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Novel Minimally Invasive VSP Er:YAG Laser Treatments in Gynecology

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ABSTRACT:

Some of the most common health problems among women that are caused by a deteriorating laxity, elasticity and tightness of mucous membranes are vaginal relaxation (and the associated loss of sexual gratification) and stress urinary incontinence. Recently, two novel minimally invasive, non-ablative Er:YAG laser techniques have been introduced, a vaginal tightening therapy IntimaLase™ and a stress urinary incontinence therapy IncontiLase™, which show the potential to become an optimal solution for many women suffering from these problems. Both treatment techniques exploit the photothermal effect of a laser beam on mucosa tissue in order to cause its shrinkage without any removal of tissue. The overall impact and burden on the patient's organism is thus minimal, as opposed to more invasive classical or laser surgical procedures.

In this paper, a special Er:YAG Pixel Screen technology used in these novel gynecological treatments, and its ablative characteristics, are first analyzed with the aim to establish a range of laser parameters for safe, single-pulse or SMOOTH mode, non-ablative treatment of mucosa tissue. The initial results of multi-center clinical studies of the IntimaLase™ and IncontiLase™ treatments are then presented. All five centers involved in the studies of the IntimaLase™ treatment reported positive results, i.e an improvement in vaginal tightness for a large majority of treated patients, with practically no adverse effects. Similarly, all four studies of the IncontiLase™ treatment showed improvement in stress urinary incontinence (SUI) for a large majority of treated patients. Many patients with mild SUI reported to become free of the symptoms of incontinence following the treatment. There were no adverse effects of this treatment reported in any of the studies.

Based on these initial clinical results, the new IntimaLase™ and IncontiLase™ gynecological treatments are promising to become a minimally invasive solution of choice for many women suffering from vaginal relaxation syndrome or stress urinary incontinence.

Key words: Er:YAG laser; vaginal relaxation, stress urinary incontinence (SUI), mucosa ablation, pixel screen technology, Smooth mode.

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I. INTRODUCTION

Mucosa is the moist tissue that, in addition to some human organs, lines body cavities that are exposed to the external environment. They are at several places continuous with skin: at the nostrils, the mouth, the lips, the eyelids, the ears, the genital area, and the anus.

A number of health problems are caused by a deteriorating laxity, elasticity and tightness of mucous membranes and the underlying adjacent tissues (muscles, etc.) The following are some of the most common problems: a) vaginal relaxation and the loss of sexual gratification in women b) involuntary loss of urine called urinary incontinence among women c) anal incontinence, and d) snoring.

Vaginal relaxation is the loss of the optimum structural architecture of the vagina. This process is generally associated with natural aging and is specially affected by childbirth, whether vaginal or not. Multiple pregnancies further increase the alteration of these structures. During the vaginal relaxation process, the

vaginal muscles become relaxed with poor tone, strength, control and support. The internal and external vaginal diameters can greatly increase with a significant stretching of vaginal walls. Under these circumstances the vagina is no longer at its physiologically optimum sexual functioning state. William H. Masters, M.D. and Virginia E. Johnson pioneered studies that concluded that sexual gratification is directly related to the amount of frictional forces generated during intercourse [1]. Friction is a function of the vaginal canal diameter, and when this virtual space is expanded it can lead to reduction, delay or absence of orgasms. Thus, vaginal relaxation has a detrimental effect on sexual gratification because of the reduction of frictional forces that diminish sexual pleasure. Several approaches have been developed to address the problem of vaginal relaxation. The most common current technique utilizes a surgical procedure for tightening the vaginal canal.

Millions of women experience involuntary loss of urine called urinary incontinence (UI). Some women may lose a few drops of urine while running or coughing. Others may feel a strong, sudden urge to urinate just before losing a large amount of urine. Many women experience both symptoms [2]. UI can be slightly bothersome or totally debilitating. For some women, the risk of public embarrassment keeps them from enjoying many activities with their family and friends. Urine loss can also occur during sexual activity and cause tremendous emotional distress [3]. Women experience UI twice as often as men. Pregnancy and childbirth, menopause, and the structure of the female urinary tract account for this difference. But both women and men can become incontinent from neurological injury, birth defects, stroke, multiple sclerosis, and physical problems associated with aging. Older women experience UI more often than younger women. But incontinence is not inevitable with age. UI is a medical problem. Incontinence often occurs because of problems with muscles that help to hold or release urine. One type of incontinence will occur if the sphincter muscles are not strong enough to hold back urine. Treatments involve injections and surgery.

Laser surgical procedures for vaginal rejuvenation are currently the most popular ones [4]. In spite of the declared minimal invasiveness, these procedures are still surgery, connected with everything present in classical surgery including the risks of serious adverse effects, relatively long recovery periods and restraining from sexual activities during this long recovery period [5]. In this regard, a non ablative laser treatment would have several advantages. When using non-ablative lasers, tissue is coagulated to cause shrinkage, but tissue is not removed. The overall impact and burden on the patient's organism would therefore be significantly reduced, but at the same time the therapy would yield good results associated with high treatment safety and quick patient recovery.

Recently, two novel minimally-invasive, non-ablative Er:YAG laser techniques have been introduced by the manufacturer Fotona: a vaginal tightening therapy (IntimaLase™) and a stress urinary incontinence therapy (IncontiLase™). Both treatment techniques exploit the photothermal effect of a laser beam on mucosa tissue. With this technique, precisely controlled VSP [6,7] laser energy pulses are delivered to selected mucosa tissue in order to non-ablatively heat the collagen within the tissue. Collagen exposed to an appropriate temperature increase results in the sudden contraction of its fibers, leading to the contraction and shrinking of the irradiated bulk tissue [7]. The thermal effect on collagen is not just momentary during exposure to increased temperature, but is continues throughout the processes of collagen remodeling and neocollagenesis [8-25], resulting in the generation of new collagen and an overall improvement of treated tissue tightness and elasticity.

While the thickness of mucosa varies, it is typically several hundred microns thick. For the controlled heat deposition into the mucosa tissue, what is needed is an effective and safe heat source that is capable of distributing heat approximately 100 microns deep into mucosa without damaging either the outside mucous tissue surface or the deeper lying surrounding tissues.

