



RESEARCH ARTICLE

SELECTIVE LASER MELTING TECHNOLOGY TOWARDS PRODUCTION OF ORTHOPAEDIC METAL IMPLANT: IN VIVO BIOCOMPATIBILITY ANALYSIS

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Abstract. The primary aim of fracture management is to fracture stabilization towards normal mobilization. Internal fixation in bone fractures is well established. Selective laser melting (SLM) represents a new class of potentially revolutionary technology in the fabrication of orthopaedic implants. This technology holds great promise for producing specialized and customized orthopaedic implants without compromising their quality. The study aims to compare the capability of SLM titanium plates as an internal fixator on fracture healing and biocompatibility in vivo. All rabbits underwent surgery to induce a transverse mid-shaft tibial fracture, which was then fixed with either an SLM titanium plate or a conventional Synthes® plate, under anaesthesia. Fracture healing, bone union and biocompatibility were monitored at weeks 3, 6, 9, 12, and 26 histologically. Both groups showed callus formation, with mild to moderate callus bridging observed at week 6. By week 26, complete remodelling of cortical bone was evident, and both types of plates showed in-situ throughout the study. These findings suggest that orthopaedic plates produced via SLM technology have comparable potential to conventional plates in terms of fracture stabilization, biocompatibility, and osteoconductivity. The outcome of this study indicates that SLM-manufactured plates could serve as alternative internal fixation of orthopaedic fracture management in future.

Keywords: Selective laser melting technology, Ti6Al4V, fracture fixation, orthopaedic implant, biocompatibility.

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1. INTRODUCTION

Tibia fractures remain a challenge in orthopaedic trauma. A fracture is defined as a break in the structural continuity of a bone. It can present either in incomplete of the cortex or in the form of a complete break with a displacement of bone fragments [1]. Usually, it is caused by an impulsive and excessive force which can be direct or indirect. The healing mechanism of a fracture can be classified into two types either by direct healing by internal remodelling or indirect healing by callus formation [1-2]. Direct healing will occur when the fracture site is completely stable with no movement. As for indirect healing, it occurs when the fracture is neither fixed nor immobile with relative stability. Fracture healing under inter-fragmentary movement occurs by callus formation that mechanically unites the bony fragments followed by hematoma forms and undergoes tissue differentiation [2-3]. To support the healing event, the implantation of an internal fixator is applied as a treatment option in orthopaedic surgery to stabilize the fracture fragments. This is required to support mechanical stabilization to achieve the optimal alignment [1-3]. Besides, stabilization also requires ensuring the function of bone can be maintained during the physiological loading of both bones and joints [4-6]. Therefore, prudent consideration in the design of orthopaedic implants involves consignment of the surface properties, material's bioinert, biomechanical properties, and even chemical properties to ensure good integration between bone and implant [5-7].

Ti6Al4V, also known as titanium (Ti) alloys, is one of the most widely used in the fabrication of orthopaedic implants [8-9]. Ti has a monopoly in the orthopaedic implant market because it offers good mechanical properties, excellent biocompatibility, osteoconductive, corrosion resistance, and high specific strength [10-11]. These values give credibility to Ti as an option towards the production of orthopaedic implants and devices for bone fractures and defects [9-11]. In Malaysia, most of the production of orthopaedic implants is made from machining technology. This technology requires an implant to be machined from a solid piece of metal stock [12]. It has been commonly used in the production of various metallic implants from various materials. However, machining technology is time-consuming in the production of implants and costly. Besides, it disables to production of customized implants and there are seemingly many leftover materials derived from this technology [9,12-13].

As an alternative, selective laser melting (SLM) technology has been introduced for manufacturing local SLM plates (Ti alloys) as an internal fixator [14]. SLM is an additive manufacturing technique that uses a laser to selectively melt and fuse powdered materials to create three-dimensional parts. SLM is a novel technological approach which has attracted most researchers and scholars, particularly in medical fields [14-15]. This technology nowadays has become interesting to focus mainly on anatomical models, tissue repair, dentistry, prosthesis, surgical instruments as well as implants [15]. Overall, SLM technology can print different types of materials including polymer, metal or combination from both materials and metal combinations [14-15]. Due to its precision and near density part, it offers to form personalized complex structures implants that are based on the anatomical structures. Furthermore, this technology offers a low cost of production, a fast-manufacturing cycle, with high reproducibility [15-17].

