

Assisting diagnosis of melanoma through the “noninvasive biopsy” of skin lesions

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Assisting diagnosis of melanoma through the “noninvasive biopsy” of skin lesions

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Abstract. In order to ensure a good prognosis, malignant melanoma needs to be diagnosed whilst the level of invasion of the tumour within the dermis is small. As an aid to clinicians undertaking this diagnosis a noninvasive system is presented which through the acquisition of a number of images recovers various internal histological information. The efficacy of this approach is assessed through a comparison of the predicted histology with that found through biopsy. The results show that useful histological information can indeed be recovered with particularly sensitive information regarding the dermal invasion of melanocytes.

1 Introduction

Melanoma is a malignant tumour of the melanin forming cells, the melanocytes; when a melanoma invades these melanocytes descend from the dermo-epidermal junction into the dermis. The depth of this invasion, or thickness, is considered by MacKie [1989] to be “the single most important prognostic factor”. Delaunay [1992] states further that “the relationship between thickness and survival is progressive but not continuous especially at the extremes: under 0.76mm thick, more than 95% of the tumours are curable; over 5 to 6 mm thick, most tumours are fatal”. To ensure a good prognosis, therefore, melanomas must be identified at an early stage, i.e. when they have not invaded deeply.

As an aid to the diagnosis of malignant melanoma, and measurement of invasion depth, Marshall [1980] claims that a histological “microscopical examination of tumour tissue is the most reliable method”. However, as he goes on to discuss “the hazards associated with ‘invasive’ methods of diagnosing pigmented lesions by incisional biopsy, or by complete local excision, have underlined the need to develop dependable laboratory procedures or tests which will make a precise differentiation between malignant and benign pigmented lesions”. There is a volume of published work using various classification algorithms which aim to address this by segmenting sets of lesion images into those which are benign and malignant. Whilst these report varying levels of success they suffer from a lack of explanation of those cases reported as false negatives, thus leading to a lack of confidence in their clinical use.

The work presented here explores the efficacy of utilising knowledge of both the structure and the optics of human skin to recover internal histological information from the external appearance of a lesion. This histological data is then presented in the form of a “noninvasive biopsy” assisting, but leaving, the final diagnosis to the clinician. By taking this approach it is hoped to develop techniques approaching the gold standard of a “microscopical examination” without the inherent problems associated with biopsy. As this approach is based on an understanding of the optical properties of human skin it is possible to identify the limitations of the system. Knowledge of this then allows such cases to be identified to the clinician, thus increasing their confidence in the results and their faith in a diagnosis.

In the studies presented here predictions of internal histology are compared with the actual histology obtained through biopsy. The results of this are very promising with many histological parameters being measurable. In particular, there is a high level of sensitivity in identifying regions where melanocytic invasion has occurred even when the depth of this invasion is small. As the ability to recognise lesions suffering these early stages of invasion is of such prognostic importance it is hoped this may prove a useful tool in the monitoring and evaluation of melanoma.

2 The model of human skin colouration

A previous paper [Cotton and Claridge 1996] presented a model of colour formation within normal human skin. The model is based on the Kubelka–Munk theory of scattering and absorption within inhomogeneous materials and the physics pertaining to their optical properties. By considering the skin to be a layered

construction of such materials: the stratum corneum, epidermis, papillary dermis and reticular dermis³, and by exploiting the physics related to the optical interface between these layers, the model generates all possible colours occurring within normal human skin. In particular, the model predicts that all skin colours have to lie on a simple curved surface patch within a three-dimensional colour space bounded by two physiologically meaningful axes, one corresponding to the amount of melanin within the epidermis and the other to the amount of blood within the dermis. These predictions were successfully verified by comparing the CIE LMS coordinates⁴ of a representative, cross-racial sample of forty skin images with the LMS coordinates predicted by the model.

The model postulated that abnormal skin conditions would cause skin colouration to deviate from the predicted surface in the colour space and this was exploited further [Cotton et al. 1997]. In particular, this paper demonstrates that it is theoretically possible to derive detailed information about the skin architecture (i.e. the thickness and pigment composition of the skin layers) grossly comparable to the information available through the microscopical examination of tumour tissue, but without incurring the problems inherent in obtaining a biopsy.

In summary, this paper predicted that if, provided with one colour and two infrared images of a lesion, it should, theoretically, be possible to recover information pertaining to the amount of epidermal melanin, dermal blood and papillary dermal thickness along with the presence, depth of penetration and concentration of any melanocytes existing within the papillary dermis for every point within the image. This information can then be presented in a variety of means ranging from showing the variation of one parameter over the lesion to combining the information to provide a full three-dimensional representation of the lesion.

