

## 2.2 Periarticular Reaction to Wear Debris of Different Ceramic Materials

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### Introduction

For the last 30 years Alumina and Zirconia ceramics constituted the ceramic materials used for the manufacturing of Total Joint Arthroplasty, thanks to the high biological and mechanical properties of these materials (Piconi and al, 2003; Piconi and Maccauro 1999). The new ceramic biocomposite ZPTA (Alumina Matrix Composites by Transformation Toughened and in situ Plateled Reinforcement) that is currently known as BioloX<sup>®</sup> delta, produced by CeramTec (namely ZPTA in the paper), improving the mechanical properties when compared to Alumina (Burger W. and Richter H.G. 2000), allowed to manufacture components which were not previously possible, and especially the small-diameter ball heads (<28 mm), thin-walled cup insert, knee and finger joints. Few paper reported the in vitro and in vivo biocompatibility tests on this new material (Willmann, et al. 2000), and in particular as ceramic joints are intended for use in younger patient (Black 1997, Schmalzried 2001), hence the ones with longer life expectations, the study of the chronic effects of small particles, in term of local and systemic toxicity, including carcinogenesis becomes more and more relevant (Archimbeck et al. 2000).

In a previous paper (Maccauro et al., 2002) we described an in vivo test suitable for the observation of biological reactions made in an animal model of chronic release of ceramic particles with the observations made in case of release of ceramic particles from THR joints due to wear or fracture.

The in-vivo model of particle release that we used is based on the implant of porous pellets formed by low cohesion grains in the patellar tendon of rabbits. Due to their poor cohesion, when rubbing against an articular cartilage, grains can be easily and progressively detached from the surface of the pellet and released to the joint space all along the nursing time of the animals. In this paper we would like to present the first results obtained, compared the biological response to Alumina, Zirconia and ZPTA ceramics).

### Materials and Methods

Ceramic pellets ( $\varnothing$  8 x 2 mm) were manufactured from Alumina, Ytria Tetragonal Zirconia Polycrystals (Y-TZP in this paper) and ZPTA precursors by cold pressing followed by pressure less sintering route. The results were compared with the ones obtained by the insertion of the ceramic precursors in form of powders in the articular joint.

Pellets are characterised by high porosity obtained stopping the sintering process during the development phase of the necks between the grains of the starting powder. Thanks to this system, the cohesion among grains in the pellets is very low.

Twenty four New Zealand White adult rabbits of both sex, minimum weight 3.3 Kg were used for the experiments and divided in 3 groups. The pellets of each ceramic were inserted into surgically created defects under both the patellar tendons of 8 rabbits for the first group. Animals were maintained in a pathogen-free environment.

At different intervals (1, 3, 6, 12 months after surgery) the animals were killed. Knee joints were harvested and submitted to macroscopic and x-rays examinations. Retrieved knees were divided in 2 groups: specimens of the first group were decalcified with EDTA, dehydrated and embedded in paraffin, sectioned and stained with hematoxylin-eosin, and observed with transmitted and polarised light microscopy. Pellets of the second group were removed, fixed in Karnovsky's solution dehydrated with alcohol, and examined by SEM (Philips 515).

Two animals of each group (Alumina, Y-TZP and ZPTA) for each implantation time, was submitted to autopsy. Lungs, liver, kidney, spleen and hearth were harvested, and the external and internal surfaces of these organs underwent macroscopic examinations. Lungs were injected with China ink for detecting tumours. Histological analysis was carried out on specimens of the organs fixed in 10% formalin, embedded in paraffin, cut in 3-5  $\mu\text{m}$  thin sections, stained with haematoxylin-eosin and resorcin-fuchsin.

## Results

The preliminary results of the study are reported in this paper: in particular the *in vivo* results at 1 month after operation of the 3 groups.

