

GN- MEBA

3-4 juillet 2019 - Poitiers

Préparation et observation de composite de ciment de phosphate de calcium injectable (ciment + sang).

Révélation de la structure organique.

François-Xavier Lefèvre, Bruno Bujoli, Jean-Michel Bouler
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INTRODUCTION :

La structure osseuse et substituts osseux



Phase minérale : 65%

Phosphate de calcium de type apatite déficiente en Ca^{2+} : CDA



Phase organique : 25%

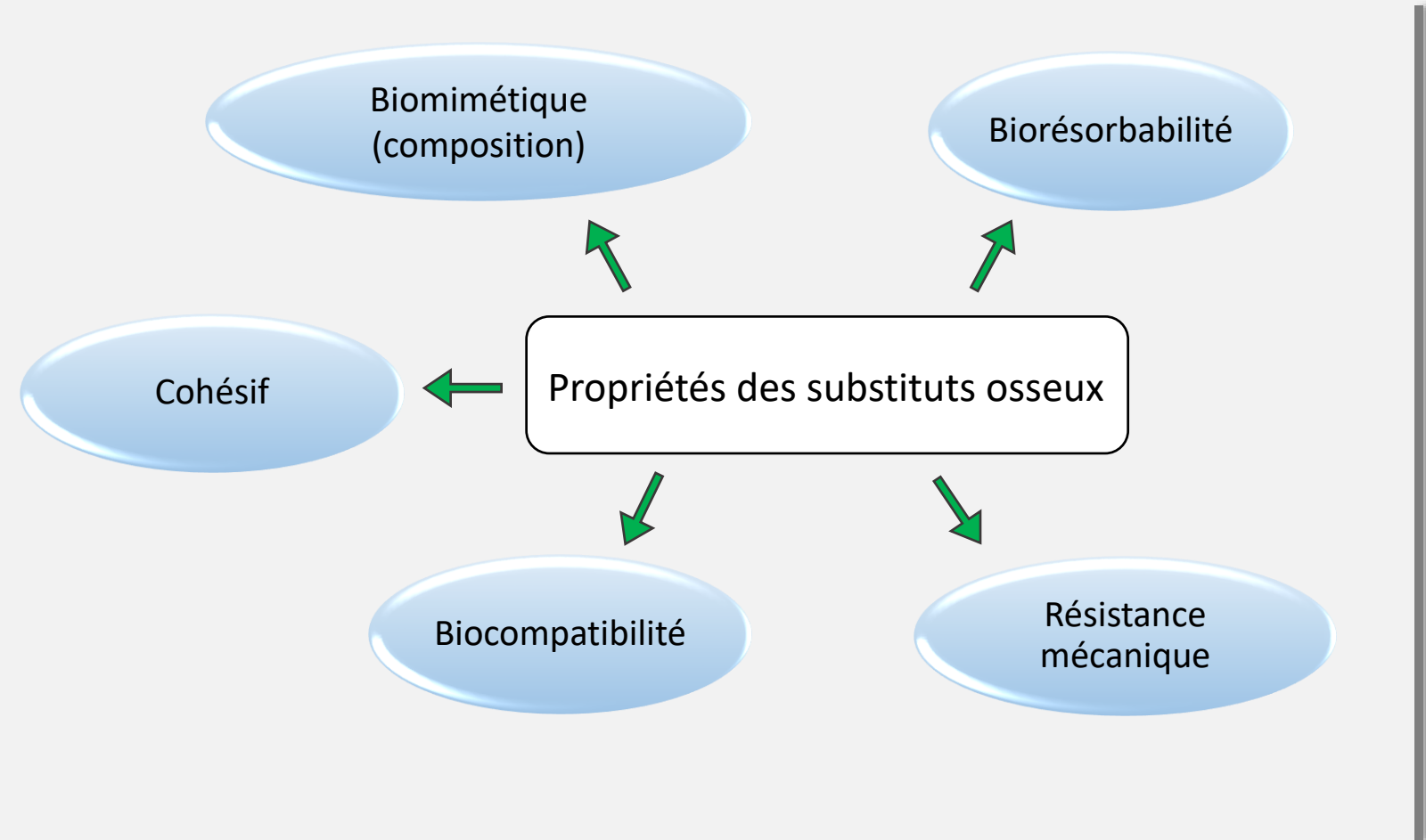
Collagène de type I

Facteurs de croissance

Eau : 10%

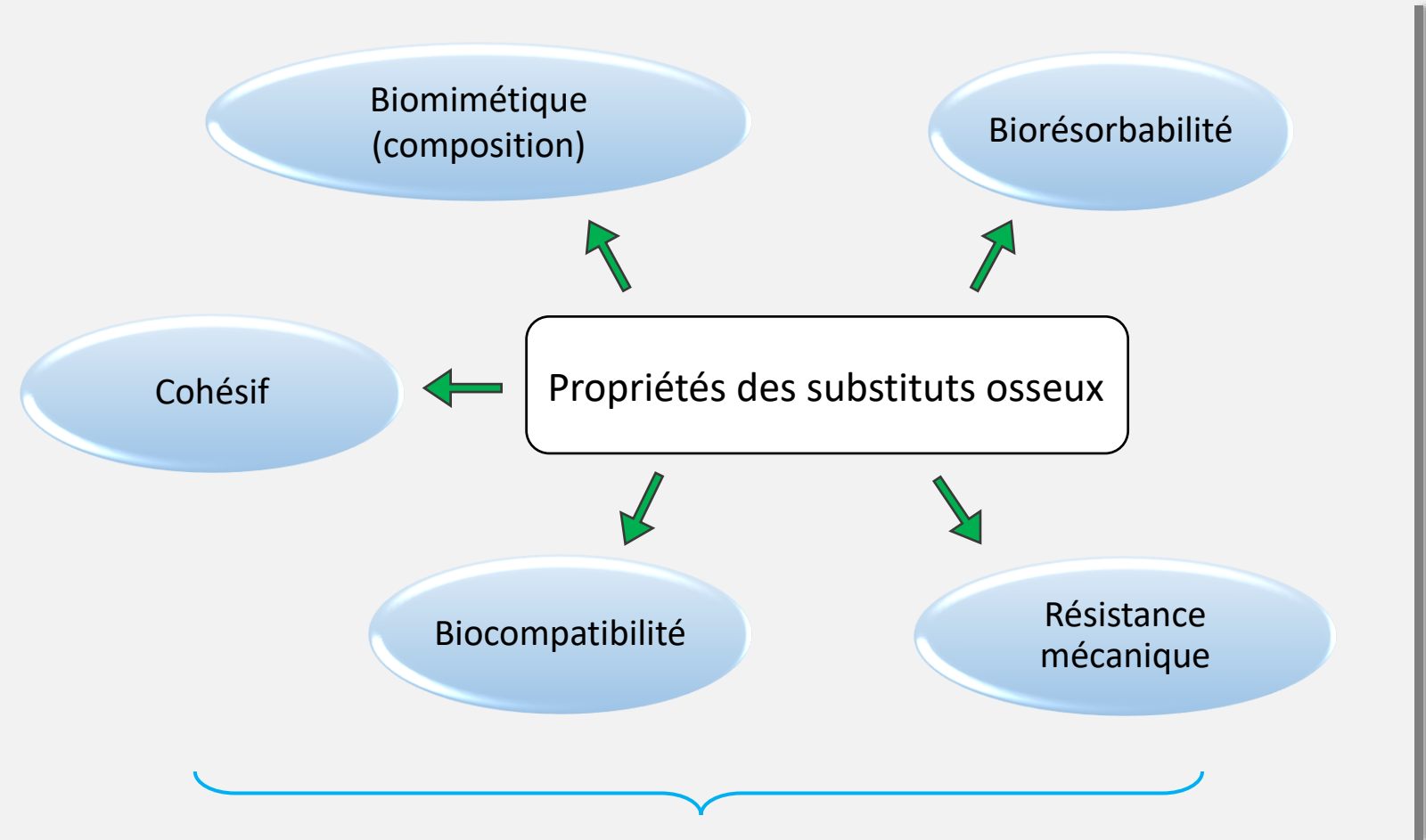
INTRODUCTION :

La structure osseuse et substituts osseux



INTRODUCTION :

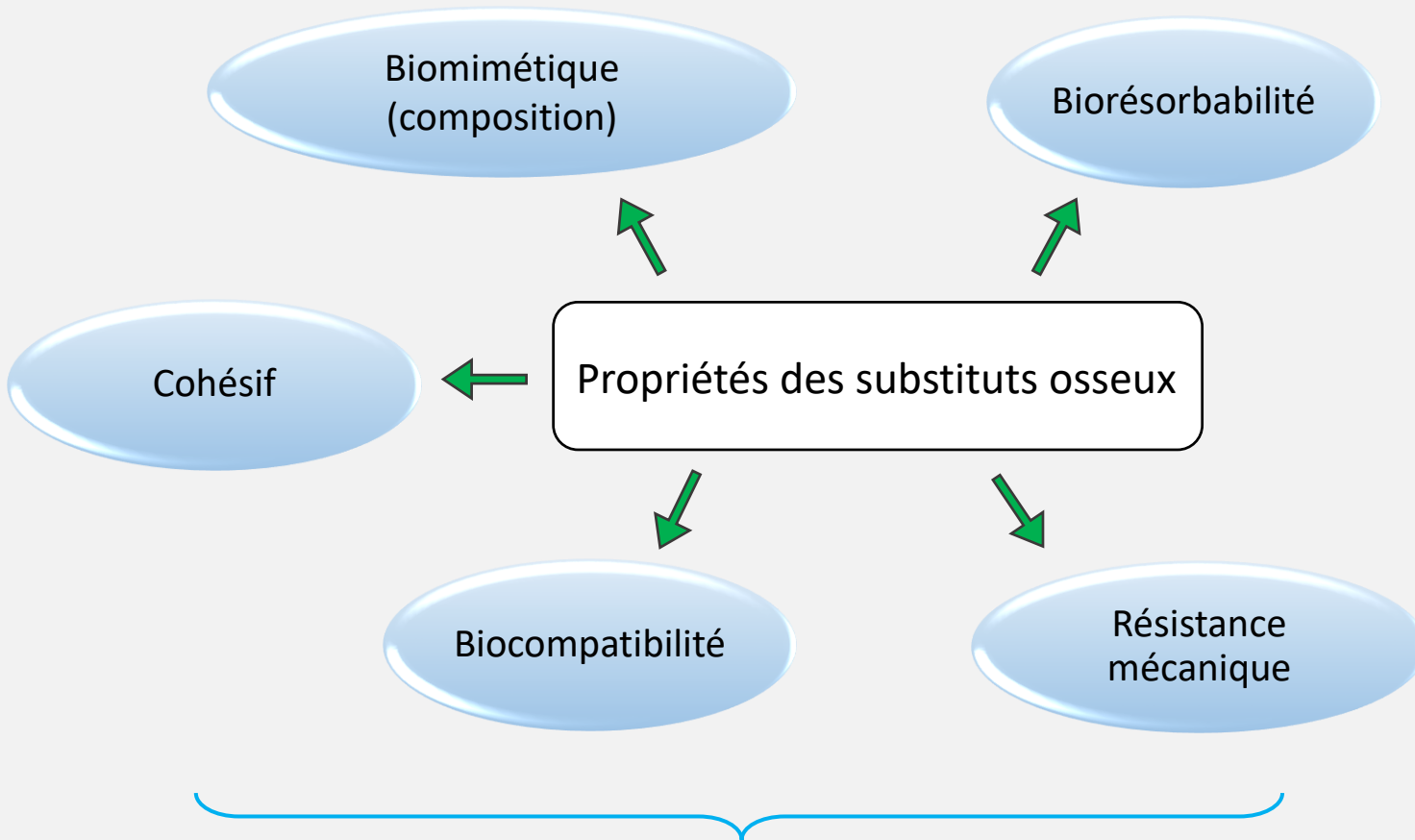
La structure osseuse et substituts osseux



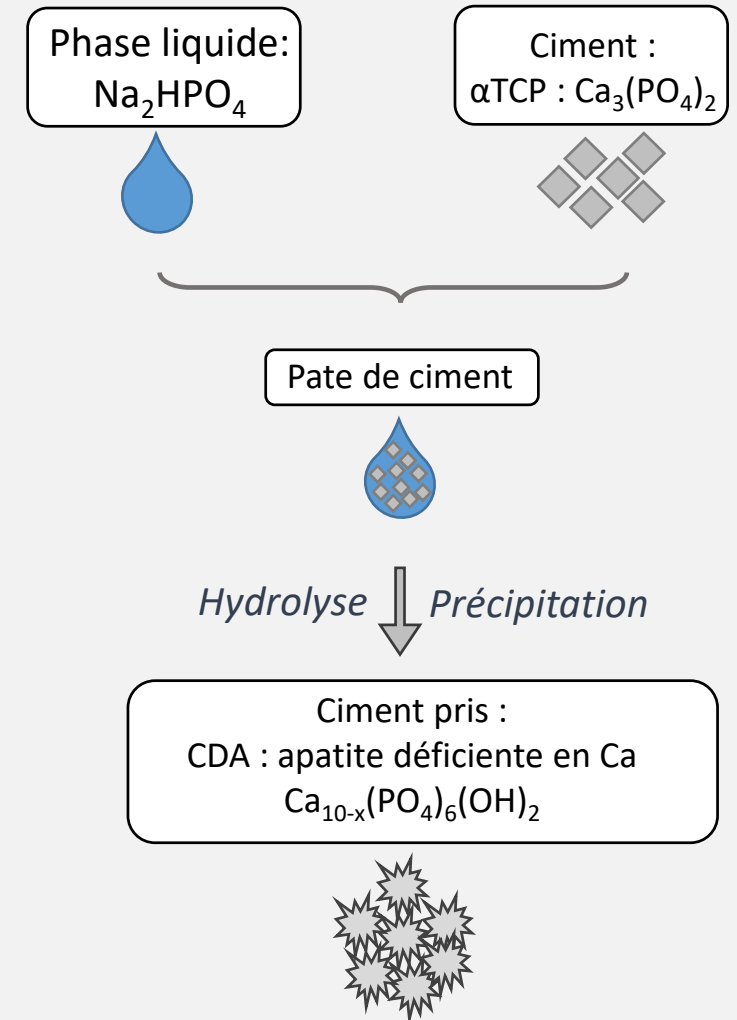
Ciment de phosphate de Ca = bon candidat

INTRODUCTION :

