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Short Communication

Advancing Oro-Dental and Cranio-Maxillo-Facial Interventions for QoL: Injectable Hydrogel and BioCeramic NanoDelivery Platforms

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Abstract

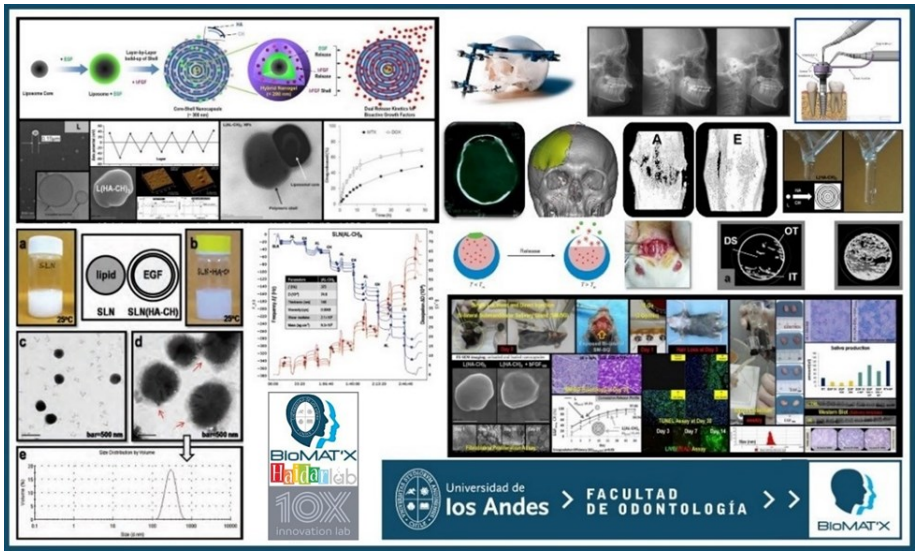
In the ever-evolving landscape of healthcare, where science, technology, and clinical practice converge, the realm of cranio-maxillo-facial and oro-dental interventions stands at the forefront of transformative possibilities. This communication embarks on an illuminating journey into the heart of this dynamic field, where innovation knows no bounds. Collaborative student engagement has been instrumental in not only exploring but also bridging the chasm between diverse scientific disciplines and the practical intricacies of clinical application. Recent strides in drug delivery mechanisms, characterized by the ingenious fusion of cells and nano-carriers, have laid the foundation for a revolution in regenerative medicine. These breakthroughs promise a future where treatments are not only precise but also meticulously controlled, enhancing patient quality of life through the amelioration of disease conditions and restoration of bodily functions. Injectable hydrogels, another trailblazing innovation, have emerged as a beacon of hope. They offer versatile solutions that promise to redefine surgical and clinical practices by affording healthcare professionals spatio-temporal control, tunability, and stimuli-responsiveness. These hydrogels unlock the potential for the targeted delivery of therapeutic agents, including cells, genes, proteins, and drugs, revolutionizing tissue engineering, regenerative medicine, and aesthetic surgical interventions. BioCeramics, a burgeoning field, is redefining conventional wisdom in bone grafting and implant technology. These biomaterials are poised to usher in a new era of innovative approaches that enhance the mechanical and biological compatibility of implants, facilitating improved clinical outcomes and patient quality of life. Moreover, this communication serves as a herald of exciting news: the inauguration of a Doctoral (PhD) Program in Dental Sciences at the prestigious Universidad de los Andes in Santiago de Chile. This program beckons forward-thinkers, visionaries, and emerging scholars to partake in pioneering research at the Laboratorio de Biomateriales, Farmacéuticos y Bioingeniería de Tejidos Cráneo Máxilo-Facial. As we embrace the future, limitless possibilities abound in this transformative health field, where advancing science and technology merge seamlessly to enhance the clinical and surgical armamentarium available for contemporary practices and users. This journey represents not only a dedication to scientific exploration yet an unwavering commitment to improving patient quality of life (QoL) and well-being thru the amalgamation of cutting-edge research, innovation, and compassionate care.

