Reunión del GEDEI Madrid 2015

Universitat de Barcelona

Biofotónica en el diagnóstico de cáncer cutáneo

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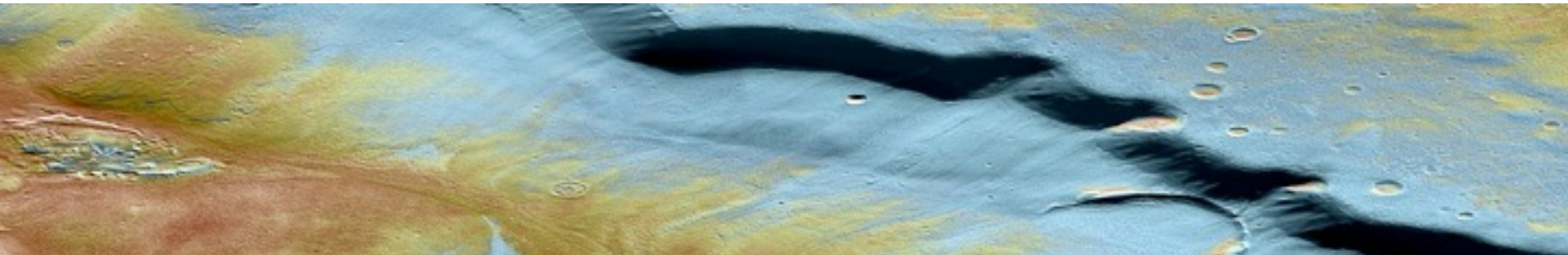
CENTRE DE TRANSFERENCIA DE TECNOLOGIA (CTT)
INSTITUT NATIONAL POLYTECHNIQUE DE TOULOUSE (INPT)
UNIVERSITA DEGLI STUDI DI MODENA E REGGIO EMILIA (UNIMORE)

Conflicts of interest

Consultant: Derm Spectra, Scibase

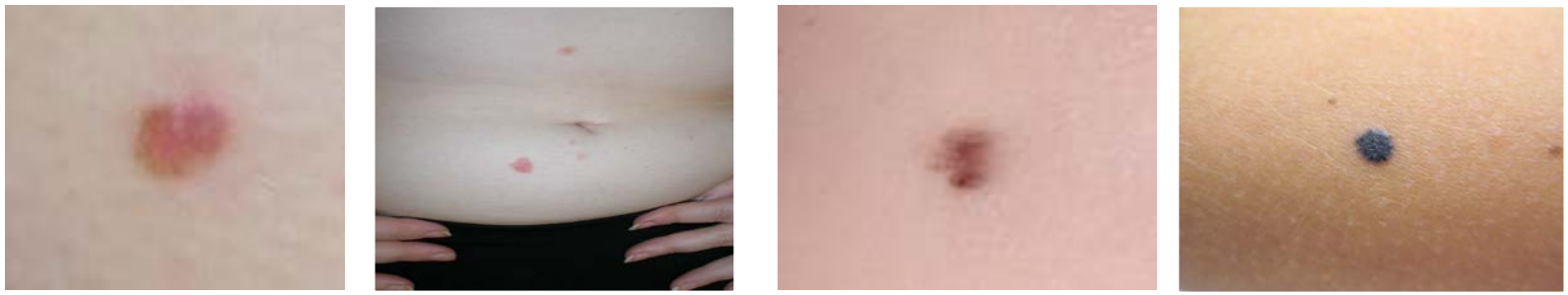
Research collaboration: Mavig, Scibase, Agfa Heathcare, Dermtech, Derma Instruments, Canfield, 3Gen, Diagnoptics

Editor of dermoscopy and confocal books



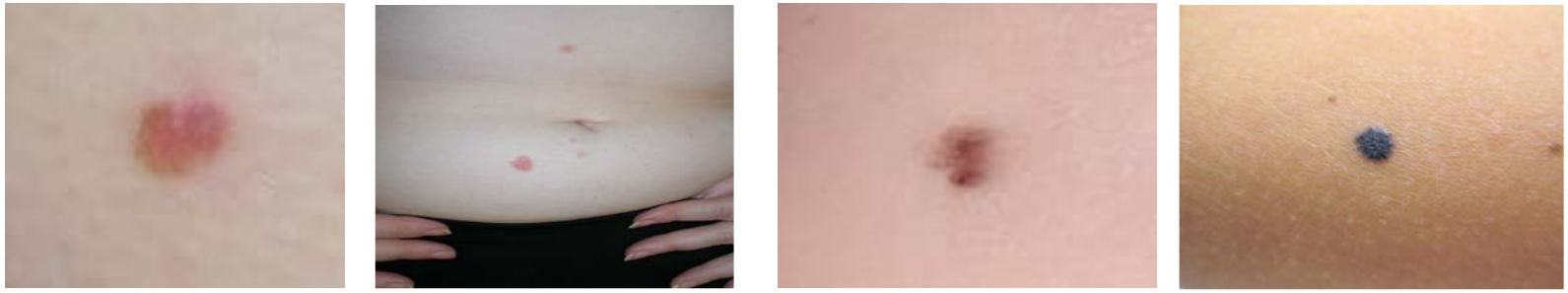
Modern diagnostic tools for early detection of melanoma

"Diagnosing melanoma by simple visual examination with the ABCD rule is incorrect in almost 1 out of every 3 melanoma diagnoses"



Wolf IH, Smolle J, Soyer HP, Kerl H. Sensitivity in the clinical diagnosis of malignant melanoma. Melanoma Res 1998; 8: 425-9.
Curley RK, Cook MG, Fallowfield ME, Marsden RA. Accuracy in clinically evaluating pigmented lesions. BMJ 1989; 299: 16-8.
Kittler H, Pehamberger H, Wolff K, Binder M. Diagnostic accuracy of dermoscopy. Lancet Oncol 2002; 3: 159-65.

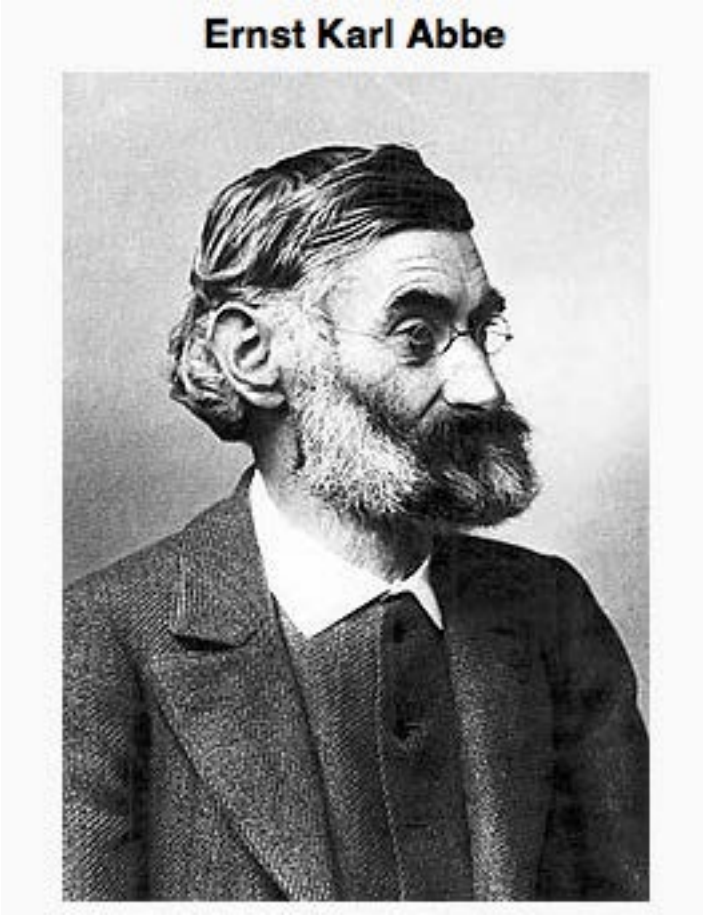
"Early diagnosis of melanoma by dermatologists is NOT saving many lives"



Wainstein A, et al. Melanoma Early Detection and Awareness: How Countries Developing Melanoma Awareness Programs Could Benefit From Melanoma-Proficient Countries. Am J Ther. 2014

Tejera-Vaquerizo A et al. Chronology of metastasis in cutaneous melanoma: growth rate model. J Invest Dermatol. 2012

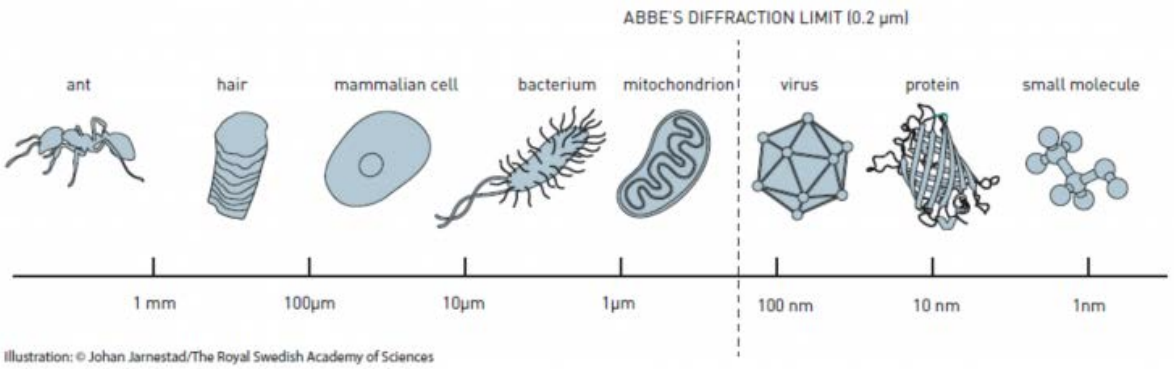
Liu W et al.Rate of growth in melanomas: characteristics and associations of rapidly growing melanomas. Arch Dermatol. 2006



1840 – January 14, 1905

Abbe is credited by many for discovering the resolution limit of the microscope, and the formula (published in 1873)

0,2 micrometers



The Nobel Prize in Chemistry 2014

Photo: Matt Staley/HHMI

Eric Betzig

Prize share: 1/3

© Bernd Schuller, Max-Planck-Institut

Stefan W. Hell

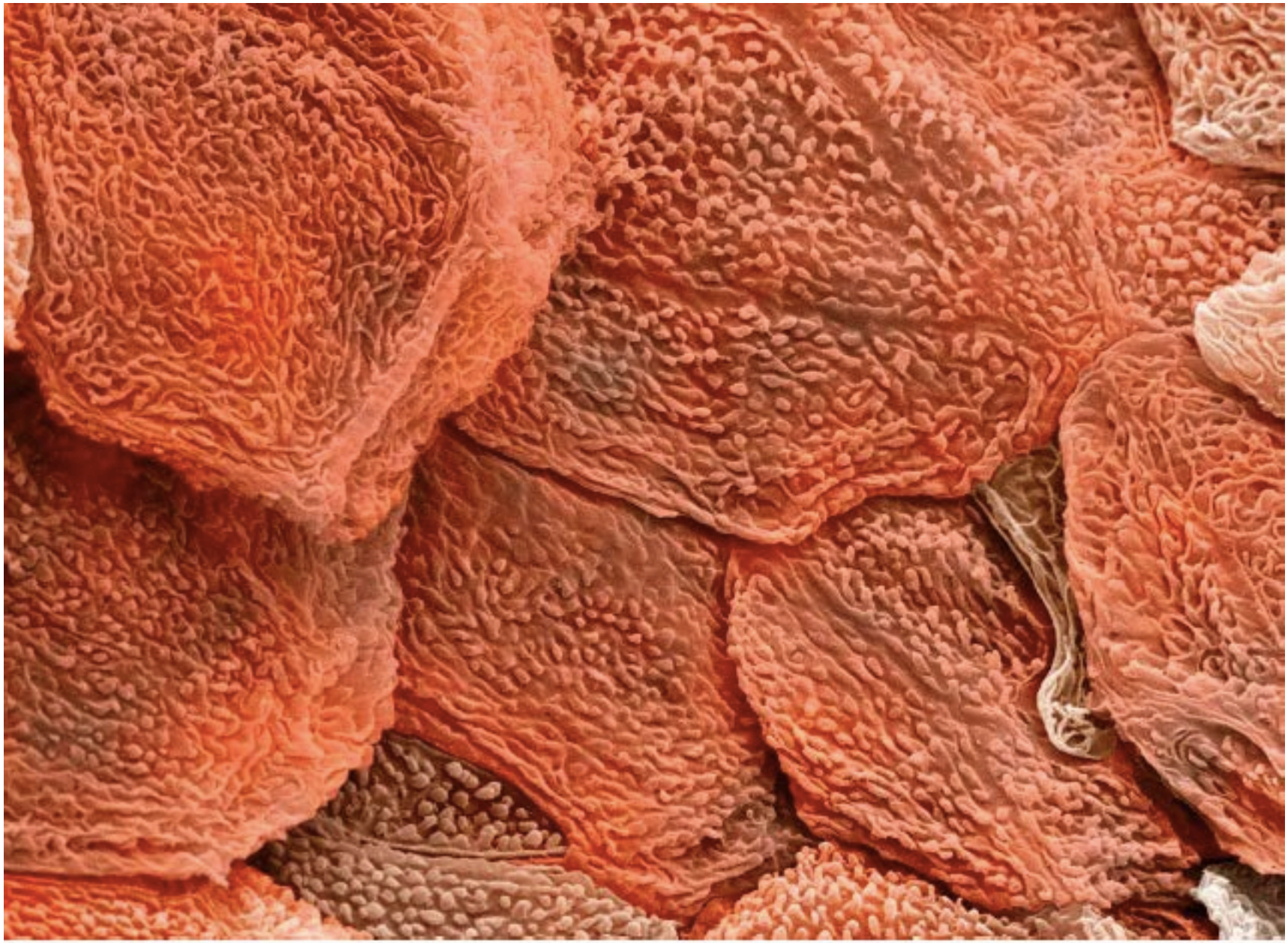
Prize share: 1/3

Photo: K. Lowder via Wikimedia Commons, CC-BY-SA-3.0

William E. Moerner

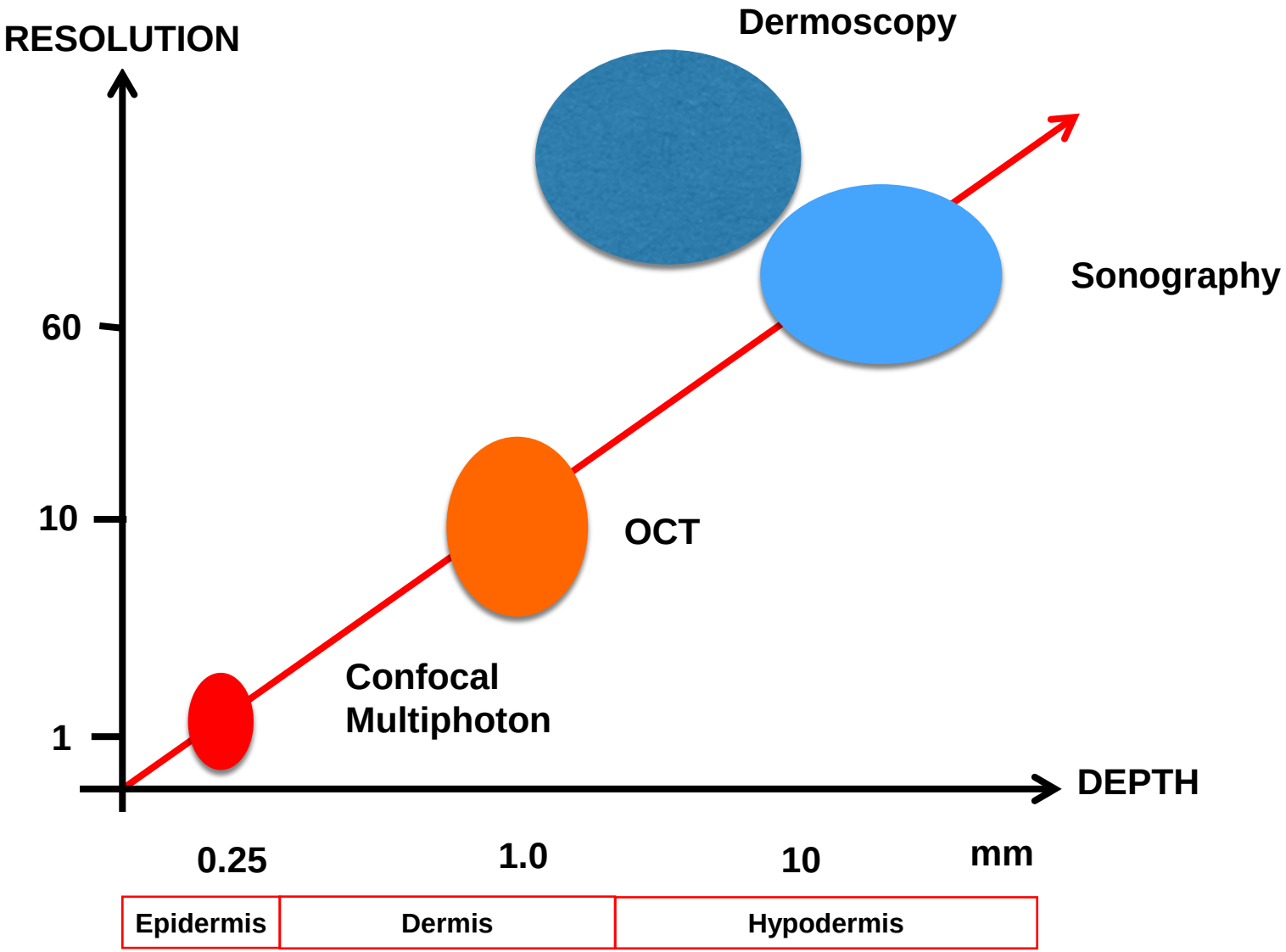
Prize share: 1/3

The Nobel Prize in Chemistry 2014 was awarded jointly to Eric Betzig, Stefan W. Hell and William E. Moerner *"for the development of super-resolved fluorescence microscopy"*.



Epidermis, SEM photograph (1840× zoom) by Andrew Syred, Science Photo Library

Resolution is limited by penetration



Non-invasive methods for skin examination

Total body photography

Dermatoscopy

Digital dermatoscopy

Wood's lamp

Confocal scanning laser microscopy

Optical Coherence Tomography

Sonography

Photoacoustic microscopy

Multispectral

Hyperspectral imaging

Raman spectroscopy

Electrical impedance spectroscopy

Tissue elastography

Reflex transmission imaging

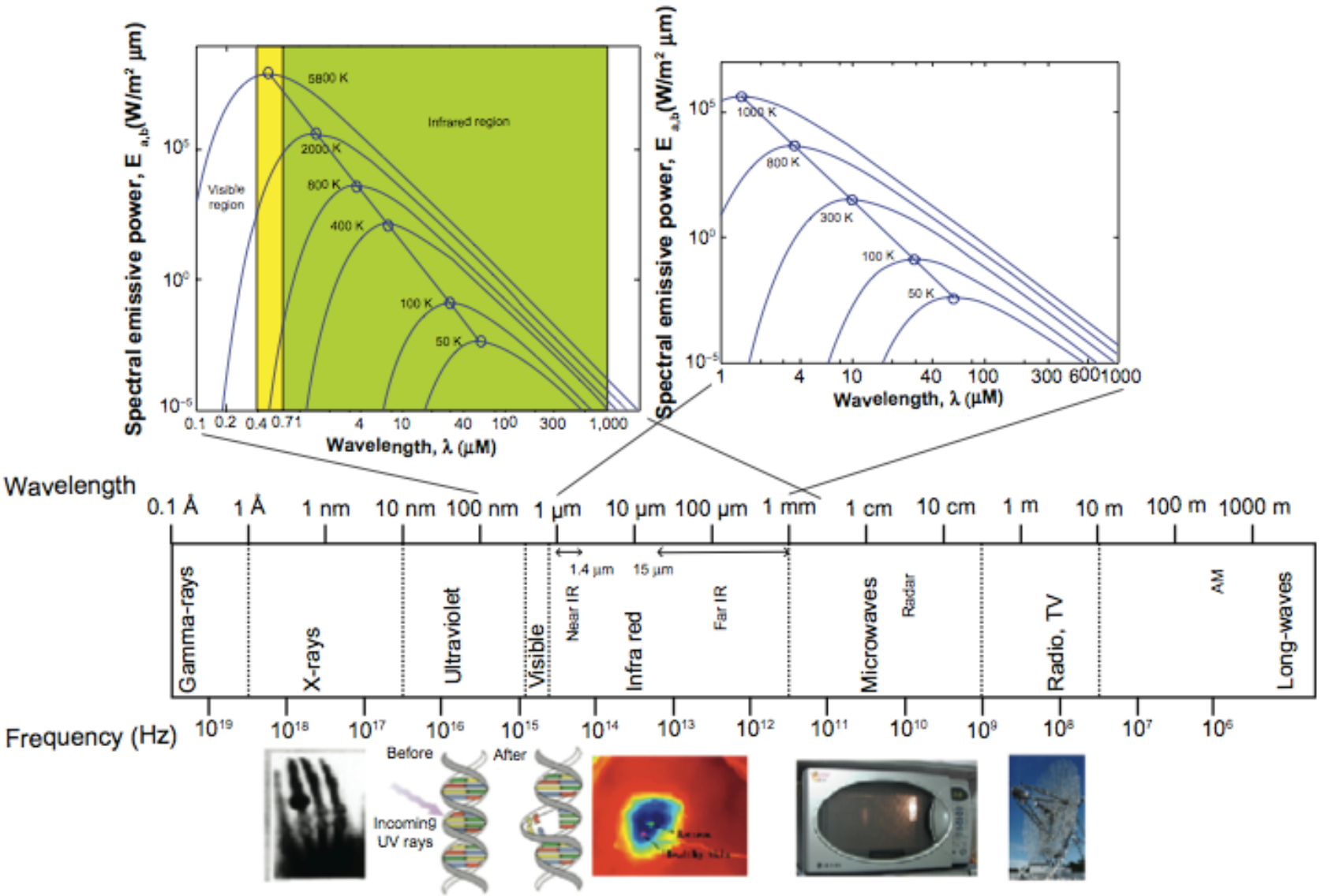
X-ray fiber diffraction

Thermal analysis

Melanoma sniffing dogs

Epidermal genetic information retrieval

Electromagnetic radiation in medical diagnosis



Herman C. Clinical, Cosmetic and Investigational Dermatology. November 2012

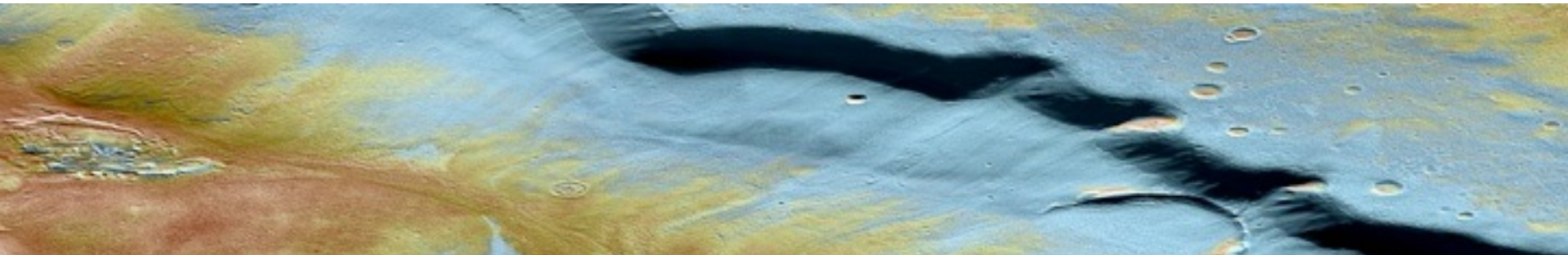
Modern diagnostic tools for early detection SKIN CANCER

Population

- General population
- High risk-patients

End users

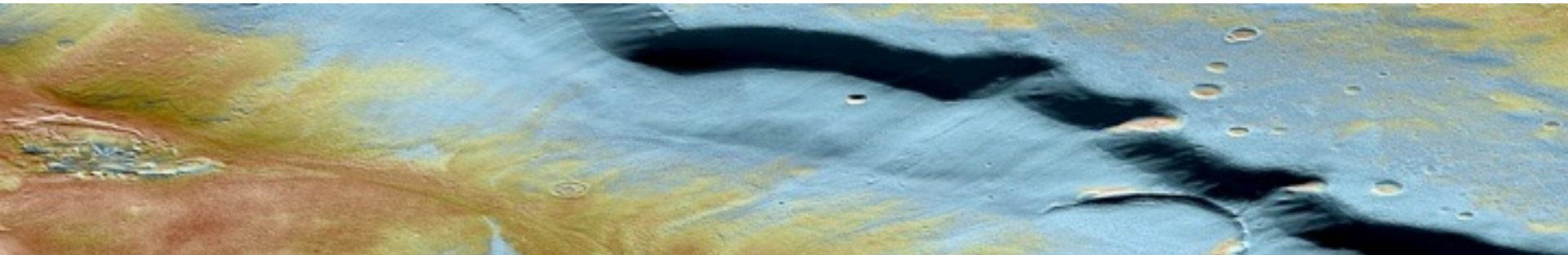
- Patients
- Nurses or general physicians
- Dermatologists
- Specialized centers



Qualitative methods

Systems that use different light to obtain images from the tissue .
Type I,II, III.
Passive methods, Available

