Significance: Aseptic loosening is the leading cause of implant failure. Currently, only the combination of medical history, physical examination and radiologic findings leads to the diagnosis of aseptic loosening. TRAP 5b is an excellent marker for periprosthetic bone turnover and a possible predictor of aseptic loosening. The aim of this study was to determine the course of TRAP 5b as well as established markers Osteocalcin, PINP and CTX in a rat model of aseptic loosening.

Methods: A rat model of aseptic loosening with continuous infusion of polyethylene particles was used. The model was first described by Kim et al. (3) and Ivase et al. (4). The implantation site and implant type were modified. Instead of K wire, anatomical shaped prostheses were implanted into the tibia. The cruciate ligament and both menisci were removed, and a 2.0 mm diameter intramedullary drill hole was made by using a 2 mm drill bit. Then, a custom made titanium tibial prosthesis was inserted press fit into the drill hole. An osmotic pump filled with 0.1 mg purified polyethylene particles and 200 μl rat serum was implanted subcutaneously on the back, connected to a cathereder leading subcutaneously to the knee joint. The osmotic pumps had to be replaced every 2 weeks. In the sham-operated group the left knee joint was exposed by a medial parapatellar approach. An osmotic pump filled only with 200μl rat serum was implanted. Bone turnover markers and bone density: Blood samples were drawn 12, 6 and 1 weeks before the surgery and on Post Operative Day (POD) #0, #7, #14, #28, #35, and #42 according to Herbert and Christensen(5). The samples were centrifuged and serum was analyzed by ELISA preoperatively for TRAP 5b activity and postoperatively for Osteocalcin, PINP, CTX concentrations and TRAP 5b activity. To verify the result of ovariectomy, bone mineral density was measured by DEXA on POD #0, #14, #28 and #42. Statistical analysis: Data were expressed as mean ± standard deviation (SD). Statistical analyses were performed using the statistics package SigmaStat™ (SPSS Inc.). A Wilk-Shapiro test for normality was conducted on all parameters. To answer the research questions, a one-way analysis of variance (ANOVA) was carried out on all groups. A Tukey post-hoc analysis was performed to determine with groups differed significantly (p<0.05).

Results: Bone density: In the prostheses group, bone density decreased significantly from POD #0 to #14 (p<0.001) and #26 (p<0.001) and #42 (p=0.008). From POD #14 to #42 a slight increase was seen. In the sham-operated group, bone density decreased significantly from POD #0 to #42 (p<0.001). There was no significant difference in bone density between prostheses and sham-operated group on POD #0 or POD #42, respectively.

Osteocalcin: In the prostheses group, highest OC concentrations were reached on POD #7 and #14. From POD #14 to #21 OC decreased significantly (p<0.001) and showed further constant decrease until #42. In the sham-operated group, highest OC concentration was reached on POD #14. From POD #14 to #21 OC decreased significantly (p=0.021) and showed also further decrease until POD #42. On POD #7, OC concentration in the prostheses group was significantly higher than OC concentration in the sham-operated group (p=0.042).

PINP: In the prostheses group, PINP increased slightly from POD #7 to #14. On POD #21 PINP concentration reached its maximum (p<0.001), decreased to the minimum on POD #28 (p<0.001). In the sham-operated group, PINP increased significantly from POD #7 to #14 (p<0.001), reached its maximum on POD #21 (p<0.001). On every POD, PINP concentration in the prostheses group was significantly higher than PINP concentration in the sham-operated group.

CTX: In the prostheses group, CTX increased significantly from POD #7 to the maximum on POD #14 (p<0.001) and decreased until POD #42 to the minimum. In the sham-operated group, CTX increased slightly from POD #7 to #14, decreased to the minimum on POD #21 (p<0.001) and reached the maximum on POD #28 (p=0.023). From POD #28 to #42 CTX decreased steadily. On POD #14 and #21 CTX concentration in the prostheses group was significantly higher than in the sham-operated group.

TRAP 5b: In the prostheses group, TRAP 5b activity reached the preoperative maximum 6 weeks before the operation and decreased to the preoperative minimum 1 week before the operation. Postoperatively, the maximum was reached on POD #7 and TRAP 5b activity decreased slowly until POD #42. Similar to the prostheses group, the postoperative maximum of the sham group was reached on POD #7 and it decreased slowly until POD #42. On every POD, TRAP 5b activity in the prostheses group was significantly higher than TRAP 5b activity in the sham-operated group (#7 p=0.002; #14 p=0.003; #21 p=0.005; #28 p=0.003; #35 p=0.029; #42 p=0.013).

Conclusion: Our investigation showed no eligibility for Osteocalcin and CTX for detecting aseptic loosening since serum concentrations of Osteocalcin and CTX seem to be influenced by several factors besides bone turnover which is in line with results from previous studies. However, for TRAP 5b, our data suggest that high activity levels show increased periprosthetic bone resorption leading to aseptic loosening. TRAP 5b is eligible for the early diagnosis of aseptic loosening. PINP indicates defective bone formation accompanying the process of aseptic loosening and could be used along with TRAP 5b for early diagnosis of aseptic loosening. Further investigations are needed to verify clinical practice and relevance of TRAP 5b.