SYLFIRM X

Clinical Paper Summary

Victory of Life ViOL

[redacted] VIOL-0000021(

Serendia, LLC
Exhibit 2044
EndyMed v. Serendia
IPR2024-00842
Ex. 2044-001

Clinical Papers of ViOL's RF Microneedling Systems

Clinical Paper

	Continuous Wave	Pulsed Wave	300㎛
Skin Reaction	1	1	
Pigmented Lesion		6	1
Vascular Lesion		2	
Skin Rejuvenation	4	3	
Scar		1	
Acne	5	1	
Etc			
Total	10	14	1

Total 24

Updated in Jan 2022

Outline

Continuous Wave

- Skin Reaction: Na Effect _4
- Skin Rejuvenation _5
- Acne _10

Pulsed Wave

- Skin Reaction _15
- Pigmented Lesion _17
- Vascular Lesion _25
- Skin Rejuvenation _27
- Scar _30
- Acne_31

300μm

- Pigmented Lesion _32

❖ Frequently mentioned articles are marked with a star sign.

Skin Reaction: Na Effect



Electromagnetic Initiation and Propagation of Bipolar Radiofrequency Tissue Reactions via Invasive Non-Insulated Microneedle Electrodes SCI(E) SCOPUS

By Jongju Na, Zhenlong Zheng, Christopher Dannaker, Sang Eun Lee, Jin-Soo Kang, and Sung Bin Cho
Scientific Reports, 2015, 5, 16735:
http://doi.org/10.1038/srep16735

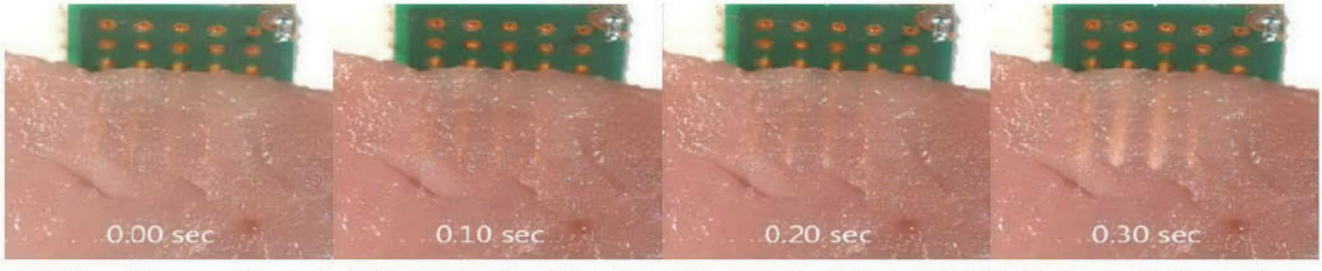
Methods

- For an experimental study of RF tissue reactions, bipolar RF energy with non-insulated microneedle electrodes (CELFIRM; ViOL) were emitted to in vivo/ex vivo micropig skin and ex vivo bovine liver tissue at varying microneedle penetration depths, RF signal amplitudes, and RF conduction times.

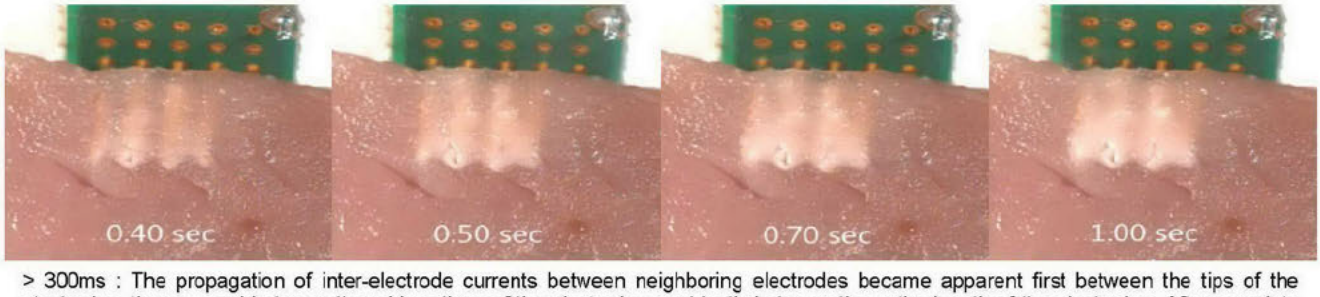
Results

- It was found in both micropig skin and bovine liver tissue that coagulation was initiated at the tip of each needle electrode when bipolar RF is transmitted to the tissue through non-insulated needles .
- As the conduction time increased, the coagulation expanded into a droplet or cocoon shape with relatively few thermal effects on the epidermis. "Na Effect"

Bipolar RF with non-insulated microneedles irradiated on Ex vivo micropig skin ay 50V, 0-7 seconds
Captured by high-speed cinematography



< 300ms : Tissue reactions were initiated at the tips of the microneedle electrodes that penetrated into the tissues. As the reactions propagated up from the tips of the microneedle electrodes, they expanded to deeper, wider, and higher areas around the microneedle. After a brief delay, the reactions continued to move upward around the body of the microneedle electrode and expand laterally.



> 300ms : The propagation of inter-electrode currents between neighboring electrodes became apparent first between the tips of the electrodes, then second between the mid-portions of the electrodes, and lastly between the entire length of the electrodes. After complete convergence of all individual coagulation areas, tissues then began to show vaporization and carbonization.

