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ON CUSTOMIZATION OF ORTHOPEDIC IMPLANTS-FROM DESIGN AND ADDITIVE MANUFACTURING TO IMPLEMENTATION

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"The more I learn, the more I realize how much I don't know"

-Albert Einstein

ABSTRACT

This doctoral thesis is devoted to studying the possibilities of using additive manufacturing (AM) and design based on computed tomography (CT), for the production of patient-specific implants within orthopedic surgery, initially in a broad perspective and, in the second part of the thesis focusing on customized clavicle osteosynthesis plates. The main AM method used in the studies is the Electron Beam Melting (EBM) technology. Using AM, the parts are built up directly from 3D computer models, by melting or in other ways joining thin layers of material, layer by layer, to build up the part. Over the last 20 years, this fundamentally new way of manufacturing and the rapid development of software for digital 3D reconstruction of anatomical models from medical imaging, have opened up entirely new opportunities for the design and manufacturing of patient-specific implants. Based on the information in a computed tomography (CT) scan, both digital and physical models of the anatomy can be created and of implants that are customized based on the anatomical models.

The main method used is a number of case studies performed, focusing on different parts of the production chain, from CT-scan to final implant, and with several aims: learning about the details of the different steps in the procedure, finding suitable applications, developing the method and trying it out. The first study was on customized hip stems, focusing on the EBM method and its special preconditions and possibilities. It was followed by a study of bone plates, designed to follow the patient-specific bone contour, in this case a tibia fracture including the whole production chain. Further, four cases of patient-specific plates for clavicle fracture fixation were performed in order to develop and evaluate the method. The plates fit towards the patient's bone were tested in cooperation with an orthopedic surgeon at Östersund hospital. In parallel with the case studies, a method for finite element (FE) analysis of fixation plates placed on a clavicle bone was developed and used for the comparative strength analysis of different plates and plating methods. The loading on the clavicle bone in the FE model was defined on a muscle and ligament level using multibody musculoskeletal simulation for more realistic loading than in earlier similar studies.

The initial studies (*papers I and II*) showed that the EBM method has great potential, both for the application of customized hip stems and bone plates; in certain conditions EBM manufacturing can contribute to significant cost reductions compared to conventional manufacturing methods due to material savings and savings in file preparation time. However, further work was needed in both of the application areas before implementation. The studies on the fracture fixation using patient-specific clavicle plates indicated that the method can facilitate the work for the surgeon both in the planning and in the operating room, with the potential of a

smoother plate with a better fit and screw positioning tailored to the specific fracture (*paper VI*). However, a large clinical trial is required to investigate the clinical benefit of using patient-specific plates. The FE simulations showed similar stress distributions and displacements in the patient-specific plates and the commercial plates (*papers III to VI*).

To summarize: the results of this thesis contribute to the area of digital design and AM in patient-specific implants with broad basis of knowledge regarding the technologies used and areas in which further work is needed for the implementation of the technology on a larger scale. Further, a method has been developed and initially evaluated for implementation in the area of clavicle fracture fixation, including an approach for comparing the strength of different clavicle plates.

Keywords: Patient-specific implants, Additive manufacturing, Electron Beam Melting, Multibody musculoskeletal analysis, Orthopedic implants, Clavicle, Finite element analysis, Computer aided design, Osteosynthesis plates, Hip stem implants.

SAMMANFATTNING

Denna doktorsavhandling har tillägnats att studera möjligheter med att använda additiv tillverkning (AT), och design baserad på informationen i en datortomografi (DT), för att ta fram patientspecifika ortopediska implantat, inledningsvis i ett brett perspektiv och i senare delen av avhandlingen med fokus på individanpassade osteosyntesplattor för komplicerade nyckelbensfrakturer. Den huvudsakliga metoden för AT som använts i studierna är ”Electron Beam Melting” metoden (EBM). Med AT byggs detaljerna upp direkt utifrån tredimensionella (3D) digitala modeller genom att smälta eller på annat sätt foga samman material i tunna skikt lager på lager. Detta fundamentalt nya sätt att tillverka detaljer, tillsammans med en snabb utveckling av programvaror för digital 3D-rekonstruktion av anatomiska modeller utifrån DT och annan medicinsk bilddiagnostik, har under de senaste 20 åren öppnat upp helt nya möjligheter inom området för design och tillverkning av patientspecifika implantat. Utifrån informationen från en DT undersökning kan i ett första skede en digital modell av anatomin skapas, följt av en additivt framställd fysisk modell. Den digitala modellen kan användas som underlag för design av implantat utifrån anatomin och den fysiska kan användas i operationsplaneringen.

Den huvudsakliga metoden som använts är ett antal praktiskt utförda fallstudier som omfattar olika delar av produktionskedjan från DT till färdigt implantat med ett flerfaldigt syfte; erhålla kunskap om detaljer i de olika stegen i produktionskedjan, hitta lämpliga tillämpningar samt att utveckla och utvärdera metoden. Den första fallstudien handlade om individanpassade höftstammar och har fokus på EBM metoden med dess speciella förutsättningar och möjligheter. Den följdes av en studie som innefattar hela produktionskedjan från DT till färdig individanpassad platta utformad för att passa patientens benkontur för fixering av en tibiafraktur. Vidare utfördes fyra fall av patientspecifika plattor för fixering av nyckelbensfrakturer för att utveckla och initiellt utvärdera metoden. Plattorna provpassades mot patienternas ben i samarbete med en ortoped vid Östersunds sjukhus. Parallellt med fallstudierna togs en metod för finita element (FE) analys av nyckelbensplattor fram som sedan har använts för jämförande hållfasthetsanalyser mellan kommersiella och patientspecifika plattor samt för jämförande analyser av olika fixeringsmetoder. Lastfallet på nyckelbenet definierades på muskel- och ligamentsnivå genom användandet av flerkroppssimulering på muskuloskeletär modell för att åstadkomma en mer realistiskt simulering jämfört med tidigare liknande studier.

De inledande studierna (*paper I och II*) visade att EBM metoden har stor potential både inom tillverkning av individanpassade höftstammar och fixerings plattor, och

att tillverkning med EBM-metoden kan under speciella förutsättningar bidra till att väsentligt minska kostnaderna jämfört med konventionell tillverkning på grund av minskad materialåtgång och tid för filberedning. Vidare arbete är dock nödvändigt inom båda dessa områden. De indikativa resultaten av studierna på individanpassade nyckelbensplattor visar att metoden kan underlätta arbetet för ortopeden både i operationsplaneringen och under utförandet av själva operationen och att det finns god potential för att åstadkomma en smidigare platta med bättre passform och med skruvpositioner och vinklar som passar den specifika frakturen (*paper VI*). För att utreda den kliniska nyttan med individanpassade plattor krävs dock en stor klinisk studie. FE-simuleringarna visade på liknande spänningsfördelning och deformationsmönster i de patientspecifika plattorna och de kommersiella (*paper III-VI*).

Sammanfattningsvis, detta avhandlingsarbete bidrar inom området för datorstödd design och AT av patientspecifika implantat med en bred kunskap gällande de tekniker som används och inom vilka områden vidare arbete krävs för att kunna implementera tekniken i större omfattning. Vidare är metoden utvecklad och initialt testad för implementering på patientspecifika plattor för nyckelbens-frakturer och omfattar också en ny metod för jämförande hållfasthetsanalys av sådana plattor.

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LIST OF PAPERS

This thesis is mainly based on the following six papers, herein referred to by their Roman numerals:

Paper I M Cronskär, M Bäckström, L-E Rännar
Production of Customized Hip Stem Prostheses – A comparison between Conventional Machining and Electron Beam Melting (EBM)
Rapid Prototyping Journal, v 19, n 5, p365-372, 2013

Selected by the journal's Editorial Team as a Highly Commended Paper of 2013

Paper II M Cronskär, L-E Rännar, M Bäckström
Implementation of digital design and solid free-form fabrication for customization of implants in trauma orthopaedics
Journal of Medical and Biological Engineering, v 32, n 2, p91-96, 2012

Paper III M Cronskär, J Rasmussen, M Tinnsten
Combined finite element and multibody musculoskeletal investigation of a fractured clavicle with reconstruction plate
Computer Methods in Biomechanics and Biomedical Engineering, p1-9, ahead-of-print, 2013

Paper IV M Cronskär
Strength analysis of clavicle fracture fixation devices and fixation techniques using finite element analysis with musculoskeletal force input
Submitted to: Medical & Biological Engineering & Computing.

Paper V M Cronskär, M Bäckström
Modeling of fractured clavicles and reconstruction plates using CAD, finite element and real musculoskeletal forces input
Wessex Institute Transactions on Biomedicine and Health, vol 17, p235-243.

Paper VI M Cronskär, L-E Rännar, M Bäckström, K-G Nilsson, B Samuelsson
Patient-specific bone plates for clavicle fractures – design, manufacturing and strength analysis
Manuscript

ABBREVIATIONS AND VOCABULARY

AM	Additive Manufacturing
CAD	Computer Aided Design
CAM	Computer Aided Manufacturing
CT	Computed Tomography
DICOM	Digital Imaging and Communications in Medicine
EBM	Electron Beam Melting
FEM	Finite Element Modeling
HIP	Hot Isostatic Pressing
MRI	Medical Resonance Imaging
PS	Patient Specific
RP	Rapid Prototyping
STL	Stereolithography
THR	Total Hip Replacement
XML	Extensible Markup Language

Acetabulum	The cup shaped socket in the hip bone
Anomalies	A deviation from normal
Anterior	Situated towards the front of the body
Anterioinferior	Situated in the front and below
Articular	relating to a joint
Aseptic loosening	Loosening of implant caused by biologic respons to wear particles and mechanical factors
Callus	Tissue that forms around a break in a bone and is converted into bone in the healing
Clavicle ligaments	se sid. 21-22
Clavicle muscles	se sid. 21
Clavicle	Collarbone
Comminuted	A fracture in which the bone is splintered or crushed into numerous pieces.
Congenital	Existing from birth
Cortical bone	Compact bone in the outer shell of most bones
Diaphysis	The shaft of a long bone
Distal	Situated away from a central point of the body
Femur	The bone of the lower limb that extends from the hip to the knee
Inferior-medial	Situated below and in the middle
Interfragmentary compression	Static compression applied to a fracture plane
Lateral	Lying away from the median axis of the body
Malunion	A fracture that has healed in a incomplete or faulty union
Medial	Lying or extending towards the median axis of the body
Medullary	Relating to the medulla of any body part or organ, (medulla = bone marrow)
Nonunion	Permanent failure of healing of a fracture.
Orthotropic	Different properties in different orthogonal directions
Osseointegration	The firm anchoring of a surgical implant by the growth of bone around it
Osteoporotic bone	Porous, fragile bone, decreased in bone mass
Osteosynthesis	The operation of uniting ends of a fractured bone (with wire or metal plate)
Osteotomy	A surgical operation in which a bone is divided, or a piece of bone is excised, as to correct a deformity

Reduction	A medical procedure to restore a fracture or dislocation to the correct alignment
Revision	A surgery performed to replace or compensate for a failed implant or to correct undesirable sequelae of previous surgery
Scapulae	Shoulder-blade
Sequelae	A negative aftereffect
Spongy bone	Light, porous bone in a honeycombed or spongy appearance
Subcutaneous	Right under the skin
Superior	Situated towards the head

TABLE OF CONTENTS

1. INTRODUCTION

Additive manufacturing (AM), including both rapid prototyping (RP) and direct fabrication is a fundamentally new way of part fabrication for which parts are processed directly from 3D computer models by successively adding layers of materials [1]. These rapidly emerging technologies, together with the development of software used for 3D reconstruction of bone and soft tissue organs and for the design and analysis of custom surgical implants, have provided new opportunities in the area of design and manufacturing of patient-specific (PS) implants over the last 20 years.

