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EFFECTS OF POLYOL COMPOSITION ON PHYSICO-MORPHOLOGICAL AND MECHANICAL PROPERTIES OF POLYURETHANE FOAMS

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PU foams as scaffolds: basic requirements

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- ✓ mechanical strength
- ✓ open porosity
- ✓ homogeneous morphology
- ✓ biocompatibility (ability to be biointegrated or bioabsorbed with no toxic effects)

Aim of our research

to design and develop **PU foams as scaffolds** for tissue engineering applications with **open porosity** and **tunable physical** and **mechanical properties** by using a previously set up foaming process

⇩

effects of **polyol composition** and **ratio between base reagents**

Foaming a polyurethane during synthesis

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polyols mixture

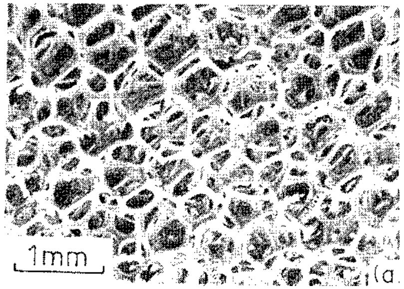
isocyanate

catalyst

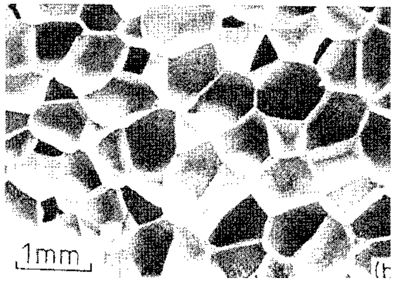
+ **water** (expanding agent)

CO_2

PU foams



open porosity, weak structure



closed porosity, strong structure

Foaming a polyurethane during synthesis – our work

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polyols mixture

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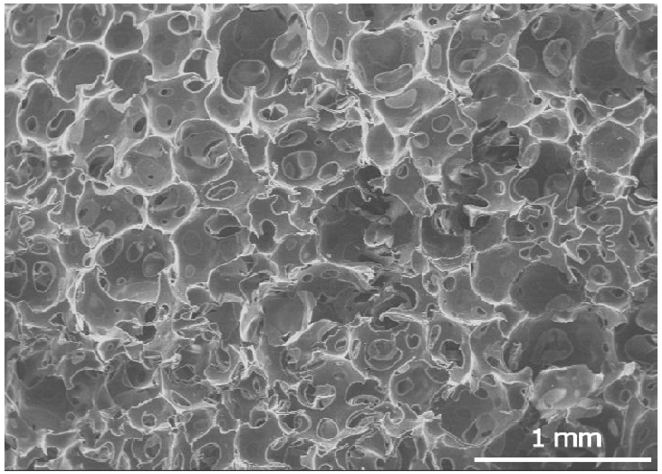
+ **water** (expanding agent)

CO_2

open cells PU foams



Previous works & results

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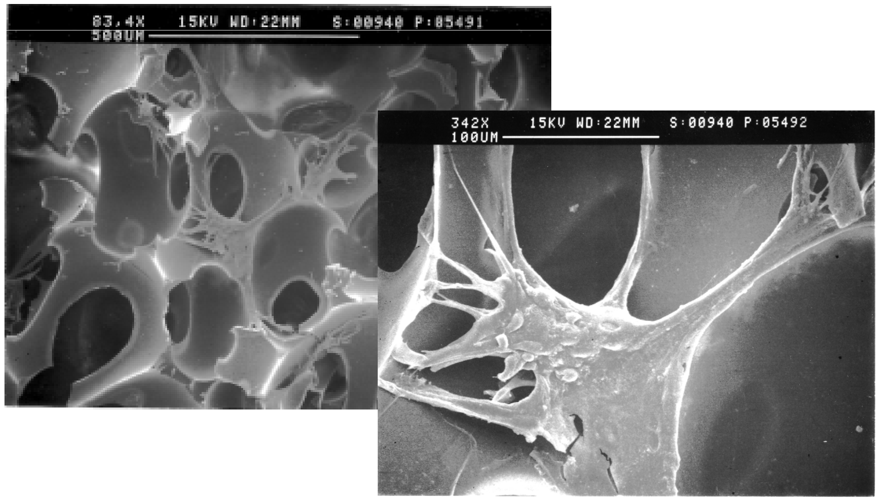
✓ by **setting up** and **controlling** the **foaming process** we are able to obtain **suitable porous structures**, with a **high percentage of open porosity**

✓ the foaming process can be adapted to produce **scaffolds with tailored properties** for regeneration of tissues with different requirements, like derma, cartilage and bone

Farè et al, Euromat 2001
Bertoldi et al, JMSMD 2010
Farè et al, EMBS 2015
Bertoldi et al, ECM 2013

✓ *in vitro* tests with different cell lines & primary cells (fibroblasts, human condrocytes, primary human osteblasts, SAOS 2 and MG63) → PU foams highly **cytocompatible**

