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# The incorporation of a zone of calcified cartilage improves the interfacial shear strength between in vitro-formed cartilage and the underlying substrate

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ABSTRACT

A major challenge for cartilage tissue engineering remains the proper integration of constructs with surrounding tissues in the joint. Biphasic osteochondral constructs that can be anchored in a joint through bone ingrowth partially address this requirement. In this study, a methodology was devised to generate a cell-mediated zone of calcified cartilage (ZCC) between the in vitro-formed cartilage and a porous calcium polyphosphate (CPP) bone substitute in an attempt to improve the mechanical integrity of that interface. To do so, a calcium phosphate (CaP) film was deposited on CPP by a sol–gel process to prevent the accumulation of polyphosphates and associated inhibition of mineralization as the substrate degrades. Cartilage formed in vitro on the top surface of CaP-coated CPP by deep-zone chondrocytes was histologically and biochemically comparable to that formed on uncoated CPP. Furthermore, the mineral in the ZCC was similar in crystal structure, morphology and length to that formed on uncoated CPP and native articular cartilage. The generation of a ZCC at the cartilage–CPP interface led to a 3.3-fold increase in the interfacial shear strength of biphasic constructs. Improved interfacial strength of these constructs may be critical to their clinical success for the repair of large cartilage defects.


## 1. Introduction

Articular cartilage is a connective tissue that forms the gliding surfaces of synovial joints, while also transferring and distributing the loads applied through the joint to the subchondral bone [1]. Cartilage damage due to disease or trauma often progresses to clinical signs of osteoarthritis because of the limited capacity for self-repair of this tissue [2,3]. Current repair strategies, including mosaicplasty, marrow stimulation and autologous chondrocyte implantation, have had limited long-term clinical success [4].

Numerous cartilage tissue engineering approaches have been developed in an attempt to improve the quality of repair tissue and the functional outcome compared to currently available surgical interventions to treat cartilage defects [5]. However, only recently have efforts to generate functionally relevant interfaces between the bioengineered cartilage and surrounding tissues in the joint received attention [6]. Because of the essential role of the cartilage–subchondral bone interface in the transfer and distribution of loads between these two tissues, it has been speculated that the long-term success of bioengineered cartilage depends on its proper integration to the subchondral bone upon implantation [7–9]. Efforts to achieve this have focused mainly on the design of biphasic constructs that mimic the native osteochondral architecture; this has been reviewed in detail by Yang and Temenoff [6]. A number of these osteochondral constructs have developed a zone of calcified cartilage (ZCC) following their implantation in cartilage defects or subcutaneously [10–12]. Our group and others have attempted to generate biphasic constructs incorporating a calcified interface generated in vitro [13–15].

The ZCC is the highly mineralized region of the deep zone of articular cartilage that interfaces and anchors the hyaline cartilage with the underlying subchondral bone. The tidemark at the interface between the hyaline and calcified cartilage maintains its mechanical integrity through collagen fibrils arranged perpendicular to the joint surface that bridge the junction between the two tissues [16]. The integrity of the interface between the ZCC and subchondral bone is ensured by the high level of interdigitation between the two tissues [17]. While the mineral content of the ZCC is significantly higher than that of bone [18], a debate exists in the literature with regards to the stiffness of the ZCC compared to subchondral bone. One study has demonstrated through a three-point bending test that the bending modulus of the ZCC is one order of magnitude lower than that of subchondral bone [19], while two nanoindentation studies have reported similar stiffness for the

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