Additive manufacturing of macro-micro-porous bioceramics for bone tissue engineering

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NEWGEN Meeting, Sofia, 13-14 October 2015

Context

Bone tissue remodeling

Autologuous graft

* Dr Joël Brie

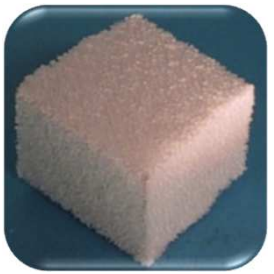
- Shape not adapted
- Second chirurgical site

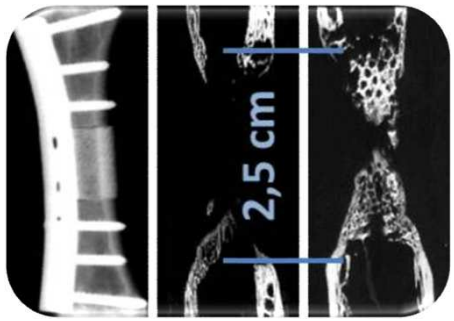
No satisfying solution

Synthetic substitutes

Porous calcium phosphates

Hydroxyapatite $Ca_{10}(PO_4)_6(OH)_2$





[Petite et al., Nature Biotech, 2000]

Large volumes → Limitations

Context

Ways to **improve osseointegration** of calcium phosphate bone substitutes

Chemical composition

Hydroxyapatite : $Ca_{10}(PO_4)_6(OH)_2$

↓

Ionic substitutions

SiHA : $Ca_{10}(PO_4)_{6-x}(\mathbf{SiO_4})_x(OH)_{2-x}$

CBPF

* Collaboration with **Dr Alexandre Rossi**

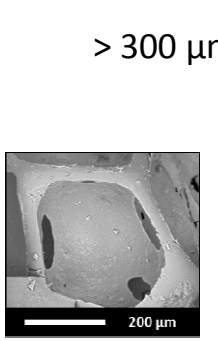
[M. Lasgorceix et al., J Mater Sci: Mater Med, 2014]

Porous architecture

Multi-scale

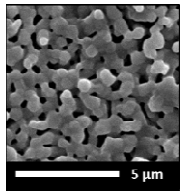
Macroporosity

> 300 µm



Microporosity

< 10 µm

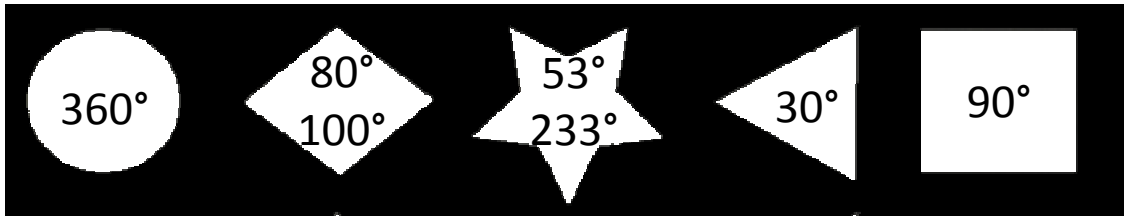


Goal

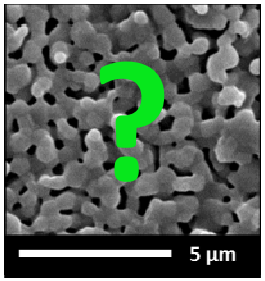
Elaboration of controlled multi-scale porous ceramics in SiHA

Ceramic process

Which geometry of macropores ?



Which microporosity ?