AM has evolved from only being applicable to the rapid manufacturing of plastic prototypes, beginning in the late 80s, to a method for the direct manufacture of end products in many different materials including biocompatible metals. The different AM methods are continuously developing (regarding surface finish, tolerances, etc.) and so are the necessary surrounding technologies. What seems impossible, too expensive or too time consuming today could, in other words, be possible tomorrow. An example in the dental field is the introduction of cone-beam CT (computed tomography). This new way for the in-office creation of volumetric images of anatomy has reduced the cost for the patient from around $1000 for a standard CT to around $200 and thus has opened up for greater use of advanced treatment planning related to AM [2].

Customization of implants has become more and more commonly used in areas such as the maxillofacial, dental and hip areas [2-7]. A medical application that has not so far received much focus, neither in research nor commercially is PS bone plates for the osteosynthesis of fractures and ostetomies in the orthopedic field. A few studies are found in the area and in closely related areas [8-11] and, regarding commercialization, only companies offering fixation plates contoured towards PS plastic models are found for fracture fixation within the orthopedic field. This is probably due to several factors. First, the time aspect – it is assumed that the time span in prior to typical fracture fixations within the orthopedic field (often trauma cases) is too short for PS design and manufacturing. However, considering the above-mentioned development of the manufacturing methods and software, the time requirements are reducing. Further, in many trauma cases the operation has to be postponed 7 to 10 days due to damage to the soft tissue. Another question is: what are the gains in proportion to the cost and effort, including the acquisition of a CT-scan? Some examples of cases where plate customization can provide value are: for some fractures close to joints, in cases where conventional plates are difficult or time consuming to reshape to achieve a good fit and for fractures close to previously acquired deformities that make plate positioning difficult. Also, in osteoporotic areas, custom designed plates can be beneficial, including the positioning and angle of screws, and when performing minimally invasive surgery, it is a great advantage to know that the plate contour is anatomically correct.

The development of PS plates for osteosynthesis cases was the focus of the second half of the work on the thesis.

When starting these doctoral studies in 2008, the research team was quite experienced in AM of plastic prototypes including medical pre-operative models, and had just recently started to use the AM method of Electron Beam Melting (EBM) for research in medical applications. Discussions were initiated with some surgeons at the orthopaedic department at Östersund hospital, introducing the special opportunities of the technology and discussing possible applications. The literature had many examples of rapid prototyping (RP) and reversed engineering within the medical field, but not many examples of using direct AM. With this starting point, the initial research approach was kept wide in order to learn about the field and investigate different medical applications that could possibly benefit from the use of AM and specifically EBM.

The aim of the first part of the thesis work was to learn about the methods for the design and additive manufacturing (using Electron Beam Melting) of patient-specific medical implants and to find suitable applications in the area.

In *paper I,* seven different PS hip stems were manufactured using the EBM method and the focus was on the additive manufacturing approach compared to conventional manufacturing methods. In *paper II,* a PS fixation plate was designed using CT images and manufactured using the EBM method. Both were interesting applications for the further work. Using EBM for hip stem implants (*paper I)* provides possibilities both to streamline the manufacturing process and to develop implants with surface structures and material mesh structures for better longevity. Using digital design and EBM for the design and manufacturing of trauma fixation plates (*paper II*) gives the potential to offer individually adapted solutions for a specific patient and actual fracture, with pre-planned screw positions and without any need for reshaping during surgery. Gains and obstacles found in the first part of the thesis work are presented in fig. 1.

	Gains	*Obstacles*	*What to do?*
Replacement of conventional machining (CNC) to EBM for production of patient-specific hip stems	Reduced material consumption Reduced file preparation time Possibilities to reduce stress shielding	The surface of medial part has to be suitable for bone ingrowths and mechanical properties To ensure mechanical properties	Optimizing surface for this application More fatigue tests and develop a method for mechanical properties control Choosing optimal post processing methods
Additive manufacturing (AM) and digitalization for individual adaption of plates within trauma surgery	Shorten surgery time (no need for reshaping) Placement of screws in optimal position and angle. Effective pre planning in accordance with the hardware	To keep down time and cost How to perform the cooperation between engineer and orthopedist To ensure mechanical properties	Develop reliable/fast modeling -method Choosing post processing methods Develop a pre plan/design outline software for the orthopedist Develop method for mechanical properties control

Figure 1. Gains and obstacles found in the first half of the thesis work [12]

The second half of the thesis focuses on further work on the PS osteosynthesis plates. The reasons for choosing that direction was that little was done in the area, less development was required in prior to implementation, and there was an opportunity for cooperation with orthopedic surgeons, which was considered essential for performing applicable research in such an interdisciplinary area as this.

The application of non-unions, and largely displaced clavicle fractures was chosen as the subject of further studies on PS plating. Operative treatment of clavicle fractures appears to be increasing, although opinions regarding the optimal treatment are divided within the orthopedic community. It should be clarified that this thesis does not underline any treatment option over another, only intends to contribute to the development of improved possibilities when the surgeon's treatment of choice is surgery using a fixation plate. The focus is on providing more optimized, smooth and adapted solutions with the aim of both shortened surgery time, facilitation of the procedure and minimizing risks and complications.

However, the clavicle bone lies close to vital organs and the skin which makes the operative procedure difficult. Also, the clavicle bone is s-shaped with a large individual variation in curvature, torsion and inclination of articular surfaces [13]. All these factors make the fit of plate important [14] and make room for improvements to the tools used in planning operations and fracture fixation. The results from the studies may, with small adjustments, be adapted to other types of fractures for which conventional plates are not fully functional.

The aim of the second part of the thesis was to test, develop and evaluate the method for the design and Electron Beam Melting manufacturing of patient-specific clavicle plates, and to perform strength analysis and development of the patient-specific plates using finite element simulation.

In *paper III*, a method for analyzing the strength of the PS clavicle plates was developed. In the literature; only one much simplified FE model of a clavicle with plate and FE models used for injury prediction, were found. Further, the experimental biomechanical studies on clavicle plates usually used greatly simplified loading cases showing inconsistent results. Therefore, a great deal of effort was put into how to define the loading case of the clavicle more realistically than in previous work (*paper III*). In *papers IV and V,* the simulation method is used to compare different fixation plates and *paper VI* presents results from four pilot studies on the design and AM manufacturing of PS clavicle plates. In these studies, the PS-method is developed and tested. Further, in *paper VI*, stresses and displacements in PS plates are compared to those of conventional plates using the above mentioned simulation method.

2. BACKGROUND

2.1. Some orthopedic implants and treatment methods

Orthopedics as a specialty was founded by Nicolas Andry, professor of medicine, who also published the first book on basic orthopedics in 1741. At that time orthopedics was about correcting deformities in children's anatomy using bandages and prostheses. What we now call orthopedic surgery is a wide field including the treatment of fractures, joint injuries, congenital disorders etc. Due to the increasing average life span, further expansion of the use of orthopedic surgery can be expected [15].

"Orthopedic implants are man-made, medical devices, manufactured from biocompatible materials for implantation in a living biological structure. Their purpose may be to replace a missing structure or to give support to a damaged structure. The most common way of fabricating metallic implants is CAD-driven machining from wrought or cast bar stock" [12].

2.1.1 Hip stem implants

A widely used type of treatment for hip joints that don't function due to fracture or disease is total hip arthoplasty (THA), see fig. 2. In a THA both the acetabulum and femur are replaced; the method was introduced on a large scale in the 1960s by John Charnley and his technical assistant Harry Craven and is even now based on Charnley's design [16]. To fixate the stem into the femur either a bone cement is used between the implant and bone (cemented fixation) or the implant surface is prepared to enhance bone ingrowths into the medial part of the stem (cementless fixation), see fig. 2. The success rate from THA is very high, but because younger patients undergo the procedure and have higher activity levels, revision surgery has become more frequent [17] and, most people can only go through 1-3 revision surgeries. The main reason for revision surgery is aseptic loosening, which is implant loosening caused by both biological and mechanical factors. Mechanical factors include micromotion between implant and bone, and stress shielding caused by a large stiffness deviation between the implant material and bone material, as explained in *paper II*. Hence, aseptic loosening caused by mechanical factors can be counteracted by firm primary stability, lowered stiffness in the implant and even stress distribution between the implant and bone. This is the area in which AM manufactured implants can contribute through a surface structure for enhanced bone ingrowths and by using lattice structures to design the implants stiffness properties, as discussed in *paper II* [12]. Further the PS shape of the stem can provide a more even load transfer between implant and bone.

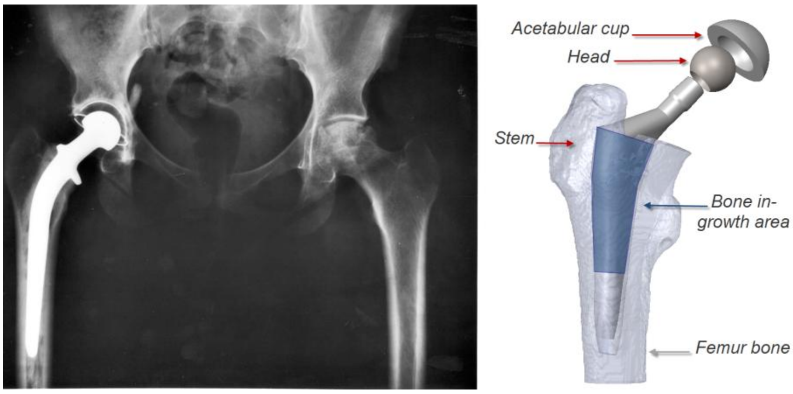

Figure 2. Left: An x-ray of a total hip replacement (THR). (*Courtesy of National Institute of Health, U.S.*). Right: The femur bone and different parts of a THR (the area for bone ingrowth is shaded in blue) [12].

2.1.2. Osteosynthesis plates and screws

Plates are devices which are used to provide fixation to fractured bone. They are differentiated by their biomechanical function and hence can have different shapes but the same function within one group. It must also be understood that the same plate can sometimes perform more than one function. One of these groups is called *protection or neutralization plates* and their purpose is to protect lag screw fixation. The *lag screw* (fig. 3c) is responsible for interfragmentary stability and the plate protects the lag screw compression in the fracture zone from torsional, bending and shearing forces in order to allow patients early movement after internal fixation.

Lag screws are used to hold bone fragments in place and are usually fastened in the direction normal to the fracture. Whenever the size and geometry of the fragments allow for lag screw fixation, the technique should be used. However, lag screw fixation cannot be positioned correctly to stabilize transverse or short oblique fractures; in these cases another group of plates called *compression plates* are used to bring stabilization and compression to the fracture. Compression is usually obtained by holes in the plate formed like inclined cylinders (fig. 3b). When the screw goes in, the plate forces the bone fragments into compression.

