Appendix S1

SUPPLEMENTARY MATERIAL AND METHODS

Technical descriptions of the included skin imaging modalities

High-frequency ultrasound imaging (HFUS). Doppler ultrasound system from Siemens was used (ACUSON Juniper Ultrasound System, HELX™, Erlangen, Germany). A regulation amount of ultrasound gel was placed on the skin to avoid compression of soft tissues under examination.

Optical coherency tomography (OCT). Different OCT devices may provide quite different images of, especially, basal cell carcinoma (BCC) lesions (8). To explore this, we used both a commercial OCT (C-OCT) system with integrated angiographic OCT (OCTA) and a prototype ultra-high resolution (UHR-OCT) system, developed by the Technical University of Denmark (DTU).

The C-OCT system (VivoSight Dx, Michelson Diagnostics, Kent, UK) has a resolution of 5.5 µm, lateral resolution of 7.5 µm and scans a skin area up to 6 × 6 mm in a single session, with a penetration depth of 1–2 mm. Integrated software provided OCTA images.

The UHR-OCT system has an axial resolution of 2.2 µm, lateral resolution 6 µm in tissue (30, 43) and is a prototype OCT system assembled at the Technical University of Denmark and NKT Photonics, Birkerød, Denmark. The field of view is 3 × 3 mm.

Reflectance confocal microscopy. The reflectance confocal microscope (RCM), a commercial Vivascope Multilaser 3000®/1500® (Mavig GmbH, Munich, Germany) in 785 nm mode, provides a penetration depth of 200–300 µm, axial resolution of 1.25 µm and lateral resolution of 0.5 µm in skin (44, 45). The lesions were scanned in image mosaics of up to 8 × 8 mm (VivaBlocks®, Mavig GmbH) or with the handheld scanner at different depths. Dermoscopy images are collected to guide RCM scanning, but it was decided not to analyse individual dermoscopy images of skin tumours in this pilot study, in order to keep the diagnostic complexity of the dataset lower, as the study focused on diagnostic accuracy of more advanced imaging technologies.

Photoacustic imaging. For photoacoustic imaging, the novel multispectral optoacoustic tomography technology, MSOT Acuity (iThera Medical GmbH, Munich, Germany), was used, equipped with a fast-tuneable laser (700–875 nm wavelength) and handheld 3D detector. Real-time 3D images are created at a field-of-view of 15 × 15 mm and a depth up to 20 mm. Spatial mapping of the intrinsic chromophores: melanin, haemoglobin (HbO_2) and deoxyhaemoglobin (Hb) is obtained through spectral unmixing. For each lesion, image sequences with a duration of approximately 2–5 s were acquired and a clear ultrasound gel was applied to the skin prior to imaging.