CASE STUDY ANALYSIS OF OSSEOINTEGRATION AND LIMB-SALVAGING TECHNOLOGY
IN ANIMAL SUBJECT’S BILATERAL OSSEOINTEGRATED IMPLANT JOURNEY WITH
POTENTIAL HUMAN TRANSLATION

by

Donna Eggert

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A Practice Inquiry Submitted to the Faculty of the

COLLEGE OF NURSING

In Partial Fulfilment of the Requirements

For the Degree of

DOCTOR OF NURSING PRACTICE

In the Graduate College

THE UNIVERSITY OF ARIZONA

2014
As members of the Practice Inquiry Committee, we certify that we have read the Practice Inquiry prepared by Donna Eggert, titled “Case Study Analysis of Osseointegration and Limb-Salvaging Technology in Animal Subject’s Bilateral Osseointegrated Implant Journey with Potential Human Translation” and recommend that it be accepted as fulfilling the Practice Inquiry requirement for the Degree of Doctor of Nursing Practice.

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Final approval and acceptance of this Practice Inquiry is contingent upon the candidate’s submission of the final copies of the Practice Inquiry to the Graduate College.

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SIGNED: Donna Eggert
ACKNOWLEDGEMENTS

My DNP journey would not have been possible without the support, dedication, belief and patience of many people who gave me encouragement while I was juggling active duty military commitments and working on my practice inquiry.

First and Foremost, I would like to thank my Practice Inquiry committee … my Chair, Dr. Sally Reel, Dr. Catherine Michaels, Dr. Ivo Abraham and Dr. Katie Sheppard who was instrumental in the success of my oral and written exams and my defense proposal. Professor Reel, thank you for your time, patience and visionary ideas in the scholarly development of my project. Your words of encouragement while I was deployed to Afghanistan will be forever etched in my heart. Professor Michaels, I am grateful for your meticulous writing guidance and mentorship which kept me focused through completion. Professor Abraham, thank you for your support organizing my outline and giving me valuable inputs with encouragement.

I am extremely appreciative of canine Jack and owner Dr. Karen McDonald for the enormous support, not only allowing “Jack” to be my case study subject but sharing his medical and progress records and providing information for my thesis preparation. I believe your labour of love allowing Jack to participate in osseointegration technology will serve to benefit many military troops in the future. A special thank you Dr. Denis Marcellin-Little and the North Carolina State University Veterinary Clinic staff. I appreciate you sharing information, time and support with Jack’s case study. Professor Marcellin-Little, thank you for letting me be a part of “Jack” journey with osseointegration implant technology.

I am grateful for the support and time spend with the staff and military amputees at the Center for the Intrepid (CFI) Armed Forces Rehabilitation Center especially hearing of the bravery and survival stories told of limb-loss and new appreciation of life. Also, I would like to thank Lucas and Amanda for their on-going administrative support from the University of Arizona.
Finally, my family … especially my parents who encouraged me to climb every step of the ladder to reach my educational goals. I miss you both and wished you were here to share this success. To my sister, Sharon, who provided me unconditional love and has always been there to support me. Thank you to my amazing, extremely talented and intelligent sons, James and Alexander who have inspired and motivated me to succeed even when it seemed impossible.

Thank you both for assisting me with multiple technical computer challenges and literally made it possible for me to complete my defense. Words cannot express how much I appreciate and love you both.

I will be forever indebted to my #1 fan, my husband Jim, who has had many sleepless nights supporting me on my doctoral journey even while I was deployed. Jim, the countless hours and gift of time could never be repaid. Your unwavering love and sheer patience made this possible. Thank you for sharing this journey with me.
DEDICATION

This Practice Inquiry is lovingly dedicated in memory of my parents, Guy and Alice; exceptionally wise people … each inspired my life through their strength, enduring faith, and boundless love for family and to the brave military men and women who have sacrificed life and limb for our great country, the United States of America.
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ABSTRACT

In the twenty-first century, new cutting-edge osseointegration technology is improving quality of life. Osseointegration is a new technique to suspend an implant prosthetic device for individuals with a limb-loss. The science of osseointegration is not clearly understood although there appears to be a special relationship between pure titanium that promotes activation of our bone building cells and bone remodelling. Direct bone-anchored osseointegration to integrate a foreign device into the body without the body rejecting the prosthesis is the new technology lacking knowledge and research clinical cases for human translation. The objective of the case study was to review the science of bone-anchored osseointegration as a limb-salvaging technique and potential translation to humans using a canine model in a well-defined control study. Aims were to enhance knowledge technology, improve mobility, decrease pain to improve quality of life and influence health care practices.

By the year 2050, the projected number of American amputees is expected to reach 3.6 million. Many people depend on artificial limbs to perform their activities of daily living. Often these limbs start developing complications associated with stump-socket designs such as separation from the human tissue, poor fit with repeated fittings, recurrent skin infections, ulcers and pressure sores due to non-uniform pressure distribution over the socket contact area and pain which decreases their mobility. Since 2001, close to 28,500 American troops have been wounded in combat in Iraq and Afghanistan. Greater than 24,600 of them have survived their injury, the highest survival rate of any war in the history of the United States. Sadly, 700 of these services members have lost at least one limb from amputations. Lower limb amputations are still performed above the knee as not enough bone can be preserved below the knee for prosthesis. Osseointegration with limb-salvaging techniques could enhance mobility and quality of life for those individuals who sacrifice their limbs defending our freedoms.
Introduction to the Study

“Between animal and human medicine there is no dividing line – nor should there be”

(Rudolf Virchow, 1900)

As of September 2012, there were 68,000 military members deployed in Afghanistan in the combat zone (Whitlock, 2012). Some of these members have suffered or will suffer traumatic limb injuries during their deployment. Between 2000 and 2011, there were 6,144 amputations among military members deployed in combat with 2,037 (33%) of them having a major limb amputation (MSMR, 2012). One out of every 195 people, have had an amputation which resulted in limb-loss in the United States (Ziegler-Graham et al, 2008). Approximately 5,000 amputations are performed yearly in the United Kingdom (Chimutengwende-Gordon et al, 2011). New limb salvaging techniques with osseointegration could be used in otherwise healthy civilian and military members who undergo amputations to save more tissue and limb function. Using veteran and warrior amputees that are relatively young and in good health make them ideal candidates for aggressive rehabilitation with osseointegrated implants to improved their mobility and decrease their pain level (Isaacson et al, 2009).

Background and Significance

Limb salvaging surgery (LSS) has become more popular in the last 20 years compared to amputations. The goal standard to treat bone and soft tissue tumors of the extremities has been amputation with only a 10-20% survival rate. Studies are now showing short-term survival rates improved 50-70% with LSS for osteosarcoma or bone cancer (Kupersmith & Somerson, 2012).

According to the National Center for Vital and Health Statistics in 2012, the average life expectancy is currently 78 years old in the United States up from 69 in 2005 (CDC, 2012). Research indicates people do not mind living longer as long as they have a good quality of life with those extra
years (CDC, 2012). People are outliving their medical implants. The average life span of an implant is 10-15 years depending on the type (Harrysson et al, 2007). Younger people are having LSS procedures, and as seniors continue to live longer, a growing number of joint replacement patients will outlast their implant (AAOS, 2012). Research needs to provide more evidence based on clinical trials to show the practice impact to meet the challenges of the growing implant population.

To date in the United States, the magnitude and distribution of orthopaedic implant devices is hard to determine with no systematic approach to gather available data. In 1988, a nationwide medical device implant one time survey was conducted by the Food and Drug Administration’s Center for Devices and Radiological Health (FDA/CDRH) in collaboration with the Center for Disease Control’s National Center for Health Statistics (CDC/NCHA) to generate the nation’s first population-based prevalence estimates of orthopaedic implant devices. They surveyed 122,310 individuals. The results showed an estimated 6.5 million orthopaedic implants were used in the United States general population in 1988, which included 1.6 million artificial joints and 4.9 million fixation devices. These orthopaedic implants comprised nearly half of all medical implants in use, 43.4% (Moore et al, 1991). No other efforts to collect data on medical device implants could be identified. Perhaps the companies kept this data and as such are proprietary.

Statement of the Problem

Amputee numbers are expected to soar in the future with the aging population and traumatic injuries. Osseointegration technology is surging at a fast pace but few surgeons possess the knowledge and expertise to perform successful limb-salvaging surgery using osseointegration technology (Webster et al, 2009). No medical or nursing protocols were found in the literature to provide knowledge on caring for the member receiving limb-salvaging surgery with osseointegration prosthesis. Without osseointegration technology, limb salvaging surgeries are saving lives and even increasing survival rates for cancer
patients who otherwise may not have survived before this booming technology. However, over time, some of these artificial limbs and implants are separating from the tissue, causing increase pain, pressure sores, infections and other discomforts (Kupersmith & Somerson, 2012). Given the young age most patients undergo limb salvage; it is likely most will require at least one and some more than one prosthetic procedures in their lifetime (Grimer & Jeys, 2012).

The concerns about prosthetics are most relevant for the military. Approximately 15% of military warriors have lost multiple limbs and a significant number have short residual limbs where socket technology, the technology associated with current prosthetic, is not an option or has been rejected by their body. Greater than 50% are not using their fixation devices as they are cumbersome and difficult to use (Moore, 1989). Younger people are having total joint procedures, and as seniors continue to live longer; a growing number of the joint replacement patients will also outlast their implant (AAOS, 2012). Implant recalls are occurring at an alarming rate due to corrosion and toxicity of the metal alloys interface with the tissues in the body (CDC, 2012). Given these issues, osseointegrated prosthesis would be helpful, but limited knowledge of osseointegrated prosthesis exists, as well as clinical protocols to guide these practices and therefore implants are lagging behind this advanced technology surge.

Translational research needs more studies that test translating research into practice intervention, and adopting new innovations which can influence health care practices. The current research and clinical trials on osseointegrated prostheses are being used for felines and canines, but the clinical practice has not been systematically studied in preclinical research. This practice inquiry addresses the potential for osseointegration prosthesis for humans by using a canine case study to describe the clinical features of the osseointegration technique, follow-up care and results.
Purpose of Study

The purpose of this case study is to review the science of osseointegration as a limb salvaging technique with potential translation to humans. Translation in this case study refers to limited preclinical animal research to clinical human research. Concepts are defined and discussed using a canine model in a well-controlled case study and looking at comparative variables of canine and human candidates for osseointegration. Based on canine case study, selection criteria for the ideal human candidate will be defined as well as risk factors described. Mitigation of those risk factors will be addressed from the perspective of the doctorally-prepared nurse practicing in collaboration with the interprofessional team. The expected outcome will be to enhance education to the patient, family and the interprofessional team to advance our practice knowledge of osseointegration. This progressive technology could provide life-changing mobility options to people, civilians and especially the wounded military warrior.

