27 settembre 2017

Melanomi cutanei: approccio diagnostico

CATERINA LONGO

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IRCCS - Santa Maria Nuova, Reggio Emilia, Italy
Università di Modena e Reggio Emilia

SKIN is an external organ...

SKIN is an external organ...

VISIBLE

SKIN is an external organ...

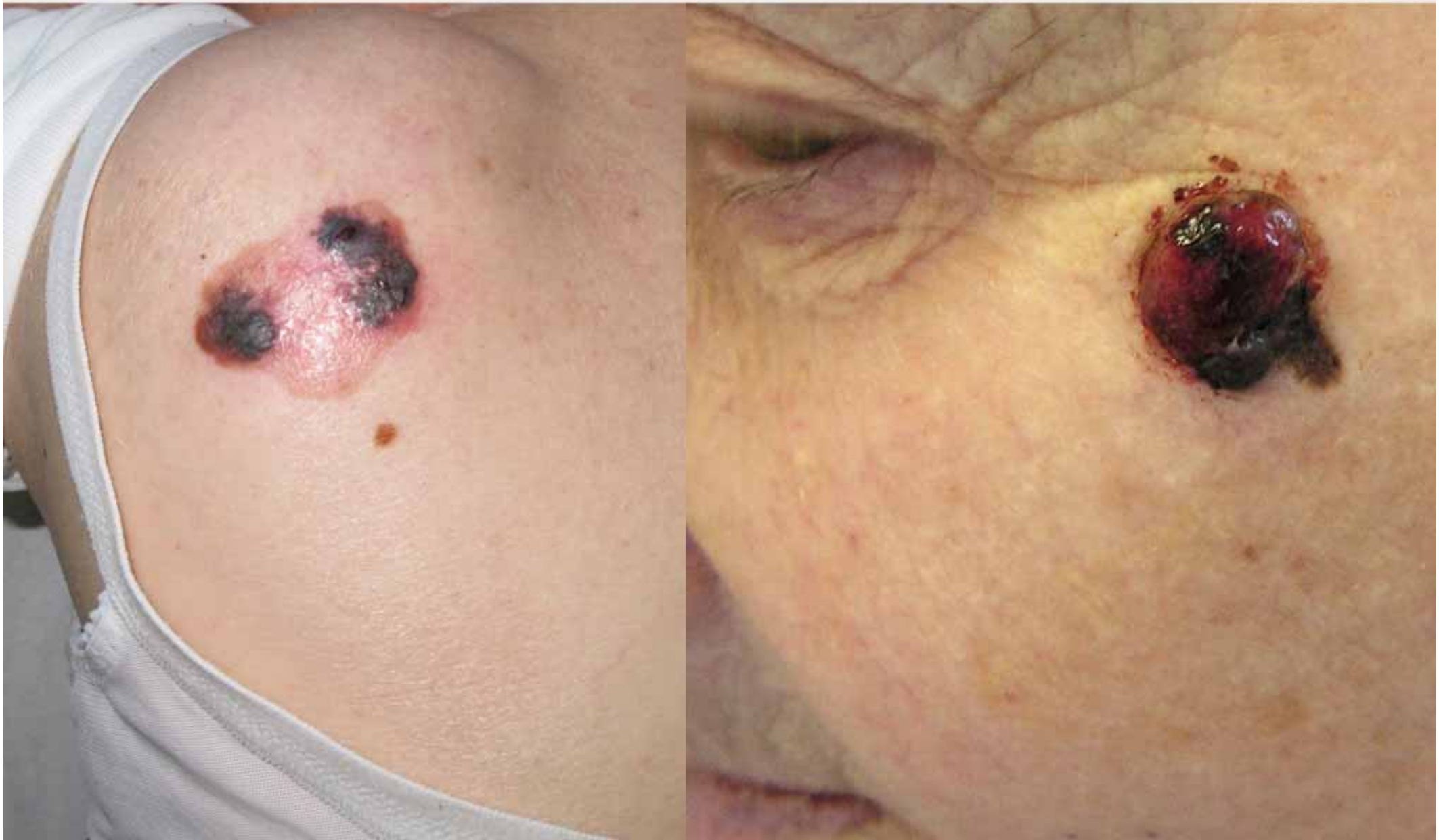
VISIBLE

EXPLORABLE!!!

Clinical examination

SEMEIOLOGY

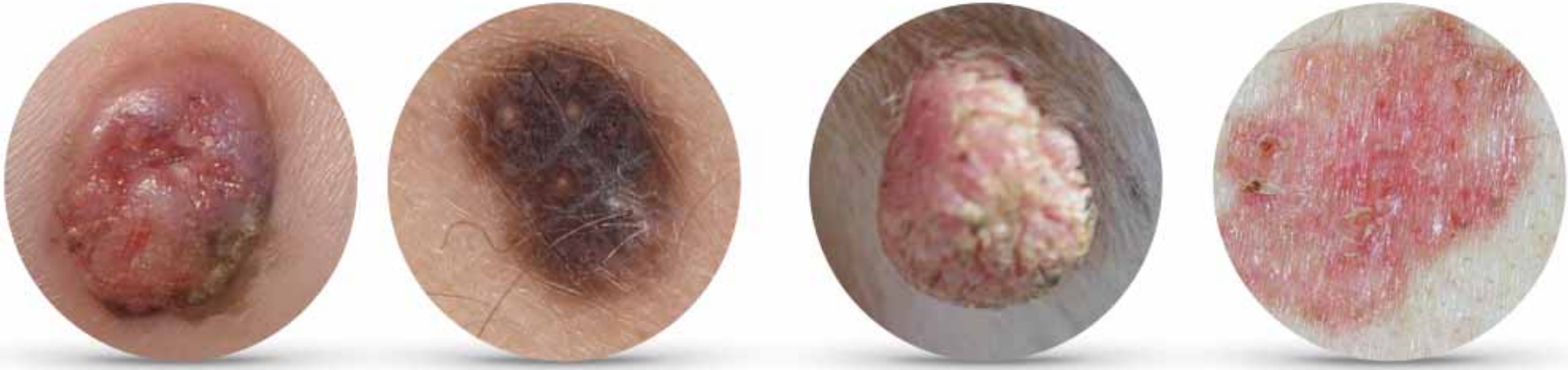
CLEAR CUT CLINICAL DIAGNOSIS




different devices
to have
a "virtual" skin biopsy

"virtual" skin biopsy

skin CANCER



Screening, early detection, education, and trends for melanoma: Current status (2007-2013) and future directions

Part I. Epidemiology, high-risk groups, clinical strategies, and diagnostic technology

Jonathan E. Mayer, BA,[a,b] Susan M. Swetter, MD,[c,d] Teresa Fu, MD,[c] and Alan C. Geller, MPH, RN[a]
Boston, Massachusetts; New York, New York; and Redwood City and Palo Alto, California

Table I. Summary of new technologies for the detection of melanoma

Technology	Definition	Pros	Cons	Sensitivity	Specificity
Dermatoscopy	Examination of skin with dermatoscope	Fewer biopsy specimens and removal of benign lesions	Increases examination time and requires clinician training	90%	90%
Total body photography	Series of photographs of all skin on body	Can detect thinner tumors than the naked eye and lower biopsy rates than serial dermatoscopy	Expensive	75%	74%
Confocal microscopy	Low power laser that creates 3-dimensional image with resolution comparable to standard histology	Able to detect subclinical disease in an area wider than that of dermatoscopy	Limited by expense and the need for specialized training	90%	86%
MelaFind	Multispectral device that uses automated software for image analysis	High sensitivity	Expensive and low specificity	96-98%	0-10%
Electrical impedance spectroscopy	Device that measures changes in tissue impedance to low voltage current flow	High sensitivity	Expensive, low specificity, requires presoaking of the lesion in saline, increases examination time	98%	25-49%
Smartphone apps	Cell phone programs that analyze self-taken photographs of suspicious lesions	Widely available, and some apps send photos to Board-certified dermatologists	Experimental and highly variable quality	7-98%	30-94%

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CONTINUING MEDICAL EDUCATION

J AM ACAD DERMATOL
OCTOBER 2014

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Part I. Epidemiology, high-risk groups, clinical strategies, and diagnostic technology