The use of Ti alloys through SLM technology in the production of the orthopaedic implant is being introduced [18]. These factors include effective powder bed fusion to create a solid layer, providing the flexibility of the implant design, good surface finish and porosity that is suitable to allow for better bone ingrowth, load-bearing implant and customization. This localized technology also did not induce toxicity either in the cellular or animal stage as reported and submitted. Although Ti alloys and SLM technology are established and reviewed, pre-clinical work data is needed. Therefore, in this study, the potential of local SLM plate (Ti alloys) as an internal fixator in animal models and its biocompatibility through in-vivo experimental settings from the histological analysis were investigated. The performance of SLM was compared to conventional implants. This data is required before the local SLM plate (Ti alloys) can be translated into a clinical trial.

2. MATERIALS AND METHODS

All animal and surgical procedures in this study adhered to the requirements of ISO/IEC 17025:2017 and were conducted at the Advanced Orthopaedic Research Laboratory, Department of Orthopaedic, Traumatology and Rehabilitation, Kulliyah of Medicine, International Islamic University Malaysia (IIUM), Kuantan, Pahang. Approval of the animal study was adhered to the Institutional Animal Care and Use Committee (I-ACUC) at IIUM, with the reference number IACUC 2022-022.

2.1 Experimental Procedure

This study investigated the effects of different implant types on the healing of mid-shaft tibial fractures in New Zealand White Rabbits (NZWR). A total of 30 rabbits (weights between 2.5 to 3.0 kg) were acclimatized and used in this study. All rabbits underwent a mid-shaft tibial fracture on the right tibia. They were randomly assigned to two groups randomly divided into two groups: Group 1 received a SLM plate, while Group 2 received a conventional Synthes® plate as a control. The animals were monitored over a period ranging from 3 up to 26 weeks to assess fracture healing and any potential complications.

2.2 Internal Fixation Fixator

The mini system Ti6Al4V titanium powder was used to fabricate the SLM plate. The SLM plate was provided by our research partner SIRIM Berhad. Synthes® plate, a commercially available plate was bought directly from Synthes Malaysia Sdn. Bhd. The healing study was accomplished with straight and six-hole plates for both types of plates.

2.3 Anaesthesia

Anaesthesia for the rabbits was administered by trained personnel. Before surgery, each rabbit was weighed to calculate the appropriate dosage of anaesthetic drugs. The sedation regime included 2.5 ml of Ketamine, 250 mg of Tiletamine/Zolazepam (Zoletil-50), and 2.5 ml of Xylazine, with a dosage of 0.2 ml/kg administered intramuscularly for induction. Maintenance was achieved with 0.1 ml/kg intravenously via the marginal veins of the ear. Surgical procedures followed standard aseptic techniques to ensure a sterile environment.

2.4 Pre-Operative Procedure

The animals were placed in a supine position. Following intramuscular anaesthesia, the surgical site was remarked and shaved from the ankle to the femur. The rabbits were then moved to the Animal Operating Room for the procedure. The surgical site was disinfected according to standard sterile protocols. All surgical interventions were conducted using aseptic techniques to prevent infection. The surgical procedure was recorded and kept using the institutional animal surgery form.

2.5 Surgical Technique

All animals underwent a surgical procedure to create a mid-shaft tibial fracture in the right tibia, following a previously established technique [12]. An incision was made through the skin, the first layer of tissue, and the second layer of muscle to expose the bone. The incision site was marked along the medial shaft of the right tibia, approximately 6 cm below the tibial tubercle and 1.5 cm above the ankle joint. A deep incision was then made along the shaft, and the anterior muscle of the right tibia was retracted medially by catspaw to expose the underlying bone. The appropriate plate (either the SLM Ti plate or the Synthes® plate) was inserted and secured with screws using a drill and screwdriver, with screw lengths determined by the depth gauge. The bone plate was tightly fixed to the bone. Once secured, the mid-shaft tibial fracture was created using an oscillating saw (Aesculap® Microspeed GD657, B Braun Melsungen AG, Germany), with the fracture positioned centrally along the metal plate. After completing the procedure, the surgical incision was closed with a bioabsorbable surgical suture

(Monosyn® 4.0, Germany) using a continuous suturing technique for the muscle and a double-layer closure with interrupted sutures for the skin. Povidone-soaked gauze and bandages were applied for wound dressing. Enrofloxacin (10 mg/kg; Batril® 5%, Bayer AG, Leverkusen, Germany) and the analgesic tramadol hydrochloride (50 mg/mL; Mabron, Medochemie LTD, Limassol-Cyprus) were administered daily via the intramuscular route for up to seven days post-implantation to prevent wound infection and manage pain as post-operative management.