Conceptual Framework

The Iowa model of research-based practice developed in 1998, revised in 2001 at the University of Iowa will guide the use of research outcomes to promote and improve healthcare practices. In the absence of published research data, this model uses case study evidence providing an algorithm to guide decisions in using research findings (Titler et al, 2001). Decisions points are guided using evidence-based practice, whether problem-focused, clinical-focused or new knowledge-focused coming from outside the organization (White & Dudley-Brown, 2012). This model encourages the nurse to ask questions during the research process that focus not only on the new research data collected but the overall outcome and if it is ready for dissemination into practice. Nurses are looking for new evidence for osseointegration in order to resolve those clinical issues for patients with prostheses.
Implants

Implanted medical devices are used in an animal or human body to restore or enhance their biological system desired state to improve mobility for activities of daily living. These medical devices are made from materials that can be used to replace tissues in the body such as dental (root implants), vascular surgeries (grafts) or orthopaedics (hip replacement) (Hagberg & Branemark, 2001; Isaacson et al, 2009). Inability to perform activities of daily living such as a not being able to walk or no teeth to eat food definitely impacts our quality of life. The challenge is finding materials to make these medical devices that our body will accept and meet our desired state of function without major risk factors.

Titanium is widely used in orthopaedic implant devices. High biocompatibility, increased resistance to corrosion and lack of toxicity on macrophages and fibroblasts make titanium an ideal choice for implant devices. Titanium also has a decreased inflammatory response with peri-implant tissues and having a surface made of an oxide layer provides the ability to repair itself by reoxidation if damaged (Browne & Gregson, 2000). Other alloys such as aluminium, niobium, nickel, tantalum, zirconium, and hafnium can be used as orthopaedic implant materials (Mavrogenis et al, 2009). Prior to titanium, implant materials devices were made of wood and then aluminium. One surgeon interviewed uses less powdered titanium and now uses a refined laser technique when making implants for models (Marcellin-Little, 2013). Laser and powdered titanium will be the primary materials discussed with bone-anchored osseointegration in the canine case study for this paper.

Science of Osseointegration

In 1952, Dr. Per-Ingvar Branemark, a Swedish professor used a titanium implant chamber to study the blood flow patterns in a rabbit bone. He noticed the chambers could not be removed once he completed his experiment and called his discovery “osseointegration”. The bone had fused into titanium with very little inflammation noted at the material tissue interface which was unusual when a foreign
material was put in the body (Branemark, 1983). Normally, a foreign material in the body would disrupt the normal wound healing, create increase inflammation, not adhere to the material-tissue interface and frequently be rejected by the body (Tillander et al, 2009). The stages of a normal wound healing process would be inflammation, formation of tissue, and remodeling of the tissue. Dr. Branemark had discovered an osseointegrated technique which would become new technology to be used in surgeries for members with a limb loss (Hagberg & Branemark, 2009).

Dr. Branemark unique technique discovery would lead to future osseointegrated transfemoral prostheses treatment in Europe with animal and humans trials. Treatment with osseointegrated transfemoral prostheses has been performed in Sweden since 1990 and involves two separate surgical procedures followed by rehabilitation (Hagberg & Branemark, 2009). The osseointegration procedure involves surgically inserting titanium implant directly into the bone of the residual limb. This implant serves as an attachment system to connect and suspend a prosthesis to the residual limb. A bone can heal around an implant resulting in a newly formed bone (Fini et al, 2004). These osteogenetic processes involve cellular and extracellular biological events that occur at the bone-implant interface, similar to the healing process in terms of an initial host response. Osteogenetic processes are regulated by growth and factors released by activated blood cells located at the bone-implant interfaces (Davies, 1998). Bone that comes in contact with an implant surface undergoes morphological remodelling and adapts to stress and mechanical loading (Mavrogenis et al, 2009). Other countries, outside the United States are using this new technique primarily for individuals with transfemoral level amputations. Due to limited trials, safety and regulatory guidance, long rehabilitation time and resources, the osseointegration procedure has not been approved by the FDA yet for use in the United States for individuals with lower limb amputations (Webster et al, 2009).
Overview of Osseointegration

Osseointegration also referred to osteointegration involves a direct structural and functional connection between ordered, living bone and the surface of a load-carrying implant. The implant is considered osseointegrated when there is no progressive relative movement between the implant and the bone it has direct contact with (Mavrogenis et al, 2009).

Osseointegration is the lack of a negative tissue response, not necessarily a biological tissue response. Titanium implants can become permanently incorporated within a bone in that the living bone could become fused with the titanium oxide layer of the implant. The only way they could be separated would be a fracture (Mavrogenis et al, 2009). However, surgeons are unable to predict the long term durability of osseointegrated titanium implants (Tillander et al, 2010). More research and clinical trials need to be done to support their durability.

Osseointegration can be enhanced or inhibited by several factors. Implant issues such as design, chemical composition, material, shape, length, and diameter, the host healing potential, mechanical stability, implant surface treatment and coating can enhance osseointegration (Rosenqvist et al, 1986, Zhang et al, 2004, Mombelli, 2006 and Wong et al, 1994). Factors that inhibit osseointegration include excessive implant mobility, radiation therapy and pharmacological agents such as cyclosporine A, warfarin and non-steroid anti-inflammatory drugs. Patient factors such as rheumatoid arthritis, nutritional deficiency, elderly, smoking and osteoporosis also inhibit osseointegration (Rosenqvist et al, 1986, Zhang et al, 2004, Mombelli, 2006 and Wong et al, 1994). While some of these factors remain controversial, literature tends to validate the importance of having a fairly healthy subject with healthy bones when being considered as an osseointegration surgery candidate.
Overview Limb-Salvaging

Current LSS involves replacing the affected bone with a substitute bone or a metal limb spare implant. Limb-salvaging surgery is complex with few surgeons skilled in the art of tissue preservation (Grimer & Jeys, 2012). The ability to remove a tumor and still be able to salvage the surrounding tendons, nerves and blood vessels for limb function takes special skills and experience. Limb-salvage surgery does not come without potential complications. Grafts or rods can break or become loose; the person may need additional surgery in the future or even need a future amputation (American Cancer Society, 2013).

Limb-sparing surgery has the potential to treat cancerous tumors by either removing the tumors without having to amputate the arm or leg limbs. Diseased bone removed due to osteosarcoma can be replaced with a bone graft. A bone graft is a piece of bone that can be from the person, another part of their body, from another person or a man-made device, an internal prosthesis to replace part or all of the bone. The prosthesis can be made from metal or other materials (American Cancer Society, 2013).

Limb salvaging techniques with tissue preservation versus amputation will be discussed as part of the conceptual framework and central to the quality of life risk and potential benefits. In limb salvaging preservation, it is imperative sufficient bone below the knee or above the hip is available to permit osseointegration (Isaacson et al, 2009).
Research studies indicate there may be functional benefits for a person to have transcutaneous osseointegration prosthesis limb-salvage surgery over conventional prosthesis or amputation surgery for lower extremity tumors, given that a viable option and sufficient tissue are available to be salvaged. Greater than 73% of the 1.04 million people in the United States with lower limb amputees report complications with their conventional prosthesis (Tillander et al, 2010). Skin problems with ulcers, sweating and irritation are a few complications that affect their quality of life (Hagberg & Branemark, 2001; Tillander et al, 2010).

Transcutaneous osseointegration is an implant that protrudes through the skin permanently and integrates as a direct bone attachment or anchor of prosthesis. Amputees are favouring this option over conventional amputation surgery prosthesis attachments. Advantages have been limited tissue breakdown, enhanced ability to function with mobility and non-restrictive range of motion (Isaacson et al, 2009). Other advantages over conventional prosthetic fittings with a socket suspension could be reduced skin irritation, limb breakdown and decreased pain (Hagberg & Branemark, 2001).
Literature Review

A few qualitative articles were found in the literature review to be informative on osseointegration technology, limb salvaging and associated quality of life measurement tools. Bone-anchored osseointegration and limb-salvaging technology literature associated with this practice inquiry case study has limited research (less than 10 articles found) available for comparison in the United States or other countries. Osseointegration, specifically transfemoral osseointegration, was introduced roughly 20 years ago with first trials in animal and human models in Europe (Pitkin, 2008). Some of these studies will be discussed to provide knowledge of limited publication on osseointegration to highlight the need for more evidence-based trials. Since our case study model for potential translation to humans will focus on bone-anchored osseointegration, the existing literature will be relevant to understand some of the technology used in this case study. No national database exist that serves to capture the current activity, trends or processes that could analyse outcomes and improve standards in peripheral interventions for limb salvage or osseointegration procedures (Davies, 2012).

In 2001, a German research article presented the first osseointegrated anchoring device designed to enable a permanent attachment of an artificial limb for an above-the-knee implantation. The subject was an 18 year old human male who underwent a two-stage operative procedure and after approximately 12 weeks of rehabilitation was able to walk without mobility aids and return to work. This individual had an amputation with complete healing of the tissues before his osseointegration procedure (Staubach & Grunde, 2001).

Literature review show osseointegration for upper extremity amputation started in 1990 in Sweden where the first titanium fixture was implanted into a thumb for trans-humeral and below the-
elbow amputation. This procedure also involved two surgical procedures; one to attach the titanium fixture to the skeleton, and a second procedure six months later to attach prosthesis (Jonsson, Winterberger & Branemark, 2011). From 1990 to April 2010, there were 37 upper limb osseointegrated cases treated and fitted with prosthesis. These patients indicated improved function and enhanced quality of life after the osseointegration procedures (Jonsson, Winterberger & Branemark, 2011).

In England, osseointegration for transfemoral amputees has been performed since 1997. Eleven candidates have undergone similar surgical experiences as mentioned in above cases. This article highlighted the physical and prosthetic advantages of direct skeletal attachment leading to improvement of function, comfort and quality of life. The importance of screening the candidate or pre-osseointegration assessment of candidates prior to their procedures is emphasized regarding the rehabilitation period (Sullivan et al, 2003).

