

Orthopaedic War Injuries: Recent Developments in Treatment and Research

CAPT Dana C. Covey, MD, MC, USN
Roy K. Aaron, MD
LTC Martin F. Baechler, MD, MC, USA
Christopher T. Born, MD, FACS
Deborah McK. Ciombor, PhD
Lt Col James A. Keeney, MD, MC, USAF
CPT Andrew W. Mack, MD, MC, USA
CDR Michael T. Mazurek, MD, MC, USN
Col Mark W. Richardson, MD, MC, USAF
Alexander Y. Shin, MD
CAPT Michael A. Thompson, MD, MC, USN

Abstract

Musculoskeletal injury is the most common type of injury among survivors of combat trauma, and combat-related trauma is challenging for an orthopaedic surgeon to treat. Methods of treatment are evolving, but significant gaps remain as knowledge of civilian trauma is extrapolated to combat trauma.

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More than 32,000 members of the US Armed Forces have been wounded during the ongoing wars in Iraq and Afghanistan, and most of them have a musculoskeletal injury.^{1,2} The most common cause of these injuries is a mortar, rocket, improvised explosive device, or other potentially lethal explosive weapon.³ Approximately 90% of wounded service members currently survive their injuries.¹ In contrast, survival rates during the war in Vietnam, the war in Korea, and World War II were 86.5%, 75.4%, and 69.8%, respec-

tively.⁴ Improved personal protection equipment and training are partly responsible for the higher survival rate. Tactical surgical intervention and rapid evacuation also are increasing the number of patients with devastating musculoskeletal injuries who survive the immediate postinjury period. The improved survival rate is accompanied by a corresponding increase in the initial and late treatment of complex musculoskeletal war injuries. In response, treatment strategies are evolving and further research is being conducted.

Intramedullary Flexible Nailing of War-Related Diaphyseal Radial Fractures

Many injuries incurred during Operation Iraqi Freedom and Operation Enduring Freedom have resulted from a high-energy mechanism and include an open, comminuted, or segmental fracture with a large zone of injury and significant soft-tissue loss. Open reduction and internal fixation with compression plate osteosynthesis is the most common method of treating an adult forearm shaft fracture. However, this technique can require extensive surgical exposure and periosteal stripping, and refracture occurs after plate removal in 3% to 22% of patients.^{5,6} Plate fixation may not be the optimal mode of treating some patients with an open diaphyseal radial fracture, as the soft-tissue dissection required for plate placement may complicate wound stabilization and healing by disturbing the periosteum over long comminuted segments. In addition,

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plate fixation requires adequate soft-tissue coverage over the plate.

Intramedullary fixation of forearm shaft fractures was introduced in 1913 by Georg Schöne, who used flexible silver pins.⁷ More recently used devices for intramedullary fixation of an adult forearm shaft fracture include Kirschner wires, Steinmann pins, Rush rods, Küntscher nails, Hackenthal bundle nails, Street square nails, Sage prebent triangular nails, and interlocking intramedullary nails.⁸⁻¹² All of these devices are intended to limit soft-tissue dissection, preserve the periosteum, minimize the length of incisions and scars, and decrease the refracture rate. Flexible titanium nails have been extensively used; results in pediatric trauma patients have been reported,^{13,14} but few data are available to guide the use of these nails in adult patients.

Walter Reed Army Medical Center Study

During the period from March 2003 to January 2008, 145 combat-related open diaphyseal radial fractures were treated at Walter Reed Army Medical Center (Washington, DC). Ten of these patients (mean age, 25.4 years; range, 20 to 39 years) were treated with flexible titanium nails. All 10 patients had a Gustilo-Anderson type III radial shaft fracture (nine type IIIA fractures and one type IIIB fracture), with concomitant severe soft-tissue trauma. Seven patients had a both-bone forearm fracture, and three had an isolated radial shaft fracture. Seven had been injured as the result of an explosive blast; two had received a military-velocity gunshot wound, and one had been injured in a motor vehicle crash. Six patients had multisystem trauma. The fracture initially had been immobilized using a plaster splint in six

patients and external fixation in four. The mean elapsed time from injury to definitive fixation was 9.8 days (range, 4 to 18 days), and the patients received a mean of 4.1 débridement procedures (range, 2 to 6 procedures) before the definitive fixation. None of the patients received immediate or delayed bone grafting.

In the seven patients with a both-bone forearm fracture, the ulnar fracture was treated first, using plate fixation to restore adequate length. The technique used for flexible titanium nail stabilization of the diaphyseal radial fractures was similar to the technique described for pediatric patients.¹⁵ For directional control during insertion, a nail with a prebent tip is used, or the nail is slightly bent at the tip before use. The nail is placed retrograde through a starting point at the radial styloid between the first and second dorsal compartments, after the tendons and superficial branch of the radial nerve have been identified and protected. A push-and-oscillate technique is used during insertion to provide better control and accuracy than malleting into position. If possible, two flexible nails are inserted as the surgeon attempts to divergently position them into the radial head for better rotational stability. The nail is cut close to the bone surface using a smooth cutter to minimize irritation of the overlying soft tissue.

The 10 patients had radiographic and clinical union at a mean 23.7 weeks after surgery (range, 12 to 48 weeks). The final follow-up time was 30.5 months (range, 13 to 58 months). Forearm synostosis required excision in three patients (two with a both-bone forearm fracture and one with an isolated radial fracture) at a mean 5 months after surgery (range, 4 to 6 months), and pain required nail removal in 1 pa-

tient. There were no postsurgical infections.