La structure osseuse et substituts osseux

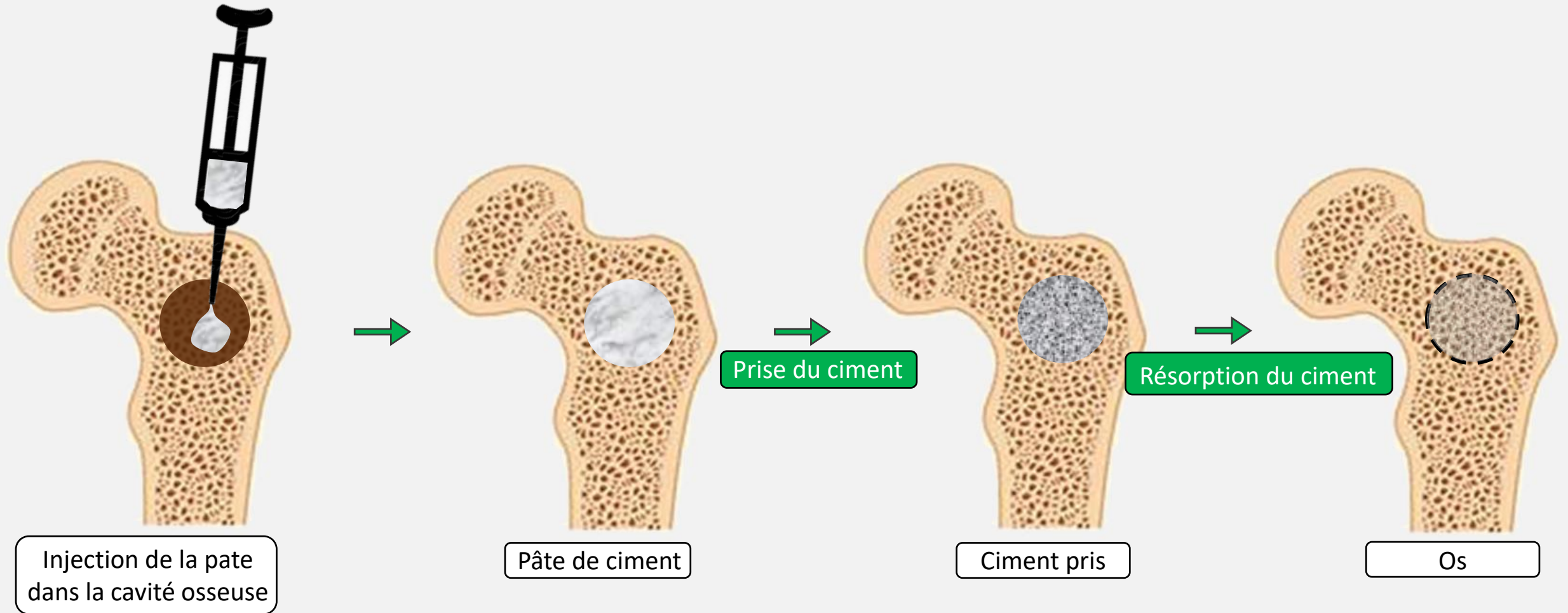


Ciment de phosphate de Ca = bon candidat



INTRODUCTION :

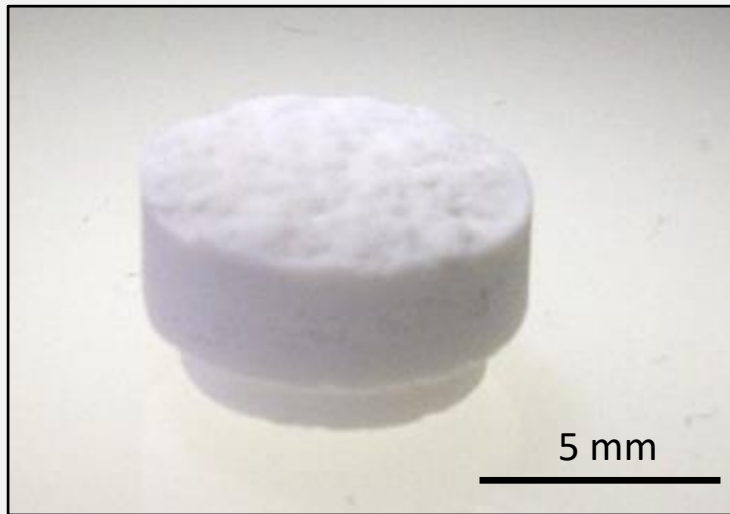
La structure osseuse et substituts osseux



INTRODUCTION :

La structure osseuse et substituts osseux

Ciment



Composite
(ciment + sang)



Composite décalcifié
(sang)

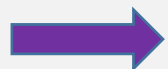
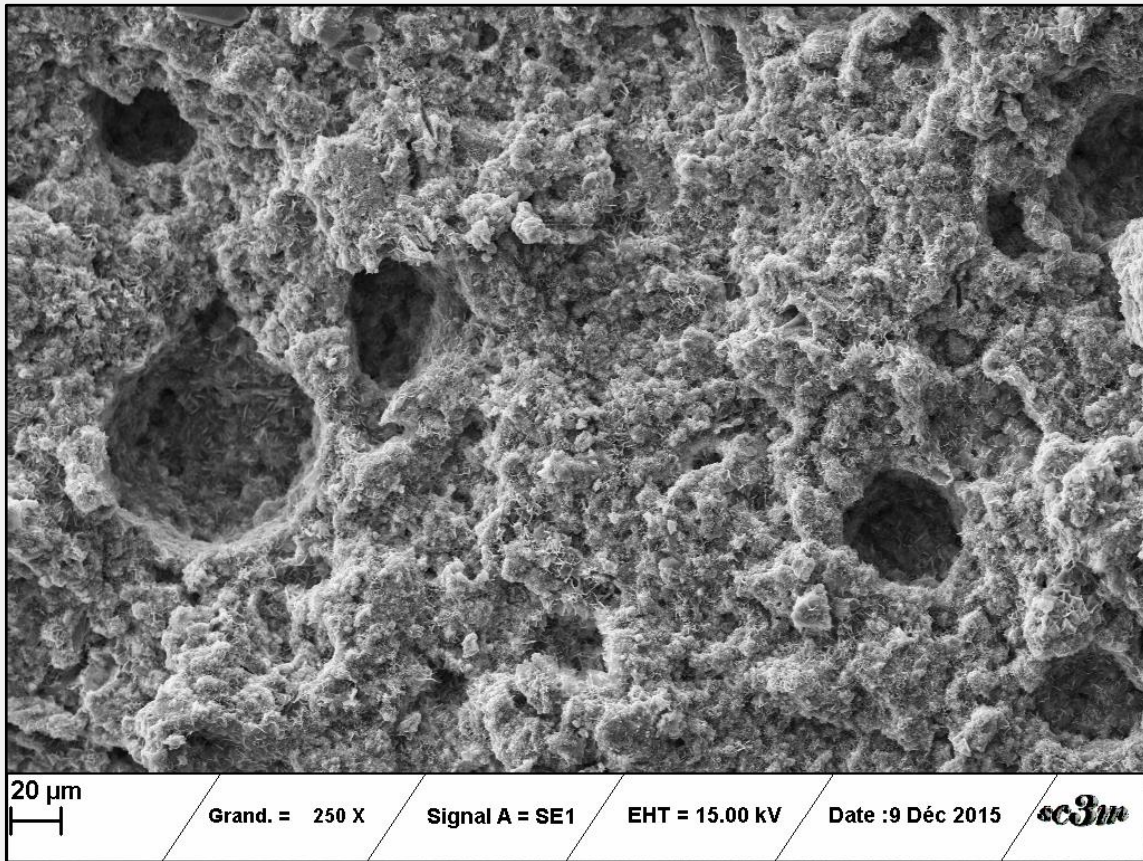


I - Ciment seul

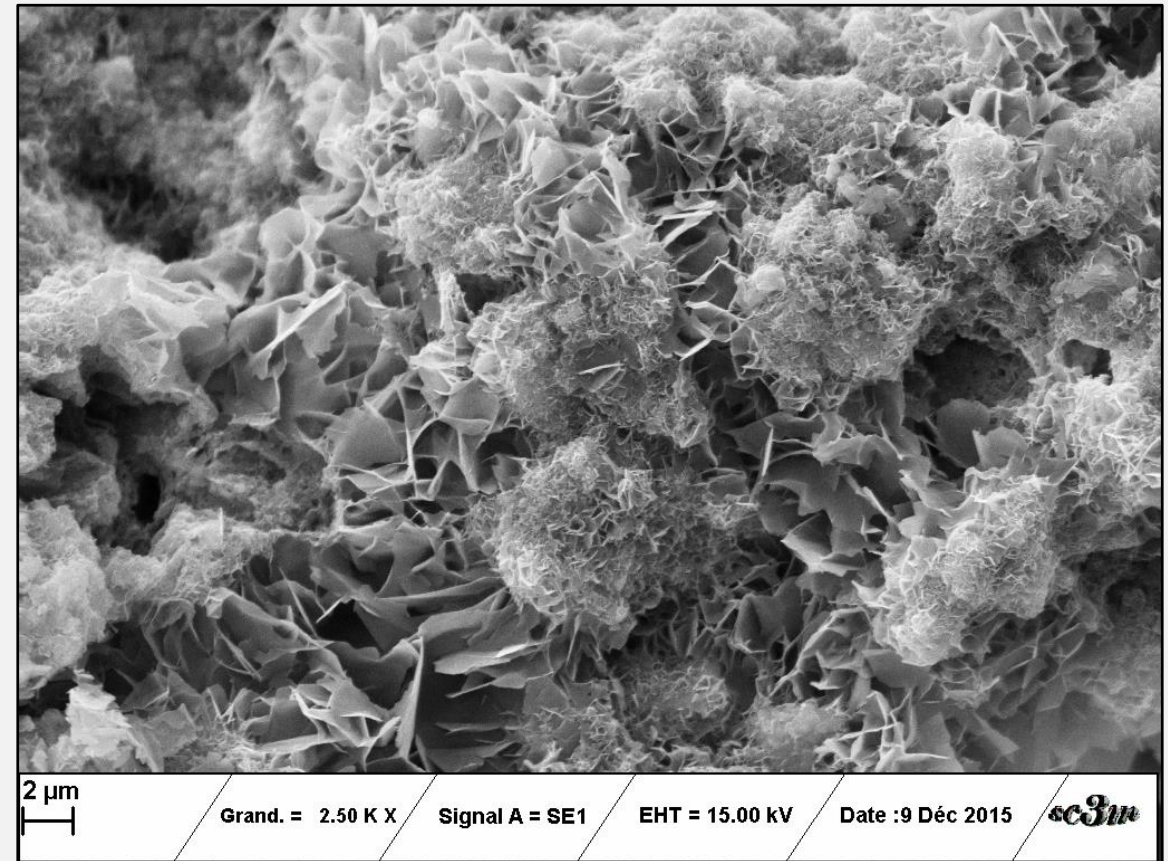
Images sur fracture



Préparation: séchage à l'air - fracture



INFOS : bulles d'air – forme des cristaux



PAS d'INFOS sur la porosité et sur l'intérieur des particules

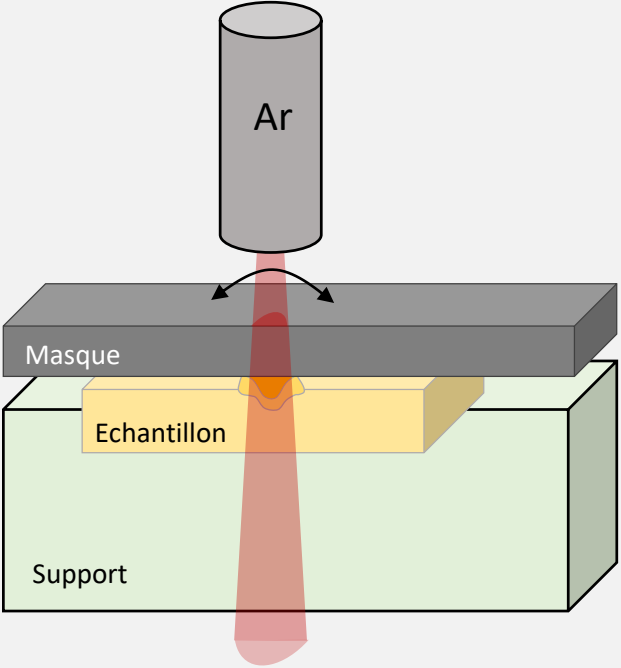
I - Ciment seul

Cross Section Polisher

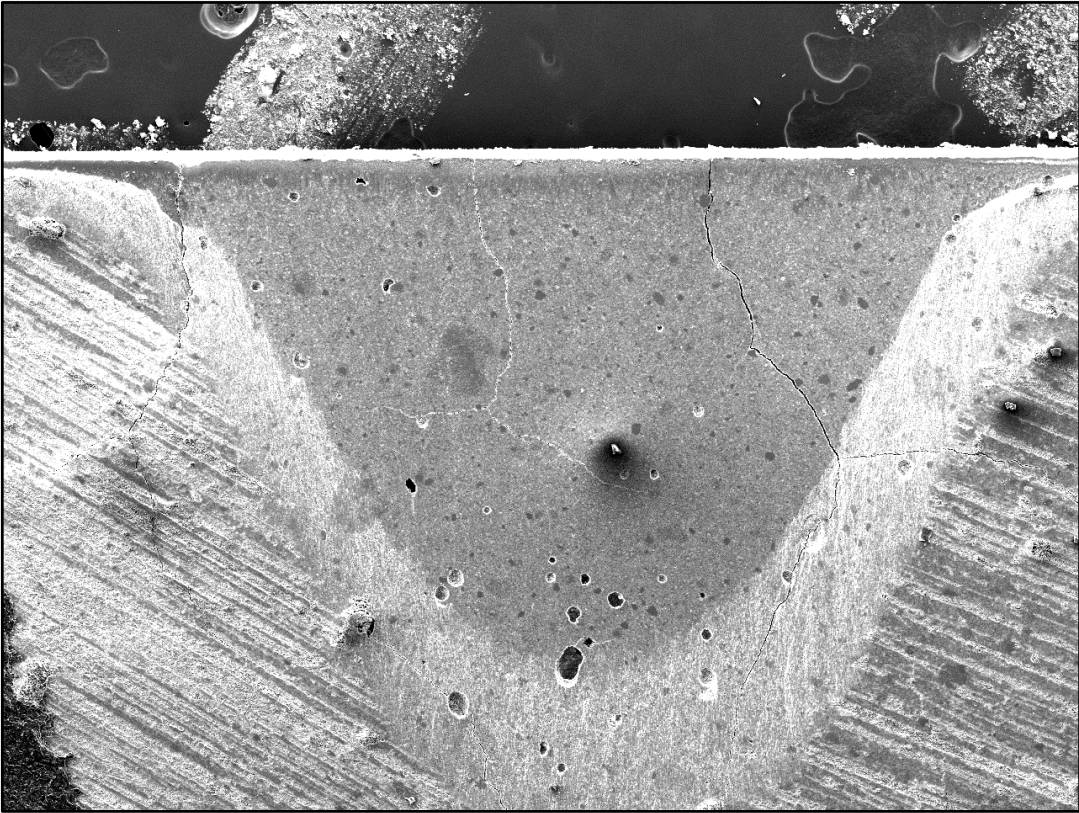
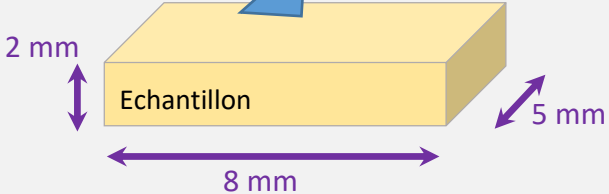


polissage ionique (CSP)

