

# An MRI-Guided HIFU-Triggered Wax-Coated Capsule for Supertargeted Drug Release

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## Introduction

### Background

- In many diseases (e.g. non-metastatic solid gastrointestinal (GI) tumors, Crohn's disease) **current treatment strategies** involve **systemic** administration of drugs.
- Spatially and temporally controlled drug release** could reduce systemic **side effects** while simultaneously increasing the **drug concentration** at the required site.
- Currently no **galenic formulations** are known which are stable in GI fluids and allow for **externally controlled and monitored drug release** in the GI tract.

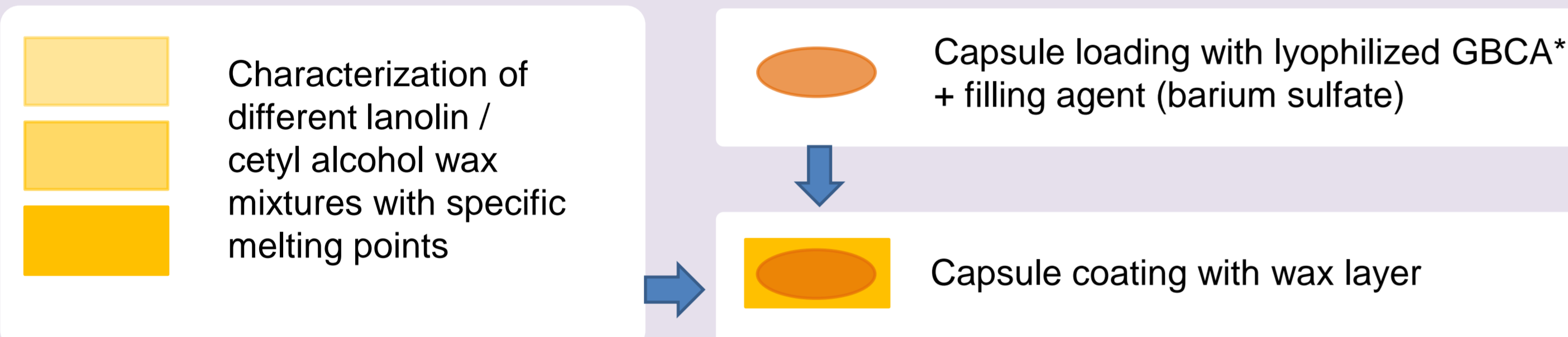
### Aim

To develop a supertargeted drug delivery system (DDS) for personalized non-invasive therapy

Property	Concept	Method
Stimuli-responsive DDS	Thermoresponsive system	Wax-coated capsule
Externally controlled trigger of drug release	Focused rise of temperature	High-intensity focused ultrasound (HIFU)
External monitoring of drug release	Imaging of T1-hyperintense signal due to drug release	Magnetic resonance imaging (MRI) + Gadolinium-based contrast agent (GBCA)