The IntimaLase™ and IncontiLase™ techniques are based on the Fotona non-ablative SMOOTH mode concept. In the SMOOTH mode, [18, 43] laser energy is transmitted as heat onto the mucosa surface, without any resulting ablation, and is then dissipated into the deeper tissue layers. Laser energy is delivered onto the mucosa tissue in a fast sequence of low-fluence laser pulses inside an overall super-long pulse of several hundred milliseconds. When the temporal separation among the pulses is longer than the thermal relaxation time of the mucous surface tissue, the surface mucous tissue has sufficient time to cool between the pulses by dissipating the heat into the deeper tissue layers. Thus temperatures required for ablation are reached at much higher fluences. And if at the same time laser energy is delivered in a time period that is shorter than the thermal relaxation time of the total mucous layer, then the deeper lying mucous layer does not have time to cool off during the laser pulse sequence. The delivered laser energy thus results in an overall non-ablative build-up of heat and creates a temperature increase within the mucous tissue. Research has shown that with the SMOOTH mode pulses, human tissue gets non-ablatively heated to a depth of 100 microns, which is just what is required for a depth-controlled thermal treatment of vaginal mucosa tissue.

There are two approaches to superficial tissue treatments: full-field and non-uniform, patterned (also called fractional) treatments (See Fig. 1) [26-42].

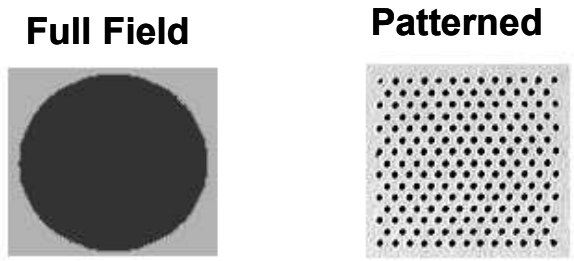

Fig. 1: As opposed to full-field treatments, patterned treatment is based on a concept of producing an array of smaller treatment "islands".

In full-field treatments, the entire surface area within the laser spot is affected by the laser. The patterned technique is based on a concept of producing an array of smaller treatment "islands" on the tissue surface. The reason to have healthy untouched spots around the heated tissue is to use the capacity of healthy spot tissue and cells for a faster immune response and healing process. Our clinical experience also shows that patterned irradiation is more comfortable to the patient, which allows practitioners to use higher fluences within the irradiated spots.

Typically, the fractional pattern is generated by focusing the laser light into small pixels (See Fig. 2). This results in relatively high local laser fluences and low energy ablation thresholds.

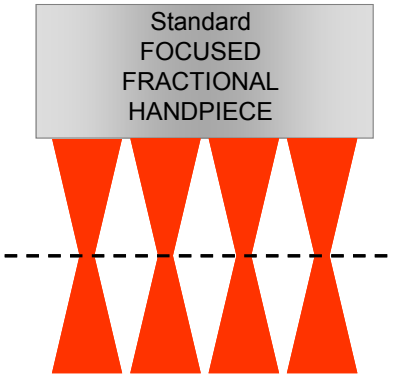

Fig. 2: Standard focused fractional technology utilizes focusing optics to focus a whole beam, or parts of the beam, to small spots located in the focal plane of the focusing optics. The beam is narrow only at the focal plane, while it spreads in both directions away from the plane. With this technology, it is imperative that the treated tissue is positioned precisely at the handpiece's focal plane.

However, there are some significant limitations when applying traditional focusing fractional technology to non-ablative laser treatment of mucosa tissue. Since a minimally invasive, non-ablative, and purely thermal treatment of mucosa is desired, the fluence F of the laser must be below or close to the ablation threshold fluence. Here, the fluence (in J/cm^2) is defined as energy density: $F = E/A$ where E is the energy of the laser pulse, and A is the spot size area. A laser-induced heating has to be provided in the mucosa tissue without overheating to prevent tissue damage and ablation. This is extremely difficult to achieve with standard focusing fractional technology since the ablation of mucosa tissue occurs already at very low laser pulse energies, and the parameter range for a safe non-ablative treatment is extremely narrow.

For the above reasons, the IntimaLase™ and IncontiLase™ techniques employ a special Pixel Screen (PS) technology to create smaller beam dots on the mucosa tissue. With the Pixel Screen technology, the full beam is divided into smaller beams by a special pixel screen (See Fig. 3). As a result, the fluence of each individual pixel beam remains comparable to that of the original full beam.

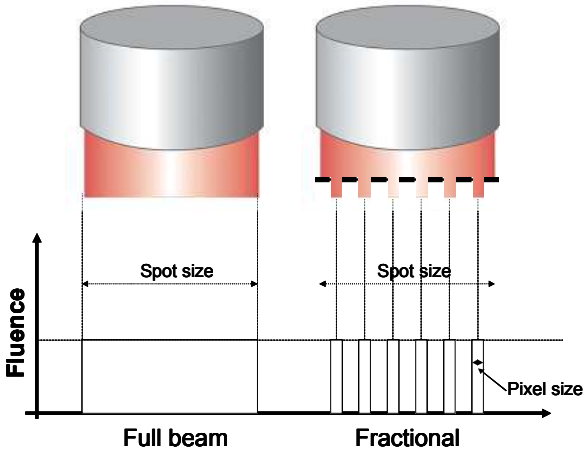

Fig. 3: Er:YAG laser Pixel Screen technology does not use any focusing optics to create smaller beams. Instead, the full beam is divided into small beams by a special pixel screen. The fluence of each individual beam thus remains unchanged and is equal to that of the full beam.

An additional advantage of the PS technology is that it enables the generation of collimated beams that do not considerably change in size with distance relative to the treated tissue. This is particularly important when treating body cavities where the treated surface is not flat or well defined. For such treatments, the focusing technology would be inappropriate since the fluence on the mucosa tissue would vary drastically depending on the distance from the emitting laser handpiece to the treated mucosa tissue surface (See Fig. 4).

