

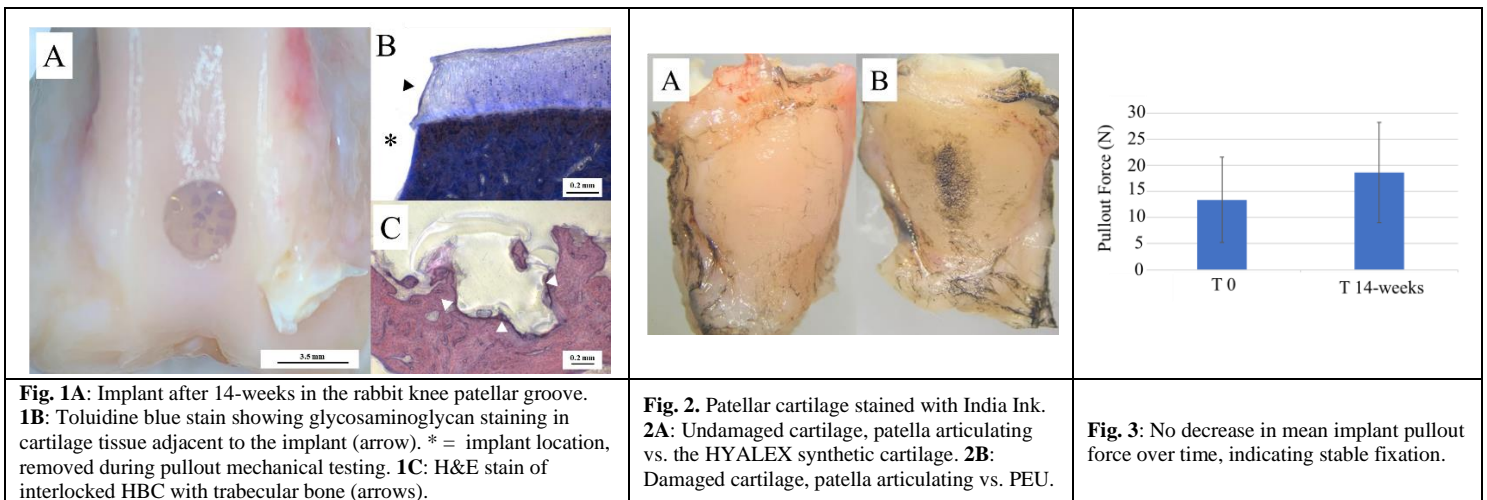
# Osteochondral defect repair using a novel synthetic cartilage implant anchored through *in situ* photocured bone cement – a long-term fixation assessment

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**INTRODUCTION** – Disruption of cartilage due to injury can result in repair tissue with inferior properties, leading to progressive degradation of surrounding healthy cartilage and large painful osteochondral lesions. Patients with symptomatic knee cartilage lesions report that quality of life is affected as much as patients scheduled for total knee replacement<sup>1</sup>. Treatment options for osteochondral lesions using regenerative approaches have variable outcomes depending on patient age and lesion size, and require long rehabilitation periods prior to resumption of normal activity levels. In contrast, cartilage replacement devices have the potential to provide rapid return to weightbearing activities even for patients who do not respond to regenerative treatments. The synthetic cartilage replacement system used in this study consists of an implant designed to have mechanical properties that are similar to cartilage and an *in situ* photopolymerizing bone cement used to anchor the implant to cancellous bone. This implant system is intended for a wide range of applications such as hemiarthroplasty and treatment of localized cartilage lesions in a variety of articular joints.