Another group is *buttress plates* which have the function of preventing axial deformity by shear or bending. These are firmly attached to the main fragments but don't have to be attached to the fragments they support and must correspond accurately to the shape of the bone (fig. 3d).

Bridging plates are used for badly comminuted fractures to maintain the length and alignment of the bone, leaving the fragments movable between the main fragments in order to generate union through the formation of a bridging callus rather than primary bone union. The plate is firmly fastened in the main fragments, in healthy bone, on each side of the comminuted segment.

The plating alternatives in areas where the anatomy is extremely complex are *reconstruction plates* (fig. 3a), which are designed to be able to be bent both in the long axis and short axis of the plate to enable a good contouring to the bone, and *specially designed plates*, which are primarily needed in areas close to joints to meet the biomechanical and anatomical requirements in these areas [12, 18].

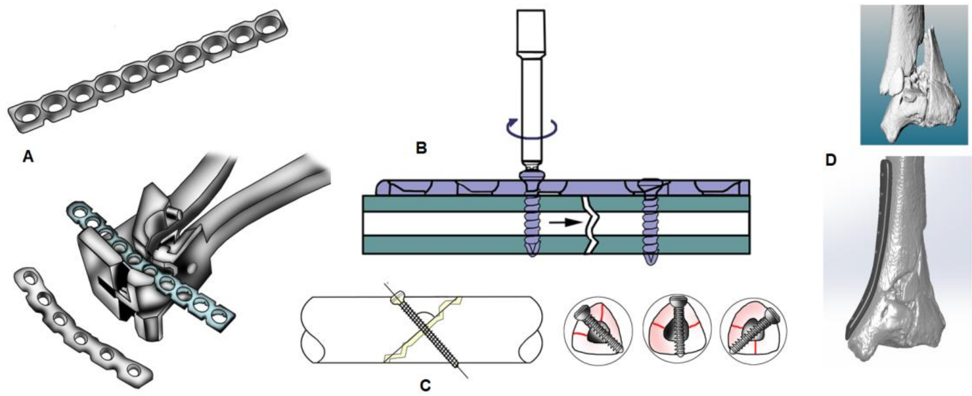

Figure 3. A) Reconstruction plate, B) Compression plate, C) Lag screw, D) Buttress plate. (*A-C from [19]*).

A common element in recent plate designs is "locking plate systems" in which the screw heads are locked by threads in the plate as well as on the screw head (fig. 4). The plate and screws work as a single construct element and all the screw/bone interfaces together make a strong union for resisting screw loosening and pullout. Some newer locking plate designs allow for variable angulations within certain limits. Using these systems, a small distance can be preserved between the bone and the plate to preserve soft tissue and circulation under the plate. Locking screws are recommended for use in osteoporotic bone and when there is a need for fixed-angle support [12, 19].

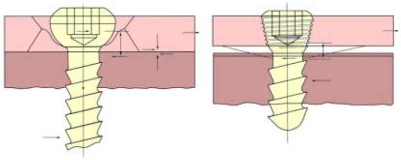

Figure 4. Left: Conventional plate screw. Right: Locked plate screw. (*From [19]*).

2.1.3. The clavicle bone

Clavicle fractures accounts for 4% of all fractures and 35-44% of all fractures of the shoulder girdle; the management of these fractures has recently evolved due to new findings about the importance of proper healing [20]. The clavicle is s-shaped with a medial anterior convexity and a lateral anterior concavity (fig. 5). The bone is narrowest approximately in the middle where the transition from convex to concave is located, and that is also the most frequent location for clavicle fractures. Further, that is an area on the clavicle bone which is not reinforced by muscles (fig. 7). The length varies proportionally with the size of the person and in a study of 150 clavicles, De Palma found a great variation both in the curvature, torsion and the inclination of the articular surfaces [13].

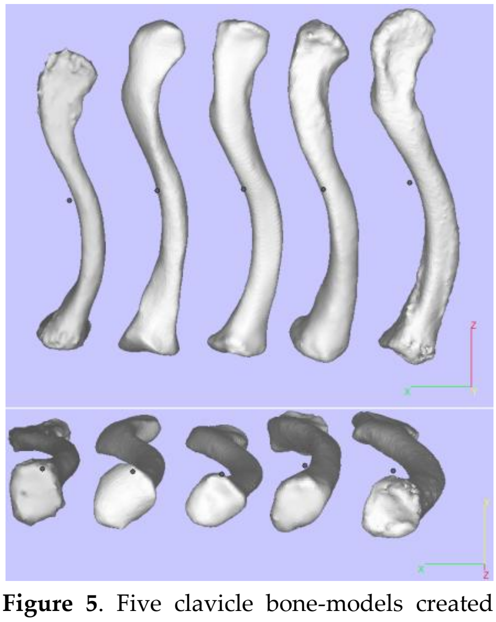

Figure 5. Five clavicle bone-models created based on patient specific CT-data, seen in top (xz) view and xy-view.

The clavicle functions as a strut that connects the arm with the trunk and is an important part of the shoulder joint, especially for providing stabilization in overhead work. It also protects underlying nerve and vascular structures. The ligaments attached to the clavicle are the coraco-clavicular ligament, (divided into conoid lig and trapezoid lig) the costo-clavicular ligament and the coraco-acromial ligament (fig. 6). The muscles attached to the clavicle are the deltoid, trapezoid, sternocleidomastoid, pectoral and subclavius muscles (fig. 7-8). The bone lies subcutaneously under the skin throughout its length and, fracture deformity hence also becomes an aesthetic issue [13, 20, 21].

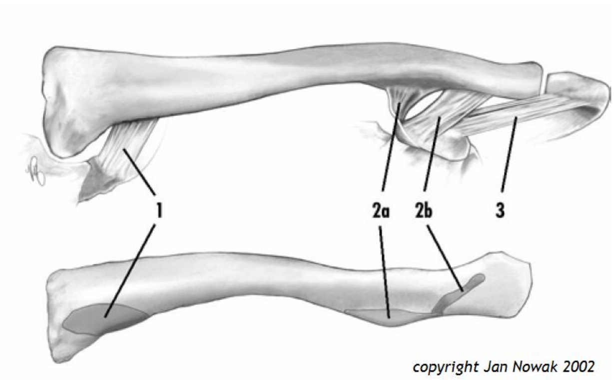

Figure 6. Ligaments attached to the clavicle:, 1=Costo-clavikular ligament, 2=Coraco-clavicular ligaments, conoid ligament (a) and trapezoid ligament (b), 3=Coraco-acromial ligament [21].

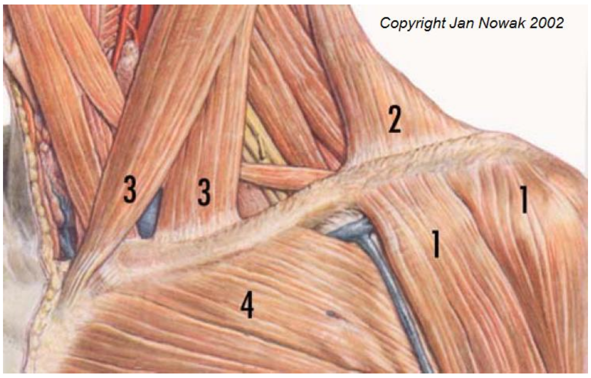

Figure 7. Muscles attached to the clavicle: 1=Deltoid m, 2=Trapezius m, 3=Sternocleidomastoid m, 4=Pectoralis major m, 5=Subclavius m (hidden) [21].

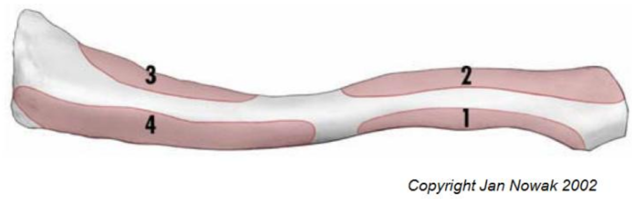

Figure 8. Muscle attachment areas on the bone seen from above (subclavius m hidden) [21].

Bone is a living material and its material properties change with age and loading. It has a greater compression than tensile stiffness and strength (due to bone mineral influence) and also an anisotropic behavior caused by microstructural organization. It is stronger and stiffer in the longitudinal direction than in the perpendicular directions [22]. There are many studies on bone properties in different types of bones, but few regarding clavicle bone properties [23].

The clavicle bone is classified as a long/tubular bone and is composed of cortical (compact) and spongy (cancellous) bone. The ratio between cortical and spongy bone differs in different parts of the bone. The cortical part is thickest in the diaphysis (midsection) of the bone while the ends of the bone are mainly built up of spongy bone material (fig. 9). The midsection is also where the most strain on the bone occurs. [22, 24].

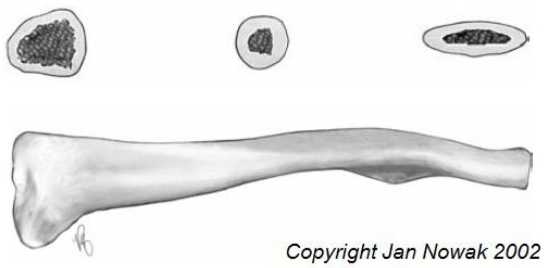

Figure 9. Light cortical and dark spongy bone material in cross-sections of the clavicle bone.

2.1.4. Treatment of clavicle fractures

Traditionally, non-operative treatment of clavicle fractures has been preferred and has shown satisfactory results [25], but cumulating evidence during recent years shows that conservative treatment (especially of mid-shaft comminuted or largely displaced fractures) leaves a great part of the patients with pain and other types of sequeale [26, 27]. These results have given rise to controversial discussions and recently there are more and more advocates for not only focusing on nonunions for operative treatment, but on the risk of nonunion with increasing age, female gender, displacement of the fracture and the presence of comminution, and also to focus on malunion, which can be responsible for pain, neurovascular symptoms ect. The variations in treatment are great between different clinics and in different countries [20]. What the optimum treatment is for these types of fractures is still under investigation.

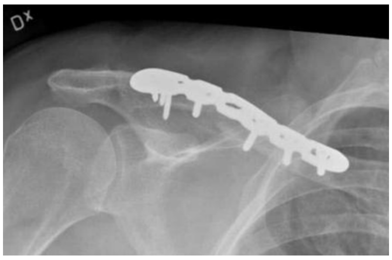

Figure 10. A clavicle fracture fixated with plate.

For the operative treatment of clavicular fractures, plating (fig. 10) and intramedullary nailing are two different options. Intramedullary devices are metal pins that are placed into the medullary cavity of the bone to provide stability. This is less invasive than plating but is not suitable when rotational stiffness is required [28, 29] and some reports show significant problems with pin migration [20]. Plating of fresh clavicular fractures also shows different outcomes in different clinical studies, but is preferred by many surgeons and in the cases of nonunion plating it seems to continue to be the treatment of choice [20]. Due to the clavicle bones s-shape and subcutaneous location (right under the skin) the contour of the plate is important; either a straight reconstruction plate can be used and reshaped during the operation to follow the bone contour, or an anatomically shaped plate can be used. Anatomically shaped plates are designed to have the shape of an average clavicle, but since the clavicle anatomy has great individual variation they often don’t fit well. In a study of 100 patients, Huang et al. (2007) found that the pre contoured plates had a poor fit on 38% of the female clavicles [30].

