Clinical Studies

Key Clinical Trials

1. Cambridge MoleMate trial 1800 lesions due for completion Oct 2010. Further assessment of *Primary Care Screening Algorithm*.
2. Australian MoleMate trial 600 lesions. Trial completed. Verified *Primary Care Screening Algorithm*.
3. Judith Hunter. 600 lesions. Trial completed. Resulted in *Primary Care Screening Algorithm*.
4. Moncrieff. 348 lesions. Trial completed.

Primary Care Screening Algorithm – MoleMate: Key Clinical results

- Increased GP sensitivity from 67% to 95%
- Increased GP specificity from 75% to 83%
- GPs would become more sensitive to melanoma increasing the number of melanomas diagnosed
- GPs would refer less benign moles increasing the quality of referrals
- The health care system saves money by missing less melanomas and referring less benign lesions
- Proven to be easy to learn in less than 2 hours

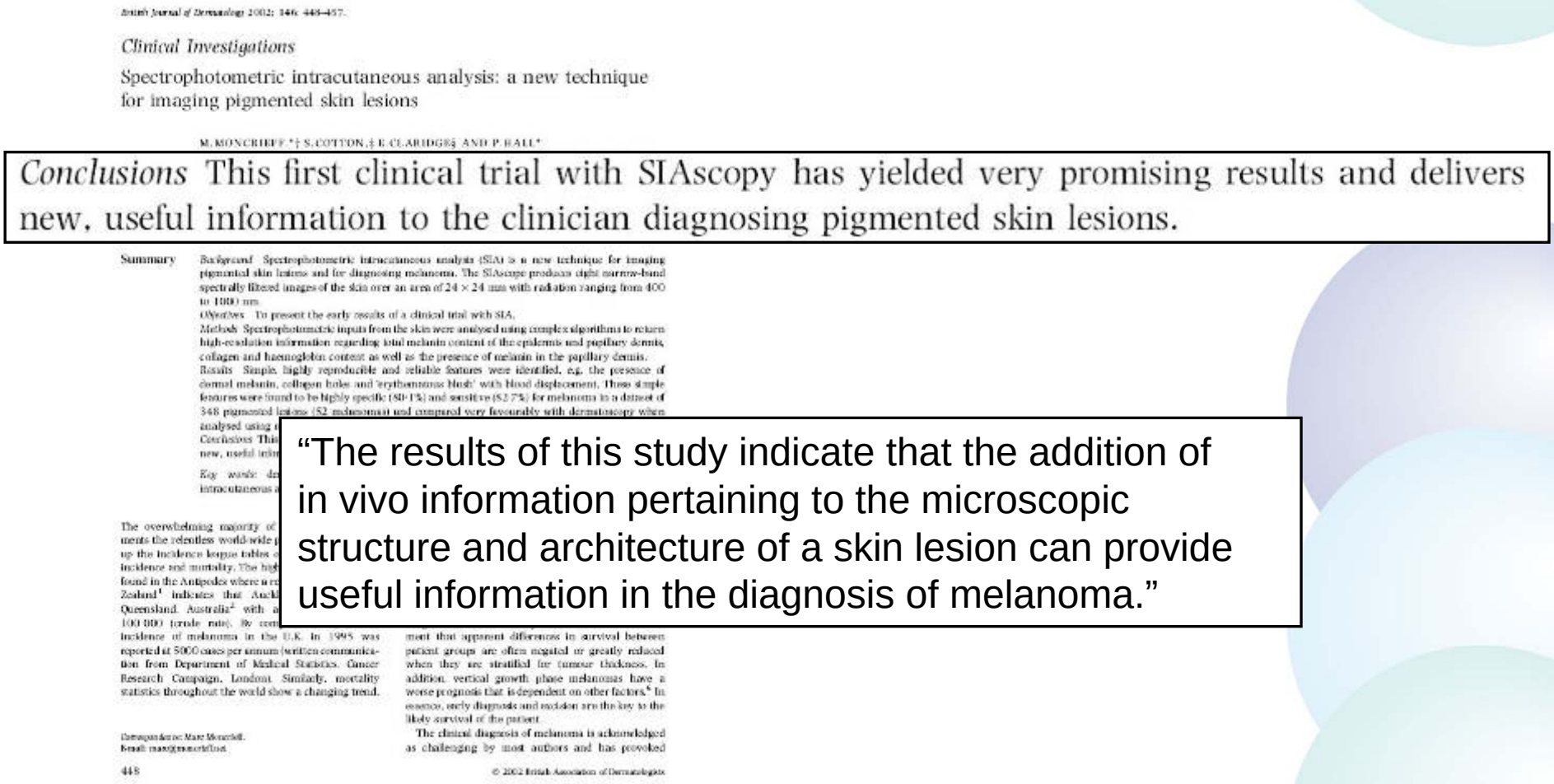
Key clinical publications

1. Moncrieff M, Cotton S, Claridge E, Hall P (2002) **Spectrophotometric intracutaneous analysis - a new technique for imaging pigmented skin lesions.**
   - *British Journal of Dermatology* 146(3), 448-457.
2. Wood A, Morris H, Emery J, Hall P. N, Cotton S, Prevost A. T. and Walter F. M. **Evaluation of the MoleMate training program for assessment of suspicious pigmented lesions in primary care.**
   - *Informatics in Primary Care, 2008, 16, pages 41-50.*
3. P J Matts, P J Dykes and R Marks. **The distribution of melanin in skin determined in vivo.**
   - *British Journal of Dermatology*. 2007, Volume 156, pages 620-628.

Pending clinical publications

1. Judith Hunter. **Development and validation of a scoring system for SIAscopic diagnosis of pigmented skin lesions in primary care.** Paper submitted to Family Practice Journal.
2. Australian MoleMate study 600 lesions. Study complete.
    - Paper being written

Conclusions - Spectrophotometric intracutaneous analysis: a new technique for imaging pigmented skin lesions.



British Journal of Dermatology 2002; 146: 448–457.

Clinical Investigations

Spectrophotometric intracutaneous analysis: a new technique for imaging pigmented skin lesions

M. MONCRIEFF,*† S. COTTON,‡ E. CLARIDGE§ AND P. HALL*