One of the patients was a 27-year-old US serviceman with a type IIIA comminuted diaphyseal left radial fracture at the junction of the proximal and middle thirds, as well as a posterior interosseous nerve neurapraxia and an 11-cm overlying dorsal soft-tissue injury (Figure 1, *A*). Despite the relatively benign appearance of the skin injury, débridement procedures revealed marked soft-tissue contusion and muscle necrosis (Figure 1, *B*). After five débridement procedures, the radial fracture was treated using flexible titanium nail fixation and delayed primary closure (Figure 1, *C*). The fracture had united 14 weeks after surgery, and at 31-month follow-up the patient had almost-symmetric forearm rotation compared with the contralateral limb (Figure 1, *D* and *E*). There was gradual spontaneous resolution of the neurapraxia.

Other Studies

Open reduction and internal fixation with compression plating is the most common method of treating an adult diaphyseal forearm fracture, and excellent union rates have been reported with this technique. In a retrospective study of 330 diaphyseal forearm fractures treated with compression plating, Anderson and associates¹⁶ found a 97% overall union rate, with minimal complications. Hadden and associates,¹⁷ in a retrospective study of 177 adult forearm shaft fractures in 108 patients, also found a 97% union rate after compression plating; the complications included surgical nerve injury in seven patients, deep infection in six, and synostosis in six. Although union of a diaphyseal forearm fracture can be reliably obtained with

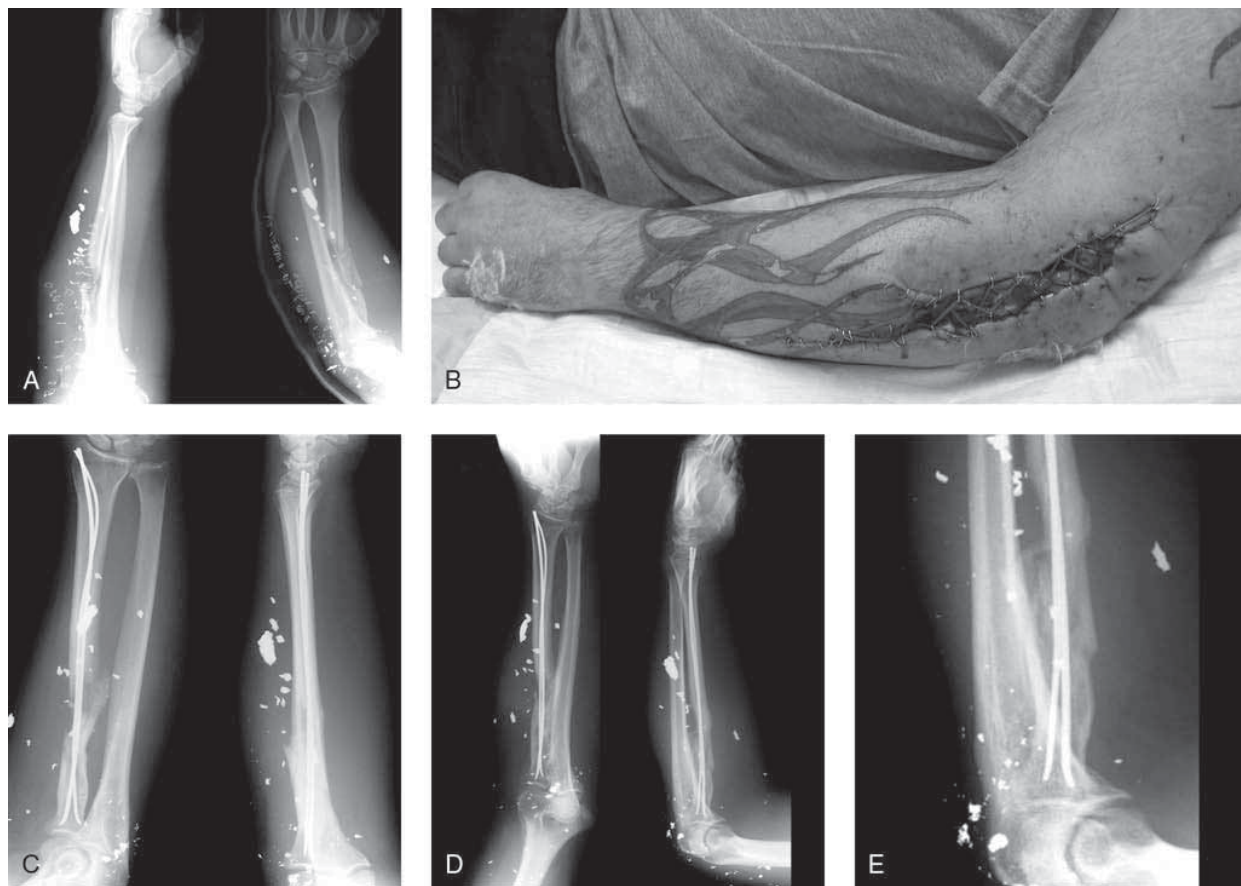


Figure 1 **A**, AP and lateral radiographs of a 27-year-old man injured by an explosive detonation, showing a type IIIA open diaphyseal radial fracture and numerous retained metallic fragments. **B**, Clinical photograph showing an 11-cm dorsal forearm wound partially approximated with vessel loops. **C**, AP and lateral radiographs of the forearm after reduction and internal fixation of the radial fracture with two flexible titanium intramedullary nails. **D**, AP and lateral radiographs taken at 14-week follow-up showing a bridging callus across the fracture. **E**, Magnified lateral radiograph of the proximal forearm showing bony healing of the fracture.

compression plate fixation, strength in the forearm, wrist, and hand is not as reliably restored. Droll and associates¹⁸ evaluated the final range of motion and strength after plate fixation of forearm fractures at a mean 5.4-year follow-up and found that plate fixation of both-bone fracture restored almost-normal anatomy and motion. Compared with the contralateral forearm, however, the injured forearm had moderately reduced strength in pronation (70% of normal), supination (68% of normal), wrist flexion (84% of normal),

wrist extension (63% of normal), and grip (75% of normal) that were highly significant (all $P < 0.0011$).

