

# Fusion of gamma scintigraphic and magnetic resonance images improves the anatomical delineation of radiotracer for the assessment of gastrointestinal transit

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**Objectives** This paper describes the use of gamma scintigraphic and magnetic resonance (MR) fusion images for improving the anatomical delineation of orally administered radiotracers used in gastrointestinal (GI) transit investigations.

**Methods** Ten healthy volunteers ingested enteric-coated gelatin capsules containing  $4.4 \pm 1.1$  MBq  $^{153}\text{SmCl}_3$ -labelled resin. Four external body markers containing  $^{153}\text{Sm}$  and Gd-DTPA were placed on the left and right lower costal margins and iliac crests of each volunteer. Anterior and posterior planar images were acquired hourly for 9 h, followed by a final single photon emission computed tomography (SPECT) image and subsequent T1-weighted images using a 1.5 T MR system. Coronal scintigraphic images were fused with MR images and assessed for diagnostic information.

**Results** The fused images revealed a combination of the tissue and organ anatomy with an overlay of the distribution of the tracer. Compared with conventional scintigraphic imaging alone, SPECT-MR fused images improved the localization of spatial and temporal movements of the radiotracer throughout the GI tract.

## Introduction

Nuclear medicine techniques are routinely applied for the quantitative assessment of gastrointestinal (GI) transit [1–13]. The commonly used radionuclides for GI imaging include  $^{99\text{m}}\text{Tc}$  for upper GI imaging (as the physical half-life of 6 h is not long enough for whole GI transit studies) and  $^{111}\text{In}$  for whole GI transit (physical half-life of 2.8 days) [1,3,14–18]. In our experience, however, a limitation of scintigraphic imaging is the lack of anatomical detail, especially with regard to the varying internal position of the nonrigid small and large bowel. These details are of value in GI transit studies, especially when the regional transit time is being assessed. Although nuclear medicine is known as the gold standard for the quantitative assessment of GI motility, scintigraphy is not

**Conclusion** Fusion of SPECT and MR images in conjunction with sequential scintigraphic images improved the assessment of segmental GI transit. These have the potential to provide more accurate diagnostic results and are visually powerful images that would have more widespread acceptance by nonspecialists. *Nucl Med Commun* 34:645–651 © 2013 Wolters Kluwer Health | Lippincott Williams & Wilkins.

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**Keywords:** gamma scintigraphy, gastrointestinal transit time, image fusion, magnetic resonance imaging, single photon emission computed tomography,  $^{153}\text{Sm}$

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always the first choice of gastroenterologists and radiologists because of the limited information on anatomical structures [1,6,7].

Abdominal imaging using MRI is gaining credibility, and there is now increasing interest in imaging protocols for the investigation of GI function [19–24]. MRI is a promising imaging technique for the investigation of GI transit, as reviewed by Marciani [23]. The advantages of MRI include the absence of ionizing radiation and excellent soft-tissue resolution. However, compared with conventional radiological methods, MRI is relatively more expensive, and repeated imaging for GI transit study in the same patient would be logistically difficult.

In the present study we sought to combine the benefits of hourly planar scintigraphic imaging (using  $^{153}\text{Sm}$  as an alternative to  $^{111}\text{In}$ , as previously reported [25–27]) with those of single photon emission computed tomography (SPECT) and magnetic resonance (MR) volumetric studies to improve the presentation of data used in the assessment of whole GI transit studies. By fusing

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Preliminary data from this study have been published in EPOS format at the European Congress of Radiology, Vienna, 2012, and this study was proudly awarded the Certificate of Merit.

scintigraphic images with MR images we aimed to develop a simple and viable method of data merger to enhance diagnostic imaging for whole GI transit assessment (Supplementary video, <http://links.lww.com/NMC/A8>).

## Materials and methods

### Preparation of $^{153}\text{Sm}$ -labelled oral dose formulation

The labelling and neutron activation of the  $^{153}\text{Sm}$  oral dose formulation were performed as reported previously [25,26]. The formulation was incorporated into a medical-grade size 1 hard gelatine capsule for human consumption. The administered activity was 5 MBq/patient.

