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UNIVERSITE DE LAUSANNE – FACULTE DE BIOLOGIE ET DE MEDECINE

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## **Colonic movements in healthy subjects as monitored by a Magnet Tracking System**

THESE

Préparée sous la direction du Professeur associé Jean-Claude Givel  
avec la collaboration du Professeur honoraire Pavel Kucera

et présentée à la Faculté de biologie et de médecine  
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par

Philippe HIROZ

Médecin diplômé de la Confédération Suisse

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*Directeur de thèse Monsieur le Professeur associé Jean-Claude Givel*

*Co-Directeur de thèse*

*Expert Monsieur le Professeur Alban Denys*

*Directrice de l'Ecole  
doctorale Madame le Professeur Stephanie Clarke*

*la Commission MD de l'Ecole doctorale autorise l'impression de la thèse de*

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Directrice de l'Ecole doctorale*

## Rapport de synthèse

### **Etude par Magnet Tracking System des mouvements coliques chez les sujets sains**

Le Magnet Tracking System (MTS) est une technique peu invasive d'investigation de la motilité de l'entier du tube digestif. Elle repose sur le suivi de la progression d'un aimant par des senseurs externes en temps réel et dans les 3 dimensions. Dans cette étude, le MTS a été utilisé pour étudier les caractéristiques de propulsion propres aux différents segments coliques ainsi que pour comparer le transit de l'aimant permanent du MTS à celui de marqueurs radio-opaques habituellement utilisés.

Dix hommes et 10 femmes ayant un transit gastro-intestinal régulier ont ingéré simultanément un aimant de MTS et une capsule contenant 10 marqueurs radio-opaques, à 20h00. Les enregistrements se sont ensuite déroulés sur 2 matinées successives de 5 heures. L'analyse des données brutes recueillies a permis de réaliser une projection spatio-temporelle de la trajectoire de l'aimant dans le tube digestif ainsi qu'une description précise de l'origine, de la direction, de l'amplitude et de la vitesse des mouvements coliques. Des radiographies d'abdomen ont permis de comparer les positions respectives des marqueurs radio-opaques et de l'aimant du MTS.

Durant 90% du temps d'enregistrement, l'aimant était immobile ou présentait des mouvements alternatifs de faible amplitude. Le reste des enregistrements consiste en activité propulsive dont 20% représentent des déplacements rétrogrades et une description très précise de 34 mouvements de masses. L'analyse des déplacements démontre une distribution bimodale des vitesses voisine de 1.5 et 50 cm / min, ce tant en direction orale que caudale. Deux tiers des distances parcourues le sont à vitesse rapide. L'analyse segmentaire confirme une progression horaire absolue supérieure dans le côlon gauche que droit. L'analyse détaillée par segment colique, reposant sur la description des déplacements enregistrés correspond aux rôles reconnus des différents segments, notamment de aire de stockage et de conditionnement du côlon ascendant ou de transit du côlon descendant. La comparaison des 2 sexes démontre un nombre plus important de mouvements, particulièrement de mouvements de masse chez l'homme. Les radiographies montrent une bonne corrélation entre la position de l'aimant et celle des marqueurs radio-opaques.

Le MTS permet ainsi une description précise des caractéristiques propulsives des différents segments coliques, notamment par l'analyse détaillée des progressions à vitesses lente et rapide et leurs directions. Des distinctions peuvent également être notées en fonction du sexe. Ces investigations offrent de nouvelles perspectives pour l'étude des troubles de la motilité digestive.

## Colonic movements in healthy subjects as monitored by a Magnet Tracking System

P. HIROZ,\* V. SCHLAGETER,† J.-C. GIVEL\* & P. KUCERA†

\*Department of Visceral Surgery, University Hospital, Lausanne, Switzerland

†Department of Physiology, University of Lausanne, Lausanne, Switzerland

**Abstract** The Magnet Tracking System (MTS) is a minimally-invasive technique of continuous evaluation of gastrointestinal motility. In this study, MTS was used to analyse colonic propulsive dynamics and compare the transit of a magnetic pill with that of standard radio-opaque markers. MTS monitors the progress in real time of a magnetic pill through the gut. Ten men and 10 women with regular daily bowel movements swallowed this pill and 10 radio-opaque markers at 8 pm. Five hours of recordings were conducted during 2 following mornings. Origin, direction, amplitude and velocity of movements were analysed relative to space–time plots of the pill trajectory. Abdominal radiographs were taken to compare the progress of both pill and markers. The magnetic pill lay idle for 90% of its sojourn in the colon; its total retrograde displacement accounted for only 20% of its overall movement. Analysis of these movements showed a bimodal distribution of velocities: around 1.5 and 50 cm min<sup>-1</sup>, the latter being responsible for 2/3 of distance traversed. There were more movements overall and more mass movements in males. Net hourly forward progress was greater in the left than right colon, and greater in males. The position of the magnetic pill correlated well with the advancement of markers. MTS showed patterns and propulsion dynamics of colonic segments with as yet unmet precision. Detailed analysis of slow and fast patterns of colonic progress makes it possible to specify the motility of colonic segments, and any variability in gender. Such analysis opens up promising avenues in studies of motility disorders.

