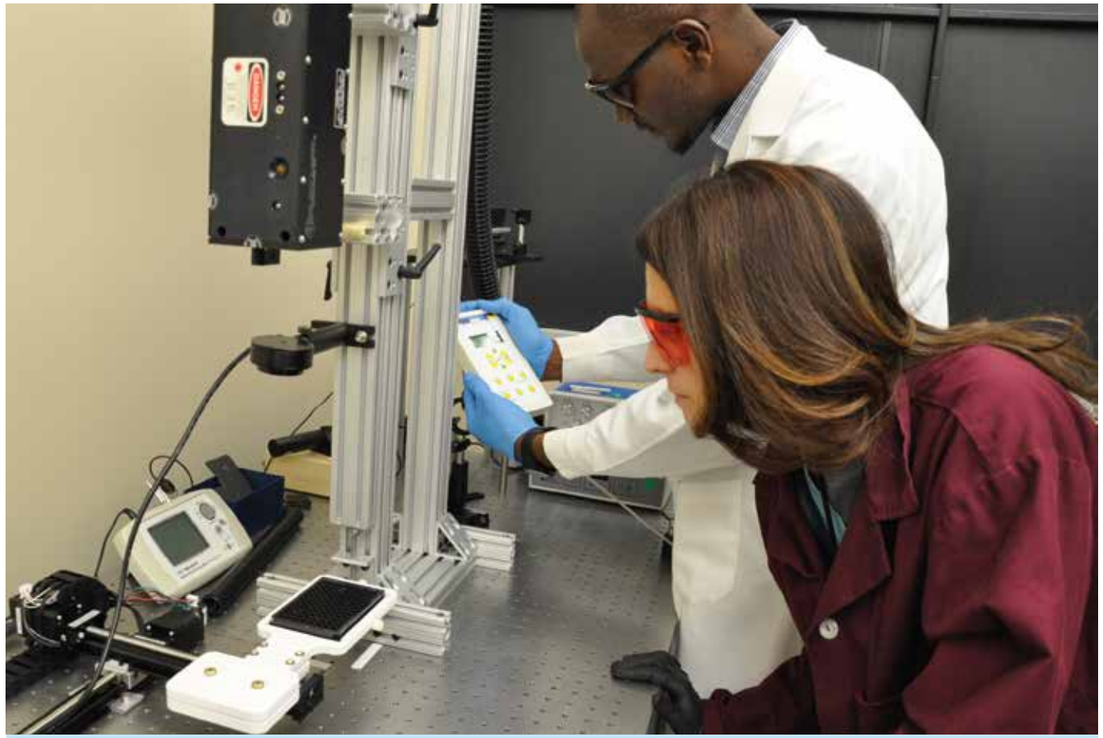
Naval Medical Research Reaches New Level by Being Interdisciplinary

By Dr. John Simecek, Cmdr. David Leal, USN, and Capt. Jonathan Stahl, USN



Dr. Nancy Millenbaugh (front) and Dr. Dickson Kirui (back) investigate how pulsed laser irradiation would maximize bacterial biofilm destruction. Photo by Flisa Stevenson.

The military and civilian medical research communities are acknowledging that even their best individual efforts cannot fully address today's complex and interconnected problems. The research process of lone scientists or small teams solving medical problems with a single-pronged approach is incongruous given our advanced and ever-evolving understanding of the disease process. Nowhere has the need for a change to this paradigm been more evident than in the dynamic realm of military medical research.

Interservice Collaborations

Battlefield injuries often present special challenges to the healing process and demand that relevant research no longer proceeds as a compartmentalized effort. Being located on Joint Base San Antonio, Texas, where many injured warfighters receive care at the San Antonio Military Medical Center, means Navy researchers see first-hand the need for a mindset change—and they have developed a new model for scientific excellence in response. Strategic planning begets thoughtful scientific hiring to create interdisciplinary teams, which are designed to "attack" a problem from numerous pathways. This new approach also encourages scientists to think imaginatively and network with other researchers to form collaborations and leverage resources. Internal collaborations, interservice collaborations, and fiscal efficiency characterize the Naval Medical Research Unit San Antonio (NAMRU-SA) approach to the business of research, and are key reasons why sponsors are excited about their capabilities and what they are accomplishing.