2.6 Harvesting Samples

All animals were euthanized using an overdose of 100 mg/ml ketamine hydrochloride (5 ml per rabbit) and administered via intravenous injection. Under sterile conditions, an incision was made to access the tibia, which was then harvested. The bone samples were fixed in a 10% Natural Buffered Formalin (NBF) solution. The rabbits were euthanized at predetermined intervals for histological analysis to evaluate fracture healing and biocompatibility. All assessments were conducted following the euthanasia and harvesting of the specimens.

2.7 Histological Interpretation

The harvested tibia samples were sectioned in the coronal plane into slices approximately 0.5 cm thick, with the plate remaining in place, using the EXAKT cutter machine. The samples were then dehydrated through a graded alcohol series and infiltrated with methyl methacrylate (Technovit 7200, Heraeus Kulzner Co., Germany). Following infiltration, the samples were embedded in methyl methacrylate, sectioned to a thickness of 80 µm (EXAKT Apparatebau systems, Norderstedt, Germany), and stained using Masson-Goldner staining. In this staining method, mineralized bone/connective tissue appears green, unmineralized bone is reddish-orange, and the plate and screws are unstained, appearing black. Histological analysis was performed using a Nikon Eclipse Ni motorized transmitted light microscope (Nikon, Japan).

3. RESULTS AND DISCUSSION

The histological interpretation results show the outcome from 3 weeks up to 26 weeks. The tibiae were extracted along with the bone plates, including the hard tissues surrounding the screw holes and the soft tissue covering the plate-screw junctions. The histological analysis further confirmed the interaction between the SLM plate and bone samples. At three weeks of the interval of post-implantation, both groups present extensive early callus formation observed around the fracture site, with prominent endosteal and periosteal reactions indicating an active bone healing process. Limited mineralization was present, endosteal periosteal in SLM group and subperiosteally in the conventional group, as indicated by the reddish-orange staining, which signifies unmineralized or immature bone, as illustrated in Figures 1(a) and (b).

Meanwhile, at week six of the interval, the healing response was positive in both groups and showed a high degree of biocompatibility. Callus formation was noted as tissues that bridge over the fracture site. The fracture site demonstrates mineralized callus formation bridging the fracture gap at SLM group as illustrated in Figure 2(a). As for the conventional group in Figure 2(b), the fracture site showed evidence of union with ongoing remodelling. Both groups showed similar phases of bone healing. The fracture gaps in both groups were completely bridged and dissolved at week nine (Figure 3(a) and (b)), indicating bone union. Early bone remodelling progressively was evident in SLM group (Figure 3(a)). Interestingly the new bone was more obvious than the previous intervals. In this phase, the bone was in union with the conventional group (Figure 3(b)). The implant interface was occupied by a newly formed bone. No signs of incompatibility were noted, and plates in situ were noted in both groups. Both plate-screw were straight and parallel with the tibia longitudinal axis.

