

THE DERMOELECTROPORATION® SYSTEM FOR TRANSDERMAL DELIVERY OF DRUGS

In this article, Gian Franco Bernabei, PhD, Chief Executive Officer, Mattioli Engineering, introduces the company's transdermal drug delivery system for the delivery of large molecules using electroporation.

In 2004, Mattioli Engineering introduced a new concept in dermatology for the transdermal delivery of high-molecular-weight therapeutics up to 1,000 kDa. The patented, proprietary technology, known as Dermo-electroporation® (DEP) is shown in Figure 1 and 2. The DEP system delivers controlled current pulses between two adjacent electrodes to increase the permeability of the skin. The effect of the electrical pulses is the opening of water-based microchannels through *stratum corneum* and epidermis.

Thus a high-molecular-weight drug filled into two adjacent gauze-pad electrodes is then delivered into the dermis. Sonic technology is also employed to enhance delivery.

The device is covered by a broad US patent estate, which includes US patent numbers: 6518538; 6535761; 6587730; 6687537; 6743215; 6748266; 6980854; 7010343;



Figure 1: The Dermo-electroporation® (DEP) System.

erable, although not yet FDA-approved. These include: Botulinum toxin, phosphatidylcholine,

“INSTEAD OF USING THE STANDARD ELECTROPORATION HIGH-VOLTAGE CONTROLLED PULSES, THAT COULD DAMAGE THE SKIN DUE TO THE UNPREDICTABLE CURRENT DENSITY, DEP APPLIES CONTROLLED CURRENT PULSES TO THE SKIN”

7083580; 7376460; 7471979; 7496401; 7520875; 7532926; and 7945321.

The device is EU CE marked and US FDA-cleared for the transdermal delivery of lidocaine. Many other drugs are successfully deliv-

aminophylline, L-carnitine, amino acids, heparin, collagen, various vitamins, various steroids, diclofenac and others.

To date, the technology has been used mainly in cosmetic dermatology for delivering sub-

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Figure 2: The Dermo-electroporation® (DEP) System and Mobile Stand.

stances like non-crosslinked hyaluronic acid, in conjunction with a microdermabrasion treatment. The microdermabrasion treatment is a standard in cosmetic dermatology and it is needed in order to have the assurance that the *stratum corneum* has a maximum permeability so that that the drug is really transdermally delivered.

The DEP technology developed by Mattioli is an improvement on the standard electroporation pulse systems that have been in use for more than a decade and are known to be able to deliver macromolecules through *stratum corneum* and epidermis.

Instead of using the standard electroporation high-voltage controlled pulses, that could damage the skin due to the unpredictable current density, DEP applies controlled current pulses to the skin. This technology works perfectly if the permeability of the *stratum corneum* is enough to enable transdermal transport.

In dermatology it is normal practice to use microdermabrasion in order to pretreat the skin for further treatment and thus has not been a problem to introduce this limitation also because Mattioli is one of the major manufacturers of microdermabrasion equipment. The reason pretreatment is included is that we limit to 100V the maximum voltage that the device applies to the skin, in order to avoid adverse effects.

Recently, in order to broaden the use of the technology, a means to verify sufficient *stratum*



Figure 3: On the DEP handpiece is mounted an optional computerised liquid dispenser that delivers the drug to the disposable cap by pushing a disposable drug-loaded syringe.

corneum permeability has been added to the equipment. This is done by measuring the electrical impedance of the skin during the current pulse. This makes it possible to check if pretreatment is needed and, further, to judge whether full microdermabrasion pretreatment is required or whether simpler pretreatment using scrubs or even gently abrasive paper would suffice.

The DEP comprises a machine body and a handpiece. On the handpiece is mounted an optional computerised liquid dispenser that delivers the drug to the disposable cap by pushing a disposable drug-loaded syringe (see Figure 3). Two sizes of syringes (10 cm³ and 20 cm³) and two handpiece sizes (small and large) are available. The typical injection speed over a skin surface of 30 cm² is between 0.5-1 cm³/min, depending on drug and handpiece size.

The device has been validated in a number of clinical studies conducted by the Department of Anatomy at the University of Florence, Italy. Amongst the many studies that have used the device, some of the most significant include:

- Pacini S, Punzi T, Gulisano M, "Transdermal delivery of Hyaluronic acid". *J of Dermatol Sci*, 2006, Vol 44, pp 169-171.
- Pacini S, Punzi T, Gulisano M, "Transdermal delivery of Clostridium Botulinum Toxin Type A by pulsed current Iontophoresis".

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- Pacini S, Punzi T, Gulisano M, Cecchi F, Vannucci S, Ruggiero M, "Transdermal delivery of heparin using pulsed current iontophoresis". *Pharm Res*, 2006, Vol 23(1), pp 114-120.
- Pacini S, Peruzzi B, Gulisano M, "Qualitative and quantitative analysis of transdermic delivery of different biological molecules by iontophoresis". *Ital J Anat Embryol*, 2003, Vol 18(Suppl2), pp 127-129
- Pacini S, Peruzzi B, Gulisano M et al, "Transdermal delivery of heparin by means of alternate current skin electroporation". *Ital J Anat Embryol*, 2004, Vol 109(1), p 223.
- De Bartolo HM, "Comparison of Mattioli Iontophoresis, Mesosystems, the U225, and Manual Injections". *Proceedings of the Illinois Society of Ophthalmology & Otolaryngology*, 2005, Vol 9(1).
- De Bartolo HM, "Scar Revision & Minimally Invasive Cosmetic Surgery using Mattioli Engineering Technology", *ibid*.
- Bacci PA, "The role of Dermo-electroporation". *Cellulite: Pathophysiology & Treatment*, 2006, Chapter 18, pp 291-299. (Published by Taylor & Francis, ISBN-10: 0-8247-2985-4/ISBN-13: 978-0-8247-2985-4)

New Transderm® Ionto DEP System

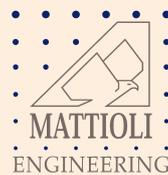


The only and Real transportable
Needles free Syringe for any skin need.

The new improved Transderm® Ionto DEP System represents the only one and real transportable "Needles free Syringe" System on the market carrying Dermoelectroporation® technology*.

The new improved Transderm® Ionto DEP System introduces:

- A New "Syringe like" handpiece design for medical controlled transdermal delivery of any ionic drug solution doctors indicate.
- Optimized MACRO molecules transdermal delivery (up to 2,000.000dalton-type a botulinum toxine** included).
- Continuous Visual indication on the skin absorption.
- Real time control on the whole treatment (delivery time, volume, flow, skin absorption).



New Delivery caps:

- 30% efficiency enhanced
- Faster then ever
- Avoids unwanted waste of products
- More comfort during session

* Dermoelectroporation® is a patented technology from Mattioli Engineering clinically proven to be able to transdermally deliver an accurate dosage of high molecular weight drugs into the body due to controlled electrical pulses.

CAUTION: Federal law (USA) restricts this medical device to sale by or on order of a physician.



BEFORE

AFTER



** Transdermal delivery of Clostridium botulinum toxin type A by pulsed current iontophoresis

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