THE *IN VIVO* STUDY OF INJECTION MOULDED 316L STAINLESS STEEL FRACTURE FIXATION PLATE

BY

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ABSTRACT

Metal Injection Moulding (MIM) is a revolutionary new class of medical implant fabrication in orthopaedics. This technology employs natural resources and holds great promises in producing large quantities of metallic parts for prosthetic implant at minimum outlay without compromising its quality. The present study was conducted to compare potential effects of MIM plate for internal fixation in fracture healing in New Zealand White (NZW) rabbits with conventional machining plate (Synthes®) as control. Following research approval by IIUM Ethics Committee (IIUM/305/20/4/10), forty rabbits were used and randomly divided into two groups. All rabbits underwent single transverse mid-shaft tibial fracture surgery and fixation under anaesthesia. The fractures were fixated with either the MIM plate or conventional plate (Synthes®). The monitoring of fracture healing was carried out at week 3, 6, 9, 12 and 26 according to ISO10993-2:2006 & ISO10993-6:2009 standards. The status of bony union was examined by means of plain radiographic assessment, macroscopic observation and, histological evaluation. There were callus formations in both groups. Bony union was evident at week 6 post-operatively, whilst bone remodelling was completed at week 26 as indicated by plain radiograph assessment and macroscopic evaluation. Histological assessment showed that both groups possessed mild to moderate callus bridging at week 3 and week 6, respectively. Complete remodelling of cortical bone was evidenced at week 26. The plate was neither broken nor bent during the study. These findings indicate that the MIM plate has equal potential to hold the fracture as the conventional plate. Therefore, the locally manufactured MIM plate has the potential to be used as an alternative internal fixator for fracture management in orthopaedic considering the value and conservation of natural resources.

ملخّص

إن نظام تقوية العظام بالألواح المعدنية (MIM)، فكرة ثورية جديدة بإمتياز في علم طب زراعة العظام. إن هذه التقنية، التي تعتمد على المصادر الطبيعية، واعدة بتوفير كمية كبيرة من الأجزاء المعدنية الصناعية لزراعتها، على الأقل خارجياً، مع الاحتفاظ بوجودها العالية. إن هذا البحث يهدف إلى تقويم الآثار المحتملة لقوالب معدنية (MIM) تمت زراعتها في أرانب نويزيلانيدية لترسخ وضمد الكسور داخلياً. وكان مع كل أرنب لوح معدني عادي (Synthes®). أما من حيث **منهج البحث**، فلقد تم اسخدام عدد أربعين أرنباً في العملية، وذلك بموافقة من لجنة أخلاقيات البحث بالجامعة الإسلامية العالمية ماليزيا، برقم (IIUM/305/20/4/10). وقد تم تأليف وأقلمة أرانب لمدة أسبوعين، وبعد ذلك تم تخدير جميع الأرانب قبل إجراء عملية جراحية لكسر العظام. ثم تمت إعادة ربط العظام إما بالقالب المعدني (MIM) أو باللوح المعدني العادي (Synthes®). تمت مراقبة ضمد الكسور خلال الأسبوع الثالث، السادس، التاسع، الحادي عشر، والسادس والعشرين، وفق المعاديير المعتمدة (ISO10993-6:2009 & ISO10993-2:2006). خلال هذا المراقبة قد تم اختبار حالة ضمد الكسور عبر المجهر، المسح الطبوغرافي العادي، وتقييم بناء الأنسجة بإعتبار أن كل حالة تحوي على ولوح معدني. وكان من المثير للدهشة أن النتائج قد أظهرت أن الطبقة لحمية العريضة قد تكونت في الحالتين معاً. وكان ترابط العظام قد بدأ واضحاً منذ الأسبوع السادس، بينما إلتئامها قد اكتمل بدخول الأسبوع السادس والعشرين. من خلال اختبار بناء الأنسجة قد ظهر أن المجموعتين يمتلكان طبقة لحمية عريضة أولية إلى متوسطة بدخول الأسبوع الثالث والسادس. بينما الضمد الكامل للعظام كان واضحاً في الأسبوع السادس والعشرين. ليست هنالك صفيحة مسكورة خلال هذه الدراسة. إن نتائج الدراسة تشير إلى أن القوالب المعدنية (MIM) قد تتمتع بنفس الميزة التي تتمتع بها الألواح المعدنية العادية في ربط الكسور وتقويتها. ولذلك يمكن استخدام القوالب المعدنية كرابط بديل لمعالجة الكسور الداخلية بالنظر إلى قيمتها الإقتصادية للمحافظة على الموارد الطبيعية.