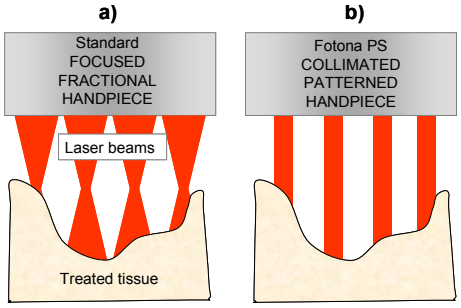

Fig. 4: a) With the focusing fractional handpiece, the beam spot size and the corresponding ablative effects depend strongly on the distance between the treated tissue surface and the handpiece. b) With the Pixel Screen handpiece, the beam spot size does not depend on the distance between the treated tissue surface and the handpiece. This allows safe and defined treatments of irregularly shaped surfaces of body cavities. Note that for both focused and collimated beams, the fluence will depend on the angle of the treated surface relative to the handpiece axis.

The ablative and thermal effects of standard full field Er:YAG lasers operating in a single pulse or SMOOTH mode are by now well understood [43-46]. Since for non-ablative thermal treatments of mucosa tissue it is of paramount importance to always remain below the ablation threshold, we have in this study carried out a study of ablative effects of Pixel Screen Er:YAG laser beams which are currently applied during IntimaLase™ and IncontiLase™ treatments. The purpose of this in-vivo histological and in-vitro triangulation measurements was to show that with the Pixel Screen technology the ablative characteristics are the same as those obtained with the full field technology. In the second part of this paper we report on the initial results of the on-going multi-center clinical studies of the IntimaLase™ and IncontiLase™ techniques using collimated full-field and collimated Pixel Screen technology handpieces.

II. MATERIALS AND METHODS

The Er:YAG laser used in the study was a Fotona Dynamis Er:YAG laser system (Fig. 5).

Fig. 5: Fotona Dynamis Er:YAG laser system.

The Dynamis laser system used in the experiment was fitted with one of the following handpieces: a) R04 or R11 full-beam handpiece; b) PS01, PS02 or PS03 Pixel Screen technology handpiece; and c) F22 focusing fractional scanner handpiece.

a) Ablation measurements

Human skin obtained during abdominal surgery was used in the study. Because of the very small volumes of ablated skin in many of the measurements, a highly accurate methodology was required to make the appropriate measurements of the ablated depths in the human tissue. To achieve this, a specialized measurement assembly has been developed and proven to be effective at the Faculty of Mechanical Engineering at the University of Ljubljana, Slovenia. This makes use of a laser profilometer running in conjunction with custom 'Volume_analyser' software [47-49]. The method is based on the optical triangulation principle. The measured surface is illuminated by a diode laser beam, formed into a light plane. The bright laser beam is visible on the illuminated surface and captured by a camera (See Fig. 6).

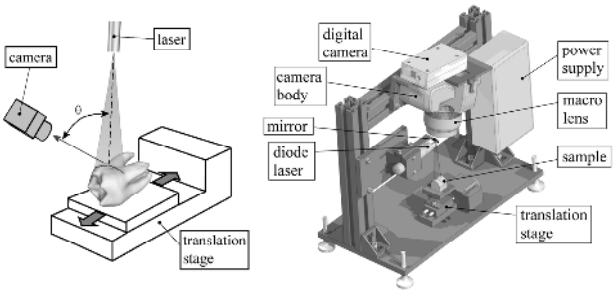

Fig. 6: Schematic showing the operation of the profilometer and the general assembly of the equipment.

The design of the system ensures highly-accurate and repeatable measurements as well as the facility for photographic recording and visual comparisons (Fig. 7).

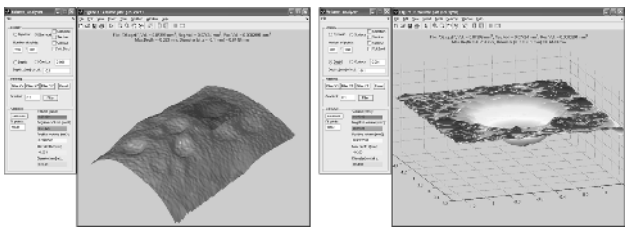

Fig. 7: Screenshots of the 'Volume_analyser' software showing various stages in volume analysis.

Typical examples of the triangulation images of Er:YAG laser-ablated holes are shown in Fig. 8.

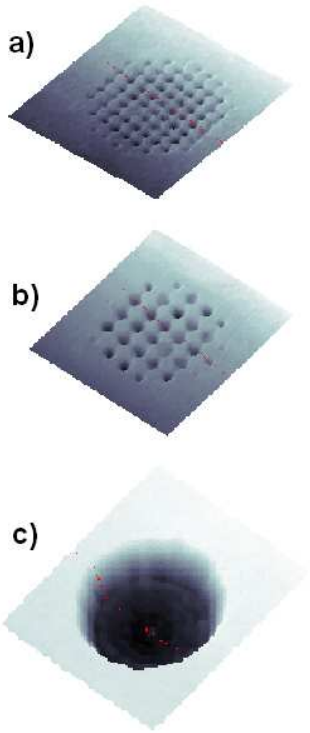

Fig. 8: Triangulation images of the ablated holes following a treatment with: a) stamping fractional handpiece PS01, position 1; 7mm overall spot size; b) stamping fractional handpiece PS01, position3; 7mm overall spot size; c) full beam handpiece R04, 7 mm spot size.

The histological data of six male patients were also analyzed. All patients consented to biopsies following the treatment with the Dynamis Er:YAG F22 scanning fractional handpiece. This part of the study was carried out by Professor Leonardo Marini from the Skin Doctors' Center of Trieste, Italy.

b) IntimaLase™ clinical treatment protocol

IntimaLase™ treatment is performed with the use of two Er:YAG collimated handpieces (R11 – full field and PS03 pixelated beam) and two handpiece adaptors (circular and straight).

In the first phase of the procedure, the full-field handpiece (R11) with circular adaptor is used to perform irradiation of the full circumference of the vaginal canal. For easier access to the vaginal canal, an additional piece of equipment called a laser speculum is used. The laser speculum serves as a guide for the handpiece with circular adaptor, allowing it to easily glide along the vaginal canal without touching it (See Fig. 9).

During the first phase of the procedure, several passes of the handpiece with circular adaptor along the vaginal canal are executed, depositing non-ablative SMOOTH mode laser irradiation to the vaginal mucosa. The laser energy delivery sequence and parameter settings are proprietary to the laser manufacturer (Fotona), which is an issue of pending patent application.