Process

Shaping

Integral microstereolithography

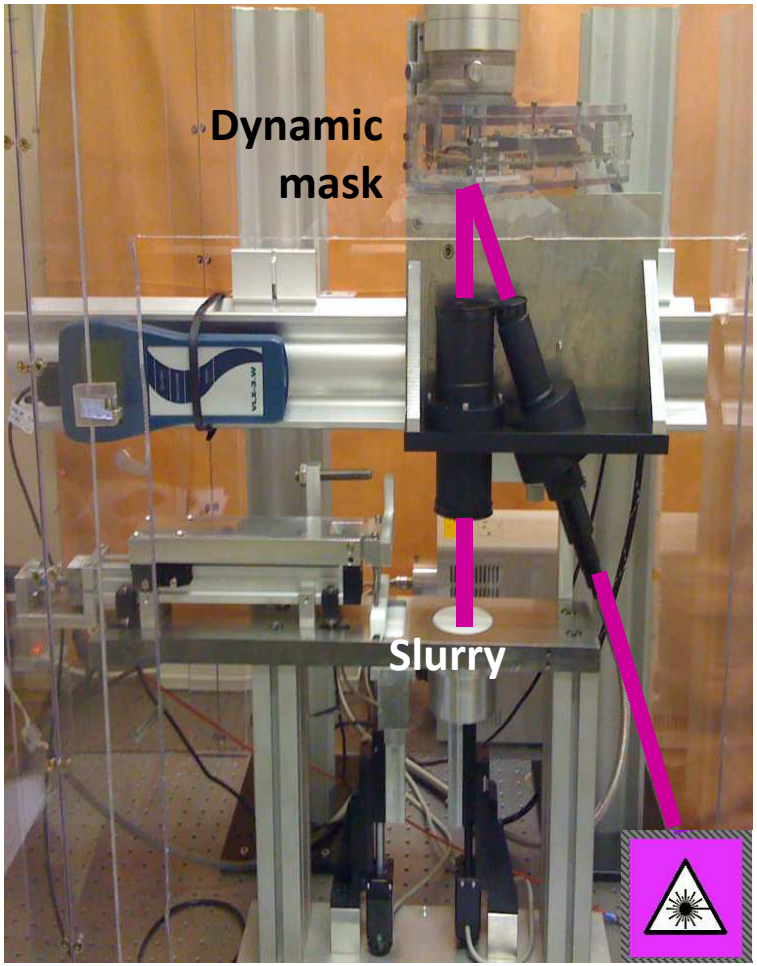
Complex shapes + Accuracy + Rapidity

Sintering

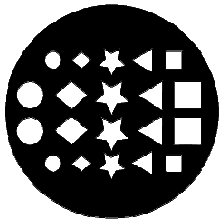
Control of microporosity amount

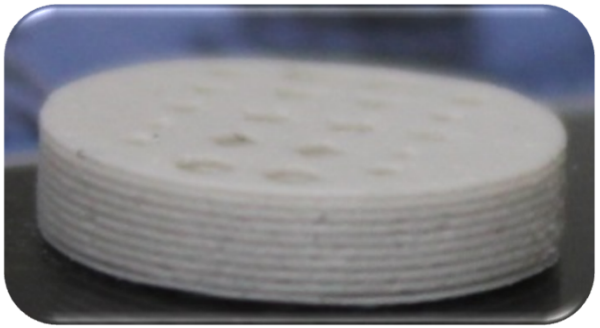
Ceramic process: shaping

Microstereolithography

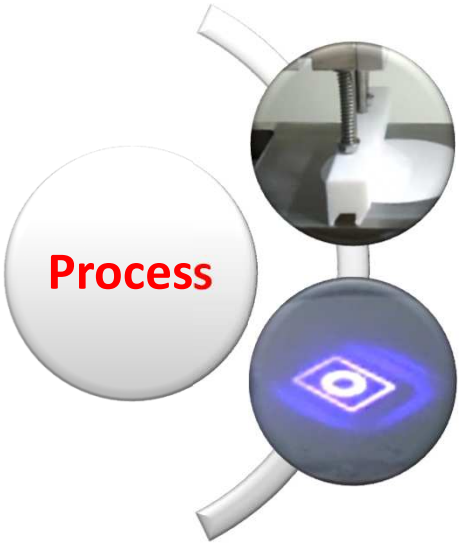


Model





Formulation of photosensitive slurries



Spread slurry thickness

Exposure time

Ceramic process: shaping

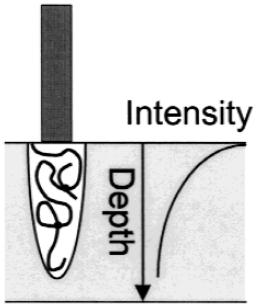
Overcure study

Vertical polymerisation

Jacobs equation: **Cd = Dp . Ln (Ei/Ec)**

Cd : cured thickness
Dp : beam penetration depth
Ei : received energy density
Ec : critical energy density

[V. Tomeckova et al., J. of Eur. Cer. Soc., 2010]
[J.W. Halloran et al., J. of Eur. Cer. Soc., 2011]
[S.P. Gentry et al., J. of Eur. Cer. Soc., 2014]



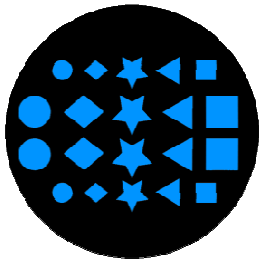
[Lee et al., J. Mater. Res., 2001]

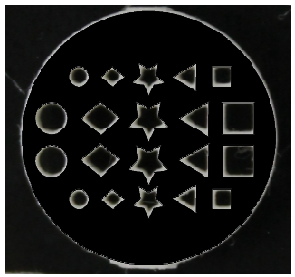
Lateral overcure

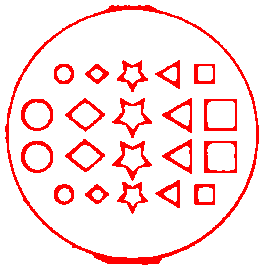
Width of polymerized lines

[Hinczewski et al., J. of Eur. Cer. Soc, 1998]
[Gentry et al., J. of Eur. Cer. Soc, 2013]

Complex geometries ?





