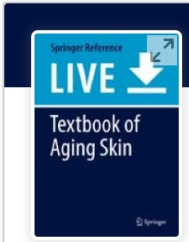
Towards data-driven quantification of skin ageing: reflectance confocal microscopy and microsampling

- Prof Tarl Prow
- Director, Skin Research Centre, Hull York Medical School, University of York
- tarl.prow@hyms.ac.uk

UNIVERSITY of York

Skin
Research Centre



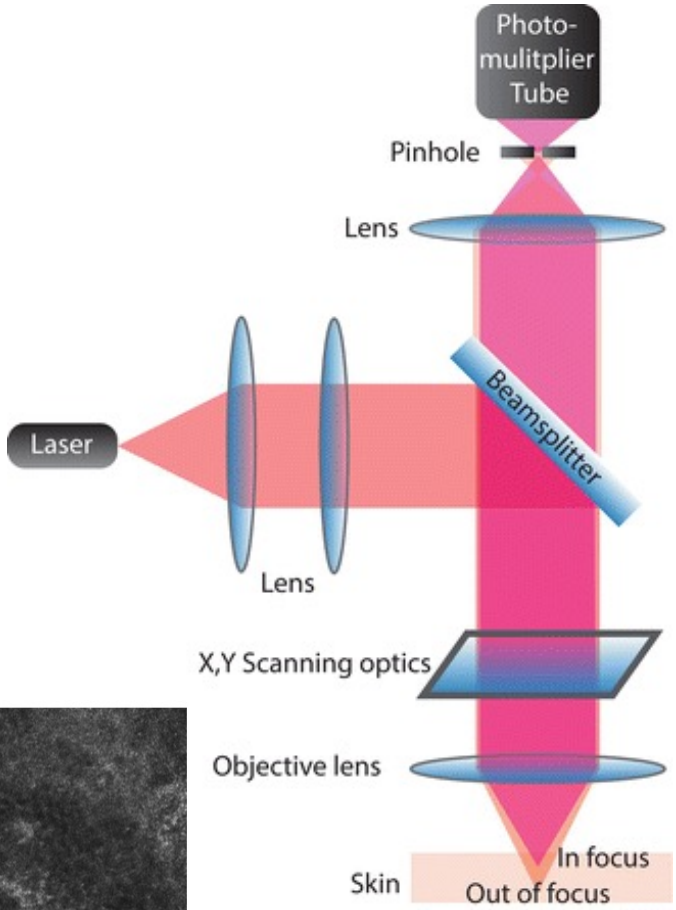
Textbook of Aging Skin pp 1–17 | Cite as

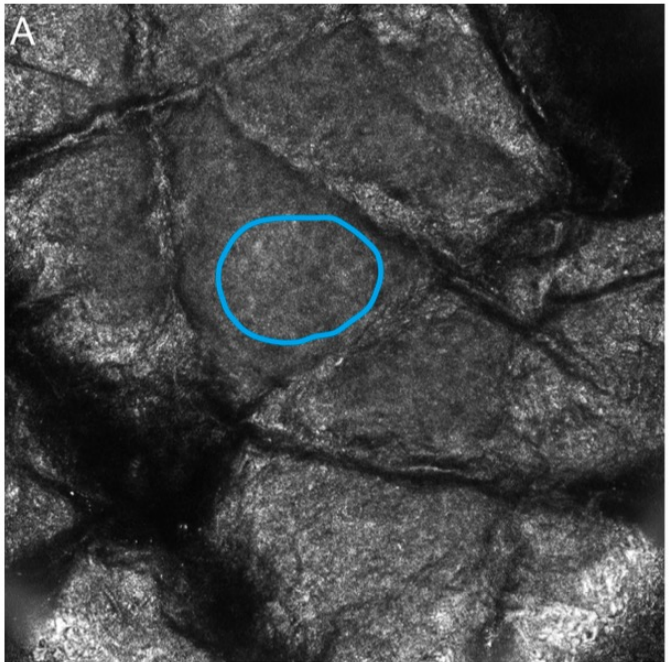
Reflectance Confocal Microscopy and Aging

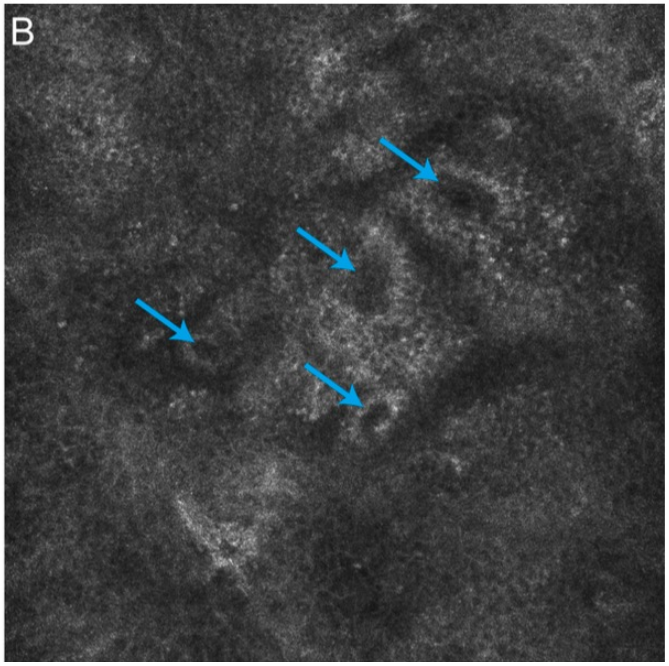
Anthony P. Raphael ✉, Danielle Tokarz, Marco Ardigò & Tarl W. Prow

