A Biofeedback System for Continuous Monitoring of Bone Healing

M. Windolf[1], M. Ernst[1], R. Schwyn[1], S. M. Perren[1], H. Mathis[2], M. Wilke[1] and R. G. Richards[1]
[1]*AO Research Institute Davos, Davos Platz, Switzerland*
[2]*Institute for Communication Systems, HSR Rapperswil, Rapperswil, Switzerland*

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Abstract: A telemetric biofeedback concept for continuous monitoring of bone healing is introduced. The system is based on an implantable electronic unit with on-board data processing of deformations or displacements of fracture fixation devices. In contrast to existing solutions, it allows for autonomous long-term data collection over several months. The system enables observing fracture motion and patient activity under daily routine conditions. Feasibility of the approach was proven in an animal experiment with an instrumented plate monitoring axial motion in a transverse osteotomy gap at the sheep tibia. Callus formation and maturation of the repair tissue was indicated by a decline of the interfragmentary motion signal over time and by changes in the animal's activity pattern. For improved understanding and interpretation of such information, extended collection of in-vivo data is the consequent next step.

1 INTRODUCTION

Flexible internal fixation is an essential modality in today's fracture treatment. It promotes secondary bone healing by imposing confined mechanical stimuli at the fracture site, while still permitting early recovery of limb function. Having reached a high level of competence, quick, safe and reliable healing is achieved in the majority of cases. Despite, healing disturbances under difficult mechanical or biological conditions such as infections, non-unions or osteoporosis remain challenging.

Acceleration of bone healing through mechanical stimulation of the repair tissue has been investigated over decades (Claes et al., 1995; Goodship and Kenwright, 1985; Perren,1979). To define the frame for an appropriate healing environment, numerous experimental studies investigated active and passive mechanical stimulation with varying motion magnitudes (Claes et al., 1995), motion frequencies (Hente et al., 2001) and directions of motion (Bishop et al., 2006; Claes et al., 2008; Epari et al., 2007). However, in clinical practice the actual mechanical circumstances at the fracture site remain a black box. Factors such as individual limb loading, patient activity, fracture patterns or configuration of the fixation hardware form a complex setting influencing the healing outcome. An objective measure to assess fracture healing under in-vivo conditions is, hence, required. Such information could be valuable to improve implant designs and application to better serve the individual requirements. Moreover, they could have a considerable impact on patient care, not only to accelerate healing, but also to steer weight bearing and early patient mobilization, detect and react on healing disturbances or define the appropriate time-point for implant removal.

Clinical methods to determine the state of healing are based on radiographic evaluation or clinical examination. Both are highly subjective. McClelland et al. (2007) showed considerable intraobserver variability and overall poor prediction performance of radiographic healing assessment criteria. Only weak correlations were found between the radiographically determined diameter of mineralized callus and fracture stiffness (Eastaugh-Waring et al., 2009).

Hence, it was suggested that measuring the load carried by a bridging implant would be an indirect but valid criterion to assess mechanical stability of the fractured bone. It is assumed that the load borne by the fixation device decreases with ongoing calcification and stiffening of the fracture callus while interfragmentary motion and strain within the fracture gap diminish (Cunningham et al., 1987).

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This load-sharing relation between implant and bone serves as basis to track the course of healing by measuring load transmission through implants.

Current telemetric solutions transmitting such data from inside the body rely on electric induction as power source. Some are meant as research tools to measure internal body loads (Bergmann et al., 2001; Wilson et al., 2009), some target clinical application (Seide et al., 2012). An induction coil, positioned at the injured limb, is required for data collection and transfer and therefore allows only short term "snapshot" measurements when long term data acquisition is actually needed for monitoring the healing progress. Short term measurements of implant deformation can be disturbed by several influencing factors such as current physiological loading of the bone or artificial conditions in a gait-lab. Natural patient behavior and individual long-term activity cannot be captured.

An alternative approach is proposed offering continuous long-term measurements (approx. 4 months) of biomechanical parameters in-vivo without external power source. An implantable and autonomously working electronic unit was developed for continuous recording of fracture motion under unimpaired natural locomotion. In a first instance the device was developed as a research system to analyze the bone healing progress under selected defined conditions.