APPROVAL PAGE

I certify that I have supervised and read this study and that in my opinion, it conforms to acceptable standards of scholarly presentation and is fully adequate, in scope and quality, as a thesis for the degree of Master of Health Sciences (Biomedical Science).

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DECLARATION

I hereby declare that this thesis is the result of my own investigations, except where otherwise stated. I also declare that it has not been previously or concurrently submitted as a whole for any other degrees at IIUM or other institutions.

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LIST OF ABBREVIATIONS

AMREC	Advanced Material Research Centre
SIRIM	Standards and Industrial Research Institute of Malaysia
MIM	Metal Injection Moulding
NZW	New Zealand White
CRES	Corrosions-resistant Steel
SS	Stainless Steel
VIM	Vertical Injection Moulding
CT	Computed Tomography
PS	Palm Stearin
PP	Polypropylene
NBF	Natural Buffered Formalin
SEM	Scanning Electron Microscope
TEM	Transmission Electron Microscope
KTX	A combination of drugs Ketamine, Tilatamine / Zolazepam and Xylazine for anaesthasia
AO/ASIF	Association for the Study of Internal Fixation
316	Type of stainless steel
ISO/IEC	International Organization for Standardization / International Electrotechnical Commission
L	Low carbon contains in stainless steel
RSSFH	Radiographic Scoring System for Fracture Healing
n-heptane	Normal Heptane
MOSTI	Minister of Science, Technology and Innovation
POP	Plaster of Paris

IIUM	International Islamic University Malaysia
Sdn. Bhd.	Sendirian Berhad
AG	German Aktiengesetz
Pty Ltd.	Propriety / Private Limited
SPSS	Statistical Package for the Social Science
IBM	IBM Corporation
Co.	Company
BR	Basic Research

LIST OF SYMBOLS

N	Newton
g	Gram
mm	Millimetre
cm	Centimetre
%	Percentage
°C	Degree Celsius
mmHg	Millimetre Mercury
rpm	Rotation per minute
µm	Micrometre
C	Carbon
Cr	Chromium
Mn	Manganese
Fe	Iron / Ferum
Ni	Nickel
®	Registered patent
™	Trademark
kg	Kilogram
<	Less than
g cm^{-3}	Gram per cubic centimetre
min	Minute
Mg/ml	Milligram per millilitre

ml/kg	Millilitre per Kilogram
SiO_2	Silicon dioxide / Quartz

CHAPTER ONE

INTRODUCTION

1.1 BACKGROUND

Orthopaedic is a medical specialty that is highly technical in nature. It employs numerous techniques and/or skills ranging from fine micro-vascular surgery to bone fixation, massive metallic and polymeric composite implants for joint replacement, as well as complex methods for external fixation of the bone. Successful usage of the orthopaedic implants requires extensive technical knowledge and skills by the practitioner and/or the surgeon. Understanding the biology of the affected tissues is an important factor that can lead to an effective result (Chapman, 2001).

In orthopaedic trauma, the energy that causes bone fractures generates a zone of injury that affected the bone and its surrounding tissues. Early observations on the external splinting had lead to belief that bone fractures are best treated by immobilization and prolonged rest. Although fractures can be recovered by non-operative treatment, the shortcoming of directly controlled position of the fracture fragments had led to problems such as mal-union and non-union. Moreover, prolonged immobilization can cause fracture illness that is characterized by joint stiffness, muscle atrophy, disuse osteoporosis and persistent oedema (Augustus, et al., 2008).

Up to the 19th century, the treatment of fracture was performed by means of external splinting. This is done to achieve an anatomical alignment of the broken bone, to relieve pain and stabilize the fragments for bone union. From biomechanical point of view, fracture fixation should have sufficient stability to such a degree that

bone healing may take place on order to reduce inter-fragmentary movement that may occur under external loading and muscle activity (Lutz & Ito, 2005).

The key factor that affects bone healing is the inter-fragmentary movement. It determines the tissue strain and the cellular reaction in the fracture healing zone. Therefore, the methods of fracture fixation will be assessed with regard to their capability to reduce the inter-fragmentary movement (Chapman, 2001). As a consequence, the operative of fracture treatments which involved new fixation technique and implants were developed in the 20th century (Lutz & Ito, 2005).

In light of these phenomena, it is clear that the focus of the fracture treatment should be on both healing and restoration to pre-injury functions. One of the methods that implant sufficient skeletal stability to restore its function is by internal fixation with metal implants (Gilardino, Chen, & Bartlet, 2009). Metal implants have been successful in fracture stabilization because they support bone functions without impairing the healing, remodeling or growth of the bone.

The first metal implants were fabricated from Vanadium steel. It is the best available alloy in the beginning of the 20th century. However, the usage of Vanadium had been controversial due to poor tissue compatibility issues. Later, modern orthopaedic surgery, three metallic alloys are employed for implant fabrication i.e stainless steel, chrome-cobalt and titanium (Golish & Mihalko, 2011).

