POLITECNICO DI TORINO

Master's Degree in Biomedical Engineering

Master's Degree Thesis

Procedure Improvement for Designing and Developing Medical Devices in Compliance with MDR and ISO 13485: Case Study on Osteotomy Plates Series

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Table of Contents

Introduction

This thesis, conducted in collaboration with INTRAUMA S.p.A., delineates the formulation of a new design and development procedure applied to a new series of orthopedic plates for osteotomy.

The aim is to optimize the internal process of medical device design and development at INTRAUMA S.p.A., emphasizing not merely the technical stages of design but also the critical pathway of documentary and regulatory compliance, specifically in alignment with the Medical Device Regulation (MDR). This pathway is crucial for obtaining CE certification and for the subsequent entry into the European market, ensuring that each manufactured medical device adheres to the highest standards of safety, efficacy, and quality.
The revision of the procedure has successfully led to a reduction in the complexity and redundancy of documentation compared to previous methods, resulting in decreased time and costs of design and development while maintaining the quality and safety standards demanded. Throughout this exposition, the applicability, usability, and efficacy of the developed procedure are validated through the design of a new osteotomy plates series. It includes the elaboration of the necessary technical documentation required for submission to the notified bodies for CE marking, from user needs and design inputs to essential outputs, through to the technical specifications and product engineering.

The development of this new design and development procedure, conducted in close synergy with INTRAUMA S.p.A., has made possible the practical application of results directly on the company's production line. The new osteotomy plates series, developed within this cooperation, is the result of the integration between academic innovation and INTRAUMA's manufacturing prowess.

Founded in 2006 in Rivoli by Nilli Del Medico and her son Riccardo, INTRAUMA S.p.A. is a leading company in the orthopedic and trauma field, specializing in the design and production of devices for internal fixation, such as the O'Nil System – Internal Fixator and Elos - Intramedullary Nail, flagship products of the company.

With a strong commitment to research and development, the company focuses on optimizing materials and manufacturing processes, closely collaborating with expert surgeons to ensure the highest quality implants that facilitate approaches to both human and veterinary traumatology. All manufacturing processes strictly adhere to the Made in Italy standards, ensuring safe and effective devices, certified according to EU MDR 2017/745 standards for distribution in Europe.

Chapter 1

Background

1.1 Anatomical Overview

1.1.1 Bones

FEMUR

The femur is the proximal bone of the hindlimb in human (Fig: 1.1). It is the longest and strongest bone in the human body. Its length is associated with a striding gait and its strength with the weight and muscular forces it is required to withstand. The head of the femur articulates with the acetabulum in the pelvic bone forming the hip joint, while the distal part of the femur articulates with the tibia (shinbone) and patella (kneecap), forming the knee joint. As the femur is the only bone in the thigh, it serves as an attachment point for all the muscles that exert their force over the hip and knee joints. The femoral shaft is a cylinder of compact bone with a large medullary cavity. The wall is thick in its middle third, where the femur is narrowest and the medullary cavity most capacious.

Proximally and distally, the compact wall becomes progressively thinner, and the cavity gradually fills with trabecular bone. Femur has a proximal rounded, articular head projecting medially from its short neck, which, in turn, is a medial extension of the proximal shaft. The distal extremity is wider and more substantial and presents a double condyle that articulates with the tibia. The extremities, especially where articular, consist of trabecular bone within a thin shell of compact bone, their trabeculae being disposed along lines of greatest stress. In standing, the femoral shafts show an inclination upwards and outwards from their tibial articulations, with the femoral heads being separated by the pelvic width [1].

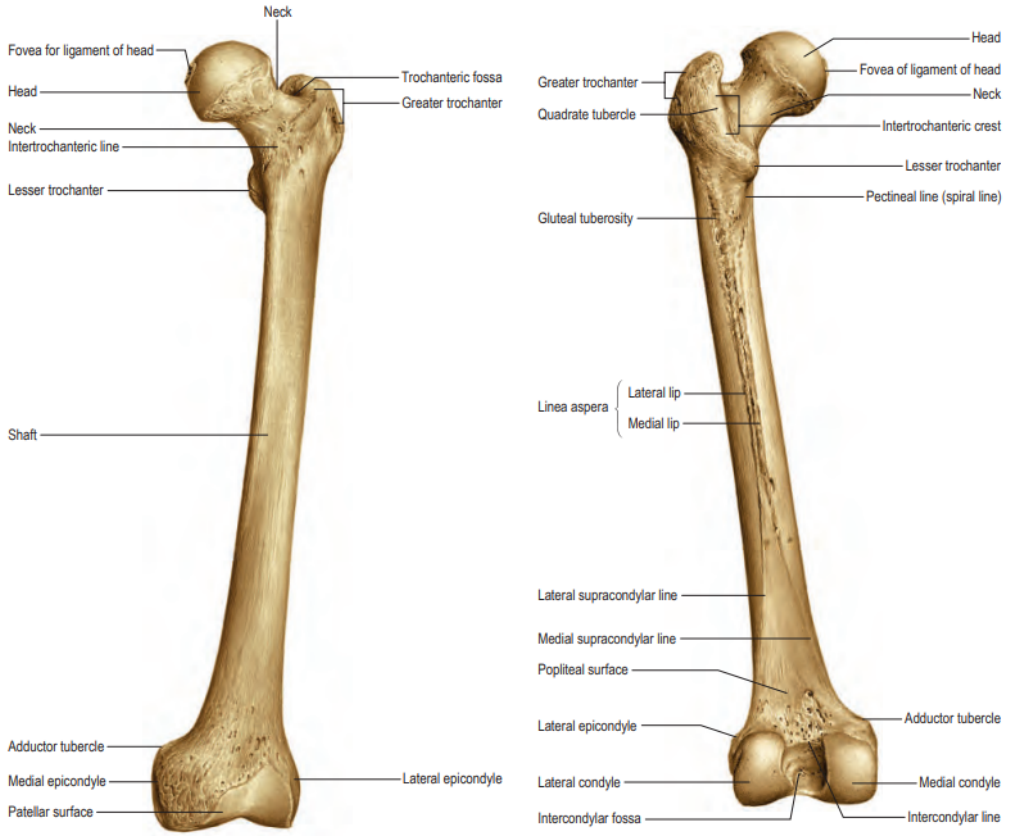


Figure 1.1: Femur [1].

The distal end of the femur (Fig: 1.2) is widely expanded as a bearing surface for transmission of weight to the tibia. It bears two massive condyles, which are partly articular. Anteriorly, the condyles are confluent and continue into the shaft; posteriorly, they are separated by a deep intercondylar fossa and project beyond the plane of the popliteal surface. The patellar surface extends anteriorly on both condyles, especially the lateral. The tibial surface is divided by the intercondylar fossa but is anteriorly continuous with the patellar surface. Regarding the structure of distal femur, trabeculae spring from the entire internal surface of compact bone, descending perpendicular to the articular surface [1].

Fractures of the distal femur are rare and severe. The most common mechanism is an indirect trauma on a bent knee, and more rarely direct trauma by crushing. The anatomy of the distal femur explains the three major types of fracture. Because of the anatomy of the distal femur, only surgical treatment is indicated to stabilize the fracture. A non-surgical treatment is a rare option [2].

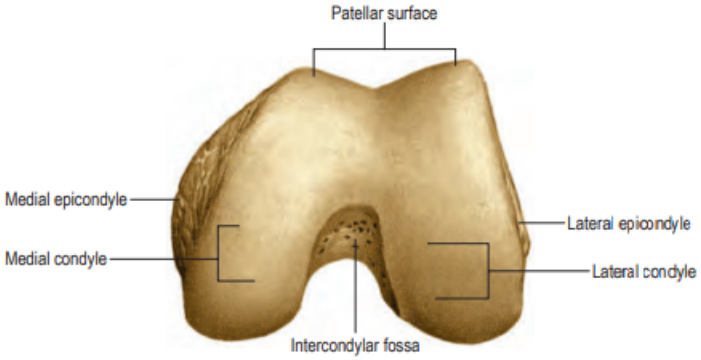


Figure 1.2: Distal Femur [1].

TIBIA

The tibia is the larger and stronger of the two bones in the lower part of the leg, commonly known as the "shin" (Fig: 1.3). Medially located in comparison to the thinner fibula, the tibia is primarily involved in weight bearing and locomotion and is susceptible to fractures due to its superficial position and its role in load bearing. The tibial shaft is triangular in section and has expanded ends, the anterior border of the shaft is sharp and curves medially towards the medial malleolus. Together with the medial and lateral borders, it defines the three surfaces of the bone. Proximally, it articulates with the femur at the tibial condyles, forming the knee joint; the tibial plateau, the upper surface of the tibia, supports the femoral condyles. Distally, there is the ankle joint, which features a prominence known as the medial malleolus, contributing to the stability of the joint. The external surface of the tibia serves as an attachment point for the tendons of the leg muscles, while the medullary canal within houses the bone marrow [1].

The **proximal end** (Fig: 1.4) bears the weight transmitted through the femur. It consists of medial and lateral condyles, an intercondylar area and the tibial tuberosity. The tibial condyles overhang the proximal part of the posterior surface of the shaft. Both condyles have articular face superior surfaces, separated by an irregular, non-articular intercondylar area. The geometry of proximal tibia has a direct influence on the biomechanics of knee joint and the tibial component is recognized to be more prone to complications compared to the femoral component [3]. The angle of inclination of the superior tibiofibular joint varies between individuals and may be horizontal or oblique. The tibial tuberosity is the truncated apex of a triangular area where the anterior condylar surfaces merge. The patellar ligament is attached to the smooth bone proximal to this, its superficial fibres reaching a rough area distal to the line. The deep infrapatellar bursa and fibroadipose tissue

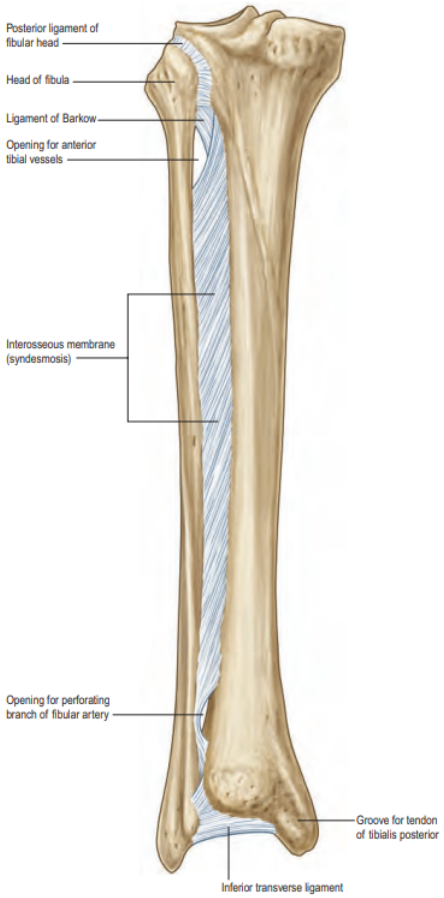


Figure 1.3: Tibia and Fibula [1].

intervene between the bone and tendon proximal to its site of attachment. The latter may be marked distally by a somewhat oblique ridge, on to which the lateral fibers of the patellar ligament are inserted more distally than the medial fibers. This knowledge is necessary for avoiding damage to this structure when performing an osteotomy above the tibial tuberosity in a lateral to medial direction [1].
The proximal tibiofibular joint is a sliding joint located between the lateral tibial condyle and the fibular head. This synovial articulation may communicate with the knee in 10% of adults. A fibrous capsule surrounds the articulation with two prominent ligaments, the anterosuperior and the posterosuperior tibiofibular ligaments, which provide additional stability. This joint has been classified into two types, horizontal and oblique. The horizontal type is associated with increased rotatory mobility and increased joint surface area, and the latter type is associated with less rotatory mobility and less joint surface area [4].

The distal end of the tibia has anterior, medial, posterior, lateral and distal surfaces and ends with the medial malleolus (Fig: 1.4). When compared to the proximal end, distal tibia is laterally rotated of approximately 30° (tibial torsion). The torsion begins to develop at birth and progresses until skeletal maturity is attained. Some of the femoral neck anteversion seen in the newborn may persist in adult females: this causes the femoral shaft and knee to be medially rotated, which may lead the tibia to develop a compensatory external torsion to counteract the tendency of the feet to turn inwards. The medial surface is smooth and continuous above and below with the medial surfaces of the shaft and medial malleolus, respectively. More laterally, the posterior tibial vessels, tibial nerve and flexor hallucis longus contact this surface. The lateral surface is the triangular fibular notch; its anterior and posterior edges project and converge proximally to the interosseous border. The distal surface articulates with the talus and is wider in front, concave sagittally and slightly convex transversely (saddle-shaped). Medially, it continues into the malleolar articular surface [1].

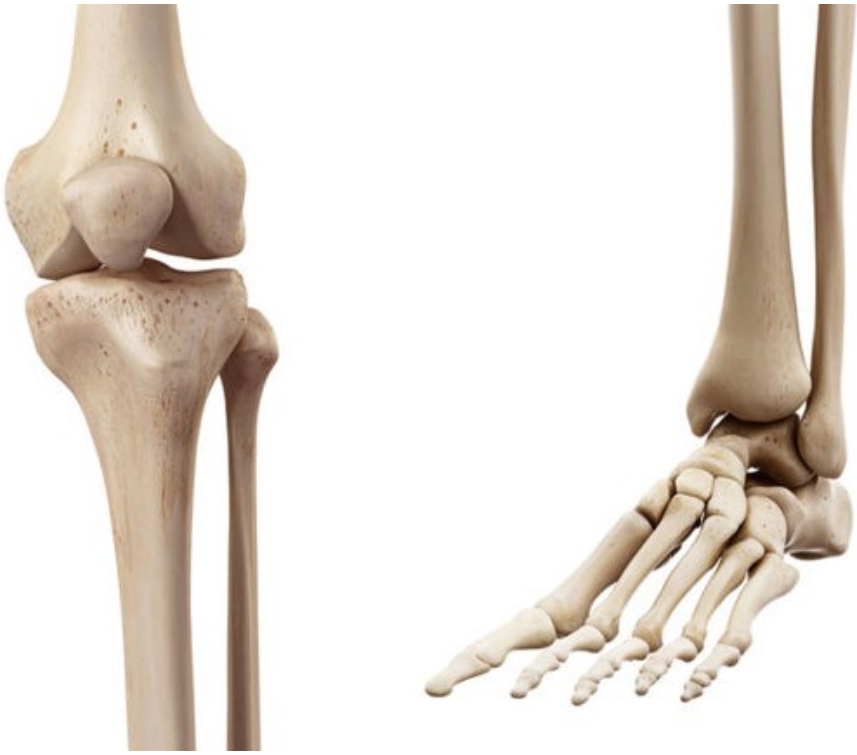


Figure 1.4: Proximal Tibia (R) and Distal Tibia (L) (Image generated by AI).

ULNA

The ulna is medial to the radius in the supinated forearm (Fig: 1.5). Its proximal end is a massive hook, concave forwards, that articulates with the distal humerus. The lateral border of the shaft is a sharp interosseous crest. The bone diminishes progressively from its proximal mass throughout almost its whole length, but, at its distal end, expands into a small, rounded head and styloid process. The ulnar shaft is triangular in cross-section in its proximal three quarters, but distally is almost cylindrical. Along its whole length, the ulna is slightly convex posteriorly. Mediolaterally, the proximal half has a slight curvature that is concave laterally and the distal half a curvature that is concave medially [1].

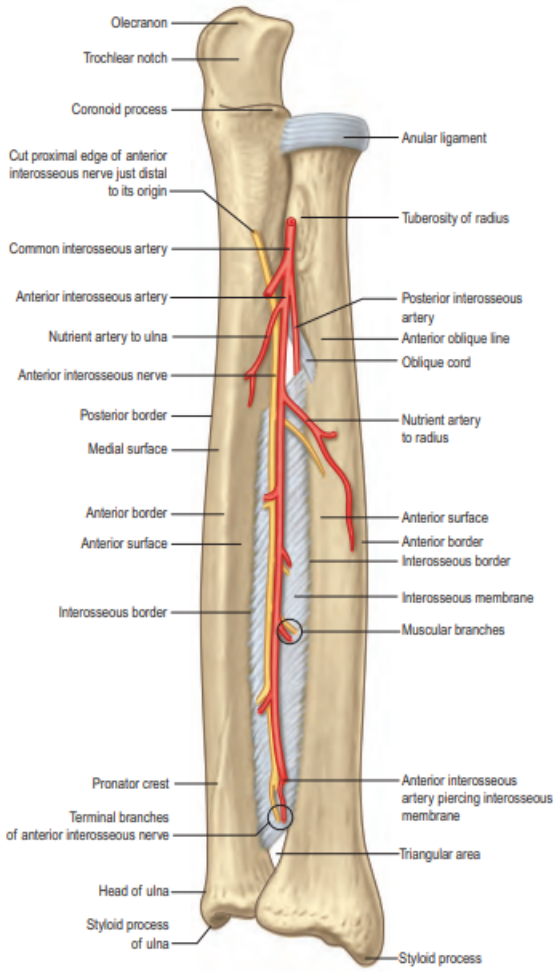


Figure 1.5: Ulna and Radius [1].

1.1.2 Joints

KNEE

The knee is the largest synovial joint in the body (Fig: 1.6) and it consists of two joints, one between the femur and tibia (tibiofemoral joint), and one between the femur and patella (patellofemoral joint). It consists of three functional compartments that collectively form a dynamic, specialized hinge joint, which permits flexion and extension as well as slight internal and external rotation [1]. The medial and lateral meniscus stabilize and cushion the tibiofemoral articulation. The medial and lateral ligaments prevent valgus or varus deformity. Within the knee joint, the anterior and posterior cruciate ligaments allow for some rotational movement of the knee while preventing anterior or posterior displacement of the tibia. The patellofemoral joint is used in knee extension [5]. The asymmetric medial and lateral condyles of the distal femur and proximal tibia have a direct influence on the biomechanics of knee joint and prostheses design [3].

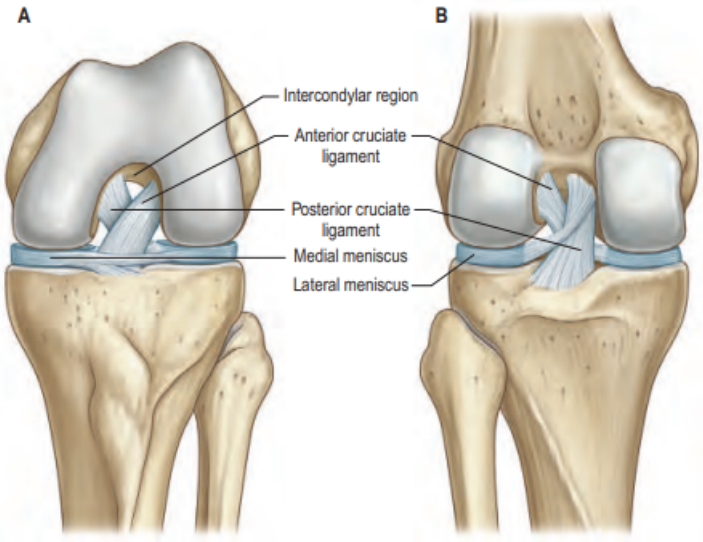


Figure 1.6: Knee Joint. Anterior view (A) and posterior view (B) [1].

ANKLE

The ankle joint, or tibiotalar joint (Fig: 1.7), is a complex mechanism that connects the leg to the foot, allowing primarily for flexion and extension movements. The

joint is a diarthrodial articulation involving the distal tibia and fibula and the body of the talus; it is the only example in the human body of a true mortise joint [1]. The distal part of the tibia, equipped with a concave articular surface and reinforced by cartilage, articulates with the talus, while the medial malleolus provides medial stability to the joint. The talus is an irregularly shaped bone with an extensive articular surface. In the tibiotalar joint, the talus mainly serves to articulate with the tibial plafond, allowing for ankle plantar flexion and dorsiflexion. The talus translates rotational forces in the foot to the tibiotalar joint and leg [6]. Ligaments, including the deltoid ligament and the tibiofibular ligaments, contribute to the joint's stability, preventing excessive movements and ensuring functional synchrony between the tibia and fibula. This complex structure supports body weight and allows adaptations on different surfaces, being essential for mobility and daily activities.

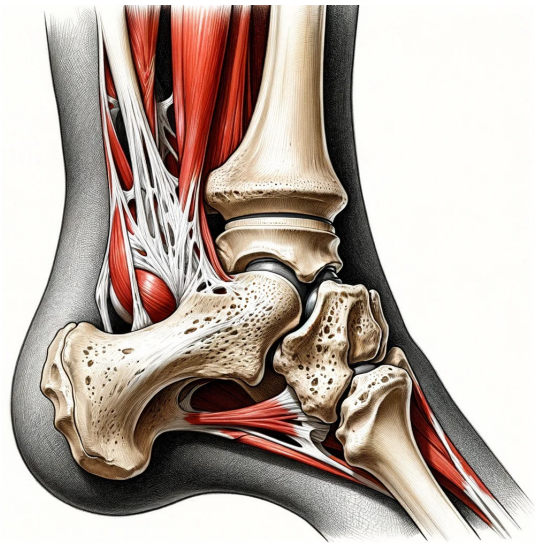


Figure 1.7: Ankle Joint (Image generated by AI).

1.1.3 Osteotomy surgery

Osteotomy literally means "cutting of the bone" (from greek: ὸστεον "bone" and $\tau o \mu \eta$ "incision"). It is a surgical procedure that involves cutting the bone, with the aim of reshape or realign a portion of bone. This operation can be performed on almost all bones in the body and primarily aims to [7]:

- correct bone deformities, whether congenital or acquired, like those resulting from fractures that have healed improperly;
- improve joint alignment;

- redistribute pressures and stresses on a joint to relieve joint pain due to degenerative conditions or to slow down the process;
- prepare the bone for further orthopedic correction procedures.

Osteotomy is therefore a versatile surgery that finds application in different areas of traumatology and orthopedics. The operation involves several steps, starting with detailed surgical planning, often assisted by advanced imaging techniques such as radiography (RX), computed tomography (CT), or magnetic resonance imaging (MRI). The most common method used when planning an osteotomy is to visualize the movement of the lower leg, in order to obtain a desired overall leg alignment. In the absence of any better evidence, the realignment usually aims towards having a straight 'mechanical axis' that passes (in the coronal plane with the knee in full extension) from the center of the hip, through the knee, to the center of the tibiotalar joint. This allows the surgeon to determine the exact position, angle and size of the bone cut needed. During the surgery, the bone is sectioned according to the predefined plan and, if necessary, is reduced or reshaped and finally stabilized using internal fixation systems, such as plates and screws, that ensure proper alignment and promote bone healing [7]. Although varying based on the location and type of osteotomy, the main steps of the surgical technique include:

1. **Incision**: an incision is made in the skin above the bone area to be treated.
2. **Osteotomy**: the surgeon performs the predefined cut on the bone, removing or adding bone portions if necessary.
3. **Fixation**: the bone is stabilized using internal fixation devices.

Trauma plates for bone fixation, made of biocompatible materials such as titanium and its alloys or stainless steel, play a crucial role in maintaining optimal alignment during the healing process. Both the design and material have been significantly refined over the years to enhance bone stability, reduce the risk of infections and minimize irritation of the surrounding soft tissues. The recovery time post-surgery can vary depending on the procedure's complexity, the patient's age and their overall health condition. Rehabilitation is highly important in the healing process, being essential for regaining strength and mobility in the treated area.
Osteotomy has been shown to be effective in improving bone and joint alignment, reducing pain, and enhancing functionality in many patients. However, as with any surgical procedure, there are risks of complications, including allergic reactions to the materials or sensitivity to foreign bodies, acute or chronic local or systemic infections, inflammatory arthritis, non-union of the bone and the need for further surgical interventions.

In conclusion, osteotomy around the knee joint supports a step-up approach to treatment and serves as an effective alternative for managing knee osteoarthritis, particularly when compared to knee arthroplasty. While knee arthroplasty carries a significant risk of postoperative infection, osteotomy presents a lower risk profile. Furthermore, younger patients undergoing knee replacement often face the possibility of needing multiple revision surgeries later in life. In contrast, osteotomy is a simpler and safer surgical option, with most patients experiencing swift and comparable recovery rates to those observed in arthroplasty [8]. This makes it an especially appealing option for younger patients or those seeking to minimize the risk and frequency of follow-up surgeries, while still effectively managing the symptoms of osteoarthritis.

Osteotomies can be divided into two main categories: one classification is based on the type of surgical technique, specifically the cut performed, while the other considers the anatomical area involved.
Classification by type of cut:

- **Wedge Osteotomy (opening/closing wedge)**: involves the removal or addition of a bone wedge to alter the bone's angle.
- **Linear Osteotomy**: a straight cut across the bone.
- **Transverse Osteotomy**: A curved transverse cut relative to the bone's longitudinal axis for correcting more complex deformities.

Classification by anatomical area:

- Distal Femoral Osteotomy (DFO)
- Proximal Femoral Osteotomy (PFO)
- High Tibial Osteotomy (HTO)
- Distal Tibial Osteotomy (DTO)
- Acetabular Osteotomy
- Mandibular Osteotomy
- Calcaneal Osteotomy
- Metatarsal Osteotomy
- Spinal Osteotomy

In the following sections, we will proceed with a detailed exploration of some of the main techniques previously listed, providing insights for a more comprehensive understanding of their applications, benefits, and surgical considerations.

The two main classifications based on surgical technique are "opening wedge" osteotomies and "closing wedge" osteotomies. These techniques aim to restore normal bone alignment and improve joint functionality but differ in how they modify the bone structure.

- **Opening Wedge Osteotomy**: this procedure involves cutting the bone and inserting a wedge of biocompatible material (such as titanium, polymer or donated bone) (Fig. 1.8). The technique is used to increase the bone's angle and improve alignment without removing any bone tissue. The opening wedge osteotomy may be preferred when it's necessary to increase the limb's length or correct specific types of deformities. An advantage of this technique is that it allows for more precise control over the correct angulation and can be used for larger adjustments than closing wedge osteotomies. However, it may involve a longer healing time due to the need for new bone to fill the opened wedge. Opening wedge osteotomies are frequently applied in correcting knee deformities, especially in the case of **varus alignment**, where opening the wedge on the knee's inner side can redistribute the load.

