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Original Article

# In vivo observation of a stomach road or 'Magenstrasse' for gastric emptying using MRI imaging in healthy humans

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SUMMARY

The presence of a 'magenstrasse', a central 'stomach road' for flow and mixing of foods and drinks in the stomach had been predicted from hydrodynamic modelling. Here a magnetic resonance imaging (MRI) tagging technique was used to gain novel insights on the intragastric motion of breakfast porridges in 17 healthy humans. They consumed two similar breakfast porridge meals on separate days and tagging images with two different delay times were acquired 15 and 45 minutes postprandially, generating 128 data sets. Motion of the gastric contents was assessed by coefficient of variation (CoV) analysis across timeframes. The data showed that postprandial movement occurred already at the first imaging point after feeding. The motion of the gastric contents occurred along the central axis of the stomach appearing as a central 'magenstrasse' reaching the stomach body/fundus region in 73% of cases.

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Only in 10% of cases the displacement and smearing of the tag lines was detected close to the stomach walls. Seven % of data sets showed antegrade (towards the antrum) motion whilst a much larger percentage of motion was observed to be only retrograde (43%) or mixed antegrade and retrograde (50%). In conclusion, the MRI tagging method allowed novel insights into the movement of stomach contents using real model porridge meals and confirmed the existence of a central 'stomach road' for intragastric flow and mixing of food.



## Introduction

The stomach is a complex organ that accommodates, grinds, dilutes, mixes and processes foods and drinks, before releasing them into the duodenum. Despite its central role in food digestion and, in turn, nutrition, it has been historically difficult to study motion, flow and mixing of foods inside the stomach in a physiological, undisturbed state due to invasiveness or limitations of the techniques involved. Increased knowledge of these processes would improve our understanding of intragastric handling of food and drinks. This could help in turn not just understanding of physiology in vivo but also the design of in vitro food digestion models which are more 'in vivo relevant' [1,2].

A MRI method that can be used to study motion of an organ and/or its contents is called 'MRI tagging'. MRI tagging is widely used in cardiac imaging [3] and it exploits the magnetisation of the tissue to visualise motion. Firstly, a grid of thin, parallel, black lines – lines with zero MRI signal – (the tags) is magnetically superimposed on the body. Then a little later an image is taken. Therefore, if a body organ remained stationary in the time between the application of the tags and the taking of the image, the black lines on the organ will still look straight and parallel, indicating that no motion has occurred. However, if an organ has moved, then the black lines on that organ will look bent in the location and direction of motion, because the organ has dragged the tags along with its motion. MRI tagging therefore provides an easy-to-interpret 'motion map' that can be used to assess the movement happening inside an organ or a sample. This principle is shown in Figure 1.

MRI tagging has had limited applications so far in the gastrointestinal field. There was an early example from our group demonstrating the potential to study stomach motility [5] and some studies exploiting the technique to monitor small bowel motility [6–8]. More recently, the tagging technique was used by our group to assess fluid movement within the human ascending colon [9].

Building on that work, this study aimed to investigate the feasibility of using the tagging method to assess the intragastric motion of breakfast porridge meals in healthy human participants and in particular, to test the hypothesis that there is a central stomach road or 'magenstrasse' [4].

## Methods and materials

### *MRI tagging method*

As briefly introduced above, the tagging method involves superimposing a series of magnetic tags in the form of parallel black lines onto the anatomy. This is carried out at a pre-defined length of time (hundreds of milliseconds) prior to acquiring the anatomical MRI image. Tissues and materials that are static will not deform the pre-applied black lines (tags), which will therefore look straight in the image, demonstrating no motion (Figure 1A). Tissues and materials that move between the application of the magnetic black lines and the acquisition of the MRI image will instead show a deformation of the lines (tags) in the direction of motion, with the deformation being proportional to the amount of motion that