Jonathan E. Mayer, BA,[a,b] Susan M. Swetter, MD,[c,d] Teresa Fu, MD,[c] and Alan C. Geller, MPH, RN[a]
Boston, Massachusetts; New York, New York; and Redwood City and Palo Alto, California

- **Dermatoscopy** increases the sensitivity of clinical evaluation for MM and has been shown to decrease the number of excised benign lesions
- **Total Body Photography** helps to detect new/thinner tumors especially in patients with numerous moles
- **Confocal microscopy** requires specialized training and may be superior to dermatoscopy for the detection of subclinical MM

DERMOSCOPY

Dermatoscope

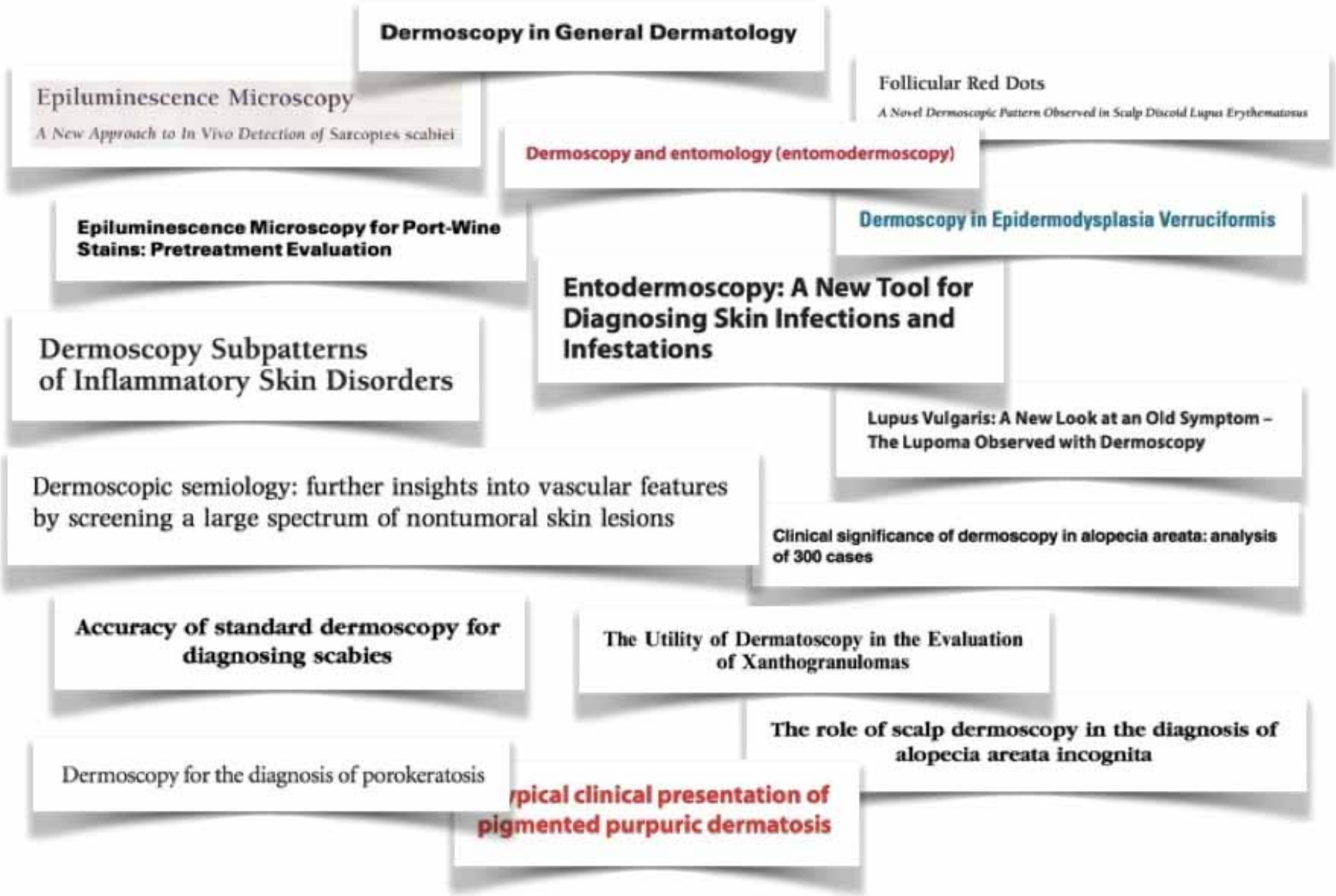
Dermatoscope

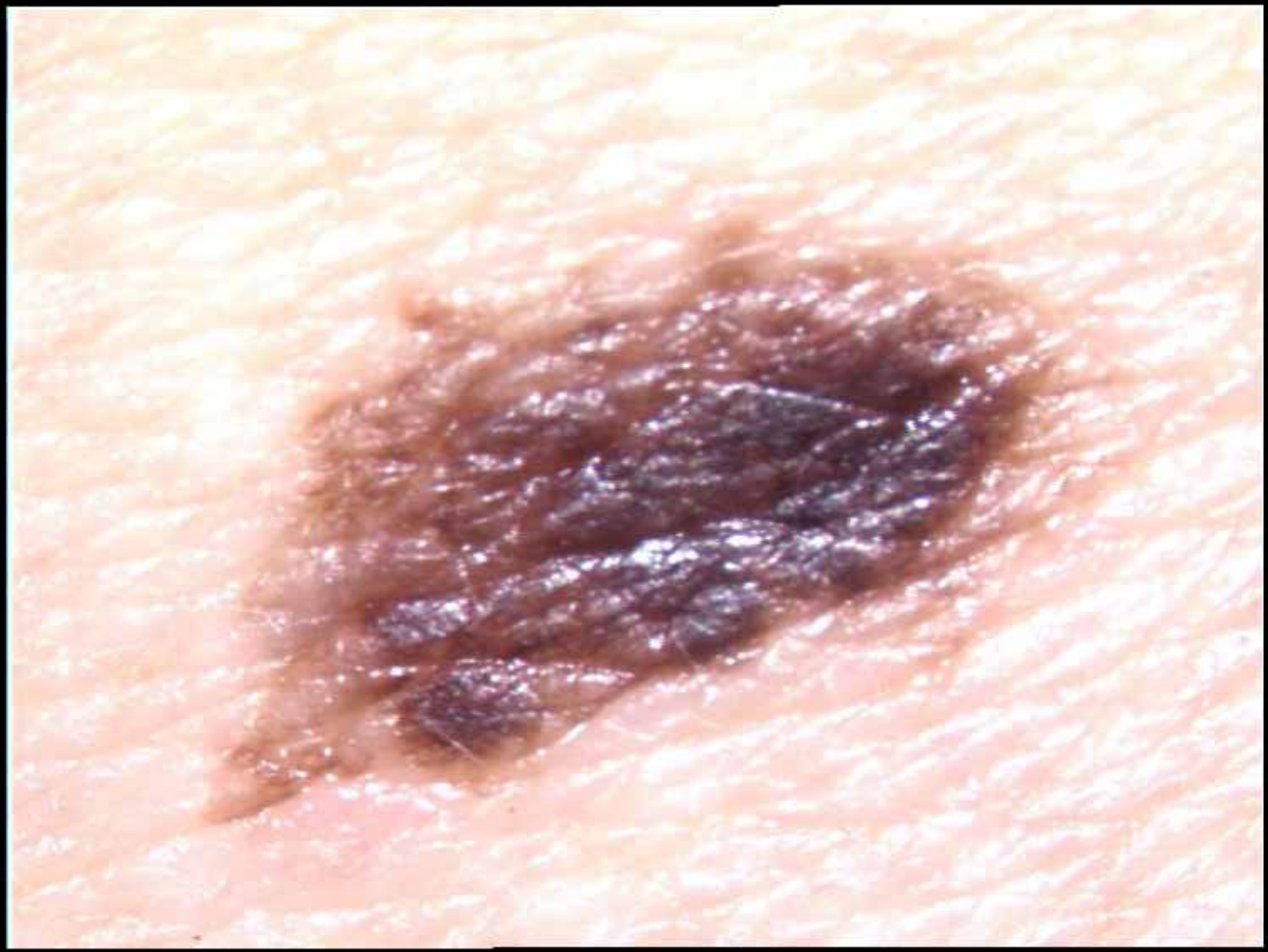
Stethoscope