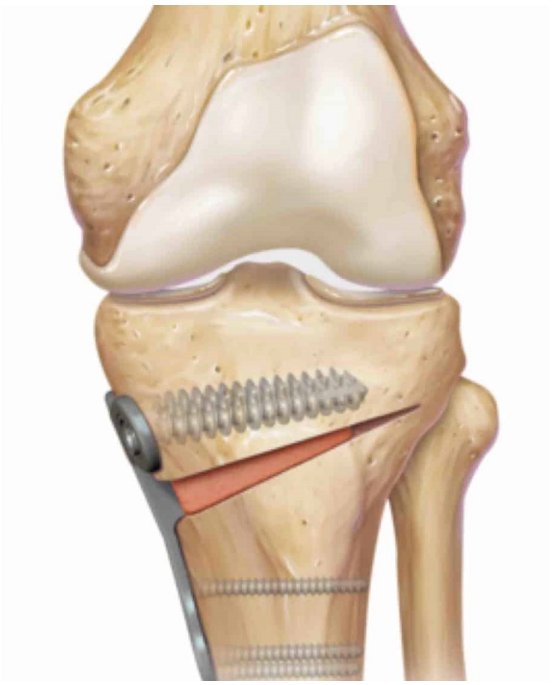


Figure 1.8: Opening Wedge Osteotomy [9].

- **Closing Wedge Osteotomy**: in this procedure a wedge-shaped bone segment is removed (Fig. 1.9) from one side while the two remaining sides are brought together and fixed. This has the effect of changing the bone's angle and, consequently, the alignment of the adjacent joint. The advantage of this technique is that the bone closure tends to be stable and allows for relatively quick healing, as the contact surface for the bone to heal is large. However, removing a bone segment can lead to a slight reduction in limb length. Closing wedge osteotomies are commonly used in treating several deformities, particularly improper knee alignments to correct excessive **valgus**.

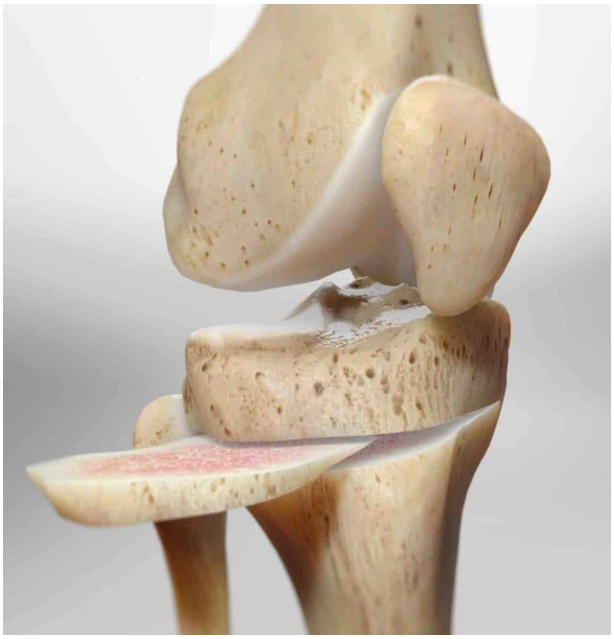


Figure 1.9: Closing Wedge Osteotomy (Image generated by AI).

The choice between an opening or closing wedge osteotomy depends on several factors, including the specific nature of the bone deformity, the patient's needs and the potential impact on the biomechanics of the involved joint. Each technique has its specific advantages and limitations. The main differences concern the modification of the limb's angulation and length and the stability of the implant. Closing wedge osteotomies remove a bone segment, which can lead to a slight reduction in limb length, this is typically not an issue unless there is a significant discrepancy in limb lengths. Conversely, opening wedge osteotomies can maintain or even increase the length, which may be desirable in certain clinical contexts. Moreover, they offer greater flexibility in adjusting the angulation since the inserted wedge can be sized to achieve the desired angulation, particularly useful in cases of complex deformities or major corrections. Regarding the healing process related

to the stability of the plate used for fixation, closing wedge osteotomies tend to offer greater post-operative stability and potentially quicker healing, since the cut bone surfaces are brought into direct contact. Opening wedge osteotomies, on the other hand, require the formation of new bone to fill the created wedge, which can extend healing times. However, the use of biocompatible materials and fixation techniques can mitigate these aspects [10].
Common contraindications to an osteotomy are the presence of an inflammatory disease and very unstable knee valgus deformity greater than 20°, because it can be associated with severe ligamentous instability. Furthermore, severe bone loss and severe valgus deformity associated with tibial subluxation greater than 1 cm are other contraindications to osteotomies, as well as severe articular disruption [11].

In summary, the choice between opening and closing wedge osteotomy is complex and must be personalized based on a detailed assessment of each patient, considering the advantages and disadvantages of each technique in relation to the specific clinical situation.

Subsequently, we will further explore the classification of osteotomy techniques, focusing specifically on the anatomical area of interest. This distinction is crucial for understanding the various surgical applications and their associated benefits. Each technique is targeted at addressing specific biomechanical and pathological issues, thereby contributing to the improvement of bone functionality and alignment.

- **High Tibial Osteotomy (HTO)**: HTO is an orthopedic surgical procedure aimed at correcting knee alignment by modifying the geometry of the proximal tibial bone. Biomechanical data suggest that a biplanar osteotomy and the use of a plate fixator are optimal technique to correctly execute a HTO [12]. This type of surgery is particularly effective for patients suffering from unicompartmental osteoarthritis or varus malalignment, conditions that most frequently affect the medial side, namely, the inner aspect of the joint.
  In detail, HTO is performed by making a cut in the tibial bone near the knee; then, depending on the specific need of the patient, a small portion of bone may be removed to create a space (opening wedge osteotomy) or the bone may be cut and then shifted (closing wedge osteotomy), changing the angle of the tibial bone and, consequently, the alignment of the entire leg. This procedure is primarily aimed at patients who have unicompartmental knee osteoarthritis with varus alignment, i.e., an inward inclination of the lower limb, leading to increased pressure and wear on the inside of the knee. By correcting the tibial angulation through HTO, as shown in Fig. 1.10, a redistribution of forces across the knee is achieved, shifting the load from the damaged areas to healthier ones.

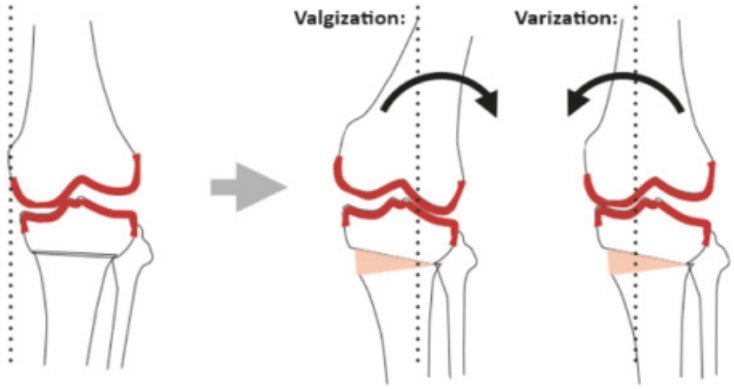


Figure 1.10: Different HTO procedures (Image generated by AI).

HTO is especially recommended for young and active patients who wish to maintain a high level of physical activity or would like to avoid other types of surgeries like total knee arthroplasty (TKA) [13]. Studies indicate that adequate stable fixation is required for the proper healing of this additive type of osteotomy to minimize the risk of non-union and loss of correction [14]. Despite the recovery period can be relatively long, with rehabilitation that may extend for several months, the long-term results include significant improvement in quality of life and pain reduction, allowing patients to return to their daily and sporting activities.

- **Distal Tibial Osteotomy (DTO)**: DTO is a surgical procedure designed to correct deformities and improve the alignment of the ankle joint. The shape of the ankle joint surface is changed by cutting and tilting the tibial plafond without osteotomy of the fibula; thereby, the inclination of the distal tibial articular surface with respect to the tibial axis is altered, with associated improvement in ankle stability [15].

  This procedure focuses on the lower part of the tibia, near the ankle joint and is often indicated for patients who present significant misalignment at this level, resulting from poorly healed fractures, degenerative diseases, or congenital deformities, all conditions that can lead to pain, difficulty in walking and the progression of degenerative conditions such as osteoarthritis [6]. The procedure illustrated in Fig. 1.11, involves cutting the distal tibial bone in a specific way to correct the irregular angulation. Depending on the nature and extent of the deformity, the osteotomy can be performed by removing or adding a bone wedge or by making a cut and shifting the bone (closing or opening wedge osteotomy).

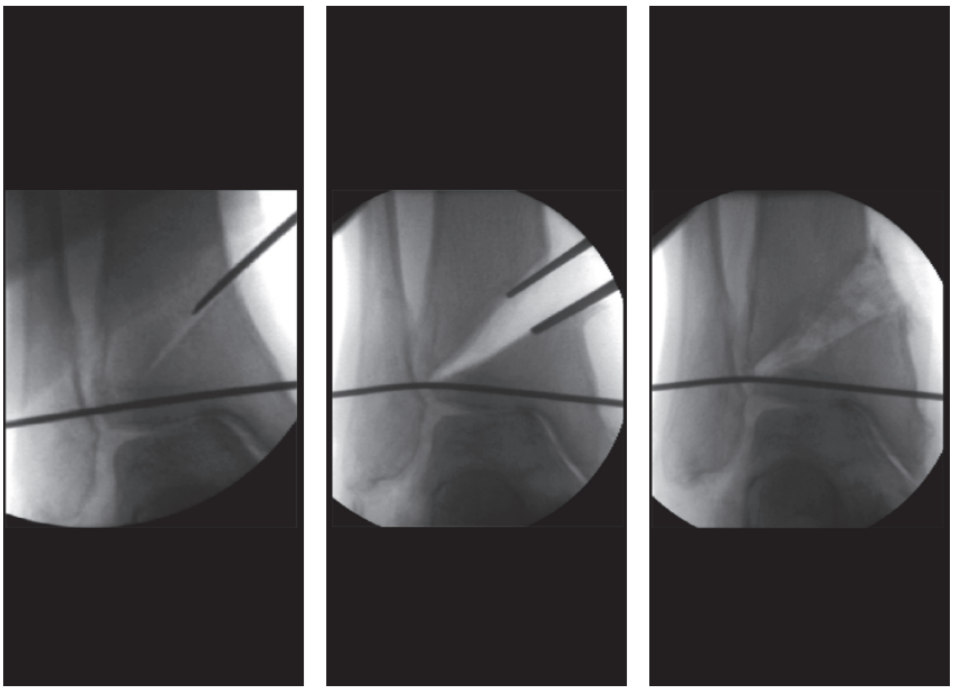


Figure 1.11: Procedure of Opening Wedge DTO [15].

DTO requires careful preoperative planning, surgical precision and a detailed post-operative rehabilitation program. It plays a crucial role in restoring strength, mobility and functionality to the ankle and foot, leading to significant improvement in quality of life and joint function, as well as a reduction in pain. DTO with joint distraction may be useful as a joint-preserving surgery for medial ankle osteoarthritis in older patients [16].

- **Distal Femoral Osteotomy (DFO)**: DFO is an advanced surgical procedure designed to correct deformities and improve the alignment of the knee joint by acting on the distal femur, the part of the femur near the knee, thereby distributing the load more evenly during walking.

  This procedure is particularly indicated for patients presenting significant valgus or varus misalignment, situations where the knee axis deviates outward or inward, respectively, from the normal alignment. This can lead to a significant reduction in pain for the patient and a slowdown in the progression of osteoarthritis. The procedure involves a controlled cut of the distal femur to reshape the bone. Depending on the nature of the deformity, an open or closed wedge osteotomy may be necessary to achieve the desired alignment, an example of closing wedge osteotomy is shown in the Fig. 1.12.

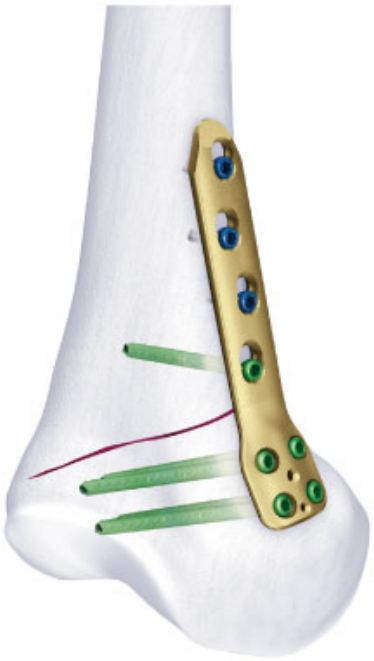


Figure 1.12: Closing Wedge DFO (LCP Plate) [17].

Opened and closed wedge DFO show similar performance, confirmed by the clinical and radiological outcome, including survival rates, that did not statistically differ [18]. Recovery from a DFO includes a targeted post-operative rehabilitation program aimed at restoring strength, mobility, and functionality to the knee, leading to a significant improvement in the quality of life and joint function, as well as a reduction in pain. Lastly, DFO has a high survival rate in the long term and osteotomy surgery significantly delaying the need for arthroplasty [19].

In addition to the types already discussed, there are several other kinds of osteotomies, each aimed at correcting specific deformities or conditions in different parts of the body. These include:

- Proximal Femoral Osteotomy (PFO): commonly used to treat hip deformities, especially in children and young adults. This procedure can correct alignment issues and load distribution on the hip joint, often related to dysplasia or diseases.
- Acetabular Osteotomy: performed to improve the alignment and functionality of the hip, especially in patients with dysplasia. It primarily aims to reposition the acetabulum for better coverage and support of the femoral head.

- Mandibular Osteotomy: this procedure is used to correct deformities of the jaw or face, including malocclusion problems that cannot be solved with orthodontic treatment alone. Mandibular osteotomies can significantly improve masticatory function and facial aesthetics.
- Calcaneal Osteotomy: aimed at correcting hindfoot deformities that can cause pain and dysfunction in walking.
- Metatarsal Osteotomy: used for the treatment of bunions.
- Spinal Osteotomy: necessary for correcting spinal deformities, it aims to restore a more natural alignment.

Each type of osteotomy has specific indications, surgical techniques and recovery protocols, based on the condition being treated and the individual needs of the patient. The selection of the appropriate type of osteotomy depends on a detailed evaluation of the bone deformity, functional goals and patient expectations, as well as the competence and experience of the orthopedic surgeon.

1.2 Surgical Plates in Traumatology and Orthopedics

A surgical plate is an implantable medical device designed to stabilize and support broken or weakened bones, facilitating the healing process and osteosynthesis.
Made from biocompatible materials such as titanium or stainless steel, this device is attached directly to the bone using screws to immobilize bone fragments in the correct position during the healing process. In **ASTM F382-17 standard** [20], a bone plate is described as a metal device with two or more holes, slots, or a combination thereof, and a cross-section that consist of at least two dimensions (width and thickness) that are generally not equal in size. The device is intended to provide alignment and fixation of two or more bone section, primarily by spanning the facture or defect.
Plates can vary in shape and size depending on their specific orthopedic or traumatological application. These devices are designed to be introduced inside the human body through precise surgical procedures, with the aim of restoring the anatomical and functional integrity of the musculoskeletal system. Consequently, the uses of bone plates are several, encompassing critical roles including fracture reduction to restore bone morphology in terms of length and alignment, and fracture fixation that ensures both absolute and relative stability. Furthermore, these plates facilitate early mobilization of the affected region, aiming for the complete recovery

of the patient, while also preserving soft tissue and bone vascularity. The different mechanical operations carried out by the plates include the transmission of forces across the bone, which facilitates the transfer of loads from one end to the other, sustaining the alignment of fracture fragments, providing stability to the fracture zone and safeguarding against overload.
Common features of orthopedic plates include, as exemplified in Fig. 1.13:

- **Anatomic contours**: plate design influenced the outcome of the biomechanics, for this reason the plates feature preformed contours that match the shape of the specific bone, facilitating surgical installation and improving alignment and stability.
- **Low profile**: this minimizes irritation of soft tissues, reducing the risk of post-operative complications.
- **Screw holes and slots configurations**: these are specially designed features to accommodate fixation screws, which anchor the plate to the bone. To ensure stability, it is essential to firmly attach the plate to the bone's surface using screws. The compressive force is then generated by applying a tightening torque to the screws, which is the rotational force used to turn them. To enhance the compression force, one can increase the applied torque or modify the plate's shape to better conform to the bone's surface.

Figure 1.13: Example of common features of Orthopedic Plates [21].

Plates also come with limitations, including extensive bone exposure during surgery and potential disruption of the blood supply. Preserving the biological integrity is crucial, as any disruption can result in significant delays in the healing process and increase the risk of infections.
Technological advancements in the field of trauma plates have led to the development of more sophisticated fixation systems, offering greater stability and promoting effective bone healing. The biomechanics of trauma plates play an important role in their effectiveness: the design must balance the need for mechanical stability with

the goal of minimizing damage to soft tissues and preserving bone vascularization. For this purpose, modern plate and screw systems are designed to reduce stress at the fracture site, evenly distributing the load across the bone and plate and to promote callus formation without impeding physiological movements.
The ongoing evolution of surgical techniques, along with advances in plate design and materials, has significantly improved patient outcomes, reducing healing times and enhancing post-operative quality of life. Plate engineering continues to evolve with the introduction of new technologies, such as 3D printing, which allows to produce custom plates based on the exact shape of the patient's bone, obtained through advanced imaging. This level of customization can further improve alignment, stability and healing.

1.2.1 Overview of Plate Classification in Medical Use

In orthopedic and trauma surgery, plates play a critical role in the treatment of bone fractures and injuries, a method of fracture management that has been used since the late 1800s [22]. The evolution of orthopedic plates over the years reflects advancements in medical technology and a deeper understanding of bone healing processes. Historically, from their initial use, these devices have undergone significant modifications to meet diverse clinical needs and improve patient outcomes. To date, there are several types, each designed for specific purposes and anatomical locations, which point to the diversity of clinical needs that may arise. The following classification will provide a brief and general description of the main types of plates used, emphasizing their mechanical distinctions, specifically how they differ in transmitting forces among screw, bone, and plate [23].

- **Locking Compression plates (LCP)** provide solid anchorage to stabilize fractures under suboptimal bone conditions, such as reduced bone density, fractures near joints, or osteoporosis. These devices (as depicted in Fig. 1.11), characterized by their ability to lock screws at a fixed angle, create a rigid system that maintains stability without the necessity for compression between the bone and the plate. However, the precise anatomical contouring of the plates is crucial for effective adaptation to the bone morphology. When applied, the plates exert pressure directly on the bone surface, which can impair blood supply by damaging vascular structures and consequently delay the bone healing process. Furthermore, LCPs require that fractured bone segments be meticulously reassembled to ensure the correct mechanical support and stabilization. Unlike some other systems where the screw head locks onto the plate, in LCP systems, the thread of the screw draws the bone towards the plate, maintaining the position of bone fragments through the pressure exerted by the plate itself.

- **O'Nil System – INTRAUMA Internal Fixator** takes a revolutionary step forward compared to LCP plates. While morphologically similar to traditional plates, it is mechanically equivalent to external fixators, yet stands out as a distinct and innovative osteosynthesis system. The key distinction lies in the interface between the self-locking screw and the support (Fig. 1.14), facilitated by a Morse taper coupling at the conical hole of the O'Nil bushing. Moreover, the O'Nil system uniquely manages the forces acting on the fracture by allowing the structure to elastically deform and return to its original state once the forces are removed, thereby providing a dynamic response to stress. This elastic behavior is crucial for managing the forces acting on a fracture, providing a dynamic response that enhances the healing process by maintaining a balance between stability and flexibility. Notably, the system incorporates new technology where the screw no longer exerts a pulling force to bring the bone towards the plate, which fundamentally changes how the device interacts with the bone. This alteration helps preserve the blood supply to the bone since the plate does not compress against it. Furthermore, the O'Nil system requires fewer screws and reduces surgery time, making the procedure less invasive. Its design, which does not require precise repositioning of bone fragments, simplifies the surgical process and may lead to quicker recoveries for patients, offering substantial advantages in clinical settings.

Figure 1.14: Detail of Morse coupling of locking screws in the O'Nil System [21].

- **Dynamic Compression Plates (DCP)** facilitate the application of constant force on the fractured bone, exerting pressure through the fracture site to promote direct contact between bone fragments and rapid consolidation. This aids in alignment and accelerates healing. DCPs utilize dynamic compression screws that slide within designated slots during bone closure and consolidation, enabling effective compression and stabilization. When used dynamically, continuous compression is maintained along the diaphyseal axis, fostering physiological consolidation and reducing the risk of failure.

- **Angular Stable Plates (ASP)** enhance the stability of bone fracture repair by using a specialized design that integrates polyaxial screws (Fig. 1.15). These screws can be fixed at predefined angles relative to the plate, forming a rigid construct that minimizes movement at the fracture site. This rigidity is crucial in cases where traditional fixation methods such as LCP and DCP might be inadequate, especially in complex fracture scenarios or in osteoporotic bones where screw grip might be compromised. The design of ASPs provides a flexible approach to screw placement, ensuring necessary stability without the precise contouring required by traditional plates, which must be exactly bent to match the bone's anatomy. This characteristic streamlines the surgical process and reduces its invasiveness. Additionally, ASPs have shown significant success in correcting both uniplanar and multiplanar deformities.

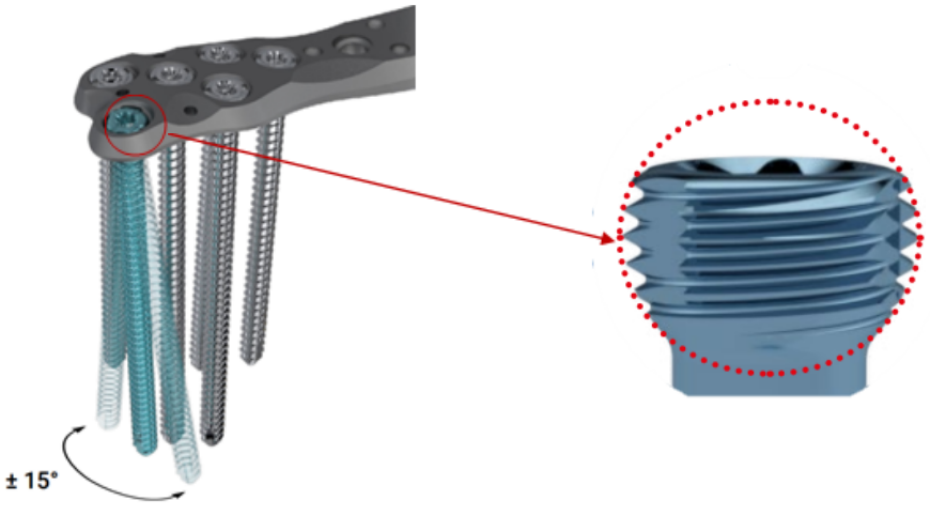


Figure 1.15: Details of polyaxial system [21].

Modern plates are typically anatomically pre-contoured, providing durable fixation within an environment that supports relative stability. This approach is less invasive and helps preserve the biological environment at the fracture site. However, the rigidity of LCP constructs can sometimes become too rigid, inhibiting sufficient interfragmentary motion, which is crucial for natural fracture healing through callus formation. In contrast, DCP and ASP systems may offer a solution by integrating the stability benefits of locked plating while still promoting fracture healing.

Furthermore, plates can be broadly classified based on their specific intended use, catering to distinct surgical needs and applications. The principal types will be outlined in the subsequent list.

- **Periarticular plates** are specifically designed to match the complex geometries of joints, providing support and stabilization in fractures that involve or are close to joints, without compromising functionality or limiting movement.

- **Periprosthetic plates** (Fig. 1.16) are specialized orthopedic devices used specifically around the areas of bone that interface with joint prostheses, such as hip or knee replacements. These plates are designed to provide support and stability in cases where there is a fracture in the bone surrounding a prosthetic joint (periprosthetic fractures) or an intramedullary nail. They typically feature complex designs with multiple screw options to allow for secure attachment in the limited bone stock typical of periprosthetic fractures. These plates may also include locking mechanisms that provide a firm, immovable fix between the plate and the screws, minimizing the risk of loosening under the mechanical loads associated with joint movement.

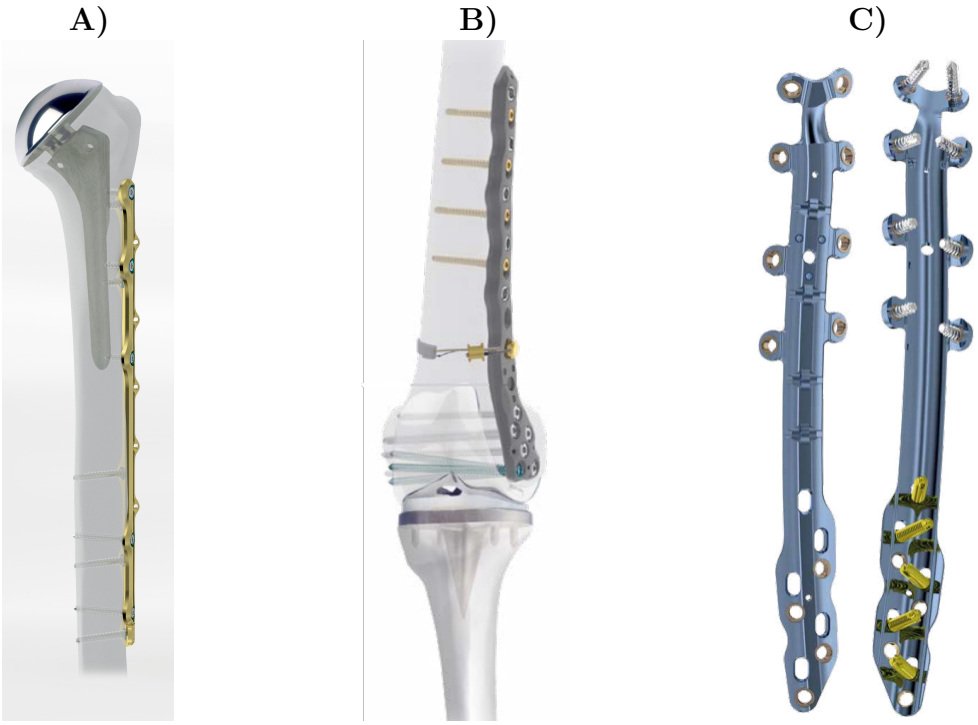


Figure 1.16: O'Nil periprosthetic plates for A) humerus periprosthetic fracture, B) distal femur and knee periprosthetic fractures, C) proximal femur and hip periprosthetic fractures [21].

- **Straight plates** (Fig. 1.17) are orthopedic devices characterized by their straight, elongated and relatively narrow structure.

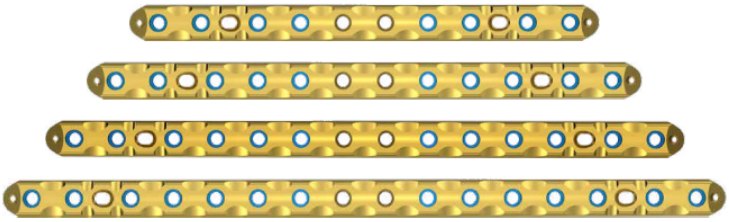


Figure 1.17: Straight supports for the treatment of diaphyseal fractures [21].