**Figure 1.** Diagram of the appearance of MRI tag lines superimposed over the stomach: (**A**) when no motion has occurred between the superimposition of the tag lines and the taking of the image, the tags all look parallel. (**B**) when motion inside the stomach has occurred the tag lines are deformed where the motion occurred and in the direction of the motion. In this particular example the diagram shows the deformation of the tag lines when a retrograde flow event, in the direction of the dotted arrow, has happened inside the stomach during the imaging procedure. (**C**) A MRI image from the study showing actual deflection of the tag lines in the direction of a backwards motion intragastric chyme motion event. The image shows a central stomach axis retrograde food movement, in the direction of the dotted arrow, indicating also the presence of a central stomach 'magenstrasse' [4].

occurred (Figure 1B) [9]. A deformation of the tags comparable to that drawn on Figure 1B will correspond to a central stomach road.

### The healthy volunteer study

#### Participants

Seventeen participants (10 females and 7 males), aged 31 (SD 11) years old, with a BMI of 24 (SD 3) kg/m$^2$ were included in this study. These tagging data were acquired as additional MRI sequences, which were acquired during a previous study but not processed nor included in the original publication [10]. The study was approved by the University of Nottingham, Medical School Research Ethics Committee (approval number F12072016). Informed written consent was obtained from each participant.

#### Experimental design

The study used a randomised, two-way crossover design that consisted of two separate test days, approximately 1 week apart. An MRI scan was performed to collect baseline images to ensure that the participants' stomachs were empty at baseline as expected in adherence to the overnight fast required. Postprandially a MRI tagging assessment of the motion of the gastric contents was done at = 15 min and 30 min later at t = 45 min. At each scan, the movement was assessed over a 20 second time period, providing 20 cine frames, 1 second apart whilst participants held their breath.

The MRI was performed on a research-dedicated 1.5T Philips Achieva MRI scanner (Philips Healthcare, Best, and The Netherlands). A cine-MRI tagged blanced turbo field echo (bTFE) single-slice sequence, positioned coronally oblique through the body and antrum of the stomach, was used to visualise the motion of the gastric contents. Delays of 300 ms and 600 ms between the application of the tag lines and acquisition of the image were used (following optimisation) to allow visualisation of the motion of the gastric contents. These delays were determined following in vitro and in vivo optimisation work which explored a range of tag delay times between 300 ms and 900 ms. The other parameters of the two scans were the same and as follows. Both scans had TR/TE 3/1.5 ms, FA 60°, thickness 15 mm, FOV 400 mm (FH), 400 mm (RL), Matrix size 256*256. Movies of the tagging data were generated by concatenating the individual images in time-sequence order. The MRI data were blinded prior to analysis, and the blind code was broken only after a blind data review was conducted.

#### Test meals

The two breakfast porridges were made from either Scottish oat flakes (Asda, United Kingdom) or pearl millet flakes (manufactured for the study in Campden BRI, UK). Both products were in the form of steam-rolled flakes. The test meals prepared for the study were cooked identically, they were iso-energetic (220 kcal each) and served with a water drink calculated to make the two meals also iso-volumetric (640 mL each). Both porridges were cooked in the same way, in that 40 g of flakes were placed in an open glass bowl, gently mixed with 270 mL of room temperature water and heated in a 900W microwave The composition of the two products is detailed in Table 1.

### Outcome measures

All the tagging movies were inspected visually to categorize the type, location and direction of movement of the gastric contents. Specifically, it was noted whether the gastric content motion was anterograde or retrograde, and the percentages of each type of motion were calculated.