The reported frequency of post-traumatic radioulnar synostosis is 1% to 6% after plate fixation of a diaphyseal forearm fracture.^{16,17,19} In theory, intramedullary nailing of a forearm fracture causes less soft-tissue disruption, especially along the interosseous space, and therefore decreases the likelihood of synostosis. However, flexible nailing did not appear to limit the formation of forearm synostosis in war-related open

radial fractures; 3 of the 10 patients required excision of synostosis to allow forearm rotation. Synostosis formation may be related to the extensive soft-tissue damage that results from a high-energy injury as well as the traumatic brain injury sustained by two of the three patients who developed forearm synostosis.

Brachial Plexus Injuries

The protection provided by military body armor is limited by the service member's mobility needs. As a result, injuries to the extremities, in-

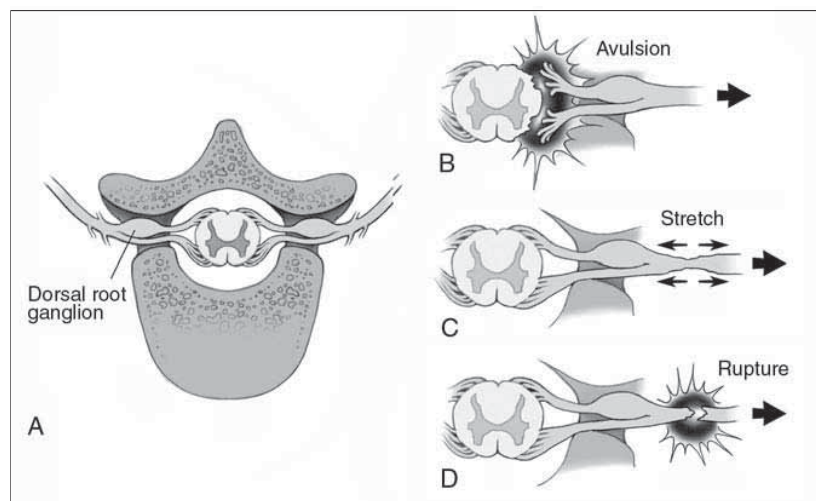


Figure 2 A, The normal relationship of the spinal cord, the nerve root, and the dorsal root ganglion. B, Preganglionic injury (proximal to the dorsal root ganglion). C and D, Postganglionic injury (distal to the dorsal root ganglion). (Reproduced with permission from the Mayo Foundation.)

cluding brachial plexus injuries, account for a disproportionately high number of the current wartime injuries caused by blasts and missiles. During World War I, neurovascular injuries to the upper limb also were relatively common. The prevailing treatment was limb amputation with no attempt to repair the vessels or nerves, although Carrel²⁰ and Guthrie²¹ had described techniques for vascular repair. In 1934, Stevens stated, "The presumption should be against operating in cases of tension or traction injuries. The chance of suture of a ruptured nerve trunk is a forlorn hope."²² The large number of penetrating injuries during World War II again brought brachial plexus injury to the attention of surgeons and led to the development of cervical myelography,²³ electromyography,²⁴ nerve action potential recording,²⁵ and the histamine test.²⁶ The British government commissioned Herbert Seddon to study peripheral nerve lesions in the hope of improving patient functioning; Seddon's

research continued for several decades and greatly contributed to knowledge of this devastating injury.²⁷⁻³² The outcome of surgical treatment for brachial plexus injury nevertheless remained poor, and in 1966 the International Society of Orthopaedic Surgery and Traumatology concluded that surgical exploration of the plexus, especially at the infraclavicular level, had no real benefit and that surgical repair of lesions was generally impossible.³³ By 1969, above-elbow amputation with shoulder arthrodesis and prosthesis fitting was frequently recommended.³⁴

The advent of microsurgery during the late 1960s improved the understanding of nerve injuries and physiology and increased interest in the repair of brachial plexus injury. Improved microsurgical techniques and novel methods of nerve repair and reconstruction were introduced. During the past two decades, the use of free-functioning muscle transfers and novel nerve

transfers, as well as an improved understanding of nerve physiology, has improved the outcomes of reconstruction. However, general knowledge of the treatments available for adult brachial plexus injury is inadequate, and many orthopaedic surgeons still believe that the best treatment is amputation and shoulder arthrodesis.

Treatment Decisions

Important factors in determining the treatment of a brachial plexus injury include the appropriateness of surgery, the timing of surgery, and the priorities for restoring upper arm function.³⁵ The appropriateness and timing decisions are among the most difficult in peripheral nerve surgery, despite improvements in electrodiagnostic and imaging studies. In general, surgery is indicated when there is no clinical or electrical evidence of recovery or no hope of spontaneous recovery, but it also is dependent on the mechanism of injury and associated injuries. Nerve injuries can be broadly categorized as preganglionic (avulsion of the nerve rootlets from the spinal cord) or postganglionic (rupture of the nerve distal to the dorsal root ganglion; Figure 2). Preganglionic nerve injury cannot be treated by reinsertion of the nerve rootlets back into the spinal cord, and alternative means of repair such as nerve transfer or neurotization should be considered. Postganglionic injury, which can include missile injuries, sharp lacerations, or ruptures, can be repaired using interpositional nerve grafts. All concomitant injuries must be considered, as they may affect the reconstruction of the brachial plexus.

