

## 5 Questions—and Answers—About MIRE Treatment

Thomas J. Burke, PhD

### Q: What is MIRE?

**A:** MIRE is an acronym for monochromatic infrared energy. The MIRE, a therapeutic device (Anodyne Therapy, LLC, Tampa, FL), delivers a single (monochromatic) wavelength of near infrared photo energy at 890 nanometers, which is emitted by an array of 60 superluminous gallium aluminum arsenide diodes (Figure 1).

Because MIRE warms the targeted epidermis only slightly, its diode array may be placed in direct contact with the skin. The 890 nanometer (nm) wavelength is within the therapeutic window of photo energy.<sup>1</sup> Moreover, photo energy in this portion of the electromagnetic spectrum has an extensive depth of penetration and significant absorption by hemoglobin, rather than water.

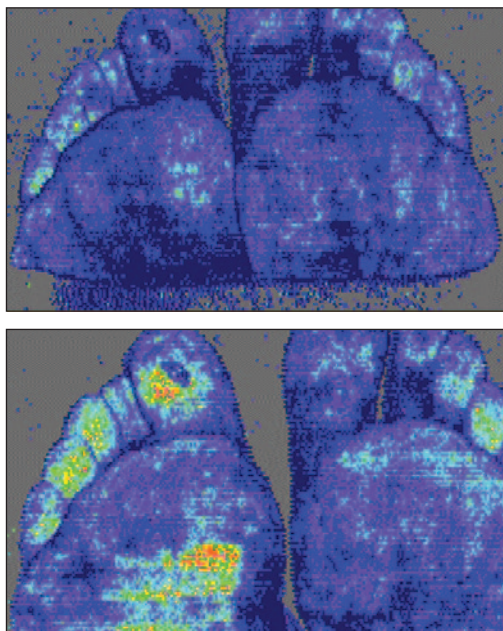
Although the therapeutic use of photo energy has been well documented internationally,<sup>1-5</sup> only recently has it been used by health care providers in the United States.<sup>6</sup> The benefits of photo energy depend on many factors, including skin contact, pulsation, wavelength, radiant power, and energy density.<sup>1,2</sup> Photo energy in the near infrared spectrum (890 nm) is delivered by diode arrays placed in direct skin contact with a flexible pad (3 cm × 7.5 cm, or 22.5 cm<sup>2</sup>). MIRE delivers pulsed adjustable radiant power of up to 10 milliwatts per diode, a power density per diode array of up to 10 milliwatts per cm<sup>2</sup>, and an energy density of up to 1.6 joules/cm<sup>2</sup>/minute. Thus, a

**Figure 1.**  
**FLEXIBLE, 60-DIODE PAD THAT EMITS 890 nm NEAR INFRARED PHOTO ENERGY**



**Figure 2.**  
**SCANNING LASER DOPPLER OF PLANTAR SURFACE OF THE FOOT, FOLLOWING 30 MINUTES OF MIRE TREATMENT**

Control perfusion is similar in both feet before treatment (top). Brighter color indicates better perfusion. Thirty minutes of MIRE treatment increases blood flow by 400% over baseline; elevating skin temperature to the same degree without MIRE increases blood flow by only 40%.



30-minute MIRE treatment can deliver up to 48 joules/cm<sup>2</sup> when the diodes are in direct skin contact.

### Q: Why is MIRE thought to be effective in treating chronic wounds?

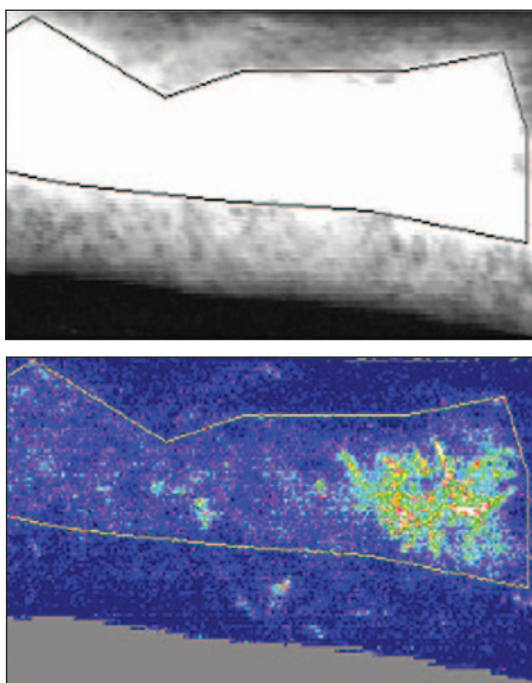
**A:** MIRE substantially increases microcirculation in the tissue under and around the diode array and increases venous flow. This reduces cellular edema in the wound site, increasing tissue blood flow and oxygenation.<sup>5,7,8</sup> Endogenous growth factor and white blood cells are delivered to healing tissue; the increased capillary blood flow promotes a positive wound healing environment.