They are designed primarily for stabilizing long bone fractures, such as those in the arms and legs. Due to their shape and design, straight plates distribute the mechanical load along the length of the bone, maintaining alignment while facilitating the natural healing process. They are mainly used for the treatment of diaphysis fractures in long bones, such as the femur and humerus.

- **Osteotomy plates** (Fig. 1.18) are specialized devices designed specifically for surgical procedures where bone cutting or osteotomy are required to correct bone deformities or align the bones properly. The primary characteristic of these plates is to stabilize and maintain the bone in the desired position after an osteotomy has been performed.

Figure 1.18: Osteotomy Plates Series from INTRAUMA O'Nil System.

Another classification of bone plates is provided by the ASTM standard (ASTM F382-17) [20], which categorizes bone plates used in general orthopedic surgery into specific types based on their structural characteristics.

- **Cloverleaf plate**: a bone plate that has one three-lobed end which contains screw holes.
- **Cobra Head plate**: a bone plate that has one flared triangular or trapezoidal end which contains multiple screw holes or slots, or both. This type of bone plate is often used for hip arthrodesis.

- **Reconstruction plate**: a bone plate that does not have a uniform width, but usually has a smaller cross-section between the screw holes or slots. The reduced cross-section between screw holes/slots facilitates contouring the bone plate in several planes. Reconstruction plates are often used in fractures of the pelvis and acetabulum.
- **Straight plate**: a bone plate with uniform width and a straight longitudinal axis. Straight plates are often used for fractures of the diaphyses of long bones.
- **Tubular Plate**: a bone plate whose cross-section resembles a portion of a tube, and which has a constant thickness or a crescent section. Tubular plates are often used for fractures of the smaller long bones (that is, radius, ulna, fibula).

This diversity in the design and application of plates highlights the importance of a careful choice of device, based on a thorough understanding of the bone injury, limb biomechanics and individual user needs. Each type of plate has unique features in terms of material, design, and clinical application. The ongoing innovation in the design of trauma plates aims to improve surgical outcomes, reduce healing times and maximize the functional recovery of the patient.

1.2.2 Osteotomy Plates

Plates used in osteotomies are precision-engineered surgical devices designed to provide support and stability to bones during the post-osteotomy healing process [10]. As illustrated in figure 1.18, osteotomy plates vary widely in design, depending on the specific requirements of the osteotomy, including the bone involved and the nature of the correction needed. They are typically used in procedures involving joints as knees, hips and jaws, but can be applied to any bone requiring realignment or length adjustment.
The primary function of osteotomy plates is to ensure that the newly aligned bone segments maintain their position securely during the healing process. They must balance stiffness and flexibility to offer optimal support without excessively stressing the surrounding bone. From an engineering point of view, these plates are crafted to conform to complex bone shapes, to optimally and evenly distribute loads and to promote effective bone regeneration while minimizing the risk of implant failure. Therefore, implant position and geometry are vital parameters to maintain stability and the design should be modified to the surface geometry of the post-correction for the proper fitting [24].
Osteotomy plates are commonly made from biocompatible metal alloys, such as titanium and its alloys, or specific stainless steels for medical use. Titanium is especially valued for its excellent corrosion resistance, biocompatibility and elasticity

similar to natural bone, thus reducing the risk of stress shielding (the reduction of stress on the surrounding bone, which can lead to its degradation).

In conclusion, osteotomy plates represent a synergy of materials science, mechanical engineering and biomechanical principles, designed to effectively support the bone healing process following an osteotomy procedure. The choice of the appropriate plate, alongside surgical technique, is essential for the success of the osteotomy and the patient recovery.

1.2.3 Composition Materials of Medical Plates

Implantable medical devices, such as surgical plates, are designed to interact with the human body in ways that support or replace biological functions. Selecting the right material for these devices is essential because it must be biocompatible, durable and tailored for the specific Intended Use.

Titanium, along with its alloys, is one of the most favored materials in the field of implantable medical devices, especially for surgical plates, due to its exceptional biocompatibility [25]. This means that titanium does not induce adverse reactions in the body, making it an ideal candidate for long-term applications. Another key property of titanium is the corrosion resistance: this is indispensable because the material must preserve its integrity and functionality in body fluid over extended periods without degrading. Moreover, titanium is known for its favorable strength-to-weight ratio, mechanical properties comparable to those of human bone, and its excellent elasticity. This minimizes the risk of adverse reactions, allowing for better bone integration and thus reducing the risk of stress shielding. There are several alloys and grades of titanium, each with specific properties and applications. The main types used for surgical devices are Pure Titanium (Grade 4), which offer superior mechanical strength, but less machinability compared to other grades of titanium, and the Ti-6Al-4V alloy (Titanium Grade 5) [26]. This alloy is the most used in medical applications because the combination of aluminum and vanadium significantly improves the mechanical strength of titanium without significantly compromising biocompatibility. The first one is commonly used for applications that require greater strength, while the second is predominantly employed in orthopedic and dental applications.

Stainless steel, on the other hand, is traditionally used in many types of medical implants due to its high strength and ability to withstand mechanical stresses [27]. However, it does not reach the level of biocompatibility of titanium, as it can release ions into the body that in rare cases may cause a reaction. Nonetheless, its durability and corrosion resistance make it a viable option for many surgical applications.

AISI 316 LVM (Low Vacuum Melted) stainless steel stands out among steels used for implantable medical devices and is widely used, in particular for orthopedic surgery, because it combines good biofunctionality and acceptable biocompatibility at low costs [28], thanks to a production process that involves vacuum melting, known to significantly improve the material's purity and properties. This type of stainless steel is designed to ensure maximum biocompatibility and corrosion resistance in critical applications where safety and long-term durability are imperative. The improvement of the chemical composition is aimed at maximising the material's resistance to corrosion by obtaining a ferrite-free metallographic structure [29]. Vacuum melting reduces the impurities that can compromise these qualities and gives the steel a homogeneous structure and a uniform distribution of alloying elements, further enhancing its mechanical properties. Its superior corrosion resistance also ensures that the material does not degrade over time, preventing the release of metallic ions that could cause adverse reactions in patients.

Cobalt-chrome alloys must also be considered, distinguished for their extraordinary wear and very highly corrosion resistance because of the natural development of a passive oxide layer inside the environment of the human body, essential characteristics for long-term implants like prostheses. They are particularly valuable in applications where an extremely smooth and wear-resistant surface is required [30], such as in knee and hip prostheses, where minimizing friction and wear between joint components is crucial for the implant's success.

To sum up, selecting the appropriate metal for an implantable medical device is based on a balance between biocompatibility, mechanical strength, corrosion resistance and the specific requirements of the surgical application. Titanium and its alloys are often preferred for most implantable applications due to their superior biocompatibility and corrosion resistance [31].

1.3 Regulatory Requirements

This section examines the regulatory framework governing the certification of medical devices. As the healthcare industry continues to evolve, stringent regulations ensure that medical devices meet rigorous safety and performance standards before they reach the market. The following subsections, will explore the specific mandates of Regulation, detailing the comprehensive criteria that medical devices must satisfy to achieve certification and compliance within the European Union.

1.3.1 MDR 2017/745

Regulation (EU) 2017/745 of the European Parliament and of the Council [32], commonly referred to as the Medical Devices Regulation (MDR), governs the marketing and monitoring of medical devices within the European Union and represents a significant advancement over the previous Medical Devices Directive (MDD). Adopted with the aim of strengthening the pre-existing regulatory framework, the MDR is designed to ensure a high level of health and safety protection for users and patients, as well as to promote fair and transparent trade in medical devices. Consequently, this thesis, conducted in collaboration with the company, aims to update compliance procedures to align with the more detailed and stringent standards set by the MDR, replacing the practices based on the less detailed and obsolete MDD Directive.

Structured with 123 articles and 17 annexes, the MDR introduces a robust regulatory environment aimed at enhancing the safety, traceability, and accountability of medical devices within the European Union. Unlike the MDD, which allowed for variability in national implementation, the MDR is a regulation that applies uniformly across all EU member states, ensuring consistent application and enforcement. This transition reflects a comprehensive approach, emphasizing a rigorous lifecycle management of medical device, from market entry through post-market surveillance. Critical to the MDR's framework is the introduction of a Unique Device Identification (UDI) system and the enhanced role of EUDAMED, the European database, which together facilitate greater transparency and monitoring capabilities. Additionally, the regulation mandates that manufacturers appoint a designated person responsible for regulatory compliance (PRRC), thereby centralizing accountability. The expanded scope of the MDR not only covers a broader array of devices but also imposes more stringent requirements on clinical evaluations, market surveillance, and the management of device-related incidents, significantly advancing the regulatory oversight compared to the MDD. These measures collectively aim to protect public health and ensure the devices' safety and performance throughout their Intended Use.

In this thesis, particular attention is given to the design and production processes of medical devices. **Annex I**, which outlines the 'General Safety and Performance Requirements,' sets the cornerstone for the safe and effective design of devices. These requirements include minimizing potential risks associated with the use and ensures that they perform correctly for their intended purpose. The design process must therefore consider all phases of the device's lifecycle, from conception to decommissioning, including safety testing, biocompatibility assessment, performance under expected conditions, and clinical efficacy.

Regarding documentation, the MDR mandates the creation of a comprehensive 'Technical File' for each device, as detailed in **Annexes II and III**. Annex II addresses the technical documentation that manufacturers must compile and maintain to demonstrate compliance with the requirements of Annex I. This documentation must be presented in a clear and organized manner to facilitate assessment by notified bodies. It should include a detailed description of the device, an explanation of its design and technical specifications, along with a comprehensive risk assessment and exhaustive documentation of tests and experimental results. It is crucial to keep the technical file up-to-date, reflecting any changes in the design or Intended Use of the device. The technical documentation must be drafted in a way that is easily searchable and unambiguous, with complete details on the design, production, and verification processes of the device. The design and development process also requires close interdisciplinary collaboration. Medical device developers must work closely with clinical experts, engineers, designers, and importantly, with patients or end-users. This collaborative approach is essential to ensure that the medical device is not only technically reliable but also tailored to the real needs and expectations of the users.
Annex III, on the other hand, deals with the technical documentation on post-market surveillance, which is crucial to ensure that medical devices continue to operate safely and effectively after being marketed, by constantly monitoring their performance and the impact on the health of users. The PMS system is tasked with systematically collecting data, which includes user feedback, complaints, information on adverse events, and any other relevant information that might indicate safety or performance issues.

In conclusion, Annexes I, II, and III of the MDR create a robust framework that medical device manufacturers must follow to ensure their products are safe and effective for human use. The design and development procedure outlined in the subsequent chapters aims to systematically integrate these MDR principles into the internal development process.

1.3.2 ISO 13485:2016

ISO 13485:2016 "Medical devices – Quality management systems – Requirements for regulatory purposes" [33] is an internationally recognized standard that ensures medical device manufacturers meet stringent regulatory requirements through their quality management systems. Its primary goal is to facilitate consistent medical device regulatory requirements and provide a guide for manufacturers to consistently meet customer expectations and regulatory standards.

The standard encompasses all stages of a medical device's lifecycle, including design, development, production, installation, and servicing, with a particular emphasis on risk management and the maintenance of effective processes for safe design. It is organized into several main sections and supplementary annexes that illustrate its relationship with European Union legislation and other relevant regulatory directives. It is important to note that while ISO 13485:2016 provides a robust foundation for regulatory compliance, it does not cover specific regulatory requirements in detail, such as those related to clinical evaluation, risk management, post-market surveillance, and the unique device identification (UDI). Organizations are required to independently incorporate these components in accordance with the relevant laws to achieve comprehensive regulatory compliance.

The most pertinent part of the document for medical device design is found in **Section 7.3**, which details the device development process. This section forms an integral part of the procedure developed in this thesis, significantly influencing the methodologies and approaches discussed in subsequent chapters. Specifically, the process begins with detailed planning of design and development, during which organizations must establish and maintain plans that outline the stages of the development process, including review, verification, and validation processes for each stage. Design inputs, including regulatory, performance, and safety requirements, must be clearly defined and unambiguous. These inputs form the basis for the design outputs, which must be meticulously documented to ensure they meet all initial inputs. Accurate documentation and validation of outputs are critical steps that confirm the design's compliance with the original specifications. Design reviews are conducted at planned intervals to assess the design's efficacy in meeting requirements and to identify and rectify any discrepancies. The final step, the final design validation, verifies the design's suitability before large-scale production, confirming that the finished devices are compliant and fit for their Intended Use. Change control is equally important; all changes to the design during the development process must be strictly managed. This includes the identification, documentation, review, and approval of changes prior to their implementation, ensuring that changes do not compromise the device's quality or compliance.

In summary, the design and development process described in ISO 13485:2016 underscores a structured approach to medical devices fabrication, essential for meeting both customer needs and regulatory requirements.

Chapter 2

Design and Development Procedure

2.1 Purpose and General Principles

The design and development procedure is crucial for the company, impacting product processes and documentation to ensure effective development of new medical devices. This chapter explores planning, control, review, validation of design processes, and management of product changes and production processes. The goal is to ensure a continuous, reliable development process maintaining performance and compliance of medical devices.

The procedure is structured into four main phases, outlining a pathway that, although standardized, adapts to the specifics of the project in terms of size, complexity, and risk. Each phase undergoes a systematic review by a functional team, including representatives from all company departments, such as marketing, research and development, production, and quality management. These reviews ensure each phase meets technical requirements, users' expectations, and current regulations. During the project reviews, which take place at the end of each development phase, the team evaluates the adequacy of the design requirements and the effectiveness of the design in meeting them. These reviews must be documented, reporting the decisions made and the rationale behind the choices. The outcomes of these reviews may include approval, requests for further validations, or modifications with detailed action plans. Finally, the process includes an audit of the design review, conducted before proceeding to the next design phase. This verification, performed by the Independent Reviewer (IR), ensures that all results are complete and that objective evidence has been adequately examined. Final approval is given only when all results are accurate and complete.

2.2 Flow-chart of Development Stages

The figure 2.1 shows the flow of the design phases to be followed as per the procedure, which will be described in detail in the following chapters.

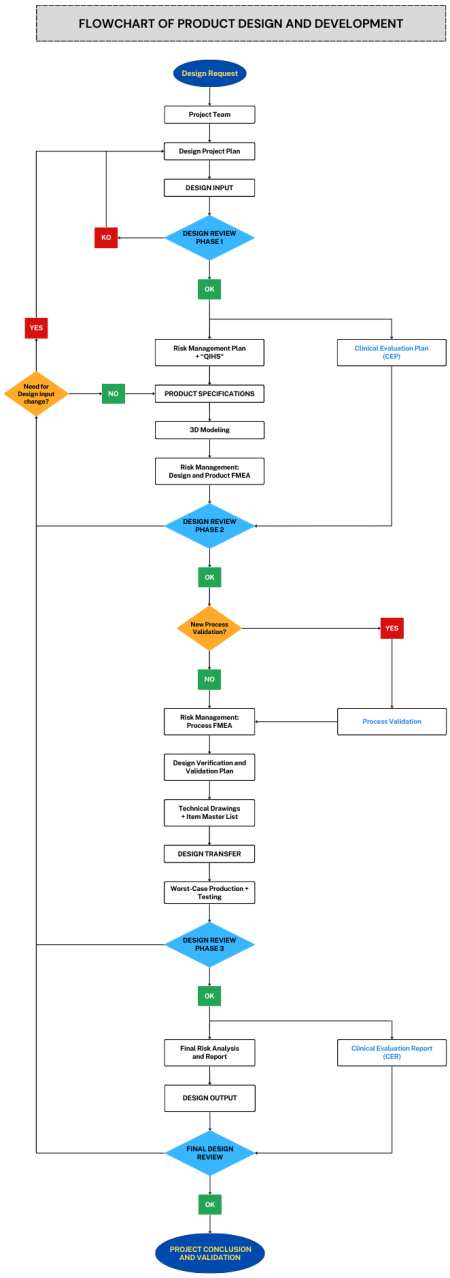


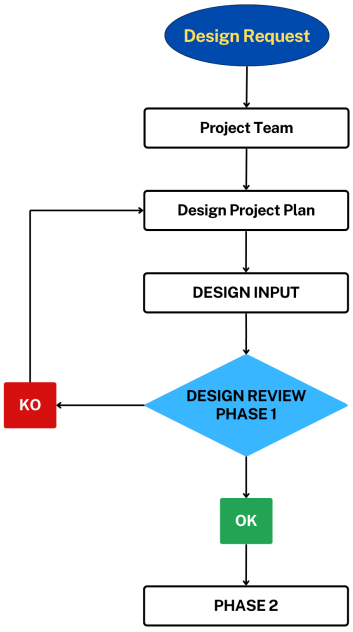
Figure 2.1: Flowchart of Design and Development Procedure.

2.3 Design Modules Features for Technical File

2.3.1 Phase 1: Project Setup and Design Input

Phase 1 of the product development cycle, as shown in Tab. 2.1, set the groundwork for subsequent stages. This phase encompasses specific design control activities and key deliverables, all meticulously documented in the Design Project Plan.

The development process is initiated by a commercial request for project development, which may be followed by a market analysis (if deemed necessary). The most important component of Phase 1 is the identification of User Needs and Design Inputs, which form the basis for the device's design criteria. Additionally, this phase involves a thorough assessment of project timelines and the composition of the project team.



Deliverables:

I. Project Request

II. Project Team

III. **Design Input**

IV. Design Project Plan

V. Market and Competitor Analysis

VI. Design Review of Phase 1

Table 2.1: Phase 1 flowchart.

Project Request

The initiation of any new product development within INTRAUMA S.p.A. begins with the formal documentation of a project request, a catalyst for the activities that follow. Typically, the initiation can be processed through a standardized "Project Request" form, or alternatively, it can be recorded during a meeting. Each project is meticulously recorded and cataloged by a unique identifier that includes a progressive number, the year, the project type, and a detailed description of request, enabling stakeholders to monitor the project's lifecycle effectively from conception through to completion.

This method ensures that the project request is not only stored in a central intranet folder for easy accessibility but also maintains the necessary transparency, traceability, and oversight of the evaluation processes and the progression of related activities.

Project Team Composition and Responsibility Matrix

The composition of the project team is the first step following the project request, where each role is assigned to an appropriate individual as defined in the **responsibility matrix** (Fig. 2.2), which is included within the procedure. The responsibility matrix is not a simple assignment of tasks, but a comprehensive diagram that tracks the involvement of business positions in the different stages of the development process.

Document Matter	**TPL**	**CEO/DIR**	**RDD/PRRC**	**DRT**	**RSV**	**RUT**	**RGQ**	**PROD**	**COM**	**MKT**	**CLIN**	**RVI**
Market Analyses	●				●				●			
Risk Management and Risk Analyses	●				●	●	●					
Product & Process FMEA	●			●		●	●	●				
Design Input / Design Output	●		●	●	●	●	●					
Product Specification	●				●	●	●					
Design Transfer	●			●	●	●	●	●				
Packaging & Labeling	●					●	●	●				
Clinical Evaluation Plan (CEP)	●		●				●					
Clinical Evaluation Report (CER)	●		●				●				●	
Biocompatibility & Sterilization	●				●		●					
Surgical Technique	●				●		●		●			
Verification & Validation	●			●	●	●	●					
Intermediate Phase Design Reviews	●	●	●	●	●	●	●		●			●
Design Final Review	●	●	●	●	●	●	●	●	●	●		●

Figure 2.2: Responsibility Matrix

It is constructed based on the current organizational structure of the company, ensuring that each team member's duties are clear and aligned with their professional capabilities and the strategic objectives of the project. The complexity and scope of the project often dictate the degree of functional involvement required; however, the structure remains flexible enough to adapt to project-specific needs without compromising the integrity and efficiency of the team.

The formal assembly of the project team is executed through the "Project Team" form, which details the responsibilities assigned to each project activity. This delineation is further reported and elaborated in the Design Project Plan, that is instrumental in guiding the project through its stages, ensuring that all team members are aligned and that the project adheres to predefined milestones and quality standards.

Design Project Plan

Subsequent to the project request and team composition, the structured approach detailed in the flow-chart referenced in the Chapter 2.2 is performed. This approach is important for maintaining control over the product development process, ensuring that all necessary activities are carried out effectively. The "Design Project Plan" form, managed by the **Project Leader** (**TPL**), who has the specific responsibility for the strategic planning of design activities, is implemented. It is similar to a Gantt chart, visually outlines the project timeline against work tasks, providing a clear schedule of when tasks should start and finish. The visualization aids in monitoring progress and coordinating different aspects of the project.
The Design Project Plan details several key aspects:

- **Identification of the main design phases**: This includes critical activities such as Verification, Validation and Design Transfer.
- **Timeline and Milestones**: Established to ensure timely progression and alignment with the project's objectives.
- **Responsibilities**: Clearly delineated for all team members to foster accountability and efficient task management.
- **Necessary time frames**: Specified for each phase to facilitate effective resource allocation and adherence to schedules.
- **Resource allocation**: Comprehensive identification of all resources involved, ensuring that the project is fully equipped to meet its defined goals.

Design Inputs and User Needs

The identification and documentation of Design Inputs and User Needs are central to the first phase of the device development process, both of which are included in the "Design Input" form. All physical and performance requirements of the device are directly tied to the articulated needs of the users, which include patients, healthcare professionals and any other stakeholders interacting with the device.

User Needs are extracted from different sources, such as market research, customer complaint data, and reviews of previously marketed or competitor devices, for a comprehensive understanding of the requirements. These needs address essential factors like surgeons' request to accommodate specific patient populations, surgical techniques, and explaining of the use of instrumentation systems. For instance, surgeons may specify the need for devices adaptable to diverse surgical approaches or robust enough to ensure safety and during operations.

Simultaneously, these identified User Needs are transformed into **Design Inputs**, which specify the functional and safety requirements the device must meet. These inputs also consider safety standards, regulatory and manufacturing requirements, and environmental compatibility; thus each one is carefully developed in order to be consistent with user needs, including aspects like intended use, functionality, performance parameters, toxicity and biocompatibility.

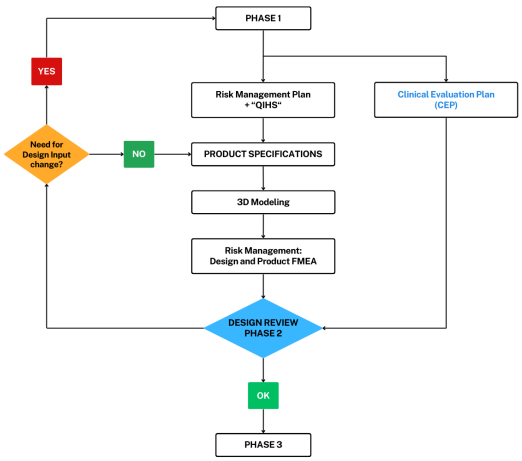
The completion of the "Design Input" form, which includes a comprehensive list of User Needs and Design Inputs, marks a milestone in the design process, as every aspect of the device's requirements is considered and documented, setting a solid foundation for the subsequent design phases. The accuracy of this approach helps maintain the project's alignment with user expectations and regulatory standards, facilitating a smooth transition to the next phase of development.

Design Review Phase 1

The end of the first step is marked by the first Design Review, which is a critical evaluation point where the deliverables of Phase 1 are reviewed to ensure that all initial requirements are met. This review is conducted using the "Design Review – Phase 1" form, where all deliverables are listed and assessed.
A positive conclusion from this review formalizes the successful completion of the initial phase and authorizes the project to transition to the subsequent design phase. This phase review ensures that the project remains in line with stipulated quality and regulatory standards and is prepared for the next stages of development with all necessary elements.

2.3.2 Phase 2: Product Architecture

The following flowchart (Tab. 2.2) depicts Phase 2 of the Product Development Cycle. The specific design control activities and deliverables to be completed in Phase 2 are documented in the Design Project Plan.



Deliverables:

I. Risk Management Plan and Design & Product FMEA

II. **Product Specification**

III. Technical Drawings

IV. CAD Models

V. Item Master List

VI. Draft of Design Outputs

VII. Clinical Evaluation Plan (CEP)

VIII. Design Review of Phase 2

Table 2.2: Phase 2 flowchart.

Phase 2 passes through the documents founding the development of product and process. In particular, the project is defined in more detail by producing documentation relating to risk management and the technical details of the product (including CAD models), we begin to collect the design outputs and draft the article codes.

Risk Management

The Risk Management Plan is a comprehensive document that outlines the tools and techniques utilized by INTRAUMA in managing risks throughout the entire lifecycle of the device. This lifecycle, as illustrated in Fig. 2.3) spans from the initial concept phase through to production, post-production, and ultimately the end of the product's life cycle.
A Risk Management Plan acts as a strategic guide to identify, evaluate, and mitigate potential risks that could impact the safety of the device. It includes procedures and methodologies to anticipate and address potential failures before they occur. One of the core methodologies included in this plan is the Failure Mode and Effects

Analysis (FMEA), which is conducted in accordance with INTRAUMA's internal risk management procedures. These procedures are not detailed within the scope of this thesis.

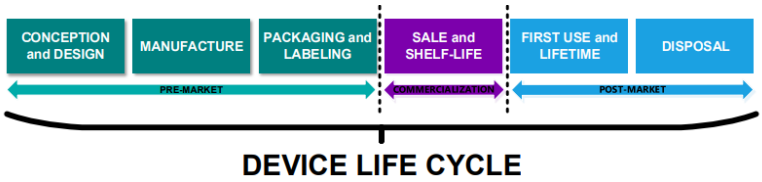


Figure 2.3: Medical Device Lifecycle.

The risk analysis process begins with the identification of design inputs that are crucial for mitigating risks. During this process, critical design characteristics are identified, these are specific attributes of the device that directly influence its safety and intended use. Identifying these characteristics early in the design phase allows for the development of robust acceptance criteria, which serve as benchmarks for ensuring that the device meets all safety and performance standards.

Product Specifications

Product specifications, which form an essential part of the technical documentation, are a detailed technical description of the requirements and characteristics that a medical device must have to comply with regulatory standards and meet the expectations of end-users. Through the use of the "Product Specifications" document, all technical characteristics of the product are incorporated into the project. This includes sizes, materials, finishes, compatibility, risk class, Intended Use, as well as a general description of the relevant anatomical compartment. By thoroughly documenting all these aspects, INTRAUMA ensures that all technical characteristics of the product are clearly reported.
Product specifications generally include:

- **General description** of the device, where are specified: Device Name, Intended Use, Intended Purpose, Intended User and Environment.
- **Description of functionalities** and **Instructions for Use**, including contraindications and potential adverse events that may occur during the use of the device. It is particularly important as it outlines how the device should be used, ensuring that users are fully informed about the correct usage of the device and any associated risks.
- **Functional and performance requirements**, namely the operational characteristics and usage modes, technical specifications and expected performance

parameters. These requirements serve as benchmarks for the design and testing phases of devices.

