Mapping skin properties in psoriasis for improved understanding of topical absorption

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INTRODUCTION

- Skin diseases such as plaque psoriasis are known to cause significant changes in skin structure and function, including hyperplasia and inflammation [1], however, there is limited understanding about how these changes impact topical drug delivery (Fig 1).
- Regulatory agencies have made it a priority to facilitate the development and approval of more affordable generic drug products. An attractive approach to improve the understanding of topical drug delivery in disease-modified skin is to develop mechanistic physiologically based pharmacokinetic (PBPK) models.
- In order to help develop these models, information characterizing the skin in healthy and diseased conditions is required at both the structural and functional levels.

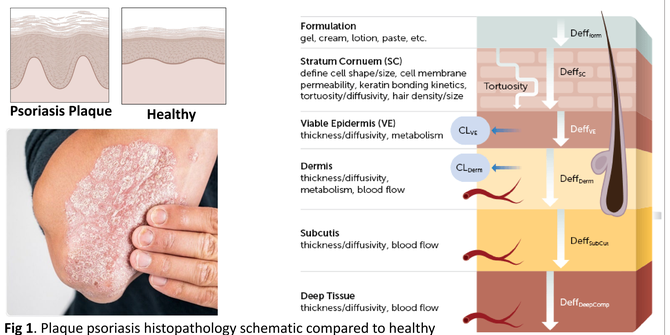

Fig 1. Plaque psoriasis histopathology schematic compared to healthy skin, and PBPK approach used by the Simcyp Simulator [2], [3].

AIM & METHODS

- We aimed to 1) create a database of structural and functional skin parameters in psoriasis and healthy skin and 2) correlate these parameters for use towards improved topical delivery predictions.
- Fifty-six adults were recruited (28 mild-severe psoriasis and 28 healthy) from January 2022 to September 2023. Functional properties (e.g., pH and trans-epidermal water loss (TEWL)) were measured non-invasively at lesion and non-lesion sites, prior to in vivo confocal microscopy and skin shave biopsy, for assessment of structural features (e.g., stratum corneum (SC) thickness and cellular dimensions) (Fig 2).

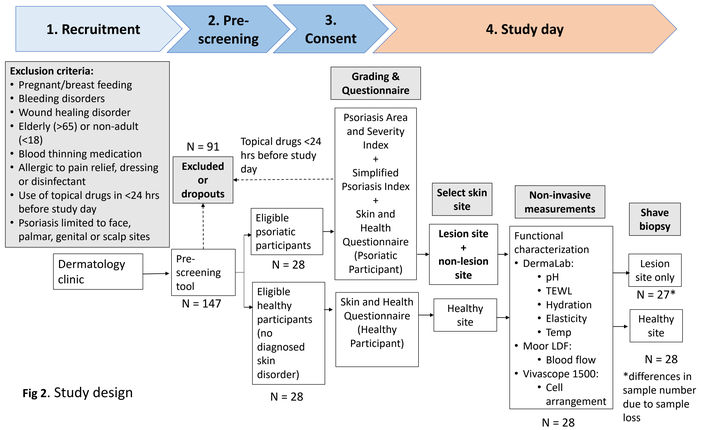

Fig 2. Study design

RESULTS & DISCUSSION

Study demographics

Characteristic	Psoriasis (n=28)	Healthy skin (n=28)
Sex	61% M	43% M
Age	48 ± 12	35 ± 12
BMI	31 ± 7	24 ± 5
Smoking (pack years)	16.0 ± 19.9	1.8 ± 6.7
Alcohol (std drinks/week)	4.1 ± 6.2	4.2 ± 4.5

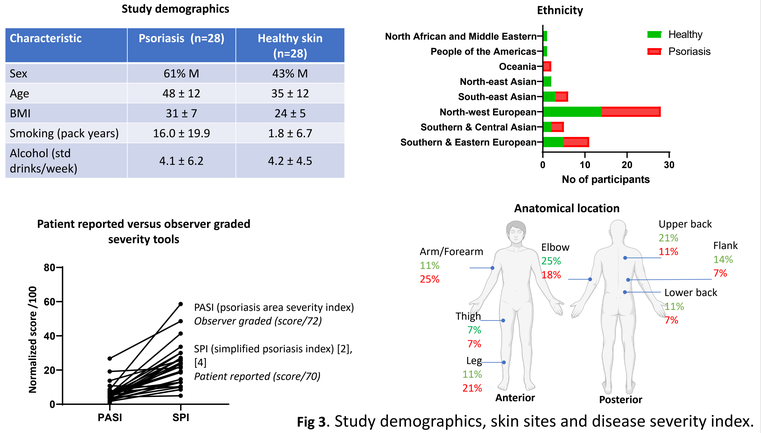

Fig 3. Study demographics, skin sites and disease severity index.

Functional changes in psoriasis (mean ± SEM), as compared to healthy skins, included elevated TEWL (16.0 ±2.4 vs 8.3±0.9 g/m2/h, P<0.001), elevated blood flow (162.2 ± 26.6 vs 37.6 ± 4.4 perfusion units, P<0.0001) and reduced hydration (28.3±4.4 vs 113.4±10.2 µS, P<0.001) (Fig 4). There was an increased site-wide SC thickness (103.8 ± 14.8 vs 26.9 ± 2.5 µm , P<0.001), however, a 42% reduction in intercellular lipid tortuosity, reflective of altered geometric packing, was observed in psoriasis (Fig 5).

