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REFLECTANCE CONFOCAL MICROSCOPY: A CRUCIAL ROLE FOR ACTINIC KERATOSIS TREATMENT MONITORING

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None

The article by Ishioka et al[1]. indicates a very important role for reflectance confocal microscopy (RCM) as a non-invasive method that can be successfully used for monitoring actinic keratosis therapeutic response to 5-fluorouracil, with an efficacy similar to histological examination. Furthermore, the results suggest that 5-fluorouracil may be a satisfactory option for therapeutic control of this condition.

This study further supports the general idea that RCM is a pivotal tool for actinic keratosis (AK) diagnosis and treatment monitoring although some considerations have to be done. The use of RCM on AKs permits to explore a wide skin area and not only a 3 to 5 mm punch biops, to avoid tissue removal and, in case of use of the handy device, to assess both several AKs and cancerization field on surrounding skin. It is well known that the aim of the topical treatment such as 5-fluorouracil is not limited to lesion-directed therapy but indeed to the whole affected area and thus a precise morphologic analysis is mandatory to assess treatment response. RCM

holds the great advantage of a total non-invasive and dynamic way to monitor a treated area over time that it's not possible with conventional histopathology in which removed tissue cannot be subsequently analyzed, and procedure generates uncontrolled skin changes. However, RCM definition of some parameters is subjective and not highly reproducible, such as the classification for dyskeratosis (atypical honeycomb). For this reason, probably the Authors decided to evaluate its extent and not the degree of atypia, that requires a more complex approach for classification or the generation of standards.[2] Computer model may be used to noninvasively evaluate keratinocyte populations as a quantitative morphometric diagnostic in skin cancer detection and evaluation of cyto-architectuarl degree of disorder, in order to provide objective and quantitative data for dyskeratosis detecton and quantification.[3]

On the other side, conventional histopathology has a greater cytologic resolution compared to RCM and makes easier the distinction from AKs and invasive forms even though RCM seems a promising tool for this differential diagnosis[4]. Notably, the Authors in the current study didn't perform any dermoscopic assessment, that would result in a more detailed AK classification[5]. However, RCM alone demonstrated AK clearance in in 45.0% (observer 1) and 32.5% (observer 2) of subjects according to RCM and in 32.5% of subjects according to histological examination. The excellent performance of RCM alone opens the question whether this imaging tool could be used as a standing alone instrument for treatment monitoring and not coupled with dermoscopy as it is required for skin cancer diagnosis.

Not surprisingly, RCM showed a good concordance among two evaluators underling that RCM features for AKs are reliable and easy. Larger randomized trials using RCM for treatment monitoring of AK therapies are needed to confirm the findings by Ishioka et al. and to change the current clinical workflow in the field of AK diagnosis and treatment monitoring. Image analysis for the quantification of key-parameters in RCM can help to objectivize the measurements and to consider the systematic use of non-invasive technologies in clinical trial to evaluate product efficacy.

References

1: Ishioka P, Maia M, Rodrigues SB, Lellis RF, Hirata SH. In vivo Confocal Laser Microscopy for monitoring of actinic keratosis treatment: a comparison with histopathologic assessment after treatment with topical 5% 5-fluorouracil. J Eur Acad Dermatol Venereol. 2017 Nov 24. doi: 10.1111/jdv.14716. [Epub ahead of print] PubMed PMID: 29178474.

2: Pellacani G, Ulrich M, Casari A, Prow TW, Cannillo F, Benati E, Losi A, Cesinaro AM, Longo C, Argenziano G, Soyer HP. Grading keratinocyte atypia in actinic keratosis: a correlation of reflectance confocal microscopy and histopathology. J Eur Acad Dermatol Venereol. 2015 Nov;29(11):2216-21. doi: 10.1111/jdv.13215. Epub 2015 Aug 14. PubMed PMID: 26274903.

3: Gareau D. Automated identification of epidermal keratinocytes in reflectance confocal microscopy. J Biomed Opt. 2011 Mar;16(3):030502. doi: 10.1117/1.3552639

4: Manfredini M, Longo C, Ferrari B, Piana S, Benati E, Casari A, Pellacani G, Moscarella E. Dermoscopic and reflectance confocal microscopy features of cutaneous squamous cell carcinoma. J Eur Acad Dermatol Venereol. 2017 Nov;31(11):1828-1833. doi: 10.1111/jdv.14463. Epub 2017 Aug 4. PubMed PMID: 28696052.

5: Pampena R, Benati E, Borsari S, Bombonato C, Lombardi M, Raucci M, Mirra M, Lallas A, Apalla Z, Papadimitriou I, Moscarella E, Kyrgidis A, Argenziano G, Pellacani G, Longo C. Tracking actinic keratosis of face and scalp treated with 0.015% ingenol mebutate to identify clinical and dermoscopic predictors of treatment response. J Eur Acad Dermatol Venereol. 2018 Jan 22. doi: 10.1111/jdv.14803. [Epub ahead of print] PubMed PMID: 29356164.