

Introduction:

General background: The objective is to investigate the degradation and mechanical properties of a degradable biomaterial*. Possible applications are reconstruction of the bone after tumour removal or filling of the gap between the implant and the femur during hip-implant revision surgery. The material consists of a porous ceramic filled with a polymer (Figure 1). The material is initially non-porous and develops a controlled porosity during the faster degradation of the polymer. Being implanted as a scaffold for bone healing purposes, the material would hence provide both sufficient initial mechanical strength and a porous ceramic structure for tissue ingrowth. Eventually, due to its degradable nature, the material will be replaced by bone. The main advantages over metal implants are avoidance of a second operation to remove the implant and a slow transfer of the load from the degrading material onto the regenerating bone instead of stress-shielding.

Further technical background: Calcium phosphate ceramics are widely used in bone healing applications due to their biocompatibility and osteoconductivity*. Porous structures are preferred since they support vascularization and proliferation of the newly generated bone. The synthesis of an inorganic-organic composite simulates the architecture of bone, which can be regarded as a ceramic/ polymer composite of biological apatite and collagen. Samples are produced via in-situ polymerization and injection moulding of the polymer into the ceramic matrix. A possible composite is composed of a β -tricalcium phosphate* matrix filled with poly (D,L) lactic acid* [1](Figure 1). The aim of this study is to compare degradation and mechanical properties of samples differing in composition and/or manufacturing method.

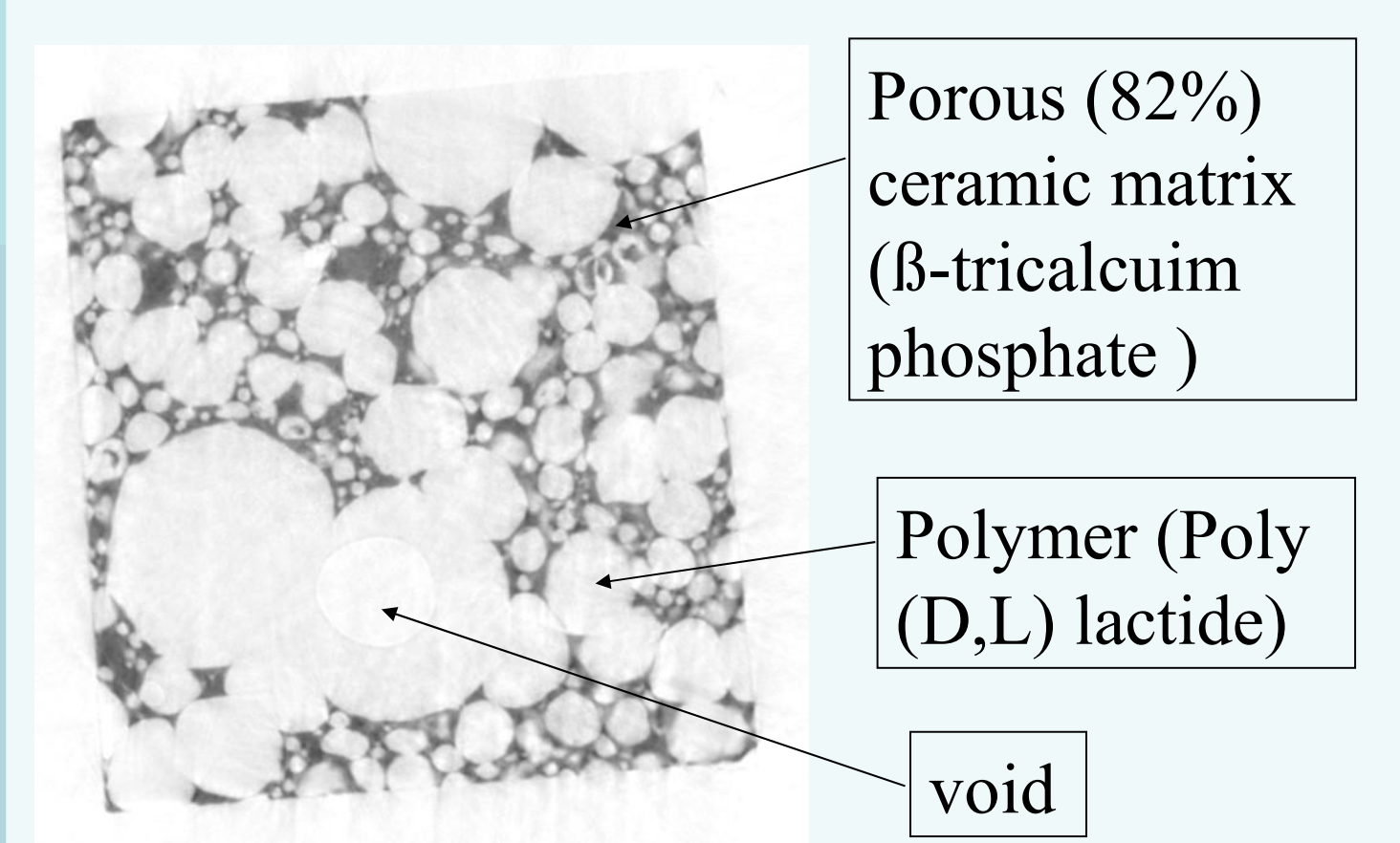
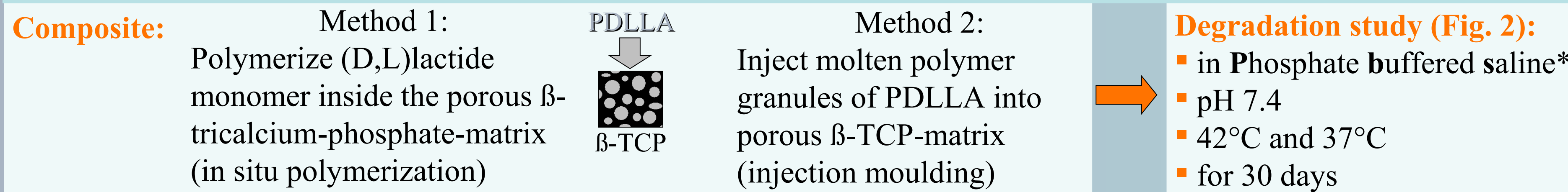


