**ABSTRACT**

**BACKGROUND:** The current standard diagnostic procedure for basal cell carcinoma (BCC) is histologic examination after invasive biopsy. Reflectance-mode confocal microscopy (RCM) offers noninvasive high-resolution imaging of human skin in vivo.

**OBJECTIVE:** The objective of this study was to explore the sensitivity and specificity of RCM for diagnosis of BCC.

**METHODS:** This was a retrospective study of RCM images from 4 institutions of 152 skin lesions representing a variety of benign and malignant diagnoses. These 152 lesions were examined clinically, with biopsies recorded for all the 83 BCCs detected. Based on a previous study, a set of 5 histologically correlated confocal imaging criteria for diagnosing BCC was established, e.g., the presence of elongated monomophic nuclei. Blinded retrospective analysis of the images from the 152 lesions was carried out by a single novice reviewer to determine the sensitivity and specificity of these 5 RCM criteria for diagnosing BCC. The accuracy of combining the probability of BCC based on examination of clinical photographs with the predicted probability of BCC based on confocal criteria was also evaluated.

**RESULTS:** The presence of two or more criteria is 100% sensitive for the diagnosis of BCC, and with 4 or more RCM criteria present the specificity was 95.7% and sensitivity was 82.9%. These results were found to have little variability across study sites and across BCC subtypes. The combination of RCM with photography-based predictions of clinical probability of BCC significantly improved the accuracy for noninvasive diagnosis of BCC.

**CONCLUSION:** RCM offers a sensitive and specific tool for the noninvasive diagnosis of BCC in vivo.