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Transungual penetration of fractional CO_2 laser: A histopathological evaluation

Sir,

Lasers are one of the most promising device-based adjunctive therapies for onychomycosis.[1] Despite many lasers being used, there is a lack of clarity regarding their mechanism of action or expected outcomes, especially regarding their extent of penetration in the nail plate, or optimum energy to be used. Ablative lasers work by increasing permeability of an otherwise impervious nail plate to topical drugs.[2] However, the extent of penetration is unclear. Regarding their clinical efficacy, there are mostly uncontrolled data.[2] As of now, lasers are approved for 'cosmetic improvement in affected nails', whereas, for cure, more rigorous trials are required, aided by microscopically visualising laser effects on the nail plate.

We attempted histopathological correlation of energy delivered and the depth of penetration achieved in toenail specimens obtained from patients operated for ingrown nail. We used a 40 watts fractional carbon dioxide (CO_2) laser, (REX CO_2 Model from AMI Laser Company), to assess the microscopic effects of fractional CO_2 laser on the nail plate. Nails, with a water content of 15–18%, should ideally respond to the wavelength of fractional CO_2 laser (10,600 nm). Fresh slivers of lateral nail plate removed during ingrown nail surgery were cleaned of surrounding tissue and irradiated with two passes of one of the four energy levels (50 mJ, 100 mJ, 150 mJ or 200 mJ) [Figures 1a and 1b]. Only one energy was delivered on one nail sliver. Two passes were given to increase the depth

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of penetration without causing damage to the surrounding nail tissue. A spot size of 2 x 2 millimeters, pulse duration of 2–10 milliseconds, pulse interval in the range of 100–300 milliseconds and ultra-pulse beam were used. A small spot size was used keeping in mind the curvature of the nail plate and the width of the slivered nail plates. The lased specimens were then formalin fixed, softened and sectioned vertically and horizontally followed by staining with hematoxylin and eosin.

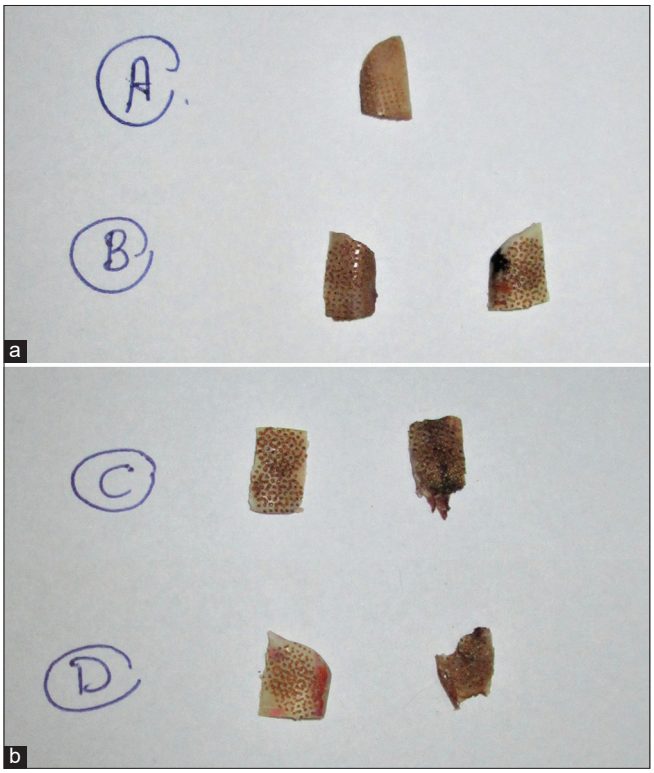

Figure 1a and b: Ingrown nail slivers removed from patients undergoing surgery were lased with different levels of energy using 40 watts fractional carbon dioxide laser

It was observed that the laser beam created uniformly sized and shaped fenestrations representing microthermal zones (MTZ) in the nail plate, ranging in diameter from 200 to 400 microns [Figures 2a and 2b]. The depth of penetration increased with the energy delivered (150–450 microns), although these could not be reliably correlated because of inadvertent oblique sectioning in some specimens. These fenestrations were lined by charred onychocytes [Figures 3a and 3b].