### Preparation of dual MR and gamma scintigraphic markers

The commercially available clinical MR contrast agent gadopentetate dimeglumine (Gd-DTPA 0.5 mol/l, Magnevist; Bayer Schering Pharma, Berlin, Germany) was used as the MR external marker in this study. In order to determine the optimal concentration of Gd-DTPA for the T1-weighted MR image, a phantom study was conducted in which different concentrations of Gd-DTPA solution ranging from 0.10 to 0.30 mg/ml with a 0.02 mg/ml step were prepared in different polyethylene vials immersed in a 1000 ml water phantom. The phantom was then placed in the body coil of a 1.5 T MR system (MR Signa HDxt; General Electric Healthcare, Waukesha, Wisconsin, USA) and imaged with a T1-weighted MR sequence. Regions of interest were drawn on the MR images, and the mean signal intensity was obtained from the region of interest of each sample. The plot of relative signal intensity to water versus Gd-DTPA concentrations (Fig. 1) showed that 0.18 mg/ml was the optimum Gd concentration for the purpose of this study.

On determination of the optimum Gd concentration, the dual MR and gamma scintigraphic markers were prepared by filling polypropylene microcentrifuge tubes with  $\sim 0.2$  ml of Gd-DTPA having 0.18 mg/ml of Gd (microcentrifuge tube 0.3 ml; Jet Biofil, Guangzhou, China). Neutron-activated  $^{153}\text{Sm}$ -labelled resin beads with activity of  $\sim 0.5$  MBq were subsequently added to the microcentrifuge tube to be used as the gamma scintigraphic marker. The tubes were then sealed and the clips of the lid were cut off and smoothed (Fig. 2).

### Healthy volunteers' study

Ethics approval (protocol number MEC 782.30) was obtained from the Medical Ethics Committee of University of Malaya Medical Centre, Malaysia, to conduct a healthy volunteer imaging study. Pregnant women were strictly excluded from the study. Ten healthy volunteers (six women and four men; age  $33 \pm 13$  years) with no history of or with active GI-related diseases were screened and recruited into the study.

Four fiducial markers containing gadolinium and  $^{153}\text{Sm}$  were attached to the anterior left and right upper and lower costal margins of each volunteer. The markers were

taped on the volunteer's skin throughout the period of the study.

Each volunteer ingested one  $^{153}\text{Sm}$ -labelled resin capsule with 250 ml of water. Immediately after administration, scintigraphic imaging was performed using a dual-detector SPECT system (Philips BrightView; Philips, Eindhoven, the Netherlands) fitted with a low-energy high-resolution collimator. Anterior and posterior 1-min planar images with the participant in the supine position were acquired using a  $103 \text{ keV} \pm 10\%$  energy window. Planar scintigraphic imaging was performed hourly for 9 h, followed by a final volumetric SPECT image acquisition of 64 angular steps over  $360^\circ$  at 15 s/view with a  $64 \times 64$  matrix size. Subsequently, the volunteer underwent an MRI scan using a 1.5 T MR system (MR Signa HDxt; General Electric Healthcare). The volunteers were scanned in the supine position using a multiarray body coil. After obtaining the standard localization and calibration scans, a volumetric T1-weighted LAVA sequence (TR 4.0 ms; TE 2.0 ms; SL 2.0 mm; 156 slices) was performed. The total MRI time including subject positioning was  $\sim 7$  min.

The volunteers were required to return to the department the next morning for a 24-h postingestion imaging study. Two-minute planar scintigraphic imaging was carried out to verify the excretion of the radioactivity from the body.

