Table I. 2016 overview of available and novel dermatologic non-invasive imaging devices

Fundamental technique and synonyms or variations	Most likely user, Examples of CE devices (bold for FDA-approved), and price range	Clinical uses and highest quality *in vivo* clinical trial result	Features typically visualized and imaging time	Advantages & unique technologic capabilities	Limitations of currently available devices	Technological developments and anticipations
Polarization techniques (dermoscopy, polarimetry)	*All dermatologists*, DermLite (3Gen), EpiScope (Welch Allyn), NevoScope (TransLite), Dermascope (American Diagnostic Corp), MoleMax (Derma Medical Systems), DermoGenius (Dermoscan), handyscope (Fotofinder), Canfield; $0.1k to $2k	Assistance of dermatologic physical exam, especially for cancer screening; melanoma vs. benign naevi sens 89%, spec 84%[a]	Modestly magnified subsurface morphology including vessels; melanin distribution and other skin cancer features; instantaneous images	Rapid skin cancer screening; wide base of experienced dermoscopy users; significant improvement in sensitivity and specificity relative to unaided clinical exam; devices do not require FDA approval (Class I)	Added value highly user- and training-dependent; low resolution images; top view image (no cross-sectional images at depth)	Mobile phone mounts and apps; advanced polarimetry techniques will extend possibilities, e.g. automatic evaluation of average nuclear morphology or tissue heterogeneity; www.dermoscopy-ids.org
Total body digital photography (TBDP), regional imaging	*Pigmented lesion experts*, Dermspectra, Canfield, FotoFinder, Molemax, Molesafe, MoleMap, MelanoScan, Dermoscan, Visiomed; $10k to $250k	Monitoring melanocytic neoplasms in high risk pigmented lesion clinics, NMSC, and inflammatory diseases	Generally same features as clinical exam; 10 min for total body	Rapidly acquire and monitor large portion of skin surface; computer algorithms help track changes and suspicious features	Challenging to rapidly present and interpret resulting large data set in clinical setting	Increasing number of commercial devices with automated image acquisition; comprehensive resource at http://isdis.net/imaging-modalities/total-body-photography/
Confocal microscopy (LSCM, CSLM, RCM)	*All dermatologists willing to invest in necessary training*, six category 1 CPT reimbursement codes; **Vivascope** (Caliber ID and Mavig, formerly Lucid), **Stratum** (Optiscan); $100k	Identify diverse lesions for which biopsy can be avoided; preoperative mapping of malignancies including lentigo maligna for reduced surgical defects; melanoma vs benign nevi sens 97%, spec 83%[a] diagnosis of equivocal lesions vs BCC sens 100%, spec 89%[b]	Microscopic structures as in H&E but only in horizontal (en face) sections; 25 min for 6 x 6 mm image stack (including prep time described in CPT 96932)	Highest accuracy; only imaging technology with Medicare reimbursement; video-rate single-lesion, histology-grade (<1 µm) resolution of cellular components based on scattered light; able to view dendrites on melanocytes (unachievable with standard H&E)	En face views best interpreted by experienced confocalist; difficult to detect invasion through dermal-epidermal junction and other depth-resolved features such as melanoma stage or HAK vs SCC; unable to image beneath papillary dermis (limited to 0.25 mm depth)	Intraoperative use, e.g. coupled to laser ablation; combination with fluorescent techniques; working group at http://www.confocal-icwg.com/