Fig. 1: X-ray computed microtomography picture of co-continuous degradable β -TCP-PDLLA composite

Materials and Methods:



Characterization of samples before and after degradation:

- Molecular weight*
- Glass transition temperature*
- Mass loss after degradation: $m_{\text{loss}} = (m_{\text{dry}} - m_{\text{original}}) / m_{\text{original}} \cdot 100$
- Water gain after degradation: $m_{\text{gain}} = (m_{\text{wet}} - m_{\text{dry}}) / m_{\text{dry}} \cdot 100$
- 3D structures of the composite (X-ray microtomography, μ CT) (Fig.2)

Mechanical testing of as-made samples:

- Compression tests of as-made composites, unfilled β -TCP matrix and pure PDLLA
- Combination of compression tests and X-ray computed microtomography (μ CT) to monitor mechanisms of sample failure

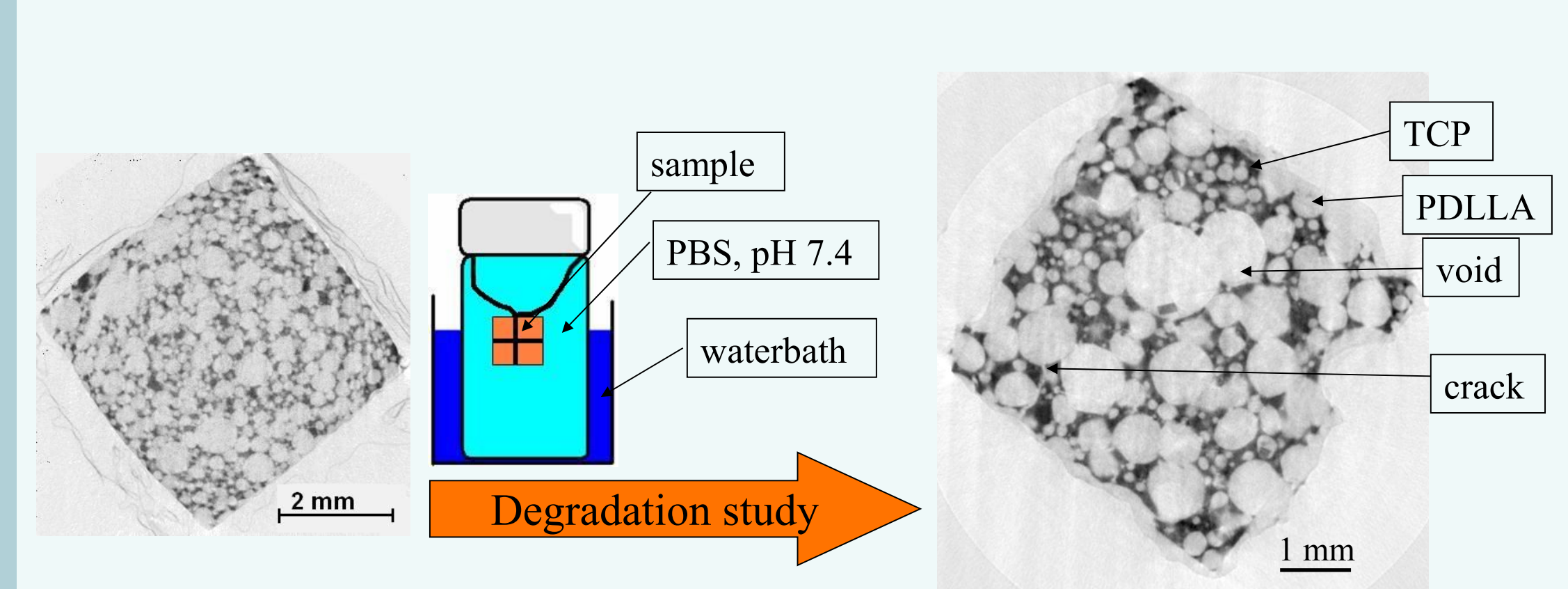


Fig. 2: μ CT pictures of TCP-PDLLA composite before and after degradation in 42°C for 30 days

Results and Discussion:

(A) Mechanical Testing of pure β -TCP and composite, combined with μ CT:

- Mechanical behaviour changed from brittle (unfilled β -TCP matrix) to elastic-plastic (TCP-PDLLA composite) (Fig. 3)

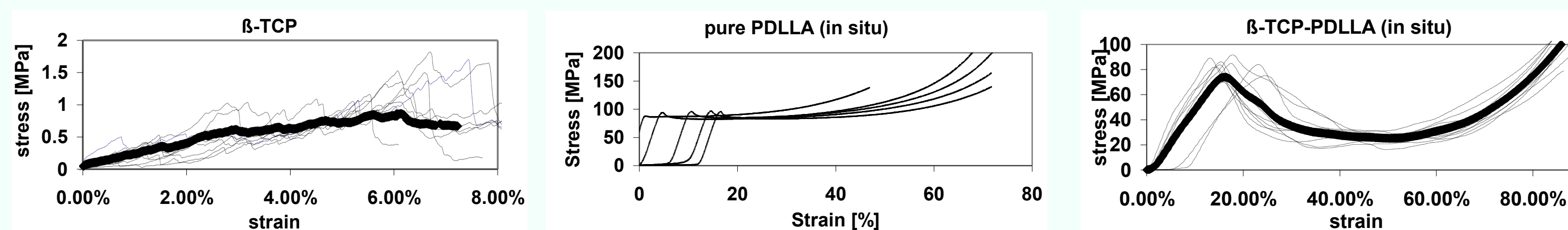


Fig. 3: Stress-strain curves of pure β -TCP, pure PDLLA and β -TCP-PDLLA composite

- Great improvement in mechanical properties (compressive strength, E-modulus) due to polymer filling (Fig. 4)