Keywords: *ToNanobiotechnology; Oro-Maxillo-Facial; Injectable Hydrogels; BioCeramics; Regenerative Dentistry; Regenerative Medicine*

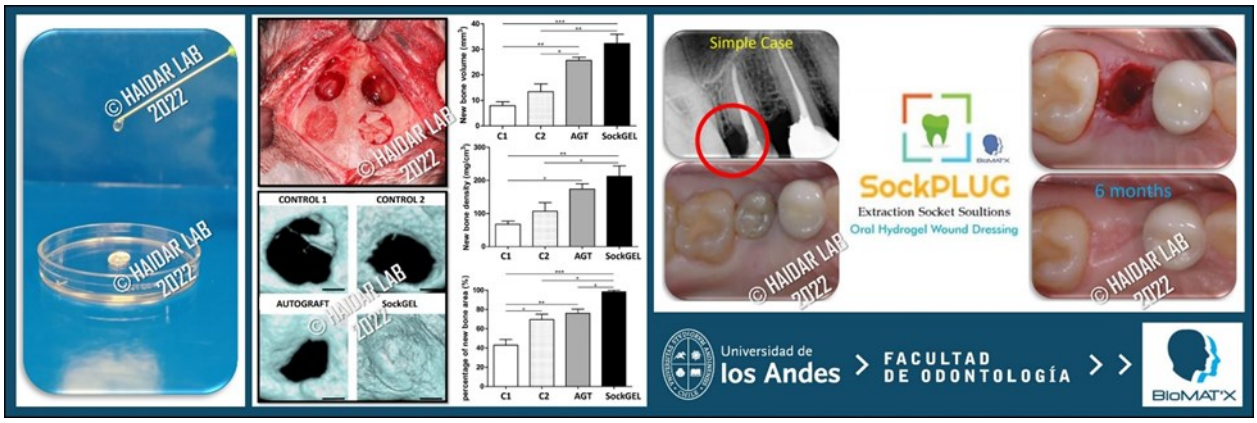
Introduction

Exploring the intersection (and synergy) of nanobiotechnology, advanced biomaterials, 3D printing, omics-based approaches, and robotic systems and more, this communication delves into the transformative potential of cranio-maxillo-facial and oro-dental interventions. Informed by collaborative student engagement, it bridges the gap between scientific disciplines and clinical practice. Recent breakthroughs in drug delivery, utilizing cells and nano-carriers, and the emergence of injectable hydrogels are poised to revolutionize regenerative medicine, offering precise, controlled treatment options. We are excited to announce the development of a new Doctoral (PhD) Program in Dental Sciences and Research at the Faculty of Dentistry, Universidad de los Andes, Chile, inviting forward thinkers to join our pioneering research at the Laboratorio de Biomateriales, Farmacéuticos y Bioingeniería de Tejidos Cráneo Máxilo-Facial, and others. As we embrace the future, limitless possibilities abound in this transformative novel field.

Innovative tissue engineering and regenerative medicine (including regenerative dentistry) solutions that incorporate nanobiotechnology, advanced biomaterials, computer assistance, three-dimensional (3D) printing, omics-based approaches, and robotic systems, amongst other emerging technologies, can offer a wide ranging potential for augmenting and improving the functional and esthetic cranio-maxillo-facial and oro-dental health profile of patients. Indeed, the bio-materials field, in general, is one of the largest and fastest growing research and innovation areas both in the scientific (and clinical/surgical) community as well as in the industry (and market). Novel biomaterials often result from collaborations between different disciplines, not limited to chemistry, biology, medicine, pharmacology, physics, mathematics, and engineering. Human activities and other biological species can and do influence the generation of natural nano-materials, nanomedicine and nanodentistry. Briefly, the global objective is to lead the innovation and implementation of new solutions and devices, for use, in diagnosis (including early disease detection), and treatment, via repairing and restoring form and function of the human body and eventually improving quality of life (QoL) and longevity; successful ageing. For example, nanodelivery (of cell/s, drug/s, protein/s, cytokine/s, bioactive agents, etc …) have thus far been successful in improving the precision (targeting), efficacy and even reducing the toxicity of many conventional cancer therapies. Overall, emphasis in this field focused on understanding, controlling, and fine-tuning the physico-chemico-mechanical and bio-characteristics and interactions (local and systemic) between the biomaterial (s) and living tissues and organs is critical and evident.

