# 1 Introduction

688 000 bone fractures were registered in Germany in 2019 with the incidence having increased by 14 % since 2009. Statistically, every adult older than 55 years has an accumulated risk of 44 % to be affected by a fracture at some point, which indicates the relevance of this public health problem for the society and the healthcare system [1]. The most common fracture localizations are at the long bones of the upper leg and the forearm. Globally, 178 million new fractures have been reported in 2019 [2].

Bone fractures can be treated by conservative management with plaster in simple cases or surgical methods with osteosynthesis devices in more complicated cases [1, 3]. Among these osteosynthesis devices, which are used to reposition and stabilize the fractured bone, are osteosynthesis plates and hexapod fixators, which are the focus of this thesis. Osteosynthesis plates essentially are flat metallic bars, which are attached to the bone on both sides of the fracture by surgical screws to bridge the discontinuity [4].

Hexapod fixators are a specialized type of external fixators, of which the major load-bearing part remains outside the body. They consist of several rings, which are placed around the fractured limb and are attached to the bone with surgical screws or tensioned wires. Rings on both sides of the fracture are connected to each other by six length-adjustable struts, so-called distractors, which enable precise repositioning of the fracture in six degrees of freedom. Attaching the hexapod fixator to the bone requires only minimally invasive surgeries, which avoid damage to the soft tissue surrounding the bone [5].

Even though the widespread use of osteosynthesis devices and methods has greatly improved fracture treatment, it is regularly reported that in about 5 % to 10 % of the cases the fracture healing is delayed, negatively affected by complications or does not occur at all [1, 2, 6]. These problems can result in a prolonged treatment duration, longer hospitalization or the need for further surgeries and therefore have a huge impact on the patients health as well as negative socioeconomic consequences [7]. In [6], an average of two full days spent in hospital for the treatment of complications after the original fracture treatment was found for a group of 315 patients in Australia. The associated average costs per patient only for the extended treatment of the complications is given as 9300 $. Similar investigations in the United Kingdom estimated the costs for the treatment of non-unions to be between 8800 $ and 99 000 $ and for the United States a value of 25 600 $ was found [6]. Even though the methods for estimating the costs, the underlying statistical data and the results vary, it can be clearly seen that complications in fracture treatment lead to significant costs in the health care system and should be further reduced whenever possible.

The monitoring of the healing process in the clinical practice of fracture treatment is normally done with planar radiography or computed tomography scans. However, these methods have some known disadvantages [8]. The interpretation of radiographic images is highly subjective and only shows a low correlation with the mechanical load bearing capabilities of the bone [9–11]. Moreover, it takes some time until new callus tissue is formed in the fracture gap, which can then be detected radiographically [12]. Because of its adverse health effects, the general availability of the devices and the associated costs, radiography is typically done in intervals of several weeks with no data points in between [2]. Therefore, radiographic methods are not able to accurately determine the status of the fracture healing process without significant delays, especially in the first weeks after the fracture occurred. Because of this, valuable time can be lost when an osteosynthesis treatment was unsuccessful, but is continued until this is detected in the next radiography. On the other hand, the patients can be allowed to apply higher loads to the fracture if an increased stability is detected earlier, which supports the healing process and reduces constraints for the patients.

It was found that measurements of the mechanical stiffness of the fracture represent a good indicator for the status of the healing process and provide objective metrics for the load bearing capability [2, 8, 12–15]. Typically, this concept is implemented by integrating strain gauges into osteosynthesis implants or external fixators. The fracture stiffness is obtained as the ratio of the measured strain to an externally applied force and over time it decreases relative to the initial value, if the fracture is healing. Several electronically instrumented osteosynthesis plates have been reported and successfully applied in clinical studies, which utilize wireless inductive power and data transfer or similar approaches to obtain measurement data [11, 16, 17].

It is assumed that there exists a window of load bearing levels, which optimally supports fracture healing [8, 18]. A certain amount of stimulation and movement in the fracture gap accelerates the generation of new bone tissue, but it must remain small enough in order not to negatively affect the healing or even damage the bone further [19, 20]. Conventionally, this aspect is addressed by certain load bearing levels that the patients should follow. For example, 10 kg partial weight bearing directly after surgery of a fracture at a leg could be recommended and increased to 20 kg after some weeks. Scales are sometimes used to demonstrate to the patients, which motions they can perform without exceeding the limits. Partial weight bearing also helps to improve the patients' quality of life when it reduces restrictions of their mobility and avoids damage to the osteosynthesis device. However, humans are generally unable to precisely estimate the weight that they apply to their legs in everyday life situations and therefore they tend to exceed the defined load limits significantly [20–22].