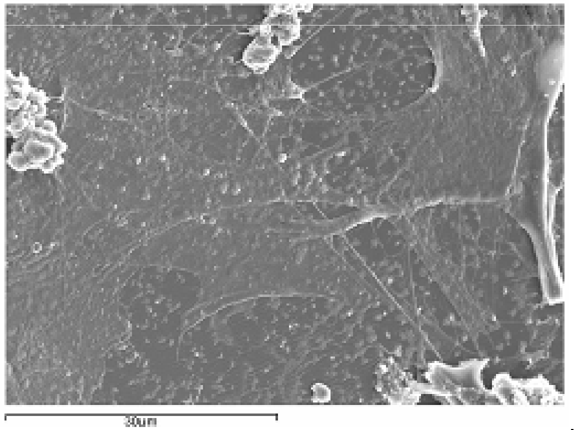


chondrocytes cultured onto PU foams for 48 hours – Tanzi et al, JABB 1998

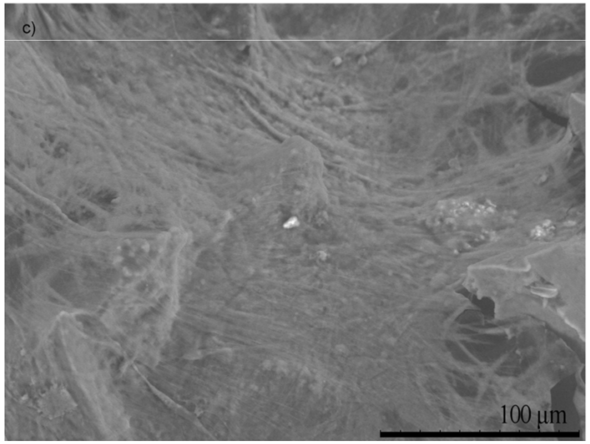
Previous works & results

✓ *in vitro* tests with different cell lines & primary cells (fibroblasts, human condrocytes, primary human osteblasts, SAOS 2 and MG63) → PU foams highly **cytocompatible**

✓ *in vitro* tests with mesenchymal stem cells (MSCs) from human bone marrow and human placenta → ability to **support stem cells differentiation** into **osteoblasts**



MSCs from hBM cultured onto PU foams for 22 days – Zanetta et al., Acta Biomater 2009



MSCs from human placenta cultured onto PU foams for 21 days – Bertoldi et al., JMSMM 2010

Previous works & results

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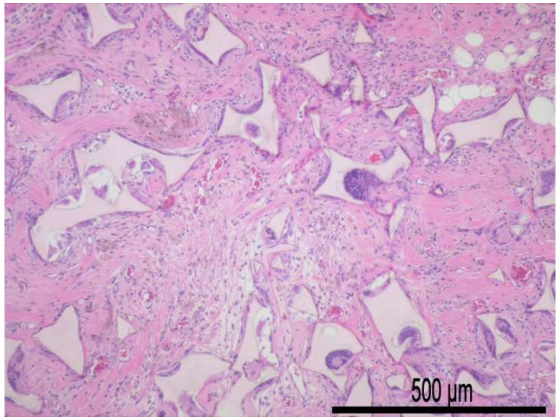
✓ *in vitro* tests with different cell lines & primary cells (fibroblasts, human condrocytes, primary human osteblasts, SAOS 2 and MG63) → PU foams highly **cytocompatible**

✓*in vitro* tests with mesenchymal stem cells (MSCs) from human bone marrow and human placenta → ability to **support stem cells differentiation** into **osteoblasts**

✓*in vivo* implantation in subcutaneous tissue of rats up to 42 weeks → PU foams highly **biocompatible**



H&H staining of PU foams implanted *in vivo* for 42 weeks – Bertoldi et al, CCT 2007

Exploiting the versatility of polyurethane to obtain PU foams with tailored properties

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by varying the foaming parameters, in particular the **polyol mixture formulation** & the **ratio among** the **PU foam reagents**, foams with different properties can be synthesized

selection of the **appropriate components &** their **ratio** for the **polyol mixture formulation**

PU foams base reagents

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Polyol mixture	**different formulation** ad hoc prepared
Isocyanate	MDI prepolymer; -NCO group content: 23.0 ± 0.5%
Expanding agent	**distilled water**
Catalyst	**Fe-acetil-acetonate**

foam prepared considering:

- ✓**stoichiometric** ratio between –NCO and –OH groups
- ✓**excess** of **isocyanate**
- ✓**defect** of **isocyanate**

Bertoldi et al, JMSMD 2015

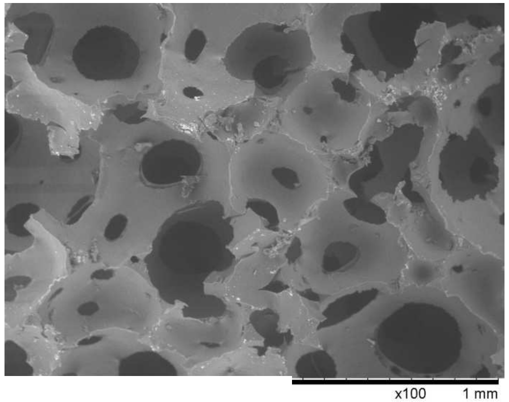
Polyol mixture formulation

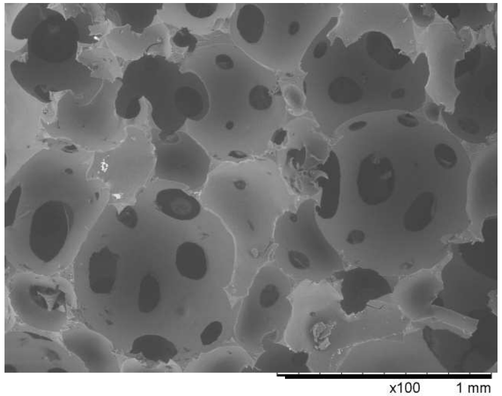
Component	Label
polyether-polyol for flexible PU foams	comp. A
polyether-urea polyol with styrene for flexible PU foams with high resilience	comp. B
amine-based tetrafunctional polyether polyol for rigid PU foams	comp. C
1,4-Butanediol (Sigma-Aldrich)	**BU**
Ethylene glycol (EG)	**EG**
Potassium Acetate in EG (Sigma Aldrich)	**AC**
DABCO 33-LV (Air Products)	**DA**