Conclusions This first clinical trial with SIAscopy has yielded very promising results and delivers new, useful information to the clinician diagnosing pigmented skin lesions.

Summary

Background Spectrophotometric intracutaneous analysis (SIA) is a new technique for imaging pigmented skin lesions and for diagnosing melanoma. The SIAscope produces eight narrow-band spectrally filtered images of the skin over an area of 24 × 24 mm with radiation ranging from 400 to 1000 nm.

Objectives To present the early results of a clinical trial with SIA.

Methods Spectrophotometric inputs from the skin were analysed using complex algorithms to return high-resolution information regarding total melanin content of the epidermis and papillary dermis, collagen and haemoglobin content as well as the presence of melanin in the papillary dermis.

Results Simple, highly reproducible and reliable features were identified, e.g. the presence of dermal melanin, collagen holes and 'erythaemmous blush' with blood displacement. These simple features were found to be highly specific (80·1%) and sensitive (82·7%) for melanoma in a dataset of 348 pigmented lesions (52 melanomas) and compared very favourably with dermatoscopy when analysed using

Conclusions This

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incidence of melanoma in the U.K. in 1995 was reported at 5000 cases per annum (written communication from Department of Medical Statistics, Cancer Research Campaign, London). Similarly, mortality statistics throughout the world show a changing trend.

ment that apparent differences in survival between patient groups are often negated or greatly reduced when they are stratified for tumour thickness. In addition, vertical growth phase melanomas have a worse prognosis that is dependent on other factors.[4] In essence, early diagnosis and excision are the key to the likely survival of the patient.

The clinical diagnosis of melanoma is acknowledged as challenging by most authors and has provoked

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"The results of this study indicate that the addition of in vivo information pertaining to the microscopic structure and architecture of a skin lesion can provide useful information in the diagnosis of melanoma."

Results - Spectrophotometric intracutaneous analysis: a new technique for imaging pigmented skin lesions.

