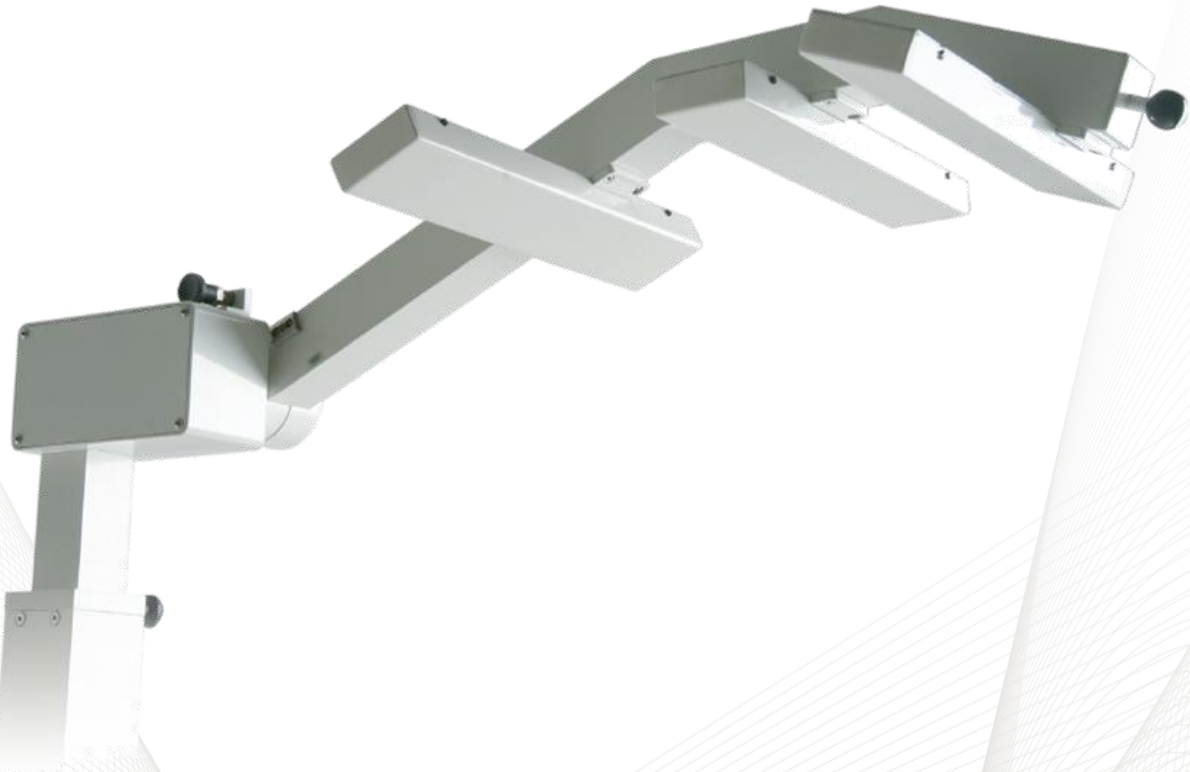
3D-MAGMA

Smart gastrointestinal functionality investigations



www.3D-magma.com

3D-MAGMA – Overview

Therapeutic approaches *for diseases of the gastrointestinal - tract - which can be caused by organic and/or functional disorders - need* ***retroaction free local functional investigations****. These local functional investigations can not sufficiently be performed by conventional methods.*

Functional disorders belong to the most common types of gastrointestinal disorders and therefore they are important also from a social-economic point of view.

3D-MAGMA offers *a* ***retroaction free investigation***
of functional processes within the ***whole gastrointestinal-tract.***

Approach

Localization of a small magnetically marked capsule by use of **3D-MAGMA**

- Bioinert magnetic capsules
  standard size: Diameter: 6 mm, Length: 16 mm, Density: < 1.5 g/cm³
- Precise 3D-realtime-tracking
  Accuracy: 3 mm
- Long term stability
- Exact local correlation of 3D-position and motility pattern
- Use in normal clinical environment without shielding of disturbing magnetic fields
- No radiation at all
- Comprehensive evaluation tool
- 3D-MAGMA is a CE certified medical device

Benefit

- Retroaction free , local motility analysis within the whole gastrointestinal-tract
- Evaluation of paths, local velocities, and typical motility patterns
- Illustration and evaluation of passages through stomach, small and large intestine