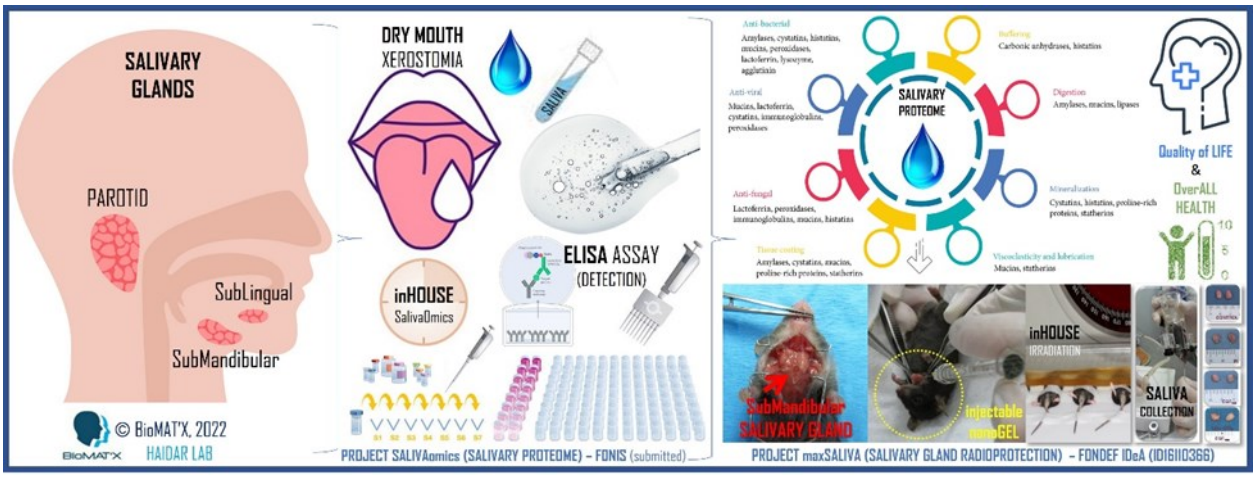


The active inspiration behind writing this article is attributed to recent interactive discussions with outstanding under graduate students attending the Faculty of Dentistry - Universidad de los Andes and participating in the **CALCIO** (Comisión de Alumnos Científica de Odontología) UANDES initiative referred to as PAI 2022-2023; Proyecto de Aproximación a la Investigación, in general, and selected/opted for participation in the "líneas de investigación en Cirugía Maxilo-Facial", in specific; a credit hour assistantship. Idea, herein, is to reflect on some of the examined concepts regarding (1) bridging-the-gap between (a) the diverse scientific disciplines as well as (b) the dental chair/clinic (chair side) and the science laboratory (bench-top), and (2) Outside-the-Box (revising the Gestalt psychology – *why the box?*) insightful, creative, innovative, and critical thinking concepts. Hence, an intentional focus on the use of specific "keywords" and terminology is integrated in this interactive piece, to further prompt the interested reader for additional curiosity, supplementary in-depth search, discussion and *applied research question design, development, evaluation, and translation*; a fun work-out and/or journey, perhaps.



Herein and for over the past century, R&D&I (research, development, and innovation) efforts have focused on optimizing drug delivery. In recent years, cells, micro and nano-particles, and combinations thereof as carriers, have emerged, mainly for facilitating superior encapsulation and controlled release pharmacokinetics. Indeed, most cells and drugs require an appropriate formulation for their successful application as pharmaceuticals. In this, the use of polymer-based hydrogel biomaterials for the delivery of drugs and recruitment of cells to promote tissue regeneration in the body is of growing interest and currently a hot research topic in pharmacology, pharmaceutics, and bio-material science; a multi/ intra-disciplinary research field. For example, hydrogels are cross-linked three-dimensional polymeric networks with unique properties such as affinity for biological fluids, tunable porosity, high water content and uptake, ease of preparation, flexibility, malleability, biocompatibility, and biodegradability. Hence, while biomimetic hydrogels have been popular for tackling pharmacological, biomedical and clinical limitations of the existing drug delivery systems, injectable hydrogels have been recently gaining more attention due to the potential spatio-temporal control, tunability and stimuli responsiveness capacities, offering significant innovative solutions in the delivery controlled and targeted delivery of therapeutics such as cells, genes, proteins and drug molecules, amongst others, with versatile platform applications in tissue engineering, regenerative medicine, implantology, functional and aesthetic surgical interventions, cancer, disease prevention and/or treatment and beyond.

