Photobiomodulation: Evaluation in a wide range of medical specialties underway

Advances in photobiomodulation have propelled the use of therapeutic applications in a variety of medical specialties, according to <u>Juanita J. Anders, PhD</u>.

During the annual conference of the American Society for Laser Medicine and Surgery, Dr. Anders, professor of anatomy, physiology, and genetics at the Uniformed Services University of the Health Sciences, Bethesda, Md., defined photobiomodulation (PBM) as the mechanism by which nonionizing optical radiation in the visible and



near-infrared spectral range is absorbed by endogenous chromophores to elicit photophysical and photochemical events at various biological scales. Photobiomodulation therapy (PBMT) involves the use of light sources including lasers, LEDs, and broadband light, that emit visible and/or near-infrared light to cause physiological changes in cells and tissues and result in therapeutic benefits.

In dermatology, LED light therapy devices are commonly

used for PBMT in wavelengths that range from blue (415 nm) and red (633 nm) to near infrared (830 nm). "Often, when PBMT is referred to by dermatologists it's called LED therapy or LED light therapy," Dr. Anders noted. "Some people are under the impression that this is different from PBMT. But remember: It's not the device that's producing the photons that is clinically relevant, but it's the photons themselves. In both cases, the same radiances and fluence ranges are being used and the mechanisms are the same, so it's all PBMT."

The therapy is used to treat a wide variety of medical and aesthetic disorders including acne vulgaris, psoriasis, burns, and wound healing. It has also been used in conjunction with surgical aesthetic and resurfacing procedures and has been reported to reduce erythema, edema, bruising, and days to healing. It's been shown that PBMT stimulates fibroblast proliferation, collagen synthesis, and extracellular matrix resulting in lifting and tightening lax skin.

According to Dr. Anders, French dermatologists Linda Fouque, MD, and Michele Pelletier, MD, performed a series of in vivo and in vitro studies in which they tested the effects of yellow and red light for skin rejuvenation when used individually or in combination. "They found that fibroblasts and keratinocytes in vitro had great improvement in their morphology both with the yellow and red light, but the best

improvement was seen with combination therapy," Dr. Anders said. "This held true in their work looking at epidermal and dermal markers in the skin, where they found the best up-regulation in protein synthesis of such markers as collagens and fibronectin were produced when a combination wavelength light was used."

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Oral mucositis and pain

PBMT is also being used to treat oral mucositis (OM), a common adverse response to chemotherapy and/or radiation therapy, which causes pain, difficulty in swallowing and eating, and oral ulceration, and often interrupts the course of treatments. Authors of a recently published review on the risks and benefits of PBMT concluded that there is consistent evidence from a small number of high-quality studies that PBMT can help prevent the development of cancer therapy—induced OM, reduce pain intensity, as well as promote healing, and enhance patient quality of life.

"They also cautioned that, due to the limited long-term follow-up of patients, there is still concern for the potential long-term risks of PBMT in cancer cell mutation and

amplification," Dr. Anders said. "They advised that PBMT should be used carefully when the irradiation beam is in the direction of the tumor zone."

Using PBMT for modulation of pain is another area of active research. Based on work from the laboratory of Dr. Anders and others, there are two methods to modulate pain. The first is to target tissue at irradiances below 100 mW/cm².

"In my laboratory, based on in vivo preclinical animal models of neuropathic pain, we used a 980-nm wavelength laser at 43.25 mW/cm² transcutaneously delivered to the level of the nerve for 20 seconds," said Dr. Anders, who is a past president of the ASLMS. "Essentially, we found that the pain was modulated by reducing sensitivity to mechanical stimulation and also by causing an anti-inflammatory shift in microglial and macrophage phenotype in the dorsal root ganglion and spinal cord of affected segments."

The second way to modulate pain, she continued, is to target tissue at irradiances above 250 mW/cm². She and her colleagues have conducted in vitro and in vivo <u>studies</u>, which indicate that treatment with an irradiance/fluence rate at 270 mW/cm² or higher at the nerve can rapidly block pain transmission.

"In vitro, we found that if we used an 810-nm wavelength light at 300 mW/cm², we got a disruption of microtubules in

the DRG neurons in culture, specifically the small neurons, the nociceptive fibers, but we did not affect the proprioceptive fibers unless we increased the length of the treatment," she said. "We essentially found the same thing in vivo in a rodent model of neuropathic pain."

In a pilot <u>study</u>, Dr. Anders and coauthors examined the efficacy of laser irradiation of the dorsal root ganglion of the second lumbar spinal nerve for patients with chronic back pain.

They found that PBMT effectively reduced back pain equal to the effects of lidocaine.

Based on these two irradiation approaches of targeting tissue, Dr. Anders recommends that a combination therapy be used to modulate neuropathic pain going forward. "This approach would involve the initial use of a high-irradiance treatment [at least 250 mW/cm²] at the nerve to block the pain transmission," she said. "That treatment would be followed by a series of low-irradiance treatments [10-100 mW/cm²] along the course of the involved nerve to alter chronic pathology and inflammation."

Potential applications in neurology

Dr. Anders also discussed research efforts under way involving transcranial PBMT: the delivery of near-infrared

light through the tissues of the scalp and skull to targeted brain regions to treat neurologic injuries and disorders. "There have been some exciting results in preclinical animal work and in small clinical pilot work that show that there could be possible beneficial effects in Parkinson's disease, Alzheimer's disease, depression, and improvement in cognition and memory after a brain injury, such as a TBI," she said.

"Initially, though, there were a lot of questions about whether you could really deliver light to the brain through the scalp. In my laboratory, we used slices of nonfixed brain and found that the sulci within the human brain act as light-wave guides. We used an 808-nm near-infrared wavelength of light, so that the light could penetrate more deeply." Using nonfixed cadaver heads, where the light was applied at the scalp surface, Dr. Anders and colleagues were able to measure photons down to the depth of 4 cm. "It's generally agreed now, though, that it's to a maximum depth of 2.5-3 cm that enough photons are delivered that would cause a beneficial therapeutic effect," she said.

Dr. Anders disclosed that she has received equipment from LiteCure, grant funding from the Department of Defense, and that she holds advisory board roles with LiteCure and Neurothera. She has also served in leadership roles for the Optical Society and holds intellectual property rights for the

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