An injectable, resorbable and pro-osteogenic cement to treat osteoporotic vertebral compression fractures

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Approximately 200 million people worldwide are suffering from osteoporosis (OP)[1], a metabolic bone disease caused by excessive osteoclasts (OCs) resorption activity that increases the risk of fracture. Particularly, vertebral compression fractures are one of the most frequent[2]. In the frame of the H2020-GIOTTO project[3], an injectable composite cement was developed to stabilize these fractures alongside stimulating bone regeneration. The cement was prepared by mixing a dry phase consisting of a mixture of powders with an aqueous phase to obtain a paste-like material, directly injectable into the fractured site.The powder component consists of α-calcium sulphate hemihydrate as matrix, strontium-containing mesoporous bioactive glasses(Sr-MBG)and zirconia particles to impart resorbability, pro-osteogenic effect and radiopacity, respectively. Furthermore, ICOS-Fc, a recombinant protein recently patented by NOVAICOS and able to decrease OC activity[4], was incorporated into the formulation to confer anti-osteoclastogenic properties exploiting two routes:biomolecule encapsulation into resorbable polymeric nanoparticles or covalent immobilisation onto Sr-MBG surface. The cement setting times were evaluated in accordance with the ASTM-C266 indicating timeframes suitable for the clinical practice. Mechanical tests conducted following the ISO-5833 demonstrated that the cement has a compressive strength value (ca.8MPa) comparable to human vertebral bodies. A radiopacity comparable to commercial reference was observed and micro-computed tomography analysis evidenced homogenous distribution of the radiopaque phase throughout its volume. In vitro release experiments revealed that the biomaterial can sustainably deliver Sr^{2+} ions up to 28 days and also functional ICOS-Fc when polymeric nanoparticles were introduced. Scratch tests with B16-F10cells proved that the ability of ICOS-Fc to inhibit OC migration was maintained also when grafted on Sr-MBG. A weight loss of about35% was detected after 1 month of immersion in Tris-HCl. Finally, the biocompatibility and the efficacy have been assessed both in vitro and in vivo in healthy and osteoporotic mice with 2% new bone volume fraction(BV/TV)formation after 28 days.

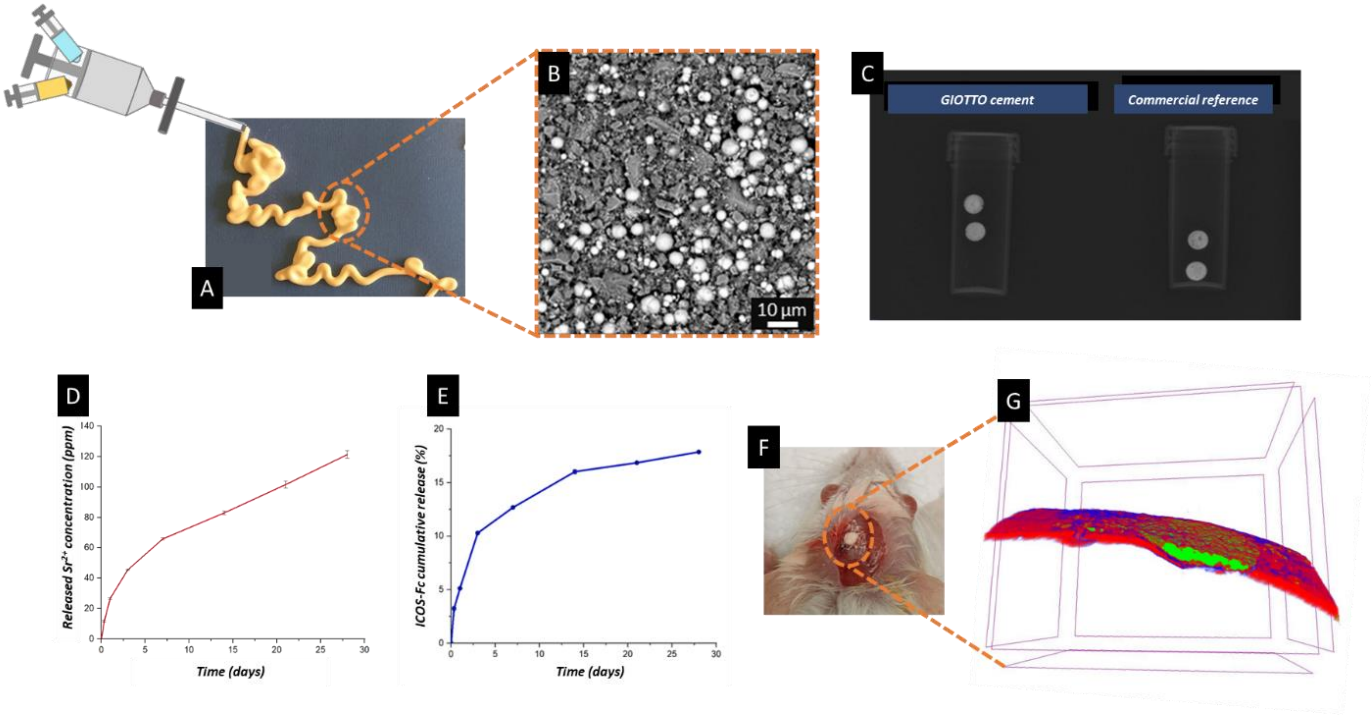

Figure: (A) injectability test of the developed cement through a 13 Gauge needle; (B) SEM images showing the great distribution of both Sr-MBG and zirconia particles (brighter spherical particles) within the calcium sulphate matrix; (C) fluoroscopy images acquired on the developed cement (left) compared to the commercial reference (right); (D) strontium ion and (E) ICOS-Fc release kinetic from the optimized cement formulation; (F) cement implanted in cranial bone defect model and (G) 3D rendering evidencing the osteointegration and new bone formation after 28 days (colour legend: blue-soft tissue, red-bone, green-cement) .

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