- Total Body Photography
- Dermoscopy
- Digital Dermoscoy

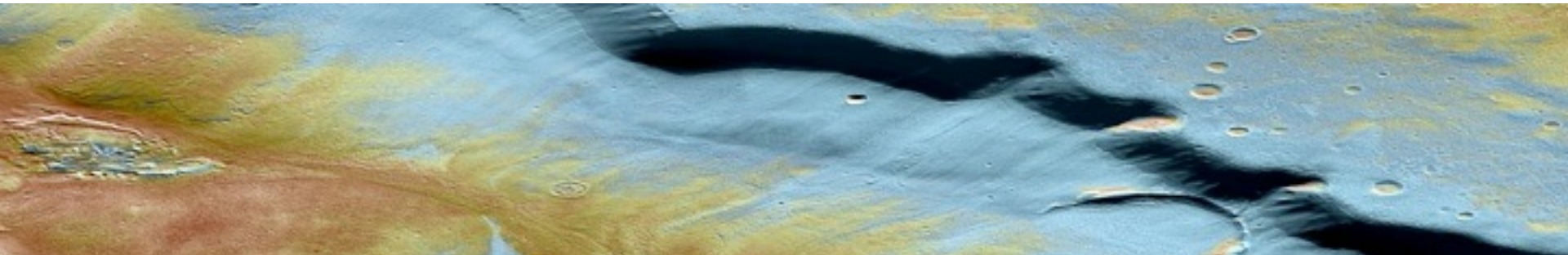


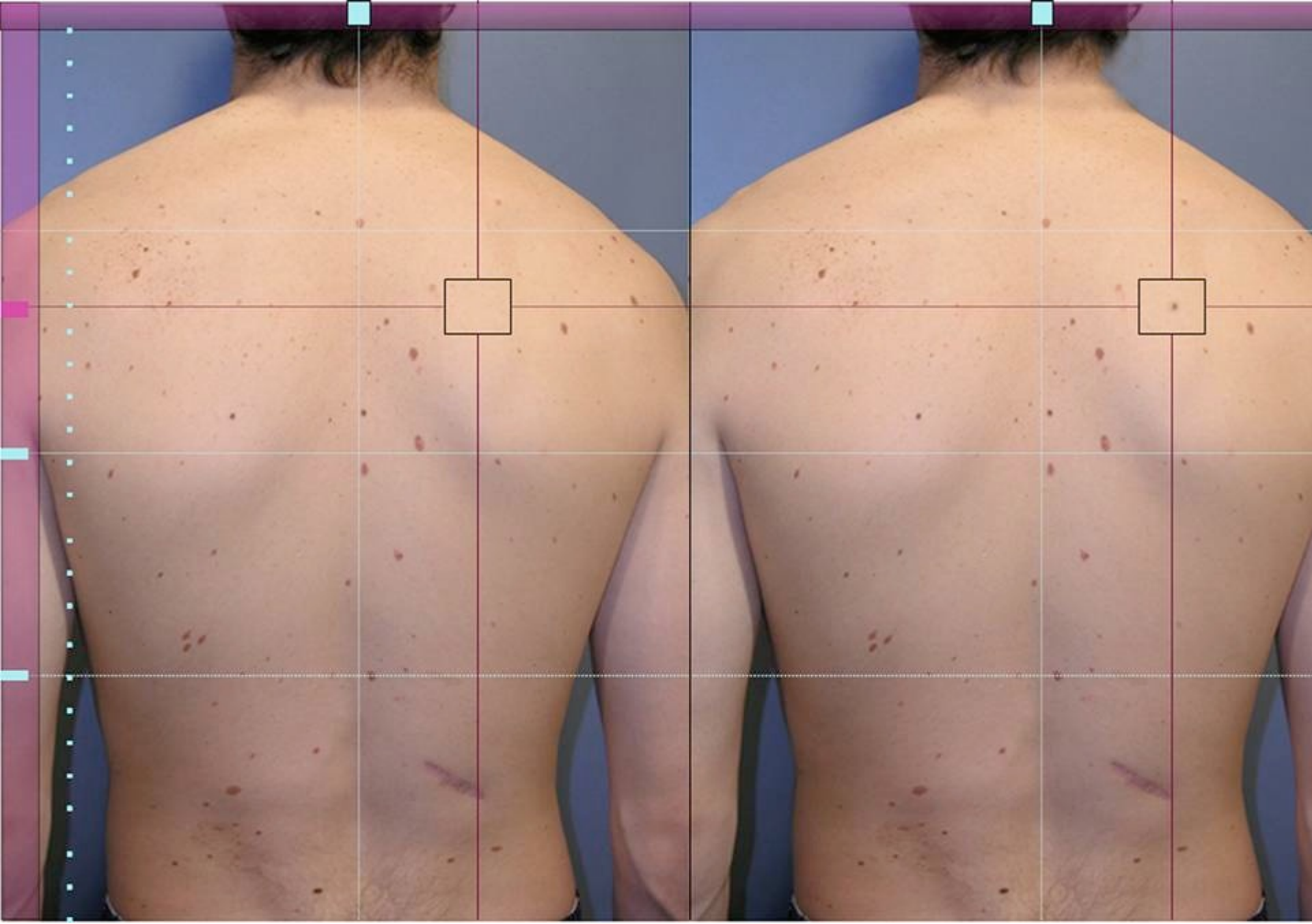
Qualitative methods

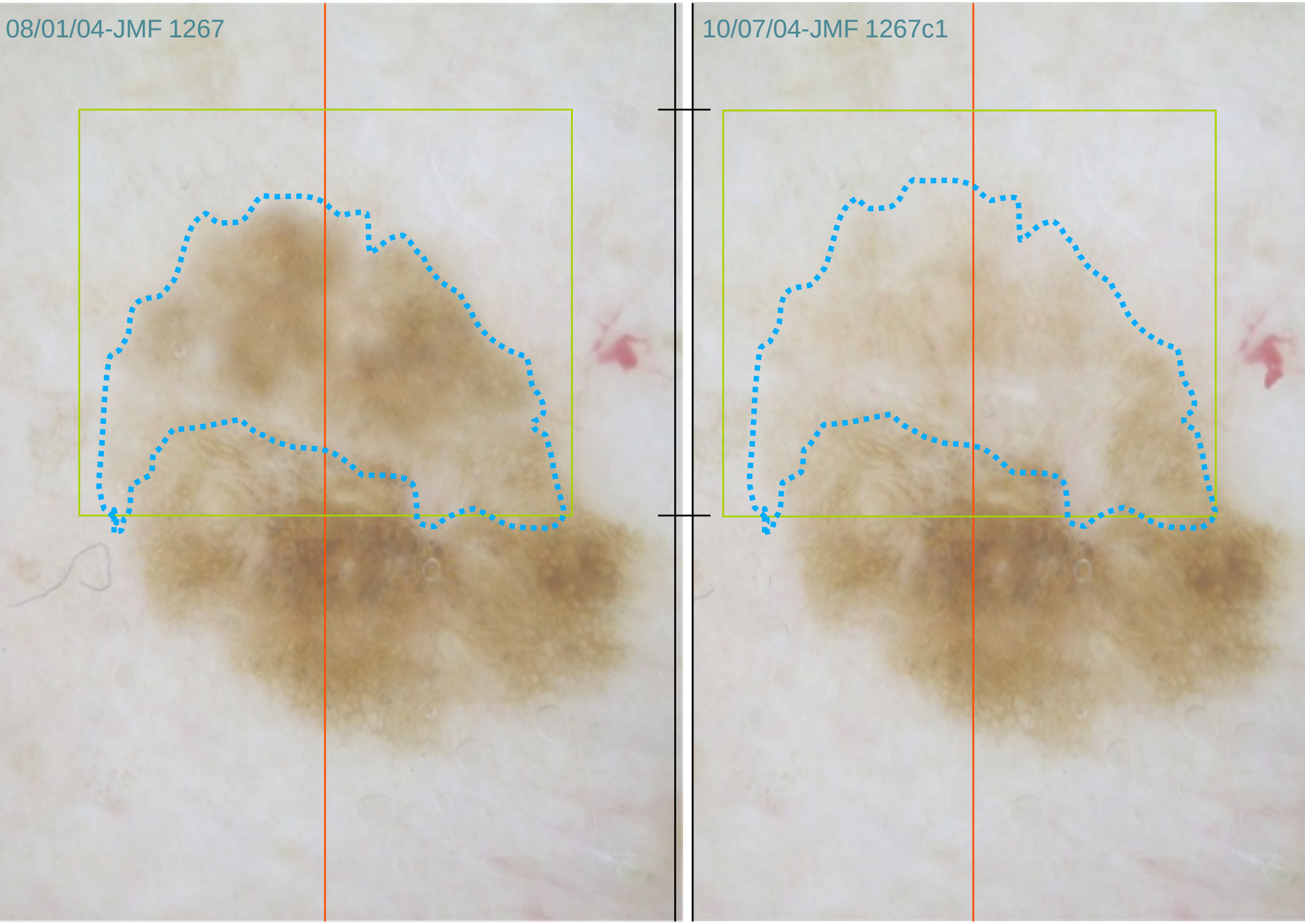
Systems that use different light to obtain images from the tissue .
Type I,II, III.
Passive methods, Available

- Total Body Photography
- Dermoscopy
- Digital Dermoscoy

- Reflectance Confocal Microscopy
- Optical Coherence tomography
- Multiphoton tomography
- RAMAN+RCM
- Photoacoustic microscopy
- Multi-Hyperspectral imaging



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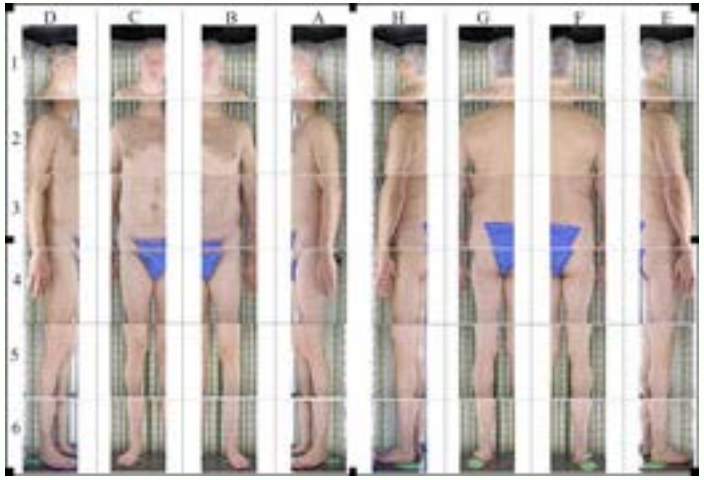
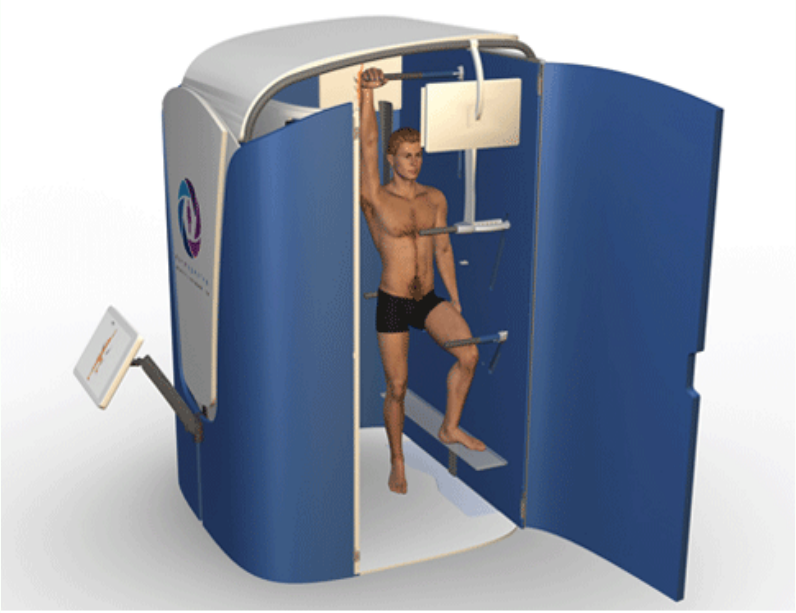


Rhett J Drugge et al. Melanoma screening with serial whole body photographic change detection using Melanoscan® technology. Dermatology Online J 15 (6): 1



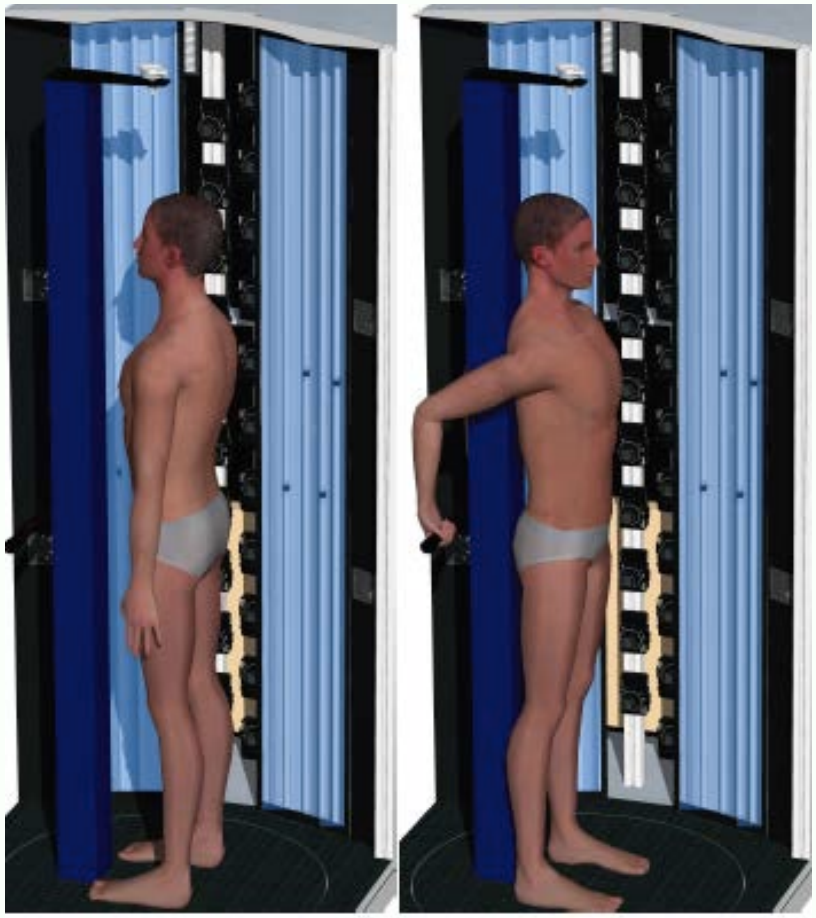
High resolution color imaging in 10 minutes

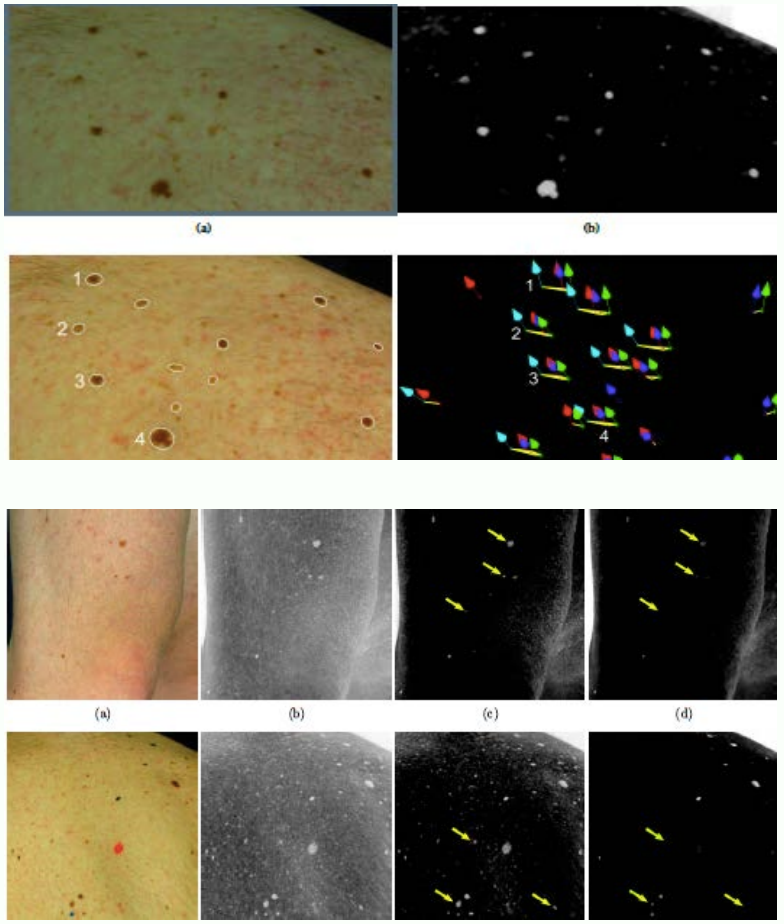
Comprehensive body imaging from head to toe (85% coverage)

Private storage of all images and date marked for easy comparison

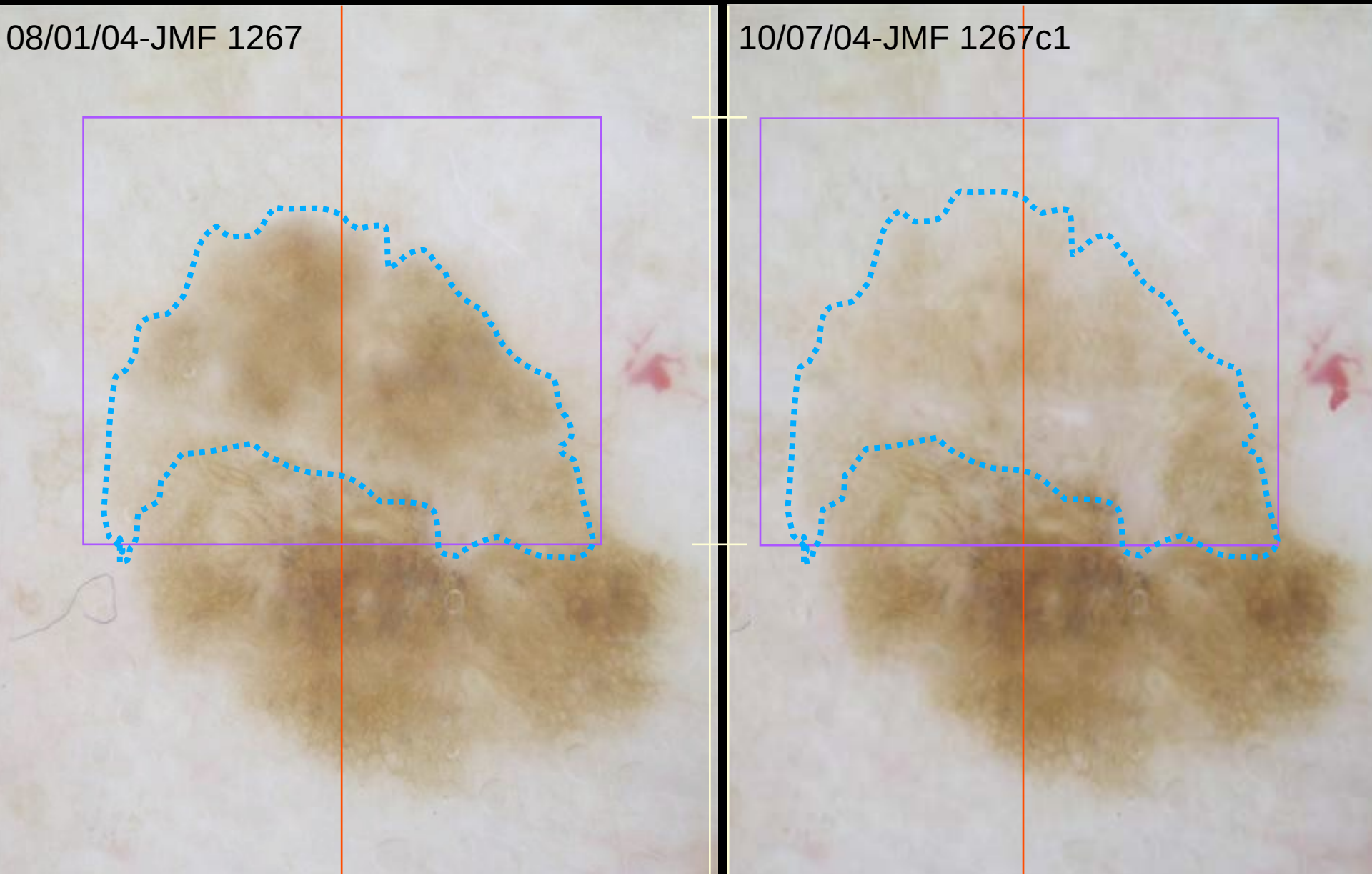
3D Total Body surface

New technologies in TBP



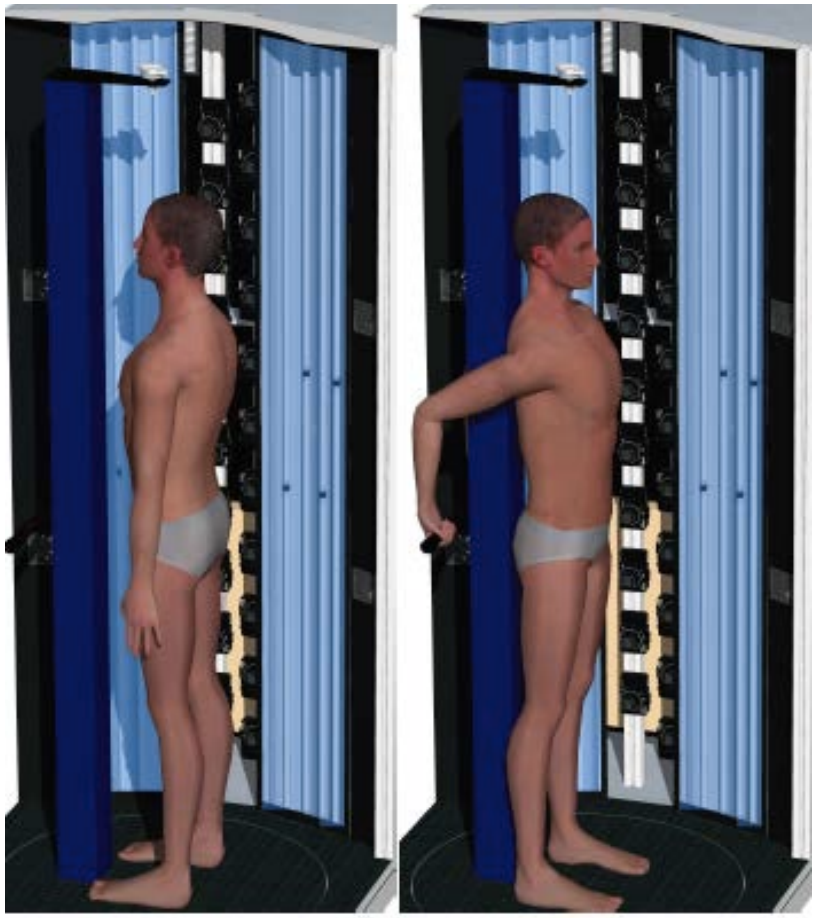


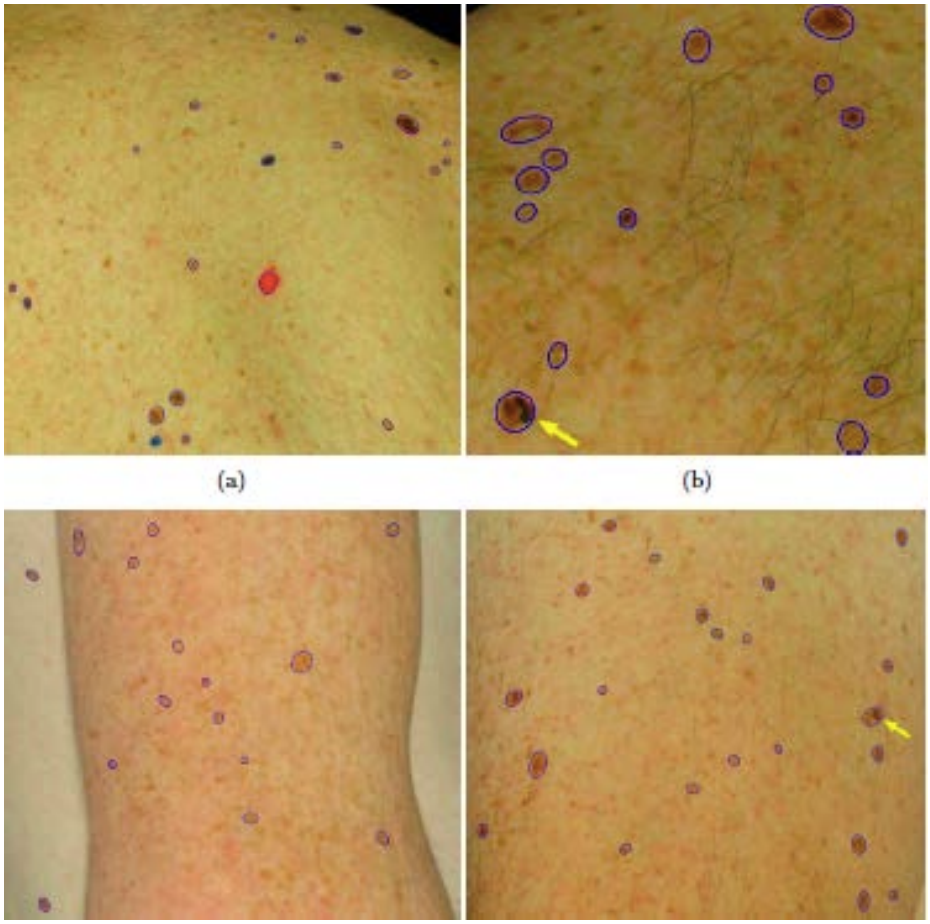
Konstantin Korotkov, Josep Quintana, Susana Puig, Josep Malvehy, Rafael Garcia. Design, Construction, and Testing of a New Total Body Skin Scanning System. IEEE Transactions on Medical Imaging 2014



Meta-analysis of digital dermoscopy follow-up of melanocytic skin lesions: a study on behalf of the International Dermoscopy Society. G. Salerni, T. Terán, S. Puig, J. Malvehy, I. Zalaudek, G. Argenziano, H. Kittler. *J Eur Acad Dermatol Venereol.* October 2012.