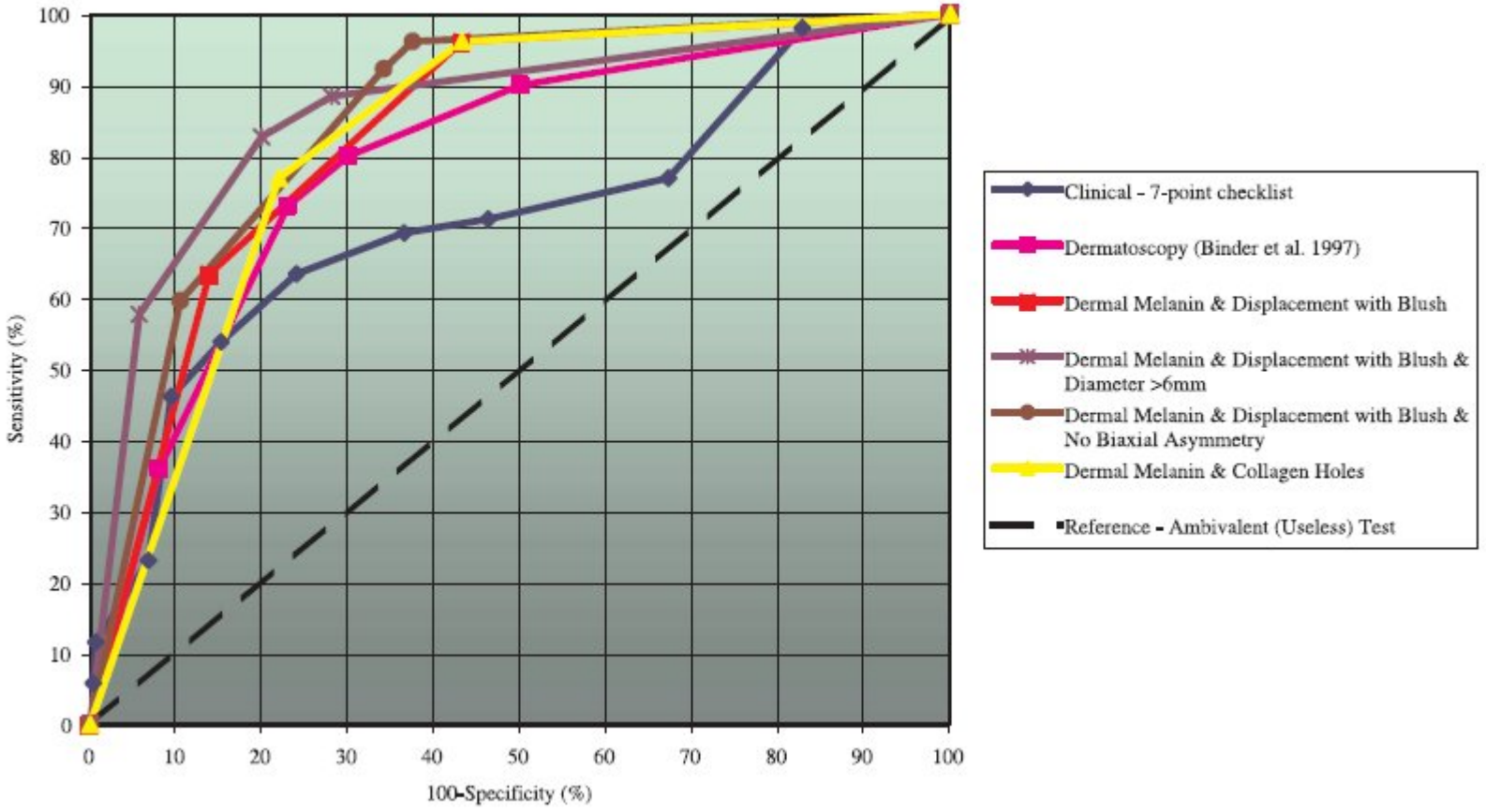
Table 3. Specificity and sensitivity analysis of SIAscopy features

Feature	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Positive LR	Negative LR
Single features						
Collagen holes	78·8 (66–87·8)	74·0 (68·7–78·7)	34·7	95·2	3·03 (2·39–3·85)	0·29 (0·17–0·49)
Blood displacement	75·0 (57·3–87)	70·3 (63–76·6)	30·7	94·1	2·52 (1·99–3·19)	0·36 (0·22–0·57)
Erythematous blush	75·0 (61·8–84·8)	65·5 (60–70·7)	27·7	93·7	2·18 (1·74–2·72)	0·38 (0·24–0·62)
Blood displacement with blush	63·5 (49·9–75·2)	84·8 (80·3–88·4)	42·3	93	4·17 (2·97–5·86)	0·43 (0·3–0·62)
Dermal melanin	96·2 (87–98·9)	56·8 (51·1–62·3)	28·1	98·8	2·22 (1·93–2·56)	0·07 (0·02–0·26)
Dermal melanin globules	88·5 (77–94·6)	66·6 (61–71·7)	31·7	97	2·64 (2·19–3·19)	0·17 (0·08–0·37)
Asymmetry	76·9 (63·9–86·3)	62·2 (56·5–67·5)	26·3	93·9	2·03 (1·65–2·5)	0·37 (0·22–0·61)
Biaxial symmetry	3·8 (1·1–1·3)	70·3 (64·8–75·2)	2·2	80·6	0·13 (0·03–0·51)	1·37 (1·25–1·5)
Biaxial symmetry not present	96·2 (87–98·9)	29·7 (24·8–35·2)	19·4	97·8	1·37 (1·25–1·5)	0·13 (0·03–0·51)
Combined features						
Dermal melanin + collagen holes	76·9 (63·9–86·3)	78 (73–82·4)	38·1	95·1	3·5 (2·67–4·52)	0·3 (0·18–0·47)
Dermal melanin + displacement with blush	96·2 (87–98·9)	56·8 (51·1–62·3)	28·1	98·8	2·22 (1·93–2·56)	0·07 (0·02–0·26)
Dermal melanin + displacement with blush + biaxial symmetry not present	92·3 (81·8–97)	65·9 (60·3–71)	32·2	98	2·71 (2·25–3·23)	0·12 (0·05–0·28)
Dermal melanin + displacement with blush + diameter ≥6 mm	82·7 (70·3–90·6)	80·1 (75·1–84·2)	42·2	96·3	2·75 (2·13–3·52)	0·25 (0·13–0·43)