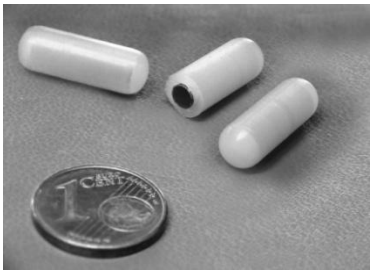
Medical examination

- Oral application of the magnetic capsule
- Real-time tracking of the magnetic capsule
- Postprocessing data evaluation

3D-MAGMA – Technology

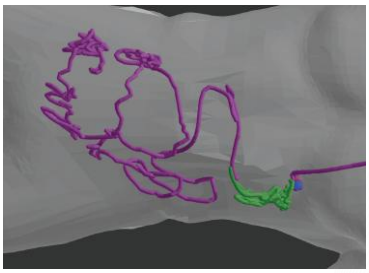
3D-MAGMA components

- 3D-MAGMA capsules
- Highly sensitive sensor system
- Evaluation software



Standard capsule

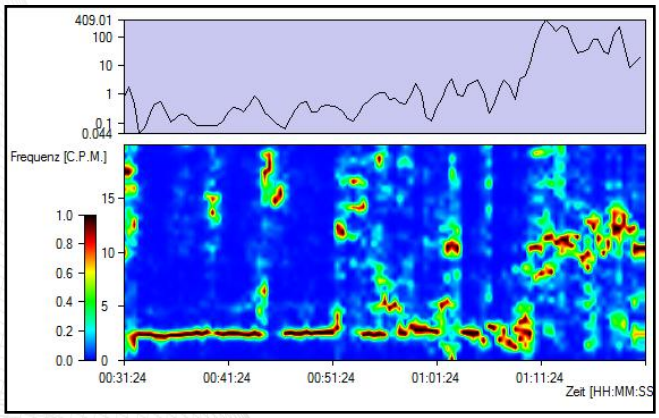
Sensor system



Capsule passage

1. The magnetic field induced by the capsule is measured by a highly sensitive magnetic field sensor array.
2. Calculation of three dimensional position and orientation of the magnetic capsule.
3. The position data serves for performance calculations.

Examples of 3D-MAGMA software calculations



- 3D capsule path
- Length of travelled path
- Local velocity profiles
- Passage durations
- Characteristic frequencies
- Local power

Motility

- Elimination of respiration and movement artifacts
- Estimation of position accuracy

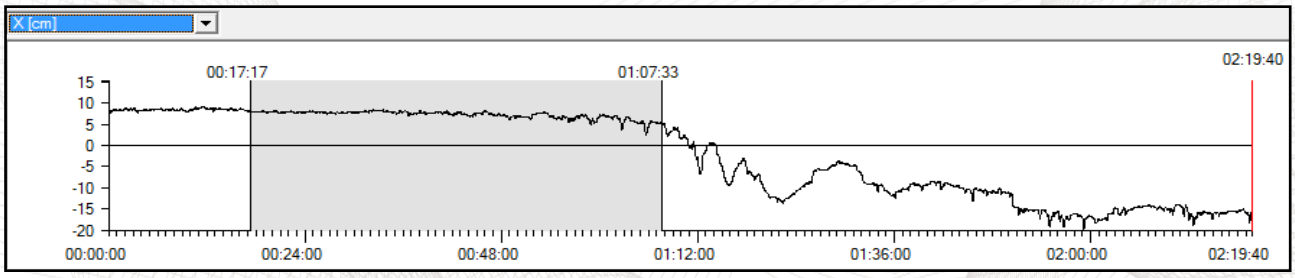


Fig.: Typical results of the 3D-MAGMA evaluation software; Above: characteristic frequency during the stomach passage (frequency within stomach: 3 $min^{-1}$and low power, frequency within small intestine: 8…12 min^{-1} and high power); Below: Path-time-diagraph.

3D-MAGMA – Potential use

3D-MAGMA is a good choice for functional examination for all conditions, which affect the gastrointestinal motility.

The patient just swallows the magnetic capsule whose movement is measured by the 3D-MAGMA during the examination.

3D-MAGMA - investigations

- Inflammatory diseases
    - Ulcerative colitis
    - Crohn's disease
    - Irritable bowel syndrome (IBS)
    - Celiac disease
- Diarrhea caused by multiple diseases
- Infections of gastrointestinal-tract
- Diabetes
- Motility changes caused by
    - Surgery
    - Drugs
    - Food
    - Age
    - Stress
- Observation of electrotherapy

3D-MAGMA – Add-ons

Magnetic active agent release system - MAARS

Use of the 3D-MAGMA together with the MAARS system for targeted agent release into the gastrointestinal tract of humans and animals **(www.pharmagnetic.com)**

- Development of new drugs
- Examination of the interactions between drugs and/ or food with the GI-system

Measurement arrangement for physiological examinations

- Chair measurement
- Upright measurement

Both modifications are useful to partially increase the speed of passage and to improve convenience of examination.

