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TITLE: A blast model of traumatic brain injury in swine

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14. ABSTRACT
Although blast-induced traumatic brain injury (BI-TBI) is a significant cause of morbidity and behavioral dysfunction in warfighters returning from Iraq, laboratory models are not currently available to study the mechanisms underlying this critical injury and develop new therapies to treat survivors. Many TBI models are performed in rodents, and data from these models have been used as a basis for several disappointing Phase III clinical trials in humans with TBI. The failure of these trials may, in part, be due to differences between the rodent and human (or pig) brain. The development of a large-animal model of BI-TBI will revolutionize the study of this pressing clinical problem and rapidly facilitate the development of novel therapies to treat injured military personnel. Therefore, the purpose of the experiments proposed is to develop a survival model of BI-TBI in swine.

15. SUBJECT TERMS
Traumatic Brain Injury, Swine, Blast, Model Development

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Annual Report for project W81XWH-08-2-0082
A blast model of traumatic brain injury in swine.

INTRODUCTION:
Task 1— Write protocols: March-April 2008.

Submit protocol to IACUC: local ISCUC approval received on 3/20/08.
Submit protocols to DOD: late March 2008; approval expected by May 2008.
Protocol has been written, submitted, approved, and renewed 1 June 2009. The VA protocol (ACORP) has not yet been reconciled with the ACURO.

Task 2— Calibration of the air cannon will take place in April-May 2008.

Two airguns were manufactured. The first is smaller with a 40 inch barrel with an internal diameter of one inch. The compression chamber, which can be inflated up to 100 psi, is 26 inches in length and has an outer diameter of 4 inches. The larger gun has a barrel 54.25 inches in length with an inside diameter of 2.5 inches. The compression chamber is 4 inches in outside diameter with a length of 36 inches. An abstract and data from airgun calibration experiments, submitted to the Military Health Research Forum, are presented below.

BODY:
The Walter Reed Army Institute of Research recently published a preprint of experiments performed at an undisclosed location. The used Yorkshire swine and had three models of blast injury, all using actual explosives (1.0 kg TNT). I will attach a .pdf of their preprint as an appendix. Their blast tube produced a mild traumatic brain injury manifested by histological changes in the brain and a minor disturbance in normal walking gait. In contrast to our airguns, their blast tube was 70 feet long and 6 feet in diameter. Recent consultations with Dr. David F. Moore (Deputy Director for Research, DVBIC, Lead Scientist, DVBIC/DCoE - AFIP Laboratory of Traumatic Brain Injury, TBI Scientific Advisor, Defense Center of Excellence for Psychological Health and Traumatic Brain Injury) and Dr. Tamara Crowder at the DoD sponsored meeting on mild traumatic brain injury have led to new insights on positioning of the animals and determining the airgun's "sweet spot".

REPORTABLE OUTCOMES AND KEY ACCOMPLISHMENTS:
ABSTRACT AND DATA FROM AIRGUN CALIBRATION EXPERIMENTS, SUBMITTED TO THE MILITARY HEALTH RESEARCH FORUM

Blast-Induced Traumatic Brain Injury
Moody, Erin; Wilke, Harland; Coppes, Valerie; Venugopal, Sandya; Panter, S Scott. San Francisco VA Medical Center.

The objective of this study was to develop a technique to help quantify brain trauma resulting from an intense explosive blast in animal models. This study is relative and

applicable to current military personnel in Afghanistan and Iraq facing traumatic head injuries from improvised explosive devices (IED). This study, along with improvements in protective body armor, will help decrease the mortality rate and long term brain injuries in US military. In order to achieve the objective, two air blast guns, using PVC piping, were constructed, each having different lengths, air chamber volumes, barrel diameters and both designed to hold up to 100 psi of pressurized air. With these air guns we produced a small scale blast to induce traumatic brain injury (TBI) in test rats. Using a digital chronometer and small pellets, we measured the air velocity over a series of controlled pressures in the air chambers. To characterize the guns and determine the velocity range, each gun underwent two (2) sets of 10 round firings at 60, 70, 80, 90, and 100 air chamber psi at a distance of one foot. The test results of round one show the small and large guns produced an average force (in Newtons (N)) of 73.9 N (± 4.67) and 499.8 N (± 63.02) , respectively, using 60 psi; 88.6 N (± 6.69) and 573.2 N (±26.14) at 70 psi: 109.7 N (± 3.37) and 656.3 N (± 36.24) at 80 psi: 123.2 N (± 7.76) and 733.7 N (± 39.45) at 90 psi and 137.1 N (± 4.63) and 817.2 N (±54.37) at 100 psi. (See Figure 1). The test results were then recorded for the second round test firing. The test results for round 2 show the small and large gun measured an average of 75.1 N (± 2.78) and 491.1 N (± 26.67); under 60 psi respectively ; 91.7 N (± 6.23) and 577.5 N (± 48.10) at 70 psi; 105.0 N (± 3.29) and 672.1 N (± 42.47) at 80 psi ; 116.N (± 6.99) and 736.1 N (± 49.32) at 90 psi and 133.4 N (± 5.63) and 792 N (± 43.46) at 100 psi (See Figure 2). In conclusion, Figure 3 shows the test ranges for round 2 are very similar to round 1 for the smaller air gun but slightly differ when comparing the large air gun. This difference could be due to operator error or test area conditions, but the ranges still fall within the standard deviation. This data shows linear and reproducible results that quantify known air velocities through the use of air blast guns. This application could help develop further research in swine models. To work with comparative velocities produced by an IED, a larger facility is needed to produce larger air blasts. These air gun velocities also indicate a need for more advanced equipment to simulate a blast in a similar way it is delivered in combat. While this study is at an early stage, it can provide a stepping stone to help in the early treatment of traumatic head injuries as well as possible improvements in military body armor.

