A non-invasive in-vivo system for recovering architectural and compositional information to guide the management of non-melanoma skin cancer

Symon Cotton[1] Peter Bjerring[2]

[1] Astron Clinica, Cambridge [2] Marselisborg Hospital, Aarhus, Denmark

Basal Cell Carcinoma and Squamous Cell Carcinoma are the most common forms of skin cancer. Many forms of treatment are now available for both of these diseases, ranging from topically applied drugs to surgery. The best choice of treatment, however, depends on whether the cancer is superficial, infiltrating or invasive with the decision being preferably made at primary care level. This paper develops a technique for differentiating between these forms of the disease, based on the optical properties on the tissue, which can be implemented utilizing low cost imaging devices.

1 Introduction

Non-melanoma skin cancer accounts for 90%[1] of skin cancers. Within the grouping of non melanoma skin cancer there are two pre-dominant forms Basal Cell Carcinoma (BCC) and Squamous Cell Carcinoma (SCC) with approximately 75%[2] being BCC's and 20%[3] being SCC's: indeed BCC is not only the most common form of skin cancer it is also the most common form of cancer in humans; it is estimated 1 in 3 Americans will develop a BCC during their life time.

Both forms of cancer are believed to be linked to Ultra Violet[4] exposure causing damage to the DNA of cells existing within the upper layers of the skin. The cancers typically cause local destruction of tissue but although they have the power to metastasise the percentage chance of metastasis is far lower than for melanoma, the more aggressive form of skin cancer.

A large number of different treatment options are now available for non-melanoma skin cancer ranging from surgical excision to light activated drugs that destroy the tumour, to locally applied cryotherapy. The decision on which treatment option is the most suitable depends largely on at which stage the cancer is in its life cycle and the site of the tumour. Both BCC's and SCC's begin life with the tumour cells confined to solely to the epidermis – SCC's are commonly called Actinic Keratosis at this stage – a stage at which they are histologically referred to as "superficial". The cancer can then penetrate and populate the dermis at which point a histologist would refer to them as "infiltrating" or "invasive". Non-surgical treatment has been shown to be effective for treating superficial cancers but is far less effective for infiltrating or invasive cases when surgery is the best option. There are many reasons to prefer a non-surgical intervention namely a better cosmetic result is often achieved and the treatment can be applied at a primary care level – something which is important when the large numbers of these cancers are considered. However, it is also not desirable to treat invasive non-melanoma cancer in such a manner as there is a possibility that not all the cancer will be destroyed therefore requiring surgery at a later stage.

Currently there is no reliable method available to assess whether such a cancer is superficial that can be applied widely enough to reach practising dermatologists and general practice. Confocal microscopy[5] can be used to view the malignant cells and indeed assess whether they are intra-epidermal or not but both the high cost and time required to assess a patient have so far confined its use to research institutions. A useful tool would therefore be one that is both effective in distinguishing superficial from infiltrating and invasive non-melanoma skin cancer and which is also applicable to a primary care setting.

2 Method

This paper outlines one such possible tool based on the interaction of light with tissue. Skin can be considered to be a layered structure with the epidermis lying over the dermis. The junction between the two layers is called the dermo-epidermal junction and anchored to this layer are cells called melanocytes that produce the pigment melanin. It is these melanocytes which dictate the colour of our skin with black skin having the same number of melanocytes as white skin but the production of melanin being higher. The melanin produced is taken up by keratinocytes in the epidermis which migrate to the surface before flaking and being discarded. The dermis, in contrast, is formed largely from collagen fibres which are tightly bound together and blood vessels.

Optically both layers exhibit markedly different properties most notably in the amount to which they scatter light. The epidermis is a low scattering regime in contrast to the dermis where the collagen fibres are on a comparable scale with the wavelengths of visible and near infrared light resulting in a strong interaction and high scattering.

Light striking the outer layer of the skin therefore first has to traverse the epidermis suffering absorption from any pigments, typically melanin, being present. The low scattering nature of the epidermis will ensure that any remaining light enters the dermis with absorption occurring from the collagen fibres and any haemoglobin present. The high scattering nature of the dermis will then return a proportion back into the epidermis which it will travel through again before being remitted from the tissue.

If the light striking the tissue is described as $I_0(\lambda)$ where λ refers to the wavelength of light, absorption due to melanin as $A(m,\lambda)$where *m* refers to the amount of melanin present and the proportion returned from the dermis as $R_d(c,h,\lambda)$, where *c* relates to the amount of collagen present and *h* haemoglobin: $I_r(\lambda)$, that proportion of light remitted from the skin can be described as $I_r(\lambda)=I_0(\lambda)A(m,\lambda)^2 R_d(c,h,\lambda)$. The $A(m,\lambda)^2$ term is due to light traversing the epidermis twice. The absorption of light by melanin $A(m,\lambda)$ can be shown to be an exponential term of the from $e^{m\alpha(\lambda)}$ where α is the absorption coefficient of melanin therefore resulting in:

$$I_r(\lambda)=I_0(\lambda)e^{2m\alpha(\lambda)}R_d(c,h,\lambda).$$

And

$$R_t(\lambda)=\frac{I_r(\lambda)}{I_0(\lambda)}=e^{2m\alpha(\lambda)}R_d(c,h,\lambda)$$ the ratio of light returned from the tissue

