

SHORT REPORT **OPEN ACCESS**

Complete Remission of Superficial Basal Cell Carcinoma Using Automatic Patting System-Assisted Topical 5-Fluorouracil Therapy: Preliminary Clinical Evidence

Francesco D'Oria^{1,2}  | Giulio Foggi^{1,2}  | Francesco Piscazzi¹  | Marco Ardigo^{1,2} 

¹Dermatology Unit, IRCCS Humanitas Research Hospital, Rozzano, Lombardy, Italy | ²Department of Biomedical Sciences, Humanitas University, Pieve Emanuele, Lombardy, Italy

Correspondence: Francesco D'Oria (francesco.doria@humanitas.it)

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ABSTRACT

Background: Topical 5-fluorouracil (5-FU) is a validated non-invasive treatment for superficial basal cell carcinoma (sBCC), but its effectiveness may be limited by suboptimal skin penetration and local toxicity.

Objectives: To evaluate a galenic 5-FU formulation delivered with Automatic Patting System (APS)-assisted transdermal enhancement in patients with sBCC.

Methods: We conducted a prospective observational study including six patients with nine clinically, dermoscopically, and Line-Field Confocal Optical Coherence Tomography (LC-OCT)-diagnosed sBCCs. Lesions were treated once weekly for 4 to 7 weeks using APS protocols combining Skin Patting and iontophoresis, with treatment intensity adapted by anatomical site. The galenic preparation consisted of a liposomal 5-FU gel. Preclinical support came from ex vivo permeation studies on dermatomed pig ear skin mounted on Franz diffusion cells, assessing 5-FU permeation and retention after APS-assisted delivery.

Results: Treatment was well tolerated, with only mild expected procedural bleeding. Five of nine lesions achieved complete response, confirmed clinically and by LC-OCT when follow-up imaging was available, whereas four lesions showed partial response. Complete remission occurred 7 to 11 weeks after treatment initiation, with no recurrence observed during follow-up of up to 9 months in lesions achieving complete response. Ex vivo studies showed significantly greater 5-FU permeation with APS-assisted treatment than with passive application at 5 h, together with increased drug retention within the skin membrane and greater delivery with extended treatment protocols.

Limitations: The small sample size, absence of a control group, and relatively short follow-up limit the generalizability of these findings.

Conclusions: In this preliminary series, five of nine sBCCs achieved complete response following APS-assisted topical 5-FU, while four showed partial response. These findings are descriptive and require confirmation in larger controlled studies.

Francesco D'Oria and Giulio Foggi contributed equally to this work and share first authorship.

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1 | Introduction

Topical chemotherapy with 5-fluorouracil (5-FU) remains a validated non-invasive option for superficial basal cell carcinoma (sBCC) [1], yet its clinical utility is often limited by the difficulty of achieving sufficient transdermal penetration while preserving tolerability [2, 3]. In a large randomized controlled trial, conventional 5% 5-FU applied twice daily for 4 weeks achieved a tumor-free rate of 80.1% at 1 year [4], while the probability of tumor-free survival at 5 years was 70.0% [5]. This limitation is particularly relevant in frail or elderly patients, in subjects with multiple lesions, and in cosmetically sensitive areas, where prolonged inflammation, crusting, and erosive reactions may negatively affect adherence and compromise the practical advantages of a tissue-sparing approach. For this reason, strategies able to enhance local bioavailability of 5-FU without proportionally increasing toxicity are of considerable clinical interest, especially when treatment is intended to be repeated over several weeks in an outpatient setting. In standard regimens, moderate-to-severe local inflammatory reactions are reported in up to 15%–60% of patients, with approximately 5% discontinuing therapy due to adverse events, highlighting the need for delivery strategies capable of improving efficacy while substantially reducing treatment-related toxicity [4].

We report a small prospective observational experience involving six patients with a total of nine clinically-, dermoscopically- and Line-Field Confocal Optical Coherence Tomography (LC-OCT)-diagnosed sBCCs treated with a galenic 5-FU formulation delivered through Automatic Patting System (APS)-assisted transdermal enhancement. In this context, LC-OCT also provided a valuable non-invasive imaging support not only for baseline lesion characterization but also for treatment monitoring, allowing serial morphological assessment of tumor response in a manner coherent with the conservative nature of the protocol. All patients underwent one treatment session per week for 4 to 7 weeks, according to APS protocols combining skin patting and iontophoresis. Complete remission, confirmed clinically and by LC-OCT imaging where available [6, 7], was achieved in a subset of treated lesions following completion of the treatment course, while the remaining lesions showed a partial response. This small prospective observational series was designed to describe the clinical outcomes and tolerability observed with APS-assisted topical 5-FU in patients with sBCC.

