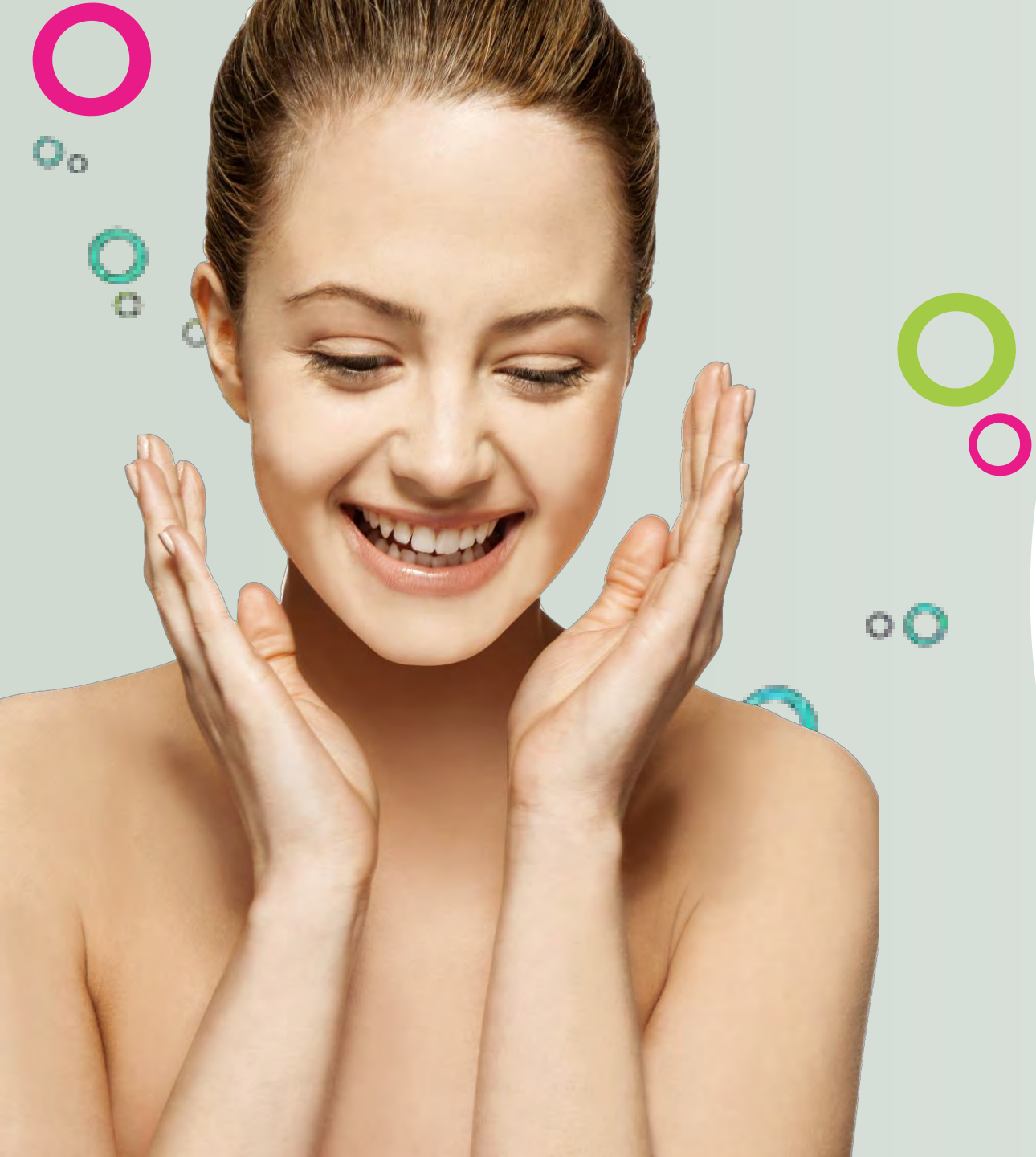

Tixel Publications

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Tixel in scientific publications

Key findings	Publications
Pretreatment with TMFI (Tixel) at low-energy pulse duration of 6 milliseconds increased the percutaneous permeation of ALA linearly over the first 5 hours from application when the compounded 20% ALA gel was used.	**A New Method for Percutaneous Drug Delivery by Thermo-Mechanical Fractional Injury.** Ronen Shavit, MSc and Christine Dierickx, MD Pub. List # 1
TMFI, in combination with the standardized application of 20% ALA cream and gel formulations, significantly enhanced skin surface PpIX fluorescence compared to no pretreatment. Additionally, TMFI increased epidermal PpIX fluorescence combined with 20% ALA cream vehicle. Thus, TMFI pretreatment and formulation characteristics exert influence on PpIX fluorescence intensities in normal skin.	**Thermo-mechanical fractional injury enhances skin surface- and epidermis- Protoporphyrin IX fluorescence: Comparison of 5-aminolevulinic acid in cream and gel vehicles.** Camilla Foged; Merete Haedersdal; Liora Bik; Christine Dierickx, Peter Alshede Phillipsen; Katrine Togsverd-Bo. Pub. list # 2

Editor's Choice

A New Method for Percutaneous Drug Delivery by Thermo-Mechanical Fractional Injury

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Background and Objectives: Percutaneous drug delivery (PDD) is a means of increasing the uptake of topically applied agents into the skin. Successful delivery of a photosensitizer into the skin is an important factor for effective photodynamic therapy. To evaluate the efficacy of pretreatment by thermomechanical fractional injury (TMFI) (Tixel®, Novoxel®, Israel) at low-energy settings in increasing the permeability of the skin to a known hydrophilic-photosensitizer medication, 5-amino-levulinic-acid hydrochloride (ALA) in compounded 20% ALA gel. To compare the effect of TMFI on ALA permeation into the skin in compounded gel to three commercial photosensitizing medications in different vehicles: ALA microemulsion gel, methyl-amino-levulinic-acid hydrochloride (MAL) cream, and ALA hydroalcoholic solution.
Study Design/Materials and Methods: Five healthy subjects were treated in two separate experiments and on a total of 136 test sites, with four topical photosensitizer preparations as follows: compounded 20% ALA gel prepared in a good manufacturing practice (GMP)-certified pharmacy (Super-Pharm Professional, Israel), 10% ALA microemulsion gel (Ameluz®, Biofrontera Bioscience GmbH, Leverkusen, Germany), 16.8% MAL cream (Metvix®, Galderma, Lausanne, Switzerland), and 20% ALA hydroalcoholic solution (Levulan Kerastick®, DUSA Pharmaceuticals, Inc., Wilmington, MA, USA). The dermal sites were pretreated by Tixel® (Novoxel® Ltd., Israel) prior to topical drug application. One site was untreated to serve as control. Protoporphyrin IX (PpIX) fluorescence intensity readouts were taken immediately and 1, 2, 3, 4, and 5 hours posttreatment.
Results: The highest average PpIX fluorescence intensity measurements were obtained for the compounded 20% ALA gel following pre-treatment by TMFI at 6 milliseconds pulse duration. After 2 and 3 hours, TMFI-treated sites exhibited an increased hourly rate in readouts of FluoDerm units, which were 156–176% higher than the control rates ($P \leq 0.004$). TMFI pre-treatment did not enhance the percutaneous permeation of either ALA or MAL following the microemulsion gel, hydroalcoholic solution, and cream applications.
Conclusions: Pretreatment with low-energy TMFI at a pulse duration of 6 milliseconds increased the percutaneous permeation of ALA linearly over the first 5 hours from application when the compounded 20% ALA gel was used. Formulation characteristics have substantial influence on the ability of TMFI pretreatment to significantly increase the percutaneous permeation of ALA and MAL. Lasers Surg. Med. © 2019 Wiley Periodicals, Inc.