If $R_t(\lambda)$ is computed at different wavelengths and then divided by one another $G(\lambda_1,\lambda_2)$ can be found where

$$G(\lambda_1,\lambda_2)=\frac{e^{2m\alpha(\lambda_1)}R_d(c,h,\lambda_1)}{e^{2m\alpha(\lambda_2)}R_d(c,h,\lambda_2)}$$

$a(\lambda_1)$ and $a(\lambda_2)$ are constants if λ_1 and λ_2 are fixed so there exist a series of constants *j* and *k* where $2ja(\lambda_1)=2kja(\lambda_2)=1$ therefore there exists Z where

$$Z(\lambda_1,\lambda_2)=\frac{e^{2mj\alpha(\lambda_1)}R_d(c,h,\lambda_1)^j}{e^{2mjk\alpha(\lambda_2)}R_d(c,h,\lambda_2)^{jk}}=\frac{e^{m}R_d(c,h,\lambda_1)^j}{e^{m}R_d(c,h,\lambda_2)^{jk}}=\frac{R_d(c,h,\lambda_1)^j}{R_d(c,h,\lambda_2)^{jk}}$$

and therefore

$$Z=\frac{R_d(c,h,\lambda_1)^j}{R_d(c,h,\lambda_2)^{jk}}=\frac{R_t(\lambda_1)^j}{R_t(\lambda_2)^{jk}}=\frac{R_t(\lambda_1)}{R_t(\lambda_2)^l}$$

$R_t(\lambda_1)$ and $R_t(\lambda_2)$ are straightforward to measure and *j* and *k* can easily be calculated by considering the absorption properties of melanin against wavelength or by experiment. The resulting term Z is independent of the melanin term being constructed solely from differences in the dermal component R_d. If wavelengths are then chosen where the haemoglobin term, *h*, is very small Z then becomes purely dependent on non-haemoglobin changes to the dermal component such as collagen and the presence of any other interesting material. Such wavelengths are easily accessible by silicon based sensors above approximately 600nm. It should therefore be possible construct images showing the variation of Z which may carry information pertinent to the structure of a skin lesion and in particular a BCC or SCC.

3 Results

To test this hypothesis images of BCC's were acquired from 10 lesions including 5 superficial and 5 infiltrating/invasive gathered from Marselisborg Hospital. The wavelengths used included 700nm and 940nm at which the absorption of haemoglobin is negligible. *Z* was then computed across each lesion.

Two examples are shown below. Figure 1 shows a histologically confirmed superficial BCC with the Z image to the right. The Z image shows little difference between the surrounding tissue and the BCC. In contrast figure 2 shows an invasive BCC with its Z image indicating a marked difference from the surrounding tissue.

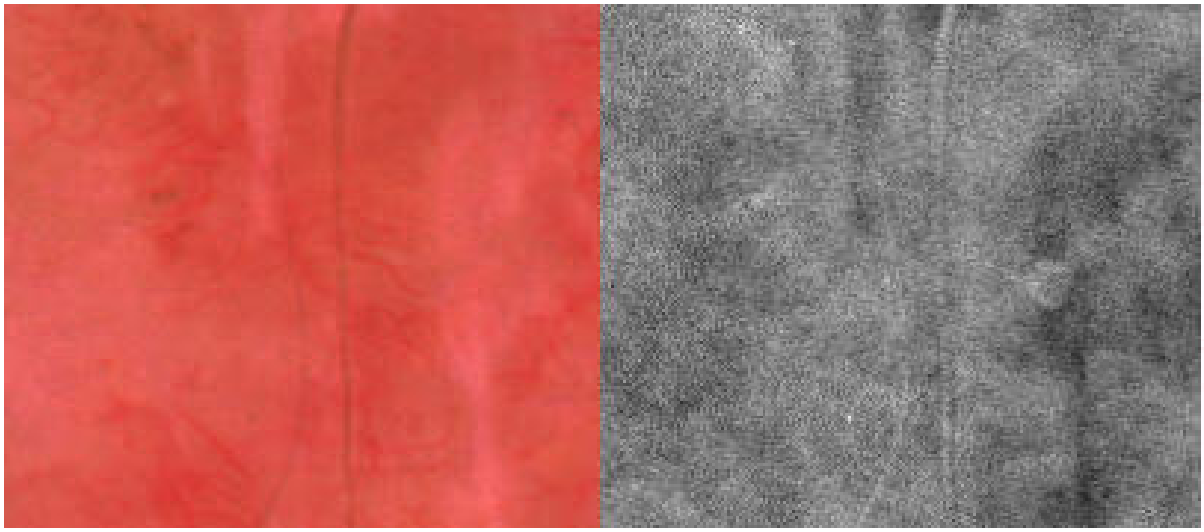

Figure 1 Superficial BCC with the Z image on the right showing no dermal involvement

