

Fractional microablative CO₂ laser treatment of vulvovaginal atrophy & the genitourinary syndrome of menopause

- **Cass DL, Sylvester KG, Yang EY, Crombleholme TM and Adzick N: Myofibroblast persistence in fetal sheep wounds is associated with scar formation. J Pediatr Surg 1997; 32 (7): 1017-1021.** Abstract: The scarless repair capabilities of the fetus are influenced by the size of the wound and the gestational age of the fetus. Whereas small wounds heal scarlessly, large wounds in the same fetus heal with scar. Myofibroblasts are specialized fibroblasts that express alpha-smooth muscle actin (alpha-SMA), a contractile cytoskeletal protein. The authors hypothesized that small fetal wounds that heal scarlessly will have a relative absence of myofibroblasts, whereas large wounds that heal with scar will have abundant myofibroblasts. In this study, an incisional wound and four punch biopsy wounds of 2, 4, 6, and 10 mm diameter were placed on the backs of 60- to 90-day-gestation fetal sheep (term, 145 days). Fourteen days after wounding, the healed fetal wounds were harvested, the repair morphology was determined (scarless, transitional repair, or scar), and the expression of alpha-SMA was analyzed by immunohistochemistry. In the second part of this study the authors analyzed the temporal expression of alpha-SMA in fetal wounds at 1, 2, 3, and 7 days after wounding in 70-day-gestation fetal sheep. In the 14-day wounds, the authors found that alpha-SMA was not expressed in any incisional or 2-mm wound that healed scarlessly, but it was expressed in all wounds that healed with scar. Overall, alpha-SMA expression strongly correlated with increasing wound size (P < .005). Myofibroblasts were seen as early as 24 hours after wounding, and at 3 and 7 days all wounds showed strong expression of alpha-SMA. These results demonstrate that although myofibroblasts are induced early in fetal wound repair, by 14 days there is a notable lack of myofibroblasts in wounds that heal scarlessly and an abundance of myofibroblasts in those wounds that scar. By determining the factors that regulate the disappearance of the myofibroblast in scarless fetal wounds, the authors hope to gain new insights into the mechanisms of scarless fetal repair
- **Orringer JS, Kang S, Johnson TM, Karimipour DJ, Hamilton T, Hammerberg C, Voorhees JJ and Fisher GJ: Connective tissue remodeling induced by carbon dioxide laser resurfacing of photodamaged human skin. Arch Dermatol 2004; 140: 1326-1332.** Abstract: OBJECTIVE: To quantitatively examine the dynamics of molecular alterations involved in dermal remodeling after carbon dioxide (CO₂) laser resurfacing of photodamaged human skin. DESIGN: Serial in vivo biochemical analyses after laser therapy. SETTING: Academic referral center, Department of Dermatology, University of Michigan, Ann Arbor. Subjects Volunteer sample of 28 adults, 48 to 76 years old, with clinically evident photodamage of the forearms. Intervention Focal CO₂ laser resurfacing of photodamaged forearms and serial biopsies at baseline and various times after treatment. MAIN OUTCOME MEASURES: Reverse transcriptase real-time polymerase chain reaction technology and immunohistochemistry were used to assess levels of type I and type III procollagens; matrix metalloproteinases (MMPs) 1, 3, 9, and 13; tropoelastin; fibrillin; primary cytokines interleukin 1beta and tumor necrosis factor alpha; and profibrotic cytokine transforming growth factor beta1. RESULTS: Production of type I procollagen and type III procollagen messenger RNA peaked at 7.5 and 8.9 times baseline levels, respectively, 21 days after treatment and remained elevated for at least 6 months. Increases in messenger RNA levels of several cytokines (interleukin 1beta, tumor necrosis factor alpha, and transforming growth factor beta1) preceded and/or accompanied changes in collagen levels. Marked increases in messenger RNA levels of MMP-1 (39 130-fold), MMP-3 (1041-fold), MMP-9 (75-fold), and MMP-13 (767-fold) were noted. Levels of fibrillin and tropoelastin rose in a delayed fashion several weeks after treatment. CONCLUSIONS: The biochemical changes seen after CO₂ laser resurfacing proceed through a well-organized and highly reproducible wound healing response that results in marked alterations in dermal structure. These quantitative changes may serve as a means for comparison as other therapeutic modalities meant to improve the appearance of photodamaged skin are evaluated.
