Bone and Soft Tissue Trauma Research at the USAISR

David G. Baer, PhD., Thomas J. Walters, PhD., MAJ Steven J. Svoboda MD, 
LTC(P) John F. Kragh, MD., Terry G. Bice, and Joseph C. Wenke, Ph.D.

US Army Institute of Surgical Research 
3400 Rawley E. Chambers Avenue 
Fort Sam Houston, TX  78234-6315 
Email: David.Baer@amedd.army.mil

ABSTRACT

Since its establishment in 1943, the United States Army Institute of Surgical Research (USAISR) has conducted research focused on improving the surgical care given to soldiers. Just as our predecessors addressed the unacceptably high impact of thermal injury on combat casualties, the Bone and Soft Tissue Research Team focuses research on combat casualties by examining the epidemiology of combat wounds to identify needed improvements in combat casualty care. This paper provides an overview of the bone and soft tissue trauma research currently being conducted at the USAISR and introduces the available combat casualty data from recent conflicts that were used to identify areas where research can achieve maximum impact on reducing the morbidity and mortality rates of combat casualties.

1.0 COMBAT CASUALTY STATISTICS

Because the Vietnam War ended over a quarter century ago, we sought data from more recent conflicts on which to base our research efforts. While we have been fortunate to have suffered relatively few combat casualties at the end of the 20th century, Operation Just Cause (Panama), Operation Desert Storm (Kuwait and Iraq) and the Battle of the Black Sea (Somalia) offered the opportunity to investigate more recent patterns of combat injury. Fortunately, the patterns of injury were documented both during and after each of these conflicts, as had been done in Vietnam by the Wound Data and Munitions Effectiveness Team (WEDMET).

Despite the great disparity in missions, environments, enemy, weaponry, and the units engaged, the distribution of wounds was surprisingly consistent in these three conflicts (Table 1 and Figure 1).

In each conflict, extremity wounds predominated, constituting between 70% to 75% of all wounds. Another interesting finding from the data collected following Operation Just Cause is the preponderance of minor to moderate wounds in combat casualties as indicated by injury severity scores (Figure 2), a finding consistent with a similar analysis of casualties from Vietnam. With this new appreciation of the importance of extremity wounds in general, and wounds of mild to moderate severity in particular, we set out to identify medical interventions which target these types of wounds.

1 The opinions or assertions contained herein are the private views of the authors and are not to be construed as official or as reflecting the views of the Department of the Army or the Department of Defense.

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Table 1: Anatomical distribution of injury as a percentage of total number of wounds in observed in soldiers wounded in action during Operation Just Cause (OJC), Operation Desert Storm (ODS) and the Battle of the Black Sea (Somalia).

<table>
<thead>
<tr>
<th>Injury Location</th>
<th>OJC</th>
<th>ODS</th>
<th>Somalia</th>
<th>Weighted Average</th>
</tr>
</thead>
<tbody>
<tr>
<td>Extremity</td>
<td>70%</td>
<td>71%</td>
<td>75%</td>
<td>71%</td>
</tr>
<tr>
<td>Thorax</td>
<td>9%</td>
<td>4%</td>
<td>7%</td>
<td>6%</td>
</tr>
<tr>
<td>Head/Neck</td>
<td>9%</td>
<td>15%</td>
<td>14%</td>
<td>13%</td>
</tr>
<tr>
<td>Pelvis</td>
<td>4%</td>
<td>2%</td>
<td>1%</td>
<td>3%</td>
</tr>
<tr>
<td>Abdomen</td>
<td>4%</td>
<td>4%</td>
<td>3%</td>
<td>4%</td>
</tr>
<tr>
<td>Eye</td>
<td>2%</td>
<td>2%</td>
<td>0%</td>
<td>2%</td>
</tr>
<tr>
<td>Spine</td>
<td>1%</td>
<td>1%</td>
<td>0%</td>
<td>1%</td>
</tr>
</tbody>
</table>

Figure 1: Anatomical distribution of wounds which were recorded for WIA in Operation Just Cause, Operation Desert Storm, and the Somalia. Data were compiled from McBride, et al [3] (Operation Just Cause), Uhorchak et al. [4] (Operation Desert Storm) and Mabry, et al. [5] (Somalia). The patterns of anatomical distribution of injury are highly consistent, and highlight that extremity wounds cause a greater number of casualties than all other wounds combined.
2.0 BATTLEFIELD TREATMENT OF FRACTURES

Of the ¾ of combat wounds that are to the extremities, a large fraction of these injuries include trauma to bone. In fact, fractures constituted 28% of the combined 941 injuries documented for Desert Storm, Just Cause, and Somalia. Not only are these an extremely common injury, fractures in combat casualties result in unusually high morbidity due to high rates of bone loss, mal-union, and osteomyelitis. To reduce the negative impact of fractures, we are developing products that start at the buddy/medic level (non-invasive pelvic band for fracture stabilization and improved splints and casts) and that continue through all echelons of treatment to definitive care (antimicrobial coated external fixator pins and antimicrobial bone graft substitute).