2 DATA ACQUISITION CONCEPT

Targeting a method for autonomous long-term data acquisition, a novel telemetric data logger unit was developed. The system comprises a microprocessor for real-time processing of sensor raw data. The sensor signal is scanned for peak values employing a custom-made peak detection algorithm. Assuming a maximum step frequency of 3 Hz, the sampling rate is set with a tenfold oversampling at 30 Hz. Together with a stroke counter, peak values are continuously cumulated. Results are stored internally at predefined logging intervals. The influence of natural variances of functional loading is thereby averaged out. Additionally, the first derivative of the raw signal is computed in real-time and the average deformation rate is calculated, considered as important parameter characterizing bone healing. To obtain a histogram of loading intensities, three peak detectors run in parallel at different amplitude thresholds to sort load strokes into distinct bins according to their magnitudes. Instead of storing and transferring the complete sensor signal, the data is transformed on-board into small packages of statistically meaningful parameters (e.g. average amplitude per stroke within a defined time interval), using an ultra-low power microcontroller (MSP430AFE253, Texas Instruments, Dallas, Texas, USA). This approach follows the hypothesis that the lion's share of such raw data lacks meaning and would anyway be discarded at post-processing.

Figure 1: Electronic unit used for on-board processing of the sensor signal with wireless interface for data tranfer via radio frequency identification (RFID).

This lean data management allows the use of an energy-efficient wireless data transfer technology. The download of the calculated parameters and settings adjustment (if required) is realized by means of Radio Frequency Identification (RFID) with a low frequency transponder (134.2 kHz). Data download is independent from the data collection process and can be done on demand at freely chosen time points. In the current system version, the patient skin is approached with an RFID transponder to a maximum distance of 3 cm to the implanted data logger. The download process for 1 month of collected data requires 12 min (at 6 h logging intervals).

Current consumption of the device is ~60 µA resulting in a battery lifetime of around 4.5 months (3 V button cell battery with a capacity of 210 mAh). Size of data logger and battery is 26 mm diameter x 7.5 mm (Figure 1).

The data collection principle is independent of the processed signal type. Two versions of the device with adapted signal conditioning have been realized for receiving signals of different sensors. 1) Connecting a conventional strain-gauge rosette, measuring implant/fixator deformation, and 2) Attaching a miniature LVDT displacement transducer (linear variable differential transformer) for measuring fracture gap motion.

In a first application, the LVDT version was used together with a research implant system in a sheep tibia model as described in the following.

3 PILOT ANIMAL STUDY

Functionality of the developed system under in-vivo conditions was investigated in an animal model. Purpose of the experiments was proving the principle, revealing technical and methodological issues and using the system to answer specific research questions. Until now, a total of 10 sheep were operated and equipped with different versions of the data logger as part of an iterative development process. Since settings and scope varied between experiments, a single case will be described in the following to illustrate the system function. Statistical evidence is, hence, not presented.

3.1 Materials and Methods

In-vivo measurements were performed in a sheep tibia osteotomy model. For stabilization of the fracture a dynamizable internal fixator system was used (AO Research Institute Davos). The implant is axially compressible and comprises a proximal and distal plate-body connected by two cylindrical rods, which act as linear guides for implant motion. Two polymer springs (Polyurethane) allow for passive dynamization of the fracture through weight bearing and muscle contraction and provide defined load sharing between bone and implant. Range of motion can be freely adjusted from rigid blocking to macroscopic axial displacement. A miniature displacement transducer (GHSM-1.0B, Singer Instruments & Control Ltd., Tirat Carmel, Israel, 2 mm measuring range) was incorporated into one of the guiding rods to measure axial plate motion (Figure 2). The electronic unit was connected via a biocompatible cable and was encapsulated in a custom-made PEEK housing (Polyetheretherketon) (Figure 3).

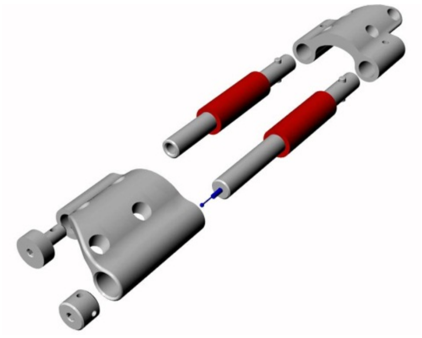

Figure 2: Exploded view of the internal fixator instrumented with a displacement transducer and polymer springs for passive dynamization of the fracture gap.