**Keywords** human colon, Magnet Tracking, motility, space–time analysis.

### INTRODUCTION

Colonic motor activity is currently investigated using manometry, barostat volume recording and imaging (radio-opaque markers, scintigraphy). These techniques and the classification of colonic motility have been extensively reviewed by Scott.<sup>1</sup> Most of the time, the colon is quiet or displays low intensity propulsive activity such as to-and-fro movements and slow propagation, the main role of which is to stir luminal content and to propel it slowly along the colon. Occasionally during the day, long-lasting contractions migrate rapidly and uninterruptedly over long distances. They were described in manometric studies as high amplitude propulsive contractions (HAPC) and they represent manometric equivalents of mass movements initially observed on standard radiographs.<sup>1</sup> Awakening, food ingestion and coffee facilitate colonic activity (gastrocolonic response).<sup>2–4</sup>

The final result of contractions, i.e. the displacement of luminal contents, is difficult to evaluate with precision as radio-imaging is time-limited and pressure events do not always predict luminal flow. Simultaneous manometric and scintigraphic records showed correlations varying from poor values up to 93% mechanical link between propagating sequences and colonic content transport.<sup>5–7</sup> Luminal flow also occurs in the absence of identifiable propagating sequences.<sup>5,7</sup> Thus, there is the need for techniques allowing for simultaneous assessment of intraluminal pressure changes and transit, if possible along the entire intestine. Pan-colonic mapping of propagating sequences in manometry represents a promising step.<sup>8</sup> With respect to displacements of luminal content, the capsule telemetric technology offers interesting possibility for recording of motility events using pills containing pH and or pressure sensors<sup>9</sup> or video-recording capabilities.<sup>10</sup>

#### Address for correspondence

Dr Pavel Kucera, Ecole Polytechnique fédérale de Lausanne (EPFL), Local AI 0145, 1015 Lausanne, Switzerland.  
Tel: +41 21 693 18 08; fax: +41 21 693 76 00;  
e-mail: pavel.kucera@epfl.ch

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The Magnet Tracking System (MTS), a simple and minimally-invasive technique, using a capsule with a permanent magnet traces with high spatio-temporal resolution the displacements of luminal content of the entire digestive tube.<sup>11</sup> In this study, colonic propulsive activity following morning colonic stimulation was recorded in healthy volunteers using MTS with the aim to analyse propulsive dynamics, to detect and quantify fast colonic movements, and to compare the transit of a magnetic pill with that of standard radio-opaque markers.

## MATERIALS AND METHODS

### Subjects

Twenty healthy volunteers (10 women aged  $24 \pm 1$  years, 10 men  $28 \pm 2$  years) were recruited for this study. All had regular daily bowel motions between 1 and 3 defecations per day, no history of gastrointestinal disease or abdominal surgery and all were non-smokers. Average body mass index was  $21.1 \pm 2.6$ . The subjects used no medications except the oral contraceptive pill. All females had a negative urine pregnancy test prior to entry into the study. Informed written consent was obtained for each subject. The protocol was approved by the Committee of Ethics of the Faculty of Medicine of the University of Lausanne.

### Magnet Tracking System

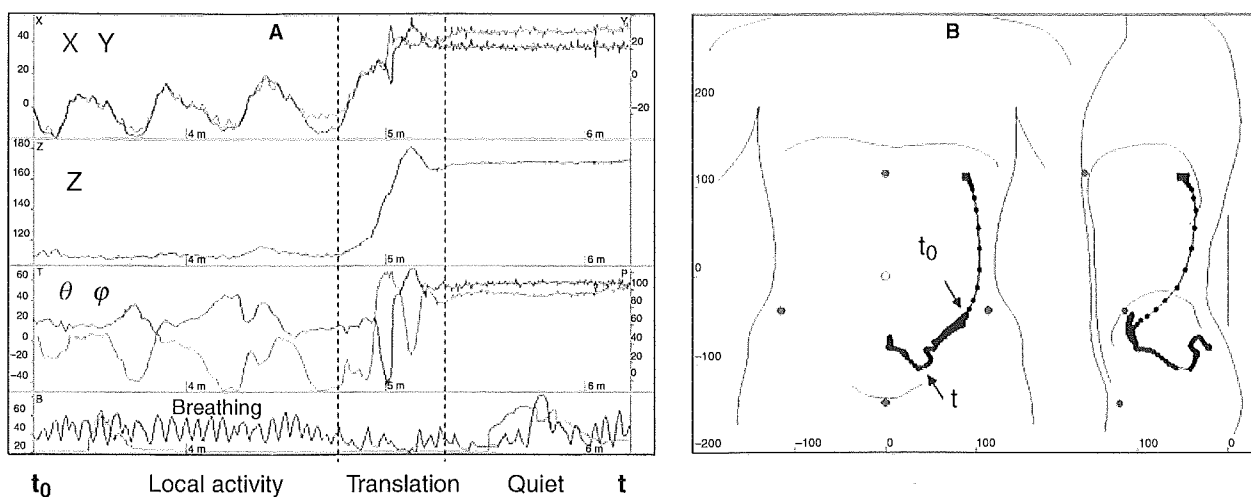
Magnet Tracking System consists of a magnetic pill, a detection matrix (4 × 4 magnetic field sensors) and dedicated software implanted in a laptop computer (MTS-adult, Motilis, Lausanne, Switzerland).<sup>11</sup> The pill used was a silicon coated capsule

( $\varnothing 5.5 \times 18$  mm) containing a permanent cylindrical magnet with a composite density of  $1.8 \text{ g cm}^{-3}$ .

Before measurements, the detection matrix was calibrated by offsetting the earth magnetic field and was then positioned over the abdomen with respect to anatomical reference points. Recording sessions lasted from 15 to 90 min during which the subject had to lay still under the detection matrix. The signals from the sensors were digitized and transmitted to the computer for processing and storage. The movement of the pill was monitored in real time by two complementary methods. Firstly, the  $x, y, z$  coordinates and two inclination angles ( $\theta, \phi$ ) of the pill were plotted with respect to time at a 10 Hz sampling frequency (Fig. 1A). In order to filter out respiratory artefacts, breathing was also recorded using a nasal thermal probe. This method simplified the search for rhythms and the analysis of progress dynamics (amplitude, direction, velocity). Secondly, the pill trajectory was continuously monitored in frontal, sagittal and transverse planes (Figs 1B and 4). Such images reflecting the luminal configuration were compared to abdominal radiographs.

