Chromophore Mapping: a New Technique to Characterize Aging Human Skin, In Vivo

Paul J. Matts Ph.D[1], Jeremy Carey Ph.D[2] & Symon D. Cotton Ph.D[2]
[1]The Procter & Gamble Company, Rusham Park Technical Centre, Egham, Surrey, UK; [2]Astron Clinica Ltd, Cambridge, UK

INTRODUCTION

It is simple fact that we judge one other, consciously or unconsciously, based in part on the aesthetic appearance of our outer integument, "skin". As the human retina responds to a narrow bandwidth of the electromagnetic spectrum (so-called "visible light", a nominal 400-700nm), the interaction of these wavelengths with skin, therefore, is of primary importance in our understanding of the way we perceive others and are ourselves perceived. A modern understanding of cutaneous optics is based largely on the development of increasingly-sophisticated mathematical models to explain the interaction of light with skin.. This understanding of cutaneous light transport highlights the surprising fact that normal human skin appearance is driven primarily by surface topography and only three internal chromophore components, that is, the concentration and spatial distribution of melanin, haemoglobin and collagen. Whereas there are a plethora of methods to characterise and quantify skin surface topography, chromophore mapping remains a remarkably un-researched area.

A new technique "Spectrophotometric Intracutaneous Analysis" ("SIA") has been developed, commercialised and shown to have excellent sensitivity and specificity in the early identification of malignant melanoma in human skin[1,2]. The technique is based upon a unique combination of dermatoscopy and contact remittance spectrophotometry. The SIA hardware comprises a hand-held imaging probe, attached by umbilical to a laptop computer, that is placed in contact with the skin surface. High-intensity LEDs illuminate the skin surface with four consecutive discreet wavebands between 400nm and 1000nm, spanning the visible spectrum and a small range of near infrared radiation. A digital image is captured for each waveband. Custom SIA algorithms then solve the complex relationship that exists between R-G-B-NiR "colour-space" and melanin-haemoglobin-collagen "histology-space", using a sophisticated model of cutaneous light-transport[3,4]. Since there is a proven one-to-one mapping between colour-space and chromophore parameters[5,6], individual chromophore parameter values can be retrieved from the model, given the colour vector obtained from each point in a colour skin image. The magnitude of each chromophore parameter is displayed at each pixel location in a separate image, giving three parametric maps: epidermal melanin, dermal haemoglobin and collagen (a dermal melanin map is also provided as a diagnostic criterion for melanoma). In short, the SIA technique is able to obtain a high-resolution white-light image of the skin over a 12x12mm area and four additional maps that display the concentration of epidermal melanin and haemoglobin, collagen and melanin in the papillary dermis, pixel by pixel.

METHODS

Whilst the SIA technique has proven highly valuable in the measurement of diseased skin, namely the early diagnosis of malignant melanoma, it was not known whether it could be used to successfully map chromophores in normal skin in order to explain changes in human cutaneous colouration with age. This present poster, therefore, describes a study to evaluate the utility of the SIA technique for this purpose:

Subjects: 400 Caucasian female subjects (Fitzpatrick skin types I-III) aged 10-70 with normal, un-diseased skin were recruited in Reading, UK. Subjects were recruited so that they fell equally across the 10-70 age range into 12 cohorts of 5 years each, containing approximately 33 subjects per cohort (i.e., Group 1, 10-15 years; Group 2, 15-20 years, etc.).

Measurement Site: the skin between the thumb and the first finger of each subject's right hand was used as the measurement site for this study. The dorsal hand was chosen as it has been shown to receive approximately one half of the dose of erythemally-effective solar UV radiation relative to vertex[7] (the face receives only one third). The dorsal hand, therefore, represented a site where we had confidence that both chronological effects and actinic damage to the chromophores of interest in this study should be well-expressed.

Measurements: Subjects were equilibrated for 20 minutes in a controlled atmosphere ($20+1^{o}C$; 50+10%RH). The measurement site on the subject's right dorsal hand was then lightly sprayed with a 20% (v/v) aqueous ethanol solution (to act as a "matching fluid"). SIA measurements were then taken; each lasted approx 6 seconds.

Image analysis: The SIA parametric maps ("SIAgraphs") constituted 8-bit 1024x1024 256 level greyscale maps of chromophore concentration in PNG image file format and, as such, were readily amenable to sophisticated image analysis techniques for calculation of a variety of relevant endpoints. The following analyses were undertaken: (a) mean global grey-scale (corresponding to mean chromophore concentration in the imaged skin field) (b) internal image standard deviation (corresponding to an index of chromophore homogeneity) and (c) for melanin SIAgraphs, contiguous cluster analysis (to identify pigmented spots) and subsequent feature (spot) count and mean spot area calculations.

