CERACELL Success Story
17 JAN 2017

Bone Therapeutics

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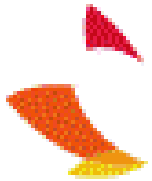
CERACELL – M-ERA.NET CONVENTION N°1318215

DEVELOPMENT OF A 3D PATIENT-TAILORED BONE PIECES COMBINING SCAFFOLD AND BONE CELLS FOR THE REPAIR OF BONE DEFECTS

PROJECT PARTNERS

imageanalysis



sirris

driving industry by technology

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OBJECTIVES

- **Main objective :** to test the feasibility of developing novel patient-tailored 3D bone tissue engineered products combining osteoblasts and 3D tailored bioresorbable ceramic scaffolds (personalised to the defect: shape, size and macro / microstructure)

- **Advantages :** enhanced bone biomechanical and biological properties which are expected to accelerate and improve bone regeneration

- **Initiation date :** 01/12/14

- **Duration :** 2 years

- **Budget :**

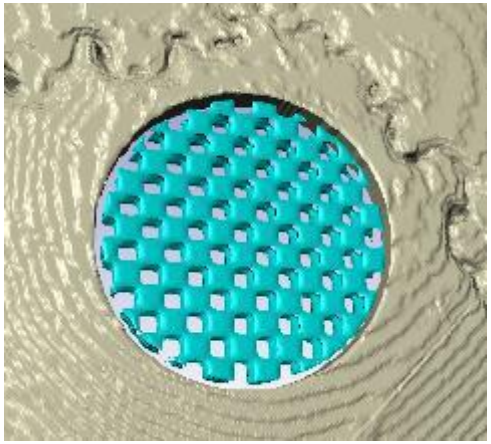
Total	**800.107,50**
Subsidies	**576.080,62**

IMAGE ANALYSIS SKILLS

- Extensive experience in image processing
  - Specialized in developing usable practice-friendly algorithms (UI, UX)

- Regulatory Compliant medical software development
- BS EN ISO:13487 ; BS EN 62304 Medical Device Software – Software life-cycle process ; CE Marked

- Commercial expertise working with hospitals world-wide



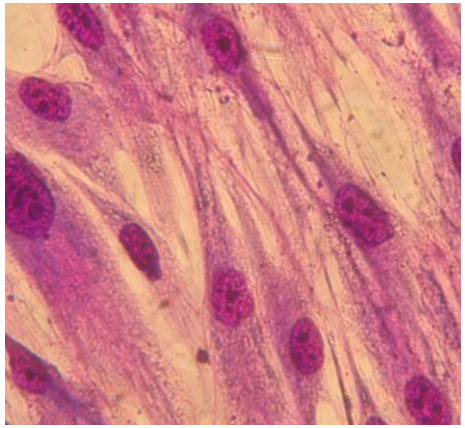
Example of CT scan sagittal view of human femoral fracture

BONE THERAPEUTICS SKILLS

- Experience in developing innovative cell products for the repair of bone tissues.

- Bone Therapeutics' products characteristics are unique in the industry because they are composed of osteoblastic cells, superior and safer than undifferentiated cells.

- Minimally invasive administration ➔ significant improvement of current standard of care and over most competitors (e.g., no open surgery, one-day clinic...)



SIRRIS SKILLS

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- Extensive experience in additive technologies
  - Experience in developing 3D-printing of (bio)ceramics using Stereolithography, debinding and sintering post-processing

- 4 AM processes ISO:13485 certified

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WORK PROGRAM

	CERACELL (projet M-ERA.net)	2014	2015											2016									
	Tâches	12	1	2	3	4	5	6	7	8	9	10	11	12	1	2	3	4	5	6	7	8	9	10	11
1	**Analyse d'images des parties osseuses manquantes (définition des parties manquantes et développement de l'algorithme)**																								
2	**Essais d'impression et évaluation de la biocompatibilité avec les ostéoblastes** .																								
3	**Reconstruction des parties osseuses manquantes par impression 3D de biocéramiques et évaluation des propriétés**																								
4	**Etude de la colonisation cellulaire des pièces biocéramiques 3D (in vitro et in vivo)**																								
5	**Exploitation, dissémination et gestion du projet**																								
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24