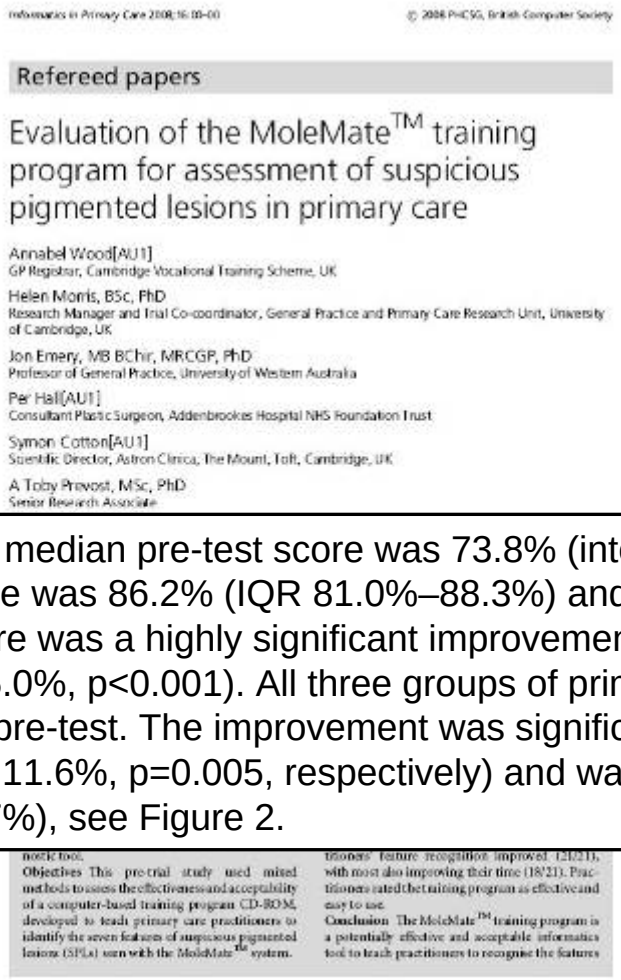
Sensitivity = true positive/(true positive + false negative); specificity = true negative/(true negative + false positive); positive predictive value (PPV) = true positive/(true positive + false positive); negative predictive value (NPV) = true negative/(true negative + false negative); positive likelihood ratio (LR) = sensitivity percentage/(100 − specificity percentage); negative LR = (100 − sensitivity percentage)/specificity percentage. Values in parentheses are the 95% confidence interval.

Results - Spectrophotometric intracutaneous analysis: a new technique for imaging pigmented skin lesions.

Receiver operator curve showing diagnostic results against dermatoscopy (current standard of care) and clinical assessment



Conclusions - Evaluation of the MoleMate training program for assessment of suspicious pigmented lesions in primary care



Refereed papers

Evaluation of the MoleMate™ training program for assessment of suspicious pigmented lesions in primary care

Annabel Wood[AU1]
GP Registrar, Cambridge Vocational Training Scheme, UK

Helen Morris, BSc, PhD
Research Manager and Trial Co-coordinator, General Practice and Primary Care Research Unit, University of Cambridge, UK

Jon Emery, MB BChir, MRCGP, PhD
Professor of General Practice, University of Western Australia

Per Hall[AU1]
Consultant Plastic Surgeon, Addenbrookes Hospital NHS Foundation Trust

Symon Cotton[AU1]
Scientific Director, Astron Clinica, The Mount, Toft, Cambridge, UK

A Toby Prevost, MSc, PhD
Senior Research Associate

Conclusion The MoleMate™ training program is a potentially effective and acceptable informatics tool to teach practitioners to recognise the features of SPLs identified by the MoleMate™ system. It will be used as part of the intervention in a randomised controlled trial to compare the diagnostic accuracy and appropriate referral rates of practitioners using the MoleMate™ system with best practice in primary care.