Implant and sensor were calibrated on a material testing machine. Axial motion was limited to 0.3 mm and the springs were preloaded with 250 N. Axial stiffness of the implant was ~530 N/mm.

Animal experiments were approved by the local ethic committee for animal health and were carried out on Swiss white alpine sheep. Surgery was performed under general anesthesia. The implant was placed on the medial aspect of the left tibia with the sensor wire exiting proximally to the electronic unit, which was positioned in a subcutaneous pocket proximal to the implant. Following fixation of the plate with eight 5.0 mm angular stable locking screws, a 3 mm transverse osteotomy was created using an oscillating saw and a guiding jig.

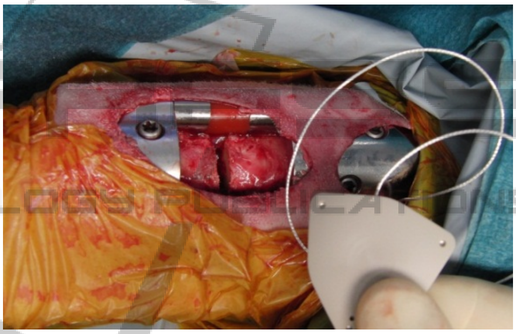

Figure 3: Implantation of the research implant system with telemetric unit in a sheep tibia model. The electronic is encapsulated in a PEEK housing and inserted proximally to the axially compressible plate.

The sheep (body weight 50 kg) was able to bear full weight immediately after surgery. A loose harness was installed during the first five days allowing the animal to rest while protecting the fixation from excessive loading. Radiographs were taken biweekly until euthanasia at 18 weeks post-operation.

Thresholds for the peak detectors were set to motion amplitudes of 0.2 mm, 0.1 mm and 0.04 mm (0.02 mm after 6 weeks). The logging interval over which measurements were averaged, was set to 12 hours, thereby generating two sets of parameters per day (daytime: 6-18 h, nighttime: 18-6 h). The recorded data was downloaded to an external computer once or twice a week. After the animal was killed at 18 weeks post-operation, both tibiae were harvested and the implant was removed from the bone. Torsional stiffness and ultimate torque was determined for operated and contralateral tibia by means of torsional mechanical testing to failure. Mechanical behavior of the implant was reevaluated after explantation and compared to the initial mechanical test results.