Living reference work entry | First Online: 01 January 2016

239 Accesses

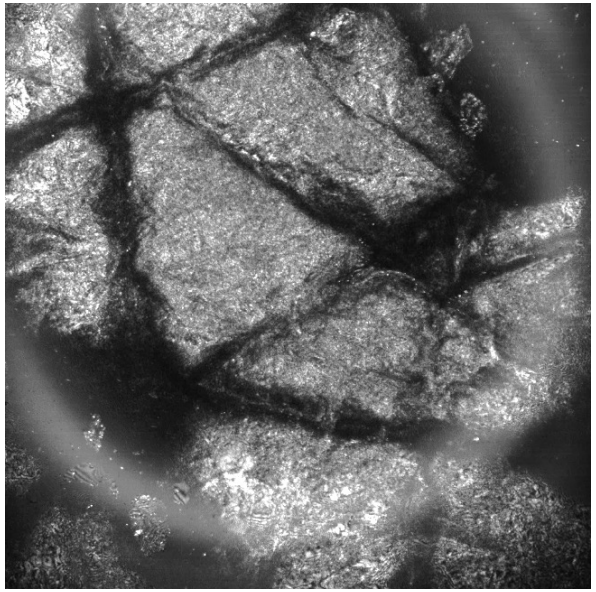




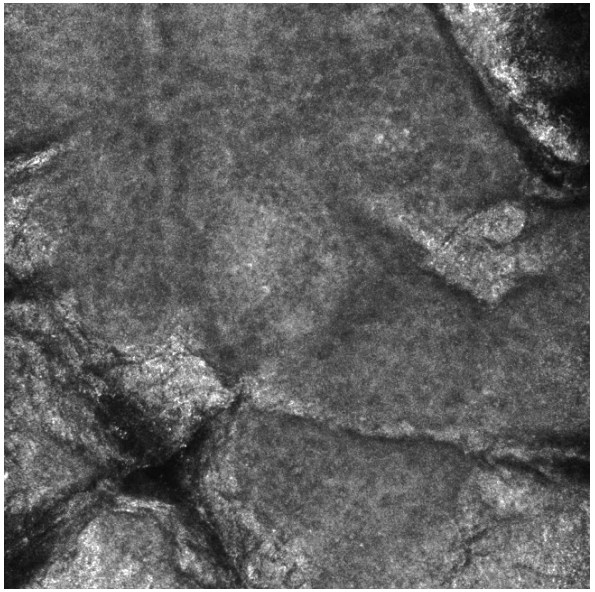


Understanding RCM depth stacks – Aims

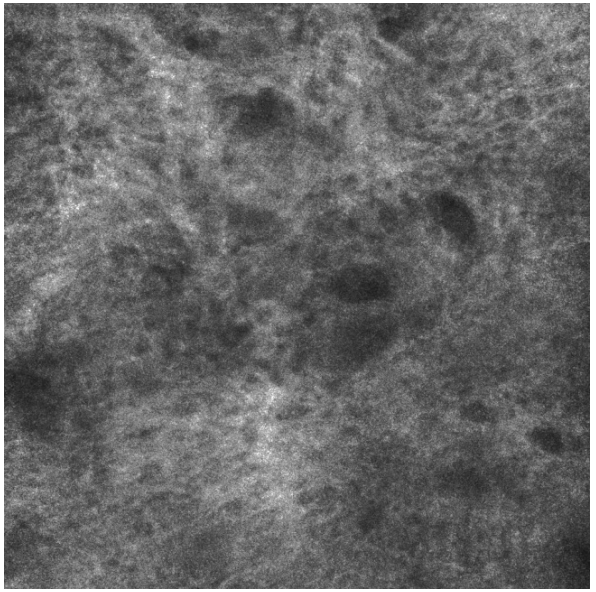
1. Automatically determine the strata of the skin in a depth stack.



Stratum Corneum



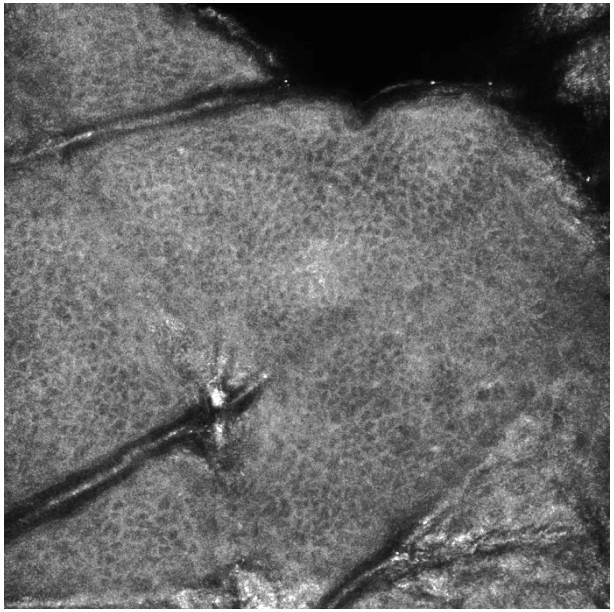
Epidermis



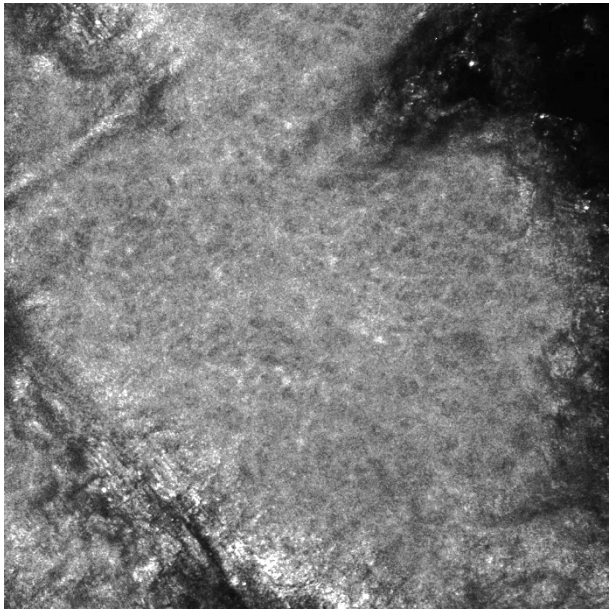
Dermis

Understanding RCM depth stacks – Aims

2. Discriminate photoaged and actinic keratosis affected skin.



Low photoageing



High photoageing

Understanding RCM depth stacks – Pilot

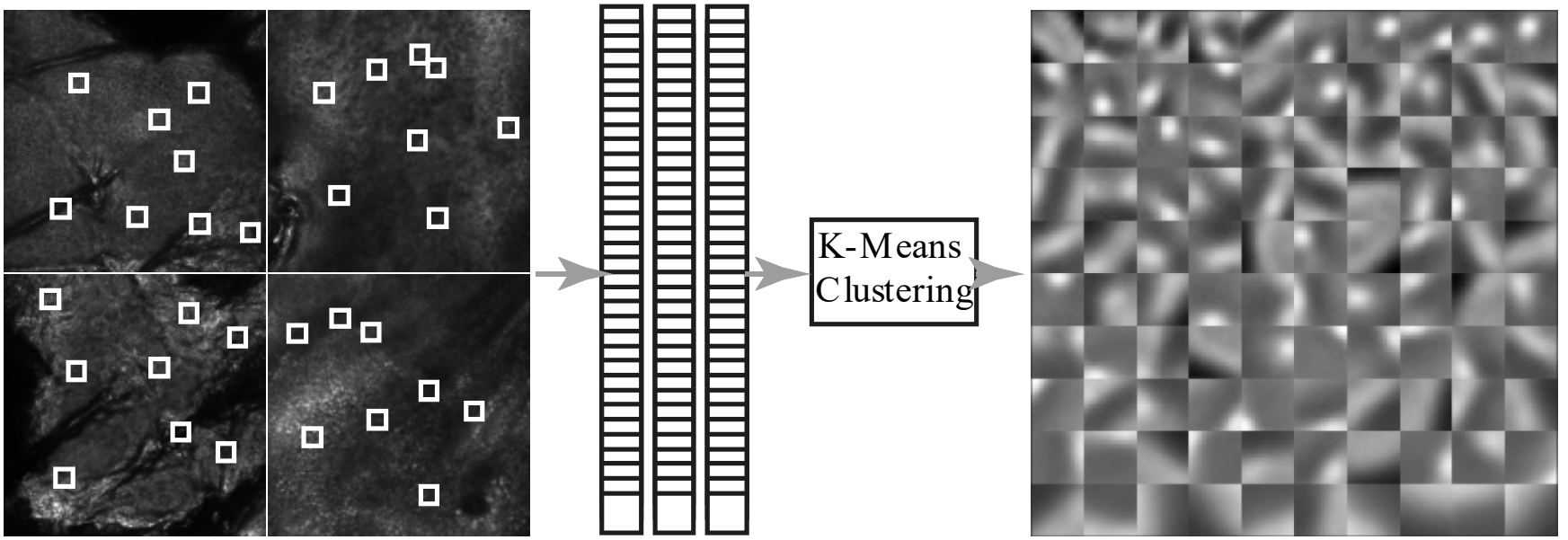
- 335 depth stacks from 52 volunteers aged 20-29 or 50-59
- Dataset used in previous publications[1,2]
- Wide range of photo-ageing in cohort

- Four distinct strata were labelled – stratum corneum, viable epidermis, papillary dermis and dermis