2.1 Pelvic Fracture Stabilizer

While pelvic fractures constitute a relatively small proportion of the fractures on the battlefield, they do occur. These fractures are caused by falls during airborne and fast-rope insertion, as well as miscellaneous accidents.
In order to improve our ability to stabilize these casualties during evacuation and the initial phases of diagnosis and treatment in echelon II medical treatment facilities, we have conducted an analysis of commercially available pelvic compression bands. Cadaveric studies conducted at the USAISR and by academia have documented the utility of these devices in stabilizing the pelvic ring, and reducing the volume of the pelvic cavity, which may aid in hemostasis. In addition, clinical experience suggests that improved stability during transport and manipulation of the patient for medical evaluation significantly reduces pain. These devices are lightweight and inexpensive, and much easier to use than improvised devices and invasive fixators. As a result, we anticipate medical evacuation vehicles will carry pelvic bands in the future.

2.2 Improved Splint/Cast

Although casts are highly effective treatment for fractures, plaster of paris requires water and is high in both volume and weight, making it a less than ideal substance in far-forward medical treatment facilities. Given the great advances in materials science in recent decades, we hypothesized that a polymer could be identified and engineered that would replicate the mechanical properties of plaster and gauze casts while greatly reducing weight. These materials are currently under development through several partnerships with both academia and industry. One promising system, a composite Kevlar mesh/polyurethane epoxy, achieves high strength and rigidity, and is extremely light weight. This composite system can be formed to an extremity as it is pliable before the epoxy completes curing then rapidly stiffens and provides mechanical stability to a fractured limb. Although the impetus for the development of this product is the burdensome weight of plaster casts, we also anticipate that these improved devices may serve as splints, particularly in Special Operations units which operate without easy access to evacuation to an echelon II facility.

Another promising line of research seeks to develop a splint that can off-load the lower extremities. Figure 3 illustrates the impact of minor extremity wounds on units in combat. In this photograph from the recent war in Iraq, a single wound to a lower extremity required three uninjured personnel to aid in evacuation. A device that would allow a soldier to remain ambulatory after injury could have a significant impact on unit effectiveness. We do not anticipate returning the wounded soldier to full function without further care, however, merely freeing other soldiers from the need to carry the casualty would significantly impact unit combat effectiveness. In addition, the casualty may be able to continue to contribute to mission success by performing limited duties such as manning a defensive position.

2.3 Antimicrobial Coated External Fixator Pins

Once a casualty with an open fracture reaches a treatment facility with surgical capability, external fixation is often used to provide mechanical stability while the soft tissue wound heals. Due to the combined effects of higher inoculum and longer delays between injury and initial surgical wound care (irrigation and debridement), external fixators are often used for extended periods. One possible outcome of this extended period of external fixation is pin tract infection, which can lead to pin loosening (loss of structural stability), osteomyelitis, and delays in conversion to internal fixation [1, 2]. In order to combat this problem, the USAISR has developed and tested several prototype antimicrobial coated external fixator pins. Of those tested, standard stainless steel or titanium pins coated with a combination of hydroxyapatite (the calcium-containing mineral found in bone) and lipid stabilized chlorhexidine (a potent antimicrobial) (Fig. 4) proved the most effective, with an 80% reduction in the rate of pin infection in a large animal model of intentionally contaminated pins [6, 7]. These coated pins have been nominated for advanced development, and investigators at the USAISR are currently working with USAMMDA and industry partners to speed the fielding of this promising product.
Figure 3: Wounds to the lower extremities have significant impact on combat units. As shown in the above photo (taken in the early days of Operation Iraqi Freedom), 3 marines were removed from fight in order to aid in the evacuation of an injured soldier unable to ambulate. ©Joe Raedle/Getty Images, reproduced with permission.