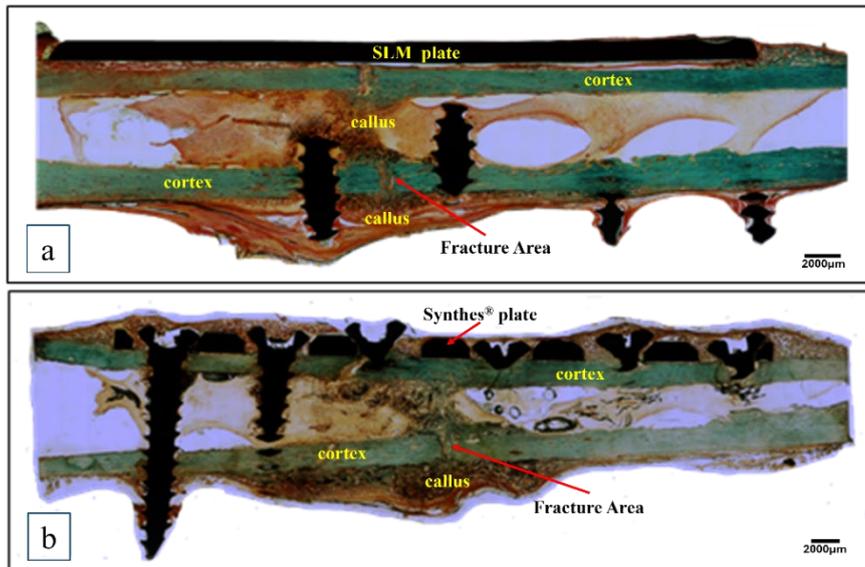


Figure 1: Rabbit tibia was embedded in Technovit® 7200 resin (Kulzner, Germany) and stained with Masson Goldner Trichrome. Sagittal view showing the fracture plate implantation in rabbit mid-shaft tibia using (a) SLM plate and (b) conventional plate. Callus formation and limited mineralization were noted at week 3. (Original magnification 40X).

In addition, at 12 weeks of post-surgery, it shows a medullary cavity and bone remodelling as illustrated in Figure 4(a) and (b). In this interval, most of the intramedullary canal had been reconstructed, indicating more advanced bone remodelling, with similar observations in both groups. Finally, at week 26 revealed that the fracture had successfully united and remodelled, with continuity observed in both the bone cortex and medullary canal. This was evidenced by the formation of mature bone tissue with few distinguishable features of fracture sites found through the histological findings (Figure 5(a) and (b)), which was attributed to the remodelling phase of the united fracture. Both groups demonstrated similar bone healing outcomes. The plate was in-situ, and no signs of incompatibility or adverse reactions were noted in both groups.

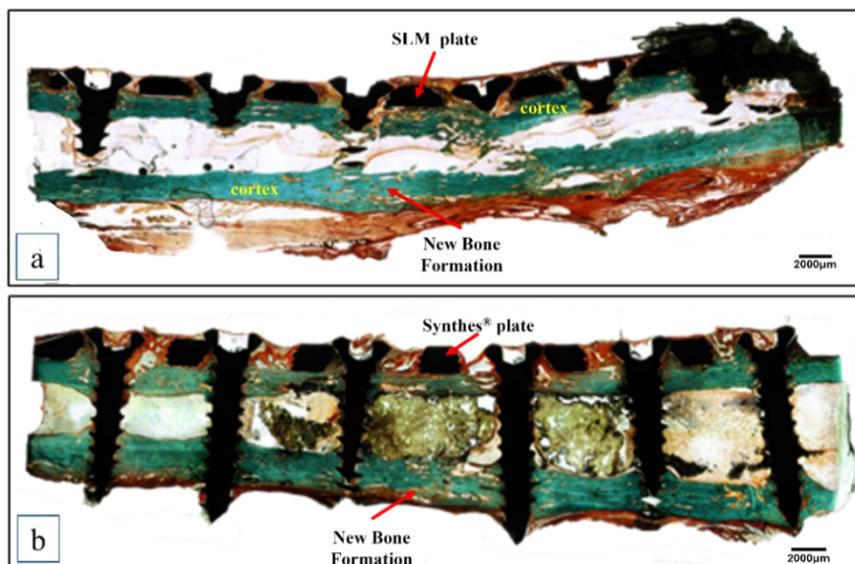


Figure 2: Rabbit tibia was embedded in Technovit® 7200 resin (Kulzner, Germany) and stained with Masson Goldner Trichrome. Sagittal view showing the fracture plate implantation in rabbit mid-shaft tibia using (a) SLM plate and (b) conventional plate. New bone formation was noted at six weeks of post-surgery. (Original magnification 40X)