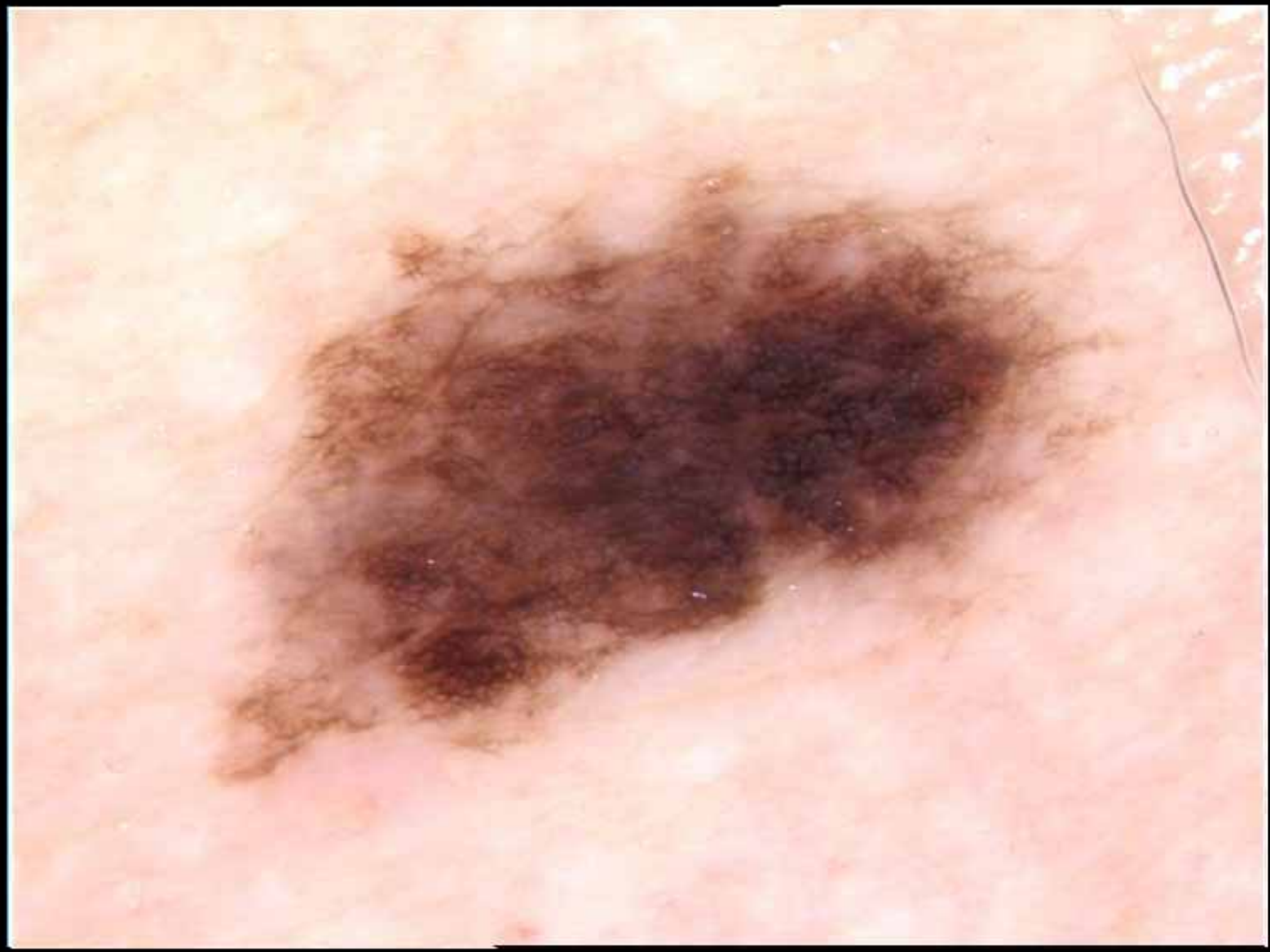
Why method of the millennium

- Cheap (average costs between 500-1000$)
- Handy (can be easy carried all day)
- Fast (allows examination of all lesions in few minutes)
- High diagnostic accuracy
- High image quality
- Allows documentation via digital photography

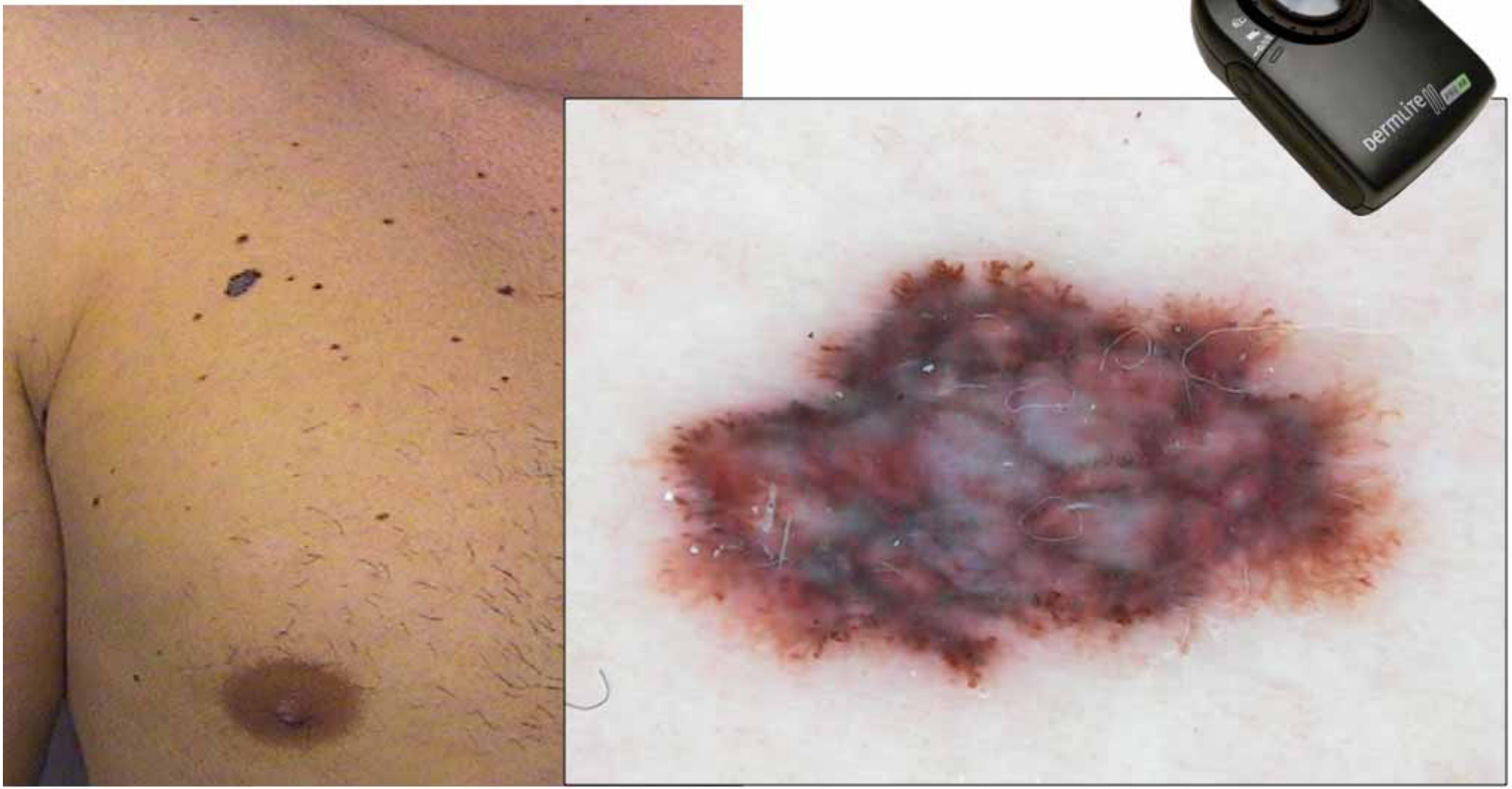
More than 35 different indications







DERMOSCOPY



Pehamberger H, Steiner A, Wolff K. In vivo epiluminescence microscopy of pigmented skin lesions. I. Pattern analysis of pigmented skin lesions. J Am Acad Dermatol. 1987;17:571-83

DERMOSCOPY

EVIDENCE-BASED DERMATOLOGY: ORIGINAL CONTRIBUTION

Is Dermoscopy (Epiluminescence Microscopy) Useful for the Diagnosis of Melanoma?