New technologies in TBP





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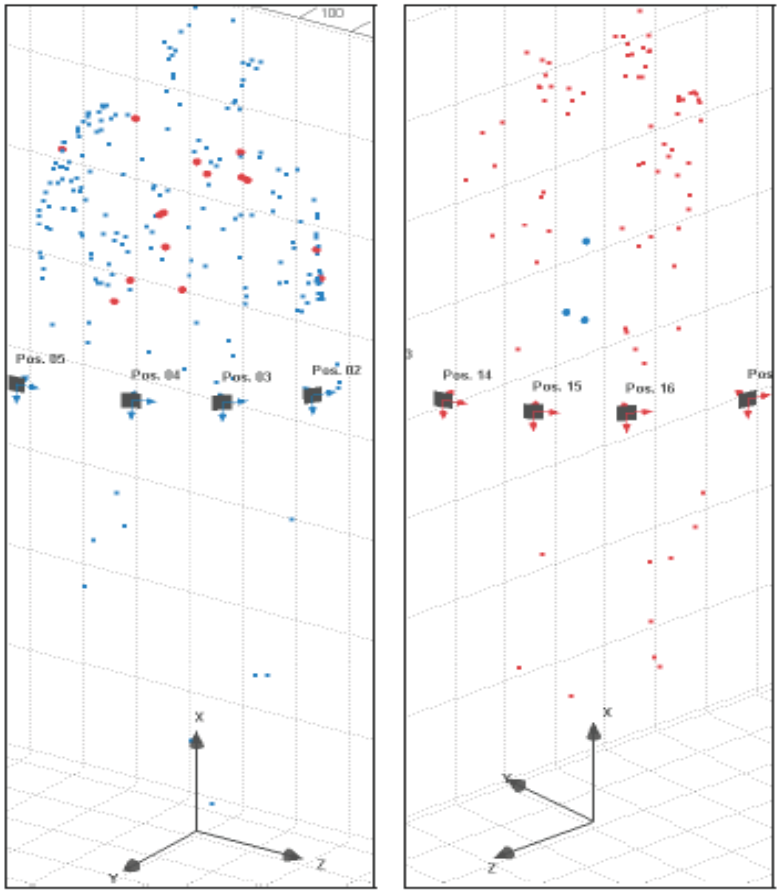
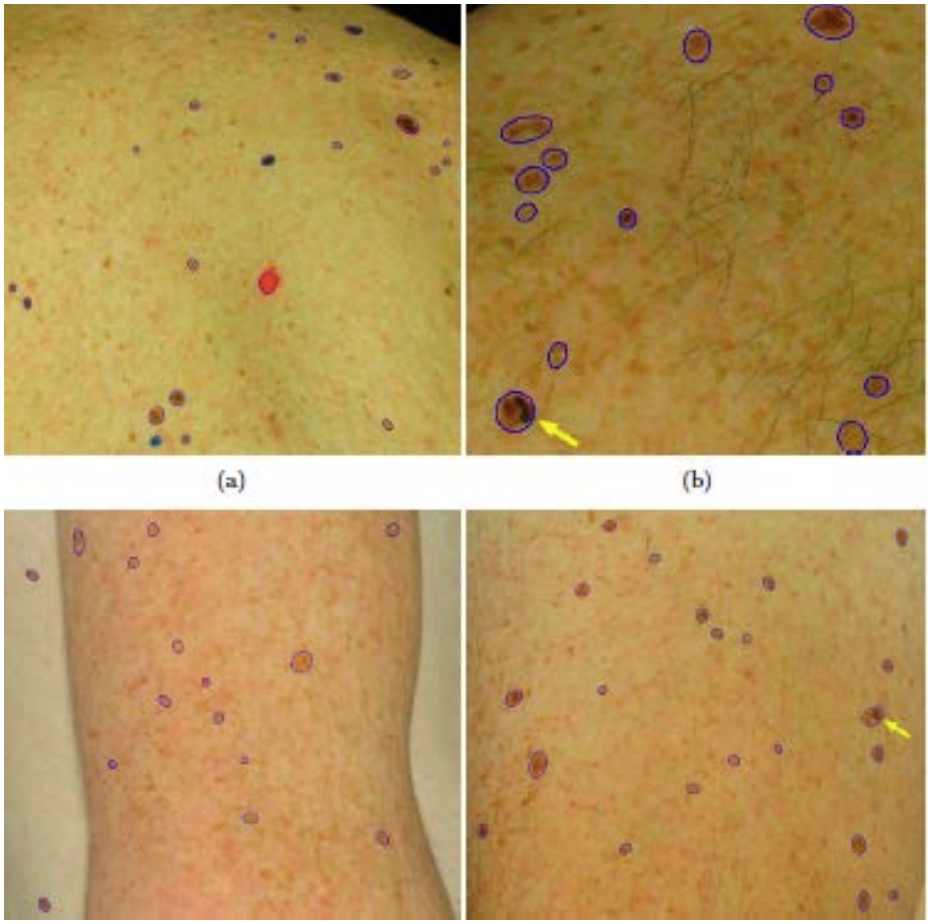
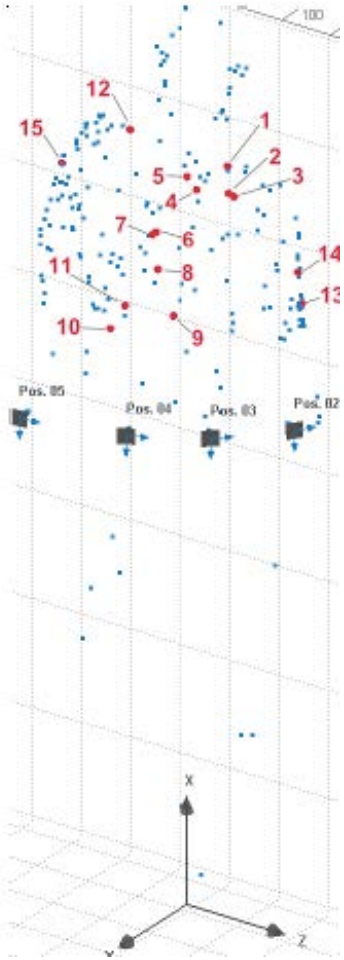
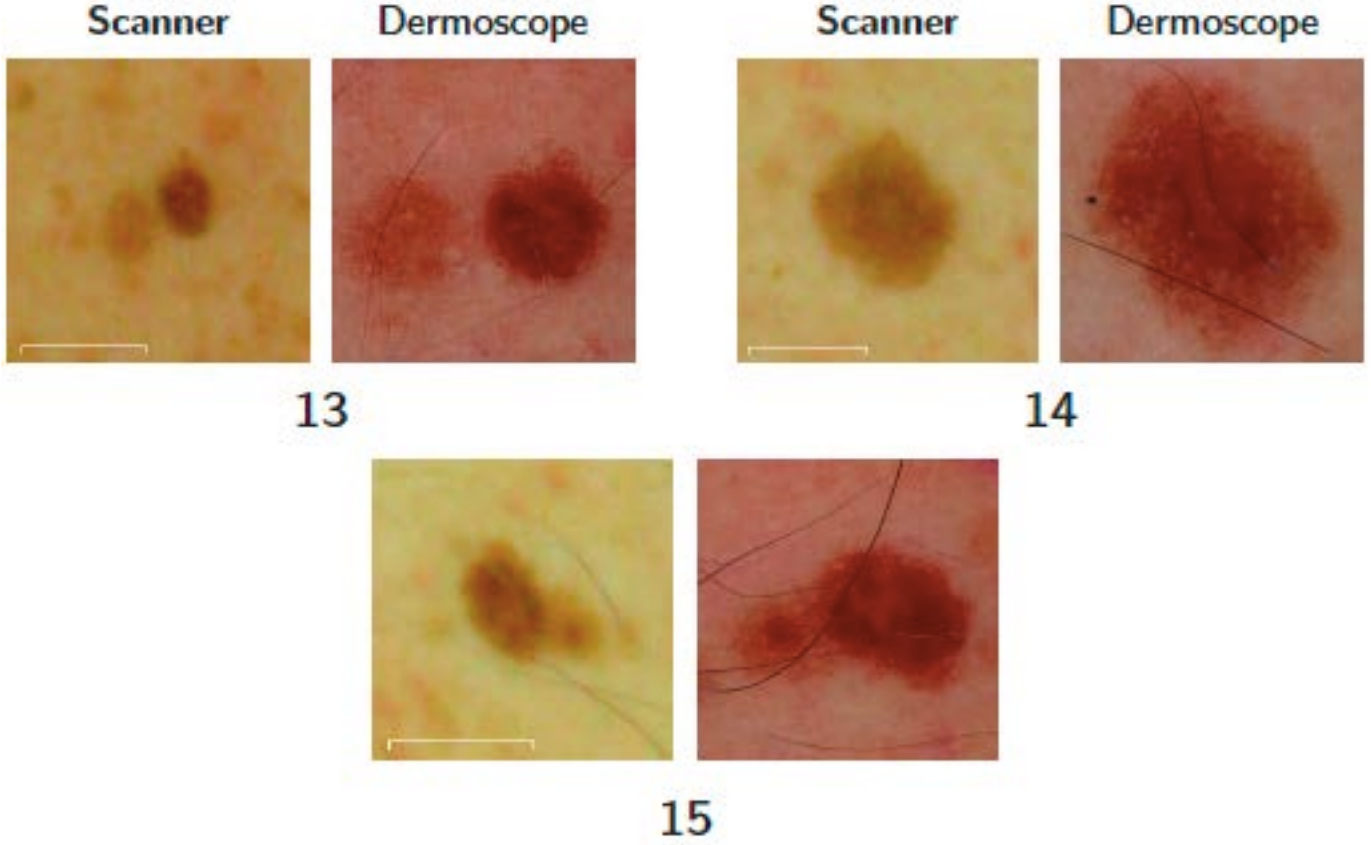




Konstantin Korotkov, Josep Quintana, Susana Puig, Josep Malvehy, Rafael Garcia. Design, Construction, and Testing of a New Total Body Skin Scanning System. IEEE Transactions on Medical Imaging 2014

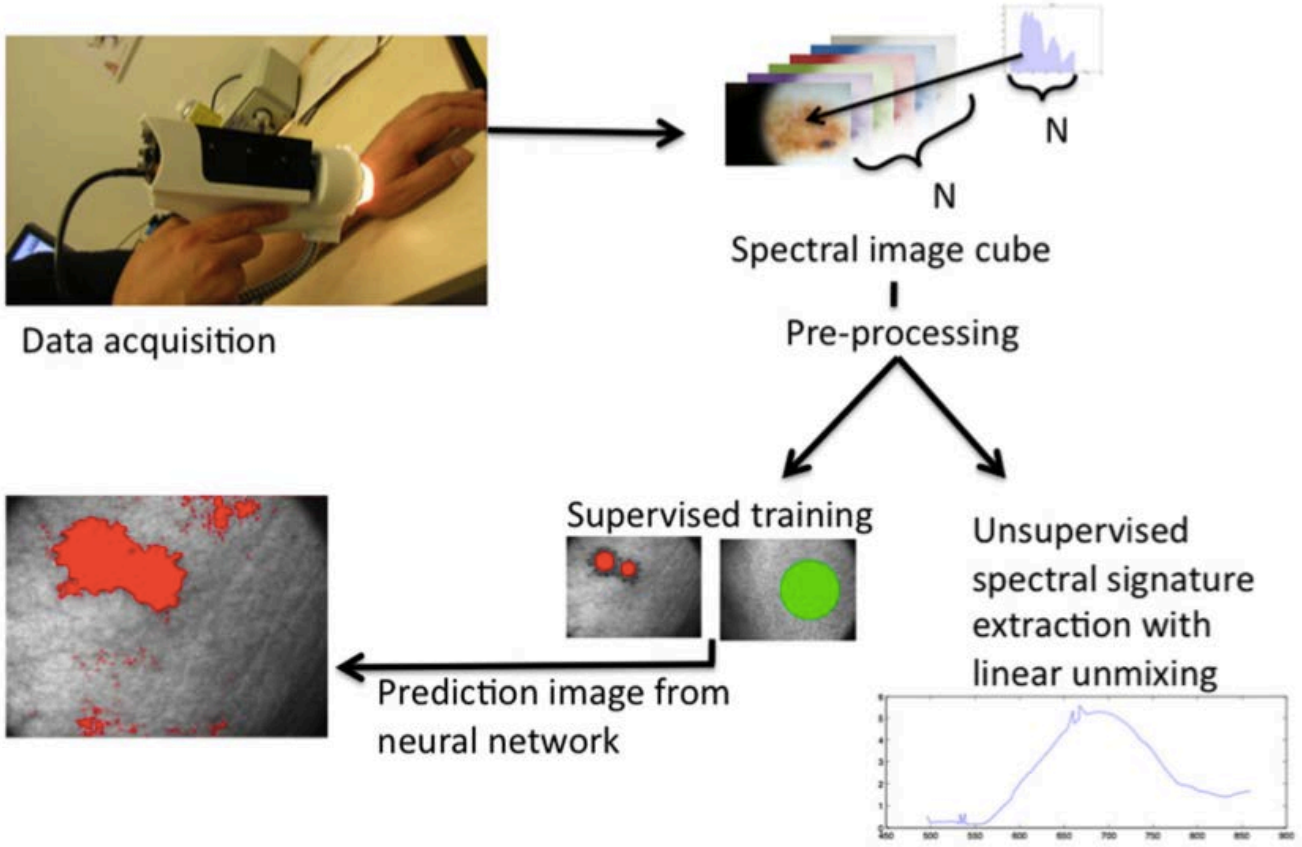
New technologies in TBP and TB dermoscopy





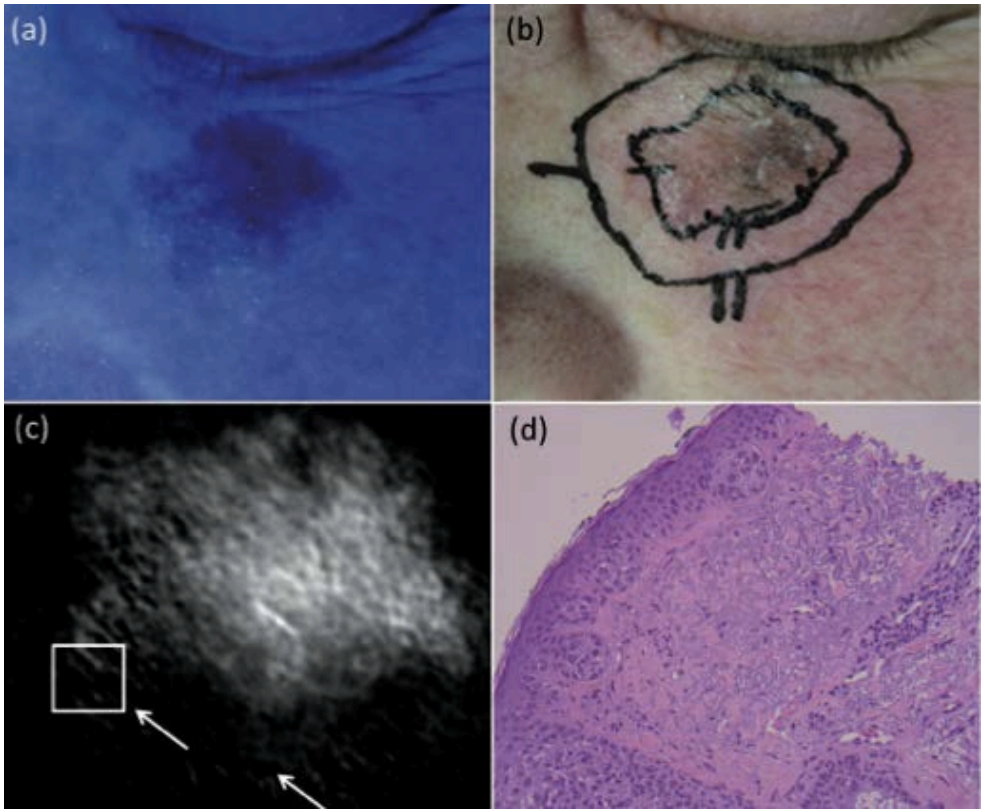
Konstantin Korotkov, Josep Quintana, Susana Puig, Josep Malvehy, Rafael Garcia. Design, Construction, and Testing of a New Total Body Skin Scanning System. IEEE Transactions on Medical Imaging 2014

Multi-Hyperspectral imaging



Neittaanmäki-Perttu N, Grönroos M, Jeskanen L, Pölönen I, Ranki A, Saksela O, Snellman E. Delineating margins of lentigo maligna using a hyperspectral imaging system. Acta Derm Venereol. 2015 May;95(5):549-52

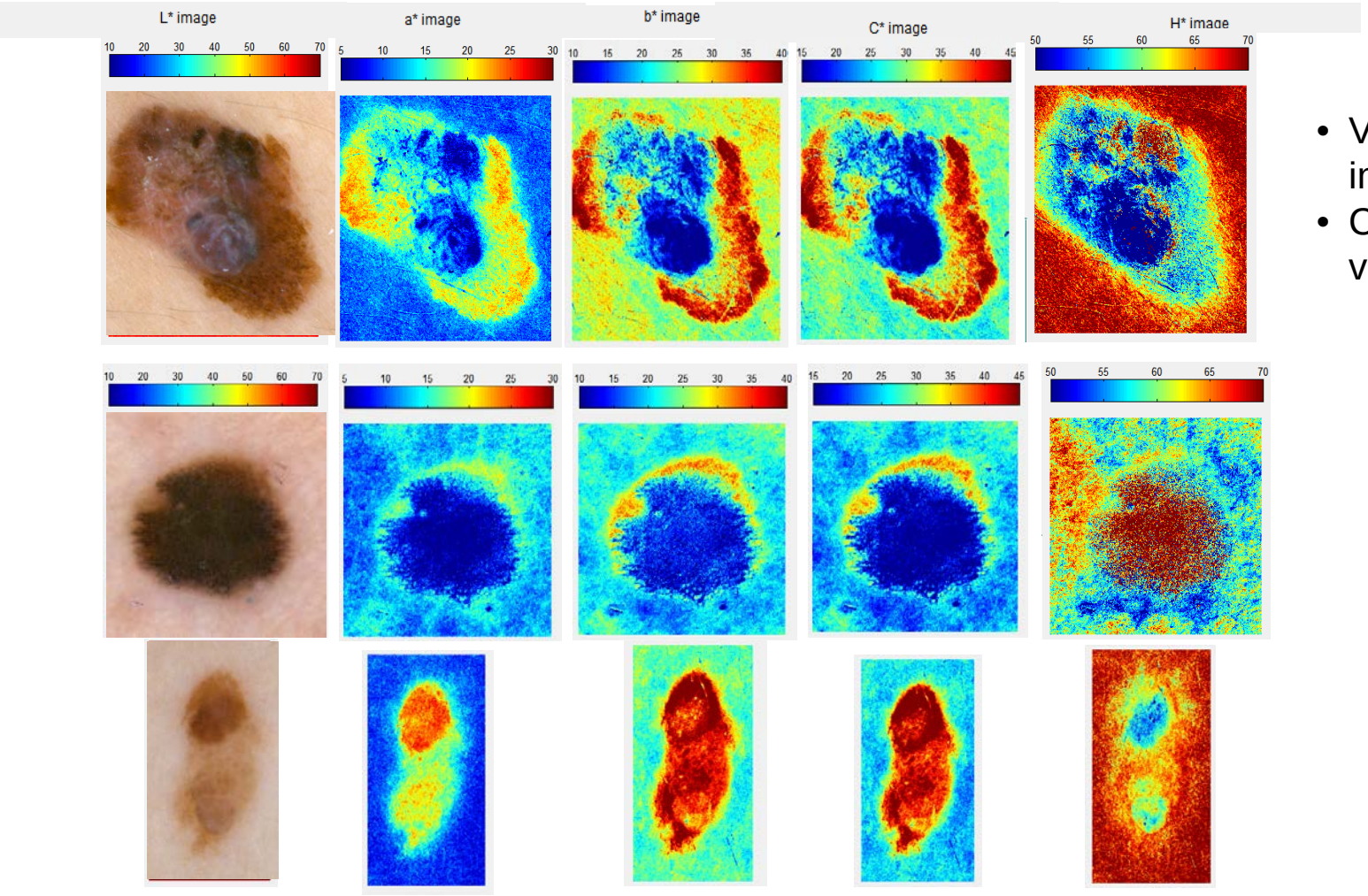
Hyperspectral imaging
Delineating margins of lentigo maligna



A total of 14 LMs and 5 LMMs in 19 pa- tients were included. HIS analysis matched the histo- pathological analysis in 18/19 (94.7%) cases while in 1/19 (5.3%) cases HIS showed lesion extension not confirmed by histopathology (false positives). Compared to clinical examination, HIS defined lesion borders more accura- tely in 10/19 (52.6%) of cases (wider, n=7 or smaller, n = 3) while in 8/19 (42.1%) cases lesion borders were the same as delineated clinically as confirmed histologically. Thus, HIS is useful for the detection of subclinical LM/ LMM borders.

Neittaanmäki-Perttu N, Grönroos M, Jeskanen L, Pölönen I, Ranki A, Saksela O, Snellman E. Delineating margins of lentigo maligna using a hyperspectral imaging system. Acta Derm Venereol. 2015 May;95(5):549-52