Measurement arrangements for animals

- Rodents (mice, rats, rabbits)
- Dogs
- Mini pigs
- Pigs
- Horses

The arrangements for animals differ in the number and position of sensors, as well as in size of the used magnetic marked capsules.

Localization of any magnetically marked object

- Localization of
  - Endoscopic capsules
  - Endoscope tips
  - Implants
  - Accidently swallowed magnets

3D-MAGMA – Technical data

3D-position determination by magnetically marked capsules

Measurement range:	whole gastrointestinal tract
Primary measurement values:	3d-position and orientation of the capsule
Secondary measurement results:	path, velocity, motility patterns, dominant frequencies, power of the marker movement, passage duration, interval oriented number of fast movements,…
Primary measurement rate:	500 samples per second
Filtered sample rate:	2 samples per second
Measuring accuracy:	3 mm
Power supply:	110-240 V, 50-60 Hz

3D-MAGMA is according to the EG guideline 93/42/EWG a medical class I product and CE marked. The following regulations are applied:

EN 60601-1: 1990	Medical electrical equipment– part 1: (IEC 601-1:1988)
EN 60601-1:1990 A1:1993	Medical electrical equipment– part 1, change A1 (IEC 601-1:1988/A1 : 1991)
EN 60601-1:1990 A2:1995	Medical electrical equipment– part 1, change A2 (IEC 601-1:1988/A2 : 1995 + corrigendum 1995)
EN 60601-1:1990 A3:1996	Medical electrical equipment– part 1: General requirements for basic safety and essential performance, change A3
EN 60601-1-2/A1:2006	Medical electrical equipment– part 1-2 , Electromagnetic compatibility (IEC 60601-1-2:2001/A1 2004)
EN 60601-1-6:2004	Medical electrical equipment– part 1: Collateral standard (IEC 60601-1-6:2004)
EN 1041:1998	Information supplied by the manufacturer with medical devices
EN 980:2003	Medical equipment, Graphic symbols, Symbols, Identification methods, labelling (process)
EN ISO 14971:2007	Risk-management for medical devices

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3D-MAGMA – FAQ

What is the size of a capsule?

- The size of 3D-MAGMA-capsules is diameter = 6 mm, length = 16 mm and comparable to standard medical capsule size.
- We offer adapted types for animal applications

Is the 3D-MAGMA reliable and safe?

3D-MAGMA measures by the capsule induced quasi-static magnetic fields. The field intensity at the sensors is in the range of the Earth magnetic field. The field intensity directly at the capsule surface is about 10 mT, what is less than the field intensity of a usual refrigerator magnet. 3D-MAGMA magnets are covered with an extraordinary stable and bioinert polymer. Therefore any contact with any body fluid can be completely excluded.
The only small risk is that a capsule remains within the appendix. This risk is not higher than for any other non indigestible food component. An additional 3D-MAGMA examination approx. one week after the primary measurement secures the successful withdrawal of the capsule.

How long does an examination take?

Natural transport processes can last for several hours. The passage of the stomach needs up to 180 minutes (usually 10 to 120 min). The complete passage of small-intestine lasts up to 360 minutes.

Are there any exclusion criteria?

- Patients with very pronounced adiposity

3D-MAGMA – Selected Literature I

Bergstrand M, Soederlind E, Weitschies W, Karlsson MO. 2009. Mechanistic modeling of a magnetic marker monitoring study linking gastrointestinal tablet transit, in vivo drug release, and pharmacokinetics. *Clin Pharmacol Ther. 2009 Jul; 86(1):77-83.*

Magnetic marker monitoring (MMM) is a new technique for visualizing transit and disintegration of solid oral dosage forms through the gastrointestinal (GI) tract. The aim of this work was to develop a modeling approach for gaining information from MMM studies using data from a food interaction study with felodipine extended-release (ER) formulation. The interrelationship between tablet location in the GI tract, in vivo drug release, and felodipine disposition was modeled. A Markov model was developed to describe the tablet's movement through the GI tract. Tablet location within the GI tract significantly affected drug release and absorption through the gut wall. Food intake decreased the probability of tablet transition from the stomach, decreased the rate with which released felodipine left the stomach, and increased the fraction absorbed across the gut wall. In conclusion, the combined information of tablet location in the GI tract, in vivo drug release, and plasma concentration can be utilized in a mechanistically informative way with integrated modeling of data from MMM studies.