The median pre-test score was 73.8% (inter-quartile range (IQR) 67.9%–78.3%), the median post-test score was 86.2% (IQR 81.0%–88.3%) and all participants improved after completing the feedback session. There was a highly significant improvement between median pre- and post-test scores (10.0%, IQR 7.6% – 15.0%, p<0.001). All three groups of primary care practitioners had higher scores in the post-test than the pre-test. The improvement was significant for GPs and GPRs (median improvement 10.4%, p=0.012 and 11.6%, p=0.005, respectively) and was in the same direction for the small PN/PA group (median 15.7%), see Figure 2.

Results - Evaluation of the MoleMate training program for assessment of suspicious pigmented lesions in primary care

Figure 2 shows that a GP can become proficient in using the system following a two hour training session

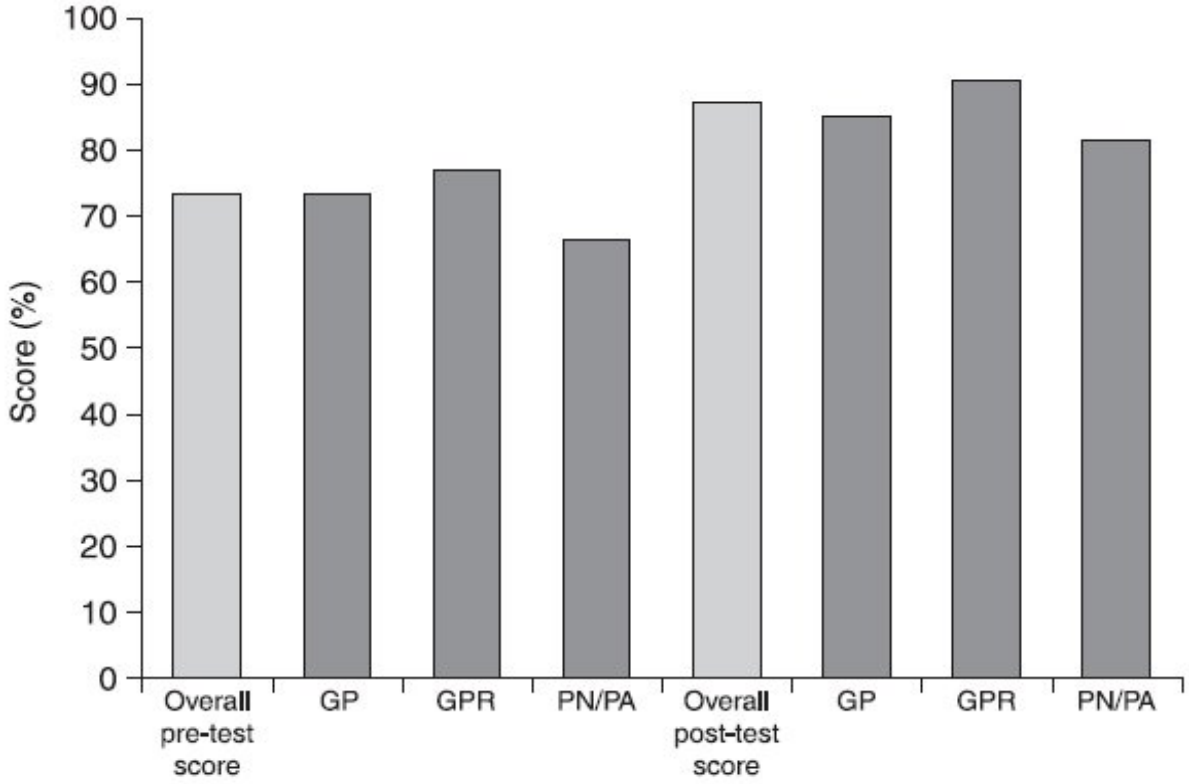
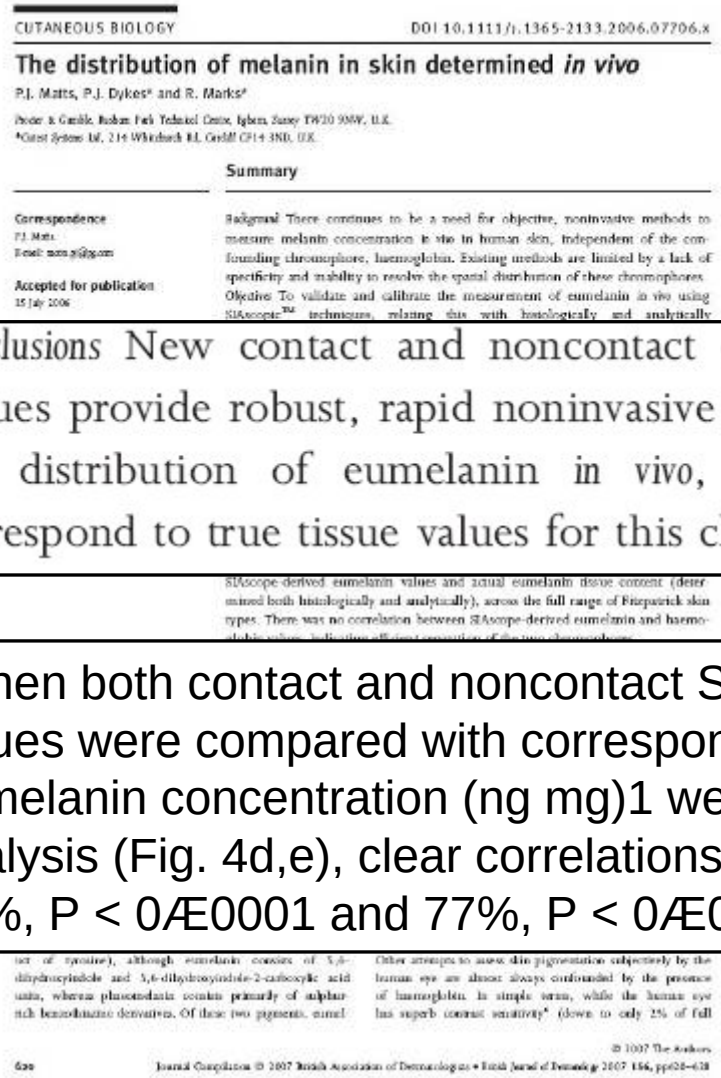


