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Military regenerative medicine

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Amid the rising toll of war-associated deaths and injuries and escalating conflicts between countries, there is a strong need to manage complex battlefield injuries by preventing further deterioration and accelerating the repair of damaged tissues. Global military powers, including the USA and China, have established scientific facilities for dedicated research into military regenerative medicine. However, there remains a gap, as most reported medical devices created for tissue repair are unsuitable for use on battlefields. In this perspective, we argue why *now* is the golden time for countries to invest in military regenerative medicine, and we propose the use of RIPE (Restorative, Individualized, Portable and Emergency) criteria to optimize technologies for tackling battlefield injuries, including rapid hemostasis, immobilization, tissue repair, and functional reconstruction. Similar to technologies such as blood plasma transfusion and portable ultrasound, which were originally developed through military investment and later found highly valuable for civilian medical use, timely investment in military regenerative medicine, as we argue, will have a positive spillover impact on public healthcare programs in the future.

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Introduction

Recent conflicts across the globe have resulted in significant casualties among military personnel and civilians. The ongoing conflict between Russia and Ukraine, which began in 2022, has resulted in approximately 80 000 fatalities and 400 000 injuries among Ukrainian forces,[1] while Russian forces have experienced between 462 000 and 728 000 casualties, including both killed and wounded personnel.[2] Since October 2023, the armed conflict between Israel and Hamas-led Palestinian militant organizations has taken a heavy toll, with 49 145 deaths and 114 190 injuries, including armed combatants and civilians.[3] Significant advancements in battlefield medicine have greatly increased survival rates; however, a larger number of soldiers are returning home with life-altering disabilities.[4] Regenerative medicine is an indispensable component of military healthcare, offering innovative approaches for treating injuries with limited medical equipment and personnel on the front line.[5] Techniques such as stem-cell therapy, tissue engineering and bioprinting show great promise for restoring damaged tissues and organs.[6] While most of these approaches are administered in specialized medical facilities, significant research is underway to streamline and miniaturize these technologies for field-based deployment.[7,8] In the future, it is expected that advanced portable systems and rapid deployment strategies will enable some of these regenerative therapies to be applied on the battlefield or as part of early post-evacuation care. By improving the immediacy and efficacy of medical interventions in challenging environments, regenerative medicine has the potential to improve survival rates and reduce the incidence of permanent disability in injured soldiers.[9] From this perspective, we believe that although significant progress has been made, most existing strategies still overlook the unique limitations of battlefield deployment. Our view is that military regenerative medicine must go beyond the incremental adaptation of civilian technology and adopt forward-looking standards tailored to combat realities.

The application of regenerative medicine in the military field can be divided into two functional modules: frontline emergency care and rear reconstruction. Frontline first aid aims to rapidly stabilize the physiological state of the wounded through short-term life support and primary regeneration techniques,[10] while rear reconstruction is dedicated to restoring the physiological function and combat capability of soldiers through the deep regeneration and repair of tissues and organs, providing medical protection and allowing their return to duty.[11] These two modules have seen substantial progress, with battlefield hemostatic biomaterials, antibacterial dressings, and portable medical devices advancing frontline emergency care.[12,13] However, frontline emergency care still faces challenges, including material stability, operational simplicity, and cost effectiveness.

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Meanwhile, engineering grafts, bioprinting technology, and advanced scaffolds show hope for off-site reconstruction.[14]

Internationally, numerous research institutions are actively engaged in regenerative medicine research specifically tailored to military medicine, and they have benefitted from significant financial support from defense organizations. In the United States, the Armed Forces Institute of Regenerative Medicine (AFIRM), led by the Wake Forest Institute for Regenerative Medicine (WFIRM), is a prominent example, receiving $40 million in funding from the Defense Health Agency in 2024.[15] The McGowan Institute for Regenerative Medicine, led by the University of Pittsburgh, received a $22 million grant from the Defense Advanced Research Projects Agency (DARPA) in 2020 to develop effective methods for regenerating muscle tissue.[16] The UK Defence Science and Technology Laboratory held a competition called 'Regenerative Medicine at the Front Line' in 2018, with funding of £500 000 for each valuable project.[17]