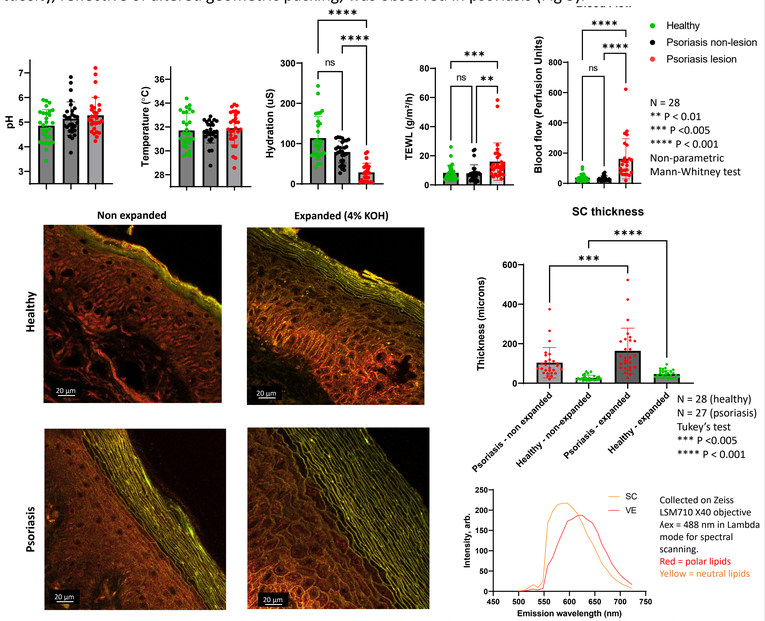

Fig 4. Functional and structural parameters for psoriasis and healthy skin. Expansion (4% KOH) was performed for visualisation of individual corneocytes

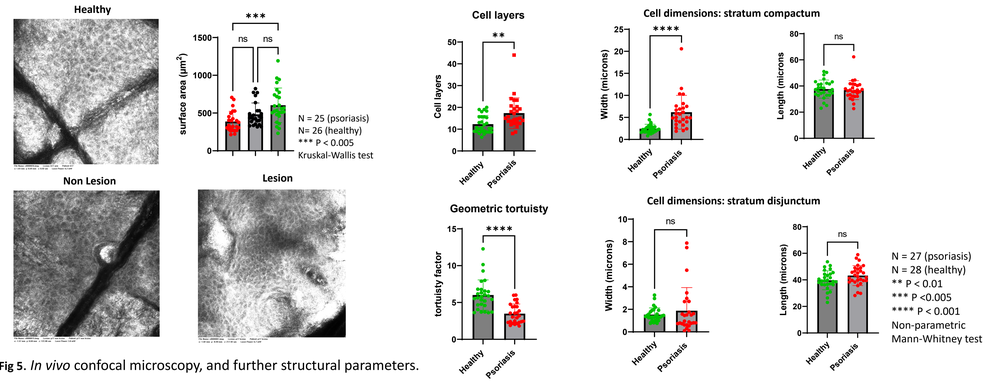

Fig 5. *In vivo* confocal microscopy, and further structural parameters.

Relationships between tortuosity factor (=lipid pathlength/SC thickness) and TEWL, among others (e.g., blood flow and skin temperature), were body-site dependent, indictive of regional differences in barrier function (Fig 6).

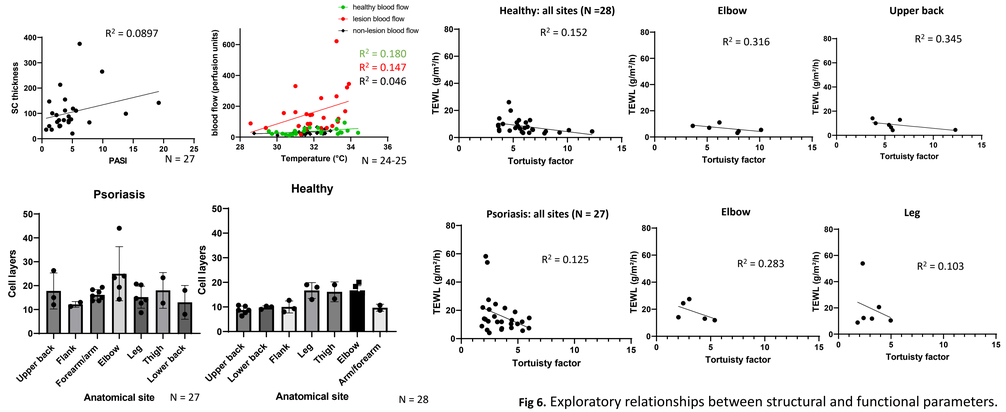

Fig 6. Exploratory relationships between structural and functional parameters.

CONCLUSIONS

- Functional skin properties and structural features were studied in fifty-six adults (28 mild-severe psoriasis and 28 healthy) using state-of-the-art methodologies. Correlations among these parameters were explored.
- Parameters (TEWL, blood flow, hydration and geometric packaging) may differ between healthy and psoriatic patients while geometric tortuosity may correlate with TEWL in certain anatomical sites.

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