2.2. Additive Manufacturing

Additive Manufacturing (AM), three-dimensional printing and rapid prototyping all refers to a group of technologies in which components are fabricated directly from computer models, built up in an additive approach by curing, depositing or consolidating thin layers of material to build up the component [1]. Each layer is built up from the cross-sectional geometry of a 3D computer model of the component. The freeform nature of AM removes many of the traditional constraints that controlled component design in traditional manufacturing like plastic injection molding or machining. By building parts layer-wise, very complex geometries can be manufactured, for example engineered lattice structures, internal channels and highly organic forms, and with some AM techniques it is even possible to produce complete assemblies including moving parts in a single build operation, see fig. 11. When designing for AM, challenges include learning the constraints that different AM technologies bring to the manufacturing, including preferred build directions, tolerances and minimum wall thickness. Further, the designers have to “unlearn” many previous manufacturing rules in order to fully benefit from the new freedom of design that comes with AM technology [2]. AM methods started to develop in the late 1980s with a technology called stereolitography and initially the technologies were only suitable for quick product visualization, but in the past decade they have evolved to a fundamentally new method for part manufacturing [1].

Figure 11. Examples of parts manufactured with AM.

The most common use of AM technology in 2012 was for direct part production and functional models. Regarding industrial use, in 2012 the medical/dental applications was the third largest sector after consumer products/electronics and motor vehicles [2]. AM is suitable for medical applications since those often have low production rates and high complexity in the geometry due to organic shapes. Also the lattice structures are interesting for medical applications as scaffolds for orthopedic tissue repair and for the design of implants with a stiffness closer to the bone’s properties. Access to medical-imaging technology used as basis for the preparation of medical models and design of implants, the use of virtual surgical planning tools and the direct metal AM fabrication for surgical implants and instruments are all increasing [2].

There are many different AM processes available for manufacturing parts in different materials, all using computer models as basis and building up the parts layer-wise. In January 2012 the ASTM International Committee F42 on Additive Manufacturing Technologies took a decision on a list for current AM process categorization. According to that list, the processes applied in this thesis are

powder bed fusion for the direct metal fabrication of implants, and ***material extrusion*** and ***material jetting*** for the manufacturing of pre-operative plastic models [2]. The technologies used are further described in the following chapters.

Different AM technologies use different support materials during the builds. This can be the same type of material as in the build, but designed in thin lattice structures and removed manually after the build, or it could be other types of materials that are removed by dissolving them in a bath of water or chemicals, for example. The purpose of support materials is to support structures, keep parts away from each other in assemblies and to lead away heat from parts of the design when needed.

2.2.1. Electron Beam Melting – a powder bed fusion technology

The powder bed fusion technology fuses selected regions of a powder bed using thermal energy. In the EBM process (by Arcam AB) the energy source is an electron beam and the process is described by the author in [12] as follows, see also fig. 12:

> "The electron beam (3) is formed by electrons emitted from a tungsten filament (1) and accelerated in a high voltage difference in the electron beam gun (2). The beam (3) is focused using two magnetic fields (4, 5) and welds consecutive layers of powder. When one layer is finished a new layer of powder is raked over the build by a movable rake (7) and the powder layer is pre-heated by the beam before it is melted to the geometry from the computer aided design (CAD) file. The powder containers (6) store powder to last for the whole build. The process takes place under vacuum with a Helium atmosphere ($2\cdot10^{-3}$mbar) and the build temperature is kept above ~700°C throughout the build to prevent stresses induced by temperature gradients" [12].

After the build is finished, the parts are left in the machine to cool down for some hours and then excess powder is removed and recycled using a special blast chamber called powder recovery system (PRS).

The layer thickness is typically between 0.05-0.2 mm and the surface structure of the EBM manufactured parts is slightly rough, with a typical R_a value between 10-50 µm. It derives primarily from the fact that the parts are built up surrounded by powder resulting in powder grains becoming attached to the surface during the melt. Also, the layer-wise approach affects the surface structure. Hence, for some applications dependent on "fine surface finish", post-processing like grinding and polishing is needed.

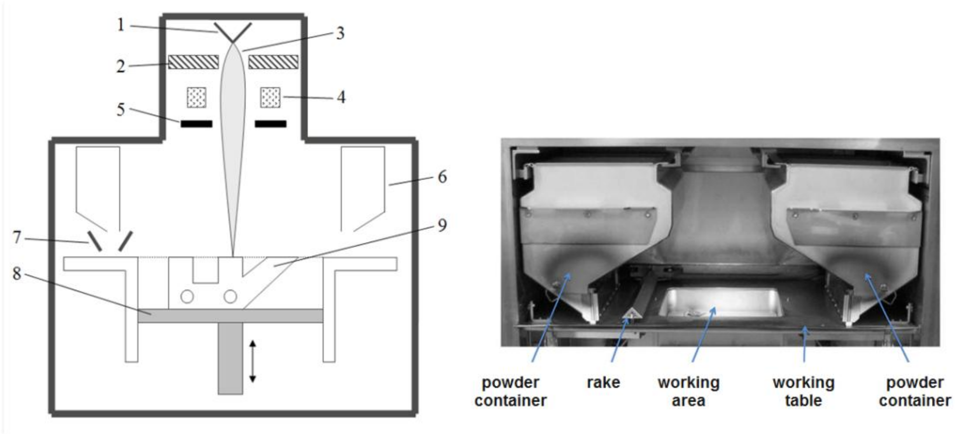

Figure 12. A schematic picture of the EBM process from [31] and a picture from inside the build area of the EBM machine.

The material used for medical applications is a Ti6Al4V ELI (grade 23) which is biocompatible and has a particle size between 45-100 μm.

Many studies have investigated material processed using the EBM method and has been shown to have adequate properties in the same range as conventionally manufactured materials, both in terms of mechanical and chemical properties [32-35] and biological response in bone [36]. Due to gas residues left in the powder granules from the powder manufacturing, the EBM processed material can contain some porosity [34, 37] and hot isostatic pressing (HIP) is recommended for use in fatigue-sensitive applications.

2.2.2. Material extrusion and material jetting

The plastic pre-operative models in the thesis are manufactured using two different AM technologies, material extrusion and material jetting. For the process of material extrusion, the material is melted and forced through a nozzle as the extrusion head or the build platform is moving in the x-y plane. When one layer is finished, the build platform moves down, or the extrusion head moves up one layer thickness. The material used is typically a filament of thermoplastic coiled onto a spool. The machine used for material extrusion is a fused deposition modeling (FDM) machine called "uPrint SE plus" (Stratasys Inc, USA) using an ABS+ material.

The material jetting process uses inkjet-printing heads with one or several nozzles to deposit droplets of build material on the build plate. The print head moves across the area and dispenses the droplets according to the layers in the computer model. The use of several nozzles enables the printing of multi-material and graded material parts. It also speeds up the process. The machine used for the material jetting is a Eden 260V (Stratasys Inc, USA) and "FullCure 835, VeroWhitePlus" was used as build material [2].

2.3. Simulation methods

2.3.1 Finite element analysis

The finite element method (FEM) was originally developed to solve complex problems in structural mechanics, but is today used for many different problems like heat transfer, fluid flow, electric fields, etc. The idea of the method is to subdivide a structure into small parts (elements), each with simple geometry and hence much easier to analyze than the original structure. The elements are connected to each other in points called nodes. That way, in a series of many simple calculations, solutions can be found for large complex structures more or less approximated, depending on the grade of simplification in the FE-model.

The FEM problem (for multiple elements) is formulated as:

$[K]\ d = f$, where $[K]$ is the stiffness matrix, d is the vector describing nodal displacements and f is the vector describing nodal forces and external forces. The relation between the known nodal forces and the unknown nodal displacements is defined by the element stiffness matrix $[K]$ which holds information about the geometry and material properties of the elements.

Important input values for FE-models, determining the accuracy of the model, therefore include: material properties of the different parts of the structure, boundary conditions, external loads on the structure, how accurately the mesh is defined and what type of elements are used. There are many ways to define the elements depending on the geometry and loading of the structure, ranging from simple one-dimensional line elements, to three-dimensional solid elements. The type of elements suitable for genuine 3-dimensional problems is the three-dimensional solid elements. Different types of solid elements are wedge, brick and tetrahedral elements. Tetrahedral elements have a good geometrical adaptability and are suitable for automatic mesh generation, while wedge and brick elements better suit manual meshing [38]. The simplest tetrahedral element has one node in each corner called a 4-node tetrahedral element. A more suitable element for stress calculations is the 10-node tetrahedral (4 corner and 6 side nodes) [38, 39].

2.3.2 Multibody musculoskeletal simulation

A musculoskeletal model is a model of the musculoskeletal system, usually defining the bones as rigid bodies constrained by joints with muscles acting as force and movement generators, that are used to analyze athletic performance, estimate musculoskeletal loads, metabolism, neuromuscular coordination etc. The software used in this thesis is the AnyBody modeling system (AnyBody Technology) which is also the one described in this chapter. Other musculoskeletal modeling systems, similar to AnyBody are SIMM/FIT (Musculographics Inc) and BRG.LifeModeler (Biomechanics Research Group, Inc) [40].

Since the human musculoskeletal system is mechanically very complex, computer models describing it have to be highly simplified in order to be efficient. Usually it is assumed to be a rigid-body system (no body deformation under the action of applied forces) allowing for the use of standard methods of multibody dynamics. Another assumption in the model is how the muscles are activated to generate a certain movement. In reality they are activated by mechanisms in the central nervous system which are not understood well enough for detailed modeling. Typically some kind of optimization is used for this assumption, and in the AnyBody modeling system the muscle forces are calculated using optimization for minimum fatigue by evenly spreading the loads over the muscles involved.

Simulation of bone-implant systems including muscle and ligament forces from musculoskeletal modeling is difficult to validate due to the difficulty of creating an experimental setup for the validation. Muscle forces cannot be measured accurately which makes the validation of the musculoskeletal models difficult. This is a problem but it also gives the models a special importance, since they might be the only way to estimate information such as the internal forces in the body [40]. An attempt to validate a musculoskeletal model of the shoulder joint in experimental setups is presented in [41] and the experimental results used as reference in that study are presented in [42].

Inverse dynamics is used in the AnyBody musculoskeletal model. This means that the muscle activation is computed based on a motion, in opposite to forward dynamics that computes the motion based on predicted muscle activation [40].

The dynamic equilibrium equation is on the form:

Cf=d, where f = $[f^{(R)}, f^{(M)}]$, $f_i^{(M)} \geq 0$, $i \in \{1,.., n^{(M)}\}$

Where f= internal forces, d= applied forces, $f^{(R)}$=joint reactions, $f^{(M)}$=muscle forces. C= the coefficient-matrix for the unknown forces.

The solution is formulated as an optimization problem on the form:

Minimize $G(f^{(M)})$,
Subject to Cf=d,
$f_i^{(M)} \geq 0$, $I \in \{1,.., n^{(M)}\}$

The objective function $G(f^{(M)})$ decides how the muscles are recruited and is also called the muscle recruitment criterion. It can be formulated in different ways, for more details refer to Damsgaard et al. [40].

Simply explained: the model is built up of rigid segments (containing mass and inertia properties of the bone, muscles, fat, etc.) connected by friction free joints. Muscles and ligaments, without mass, create forces at origins and insertions on the bones. One muscle can be described by several points to address the whole muscle attachment surface. Inputs into the model are movement and external forces and outputs are muscle forces and joint reaction forces.