The problem of missing feedback for partial load bearing can be addressed by a continuous monitoring of the mechanical loads affecting the fracture and by warning the patients if they exceed an overload threshold [8, 17]. However, none of the electronically instrumented osteosynthesis plates reported in literature are capable of autonomously measuring the mechanical loads and directly sending them to the patients, which is necessary for an efficient overload detection. Most of them rely on an active wireless power transfer to be operated and those, which have an energy storage, do not have enough energy available for continuous data transmission.

To overcome this limitation, a demonstrator for a new electronic osteosynthesis implant was developed as part of this thesis, which utilizes a strain gauge attached to an osteosynthesis plate as a sensor, and has an integrated energy storage, which can be recharged via an inductive wireless power transfer link. A Bluetooth Low Energy (BLE) transceiver is used to transmit the measured data to an external reader device without relying on an inductive data transmission, which is highly susceptible to misalignment. This enables a continuous overload detection. An application-specific integrated circuit (ASIC) was designed for the sensor interface to minimize the power consumption and therefore increase the autonomous operating time. Moreover, the ASIC allows a higher level of functional integration, which is an advantage for implants, in which the available space is always very limited.

The same concept was also applied to a newly developed electronic hexapod fixator, which uses force sensors integrated into the six distractors for indirect measurements of the fracture stiffness. Each distractor is equipped with an electronic module, which integrates a sensor interface, batteries, a power management system and a Bluetooth Low Energy transceiver for wireless data transmission. The force measurements from all distractors are sent to an overload indicator, which is a portable battery-powered device that calculates the total force affecting the hexapod fixator. The overload indicator activates an optical and acoustical alarm if the threshold for the acceptable mechanical load is exceeded. This enables a reliable monitoring of the healing process and a continuous overload detection.

Moreover, an optical proximity sensor is attached to each distractor to automatically measure its length. These measurements are required during applications like limb lengthening procedures or the correction of complex fractures over a longer period. In these cases, the patients have to iteratively adjust the distractor lengths according to a treatment plan. Since the distractors are often hard to reach, the manual length measurement is error-prone and limits the patients autonomy if they cannot do it by themselves. The only solutions for automatic length measurements, which have been published so far, rely on electric motors, rotary encoders and large battery packs, which are bulky and add a significant amount of weight to the hexapod fixator [23–26]. The electronic hexapod fixator developed as part of this work, is the first one that implements an automatic length measurement of the distractors with small optical proximity sensors that do not add bulky motors and battery packs. Moreover, it is the only hexapod fixator that combines electronic length measurements and measurements of the mechanical loads affecting the fracture.

The development of an electronic osteosynthesis device is a highly interdisciplinary project, which has to cover medical requirements, information about the biomechanical behavior of fractures, mechanical design of the load-bearing components, sensor physics, electronics design, embedded software development and many other topics. Without the cooperation, support and experience of a larger team, an individual person would most likely not be able to achieve any meaningful results in this research area. The work presented in this thesis was embedded in two research projects, the IOMon project (KMU-innovativ: Medizintechnik, 13GW0199) for the electronic osteosynthesis implant and the SmartFix project (KMU-innovativ: Medizintechnik, 13GW0642) for the electronic hexapod fixator, which were both supported by grants from the German Federal Ministry of Research, Technology and Space (BMFTR). The developed medical devices are the result of combining the electronic components, presented in this thesis, with the mechanical components [27] and other contributions from the project partners. The focus of this work will be on the design of the electronic components, which was performed by the author, but other contributions like the mechanical parts of the devices will inevitably also be shown in some cases. Those contributions will only be explained as much as necessary within the context of this work and results achieved by others will be indicated when it is not obvious.

After the introduction, this thesis is structured into four additional chapters. Chapter 2 describes the fundamentals of osteosynthesis devices, the main functional modules from which medical instrumentation systems are built and the basics of analog integrated circuit design. In chapter 3 the electronic osteosynthesis implant is presented. This is further segmented into a I. demonstrator based on commercially available electronic components, which is used as a proof of concept, the design of the ASIC for the sensor interface and a II. demonstrator based on this ASIC. The electronic hexapod fixator is described in chapter 4 and the thesis ends with a conclusion and an outlook in chapter 5.

