
**ABSTRACT**

**BACKGROUND:** Photodynamic therapy (PDT) with methyl aminolaevulinate (MAL) is an approved noninvasive treatment option for basal cell carcinoma (BCC). In vivo reflectance confocal microscopy (RCM) is a noninvasive imaging technique that has proved useful for in vivo real-time cytomorphological analysis of BCC cells infiltrating the epidermis. **OBJECTIVES:** To investigate the use of in vivo RCM to assess the persistence of BCC cells surviving MAL-PDT. **METHODS:** In vivo RCM images of 20 biopsy-proven BCCs were taken before patients underwent a treatment cycle with MAL-PDT. Follow-up after 3 months was performed using clinical examination, RCM and conventional dermoscopy. Treated areas also underwent a targeted 3-mm punch biopsy for standard haematoxylin and eosin histology stain to establish the clinical and instrumental correlation of the treatment outcome. **RESULTS:** Three months after PDT, clinical examination established that two out of 20 BCCs were persistent; dermoscopy found three out of 20 residual BCCs, but RCM showed that one of these lesions was a false positive, and showed persistent BCC foci in five out of 20 lesions. Histological analysis of targeted biopsies confirmed these results. **CONCLUSIONS:** RCM provided noninvasive, early detection of incipient recurrences of BCC after MAL-PDT. RCM findings steered targeted biopsies and surgical removal, or a new MAL-PDT, of these subclinical recurrences with minimal invasiveness.