Key words: percutaneous drug delivery; percutaneous permeation; diffusion; thermomechanical fractional injury; transepidermal drug delivery; tixel

INTRODUCTION

The therapeutic efficacy of topical drugs is correlated with both inherent potency and ability to penetrate the various skin layers. The principal barrier to drug permeation is the stratum corneum (SC), which has a structure of "brick" (corneocyte) and "mortar" (lamellar membranes). It consists of approximately 15 sublayers with a total thickness of 20 μm. The structure of the SC serves multiple barrier functions to protect internal cells and tissues while maintaining the internal environment and normal cellular functions [1]. The importance of the water content of the SC in determining its properties is well-documented. Warner et al. [2] reported a continuous increase in the water content of the SC, ranging from 15 to 25% at the skin surface to a constant level of approximately 70% in the viable stratum granulosum (SG) [3]. The mechanical properties of the SC are highly

Abbreviations: AFXL, ablative fractional laser; ALA, 5-aminolevulinic acid hydrochloride; CZ, coagulation zone; DSP, digital signal processing; FDU, FluoDerm Units; GMP, good manufacturing practice; HAZ, heat-affected zone; IR, infra-red; MAL, methyl-amino-levulinic acid hydrochloride; MAZ, micro-thermal ablation zone; PDD, percutaneous drug delivery; PDT, photodynamic therapy; PpIX, protoporphyrin IX; RH, Relative humidity; SC, stratum corneum; SG, stratum granulosum; TMFI, thermomechanical fractional injury; USP, United State Pharmacopeia.

Conflict of Interest Disclosures: All authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest and have disclosed the following: RS is the Chief Technical Officer of Novoxel Ltd. and CD has no conflicts of interest.

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Thermo-Mechanical Fractional Injury Enhances Skin Surface- and Epidermis- Protoporphyrin IX Fluorescence: Comparison of 5-Aminolevulinic Acid in Cream and Gel Vehicles

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Background and Objectives: Thermo-mechanical fractional injury (TMFI) impacts the skin barrier and may increase cutaneous drug uptake. This study investigated the potential of TMFI in combination with 5-aminolevulinic acid (ALA) cream and gel formulations to enhance Protoporphyrin IX (PpIX) fluorescence at the skin surface and in the skin.
Study Design/Materials and Methods: In healthy volunteers ($n = 12$) a total of 144 test areas were demarcated on the upper back. Test areas were randomized to (i) TMFI (6 milliseconds, 400 μm at a single pass) or no pretreatment and (ii) 20% ALA in cream or gel formulations. Skin surface PpIX fluorescence was quantified by PpIX fluorescence photography and photometry in 30-minute intervals until 3 hours. PpIX fluorescence microscopy quantified separate PpIX fluorescence in the epidermis, and in superficial-, mid-, and deep- dermis from punch biopsies sampled after 3 hours of ALA incubation. Local skin reactions (LSR) and pain intensities (numerical rating scale 0–10) were evaluated immediately, at 3 hours and 14 days after the intervention.
Results: TMFI exposure before photosensitizer application significantly increased *skin surface* PpIX fluorescence, both for ALA cream (TMFI-ALA-cream 7848 arbitrary units [AU] vs. ALA-cream 5441 AU, 3 hours, $P < 0.001$) and ALA gel (TMFI + ALA-gel 4591 AU vs. ALA-gel 3723 AU, 3 hours, $P < 0.001$). The TMFI-mediated increase in PpIX fluorescence was similar for ALA-cream and -gel formulations ($P = 0.470$) at the skin surface. In the *epidermis*, PpIX fluorescence intensities increased from combination treatment with TMFI and ALA-cream (TMFI + ALA-cream 421 AU vs. ALA-cream 293 AU, $P = 0.034$) but not from combination with TMFI and ALA-gel (TMI + ALA-gel 264 AU vs. ALA-gel 261 AU, $P = 0.791$). *Dermal* fluorescence intensities (superficial-, mid-, or deep dermis) were unaffected by TMFI pretreatment in both ALA-cream and ALA-gel exposed skin ($P = 0.339$). ALA-cream generally induced higher PpIX fluorescence intensities than ALA-gel (skin surface $P < 0.001$ and epidermis $P < 0.03$). TMFI induced low pain intensities (median 3) and mild LSR that were resolved at 14 days follow-up.
Conclusion: Given the present study design, TMFI, in combination with the standardized application of 20% ALA cream and gel formulations, significantly enhanced skin surface PpIX fluorescence compared to no pretreatment. Additionally, TMFI increased epidermal PpIX fluorescence combined with 20% ALA cream vehicle. Thus, TMFI pretreatment and formulation characteristics exert influence on PpIX fluorescence intensities in normal skin. Lasers Surg. Med. © 2020 Wiley Periodicals LLC

Key words: 5-aminolevulinic acid; actinic keratoses; fluorescence microscopy; Protoporphyrin IX; photodynamic therapy; stratum corneum; thermo-mechanical fractional injury; thermo-mechanical system; vehicle viscosity

INTRODUCTION

Topical photodynamic therapy (PDT) in dermatology is based on light activation of the endogenous photosensitizer

Conflict of Interest Disclosures: All authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest and have disclosed the following: TMFI device was loaned by Novoxel (Novoxel LTD., Israel) for this particular study, accompanied by a research grant to Bispebjerg Hospital, represented by Merete Haedersdal, Novoxel Ltd. had no influence on data collection or interpretation of results. CD, CF, KTB, LB, and PAP have no conflicts of interest.