- **Technical requirements**, i.e. a description of the user interface, expected lifespan and the implementation of calibration and maintenance guidelines.
- **Regulatory requirements**, applicable regulations and device classification (depending on the country where it will be marketed).
- **Manufacturing requirements**, with information about the materials used and surface finishing.
- Any **related devices and compatibility** with other devices or instruments have to be outlined.

Finalization of Technical Drawings and CAD Models

Phase 2 requires the finalization of 3D models constructed using the company's modeling software. CAD (Computer-Aided Design) models are digital representations of the product, offering a three-dimensional view that allows for detailed visualization and analysis. These models are integral to the design process as they enable designers to examine the product from all angles, assess the fit and function of individual components, and make necessary adjustments before physical prototypes are created. Finalizing these CAD models ensures that all aspects of the design are refined and optimized for production.

Additionally, Phase 2 necessitates the completion of technical drawings at the finished product level. By "finished product level," we refer to technical drawings that include the product's bill of materials (BOM), laser marking plan, and surface finish specifications. Technical Drawings are precise representations of the product, detailing all necessary dimensions, materials, and processes required for manufacturing that serve as a guide for the production process. The inclusion of the BOM in these drawings lists all the materials and components needed, while the laser marking plan specifies any markings required for identification or regulatory compliance. Surface finish specifications describe the final texture and treatment of the product surfaces, which can affect both aesthetics and functionality.

Item Master List

The Item Master List is a catalog of project-specific item part numbers, with descriptions, drawing codes and **UDI-DI codes**. It is produced using the "Item Master List" form, crucial for maintaining organized and accessible records of all

components and versions associated with the device. The Unique Device Identification (UDI) system, required by the MDR 2017/745, enhances the traceability and safety of medical devices. The UDI-DI (Device Identifier) is a part of this system, providing a unique identifier for each device model, linking it to detailed information about the product.

The Project Leader (TPL) is responsible for providing a complete and updated Item Master List, which must clearly state all versions of the device in their latest revisions. A non-final version of the document is provided at this stage, which will be updated in the next phase with process and design transfer data.

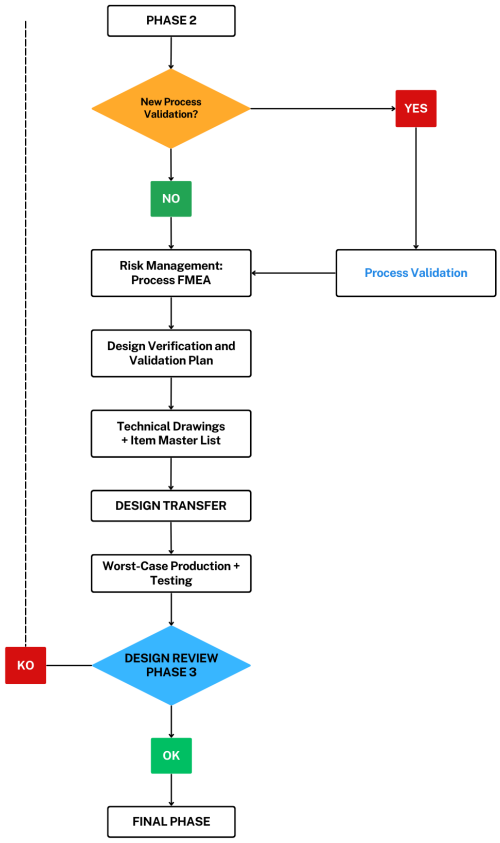
Design Review Phase 2

The Phase 2 review is conducted to evaluate and verify the deliverables completed during this stage. The first prerequisite for accessing this review is the successful completion and review of Phase 1. Using the "Design Review – Phase 2" form, it ensures that all technical drawings, CAD models, and related documentation meet the stipulated quality standards. A draft document that collects design outputs is also compiled and will be completed in the next stage (see next chapter for details). A successful review marks the formal closure of Phase 2 and authorizes the transition to the next design phase, ensuring that the project remains on track and adheres to all predefined criteria.

2.3.3 Phase 3: Industrialization and V&V Protocols

The Table 2.3 depicts the Phase 3 of the Product Development Cycle. The specific design control activities and deliverables to be completed in this phase are documented in the Design Project Plan.

During Phase 3, all activities related to project verification, validation, and industrialization take place. Based on these, the Design Output, as well as the Design Project Plan and Product Specifications, will be updated as necessary and additional inputs may also be generated. New or modified inputs will be recorded using the "Design Input" forms. Should any ambiguous or conflicting design inputs arise during the project, they will be resolved and approved by the project team. Each identified design input will correspond to a specific design output.
Packaging and Labeling development, including the design of both primary and secondary packaging, is also conducted in this phase. This may trigger a specific packaging development protocol. If the device under development is similar in design, geometry, weight and intended use to an existing device, packaging development can be managed through the creation of an equivalence document.



Deliverables:

I. Process FMEA

II. Worst Case Analysis

III. **Design Transfer**

IV. Verification/Validation Protocol

V. Bill of Material (BOM) and Product Process Flow definition

VI. Packaging & Labeling Specification

VII. Instructions for Use (IFU)

VIII. Technical Drawings

IX. Update Item Master List

X. Draft of Design Outputs

XI. Design Review of Phase 3

Table 2.3: Phase 3 flowchart.

Process FMEA

Process FMEA is a structured technique for identifying and evaluating potential failures in production processes. By analysing the causes, failure modes, and their effects, the impact of each failure on product quality and process performance is determined. It is used to identify critical areas where problems may occur, allowing for the implementation of preventive actions to improve reliability and reduce associated risks. This methodology aids organizations in optimizing processes, enhancing product quality, and mitigating risks.
The Process FMEA document must be attached to the design transfer checklist. If the manufacturing routing involves new or not yet implemented production processes, a process validation procedure must be initiated, which must include, in the case of a non-special process, at least **IQ** (Installation Qualification) and **PFMEA** (Process FMEA).

Worst-Case Analysis

The Worst-Case Analysis is a methodology used to evaluate the behavior and performance of a system or its components under the most unfavorable conditions possible. In the context of a range of mechanical plates, this analysis aims to identify the plate with the weakest resistance and performance characteristics, ensuring that the test results are valid for the entire range. This approach optimizes time and resources by testing only the weakest plate, thereby guaranteeing that all other plates, which perform better, meet the required standards.
The process begins with identifying the key parameters that influence the strength and durability of the plates, followed by assessing their variations. Through simulations and mathematical models, the behavior of the plates under various stress conditions is predicted, allowing for the selection of the plate with the most unfavorable combination of parameters. Once identified, this plate undergoes rigorous mechanical testing. The results are then used to validate the entire range, ensuring that all plates meet the quality and safety requirements, reducing the risk of failure, and enhancing the overall reliability of the product.

Design Transfer and Device Master Record (DMR)

The Design Transfer can be considered the link between the design and production stages of product and it ensures that the design is translated into production specifications. Although it is considered the final design control phase, design transfer activities is usually carried out starting early during the development process and run concurrently with other activities. This approach ensures that the devices used in the design validation phase are manufactured using the validated methods and procedures intended for series production.
During this stage, **the design transfer is limited to the worst-case products** that will undergo laboratory testing. The results of the design transfer process is the creation of the Device Master Record (DMR). Depending on the product or device, DMR elements must include at least the following:

- **Bill of materials** - The manufacturing BOM consists of the components and subcomponents assembled to create the final part. The packaging BOM consists of the packaging materials, labels and IFUs to create the final packaged part. BOMs are inserted in the Enterprise Resource Planning Software (ERP).

- **Manufacturing Routings** - The manufacturing routings include the work steps, procedures and relevant documents required to manufacture the products internally. This step should include a review of procedures and documents to ensure the product has been included. The routings are stored in the ERP.

- **Package Insert** - Package insert needs to be completed and documented with any device instructions. It includes the IFUs.
- **Labeling** - Labeling needs to be complete and documented.
- **Technical drawings** - Technical drawings detail the dimensions, material specifications and process required to manufacture the finished part. Technical drawings are stored in the File System and the updated list of currently valid technical drawings is reported in the document "Elenco disegni".
- **Quality control sheets**.

The **Design Transfer Leader** (DTL) will be assigned by the project team. The person responsible for the design transfer can be a representative from quality engineering or operational engineering.
A complete list of deliverables for the project transfer is documented in the project transfer checklist in form "Design Review – Phase 3" and must be completed prior to the final project review. An uncompleted deliverable will be considered an open action item and will require an action plan. Before proceeding with the transfer of the project, a justification must be provided as to why the action plan is acceptable.

A *Make vs Buy* confirmation for the project scope will be established with the design transfer checklist:

- *Make* = All scope items are produced/assembled internally.
- *Buy* = All items in scope are produced externally.
- *Make* & *Buy* = Scope items are produced internally and produced externally.

Verification/Validation Tests & Protocols

It is necessary to draw up the appropriate design verification and validation protocols. **Design verification** aims to ensure that the design outputs conform to the requirements specified by the design inputs, to eliminate possible design errors or optimize the performance of the design process. If some checks and validations are not carried out because previous devices are already appropriate for the ongoing project, it is still necessary to draw up an equivalence note. If reports or equivalence documents are collected during this phase, these documents can already be reported in the design output document. The assessment conducted during the **validation activity** considers the functional requirements, safety and performance requirements, and interference requirements, as well as product labeling to ensure that it complies with legal requirements and reference standards, and at the same time understandable and useful for the intended user.

The validation activities must be conducted using devices belonging to the initial production, or their equivalents, in actual or simulated modes of use and produced as defined in the DMR. The rationale justifying the choice of the product used in the validation protocol (worst case) must be recorded and a validation plan must be drawn up which includes the methods, acceptance criteria and, where appropriate, statistical techniques with the related rationale for the sample size used. This validation plan must include a clinical evaluation of the product in accordance with art. 61 of the MDR.

Test samples for the design verification activities must be representative of the final product design and/or feature being tested. Test parts should be representative of the final manufacturing process. Critical features tested should be inspected to verify design intent. If there are differences between test parts and production parts, an equivalence rationale must be included in the appropriate file. The methods of execution of these activities must be described, as well as the description of the test and functional operating conditions, the parameters of acceptability of the results (these must be defined before conducting V&V activities) and, where appropriate, statistical techniques with the related rationale for the sample size used. In the case of products whose indication of use includes connection or interface with other devices, the verification must include confirmation that the outputs satisfy the inputs when the devices themselves are connected or interfaced with each other.

Design V&V activities are typically based on risk analysis and may include the following:

- Finite element analysis;
- Tolerance analysis;
- Experimental analysis, as physical and chemical analysis;
- Performance test (i.e. mechanical tests, shipping test);
- Packaging, sterilization and shelf-life validations;
- Biocompatibility evaluation.

In particular, for **Mechanical Testing**, products will be tested in accordance with current technical specifications which will refer to documented protocols and standards, where applicable. Test protocols and acceptance criteria should be established and documented before testing begins. Where appropriate, verification protocols will be reviewed and approved by a qualified person upon completion of the document or prior to verification activity.

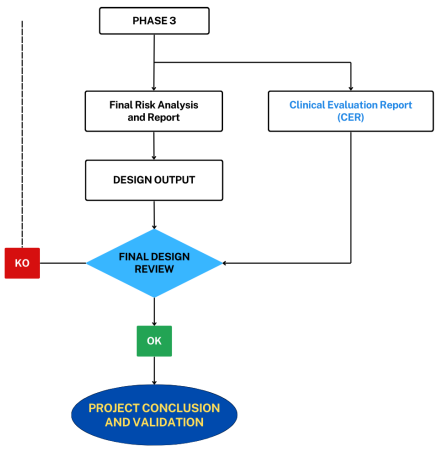
For the **Sterilization Validation**, once the sterilization method is determined, development of a sterilization validation protocol is initiated or, if the proposed device is similar in design and manufacturing to an existing device, an equivalence document can be written. Regarding the determination of the shelf life, the same assessments expressed previously can be applied.

Design Review Phase 3

The Phase 3 review is conducted to evaluate and verify the deliverables completed during this stage. The first prerequisite for accessing this review is the successful completion and review of Phase 2. Using the "Design Review – Phase 3" form, this review ensures that all verification, validation, and industrialization activities, including updated Design Outputs document and risk analysis (Process FMEA), meet the required standards.
A successful review signifies the formal closure of Phase 3 and authorizes the project to advance to the final stages of development.

2.3.4 Final Phase: Design Output and Project Closure

The following table 2.4 represents the Final Phase of the development procedure. The design control activities and deliverables to be completed in this last phase of the product development process are documented in the Design Project Plan.



Deliverables:

I. **Design Output**

II. Verification & Validation Reports

III. Clinical Evaluation Report

IV. General Safety and Performance Requirements (GSPR)

V. Surgical Technique

VI. Final Design Review & Project Validation

Table 2.4: Phase 4 flowchart.

During the Final Phase, all documents integral to the product development process are finalized. This includes the collection and consolidation of all verification and validation test reports, ensuring that the Design Output is comprehensively updated to reflect all relevant documents and maintain conformity with the design inputs. The Clinical Evaluation Report (CER), the General Safety and Performance Requirements (GSPR) assessment and the Surgical Technique are drafted. Additionally, Design Transfer is completed for all part numbers within the project's scope, ensuring that production specifications are fully developed and ready for implementation. The Final Phase also involves the critical step of the Final Design Review, which serves as the ultimate validation of the entire project. This review verifies that all design outputs align with the initial design inputs and regulatory standards.

Upon successful completion, the project transitions to the creation of the **Technical File** required for CE certification. This technical file, compiling all developed documents and reports, is then submitted to the notified bodies, marking the conclusion of all development activities.

Design Outputs

Design outputs are the definitive product characteristics that enable the subsequent phases of activity to be carried out efficiently, leading to production and supply. These outputs are collected throughout the entire product development cycle, starting from Phase 2 with the product specifications, continuing through all phases, and culminating in this final phase.
Design outputs are essentially the collection of documents that must meet the requirements established in the design inputs, providing detailed guidance on how to create and maintain the product. They include comprehensive technical documentation that facilitates the identification of the product, its characteristics and performance, as well as the implementation and control of the entire production process. By detailing every aspect of the product, from its materials and dimensions to its functional requirements and performance parameters, Design Output records typically encompass product specifications, technical drawings, work instructions, quality assurance procedures and packaging and labeling specifications. As the design process progresses, documentation and reports are continuously generated and references to these documents are systematically inserted into the appropriate "Design Output" form.

Design Validation involves activities aimed at ensuring that the product, as designed and manufactured, conforms to the defined inputs. This validation process considers a lot of factors, including the knowledge and capabilities of the intended user, operating instructions (such as the Surgical Technique), compatibility with

other systems, the environment in which the product will be used, and any usage restrictions. Design validation activities are typically driven by risk analysis to ensure thorough examination and mitigation of potential risks.
Output validation methods and activities may include:

- Surgeon review and evaluation.
- Functional tests in cadaver, animal, or synthetic (sawbones) materials.
- Animal/Biological analysis.
- Usability testing.
- Validation of labeling materials, including Instructions for Use (IFU) and training materials.
- Instrument cleanability, reprocessing, assembly and disassembly.

The results of the design validation are comprehensively documented in the Final Design Review phase, which ensures that there are no doubts or unresolved discrepancies between the device specifications (outputs) and the user needs/design inputs or the Intended Use of the product. The comprehensive and continuous process of collecting and validating design outputs underscores the commitment to quality and safety throughout the entire product lifecycle.

Clinical Evaluation Report (CER)

The Clinical Evaluation Report (CER) is an important document in the medical device sector, essential for ensuring the safety of a device. The CER compiles and evaluates all available clinical data related to the medical device, including information from clinical studies, scientific literature, adverse event reports, and other pertinent sources. The assessment is integral to the CE certification process, which is mandatory for the commercialization of medical devices in Europe. A thorough clinical evaluation is an ongoing process, extending beyond the initial submission of the CER. Manufacturers are required to regularly update the report to incorporate new clinical data and ensure ongoing compliance with current regulations. This continuous evaluation process ensures that medical devices maintain an appropriate safety and efficacy profile throughout their lifecycle.
The CER includes detailed information on product descriptions, indications, contraindications, intended users, intended patient population, risks, and **Post-Market Clinical Follow-up** (PMCF) plans. These PMCF plans are based on risk assessments and recommendations from notified bodies. The report is periodically updated with new product performance information derived from the **Post-Market Surveillance process** (PMS), ensuring that the latest clinical data is reflected.

For line extensions, the PMCF plan must be reviewed and updated if necessary to ensure continued compliance and relevance. It is important to note that for projects involving only instruments, a final CER is not required. Instead, the first useful update of the CER for the implants used with these instruments will also encompass all literature related to the instruments.

In summary, the CER is a living document that plays an essential role in the regulatory framework for medical devices, ensuring that they remain safe and effective for their Intended Use through continuous monitoring and evaluation of clinical data.

Final Review & Project Validation

The culmination of the product development process involves the collection and review of all final reports and outputs, including the Test Reports, Risk Analysis Report, Design Transfer final documentation, Surgical Technique description, General Safety and Performance Requirements (GSPR) assessment and other critical documents. This compilation ensures that every aspect of the design and development process is thoroughly documented and ready for the **Final Validation**.
The Final Design Review of the project is conducted to examine the conformity of the outputs to the design inputs. This review is formalized using the "Final Design Review & Validation" form, which includes a complete list of deliverables obtained during the Final Phase. This activity marks the conclusion of the design phases and certifies the project's readiness for series production.

Essentially, the Final Design Review serves as a Final Validation of the entire project. It signifies the transition from development to production. Upon successful completion of the Final Review, the project moves forward to the creation of the Technical File, which is essential for CE certification. The Technical File, which includes all developed documents and reports from the design and validation activities, is then submitted to the notified bodies. This step marks the end of all development activities and the project's readiness for market entry.

Thus, the Final Design Review not only certifies the suitability of the project for series production but also validates the entire development process, ensuring that the product is fully compliant and ready for regulatory approval and commercial distribution.

2.4 Results

The implementation of the new design and development procedure for medical devices at INTRAUMA S.p.A. has yielded a series of positive results, despite the complex and multifaceted nature of the process. Firstly, one of the most significant outcomes has been the optimization of the design process, which has led to a substantial reduction in both the time and, indirectly, the costs associated with product development and related documentation. This efficiency has been achieved through the elimination of redundant documentation and the standardization of design and verification phases, ensuring a more streamlined and coherent workflow. The rigorous application of Risk Analysis (FMEA), Clinical Evaluation (CER), and technical specifications has ensured that each device not only complies with current regulations but also meets the end users' expectations in terms of safety and performance.
Another important outcome pertains to the transparency and traceability of the development process. Detailed documentation and the use of standardized forms, such as the "Design Input," "Design Output," and "Item Master List," have enhanced the traceability of design decisions and modifications made throughout the product lifecycle. This level of detail facilitates both internal reviews and compliance audits, making the CE certification process more straightforward.

Evaluating the effectiveness of the new updated procedure has demonstrated that the current approach is more advantageous compared to the previous procedure. Clear and concise forms have eliminated redundant documentation, reducing the time required for their completion and simplifying the identification of involved resources. Clarity and traceability have increased process transparency, making the overall workflow more linear and manageable. Furthermore, the procedure has been designed to be highly usable, with broad applicability to different products. Most modules have been created to be applicable to similar product families (e.g., plates, or screws, or instruments), ensuring homogeneity across company projects. This standardization not only facilitates the implementation of the procedure but also makes the documentation easier to read and understand during audits, which is essential for ensuring that the product can be quickly introduced to the market.

The **phase reviews** are an innovative feature, optimized to ensure compliance with the new MDR 2017/745, requiring oversight by an Independent Reviewer and final approval from the management. Each phase of the process will be frozen since the positive conclusion of the phase's review, ensuring that all responsibilities are clearly defined and documented. Signatures on the documents certify that all deliverables have been completed.

Chapter 3

Case Study: Development of Osteotomy Plates Series

In this chapter, the design and development procedure outlined in Chapter 2 will be applied to the creation of a new series of osteotomy plates. INTRAUMA S.p.A. aims to innovate and enhance its product offerings for several reasons, including the need to meet the most recent standards and address evolving market and user requirements. The current series of osteotomy plates, known as the "Legacy" series, was submitted and approved under Directive 93/42/EEC. This directive, established in 1993 by the European Economic Community (EEC), set standards for the safety and performance of medical devices. However, the Legacy plates are not fully aligned with modern market features, such as anatomical design, which ensures a better fit to bone contours, and the option for polyaxial screws, allowing for greater flexibility in surgical procedures and improved fixation.

Osteotomy plates are medical devices used in surgical procedures to correct bone deformities by cutting and realigning the bone. These plates stabilize the bone during the healing process, ensuring proper alignment. The new series of osteotomy plates will incorporate several innovative features to address the shortcomings of the legacy series and meet modern surgical demands. One of the primary innovations in the new series will be the adoption of an anatomical design. This design will ensure that the plates conform more naturally to the bone structure, reducing discomfort and improving patient outcomes. Additionally, the new plates will be manufactured from titanium instead of stainless steel, which was used in the legacy series. Titanium offers several advantages, including superior biocompatibility, reduced weight, and increased strength, which collectively enhance the performance of the plates. Others innovative feature for the new osteotomy plates are improved

fixation mechanisms with polyaxial screws and advanced surface treatments to promote better bone integration. The design will also focus on versatility, allowing for use in a variety of osteotomy procedures and different anatomical sectors, providing surgeons with greater flexibility in treatment options.

3.1 Project Overview

This thesis presents the most significant documents related to the development of osteotomy plates, focusing on those that are crucial for the development procedure. Subsequent sections cover the design process, manufacturing considerations, clinical evaluations and regulatory compliance. Each subsection will provide insight into the critical aspects of the project, highlighting the methodologies and innovations that underpin the development of these medical devices. The goal is to provide a comprehensive understanding of the stages involved in bringing osteotomy plates from concept to final production.

3.1.1 Project Request

The design request focuses on developing a new series of osteotomy plates, specifically for tibial and femoral applications. The individual who initiates the claim is responsible for specifying the type of claim in the appropriate form, as described herein:

- New Product & New submission of Legacy Devices.
- Human Application.

Next are the requirements of the application:

- **Product type:** Plate & Instruments.
- **General description:** The **INTRAUMA Osteotomy System** are intended for use in conjunction with bushings, locking screws, and polyaxial screws to provide robust fixation for osteotomies. The targeted anatomical areas include the distal femur, proximal and distal tibia and the ulna diaphysis. This product family addresses osteoarthritis and various deformities such as varus or valgus bone angles, rotational misalignments, and leg-length discrepancies. These plates will consist of plates available in different configurations, depending on the anatomical focus, in left or right side.
- **General requirements:** Single-use device, reusable surgical instruments and sterile packaging.

- **Materials and surface finishing:** Materials include stainless steel and pure titanium, with surface finishes such as mirror polishing, type III anodization, and silver coating.
- **Related Devices & Feature:** Additional components include locking screws, cortical screws, MultiAx screws with specific osteotomy instrumentation for standard surgical technique.

The project involves the commercialization of products in Europe and the U.S., targeting an availability time of about six months, focusing on the development of reusable surgical instruments and sterile packaging.
This project also includes updating the design and development documentation for Legacy devices previously submitted under Directive 93/42/EEC.

3.1.2 Competitor and Market Analysis

The objective of this chapter is to provide a general overview of the osteotomy plate market and analyze INTRAUMA's main competitors, with the aim of identifying opportunities and challenges within the competitive landscape. This analysis focuses on market data published by "Ministero della Salute" [34] [35] for the years 2019, 2020, and 2021, examining medical devices exclusively marketed in Italy. the most influential competitors were identified to understand which products are most attractive to customers.
A preliminary market analysis offers several strategic advantages. Firstly, it enables us to assess the market share currently held by the leading players and estimate the overall growth-rate of the sector. This is essential for determining whether it is feasible and beneficial to expand with a new product. Moreover, a detailed market analysis helps to identify areas where competitors have strengths or weaknesses, allowing the company to develop a product that not only meets clinical needs but is also competitive in terms of price and quality. In addition, analyzing competitors and market dynamics is useful for making informed and strategic decisions in the development and commercialization of New Osteotomy Plates.

MARKET ANALYSIS

The Italian market for osteotomy plates, presented in the chart below (Fig. 3.1), reached an overall value of approximately €440,000 in 2019. The main players in this market were *Arthrex*, with a 38.9% share, followed by *DePuy-Synthes* with 31.9% and *THI (Total Healthcare Innovation)* with 16.5%. Other relevant competitor is *NEWCLIP* with 5.1%, while INTRAUMA held a marginal market share of 0.4%.

In 2020, the market experienced a significant decline, settling at just over €250,000, with *Arthrex* increasing its share to 41.1% and *DePuy-Synthes* to 33.5%, while INTRAUMA remained stable.

In 2021, the market rebounded to above €320,000, with *Arthrex* (37.8%) and *DePuy-Synthes* (37.5%) continuing to dominate, while INTRAUMA maintained a marginal presence with 0.5%.

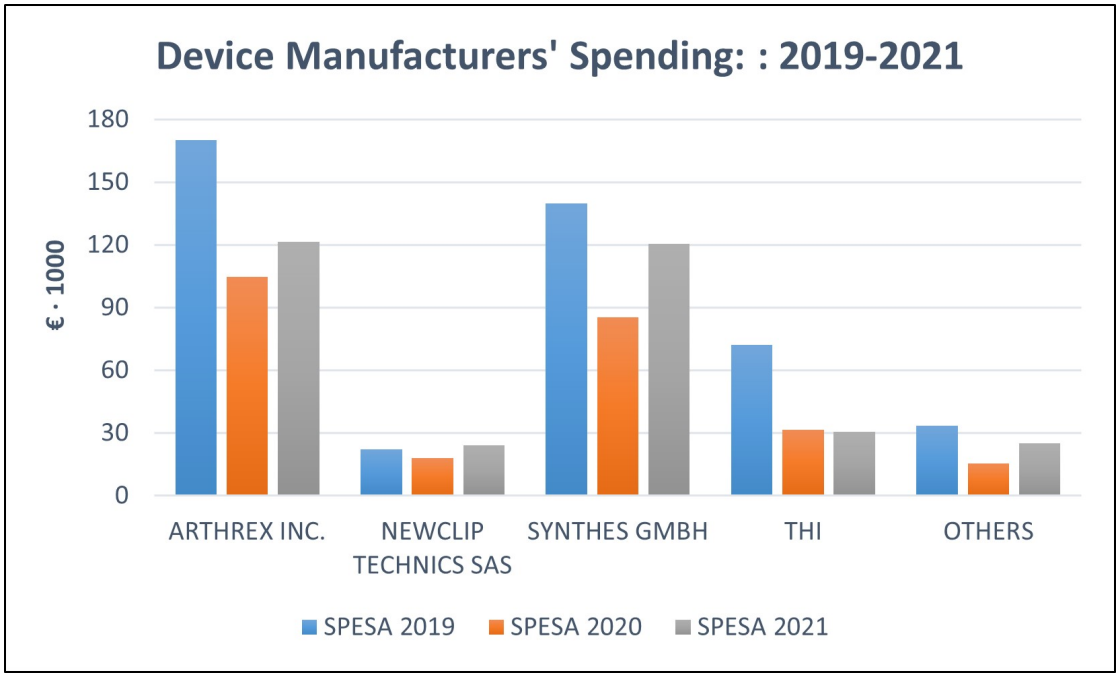


Figure 3.1: Device manufactures' spending for the years 2019-2020-2021.