## Methods

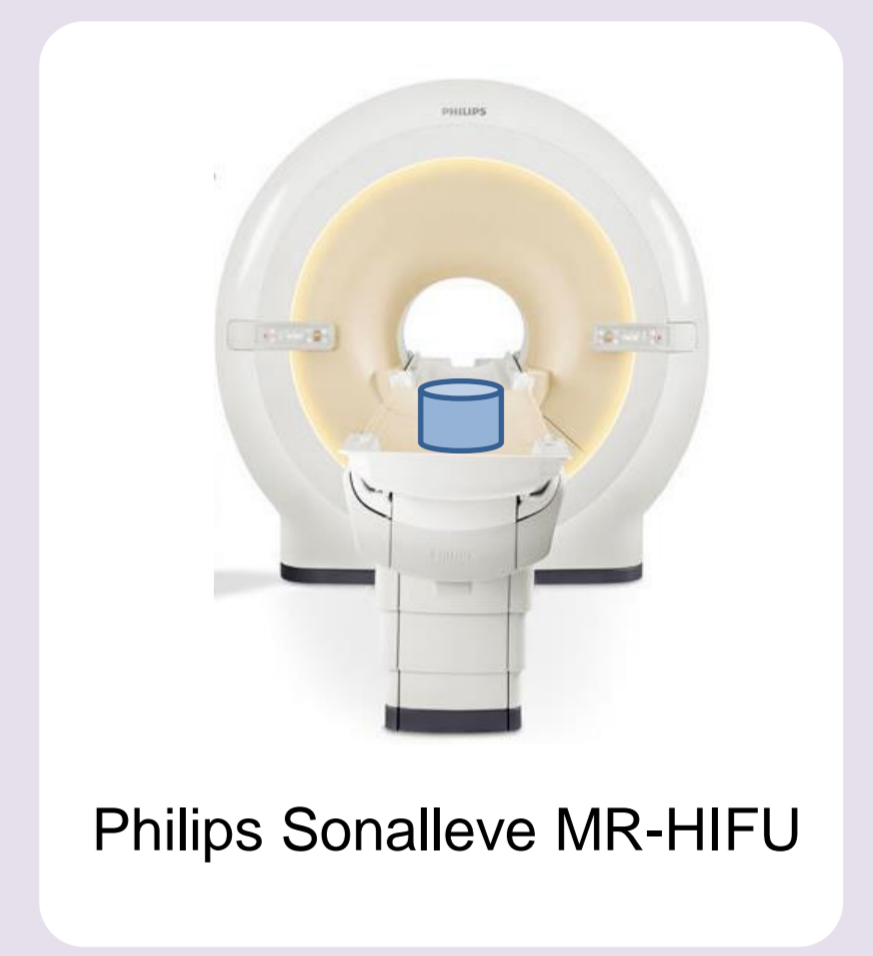
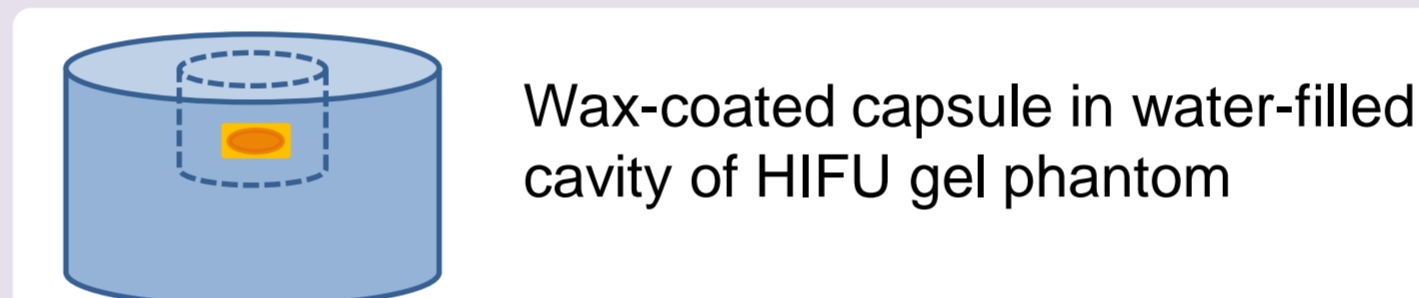
### Development of wax-coated capsule