Results of a Meta-analysis Using Techniques Adapted to the Evaluation of Diagnostic Tests

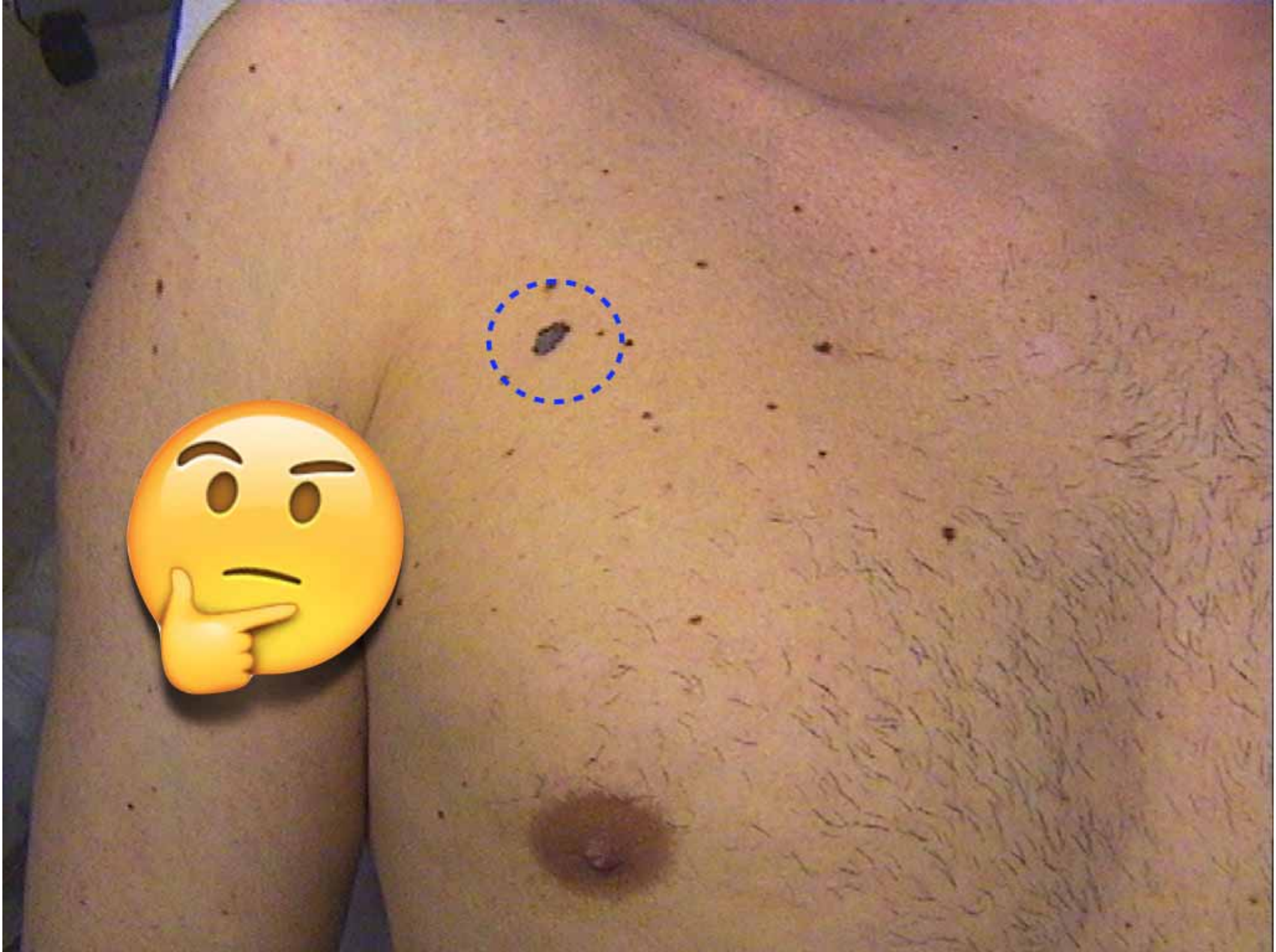
Marie-Lise Bafounta, MD; Alain Beauchet, MD, PhD; Philippe Aegerter, MD, PhD; Philippe Saiag, MD