Movement of the gastric content was then assessed by calculating the coefficient of variance (CoV) as previously described [9]. Briefly, movement of the gastric contents tags leads to changes in the signal intensity from frame to frame. The variation in the signal intensity can thus be quantified to provide a single number related to the amount of gastric contents motion present in that data set. Firstly, both the mean signal intensity (MI(x, y)) and standard deviation (STDEV (x, y)) was calculated on a pixel-by-pixel basis through the dynamic frames over the stomach region of interest using software custom-written in IDL® (Research Systems Inc, Boulder, CO, USA), which provided maps of both mean intensity and standard deviation. In the standard deviation maps, the voxels in which the signal intensity

**Table 1**
Breakfast porridge test meal characteristics per served portion[a]

| | SOP | PMP |
|---|---|---|
| Weight (g) of cooked product served | 400 | 415 |
| Volume of Water drunk with cooked product served (mL) | 240 | 304 |
| Total volume (mL) = volume of cooked product served + water drunk (mL) | 640 | 640 |
| Energy (kJ) | 920 | 920 |
| Energy (kcaL) | 220 | 220 |
| Protein (kjeldahl, g) | 7.2 | 6.6 |
| Total carbohydrate (by difference, g) | 42.0 | 44.4 |
| Carbohydrate (avail, g) | 34.0 | 37.4 |
| Total sugars (enzymic, g) | 1.6 | 1.7 |
| Fat (Weibull-Stoldt, g) | 4.4 | 3.3 |
| Saturates (g) | 0.8 | 0.8 |
| MUFA (cis, g) | 2.0 | 0.8 |
| PUFA (cis) | 1.2 | 1.7 |
| Trans fatty acids (g) | 0.4 | 0.4 |
| Total fibre (AOAC, g) | 8.0 | 7.5 |
| Moisture (oven102°C) | 345.2 | 359.4 |
| Ash (at 525°C) | 1.2 | 1.1 |
| Protein N Factor | 6.3 | 6.3 |
| Equivalent salt (g) | 0.4 | 0.4 |

[a] SOP, Scottish oats porridge and PMP, pearl millet porridge.

changed during the scan due to movement have a larger standard deviation than static structures, such as the liver.

The average coefficient of variation (%COV) for the tagged scan was then calculated from the following equation:

$$\%COV = 100 \times STDEV_R / MI_R$$

where ($STDEV_R$) is the average STDEV and ($MI_R$) is the average mean intensity within that region of interest. Four regions of interest were outlined on the images using Analyze9™ (Mayo Clinic, Rochester, NY, USA): the proximal stomach, distal stomach, whole stomach and liver (as control). Accordingly, increased motion causes higher displacement and/or smearing of the tag lines which in turn results in higher CoV values.

### *Statistics*

Prism version 6.07 (Graph Pad Software Inc., La Jolla, CA, USA) was used for descriptive and statistical analyses. All data are presented as mean ± SEM unless otherwise indicated. The data were assessed for normality using the Shapiro–Wilk test. Comparisons of gastric contents between SOP and PMP were made with the use of Student's paired t test (2 tailed). When data were normally distributed differences were compared using parametric statistics methods.

## Results

Application of the MRI tagging technique was successful. Displacement and smearing of the tag lines were observed in the stomach, revealing postprandial motion events of the intragastric porridge chime, in 82% of all data sets. As expected, the tag lines remained intact in the liver control area for all data sets (Figure 1C).

Visual inspection of the images showed that postprandial movement occurred early, visible already at the first imaging point after feeding (t = 15 min). In 90% of all data sets where motion was visible, the motion of the gastric contents occurred along the central axis of the stomach appearing as a central 'magenstrasse' [4], as depicted in Figure 1. This 'street of the stomach' reached the stomach body/fundus region in 73% of cases, with only 33% of cases displaying chyme motion in the antral area only.

Only in 10% of cases the displacement and smearing of the tag lines was detected close to the stomach walls.

Considering the data sets where motion was visible, only a smaller fraction of these sets (7%) presented with motion that was antegrade (i.e. from the body/fundus towards the antrum). A much larger percentage of motion (43%) was observed to be only retrograde (i.e. from the antrum towards the body/fundus) or mixed, some antegrade and retrograde within the same movie data set (50%).

