Recognizing that a cure lies in timely detection, dermatologists strive to diagnose malignant melanoma (MM) at the earliest possible stage. The desire to achieve this goal without injudiciously and unnecessarily excising many benign lesions has led to numerous techniques that assist clinicians in differentiating nevi from MM, including clinical mnemonics and algorithms, optical imaging instruments, and computer-assisted diagnostic systems. Most of these seemingly diverse methods rely on evaluating the in vivo morphology of lesions. In this issue, Guitera et al. compare dermoscopy with reflectance confocal microscopy (RCM) in an attempt to determine which imaging modality facilitates accurate diagnosis of melanocytic lesions using diagnostic parameters such as sensitivity and specificity.