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Cartilage degeneration in the goat knee caused by treating localized cartilage defects with metal implants

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Summary

Objective: The purpose of the current study was to investigate the feasibility of applying defect-size femoral implants for the treatment of localized cartilage defects in a 1-year follow-up model.

Methods: In 13 goats, a medial femoral condyle defect was created in both knees. Defects were randomly treated by immediate placement of an oxidized zirconium (OxZr) ($n = 9$) or cobalt–chromium (CoCr) implant ($n = 9$) or left untreated ($n = 8$). Six un-operated knee joints served as a control. Animals were sacrificed at 52 weeks. Joints were evaluated macroscopically. Cartilage quality was analyzed macroscopically and microscopically and cartilage repair of untreated defects was scored microscopically. Glycosaminoglycan (GAG) content, release and synthesis were measured in tissue and medium. Implant osseointegration was measured by automated histomorphometry.

Results: Cartilage repair score of the defects was 13.3 ± 3.0 out of 24 points (0 = no repair, 24 = maximal repair). Articular evaluation scores decreased (indicative of degeneration) in untreated defects and in defects treated with either implant ($P < 0.05$). Macroscopical, microscopical and biochemical analysis showed that the presence of untreated defects and the implants caused considerable degeneration of medial tibial plateau, and to a lesser extent of the lateral compartment. Mean bone-implant contact was extensive and not different between materials ($39.5 \pm 28.1\%$ for OxZr and $42.3 \pm 31.5\%$ for CoCr) ($P = 0.873$).

Conclusions: Considerable cartilage degeneration was induced in the articulating cartilage of the medial tibial plateau 1 year after creating an osteochondral defect in the medial femoral condyle. Treating this defect with a small metal implant, made of either OxZr or CoCr, could not prevent this degeneration. Further optimization of defect-size implants and their placement is required to make this the therapy of choice for the treatment of local cartilage defects.

Key words: Oxidized zirconium, Cobalt–chromium, Small metal implant, Cartilage defect, Knee.

Introduction

Localized cartilage defects in the knee are associated with disability and symptoms such as joint pain, locking phenomena and reduced or disturbed function. Moreover, these defects predispose to severe forms of osteoarthritis[1]. The surgical treatment of localized cartilage defects is usually aimed at stimulation of biological repair, including subchondral perforation[2,3], osteochondral transplantation, and autologous chondrocyte transplantation. Although these biological repair treatment modalities are well established[4,5], they have limitations. Often, fibrous or fibrocartilaginous tissue is formed, which is frequently followed by progressive joint degeneration, often resulting in an indication for further surgical intervention, such as an osteotomy, joint distraction[1], a hemiarthroplasty or a total joint replacement[1].

A proposed alternative for the treatment of localized (osteo)chondral defects is the use of defect-size metal implants filling the cartilage defect, thereby re-establishing the integrity of the joint surface. Although this treatment modality has already been applied in humans after trauma of the knee, hip, toe and shoulder[6–8], there is no experimental evidence suggesting its efficacy as an alternative to the established surgical treatments. In fact, in a rabbit model, defect-sized implants inserted in knee defects were found to induce considerable cartilage degeneration of the opposing articulating cartilage of the tibia[9,10]. However, this may have been due to the sensitivity of such a small animal model to small deviations in surgery procedures. The thickness of healthy adult rabbit knee cartilage thickness is 0.3 mm, whereas healthy goat knee cartilage is 0.7–1.5 mm thick[11]. Thus malpositioning of only 1 mm or less might have fewer consequences in a goat knee.

Vital in the application of non-degradable implants are their biomechanical and wear characteristics. Currently, cobalt–chromium (CoCr) alloy is a frequently employed material for hemiarthroplasty bearing surfaces, however, even given the wide implementation, some downsides are described[12,13]. For example, failure of CoCr hemiarthroplasty hip prostheses was found, due to pain and erosion of acetabular articular cartilage and bone[14]. Therefore,

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ceramic bearing materials such as oxidized zirconium (OxZr) have sparked renewed interest, based on *in vivo* properties such as better scratch resistance, less surface roughness after articulation against third body debris such as bone cement, a lower friction coefficient and more elasticity, while maintaining equivalent device fatigue strength[15–21]. Therefore, it could be hypothesized that this material would be suitable as an articulating surface in treatment of cartilage defects, joint trauma and early, localized osteoarthritis using defect-sized non-degradable implants. However, the postulated superiority of this material has not been proven *in vivo*, where not only articulation, but also osseointegration and surgical aspects define the functionality of an implant. To verify the applicability of local implants in the treatment of cartilage defects in a large animal model (in an effort to avoid the propensity of small animal models for suboptimal implant positioning) and to evaluate whether OxZr would confer an advantage over CoCr in terms of joint and cartilage integrity and implant fixation, we used an *in vivo* model in which a femoral tack (similar to the abovementioned rabbit studies) of either material was applied to a localized defect in a goat knee joint.

Materials and methods

EXPERIMENTAL DESIGN

This research was approved by the Institutional Animal Care Committee of the Utrecht University (approval number DEC04.07.057). In thirteen adult female Dutch milk goats, a standardized medial femoral condyle defect was created in both knees. The defects were randomly treated with either an OxZr (nine knees) or CoCr (nine knees) press fit implant (∅articulating surface 5.0 mm; length 13.5 mm) or left untreated (eight knees). As a control group, the un-operated left knees of six goats (six knees) included in a separate study were used. The experimental animals were killed 52 weeks after surgery. Macroscopic articular evaluation was performed immediately before creating the defect and 52 weeks after treatment. Tibial and femoral cartilage quality was evaluated by macroscopic, microscopic, and by biochemical analysis. After 52 weeks, implant osseointegration was measured by automated histomorphometry and defect healing of the untreated defects was scored microscopically. All results are described as mean ± standard deviation.