NAMRU-SA is one of eight subordinate research commands in the global network of laboratories operating under the Naval Medical Research Center, Silver Spring, Maryland. To improve medical outcomes related to NAMRU-SA's mission and capabilities in combat casualty care and craniofacial health and restorative medicine, this collaborative approach not only is necessary, it also makes great scientific sense. NAMRU-SA is reengineering wound healing, infection control, and dental treatments with a diverse team of scientists and clinicians from across the United States, encompassing molecular and cellular biologists, biomedical engineers, microbiologists, immunologists, physiologists, and healthcare specialists including surgeons and dentists.

Reengineering Wound Healing

NAMRU-SA's purposeful integration of scientific disciplines and a value-conscious approach to research provides an interdisciplinary view of the problem under investigation and leads to cutting-edge solutions and product-driven research. For example, recent statistics reveal that approximately 65 percent of battlefield injuries are related to head, face, or neck trauma and that antibiotic-resistant infections in these areas increase death, illness, and direct costs of treatment by 30 to 100 percent. Improved craniofacial wound management and infection control is essential for decreased morbidity and mortality in Sailors and Marines, controlling healthcare costs, and improving service members' quality of life in terms of both function and esthetics. To that end, NAMRU-SA launched a collaborative initiative involving biomedical engineers, cell biologists, immunologists, mechanical engineers, biomaterials experts, and dentists. The team developed a novel approach to creating biocompatible nanofibers to enhance wound treatment, especially wounds to the craniofacial region. The biocompatible nanofiber scaffold is designed to promote tissue repair by forming a surface that mimics the natural cellular environment while simultaneously releasing bioactive molecules to accelerate healing and potentially minimize the formation of scar tissue.

To synthesize the nanofibers, NAMRU-SA's biomedical engineering team constructed a custom electrospinning apparatus. The device produces the nanofibers by spraying a polymer solution through a spinneret under an applied electric field. The electric field induces a charge in the polymer solution, leading to the elongation of droplets into a thin, continuous fiber of submicron diameter. The nanofiber composition and structure, including spray pattern and strand size, are readily controlled during the electrospinning process, enabling the user to tailor nanofibers to a wide variety of biomedical applications.

Once the process is optimized, scientists plan to integrate nanofibers into coatings for use on medical materials to improve treatment for craniofacial injuries. These nanofibers can deliver bioactive agents at a sustained rate and can be assembled into a 3D architecture to guide cell behavior. This endeavor has led to a collaborative effort with the US Army Dental and Trauma Research Detachment to develop a novel bandage that will contain therapeutic agents to improve healing and decrease scar formation in military trauma patients.

The success of the electrospinning technology and nanofibrous scaffolding was directly attributable to the comprehensive team approach applied to the problem. Every team member brought a unique perspective and skill set to the issue and resulting end product. Industry has used a similar process to spin plastic and polyvinyl fibers into household items such as air filters, but developing a technique and accompanying device that could transform organic elements into engineered tissue, and then transport and deliver drugs to fight infection and promote proper natural healing, is complex and poses serious challenges. The absence of any one idea or perspective may have derailed the project or resulted in a less-than-optimal outcome.

The electrospinning apparatus can reliably produce nanofibrous scaffold and the fibers can be embedded with growth factors, medications, and other materials of interest. The implications of these new capabilities cannot be overstated. This technology will be increasingly used to fabricate nanofibrous scaffolds for a multitude of tissue-engineering purposes related to tissue repair or regeneration because of its cost-effectiveness, relative simplicity, and ability to scale up scaffold production. Scaffolds of various shapes and sizes can be constructed, while at the same time fiber orientation, composition (blended fibers), and dimensions can be controlled precisely. In addition, these ultrafine fibers can be woven using a variety of natural and synthetic components. Scaffolds generated by this method offer the additional advantage of being able to incorporate bioactive components such as growth factors. Growth factors can then be released in a controlled and continuous manner while the scaffold still possesses adequate mechanical properties to serve as a physical wound dressing. While development of the nanofiber technology is ongoing, these nanofiber materials offer the potential to improve patient outcomes and reduce costs associated with wound treatment.

Cmdr. David Leal (left) demonstrates the Optical Coherence Tomography (OCT) system to Capt. Denise Smith (right). The OCT is a laser device that shows dentists subtle discrepancies and cracks in a tooth that cannot be seen in a regular dental exam. Opposite, electrospinning has become a common technique in the production of polymer nanofibers; the polymer jet is being ejected towards a collector plate. Photos by Flisa Stevenson.

