ASSESSMENT OF PATIENTS'OUTCOME IN LASER SKIN RESURFACING

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LIST OF ABBREVIATIONS

CNN: Congenital Nevomelanocytic Naevi.
CO_2: Carbon Dioxide.
CPG: Computer Pattern Generator.
CW: Continuous Wave.
EM: Electro-Magnetic.
Erb:YAG: Erbium Yttrium Aluminum Garnet.
HZ: Hertz.
IR: Infrared.
J: Joule.
L.S.R: Laser Skin Resurfacing.
Mic.Sec: Micro-Second.
MJ: milli-Joule.
msec: Milli-Second.
Nd:YAG: Neodymium Yttrium Aluminum Garnet.
nm : Nano-meter.
OPD: Optical Penetration Depth.
PSL: Pigmented skin lesion.
R.T.D: Residual Thermal Damage.
SCC: Squamous Cell Carcinoma.
TCA: Trichloro-Acetic Acid.
μm: Micrometer.
μsec: Microsecond.
W: Watt.
S.derm: Superficial dermis.
D.dermis: Deep dermis.
Epid: Epidermis.

SUMMARY

Applications of lasers in plastic surgery and dermatology began in the early 1960's, over the last few decades many types have been developed including Ruby laser, Dye laser, Nd:YAG laser, Er:YAG laser, and Carbon dioxide laser.

Carbon dioxide (CO_2) laser skin resurfacing has rapidly become the treatment of choice for rejuvenation of photo-ageing skin and ablation of other skin lesions. Pulsed Erbium:Yttrium-aluminum-garnet (Er:YAG) laser skin resurfacing is currently being explored for treatment of similar skin conditions.

The indications for laser skin resurfacing includes: facial wrinkling, acne scarring, scars, actinic cheilitis, some pigmented lesions, rhinophyma and benign tumours such as syringoma, trichoepithelioma, dermatosis papulosa nigra, xanthelasma, adenoma sebaceum, sebaceous hyperplasia, epidermal naevi, and others.

Four mechanisms are involved in laser resurfacing:

1- Single-pulse vaporization.

2- Collagen shrinkage and skin tightening.

3- New collagen formation and remodeling of collagen.

4- Multipulse coagulation of collagen.

Both the CO_2 laser and the Erb:YAG laser have unique qualities that can be exploited during resurfacing. The CO_2 laser is unique in the following ways:

1- Hemostasis is achieved.

2- A plateau of ablation is reached, limiting resurfacing depth if proper treatment protocols are followed.

3- Collagen (skin) tightening occurs as heat-related phenomenon, resulting in correction of loose tissue and atrophic scars.

4- The first pass causes an epidermal/dermal split that allows easy and complete removal of epidermis with a single pass.

The Erb:YAG laser is unique in the following ways:

1- Minimal residual thermal damage or tissue heating occurs.

2- This pure-ablation laser continues to ablate with each pass and does not reach an ablation plateau with depth.

3- Only minimal tissue water is required for laser tissue interaction.

The most successful use of lasers for skin resurfacing would be to take advantage of each laser's unique benefit and to eliminate any disadvantages as much as possible.

Accordingly, a prospective study was arranged to examine the effect of Erb:YAG laser, CO_2 laser, and a combined CO_2-Er:YAG laser in skin resurfacing in terms of depth of injury and long term effect on histological appearances after laser skin resurfacing by each laser.

Twenty patients were recruited and a skin resurfacing test patch was performed using each laser (CO_2, Erb:YAG, and combined CO_2/Erb:YAG) on the post auricular area. A biopsy was taken from each test patch six hours after the operation.

Six months later another biopsy was taken from each test patch area of each laser (CO_2, Erb:YAG, CO_2/Erb:YAG) in seven patients. One year following the first operation, biopsies were taken from the test patch areas in eight other patients.

Biopsies were examined histologically to determine the differences between the three lasers in terms of their effect on the histological appearance related to original depth of injury.

The histological assessment of epidermal and dermal changes in the three groups of biopsies after the use of three types of lasers:

The first group (6h post test patch)

Greater damage in the epidermis was associated with Erb:YAG use. Most specimens with focal epidermal residue were found in the biopsies after test patches with CO_2 laser. No biopsies showed focal epidermal residue after test patches with Erb:YAG laser.

Following the statistic analysis of the result in this group, it was found:

In relation to the depth of injury to epidermis: There was a statistically significant difference in the depth of ablation between the CO_2 and Erbium groups. $P = 0.007$ (exact test).

In relation to the depth of injury to dermis and inflammatory response: There was trend towards deeper dermal injury in the Erb compared with the CO_2/Erb and the CO_2 groups. $P = 0.093$ and $P = 0.162$ (exact test). There was significantly more inflammation at 6 hours in the CO_2 compared with the Erb group $P < 0.05$ (chisquare test), and the CO_2/Erb compared with the Erb group $P < 0.025$ (chisquare test).

The results suggest that the overall injury (ablation + RTD) was similar in the three groups as planned from the known characteristics of the three lasers ie deeper ablation in the Erb group and more residual thermal damage in the CO_2 and CO_2/Erb groups.

Biopsies in the second and third groups (6months, 1 year post test patch) have shown:

Many of the slides showed full recovery with normal looking epidermis and dermis. Some showed altered epidermis with either flattened epidermis with loss of rete pegs or complex branching of the rete pegs or a combination of these appearances. There was no significant difference between the CO2/CO2 + Erb, CO2/Erb or CO2 + Erb/ Erb groups (P = 1.279, P = 0.824 and P = 0.908 respectively using exact tests)

The results in all of the three groups suggest that:

with an equivalent depth of injury i.e. deeper ablation but less collateral heat damage Erb:YAG laser produces similar long term histological changes as CO_2 or Erb/CO_2 lasers.

There appears to be few long-term changes to dermal architecture with laser resurfacing

Another part of this study looked at a group of patients who had pigmented skin lesions like congenital compound naevi, hairy naevi, and others. All of those patients had poor results with Q.Switched Ruby laser treatment, and all of them were treated with CO_2 or Erb:YAG lasers.

This study looked at the outcome of laser ablation in relation to the diagnoses and depth of lesion, which was confirmed with biopsy.

38% of patients with congenital pigmented neavi had good results, but none of the naevi had gone completely. 70% of epidermal naevi had good results. Although 100% of the lentigo maligna lesions disappeared we do not recommend the laser ablation as a treatment of choice due to the tendency of the lentigo maligna lesions to develop malignant melanoma. All of actinic keratosis lesions cleared completely.

There was a significant correlation between the depth of a pigmented skin lesion and its response to laser ablation with all the lesions which were either gone or had a good result being in either the epidermis or superficial dermis $P < 0.001$ (chisquare test).

Another group of patients who had benign superficial tumors, like epidermal naevi, syringomas, and others, were looked at to find out the outcome of laser treatment after using either CO_2 or Erb:YAG laser.

The conclusion that the superficial lesions did achieve better results than the deeper pigmented skin lesions covers the finding following the laser ablation for benign superficial tumours, where only the superficial lesions (xanthalasmas) had disappeared.

Finally; a small group of patients with disseminated superficial actinic prokoratosis (DSAP) were treated with CO_2 laser resurfacing. The outcome of this treatment was assessed, to find out the effect of laser resurfacing on this rare and very difficult to treat skin condition.

INTRODUCTION

For many years mechanical or chemical removal of the outer layers of skin has been used in the treatment of many skin conditions. More recently lasers have been used for the same purpose. Laser stands for (**L**ight **A**mplification by the **S**timulated **E**mission of **R**adiation).[1] Lasers have been in medical use for nearly Forty years. The laser light has three specific characteristics, which makes it different from the ordinary light. The laser light is coherent, monochromatic and collimated (low divergence).

Lasers differ from other surgical tools that can cut, coagulate and/or ablate, because lasers can be selective for a particular target (chromophore). They can achieve precisely controlled tissue damage, and they are often less painful with a quicker recovery. The principal of selective photothermolysis is important in the cutaneous use of lasers in plastic surgery and dermatology. Selective photothermolysis occurs when laser light of a specific wavelength is preferentially absorbed by the desired target, the exposure duration (pulse-width) is less than the thermal relaxation time of the target, and the energy is sufficient to heat and destroy the target. Target chromphores in cutaneous use of lasers are Oxyhaemoglobin, Melanin, Inks (tattoo), and Water.

In plastic surgery and dermatology many different lasers are used,which differ in their wavelengths, and therefore the specific target, which can be treated.

The main therapeutic indications for cutaneous lasers are: Vascular lesions such as capillary vascular malformations, leg veins, pigmented lesions, tattoos, hair removal, and skin resurfacing. This study will focus on laser skin resurfacing and ablation.

Laser skin resurfacing is removing the outer layers of skin, the epidermis and upper dermis, using lasers where water is the target chromophore. This introduction will be concentrating on Carbon dioxide lasers and Er:YAG lasers which are the commonest resurfacing lasers.

Many grand claims have been made for the results of cutaneous laser treatment. In this introduction different opinions about laser skin resurfacing are explored. The results particularly of laser skin resurfacing are difficult to quantify. Objective improvement in for example the depth of acne scarring is extremely difficult to quantify. Although, photographs are widely used, slight change in lighting can have a profound effect on the appearance of scars or wrinkles. Measuring profiles of scars is fraught with potential error; scales used to measure improvement in patient's psychological view of their condition are by nature subjective and often reflect background mental health problems. As changes in dermal collagen have been noted to be so important in the result of laser skin resurfacing (LSR), the results in this study have been assessed using histological appearances whenever possible.

In this introduction some important points are highlighted:

- Laser development.
- Laser tissue interactions.
- Collagen structure and collagen shrinkage.
- Biological characteristic of wound healing.
- Indications for carbon dioxide laser treatment.
- Finally the study outline and aims of this study.

Carbon dioxide (CO_2) laser resurfacing of skin has rapidly become the treatment of choice for treating depressed scars and rejuvenation of photo-aged facial skin. Erbium:Yttrium-Aluminium-Garnet (Erb:YAG) laser resurfacing is currently being explored for similar treatment of skin.

Although surgical revision of depressed scars has been the treatment of choice for many decades, it leads to fresh scarring and may lead to scar stretching especially on the face where the muscles pull on the edge of the scars and increase it's width. Dermabrasion was also used in treating depressed scars, but it is difficult to control the depth of injury and it causes bleeding. Therefore, laser resurfacing has advantages in treating depressed scars by removing the edges with a high degree of precision, without risk of further scar stretching, and also leads to new collagen formation in the dermis.

One must understand the pathophysiology of photo-damaged skin, details of

laser-tissue interaction, factors in the proper choice of patients, and optimal laser treatment parameters. In addition, knowledge of photo-ageing of skin and its modulation with topical agents, allows choices to be made in the determination of pre-operative and post-operative regimens.

Interest has surrounded facial rejuvenation for centuries. The use of topical agents such as soured milk, vegetable extracts, and mud packs have been documented in ancient civilisations. However, only in the last decade has rejuvenation been approached from a scientific direction. Much attention has been focused on 'anti-ageing' therapies. In particular, the use of retinoic acid, alpha-hydroxy acids, and antioxidants in conjunction with sunscreens and sun blocks to prevent or reverse the photo-ageing process has been investigated. Although these agents may have significant benefits, they generally fall short of the clinical expectations of those using them as a primary rejuvenation treatment.

To achieve a more dramatic clinical endpoint, a variety of chemical agents have been used to induce a layer of necrosis of variable depths, effectively peeling away the outermost layer of sun-damaged skin, with subsequent dermal healing and re-epithelialisation resulting in a more youthful appearance. Similar results have been achieved by mechanically removing these outer layers with dermabrasion. More recently the CO_2 and Erb:YAG lasers have been used to ablate and rejuvenate the skin

CARBON DIOXIDE LASER

Although physicians showed considerable interest in development of resurfacing parameters with the CO_2 laser in the early to middle 1980s, the safety profile for use of continuous-wave (CW) CO_2 laser prohibited its use in this manner. Successful low-fluence CW CO_2 laser removal of the epidermis was reported[2,136] as well as revision of skin grafts[3] and treatment of acne scars[4] in 1985 through 1991. However, this technique was found to be too risky to use over large surface areas because of its high risk of scarring. The more limited use of the CO_2 laser in combination with TCA peeling was reported first by Brauner and Schliftman[4] in 1987 and by David et al[5] in 1989 for the treatment of wrinkling.

CO_2 Laser development

At first the only lasers available were those having wavelengths in the visible spectrum, so treatment was limited to pigmented lesions, particularly those with a very dark colour. This requirement limited significantly the application of lasers surgically. This changed with the development of the carbon dioxide (CO_2) in 1964, which was followed by a wide surgical application of this laser.

The CO_2 laser emits a continuous beam having a wavelength of 10,600 nm, which is absorbed by biologic tissues regardless of pigmentation or vascularity because its target of interaction is water.

The early use of the CO_2 laser in cutaneous surgery was as an excisional or destructive instrument for malignancies,[6-9,10,11-14] in the management of burns,[15,16] and for debridement of decubitus ulcers.[17] Although the CO_2 laser has been referred to as the workhorse of dermatologic lasers, many practitioners in plastic surgery and other specialities became disenchanted with it because of the realisation that thermal damage was difficult to control. Laser manufacturers responded to this situation by developing pulsed CO_2 laser systems.

The traditional CO_2 laser continuous beam could be electronically shuttered to produce pulses of 0.1 to 1 sec duration with consistent power, but this could not predictably prevent thermal diffusion.[18] Therefore superpulsed systems were developed with peak powers 2 to 10 times higher and pulse duration's 10 to 100 times shorter than the conventional CO_2 laser. The development of superpulsed CO_2 lasers, in conjunction with Anderson and Parrish's development of the theory of selective photothermolysis[18] and work being done on burn debridement, allowed the potential for defining the necessary laser parameters for skin resurfacing.

Weinstein[19] reported the first series of patients treated with the high-energy, pulsed CO_2 laser for cosmetic benefit. She reported 36 patients who had upper and lower lid laser blepharoplasty in conjunction with periorbital resurfacing. Excellent results (complete eradication of static periocular lines) were seen in 81%; re-epithelialization required 8.4 days on average and erythema 4.7 weeks to fade. One patient had transient scarring, one had transient ectropion, and three had mild hypopigmentation. The initial use of the laser was confined to the perioral and periorbital regions, because these areas were most difficult to treat by traditional methods. Improvement in pre-treatment photo-damage by approximately 50% or more was reported by Fitzpatrick et al[20]. It became apparent that full-face resurfacing was possible and resulted in even better cosmetic improvement.

Simultaneously, the SilkToutch scanning system (Sharplan Laser Corp) was being developed and used for laser cutaneous resurfacing. Two reports of 47 patients and 40 patients showed an average improvement of greater than 50% and 3.5 on a scale of 6.0.[21,22] Erythema was seen to last 1 to 4 months or average 6 weeks. Persistent erythema was seen to correlate with depth of ablation. Post-inflammatory hyperpigmentation was the most common complication, occurring in 17%, exclusively in patients with skin types III or IV. Bacterial infections occurred in 6%, with herpes simplex disseminating in one patient.

A third laser, the SurgiPlus XJ150 (Sharplan) uses two paired 200-mJ energy peaks rather than a single 500-mJ peak as in coherent UltraPulse CO_2 laser. With a peak of 200-mJ, very little energy actually exceeds the irradiance required for tissue vaporisation, thus, an increased number of laser passes was found to be necessary for treatment, and a 63% mean average improvement was seen, compared with 82% mean improvement after UltraPulse laser treatment.[23]

The recent advances in high-energy, pulsed CO_2 lasers, combined with the development of safe and effective treatment protocols, have resulted in an explosion of interest, promotion, and use of these lasers for rejuvenation of skin.

Delivery System and Laser-Tissue Interactions

A study regarding the effect of pulse duration on the ablation threshold and residual thermal damage[24] revealed a number of significant findings regarding the laser-tissue interaction. These findings concluded that (1) when tissue ablation occurs, the pulse duration is not critical because a rapid temperature drop occurs just below the ablation front,[25,26] (2) residual thermal damage in this situation approaches a theoretic minimum of 50 μm,[25,27,28] and (3) an

increase in pulse width causes increased thermal damage at the edges of craters resulting from a gaussian beam. Also, an increase in the ablation threshold at longer pulse durations is related to thermal diffusion during the pulse. To confine thermal damage the velocity of ablation is critical and requires a value of 0.65 cm/sec or greater to achieve minimal thermal damage.

The ablation depth per pulse at 7.5J/cm^2 was found to be 35 μm, too small to account for the clinical improvement seen in two or three passes of the CO_2 laser in treating wrinkles measuring 300 μm in depth.

As an alternative to pulsed delivery, a CW CO_2 laser may be used with a scanning system that sweeps the beam across the tissue sufficiently rapidly for the tissue dwell time to be less than the thermal relaxation time of the tissue. Simulating the effect of the pulsed delivery system.[21]

The laser beam may be delivered using a focused system, in which the beam is focused with lenses to a point having maximal fluence or irradiance. The distance from that focal point is a major determinant of tissue reaction, resulting in decreasing energies with increased hand piece-to-tissue distances. Alternatively, the beam may be delivered in a collimated manner, in which the beam is parallel and nondivergent, having the same fluence or irradiance independent of handpiece-to-tissue distance.

Although several new lasers were introduced in the mid-1990's, two laser systems have been used to pioneer this field and have generated virtually all the published data: the UltraPulse laser (Coherent) and the SilkTouch scanner (Sharplan). The UltraPulse laser can deliver up to 500 mJ in a single pulse with a duration of less than 1msec, and it is used with computerised pattern generator (CPG) .[29,30]

The Sharplan system uses a standard CW CO_2 beam focused to 200-μm spot that is manipulated through rotating mirrors to scan tissue rapidly, resulting in a tissue dwell time of less than 1msec. Scanning patterns of 4, 6, or 9 mm may be chosen. In clinical use two passes with the Sharplan SilkTouch system appears to be approximately equal to three passes with the UltarPulse laser in terms of the amount of tissue removal and the depth of residual thermal necrosis.[31]

Experimental data and theoretical calculations reveal the necessary pulse fluence to vaporise epidermal tissue to be approximately $5J/cm^2$.[32] To use a large spot size and deliver a pulse less than 1msec, to achieve this threshold fluence, a very high irradiance is necessary. When a spot size of 2.5 mm is used, 250mJ must be delivered in less than 1msec[33]. This is generally delivered with a gaussian beam, so a peripheral ring of about 10% may exist in which this threshold is not reached. This suprathreshold energy will immediately vaporise intracellular water, leaving behind cellular proteinaceous debris. The

depth of the vaporisation is proportional to the pulse energy. However, when the laser is interacting with the dermis, a new situation exists. Water is now primarily extracellular, in the dermal matrix, which is dominated by the structural proteins collagen and elastin. Type I collagen will melt at temperatures greater than 60° C but requires fluences much greater than 5J/cm^2 for vaporisation. Non-vaporisation heating of dermis will have little adverse effect as long as the pulse width is less than 1msec and pulses are delivered to the same tissue spot at a rate less than 5Hz. If the delivery rate is greater than this, heat will accumulate between pulses, and thermal damage by diffusion may occur. This can result in poor wound healing or scarring.

Most histologic studies have shown the first CO_2 laser pass to result in epidermal ablation and the subsequent passes to result in a variable depths of dermal ablation and necrosis. The amount of thermal necrosis has also been shown to correlate with both pulse energy and number of passes, with each pass delivering the same amount of energy with less vaporisation and more extensive heat absorption because of the layer of desiccated tissue at the treatment surface.[34,35,36,37]

One published report has correlated clinical signs with anatomic depth of ablation.[38] A pink colour of tissue was found to correlate with superficial papillary dermis, chamois-cloth appearance for deeper papillary dermis, and waterlogged cotton-thread appearance for reticular dermis. A second report has

received a tremendous amount of attention in which colour changes were stated to be an indication of depth of ablation: pink indicating epidermis, grey indicating papillary dermis, and chamois yellow indicating reticular dermis.[39] These colour changes are actually a misinterpretation of anatomic changes and not a reliable indicator of tissue depth. If little residual thermal necrosis (less than 30 μm) exists, thermal reaction will not be sufficient to coagulate fine papillary vessels, and the tissue will be pink because of the visible capillary blood flow. This is typical of the appearance of the tissue after a single laser pass removing the epidermis. After a second or third laser pass, the laser is reacting with the dermis and leaves 70 to 100 μm of thermal necrosis, adequate for haemostasis and resulting in whitish grey tissue. Further laser passes tend to leave more thermal injury, not an indication of penetration into the reticular dermis.

One study used post treatment biopsies to compare the pulsed CO_2 lasers with a CW CO_2 laser. After one, two, and three passes, the depth of residual thermal damage measured 30, 80, 150 μm, respectively, with the SilkTouch; 30, 100, and 150 μm with the SurgiPulse laser; and 20, 50, and 70 μm with the UltraPulse laser.[40] The CW CO_2 laser left a 400 μm layer of thermal necrosis.

Although early studies appeared to show a relatively constant amount of tissue to be ablated per pass[41] (approximately 75 μm), it became clear in clinical use

that a decreasing amount of tissue was ablated per pass. Fitzpatrick[42] reported in a study that an ablation plateau was reached after three or four passes at 225 to 250 μm using pulsed CO_2 laser. The same study showed that residual thermal necrosis has a linear relationship with both pulse energy and number of passes, with single-pulse thermal necrosis gradually increased to a maximum of 100 μm at pass number seven. However, pulse stacking had a marked impact on residual thermal necrosis, because double pulses added significantly more thermal injury per pass and triple pulses even more per pass, about 30 μm. This additional thermal injury may significantly affect wound healing and result in a much deeper wound than intended. This may be a significant factor in causing scarring, hypopigmentation, or poor wound healing. When using single pulses the vaporisation in laser resurfacing plateaus at a depth of 250 to 300 μm in the dermis, which is too superficial to result in scarring because of the wound depth alone. Therefore, adherence to proper treatment techniques is critical in avoiding excessive thermal injury.

Increases in Grenz zone collagen have been reported after laser resurfacing[43-46], This new collagen formation and remodelling may be a significant factor in achieving rejuvenation of facial photo-damage, as well as an improvement in atrophic scars. A discernible shrinkage of the skin is visible as the laser reacts with dermis, tightening loose folds of skin. This is thought to be a result of heat-induced collagen shrinkage.[20]

When the CO_2 laser interacts with tissue, three distinct zones of tissue alteration correlate to the degree of tissue heating. The zone of direct impact results in vaporisation of intracellular water and tissue ablation. Underlying this is a zone of irreversible thermal damage and denaturation resulting in tissue necrosis. Below this layer is a zone of reversible, non-lethal thermal damage, in which collagen shrinkage is thought to occur, accounting for the visible tissue tightening observable as the CO_2 laser interacts with the dermis.

The carbon dioxide laser possesses intrinsic properties that enhances its usefulness in laser skin resurfacing (LSR), the most important of which is the high absorption coefficient for tissue water (approximately 800 cm^{-1}at room temperature) [47]. This permits minimal residual thermal damage (RTD) if one of the following conditions is satisfied: (1) the power density (fluence divided by exposure time) is sufficient that vaporisation significantly outpaces the speed of thermal diffusion; (2) the energy delivered in less than the thermal relaxation time (tau); or (3) the fluence is small enough that only a thin layer of collagen is denatured.

Energy density (fluence or radiant exposure) is often cited when characterising tissue effects in laser dermatology. Indeed, for pulsed laser applications where pulse duration is approximately tau, this parameter serves as an adequate determinant of the laser-tissue interaction. However, in LSR, pulse duration may vary as much as 10-fold between different devices, and follows that power

density is more useful parameter in determining RTD and vaporisation depth in LSR. Fig 1(Appendix A)

Despite literature extolling the virtues of ablation in carbon dioxide LSR[47], dermal ablation is minimal (<20 μm per pass) in typical applications where relatively low average fluences are used (approximately 7J/cm^2). Moreover, it has never been established that dermal ablation is necessary for clinical efficacy. Accordingly, an understanding of carbon dioxide LSR can be based primarily on non-ablative tissue heating. In short, for carbon dioxide laser with typical fluences, the depth of RTD, rather than the depth of dermal ablation, largely determines the depth of injury. More precisely, the total depth of dermal injury is the sum of a thinly ablated layer (if ablation occurs at all) plus the thermally damaged base.

Pulse duration plays a major role in restricting RTD. Optimally, the exposure time should not exceed tau for a heated layer of water (the primary chromophore for infrared radiation) at 10,600 nm. Thermal relaxation time (for a planar geometry) is defined by tau=delta^2/4kappa, where delta is the optical penetration depth (OPD) for homogeneously absorbing layers (such as tissue water for infrared applications). In contrast, for discrete absorbers, i.e., the melanosome, tau is defined in terms of the particle size; "kappa" is the thermal diffusivity, a quantity based on the thermal conductivity and specific heat of the medium. Conceptually, tau represents the time for a heated layer to cool to

37% of its peak temperature. The OPD of laser irradiation is defined as the depth where fluence is attenuated to 37% of its value. The often used 'thermal relaxation time of the skin' is meaningful only when used for specific wavelengths (or specific skin structures, i.e., the epidermis). When used with reference to the skin in general, the frequently reported tau of 1 msec is meaningful only for 10600 nm radiation.

If energy is delivered in less than tau, commonly applied models predict that heating will be confined to the OPD during the laser pulse. However, the depth of RTD is usually 3 to 4 times the OPD. The reason for this is because there is some heat diffusion during the pulse even with very short exposures, and deeper tissue heating occurs after the pulse. In practice, tau is only an approximation and does not predict the absolute time it takes tissue to cool.

