CHAPTER 5

GENERAL DISCUSSION
AND FUTURE PERSPECTIVES
GENERAL DISCUSSION

Titanium plates and screws are currently regarded as the gold standard for fixation of bone fragments in the maxillofacial skeleton. As with any material, there are aspects that are undesirable and should be improved to meet the ideal characteristics for fixation. From the point of view of an ideal fixation system, there is a continuous drive to create a fixation system that disappears from the human body without any residues as soon as it has fulfilled its function, i.e. undisturbed healing of the bone segments. As stated in the introduction of this thesis, biodegradable plates and screws could be a suitable material as they dissolve in the human body. The known pros and cons of both titanium and biodegradable plates and screws are described in detail in the introduction. In this thesis, a systematic review was performed to investigate the clinical efficacy and safety of biodegradable plates and screws. Subsequently, in vitro studies were performed to establish the mechanical properties of biodegradable plates and screws. Finally, a clinical trial was performed in order to establish whether these plates and screws could be used safely and effectively at large-scale and fit into the current treatment protocols and guidelines in maxillofacial surgery.

Based on a systematic review of literature (122) regarding the clinical efficacy and safety of titanium and biodegradable plates and screws, a definitive conclusion regarding the fixation of fractured bone segments and osteotomies with respect to their long-term performance in maxillofacial surgery could not be drawn. Lack of sufficiently powered, high quality and appropriately reported (randomized) controlled clinical trials are the main reasons. Moreover, the application of biodegradable plates and screws for mandibular fractures and osteotomies without using IMF has not been thoroughly investigated.

The mechanical properties of biodegradable plates and screws appeared to have less favourable strength and stiffness compared with titanium plates and screws (130;135;146). These lower strength and stiffness values apply for the functional unit characteristics, plate and screws together, as well as for the torsion characteristics of the screws. Despite the inferior mechanical characteristics, the above-mentioned review (122) presented uneventful clinical case series using biodegradable fixation devices. This raises the question as to whether the effectiveness and safety of biodegradable plates and screws will be at least non-inferior to the high success rates (more than 95%) of titanium plates and screws in large patient series. Adequately powered randomized controlled trials needed to be conducted to draw definitive conclusions regarding the effectiveness and safety of biodegradable plates and screws for bone healing in maxillofacial surgery.

The manufacturers of biodegradable plates and screws increased the dimensions to compensate for the inferior mechanical characteristics. The dimensions of the LactoSorb system are relatively bulky compared with the subtle dimensions of the Inion CPS and BioSorb FX biodegradable systems. It has been concluded that these bulky dimensions are responsible for the relatively good mechanical properties of the LactoSorb system (130;135). As the dimensions of biodegradable plates and screws are larger compared to titanium devices, it was not desirable to include the relatively bulky plates and screws of the LactoSorb system in the RCT. The manufacturers of the BioSorb FX system used a special self-reinforcement principle to enhance the mechanical characteristics in order to keep the dimensions within acceptable limits.

The application of biodegradable plates and screws is commonly limited to upper- and midface fractures and osteotomies. Most manufacturers discourage the use in the mandible unless in conjunction with 6 weeks of IMF. The use of IMF would be a step back in history. Inion Ltd. is the only exception and can be used to fixate fractures and osteotomies of the mandible according to the manufacturer. IMF should additionally support the fixation only in complex or comminuted cases. As the inclusion- and exclusion criteria of the RCT resulted in exclusion of these cases, and the regular mandibular fractures and osteotomies could be stabilized without using IMF, Inion CPS plates and screws were chosen to use in the RCT. Little data were available for the Inion CPS plates and screws as the material was relatively new onto the market. After contacting the manufacturer of the Inion CPS system, we received the proof of an article of Nieminen et al. published later in 2008 (148). The authors investigated the tissue reactions and mechanical strength of the Inion CPS plates and screws during the course of degradation. The materials were implanted to the mandible and in the dorsal subcutis of 12 sheep. The animals were sacrificed at 6-156 weeks. In light microscopy, the in vivo implant material began to fragment at 52 weeks and could not be detected at 104 weeks. No significant foreign body reactions were seen in the mandibles. The dorsal subcutis disclosed mild reactions which were not of clinical significance. These findings suggest that Inion CPS plates can be used safely for fixation of the bony structures in the maxillofacial skeleton. Definitive proof of full degradation and resorption is still lacking, as it is for all biodegradable systems investigated in this thesis.

In order to accomplish the main aim of this thesis, ‘to establish the effectiveness and safety of biodegradable plates and screws to fix bone segments in the maxillofacial skeleton as a potential alternative to metallic ones’, the clinical aspects were investigated in a randomized controlled clinical trial using the Inion CPS biodegradable fixation system (Buijs et al., submitted). The Intention To Treat analysis (ITT-analysis) and the Per Protocol analysis (PP-analysis) yielded that Inion CPS biodegradable plates and screws did not perform inferiorly to titanium plates and screws regarding bone healing after 8 weeks for maxillofacial fractures (except for Le Fort I fractures) as well as osteotomies. This implies that the biodegradable system can be safely used without IMF, also for load bearing situations like bilateral sagittal split osteotomies and non-comminuted mandibular fractures. Also regarding the secondary outcome measures, it can be concluded that there are no important differences between the two investigated systems.