### Protocol

The protocol was designed to capture colonic responses to morning stimuli known to enhance motility (viz. awakening, physical activity, breakfast, coffee). On day zero (D0), at 8 pm, about an hour after eating their own dinner, the subjects ingested the magnetic pill together with a capsule of 10 radio-opaque polyurethane markers containing 40% barium sulphate (P & A Mauch, Münchenstein, Switzerland). The subjects slept in a special room designated for the experiment until 6 am. On day 1 (D1), monitoring was started immediately after waking up but was interrupted at 7 am when a standard 640 kcal breakfast containing 45% of fat, 45% carbohydrate and 10% protein was served. Recording was resumed at the end of the meal after about a 15 min. At 9 am, it was again interrupted for a coffee break for about 10 min (1 dL cup of black Nespresso coffee: professional café Forte). Afterwards, recordings lasted until 11 am when the



**Figure 1** Real time displays of the magnetic pill position in the colon of a male volunteer after waking up. [A] 3 min segment ( $t_0 - t$ ) of an on-line record: the pill position is expressed in five coordinates [ $x, y, z$  in mm and  $\theta, \phi$  in degrees]. The record shows three rhythmic to- and -fro oscillations (2.2 cycle per min) before a net displacement of 18 cm in 40 s followed by a quiet period. Respiratory frequency is also recorded by a thermal nasal probe in order to filter out breathing interference with the magnet movement. [B] Two-dimensional plot of this record in the frontal and lateral views locates the  $t_0 - t$  period at the end of a descending mass movement starting from the splenic flexure, which has reached the sigmoid segment and then continues to the rectum. One dot per second.

volunteers were let free until the evening. An identical recording protocol was followed on day 2 (D2). Short breaks were occasionally allowed on demand to let the subject stretch and walk. A standard abdominal radiograph was taken at the end of the first morning for the 10 first volunteers and at the end of the second morning for the last 10.

Volunteers who had expelled the pill during D1 (confirmed by MTS and radiograph) ingested another magnetic pill at 8 pm to allow recordings on the second day following an identical protocol. At the end of D2, the presence of the pill was checked daily until its elimination was confirmed.

### Analysis

The instantaneous anatomical position of the pill was identified by comparing data from the temporal and spatial displays (rhythms, previous and future trajectory) with radiographs (Figs 1B, 2A and 5A). Artefactual disturbances such as sneezing, coughing or volunteer movements were screened based on each individual record notes. They were also traced by their typical pattern on recording as a sudden fast change with return to the exact same previous position in less than 3 s. Furthermore the respiratory tracing could help filter out breathing movements.

A plot of the position of the pill with respect to three reference planes was linked to anatomical position and stimulating factors

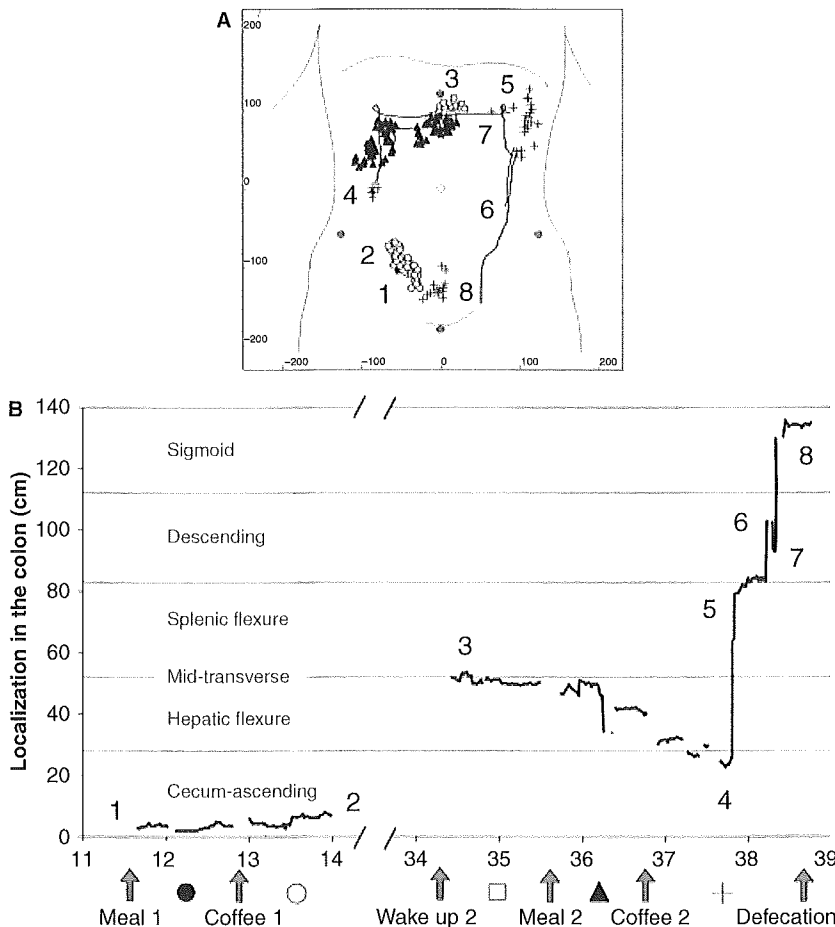
such as awakening or eating. Fig. 2A shows that a fairly good representation of the transit may be obtained despite interruptions in the recording. A space-time representation was obtained by plotting the position of the pill along the colon with respect to time (Fig. 2B). Such a linear representation enables the calculation of velocity of motion and also, by measuring the distances traversed in antegrade and retrograde directions the net forward progress of the pill. Distances covered by the magnet between recordings were approximated by comparing colonic plots with standard abdominal radiographs.