The effect of a gaussian beam after single and multiple pulses

It is instructive to examine the tissue effects of a Gaussian beam (Fig 2-Appendix A) after single and multiple pulses in a single spot. In this manner the effects of broad range of fluences can be analysed in a single specimen in carbon dioxide LSR. On the other hand, the use of this profile has contributed to confusion in LSR regarding tissue ablation. A Gaussian beam (seen in the msec and continuous wave systems , but not the micsec system) distributes energy density like a bell-shape curve. The spot diameter is defined in terms of

the distance from the centre of the beam at which the fluence falls to 14% of the Maximum[47]. The average fluence is defined by the energy divided by the spot diameter, and the fluence at the centre is twice this average. A particular site on the skin surface is likely to see a sub-ablative fluence in one pass, followed by supra-ablative fluence in the next pass, due to the energy distribution pattern, and the unlikelihood of directly overlapping beam profiles in second and third passes when operating in a typical manner (complete one pass, then wipe and return to the site). The impact of the Gaussian beam becomes especially apparent when working with higher fluences (ablation regime >10 J/cm^2 or when applying >20 passes with 7 J/cm^2 and holding the handpiece in a constant position, i.e., in attempting to remove a seborrhoeic keratosis). In this case an ablation defect mirrors the beam profile, and the crater looks like a raindrop in the sand rather than cylindrical defect (Fig 3-Appendix A).

COLLAGEN STUCTURE:

Collagen is protein that undergoes self-assembly into macromolecular structures. Collagen solutions will readily polymerize into collagen fibrils that are indistinguishable from those found in vivo. Reactive Carbonyl moieties generate intermolecular cross-links (collagen aldehydes reacting with other collagen amino acids), uniting the collagen molecules into a continuous polymeric network.[59] Thus collagen molecules, which contain carbonyl groups,

self-assemble into fibres, which then become cross-linked because of reactions between the carbonyl groups and other amino acids of adjoining molecules. This structure is maintained by hydrogen bonds.

Collagen protofibrils are composed of laterally aggregated, staggered molecules, which when cross-linked, form a strong macroscopic three-dimensional network. The molecular stagger results from interactions between the amino acid side chains and consequently has the requisite precision to bring the lysyl side chains into proximity to form intermolecular cross-links.[60] This occurs in a spontaneous, progressive manner. As previously mentioned, this precise intermolecular cross-linking is species specific, because the relative abundance of different cross-links varies greatly depending on the tissue of origin of the collagen.[59]

Flexibility in side-chain interactions suggest that rather a unique reaction being involved, a myriad of conformations occur at the molecular surfaces.[60] The fluidity of the surface domains would allow collagen molecules in soft tissues to slip relative to one another when stress is applied.[61]

Collagen Shrinkage

Collagen fibres provide the framework and mechanical strength of skin. The microscopically visible fibre is composed of a bundle of fibrils that is readily

distinguishable by electron microscopy. These fibrils are made up of a unit filament, the protofibril, which has the same chemical and configurational structure as collagen molecule.

The collagen molecule is a highly unique and unusual protein, containing three polypeptide chains in a helical conformation with the presence of hydroxyproline and hydroxylysine. The repetitive positioning of glycine at every third amino acid locus accounts for its unique helical conformation.

Intermolecular cross-links provide collagen connective tissue with unique physical properties of high tensile strength and substantial elasticity. This cross-linking is mediated by the copper-dependent enzyme lysyl oxidase and can be chemically inhibited by B-aminopropionitrile. This cross-linking reaction is also inhibited by heat and photonic energy.

Thermal Effects

The response of collagen to heat is different compared to that of other body tissues. The hydrothermal shrinkage of collagen fibres has long been recognized as a characteristic of collagen.[48] The mechanism of this thermal contraction is proposed to be a molecular structure transition between the triple helix and a random coil.[49] Temperature elevation ruptures the ultrastructural cross-links that stabilise the collagen helix and results in immediate contraction

in the fibres to about one-third their original length, with corresponding increase in the calibre of individual fibres without alteration in the structural integrity of tissue. Although the application of heat dissociates the interpeptide bonds, the cross-linkage between tropocollagen molecules remains intact, and the contraction of these linked molecules leads to shortening of the collagen fibre.[50]

The viscosity of a tropocollagen solution drops sharply at 39° C as the helical structure is disrupted to random coils and gelatin is formed. This same type of reaction with intact collagen results in visible shrinkage along the long axis of collagen fibres and occurs at a very specific temperature. Rabbit cornea has been shown to shrink 40% to 50% at 65° C.[48] Mammalian collagen, including human sclera and skin tissue, shrinks at 61° to 63° C, whereas human cornea shrinks at lower temperatures, 55° to 58° C.[51] Changes in birefringence (double refraction), indicating thermal coagulated collagen with unravelling of collagen fibrils and loss of unique striations, reportedly occurs at 70° to 75° C.[52]

In the photo-thermal effect induced by laser irradiation of tissue, Thomsen[52] separates these biologic thermal effects into three different thermodynamic processes:

1) Lower-temperature (about 43° - 100° C) damage by heat accumulation processes, which may be lethal or non-lethal depending on times of heat

exposure

2) Higher-temperature (100° C +) effects, dominated by water vaporisation and effects of water vapour release

3) High-temperature ablation (about 300° - 1000° C), resulting in tissue vaporisation, combustion, molecular dissociation, and plasma formation.

Thermal Coagulation

The visible thermal changes seen in collagen on light microscopy represent thermally induced, irreversible alterations of proteins and other biologic molecules, organelles, membranes, and adjacent cells, referred to as thermal coagulation. These alterations are caused primarily by thermal denaturation of structural proteins, are seen immediately after heating, and are always lethal. This differs from the low temperature tissue injury, which may be demonstrable with electron microscopy or enzyme histochemistry in the first 24 hours, or through light microscopy 48 to 72 hours after cellular death. Non-lethal changes may be more difficult to document because staining artefact can mimic the pathologic alterations.

Thermally induced partial loss and complete loss of native birefringence and hyalinisation of thermally coagulated collagen are easily recognisable. The normally seen birefringence is related to the regular arrangement of molecules forming the collagen fibrils. Thermally coagulated collagen examined by

electron microscopy reveals unravelling of collagen fibrils with loss of the unique striations of collagen and an increase in fibrillar diameters.[53] The unravelled strands merge, and the individual fibres becomes less distinct, forming the swollen, hyalinized (glossy) collagen fibres seen with light microscopy. Birefringence changes induced by thermal reaction in collagen include a gradual loss of bright image intensity as well as colour shifts of histologic stains. The loss of bright image intensity in thermally coagulated collagen may result from thermal disruption of the intermolecular bonds of collagen, leading to destruction of the regular arrangement among collagen molecules. The unravelling of collagen fibrils may expose new dye-binding sites and thus result in the colour shifts seen. Normal fibres have been found to be intermixed with altered fibres in examination of tissue-welding sites induced by thermal changes from laser irradiation.[54,55,56]

The easily recognisable changes of thermal necrosis of collagen reflect the effects of higher temperatures (70° - 75° C) that also result in cellular death, and therefore are not necessarily desirable in resurfacing procedures, at least not greater than 200 to 300 μm in depth. Whether more subtle alterations in birefringence and colour shifts can be definitively correlated with corresponding electron microscopy changes, and shown to represent a layer of non-lethal thermal injury, but irreversible structure change, has not been demonstrated.

One issue confounding the clinician is the often-quoted temperature of 65° C as the shrinkage point of collagen.[47] This number is only accurate for relatively long exposure, in the order of several seconds, somewhat longer than pulsed lasers. In fact there is no true shrinkage temperature for collagen, but only a range of temperature-time combinations. Protein denaturation is a rate process characterised mathematically by the Arrhenius equation. For every 5° C decrease in temperature, a 10-fold increase in time is needed to achieve the same degree of denaturation. However, it is unclear if this time temperature reciprocity holds for very short time exposures, for which denaturation kinetics are unknown. Zweig et al,[47] have suggested that the shrinkage temperature for msec-domain exposure must exceed 85° C.

There are distinct staining zones observed after multiple-pass carbon dioxide LSR. These are related to temperature gradient as a function of depth. Typically, there is a very fine (1 to 2 μm) zone of intense basophilia, and sometimes char, overlying a much larger basophilic zone about 60 to 100 μm thick (zone I). Deep to this, there is a zone composed of a mixture of basophilia and hypereosinophilia about 10 to 20 μm thick (zone II). Finally, there is a third zone that stains hypereosinophilic and extends an additional 30 to 250 μm, depending on the laser parameters (zone III). Different staining properties are due to variable states of denaturation, where staining reaction is dependent on exposed sites for dye binding.

The basophilic-staining zone (zone I) corresponds to depth where little to no birefringence is observed. This is typically referred to as the coagulative zone (and is the entity commonly referred to as RTD in literature). In the mixture zone (zone II), there is a slight decrease in overall birefringence, as this zone demonstrates focal areas of intact fibres admixed with areas with complete loss of birefringence. In the transition zone (zone III), birefringence is similar to normal-appearing untreated collagen.

Ultrastructurally, Kirsch et al,[57] differentiated three zones based on fibril alteration by electron microscopy. Their study concluded that a zone comprising a mixture of denatured and native fibrils occurred sandwiched between normal and completely denatured zones. The width of the zone featuring the mixed fibrils was only 10 to 20 μm; most likely this zone coincides with the zone II (explained before).

Zweig et al,[47] identified a transition zone by routine staining that coincides with the hypereosinophilic zone III (explained before). The electron microscopy on tissue in this zone showed retained birefringence and noted that fibrils were only slightly thickened and retained their periodicity. This suggests that subtle tinctorial change on hematoxylin-eosin staining may be more sensitive than even electron microscopy in detecting early denaturation.

In general, however, researchers agree that the thermal profile of laser-tissue interaction must be controlled to prevent excessive tissue heating and thermal necrosis when performing laser resurfacing. If, in addition, a tissue layer of collagen can be heated in the range of 60 to 70 C to achieve the desired shrinkage without completely denaturing collagen or changing the skin's structural integrity, and if this thermally altered collagen persists in this state, then maintenance of this shortened, tightened condition wound be achieved. Replacement of this altered collagen in the healing process might cause regression of the collagen contraction.[58]

Collagen Denaturation

The first step in collagen denaturation is rupture of hydrogen bonds between strands of the triple helix so that the helix transforms into three random-coil molecules. The loss of these intra-chain hydrogen bonds (which temporally coincides with the bulk of collagen denaturation by sensitive calorimetry methods) results in a rapid rise in tension if the fibre is held at constant length. In some animal studies, further heating induces partial relaxation through rupture of intermolecular heat-labile covalent cross-links (the tension actually begins to decrease as temperature rises beyond 70° C over several minutes).[47] Intermolecular cross-links in human skin, however, are heat stable so that further heating results in continued increases in tension (although at slower rate than with hydrogen-bond rupture). Remarkably, even after denaturation is

complete, in human skin there is additional fibre shortening with increasing temperature. This is most likely due to hydrolysis of peptide bonds.[47]

Denaturation begins well before visible collagen shrinkage and probably before globally apparent microscopic architectural changes on routine microscopy (including birefringence loss). Even with early electron microscopy changes (granular disintegration of cross-links), contraction is not visible. It follows that critical mass of fibrils must be denatured before bulk shrinkage is observed. This has been confirmed by Allain et al,[47] who observed that it is the number of participating molecules within the bulk-denatured extracellular matrix that results in the amplitude of tension and shrinkage. This is supported by recent observations by Weisberg et al,[47] that (1) additional shrinkage may be observed in skin despite identifiable increase in RTD and (2) the fluence threshold for shrinkage exceeded that of RTD in their in vivo experiment.

Studies of thermokeratoplasty, in which corneal flattening is achieved through application of heat, have shown that in the corneal stroma the highest temperatures do not achieve additional shrinkage, but rather result in thermal injury and necrosis.[48,62] White et al[63,64] and Kopchok et al[65] have shown in tissue-welding studies that collagen bonding occurs if tissue apposition is precise and the temperature is controlled to prevent denaturation of tissue elements. Higher energies and higher temperatures have also been shown to disrupt the laser seal when tissue-welding vessels.[66,67] Furthermore, kinetic

modelling of the laser-tissue-fusion process was done with guidelines such that excessive heating desiccates collagen fibres to a brittle state unsuitable for fusion.[68] Clearly, overheating collagen is counterproductive.

On the other hand, a number of studies have demonstrated that the percent shrinkage of collagen is directly proportional to the heat applied to tissue while remaining within a narrow range and without exceeding the excessive heat threshold.[45,57,69,70,71] However, when evaluating percent shrinkage of various tissues, the clinician must keep in mind that the degree of shrinkage of tissue will depend not only on the collagen contraction, but also on the mechanical properties of the surrounding tissue.

Biological Characteristic of Wound Healing

The distinct zones of RTD in carbon dioxide LSR distinguish it from other resurfacing modalities. What follows is a narrative of wound healing with carbon dioxide LSR based on pigskin and human experiments.[47] During carbon dioxide LSR (two to four passes), the deepest portions of the basophilic-staining zone as well as the zone of mild hypereosinophilic collagen staining (transition zone, Fig 4-Appendix A) are the critical zones for modulation of wound healing. Within these areas immediately after treatment (within 30

minutes), vascular stasis and slight nuclear hyperchromasia of fibroblasts occur. Tissue viability stains show these fibroblasts to be metabolically active, whereas, as expected, fibroblasts in the upper and mid-basophilic-staining zone are necrotic.

One day after treatment, the basophilic zone is still intact microscopically. Within and just subjacent to this zone, neutrophils extend to the deepest aspect of the zone of mild hypereosinophilia (transition zone). Within this transition zone, tissue vitality stains show fibroblast death but retains birefringence (thus confirming the greater sensitivity of cells to higher temperatures than collagen, typically only 10% of cellular protein must be denatured for death, and these are often not as thermally stable as the crystalline collagen matrix).

By two days after treatment, there is no further extension of fibroblasts death. The basophilic-staining layer begins to slough in some regions, whereas in others, where there is less inflammation focally, a portion of this completely denatured collagen is retained (zone I). Overlying this remnant of thicker basophilic zone seen on day one, a compact layer of fibrinous debris is occasionally observed (consistant with the crust, grossly). In other cases, it appears that both this debris and the entire basophilic-staining zone have sloughed (Fig 4- Appendix A). Deep to this layer, the hypereosinophilic zone continues to show fibroblast death but retention of birefringence. Remarkably, necrotic fibroblast nuclei and even the collagen fibres show a more horizontal

orientation than adjacent normal fibres of equivalent depth. This re-orientation might be due to stresses by overlying attached shrunken collagen, and facilitated by slight changes in the deeper collagen fibres that increases their malleability. Interestingly, studies with and without occlusive dressings show different wound-healing responses. With dressings, the basophilic zone tends to remain intact and later become integrated within newly forming granulation tissue, and re-epithelialization tends to occur superficially to this zone (Fig 5-Appendix A). These specimens suggest that the basophilic-staining zone might play a direct role in resetting the lattice size for new collagen deposition and thus preserving a portion of the initial wound shrinkage. In contrast, in wounds treated with less occlusive methods (i.e., application of only petrolatum), there is more pronounced inflammation and sloughing of most of the basophilic zone after two days (Fig 4-Appendix A).

During and after carbon dioxide irradiation, there is immediate contraction roughly proportional to the amount of dermal RTD over a range of 20 to 120 μm (for similar laser devices, i.e., pulsed vs. scanning). The associated area percentage of contraction ranges from 5% to 18%. Beyond 150 μm RTD, immediate contraction does not exceed 30%. After a portion of denatured collagen sloughs (day one to two), some initial shrinkage is lost, and the area is restored to an intermediate value between its original and minimum size. This may be due to re-hydration (the basophilic zone prevents further wound

desiccation after injury) and release of the tethering effects of the basophilic zone. A second contraction then occurs after carbon dioxide LSR (day five to ten) that is presumably due to myofibroblasts.

By five days after treatment in multiple-pass carbon dioxide wound, partial re-epithelialization occurs and early granulation tissue can be observed. Focal remnants of basophilic-staining collagen persist underlying this neo-epidermis. Within areas of persistent denatured collagen, viable fibroblasts have presumably replaced necrotic ones observed one and two days after the laser procedure. By seven days after treatment, there is a robust zone of granulation tissue approximately 200 to 350 μm thick underlying the epidermis. Areas of denatured collagen are occasionally still identifiable by polarisation or routine microscopy deep to the neo-epidermis. Seventeen days after treatment, the granulation tissue has become more organised but retains a thickness of approximately 300 μm. There is a greater fibroblast density, nuclear size, and vascularity vs. wounds of similar depth achieved with dermabrasion or Erbium:YAG laser. Between seventeen and sixty days after treatment with multiple-pass carbon dioxide laser, there is a slow relaxation (increase in area) resulting in most wounds reaching 90% to 95% of their original size. Histologically, the thickened hypercellular dermis becomes more compact (usually 150 to 200 μm thick) and collagen rich. Also, there is increasing horizontal alignment of collagen and elastic fibres.

This sequence of events is different after dermabrasion and Erbium:YAG resurfacing (carried to the same depth of injury, where depth of injury equals the depth of the tissue removal plus the depth of zone I RTD). There is only slight immediate wound contraction (3% to 7% of original area), less than 50 μm RTD, and imperfect haemostasis. By one day after surgery, there is an irregular band of polymorphonuclear leukocytes extending from the wound surface to 200 μm deep in the dermis. Fibrin can also be seen as a layer up to 100 μm thick at the wound surface. In the absence of an occlusive dressing desiccation is pronounced, compared with multiple-pass carbon dioxide wounds.[47] There is also more rapid re-epithelialization (three to five days). Wound contraction begins only two to three days after surgery; there is no delay or biphasic contraction pattern as noted for carbon dioxide wounds. Microscopy, 60 days after injury, shows less tightly packed collagen fibres with a less horizontal orientation than in multiple-pass carbon dioxide wounds. Also the elastic fibres are finer and more vertically oriented than in untreated skin. By 60 days after treatment, the initial wound contraction almost completely regresses in all cases of conservative Erbium:YAG LSR and dermabrasion wounds (wounds with less than 200 μm of dermal ablation).

What differentiates carbon dioxide laser from other resurfacing strategies of similar depth? It has been suggested that the method of injury is irrelevant but, rather, the total depth determines the subsequent healing cascade. Certainly

this is attractive, since such dissimilar injuries as dermabrasion, chemical peeling, Erbium:YAG, and carbon dioxide laser all can achieve adequate improved cosmesis. However, some studies suggested that RTD independently modulates wound healing.[47]

The wound contraction profiles of carbon dioxide wounds and purely ablative injuries (i.e., conventional Erbium:YAG and dermabrasion) suggest an initial healing delay in carbon dioxide-treated sites; explanations include the time interval for basophilic collagen sloughing, small vessel occlusion, and reduction in early myofibroblast activity.[47] After this initial delay, most studies show greater and more sustained increases in wound-healing factors in carbon dioxide wounds vs. their scalpel counterparts. For example, one study showed more and earlier epidermal growth factor expression after carbon dioxide laser incisions vs. scalpel wounds.[47] Pogrel et al[47] found that carbon dioxide incisions showed earlier and greater hyaluronidase activity than scalpel incisions in rats. Hyaluronidase activity was also increased over a longer period of time after surgery. They suggest that the prolonged activity might be related to the later neo-vascularization in laser wounds. Recently, Harmon et al[47] showed higher levels of platelet cell adhesion molecule after six weeks in carbon dioxide vs. Erbium:YAG laser wounds where the depth of injuries (as assessed by depth of ablation plus depth of RTD) were similar. Smith et al[47] have shown an increase factor 13, vimentin, and actin expression after pulsed

carbon dioxide laser injury in a pig but did not compare those findings with non-carbon dioxide wounds.

It is less clear how thermal injury modulates the pattern and quantity of new collagen deposition. Li et al[47] have shown that there was up to three times the collagen content in burn wounds as there was in freezing wounds in rat skin. Margolis et al[47] showed a greater and more sustained elevation in collagen content after carbon dioxide injury vs. 50% trichloroacetic acid and dermabrasion wounds in mouse skin. Luomanen et al[47] showed more collagen formation at four weeks in carbon dioxide laser wounds than in comparable scalpel wounds in rat oral mucosa. Recently it has been shown that collagen fragments can stimulate new collagen deposition, and the directed migration of fibroblasts and the associated alignment of fibrils.[47] The P15 residue, which presumably is released during the thermal denaturation of collagen, may be responsible for induction of mechanical stresses that in turn increase the proliferation of fibroblasts over injuries where collagen degradation proceeds solely through enzymatic pathways. Furthermore, the tractional forces generated by the initial collagen shrinkage may exist long enough to re-orient the newly synthesised extracellular matrix. Despite the above argument for role for denatured collagen in directing fibroblast migration, it should be noted that a recent study[47] showed no difference ultrastructurally between collagen fibres

180 days after treatment in dermabrasion and carbon dioxide laser sites in a pig.

In summary, LSR wounds can be categorised into three types: (1) wounds combining little dermal ablation (less than 50 μm) and thermal RTD greater than 60 μm (typical carbon dioxide LSR); (2) wounds combining little dermal ablation and less than 60 μm RTD (conservative Erbium:YAG LSR); and (3) wounds with moderate dermal ablation (50 to 150 μm) and less than 50 μm RTD (typical Erbium:YAG LSR). In human side-by-side Erbium:YAG-carbon dioxide study (with all three wound types),[47] it has been shown that re-epithelialization and resolution of erythema were slightly faster with Erbium:YAG laser, even where apparent depths of injury were equivalent. The final fibroplasia zones at six months were thinner for Erbium:YAG vs carbon dioxide laser. This consists with the pig study discussed above and suggests that RTD in carbon dioxide laser wounds intrinsically affects healing, and that more long-term wound contraction and fibroplasia per micrometer depth of injury is achieved with the carbon dioxide laser. The final zone of fibroplasia for a specific carbon dioxide device, roughly varies as the layer of RTD in carbon dioxide laser wounds, whereas for Erbium:YAG laser wounds, the thickness of the zone reflects the depth of ablation. Generally, to create equivalent zones of fibroplasia and erythema, Erbium:YAG depths of ablation must be at least 1.5 to 2 times that of RTD depth with carbon dioxide.

Other studies analysed specimens from the skin after LSR, Manner et al[72] reported, after CO_2 LSR to upper eyelids, that the epidermis regenerated within 7 to 10 days. By three months, the epidermis revealed flattening of the rete peg pattern with restoration of polarity, keratinocytes, and melanocytes. The three month dermis demonstrated a fibrotic repair zone (500-700 μm), new elastic fibres, and telangiectatic capillaries. Muccini et al[73] treated solar elastosis with epithelial preservation using A 980 diode laser with a spherical optic handpiece to focus the light in the dermis. The tissue showed shrinkage (16% at 8W) similar to three passes of the scanned CO_2 laser treatment (15%). Thermal damage in the dermis was similar to the RTD left after LSR with scanned CO_2 laser. After 21 days the tissue showed new collagen and abundance of young elastin fibres. In a pilot ultrastructural evaluation of human pre-auricular skin before and after high-energy pulsed CO_2 laser treatment, Ratner et al[73] found that; treatment with the high-energy pulsed CO_2 laser appears to reverse the epidermal and dermal changes of photo-ageing on an ultrastructural level. Before the laser treatment, the ultrastuctural changes characteristic of photodamaged skin were evident. Immediately after treatment, there was extensive coagulation necrosis of the epidermis and papillary dermis. Thirty days after treatment, there was no evidence of intercellular or intracellular oedema, and differentiation of the epidermal keratinocytes, with a loss of keratinocyte dysplasia was seen. Increased numbers of desmosomes and tonofibrils were noted.

New deposition of collagen was presented in the papillary dermis. The ultrastuctural findings seen at ninety days after treatment were similar to those seen at thirty days, apart from increased organisation of collagen fibres in the papillary dermis. In histological comparison of Coherent 5000C Ultrapulse CPG versus Sharplan Silk Touch CO_2 lasers, Trelles et al,[74] reported that; although tissue recovered faster on the Coherent side at seven days control, at ninety days the collagen was better compacted and organised on the Sharplan side. Similarly, the quantity of the elastin was significantly more enhanced on the Sharplan side. Which means that irradiated laser energy density in relation to time and the way that it is delivered, should play an important role at the moment of producing collagen shrinkage. The SilkTouch delivers laser energy more aggressively, thereby producing a more intense inflammatory tissue reaction, which results in slower recovery of the tissue, compared with the Coherent CPG. More active enhancement of vascularisation found in the Sharplan is likely to be the reason for more effective collagen proliferation and compaction. These changes, together with the increase in elastin in the dermis, may produce longer lasting effects in the skin resurfacing. Shim et al,[75] agrees with the others when he reported increases in collagen layer thickness in skin biopsies from rhytides post CO_2 laser treatment. Finally Cotton et al,[76] confirmed as well that ninety days after CO_2 laser treatment, the sub-dermal and dermal repair zone consist of compact new collagen fibres overlying collagen with evidence of solar elastosis.

INDICATIONS OF CO2 LASER TREATMENT

The CO_2 laser can be used in many situations, but is not always the best procedure. We will talk only about the applications where the CO_2 laser has been advocated as the treatment of choice in the literature.

Lesions for which CO2 laser is potentially treatment of choice

Although lesions in this group may be treated with other therapeutic modalities, the CO_2 laser offers significant benefits so that it may be considered as first line treatment. Most of these lesions are said to be best treated with the CO_2 laser because of the difficult surgical sites, the need for precision, or control of bleeding and swelling. The CO_2 laser allows more aggressive local therapy and, avoids excisional surgery. However it should be noted that it does not allow histological examination of tissue, for example, in actinic chelitis unless a shave biopsy is performed first, and it can be a slow method of tissue removal for example, in a large rhinophyma. Also, where a large amount of tissue is removed, as in rhinophyma, there is significant collateral heat damage which may delay healing.