Spectral (multispectral, hyperspectral, RGB, infrared thermography) imaging	*Few dermatologists*, category 3 CPT codes for research use; **MelaFind** (Melasciences) $30k; **SIAscope** (MedX) with SIMSYS or MoleMate software $6k - $8k; Dermlite II MS (3gen) $1k; TiVi (WheelsBridge) $20k	Help triage pigmented lesions for biopsy; for melanoma vs nevus, Melafind sens 98.3%, spec 9.9%[c] whereas SIAscope sens 80%, spec 76%[d]; clinical research with TiVi	Macroscopic views of erythema and blanching, oxy- & deoxyhaemoglobin and melanin; Siascope 5s for single 11 x 11 mm image; Melafind 45s for single image up to 22 x 22 mm; TiVi 30fps wide field or single lesion	Mapping of some chemical components through entire thickness of skin (to 2.5 mm deep) based on light collection at numerous frequencies; often combined with polarization technique	Large data set interpretation highly dependent on training set that computer algorithms use; top view image (no cross-sectional images at depth)	Research needed correlating spectral properties of skin to disease; handheld spectral polarization camera probes operating on tablets
Optical coherence tomography (low coherence interferometry, FF-OCT, GD-OCT)	*Few academic dermatologists*, **Vivosight** (Michelson Diagnostics), Light-CT (LLTech), **Skintell** (Agfa), Nitid (DermaLumics), SkinDex300 (ISIS Optronics); $130-$180k	Depth demarcation and reduction of presurgical biopsy rate for BCCs; dynamic blood flow imaging; as adjunct to expert dermoscopy exam, sens not significantly improved, but spec for BCC improved from 54% to 75%[e]	Macroscopic structures (e.g. blood vessels, DEJ, BCC border); Vivosight 20s for 6 x 6 mm image stack; Skintell <2s for 1.8 x 1.5 x 1 mm 3D volume; Light-CT 1 min for 10 x 10 mm image	Optical analogue of ultrasound; images relatively deep in dermis (~1 mm), able to image flow with speckle variance or Doppler; images in same plane of view (vertical) as traditional H&E	Diagnostic accuracy limited by lateral resolution (Vivosight 8 µm, Skintell 3 µm with adaptive optics). FF-OCT overcomes this (Light-CT resolution 1 µm) but in excised tissue and limited to 0.2 mm depth	Intraoperative Mohs margins with FF-OCT; OCT elastography; molecular imaging; polarization-sensitive OCT; potential resolution improvement with Gabor domain liquid lens or Mirau interferometer
Interferometry (dynamic light scattering, laser Doppler flowmetry, LDPI, laser speckle imaging, LSPI, LSFG, LASCA, MESI)	*Research centres*, FluxExplorer (Microvascular Imaging), Moor, Perimed, Lisca	Skin grafts, vascular lesion treatment monitoring, patch test quantification, Raynaud's scoring, scar evaluation; in detection of active morphea sens 80% spec 77% in single-centre trial[f]	Colour-coded perfusion image reflecting blood flow level or velocity; imaged area adjustable; 1s for 50 x 50 mm	Low cost, non-contact; rapidly evaluates blood flow over a large area (up to 500 x 500 mm)	Lower resolution (>100 µm)	Combination with OCT
Vibrational spectroscopy (Raman, FTIR)	*Research centres*, gen2-SCA (RiverD) $100k to $250k; Aura (Verisante) $65k	Determining skin hydration, antioxidant levels, and distribution of cosmetics and other topical treatments; diagnostically, benign (including SK) vs. malignant (including AK) lesions had sens 90–99%, spec 75–20% in single-centre trial[g]	Molecular composition and biochemical information; single point or depth-resolved spectra acquired in seconds but without yielding actual images	Quantitative measurements of many known compounds already available, e.g. carotenoid antioxidants, NMF, urea, lactate; theoretically any molecule will have unique Raman signature	Rapid high resolution volumetric imaging impractical as Raman effect (inelastic scattering) several orders of magnitude weaker than reflectance (elastic scattering) or fluorescence; spectra are difficult to interpret for unknown compounds	Research needed correlating Raman signatures to disease; more complex non-linear implementations (e.g. CARS, stimulated Raman) enable rapid imaging for some specific chemical signature lines