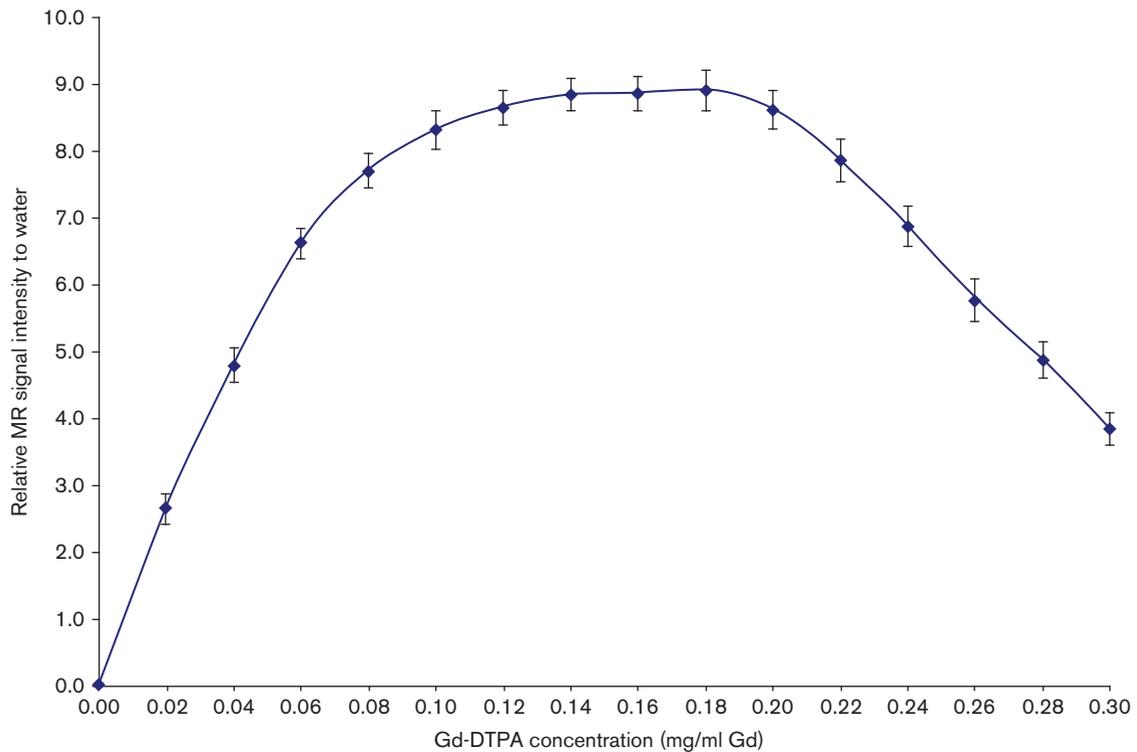
### Image postprocessing and data analysis

Gamma scintigraphic images were processed and analysed using dedicated nuclear medicine software (Extended Brilliance Workspace V3; Philips, Eindhoven, the Netherlands). Alignment was carried out by superimposing the images on the basis of the fiducial external markers. Sequential planar images were concatenated into a dynamic display to allow better visualization and interpretation of anatomical information. The GI tract was segmented into seven regions: the stomach, the small intestine, the ileocaecal junction, the ascending colon, the transverse colon, the descending colon, and the rectosigmoid. The site and extent of  $^{153}\text{Sm}$  radioactivity were recorded at each imaging time point. In addition, the regions and times at which the  $^{153}\text{Sm}$  capsule started to disintegrate were also recorded. A graph was finally plotted to show the track of  $^{153}\text{Sm}$  radioactivity in the GI tract at each time point.

The MR data were displayed as volumetric T1 (LAVA)-weighted images. Maximum intensity projections of 3 mm thickness were generated using the T1-weighted coronal images. The Gd-DTPA markers were identified on the basis of their characteristic shape and a homogeneous intense signal.

