Lesion compression during light activation may improve efficacy of photodynamic treatment of basal cell carcinoma

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LESION COMPRESSION DURING LIGHT ACTIVATION MAY IMPROVE EFFICACY OF PHOTODYNAMIC TREATMENT (PDT) OF BASAL CELL CARCINOMA (BCC): PRELIMINARY RESULTS AND RATIONALE.

Key words: Photodynamic therapy, BCC, IPL, haemoglobin, optical-coherence-tomography (OCT), compression.

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Roozeboom et al[1] reported high recurrence rates at 3 years for photodynamically-treated superficial-BCCs, particularly on the head and neck of younger patients. Vasculature within the dermis is more prominent in these areas[2] and flushing is more noticeable when lesions on faces are treated (personal observation) (Fig.1). Therefore, we hypothesize that haemoglobin may be interfering with treatment.

We present PDT of BCCs using methylaminolevulinic-acid (MAL) cream with a modified protocol. Activation is performed in 2 phases; a first-phase using 630nm red-light (*Aktilite CL16, Galderma, Sweden*) immediately followed by a second-phase using intense-pulsed-light (IPL) (*BBL, Sciton*, *Ca, USA*) with long-pulsed, non-thermal settings and applied with compression to the lesion to blanch the skin. Fig.1 shows typical blanching from compression.

Thirty-six BCCs from 35 patients (age range; 26 - 80, mean; 54) up to a thickness of 2mm have been treated in a 24-month period. Clinical diagnosis of BCC has been supported by

histopathology (17 tumours) and/or optical-coherence-tomography (OCT) (*VivoSight, Michelson Diagnostics, UK*) (23 tumours). Eighteen tumours were nodular, 17 tumours were superficial, and 1 tumour was morphoeic. Twenty-two of 36 tumours were located on the face including 17 tumours within the "H-zone". The MAL incubation time was 3 hours and a maximum of 2 treatments have been performed. Lesions were gently curetted prior to treatment in order to remove scale but aiming not to draw blood. Typical fluence per treatment consisted of 37.5Jcm^{-2} *Aktilite* followed by 30Jcm^{-2} *BBL* (2 passes, 15Jcm^{-2} per pass) or 22.5Jcm^{-2} *Aktilite* followed by 45Jcm^{-2} *BBL* (3 passes, 15Jcm^{-2} per pass). The 560nm cut-off filter was used in 34/36 tumours. The 515nm cut-off filter was used in 2/36 tumours. The follow-up period has been 3-24 months (mean: 10 months).

There has been no clinical and/or OCT evidence of recurrence in 35 of 36 tumours. The lesion that did not clear completely was a cryotherapy-recurrent 4cm diameter nodular tumour on a forearm. At follow-up 3 months later, a 4mm nodular focus of tumour remained and this was simply excised. The remaining tumour area was clear both clinically and on OCT-scanning. The low rate of incomplete clearance using this modified protocol, on this limited sample where 50% of tumours were nodular, is encouraging.

Successful PDT depends on adequate presence of photosensitiser, light and oxygen to tumour. Oxygen is consumed during the activation process and is displaced from haemoglobin. This results in significant production of deoxyhaemoglobin[3,4], which absorbs 630nm light far more strongly than oxyhaemoglobin.[5] It is therefore plausible that during photodynamic-activation of BCC, the peritumour stroma becomes perfused with blood (flushing) that has a high concentration of deoxy-Hb, interfering with the passage of light to tumour**.** Removing haemoglobin will mean more light reaches tumour; enhanced optical scattering from dermal collagen may be fundamental in this regard[6]. In our protocol, firm pressure on the IPL-head squeezes out blood from dermal-vessels. Firm pressure may also shorten the pathlength for the activating-light, as BCCs are often gelatinous - this is evident as liquefactive-necrosis on OCT-imaging (Fig.2).