The two infrared images, one slightly further into the infrared than the other, are required to allow quantification of the papillary dermal thickness. This parameter has a profound effect on the colouration of a lesion [Cotton et al. 1997] which can lead to “lesions only varying in this parameter being wrongly classified [as being suspect]”. Indeed it is possible to find malignant invasive melanomas with an identical colouration to that of simple warts. The paper goes on further to suggest that “this result casts doubt on the effectiveness of using purely colour information in the diagnosis of malignant melanoma”.

3 Comparing predicted histology with that found through biopsy

As a means of determining the validity of this approach a set of lesion images were obtained by Mr Per Hall using one camera loaded with colour slide film and another loaded with Kodak High speed infrared film. These lesions were then excised and biopsies were performed by Dr Jeremy Rashbass. In brief, the aim of this experiment is to compare the actual biopsies, and information obtained from examination of these biopsies, with that predicted by the system.

In a discussion of the results the three lesions shown in figure 1 will be studied. These are: case 1, a superficial spreading melanoma; case 2, a noninvasive lentigo maligna, and case 3, a compound naevus. The histological reports identify the lentigo maligna as showing “no invasion into the underlying dermis”, whilst both the melanoma and compound naevus show “cells [melanocytes] in the dermis”. It should be noted that although the melanoma and compound naevus both exhibit dermal melanocytes, the compound naevus is benign and indeed this is true of many skin conditions. It is worth, therefore, reiterating that, at this stage, the actual diagnosis is performed by a clinician with the system solely providing useful histological information. Cross sections showing the pathology of the malignant melanoma and lentigo maligna are shown in figure 2 where the epidermis is seen as a continuous dark band with the stratum corneum above and the dermis below. Within the melanoma invading melanocytes can be clearly seen as the dark areas existing within the dermis.

The first stage in processing these images is to utilise the infrared images to recover the thickness of the papillary dermis. This information in itself may prove useful in the formation of a diagnosis with, for example, Roses et al. [1983] reporting that “the morphological evidences of regression are marked thickening and fibrosis of the papillary dermis”. Following this, a transformation can be applied to the colour lesion images resulting in their appearance assuming the papillary dermal thickness was constant. This then removes the previously discussed problem of lesions varying in this parameter being confused with cases where melanocytes exist within the papillary dermis. A comparison of this transformed colouration with that predicted for human skin [Cotton et al. 1997] can now be performed thus allowing areas where melanocytes exist within the

³The dermis is subdivided into two histologically distinct layers the papillary dermis and reticular dermis. The papillary dermis is situated directly below the epidermis and is distinguishable from the lower reticular dermis by the differing structure of its collagen fibres.

⁴This refers to CIE “Commission Internationale de l’Eclairage” colourimetric system. which defines three colour-matching functions L, M and S.

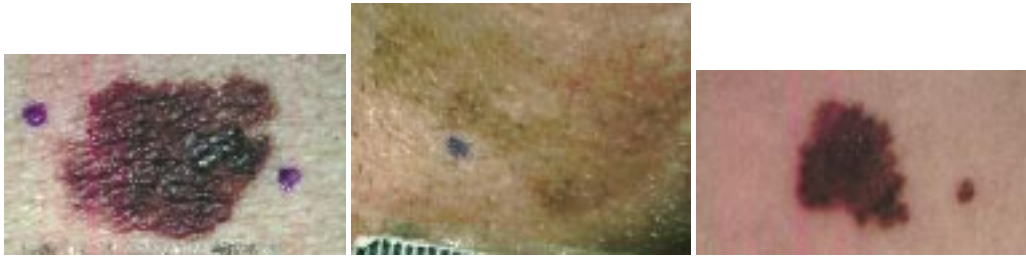


Figure 1: The lesions analysed. From left: case 1, superficial spreading melanoma; case 2, non invasive lentigo maligna and case 3, compound naevus.

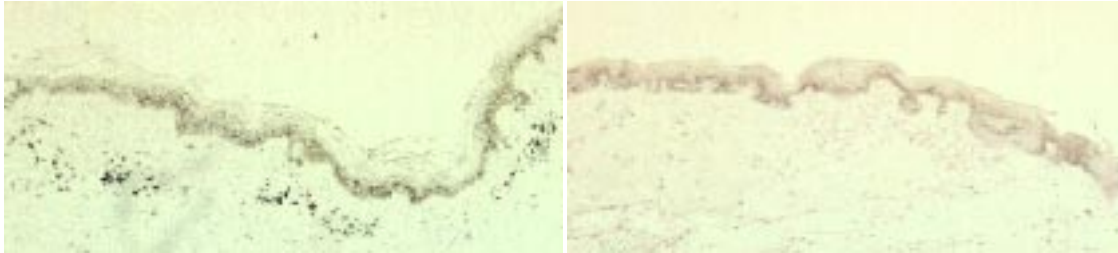


Figure 2: Pathology of, left, the malignant melanoma and, right, the lentigo maligna. Invading melanocytes can be clearly seen within the melanoma as the dark areas existing within the dermis.

papillary dermis to be identified. These can be seen in figure 3 where the size of the deviation from the predicted skin colouration is shown with high values indicating the presence of dermal melanocytes.