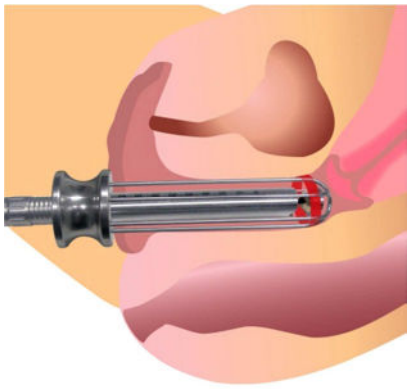

Fig. 9: IntimaLase™ laser-beam delivery system (developed by Fotona d.d.) enabling 360° irradiation of the vaginal canal.

When this phase is completed, the R11 handpiece and circular adaptor are replaced with a PS03 and straight adaptor, and the laser speculum is removed from the vaginal canal. In the second phase of the IntimaLase™ procedure, a pixilated, non-ablative SMOOTH mode laser irradiation is delivered to the mucosa of the vestibule and introitus, again in several passes with the aim to fully and thoroughly heat these areas and thus induce collagen shrinkage, remodeling and new collagen synthesis.

c) IncontiLase™ clinical treatment protocol

IncontiLase™ treatment is performed with the use of the same handpieces and adaptors as are used for IntimaLase™, but here one more adaptor (angular) is needed.

The first phase of IncontiLase™ treatment is similar to the first phase of the previously described IntimaLase™ procedure – the laser speculum is introduced into vaginal canal and a handpiece with adaptor is introduced into laser speculum (See Fig. 10). The difference is that with IncontiLase™ the PS03 handpiece with angular adaptor is used as the laser beam delivery system, with the aim to deposit a pixelated laser beam to (and along) anterior vaginal wall. Several passes of the handpiece with angular adaptor along anterior vaginal wall are executed, depositing pixelated non-ablative SMOOTH mode laser irradiation to the mucosa of the anterior vaginal wall. Upon completion of the appropriate number of passes along the anterior wall, the handpiece and adaptor are changed to the R11 and circular adaptor, and an additional pass with full beam is deposited to the whole vaginal canal circumference.

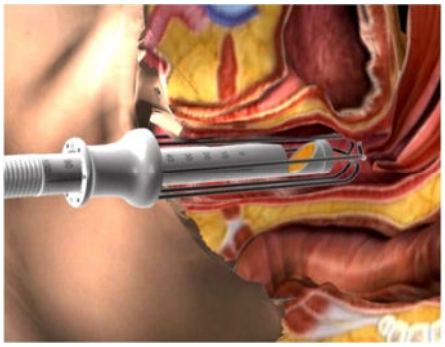

Fig. 10: IncontiLase™ laser beam delivery system (developed by Fotona d.d.) enabling perpendicular irradiation of the anterior vaginal wall.

The final part of the IncontiLase™ procedure is the same as the second phase of IntimaLase™ procedure already described – using the PS03 and straight adaptor, the vestibule and introitus areas are properly irradiated.

III. RESULTS

a) Ablation results

Figure 11 shows the measured ablation depth per pulse for a case when a full beam Er:YAG handpiece (R04) was used. The laser pulse energy is a good predictor of the ablative depth only when the same spot size is used. For the same fluence at different spot sizes, the pulse laser energy will vary considerably, while the ablative depth will be the same. As can be concluded from Fig. 11, the ablative effect will be the same for the same fluence but not for the same pulse energy. For example, at a fluence of 5 J/cm², an ablative depth of approximately 10 µm will be achieved with a pulse energy of: 350 mJ with a 3 mm spot size, 980 mJ with a 5 mm spot size, and 1920 mJ with a 7 mm spot size.

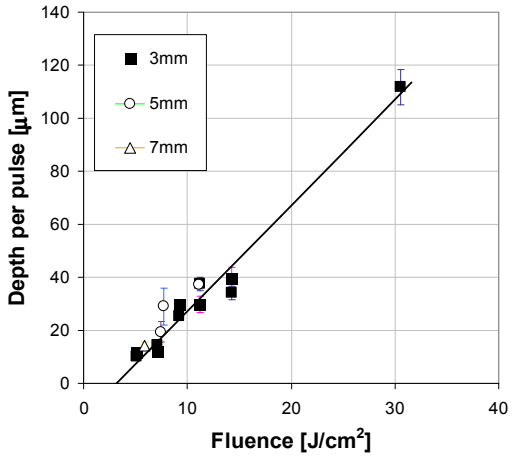

Fig. 11: Dependence of ablation depth on laser pulse fluence and spot size, as measured with the laser triangulation method (full beam R04 handpiece, 300 µs pulse duration). The ablation depth (D) depends linearly on the maximal pulse fluence within the pixel as D= k x (F-F_{th}) where K = (3.7 +- 0.3) µm cm²/J.

Figure 12 shows the ablation depths for different full beam and PS type handpieces. As can be seen from the data, the ablative depths of Pixel Screen technology handpieces follow the same linear dependence on laser fluence as the corresponding full beam handpieces, independently of the handpiece type. The ablation threshold fluence, F_{th}, as determined from the linear fit is at 2.4 J/cm² for both the PS and full-field handpieces.

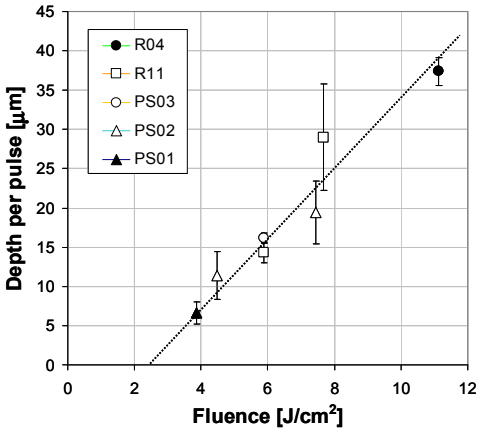

Fig. 12: Dependence of ablation depth on laser pulse fluence and handpiece type, as measured with the laser triangulation method (7 mm spot size, 300 µs pulse duration). The ablative depths follow the same linear dependence of laser fluence, independently of the handpiece type. The ablation depth (D) depends linearly on the maximal pulse fluence within the pixel as D= k x (F-F_{th}) where K = (3.8 +- 0.3) µm cm²/J.

Since the triangulation method is not suitable for measuring very deep holes, the ablative effect of the focusing fractional scanner handpiece F22 was measured by obtaining histological results following the Er:YAG laser treatments. A typical histological picture of a hole in the human skin following treatment with the F22 handpiece is shown in Fig. 13.

