

## Echo-Planar Imaging of Gaviscon Alginate Rafts in Vivo.

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### Introduction

Liquid Gaviscon (LG) and Gaviscon Advance (GA) are established alginate biopolymer formulations used in the treatment of gastroesophageal reflux disease. So far direct visualisation of alginate rafts in the stomach has proven difficult due to limitations in the techniques used. Several reports though have proven the potential of conventional MRI<sup>1</sup> and EPI<sup>2,3</sup> in imaging gastric function and the gastric contents<sup>4</sup> and a recent abstract reported a preliminary experience of visualisation of Gaviscon rafts using MRI<sup>5</sup>. The true snap-shot nature and the inherent contrast between gels and liquids of EPI could provide a unique tool for monitoring alginate rafts in vivo.

Therefore, our aim was to evaluate the use of EPI in assessing, non-invasively, the formation, location and retention of intragastric alginate rafts of LG and GA in healthy subjects. Secondly, to evaluate the use of  $T_2$  measurements to monitor changes in the physicochemical properties of the rafts.

### Methods

Six healthy subjects attended fasted on 2 sessions each, and ingested 200ml of fat to slow gastric emptying: after 20min they ingested 500ml of a liquid test meal (60% water, 10% sugar and 30% concentrated lemon juice). 5min later they received (randomly) a single oral dose of 20ml LG or 10ml GA (Reckitt Benckiser Healthcare, Hull, UK).

One volume and one  $T_2$  measurement data set were acquired every 15min until the stomach appeared empty. 5min later the volunteers rapidly drank 500ml water and a further volume scan was acquired. Subjects were kept supine on the bed outside the magnet bore between scanning. This study was approved by the local Ethics Committee and subjects gave informed written consent.

Single-shot, half-Fourier EPI images were acquired on a whole-body, purpose-built, 0.5T EPI scanner. Volume sets were acquired using half-Fourier transverse rapid multislice spin-echo EPI with TE=20ms. A 72 by 128 matrix, 3.5mm by 2.5mm in-plane resolution and a slice thickness of 1cm were acquired.  $T_2$  data-sets were acquired on the digesta using a multi-echo EPI sequence<sup>6</sup> based on inverting hyperbolic secant pulses (4 echo times from 74 to 731ms, repeated 3 times with TR=10 s). Changes in total volume and  $1/T_2$  were plotted against time for both the raft and meal.

Results were expressed as mean(SEM). Treatment differences and trends were analysed using ANCOVA and Page's test.

### Results

In vitro the test meal allowed repeatable raft formation for both products. The EPI images showed good contrast between raft and liquid meal. In vivo raft formation was observed in all experiments for both LG and GA. It is worth noting that in the supine position the raft floated in the antro-pyloric region and thus emptied progressively with the liquid meal.

At t=45min after dosing the raft volumes were 61(8)ml for LG and 66(2)ml for GA. After the meal emptied a raft was still seen in the stomach in 60% of cases for LG and in 100% for GA.

The 3D reconstructions showed precise details of the stomach anatomy and spatial distribution of the floating rafts (Figure 1).

The  $T_2$  measurements were able to assess dynamic changes in the raft properties in vivo. The  $1/T_2$  values for the raft were higher than those for the underlying liquid meal at all time points up to 75 min for both treatments.  $1/T_2$  for the raft decreased significantly over time ( $p=0.01$ ) while  $1/T_2$  for the liquid meal increased ( $p<0.001$ ).

Statistical analysis suggested the possibility of treatment differences, but due to the small sample size no definitive conclusions could be drawn.

### Discussion

The data show that it is possible to visualise LG and GA alginate rafts in the gastric lumen using EPI. We chose a spin-echo EPI module with 20ms echo-time to increase the  $T_2$  contrast between raft and liquid meal whilst refocusing  $T_2^*$  effects. Half-Fourier EPI was used because of the short  $T_2^*$  of the raft. The difference in  $1/T_2$  between raft and liquid meal was expected due to the gel matrix restricting water mobility and to cross-relaxation effects between bulk water and gel hydroxyls. Furthermore,  $CO_2$  bubbles are trapped in the raft and the magnetic susceptibility effect also affects the its  $T_2$ . Interpretation of the dynamic changes observed is therefore complex. A decrease in  $1/T_2$  could be explained with a slow degrading of raft coherence and/or with a release of  $CO_2$  from the gel matrix with time. A  $1/T_2$  increase in the liquid phase may suggest a slow leakage of degraded gel matrix into it. However, although indicative of dynamic changes, it was not possible to differentiate between the gel and the  $CO_2$  effects from our data. Further investigation is required to relate the  $T_2$  values to the dynamics of raft formation. Additional water diffusion and proton density MRI measurements could prove useful.

### Conclusion

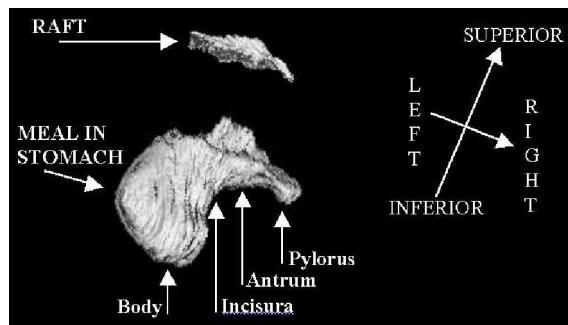
This study demonstrates the use of EPI in the visualisation of Gaviscon alginate rafts in vivo, non-invasively without the need to use radioactive labels or contrast agents. The EPI investigation was well tolerated by subjects and could allow serial comparison of different products using larger sample sizes.

### References

1. W Schwizer et al, *Gastroenterol.* **103**:369-376 (1992).
2. MK Stehling et al, *Radiology* **171**:41-46 (1989).
3. DF Evans et al, *Gut* **34**:848-852 (1993).
4. J Wright et al, *Gastroenterol.* **110**(4SS):A781 (1996).
5. RS Paterson et al, *J. Pharm. Pharmacol.* **52**(SS):8 (2000).
6. D Tyler et al, *Proceedings 8<sup>th</sup> ISMRM*:432 (2000).

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**Figure 1:** 3D reconstruction of a Gaviscon Advance raft and of the underlying meal in the gastric lumen at t=95min.