Following the identification of regions where melanocytes exist within the papillary dermis the system can be used to quantify both the concentration of said melanocytes and their penetration within the papillary dermis. This concentration is shown in figure 4 with areas of high melanocyte concentration shown as bright areas. As the border of melanocytic invasion is identified, this also allows investigation of the differing invasive growth patterns of benign and malignant lesions. Points of note are the lack of any invasion within the lentigo maligna and the differing appearance of the invasive pattern pertaining to the melanoma and compound naevus.

Quantification of the invasion depth is harder with the current system being limited to being able to “measure” only a certain distance into the papillary dermis. This then results in measures for dermal penetration in the form of “at least 0.3 mm”. It should be noted that due to the scattering properties of the papillary dermis melanocytes existing deeper than this will still be identified, but the accuracy to which this invasion depth can be measured is less. This difficulty can be predicted from an analysis of the underlying theory and requires a marked increase in the sensitivity and accuracy of the image acquisition system to increase this limit. It should be stressed that this is purely a practical problem which could be overcome through the development of such a suitable system. Even without such improvements, however, the system is extremely sensitive in identifying and quantifying the depth of melanocyte intrusion in the early stages of invasion.

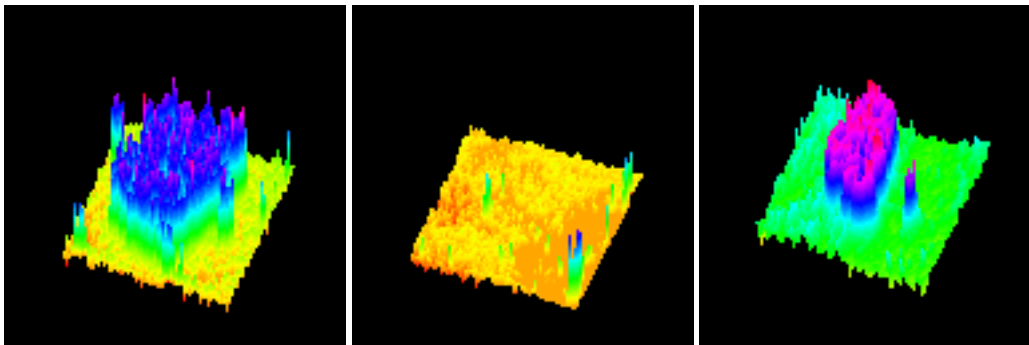


Figure 3: “Cottongrams” showing areas where melanocytes exist within the papillary dermis. From left: case 1, case 2 and case 3.



Figure 4: Concentration of melanocytes within the papillary dermis with concentration represented as brightness. From left: case 1, case 2 and case3.

The result of this analysis is to agree with the histological information obtained through biopsy regarding the lack of invasion within the lentigo maligna and the presence of invasion within the melanoma and compound naevus. Regarding diagnosis the shape of this invasive border and the manner in which the concentration varies over the lesion is extremely useful.

4 Conclusion

The efficacy of quantifying various internal histological features through a “noninvasive biopsy” with the aim of assisting clinicians in the diagnosis and monitoring of suspicious skin lesions does indeed seem justified. In particular, the high sensitivity of the system with regard to the identification and quantification of dermal invasion should assist in the early diagnosis of such cases and as such markedly improve their prognosis.

It is not suggested that this approach should replace biopsy as the method of diagnosis for there are numerous features important to formulating a diagnosis that are only available through a microscopical examination of tumour tissue. However, it is envisaged assisting in increasing the sensitivity achieved within the initial screening process which leads to the selection of lesions referred for biopsy. As the system is based on a set of lesion images which could be obtained at a clinic local to the patient, this may also allow a greater proportion of screening to take place at such clinics.

It could be of particular importance in the monitoring of suspicious lesions. For instance, lentigo maligna typically present as large brown macules often on the face and can exist in a benign state for many years. Currently, these are monitored either visually or by standard photographic means with the aim of observing changes which may suggest a progression to invasive lentigo maligna melanoma. By monitoring these using the described system regions of invasive growth could be identified at an early stage assisting greatly in this monitoring process.

This paper concentrated on the use of information relating largely to lesion invasion. As described earlier, however, there are many other histological parameters made available by the system and these could also contribute towards forming a diagnosis. For instance variations in the amount of epidermal melanin and signs of regression are sometimes indicative of malignancy and as such would provide useful information to a clinician.

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