Systemic reviews were shown to highlight a surge in limb-salvaging surgery over amputation with short-term survival rates improving especially with osteosarcoma (Kupersmith & Somerson, 2012). Some dated articles even suggested a forward trend preference toward limb salvage surgery for sarcomas in the extremities (DeGroot & Ellison, 1995). With improved healthcare screening and preventive care, people are living longer, taking better care of them self and using new innovative technology to stay highly functional. Literature also supports the notion that traumatic injuries are on the rise with military members exposed to combat and people in traffic accidents, which serve to increase amputee numbers in the future. In 2012 during Operation Enduring Freedom (OEF) and Operation Iraq Freedom (OIF) statistics reflect 87% of the military soldier amputations as major limb amputations (Fischer, 2013).

Research indicates military members in combat are surviving catastrophic injuries, compared to previous conflicts, primarily due to improved body armour gear and medical management of injuries in
the field with quicker evacuation from the combat zone (Webster, 2009). Individuals, who have survived however, are coming home with more limb amputations complicated with orthopaedic, soft tissue, vascular, and neurological injuries. Some of these amputations have shortened residual limb length where socket technology with conventional prosthesis has a limited ability to provide adequate prosthetic suspension. Another group of military members with amputations have significant heterotopic bone formation, which makes using socket technology painful and limited their mobility and quality of life (Webster, 2009).

**Osseointegration Studies**

Dr. Webster (2009) and his colleagues conducted a prospective survey of perceptions and acceptance of osseointegration among individuals with lower limb amputations. Of the 73 participants who completed surveys, 33% stated they would consider an osseointegration procedure for a prosthetic attachment. They cited anticipated advantages being improvements in their prosthetic function, feeling secure of the suspension system, an improved activity level with increase walking ability and ease of prosthetic attachment. Of those who would not consider having the osseointegration procedure, participants cited concern for activity limitations due to potential implant failure, rehabilitation time, risk of broken bone in the limb and concern over potential infection. Characteristics correlated with a participant considering an osseointegration procedure include: living in a rural community, problems with a prosthesis falling off and pain that could interfere with their daily activities (Webster et al, 2009).

**Limb-Salvage Surgery (LSS) Versus Amputation**

Studies depicting functional benefits after limb salvage and amputation for lower extremity bone and soft tissue tumors are showing inconsistent results. Bias can occur with subjective and objective tests used in LSS and amputation studies depending on your perspective (Kupersmith & Somerson, 2012). Since the 1970’s, advancement in precision imaging techniques with Computed Tomography (CT) and
Magnetic Resonance Imaging (MRI) scans have made it easier for the physician to define the extent of a tumor and remove it without resorting to amputation. It is estimated that 85% of extremity sarcomas are now being treated with LSS (Bacci et al, 1991).

As previously stated, for years the gold standard to treat bone and soft tissue tumors of the extremities have been amputation. However, in the last 20 years, LSS surgery has become more of a popular choice especially for cosmetic reasons, preserving uninvolved tissue and improving functional abilities compared to amputations (Kupersmith & Somerson, 2012). Reasons for LSS and amputation include trauma and vascular diseases. Studies often focus more on tumors of the bone and soft tissue of the extremities primarily because these diseases affect young healthy people with few comorbid conditions, good preoperative functions and a greater possibility of having maximal functional abilities after surgery (Kupersmith & Somerson, 2012).

**Human Limb-Salvaging Study**

A longitudinal Swedish research study at the University of Gothenburg was performed on human osseointegrated amputation prostheses. The experimental study focused on improving the quality of life for 100 patients who had received osseointegrated transfemoral amputation prostheses. A treatment protocol; Osseointegrated Prostheses for the Rehabilitation of Amputees (OPRA), a Quality of Life (QOL) measurement tool was introduced in 1999. The population was intended for 100 patients who had received 106 implants between May 1990 and June 2008 with the majority of amputees due to trauma (Hagberg & Branemark, 2009).

In this study, a Swedish professor, Dr. Per-Ingvar Branemark discovered that implants made of commercially pure titanium provided a stable anchor for an implant in living bone tissue. These 100 patients were treated at the Sahlgrenska University Hospital in Sweden with a focus on the OPRA protocol. This involved two surgical sessions, 6 months apart that involved titanium implants prosthesis
surgery. Major soft-tissue surgery was performed with the patient immobilized 10 to 12 days for critical healing of the skin penetration area. Researchers theorized that osseointegration with bone mineralization takes 6 months. They compared the healing around the implant like a fracture healing which can take about 6 months (Hagbergy & Branemark, 2009).

Early in the study, researchers discovered a rapid increase in implant loading could lead to the implant loosening. Using a pain management scale (1 to 10), they quickly discovered that pain during rehabilitation indicated overload and should be avoided if the patient was expected to recover. The protocol increased loading of the bone-implant unit to prepare for unrestricted artificial limb use. The protocol stipulated the patients needed to perform gentle exercises to prevent contractures and gradually start weight bearing and prosthetic gait training exercises. They were given defined instructions to follow and give feedback on their survey of their progress or lack of progress (Hagbergy & Branemark, 2009).

Analysis of this study shows only 18 of the 100 patients discussed actually participated in the OPRA protocol due to the timeline. The patients who did not participate in the OPRA protocol reported decreased quality of life issues that centered on pain, swelling in prosthetic socket with skin rashes and sores (Gallagher & Maclachlan, 2001). Results showed 94% of the 18 patients who followed the protocol reported success at the 2 year follow up appointment (Hagbergy, Branemark, Gunterbergy & Rydevik, 2008-2011). Of the 100 patients, 20 have had their implant removed for various reasons, 13 have been retreated and 11 of the 100 patients still have no implant today (Hagbergy & Branemark, 2009).

This on-going longitudinal study could provide promising results with this rehabilitation protocol for future discussion. Researchers clearly indicate the significance of having the entire interprofessional team educated on the protocol, performing a thorough preoperative evaluation and educating the patient on realistic expectations of mobility outcome from the surgery. Researchers emphasize that the OPRA protocol could make everyday life easier for patients experiencing war causalities, traffic accidents,
tumors and other traumatic injuries at younger ages (Hagbergy & Branemark, 2009). Results support the ideal osseointegrated surgical candidate being younger with higher healing factors.

**Canine Limb-Salvaging Study**

Literature reviews indicate little research was published on large animal models for transcutaneous osseointegration prosthesis in the 1990’s into early 2000. The osseointegration research success in Europe with human trials captured the attention of researchers to study animal models. In 2008, a canine model had successful transcutaneous osseointegrated titanium stem implanted in the leg. At the two year follow-up, the canine was running on the prosthetic leg and was free from infection (Drygas et al, 2008).

**Focus of Translational Study**

This chapter will describe the comparative methods used to investigate osseointegration currently used with felines and canines as well as consideration of translating osseointegration research from preclinical to clinical research for humans. Context for this chapter is that new osseointegration techniques show great promise although knowledge deficits exist for this technology as well as clinical research cases studies performed in the United States. The technology must be understood to discuss osseointegration limb salvaging techniques with potential translation to humans. Osseointegration limb salvaging has broad implications for all healthcare providers who render primary or specialty to patients and particular relevance for the military population. This chapter will be begin with a review of comparative variables of canine and human candidates for osseointegration and then proceed to specific criteria and risk factors for providing osseointegration to humans, followed by the specific methodology used for case study analysis for a canine osseointegration surgery.
Similarities of Human Versus Canine Skeleton Structures

Innovative research has been on-going for years trying to find an optimal interface between bone and orthopaedic or dental implants. Finding an implant material that has biocompatibility, mechanical stability and safety require rigorous testing. Animal models have become part of this implant testing environment which is essential prior to clinical testing in humans. Bone implant testing has occurred in dogs, goats, sheep, pigs and rabbit models (Pearce et al, 2007).

Animal Models

Similarities between animal models and human bone show minor differences with bone composition especially when looking at remodeling around the bone structures. While the pig has some likeness with human bone, their size and ease of handling make pigs challenging to work with. The rabbit has the least similarities to human bone. The dog, sheep and goat shows the most promise in testing animal models with bone implant materials (Pearce et al, 2007). The size of the animal is important to ensure it is appropriate for the number and size of implants chosen (Schimandle & Boden, 1994).

There is probably no ideal model and few animals or humans are volunteering to be test models especially with moral and ethical controversial issues surrounding their use.

Bone Implant

One of the challenges in finding the ideal bone-implant interface is biocompatibility with the body. The bodies of animals and humans tend to reject foreign objects. To avoid adverse tissue responses, we must find a material strong enough with corrosion resistance with elasticity similar to bone, to minimize bone resorption that occurs around foreign objects (Pearce et al, 2007). The main function of the human skeletal system is for balance support, protection, storage and formation of blood cells. The bone consists of spongy and compact bone tissue. The compact bone has a high density which brings strength and stiffness to the skeletal structure while the spongy bone has a high porosity and can absorb a
lot of energy distributing our loads (Hamill & Knutzen, 1995). The shape of bone is poised to have high strength to weight ratio and depending on the bone, it can remodel by growth or removal of bone tissue. A bone becomes weaker if there is not enough stress acting on the bone or too much stress is applied (Fung 1981). Titanium has a relatively low elastic modulus which makes it similar to the stiffness of a human bone than other materials (Leyens et al, 2003).

The most common types of implant designs used in animal models are rod shaped (cylindrical) or screw-type (threaded) designs. The screw design is used more frequently due to its’ properties of stability and not requiring an exact fit for bone integration (Carlsson et al, 1988). The International Standard (ISO) 10993-6 (1994) recommend implants be made of material already in clinical use. Orthopaedic bone screw-type implants should have at least 4.5mm screws for larger species such as a dog, pig or sheep (Huffer et al, 2006). Implant-related factors such as design, chemical composition, shape, length, material, implant surface treatment and coatings can enhance osseointegration (Marco, 2005). Table 1 depicts bone characteristics that must be taken into account with osseointegration.