Hocke M, Schoene U, Richert H, Goernert P, Keller J, Layer P, Stallmach A. 2009. Every slow-wave impulse is associated with motor activity of the human stomach. *Am J Physiol Gastrointest Liver Physiol. 2009 Apr; 96(4):G709-16.*

Using a newly developed high-resolution three-dimensional magnetic detector system (3D-MAGMA), we observed periodical movements of a small magnetic marker in the human stomach at the typical gastric slow-wave frequency, that is 3 min(-1). Thus we hypothesized that each gastric slow wave induces a motor response that is not strong enough to be detected by conventional methods. Electrogastrographies (EGG, Medtronic, Minneapolis, MN) for measurement of gastric slow waves and 3D-MAGMA (Innovent, Jena, Germany) measurements were simultaneously performed in 21 healthy volunteers (10 men, 40.4+/-13.6 yr; 11 women, 35.8+/-11.6 yr). The 3D-MAGMA system contains 27 highly sensitive magnetic field sensors that are able to locate a magnetic pill inside a human body with an accuracy of +/-5 mm or less in position and +/-2 degrees in orientation at a frequency of 50 Hz. Gastric transit time of the magnetic marker ranged from 19 to 154 min. The mean dominant EGG frequency while the marker was in the stomach was 2.87+/-0.15 cpm. The mean dominant 3D-MAGMA frequency during this interval was nearly identical; that is, 2.85+/-0.15 movements per minute. We observed a strong linear correlation between individual dominant EGG and 3D-MAGMA frequency (R=0.66, P=0.0011). Our findings suggest that each gastric slow wave induces a minute contraction that is too small to be detected by conventional motility investigations but can be recorded by the 3D-MAGMA system. The present slow-wave theory that assumes that the slow wave is a pure electrical signal should be reconsidered.

Kosch O, Osmanoglou E, Hartman V, Strenzke A, Weitschies W, Wiedenmann B, Moennikes H, Trahms L. Investigation of gastrointestinal transport by magnetic marker localization. *Biomed Tech (Berl) 2002; 47 Suppl 1 Pt 2:506-9.*

The method of magnetic marker monitoring MMM with a biomagnetic measurement system allows the tracking of the transport of solid drug forms with high spatiotemporal resolution. This technique enables to display the path and the disintegration of the magnetic marked pharmaceutical dosage form via the decrease of its magnetic moment. The method was used to assess exogenous factor on the esophageal transport of orally administered solid drug forms in five healthy volunteers. In a drug delivery study we have applied the MMM to monitor the path of a tablet during the gastrointestinal passage and to visualize the disintegration in the small intestine by the magnetic moment of the tablet. The signal to noise ratio of the measurement data was improved by ICA filtering.

3D-MAGMA – Selected Literature II

Richert H, Kosch O, Goernert P. Magnetic Monitoring as a diagnostic Method for Investigating Motility in the Human Degestiv System. *Magnetism in Medicine: A Handbook, Second Edition 2007; 481-498.*

Magnetic monitoring has been developed within the last few years and, for some applications such as the investigation of dissolution process it is already in regular use. A large number of investigations of human GI tract motility have demonstrated the potential of magnetic monitoring based in the fact that the method does not use ionization radiation and has no other harmful affects. Moreover, the informational content obtained with regard to local motility patterns exceeds that of any other currently available investigational method for the human intestine.
The correlation of local velocities, and especially the unique motility patterns of specific known diseases, might lead to an earlier diagnosis of functional disease in the human digestive system. Indeed, initial correlations between local velocity and BMI have already established that there are significant differences between healthy volunteers and patients with different diseases.
The specific properties of the described magnetic monitoring systems (SQUID and forward or inverse AMR) are highly complementary. While investigations of GI tract motility in normal clinical environments are possible with AMR sensor systems, dissolution processes to help understand absorption can be investigated with SQUID systems. Nonetheless, while much effort is required to reduce electromagnetic interference, the system has extremely high sensitivity.
In all cases magnetic monitoring investigations are noninvasive and the patient need swallow only a small magnetic pill. Consequently, the acceptance of this method is expected to be very high. However, before magnetic monitoring can be used widely for diagnostic purposes, important correlations between motility patterns and specific GI tract diseases must established. To date, the data obtained have revealed some interesting relationships and will, undoubtedly, provide much more information in future.