1. Wurm et. al, 2012, BJD;
2. Raphael et. al, 2013, Exp. Derm.

Bag of features

Learning a visual dictionary

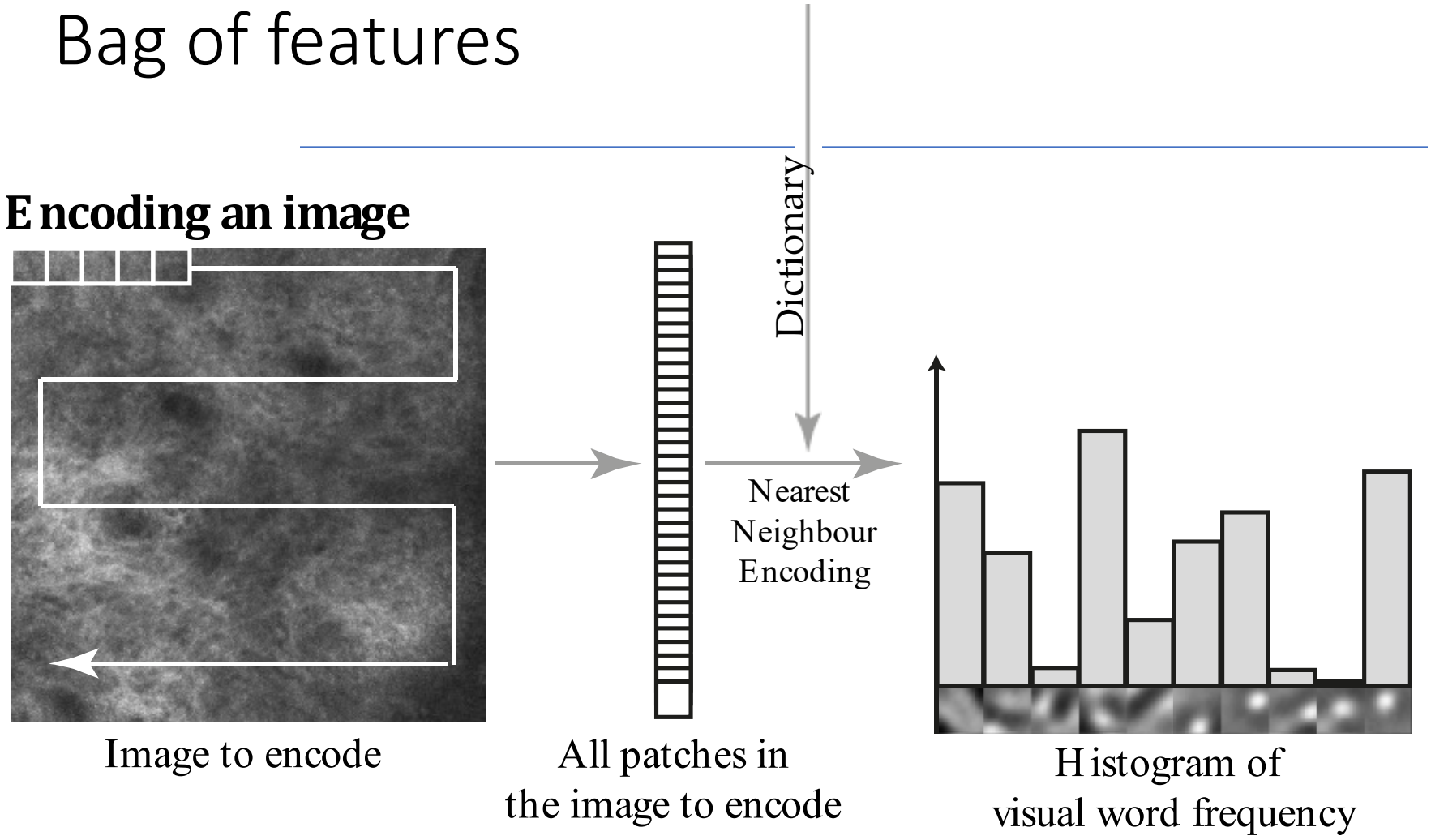


Training images

Patches from random locations

Clustered patches form a dictionary

Bag of features



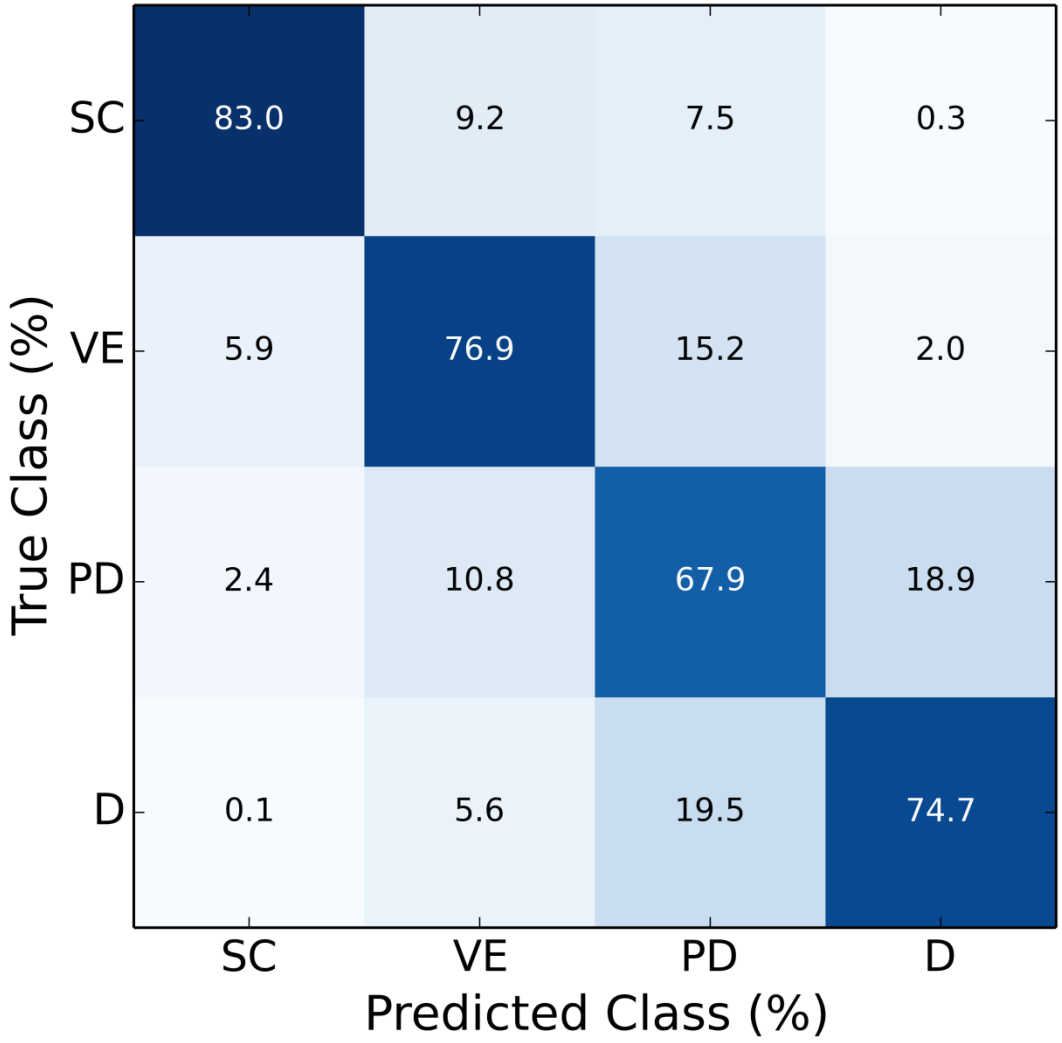
Understanding RCM depth stacks – Classification

- Separate test set has been held out for final performance estimation
- Small dictionary size (256 words)
- Random forests used as classifier
- 5-fold cross validation used with fixed parameters
- Dictionary learned separately on each fold