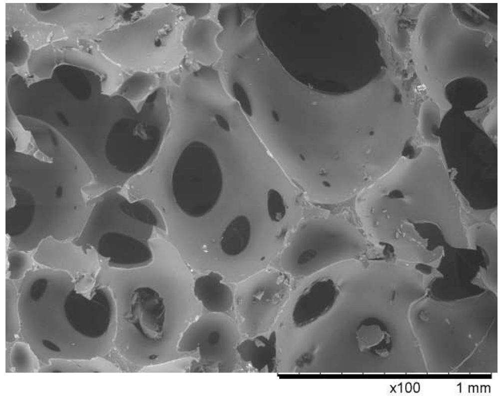
chain extender (BU, EG)

catalyst (AC, DA)

Influence of polyol composition – morphological properties







85% A – 10% B – 2% C
isocyanate excess

85% A – 10% B – 2% C
stoichiometric ratio

73% A – 20% B – 3% C
isocyanate defect

NO influence of polyol composition and reagent ratio on **morphological properties**

Influence of polyol composition – morphological properties

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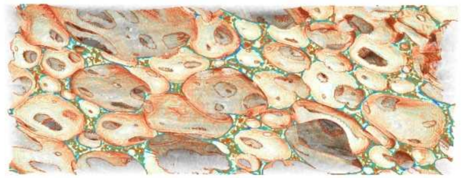
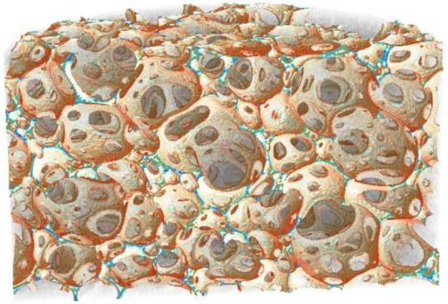
85% A – 10% B – 2% C
isocyanate excess



85% A – 10% B – 2% C
stoichiometric ratio

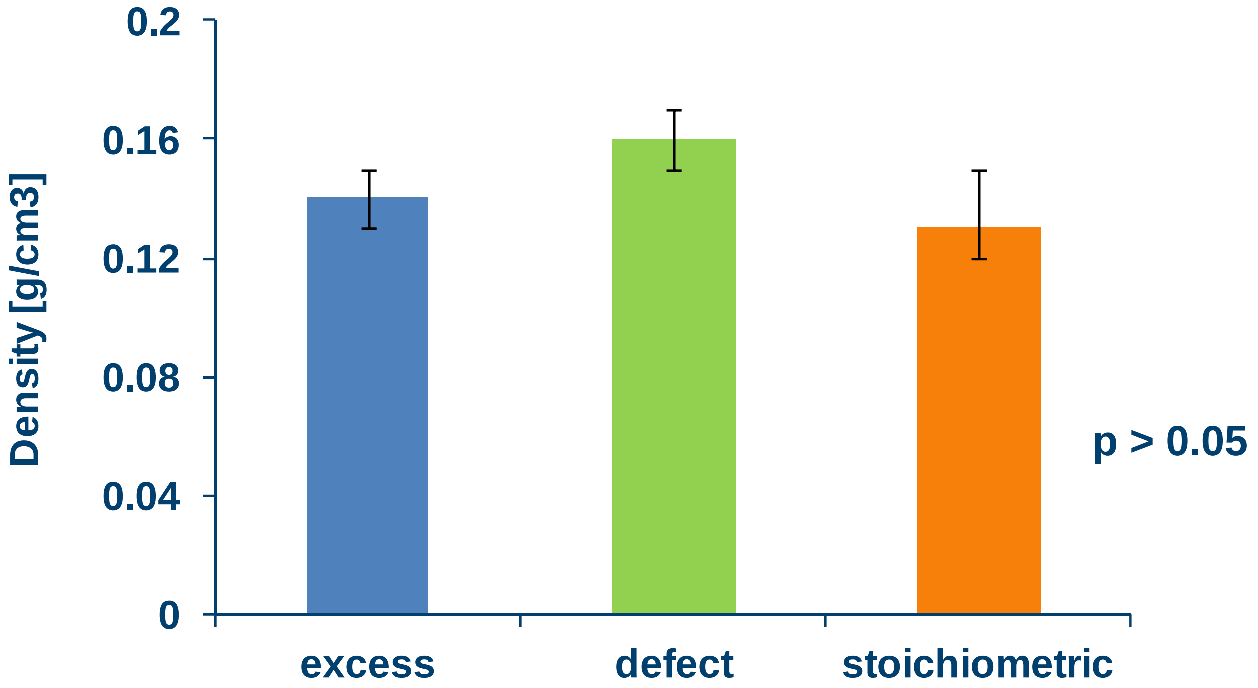


73% A – 20% B – 3% C
isocyanate defect

NO influence of polyol composition and reagent ratio on **morphological properties**

Influence of polyol composition – density

86%A – 10%B – 2%C



NO influence of reagent ratio on **density**

Influence of polyol composition – open porosity by micro-CT

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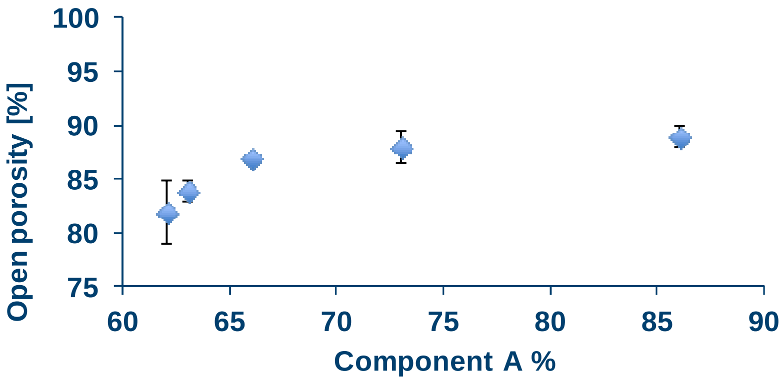