Considering the entire three-year period (Fig. 3.2), the Italian market for osteotomy plates totaled approximately €1 million. *Arthrex* and *DePuy-Synthes* demonstrated a strong and continuous presence, while INTRAUMA's market share remained very low, indicating a significant opportunity for growth and improvement.
This trend suggests that despite annual fluctuations, there is a constant and potentially growing demand for osteotomy plates, offering INTRAUMA the opportunity to expand its presence and capture a more substantial market share through product innovation and differentiation.

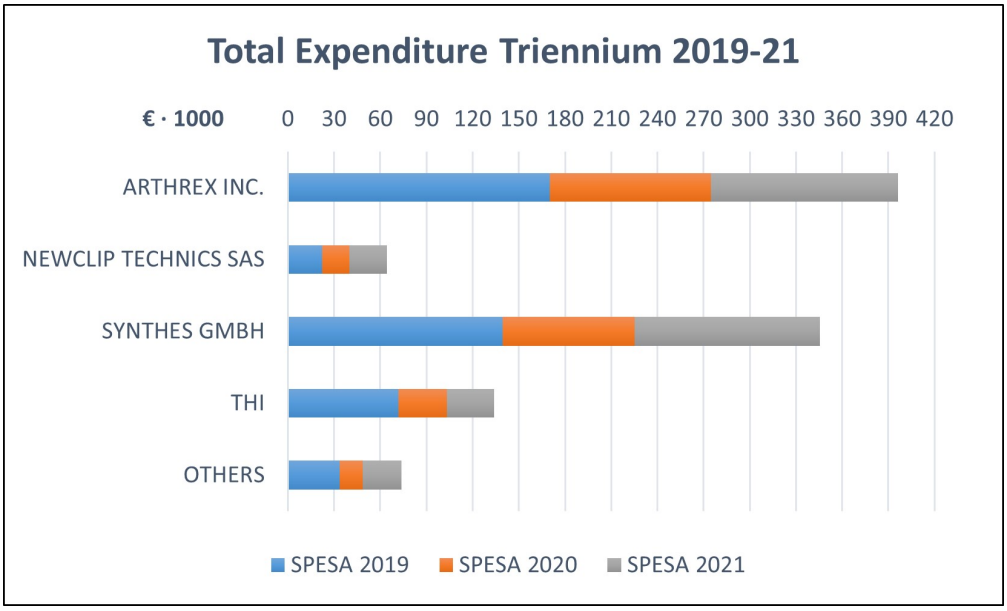


Figure 3.2: Total Expenditure in the three years period.

COMPETITOR ANALYSIS

INTRAUMA's main competitors in the osteotomy plate market include companies such as *Arthrex*, *DePuy-Synthes* and *NEWCLIP*. *Arthrex* offers solutions like the ContourLock™ LDFO and PEEKPower™ HTO plates for the femur and tibia, while *DePuy-Synthes* markets a line of TomoFix plates for the same anatomical areas. *NEWCLIP*, on the other hand, with Activmotion and Activmotion S series offers a wide range of plates for femoral and tibial osteotomies, including models specifically designed for derotation and closing osteotomies. This diversity of offerings enables competitors to meet a broad spectrum of clinical needs.
Through competitor analysis, the major strengths and weaknesses of existing products in the market were highlighted. *Arthrex* and *DePuy-Synthes* plates are particularly appreciated for their anatomical design and plate robustness. *NEWCLIP* stands out for its variety of available models, offering versatile solutions for different clinical scenarios. However, INTRAUMA's products can effectively compete by introducing innovations such as anodized surfaces and the use of various types of screws, including polyaxial screws, enhancing the versatility and ease of use of the plates. The table below, shown in Fig. 3.3, provides an overview of the key specifications and requirements of INTRAUMA's new products compared to those of the main competitors, highlighting the strengths and weaknesses of each.

Specifications	INTRAUMA Goals	Competitors			
		Arthrex	*DePuy-Synthes*	*NEWCLIP*	*Newdeal*
Anatomic Design	X		X	X	X
Stainless Steel Plates Series	X				
Pure Titanium Plates Series	X	X	X		
Titanium Alloy Plates Series				X	X
Anodized surface	X		X	X	X
Presence of K-Wires holes	X	X		X	
Possibility to use locking screws	X	X	X	X	X
Possibility to use cortical screws	X	X	X	X	
Possibility to use polyaxial screws	X			X	X
Opening wedge osteotomy	X	X	X	X	X
Closing wedge osteotomy	X		X	X	

Figure 3.3: Competitors' features.

PREDICATE DEVICES IDENTIFICATION

To guide the development of new osteotomy plates, INTRAUMA has selected a Predicate Devices from the main competitors. For instance, for distal femoral plates, the **TomoFix** plates from *DePuy-Synthes* were chosen, while for proximal tibial plates, **Activemotion** models from *NEWCLIP* were selected. This selection is essential not only for having a consolidated benchmark but also for facilitating performance comparisons. Although mechanical and biological performance tests between the new INTRAUMA products and those of the competitors are not mandatory, the option to perform them could prove advantageous. Achieving equal or better results compared to the predicate devices can facilitate the device submission phase and validate the performance of the new plates, ensuring that they meet clinical requirements and offer competitive advantages in the market.
In conclusion, the market and competitor analysis provide INTRAUMA with a clear understanding of the competitive landscape, highlighting opportunities to differentiate and enhance its product offerings in the osteotomy plate market.

3.1.3 Design Project Plan

In the context of the development of new osteotomy plates series, the Gantt chart is an invaluable tool for initiating, planning, and managing the project at each stage. It helps to coordinate human and material resources and ensures that all activities are carried out on schedule. Indeed, TPL organizes each phase temporally to avoid delays and overlaps. The Gantt chart highlights dependencies between different phases, allowing potential bottlenecks to be identified and critical activities to be planned in order to avoid compromising the entire project.

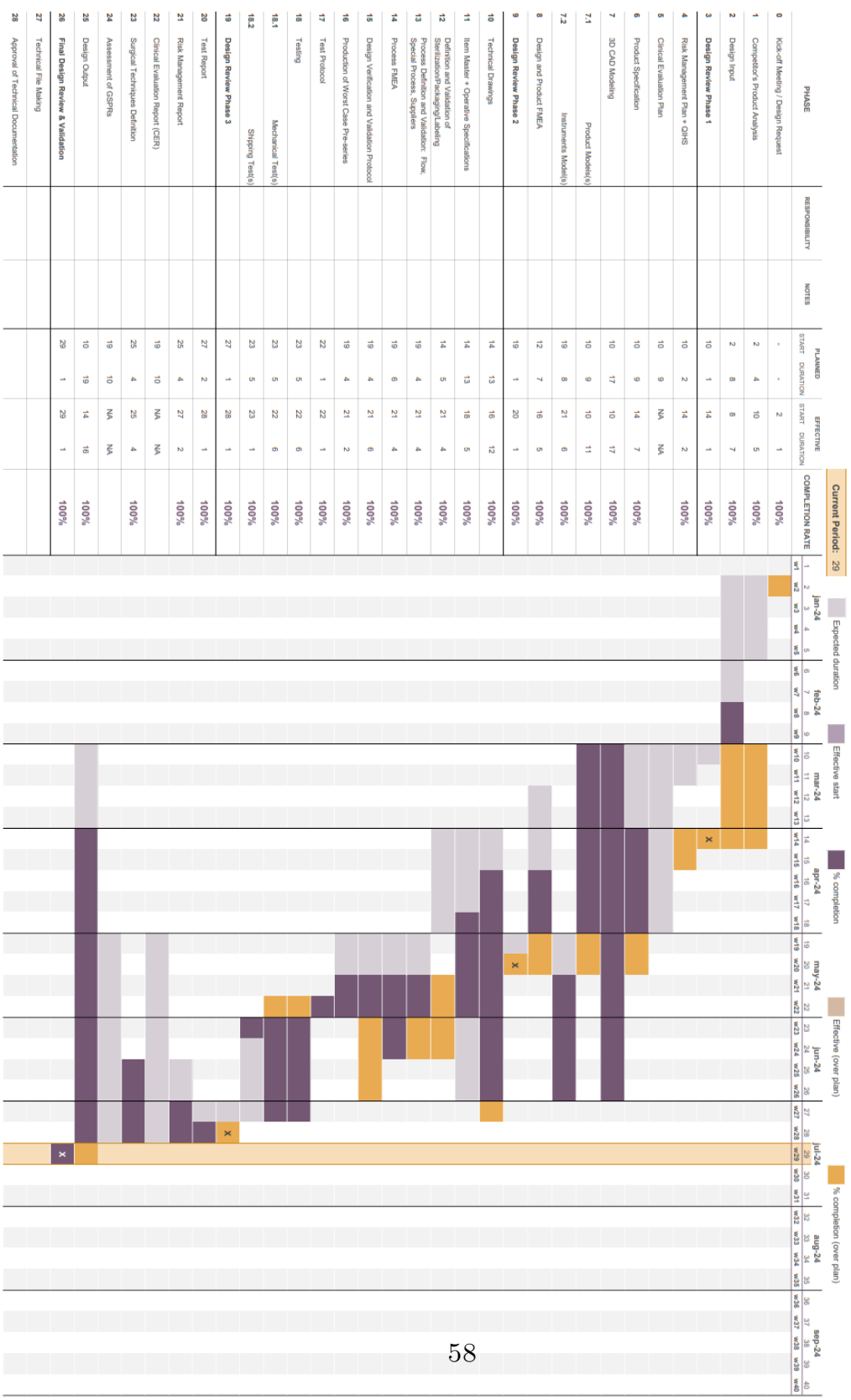


Figure 3.4: Design Project Plan.

From the diagram shown in figure 3.4, it is evident that:

- Design Reviews ensure that each milestone is carefully planned and conclude each stage.
- Risk management activities are integrated into the various phases, thereby demonstrating a proactive approach to security.
- Production and testing stages, including CAD modeling, pre-series production, and mechanical testing, are properly planned by TPL.

The diagram depicts the chronology of the project, encompassing the initial kick-off meeting and the subsequent approval of the technical documentation. This timeline extends over a six-month period and is represented horizontally, thereby facilitating a coordinated and systematic approach to the development of new plates. The clear delineation of responsibilities and the smooth progression of the project are further enhanced by this visualization. Furthermore, the real-time tracking of activities (updated with each review) offers a transparent representation of both completed and upcoming project milestones.

3.2 Specific Design Inputs

The design inputs and user needs of osteotomy plates are focused on several aspects. The plates are designed to correct bone deformities and stabilize bone after femur, tibia, or ulna osteotomy surgery. They must offer modular solutions, adapting to different anatomical and surgical needs, with special attention to compatibility with existing INTRAUMA screws and instruments. Intraoperative stability is ensured using K-wires, while osseointegration is facilitated through an anatomical, rounded shape that reduces soft tissue irritation. In addition, the plates must be able to withstand the normal forces of daily activity, providing a firm and secure internal fixation. The use of biocompatible materials that conform to ISO standards is essential to prevent adverse reactions and ensure patient safety. These design inputs, which are aimed at optimizing the functionality and durability of the plates, will be further explored in the document in the appendix of this thesis (see Appendix A). The latter document will provide a comprehensive overview of user needs and design inputs, which are briefly detailed below:

- **Intended Use:** The INTRAUMA Osteotomy System is intended for osteotomies, bone and joint deformities, fixation of fracture and malalignment. Plates are designed to provide internal fixation of osteotomies of distal femur, proximal tibia, distal tibia and ulna diaphysis in adults.

- **Regulatory Specifications:** The implants are intended for the European and US markets. In accordance with the Medical Device Regulation (MDR) 2017/745, the devices are classified as Class IIb (Rule 8). In the U.S. they are classified as HRS – Device Class II.

- **Related Devices and Compatibility:** The plates are compatible with existing and new INTRAUMA screws and bushings, ensuring intraoperative stability via K-wires. The use of O'Nil bushings and MultiAx screws allows for the distribution of loads and facilitates variable angulation, thereby improving the engagement with bone fragments.

- **Technical Features and Dimensions:** The plates have been designed to facilitate osseointegration and to minimize the potential for tissue irritation, due to their anatomical shape. In order to withstand the normal forces produced by patient activity, the plates must comply with the ASTM F382 standards. The dimensions of the femur, tibia, and ulna plates are designed to accommodate specific anatomical needs.

- **Materials and Biocompatibility:** Implants are made of AISI 316 LVM or CP-Ti Gr.4, materials selected for their biocompatibility and compliance with ISO 5832 series and ASTM F67/F138 standards, thereby ensuring safety and reducing the risk of adverse reactions.

- **Manufacturing, Surface Finishing and Special Processes:** The manufacturing processes include machining, surface finishing, quality control, packaging and sterilization, as well as packaging and labeling. The finishing options include anodization and polishing.

- **Risk Management:** Risk analysis involves the use of FMEA (Failure Mode and Effects Analysis) to identify and mitigate potential risks, ensuring a proactive approach to safety management throughout the development and production cycle.

- **Surgical Instruments:** In addition to existing compatible instruments, new surgical instruments have been developed to facilitate the insertion and fixation of plates. These instruments have been designed to be biocompatible, easy to clean, sterilize and reprocess, thereby optimizing the safety of reuse and efficacy during surgical use.

3.3 Product Specifications

The Product Specification document (see Appendix B) delineates the INTRAUMA Osteotomy System, intended for the internal fixation of osteotomies in the distal femur (DFO), proximal tibia (HTO), distal tibia (DTO), and ulna diaphysis in adults. The Osteotomy System includes one or more plates specifically tailored for each anatomical area according to the intended use, eliminating the need for additional intraoperative modeling. The plates (detailed in Appendix YY) are available in left and right configurations (except for ulna and distal tibia, which are unilateral) and are manufactured from **AISI 316 LVM stainless steel** or **Grade 4 titanium (CP-Ti Gr.4)**, both materials compliant with ASTM F67 and F138 standards and the ISO 5832 series. The titanium variants feature surface treatments such as **Type III Anodization** or **BACT** (a special coating treatment provided by INTRAUMA), while the stainless steel plates are **polished**.

All devices exhibit an anatomical conformation with a low profile and rounded edges to minimize soft tissue irritation. Additionally, the tapered end of each plate facilitates insertion, and screw protrusion is minimized to reduce potential irritation and enhance patient comfort. The plates are equipped with preassembled bushings for the accommodation of locking screws, which simplify screw insertion and stabilize the system without cross-threading. Furthermore, the plates include spherical compression slots to facilitate intraoperative approximation of bone fragments (only for the closing osteotomy plates) and holes for polyaxial screws, which can be inclined ± 15 degrees relative to the hole axis. The document also provides an overview of the Legacy devices, highlighting the main differences compared to the new devices in terms of materials, design, and technical specifications.

The indications for the use of the System are described, which include bone fixation following osteotomies of the distal femur, proximal and distal tibia, and ulna diaphysis. These devices are recommended for the treatment of bone and joint deformities, correction of varus or valgus malalignments caused by trauma or pathology, and treatment of unicompartmental osteoarthritis of the knee. They are also indicated for arthrodesis and pseudarthrosis, fracture fixation, and support complex procedures such as high tibial osteotomy (HTO) with ligamentoplasty. It is crucial to adhere to the specific instructions to avoid surgical complications and to combine the O'Nil system components exclusively with those provided by INTRAUMA. The system also includes specific surgical instruments to ensure procedural efficacy. The sections on contraindications, adverse events, warnings and precautions emphasize the importance of avoiding the system's use in the presence of critical pathologies and general medical conditions that impair healing.

3.4 Design Transfer

The design transfer phase represents a pivotal juncture in the medical device development process, during which the finalized design is transferred from the development team to manufacturing. This phase serves to guarantee that the product can be consistently produced to meet the requisite specifications and quality standards. In this thesis, the focus will be on certain activities of the design transfer, excluding specific documents related to production.

3.4.1 CAD Models & Technical Drawings

At this phase, computer-aided design (CAD) models were created using SolidWorks software and technical drawings are produced for all osteotomy plate models in the new series. The threedimensional visualization provided by the CAD models allows for the optimization of the design prior to physical prototyping. The technical drawings, which include a complete bill of materials, a laser marking plan and surface finish specifications, provide all the dimensions and materials needed for production. This ensures that the plates are well designed both aesthetically and mechanically.

3.4.2 Special Process

STERILIZATION

The sterilization process designated for the medical devices at issue adheres to the INTRAUMA Internal Protocols, already validated and currently employed for the devices of O'Nil System. The Osteotomy Plates can be assimilated to the product families that were identified as representative sample during the validation of the sterilization process and which were therefore subjected to the necessary tests to establish the sterilization dose (VDmax25 method) and conduct routine dose audits.

In particular, the product *Autolocking Screw* is considered the worst case for O'Nil System in relation to its raw material (Titanium Gr.5 ISO 5832-3) and its threaded profile. Titanium is considered worst case due to its porosity which increases the surface area for potential contact with external agents. The other characteristics do not vary significantly from product to product; therefore, the product *Autolocking screw* is considered representative of the O'Nil Screws and Plates product families.

Plates also fall into the Screws family for the following reasons:

- similar raw materials.
- similar process flow:
  - similar processing for chip removal.
  - manual mirror polishing does not influence the process since cleaning phase takes place downstream in a clean room in controlled mode.
  - laser marking does not influence the process since cleaning phase takes place downstream in a clean room in controlled mode.
  - bushings assembly takes place in a clean room in controlled mode.
  - the screws are the worst case compared to plates since the threads are free and therefore potentially contaminated, compared to plates, where the threads are protected by bushings.
- screws are produced in much greater numbers than plates (estimated ratio 5 to 1).

Based on these observations, the specific methods and parameters for sterilization of INTRAUMA medical devices already on the market can also be applied to the Osteotomy Plates, thereby ensuring equivalent effectiveness and safety.

The **sterilization method** chosen for the Osteotomy Plates is **Gamma Ray sterilization**. The specified sterilization dose for this method is 25 kGy. The Irradiation Process will be performed according to ISO 11137.
All plates of INTRAUMA Osteotomy System will be provided sterile; therefore, it is NOT necessary for the end-user to sterilize the device.
The estimated **shelf life** for keeping the sterility condition of the device packed and maintained in integrity is defined in **10 years** (expiry date), based on shelf-life and packaging validation protocol activities and results.

PACKAGING

The Osteotomy Plates will be packaged according to the instructions described INTRAUMA Internal Protocols, which is currently used to package the devices of O'Nil System. All plates fall within the dimensions, material, weight, shape, and general geometry of previously tested plates packaged. Tested plates show same features of the devices at issue as follow:

- They are manufactured using the same surgical grade metallic materials.

- The weight of devices is similar.
- The geometry complexity and shape are equivalent.
- They are subject to the same production and decontamination processes.
- They are packed into the same packaging material, using the same sealing and labelling processes.

The Osteotomy Plate is packaged in accordance with the principles of aseptic technique. There are two levels of packaging implemented during the manufacturing process:

- **Preliminary Packaging** (Sterile Barrier System): the product is packed in a double barrier with the application of a sterilization indicator reporting the evidence of the exposure to Gamma rays. This guarantees the aseptic opening and sterility preservation for the shelf life of devices. The preliminary packaging selected is **OPA/PE**.
- **Final Packaging** (Protective Packaging): product packaging is completed with the final package box, including the identification labels and informational leaflet (where applicable). It is responsible for preserving package characteristics during distribution, storage and handling. The final packaging selected is **Carton Box**.

LABELING

The Osteotomy Plates labels are specified in INTRAUMA Internal Protocols, where the complete list of labels is described. Labels designated are currently employed for other devices of O'Nil System with similar Intended Use. The configuration is designed for straightforward product identification and to ensure easy and quick detection of key product information on implant packaging. The labeling for the Osteotomy Plates includes both internal and external components.

The **Internal Labeling** are included inside the Final Packaging as described below:

- Internal product label and Gamma Ray sterilization process indicator attached to the Preliminary Packaging (1 pc/each type of label);
- Surgical note labels not adhered but inserted folded, thanks to dedicated grooving, in the Final Packaging (5 pcs).

Regarding **External Labeling** eIFU (electronic Instructions for Use), external product labels and identificative colored labels are provided. The External Labeling is adhered to the Final Packaging (1 pc/each type of label).
The expiry date (related to shelf-life) is clearly indicated on the product labels with appropriate symbol according to EN ISO 15223-1.

3.4.3 Worst-Case Analysis

Due to the variety of device models for fracture applications, a comprehensive rationale based on the cross-sectional characteristics of the plates is developed. This approach allows to systematically compare plates that have similar intended uses and identify the most critical among them. Consequently, the worst-case scenario can be determined, which will become the primary focus of the mechanical testing. This analysis covers both the new Osteotomy Plates and the "Legacy" series, providing a thorough examination of each. Understanding the weakest point is crucial, as it could potentially lead to implant failure or breakage when subjected to expected loads. These loads are derived from extensive bibliographic research and are representative of the most challenging scenarios in different bone applications. This approach helps in identifying potential failure points.

PROCEDURE

The primary distinction among plates of the same family was based on the material composition: titanium plates were chosen for mechanical evaluation due to the superior mechanical properties of stainless-steel plates, despite both having the same shape and dimensions. The decision to focus on titanium in bending tests is based on several reasons related to the intrinsic differences between the two materials. Firstly, stainless steel has nearly twice the modulus of elasticity of titanium, meaning it is less flexible and more rigid, while titanium's modulus is lower and comparable to that of natural bone. Titanium also has greater ductility, deforming in a more predictable and gradual manner under load. In bending tests, this results in greater flexion under load, allowing for a more precise identification of critical points of fracture or yielding. This decision directly influences the exclusion of the INTRAUMA Legacy Plates from the current analysis.
Having established titanium as the material for the plates to be tested, the identification of the weakest zone requires finding the critical section of the plates, according to the following criteria:

- the area has a poor section;
- the area is characterized by shape and/or thickness changes that can impact on the loads bearing;

- presence of holes and/or slots that further reduce the area section.

After identifying the weakest zone, the moment of inertia of that area is calculated using either Solidworks® or MATLAB software, depending on the methodologies specified in the internal INTRAUMA procedure. Each method returns the main geometric properties of the section of interest, including the Moment of Inertia, the Bending Section Modulus, the Maximum Bending Moment that the section can withstand, the Maximum extension from the neutral axis and the specific physical dimensions of width and thickness of the section. The final step is the calculation of **Maximum Bending Moment** as described in the related document.

The methodology described above allows for the identification of the worst case among the plates in the family. This is achieved by selecting the plate that has the lowest value of this critical parameter, as this will be the one most prone to failure under bending loads (similar to anatomical loads). Indeed, when the plate is subjected to these loads, the weakest section is likely to break first, indicating the critical point, which will have to be analyzed and on which the tests will focus. Selected plate will serve as the benchmark for the entire family and will undergo mechanical testing. Should the benchmark plate meet or exceed these standards, the findings will then be applicable to the entire range of plates, thereby confirming the safety and efficacy of the entire range of plates under the most demanding conditions.

CROSS-SECTION EVALUATION FOR FEMUR OSTEOTOMY PLATES

I. *Lateral DFO Plate*
As shown in Figure 3.5, the models (left and right side) have same shape and size, therefore the 633.3101 (L) is chosen to be evaluated. Upper holes should be used to lock the plate into the proximal fragment of the tibia bone while the holes in the lower portion should be used to lock the distal one. Consequently, 6 cross-sections are chosen to be compared, excluding the section involving the last hole at the lower end because of its negligible influence on the overall stability.

Sections A-A, B-B and C-C are designed to investigate the strength of the upper portion corresponding to the centers of the holes, while the other sections, from D-D to F-F, are intended to evaluate the strength of the plate shaft sections. The cross-section E-E has clearly higher properties (the K-wire hole is significantly smaller than the others), as does the entire solid part connecting the head to the shaft, therefore they are not considered.

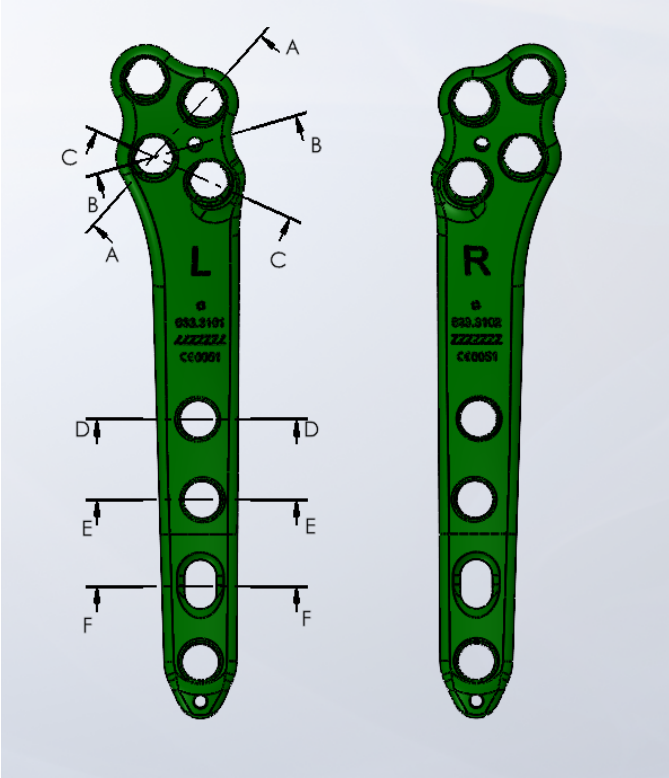


Figure 3.5: Evaluation of 633.3101-2 plates.

II. *Medial DFO Plate*
As shown in Figure 3.6, the models (left and right side) have same shape and size, therefore the 633.7101 (L) is chosen to be evaluated. Upper holes should be used to lock the plate into the proximal fragment of the tibia bone while the holes in the lower portion should be used to lock the distal one. Consequently, 4 cross-sections are chosen to be compared, excluding the section involving the last hole at the lower end because of its negligible influence on the overall stability.

