthy volunteers with disturbed motility in patients with neuromuscular bowel disorders provides further indication of the potential diagnostic value of the method.

ACKNOWLEDGMENTS AND DISCLOSURES

Supported in part by Given Imaging, the Spanish Ministry of Education (Dirección General de Investigación, SAF 2006-03907), the Spanish Ministry of Health (Ayuda para contratos post-formación sanitaria especializada, CM05/00012) and Fundació La Marató TV3 (MARATV3_072010). Ciberehd is funded by the Instituto de Salud Carlos III.

The authors thank Sara Mendez for performing and visualizing the studies; Santi Segui, Panagiota Spyridonos, Fernando Vilariño and Petia Radeva for their contribution to the computer vision analysis program; Maite Casaus and Anna Aparici for technical support; and Gloria Santaliestra for secretarial assistance.

FINANCIAL DISCLOSURE

Supported in part by Given imaging.

COMPETING INTERESTS

The authors have no competing interests.

REFERENCES

1. Iddan G, Meron G, Glukhovsky A *et al.* Wireless capsule endoscopy. *Nature* 2000; **405**: 417.
2. Malagelada C, De Iorio F, Azpiroz F *et al.* New insight into intestinal motor function via non-invasive endoluminal image analysis. *Gastroenterology* 2008; **135**: 1155–62.
3. Igual L, Vitria J, Vilariño F *et al.* Automatic discrimination of duodenum in wireless capsule video endoscopy. In: Stolen JV, Verdonck P, Nyssen M, Haueisen, eds. *IFMB Proceedings* Berlin: Springer, 2009: 1536–9.
4. De Iorio F, Malagelada C, Azpiroz F *et al.* In search for new parameters of intestinal motor activity in humans. *Gastroenterology* 2006; **130**: A473.
5. Rouillon J-M, Azpiroz F, Malagelada J-R. Sensorial and intestino - intestinal reflex pathways in the human jejunum. *Gastroenterology* 1991; **101**: 1606–12.
6. Serra J, Azpiroz F, Malagelada J-R *et al.* Modulation of gut perception by spatial summation phenomena. *J Physiol* 1998; **506**: 579–87.
7. Serra J, Azpiroz F, Malagelada J-R. Mechanisms of intestinal gas retention in humans: impaired propulsion versus obstructed evacuation. *Am J Physiol* 2001; **281**: G138–43.
8. Gregersen H, Rittig S, Kraglund K *et al.* The effects of glucagon and glucagon-(1-21)-peptide on antroduodenal motility in healthy volunteers. *Scand J Gastroenterol* 1988; **152**: 42–7.
9. Russ J. *The Image Processing Handbook*, 5th edn. Boca Raton, FL: CRC Press, 2007.
10. Vilariño F, Spyridonos P, Azpiroz F *et al.* Cascade analysis for intestinal contraction detection. *Int J CARS* 2006; **1**: 9–10.
11. Noble WS. What is a support vector machine? *Nat Biotechnol* 2006; **24**: 1565–7.
12. Spyridonos P, Vilariño F, Vitrià J *et al.* Anisotropic feature extraction from endoluminal images for detection of intestinal contractions. *Lect Notes Comput Sci* 2006; **4191**: 161–8.
13. Vilariño F, Spyridonos P, Vitrià J *et al.* Linear radial patterns characterization for automatic detection of tonic intestinal contractions. *Lect Notes Comput Sci* 2006; **4225**: 178–87.
14. Vilariño F, Spyridonos P, Vitria J *et al.* A machine learning framework using SOMs: applications in the intestinal motility assessment. *Lect Notes Comput Sci* 2006; **4225**: 188–97.
15. Rubner Y, Tomasi C, Guibas LJ. The earth mover's distance as a metric for image retrieval. *Int J Comput Vis* 2000; **40**: 99–121.
16. Rouillon J-M, Azpiroz F, Malagelada J-R. Reflex changes in intestinal tone: relationship to perception. *Am J Physiol* 1991; **261**: G280–6.
17. Schirra J, Houck P, Wank U *et al.* Effects of glucagon-like peptide-1(7-36)amide on antro-pyloro-duodenal motility in the interdigestive state

and with duodenal lipid perfusion in humans. *Gut* 2000; **46**: 622–31.

18 Caldarella MP, Serra J, Azpiroz F *et al.* Prokinetic effects in patients with intestinal gas retention. *Gastroenterology* 2002; **122**: 1748–55.

19 Malagelada JR, Robertson JS, Brown ML *et al.* Intestinal transit of solid and liquid components of a meal in health. *Gastroenterology* 1984; **87**: 1255–63.

20 Serra J, Azpiroz F, Villoria A *et al.* Intestinal gas correlates with the severity of intestinal motor dysfunction. *Neurogastroenterol Motil* 2006; **18**: A394.