- **Mak K, Manji A, Gallant-Behm C, Wiebe C, Hart DA, Larjava H and Häkkinen L: Scarless healing of oral mucosa is characterized by faster resolution of inflammation and control of myofibroblast action compared to skin wounds in the red Duroc pig model. J Dermatol Sci 2009; 56: 168-180 (DOI: doi:10.1016/j.jdermsci.2009.09.005).** Abstract: BACKGROUND: Scar formation following skin trauma can have devastating consequences causing physiological and psychosocial concerns. Currently, there are no accepted predictable treatments to prevent scarring which emphasizes a need for a better understanding of the wound healing and scar formation process. OBJECTIVES: Previously it was shown that healing of small experimental wounds in the oral mucosa of red Duroc pigs results in significantly reduced scar formation as compared with equivalent full-thickness skin wounds. In the present study, scar formation was assessed in 17 times larger experimental wounds in both oral mucosa and skin of the red Duroc pigs. METHODS: Equivalent experimental wounds were created in the oral mucosa and dorsal skin of red Duroc pigs, and scar formation, localization and abundance of key wound healing cells, transforming growth factor-beta (TGF-beta) and phosphorylated Smad3 (pSmad3) were assessed. RESULTS: Oral mucosal wounds displayed significantly less clinical and histological scar formation than did the corresponding skin wounds. The number of macrophages, mast cells, TGF-beta and pSmad3 immunopositive cells was significantly reduced in the oral mucosal wounds as compared with skin wounds during the maturation stage of the healing process. Although the number of myofibroblasts was significantly elevated, the oral mucosal wounds showed significantly less contraction than did the skin wounds over time. CONCLUSIONS: Earlier resolution of the inflammatory reaction and reduced wound contraction may promote scarless oral mucosal wound healing. In addition, scar formation likely depends not only on the number of myofibroblasts but also on the extracellular environment which regulates their function.
- **Wong JW, Gallant-Behm C, Wiebe C, Mak K, Hart DA, Larjava H, Häkkinen L: Wound healing in oral mucosa results in reduced scar formation as compared with skin: evidence from the red Duroc pig model and humans. Wound Repair Regen 2009; 17: 717-729 (DOI: DOI:10.1111/j.1524-475X.2009.00531.x).** Abstract: Scar formation is a common, unwanted result of wound healing in skin, but the mechanisms that regulate it are still largely unknown. Interestingly, wound healing in the oral mucosa proceeds faster than

in skin and clinical observations have suggested that mucosal wounds rarely scar. To test this concept, we created identical experimental wounds in the oral mucosa and skin in red Duroc pigs and compared wound healing and scar development over time. We also compared the pig oral mucosal wound healing to similar experimental wounds created in human subjects. The findings showed significantly reduced scar formation at both clinical and histological level in the pig oral mucosa as compared with skin 49 days after wounding. Additionally, the skin scars contained a significantly increased number of type I procollagen immunopositive cells and an increased fibronectin content, while the oral mucosal wounds demonstrated a prolonged accumulation of tenascin-C. Furthermore, the pig oral mucosal wounds showed similar molecular composition and clinical and histological scar scores to human oral mucosal wounds. Thus, the reduced scar formation in the pig oral mucosa provides a model to study the biological processes that regulate scarless wound healing to find novel approaches to prevent scar formation in skin.

- **Gallant-Behm CL, Du P, Lin SM, Marucha PT, DiPietro LA and Mustoe TA: Epithelial regulation of mesenchymal tissue behavior. J Invest Dermatol 2011; 131: 892-899 (DOI: 10.1038/jid.2010.420).** Abstract: Fibroproliferative scars are an important clinical problem, and yet the mechanisms that regulate scar formation remain poorly understood. This study explored the hypothesis that the epithelium has a critical role in dictating scar formation, and that these interactions differ in skin and mucosa. Paired skin and vaginal mucosal wounds on New Zealand white (NZW) rabbits diverged significantly; the cutaneous epithelium exhibited a greater and prolonged response to injury when compared with the mucosa. Microarray analysis of the injured epithelium was performed, and numerous factors were identified that were more strongly upregulated in skin, including several proinflammatory cytokines and profibrotic growth factors. Analysis of the underlying mesenchymal tissue demonstrated a fibrotic response in the dermis of the skin but not the mucosal lamina propria, in the absence of a connective tissue injury. To determine if the proinflammatory factors produced by the epidermis may have a role in dermal fibrosis, an IL-1 receptor antagonist was administered locally to healing skin wounds. In the NZW rabbit model, blockade of IL-1 signaling was effective in preventing hypertrophic scar formation. These results support the idea that soluble factors produced by the epithelium in response to injury may influence fibroblast behavior and regulate scar formation in vivo.