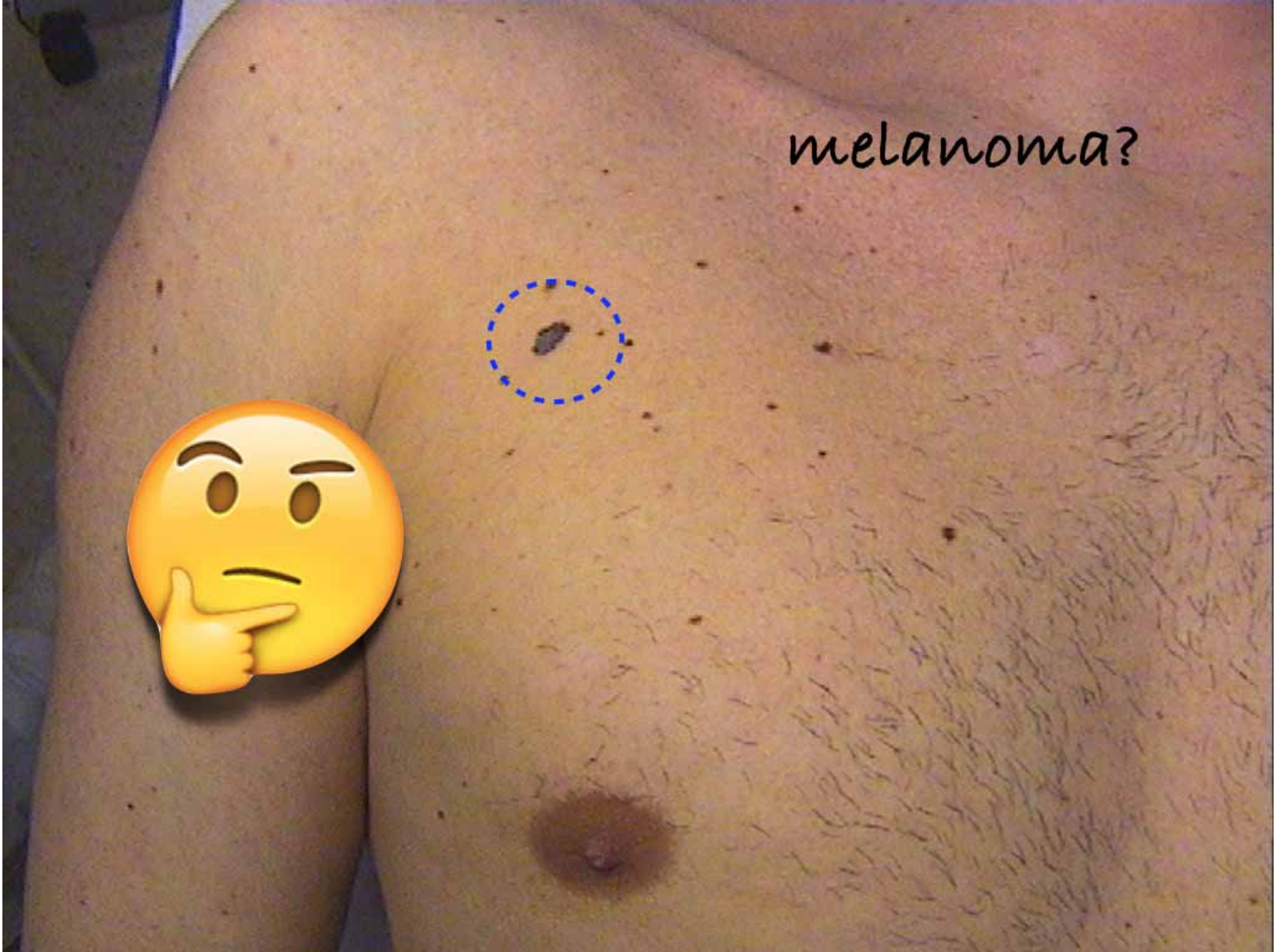
Dermoscopy — Review

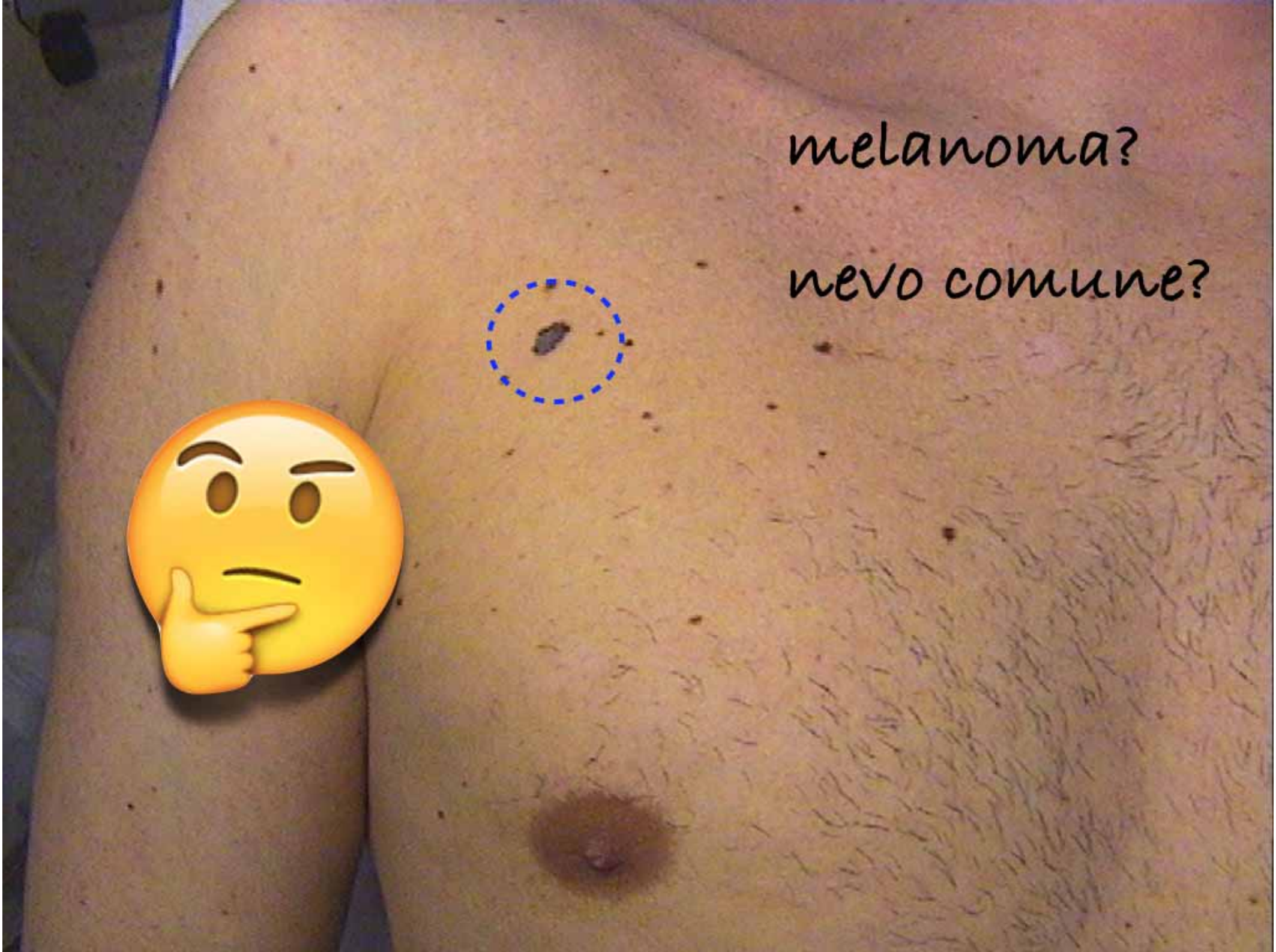
Diagnostic accuracy of dermoscopy

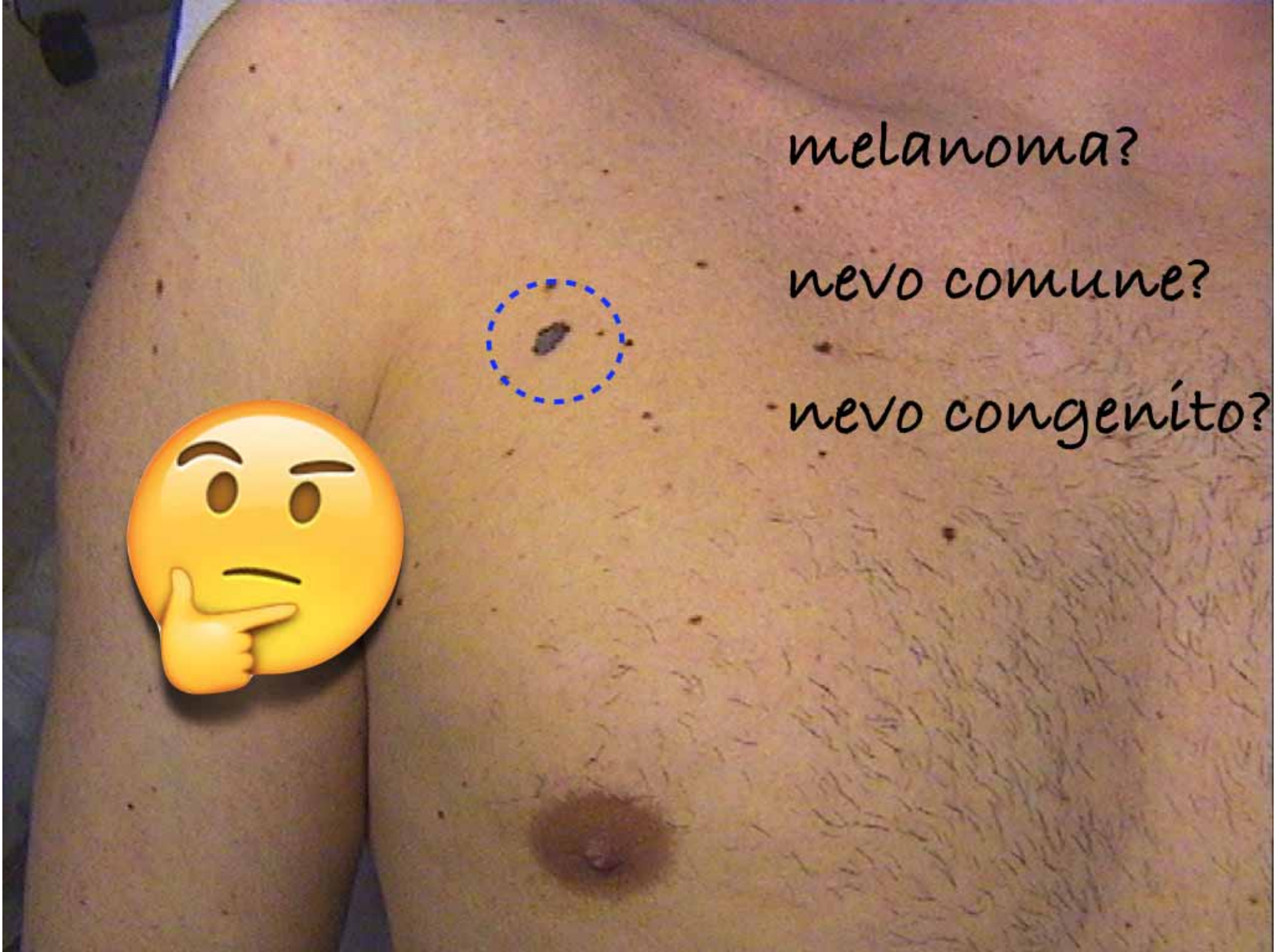
H Kittler, H Pehamberger, K Wolff, and M Binder