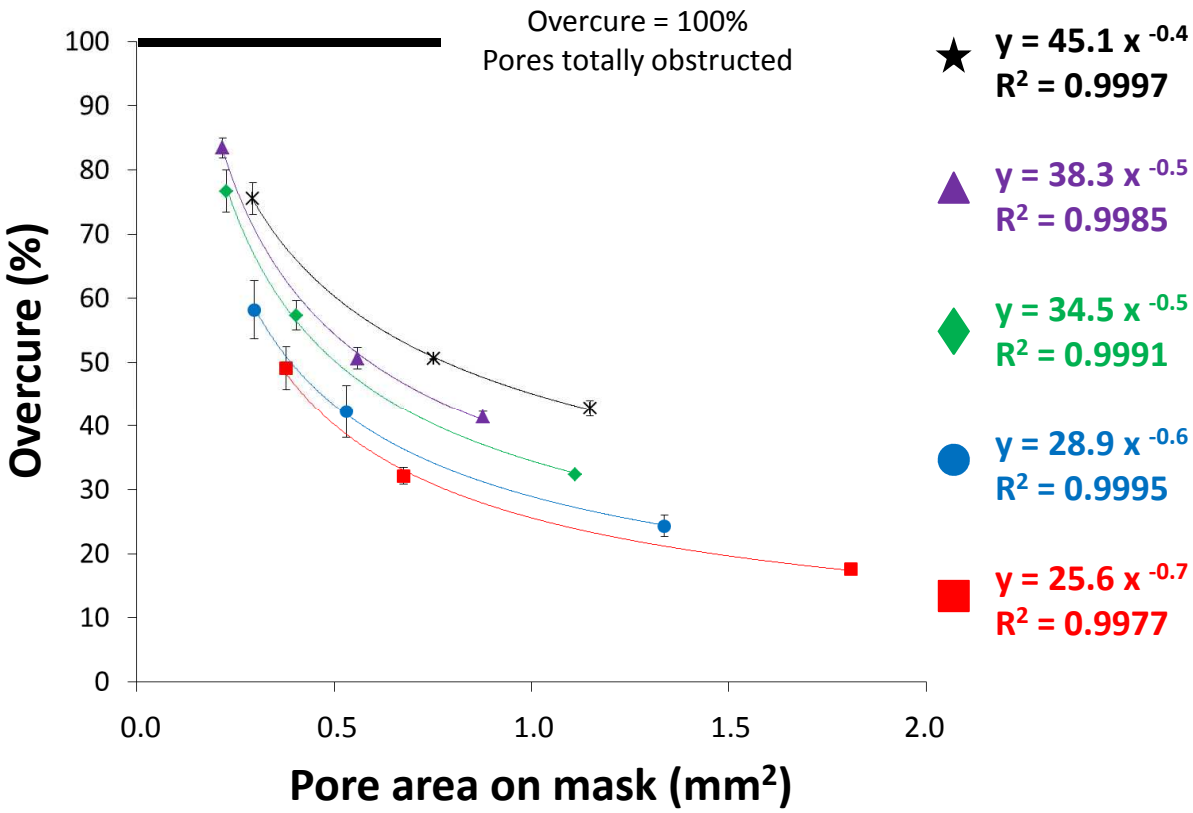


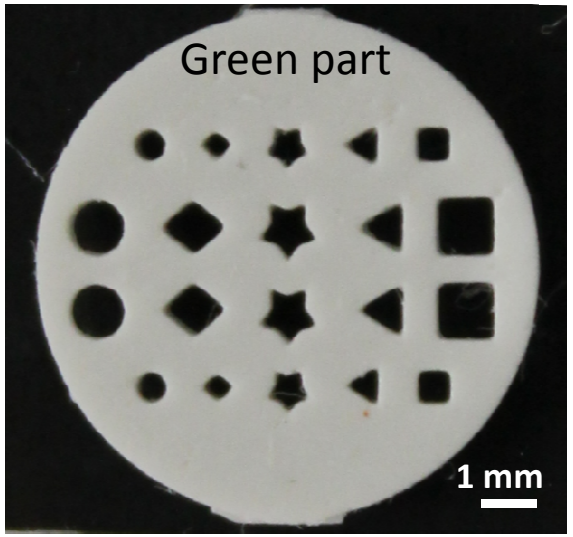
$$S = \frac{Overcured\ area}{Theoretical\ empty\ area} \times 100$$