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Tixel in scientific publications

Key findings	Publications
By using Tixel for drug delivery, we have demonstrated for the first time an increased permeability of hydrophilic active compounds. Fractional ablation of the upper layer of the skin carried out by the Tixel's pretreatment procedure can result in an enhanced transdermal delivery of poorly permeable drugs.	**A Novel Thermo-mechanical System Enhanced Transdermal Delivery of Hydrophilic Active Agents by Fractional Ablation** Amnon C. Sintov, Maja A. Hofmann Pub. list # 3

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A novel thermo-mechanical system enhanced transdermal delivery of hydrophilic active agents by fractional ablation

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ABSTRACT

The Tixel is a novel device based on a thermo-mechanical ablation technology that combines a sophisticated motion and a temperature control. The fractional technology is used to transfer a very precise thermal energy to the skin thereby creating an array of microchannels, accompanying by no signs of pain or inconvenience. This study aimed to evaluate the effect of the Tixel on the skin permeability of three hydrophilic molecular models: verapamil hydrochloride, diclofenac sodium, and magnesium ascorbyl phosphate. Tixel's gold-platted stainless steel tip heated to a temperature of 400 °C was applied on skin for 8 ms or 9 ms at a protrusion of 400 μm (the distance in which the tip protrudes beyond the distance gauge). The experiments were carried out partly *in vivo* in humans using a fluorescent dye and a confocal microscopy and partly *in vitro* using porcine skin and a Franz diffusion cell system. The results obtained in this study have shown that (a) no significant collateral damage to the skin tissue and no necrosis or dermal coagulation have been noted, (b) the microchannels remained open and endured for at least 6 h, and (c) the skin permeability of hydrophilic molecules, which poorly penetrate the lipophilic stratum corneum barrier, was significantly enhanced by using Tixel's pretreatment.

1. Introduction

Transdermal drug delivery has been well-established as a potentially advantageous alternative for many therapeutically active compounds to the parenteral and oral routes. The adverse effects due to fluctuations in plasma drug levels, the high portion of hepatic first-pass metabolism (or other factors leading a low bioavailability), as well as a short biological half-life have been important reasons to intensively explore ways how to circumvent the skin barrier. The highly lipophilic nature of the skin provides the main barrier for influx of drugs and environmental chemicals into the body. The lipophilic properties are related to the outermost keratinizing layer, the stratum corneum (10–20 μm thickness), which is impermeable to most therapeutically active compounds, in particular high-molecular weight, hydrophilic or charged substances. Nonetheless, the advantages of transdermal drug delivery have motivated intensive research activity for the purpose of circumventing the skin barrier with optimal solutions (Barry, 2001; Davis et al., 2002). Various methods have been studied, such as those based on chemical enhancers (Walters, 1989; Smith and Maibach, 1995; Ben-Shabat et al., 2007), or those rely on physical techniques including microneedles (Henry et al., 1998; McAllister et al., 2000), iontophoresis (Singh et al., 1999; Marro et al., 2001; Guy et al., 2001 Sintov and Brandys-Sitton, 2006), electroporation (Prausnitz et al., 1993; Riviere et al., 1995; Vanbever et al., 1994, 1996; Prausnitz, 1999; Hu et al., 2000), ultrasound (Ogra et al., 2008), as well as a diversity of thermal ablation techniques (Sintov et al., 2003; Park et al., 2008; Bachhav et al., 2010, 2013; Lee et al., 2011). Thermal ablation for transdermal drug delivery has included lasers (Bachhav et al., 2010, 2013), radiofrequency (Sintov et al., 2003), or superheated steam (Lee et al., 2011) devices. A pioneering work by Park et al. (2008) has shown, by screening a broad range of temperatures (25°–315 °C) and durations (100 ms–5 s), that skin permeability strongly depends on the temperature and less on the duration of heating so even shorter durations (i.e., on a microsecond timescale) might be sufficient. Lee et al. (2011) later developed a microdevice that ejects superheated steam during only 100 μs at the skin surface, demonstrating a selective removal of stratum corneum of cadaver skin without significant collateral damage to the inner tissue. Recently, a thermo-mechanical ablation (TMAb) technology has been proposed (Lask et al., 2012; Elman et al., 2016), demonstrating

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Tixel in scientific publications - cont.

Key findings	Publications
TMA used immediately prior to ALA application may enhance the effectiveness of PDT in the treatment of acne with minimal side effects, reduced downtime, and fewer sessions. The exact mechanism of TMA assisted PDT is still to be understood.	**Thermo-mechanical ablation assisted photodynamic therapy for the treatment of acne vulgaris. A retrospective chart review of 30 patients.** Y. Hilerowicz, O. Friedman, E. Zur, R. Ziv, A. Koren, F. Salameh, Joseph N. Mehrabi, O. Artzi Pub. list # 4
Wound healing after thermomechanical skin ablation is much faster compared with other fractionated ablation methods. Treatment intervals of 2–4 weeks could be recommended.	**Wound Healing Process After Thermomechanical Skin Ablation** Georgios Kokolakis, Leonie von Grawert, Martina Ulrich, Juergen Lademann, Torsten Zuberbier, and Maja A. Hofmann Pub. list # 5

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Thermomechanical Ablation-Assisted Photodynamic Therapy for the Treatment of Acne Vulgaris. A Retrospective Chart Review of 30 Patients

Yuval Hilerowicz,[1] Or Friedman,[2] Eyal Zur,[3] Roni Ziv,[4] Amir Koren,[1,4] Fares Salameh,[1] Joseph N. Mehrabi,[5] and Ofir Artzi[1,4]

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Background and Objectives: Acne vulgaris, a chronic inflammatory disease, affects more than 90% of teenagers. The first-line treatments for acne vulgaris are topical and oral medications, mainly antibiotics and retinoids. However, antibiotic resistance of *Propionibacterium acnes*, contraindications, partial response, significant adverse effects, or recurrence creates demand for novel treatment options in acne. Aminolevulinic acid (ALA) photodynamic therapy (PDT) is a well-established modality in the treatment of acne. Nevertheless, PDT has limitations: it may not be effective for every patient; several treatments are usually required to achieve sufficient outcome; incubation time is 1–3 hours; treatment pain and post-treatment downtime may be difficult for some patients to endure; and adverse effects may occur. This retrospective chart review was conducted to evaluate the efficacy and safety of PDT, assisted by a thermomechanical ablation (TMA) fractional injury device in the treatment of patients with moderate to severe acne.
Study Design/Materials and Methods: We conducted a retrospective chart review of 30 acne patients treated with TMA immediately before 5% ALA application with an incubation time of 1 hour and exposure to 60 J/cm^2 red light (630 nm). Patients received up to three monthly treatments and were followed for 16 weeks. Two independent investigators evaluated the subject outcomes according to high definition photographs taken at baseline, before each treatment and at follow-up visits. Three acne grading methods were used: Acne Grading Scoring System (AGSS), the Leeds revised acne grading system, and the general response to the treatment score. Patients also provided self-assessments of improvement using the patient global impression of change (PGIC).
Results: Compared with baseline, the AGSS has showed a statistically significant reduction of 26.7% and 23.7%, respectively, at weeks 8 and 16 after final treatment. The Leeds score showed 65.2% and 60.6% improvement at the respective visits. The overall response rate was graded 3.3 ± 0.5 out of 4. PGIC score given by the patients was 5.5 out of 7, reflecting high satisfaction.
Conclusion: TMA used immediately prior to ALA application may enhance the effectiveness of PDT in the treatment of acne with minimal side effects, reduced downtime, and fewer sessions. The exact mechanism of TMA-assisted PDT is still to be understood. Lasers Surg. Med. © 2020 Wiley Periodicals, Inc.

Key words: acne vulgaris; photodynamic treatment; ALA; tixel

INTRODUCTION

Acne vulgaris is a common condition among teenagers and adults, which might result in scarring [1]. Although highly effective, many patients refuse systemic treatment or pose relevant contraindications [1].