Another prevalent R&D&I topic is bioCeramics. The use of ceramics in biological environments and biomedical applications is of enduringly increasing importance, as is the understanding of how biology works with minerals to develop strong materials suitable for the clinic. Herein, bioCeramics have been revolutionizing the biomedical field in the form of bone grafts, fillers, implants, and metal implant surface coatings for use in humans. Likewise, efforts are focusing on understanding and improving the biocompatibility, physico-chemical and mechanical properties of such materials and devices, with the attention directed towards the development and potential use of ceramic/ceramic composites, at micro-nano and pico-scales. Indeed, exciting and potential opportunities are associated with the design, development and use of nanobioceramics as tissue and body-interactive materials, facilitating healing and repair, or promoting the regeneration of tissues, therefore restoring physiological functions. Ceramic-based and/or ceramic-incorporated biomaterials are being biologically evaluated through numerous in vitro, in vivo and clinical tests. Safety of ceramic components and mechanical stability (preventing deformation under physiological conditions) and strength upon loading are major issues.

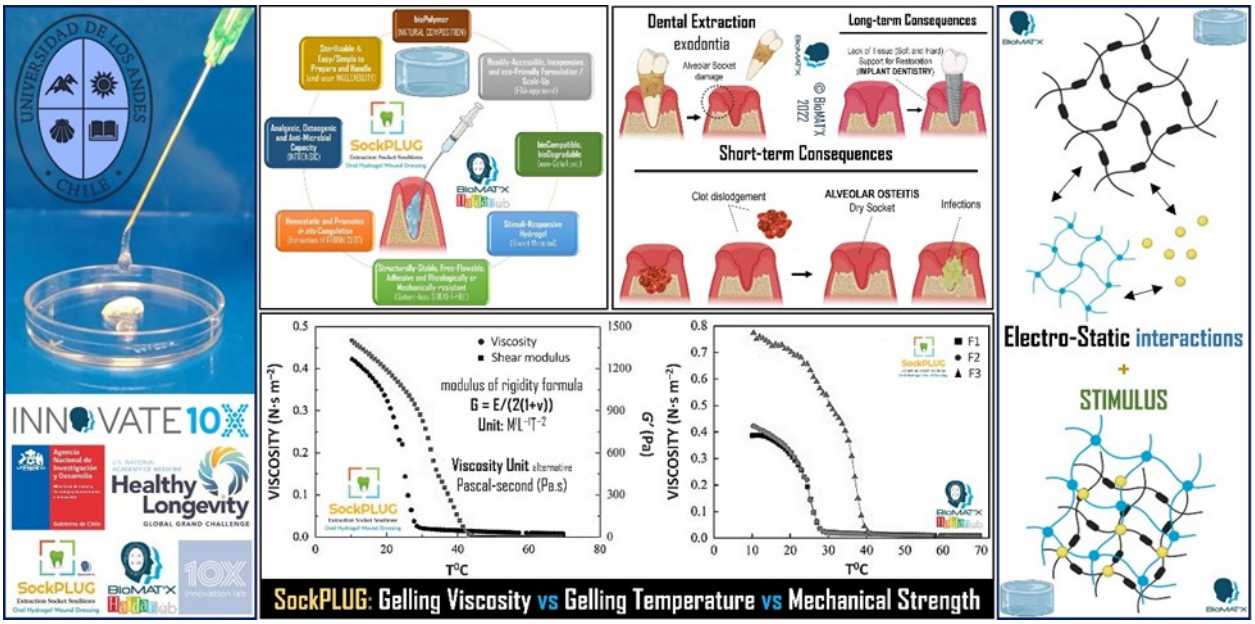


Current Challenges and Opportunities in the Oro-Dental and Cranio-Maxillo-Facial Field