Ceramic process: shaping

Quantification of lateral overcure

Mathematical laws: $y = a\,x^{n}$

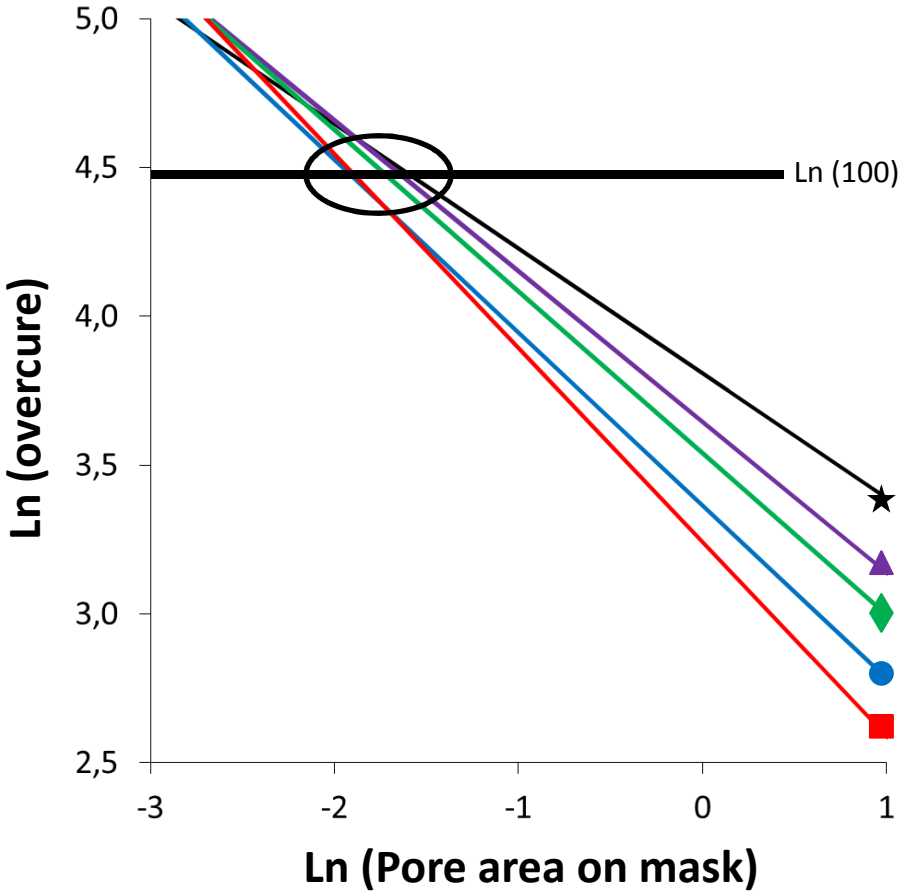


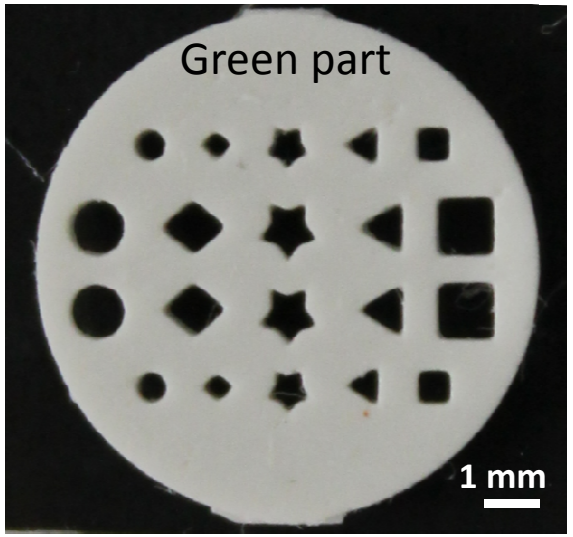


Ceramic process: shaping

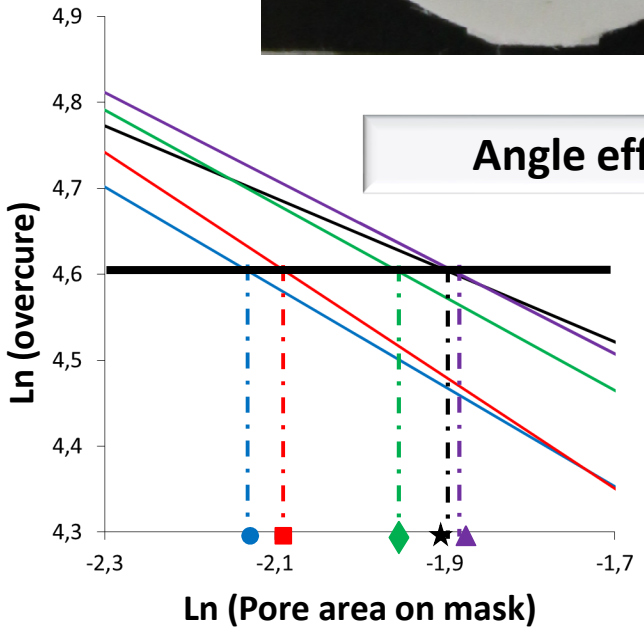
Quantification of lateral overcure

Logarithmic transformation → Linear law → Extrapolation





Overcure = 100%
Pores totally obstructed



Angle effect

Ceramic process: shaping

Quantification of lateral overcure

Angle effect

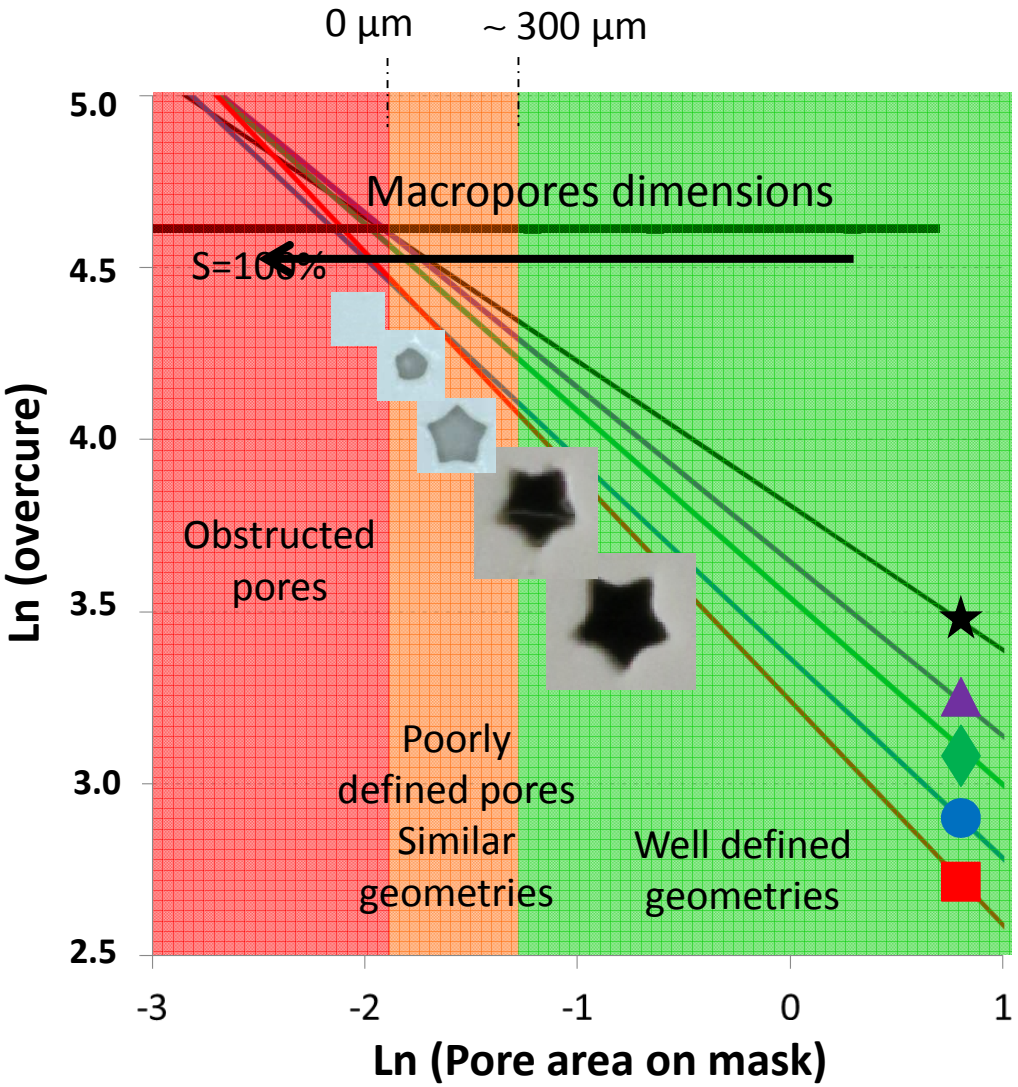
Angle

53 ° 60° 80° 90°

S = 75 % S = 71 % S = 66 % S = 50 %

Overcure

Ceramic process: shaping



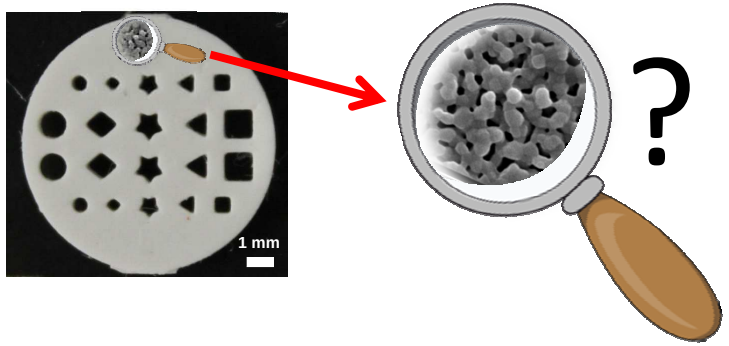
Range of desired pore size:
> 300 µm

Process adapted to macropores shaping with controlled geometries in the desired size range