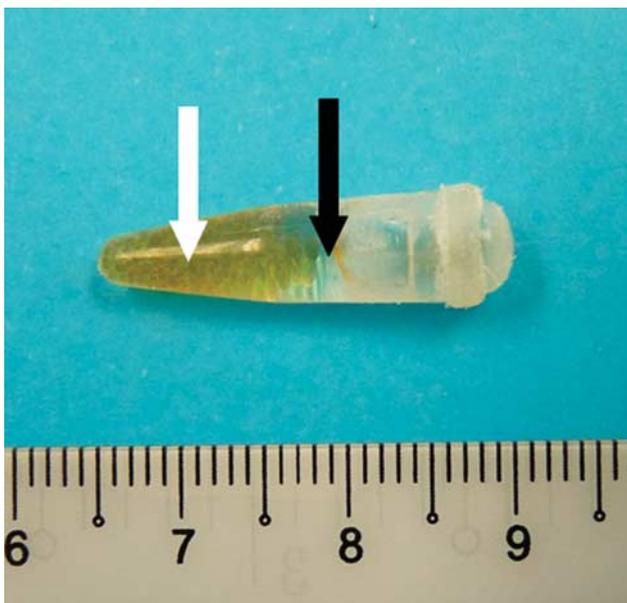
Image processing software, Medical Image Processing, Analysis and Visualization (MIPAV; Centre for Information

Fig. 1



Graph of relative MR signal intensity to water versus concentration of Gd-DTPA showing the optimum concentration of Gd at 0.18 mg/ml in the T1-weighted sequence. Gd-DTPA, gadopentetate dimeglumine; MR, magnetic resonance.