- **Gaspar A, Addamo G and Brandi H. Vaginal Fractional CO₂ Laser: A Minimally Invasive Option for Vaginal Rejuvenation. Am J Cosmet Surg 2011; 28(3): 156-162 (DOI: 10.5992/0748-8068-28.3.156).** Abstract: Introduction: To provide evidence that the use of a fractional CO₂ laser in combination with platelet-rich plasma (PRP) locally in the vagina mucous with minimal to moderate atrophy and pelvic floor exercise with perineometer would have effects of greater impact in the 3 layers of vaginal walls, including an important decrease of discomfort during sex. Materials and Methods: The study was composed of 2 groups: a study group and a control group. The main consultation purposes were vaginal dryness, dyspareunia, and local irritation. The study group underwent PRP, CO₂ laser, and pelvic exercise, whereas only PRP and pelvic exercise were applied to the control group. We used a special vaginal scanner, which was able to fractionize the laser and could be inserted in the vagina. Both groups were evaluated with a sexual questionnaire and vaginal biopsies. Results: An important improvement of vaginal mucous histology and a decrease of discomfort during sex were observed in most patients in the study group compared with the control group. Conclusion: Through the local use of vaginal fractional CO₂ laser, PRP, and pelvic floor exercises in women with symptoms of vaginal atrophy, beneficial effects are exerted in the 3 layers of the vagina rather than only the epithelium, as achieved with estrogens. We also observed a significant decrease of discomfort during sex. More data will be needed to better address the use of this new procedure.
- **Perino A, Cucinella G, Tiberio C, Martorana A, Venezia R, Calagna G. Fractional CO₂ Laser: the new frontier for the treatment of vulvovaginal atrophy symptoms. Giorn.It.Ost.Gin. 2014; 36(3): 405-408.** Abstract: The vulvo-vaginal atrophy (VVA) is a chronic condition characterized by gradual involution of the mucous membranes and vulvo-vaginal tissues, which is manifested in the climacteric phase. Numerous therapeutic options, hormonal and non-hormonal, have been proposed to alleviate the symptoms related to VVA, but to date none of them is able to guarantee long-term effects. The use of Fractional CO₂ Laser technology applied to the vulvo-vaginal area represents an innovative procedure to make a real "regeneration treatment" of the vaginal tissues. In fact, it is possible to spread the laser energy in the various layers of the vaginal wall, reactivating the synthesis of extracellular matrix and collagen, with the recovery of tissue tropism and improved VVA-related disorders.
- **Salvatore S, Nappi RE, Zerbinati N, Calligaro A, Ferrero S, Origoni M, Candiani M, Leone Roberti MU. A 12-week treatment with fractional CO₂ laser for vulvovaginal atrophy: a pilot study. Climacteric. 2014; 17: 363-369 (DOI: 10.3109/13697137.2014.899347).** Abstract: OBJECTIVE: This pilot study aimed to assess the efficacy and feasibility of fractional CO₂ laser in the treatment of vulvovaginal atrophy (VVA) in postmenopausal women. METHODS: VVA symptoms were assessed before and after three applications of laser over 12 weeks in 50 women (age 59.6 +/- 5.8 years) dissatisfied with previous local estrogen therapies. Subjective (visual analog scale) and objective (Vaginal Health Index Score, VHIS) measures were used during the study period to assess VVA. Quality of life was measured by using the SF-12. A subjective scale to evaluate the degree of pain related to the laser application and the degree of difficulty to perform the laser procedure was used. RESULTS: Fractional CO₂ laser treatment was effective to improve VVA symptoms (vaginal dryness, vaginal burning, vaginal itching, dyspareunia, dysuria; p < 0.001) at 12-week follow-up, as well as the VHIS (13.1 +/- 2.5 at baseline vs. 23.1 +/- 1.9; p < 0.001). Both physical and mental scores of quality of life were significantly improved in comparison with baseline (p < 0.001). Satisfaction with the laser procedure was reported by 42 women (84%) and a minimal discomfort was experienced at the first laser application, mainly because of the insertion and the movements of the probe. Finally, the technique was very easy to perform in all women starting from the second application at week 4 and no adverse events were recorded during the study period. CONCLUSIONS: A 12-week treatment with the fractional CO₂ laser was feasible and induced a

significant improvement of VVA symptoms by ameliorating vaginal health in postmenopausal women. Further controlled studies should be performed to confirm the present data and to assess the long-term effects of the laser procedure on vaginal tissues.

