Intragastric Volume Changes after Intake of a High-Caloric, High-Fat Breakfast in Healthy Human Subjects Investigated by MRI

M. Koziolek, M. Grimm, G. Garbacz, J-P. Kuehn, W. Weitschies
University of Greifswald

Purpose
The effect of food on drug release and absorption is a challenging biopharmaceutical problem. Meal ingestion can influence drug plasma levels by changing one or more pharmacokinetic parameters of an API and may affect both, therapy efficacy and safety. Therefore, clinical studies on food effects are demanded by the authorities. For these studies, the FDA recommends a high-calorie (800-1000 kcal) and high-fat (> 50% calories from fat) standard breakfast. According to the respective FDA guidance, the dosage form tested is ingested together with a glass of water (240 mL) 30 min after beginning of meal intake.

Methods
In the present study, 12 healthy human subjects (18-50 years old) received the FDA standard breakfast after an overnight fast (> 8 h). Magnetic resonance imaging (MRI) performed with a commercially available 1.5 T MRI scanner was used to visualize and determine the gastric content volume (GCV) over a period of more than 6 h. Moreover, the hypothesis of a stomach road (“Magenstrasse”) allowing the fast emptying of water from the fed stomach was investigated by T2-weighed sequences. Therefore, subjects drank 240 mL water representing the water volume ingested with drug intake. Data were analyzed using OsiriX Imaging Software 3.9.

Results
The results revealed that the initial GCV after meal intake was higher than the sum of total meal volume and fasting GCV owing to salivary and gastric secretions. Within time of investigation, GCV decreased constantly. The return into fasted state was not reached within at least 4 h. Regarding the stomach road, the water ingested directly flew into the antrum and subsequently, was rapidly emptied.

Conclusion
We revealed that the overall gastric emptying proceeded with a nearly constant rate. Moreover, none of the subjects was fasted within 4 h after ingestion of the standard breakfast recommended by the FDA. This may have consequences for the administration of drugs that are showing a reduced bioavailability after ingestion with food, as the common intake advice is 1 h before or 2 h after a meal.