VIOL-00000219
Ex. 2044-004
CX-2855C.4

Continuous Wave: Skin Rejuvenation



Comparison of efficacy and safety of fractional radiofrequency and fractional Er:YAG laser in facial and neck wrinkles: Six-year experience with 333 patients SCI(E) SCOPUS

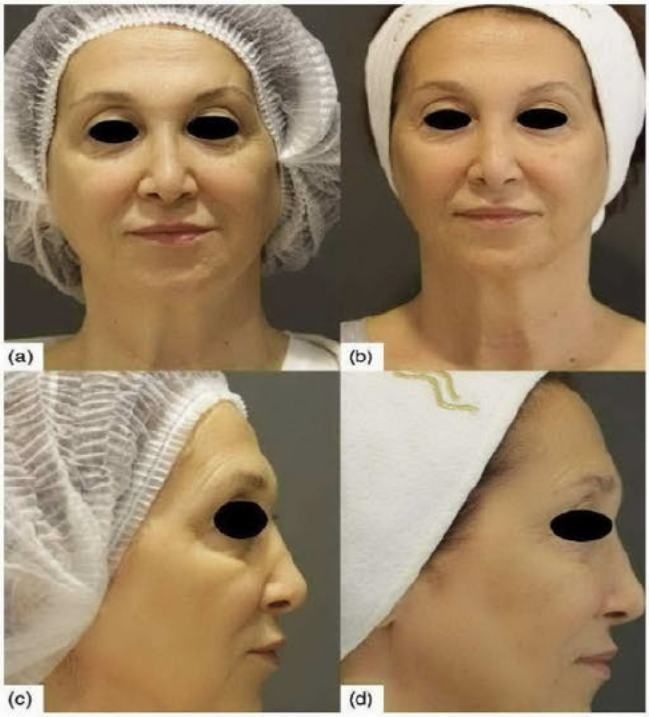
By Zehra A Serdar, and Asli Tatliparmak
Dermatologic Therapy, 2019, 32(5), e13054:
http://doi.org/10.1111/dth.13054

Methods

- 333 patients with facial wrinkles were treated with fractional RF (SCARLET; ViOL) and fractional Er:YAG laser for skin rejuvenation.
  - Patients: aged between 36 and 85 years, mean age of 49.8+7.9 years
  - 133 patients for fractional RF and 200 patients for fractional Er:YAG
  - Fractional RF: F(face) mode, power 8, intensity of 50-70mJ, 1.0-1.5mm on periorbital area, 2.0-2.5mm on nasolabial, jaw line and perioral area, 3.0-3.5mm on submental and neck area
  - Fractional Er:YAG laser: PSO3 handpiece, short pulse mode, 40-50J/cm2, 10hz on periorbital area / F-runner handpiece, short pulse mode, 40-50J/cm2, 10hz on nasolabial, jawline and perioral area / R11 handpiece, smooth mode, 2J/cm2, 10hz on submental and neck area
  - 3 treatment sessions at one month intervals

Results

- Fractional RF treatment was more effective for perioral, nasolabial, jawline, neck areas whereas fractional Er:YAG laser treatment was more effective for the periorbital areas.
- There are no statistically significant difference in side effects between two treatment groups.



(A), (C) Before
(B), (D) 2 months after 3 sessions of fractional RF treatment



(A), (C) Before
(B), (D) 2 months after 3 sessions of fractional Er:YAG treatment

VIOL-00000220

Ex. 2044-005

CX-2855C.5

Continuous Wave: Skin Rejuvenation



Clinical Study of Facial Wrinkle Treatment with Fractional Microneedle Radio Frequency System
By Hyoun Jun Park, Hyoung Moon Kim, and Myung Jin Oh
Medical Lasers, 2014, 3(2), 59-64:
http://doi.org/10.25289/ML.2014.3.2.59

Methods

- 204 Korean patients with facial wrinkles at 3 study centers, were treated with fractional microneedle RF system (SCARLET; ViOL).
  - Patients: 80 male, 124 female; mean age of 47.3 years, ranging from 26 to 68 years, Fitzpatrick skin type III-IV
  - Treatment: 0.8-3.0mm, level 6-8, 100-200ms, 1-3 passes for 1-3 sessions at average 4-week intervals

Results

- Of 204 patients, 54 had near total improvements (>75%), 86 had marked improvement (51-75%), 50 had moderate improvement (26-50%), and 14 had minimal improvement (0-25%).
- Mild post-inflammatory hyperpigmentation was found in only 2 patients, which spontaneously resolved within one month.



(A) Baseline
(B) 2 months after 2 sessions of fractional RF treatment



(A) Baseline
(B) 3 months after 3 sessions of fractional RF treatment



(A) Baseline
(B) 2 months after 2 sessions of fractional RF treatment

[redacted]

Continuous Wave: Skin Rejuvenation



Skin rejuvenation by microneedle fractional radiofrequency and a human stem cell conditioned medium in Asian skin: a randomized controlled investigator blinded split-face study

SCOPUS

By Kyu Young Seo, Dong Hyun Kim, Sang Eun Lee, Moon Soo Yoon, and Hee Jung Lee

Journal of Cosmetic and Laser Therapy, 2013, 15(1), 25-33: http://doi.org/10.3109/14764172.2012.748201