- **Salvatore S, Leone Roberti Maggiore U, Origoni M, Parma M, Quaranta L, Sileo F, Cola A, Bains I, Ferrero S, Candiani M, Zerbini N. Microablative fractional CO2 laser improves dyspareunia related to vulvovaginal atrophy: a pilot study. Journal of Endometriosis 2014; 6(3): 150-156 (DOI: 10.5301/je.5000184).** Abstract: OBJECTIVE: This pilot study aimed to assess the efficacy in treating sexually active menopausal patients who had dyspareunia related to vulvovaginal atrophy (VVA). MATERIALS AND METHODS: The intensity of VVA symptoms was recorded for each patient. Patients were administered the Short Form 12 (SF-12) and the female sexual function index (FSFI) to assess quality of life and sexual function, respectively. An objective evaluation of female urogenital health was performed using the Gloria Bachman Vaginal Health Index (VHI). RESULTS: At 12-week follow-up, the laser treatment was efficacious in improving dyspareunia in 100% of patients included in the study (n = 15). The intensity of dyspareunia significantly decreased from baseline (8.7 ± 1.0) to 12-week follow-up (2.2 ± 1.0 ; $p < 0.001$). In addition, all other VVA symptoms significantly ameliorated at the same follow-up. Furthermore, after the treatment, a significant improvement in quality of life (QoL) and sexual function were shown. CONCLUSIONS: This pilot study demonstrated that treatment with the microablative fractional CO2 laser of patients with dyspareunia related to VVA was efficacious at 12-week follow-up.
- **Perino A, Calligaro A, Forlani F, Tiberio C, Cucinella G, Svelato A, Saitta S, Calagna G. Vulvo-vaginal atrophy: a new treatment modality using thermo-ablative fractional CO2 laser. Maturitas 2015; 80: 296-301 (DOI: 10.1016/j.maturitas.2014.12.006).** Abstract: OBJECTIVE: To evaluate the efficacy and feasibility of thermo-ablative fractional CO2 laser for the treatment of symptoms related to vulvo-vaginal atrophy (VVA) in post-menopausal women. METHODS: From April 2013 to December 2013, post-menopausal patients who complained of one or more VVA-related symptoms and who underwent vaginal treatment with fractional CO2 laser were enrolled in the study. At baseline (T0) and 30 days post-treatment (T1), vaginal status of the women was evaluated using the Vaginal Health Index (VHI), and subjective intensity of VVA symptoms was evaluated using a visual analog scale (VAS). At T1, treatment satisfaction was evaluated using a 5-point Likert scale. RESULTS: During the study period, a total of 48 patients were enrolled. Data indicated a significant improvement in VVA symptoms (vaginal dryness, burning, itching and dyspareunia) ($P < 0.0001$) in patients who had undergone 3 sessions of vaginal fractional CO2 laser treatment. Moreover, VHI scores were significantly higher at T1 ($P < 0.0001$). Overall, 91.7% of patients were satisfied or very satisfied with the procedure and experienced considerable improvement in quality of life (QoL). No adverse events due to fractional CO2 laser treatment occurred. CONCLUSION: Thermo-ablative fractional CO2 laser could be a safe, effective and feasible option for the treatment of VVA symptoms in post-menopausal women.