Hyperspectral: visual representation of distribution of colours

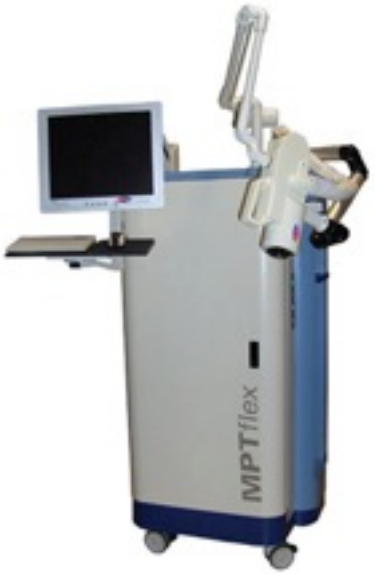


- Visual interpretation
- Computer vision analysis

Hyperspectral images in Melanoma : Diagnoptics project

New imaging technology in skin cancer

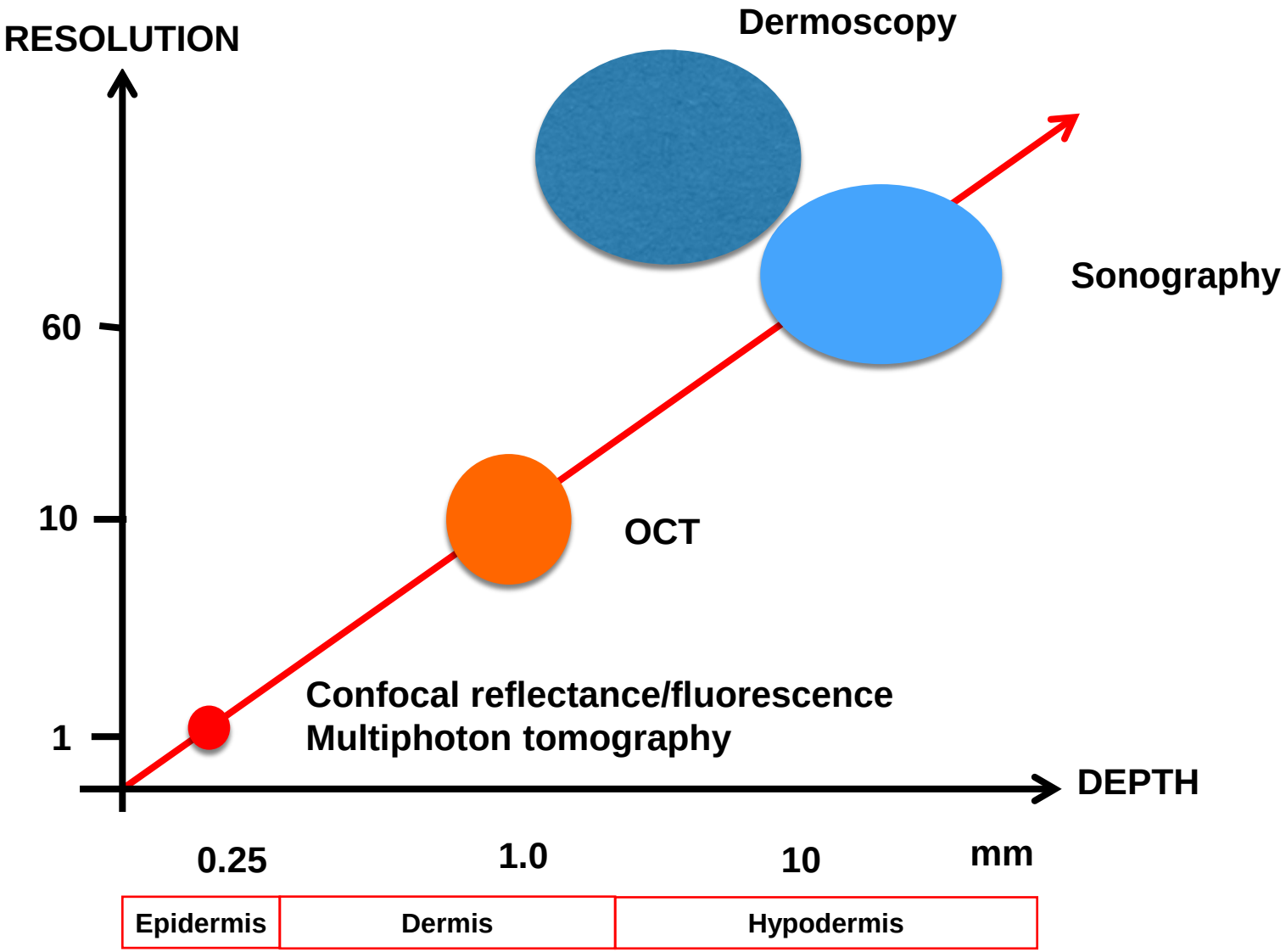
IN VIVO CONFOCAL MICROSCOPY



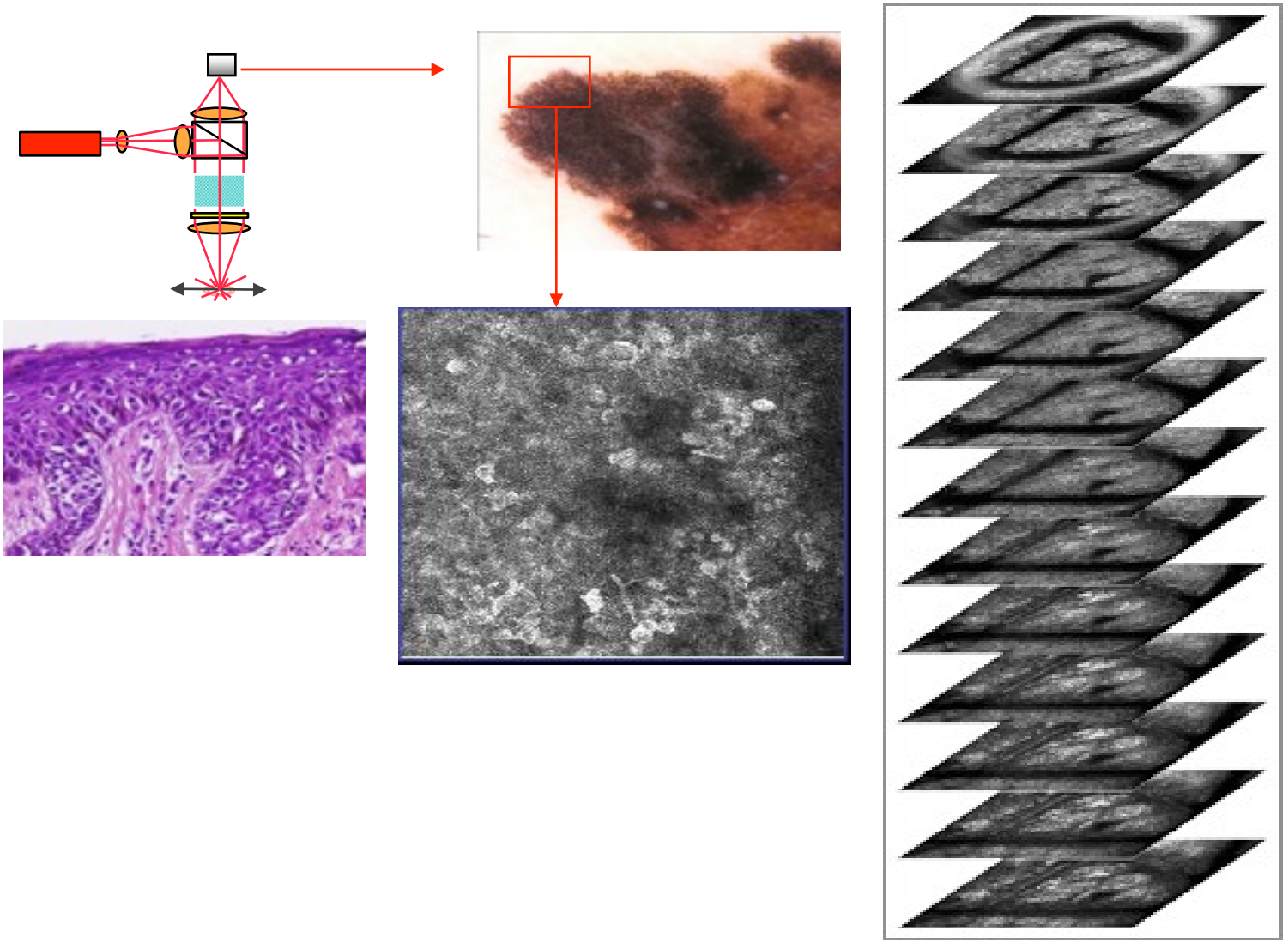
MULTIPHOTON MICROSCOPY

OPTICAL COHERENCE TOMOGRAPHY

Resolution and penetration

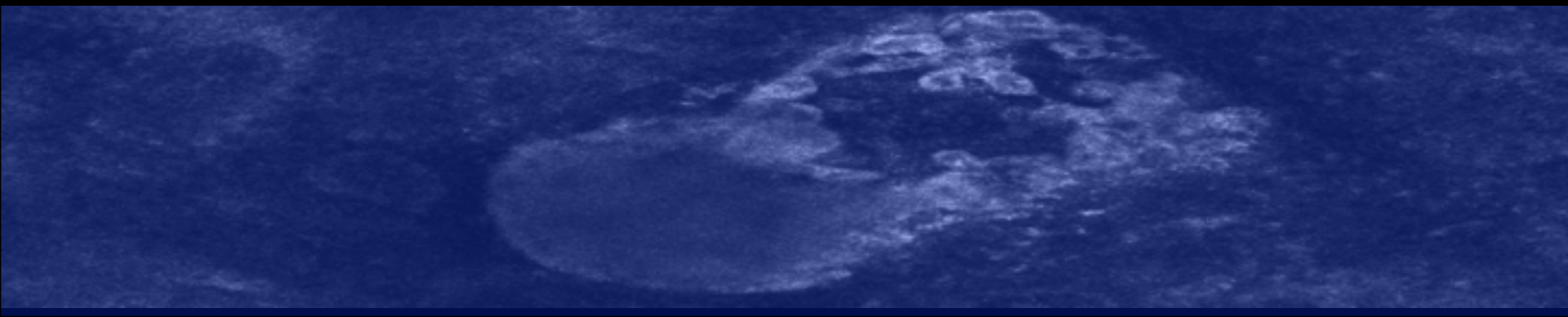


Reflectance confocal microscopy



Principles of Confocal Imaging

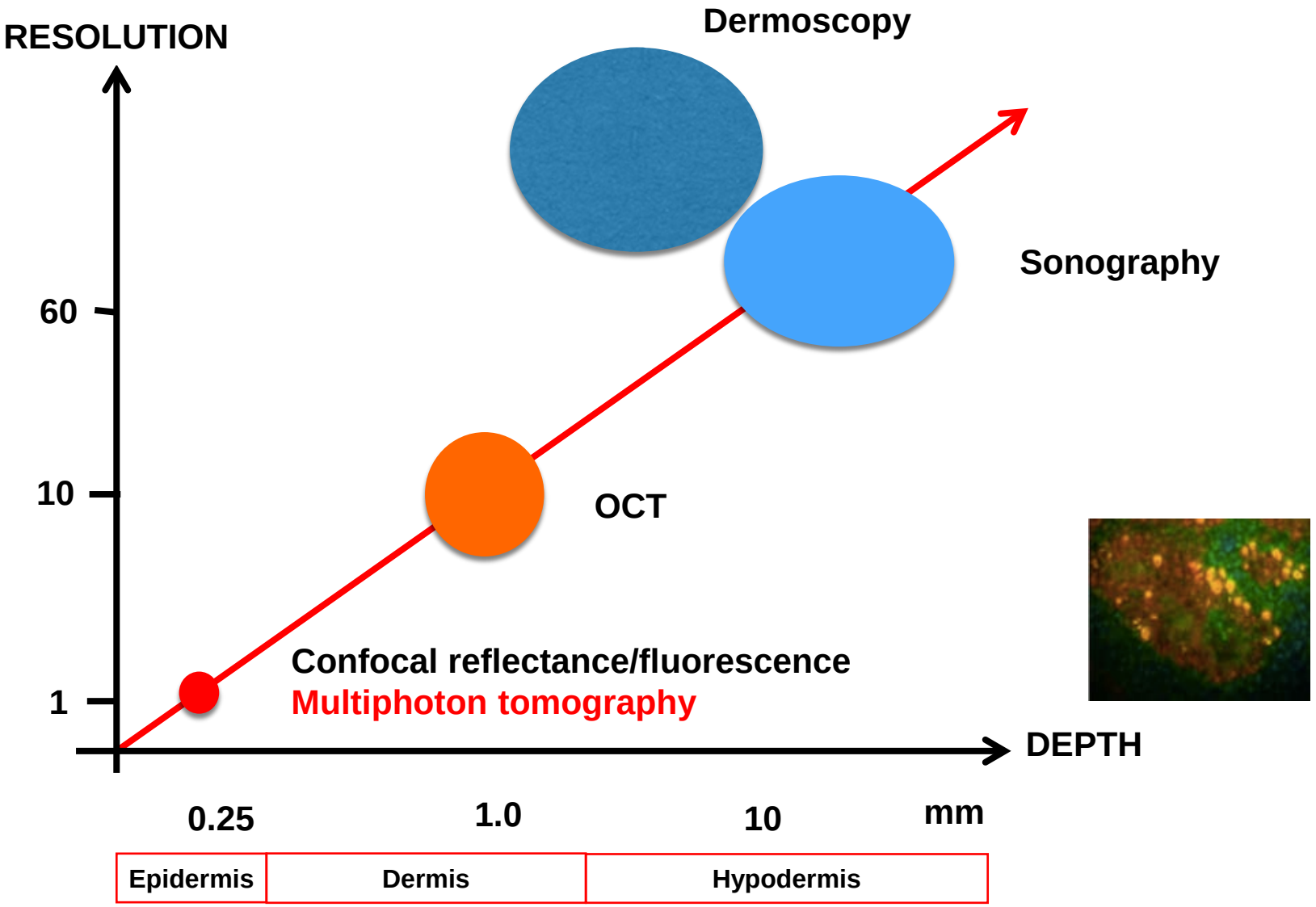
- The pigment **melanin** within the epidermis has a high refractive index, in fact higher than keratin.
- The confocal microscope images keratinocytes in the **epidermis, erythrocytes and leukocytes in capillaries within the papillary dermis and collagen bundles** within the dermis to a **depth of 100-200 µm at the 830 nm wavelength**.



Hand held RCM

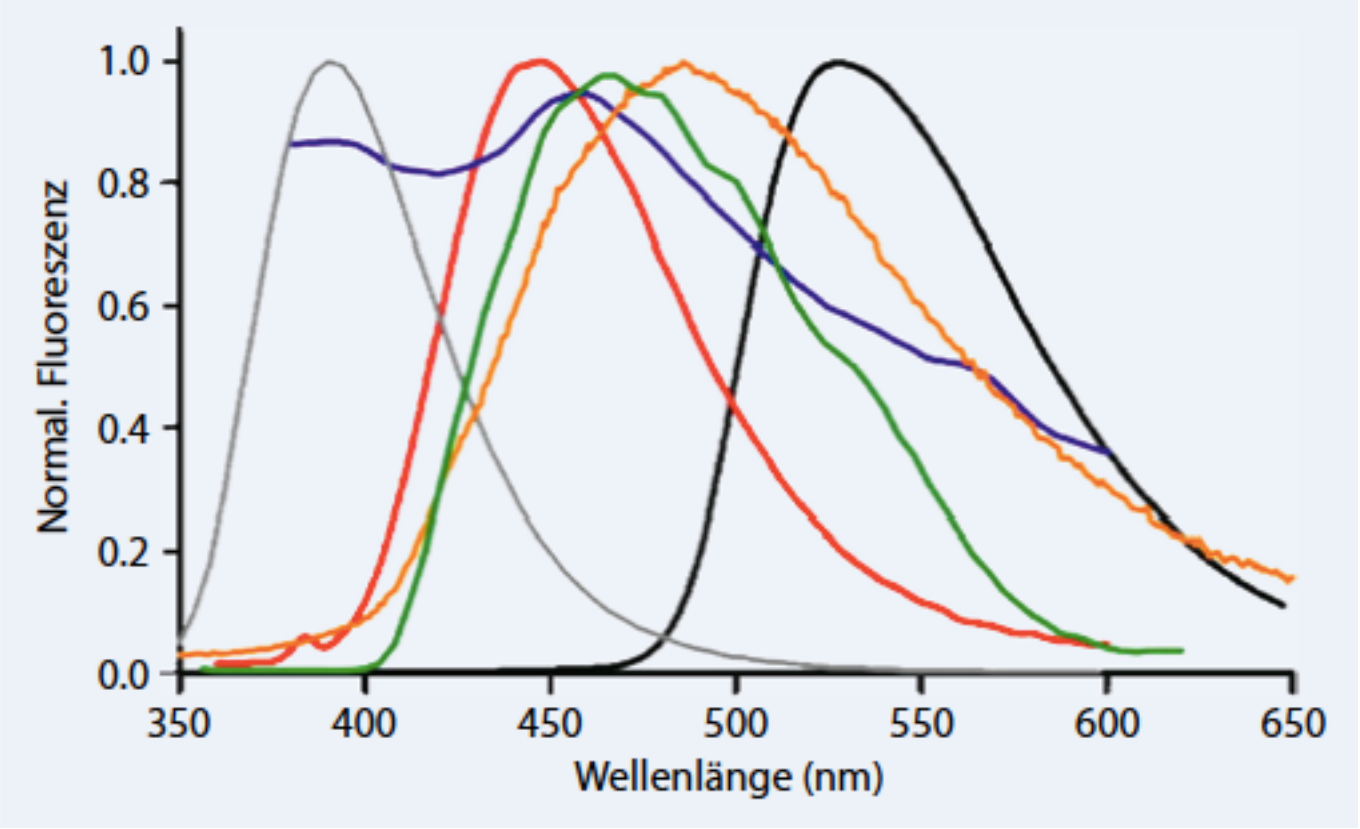
Fast examination (1-5 minutes)
Facial areas

Resolution is limited by penetration

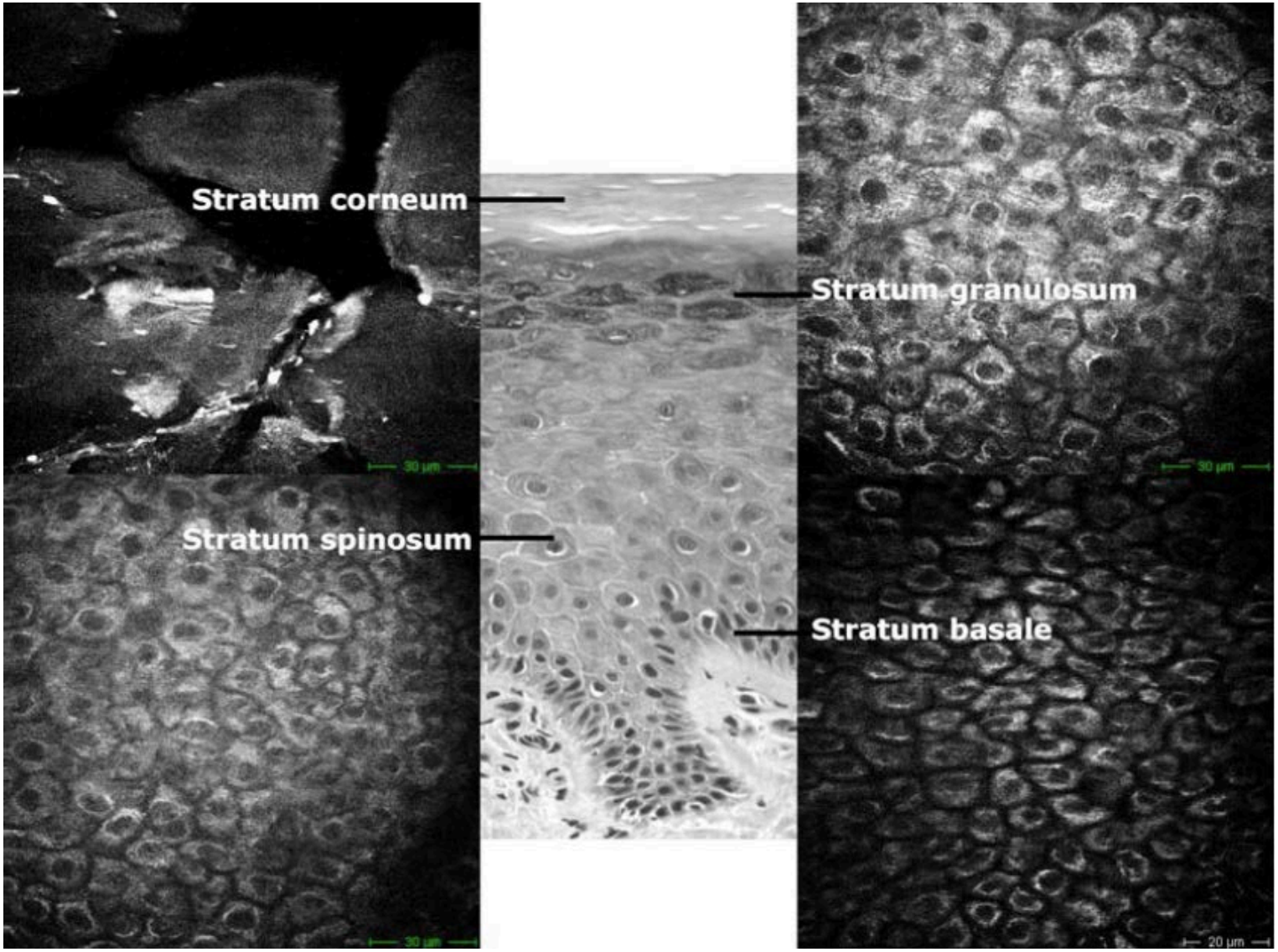


Multiphoton tomography

Simultaneous excitation of endogenous fluorophores by two or more photons of low energy in the NIR



M. Kaatz, K. König. Multiphotonenmikroskopie und In-vivo-Multiphotonentomographie in der dermatologischen Bildgebung. Hautarzt 2010

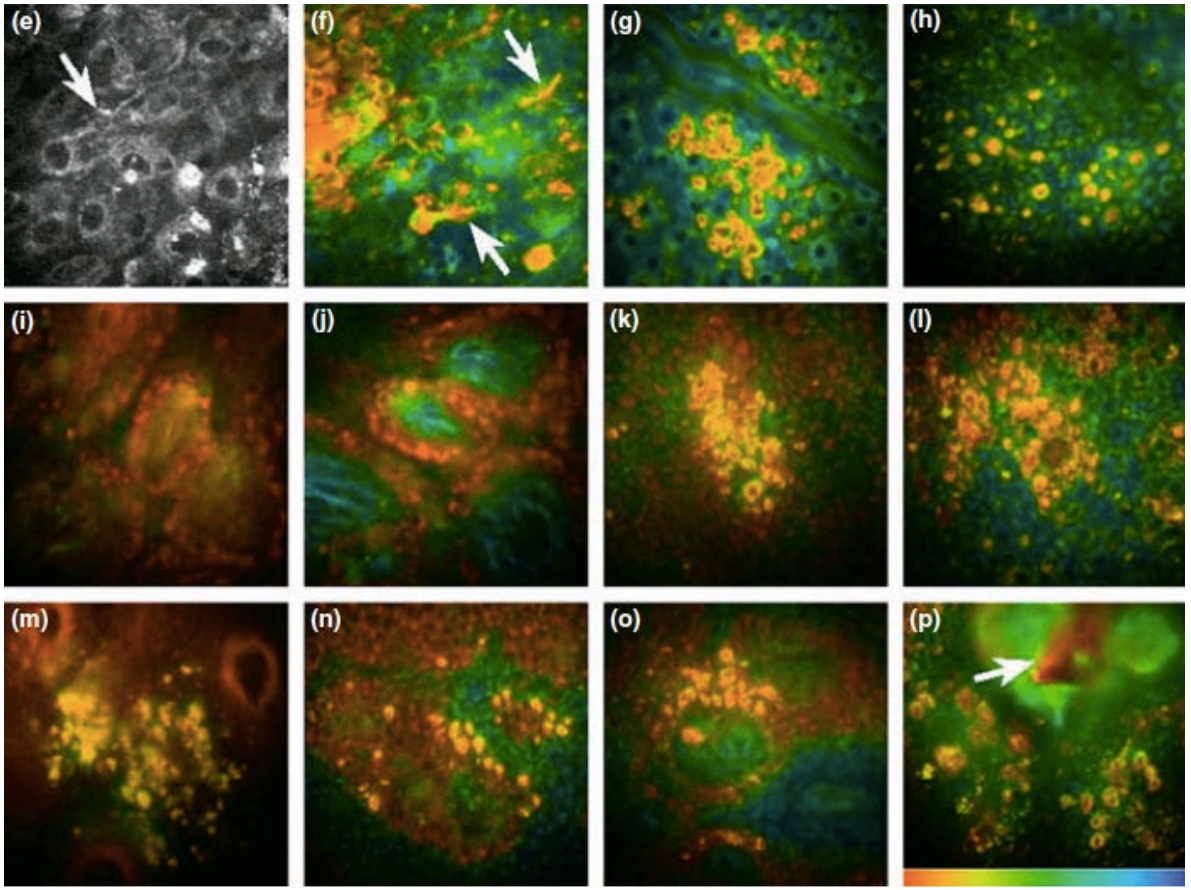


M. Kaatz, K. König. Multiphotonenmikroskopie und In-vivo-Multiphotonentomographie in der dermatologischen Bildgebung. Hautarzt 20

Dimitrow E, Riemann I, Ehlers A et al (2009) Spectral fluorescence lifetime detection and selective melanin imaging by multiphoton lase tomography for melanoma diagnosis. Exp Dermatol 18:509–515

Multiphoton tomography

Combination of MPT and FLIM (fluorescence life time excitation). 200 microm resolution

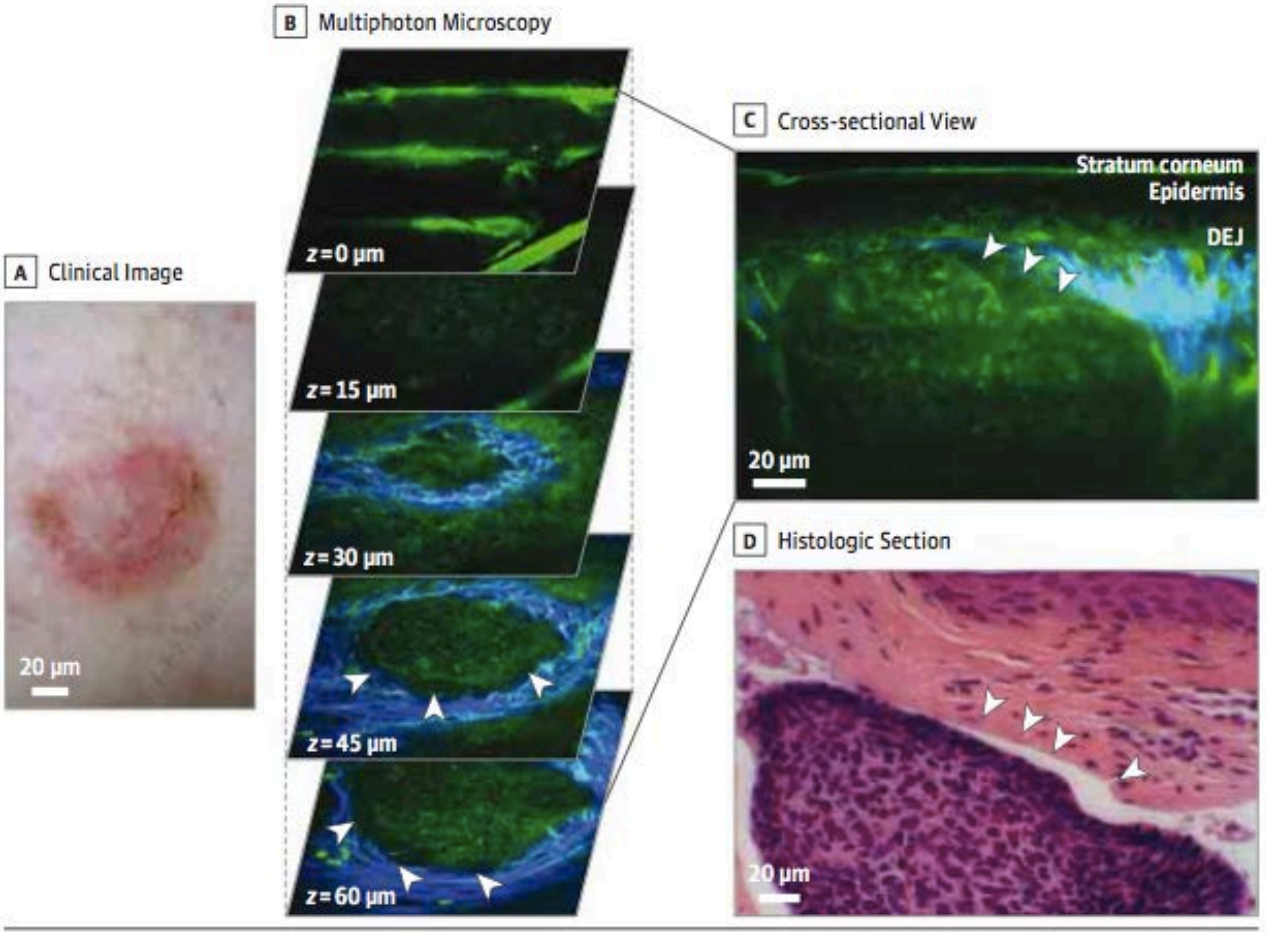


Federica Arginelli et al. High resolution diagnosis of common nevi by multiphoton laser tomography and fluorescence lifetime imaging. Skin res and technol 2013

Original Investigation

In Vivo Multiphoton Microscopy of Basal Cell Carcinoma

Mihaela Balu, PhD; Christopher B. Zachary, MD; Ronald M. Harris, MD; Tatiana B. Krasieva, PhD; Karsten König, PhD; Bruce J. Tromberg, PhD; Kristen M. Kelly, MD