2 à 6 kV - jusqu'à 99 h



1 mm



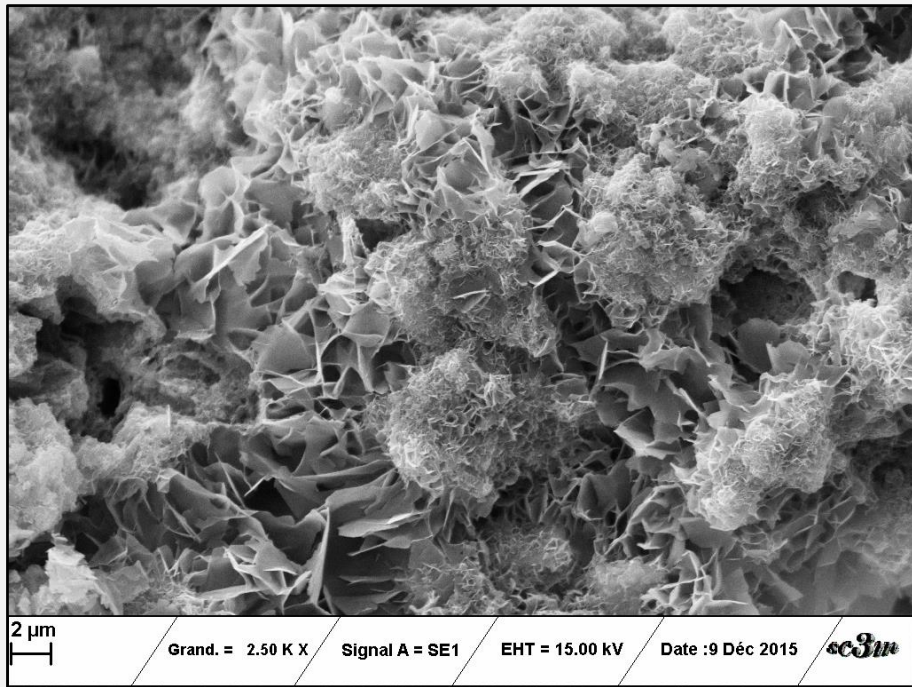
Conditions : 5,5 kV - 5 h

I - Ciment seul

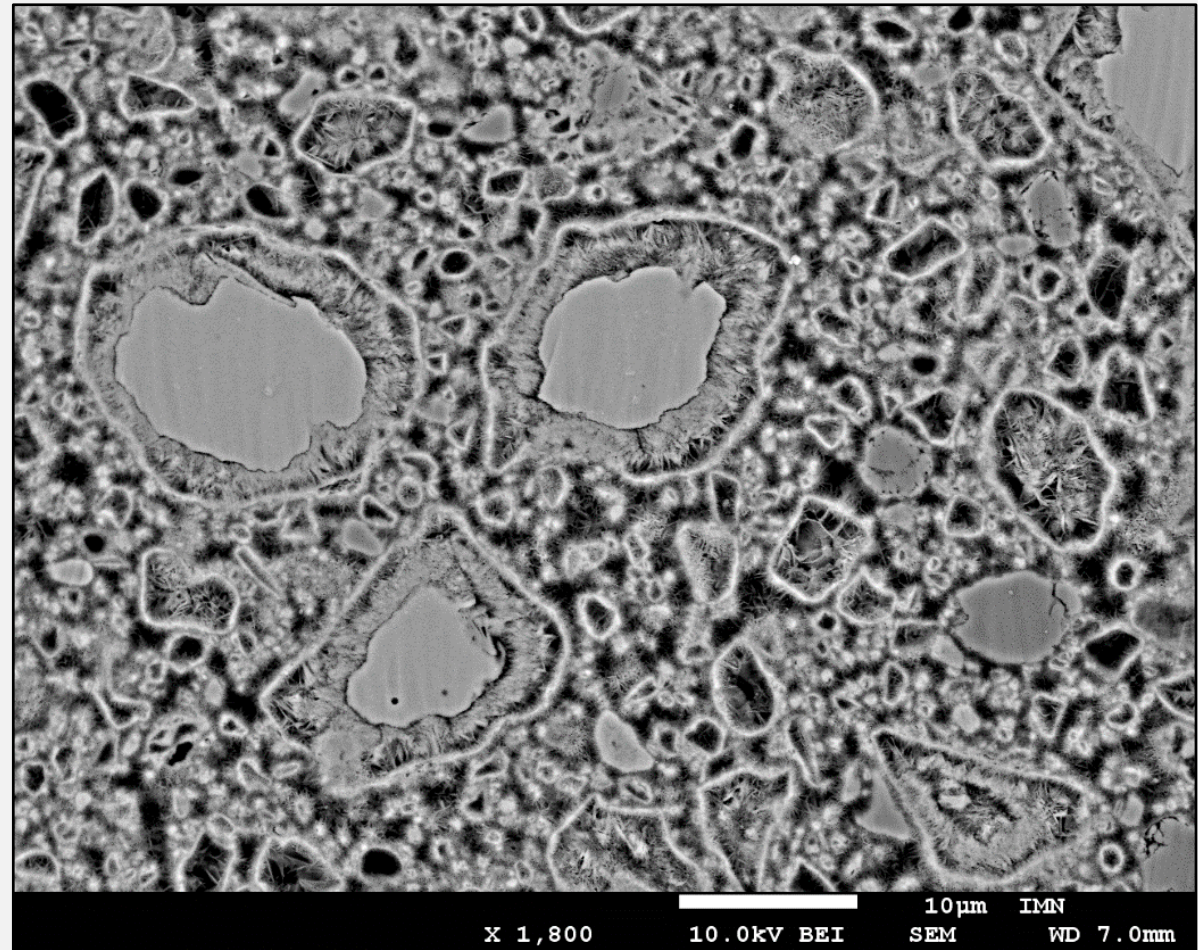
Images sur ciment poli



Préparation: séchage à l'air - CSP



secondaires



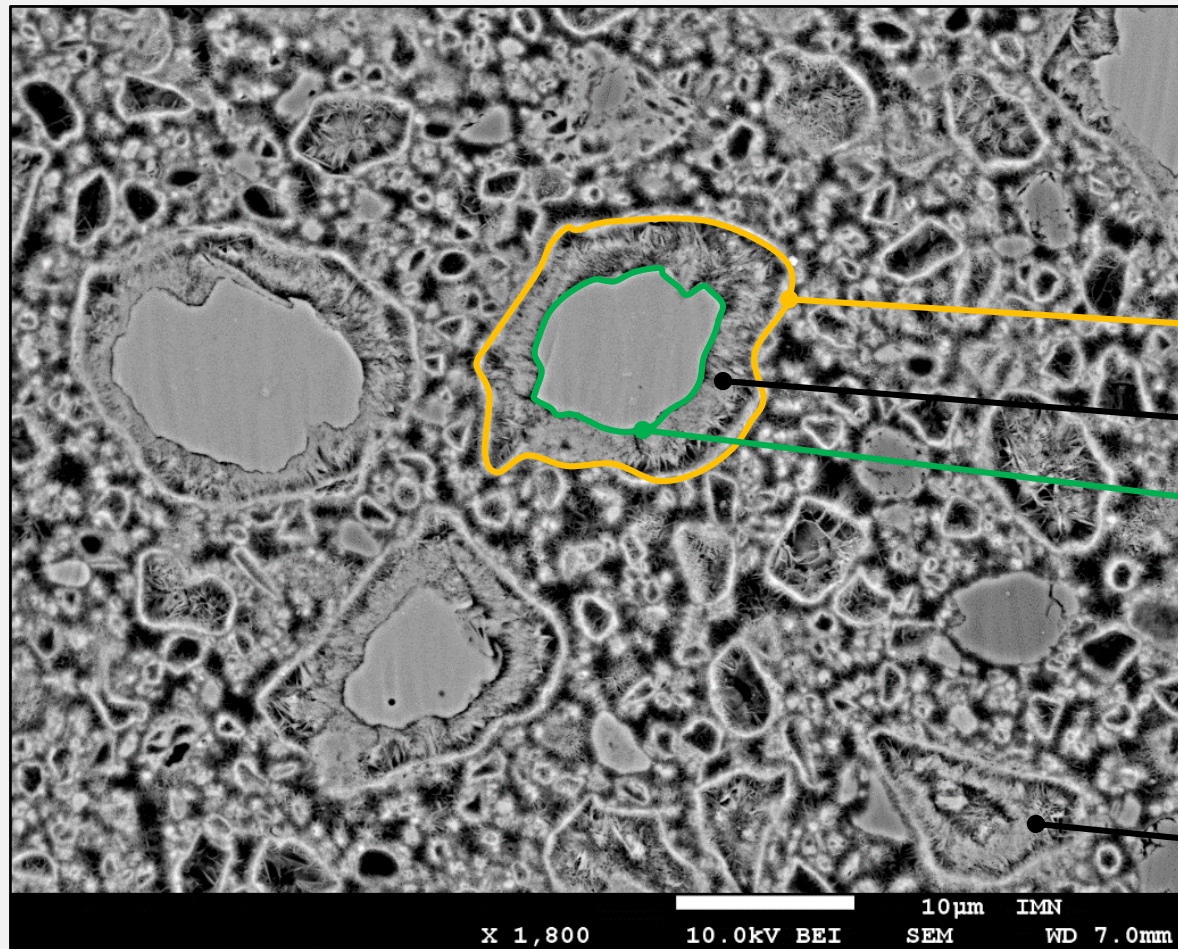
rétrodiffusés

I - Ciment seul

Images sur ciment poli



Préparation: séchage à l'air - CSP



Particule α -TCP originelle

Zone transformée (CDA)

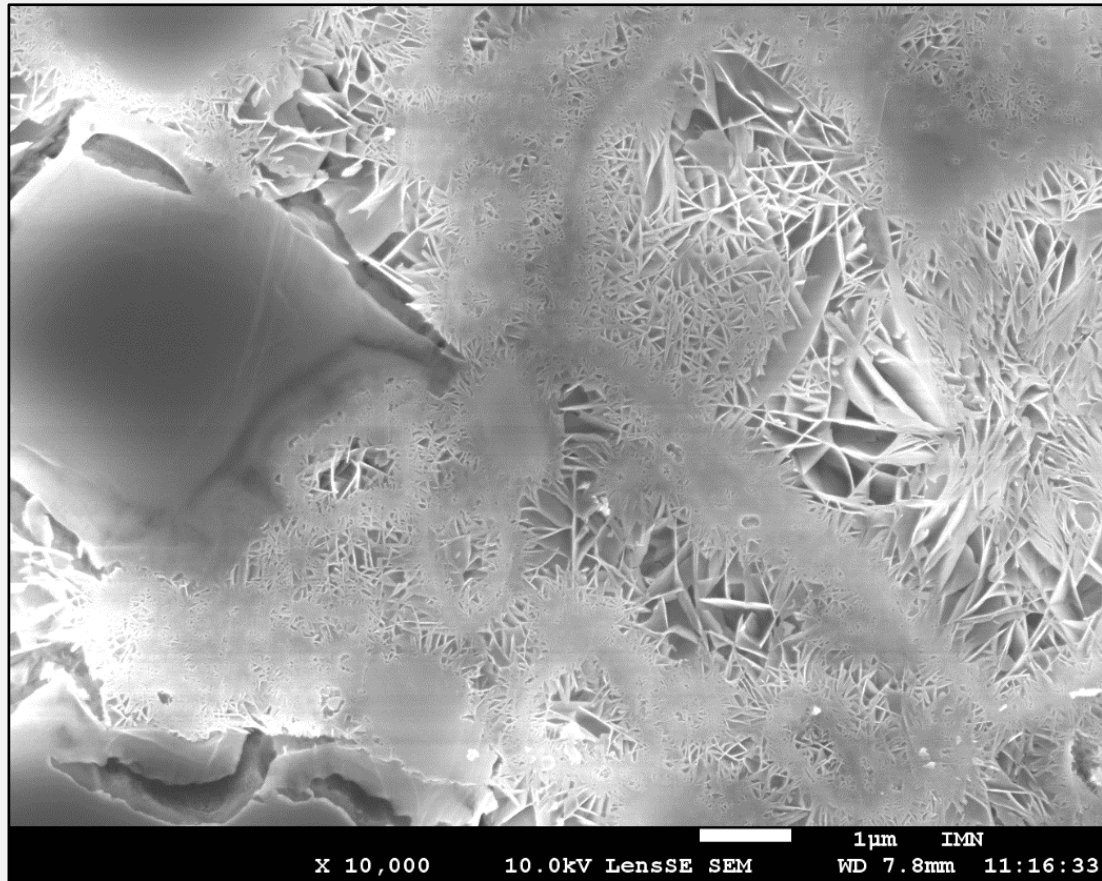
Zone non transformée (α -TCP)