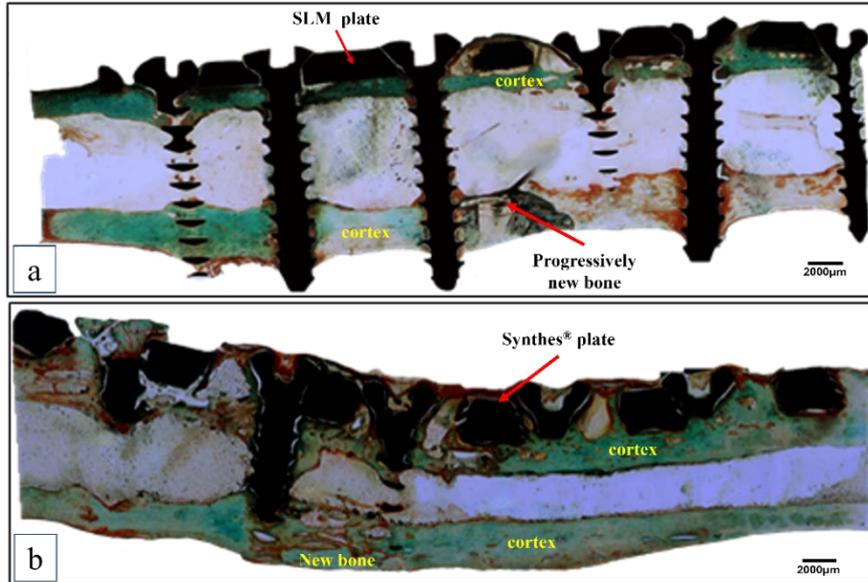


Figure 3: Rabbit tibia was embedded in Technovit® 7200 resin (Kulzner, Germany) and stained with Masson Goldner Trichrome. Sagittal view showing the fracture plate implantation in rabbit mid-shaft tibia using (a) SLM plate and (b) conventional plate. Fracture has been united, and remodelling is also evident at nine weeks of post-surgery. (Original magnification 40X).

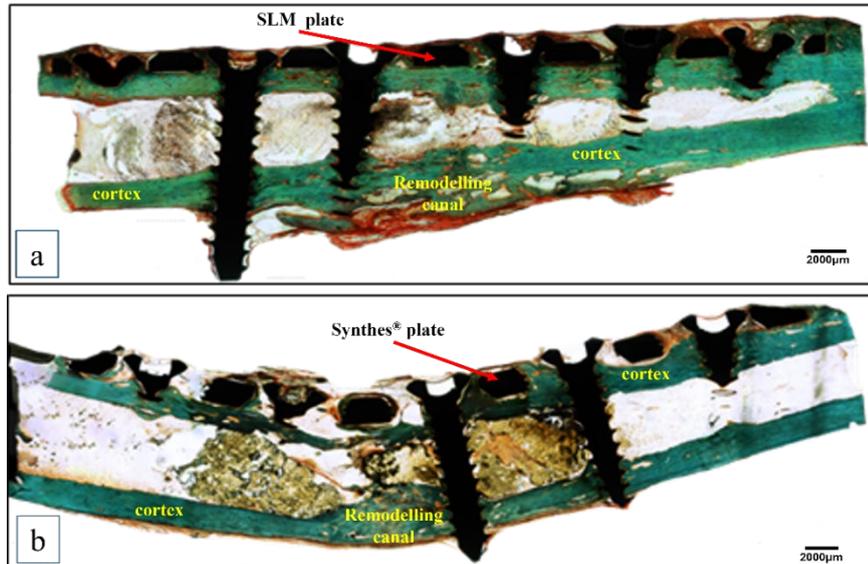


Figure 4: Rabbit tibia was embedded in Technovit® 7200 resin (Kulzner, Germany) and stained with Masson Goldner Trichrome. Sagittal view showing the fracture plate implantation in rabbit mid-shaft tibia using (a) SLM plate and (b) conventional plate. Remodelling of intramedullary is noted at twelve weeks of post-surgery. (Original magnification 40X).