Measurement of the Coefficient of Variation (CoV) percentage values allowed a more quantitative assessment of the amount of motion. The mean values for the CoV in the four different regions of interest drawn (the antrum, body/fundus, whole stomach and liver) are shown in Table 1, with the values reported for both postprandial image acquisitions times t = 15 min and t = 45 min and both tag delay times (300 ms and 600 ms). The two porridge meals were similar and no significant differences in CoV tagging values between them were observed, hence all data were pooled together to increase power. Furthermore, gastric contents for both meals were not significantly different. Table 2 reports the number of data sets analysed in each case out of the 34 acquisition available as a small number of data sets had breathing artefacts and/or imperfect slice positioning.

The small difference in CoV values in the liver between 300 ms and 600 ms delay was expected because of a change in intensity of the tag line at the longer delay time.

## Discussion

The presence of a stomach 'magenstrasse', a central 'stomach road' for flow and mixing of foods and drinks in the stomach had been predicted some time ago by Pal and colleagues using hydrodynamic modelling and boundary MRI data on stomach wall contractility [4]. The phenomenon could have potential implications for physiology and nutrition. This work has for the first time observed directly the 'magenstrasse' in vivo using 'real life' porridge meals and MRI tagging methods. The CoV was higher in the antrum indicating that in that region, as expected, motion and mixing of the stomach contents is stronger. However the data showed that the 'magenstrasse' extended to the stomach body/fundus in 73% of cases. This contradicts the common idea that the stomach empties chyme only from the antrum and is in keeping with the previous modelling work [4]. It is worth noting that our work ehre used a nutrient, small particulate porridge meal and that this 'central road' observation may not apply to more solid meals. Indeed the original computer modelling was demonstrated for a liquid nutrient meal, not a solid meal [4].

**Table 2**
Coefficient of variation CoV (%) (mean ± SEM) in the four different regions of interest (distal and proximal part of stomach, whole stomach and liver control). The CoV values are reported for the two different postprandial time points and the two different tag delay times. Data from both porridge meals were pooled together and the available number n of datasets is also indicated

| Imaging tag delay | Region of interest | CoV (%) at $t = 15$ min postprandially | CoV (%) at $t = 45$ min postprandially | $P$ Value[a] |
|---|---|---|---|---|
| Shorter tag delay 300 ms | Number of data sets | n = 34 | n = 31 | |
| | Antrum | 31 ± 2[b] | 25 ± 2 | 0.0010 |
| | Body/fundus | 24 ± 1[b] | 26 ± 2 | 0.6587 |
| | Whole Stomach | 26 ± 1 | 25 ± 1 | 0.7104 |
| | Liver control | 9.7 ± 0.4 | 10.1 ± 0.4 | 0.2673 |
| Longer tag delay 600 ms | Number of data sets | n = 33 | n = 30 | |
| | Antrum | 26 ± 1[c] | 22 ± 1 | <0.0001 |
| | Body/fundus | 21 ± 1[c] | 20 ± 1 | 0.6418 |
| | Whole Stomach | 22 ± 1 | 20 ± 1 | 0.1072 |
| | Liver control | 6.8 ± 0.2 | 7.0 ± 0.3 | 0.1627 |

[a] the data were normally distributed and differences were assessed using two-tailed, paired Student's t test.
[b] regional areas different from each other at the same time point t=15 with $P$<0.0001 at sorter tag delay.
[c] regional areas different from each other at the same time point t=15 with $P$<0.0001 at longer tag delay.

We observed both anterograde and retrograde direction of flow events inside the stomach. Previous MRI work had shown the bi-directionality of stomach flow events using a fatty liquid meal and a different flow sensitive MRI technique [11].