TABLE 1. Canine versus Human Bone Characteristics (Eggert, 2014)

<table>
<thead>
<tr>
<th></th>
<th>Canine Bone</th>
<th>Human Bone</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td>Significantly higher bone-implant interface strength in younger animals due decrease in bone remodeling ability with age (Magee et al, 1989)</td>
<td>Similar bone-implant interface, bone strength decreases with advancing age</td>
</tr>
<tr>
<td><strong>Microstructure</strong></td>
<td>Mixed predominantly comprised secondary osteonal bone in center cortical bone with plexiform bone (Wang et al, 1998)</td>
<td>Has a secondary osteonal structure (osteons &gt;100um containing blood vessels &amp; cement lines forming boundary between adjacent lamellae) (Kuhn et al, 1989)</td>
</tr>
<tr>
<td><strong>Plexiform or Laminar bone</strong></td>
<td>Found in rapidly growing animals (Wang et al, 1998)</td>
<td>Found occasionally in children during periods of rapid growth</td>
</tr>
<tr>
<td><strong>Trabecular bone</strong></td>
<td>Similar to humans Trabecular bone from distal femur similar mechanical &amp; mass properties of human bone</td>
<td>Similar to canine Trabecular bone from distal femur similar mechanical &amp; mass properties of canine bone</td>
</tr>
<tr>
<td></td>
<td><strong>Canine Bone</strong></td>
<td><strong>Human Bone</strong></td>
</tr>
<tr>
<td>----------------------</td>
<td>--------------------------------------------------------------------------------</td>
<td>--------------------------------------------------------------------------------</td>
</tr>
<tr>
<td><strong>Strain resistance</strong></td>
<td>Trabecular bone can withstand higher compressive strains before failure than human bone (Kuhn et al, 1989)</td>
<td>Trabecular bone has lower compressive strains before failure than canine bone</td>
</tr>
<tr>
<td><strong>Macrostructure</strong></td>
<td>Biological more suitable as human model (Aerssens et al, 1981)</td>
<td>Similar characteristics to canine bone</td>
</tr>
<tr>
<td><strong>Size</strong></td>
<td>Smaller bone dimensions</td>
<td>Long bone dimensions</td>
</tr>
<tr>
<td><strong>Shape</strong></td>
<td>Discrepancy to human (varies)</td>
<td>Discrepancy to canine (varies)</td>
</tr>
<tr>
<td><strong>Mineral density</strong></td>
<td>Significantly higher levels</td>
<td>Significantly lower levels</td>
</tr>
<tr>
<td><strong>Bone composition</strong></td>
<td>Similar (ash weight, extractable proteins)</td>
<td>Similar (ash weight, extractable proteins)</td>
</tr>
<tr>
<td><strong>Bone density</strong></td>
<td>Similar characteristics (Aerssens et al, 1998)</td>
<td>Similar characteristics</td>
</tr>
<tr>
<td><strong>Cortical/Cancellous</strong></td>
<td>Similar water/organic/ash fraction</td>
<td>Similar water/organic/ash fraction</td>
</tr>
<tr>
<td><strong>Mineral composition</strong></td>
<td>No significant difference</td>
<td>No significant difference</td>
</tr>
<tr>
<td><strong>Bone remodeling rate</strong></td>
<td>Significantly different from human which is important with implant modifications: has higher remodeling rate (Bloebaum et al, 1991)</td>
<td>Significantly different from canine: has lower remodeling rate (Fernandez-Tresgrirres et al, 2006)</td>
</tr>
<tr>
<td><strong>Implant changes</strong></td>
<td>More evident in canine models due higher rate of remodeling (Bloebaum et al, 1991)</td>
<td>Less evident in human models due lower rate of remodeling</td>
</tr>
<tr>
<td><strong>Bone turnover rates</strong></td>
<td>Structural similarities in trabecular bone turnover between canine and humans</td>
<td>Structural similarities in trabecular bone</td>
</tr>
<tr>
<td></td>
<td>Turnover highly variable between bone sites (Kimmel &amp; Jee, 1982)</td>
<td>Remodeling of total bone mass per year is 5-15% with whole body trabecular bone turnover rate from 10-15% to 40-55% per year (Fernandez-Tresguerre et al, 2006)</td>
</tr>
</tbody>
</table>

Picking an animal model that shows similarities with humans, both physiological and pathological is important when deciding implant selections especially with bone modelling and translation for human use (ISO 10993-6, 1994). The dog species is used most often for musculoskeletal and dental research. A fair amount of literature comparing canine and human bone has been done making the dog model ideal in animal and human orthopaedic comparisons (Pearce et al, 2007). Between 1970 and 2001, dogs were used in 9% of all orthopaedic animal model studies (Martini et al, 2001). Dogs, due to their tractable nature typically do well in the post-operative healing stage and can be trained to
participate in their rehabilitative treatment much like humans. Often ethical issues arise when discussing
animals in research especially since they are companion to humans (Wang et al, 1998).

Another interesting facet is reviewing the fracture properties in canine bone with human bone.
There is a secondary osteonal structure (osteons with blood vessels and cement lines that form a boundary
between adjacent lamellae) in adult human bone. However, canine bone has a mixed microstructure; a
secondary osteonal bone in the center of cortical bone called a plexiform bone adjacent to the periosteum
and endosteum (Wang et al, 1998). This plexiform or laminar bone is mostly found in large, rapidly
growing animals and sometimes in children during their stages of growth (Jee et al, 1970). While it is
formed more rapidly than secondary osteonal tissue, the bone has greater mechanical support than woven
bone. Even though there are similarities in organic composition, canine bone has a higher mineral density
than human bone (Wang et al, 1998).

The trabecular bone from the distal femur in humans and dogs has similar mass and mechanical
properties although different coefficients to strain resistance exist. The trabecular bone in a canine can
withstand higher compressive strains than humans before the bone fails (Kuhn et al, 1989). The dog and pig
resemble the human bone density factor.

The characteristic properties associated with human bone are also associated with canine bone

Another difference between human and canine bone is the rate of bone remodeling, this can be
significant when assessing implant modifications. The human bone has a lower rate of remodeling than
the canine bone (Bloebaum et al, 1993). For the purpose of this translational study, we will not discuss
this in detail although there are unique advantages and disadvantages in the discussion of bone tissue
response to implant material for a proposed model.
The literature tends to validate the importance of having a fairly healthy subject with healthy bones when being considered as an implant surgery candidate.

FIGURE 2. Candidate Selection Criteria Variables (Eggert, 2014)

Inclusion and Exclusion Criteria for Osseointegration Surgery

This case study will investigate an experimental implant animal model with potential translation to human models. A framework needs to be established that covers inclusion and exclusion criteria to focus the descriptive animal case study and narrow down the topic. Inclusion criteria for the case study is limited to loss-of-limb due to traumatic injuries and those with good wound healing potential such as a healthy canine with no co-morbidities who had a traumatic injury earlier in life resulting in no back paws. A human translation case could be the healthy military member who suffered a traumatic injury resulting in loss of a limb who may be a candidate for limb-salvaging surgery. Exclusion criteria for the study
would be amputations and loss-of-limb cases due to diseases with poor wound healing prognosis that were not traumatic in nature. Diseases such as diabetes, limb necrosis or high infection risk burn subjects, severe peripheral vascular diseases, specific drug treatments (chemotherapy or corticosteroids), growing children or age greater than 70, pregnancy or excessive body weight (100 Kg) are not included in this case study analysis (Hagberg & Branemark, 2009). These subjects are viewed as potentially unsuccessful surgical candidates for limb-salvaging and may have risk factors that outweigh the potential benefits.

**Ideal Human Candidate for Osseointegration**

The ideal human candidate for osteointegration would have selective criteria in a well-controlled case study. Criteria to include youthfulness, fairly healthy individual without chronic diseases and good wound healing abilities with a positive attitude, good rehabilitation potential and a strong motivation for survival. For example, a young otherwise healthy military member without co-morbidities with family and financial resources could be a strong candidate, especially if they had good wound healing abilities and free from infections or illnesses. Resilience would be a necessity for the long rehabilitation period and ability to cope successfully with issues that may arise during their rehabilitation. A supportive network of professionals on the interprofessional team is paramount, not only for continuity of care but to ensure appropriate protocols and safety regulations are followed. The military member could be an ideal participant in a well-controlled osseointegration study.

**Ideal Canine Candidate for Osseointegration**

Ideal canine subjects for osseointegration surgery should meet similar criteria as human candidates. Jack, our canine subject for this translational case study was considered the ideal candidate. He was a healthy subject with no co-morbidities, possessed strong resilience, considered low risk for infection with great rehabilitation potential. Jack’s youth, good bone structure, good wound healing properties, extremely supportive owners with financial resources were motivated to give Jack improved
mobility, to enhance his quality of life. A thorough description of Jack’s candidacy will be discussed in the case study chapter.

**Risk Factors and Challenges with Osseointegration**

Some of the challenges associated with osteointegration include risk factors that could produce an adverse outcome. Risk factors to consider include: the type of implant and longevity, age, bone strength and density, potential for infection, skin breakdown at the implant interface site and osteointegration rejection. Other risk factors include: complications from surgical intervention, lack of support and economic challenges with cost factors, motivation and survivability instincts (Mavrogenis et al, 2009). Excessive implant mobility and radiation therapy can inhibit osseointegration (Giori et al, 1995; Kudo et al, 2001). The role of radiation therapy remains controversial, however, it appears to delay bone remodelling pre and post-osseointegration procedures, depending on the radiation dose and bone tissue response (Kudeo et al.) other factors shown to inhibit osseointegration are patient-related such as osteoporosis, advanced age, nutritional deficiency, smoking, rheumatoid arthritis, and renal insufficiency (Rosenqvist, et al, 1986; Zhang et al, 2004; Mombelli & Cionca, 2006). These risk factors should be identified early when screening a potential subject for osseointegration procedures.

Research indicates the average useful implant life is 10-15 years depending on the patient, implant type, material used for the implant and fixation method (Harrysson et al, 2007). A younger person receiving an implant with the average human lifespan of 79 years old could possibly require one to three implants in the course of their life which exposes them to surgical risk factors as well as osteointegration rejection (CDC, 2012).
**Methodology**

The methodology for the osseointegration canine case study, including this new osseointegration technology, methods and instruments will be discussed. The surgeon will be introduced with his research focus and a brief discussion of his previous model surgeries.

**Case Study Methodology**

A qualitative descriptive case study will be used to present the osseointegration surgery for Jack, a canine. Case study is “A research method involving a thorough, in-depth analysis of an individual, group, or other social unit” (Polit & Beck, 2012, p. 721). Case studies may be qualitative or quantitative. This is a single case and instrumental study in order to describe a representational case of osseointegration surgery to enhance our knowledge of current evidence of osseointegration surgery.

