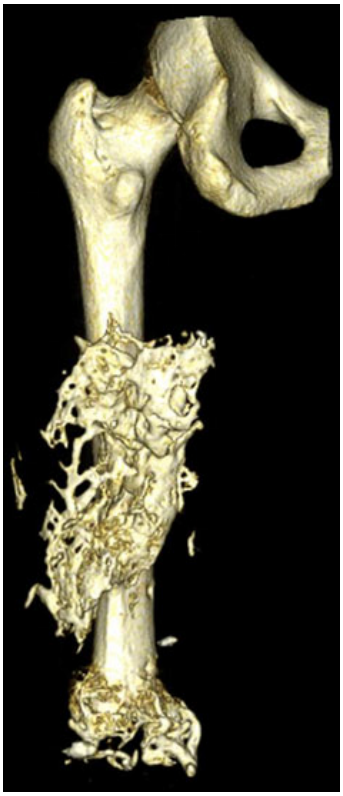
Heterotopic Ossification Research

Dr. Brad M. Isaacson, PhD

Background of Heterotopic Ossification (HO) in the Military



Medical reviews from Operation Enduring Freedom (OEF) and Operation Iraqi Freedom (OIF) have indicated that approximately 70% of war wounds involve the musculoskeletal system, largely in part from the use of improvised explosive devices (IEDs) and rocket propelled grenades (RPGs). Given the intense nature of blast injuries (which require rapid tourniquet use, debridement and surgical intervention), HO has been reported to occur in approximately 63%-65% of wounded service members with limb loss/major extremity injuries. Most concerning is that approximately 20-40% of these affected patients will require surgery to excise their ectopic masses. Symptomatic HO delays rehabilitation regimens and often requires modifications to prosthetic limb componentry and socket size.

← **Figure 1:** Three-dimensional reconstruction of HO demonstrating both boney islands and complete connection to the femur of a service member who sustained a traumatic injury.

There are currently no known mechanisms for quelling or preventing metabolically active HO. Therefore, our team of physicians and scientists have designed several studies to further understand this pathological condition and plan improved surgical schedules to reduce recurrence.

Study #1: Establishing the Mineral Apposition Rate of Heterotopic Ossification for Prevention of Recurrence in Wounded Warriors

- **Purpose:** Study 1 is focuses on reducing HO recurrence in our wounded service members using detailed histological analysis and clinical predictors prior to resection. While much is known about human cortical and cancellous bone, ectopic bone remains an under investigated pathological bone disorder, significantly affecting injured warfighters and the general population.

- **Results to Date:** The team has successful recruited 83% of our intended sample size (33/40) who required HO removal at Walter Reed National Military Medical Center (WRNNMC). Data has indicated that HO growth rate is related to anatomical location and that all masses removed by our physicians were still actively modeling/remodeling at the time of surgical intervention (Figures 2 and 3). Histological data demonstrated that HO grows on average 1.6x faster than non-pathological human bone. In the future, surgeons may be able to use the bone growth equation developed by our team as a tool for planning resection time periods to mitigate recurrence.

- **Budget Total:** $681,410

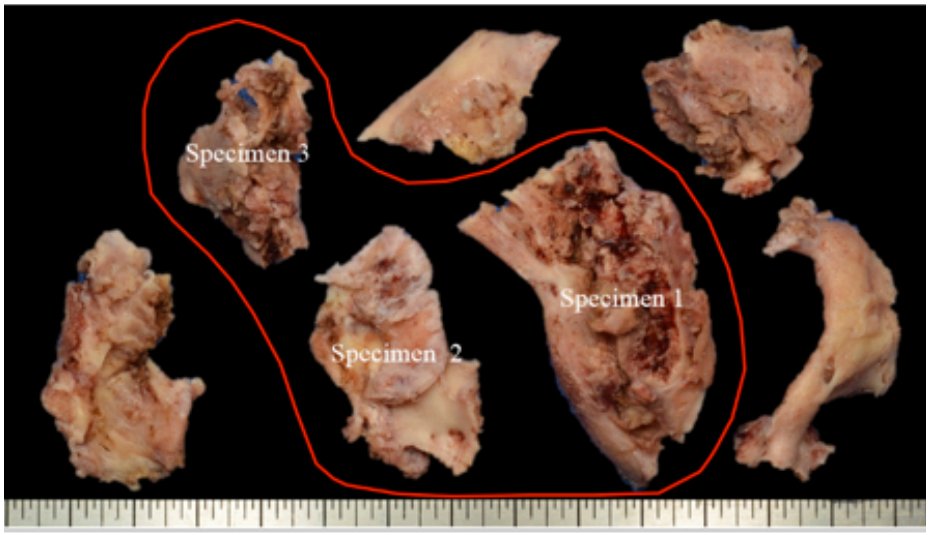


Figure 2: Bone specimens collected from a wounded warrior undergoing ectopic bone removal in their residual limb. Note the large volume of bone tissue that precluded rehabilitation.