Methods

- 15 female patients with various signs of aging such as visible lines, wrinkles and widened pores, were treated for a split-face study with microneedle fractional RF (SCARLET; ViOL) and stem cell conditioned medium.
  - Patients: ranging from 41 to 64 years, mean age 53.8±3.21, Fitzpatrick skin types III-IV
  - One side: RF treatment alone (plus 1.5ml of normal saline)
  - The other side: RF plus stem cell conditioned medium
    - RF treatment : a single, non-overlapping pass
    - Stem cell conditioned medium: 1.5ml of hESC-EPC CM (conditioned medium of human embryonic stem cell – derived endothelial precursor cells) *including epidermal growth factor (EGF), fibroblast growth factor-2 (FGF-2), fractalkine, granulocyte macrophage colony stimulating factor (GM-CSF), interleukin-6(IL-6), platelet derived growth factor-AA (PDF-FAA) and vascular endothelial growth factor (VEGF)
  - 3 sessions every 4 weeks

*

Results

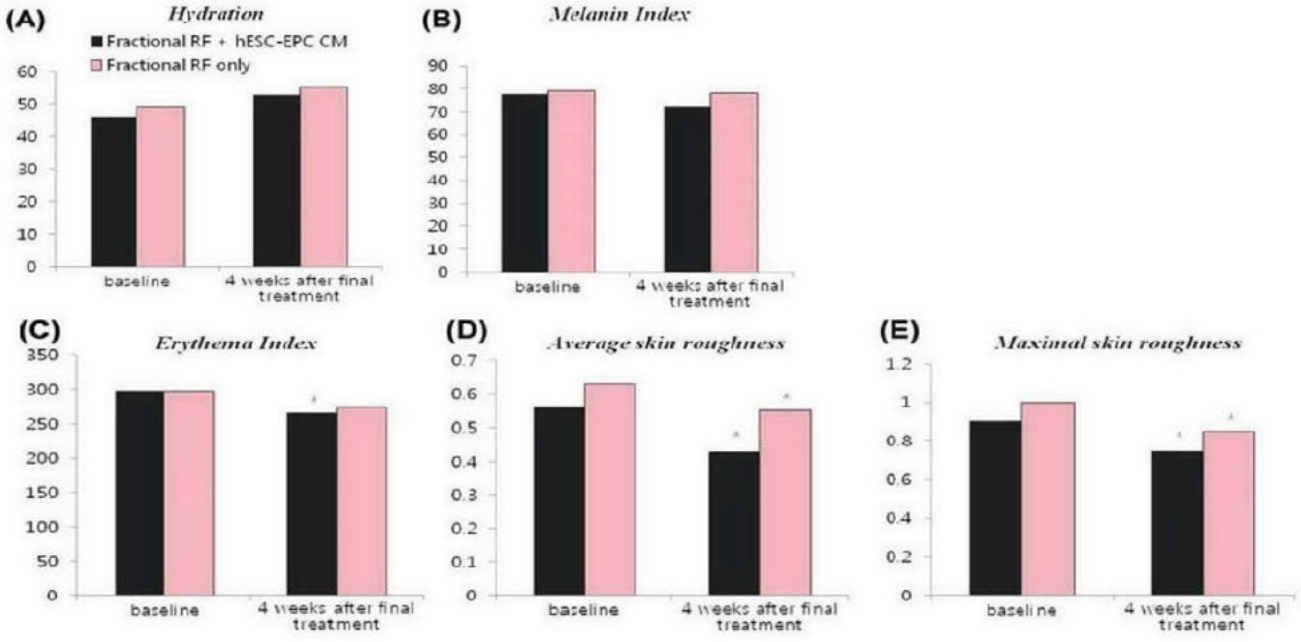
- All patients showed clinical improvement on physician's global assessment and patient satisfaction scores on both sides of their faces.
- Among objective biophysical measurements, improvement in hydration, melanin, erythema index and especially skin roughness was noticed.
- Stem cell conditioned medium provided a synergistic effect on improvements of skin roughness, which was statistically significant.
- Histologic examination revealed marked increase in dermal thickness and dermal collagen content.
- Side effects were minimal.

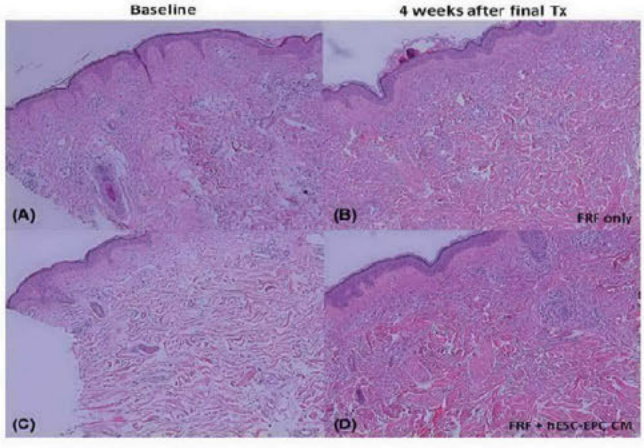
VIOL-00000222

Ex. 2044-007

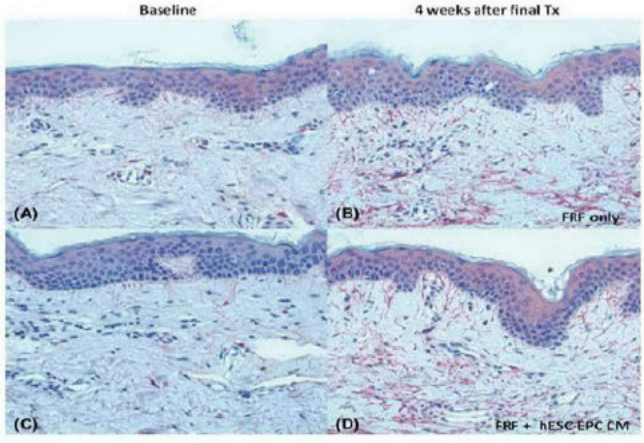
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Continuous Wave: Skin Rejuvenation