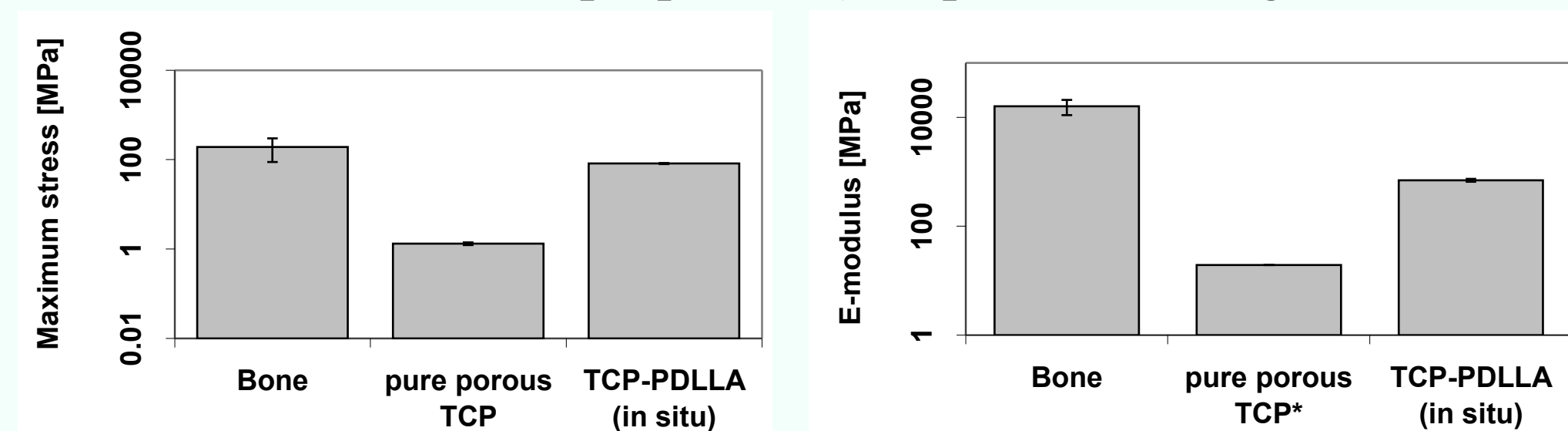


Fig. 4: Maximum stress-to-failure and E-modulus for pure β -TCP (n= 14), β -TCP-PDLLA (n= 10) composite and bone

- Failure of composite due to fracture of the ceramic struts (Fig.5)
- Stress deflection by crack bridging around the polymer phase (Fig. 5) results in debonding of polymer along the crack lines

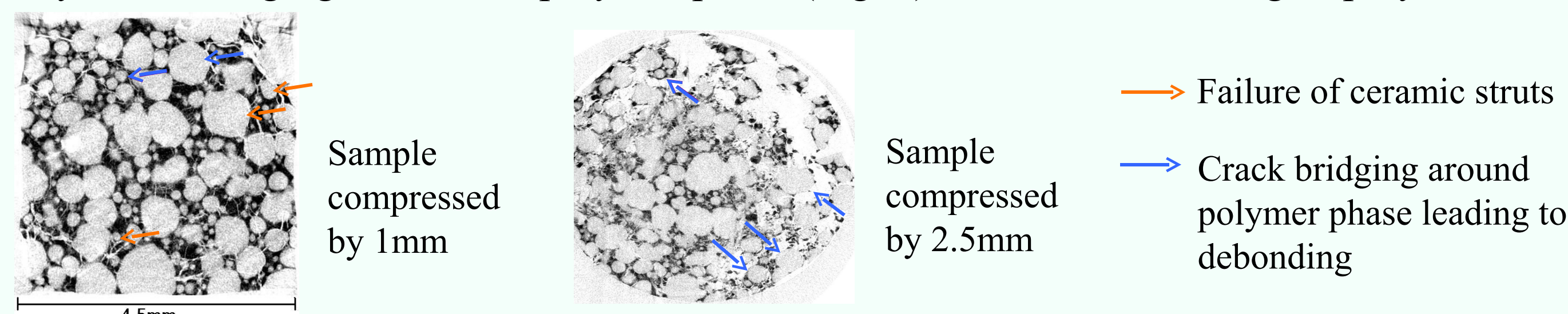


Fig. 5: μ CT picture of β -TCP-PDLLA composite under compression

(B) Degradation study of β -TCP-PDLLA composite (Fig. 6):