The colon was arbitrarily divided into five segments: caecum with ascending colon, hepatic flexure with right transverse colon, left transverse colon with splenic flexure, descending colon and sigmoid colon.

With the use of software, propulsive and non-propulsive periods were identified. Propulsive periods were those with displacements of at least 4 cm, either antegrade or retrograde, and of average speed  $>4 \text{ cm h}^{-1}$  (e.g., Fig. 1A).

Mass movements were defined as having a distance  $>10 \text{ cm}$  completed in  $<1 \text{ min}$ . Displacements at  $<10 \text{ cm min}^{-1}$  were defined as slow and those at  $\geq 10 \text{ cm min}^{-1}$  as fast (Fig. 3).

Segmental and gender analysis were based on: (i) frequency of propulsive and non-propulsive periods, (ii) number of mass movements, (iii) total (i.e. antegrade plus retrograde) displacement per recording hour, (iv) net forward progress per recording hour (i.e. antegrade minus retrograde displacements) and (v) fraction of trajectory completed at fast velocity.



**Figure 2** Space-time representations of colonic propulsive activity in one male volunteer. (A) Frontal anatomical plot illustrating colonic transit. On day 1, the plot of the pill position shows oscillatory movements in the caecum (after coffee,  $\circ$ , 1–2). On day 2, after waking up, it is found in the transverse colon ( $\square$ , 3) from where it returns after breakfast to the ascending colon ( $\blacktriangle$ , 4). After coffee, it quickly covers the entire colon with a short to- and -fro oscillation at the splenic angle ( $+$ , 5–8). (dots:  $1 \text{ min}^{-1}$ , lines: mass movements at  $\geq 10 \text{ cm s}^{-1}$ ). (B) Linear space-time plot of the same experiment and with identical labels enables evaluation of the dynamics of transit. On day 1 morning, the pill advances (1–2) very slowly (about  $5 \text{ cm}$  in  $150 \text{ min}$ ). The remaining day and night (2–3) were not recorded. On day 2 morning, the pill is found quiet about  $45 \text{ cm}$  further in the colon (3) from where, after breakfast, it slowly returns ( $30 \text{ cm}$  in  $3 \text{ h}$ ). After coffee, it then quickly covers the entire remaining colon (4–8) with a short pause and to- and -fro oscillation (6–7). The net advancement of the pill is about  $135 \text{ cm}$  but the total covered distance is at least  $40 \text{ cm}$  longer. Comparison with A fixes the plot with respect to colonic anatomy.

Total transit time was defined by the time interval between ingestion and elimination of the pill. Elimination time was recorded or deduced from volunteer information. When the pill was still present after D2, its final position was recorded.

The correlation between the positions of the pill and radio-opaque markers was studied on standard abdominal radiographs where the colon was divided in eight zones: caecum, ascending, hepatic flexure, transverse, splenic flexure, descending, sigmoid and rectum. In each zone, the number of radio-opaque markers was determined and plotted against the zone containing the pill (Fig. 5). Thus the advancement or delay of the pill relative to the markers was quantified.

## Statistics

ANOVA and *F*-tests were used to evaluate segmental and gender differences. *P* < 0.05 was taken as a significance criterion.

## RESULTS

All volunteers completed the study without complications and were quite unaware of the presence of the pill.

### Recording time

Altogether 137 h of recordings were conducted. Periods not recorded were accounted for breaks for meal, coffee and short exercises and for early pill elimination during protocol period. Two morning only records were collected in two subjects and one other had recording of the small intestine during D1 but expelled it during the night so that no colonic records were obtained.

Altogether 55 h of recordings were localized in the small bowel. Much variation was observed among the subjects. Seven subjects started the morning recordings on D1 with the pill already in the colon as two others displayed only recordings in the small intestine. Six subjects eliminated the pill on D1 and therefore ingested a second pill and a capsule of radio-opaque

markers. One of them (a male) eliminated his second magnetic pill again during D2.

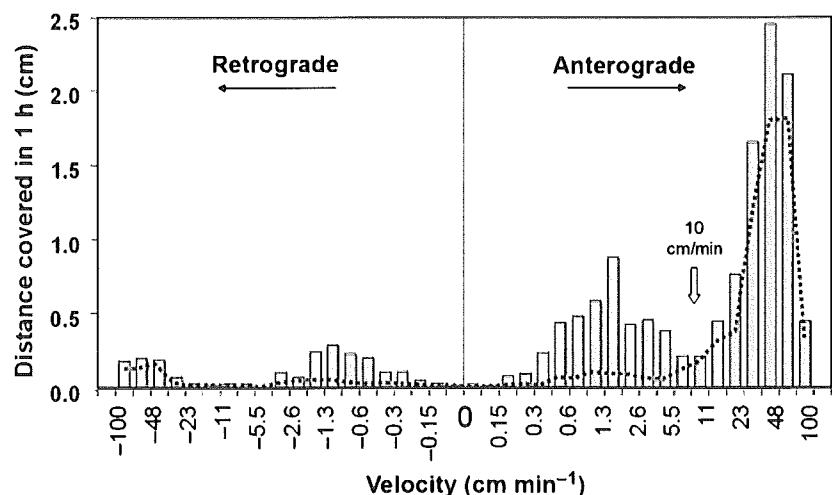
The pill spent a total of 82 h within the colons of the different volunteers, approximately half for males and females (Table 1). On average,  $4.6 \pm 1.8$  h per subject were recorded in the colon. The times spent in each colonic segment were as follows: 42% in the caecum-ascending, 11 and 23%, respectively in the first and second part of the transverse, 7% in the descending and 17% in the sigmoid colon (Table 1).