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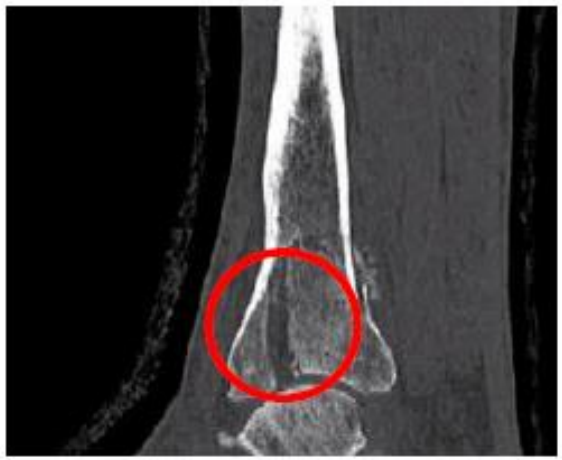
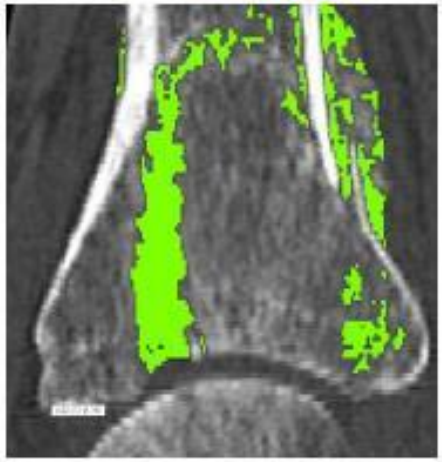
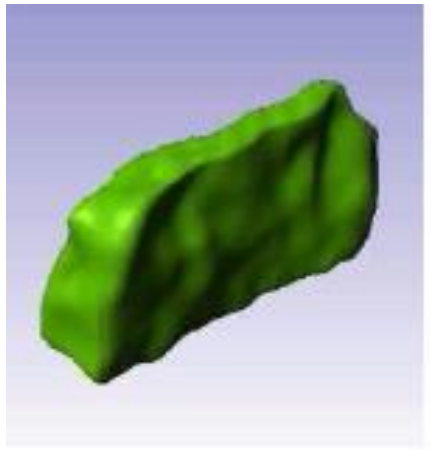
WORK PACKAGE 1 : SOFTWARE DEVELOPMENT (I.A.)

- Definition of the missing bone part (in collaboration with Bone Therapeutics)
- Development of the algorithm/software (in collaboration with Sirris)







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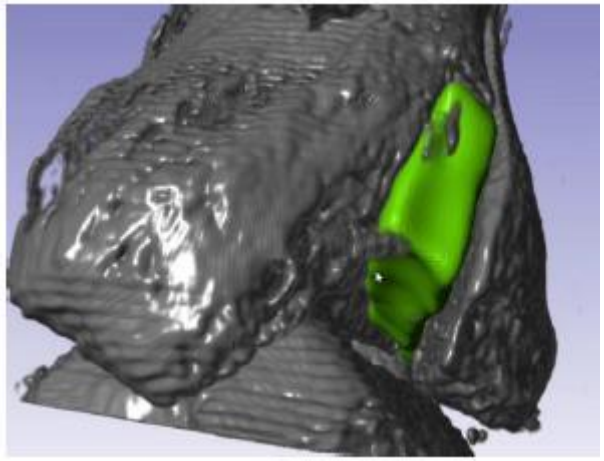