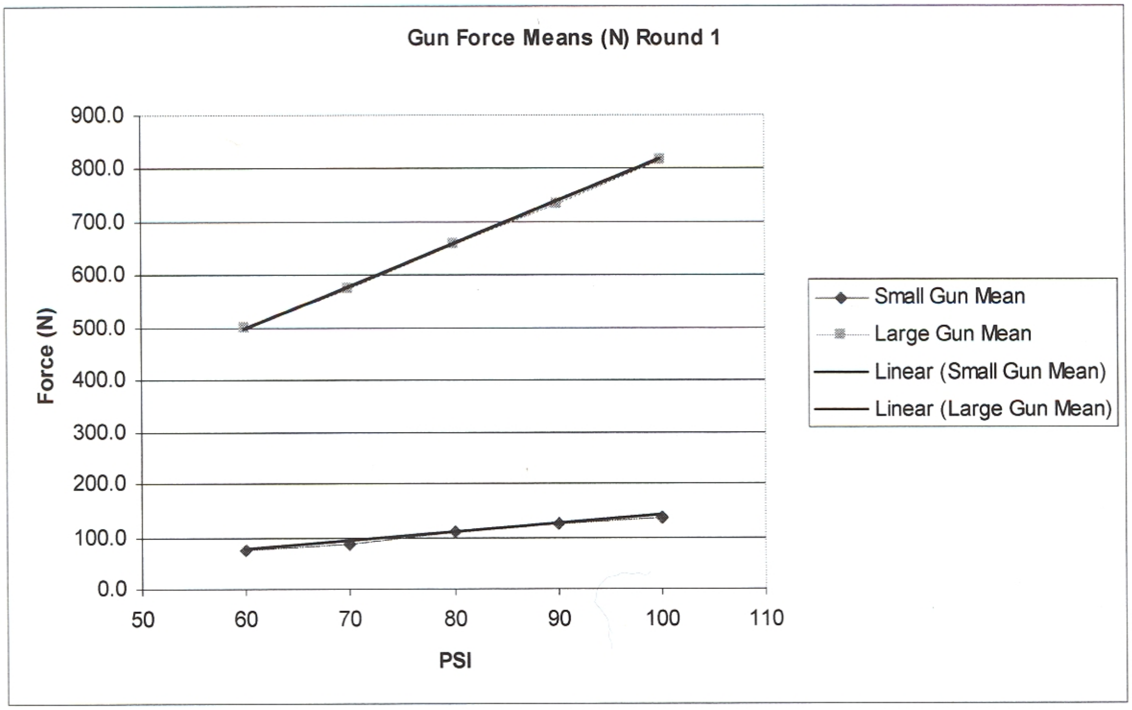

Figure 1- The mean velocity ranges in the small and large gun after the first round of testing.