The timing of surgical intervention depends on the type and mech-

anism of injury. After a sharp, open injury, immediate exploration and primary repair of the injured portion of the brachial plexus can facilitate end-to-end repair of the injured nerves. If the open injury is secondary to blunt trauma with nerve avulsion, the ends of the lacerated nerve should be tagged, and repair should be delayed for 3 to 4 weeks; at that time, the injured nerve ends will be demarcated, and the zone of nerve injury can be better identified. A low-velocity gunshot wound should be observed because most such injuries are neurapraxic. However, high-velocity gunshot wounds are associated with significant soft-tissue damage and usually require surgical exploration.

The timing of surgery for a stretch injury is controversial; however, most authors agree that a period of observation along with serial clinical and electrodiagnostic examination may be helpful in determining the type of surgical treatment required. Early surgical intervention may not allow sufficient time for spontaneous reinnervation, but an overly long delay may lead to unnecessary motor end plate and reinnervation failure. Early exploration and reconstruction (3 to 6 weeks after injury) are recommended when there is a high suspicion of root avulsion. Routine exploration is recommended 3 to 6 months after the injury and allows for serial examination to determine if spontaneous recovery will occur in proximal muscles. Delayed surgery (6 to 12 months after injury) or late surgery (more than 12 months after injury) portends poorer outcomes because the time required for the nerve to regenerate to the target muscles is greater than the survival time of the motor end plate after denervation. In late surgical reconstructions, options other than nerve

transfers/grafting should be considered. These options include the use of free functioning muscle transfers or tendon transfers.

When surgical treatment of an acute brachial plexus injury is performed, ideally it should be undertaken within 6 months of injury.³⁵ Nerve grafting or nerve transfer is less successful between 6 to 9 months because of the time-dependent degradation at the motor end plate of the end organ. After 1 year has elapsed, alternatives to nerve grafting and neurotization usually should be considered.

The treatment priorities for a brachial plexus injury include restoration of elbow flexion and shoulder stability. Additional function, including rudimentary grasping and elbow extension, frequently can also be restored. In restoring function to a flail extremity, elbow flexion usually is considered the highest priority;³⁵ in descending order of importance, other priorities are shoulder abduction and stability, hand sensibility, wrist extension and finger flexion, wrist flexion and finger extension, and intrinsic hand function.

Surgical Treatment

Brachial plexus reconstruction is considered either primary or secondary. Primary reconstruction is the initial surgical treatment. It can include direct nerve surgery (direct repair, neurolysis, nerve grafting, nerve transfer), soft-tissue surgery (free-functioning muscle transfer), or both. Secondary reconstruction may be necessary to augment partial recovery or obtain function. It can include soft-tissue reconstruction (tendon or muscle transfer, free muscle transfer) or bony procedures (arthrodesis, osteotomy) but typically not nerve surgery. Often, a combination of techniques is used.

Interpositional nerve grafting still has a significant role in the treatment of brachial plexus injury and often is used with newer techniques.

Nerve Transfers (Neurotization)

In a nerve transfer, a functioning but relatively unimportant nerve is transferred to a distal but more important denervated nerve. A nerve transfer may be preferable to interpositional grafting because the transferred nerve can be placed close to the donor nerve's entrance into a muscle, which in turn would decrease the time to reinnervation.

Several nerves can be used as a source for neurotization. The commonly used donor nerves include the spinal accessory nerve (cranial nerve XI), motor and sensory intercostal nerves, and the medial pectoral nerve. The intercostal nerves are among the most common extraplexal sources for neurotization (Figure 3) and have been used with excellent results for both motor and sensory nerve transfers.

More than a decade ago, several surgeons in Asia began using the phrenic nerve and contralateral C7 (or hemicontralateral C7) nerve in an effort to expand the pool of extraplexal donor nerves and improve outcomes. This type of nerve transfer now is used in several centers around the world.³⁵⁻⁴³ The deep cervical plexus and hypoglossal nerve (cranial nerve XII) have also been used for motor recovery, although the reported results have been poor.⁴⁴

Neurotization for shoulder abduction can easily be obtained by transferring the spinal accessory nerve or phrenic nerve to the suprascapular nerve.³⁴ These two transfers have the benefit of requiring no additional interpositional nerve grafts and allowing a direct coaptation of the nerves. If additional

nerve sources are available, neurotization of the axillary nerve or nerve grafting from C5 is recommended to provide additional shoulder stability and abduction.

Two popular options are available for restoring elbow flexion in a pa-

tient with an upper trunk avulsion injury: transfer of the medial pectoral nerve to the musculocutaneous nerve or the biceps branch and transfer of a fascicle from the ulnar nerve to the motor branch of the biceps, which is known as the Oberlin transfer⁴⁵

(Figure 4). In addition, deltoid function can be restored by transfer of a branch of the triceps to the posterior axillary nerve^{46,47}(Figure 5).

The contralateral C7 or hemicontralateral C7 nerve can be used with a vascularized ulnar nerve graft (for a complete plexus avulsion injury) or with a sural nerve graft to bring a large number of motor axons to the injured side.^{39,40,48} When used with a vascularized ulnar nerve graft, the contralateral or hemicontralateral C7 nerve can be used to innervate the median nerve in the hope of obtaining useful finger flexion and protective sensation in the median nerve distribution.

Free Muscle Transfer

Advances in microsurgical technique have led to innovations in surgical reconstruction of the upper extremity after brachial plexus injury. A free-functioning muscle transfer is the transplantation of a muscle and its neurovascular pedicle to a new location where it will be reinnervated by a donor nerve and provide a new function. The muscle is powered by neurotizing the motor nerve to the flap, and the circulation of the transferred muscle is restored with microsurgical anastomosis of the donor and recipient vessels. Reinnervation of the transferred muscle by the donor nerve begins within several months, and eventually the muscle begins to contract and gains independent function.