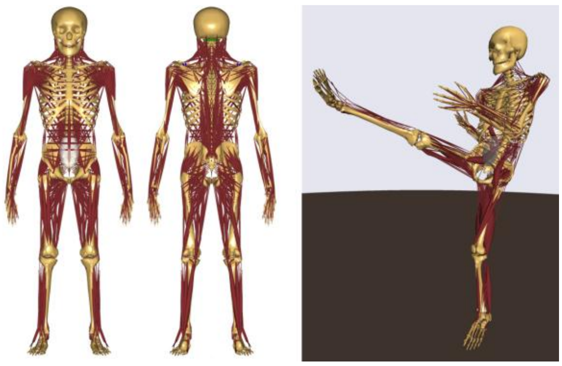

Figure 14. Multibody musculoskeletal manikins from the AnyBody software.

To simulate the muscle and ligament forces acting on a certain bone using the AnyBody modeling system, a 3D model of the bone is imported into the system, oriented and scaled to fit the model and subjected to multibody musculoskeletal analysis in the desired body position (or movement). One output file-format available from the AnyBody modeling system (containing the resulting muscle forces and joint reactions) is the Extensible Markup Language (XML) format, which was the one used in this thesis. More details about the combination of the musculoskeletal forces and the FE-simulations are found in the methods chapter, under 3.2.2.

3. METHODS

Due to the broad initial research aim and the need to gain an understanding of several new areas and technologies, the two initial studies (*papers I and II*) were built on practical cases, including the performance of the different parts of the production chain, from CT-scan to final implant, with the first focusing on the EBM manufacturing and the second on the whole production chain.

In *paper I,* a batch of seven PS hip stems were manufactured, both with EMB technology and with conventional machining, in cooperation with a company (hereafter called CC) providing customized hip stems manufactured in titanium using CNC-machining. The PS hip stems were designed by the CC for a good fit into the femur and also to correct anomalies in the patient's anatomy; fig. 15 shows the studied batch of implants.

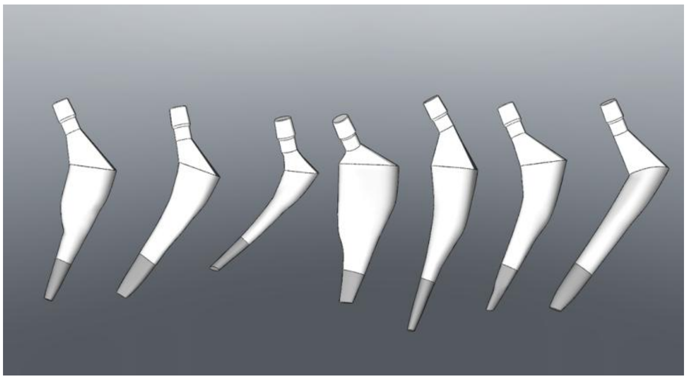

Figure 15. An ordinary batch of seven customized hip stems, designed by the CC.

The two methods were compared according to the cost of: the material, time for preparing the manufacturing files and manufacturing. A complete time and cost breakdown was only available for the EBM manufactured implants due to the confidentiality policy of the CC.

Uncemented fixation is used for the PS stems and the CC uses titanium powder sputtering and hydroxyapatite coating on the medial part of the stem to enhance bone ingrowth. Earlier studies have shown that the EBM manufactured material enhance osseointegration [43-45] and it was assumed that by further development, a decent surface for the bone ingrowth area could be directly manufactured with the EBM method, leaving out the need for powder sputtering. The comparisons were therefore made under the assumption that a functional surface can be developed, both in terms of bone ingrowth and mechanical properties. Initial studies on the coarse surface structure´s impact on the fatigue properties were performed, using coarse and post processed test-bars. The cone part (circular part at the top) was machined by a turning operation and the rest of the stem, excluding the bone ingrowth area in the middle (fig. 2) were manually grinded and polished, to reach the same tolerances as the CC stems.

The study in *paper II* not only focused on the manufacturing but in addition involved the part of the production chain from CT-scan to 3D computer model for use in AM. This study is more similar to the rest of the case studies in the thesis and the method used is included in the following presentation.

The initial literature study and the results from the two initial studies (*papers I and II*) formed the basis of the methodology outline for use in the continuing studies of PS clavicle osteosyntesis plates. This includes the following actions (see also fig. 16):

1. Digitalization of fracture (and mirrored non-fractured bone)
    a. Acquisition of CT-scan
    b. Creating 3D model of fractured bone
    c. Digital reduction of fracture
2. Modeling of patient-specific bone plate
    a. Modeling strategies
    b. Strength analysis of patient-specific plates
    c. Reversed engineering used to reproduce the geometry of the commercial comparing plates used in the FE-study.
3. Additive manufacturing
4. Post processing, cleaning and sterilization
5. Initial evaluation of the method

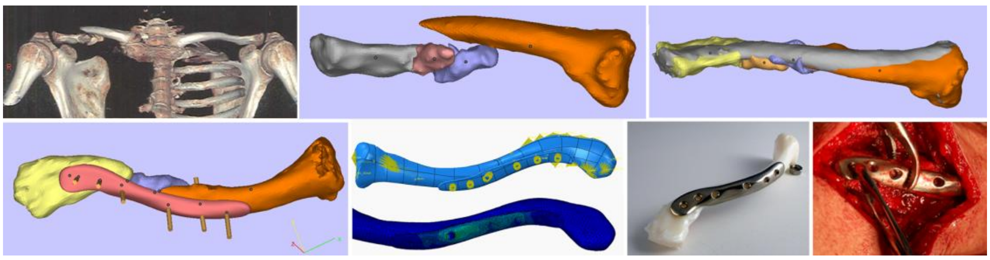

Figure 16. Parts of the method used: CT-scan, 3D model of fracture, digital reduction of fracture, PS-plate design, strength analysis, AM manufactured and post-processed plate, test-fit in surgery.

Four gradually refined case studies, including actions 1 to 5, have been performed on clavicle fractures in cooperation with an orthopedic surgeon at the orthopedic department of Östersund hospital in order to develop and initially evaluate the PS-plate method (*Paper VI*). Actions 2b and 2c, regarding strength analysis, were performed in parallel with the case studies and were not included in each individual case.

It was important to get insight into how the plates are used, how the orthopedic surgeons work and the challenges in their work, therefore observation during some operations were part of the second half of the thesis work.

3.1. Digitalization of fracture

Prior to the development of PS medical devices using AM, accurate three-dimensional digital representation of the anatomy has to be acquired. In this thesis work, the materialise software (Materialise, Belgium) has been used for that purpose.

First, volumetric data of the relevant anatomy has to be acquired. Two medical imaging techniques used in that aspect are magnetic resonance imaging (MRI) and CT. CT shows better contrast between bone and soft tissue and thus is the technique used for medical imaging of bone. The output from a CT scan is a large series of 2D slices of data, which together represent the 3D geometry. The representation of the geometry can be made more or less exact by varying the slice thickness and resolution. The format of the images follows the medical industry standard, called DICOM (digital imaging and communications in medicine). The soft tissue was removed from the CT data using a threshold segmentation technique in which pixels are distinguished within the images by their grey scale values, also known as Hounsfield units, where the highest number represents the densest bone. That can either be done by the radiotherapist or afterwards by the engineer using suitable software. For better efficiency, in these cases the (DICOM) images were segmented by the radiotherapist and in some cases a refined segmentation was made at the university.

The segmented bone parts were then modeled into 3D models using the Mimics software (fig. 17). Further in many cases the 3D models were smoothed and in some cases cavities resulting from imprecise segmentation or bad bone quality were closed using the same software. The files were saved in the stereolitography (STL) format. In the STL file format the surface contours are described by triangular elements; the STL file format is widely used as basis for AM. Depending on the purpose of the model: FE-analysis, basis for implant modeling or basis for AM of a pre-operative plastic bone model, the original STL-files could be used or needed to be further refined.

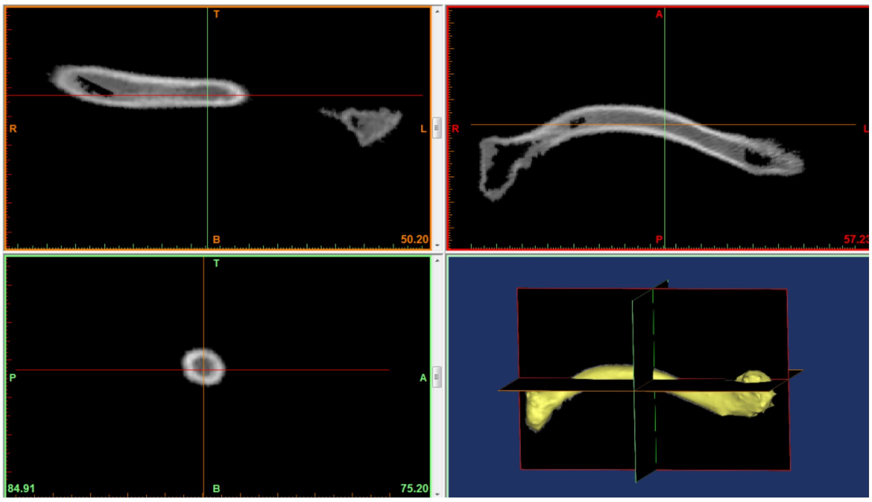

Figure 17. CT-images imported into the Mimics (Materialise) software showing gray scale values in different cross- sections of a clavicle, and down to the right a 3D reconstruction of the bone.

In order to design an osteosynthesis plate to fit the actual fracture, the bone model usually has to be digitally reduced, in other words, the bone fractions moved closer to their original position, according to the reduction performed in the surgical procedure. For that purpose, bone fractions touching each other, (and therefore becomes joined in the computer model), first had to be separated from each other. In *paper II* different ways of separating bone fractions and moving them to the correct positions are described. In *paper VI* the radiotherapist created separate data sets for the different fractions. Hence a separate 3D STL model could be created for each fragment, the fragments imported into the same file and then moved into the desired positions (fig. 16).

3.2. Modeling and analyzing patient-specific bone plates

3.2.1. Plate modeling strategies

The above described 3D STL-representation of the bone is the basis for modeling the PS plate. In *paper II*, some different modeling techniques are compared to each other: surface modeling using Rhinoceros (by Mc Neal), solid modeling using Solid

Works (by Dassault Systemes) and a technique specially developed for implant/ plate modeling on anatomy using a software called 3-Matic (by Materialise). All three have their own advantages and drawbacks. As described in *paper VI*:

> “There are two primary aims when modeling a customized plate. The first is to create a plate that follows the bone contour smoothly without any need for reshaping during surgery. The second is to design the plate (including the screw holes) for optimal fixation of the actual fracture. The preconditions for how to do this are dependent on the fracture and how it will be reduced during the surgery”.