ANIMALS

Thirteen adult female Dutch milk goats, aged 3.1 ± 0.28 years and weighing 66.4 ± 8.7 kg were used for surgery. The un-operated left knees of six adult female Dutch milk goats aged 2.4 ± 0.28 years and weighing 65.6 ± 5.7 kg were used as a control group. These goats were used in a separate (unpublished) study (approval number DEC04.07.057). The number of animals needed for this study was determined by a power analysis. The power was 0.8 and α was 0.05. The data used for this analysis were obtained from biochemical analysis as described previously[22]. Food and water was given *ad libitum*. General health and care conditions were monitored by the laboratory animal welfare officer.

IMPLANTS

Implants were custom-manufactured to our design specifications by Smith & Nephew (Memphis, TN, USA). The size of the implant was 13.5 mm (length) by 5.0 mm (diameter-articulating surface). The articulating shape of the implant was designed after a study on goat cadaver knees and tested in a pilot study [Fig. 1(A, B)].

SURGERY

After acclimatizing for at least 3 weeks in the animal care facility, 1 day prior to surgery, a topical fentanyl application bandage was given as pain medication. The goats were weighed pre-operatively. Surgery was performed on both knees, under general inhalation anaesthesia using an isoflurane (2% in air) gas mixture (Abbott Laboratories, ASTPharma, The Netherlands) preceded by detomidine hydrochloride sedation (Pfizer, The Netherlands) and antibiotic prophylaxis (Augmentin®, GlaxoSmithKline, United Kingdom). All surgical procedures were carried out under aseptic conditions and by the same surgeon (RC), who had gained specific experience in the course of a pilot study. The medial femoral condyle was exposed through a medial parapatellar incision, without dislocating the patella. After inspecting the joint and determining the location for implantation, a drill (diameter 5.0 mm) was used to create a standardized full-thickness cartilage defect not penetrating the subchondral bone layer (2.0 mm deep). To place the implant, the defect was drilled deeper (3.0 mm) and subsequently, the implant was placed flush to the surrounding cartilage surface by tapping the implant into place using a specially designed tamp with a polyethylene head, as previously described[9,10]. After insertion, the implants were visually inspected and manually tested for fixation. Following lavage, the joint, subcutis and skin were closed in three layers using sutures. Additional post-operative pain relief was provided by buprenorphin (Schering−Plough, The Netherlands). Until 5 days post-operatively, ampicillin (Albipen®, Intervet, The Netherlands) was given. Post-operatively, the goats

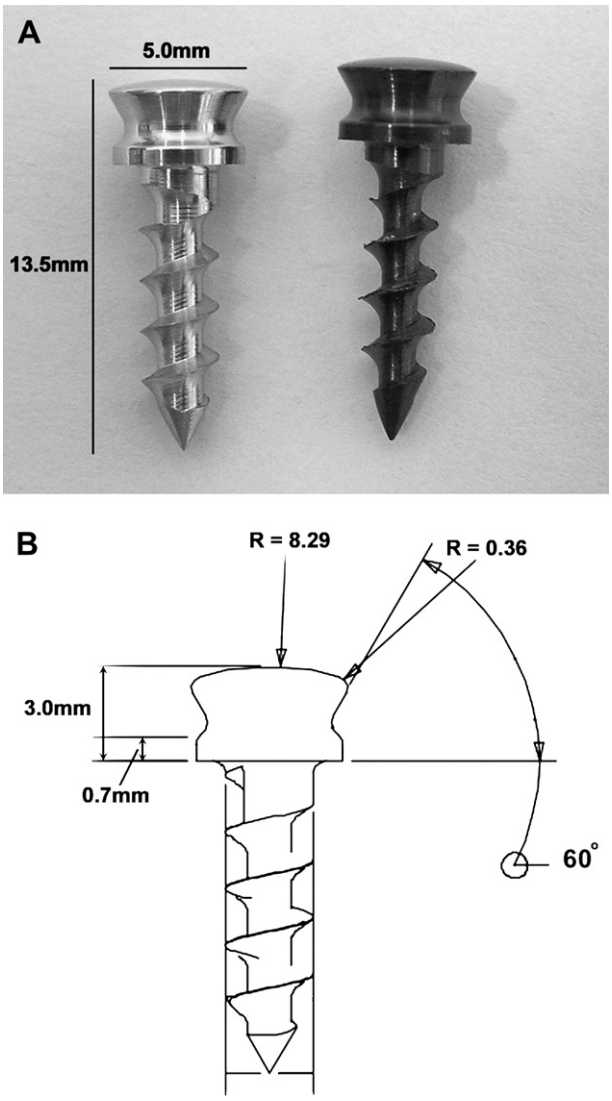

Fig. 1. A. Femoral tack implant made of CoCr (left) and OxZr (right). The OxZr components were produced from a wrought zirconium alloy (Zr-2.5%Nb) that was oxidized by thermal diffusion to create a zirconia surface, which is approximately 5 μm thick, and then polished to produce an articular surface as smooth as that of the CoCr component ($R_a < 0.03$ μm). The CoCr components were produced from a cast CoCr alloy [American Society for Testing and Materials (ASTM F75)] and polished afterwards. The threads on the implants were designed for osseointegration. B. Technical drawing of the implant.