Pressure forces in the TIM-agc, an Advanced Gastric Compartment that simulates shape and motility of the stomach.

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INTRODUCTION

The Advanced Gastric Compartment (TIM-agc) is a new gastric compartment of the TNO gastro Intestinal Model (TIM-1). This compartment is designed to study the behavior of food and dosage forms with simulation of shape and motility of the human stomach.

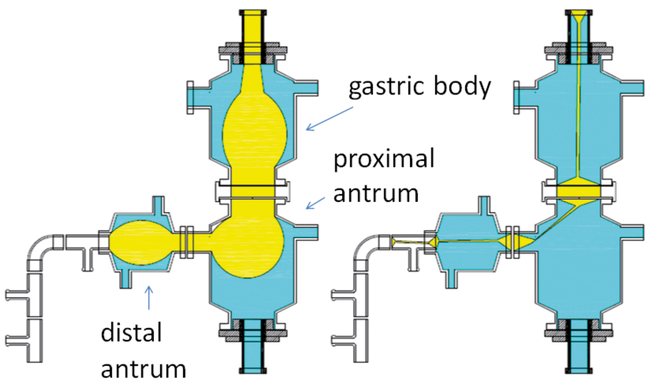

Figure 1. *Schematic representation of the Advanced Gastric Compartment, TIM-agc, filled (left) and empty (right).*

The TIM-agc consists of three parts that can be contracted independently (Fig. 1):

- The upper part presents the gastric body with a flexible wall that gradually contracts to simulate reduction of gastric volume during emptying.
- The antrum consists of two parts that represent the proximal and distal antrum, respectively.
- Contractions of the antrum sections are synchronized to simulate antral waves. A valve is synchronized with an antral wave to simulate the opening of the pyloric sphincter during gastric emptying.
- Motility patterns as well as gastric emptying, secretion of digestive fluids and pH profiles are dictated by a predetermined protocol that describes a specific condition (e.g. fed or fasting) in time.

The Smartpill® technology (Fig. 2) is a device that is used to study gastro-intestinal motility. After swallowing, the pill transmits *in situ* data on pressure, pH and temperature to a portable receiver while traveling through the gastro-intestinal tract. Data are imported into a computer for further analysis.

Figure 3. *Smartpill ® technology*

OBJECTIVE

Aim of this study was to compare the gastric pressure forces in the TIM-agc with those observed *in vivo* with the use of the Smartpill® technology.

METHODS

- The TIM-agc was programmed to simulate a basic motility pattern and a pattern simulating a housekeeper wave.

During the basic motility pattern, the gastric content is pushed gradually into the antral part 3 times per minute to simulate an antral wave. After that, the content is pushed back from the antrum part into the bottom part to simulated retro-pulsion. Both the bottom part and the antrum part are not fully squeezed during this pattern. The housekeeper wave is simulated by a pattern that fully squeezes all three part in consecutive order starting with the body part. This forces the compartment to empty completely.

- The Smartpill® was introduced into the TIM-agc to measure the actual pressure as applied on the pill.
- *In vivo* gastric pressure profiles were obtained with a Smartpill® in healthy persons. Pressure peaks were analyzed on height and shape.
- The programmed pressure peaks produced by the TIM-agc were compared with those obtained *in vivo*.

RESULTS

- Directly after introduction into the TIM-agc, the Smartpill® settled in the proximal antrum, the bottom of the compartment. During simulation of the digestive phase with the basic motility pattern, the pill stayed at this position.

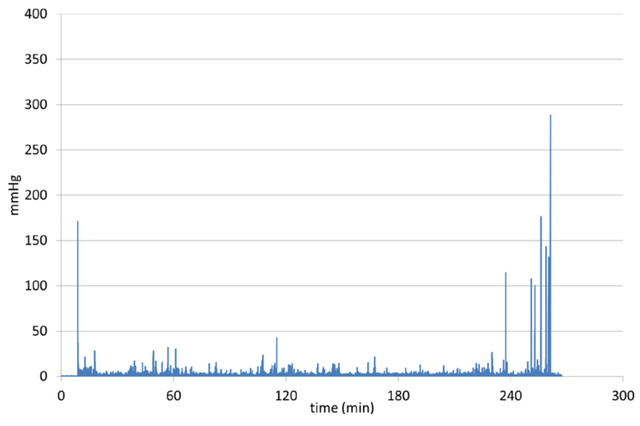

Figure 5. *Example of an in vivo gastric pressure profile measured with a Smartpill®.*

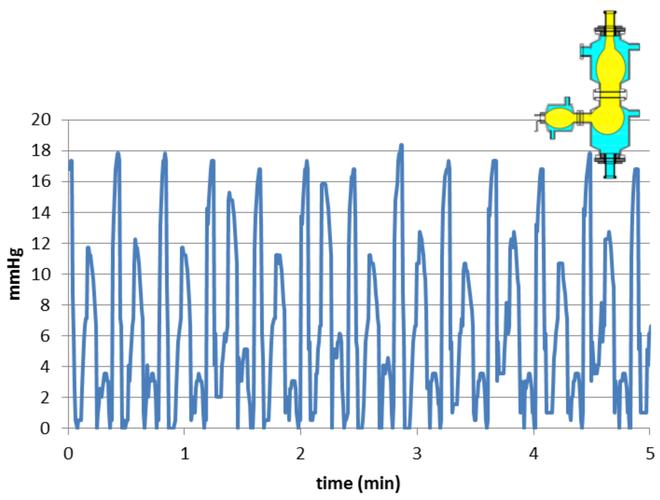

Figure 3. *In vitro gastric pressure profile measured in the TIM-agc during a basic motility pattern.*

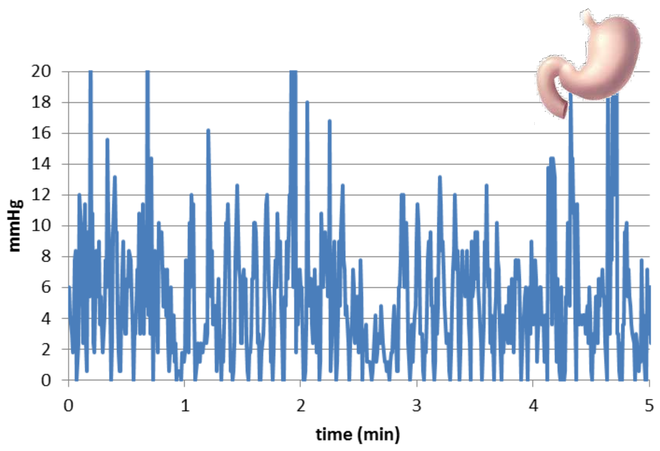

Figure 4. *In vivo gastric pressure profile measured with a Smartpill® during the digestive phase.*

- The pressure forces measured in the TIM-agc (Fig. 3) were similar to those observed *in vivo* (Fig. 4).
- During simulation of the housekeeper wave, pressure peaks of 100-200 mmHg were measured caused by squeezing of the flexible wall. These pressures are in the same range as observed in humans (Fig. 5).

CONCLUSION

These experiments indicate that the advanced gastric compartment (TIM-agc) allows realistic *in vitro* simulation of *in vivo* pressure profiles during gastric residence of a dosage form.

ACKNOWLEDGEMENTS

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