Identifying specific information about investments into regenerative medicine by military institutions in some countries is not trivial due to the sensitive nature of military budgets and strategic research. However, multiple news reports indicate that the defense organizations of multiple countries are pursuing advancements in regenerative medicine. Due to the sensitive information involved in battlefield casualty data and military research funding, the information cited in this study mostly comes from government reports, official websites, and authoritative media reports (see Fig. 1 and Table 1). We acknowledge their limitations, but these sources are currently the most reliable information publicly available. The Trauma Repair and Tissue Regeneration Research Center within the Medical Innovation Research Department at the General Hospital of the Chinese People's Liberation Army has achieved breakthroughs in challenging areas such as sepsis and chronic refractory wounds to reduce the mortality and disability rates associated with war-related trauma.[18] Alexander Sergeyev, President of the Russian Academy of Sciences, asserted that regenerative medicine has significant importance for military applications and that the Russian Academy of Military Medical Sciences is actively advancing this field by developing techniques for organ printing at the cellular level.[19] Similarly, the Institute of Biomedical Research of the Armed Forces (IRBA) attached to the French Military Health Service (Service de Santé des Armées, SSA) is dedicated to research into regenerative and translational medicine.[20]

Regenerative military medicine has distinct requirements

While regenerative medicine in traditional healthcare also focuses on restoring function and repairing damaged tissues, the unique challenges of battlefield conditions necessitate a distinct approach. These differences arise from a stark contrast between civilian and military medical environments, including the urgency of the medical situation; resource limitations in combat zones; and a wider range of injuries, from minor to life-threatening conditions; however, in civilian environments controlled long-term care is more readily available. Here, we propose the use of the RIPE strategy (Restorative, Individualized, Portable and Emergency) to evaluate the suitability of technologies for use in military regenerative medicine. Unlike traditional checklists, RIPE not only exists as a descriptive framework but also serves as a guiding principle for innovation. For example, "Restorative" emphasizes rapid functional recovery rather than simple long-term repair; "Portable" emphasizes operability and logistics feasibility in extreme environments; and "Emergency" focuses on the immediacy of intervention rather than the complexity of treatment.

However, balancing these four dimensions simultaneously still leads to many challenges, including biological stability, the miniaturization of complex therapies, and cost-effective large-scale production, all of which are key directions that urgently need to be addressed in future research. In addition, logistical challenges remain critical bottlenecks, including dependence on complex and bulky infrastructure, as well as limitations related to low-temperature storage, which significantly hinder the feasibility of frontline applications. To address these challenges, feasible solutions include integrating multifunctional biomaterials to improve biological stability, developing modular and miniaturized treatment platforms for on-site deployment, and adopting scalable biomanufacturing technologies to reduce costs. These directions not only highlight the feasibility of overcoming current obstacles but also provide specific pathways for translating regenerative medicine into battlefield applications.

Fig. 2 presents the RIPE framework, showing how the Restorative, Individualized, Portable, and Emergency components function as an integrated system to guide regenerative strategies in battlefield contexts. This also highlights the contrast with civilian healthcare, underscoring the emphasis on rapid, portable, and mission-oriented solutions under combat conditions. At the same time, it should be pointed out that regenerative military medicine not only relies on biomaterials but also requires multidimensional methods such as cell therapy, genetic and molecular interventions, tissue engineering, and biomanufacturing. This article focuses on biomaterials as its core, but other strategies are also key components in promoting the development of this field.

Restorative

Military regenerative medicine differs from civilian regenerative medicine in that it requires the injured party to regain mobility within a short period of time. As such, researchers are developing technologies to repair blood vessels, nerves, and muscles simultaneously, and these technologies need to be able to deal with complex injuries on the battlefield, such as blast injuries and wounds contaminated with heavy metals, radionuclides, phosphorus, and metal fragments, which are rare in civilian cases.