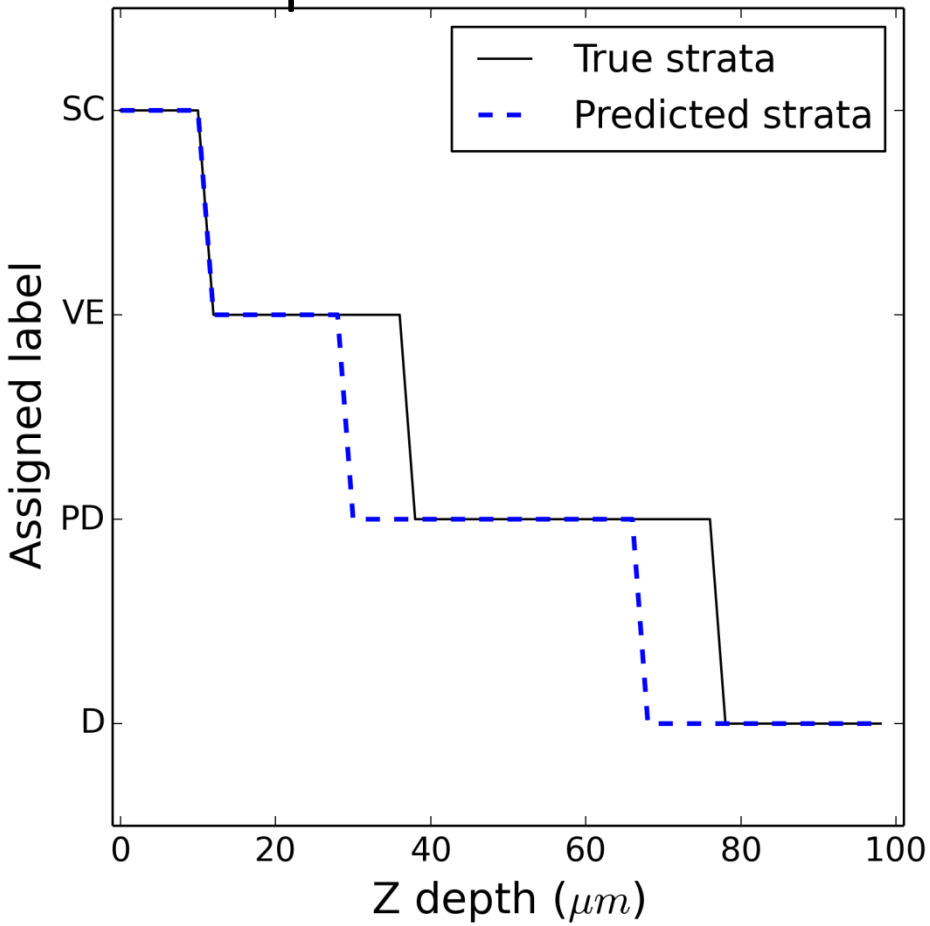
- No optimisation of parameters

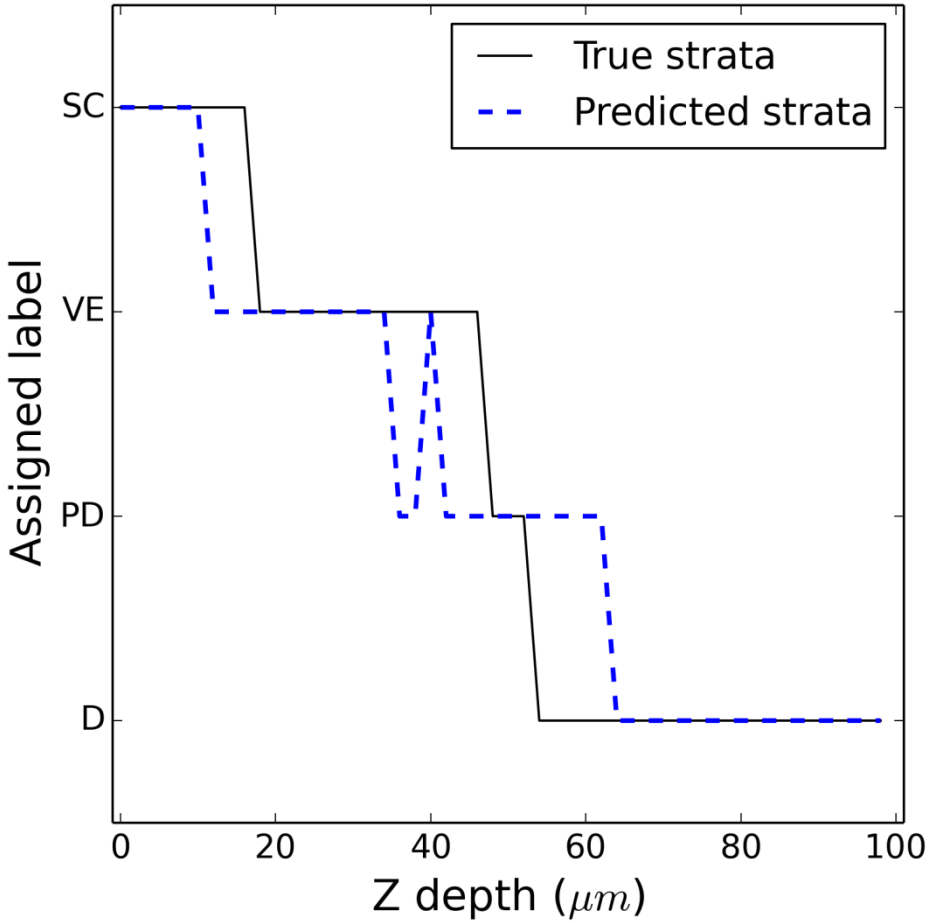
Understanding RCM depth stacks – Results

Accuracy:
74.9 ± 1.5%



Understanding RCM depth stacks – Output





Understanding RCM depth stacks - Conclusions

- K-means learns representative visual words to describe the RCM imagery
- Simple classifiers can generate a physically realistic understanding of the skin

Received: 14 June 2021 | Accepted: 15 June 2021

DOI: 10.1111/ics.12720

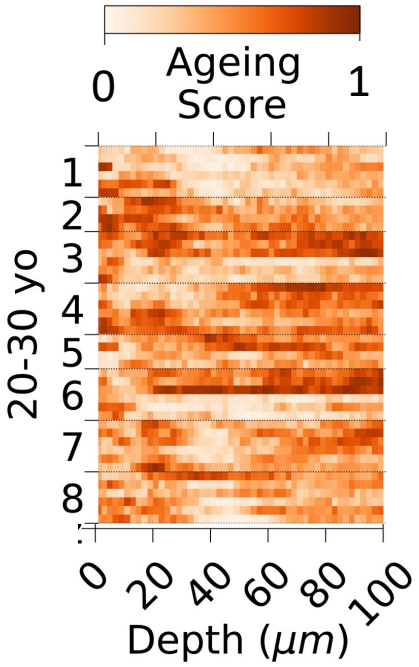
International Journal of Cosmetic Science
SOCIÉTÉ FRANÇAISE DE COSMÉTOLOGIE

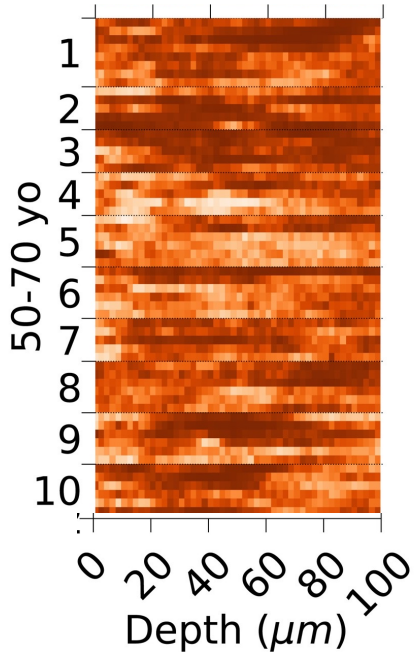
ORIGINAL ARTICLE

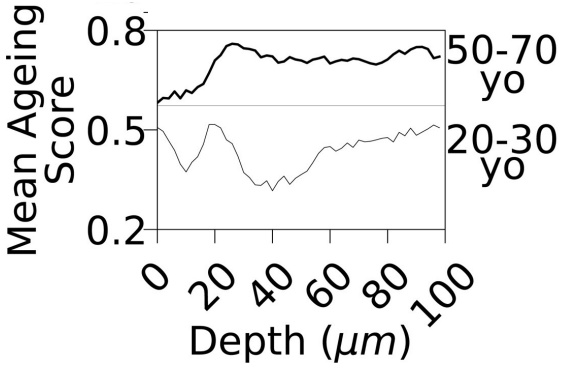
Towards data-driven quantification of skin ageing using reflectance confocal microscopy

Samuel C. Hames[1,2] | **Andrew P. Bradley**[2,3] | **Marco Ardigo**[1,4] | **H. Peter Soyer**[1] | **Tarl W. Prow**[1,5]

- En-face sections of reflectance confocal microscopy depth stacks
- dorsal and volar forearm
- 74 volunteers, 20-30 & 50-70 yo
- 36/18/20 training/testing/validation







Publications

Towards data-driven quantification of skin ageing using reflectance confocal microscopy.