In vitro studies were performed to establish the mechanical properties of biodegradable plates and screws during the course of degradation. The materials were implanted to the mandible and in the dorsal subcutis of 12 sheep. The animals were sacrificed at 6-156 weeks. In light microscopy, the in vivo implant material began to fragment at 52 weeks and could not be detected at 104 weeks. No significant foreign body reactions were seen in the mandibles. The dorsal subcutis disclosed mild reactions which were not of clinical significance. These findings suggest that Inion CPS plates can be used safely for fixation of the bony structures in the maxillofacial skeleton. Definitive proof of full degradation and resorption is still lacking, as it is for all biodegradable systems investigated in this thesis.

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In contrast, the handling characteristics showed a remarkable difference, indicating that biodegradable plates and screws performed significantly less compared to titanium plates and screws. This is because biodegradable plates and screws are weaker and, more particularly, bulkier in terms of dimensions. These large dimensions remain a problem, especially in the small and subtle areas of the midface where thin bones are present. The large dimensions as well as the inferior mechanical characteristics are the main reasons for the high amount (22%) of peri-operative switches from biodegradable to titanium plates and screws.

Besides the clinical aspects, the costs were also evaluated. It can be concluded that there is no significant difference between the Inion CPS biodegradable and the titanium plates and screws. The application of the biodegradable plates is slightly more expensive compared to titanium ones. However, productivity losses of people are the main costs. Following a post-operative period of 1 year, or perhaps even longer, one could draw definitive conclusions regarding the cost-effectiveness of the biodegradable plates and screws and whether the potential advantages of biodegradable plates and screws could be ‘confirmed’. Patient’s potential productivity gains could resolve the negative aspects of the peri-operative switches of biodegradable plates and screws.

The skeletal stability of the bone segments is an important variable which is evaluated in the RCT by assessing the dental occlusion and the positional change of the bone segments. During the 8-weeks follow-up the main focus was on bone healing (primary outcome measure). The skeletal stability will be evaluated after 1 year follow up. Skeletal structures may change especially during the first postoperative year (relapse; postoperative orthodontics). After 1 year the skeletal structures will be more reliable making complete effect size measurement of the skeletal stability possible.

It is generally accepted that the strength and stiffness of different titanium plates and screws are comparable. This is also applicable for biocompatibility as is investigated in the study of Langford in 2002 (149). In this way, it can be concluded that the KLS Martin titanium system, which is used in the RCT, has a good generalizability for other titanium systems. Regarding the Inion CPS biodegradable system, the generalizability of the mechanical aspects is limited to the BioSorb FX, and LactoSorb. These systems represent comparable mechanical characteristics (135). The other biodegradable systems investigated in the study, performed significantly inferior. With respect to the biocompatibility, the generalizability of Inion CPS plates and screws is difficult as a result of the various co-polymer composition used to manufacture the different biodegradable plates and screws. Although many studies report promising results, ultimate biocompatibility and complete resorption has never been proven. It can be concluded that the results of the randomized controlled trial can be extrapolated to at least 2 of the investigated biodegradable plate and screw systems (BioSorb FX and LactoSorb).

Based on the results of the RCT performed in this thesis, it is concluded that biodegradable plates and screws do not perform inferior to titanium regarding a follow-up period of 8 weeks. The high percentage of switches is a threat to a widespread acceptance of biodegradable plates and screws in the current treatment protocols and guidelines in maxillofacial surgery. The follow-up period of 1 year will provide more clarity about the potential differences in plate removal operations and thus the potential gain in effectiveness in the treatment of fractures and osteotomies of the maxillofacial skeleton.

The 1 year follow up results will also provide more information about the skeletal stability, biocompatibility, and resorption aspects of Inion CPS plates and screws. Further research is performed and will be published in the near future.

**FUTURE PERSPECTIVES**

Despite the results of the RCT, some reservations remain regarding the use of biodegradable plates and screws in maxillofacial surgery. There may be alternatives that can contribute to finding the ideal fixation system. One such development is the welding technique incorporated in the SonicWeld Rx system (Gebrüder Martin GmbH & Co., Tuttingen, Germany). A biodegradable pin is placed onto an ultra-sound activated sonic electrode, called a sonotrode, and inserted into the borehole. As a result of the added ultra-sound energy, the thermoplastic biodegradable pin will melt, resulting in a flow of biodegradable polymers into the cortical bone layer and the cavities of the underlying cancellous bone. At the same time the biodegradable plate and pinhead fuse. Due to the welding technique, the handling characteristics as well as the mechanical properties are greatly enhanced (146). These two aspects were the main reasons for the high amount of peri-operative switches reported in the randomized clinical trial. Despite these promising results (146), the SonicWeld Rx system is considered not to be suitable for fixation of mandibular fractures and osteotomies according to the manufacturer (KLS Martin). The present co-polymer composition (50% L-lactide and 50% D-lactide) is not sufficient to fix mandibular fractures and osteotomies in a stable manner. Different co-polymer(s) (compositions) with improved mechanical characteristics could be used in conjunction with the welding technique to achieve strong and easy to apply biodegradable plate and screw systems. Important prerequisites, i.e. the biocompatibility and biodegradability of these polymers, should be taken into account since they are important potential advantages of biodegradable plates and screws. One should critically appraise the biocompatibility, biodegradability, and finally the resorption of these polymers as up till now there is no evidence regarding the complete resorption of biodegradable plate and screws to the electron microscopic level. Future of research of biodegradable plates and screws will be determined to a large extent by the above factors since the main rationale for using biodegradable plates and screws is their disappearance after fulfilling their function (bone healing).