Table I. Contd.

Fluorescence (autofluorescence lifetime imaging, photodynamic diagnosis, fluorescence videomicroscopy)	*Research centres*, SkinSpect (Spectral Molecular Imaging)	Presently early research phase; not used as single modality; primarily used to enhance confocal images, especially in perioperative imaging	Images of added or intrinsic fluorescent compounds	Fluorescent agents can improve contrast of other modalities; fluorescence lifetime measurements, when used, are sensitive to microenvironment of detected compounds	Little dermatologic clinical data; limited by width of fluorescence absorption and emission lines and few FDA-approved exogenous fluorescent compounds (fluorescein, indocyanine green, methylene blue)	Much R&D needed
Diffuse optics (spatial frequency domain imaging)	*Research centres and wound care physicians*, Ox-Imager (Modulated Imaging) $100k	Presently early research phase; preliminary data in wound monitoring, burn thickness assessment, and surgical flap viability prediction based on blood supply	Haemoglobin total concentration and oxygenation; optical properties of skin (scattering, absorption); 1s for two frequency scan, 25s for full scan	Non-contact imaging of large area (size adjustable up to 200 x 150 mm)	Little dermatologic clinical data; low resolution (>100 µm)	Much R&D needed
Nonlinear optical imaging (multiphoton, SHG, two photon fluorescent, coherent Raman, CARS, stimulated emission imaging)	*Few research centres*, DermaIinspect, MPTflex (JenLab) $400k	Presently early research phase; preliminary data for diagnosis of melanoma vs benign nevi sens 75%, spec 80%[h]	Similar features as corresponding linear modalities above; molecular composition and microscopic structures; few seconds for 0.35 x 0.35 mm image at single depth	High resolution (<1 µm) sensitive and label-free quantitative measurements of many intrinsic chemicals (such as collagen, NADH, pheo- and eumelanin)	High laser cost; current CE device has higher laser intensities, much slower imaging, and slightly worse depth (about 0.2 mm) than confocal	Much R&D needed; impressive basic science results in questions of immune cell interactions, stem cell trafficking, and metabolism (including redox ratios); more advanced setups including pump-probe dynamics under development
Photoacoustic imaging (optoacoustic tomography, photoacoustic microscopy)	*Few research centres*, inSight, MSOT Acuity (iThera) $150k–$350k	Presently early research phase; preliminary data for detection of melanoma mets in sentinel lymph nodes sens 100%, spec 49%[i]	High-contrast, absorption-based images of melanin, oxy-, deoxyhemoglobin, lipids, and external dyes (such as indocyanine green); 5 min for 5 x 5 x 1.5 mm 3D volume at 8 µm resolution	Combines optical and ultrasound imaging; excellent melanin contrast (50x better than light microscopy); only method that can tune between extremely high resolution images (to 0.1 µm) and depth (> 10 mm), e.g. 4 µm resolution at 5 mm depth	Little dermatologic clinical data	Much R&D needed; early data suggests sensitive detection of melanoma metastases in circulation and lymph nodes; high resolution microvasculature assessment; pilosebaceous unit imaging

[a]Langley RG. Dermatology 2007; 215: 365–372 – (125 patients single centre). [b]Guitera P. J Invest Dermatol 2012; 132: 2386–2394 – (663 patients multicentre). [c]Monheit G. Arch Dermatol 2011; 147: 188-194 – (1,251 patients multicentre). [d]Tomatis S. Phys Med Biol 2005; 21; 50: 1675–1687– (1,278 patients single centre). [e]Ulrich M. Br J Dermatol 2015; 173: 428–435 – (250 patients multicentre). [f]Weibel L. et al. Arthritis Rheum 2007; 56: 3489–3495 – (111 lesions). [g]Zhao J. et al. Analyst 2016; 141: 1034–1043– (127 lesions tested). [h]Dimitrow E. et al. J Invest Dermatol 2009; 129: 1752–1758 – (53 lesions). [i]Stoffels I. et al. Sci Transl Med 2015; 7: 317ra199 – (41 sentinel lymph nodes from 20 patients).

CE: European certification; AK: actinic keratosis; BCC: basal cell carcinoma; CARS: coherent anti-stokes Raman scattering; CLSM: confocal laser scanning microscopy; CPT: current procedure terminology; DEJ: dermoepidermal junction; FF-OCT: full-field optical coherence tomography; FTIR: Fourier transform infrared spectroscopy; GD-OCT: Gabor domain optical coherence tomography; H&E: hematoxilin and eosin; HAK: hyperkeratotic actinic keratosis; LASCA: laser speckle contrast analysis; LSCM: laser scanning confocal microscopy; MESI: multi-exposure speckle imaging; MSOT: multispectral opto-acoustic tomography; NMF: natural moisturising factor; OCT: optical coherence tomography; R&D: research and development; RCM: reflectance confocal microscopy; SCC: squamous cell carcinoma; Sens: sensitivity; SHG: second harmonic generation; SK: seborrhoeic keratosis; Spe: specificity.