Figure 2 Comparing median pre- and post-test scores between GPs (*n*=8), GPRs (*n*=10) and PN/PAs (*n*=3)

Conclusions - The distribution of melanin in skin determined in vivo.



CUTANEOUS BIOLOGY DOI 10.1111/j.1365-2133.2006.07706.x

The distribution of melanin in skin determined *in vivo*

P.J. Matts, P.J. Dykes* and R. Marks*

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Summary

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Accepted for publication
15 July 2006

Background There continues to be a need for objective, noninvasive methods to measure melanin concentration in vivo in human skin, independent of the confounding chromophore, haemoglobin. Existing methods are limited by a lack of specificity and inability to resolve the spatial distribution of these chromophores.
Objective To validate and calibrate the measurement of eumelanin in vivo using SIAscopic™ techniques, relating this with histologically and analytically

Conclusions New contact and noncontact chromophore SIAscopic mapping techniques provide robust, rapid noninvasive measures of the concentration and spatial distribution of eumelanin *in vivo*, independent of haemoglobin, which correspond to true tissue values for this chromophore.

SIAscope-derived eumelanin values and actual eumelanin dioxe content (determined both histologically and analytically), across the full range of Fitzpatrick skin types. There was no correlation between SIAscope-derived eumelanin and haemo-

"When both contact and noncontact SIAscope mean greyscale values were compared with corresponding values for mean eumelanin concentration (ng mg)1 wet tissue) by simple regression analysis (Fig. 4d,e), clear correlations were obtained for each (r2 ¼ 84%, P < 0Æ0001 and 77%, P < 0Æ0001, respectively)."

tor of tyrosine), although eumelanin consists of 5,6-dihydroxyindole and 5,6-dihydroxyindole-2-carboxylic acid units, whereas pheomelanin contains primarily of sulphur-rich benzothiazine derivatives. Of these two pigments, eumel-

Other attempts to assess skin pigmentation subjectively by the human eye are almost always confounded by the presence of haemoglobin. In simple terms, while the human eye has superb contrast sensitivity* (down to only 2% of full

