

# Lipids infused into the jejunum accelerate small intestinal transit but delay ileocolonic transit of solids and liquids

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## Abstract

**Background**—Various nutrients are known to alter small intestinal motility patterns although their effect on transit of fluids and solids in man is not clear.

**Aims**—To determine small intestinal transit of solids and liquids during perfusion with lipids, protein, and non-energy solutions.

**Methods**—Twenty eight healthy volunteers received a jejunal infusion (1 ml/minute for 30 minutes) of one of four solutions: a lipid or a protein solution (4.18 J/ml), a non-absorbable electrolyte solution containing polyethylene glycol, or 0.9% sodium chloride. As solid phase marker 1 g of amberlite resin pellets labelled with  $^{111}\text{InCl}_3$  was added;  $^{99\text{m}}\text{Tc}$  DTPA was used as a fluid phase marker. Images were obtained on a gamma camera at 10 minute intervals for four hours or until all radiolabel was detected in the colon.

**Results**—Intestinal transit of solids and liquids from the duodenojejunal junction to the caecum was simultaneous, and independent of the energy content of the solution infused. Lipid infusion accelerated transit through the small intestine but delayed transport of chyme along the ileocolonic junction. After protein small intestinal transit was slowest; ileocolonic transit on the other hand was fastest with protein. Transit of the non-energy solutions was in between that of the nutrient solutions.

**Conclusions**—Transit times through the small intestine and the ileocolonic junction were influenced by the luminal contents. In the small intestine fat induced significantly faster transit compared with proteins, but delayed ileocolonic transit. Once in the small intestine, solids and liquids transit the small bowel together, independent of the luminal content.

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Keywords: small intestine; ileocolonic junction; transit; nutrients; lipids; proteins

The differential transit of solids and liquids along the gastrointestinal tract is best described at the level of the stomach.<sup>1</sup> Fluids are separated from solids at the antroduodenal junction and are emptied into the duodenum in an exponential fashion. Solids are initially retained in the stomach, triturated, and then

emptied in a linear fashion. Various nutrients and non-energy solutions in the gastric and intestinal lumen can modulate gastric emptying, thus delaying or accelerating gastric emptying of liquids and solids.<sup>1</sup> In particular, fat in the gastrointestinal lumen is known to regulate gut motility in a potent manner, acting to inhibit gastric emptying<sup>2</sup> and duodenal transit.<sup>3</sup>

In the small intestine transit of chyme is discontinuous and it has been suggested that periods of slow transit alternate with bursts of rapid flow.<sup>4</sup> Results of studies investigating differential transit of liquids and solids along the small bowel are controversial.<sup>5-7</sup> Observations in dogs fed a mixed meal suggested that liquids moved along the small intestine faster than solids.<sup>5</sup> In a study in man similar duodenocaecal transit times were calculated for solids and liquids, when different rates of gastric emptying were corrected for mathematically.<sup>6</sup> However, when a carbohydrate solution was infused into the distal small bowel together with scintigraphic markers for the liquid and the solid phase, the ileum was able to discriminate liquids from solids while the ileocolonic junction was not.<sup>7</sup> Furthermore, several studies using liquid markers suggested that ileal emptying occurs in a linear fashion,<sup>6,8</sup> while others suggested bolus transfer of liquids<sup>7,9</sup> and also of solids<sup>7,10</sup> from the small bowel to the colon.

Furthermore, the composition of chyme in the small intestine had an effect on transit<sup>11,12</sup>; an increase in unabsorbable carbohydrates accelerated small intestinal transit.<sup>11</sup> Infusion of lipids into the ileum delayed small intestinal transit via a mechanism called the "ileal break" while jejunal lipid infusion had no delaying effect.<sup>12</sup> The role nutrients play in the upper small intestine in regulating the differential transit of the solid and liquid phase along the small intestine has not yet been studied in detail. In the present study we quantified small intestinal transit of liquids and solids and transit across the ileocolonic junction after jejunal infusion of small amounts of nutrients and non-energy solutions. Both physical phases were introduced into the jejunum simultaneously, thus avoiding different gastric emptying rates for solids and liquids, and subsequently were quantified independently using scintigraphy. As markers for solid residue we used indium-111 labelled resin pellets with an average diameter of 1 mm. Liquid transit was assessed with technetium-99m which was mixed into either a nutrient solution (lipid, protein) or a non-energy electrolyte solution.

