FROM TISSUE ENGINEERING IN ORTHOPEDY AND DENTISTRY TO REGENERATIVE CARDIOLOGY AND NEUROLOGY

Franco Rustichelli

Department Disco, Università Politecnica delle Marche, Ancona, Italy
Istituto Nazionale di Biostrutture e Biosistemi, Rome, Italy

Advanced Tomographic Techniques based on Synchrotron Radiation in Regenerative Medicine

A short introduction will be given of the standard *X-Ray micromotography*, which allows a good visualization at 3D level of biomaterials , mineralized tissues and of the spatial distribution of injected stem cells. However this technique fails to finely discern soft tissues. This limitation is overcome by using a recently developed technique, the *X-Ray holotomograpy* which is also able to visualize at 3D level the microvascular network, without any need of contrast agents.
This technique express the maximum of its potentialities in conjunction with *phase contrast radiography.*

Applications in Bone Tissue Engineering and Dentistry

A first application of these techniques concern investigations of the microstructural properties of bone engineered from bone marrow stromal cells. 3D images were obtained and the volume fraction, the average thickness and distribution of newly formed bone were evaluated as a function of the implantation time. By using the *X-ray microdiffraction technique* it was possible to investigate the structure of engineered bones inside a scaffold pore.
The *X-ray holotomography* was used to visualize, at three-dimensional (3D) level, microvascular networks, and to extract quantitative structural data in a bone-engineered construct related to orthopaedy.
Moreoever X-Ray holotomography was used to investigate the structure of the bone regenerated, in a *clinical experiment*, in areas of mandibles with large bone defects, by deposition of mesenchymal stem cells derived from dental pulp.

Applications in Regenerative Cardiology and Neurology

Then the results will be presented of a neurological study in connection with attempts to repair muscle damage in Duchenne muscular dystrophy, by transplanting intraarterially myogenic stem cells into the muscle itself. Several *in vivo* microtomographic visualizations were obtained for

different times after injection in homozygous *scid/mdx* mices, by obtaining a quantitative information of the kynetics of diffusion of the stem cells in the muscular tissue.
After that, an experiment will be presented related to the use of stem cells to repair infarcted hearts. The above mentioned imaging techniques were used to detect, with high resolution, the 3D spatial disrtibution of rat cardiac progenitor cells in ex vivo conditions,inside the rat infartecd rat early after injection.

The New COST BIONECA ACTION

Finally the new COST BIONECA ACTION will be presented. Cardiovascular diseases are the leading cause of death in the western world. A progressively ageing population is increasingly affected by neurological diseases, which brings a negative impact on European economies with more than 1 billion euros cost per year.
One of the most promising strategies is based on stem cell applications for cardiovascular and neurological diseases and on the employment of biomaterials for supporting cultivation and integration of stem cells in disease-affected tissue. On this basis we conceived a project having the title: Biomaterials and advanced physical techniques for Regenerative Cardiology and Neurology. (BIONECA) which was written with several colleagues of different disciplines and submitted to COST Organization, which approved it, with start on March15, 2017, and lasting 4 years. At present 36 countries joined BIONECA:
The main goal of BIONECA is to establish an intensive interaction among top-level European Institutions of different scientific communities (**physics, chemistry, mathematics, informatics, biomaterials science, material engineering, nanotechnology, surface science, rapid prototyping, advanced imaging technology, cell biology, molecular biology, tissue engineering, regenerative cardiology, and regenerative neurology**) in order to induce significant progresses in Regenerative Cardiology and Regenerative Neurology with a consequent reduction of deaths and costs associated to brain and heart diseases.