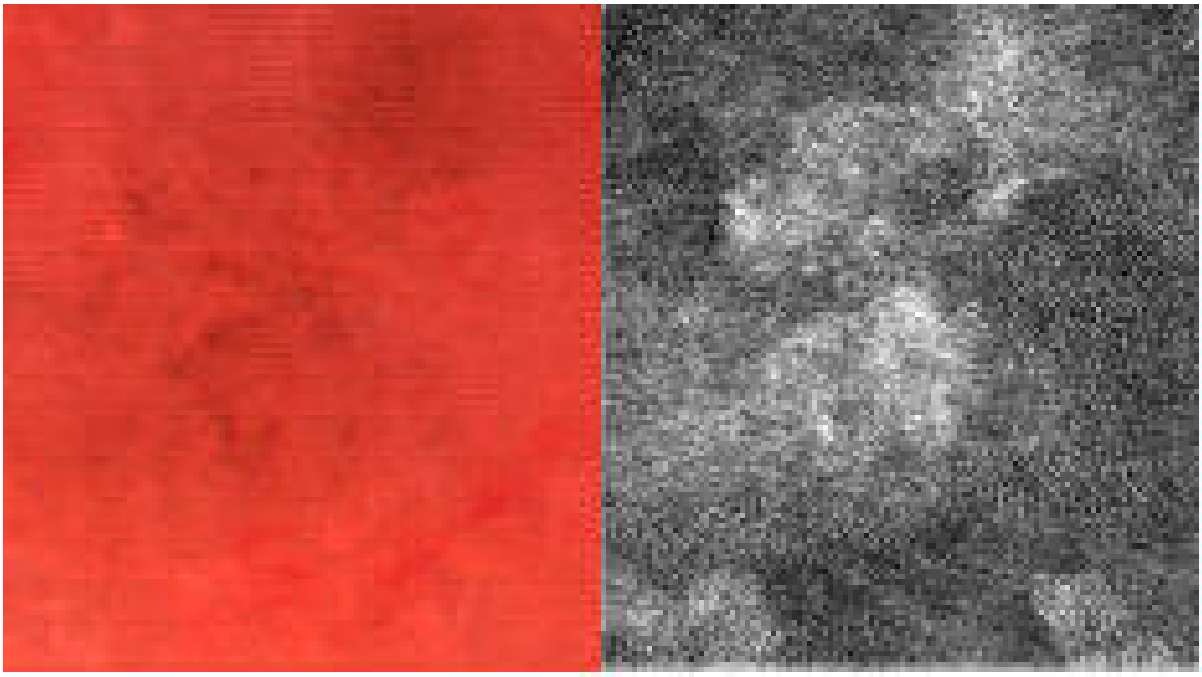

Figure 2 Invasive BCC with the Z image on the right showing marked dermal involvement

This pattern replicated itself through out all ten lesions with the invasive and infiltrating BCC's showing deviations on the Z image compared with the surrounding tissue whilst the superficial BCC's showed no such deviation.

4 Discussion

The Z image construction and analysis produced information able to separate superficial from infiltrating and invasive BCC's. This information is important in the management of the most common form of cancer in human's allowing a clinician to treat superficial BCC's quickly and simply without surgery whilst ensuring that those that require surgery undergo a procedure with minimum delay. Another important consideration is that the technology required to implement this technique is readily available in the form of CCD and CMOS digital cameras although controlled illumination at specific wavelengths is required. This study only examined BCC's but it is a reasonable, although untested, hypothesis that a similar approach may yield information in the case of SCC's.

5 Further work

The analysis in this paper specifically utilized near infrared wavelengths where the absorption of haemoglobin is low. This however limits the resolution of information relating to the disruption of collagen due to the cancer, if a lower frequency is used – for instance blue and green light – the spatial resolution of the collagen increases although there is artefact due to cross over with haemoglobin. This increase in resolution however appears to allow good discrimination of the edge of the cancer, something which is important in planning surgery, particularly Mohs surgery. Figure 3 below shows an example computed at these shorter wavelengths showing the extent of collagen disruption.

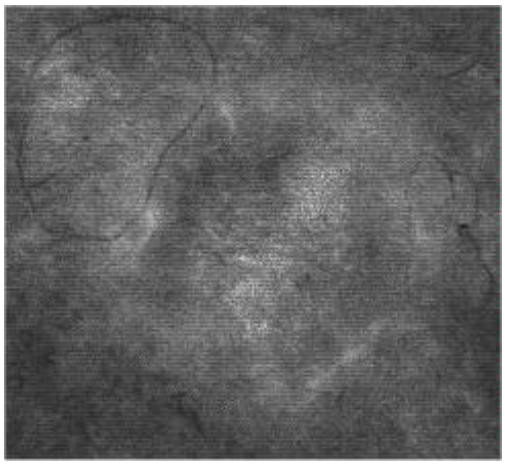

Figure 3 Collagen disruption showing in the Z value computed at shorter wavelengths

6 References

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