BACKGROUND:Frozen histological sections are currently used for intra-operative margin assessment during Mohs surgery. Fluorescence confocal microscopy (FCM) is a new tool, which offers a promising and faster alternative to frozen histology. OBJECTIVE:The aim of the present study is to prospectively evaluate in a clinical setting, the accuracy of FCM as compared to frozen sections in BCC’s margin assessment. METHODS: Patients with BCC, scheduled for Mohs surgery were prospectively enrolled. Freshly-excised surgical specimens were first examined through FCM and then frozen sections were evaluated. Permanent sections were finally obtained, in order to validate our sample technique. A blind re-evaluation was also performed for discordant cases between FCM and frozen sections. Sensitivity and specificity levels, as well as positive and negative predicting values were calculated and ROC curves were generated. RESULTS: We enrolled 127 BCCs in as many patients (40.2% females). A total number of 753 sections were examined. All BCCs were located on the head and neck area. When evaluating the performance of FCM as compared to frozen sections 79.8% sensitivity, 95.8% specificity, 80.5% positive predicting and 95.7% negative predicting values were found (Area Under the Curve: .88, 95%CI .84-.92; P<.001). A total of 49 discordant cases between FCM and frozen sections evaluations were blindly re-evaluated, of which 24 were false positive and 25 false negative. The performance of FCM and frozen sections was also evaluated according to the final histopathological assessment. CONCLUSIONS: We found high levels of accuracy for FCM as compared to frozen sections evaluation, in intra-operative BCC’s margin assessment during Mohs surgery. Some technical issues still prevent a wide use of this technique, but new upcoming devices promise to overcome these limitations. This article is protected by copyright. All rights reserved. This article is protected by copyright. All rights reserved. KEYWORDS: Mohs surgery; basal cell carcinoma; ex vivo confocal microscopy; fluorescence confocal microscopy; skin cancer PMID: 30512198 DOI: 10.1111/bjd.17507