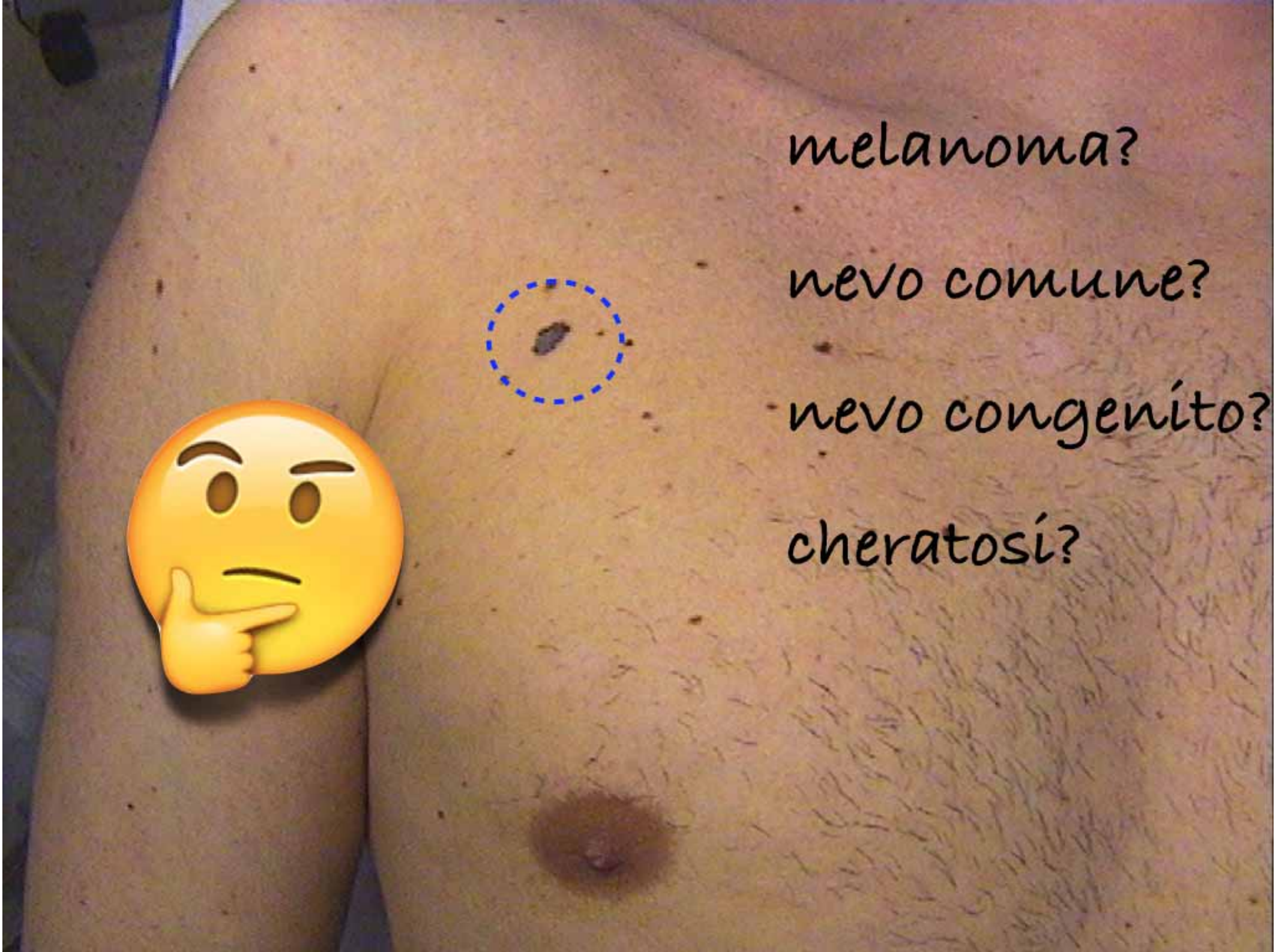
In the hands of experts, diagnostic accuracy improved from 15 to 35% with dermoscopy