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Original Investigation

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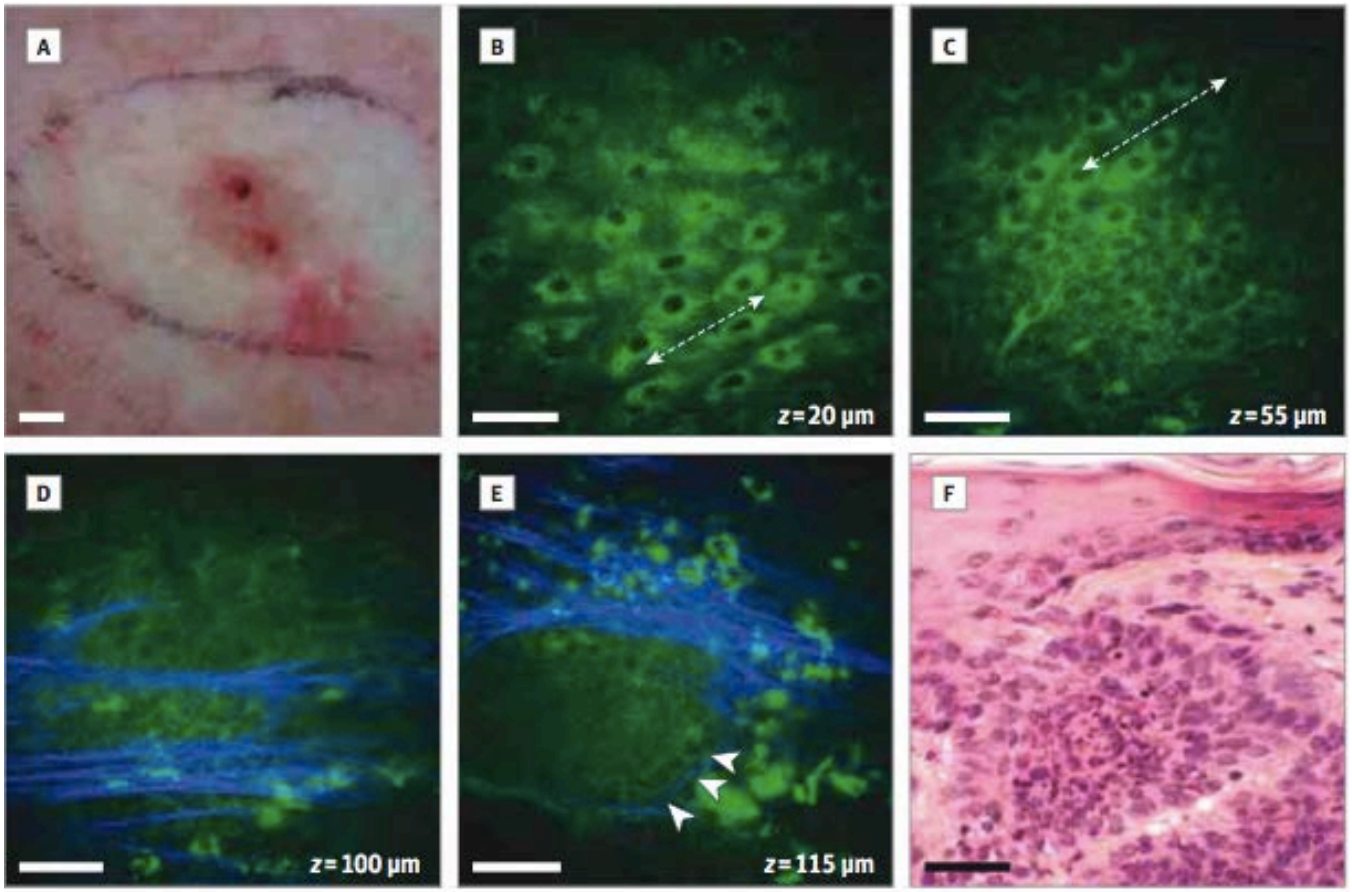
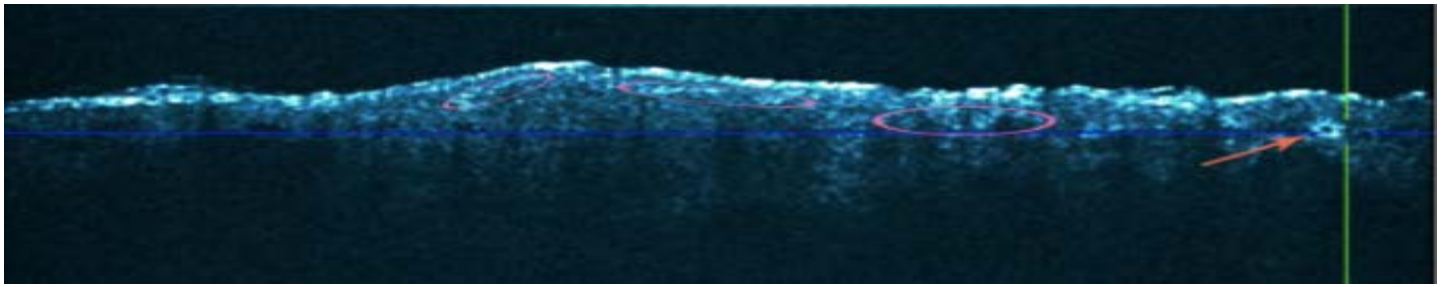


Federica Arginelli et al. High resolution diagnosis of common nevi by multiphoton laser tomography and fluorescence lifetime imaging. Skin res and technol 2013

HIGH –DEFINITION OPTICAL COHERENCE

OCT is a noninvasive, in vivo imaging method, which captures high-resolution (⌠m), 3D images of biological tissue.

OCT is an interferometric technique using relatively long-wavelength light in the near-IR portion of the spectrum, which is able to penetrate into the scattering medium (deeper than CSLM).



Patel JK, Konda S, Perez OA, Amini S, Elgart G, Berman B. Newer technologies/techniques and tools in the diagnosis of melanoma. Eur J Dermatol. 2008;18(6):617–631

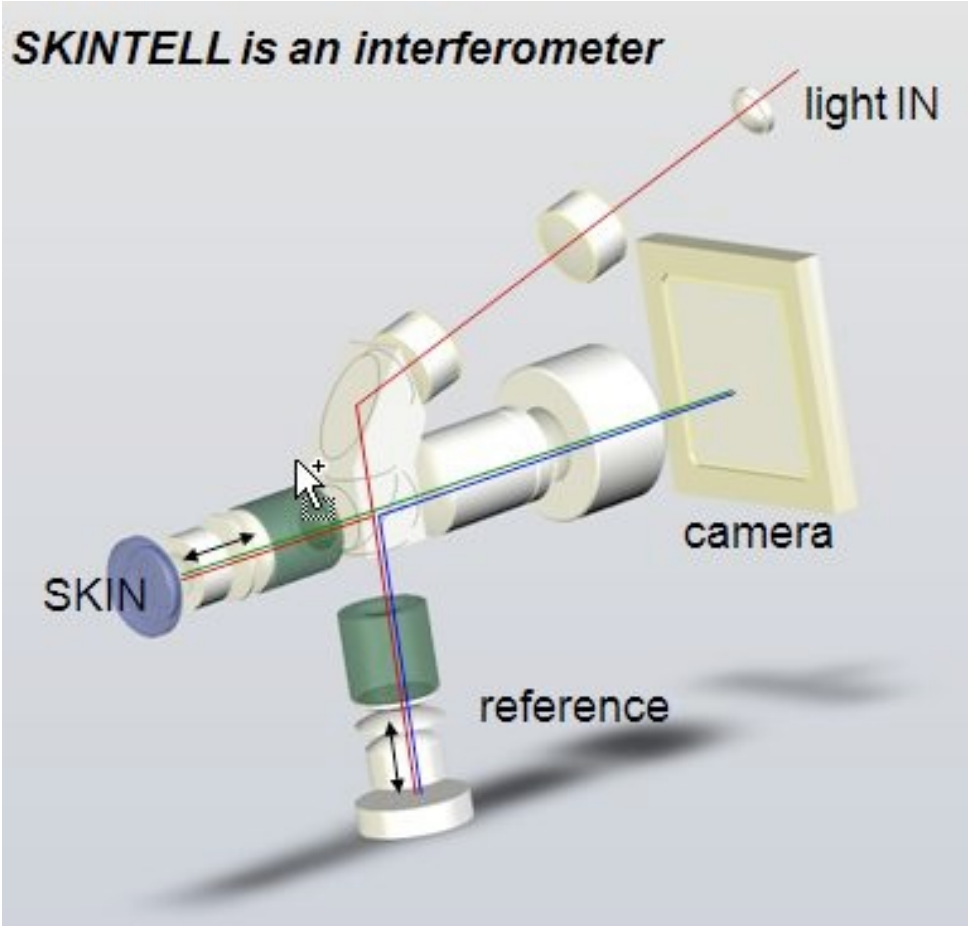
HIGH –DEFINITION OPTICAL COHERENCE

An image is generated
not by the light intensity directly like in dermoscopy

but by the strenght of the interference signal

Result is:

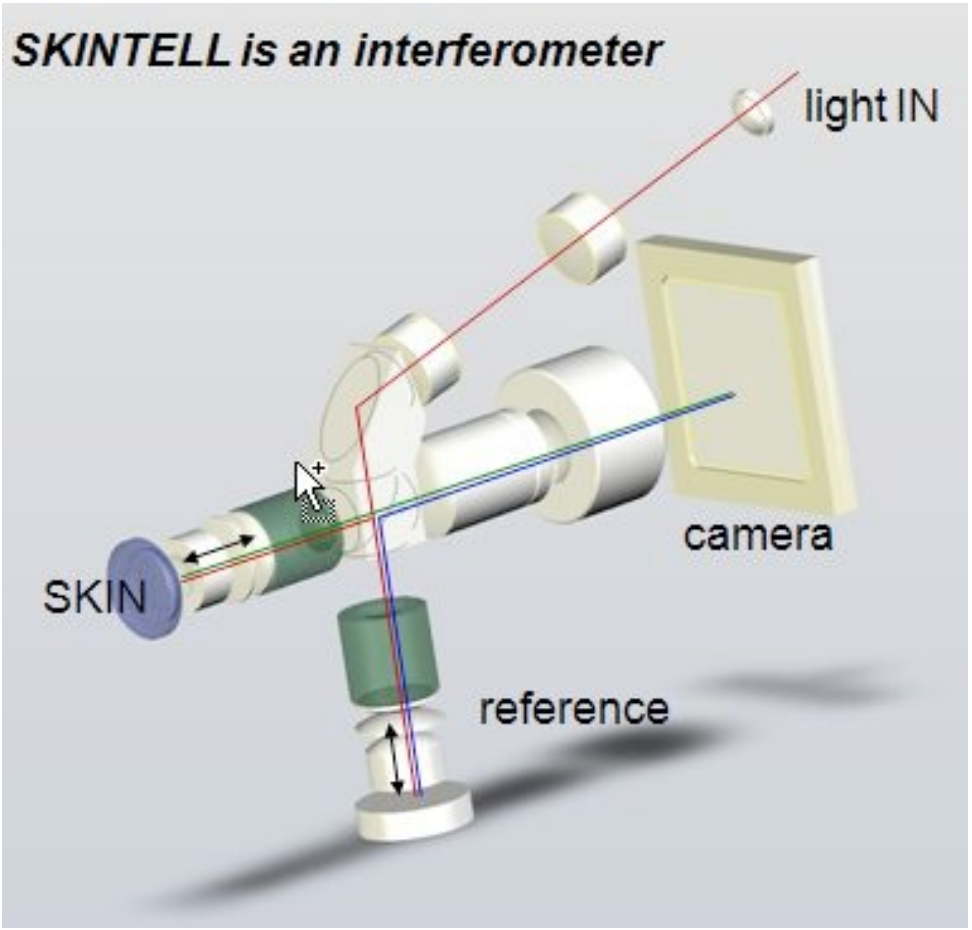
1. **Scattered light is blanked out**
2. **Depth selection becomes possible**



Courtesy of Marc Boone

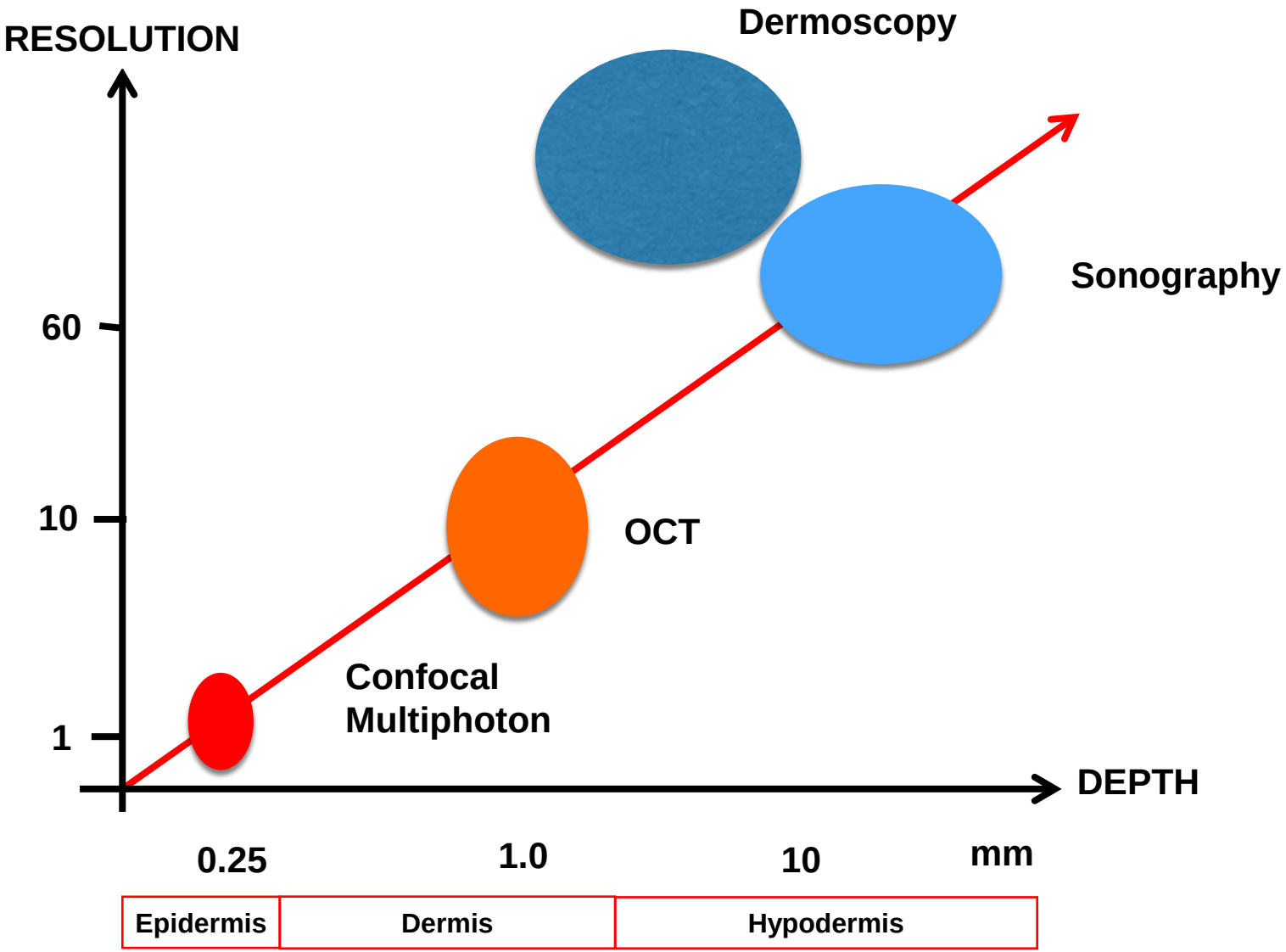
HIGH –DEFINITION OPTICAL COHERENCE

- Lower resolution than Reflectance confocal microscopy
- Higher depth of tissue examination (500 microm)
- 3 dimensional reconstruction

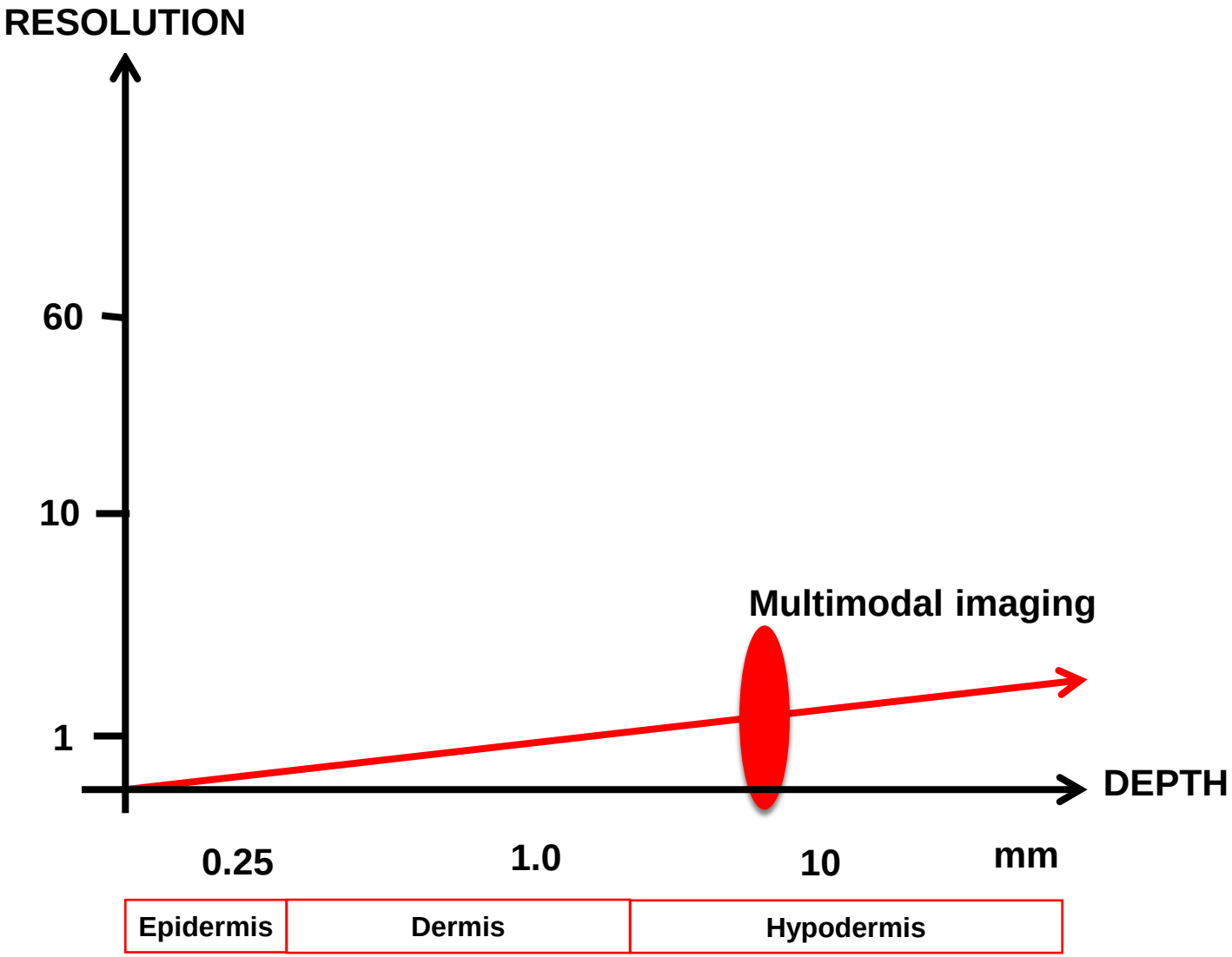


Courtesy of Marc Boone

Resolution is limited by penetration



Multimodal microscopy

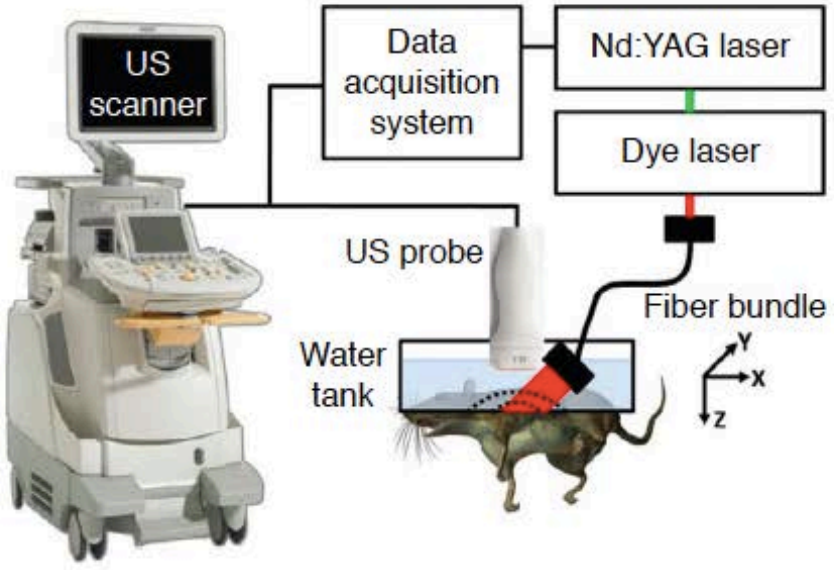


Multimodal microscopy

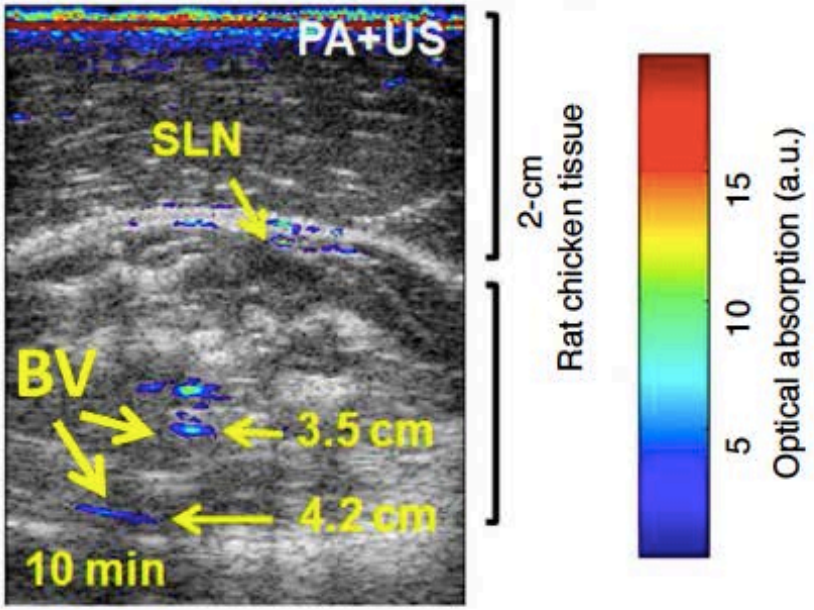
Superdepth, superresolution,
and superb contrast

Photoacoustic microscopy

Pulsed laser+ US detector



A

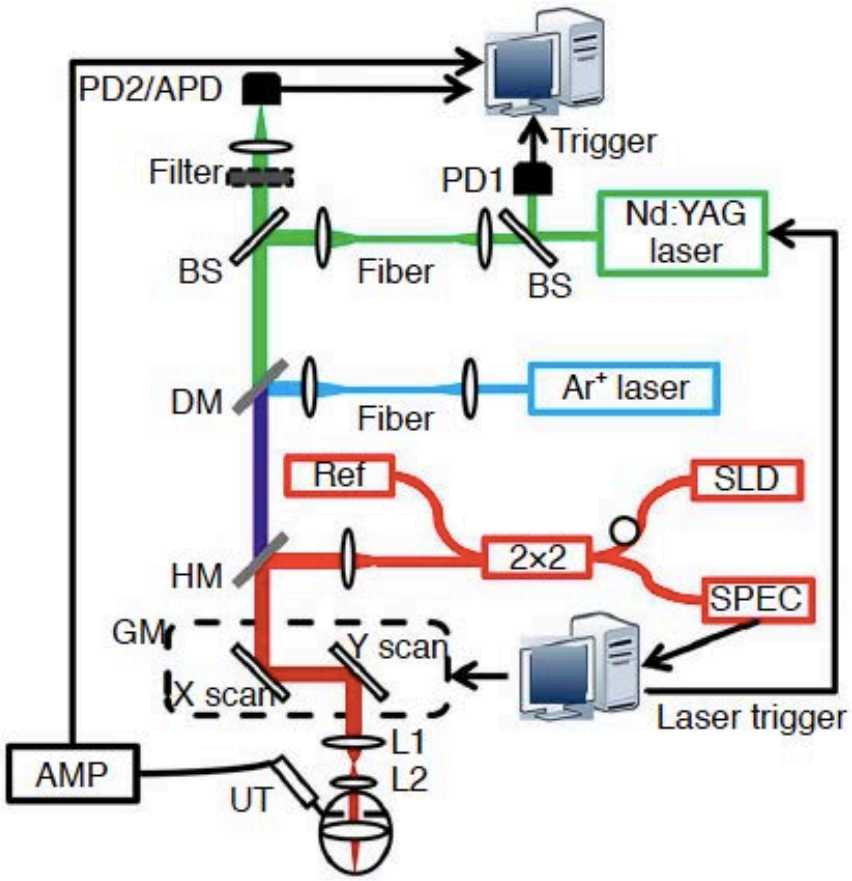


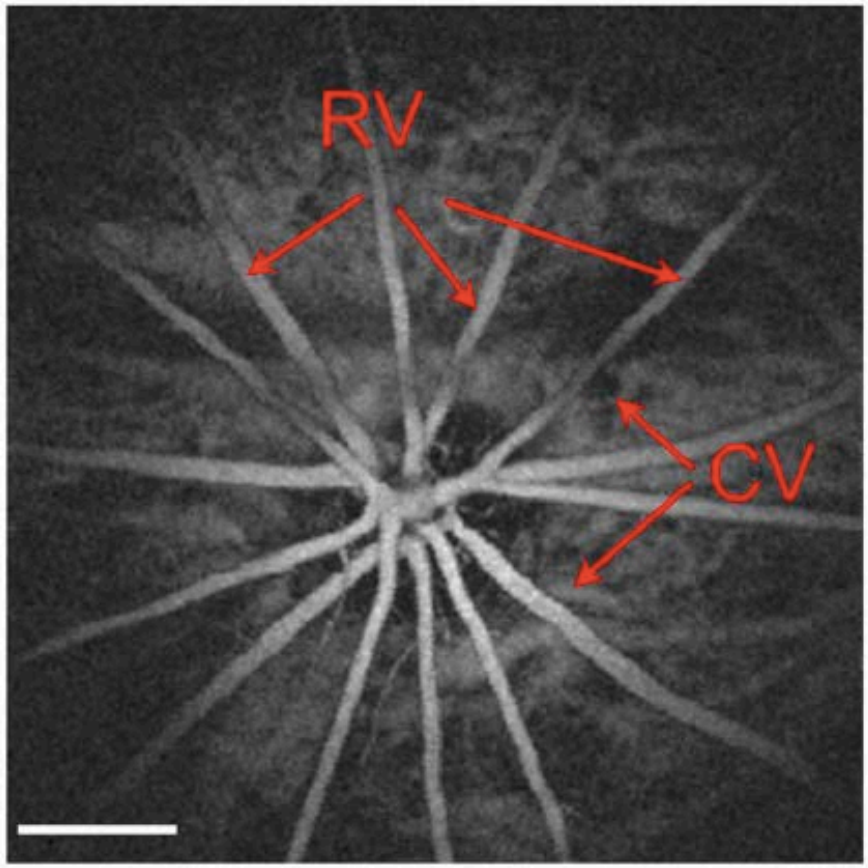
B

Jeesu Kim, Donghyun Lee, Unsang Jung, Chulhong Kim. *Photoacoustic multimodal platfforms*Photoacoustic imaging platforms for multimodal imaging. Ultrasonography 2015;34:88-97