2 | Materials and Methods

2.1 | APS Technology and Mechanism of Action

The APS relies on a patented Skin Patting technology, which integrates controlled micro-dermoincision and radial acoustic waves to enhance microcirculation, stimulate local metabolic activity, and promote transdermal delivery of active substances. According to the technical documentation of the device, these combined actions are intended to generate an immediate increase in local blood microcirculation and tissue oxygenation, together with a stimulation of cellular metabolism that may favor the uptake and distribution of topically applied compounds. The broader biological rationale is that a transiently activated and mechanically conditioned cutaneous environment may be more receptive to hydrophilic drugs that otherwise permeate poorly

through the intact stratum corneum. Micro-dermoincision is produced by a dual-cone system capable of generating micro-trauma limited to the epidermis, sparing the basal membrane; this induces fibroblast activation and facilitates penetration of topical drugs. More specifically, the handpiece is described as containing multiple protuberances with a dual-cone architecture: a lower cone places the skin under tension, while the upper cone penetrates within the epidermal layer and creates multiple controlled micro-injuries without disrupting deeper structures. This feature may provide a mechanistic explanation for enhanced penetration while limiting micro-injury to the epidermal layer. The associated acoustic wave stimulation has also been proposed to influence local vascular and metabolic activity and potentially contribute to transdermal drug delivery [3].

2.2 | Role of Iontophoresis in Drug Delivery

For drug delivery, iontophoresis enhances the passage of hydrophilic molecules such as 5-FU by transiently widening epidermal intercellular spaces [8–10]. Recent evidence supports its role in dermatologic drug delivery, including skin-directed oncologic and pre-oncologic applications [11]. Within APS, skin patting may create temporary micro-pathways, while iontophoresis complements this effect by favoring deeper and more homogeneous drug distribution (Figure 1).

2.3 | Treatment Protocol

In our protocol, treatment intensity was based on permeation-derived parameters: head-and-neck lesions were treated with skin patting and iontophoresis for 3 min each at 20% power, whereas trunk and extremity lesions were treated for 3 min each at 30% power. These settings were adapted according to anatomical site and differences in skin characteristics and treatment tolerability.

2.4 | Clinical, Dermoscopic, and LC-OCT Evaluation Schedule

Clinical response was assessed through a predefined follow-up schedule integrating clinical examination, dermoscopy, and non-invasive imaging, consistent with the role of these techniques in supporting dermatological decision-making and conservative management [12]. At baseline, each lesion underwent clinical examination, standardized photography, dermoscopy, and LC-OCT to support the diagnosis of superficial basal cell carcinoma and document pretreatment morphology.

Before each weekly APS-assisted 5-FU session, lesions were clinically reassessed, and local tolerability, expected bleeding, pain or discomfort, inflammatory reaction, and adverse events were recorded.

Dermoscopy was repeated during treatment and at post-treatment visits to assess persistence or disappearance of basal cell carcinoma-associated structures. LC-OCT was repeated when available, especially in clinically cleared or equivocal lesions, to evaluate residual basal cell carcinoma nests, mill-efeuille pattern, clefting, or other architectural criteria.