Fig. 2

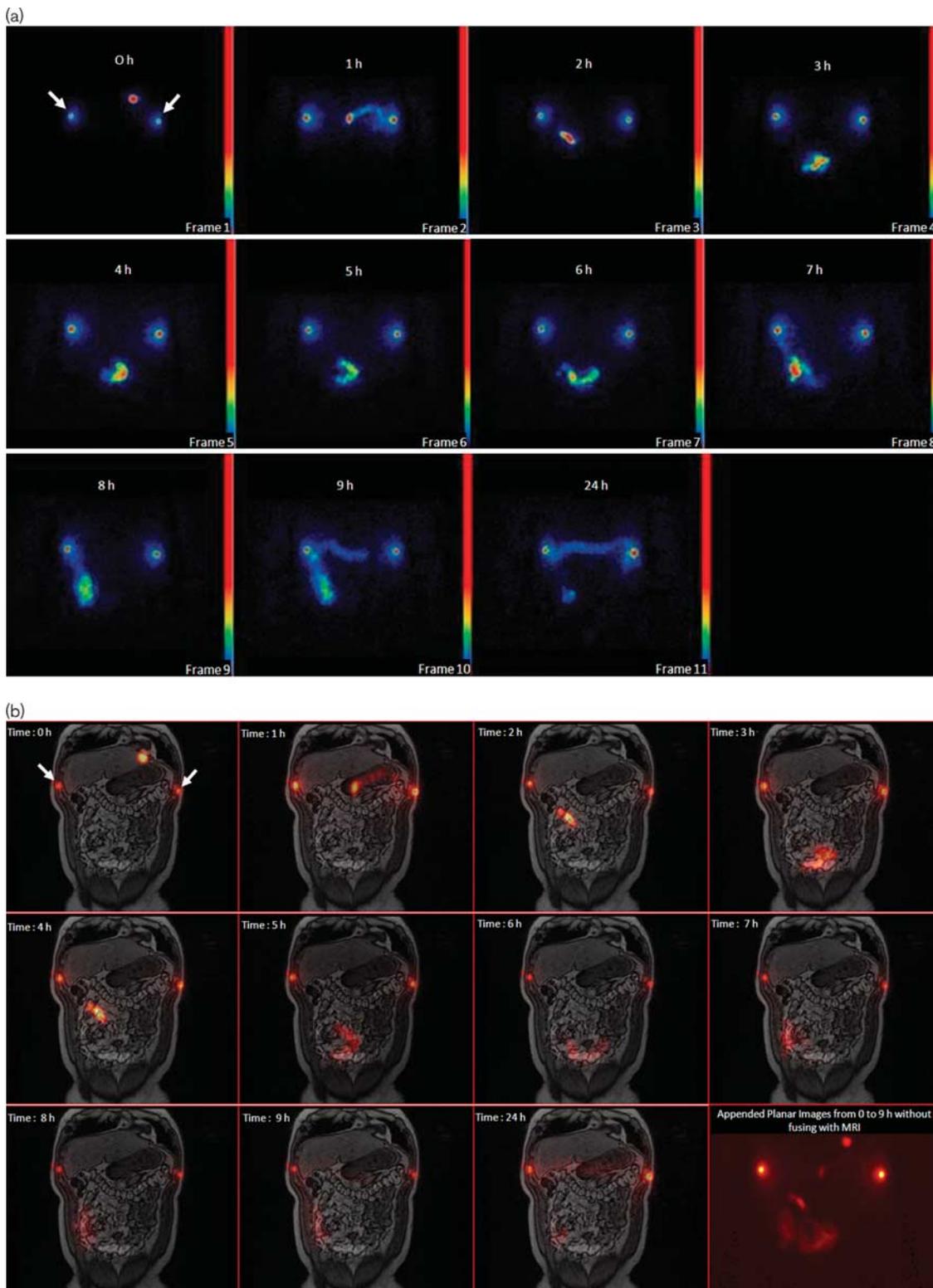


A microcentrifuge tube containing 0.2 ml of 0.18 mg/ml Gd-DTPA (MRI marker, black arrow) and 0.5 MBq  $^{153}\text{Sm}$ -labelled resin beads (gamma scintigraphic marker, white arrow).

Technology, National Institutes of Health, Bethesda, Maryland, USA), developed by the Johns Hopkins University, Maryland, USA, was used to process and fuse the volumetric images from SPECT and MRI. MIPAV is an open-access software used for visualization, analysis and processing of the Digital Imaging and Communications in Medicine (DICOM) images (available at: <http://mipav.cit.nih.gov>). The SPECT data were first reconstructed in the coronal plane so that they could be aligned with the reformatted coronal MR images. Registration of the coronal, SPECT and MR images was carried out using the least squares method based on the four external body markers. The images from the two modalities were then fused, and the blending ratio was adjusted according to preference. The fused coronal images were then saved in a multimodality DICOM format. Finally, each of the 11 planar scintigraphic images was superimposed onto the SPECT-MR fused image, and registration was again based on the external body markers. These fused, planar SPECT-MR images were viewed sequentially in the cine mode.