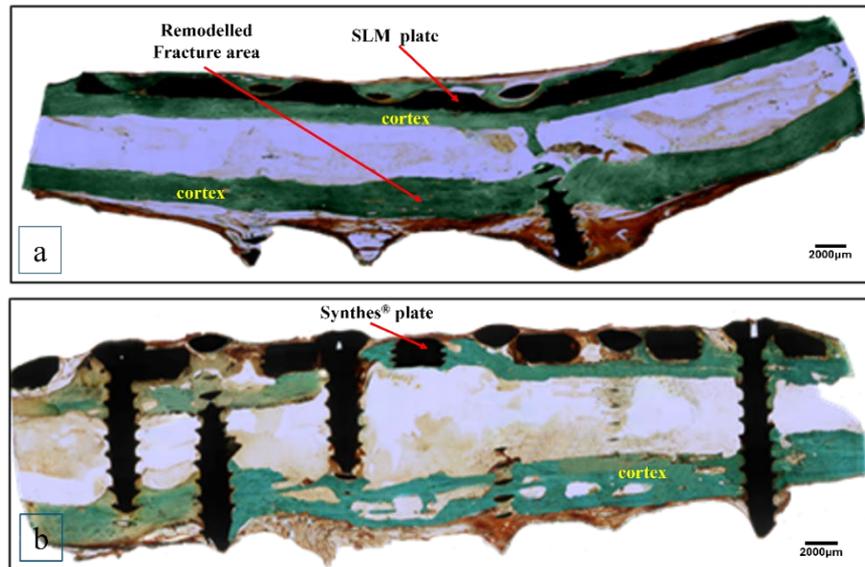


Figure 5: Rabbit tibia was embedded in Technovit® 7200 resin (Kulzner, Germany) and stained with Masson Goldner Trichrome. Sagittal view showing the fracture plate implantation in rabbit mid-shaft tibia using (a) SLM plate and (b) conventional plate. The fracture has successfully been united and remodelled at twenty-six weeks of post-surgery. (Original magnification 40X)

In this study, the potential of the local SLM plate as the internal fixator for bone fractures was assessed in vivo model comparison with the conventional machining plate i.e. Synthes®. Overall, no significant histological finding difference was noted in both groups. These in vivo results evidenced immediate contact healing between implant and bone. This outcome also reveals an early indicator that the localized SLM plate is biocompatible, and it is comparable to the conventional group. Fracture healing events, involve three main phases: i.e. inflammation, reparation and remodelling [1]. During the inflammatory phase, a hematoma forms at the fracture site within the first few hours to days post-fracture [1-2]. As vascular ingrowth progresses, osteoid is secreted and mineralized, leading to the formation of a soft callus at the fracture site, typically within the first 4 to 6 weeks [1-2,4]. Therefore, to stabilize the fracture fragments, an internal fixator was applied and required to protect and support the callus during the healing event. This fixation also supports the ossification of the callus. Consequently, a bridge was later formed by the initially formed woven bone between the fracture fragments [1,3]. In the present study, the formation of a bridging callus was noted in week 3 as illustrated in Figure 1. The present findings indicate that local SLM and conventional plates provide good support for fracture fragments.

Tibia fractures are common in orthopaedics, and due to the limited blood supply to the tibia, resulting from its thin subcutaneous muscle tissue, these fractures are prone to delayed healing and non-union after surgery [1-3]. Fracture healing is considered completed when remodelling has taken place. It is considered normal healing when the bone returns to its original structure, shape and mechanical function. Once the fracture has been fully bridged, it is essential for this new bone to adapt its function [1,4-5]. Supported by the outcome of this study, bone remodelling was present at week 26 (Figure 5) respectively in both groups. Therefore, in accordance with the previous studies, the present results confirmed that the local SLM and conventional plates were capable of supporting bone healing events effectively. This had reduced inter-fragmentary motion of the fracture site and thus helped the healing process in producing a new bone that was almost similar to its original form. It is interesting to note that there was no difference in healing patterns between local SLM and conventional plates. The use of Ti alloy plates as internal fixators to stabilize fracture fragments has become prevalent in the manufacture of orthopaedic implants [5-6]. This is attributed to its excellent mechanical properties, osteoconductivity, biocompatibility, low density, high corrosion resistance, and relatively low Young's modulus [9-10]. These characteristics make titanium alloys a preferred material for producing orthopaedic implants using Selective Laser Melting (SLM) technology. SLM titanium plates offer an

advanced solution by overcoming the mechanical limitations of conventional implants. Biomechanically, these plates enhance load-sharing by modulating stiffness through optimized lattice structures and tailored porosity, minimizing stress shielding and promoting physiological bone loading [9-11]. The ability to fine-tune mechanical properties ensures adaptive stiffness, facilitating better integration with bone tissue [10-11]. Additionally, SLM plates enable controlled micromotion at the fracture site, promoting secondary bone healing by stimulating callus formation through mechanotransduction, as demonstrated by the presence of callus at week 3 (Figure 1(b)).