For bones with bilateral symmetry in the body (for example the clavicle) there is the opportunity to use both the fractured reduced- and the opposite non-fractured bone as basis for plate modeling. Using the non-fractured bone is easiest in terms of modeling technique since there is a smooth surface to use as basis without any fracture edges to bridge. In such cases the fractured reduced bone can be imported into the same file as the mirrored one (fig. 16) to be used when deciding screw positions and other design details. This approach is applicable when the reduction can be performed so that the reduced bone model has a shape which is close to the original bone and hence also to the mirrored non-fractured bone. In these cases surface modelling technique is suitable. The plate is modelled by creating a smooth surface that follows the bone contour. The plate contour is drawn on the surface, trimmed and given an appropriate plate thickness (fig. 18). This was the approach in cases 1-3 in *paper VI* for which the Rhinoceros software was used.

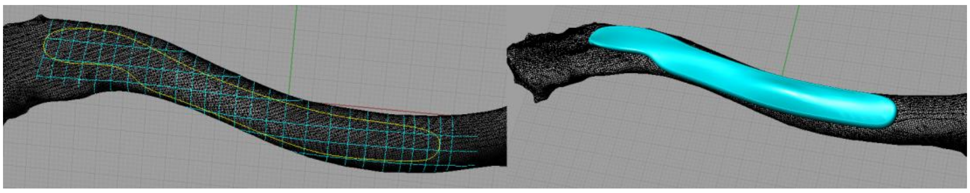

Figure 18. Left: A mesh projected on the bone surface to create a matching surface and the contour of the plate. Right: The trimmed surface with thickness forming the PS-plate.

For more severe fractures which do not allow bilateral symmetry in the reduction, the plate has to be modeled based on the digitally reduced bone model to follow its curvature. This can be the case when an osteotomy has to be done or when there is an earlier obtained deformity which the plate contour and shape has to match. The fracture edges on the surface of a reduced bone model complicate the modelling. In the fourth case in *paper VI* a solid modeling approach was assumed to be more efficient due to a complicated reduced fracture, including an osteotomy.

In this case, the plate was designed by drawing six cross-sectional sketches of the plate shape based on the bone geometry and connecting these using a loft command (Solid Works) (fig. 19). One problem was that the STL-mesh of the bone could only be imported as a visual reference in Solid Works, to which it is not possible to connect the cross-sectional sketches. Therefore, the STL-meshes of the fractured bone parts were converted into solid computer aided design (CAD) models using RhinoResurf (Rhinoceros, Mc Neal), imported into the same file and reduced according to the surgeons guidelines to form the basis for the plate modeling.

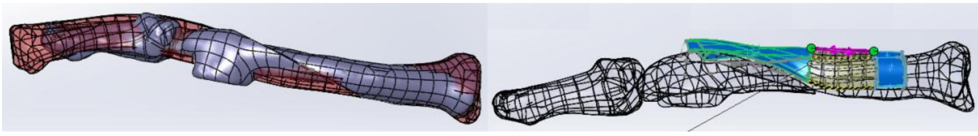

Figure 19. Left: The reduced bone model including the mirrored bone. Right: the start of the loft modeling of a PS-plate.

3.2.2. Finite element analysis on the clavicle with fixation plate

The finite element method was used in *papers III – VI* to perform comparative stress and displacement analysis on different clavicle bone plates- and fixation methods. The FE solver Abaqus (Dassault Systemes) was used for all analyses in the thesis. Preparations for the FE calculations included; 1) creation of finite element mesh from the STL-mesh of the clavicle bone, 2) definition of boundary conditions and external forces to be applied on the system, 3) modeling of different type of plates and 4) defining the material properties for the bone and the plates.

It was soon realized that points 1, 2 and 4 are very dependent on each other and need to be dealt with in that context. There is a lack of data in the literature, about the material properties of the clavicle bone. Even for bones with material properties that are more commonly studied, like the tibia or the femur, the results from cortical bone property studies differs greatly [46].

When, as in this case, the FE-analysis is based on real bone geometry obtained from a CT scan, it is possible to use the CT image density information (the gray scale values), (fig. 17) to translate to PS material properties of the bone, which has shown the potential to entail better results in a study by Li et al [47]. Initially, that approach was regarded as an option.

Further, data about definitions of the loads and boundary conditions on the clavicle bone were also difficult to find in the literature. Few previous FE-studies of clavicles were found, and they mainly focused on injury prediction in traffic accidents. One FE model including a clavicle with bone plate, but without screws, and with a simplified loading case was found [48]. Regarding the results of earlier biomechanical clavicle plate studies, also simplified loading cases like axial compression or cantilever bending were used and there seemed to be an inconsistency in the results probably due to the differences in test modes. Hence it was decided to primarily focus on the loading case, by combining multibody musculoskeletal simulation with FE analysis, taking a step closer to a more realistic simulation, as described in *paper III.* Using multibody musculoskeletal simulation, the loads are simulated on a muscle and ligament level. The simulations were based on the eating motion, more precisely the static position when holding a weight of 0.5 kg, in front of the mouth with the elbow away from the body, simulating an arm position allowed during the early rehabilitation (before no healing has occurred), see fig. 22.

In order to import material properties based on the CT-density into the FE-solver, the bone model must not be scaled or re-orientated. To be able to perform the simulation using the AnyBody modeling system, the bone model has to be re-oriented and slightly scaled. Hence, the decision was to focus on realistic loading and a simplified material definition.

The cortical bone is anisotropic, being stronger and stiffer in the longitudinal direction than in the perpendicular directions [22]. For the definition of the cortical material property in the calculations a reference was chosen, defining the cortical bone as an anisotropic material with a Young's modulus of 18 GPa in the longitudinal direction and 8 GPa in the transversal direction [49].

Another question about the definition of the bone's material property was whether the bone should be split into a cortical and a spongy part or not. In the first model the spongy part of the bone was removed from the bone mesh leaving a cavity inside the cortical part of the bone. The separation complicated the modeling a lot. It was assumed that the inner part of the bone did not have much influence on the stresses and displacements in the plate, which was the main focus. Therefore, a number of different models comparing the plate stresses and displacements on bones with and without cavity for the spongious part and with different material definitions for the cortical part were performed in *papers III and IV*, finally resulting in a simplified solid model of the bone with cortical material properties throughout the whole structure. Also, in *paper IV*, a sensitivity analysis was performed, on different ways to define the muscle attachment surfaces.

The procedure for combining the FE-model with the multibody musculoskeletal load case is graphically presented in fig. 5 in *paper III*, starting with converting the STL-mesh of the bone and the XML-file from the multibody musculoskeletal simulation, into one input file to the FE solver. That procedure results in an FE-model containing a mesh representation of the bone; in Abaqus a so called, "orphan mesh". In such a model the bone cannot be modified or remeshed, and so the whole procedure has to be performed from the beginning to analyze each plate that requires new screw holes in the bone. Another problem with the orphan mesh was that when refining the mesh to be of FE-analysis quality, the surfaces become somewhat modified and the screw hole surfaces became too uneven to be constrained towards the cylindrical screw surfaces, in the FE-model, see fig. 20.

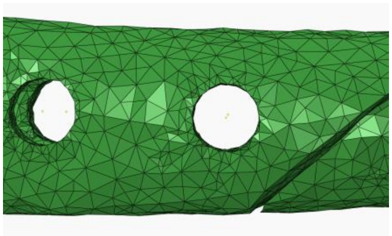

Figure 20. Orphan mesh.

To make the model more functional for the comparison of stress analyses between different types of plate designs, the bone mesh was converted into a solid CAD model using RhinoResurf (in *papers IV-V*). The solid model was imported into the FE model which contains the muscle and ligament forces which are coupled to selected areas of the orphan mesh, representing the muscle and ligament attachment areas. Together, the muscles and ligaments are represented by 15 coupled points, each with an x, y and z force component, resulting in a total of 45 concentrated forces. The solid bone model was oriented in the same position as the orphan mesh which was later used as a starting model in the analyses of the different plate designs (fig. 21). Boolean operations were used in the Abaqus software to create the different screw-hole configurations in the bone depending on each type of plate. Then the solid bone was meshed and the muscle and ligament attachment areas were redefined on the new mesh.

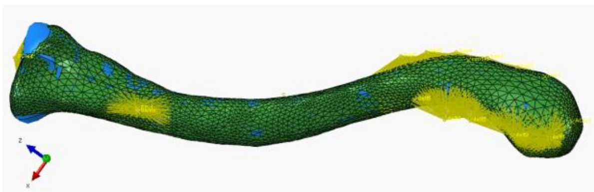

Figure 21. The FE starting model including the green orphan mesh, the blue solid bone model and the concentrated forces coupled to the mesh describing the muscle and ligament forces and reactions.

This meant that only the procedure described by red arrows in fig. 22 had to be performed in order to analyze different plates and plating methods under the same loading conditions. Possibly there is a commercial solution to this problem, (for another FE-software) that was found in the latter part of the thesis work and has not been tried out during this work [50].

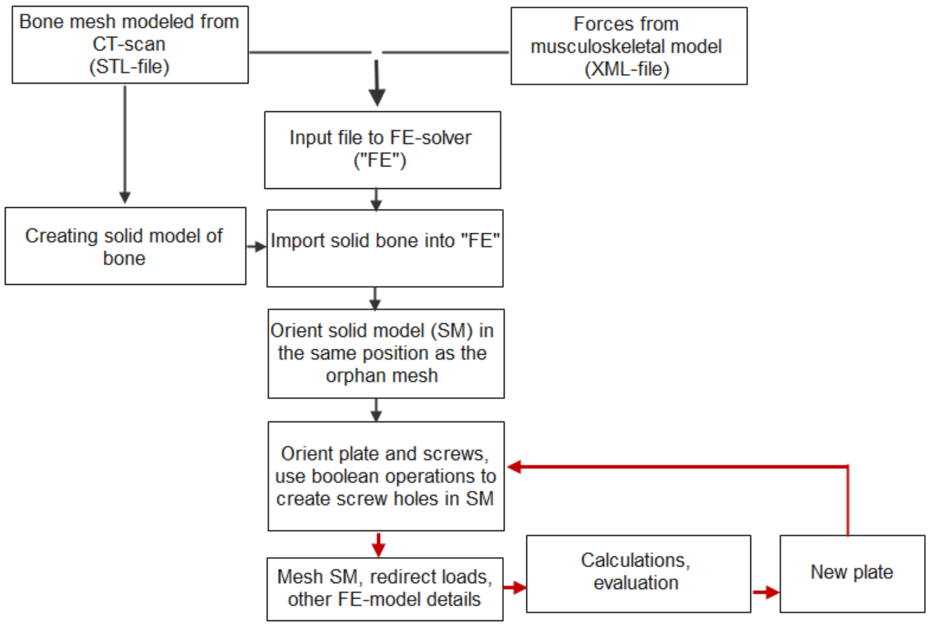

Figure 22. The workflow of combining musculoskeletal forces with the FE-model and how it was shortened (red arrows) by converting the bone mesh into a solid CAD-model.

