The Ingetissos project

Following severe facial trauma leading to an important loss of bone structure, it may prove necessary to envisage bone grafts. One of the techniques currently applied is to make an auto-graft (taking a bone from one spot of a patient's body for use at another place), but this is always heavy and painful surgery at best. To remedy the situation, the UTC-BMBI Lab (Bio-Mechanical and Bio-Engineering) has been working for several years to produce a bio-hybrid tissue (comprising a biomaterial (1) in which stem cells have been implanted and grown), with biological and mechanical characteristics that facilitate use by the surgeons operating and ensuring better later tolerance by the patient.

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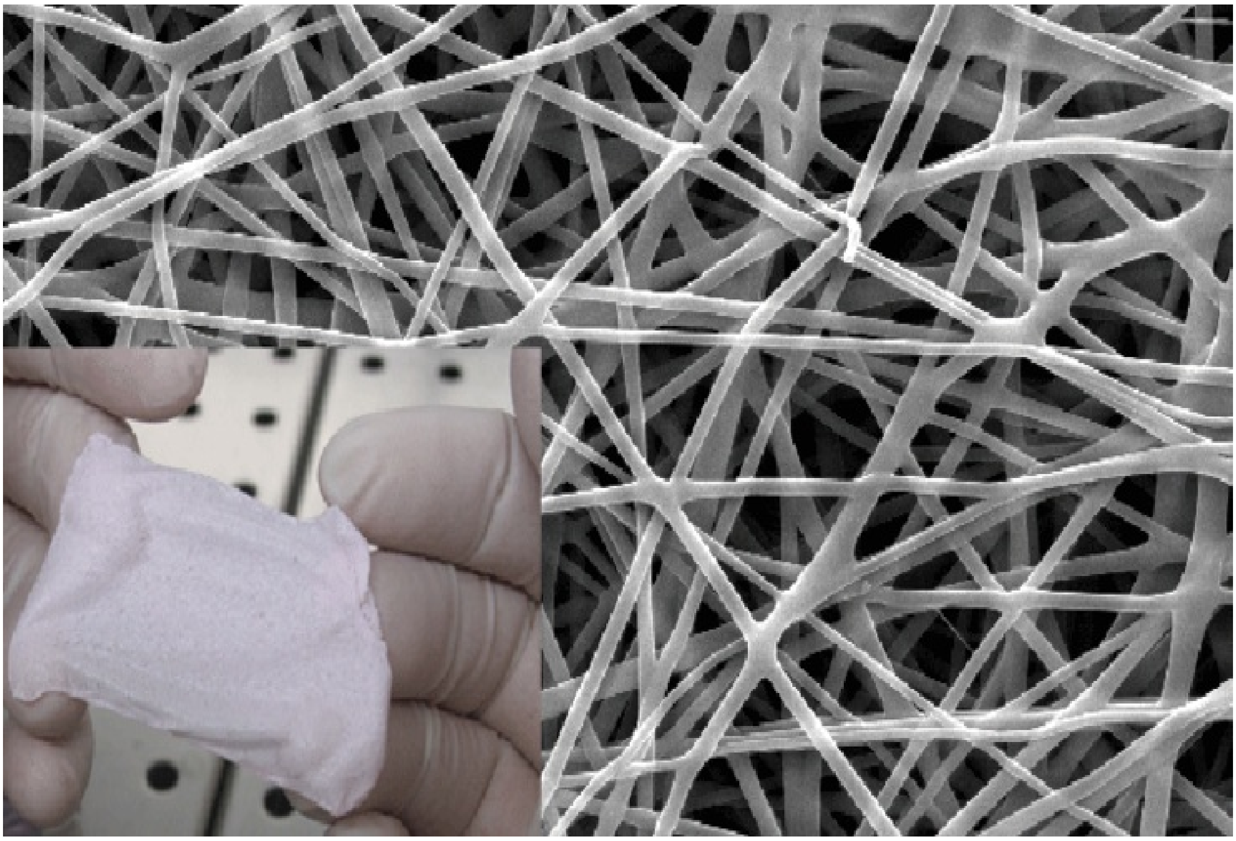

