Structural and functional characterisation of 3D printed pharmaceutical dosage forms by means of high-resolution X-ray CT

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3D Printing in Pharmaceutical Technology

3D printing technology is one of the most promising advances in modern pharmaceutical technology. **Fabrication of dosage forms with bespoke designs** is now made possible and **opens new highways towards personalisation of medication** with potential to revolutionize pharmacotherapy. Applications include fabrication of **polypills** for patients receiving a range of medications, **on-site production** (e.g. hospitals) of dosage forms **tailored to patients' needs** and **cost-effective** production of sophisticated designs in the productions line.

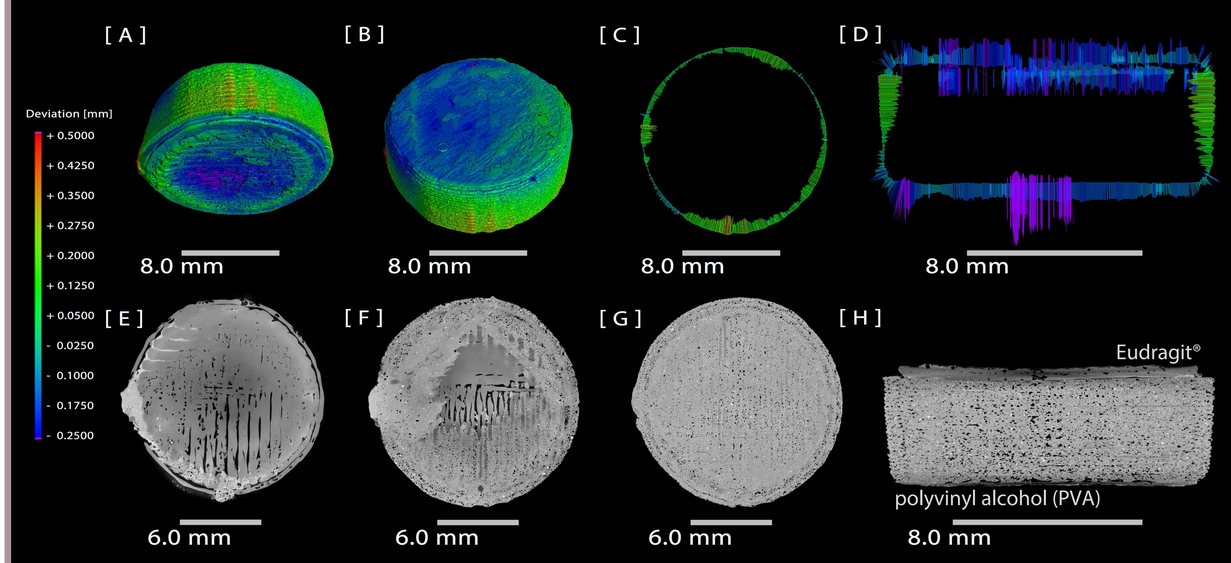
Quality Control, Structural and Functional Characterization

3D printing inherently produces objects that deviate from the ideal designed template for reasons specific to each 3D printing method. **Microfocus X-ray Computed Tomography**, µCT, is a high resolution non-destructive volume imaging technique that amongst others **allows for**:

- ⌘ ***defect & porosity analysis*** (*µCT imaging* ► *Feature extraction* ► *Quantification*)
- ⌘ ***dimensional accuracy analysis*** (µCT imaging ► Surface extraction ► Comparison with CAD ► Quantification)
- ⌘ **functional characterisation** (*in situ* or *ex situ* time-resolved µCT imaging).

Case study 1 | Dimensional accuracy analysis

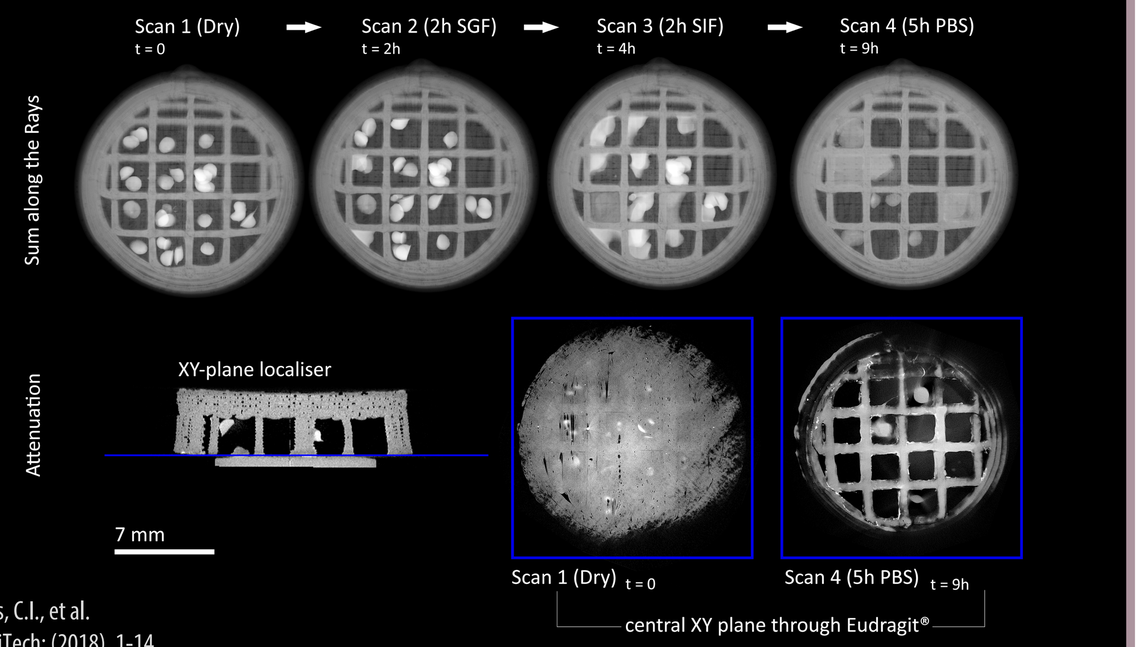
Nominal (CAD) *vs* Actual (printed product) Comparison



Gioumouxouzis, C.I., et al. Eur J Pharm Sci.120 (2018): 40-52.

