**ABSTRACT**

**BACKGROUND:** Early detection of melanoma is the main objective to ensure a high survival rate. In some cases melanoma diagnosis still remain difficult and this leads to unnecessary excisions.

**OBJECTIVE:** The aim of this study was to detect the most relevant Reflectance confocal microscopy (RCM) features for the detection of dermoscopic difficult melanomas. **METHOD:** A total of 322 lesions were selected from database and were evaluated on dermoscopy according to the 7-point checklist score, in blind from histological diagnosis. We classified the lesions into three categories: (i) 'featureless' lesions with score ranging between 0 and 2; (ii) 'positive-borderline' moles with score between 3 and 4 and (iii) 'positive-clear cut' lesions with score from 5 to 10. We evaluated confocal features of the 'featureless' lesions and of the 'positive-borderline' lesions. Evaluated confocal features were as follows: presence of pagetoid cells, cell shape (roundish or dendritic) and number (< 5 or >5 cells per mm2), overall architecture (ringed, meshwork, clods and non-specific pattern); architectural disorder, presence of cytological atypia (>5 cells per mm2 ) and cells arranged in nests. **RESULTS:** Among 322 lesions 70 were melanomas and 252 were nevi. According to the classification based on the 7-point checklist score, 130 'featureless lesions' (score 0-2) including six melanomas, and 102 'positive-borderline' moles (score 3-4) including 17 melanomas, were identified. Round pagetoid cells >5 cells per mm2 and/or architectural disorder on RCM were found in all of six melanomas with featureless dermoscopy. Round pagetoid infiltration and five or more atypical cells at the DEJ were found in 16 positive 'borderline melanomas'. **CONCLUSIONS:** RCM represents a rapid non-invasive technique that can aid early diagnosis of dermoscopic difficult melanomas. Use of RCM on lesions with clinical and/or dermoscopic suspect of malignancy may reduce the number of unnecessary excision increasing the rate of accurate diagnoses.