- Influence of sample manufacturing method:**
 - Injection moulded materials show no significant mass loss after 30 days degradation for both temperatures.
 - In situ polymerized samples have lost 20% of their initial mass when degraded for 30 days in 42°C, whereas only 2% mass is lost at 37°C.
 - In situ polymerized samples show higher water uptake (>60%) than injection moulded samples (<40%).
 - Polymer swelling during degradation leads to sample cracking (Fig.2)
- Influence of degradation temperature:**
 - Mass loss of in situ polymerized samples is accelerated at increased temperature (20% mass loss at 42°C vs. 2% mass loss at 37°C).
 - Higher water gain for both types of samples at increased temperature due to higher flexibility of molecular chains.

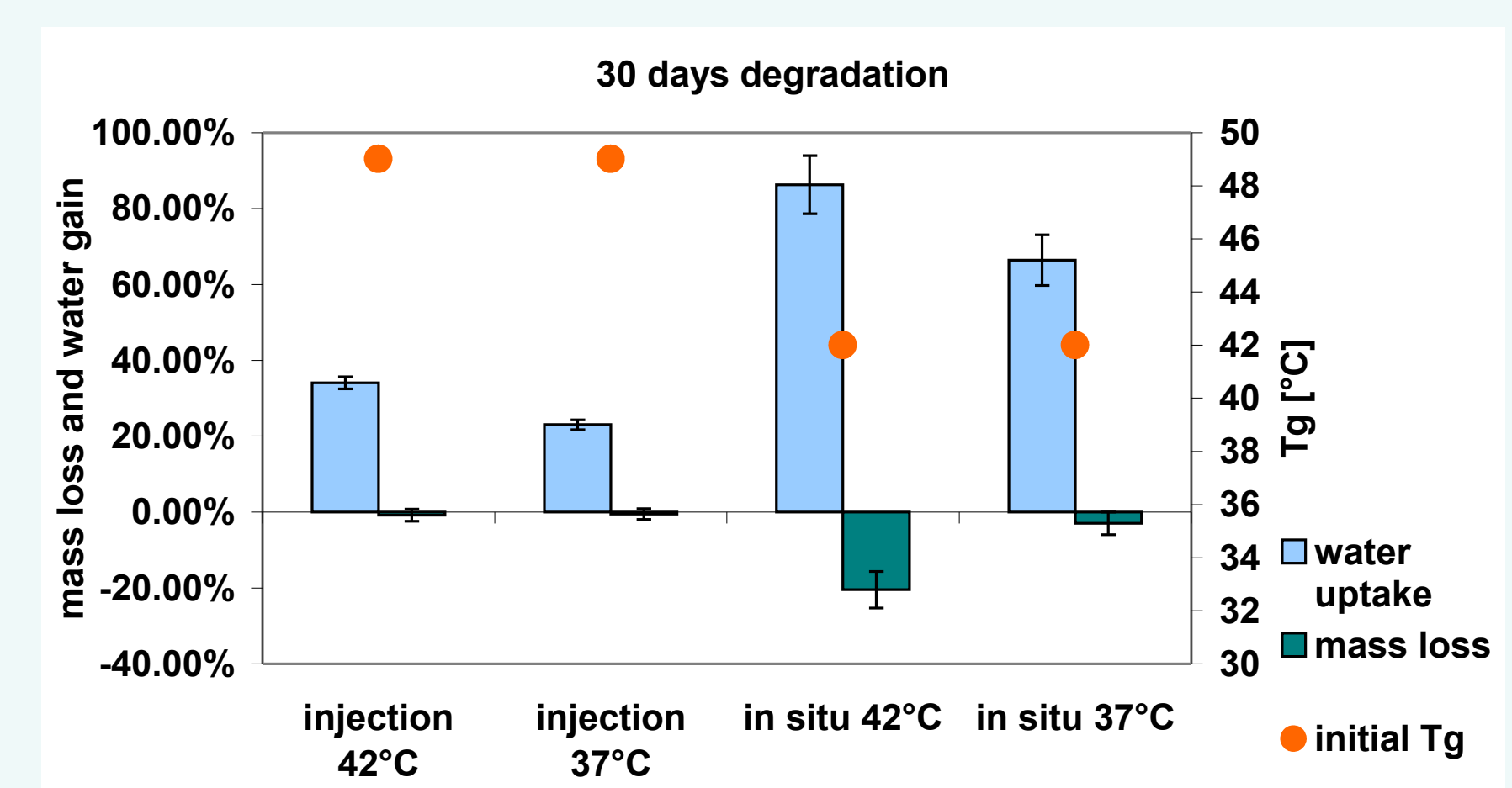


Fig. 6: In-situ-polymerized and injection moulded β -TCP-PDLLA samples after 30 days degradation in 37°C and 42°C