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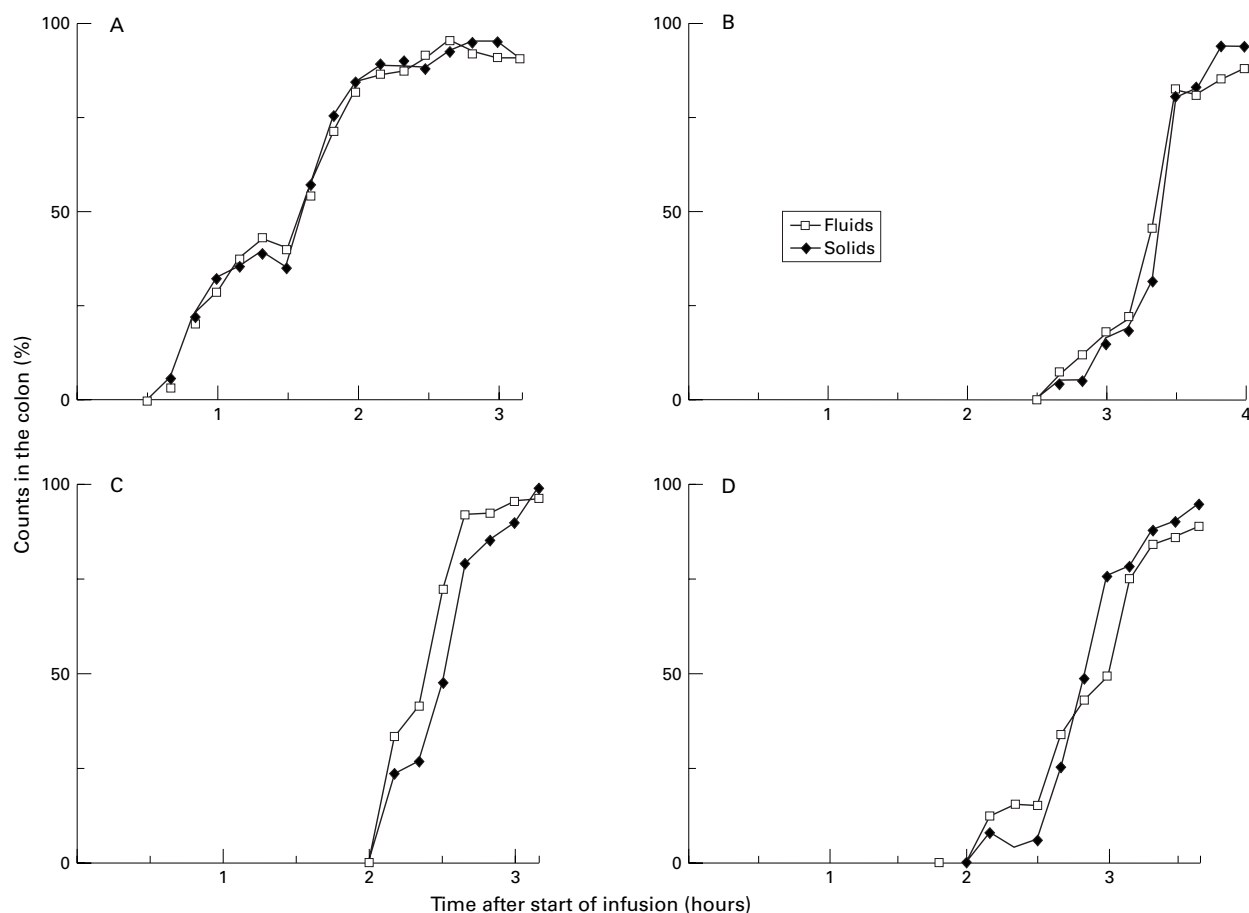


Figure 1 Individual examples of transit of solid and liquid radiolabel from the small intestine into the colon. (A) Lipid, (B) protein, (C) saline, and (D) poorly absorbable solution.

## Methods

### EXPERIMENTAL SUBJECTS

Studies were carried out in 28 healthy volunteers, aged 18 to 30 years (21 men, seven women) who were recruited by public advertisement. None had a history of gastrointestinal disease or abdominal surgery other than appendectomy. Subjects did not take any medication known to alter gastrointestinal motility. Written consent was obtained for the protocol which had been previously approved by the ethics committee of the Medical Faculty at the University of Vienna.

