

Light-emitting diodes (LEDs), developed for NASA Space Shuttle plant growth experiments, are being used in the treatment of wounds.

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Medical College of Wisconsin study in conjunction with NASA:

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- The Phase I effort achieved its objective of ascertaining and demonstrating the efficacy of light therapy using LEDs, alone and in conjunction with hyperbaric oxygen, in the treatment of wounds.
- Phase II results in speeding the early phase of wound closure were particularly successful.
- Doctors at the Medical College of Wisconsin have examined how LEDs can help heal oral mucositis (severe oral sores caused by chemotherapy and radiation), diabetic skin ulcers, and serious burns. (Preventing oral mucositis improves the patients' ability to eat and drink and may also reduce the risk of infections in patients with compromised immune systems.)
- NASA LED arrays have already flown on Space Shuttle missions for studies of plant growth.
- Improved wound healing may have multiple applications, including civilian medical care, military situations, and long-term space flight.
- Phase II objectives have included the development of a tri-photon light source and human clinical trials at the Medical College of Wisconsin.
- The FDA pre-approved the procedure.
- Verification of operation in ISS environment to be determined. Wounds are slow to heal in a microgravity environment. Muscle and bone atrophy are well documented in astronauts, and various minor injuries have been reported not to heal until landing on Earth. LED therapy could keep what would be termed as minor wounds on Earth from becoming mission-catastrophic in space.
- While under contract to NASA, LEDs have been utilized as part of a cancer treatment. In Special Operations, LED arrays could be used for improved wound healing and in the treatment of problem wounds, as well as speeding de-conditioned personnel to full-duty performance.

- LED usage has been approved by the Naval Special Warfare Command.
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"The Use of NASA Light-Emitting Diode Near-Infrared (IR) Technology for Biostimulation"

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This work is supported and managed through the NASA Marshall Space Flight Center - SBIR Program. Studies on cells exposed to microgravity and hypergravity indicate that human cells need gravity to stimulate growth. As the gravitational force increases or decreases, the cell function responds in a linear fashion. This poses significant health risks for astronauts in long-term space flight. The application of light therapy with the use of NASA LEDs will significantly improve the medical care that is available to astronauts on long-term space missions. NASA LEDs stimulate the basic energy processes in the mitochondria (energy compartments) of each cell, particularly when near-infrared light is used to activate the color sensitive chemicals (chromophores, cytochrome systems) inside. Optimal LED wavelengths include 680, 730 and 880 nm and our laboratory has improved the healing of wounds in laboratory animals by using both NASA LED light and hyperbaric oxygen. Furthermore, DNA synthesis in fibroblasts and muscle cells has been quintupled using NASA LED light alone, in a single application combining 680, 730 and 880 nm each at 4 Joules per centimeter squared.

Muscle and bone atrophy are well documented in astronauts, and various minor injuries occurring in space have been reported not to heal until landing on Earth. An LED blanket device may be used for the prevention of bone and muscle atrophy in astronauts. The depth of near-infrared light penetration into human tissue has been measured spectroscopically. Spectra taken from the wrist flexor muscles in the forearm and muscles in the calf of the leg demonstrate that most of the light photons at wavelengths between 630-800 nm travel 23 cm through the surface tissue and muscle between input and exit at the photon detector. The light is absorbed by mitochondria where it stimulates energy metabolism in muscle and bone, as well as skin and subcutaneous tissue. Long term space flight, with its many inherent risks, also raises the possibility of astronauts being injured performing their required tasks. The fact that the normal healing process is negatively affected by microgravity requires novel approaches to improve wound healing and tissue growth in space. NASA LED arrays have already flown on Space Shuttle missions for studies of plant growth and the U.S. Food and Drug Administration (FDA) has approved human trials. The use of light therapy with LEDs can help prevent bone and muscle atrophy as well as increase the rate of wound healing in a microgravity environment, thus reducing the risk of treatable injuries becoming mission catastrophes.

Space flight has provided a laboratory for studying wound healing problems due to microgravity, which mimic traumatic wound healing problems here on earth. Improved wound healing may have multiple applications that benefit civilian medical care, military situations and long-term space flight. Enhancing the soldier's tissue responses to injury may lead to battlefield resilience and medical independence. Counter-measures to chemical, biological and radioactive weapons exposures which are based on biostimulation of natural tissue regeneration mechanisms could be more universally safe and effective than conventional drugs and surgical modalities. Regeneration of wounded organs and limbs may also be possible if biostimulation could re-awaken molecular events leading to re-growth of tissue.

Near infrared (IR) light has documented benefits promoting wound healing in human and animal studies. Our preliminary results have also demonstrated two to five-fold increases in growth-phase-specific DNA synthesis in normal fibroblasts, muscle cells, osteoblasts, and mucosal epithelial cells in tissue cultures treated with near-IR light. Our animal models treated with near-IR have included wound healing in diabetic mice and ischemic bipedical skin flap in rats. Near-IR induced a thirty percent increase in the rate of wound closure in these animal models. Dose- and time-dependent increases in vascular endothelial growth factor (VEGF) and fibroblast growth factor (FGF-2) occurred in animals treated with near-IR. Human studies have included the use of near-IR to prevent ulcerative mucositis resulting from high doses of chemotherapy and radiation. Widely published reports, including those from our laboratory, described accelerated recovery from musculoskeletal injuries, hypoxic-ischemic wounds, burns, lacerations, radiation necrosis, and diabetic ulcers with the use of near-IR.

Lasers have some inherent characteristics which make their use in a clinical setting problematic, including limitations in wavelength capabilities and beam width. The combined wavelengths of light optimal for wound healing cannot be efficiently produced, and the size of wounds which may be treated by lasers is limited. Light-emitting diodes (LEDs) developed for NASA manned space flight experiments offer an effective alternative to lasers. These diodes can be made to produce multiple wavelengths, and can be arranged in large, flat arrays allowing treatment of large wounds.

We are now investigating new collaborations with the Defense Advanced Research Projects Agency (DARPA) for military applications of LED wound healing technology in military medicine. Several uniquely military situations and indications could be addressed, optimizing near-IR parameters for wound healing via LEDs during extended missions under conditions separated from medical personnel. These include burns, chemical agents, radiation, biological agents and highly infected flesh-eating wounds (with and without extended burns) typical for the hygienic conditions occurring in battle fields, also infectious diseases and external wounds occurring in environments with no solar irradiation, low oxygen and high carbon dioxide (submarines). The dramatic results

with use of near-IR LED light to prevent digestive mucosal lesions (mucositis) and pain in cancer patients, after high-dose chemotherapy and radiation, suggest the potential for military use of near-IR light to treat U.S. troops exposed to chemical and radioactive warfare agents in the field. These examples illustrate the many possible military uses for this technology. These life-saving applications require especially accelerated wound healing, rapid reduction of infections and pain modulation.

Regeneration of muscles in amphibians has also been produced by near-IR therapy. The potential for regeneration of human tissue also deserves study. Central nervous system regeneration would be of particular benefit. Thus far, we have demonstrated that the best results for wound healing occur at wavelengths of 670 nm and 880 nm using 4 to 8 joules/cm², applied at power densities of approximately 50 mW/cm². However, studies to determine molecular mechanisms could lead to the optimization for current uses, as well as open up new applications.

Despite numerous reports on the benefits of near-IR on wound healing and rehabilitation over the last decade, the basic mechanisms of its action remain poorly understood. Britton Chance's group has reported that about 50% of near-IR light is absorbed by mitochondrial chromophores, such as cytochrome oxidase. However, the underlying cellular and molecular events are still unknown.