**ABSTRACT**

**BACKGROUND:** Real-time near-infrared confocal laser scanning microscopy (CM) offers an unprecedented method for confirming the clinical diagnosis of actinic keratosis (AK) without biopsy.

**METHODS:** Seven patients with clinically diagnosed AK underwent CM imaging over the lesion and over adjacent normal-appearing skin. Biopsy specimens were obtained from the presumed AKs in 4 patients.

**RESULTS:** CM detected lesional pathologic features of hyperkeratosis (71%), lower epidermal nuclear enlargement and pleomorphism (100%), and architectural disarray (57%). In contrast, cytologic atypia and architectural disarray were apparent in one patient (17%) over the adjacent, clinically normal skin. Three of 4 biopsy specimens confirmed the clinical diagnosis of AK, whereas one revealed invasive squamous cell carcinoma. Without optimizing CM for imaging hyperkeratotic skin lesions, the limited depth of penetration reached the stratum basale in only 3 lesions, precluding detection of dermal invasion in the others.

**CONCLUSION:** Depth of penetration currently imposes a major limitation on CM in the diagnosis of AKs, especially in hypertrophic and hyperkeratotic lesions, which are more likely to be malignant. However, CM may become an alternative to biopsy, and its limitations may be overcome by future technologic advances in optical penetration or by simply removing the hyperkeratotic stratum corneum.