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steel had been controversial due to its poor compatibility issues. Later in modern orthopaedic surgery, three metallic alloys are employed for implant fabrication i.e. stainless steel, titanium and cobalt-chromium.

Nowadays, stainless steel 316L plate has been widely used for orthopaedic and dental implants due to its ability to form a direct bone to metal contact. The plate has good properties in terms of mechanical strength, biocompatibility and corrosion resistance (Ying, Jean, & Her, 2013). Those properties make it as the most commonly used material for internal fixation of the bone fracture. Hypothetically, the internal fixation technique provides sufficient stability for bone healing to occur by stimulating the callus formation. Research has been directed at modifying implant surfaces to achieve a more rapid and extensive stabilization as well as integration of the device in bone (Yang, Kabel, & Van Rietbergen, 1998). In medical application especially in the orthopaedic field, most surgeons opted for the 316L stainless steel plates due to their availability in different sizes and shapes. The demand of the plates is high but the price is expensive (Omar, Mustapha, Istikamah, & Ali, 2007).

Current metal implants used in Malaysia for internal fixation are made from conventional machining process. Machining is simply known as an action that requires an implant to be machined from a solid piece of metal stock. It is widely used especially in the production of metal implants in orthopaedic field since it is suitable for various work materials and can produce a variety of shapes and geometric features for the metal implants (McKinley, 2006).

However, conventional machining process requires advanced machining operation and it is time consuming since it requires more time to shape the metal compared to other processes. In addition to that, there will be leftover materials from the machining process which is considered as a waste, which subsequently will

increase the production cost of the metal implants. The price in the market will be going up and cause an economical strain in health sector (Mikell, 2010).

In order to reduce the production cost of the metal plates, a new techniques which is known as Metal injection molding (MIM) is developed. This technique utilizes the flexibility of both materials (i.e. powder metallurgy) and the design (i.e. plastic moulding) (Omar & Zulkifly, 2014). It shapes a component according to the intended size through an injection moulding process (Tandon, 2001). With it's properties that are comparable, or even better than the conventional machining process, this MIM technique is suitable for the production of a small complex-shaped parts with outstanding mechanical strength. If the shape allows the production of the part by, for example, conventional pressing and sintering, MIM would in most cases be too expensive. However, if the required number of complex parts is huge enough for large-scale production, MIM is cheaper than machining plate (Ismail, Omar, Subuki, Abdullah, Ali, & Hassan, 2007).

Previous study had done on MIM implant's biomechanics and toxicology studies have produced positive result (Abdullah, Omar, & Zulkifly, 2014). In addition to that, plates or implants produced via MIM process have high final density and close porosity. Details on MIM plates and conventional machining plates as well as their significance usage in orthopaedic field especially in the area of bone fracture fixation were provided in Chapter 2 of this thesis.

This present study aimed to evaluate the potential of MIM plate to hold the bone fracture in a rabbit model. The conventional plate Synthes® was used as control. The outcomes of this *in-vivo* study were assessed by means of plain radiograph, gross examination and undecalcified histological analysis. The complete materials and methods of the study were addressed in Chapter 3 of this thesis. In brief, the MIM

stainless steel plate was implanted on 20 of New Zealand White (NZW) rabbits or *Oryctolagus cuniculus*. The rabbits were assigned into two groups. Each group was subdivided into five groups based on the interval periods (i.e. week 3, 6, 9, 12 and 26) as per recommendation by the ISO 10993-6:2009. Experimental bony fractures were created at rabbit's tibia. The fractures were fixed with either MIM plate or conventional plate; the control. All rabbits were sacrificed at each time point post-implantation. The implantation site of the bones were harvested *en bloc* for evaluation purpose. The results of this study were described in Chapter 4 and discussed in Chapter 5 of this thesis.

The MIM technique has now become a very useful tool in producing orthopaedic implants. This technology will serve as alternative that holds great promises for efficient bone fracture management in orthopaedic. Its establishment perhaps, should be explored further since it could contribute to the local economy expansion and wealth creation of the country.

1.2 RESEARCH QUESTION

Could the MIM plate have the ability to perform as good as the conventional plate?

1.3 HYPOTHESIS

MIM plates could perform as good as conventional plate

1.4 OBJECTIVES

This study embarked the following objectives:

1. To evaluate the potential of MIM plate as an internal fixator for bone fracture in a rabbit model with the Synthes® plate as control.
2. To compare between the unification (or, union) of a bone fracture that fixed with the MIM plate and Synthes® plate using plain radiograph, gross examination and undecalcified histology.