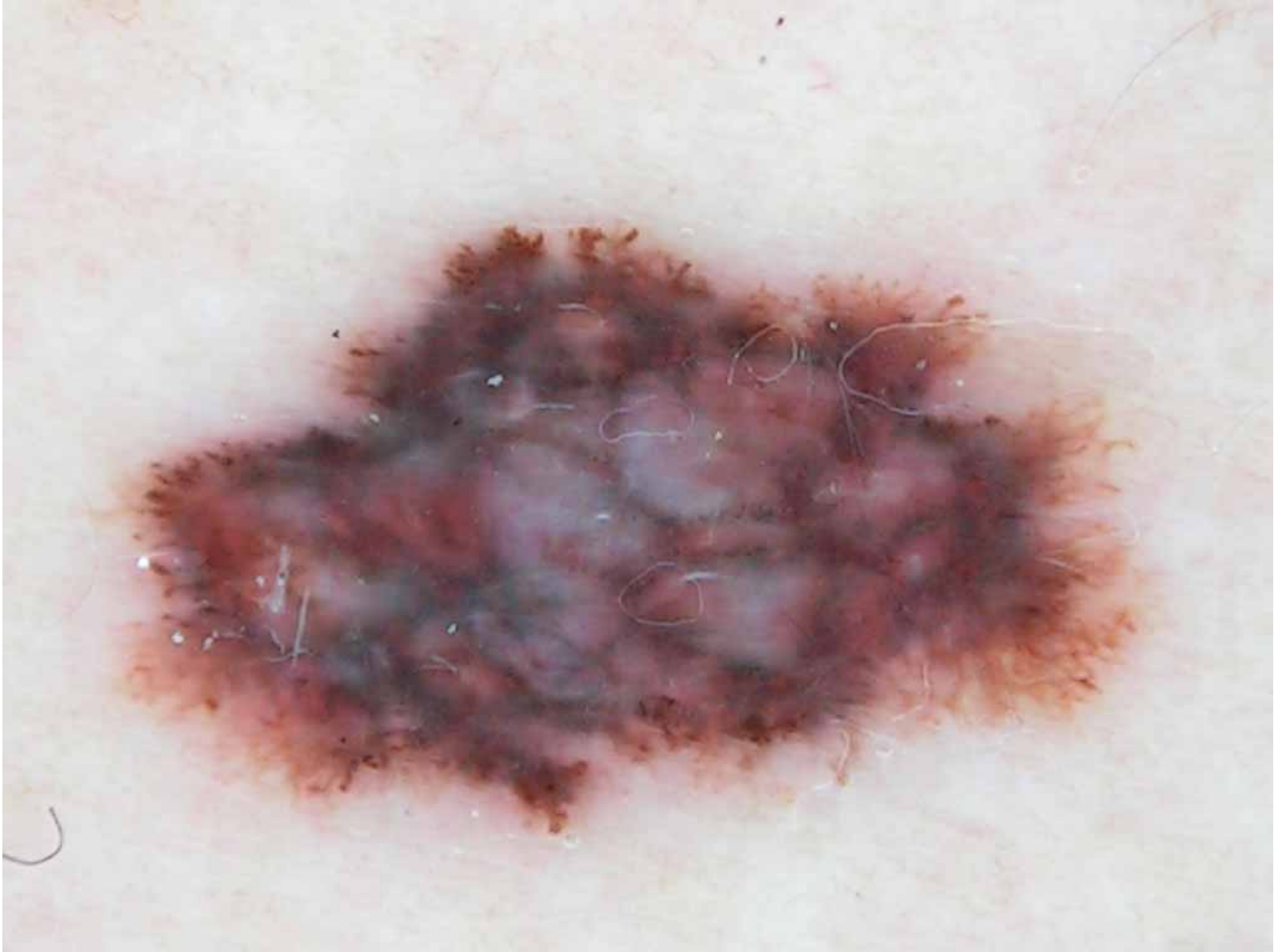


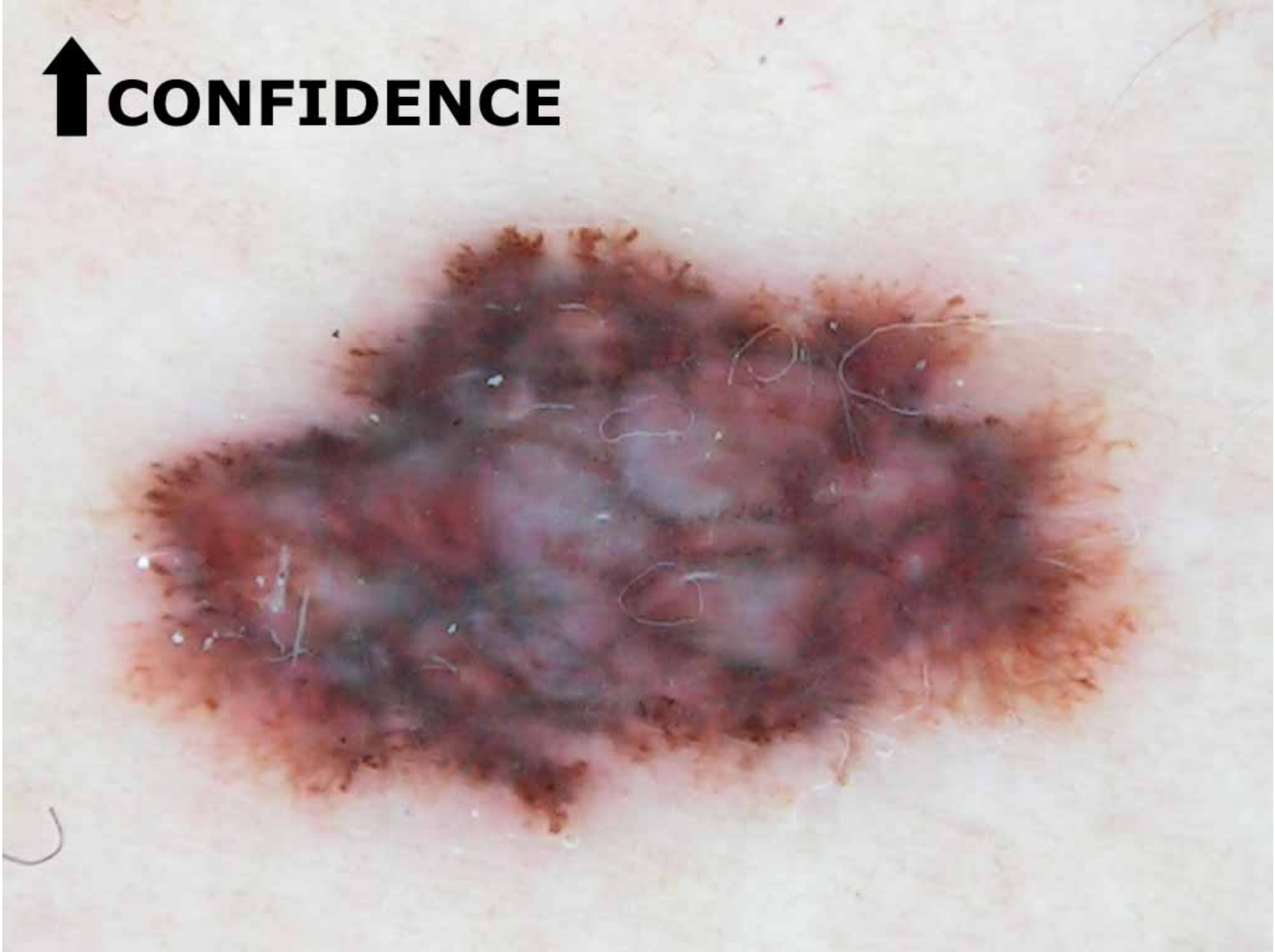

melanoma?

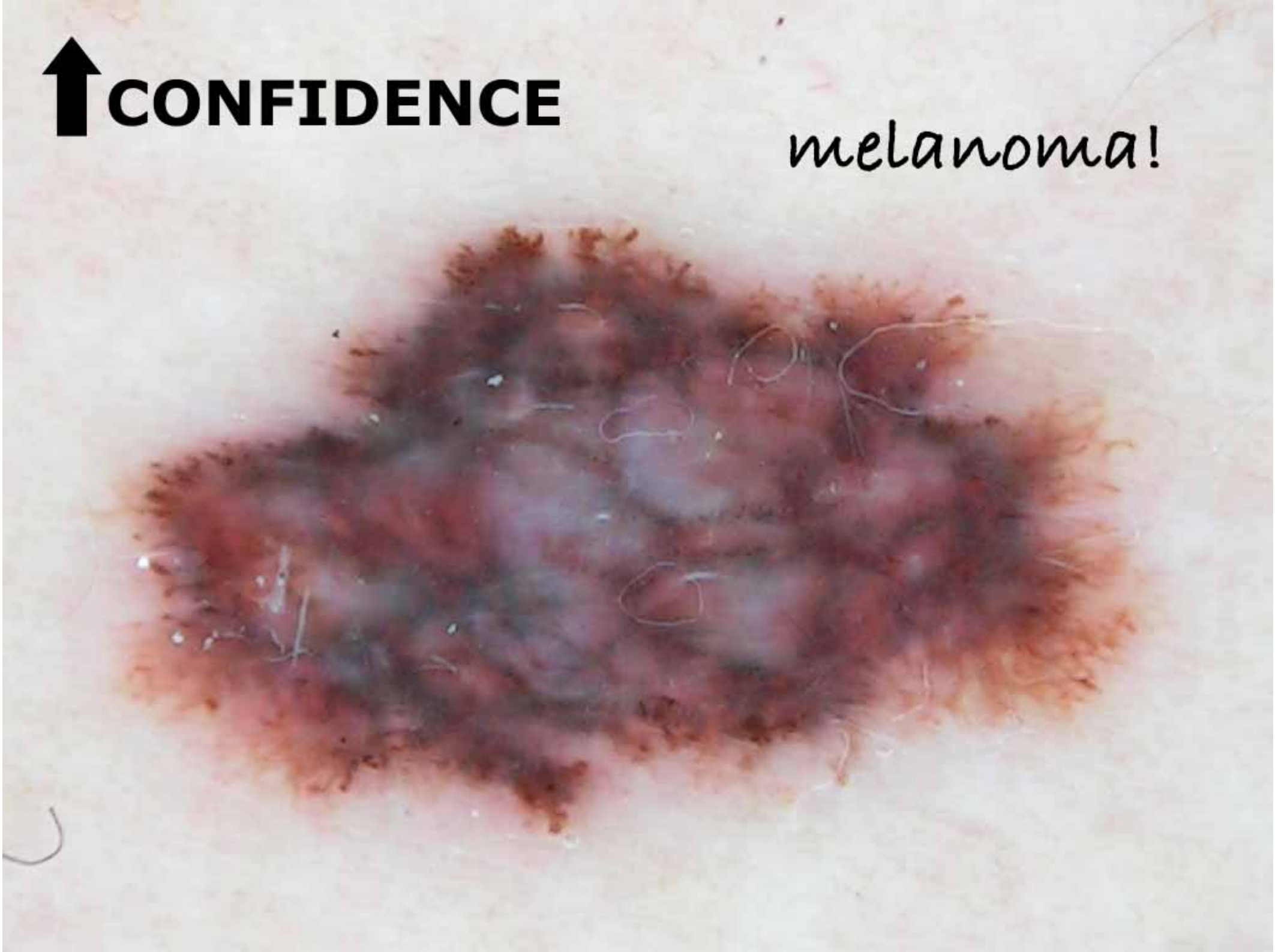

melanoma?
nevo comune?