Infection Control that Pushes the Edge of Technology

Another example of NAMRU-SA's contemporary and integrated research approach is in the area of infection control. Bacterial wound infections are problematic for military and civilian populations around the world. Two of the major challenges for successful treatment of maxillofacial (face and mouth) wounds in particular are multidrug resistance and formation of biofilms (bacteria growing in slime-enclosed aggregates). The high level of infection in facial injuries and the difficulties encountered during extended military evacuation procedures contribute to severe soft tissue breakdown that results in delayed healing, increased scarring, scar contracture, deformities, long-term functional deficits, and difficulty with facial reconstruction.

NAMRU-SA is addressing these challenges by assembling an interdisciplinary team with expertise spanning chemistry, virology, molecular immunology, and structural biology to physics, mathematics, and nanomedicine to develop innovative therapeutic strategies as alternatives to conventional antibiotics. This pioneering team proposed a two-phased approach to solving multidrug resistance and biofilms. One arm of the research focuses on using laser-induced opto-acoustic treatment, which is pulsed laser light and energy absorbing nanomaterials to physically damage the infectious agent through generation of heat and shock waves. A major advantage of this approach is that the efficacy of the technique at eradicating pathogens would not depend upon level of antibiotic resistance, growth rate, or metabolic status. Another arm of the study involves developing compounds that can break through biofilms to enhance the activity of antibiotics and help debulk infectious lesions. The ultimate contributions of this research will be new technologies and products for improved treatment of antibiotic resistance and biofilm infections, essential for preservation of soft tissues and optimal cosmetic and functional outcomes following maxillofacial injuries.

Preventive Dental Care to the Extreme

Preventive dental care is often categorized as routine, but fractured teeth and restorations are the most commonly reported dental emergencies among military personnel.

Recent statistics from Soldiers serving in Iraq place the cost of these types of emergencies at more than $20 million a year, not accounting for degradation of unit operational capability. A large number of these emergencies occur because of a gap in current dental diagnostic technology that prevents accurate characterization of enamel cracks. Transillumination, for example, uses visible light to highlight the fracture, but visible light scatters when reflected on enamel and does not allow the clinician to determine the depth or extent of the fracture. In addition, the most basic diagnostic test, X-Ray, is quick but cannot be used to evaluate cracks unless the fracture is grossly displaced.

The disparity between requirement and capability drove NAMRU-SA's craniofacial health research team to explore various industry technologies that could be adapted and other basic technology that was suitable for modification. The team of dentists, engineers, and technicians is evaluating a technology called optical coherence tomography (OCT) that has the potential to provide significant diagnostic images that will aid dentists in evaluating enamel cracks and the need for further intervention. OCT is a laser-based system that allows one to visualize subtle discrepancies and cracks in a tooth not able to be seen during a routine dental exam. The laser uses nonionizing laser light to obtain subsurface images of translucent or semitranslucent materials at a resolution of better than 10 micrometers, and then creates an instant, clear 2D and 3D tissue images by rejecting background scatter signals or light directly reflected from the surface of interest. The most appealing features of OCT are that no special preparation of the biologic sample or subject is needed and images can be obtained in a noninvasive and nonionizing manner. These characteristics translate to a highly effective, quick, easy-to-use instrument with no damage to biologic tissue. The NAMRU-SA team is completing research with the technology by testing extracted restored and nonrestored teeth with simulated chewing stress applied by a mechanical testing device to propagate cracks. Enamel crack propagation will be evaluated using images from a Micro CT scanner and they will be compared to the images produced by the OCT. On successful evaluation and development of a diagnostic predictive model, the research team will work on a hand-held device that would be suitable for use in military dental clinics.

Science with a Purpose

With the current call for improved Sailor and Marine readiness and greater effectiveness for every dollar spent, the philosophy of efficient repurposing of existing technology

and team-driven design of functional devices is an important step forward in a research culture that is traditionally compartmentalized and can labor unnecessarily too early in the research continuum.

The command's goal is science with a purposeful strategic plan designed to approach problems from an interdisciplinary viewpoint while leveraging resources to the greatest extent possible. The NAMRU-SA vision of decreasing time from bench to battlefield is critical to ensuring relevancy, purpose, and longevity in an ever-evolving military landscape.

About the authors:

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