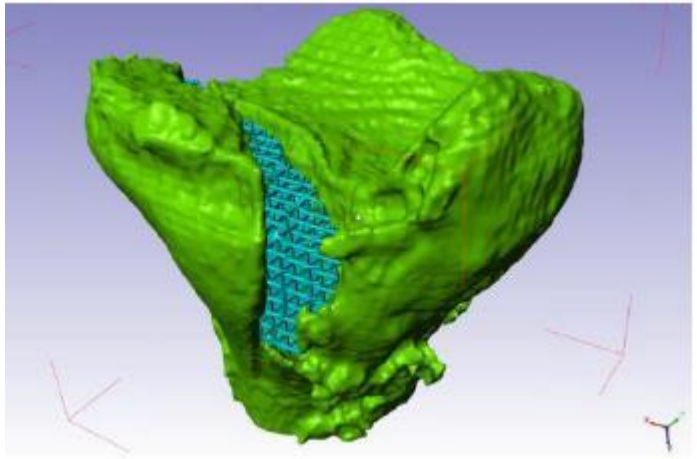

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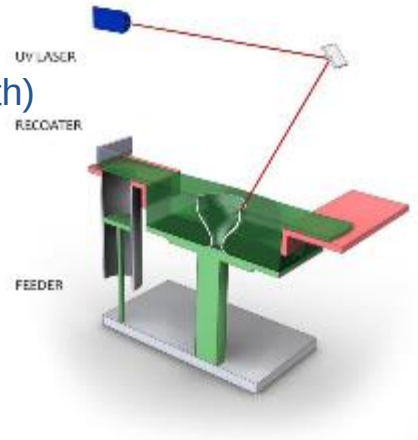
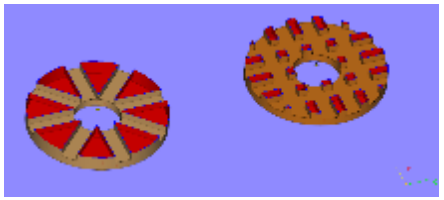
WORK PACKAGE 2 : 3DP AND BIOCOMPATIBILITY TESTS

- Stereolithography of high viscosity paste material
  - 2 geometries for biocompatibility tests (sent to BT)
  - Cubes and lattices for physical tests (density, strength)
  - 5 bioceramic compositions:
    - HA 100%
    - HA 60% - TCP 40%
    - HA 40% - TCP 60%
    - HA 20% - TCP 80%
    - TCP 100%





- Quick optimization of paste formulations, process parameters and thermal post-treatments
- Following biocompatibility tests

  → TCP 100% is the best choice (see WP 4)

  → Full optimization of TCP 100% formulation and parameters

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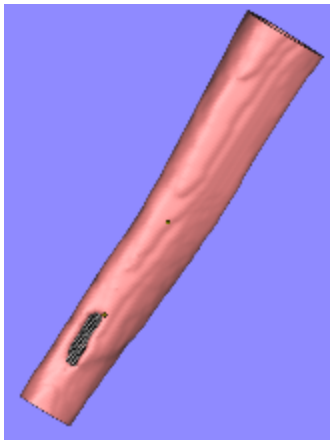
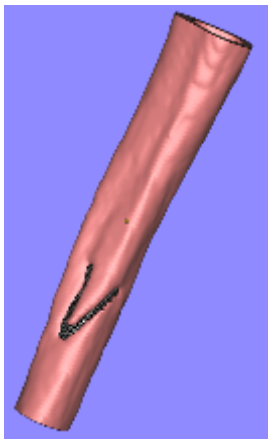
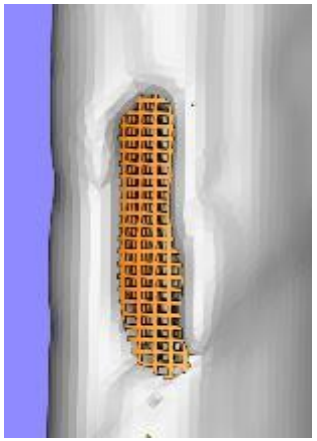
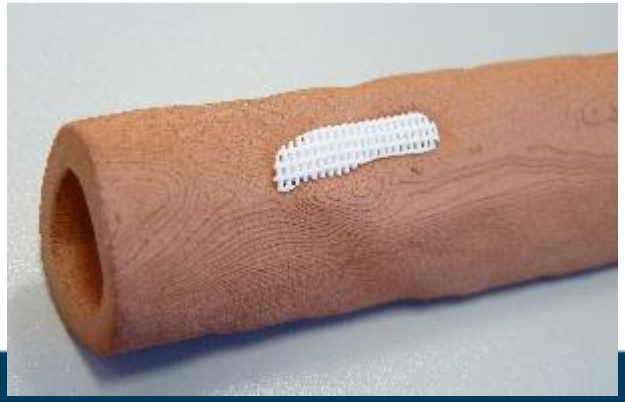
WORK PACKAGE 3 : 3DP OF MISSING BONE