### EXPERIMENTAL PROCEDURE

The 28 volunteers were randomly allocated to four groups ( $n=7$  in each) to receive an infusion of either lipid, protein (albumin), normal saline, or a poorly absorbable electrolyte solution containing polyethylene glycol 4000 (PEG), into the distal duodenum. Fluids were labelled with 1.5 mCi  $^{99m}\text{Tc}$ -diethylenetriaminepentaacetic acid (DTPA) to monitor their movement along the small intestine scintigraphically. As a solid phase marker, 1 g Amberlite 120 IRP cation exchange resin pellets (Sigma Chemical Co., St Louis, USA) (diameter 0.5–1.8 mm, density 1.2), radiolabelled with 0.1 mCi  $^{111}\text{InCl}_3$ , were used.<sup>13</sup>

After an overnight fast, subjects swallowed a single lumen polyvinyl tube (outer diameter 1.5 mm) with openings at the tip and 1, 2, 3, and 4 cm proximally to the tip of the tube. The tube was positioned under fluoroscopy so that the tip was at the ligament of Treitz. Twenty minutes after the tube was in place the solid phase markers were injected into the tube and then rinsed down the tube with the infused solutions. Infusion rates were 1 ml/min for 30 minutes, corresponding to an energy delivery rate of 1 kcal (4.18 J) per minute for both protein and lipid solutions. Volunteers received 30 ml of either a 10% lipid emulsion (Intralipid, Kabi Pharmacia, Uppsala, Sweden: 17% fractionated soya oil, 1% fractionated ovolcithin, 2% glycerol; 350 mmol/l), a 10% solution of albumin (Behring Institut, Vienna, Austria; 390 mmol/l), 0.9% saline, or Golytely, a poorly absorbable, iso-osmotic, isotonic electrolyte solution<sup>14</sup> containing 59 g PEG 4000, 125 mEq/l sodium, 10 mEq/l potassium, 35 mEq/l chloride, 80 mEq/l sulphate, and 20 mEq/l bicarbonate (30 mmol/l). After 30 minutes the infusion was terminated and the tube was gently removed.

### GAMMA CAMERA IMAGING

Simultaneous with the infusion of fluids, gamma camera imaging was started in order to monitor the movement of radiolabel along the small intestine. Scans were taken every 10 minutes for

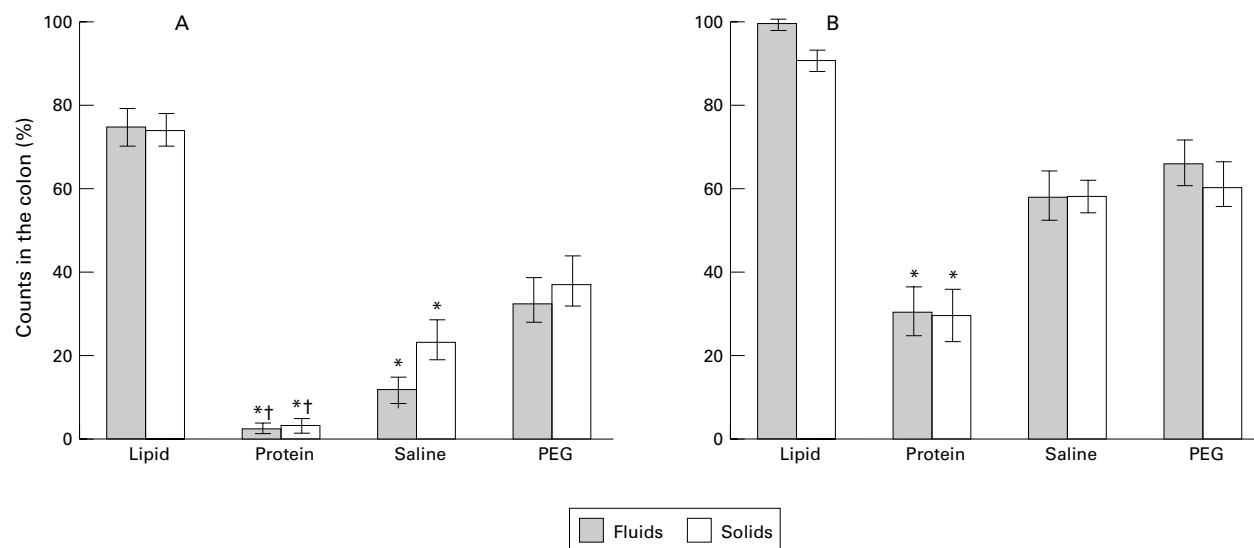


Figure 2 Percentage of counts in the colon at (A) two and (B) three hours after start of isotope infusion. \*Significant versus lipid; †significant versus PEG.