The macroscopic and nutritional properties of the two porridges were very similar and this was reflected in the lack of difference in tagging appearance or CoV values. As such the data were pooled together to increase power. The tag lines remained intact in the liver region and provided lower CoV values as expected, because of the negligible liver motion during a breath hold and provide a good indication of the noise of the measurement. There was however a statistical difference in the measurements using the different imaging delay times in the liver and is a consequence of the recovery of the magnetisation in the tagged regions; with a longer delay time allowing for more recovery and hence a higher signal. This higher signal translates into a lower CoV as the contrast between the tag lines and surrounding tissues is reduced. The regions of interest defined in the stomach showed higher CoV compared with the liver, which indicates that the contents of the stomach were moving and mixing during the acquisition time, however they also showed a larger reduction in CoV with increased delay time which is discussed further in the next section.

Motion can be detected visually in the tagging images and movies. The CoV method of analysis provides quantitative information on the movement. Two delay times between the application of the tags and the imaging were tested. The shorter delay times resulted in higher CoV. This may be for two reasons. The tag lines in the shorter, 300 ms delay images are darker and could yield a larger CoV for the motion of the stomach contents [9]. However, the longer 600 ms delay allows more time for the contents to move and can be more useful to study slower intragastric motion. It can however result in greater smearing of the tag lines in the images if large-scale motion was present, thus reducing the variability between cine frames [3].

This study had limitations. One was the positioning of the scanning single slice across the stomach, which was operator-dependent. The single slice may not encompass all regions of the stomach depending on anatomic variability. Motion in the presence of gas also cannot be determined. A good breath hold is needed to achieve good quality images. Also, this method is only sensitive to motion perpendicular to the tag lines, and cannot capture three-dimensional motion. The tagging method at present requires a cardiac MRI specialist package that not all MRI scanners have installed as basic configuration and if such package is present some parameter modifications may be needed to run it for this type of application. We also pooled together two sets of meal data which, statistically, may not be entirely in-dependent from each other. The main aim of the work was however to observe the stomach 'central road' using imaging rather than to compare differences between interventions.

Future applications might also include studying patients with functional dyspepsia in whom disordered motility is suspected to underlie symptoms yet conventional gastric emptying studies fail to identify any abnormality.

## Conclusion

In conclusion, the MRI tagging method can be used to visualise and assess the movement of stomach contents using real model porridge meals. Further analysis of the tag line deformation on a frame-by-frame basis could provide more information on the movement of the contents. In future work, this technique could be applied to different meals to observe gastric mixing processes and to increase our knowledge of its relationship with gastric emptying as well as endocrine, glycaemic and appetite responses. The effect of texture (e.g. liquid versus particulate or gels) on intragastric motion and mixing could be investigated. Increased knowledge of motion events in the stomach in vivo will inform in vitro models which will increase in turn their in vivo relevance.

## Author contributions

Designing: Jaber Alyami, Caroline L. Hoad, Luca Marciani, Robin C. Spiller, Penny A. Gowland, Analysis and Software: Caroline L. Hoad, Validation: Jaber Alyami, Luca Marciani, Caroline L. Hoad,

Formal analysis: Jaber Alyami, Writing—original draft preparation: Jaber Alyami, Fahad Almutairi, Luca Marciani, Writing—review and editing: Luca Marciani, Caroline L. Hoad, Robin C. Spiller., Moira A. Taylor, Fahad Almutairi, Walaa Alsharif, Visualization: Caroline L. Hoad, Supervision: Moira A. Taylor, Luca Marciani, Project administration: Jaber Alyami, Funding Acquisition: Fahad Almutairi, Jaber Alyami, Walaa Alsharif. All authors have read and agreed to the published version of the manuscript.

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## Institutional review board statement

The study was conducted according to the guidelines of the Declaration of Helsinki, and approved the study was approved by the University of Nottingham, Medical School Research Ethics Committee (F12072016).

## Informed consent statement

All participants gave written informed consent.

## Data availability statement

The study was conducted at the Sir Peter Mansfield Imaging Centre located at the University of Nottingham.

## Conflicts of interest

The authors declare no conflict of interest.

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