Actinic cheilitis

The best example in this group is the treatment of actinic cheilitis. Although this condition has also been treated with excisional vermilionectomy,[76] liquid nitrogen cryosurgery,[76,77] and 5-fluorouracil,[78,79] the CO_2 laser offers the benefits of less scarring, shorter healing time, and less pain with a procedure that is both simple and more effective. Again, however, the avoidance of thermal damage beneath the vaporised lesion is critical in achieving these goals.

David reported[80], in 1985, the successful treatment of eight cases, with an average follow-up of 34 months. Since then the results of treatment of 123 patients with an average follow-up of 11 to 36 months have been reported.[81,82,83] Only two of these patients were found to have local recurrences.

Healing time was reported to range from 3 to 8 weeks. One group reported a mean of 98.5% re-epithelialized at 4 weeks.[83] Scarring was from 8%[83] to 23%.[84]

A low risk of scarring is related to both proper wound care with avoidance of infection[84] and prevention of thermal damage to the healing vermilion surface. This can be achieved with a proper choice of pulse parameters and attention to

details of laser-tissue interaction. A third factor is the depth of vaporisation. Because the variegated appearance of the vermilion surface and the potential for undiagnosed occult SCC, surgeons tend to vaporise the surface to a deeper level than necessary. Because actinic cheilitis is a purely epidermal process in an area devoid of hair follicles, superficial treatment that completely removes the epidermis should be adequate.

Finally; although laser resurfacing was considered in the literature to be the treatment of choice in actinic cheilitis, we still believe that surgical excision (vermilionectomy) has an important role in treating actinic cheilitis, as it allows the precise pathologic diagnosis, and it usually takes about one week for the wound to heal after vermilionectomy.

Rhinophyma

Treatment of Rhinophyma has been accomplished by dermabrasion, sculpting with scalpel or razor blade or a dermatome, cryosurgery destruction, electro-surgical destruction, and the CO_2 laser.[85-94]

Dermabrasion is generally a difficult procedure because of technical factors involved and often leaves incomplete results. The use of cryosurgery to obtain an even depth of tissue destruction is very difficult and often results in incomplete destruction and scarring or hypopigmentation. Use of thermal scalpel and thermal destruction gives easier tissue removal but has a significant

risk of scarring from heat conduction to deeper tissues. Sculpting with scalpels, razors, and dermatomes leads to significant bleeding, which requires excessive coagulation for haemostasis, and compounds the difficulty to achieving a smooth tissue plane as an end point because of poor visualisation and uneven tissue contouring, and focal tissue destruction if the electrocautery is used. Use of the CO_2 laser is advantageous because of the greater precision and ease of tissue removal, and the ability to sculpt the nasal contours precisely, and with good haemostasis.[95] However, a definite risk of scarring exists from heat conduction when a CW CO_2 laser is used and tissue removal is taken to a deep level.[96] The UltraPulse CO_2 laser allows greater freedom in removal of bulky tissue with decreased risk of scarring, but does not completely eliminate this risk, and the surgeon must pay close attention to presentation of the oil gland structures.

With major Rhinophyma, laser excision of excessive tissue before vaporisation is helpful.[91] During vaporisation the dermis contracts and causes expression of sebum from the sebaceous glands. This, as well as squeezing the nose and producing sebum extrusion, is a sign that intact sebaceous glands remain and that vaporisation has not extended to depth below these glands and will not result in healing with scarring.[94]

In spite of what has been published in the literature, it is fair to say that in our practice we still treat major Rhinophyma with surgical shaving, because it

offers shorter operating time and less risk of scarring especially when we use Sharplan 40C (SilkTouch) CO_2 laser which causes a deeper layer of RTD.

Epidermal naevi

Removal of linear epidermal naevi can be very difficult, and these lesions were virtually difficult to treat before the advent of the CO_2 laser.[97,98] Treatment by dermabrasion is almost invariably followed by lesion recurrence if the treatment is superficial or by scarring if the treatment is more aggressive. Excision of the lesions is usually not an option because of their size and location. Vaporisation of these lesions with use of the CO_2 laser has been much more successful in prevention of both scarring and recurrence.

The degree of precision achievable with the CO_2 laser is not possible with other modalities, but a fine line exists between excellent results without lesion recurrence and ablating too deeply, resulting in healing with some degree of scarring.

Benign dermal tumours

Another area where the CO_2 laser offers definite advantages is in vaporisation of selected benign dermal tumours. These include neurofibromas,[99] granuloma faciale,[100] syringomas,[101,102] sebaceous hyperplasia, adenoma sebaceum of tuberous sclerosis,[103,104], and others[105,106]. These dermal tumours have been and still are treated by a variety of other surgical techniques, including excision and repair, shave excision, dermabrasion, cryosurgery, electrocautery, and others. However all these techniques have had one or more of the following disadvantages: scarring or surface textural change, cumbersome or slow surgical technique, lesion recurrence, and incomplete lesion removal.

The primary advantages of the CO_2 laser for removal of these lesions are extreme precision, leaving minimal damage to adjacent normal tissue, and the ability to achieve microscopic control by magnified intra-operative visualisation of the vaporised site. In addition, the speed of the treatment of multiple lesions, the bloodless field, and the diminished post-operative pain and swelling are definite advantages.

Other superficial lesions

Another area where the pulsed CO_2 laser may offer distinct clinical advantages is in treatment of various lesions limited to the superficial dermis and epidermis in difficult surgical locations.

Cutaneous resurfacing procedures and rejuvenation of skin

The capability of the CO_2 laser to vaporise discrete cutaneous tumours precisely, as well as treat larger cutaneous surface areas with excellent cosmetic results, has led to its use for various resurfacing procedures for cosmetic benefit.

Focal and discrete irregularities such as acne scars, chickenpox scars, and others,[107-109] have been reported to respond with excellent cosmetic results to CO_2 laser vaporisation.

In terms of skin rejuvenation, CO_2 laser skin resurfacing plays a significant role in obtaining improvement in skin appearance, and good cosmetic results.

OTHER RESURFACING LASERS

It is often stated that one of the main limitations of CO_2 laser is the extensive erythema that persists for one to three months. Because of these perceived disadvantages, manufacturers have marketed lasers that may be capable of

resurfacing with greater ease, more superficially, and with delivery of less heat to the treated tissue.

Erbium:YAG Laser

The Erbium:Yttrium-Aluminum-Garnet (Erb:YAG) laser produces light in the near infra-red (IR) portion of the electromagnetic spectrum at 2.94 μm.

The broad water-absorption band extends from just under 2μm to beyond 10μm, ensuring superficial absorption of near-IR light. The Erb:YAG laser ablates approximately 15 to 20 μm of skin and leaves such a thin layer of thermal damage (5 μm) that is not haemostatic. The Erb:YAG laser has a macropulse of approximately 250 μsec, made up by a train of 1μsec micropulses.[110]

Because of the high coefficient for absorption of water, very little tissue water is necessary for tissue reaction, allowing deep or very superficial vaporisation, but both being done with minimal thermal injury. This may result in some unique clinical benefits, such as treatment of scars; treatment of the neck, chest, hands, and arms[111]; and removal of superficial photodamage wrinkling with faster healing and decreased erythema.[112]

The coefficient of absorption of water in the CO_2 laser (10.6 μm) is approximately 790/μm, whereas in the Erb:YAG laser (2.94 μm) is

approximately 13,000/μm, which means that it is 16 times greater in the Erb:YAG laser than the CO_2 laser. This results in the Erb:YAG laser energy being absorbed much more readily in a thinner layer of tissue than with the CO_2 laser, also results in efficient tissue ablation with very little scattering of the beam and minimal residual thermal damage.

No shock-wave effect occurs in tissue, but clinically a pressure-wave effect seems to occur relative to the explosive vaporisation that results when delivering rapidly large amounts of energy to a thin layer of tissue. The Erb:YAG laser therefore can be viewed as essentially a pure vaporisational or ablative laser, with insignificant thermal damage.

This has resulted in a new wave of enthusiasm for resurfacing, specifically with the Erb:YAG laser. However, because of the newness of the technology and its promotion by eager physicians and laser manufacturers, a number of myths regarding the Erb:YAG laser have been generated. These myths hold some element of truth but are based on generalisation of those elements. These myths are:

1) The Erb:YAG laser is painless and requires no anaesthesia. The Erb:YAG can be used to remove the epidermis painlessly, because no nerve endings exist in the epidermis and insufficient heat is generated to stimulate the

papillary dermal nerves. However, once the dermis is reached with a second pass of the laser, pain occurs just as readily as with any laser.

2) Healing is faster with the Erb:YAG laser, and redness (erythema) is minimal or less prolonged. The Erb:YAG laser does vaporise thinner layers of tissue than the CO_2 laser and with less residual thermal injury to tissue, but the healing time correlates with the total depth of injury, not the depth per pass. Equal results require equal depths of treatment. The total depth of injury is the depth of ablation plus the depth of thermal damage.

3) Side effects are reduced with Erb:YAG laser, resulting in safer treatment. Side effects such as hypopigmentation, scarring, erythema, and slow healing are generally depth related and therefore are reduced with more superficial treatment. Therefore if the Erb:YAG laser is used in a more superficial manner, the incidence of complications would be expected to be diminished as well. However the same statement may be made regarding CO_2 laser resurfacing.

COMBINATION LASER TREATMENT

Both the CO_2 laser and the Erb:YAG laser have unique qualities that can be exploited during resurfacing. The CO_2 laser is unique in the following ways:

1) Haemostasis is achieved.

2) A Plateau of ablation is reached, limiting resurfacing depth if proper treatment protocols are followed.

3) The first pass causes an epidermal/dermal split that allows easy and complete removal of the epidermis with a single pass.

The Erb:YAG laser is unique in the following ways:

1) Minimal residual thermal damage or tissue heating occurs.

2) It continues to ablate with each pass and does not reach an ablation plateau with depth.

3) Only minimal tissue water is required for laser-tissue interaction.

The most successful use of lasers for resurfacing would use each laser to take advantage of its unique benefit and to eliminate the disadvantages of each as much as possible. Accordingly one laser can be used in specific cases, or both lasers can be used one after the other in some other cases of laser skin resurfacing. On the other hand some machines allow both lasers to be used simultaneously.

Many reports have been published about the use of Erb:YAG laser and the differences between Erb:YAG laser, CO_2 laser and other modalities of skin resurfacing.

Perez et al,[113] reported ,after treatment of facial rhytides with Erb:YAG laser, that all patients showed some degree of improvement of their rhytides. Re-epithelialisation occurred between 3 and 8 days. All evidence of erythema resolved between 3 and 6 weeks after treatment. It needed five to six passes to ablate the papillary and superficial layer. Therefore the Erb:YAG laser plays a significant role in the treatment of superficial and mid-depth rhytides. Alster,[114] reported, after looking at the clinical and histologic evaluation of six Erb:YAG lasers, that equivalent clinical and histologic results were seen after each of the six Erb:YAG laser treatments. Therefore Erb:YAG laser resurfacing can be used to significantly improve mild cutaneous photodamage. Goldberg DJ,[115] reported good results after using the Erb:YAG laser for treatment of neck rhytides. Therefore Erb:YAG laser may be used to improve photodamaged skin in areas where the risk of using CO_2 laser is high. Goldman MP,[116] reported as well that photo-aged skin of the neck can be effectively treated with the Erb:YAG laser with minimal adverse effects. Manaloto RM et al, Kopelman J, and Weiss RA,[117-119] reported that the Erb:YAG laser is an ideal laser for treatment of mild to moderate periorbital rhytides. Patients achieve approximately 75% improvement, erythema fades quickly, re-epithelialisation is rapid and side effects are minimal.

In comparison of Erb:YAG and CO_2 lasers in resurfacing of facial rhytides. Khatri KA et al,[120] reported that Erb:YAG laser is safe and effective in

removing facial rhytides. Patients treated with Erb:YAG laser recovered more quickly from the procedure than those who received CO_2 laser treatment. Millman AL et al,[121] treated two groups of patients who underwent eyelid resurfacing. The first group was treated with two passes of Erb:YAG laser followed by one pass of the CO_2 laser. The second group was only treated with the CO_2 laser (two passes). He reported that combining both lasers shortened re-epithelialisation time and duration of erythema . Histopathologic examination disclosed less residual thermal damage (RTD) in dermis with combined lasers treatment. Goldman MP et al,[122] treated one side of the face in a group of patients with CO_2 laser followed by Erb:YAG laser, and on the other side of the face CO_2 laser alone. He reported that treatment with Erb:YAG laser after CO_2 laser, results in a decreased incidence of adverse sequelae without a noticeable difference in the degree of wrinkle improvement. Collawn SS and Weinstein C,[123-124] reported that, for deeper rhytides , multiple passes with CO_2 laser is the treatment of choice. For moderate rhytides, the CO_2 laser can be used for the first pass followed by one or multiple passes with the Erb:YAG laser. Erb:YAG laser when used alone is beneficial for removing fine wrinkles and discoloration.

After using the Erb:YAG laser in skin resurfacing in Asians, Polnikorn N et al,[125] reported that significant improvement was noted in all patients, shorter periods for re-epithelialisation and erythema duration were noted when

compared to previously reported results following CO_2 laser resurfacing. Therefore the Erb:YAG laser is safer and effective in the treatment of Asian skin.

UNCOMMON LASERS

Goldberg DJ et al[126] reported the use of Q Switched Nd:YAG laser at 1064nm in skin resurfacing. Muccini JA et al[127] reported laser treatment of solar elastosis with epithelial preservation using a 980 μm diode laser. In comparison with CO_2 laser skin resurfacing, the tissue showed shrinkage (16%) similar to three passes of CO_2 laser treatment (15%). Thermal damage in the dermis was similar to the residual thermal damage left after laser resurfacing with CO_2 laser. After 21 days the tissue showed new collagen and abundance of young elastin fibres.

Finally, it is obvious from this introduction that opinions vary in terms of favouring the use of CO_2 laser, Erb:YAG laser, or both lasers together. Some authors believed that the residual thermal damage (RTD), which happens with the use of CO_2 laser in skin resurfacing, plays an important role in collagen shrinkage and new collagen formation. Ross E.[128] Li AK et al, Luomanen M et al, and others.[47]

Other authors reported that the residual thermal damage is not an important factor for collagen shrinkage and new collagen formation. Campell JP et al[47], in 1998 reported that there was no difference Ultrastructurally between collagen fibres 180 days after treatment in dermabrasion and CO_2 laser sites in pigs.

Utley DS et al,[129] reported that after 7 days, all groups of patients after laser treatment with CO_2, or CO_2/Erb:YAG, or Erb:YAG, or Erb:YAG/CO_2 were re-epithelialised and showed equal new-collagen formation. Hughes PS,[130] Reported that laser skin resurfacing with Erb:YAG laser causes skin contraction up to 14% in spite of the minimal residual thermal damage (RTD).

STUDY OUTLINE

All the authors have looked at the results of laser skin resurfacing in limited number of patients, none of them have reported long term follow up (one year or more). Although clinical improvement is often noted to continue for 6-12 months, nobody has reported results after using Erb:YAG/CO_2 laser simultaneously in laser skin resurfacing. Therefore we have planned to look at the long term effect of laser skin resurfacing using CO_2 laser alone, or CO_2/Erb:YAG laser simultaneously, or Erb:YAG laser alone as an essential

part in our work of the assessment of patients outcome in laser skin resurfacing.

Objective improvement in the depth of acne scarring is extremely difficult to quantify. Although photographs are widely used, slight change in lighting can have a profound effect on the appearance of scars or wrinkles. Measuring profiles of scars has considerable potential for error; scales used to measure improvement in patient's psychological view of their condition are by their nature subjective and often reflect background mental health problems. As changes in dermal collagen have been noted to be important in the result of laser skin resurfacing (LSR), this study looked at the long term histological appearances after LSR as an objective method to compare different types of lasers.

Laser treatment parameters such as energy settings and number of passes were selected according to the manufacturers technical manuals and clinical experience to cause a similar total injury ie ablation + RTD in the different test patches corresponding with the widely accepted clinical impression that tissue ablation with Erb:YAG laser has to be deeper to get a similar result to that obtained with a CO_2 laser. The treatment parameters used were those recommended by the manufacturers and in widespread clinical use. The parameters vary in relation to the treatment site and the characteristics of each

type of laser following the principles of the laser-tissue interaction[25,26,27,28,31,34,35,36,37]. These principles were explained in page 12-16.

It is known from previous studies that CO_2 laser reaches plateau of ablation after three or four passes[42], The injury consists of ablation + RTD[47], while the CO_2 LSR causes little dermal ablation (less than 50μm) and RTD greater than 60μm, the Erb:YAG LSR causes moderate dermal ablation (50 to 150μm) and less than 50μm RTD[110].

Clinical observation through the passes were used to assess the depth according to the colour in CO_2 laser and bleeding point in the Erb:YAG laser.

The other part of this work included looking at the outcome of laser skin resurfacing in a group of patients who had pigmented skin lesions and poor results after treatment with Q.S.Ruby laser, in addition to looking at the outcome of laser skin resurfacing in a group of patients who had benign epidermal tumours. Finally, this study looked at the outcome of laser skin resurfacing in a group of patients with a very rare skin condition (Porokeratosis), which is very difficult to treat.

Therefore the aims of this study are:

1) To determine the long term histological appearances after laser skin resurfacing using three types of lasers and to use that as an objective method to compare different types of lasers.

2) To determine whether laser ablation is effective in pigmented skin lesions

3) To determine whether laser ablation is an effective treatment for benign epidermal tumours and other rare skin condition (Porokeratosis).

METHODS

According to the aims of this study the methods can be considered in three parts:

1) Methods to determine the long term effect on histological appearances after laser skin resurfacing using different types of lasers.

2) Methods to determine the effect of laser ablation (resurfacing) in benign pigmented skin lesions.

3) Methods to determine the effect of laser ablation (resurfacing) in benign superficial tumours and other rare skin condition (Porokeratosis).

These methods will be explained in detail in this section.

1. Methods to find out the long-term effect of Erbium/CO_2 lasers resurfacing on histological appearances.

A prospective study was performed to identify the different effects between different types of lasers in skin resurfacing in terms of depth of injury and long-term influence on histological appearances. A protocol was written for this study including a special consent form for the patients, and ethical committee approval was obtained.

Subjects: Twenty patients agreed to participate in this study. All of these patients had facial laser skin resurfacing. The purpose of this study and the

details of the procedure were explained to each patient. Each patient signed a consent form before the procedure.

Lasers: Three types of lasers were used.

1) Carbon dioxide laser, Sharplan 40C (SilkTouch). This laser is a gas-type laser (the active medium is gas-CO_2). It is a class IV laser.[137] This laser has a wavelength of 10600 nm, which is in the far infrared part of the electromagnetic spectrum, and is invisible. This wavelength is readily absorbed by water (which is the target in tissue) during laser skin ablation and resurfacing. The absorption coefficient of water for 10600nm W/L is very high (800/cm), therefore the optical penetration depth for that specific wavelength (10600nm) is minimal, which means a very thin layer of the skin will have the effect of thermal interaction which will lead, at the end, to vaporisation and ablation of that thin layer of epidermis and dermis. This laser has three operation modes: continuous wave, superpulse, and pulser. Each operation mode can be used with one of the three tissue exposure modes, which are (continuous, single pulse, and repeat pulse). The superpulse and pulser operation modes are not used in skin resurfacing (used in drilling and cutting only). Therefore for skin resurfacing and ablation we selected the continuous wave from the operation mode with the repeat pulse from tissue exposure modes using the SilkTouch flash scanner. The continuous wave beam is made to quasi-pulse using shutter to turn the beam on and off. Maximum output

power is 40 Watt; an output of 16 watt was used in this study. The hand pieces are 200mm, 125mm, 50mm, and 80mm. Only 125mm and 200mm are suitable for skin resurfacing. The hand piece 200mm was used in this study. Finally a 9mm scan was used in this study using the SilkTouch flash scanner.

2) 3 Derma K Erbium laser and Derma K Erbium/CO_2 laser (one machine). This laser system incorporates an Erbium:YAG laser and a CO_2 laser. The Erb:YAG laser emits infrared light with a wavelength of 2940nm, a wavelength which corresponds to peak absorption in water. The absorption coefficient of water for 2940nm W/L is 13000/cm; therefore the optical penetration depth is minimal. The effective absorption depth of Erb:YAG laser is 5 μm, 10 times less than that of the CO_2 laser. Ideally ablation of the skin is achieved by the Erb:YAG laser and the controlled thermal damage is produced by the CO_2 laser when both lasers are used simultaneously. The Derma K System specification is shown in a table in Appendix A.

Duty Cycle: The duty cycle is the percentage of time the CO_2 remains on between the Erb:YAG pulses. The start of the CO_2 cycle is synchronised with that of the Erb:YAG and thus both laser energies are delivered simultaneously. The CO_2 beam continues after the Erb:YAG pulse, for a duration that is

determined by the selected duty cycle. If the duty cycle is less than 100% the CO_2 laser beam is pulsed.

An example of a pulse repetition rate of 10 pulses per second and 50% duty cycle of the CO_2 laser is shown in the diagram (Appendix A). The parameters of the laser were selected according to its technical manuals. Clinical observation through the passes were used to assess the depth according to the colour in CO_2 laser and bleeding point in the Erb:YAG laser.

Test Patches: Three test patches were performed behind the left ear in each patient. The numbers and types of these test patches are summarised in the table (1) below, followed by the details of each test patch.

	20 pts (total no)	**Area**	**Type of laser**
First test patch	20	Post-auricular	CO_2 laser
Second test patch	20	Post-auricular	Erb/CO_2 laser
Third test patch	20	Post-auricular	Erb:YAG laser
Total no of patches	60		

Table (1): Test patches details.

In the first test patch the Sharplan SilkTouch CO_2 laser was used, four passes, with 16 Watt, 200mm hand piece, and 9mm scan. Wiping was performed after all passes except the last one, using normal saline.

In the second test patch three passes, using ESC Derma K Erb/CO_2 laser, were performed, with 1.7J for Erb:YAG laser, 2 Watt for CO_2 laser, 10 pulses per second (pps), 30% duty cycle, 20% overlap between treatment spots, 3 mm spot size, and 1 cm scan. The second pass was performed perpendicular to the first pass (and the third pass at 45 degree to the previous pass), thus assuring uniform coverage of the entire area of treatment.

In the third test patch: Five passes were performed, using ESC Derma K Erb:YAG laser, with 1J, 3 mm spot size, 1 cm scan, and 20% overlap between treatment spots.

Biopsies (BXs): Using loupes for magnification, biopsies 6 hours post test patches were taken at the edge of the laser test patches (9 O'clock) to include approximately 50% normal and 50% injured skin. Biopsies at 6 months and 1year were taken medial to the previous biopsy scars so contained only previously injured skin. Biopsies were taken and grouped into three groups, as it is shown in table 2 (next page), followed by detailed explanation.

	Time of BX	No of patients	Total no of BXs
First group of BXs	Six hours post-operation	20	60
Second group of BXs	Six months post-operation	7	21
Third group of BXs	12-13 months post-operation	8	24
Total no of BXs in all groups			105

NB: Five patients lost to follow up.

Table (2): Biopsies in each group after laser test patches.

First group of biopsies: Biopsies were taken from all test patches in all patients six hours post operatively, under local anaesthesia using 0.5% Marcaine with 1/200,000 Adrenaline which was infiltrated in the area of post auricular skin at the time of the operation while patients were under general anaesthesia.

Second group of biopsies: Biopsies were taken from the three areas of test patches in 7 patients, under general anaesthesia, during a secondary facial laser resurfacing, six months after the first one.

Third group of biopsies: Biopsies were taken from all test patches in 8 patients under general anaesthesia during another procedure of facial laser resurfacing 12 -13 months after the first operation. (5 patients lost to follow up).

Histological Examination of Biopsies: All biopsies were cut, stained with Hematoxylin and Eosin, and examined under the light microscope.
Both the epidermis and dermis were assessed in each of the three groups (6 hours post laser treatment, 6 months post first laser treatment, 12-13 months post first laser treatment). Observations made by the pathologist were blinded to the laser used.

The epidermal changes in the first group (6 hours post laser treatment) were graded as follows: 1) Focal residue of the epidermis.

2) Complete loss in the epidermis.

3) Hair follicle involvement in the zone of injury.

The dermal changes in the first group (6 hours post laser treatment) were graded as follows: 1) Normal appearance of dermis.

2) Superficial injury in the dermis.

3) Deeper injury in the dermis.

4) Presence of inflammation in the dermis.

The changes in the epidermis and dermis were assessed in the other two groups (that will be explained in the results section).

2. Methods to find out the effect of laser ablation (resurfacing) in pigmented skin lesions.

This study looked at the results of skin resurfacing in 46 patients; all of them had benign pigmented skin lesions, which have been treated with laser skin resurfacing (ablation). In 38 patients the diagnosis was proven by biopsy, (in the other 8 patients we did not perform a diagnostic biopsy due to easy clinical diagnosis and cosmetic reason). In these patients, the outcome of laser skin resurfacing (ablation) in benign pigmented skin lesions was looked at, in relation to diagnosis and depth of lesion.

3. Methods to find out the effect of laser ablation (resurfacing) in benign superficial tumours, and other rare skin conditions.

Eleven patients were looked at. All of them had non-pigmented benign skin lesions which were diagnosed as shown in table (3), (next page).

Diagnosis	Xanthal-smas	Syring-omas	Tubero-Scleroses	Darier's disease	Granuloma-Anulare	Poroke-ratosis
No of pts	3	2	2	1	1	2

Table (3): Patients with benign superficial tumours.

3 patients had xanthelasmas, 2 patients had syringomata, 2 patients had tuberous scleroses, 1 Patient had Darier's disease, 1 patient had granuloma-annulare, 2 patients had porokeratosis (DSAP). Eight of these patients had diagnostic biopsies.

All of those patients were treated by laser skin resurfacing (ablation), using either CO_2 laser or Erb:YAG laser. The outcome of laser skin resurfacing (ablation), in these patients, was looked at, in relation to the diagnosis and the depth of the lesions.