Functional characterisation | Case Study 2

Controlled drug release from alginate beads encapsulated in pH-responsive 3D printed carrier



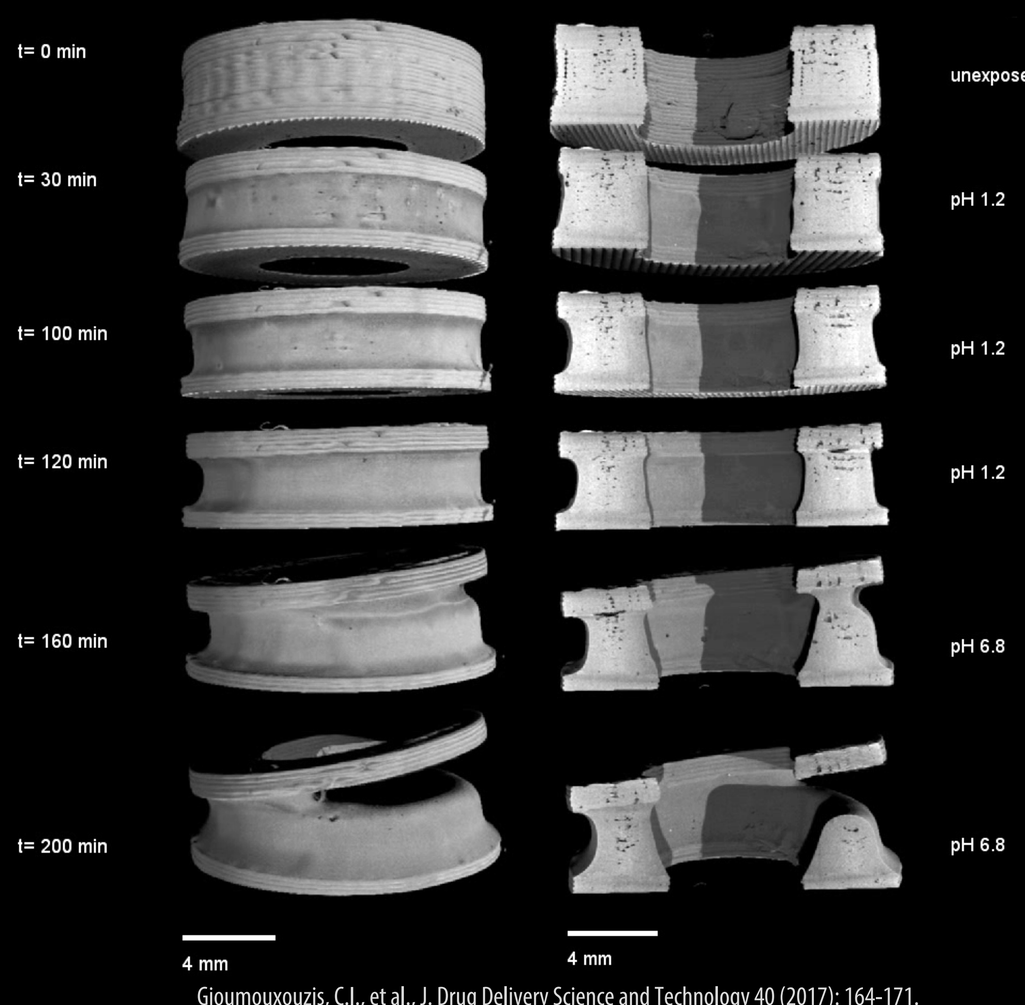
Gioumouxouzis, C.I., et al. AAPS PharmSciTech: (2018), 1-14.

Case Study 1 | [a-d] **Deviation map of printed object's surface from the nominal values of the CAD design**; [e-g] CT slices trough the PVA layer, the PVA/ Eudragit® layer interface and the centre of Eudragit®; [h] cross-section through the XZ plane **Sample: flat cylindrical with smoothed edges; Constituents: water-soluble PVA (+ glimepiride), Eudragit® RL (+ Metformin)**

Case Study 3 | Dissolution of printed dosage form in simulated gastro-intestinal environment Timestamps describe the "total exposure time" to the respective medium. **Sample**: Hollow cylinder dosage form (0.25 mm height); **Constituents**: water-insoluble polylactic acid (PLA), water-soluble PVA + model drug (mannitol and hydrochlorothiazide);

Functional characterisation | Case Study 3

Dissolution over time for zero-order kinetics drug release



Gioumouxouzis, C.I., et al., J. Drug Delivery Science and Technology 40 (2017): 164-171.

Case study 2 | top row: *Sum along the Rays* renderings of the printed form at its initial/dry state (scan 1), after 2h exposure to simulated gastric fluid (scan 2), consequent 2h exposure to simulated intestinal fluid (scan 3), followed by 5h exposure to PBS (scan 4). Bottom row: CT slices through the Eudragit®-based layer before and after the 9h exposure to the various solutions ; **Sample:** Eudragit® L100-55 / Eudragit® S100 (pH responsive leyer), polylactic acid (PLA), alginate particled (+5-Fluorouracil)

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