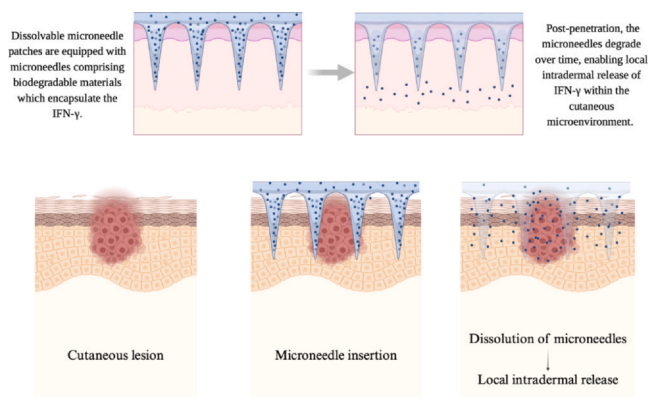


A-140

IFN- γ -Loaded Dissolvable Sugar Microneedles for Local Intradermal Delivery in Cutaneous Squamous Cell CarcinomaT. Akmandor^{1,2}, S. Outram¹, C. Russo¹, E. Loizidou^{1,3}¹ Middlesex University, Department of Natural Sciences, London, United Kingdom² University College London Hospitals NHS Foundation Trust, Department of Cellular Pathology, London, United Kingdom³ University College London, School of Pharmacy, London, United Kingdom

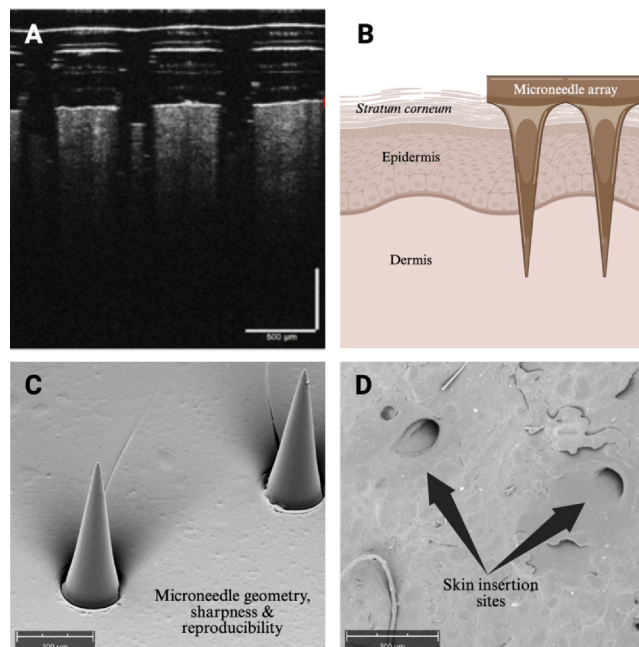
Background: Cutaneous squamous cell carcinoma (cSCC) is a common non-melanoma skin cancer in which local immune modulation is clinically relevant. Interferon-gamma (IFN- γ) is a key immunomodulatory cytokine; however, its clinical application in skin disease is limited by challenges associated with controlled local delivery. Dissolvable microneedles offer a minimally invasive approach to bypass the stratum corneum and enable intradermal delivery of biologics. This study aimed to develop IFN- γ -loaded dissolvable sugar-based microneedles and evaluate their structural integrity and ability to achieve reproducible intradermal penetration in skin-relevant models.



Conceptual schematic of dissolving microneedle-mediated IFN- γ delivery. Microneedles penetrate the stratum corneum and dissolve following insertion, enabling local intradermal cytokine release within the cutaneous microenvironment. The approach is intended for localised cutaneous immunomodulation.

Methods: IFN- γ -loaded dissolving microneedles were fabricated using a sugar-based matrix via micro-moulding. Microneedle morphology and structural integrity were assessed using scanning electron microscopy (SEM). Intradermal penetration and delivery depth were evaluated using ex-vivo human skin and optical coherence tomography (OCT), with penetration depth assessed across multiple insertion sites.