# 2 Fundamentals

In this chapter an overview of osteosynthesis devices, medical instrumentation systems and CMOS analog integrated circuit design is given. This introduces the fundamentals for the following chapters, in which the electronic osteosynthesis implant, the application specific integrated circuit (ASIC) and the electronic hexapod fixator will be presented in detail.

## 2.1 Osteosynthesis

Osteosynthesis describes the surgical treatment of bone fractures to reposition and stabilize the bone fragments [4, 28]. The target is to support the natural fracture healing, to enable partial load bearing of the patients and to avoid deformities [29]. Osteosynthesis treatment is typically done with the help of medical devices, which are connected to both sides of the fracture and can carry mechanical loads. These devices include osteosynthesis plates, external fixators, intramedullary nails, Kirschner wires and other more specialized solutions [3, 4, 30]. Osteosynthesis devices can generally be categorized into two groups - internal and external fixators. Internal fixators like osteosynthesis plates or intramedullary nails are fully implanted and attached to the bone with surgical screws. The main part of external fixators on the other hand remains outside the body and is connected to the fractured bone with Schanz screws or Kirschner wires, which require only minimally invasive surgery for implantation [30].

In this section the fundamentals of bone fractures and their healing process will be presented. The focus will then be on osteosynthesis plates from the group of internal fixators and hexapod fixators, which are a specialized realization of an external fixator, because these are the two osteosynthesis devices, for which electronic instrumentation systems have been developed as part of this thesis. Moreover, an overview of the state of the art of electronically instrumented osteosynthesis implants and hexapod fixators is presented in the following paragraphs.

### 2.1.1 Bone Fractures

Bones fulfill several tasks in the human body. They are mainly responsible for providing structural stability, protecting internal organs and providing attachment points for other components of the musculoskeletal system, which enables humans to move. Moreover, the cellular blood components are generated in the bone marrow and the bone tissue serves as a reservoir for calcium and phosphate in the mineral metabolism of the human body [3, 31]. Bones mainly consist of a hard outer layer, which is called cortical bone, and a porous, spongy, more flexible internal tissue close to the ends of long bones and inside flat bones, which is called cancellous bone. The bone marrow is located around the porous cancellous bone and in a marrow cavity in long bones [3, 32]. Bones undergo a continuous process of remodeling and adaption performed by osteoblasts, which are cells that synthesize and shape new bone tissue, and osteoclasts, which reabsorb bone. An important stimulus that affects this process is mechanical stress. According to Wolff's law, bone is remodeled along lines of mechanical stress so that it is improved where more stability is needed [3, 31]. This means that the bone becomes more dense and stable in those regions where it is mechanically loaded and bone tissue is reabsorbed when the loading decreases. The process described by Wolff's law allows the bone to be continuously adapted to changing external factors.

A bone fracture is defined as a partial or complete disruption of the continuity of cortical or cancellous bone [3]. Causes for fractures can be accidents in traffic, household activities or sports for example [33]. Fractures are differentiated between "closed" if the skin over the fracture remains intact and "open" if that is not the case. Depending on the number of fragments as well as the localization, orientation and pattern of the fracture, they can be categorized further.

With direct and indirect fracture healing, two different processes of bone recovery are known. Direct healing only occurs if the fracture is repositioned exactly without any gap. If this condition is fulfilled, the bone healing occurs as part of the remodeling process and is comparatively fast. However, direct healing does not happen very often because of the strict requirements. Therefore, indirect fracture healing, which takes place in three partly overlapping steps, is the typical scenario. In the vascular phase, a hematoma occurs, which is infiltrated by cells that reorganize its structure and create small blood vessels. Dead cells are also removed in this phase. Soft callus tissue then starts to form in and around the fracture gap. When this soft callus is transformed into hard callus in the metabolic phase about four to six weeks after the injury, that is the first sign of successful healing that can be detected with the help of radiography [18]. In the mechanical phase, the process of remodeling performed by the osteoblasts and osteoclasts takes over. The hard callus, which typically occupies a larger volume than the intact bone did before the fracture, is continuously removed and replaced by cortical and cancellous bone. Complete healing of the fracture can take up to several years [3, 18, 19].

Fracture healing benefits from a small amount of micro-motion in the fracture gap to stimulate callus formation and bone remodeling according to Wolff's law. However, if there is too much strain on the fracture, healing can be delayed or even prevented [18]. Osteosynthesis plates and hexapod fixators are regularly used to reposition and stabilize a fracture so that the strain is limited and the healing process is supported. An overview of these osteosynthesis devices will be given in the following sections. Alternative methods can also be closed repositioning of the fracture and the use of plaster casts in less complex cases [3]. Conventionally, planar radiography or computed tomography scans (CT scan) are used in intervals of several weeks for monitoring the healing process [3, 31, 34].