Photodynamic therapy (PDT) has been used as an alternative and effective evidence-based treatment for acne vulgaris since 2000 [2,3]. PDT is not effective for every patient. In most patients, several treatments are required to achieve an improvement. They are frequently associated with pain, downtime, and adverse effects. Preceding skin manipulation is aimed to enhance photosensitizer absorption and employed to improve PDT outcome, reduce pain and adverse effects, and ease downtime. Laser-assisted PDT has been advocated by many studies with impressive results when fractional

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Wound Healing Process After Thermomechanical Skin Ablation

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Background and Objectives: Energy-based devices have been widely applied for skin ablation. A novel ablation technique based on thermomechanical principles (Tixel©) has been recently developed. The aim of this study was to examine the wound-healing process and clinical aspects after thermomechanical skin ablation.
Study Design/Materials and Methods: Six female participants were treated with Tixel© on healthy skin of the dorsal side of the right forearm in a single session with a 600 µm protrusion and 12 milliseconds pulse. The treated area was examined with confocal laser scanning microscopy on day 1, 2, 7, and 14 after treatment. Clinical symptoms were evaluated at the same time-points.
Results: All patients developed erythema and mild edema on the treated areas, which completely disappeared within 14 days. No post-inflammatory hyperpigmentation or scarring was observed. Thermomechanical skin ablation resulted in the formation of homogeneous micro-ablation zones. Two weeks after ablation, the honeycomb patterns of the epidermis in all examined layers was thoroughly restored. Thus, wound-healing was completed.
Conclusions: Wound healing after thermomechanical skin ablation is much faster compared with other fractionated ablation methods. Treatment intervals of 2–4 weeks could be recommended. Lasers Surg. Med. © 2020 The Authors. *Lasers in Surgery and Medicine* published by Wiley Periodicals, Inc.

Key words: thermomechanical skin ablation; Tixel©; wound-healing

INTRODUCTION

Skin ablation employing energy-based devices has increasingly attracted interest in the last few years. Not only for cosmetic purposes like antiaging, resurfacing, or treating scars but also for therapeutic applications, skin ablation is a well-established efficacious procedure. Side effects including thermal injury, crusting, long-lasting erythema, or hyperpigmentation may prolong the healing process [1]. Dividing the energy into fractions ensures deep dermal penetration of the energy with minimal affection of the epidermis. Thus, rapid recovery times are achieved compared with traditional ablative lasers [2].

Several ablative and non-ablative laser devices have been developed to improve skin laxity in the last decade, providing physicians with a wide palette of treatment options.

Currently, ablative fractionated CO_2 or Erbium:Yag lasers and bipolar radiofrequency are the most commonly applied techniques [2,3]. Novel technologies have also emerged that use sources of energy other than light, such as high-intensity focused ultrasound [4].

In the last few years, the development of a new technology based on thermomechanical principles offers a new treatment modality. A precise thermal energy is fractionally transferred to the skin creating an array of microchannels, minimizing downtime, and side effects compared with other fractional skin ablation techniques [5,6].

Confocal laser scanning microscopy (CLSM) is a non-invasive device, which visualizes the superficial layers of the skin *in vivo* in real-time. CLSM allows very detailed imaging with almost histopathological resolution of the epidermis and papillary dermis. The penetration depth is about 250 nm. CLSM was chosen to analyze the wound-healing process, as it is a non-invasive device able to regularly evaluate deeper skin layers. Therefore, the wound-healing process can be monitored over time without the need of surgical intervention [7].

The aim of this proof-of-concept trial was the investigation of the underlying wound-healing processes after skin ablation with thermomechanical ablation (TMA) and their correlation with clinical aspects.

Conflict of Interest Disclosures: All authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest and none were reported.
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Tixel in scientific publications - cont.

Key findings	Publications
Thermal breakage of the stratum corneum using Tixel to increase skin permeability for botulinum toxin type A in the treatment of facial flushing of rosacea seems both effective and safe.	**The Toxic Edge - A Novel Treatment for Refractory Erythema and Flushing of Rosacea.** Or Friedman, MD, Amir Koren, MD, Roni Niv, MD, Joseph N. Mehrabi, BSc and Ofir Artzi, MD Pub. list # 6
Thermomechanical drug delivery of TAC and 5-FU is safe and effective. This is a promising option for the treatment of keloid scars, particularly in the pediatric population.	**The Scar Bane Without the Pain: A New Approach in the Treatment of Elevated Scars: Thermomechanical Delivery of Topical Triamcinolone Acetonide and 5-Fluorouracil** Ofir Artzi, Amir Koren, Roni Niv, Joseph N. Mehrabi, Or Friedman Pub. list # 7

The Toxic Edge—A Novel Treatment for Refractory Erythema and Flushing of Rosacea

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Purpose: Rosacea is a common, chronic facial skin disease that affects the quality of life. Treatment of facial erythema with intradermal botulinum toxin injection has previously been reported. The primary objective of the study was the safety and efficacy of thermal decomposition of the stratum corneum using a novel non-laser thermomechanical system (Tixel, Novoxel, Israel) to increase skin permeability for Botulinum toxin in the treatment of facial flushing of rosacea.
Methods: A retrospective review of 16 patients aged 23–45 years with Fitzpatrick Skin Types II to IV and facial erythematotelangiectatic rosacea treated by Tixel followed by topical application of 100 U of abobotulinumtoxin. A standardized high-definition digital camera photographed the patients at baseline and 1, 3, and 6 months after the last treatment. Objective and subjective assessments of the patients were done via Mexameter, the Clinicians Erythema Assessment (CEA), and Patients self-assessment (PSA) scores and the dermatology life quality index (DLQI) validated instrument.
Results: The average Maxameter, CEA, and PSA scores at 1, 3, and 6 months were significantly improved compared with baseline (all had a P-value <0.001). DLQI scores significantly improved with an average score of 18.6 at baseline at 6 months after treatment ($P < 0.001$). Self-rated patient satisfaction was high. There were no motor function side-effects or drooping.
Conclusion: Thermal breakage of the stratum corneum using the device to increase skin permeability for botulinum toxin type A in the treatment of facial flushing of rosacea seems both effective and safe. Lasers Surg. Med.

Key words: botulinum toxin; erythema; flushing; rosacea; drug delivery; percutaneous permeating; fractional skin ablation

INTRODUCTION

Rosacea is a chronic, relapsing inflammatory skin disease [1]. Symptoms include persistent facial erythema, papules, pustules, telangiectasia, and recurrent flushing [1]. The red, pimply facial rash can cause embarrassment, low self-esteem, anxiety, and have a considerable adverse effect on quality of life [2–4]. The prevalence of rosacea across populations is reported to range from less than 1% to 22% and is characterized by episodes of exacerbation and remission. [5–6]. Symptoms only partially respond to therapy and tend to recur. Frequently prescribed treatments include topical, oral, and light-based therapies [1]. Intradermal botulinum toxin has been investigated as a novel treatment of facial erythema and flushing [7–11]. Botulinum toxin (BTX) blocks the release of the neurotransmitter acetylcholine from peripheral nerves and thus might alter cutaneous vasodilatation [12–13]. Due to its characteristics and high molecular weight, BTX cannot penetrate the highly impermeable stratum corneum while applied to bare skin [14].