Particule α -TCP complètement transformée

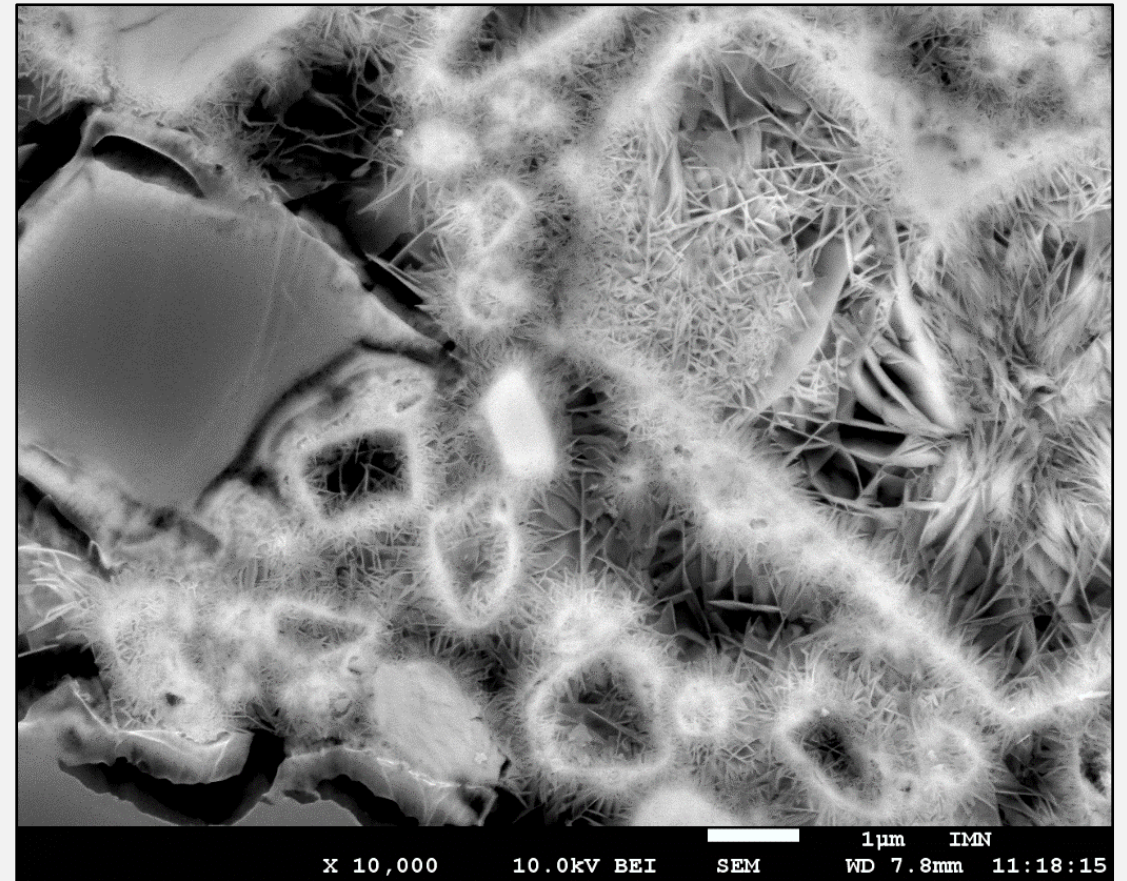
rétrodiffusés

I - Ciment seul

Images sur ciment poli



secondaires

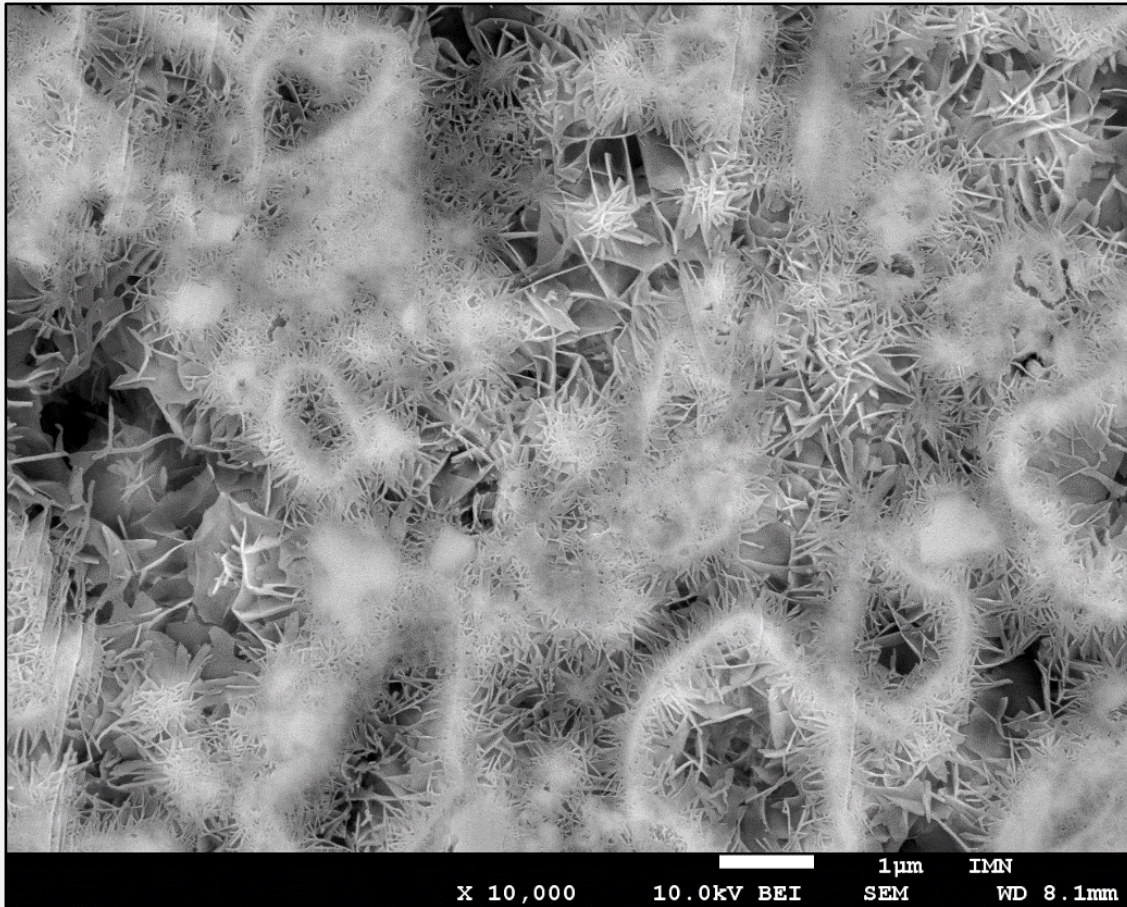


rétrodiffusés

II-Composite MEB sur CSP ciment + sang



Préparation: séchage à l'air - CSP



33 % de sang dans la pate de ciment

90% d'eau dans le sang



3,3 % de matière organique dans le
composite sec

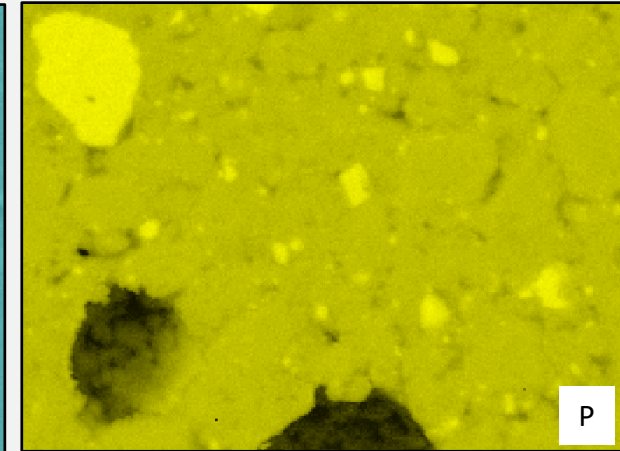
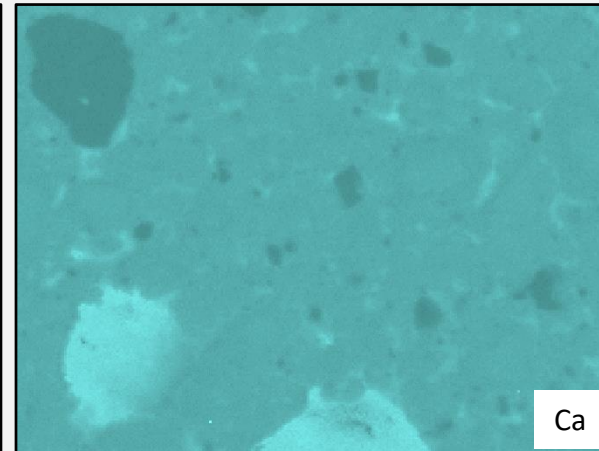
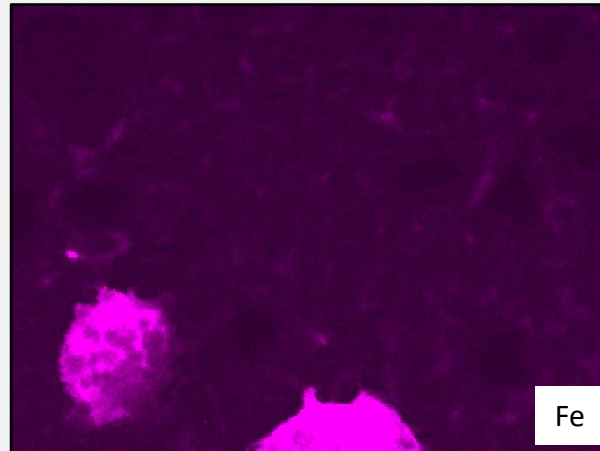
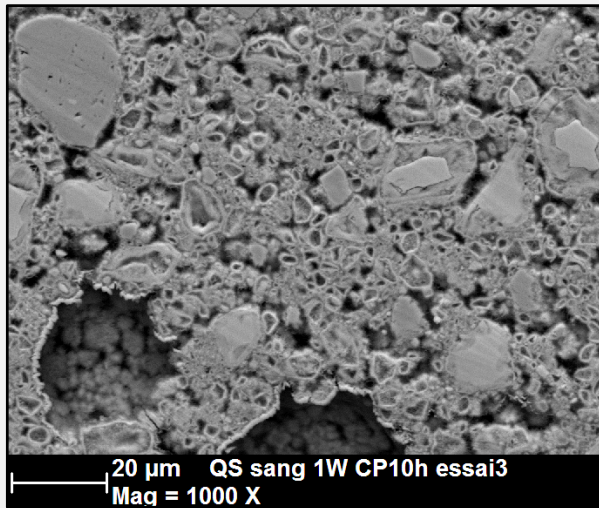
rétrodiffusés

II-Composite

EDS sur CSP ciment + sang



Cartographies A%



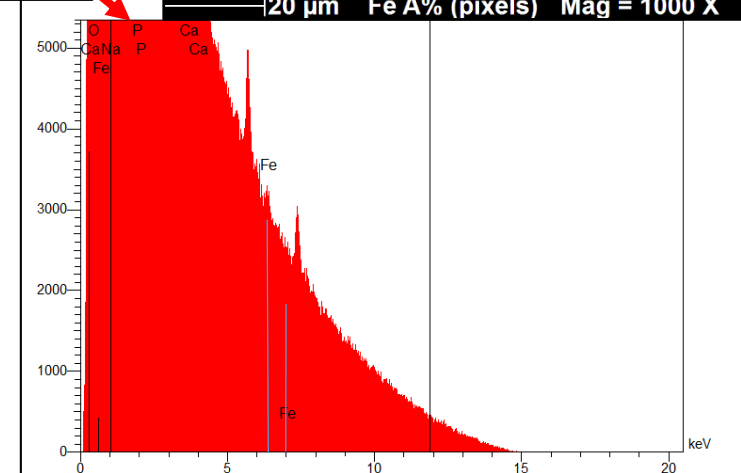
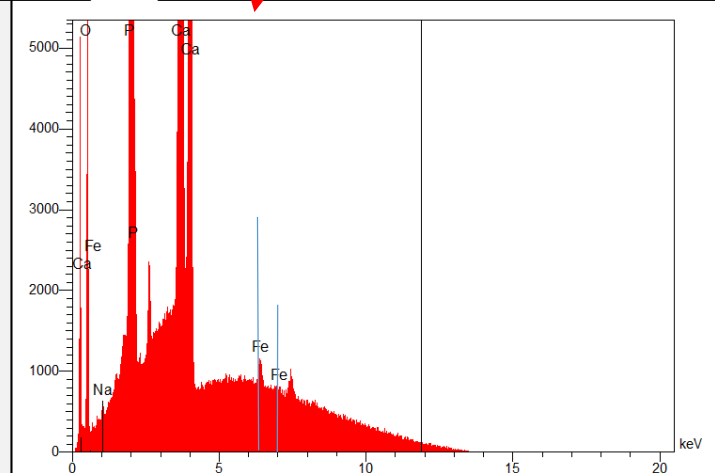
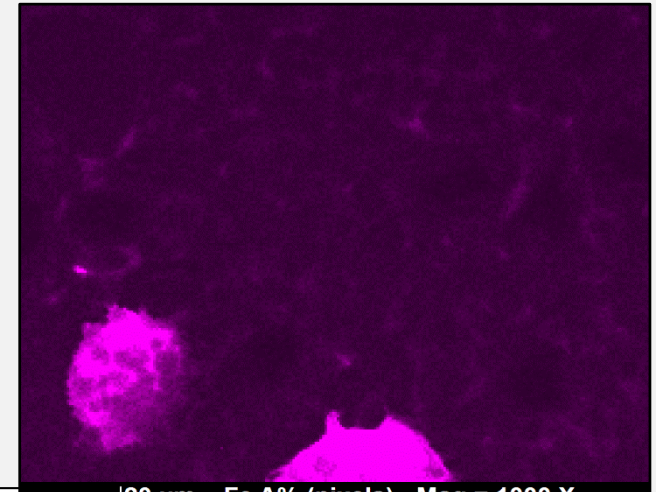
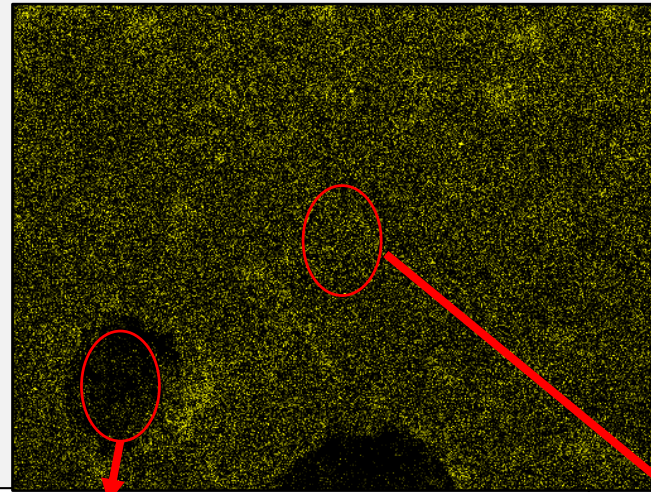
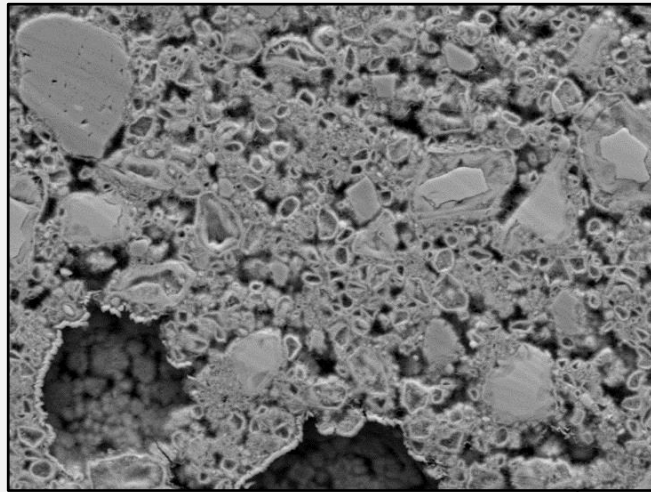
II-Composite

EDS sur CSP ciment + sang



Nombre de coups (Fe)

% atomique (Fe)

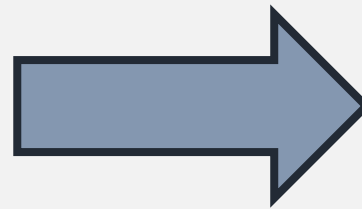


III-Composite décalcifié

Décalcification des composites



Composite
(ciment + sang)



Composite décalcifié
(sang)