Photoacoustic microscopy

PAM/OCT imaging system (PAT)

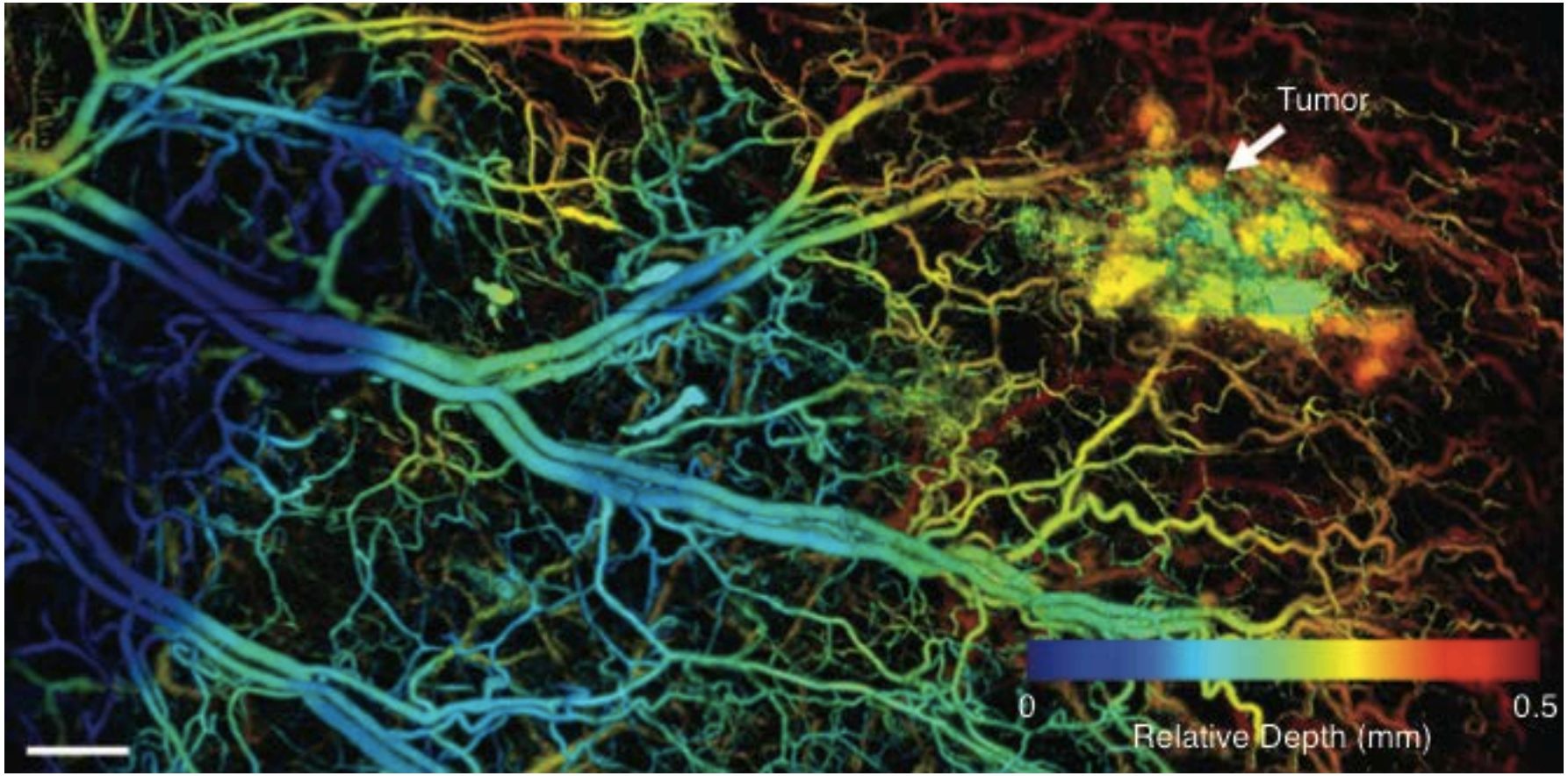




Jeesu Kim, Donghyun Lee, Unsang Jung, Chulhong Kim. *Photoacoustic multimodal platfforms*Photoacoustic imaging platforms for multimodal imaging. Ultrasonography 2015;34:88-97

Photoacoustic microscopy

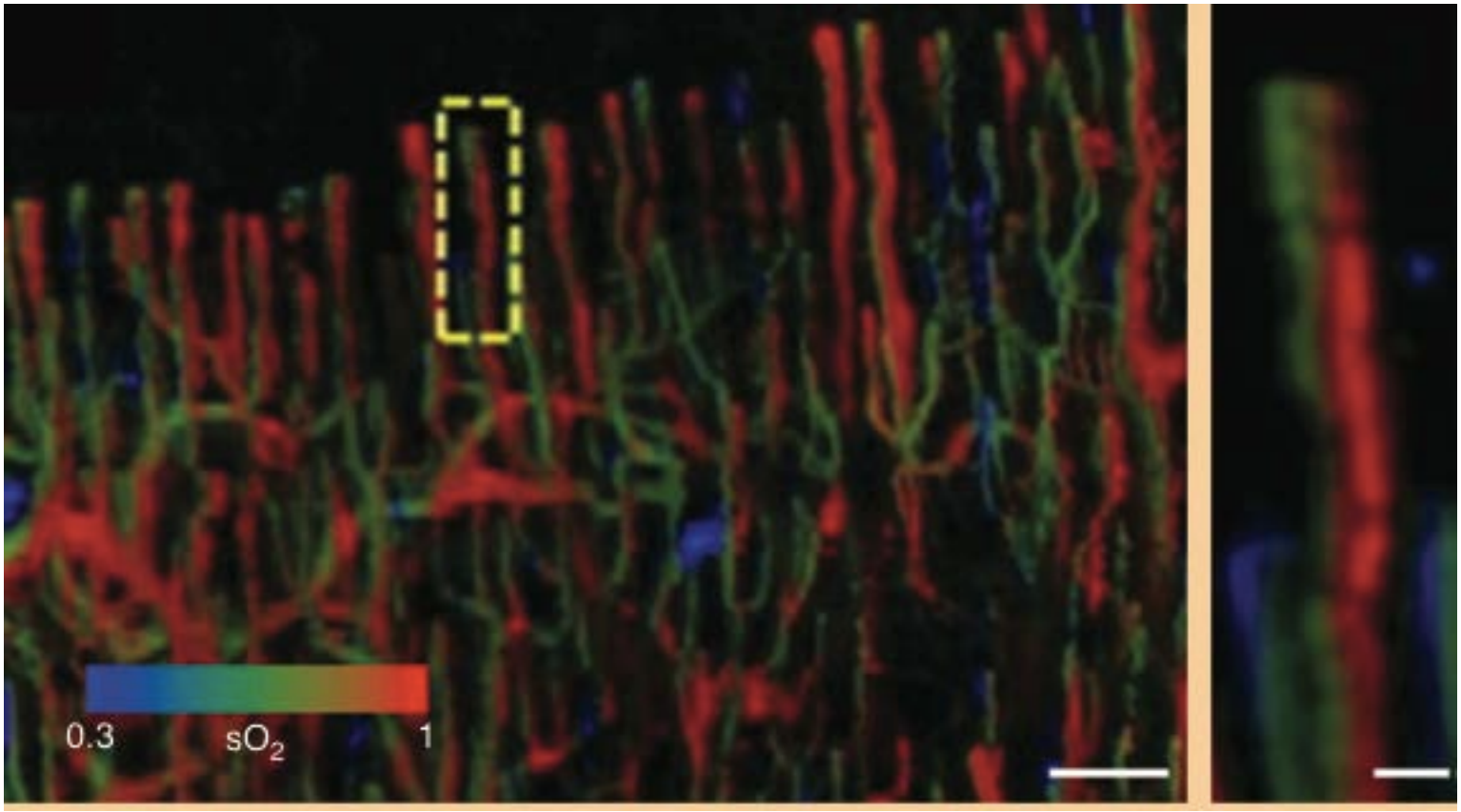
PAM/OCT imaging system



Jeesu Kim, Donghyun Lee, Unsang Jung, Chulhong Kim. *Photoacoustic multimodal platfforms*Photoacoustic imaging platforms for multimodal imaging. Ultrasonography 2015;34:88-97

Photoacoustic microscopy

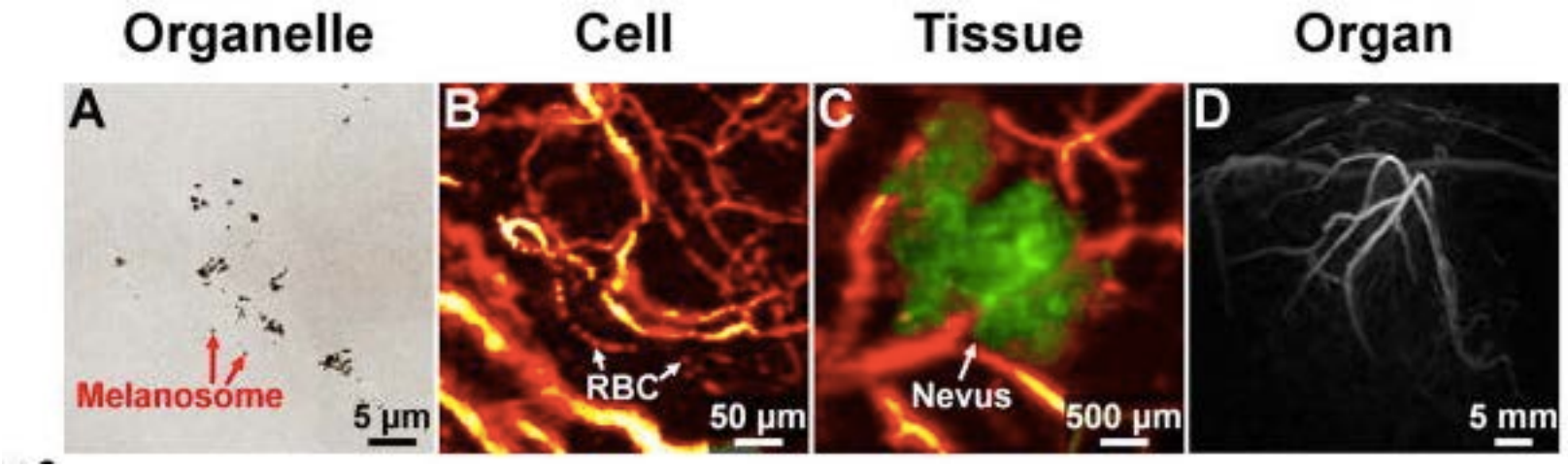
PAM/OCT imaging system



Wang LV. Multiscale photoacoustic microscopy and computed tomography. Nat Photonics. 2009 Aug 29;3(9):503-509

Photoacoustic microscopy

PAM/OCT imaging system

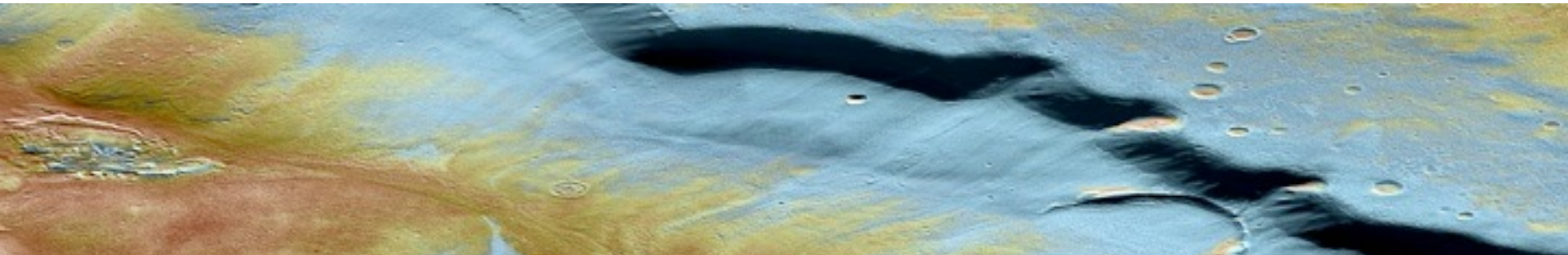


L. H. V. Wang and S. Hu, “Photoacoustic tomography: In vivo imaging from organelles to organs,” Science, vol. 335, no. 6075, pp. 1458–1462, 2012

Quantitative methods using automatised algorithms

Systems that use different physical measures to obtain information from the tissue .
The system is providing an automatised analysis and final classification to the end user.

- Multi-Spectral Imaging (Melafind)
- Electrical impedance Spectroscopy (EIS) (SCIBASE)
- Raman



MelaFind (Multi-Spectral Imaging)

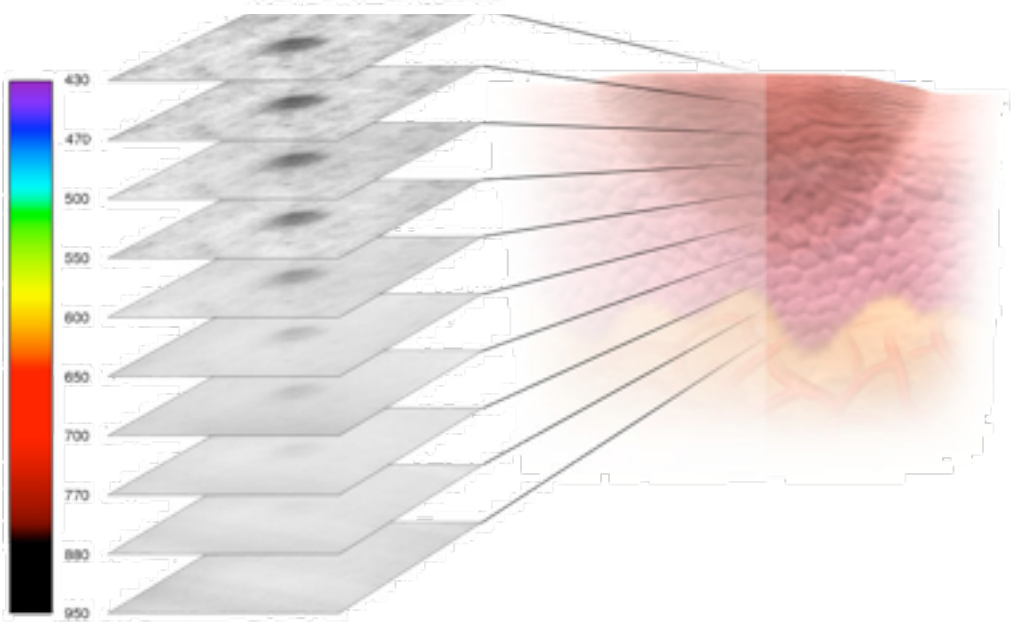
Noninvasive, fully automatic, computer-vision diagnostic system (type 2)

Designed as an aid to detection of early melanoma and developed to identify PLs that should be considered for biopsy to rule out melanoma.

Multi-Spectral Imaging

MelaFind acquires digital multispectral images of a PL in 10 different spectral bands, from blue (430 nm) to near infrared (950 nm).

MelaFind uses automatic image analysis and statistical pattern recognition to help identify lesions to be considered for biopsy to rule out melanoma.



MelaFind

1. Emits multiple wavelengths of light
2. Captures lesion images
3. Analyzes images

4.Separates pigmented lesions from melanoma

ONLINE FIRST

The Performance of MelaFind

A Prospective Multicenter Study

Gary Monheit, MD; Armand B. Cognetta, MD; Laura Ferris, MD, PhD; Harold Rabinovitz, MD; Kenneth Gross, MD; Mary Martini, MD; James M. Grichnik, MD, PhD; Martin Mihm, MD; Victor G. Prieto, MD, PhD; Paul Googe, MD; Roy King, MD; Alicia Toledano, ScD; Nikolai Kabelev, BCSc; Maciej Wojton, MS; Dina Gutkowicz-Krusin, PhD

Setting: Three academic and 4 community practices in the US

Patients: 1632 lesions (including 127 melanomas—45% in situ—with median Breslow of invasive lesions, 0.36 mm)

Metric	Positive Lesion Set[b]	
	MM, HGDN, AMP, or AMH	MM
Sensitivity	98.3 (172 of 175)	98.4 (125 of 127)
Specificity	10.8 (157 of 1457)	10.5 (158 of 1505)
Positive predictive value	11.7	8.5
Negative predictive value	98.1	98.8
Biopsy ratio	7.6:1	10.8:1

Trial Registration: clinicaltrials.gov Identifier: NCT00434057

Arch Dermatol. 2011;147(2):188-194.

Medical Devices

Products and Medical Procedures

Device Approvals and Clearances

Recently-Approved Devices

2012 Device Approvals
2011 Device Approvals
2010 Device Approvals
2009 Device Approvals
2008 Device Approvals
2007 Device Approvals
2006 Device Approvals
2005 Device Approvals
2004 Device Approvals
2003 Device Approvals
2002 Device Approvals
2001 Device Approvals
2000 Device Approvals

MelaFind® - P090012

This is a brief overview of information related to FDA's approval to market this product. See the links below to the Summary of Safety and Effectiveness Data (SSED) and product labeling for more complete information on this product, its indications for use, and the basis for FDA's approval.

Product Name: MelaFind®
PMA Applicant: MELA Sciences, Inc.
Address: 50 South Buckhout Street, Suite 1, Irvington, NY 10533
Approval Date: November 1, 2011
Approval Letter: http://www.accessdata.fda.gov/cdrh_docs/pdf9/p090012a.pdf

What is it? An optical imaging and analysis device used in the detection of melanoma among atypical skin lesions.

How does it work? The device uses light to image the skin through a layer of isopropyl alcohol to generate a positive or negative result based on predefined image analysis algorithms.

When is it used? The device is used when a dermatologist chooses to obtain additional information on atypical skin lesions for a decision to biopsy.

What will it accomplish? MelaFind will provide the dermatologist with additional information about atypical skin lesions. This additional information may help a dermatologist find additional melanomas that may not have been found without the use of the device.

When should it not be used? There are no contraindications.

Additional information: Summary of Safety and Effectiveness and labeling will be available online.

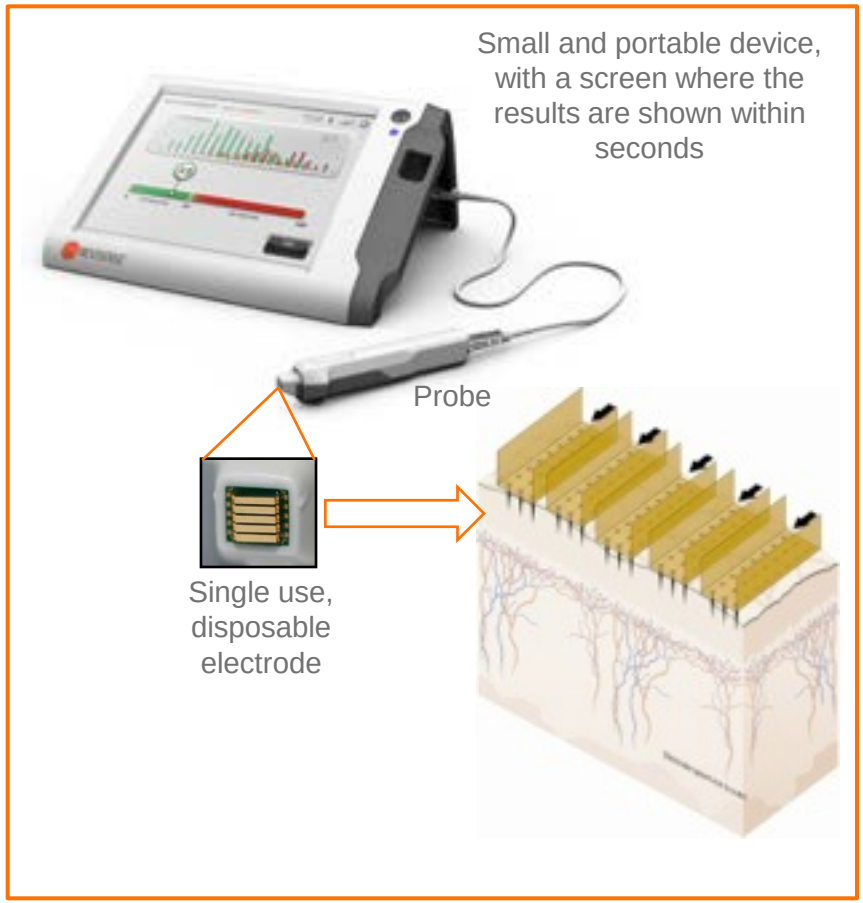
Page Last Updated: 12/04/2012
Note: If you need help accessing information in different file formats, see Instructions for Downloading Viewers and Players.

Electrical impedance Spectroscopy (EIS)

Technology and method

Overview

- EIS is a measure of the overall resistance within the tissue at alternating currents of various frequencies
- EIS is measured by applying an unnoticeable and harmless alternating electrical current onto the skin and measure the response
- The frequencies used in the applied signal relate to clinically relevant properties, such as composition of intra and extra-cellular environments, cell shape and size and cell membrane composition
- The CE marked technology platform consists of a handheld probe with a disposable electrode connected to a device analysing the signals
  - Aside from the disposable electrode other parts of the device are made of standard components
- Algorithm development based on >4,000 lesions with 500 Malignant Melanoma measurements in International Multicenter Melanoma Training Studies (IMATS)
- The system gives on-screen results within seconds

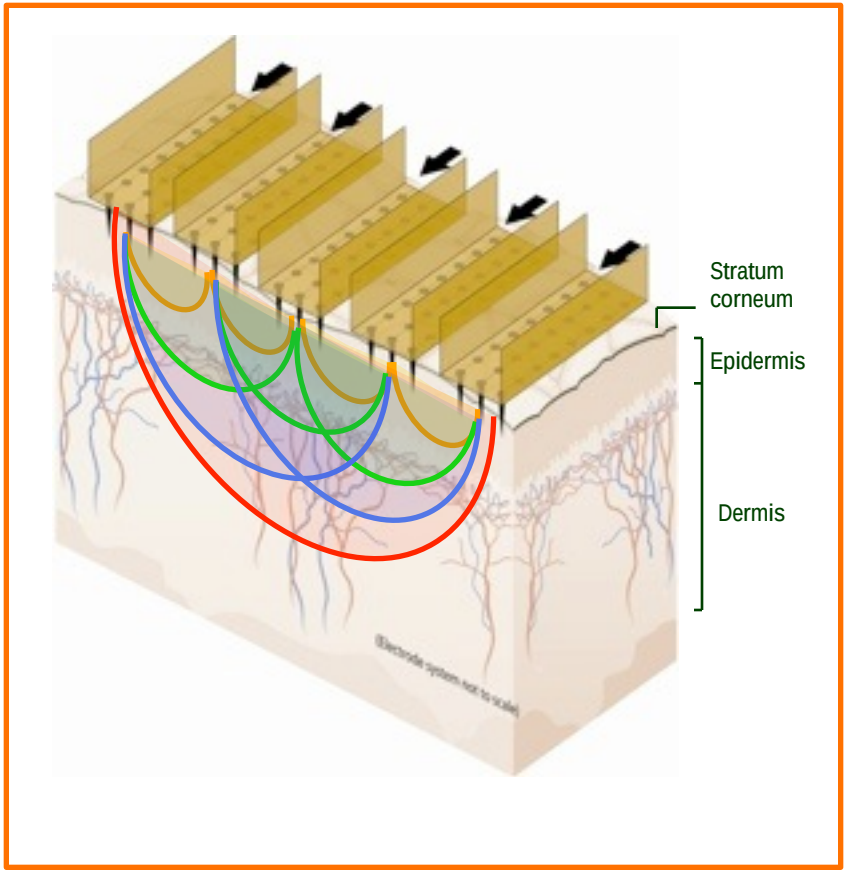


Electrical impedance Spectroscopy (EIS)

Principle of microinvasive impedance

Description

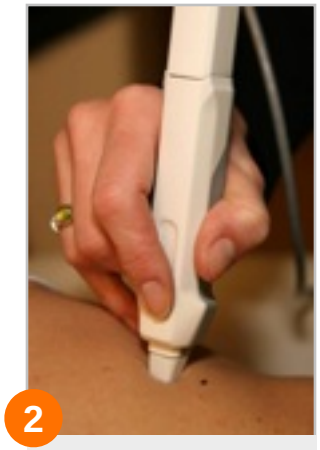
1. The pins penetrate into the stratum corneum
2. Impedance is measured in the viable skin under stratum corneum
3. Alternating current is transmitted from one electrode bar to another at 35 predefined frequencies that relate to clinically relevant properties in the skin
4. Amplitude and phase shift in the receiving signal are measured at the receiving electrode bar for each of the 35 frequencies
5. In order to cover the lesion in both width and depth, the measurement is performed in 10 permutations covering both shallow measurements between neighbouring electrode bars as well as deeper measurements between more distant electrode bars



Electrical impedance Spectroscopy (EIS)

Measurement process – three simple and painless steps with results within seconds

1 **Clean and moisten the skin**



2 **Perform a reference measurement close to the lesion**

3 **Perform lesion measurement(s)**

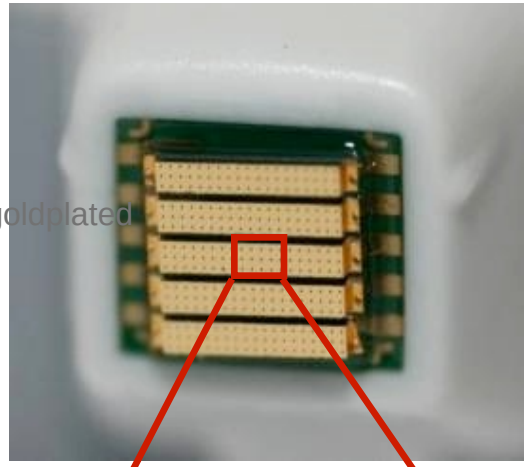
On screen results (benign or malignant)…