Sections A-A is designed to investigate the strength of the upper portion corresponding to the centers of the holes, while the other sections, from B-B to D-D are intended to evaluate the strength of the plate shaft sections. The entire solid part connecting the head to the shaft has clearly higher properties, therefore it is not considered.

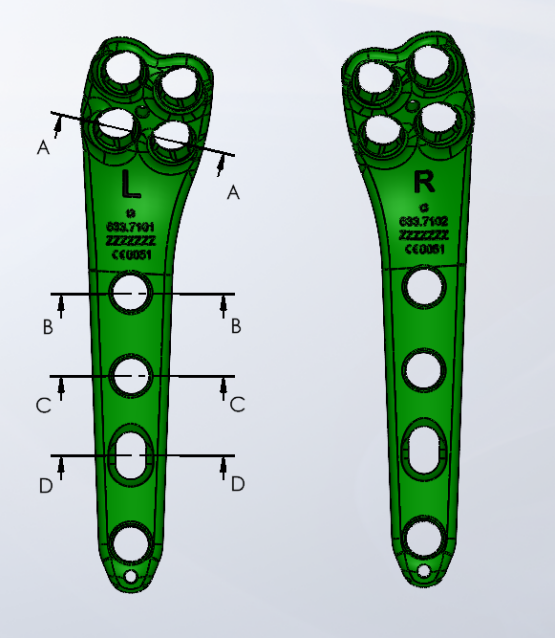


Figure 3.6: Evaluation of 633.7101-2 plates.

CROSS-SECTION EVALUATION FOR TIBIA OPENING OSTEOTOMY PLATES

The following assessment evaluates the Opening Osteotomy Titanium Plates cross-sections to identify the weakest zones and critical sections. The subsequent subparagraphs analyze each plate individually.

III. *Medial Opening HTO Plate*
As shown in Figure 3.7, the models (left and right side) have same shape and size, therefore the 641.8101 (L) is chosen to be evaluated. Upper holes should be used to lock the plate into the proximal fragment of the tibia bone while the holes in the lower portion should be used to lock the distal one. Consequently, 5 cross-sections are chosen to be compared, excluding the section involving the last hole at the lower end because of its negligible influence on the overall stability.

Sections A-A and B-B are designed to investigate the strength of the upper portion corresponding to the centers of the holes, while the other sections from C-C to E-E are intended to evaluate the strength of the plate shaft sections. The cross-section D-D has clearly higher properties (the K-wire hole is significantly smaller than the others), as does the entire solid part connecting the head to the shaft, therefore they are not considered.

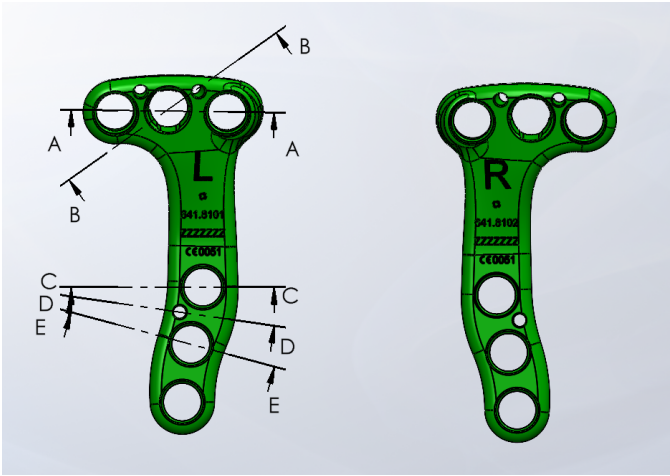


Figure 3.7: Evaluation of 641.8101-2 plates.

IV. *Medial Opening HTO Plus Plate*
As shown in Figure 3.8, the models (left and right side) have same shape and size, therefore the 641.8201 (L) is chosen to be evaluated Upper holes should be used to lock the plate into the proximal fragment of the tibia bone while the holes in the lower portion should be used to lock the distal one. Consequently, 6 cross-sections are chosen to be compared, excluding the section involving the last hole at the lower end because of its negligible influence on the overall stability.

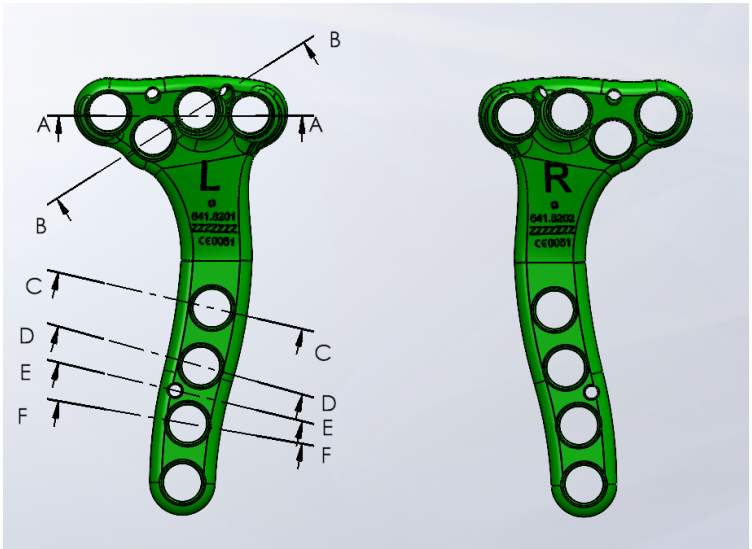


Figure 3.8: Evaluation of 641.8201-2 plates.

Sections A-A and B-B are designed to investigate the strength of the upper portion corresponding to the centers of the holes, while the other sections from C-C to F-F are intended to evaluate the strength of the plate shaft sections. The cross-section E-E has clearly higher properties (the K-wire hole is significantly smaller than the others), as does the entire solid part connecting the head to the shaft, therefore they are not considered.

V. *Medial Opening HTO Plate with Ligamentoplasty*
As shown in Figure 3.9, the models (left and right side) have same shape and size, therefore the 641.8301 (L) is chosen to be evaluated. Upper holes should be used to lock the plate into the proximal fragment of the tibia bone while the holes in the lower portion should be used to lock the distal one. Consequently, 5 cross-sections are chosen to be compared, excluding the section involving the last hole at the lower end because of its negligible influence on the overall stability.

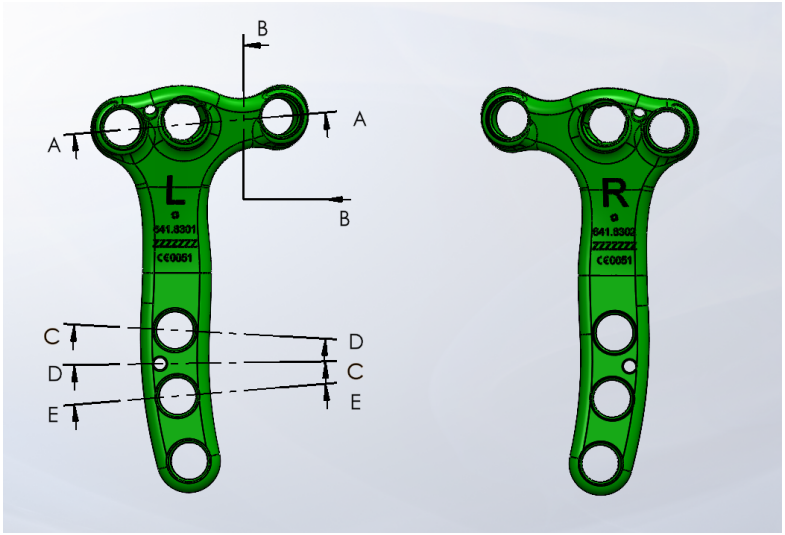


Figure 3.9: Evaluation of 641.8301-2 plates.

Section A-A is designed to investigate the strength of the upper portion corresponding to the centers of the holes, while section B-B is created to evaluate the thickness reduction that the plate undergoes in the sloped part. The other sections from C-C to E-E are intended to evaluate the strength of the plate shaft sections. The cross-section D-D has clearly higher properties (the K-wire hole is significantly smaller than the others), as does the entire solid part connecting the head to the shaft, therefore they are not considered.

VI. *Medial Opening HTO Plate Short*

As shown in Figure 3.10, the models (left and right side) have same shape and size, therefore the 641.8401 (L) is chosen to be evaluated. Upper holes should be used to lock the plate into the proximal fragment of the tibia bone while the holes in the lower portion should be used to lock the distal one. Consequently, 4 cross-sections are chosen to be compared, excluding the section involving the last hole at the lower end because of its negligible influence on the overall stability.

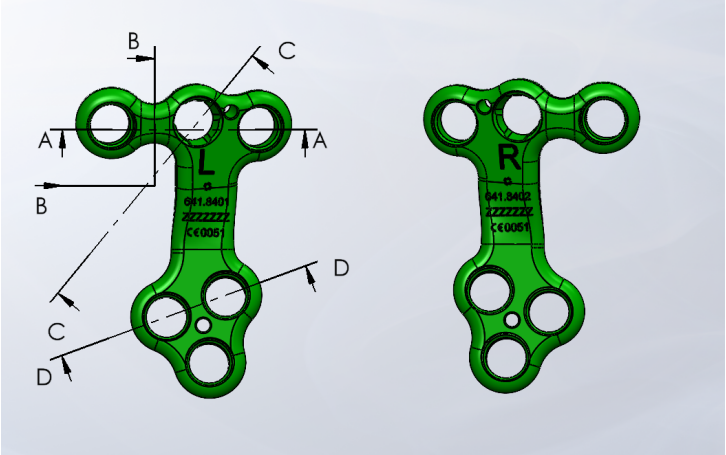


Figure 3.10: Evaluation of 641.8401-2 plates.

Sections A-A and C-C are designed to investigate the strength of the upper portion corresponding to the centers of the holes, while section B-B is created to evaluate the thickness reduction that the plate undergoes in the sloped part. The cross-section D-D includes two holes and passes through their centers, following the curvature, and is intended to evaluate the strength of the plate shaft sections. The entire solid part connecting the head to the shaft has clearly higher properties, therefore it is not considered.

VII. *Medial Opening DTO Plate*

As shown in Figure 3.11, the 643.7201 plate is evaluated. Upper holes should be used to lock the plate into the distal fragment of the tibia bone while the holes in the lower portion should be used to lock the proximal one. Consequently, 3 cross-sections are chosen to be compared, excluding those that include the last and the first hole at both plate ends, due to their negligible influence on the overall stability.

Sections A-A is designed to investigate the strength of the upper portion corresponding to the centers of the holes, while sections B-B and C-C are intended to evaluate the strength of the plate shaft sections. The entire solid part connecting the head to the shaft has clearly higher properties, therefore it is not considered.

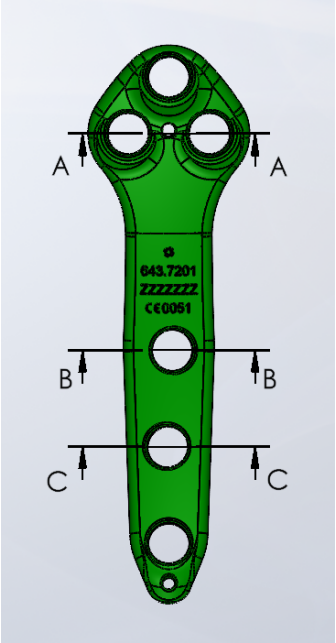


Figure 3.11: Evaluation of 643.7201 plate.

CROSS-SECTION EVALUATION FOR TIBIA CLOSING OSTEOTOMY PLATES

VIII. *Lateral Closing HTO Plate*

As shown in Figure 3.12, the models (left and right side) have same shape and size, therefore the 641.2101 (L) is chosen to be evaluated. Upper holes should be used to lock the plate into the proximal fragment of the tibia bone while the holes and the slot in the lower portion should be used to lock the distal one. Consequently, 4 cross-sections are chosen to be compared, excluding the section involving the last hole at the lower end because of its negligible influence on the overall stability.

Section A-A is designed to investigate the strength of the upper portion corresponding to the centers of the holes. The sections B-B and C-C are created to evaluate the thickness reduction that the plate undergoes at the

beginning and end of the inclined portion. The last section D-D is intended to evaluate the strength of the plate shaft at the screw hole.

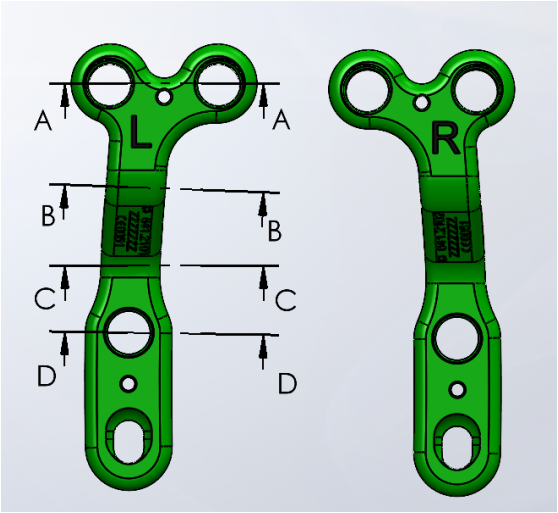


Figure 3.12: Evaluation of 641.2101-2 plates.

IX. *Medial Closing HTO Plate*

As shown in Figure 3.13, the models (left and right side) have same shape and size, therefore the 641.8501 (L) is chosen to be evaluated. Upper holes should be used to lock the plate into the proximal fragment of the tibia bone while the holes and the slot in the lower portion should be used to lock the distal one. Consequently, 5 cross-sections are chosen to be compared, excluding the section involving the last hole at the lower end because of its negligible influence on the overall stability.

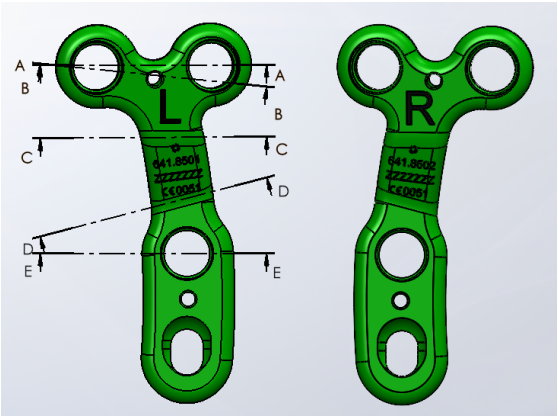


Figure 3.13: Evaluation of 641.8501-2 plates.

Sections A-A and B-B are designed to investigate the strength of the upper portion corresponding to the centers of the holes. The sections C-C and D-D are created to evaluate the thickness reduction that the plate undergoes at the beginning and end of the inclined portion. The last section E-E is intended to evaluate the strength of the plate shaft at the screw hole.

X. *Antero-Lateral Closing DTO Plate*
As shown in Figure 3.14, the models (left and right side) have same shape, therefore the 643.2101 (L) is chosen to be evaluated. Upper holes should be used to lock the plate into the distal fragment of the tibia bone while the holes and the slot in the lower portion should be used to lock the proximal one. Consequently, 5 cross-sections are chosen to be compared, excluding the section involving the last hole at the lower end because of its negligible influence on the overall stability.

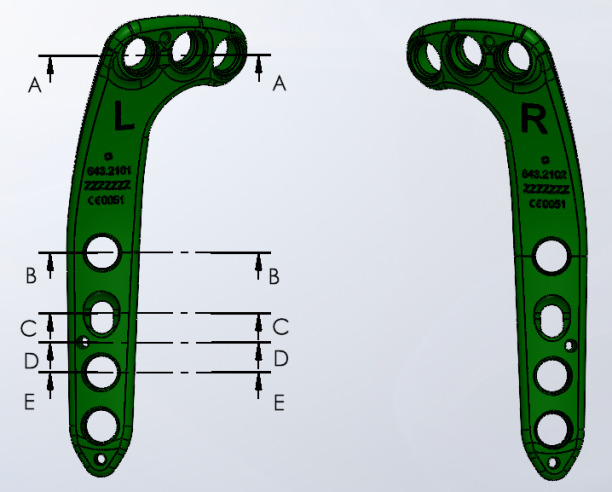


Figure 3.14: Evaluation of 643.2101-2 plates.

Section A-A is designed to investigate the strength of the upper portion corresponding to the centers of the holes. The other sections, from B-B to E-E, are intended to evaluate the strength of the plate shaft sections. The cross-section D-D has clearly higher properties (the K-wire hole is significantly smaller than the others), as does the entire solid part connecting the head to the shaft, therefore they are not considered.

XI. *Medial Closing DTO Plate*
As shown in Figure 3.15, the 643.7101 plate is evaluated. Upper holes should be used to lock the plate into the distal fragment of the tibia bone while the holes and the slot in the lower portion should be used to lock the proximal

one. Consequently, 4 cross-sections are chosen to be compared, excluding those that include the last and the first hole at both plate ends, due to their negligible influence on the overall stability.

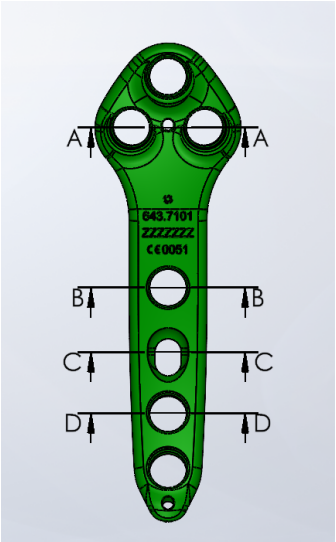


Figure 3.15: Evaluation of 643.7101 plate.

Sections A-A is designed to investigate the strength of the upper portion corresponding to the centers of the holes, while sections B-B, C-C and D-D are intended to evaluate the strength of the plate shaft sections. The entire solid part connecting the head to the shaft has clearly higher properties, therefore it is not considered.

WORST-CASE ANALYSIS RESULTS

In the assessment of orthopedic plates designed for tibia osteotomy, a fundamental distinction between opening and closing osteotomy procedures justifies the exclusion of plates for closing osteotomy from bending tests. Opening osteotomy involves the insertion of a bone wedge or another similar implant to increase the gap between the bone ends, subjecting the plates to greater mechanical stresses, particularly in flexion, due to increased tensile and compressive forces. In contrast, closing osteotomy involves the removal of a bone segment, leading to the approximation and compression of the two free ends. The absence of a wedge between the two parts of the osteotomized bone significantly reduces mechanical forces, since the bone is compressed along its axis, mainly generating compressive rather than flexural forces. This direct compression significantly decreases the on the plate, resulting in generally lower and less critical loads. Therefore, the plates used in closing osteotomy, generally smaller and designed to withstand lower loads, do not require

the inclusion in the worst-case testing for bending stress evaluation of tibia plates, as the operational conditions are significantly less severe compared to those of opening osteotomy plates.

Finally, all results are summarized in two tables (Fig. 3.16 and Fig. 3.17) where the **Bending Resistance Modulus** and the **Maximum Bending Moment** are calculated for all cross-sections of each plate in the Opening Osteotomy Titanium Plates group and DFO Plates group. This calculation provides valuable insights into the bending strength of each plate under flexural loading conditions, allowing for a comprehensive comparison.
The cross-sections (column 3) highlighted in blue were evaluated using Method A (with SolidWorks software) detailed in the procedure, while those in orange were made using Method B (with MATLAB software).

Code	Representative Plate	Cross-section	I_xx (mm^4)	X_Max (mm)	W_Fx (mm^3)	Mf_X_max (N*mm)
x33.3101-2	633.3101A	A-A	76.83	13.37	27.64	13348.17
		B-B	73.26	12.52	29.30	14153.45
		C-C	59.12	12.26	20.89	10090.09
		D-D	44.51	7.07	17.22	8319.38
		E-E	40.99	7.48	15.78	7621.75
		F-F	36.18	6.69	13.72	6625.99
x33.7101-2	633.7101A	A-A	104.72	12.05	25.92	12518.29
		B-B	59.17	7.40	21.08	10183.26
		C-C	47.78	6.87	17.52	8464.10
		D-D	40.40	6.30	14.38	6944.20

Figure 3.16: Summary table of DFO Osteotomy Plates cross-sections properties.

Code	Representative Plate	Cross-section	I_xx (mm^4)	Y_Max (mm)	W_Fx (mm^3)	Mf_X_max (N*mm)
x41.8101-2	641.8101A	A-A	71.92	3.14	22.90	11063.01
		B-B	43.34	2.27	19.09	9220.83
		C-C	10.50	1.85	5.68	2742.86
		E-E	8.90	1.87	4.76	2300.56
x41.8201-2	641.8201A	A-A	161.53	3.86	41.85	20212.42
		B-B	37.40	2.81	13.31	6428.54
		C-C	10.45	1.85	5.66	2733.78
		D-D	9.73	1.86	5.23	2527.46
		F-F	8.66	1.86	4.64	2242.47
x41.8301-2	641.8301A	A-A	187.34	4.33	43.26	20896.72
		B-B	24.16	1.70	14.21	6864.85
		C-C	10.50	1.85	5.69	2748.66
		E-E	8.88	1.88	4.71	2276.79
x41.8401-2	641.8401A	A-A	104.89	3.66	28.66	13842.04
		B-B	9.51	1.51	6.30	3042.26
		C-C	21.39	2.24	9.55	4612.22
		D-D	31.45	2.22	14.17	6841.85
x43.7201	643.7201A	A-A	25.83	2.07	12.47	6022.28
		B-B	14.65	1.82	8.06	3893.84
		C-C	12.07	1.79	6.74	3257.47

Figure 3.17: Summary table of Tibia Osteotomy Plates cross-sections properties.

With regard to the Femur Plates, the lower Maximum Bending Moment, which identifies the worst case, is found in section F-F of plate 633.3101 – **Lateral DFO Plate**, which is the weakest section overall. This plate has been chosen as a benchmark for the mechanical tests. In contrast, for the Tibia Plates, the lower Maximum Bending Moment is found in the section F-F of plate 641.8201 – **Medial Opening HTO Plus Plate**, the weakest section overall. It has been chosen as a benchmark for the Mechanical Tests.

3.4.4 Test Protocols

Test protocols aim to define tests methods and setup that will be used to assess the mechanical performance of the INTRAUMA Osteotomy Plate, in accordance with the standard **ASTM F382-17**. This assessment will demonstrate that the device meets the mechanical performance requirements. The mechanical strength test was conducted in the PAsTIs Laboratory at the Polytechnic University of Turin (*PoliTo*), located in Turin, Italy.

The testing system depicted in Fig. 3.18, consist of a load machine, which features a lower base for securing the support rollers and an upper fixture for affixing the loading rollers. In between these, the bone plates along with their own extensions will be mounted. Due to the lack of a sufficiently extended section in the tested plates, as per specification ASTM F382-17 A1.6.2, rigid extension segments have been employed. These extensions serve to effectively elongate the bone plates, enabling the evaluation through the 4 Point Bend test method.

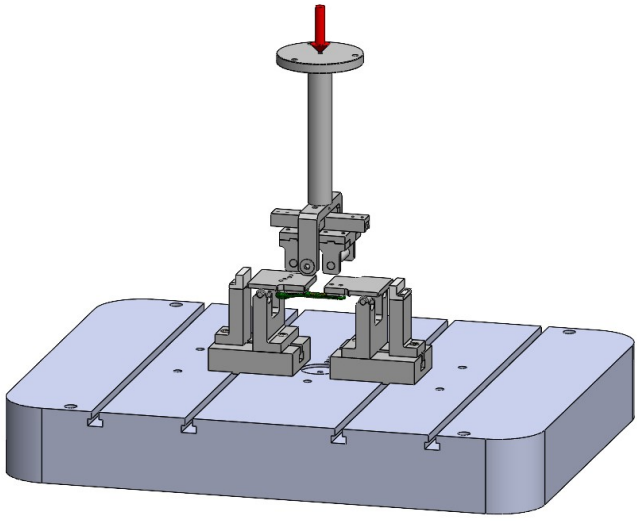


Figure 3.18: Test equipment and setup.

Two different types of tests are planned:

- **Test A** adheres to ASTM F382-17 – **Annex A1**. The devices under examination are plates with bushings, manufactured from Cp. Titanium Gr.4, in accordance with ISO 5832-2. The test type is **Static 4 Points Bending**, and the number of samples required is 5. The plates to be tested have been identified as the worst case in the respective analysis.
- **Test B** adheres to ASTM F382-17 – **Annex A2**. The devices under examination are plates with bushings, manufactured from Cp. Titanium Gr.4, in accordance with ISO 5832-2. The test type is **Fatigue 4-Points Bending**, and the estimated number of samples required is 10. However, this number may differ during the test to converge and confirm the fatigue limit. The plates to be tested have been identified as the worst case in the respective analysis.

The ASTM F382-17 standard mandates that at least five plates undergo static testing, with an additional minimum of five plates subjected to dynamic testing. For it, the standard specifies that the plates must reach a "runout" of at least **1 million cycles** at a frequency of $5Hz$. Runout is defined as the threshold where a specimen endures the designated number of cycles without experiencing failure, thereby demonstrating its endurance under repetitive loading conditions. To satisfy these requirements, an estimated 10 dynamic tests are planned, as the initial tests are useful for determining the fatigue failure load that allows the plates to achieve runout.

3.5 Main Outputs

3.5.1 Laboratory Testing

The mechanical strength test was conducted in the laboratory of the Polytechnic University of Turin (PoliTo), located in Turin, Italy. The laboratory, known as PAsTIs, is responsible for conducting these critical tests, following the established test protocol (see Chapter 3.3.4), which details all the specific parameters of the planned tests.
The tests are still ongoing, as the dynamic tests require a considerable amount of time to complete. Although an estimated ten samples are expected to converge and establish the fatigue limit, this number may vary during the process. Multiple plates are tested to ensure accurate determination of the **fatigue limit**, as it helps in identifying consistent performance under repetitive loading conditions. This allows for the establishment of the boundary load, which is the fatigue limit below which the plate is considered safe for a lifetime.

3.5.2 Design Output of Osteotomy Plates

The design outputs of this project are comprehensively documented in a dedicated output document (see Appendix C). Each output is associated with the specific input and is accompanied by a reference document collected throughout the entire product development cycle. This output document serves as evidence that all inputs have been satisfied with a corresponding output (Input/Output Verification). By meticulously mapping each input to its resulting output, the document ensures that the design process is thorough and meets all predetermined requirements. This approach guarantees that every aspect of the project has been addressed and validated, thereby demonstrating the successful fulfillment of all design criteria.

This document serves as a comprehensive summary of the project and will be presented during the audit by the notified bodies. The document's clarity and completeness ensure comprehensive and accurate reflection of the entire development process. In addition to the outputs reported in the designated module, which are subject to the final review, further outputs include the Clinical Evaluation Report (CER), the surgical technique documentation, and all project validation reports. The CER provides a comprehensive analysis of clinical data to confirm the safety and performance of the device. The surgical technique documentation offers detailed guidelines and protocols for the correct usage and application of the osteotomy plates during surgical procedures. These supplementary documents serve to reinforce the soundness and reliability of the design outputs.

