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Repetitive reduction lead to significant elevated IL-6 and decreased IL-10 levels in femoral osteotomies: A quantitative analysis of a robot-assisted reduction process in a rat model

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ABSTRACT

Introduction: The field of robot-assisted fracture reduction has been developed by several research groups over more than one decade by now, with the main goals of increasing the fracture reduction accuracy. However, the influence of different reduction paths to patients' physiology is not fully known yet. The aim of our study was to compare the impacts of a robot-assisted direct reduction path versus an artificially prolonged reduction path by measuring the cytokine responses in an *in vivo* rat model.
Materials and methods: Thirty-six male CD© rats were assigned into three groups with an external fixator and osteotomy on the left femur. Seven days later, the robot was attached and one group was reduced in a single attempt, while the other group underwent 10 attempts by the robot. The third group was the control group without reduction. Before, and as well as 6, 24 and 48 h after the reduction process blood samples were collected. IL-1, IL-6, IL-10, IL-17, and MCP-1 concentrations where analysed via ELISA or cytometric bead assay. Muscle biopsies in the osteotomy area were collected 48 h after the reduction process for histological analyses. Statistical significance was set at $p \leq 0.05$.
Results: Analysis of the cytokines showed that the pro-inflammatory cytokine IL-6 of the Ten-Attempts reduction group significantly increased 6 h after reduction compared to the control group. IL-6 further showed markedly elevated levels 6 h after surgery in the Ten-Attempts reduction group compared to the Single-Attempt reduction group. On the anti-inflammatory side, IL-10 showed a significant decrease in the Ten-Attempts reduction group 6 h after reduction compared to the Single-Attempt reduction and control group. Muscle biopsies showed a significant increase of pathological changes in both reduction groups and an increase in the severity of bleedings of the Ten-Attempts reduction group compared to the Single-Attempt reduction and control group.
Conclusion: A direct and gentle reduction procedure as feasible by the aid of a robot is preferable over a prolonged reduction in terms of cytokine response and tissue changes.
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Introduction

Femoral fractures belong to the most common injuries of the long bones in multiple trauma patients [1]. According to the literature, 90% of the multiple injured patients have one or more fractures of the extremities [2,3]. Today, multiple robot-assisted devices exist in the field of orthopaedic surgery [4–6]. The main goals of robot-assisted surgery are to increase the fracture reduction accuracy by reaching anatomically correct bone alignments, and also to relieve the surgeon from X-ray exposure as well as from the exhausting task of fracture manipulation against strong soft-tissues as in the femur [7]. Especially robotized procedures with their precise and well controlled motions have the potential to achieve a more gentle and tissue preserving surgical outcome. Fuchtmeier [7], Koo [8] and Oszwald et al. [9] have already described the *in vitro* use of a precise robotic-guided reduction in femoral shaft fractures. However, the influence of different reduction paths to the patients' physiology is not fully understood

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yet. Therefore, the aim of our study was to compare the impacts of a robot-assisted direct reduction path versus an artificially prolonged reduction path in an *in vivo* rat model by measuring the concentration of plasma cytokines, which are secreted during the inflammatory phase of the fracture healing process and by analysing soft-tissue damages of muscle biopsies after the reduction process. For this reason, the *ex vivo* rat model of Oszwald et al. was adapted for *in vivo* use.

Materials and methods

Animal care

Experiments were carried out in accordance with the German Animal Welfare Legislation, and were approved by the local institutional animal care and research advisory committee and permitted by the local government of Lower Saxony, Germany (Approval number: 33.9-42502-04-12/0727). The experiments were performed in 36 male CD© rats aged 12–14 weeks and weighing 350 ± 50 g. The animals were obtained from Charles River Laboratories (Charles River, Sulzfeld, Germany). They were held under specific pathogen free conditions in the central animal facility of our institution. Throughout the study, pellet chow and water were available *ad libitum*. Lighting was maintained on a 12-h light and dark cycle and a temperature of 20 ± 2 °C.

Group distribution

Rats were randomly assigned to one of the three groups. Each group consists of 12 animals. The sample size was calculated by statistical power analysis on http://www.biomath.info/power/ttest.htm. All groups received a fixation of the femur with an external fixator and subsequent osteotomy. The Single-Attempt reduction group received a distraction of 2 mm followed by a vertical displacement of first 5 mm up and then 10 mm down. Finally, the bone is moved back to the starting position. The Ten-Attempt reduction group received the same reduction path with 10 repetitions. The control group received no reduction attempts.