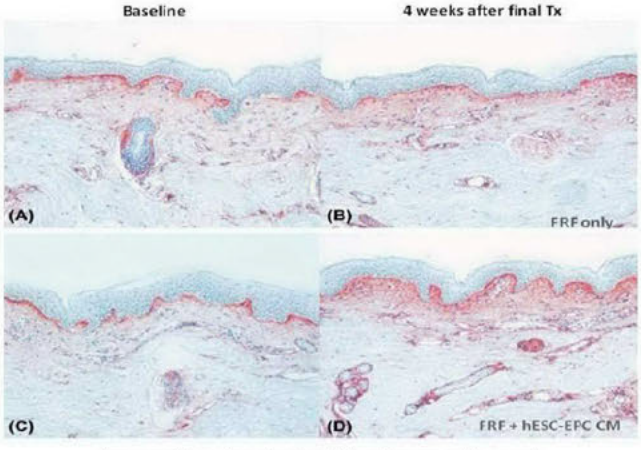




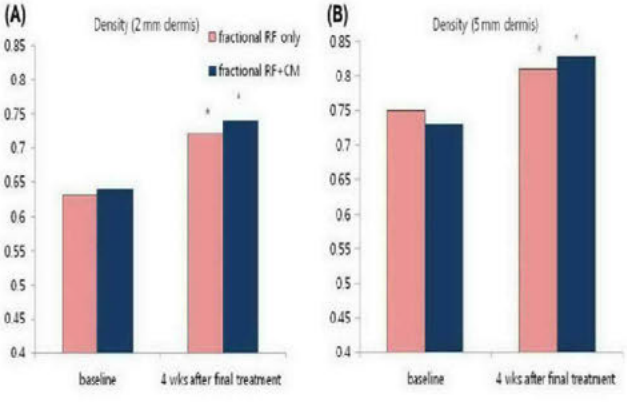
Dermal remodeling and neocollagenesis after microneedle fractional radiofrequency in H & E stain



Immunohistochemical staining for fibrillin-1



Immunohistochemical staining for procollagen-1



Quantitative assessment of the density of procollagen within 0.2mm and 0.5mm of dermis from basement membrane

VIOL-00000223

Ex. 2044-008

CX-2855C.8

Continuous Wave: Skin Rejuvenation



Skin rejuvenation by microneedle fractional radiofrequency treatment in Asian skin: clinical and histological analysis

SCI(E) SCOPUS

By Kyu Young Seo, Moon Soo Yoon, Dong Hyun Kim, and Hee Jung Lee

Lasers in Surgery and Medicine, 2012, 44(8), 631-636:

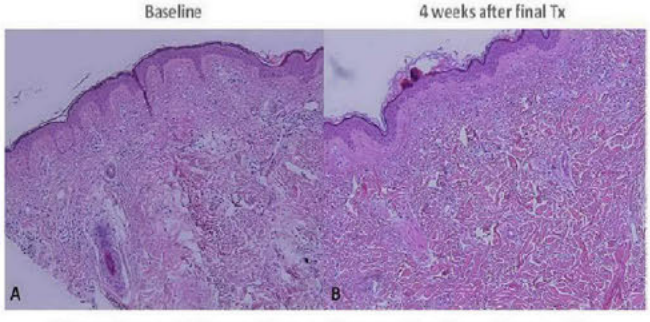
http://doi.org/10.1002/lsm.22071

Methods

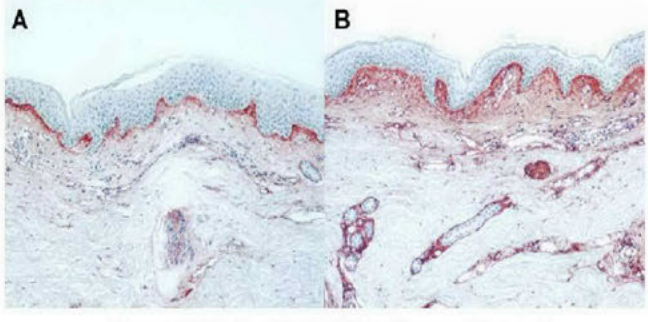
- 25 female patients with various signs of aging such as visible lines, wrinkles, and widened pores, were treated with fractional RF device (SCARLET; ViOL).
  - Patients: ages from 41 to 64 years, mean age 54.2±3.21, Fitzpatrick skin types III and IV
  - Treatment: a single pass, no-overlapping over the indicated area, 0.5mm on periorbital area, 0.8mm on forehead, 1mm on chin and temple, 2mm on cheeks
  - 3 sessions every 4 weeks

Results

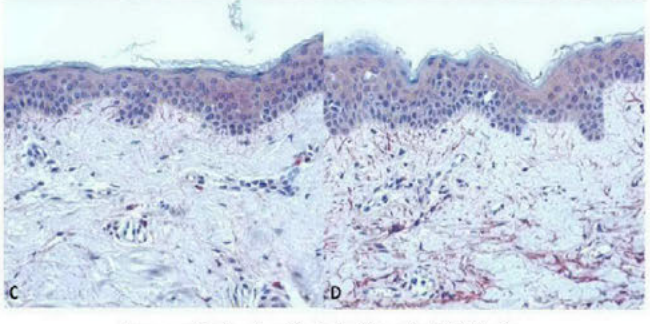
- All patients showed clinical improvement on physician's global assessment and patient satisfaction scores.
- Among objective biophysical measurements, improvement in hydration and skin roughness was noticed.
- Histological examination revealed marked increase in dermal thickness, dermal collagen content and dermal fibrillin content.
- Side effects were minimal.