Chapter 4

Conclusion

The thesis project focused on the updating and optimization of the design and development procedure for medical devices at INTRAUMA S.p.A., with particular attention to the requirements of the new Medical Device Regulation (MDR) 2017/745 and the ISO 13485:2016 standard. The objective was to submit clear and well-structured documentation to notified bodies for obtaining the CE mark and commercializing the product. This project resulted from close collaboration with the company, which required the updating of its previous internal procedure based on the now obsolete Medical Device Directive 93/42/EEC. The work considered both the documentary update concerning the development and production processes of existing market products (Legacy Devices) and the design of new medical devices.

The final result, represented by the definition of the new procedure and related documentation, significantly improved the efficiency of the internal design and development process. This was demonstrated in the thesis through the development of a new series of medical devices. Additionally, the procedure achieved considerable time savings as the documentation is clearer and less redundant compared to the previous version. The time savings benefit is currently being evaluated since the procedure has been recently implemented; however, initial results already indicate a significant reduction. Further analyses and evaluations will be conducted following submission to notified bodies to verify and confirm the benefits derived from the update.

The experimental tests, conducted on the worst-case scenario of the device family at the laboratory of the Polytechnic University of Turin, represent the culmination of the work. These tests are essential as they verify and validate the product's performance, confirming its safety and efficacy.

However, a multitude of opportunities for further development exist. One area

of particular interest involves adapting to the regulatory requirements of entities beyond those considered so far, in line with the expansion of the commercialization market. For instance, it may be necessary to comply with the regulations of the Food and Drug Administration (FDA) for entering the United States market.

Appendix A

Design Input

IMPLANTS

LINE NUMBER	*USER NEEDS*	*DESIGN INPUT*
1. *Intended Use*		
1.1. Intended Use	The System is intended for use in orthopedic surgical procedures requiring the correction of bone deformities or the stabilization of the bone following osteotomies of the femur, tibia and ulna in adult patients.	1.1.1. Intended Use The INTRAUMA Osteotomy System is intended for osteotomies, bone and joint deformities, fixation of fracture and malalignment. Plates are designed to provide internal fixation of osteotomies of distal femur, proximal tibia, distal tibia and ulna diaphysis in adults.
1.2. Indications for Use	The System is indicated for osteotomies, malunions and non-unions, fixation of fractures and correction of deformities and varus/valgus misalignment caused by injury or disease. The fixation system offers modular solutions to adapt to the specific anatomical and surgical needs of each bone segment in different anatomical locations.	1.2.1. Indications for Use The INTRAUMA Osteotomy System is used in conjunction with O'Nil bushings and locking screws, cortical screws and MultiAx screws to provide fixation following osteotomies of: - distal femur, - proximal and distal tibia, - ulna diaphysis. The system is specifically recommended for use in treatment of osteotomies, bone and joint deformities or misalignment, malunion or non-union and fractures.
2. *Regulatory Specifications*		
2.1. Trauma Classification	Clear classification of trauma types that the implants aim to manage.	2.1.1. AO-OTA Classification N/A
2.2. Device Regulatory Classification	Implants are intended to be marketed in the European and USA markets.	2.2.1. General Regulatory Definitions • Implantable • Invasive • Long Term Use • Not Reusable • Sterile
		2.2.2. MDR 2017/745 Classification (Annex VIII) • Class: IIb • Rule: 8
		2.2.3. FDA Classification • Reg. No.: 888.3030 • Product Code: HRS • Product Name: Plate, Fixation, Bone • Device Class: II
3. *Related Devices and Compatibility*		
3.1. Related Devices	Femur Osteotomy System details, including new and Legacy devices.	3.1.1. **Femur Plates'** Related Devices • O'Nil bushings • O'Nil locking screws • MultiAx screws • Cortical screw For Legacy Plate: • O'Nil bushings • O'Nil locking screws
	Tibia Osteotomy System details, including new and Legacy devices.	3.1.2. **Tibia Plates'** Related Devices • O'Nil bushings • O'Nil locking screws • MultiAx screw • Cortical screw (only for closing osteotomy) For Legacy Plates: • O'Nil bushings • O'Nil locking screws
	Ulna Osteotomy System details.	3.1.3. **Ulna Plates'** Related Devices • O'Nil bushings • O'Nil locking screws • Cortical screw

LINE NUMBER	USER NEEDS	DESIGN INPUT
3.2. Compatibility	All plates will be compatible with existing and new INTRAUMA screws, bushings and instruments.	3.2.1. Compatibility All plates will be compatible with existing and new INTRAUMA screws and bushings by having appropriate mating geometry to ensure full seating. Additionally, a new specific instruments set is provided for surgical treatment.
	Need for intraoperative implant stability through the use of wires.	3.2.2. K-Wire Stabilization All plates have holes for temporary intraoperative implant stabilization using K-wires.
3.3. Mating Components	Appropriate bushings size offering and mating assured.	3.3.1. O'Nil Bushings The intended function of the bushings is to accommodate locking screws, facilitating their insertion into the plate and stabilizing the system. The bushing is internally conical and presents an external tapered or straight thread; the external thread is necessary for the fixing on the plate while the internal conical shape allows the conical coupling with the screw (patented feature of the O'Nil Fixation System).
	Appropriate self-locking screws size offering and mating assured.	3.3.2. O'Nil Locking Screws Locking screws presents a conical head and they are used to transfer loads to the plate. They are housed inside dedicated bushings preassembled on the plates that allow locking through the conical coupling, without the possibility of cross threading between screws and support. This conformation allows a fixed axis to the screw in respect of the hole axis.
	Appropriate cortical screws size offering and mating assured.	3.3.3. Cortical Screws Cortical screws are placed into the designated spherical slots to achieve interfragmentary compression. This direct coupling serves to secure the plate in conjunction with the bone.
	Appropriate polyaxial screws size offering and mating assured.	3.3.4. MultiAx Screws MultiAx screws, inserted into dedicated conical threaded holes, facilitate load distribution to the plate and allow for angulation up to approximately ±15° in any direction from the hole's axis. These screws can be oriented arbitrarily within a 30° range from the nominal axis, enhancing engagement with bone fragments.
4. *Technical Features and Sizing*		
4.1. General Features	Plates will be designed to promote osteointegration, ensuring a solid internal fixation. They require an anatomical shape and aim to minimize the irritation of tissues.	4.1.1. External Design All plates have an anatomical conformation, developed by taking Sawbone Medium Tibia models as reference. The Osteotomy System includes a specific plate for each anatomical area according to the Intended Use and does not require further modeling or intraoperative contouring. The implants are designed with rounded edges for patient comfort and feature a limited-contact shaft profile that minimizes plate-to-bone contact to preserve blood supply. In addition, the tapered end of each plate facilitates insertion and screw protrusion has been minimized to reduce soft tissue irritation.
	All plate must be immediately recognizable by the Intended Users.	4.1.2. Product Identifications Implant will have appropriate identification marking on the device and clear labeling configuration on implant packaging.
	All plates must mechanically resist the stresses according to the Intended Use and standard requirements.	4.1.3. Mechanical Performance All plates must be able to withstand normal forces produced by patient activity. The mechanical strength of Osteotomy Plates is investigated according to ASTM F382 - Standard Specification and Test Method for Metallic Bone Plates, following a worst-case analysis to indicate which plate should be tested.

LINE NUMBER	USER NEEDS	DESIGN INPUT
	Products must arrive to Intended Users in optimal condition without damage due to transportation or loss of sterility, fully functional to ensure patient safety.	4.1.4. Shipping Requirements Shipping Test will be provided to ensure compliance with the regulation and complete safety of transportation. The evaluation of shipping system will be performed according to ASTM D4169 - Standard Practice for Performance Testing of Shipping Containers and Systems.
	The assessment of the safety and compatibility of a medical device in the Magnetic Resonance (MRI) Environment is essential to guarantee patient safety. Implants design should prevent interference with the operation of MRI equipment, as well as protection from damage or malfunction during exposure to high-intensity magnetic fields.	4.1.5. MRI Compatibility A device evaluation in the MRI environment will be conducted according to standards and scientific literature. The assessment should consider the potential risks associated with overheating, movement or malfunction of the device within the MRI environment. Instructions for Use must include all pertinent information regarding MRI safety and compatibility.
4.2. Product Sizing	Appropriate dimensions for the Intended Use.	4.2.1. Femur Plates Sizing ▪ Distal Plates: • Size: Standard • Side: Left, Right Legacy Plate (Femur model): • Unilateral configuration, single size.
		4.2.2. Tibia Plates Sizing ▪ Proximal Plates: • Size: Short, Medium, Standard, Long • Side: Left, Right ▪ Distal Plates: • Size: Standard • Side: Left, Right, Unilateral Legacy Plates (Tibia models): • Left/Right for addiction models and unilateral for subtraction model, standard size
		4.2.3. Ulna Plates Sizing: • Size: Standard • Side: Unilateral
4.3 Specific Features	Screw Holes/Slots options and location according to the Intended Use.	4.3.1. Holes/Slots Configurations of Femur Plates • Holes for O'Nil bushings • Holes for MultiAx screws • Holes for K-Wire insertion • Slot for compression screws Legacy Plate: • Holes for O'Nil bushings
		4.3.2. Holes/Slots Configurations of Tibia Plates • Holes for O'Nil bushings • Holes for MultiAx screws • Holes for K-Wire insertion • Slot for compression screws (for closing osteotomy) Legacy Plates: • Holes for O'Nil bushings • Holes for K-Wire insertion
		4.3.3. Holes/Slots Configurations of Ulna Plates • Holes for O'Nil bushings • Holes for K-Wire insertion • Slot for compression screws • Hole/Slot dedicated for instruments
5. *Materials*		
5.1 Materials	Appropriate bulk material for the Intended Use.	5.1.1. Bulk Implants Materials Substrate material to be: • CP-Ti Gr.4 – ISO 5832-2, ASTM F67 • AISI 316 LVM – ISO 5832-1, ASTM F138 Legacy Devices: • AISI 316 LVM – ISO 5832-1, ASTM F138

LINE NUMBER	USER NEEDS	DESIGN INPUT
		5.1.2. Materials of Related Devices Substrate material of Related Devices to be: • Ti-6Al-4V (Ti Gr.5) – ISO 5832-3, ASTM F136
5.2 Biocompatibility	Intended Users require that implants be biocompatible, ensuring materials used do not trigger adverse responses in the body and securing the device's safety and effectiveness within its Intended Use Environment.	5.2.1. Biocompatibility Biocompatibility tests for cytotoxicity, sensitization and irritation must be conducted to ensure safety and compliance with regulatory requirements according to ISO 10993 standards. Material selection must ensure the absence of toxicity, immunogenicity and carcinogenicity, minimizing contamination risks and facilitating sterilization. Further assessments will be conducted during the development phase in accordance with ISO 10993 Series.
6. *Manufacturing Requirements*		
6.1. Manufacturing Requirements	Appropriate surface finishing and coating option.	6.1.1. Surface Finishing/Coating Options Coating option to be: • Anodization Type III (CP-Ti Gr.4) • BACT (CP-Ti Gr.4) • Polishing (AISI 316 LVM)
	Devices must be able to be properly manufactured by INTRAUMA, according to the standard/specific manufacturing process for similar devices.	6.1.2. Main Manufacturing Process • Machining • Surface Finishing • Coating (if necessary) • Quality Control • Marking • Cleaning • Assembly • Packaging • Sterilization • Labeling
6.2. Cleaning	Devices must be designed to facilitate efficient cleaning, effectively removing all biological debris and contaminants prior to sterilization.	6.2.1. Cleaning Process The design of the plate geometry aims to ensure the effective removal of all biological contaminants and organic materials before use. This involves the use of corrosion-resistant and detergent-tolerant materials.
7. *Sterilization, Packaging and Labeling*		
7.1. Sterilization	Appropriate implants sterilization to ensure biocompatibility, acceptable bioburden and decontamination level (according to ISO 10993).	7.1.1. Sterilization Process Implant will be provided sterile, according to the INTRAUMA standard/specific manufacturing process for similar devices.
7.2. Packaging	Appropriate implants packaging: it will facilitate implant sterilization and will protect the sterility of the implant in storage and in transit.	7.2.1. Packaging Specifications Materials for packaging are chosen based on their physical and chemical properties, product compatibility, and regulatory compliance, according to EN ISO 11607 and ASTM D4169. Implants must remain sterile through normal handling and normal transportation of package.
	Devices must maintain its functionality and safety over an extended period (expiry time), ensuring clinical effectiveness and reducing the frequency of replacement. A reliable shelf life minimizes waste and guarantees that devices are always available when needed.	7.2.2. Shelf-Life Assessment Materials and devices must maintain integrity and performance over time, adhering to EN ISO 11607. Packaging should protect the device from moisture, light, and contamination. Stability tests to evaluate the effects of time and environmental conditions must be conducted to validate shelf life, ensuring safety and effectiveness until the expiry date.
7.3. Labeling	Appropriate implants labeling to clearly visually identify the product.	7.3.1. Labeling Specifications Its configuration is designed for straightforward product identification and to ensure easy and quick detection of key product information on implant packaging, according to EN 1041 and EN ISO 15233.

LINE NUMBER	USER NEEDS	DESIGN INPUT
	Each device shall be accompanied by the information needed to identify the device and its manufacturer and communicate safety and performance related information to the Intended User.	7.3.2. IFU Specifications The Instructions for Use (IFU) must include information, warnings and precautions on preventative maintenance, cleaning, sterilization, handling, storage, disposal and all main processes involving the product. Additionally, there must be explicit clarification about disclosing any residual risks.
8. *Risk Analysis*		
8.1. Risk Analysis	Need for design risk management and hazard identification in the preliminary stages of design.	8.1.1. Preliminary Risk Analysis The Design Risk Analysis will be developed/updated according to the established Risk Management Plan. The risk management is performed according to "EN ISO 14971 Medical Devices - Application of risk management to medical devices, with the application of FMEA (Failure Mode and Effects Analysis)". The preliminary stage also involves the compilation of "Questions for Hazard Identification related to Safety".
	Need for Process FMEA and Product FMEA to identify, analyze, control and mitigate risks throughout the development and production stages.	8.1.2. Risk Analysis Process FMEA and Product FMEA will be developed/updated according to the established Risk Management Plan. The findings from these FMEA analyses will be meticulously documented in the Risk Management Report.

INSTRUMENTS

LINE NUMBER	USER NEEDS	DESIGN INPUT
9. *Instruments Specifications*		
9.1 Instruments	The existing INTRAUMA instruments selected must be fully compatible and integrable with the Osteotomy System and its surgical technique, thus contributing to the effectiveness and efficiency of the procedures without compromising patient safety.	9.1.1. Existing Instruments Selection • K-Wire • K-Wire Guide • Drill Bit • Drill Guide • Screwdriver • Depth Meter
	Need to develop new surgical tools that facilitate the insertion and fixation of the new plates.	9.1.2. New Instruments • Chisel Type 1 • Standard • Narrow Wedge • Wedge impactor • Multipurpose Handle • Tissue Protector • Spreader Set • Cutting Guide Body • Pin Guide • Alignment Rod
9.2. Compatibility	New and existing instruments must be compatible with INTRAUMA Plates and all related devices.	9.2.1. Compatibility of Instruments Both new and existing instruments must be completely compatible with the Osteotomy Plates and any related devices, featuring a design with the appropriate geometry to ensure secure integration without any risk to safety into the surgical procedure.

LINE NUMBER	USER NEEDS	DESIGN INPUT
10. *Materials*		
10.1. Materials	Appropriate bulk material for the Intended Use.	10.1.1. Bulk Instruments Materials Substrate material to be: • Metal for surgical instruments (ISO 7153-1, ASTM F899) • Medical Grade Plastics (USP Class IV) • Silicone (USP Class IV)
10.2. Biocomatibility	Intended Users require that instruments be biocompatible, ensuring materials used do not trigger adverse responses in the body and securing the device's safety and effectiveness within its Intended Use Environment.	10.2.1. Biocompatibility of Instruments Biocompatibility tests for cytotoxicity, sensitization and irritation must be conducted to ensure safety of instruments and compliance with regulatory requirements according to ISO 10993 standards. Material selection must ensure the absence of toxicity, immunogenicity and carcinogenicity, minimizing contamination risks and facilitating sterilization. Further assessments will be conducted during the development phase in accordance with ISO 10993 Series.
11. *Technical Features*		
11.1. Cleaning	Surgical instruments must be designed to facilitate efficient cleaning, effectively removing all biological debris and contaminants prior to sterilization.	11.1.1. Instruments Cleaning The design of the instruments aims to ensure the effective removal of all biological contaminants and organic materials before use. This involves the use of corrosion-resistant and detergent-tolerant materials, coupled with a design that promotes smooth, non-porous surfaces and eliminates hard-to-clean crevices.
11.2. Sterilization and Reprocessing	Surgical instruments must be designed for easy and complete sterilizability, minimizing the risk of contamination and ensuring the highest patient safety during Intended Use. It is necessary for the instruments to be compatible with effective and standardized sterilization methods, in accordance with current regulations.	11.2.1. Instruments Sterilization Instruments design will prioritize ease of sterilization, which is essential for ensuring patient safety. The geometric design of the instruments will be optimized to ensure that all surfaces are easily accessible to sterilizing agents. This approach strictly adheres to the requirements of EN ISO 17665 and ANSI/AAMI ST79.
	Users require that instruments be reprocessed safely and effectively to maintain their functionality, sterility, reliability and safety for repeated surgical use. Proper reprocessing reduces the risk of infection and extends the lifespan of the instruments. Clear instructions for use and maintenance are also necessary to ensure all procedures are correctly followed, maintaining the instrument in optimal operating condition.	11.2.2. Instruments Reprocessing Instruments will be made of corrosion-resistant materials to ensure durability and safety. They will be designed for easy cleaning, disinfection and sterilization. Materials must withstand repeated reprocessing cycles without degradation. The minimum number of reprocessing cycles required to maintain material integrity and functionality will be evaluated. Reprocessing instructions will be included in the IFU, where cleaning agents, methods and parameters will be specified.
11.3. Usability	The instruments set needs to be efficacious, easy to use and reusable, ensuring complete safety. Healthcare professionals can utilize these tools efficiently with minimal training.	11.3.1. Instruments Usability Instruments will be developed with a focus on user-friendly and ergonomic design, ensuring the tools are efficacious and easy to use. They are designed to be washed and reused multiple times after sterilization, enhancing both sustainability and operational safety.
11.4. Specific Features	Possibility of minimally invasive surgical application to facilitate procedures with reduced patient impact.	11.4.1. Mini-Invasive Technique N/A
	Possibility of implant removal.	11.4.2. Removal Option All plates will be designed to allow insertion of removal instruments.

Appendix B

Product Specification

1. *GENERAL DESCRIPTION*

1.1. Product Description

The INTRAUMA Osteotomy System is intended for osteotomies, bone and joint deformities, fixation of fracture and malalignment. Plates are designed to provide internal fixation of osteotomies of distal femur, proximal tibia, distal tibia and ulna diaphysis in adults. The System is used in conjunction with O'Nil bushings and locking screws, cortical screws and MultiAx screws to provide bone fixation. The INTRAUMA Osteotomy Plates, both Legacy and New Series, are included in the devices of *O'Nil System – Internal Fixator*, manufactured by INTRAUMA S.p.A.

NEW INTRAUMA PLATES

The fixation system offers modular solutions to adapt to the specific anatomical and surgical needs of each bone segment in different anatomical locations. The plates are divided into four main series, each designed for application on distinct anatomical parts. The System is specifically intended for:

- **DFO**: Distal Femur Osteotomy.
- **HTO**: High Tibia Osteotomy (proximal end).
- **DTO**: Distal Tibia Osteotomy.
- **Ulna** Osteotomy.

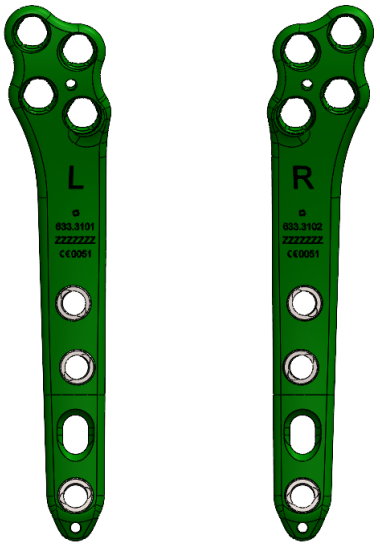
The plates are available in left (L) and right (R) configurations for all anatomical district except for the ulna, and unilateral configuration for the ulna and distal tibia plates.
All plates have an **anatomical conformation**, developed by taking Sawbone Medium Tibia models as reference. The fixation system includes a specific plate for each anatomical area according to the Intended Use and does not require further modeling or intraoperative contouring. The implants are designed with **rounded edges** for patient comfort and feature a **limited-contact shaft profile** that minimizes plate-to-bone contact to preserve blood supply. In addition, the **tapered end** of each plate facilitates insertion and screw protrusion has been minimized to reduce soft tissue irritation.

The materials selected for the New Osteotomy Plates are **AISI 316 LVM stainless steel**, in compliance with ISO 5832-1 and ASTM F138 standards, and **Pure Grade 4 Titanium**, in compliance with ISO 5832-2 and ASTM F67 standards, both known for their optimal properties in medical applications. AISI 316LVM stainless steel is chosen for its good corrosion resistance and biocompatibility; notably, the Low-carbon Vacuum-Melted steel variant also minimizes adverse reactions within the body. Titanium Gr.4 is favored for its high strength, light weight and excellent biocompatibility.

In each of New Plates Series, there are three variants that shares the same design but different material: one in AISI 316 LVM and two in Pure Titanium (Cp. Ti Gr.4). Titanium plates have different surface treatments: **Type III Anodization** (Ti-color) or **BACT** are offered. For stainless steel plates, **polishing** is the surface treatment of choice. All related devices are made of titanium alloy (Ti Gr.5), also known as Ti-6Al-4V, in compliance with ISO 5832-3 and ASTM F136 standards.

To provide a clearer understanding of the different plate designs available within the series, the following is an overview of each type of plate.

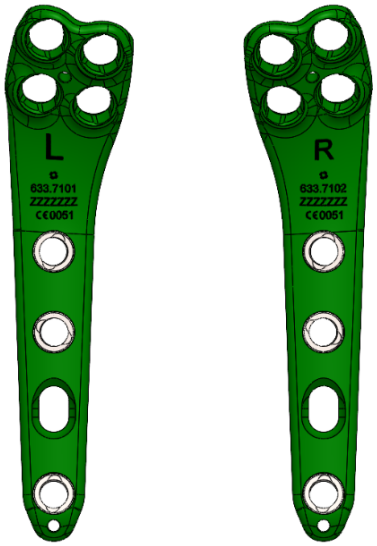
Lateral DFO Plate – 633.3101-2



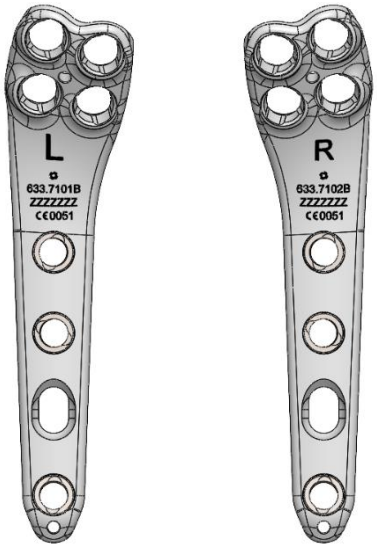
Lateral DFO Plate - BACT – 633.3101-2B

Lateral DFO Plate – 733.3101-2

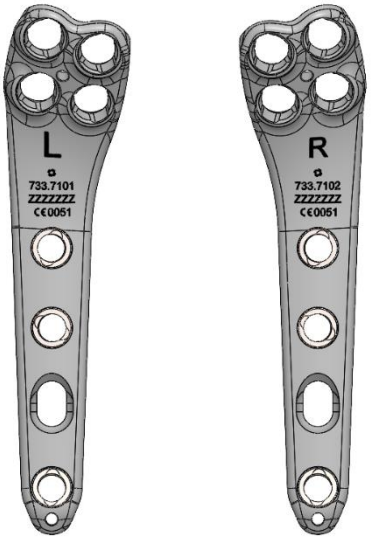
Medial DFO Plate – 633.7101-2



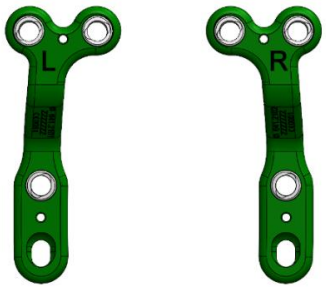
Medial DFO Plate - BACT – 633.7101-2B



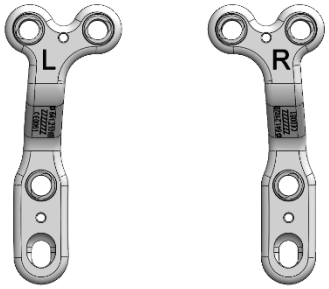
Medial DFO Plate – 733.7101-2



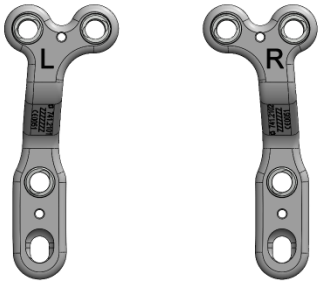
Lateral Closing HTO Plate – 641.2101-2



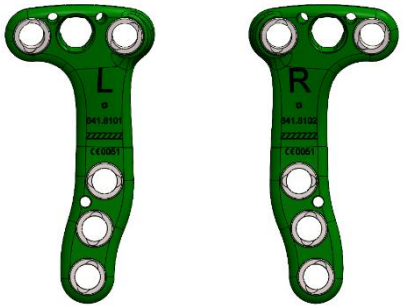
Lateral Closing HTO Plate - BACT – 641.2101-2B