Ceramic process: sintering

Control of open microporosity amount

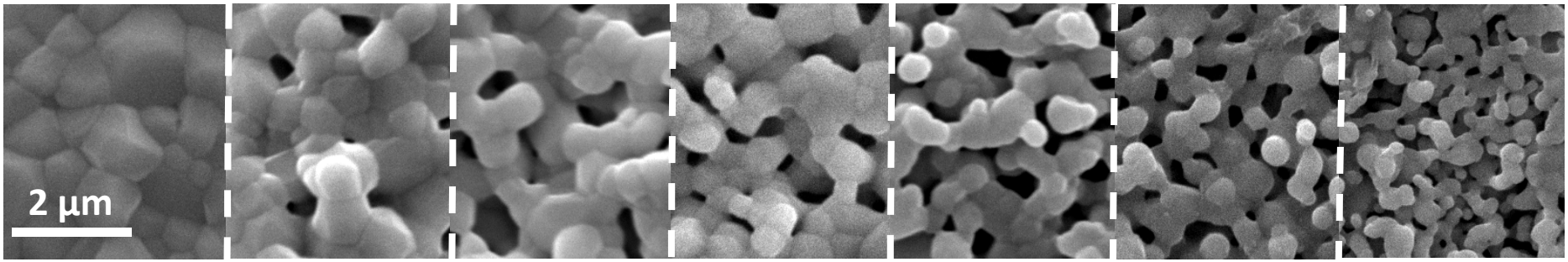
Choice of sintering parameters



T

t

1240°C	1220°C	1200°C	1180°C	1160°C	1160°C	1160°C
2h	2h	2h	2h	2h	30min	15min



0,5 %	15 %	23 %	28 %	32 %	36 %	37 %

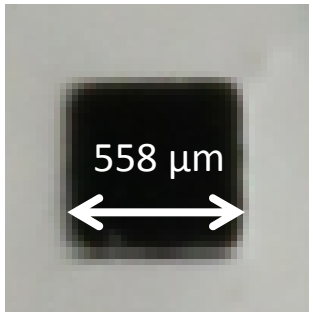
Controlled open microporosity amount (± 1 %)