- **Salvatore S, Nappi RE, Parma M, Chionna R, Lagona F, Zerbini N, Ferrero S, Origoni M, Candiani M, Leone Roberti MU. Sexual function after fractional microablative CO2 laser in women with vulvovaginal atrophy. Climacteric 2015; 18: 219-225 (DOI: 10.3109/13697137.2014.975197).** Abstract: Objective To investigate the effects of fractional microablative CO2 laser on sexual function and overall satisfaction with sexual life in postmenopausal women with vulvovaginal atrophy (VVA). Method This prospective study included 77 postmenopausal women (mean age 60.6 ± 6.2 years) treated for VVA symptoms with the fractional microablative CO2 laser system (SmartXide(2) V(2)LR, Monalisa Touch, DEKA, Florence, Italy). Sexual function and quality of life were evaluated with the Female Sexual Function Index (FSFI) and the Short Form 12 (SF-12), respectively, both at baseline and at 12-week follow-up. A 10-mm visual analog scale was used to measure the overall satisfaction with sexual life and the intensity of VVA symptoms (vaginal burning, vaginal itching, vaginal dryness, dyspareunia and dysuria) before and after the study period. Results We observed a significant improvement in the total score and the scores in each specific domain of the FSFI at 12-week follow-up compared to baseline ($p < 0.001$). After concluding the laser treatment, the overall satisfaction with sexual life significantly improved ($p < 0.001$). Seventeen (85%) out of 20 (26%) women, not sexually active because of VVA severity at baseline, regained a normal sexual life at the 12-week follow-up. Finally, we also found a significant improvement in each VVA symptom ($p < 0.001$) and in quality-of-life evaluation, both for the scores in the physical ($p = 0.013$) and mental ($p = 0.002$) domains. Conclusions Fractional microablative CO2 laser treatment is associated with a significant improvement of sexual function and satisfaction with sexual life in postmenopausal women with VVA symptoms.
- **Salvatore S, Leone Roberti MU, Athanasiou S, Origoni M, Candiani M, Calligaro A, Zerbini N. Histological study on the effects of microablative fractional CO2 laser on atrophic vaginal tissue: an ex vivo study. Menopause 2015; 22(8): 845-849 (DOI: 10.1097/gme.0000000000000401).** Abstract: OBJECTIVE: Microablative fractional CO2 laser has been proven to determine tissue remodeling with neof ormation of collagen and elastic fibers on atrophic skin. The aim of our study is to evaluate the effects of microablative fractional CO2 laser on postmenopausal women with vulvovaginal atrophy using an ex vivo model. METHODS: This is a prospective ex vivo cohort trial. Consecutive postmenopausal women with vulvovaginal atrophy managed with pelvic organ prolapse surgical operation were enrolled. After fascial plication, the redundant vaginal edge on one side was treated with CO2 laser (SmartXide2; DEKA Laser, Florence, Italy). Five different CO2 laser setup protocols were tested. The contralateral part of the vaginal wall was always used as control. Excessive vagina was trimmed and sent for histological evaluation to compare treated and nontreated tissues. Microscopic and ultrastructural aspects of the collagenic and elastic components of the matrix were studied, and a specific image analysis with computerized morphometry was performed. We also considered the fine cytological aspects of connective tissue proper cells, particularly fibroblasts. RESULTS: During the study period, five women were enrolled, and 10 vaginal specimens were finally retrieved. Four different settings of CO2 laser were compared. Protocols were tested twice each to confirm histological findings. Treatment protocols were compared according to histological findings, particularly in maximal depth and connective changes achieved.

All procedures were uneventful for participants. **CONCLUSIONS:** This study shows that microablative fractional CO₂ laser can produce a remodeling of vaginal connective tissue without causing damage to surrounding tissue.

- **Zerbinati N, Serati M, Origoni M, Candiani M, Iannitti T, Salvatore S, Marotta F, Calligaro A. Microscopic and ultrastructural modifications of postmenopausal atrophic vaginal mucosa after fractional carbon dioxide laser treatment. *Lasers Med.Sci.* 2015; 30: 429-436 (DOI: 0.1007/s10103-014-1677-2).** Abstract: Vaginal atrophy occurring during menopause is closely related to the dramatic decrease in ovarian estrogens due to the loss of follicular activity. Particularly, significant changes occur in the structure of the vaginal mucosa, with consequent impairment of many physiological functions. In this study, carried out on bioptic vaginal mucosa samples from postmenopausal, nonestrogenized women, we present microscopic and ultrastructural modifications of vaginal mucosa following fractional carbon dioxide (CO₂) laser treatment. We observed the restoration of the vaginal thick squamous stratified epithelium with a significant storage of glycogen in the epithelial cells and a high degree of glycogen-rich shedding cells at the epithelial surface. Moreover, in the connective tissue constituting the lamina propria, active fibroblasts synthesized new components of the extracellular matrix including collagen and ground substance (extracellular matrix) molecules. Differently from atrophic mucosa, newly-formed papillae of connective tissue indented in the epithelium and typical blood capillaries penetrating inside the papillae, were also observed. Our morphological findings support the effectiveness of fractional CO₂ laser application for the restoration of vaginal mucosa structure and related physiological trophism. These findings clearly coupled with striking clinical relief from symptoms suffered by the patients before treatment.
