The CO2 Micro Ablative Laser for Treatment of Genitourinary Syndrome of Menopause

What we know...and what we don’t know

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Objectives

• Mechanism of action of CO2 laser
• Indications
• Review of literature
• Clinical trials in progress
Normal Vaginal Wall Mucosa Histology and Function

• Epithelium
  – non-keratanized, stratified squamous cells (superficial, intermediate and parabasal layers)
  – Glycogen production
• Lamina propria
  – Synthesis of collagen, hyaluronic acid and proteoglycans which help diffuse moisture

• Together, 1 mm thick
• Requires:
  – Adequate blood supply
  – Multiple cell layers
    • to synthesize & produce glycogen
Vaginal Mucosa

Pre-menopause

Atrophic

Epithelium

Lamina Propria

Epithelium

Lamina Propria
Treatment Protocol

- 3 Treatments
- 6 week interval
- Vaginal, vestibular and vulvar tissue treated
- No anesthesia required
- Annual maintenance treatment recommended
Fractional Ablation

Colposcopic View of Vaginal Mucosa Immediately Post Treatment
Mechanism of Action

- Fractionated beams of light penetrate small areas of tissue.
- Small ablated wounds are created in mucosal epithelium and lamina propria.
- Sufficient energy so lateral “spared tissue” also treated.
CO2 Ablation Laser Creates a Wound to Activate the Body’s Own Repair Mechanism

- Chemotaxis
- Phagocytosis
- Neo-collagenesis
- Collagen remodeling
- Angiogenesis
- Epithelialization
- Glycosaminoglycans (GAG) formation
Pre and Post Treatment

Histologic Evidence

Zerbinoti: Microscopic... modifications of postmenopausal atrophic vaginal mucosa after fractional CO2 laser treatment
laser treatment, vaginal walls are thinner and less elastic with loss of rugations (A); yellow ring highlights petechial atrophy.
PUBLISHED DATA

**TABLE II - VHI SCORES, PREVALENCE AND INTENSITY OF SYMPTOMS RELATED TO VULVOVAGINAL ATROPHY DURING THE STUDY**

<table>
<thead>
<tr>
<th></th>
<th>Baseline (T1) (First laser)</th>
<th>4-week follow-up (T2) (Second laser)</th>
<th>8-week follow-up (T3) (Third laser)</th>
<th>12-week follow-up (T4)</th>
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<tbody>
<tr>
<td>VHI (mean ± SD)</td>
<td>12.9 ± 3.0</td>
<td>17.8 ± 2.0*</td>
<td>19.0 ± 2.2*†</td>
<td>22.1 ± 2.3*‡</td>
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<td>Dyspareunia (no., mean ± SD)</td>
<td>8.7 ± 1.0 (n = 15)</td>
<td>3.5 ± 0.8* (n = 15)</td>
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<td>Vaginal dryness (no., mean ± SD)</td>
<td>7.2 ± 1.1 (n = 13)</td>
<td>2.8 ± 0.7* (n = 13)</td>
<td>1.5 ± 1.1*† (n = 13)</td>
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<td>Vaginal burning (no., mean ± SD)</td>
<td>6.9 ± 2.7 (n = 13)</td>
<td>2.5 ± 0.9* (n = 13)</td>
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<td>Vaginal itching (no., mean ± SD)</td>
<td>5.6 ± 1.3 (n = 11)</td>
<td>2.5 ± 0.9* (n = 11)</td>
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<td>Dysuria (no., mean ± SD)</td>
<td>5.1 ± 0.9 (n = 9)</td>
<td>2.9 ± 0.7* (n = 9)</td>
<td>1.6 ± 0.8*† (n = 9)</td>
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N=15
Salvatore et al. 12-week treatment with fractional CO2 laser for vulvovaginal atrophy Climateric 2014

VHI Scores and Symptoms

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N=50
Salvatore: Sexual function after fractional microablative CO2 laser in women with VVA Climacteric  2014

Female Sexual Function Index Scores

Figure 1  Female Sexual Function Index scores at baseline and at 12-week follow-up

N=77
Salvatore Sexual function after fractional microablative CO2 laser in women with VVA Climacteric 2014

VVA Symptoms

Table 2  Presence and severity of vulvovaginal atrophy symptoms in our study sample. Data are given as mean ± standard deviation (95% confidence interval)

<table>
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<th>Number of women (%)</th>
<th>Baseline</th>
<th>12-week follow-up</th>
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<tr>
<td>Vaginal dryness (cm)</td>
<td>69 (89.6%)</td>
<td>8.4 ± 2.0 (7.9–8.9)</td>
</tr>
<tr>
<td>Vaginal burning (cm)</td>
<td>66 (85.7%)</td>
<td>6.2 ± 2.7 (5.6–6.9)</td>
</tr>
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<td>Vaginal itching (cm)</td>
<td>64 (83.1%)</td>
<td>6.4 ± 2.7 (5.7–7.1)</td>
</tr>
<tr>
<td>Dyspareunia (cm)</td>
<td>52 (91.2%)</td>
<td>8.4 ± 2.4 (7.8–9.1)</td>
</tr>
<tr>
<td>Dysuria (cm)</td>
<td>60 (77.9%)</td>
<td>5.7 ± 2.8 (5.0–6.4)</td>
</tr>
</tbody>
</table>

* Statistically significant difference in comparison with baseline (p < 0.001 for each); †, measured on a 10-cm VAS scale (range: 0–10); ‡, calculated out of the 57 women who were sexually active at baseline.
N=40

• Breast Cancer Survivors
• 5 laser treatments, q 4 weeks
• FSFI, QOL, VVA symptoms
• 33 (77%) were “satisfied” at 20 weeks