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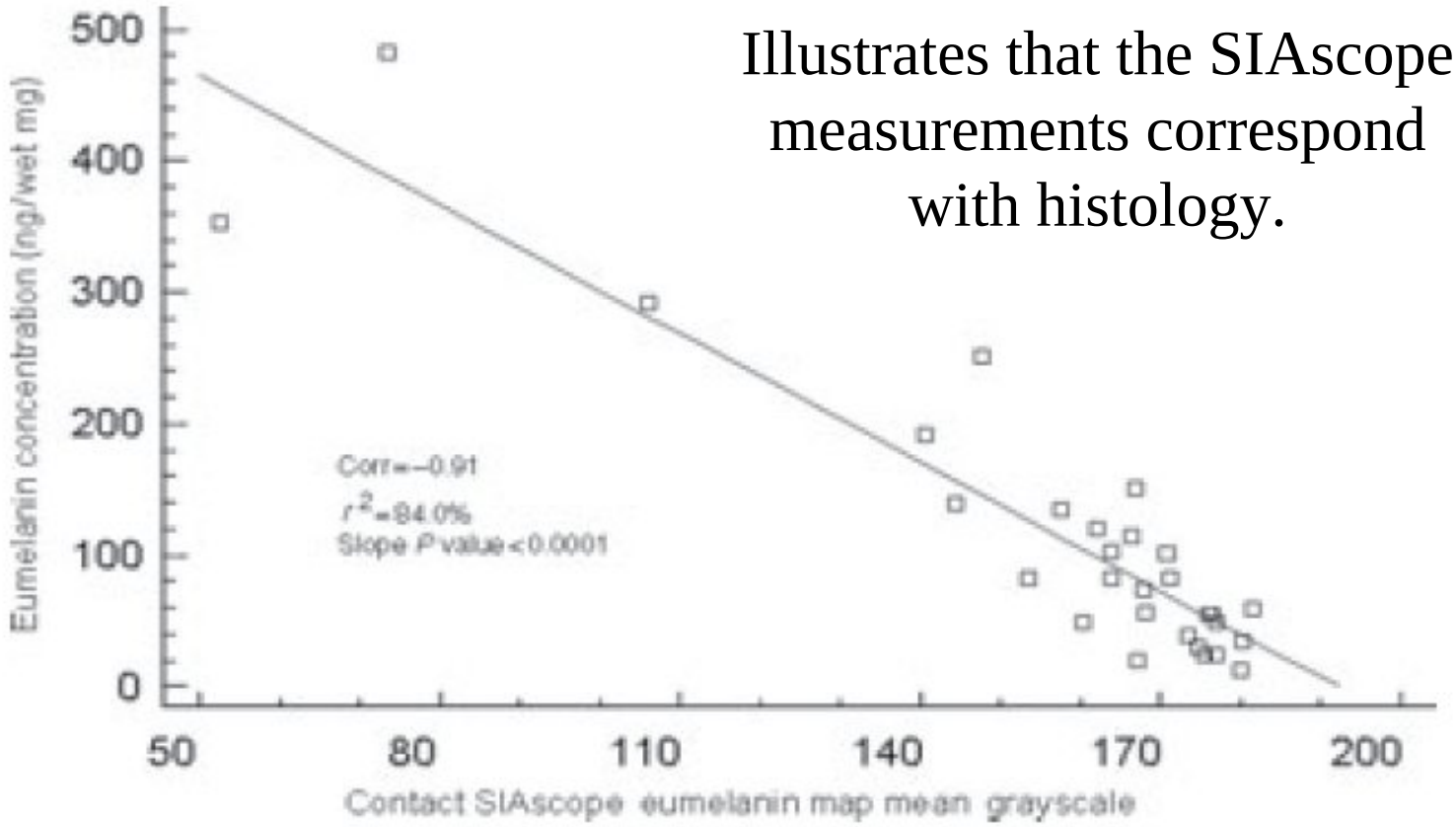
Results - The distribution of melanin in skin determined in vivo.



Illustrates that the SIAscope measurements correspond with histology.

Conclusions - Development and validation of a scoring system for SIAscopic diagnosis of pigmented skin lesions in primary care

Submitted for publication. Shows improvement over Moncrieff paper and is basis of both Australian and Cambridge trial.

"The new PCSA was tested against the 208 lesions in the Validation Lesion dataset, which included 6 suspicious lesions and two melanomas. The performance of the PCSA is presented in Table 3. Simulation modeling with a higher prevalence of melanomas in the dataset confirmed high sensitivity and specificity for the diagnosis of melanoma with the PCSA (Figure 4). The mean sensitivity and specificity of the PCSA for the diagnosis of melanoma was 94.0% and 83.5% respectively."

Conclusions - Spectrophotometric Intracutaneous Analysis (SIAscopy)

25 **Spectrophotometric Intracutaneous Analysis (SIAscopy)**

Paul J. Matts
Procter & Gamble, Egham, U.K.
Symon D. Cotton
Astron Clinica, Cambridge, U.K.