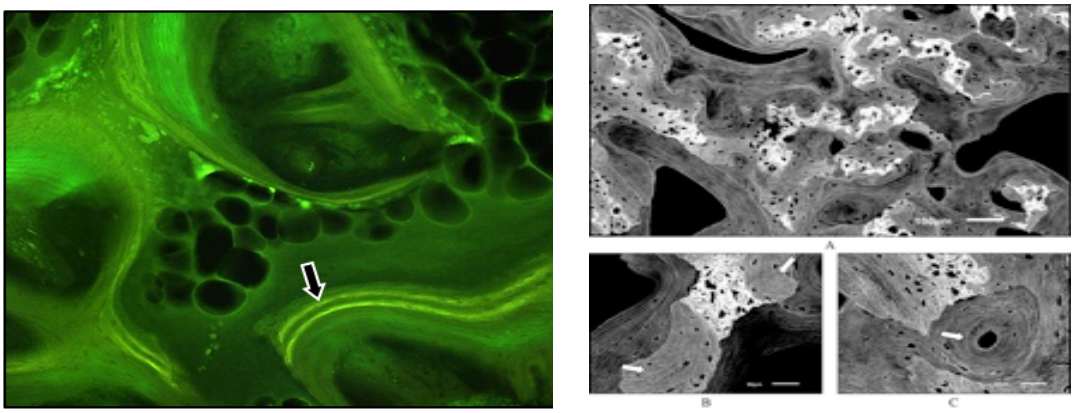


Figure 3: Images used to determine bone growth rates of ectopic bone (left) and detailed scanning electron microscopic analysis showing various stages of bone remodeling (right).

Study 2: Establishing the Mineral Apposition Rate of Heterotopic Ossification for Prevention of Recurrence in Veterans

- **Purpose:** Study #2 utilizes the same key histological/clinical predictors as demonstrated in Study #1, but evaluates HO growth/maturation in veterans undergoing total hip arthroplasty and total knee arthroplasty. There is reason to believe that HO develops differently depending on traumatic inducing agent, and to date, no persons have examined this for this underserved patient population. Understanding HO formation in veterans would have a significant impact on clinical care for the military and civilian patients.

- **Results to Date:** Our team has recruited 10% of our intended target (2/20) and histological data is currently being processed.

- **Budget Total:** $228,508

Study #3: Investigation of a Translatable Animal Model in Order to Understand the Etiology of Heterotopic Ossification

- **Purpose:** Study #3 is intended to serve as a pilot study to create a translatable animal model in order to better understand HO etiology. While small rodent models exist for HO research, there is not a large animal model that can accurately bridge the gap between research and clinic. Therefore our team has developed an ovine study that will evaluate real-life combat factors such as bacterial biofilms, use of a tourniquet, wound vac and trauma to investigate HO growth/maturation. We hypothesize ectopic bone will develop floridly and this model with lead to an increased understanding of these factors and improved rehabilitation regimens/treatment strategies.

- **Results to Date:** N/A – this study is slated to being March 2015.

- **Budget:** $299,331.02

Study 4: Assessing the Primary Factors for HO Development in an Ovine Model

- **Purpose:** This research projects will build upon Study #3 and will evaluate 12 distinct groups to determine which of the factor(s) note above contribute most significantly to HO. This will be a large cohort study and detailed statistical analysis will be conducted upon completion.

- **Results to Date:** N/A – this study is not currently funded

- **Budget:** $820,164.00

About the team: Dr. Brad Michael Isaacson leads the HO team and holds a Bachelors of Science in Mechanical Engineering from Widener University, PhD in Biomedical Engineering from the University of Utah and is completing his Masters of Business Administration and Masters of Finances degrees from Boston College. Shortly after finishing his PhD, Dr. Isaacson completed his post-doctorate fellowship at Walter Reed Army Medical Center in the Integrated Department of Physical Medicine and Rehabilitation and Orthopedics. In 2011, Dr. Isaacson and Dr. Paul Pasquina started the Center for Rehabilitation Sciences Research (CRSR), an organization dedicated to improving the quality of life for wounded warriors with orthopedic and neurological trauma. Dr. Isaacson currently serves as the Program Manager for CRSR and is a lead scientist for the Henry M. Jackson Foundation. Dr. Isaacson was the recipient of a prestigious predoctoral rehabilitation fellowship from the Department of Veterans Affairs (only 1/10 awarded nationwide) and two orthopedic scholarships from the University of Utah for his military-centric research.

Key Accomplishments: Dr. Isaacson and his team are the first team to quantify the rate of HO bone growth in wounded warriors and analyze this ectopic growth using detailed histological analysis (SEM/light microscopy). The team is making great strides at improving surgical schedules to mitigate recurrence and help our injured service members.