[1]Department Disco, Universita' Politecnica Delle Marche, Ancona, Italy, [2]Dipartimento Di Medicina Sperimentale, Secondo Ateneo Di Napoli, Napoli, Italy, [3]Dipartimento Di Scienze Chirurgiche E Morfologiche, Universita' Dell'Insubria, Varese, Italy, [4]Dipartimento Di Scienza Della Salute, Universita Del Piemonte, Novara, Italy, [5]Dipartimento Di Scienze Mediche, Universita' Di Chieti E Pescara, Chieti, Italy.

In recent years there has been an increasing interest in a novel approach to evaluate human bone biopsy specimens by means of synchrotron micro-tomography (SCT). Using SCT, bone regeneration subsequent to grafting hosting sites with different types of biomaterials (with or without stem cells seeding) is recently explored. Evaluation of the amount of bone formed is usually based on 2-D histomorphological data obtained from one or several histological sections.

If the regenerative potential of neighboring tissues with different morphology (alveolar process, unmineralized extracellular matrix involvement, regenerated vessels, etc.) on a defect or space to regenerate is not clearly verified or unknown, 3-D analyzing methods like high resolution SCT are indicated to explore the dynamic and spatial distribution of regenerative phenomena in such complex anatomic structures.

Moreover the use of advanced techniques like phase contrast tomography (PCT) and holotomography (HT) allow to visualize components with low attenuation coefficient, like blood vessels.

In the present lecture the most recent breakthroughs in Clinical Regenerative Dentistry will be shown, demonstrating the unique capabilities of the SCT in offering not only an advanced characterization of different biomaterials (to understand the mechanism of their biological behavior as bone substitute) but also to investigate the growth kinetics of regenerated bone in different dental implants retrieved from humans.

Implant survival, bone regeneration, graft resorption, neo-vascularization and morphometric parameters (including anisotropy and connectivity index of the structures) were evaluated by microCT and HT at different times from implantation or grafting in human bone defects.

Development of Biomimetic Microengineered Hydrogel Fibers for Tendon Regeneration

R. Costa-Almeida[1,2], L. Gasperini[1,2], M. T. Rodrigues[1,2], P. Babo[1,2], J. F. Mano[1,2], R. L. Reis[1,2], M. E. Gomes[1,2];

[1]3B's Research Group, University of Minho, Guimarães, PORTUGAL, [2]ICVS/3B's – PT Government Associate Laboratory, Braga/Guimarães, PORTUGAL.

Musculoskeletal diseases are one of the leading causes of disability worldwide. Tendon injuries are responsible for substantial morbidity, pain and disability. Tissue engineering strategies aim at translating tendon structure into biomimetic materials. The main goal of the present study is to develop microengineered hydrogel fibers through the combination of microfabrication and chemical interactions between oppositely charged polyelectrolytes. For this, methacrylated hyaluronic acid (MeHA) and chondroitin sulfate (MeCS) were combined with chitosan (CHT). Hydrogel fibers were obtained by injecting polymer solutions (either MeHA or MeHA/MeCS and CHT) in separate microchannels that join at a y-junction, with the materials interacting upon contact at the interface. To evaluate cell behavior, human tendon derived cells (hTDCs) were isolated from tendon surplus samples during orthopedic surgeries and seeded on top of the fibers. hTDCs adhered to the surface of the fibers, remaining viable, and were found to be expressing CD44, the receptor for hyaluronic acid. The synthesis of hydrogel fibers crosslinkable through both physical and chemical mechanisms combined with microfabrication technology allows the development of biomimetic structures with parallel fibers being formed towards the replication of tendon tissue architecture.

Acknowledgments: The authors would like to thank Portuguese funds through FCT - Fundação para a Ciência e a Tecnologia in the framework of FCT-POPH-FSE, the PhD grant SFRH/BD/96593/2013 of R.C-A, to the project RL3 -TECT -NORTE-07-0124-FEDER-000020 cofinanced by ON.2 under the National Strategic Reference Framework (NSRF), through the European Regional Development Fund (ERDF) and the European Research Council for the project ComplexiTE grant agreement ERC-2012-ADG 20120216-321266.

Development of Novel Biodegradable and pH-sensitive Nanocarrier based on Self-assembling Polypeptides

L. W. Wang, T. W. Wang;

Department of Materials Science and Engineering, National Tsing Hua University, Hsinchu, TAIWAN.

Polymeric nanoparticles have shown promising potential as carriers for drug delivery. The structural stability of delivery vehicle and effective release of encapsulated therapeutic drugs are crucial for drug delivery system. In this study, the biodegradable pH-sensitive nanoparticles composed of natural polypeptides and calcium phosphate (CaP), have been developed. We utilized two different amphiphilic sequences, poly(ethylene glycol)3400-aconityl linkage- poly(L-glutamic acid)- poly(L-histidine)-poly(L-leucine) and LyP1-poly(ethylene glycol) 1100-poly(L-glutamic acid)- poly(L-histidine)-poly(L-leucine), to self-assemble into nanoparticles in aqueous phase. The biostable nanoparticles provide three distinct functional domains: the hydrated PEG outer corona for prolonging circulation time, the anionic PGlu shell for CaP mineralization, and the protonation of PHis shell for facilitating anticancer drug release at target site. The active targeting ligand, LyP-1, is served to bind to lymphatic endothelial cells in tumor for the reduction rate of metastasis. The resulting mineralized Dox-loaded particles (M-DOX NPs) with negative charge (-21.9 ± 1.6 mV) have a smaller size 179.4 ± 33.9 nm at pH 7.4, but particles at pH 5.0 have a doubled size (291.2 ± 25.1 nm) and positive charged (21.7 ± 2.1 mV), implying the protonation of polyhistidine. From the release profile, M-DOX NPs effectively reduce the leakage at physiological pH value comparing to DOX NPs, and both nanoparticles facilitate the encapsulated drug release at acidic condition. The biocompatible pH-sensitive drug carriers can effectively release anti-cancer drug in acidic condition to obtain sustained controlled release as promising carriers for anti-tumor drug delivery.

Implementation of Nanorough Surface Treatments to Improve Bone-Anchored Hearing Aid Integration

M. Stolzoff[1], J. E. Burns[2], A. Aslani[2], E. J. Tobin[2], T. J. Webster[3];

[1]Bioengineering, Northeastern University, Boston, MA, [2]N2 Biomedical, Bedford, MA, [3]Chemical Engineering, Northeastern University, Boston, MA.

Bone-anchored hearing aids (BAHA) are used in patients with hearing loss that cannot be resolved using typical air-conduction hearing aids. These devices work using sound processors mounted outside of the skull that transmit amplified sound into an implant (often titanium screws) embedded into the mastoid, which conducts sound waves directly to the cochlea, bypassing the external and middle-ear pathology. In percutaneous implants, up to 17% of patients have adverse skin reactions around the implant despite strict hygiene practices, causing revisional surgery and possible explantation of the device. This is particularly problematic with pediatric patients, who also experience implant failure (up to 15%) due to inadequate osseointegration. For children, whose hearing cognition and speech/language development are in a critical stage, failure rates up to 37% with up to 25% requiring implant explantation. To address this problem, we investigated the use of nano-featured surfacing for these implants to both reduce infection and inflammatory responses while improving osseointegration. Nanomaterials have been found to have a profound effect upon cell-material interactions, including the prevention of bacterial proliferation and biofilm formation as well as heightened mammalian cell growth for tissue regeneration. To implement this, we employed ion-beam assisted deposition