CONCLUSION

Whereas even modern high-resolution imaging still only describes skin appearance, SIAscopy explains it by separating the molecular components responsible for that appearance in the first place. In this way, SIAscopy provides the clinician and researcher alike with a powerful new tool to both measure and characterize human skin.

at all pixel locations. This approach requires two inputs: the first is a set of parameters that characterize a given tissue by specifying its components, their optical properties, their quantities, and their geometry; the second is a method for computing the remitted spectra from the given parameters.

CONSTRUCTION OF THE MATHEMATICAL OPTICAL MODEL OF HUMAN SKIN

The skin consists of a number of layers with distinct functions and optical properties as shown in Figure 1. Light incident to the skin penetrates the superficial layers, and while some of it is absorbed, much is remitted back and can be measured.

The stratum corneum is a protective layer consisting of keratinized squamous cells (corneocytes), and it varies in thickness across the body. Apart from forward scattering of incident light, it is optically neutral (4). The epidermis is composed of several layers of differentiating keratinocytes and also contains pigment-producing cells, melanocytes, and their product, the melanins. The melanins are complex heteropolymers that strongly absorb short-wavelength radiation, i.e., light in the blue part of the visible spectrum and radiation in the ultraviolet (UV) waveband (in the latter case, therefore, acting as a filter to protect the deeper layers of the skin from the well-documented harmful effects of UV radiation). Within the epidermal layer, there is very little scattering and that which does occur is forward directed. This means that all light not absorbed by melanin can be considered to pass into the dermis. The dermis is composed largely of collagen fibers, and in contrast to the epidermis, it contains sensors, receptors, blood vessels, and nerve endings. Hemoglobin, present in blood vessels within the dermis, acts as a selective absorber of light. The dermis consists of two structurally different layers, papillary and reticular, which differ principally in the size of collagen fibers. The scale of the collagen fibers in the papillary dermis (diameter of an order of magnitude less than the incident visible light) makes this layer highly scattering, i.e., any incoming light is scattered with a proportion directed back toward the skin surface. The scatter is greatest at the blue end of the spectrum, decreasing with increasing wavelength

Cambridge NHS trial

Addenbrooke's NHS Trust

NHS ASTRON CLINICA
THROWING LIGHT ON SKIN HEALTH

NHS National Institute for Health Research
School for Primary Care Research

UNIVERSITY OF CAMBRIDGE
General Practice and Primary Care Research Unit
Department of Public Health & Primary Care

- Institute of public health Cambridge University UK
- 1800 Lesions
- 15 GP practices
- 16 months
- Due to complete Oct 2010
- Will report on both clinical results and cost savings to the health care system
- As of 18 August 2009: 700 patients/750 lesions recruited

UK Political Radar

CANCER RESEARCH UK

DH Department of Health

January 2009
Volume 2, Issue 1

NAEDI Newsletter

National Awareness and Early Diagnosis Initiative

Inside this issue:

Welcome to the second edition of the NAEDI newsletter. It's been a busy few months since the first issue back in July last year – not least because of the launch conference that took place in November. The day attracted around 300 delegates and was so popular that, reluctantly, we had to turn people away. Feedback from the event has been overwhelmingly positive – many thanks to all who gave their time to make the day such a success.

“Promoting earlier presentation”

The NAEDI Launch Conference

Overview of the National Awareness and Early Diagnosis Initiative

Professor Mike Richards, national cancer director, gave the opening and concluding presentations of the conference.

In his first, he spoke of the core hypothesis on which NAEDI is based – ‘delays’ can occur at different steps in the pathway to diagnosis. And because of delay, cancer in the UK is more often diagnosed at an advanced stage, contributing to poor survival rates and, ultimately, a significant number of deaths that could be avoided. Professor Richards then briefly outlined each of the NAEDI work streams and updated on progress that’s been made.

The seven work streams

- Awareness measurement
- Promoting earlier presentation
- Reducing primary care delay
- Key messages
- Review the evidence base
- International comparisons
- New research

“Promoting earlier presentation”

The NAEDI Launch Conference

Overview of the National Awareness and Early Diagnosis Initiative

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The seven work streams

- Awareness measurement
- Promoting earlier presentation
- Reducing primary care delay
- Key messages
- Review the evidence base
- International comparisons
- New research

NICE guidance on cancer services update November 2009, Draft for consultation

- "It is estimated that **24% of primary care workload** is related to the diagnosis and **management of skin conditions**, including skin lesions."
- "Approximately **88% of two-week wait urgent referrals for suspected skin cancer turn out to be non-malignant**, highlighting a need for better training in primary care on the recognition of skin cancer."