- **Perino A and Calagna G: A new approach to treatment of vulvo-vaginal atrophy. *Maturitas* 2015; 81, 499 (DOI: 10.1016/j.maturitas.2015.03.003).** Abstract: Based on our recent published experience, your suggestion to utilize fractional CO₂ laser for treatment of VVA symptoms in post-menopausal women aged over 70 years is an interesting proposal. However, the possibility of extending the treatment to women with severe contraindications to hormonal treatments, such as cancer survivors, seems to be of primary importance. As previously reported, patients with estrogen-dependent malignancies are at high risk of severe VVA symptoms and sexual dysfunction and an increase in the incidence and progression of gynecological symptoms following chemotherapy and/or endocrine therapy was demonstrated. Up to 75% of breast cancer survivors experiences urogenital symptoms, with relevant reduction of Quality of Life. Although there are few data regarding the use of vaginal estrogens in women with gynecological hormone-responsive cancers, this treatment is actually the most common approach for these patients, after careful counseling and discussion with the oncology team [3,4]. Therefore, we support your idea of a follow-up study on the effects of laser treatment on a population of cancer-survivor women. Moreover, considering clinical observations about sexual function and vaginal changes after radiotherapy, our group is working on a new project on patients treated for cervical and endometrial cancer by RT. To achieve an effective treatment for VVA disorders is a key point of the patient care in our aging society. Even more, the possibility of a safe "non-hormonal" option for the risk patients should be a primary goal. According to our results, fractional CO₂ laser has proved to be a safe and effective modality of treatment of VVA symptoms for patients in the early phase of menopause. Further studies are needed in order to assess the usefulness of this technique on elderly women and cancer survivor patients.
- **Singh A, Swift S, Khullar V, Digesu GA. Laser vaginal rejuvenation: not ready for prime time. *Int Urogynecol J* 2015; 26:163–164 (DOI: 10.1007/s00192-014-2588-2).**
- **Maggiore ULR, Candiani M, Salvatore S. Comments on Singh et al.: Laser vaginal rejuvenation: not ready for prime time. *Int Urogynecol J* 2015; 26:783 (DOI: 10.1007/s00192-015-2644-6).**
- **Digesu A. Laser vaginal rejuvenation: not ready for prime time - response to comments by Maggiore et al. *Int Urogynecol J* 2015; 26:785 (DOI: 10.1007/s00192-015-2647-3).**
- **Hutchinson-Colas,J. and Segal,S. (2015) Genitourinary syndrome of menopause and the use of laser therapy. *Maturitas*, 82, 342-345 (DOI: 10.1016/j.maturitas.2015.08.001).** Abstract: Genitourinary syndrome of menopause is a common condition that left untreated can progress and negatively affect quality of life and sexual function. Laser therapy has a therapeutic role for several gynecologic conditions and most recently has gained interest as a non-hormonal treatment for genitourinary syndrome of menopause (GSM). The laser is well tolerated and may increase thickness of the squamous epithelium and improve vascularity of the vagina. These morphological changes presumably alleviate symptoms of dryness, dyspareunia, and irritation. However, the duration of therapeutic effects and safety of repeated applications at this point is not clear. Further research is needed in the form of controlled studies of the laser and other non-hormonal GSM therapies. The objective of this paper is to review the existing literature describing laser therapy for GSM.