Weitschies W, Cardini D, Karaus M, Trahms L, Semmler W. Magnetic marker monitoring of esophageal, gastric and duodenal transit of non-disintegrating capsules. *Pharmazie 1999 Jun; 54 (6): 426-30.*

The purpose of the study was to investigate in detail the esophageal, gastric and duodenal passage of non-disintegrating capsules in a fasted, healthy volunteer using Magnetic Marker Monitoring (MMM). Five independent experiments were performed. In each case the same healthy male volunteer ingested one magnetically marked capsule after fasting for at least 8 h. The magnetic dipole fields of the capsules were recorded by biomagnetic multichannel measuring equipment. The positions of the capsules were calculated from the recorded data by methods established in magnetic source imaging. The esophageal, gastric and duodenal passages of the capsules were successfully reconstructed from all recorded data sets. The spatial resolution of the capsules' three-dimensional positions in the organs of the gastrointestinal tract was within a range of several millimeters, with a chosen temporal resolution of up to four milliseconds. The esophageal transit times were between 3-13 s, the gastric residence times were between 14-133 min and the duodenal transit times were between 7-245 s. The data demonstrate that Magnetic Marker Monitoring permits the detailed investigation of the gastrointestinal transit of solids.

Weitschies W, Wedemeyer RS, Kosch O, Fach K, Nagel S, Söderlind E, Trahms L, Abrahamsson B, Moennikes H. Impact of the intragastric location of extended release tablets on food interactions. *J Control Release 2005 Nov 28; 108(2-3):375-85.*

Gastrointestinal motility and transport as well as concomitant food intake are factors that are known to influence pharmacokinetics derived after intake of extended release dosage forms. However, the mechanisms behind these influencing factors are mostly unknown. In this study the gastrointestinal transit and the in vivo drug release of magnetically labelled extended release tablets containing felodipine were monitored together with the drug absorption phase of pharmacokinetics under fasting and fed conditions in six healthy volunteers using Magnetic Marker Monitoring. It was found that the in vivo drug release profiles of the tablets compared well under fasting and fed conditions. However, the plasma concentration profiles were strongly influenced by concomitant food intake. This could be attributed to elongated residence of the tablets in proximal parts of the stomach, resulting in delayed drug absorption and the occurrence of late high plasma peak concentrations. The lag time until the first appearance of felodipine in plasma and the residence time of the tablets in the proximal stomach, were found to be directly correlated. The study shows that increased plasma peak drug concentrations after intake of extended release formulations together with food can be explained by poor mixing in the proximal part of the stomach and are not necessarily due to failure of the formulation to control drug release (dose dumping).

3D-MAGMA – Selected Literature III

Weitschies W, Kosch O, Moennikes H, Trahms L. Magnetic Marker Monitoring: An application of biomagnetic measurement instrumentation and principles for the determination of the gastrointestinal behavior of magnetically marked solid dosage forms. *Adv Drug Deliv Rev. 2005 Jan 15; 57(8):1210-22.*

Magnetic Marker Monitoring offers an alternative to investigate the behavior of solid dosage forms in the organs of the gastrointestinal tract without the need to apply radiation. For Magnetic Marker Monitoring, the dosage form is marked as a permanent magnetic dipole by the incorporation of small amounts of ferromagnetic material, as for example the colorant black iron oxide, and subsequent magnetization. Thereby, the dosage form is labeled as the source of a well defined magnetic field, which can be measured using a measurement technique that is established for biomagnetic investigations. Using the established concepts for magnetic source localization, the three dimensional localization and orientation as well as the strength of the magnetic source can be reconstructed from these magnetic measurement data as a function of time. Furthermore, it is possible to gain quantitative information on the disintegration of dosage forms in vivo. Examples are given for results obtained concerning the esophageal transit, the gastric and the intestinal behavior of capsules and tablets.

Maqbool S, Parkman HP, Friedenberg FK. Wireless capsule motility: comparison of the SmartPill GI monitoring system with scintigraphy for measuring whole gut transit. *Dig Dis Sci. 2009 Oct;54(10):2167-74*

