**ABSTRACT**

**BACKGROUND:** Successful treatment of melanoma depends on early diagnosis, but its varied clinical presentation means that no single noninvasive method or criterion can provide reliable detection in all cases. **OBJECTIVES:** To determine whether combining sequential dermoscopy imaging with Reflectance Confocal Microscopy (RCM) can improve melanoma detection and reduce the burden of unnecessary excisions. **METHODS:** Retrospective study with median follow-up of 25 months. Included equivocal pigmented lesions that lacked clear dermoscopy criteria for melanoma at baseline but were excised subsequently because of changes during digital monitoring. RCM imaging was performed before excision. Main melanoma dermoscopy features, 7-point checklist score at baseline, and changes in structure and/or color, and development of new melanoma-specific criteria at follow up (scored as major, moderate or minor) were considered. Main melanoma RCM criteria were evaluated and diagnosis was made. Histopathologic diagnosis was the reference standard for defining parameter frequency and diagnostic accuracy. **RESULTS:** Seventy lesions were included. Major changes were more frequently correlated with melanoma diagnosis, although one-third (4/12) of melanomas showed moderate or minor changes. Cytological atypia and architectural disarrangement on RCM were correlated with melanoma diagnosis. A correct melanoma diagnosis was achieved with RCM in almost all cases (11/12, 92%). Referring for excision only lesions with RCM positive features and/or presenting major changes at digital dermoscopy follow-up, theoretically 27 out of 58 nevi could be saved from surgery. **CONCLUSIONS:** Integration of RCM in the clinical and instrumental strategy for managing difficult pigmented lesions provided additional diagnostic information useful in the decision-taking process.