All PSL lesions and benign superficial tumours were treated either CO_2 Sharplan Silk Touch laser 10600nm or Erb/Yag laser. CO_2/Erb laser was not used to treat these groups.

The parameters for CO_2 laser were: Output power 16-18 watt for hand piece 200mm, 9mm scan, 3-4 passes, and 5-7 watt for hand piece 125mm, 3-4 passes. The hand piece was selected according to the site and area of the

lesion. Wiping was performed after all passes except the last one.

The parameters for Erb:YAG laser were 1.5 J, 7mm spot size, 5-7 passes. No wiping was performed.

Treatment was repeated if needed in six months interval. The follow up period was 12-36 months.

RESULTS

According to the aims and methods in this study, the results in this section have been divided into three parts:

1) Results of the long –term effect of Erbium/CO_2 lasers resurfacing on histological appearances.

2) Results of the effect of laser ablation (resurfacing) in benign pigmented skin lesions.

3) Results of the effect of laser ablation (resurfacing) in epidermal tumours and other rare skin condition (porokeratosis).

1. Results of the long-term effect of Erbium / CO_2 laser resurfacing on histological appearances.

This part of the results includes three groups:

A- First group, which includes the results of the biopsies that were taken 6 hours post laser test patches.

B- Second group, which includes the results of the biopsies that were taken six months post laser test patches.

C- Third group, which includes the results of the biopsies that were taken 12-13 months post laser test patches.

FIRST GROUP

Three biopsies (6 hours after test patches with CO_2 laser, Erb:YAG laser, and Erb:YAG&CO_2 simultaneously) were taken from the post-auricular skin in 20 patients. Changes in both epidermis and dermis were assessed.

Epidermal changes:

The epidermal changes were categorized as: Normal, focal residual of epidermis, complete loss of epidermis, involvement of hair follicle, and not assessable. These changes in relation to laser type are tabulated in the table 4.

Laser type	**Normal**	**Focal residual**	**Complete loss**	**Hair follicle involvement**	**Not assessable**
CO_2	5	6	7	5	2
CO_2/Erb: YAG	1	4	14	9	1
Erb:YAG	4	0	16	8	0

Table (4): Epidermal changes in the first group

NB: Normal: histological section taken from uninjured, normal half of biopsy. Due to blinding of pathologist and handling difficulties due to small size of biopsies further sections were not assessed. Small part of normal adjacent skin was taken with all 6 hours biopsies.

It was clear from the results of epidermal changes, (table 4), that there was greater damage associated with Erb:YAG use. While 7 cases had complete loss of epidermis following the test patches with CO_2 laser, there was 14 cases of complete loss of epidermis biopsies after test patches with Erb:YAG/CO_2, and 16 cases complete loss of epidermis after test patches with Erb:YAG laser. Most specimens with focal epidermal residue were found in biopsies after test patches with CO_2 laser. No biopsies showed focal epidermal residue after test patches with Erb:YAG laser.

Dermal changes:

Dermal changes were categorized as: normal, superficial injury, deeper injury, inflammation, and not assessable. These changes in the dermis in relation to the laser type are tabulated in table 5.

Laser type	**Normal**	**Superficial**	**Deeper**	**Inflammation**	**Not_Assessable**
CO_2	9	9	1	6	1
CO_2/Erb	2	15	2	10	1
Erb:YAG	4	9	7	3	0

Table (5): Dermal changes in first group.

In tab (5): 5/9 normal dermis (CO_2), 1/2 normal dermis (CO_2/Erb), and 4/4 normal dermis (Erb) showed normal epidermis due to miss orientation while cutting the biopsies.

SECOND AND THIRD GROUPS

In 7 patients, biopsies from test patch areas were taken 6 months post first laser treatment (second group). In 8 patients, biopsies from test patch areas were taken 12-13 months post first laser treatment (third group).

In both groups, all specimens, which could be assessed, showed intact epithelium. In all but one, there was no obvious dermal abnormality. This single case showed some inflammation associated with a blocked hair follicle.

In cases where changes were seen, the main features were either flattening of the epithelium with some loss of rete pegs (**flattened)** or conversely, an increase in the complexity of branching of rete pegs (**complex)**. Some cases showed both (**variable)**. The data at 6 months post first laser treatment (second group), and 12-13 months post first laser treatment (third group) are tabulated in table (6) and table (7) as shown (next page):

Laser type	Normal	Flattened	Complex	Variable	Not assessable
CO_2	3	1	2	1	0
CO_2/Erb	2	0	3	2	0
Erb:YAG	2	1	0	2	2

Table (6): Results of BXs 6 months post first laser treatment (second group).

Laser type	Normal	Flattened	Complex	Variable	Not assessable
CO_2	0	4	1	3	0
CO_2/Erb	1	1	1	4	1
Erb:YAG	2	0	2	4	0

Table (7): Results of biopsies 12-13 months post first laser treatment (third group).

According to the figures in the previous tables (6&7), the late changes could be summarised as:

- Some loss of the rete pegs (flattened epidermis). Most common after the use of CO_2 laser.

-Some complex branching (increase in the complexity of branching of rete

pegs). More after the involvement of Erb:YAG laser.

- Some variable (flattened epidermis and increase in the complexity of rete pegs). Mostly when the Erb:YAG laser was involved.

- No obvious changes in dermis in both groups (6 months, 1 year).

- No obvious difference between both groups (6 months, 1year).

Statistic analysis of results:

Contingency tables were drawn up combining results where appropriate (table 8 to19). Data was analysed using chisquared tests where appropriate on minitab version 8.Where n<40 and more than one cell had an expected frequency <5 Fisher's exact test was used as described in Kirkwood B. Essentials of medical statistics, page 95, chapter 14, Blackwell 1988. Calculations were performed using the scientific calculator on windows XP.

FIRST GROUP(6 HOURS POST TEST PATCHES):

Depth of Epidermal Damage: Tab (8,9,10)

	Focal residual (Superficial)	**No epidermis (Deep)**	**Total**
CO_2	6	7	13
CO_2/Erb	4	14	18
Total	10	20	31

Tab (8) Epidermal damage CO_2, CO_2/Erb. P= 8.686 (exact test)

	Superficial	Deep	Total
CO_2	6	7	13
Erb	0	16	16
Total	6	23	29

Tab (9) Epidermal damage CO_2, Erb. P = 0.0072 (exact test)

	Superficial	Deep	Total
CO_2/Erb	4	14	18
Erb	0	16	16
Total	4	30	34

Tab (10) Epidermal damage CO_2/Erb, Erb. P = 0.131 (exact test)

Dermal Damage: tab (11,12,13).

	Superficial	Deep	Total
CO_2	9	1	10
CO_2/Erb	15	2	17
Total	24	3	27

Tab (11) Dermal damage CO_2, CO_2/Erb. P = 1.394 (exact test)

	Superficial	Deep	Total
CO_2	9	1	10
Erb	9	7	16
Total	18	8	26

Tab (12) Dermal damage, CO_2, Erb. P = 0.162 (exact test)

	Superficial	Deep	Total
CO_2/Erb	15	2	17
Erb	9	7	16
Total	24	9	33

Tab (13) Dermal damage, CO_2/Erb, Erb P = 0.093 (exact test)

Inflammation: Tab (14,15,16).

	Inflammation	No inflammation	Total
CO_2	6	4	10
CO_2/Erb	10	7	17
Total	16	11	27

Tab (14) Inflammation, CO_2, CO_2/Erb. P > 0.5 (χ^2 test)

	Inflammation	No inflammation	Total
CO_2	6	4	10
Erb	3	13	16
Total	9	17	26

Tab (15) Inflammation, CO_2, Erb. $P < 0.05$ (χ^2 test)

	Inflammation	No inflammation	Total
CO_2/Erb	10	7	17
Erb	3	13	16
Total	13	20	33

Tab (16) Inflammation. CO_2/Erb, Erb $P < 0.025$ (χ^2 test)

SECOND AND THIRD GROUPS (6 MONTHS AND 1YEAR):

Epidermal Alteration:

	Normal epidermis	Altered epidermis	Total
CO_2	3	12	15
CO_2/Erb	3	11	14
Total	6	23	29

Tab (17) Epidermal appearance. CO_2, CO_2/Erb $P = 1.278$ (exact test)

	Normal epidermis	Altered epidermis	Total
CO_2	3	12	15
Erb	4	9	13
Total	7	21	28

Tab (18) Epidermal appearance. CO_2, Erb. P = 0.824 (exact test).

	Normal epidermis	Altered epidermis	Total
CO_2/Erb	3	11	14
Erb	4	9	13
Total	7	20	27

Tab (19) Epidermal appearance. CO_2/Erb, Erb. P = 0.908 (exact test)

Biopsies 6 hours post test patches

These biopsies were taken at the lateral edge of the laser test patches to include approx 50% normal and 50% injured skin however due to the small size of the specimens sectioning led to some of the final histology slides containing only the uninjured skin ie those slides assessed as normal.

Depth of injury to epidermis

There was a statistically significant difference in the depth of ablation between the CO2 and Erbium groups P = 0.007 (exact test) (tab 9),with total loss of epidermis and a deeper depth of ablation in the Erbium group. The combined CO2 + Erbium laser caused an intermediate depth of ablation not significantly different from either the CO2 or Erbium groups (P = 8.686 and P = 0.131 respectively using an exact test), (tabs 8,10).

Depth of injury to dermis and inflammatory response

There was trend towards deeper dermal injury in the Erb compared with the CO2 + Erb and the CO2 groups P = 0.093 and P = 0.162 (exact test), (tab13,12), but not in the CO2 /CO2 + Erb group P = 1.394, (tab11). The much more obvious difference was in the inflammatory response in the dermis with significantly more inflammation at 6 hours in the CO2 compared with the Erb group P < 0.05 (chisquare test), (tab15), and the CO2 + Erb compared with the Erb group P < 0.025 (chisquare test), (tab16). There was no significant difference between the CO2 and CO2 + Erb groups P > 0.5 (chisquare test), (tab14).

These results suggest that the overall injury (ablation + RTD) was similar in the 3 groups as planned from the known characteristics of the 3 lasers ie

deeper ablation in the Erb group and more residual thermal damage in the CO2 and CO2 + Erb groups.

Biopsies at 6 months and 1 year

These biopsies were taken medial to the previous biopsy scars so contained only injured skin. Many of the slides showed full recovery with normal looking epidermis and dermis. Some showed altered epidermis with either flattened epidermis with loss of rete pegs or complex branching of the rete pegs or a combination of thes e appearances. There was no significant difference between the CO2/CO2 + Erb, CO2/Erb or CO2 + Erb/ Erb groups ($P = 1.279$, $P = 0.824$ and $P = 0.908$ respectively using exact tests), (tabs 17,18,19)

The results in all of the three groups shows that:

with an equivalent depth of injury i.e. deeper ablation but less collateral heat damage Erb:YAG laser produces similar long term histological changes as CO_2 or Erb/CO_2 lasers.

There appears to be few long-term changes to dermal architecture with laser resurfacing.

NB: All the details of the data, and examples of biopsies (histological appearances) are shown in appendix B.

2. Results of the effect of laser resurfacing (ablation) in pigmented skin lesions (PSL)

The results of laser treatment were assessed in 46 patients. All patients had benign PSLs, and all were treated with laser resurfacing (ablation). The diagnosis in these pigmented skin lesions and the number of patients in each condition are shown in table (20):

Diagnosis	**Number of patients**
Congenital pigmented naevi	19
Epidermal naevi	10
Lentigo maligna	5
Actinic keratosis	7
Becker's naevus	1
Organoid naevus	1
Benign fibroepithelial polyp	1
Angio-keratoma	1

Atrophoderma vermiculatum	1

Table (20): Number of patients according to the diagnosis in PSLs

In all of the patients but eight, the diagnosis was confirmed by biopsy. In these eight patients where the diagnosis was not confirmed by biopsy, the clinical diagnosis was: benign solar keratosis, four patients, and congenital naevi, four patients.

The number of laser treatments in pigmented skin lesions, are shown in table (21):

No of RXs	**One RX**	**Two RXs**	**Three RXs**	**Five RXs**
No of patients	25	15	5	1

Table (21): Number of laser treatments in pigmented skin lesions.

25 Patients were treated once, 15 Patients were treated twice, 5 Patients were treated tree times, and one patient was treated five times, who was diagnosed with epidermal naevus syndrome, which covered a large area of his skin.

The results were classified into four types:

1) Gone, where the lesion has disappeared.

2) Good, where there was obvious improvement and the patient was satisfied.

3) Moderate, where there was little improvement and the patient was unsatisfied.

4) Poor where there was no improvement.

The results were assessed in each condition of benign pigmented skin lesions:

Congenital Naevi: The results of laser ablation in patients diagnosed with congenital pigmented naevi, are summarised in table (22):

Results	**Good**	**Moderate**	**Poor**
19 patients	8	10	1

Table (22): Results of, laser treatment, of congenital naevi.

19 patients: 8 patients had good results, 10 patients had moderate results, and 1 patient had a poor result. Therefore 38% of patients with congenital pigmented naevi had good results, but none of these naevi have gone completely.

Epidermal Naevi, 10 Patients: The results of laser ablation in patients with epidermal naevi are summarised in table (23) (next page).

Results	Good	Moderate
10 patients	7	3

Table (23): Results of laser treatment for epidermal naevi

7 patients had good results, 3 patients had moderate results, therefore 70% of patients with epidermal naevi had good results, although, the Epidermal Naevi are usually superficial in their depth, none of them had complete clearance of the lesion. That might be due to the involvement of the pilo-sebaceous unit with the disease. That will cause incomplete clearance and recurrence of the epidermal naevi.

Lentigo maligna, 5 patients: all of these patients had complete initial clearance of the lesions with one late recurrence. Although the results after laser ablation were very good, (100% clearance), we do not recommend the laser ablation as the treatment of choice in patients with lentigo maligna PSL. This is due to the tendency of lentigo maligna lesions to develop malignant melanoma. In our practise two patients have been referred for laser ablation of lentigo maligna, and when the lentigo maligna lesions were excised, evidences of malignant melanoma in the lesions of lentigo maligna were found. Therefore the treatment of choice of lentigo maligna is complete surgical excision whenever possible, and the laser ablation is indicated only when surgical excision carries high

morbidity, as in lentigo maligna covering most of the cheek or the ear. In that case patient will be followed up for a long time.

In actinic keratosis, 7 patients: all lesions in all of the patients have gone. Therefore 100% of patients with actinic keratosis had complete clearance after laser ablation. Actinic keratosis is a superficial lesion, which does not go deeper than the epidermis. This explains the complete clearance of actinic keratosis following laser ablation.

One patient, in each other condition, was treated. The result in each of them was: good result in the patient with angio-keratoma, the lesion has gone in the patient with benign fibroepithelial polyp, good result in the patient with organoid naevus, moderate result in the patient with atrophoderma vermiculatum, and poor result in the patient with Becker's naevus.

Although it was not possible to reach a conclusion after the treatment of one patient in each condition, it was obvious that the superficial lesions had better results than the deeper lesions.

The relation between the depth of pigmented skin lesion and the results after laser ablation:

The Depth of the PSL was assessed with biopsies in 38 patients from 46. 8 cases, where there was no biopsy, were excluded from the depth/ results analysis. The data was analysed as shown in the following tables:

Gone	Good	Moderate	Poor	Total
9	17	11	1	38

Tab (24) The results in Biopsy group in PSL.

All lesions, which had gone (9), where in the epidermis in there depth.

Lesions, with good results, had their depth as follows tab (25):

Epidermis	Superficial dermis	Deep dermis	Total
7	10	0	17

Tab (25) Depth of PSL with good result.

The depth in the lesions, which had moderate results, was as shown in tab (26).

Epidermis	**Superficial dermis**	**Deep dermis**	**Total**
3	0	8	11

Tab (26). Depth of PSL with Moderate result

All the three lesions, which had depth in the epidermis, were epidermal naevi.

Finally one lesion had poor result, and the biopsy confirmed deep dermal involvement.

In the congenital pigmented naevi group (19 pts), 15 patients had biopsies to confirm the depth. There results varied according to the depth. Tabs (27&28).

Gone	**Good**	**Moderate**	**Poor**	**Total**
0	8	7	0	15

Tab (27). Results in Cong.P.Naevi.

Epidermis	S.dermis	Deep dermis	Total
0	7	8	15

Tab (28). Depth of Cong P.Naevi.

7 patient s out of 8, who had good results, their lesions were in the superficial dermis. All the moderate results lesions had deeper dermal depth.

According to the previous results in the relation between the laser ablation outcome and depth of PSL a statistic analysis was done as follows:

	Gone/Good	Moderate/Poor	Total
Epid /S. dermis	26	3	29
Deep dermis	0	9	9
Total	26	12	38

Tab (29) the relation between depth and results in PSL. $P < 0.001$ (χ^2 test)

	Gone	Good	Moderate	Poor	Total
Epidermis	0	0	0	0	0
S. dermis	0	7	0	0	7
D. Dermis	0	1	7	0	8
Total	0	8	7	0	15

Tab (30) the results according to the depth in Cong. P.N. P = 0.001 (exact test).

CONCLUSIONS:

Pigmented skin lesions

There was a significant correlation between the depth of a pigmented skin lesion and its response to laser ablation with all the lesions which were either gone or had a good result being in either the epidermis or superficial dermis P < 0.001 (chisquare test). Tab (29)

Congenital Pigmented Naevi

All except one of the naevi that had a good response were in the superficial dermis and all those with a moderate or poor response were in the deep dermis P = 0.001 (exact test), tab (30). None of the naevi were completely removed and it seems likely that a degree of scarring would probably have to be accepted to allow complete ablation

Complications of laser treatment of pigmented skin lesions

The complications following the laser treatment in 46 patients are shown in table (31).

Complication	**No of patients**	**Diagnosis**
Recurrence	3	Epidermal naevi
Scarring	1	Epidermal naevi
Recurrence	1	Lentigo Maligna

Table (31): Complications of laser treatment for pigmented skin lesions.

There were three cases of recurrence of epidermal naevi, and one case of recurrence in lentigo maligna. One patient had scarring after the laser treatment to the epidermal naevi on his trunk.

NB. See data of CO_2 laser treatment to pigmented skin lesions in Appendix C.

3. Results of the effect of laser resurfacing (ablation) for benign superficial tumours, and other rare skin conditions:

The results of laser ablation, in 11 patients, were assessed. These results are summarised in table (32).

Diagnosis	No of patients	Results
Xanthalasmas	3	Gone
Syringomas	2	Good
Tubero-sclerosis	2	Good
Darier's disease	1	Good
Granuloma anulare	1	Good
porokeratosis	2	Good/Gone

Table (32): Results of laser treatment in benign superficial tumours.

Three patients had xanthelasmata. In all of these patients the xanthelasmata had gone after laser ablation. Therefore, 100% clearance was achieved in xanthelasma after laser ablation. Two patients had syringomata on the cheeks and eyelids. After laser ablation there was good improvement and the patients

were satisfied. Two patients had tuberous sclerosis. Both patients achieved good improvement after laser ablation. One patient had Darier's disease. That patient achieved good improvement after laser ablation. Another patient had had granuloma-annulare at her wrist. She also achieved good improvement after laser ablation. Finally, two other patients had porokeratosis. One of these patients had good improvement after laser ablation to the lesion on his arm, while the other patient had complete clearance of lesions on his leg after laser ablation. All patients received 1-2 laser treatments; one patient had infection and hyperpigmentation after laser ablation to porokeratosis on his leg.

NB: The data is found in Appendix D.

DISCUSSION

The discussion in this section will consider the same three parts, which were explained in the previous sections. These parts are:

1) Discussion in relation to the results of the long-term effect of laser resurfacing on histological appearances.

2) Discussion in relation to the results of the effect of laser ablation (resurfacing) of benign pigmented skin lesions.

3) Discussion in relation to the results of the effect of laser ablation (resurfacing) of benign superficial tumour and other rare skin condition.

1. Long-term effect of Erbium/CO_2 laser resurfacing on histological appearances.

Before starting the discussion about the long term effect of CO_2, CO_2/Erb, and Erb:YAG laser, it is useful to highlight the important characteristics in each of CO_2 laser and Erb:YAG laser. This will help in understanding the effect of each laser in wound healing process after laser skin resurfacing (LSR).

While, the CO_2 laser has a wavelength of 10,600 nm with coefficient absorption of water approximately 790/μm, the Er:YAG laser has a wavelength of 2,940nm with coefficient of absorption of water 13.000/μm, more than 16 times greater than that of the CO_2 laser. This results in its energy

being absorbed more readily in thinner layers of tissue than the CO_2 laser. In other words the optical penetration depth (OPD) of the CO_2 laser is much higher than the (OPD) in Erb:YAG laser.

If energy is delivered in less than the thermal relaxation time (tau), heating will be confined to the OPD during a laser pulse. However, the depth of residual thermal damage (RTD) is usually 3-4 times the OPD. This is because there is some heat diffusion during a laser pulse, even with a very short exposure. And deeper tissue heating occurs after the laser pulse. Therefore the CO_2 laser causes residual thermal damage much deeper than the Erb:YAG laser. In other words the main effect of CO_2 laser in laser resurfacing is tissue heating, whilst in laser resurfacing with Erb:YAG laser, it is tissue ablation.

The previous points about CO_2 and Erb:YAG laser characteristics explain the results in the first group of biopsies (6 hours post laser test patches), it was clear in those results that deeper ablation of the dermis was associated with the use of Erb:YAG laser due to its main effect of tissue ablation. From the results of the dermal changes in the first group of biopsies (6 hours after laser test patch), it was clear that while the deeper damage of dermis was most common after the use of Erb:YAG laser, the commonest cases of inflammation were when the CO_2 laser was involved. This could be explained because the main effect of the CO_2 laser is causing residual thermal damage, whereas the main effect of the Erbium laser is ablation of tissue.

These results suggest that the overall injury (ablation + RTD) was similar in The 3 groups as planned from the known characteristics of the 3 lasers ie Deeper ablation in the Erb group and more residual thermal damage in the CO2 and CO2 + Erb groups.

The thermal effect on collagen shrinkage and denaturation is well documented. Thermally coagulated collagen examined by electron microscope shows unravelling of collagen fibrils with loss of the unique striations of collagen and an increase in fibrillar diameters.[53] The unravelled strands merge, and the individual fibres become less distinct, forming the swollen, hyalinized (glossy) collagen fibres seen with light microscopy.

It is often quoted that a temperature of 65° C is the temperature of shrinkage point of collagen.[47] This number is only accurate for relatively long exposure, on the order of several seconds, somewhat longer than for pulsed lasers. Zweig et al,[47] have suggested that the shrinkage temperature for msec-domain exposure must exceed 85° C.

Three distinct staining zones have been observed after multiple-passes of CO_2 laser skin resurfacing. These are related to temperature gradient as a function of depth[47]. Typically there was a very fine (1-2 μm) zone of intense basophilia, then 60-100 μm of basophilic zone (zone I). 10-20 μm mixture of basophilia and hypereosinophilia (zone II). 30-250 μm of hypereosinophilia (zone.III).

Zone I corresponds to depth where little or no birefringence is observed; it is called the coagulative zone and known as RTD. In zone II there is decrease in overall birefringence. In zone III, birefringence is similar to normal-appearing untreated collagen.

Zweig et al,[47] identified a transition zone by haematoxylin-eosin staining that coincides with the hypereosinophilic zone III. The electron microscopy on tissue on this zone showed retained birefringence and noted that the fibrils were only slightly thickened and retained their periodicity. This suggests that subtle tinctorial change on hematoxylin-eosin staining may be more sensitive than even electron microscopy in detecting early denaturation.

Many studies have demonstrated that the percent shrinkage of collagen is directly proportional to the heat applied to the tissue while remaining within a narrow range and without exceeding the excessive heat threshold.[45,57,69-71]

During and after CO_2 laser treatment, there is immediate contraction roughly proportional to the amount of dermal RTD over a range of 20 to 120 μm. After a portion of denatured collagen sloughs (day one to two), some initial shrinkage is lost. This may be due to rehydration. A second contraction then occurs after carbon dioxide laser skin resurfacing (day 5-10); that is presumably due to myofibroblasts.

After CO_2 LSR focal remnants of basophilic-staining collagen persist underlying the neo-epidermis, which is started to form five days after

treatment. Within areas of persistent denatured collagen, viable fibroblasts have presumably replaced necrotic ones observed one and two days after the laser procedure. By seven days post treatment, there is a robust zone of granulation tissue approximately 200-300 μm thick underlying the epidermis. Seventeen days post treatment, the granulation tissue has become more organised but retains a thickness of approximately 300 μm. Between seventeen and sixty days post treatment, there is slow relaxation (increase in area) resulting in most wounds reaching 90% to 95% of their original size. Histologically, the thickened hypercellular dermis becomes more compact (150-200 μm), and collagen rich. Also there is increased horizontal alignment of collagen and elastic fibres. Shim et al,[75] agree with others when they reported increase in collagen layer thickness in skin biopsies from rhytides, post CO_2 laser treatment. Cotton et al,[76] confirmed as well that, ninety days after CO_2 laser treatment, the sub-dermal and dermal repair zone consist of new collagen fibres overlying collagen with evidence of solar elastosis.

This sequence of events is different after treatment with Erb:YAG laser skin resurfacing, when it carries the same depth of injury (RTD plus the depth of ablation). Immediate wound contraction is slight (3%-7% of original area). Wound contraction begins only 2-3 days after surgery. There is no delay or biphasic contraction pattern as noted for carbon dioxide wounds. After 60 days there are fewer collagen fibres with less horizontal orientation than in CO_2

laser wounds. By 60 days after treatment, the initial wound contraction almost completely regresses.

Therefore, what differentiates CO_2 laser skin resurfacing from Erb:YAG laser skin resurfacing of similar depth is not the method of injury, which is irrelevant, but rather the total depth of injury determines the subsequent healing cascade.

Opinions about the relation between the residual thermal damage (RTD) and the outcome of the laser skin resurfacing vary.