Ceramic process

Microporosity 23 %

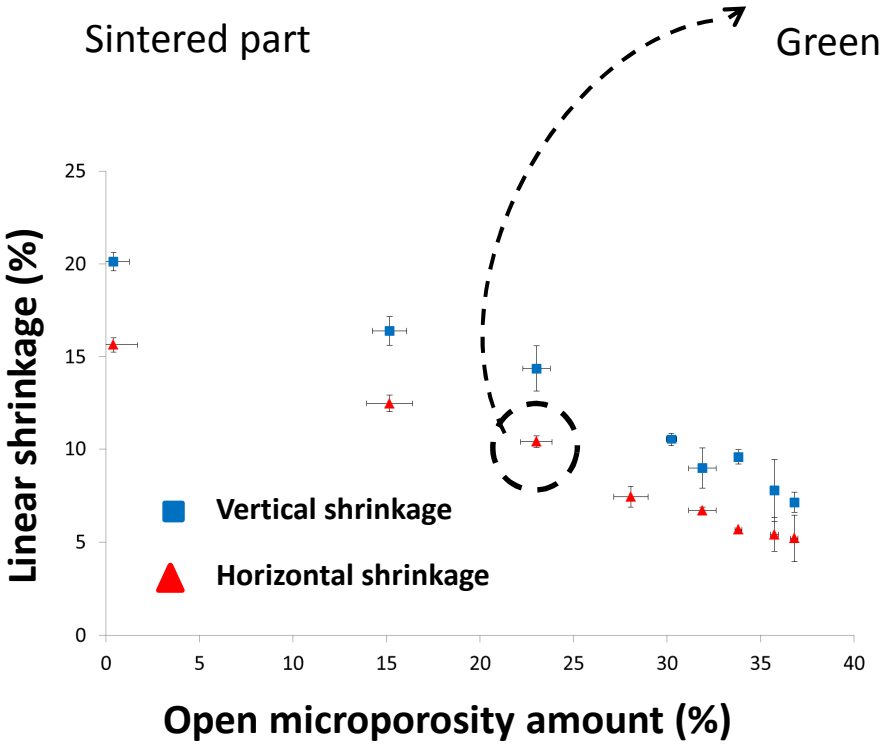
Sintering

Shrinkage



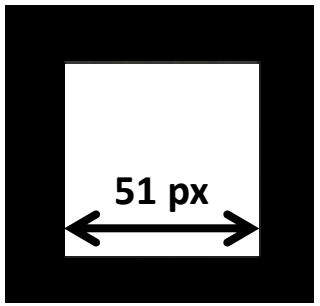
Sintered part

Green part

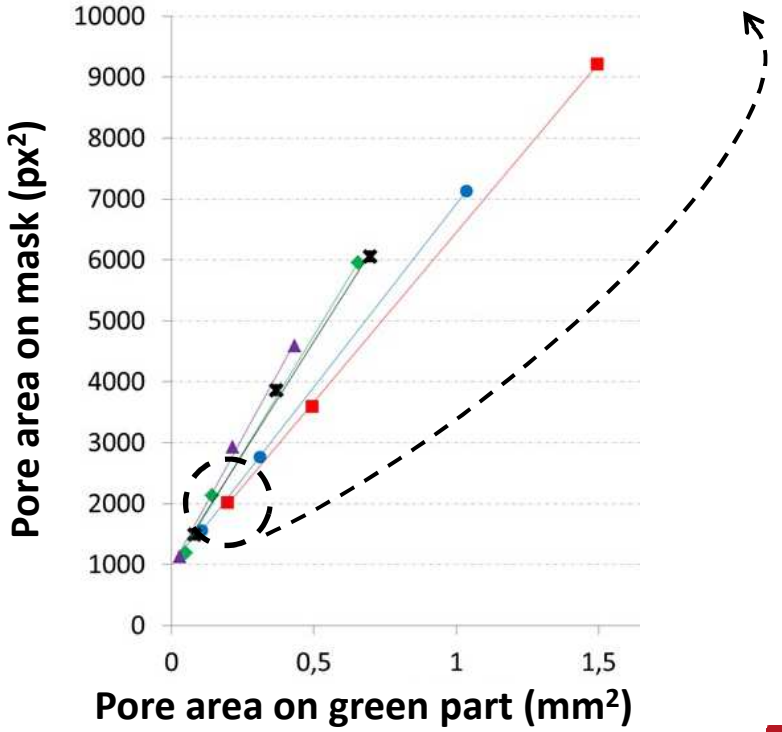


Microstereolithography

Overcure



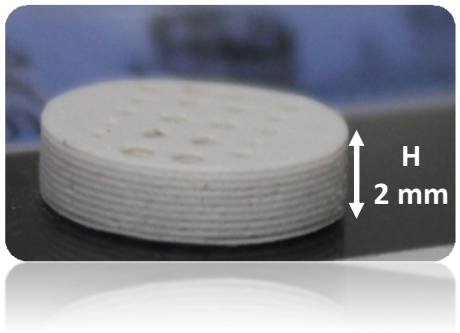
Dimensionned mask

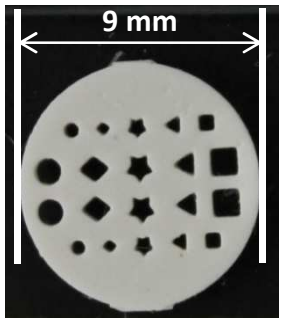


→ **Predictive dimensioning model**

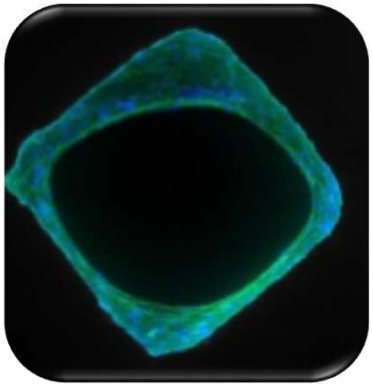
Biological evaluation

Model ceramic substrates

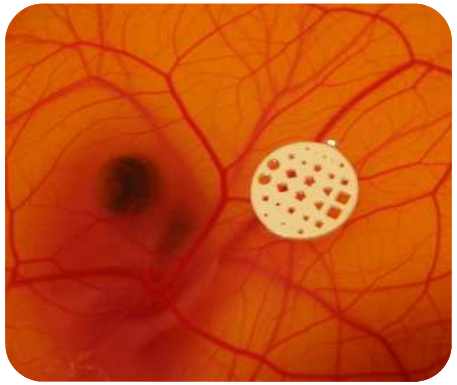


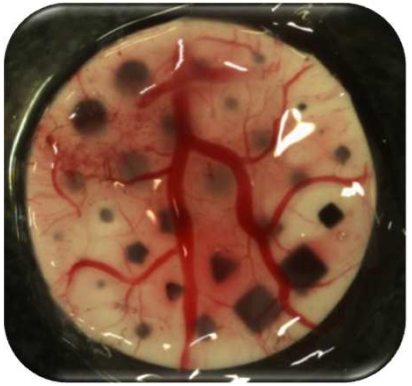


Cellular colonisation *in vitro*



Vascularisation *ex ovo*



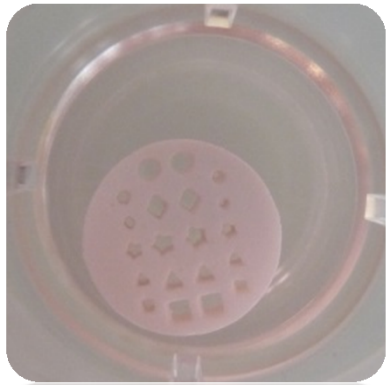


* Collaboration with **Dr Urda Rüdrich**

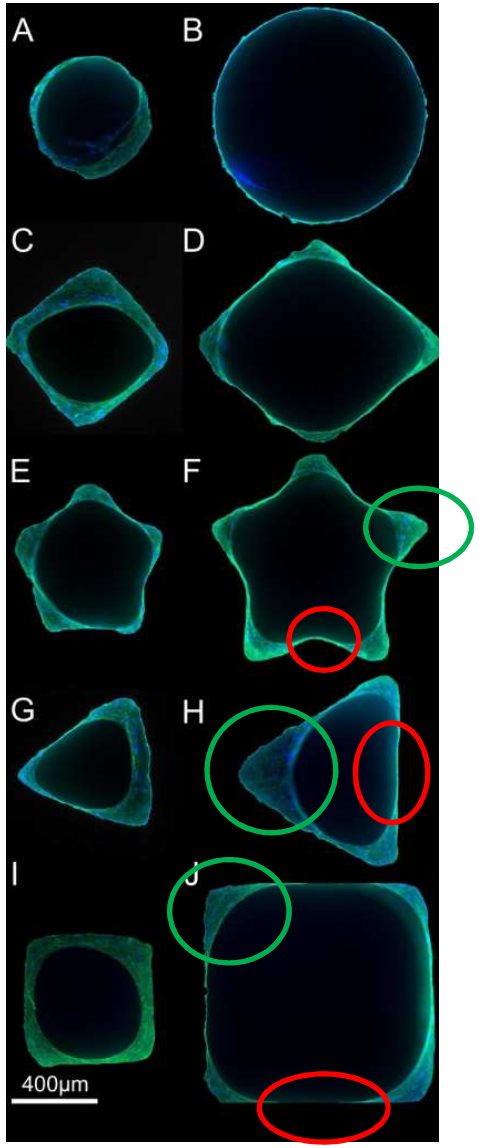
* Collaboration with : **Dr A. Magnaudeix, Dr F. Lalloué**

