

delivery of AuNPs with dissolvable microneedles in the skin would enhance the OCT image contrast between normal and disease skin. AuNPs (87 nm in diameter) were mixed in sodium carboxymethyl cellulose solution (CMC). CMC is water soluble and mechanically robust in dry form. They developed dysplasia in one cheek pouch by applying 0.45%(w/v) 9,10-dimethyl-1,2-benzanthracene in mineral oil topically three times a week for 10 weeks. They applied AuNPs with dissolvable microneedles and dissipated them by ultrasound (US) on the cheek pouch. After the treatment, the cheek pouch tissue was harvested, fixed in 10% formalin buffer, and embedded in paraffin for sectioning. The tissue sections were imaged by spectral domain-OCT (SD-OCT). The OCT images showed morphological differences between dysplasia and normal skin. Quantitative analysis was performed from image data. The data showed alternations in epithelial stratification, one with disruptive and the other one with well-aligned morphologies. Analysis of quantitative depth-dependent distributions of OCT signal intensity indicated that OCT signal intensity was increased in the stratum corneum in dysplastic tissue after treatment. In normal skin, there were significant signal intensity differences before and after the AuNP application. However, little information was obtained in terms of the nanoparticle penetration profile. Overall, their hypothesis was supported by the data that the application of AuNPs could achieve clear quantitative imaging-based differences between dysplastic and normal tissues.

In 2019, Ruini et al. employed OCT to investigate the effect of ingenol mebutate in actinic keratosis (AK) and subclinical AK (sAK) [26]. Twenty patients (Fitzpatrick skin type II-III) with multiple AKs were recruited. Ingenol mebutate 0.015% gel was applied within a 25 cm² area on the face or scalp at the time of enrollment and the following two consecutive days. Clinical, dermoscopic, reflectance confocal microscopy, and OCT images were taken at the time of enrollment (T = 0), at day 4 (T1), at day 14 (T2), and at day 56 (T3). OCT images show hyperkeratosis and crusting, irregular layering, and a broadened epidermis. By day 56, thickening of the epidermis was improved by the treatment. For sAK, there was a restoration of the epidermal dermal junction by OCT images after 56 days. These findings were confirmed by images from RCM and dermoscopy. OCT images were analyzed by measuring the mean epidermal thickness. There was a significant reduction in epidermal thickness AK from 0.22 mm to 0.15 mm after 56 days and from 0.2 mm to 0.11 mm in sAK after 56 days. The limitation is that OCT does not provide cellular resolution, but it does allow the visualization of structural patterns. The main histological features of AKs that OCT can provide are hyperkeratosis, thickening, and disruption of the dermal layers. No drug penetration profile was obtained from the OCT images. This study shows the multiple noninvasive in vivo imaging modalities to monitor the pharmacological effects on skin disease over a period of time.

56.9 REFLECTANCE CONFOCAL MICROSCOPY

RCM is a widespread imaging approach technology that is being used clinically to monitor skin morphology with quasi-histological skin images to a depth of 200 to 250 μm , including the entire epidermis and upper dermis. Recently, Haedersdal et al. (2019) published a study that used both RCM and OCT imaging approaches to visualize and quantify gold nanoparticle delivery in the facial skin of acne patients and healthy participants. They also applied laser treatment to the skin to enhance the nanoparticle delivery. RCM images from the initial experiment showed the morphology of channels created by laser application in each skin layer (epidermis, dermoepidermal junction, and papillary dermis). Gold nanoparticles were seen as hyperreflective spots in RCM images that resembled previously reported signatures. Nanoparticle penetration was confirmed by OCT. RCM imaging is useful for this application to 150 to 200 μm deep, whereas OCT can image much deeper but has less information in that data. The quantitative measurement of gold nanoparticle delivery in skin strata was calculated by analyzing the signal from the laser channels in the RCM images. This study demonstrated that RCM and OCT can successfully be used to visualize gold nanoparticle delivery into the skin and the effects on skin caused by applications.