Free-functioning muscle transfer was first used for injuries that were more than 12 months old. Free-functioning muscle transfer also has been used as a salvage procedure after unsuccessful nerve reconstruction.^{34,49-52} Because free muscle transfer was successful in late surgery, it has been incorporated into early reconstruction.

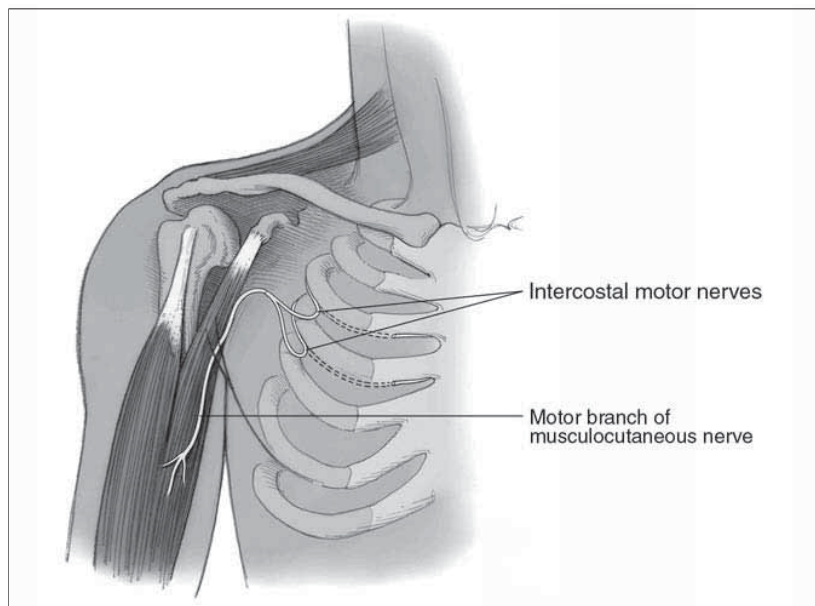


Figure 3 Intercostal motor nerve transfer for neurotization of the biceps branch of the musculocutaneous nerve. (Reproduced with permission from the Mayo Foundation.)

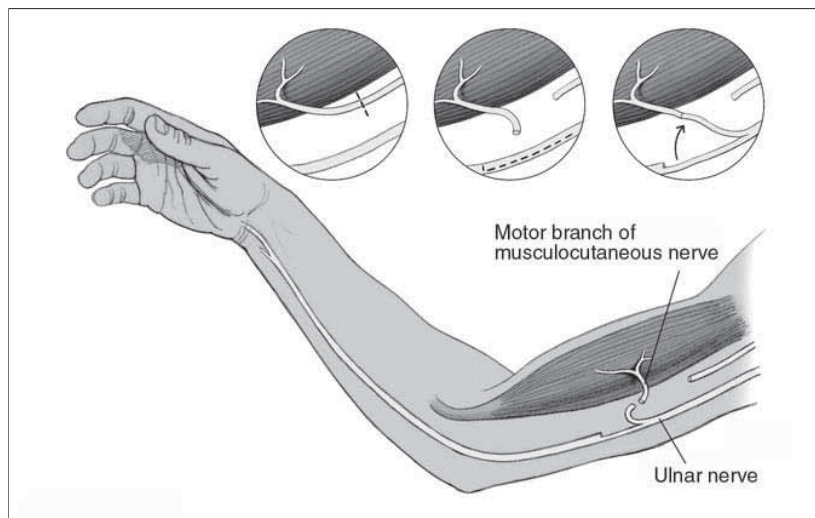


Figure 4 A portion of the functioning ulnar nerve can be transferred to the biceps motor branch to restore elbow flexion in an upper trunk injury. (Reproduced with permission from the Mayo Foundation.)



Figure 5 A through C, When the triceps is spared and restoration of axillary nerve function is needed, a branch of the triceps can be transferred to the posterior axillary nerve. **A**, Via a posterior approach, the deltoid is identified and elevated. The quadrilateral space and triangular interval are identified. **B**, The axillary nerve and a triceps branch are identified. The axillary nerve is divided as far anterior as possible, and the triceps branch is divided as distal as possible. **C**, The two nerves are then coapted under the operative microscope. (Reproduced with permission from the Mayo Foundation.)

Free muscle transfers are most commonly used to provide reliable elbow flexion.^{34,50-52} The gracilis has a proximally based neurovascular pedicle, which allows relatively early reinnervation, and a long tendon, which reaches into the forearm for hand reanimation; as a result, the gracilis is one of the most commonly used muscles for brachial plexus reconstruction. The gracilis can be used for restoration of biceps function (Figure 6), wrist extension, and finger flexion or for a double-muscle transfer in the two-stage Doi procedure,⁵¹ in which both gracilis muscles are transferred to restore elbow flexion and extension, wrist extension, and finger flexion.

A single-stage gracilis muscle transfer can be used in a complete acute brachial plexus injury to restore elbow flexion and extension, shoulder abduction and external rotation, and rudimentary grasp. The brachial plexus is first explored, and any usable nerve roots are used to target the

shoulder. If no nerve roots are available, a hemicontralateral C7 nerve is used to motor the axillary and suprascapular nerves through nerve grafts. Elbow flexion is restored by the transfer of two intercostal motor nerves. A free-functioning muscle transfer is used to obtain finger flexion and is motored by an additional two intercostal nerves. Triceps function is restored by using the spinal accessory nerve with a nerve graft to the radial nerve. Finally, sensation is restored with an intercostal sensory nerve transfer to the lateral cord contribution of the median nerve.