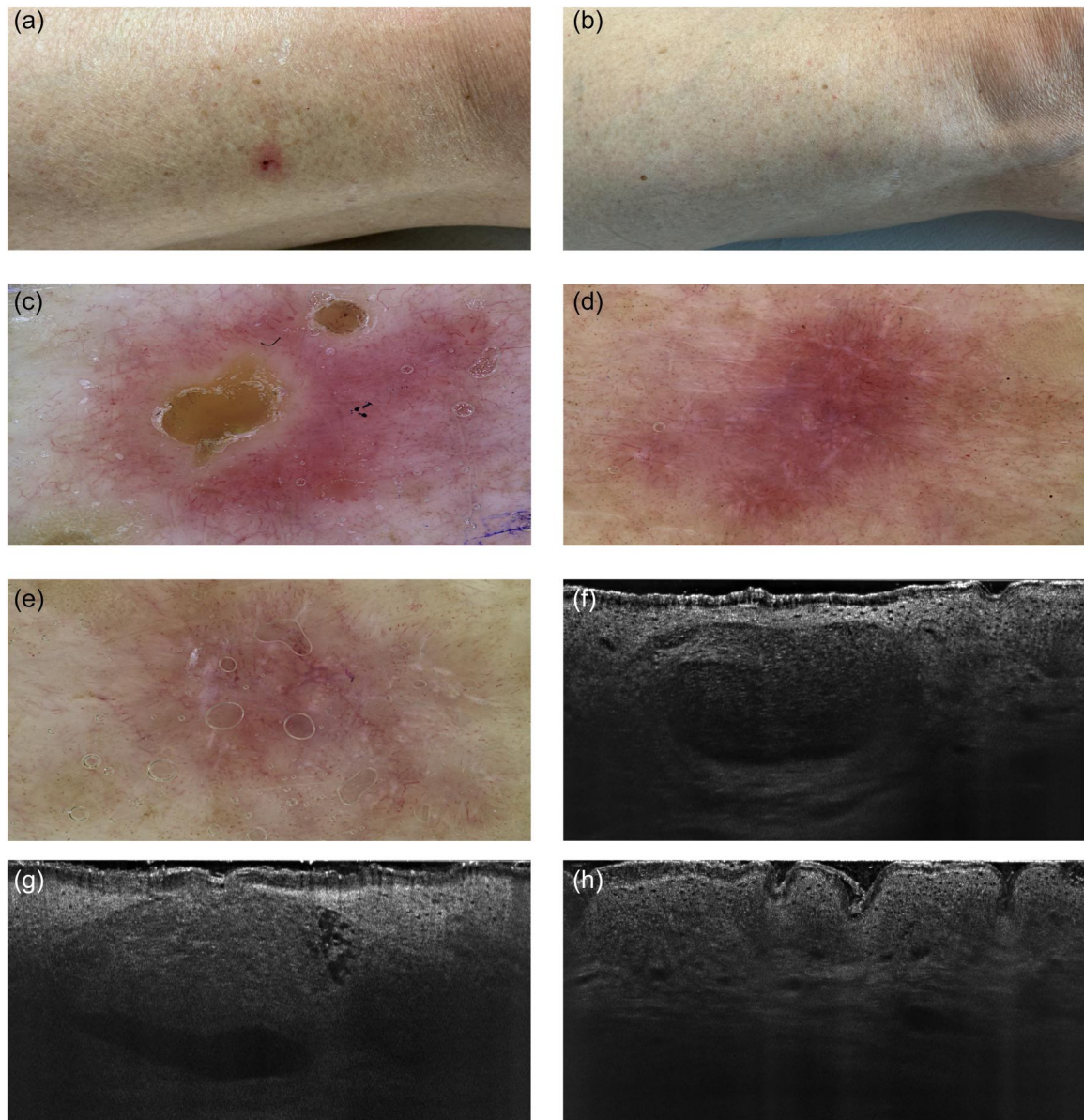


FIGURE 1 | Representative clinical, dermoscopic, and line-field confocal optical coherence tomography (LC-OCT) images of lesion 1 (L1) before, during, and after treatment with Automatic Patting System (APS)-delivered 5-fluorouracil (5-FU); (a) clinical image at the start of treatment: the lesion was located on the right lateral thigh of a 65-year-old male patient and was clinically suspicious for superficial basal cell carcinoma (sBCC), appearing as an erythematous macule with an area of erosion; (b) clinical image after 9 months from treatment initiation, showing complete clinical remission of the lesion, with only minimal residual erythema; (c) dermoscopic image at baseline, showing two areas of erosion on an erythematous background; (d) dermoscopic image at 4 weeks from the start of treatment, showing a pattern that, in our experience, recurred in almost all lesions treated with this methodic: hairpin vessels on an erythematous background and shiny white structures, in the form of lines and strands; (e) dermoscopic image at 7 weeks from the start of treatment, immediately before the last application, showing a reduction in lesion extent, with persistence of the pattern observed in panel (d); (f) LC-OCT vertical scan of a portion of the lesion at baseline, depicting a BCC nest with a classic millefeuille pattern in continuity with the epidermis and clefting visible in the deeper portion of the lobule, both features typical of sBCC; (g) LC-OCT vertical scan of a portion of the lesion at 1-week follow-up, showing a BCC nest (again identified by the millefeuille pattern), with an area of cell discohesion within the nest, plausibly caused by treatment and suggestive of initial tumoral cell necrosis; (h) LC-OCT vertical scan of a portion of the lesion at 7 weeks, immediately before the last 5-FU application, showing normal skin with only an increased number of vessels in the superficial dermis, consistent with the concomitant clinical picture of an erythematous lesion; this LC-OCT appearance was observed across the entire lesion, confirming BCC remission.