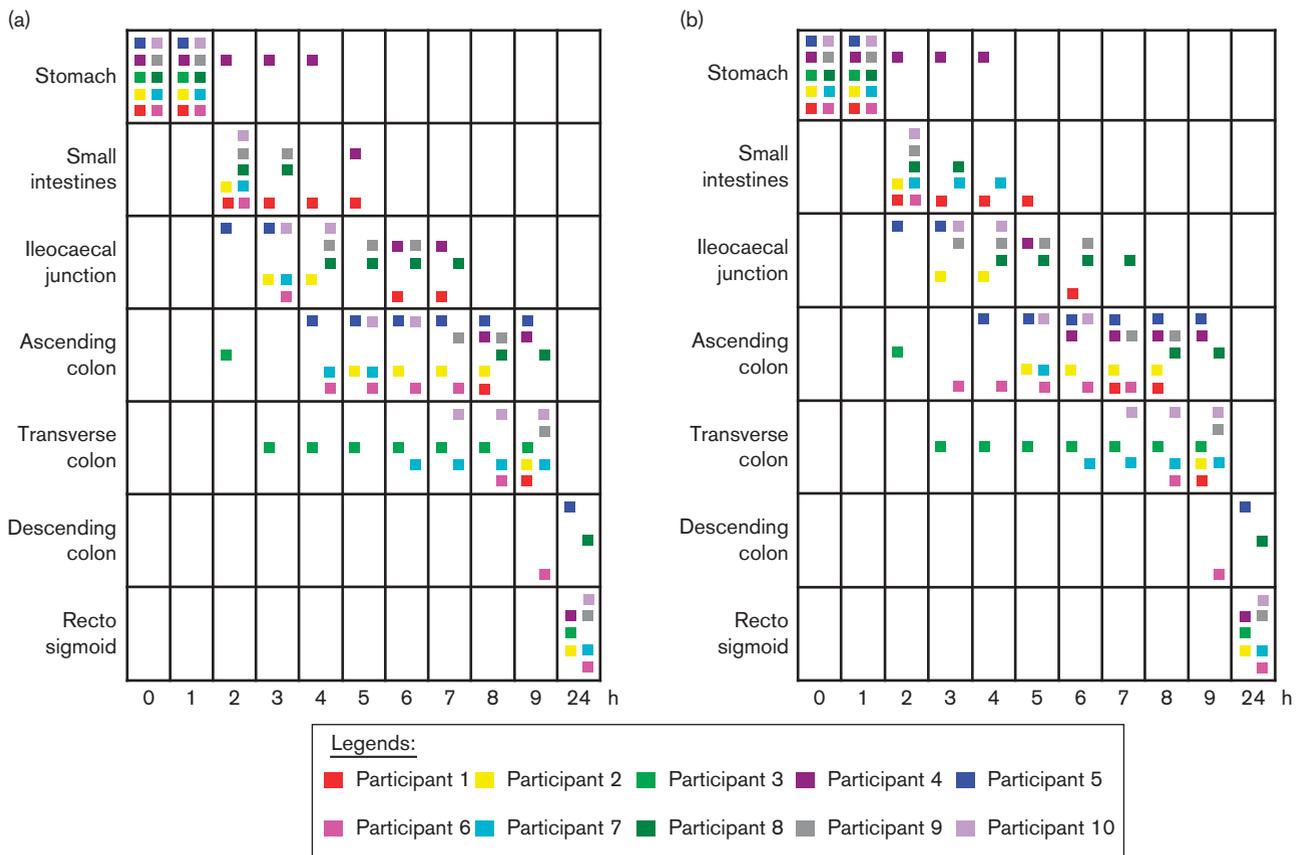
The transit of the  $^{153}\text{Sm}$ -labelled formulation through the GI tract was assessed using both planar scintigraphic images and SPECT-MR fused images on two separate occasions. The two sets of interpreted results were then compared.

Fig. 3



(a) Planar scintigraphic images at a 1-h interval and a final image at 24 h after ingestion. The capsule started to disintegrate at 5 h after ingestion at the ileocaecal junction. The white arrows point to the external body markers. (b) The sequential coronal series of SPECT and MR fused images shows the transit of the  $^{153}\text{Sm}$  formulation (represented in a warm colour palette) through the GI tract. Two external markers containing both  $^{153}\text{Sm}$  and Gd-DTPA (white arrows) were placed at the left and right lower costal margins of the volunteer. The last panel at the right bottom shows the appended images from scintigraphic imaging alone without fusion with MRI data. Gd-DTPA, gadopentetate dimeglumine; GI, gastrointestinal; MR, magnetic resonance; SPECT, single photon emission computed tomography.

Fig. 4



Comparison of localization of the <sup>153</sup>Sm-labelled formulation in the GI tract using (a) scintigraphic images alone and (b) fused SPECT-MR images. The colour-coded boxes represent the location of the <sup>153</sup>Sm-labelled resins with time for each individual participant. GI, gastrointestinal; MR, magnetic resonance; SPECT, single photon emission computed tomography.

**Results**

**Gamma scintigraphic images**

The <sup>153</sup>Sm-labelled resin was clearly visualized in all the scintigraphic images as a single hot spot when the capsule was intact, and the activity was seen to disperse when the capsule disintegrated. Figure 3a shows a sequential planar image at a 1-h interval and a final image at 24h after ingestion. The transit of the radiotracer along the GI tract and the site of capsule disintegration could be seen by concatenating all the planar images into a dynamic display. Figure 3b shows the sequential coronal series of SPECT-MR fused images. The fusion of MR images with SPECT and planar scintigraphic images was seen to enhance the anatomical delineation of the radiotracer within the GI tract.