**Pattern-Matching Strategy**

Yin (1994) discussed a technique called, “pattern-matching”. This strategy of comparing established empirical research-based patterns to predictable patterns will be used with osseointegration technology. Basically, if the pattern matches, the internal reliability of the analysis is enhanced. The methodology with pattern-matching has four stages: design the case study, conduct the case study, analyse the case study evidence, and develop the conclusions, recommendations and implications (Yin, 1994 & Tellis, 1997). The notion of comparison between the predicted and the actual pattern may have no quantitative value but can be used in qualitative and descriptive cases (Yin, 1994). Due to limited research on this new osseointegration fabrication technology, this strategy will be used with this case study to compare and theorize potential translation for animal and human use.

**Sample**

This descriptive qualitative case study is focused on Jack (n=1) the canine. Although his surgeon had performed 11 osseointegration surgeries, one feline and 10 on canines, for the purposes of this
inquiry, Jack was selected as a case study having undergone bilateral implants with osseointegrated prosthesis.

Data Collection Methods with Limitations

As the primary researcher, data collection will come from retro-medical chart reviews, observation of the canine model, interviews with surgeon and surgical team, other stakeholders involved in osseointegration implant fabrication, medical and nursing staff, technicians and the canine owner. Data collection is challenging due to remote geographical locations of case files from researcher. The surgeon is associated with a clinic in North Carolina, the canine subject lives in Arizona and researcher is located in Texas. The timeline to collect and exchange data has taken several months. Canine “Jack’s” medical records provided source documents for study. The credibility of data from Jack’s records was reliable based on his actual surgical course and confirmed with interview from surgeon, medical staff and canine owner. The primary source of information on Jack’s surgical journey, QOL reports and rehabilitation progress are attributed to the surgeon and the canine owner.

Expected Outcomes

The animal osseointegration surgical cases were costly, not currently practical, were experimental in nature and lacked regulatory guidance and polices. Due to these factors, they are currently not approved to be performed in the United States. The implant fabrication models are still patent-pending. Obviously, with more clinical cases, the implant model fabrications and limb-salvaging techniques will improve as well as the surgeon’s skill level in performing the surgery. Once this occurs, expect more companies to take an interest in the manufacturing aspect of osseointegration technology.

Since these are benchmark cases with new technology, bias is expected with clinicians, subject owners and other stakeholders in measuring QOL success. Mobility is a QOL indicator and any improvement in mobility can be attributed to this osseointegrated technology. This may prove to be valid
in some of the implant surgical cases. McGonigle and Mastrian (2012) imply evidence-based research can stimulate our practice knowledge and with other collaborative team members are integrated into our clinical practice to make an impact on our practice.

**Context for Translating Research from Pre-clinical to Clinical Research**

**The Surgeon**

A veterinary orthopaedic surgeon at the North Carolina State University (NCSU) College of Veterinary Medicine was embarking on new osseointegration technology. His successful novel prosthetic implant surgeries on animals with amputations in the veterinary world are showing promise for human translation. Canine Jack’s surgeon has written approximately 100 peer-reviewed research articles with emphasis on joint arthroplasty, circular external fixation, biomanufacturing and biomodeling. His primary research efforts encompass distraction osteogenesis, biological response to orthopaedic implants and canine developmental orthopaedic diseases. In addition to performing our case study canine’s bilateral osseointegrated lower leg implant surgery, he also performed the first osseointegrated implant unilateral surgery in the world on another canine (NCSU College of Veterinary Medicine, 2012).

**Translational Research**

Canine Jack’s surgeon is involved in translational research that promotes scientific discovery and been working with transdermal osseointregation for 8 years with his specialty in biomodeling (Marcellin-Little, 2013). His goal working with the Center for Comparative Medicine and Translational Research (CCMTR) is to facilitate the clinical application of this scientific discovery into improving health outcomes for animals and humans. The mission of the CCMTR directs the center of their translational research around patients with their involvement in clinical studies to generate new evidence-based knowledge to broaden technology in clinical practice (CCMTR, 2012).
This remarkable surgeon pioneered osseointegrated implants for felines and canines missing a limb. He is currently conducting a study to determine the feasibility of a novel limb-sparing osseointegrated implant for treating canine osteosarcoma, which is the most frequent bone tumor in canines. Primarily, the distal portion of the radius (the bone of the front limb just above the wrist is typically the site of infection). A standard treatment for this cancer is to remove the tumor by amputation or limb-sparing surgery followed by chemotherapy (CCMTR, 2013).

Canine Jack’s surgeon’s study serves to preserve limbs of these canines and provide a quality of life they did not have before. The insights gain through these clinical trials hope to benefit efforts to treat human osteosarcoma which is the eighth most common form of childhood cancer (CCMTR, 2013).

Prior Osseointegrated Implant Surgeries

In 2005, canine Jack’s surgeon performed the world’s first osseointegrated implant (prothetic foot) surgery on a feline. This first unilateral implant fabrication took 4 hours to make, while the surgery only took 3 hours, with a soft tissue reconstruction done on the femur. He rehearsed three to four times with model implants prior to performing the surgery and still has enhanced concerns, since investigative research with mechanical orthosurgery has still not been sanctioned (Marcellin-Little, 2013).

In early 2011, this same surgeon performed the first front limb surgery on a canine. He noted less granulation tissue observed with this case which increased the canine’s resistance to infection. He discussed the left ball free-form of conventional titanium screw and seal soft tissue making a smooth surface and prothesitic portion during the canine’s surgical procedure. Infection is still the surgeon’s number one concern with any osseointegrated surgery. Other surgeons have the same concern (Marcellin-Young, 2013). Although osseointegration was introduced about 20 years ago, the challenge with this technology remains the infection potential, especially at the skin-pylon interface (Pitkin, 2008).
In his study, the surgeon is comparing the designs of his implant models against one another to determine which design represents the properties of natural bone and are biomechanically superior. The novel plate designs of these models can be tailored and customized to meet the requirements of individual patients (CCMTR, 2013). Each model case brings increase experience on model fabrication and improved surgical techniques with this new bone-anchored osseointegration technology.

**Case Study of Canine Jack’s Osseointegration Journey**

An historical account of canine subject, Jack and his journey to get two feet through osseointegration surgery that gave him four good feet is the case study. Jack’s story will be described with graphic figures, models, interviews and photography to illustrate his amazing journey and how innovative osseointegrated technology, surgical skill and a labour of love from extraordinary owners, improved his mobility options and quality of life. The technology used in his case will have great significance when discussing limb-salvaging techniques with potential translation to humans as well as future implications for healthcare providers, medical and nursing in providing specialty care for these types of patients.

**FIGURE 3.**  A Jack with no Back Paws,  B Jack with Owner’s Post-surgery,  C Jack at Home with Rubber Chair Tips
Jack, an American Staffordshire terrier mix (pit-bull mixed per his owner) estimated to be around six years old (per medical record May 31, 2007), lost both back paws as a young male puppy. While it is unknown how Jack lost his back paws, it has been speculated the amputations were a result of traumatic injury and not congenital. Veterinary x-rays indicate the paws may have been cut off at an early age (NC Vet clinic, 2012). There is no history for Jack prior to 2008 or between 2008 and 2010 (McDonald, 2013).

Relevant History

Fortunate for Jack, his to-be owners went to an animal shelter in Virginia in 2010 looking for a disabled dog that needed extra care and attention. Records at the ASPCA indicated Jack had been sheltered and adopted once before. After two years, his owner died and Jack was return to the shelter. The current owner spent four days at the shelter observing pit bulls and kept coming back to Jack as her choice to join their family. She recounts both her and Jack “picking” each other. They were quickly impressed with his intelligence, resilience and affectionate loving attitude. Jack took great delight in simple pleasures; a soft bed or touch, a belly rub, a roll in the grass and according to his owners, did not seem to realize he was disabled (McDonald, 2013).

The family moved to Arizona where Jack’s quality of life changed from shelter life in a cage to a large spacious home with the Arizona desert to explore. He lived primarily indoors with two felines and ventured outside on a leash. Outside of his orthopaedic issues, Jack is described as a healthy canine, with a normal hardy appetite (eats 1¾ cups of Science Diet Canine Large Breed twice daily), has no acute or chronic illnesses and was on no medications. Jack quickly adapted to his new environment and became well-integrated with his new family (McDonald, 2013).
Pre-Surgery Mobility

Jack ambulated around the house by supporting himself solely on his front limbs which appeared strenuous. He would become fatigue after walking short distances although seemed to have adjusted to using his front legs for mobility. His shoulders and forearms were massive and muscular while his hips and hind legs were tiny. The owners noted him guarding his hind limb stumps which appeared painful and he licked them intermittently, throughout the day. They observed Jack’s hind limbs to tremble on occasion, as though he was in pain. In one isolated incident, his pet sitter bumped his hind-end accidentally while walking by and he yelped out in pain. They interpreted this cry as pain and sought out devices and gadgets to decrease this discomfort. These devices ranged from a two-piece harness and booties to a hip sling and a ramp.

The concern for health risk factors of arthritis and other mobility injuries led Jack’s owners to explore options that would decrease his pain and improve his comfort. A wheelchair for Jack called his “chariot” would instantly improve his mobility efforts. He quickly realized this chariot would allow him to go on longer walks and run which he was unable to do before. The mere sound of the chariot coming out of the closet got Jack excited. Unfortunately, the chariot did not address his discomfort and pain. This realization led his owners on a journey to find a solution that could improve Jack’s long term mobility and enhance his mobility. A referral from their veterinary provider in December of 2010, to a veterinary orthopaedic surgeon in North Carolina would secure them an appointment for Jack, before the year had ended. This surgeon would introduce new osseointegration technology that served to alter the course of Jack’s life (McDonald, 2013).

Mobility Options and Cost

Their discussion with this orthopaedic surgeon would open up promising options for their consideration. Some non-invasive options included an external prosthesis, an inexpensive harness or a
cart to use outside for comfort. An invasive option was a surgical free-form implant procedure which would require hospitalization, could be costly and ran the risk of infection and other complications for Jack. The initial cost estimate for a diagnostic and treatment procedure for osseointegrated prosthesis of limbs varies from $12,000 to $16,000. This breaks down to $6,000 to $8,000 per side (NCSU Hospital & Marcellin-Little, 2013). The surgeon wanted them to be well-informed and consider all options before making a decision. He explained the experimental aspects of the osseointegrated implant surgery, his case study and the associated risk factors (Marcellin-Little, 2013). The owners were focused on a long term solution to improve Jack’s mobility, decrease his pain and provide a happier life. They had already tried some non-invasive options which seem only to have short-term benefits. After weighing the risks and benefits of the options, they chose the osseointegration implant surgery (McDonald, 2013).