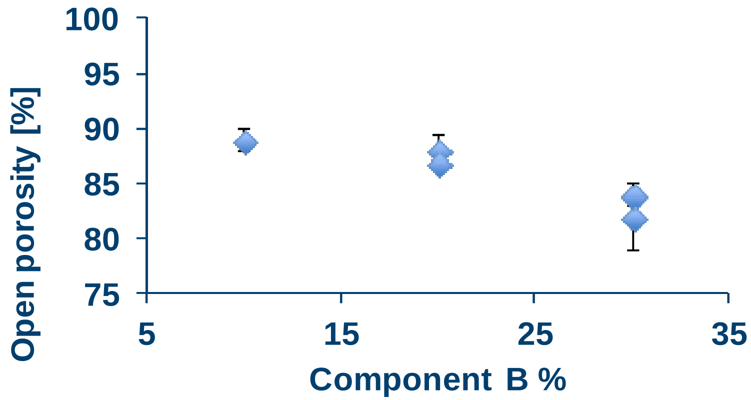

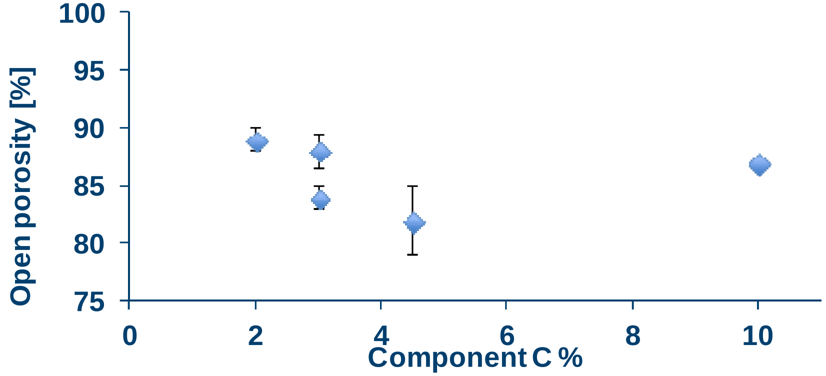

isocyanate defect

- ↑ **comp. A → ↑ open porosity**
- ↑ **comp. B → ↓ open porosity**

Influence of polyol composition – open porosity by micro-CT

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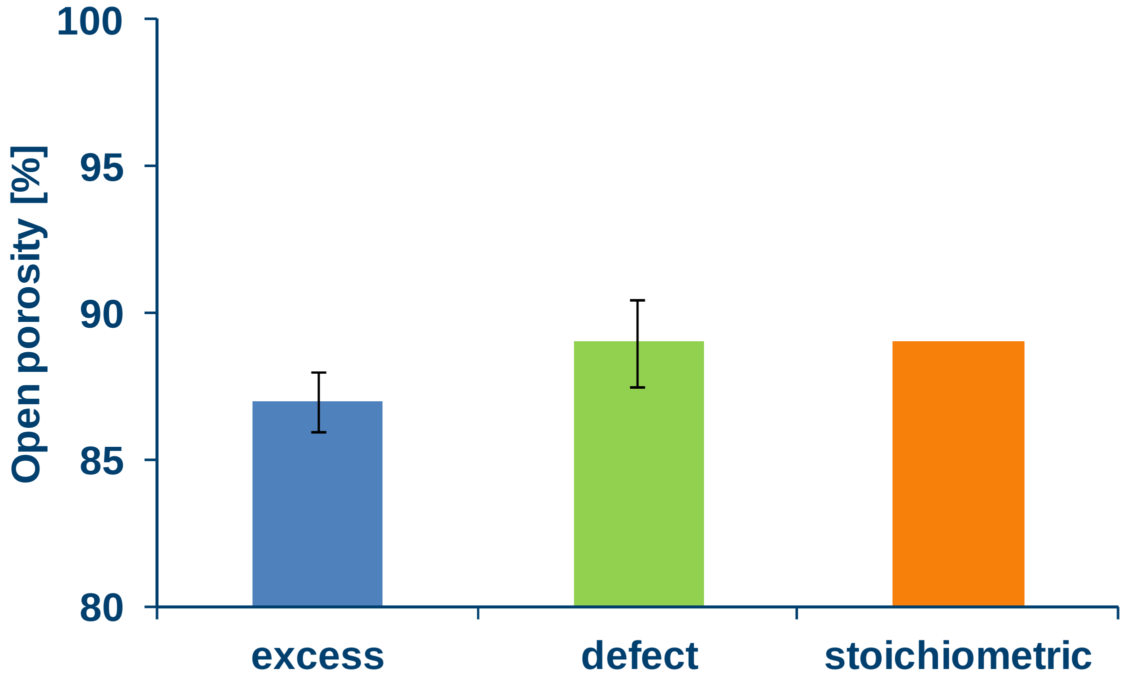
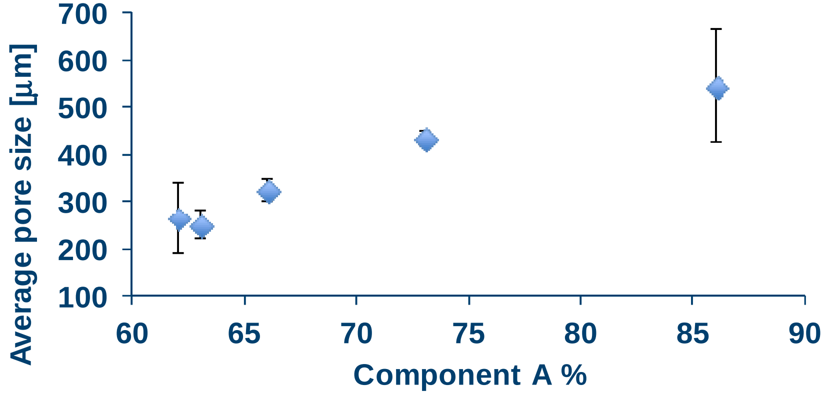
86%A – 10%B – 2%C