Results: IFN- γ -loaded microneedles demonstrated uniform geometry and intact needle tips suitable for skin insertion. SEM confirmed consistent microneedle architecture, while OCT imaging demonstrated reproducible disruption of the stratum corneum and formation of intradermal microchannels extending into the viable epidermis and superficial dermis. Penetration depth was consistent across multiple microneedles within each array, supporting reliable intradermal delivery.



Structural integrity and skin penetration of dissolving microneedle arrays. (A) OCT imaging demonstrating consistent microneedle penetration into skin. (B) Schematic illustrating microneedle insertion across skin layers. (C) SEM showing microneedle geometry and tip sharpness. (D) SEM of skin surface confirming microneedle insertion sites.

Conclusions: This study demonstrates the feasibility of delivering IFN- γ -loaded dissolving microneedles into human skin using a minimally invasive approach. These findings support the potential of dissolvable microneedles as a local intradermal delivery platform for cytokine-based strategies in cutaneous squamous cell carcinoma, with future work required to evaluate pharmacodynamic and biological effects.

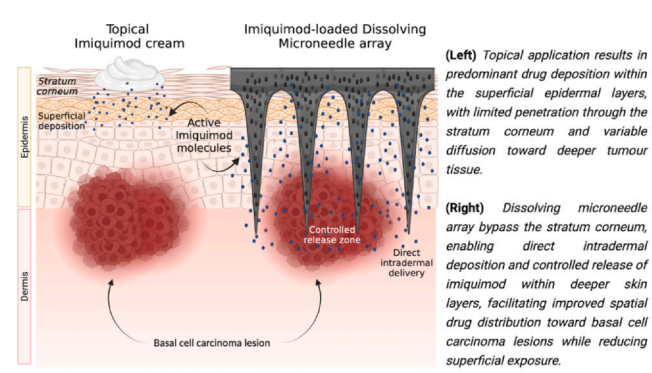
<https://doi.org/10.1016/j.ejcskn.2026.101112>

A-141

Imiquimod-Loaded Dissolving Microneedles for Enhanced Dermal Penetration in Basal Cell Carcinoma Immunotherapy: A Feasibility and Delivery Study

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Background: Topical imiquimod is widely used for the treatment of superficial basal cell carcinoma (sBCC) however its clinical efficacy is limited by variable stratum corneum penetration, prolonged treatment courses, and frequent local skin reactions. Improving intradermal delivery while reducing epidermal exposure could enhance both efficacy and tolerability in dermatology. The aim of this study is to develop and characterise a dissolving microneedle (MN) platform for imiquimod delivery designed to improve dermal penetration and enable targeted local immunotherapy for basal cell carcinoma.



Schematic comparison of topical versus dissolving microneedle-mediated intradermal delivery of imiquimod. Topical application shows barrier-limited epidermal diffusion, while microneedles bypass the stratum corneum, enabling direct intradermal release and targeted distribution of imiquimod toward basal cell carcinoma lesions.

Methods: Imiquimod-loaded dissolving microneedles were fabricated using a sugar-based polymer matrix via micro-moulding technology. Microneedle morphology, mechanical integrity, and dissolution kinetics were assessed using optical and scanning electron microscopy. Drug incorporation and in-vitro release profiles were evaluated by UV-spectrophotometry and analytically validated using HPLC calibration modelling. Penetration depth and transport behaviour were examined using multilayered skin-mimetic models and diffusion-based receptor-phase analysis, with a topical imiquimod formulation used as a comparator.

Results: Imiquimod was successfully incorporated into dissolving microneedles with consistent uniform geometry and sufficient mechanical strength to penetrate the outer skin barrier. The MN arrays achieved rapid insertion and complete dissolution within minutes, enabling controlled release of imiquimod into deeper tissue layers. In-vitro release studies demonstrated sustained drug liberation from the microneedle matrix compared with free drug application, supporting enhanced intradermal availability. HPLC quantification confirmed reproducible drug loading and measurable receptor-phase recovery following microneedle delivery. Comparative analysis demonstrated formulation-dependent delivery performance, with microneedle-mediated delivery showing quantifiable intradermal transport relative to conventional topical application.