Individualized

Unlike the highly individualized treatments emphasized in civilian regenerative medicine, this aspect is often difficult

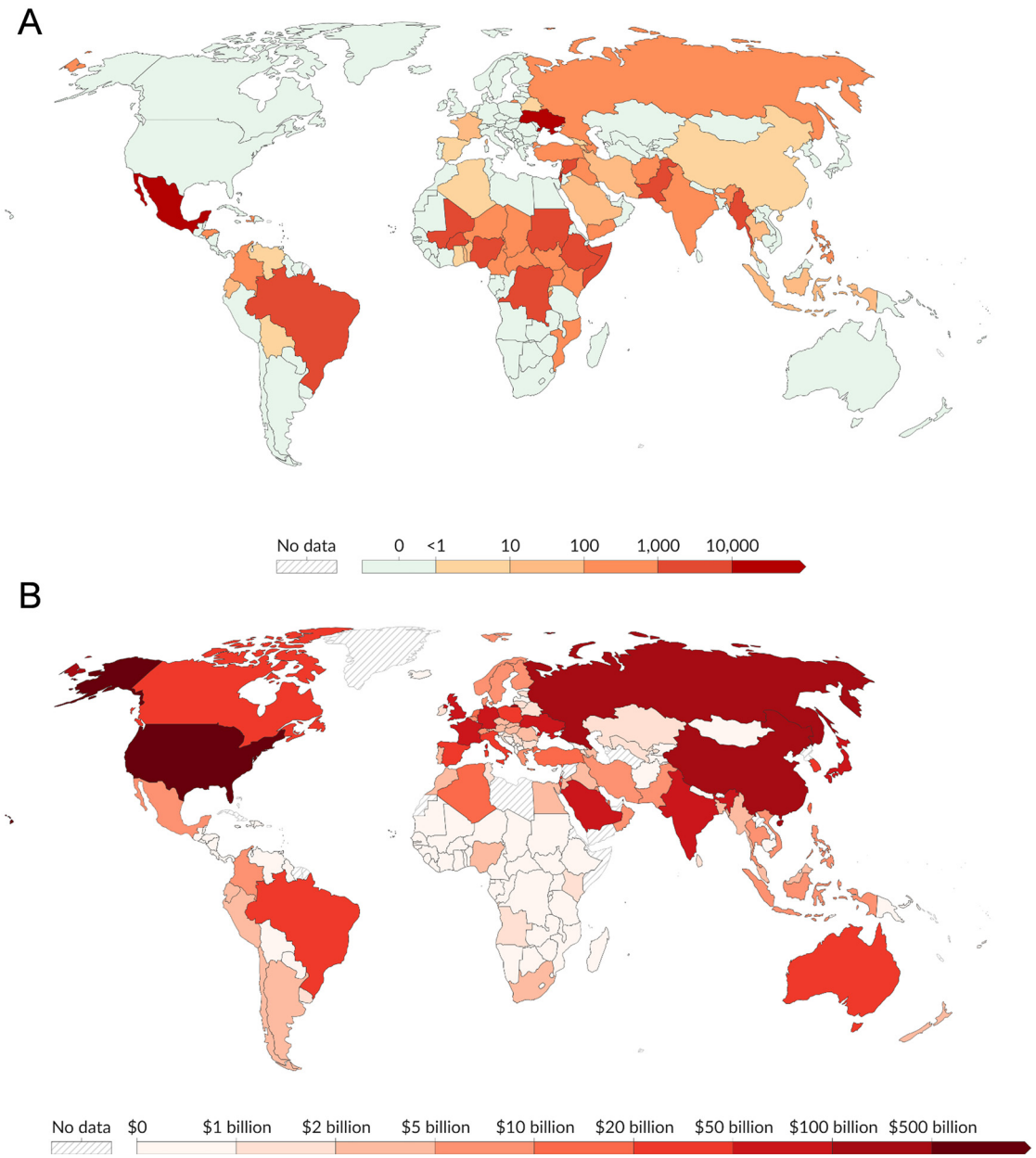

Fig. 1 Relevant military information in 2023. (A) The number of deaths due to armed conflict in 2023. (B) Military expenditure in 2023, including military and civilian personnel, operations and maintenance, procurement, military research and development, infrastructure and assistance. Data obtained from https://ourworldindata.org/military-personnel-spending and https://ourworldindata.org/war-and-peace.

and costly to achieve in frontline emergencies. Military regenerative medicine emphasizes a strategy of stratification and task orientation, which classifies and optimizes plans based on the trauma type, battlefield environment, and combat tasks to achieve a balance between feasibility and adaptability, in order to meet the rapid response needs of battlefield environments.