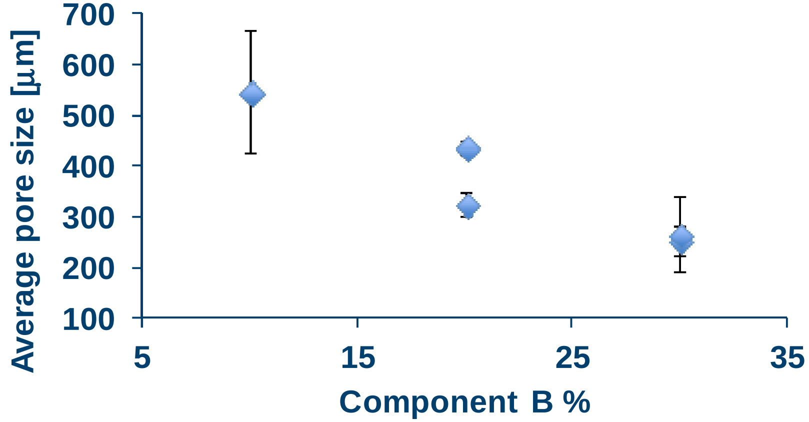
p > 0.05

NO influence of reagent ratio on **open porosity**

Influence of polyol composition – average pore size by micro-CT



isocyanate defect



- ↑ comp. A → ↑ average pore size
- ↑ comp. B → ↓ average pore size

Influence of polyol composition – average pore size by micro-CT

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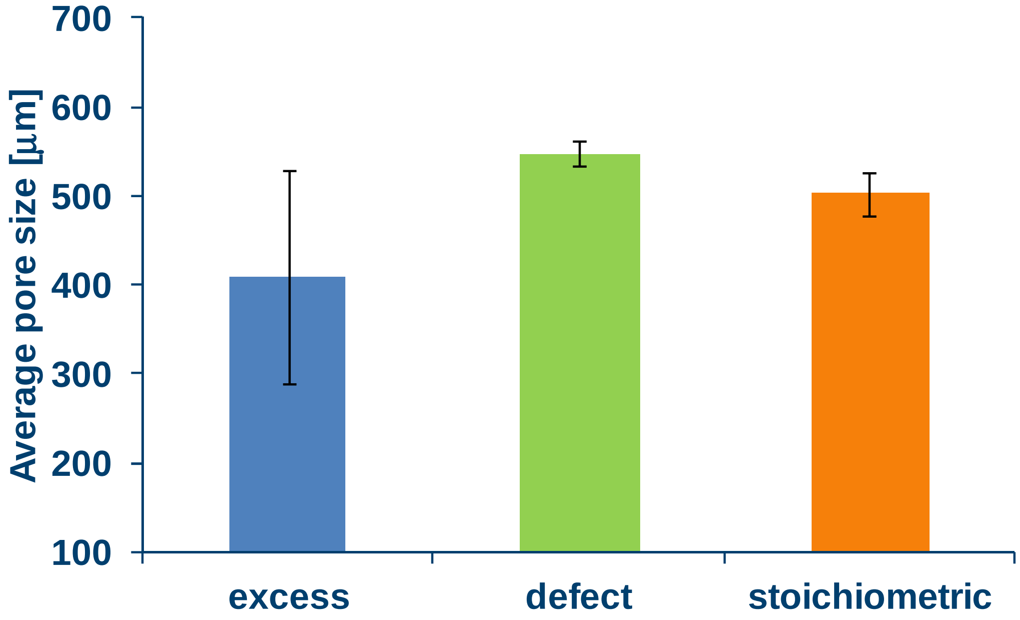
86%A – 10%B – 2%C



$p > 0.05$

NO influence of reagent ratio on **average pore size** due to a **high standard deviation**