### Total transit time

The total transit time (TTT) from ingestion to elimination was highly variable. The shortest TTT was observed in one male with 13.25 h on D1 and 13.75 h on D2. Three females and four males showed TTT between 14 and 24 h. Three other male subjects eliminated the pill on the second morning with TTT of 37.5, 37.5 and 39 h. The seven remaining subjects (six females and one male) did not evacuate the pill during the experiment and thus had a TTT greater than 39 h. Among them, the pill ended up in the sigmoid of one male and two females, in the transverse colon for another two females, and in the ascending colon for the remaining two females.

### Colonic activity

Anatomical and linear space-time colonic plots were obtained for all subjects and colonic activity was analysed in detail. During 90% of the time, non-propulsive periods were recorded where the pill remained still or underwent small to-and-fro displacements and rotations. Such non-propulsive periods were interrupted by intervals of propulsive activity in either



**Figure 3** Analysis of propulsive velocities in the colon. Histogram of distances covered at different velocities (measured as mean value for 1 cm traversed) shows a very large spectrum, yet identical in both antegrade and retrograde directions. From the bimodal distribution, it can be deduced that 1/3 and 2/3 of the colon are traversed respectively by slow ( $<10$   $\text{cm min}^{-1}$ ) and fast ( $\geq 10$   $\text{cm min}^{-1}$ ) antegrade movements. Retrograde displacements are much fewer. The interrupted line represents the distances covered by mass movements ( $>10$  cm).

direction. The average net colonic distance traversed by the pill per subject was  $61 \pm 43$  cm of which 25% was computed during periods not recorded.

### Velocity of progress

The histogram of velocities (Fig. 3) showed a bimodal distribution that was identical for antegrade and retrograde directions. The value of  $10 \text{ cm min}^{-1}$  separating the two peaks, around  $1.5 \text{ cm min}^{-1}$  and around  $50 \text{ cm min}^{-1}$ , was taken as a mathematical boundary between fast and slow displacements. Fast displacement accounted for 65% of the total displacement.

### Large movements

Thirty-four fast large (>10 cm) movements were identified in 12 different subjects. These mass movements (e.g., Figs 1, 2 and 4) originated in every colonic segment and extended for several segments (Table 1). They occurred more frequently in the left colon with 23 starting after the mid-transverse. Eleven mass movements were longer than 20 cm, the longest traversing 36 cm from the ascending colon to the splenic flexure in 35 s (Fig. 4A). Five retrograde mass movements were also recorded among three subjects, the greatest one extending to 13 cm.

Slow large and continuous displacement covering tens of cm with a mean velocity around  $1 \text{ cm min}^{-1}$  were also recorded. Such displacements, illustrated in Fig. 4C, D, were recorded in every colonic segment and in both directions.

On 13 occasions, great shifts in positions were detected after breaks in recordings. Interestingly, in seven of those shifts the pill was found more proximally after the break than before, so that

these displacements were interpreted as retrograde. At least three of them could have been mass movements because the breaks were shorter than 1 min.

### Segmental differences (Table 1)

In the *caecum-ascending colon*, slow oscillatory movements were mostly recorded resulting in the slowest net forward progress (Table 1). Mass movements were captured transporting quickly the pill from this segment to the hepatic flexure (Fig. 4A) or deduced from shifts in the pill position before and after a break (Fig. 4C). Retrograde displacements of great amplitude were recorded especially after coffee or meal (Fig. 2A).

In the *hepatic flexure-mid transverse* segment, despite the least activity, the total displacement and net forward progress partially accomplished by mass movements, were comparable to the next segment (Table 1).

The *mid-transverse-splenic flexure* segment showed the highest variability in progress patterns, with antegrade and retrograde displacements equally represented and well documented fast and slow velocities.

The *descending colon* segment showed the highest frequency of propulsive periods, highest total displacement per hour and highest net forward progress (about 87% of the total distance traversed by the pill, Table 1). These displacements were mainly due to mass movements. Thus, despite the shortest recording time (7%), descending movements were observed in great detail: after an initial to-and-fro activity in the upper descending colon, a propulsive movement would take the pill slowly (Fig. 4D) or more often rapidly (Figs 2A and 4B) to the sigmoid.