Regenerative and Restorative Treatment of Severe Limb Trauma

The need for increased medical attention to limb loss was heightened by the return from Operation Iraqi Freedom and Operation Enduring Freedom of service members with devastating extremity injuries. Although body armor often preserves

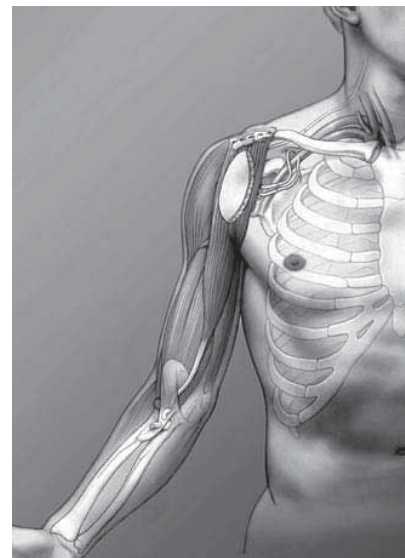


Figure 6 A free gracilis muscle transfer can be used for elbow flexion. The proximal end of the gracilis is secured to the clavicle. Vascular inflow and outflow are via the thoracoacromial trunk, and the muscle is powered by the spinal accessory or intercostal motor nerves. Distally, the gracilis tendon is woven into the biceps tendon. (Reproduced with permission from the Mayo Foundation.)

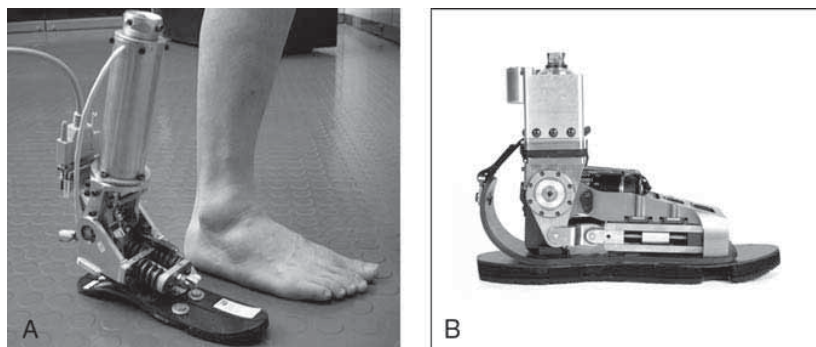


Figure 7 A, A prototype ankle-foot prosthesis requiring connection to a computer. B, The current ankle-foot prototype with self-contained battery pack and microprocessors (weight, 3.8 lb).

life by protecting the head, chest, and abdomen, survivors can suffer from mutilating upper or lower extremity injury or limb amputation. The Center for Restorative and Regenerative Medicine at Brown University and the Providence Veterans Affairs Medical Center (Providence, RI) is investigating technologically advanced solutions for the restoration of limb function after traumatic injury, with funding from the US Department of Veterans Affairs Rehabilitation Research and Development Service. The center's multidisciplinary approach to prosthesis design, tissue engineering, biomaterials, neurotechnology, and rehabilitation converges in the concept of a composite or biohybrid limb that is composed of both biologic and synthetic materials; the limitations of each type of material theoretically can be overcome by integrating them. The center's long-term goals are to develop biomimetic prostheses, optimize the human-prosthesis interface with neurocontrol devices, improve osseointegrated fixation, and lengthen short residual limbs. Research also is focused on techniques for tissue restoration through tissue engineering and regenerative medicine. Success will de-

pend in part on the development of rehabilitation strategies using computer-based virtual technology and other modalities.

Biomimetic Prosthetics

Currently available prostheses are not responsive to the intent of the user. The stiffness of human lower extremity joints varies with walking speed, and the joints store return energy at a predictable level. In contrast, a conventional prosthesis has fixed mechanical properties, requires a significant increase in metabolic energy use, and does not readily accommodate changes in walking speed. The patient may be forced to accommodate an asymmetric gait pattern and may have difficulty in changing direction and maintaining balance. The goal of current research is to develop joints that use biomimetic control, musclelike actuation, and neurosensors to achieve greater responsiveness to the user's actions and wishes. A system designed to mimic the normal stiffness and damping of a joint (joint impedance) will be coupled with a mechanical power source to improve peak power, torque, and velocity during walking.

Research has led to an ankle-foot prosthesis that better mimics the biomechanics of the normal limb during walking. By using a controlled dorsiflexion spring supplemented with additional energy, the patient can add power to the joint during plantar flexion. Sensors and microprocessors allow stiffness to change and joint position to be controlled within each phase of the gait. The current system has four primary mechanical elements: a motor, transmission, series springs, and leaf-spring foot. Figure 7, A, shows a prototype ankle-foot prosthesis that required connection to a computer. The most recent model, shown in Figure 7, B, has microprocessors and a self-contained battery pack, and it weighs only 3.8 lb. The patient uses a graphic interface to select both the spring stiffness and the power generated during specific phases of gait. Pilot studies found that the system improves shock absorption during heel strike and allows a relatively smooth transition from controlled plantar flexion to controlled dorsiflexion. This system also appears to allow a more natural gait than a conventional passive prosthesis.⁵³

Neurotechnology

The possibility of linkages between a robotic prosthesis and nerve tissue has emerged with advances in microelectronics and the understanding of neural plasticity. Mathematical algorithms can be used in conjunction with microelectronic sensors to allow complex patterns of neural activity to be translated into control outputs for a prosthetic device. The technology is based on neural spiking, a source of information-rich, rapid, and complex control signals from the nervous system, which can be decoded

and transformed into movement commands. The ability to read and translate these brain wave patterns has led to the emergence of closed-loop neuromotor prosthesis (NMP) technology. NMP research combines the disciplines of biomedicine, neuroscience, mathematics, computer science, and engineering to develop bidirectional interaction between the human nervous system and external devices. The application of NMP technology has the potential to restore lost neurologic function and provide relatively precise control of physical devices, including prosthetic limbs and semi-autonomous robots.