### 2.1.2 Osteosynthesis Plates

The initial use of osteosynthesis plates in fracture treatment dates back to the year 1886, when Carl Hansmann reported the first application at a fracture of a long bone. Before that, other osteosynthesis implants like screws, wires and nails had already been used. With the introduction of antiseptic wound treatment in 1877, a slow shift had started from open surgery being a last resort to it becoming the primary treatment for many types of fractures. Towards the end of the 20th century, several improvements of osteosynthesis plates have been developed. These include limited contact plates, which reduce damage inflicted on the soft tissue and blood vessels surrounding and supplying the bones. Together with less invasive surgery methods this approach improved the fracture healing process. Moreover, the invention of locking plates, which create angular-stable connections between the plate and the surgical screws, enabled the transfer of mechanical loads between the plate and the bone without relying on friction between them. These plates allow the transfer of forces and moments in all degrees of freedom while keeping a gap between the plate and the bone to limit soft tissue damage [28, 29, 35]. Angular-stability is often achieved with the help of a second thread at the head of the screws which locks them to the plate by screwing into a lip or a thread in the holes of the plate [36].

Fig. 2.1 shows a collection of osteosynthesis plate samples including small plates used for foot surgery as well as larger ones for long bones in the lower limbs. The second and third plate from the top on the left side are a femur and a tibia plate, which are used for the treatment of fractures in the upper leg (femur) and the shinbone (tibia). Osteosynthesis implants similar to these will be used more often as sample applications throughout this thesis, because overload detection is especially relevant for fractures at the lower limbs.

Figure 2.1: Collection of osteosynthesis plates for various fracture localizations like the leg and foot. The second and third implant from the top on the left side are examples for a femur and a tibia plate, which are applied at the upper leg and the shinbone, respectively.

Osteosynthesis plates are typically made from titanium or medical grade stainless steel. The basic shape often resembles a flat bar with several holes at the ends or distributed along the length of the plate, to which the surgical screws can be attached. Various designs of osteosynthesis plates are available, which are adapted to the shape of the bones and the surrounding biological environment at many different fracture localizations. Important properties of these implants are biocompatibility and mechanical stability to withstand the loads applied to a fractured bone. At the same time osteosynthesis plates have to be small enough for the inherently limited space in the human body. Moreover, they should ideally have a flexibility similar to the bone so that they do not disturb its remodeling by locally shielding regions of the bone from the externally applied loads [4, 29]. This short overview of requirements for osteosynthesis implants already shows that each device always represents a compromise between contradicting design goals.

In Fig. 2.2 an example of a tibia plate attached to an artificial shinbone is depicted. The artificial bone was cleanly cut to approximately model a fracture. Six angular-stable screws attach the plate to both sides of the fracture. In realistic cases, the cut line would normally be less ideal and the fracture gap would probably be reduced during surgery so that less new bone tissue has to form.

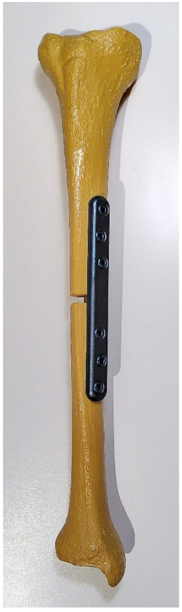

Figure 2.2: Model of a tibia plate attached to an artificial bone in the shape of a right shinbone (tibia).

### 2.1.3 Electronically Instrumented Osteosynthesis Implants

As described in the introduction in chapter 1, the state of the art fracture treatment has some limitations in the monitoring of the healing process and the prevention of mechanical overloads, even though modern osteosynthesis plates in general represent good solutions for the biomechanical requirements. Since the 1960s, experiments with strain gauges attached to external fixators have been performed [13]. An additional measurement of the external reference force applied to the fracture provides an approximation for the stiffness as the fraction of strain over force. This stiffness of the biomechanical system, which consists of the fractured bone, its surrounding soft tissue and the osteosynthesis device, proved to be a good indicator for the healing process. In clinical studies it enabled the differentiation between healing patterns including delayed healing or the absent of healing. An increasing fracture stiffness correlates with a higher weight bearing capability and an