Portable

Battlefield first aid often occurs in harsh environments, and portability ensures that regenerative medicine can be carried out in a timely manner. This necessitates medicines that are lightweight and that can be ideally stored at room temperature with extended shelf lives.

Emergency

Military regenerative medicine requires emergency treatment of the wounded, rapid hemostasis, anti-infection treatment and stabilization of injuries on the frontline. Methods for simple tissue repair in the field are also being explored to minimize complications and ensure the safety of the wounded.

Table 1 List of institutions engaged in military regenerative medicine research

Country	Institution	Location	Research focus	Latest budget (USD, millions)
USA	Armed Forces Institute of Regenerative Medicine (AFIRM): • Wake Forest Institute for Regenerative Medicine (WFIRM)[15]	North Carolina	• Craniofacial regeneration • Extremity regeneration • Genitourinary/lower abdomen • Skin and wound healing • On-demand blood • Cellular therapies for trauma	2024–2028: 40
USA	McGowan Institute for Regenerative Medicine[16]	Pittsburgh	Regrowing muscle tissue after combat injuries	2020–2024: 22
USA	•Uniformed Services University (USU) •Walter Reed National Military Medical Center (WRNMMC) •National Institutes of Health (NIH)[21]	Maryland	Regenerative medicine for traumatic brain injury (TBI)	2024–2029: 69.92
United Kingdom	Defence Science and Technology Laboratory (DSTL) - Defence and Security Accelerator[22]	Wiltshire	• Bioengineered blood components • Preservation and regeneration of soft tissues using biophysical approaches	Jan-Mar 2024: 48 Jul-Sep 2024: 30
United Kingdom	National Center for Sports & Exercise Medicine[23]	East Midlands	Technologies to advance musculoskeletal injury prevention, rehabilitation and return to work	Undisclosed
France	Defense Innovation Agency	Paris	• Hydrogels to restore volumetric muscle loss • Laser-assisted bioprinting of muscle tissues	Undisclosed
People's Republic of China	Chinese PLA General Hospital[18]	Beijing	Trauma repair and tissue regeneration	Undisclosed