Figure 4 shows the spatial and temporal distribution of the radiolabelled resin through the GI tract in each individual participant, as indicated by colour-coded boxes. The interpreted results from conventional scintigraphic images and SPECT-MR fusion images were compared.

**Single photon emission computed tomography-magnetic resonance fused images**

Image fusion using the MIPAV analysis software provided an informative display of the position of the tracer in the GI tract. Comparisons of the two sets of results, one from scintigraphic images alone and the other from SPECT-MR fused images, showing the transit of the tracer in the GI tract, are shown in Tables 1 and 2, respectively.

**Discussion**

GI imaging has advanced enormously in the last two decades. Hybrid imaging and image fusion such as SPECT-CT, PET-CT and more recently PET-MR are playing a role in enhancing the diagnostic quality of many investigations. SPECT-MR machines are not yet commercially available; however, in the present study we have explored the feasibility of gamma scintigraphy and MR postimage fusion for whole GI transit imaging. MRI was chosen as the hybrid modality because of the good soft-tissue discrimination and the absence of ionizing radiation.

**Table 1 Comparison of radiologist’s interpretation using SPECT-MR fused images and scintigraphic images alone**

Participant	Time (h)																				
	1.0		2.0		3.0		4.0		5.0		6.0		7.0		8.0		9.0		24.0		
	GS	Fused	GS	Fused	GS	Fused	GS	Fused	GS	Fused	GS	Fused	GS	Fused	GS	Fused	GS	Fused	GS	Fused	
1	ST	ST	SI	SI	SI	SI	SI	SI	SI	SI	SI	ICJ	ICJ	ICJ	AC	AC	AC	TC	TC	EX	EX
2	ST	ST	SI	SI	ICJ	ICJ	ICJ	ICJ	AC	AC	AC	AC	AC	AC	AC	AC	AC	TC	TC	RS	RS
3	ST	ST	AC	AC	TC	TC	TC	RS	RS												
4	ST	ST	ST	ST	ST	ST	ST	SI	ICJ	ICJ	AC	ICJ	AC	AC	AC	AC	AC	AC	AC	RS	RS
5	ST	ST	ICJ	ICJ	ICJ	ICJ	AC	AC	AC	DC	DC										
6	ST	ST	SI	SI	ICJ	AC	AC	AC	AC	AC	AC	AC	AC	AC	TC	TC	DC	DC	RS	RS	
7	ST	ST	SI	SI	SI	SI	ICJ	SI	AC	AC	TC	TC	TC	TC	TC	TC	TC	TC	TC	RS	RS
8	ST	ST	SI	SI	SI	SI	ICJ	ICJ	ICJ	ICJ	ICJ	ICJ	ICJ	ICJ	AC	AC	AC	AC	DC	DC	
9	ST	ST	SI	SI	SI	ICJ	ICJ	ICJ	ICJ	ICJ	ICJ	ICJ	ICJ	AC	AC	AC	TC	TC	RS	RS	
10	ST	ST	SI	SI	ICJ	ICJ	ICJ	ICJ	AC	AC	AC	AC	TC	TC	TC	TC	TC	TC	RS	RS	

AC, ascending colon; DC, descending colon; EX, excreted (no radioactivity detected); fused, fused SPECT and MR image; GS, gamma scintigraphy alone; ICJ, ileocaecal junction; MR, magnetic resonance; RS, rectosigmoid; SI, small intestines; SPECT, single photon emission computed tomography; ST, stomach; TC, transverse colon.

