

## Combination of Fractional CO<sub>2</sub> Laser and Imiquimod in Pigmented Basal Cell Carcinoma: Preliminary Clinical Observations

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### Introduction

Basal cell carcinoma (BCC) is the most common cutaneous malignancy, with rising incidence rates. Typically presenting as a solitary or multiple lesions, surgical excision remains the gold standard treatment; however, non-surgical options are gaining traction, particularly for patients unable or unwilling to undergo surgery. Systemic immunotherapy, reserved for advanced BCC, often has limited use due to significant side effects. Among non-surgical treatments, imiquimod, a topical immunotherapeutic agent approved for superficial BCC, has demonstrated efficacy. Acting as an agonist of toll-like receptors 7 and 8, imiquimod stimulates innate immune cells, promoting adaptive immune responses through cytokine and chemokine production [1]. Physical

modalities like cryotherapy are also approved for superficial BCC, but the use of conventional CO<sub>2</sub> lasers has been studied less, with few reports. Over the past decade, fractional CO<sub>2</sub> laser therapy has emerged as a novel technique to enhance topical drug absorption through laser-assisted drug delivery (LADD). This combination approach is particularly useful for deeper subtypes, such as pigmented and nodular BCC, where imiquimod's dermal penetration is insufficient. Beyond its facilitative role, laser therapy itself has demonstrated immunomodulatory properties, including local immune activation, tumor mass reduction, and the induction of resistance to tumor reinoculation [2]. Despite these advances, non-surgical therapies yield lower complete response rates than surgery, necessitating rigorous post-treatment monitoring. Dermoscopy is widely used for follow-up but

may present limitations, such as overlapping features with other lesions, and the presence of features like fine telangiectatic vessels or whitish areas may not definitively indicate tumor persistence [3]. Reflectance confocal microscopy (RCM), offering superior sensitivity and specificity, is more effective for detecting tumor persistence and recurrence in BCC and other non-melanoma skin cancers (NMSC) [4,5].

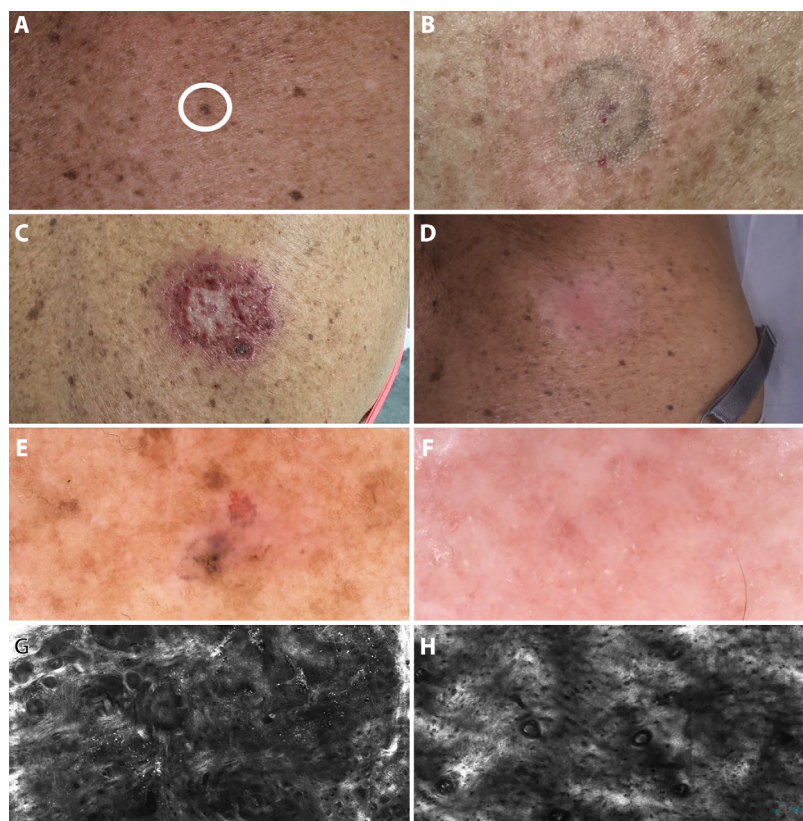
## Case Presentation

We report the case of an 83-year-old female with a pigmented lesion on her left back diagnosed as pigmented BCC (pBCC) via dermoscopy and RCM. The patient refused surgery due to cosmetic concerns and accepted an off-label combination of fractional CO<sub>2</sub> laser and imiquimod cream. Dermoscopy revealed structureless gray-blue areas, arborizing vessels, and gray nests, while RCM identified basaloid islands in the deep dermis, peripheral clefting, palisading of nuclei, bright dendritic cells, and tortuous vessels (Figure 1).

Fractional CO<sub>2</sub> laser was performed biweekly to create epidermal channels, facilitating imiquimod penetration into the dermis where BCC nests were located. Imiquimod was applied five days weekly for six weeks. At the 8-week follow-up, RCM revealed no residual BCC feature, demonstrating collagen fiber remodeling and the absence of basaloid islands. Excellent cosmetic results were achieved, with no scarring or discoloration. Follow-ups at 12, 24 weeks, and one year confirmed sustained remission, with no evidence of recurrence on RCM.

## Conclusion

This case highlights the potential of laser immunotherapy as an effective, minimally invasive treatment for pBCC, offering robust clinical responses and excellent cosmetic outcomes [2]. Advanced imaging modalities like RCM are invaluable for monitoring, enabling early detection of recurrence. These findings underscore the need for further clinical



**Figure 1.** (A) Pigmented macular lesion on the right scapular region pre-treatment. (B) Right scapular area post-treatment with fractional CO<sub>2</sub> laser. (C) Local inflammatory reaction in the right scapular area after imiquimod cream application. (D) Complete lesion resolution with minimal dyspigmentation 12 weeks after initiating laser-immunotherapy. (E) Pre-treatment dermoscopy showing a structureless area with gray-blue nests and arborizing telangiectatic vessels, consistent with BCC. (F) Dermoscopy at 12-week follow-up showing absence of BCC features. (G) Pre-treatment confocal microscopy (RCM) showing basaloid islands with peripheral clefting, palisading of nuclei, bright dendritic cells, and tortuous vessels. (H) RCM at 12-week follow-up showing significant collagen remodeling and absence of basaloid island.

trials to validate combined non-surgical therapies for BCC and NMSC, paving the way for personalized treatments that prioritize both efficacy and patient quality of life.

**Ethical Approval:** The study was a retrospective evaluation conducted in accordance with the principles of the Declaration of Helsinki and the International Council for Harmonization and Good Clinical Practice guidelines. Written informed consent was obtained from the patient to publish this paper.

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