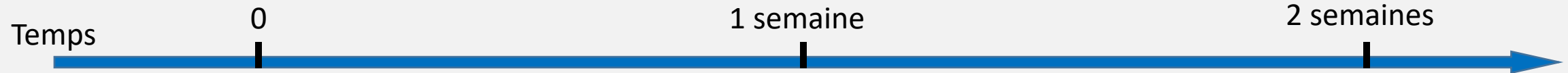
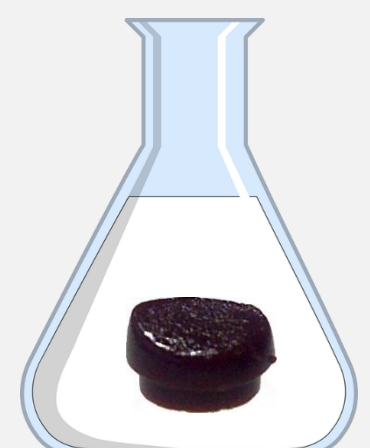
III-Composite décalcifié

Décalcification des composites



EDTA + NaOH 10% masse
pH 7
30 mL

Renouvellement:
EDTA + NaOH 10% masse
pH 7
30 mL



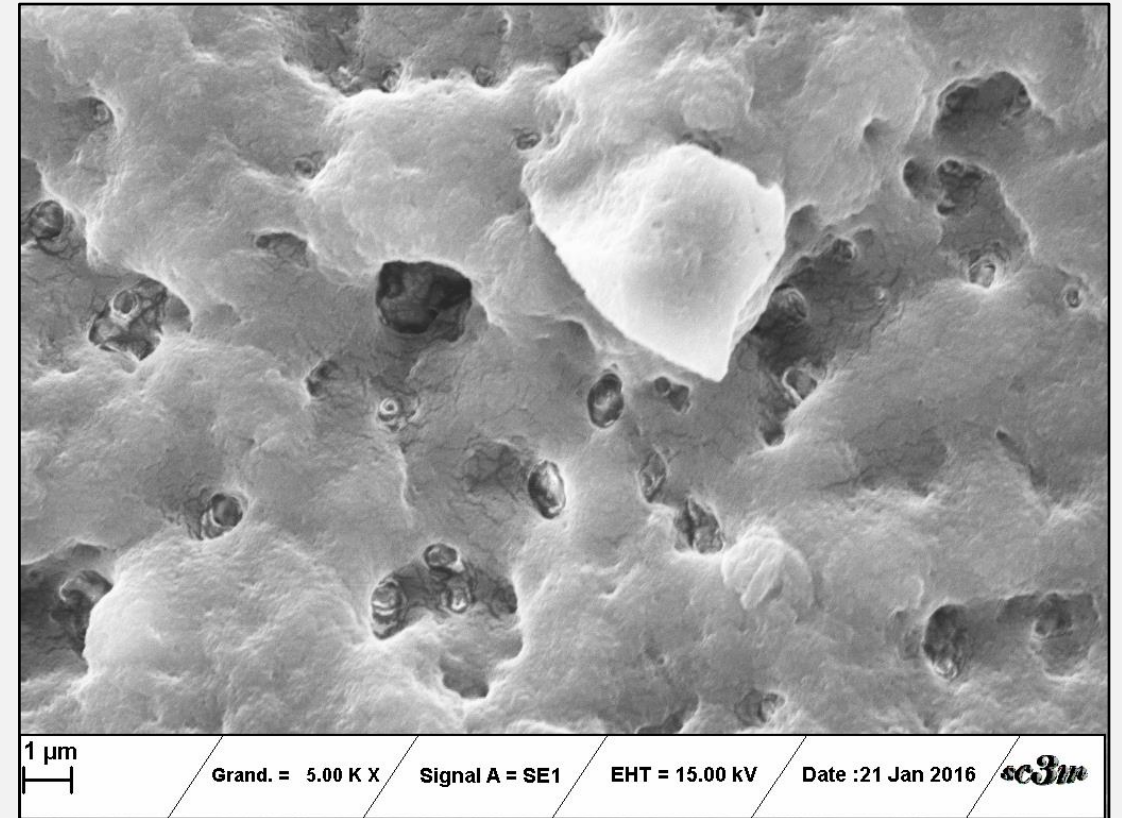
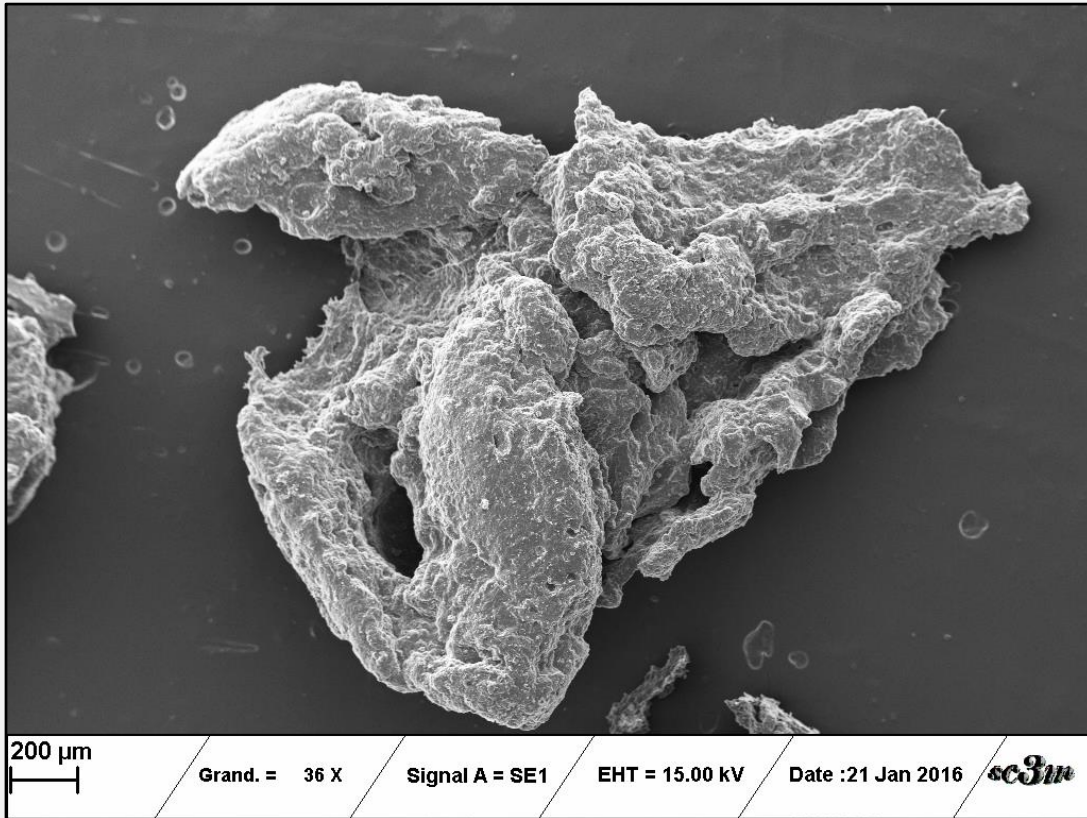
Agitation légère à la main tous les jours

III-Composite décalcifié

Séchage normal



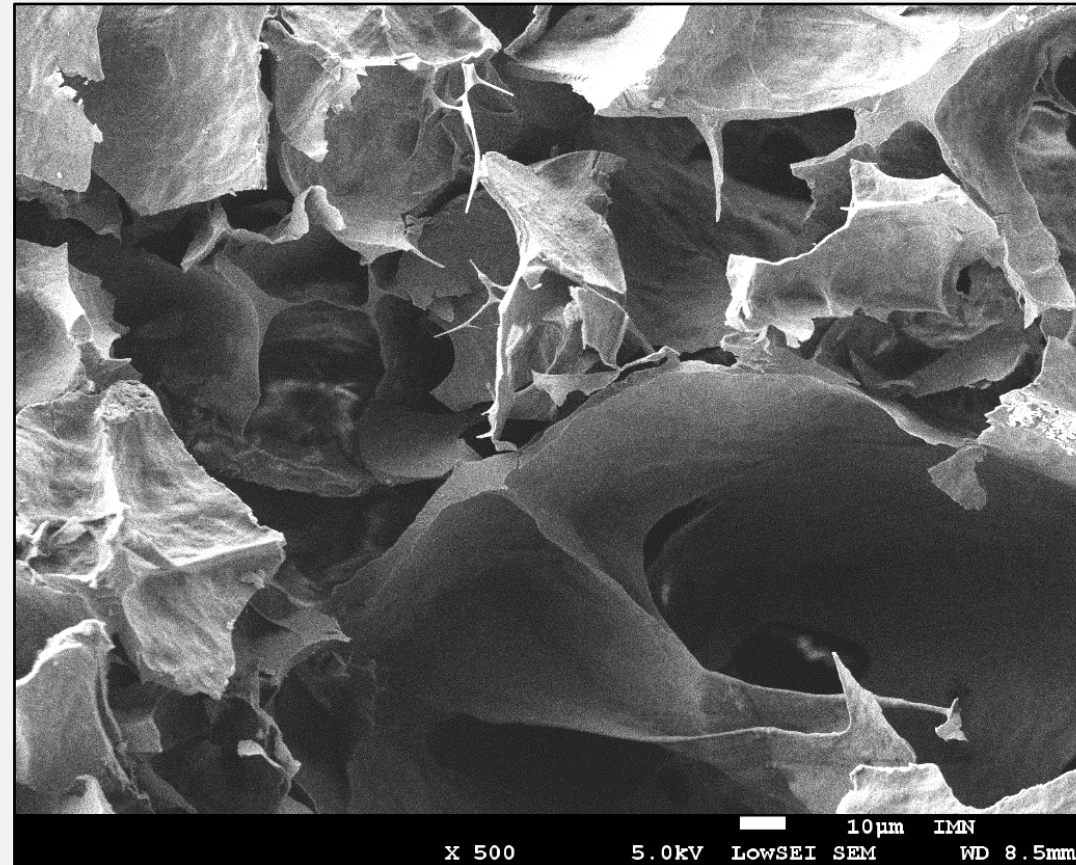
Séchage à l'air



III-Composite décalcifié Lyophilisateur

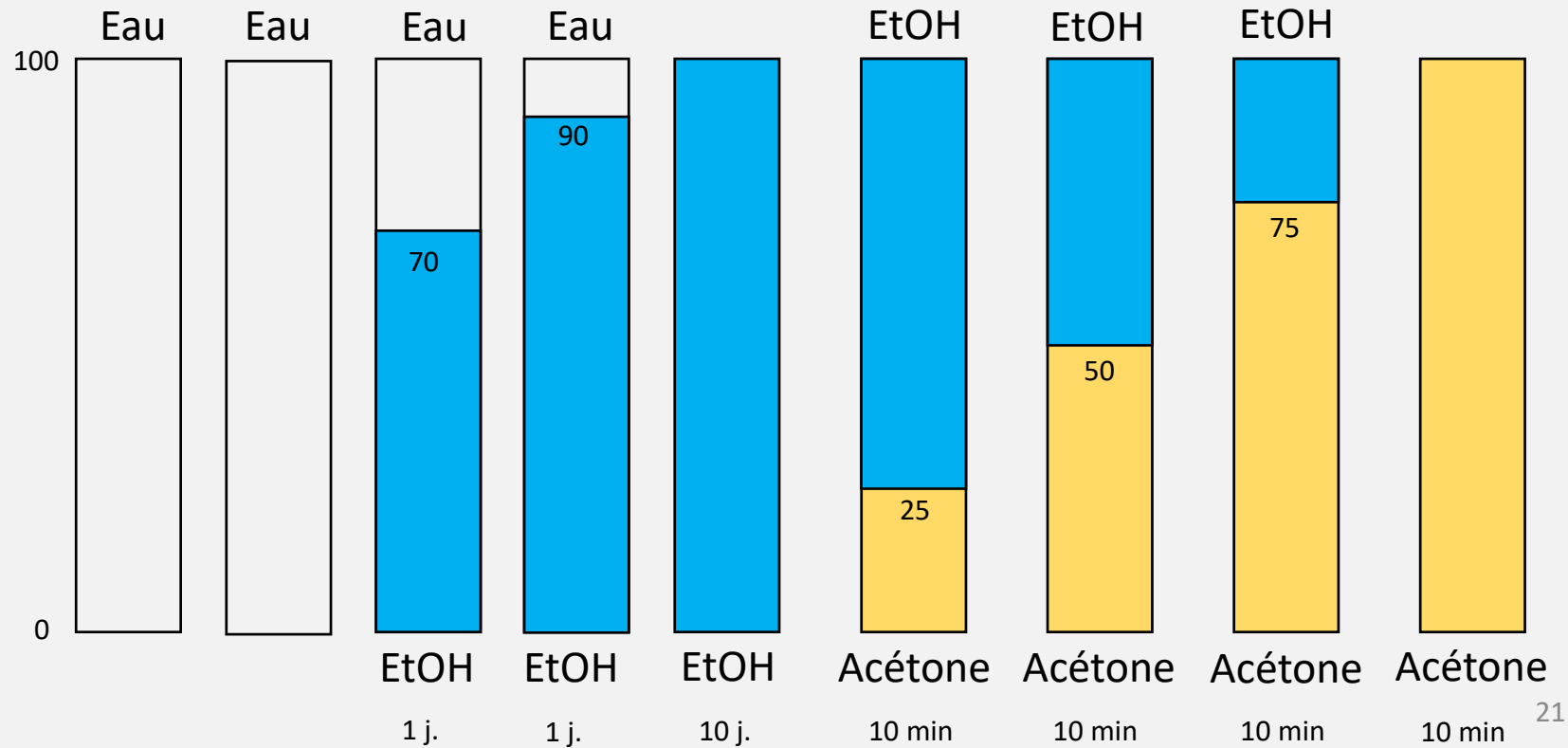
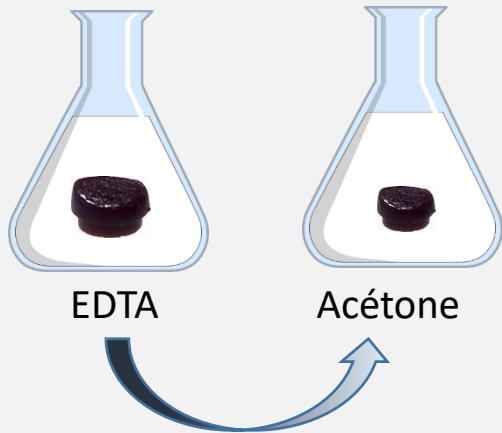


Séchage au lyophilisateur :



