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Articular damage caused by metal plugs in a rabbit model for treatment of localized cartilage defects

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Summary

Objective: Currently, the surgical treatment of localized cartilage defects has limitations. Alternatively, localized cartilage defects may be treated with small biocompatible metal cartilage tacks. Our purpose was to investigate the applicability of defect-size femoral implants. Different bearing materials, cobalt–chromium (CoCr) and oxidized zirconium (OxZr), were tested to evaluate the effect on opposing cartilage quality and osseointegration at different insertion depths.

Methods: In 18 adult female New Zealand White rabbits, a medial femoral condyle defect was filled with either an OxZr or a CoCr implant (∅ articulating surface 3.5 mm; fixating pin of 9.1 mm length), placed flush, 1 mm deep or 1 mm protruding with respect to the level of the surrounding cartilage. Animals were sacrificed after 4 weeks. Tibial cartilage quality was scored microscopically and osseointegration measured by automated histomorphometry.

Results: Considerable articulating cartilage erosion was found in all conditions. Tibial cartilage quality was least compromised when both implants were placed flush compared to deep ($P = 0.01$) or protruding position ($P = 0.004$) and was better for OxZr compared to CoCr ($P = 0.011$) when left protruding, while no differences were found when placed deep of flush. Most bone formation around the fixating pin was observed in a protruding position ($P = 0.01$). In deep position, more bone–implant contact was observed with CoCr compared to OxZr ($P = 0.02$).

Conclusions: OxZr and CoCr implants showed good osseointegration when used as a localized cartilage defect treatment in the rabbit knee; however, opposite cartilage damage was observed in all cases. Placement flush to the surrounding cartilage seems essential and when left protruding OxZr may be less erosive. In conclusion, caution is warranted using small metal implants for the treatment of localized cartilage in the human patient.

Key words: Cartilage defect, Cartilage repair, Knee, Oxidized zirconium, Cobalt–chromium, Rabbit, Small metal implant, Mankin score, Osseointegration.

Introduction

Localized cartilage defects are frequently associated with disability and with symptoms such as joint pain, locking phenomena and reduced or disturbed function. Moreover, such lesions are generally believed to progress to severe forms of osteoarthritis[1].

When conservative treatment options fail, there are several surgical possibilities. A localized treatment, which maintains the surrounding and opposite healthy cartilage, is preferred. Currently, the surgical options for the treatment of localized cartilage defects are primarily aimed at biological repair, including joint lavage and débridement, subchondral drilling, osteochondral transplantation, and autologous chondrocyte transplantation. Although these biological repair treatment modalities are promising, currently, limitations persist. Often fibrous or fibrocartilage tissue is formed, frequently followed by progress of joint degeneration and eventually results in an osteotomy, a hemiarthroplasty or a total joint replacement.

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A promising alternative for the treatment of localized defects is the use of defect-size metal implants for localized cartilage defects, as have already been applied in trauma of the knee, hip, and shoulder[2–4]. The current implants consist of a titanium screw and a cap device. The success of this approach depends on various factors. First, since localized implants will articulate against healthy unaffected cartilage, it is anticipated that the position of the implant in relation to the adjacent tissues will affect the articulating surfaces. As yet, it is not clear whether placing an implant flush with the surrounding cartilage, or rather slightly depressed is best in terms of articulating surface integrity. And second, the implant should be well fixed in the joint to maintain articular congruity and limit subchondral alterations, and thus the materials used should allow for osseointegration of the implant.

Important in these considerations are the implant materials, in terms of effects on both articulation and osseointegration. A metallic knee hemiarthroplasty was introduced in the 1950s by MacIntosh and McKeever. Despite initial good to excellent results, this prosthesis never became popular[5,6]. Currently, cobalt–chromium (CoCr) alloy is a frequently employed material for hemiarthroplasty bearing surfaces, however, even given the wide implementation, some downsides are described[7–9]. For example, failure of hemiarthroplasty

hip prostheses was found, due to pain and the erosion of acetabular articular cartilage and bone. These might be the result of design specifications and/or the bearing material used[10].

Therefore, interest has regained in ceramic bearing materials for articulation in treatment of cartilage defects, joint trauma and early, localized osteoarthritis. A major disadvantage of ceramics is that they are brittle, so novel bearings such as oxidized zirconium (OxZr), aluminum oxide (Al_2O_3), and CoCr coated with ceramics such as titanium nitride (TiN) or titanium niobium (TiNb) oxynitride are being developed, which are not brittle. In particular, OxZr was shown to exhibit a number of relevant beneficial characteristics *in vitro*, 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[10–15]. A comparative friction test showed that the coefficient of friction was lower for OxZr compared to the CoCr alloy when rubbed against bovine articular cartilage[10], which was further confirmed by an *in vitro* pin-on-disk wear study demonstrating that cartilage thickness decreased to a smaller extent when articulated against OxZr compared to CoCr alloy[16]. 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 this end, we developed an *in vivo* model in which a femoral tack implant is applied to a localized defect in a rabbit knee joint. In this model, opposing cartilage quality, biocompatibility, and osseointegration are studied with varying implant positions, comparing the commonly used CoCr with OxZr as bearing materials.