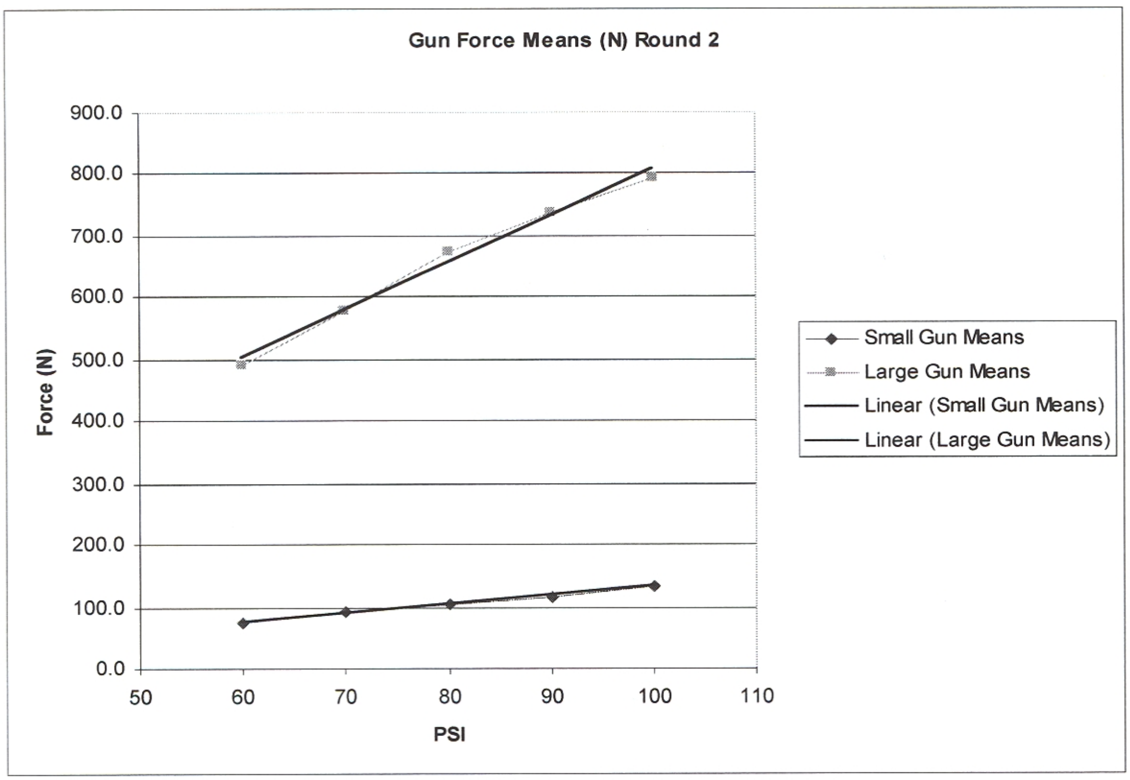

Figure 2- The mean velocity ranges in the small and large fun after the first round of testing.

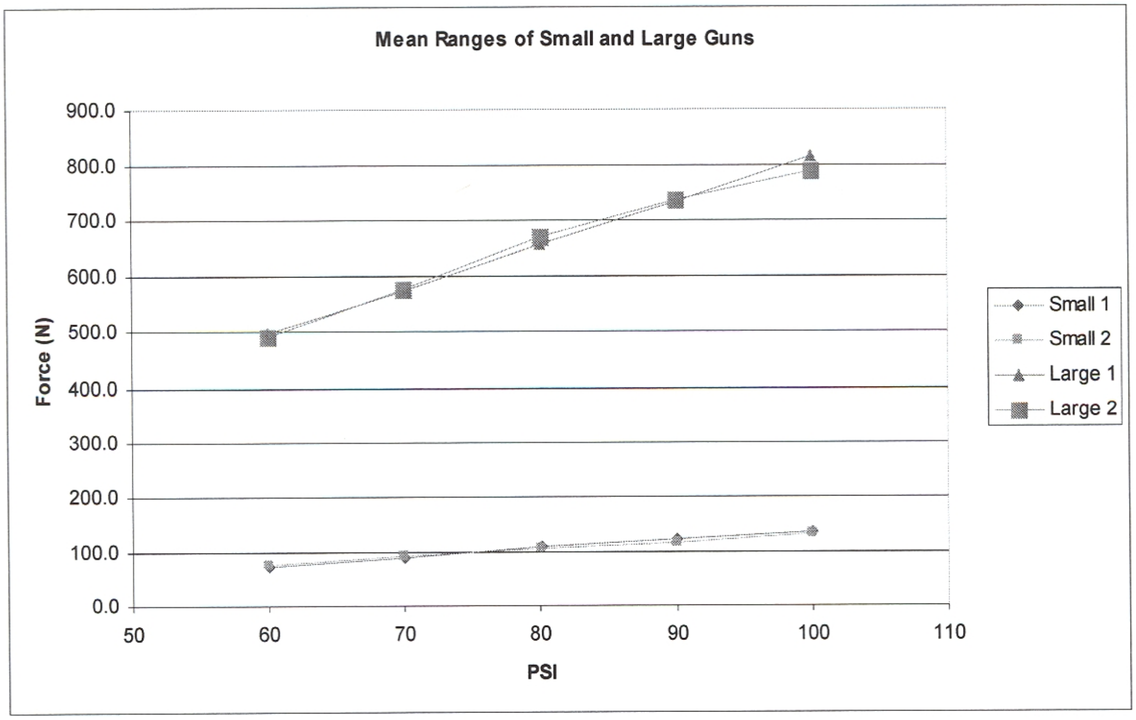

Figure 3- Comparison of the mean ranges between the two rounds between the small and large guns.

CONCLUSIONS:
I recently attended a meeting entitled "Non-Impact, Blast-Induced Mild Traumatic Brain Injury" (held May 12-14, 2009 in Washington, DC) and a second meeting entitled "The Brain at War" (28 May at the San Francisco VAH), and my conclusion from both of these meetings, the WRAIR manuscript, and our own preliminary data is that humans are much more sensitive to blast-induced mild traumatic brain injury (TBI). Another conclusion is that isolated blast TBI probably does not exist. Following blast exposure, the patient will most likely suffer a secondary impact injury, perhaps with the ground, rocks, metal, concrete, or wood. In addition, Dr. (COL) Charles Hoge (WRAIR) has published convincing data showing that mild TBI is probably indistinguishable from persistent post-concussive symptoms, or even post-traumatic stress disorder, both of which are difficult to discern in animals. The next task is to reconcile the ACORP with the ACURO

REFERENCES:
None.

APPENDICES;
Please find attached the report from scientists at WRAIR.

SUPPORTING DATA:
Embeded