Disruption of the outer stratum corneum by mechanical, chemical, or physical approaches increases skin permeability [15–17]. Selective thermal ablation of stratum corneum dramatically increased skin permeability for transdermal drug delivery [18–19]. Above 360°C, transdermal flux increased by many orders of magnitude. [20].

This study aimed to assess the safety and efficacy of a novel non-laser thermal resurfacing system (Tixel, Novoxel, Israel) of increasing skin permeability for botulinum toxin type A in the treatment of patients with resistant facial flushing of rosacea. The system has already been demonstrated to significantly increase the permeability of several topically applied medications [21,22].

METHODS

A retrospective review of 16 patients ages 23–45 years (average 41 years) treated in a single center between January 2017 and March 2018. The standard treatment reviewed consisted of a novel thermomechano-ablative

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ORIGINAL RESEARCH

The Scar Bane, Without the Pain: A New Approach in the Treatment of Elevated Scars: Thermomechanical Delivery of Topical Triamcinolone Acetonide and 5-Fluorouracil

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ABSTRACT

Introduction: Keloids are challenging to treat due to their inadequate response to treatment and high recurrence rate. Intralesional triamcinolone acetonide (TAC) injection with or without 5-fluorouracil (5FU) is considered the first-line treatment for keloids. Three significant disadvantages of intralesional injections are the pain associated with the procedure, the uneven topography, and epidermal atrophy. Fractionated ablative carbon dioxide (CO_2) laser-assisted drug delivery (LADD) of the topical solution can help facilitate transdermal drug delivery and shows promise in scar remodeling. This study examined the use of a thermomechanical device (Tixel, Novoxel) to facilitate the transdermal delivery of TAC and 5-FU in the treatment of keloid scars.
Methods: Seven patients each received eight topical thermal ablations, with one ablation performed every 2–3 weeks. TAC and 5FU were applied after each ablation. Outcomes were evaluated using the Vancouver Scar Scale (VSS), and pain was assessed using the Visual Analog Scale (VAS).
Results: Mean keloid VSS reduced from 8.6 ± 1.2 to 5 ± 2.7 after the eight treatments. Mean treatment pain VAS score was 2.4 ± 0.7. Patients rated their satisfaction level as moderate–high. No severe adverse reactions were noted.
Conclusion: Thermomechanical drug delivery of TAC and 5-FU is safe and effective. This is a promising option for the treatment of keloid scars, particularly in the pediatric population.

Keywords: Keloid; Fluorouracil; Fractional skin ablation; Percutaneous permeating; Resurfacing; Scar; Tixel; Transdermal drug delivery; Triamcinolone

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INTRODUCTION

Keloid scars are an uncommon but severe result of impaired wound healing. Keloid scars may develop after acne vulgaris, trauma, surgical incisions, burn injuries, or without an obvious

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Tixel in scientific publications - cont.

Key findings	Publications
Thermomechanical decomposition of the stratum corneum, in combination with topical application of TAC and 5-FU, is a safe, relatively painless, and efficient modality for the treatment of pediatric hypertrophic burn scars.	**A new approach in the treatment of pediatric hypertrophic burn scars: Tixel-associated topical triamcinolone acetonide and 5-fluorouracil delivery** Ofir Artzi MD, Amir Koren MD, Roni Niv MD, Joseph N. Mehrabi, Jacob Mashiah MD, Or Friedman MD Pub. list # 8
Enhanced percutaneous delivery of beta-blockers is a safe and efficient topical therapy for infantile hemangioma.	**Enhanced percutaneous delivery of Beta-blockers using thermal resurfacing drug delivery system for topical treatment of infantile hemangiomas.** Jacob Mashiah, MD, Efrat Bar-Ilan, MD, Amir Koren, MD, Or Friedman, MD, Eyal Zur, RPh, Ofir Artzi, MD Pub. list # 9

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ORIGINAL CONTRIBUTION

JCD Journal of Cosmetic Dermatology | WILEY

A new approach in the treatment of pediatric hypertrophic burn scars: Tixel-associated topical triamcinolone acetonide and 5-fluorouracil delivery

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Abstract

Background: Pediatric hypertrophic burn scars are challenging to treat due to their widespread nature and pain associated with the treatment. Intralesional triamcinolone acetonide (TAC) injection with or without 5-fluorouracil (5FU) is considered first-line treatment for severe hypertrophic scars. The pain associated with the procedure, the uneven topography, and epidermal atrophy, all limit the application of this treatment modality.

Aims: We sought to evaluate the clinical effectiveness and safety profile of a novel thermomechanical system (Tixel, Novoxel) for transdermal delivery of a topical solution containing TAC and 5-FU in the treatment of hypertrophic scars.

Patients/Methods: A retrospective study of pediatric hypertrophic burn scars treated between 2015 and 2017 was performed. Epidemiologic, treatment data, effectiveness score, and safety were reviewed.

Results: Four children (one male and three females, ages 3-10 years old) with hypertrophic burn scars treated with the Tixel device were evaluated. Mean scar VSS was reduced from 8.4 ± 0.8-5.2 ± 0.5 (P-value – .001) after eight treatments. The mean improvement of toughness, thickness, color, and general aesthetic impression was 3.1 ± 0.43 → 2.2 ± 0.31, 3.4 ± 0.5 → 1.9 ± 0.63, 2.7 ± 0.21 → 2.4 ± 0.25, and 3.23 ± 0.44 → 1.6 ± 0.64, respectively. Mean treatment pain VAS score was 1.74 ± 0.9. Patient's parents rated their satisfaction level as "moderate-high." No topical or systemic complications were observed.

Conclusion: Thermomechanical decomposition of the stratum corneum, in combination with topical application of TAC and 5-FU, is a safe, relatively painless, and efficient modality for the treatment of pediatric hypertrophic burn scars.

KEYWORDS
burn scars, fluorouracil, fractional skin ablation, hypertrophic, Percutaneous permeating, resurfacing, scar, Tixel, transdermal drug delivery, triamcinolone

Dermatology

Research Article

Dermatology
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Enhanced Percutaneous Delivery of Beta-Blockers Using Thermal Resurfacing Drug Delivery System for Topical Treatment of Infantile Hemangiomas

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Keywords
Beta-blockers · Enhanced percutaneous delivery · Infantile hemangioma · Pediatric dermatology · Tixel

Abstract
Background: Infantile hemangiomas (IHs) are the most common vascular tumors in children. In the past few years, topical beta-blockers (bBs) have been reported to be an effective treatment of superficial IHs. ***Objective:*** We sought to evaluate the clinical effectiveness and safety profile of enhanced percutaneous delivery of bBs for the treatment of IH. ***Methods:*** A retrospective study of all cases of IHs treated with enhanced percutaneous delivery of bBs between 2018 and 2019 was performed. Epidemiologic, clinical, and treatment data, including effectiveness score and safety, were reviewed. ***Results:*** The study included 11 patients with a total of 11 IHs. Of the total number of IHs, 7 (63.7%) showed a good response to treatment and 4 (36.3%) had a partial response; thus all patients (100%) had good or partial response to treatment. No systemic or local adverse effects were reported. ***Limitations:*** This is an uncontrolled retrospective study. ***Conclusion:*** Enhanced percutaneous delivery of bBs is a safe and efficient topical therapy for IH.