The plates used in the FE-analyses are modeled as described in chapter 3.2.1, except for the commercial plates used as references in the study. Two different commercial plates are included in the study. One "LCP Reco-Plate 3.5 straight, 6 holes" (DePuy Synthes) which is a straight reconstruction plate with notches along the plate for contouring during the surgery. Reverse engineering was used in order to digitalize a straight LCP Reco-plate. A FARO Titanium measurement arm with laser scanner was used to scan the plate and CAD software, Solid Works and Rhinoceros were used to model the plates based on the laser-scan (described in *paper III*). The CAD model was later bent and twisted in the Solid Works software to fit the contour of the bone model in two different plate positions: superior, which is on top of the bone, and anterior, which refers to a placement more in the front of the bone. These are two different plating techniques currently used for clavicle plating. The second commercial reference plate in the study was a "LCP

Sup-Ant Clavicle Plate 3.5, 7 holes" (DePuy Synthes) which is a pre-contoured plate, designed to fit an average clavicle, having a placement starting medially somewhat in the anterior position and ending in a more superior position. The LCP Sup-Ant is considered to be a secure plate as regards the strength of clavicle fixation, and was hence considered to be a good reference for comparison with the PS plates. This plate was also digitalized using scanning and CAD modeling. The FE model with a PS plate can be seen in fig. 23. For the force magnitudes in each muscle and ligament and other FE model details, see *papers III-IV*. The model was used to compare the stresses and displacements in three different customized plates with those of the commercial plates and to analyze the commercial plates in different positions and with and without the use of a lag screw to fixate the fracture.

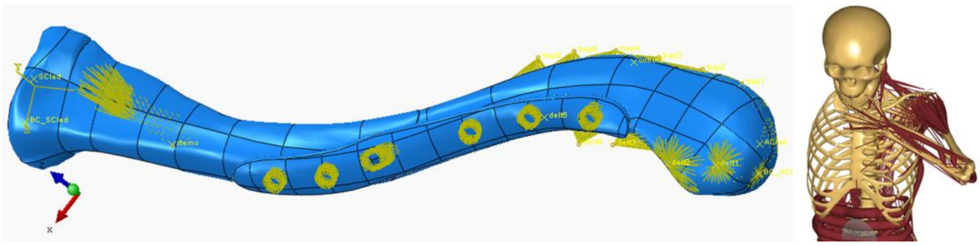

Figure 23. Left: The FE-model with a patient-specific plate. Right: The arm position in the musculoskeletal model.

3.3. Additive Manufacturing

The first study in this thesis has the greatest focus on the actual additive manufacturing process in which the EBM-method is compared to conventional machining for the manufacturing of PS hip stems (*paper I*). The times used for the file preparation, EBM manufacturing and different parts of the post-processing were taken, and the amount of wasted material in the EBM manufacturing was measured. This chapter primarily presents the use of AM for manufacturing the plates and pre-operative models in the case studies on PS clavicle plating (and tibia plating) from *papers II and VI*.

The five (including the tibia-plate) case studies on PS plates all ended with additively manufactured prototypes or final products for the plates. By taking the studies all the way to a prototype or end product, important design details that would have been missed with a more theoretical approach were discovered. Practical performance was seen as an important part of the work, according to the discussion in chapter 2.2 about the possibilities and constraints of AM and, in this case, the EBM method. Examples of such details are: how can the desired screw hole pattern (including screw angles) be efficiently manufactured with EBM and post-processing? Is it important to model the plate radii correctly in the CAD-model? And how to make the threading in the plate holes in order to use a locking screw attachment?

After the digital models of the plates were finished and saved in the STL format, these files were prepared for manufacturing with EBM technology (by Arcam AB) using Magic's software (Materialise) and ARCAM´s build assembler software. The plates were oriented on the start plate according to fig. 24 a and b, to keep down manufacturing time and the need for support materials.

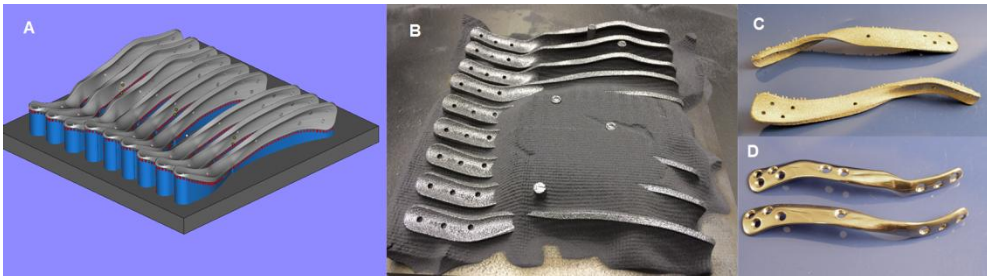

Figure 24. A) Preparation file for EBM manufacturing. Support materials in blue. B) Manufactured plates before excess powder is removed. C and D) Plates before and after post processing.

After the EBM build was finished, excess powder was removed (sifted and later reused) in the PRS and finally the support materials were manually removed.

Manufacturing time is primarily determined by the number of layers in the build (the height). The time used for the manufacturing (excluding machine preparations, cooling the system and recycling unused powder) of several bone plates in a single build was around five hours and was only slightly lengthened by the increased number of plates when having approximately the same height, as discussed in *paper II*. The total EBM time including machine preparations etc., was around ten hours both in *papers II and VI*.

The EBM process has in earlier work shown to be suitable for the manufacturing of medical implants: In Europe, orthopedic implants from the EBM technology have been used since 2007 and about 20 000 implants have been implanted in patients. Two European companies and one American company have gotten their EBM manufactured implants certified for serial production. Earlier successful operations with PS, EBM manufactured implants are presented in [3, 51].

3.4. Post-processing, cleaning and sterilization

The EBM manufacturing approach of building up the parts layer-wise and melting the material surrounded by powder, results in a slightly rough surface with an R_a value that is typically 10 -50 µm. The rough surface can be preferable for some implants or parts of implants for which enhanced bone ingrowth is desirable, as discussed in *paper I*. In some cases it doesn't matter whether the surface is smooth or rough but for the fixation plates it is preferable to have a smooth surface that counteracts tissue adhesion, in case the plate has to be removed later on. Hence, post processing including grinding and polishing of the plate surfaces and also completion of the details for the screw holes was done afterwards.

In the modeling phase, guide holes with a diameter of 2 mm were created, showing the position and angle of the screw holes. These were used as guides while drilling the holes. The size of the holes was chosen to be big enough to be used as guides and small enough to make sure that all surface roughness porosity was removed. More work regarding these details is needed as well as for the most feasible way of threading holes for locking screws, how to design the countersinks and how much freedom of screw angle variation is needed.

Cleaning and sterilization of the plates were performed at the Östersund hospital. The plates were washed in a washer-disinfector using Suma Med Super LPH (SealedAir Corp, USA), for 60 minutes in 90°C, and then packed in sterile bags followed by standard steam-sterilizing for 60 minutes.

3.5. Initial evaluation of the method

3.5.1. Test cases

The method described above was initially evaluated by trying out the fit of the plates in four operation cases, presented in *paper VI*. These cases also brought important input to the continuous development of the method. The trials were performed in cooperation with one orthopedic specialist at the hospital of Östersund. In the first three cases the PS plates were test fitted during ordinary operations and then replaced by commercial plates. In two of these cases, plastic AM models of the bone were used as support when contouring the commercial plate. The fourth case was a complicated fracture for which the surgeon's assessment was that no conventional method and fixation devices would be functional. Therefore the PS method was used to offer a more adapted plate and to support the surgeon, in the preplanning and performance of the surgery.

Conventional plates were also available in the operating room for the surgeon's freedom of choice. All patients were informed about the trials and gave their consent.

3.5.2. Surgical planning and interaction between surgeon and engineer

To be able to advance in this interdisciplinary area comprising both engineering and medical competence, functional methods for cooperation are important. The orthopedic surgeon, who is the medical expert and responsible for the operation has to confirm the implant system from the medical point of view, without having to invest much time in the design procedure. The engineer confirms it from the mechanical point of view. In *paper II* a proposal for cooperation between the surgeon and the engineer is presented and similar approaches can be found by resellers of other types of PS implants [52, 53]. In the cases in this thesis, the interaction between the surgeon and the engineers has been through personal meetings.

When using digital implant design based on the CT-representation of the fracture, lots of digital information is produced that can be useful for the surgeon during pre-planning or as basis for manufacturing plastic pre-planning models. Examples of useful models are: models of the initial fracture for planning of the fracture reduction (of severe fractures), models of malunions that need corrective osteotomy and models of the mirrored non-fractured bone to be used as a basis for contouring conventional plates prior to surgery. In the clinical cases in this thesis, the digital material and plastic pre-operative models have been occasionally used by the cooperating surgeon. This pre-operative material could be better utilized but how to do that lies outside of the scope of this thesis. In the fourth clavicle case the preoperative planning is more in focus since it was an unusually complicated case including both a malunion and a nonunion and the surgeons choice was to use osteotomy to correct the malunion. First, the osteotomy was digitally performed (fig. 25), and then a PS saw guide was designed and additively manufactured to be used as support in order to perform the osteotomy as planned.

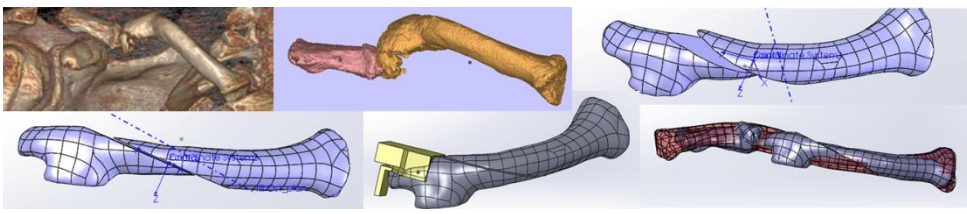

Figure 25. Digital osteotomy planning

Further, a plastic bone model of the malunion and nonunion were manufactured and used to perform a "trial operation" to verify the method and the plate, in prior to the surgery (fig. 26). The plastic bone model was attached to a wooden board using pins and the operation was performed step by step, using standard surgery equipment.

Figure 26. Test operation on plastic bone in prior to surgery.

Paper II presents a proposed method for quality control that is based on continuous use of AM for implant manufacturing. In the pilot clavicle fixation case, the strength of the plate was verified by dimensioning the plates similar to the LCP Sup-Ant plate, which is a reliable plate regarding the strength of clavicle fixation, and HIP treating the material to ensure full material density and good fatigue properties. Knowing that the EBM processed material's properties are in the same range or better than conventionally manufactured ones (chapter 2.2.1) ensures the strength of the plates. The material used for the plate manufacturing is the Ti6Al4V ELI (grade 23), which is a standard material for the use in medical implants.

4. RESULTS

4.1. Initial studies

The aim of the first part of the thesis work was to learn about the methods for the design and additive manufacturing (using Electron Beam Melting) of patient-specific medical implants and to find suitable applications in the area.

The results from the initial studies (*papers I and II*) are partly presented in fig. 1 and show that EBM technology has great potential, both for the manufacture of hip stems and for the manufacture of customized fixation plates. *Paper I* showed the EBM technology's feasibility for the manufacture of custom designed hip stems (compared to conventional machining). Under the assumption that the surface for bone in-growth on the middle of the stem can be left intact or with little post-processing the cost for the manufacturing could be significantly lowered by using the EBM method. These savings are due to reduced material consumption and file preparation time. However, the precondition of a surface structure sufficient both for bone in-growth and mechanical properties is also the main issue that needs solving, since the coarse surface structure indicates significant reduction in the fatigue strength. On the other hand, the coarse bone-ingrowth area is in the middle of the stem, where the stem is thick and hence is not a load sensitive area. Further the EBM process has evolved since this study was performed and enables a finer surface structure and less porosity in the material. The mean R_a value of the test bars in *paper I*, was 97 μm and now it is typically between 10 and 50 μm which show how fast the preconditions changes in this area and that new possibilities are arising for the technology to be implemented. In *paper II* a contribution was made to the development of a routine for the design and manufacture of PS plates, which demonstrated the possibilities for producing these types of plates within the time limit associated with a certain type of trauma fracture. Further, developments were needed in the method for the modeling, post-processing, interdisciplinary cooperation-routines and mechanical properties control. In the second part of the thesis work, the PS plate modeling method and methods for strength simulations were the primary focus.