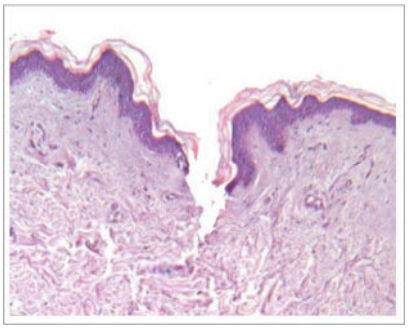

Fig. 13: A histological picture of an ablated pixel, using the scanning fractional handpiece F22 (laser energy 7 mJ).

The dependence of the ablation depth on the F22 handpiece pulse energy as obtained from histological pictures is shown in Fig. 14. Corresponding laser fluences are calculated from the nominal pixel spot size of 250 µm, and taking into account that the laser intensity varies across the pixel according to an Airy

function. The local fluence is largest at the center of the pixel, and is calculated to be larger than the average fluence across the pixel by approximately a factor of 2.3.

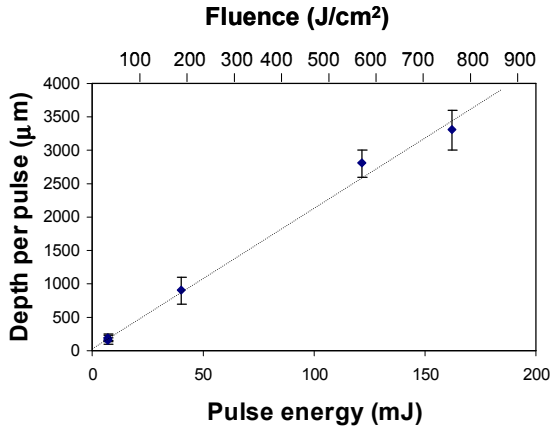

Fig. 14: Dependence of ablation depth on laser pulse energy for the F22 scanning fractional handpiece, as obtained from histological results. Maximal pixel fluences that correspond to laser pulse energies within the 250 µm diameter pixel are also shown. The ablation depth (D) depends linearly on the maximal pulse fluence within the pixel as $D = k \times (F - F_{th})$ where K = (4.3+- 0.3) µm cm²/J.

It is important to note that although the study was performed on the human skin, the results apply also to mucosa tissue. Namely, the Er:YAG laser wavelength is pigment non-specific, and is absorbed only by the water contained in the human tissue.

b) Clinical results using IntimaLase™ protocol

Dr. Mario A. Rivera D. from GynDermo Laser Clinic has reported on two studies of laser vaginal tightening, using the IntimaLase™ protocol [50]. The first group of 135 patients was treated in the period from June 2009 to September 2010. On 1 month follow-up after the first session of IntimaLase™ treatment, 122 (90.4%) patients expressed their satisfaction with the tightening improvement, while 13 patients (9.6%) declared improvement, but asked for a second session. On the next follow-up interviews at 3 months and 6 months, all patients expressed their satisfaction with tightening improvement. The second group of 27 patients was treated during March 2011 with a single session of IntimaLase™ therapy. In an attempt for better quantification of the results, Dr. Rivera used the McCoy Female Sexuality Questionnaire (MFSQ) to measure changes in sexual gratification. For objective measurement of vaginal tissue shrinkage vaginal canal dimensions were measured before and after the treatment. Results of the MSFQ showed an average improvement of 8.5 points on a 36 point scale. Vaginal tightening was achieved in all patients, ranging from 3% to 28%, resulting in an average shrinkage of 17% (or 12 mm), as shown in Fig.15.

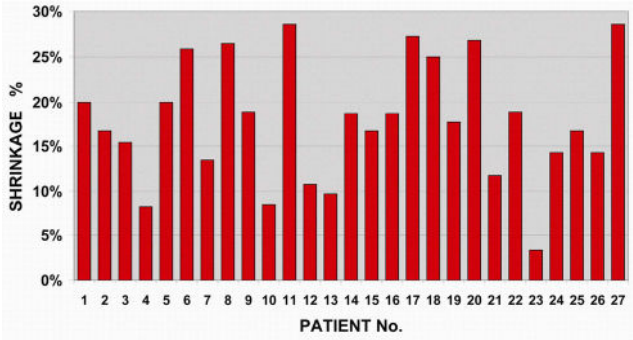

Fig. 15: Shrinkage of the vaginal canal after a single IntimaLase™ treatment, as measured by Dr. Rivera on 27 women.

There were no adverse effects nor any complications observed either by the clinician or reported by patients.

Dr. Ivan Fistonic from Fistonic Gynecology Clinic has evaluated the efficacy and safety of the IntimaLase™ procedure in his pilot study conducted on 17 women in a period between September 2010 and January 2011 [51]. Before the treatment all patients were submitted to measurements of pelvic floor muscle strength and endurance and were asked to respond to a short form of the Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire (PISQ-12) [52]. Follow-ups were performed at 1 month and 3 months after the treatment. Results (see Fig. 15) showed an average improvement in PISQ-12 value of 2.4 points (an increase of average value from 39.0 to 41.4). Perineometric measurements giving values of maximal and average pelvic floor muscle pressure, as well as duration of vaginal squeeze, also showed nice improvement at 1 month after the treatment, among which the duration of vaginal squeeze was significantly higher ($P<0.028$).

All patients but one were clear of any adverse effects. However, there was one patient which had mild burns along the vaginal canal, which normally re-epithelized in a few days, leaving no scars. This adverse effect was attributed to an overdosing of laser irradiation due to the laser operator's learning curve.

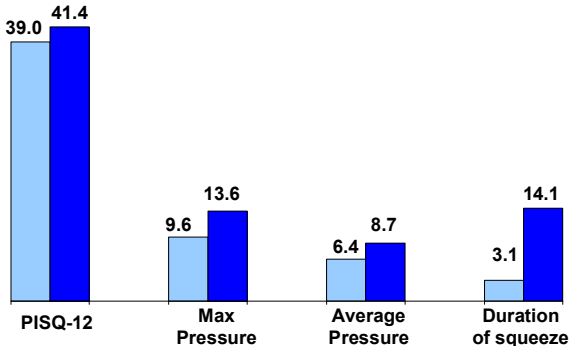

Fig.16: Results of Dr. Fistonic's IntimaLase™ pilot study showing improvement in all measured parameters.

