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Research Paper

Superior biofunctionality of dental implant fixtures uniformly coated with durable bioglass films by magnetron sputtering

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ABSTRACT

Bioactive glasses are currently considered the suitable candidates to stir the quest for a new generation of osseous implants with superior biological/functional performance. In congruence with this vision, this contribution aims to introduce a reliable technological recipe for coating fairly complex 3D-shaped implants (*e.g.* dental screws) with uniform and mechanical resistant bioactive glass films by the radio-frequency magnetron sputtering method. The mechanical reliability of the bioactive glass films applied to real Ti dental implant fixtures has been evaluated by a procedure comprised of "cold" implantation in pig mandibular bone from a dead animal, followed by immediate tension-free extraction tests. The effects of the complex mechanical strains occurring during implantation were analysed by scanning electron microscopy coupled with electron dispersive spectroscopy. Extensive biocompatibility assays (MTS, immunofluorescence, Western blot) revealed that the bioactive glass films stimulated strong cellular adhesion and proliferation of human dental pulp stem cells, without promoting their differentiation. The ability of the implant coatings to conserve a healthy stem cell pool is promising to further endorse the fabrication of new osseointegration implant designs with extended lifetime.

1. Introduction

The international dental implants market experienced a continuous growth in the last decade, slightly fading only during the global financial crisis, followed by a strong revival from 2013 to a level rated at 6.4 billion dollars (http://www.marketsandmarkets.com/PressReleases/dental-implants-market.asp, 2015a). Reputed economic research agencies forecast a continuous strong rise in the Compound Annual Growth Rate (CAGR) in coming years: Transparency Market Research—CAGR ~7.3% (http://www.marketsandmarkets.com/PressReleases/dental-implants-market.asp, 2015a) until

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2018; TechNavio—CAGR of ~5.4% from 2012 to 2016 (http://www.technavio.com/report/global-dental-implants-market-2012-2016, 2015b); Persistence Market Research—CAGR ~9.7% for the 2014–2020 period (http://www.persistencemarketresearch.com/mediarelease/dental-implants-market.asp, 2015c).

The evolution of dental implants' market is determined by economical aspects, and changes in cultural perception on health and lifestyle of the society (http://www.transparenc;ymarketresearch.com/dental-implants-market.html, 2015d; http://www.dentaleconomics.com/articles/print/volume-100/issue-12/features/trends-in-implant-dentistry.html, 2015e; http://www.dental-tribune.com/articles/business/americas/11737_dental_implants_market_expected_to_double_by_2018.html, 2015f): (i) life expectancy (the edentation problem becomes more acute with the increase of the population age); (ii) demographics in certain regions of the world; (iii) oral hygiene concerns; (iv) sociological and cultural reasons (in the collective mentality a pleasant appearance enhances the perception of a more dynamic, professional and trustworthy individual); (v) per capita incomes in the emerging economies; (vi) implants' availability due to an increased number of certified producers; (vii) advanced therapeutic biomedical progress and new technologies advertised through diverse media channels. According to a recent study of the American Association of Oral and Maxillofacial Surgeons (http://www.dentaleconomics.com/articles/print/volume-100/issue-12/features/trends-in-implant-dentistry.html, 2015e), 69% of adults with ages between 35 and 44 in USA have lost at least one tooth due to accidents or dental disease, while by age 74, 26% of adults are edentulous. The American Academy of Implant Dentistry reported that 3 million people have dental implants in USA, and that the number is growing by 500,000 a year (http://www.bluemcare.com/en/blogs/nieuws/good-news-for-bluem-dental-implants-market-expecte/, 2015g). Yet, Europe is the largest dental implants market with a share of ~42% of the global market (http://www.marketsandmarkets.com/PressReleases/dental-implants-market.asp, 2015a), followed by North America, and by the countries with major booming economies and a large population (China, India, Brazil). Such demand stimulates the search for more effective manufacturing processes and implants with superior functionality and fast healing responses.

Titanium (Ti) based materials, first introduced in clinical practice in the '40s (Bothe et al., 1940; Nakajima and Okabe, 1996), have a dominant share of the dental implants market due to a set of relevant properties: (i) corrosion resistance and compatibility in biological environments; (ii) excellent mechanical properties and reduced mass density. A smaller market share appertains to implants fabricated from another bioinert material: zirconia (*e.g.* CeraRoot®).

