# OSTEOCHONDRAL DEFECT REPAIR USING A NOVEL TISSUE ENGINEERING APPROACH – SHEEP MODEL STUDY

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## Introduction

Current strategies for treatment of diffuse joint degeneration utilize replacement of the whole degenerated joint with implants made of metals, ceramics, or polymers. While this has provided excellent treatment outcome for periods up to 15 years or so, approximately 20% of treated patients require revision procedures after this period, primarily due to adverse host response to liberated wear debris (endosteal osteolysis) and/or significant bone loss due to stress shielding of bone for adjacent to certain implant designs. Younger patients (40- and 50-year olds), therefore, may require 2 or more revision surgeries during their lifetime. Early intervention and repair of localized defects caused by trauma-induced damage to a joint surface could reduce the need for such treatment. However, currently a reliable method for achieving early repair of focal defects is not available. As a result, localized lesions can progress to more diffuse degenerative changes requiring eventually whole joint replacement with its associated long-term limitations. The goal of our study has been the development of a novel method for the repair of localized osteochondral damage at an early stage using a tissue engineering strategy. The approach involves the use of in 'biphasic' constructs consisting of articular cartilage formed *in vitro* from autologous donor cells attached through tissue ingrowth to regions of a porous biodegradable inorganic substrate. This biphasic construct when implanted into an osteochondral defect site is designed to achieve secure anchorage through bone ingrowth into regions of the porous construct not occupied by cartilage while establishing close approximation of the *in vitro*-formed cartilage with surrounding host cartilage.

## Methods

Porous calcium polyphosphate (CPP) substrates were formed by sintering CPP powders made in our laboratory as described elsewhere [1]. The resulting substrates were about 65% dense with a network of interconnected pores of size suitable for rapid bone ingrowth (average pore size ~ 75 μm). Articular cartilage was harvested from sheep knee joints and chondrocytes isolated by sequential enzymatic digestion under sterile conditions as described previously [2]. The chondrocytes ($2x10^6$ cells for a 4mm diameter plug) were re-suspended in 25μl of Ham's F12 with 5% autologous serum and placed on the top of the porous substrates and cultures grown for 8 weeks under standard culture conditions at 37°C. The resulting biphasic implants were gently but snugly pressed into a prepared site in the sheep femoral condyle. Control sites that received CPP alone (lacking an *in vitro*-formed cartilage over-layer) were also included. Up to three implants were placed in the lateral or medial femoral condyle of the leg opposite to that from which chondrocytes were harvested for *in vitro* cartilage formation. Animals were euthanized at either 3 or 9 months and the implants and surrounding tissues retrieved. The retrieved samples were used for assessment of histological, biochemical and mechanical properties of the *in vitro*-formed cartilage.

## Results

The initial *in vivo* studies employing 'biphasic' constructs to repair defects in sheep knee joints have provided encouraging results with secure implant fixation to host bone being achieved by bone ingrowth by 3-months and good integration of *in vitro*-formed cartilage with the adjacent host cartilage at that time. This structure was maintained at 9 months. *In vivo* degradation of the CPP construct was observed in keeping with previously reported animal studies [3]. Comparison of cartilage characteristics after the 3- and 9-month implantation periods indicated hydroxyproline (collagen) levels increased from 60% to 82% relative to values determined for nearby host cartilage, and relative GAG levels (proteoglycans) increased from 62% to 72%. Mechanical testing of the *in vitro*-formed cartilage indicated that after 3 and 9 months *in vivo*, the equilibrium modulus of the *in-vitro*-formed cartilage was ~ 45% that of native host cartilage.

## Conclusions

The study supported the potential use of *in vitro*-formed cartilage anchored to a biodegradable calcium polyphosphate construct for the repair of early cartilage/subchondral bone defects.


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**References**

[1] Pilliar RM et al, Biomaterials 22:963-72, 2001
[2] Waldman SD et al, J Biomed Mater Res 62:323-330, 2002
[3] Grynpas MD et al, Biomaterials 23:2063-70, 2002


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