four hours or until all radiolabel had entered the colon. The gamma camera (Digital Gamma camera GCA-901A, Toshiba Corp., Japan) had a large field of view and a medium energy parallel hole collimator (matrix size: 128×128).  $^{99m}\text{Tc}$  counts were determined at a 140 keV  $\pm$  20% window,  $^{111}\text{In}$  counts at a 247 keV  $\pm$  20% window. Images were obtained at 10 minute intervals with a gamma camera in an anterior and posterior position. Acquisition time was one minute. Data from the scans were stored on an on line computer (Toshiba, Japan) for later analysis. A marker was taped over the xiphisternum to facilitate alignment of serial images.

A variable region of interest (ROI) program quantified the radiolabels that had entered the colon. Counts were decay corrected to time zero and corrected for Compton scatter from the indium into the technetium window. The geometric mean of the anterior and posterior images was calculated, thus minimising errors due to movement of counts in the anteroposterior direction. Counts in the colon were expressed as percentage of total abdominal counts.

#### DATA ANALYSIS AND STATISTICS

For transit measurement the beginning of fluid infusion was considered as time 0 minutes.

Parameters of small intestinal transit of liquids and solids were: (a) initial transit—that is, the time of onset of small intestinal emptying into the colon; and (b) the percentage of technetium and indium counts that had left the small intestine at hours 2 and 3.

Ileocaecal transit was calculated as the time from the start of colonic filling until the time at which 50% of  $^{99m}\text{Tc}$  and  $^{111}\text{In}$  counts had entered the colon (T50%). Colonic filling was considered to be a “bolus” filling when more than 10% of total counts moved into the colon within 10 minutes, as defined in previous studies.<sup>7 10 15</sup> “Linear movement” was defined as ileocaecal transfer of counts at a rate below 10% of counts during a 10 minute period.

Parameters of small intestinal and ileocaecal transit of both solids and fluids were compared by the Student's *t* test for paired and unpaired data, respectively, and the Wilcoxon rank sum test for parametric and non-parametric parameters. A *p* value of less than 0.05 was considered significant. Results are expressed as mean (SEM). Bonferroni correction was applied for multiple comparisons.

#### Results

During the 30 minute infusion period indium and technetium distributed uniformly over the small intestine. After the end of infusion radiolabels moved quickly to the distal small intestine, collected there, and then moved in bulk into the terminal ileum.

#### SMALL INTESTINAL TRANSIT

Examples of the transit of solids and liquids from the small intestine into the colon (colonic filling curves) are given in fig 1.

#### Transport of fluids and solids along the small intestine

$^{99m}\text{Tc}$  and  $^{111}\text{In}$  moved along the small intestine together, independent of the composition of the solution that was infused (figs 1 and 2). The start of small intestinal emptying of solids and liquids was always simultaneous; thereafter solids and liquids always moved together in all four infusion groups. The percentage of counts that had entered the colon after two and three hours (fig 2) was also similar for both isotopes ( $p > 0.05$ ).

Subsequently, if not stated otherwise, the results of fluid transit are given only.

#### Small intestinal transit of lipids versus proteins and non-energy solutions

Table 1 shows the time from the start of the infusion until when the first counts could be localised in the caecum: this initial transit was shortest after lipids ( $p < 0.001$  versus protein and  $p < 0.05$  versus saline) and longest after protein ( $p < 0.01$  versus poorly absorbable solution).

Table 1 Start of small intestinal emptying

	Minutes after start of infusion
Lipid	50.0 (8.2)
Protein	175.7 (15.5)*†
Saline	122.8 (1.8)*
Poorly absorbable solution	95.7 (20.6)

Results are expressed as mean (SEM). Small intestinal transit is expressed as the time after infusion when first counts arrived in the caecum; the head of the technetium and indium counts always moved together and arrived in the colon simultaneously. \*Significant *v* lipid; †significant *v* the poorly absorbable solution.