4.2. Patient-specific clavicle plate method

The aim of the second part of the thesis was to test, develop and evaluate the method for the design and Electron Beam Melting manufacturing of patient-specific clavicle plates, and to perform strength analysis and development of the patient-specific plates using finite element simulation.

The four cases of designing and manufacturing PS clavicle plates were successfully performed, including an approach on how to model and manufacture plates with screw positioning tailored to the reduced fracture. The plates were confirmed by the surgeon to have a good fit on the reduced fracture without any need for reshaping (*paper VI*). The initial evaluation indicates that the method facilitates the work for the surgeon, both during the pre-planning and in the operating room, and that a smoother plate (compared to the commercial) is achieved, with a more optimized screw positioning and no need for reshaping during surgery (*Paper VI*). The steps of the design and manufacturing procedure used, with alternative routes depending on the requested final product and what type of bone model to use as basis for the plate modeling, are shown in fig. 27. It also shows where the medical expertise has to be involved. The times used for the different steps of the routes (green and red) are presented in *paper VI*.

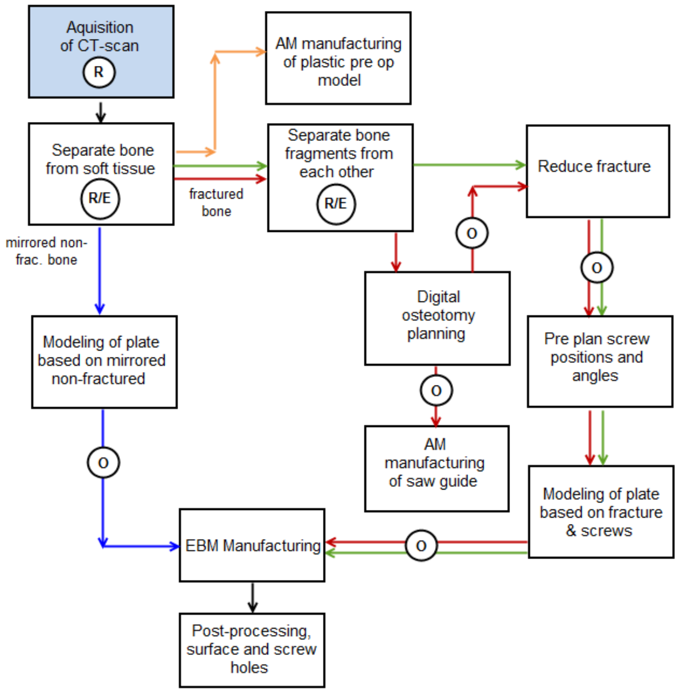

Figure 27. A schematic picture of different routes in the design and manufacturing procedure of EBM manufactured fixation plates and pre-operative models. R=performed by the radiotherapist, R/E=performed by radiotherapist or engineer, O=confirmation by the orthopedist. Start of the route in blue square.

In the fourth study the method for osteotomy planning combined with plate customization was carried out according to plan except for some small deviations presented in *paper VI*. The surgeon's subjective experience was that both the PS plate and the pre-planning tools facilitated the surgery and improved the results. In the 3-months follow-up report it is described as a successful operation and both the orthopedic surgeon and the patient were satisfied with the results.

4.3. Finite Element simulations of clavicle plates

A method for comparing stresses and displacements between different clavicle plates with improved detailing in the loading conditions compared to previous published works was developed and used in *papers III-VI*.

Analyses using the method show that the type of fracture and whether the fracture is stabilized using a lag screw or not make a big difference in the stress (Von Mises) distribution in the fixation plates as can be seen in fig. 28. The analyses without lag screws are to the left and the ones with lag screws are to the right, marked with "L". The only analysis on a multifragmentary fracture is labeled with *.

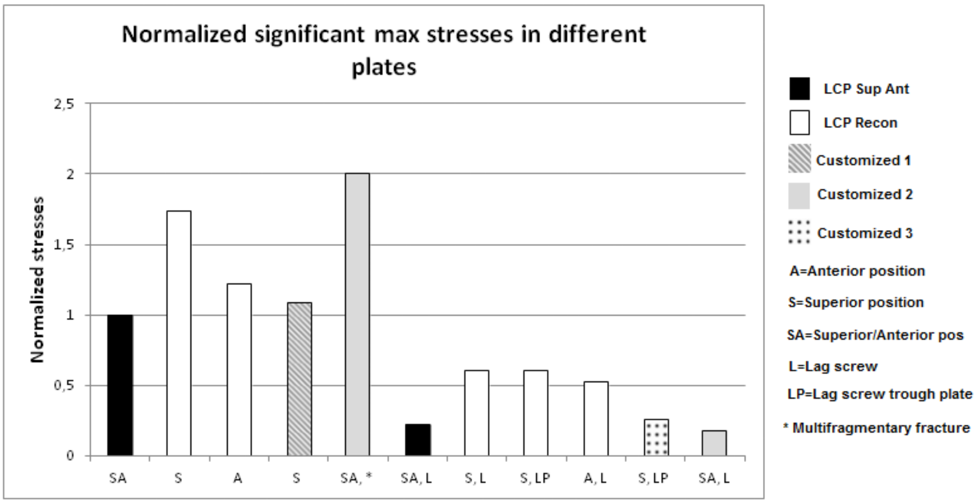

Figure 28. Summarized results from FE studies (from *papers IV-VI*).

The significant maximum stresses in the LCP Sup-Ant and the customized 2 and 3 (modeled on a single fracture and all using lag screw fixation) were in the same magnitude. Only one customized plate was analyzed on a single fracture without the use of a lag screw. That plate (Customized 1) also showed to have a significant maximum stress in the same magnitude as the comparing plates (without lag screw fixation). The customized 1, was thinner than the conventional plates, but was more cup-shaped around the bone (*paper V*).

Further, for this loading case in combination with the type of fracture, the anterior placement showed lower stresses compared to superior placement, both with and without the use of lag screws but with a more significant difference for the plates without lag screw fixation; see the white bars in fig 28. The customized 2, modeled on a multifragmentary fracture, showed significantly raised stresses due to the long plate section, bridging the non-fixed bone fragment.

5. DISCUSSION AND FUTURE WORK

Additive manufacturing also called 3D-printing, is a fundamentally new way of manufacturing parts layer-wise from 3D computer models. These methods has rapidly developed over the past 20 years, from being a way of quick product visualization to direct part manufacturing in many materials, including metals. Over the same time period there has been rapid development in software for making medical/anatomical models and for the handling and use of such.

These new technologies have shown to be useful in medical applications, typically for PS implants and planning. Further, the EBM method has been successful both in Europe (Adler Ortho and Lima Corporate) and in the USA (Exactech) for serial production of acetabular cups with a special surface structure to enhance bone ingrowth. With further research and development and as more surgeon´s get to know of the possibilities, new ways to take advantage of the technology will continuously arise. Working with this thesis has made me realize how essential it is to have close cooperation between medical professionals and professionals on the technical side. Making PS devices involves a special interaction between the two professions. Each final product is unique and designed by an engineer and a surgeon in some kind of interaction. An alternative to the close cooperation would be to educate people with knowledge in both areas.

Based on good cooperation or interdisciplinary knowledge, new practical applications are possible when old limiting laws regarding design and manufacturing no longer apply. One example is the young woman who got a 3D printed hip implant allowing her to move from a wheelchair to walking on her own [54].

As previously mentioned, one reason that there is little activity and research carried out in the area of PS plates for osteosynthesis of fractures within the orthopedic field, is the short time limits available for their design and manufacture. In the clavicle cases, the time used greatly differed depending on the case but in one case the time from the CT-scan to the delivery of plate to the hospital was two days, which shows potential even within trauma surgery since the operation often is postponed by 7-10 days due to soft tissue damage.

Regarding the FE simulations, the initial aim was to use the FE-method to optimize the plate according to material distribution and the shape of the plate. Due to a lack of input data in the literature regarding material and loading of the clavicle bone, a large amount of time was put into the definition of the boundary conditions before it was used for analysis. The combination of the practical cases and the theoretical calculations has led to reflections on: to what extent is it actually possible to optimize fixation plates when there are so many uncertain factors involved? The position and type of fracture, how the operation is finally performed, the bone properties of the patient, what the patient does during the rehabilitation, not to mention the biology influencing the healing of the bone. These conditions apply both for PS and conventional plates. However, it is always possible to use simulation to obtain a much better understanding of the case and to find the factors with the greatest impact and, on that basis, to optimize the plates to some extent.

The approach for improving the definition of the boundary conditions was to combine the FE-model with multibody musculoskeletal simulation, aiming for realistic loading case. A combination of these two can, with development, be used in a broader aspect "to simulate different types of fractures, various stages of the healing process, different loads and positions of the body, and combinations of the factors mentioned above. Hence, it can be used to study fixation methods, suitable body movements during rehabilitation, optimization of new plates, verification of the strength of customized implants, etc" as discussed in *paper III*.

Experience from the case studies and the strength analyses has resulted in some guidelines for use in continuing work on designing PS clavicle plate solutions. Always aim at facilitating the lag screw fixation of the fracture gap; if the bone can be stabilized the plate can have a leaner design. Further, designing the plates with a more or less twisted design, medially, starting in an anterior position and ending in a more superior position seems to be functional. The advantages of lateral superior placement are that there is less need to detach muscles than with anterior placement and that plate placement is easier. The advantages of medial anterior positioning are that it reduces the risk of damaging surrounding structures; it entails less plate prominence, easier drilling and screw insertion under the skin [55].

To summarize: the results of this thesis contribute to the area of digital design and AM in patient-specific implants with broad basis of knowledge regarding the technologies used and areas in which further work is required for the implementation of the technology on a larger scale. Further, a method has been developed and initially evaluated for implementation in the area of clavicle fracture fixation, including an approach for comparing the strength of different clavicle plates. The initial evaluation of using PS plates for osteosynthesis of the clavicle shows great potential of: *achieving a smooth plate adapted to the fracture in terms of shape and screw positioning*, *facilitating the surgeon's work,* and *saving some valuable time in the operating room*.

Future work will be performed to further develop and streamline the design and production chain from CT scan to final plate, including details regarding the post-processing for different functions of the screw holes. The preliminary results on the clavicle fixation method will be a good starting point, to begin discussions with medical expertise about future research collaboration, and about possible use of the method in other types of fractures for which the conventional plates are not fully functional. Another interesting area in which a great potential is seen, is the area of digital PS osteotomy planning and AM of saw guides for the use in osteotomies, in the orthopaedic field.

Regarding the strength simulations, important future work is to perform multibody musculoskeletal simulations in more relevant body positions to be used in the FE-simulations for a better understanding of the loading. The screw bone interactions should also be modeled in better detail since screw pull-out and loosening often is a bigger problem than plate breakage. Further, the FE-model has to be validated in some way towards experimental tests in order to be used alone to confirm the strength of the PS plates.

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