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Diagnosis of congenital pigmented macules in infants with reflectance confocal microscopy and machine learning

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1 **Title: Diagnosis of congenital pigmented macules in infants with reflectance confocal**
2 **microscopy and machine learning**

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43 **To the Editor**

44 Congenital pigmented macules (CPM) can be clinically and dermoscopically equivocal in infants,
45 making the differential diagnosis between Café au Lait Spot (CLS) and Congenital Melanocytic Nevus
46 (CMN) difficult. Reflectance confocal microscopy (RCM) may reveal morphological patterns,
47 differentiating CMN from CLS at the bedside and changing management/follow-up of these lesions.

48 A retrospective study was performed to describe the RCM patterns of
49 dermoscopically equivocal CPM and to compare it on CLS and CMN. CPM cases were
50 analysed and classified either CLS or CMN by a skin biopsy or by clinical characteristics
51 and/or dermoscopic evolution during follow-up. RCM acquisition took 5-30 minutes per
52 patient (handheld RCM Vivascope 3000® -CALIBER, Rochester, NY, USA). Frequencies of each
53 clinical and RCM pattern for CLS and CMN were calculated.¹ Images evaluation was
54 performed by three experts in a blinded manner and the inter-expert agreement was
55 analysed. Finally, a pretrained convolutional neuronal network combined with a Support
56 Vector Machine algorithm, was trained to automatically classify CLS and CMN based on RCM
57 images at the dermal-epidermal junction.

58 Among 30 children with CPM (mean age 33.7 months; standard deviation (SD) 31
59 months), 20 patients were diagnosed with CLS and 10 with CMN. The mean follow-up
60 duration was 72 months (SD 40). CPM locations were: face (33%), back (23%), abdomen
61 (20%), arms (3%) and legs (20%). Clinically, hair was more commonly observed on CMN than
62 CLS, however no significant difference was observed for lesion's color or regular/irregular
63 border. 7943 RCM images from 30 patients, were acquired at first dermatology
64 consultation. RCM images of CMN (figure 1) were the only class characterized by the
65 presence of nests (CMN: 100% vs CLS:0%, $p < 0,001$). In contrast, RCM images of CLS (figure
66 2) were characterized by the presence of bright peri-papillary rings (CLS: 100% vs CMN: 30%,

67 p <0.001) and enlarged peri-papillary rings (CLS: 100% vs CMN: 10% p <0.001). Honeycomb
68 and cobblestone epidermis patterns usually described on RCM images and presence of
69 melanophages on the dermis were studied and not significantly different between both sets.
70 The blind retrospective evaluation exhibited an excellent inter-observer agreement for the
71 presence of nests and bright peri-papillary rings (kappa coefficient (κ) = 1) and enlarged peri-
72 papillary rings (κ = 0.84). The classifier by cross-validation showed an accuracy of 89.1% to
73 discriminate CMN to CLS with respectively 85.5% and 92.8% of good predictions.

74 There are very few data describing CMN and CLS diagnostic criteria in RCM in infants.
75 Prodinge *et al.*² demonstrated the diagnostic value of RCM in a single case of nevus spilus.
76 Zeng *et al.*³ described the RCM characteristics of facial hyperpigmented lesions in a series of
77 adults.

78 Our results demonstrated that CLS can be differentiated from CMN by specific
79 characteristics and different patterns on RCM images. Machine learning can be combined
80 with RCM to assist the image's interpretation and to increase the diagnostic accuracy in the
81 differentiation of CPM. RCM seems to be a non-invasive helpful diagnostic tool in difficult to
82 diagnose and dermoscopically equivocal CPM cases.

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111 **Figure 1:**

112 RCM at the level of the dermal epidermal junction showing numerous bright melanocytic

113 nests: congenital melanocytic nevus

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135 **Figure 2:**

136 RCM at the level of the dermal epidermal junction showing bright and enlarged peripapillary

137 rings: café-au-lait spot.

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