Surgeon Interview

This prominent surgeon has been interviewed several times on his interest of challenging orthopaedic cases that are not treated successfully by conventional methods. In finding ideal candidates for modelling or custom osseointegration surgeries, he looks for healthy animals with complex deformities or abnormal joints. Jack met his ideal canine candidate for this surgery (Marcellin-Little, 2013).

In discussing the steps involved in developing a custom prosthesis or model, the surgeon relays the foundation is based on the x-ray computed tomography (CT) scan. The CT is a technology that uses computer processed x-rays to show images of a scanned object to see what is inside of it without having to cut into it. The CT with high tech software is used to translate the CT scan data to a computer-aided design (CAD) file. A widely used program called “Mimics” is often used. This CAD file is then inputted into one of several machines that can actually make the replica or model. This process is called rapid prototyping (RP) which involves several techniques. Some machines will make the model directly into a
polymer such as plastic, polyurethane or wax impregnated plaster. A technique referred to as “room
temperature vulcanization” can be used to create a silicone mold based on the original design or a cast or
mold can be made directly with a hollow mold. A replicate model can be made multiple times using other
materials that can be cast or injected directly into the mold (Marcellin-Little, 2013).

Canine Jack’s surgeon reports at NC State, his models are used using a process known as
Stereolithography (SLA). The CAD file is fed into a machine, where a laser will solidify liquid plastic
poured in subsequent layers to build up to the final model. The custom implants are made from metal.
Various metals are used to create custom implants and at NC State, they use a process called electron
beam melting (EBM) to customize their implants. They make different sizes and replicas identical to the
original bone which they use for diagnostic purposes and the design and rehearsal of a surgical procedure
(Marcellin-Little, 2013).

Cost

After Jack was identified as a candidate for osseointegration technology surgery, a CT scan was
the initial expense done for diagnostic purposes. In addition, an initial workup is performed to determine
baseline status surrounding any surgical candidate to determine their readiness and potential risk factors
for surgery. There is a cost for the design and production of the implant model, which can be as little as
$100 to $1000 for a larger model. The average is $200 to $300 for a single model. Often two models are
made; one as a reference and one used for design and rehearsal of the surgery. If a custom implant or
prostheses is required, the cost is greater due to the cost of the metal, which always cost more to produce
(Marcellin-Little, 2013).

Design cost can vary. Jack’s surgeon estimates a human custom implant may cost as much as
$30,000. The time and expertise involve with engineering, use of new technology, manufacturing and
finishing of implants can be expensive. In addition, machines, software, training and design associated
add cost. In a non-profit business, the expense can be less costly. The surgeon reports his clinic benefits are non-profit. Their implants cost a few thousand dollars depending on the implant complexity. He highlights his purpose is not to make money, but to streamline a design process. Obviously, the more models required, the greater the cost. The more streamlined, the lower the cost to produce the models (Marcellin-Little, 2013).

**Timeline for Osseointegration Implant Model Development**

Once the CT scans have been done, the timeline to complete models has decreased from several months to roughly a week, if no complications or problems develop. Jack’s surgeon advocates use of implant models versus natural samples in research when possible. His first implant fabrication was four hours and now it is down to two hours for fabrication. The challenge of collecting samples from live or deceased patients is difficult. Creating your own samples to precision with models that can be reproduced, and readily available for testing, is an attractable feature. In the future, virtually testing will replace mechanical testing especially in our digital age. In time, virtual technology and the ability to rehearse surgeries could decrease cost and health risk to the customer. Perhaps we could identified potential health risk, complications and avert them before we do the surgery (Marcellin-Little, 2013).

**Jack’s Unique Osseointegration Implants**

Jack did not travel to see the Engineers at NC State University College of Veterinary Medicine to get his custom-made bilateral transdermal osseointegrated prostheses and screws, his 3D X-rays did. His CT scans were used to make these rehearsal and final customized implants. His hind leg screws were donated by SynthesVeterinary (Marcellin-Little, 2013). Jack did not see his surgeon again after his initial evaluation in December 2101, until he arrived in NC for his surgery. Jack’s new prosthesis has a metal end attached to his bone, which allows him to easily snap attachments on and off. This same process could take as long as 30 minutes with a conventional prosthetic which may present a problem for
someone, if they had to go quickly to the bathroom (Harrysson & Grager, 2013). This time saver, with mobility options could be significant in human translation. Cumbersome fixation or prothetic devices that are difficulty to work with can be a quality of life issue with people in today’s fast-pace environment. Easy snap on devices that have quick release devices will be more convenient and sought after for people on the move.

![Images of prosthetic implants and devices](image)

**FIGURE 4.** A Jack’s Rehearsal Implants, B Prosthetic Feet, C Jack’s Osseointegrated Implant and Prosthesis

### 3D Printing

A NCSU professor used a 3D printer which allowed him to attach tiny beads to the metal that helped canine Jack’s bone attach itself to the prosthetic (Harrysson, 2013). This printer also allowed the surgeon to perfectly match the contours of Jack’s bone to the socket of the prosthetics (Marcellin-Little, 2013).

Three-dimensional (3D) printing provides innovative technology that can change the course of future applications from biomedical implants to exploring space. A machine that can create a three-dimensional object also known as rapid prototyping, solid freeform fabrication, direct manufacturing and additive manufacturing. The 3D process starts by using a computer to create a three-dimensional model of
an object using a computer-added design (CAD) program. Precise height, width and depth of an object you want to fabricate can be designed to your object specifications (Shipman, 2011).

The next step in this process is to convert your model into a Stereolithography (STL) file. This conversion process takes your 3D model in CAD and maps its surface using a series of connected triangles. The STL file is then put through a program that slices the model into wafer-thin layers and maps where the plane of each layers intersects with the legs of various triangles. Each of the intersections is represented by a dot. Once you connect the dots, you see the profile of the particular layer of the 3D model. The profile than tells the 3D printing machine how to draw each of the layers. The layers will pile up on top of one another and you have your finished product (Shipman, 2011). This technology creating 3D models will be a marketing initiative for future model cases in animal and human cases. In addition to Jack’s case, 3D printing was used on nine animals since these experimental procedures started in 2005 with varying degrees of success (Marcellin-Little, 2013). Each case brings them closer to perfecting the osseointegration procedures.

**Computer Modeling with Electronic Beam Machine (EBM)**

The type of machine used for canine Jack’s 3D x-rays was an Electron Beam Machine (EBM). This machine use electron beams to melt metallic powders into layer after layer of the functioning metal parts and was used to make Jack’s final implants. Some machines use lasers instead of electron beams to do the same thing. If you need any replacement parts, this type of technology now exist to custom-make your design (Shipman, 2011). Jack’s surgeon uses more refined laser technique now and less powdered titanium with his models. He performs fabrications from 25 different machines with his implant technology skills (Marcellin-Little, 2013).
FIGURE 5. **A** Large Electronic Beam Machine, **B** Jack’s Final Titanium Implant Models (Marcellin Little, 2012-2013 with permission granted to use)

The EBM is three dimensional. The EBM made the customized implants from viewing Jack’s CT scan only. The engineers put in an engineering software program into the EBM to assist with the implant construction. The implants were made from 7 to 8 screws, like a glove and mitten. They wrap around the bone and fits perfectly for stability with these screws. Future rings will have threaded screws into the implant and will be sutured in place (NC CVM & Marcellin-Little, 2012). The stability is the screwed ring onto the implant and sutured subcutaneous tissue to the ring. This process takes roughly 8 weeks.

The sutured ring is temporary and holds the skin down in place temporarily while healing. Subcutaneous tissue grows through the mesh part of the basket and prevents the skin from retracting. The basket is the only permanent stability. The suture ring will be removed so you have just the implant that has the subcutaneous basket in place (NC CVM & Marcellin-Little, 2012).

**Journey to Surgery**

Jack and his owner, travelled to NC State University’s College of Veterinary Medicine Surgery Center for Jack’s surgery on May 1, 2013 to implant custom made bilateral transdermal osseointegrated
prostheses (MacDonald & Marcellin-Little, 2013). The experimental procedure, done by only two veterinarians in the United States, offers Jack the best hope to improve his mobility, comfort and quality of life and could one day offer this same hope to people (McDonald, 2013).

Jack and his owner arrived at the NC University Veterinary Teaching Hospital (VTH) after a two to three-day automobile road trip from Arizona. On arrival, the surgeon with his clinical team (veterinarians, residents, students and technicians) evaluate Jack’s general health for his surgery. His baseline health status had not changed from their initial consultation assessment. While he was anxious being in a new place, Jack was found to be healthy without infections or acute illness and a good candidate for prosthetic osseointegration surgery (Marcellin-Little, 2012).

Jack was admitted to the NC VTH on April 30, 2012 and started his prep for osseointegration surgery which would occur on May 1, 2012. He experienced a similar pre-operative prep a human would experience with a pre-operative assessment, medication and visit with providers from anaesthesiology and surgery. Like a human minor with their parent, his informed consent would be reviewed and discussed with the surgeon by his owner. His weight (26.7 kg) would be obtained as well as his vital signs which were considered within normal limits for a canine. He was anxious panting and did not appear to like his hind legs touched or manipulated by staff. Jack would be given nothing by mouth (NPO) overnight to avoid potential aspiration during his surgery. No indications were observed or reported he was in pain or had any physical ailments that would prohibit his surgery (NC VTH & Marcellin-Little, 2012).

Surgery Course

On the day of Jack’s surgery, his owner would visit with him, provide emotional comfort and reassurance (much like a human to a human going to surgery), send him off to the operating room and spend roughly 6 hours in the waiting area patiently waiting to hear the outcome of the surgery and future prognosis for Jack from the surgical team (McDonald, 2012).
The surgical team consisted of the primary surgeon with 3 assistant surgeons, 2 anaesthetists and a veterinary student. A muzzle was on standby for safety for needle insertions which is normal protocol for canine surgery. Jack received an epidural for medications to include an antibiotic to prevent infection (Cefazolin); medications for pain (Carprofen, Remifentanil, Lidoaine, Ketamine) as well as anaesthesia medication (Propofol, Buprenorphine) to sedate for the surgical procedure. He had continuously fluids (Lactated Ringers Solution) given and placed on a ventilator with his oxygen saturation levels monitored continuously. His vital signs and pain level was monitored throughout the surgery (NC VTH, Marcellin-Little, 2012 & McDonald, 2012). Jack’s pre-operative diagnosis was documented as “partial amputation of pes bilaterally” and post-operative diagnosis, “bilateral hind limb transdermal osseointegration implants and rods”. Post-operative, Jack kept his epidural line in place for future medications. Sterile dressings were applied to his surgical sites with protective splints placed around his extremities. He was stabilized and sent to the intensive care unit ward for post-operative care (NC VTH, Marcellin-Little, 2012 & McDonald, 2012).