The NMP system consists of a platform the size of a match head, with 100 thread-thin electrodes that barely penetrate the surface of the motor cortex (from which commands to move the hand emanate; Figure 8). The pattern of neuronal signals is decoded by a computer and transformed into the motion of a cursor on a computer monitor. The user can move the computer mouse by thinking. This neural

command signal has been used by patients with tetraplegia to control computer software or a television remote control device.^{54,55}

Current research is focused on developing advanced NMP technology with integrated microscale signal processors, innovative broadband optical telemetry and powering, and miniaturized processors. The long-term goal is to create a closed-loop system that would provide a feedback signal from the effector to the brain. Research also is underway to develop a fully implantable wireless multi-neuron sensor that could be used as a platform for whole-body prosthetic networking through cortical interfaces. These technologies ultimately may enable direct brain control of an artificial limb or paralyzed muscles.⁵⁶

Regenerative Medicine

Research in regenerative medicine focuses on the use of engineered biologic tissue to restore function lost to trauma or disease. Tissue-engineering strategies use a combination of cell-based approaches in-

cluding delivery of the growth-factor proteins that guide the differentiation of stem cells into mature cells capable of forming cartilage, bone, and nerve. In addition, structural biomaterials using nanotechnology are being developed.

Synovial fibroblasts for enriching cartilage repair in a pig model are produced by harvesting synovial membrane, enzymatically digesting it, and isolating the primary synovial cells. The isolate consists of mesenchymal stem cells and synovial fibroblast stem cells, which are separated as shown in Figure 9; the fibroblast

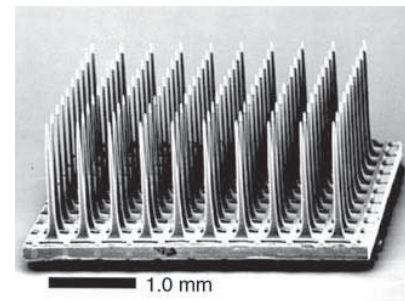


Figure 8 Match head-size NMP platform with 100 thread-thin electrodes.

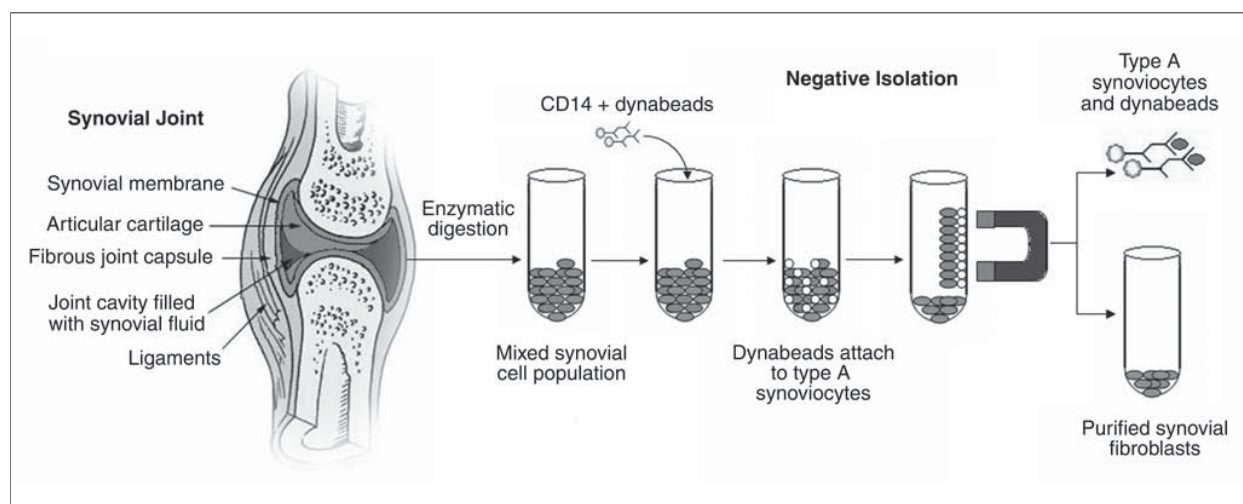


Figure 9 Enrichment of synovial fibroblasts for cartilage repair can be produced by harvesting synovial membrane, enzymatically digesting it, and isolating the primary synovial cells.

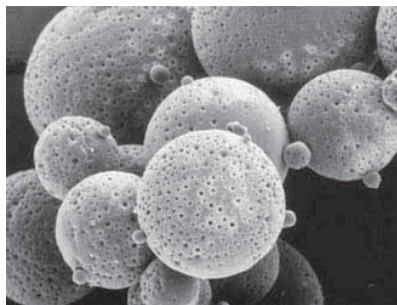


Figure 10 Bioerodable polymer microspheres made of polylactic or polyglycolic acids become part of a scaffold that supports and enhances cell growth.

stem cell line is differentiated into cartilage cells by exposure to specific sequences of growth factors. Fibroblast growth factor-2, transforming growth factor- β -1, and insulinlike growth factor-1 are released to mimic the developmental sequences for proliferation, differentiation, and cartilage matrix synthesis. These sequencing growth factors can be encapsulated into bioerodable polymer microspheres with greater than 90% bioactivity. The microspheres are made of polylactic or polyglycolic acids and become part of a scaffold that supports and enhances cell growth (Figure 10).

Nanomaterials, with one dimension less than 100 nm, have unique, tailorable surface energy properties that control the cell interactions leading to tissue growth and repair. Nanostructured materials hold promise for many tissue engineering applications, including the manipulation of traditional implant materials so they will possess biologically inspired nanometer surface features that can increase tissue growth.