Figure 2 shows the counts that had entered the colon two and three hours after the start of the infusion. At hour 2, significantly more counts had entered the colon after lipid infusion compared with all other solutions ( $p < 0.001$  versus protein,  $p < 0.001$  versus saline,  $p < 0.05$  versus PEG), and counts were lowest after proteins (NS versus saline,  $p < 0.05$  versus PEG). At hour 3, essentially all counts had entered the colon after lipid infusion (98 (2)%) whereas only 30 (13)% of counts were in the colon when proteins were infused ( $p < 0.01$ ). For the two non-energy solutions values were in between those of the two nutrient solutions (fig 2).

#### ILEOCAECAL TRANSIT

Movement of both fluids and solids into the caecum occurred largely as a series of boluses (see fig 1). The number of boluses (between one and three boluses, mean over all groups: 2.2) and duration of boluses (data not shown) was similar for all solutions.

#### Transport of fluids and solids through the ileocaecal junction

Within all infusion groups T50% ileocaecal transit—that is, the time from the start of colonic filling until when 50% of counts had entered the colon, were similar for  $^{99m}\text{Tc}$  and  $^{111}\text{In}$  (table 2). Furthermore, number and duration of boluses did not differ between the isotopes (data not shown).

#### Ileocaecal transit of lipids versus proteins and non-energy solutions

Table 2 shows T50% ileocaecal transit: transit of lipids was slower compared with protein ( $p < 0.01$ ) and saline ( $p < 0.01$ ); the difference with respect to PEG was not significant ( $p > 0.05$ ). Protein moved fastest along the ileocaecal region ( $p < 0.05$  versus PEG, NS versus saline).

Table 2 Duration of colonic filling

	T50% (min)	
	Fluids	Solids
Lipid	128.3 (7.0)	123.3 (5.4)
Protein	66.7 (12.0)*†	66.7 (18.6)*†
Saline	97.1 (6.8)*	94.3 (6.9)*
Poorly absorbable solution	115.7 (11.1)	115.7 (11.1)

Results are expressed as mean (SEM). Ileocolonic transit expressed as T50%—that is, the time from the start of ileal emptying to the time when 50% of counts had entered the colon.

\*Significant *v* lipid; †significant *v* the poorly absorbable solution.

## Discussion

Transit of solids and liquids from the duodenojejunal junction to the caecum was simultaneous, independent of the energy content of the solution infused. However, small intestinal transit and ileocolonic transit were affected differently by the solutions used in our study.

All the infusions flushed the leading edges of both the solid and the liquid phase label together through the small intestine and into the caecum, and after two and three hours the difference between solid and liquid radiolabel that had emptied from the small intestine was minimal. Similarly, in a study quantifying small intestinal transit of solid and liquid meal components equal transit rates of both physical phases were described after correcting for different gastric emptying of solids and liquids.<sup>6</sup> However, in this study the gamma camera was only positioned in an anterior position. Thus errors in quantitating radioactivity due to movement of counts in the antero-posterior dimension<sup>16</sup> could not be corrected for. In fasting subjects, transit of different solid materials was independent of size and weight once they were in the small intestine.<sup>17</sup> Other data suggesting that in the ileum solids and liquids again might be separated when subjects were fasting,<sup>7</sup> cannot be supported by our present results. We presume that in our study the small amounts of nutrients (0.13 MJ) we have infused are very unlikely to have induced a fed pattern. We did not record motor activity as intubation of the small intestine is known to alter transit<sup>18</sup> and thus we avoided prolonged tube placement. However, there is no clear answer in the literature as to whether the post-pyloric tube might have influenced our results.

The size of the resin pellets we used as markers for solids was well in the range of the particulate matter that leaves the stomach after a meal: indigestible solids, mainly fibres from vegetables and fluids, are triturated in the stomach and enter the small intestine as relative small particles under 2 mm in diameter.<sup>19,20</sup> The infusion rate of 1 kcal (4.18 J) per minute was chosen to be in the range reported for gastric emptying of energy loads after a meal.<sup>21</sup> We decided to infuse only a small bolus into the proximal intestine; lack of discrimination of solids and liquids during continuous infusion of larger volume loads could have been due to flushing both phases together through the small bowel rather than due to the motor effect of the small intestine.

