Introduction
If given intermittently, parathyroid hormone (PTH) activates bone formation via initiation of osteoblastic activity. Recent animal studies have demonstrated that PTH can enhance the mechanical strength and callus volume of healing fractures in rats [1]. Implant fixation is in part dependent on the bone density adjacent to it and may be considered as the end result of a fracture healing response elicited by implantation. PTH could therefore be promising for enhancement of orthopedic implant fixation. The aim of the present study is to evaluate first how quick the onset of such an effect would be on stainless steal screws and second if PTH is able to increase the contact area between bone and implant.

Materials and Methods
The threaded part of the stainless steal screws was 1.7 mm in diameter (thread M1.7) and 3mm long. The screw heads fitted with a specially constructed device for pull-out measurement. The metal rods,which were used for establishing bone contact fraction were also made of stainless steal. The rods were 5mm long with a diameter of 2mm. First, 8 Sprague-Dawley rats received one screw in the left tibia. These screws were used for immediate pull-out strength measurement. Then in 30 Sprague-Dawley rats one screw was inserted in the left tibia and one rod in the contralateral tibia. After implantation, the rats were randomly divided in two groups with equal numbers. One group was injected subcutaneously with human PTH (1-34) at a dose of 60 µg/kg BW/injection. The second group was injected with vehicle only. The injections were given three times a week starting on the operating day. Five control and 5 PTH-treated rats of each group were killed after 1, 2, and 4 weeks.

After the animals were sacrificed the metal rods were carefully removed. The tibial segments around the hole of the rods were prepared by standard histological techniques. Thus, the linear tissue surfaces, that had been in contact with the surface of the rod, could be analyzed. All specimens were blinded and examined in random order. The contralateral tibiae were frozen immediately after retrieval until all specimens were harvested. After thawing all left tibiae at the same day at room temperature for over 2 hours, a pull-out test was performed in random order. The pullout strength was measured as the peak force when the screw loosened from bone. Pullout results and bone contact index were then tested for significance using one way ANOVA followed by Fisher’s PLSD-test at the 0.05 significance level.

Results
Three of the tested pull-out screws (all controls) were grossly loose. In these, the pull-out strength was defined as 0. All other implants seemed clinically stable. The pullout strength from the rats killed immediately after implantation was 12 (SD 7) N. PTH increased the pull-out strength compared with the vehicle from 33 (SD 17) to 43 (SD 4) N after 1 week, from 23 (SD 24) to 58 (SD 13) N after 2 weeks, and from 41 (SD 12) to 100 (SD 15) N after 4 weeks (Figure 1). After failure, the force immediately went down close to 0 N. In the controls, the pullout force did not increase after 1 week (r² 0.03), but the PTH treated specimens became gradually stronger (r² 0.8). By post-hoc test, both groups at 1 week were higher than directly after implantation, and there was a significant effect of PTH at 2 and 4 weeks. By histology, PTH treatment caused a substantial and significant increase in bone contact fraction, already after one week, followed by a slight increase over time (Table 1). There was no significant effect of PTH treatment on the body weight of the rats or the ash weight of the femurs.

Table 1 Bone contact fraction over time

<table>
<thead>
<tr>
<th></th>
<th>One week Mean (SD)</th>
<th>Two weeks Mean (SD)</th>
<th>Three weeks Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>0.45 (0.04)</td>
<td>0.35 (0.16)</td>
<td>0.45 (0.13)</td>
</tr>
<tr>
<td>PTH</td>
<td>0.69 (0.08)</td>
<td>0.70 (0.16)</td>
<td>0.78 (0.18)</td>
</tr>
</tbody>
</table>

Discussion
In this study, intermittent PTH treatment increased bone implant contact already after one week (3 injections), and it enhanced implant pull-out strength already after two weeks. The early onset of PTH effects in the present study suggests that intermittent PTH treatment might be considered as a possible drug to enhance early incorporation of orthopedic implants. In a previous experiment we found a 3-fold increase in removal torque with similar screws after 4 weeks of PTH treatment [2]. We thought the reason for this phenomenon could be an increased bone apposition to the implant. The present study showed this to be the case, although the geometry of the screw threads made morphometric assessment of tissue contact difficult, so in the present study we used rods that created a straight interface.

In contrast, pull-out strength appears mostly to be dependent on the bone surrounding the implant and less on the properties of the interface because of the geometry of the implants. The threads constitute an efficient load transfer mechanism without the need to depend on generation of shear stresses in the interface region [3]. The increased pull-out strength thus indicates more or stronger bone surrounding the screw.

References

Supported by the Swedish Medical Research Council (2031)