# Study Confirms Electroporation Advantage

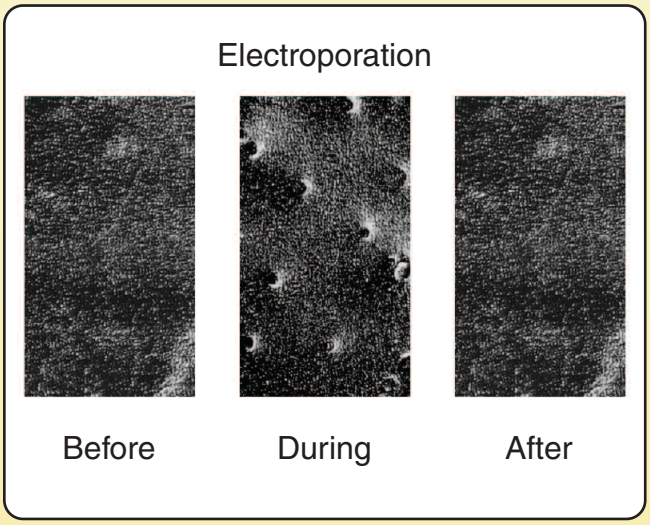
## 500 Times More Effective vs. Iontophoresis

By Bob Kronemyer, Associate Editor

Expanding therapeutic opportunities presented by transdermal delivery of drugs has a major benefit in the area of aesthetics. Transdermal drug delivery has advantages over oral, injection or intravenous administration due to its non-invasive nature, convenience, lack of trauma and avoidance of first pass degradation or absorption in the gastro-intestinal tract. Highly localized treatment is possible with the benefit of absorption into the dermal blood supply and the lymphatic system.

Several device manufacturers claim an ability to deliver topicals through the epidermis and achieve significant penetration in deeper layers of tissue to duplicate the efficiency of a syringe injection. Efficient delivery of materials to a significant tissue depth mandates that the concentration and quantity of topical be maintained without significant dilution. Penetration must therefore be fast and not limited by the sparse distribution of the appendages in tissue. Reality suggests that the technology and method used for delivery is the most important factor in duplicating syringe injection techniques.

Understanding technology differences may have a significant impact on a practitioner's choice of equipment for transdermal delivery and the potential success experienced by patients.




Previously, the potential of transdermal delivery was restricted by the need to limit drugs to a molecule size sufficient to migrate through an intact stratum corneum. The protective qualities of the stratum corneum exclude the transfer of all but the smallest molecule ingredients. Needle injection is efficient in delivering medication to a required depth in tissue but includes downsides. While these downsides may be insignificant in non-aesthetic medicine, they are critically important to those patients undergoing aesthetic therapy, especially in applications where multiple injections are required over several sessions of treatment.

The technology associated with transdermal drug delivery, in particular iontophoresis, electropermeabilization and electroporation is complex and most often familiar to those in the fields of molecular and cellular biophysics. Iontophoresis devices are often promoted as electroporation systems and claim transfer of materials to a significant depth in tissue despite the fact that the technology they use is entirely unsuited for this purpose.

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So what are the essential differences between iontophoresis and electroporation? Iontophoresis relies on active transportation of a drug within an electric field using a simple Galvanic current. Research performed at the Roswell Park Cancer Institute in Roswell, N.Y., found that iontophoresis typically delivers 100 times less drug volume than an injection but provides higher local concentrations than oral administration.* In applications that attempt to duplicate injection mesotherapy for the treatment of cellulite, this downside may be significant.

*A Pulsed Electric Field Enhances Cutaneous Delivery of Methylene Blue in Excised Full Thickness Porcine Skin: *Journal of Investigative Dermatology* (1998) 111, 457-463; doi:10.1046/j.1523-1747.1998.00301.x: Johnson, Gallo, Hui and Oseroff department of molecular and cellular biophysics and dermatology, Roswell Park Cancer Institute, Buffalo, N.Y.

Success of injection mesotherapy for cellulite, or injections for reduction of deeper fat masses demands that a specific amount of drug – kept close to its original concentration and without significant dilution – is placed at an optimum depth.

In iontophoresis the potential pathways for ingredients are restricted, forcing the majority of drugs to permeate the skin via appendageal pores such as hair follicles and sweat glands. These routes only account for about 0.1% of the skin's surface, making drug delivery via iontophoresis inefficient when a large area of tissue requires treatment. Moreover, penetration via the appendages is slow therefore dilution is a factor influencing potential success. In contrast, the number of transdermal pathways, available via electroporation, is over 500 times greater than with iontophoresis.

To improve absorption and defeat the protective qualities of the stratum corneum, iontophoresis device manufacturers sometimes recommend removing layers of the epidermis via microdermabrasion. While this may seem to enhance permeability, this step is not required with electroporation. Cellulite treatments most often address upper thigh and buttock areas therefore the use of any form of microdermabrasion as a pretreatment would seem impractical, time consuming, uncomfortable and extremely messy.

Electroporation is the basic mechanism of tissue injury in high-voltage electric shock and occurs as a result of the re-orientation of lipid molecules to form hydrophilic pores or microconduits. For example, the technique used in the DermaWave No-Needle Mesotherapy (NNM) System (DermaWave, Loxahatchee, Fla.), uses short, intense electric pulses that alter the electrical potential and form aqueous pores in the membrane. These pores, or microconduits, are very numerous providing the opportunity to deliver compounds evenly into tissue without the need to alter, change or remove the stratum corneum. Radioisotope lymphography studies confirm transfer of topical medication into the lymphatic system in less than 20 minutes and even distribution and retention in tissue up to 24 hours.

Electroporation proceeds in a domino like manner across tissue with the strongest effect being directly beneath the drug application accessory. Significantly, some device manufacturers utilize separate accessories for the delivery of electrical pulses and application of topicals. This technique has some problems, since efficient electroporation requires that the electrical energy is delivered in a consistent manner to tissue with simultaneous delivery of medication. Microconduits return to pre-treatment size a few milliseconds after the pulse is turned off and dilation time may be augmented by increasing the duration of the pulsing waveform. However, to achieve maximum transport potential, treatment strategy requires that the applicator is in relatively continuous contact with the tissue area to be treated.

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Electroporation delivery of Methylene Blue (MB) showed much greater penetration than dye delivered by iontophoresis – which provided minimal penetration – in the Roswell study. Material delivery is enhanced by energy in the form of pulses, and even at low electroporation levels delivery of MB was dramatically higher than with iontophoresis.

The DermaWave NNM System, utilizes additional strategies to enhance the transdermal delivery aspects of treatment. Electroporation is preceded by a strategy that focuses on increasing cell permeability, metabolic rate and blood perfusion. This system also uses additional electric waveforms delivered sequentially or in combination with the electroporation waveform. This treatment protocol may be used in combination with proprietary gel formulations designed by College Pharmacy, Colorado Springs, Colo. who offers transdermal gels for facial skin rejuvenation, cellulite and fat reduction. New applications being tested include electroporation gels for hyperpigmentation and scar reduction.