Post-treatment assessments were scheduled after treatment completion, approximately 6 to 12 weeks from treatment initiation, and then during routine dermatologic follow-up. The actual follow-up duration for each lesion is reported in Table 1.

Complete response was defined as the disappearance of the clinically and dermoscopically visible lesion, with the absence of residual basal cell carcinoma features on LC-OCT when available. Partial response was defined as improvement with residual clinical, dermoscopic, or LC-OCT findings, need for

TABLE 1 | Clinical characteristics, treatment details and outcomes of treated lesions.

Patient		Lesion site	Treatment modality	Number of sessions/weeks	Follow-up	Clinical outcome	Adverse events (AEs)
Lesion ID	(Sex, Age)						
P 1, L 1	M, 65	Right anterior lower leg	5-FU Delivery/week	6	9 m	CR—clinical remission at 7 weeks, LC-OCT confirmed; no recurrence at 9 m	No AEs
P 1, L 2	M, 65	Right anterior thigh	5-FU Delivery/week + topical 5-FU once a day for 1 month	7	9 m	CR—clinical remission at 11 weeks; stable at 9 m	No AEs
P 1, L 3	M, 65	Right lateral thigh	5-FU Delivery/week	6	9 m	CR—clinical remission at 7 weeks; LC-OCT confirmed remission; no recurrence at 9 m	No AEs
P 2, L 4	M, 83	Posterior helix of the left ear	5-FU Delivery/week	6	7 m	CR—clinical remission at 8 weeks; no recurrence at 9 m	Bleeding during treatment; no other AEs
P 2, L 5	M, 83	Left temporal scalp	5-FU Delivery/week	4	1 m	PR—lesion was still under treatment at the time of publication	No AEs
P 3, L 6	F, 79	Right forehead	5-FU Delivery/week	5	3 m	PR—persistence at 3 months, requiring initiation of topical imiquimod	No AEs
P 4, L 7	M, 62	Left upper anterior chest	5-FU Delivery/week	6	7 w	CR—clinical remission at 7 weeks; LC-OCT confirmed	No AEs
P 5, L 8	M, 80	Right upper anterior chest	5-FU Delivery/week (only patting, no iontophoresis)	6	6 w	PR—lesion improvement; patient is scheduled for reassessment at subsequent follow-up visits	Bleeding during treatment, no other AEs
P 6, L 9	F, 69	Presternal chest	5-FU Delivery/week	6	6 w	PR—lesion improvement; patient is scheduled for reassessment at subsequent follow-up visits	No AEs

Abbreviations: AEs, adverse events; CR, complete response; F, female; L, lesion; LC-OCT, line-field confocal optical coherence tomography; M, male; m, months; P, patient; PR, partial response; w, weeks; 5-FU, 5-fluorouracil.

additional therapy, or planned reassessment. Recurrence was defined as reappearance of clinically, dermoscopically, or LC-OCT-suspected basal cell carcinoma at a site previously classified as complete response.

2.5 | Galenic Formulation and Preclinical Permeation Evidence

The galenic preparation consisted of a liposomal 5-FU gel designed to enhance epidermal absorption and retention [13]. Preclinical permeation studies using dermatomed pig ear skin mounted on Franz diffusion cells showed that APS stimulation significantly increased 5-FU permeation compared with passive application. In these experiments, samples were collected over 5 h and analyzed by HPLC, with four replicates for each condition.

A 3-min skin patting phase followed by 3-min iontophoresis significantly increased permeated 5-FU at 5 h compared with passive application (mean difference: $325.4 \mu\text{g}/\text{cm}^2$, 95% CI 276.0–374.8; $p < 0.01$). Membrane-associated 5-FU increased from 11.65 ± 1.80 in the reference condition to 22.86 ± 3.47 after the 3 + 3-min protocol and to 28.45 ± 10.00 after the 4 + 4-min protocol, suggesting enhanced transmembrane flux and local reservoir formation. The combined sequence of skin patting followed by ionic stimulation was more effective than skin patting alone, supporting a synergistic interaction between the two treatment phases.

