

In vivo gastrointestinal transit study using double-labelled markers

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Introduction

Functional gastrointestinal disorders frequently affect the transit time of material through the gastrointestinal tract. A number of studies have been presented in the past to study the transit of dosage forms [1-4] and many techniques have been used previously including radiopaque markers [5], non-absorbable markers [6] or calculating the transit time on the basis of the appearance of the marker in the x-ray or in the stools [6]. The main disadvantages of these techniques are the use of radiation or the lack of precision in the estimate of transit times due to the analysis of a single stool. This abstract presents the first pilot in vivo study measuring gastrointestinal transit with MRI and purpose built plastic capsules, double labelled with a fluorine agent (perflubron, PFOB) and a gadolinium (Gadoteridol, Gd-HP-DO3A) solution.

Aim: to determine which of the two capsule fillings produced the best images for detection of capsule location.

Methods

Capsule preparation:

Plastic capsules were made from Polyoxymethylene, with the shape of a size 0 gelatine capsule for oral drug dosage, fig. 1. The capsules were closed, glued and filled with a needle from a hole on the top that was then closed with a plastic screw. They were filled with 0.2 ml of 15µM Gadoteridol solution (1H MRI marker) together with 0.6 ml of PFOB (19F MRI marker). 10% of the capsules prepared in each batch were tested for leakage: they were filled with 0.8 ml of blue food colour and individually immersed in 45 ml of water in a water bath with movement, at body temperature for 3 days. 1 ml samples were taken from the bath every 3 hours up to 72 hours. A UV/VIS Jenway Model 6105 spectrophotometer was used to establish any leakage of colour from the samples.

In vivo study:

Two healthy volunteers were imaged on a 3T Philips Achieva system on 4 consecutive days. They received a breakfast of a rice pudding and pure orange juice [7] and, after a baseline scan, they swallowed 4 capsules with water ad libitum. They were scanned immediately after this and then hourly up to 5 hours after dosage and then at 24, 48 and 72 hours. A range of MRI sequences were used to image the gut. Three proton sequences were acquired with the body coil: dual FFE sequence (TR/TE1/TE2 (ms) = 126 / 2.3 / 5.8, rec. res. = 1.56 x 1.56 mm², 15 slices thickness 5 mm) for anatomical detail; Haste (TSE) (TR=1667 ms, TE=65 ms, rec. res. = 1.56 x 1.56 mm², 10 slices 10 mm thick) on which both Gadoteridol and PFOB have low intensity; heavily T1-weighted TFE sequence (TR=4.6 ms, TE=2.3 ms, rec. res. = 1.14 x 1.14 mm², thickness 3 mm), on which Gadoteridol is high intensity and the PFOB is low intensity. Fluorine images were acquired with a PulseTeq surface fluorine coil without moving the volunteer: an FFE sequence was acquired (TR=350 ms, TE=3.0 ms, rec. res. = 2.5 x 2.5 mm², 3 slices 100 mm thick), displaying the PFOB with high intensity and no proton signal.

Results

Capsule preparation: No leakage was found in any of the capsules tested.

In vivo study: Table 1 summarises the results for this pilot study. At 2 hours, the 4 capsules were visible in the stomach for both volunteers (example in fig. 2). From 2 to 5 hours the capsules were seen in the small bowel for both subjects. Fig. 3 shows 1H images of capsules in the small bowel and the corresponding fluorine image, which has a thick slice so that all the capsules are seen in one image. At 24 hours, for Sub1 two capsules were found in the transverse colon and 2 in the rectum, whilst for Sub 2, 1 capsule was found in the descending colon and 2 in rectum. At 48 and 72 hours no capsules were found for both volunteers.

Discussion

The subjects tolerated the study procedures well and the capsules were evacuated within 48 hours. The capsules were detected in the gut for both volunteers at all time points until evacuation. By using the range of sequences and marker tracers, one can easily differentiate the bright signal of the Gd in the capsules from the structures nearby and the fluorine image gave confirmation of their position. However, in most cases the fluorine coil had to be repositioned after the exact location of the capsules was established by the 1H images because the 19F coil sensitivity doesn't cover the entire GI tract. In future it would be possible to perform clinical studies of GI transit using just 1H labelled capsules assessing transit from the geometric centre of the 4 capsules [8].

References

[1] Schiller et al Aliment Pharmacol 22 (2005) [2] Schwarz et al. MRM 48 (2002) [3] Buhmann et al Eur Radiol 17 (2007) [4] Hahn et al. ISMRM Proc. 6804 (2010) [5] Hinton et al. Gut 10 (1969) [5] Higgs et al. Gut 16 (1975) [6] Cummings et al. Gut 17 (1976) [7] Marciani et al. Gastroenterology 138 (2010) [8] Camilleri et al. Gastroenterology 103 (1992)

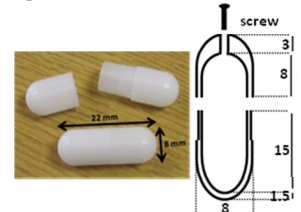


Figure 1 Manufactured capsules and size in mm.

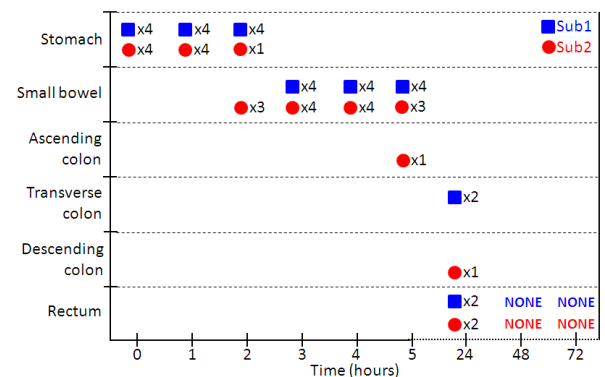


Table 1 Position of the capsules for the 2 subjects over time.

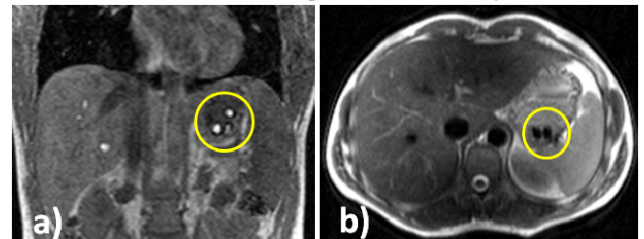


Figure 2 Dual FFE (a) and the Haste (b) images for Sub 1 at t=0, showing the 4 capsules (highlighted) in the stomach.

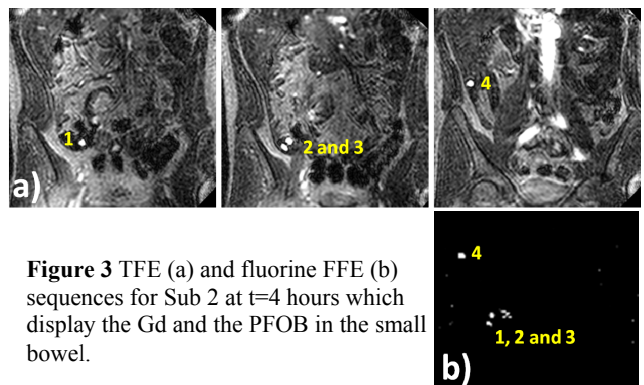


Figure 3 TFE (a) and fluorine FFE (b) sequences for Sub 2 at t=4 hours which display the Gd and the PFOB in the small bowel.