Influence of polyol composition – interconnection by micro-CT

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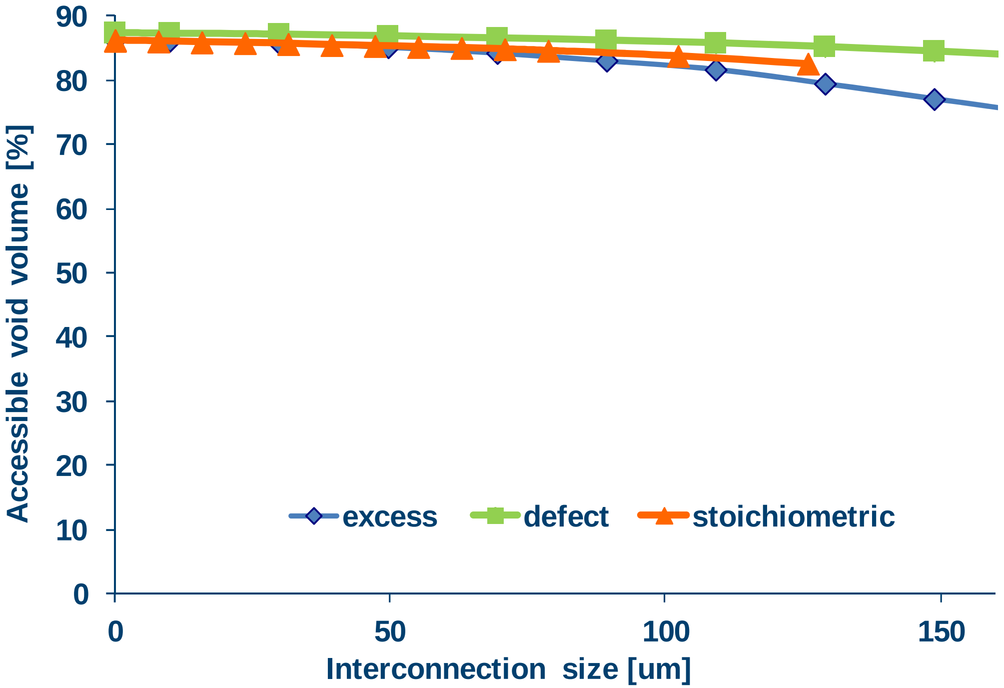
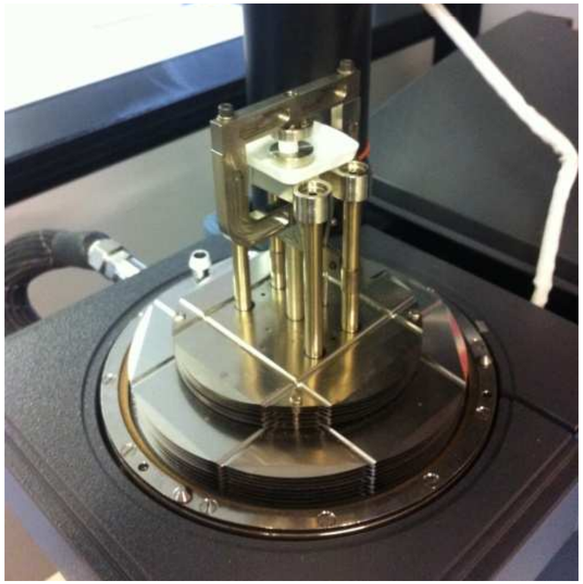
86%A – 10%B – 2%C



NO influence of reagent ratio on **pore interconnection**

Influence of polyol composition – mechanical properties

- ✓ uniaxal compressive test in dry & wet condition
- ✓ n=3; Ø=6 mm; h=4 mm
- ✓ deformation ramp 2.5%/min up to 50% & 5%/min up to 0
- ✓ T=37°C



Influence of polyol composition – mechanical properties

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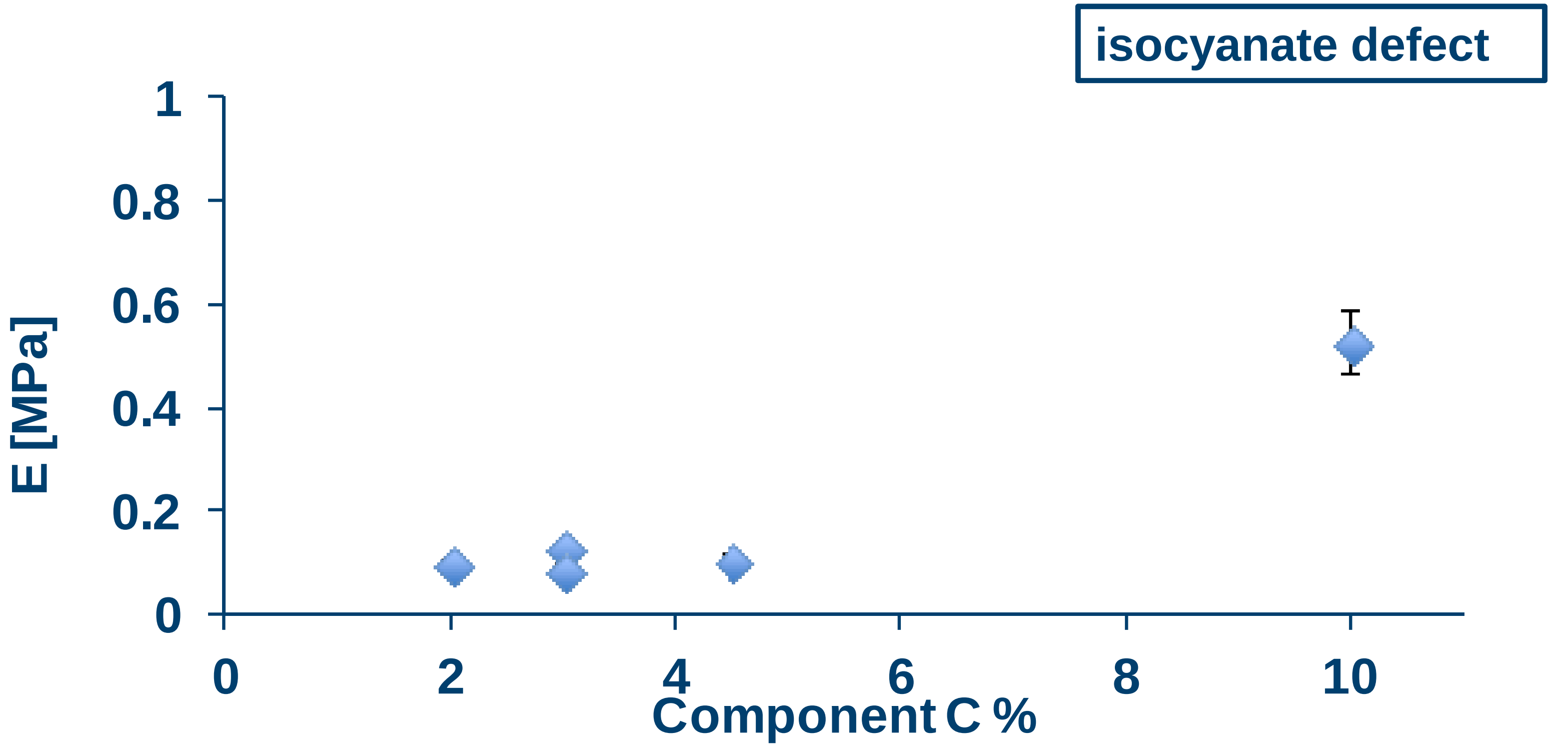
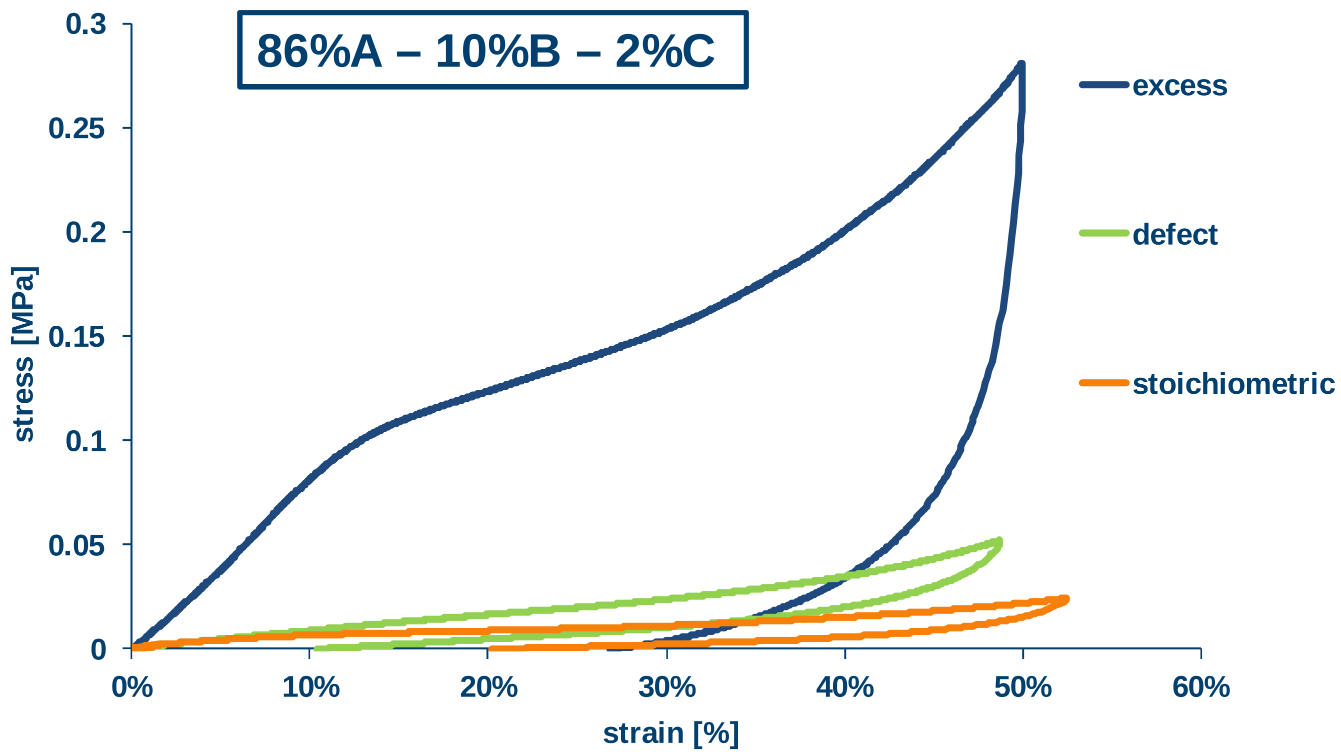


