SYSTEMIC SPREAD OF TITANIUM WEAR DEBRIS: TARGET IDENTIFICATION IN A RABBIT MODEL

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INTRODUCTION: Local effects of wear debris, leading to osteolysis and aseptic loosening, are frequently reported in the literature. While much knowledge has been gained about the local reactions, relatively little is known concerning the dissemination of wear debris beyond the periprosthetic tissues and the systemic reactions. Wear particles, phagocytosed by macrophages, may enter the lymphatic system or may use hematogenous pathways. As shown by a recent study (1), wear particles were detected in the para-aortic lymph node, liver and spleen of patients studied post mortem. The aim of the present study was the identification of target organs and the analysis of histopathological responses to wear debris in affected organs using a rabbit model.

METHODS: Titanium wear particles with known characteristics (mean diameter 0.63 µm), were used to produce an overload of wear particles in a bony cavity (8mm depth, 2,5mm diameter), close to the knee joint of a rabbit. The drilling direction was parallel to the joint line. After insertion of the wear debris the drill hole was covered with a periostal flap. Skin closure was performed using non-resorbable materials.

Seven rabbits were operated by the same surgeon, randomized right/left to filled/empty defect. All animals were sacrificed after 16 weeks. Six health rabbits taken from stock underwent euthanasia and served to establish baseline values for metal concentration measurements in tissues.

The spleen, liver, left and right kidney, and the lymph nodes of the right and left femur were removed and cut into half. Metal concentrations of the moieties were determined using inductively coupled plasma – optical emission spectroscopy (ICP-OES) with a limit of determination of 2ng/mg titanium in freeze-dried tissue. The remaining, non-lyophilized organ samples as well as the femoral condyles of the left and right knee were fixed in formalin and embedded in paraffin and PMMA respectively. Microtome sections (6µm) were prepared. The femoral condyles as well as the soft tissue samples were colored using three different staining techniques: hematoxylin and eosin, Perl´s Prussian Blue and alcian blue. All specimens were examined by light microscopy, up to 1000x magnification.

RESULTS: After 16 weeks, wear debris was still present inside the insertion location. No signs of inflammation or necrosis could be detected. Particles were also found in the surroundings, encapsulated in the fibrous tissue. The spleen of all experimental rabbits exhibited titanium concentrations above the limit of determination (Tab.1), while no titanium was detected in the spleen of the untreated rabbits. Also, for any animal, all other organ samples displayed concentration values below 2 ng/mg.

	Animals						
	1	2	3	4	5	6	7
Ti (ng/mg)	3.16	4.94	9.78	5.67	2.83	5.66	3.04

Table 1: Titanium concentration in the spleen

Opaque particles were identified histologically in sections of the spleen. The particles appeared dark brown to black. The foreign material was either encapsulated in vacuolated macrophages or accumulated near trabeculae of the spleen. No cellular response as for example granulomous inflammation, fibrosis or necrosis could be detected. No particles were identified in other investigated organs and the lymph nodes.

DISCUSSION & CONCLUSIONS: Since no wear debris was found in the lymphatic system and in the liver, this study suggests that immediate hematogenous dissemination of wear debris may be an alternative possibility. In all seven rabbits titanium was identified in the spleen using quantitative measures. Although at the present time we are unable to draw further conclusions about the role of the lymphatic system regarding particle transport, the consistency of the findings suggests hematogenous pathways to remote organs as the principle route for early dissimination of wear debris. The macrophages with ingested particles suggest either an active transport from the periprosthetic tissue to the spleen or a local processing. The mild cellular reaction of the spleen is consistent with recent findings in total joint replacement patients (1). Further studies should elucidate the influence of particle size, shape and material composition on the pathway, as well as the long-term systemic cellular reaction.

REFERENCES: (1) R.M. Urban et all (2000) *Dissemination of wear particles to the liver, spleen and abdominal lymph nodes of patients with hip or knee replacement*. JBJS 82-A, No.4