Currently, the tissue developed by UTC-BMBI is produced in a bio-reactor with a carpet of hydroxyapatite granules, a material commonly used to fill in bone damaged zones. The stem cells (extracted from a bone marrow of the patient) are spread on the carpet where they implant and cement the granules together to form a sheet. The stem cells then begin to differentiate into bone cells, where the biomaterial induces naturally the differentiation process. "This is more efficient than introducing differentiating factors, which as yet are not well identified and could not be authorized for clinical tests", underlines Cécille Legallais, research scientist at the UTC-BMBI Laboratory. "After 5 weeks, we carry out our own tests to make sure the cells have really become bone tissue".

Obtaining a 'manipulatable' tissue sheet

"Since the tissue we aim to produce will in the long run be used for maxillofacial reparatory bone surgery (infilling), the clinician surgeons must be able to manipulate it and model it to exactly mold the shape required. "Often, in tissue engineering, we use a small plaque only a few millimeters thick. But for face surgery, this

cannot be used, explains Cécille Legallais. "Our approach is to obtain a sheet that can be manipulated by the surgeons. They will be able to shape the implant, slice and incise it, fold it as a function of the exact shape of the cavity to be infilled. The idea is to make a tissue that will be just as strong as the bone was, but to make it far easier to use by the surgeons to do their infilling operations."

At the beginning of the project, the tissue created was only characterized by its biological functions. "For example, for bone grafts, the question is to see if the tissue will effectively produce bones", adds Cécille Legallais. *"As we saw it, it was useful and logic to characterize the tissue created from a mechanical point of view. This called for further, complementary skills in material sciences and engineering. We therefore identified specialists of polymer engineering in UTC itself."* The UTC-BMBI team then met with Fahmi Bedoui, senior lecturer at the UTC-Roberval laboratory who had solid experience in the field. He was very interested in the project. A PhD student was recruited in October 2012, thanks to a joint financial support from the Region + CNRS. *"Very rapidly, we focused on a research subject several other partners: the teaching hospital at Amiens who provide the stem cells and the Institut Fair Face" (cf. intra), details Cécille Legallais. "And that was how the Ingetissos Project came to be*".

Next step: reinforcing biohybrid tissues

The arrival of Fahmi Bedoui in the research team allowed them to characterize the breaking point of the tissue. "We realized, after some static traction tests, that out issue broke relatively rapidly and that we needed to reinforce the solid part of the implant", he adds. "We then carried out microscope tests to see how the sheet is damaged, and what role the granules play. The microscope tests allows us to see that there was a strong attachment between the tissue and the granules and that the weak features lay in the tissue itself." Then the research team focused on ways to strengthen the tissue sheet. *"We decided to replace the granules by a polymer fibre containing coumarone resin (2). We project these fibrates* *onto a random flat surface to as to build up the 3D tissue. The cells envelop the granules and fill in the spaces*", explains Fahmai Bedoui. *"The cells colonize the granules and move on to a system of cells in a 3D material, which strengthens ad guarantees the mechanical properties."*

This tissue is currently in development. But in some 2 to 3 years, the first clinical tests on animals will be conducted and if all goes well, the first human tests will take place in 5 years or less. The potential for strengthened tissues goes beyond medical uses. As Fahmi Bedoui explains: *"Development of such tissues should lead to job creation, inasmuch as these are non-delocalisable activities with high added value. They will be created near the patients, since we shall have to, be very reactive and comply strictly with stringent sanitary requirements."*

(1) In the framework of this project, this refers to a bio-medical, bio-compatible and bio-resorbable material, of either natural or synthetic composition.

(2) A synthetic compound inspired by an existing natural compound.