Hames SC, Bradley AP, Ardigo M, Soyer HP, Prow TW.

Int J Cosmet Sci. 2021 Aug;43(4):466-473. doi: 10.1111/ics.12720. Epub 2021 Jul 26.

PMID: 34133771

Item in Clipboard

Automated Segmentation of Skin Strata in Reflectance Confocal Microscopy Depth Stacks.

Hames SC, Ardigò M, Soyer HP, Bradley AP, Prow TW.

PLoS One. 2016 Apr 18;11(4):e0153208. doi: 10.1371/journal.pone.0153208. eCollection 2016.

PMID: 27088865 **Free PMC article.**

Item in Clipboard

Automated detection of actinic keratoses in clinical photographs.

Hames SC, Sinnya S, Tan JM, Morze C, Sahebian A, Soyer HP, Prow TW.

PLoS One. 2015 Jan 23;10(1):e0112447. doi: 10.1371/journal.pone.0112447. eCollection 2015.

PMID: 25615930 **Free PMC article.**

Item in Clipboard

Counting actinic keratosis - is photographic assessment a reliable alternative to physical examination in clinical trials?

Sinnya S, O'Rourke P, Ballard E, Tan JM, Morze C, Sahebian A, Hames SC, Prow TW, Green AC, Soyer HP.

Acta Derm Venereol. 2015 May;95(5):604-5. doi: 10.2340/00015555-2040.

PMID: 25572587 **Free article.** No abstract available.

Item in Clipboard

The future of keratinocyte skin cancer surveillance: automated image analysis to identify and monitor keratinocyte dysplasia.

Hames SC, Prow TW.

Curr Probl Dermatol. 2015;46:77-84. doi: 10.1159/000366540. Epub 2014 Dec 18.

PMID: 25561210

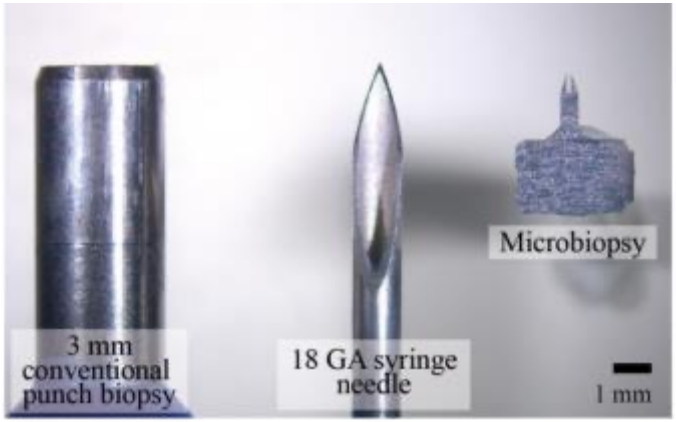
Item in Clipboard

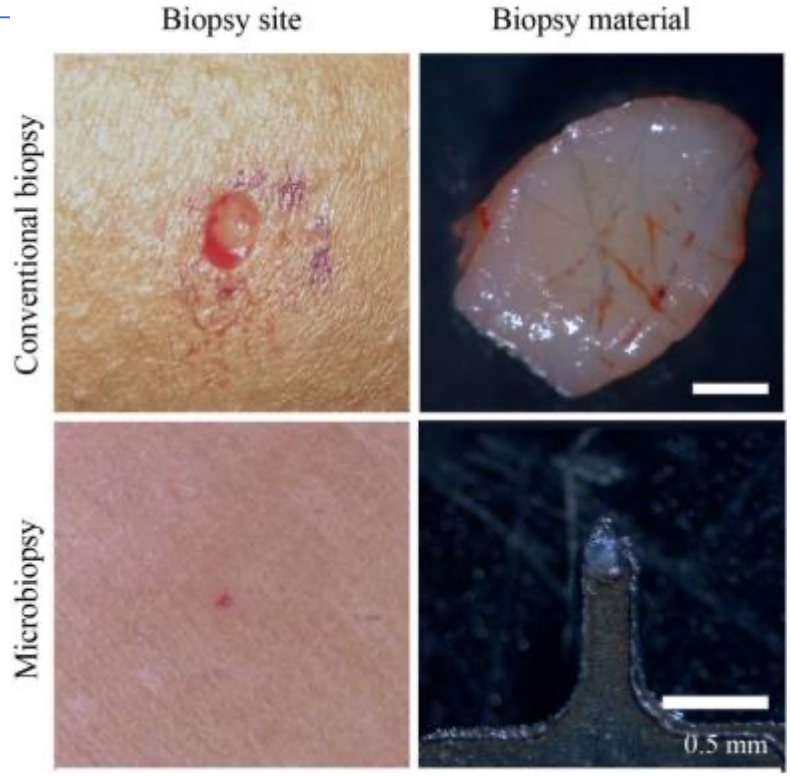
Skin Microbiopsy Introduction

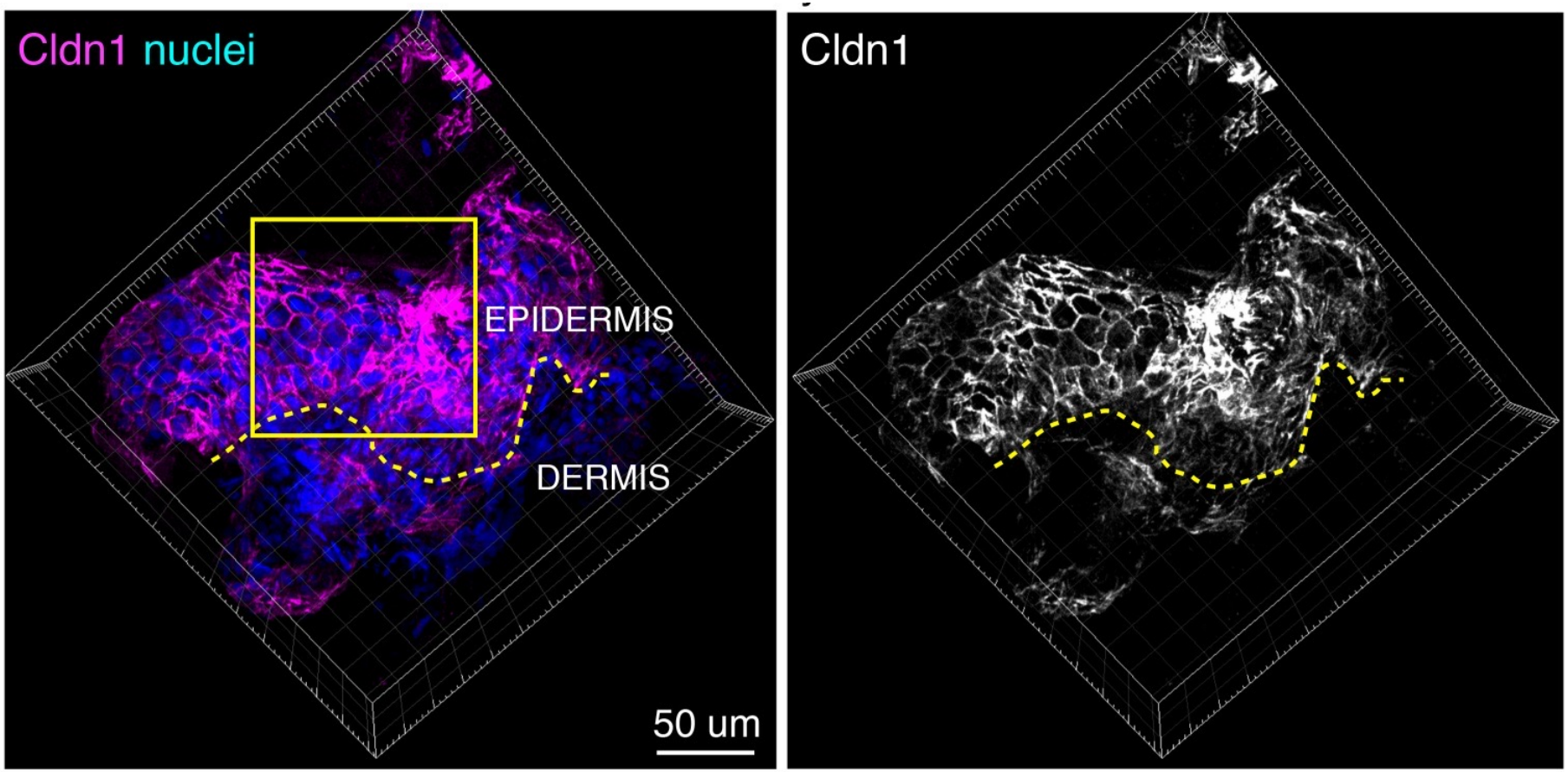
Addressing unmet needs in skin research:

- Enabling patients to sample there skin at home, as often as needed
- Minimally invasive DNA, RNA, Protein and drug sampling from living skin
- Medical, cosmetic and pediatric sampling
- Non-destructive sampling of the same area repeatedly

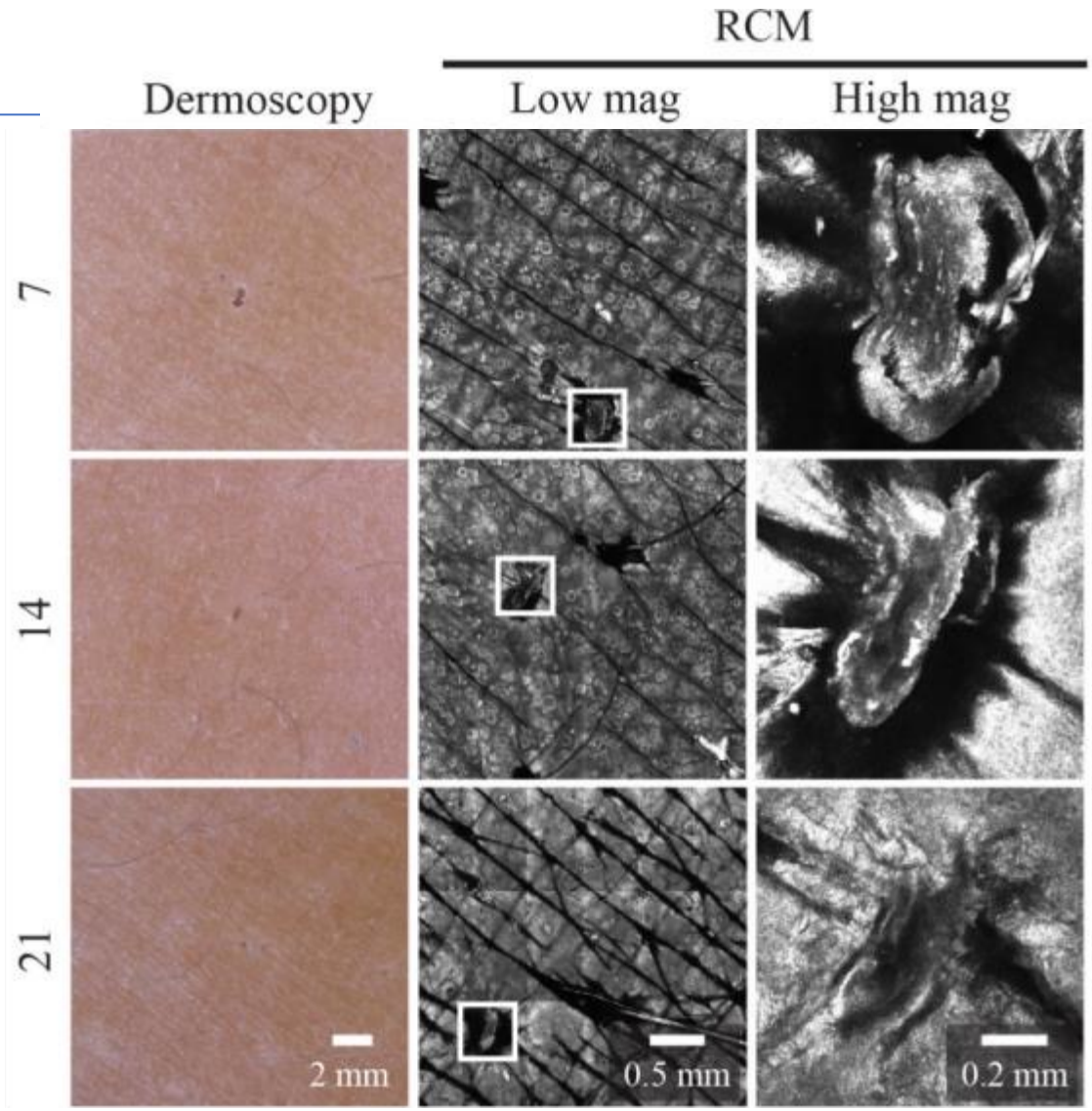
Conventional punch biopsy and Microbiopsy