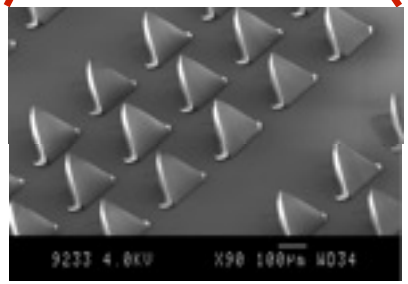
…within seconds

Electrical impedance Spectroscopy (EIS)

The patented microinvasive electrode

The electrode consists of 5 goldplated electrode bars





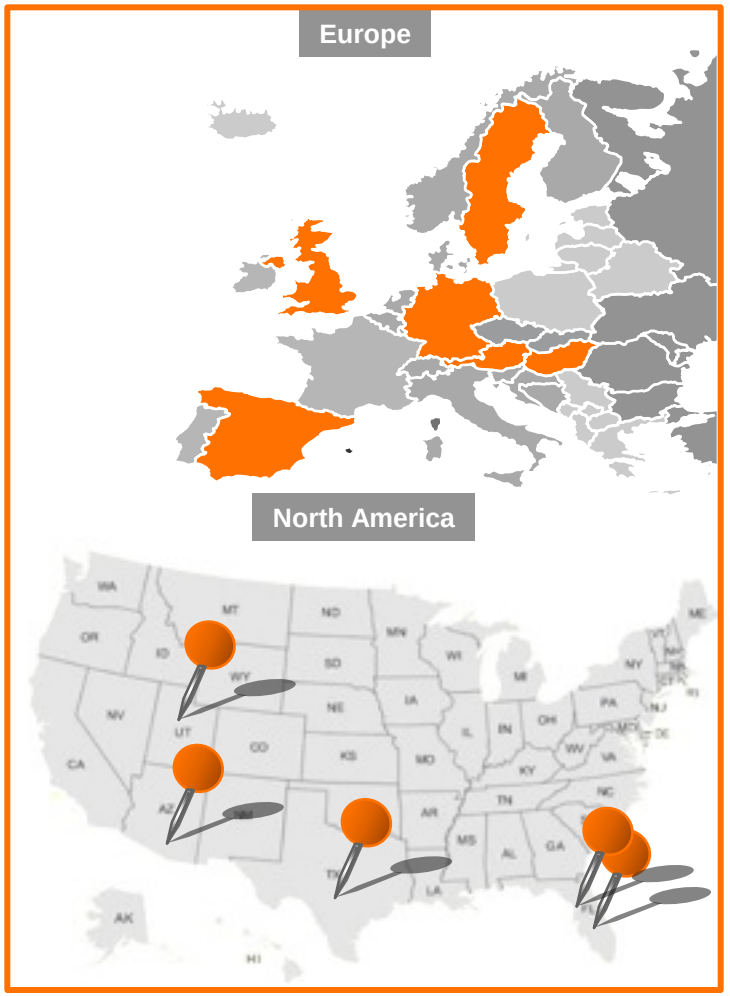
On the surface of each electrode bar there are 45 microscopic spikes (length ~150 µm and width ~40 µm)

Electrical impedance Spectroscopy (EIS)

Pivotal study – overview

SciBase International Melanoma Pivotal Study

Purpose	The final SIMPS pivotal study was performed with the objective to provide scientific evidence of the accuracy of the SciBase system in detecting Malignant Melanoma. As the study is designed to provide scientific evidence of the methods' accuracy, it also provides the basis for a regulatory approval in the US
Design overview	The study was run as an international, multicenter, prospective, non controlled and non randomised clinical trial conducted at both private and academic dermatological centers. Prior to initiation, the study was approved by national and local ethics committees and carried out in accordance with international conference of harmonization of good clinical practice (ICH-GCP)
Geography	The study was run in both Europe and the US with 22 participating clinics in UK, Germany, Sweden, Hungary, Austria, Spain and the US (17 clinics in Europe and 5 clinics in the US)
Size	In total 2,400 lesions were included in the study, which is the largest prospective study ever conducted in melanoma detection



Electrical impedance Spectroscopy (EIS)

Pivotal study – top line results *

- Median Breslow thickness: 0,4 mm

• Age Groups 30 years and above
† SCC = Squamous cell carcinoma
‡ BCC = Basal cell carcinoma

Clinical performance of the Nevisense system in cutaneous melanoma detection: an international, multi-centre, prospective and blinded clinical trial on efficacy and safety. *J, Malvehy, A. Hauschild, C. Curiel-Lewandrowski, P. Mohr, R.Hofmann-Wellenhof, R.Motley, C.Berking, D.Grossman, J.Paoli, C.Loqua, J. Olah, U. Reinhold, H. Wenger, T. Dirschka, S. Davis, C. Henderson, H.Rabinovitz, J.Welzel, D.Schadendorf, U.Birgersson.* BJD 2014

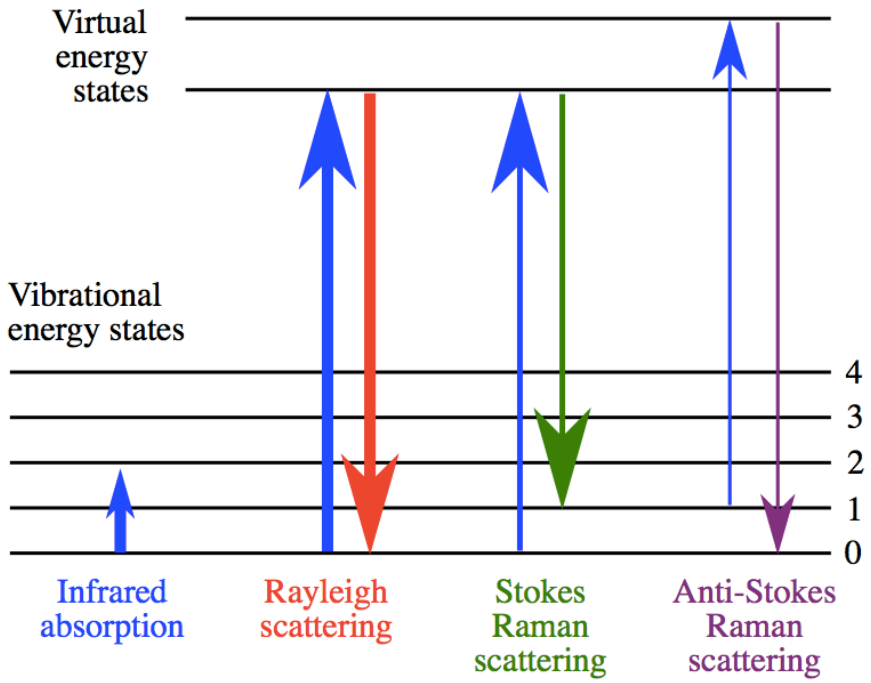
Exclusion Reason	No. Lesions		Source
	No	%	
Lesions included	2416		
Signed Informed Consent Form Missing	1	0,04%	Investigator 11.0%
Withdrawal	17	0,7%	
Not eligible (i.e. inclusion/exclusion)	61	2,5%	
Major Protocol Violation	29	1,2%	
Measurement not acquired	60	2,5%	
Coverage***	98	4,1%	
Not eligible histopathology (preparation quality)	8	0,3%	Pathology 4.1%
Missing histopathology*	39	1,6%	
Inaccurate mapping of histopathology†	7	0,3%	
No Consensus‡	44	1,8%	
Poor Reference Quality**	95	3,9%	Device related 4.5%
Device failure	14	0,6%	
Eligible Lesions	1943		

Sir C.V. Raman
Nobel Prize of Physics in 1930

RAMAN

Vibration profiles specific of some molecules in the tissue can be induced by photons.

These methods have been introduced for the diagnosis of skin tumors.



Gniadecka M, Philipsen PA, Sigurdsson S, et al. Melanoma diagnosis by Raman spectroscopy and neural networks: structure alteration in proteins and lipids in intact cancer tissue. J Invest Dermatol. 2004;122(2):443–449.

Nijssen A, Bakker Schut TC, Heule F, et al. Discriminating basal cell carcinoma from its surrounding tissue by Raman spectroscopy. J Invest Dermatol. 2002;119(1):64–69

IR and RAMAN

IR and Raman spectroscopy provide details regarding the chemical composition and molecular structure of substances in cells and biological tissues, and they are considered to be vibrational spectroscopic techniques.

IR spectroscopy measures absorbed radiation, and can serve as a visualization tool to aid the pathologist in evaluating tissue specimens

Rigel DS, Roy M, Yoo J, Cockerell CJ, Robinson JK, White R. Impact of guidance from a computer-aided multispectral digital skin lesion analysis device on decision to biopsy lesions clinically suggestive of melanoma. Arch Dermatol. 2012;148(4):541–543

Krafft C, Sergo V. Biomedical applications of Raman and infrared spectroscopy to diagnose tissues. Spectroscopy. 2006;20(5–6): 195–218

RAMAN

Confocal Raman microspectroscopy has been used to study structures in up to 200-⌠m depth

The combination of Raman spectroscopy and Confocal Scanning Laser Microscopy (CSLM) offers the ability to analyze sections and layers of the skin without physically dissecting the tissue.

The feasibility of these methods for the diagnosis of skin cancers

Gniadecka M, Philipsen PA, Sigurdsson S, et al. Melanoma diagnosis by Raman spectroscopy and neural networks: structure alteration in proteins and lipids in intact cancer tissue. J Invest Dermatol. 2004;122(2):443–449.

Nijssen A, Bakker Schut TC, Heule F, et al. Discriminating basal cell carcinoma from its surrounding tissue by Raman spectroscopy. J Invest Dermatol. 2002;119(1):64–69

A revolutionary advancement in skin cancer detection

verisante.com
TSX-V: VRS
OTCQX: VRSEF
FRANKFURT: V3T

verisante™

aura™

Verisante's Aura™ is a novel, multimodality imaging and spectroscopy system designed to aid in the detection of skin cancer. This system provides valuable information by identifying spectral changes associated with the biochemistry of skin cancer cells in less than a second; providing immediate results.

Early Detection Saves Lives

The Facts on Skin Cancer

Early Detection Saves Lives

Jointly developed by the BC Cancer Agency and the University of British Columbia, and refined and tested at the Skin Care Centre at Vancouver General Hospital, this patent protected technology has already been used in a human clinical study spanning six years on approximately 1,000 lesions. Results published in the peer-reviewed journal *Cancer Research* showed that for sensitivities between 95% and 99%, specificities ranged between 66% and 24%. According to an Australian study, the sensitivity of clinical diagnosis for malignant melanoma is approximately 33.8%.

Verisante's Aura™ will help to automate the current process of diagnosis, allowing rapid scanning of the 20 – 40 skin lesions on "at risk" individuals. No longer will patients need to suffer through long wait times to see a dermatologist, as scans may be accomplished quickly by trained technicians or assistants. Verisante's Aura™ will greatly aid healthcare professionals, delivering significant clinical impact through improved patient outcomes and reduced wait times.

The Verisante product development team is led by award-winning pioneers in the field of cancer imaging. In addition, the Company is proud to have world renowned experts in cancer detection involved with our technical and medical team.

Aura™ has been approved for sale in Canada, the EU and Australia.

The Facts on Skin Cancer

- Skin cancer is the most common form of cancer, and most rapidly increasing
- Every hour, one person in the United States dies of melanoma
- 50% of people over the age of 65 in the US will be affected by skin cancer
- One in six Canadians will develop skin cancer during their lifetime
- Survival rate of patients where the disease is detected early is 99%
- Survival rate of patients with advanced stage melanoma skin cancer is 15%
- The treatment of advanced stage melanoma costs 2200% more than early stage melanoma
- The annual treatment cost of treating skin cancer in the United States is estimated at USD $3.0 billion

Clinical Studies

Cancer Research

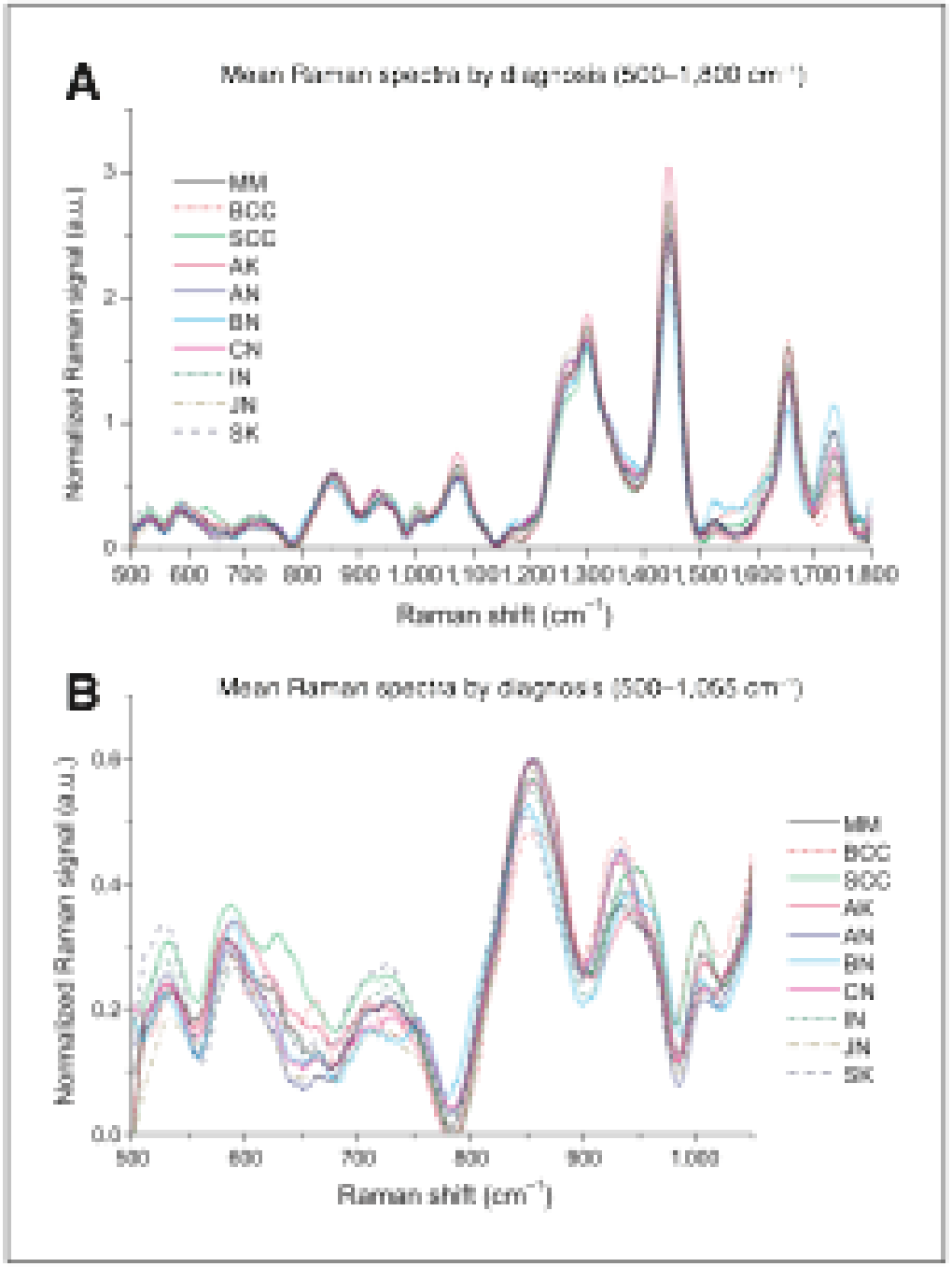
Real-time Raman Spectroscopy for *In Vivo* Skin Cancer Diagnosis

Harvey Lui[1,2], Jianhua Zhao[1,2], David McLean[1], and Haishan Zeng[1,2]

Abstract

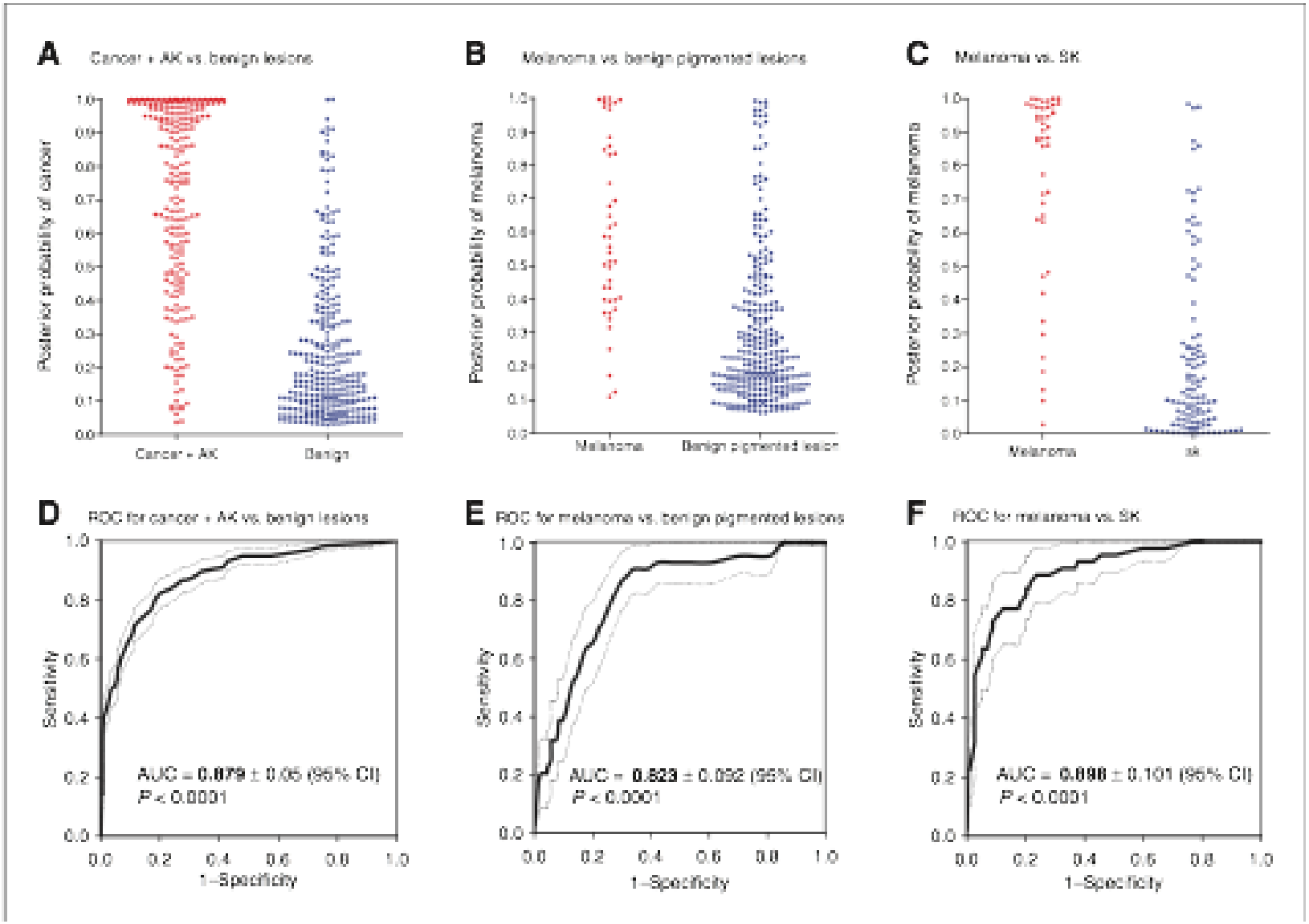
Raman spectroscopy is a noninvasive optical technique capable of measuring vibrational modes of biomolecules within viable tissues. In this study, we evaluated the application of an integrated real-time system of Raman spectroscopy for *in vivo* skin cancer diagnosis. Benign and malignant skin lesions ($n = 518$) from 453 patients were measured within 1 second each, including melanomas, basal cell carcinomas, squamous cell carcinomas, actinic keratoses, atypical nevi, melanocytic nevi, blue nevi, and seborrheic keratoses. Lesion classification was made using a principal component with general discriminant analysis and partial least-squares in three distinct discrimination tasks: skin cancers and precancers from benign skin lesions [receiver operating characteristic (ROC) = 0.879]; melanomas from nonmelanoma pigmented lesions (ROC = 0.823); and melanomas from seborrheic keratoses (ROC = 0.898). For sensitivities between 95% and 99%, the specificities ranged between

For sensitivities between 95% and 99%, the **specificities ranged between 15% and 54%**. Our findings establish that real-time Raman spectroscopy can be used to distinguish malignant from benign skin lesions with good diagnostic accuracy comparable with clinical examination and other optical- based methods



Spectral results plotted for lower frequency range only (500– 1,055 cm1)
Variability according to lesion diagnosis.

The y-axis scales for A and B are different. AK, actinic keratosis; AN, atypical nevus, BN, blue nevus; CN, compound nevus; IN, intradermal nevus; JN, junctional nevus; MM, malignant melanoma; SK, seborrheic keratosis.



Lesion classification by Raman spectroscopy based on PC GDA analysis. Skin cancer þ actinic keratosis, including MM, BCC, SCC, AK, n ¼ 232) from benign skin disorders (including atypical nevi, blue nevi, compound nevi, intradermal nevi, junctional nevi, seborrheic keratosis, n ¼ 286; A), melanoma (n ¼ 44) from benign pigmented skin diseases (including atypical nevi, blue nevi, compound nevi, intradermal nevi, junctional nevi, seborrheic keratosis, n ¼ 286; B), and melanoma (n ¼ 44) from seborrheic keratosis [(n ¼ 114); C]. D–F

IDIBAPS

Melanoma Unit. HCP. Barcelona

Director	J. Malvehy
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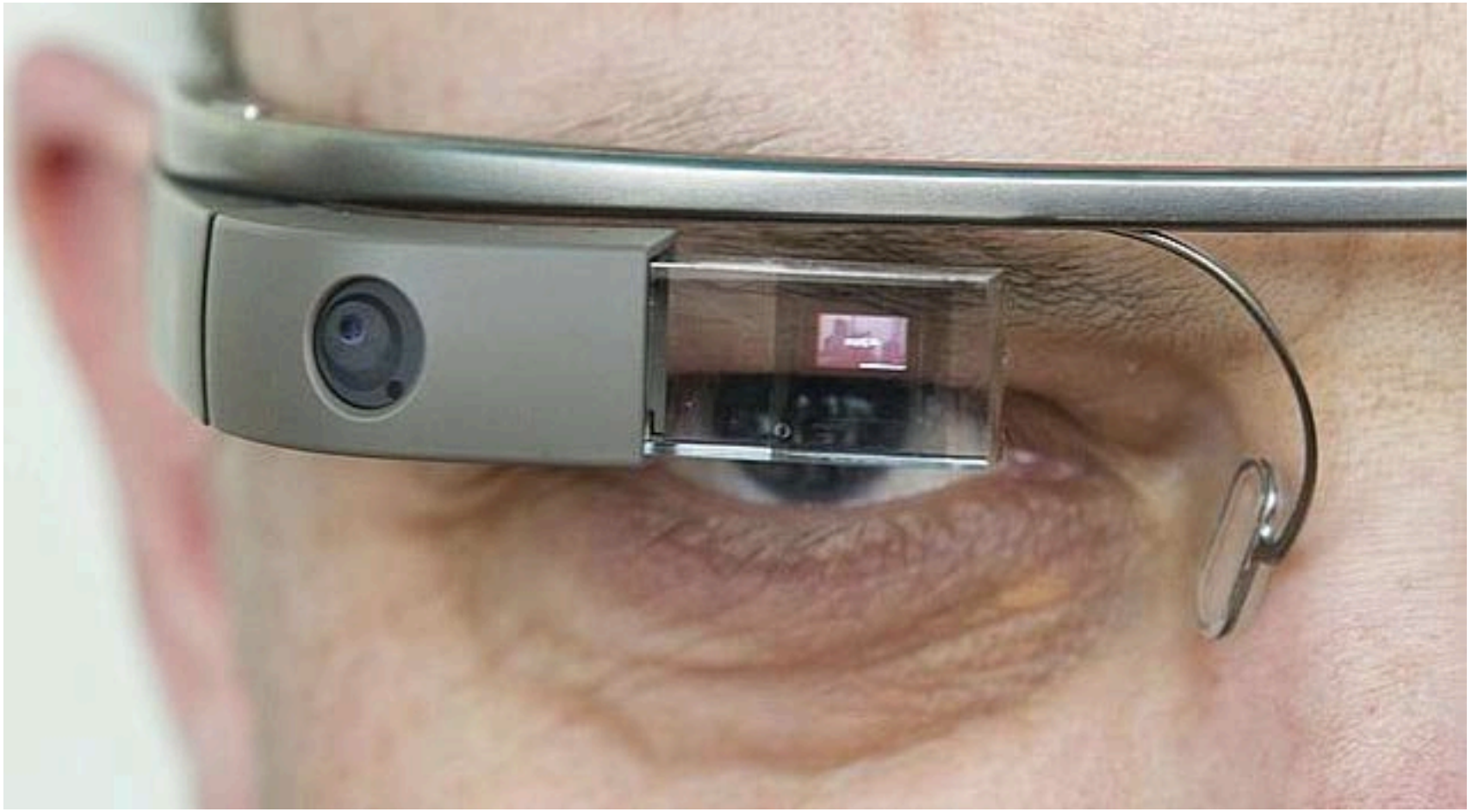
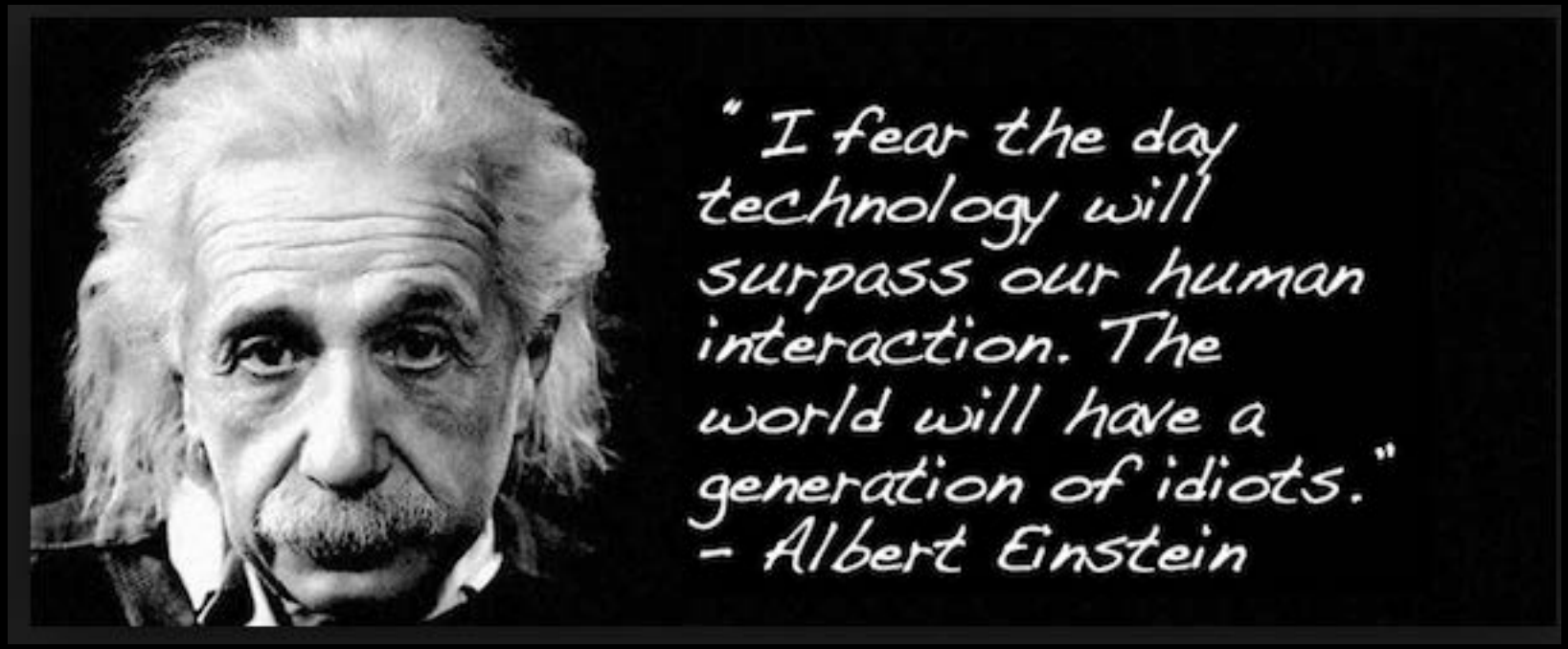
Dermatopathology	A. Alós, A.Díaz
Surgery	R. Rull
Radiotherapy	C. Conill
Immunotherapy	R. Vilella, J. Mila
Nuclear Med.	S. Vidal
Image Dx.	O.Chirife, M. Sánchez, R. Vilana
M.Oncology	A.M.Arance
Genetics	C. Badenas, JA. Puig, M. Milà, R. Cervera
Research Fellows	I. Alarcon, T. Martinez , V. Martins
Research nurses	P. Iglesias, D. Gabriel, M.Dominguez, Abel Caño
Psychologist	M. González