- **Salvatore S, Athanasiou S and Candiani M: The use of pulsed CO₂ lasers for the treatment of vulvovaginal atrophy. *Curr Opin Obstet Gynecol* 2015; 27: 504–508 (DOI: 10.1097/GCO.0000000000000230).** Abstract: Purpose of review: This article reviews the literature regarding the safety and efficacy of the use of a pulsed CO₂ laser for the treatment of vulvovaginal atrophy (VVA). Recent findings: Prospective observational studies have demonstrated histological changes after the use of pulsed CO₂ laser vaginally in atrophic conditions. Increased collagen and extracellular matrix production has been reported together with an increase in the thickness of the vaginal epithelium with the formation of new papilla. Three different observational studies reported a significant improvement of VVA assessed subjectively (with a 10-point visual analogue scale) and objectively (using the Vaginal Health Index) after a cycle of three treatments of pulsed CO₂ laser. Also sexual function (assessed with the Female Sexual Function Index) and quality of life (evaluated

with the SF12 questionnaire) significantly improved. No complications or side effects were reported during or after the laser procedure that was performed in an outpatient setting. Summary: Increasing evidence with histological and clinical data supports the use of pulsed CO₂ lasers in the treatment of VVA; however, no randomized control trial (sham versus treatment) has yet been produced and no data on the duration of therapy are currently available. Keywords: dyspareunia, pulsed CO₂ laser, quality of life, sexual function, vaginal dryness, vulvovaginal atrophy.

Fractional microablative CO₂ laser treatment of the skin in Ob/Gyn

- **Saedi N, Petelin A, Zachary C. Fractionation: a new era in laser resurfacing. Clin.Plast.Surg. 2011; 38: 449-461, vii (DOI:10.1016/j.cps.2011.02.008).** Abstract: Fractional photothermolysis combines the benefits of fully ablative lasers with significantly reduced downtime and fewer complications. Skin is treated in a fractional manner, with narrow cylinders of tissue being thermally heated and normal adjacent skin left unaffected, and the fractional devices have shown effectiveness in treating a variety of conditions, especially scarring and photodamage. There are many devices that use fractional photothermolysis, and practitioners are becoming more adept at using optimal parameters to induce near CO₂ laser benefits. Fractionated lasers have become the cornerstone of a minimally invasive treatment regimen and have ushered in a new era of laser skin rejuvenation.
- **Filippini M and Farinelli M. Use of the MonaLisa Touch® Treatment for post-partum dyspareunia. A pilot study. Social Security Institute San Marino December 2014.** Abstract: Objectives: This pilot study aimed to assess the efficacy in treating perineal pain symptoms in women who had late post-partum dyspareunia. Materials and Methods: The study involved six patients who had late post-partum dyspareunia. Over a time period from January 1, 2013 through August 31, 2014, patients were subjected to MonaLisa Touch® CO₂ laser treatment. Results: Study results showed that two months after the treatment, out of a total of six patients, four treated for pain following episiorrhaphy or vaginal tear reported improvement of symptoms. Of the other two patients who underwent cesarean section, one has noticed a significant improvement while the other patient had modest pain reduction after two treatments. Conclusions: This pilot study has shown the effectiveness of the MonaLisa Touch® fractional CO₂ laser treatment in patients with post-partum perineal pain.
- **Choi,J.E., Oh,G.N., Kim,J.Y. et al. Ablative fractional laser treatment for hypertrophic scars: comparison between Er:YAG and CO₂ fractional lasers. J.Dermatol.Treat., 2014; 25: 299-303.** Abstract: BACKGROUND: Nonablative fractional photothermolysis has been reported to show early promise in the treatment of hypertrophic scars, but there are few reports on ablative fractional photothermolysis for the treatment of hypertrophic scars. AIM: To evaluate and compare the efficacy and safety of Er:YAG fractional laser (EYFL) and CO₂ fractional laser (CO₂FL) for treatment of hypertrophic scars. METHODS: Thirteen patients with hypertrophic scars were treated with 2,940 nm EYFL, and ten were treated with 10,600 nm CO₂FL. An independent physician evaluator assessed the treatment outcomes using Vancouver scar scale (VSS) and 5-point grading scale (grade 0, no improvement; grade 1, 1-25%; grade 2, 26-50%; grade 3, 51-75%; grade 4, 76-100% improvement). Patients are queried about their subjective satisfaction with the treatment outcomes. RESULTS: After the final treatment, average percentage changes of VSS were 28.2% for EYFL and 49.8% for CO₂FL. Improvement was evident in terms of pliability, while insignificant in terms of vascularity and pigmentation. Based on physician's global assessment, mean grade of 1.8 for EYFL and 2.7 for CO₂FL was achieved. Patient's subjective satisfaction scores paralleled the physician's objective evaluation. CONCLUSION: CO₂FL is a potentially effective and safe modality for the treatment of hypertrophic scars, particularly in terms of pliability.