INTRODUCTION: Assessment of whole gut transit, by radio-opaque markers or scintigraphy, is used to evaluate patients with constipation for slow gastrointestinal transit. Wireless capsule motility, using the SmartPill GI monitoring system, samples and transmits intraluminal pH, pressure, and temperature data from a capsule at regular intervals as it traverses through the gastrointestinal tract; from these, gastric emptying and whole gastrointestinal tract transit can be assessed. The objective of this study was to compare the SmartPill with whole gut transit scintigraphy to determine whether the SmartPill system could serve as a test for measurement of whole gut motility and transit. METHODS: Ten healthy, asymptomatic subjects underwent simultaneous whole gut scintigraphy and SmartPill assessment of whole gut transit. RESULTS: All subjects completed the study per protocol and experienced natural passage of the pill. Capsule residence time in the stomach correlated very strongly with percent gastric retention of the Tc-99 radiolabel at 120 min ($r = 0.95$) and at 240 min ($r = 0.73$). Small bowel contraction-min(-1) measured by the SmartPill correlated with small bowel transit % ($r = 0.69$; $P = 0.05$) and with isotopic colonic geometric center at 24 h after ingestion ($r = 0.70$, $P = 0.024$). Capsule transit time correlated with scintigraphic assessment of whole gut transit. CONCLUSIONS: SmartPill capsule assessment of gastric emptying and whole gut transit compares favorably with that of scintigraphy. Wireless capsule motility shows promise as a useful diagnostic test to evaluate patients for GI transit disorders and to study the effect of prokinetic agents on GI transit.

Hasler WL, Saad RJ, Rao SS, Wilding GE, Parkman HP, Koch KL, McCallum RW, Kuo B, Sarosiek I, Sitrin MD, Semler JR, Chey WD. Heightened colon motor activity measured by a wireless capsule in patients with constipation: relation to colon transit and IBS. *Am J Physiol Gastrointest Liver Physiol. 2009 Dec;297(6):G1107-14.*

Relationships of regional colonic motility to transit in health, constipation, and constipation-predominant irritable bowel syndrome (C-IBS) are poorly characterized. This study aimed to 1) characterize regional differences in colon pressure, 2) relate motor differences in constipation to colon transit, and 3) quantify the role of IBS in altered contractility with constipation. Colon pH and pressure were measured by wireless capsules in 53 healthy and 36 constipated subjects. Numbers of contractions >25 mmHg and areas under curves (AUC) were calculated for colon transit quartiles by time. Constipation was classified as normal transit (<59 h), moderate slow transit (STC) (59-100 h), and severe STC (>100 h). Twelve out of 36 constipated subjects had C-IBS; 24 had functional constipation. Numbers of contractions and AUCs increased from the first to the fourth quartile in health ($P < 0.0001$). Mean numbers of contractions in constipated subjects were similar to controls. Mean AUCs with normal transit ($P = 0.01$) and moderate STC ($P = 0.004$) but not severe STC ($P = NS$) were higher than healthy subjects. IBS was associated with greater mean numbers of contractions ($P = 0.05$) and AUCs ($P = 0.0006$) vs. controls independent of transit. Numbers of contractions increased from the first to fourth quartiles in moderate STC, C-IBS, and functional constipation; AUCs increased from the first to fourth quartiles in all groups (all $P < 0.05$). In conclusion, colon pressure activity is greater distally than proximally in health. Constipated patients with normal or moderately delayed transit show increased motor activity that is partly explained by IBS. These findings emphasize differential effects on transit and motility in different constipation subtypes.

3D-MAGMA – Selected Literature IV

Sarosiek I, Selover KH, Katz LA, Semler JR, Wilding GE, Lackner JM, Sitrin MD, Kuo B, Chey WD, Hasler WL, Koch KL, Parkman HP, Sarosiek J, McCallum RW. The assessment of regional gut transit times in healthy controls and patients with gastroparesis using wireless motility technology. *Aliment Pharmacol Ther. 2010 Jan 15;31(2):313-22.*

BACKGROUND: Wireless pH and pressure motility capsule (wireless motility capsule) technology provides a method to assess regional gastrointestinal transit times. AIMS: To analyse data from a multi-centre study of gastroparetic patients and healthy controls and to compare regional transit times measured by wireless motility capsule in healthy controls and gastroparetics (GP). METHODS: A total of 66 healthy controls and 34 patients with GP (15 diabetic and 19 idiopathic) swallowed wireless motility capsule together with standardized meal (255 kcal). Gastric emptying time (GET), small bowel transit time (SBTT), colon transit time (CTT) and whole gut transit time (WGTT) were calculated using the wireless motility capsule. RESULTS: Gastric emptying time, CTT and WGTT but not SBTT were significantly longer in GP than in controls. Eighteen percent of gastroparetic patients had delayed WGTT. Both diabetic and idiopathic aetiologies of gastroparetics had significantly slower WGTT ($P < 0.0001$) in addition to significantly slower GET than healthy controls. Diabetic gastroparetics additionally had significantly slower CTT than healthy controls ($P = 0.0054$). CONCLUSIONS: In addition to assessing gastric emptying, regional transit times can be measured using wireless motility capsule. The prolongation of CTT in gastroparetic patients indicates that dysmotility beyond the stomach in GP is present, and it could be contributing to symptom presentation.