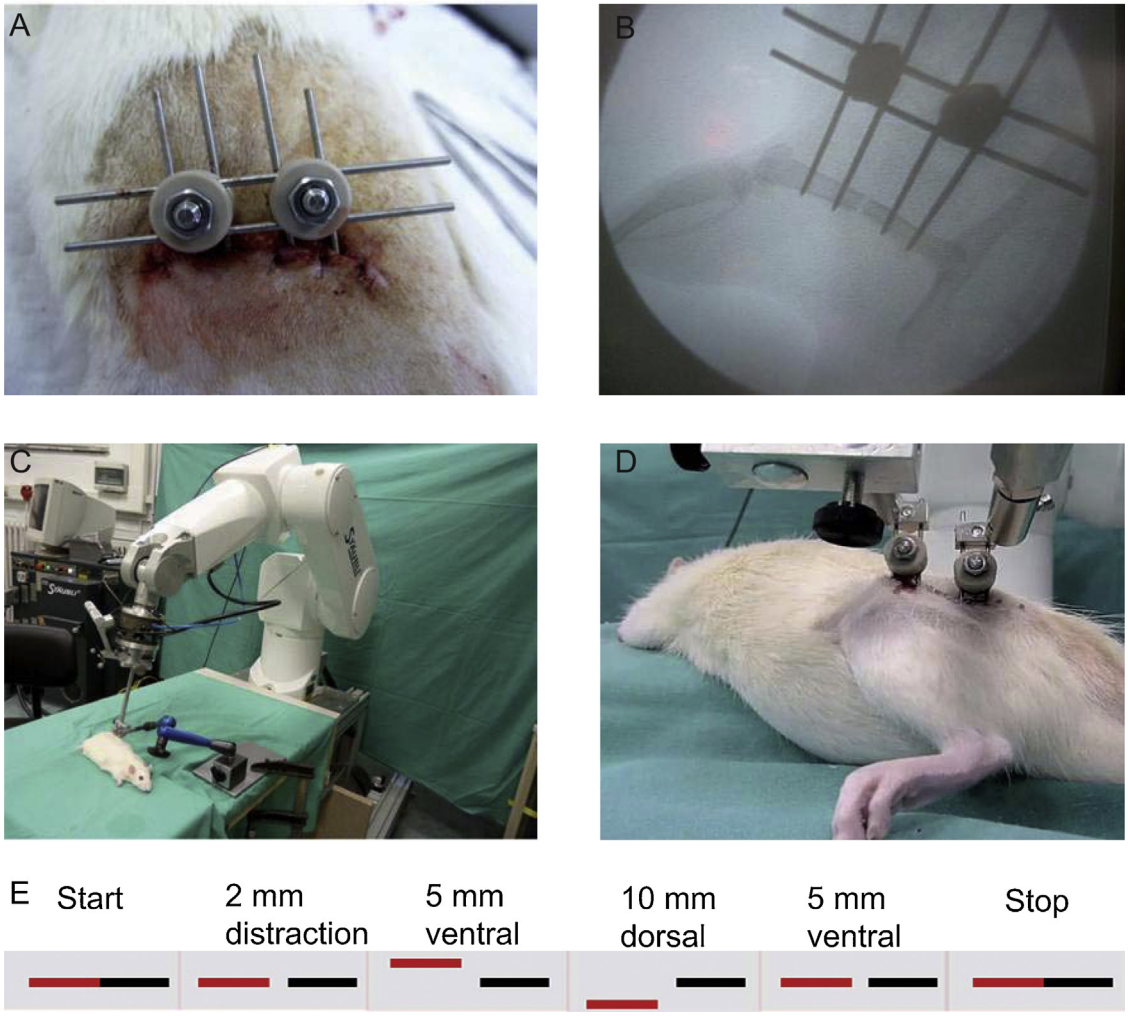

Fig 1. Operation procedure.
(A) Rat external fixator. This fixator consisted of two dynamic fixation discs which were connected by two horizontal rods (1.2 mm in diameter). (B) X-ray of the external fixator and the osteotomy, which was performed between the two centre pins using a 0.44 mm Gigli saw. (C) Reduction set up: The reduction is performed by an industrial robot, Stäubli RX 90, with its standard robot control unit, a CS7B. The robot is controlled from a Windows PC with a self-made control Software written in C++. (D) Reduction manoeuvre: After removing the two stabilizing horizontal rods, the robot performed the previously programmed path according to the experimental group. Group A received a fracture reduction on a direct path, whereas group B received the prolonged reduction path using 10 repetitions. Group C (control) received no reduction. (E) The path used for our tests consisted of a distraction of 2 mm, followed by a vertical displacement of first 5 mm up and then 10 mm down. Finally, the bone was moved back to the starting position for an anatomically correct reduction of the fracture.

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