The incorporation of porous regions at the implant-bone interface promotes osseointegration, enhancing implant stability through mechanical interlocking. Based on existing knowledge and the authors' perspective, future research in this field should focus on defining an optimal range of rigidity that provides stable fixation for primary healing while maintaining a degree of flexibility to support strong bone union through partial secondary healing. From a biomechanical view, previous studies on the production of SLM implants have demonstrated promising results [15-19]. The biomechanical performance of these implants is further improved by smooth geometric transitions that reduce stress concentrations and enhance fatigue resistance, ensuring long-term durability [15]. SLM technology also enables the design of dynamic plates with variable stiffness, facilitating progressive load transfer throughout different healing phases [16-18]. Additionally, integrated locking screw mechanisms improve construct stability by distributing stresses more evenly under axial, shear, and torsional loads. These advanced mechanical properties make SLM titanium plates particularly suited for complex fractures, as they provide a synergistic balance between mechanical support and biological healing, leading to improved long-term outcomes [18-20]. Recent findings indicate that locally produced SLM plates exhibit mechanical properties comparable to those of conventional plates. Furthermore, these local SLM plates are biocompatible, safe for cellular activity, and meet international standards for medical devices. Studies have shown that both local SLM and conventional plates are effective in stabilizing fracture fragments throughout the remodelling process, ensuring successful healing.

This study was conducted to further investigate the capability of the local SLM plate as an internal fixator in the orthopaedic field. To validate this hypothesis, the fracture model of the rabbit tibia was used to examine the patterns of bone fracture healing and its biocompatibility. The Masson Goldner Trichrome staining was employed to show the clear interaction between the bone and local SLM implant up to 26 weeks. Histological analysis revealed a good interaction between bone and local SLM at the implantation site which is comparable to the conventional plate. The present result showed there was no evidence of soft tissue reaction to either type of plate, suggesting that both plates are suitable for *in vivo* implantation without inducing adverse tissue responses, confirming their bioinert nature. Apart from that, the result also revealed that there was no structural deformity in both types of plates. The plates were also properly located on their original implanted site. The fracture was fully consolidated when stabilized with a six-hole plate [5-6], indicating that the local SLM plate performs comparably to conventional plates in terms of physical properties. The healing pattern at the implantation site was progressive for both plates, with the fracture healing effectively after the application of the local SLM plate, without any soft tissue reaction. This study demonstrates that normal bone anatomy was restored by week 26, as bone remodelling was observed (Figure 5). The local SLM plate sustained its function consistently from the initial fixation until remodelling occurred in week 26. The ability of the local SLM plate to hold fracture fragments was comparable to that of the conventional plate. Supported by prior research [15-16], this suggests that local SLM plates are as effective as conventional plates in facilitating the fracture healing process. Furthermore, the different manufacturing methods of the plates did not result in significant differences in their biocompatibility or ability to stabilize fracture fragments [15,19]. Understanding biomechanical forces and biocompatibility is crucial for optimizing the healing process and achieving complete bone remodelling [19-20]. Moreover, biomechanical data can help stimulate bone remodelling and determine the required stability of implant materials during fracture healing, reducing the risk of implant failure.

Overall, based on data analysis retrieved at both intervals, this study has proven that the local SLM plate had successfully worked as an internal fixator by supporting the healing event at the fracture site. In addition, the local SLM plate remained *in situ*, straight, stable and showed good

osteointegration which is comparable to the conventional plate. Furthermore, the application of SLM technology would be an ideal initiative towards the production of customized or personalized orthopaedic implants. Although this intervention showed a promising outcome, further assessment through the scanning electron microscope observation is suggested. This analysis is recommended to be conducted in the future as it can evaluate more valuable information on the bone structure and morphology during healing events in detail. Besides, this method provides information such as trabecular bone surfaces, osteoclast-bone interfaces, cartilaginous surfaces or structures, implant surfaces, implant-tissue interfaces and more in detail.

4. CONCLUSIONS

The study has shown a comparable outcome of using the orthopaedic implants produced through SLM technology. The findings demonstrate the potential of SLM technology towards the production of orthopaedic implants as internal fixators in a pre-clinical setup. Both groups show bone remodelled and biocompatible at the end of the study interval (26 weeks). In conclusion, the study shows that local SLM plates (Ti alloys) can support fracture fragments of the tibias of NZWR as they give good results. This is supported by the results obtained from histological interpretation. These findings may pave the possibility for clinical trials and applications in future.

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Author Contributions

All authors contributed toward data analysis, drafting and critically revising the paper and agree to be accountable for all aspects of the work.

Disclosure of Conflict of Interest

The authors have no disclosures to declare

Compliance with Ethical Standards

The work is compliant with ethical standards. The ethical approval was obtained from the IIUM Animal Care and Use Committee (I-ACUC), with approval letter reference number: IACUC 2022-022.

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