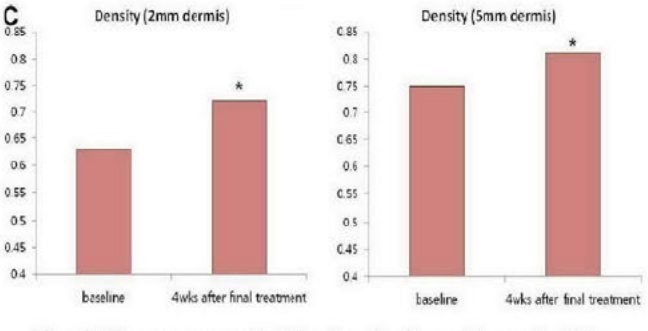
Dermal remodeling and neocollagenesis after microneedle fractional RF in H&E stain



Immunohistochemical staining for procollagen-1



Immunohistochemical staining for fibrillin-1



Quantitative assessment of the density of procollagen-1 within 0.2mm and 0.5mm of dermis from basement membrane

VIOL-00000224

Ex. 2044-009

CX-2855C.9

Continuous Wave: Acne



Safety of Combined Fractional Microneedle Radiofrequency and CO_2 as an Early Intervention for Inflammatory Acne and Scarring Treated With Concomitant Isotretinoin SCI(E) SCOPUS

By Jihee Kim, Young In Lee, Jemin Kim, Jin Young Jung, Won Jai Lee, and Ju Hee Lee

Dermatologic Surgery, 2020, 46(10), e71-e77:
http://doi.org/10.1097/DSS.0000000000002364

Methods

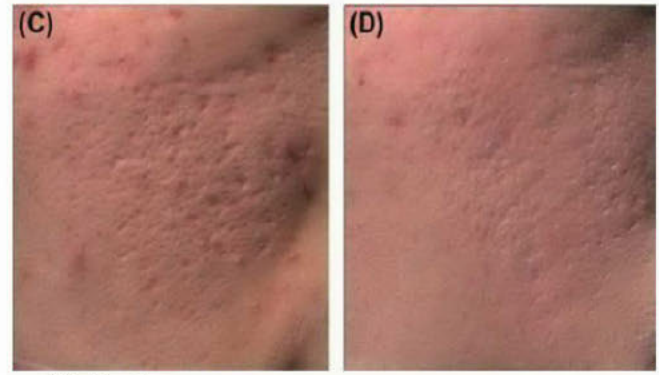
- 71 patients with inflammatory acne and acne scars received combination treatment with fractional microneedling radiofrequency (FMRF) (SCARLET; ViOL) and CO_2 ablative fractional laser (AFL).
  - Patients: 33 men and 38 women, mean age of 24.8 years, ranging from 19 to 38 years, Fitzpatrick skin types II to IV, Korean
  - 43 patients with inflammatory lesions and 28 patients with scars only
  - FMRF: 2.0-2.8mm, intensity 8-10 with a density of 25 microscopic treatment zones (MTZ)s/cm²
  - AFL: 100mJ with a density of 100 MTZs/cm², which correlates with 15.6% coverage and an ablation depth of 1,168 μm
  - Average 3.31 treatments at every 4-6 weeks
- For 43 of the 71 patients, concomitant treatment were conducted with systemic isotretinoin during the intervention or discontinued treatment within 3 weeks.

Results

- The mean scar global assessment score significantly decreased after combination treatment.
- Patients with inflammatory acne showed a significant decrease in the number of inflammatory lesions.
- Patients with concomitant low-dose isotretinoin use reported a further decrease in scar global assessment score.
- There were no reported persistent side effects, including prolonged inflammatory reaction or scarring.



(A) Baseline
(B) 4 months after 3 sessions of combination FMRF and AFL treatment while continuing systemic isotretinoin



(A) Baseline
(B) 4 months after 3 sessions of combination FMRF and AFL treatment while continuing systemic isotretinoin

VIOL-00000225

Ex. 2044-010

CX-2855C.10

Continuous Wave: Acne



The Efficacy and Safety of Bipolar Radiofrequency Treatment with Non-Insulated Penetrating Microneedles for Acne Vulgaris and Acne Scars

By Ganesh S. Pai, Mouhamad Kashmar, Young Koo Kim, and Jongju Na

Medical Lasers, 2015, 4(1), 10-15:

http://www.doi.org/10.25289/ML.2015.4.1.10

Methods

- 316 patients with moderate to severe acne vulgaris and/or mild to severe acne scarring, were treated with bipolar non-insulated microneedle RF (SCARLET; ViOL) treatment.
  - Patients: 195 males and 121 females, ages ranging from 18-34 years, mean age of 28.2, Fitzpatrick skin types IV-V, 119 patients from India, 109 patients from Saudi Arabia and 88 patients from Korea
  - Treatment: 300ms, 3mm, intensity 7, 2 passes over the entire face, additional pass to severe pustular lesions and/or acne scars
  - 2-4 sessions at 1-month interval

Results

- Clinical assessment revealed minimal improvement (0-25%) in 21 patients, moderate improvement (26-50%) in 78 patients, marked improvement (51-75%) in 133 patients and near total improvement (>75%) in 84 patients.
- Temporary aggravation of acne vulgaris or folliculitis, which spontaneously resolved within 3 weeks, was noted in 9 patients. Otherwise, no remarkable side effects were recorded.