FIGURE 6.  A Jack’s Left Paw Front View, B Jack’s Right Paw, C Left Paw Backside View, D Right Paw

The experimental surgery to attach two titanium feet to the bone on Jack’s hind legs took the primary surgeon and his surgical team 6 hours to perform. Photos above show different views of Jack’s left and right paw implants in May 2012. Expected swelling occurred as the skin was stretched around the basket and sutured to the implant surface. The surgery was described a success by the medical team as
well as the canine owners (Marcellin-Little & McDonald, 2012). The surgeon had a practice surgery with the rehearsal implant and prosthetic models before Jack’s experimental surgery. The surgeon emphasized it was imperative that Jack’s skin grows into the basket which is key for the implants around the shaft joints. Mesh is the subcutaneous basket; mesh with holes where the muscle and subcutaneous tissue is brought into the basket and the epidermis wraps around the basket. One limiting factor with prior surgical cases has been the basket being too big which caused complications especially on the first animal model, with the stretch being too hard to wrap the subcutaneous tissue into the basket. Jack was the sixth and seventh of the eleven surgical cases in his study. There have been four more single implants surgeries since Jack’s surgery. His surgeon reports his average implant surgery takes eight hours (Marcellin-Little, 2012).

Post-Operative Clinical Care

The staff at NC VTH documented Jack’s clinical progress notes using a Subjective, Objective, Assessment and Plan (SOAP) format. This format is used to document human subject progress in civilian and military hospitals. Most of Jack’s daily progress notes followed this format describing his behaviour being pleasant and rambunctious during the day with resting well at night, with a few exceptions. One note indicated he was sometimes hard to work with and snapped at the overnight technicians (NC VTH, 2012).

Jack was in a strange environment with a different routine with people manipulating his body and legs that he did not like even before surgery. He still had anesthesia in his body with limited mobility and was on medications when he normally took none. It can be surmised that any subject, animal or human would have some adjustment issues with these traumatic changes. The hospital progress notes emphasis how Jack’s attitude and cooperation would improve when his owner was present which was during most of his hospital stay. Her presence was pinnacle in his recovery and rehabilitation success. She had
extraordinary devotion and concern for her companion. A staff member documented that once Jack’s owner came and took him out for walks, he appeared excited, less anxious and cooperative (NC VTH & Marcellin-Little, 2012).

Jack’s vital signs were monitored on the ward with his comfort level assessed throughout the day. Objective and subjective signs of pain were assessed every four hours. Fentanyl medication helped control his pain as did oral medication. Jack took his post-operative medication without any difficulty. Fentanyl was discontinued around May 9, 2012 with any sign of pain managed by the oral medications (NC VTH & Marcellin-Little & McDonald, 2012).

Jack ambulated well in his cage using his front limbs with no problems noted with urination or defecation. A weight bearing restriction was put on his back limbs to avoid strain on his osseointegrated implants while he was healing. His owner and the hospital staff would take Jack for a 10 minute walk outside every six hours holding up his hind legs using a harass that strapped around his body. He was positioned in a wheel-cart where his left hind limb was at least 1 inch off the ground and the right hind limb at least 1 ½ inches above the ground. Jack seemed to enjoy his walk especially the time with his owner (NC VTH, Marcellin-Little & McDonald, 2012).

Jack had a good appetite with a return to his diet of Mix Hill wet and dry adult food every 12 hours. His weight was 27.4 kg with no weight lost reported. He received water as needed (NC VTH, 2012). Jack made positive progress every day while in the hospital, became accustom to his surroundings and cooperative (Marcellin-Little, 2012).

The post-operative medication schedule (Table 2) worked well for Jack and his discomforts. The Tramadol was bitter which was given separately. Jack’s discharge medications changed slightly to include: a non-steroidal anti-inflammatory, Carprofen (Rimadyl) 50 mg, 1 tablet by mouth every 12 hours for 7 days; an analgesic, Gabapentin 200 mg (2 tablets) by mouth every 8 hours for neuropathic pain; a
transdermal Fentanyl patch, 75 mcg that would provide pain relief for 4 to 5 days before replacing the patch and antibiotic, Cephalexin 500 mg by mouth every 8 hours to decrease infection potential (Marcellin-Little & McDonald, 2012).

**TABLE 2. Post-Operative Medication Schedule (McDonald, 2012)**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>#</th>
<th>Freq</th>
<th>8am</th>
<th>2pm</th>
<th>4 pm</th>
<th>8pm</th>
<th>12MN</th>
<th>2am</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carprofen</td>
<td>50 mg</td>
<td>% tab</td>
<td>Q12H</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trazodone</td>
<td>100 mg</td>
<td>1 tab</td>
<td>Q12H</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Gabapentin</td>
<td>100 mg</td>
<td>2 cap</td>
<td>Q8H</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cephalexin</td>
<td>500 mg</td>
<td>1 cap</td>
<td>Q8H</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tramadol</td>
<td>50 mg</td>
<td>1 tab</td>
<td>Q8H</td>
<td>X</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heparin flush</td>
<td>15 ml</td>
<td>Syringe</td>
<td>Q6H</td>
<td>X</td>
<td></td>
<td></td>
<td>X</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Jack had daily dressing changes on his wounds performed by the surgeon and hospital staff. The skin started healing and improving around the osseointegrated implants. His bilateral custom designed transdermal osseointegrated titanium implants were placed at the level of his tarsi. The surgeon noted Jack’s implants had a design feature that promoted healing and health of the skin implant interface which is a crucial part of the success of a transdermal osseointegrated implant. This type of implant promotes osteogenesis by allowing the bone, over time, to be incorporated into the prosthetic device. This is the actual stability of his implant (Marcellin-Little, 2012).

Jack was discharged May 10, 2012 with his jugular catheter in place to spend time with his owner who was in a nearby hotel. He spent 11 days in the hospital and made remarkable progress (Marcellin-Little & McDonald, 2012). The owner brought Jack back to the veterinary hospital for bandage changes and for the surgeon to assess wound healing progress. The owner also became well-versed in the dressing change procedures (McDonald, 2012).

**Jack’s Rehabilitation**

In just 2 weeks post-surgery, Jack’s skin around the implants showed improvement. The goal is to maximize the chances of uncomplicated healing with the interfaces between the skin and implant and
between the implant and the bone. The surgeon highlighted the possible complications that could occur to
the owners of infection (of skin and/or bone), weakening or complete failure of the implant (Marcellin-
Little, 2012).

FIGURE 7. A Jack’s Left Paw Implant, B Right Paw Implant, C Right Paw Implant (Larger View)

Photos taken June 2012, a month after the surgical procedure illustrates the subcutaneous tissue
wrapped around the left and right paw implants with an appearance the tissue is adapting to the implant.
Black tissue at the extremity does not indicate the skin is dead (Marcellin-Little, 2013). Some granulation
in tissue remodeling sloughs off creating this appearance. The perforated basket under the skin allows the
subcutaneous and skin to grow into each other and secure the skin in place while limiting proximal
retraction. Jack had his suture ring removed during his dressing change on May 31, 2012. For complete
healing, epithelialization needs to occur with no necrotic skin and decreased drainage from the site
(Marcellin-Little, 2013).
FIGURE 8. Jack’s Extremity x-ray Reveals 2 Titanium Implants Attached to Hind Feet (Marcellin-Little, 2013)

An x-ray taken at the NC Vet Clinic in October 2013 confirms placement of two titanium feet implants in canine Jack’s hind legs (Marcellin-Little, 2013).

FIGURE 9. A Jack on Carpet 1/2013, B Dressing Change with Surgeon/Owner, C Jack and Researcher

Jack’s surgeon, a pharmacy student and this researcher observed the owner performing wound care on Jack in November 2013. The owner, an experience nurse has a routine which seem to work well for her and her companion. The bond of compassion between Jack and his owner is remarkable. The surgeon performed a physical assessment and was impressed with Jack’s improved mobility and
outstanding care provided by the owner. Outside of some adjustments needed with external prosthetic devices, Jack is healing well without any infections noted to date (Marcellin-Little & McDonald, 2013).

![Images of Jack walking on implants, grass, and running on implants.](image)

**FIGURE 10.** A Jack Walking on Implants, B Walking on Grass, C Running on Implants

**Owner’s Perspective**

Jack is back at home in Arizona and enjoying his improved mobility. He walks the “desert-loop” near his home which is 1½ miles. Jack’s longest hike has been 3.7 miles with his implants. In Virginia, before his osseointegration surgery, Jack could only walk 100 yards before getting tired and laying down to rest. Walking in the desert has been hard for him, primarily because of the terrain. He now has a patch of grass he enjoys which probably brought back fond memories of Virginia grass (McDonald, 2013).

Jack’s owner gained a lot of practice changing Jack’s dressings and performing daily wound care. Jack appears to like this ritual as it gave him an opportunity to lick his stumps without the booties impeding his access. The owner reports for 2 months after his surgery, Jack had oozing and a crusted area around the ring. She cleaned the area with Q-tips and irrigated the stumps. She observed that when Jack licked the wound, it distributed the tissue and felt he cleaned his own wound. While she questions if she should let him lick his stump, it appears to bring him comfort. She relays a vet surgical fellow telling her that Jack’s mouth is clean and human mouths are worse, which could be controversial in translating infection potential to humans (McDonald, 2013). Jack has had no infections since surgery, which the
owner attributes to her cleaning his stumps with an antiseptic rinse. She reports that when she takes off his booties, he licks his wound for a few minutes. She then applies the rinse solution given to her from the NC vet clinic and then he does not lick. She cleans the stumps than puts the dressing back on (McDonald, 2013).

The owner reports Jack’s appetite is good. He eats human and dog food with a high protein content. An average meal for Jack is boiled chicken. She gives him some can dog food and adds an egg. His high protein for wound healing boosted his immune system. He originally had a questionable mouth infection although it could not be located in the medical records. Jack uses medicine from human’s formulary and does not appear to have any difficulty taking his medication. He drinks plenty of water, which is helpful living in the dry Arizona desert climate (McDonald, 2013).