Biological evaluation

Cellular colonisation *in vitro*



7 days



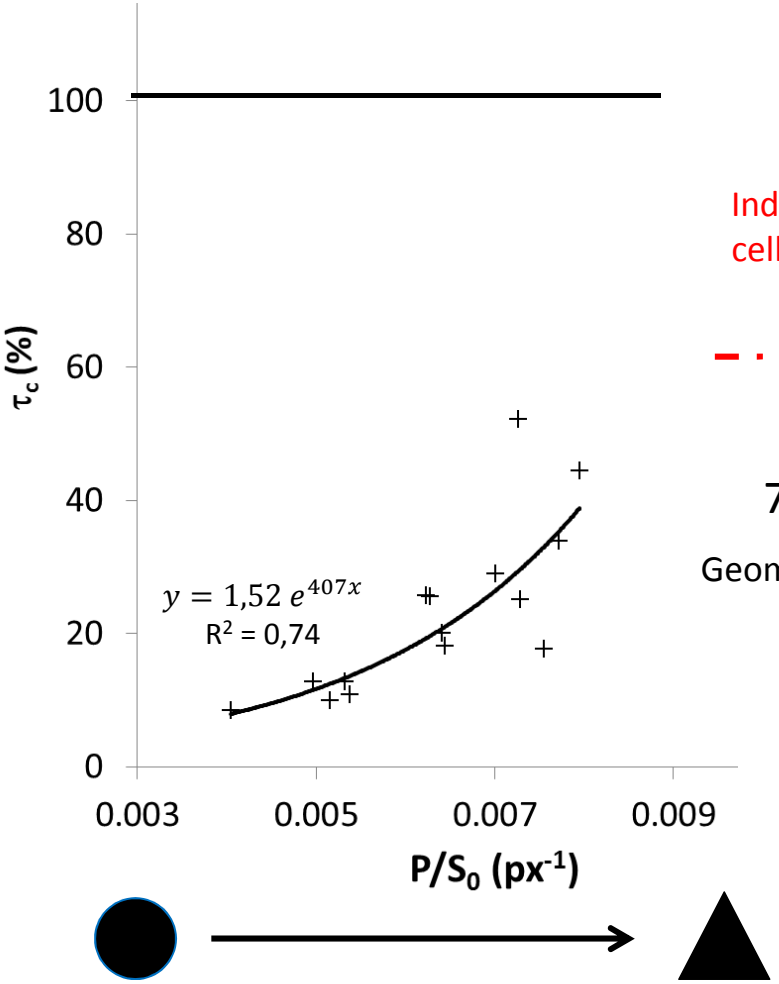
Preferential repartition in sharp angles and concave areas

Flat or convexe edges → migration decrease

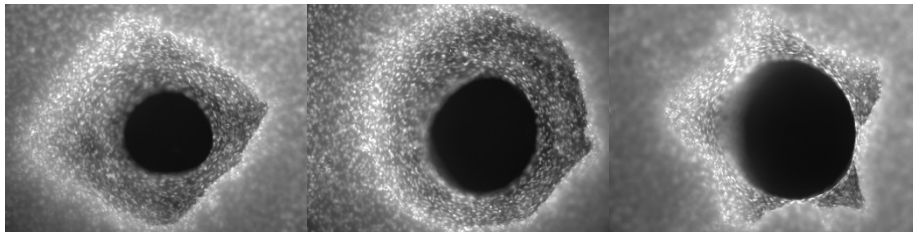
* Collaboration with **Dr Urda Rüdrich**

Biological evaluation

Cellular colonisation *in vitro*

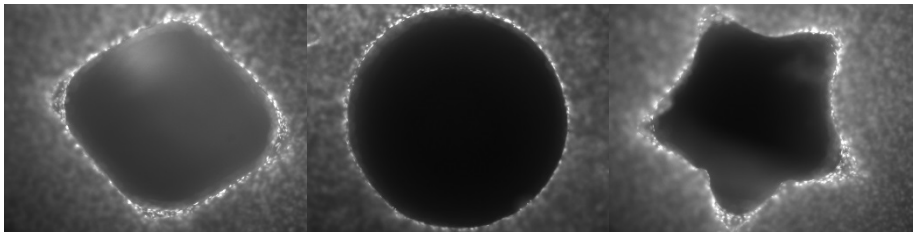


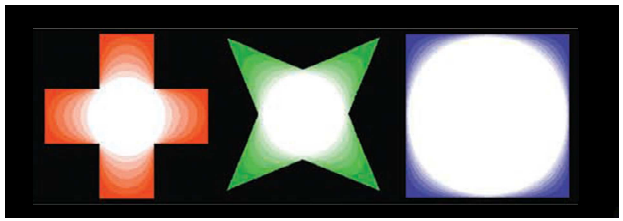
Independent cell behavior



7 days

Geometry effect

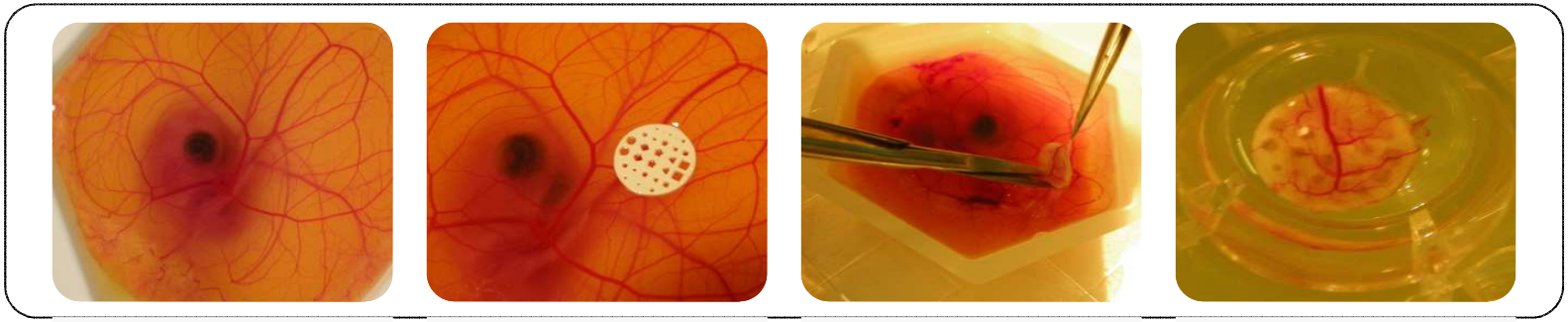




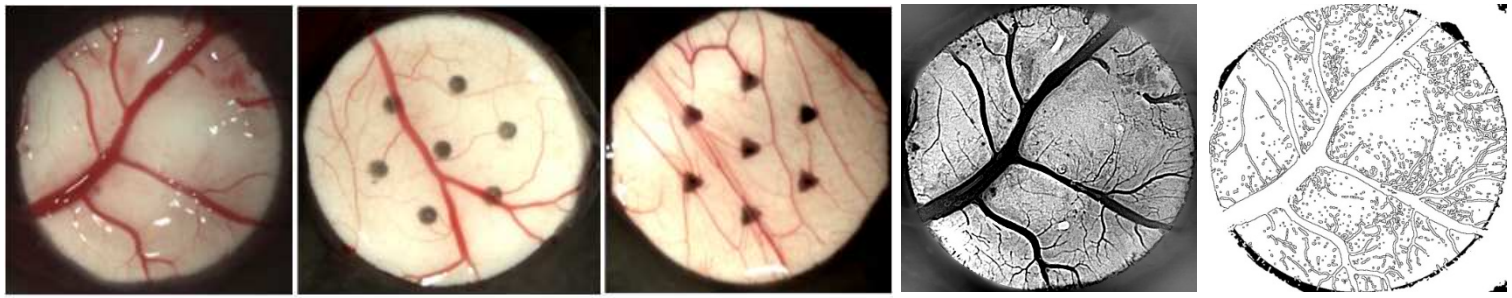
[C. Bidan et al., Adv Healthcare Mater, 2013]