In this study's results for the second and third groups of biopsies (6 months, and 12-13 after first laser treatment), there was no clear evidence that any of the three lasers (CO_2, CO_2/Erb, and Erb:YAG) was superior for the other two lasers in relation to long term outcome and effect on histological appearances. There were no obvious changes in dermis in both groups, and there was no significant difference between groups.

This study's results show that, within an equivalent depth of injury (RTD plus depth of ablation),laser skin resurfacing produces similar long-term histological changes no matter what type of laser is used.

Some authors still believed that the residual thermal damage (RTD) plays an important role in collagen formation Ross E,[128] Li AK et al, Luomanan M et al and others.[47] Harman et al[47] showed higher levels of platelet cell adhesion molecule after six weeks in carbon dioxide laser vs Erb:YAG laser wounds where the depth of injuries (as assessed by depth of ablation plus depth of RTD) were similar.

Other authors reported that the residual thermal damage is not an important factor for collagen shrinkage and new collagen formation. Campell JP et al,[47] in 1998 reported that there was no difference ultrastructurally between collagen fibres 180 days after treatment with dermabrasion and CO_2 laser sites in pig. Utley DS et al,[129] reported that after seven days, all groups of patients after treatment with (CO_2, CO_2/Erb, Erb/CO_2, Erb:YAG) lasers were re-epithelialised and showed equal new collagen formation. Hughes PS,[130] reported that laser skin resurfacing with Erb:YAG laser causes skin contraction up to 14% in spite of the minimal RTD.

It was difficult to compare the results in this study, in relation to the long term outcome in laser skin resurfacing using three lasers (CO_2, CO_2/Erb simultaneously and Erb:YAG) with other reports, because all other authors have looked at the results of laser skin resurfacing in limited numbers of patients, none of them have reported long term follow up (one year or more),

and none of them have reported the results of laser skin resurfacing by CO_2/Erb laser simultaneously.

2. The effect of laser resurfacing (ablation) in pigmented skin lesions.

Forty-six patients had pigmented skin lesions, and were treated by laser resurfacing (ablation). In terms of diagnosis these patients were classified in subgroups as follows:

1) Congenital pigmented naevi (congenital nevomelanocytic naevi-CNN-):

19 patients with large CNN were treated. 8 of them (38%) had good improvement where the lesions faded, but none of these lesions have disappeared completely.

Congenital nevomelanocytic naevi (CNN) are pigmented lesions of the skin, usually present at birth; rare varieties of CNN can develop and become clinically apparent during infancy. CNN may be any size from very small to very large. CNN are benign neoplasms composed of cells called nevomelanocytes, which are derived from melanoplasts. All CNN regardless of size may be precursors of malignant melanoma. To our knowledge there was no reports of the result of treating CNN in large number of patients by laser ablation. These results did not show complete clearance in any of the 19

patients who were treated with laser ablation. When the depth of the treated CNN lesions was considered, all of them were in the dermis, and some of them were very deep in the reticular dermis. This could explain the results, when none of these lesions disappeared completely.

According to the results of laser ablation in CNN lesions (incomplete clearance), and bearing in mind the risk of developing malignant melanoma, we believe that the treatment of choice in CNN should be surgical excision whenever it is possible. When surgical excision has a high morbidity, laser ablation could help to achieve some improvement to keep the CNN lighter in colour. Best results when treatment starts in early ages, multiple treatments, and long time follow up.

2) Epidermal Naevi:

10 patients were treated, 7 of them (70%) had a good result where the lesions improved significantly but without complete clearance.

Removal of epidermal naevi can be very difficult. Many types of treatment were used before the laser ablation. None of them was a complete success.[97,98] Dermabrasion, where it is difficult to control the depth of treatment, is followed by recurrence of the lesions if the treatment is superficial, and if the dermabrasion is deep it will cause scarring. Surgical excision of epidermal naevi is most of the time not indicated because of the high level of morbidity due to the size and location of the lesions.

The degree of precision achieved with laser ablation is not possible with other modalities, but a fine line exists between excellent results without lesion recurrence, and ablating too deeply, resulting in healing with some degree of scarring. Although, the epidermal naevi are usually superficial in depth, none of our patients had complete clearance of the epidermal naevi. That might be due to the involvement of the pilo-sebaceous unit in the disease. That explains the incomplete clearance and recurrence of the epidermal naevi, which we saw in three of our patients.

3) Lentigo Maligna:

Five patients were treated. All of them had complete initial clearance of the lentigo maligna. In spite of the complete disappearance of lentigo maligna lesions after laser ablation, and bearing in mind that lentigo maligna can extend into the hair follicles and may thus reach the mid-dermis even in the preinvasive stage, and considering the risk of developing lentigo maligna melanoma, we do not recommend laser ablation as the treatment of choice in patients with lentigo maligna. Two patients have been referred to our Unit for laser ablation of lentigo maligna, and when the lesions were surgically excised, a lentigo malignant Melanoma was found. Therefore the treatment of choice is complete surgical excision. Laser ablation is indicated when surgical excision carries high level of morbidity, as in a lesion of lentigo maligna covering a

large area of skin on the face. In that case patients should be followed up for a long time.

4) Actinic Keratosis:

Seven patients were treated. All of them had complete clearance of actinic keratosis after laser ablation. Actinic keratosis is epidermal lesion, which explains the complete clearance after laser treatment. Many modalities have been used to treat actinic keratosis, for instance local application to the lesion of 5% 5-fluorouracil cream over a period of several days to weeks, short exposure to liquid nitrogen alone or followed in three days by topical application of 5% 5-fluorouracil cream. Laser ablation is one modality of treatment to actinic keratosis. It is effective because actinic keratosis is a superficial lesion; it is fast and easy to control.

5) Other Conditions:

Five conditions, with one patient from each condition treated. These conditions were angio-keratoma, benign fibroepithelial polyp, organoid naevus, atrophoderma vermiculatum, and Becker's naevus.

Good results after laser ablation were achieved only for fibroepithelial polyp, and angio-keratoma conditions, where lesions were superficial. In the other conditions the results were poor.

Although, it is obvious from the results that laser ablation gives better results

when the lesions are more superficial, it was difficult to draw conclusions after treating one patient in each of these conditions.

Summary: Considering the results of laser ablation in pigmented skin lesions, in this study the indications of laser ablation in pigmented skin lesions could be summarised as:

1) An effective treatment in actinic keratosis and Epidermal naevi. Here the lesions are superficial (epidermal).

2) Treatment is an option for improving the appearance of congenital pigmented naevi too extensive or in a site unsuitable for surgical excision. Laser ablation can achieve results which vary according to the depth of the lesion, it is uncommon that laser ablation would clear the lesion completely.

3) Laser ablation is not the treatment of choice, and it is not recommended unless the surgical excision carries high risk of morbidity, as in lentigo maligna lesions, and organoid naevi.

3. Laser resurfacing (ablation) in benign superficial tumours, and other rare skin conditions.

11 patients were treated by laser ablation. The results of this treatment will be discussed according to the diagnosis of the benign superficial tumour as follows:

1) Xanthelasmas: Three patients with large xanthalasmas were treated. All of them had complete clearance of the Xanthelasmas of their eyelids. Xanthelasma palpebrarum (eyelid xanthelasma) may or may not be associated with hyperlipoproteinemia. It is limited in depth to the superficial dermis and epidermis. Many modalities of treatments have been used to treat xanthelasma. Excision, electrodessication, application of trichloroacetic acid, and laser ablation have been used.[131] Laser treatment offers distinct clinical advantages especially when surgical excision is difficult. In our personal experience we found that treating xanthelasmas by laser ablation using the Erb:YAG was better than using the CO_2 laser (Sharplan 40C), but with small xanthalasmas healing is quicker with surgical excision.

2) Syringoma: Two patients were treated. They had good improvement after laser ablation. Syringoma is a benign adenoma of the intraepidermal eccrine ducts. It is 1-2 mm, skin coloured in yellow. The lesion has a specific histologic pattern: many small ducts in the dermis with comma like tails with

the appearance of 'tadpoles'. Many modalities of treatment have been used including electrosurgery, dermabrasion, and laser ablation.[101]

The primary advantages of the laser ablation for removal of these lesions are precision, leaving minimal damage to the adjacent normal tissue, the speed of the treatment and of multiple lesions, the bloodless field, and the diminished post-operative pain and swelling are definitive advantages.

3) Tuberous sclerosis (angiofibromata, adenoma sebaceum):

Two patients were treated by laser ablation. Both patients achieved good improvement after laser ablation.

Tuberous sclerosis is an autosomal dominant disease arising from a genetically programmed hyperplasia of ectodermal and mesodermal cells and manifested by a variety of lesions in the skin, and other organs.

The skin lesions are white macules, and angiofibromata and adenoma sebaceum. The laser treatment has been used in treating skin lesions in tuberous sclerosis.[103]The laser has the same advantages as in the treatment of Syringoma (previous paragraph).

4) Darier's disease: One patient has been treated by laser resurfacing. She had improved after two sessions of treatments.

Darier's disease is a very rare condition and laser ablation offers some advantages, but it would not be able to cure the hyper-keratotic skin, and laser treatment needs to be repeated.

5) Granuloma annulare: One patient has been treated by laser ablation for granuloma annulare on her hand. That patient had good improvement after laser treatment. Granuloma annulare is an asymptomatic chronic dermatosis of the dermis which exhibits papules in an annular arrangement, commonly arising on the dorsa of hands and feet, elbows, and knees. Many modalities of treatment have been used to treat granuloma annulare, including topical corticosteroids, intralesional triamcinolone, and cryospray. There are no previous reports of laser ablation to granuloma annulare. Although it is very difficult to reach a conclusion after the treatment of one patient, it was clear that the laser treatment in that case has shown a good improvement. This condition may also respond to 585nm pulsed dye laser treatment.

6) Porokeratosis (DASP): Two patients have been treated by laser ablation. One of them had a good improvement, while the other one had complete clearance of porokaratosis lesions on his leg.

Porokeratosis is a disorder of epidermal keratinization with several clinical variants: Classic mibelli, palmoplanter, linear, and disseminated superficial actinic porokeratosis (DSAP), which our patients had.

The etiology is probably a combination of immunologic cause, and a maturation disorder of epidermal cells. Two types of laser were used to treat porokeratosis: Dye laser[132,133] and CO_2 laser.[134,135] All reports showed a favourable response to laser treatment. Considering that the porokeratosis is a

superficial lesion in depth (epidermis), a good result after laser ablation is expected. Therefore laser ablation can be recommended for porokeratosis conditions.

Although it is difficult to draw a conclusion from the anecdotal results in 1 or 2 patients for each condition of benign superficial tumours and other rare skin condition, it is obvious that the laser ablation has a wide range of applications in many types of superficial skin lesions.

In conclusion, laser resurfacing (ablation) is an important treatment for benign pigmented skin lesions and superficial benign skin tumours. The depth of the lesion is the main factor in achieving good results or complete clearance.

The superficial lesions (epidermal, superficial dermis) are usually easier to resolve after the laser ablation, while the deeper lesions (mid dermis, deep dermis) can improve but they will never disappear completely unless some scarring is accepted. Therefore the diagnostic biopsy is an essential step to find the depth of the lesion, which can determine the prognosis before starting laser treatment.

It is important to understand the variables in each type of laser. This will lead to the best outcome for laser treatment.

Understanding the pros and cons of each type of laser treatment is essential to

achieve good results, low complication rate, and therefore patient satisfaction Finally it is useful to remember that complete clearance in some cases is rare unless some scarring is accepted.

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APPENDIX A

Figure 1, 2, 3, 3*, 4 and 5
System specifications of Derma k laser
Example of Duty cycle in Derma k laser.

Figure 1

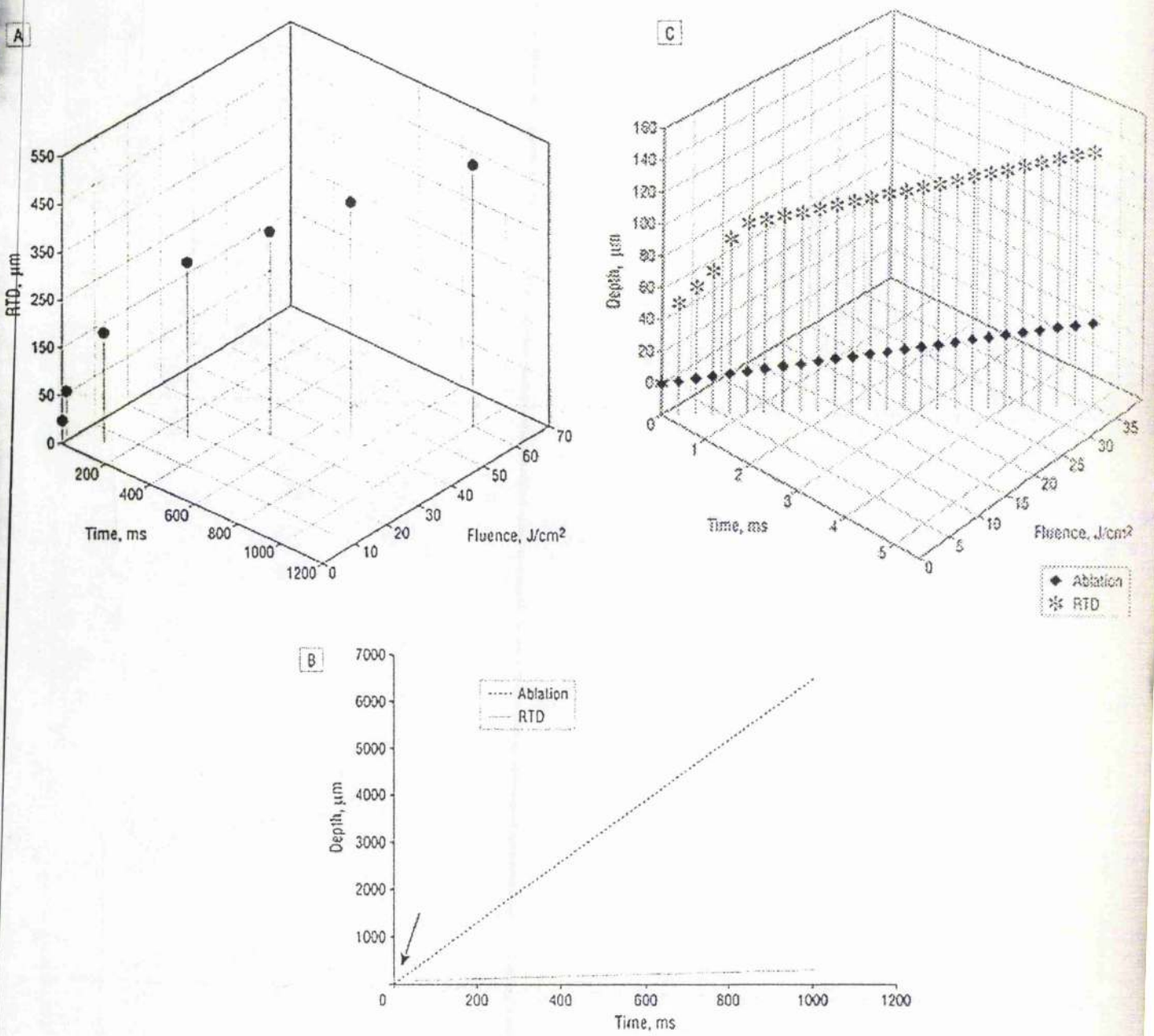

Figure 1. A, This graph shows the effects of pulse duration and fluence for a low power density, 60 W/cm^2 . This scenario occurs, for example, when treating a wart with a setting of 5 W and a 3-mm spot (defocused). Note that by the end of 1 second, residual thermal damage (RTD) has increased to nearly 500 microm. Ablation is negligible at this power density. B, Note the depths of ablation and RTD for a high power density, 10,000 W/cm^2 (like that used in laser skin resurfacing (LSR) over the same time scale. By the end of 1 second, ablation has increased to deeper than 6 mm, but RTD has remained relatively constant at 150 to 200 microm. In LSR, we restrict the exposure time to 0.5 to 5 milliseconds (part of graph denoted by arrow). With longer exposures, ablation depth increases rapidly. This might be desirable when cutting tissue, for example, and can be accomplished by focusing 5 W into a 0.2-mm beam. C, This graph depicts the influence of pulse duration and fluence (for power density x 10,000 W/cm^2) over the narrow range of parameters used in LSR for photodamage. The graph is an enlarged version of the small region denoted by the arrow in B. Note the narrow ranges of both RTD and ablation.

From: Ross: Arch Dermatol, Volume 135(4).April 1999.444-454

Figure 2

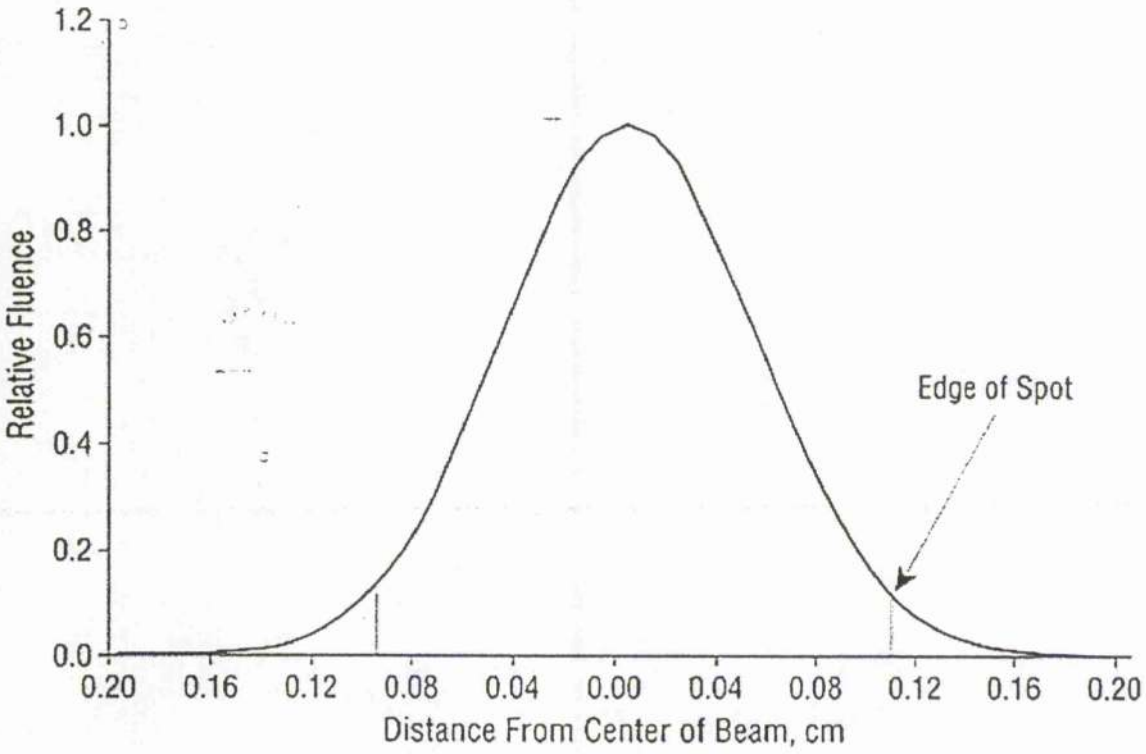

Figure 2. The relative fluence of a representative Gaussian beam.

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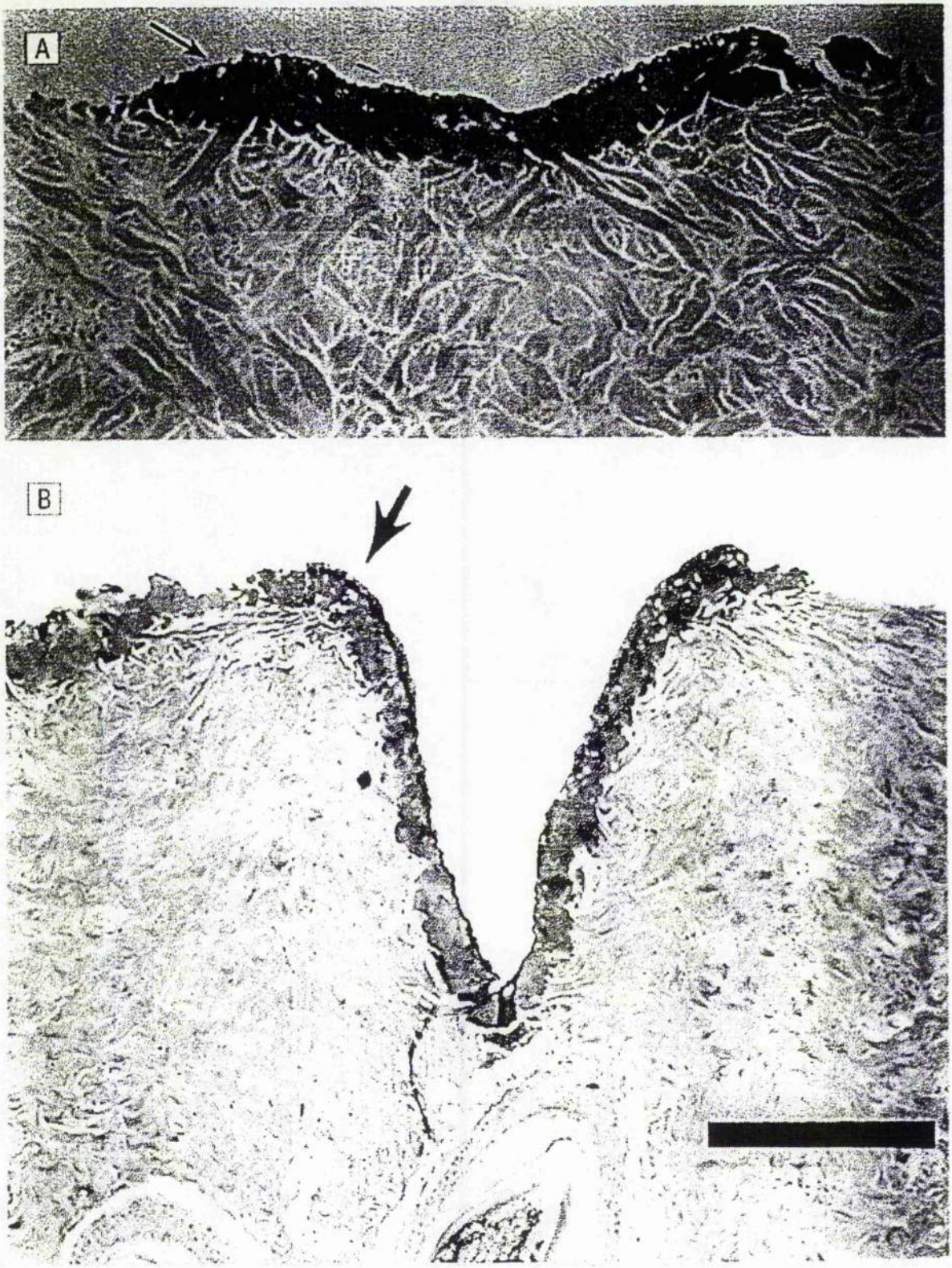

Figure 3. A, Pigskin dermis after 1 pass with millisecond-domain carbon dioxide laser, average fluence 10 J/cm^2, 1-mm spot, Gaussian beam profile (arrow indicates where local surface fluence is approximately 3 J cm^2; original magnification x100). B, After 10 passes, average fluence 10 J/cm^2 (original magnification x40) (bar=400 microm, hematoxylin-eosin stain, both A and B).

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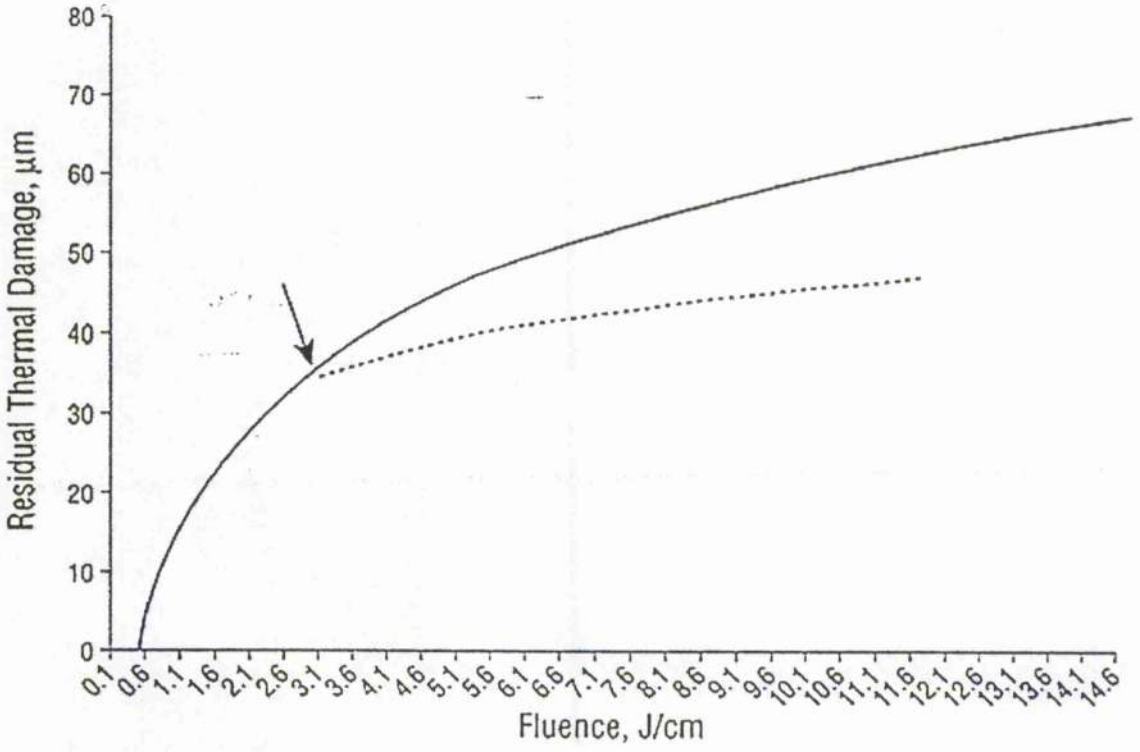

Figure 3 Graph of residual thermal damage vs fluence for a millisecond-domain carbon dioxide laser. Arrow designates ablation threshold. Dotted line indicates predicted residual thermal damage with ablation. Note resemblance of the graph to the inverted profile of denatured collagen at the edge of (Figure 3), A (arrow). This graph is based on a simple model for tissue heating using the Beer law.