Camilleri M, Thorne NK, Ringel Y, Hasler WL, Kuo B, Esfandyari T, Gupta A, Scott SM, McCallum RW, Parkman HP, Soffer E, Wilding GE, Semler JR, Rao SS. Wireless pH-motility capsule for colonic transit: prospective comparison with radiopaque markers in chronic constipation. *Neurogastroenterol Motil. 2010 Aug;22(8):874-e233.*

Abstract Background Colon transit (CT) measurements are used in the management of significant constipation. The radiopaque marker (ROM) method provides limited information. Methods We proposed to validate wireless motility capsule (WMC), that measures pH, pressure and temperature, to ROM measurement of CT in patients with symptomatic constipation evaluated at multiple centers. Of 208 patients recruited, 158 eligible patients underwent simultaneous measurement of colonic transit time (CTT) using ROM (Metcalf method, cut off for delay >67 h), and WMC (cutoff for delay >59 h). The study was designed to demonstrate substantial equivalence, defined as diagnostic agreement >65% for patients who had normal or delayed ROM transit. Key Results Fifty-nine of 157 patients had delayed ROM CT. Transit results by the two methods differed: ROM median 55.0 h [IQR 31.0-85.0] and WMC (43.5 h [21.7-70.3], $P < 0.001$. The positive percent agreement between WMC and ROM for delayed transit was approximately 80%; positive agreement in 47 by WMC/59 by ROM or 0.796 (95% CI = 0.67-0.98); agreement vs null hypothesis (65%) $P = 0.01$. The negative percent agreement (normal transit) was approximately 91%: 89 by WMC/98 by ROM or 0.908 (95% CI = 0.83-0.96); agreement vs null hypothesis (65%), $P = 0.00001$. Overall device agreement was 87%. There were significant correlations ($P < 0.001$) between ROM and WMC transit (CTT [$r = 0.707$] and between ROM and combined small and large bowel transit [$r = 0.704$]). There were no significant adverse events. Conclusions & Inferences The 87% overall agreement (positive and negative) validates WMC relative to ROM in differentiating slow vs normal CT in a multicenter clinical study of constipation.

Weitschies W, Blume H, Moennikes H. Magnetic marker monitoring: high resolution real-time tracking of oral solid dosage forms in the gastrointestinal tract. *Eur J Pharm Biopharm. 2010 Jan; 74(1):93-101.*

Knowledge about the performance of dosage forms in the gastrointestinal tract is essential for the development of new oral delivery systems, as well as for the choice of the optimal formulation technology. Magnetic Marker Monitoring (MMM) is an imaging technology for the investigation of the behaviour of solid oral dosage forms within the gastrointestinal tract, which is based on the labelling of solid dosage forms as a magnetic dipole and determination of the location, orientation and strength of the dipole after oral administration using measurement equipment and localization methods that are established in biomagnetism. MMM enables the investigation of the performance of solid dosage forms in the gastrointestinal tract with a temporal resolution in the range of a few milliseconds and a spatial resolution in 3D in the range of some millimetres. Thereby, MMM provides real-time tracking of dosage forms in the gastrointestinal tract. MMM is also suitable for the determination of dosage form disintegration and for quantitative measurement of in vivo drug release in case of appropriate extended release dosage forms like hydrogel-forming matrix tablets. The combination of MMM with pharmacokinetic measurements (pharmacomagnetography) enables the determination of in vitro-in vivo correlations (IVIC) and the delineation of absorption sites in the gastrointestinal tract.

Every slow wave impulse is association with motor activity of the human stomach

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Introduction

The electrical frequency signals of the human gastric intestinal system can detected by using surface electrodes. The recording taking by electrogastrogram (EGG) reflects only slow wave activity and not occurrence of stomach contractions.
This study was designed to investigate the typical human gastric slow wave frequency of 3/min with a newly developed high resolution 3 dimensional magnetic detector system – 3D-MAGMA.
The aim of the study was the verification that each gastric slow wave induces a motor response which is not strong enough to be detected by conventional methods for evaluation gastric motility like manometry, x-ray imaging or MR imaging.

Methods

Subjects
21 healthy volunteers (11 men and 10 women) participated in the study. Mean age of the women was 35.8 11.6 years, of the men it was 40.4 13.6 years. All subjects had been fasting for at least 8 hours.