\* 0.2 mL gadoteric acid meglumine 0.5 mmol/mL, Dotarem®

### MRI-guided HIFU-triggered drug release

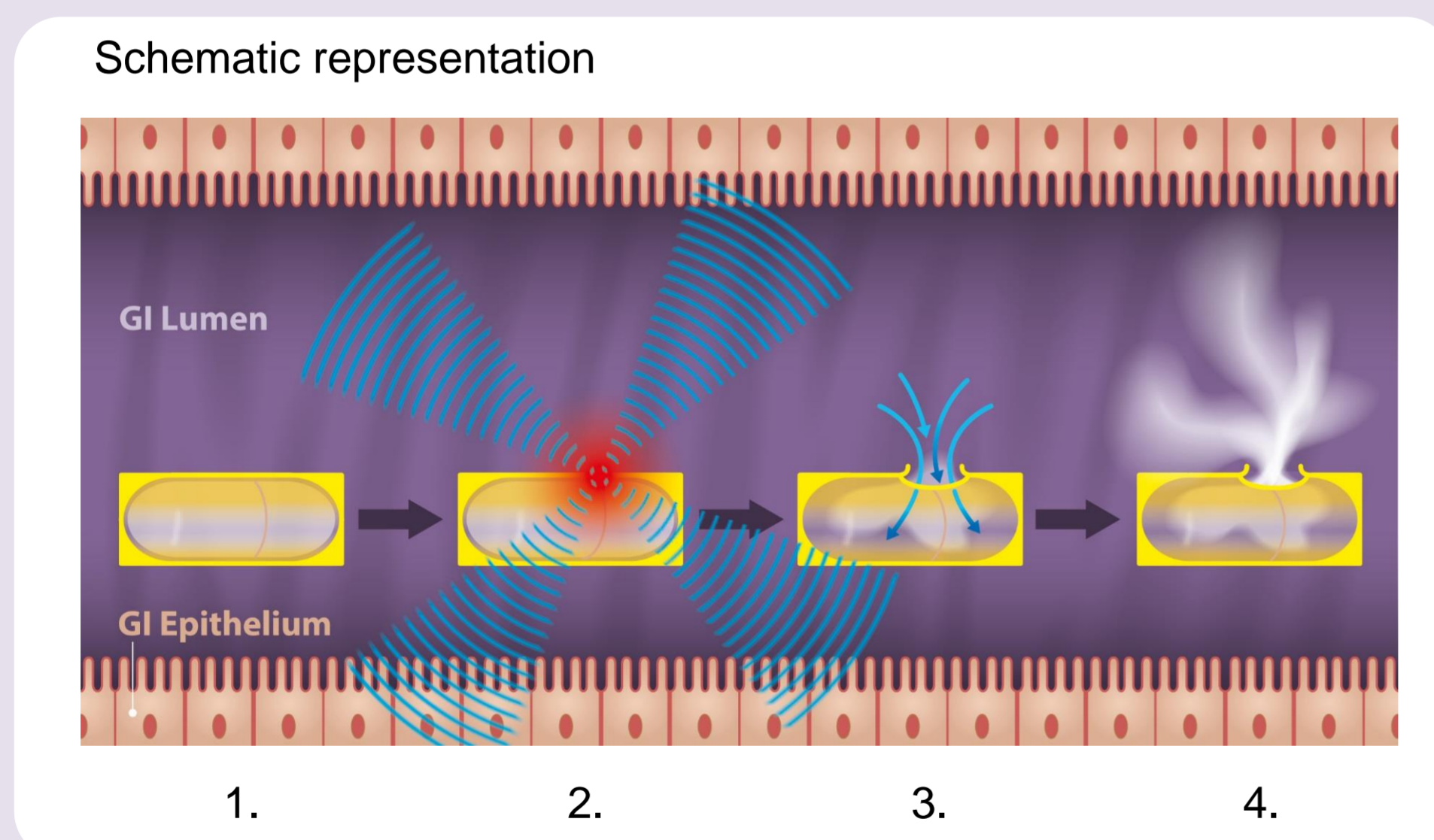
- MRI-guided HIFU is clinically validated for non-invasive thermal ablation of breast and prostate cancer.
- Externally triggered highly localized temperature increase
- Applied HIFU pulse to melt a hole into the wax coating of the capsule: 200 W, 1195 kHz