Dr. Paolo Guimaraes from GyneLaser has also reported on a laser vaginal tightening study using the IntimaLase™ treatment protocol [53]. Twenty-three patients were treated during a period from August to December 2011. All patients received a single session of IntimaLase treatment. In this study, the patients' male partners were also interviewed regarding any improvement of tightness sensation. Interviews were made on follow-ups at 1 month, 2 months and 4 months after the treatment.

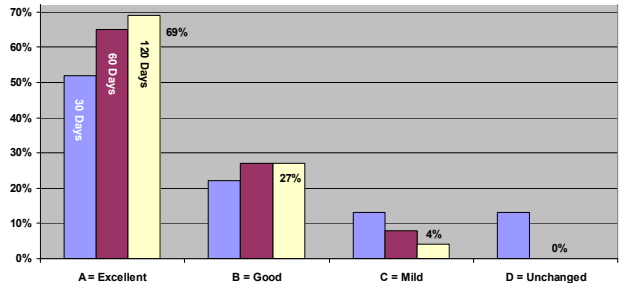

Fig.17: Male partners' evaluation of tightness improvement at three follow-ups (1M, 2M and 4M). The results show continuous improvement during the observation period of 120 days.

At 1 month follow-up, 87% of partners reported mild-to-excellent improvement, while 13% responded that there was no improvement (See Fig. 17). However through time more and more partners reported better and better improvement. At four months (120 days) after the treatment, 69% of partners assessed their improvement as excellent, 27% as good and 4% as mild. None of the patients' partners claimed "no improvement" either on the 60 or 120 day interviews. No adverse effects were observed either by the clinician or patients.

Dr. Jorge Gaviria from the Aldana Laser Center has reported on a study which was performed during June 2011 and January 2012 on 21 patients, with two sessions of IntimaLase™ treatment [54]. The interval between sessions was 15-30 days. Before the beginning of the treatment, patients responded to PISQ-12 questionnaires and were submitted to POP-Q measurements [55]. The measurements were repeated also before the second treatment session. At 3 months after the second session, patients and their partners were asked to assess the improvement of their vaginal tightness and the improvement of sexual gratification, responding to a specially designed Laser Vaginal Tightening (LVT) questionnaire.

A large majority of the patients (20/21 or 95%) assessed the change of their vaginal tightness as strongly or moderately improved, the remaining one (5%) as mildly improved – however all patients reported an improvement. Also, all of the patients' partners reported improved sensation of tightness; 85% of them assessed this sensation improvement as strong or moderate. Out of 21 patients, 20 reported better sex after the treatment (See Fig. 18). Patients described improvement as: better sensation (95.2%), better orgasm (57.1%) and more orgasms (14.3%).

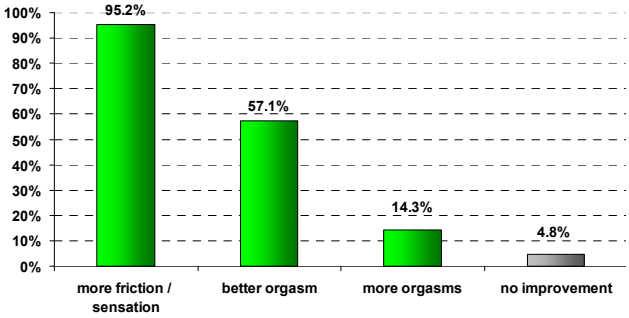

Fig. 18: Patients' assessment of sexual gratification improvement after IntimaLase™ treatment.

Results of POP-Q measurements showed that 5 patients (23.8%) had prolapses of stages 1 to 3, but all of them improved after the first session of IntimaLase™ (See Fig. 19). The IntimaLase™ treatment was found to be safe and easily tolerable. No adverse effects were observed.

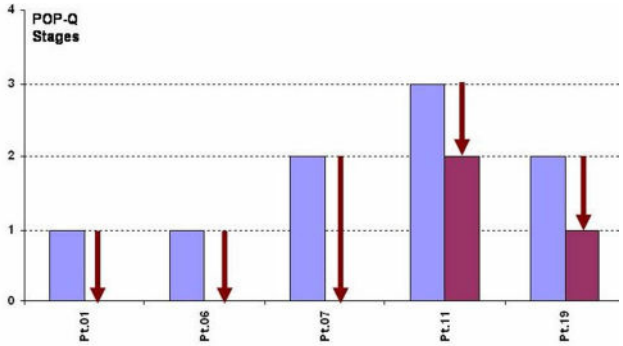

Fig. 19: All patients having prolapses showed improvement after the first treatment session. Three of them didn't have prolapses after the treatment (stage 0).

The Skintima Clinic team of doctors: Dr. Victor Garcia, Dr. Alberto Gonzalez, Dr. Andres Lemmo, Dr. Sofia Herrera and Dr. Zulybeth Rodriguez have presented their results of laser vaginal tightening (IntimaLase™) treatments performed on 29 patients in a period between October 2011 and January 2012 [56]. All patients responded to an IFSF (feminine sexual function index) questionnaire [57] prior to treatments and also at follow-ups at 21 days after the first IntimaLase™ treatment (See Fig. 20). At this first follow-up 16 patients (55.2%) expressed a desire for further improvement of their vaginal tightness and were submitted to a second session of IntimaLase™ therapy. A subjective improvement was observed in 96.6% (28/29) of the cases.

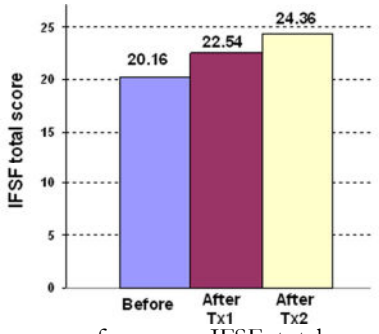

Fig. 20: Increase of average IFSF total score after each session of IntimaLase™ treatment.