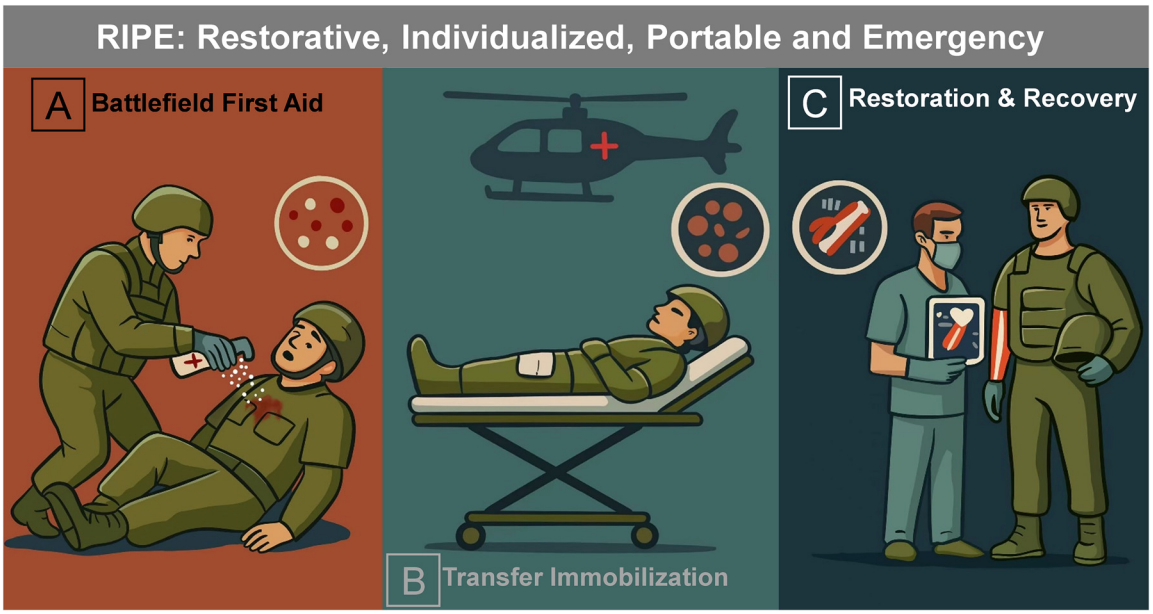

Fig. 2 A schematic diagram showing how biomaterials are being used in regenerative military medicine. (A) On-site hemorrhage control and life-saving interventions immediately after injury. (B) The initial immobilization and safe transport of wounded soldiers to prevent secondary injuries. (C) Individualized rehabilitation and functional restoration to accelerate return to service.

Biomaterials for regenerative military medicine

The word "biomaterial" is defined as a material that interacts with biological systems, including changing its own structure or inducing tissue transformation, for any type of therapeutic or diagnostic activity.[24] Regenerative biomaterials can serve not only as structural supports and delivery carriers but also as regulators of molecular signaling and cellular behavior, guiding tissue regeneration even in the absence of active drugs or cells.[25] In addition, these bioma-

terials can reduce the risk of infection and promote a more favorable healing environment by adsorbing and neutralizing pollutants such as metal ions[26] and microorganisms.[27,28] Military biomaterials should facilitate effective treatment during delayed evacuation and promote tissue regeneration upon transfer to advanced care facilities.[29] Here, we summarize the different ways in which biomaterials have or can be applied in regenerative military medicine. We note that the majority of the publicly available scientific literature on military regenerative medicine comes from the United States, likely reflecting both their leading role in the field and a higher degree of transparency.

Hemostasis

Hemorrhage, especially incompressible hemorrhage in the visceral and junctional regions, remains the leading cause of preventable death on the battlefield.[30] In the recent Russia-Ukraine conflict, vascular injuries and the widespread, sometimes inappropriate, use of tourniquets have highlighted both the effectiveness and risks of current frontline practices.[31,32] This underscores the urgent demand for hemostatic strategies that are rapid, reliable, and safe.

Ideal battlefield agents are expected to achieve rapid hemostasis, maintain effectiveness for hours, and be portable, cost-effective, biocompatible, and easily removable without residue.[33] Current TCCC guidelines recommend kaolin-based Combat Gauze as a first-line hemostatic dressing, supported by clinical validation in both the U.S. and Israel Defense Forces studies.[34,35] Other approved options include chitosan-based dressings such as Celox Gauze and ChitoGauze, as well as novel mechanical or bioengineered devices like X-Stat mini-sponges and the iTClamp, which address junctional and cavity bleeding with distinctive mechanisms.[36–39] Notably, the 2024 TCCC guidelines did not introduce new products, reflecting both the maturity and limitations of currently used solutions.[40]

Emerging bioengineered materials aim to overcome these constraints by integrating strong adhesion, antimicrobial capacity, and compatibility with contaminated battlefield environments. Examples include DNA hydrogels, water-responsive shrinkable films, porous sponges, cryogels, and polysaccharide- or hydrogel-based adhesives with antibacterial properties.[41–48] Although these biomaterials are currently in the prototype phase, Public Law No. 115-92 authorizes the FDA to accelerate the approval of defense-related medical products[49] so they may be rapidly deployed on the battlefield.

While these advanced hemostatic products are primarily used to rapidly control bleeding in trauma situations, hydrogels and chitosan can also promote wound healing. As an example, the DGA (French General Directorate of Armaments) funded a study of chitosan-based physical hydrogels for promoting skin regeneration after third-degree burns, where the new tissue closely resembles natural skin, especially in its aesthetic aspects, and shows great flexibility.[50]

Transfer immobilization

Immobilization of fractured parts of the body during casualty transport reduces further damage caused by movement, prevents secondary tissue and vascular damage, and reduces the risk of fat embolisms.[51] The U.S. Army TCCC Combat Lifesaver course recommends that burns, fractures, and other soft-tissue injuries should be treated appropriately with splints and dressings before evacuating the wounded. A range of biomaterials has been developed to address challenges relating to immobilization during transfer.

