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Measuring fasted state gastric motility before and after a standard BA/BE 8 oz drink of water: validation of new MRI imaging protocols against concomitant perfused manometry in healthy participants

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BACKGROUND:

The gastrointestinal (GI) environment in which drug products dissolve has not been studied in detail due to limitations, especially invasiveness of existing techniques. Little *in vivo* data is available on undisturbed GI motility to improve relevance of predictive dissolution models and bench dissolution techniques. Recent advances in magnetic resonance imaging (MRI) methods could provide novel data and insights [1-2]. The conventional method for measuring gastrointestinal motility is via a manometric technique involving intubation, but it is possible to measure GI motility with MRI.

OBJECTIVE(S)

To develop and validate, against concomitant perfused manometry, a new MRI method to measure stomach motility in the fasted state before and after the standard BA/BE 8oz dose of water.

METHOD(S)

A single-centre, open-label design consisting of a screening visit and two study days. Eighteen healthy participants (12 male, 29±10 years old, BMI 24±2 kg/m^2), completed both study visits. Each study day (Figure1), the subjects fasted overnight and were intubated with a 16 channel small bowel water perfused catheter with a balloon on the tip to check positioning. The MRI and manometry data were recorded as shown in Figures 2 & 3. MRI scanning was carried out supine using a 1.5T General Electric scanner. The data was acquired using a FIESTA sequence.

The cine-MRI images were processed using MRManometry software (Motilent, London, UK) (Figure 4) and the area under the curve (AUC) was calculated (mm × second). The manometry data was analysed using Medical Measurement System, Enschede, The Netherlands, and the AUC was calculated (mmHg × second)

The protocol was registered with Clinical Trials.gov with identifier NCT03191045.

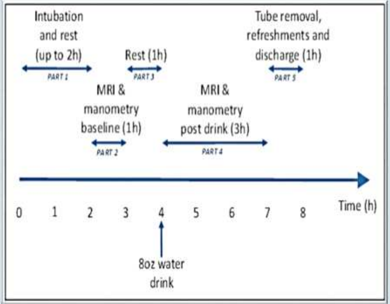

Figure 1: Schematic diagram of the MRI study day protocol.

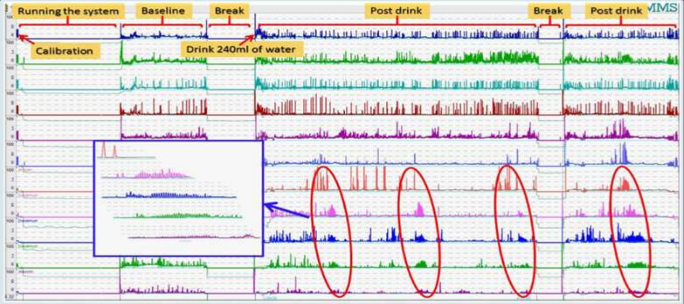

Figure 2: Perfused manometry traces over the study day of one healthy participant.

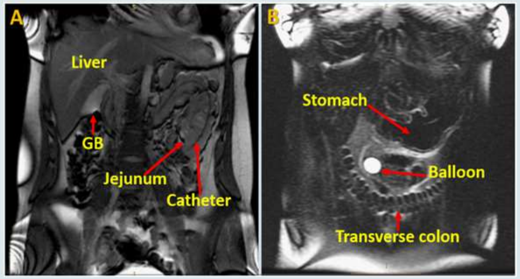

Figure 3: A. MR image showing the catheter in the jejunum and B. MR image showing the inflated balloon at the tip of the catheter inside the small bowel of the participant.

RESULT(S)

The study procedures were well tolerated and all 18 participants returned for their second visit. Under MRI guidance, over 90% of intubations reached the duodenum, of which 48% reached the jejunum. The dynamic, cine MRI captured stomach contractions and the perfused manometry traces allowed good quality concomitant monitoring of the motility of the upper GI tract in the participants (Figure 5). The MRI motility AUCs significantly correlated with the corresponding perfused manometry AUCs (r=0.850, P < 0.001) (Figure 6).

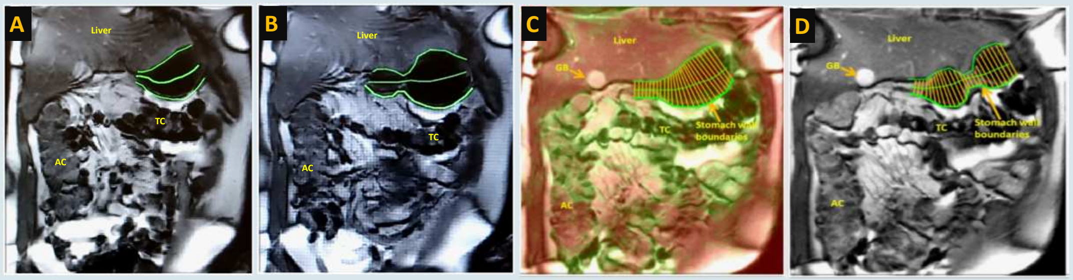

Figure 4: A and B: MRI movies of the stomach during, respectively, quiescence and contractile activity. C and D examples of quantitative measurements of the luminal diameters of the stomach (represented in yellow) as the distance between the stomach boundaries and the stomach midline (in green). D shows a pronounced stomach contraction.

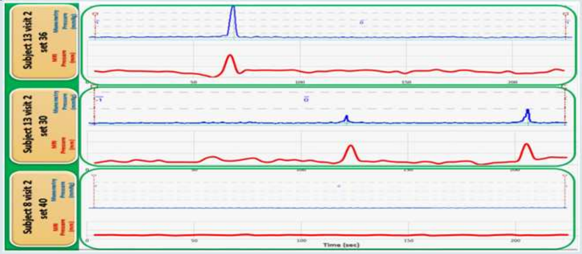

Figure 5: MRI motility spatio-temporal plots (in red) and corresponding perfused manometry traces (in blue) from different subjects across different time points during antral contractions and baseline.

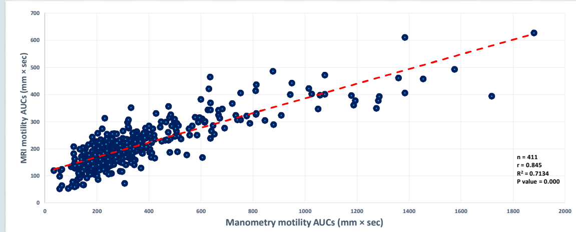

Figure 6: Plot of MRI motility AUCs against the corresponding perfused manometry AUCs.

CONCLUSION(S)

These new validated MRI protocols to measure stomach motility can help to conduct studies with drugs to measure motility and therefore, improve the in *vitro*/in *vivo* relevance of predictive dissolution studies of oral dosage forms.

FUNDING/REFERENCES

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