The art and science of oro-maxillo-facial reconstruction is of great interest for contemporary oral and maxillofacial surgeons; in search for better bioengineering strategies and biomaterials: a core driver for bio-dental research, today. Indeed, our current clinical/surgical armamentarium, strategies, procedures, and approaches used to reconstruct and heal complex defects, including different bone grafting methods, such as autologous bone grafts, allografts, bone-graft substitutes, distraction osteogenesis, guided bone regeneration (GBR) and/or more recently, computer-/PC-aided GBR/ implantology (and membranes) are deemed restricted, daily. This is often *multi-factorial*; whether due to limited self-renewal capacity of the defect and/or the limited donor supply, increased morbidity, risk of antigenicity and foreign body reactions, and limited mechanical strength (and/or inadequate space maintenance over time), all often associated with the grafts used. Accessibility, availability, and operative-associated time, cost as well as expertise, do contribute as well. It can be sturdily stated that regenerative medicine and tissue engineering significantly direct the ongoing design, development, characterization, evaluation, optimization, and translation efforts of/for novel biomaterial-based solutions for use or application in oro-dental and cranio-maxillo-facial surgery indications including, but not limited to, localized site development (post-harvesting), maxillary sinus floor lift (augmentation), distraction osteogenesis (and histiogenesis), salivary gland radio-protection, and/or or extraction socket preservation, to list a few. Herein, nano-scaled injectable hydrogels as well as electrospun nanofibers and/or 3D-bioprinted implantable scaffold matrices (or the combination thereof considerable progress lately) are fine examples. Indeed, maxillary, and mandibular alveolar bone regeneration and periodontal defect repair have been, to a great extent the leading applied R&D&I focus, in clinical practice, through a series of major recent advancements. Injectable (biocompatible) hydrogels, for example, whether prepared using natural (alginate, chitosan, collagen, elastin, fibrin, gelatin, hyaluronic acid) and/or synthetic polymers (polyethylene glycol/PEG, polyvinyl alcohol/PVA, polylactic-co-glycolic acid/PLGA, polyhydroxyethyl methacrylate/ PHEMA), and/or fabricated via physical (based on electrostatic forces) or chemical (cross-linking methods) processes, and or designed to combine favorable physico-chemico-mechanical properties as interpenetrating polymer network hydrogels (IPN), double-network hydrogels (DN), or even programmable hydrogels and 3D printed hydrogels (recently combined with electro-spinning fabrication), have led to the introduction of a novel class of "tunable" biomaterials; smart injectable hydrogels, which besides holding a porous framework mimicking the extracellular matrix thereby allowing for cellular encapsulation/transplantation and proliferation, can match any defect (irregular, in particular) and deliver/release the bio-load, in a controllable manner. Furthermore, such pharmaco-kinetics can be modulated by any specific stimuli. Today, for bone tissue engineering and osteogenesis *per se*, such innovative hydrogels and scaffolds to supplement our clinical armamentarium and platform, require further spatio-temporal optimization in terms of (a) cellular penetration/seeding control and (b) micro/macro-scale or level rheology (mechanical properties and biodegradation mechanism for different clinical indications/scenarios); aspects that are currently being investigated and technical challenges that will be addressed, for their safe and efficacious biomedical use.

Despite recent advances that continue accruing, including that several Injectable (and smart) Hydrogels and bioCeramics have already received US-FDA approval, are under-study in clinical trial stage and/or are already commercially available in the market, limitations (and therefore, opportunities for further R&D&I) exist. Chile is no exception. Such, whether based on natural or synthetic (or hybrid) polymers and constituents, include challenges in structural chemistry, phase transition, synthesis, cross-linking, mechanical stability, visco-elasticity and porosity, in situ load release profile and pharmaco-kinetics (and dose-responsiveness) over time, biodegradability, immunological compatibility, host-immune responses, lack of molecular-level studies; formulation and fabrication costs, administration route (injectable vs implantable), data analysis from quality clinical trials, GMP (good manufacturing practices) scale-up processes or strategies and/or application-specific regulatory obstacles- *topics that still entail necessity/need and challenging opportunities for more extensive research, funding and impactful contribution*; part of ongoing effort at our BioMAT'X I+D+i Group and Laboratory.

Excitingly, we are pleased to announce the launch of our new Doctoral Program in Dental Sciences at Universidad de los Andes in beautiful Santiago de Chile. This new program (https://www.uandes.cl/investigacion-y-doctorado/ doctorados/doctorado-en-ciencias-odontologicas/) offers an unparalleled opportunity for aspiring researchers and dental professionals to delve deeper into this transformative field. We invite potential candidates to apply for enrollment and be part of the cutting-edge research and innovation happening at our HAiDAR I+D+I Laboratorio de Biomateriales, Farmacéuticosy Bioingeniería de Tejidos Cráneo Máxilo-Facial. ***Your journey towards pioneering the future begins here!***



Conflict of Interest

The author declares no conflict of interest.

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