Introduction

Infantile hemangiomas (IHs) are the most common vascular tumors in children with an incidence of 4–10%, they are caused by proliferation of endothelial cells. Their natural history comprises of a rapid proliferation in the first months of life, followed by an involution phase that can take several years [1–3]. While most of the IHs does not require treatment, it is beneficiary and even obligatory in cases of IHs in high-risk distribution imposing dysfunction, disability, or disfiguration such as the eyes, nose, and throat. Treatment can also prevent post involution atrophy, telangiectasia, fibro-fatty tissue, and skin laxity which commonly occur in superficial hemangiomas [4–6].

Since the discovery of the effect of propranolol on IHs, oral propranolol is considered the first-line treatment for IHs [7]. In light of the possible adverse effects (AEs) profile of the systemic treatment, topical beta-blockers (bBs), namely propranolol hydrochloride and timolol maleate, are widely used for the treatment of superficial IHs [8–10], with an improvement in up to 90% of the cases, minor local AEs, and without any reported systemic AEs [11, 12]. The use of lasers, microneedles, as well as radio frequency waves, as topical drug delivery systems can en-

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Tixel in scientific publications - cont.

Key findings	Publications
Tixel treatment followed by topical application of Botulinum Toxin can be considered in the treatment of Hailey-Hailey disease. This approach is less invasive, less painful and yet effective as well as safe.	**An Enhanced Transcutenous Delivery of Botulinum Toxin for the Treatment of Hailey-Hailey Disease.** Bar Ilan E, Koren A. Shehadeh W., Mashiah J., Sprecher E., Artzi O. Pub. list # 10
The use of drug delivery system combined with topical rapamycin has no adverse effects, improves the results of PDL treatment for port wine stains, and can reduce the total number of required PDL sessions.	**Treatment of Port Wine Stain with Tixel Induced Rapamycin Delivery Followed by Pulse Dye Laser Application.** Ofir Artzi, Jos N. Mehrabi, Lee Heyman, Or Friedman, Jacob Mashiah. Pub. list # 11

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ORIGINAL PAPER

DERMATOLOGIC THERAPY WILEY

An enhanced transcutaneous delivery of botulinum toxin for the treatment of Hailey–Hailey disease

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Abstract

Successful treatment of Hailey–Hailey disease with intradermal botulinum toxin injections has been previously reported. The main disadvantages of this treatment are the excruciating pain and the risk of infections due to the numerous injections. We sought to evaluate the clinical effectiveness and safety profile of a novel approach using an energy-based device (Tixel, Novoxel, and Israel), followed by the topical application of botulinum toxin Type A for the treatment of Hailey–Hailey disease. A retrospective study of all cases of histologically diagnosed cases of Hailey-Hailey disease treated with Tixel device followed by topical application of botulinum toxin between 2018 and 2019 was performed. Epidemiologic, clinical, and treatment data, including effectiveness score and safety, were reviewed. The study included eight patients, of whom seven patients (87.5%) showed good or partial response. No systemic or local adverse effects were reported. There was no difference in effectivity between different body areas. Response to treatment ranged between patients with an average duration of 7.125 months after the second treatment. Tixel treatment followed by topical application of botulinum toxin can be considered in the treatment of Hailey–Hailey disease. This approach is less invasive, less painful, and yet effective as well as safe.

KEYWORDS
botulinum toxin, drug delivery, Hailey–Hailey disease

1 | INTRODUCTION

Hailey–Hailey disease or familial benign chronic pemphigus, first described in 1939 (Hailey & Hailey, 1939), is a rare chronic genetic blistering dermatosis, primarily involving the intertriginous areas, presenting with flaccid vesicles that can easily rapture, macerated fissured skin with chronic moist and vegetation (Burge, 1992), pain and malodor, significantly impairing patients' quality of life. The current treatment modalities comprise of corticosteroids, topical antimicrobials, oral antibiotics, laser ablation, photodynamic therapy, electron beam radiotherapy, dermabrasion, glycopyrrolate, afamelanotide, naltrexone, and botulinum toxin Type A (Campbell, McGrath, & Corry, 2018; Chiaravalloti & Payette, 2014; Farahnik et al., 2017; Kollman & Bass, 2018). Unfortunately, the disease is difficult to control and is recalcitrant to conventional therapies.

Treatment with botulinum toxin was first described in 2000 (Lapiere, Hirsh, Gordon, Cook, & Montalvo, 2000) with promising, several months lasting, results (Charlton, Stewart, & Rosen, 2018; Friedman, Koren, Niv, Mehrabi, & Artzi, 2019; Kothapalli & Caccetta, 2019). The main disadvantages of this treatment are the high cost of the toxin and the excruciating pain as well as the risk of infections due to the numerous needle punctures. Unfortunately, the skin barrier prevents the absorption of botulinum toxin while applied topically. Our case series study describes the clinical effectiveness and safety profile of a novel approach using an energy-based device (Tixel, Novoxel, and Israel) that thermally decomposes the stratum corneum,

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ORIGINAL PAPER

DERMATOLOGIC THERAPY WILEY

Treatment of port wine stain with Tixel-induced rapamycin delivery following pulsed dye laser application

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Abstract

Although pulsed dye laser (PDL) is considered the gold standard treatment for port wine stains (PWS), post PDL revascularization is one of the main causes of incomplete regression and recurrence. Recently, topical sirolimus have been shown to improve treatment outcome probably through minimizing post-laser revascularization. We sought to evaluate the added value of the Tixel drug delivery system (DDS) to the PDL and topical rapamycin treatment for PWS. This case series includes three teenager patients with previously treated PWS with PDL. Upon enrollment, every stain was divided into A and B halves for treatment assignments to the following regimens: (A) PDL + DDS + rapamycin; (B) PDL + rapamycin. Subjects were instructed to apply rapamycin topically over the PWS twice daily for the entire treatment period. Assessment of the treatment and adverse reactions as well as photographs was performed at baseline and before every PDL treatment. There were clinically significant differences in blanching responses favoring PWS receiving PDL + DDS + rapamycin as compared to PDL + rapamycin alone. Transient hyperpigmentation was noted in one patient. Two patients developed mild transient irritation and dermatitis following the treatment on both halves. The use of drug delivery system combined with topical rapamycin has no remarkable adverse effects, improves the results of PDL treatment for port wine stains, and can reduce the total number of required PDL sessions.

