**Biocompatible flexible piezoceramic thin films for biomedical applications**

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In the last years there was an increased interest in developing piezoceramic materials for bone repair. Indeed several research studies evidenced that osteogenic regeneration and implant osseointegration could be actively improved by transforming electrical stimuli into mechanical loading necessary for cell signaling through mechanotransduction [1,2]. This process could help to overcome the so-called stress shielding, which occurs around implants and contribute to bone tissue loss and implant loosening [2]. In order to employ the piezoceramic materials in suitable devices for bone repair, it must first be tested if mesenchymal progenitors would be able to respond to these piezoceramics without being exposed to increased toxicity. In this study we report the synthesis of functional biocompatible piezoceramic $(Ba,Ca)(Zr,Ti)O_3$ (BCZT) thin films with enhanced piezoelectric properties. The high piezoelectric coefficients and dielectric constants, which make this material very appealing for a variety of applications in photonic, piezoelectric and electronic devices, are not the only advantages of BCZT system. Another significant perspective, given by the specific properties of BCZT as lead-free non-toxic material, regards its applicability in biology and medicine field, from fundamental biological studies to tissue engineering. We have first studied this $BaTiO_3$-based material suitably doped with Ca and Zr in order to optimize its composition in the phase diagram region where maximization of physical properties of interest can be obtained [3]. BCZT thin films have been grown from these targets and investigated by different techniques [4]. We have employed two pulsed laser-based techniques: classical pulsed laser deposition (PLD) and matrix-assisted pulsed laser evaporation (MAPLE). The MAPLE technique was specially developed for integration with polymeric/organic/biological materials and allows both the deposition of organic/polymer materials that would be damaged in a classical PLD process, as well as deposition on flexible polymer substrates, which is of high interest for integration of piezoactive thin films in flexible microdevices. PLD films have been grown on Pt/Si substrates while MAPLE films have been deposited on flexible polymer Kapton substrates coated with Pt. BCZT thin films grown by both techniques show similar structural properties and high piezoelectric coefficients [5]. The assessment of cell adhesion and osteogenic differentiation onto BCZT materials has been further investigated. It has been proved for the first time that BCZT films on Kapton polymer substrates provide optimal support for osteogenic differentiation of mesenchymal stem cells in the bone marrow. Laser-based approaches to obtain BCZT as biomaterials which support cellular adhesion, proliferation and differentiation can have an important impact to their exploitation in a variety of biomedical applications. Thus, by modulating the properties of BCZT thin films, the response of mammalian cells *in vitro* (adhesion, proliferation, migration, electrical stimulation and differentiation) can be adapted to the envisaged application. Therefore the results presented here can be of more general relevance for other biocompatible piezoactive materials and their applications in the biotechnology field.

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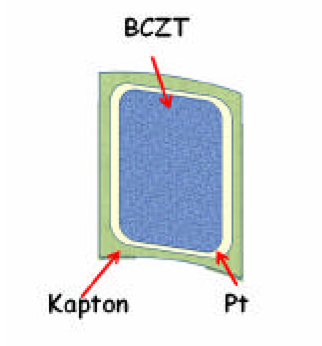


Figure 1. Sketch of a BCZT/Pt/Kapton structure.

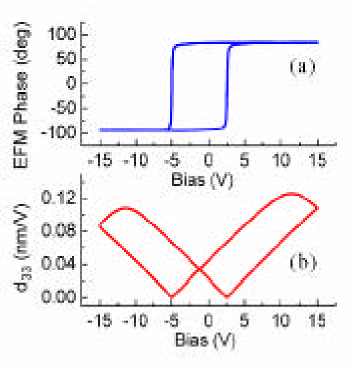


Figure 2. Piezoelectric response (phase and amplitude) of BCZT/Pt/Kapton.

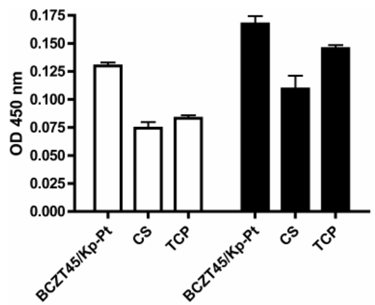


Figure 3. Proliferation rate by metabolic activity measurement of human epithelial embryonic kidney HEK 293 T (white) and human malignant melanoma A375 cells (black) grown for 48 h on BCZT/Pt/Kapton film, glass CS and TCP.

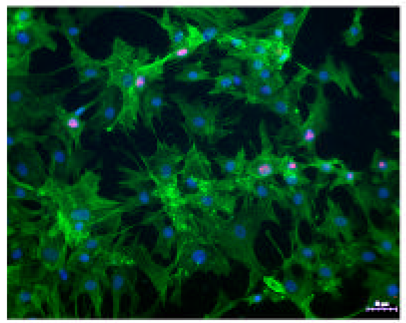

Figure 4. Spreading and proliferation of cells on BCZT/Pt/Kapton at 14 days postosteoinduction in osteogenic conditions.