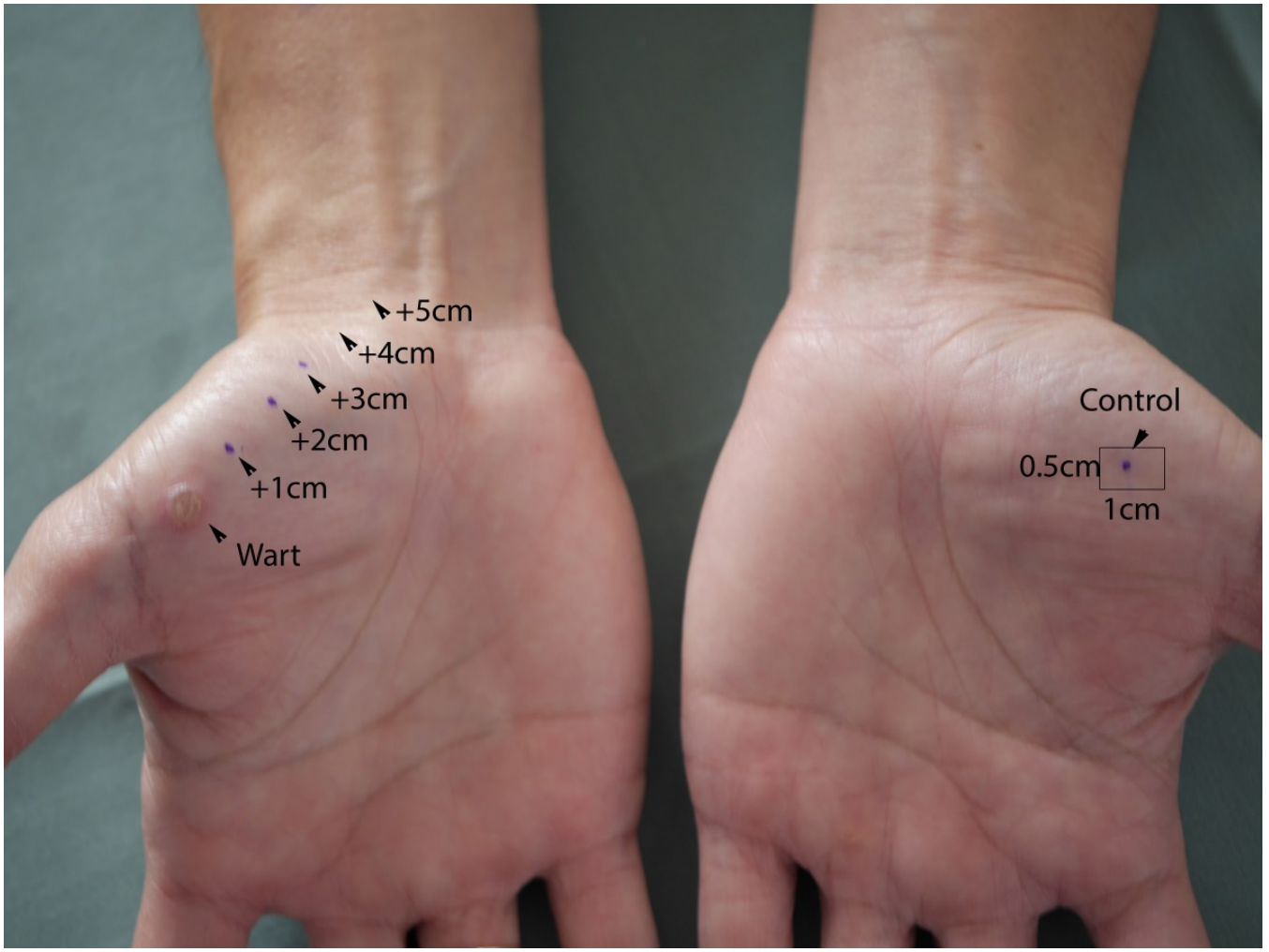



Cldn1 nuclei
EPIDERMIS
DERMIS
50 um
Cldn1

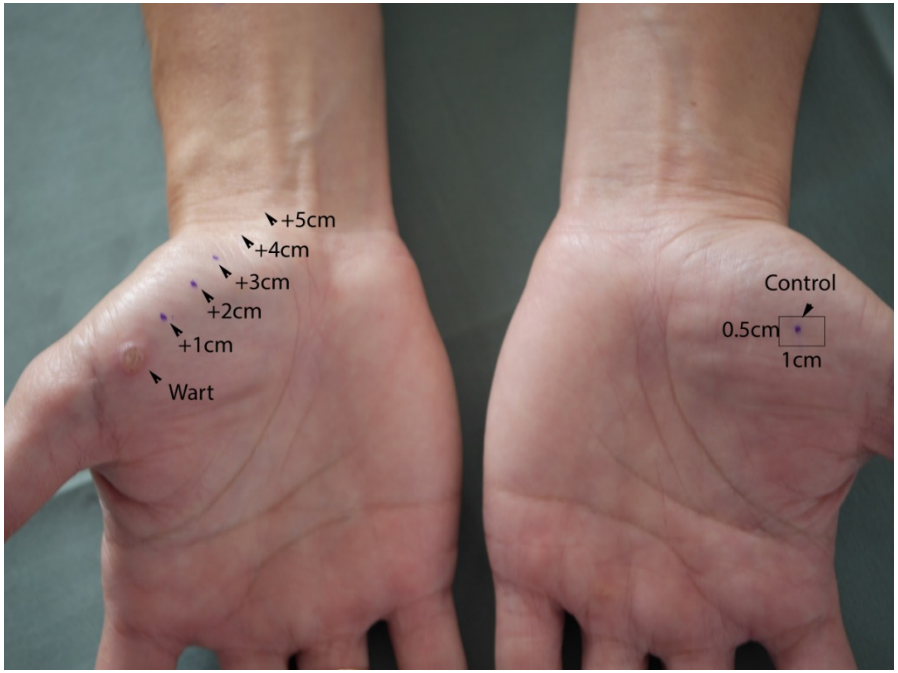
Clinical follow-up of microbiopsy site

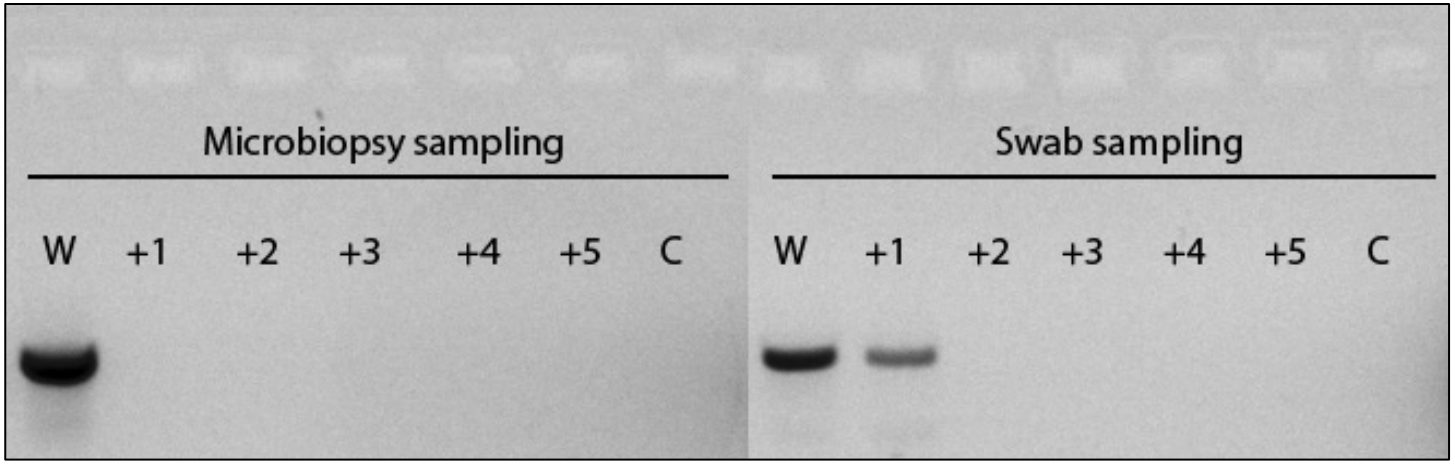


Spatial micro-sampling for genetic analysis:
Spatial distribution of HPV DNA in cutaneous warts



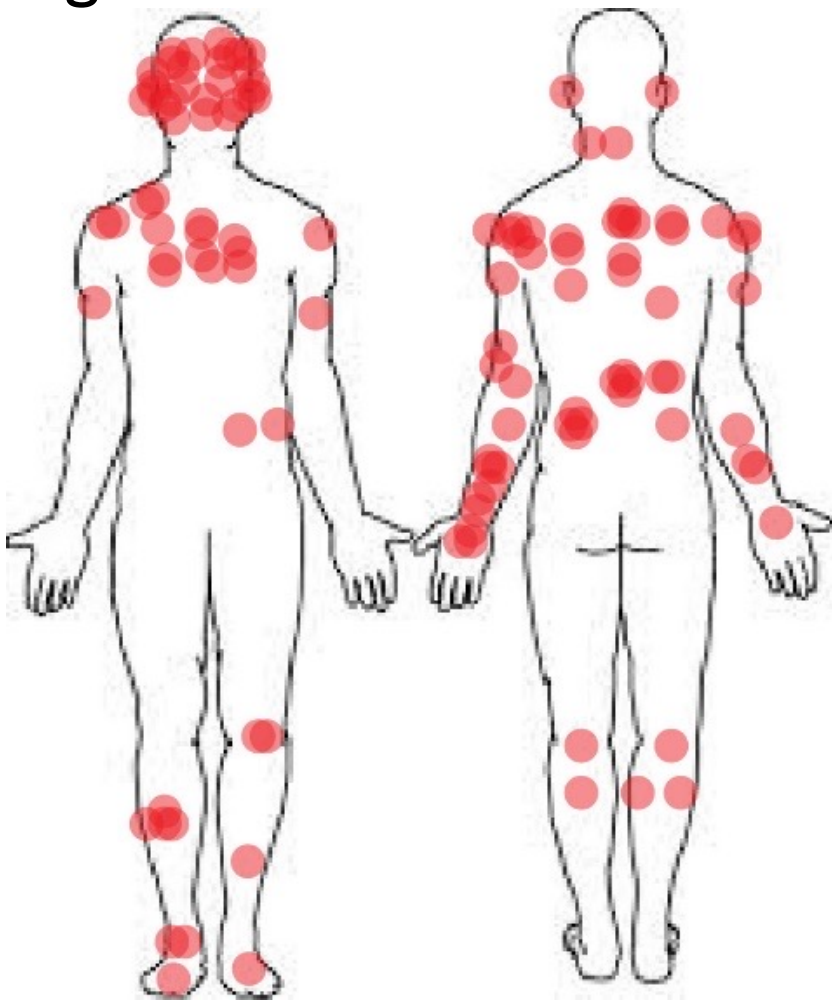
- Microbiopsy DNA yield was in the range of 1 – 2ng.
- Multiplex PCR for four of the most frequent wart-causing HPV types, 1, 2, 27, and 57.
- HPV Type 27 was found.