CLÍNIC BARCELONA Hospital Universitari




" I fear the day
technology will
surpass our human
interaction. The
world will have a
generation of idiots."
- Albert Einstein

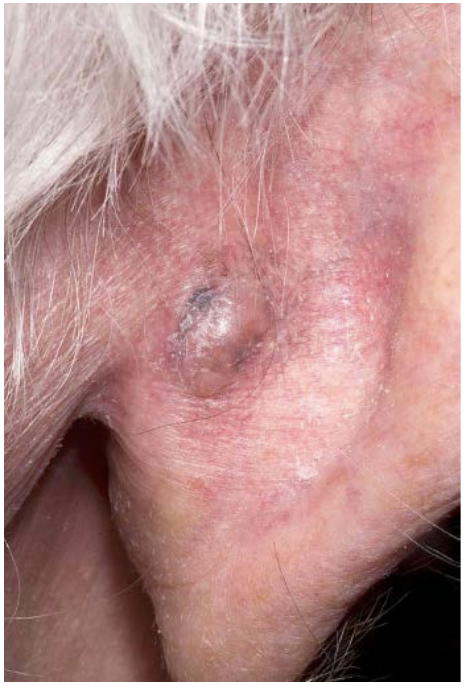

960
A

Animal diagnostic accuraccy in medicine

CASE REPORT

Canine olfactory detection of malignant melanoma

Leon Frederick Campbell,[1] Luke Farmery,[2] Susannah Mary Creighton George,[3] Paul B J Farrant[3]



A 75-year-old white Caucasian man presented to the dermatology clinic after his pet dog licked persistently at an asymptomatic lesion behind his right ear. The patient was previously unaware of the lesion.

Campbell LF, et al. BMJ Case Rep 2013. doi:10.1136/bcr-2013-008566

PLOS ONE

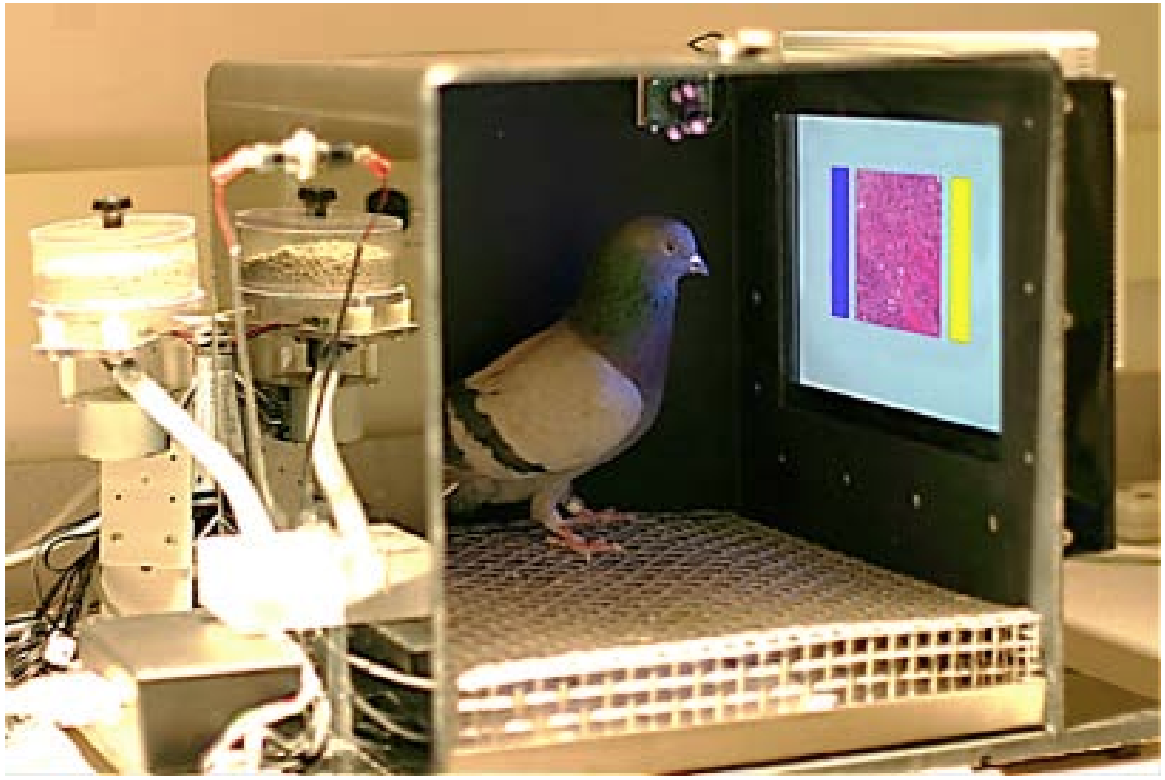
RESEARCH ARTICLE

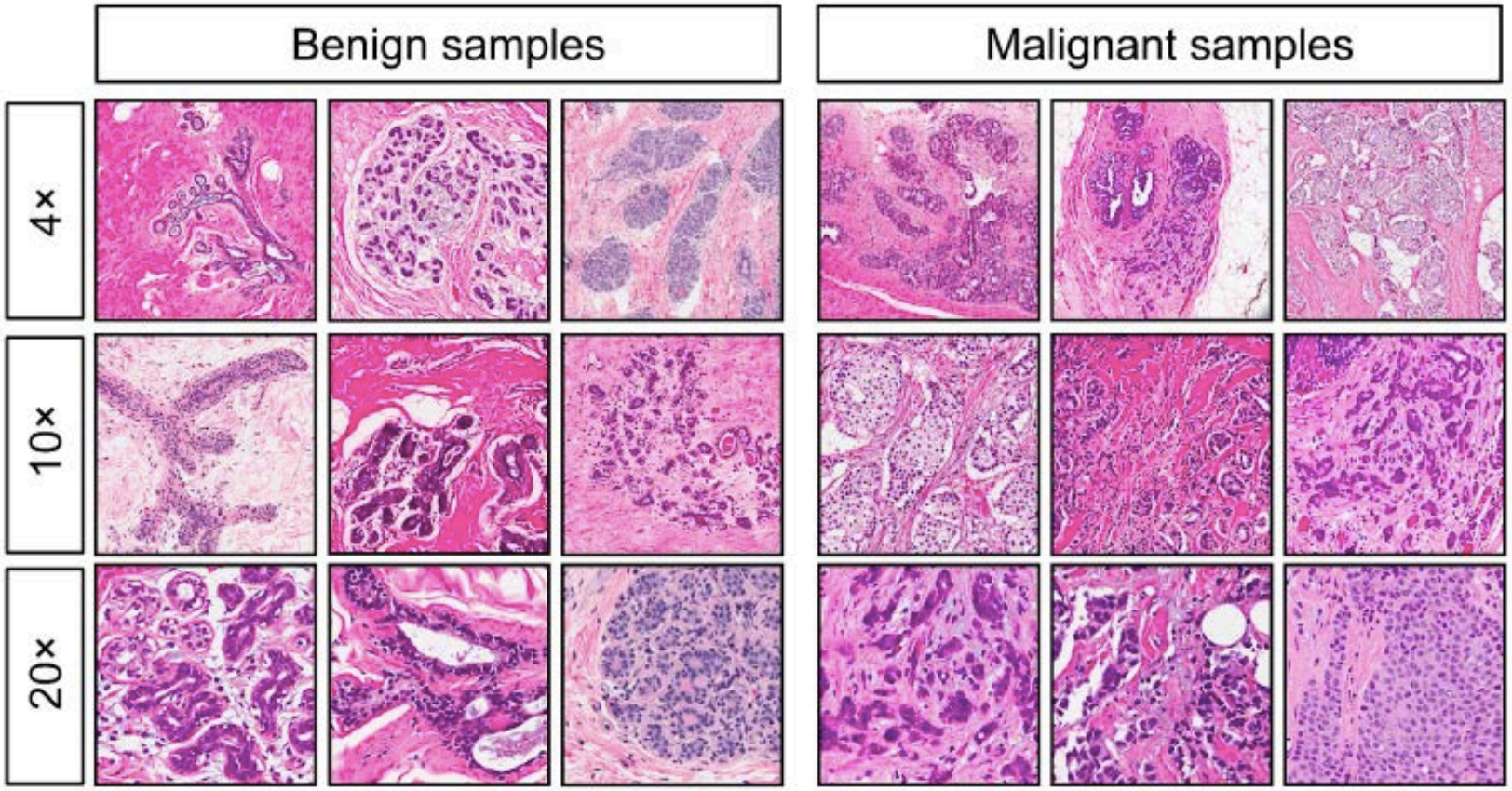
Pigeons (*Columba livia*) as Trainable Observers of Pathology and Radiology Breast Cancer Images

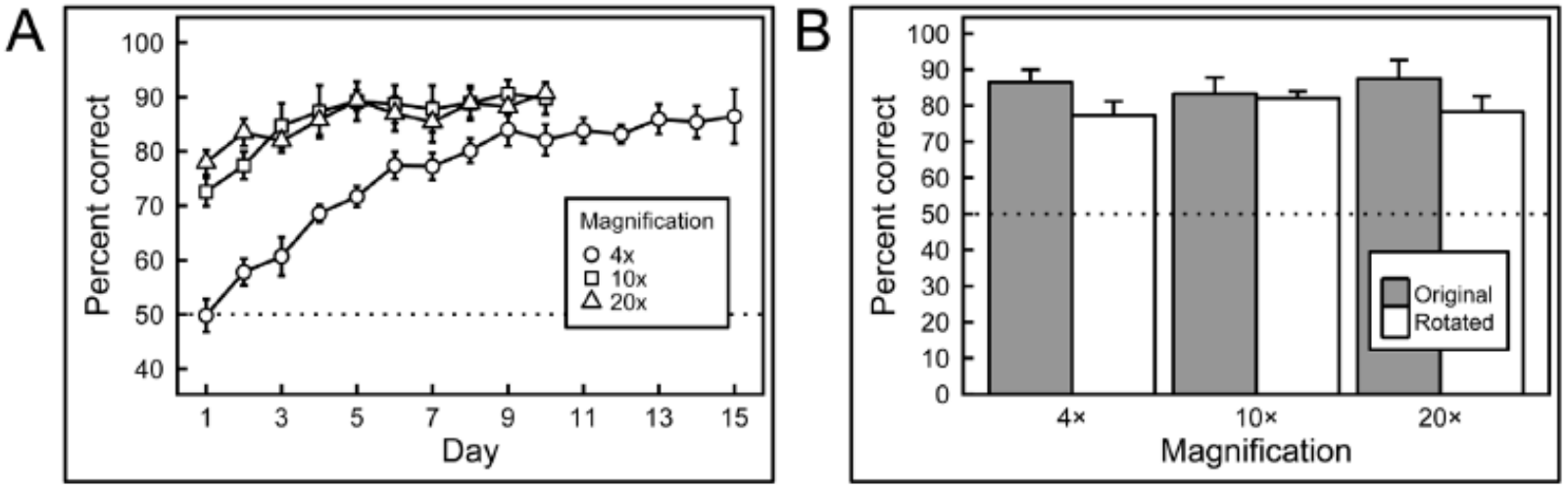
Richard M. Levenson[1]*, Elizabeth A. Krupinski[3], Victor M. Navarro[2], Edward A. Wasserman[2]*

1 Department of Pathology and Laboratory Medicine, University of California Davis Medical Center, Sacramento, California, United States of America, **2** Department of Psychological and Brain Sciences, The University of Iowa, Iowa City, Iowa, United States of America, **3** Department of Radiology & Imaging Sciences, College of Medicine, Emory University, Atlanta, Georgia, United States of America

* levenson@ucdavis.edu (RML); ed-wasserman@uiowa.edu (EAW)



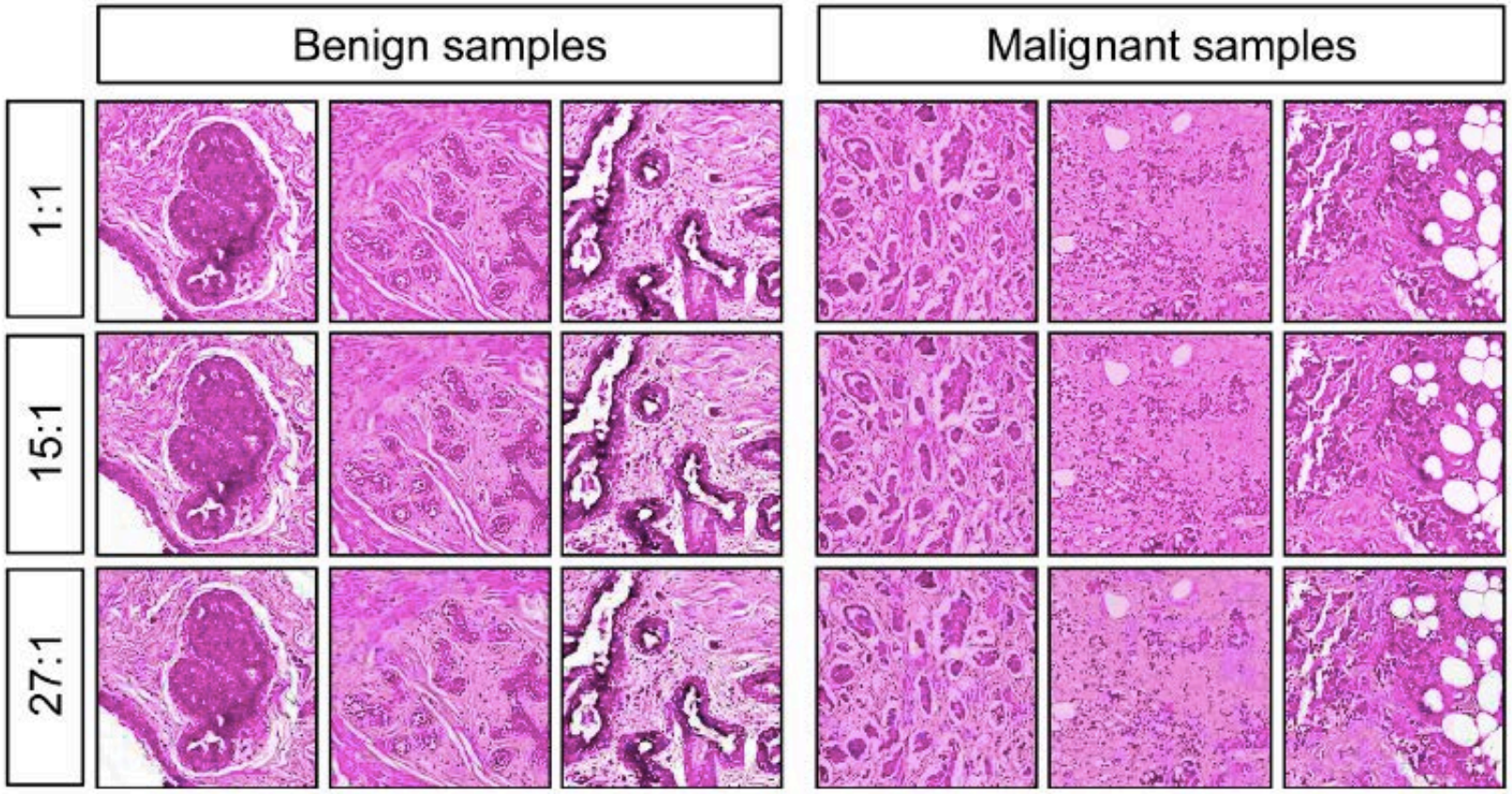

Benign samples
Malignant samples
4×
10×
20×

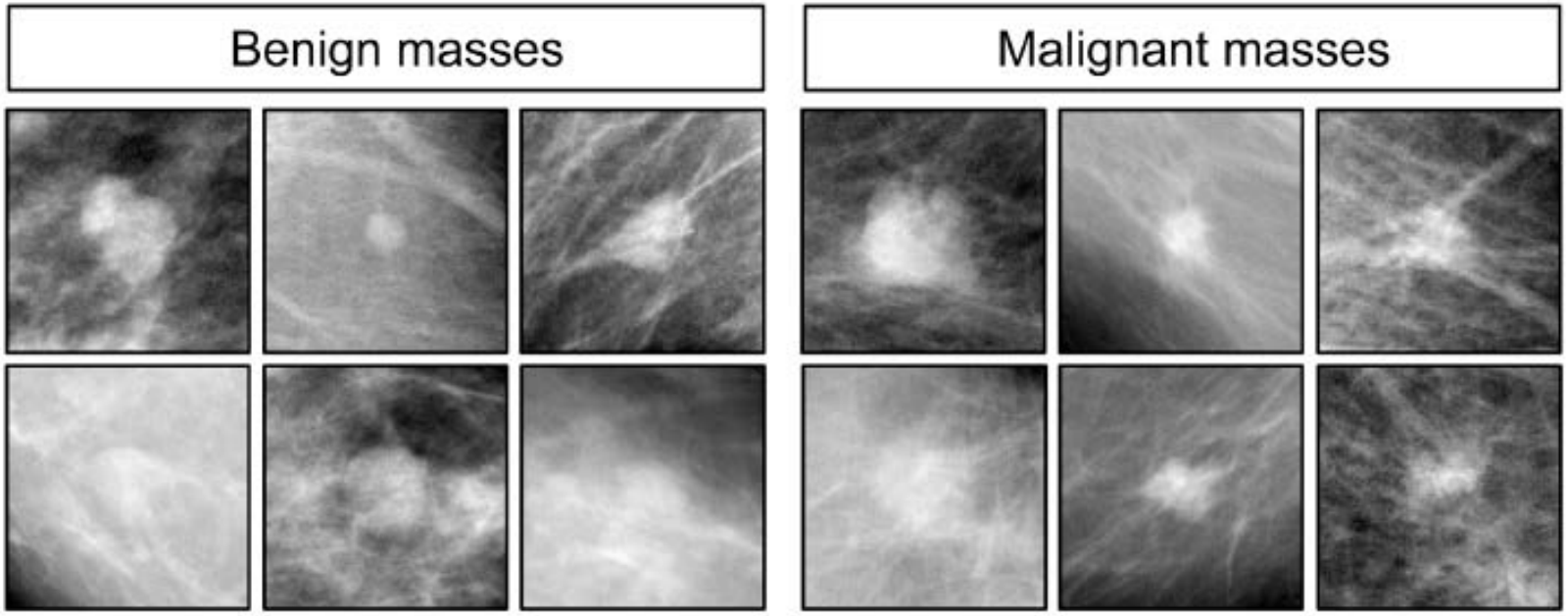


Results of training with breast histopathology samples at different magnifications and rotations.

A) When first trained with 4 magnification images the birds performed at chance levels of accuracy, but quickly learned to discriminate. Subsequently, when the birds were exposed to higher magnifications samples, their performance commenced at accuracies above chance (but below their final performance at lower magnification they had previously been exposed to), and improved further with training.

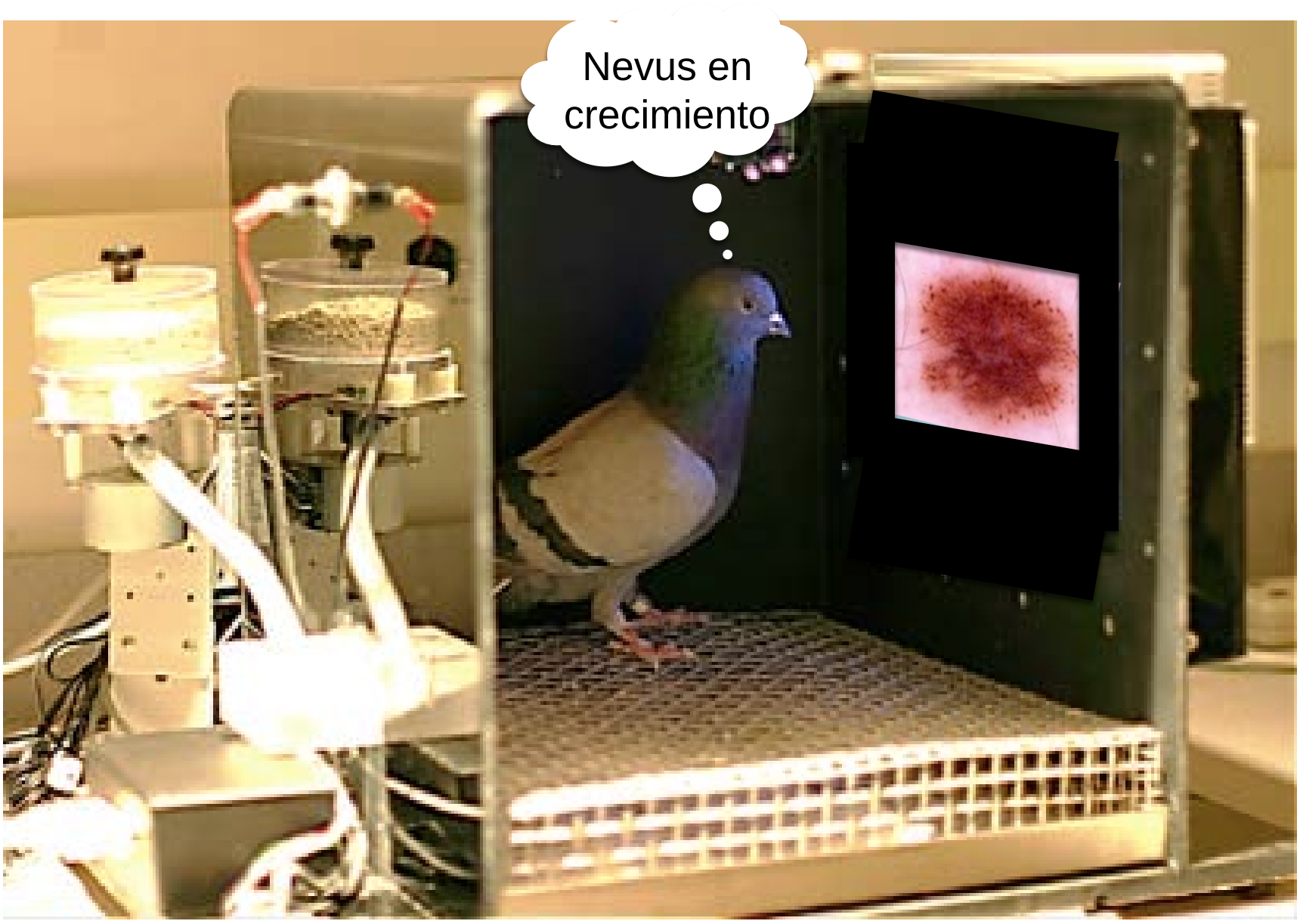
B) Introducing rotated versions of the training stimuli did not significantly affect performance at any of the magnifications.


Benign samples
Malignant samples
1:1
15:1
27:1



Examples of benign (left) and malignant (right) masses in mammograms.
Subsequent biopsy established histopathology ground-truth.

The birds proved to be similarly capable of detecting cancer-relevant microcalcifications on mammogram images. However, when given a different (and for humans quite difficult) task—namely, classification of suspicious mammographic densities (masses)—the pigeons proved to be capable only of image memorization and were unable to successfully generalize when shown novel examples.


Nevus en
crecimiento