Continuous Wave: Acne



Use of fractionated microneedle radiofrequency for the treatment of inflammatory acne vulgaris in 18 Korean patients SCI(E) SCOPUS

By Sang Ju Lee, Ja Woong Goo, Jaeyong Shin, Won Soon Chung, Jin Moon Kang, Young Koo Kim, and Sung Bin Cho
Dermatologic Surgery, 2012, 38(3), 400-405:
http://doi.org/10.1111/j.1524-4725.2011.02267.x

Methods

- 18 patients with moderate to severe acne vulgaris, were treated with fractionated microneedle RF (SCARLET; ViOL).
  - Patients: 15 male and 3 female, mean age 2.39, ranging from 19-33, Fitzpatrick skin type IV
  - Treatment: 100(off)–500(on)–100(off) ms, 3mm, intensity 7, 2 passes over the entire face, additional pass to sever pustular lesions
  - 2 sessions at 1-month intervals

Results

- Evaluation of improvement in terms of number of inflammatory acne lesions, showed that 2 patients had near total improvement (>75%), 8 patients had marked improvement (51-75%), and 6 patients had moderate improvement (26-50%).
- Evaluation of Improvement in terms of lesion severity showed that 1 patient had near total improvement, 8 patients had marked improvement, and 7 patients had moderate improvement .
- No patient had worsening of inflammatory acne lesions.



(A) Before
(B) 2 months after the final treatment



(A) Before
(B) 2 months after the final treatment



(A) Before
(B) 2 months after the final treatment

VIOL-00000227

Ex. 2044-012

CX-2855C.12

Continuous Wave: Acne



A split-face comparison of a fractional microneedle radiofrequency device and fractional carbon dioxide laser therapy in acne patients SCOPUS

By Jung U Shin, Soo Hyung Lee, Jin Young Jung, and Ju Hee Lee

Journal of Cosmetic and Laser Therapy, 2012, 14(5), 212-217: http://doi.org/10.3109/14764172.2012.720023

Methods

- 20 patients with acne vulgaris were treated with fractional microneedle radiofrequency (MRF) (SCARLET; ViOL) and CO_2 fractional laser system (FS) for a split-face study.
  - Patients: 9 women and 11 men, aged 15-28, Fitzpatrick skin types III-IV
  - One side: MRF treatment
  - The other side: FS treatment
    - MRF: 1.5-2.5mm, intensity 8 with a density of 25 MTZ/cm2, 2 passes
    - FS: 80mL with a density of 100 spots/cm² (15.6% coverage and an ablation depth of 1168μm), 2 passes
    - 1-2 sessions

Results

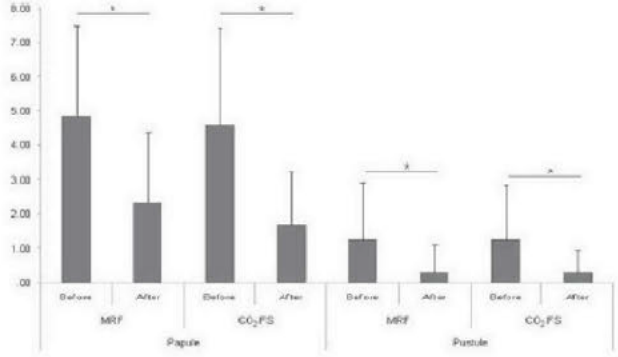
- Most of the patients improved based on clinical and photographic assessments 3 months after the treatment.
- No significant differences in physician-measured parameters, patient ratings, or intraoperative pain ratings were found, although downtime was significantly longer for the FS treated side.



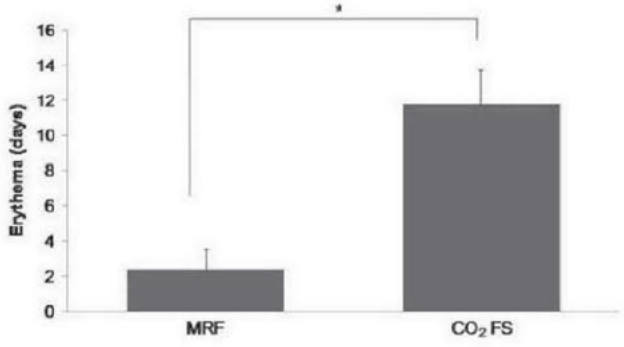
(A) Before (B) 3 months after MRF treatment



(A) Before (B) 3 months after FS treatment



The mean ±SD number of papules and pustules



The mean duration of erythema

VIOL-00000228

Ex. 2044-013

CX-2855C.13

Continuous Wave: Acne



Evaluation of the efficacy of RF microneedling and oral isotretinoin in comparison with oral isotretionoin alone in the treatment of acne vulgaris

Intisar Ahmed Hasan, Zahraa Najah Mahdi, Rana Khalid Obeed
Advances in Dermatology and Allergology/Postępy Dermatologii i Alergologii, 2022
https://doi.org/10.5114/ada.2022.124109

Methods

- 40 moderate acne patients.
  - Patients:
    - Group A : 13 females, and 7 males, 23.8 years old, 58.95 kg
    - Group B : 15 females and 5 males, 24.4 years old, 56.4 kg.
  - Treatment :
    - Group A : isotretinoin daily with an automated RF microneedling device (SCARLET; ViOL) monthly 4 times.
    - Group B : isotretinoin alone daily.