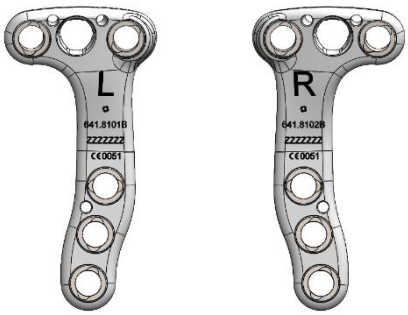
Lateral Closing HTO Plate – 741.2101-2



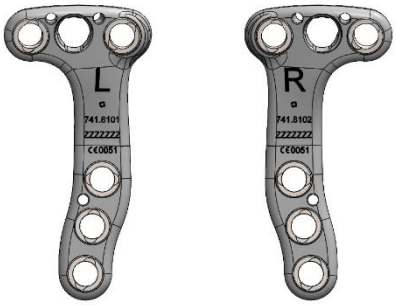
Medial Opening HTO Plate – 641.8101-2



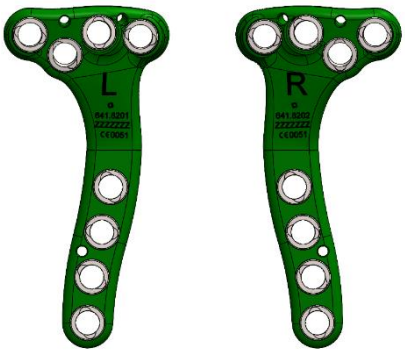
Medial Opening HTO Plate - BACT – 641.8101-2B



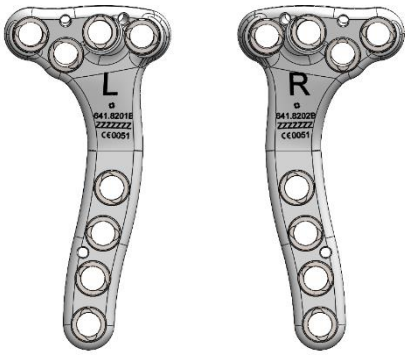
Medial Opening HTO Plate – 741.8101-2



Medial Opening HTO Plus Plate – 641.8201-2



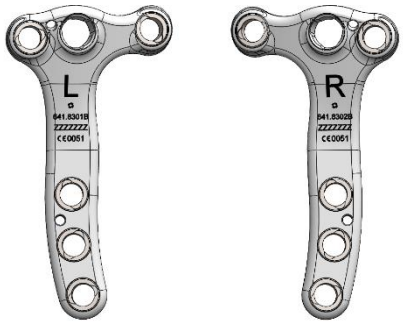
Medial Opening HTO Plus Plate - BACT – 641.8201-2B



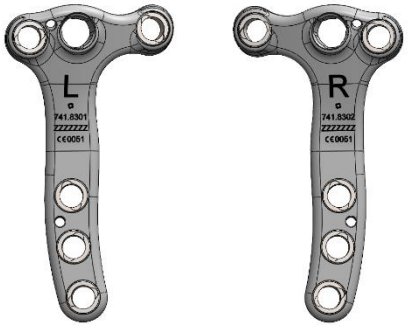
Medial Opening HTO Plus Plate – 741.8201-2

Medial Opening HTO Plate with Ligamentoplasty – 641.8301-2

Medial Opening HTO Plate with Ligamentoplasty - BACT – 641.8301-2B

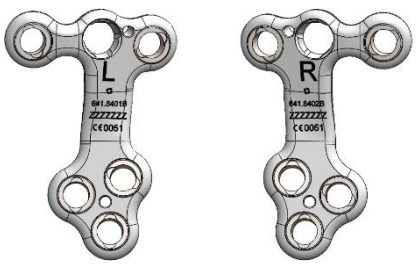


Medial Opening HTO Plate with Ligamentoplasty – 741.8301-2



Medial Opening HTO Plate Short – 641.8401-2

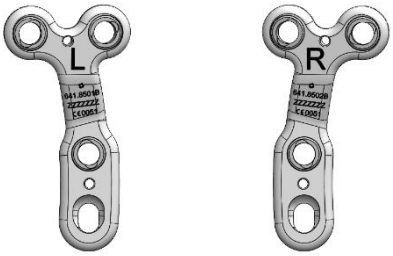
Medial Opening HTO Plate Short - BACT – 641.8401-2B



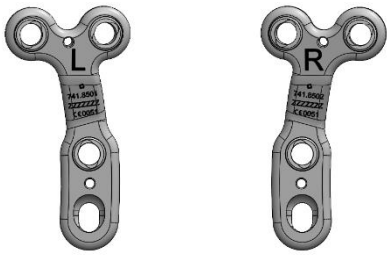
Medial Opening HTO Plate Short – 741.8401-2

Medial Closing HTO Plate– 641.8501-2

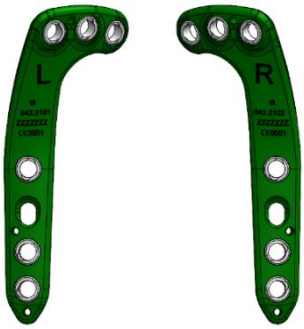
Medial Closing HTO Plate – 641.8501-2



Medial Closing HTO Plate – 641.8501-2



Antero-Lateral Closing DTO Plate – 643.2101-2

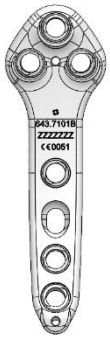


Antero-Lateral Closing DTO Plate - BACT – 643.2101-2B

Antero-Lateral Closing DTO Plate – 743.2101-2

Medial Closing DTO Plate – 643.7101

Medial Closing DTO Plate - BACT – 643.7101B



Medial Closing DTO Plate – 743.7101

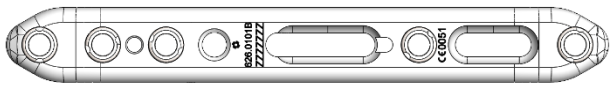
Medial Opening DTO Plate – 643.7201

Medial Opening DTO Plate - BACT – 643.7201B

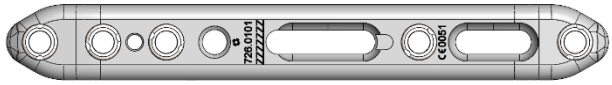
Medial Opening DTO Plate – 743.7201

Ulna Osteotomy Plate – 626.0101

Ulna Osteotomy Plate - BACT – 626.0101B



Ulna Osteotomy Plate – 726.0101



The base structure of the system includes the following components:

- Osteotomy Plates
- O'Nil Bushings – 3 different diameters, refer to Item Master List for codes,
- Locking Screws – 3 different diameters, refer to Item Master List for codes,
- Cortical Screws – 3 different diameters, refer to Item Master List for codes,
- MultiAx Screws, located in the proximal part of the plates, only for Medial Opening HTO and DFO Plates.

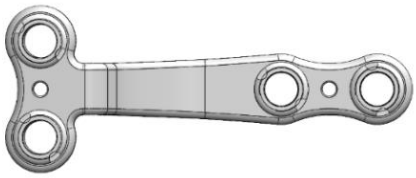
All plates are equipped with preassembled bushings for the housing of locking screws, with a fixed inclination on intersecting planes. They facilitate the screw insertion into the plate and stabilizing the system without cross threading between screws and support. The bushing is internally conical and presents an external tapered or straight thread; the external thread is necessary for the fixing on the plate while the internal conical shape allows the conical coupling with the screw (patented feature of the O'Nil Fixation System). Locking screws presents a conical head and they are used to transfer loads to the plate. This conformation allows a fixed axis to the screw in respect of the hole axis.
The implants developed for the closing osteotomy are equipped with spherical compression slots to facilitate the intraoperative approximation of the fragments using cortical screws. This direct coupling serves to achieve interfragmentary compression and to secure the plate in conjunction with the bone.
DFO plates and medial opening HTO plates (excluding the Medial Opening HTO Plus Plates) have a specific conical threaded hole for the insertion of a polyaxial screw, which has an inclination up to approximately ±15 degrees in any direction from the hole's axis. These screws can be oriented arbitrarily within a 30° range from the nominal axis, enhancing engagement with bone fragments.
Each plate is also equipped with holes for temporary stabilization of the implant using K-Wire.
This flexibility in coupling and plate selection will significantly increase the chances of surgical success, enhancing the stability of osteosynthesis and promoting effective bone healing.

The devices will be compatible with new specific osteotomy instruments. Indeed, the development of a complete set of instruments to be used during the surgery is planned. It is NOT possible to use different instruments than what is specified. Also, the surgical technique must be based, as far as possible, on the INTRAUMA surgical instruments covered by CE/FDA mark.

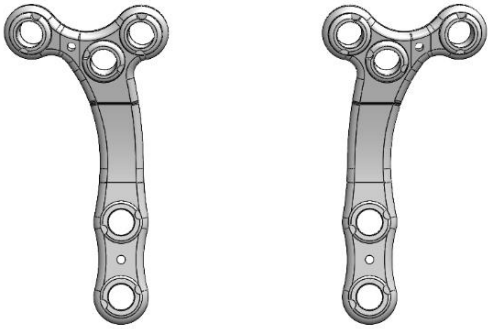
LEGACY DEVICES *(CE marketed according to 93/42/EEC)*

To provide a clearer understanding of the different plate designs available within the series, the following is an overview of each type of plate.

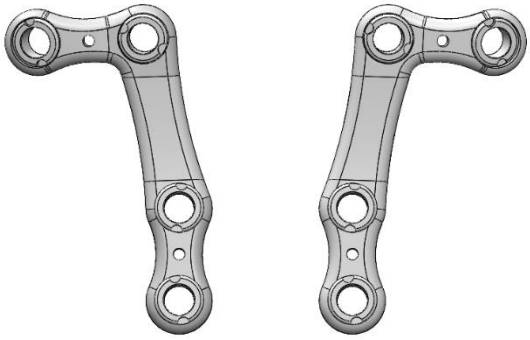
- **Tibia osteotomy by subtraction - 151.5000**



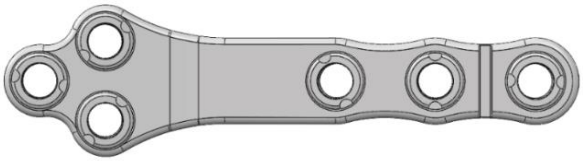
- **Tibia osteotomy by addiction - 151.5001-02**



- **L Tibia osteotomy by addiction - 151.5101-02**



- **Femoral osteotomy plate - 152.2001**



The material selected for the Legacy Osteotomy Plates are **AISI 316LVM stainless steel**, in compliance with ISO 5832-1 and ASTM F138 standards. AISI 316 LVM stainless steel is chosen for its good corrosion resistance and biocompatibility; notably, the Low-carbon Vacuum-Melted steel variant also minimizes adverse reactions within the body. The surface finishing chosen for Legacy Plates is **polishing.**

All related devices are made of titanium alloy (Ti Gr.5), also known as Ti-6Al-4V, in compliance with ISO 5832-3 and ASTM F136 standards.

The base structure of the system includes the following components:

- Osteotomy Plates,
- O'Nil Bushings – refer to Item Master List for codes,
- Locking Screws – refer to Item Master List for codes.

All plates are equipped with preassembled bushings for the housing of locking screws, with a fixed inclination on intersecting planes. They facilitate the screw insertion into the plate and stabilizing the system without cross threading between screws and support. The bushing is internally conical and presents an external tapered or straight thread; the external thread is necessary for the fixing on the plate while the internal conical shape allows the conical coupling with the screw (patented feature of the O'Nil Fixation System). Locking screws presents a conical head and they are used to transfer loads to the plate. This conformation allows a fixed axis to the screw in respect of the hole axis.
Each plate is also equipped with holes for temporary stabilization of the implant using K-Wire.
The devices will be compatible with the existing INTRAUMA instruments set (5/PFF Series Instrument Set). It is NOT possible to use different instruments than what is specified.

1.2. Indications for Use

1.2.1. Indications

The INTRAUMA Osteotomy System is used in conjunction with O'Nil bushings and locking screws, cortical screws and MultiAx screws to provide fixation following osteotomies of:

- Medial and Lateral Distal Femur.
- Medial and Lateral Proximal Tibia.
- Medial, Lateral and Anterolateral Distal Tibia.
- Ulna Diaphysis.

The devices are recommended for use in the treatment of osteotomies, correction of bone and joint deformities and malalignments, treatment of malunion and non-union and fixation of fractures.
Osteotomy Plates can be used to treat the following types of pathologies:

- Treatment of bone and joint deformities: correction of varus or valgus malalignments caused by injuries or diseases, treatment of idiopathic or post-traumatic varus or valgus deformity, treatment of single-compartment osteoarthritis (OA) of the knee.
- Knee osteotomy for procedural adjustment for uneven pressure distribution.
- Treatment of arthrodesis and pseudarthroses.
- Fixation of fractures.

Furthermore, the plates are specifically designed to support complex surgeries such as:

- Dedicated plate for HTO with ligamentoplasty.
- MultiAx System to avoid an ACL tunnel in the proximal tibia.
- HTO could be performed prior to or concurrently with reconstructive procedures.

1.2.2. Contraindications

The devices are intended for use only in accordance with the instructions provided. Any other use is contraindicated.
It is crucial to understand that combining components of the "O'Nil System" with those of other systems can lead not only to device damage but also to significant surgical complications. Therefore, INTRAUMA strictly prohibits the use of O'Nil System components in conjunction with components of other systems not supplied by the company.

It is contraindicated to implant the devices in the presence of active (acute or chronic, local or systemic) or latent infection and under general medical conditions such as:

- Insufficient quantity or quality of bone
- Altered blood supply
- Pulmonary insufficiency or acute respiratory distress syndrome, gaseous embolism
- Presumed or confirmed allergy or intolerance to the metal used or sensitivity to foreign bodies
- Obesity
- Pregnancy
- Patient not inclined to following the physician's instructions or a patient suffering from neurological disorders and therefore unable to follow the physician's instructions
- Inflammatory arthritis
- Tricompartmental osteoarthritis

1.2.3. Adverse Effects

Complications may include, but are not limited to, breaking, bending, loosening, loss of fixation, suboptimal union, and disunion. In addition to anticipating the risks associated with orthopedic implants, such as failure and fracture of the implant, it is necessary to inform and discuss with the patient possible adverse tissue reactions and other complications, such as:

- Intrinsic risks associated with anesthesia and surgery that include hemorrhage, hematoma, serum hematoma, embolism, edema, stroke, excessive bleeding, phlebitis and wound or bone necrosis.
- Osteolysis (progressive bone resorption). Osteolysis can be asymptomatic and therefore routine periodic radiographic examination is vital to prevent any serious future complication.
- Fatigue fracture of the osteosynthesis component can occur as a result of trauma, strenuous activity, loss of fixation, non-union, or excessive weight.
- Allergic reactions to materials, metal sensitivity or reactions to wear debris that may lead to histological reactions, pseudotumor and aseptic lymphocytic vasculitis-associated lesions (ALVAL).
- Delayed wound healing or deep wound infection (early or late) which may necessitate removal of the osteosynthesis devices. On rare occasions, arthrodesis of the involved joint or amputation of the limb may be required.
- Temporary or permanent nerve damage, peripheral neuropathies and subclinical nerve damage as possible result of surgical trauma resulting in pain or numbness of the affected limb.
- Damage to blood vessels or hematoma and cardiovascular disorders including venous thrombosis, pulmonary embolism, or myocardial infarction.
- Undesirable shortening or lengthening of the limb.

1.2.4. Warnings and Precautions

Handle the device carefully. All devices have been designed for Professional Use only. Surgeons responsible for supervising the use of the implants must be thoroughly familiar with orthopedical procedures and they have an adequate understanding of the product philosophy. Prior to surgery, surgeons must become familiar with the devices, instruments and surgical procedures, including application and removal.

Failure of fracture immobilization, bending or breaking of plates and screws will occur when excessive or repeated stresses are transmitted on the implant. It is essential to consider the following factors:

- Patient weight. Overweight or obese patients put undue stress on the implant, leading to failure.
- Patient lifestyle. If the patient engages in muscular exertion, running, lifting, or walking during their occupation or other activities, these movements could also contribute to implant failure.
- Senility, mental illness, drug abuse and alcoholism. Such conditions may result in the patient failing to observe the limitations and precautions to be followed, thereby increasing the risk of failure.
- Correct use of the implant and related devices and instruments is of the utmost importance. It is imperative to follow the operative technique and to use only the specific instruments manufactured and supplied by INTRAUMA.
- Devices intended for implantation are disposable and are not to be reused under any circumstances. If any implant has come into contact with any fluid body, it must be considered as having been used.
- In cleaning and disinfection steps, all cleaning solutions should be prepared according to the manufacturer's instructions.

Detailed information about the use and limitations of the implant should be provided to the patient. The surgeon must also inform the patient who is to receive the implant that the safety and durability of the implant is affected by the above factors.

FOR STERILE PRODUCT: Prior to the utilization of the implant, it is imperative to check the integrity of the packaging and verify the expiry date on the label. Implants must only be accepted and used if the sterile inner pouches, outer packaging and product identification label are found to be intact, untampered with. It is absolutely forbidden to use a component supplied in sterile packaging if its packaging is found to be open or damaged. Resterilization of sterile implants is absolutely prohibited.

2. *COMPETITORS' PRODUCT ANALYSIS*

2.1. Competitor and Market Analysis

The Competitor's Product and Market Analysis for the development of INTRAUMA Osteotomy Plates was carried out, focusing on a detailed examination of current competitors of INTRAUMA and the Italian market trend. Key sources for this analysis included data published by the "*Ministero della Salute*" covering the years 2019, 2020 and 2021, about the Italian Public Market, as well as relevant product brochures, articles and surgical technique descriptions.

3. *COMPATIBILIY AND COUPLING TO OTHER DEVICES*

3.1. O'Nil Bushings

New Devices	Legacy Devices	Part No.	Description
☒	☐	20.0002A	Bushing M4.5 Ø4.7 mm
☒	☐	30.0006A	Bushing M6 Ø6.2 mm
☐	☒	50.0004A	Bushing M7 Ø8.5 mm
☒	☒	50.0006A	Bushing M7 Ø8.5 mm

3.2. Bone Screws

LEGACY Screws:

New Devices	Legacy Devices	Part No.	Description	Socket	Material
Locking Series					
☒	☐	101.36xx	Autolocking Screw Ø3.6 mm	HL	Titanium Alloy
☒	☒	101.48xx	Autolocking Screw Ø4.8 mm	HL	Titanium Alloy
☐	☒	150.45xx	Autolocking Screw Ø4.8 mm	HEX	Titanium Alloy
Cortical Series					
☒	☐	102.48xx	Cortical Screw Ø4.8 mm	HL	Titanium Alloy
MultiAx Series					
☒	☐	103.48xx	MultiAx Screw Ø4.8 mm	HL	Titanium Alloy
☐	☐	120.23xx	MultiAx Screw Ø2.5 mm	HL	Titanium Alloy
☐	☐	120.28xx	HSP Screw Ø2.8 mm	HEX	Titanium Alloy

NEW Screws:

New Devices	Legacy Devices	Part no.	Description	Socket	Material
Locking Series					
☒	☐	101.28xx	Autolocking Screw Ø2.8 mm	HL	Titanium Alloy
Cortical Series					
☒	☐	102.28xx	Cortical Screw Ø2.8 mm	HL	Titanium Alloy
☒	☐	102.36xx	Cortical Screw Ø3.6 mm	HL	Titanium Alloy

3.3. Surgical Instruments

3.3.1. Instrument Sets

New Devices	Legacy Devices	Part no.	Description
☒	☐	New Set	-
☐	☒	SET50/PFF	5/PFF Series Instrument Set

3.3.2. New Surgical Instruments

	Features
☒	Reusable
☒	Non-Sterile
☒	Standard Surgical Approach

Appendix C

Design Output

Category	Topic	Input Ref.	Design Output	Output Ref.
Intended Use	*Intended Use*	• DI.1.1.1. Intended Use The INTRAUMA Osteotomy System is intended for osteotomies, bone and joint deformities, fixation of fracture and malalignment. Plates are designed to provide internal fixation of osteotomies of distal femur, proximal tibia, distal tibia and ulna diaphysis in adults.	▪ Intended Use Statement ▪ Product Description	▪ Product Specifications
	Indications for Use	• DI.1.2.1. Indications for Use Osteotomy System is used in conjunction with O'Nil bushings and locking screws, cortical screws and MultiAx screws to provide fixation following osteotomies of: - distal femur, - proximal and distal tibia, - ulna diaphysis. The system is specifically recommended for use in treatment of osteotomies, bone and joint deformities or misalignment, malunion or non-union and fractures.	▪ Product Description ▪ Anatomy Focus ▪ Indications, Contraindications, Adverse Effect ▪ Clinical Evaluation ▪ Risk Analysis	▪ Product Specifications ▪ IFU O'Nil System ▪ CEP O'nil System ▪ Risk Management Plan O'Nil System
Regulatory Specifications	*Trauma Classification*	• DI.2.1.1. AO-OTA Classification	N/A	N/A
	Regulatory Classification	• DI.2.2.1. General Regulatory Definitions • DI.2.2.2. MDR 2017/745 Classification • DI.2.2.3. FDA Classification	▪ Main Regulatory Classification ▪ Other International Regulatory Classifications	▪ Product Specifications ▪ Regulatory Definitions
Related Device and Compatibility	*Related Devices*	• DI.3.1.1. Femur Plates' Related Devices • DI.3.1.2. Tibia Plates' Related Devices • DI.3.1.3. Ulna Plates' Related Devices	▪ Product Specification ▪ Related Devices Specifications ▪ BOM Specifications ▪ Technical Drawings	▪ Product Specifications ▪ Item Master List ▪ Technical Drawings
	Compatibility	• DI.3.2.1. Compatibility • DI.3.2.2. K-Wire Stabilization	▪ Product Description ▪ Compatibility Specifications ▪ Technical Drawings	▪ Product Specifications ▪ Technical Drawings
	Mating Components	• DI.3.3.1. O'Nil Bushings • DI.3.3.2. O'Nil Locking Screws • DI.3.3.3. Cortical Screws • DI.3.3.4. MultiAx Screws	▪ BOM Specifications ▪ Technical Drawings	▪ Item Master List ▪ Technical Drawings

Category	Topic	Input Ref.	Design Output	Output Ref.
Technical Features and Sizing	*General Features*	• DI.4.1.1. External Design • DI.4.1.2. Product Identifications • DI.4.1.3. Mechanical Performance • DI.4.1.4. Shipping Requirements • DI.4.1.5. MRI Compatibility	▪ Product Specification ▪ Code List/Part Numbers ▪ Technical Drawings ▪ Process Flow Definition ▪ Worst Case Analysis ▪ Testing ▪ Risk Analysis	▪ Product Specifications ▪ Item Master List ▪ Technical Drawings ▪ INTRAUMA Plates Process ▪ Worst case analysis of femur and tibia osteotomy plates ▪ Test protocol for femur plates ▪ Test protocol for tibia plates ▪ Design FMEA ▪ Product FMEA ▪ Process FMEA
	Product Sizing	• DI.4.2.1. Femur Plates Sizing • DI.4.2.2. Tibia Plates Sizing • DI.4.2.3. Ulna Plates Sizing	▪ Product Description ▪ Code List/Part Numbers ▪ Technical Drawings	▪ Product Specifications ▪ Item Master List ▪ Technical Drawings
	Specific Features	• DI.4.3.1. Holes/Slots Configuration of Femur Plates • DI.4.3.2. Holes/Slots Configuration of Tibia Plates • DI.4.3.3. Holes/Slots Configuration of Ulna Plates	▪ Product Description ▪ BOM Specification ▪ Technical Drawings	▪ Product Specifications ▪ Item Master List ▪ Technical Drawings
Materials	*Materials*	• DI.5.1.1. Biocompatible Bulk Materials • DI.5.1.2. Materials of Related Devices	▪ Product Description ▪ Technical Drawings	▪ Product Specifications ▪ Technical Drawings
	Biocompatibility	• DI.5.2.1. Biocompatibility	▪ Biocompatibility evaluation	▪ Medical Device Biocompatibility Validation
Manufacturing Requirements	*Manufacturing Requirements*	• DI.6.1.1. Surface Finishing/Coating Options • DI.6.1.2. Main Manufacturing Process	▪ Product Description ▪ Process Flow Definition ▪ Technical Drawings ▪ Risk Analysis	▪ Product Specifications ▪ INTRAUMA Plates Process ▪ Technical Drawings ▪ Process FMEA
	Cleaning	• DI.6.2.1. Cleaning Process	▪ Process Flow Definition ▪ Risk Analysis	▪ INTRAUMA Plates Process ▪ Process FMEA
Sterilization, Packaging and Labeling	*Sterilization*	• DI.7.1.1. Sterilization Process Implant will be provided sterile, according to the INTRAUMA standard/specific manufacturing process for similar devices.	▪ Sterilization Process Features ▪ Risk Analysis	▪ Sterilization, Packaging & Labeling Document ▪ INTRAUMA Plates Process ▪ Process FMEA
	Packaging	• DI.7.2.1. Packaging Specifications • DI.7.2.2. Shelf-Life Assessment	▪ Packaging Configuration and Specifications ▪ BOM Specifications ▪ Shelf Life Evaluation ▪ Risk Analysis	▪ Sterilization, Packaging & Labeling Document ▪ Item Master List ▪ Process FMEA

Category	Topic	Input Ref.	Design Output	Output Ref.
	Labeling	• DI.7.3.1. Labeling Specifications • DI.7.3.2. IFU Specifications	▪ IFU/Labeling Configuration and Specifications ▪ BOM Specifications ▪ Risk Analysis	▪ Sterilization, Packaging & Labeling Document ▪ IFU O'Nil System ▪ Item Master List ▪ Process FMEA
Risk Analysis	*Risk Analysis*	• DI.8.1.1. Preliminary Risk Analysis • DI.8.1.2. Risk Analysis	▪ Risk Management Plan ▪ Question for Identification of Hazard related to Safety ▪ Risk Analysis	▪ Risk Management Plan O'Nil System ▪ Questions for Identification of Hazards Related to Safety (QIHS) - O'Nil System ▪ Design FMEA ▪ Product FMEA ▪ Process FMEA
Instruments	*Instruments Specifications*	• DI.9.1.1. Existing Instruments Selection • DI.9.1.2. New Instruments • DI.9.2.1. Compatibility of Instruments	▪ Product Description ▪ Instruments Specification ▪ Compatibility Specifications ▪ Technical Drawings	▪ Product Specifications ▪ Technical Drawings
	Materials	• DI.10.1.1. Bulk Instruments Material • DI.10.2.1. Biocompatibility of Instruments	▪ Technical Drawings ▪ Biocompatibility evaluation	▪ Technical Drawings ▪ Medical Device Biocompatibility Validation
	Technical Features	• DI.11.1.1. Instruments Cleaning • DI.11.2.1. Instruments Sterilization • DI.11.2.2. Instruments Reprocessing • DI.11.3.1. Instruments Usability • DI.11.4.1. Mini-Invasive Technique • DI.11.4.2. Removal Option	▪ Process Flow Definition ▪ Cleaning Process ▪ Sterilization Process ▪ Technical Drawings	▪ INTRAUMA Instruments Process ▪ Cleaning Validation Protocol ▪ Sterilization Validation Protocol ▪ IFU O'Nil System ▪ Technical Drawings

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