3 | Results

Nine LC-OCT-confirmed sBCCs were treated with weekly APS-assisted 5-FU sessions for 4 to 7 weeks. Therapies were well tolerated, with only mild, expected bleeding during the procedure. This procedural bleeding was limited and consistent with the superficial epidermal micro-trauma expected from the device mechanism, without evidence of major immediate complications or treatment-limiting intolerance. Overall, treatment resulted in a complete response in five lesions and a partial response in four lesions. Complete clinical remission was achieved between 7 and 11 weeks from treatment initiation and was confirmed by LC-OCT imaging in lesions with available follow-up scans. In lesions achieving complete response, no recurrences were observed during follow-up of up to 9 months. Partial responses were characterized either by persistent disease requiring additional therapy or by clinical improvement with lesions still under evaluation or scheduled for reassessment at subsequent follow-up visits. No severe inflammatory reactions or treatment discontinuations were observed in this small cohort [4].

4 | Discussion

In this preliminary case series, complete response was observed in five of nine treated sBCCs, while four lesions showed partial response. Ex vivo experiments showed increased 5-FU permeation following the combined APS protocol, while complete clinical response was observed in five of nine treated lesions. The ex vivo findings provide mechanistic information on drug

delivery under the experimental conditions tested: the liposomal vehicle may improve residence at the cutaneous surface, while skin patting and iontophoresis may facilitate the cutaneous delivery of 5-FU [13]. This interpretation is also consistent with recent systematic evidence highlighting iontophoresis as a versatile strategy for improving topical drug delivery in dermatology [11].

This study has several limitations. The small sample size (six patients, nine lesions) and the absence of a control group preclude any assessment of comparative efficacy vs. conventional 5-FU or other established treatments. Diagnosis and response assessment were based on clinical examination, dermoscopy, and LC-OCT without histopathological confirmation, and LC-OCT follow-up was not available for all lesions. Follow-up was relatively short and heterogeneous, limiting assessment of response durability and recurrence. Treatment duration and APS parameters varied according to lesion location, while the use of a liposomal galenic 5-FU formulation does not allow the relative contribution of the formulation and APS-assisted delivery to be distinguished. Finally, the ex vivo permeation experiments were performed on porcine skin and may not fully reproduce drug delivery in human sBCC in vivo.

Given these limitations, no clinical recommendation regarding APS-assisted 5-FU can be made at this stage.

5 | Conclusions

Larger controlled studies are warranted to define long-term efficacy, optimal treatment parameters, and comparative outcomes vs. standard therapies. Such studies should include standardized imaging follow-up, appropriate control groups, and longer observation periods to assess response durability, recurrence risk, and the contribution of APS-assisted delivery to the observed clinical outcomes.

Author Contributions

Francesco D'Oria: conceptualization, methodology, investigation, data curation, writing – original draft, writing – review and editing. **Giulio Foggi:** methodology, investigation, data curation, writing – original draft, writing – review and editing. **Francesco Piscazzi:** methodology, investigation, writing – review and editing. **Marco Ardigo:** conceptualization, supervision, writing – review and editing. All authors have read and approved the final version of the manuscript.

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The authors have nothing to report.

Ethical Approval

The study was conducted according to the ethical principles outlined in the Declaration of Helsinki (1975, last revised 2024) and in compliance with applicable privacy regulations, including Regulation (EU) 2016/679 (GDPR).

Patient Consent

The patients in this manuscript gave written informed consent for participation in the study and for the publication of their case details, including photographs and any other potentially identifying information.

Conflicts of Interest

M. Ardigò has received consulting fees from Pierre Fabre and has participated in lectures, presentations and advisory boards for Almirall, Kyowa Kirin, Pierre Fabre, Recordati Rare Diseases and Cantabria Labs. All other authors declare no conflicts of interest.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