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# Treatment Options

**Figure 3.**  
**HEALED VENOUS ULCER TREATED WITH MIRE, DID NOT REOCCUR**

Scanning laser Doppler (bottom) taken of a venous stasis ulcer 3 years after healing (original ulcer area is outlined by the polygon in the top scan). Blood flow remains higher in the healed, scar-free wound compared with the untreated skin (outside the polygon), despite no additional MIRE treatment following wound healing.



Tests conducted with a scanning laser Doppler (SLD; Moor Instruments Ltd, UK) demonstrate that MIRE increases local microcirculation by up to 3200% after a 30-minute treatment (data on file, Anodyne Therapy) (Figure 2). Follow-up SLD scans, taken 3 years after wound healing with adjunctive MIRE use, showed that microcirculation in the healed, original wound site is substantially greater than in the adjacent intact, untreated, unwounded tissue (data on file, Anodyne Therapy) (Figure 3).

The increase in circulation attributable to 890 nm and/or MIRE are based, in part, on the release of small amounts of nitric oxide (NO) from the hemoglobin in the red blood cells (RBCs) passing through vessels beneath the diode array.<sup>7</sup> MIRE may also increase NO formation by endothelial cells in blood vessels at the treatment site. Both endothelial cells and RBCs produce small, physiologic concentrations of NO from L-arginine via nitric oxide synthase (NOS). NO is the body's most powerful vasodilator. Small amounts increase cyclic guanosine monophosphate (cGMP) and result in relaxation of contractile proteins found in the smooth muscle walls of vascular tissue,

underscoring NO vasodilatory action.<sup>8</sup>

Every cell in the skin produces NO, therefore, NO is closely associated with the wound healing process.<sup>9</sup> After tissue injury, the inducible isoform of NOS (iNOS), partly formed by macrophages, is associated with the early, inflammatory phase of wound healing.<sup>10</sup> During this process, extremely high concentrations of NO are formed locally. Constitutive NOS (cNOS) and the generation of small NO concentrations are crucial to many cellular processes involved with later stages of wound healing. For example, NO is a powerful stimulator of cell division (proliferation) and maturation (differentiation), including formation of appropriate cell receptors for growth factors.<sup>10,11</sup> NO is also a powerful and necessary mediator of neovascularization (ie, the formation of new and, eventually, mature blood vessels [angiogenesis] and lymph ducts to nourish the healing tissue).<sup>11-13</sup> NO increases the number of fibroblasts (fibroblastic proliferation) and enhances collagen formation for the healing wound.<sup>14,15</sup> Finally, L-arginine and NO are necessary for the proper cross-linking of collagen fibers, via proline, to minimize scarring and maximize the tensile strength of healed tissue.<sup>16,17</sup>

## Q: What is the treatment protocol for MIRE?

**A:** The treatment protocol developed by Anodyne Therapy is 20 to 30 minutes, 1 to 2 times per day, 3 to 7 times per week, for all wounds, depending on patient availability for treatment in a health care facility.

A clear plastic barrier covers the wound site and a diode array is placed either over the wound or as close to the wound as possible. Areas of tunneling should be treated with diode arrays before the main wound site is treated to prevent the wound from closing before the tunnel. Additional placement of 1 or more diode arrays over large arteries and veins proximal to the wound site may prove beneficial in patients with severely compromised peripheral circulation.

## Q: For which wound types is MIRE treatment indicated?

**A:** In 1994, the FDA cleared MIRE for increasing circulation and reducing pain (data on file, Anodyne Therapy). Therefore, MIRE is an appropriate adjunctive therapy for any wound that has not responded to conservative wound treatment and would benefit from increased microcirculation through stimulation of the release of additional NO.<sup>13,17</sup> MIRE is particularly useful in the adjunctive treatment of neuropathic foot wounds in patients with diabetes. Persons with diabetes typically produce low amounts of NO<sup>18</sup>; the NO they do produce is tightly bound to hemoglobin.<sup>19</sup> Additionally, wound healing in the patient with diabetes is slowed by disease-related poor circulation to the wound site and by neuropathy. MIRE stimulates microcirculation to these wounds; the increased circulation possibly

accounts for the reported symptomatic reversal of any associated neuropathy.<sup>20</sup>

Case reports (data on file, Anodyne Therapy) show that adjunctive use of MIRE is effective in the treatment of pressure ulcers, venous ulcers, ischemic and postsurgical wounds, and wounds caused by chemical agents or radiation. The analgesic effect of NO<sup>21</sup> may also reduce the associated pain and the use of pain-relieving medications.<sup>22</sup> Published clinical studies using other photo energy delivery methods further support this use.<sup>23,24</sup>

### Q: When is MIRE contraindicated?

A: Generally, MIRE is not contraindicated for any wound. However, because small increases in NO generated by cNOS activity may inhibit iNOS activity,<sup>25</sup> early use of MIRE during the inflammatory phase of wound healing may decrease this activity before it is warranted. Additionally, MIRE should not be used on cancerous lesions, on patients with an active malignancy, or on patients who are pregnant or likely to be pregnant. ●

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