Macroscopic analysis of the retrieved rabbit knees showed the presence of fibrosis around the joint at 1 month after operation, independently on the materials tested, fixing in flexion the knees. X-ray showed the presence of ceramic fragments in the articular spaces, with Alumina and Y-TPZ pellets, but not in case of ZPTA. Histologic sections in case of Alumina showed ceramic particles within histiocyte-like cells as finely dispersed intracytoplasmatic granules or as yellow-brown bigger granules in extracellular matrix of a synovial-like tissue. Giant cells containing bigger ceramic fragments were rarely seen. Y-TZP grains appeared or as dark structure in the intercellular space, or as microscopic yellow amber grains found in intra or in extra cellular sites, scattered in areas of cell reaction containing mononuclear histiocyte-like cells. Membranes were characterised by avascular fibrous tissue. In case of ZPTA a tissue membrane containing multinuclear cells surrounded the retrieved pellets. Granules were not visible at histology. The peripheral organs did not show pathological changes neither tumours. SEM of the membranes surrounding pellets showed the presence of ceramic grains: in case of Alumina particles appeared as alone or aggregate due to electrostatic reactions, in case of Y-TZP and in case of ZPTA particles were usually alone (average  $\text{Ø}$  2  $\mu\text{m}$ ).

## Discussion

It is well known that wear is the key factor to arthroprostheses' lifetime: at local level the cascade of events induced by reactions to wear debris is still the most frequent cause of implant failure and revision, while the ions released by wear debris originate systemic reactions, depending on their transport by the blood

flow to peripheral organs, thanks to the vascularization of the reactive membrane surrounding the implant. (Schmalzried and Callaghan 1999, Urban et al. 2000, Archimbeck et al. 2000, Fisher et al 2001, Sedel 2001, Dumbleton et al. 2002). The biocompatibility tests for a candidate biomaterial for Orthopaedic implants should similar the biological events which take place in presence of biomaterial or its wear products.

The *in vivo* tests used to evaluate tissue reactions to particulate materials analyze the biological response to the particle directly injected in the joint (Rae et al 1986), or in packing the powders on a suitable carrier, like e.g. into the groove in a PMMA cylinder, and in implanting the carrier into the joint (Kubo et al 1999). These methods have some limits: particles injection is similar to the clinical situation of massive release of particles in case of catastrophic failure of the implant, but is different from the usual clinical situation of chronic release of wear debris, that is low in case of metals and very low in case of ceramics; the use of PMMA as carrier may influence the results obtained due the contamination of different materials.

Moreover in case of ceramic materials the *in vivo* tests should evaluate the chronic effects of the materials in order to predict if the material tested may really be used in younger patients, that will make use of the implant for longer times (e.g. thirty years, or more).

The method used analyzed the local and systemic effects to Alumina, Y-TZP and ZPTA ceramics. Each pellets consisted of only one material without contaminations of cement or any other carrier. The entity of cohesion is crucial in the effects as well as the animal joint motion: we observe more particles at 1 month after operation released from Alumina and Y-TZP than from ZPTA, either at XRay either histology, and only with SEM we observed the presence of ceramic particles in the periprosthetic tissue.

The reaction to the Alumina an Y-TZP ceramic particles in the articular joints was the formation of fibrous tissue, characterized by the absence of blood vessels, and by a cellular reaction depending on the size of the particles released. We observed in our specimens the presence of few giant cells, clearly related to ceramics only. In case of ZPTA ceramics multinuclear cells were present in the periprosthetic membrane: no vessels were seen in the tissue.

The membranes were poor in vessels in case of Alumina and Y-TZP and no vessels were seen in presence of delta at 1 month after operation, showing that materials do not induce an inflammatory reaction similar to the one induced by metals (Willert et al. 1996). We remark that lymphatic vessels collect particles and transport materials to the peripheral organs, and is related to a possible systemic toxicity of materials: the absence of vessels as observed in case of ZPTA may be an indirect sign of low toxicity and of systemic safety in case of implantation in younger patients. No tissue damages were seen in the peripheral organs whatever materials were used, no tumours were seen in the animals.

Obviously more information should be kept from the long term results for confirming the suitability of the materials, and the absence of cancer risk of these ceramics.

## Conclusions

We conclude that the method proposed may be considered a useful system for evaluating the chronic effects of ceramic materials, thanks to the friction of

low cohesive materials against cartilage and release of low entity of wear debris, comparable to the in vivo situation of well performing prostheses, implanted in younger patients with a longer expectation.

At 1 month after operation we did not observe local or systemic toxicity due to material tested, neither tumours developed.

A poor in vessels membrane surrounds Alumina and Y-TZP pellets, revealing the lack of inflammatory reaction to these materials, with a possible transport of debris released to the peripheral organs; in particular the absence of vessels observed in the tissue membranes surrounding ZPTA seems to reveal that this material is especially indicated in younger patients.

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