Formulation	Matrix composition (CMC/MAL/TRE/SUC, %)	Receptor phase IMQ @96h (mean ± SD)	Skin IMQ (mean ± SD)
Comparator	Topical IMQ	0.0128 ± 0.0007	0.0577 ± 0.0113
MN_1	40/40/20/-	0.0124 ± 0.0000	0.0295 ± 0.0177
MN_2	40/45/15/-	0.0116 ± 0.0001	0.0171 ± 0.0049
MN_3	40/50/10/-	0.0116 ± 0.0001	0.0153 ± 0.0013
MN_4	40/40/-/20	0.0338 ± 0.0308	0.1378 ± 0.0097
MN_5	40/45/-/15	0.0403 ± 0.0409	0.1823 ± 0.0250
MN_6	40/50/-/10	0.0416 ± 0.0181	0.1475 ± 0.0026

Formulation composition + quantified IMQ delivery (HPLC-derived concentration, mg/mL)

Conclusions: This feasibility and delivery study demonstrates that dissolving microneedles can bypass the stratum corneum to

enable analytically validated, quantifiable intradermal delivery of imiquimod, offering a promising platform to optimise topical immunotherapy for basal cell carcinoma. The platform provides a translational foundation for subsequent pharmacodynamic and tumour-specific evaluation. This approach may improve local drug bioavailability while reducing superficial irritation, supporting further translational evaluation in dermato-oncology

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A-632

Investigating alterations in autophagy signalling during development and progression of cutaneous Squamous Cell Carcinoma

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Background: Cutaneous Squamous Cell Carcinoma (cSCC) is a non-melanoma skin cancer arising in keratinocytes. Most cSCC cases develop from premalignant lesions known as actinic keratosis (AK). While most cSCC are effectively treated through surgical excision, a subset are classified as high-risk and may progress to invasive or metastatic disease. Since many gene mutations identified in cSCC are also present in normal skin and AK, distinguishing the molecular events that specifically drive malignant progression remains challenging. Investigating alterations in key cellular pathways may provide insight into the mechanisms underlying this transition. Autophagy, a key process in which damaged or unnecessary cellular components are sequestered into autophagosomes and degraded, has emerged as a potential contributor to cSCC pathogenesis. High mutational frequency in autophagy-related genes has been identified in RNA sequencing datasets from both cSCC and AK, from which it can be hypothesized that deregulation of autophagy may be driving the progression of cSCC and could provide a novel therapeutic avenue.

Methods: Preliminary in vitro autophagic flux assays have revealed that autophagic flux is blocked in premalignant cSCC cell lines, while active in metastatic cell lines. To investigate this further, the expression of key autophagic proteins, LC3, p62 and NDP52, were examined in AK and cSCC tissue using a cell DIVE multiplex immunofluorescence (IF) platform. LC3 is a marker for autophagosome formation, while p62 and NDP52 are cargo-receptors proteins that recruit target proteins to be degraded by autophagy. Accumulation of these proteins therefore indicates failed autophagic clearance, so LC3, p62 and NDP52 colocalization was used to indicate regions of autophagic impairment.

Results: In AK samples, autophagy marker accumulation was higher in regions exhibiting more severe dysplasia compared with normal epidermis or regions of mild dysplasia, tying increasing dysplastic severity with autophagy deregulation. In primary cSCC samples, autophagy markers were also elevated within tumour masses relative to distant epidermal and dermal regions; however, expression patterns were highly heterogeneous across tumour samples. This variability enabled classification of tumours into autophagy-deficient or autophagy-intact phenotypes – where autophagy-intact tumours were typically well-differentiated and highly keratinised, whereas autophagy deficient tumours tended to be poorly-differentiated.

Conclusions: In conclusion, impaired autophagy may contribute to the transition of normal epidermis to AK lesions. Contrastingly, cSCC tumours appear to segregate into autophagy-intact or autophagy-impaired phenotypes, suggesting that autophagy status may