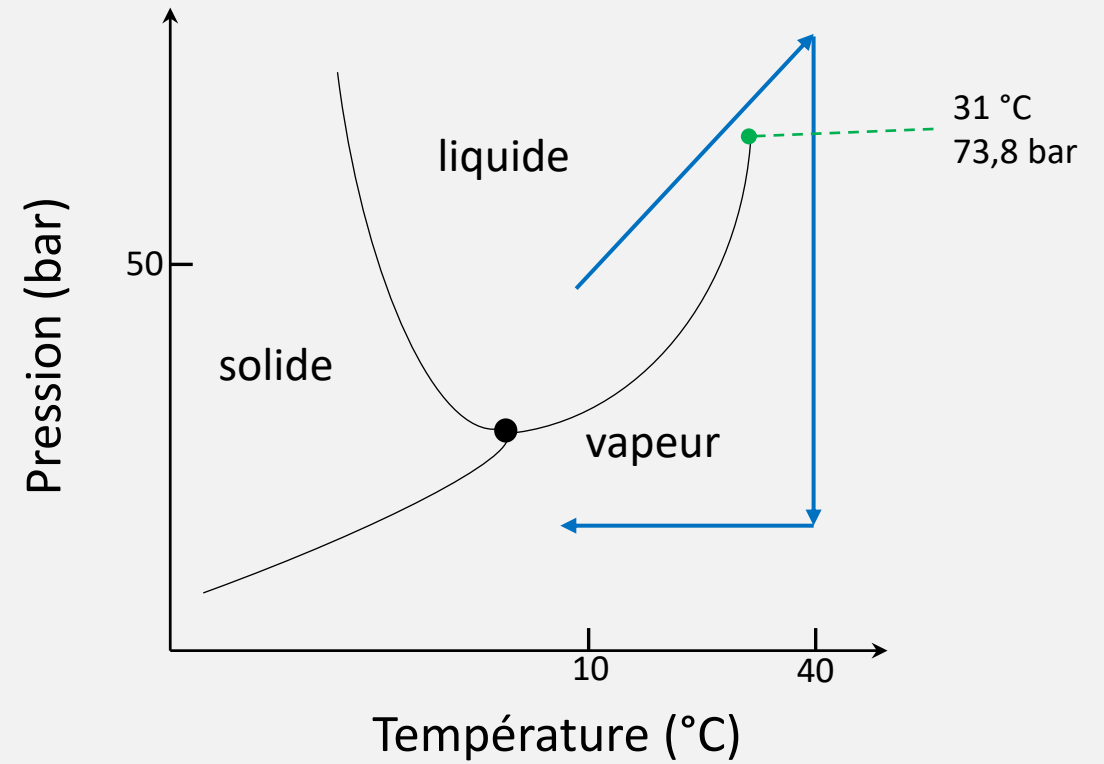
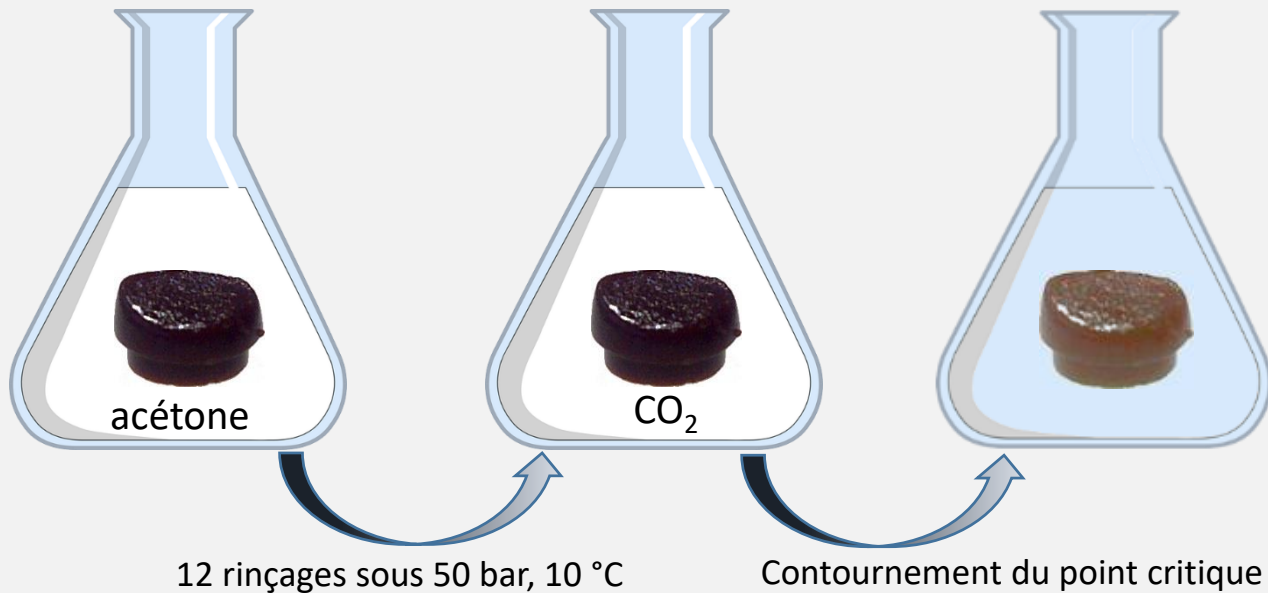
III-Composite décalcifié

Contournement de point critique – CO₂

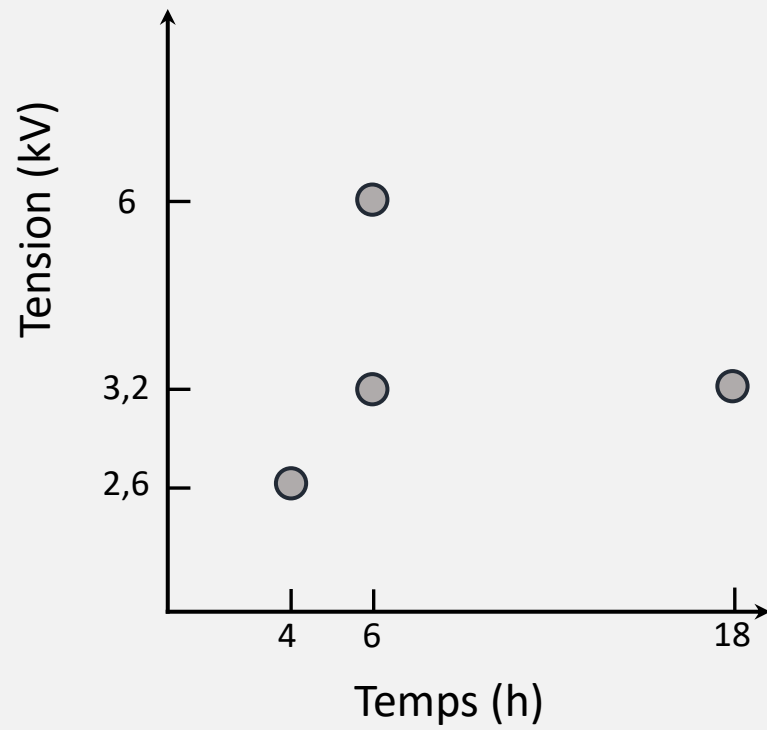


III-Composite décalcifié

Contournement de point critique – CO₂



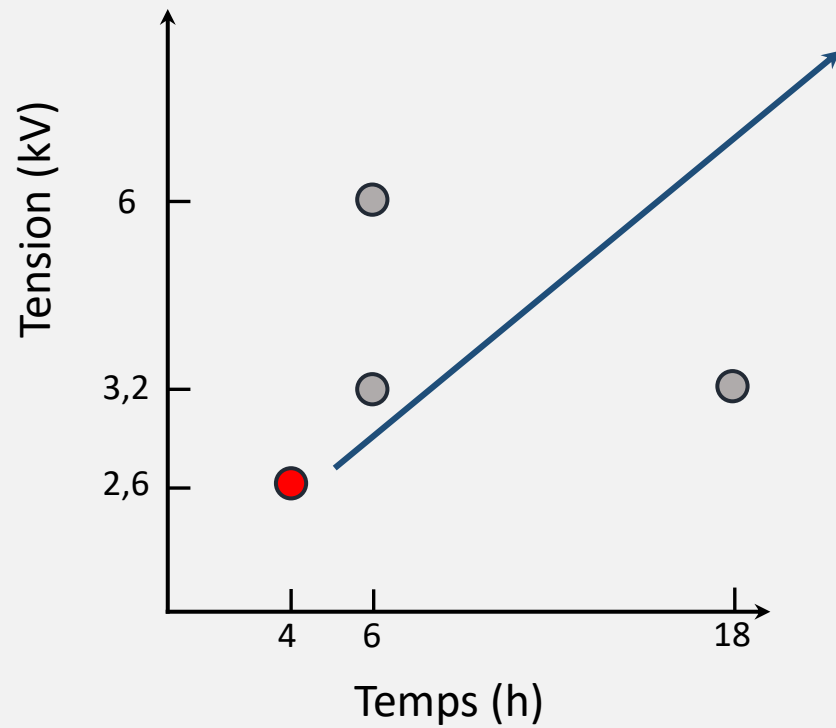
III-Composite décalcifié CSP : différents réglages



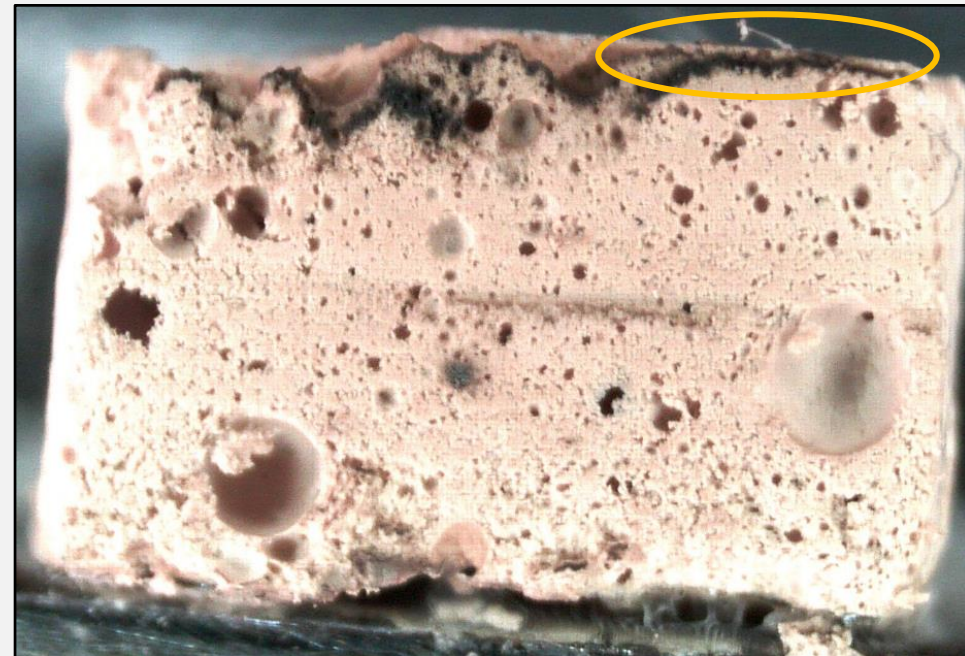
III-Composite décalcifié CSP : différents réglages



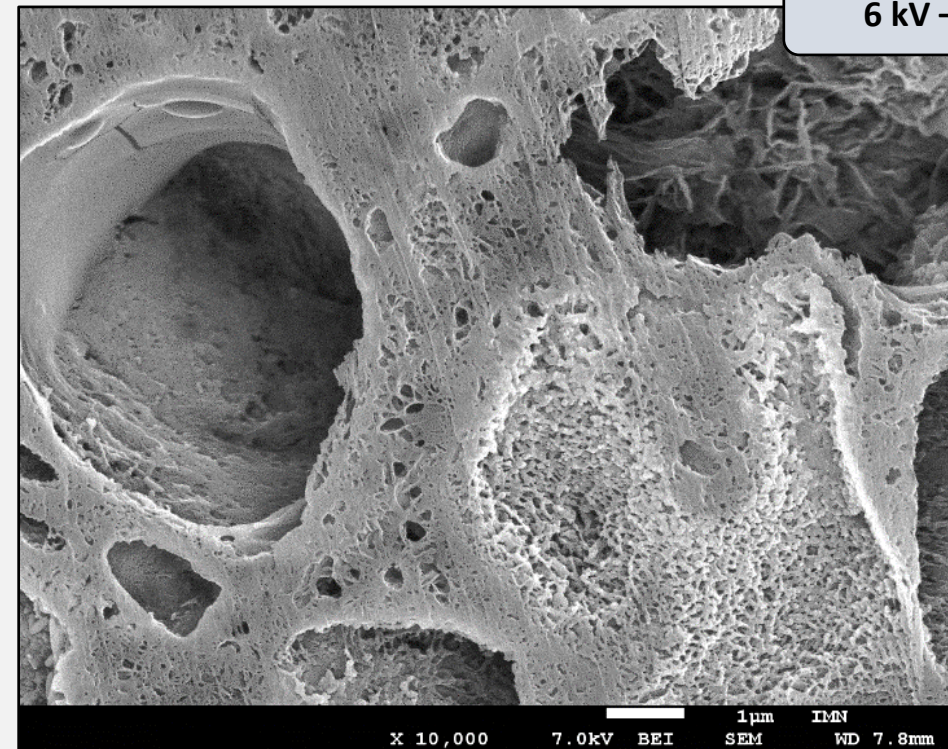
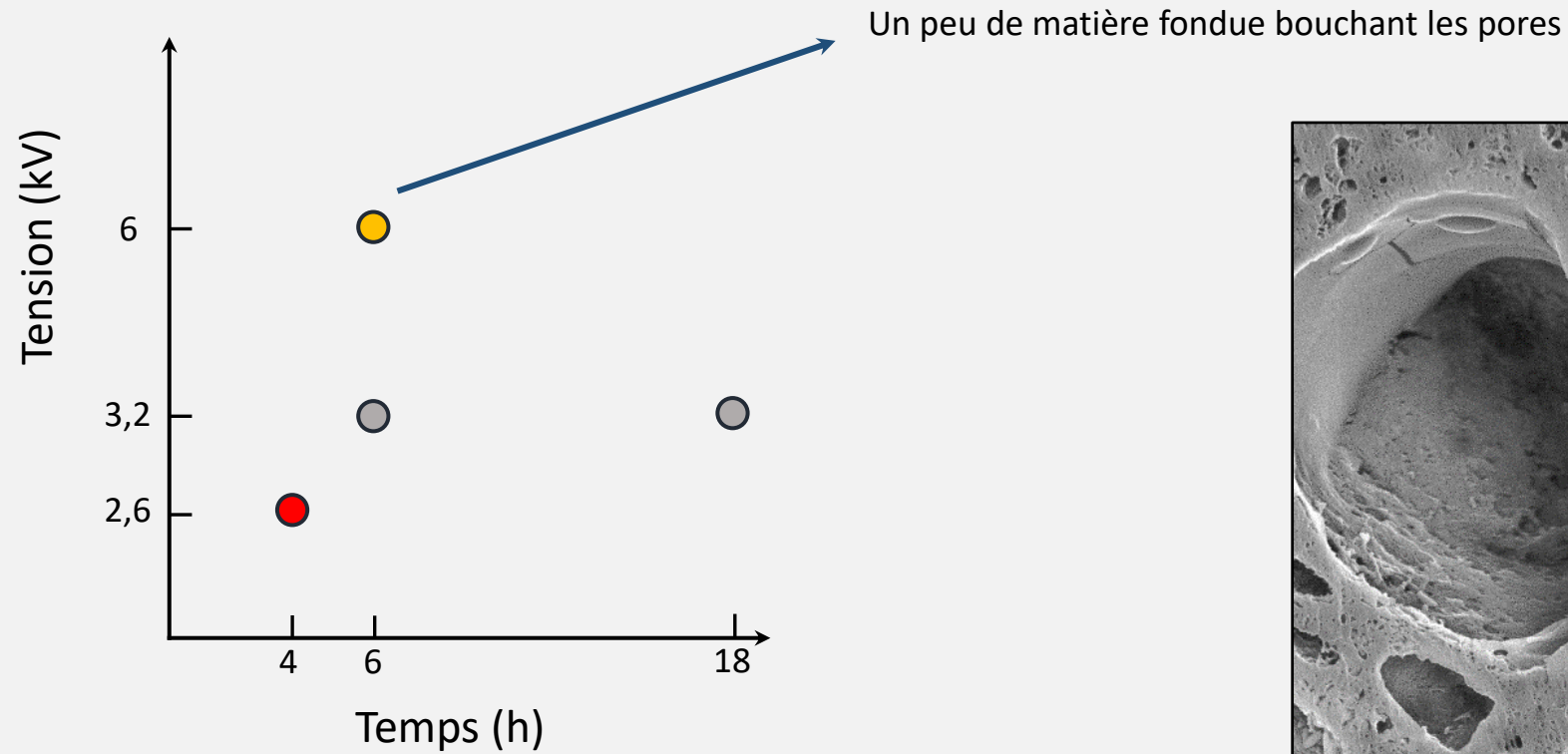
Echauffement mais pas de polissage : collerette noire au dessus