It is expected that animals that have implants at the end of their stumps will have longer recovery periods (Marcellin-Little, 2013). Jack’s owner discusses how the black tissue originally on his stumps was too painful to bear weight prior to his limb-salvage osseointegration surgery. He built up callus on his stumps. There was no fur around the area and no necrosis occurred. She did see one small black tissue section that sloughed off. This was abnormal tissue that could not be salvaged (McDonald, 2013). Successful tissue salvaging involves preservation of as much tissue as possible with good vascularity (Marcellin-Little 2013).

The owner feels the osseointegration implant surgery has definitely been a success in changing Jack’s mobility and quality of life. She does not regret their decision to have the surgery and is very appreciative she was introduced to Jack’s amazing surgeon. She does verbalize concerns over Jack not wearing the prosthetic feet that screw into his implants. They looked uncomfortable for him and seem to limit his mobility efforts so he is not wearing them. She describes how he walks and runs with the implants with rubber booties on every day, without the prostheses and without pain or discomfort noted.
The owner states Jack has hyperextension with limited right flexion. He is not flexing his ankle. She describes his movement similar to a ballerina on their toes. Jack has summer and winter booties that go over his paws with Velcro strips, like hiking socks (McDonald, 2013).

![Figure 11](image1.png)

**FIGURE 11.** A Implant Cap/Rubber Tip, B Cap Inside Rubber Chair Tip, C Worn out Rubber Caps

![Figure 12](image2.png)

**FIGURE 12.** Chair Tip on Osseointegrated Implant

Jack’s prosthetic feet were made to screw into the implant for the purpose of ambulation. The bandages in post-implant surgery cover up the interface between the screw and the implant although do reveal the rubber ball prosthetic feet. The owner improvised by purchasing some stool caps and rubber chair tips from a local hardware store until another solution was decided regarding Jack not wearing his prosthetic feet (McDonald, 2013).

The owner thought the stool caps and chair caps were a perfect fit on his paws and fit tight. The stool caps wore down. With the chair tips on, he walked on the rocks without booties less than two weeks.
Jack wore out the rubber tips and broke two of them. The hard plastic breaks down easy on rocks. The owner tried several different types of chair tips and put a spacer in them to prevent them from going all the way down to possibly, endanger the implant. No physical pressure or tissue damage occurred which was considered amazing by the surgeon. This once again, was attributed to the outstanding care Jack was receiving by his owner.

The NCSU Engineers had matched the threads on the implants for the prosthetic feet. They are now researching another model prosthetic device that Jack may like to wear as prosthetic feet. Until then, he walks, runs, plays and appears to like his chair caps over his implants devices (McDonald, 2013).

In May 2013, Jack celebrated his one year anniversary from surgery and eight months afterwards, he continues to remain free of infection and from all accounts has a much improved quality lifestyle (McDonald & Marcellin-Little, 2013). Jack continues to be the only canine to date, with bilateral paw implants (NC Vet Medicine Clinic, 2013). Jack’s surgeon describes his and his team’s passion is to help wounded military warriors of the future. He feels this is what motivates them to strive for perfection. The translation to humans is what he calls, “eye on the prize” (Marcellin-Little, 2013).

**Discussion**

The primary focus of this well-controlled animal case study analysis revolved around limb salvaging techniques with innovative osseointegration technology to improve physical mobility and quality of life. Our canine subject Jack went from a limited mobility status with 2 feet and no paws to 4 good feet that allowed him to walk and run longer distances with improved mobility options. This animal case study success supports why a canine is a good model for potential translation from preclinical to clinical research. The similarities in selection criteria from bone structure of the canine to the functional mobility with activities improving his quality of life. The data provided by the medical team, Jack’s owners and witnessed by this researcher supports this clinical outcome.
Some of the limiting factors of translating this preclinical research to clinical research in humans involve the experimental status of this technology, the lack of hard evidence for animal research, cost factors, no regulations and especially limited research and clinical trials. The experimental aspect of his limited sample case study lacked regulatory guidance and FDA approval to be performed in the United States. There is limited research supporting these experimental techniques as well as limited knowledge of limb-salvaging and osseointegration technology available to surgeons and clinical staff who treat these patients. It would be difficult for practitioners to provide education to patient and family members when they lacked the osseointegration knowledge themselves. The cost alone would be a limiting factor to many people. Model fabrication can be expensive, especially with an average of 1 to 2 implant models needed for a practice surgery, not counting the final models and limb-salvaging surgery plus rehabilitation costs. A company donated part of Jack’s prosthetics although his owner reports he does not wear them, because they are uncomfortable and he does not like them.

There are factors facilitating translating this preclinical research to clinical research in humans. The rapid advances in technology with improved implant model fabrications, patient-centered value for addressing mobility, pain and quality of life, need for military injured as well as the need for life coverage in particular the military.

The surgeon and canine Jack with owner, travelled to San Antonio Texas to meet with this researcher for interviews, perform an updated evaluation on Jack’s progress and guest lectured at the Center for the Intrepid (CFI), the National Armed Forces Physical Rehabilitation Center, to share his osseointegrated technology with military and civilian surgeons. Other stakeholders were added to the interprofessional team to discuss implant fabrication and design for future model cases. This researcher arranged a briefing for the surgeon with other medical practitioners and engineers doing human osseointegrated fabrication and human model surgical cases at the CFI. A future tour of the fabrication
lab for new human implant and prosthetic technology at the Intrepid will enhance the study preparation for future collaboration.

The Iowa Model of Evidence-Based Practice guides design and implementation of evidence based practice for a health organization. The model is initiated with problem or knowledge focused questions that tap knowledge from research national guidelines, philosophies of care, as well as data related to risk process improvement, benchmarking, financial and clinical problems. New knowledge of osseointegration can raise questions about this approach to prosthetics. Moreover, the clinical problem of prosthetic failure over a lifetime can also raise questions about what is best practice for prosthetics. This model encourages the nurse to ask questions during the research process that focus not only on the new research data collected, but the overall outcome and readiness for dissemination into practice.

Strengths of Study

One of the greatest strengths of this case study has been the interprofessional team of stakeholders and their cooperation and willingness to share knowledge and education on this innovative research technology. The thirst for knowledge provided motivation to work together. The overwhelming support of Jack’s owner, the surgeon and staff at the NCSU clinic as well as the hospital and military CFI center staff in providing critical information to researcher was a definite strength. The in-person interviews and observations of canine Jack, his owner, the primary surgeon, the surgeons at the CFI and other staff were invaluable to the study analysis. The information was based on reliable data based on raw data of actual incidents. The credibility of the data from canine Jack’s clinical records was reliable based on his actual surgical course.

Limitations and Challenges

One of the challenges and limitations of this study has been the geographic location of the participants. The members were located in North Carolina, Texas and Arizona with several of them
traveling frequently to other states and other countries. The timeline receiving and giving information slowed down the case study progress. Unclear if this could have been avoided.

Evidence gleamed from research studies on osseointegration is limited since this is new technology, especially bone-anchored osseointegration. The small sample size and nature of the technology advances does not lend to experimental or quasi-experimental design. This is one reason the surgeon has not published his clinical trials. He wants to gather more clinical data and perform more clinical cases to gain clinical significance with his research study.

**Lesson Learned**

Performing a case study analysis on new, evolving technology innovations with limited research evidence and access to resources, can be challenging and time consuming.

**Importance of Osseointegration Techniques in Nursing**

In addition to contributing to nursing scholarship, new knowledge in osseointegration techniques can assist the doctorally-prepared nurse leader in clinical practice caring for these patients and using referrals for specialty care. Advanced nurses can provide education for the patient and their family to recognize deteriorating conditions associated with implants and mitigate risk factors with patients as they develop. Nurses can participate and advocate for more osseointegration research especially with well-controlled clinical trials in bone-anchored osseointegration. As part of the interprofessional team, they can develop osseointegration protocols to deal with patients to create quality standards and establish best practices in the clinical arena.

**Mitigation of Risk Factors**

The doctorally-prepared nurse as part of the interprofessional team, can mitigate risks associated with osseointegration surgery and advance this new technology in clinical practice. Advance practice nurses are in a unique position in the clinical setting to promote education of new technology, identify and
monitor abnormalities and changes in a patient’s condition as well as promote good skin care and infection prevention associated with osseointegration procedures. As an advocate for change, they can promote healthcare policy that ensures quality and safety initiatives are included with regulatory guidance to decrease harmful risk factors. Documentation of subtle changes in a patient’s condition could detect osteointegration difficulties and good wound care could prevent further deterioration.

**Future Research**

The scientific discovery of new technology merges with the practitioner’s ability to translate this technology into clinical application and practice to improve the health and quality of life in animals and humans. Until the FDA approves bone-anchored and transfermoral osseointegration limb salvaging procedures for humans in the United States, we will continue to evaluate animal case study outcomes and the benefits and challenges they present. Obviously, multiple well-controlled clinical trials and case studies need to be done to validate osseointegration studies for translation.

New custom-made osseointegrated implants tailored to fit our physical specifications could help improve our physical mobility (Chimutengwende-Gordon et al, 2011). Translational research needs to stay patient-centric where the patient drives the research objectives in all aspects with the interprofessional team. New evidence-based osseointegration technology knowledge should be translated into clinical practice to enhance animal and human quality of life. Changing health care culture to be evidence-based practice environments and accepting new knowledge to disseminate can be challenging. Strategies to translate research and new knowledge into practice should be guided by a conceptual model (White & Dudley-Brown, 2012).
Permission was obtained from Dr. Karen McDonald to use the information she provided on her canine, “Jack” in its entirety for inclusion in this case study to include pictures, medical records, interviews and other documents on Jack’s progress to date.
APPENDIX B

THE UNIVERSITY OF ARIZONA-ANIMAL SUBJECTS IRB DISCLAIMER
No IRB animal or human model permissions were required for this case study as neither model was being used or manipulated in the study. Both animal and human subject IRB’s from the University of Arizona were consulted at the beginning of the case study and both agreed no permission was necessary for this case study.
REFERENCES


Center for Comparative Medicine & Translational Research (CCMTR). (2012-2013).


MacDonald, K. (2013). kmacdonald@matrix45.com, Tucson Arizona


North Carolina Veterinary Hospital (NC VTH). (2012-2013).