The ventral nail plate and subungual keratin are mostly infected by fungi and most topical drugs show a little diffusion till here. Drug concentration may reduce up to 1000 times preventing attainment of minimum inhibitory concentration. Fractional CO_2 laser creates microthermal zones that enhance penetration of topical agents into nail bed and matrix. Our work provides objective evidence for the same. A recent study bolstered the argument that nail fenestration improves drug delivery 3-4 fold after 42 days and should be used as pre-treatment for onychomycosis.[3] Fractional CO_2 laser offers a simple means to achieve this as visualised in our study. Fractional CO_2 laser alone versus a combination with topical antifungals has improved response rate from 50% to 71% indicating that besides the proposed fungicidal effect of laser, its role in increasing penetration of topical drugs is also at work.[1]

Neev *et al*. had evaluated four ablative lasers (solid-state erbium: yttrium-aluminium garnet (Er:YAG) [2.94 mm, 250

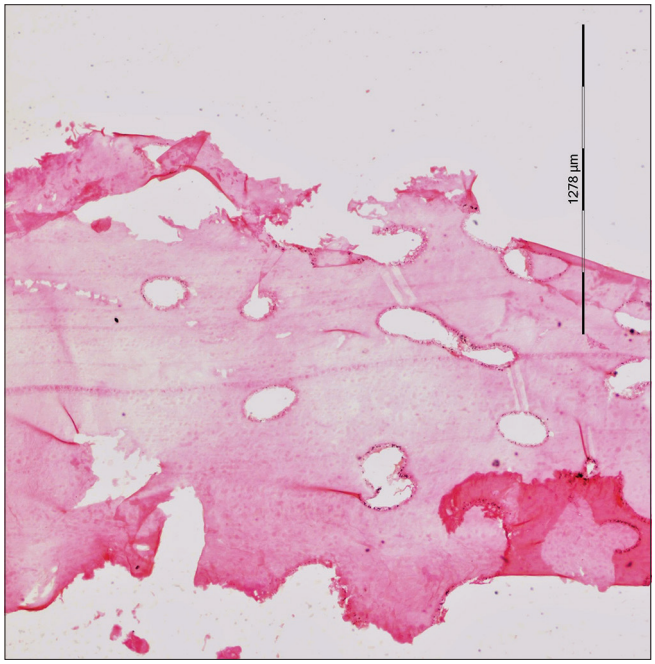

Figure 2a: Horizontal sectioning of the samples lased at 50 mJ showing fenestrations produced reflecting the microthermal zones of the laser beam (hematoxylin and eosin, ×400). The fenestrations are lined by a zone of necrosis

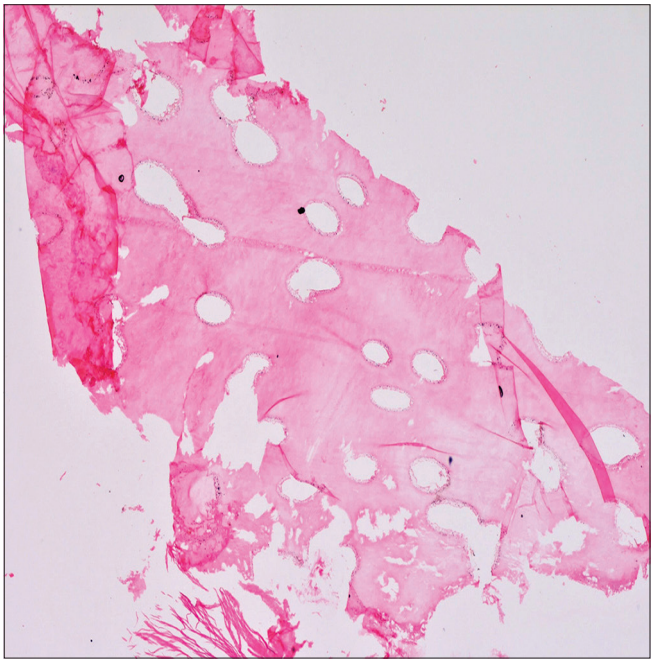

Figure 2b: Horizontal sectioning of the samples lased at 150 mJ showing fenestrations produced reflecting the microthermal zones of the laser beam (hematoxylin and eosin, ×400). The fenestrations are lined by a zone of necrosis