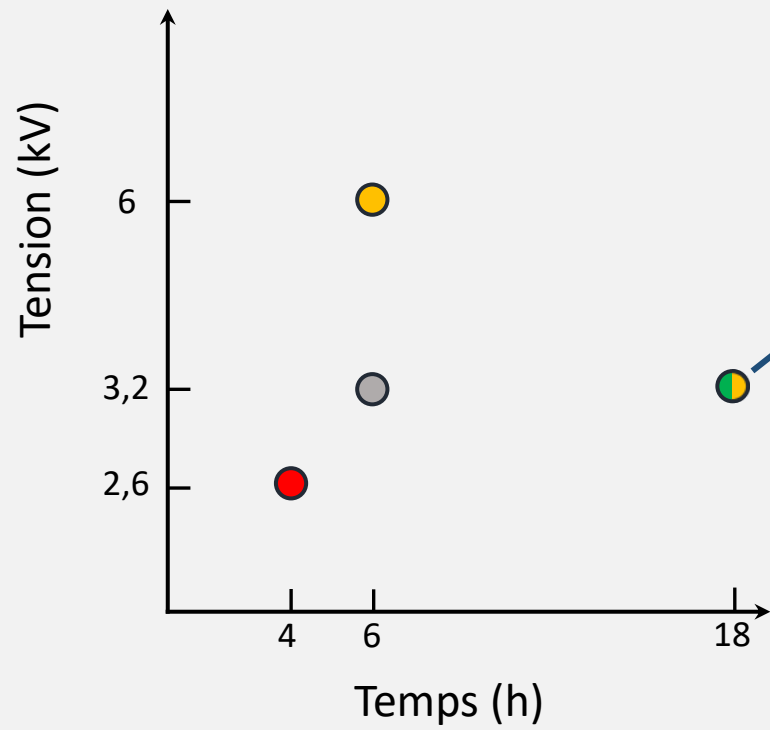
2,5 mm



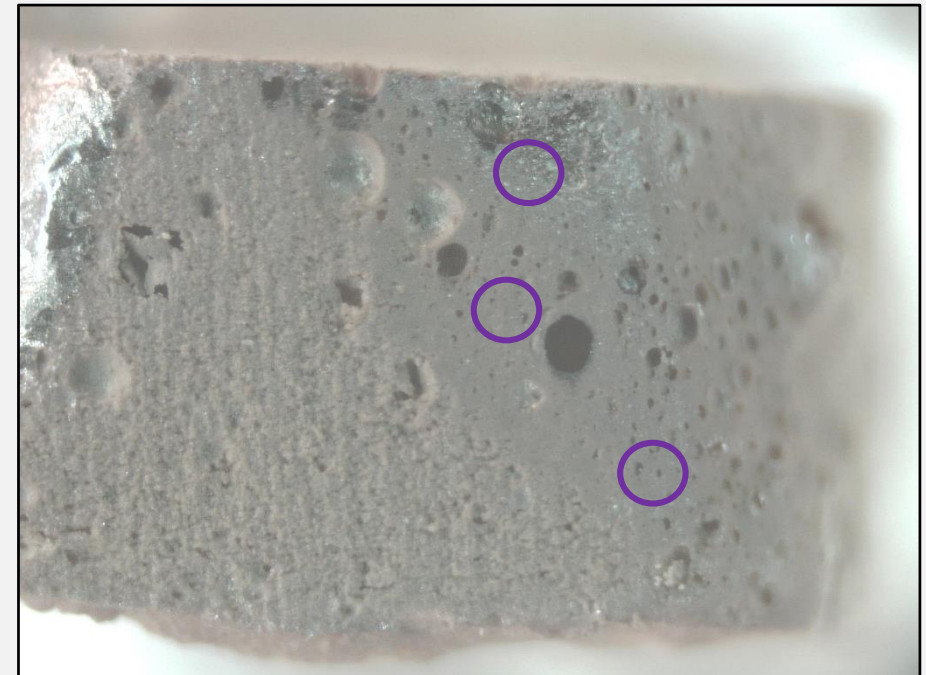
III-Composite décalcifié CSP : différents réglages



III-Composite décalcifié CSP : différents réglages



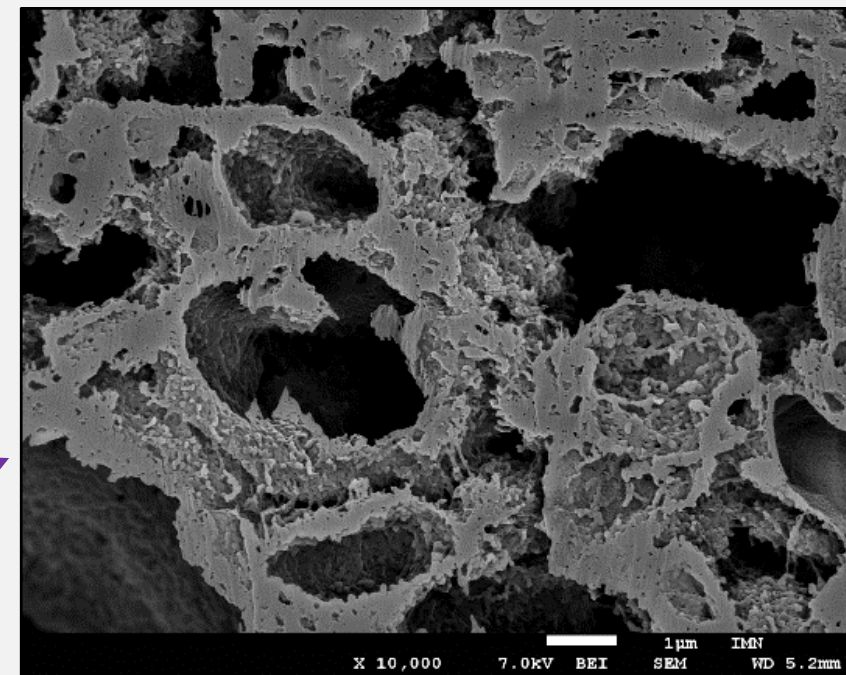
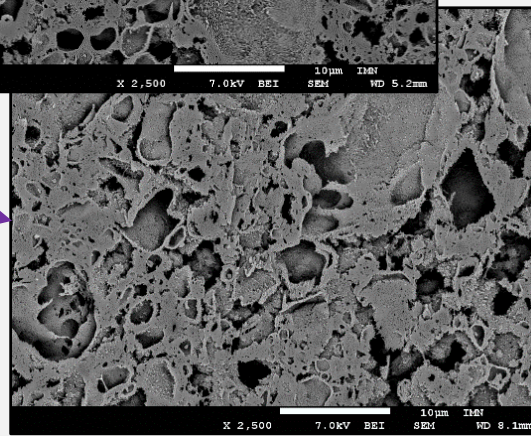
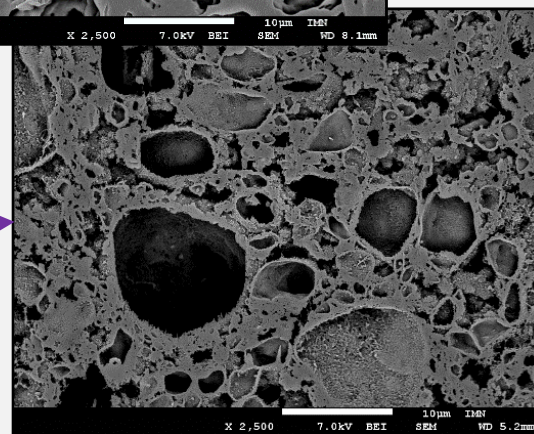
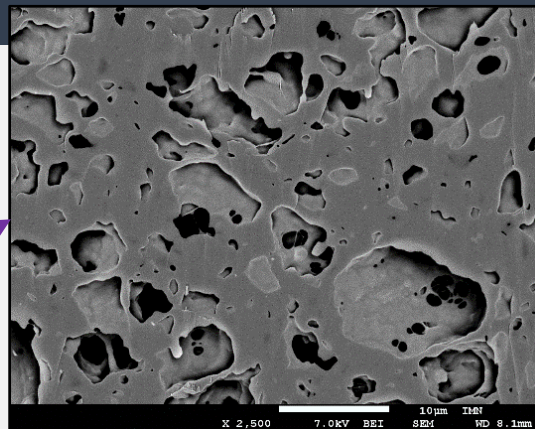
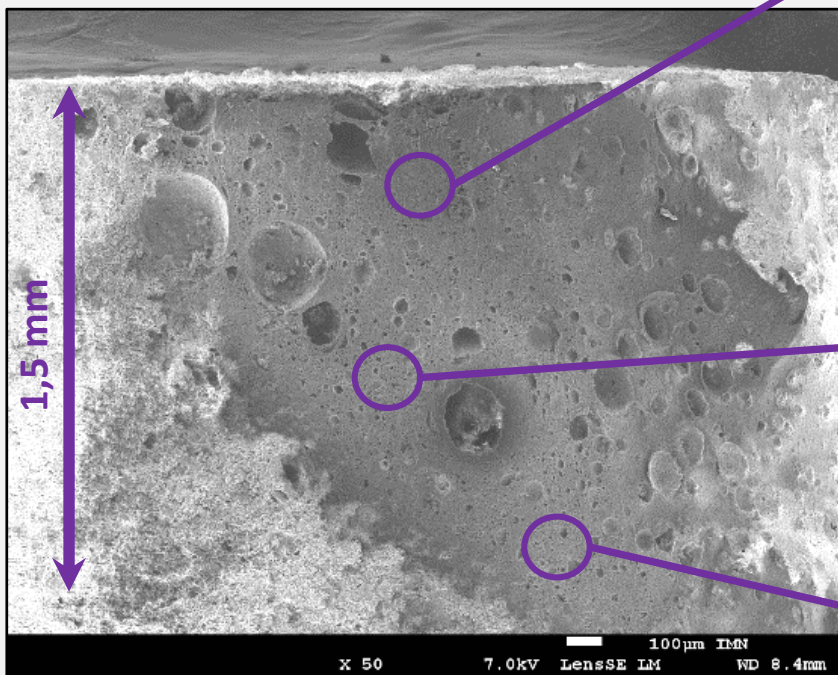
OK mais 3 zones de polissage



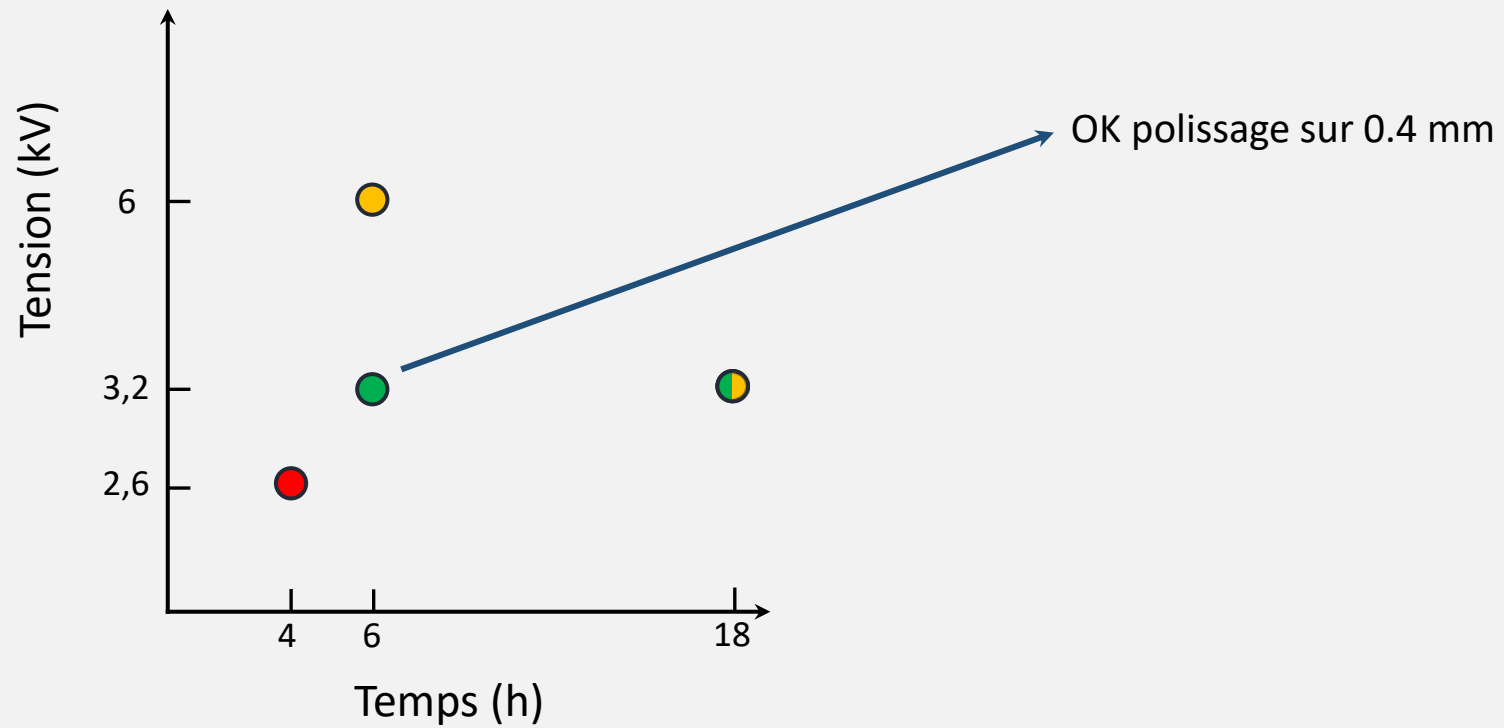
III-Composite décalcifié CSP : différents réglages