Results

- Evaluation of improvement using GAAS(global acne assessment scale) showed that Group A had better results than group B.
- After 12 weeks, group A started showing better GAAS outcomes than group B

Pulsed Wave: Skin Reaction



In vivo skin reactions from pulsed-type, bipolar, alternating current radiofrequency treatment using invasive noninsulated electrodes SCI(E) SCOPUS

By S B Cho, J Na, Z Zheng, J M Lim, J-S Kang, J H Lee, and S E Lee

Skin Research and Technology, 2018, 24(2), 318-325: https://doi.org/10.1111/srt.12433

Methods

- A pulsed-type, bipolar alternating current RF device equipped with noninsulated microneedle electrodes (SYLFIRM; ViOL), were performed on in vivo hairless mouse with 2 different settings.
  - Type A: 3 pulse cycles at a gated on-time pulse width of 40 milliseconds and a power of 3.3watts/pulse pack
  - Type B: 5 pulse cycles at an on-time pulse width of 30 milliseconds and a power of 3 watts/pulse pack
  - With 3.0mm over 1 pass without overlapping

Results

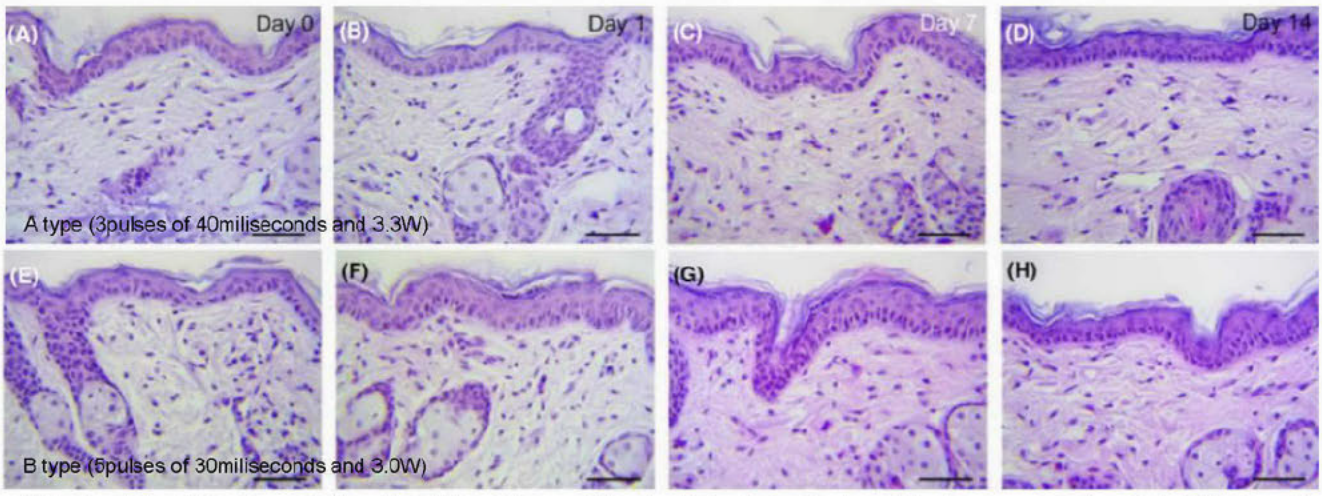
- Pulsed-type, bipolar RF energy induces structural and ultrastructural changes in basement membranes and vascular components in hair less mouse skin.
- The pulsed-type delivery of RF signal at a very short conduction time induced a resistive electrothermal response, starting from the margins of dermal components, such as basement membrane and blood vessels, just prior to the occurrence of the Na effect around each electrode.

VIOL-00000230

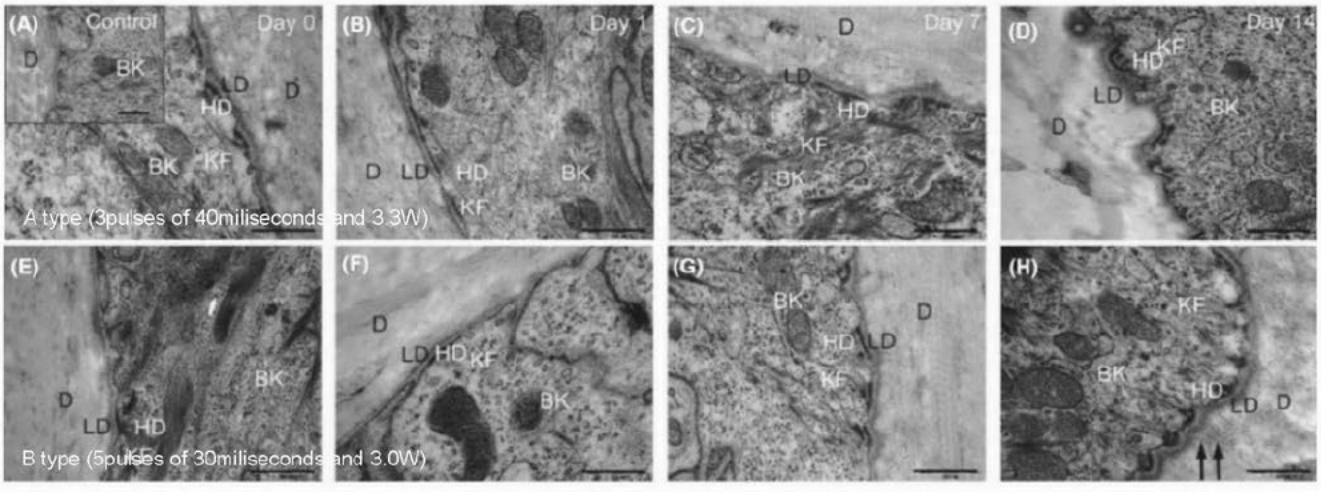
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CX-2855C.15