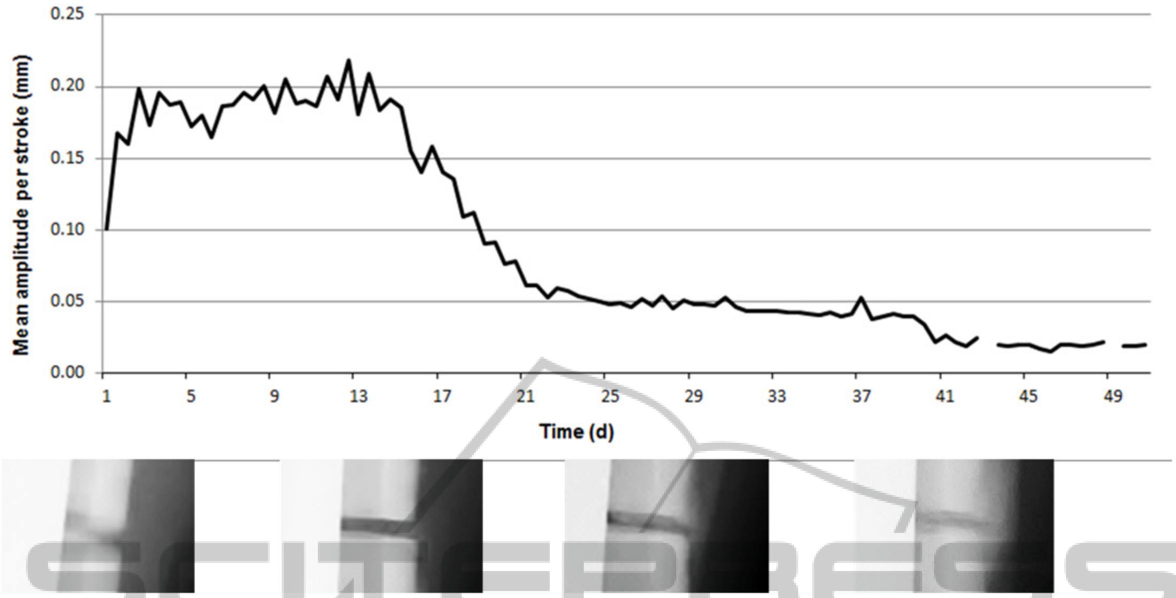

Figure 4: Recorded axial motion per load cycle over time. Displayed values are averaged over an interval of 12 hours. Below the corresponding radiographs (AP direction) are shown on the same time scale.

3.2 Results

Data logger, sensor and implant kept functioning throughout the experiment (18 weeks). No pathological reactions of the animal to the system were observed.

Mean axial displacement per stroke increased from initially 0.1 mm after operation to around 0.2 mm within the first three days. It then temporarily decreased again to 0.15 mm at day 6, before reaching the highest displacement of 0.22 mm at day 12. From the beginning of the third week post-surgery, a rapid reduction of the mean stroke amplitude was found, followed by a slower decrease until the minimal threshold of 0.02 mm was reached after eight weeks post-operation. A step in the displacement curve after day 40 is caused by changing the lowest detector threshold to 0.02 mm. (Figure 4).

A maximum of 480 strokes per hour was recorded at the second day after surgery (Figure 5). From day 3 the number of strokes/h decreased and stabilized at a level of 50 - 100 strokes/h for the following three weeks before the detected activity faded out. Number of strokes was consistently higher during daytime than during night (Figure 5).

While initially the strokes divided equally into the three intensity bins according to displacement magnitude, the number of strokes in the highest bin (≥0.2 mm) increased to 50% within the first 10 days. During the following two weeks, number of strokes in the lowest bin (amplitude 0.04-0.1 mm) increased continuously until no more strokes above 0.2 mm and above 0.1 mm were recorded after 4 and 5 weeks respectively.

First signs of callus formation on radiographs were found four weeks post-operation; bridging was observed after six weeks. Mineralization and size of callus then gradually increased reaching a maximum at 8 to 10 weeks post operation.

Torsional stiffness of the operated limb was 4.3 Nm/deg (77% of contralateral). Ultimate torque to failure yielded 58.5 Nm (72% of contralateral).

At the end of the test axial gliding of the plate remained possible, but implant mechanics were found altered by the biological environment. Spring preload was reduced while stiffness of the plate had slightly increased.

4 DISCUSSION AND OUTLOOK

A telemetric implantable data collection system for continuous monitoring of bone healing was introduced and successfully tested in an animal experiment. To the authors' knowledge, this is the first time such data could be acquired over a complete fracture healing cycle. The general principle of indirect healing assessment by measuring fixator deformations (Evans et al., 1988) was confirmed by a decline of the motion signal while fracture callus forms. A stable response of the derived signal over days and weeks supports the