3,2 kV – 18 h



III-Composite décalcifié CSP : différents réglages

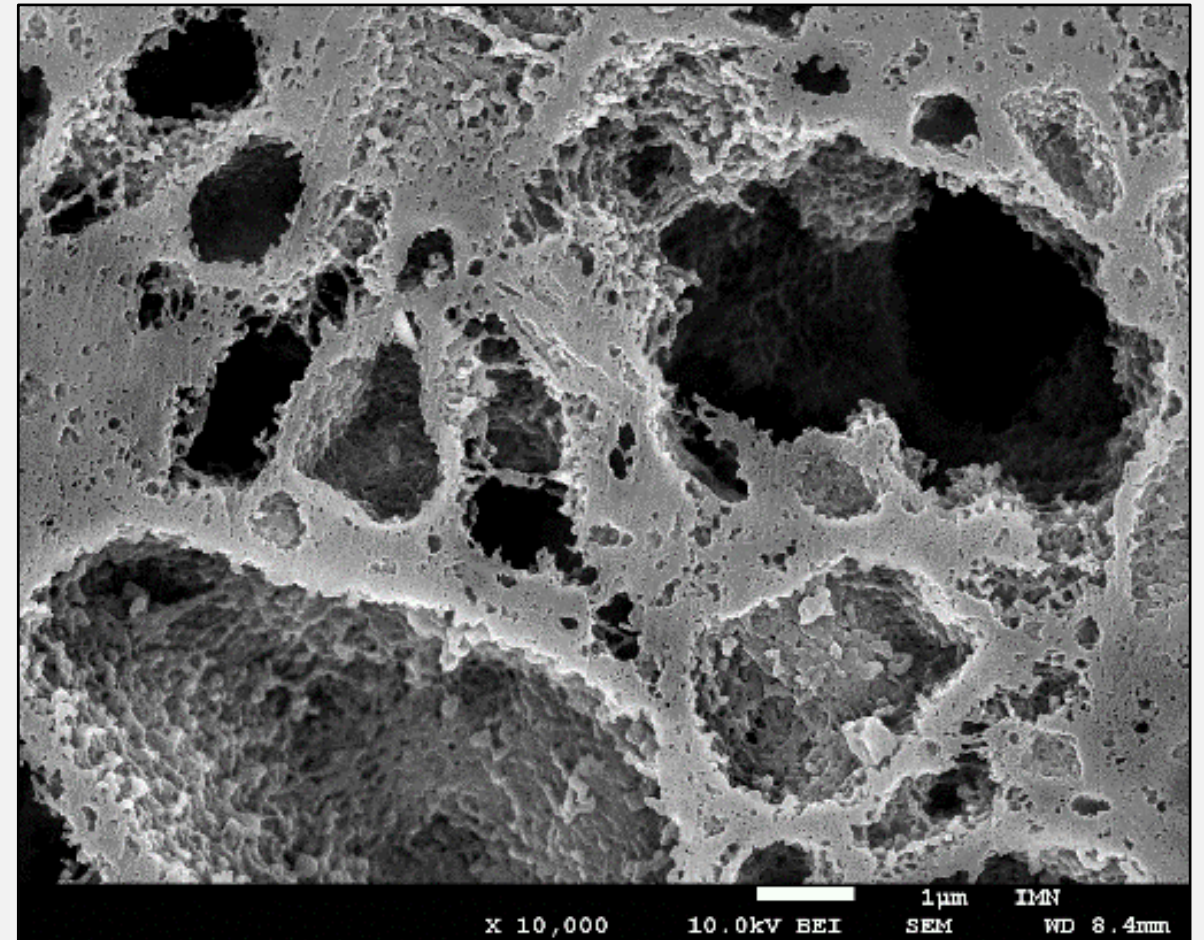
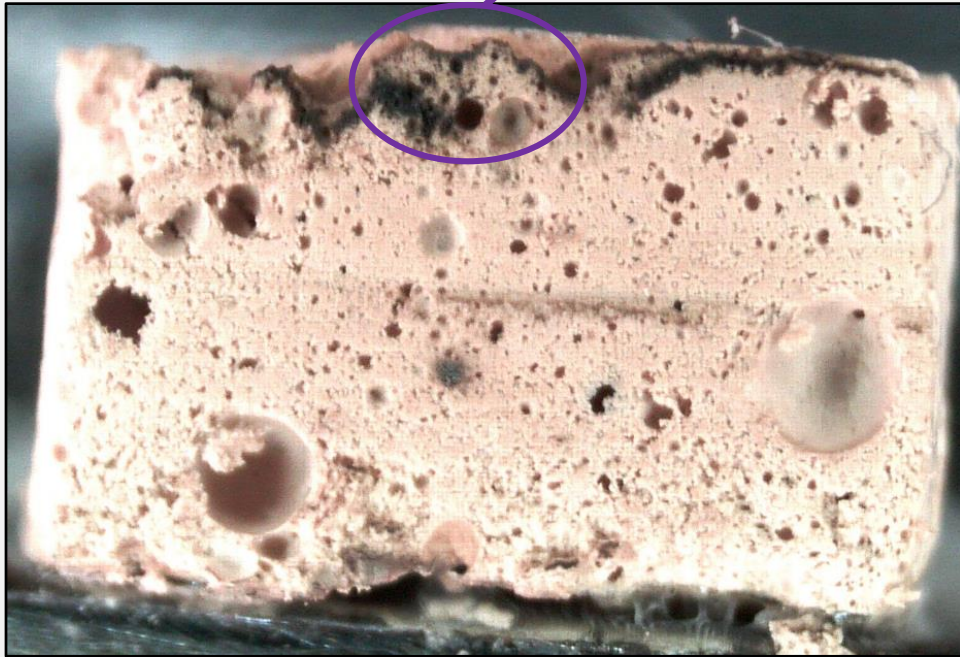


III-Composite décalcifié CSP : différents réglages

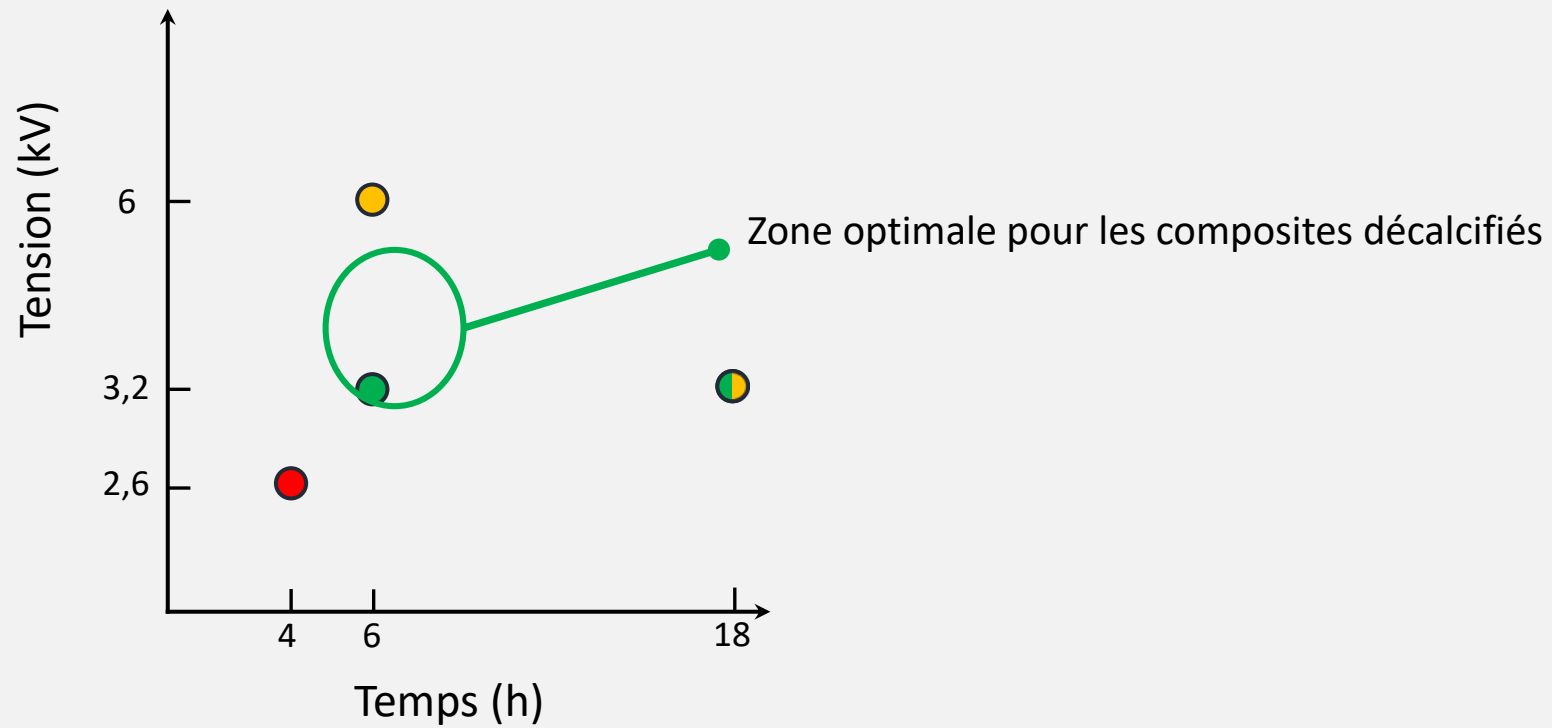


3,2 kV – 6 h

Zone polie



III-Composite décalcifié CSP : différents réglages



Remerciements

Institut des Matériaux de Nantes IMN
Nicolas Stéphant



Full length article

A straightforward approach to enhance the textural, mechanical and biological properties of injectable calcium phosphate apatitic cements (CPCs): CPC/blood composites, a comprehensive study

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ARTICLE INFO

Article history:

Received 4 May 2017

Received in revised form 21 August 2017

Accepted 28 August 2017

Available online xxxxx

Keywords:

Calcium phosphate composites

Blood clot

Bone regeneration

Organic and inorganic networks

In vivo

ABSTRACT

Two commercial formulations of apatitic calcium phosphate cements (CPCs), Graftys® Quickset (QS) and Graftys® HBS (HBS), similar in composition but with different initial setting time (7 and 15 min, respectively), were combined to ovine whole blood. Surprisingly, although a very cohesive paste was obtained after a few minutes, the setting time of the HBS/blood composite dramatically delayed when compared to its QS analogue and the two blood-free references. Using solid state NMR, scanning electron microscopy and high frequency impedance measurements, it was shown that, in the particular case of the HBS/blood composite, formation of a reticulated and porous organic network occurred in the intergranular space, prior to the precipitation of apatite crystals driven by the cement setting process. The resulting microstructure conferred unique biological properties to this material upon implantation in bone defects, since its degradation rate after 4 and 12 weeks was more than twice that for the three other CPCs, with a significant replacement by newly formed bone.

Statement of Significance

A major challenge in the design of bone graft substitutes is the development of injectable, cohesive, resorbable and self-setting calcium phosphate cement (CPC) that enables rapid cell invasion with initial mechanical properties as close as bone ones. Thus, we describe specific conditions in CPC-blood composites where the formation of a 3D clot-like network can interact with the precipitated apatite crystals formed during the cement setting process. The resulting microstructure appears more ductile at short-term and more sensitive to biological degradation which finally promotes new bone formation. This important and original paper reports the design and in-depth chemical and physical characterization of this groundbreaking technology.

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publications

Design and properties of a novel radiopaque injectable apatitic calcium phosphate cement, suitable for image-guided implantation

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Received 12 September 2017; revised 9 November 2017; accepted 18 November 2017

Published online 00 Month 2017 in Wiley Online Library (wileyonlinelibrary.com). DOI: 10.1002/jbm.b.34059

Abstract: An injectable purely apatitic calcium phosphate cement (CPC) was successfully combined to a water-soluble radiopaque agent (i.e., Xenetix®), to result in an optimized composition that was found to be as satisfactory as poly(methyl methacrylate) (PMMA) formulations used for vertebroplasty, in terms of radiopacity, texture and injectability. For that purpose, the Xenetix dosage in the cement paste was optimized by injection of the radiopaque CPC in human cadaveric vertebrae under classical PMMA vertebroplasty conditions, performed by interventional radiologists familiar with this surgical procedure. When present in the cement paste up to 70 mg mL⁻¹, Xenetix did not influence the injectability, cohesion, and setting time of the resulting composite. After hardening of the material, the same observation

was made regarding the microstructure, mechanical strength and alpha-tricalcium phosphate to calcium deficient apatite transformation rate. Upon implantation in bone in a small animal model (rat), the biocompatibility of the Xenetix-containing CPC was evidenced. Moreover, an almost quantitative release of the contrast agent was found to occur rapidly, on the basis of *in vitro* static and dynamic quantitative studies simulating *in vivo* implantation. © 2017 Wiley Periodicals, Inc. *J Biomed Mater Res Part B: Appl Biomater* 00B: 000–000, 2017.

Key Words: calcium phosphate, radiopaque agent, injectable cement, image-guided implantation, bone reconstruction

Received: 3 January 2019 | Revised: 5 April 2019 | Accepted: 10 April 2019

DOI: 10.1002/jbm.b.34395

ORIGINAL RESEARCH REPORT



In vivo resorption of injectable apatitic calcium phosphate cements: Critical role of the intergranular microstructure

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⁵ONIRIS, Nantes Atlantic College of Veterinary Medicine, Nantes, France

Correspondence

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Acta Biomaterialia xxx (2019) xxx–xxx

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Abstract

The *in vivo* resorption rate of two injectable apatitic calcium phosphate cements used in clinics (Graftys® HBS and NORIAN®) was compared, using a good laboratory practice (GLP) study based on an animal model of critical-sized bone defect. To rationalize the markedly different biological properties observed for both cements, key physical features were investigated, including permeability and water-accessible porosity, total porosity measured by mercury intrusion and gravimetry, and microstructure. Due to a different concept for creating porosity between the two cements investigated in this study, a markedly different microstructural arrangement of apatite crystals was observed in the intergranular space, which was found to significantly influence both the mechanical strength and *in vivo* degradation of the two calcium phosphate cements.