### Table 2. Assessment of change in symptoms of VVA

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Baseline to Tx1</th>
<th>Baseline to Tx2</th>
<th>Baseline to Tx3</th>
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<tr>
<td></td>
<td>Improvement</td>
<td>P</td>
<td>Improvement</td>
</tr>
<tr>
<td>Pain</td>
<td>1.1 ± 2.9</td>
<td>0.051</td>
<td>1.6 ± 3.4</td>
</tr>
<tr>
<td>Burning</td>
<td>1.3 ± 2.5</td>
<td>0.015</td>
<td>1.7 ± 2.4</td>
</tr>
<tr>
<td>Itching</td>
<td>1.1 ± 2.0</td>
<td>0.006</td>
<td>1.6 ± 1.9</td>
</tr>
<tr>
<td>Dryness</td>
<td>4.8 ± 2.9</td>
<td>&lt;0.001</td>
<td>5.1 ± 2.9</td>
</tr>
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<td>4.3 ± 2.8</td>
<td>&lt;0.001</td>
<td>5.3 ± 2.8</td>
</tr>
<tr>
<td>Dysuria</td>
<td>0.6 ± 2.1</td>
<td>0.154</td>
<td>0.9 ± 2.2</td>
</tr>
</tbody>
</table>

VVA, vulvovaginal atrophy.

*Improvement measured on a Visual Analog Scale (0 to 10, where 0 = none and 10 = extreme), listed as mean ± SD. Cutoff for statistical significance was P > 0.05.*

N=30
Sokol, Karram: An assessment of safety and efficacy of fractional CO2 laser system for the treatment of vulvovaginal atrophy
Menopause 2016

FIG. 2. Distribution of dilator size data for participant population (n = 30), shown as percentages of women able to comfortably accept an XS, S, M, or L vaginal dilator at each of four time points (before treatments 1, 2, and 3 as well as final follow up). Three participants were lost to follow-up. L, large; M, medium; S, small; XS, extra small.
Pieralli et al: Fractional CO2 laser for (VVA) ... breast cancer survivors Arch Gynecol Obstet March 2016

• At 4 months,
  – 76% satisfied, or very satisfied
  – 12% dissatisfied

• At 12 months
  – 52% satisfied, or very satisfied
Pagano, et al Fractional CO2 laser for VVA in women treated with chemotherapy and/or hormonal therapy for breast cancer

FIG. 2. Median VAS values at different times for reduced sensitivity during sexual intercourse (A), dyspareunia (B), and dysuria (C). T, time; VAS, visual analog scale.
Trials in Progress

• Velvet Trial-
  – Local vaginal estrogen v. CO2
• Lichen Sclerosis
• Vestibulodynia
• Effect on pelvic fascia
Safety Data

- Laser energy penetrates to a maximum depth of 200 mm.
- No significant adverse events reported
What We DO Know

• Effective treatment for vaginal atrophy and dyspareunia
• Safe
• Well tolerated
Emerging Indications

• Lichen Sclerosis
• Recurrent UTI
• Urinary urgency, burning
• Recurrent vaginitis
• Vestibulodynia
• Pre-vaginal surgery to increase vascularity
What We Don’t Know

• Long-term efficacy and safety data lacking
• Impact of recurrent treatments
• Special Circumstances
  – Post Radiation
  – Co-Morbidities
What it is Not For

• Vaginal “rejuvenation” or “tightening”
• Orgasmic dysfunction
• Stress incontinence
• Sexual satisfaction in the absence of atrophy
“The CO2 is indicated for incision, excision, ablation, vaporization and coagulation of body soft tissues in medical specialties including aesthetic (dermatology and plastic surgery), podiatry, otolaryngology (ENT), gynecology, neurosurgery, orthopedics, general and thoracic surgery (including open and endoscopic), dental and oral surgery and genitourinary surgery. “
# Radio-Frequency ≠ CO2 Laser

<table>
<thead>
<tr>
<th>CO2 Laser</th>
<th>Radiofrequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Mona Lisa Touch</td>
<td>• ThermiVa</td>
</tr>
<tr>
<td>• Femilift</td>
<td>• ReVive</td>
</tr>
<tr>
<td>• ItimaLase</td>
<td>• Venus Fiore</td>
</tr>
<tr>
<td>• Femtouch</td>
<td>• Viveve</td>
</tr>
<tr>
<td>• Diva</td>
<td>• Protégé Intima</td>
</tr>
<tr>
<td>• GyneLase</td>
<td>• Pelleve</td>
</tr>
<tr>
<td>• CO2RE Intima</td>
<td></td>
</tr>
<tr>
<td>• Valayza</td>
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</table>
Radiofrequency Devices

• Non-Invasive Energy Based Systems
• RF waves heat connective tissue to ~42 degrees C
• Vaginal “rejuvenation”
  – Marketing term, not scientific
  – Umbrella which includes restoring “optimal” structure and function of the vagina post childbirth, menopause
  – Claims to improve
    • Vagina dryness
    • Laxity
    • Sexual satisfaction
    • Orgasmic function
Radiofrequency “Data”

  - Self-reported vaginal tightness improved in 67% of subjects at one month post-treatment; in 87% at 6 months. N=24

- **ThermiVa: The Revolutionary Technology for Vulvovaginal Rejuvenation and Noninvasive Management of Female SUI.** J Obstet Gynaecol India. 2016 Apr
  - It seems that the time has come, when women shall ever be grateful to their gynecologist for management of SUI with ThermiVa without an incision.” (no data)

- **Transcutaneous temperature controlled radiofrequency for orgasmic dysfunction**

  - 25 women, self reported orgasmic dysfunction post treatment with radiofrequency said they reached orgasm 50% faster