1. FINAL PUBLISHABLE SUMMARY REPORT (This section normally should not exceed 2 pages.)

The generation of biocompatible materials, with enough reactivity for cells to attach easily, and a macroporous structure that allows the three dimensional colonization of deep areas of the scaffold is nowadays the main objective of bone tissue regeneration research.

To achieve this objective, several approaches have been tested taking into account the surface quality (physical, chemical and topographical) as a key influencing factor to elucidate future bone tissue growth along the scaffolds.

1. Carbon Nanotubes - Mesoporous Silica composites for bone regeneration and drug delivery.

Silica based materials, in their form of glasses or as ordered mesoporous networks, are widely used as base materials for the fabrication of implants that allow bone regeneration. Due to their textural properties, large surface area and large pore volume, they are also suitable as drug delivery devices. It has been studied for the first time, the synthesis of a composite material in order to achieve the future possible control of the cell regeneration using well known properties of mesoporous silica and carbon nanotubes (CNTs).

The addition of CNTs to the base materials can produce a three dimensional electrical conducting network, which could be used to provide electrical stimulation for increasing cellular proliferation allowing the control of the cell activity. This could be an improvement in the performance of mesoporous silica itself.

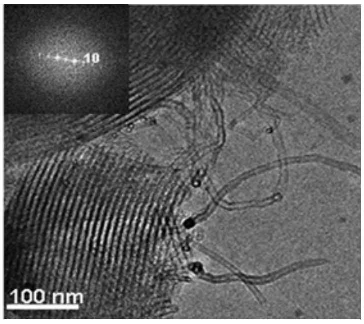

Fig. 1 Transmission Electron Microscopy (TEM) images and its corresponding FT diffractograms of SBA- 15–CNTs 2%

This research has successfully prepared uniform and homogeneous SBA-15–CNTs composites.
The addition of the CNTs, improves bioceramic properties as they become conductors, broadening thus the possible applicability of these new controllable systems. It is worth mentioned that the resistivity values decreased drastically with the increase of CNT percentage, with a reduction of up to 8 orders of magnitude, from 1 x 10^{11} Ω for pure SBA-15 to 1x 10^{3} Ω for SBA-15 with 5% CNTs.
This is direct evidence that electrical stimulation can be performed as the composites proved to be high current conductors.
Nowadays cell proliferation studies are being made with these composites as substrates. Osteoblast-like cells (HOS) are being stimulated with electrical currents from 1-10 μA, further experimental research data will be published.

2. Hydroxyapatite systems for bone regeneration.

The main requirement in bone tissue engineering is to enhance the chemical reaction leading the formation of nanoapatites as precursors of newly formed bone. To this end, it is necessary to design highly porous pieces, which must also include a certain degree of macropores to ensure bone oxygenation and angiogenesis.

2.1 Bimodal meso/macro porous hydroxyapatite coatings

New coatings technologies require the possibility of depositing porous coatings with higher specific surface areas for increasing the implant tissue contact interface, thereby improving the bone implant integration. Porous structures would also permit the attachment of biologically active molecules on these surfaces to improve the tissue response. Highly homogeneous, adhesive and crack-free coatings of pure porous nanocrystalline HA have been deposited onto Ti6Al4V substrates.

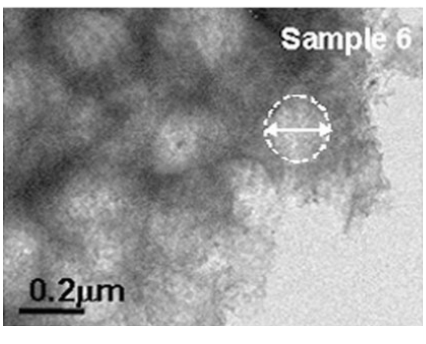

Fig.2. TEM images corresponding to the HA-films onto Ti6Al4V In the image of sample 6 a micropore of 0.2 μm is highlighted.

The porous network has been synthesized by using F127 as structure directing agent through EISA method. For the first time, by increasing the F127/TIP molar ratio a bimodal porous network has been obtained composed by mesopores around 4.5–10 nm and a macroporous network of around 0.2 μm. As these films present mesopores between 4.5 and 10 nm, they are very promising candidates to be loaded with biologically active molecules of certain sizes that could be confined inside the pores (peptides, proteins or growth factors), which might help cell attachment to the surface.