EGG
For recording of slow wave activity electrogastrographies (EGG; Medtronic, Minneapolis, USA) were performed. The system consists of four channels for the electric signals plus one channel to filter out artefacts. The signal channels were positioned above the larger curvature of the stomach, channel one over the fundic region to channel four over the antral region. The data were measured at a frequency of about 104 Hz, filtered, averaged and recorded with a frequency of 1 Hz.

3D-MAGMA
The magnetic monitoring system 3D-MAGMA (3D-MAGMA, Matesy GmbH, Jena, Germany) contains 27 highly sensitive magnetic field sensors which are arranged above the abdomen of the volunteer (Fig. 2). The system measures the magnetic field of a small permanent magnetic capsule. The capsule (Fig. 1) comprises a magnetic core and a bio-inert polymer shell (outer diameter: 6 mm, overall length: 18 mm, specific weight: approx. 2 g/cm^3). Such a capsule moves - driven by the natural peristalsis- through the complete gastrointestinal tract.
The 3D-MAGMA-system allows the real time monitoring of a single capsule in three-dimensional space with a position error less than 5 mm and orientation error less than 2 within the whole gastrointestinal tract at a measurement frequency of up to 50 Hz. It can be used in a normal clinical environment without any special precautions.

Fig. 1: Magnetic Marker PE-cover

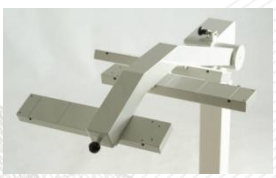

Fig. 2: 3D-MAGMA – measurement system

Procedere
First, the EGG electrodes were placed on the abdominal surface. After the volunteer was placed under the 3D-MAGMA the magnetic pill was swallowed with 70 ml water. Recordings were started. The measurement ended with the passage of the magnetic pill through the pylorus.

Results

The mean gastric transit time of the marker was 62.42 40.53 min. The shortest transit time was 19.13 min, the longest 154.07 min.

The mean frequency of the movement of the magnetic marker while the marker was placed in the stomach was 2.85 0.15 mpm (movements per minute). The mean frequency of the recorded slow wave activity using the EGG was 2.87 0.15 cpm (counts per minute). EGG and 3D-MAGMA data did not differ between male and female subjects and did not depend on the age of the volunteers.

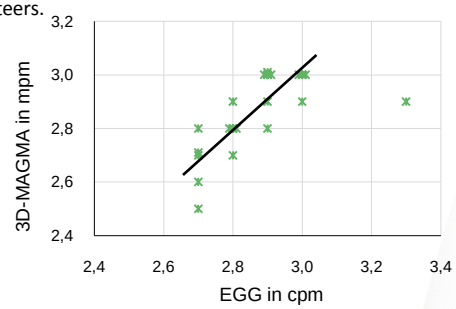

Fig. 3: Correlation of 3D-MAGMA and EGG data

Overall, there was a strong linear correlation between the dominant frequencies of the 3D-MAGMA signal and the dominant frequencies of the EGG in all 21 volunteers as shown in figure 3 (r=0.66, p=0.0011). EGG and 3D-MAGMA data became even more obvious (R=0.8265, p>0.0001) within the 95th percentile of the group of volunteers.

When the magnetic marker was placed on the abdomen of a healthy volunteer without direct contact to the abdominal wall no dominant frequency could be detected with the 3D-MAGMA system in the range of 0.5 to 30 mpm while the simultaneously performed EGG showed the expected dominant frequency of about 3 counts per minute (2.75 cpm).
Measurements obtained in the same subject after ingestion of the magnetic marker into the stomach immediately showed parallel dominant frequencies of 2.64 cpm in the EGG signal and 2.64 mpm in the 3D-MAGMA signal. Similar results were also obtained in the other 3 volunteers in whom these experiments were performed.

To test intra- and interindividual variability of the measurements, parallel 3D-MAGMA and EGG studies were repeated in 4 healthy volunteers 4 times on different days. For the 3D-MAGMA data the intra-individual variation coefficient was 3.55% and the inter-individual variation coeffi-cient was 6.35% reflecting a very good reproducibility.

Conclusion

These data demonstrate that gastric slow waves recorded by EGG an and small movements of an intragastric marker recorded by the 3D-MAGMA system occur at the same frequency in fasting healthy volunteers. Thus, in contrast to previous assumptions every gastric slow appears to bee physiologically association with gastric contraction.
In particular, the combination of EGG and highly sensitive motility measurements such as 3D-MAGMA may offer new insights into gastric physiology and pathophysiology and may become a meaningful diagnostic device for important diseases such as gastroparesis, postsurgical conditions and functional dyspepsia.