- Study on human tibia bone
- Files from IA with tailored lattice structure
  - Using developed software
  - Using optimised pore size from WP 2
- 3DP of generated file and post-treatments
  - Using optimized parameters
- Physical characterization
  - Final density: 96% (4% porosity in material)
  - Sintering shrinkage: ~25%
- Mechanical characterization on lattice blocs (ISO:13175)
  - Young modulus: 1.315 MPa
  - Maximum strength: 10 MPa
  - Elongation: 6%



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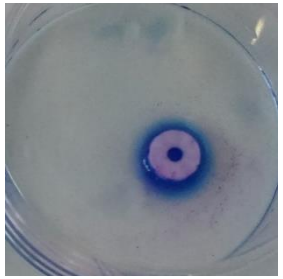
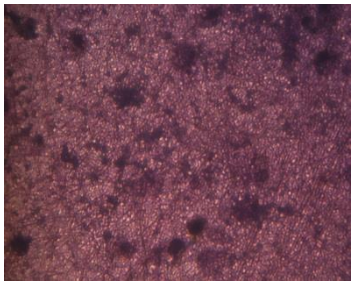
WORK PACKAGE 4 : CELL COLONIZATION STUDIES (BT)

- Evaluation of the biocompatibility of the small bioceramic cylinders with osteoblasts
  - *Cytotoxicity assay (according to the ISO 10993 part 5)*
  - *Direct contact culture followed by a phenotype analysis by FACS*



Negative control

Positive control



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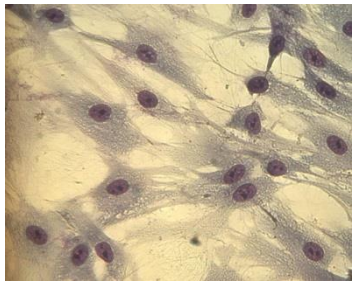
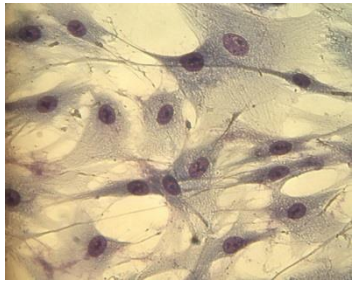


HA 100%

TCP 100%



- Assessment of the *in vivo* preclinical safety and efficacy of the tailored 3D bioceramic pieces combined with osteoblasts in a rodent bone-defect model

EXPECTED DELIVERABLES

- Accurate analysis and reconstitution of large bone defect (images) in 3D files or other instructions for the 3D bioprinting of bioresorbable ceramic scaffolds (Image Analysis)

- **Printing of 3D image-tailored bioresorbable ceramic pieces** mimicking the patient defect (SIRRIS)

- ***In vitro*** demonstration of the biocompatibility of the 3D image-tailored bioresorbable ceramic pieces with osteoblasts and of the maintenance of their osteogenic properties (mineralisation capacity, enzymatic activities) (BT)

- ***In vivo*** preliminary studies in a rodent bone defect model to assess the enhanced bone reconstruction properties and biocompatibility of the combined products (BT)

Questions ?

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