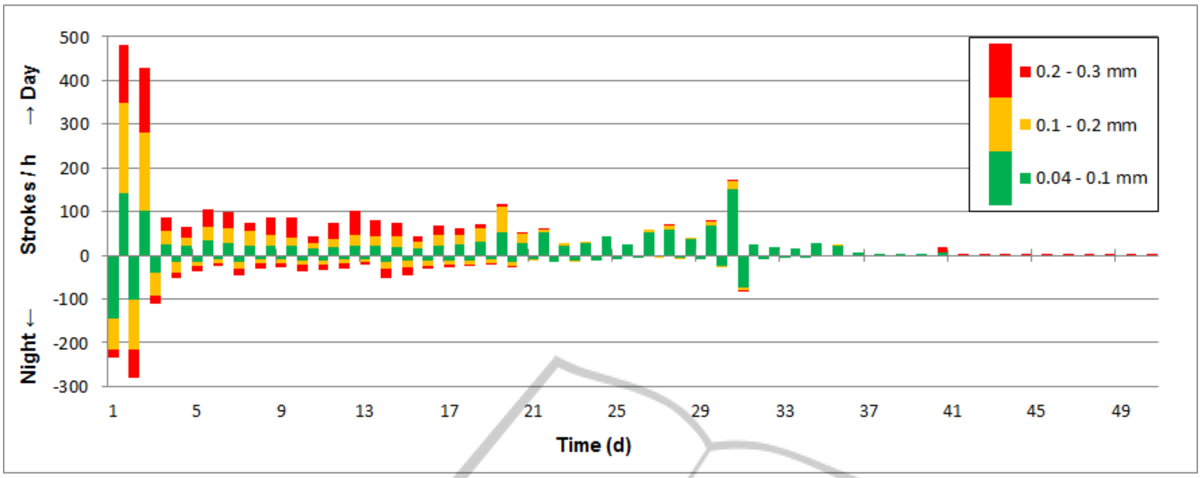

Figure 5: Number of strokes per hour recorded in time intervals of 12 hours. Green bars represent strokes with an amplitude less than 0.1 mm, yellow bars strokes from 0.1 mm to 0.2 mm and strokes with an amplitude greater than 0.2 mm are marked in red. Bars for daytime activity point upwards, nighttime downwards.

underlying assumption that variations in functional loading can be averaged out. Here 12 h averaging intervals were chosen; other timespans could be considered. In the present setting, parameters derived from the biofeedback system indicated changes in fracture motion earlier than healing became apparent on radiographs. Whether this is a valid observation remains to be clarified. It could also be attributed to the mechanical behavior of the research implant used. Preloading the springs acts as a filter shielding the fracture from low intensity strokes. The plate is, hence, more responsive to stiffness changes.

In contrast to other solutions (Seide et al., 2012) the data logger system also enables assessment of the patient activity. Onset of bone healing is reflected by an increasingly unbalanced stroke-intensity distribution. With ongoing fracture consolidation, occurrence of high-intensity strokes is fading out in favor of lower stroke intensities.

Overall patient activity in terms of number of strokes per time-interval is another interesting parameter which may contribute to a better understanding of healing processes in the future. A pronounced activity of the animal directly after surgery became obvious, but was not necessarily to be expected. This cannot be explained with individual animal behavior since a general tendency was seen in all tested animals. Pain medication during the first days after surgery may be a reason for accentuated limb loading. It is unclear how this initial activity peak influences the healing process and if the behavior can also be found in humans.

To better understand such information and to reach an evidence level, the consequent next step is to build up a database. Distinct healing patterns for normal and aberrant courses of healing could be extracted and interpreted (Burny et al., 2012; Claes et al., 2002). Ideally, data collection should concentrate on human patients to increase the significance of results. Therefore, a strategy is followed where data can be acquired at minimal patient risk. As a first step, measurement in combination with external fixation is an interesting approach (Claes et al., 2002). A non-implantable, external prototype has been developed for this purpose. The device can be attached to an external fixator measuring sidebar deflections without body contact. A study to collect clinical pilot data is in preparation.

Technically, the described data logger is still in a prototype stage to be used for research purposes. Several minor issues crystalized during animal testing including robustness of the firmware, timing accuracy of the internal clock, cable breakage or sealing of the housing. The next generation data logger is currently under development targeting accelerated data transfer, increased communication range and miniaturization. A size reduction of the electronics unit is an interesting future option for a potential internal application in human patients. However, this may only be considered at a later stage, when a distinct analysis of acquired pilot data has been performed regarding potentials and benefits for clinical fracture treatment.

Another future concept is the idea of active modulation of fixation stiffness according to individual healing progressions. The potential of such an approach is still unknown; further research is required (Epari et al., 2013). The electronic unit is already prepared not only to connect sensors, but also actuators to perform defined actions for a closed-loop control strategy.

5 CONCLUSIONS

A telemetric biofeedback concept for continuous monitoring of bone healing was introduced. The system allows for autonomous long-term data collection over several months, carrying a high potential to significantly improve fracture care. Feasibility of the approach was proven in an animal experiment. Collection of further in-vivo data - also in humans - is the consequent next step.

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