References

1. C. Bichakjian, A. Armstrong, C. Baum, et al., "Guidelines of Care for the Management of Basal Cell Carcinoma," *Journal of the American Academy of Dermatology* 78 (2018): 540–559, <https://doi.org/10.1016/j.jaad.2017.10.006>.
2. I. A. Alvi, J. Madan, D. Kaushik, S. Sardana, R. S. Pandey, and A. Ali, "Comparative Study of Transfersomes, Liposomes, and Niosomes for Topical Delivery of 5-fluorouracil to Skin Cancer Cells: Preparation, Characterization, In-Vitro Release, and Cytotoxicity Analysis," *Anti-Cancer Drugs* 22 (2011): 774–782, <https://doi.org/10.1097/CAD.0b013e328346c7d6>.
3. Y. W. Naguib, A. Kumar, and Z. Cui, "The Effect of Microneedles on the Skin Permeability and Antitumor Activity of Topical 5-Fluorouracil," *Acta Pharmaceutica Sinica B* 4 (2014): 94–99, <https://doi.org/10.1016/j.apsb.2013.12.013>.
4. A. H. Arits, K. Mosterd, B. A. Essers, et al., "Photodynamic Therapy Versus Topical Imiquimod Versus Topical Fluorouracil for Treatment of Superficial Basal-Cell Carcinoma: A Single Blind, Non-Inferiority, Randomised Controlled Trial," *Lancet Oncology* 14 (2013): 647–654, [https://doi.org/10.1016/S1470-2045\(13\)70143-8](https://doi.org/10.1016/S1470-2045(13)70143-8).
5. M. H. E. Jansen, K. Mosterd, A. H. M. M. Arits, et al., "Five-Year Results of a Randomized Controlled Trial Comparing Effectiveness of Photodynamic Therapy, Topical Imiquimod, and Topical 5-Fluorouracil in Patients With Superficial Basal Cell Carcinoma," *Journal of Investigative Dermatology* 138 (2018): 527–533, <https://doi.org/10.1016/j.jid.2017.09.033>.
6. T. Wolswijk, F. Adan, P. J. Nelemans, A. Defauwes, and K. Mosterd, "Optical Coherence Tomography for Diagnosing Recurrent or Residual Basal Cell Carcinoma After Topical Treatment: A Diagnostic Cohort Study," *Journal of the American Academy of Dermatology* 89 (2023): 728–733, <https://doi.org/10.1016/j.jaad.2023.06.033>.
7. C. Gust, S. Schuh, J. Welzel, et al., "Line-Field Confocal Optical Coherence Tomography Increases the Diagnostic Accuracy and Confidence for Basal Cell Carcinoma in Equivocal Lesions: A Prospective Study," *Cancers* 14 (2022): 1082, <https://doi.org/10.3390/cancers14041082>.
8. J.-Y. Fang, C.-F. Hung, Y.-P. Fang, and T.-F. Chan, "Transdermal Iontophoresis of 5-Fluorouracil Combined With Electroporation and Laser Treatment," *International Journal of Pharmaceutics* 270 (2004): 241–249, <https://doi.org/10.1016/j.ijpharm.2003.10.025>.
9. I. P. Gross, A. L. Lima, L. L. Sá-Barreto, G. M. Gelfuso, and M. Cunha-Filho, "Recent Advances in Cutaneous Drug Delivery by Iontophoresis," *Expert Opinion on Drug Delivery* 22 (2025): 857–874, <https://doi.org/10.1080/17425247.2025.2490267>.
10. B. Priya, T. Rashmi, and M. Bozena, "Transdermal Iontophoresis," *Expert Opinion on Drug Delivery* 3 (2006): 127–138, <https://doi.org/10.1517/17425247.3.1.127>.
11. F. Piscazzi, F. D'Oria, M. A. Ramirez, and M. Ardigò, "Iontophoresis-Based Topical Drug Delivery for Dermatologic Conditions: A Systematic Review," *Pharmaceutics* 19 (2026): 765, <https://doi.org/10.3390/ph19050765>.
12. B. Bălăceanu-Gurău, M. Liberi, F. D'Oria, G. Foggi, G. Rezze, and M. Ardigò, "Value of Reflectance Confocal Microscopy in Guiding

Dermatological Decision-Making: Insights From Facial, Body and Oral Lesion Assessment," *Skin Health and Disease* 6 (2026): 343–345, <https://doi.org/10.1093/skinhd/vzag007>.

13. N. R. Khan and T. W. Wong, "5-Fluorouracil Ethosomes – Skin Deposition and Melanoma Permeation Synergism With Microwave," *Artificial Cells, Nanomedicine, and Biotechnology* 46 (2018): 568–577, <https://doi.org/10.1080/21691401.2018.1431650>.

Supporting Information

Additional supporting information can be found online in the Supporting Information section.

Supporting File: jvc270444-sup-0001-STROBE-checklist.doc.