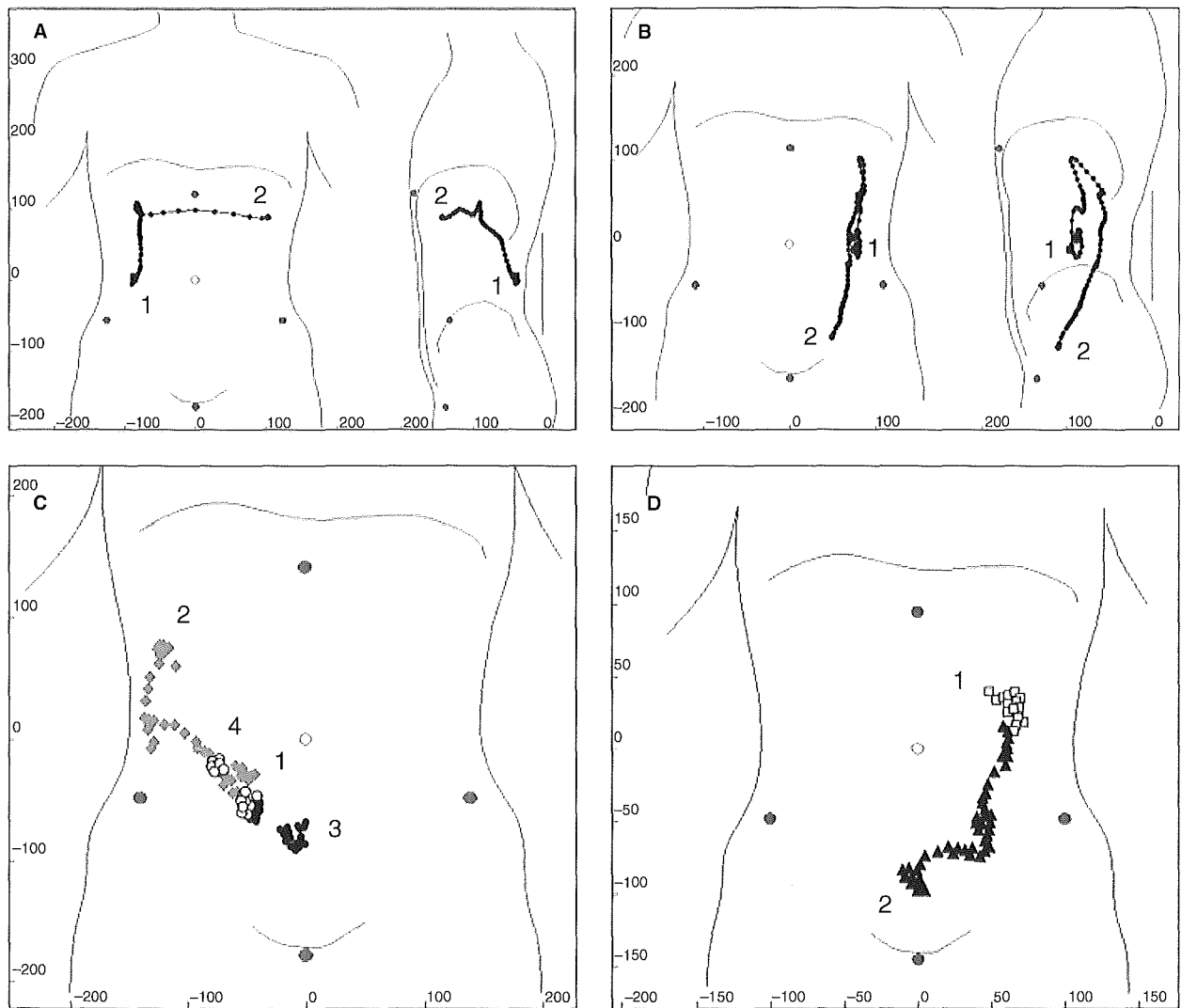
In the *sigmoid colon* segment, mostly slow progress towards rectum was observed.

**Table 1** Colonic propulsive activity according to position and gender

	Caecum & Hepatic flex. ascending & R transverse	L transverse & splenic flex.	Descending	Sigmoid	♀ mean /sum	♂ mean /sum	P <sup>1</sup>	Right colon mean/sum	Left colon mean/sum	P <sup>2</sup>	
Recording time (h)	33.8	8.6	19.2	6.4	14.4	43.3	39.1	ns	42.4	40	ns
% of time spent in displacements	11.2	5.5	11.9	17.5	11.2	9.9 ± 9.6	12.9 ± 5.9	ns	10.1	12.5	<0.05
Mass movements° ♀   ♂	4   2	5   6	6   9	4   10	3   10	12*	22*	<0.01	12**	28**	<0.01
Total displacement per recording hour (cm)	7.1	17.2	16.8	34.7	15.4	9.5 ± 8.8	19 ± 9.6	0.055	9.1	19.2	<0.05
Net forward progress per recording hour (cm)	2.6	7.3	9.4	30.2	13.5	6.7 ± 9.0	10.9 ± 6.2	ns	3.6	14.2	<0.05
Displacement with fast velocity (%)	28	80	66	87	70	65 ± 43	65 ± 27	ns	47	72	<0.02

Total displacement and net forward progress are represented per hour of recording. The *P* values concern respectively the differences between the genders (*P*<sup>1</sup>) and between the right and left colon (*P*<sup>2</sup>). °Number of mass movements corresponding to those starting in, passing through or ending in a given colonic segment. \*Number of individual mass movements recorded by gender. \*\*Number of mass movement recorded starting, passing through or ending in the right or left colon. ns, non-significant.





**Figure 4** Examples of mass movements and of slow movements. (A) 35 cm of ascending and transverse colon traversed in one continuous mass movement lasting 36 s, average speed  $1 \text{ cm s}^{-1}$ . Male, 10 min after coffee. Frontal and lateral projections. 1, 2: starting and ending positions. One dot per second. (B) continuous retrograde (13 cm, 20 s) then antegrade (28 cm, 45 s) mass movement in the descending and sigmoid colon, average speed  $0.6 \text{ cm s}^{-1}$ . Female, 8 min after coffee. Frontal and lateral projections. 1, 2: starting and ending positions. One dot per second. (C) Anatomical plot, after waking up the first time, showing slow colonic progress ( $\blacklozenge$ , 1–2) followed by a return to caecum after breakfast ( $\bullet$ , 2–3) and again a slow antegrade displacement ( $\circ$ , 3–4). One dot per min. (D) Anatomical plot after breakfast on day 2, showing a slow descent from the splenic angle to the sigmoid (15 cm in 70 min). One dot per min.