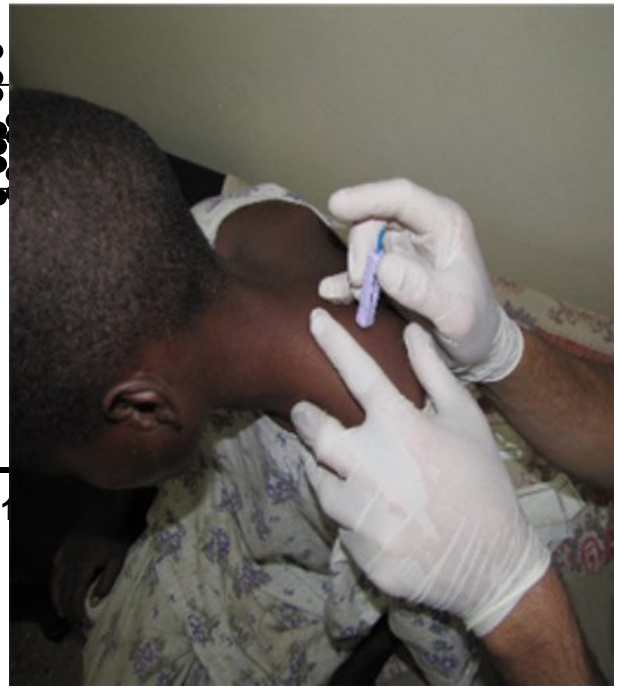


Microbiopsy sampling:
Body sites and ages

- Together we collected
  - 5x microbiopsies from 117 lesions prior to conventional biopsy
  - 5x perilesional microbiopsies from the 117 sites
  - Total of 1,170 microbiopsies from 106 volunteers
- There were 290 microbiopsies taken from the head and neck region and 880 from the rest of the body.
- No adverse events were recorded



Volunteer Ages Sampled by M



0

21-30 41-50 61-70 51-60 71

Age of volunteers

Quick Microbiopsy facts

- >10,000 microbiopsies have been made
- >2200 microbiopsies have been performed on volunteers
  - 1/3 of these have been taken from the face and neck
- 16 sites around the globe are using microbiopsy
  - USA, Brazil, Germany, UK, Israel, Japan, Africa and Australia

Publications

1. Minimally invasive microbiopsy for genetic profiling of melanocytic lesions: A case series. Jain M, Autuori I, Everett N, Harris U, Yamada M, Prow T, Busam K, Marchetti MA, Halpern AC, Orlow I.J Am Acad Dermatol. 2022 Oct;87(4):903-904. doi: 10.1016/j.jaad.2021.12.018. Epub 2021 Dec 16.PMID: 34922919
2. Microbiopsy-based minimally invasive skin sampling for molecular analysis is acceptable to Epidermolysis Bullosa Simplex patients where conventional diagnostic biopsy was refused. Yamada M, Melville E, Cowin AJ, Prow TW, Kopecki Z.Skin Res Technol. 2021 May;27(3):461-463. doi: 10.1111/srt.12971. Epub 2020 Oct 22.PMID: 33089542
3. A minimally invasive clinical model to test sunscreen toxicity based on oxidative stress levels using microbiopsy and confocal microscopy - a proof of concept study. Yamada M, Lin LL, Hang LYT, Belt PJ, Peter Soyer H, Raphael AP, Prow TW.Int J Cosmet Sci. 2020 Oct;42(5):462-470. doi: 10.1111/ics.12646. Epub 2020 Aug 30.PMID: 32619281
4. Absorbent Microbiopsy Sampling and RNA Extraction for Minimally Invasive, Simultaneous Blood and Skin Analysis. Lei BUW, Yamada M, Hoang VLT, Belt PJ, Moore MH, Lin LL, Flewell-Smith R, Dang N, Tomihara S, Prow TW.J Vis Exp. 2019 Feb 21;(144). doi: 10.3791/58614.PMID: 30855573
5. 'Mind your Moles' study: protocol of a prospective cohort study of melanocytic naevi. Koh U, Janda M, Aitken JF, Duffy DL, Menzies S, Sturm RA, Schaider H, Betz-Stablein B, Prow T, Soyer HP, Green AC.BMJ Open. 2018 Sep 19;8(9):e025857. doi: 10.1136/bmjopen-2018-025857.PMID: 30232117 Free PMC article.
6. Minimally invasive microbiopsies: a novel sampling method for identifying asymptomatic, potentially infectious carriers of Leishmania donovani. Kirstein OD, Abbasi I, Horwitz BZ, Skrip L, Hailu A, Jaffe C, Li LL, Prow TW, Warburg A.Int J Parasitol. 2017 Sep;47(10-11):609-616. doi: 10.1016/j.ijpara.2017.02.005. Epub 2017 Apr 26.PMID: 28455239 Free PMC article.
7. Microbiopsy Biomarker Profiling in a Superficial Melanoma Resembling a Pigmented Basal Cell Carcinoma. Sobarun P, Hoang VL, Yamada M, Lambie D, Soyer HP, Prow TW.JAMA Dermatol. 2017 Apr 1;153(4):334-336. doi: 10.1001/jamadermatol.2016.5537.PMID: 28196220
8. Skin microbiopsy for HPV DNA detection in cutaneous warts. Tom LN, Dix CF, Hoang VL, Lin LL, Nufer KL, Tomihara S, Prow NA, Soyer HP, Prow TW, Ardigo M.J Eur Acad Dermatol Venereol. 2016 Dec;30(12):e216-e217. doi: 10.1111/jdv.13548. Epub 2016 Feb 8.PMID: 26854066
9. BRAF wild-type melanoma in situ arising in a BRAF V600E mutant dysplastic nevus. Tan JM, Lin LL, Lambie D, Flewell-Smith R, Jagirdar K, Schaider H, Sturm RA, Prow TW, Soyer HP.JAMA Dermatol. 2015 Apr;151(4):417-21. doi: 10.1001/jamadermatol.2014.3775.PMID: 25607474
10. Effects of ex vivo skin microbiopsy on histopathologic diagnosis in melanocytic skin lesions. Banan P, Lin LL, Lambie D, Prow T, Soyer HP.JAMA Dermatol. 2013 Sep;149(9):1107-9. doi: 10.1001/jamadermatol.2013.5020. PMID: 23864191 Free article.
11. The opportunity for microbiopsies for skin cancer. Prow TW, Lin LL, Soyer HP. Future Oncol. 2013 Sep;9(9):1241-3. doi: 10.2217/fon.13.88. Epub 2013 May 9.PMID: 23654202 Free article.
12. **Microbiopsy engineered for minimally invasive and suture-free sub-millimetre skin sampling. Lin LL, Prow TW, Raphael AP, Harrold Iii RL, Primiero CA, Ansaldo AB, Soyer HP.F1000Res. 2013 May 2;2:120. doi: 10.12688/f1000research.2-120.v2. eCollection 2013.PMID: 24627782 Free PMC article.**

We are a new Centre developing new industry partnerships at scale

University of York

Skin Research Centre

What we have to offer:

- Advanced technologies (microbiopsy, spatial transcriptional
- profiling, single cell sequencing…)
- Clinical access to volunteers across a wide range of age and ethnicity

- 12 permanent, flexible positions (Lecturer to Professor) with start-up packages and PhD student placements to align with industry partners
- Dedicated research space, clinical suite, office space for business development
- Access to the latest research technologies for imaging, molecular analysis and bioinformatics
- 40+ resident researchers working in translational skin research in 5 laboratories globally recognised for excellence
- Support from the highest levels within the University of York for leverage

2022

Acknowledgements

Prof Peter Soyer
Dr Jean Tan
Dr Priyam Sobarun

Prof Albert Juhasz
Dr Dario Arrua

Prof Matt Brown
A/Prof Paul Leo
Dr Tony Kenna

Prof Tilo Bierdmann
Dr Martin Köberle
Dr Yacine Amar

Prof Anna Mandinova
Prof Sam Lee

Prof Alan Halpern

A/Prof Conor Evans
Prof Charles Lin

Prof Alon Warburg
Dr. Oscar Kirstein

Dr Paul Annells

Dr Paul Belts
A/Prof Michael Freeman