Biological evaluation

Ex ovo : chorioallantoic membrane of the chick embryo



Incubation | Grafting on CAM | Explantation | Observation



Validation of the innovative *ex ovo* method

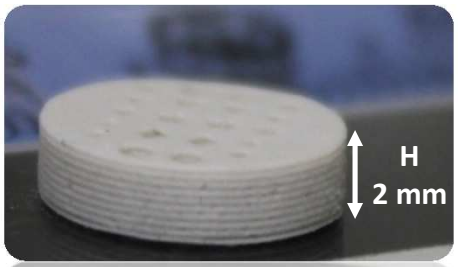
* Collaboration with **Dr A. Magnaudeix, Dr F. Lalloué**

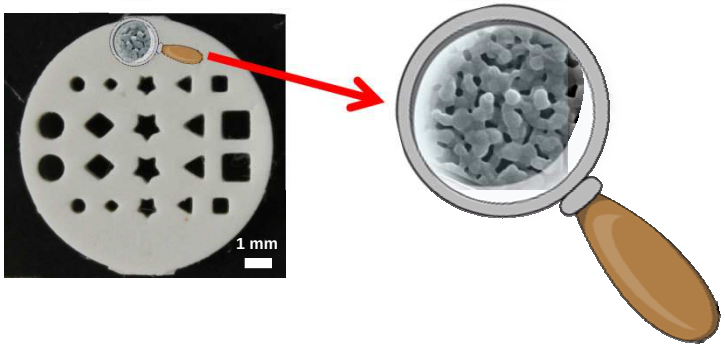
Conclusions

Microstereolithography + Sintering

Adapted technique

Dimensioning model





→ Macro-micro-porous ceramics with controlled architecture in SiHA

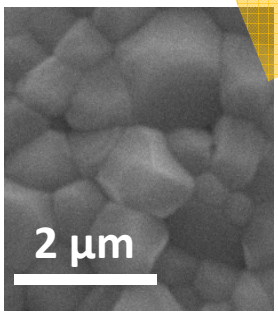
Applications

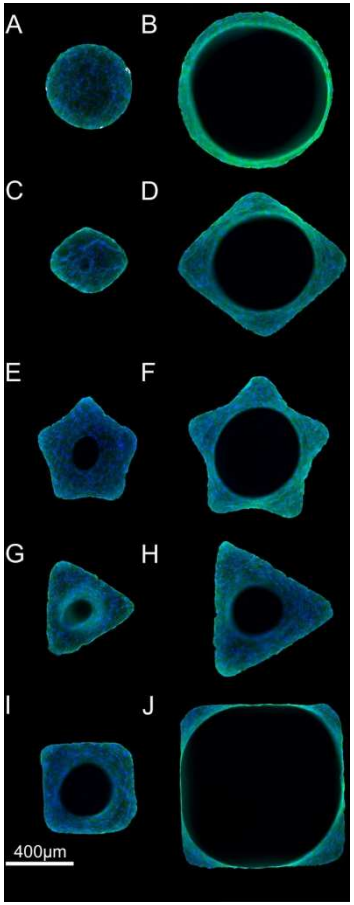
Bone tissue engineering
→ Tailored implants with multiscale porosity

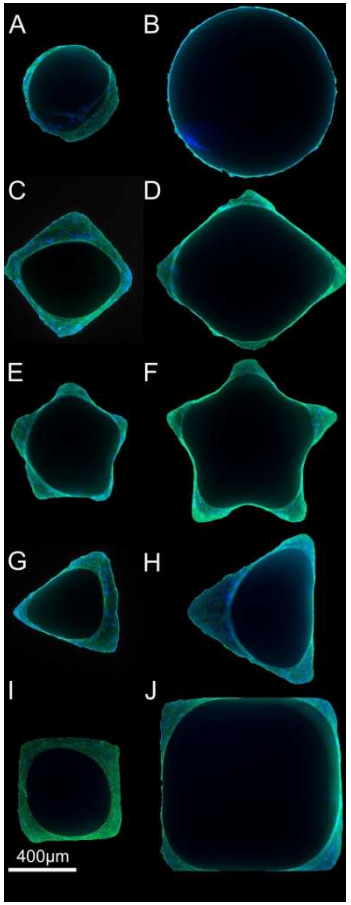
Other applications in ceramic


Thank you for your attention

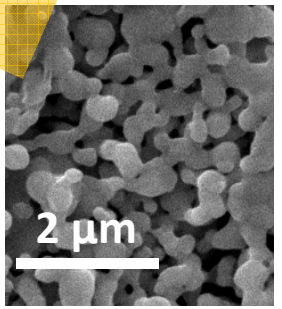
0.5% microporosité





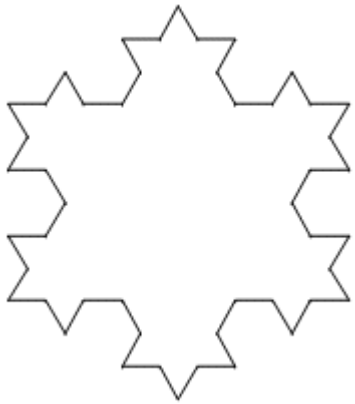


23% microporosité



Work in progress

Salient angles + Maximisation P/S_0 = Broken lines



→ ***In vivo*** **studies of 3D implants with defined porous architecture**