Image analysis interval data were treated using multi-factor ANOVA techniques with age as the main factor (grouped per 5-year cohort). Results constituted the SIAgraphs themselves and plots of image analysis LSD means and errors vs respective age group, shown in Figure 1 bellow.

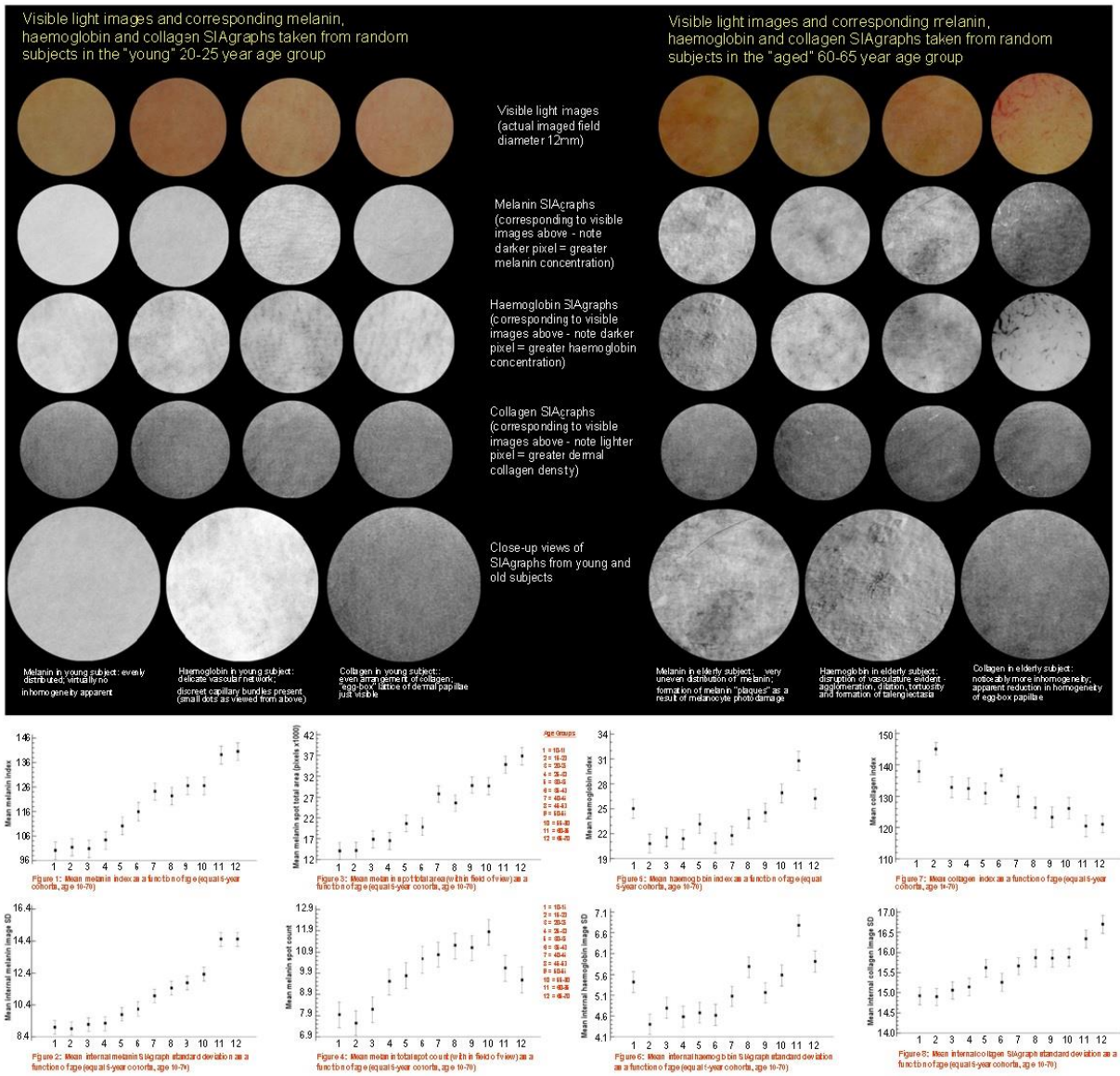

Figure 1.