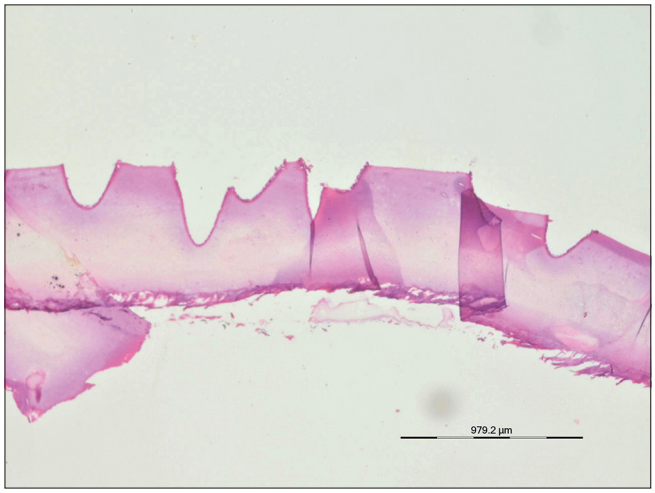

Figure 3a: Vertical section of a sample lased at 100 mJ showing craters reflecting the microthermal zones of the laser beam (hematoxylin and eosin, ×400)

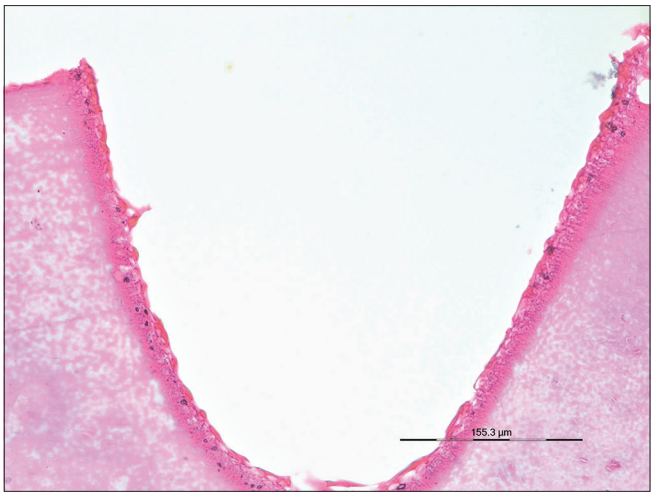

Figure 3b: Vertical section of a sample lased at 100 mJ showing craters reflecting the microthermal zones of the laser beam (hematoxylin and eosin, ×400)

ms], a holmium: yttrium-scandium-gallium garnet (Ho:YSGG) [2.08 mm, 250 ms], a xenon monochloride (XeCl) excimer [308 nm, 15 ns] and a solid-state ultrashort pulse laser [1.05 mm, 350 fs]),[4] comparing their 'ablation rates' by measuring the number of pulses needed to produce a complete perforation of the cadaver nail plate.[4] In our series, we used fresh specimens from patients with ingrown nail. We also kept the number of passes uniform, while varying the energies used. The aim was not to perforate the nail plate visibly (which will be painful *in vivo*), but to estimate the depth of penetration and histological effects produced. Neev *et al*. reported best ablation efficiency with ultrashort pulsed laser (1 mm/mJ) with minimal cracks, whereas Er:YAG laser (80 mm/pulse) achieved maximum material removal per pulse. Cracking damage was appreciated to a higher extent with both Ho:YSGG and Er:YAG. For XeC1, however, evaluation was done with a scanning electron microscope. We used light microscopy which demonstrated thermal damage confined to the areas surrounding microthermal zones, reflecting the vastly improved laser systems of today. There were no areas of cracking or denaturation except for the walls of the craters. The 2940 nm Er:YAG laser for *in vivo* fractional ablation to increase topical amorolfine lacquer delivery has also been reported to increase nail plate free of disease with negligible collateral damage.[5]

To conclude, our study provides objective evidence of fractional CO_2 laser penetration through nail plate with deeper fenestrations seen with higher energies. Thus, use of lower energies could help avoid nail bed damage. Even though higher energies could destroy fungus by thermal effect, this would require histopathological studies involving infected nails. Augmented drug penetration may be of use not only in onychomycosis but also in other conditions with thickened nails. These *in vitro* results can be useful for planning *in vivo* trials focussing on patient comfort and protection of underlying nail bed.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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