The osseointegration of Ti dental implants can be enhanced by two main surface engineering approaches: (i) topographical and physico-chemical modifications (via machining, grit-blasting, acid-etching, anodic oxidation, laser processing (Ballo et al., 2011; Bosco et al., 2012), cold-plasma treatment (Yoshinari et al., 2011) or photofunctionalization (Suzuki et al., 2013); (ii) chemical alterations (by addition of growth factors (Gaviria et al., 2014; Le Guehennec et al., 2007) or by coating with a continuous, mechanical resistant bioactive layer (Bosco et al., 2012; Gaviria et al., 2014; Le Guehennec et al., 2007).

The bioactive materials, including bioglasses/glass–ceramics and calcium phosphate-based bioceramics, possess unique biologic qualities (Hench, 1991; Zhao et al., 2011). When in contact with the physiological environment they stimulate bony tissue repair and lead to the creation of a strong bond between the surrounding tissue and the medical device (Hench, 1991; Bachar et al., 2013; Li et al., 2014; Shen et al., 2015; Kapoor et al., 2015). Dental implants are currently coated with hydroxyapatite [HA, $Ca_{10}(PO_4)_6(OH)_2$] or biphasic calcium phosphates (CaP) [HA+β-$Ca_3(PO_4)_2$] layers deposited by plasma spraying (Ong and Chan, 2000). Their share from the global market is not large, but is in a continuous rise (Bosco et al., 2012; Gaviria et al., 2014). However, plasma spraying technology is quite expensive and produces thick coatings susceptible to delamination, containing hardly reproducible residual phases with unpredictable biological behaviour, due to thermal stresses and/or compositional gradients induced by the high/transient temperatures involved (Epinette and Manley, 2004; Miyazaki and Kawashita, 2013). Moreover, delamination debris (in form of chips/cutting blades) is prone to inflict serious injuries/wounds in the implantation site.

Bioglasses (BG) are osteoproductive and possess the highest index of bioactivity, reflected in their ability to form a strong and enduring bond with the living tissues in a very short time. The first compositional system – 45S5 Bioglass® (wt%: SiO_2—45, Na_2O—24.5, CaO—24.5, P_2O_5—6) – was patented in the early '70s by Hench, 1991, 2006). Nowadays, 45S5 Bioglass® and S53P4 BonAlive® (wt%: SiO_2—53, Na_2O—23, CaO—20, P_2O_5—4) formulations, are considered the bioactive glass gold standards, being currently the only melt-quenched BGs accepted by the USA Food and Drug Administration for use in clinical practice (Massera et al., 2012; Vallittu et al., 2015). However, the significant mismatch in the thermal expansion coefficients (CTE) of these classical BG systems ($\sim$15–17 $\times 10^{-6}\,°C^{-1}$) and Ti and its medical grade alloys ($\sim 9.2 \times 10^{-6}\,°C^{-1}$), limits their use to applications bearing low biomechanical loads such as: bone fillers, scaffolds, auricular implants, treatment or repair of eye shelf or frontal sinus (Karlsson and Hupa, 2008; Fagerlund et al., 2012; Jones, 2013; Jones and Clare, 2012; Hench, 2013). The high Na_2O content and the related fast degradation rate of 45S5 Bioglass® and S53P4 BonAlive® might be inappropriate for durable implant coatings. However, in some cases remnants of S53P4 were still observed after several year post-implantation (Lindfors et al., 2010; Massera et al., 2014).

Incorporating other components (*e.g.* MgO, CaF_2, B_2O_3, and/or ZnO) into the classical formulations enabled reducing the CTEs mismatch and *in vitro* degradability, without affecting the osteoinduction capacity (Massera et al., 2012; Jones and Clare, 2012; Goel et al., 2012; Agathopoulos et al., 2006; Tulyaganov et al., 2011; Al-Noaman et al., 2013), suggesting the feasibility of manufacturing mechanically reliable BG implant coatings. Although frantic attempts to accomplish reliable BG coatings (onto almost exclusively flat substrates) by employing either well-established or novel physical and chemical deposition technologies (Sola et al., 2011; Verné, 2012) have been carried out, BG coated Ti implants are not yet available for medical practice.