- ↑ comp. C → ↑ elastic modulus → ↑ cross-linking

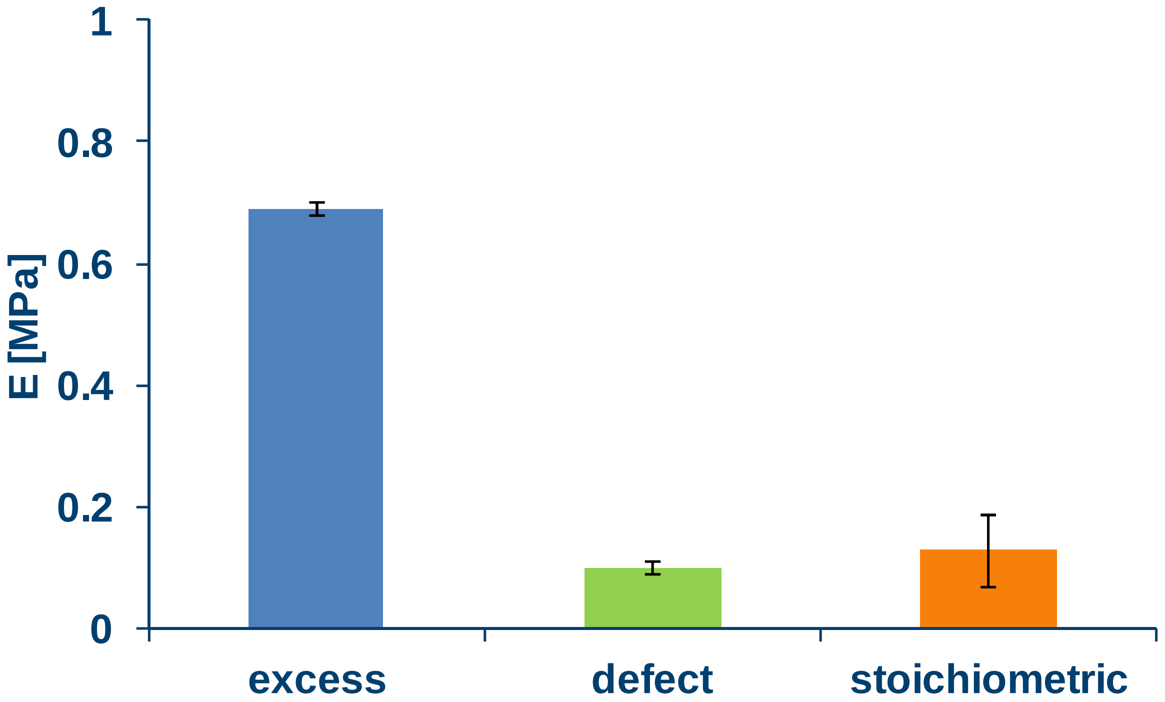
Influence of polyol composition – mechanical properties