Tissue engineering and biomaterials are combined in transcuteaneous osseointegrated device research. Direct attachment of the prosthesis to bone could allow a user to experi-

ence enhanced feedback, called osseoperception, because contact through the body would not be buffered by the skin-muscle interface. Pain could be decreased by avoiding direct skin contact and pressure. However, breakdown of the skin-prosthesis interface can lead to infection and metal corrosion, and this difficulty must be resolved before an effective osseointegrated device can be developed. Research continues into the development of an environmental seal that will integrate the epidermis and dermis with the metal implant by promoting adhesion or growth into a porous prosthetic surface.

Rehabilitation

The application of advanced technologies to rehabilitation of a patient's physical and emotional injury requires a holistic approach. The use of virtual immersive environments and motion analysis is being researched. Virtual reality and motion analysis can be integrated to explore the patient's reaction to stress, simulate a vocational environment, or enhance high-performance training (especially as related to spatial navigation and mobility). Virtual reality can be used to diagnose and treat physical and emotional injury through patient exposure to challenging visual, auditory, vestibular, tactile, and other sensory experiences in a safe, structured setting. In particular, posttraumatic stress disorder can be diagnosed and treated using virtual reality immersive environments. These virtual reality systems are designed to re-create an experience representative of combat the components include a computer-based program; a head-mounted display or high-resolution wall display with three-dimensional spatial-audio head-and-limb tracking systems; a

vibration platform; and a scent machine. Advanced feedback using wireless sensors can measure psychophysiological arousal following acute stress.

New tools are being developed to measure functional outcomes and assess the effectiveness of current interventions in clinical practice. For patients with a lower extremity amputation and an advanced prosthesis, these assessment tools also allow quality-of-life and mobility testing. Self-reporting and physical performance testing are being used to refine the ability to measure improved physical function.

The Status of War-Related Extremity Injury Research

Modern body armor, forward placement of surgical resources, rapid movement of patients from the point of injury to medical care, and a robust medical evacuation system capable of providing intensive care are being used in the current Iraq and Afghanistan conflicts. As a result, the likelihood that a service member will survive a battlefield injury is greater than in any other war in history. The reconstructive challenges also are unlike those encountered in earlier wars.

The American Academy of Orthopaedic Surgeons (AAOS), the Orthopaedic Trauma Association, and the Society of Military Orthopaedic Surgeons recognized that knowledge of civilian blunt trauma and low-velocity gunshot wounds cannot be simply extrapolated to combat trauma produced by explosive munitions and high-velocity bullets. In response, AAOS organized a series of symposia on extremity war injuries (EWI). The first EWI symposium, "State of the Art and Future Directions," was held in 2006 and summarized in a supple-

ment to *Journal of the American Academy of Orthopaedic Surgeons*.⁵⁷ Symposium sessions dealt with prehospital care and patient transportation related to extremity injury, wound care, musculoskeletal infection, stabilization of long-bone injury, treatment of segmental bone defects, and post-amputation care. The organizers recommended establishment of a joint military and civilian advisory board as well as improvements in pre-deployment training for the treatment of extremity injuries. Research objectives and priorities were established for improving the clinical care of wounded service members (Table 1).

The 2007 EWI symposium primarily dealt with issues related to the battlefield care of extremity injury and its effect on functional outcome. Best practice guidelines were established as a result of the meeting. The 2008 symposium focused on definitive care and attempted to identify the available evidence for the treatment of complex conditions, including massive bone loss, soft-tissue defect, and heterotopic ossification.

Congress established the Orthopaedic Trauma Research Program (OTRP) largely because of the efforts of AAOS and the high visibility of the EWI symposia. The OTRP is intended to complement, expand, and broaden the orthopaedic trauma research funded by the US Department of Defense, the National Institutes of Health, and private industry.⁵⁸ This program, which funds grants for up to 5 years, is run by the US Army Institute of Surgical Research to advance military and civilian research into treatments, products, and guidelines for the care of battlefield-injured patients. The OTRP research priorities closely resemble those established during the

Table 1
EWI Research Priorities

Reliable data collection system
Treatment timing
Débridement techniques
Patient transport
Wound coverage
Antibiotic treatment
Treatment management of segmental bone defects
Development of an animal model to simulate blast injury
Postamputation issues
Treatment and prevention of heterotopic ossification

first EWI symposium (Table 2). The number of grant proposals submitted to OTRP grew from 60 in 2006 to 96 in 2007 (J. Wenke, US Army Institute of Surgical Research, personal communication, 2008). However, the program is limited by its level of funding by the Department of Defense, which fell from \$7.5 million in fiscal year 2006 to \$6.8 million in 2007 and \$4.9 million in 2008.^{57,59}

Summary

The care of patients who sustain orthopaedic war injuries continues to evolve. New techniques for the fixation of open, comminuted, battlefield fractures having large zones of injury and soft-tissue loss are being developed. Recent advances in surgery for brachial plexus injuries have improved the previously poor prognosis for those sustaining combat-related brachial plexus wounds. The use of free-functioning muscle transfers and novel nerve transfers, as well as an improved understanding of nerve physiology, has improved the outcomes of reconstruction. Advances in restorative and regenerative medicine include the development of biomimetic prostheses, optimization of the human-prosthesis inter-

Table 2
OTRP-Funded Research Topics

Healing of segmental bone defects
Wound infection
Prevention of heterotopic ossification
Healing of massive soft-tissue defects
Tissue viability assessment and technologies for wound irrigation and débridement
Translation of research into practice

face with neurocontrol devices, improved osseointegrated fixation, and lengthening of short residual limbs. Lessons learned from earlier conflicts have been instrumental in shaping important aspects of current orthopaedic practice, and the current war will also stimulate advances in the treatment of high-energy, complex musculoskeletal trauma.

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