2.2 Macroporous sol-gel hydroxiapatite molding via confinement into shaped polymers

Acrylate salts and acrylamide have been extensively used for retaining or absorbing large amounts of water or ionic species. This polymers´ capability has been used as a new way to obtain porous spheres of nanocrystalline hydroxyapatite. Macroporous nanostructured HA with a pore size between 50μm-500μm are obtained when using the hydrogel as template. The removal of the template gives rise to the formed sphere and the size and shape of the formed material can be determined by the template contour. The use of this type of polymer constitutes not only an easy way to obtain beads but it is also possible to form different scaffolds sizes and shapes due to the polymer's versatility. This work will be sent for publication shortly and presented this current year in the European Biomaterials Conference.

3. Biopolymer-coated hydroxyapatite foams

3.1 A new antidote for heavy metal intoxication and water purification.

Novel 3D-macroporous biopolymer-coated hydroxyapatite foams are potential devices for the treatment of heavy-metal intoxication by ingestion. These foams are designed to exhibit a fast and efficient metal ion immobilization into the HA structure in acidic media. The capture process of metal ions is stable, not releasing any metal ion when the foams are soaked in clean basic media afterwards. These two steps mimic a digestion process.

Moreover, these foams are potential devices for the treatment of lead, cadmium and copper contamination of consumable waters. These foams have exhibited a fast and effective ion metal immobilization into the HA structure after an in vitro treatment mimicking a serious water contamination case**.**

3.2. Performance of the coated foams as bone implant for tissue engineering.

Hydroxiapatite three-dimensional foams have an improved mechanical performance as the coating provides and confers to them flexibility and handle ability. The surgical management of this HA foam is simple, allowing the surgeon to carve the appropriate design for a particular bone defect. His experimental in vivo behavior offers promising results as an eligible scaffold for clinical applications, mainly in Orthopaedics and Dentistry. These results will be published shortly and presented this current year in the European Biomaterials Conference.

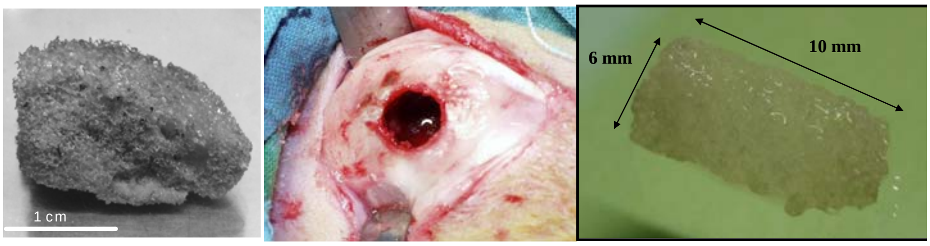

Fig. 4 Digital image of a) the biopolymer-coated foam, b) created bone defect, c) foam cylinder with bone defect dimensions.

4. Current active lines opened during the course of the project.

4.1 Graphene Oxide for photothermal therapy. The hyperthermal therapy of tumors has been investigated as a minimally invasive alternative to surgery that can induce lethal damage to cellular components at temperatures above 40 ºC.

4.2 3D scaffolds functionalized and reinforced with recombinant protein polymers for regenerative medicine. The objective is to use a novel recombinant elastin-like polymer in combination with HA scaffolds to enhance the biological activity of implants.

5. Potential impact and use and any socio-economic impact

Social-economical benefits are implicit on the research on new materials for medical applications, such as those this project deals with. Biomaterials represent an important market share on the health key sector. For example, given that a large number of people, nearly 75 million patients on a worldwide basis, suffer from osteoporosis or bone cancer. The number of required implants is increasing and so is the number of materials required to regenerate and repair the human body. The aim of this project was to improve the health- related quality of life for people with musculoskeletal disorders throughout the world by giving new approaches to produce bone substitutes/regenerators.

Moreover, the biopolymer coated foams presented are also a new route to avoid human poisoning via oral administration that can be used in before intestinal absorption or without requiring hospital admission. The foams also contribute to the research for ensuring a more sustainable management of the environment and its resources is catalogued as one of the main technologies and services to be funded and studied. They could provide a new treatment with high effectiveness without high financial costs or the need of water purification infrastructures.