In order to determine the effect of luminal contents on small bowel transit we bypassed the stomach and duodenum, thus also avoiding digestion of the tested nutrients before they entered the test segment. Although the energy content of our nutrient solution was low we found a pronounced differential effect on small intestinal transit—from the duodenojejunal junction to the caecum—and ileocolonic transit. When various nutrient meals were infused into the canine jejunum, characteristic contraction patterns were produced depending on the nutritive content of the meal.<sup>22,23</sup> Transit rates of nutrient meals were slower compared with a non-energy control meal.<sup>22</sup> In our present study

small intestinal transit of solids and liquids was fastest after infusion of lipids; transit was slower after infusion of the non-energy PEG solution, and even slower after normal saline and protein infusion. On the other hand, ileocolonic transit was slowest after fat infusion. Fat in the gastrointestinal lumen is known to delay gastric emptying<sup>2</sup> and duodenal transit.<sup>3</sup> Further down the gastrointestinal tract, in the ileum, fat again exerts an inhibitory effect on gastric<sup>24</sup> and jejunal motility<sup>25</sup> via a mechanism called the “ileal brake”. Current knowledge about the localisation of mucosal fat absorption in the small intestine is poor. However when the distal half of the small intestine was removed in dogs, distal fat recovery increased from a physiologically malabsorbed 10% of ingested lipids to up to 90%.<sup>26</sup> Removing the proximal half of the small intestine had only a small effect on fat absorption, since only 24% of ingested lipids were recovered distally.<sup>26</sup> If these observations are taken to suggest a bigger role of the distal small bowel in lipid absorption, the effect of fat on transit patterns in our study can be interpreted as allowing more time for the distal small bowel to absorb luminal fat.

The fate of proteins, once they reach the jejunum, is also not clear and the amount that were hydrolysed in our experiment cannot be quantified. However, the small amount of albumin we infused into the jejunum significantly delayed small intestinal transit compared with the other solutions tested and significantly accelerated ileocolonic transit. This effect of proteins on small bowel transit might argue for a protein brake on the proximal small intestine to allow for hydrolysis of proteins and peptides. Further studies are needed to confirm this hypothesis.

As non-energy control solutions we used a non-absorbable solution containing PEG and an easily absorbable saline solution. Although differences in intestinal transit between the two solutions did not reach statistical significance, small intestinal transit tended to be faster after PEG and ileocolonic transit tended to be delayed. This may suggest a volume effect on transit, which is supported by others.<sup>27–28</sup>

Direct application of radiolabel into the small bowel allowed us to avoid variable input of radiolabelled solutions into the small intestine due to gastric emptying. We infused only a small bolus of isotopes that, at the end of the infusion, quickly collected in the distal small intestine. Isotopes seemed to be stored there for a period of time before being emptied into the colon in one to three bolus movements. This supports the concept of the distal small intestine being a region of storage or an “intestinal stomach”.<sup>7, 18, 29, 30</sup>

Small intestinal flow during fasting is largely intermittent and peaks of flow coincide with the passage of the activity front of the migrating motor complex.<sup>31</sup> On the other hand, half of the intestinal flow in the fasting period is unassociated with the activity front.<sup>31</sup> We did not record motor activity in our study and standardised the infusion to begin 20 minutes after the tip of the tube had reached its position at the

ligament of Treitz. Further studies are required in order to clarify the effect of the different phases of the migrating motor complex on small intestinal transit of small nutrient boluses.

We did not encounter problems of discrimination between the distal ileum and the caecum in the scintigraphic images. With a fixed marker at the abdominal wall we aligned images at the end of the study, when all radioactivity was in the colonic region, with each previous frame. Overlap between the small intestine and the colon was also no problem as isotopes did not spread out in the whole small intestine for a longer period.

Infusion of specific single nutrients into the jejunum does not simulate a physiological process. However, our technique allows quantification of the influence of various intraluminal contents on intestinal transit. We are confident that this and further studies will help in the understanding of the differential effect of meal composition<sup>11, 12</sup> and composition of enteral nutrient formulas on small intestinal physiology.

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