Introduction: Aseptic loosening is the most frequent cause of implant failure in total hip arthroplasty (THA). Although cementless implants may be beneficial, failure rate was still found by some authors to be increased in patients with osteonecrosis of the femoral head (ON-FH). Since implant loosening is commonly associated with periprosthetic bone loss in cementless THA, bisphosphonates have been proved to be beneficial by several authors, although a direct link between periprosthetic bone loss and aseptic loosening has not been shown so far. On the other hand, it is well evidenced that low initial fixation and early migration precedes and predicts long-term failure rate of both, the acetabular and femoral component in THA. Moreover, we previously found that revision surgery because of aseptic loosening was linked to an increased early subsidence in patients with ON-FH(1). For this, implant failure due to aseptic loosening still remains a major concern in THA, while very few is known about the efficacy of bisphosphonates to prevent early implant migration, however.

Materials and Methods: This double-blind, randomized, controlled study was primarily designed to evaluate whether a single infusion of 4 mg of zoledronic acid is sufficient to prevent implant migration determined by the EBRA-digital method. Secondary objectives included assessments of biochemical parameters reflecting bone turnover inter alia. The protocol was developed by the investigators as accepted by the local ethic committee, and the study was performed independently from any industrial sponsorship. Fifty patients were consecutively enrolled between July 2002 and March 2005 to receive either 4 mg zoledronic acid (ZOL) or saline solution (CTR) one day after THA (Zweymüller system, cementless). The main inclusion criterion was the diagnosis of end-stage osteonecrosis of the head based on clinical and radiographic findings, which was confirmed by MRI and/or microscopic examination. The patients had to be willing to complete a minimum follow-up period of 2 years. Plain radiographs were performed postoperatively and all parameters were evaluated at each follow-up meeting interval at 7 weeks, 6 months, 1 year, and yearly thereafter during a median follow-up period of 2.8 years.

Results: An acute rise in bone resorption markers was found with a peak at 7 weeks after surgery (ICTP, P<0.0001; and CrossLaps, NS; Wilcoxon Signed Rank test), thereafter continuously decreasing below baseline levels (P<0.05 at 1 and 2 years for CrossLaps and ICTP, Wilcoxon Signed Rank test). The bone formation marker osteocalcin (OC) also significantly increased after THA, but peaked at 6 months (P<0.05, Wilcoxon Signed Rank test) and remained significantly increased during the whole follow-up period compared to preoperative values – Figure 1A. This was accompanied by an increasing subsidence of up to -1.2 mm ± 0.6 SD at 2 years in CTR (P<0.001). Less but a similar, near curve-linear shaped migration pattern was also found for the acetabular component, with an averaged medialization of 0.6 mm ± 1.0 SD and a cranialization of 0.6 mm ± 0.8 SD at 2 years (P<0.05, Friedman ANOVA) at 2 years – Figure 1B. Treatment with ZOL significantly suppressed the values of CrossLaps within 7 weeks post surgery, which remained significantly decreased during follow-up (P<0.0001, Wilcoxon Signed Rank test) as well when compared to CTR at each follow-up interval (P<0.0001, Mann-Whitney U test). Similarly, the values of OC were also significantly decreased in ZOL compared with CTR during the follow-up (P<0.05, ANOVA), but changes compared to baseline values failed statistical significance (Wilcoxon Signed Rank test) – Figure 1A. The significant reduction in bone turnover markers was accompanied by a complete prevention of cup migration in both, the transverse and vertical direction (P<0.05, ANOVA), while there was only a trend to a decreased subsidence in stems (-0.91 mm ± 0.51 SD versus -1.18 mm ± 0.64 SD at 2 years after THA) – Figure 1B.

Discussion: The study provides useful data which demonstrate that a single infusion of zoledronic acid is a save and sufficient method to reduce and prevent implant migration of THA. Importantly, the migration of the acetabular compo-