For soft-tissue injuries, immobilization materials should remain flexible to accommodate muscle contraction and skin dynamics, while reducing secondary injury. Advances include collagen-based dressings with long-acting analgesic effects for burn wounds,[52] as well as polyvinyl alcohol fillers designed to temporarily stabilize volumetric muscle loss.[53]

In contrast, fractures and hard-tissue injuries require stronger structural support. Emerging approaches include bioinspired splints mimicking insect-wing mechanics[54] and rapidly curing foams that form lightweight external fixation shells, which can also be loaded with therapeutic agents. Compared with traditional splints, these advanced biomaterials provide better conformity and mechanical compatibility, facilitating safer casualty transport. Nonetheless, achieving organ and tissue regeneration after transfer to medical facilities remains a major challenge.

Tissue regeneration

The combination of modern protective equipment and battlefield medicine has led to a marked increase in casualty survival rates, but more powerful weapons have also led to correspondingly more severe casualties that become permanent disabilities. During the Russia-Ukraine conflict, 89% of the wounded in the Ukrainian army had limb injuries, of which 76% had bone defects. The number of amputees increased significantly due to the war.[55] Regenerating the limbs and organs of wounded soldiers, including bones and muscles, is therefore a priority to protect the long-term health of war veterans.

In bone and cartilage regeneration, biomimetic collagen scaffolds provide microenvironments that mimic natural bone and stimulate host cell migration and growth,[56] while protein hydrogel scaffolds with elastin-based entanglements show mechanical properties similar to cartilage, enabling *in vivo* cartilage regeneration.[57] Stem-cell-loaded hydrogels, composite scaffolds combining TyrPC and TCP, and next-generation products such as AMP2 also demonstrate potential to promote bone healing when large defects are involved.[58–62] These technologies often rely on stem-cell preparation, cold-chain preservation, and professional surgical teams, so their application in frontline emergency environments is limited, and they are more suitable for implementation after transport to rear medical facilities.

For soft-tissue and muscle regeneration, 3D bioprinting is a leading approach, allowing the creation of layered multicellu-

lar tissues for skin, muscle, and nerve repair in a personalized manner.[63–67] *In situ* bioprinting and portable devices further extend this technology to battlefield emergencies.[7,68–70] Although portable *in situ* bioprinting has possibilities for frontline applications, it still requires specially trained technicians and sufficient logistical support, resulting in operational and logistical limitations when it comes to large-scale trauma treatment. Other biomaterial strategies include microneedle platforms for immunomodulation and protein extraction to promote wound healing,[71,72] porous scaffolds that integrate into host tissue with minimal inflammation,[73] and shape-memory polymers or oxygen-generating systems to address volumetric muscle loss and ischemia.[74,75] Innovative organ repair strategies, such as micro-liver generation in lymph nodes and exosome-based therapies for lung injuries, have also been explored.[76,77] This type of organ repair solution is currently mainly in the experimental or exploratory stage in rear hospitals, and suitable conditions do not exist for its rapid application on the front line.

Peripheral nerve regeneration remains especially challenging. Conduits, nerve tape devices, and biomimetic hydrogels have been proposed to guide axonal growth and improve functional recovery after battlefield nerve injuries.[78–80] Gene delivery techniques, such as tissue nano-transfection (TNT), are being investigated to accelerate repair.[81] Gene delivery technologies such as TNT rely on high-precision equipment and safe environments, and they are therefore mainly limited to rear research and clinical trials. Frontline personnel are more likely to rely on simplified catheters or scaffolds for initial nerve repair. Vascularized constructs are equally critical: bioengineered human acellular vessels (HAVs) have already been applied in combat-related vascular trauma with promising potency outcomes in clinical follow-ups.[82,83] HAVs, as ready-made implantable blood vessels, are closer to being a solution that can be quickly deployed on the front line, but this approach still requires certain surgical skills and sterile operating conditions.