**METHODS** – The novel implant material (HYALEX™ synthetic cartilage, Hyalex Orthopaedics) was manufactured from a hydrated interpenetrating dual polymer network based on polyether urethane (PEU), and engineered to be hydrophilic to provide a durable, lubricious, low friction interface with native articular cartilage. The implant also had a hydrophobic PEU backside surface optimized for fixation to bone using a photopolymerizable bone cement (HYALEX™ bone cement (HBC), Hyalex Orthopaedics). HBC is an *in situ* curing polyurethane-based bone cement comprised of a mixture of components used in dental and orthopaedic bone cements. Implants (3.5 mm in diameter) were gamma sterilized using a nominal dose of 40 kGy and HBC was sterilized via filtration. After passing cytotoxicity, pyrogenicity, acute systemic toxicity and intracutaneous irritation testing following ISO 10993 and GLP guidelines (NAMSA), a standard rabbit patellar groove knee defect model was chosen to assess long-term implant fixation with HBC, since this model is widely used to evaluate cartilage treatments<sup>2</sup>. A total of 22 skeletally mature New Zealand white rabbits were included in the study, conducted following GLP guidelines (NAMSA), assessing 11 rabbits after implantation (T0) and the remaining at 14-weeks (T14-weeks). One device was implanted into the patellar groove of each knee. A 3.6 mm diameter defect was created using a drill bit and reamer, followed by pulse lavage to remove bone debris and bone marrow. HBC was applied to the defect site and implant backside, and the implant was subsequently inserted. The bone cement was photopolymerized using visible light through the clear implant. Rabbits were allowed to ambulate *ad libitum* immediately following the procedure. Primary endpoint assessment consisted of a mechanical test to quantify the maximum tensile pullout force as a measure of fixation strength (displacement rate = 0.6 mm/min). Secondary endpoints included gross implant assessment, implant surface characterization using ATR-FTIR and environmental SEM (eSEM), articulating cartilage integrity determined by India Ink staining<sup>3</sup>, and histology of cartilage in contact with the implant and trabecular bone in contact with HBC.

**RESULTS** – Eleven rabbits (22 implants) were evaluated at T0 and seven rabbits (14 implants) were evaluated at 14-weeks. Four rabbits were excluded due to post-operative complications unrelated to the device. Implants successfully remained *in situ* after 14-weeks, showing no evidence of subsidence, cartilage degradation at the margins or tissue overgrowth around the implant. Bearing surfaces were grossly (**Fig. 1A**) and microscopically unchanged, determined by eSEM. ATR-FTIR spectra of the bearing surface showed no measurable change in to the surface chemistry *in vivo* as compared to control spectra (non-implanted devices), indicating long-term biostability of the implant material. Cartilage tissue adjacent to the implant was normal (**Fig. 1B**), and trabecular bone remodeled around interlocked HBC, without the presence of fibrous tissue at the interface (**Fig. 1C**). Patellar surfaces exhibited no India Ink staining, indicating preservation of healthy opposing cartilage following long-term articulation against the implant (**Fig. 2A**). The exception was one instance of implant insertion with the hydrophobic PEU backside articulating against the patella for comparison, which resulted in visible evidence of cartilage damage (**Fig. 2B**). The mean pullout forces were 13.41±8.20 N and 18.64±9.63 N at T0 and T14-weeks, respectively. All pullout testing failures occurred at the HBC-bone interface. There was no statistically significant difference in pullout force with time (t-test: p=0.09), indicating that HBC provides stable long-term implant fixation (**Fig. 3**).



**DISCUSSION** – A well-established rabbit model was used to evaluate cartilage replacement with a cartilage-like synthetic material *in vivo*. The results of this study confirmed that the device was highly compatible with cartilage. The lack of patellar surface staining with India Ink and normal histological appearance of patella cartilage with good glycosaminoglycan retention demonstrates the potential advantage of using an inherently lubricious material as a cartilage replacement implant. In contrast, articulation against a nonlubricious surface such as PEU can initiate irreparable cartilage damage. The implants remained well-fixed *in situ* using photopolymerizable HBC. This polyurethane-based bone cement was specifically formulated to form a strong, stable attachment to the hydrophobic PEU back surface of the implant and interlock with trabecular bone, as evidenced by consistent pullout failure at the cement-bone interface after implantation.

**SIGNIFICANCE** – Preclinical evaluation of a synthetic cartilage implant demonstrated successful long-term fixation and preservation of the opposing cartilage surface in a rabbit knee model, showing promising initial results that may allow early intervention cartilage resurfacing in patients suffering from painful cartilage lesions or in hemiarthroplasty for osteoarthritic joints.

**REFERENCES** – 1. Heir, S. *et al*, Am J Sports Med. 2010. 2. Cook, J. L., *et al*, Bone Joint Res. 2014. 3. Laverty, S., *et al*. Osteoarthritis Cartilage 2010.