KEYWORDS
drug delivery, port wine stain, pulsed dye laser, rapamycin, Tixel

1 | INTRODUCTION

Port wine stains (PWS) are congenital cutaneous vascular malformations, affecting approximately 0.3% of newborns, occurring as an isolated vascular malformation, or in association with capillary malformation syndromes (Kalick, Goldwyn, & Noe, 1981). They do not regress with age and in some cases may enlarge, darken, and develop thickening and hypertrophy of the surrounding soft tissue (Kalick et al., 1981; Lanigan, 1998; Nelson, Jia, Phung, & Mihm, 2011). Pulsed dye laser (PDL) remains the gold standard treatment of PWS (Griffin, Foshee, Finney, & Saedi, 2016). While it is very effective at producing initial lightening of PWS lesions, post PDL revascularization contributes to frequent recurrence and treatment failure. Resolution of PWS, as defined by persistent blanching of the lesion, is reported in less than 10–20% of cases. The revascularization is postulated to occur through post-laser angiogenesis via the induction of hypoxia inducible factor-1a (HIF-1a) and VEGF pathways (Anderson & Parrish, 1983; Chowdhury, Harris, & Lanigan, 2001; Frohm Nilsson, Passian, & Wiegleb Edstrom, 2010; Goldman, Fitzpatrick, & Ruiz-Esparza, 1993; Sajan et al., 2013; Scherer, Lorenz, Wimmershoff, Landthaler, & Hohenleutner, 2001; Tan et al., 1986; van der Horst, Koster, de Borgie, Bossuyt, & van Gemert, 1998). Sirolimus (rapamycin), a

Tixel in scientific publications - cont.

Key findings	Publications
Tixel may be used safely for ablative and non-ablative resurfacing with low pain, low downtime, and quick healing. Subject's satisfaction was 75% and wrinkle attenuation was achieved in 75% of the cases. There was no incidence of bleeding, scarring, or post-inflammatory hyperpigmentation.	**Fractional Treatment of Aging Skin with Tixel, a Clinical and Histological Evaluation**. Monica Elman, Nathalie Fournier, Gilbert Barnıon, Eric F. Bernstein and Gary Lask. Pub. list # 12
A resonating thermo-mechanical array of high temperature (350 – 400°C) rods is capable of producing an array of craters identical to those produced with pulsed CO2 lasers.	**Fractional vaporization of tissue with an oscillatory array of high temperature rods – Part I: *Ex vivo* study** GARY LASK MD, MONICA ELMAN MD , NATHALIE FOURNIER, MD & MICHAEL SLATKINE, PhD Pub. list # 13

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JOURNAL OF COSMETIC AND LASER THERAPY
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CASE REPORT

Fractional treatment of aging skin with Tixel, a clinical and histological evaluation

Monica Elman[1], Nathalie Fournier[2], Gilbert Barnéon[3], Eric F. Bernstein[4], and Gary Lask[5]

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ABSTRACT
Objective: This study presents clinical results of Tixel, a new fractional skin resurfacing system based on thermo-mechanical ablation technology. Tixel employs a hot (400°C) metallic tip consisting of 81 pyramids. Treatment is performed by rapidly advancing the tip to the skin for a preset tip–skin contact duration. Thermal energy transfer to the skin creates micro-craters by evaporation. **Methods:** Treatment results with tip types, D and S, with high and low thermal conductivity, were evaluated. Twenty-six subjects received three facial treatments, with 4–5-week intervals between treatments, without analgesia or cooling. In addition, histopathologies of Tixel and CO_2 laser were performed. **Results:** Crater properties are related to contact duration and to thermal conductivity. The D tip created char-free ablative craters 100–320 μm wide with a thermal zone 100–170 μm deep. The S tip created non-ablative coagulation preserving the epidermis. Skin complexion improvement was achieved in all subjects; average treatment pain of 3.1/10, downtime of 0–1 days, and erythema clearance of 3.5 days. Subject's satisfaction was 75% and wrinkle attenuation was achieved in 75% of the cases. There was no incidence of bleeding, scarring, or post-inflammatory hyperpigmentation. **Conclusions:** Tixel may be used safely for ablative and non-ablative resurfacing with low pain, low downtime, and quick healing.

ARTICLE HISTORY
Received 9 December 2014
Accepted 12 April 2015

KEYWORDS
Ablation; fractional; resurfacing; skin rejuvenation; thermal model

Introduction

Fractional laser resurfacing technologies are widely used in dermatology. Short-pulse CO_2 lasers are generally considered to be among the best modalities for high-precision ablation of thin tissue layers without bleeding and with minimal collateral damage (1). They are widely utilized in skin fractional skin resurfacing (2,3) for improved skin texture and fine wrinkles. Treatment is painful, requiring pre-application of analgesic creams and protective eyewear. Downtime is about 5 days. With a penetration depth of only 30–50 μm by the 10.6-μm wavelength laser beam into tissue, it is possible to vaporize crater arrays of skin down to the papillary dermis or deeper, and achieve excellent skin resurfacing results. With an array of –100–250 μm focused beam spots, fractional resurfacing of –12–20% of the skin surface ensures fast healing. The energy responsible for vaporization of tissue with a CO_2 laser is purely thermal. In the vaporization process, the temperature produced by a single-pass laser beam attains –350–400°C in the crater (4).

Since thermal energy causes tissue vaporization, one may expect that by bringing a metallic element having high thermal conductivity, heated to a temperature of –350–400°C, in contact with the skin for a duration of a few milliseconds and a depth of –50–150 μm, an ablative effect which is clinically identical to the CO_2 laser effect will occur.

The objective of the current article is to present a novel thermo-mechanical ablation (TMA) technology and to show clinical and histopathology data using the Tixel device. A comparison to fractional CO_2 laser histology is also provided.

Materials and methods

The Tixel

The Tixel (Novoxel, Germany) is a thermo-mechanical system for fractional ablation. It applies a tip, made of metallic, gold-plated biocompatible materials (Figure 1A). The tip is fixated at the distal section of the Tixel's handpiece which is equipped with a linear motor (Figure 1B). The tip's active surface consists of an array of 81 (9 × 9) pyramids evenly spaced within

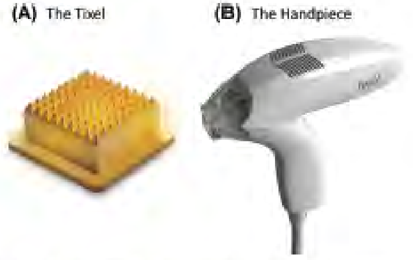

Figure 1. (A) D and S types of Tixel pyramidal tip array. (B) Tixel handpiece.