Figure 4: Antimicrobial coated external fixator pins. The pins shown in panel A are commercially available stainless steel (1) and titanium (2) self tapping external fixator pins that have been coated with lipid stabilized chlorhexidine and hydroxyapatite in order to improve the stability of the interface between the bone and the pin and reduce the incidence of pin tract infection related complications. Panel B shows sections of coated pin placed onto a Petri dish seeded with Staphylococcus aureus bacteria. The clear region surrounding each pin section indicates that bacteria were un-able to grow around these pins and is indicative of the effective local antibacterial action of the coated pins.
2.4 Antimicrobial Bone Graft Substitute

Grossly contaminated open fractures are commonly treated with prophylactic local antibiotics. Local delivery of antibiotics involves the implantation of antibiotic impregnated cement beads that are fabricated in the operating room by combining polymethylmethacrylate and an antibiotic, and hand forming this paste into small spheres. These beads elute antibiotic for a period of 2 to 6 weeks, then become nothing more than a foreign body, which requires surgical removal. Thus the currently available treatment for a grossly contaminated open fracture requires multiple surgeries. Furthermore, these cement beads are not FDA approved, do not enhance healing, may in fact negatively impact healing, and delay autologous bone graft placement. The repeated implantation and removal of antimicrobial polymethylmethacrylate beads require multiple surgeries resulting in extended hospital stays and convalescence. The USAISR is currently conducting research to test a single product that can serve both as the antimicrobial implant to sanitize the wound as well as an osteoinductive matrix to reduce the number of surgeries to a single trip to the operating room, and thereby speed wound healing. Our research program to develop and test antimicrobial bone graft substitutes was the subject of an article by Beardmore et al.[8]. We believe that improved splints, non-invasive pelvic stabilizers, and antimicrobial external fixator pins can improve combat casualty care beginning at the level of self and buddy aid, through combat medic care and stabilization, to repair in surgery capable treatment facilities.

3.0 SOFT TISSUE TRAUMA CARE

Soft tissue trauma that occurs as the result of combat wounds is a diverse category which includes the entire spectrum of injuries from minor to severe. While it is tempting to ignore the need to treat minor wounds in favor of focusing on wounds that are life-threatening, the statistics cited above highlight the need to address the entire spectrum of wounds. Although minor wounds have less impact on the individual soldier, they are by far the most common, and even moderate decrements in soldier health can have severe impacts on unit capability when multiplied by their high incidence rate. A minor wound that may require only minimal care is at risk for infection. Data from Somalia [5] as well as from British casualties in the Falkland Islands Campaign [9] show that approximately 15% to 20% of combat wounds result in infection. Infected wounds result in increased morbidity and mortality when compared to similar wounds that are not infected, and lead to longer hospitalization. USAISR has focused soft tissue trauma research on preventing infectious complications in mild, moderate and severe wounds, improving wound care for soft tissue wounds which require treatment in a forward medical treatment facility, and reducing the rate of limb loss due to tourniquet application.

3.1 Prevention and Treatment of Wound Infection

In order to reduce the rate of both soft and hard tissue infection, the USAISR initiated a program to push antibiotic therapy into the pre-hospital phase of medical care. For conventional forces, antibiotics are currently unavailable in the field. Although some Special Force medics carry and administer antibiotics, current drugs require intravenous access, which can be problematic in the far-forward environment. A review of the relevant literature showed that the pharmaceutical industry has developed promising oral antibiotics with low toxicity, excellent bioavailability, and long half-lives. In collaboration with the US Special Operations Command, the USAISR convened a panel of military and civilian subject matter experts, representing Military Medicine, Infectious Disease, Surgery, Pharmacology, and Microbiology to review currently available, FDA approved antibiotics for self-aid. The consensus of the panel was that gatifloxacin (Tequin®) is the most appropriate drug for self-administration any time a combat wound results in a break in the skin. This recommendation has been made to the Doctrine Developers (AMEDD Center and School Directorate of Doctrine and Combat Development) and is currently being implemented.
3.2 Advanced Wound Dressings

The gauze field first-aid dressing and recently developed and fielded hemostatic dressings provide wounded soldiers with excellent tools for the control of hemorrhage. However, these dressings are not practical for the protection of mild to moderate wounds [10]. Interviews with combat medics indicate that the standard field dressings will often slide distally if a casualty resumes normal activities. The failure to properly protect mild to moderate wounds from both bacterial contamination and further mechanical damage can be the source of high wound infection rates and an unacceptable degradation of individual performance. In order to provide a dressing for these wounds, we have initiated research on dressings that can be sprayed, painted, or dusted on to soft tissue wounds to provide a barrier to contamination and abrasion. Work to date has identified an extremely promising polymer product developed by an industry partner, and modified to meet the need for a combat wound dressing. In order to assess the efficacy of this dressing, we have conducted tests utilizing an animal model of a contaminated soft tissue wound. This product out-performed other candidate products, and has the potential to serve as paint on protection that will reduce pain and wound infection, while speeding healing and maintaining maximum individual performance, thus reducing the need for evacuation. A clinical trial is currently in progress as an initial step toward transition of this product to advanced development and fielding.