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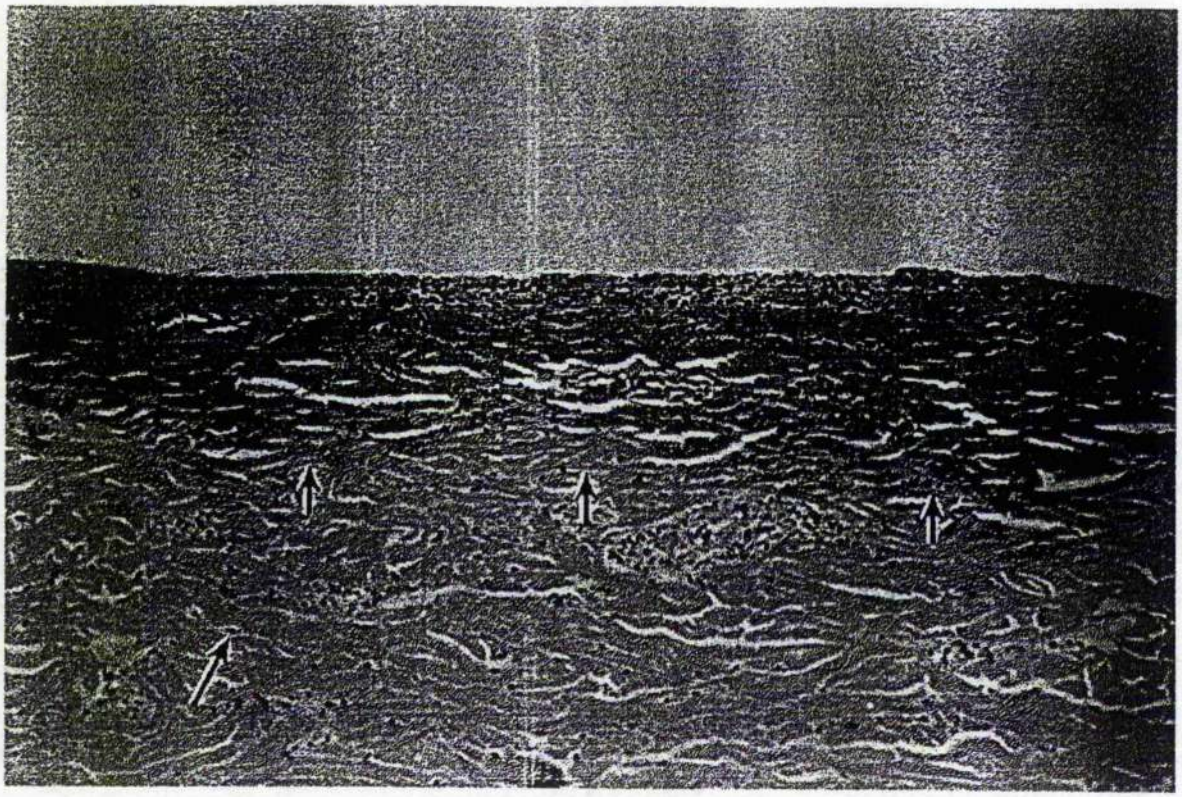

Figure 4 Pigskin 2 days after carbon dioxide laser skin resurfacing, 3 passes, with wiping, 7 J/cm^2, millisecond laser, with only petrolatum applied to the wound. Most of the basophilic zone has already sloughed. Note necrotic fibroblasts in the transition zone (which extends to the level of the short arrows, where there is a subtle change in collagen staining). At the base of the photograph are a few plump, viable fibroblast nuclei (long arrow) (hematoxylin-eosin, original magnification x200).

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Figure 5

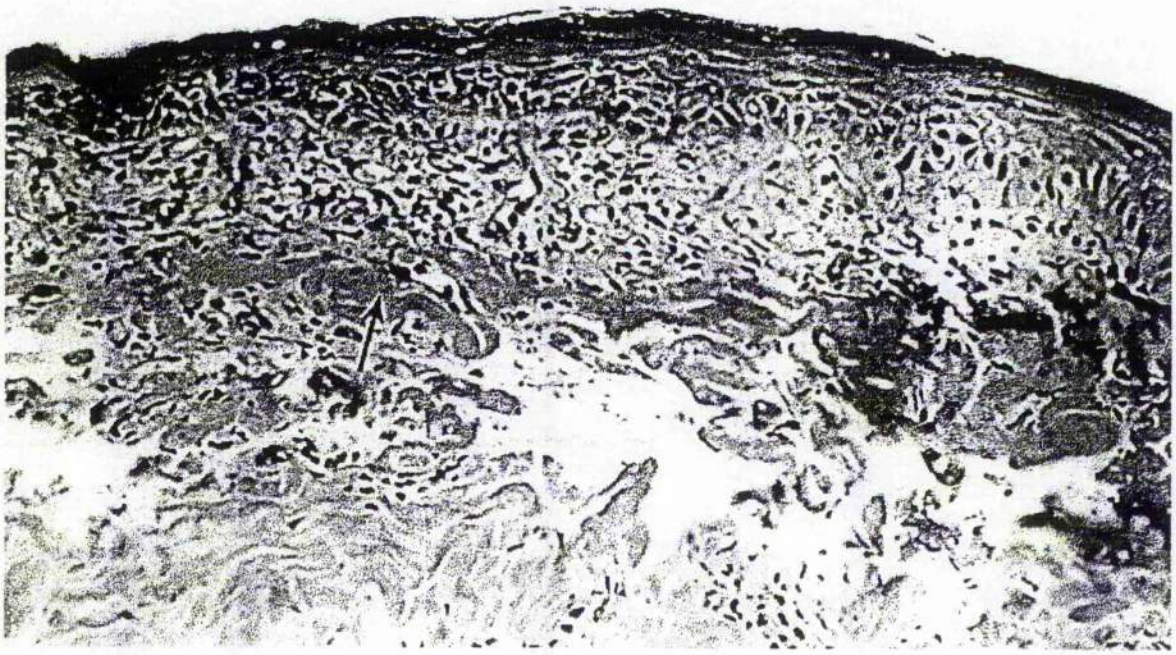

Figure 5. Pigskin 7 days after carbon dioxide laser skin resurfacing, 3 passes, with wiping, 7 J/cm^2 , millisecond laser, with occlusive dressings (OpSite; Smith and Nephew, Largo, Fla). Note areas of retained basophilic-staining collagen intermixed and subjacent to neoepidermis (arrow). This may serve as a shrunken template for new collagen deposition (hematoxylin-eosin, original magnification x200).

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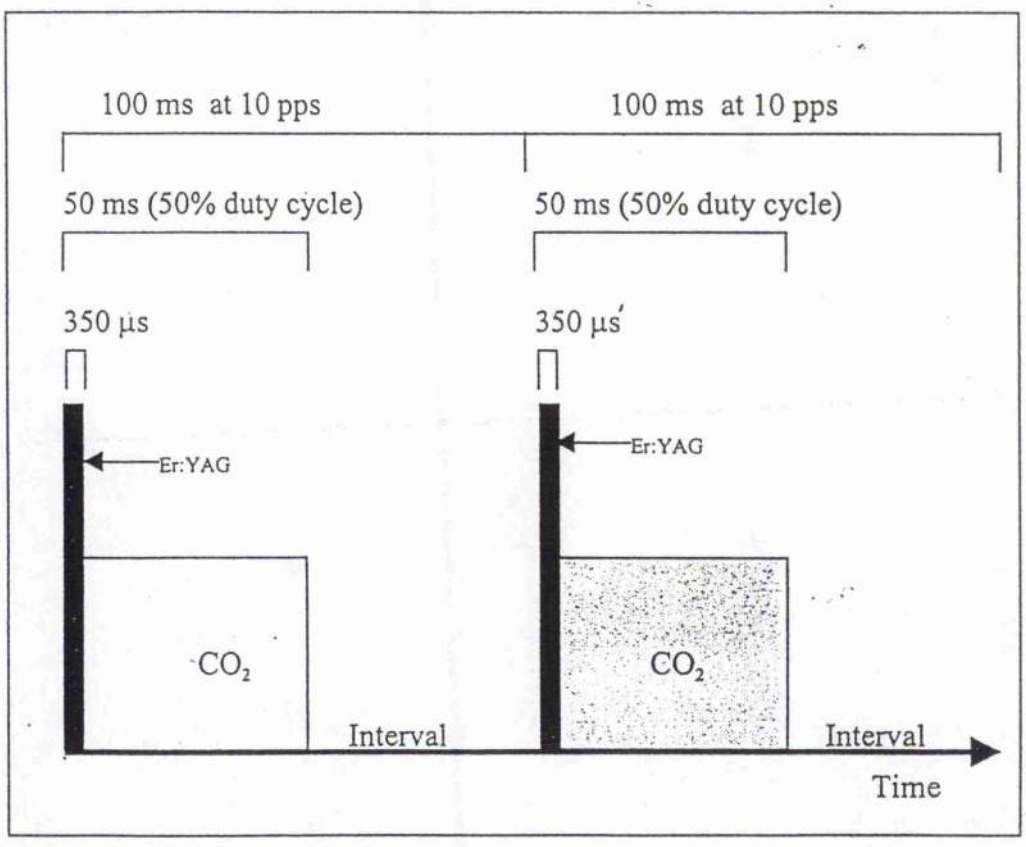
System Specifications

Operating Mode	Er:YAG alone	CO_2 alone	Er:YAG/ CO_2 combined
Laser Type	Er:YAG	CO_2	Er:YAG/ CO_2
Wavelength	2.94 microns	10.6 microns	2.94 and 10.6 microns
Emission mode	Pulsed	CW	Pulsed
Exposure mode	Continuous, single burst	Continuous, repeat pulse	Continuous, single burst
Average Power	Up to 20 watts	Up to 10 watts	Up to 30 watts
Pulse Energy	Up to 1.7 joules		Er:YAG: UP to 1.7 joules
Pulse Duration	350 microseconds	Up to 100% duty-cycle	Er:YAG: 350 microseconds CO_2: Up to 100% duty-cycle
Pulse Repetition Rate	5 to 12 pulses per second	10 pulses per second	5 to 12 pulses per second CO_2 synchronized with Er:YAG


100 ms at 10 pps
100 ms at 10 pps
50 ms (50% duty cycle)
50 ms (50% duty cycle)
350 µs
350 µs
Er:YAG
Er:YAG
CO_2
CO_2
Interval
Interval
Time

Duty Cycle:

APPENDIX B

-Analyzed data of the result of long term effect of CO_2, Erb/CO_2, Erb:YAG laser resurfacing on the new collagen formation.
-Examples of the histopathology appearance of the skin after resurfacing with CO_2, CO_2/Erb, Erb:YAG lasers.

Results of Long Term Effect of Erbium/CO2 Laser Resurfacing on New Collagen Formation

First Group: (Biopsies after 6 hours post laser test patches).

Epidermal Changes:

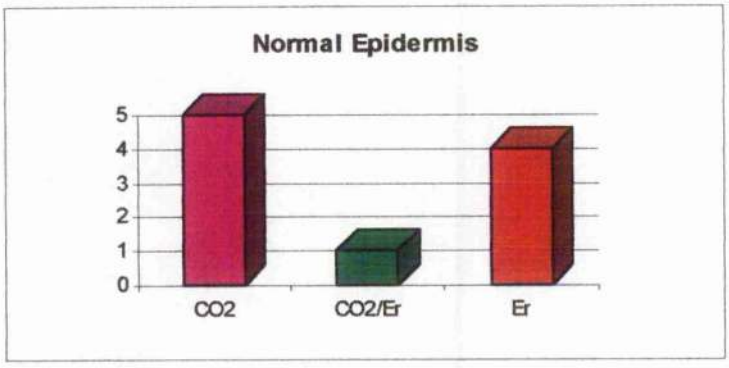


Figure 1: Shows No of biopsies, where there was disorientation and the cut was through the normal epidermis at the edge of each biopsy.

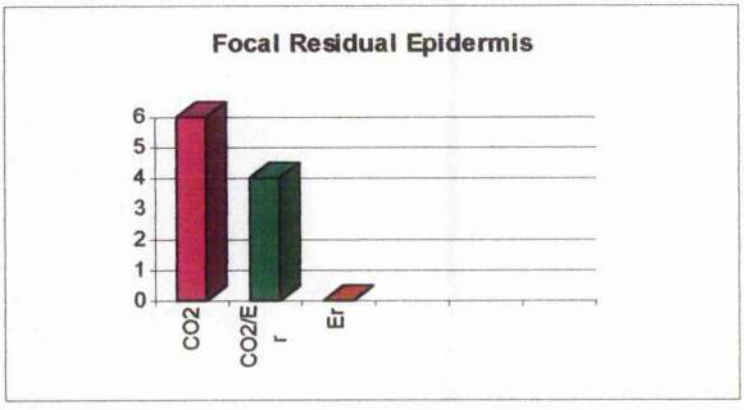


Figure 2: Most of the focal residual epidermis were after the use of CO2 laser.

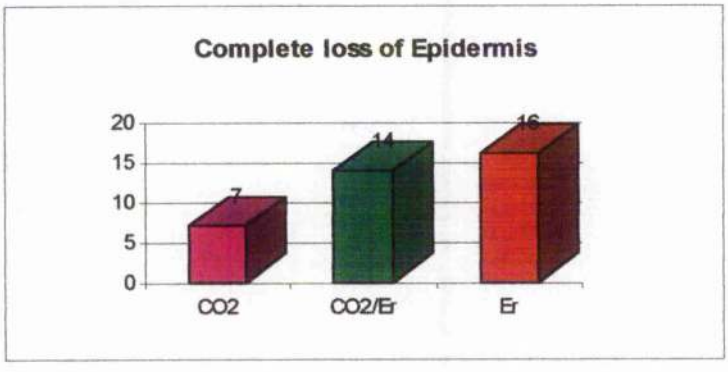


Figure 3: Most of the complete loss of epidermis was in the cases when Er:YAG laser was involved.

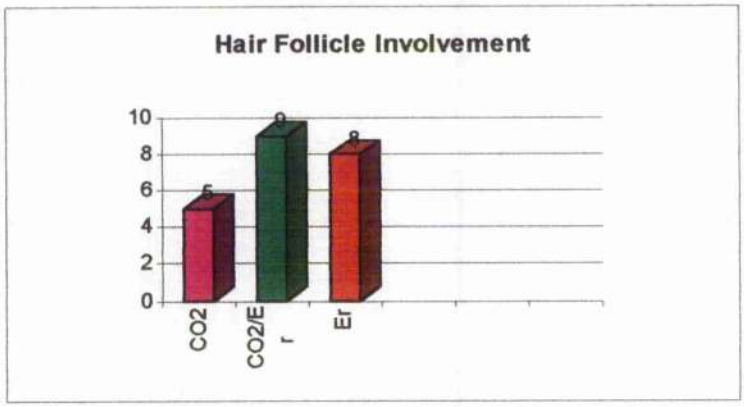


Figure 4: Hair follicle involvement was most common when Er:YAG laser was involved.

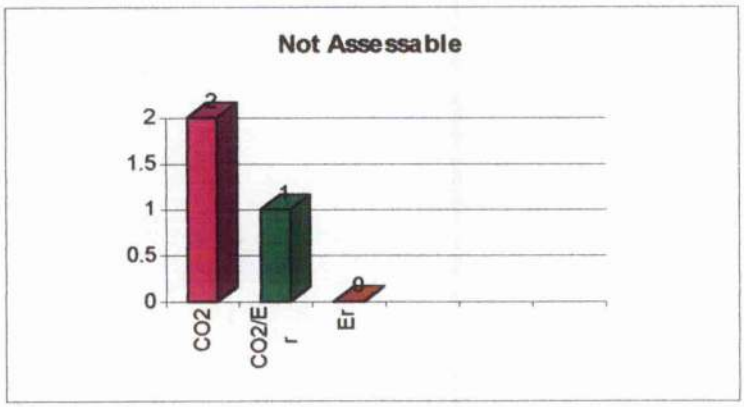


Figure 5: Not assessable cases for Technical reasons.

Dermal Changes:

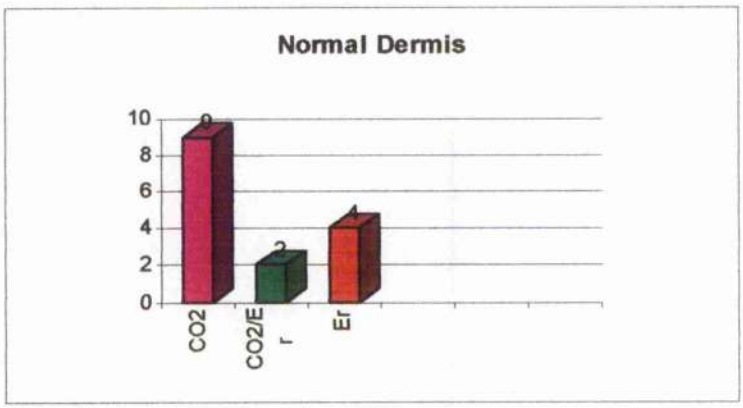


Figure 6: Most near normal appearance of dermis was in the biopsies after the test patches with CO2 laser.

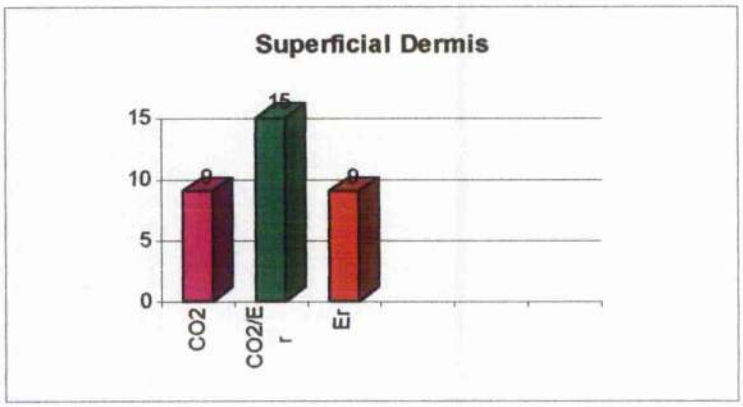


Figure 7: The involvement of Er:YAG laser increased the depth of damage in the dermis.

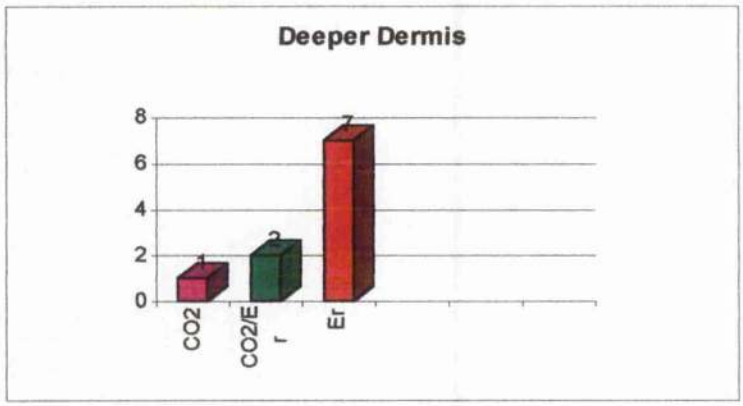


Figure 8: Deeper damage of the dermis when Er:YAG laser was used.

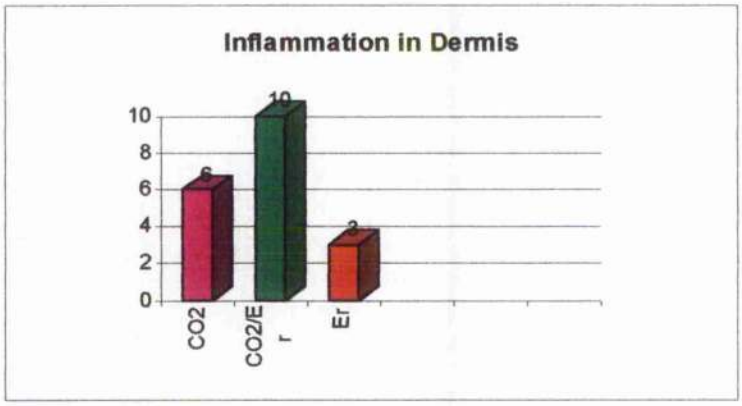


Figure 9: The least inflammation was when Er:Yag laser was used alone.

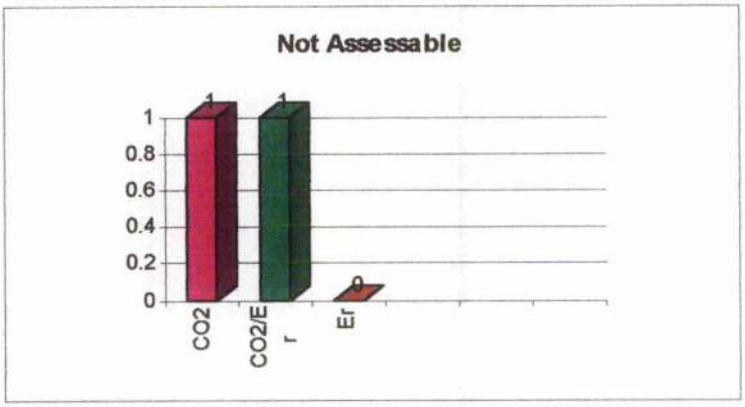


Figure 10: Not assessable for technical reasons.

Second Group: (Biopsies 6 months post first laser treatment).

Epidermal Changes:

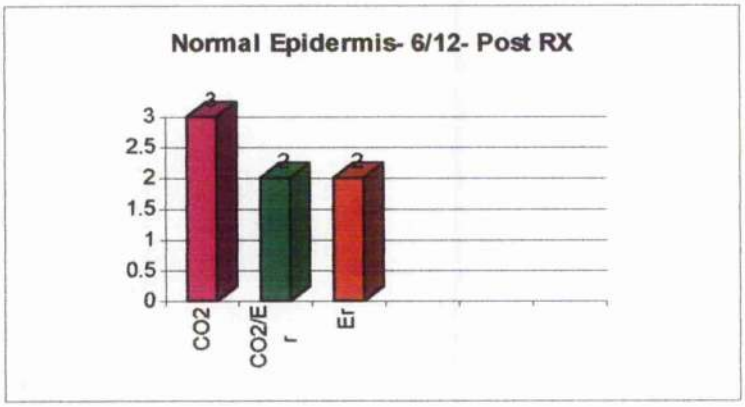


Figure 11. No obvious changes in the epidermis.

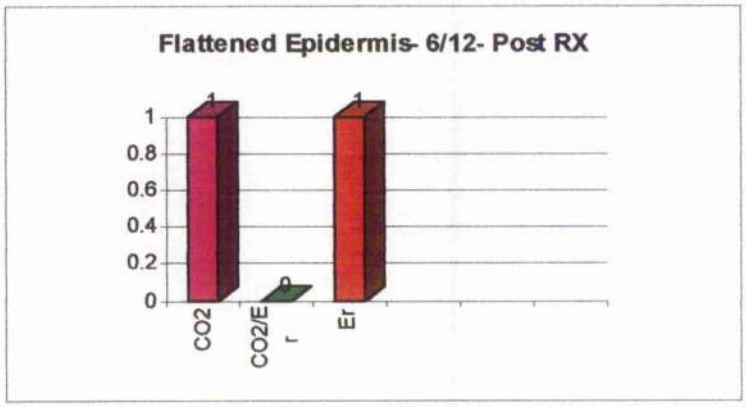


Figure 12: Flattening of the epidermis with some loss of rete pegs.

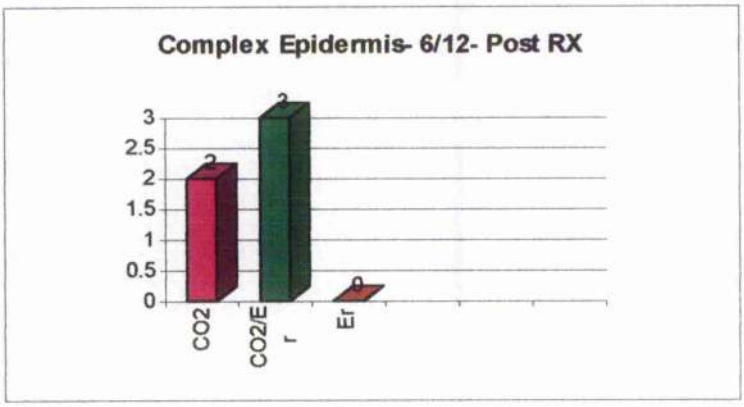


Figure 13: An increase in the complexity of branching of rete pegs.

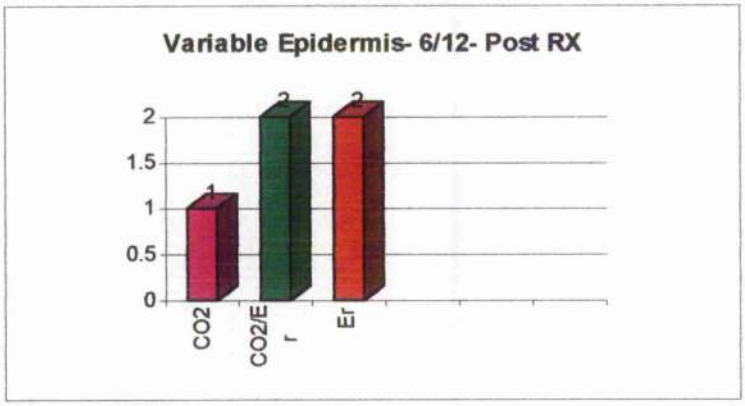


Figure 14: Both flattening of the epithelium and increase complexityof branching of rete pegs.