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Monica Elman and Nathalie Fournier are equal contributors to this paper.
Color versions of one or more of the figures in the article can be found online at http://www.tandfonline.com/ijcl

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ORIGINAL RESEARCH REPORT

Fractional vaporization of tissue with an oscillatory array of high temperature rods – Part I: *Ex vivo* study

GARY LASK[1], MONICA ELMAN[2], NATHALIE FOURNIER[3] & MICHAEL SLATKINE[4]

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Abstract
Background: Short pulse duration (–0.1–5 milliseconds) CO2 lasers are perceived as excellent tools for vaporization of craters arrays in fractional skin resurfacing. *Objectives:* To present a thermo-mechanical ablation technology, which affects tissue identically to fractional CO2 lasers, however at a fraction of the size and cost of a laser. *Material and methods:* The new technology is based on heating an oscillating array of thin metallic rods to a temperature of 400°C and advancing the rods into tissue down to a precise pre-selected depth for a duration of 0.1–5 milliseconds. As a result, an array of crater is vaporized with identical properties of those produced by CO2 lasers. An *ex vivo* test was performed with a thermo-metallic rod array prototype. *Results:* Arrays of 10 × 10 vaporized micro-craters of 350 micron diameter, 200 micron depth have been produced with lateral thermal damage of 80 micron while thermal damage below craters was 80–250 micron. *Conclusions:* A resonating thermo-mechanical array of high temperature (350–400°C) rods is capable of producing an array of craters identical to those produced with pulsed CO2 lasers.

Key Words: *skin resurfacing, CO2 lasers, fractional, wrinkles*

Introduction

Short pulse CO2 lasers are generally considered among the best tools for high precision ablation of thin layers of tissue without bleeding and with minimal collateral damage (1). They are widely utilized in skin resurfacing, including fractional skin resurfacing (2,3). By operating a 10.6 micron CO2 laser with energy density above a threshold of –5 J/cm² and pulse duration below few milliseconds (0.1–5 milliseconds), vaporization rate is faster than thermal diffusion into tissue and collateral thermal necrosis is –100–150 micron. With only 30–50 micron penetration of the 10.6 micron wavelength laser beam into tissue, it is possible to vaporize craters arrays of skin down to or deeper than the papillary dermis and achieve excellent skin resurfacing results. With an array of –100–500 micron focused beam spots, fractional resurfacing of –12–20% of the skin surface ensures fast healing. The energy responsible for the vaporization of tissue with a CO2 laser is purely thermal. The tissue parameters, which quantitatively dictate the threshold energy for vaporization with only 100–150 micron collateral damage, are the vaporization energy of tissue which is –3000 J/cm³ (4) and the beam penetration in tissue (30–50 micron). In the vaporization process, temperature craters produced by a single pass laser beam attain –350° C (5).

Since thermal energy is responsible for tissue vaporization, we may expect that by bringing a metallic element of temperature –350° C in contact with the skin for a duration of less than –0.1–5 milliseconds and depth –50–250 micron, a clinical ablative effect which is identical to the CO2 laser effect will occur. However, such extremely fast and accurate thermo-mechanical procedure with a 350° C array enclosed in a small size comfortable handpiece requires very specific geometrical, mechanical and thermal design, which has recently been developed in our laboratory. The objective of the current article is to describe the general design principles a the new 'ThermiXel' thermo-mechanical technology, which acts identically to a short pulse CO2 laser and can be used in a variety of surgical applications including fractional skin resurfacing. The advantage of the

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ASLMS 2020 Abstracts

Key findings	Pending Publications
The thermo-mechanical fractional ablative device is safe and effective for the treatment of peri-orbital lines and laxity in Asian.	**A Prospective Study of the Safety and Efficacy of a Thermo-Mechanical Fractional Ablative Device for Periorbital Rejuvenation in Asians.** Kwankamol Woottisheattapaiboon, M.D., Woraphong Manuskiatti, M.D., Nudpanuda Tevechodperathum, M.D. Pub. list # 14

A Prospective Study of the Safety and Efficacy of a Thermo-Mechanical Fractional Ablative Device for Periorbital Rejuvenation in Asians

Kwankamol Woottisheattapaiboon, M.D., Woraphong Manuskiatti, M.D., Nudpanuda Tevechodperathum, M.D.

Department of Dermatology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand

Background: Demand for noninvasive procedure to correct the unattractive feature of peri-orbital area is increasing because of the popularity of aesthetic medicine. However, data on the safety and efficacy of noninvasive procedures for treatment of periorbital photo-damaged skin in Asians are limited.

Objective: This prospective, self-controlled study was conducted to evaluate the safety and efficacy of a thermo-mechanical fractional ablative device for the treatment of photo-damaged peri-orbital skin in Asians.

Materials and Methods: Twenty females (mean age of 48.7 years old) with skin type IV with peri-orbital line and laxity were enrolled. All subjects were treated with a fractional thermo-mechanical device (a tip protrusion of 400 µm and a pulse duration of 10 milliseconds), every 4 weeks for a total of 5 treatments. Objective (measurement of skin color and roughness using 3D photography and skin elasticity analysis using cutometer) and subjective [evaluated using the Physician Global Aesthetic Improvement Scale (GAIS) by two blinded dermatologists] assessments were obtained at baseline and at 1 and 3 months after the final treatment.

Results: GAIS assessments at 3 months after the last treatment indicated that 55.6%, 22.2% and 11.1% of the subject showing improvement, much improvement and very much improvement of their peri-orbital wrinkles and laxity, respectively. Improvement progressed significantly from 1- to 3-month follow-up. There was statistically significant brown lift ($P<.001$), comparing between baseline and 3 months after the final treatment. Reductions in periorbital indentation and wrinkles corresponded to clinical evaluation. Mild-moderate post-inflammatory hyperpigmentation (PIH) was observed in 22% of the subjects. All PIH was temporary and resolved on an average of 4 weeks.

Conclusions: The thermo-mechanical fractional ablative device is safe and effective for the treatment of peri-orbital lines and laxity in Asian.

Publication Pending

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ASCRS 2020 Abstract (to be published)

Key findings	Pending Publication
Tixel treatment significantly improves clinical signs and symptoms of dry eye and it is a proven technology for dry eye treatment. Patients impression of Tixel was subjectively better than testing revealed and quite impressive compared to IPL treatments.	A Prospective Study Assessing the Impact of Tixel, a Novel Treatment on Dry Eye Symptoms and Signs. Sunil Shah, Debarun Dutta, Ludger Hanneken, Marisa Martins, Toni Qualey, Mukesh Taneja, Shehzad Naroo

Publication Pending

NoVoxel®

Case Reports

Key findings	Publications
Anti-aging and rejuvenation users know about the difficulties of treating the neck and décolleté. This alternative treatment method shows an impressive response of the areas to be treated. As a side effect, it was also shown that the skin cells in the area of the vitiligo sites are activated. This should be discussed through further case reports in medicine and aesthetics and supported by studies, so that thermomechanical infiltration could possibly be used more frequently.	**The neck doesn't lie - Tixel® the safe and low-risk treatment option for the treatment of wrinkles in the neck area: Case Report** Dr. med. Arna Shab[1], Dr. med. Catharina Shab[1] [1]Private practice for dermatology and aesthetic medicine, Frankfurt am Main

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Neurotoxins and dermal Fllers are the foundations of all aesthetic medical practice. However, to be able to truly reverse the effect of photodamage and skin ageing, skin resurfacing treatment is often needed. Tixel is a new skin resurfacing device that has largely taken over from deep chemical peels and fractional CO2 laser in my practice. So far, I have been very impressed with the device; the results are pleasing to the patients and the side effects appear to be minimal.	**Treating Severe Photo ageing** **Dr. Harryono Judodihardjo**

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Thank you

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