INTRODUCTION: Bone grafts should be biocompatible, mechanically stable, and replace with new bone over time. Morcellized bone allograft is the gold standard for grafting large defects such as in revision hip arthroplasties. BMPs can increase bone formation around allografted implants, but are also associated with increased graft resorption and implant instability. Bone resorption can be inhibited by bisphosphonates.

In the present study, we hypothesized that topical bisphosphonate (Pamidronate, Mayne Pharma) in combination with rhBMP2 (InductOs, Wyeth) would give increased mechanical implant fixation and increased new bone formation without marked allograft resorption. We evaluated both porous-coated Titanium (Ti) and Hydroxyapatite (HA) implants.

METHODS: Following approval from Animal Care committee, four 2.5 mm gap implants were inserted into the proximal part of both humeri of each of 16 dogs (Fig. 1). Fresh frozen allograft, with or without intervention treatment, was impacted in the gap surrounding the implant. Interventions were rhBMP2 and pamidronate. The rhBMP2 was mixed into the allograft (0.45 mg/cm³ allograft). The pamidronate was added topically to the allograft by soaking 1 cm³ graft in 4 ml pamidronate (9 mg/ml) for 3 minutes and drained. Half the dogs received Ti-implants, the other half HA-implants.

The 4 treatment groups were:
1. allograft alone (CONTROL)
2. allograft + rhBMP2 (BMP)
3. allograft + pamidronate (BP)
4. allograft + rhBMP2 + pamidronate (BMP+BP)

The observation time was 4 weeks.

Implant fixation was evaluated blinded by mechanical push-out test and stereological histomorphometry on vertical sections. Mechanical data were normally distributed and evaluated by one-way ANOVA followed by paired t-test. Histological data were evaluated non-parametrically with Friedman’s test followed by Wilcoxon signed rank test. Group (mean or median) differences were considered significant for p<0.05.

RESULTS: For both Ti and HA implants, the control-groups had significantly better mechanical fixation than all other treatments. The fixation was twofold higher in the control group than in the BMP group and more than 20-fold higher than in the pamidronate (BP) and the BP+BMP groups. (Fig. 2) HA implants were twice as well fixed as the corresponding Ti implants.

HA implants had less fibrous tissue and more new bone compared to Ti implants. Fractions of allograft were the same (Fig. 3).

The rhBMP2 group had more new bone and much less fibrous tissue than the mechanically superior control group. However, there was almost no allograft left in the rhBMP2 group due to resorption (Fig 3). Pamidronate appeared to block bone metabolism around the implants: The allograft was preserved, but only minor new bone was formed, with and without rhBMP2. In the pamidronate group there was a dense, thick fibrous capsule around the implants, but this membrane did not form in the combined pamidronate-BMP2 group (Fig 3).

DISCUSSION: Topical pamidronate and rhBMP2 in combination and alone weakened the mechanical fixation of the implants compared to grafted controls. rhBMP2 gave abundant new bone formation and reduced fibrous tissue, but increased resorption of the allograft, giving a perhaps transient but critical period of weakened implant fixation. Pamidronate seemed to completely block bone metabolism, This preserved the impacted allograft, but no new bone was formed and fixation remained mechanically weak.

The experiment confirms previous reports of mechanical instability of implants when BMPs are added to grafted periprosthetic defects. The negative results may be influenced by several factors not studied here, including carrier, release profile, dosage and administration, warranting further preclinical testing in relevant implant models.

The experiment also confirms the ability of HA-coated surfaces to increase implant biocompatibility and implant anchorage in living bone. In mimicking impaction grafting of hip joint replacements, this unloaded implant model in healthy bone has several limitations: It lacks joint fluid pressure, direct load and the revision environment of compromised bone. However, this basic experimental model is well controlled with a plasma sprayed surface identical to that used in human uncemented hip implants. It provides the environment to study four treatment groups in one animal, and permits a gap large enough for impaction grafting.

The results suggest caution and further experimental research before augmenting clinical hip arthroplasties with BMPs or bisphosphonates.

ACKNOWLEDGEMENTS: Biomet Inc., Warsaw, IN, USA for implants. Unconditional financial support by the Augustinus Foundation (Denmark), the Interdisciplinary Research Group Nanoscience & Biocompatibility (Danish Research Council, Grant no: 2052-01-006).

AFFILIATED INSTITUTIONS: **Department of Biostatistics, Aarhus University, Denmark

53rd Annual Meeting of the Orthopaedic Research Society
Poster No: 1748