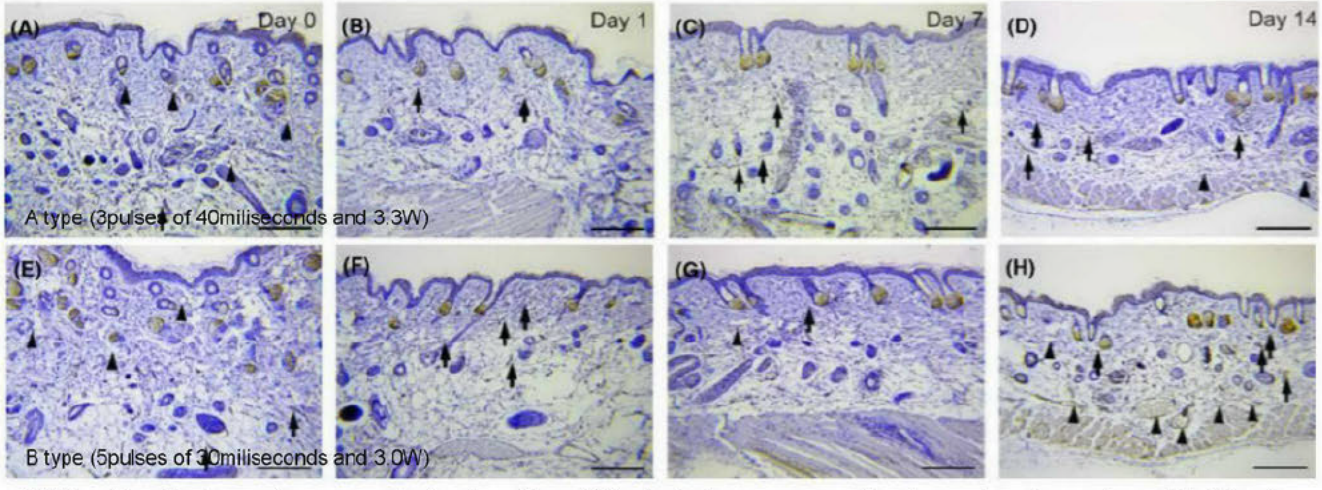
Pulsed Wave: Skin Reaction



Histochemical staining for periodic acid-Schiff and Immunohistochemical staining for type IV collagen revealed marked thickening of basement membranes. Original magnification ×400, scale bar = 50 μm



Transmission electron microscopy demonstrated that pulsed-RF treatment resulted in higher electron-dense and remarkably thicker lamina densa, as well as increases in anchoring fibrils, compared with untreated control specimens. Scale bar = 500 nm
*BK: Basal Keratinocyte *D : Dermis *HD: Hemidesmoson KF: Keratin Filament *Ld : Lamina Densa



CD31-positive blood vessels were smaller in size with a slit-like luminal appearance, without excessive damage to endothelial cells. Original magnification ×100, scale bar = 200 μm. * CD31: platelet endothelial cell adhesion molecule-1, a multifunctional cell adhesion molecule involved in numerous physiologic processes within the vasculature

VIOL-00000231
Ex. 2044-016
CX-2855C.16

Pulsed Wave: Pigmented Lesion



Therapeutic Effects of New Pulsed-Type Microneedling Radiofrequency for Refractory Facial Pigmentary Disorders
By Byeong Jin Park, You Jin Jung, Young Suck Ro, Sung Eun Chang, and Jeong Eun Kim
Dermatologic Surgery, 2022:
https://doi.org/10.1097/DSS.0000000000003367

Methods

- 44 patients with melasma or Riehl melanosis received pulsed-type microneedling RF (SYLFIRM; ViOL) treatment.
- Gene array and immunohistolochemical staining including melan-A, Fontana silver, DC44, basic fibroblast growth factor (bFGF), and periodic acid-Schiff were performed.
  - Patients: age from 25 to 69 years, mean age of 47.18 years, 42 female and 2 male, 24 with melasma and 20 with Riehl melanosis
  - Treatment: 1.0-1.5mm, 1.39-1.59J/cm², 2-3 passes and < 10% overlap for 5 treatments at 2-week intervals

Results

- Most of the patients showed clinical improvement.
- Erythema index, melasma index, and transepidermal water loss decreased after the first treatment.
- Histopathologic examination showed decreased of melanin pigment, melanophages, and blood vessel proliferation but thickened basement membrane after treatment.
- Expression of CD44 and b-FGF was decreased after treatment.
- There were no serious adverse events reported during the study.

VIOL-00000232
Ex. 2044-017
CX-2855C.17