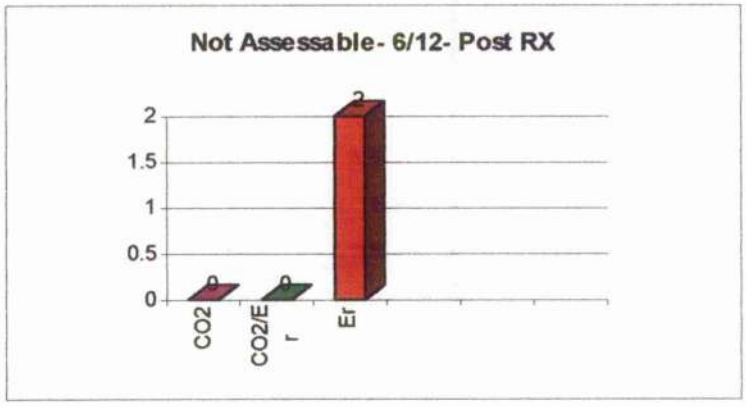


Figure 15: Not assessable for technical reasons.

Third Group: (Biopsies after 12-13 months post first laser treatment).

Epidermal Changes:

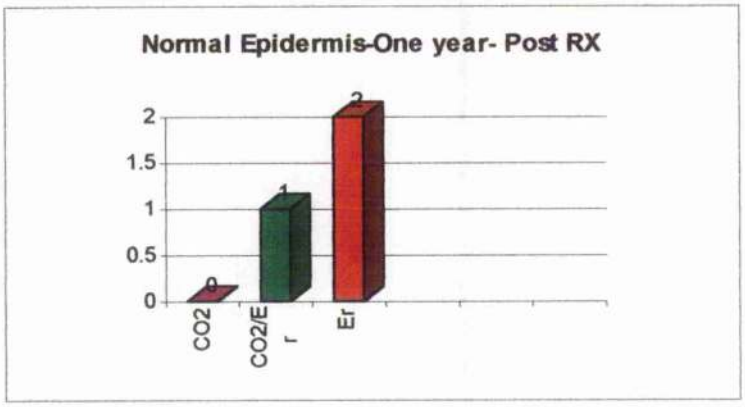


Figure 16: No obvious changes in the epidermis.

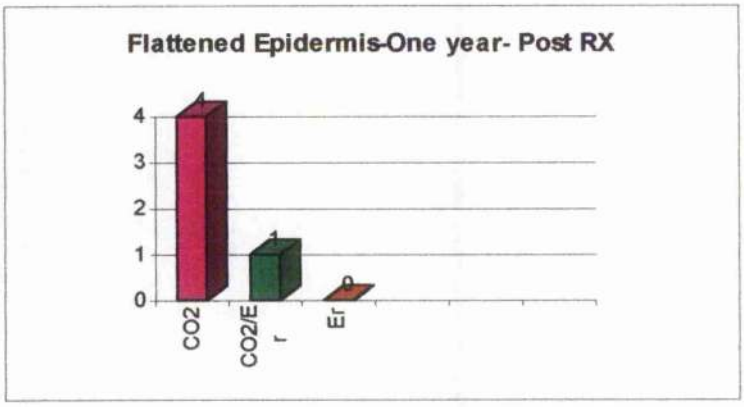


Figure 17: Flattening of the epithelium with some loss of rete pegs.

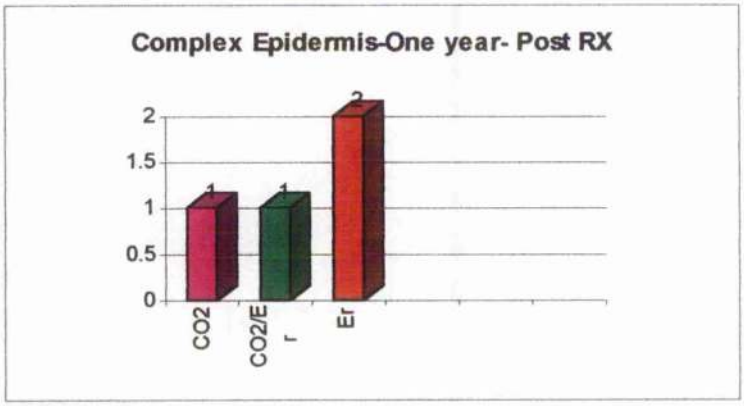


Figure 18: An increase in the complexity of branching of rete pegs.

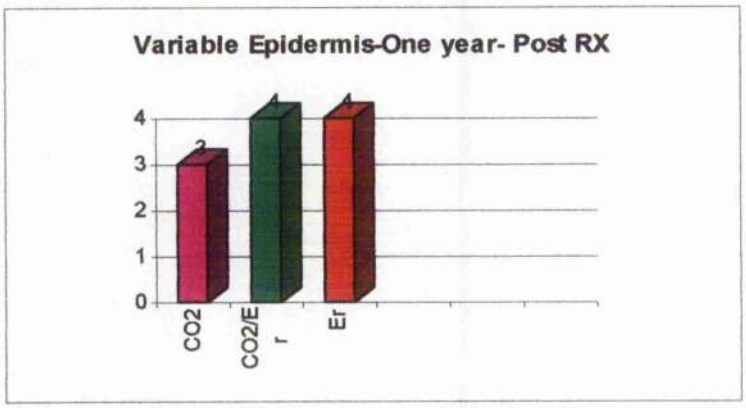


Figure 19: Both flattening of the epithelium and increase complexity of branching of rete pegs.

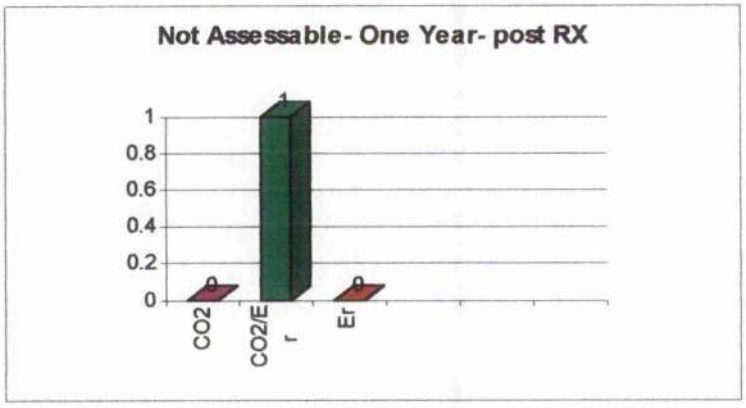


Figure 20: Not assessable for technical reasons.

Summary of Late Changes:

. Some loss of rete pegs.

. Some complex branching.

. No obvious changes in dermis.

. No obvious difference between groups.

. No obvious changes in dermis.

. No obvious difference between groups.

NP: In the next few pages examples of the the histopathologic appearance of the skin after laser resurfacing with CO2, CO2/Er:YAG, And Er:YAG lasers as follows:

1,2- CO2 laser, 6 hours post laser test patch: Evidence of focal residuals of epidermis, and hair follicle involvement, and inflammation in the dermis.

3-Er/CO2 laser, 6 hours post laser test patch: Clear evidence of total loss of epidermis in addition to superficial dermal damage.

4-Er/CO2 laser, 6 hours post laser test patch: some focal residuals of epidermis.

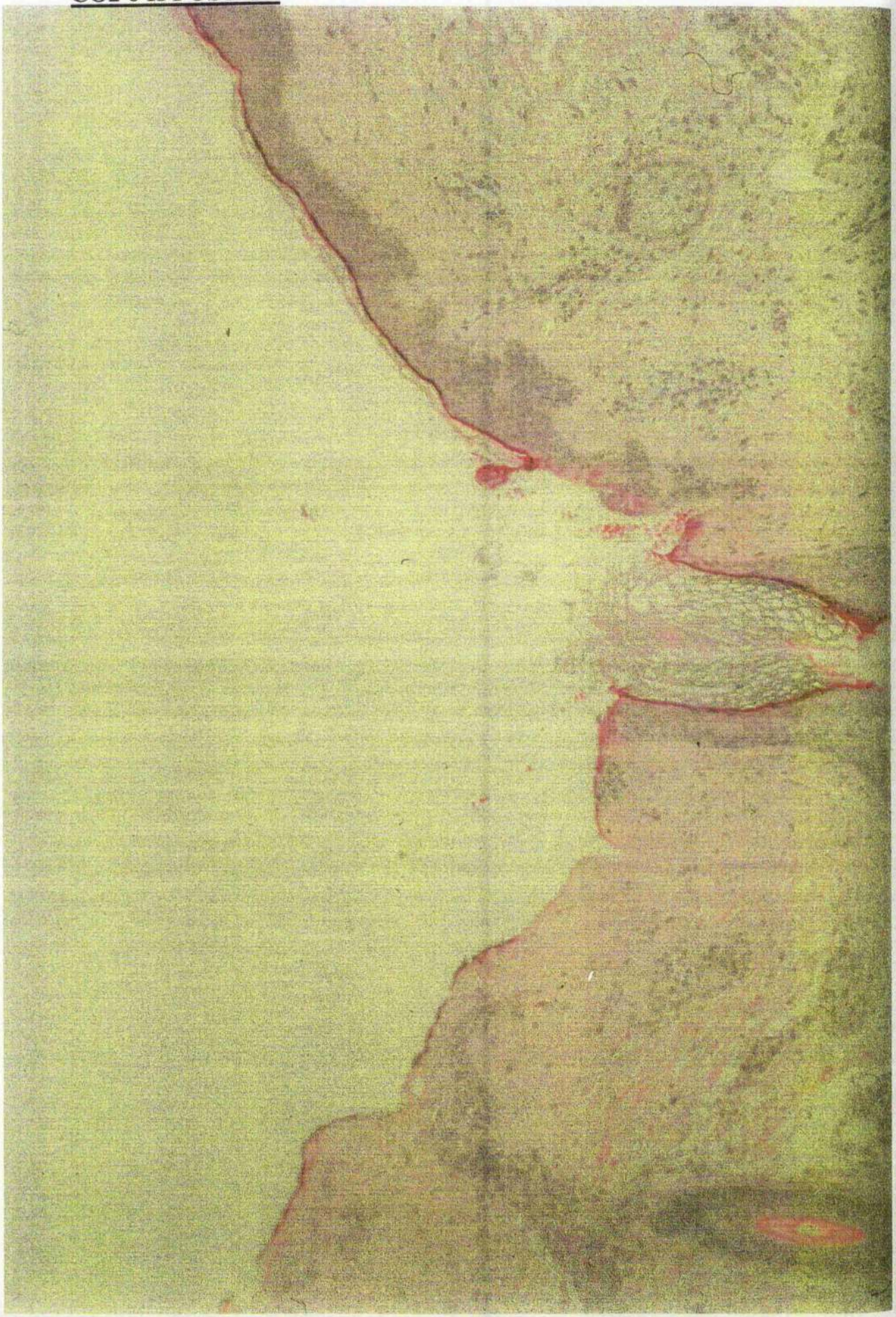
5,6- Er:YAG laser, 6 hours post laser test patch: Complete loss of the epidermis and deeper damage to the dermis.

7- CO2 laser, 6 months post laser treatment: Normal dermis with no obvious changes, some flattening in the epithelium and complexity of branching of the rete pegs (Variable).

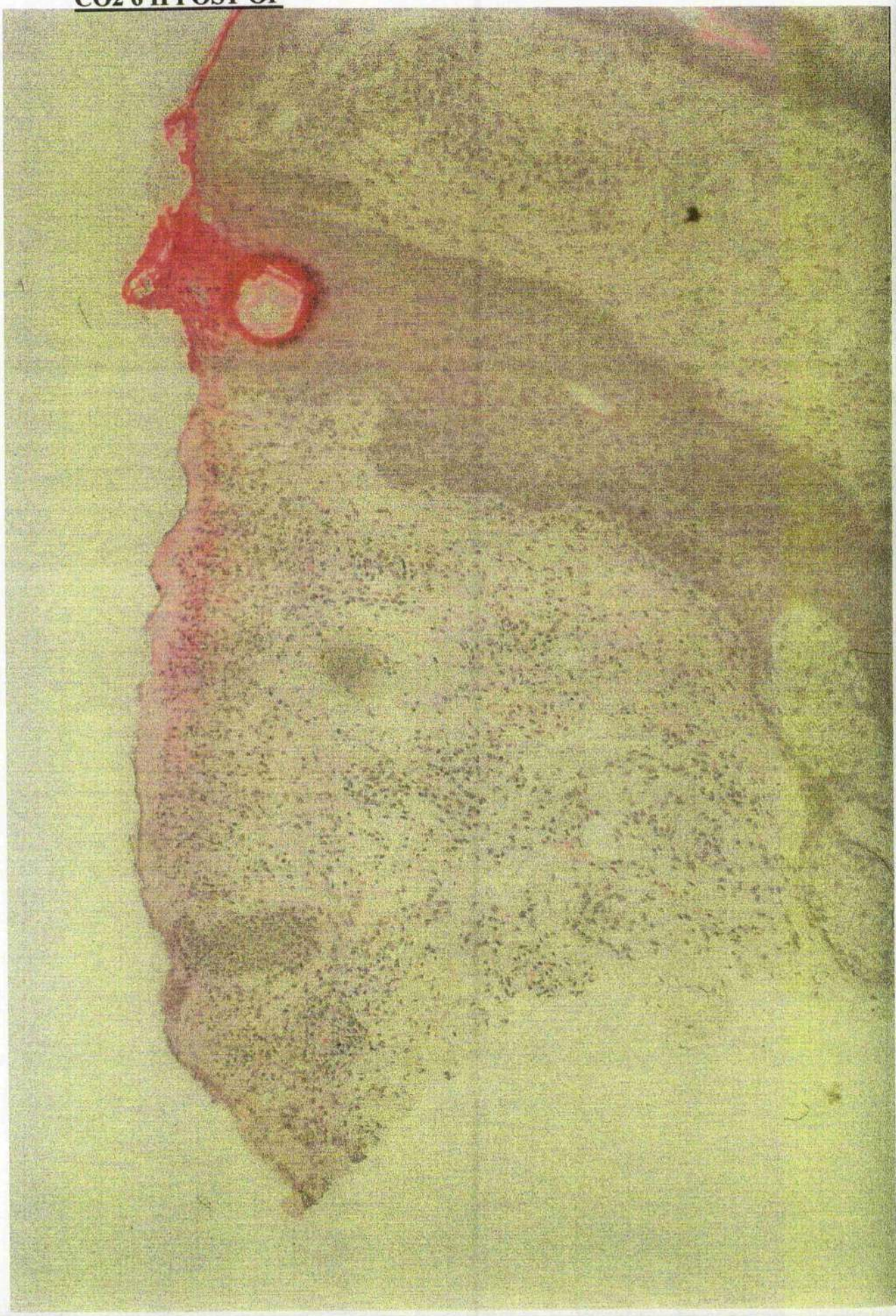
8- Er/CO2 laser, 6 months post laser treatment: Normal dermis, deep complexity of branching of the rete pegs (Complex).

9- Er:YAG laser, 6 months post laser treatment: Normal dermis, flattening in the epithelium (Flattened).

CO2 6 H POST OP



CO2 6 H POST OP

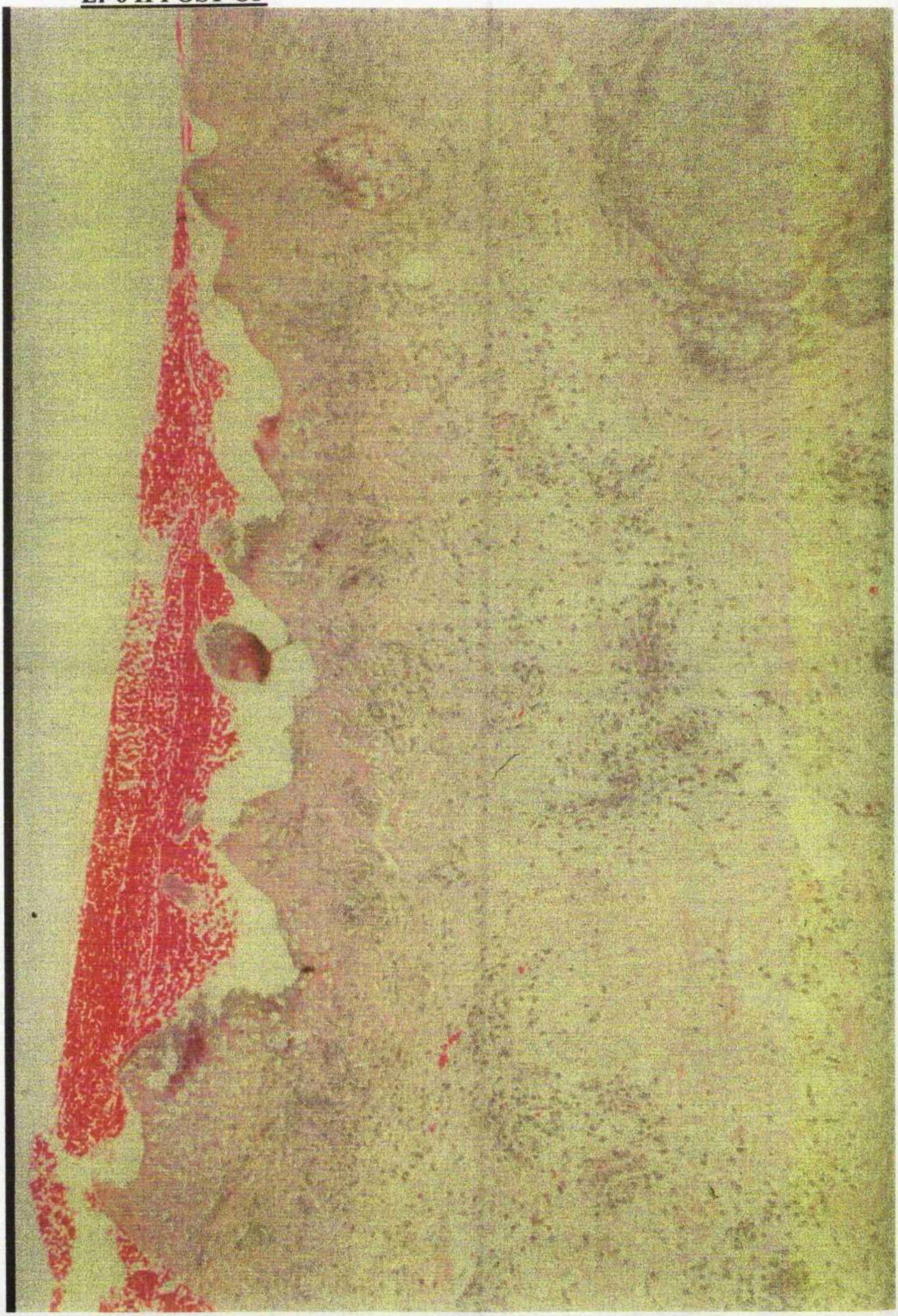


CO2/Er 6 H POST OP

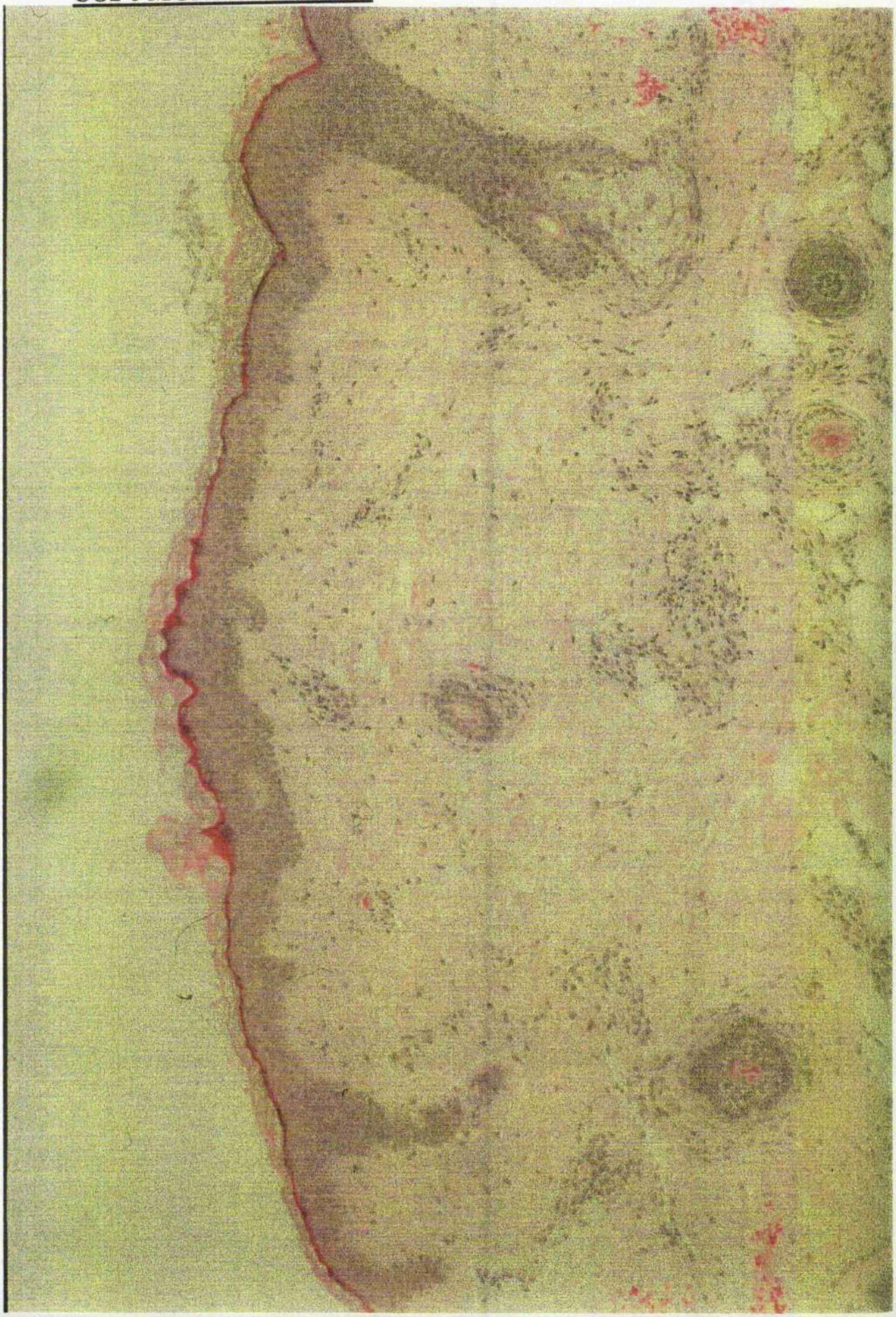
CO2/Er 6 H POST OP

Er 6 H POST OP

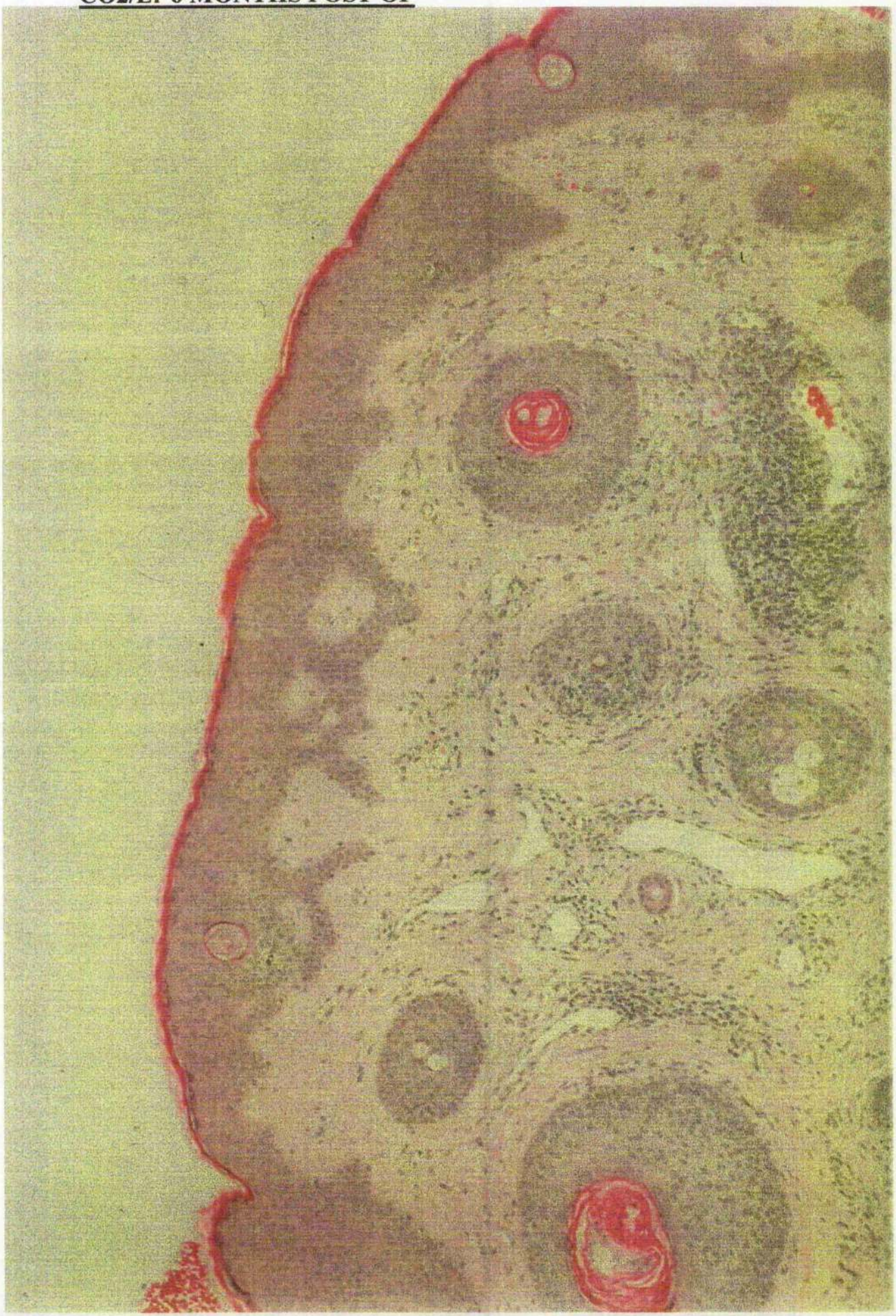
Er 6 H POST OP



CO2 6 MONTHS POST OP



CO2/Er 6 MONTHS POST OP



Er 6 MONTHS POST OP

APPENDIX C

- Data of laser resurfacing in pigmented skin lesion (PSL).
- Analyses to the of laser skin resurfacing in PSL