## Results / Discussion

### Development of wax-coated capsule

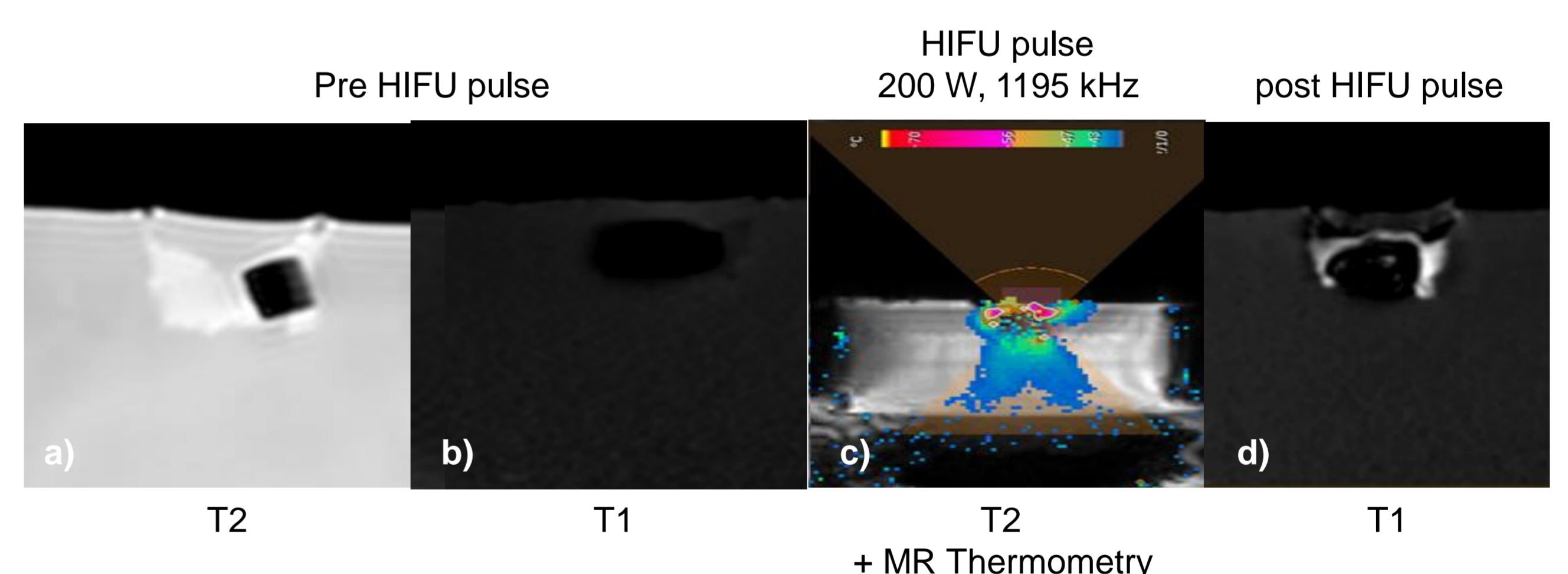
- Most suitable wax mixture: lanolin / cetyl alcohol 1:1 (m:m)
  - ✓ mp = 43°C (stable at body temperature)
  - ✓ Highly resistant to simulated gastric and intestinal fluid



- The wax-coated capsule is **resistant to GI-fluids at body temperature** → no premature release
- Melting of a focused hole into the wax coating** by an external **HIFU pulse**: 200 W, 1195 kHz
- Water influx** from the GI lumen into the capsule.
- Dissolution and **outflux of GBCA** through the hole in the coating.

### MRI-guided HIFU-triggered drug release

Proof of concept for a novel application of MRI-guided HIFU for supertargeted drug release:



- Localization of the capsule** due to its T2-hypointensity on T2-weighted MR images.
- Lack of a T1-hyperintense signal prior to the HIFU pulse shows that **non-hydrated lyophilized GBCA** is not T1-hyperintense.
- Application of a **HIFU pulse** guided by T2-weighted MRI and temperature monitoring using MR thermometry.
- The hyperintense T1 signal on T1-weighted MR images proves **outflux and hydration of GBCA** after the HIFU pulse.

## Conclusion

- Development of a **novel thermoresponsive wax coated capsule**
  - Highly resistant to simulated gastric and intestinal fluids
  - Stable at body temperature
  - Releasing its cargo at  $T \geq 43^\circ\text{C}$ , promising non-invasive HIFU application
- Proof of concept for a **novel application of MRI-guided HIFU** for supertargeted drug release

## References

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