- **Marquardt,Y., Amann,P.M., Heise,R. et al. Characterization of a novel standardized human three-dimensional skin wound healing model using non-sequential fractional ultrapulsed CO₂ laser treatments. Lasers Surg.Med. 2015; 47: 257-265.** Abstract: BACKGROUND AND OBJECTIVE: At present, there is no standardized in vitro human skin model for wound healing. Therefore, our aim was to establish and characterize an in vitro/ex vivo three-dimensional (3D) wound healing model, which we employed to analyze the effects of dexpanthenol on wound healing and gene regulation. MATERIALS AND METHODS: The novel human 3D skin wound healing model using scaffold and collagen 3D organotypic skin equivalents was irradiated with a non-sequential fractional ultrapulsed CO₂ laser. These standardized injured full-thickness skin equivalents enable qRT-PCR, microarray, and histological studies analyzing the effect of topically or systemically applied compounds on skin wound healing. RESULTS: These human laser-irradiated skin models were found to be appropriate for in vitro wound healing analysis. Topical treatment of skin wounds with a 5% dexpanthenol water-in-oil emulsion or two different 5% dexpanthenol oil-in-water emulsions clearly enhanced wound closure compared to laser-irradiated untreated control models. To find out whether this positive effect is caused by the active substance dexpanthenol, laser-irradiated skin models were cultured in calciumpantothenate containing medium (20 mug/ml) compared to skin equivalents cultured without calciumpantothenate. 3D models cultured in calciumpantothenate revealed considerably faster wound closure compared to the control models. Quantitative RT-PCR studies showed enhanced mRNA expression of MMP3, IL1alpha, keratin-associated protein 4-12 (KRTAP4-12), and decreased expression of S100A7 in laser-irradiated skin models cultured in medium containing calciumpantothenate. CONCLUSION: This novel standardized human 3D skin wound healing model proves useful for topical pharmacological studies on wound healing and reveals new insights into molecular mechanisms of dexpanthenol-mediated effects on wound healing. In addition, these novel 3D model systems can be used to monitor ex vivo effects of various laser systems on gene expression and morphology of human skin.
- **Cox JA, Dainer M, Shumaker PR. Ablative fractional laser resurfacing for abdominal scar contractures in pregnancy. Obstet.Gynecol. 2015; 125: 924-926.** Abstract: BACKGROUND: Fundal growth during pregnancy can lead to unremitting discomfort and skin breakdown in patients with extensive abdominal scarring. CASE: A 31-year-old primigravid woman at 30 weeks of gestation

presented to the department of dermatology with constant abdominal discomfort, itch, and sleep disturbance secondary to increasing tension associated with existing abdominal scars. An outpatient course of ablative fractional laser resurfacing was initiated in consultation with the dermatology department, resulting in immediate and durable symptom relief and visible abdominal expansion. No complications were observed, and the patient delivered a healthy newborn at term. CONCLUSIONS: Ablative fractional laser resurfacing is a minimally invasive therapeutic alternative for treating pregnant patients with symptoms related to restrictive scarring of the abdomen.

- **Lee A, Lim A, Fischer G. Fractional carbon dioxide laser in recalcitrant vulval lichen sclerosis. Australasian Journal of Dermatology, in press (doi: 10.1111/ajd.12305) 2015.** Abstract: Vulval lichen sclerosis is an uncommon skin condition that can usually be managed with topical corticosteroids to maintain remission. However, there is a subset of patients in whom it remains recalcitrant despite treatment with super-potent topical corticosteroids. We report a case series of four patients undergoing fractional carbon dioxide laser resurfacing and one with ablative carbon dioxide laser for severe, hyperkeratotic vulval lichen sclerosis not responding to super-potent topical corticosteroids. In these patients, carbon dioxide laser was successful in achieving remission. Their vulval lichen sclerosis was subsequently able to be maintained with topical corticosteroid treatment.
- **Jeffery S. Fractional CO₂ laser therapy: A paradigm shift in managing burns and scarring. Trauma 2015; 17(3): 163–165 (DOI: 10.1177/1460408615580204).**