Materials and methods

EXPERIMENTAL DESIGN

This research was approved by the Institutional Animal Care Committee of the Utrecht University (approval number DEC 04.07.057). In 18 adult female New Zealand White rabbits, a standardized medial femoral condyle defect was filled with either an OxZr (left knee) or a CoCr (right knee) press fit implant (∅ articulating surface 3.5 mm; length 9.1 mm). Implants were placed flush with the surface of the surrounding cartilage ($n = 9$), 1 mm deep ($n = 5$) or 1 mm protruding ($n = 4$). After 4 weeks, the animals were sacrificed. Tibial cartilage quality was scored blinded by macroscopically and microscopically evaluations. Osseointegration was determined using histomorphometry.

ANIMALS

Eighteen adult female New Zealand White rabbits aged 34 weeks and weighing 3.8 ± 0.3 kg (mean ± standard deviation) were used. Food and water were given ad libitum. The animals' general health and care conditions were recorded in a diary of well being for each rabbit separately and monitored by the laboratory animal welfare officer.

IMPLANTS

Implants were custom-manufactured by Smith & Nephew, Memphis, TN, USA. The OxZr components are produced from a wrought zirconium alloy (Zr−2.5% Nb) that is 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 a CoCr component ($R_a < 0.03$ μm). The CoCr components were produced from a cast CoCr alloy (ASTM F75) and polished afterwards. The size of the implant was 9.1 mm in length with a 3.5 mm diameter-articulating surface. The articulating shape of the implant was designed after a study on cadaver knees and tested in a pilot study [Fig. 1(A and C)].

SURGERY

After acclimatizing for at least 2 weeks in the animal care facility, 1 day prior to surgery, Baytril® (0.3 ml 2.5% enrofloxacin, Bayer, Leverkusen, Germany) was given. The rabbits were weighed pre-operatively. Surgery was performed on both knees, under general inhalation anesthesia and aseptic conditions. Pre-medication was given by an intramuscular injection of 4 mg acepromazinemaleate (Vetranquil®, Sanofi Sante BV, Maassluis, The Netherlands) and 4 mg methadone (methadone-HCl). Anesthesia was initiated by an intravenous injection of 8−10 mg etomidate (Hypnomidate®, Janssen Pharmaceutica BV, Tilburg, The Netherlands).

All surgical procedures were carried out by the same surgeon (RC), who gained specific experience during 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, an air-pressurized drill was used to insert a K-wire (diameter 1 mm, depth 1 cm) creating a pilot hole perpendicular to the surface in all directions in the load bearing area. After removing the K-wire, a drill (diameter 3.5 mm) was used to create a standardized osteochondral defect (diameter 3.5 mm, depth 2.1 mm.). Although threads are present on the implant, these were designed for osseointegration after implantation, and not for rotation during the placement procedure. Therefore, the implants were placed flush with ($n = 9$) either 1 mm too deep ($n = 5$) or 1 mm protruding from the surface of the surrounding cartilage ($n = 4$), by hammering using a specially designed tamp with a polyethylene head [Fig. 1(B)]. The joint was lavaged and closed in three layers. After surgery, the rabbits stayed on the intensive care unit (ICU) during 24 h. Subsequently, the rabbits were placed in separate cages and were allowed to move freely. Until 3 days post-operatively, Baytril® was given.

The implants were visually inspected and manually tested for loosening. After 4 weeks, the animals were killed using an overdose of Euthesate® (pentobarbital). All rabbits were weighed post-mortem. The hind legs were disarticulated at the hip joint and taken to the orthopaedic laboratory.

RADIOGRAPHS

Pre-operatively, fluoroscopy was used in an anterior−posterior (AP) and a mediolateral (ML) direction to confirm the normal anatomy and the size of the bone. Immediately post-implantation, fluoroscopy was used to confirm the desired depth positioning of each implant and examine surgical complications such as fractures. After killing the animals (day 28), fluoroscopy was used to check for implant malpositioning, loosening (sclerotic zones and radiolucency surrounding the implant), movement from original position, or other complications. Subsequently, all joints were opened and the implant was manually checked for loosening and a possible implant bone interface.