The *left colon* (from mid-transverse to sigmoid) showed two times higher total displacement, a significantly higher net forward progress and a significantly higher fraction of displacement at fast velocity than the right colon.

**Gender differences**

On average, males had about twice as high total displacement and net forward progress per hour than females. Males had significantly more mass movements than females, mainly in the left colon but,

interestingly, the slow and fast velocities were represented similarly in both genders.

**Radio-opaque markers**

Ten radiographs were taken on D1 and another 10 on D2 (examples in Fig. 5A, B). Four subjects among those with radiographs on D2 expelled the pill on D1 and received second pill and radio-opaque markers. In these cases, the radiograph done on D2 corresponded to a superposition of standard radiographs at 15 and 29 h. From 240 radio-opaque markers 98% were

localised with certitude. About 20% were eliminated at the time of the radiograph. As expected, a variable scattering of radio-opaque markers was observed. The magnetic pill was never found ahead of all the radio-opaque markers. It was found one zone behind all the radio-opaque markers in two females on D1, but it was never behind the radio-opaque markers on D2. In two cases on D2, the magnetic pill and all the radio-opaque markers had already been eliminated. About 60% of the radio-opaque markers were found clustered in the zone containing the magnetic pill (Fig. 5C).

## DISCUSSION

On one hand, the present study using a novel minimally invasive magnetic tracking device elaborates on many facts confirmed and demonstrated previously by conventional techniques of investigation:

### Activity

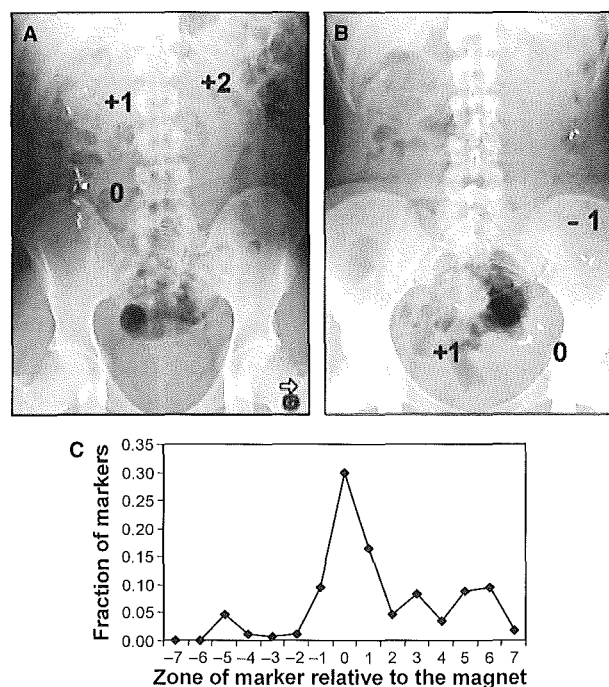
The colon shows mostly no or low activity.<sup>1,12</sup> In our study, this non-propulsive activity (displacements < 4 cm h<sup>-1</sup>, small to-and-fro oscillations, rotations) represents 90% of the recorded time. The criteria for propulsive movements (>4 cm, >4 cm h<sup>-1</sup>) were selected to separate noise and artefacts from true displacements and propulsive activity. Indeed, by decreasing these values the number of detected events increases but their interpretation becomes uncertain. On the contrary, by increasing these values, the interpretation is easy but true events may be missed. Calculations using different criteria led to slightly different absolute values for the total displacement (not shown), but did not modify the conclusions.

### Direction of movement

Studies using scintigraphy<sup>13-15</sup> or manometry<sup>5,16</sup> reported that retrograde activity is less frequent and less intense<sup>5,8,14,17</sup> and localised especially in the descending or transverse segments.<sup>13,18</sup> We also found retrograde displacement of the colonic content from the transverse colon to the ascending colon and inside the ascending colon itself<sup>5</sup> (Fig. 2A).

### Mass movements

These were present in all segments and oriented mostly antegradely. The largest one was of 35 cm but the velocity never exceeded 100 cm min<sup>-1</sup> (mean value on 1 cm trajectory). In the literature, the record length



**Figure 5** Progress of magnetic pill and radio markers. (A) Day 1, 15 h after ingestion, male subject. The magnetic pill, shown as a bright dot, and seven markers, shown as short lines, are in the same zone (ascending colon), two markers are 1 zone ahead (hepatic angle) and one marker is 2 zones ahead (left transverse) indicated by +1,+2. (B) Day 2, 39 h after ingestion, female subject. The pill and two markers are in the same zone (sigmoid), four markers are 1 zone behind (descending), indicated by -1, and one marker is 1 zone ahead (rectum), indicated by +1. Three markers were already eliminated. (C) Spread of the visible markers relative to pill position. The markers showed a tendency to advance slightly faster but 60% were nevertheless clustered around the pill. Markers:  $n = 240$ ; 98% identified, 20% eliminated (for definitions of zones see Materials and methods).

and velocity belongs to a movement from caecum to sigmoid colon in less than one minute.<sup>15</sup> The propulsion velocity obtained by MTS was between 0.2 and 1 cm s<sup>-1</sup> when calculated over a 10 cm trajectory, and never exceeded 1.7 cm s<sup>-1</sup> when calculated over 1 cm trajectory (Fig. 3). These values, comparable to those found for propagated pressure events<sup>13,17</sup> are however situated at the lower side of the span defining the high amplitude propagated pressure sequences, i.e., 0.2–12 cm s<sup>-1</sup>.<sup>1,5</sup> This again points to incomplete correlation between pressure events and luminal displacements. As the magnetic pill is a solid marker within a semi-liquid content, it may retard behind a propagating pressure sequence, especially in non-occlusive contractions. This seems to be supported by the fact that smaller and lighter radio-opaque markers show a slight tendency to overtake the pill (Fig. 5C). However it is more likely that during the morning sessions, we captured mostly the pre-expulsive and rather slow motor patterns.<sup>19</sup>

Large retrograde displacements (maximum observed 13 cm) were closely followed by continuous movement taking the pill through the whole descending colon to the sigmoid colon (Fig. 4B). Such sequences resemble those of retrograde and antegrade HAPC preceding bowel movements reported previously.<sup>20</sup>

### Motility patterns in colonic segments

As a short protocol was preferred to extensive and tiresome continuous recordings, a precise prediction of pill arrival into the colon was not possible and, consequently, the colonic records started in variable segments.