**Table 2 Comparison of regional GI transit time in hours, using fused SPECT-MR images and scintigraphic images alone (n=10)**

Participant	Stomach emptying (less than)		SI		ICJ		AC		TC		DC		RS	
	GS	Fused	GS	Fused	GS	Fused	GS	Fused	GS	Fused	GS	Fused	GS	Fused
1	2	2	2	2	6	6	7	7						
2	2	2	2	2	3	3	5	5	9	9				
3	2	2					2	2	3	3				
4	5	5	5		6	5	8	6						
5	2	2			2	2	4	4						
6	2	2	2	2	3		3		8	8	9	9		
7	2	2	2	2	4		5	5	6	6				
8	2	2	2	2	4	4	8	8						
9	2	2	2	2	4	3	7	7	9	9				
10	2	2	2	2	3	3	5	5	7	7				
Average	2.3	2.3	2.4	2.0	3.9	3.7	5.4	5.4	7.0	7.0	9.0	9.0	N/A	N/A
SD	0.9	0.9	1.1	0.0	1.4	1.4	2.1	1.8	2.3	2.3	N/A	N/A	N/A	N/A

Blank spaces indicate data not available.

AC, ascending colon; DC, descending colon; fused, fused SPECT and MR image; GS, gamma scintigraphy; ICJ, ileocaecal junction; N/A, data not available because of insufficient data points; MR, magnetic resonance; RS, rectosigmoid; SPECT, single photon emission computed tomography; SI, small intestines; TC, transverse colon.

Use of a fiducial marker containing both the MR and scintigraphic contrast agents provided a satisfactory landmark for image fusion. The marker is easily prepared, safe and inexpensive. The commercially available micro-centrifuge tube was used because it is commonly available, small and rigid, as well as convenient to use. From our earlier phantom experiment, 0.18 mg/ml Gd-DTPA was found to produce the optimum signal in T1-weighted images. Precaution needs to be taken by ensuring that the cover of the tube is completely sealed to ensure that there is no leakage of the contrast agents.

Because of logistical constraints, scintigraphy and MRI were performed separately with a time difference of ~7 min in this study. In some hospitals in which the nuclear medicine and MRI departments are located far apart, patients should be advised to use a wheel chair or trolley bed during transfer to minimize any effects of physical exertion or organ movement.

One important feature of the MIPAV software is its ability to perform image registration and superimposition of DICOM images from various modalities. To fuse three-dimensional volumetric data, a minimum of four

landmarks on both sets of data are required. After image fusion, the blending ratio could be adjusted according to user’s preference to change the weightage of SPECT and MRI data. A number of image software platforms are available for this purpose; however, the landmark least squares algorithm is recommended for rigid transformation.

When compared with scintigraphic images alone, SPECT-MR postfusion images with superimposed sequential planar scintigraphic images combine both morphologic and functional data, providing a more accurate localization of the distribution of the tracer in GI motility examinations. In general, on comparing the two techniques no major differences were seen in the overall transit time assessment, except for some discrepancies in the defined regions of the small intestine, ileocaecal junction and ascending colon. Although this image fusion required patients to undergo an additional MRI and SPECT, our preliminary assessment showed that it did help to reduce the interpretation time by ~15 min on average as the location of activity could be better defined with planar SPECT-MR image fusion. However, further work is required to quantify the time saved against the added

cost of and time taken to perform MRI and SPECT. It would also be possible to overlay planar anterior and posterior images onto coronal MR images as a more rapid alternative to full-SPECT acquisition.

Following the initial promising results from this study, we would advocate that this method of display and interpretation offers improved visualization of GI transit in both clinical and research imaging studies. The same method can also be used in other radiopharmaceutical examinations such as in examinations using  $^{111}\text{In}$ -labelled resin for whole GI transit investigation.

## Conclusion

Fusion of sequential scintigraphic and MR images improves the assessment of segmental GI motility by facilitating accurate delineation of the tracer anatomically, as compared with the traditional method of using scintigraphic images alone. The added anatomical data from MRI aided the interpretation of the localization of the tracer in the GI tract and reduced the diagnostic interpretation time.

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## Conflicts of interest

There are no conflicts of interest.

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