**ABSTRACT**

**BACKGROUND:** Ex-vivo confocal laser-scanning microscopy offers rapid imaging of excised tissue specimens without conventional histotechnical procedures. As vertical sections are prepared, morphological features can be assessed according to standard criteria used in conventional histopathology.

**OBJECTIVES:** To validate the diagnostic confocal examination of squamous cell carcinoma (SCC) in microscopy-guided surgery.

**METHODS:** Four independent observers received standardized instructions about diagnostic confocal microscopy features of SCC. Subsequently, 120 confocal images of fresh excisions from SCC or normal skin, imaged using a commercially available, near-infrared, reflectance confocal laser-scanning microscope, were evaluated by each observer.

**RESULTS:** General morphology, such as location, size and shape of the cancer area could be visualized by the imaging system. Furthermore, densely packed and irregularly organized nuclei and nuclear atypia could be delineated. Overall, a sensitivity of 95% and a specificity of 96.25% were achieved by the four observers (positive predictive value 96.25%, negative predictive value 95.23%).

**CONCLUSIONS:** This study provides a set of well-described morphological criteria with obvious diagnostic impact which should be used in further investigations. In the future, confocal laser-scanning microscopy may guide microsurgery of any skin cancer.