Our experience with the *Sciton* IPL is that pulse-durations of 200ms or longer are without risk of thermal-effects when paired with fluences of up to 15J with each pass (on untanned skin). Oxygen shortfall should not be an issue when IPL is used for second-phase treatment as reactive

hyperaemia following red-light activation, together with Hb-oxygen dissociation from heat that is generated[7,8], should compensate for oxygen that is photochemically-consumed. Compression removes haemoglobin but not the dissociated "free" oxygen.

Treatment of BCCs with a 2-phased PDT compression protocol shows encouraging results. Further research is warranted to confirm our findings and to separate the possible mechanisms involved.

FIGURE LEGENDS

Figure 1. Nodular BCC undergoing PDT on the nose. Flushing & blanching.

The tumour is compressed using the back surface of a curette. (a) Blanching is demonstrated surrounding the curette. (b) The curette is quickly released revealing the blanched tumour. (c) Re-perfused tumour is evident.
The images also demonstrate flushing following 5-minutes ($22.5 Jcm^{-2}$) red-light activation.

Figure 2. OCT image of a deformable nodular BCC.

Image size 6 mm x 2 mm. Arrow shows 1 mm depth extent of BCC. (a) Black area: Necrotic liquid core of tumour (b) Lighter band under BCC nodule: collagen-rich normal dermis which is strongly optically scattering.

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The patients in this manuscript have given written informed consent to publication of their case details.

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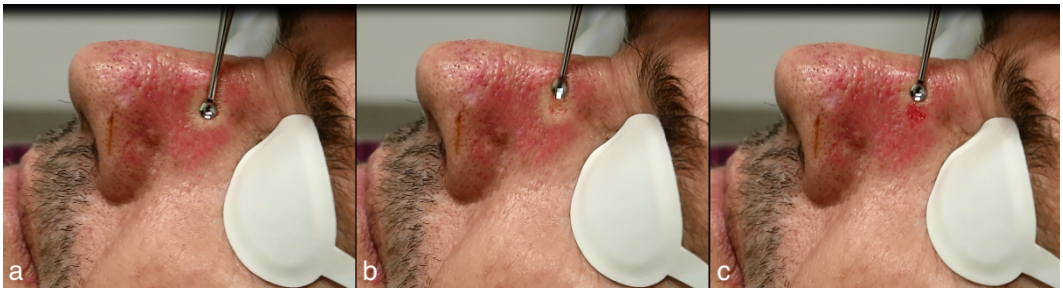

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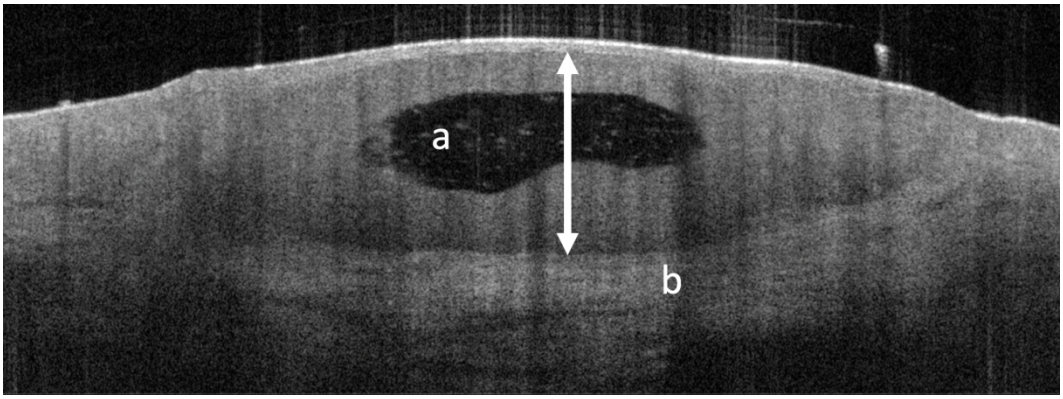

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