The results of the IFSF total score improved after the treatment with statistical significance ($P<0.05$). Most of the particular IFSF categories (desire, arousal, lubrication, orgasm, satisfaction and pain) improved as well, especially lubrication (from 3.02 to 3.95 after Tx1 and to 4.09 after Tx2) and satisfaction (from 3.05 through 4.05 to 4.22). No adverse effects were observed.

c) Clinical results using IncontiLase™ protocol

Dr. Mario A. Rivera D. from GynDermo Laser Clinic treated 115 patients suffering from Stress Urinary Incontinence (SUI) using the IncontiLase™ protocol during the period from March to August 2009 [50]. Out of the treated patient group, 77 patients had a mild form of SUI, while 37 had moderate and 1 patient had severe SUI. After the first session of IncontiLase treatment, 62 (89.6%) patients with mild and 29 (76.3%) patients with moderate SUI reported to be healed, while the others were submitted to the second session of IncontiLase™. At follow-up at 1 month after the second session, an additional 6 patients (of 8 treated) with mild SUI and 5 patients (of 9 treated) with moderate SUI were healed, thus raising the success rate to 97.4% for mild and 89.5% for moderate SUI (See Fig. 21). Of the remaining 6 patients (5.2%), one patient with severe SUI was submitted to TVT surgery, while the other 5 reported improved, but not healed SUI.

There were no adverse effects reported either by the clinician or the patients.

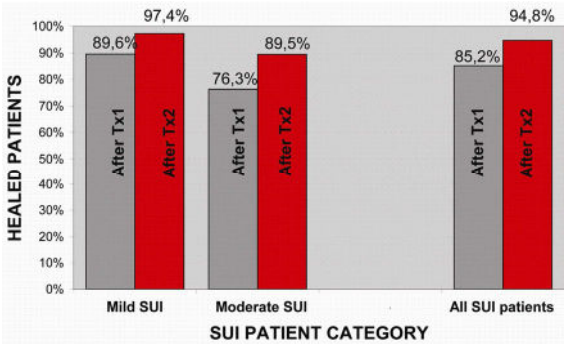

Fig. 21: Healing outcome of the IncontiLase™ treatment performed on 115 women with mild-to-moderate SUI.

Dr. Ivan Fistonic from Fistonic Gynecology Clinic has reported on his pilot study [51], that among 17 patients treated for vaginal tightening, there were 6 patients having also stress urinary incontinence on which he performed also the IncontiLase™ treatment. These patients' SUI was assessed with the ICQI-UI short form questionnaire [58] and Q-tip measurement [59] before the treatment and at 1 and 3 months follow-ups (See Fig. 22).

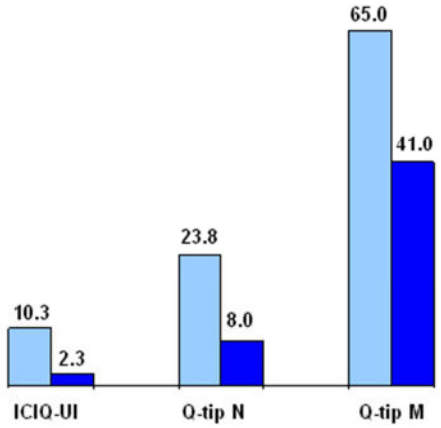

Fig. 22: Improvement of SUI after IncontiLase™ treatment: the average score of the ICIQ-UI questionnaire at 1 month follow-up showed significant reduction, and both Q-tip average angles were reduced as well.

All patients improved, having average ICIQ-UI score reduced from 10.3 to 2.3 (statistical significance at $P<0.02$) and Q-tip angles in normal position reduced from an average angle of 23.8° to 8.0° and under the pressure (exercising the Valsalva maneuver) from 65° to 41°. There were no adverse effects reported.

Dr. Paolo Guimaraes from GyneLaser has reported on a study during which 28 patients were treated according to the IncontiLase™ protocol during the period from August to December 2011 [53]. All patients received a single session of IncontiLase™ treatment. On follow-up visits at 1 month, 2 months and 4 months patients were asked to assess the results of the treatment using a four-grade scale with the following grades: A-excellent (without SUI symptoms), B-moderate improvement, C-slight improvement and D-no change.

As shown in Fig. 23, at the first (1M, or 30 Days) follow-up there were 87% of patients with improvement (43% with an excellent A grade) and 17% of patients without changes. Over time the SUI further improved, so that at 120 days (4M) only 6% of patients were still reporting no change, while 94% of patients reported improvement and 68% of all patients claimed to be free of SUI symptoms. No adverse effects were observed.

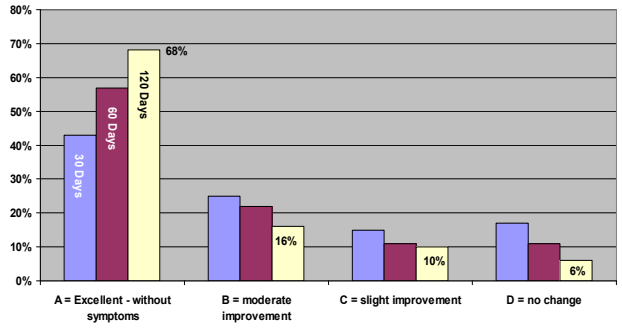

Fig. 23: Results of IncontiLase™ treatment on 28 Brazilian women. Improvement increased steadily during the first four months of follow-up. As the end of this period, 2/3 of all patients declared to be without symptoms of incontinence.

Dr. Ferit Saracoglu from Numune Research and Training Hospital has reported on his experiences with treating stress urinary incontinence and laser vaginal tightening using a single session of the IncontiLase™ or IntimaLase™ protocols, depending on the patients' indication [60]. Thirteen patients were recruited in this pilot study, nine (9) of them having reported SUI, while the remaining four (4) wanted to be treated for vaginal relaxation syndrome and were submitted to the IntimaLase™ protocol. All patients were submitted to several evaluations before and at 6 weeks after the treatment. The measurement tools used were: perineometric and prolapse (POP-Q) measurements and PISQ-12 and ICIQ-UI questionnaires.

All assessments showed improvements after the treatments and there were no adverse effects reported.

Perineometric measurements showed increases in all three measured values: maximal pressure on average increased from 18.0 to 23.8 mm Hg, average pressure from 11.2 to 17.9, while the duration of vaginal squeeze on average increased from 5.1 to 5.3 seconds (See Fig. 24).