3.3 Wound Irrigation and Tissue Viability

For a typical traumatic wound, devitalized tissue is debrided and wounds are irrigated with what is usually described as “copious” or “adequate” volumes of sterile saline. While inexpensive in a fixed treatment facility, sterile saline can be an extreme logistical load for the deployable treatment facility, especially if current dogma is followed and 8 to 12 liters of saline are used to irrigate each wound. In order to minimize the weight and volume of fluid consumed for initial wound care, investigators at the USAISR are progressing on two fronts.

First, we are attempting to reduce the volume of fluid required for debridement using improved delivery devices and irrigation fluids. Because combat casualties have evacuation times that are longer than the typical civilian trauma patient, we are currently developing an animal model of combined bone and soft tissue damage and contamination. This model will include a delay after contamination and before irrigation to more closely mirror extended evacuation times. This model will serve as the test-bed for innovations that may reduce logistical loads such as use of potable water for irrigation, irrigation fluid additives (detergents or antimicrobials), pulsatile pressure delivery, and parallel flow delivery. In particular, we will investigate the ability of each of these technologies to meet or exceed the reduction in contamination provided by 10 liters of sterile saline.

Second, we are working to minimize the loss of salvageable tissue through the development of technologies to visualize tissue viability. After conducting an extensive survey of emerging technologies for non-invasively interrogating tissue, Optical Coherence Tomography was identified as the most promising. As there is already extensive industry and academic investment in the development of the core technology, the USAISR entered into a partnership with the Beckman Laser Institute (BLI, University of California, Irvine) to adapt this emerging technology to address the military medicine need. While the technical details of this technology are beyond the scope of this paper, devices in development at BLI have already shown promise in producing images of epidermis and endothelium with sub-cellular resolution. Research conducted at the USAISR will attempt to determine if this imaging modality will be similarly successful in imaging other tissues, and whether these images will be useful as a diagnostic for tissue viability. Our technological goal is the development of a non-invasive, near real time, optical biopsy device which can be used to delineate margins of salvageable tissue. While this work is in the very early stages, a prototype device has been constructed and is currently under initial testing and validation.
3.4 Advanced Tourniquets

Though long out of favor, tourniquets for hemorrhage control when tactical or logistic restraints prevent immediate access to surgical intervention have been returned to use as self or buddy aid (for information regarding the recently fielded one-handed tourniquet, interested readers are referred to the article by Ryan, et al., this issue). While tourniquets do provide a potentially life-saving capability to the soldier, their use is not without risk. When discussing the use of tourniquets for far-forward use, the phrase “life over limb” is often used to describe the trade-off between life-saving hemostasis and the potential for subsequent amputation of a limb after tourniquet use. Our goal is to minimize the negative impact of tourniquet application by conducting research on several fronts, including investigating the pathophysiology of tourniquet injury, developing guidelines for nerve and muscle preserving tourniquet use guidelines, developing novel tissue salvage drug therapies, and designing a second generation tourniquet that is both hemostatic and soft tissue friendly. Readers interested in current research efforts on the effect of tourniquet injury and hemorrhage, and the development of protective use guidelines and therapies are referred to the article by Walters, et al. in this publication.

4.0 CONCLUSION

Though combat wounds cover virtually the entire spectrum of trauma, analysis of available statistics permits us to predict where soldier-focused research and development can have the greatest impact. Additionally, nascent trends in military doctrine such as the development of the Objective Force and an increased reliance on Special Operations units to shape the battlefield highlight the need for innovation in field medicine. The reduction of logistic loads to improve unit deployability and increased dispersion on the future battlefield will demand reduced reliance on medical evacuation and an increased effort to deliver initial medical care as far forward as possible. By providing our soldiers with improved trauma care we seek to reduce the need for immediate medical evacuation from the battlefield while simultaneously mitigating the impact of extended evacuation. This in turn will reduce the adverse effects of injury, reduce workload and logistical requirements for theater medical assets, and increase the speed and number of soldiers returned to duty following wounding.

While current efforts are focused on those problems where we can achieve maximum impact in the near term, continued improvements in combat casualty care require us to advance our understanding of the pathophysiology of trauma. In addition to the research outlined above, investigators in the Bone and Soft Tissue program are involved in longer range research programs with the goal of improving wound healing after initial stabilization and repair of trauma. These efforts include characterizing factors which facilitate regrowth of bone following fracture, improving muscle regeneration to maximize recovery of strength, modulating nerve regeneration after injury and accelerating re-epithelialization of skin defects. We foresee that these lines of research will continue to advance the art and science of caring for combat casualties in order to minimize the impact of injury on our soldiers and the units that depend on them.
5.0 REFERENCES