Conclusions and Future Work

(A) Mechanical Testing:

- Mechanical properties of porous β -TCP can be significantly improved by infiltration with polymer.
- Next step: Influence of manufacturing process and degradation on mechanical properties will be studied.

(B) Degradation study:

- Method of sample manufacture and degradation temperature have a remarkable impact on degradation behaviour.
 - Increased swelling due to residual monomer and lower molecular weight in in-situ polymerized samples.
 - Slower degradation of injection moulded samples due to higher initial molecular weight* and Tg*.
- Swelling of PDLLA during degradation leads to crack formation in β -TCP matrix.
 - Next step: Investigate new samples filled with PLLA mixed with lauric acid, a fast degrading system for which only 4% water uptake is reported [2].

*Glossary

Biomaterial: „A material intended to interface with biological systems to evaluate, treat, augment, or replace any tissue, organ, or function of the body.“ (Williams dictionary of biomaterials)

Osteoconductive: Upon implantation, osteoconductive materials allow vascular ingress, cellular infiltration and attachment and formation of bone on their surface.

β -tricalcium phosphate (β -TCP): Chemical formula: $\text{Ca}_3(\text{PO}_4)_2$, density: 3.07gcm⁻³. Degrades after implantation into the body via chemical dissolution to calcium and phosphate salts or cell mediated degradation. The great advantage of the use of β -TCP is that instead of replacing natural tissue it will be regenerated to its full functions.

Poly (D,L) lactic acid (PDLLA): Biodegradable, amorphous polymer, consisting of the chiral lactic acid in both its chiral stereoisomeric forms (D,L). The degradation time of PDLLA is size-dependent. Plates (2mm thickness) are reported to fully degrade within 15 weeks whereas PDLLA films (0.3 mm thickness) lost only 25% of their weight after 30 weeks of *in vitro* exposure at physiological conditions [3].

Phosphate buffered saline (PBS): A buffer solution commonly used for dissolution study biomaterials. It is a salty solution containing sodium chloride, sodium phosphate and potassium phosphate. The buffer helps to maintain a constant pH. The concentration usually matches the human body.

Molecular weight: The sum of the weight of all atoms in one polymer molecule. A low initial molecular weight results in faster dissolving polymer since more hydrophilic endgroups are present and the molecules are more rapidly degraded to be small enough to go into solution.

Mw: weight-average molecular weight. Takes into account that high-Mw-species have larger impact. Reflects properties such as viscosity and toughness much better. $M_w = \sum N_i M_i^2 / \sum N_i M_i$

Mn: number-average molecular weight. Better reflects the molecular weight of the most numerous species. It is directly related to the scission of polymer chains during degradation. $M_n = \sum N_i M_i / \sum N_i$

N_i: number of molecules; **M_i:** molecular weight

Glass transition temperature (Tg): The temperature at which a polymer is in transition between the glassy and rubbery state. Amorphous polymers are rubbery when they are held at temperatures above their Tg. Below Tg, the material is glassy. Hence many properties of the polymer change above their Tg.

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References: [1] D. F. Farrar, M. Brown, M. Hall, J. E. Brunelle, N. J. Cotton, R. Berube, J. Lipchitz, *US Patent*, 2005. [2]: Renouf-Glauser, A.C., Rose, J., Farrar, D., Cameron, R.E. 2005, *Biomaterials*, 26(15), pp. 2415-2422. [3] Grizzi I, et al., *Hydrolytic degradation of devices based on poly (DL-lactic acid) size- dependence*. *Biomaterials*, 1995. 16: p. 305-311.