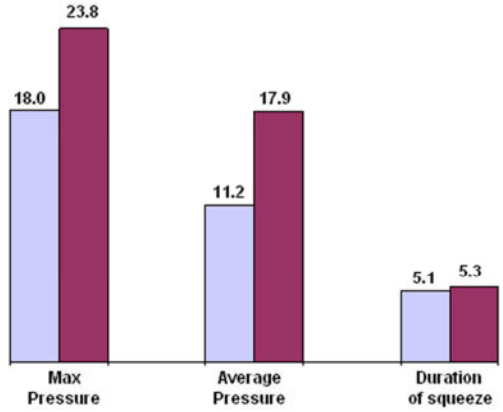

Fig. 24: Results of perineometric measurements before and 6 weeks after the treatment.

The pelvic organ prolapse quantification exam (POP-Q) (See Fig. 25) showed that all 13 patients had various stages of prolapse, most of them (9) had prolapse of stage 1, while 3 patients had stage 2 and one patient had stage 3. On follow-up at 6 weeks after the treatment only 12 patients were measured and 6 of them (50%) improved their prolapse stages, 5 patients by one stage, while one patient (having stage 3), improved by two stages .

POP-Q Stage	No. of Patients	
	Before	After
0	0	3
I	9	8
II	3	1
III	1	0
IV	0	0

Fig. 25: Improvement of prolapse stages after a single session of laser treatment.

All patients responded to the PISQ-12 questionnaire before and at 6 week follow-ups. Results showed an average improvement in PISQ-12 value of 5.2% (an increase of average value from 29.6 to 31.1 points) (See Fig. 26).

Nine patients treated for SUI answered the ICIQ-UI questionnaire before the treatment and 6 weeks after. Results showed an average improvement of 22.4%, with average score reduction from 13.9 to 10.8 points (See Fig. 26).

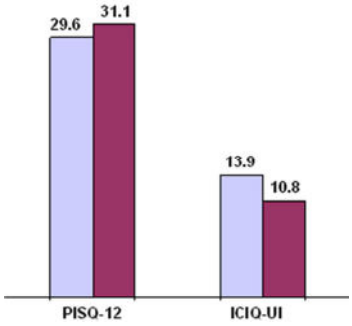

Fig. 26: Results of the questionnaires PISQ-12 (left) and ICIQ-UI (right) before and 6 weeks after the IncontiLase™ treatment.

IV. DISCUSSION

Our measurements have shown that the Pixel Screen technology allows superficial treatments of mucosa tissue with a sufficiently wide range of laser parameters for non-ablative single-pulse or SMOOTH mode technique. The difference in the ablation threshold and ablative effects between a focusing fractional handpiece and a Pixel Screen patterned handpiece is shown in Fig. 27.

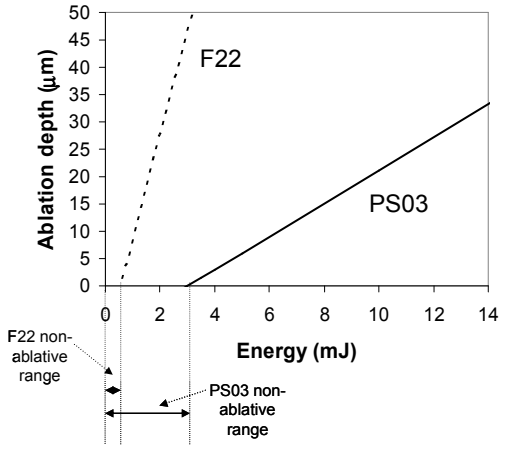

Fig. 27: Comparison of the ablative effects of a standard focusing fractional handpiece (Fotona F22) and a Pixel Screen handpiece (Fotona PS03). The Pixel Screen handpiece has a wider range of non-ablative treatment parameters. Calculations are based on data from Figs. 12 and 14.

With a focusing handpiece, the ablation starts and increases very quickly with laser energy. In comparison, the Pixel Screen technology allows a much wider range and control of non-ablative treatment parameters.

Even more importantly, and as discussed in the Introduction, the Pixel Screen technology allows the generation of collimated beams, which is critically important when treating uneven and curved body cavities. For such treatments, the focusing technology would be inappropriate since the fluence on the mucosa tissue would vary drastically depending on the distance between the emitting laser handpiece and the treated mucosa tissue surface (See Fig. 28).

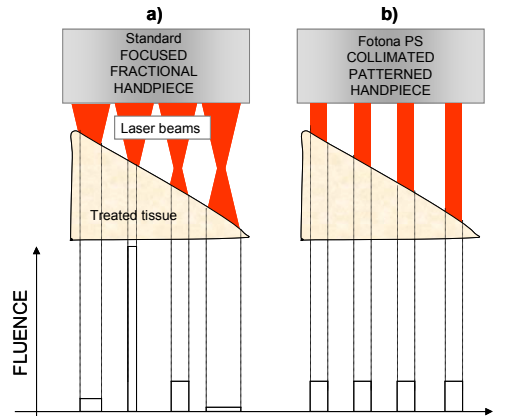

Fig. 28: a) With the focusing fractional handpiece, the fluence on the treated tissue surface and the corresponding ablative effects depend strongly on the distance between the treated tissue surface and the handpiece. The fluence can uncontrollably vary from dangerously high to insufficiently low values; b) With the Pixel Screen handpiece, the fluence and the ablative effects do not depend on the distance between the treated tissue surface and the handpiece. This allows safe and defined treatments of irregularly shaped surfaces of body cavities.

Note that for both focused and collimated beams, the fluence will vary also depending on the angle of the treated surface relative to the handpiece axis.

V. CONCLUSIONS

The relatively wide range of safe, non-ablative treatment parameters combined with the collimated beam characteristics of the Pixel Screen technology Er:YAG handpieces have enabled new minimally invasive gynecological procedures such as IntimaLase™ for vaginal tightening, and IncontiLase™ for treating stress urinary incontinence. The ability to use the Pixel Screen handpieces in a collimated beam configuration is of critical importance when treating uneven and curved body cavities.

Based on the presented initial clinical results, the IntimaLase™ and IncontiLase™ treatment protocols are promising to become minimally invasive solutions of choice for many patients suffering from vaginal relaxation syndrome and stress urinary incontinence. Further clinical studies are currently under way in several international clinical centers in order to confirm the safety and efficacy of the new treatment on a larger number of patients and with longer follow-up times, some of which have already exceeded 12 months [61, 62].

Acknowledgment

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