➢ ↑ **isocyanate** ⟶ more **viscoelastic behaviour** & **higher stiffness** and **strenght**

Influence of polyol composition – mechanical properties

86%A – 10%B – 2%C



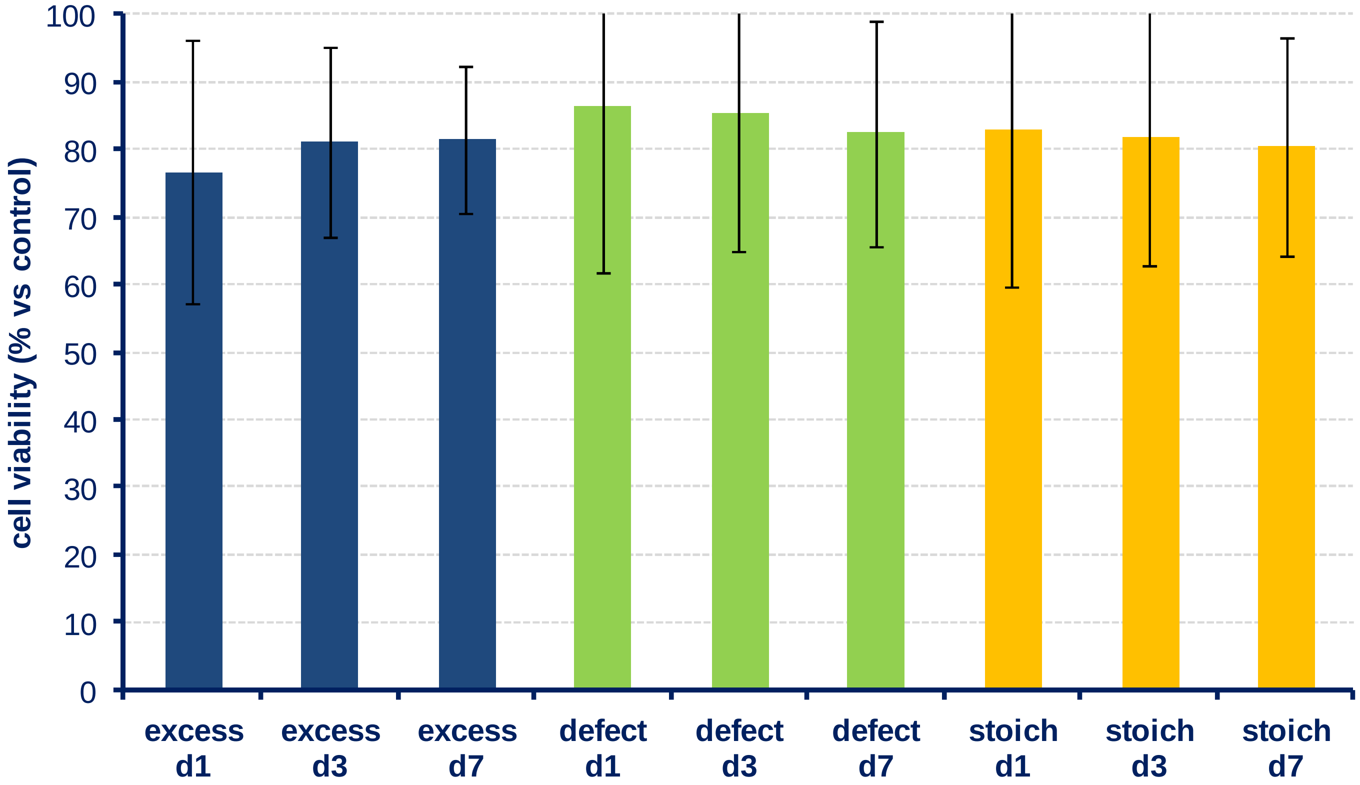
$p < 0.05$

- ↑ isocyanate → ↑ elastic modulus → ↑ stiffness

In vitro indirect cytocompatibility tests

- Materials:
  - **excess, defect and stoichiometric PU foam (86%A – 10%B – 2%C)**
  - control: complete culture medium (DMEM)
- Disinfection: 70% v/v ethanol/sterile water
- **Eluates in DMEM, timepoints: t = 1, 3, 7 days**
- **L929**, murine fibroblast cell line, cell density = 10^5 cell/sample
- @ **24 hours** (cells in contact with eluates):
  - biochemical assay: MTT assay
- test performed in triplicate

In vitro indirect cytocompatibility tests



- **good cell viabilit**y ⇒ no release of low MW products
- no significant difference ($p>0.05$) among PU foam composition

Conclusions & future works

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- ✓ **tunable** morphological and mechanical properties **by varying polyol mixture components and ratio**
- ✓ very **good** value (> 80%) of **open porosity** for all the tested composition
- ✓ **NO cytotoxic effects** even with excess of isocyanate

Conclusions & future works

- ✓ **tunable** morphological and mechanical properties **by varying polyol mixture components and ratio**
- ✓ very **good** value of **open porosity** for all the tested composition
- ✓ **NO cytotoxic effects** even with excess of isocyanate

- ➢ verifying **cytocompatibily** with cell line and primary cells
- ➢ production of composites with calcium phosphates for bone tissue engineering
- ➢ investigate **different applications** as scaffolds for tissue engineering

Thank You!!

Please write to **serena.bertoldi@polimi.it** for any information & request