D.O.B	DIGNOSES	SITE	BX	NO/RX	RESULT	COMPLICATIONS	DEPTH
29/08/60	A.KERATOSIS	TEMPLE	ACTINIC KERATOSIS	1	GONE	NIL	EPIDERMIS
18/07/48	A.KERATOSIS	CHEEK	ACTINIC KERATOSIS	1	GONE	NIL	EPIDERMIS
19/08/69	A.KERATOSIS	CHEEK	ACTINIC KERATOSIS	1	GONE	NIL	EPIDERMIS
20/11/79	NAEVUS	CHEEK	ANGIOKERATOMA	2	GOOD	NIL	SUPERF. DERMIS
13/08/83	NAEVUS	CHEEK	ATROPHODERMA VERMICULATUM	3	MODERATE	NIL	DERMIS
05/07/89	NAEVUS	NECK	B.FIBROEPITHELIAL POLYP	1	GONE	NIL	EPIDERMIS
13/11/87	NAEVUS	CHEEK	BECKER'S NAEVUS	1	POOR	NIL	DEEP. DERMIS
12/11/79	NAEVUS	ARM	CONG COMP NAEVUS	1	MODERATE	NIL	MID DERMIS
01/09/79	NAEVUS	BACK	CONG COMP NAEVUS	1	GOOD	NIL	SUPERF. DERMIS
05/12/93	NAEVUS	BACK	CONG COMP NAEVUS	1	GOOD	NIL	DERMIS
04/03/89	NAEVUS	ABDOMEN	CONG COMP NAEVUS	1	GOOD	NIL	SUPERF. DERMIS
30/03/93	NAEVUS	LEG	CONG COMP NAEVUS	1	GOOD	NIL	SUPERF. DERMIS
28/05/88	NAEVUS	LEG	CONG INTRADERMAL N	1	MODERATE	NIL	DERMIS
11/06/97	NAEVUS	LIP	CONG INTRADERMAL N	1	GOOD	NIL	SUPERF. DERMIS
28/04/97	NAEVUS	CHEEK	CONG INTRADERMAL N	1	MODERATE	NIL	MID DERMIS
22/04/93	NAEVUS	TRUNK	CONG INTRADERMAL N	2	MODERATE	NIL	MID DERMIS
02/06/95	NAEVUS	LIP	CONG INTRADERMAL N	2	GOOD	NIL	SUPERF. DERMIS
01/08/82	NAEVUS	LEG	CONG INTRADERMAL N	1	MODERATE	NIL	DERMIS
18/04/78	NAEVUS	ARM	CONG INTRADERMAL N	2	MODERATE	NIL	DERMIS
09/10/91	NAEVUS	EYELIDS	CONG INTRADERMAL N	1	GOOD	NIL	SUPERF. DERMIS
24/01/95	NAEVUS	CHEEK	CONG INTRADERMAL N	2	GOOD	NIL	SUPERF. DERMIS
02/07/86	NAEVUS	BACK	CONG INTRADERMAL N	3	MODERATE	NIL	MID DERMIS
29/12/85	NAEVUS	TRUNK	EPIDERMAL NAEVUS	2	MODERATE	NIL	EPIDERMIS
31/03/92	NAEVUS	TRUNK	EPIDERMAL NAEVUS	2	GOOD	NIL	EPIDERMIS
10/11/61	NAEVUS	LEG	EPIDERMAL NAEVUS	3	MODERATE	NIL	EPIDERMIS
27/06/86	SEB NAEVUS	AXILL FOLD	EPIDERMAL NAEVUS	1	MODERATE	NIL	EPIDERMIS
07/01/86	NAEVUS	TRUNK	EPIDERMAL NAEVUS	3	GOOD	RECURRENCE	EPIDERMIS
16/09/87	NAEVUS	CHEST	EPIDERMAL NAEVUS	1	GOOD	NIL	EPIDERMIS
23/07/33	NAEVUS	FOREHEAD	EPIDERMAL NAEVUS	2	GOOD	RECURRENCE	EPIDERMIS
27/09/85	NAEVUS	CHEEKS	EPIDERMAL NAEVUS	5	GOOD	NIL	EPIDERMIS
13/12/85	NAEVUS	TRUNK	EPIDERMAL NAEVUS	5	GOOD	SOME SCARRING	EPIDERMIS
24/04/76	NAEVUS	NECK	EPIDERMAL NAEVUS	1	GOOD	RECURRENCE	EPIDERMIS
	L.MALIGNA	NOSE	L.MALIGNA	1	GONE	NIL	EPIDERMIS
26/09/19	L.MALIGNA	CHEEK	L.MALIGNA	2	GONE	RECURRENCE	EPIDERMIS
26/09/29	L.MALIGNA	HAND	L.MALIGNA	2	GONE	NIL	EPIDERMIS

04/09/66	L.MALIGNA	NOSE	L.MALIGNA	1 GONE	NIL	EPIDERMIS
10/02/40	L.MALIGNA	EAR	L.MALIGNA	1 GONE	NIL	EPIDERMIS
12/05/62	NAEVUS	ARM	NO	2 MODERATE	NIL	
23/08/87	NAEVUS	EAR	NO	1 MODERATE	NIL	
28/05/24	B.SOLAR KERATOSIS	NOSE	NO	1 GONE	NIL	
03/01/60	B.SOLAR KERATOSIS	NOSE	NO	1 GONE	NIL	
27/03/36	B.SOLAR KERATOSIS	CHEEK	NO	1 GONE	NIL	
17/10/84	NAEVUS	CHEEK	NO	2 POOR	NIL	
20/11/79	NAEVUS	EYELIDS	NO	2 MODERATE	NIL	
23/08/22	B.SOLAR KERATOSIS	TEMPLE	NO	2 GONE	NIL	
21/03/71	ORGANOID NAEVUS	TEMPLE	ORGANOID NAEVUS	2 GOOD	NIL	SUPERF. DERMIS

COMMENTS

RECURRENCE
SHAVED+CO2

SORE, PT NOT KEEN FOR RX

DEEP,

BETTER ON THE PEREPHERAL
DEEP

DEEP
DEEP

H/O CURRETAGE

RECURRENCE

RECURRENCE

SCARRING
RECURRENCE

RECURRENCE

CONG. PIGM.N
CONG. PIGM.N

CONG. PIGM.N
CONG. PIGM.N

DATA ANALYSES OF PSL'S RESULTS FOLLOWING LASER ABLATION.

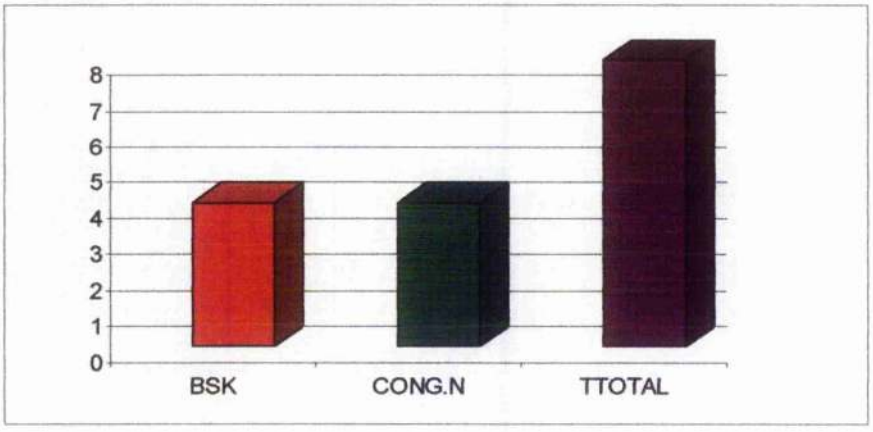
DIAGNOSIS OF PSL /TREATED WITH LASER ABLATION

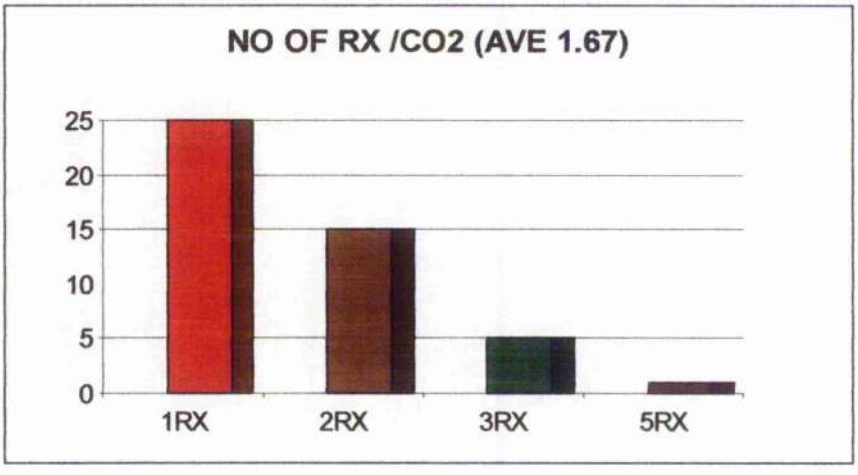
Cong. Pig. n	Epid. n	Lentigo. M	Actinic. K	Others	Total
19	10	5	7	5	46

OTHERS:

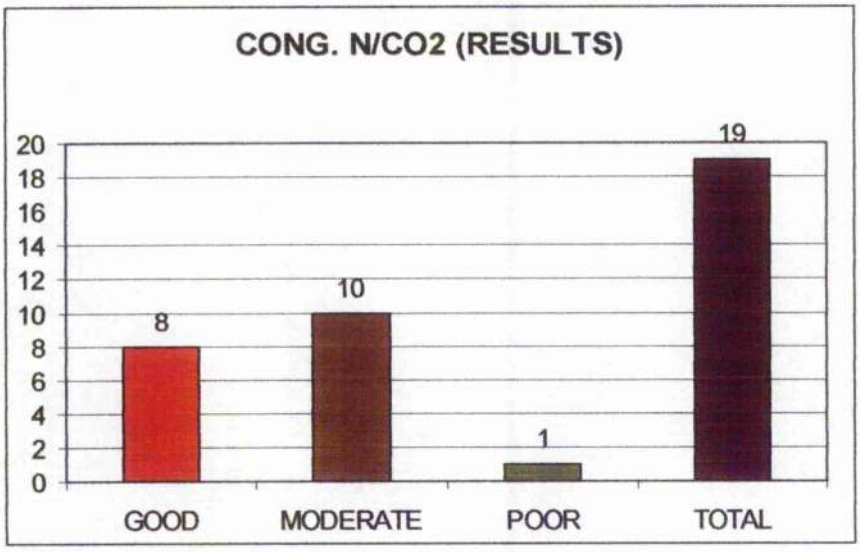
Becker's n	Organoid n	Ben. Fib. Epith. Polyp	Angio-keratoma	Atrophoderma vermiculatum
1	1	1	1	1

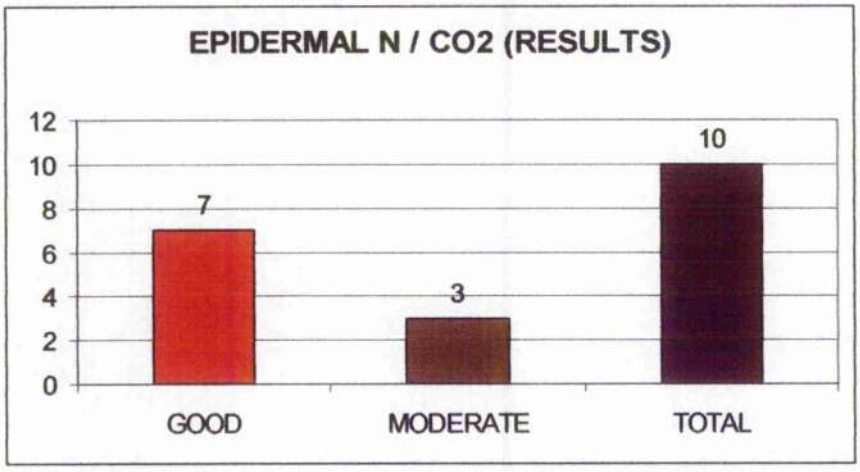
PT'S WITH NO BX/CO2

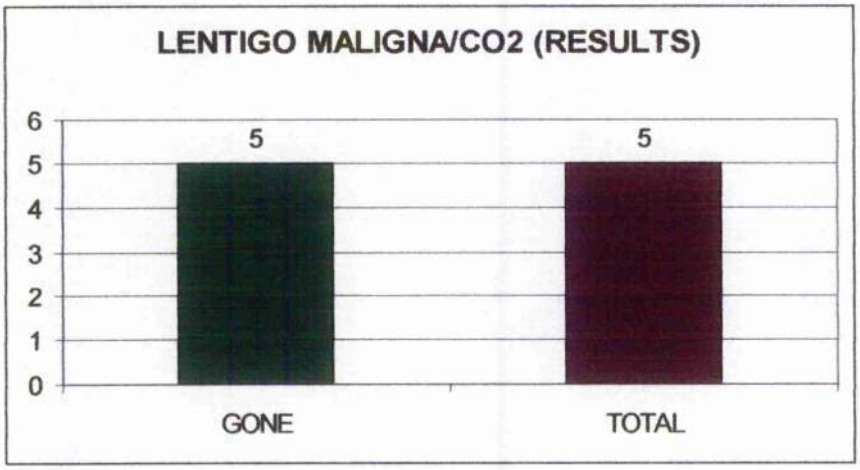


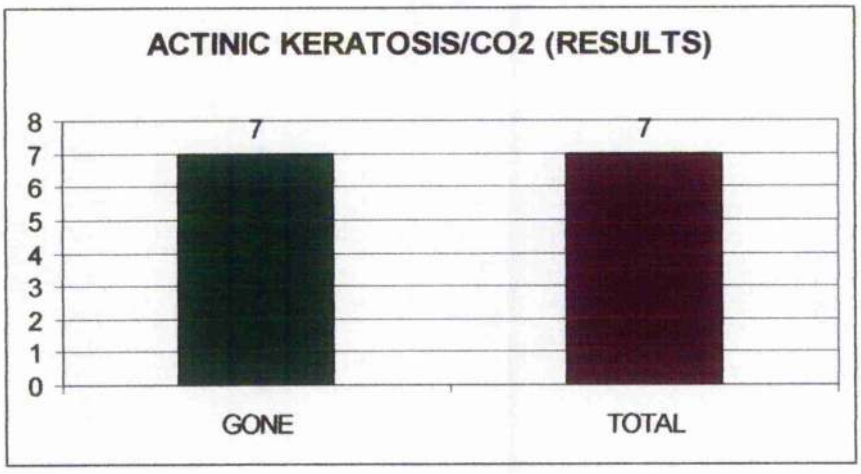


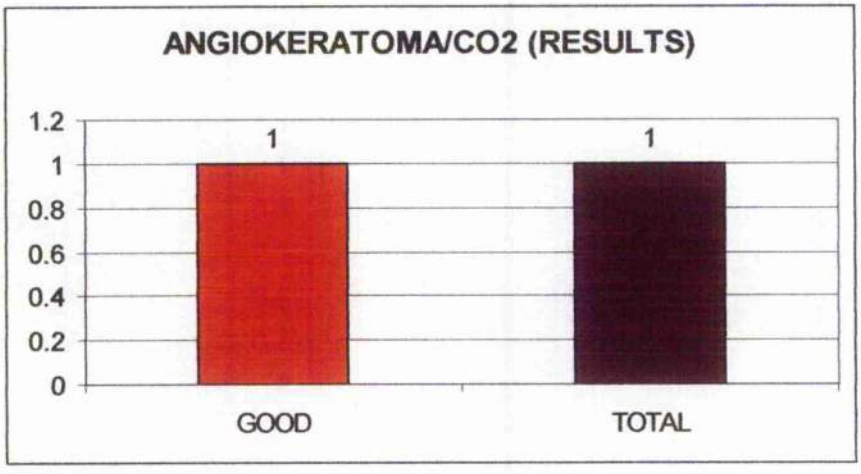
RESULTS OF LASER ABLATION OF PSL:

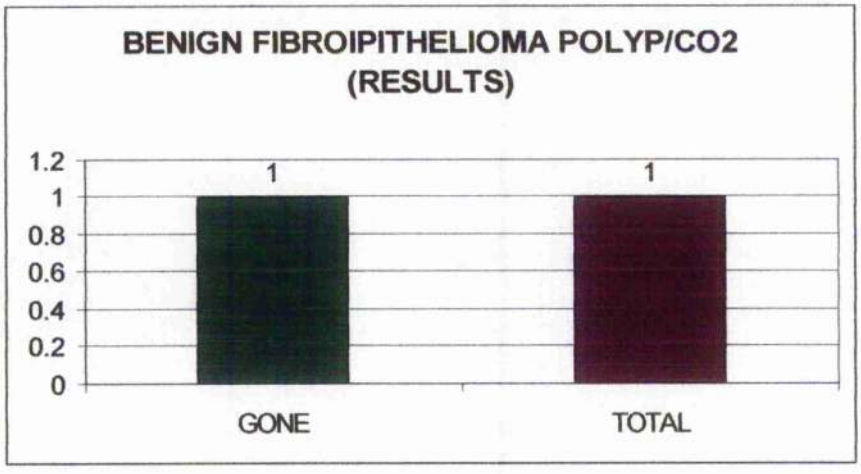


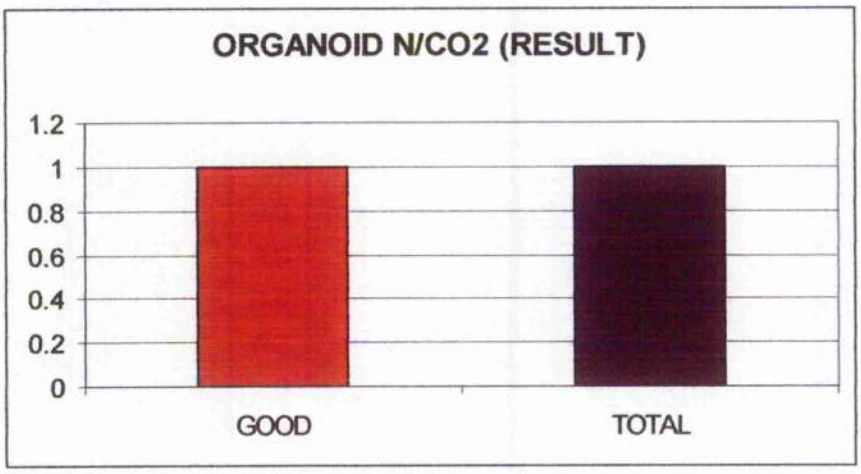


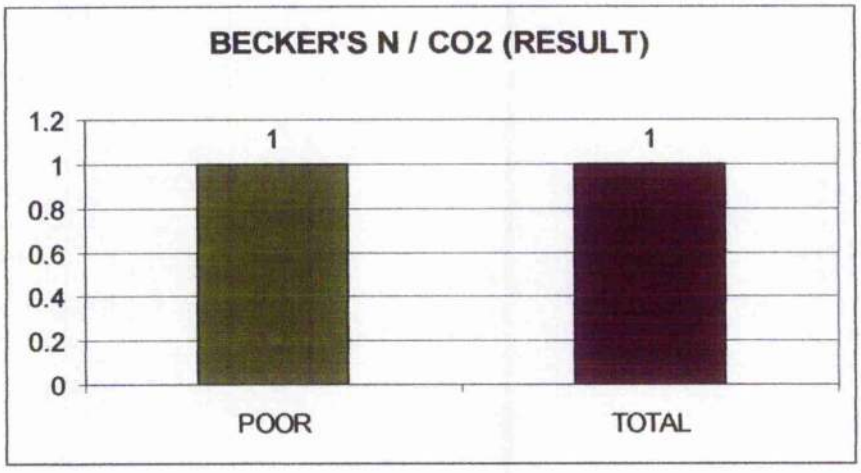


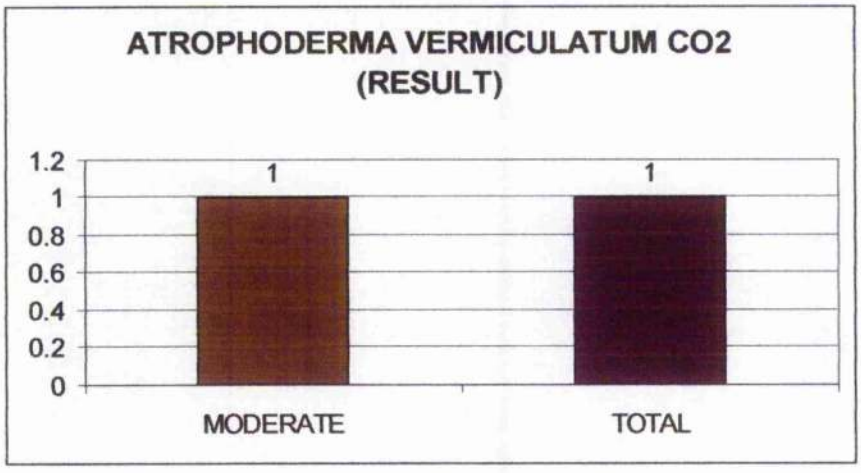

ACTINIC KERATOSIS/CO2 (RESULTS)
8
7
6
5
4
3
2
1
0
7
7
GONE
TOTAL


ANGIOKERATOMA/CO2 (RESULTS)
1.2
1
0.8
0.6
0.4
0.2
0
1
1
GOOD
TOTAL


BENIGN FIBROIPITHELIOMA POLYP/CO2 (RESULTS)
1.2
1
0.8
0.6
0.4
0.2
0
1
1
GONE
TOTAL


ORGANOID N/CO2 (RESULT)
1.2
1
0.8
0.6
0.4
0.2
0
GOOD
TOTAL

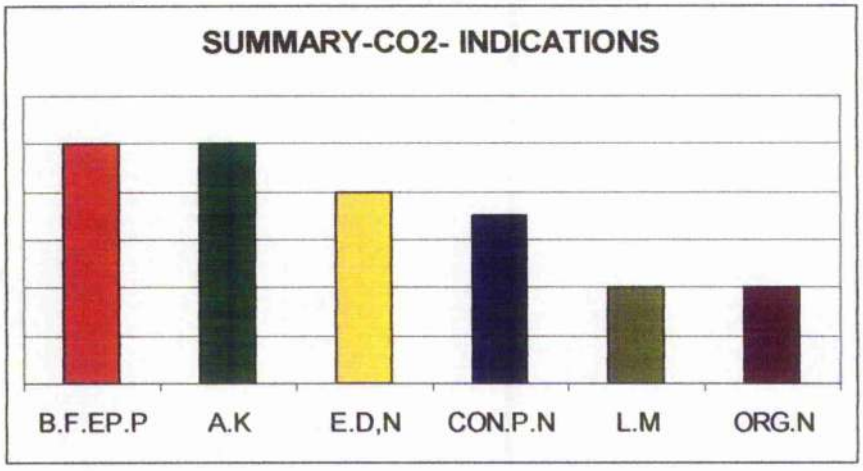

BECKER'S N / CO2 (RESULT)
1.2
1
0.8
0.6
0.4
0.2
0
1
1
POOR
TOTAL


ATROPHODERMA VERMICULATUM CO2 (RESULT)
1.2
1
0.8
0.6
0.4
0.2
0
1
1
MODERATE
TOTAL

COMPLICATIONS OF LASER ABLATION IN PSL

RECURRENCE: Epidermal N 3
L. Maligna 1

SCARRING: Epidermal N 1



APPENDIX D

- Data of laser skin resurfacing in benign superficial tumours and other rare skin condition.

DIGNOSES	SITE	BX	NO/RX	RESULT	ANAESTESIA	DEPTH	COMPLICATIONS
DARRIER'S DISEASE	CHEEK	DARRIER'S DISEASE	2	GOOD	GA		NIL
GRANULOMA ANNULARE	HAND	GRANULMA ANNULARE	1	GOOD	LA	DERMIS	NIL
POROKERATOSIS	ARM	POROKERATOSES	1	GOOD	LA	EPIDERMIS	NIL
POROKERATOSIS	LEG	POROKERATOSES	1	GONE	LA	EPIDERMIS	INFECTION, HYPERPIGMENTATION
SYRINGOMATA	CHEEK	SYRINGOMA	1	GOOD	LA	DERMIS	NIL
SYRINGOMATA	CHEEK	SYRINGOMA	1	GOOD	GA	DERMIS	NIL
TUBERO SCLEROSIS	CHEEK	TUBERO SCLEROSIS	1	GOOD	GA	DERMIS	NIL
TUBERO SCLEROSIS	CHEEK	TUBERO SCLEROSIS	2	GOOD	GA	DERMIS	NIL
XANTHALASMA	EYELIDS	NO	2	GONE	LA		NIL
XANTHALASMA	EYELIDS	NO	1	GONE	GA		NIL
XANTHALASMA	EYELIDS	NO	1	GONE	LA		NIL