DISCUSSION

Visual inspection of the chromophore SIAgraphs of young and aged subjects reveal a dramatic contrast, particularly for the melanin and haemoglobin chromophores. In short, in young skin, these chromophores are distributed in an extremely homogeneous manner, consistent with the delicate, even palette of youth. With age, a significant increase in both total concentration and inhomogeneity is evident for both chromophores. This is wholly consistent with the known changes in these chromophores as a function of actinic ageing - namely the accumulation of damaged melanogenic units (producing hyper-melanotic lesions such as solar lentigos, diffuse hyperpigmentation and hypo-melanotic lesions such as idiopathic guttate hypomelanosis) and damaged vasculature (including telangiectasia and low-grade purpura)[7,8]. These visual observations were confirmed emphatically by objective analysis of the SIAgraphs by custom algorithms. Results confirmed an apparent "lag" phase for total skin concentrations of both chromophores (lasting until approx age

30 for melanin and 40 for haemoglobin), after which there was a steady increase in each chromophore total concentration. There was also a concurrent progressive increase in inhomogeneity of each pigment. More detailed analysis of the melanin SIAgraphs revealed a progressive accumulation of melanin "spots" across a lifetime, with a linear increase in total spot area and an apparent merging of spots at approximately age 50-55 (continued area increase with parallel drop in spot count).

Visual inspection of the collagen SIAgraphs reveal an apparent overall loss with age both of density and the fine "egg-box" lattice attributed to dermal papillae. Once again, these subjective observations are supported by analysis of the SIAgraphs. A progressive decrease in collagen density was noted across the entire age span, accompanied by a progressive decrease in homogeneity. These trends fit extremely well with the known progressive atrophy of dermal papillae and total dermal collagen bulk, consistent with intrinsic and extrinsic ageing[9]. The observations of this current study were predicted and modeled by one of the present authors[10]. A model was proposed that described human skin texture and color changes with age in the unorthodox terms of "amplitude" and "frequency". The principle components of human skin color, namely melanin and haemoglobin, both display overall increases in total concentration (increased "amplitude") and heterogeneity (decreased "frequency") as a function of chronological / actinic ageing. Effective treatments to improve appearance, therefore, need to reverse this effect. Overall, therefore, these data appear to confirm chromophore mapping using the SIA technique as a remarkable new tool to characterize and *explain* the visual appearance of ageing skin.

1. Moncrieff M, Cotton S, Hall PN & Claridge E, Extracting the diagnostic features if skin surface microscopy for pigmented skin lesions using spectrophotometric intracutaneous analysis. *Medical Image Understanding and Analysis*, 49-52, 2000

2. Moncrieff M, Cotton S, Claridge E & Hall P, Spectrophotometric intracutaneous analysis - a new technique for imaging pigmented skin lesions. *Brit. J. Derm.* 146(3), 448-457, 2002

3. Claridge E, Cotton S, Hall P &Moncrieff M, From colour to tissue histology: Physics based interpretation of images of pigmented skin lesions. *Medical Image Computing and Computer-Assisted Intervention - MICCAI'2002. LNCS 2488, vol I, 730-738, 2002*

4. Claridge E, Preece, S, An inverse method for the recovery of tissue parameters from colour images. *Information Processing in Medical Imaging*, LNCS 2732, 306-317, 2003

5. Cotton, S.D., Claridge, E. (1996) Developing a predictive model of human skin colouring. *Proceedings of the SPIE Medical Imaging*, vol 2708, 814-825, 1996

6. Cotton S, Claridge E, Hall PN, A skin imaging method based on a colour formation model and its application to the diagnosis of pigmented skin lesions. *Proceedings of Medical Image Understanding and Analysis* 99, 49-52, 1999

7. Griffiths, C.E.M., The clinical identification and quantification of photodamage, *Brit. J.Dermatol*., 127 (Suppl. 41), 37-42, 1992

8. Gilchrest, B.A., Blog, F.B. and Szabo, G. Effects of ageing and chronic sun exposure on melanocytes in human skin. *J. Invest. Dermatol*. 73, 141-143, 1979

9. Sauermann, K, Clemann, S, Jaspers, S, Gambichler, T, Altmeyer, P, Hoffmann, K, Ennen, J, Age related changes in human skin investigated with histometric measurements by confocal laser scanning microscopy *in vivo*, *Skin Res. Tech*., 8, 52-56, 2002

10. Matts, PJ, Understanding and measuring the optics that drive visual perception of skin appearance, in *The Essential Stratum Corneum*, Dunitz, 213-222, 2002

This work was supported in full by The Procter & Gamble Company