Overall, while substantial progress has been achieved, translating regenerative strategies into deployable solutions for battlefield medicine requires overcoming logistical, manufacturing, and ethical challenges, aligning with the RIPE framework.

Outlook

With the rise in conflicts and more powerful weapons, soldiers have faced an increasing risk of injuries from small-caliber guns, improvised explosive devices (IEDs), and short-range rockets in low-intensity military conflicts in recent years. While there are high survival rates among soldiers, they often suffer from injuries and permanent disabilities. One recent example is Russia's use of long-range heavy weapons in the Russia-Ukraine conflict, resulting in rising numbers of Ukrainian soldiers suffering from devastating injuries, with casualty rates for Ukrainian soldiers deployed to the theater of operations being roughly five times those of U.S. forces.[84] A large proportion of Ukrainian casualties involve complex traumatic injuries, including fractures and soft-tissue, muscle, joint, and nerve injuries, which accounted for more than two-thirds of all casualties, most of which required amputation. In April 2023, a rehabilitation center called "the Superhumans Center" was set up in Lviv, where 400 prosthetic limbs were fitted to more than 300 injured people using bionic 3D printing technology developed by the British company, Open Bionics.[85] With the complexity of modern forms of warfare and the diversity of battlefield injuries, the need for battlefield treatment has expanded from pure first aid to the field of regenerative medicine.

The U.S. Army Battlefield Injury Management Technology Development Workshop discussed how bioengineering could improve soldiers' survivability in high-intensity conflicts by 2035. Experts identified emergency treatment at the point of injury, interventional treatment during evacuation, and the restoration of intact limb form and function in a rear advanced care facility as the three goals of battlefield treatment, and recommended the use of biomaterials for the regeneration and repair of soft-tissue wounds, muscle loss, and organ defects.[29] Therefore, the direction of military regenerative medicine should be towards emergency treatment at the point of injury, life support *en route*, and eventual regeneration of limbs and organs with the help of bioengineering technology. When evaluating the effectiveness and applicability of regenerative medicine products in the context of military applications, this can be done in terms of the RIPE criteria, which not only reflect the specificity of military needs but also provide a clear direction for future research and product development. Currently, most research into regenerative medicine is limited to the lab scale or, at most, clinical testing, with poor adaptation for use on battlefields where conditions are harsher. It is also worth highlighting that the military has been receptive to adopting novel healing technologies and prefers to work with companies and research institutions, which already have proofs of concept in preclinical animal settings for quicker translational use.

Although military and civilian regenerative medicine share many principles, they differ fundamentally in their goals and contexts. Military regenerative medicine is intended for rapid, on-the-spot application under harsh and unpredictable conditions. From our perspective, the key to future development lies in balancing cutting-edge technology with on-site deployment, that is, pursuing therapies that are both scientifically innovative and suitable for practical combat environments. In addition, frontline medical environments generally lack professionally trained personnel, posing additional challenges for the deployment of regenerative medicine products. Therefore, there is an urgent need to develop simplified, portable, and non-professionally operated solutions.

The development of military regenerative medicine not only involves advancements in technology but also the advocacy of a new culture centered on human beings, an ideal that contrasts with the realities of military conflict, where lives are routinely at risk. Soldiers are a vital asset, and their health should

be maintained not only through timely repair of battlefield injuries but also *via* preventive health-management strategies and long-term post-war care. It is also worth noting that this technology has potential dual-use concerns, and its practical application may involve trade-offs in resource allocation. Contradictions may arise between military R&D goals and medical ethics, making it necessary to carefully evaluate the application value under ethical scrutiny. Thoroughly addressing these issues can help promote technological progress while ensuring social and moral acceptability. Ultimately, the goal of military regenerative medicine is to transcend battlefield needs, serve a wider range of civilians, and contribute to world peace. Similar to technologies such as portable ultrasound and plasma transfusion, which were initially invented for military use but later found broad civilian applications, greater investment in regenerative military medicine is likely to generate positive spillover effects for treating diverse medical conditions outside of military settings.

Conflicts of interest

There is no conflict of interest to declare.

Data availability

There is no available data as this is a perspective article.

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