T4007

Fasted and Fed Motility of the Undisturbed Small Bowel: Development of Novel MRI Methods to Advance In Vivo Predictive Dissolution Studies

A. Khalaf[1], C.L. Hoad[1,2], A. Menys[3], D. Mudie[4,5], J. Wright[1], K. Heissam[1], N. Abrehart[1], P.A. Gowland[2], G.E. Amidon[4], R.C. Spiller[1], G.L. Amidon[4] and L. Marciani[1]

[1]Nottigham Digestive Diseases Centre, University of Nottingham; [2]Sir Peter Mansfield Imaging Centre, University of Nottingham; [3]Motilent Ltd, UK; [4]College of Pharmacy, University of Michigan; [5]Capsugel, Bend, OR

CONTACT INFORMATION: Luca.Marciani@nottingham.ac.uk

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PURPOSE

The rate and extent of drug dissolution and absorption from solid oral dosage forms is highly dependent upon gastrointestinal motility [1, 2]. However, the ability to measure small bowel motility is limited as current methods have poor spatial resolution or are invasive. Previous studies [3, 4] showed the ability of magnetic resonance imaging (MRI) to acquire dynamic movies of small bowel motility across the whole abdomen and to quantify outcome parameters of motility. This however is usually done on a bowel prepared and filled with luminal contrast media to distend the walls which may itself disturb underlying physiology and may have a stimulatory effect on motility.

OBJECTIVE

This study therefore aimed to develop MRI methods to quantify outcome parameters of the motility of the undisturbed small bowel in the fasted and fed state in healthy volunteers (HVs).

METHODS

Fifteen HVs gave informed written consent and took part. A fasted state baseline MRI scan was taken in the morning, after an overnight fast. The participants were then fed a 400g, 204 kcal soup meal after which a fed state MRI scan was acquired. The dynamic data was registered using validated software (DRAM, Motilent, UK) [3]. The results of the registration were summarised as a novel spectral parametric map (SP Map) combineing information from bowel deformation and luminal intensity to produce a single spectral power map. A summary of total gut spectral power was produced by placing a global ROI across the small bowel to produce a mean SP Map score.

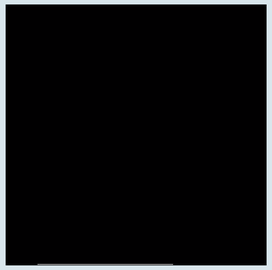
RESULTS

(mean±SEM) The total power was the small bowel motility outcome parameter that was able to detect fasting state motility and provided the widest dynamic range response to the fed state. The figure left and centre panels show the fasting and fed state motility maps respectively for one participant. Key findings showed:

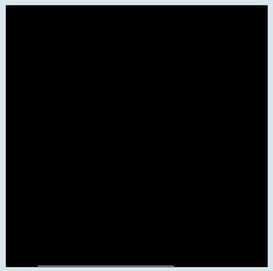
1) Using this metric the fasted small bowel motility was 39±3a.u., which increased significantly to 87±7a.u. in the postprandial state, $p<0.0001$ (individual data in the right panel of the figure).

2) Agreement between the two observers when analyzing 13 motility datasets was good, Spearman's r-value 0.91.

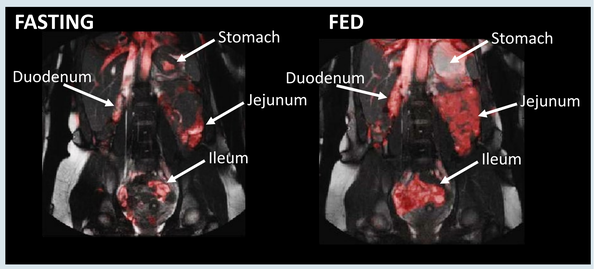
3) Intra-observer reliability was high with intra-class correlation coefficient ICC 0.929 for one observer and 0.991 for the other observer repeating analysis of 13 motility data sets.

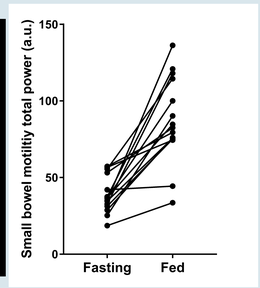


Fasting state motility movie



Fed state motility movie





Fasting and fed motility maps and total power graph

CONCLUSIONS

These are novel MRI insights into the motility of the undisturbed fasting and fed small bowel. The methods will be useful to study the time scales of contractile activity and regional patterns along the gastrointestinal tract. Information on small bowel motility can be obtained in conjunction with mapping the bowel liquid pockets using MRI [5]. This combined insights can help advancing in vitro/in vivo predictive dissolution studies of oral dosage forms under similar, undisturbed conditions.

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