The caecum-ascending segment showed the slowest total displacement and net forward progress. This is in agreement with reports of solid residue retained in the unprepared right colon for long periods,<sup>21</sup> and with the concept of the ascending colon as a site of low grade mixing and storage activity and slow emptying.<sup>5</sup> However, mass movements were also observed (Fig. 4A) as reported previously.<sup>21</sup> The hepatic flexure-mid transverse colon was mostly inactive with propulsive periods representing only 5.5% of the recorded time but resulting in relatively large displacements covered at high speed. Retrograde displacements from transverse colon to the mid-ascending colon interpreted as responsible for intraluminal mixing,<sup>14</sup> were also present (Fig. 2A). Our results suggest less mixing activity but confirm a role in storage function. The splenic flexure showed intense antegrade and retrograde displacement at slow and high velocities and also mass movements in both directions. This confirms findings obtained by instillation of scintigraphic isotope into the splenic flexure resulting in postprandial retrograde movements into the transverse as well as antegrade progress towards the sigmoid.<sup>13</sup> This segment thus seems to link the mixing-storing and the excretory functions of the colon and might play a determining role in separating faecal content from that needing still more processing. This is consistent with the suggestion that the transverse colon and splenic flexure may act as a pacemaking region.<sup>16</sup> The descending colon had the highest frequency of propulsive periods and the highest total displacement and net forward progress. It showed also the highest incidence of large movements, often following normal 'morning stimuli', thus confirming the reactivity of distal colon to eating<sup>22,23</sup> perhaps linked to a predefecatory activity.<sup>20</sup>

Many large amplitude movements took the pill from splenic flexure to the sigmoid either by a slow but continuous displacement (Fig. 5A) or by a few fast

mass movements lasting seconds (Fig. 2A). Retrograde displacements did appear in the mid-descending but never transported the content back to the transverse colon. This supports the hypothesis of the descending colon as a conduit between the storage and excretory areas.<sup>15,21</sup> The sigmoid colon displayed a lower activity than the descending colon with fast colonic displacements but no mass movements.

### Gender differences

Males had almost twice as much total displacement and net forward progress than values found in females. These differences, just at the limit of statistical significance, quantitatively support the results of 24 h ambulant manometry indicating that the activity of the transverse-descending colon of healthy women is lower.<sup>3</sup> More data are needed for further analysis and physiological interpretation of such differences.

### Total (oro-anal) transit time

A highly variable TTT was observed, among the volunteers despite self reported similar bowel habits. No correlation between the number of bowel movements per day and the movement of faeces through the colon has been found.<sup>15</sup> The average gastrointestinal transit seems to be faster in men than in women, as indicated in some studies<sup>24,25</sup> but not in others.<sup>26</sup> Because of a considerable variability the debate remains open.

On the other hand, this study also demonstrates new discoveries:

Motility characteristics, such as segmental transit time, propulsive and non-propulsive periods, frequency, types and dynamics of progress, and a detailed description of mass movements were obtained in all colonic regions.

On the basis of analysis of space-time plots, a colonic motility profile could be drawn for each subject, which greatly facilitated the evaluation and interpretation of recorded data. So far, no other technique can give such precise information.

Progress velocities were shown to be identical for both antegrade and retrograde displacements and for both genders. Each colonic segment showed long periods of slow displacements replaced by short periods of fast displacements, often mass movements. Slow progress seems to be essential not only for its role in mixing but also for distal transport of luminal contents over long distance. Slow and fast displacements account respectively for 1/3 and 2/3 of progress. Retrograde displacement was clearly demonstrated as

part of the colonic motility pattern in every colonic segment. The total distances traversed by the magnetic pill were in males and females respectively 1.5 and 2 times longer than the total length of the colon. This difference is due to more frequent mass movements (especially retrograde) occurring in the male left colon. Sixty percent of the radio-opaque markers were clustered around the pill. This finding, even though awaiting confirmation from more extensive studies, suggests that, despite different dimensions and mass, the magnetic pill and markers follow displacements of luminal contents with a similar velocity.

MTS is a well tolerated, minimally invasive technique that monitors colonic motility without interference with digestive functions. MTS provides space-time colonic maps from which information about propulsion dynamics is derived with as yet unmet precision in amplitude, direction, velocity and trajectory of colonic contents.

Our results mostly confirm and broaden many findings obtained with currently used clinical techniques, refine analysis of luminal content transit along the colon and clearly indicate the complexity of colonic propulsion dynamics. Segmental and gender motility patterns were recognized, especially based on retrograde displacements and slow progress.

This study emphasizes the advantage of high space-and-time resolution in the analysis of colonic transit. MTS opens promising perspectives for investigation and management of conditions associated with motility disorders.

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## SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article:

**Figure S1.** Mass movement as recorded by MTS in a male volunteer 10 min after drinking a black coffee.

**Figure S2.** Space–time representation as recorded by MTS illustrating colonic transit in one male volunteer.

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