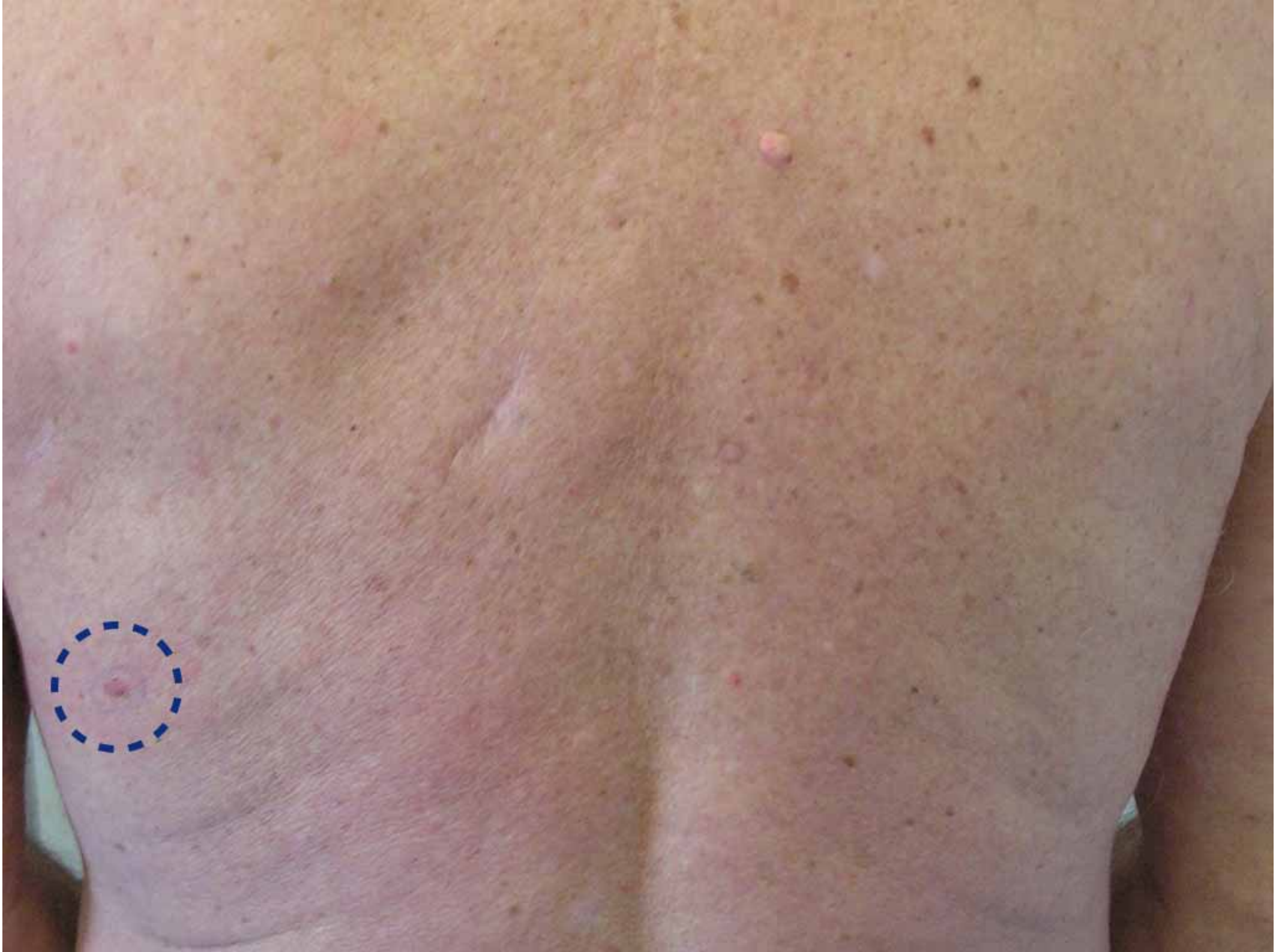

melanoma?
nevo comune?
nevo congenito?

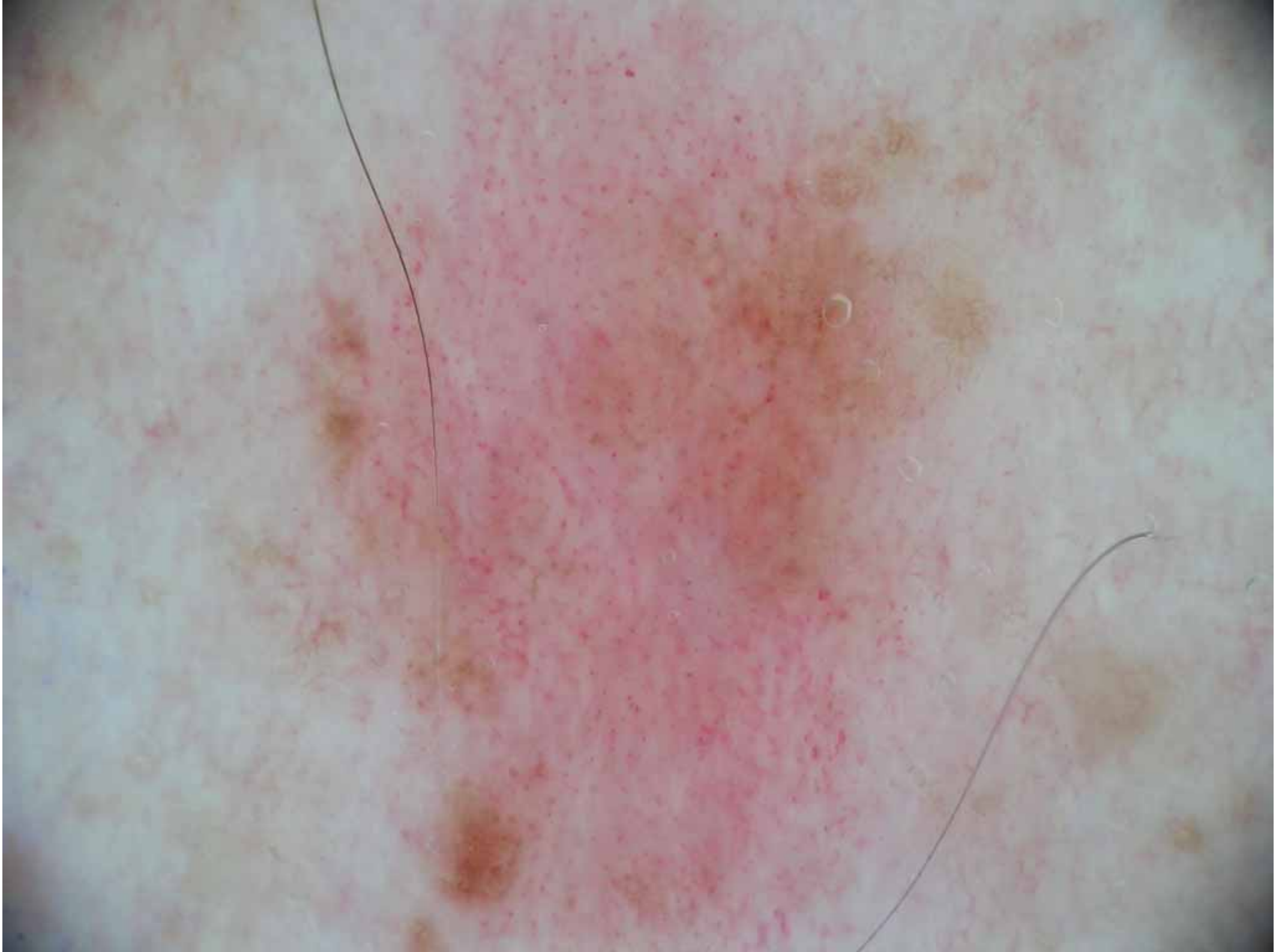

melanoma?
nevo comune?
nevo congenito?
cheratosi?




CONFIDENCE


CONFIDENCE
melanoma!






SENSITIVITY

J Am Acad Dermatol 2011 ORIGINAL ARTICLE

Accuracy in melanoma detection: A 10-year multicenter survey

Giuseppe Argenziano, MD, Lorenzo Cerroni, MD, Iris Zalaudek, MD, Stefania Staibano, MD, Rainer Hofmann-Wellenhof, MD, Nicola Arpaia, MD, Renato Marchiori Bakos, MD, MSc, Brigitte Balme, MD, Jadran Bandic, MD, Roberto Bandelloni, MD, Alexandra M. G. Brunasso, MD, Horacio Cabo, MD, David A. Calcara, BS, Blanca Carlos-Ortega, MD, Ana Carolina Carvalho, MD, Gabriel Casas, MD, Huiting Dong, MD, Gerardo Ferrara, MD, Raffaele Filotico, MD, Guillermo Gómez, MD, Allan Halpern, MD, Gennaro Ilardi, MD, Akira Ishiko, MD, PhD, Gulsen Kandiloglu, MD, Hiroshi Kawasaki, MD, Ken Kobayashi, MD, Hiroshi Koga, MD, Ivanka Kovalyshyn, MD, David Langford, MB, ChB, Xin Liu, MD, Ashfaq Marghoob, MD, Massimo Mascolo, MD, Cesare Massone, MD, Laura Mazzoni, MD, Scott Menzies, MBBS, PhD, Akane Minagawa, MD, Loredana Nugnes, MD, Fezal Ozdemir, MD, Giovanni Pellacani, MD, Stefania Seidenari, MD, Katherine Siamas, MD, Ignazio Stanganelli, MD, William V. Stoecker, MD, Masaru Tanaka, MD, Luc Thomas, MD, Philipp Tschandl, MD, and Harald Kittler, MD

A large number of BENIGN lesions, with equivocal dermoscopic aspects or history of change, are excised to rule out a MELANOMA

NNE: number needed to excise

NNE in Specialized Centers (Dermoscopy):

1 : 8.7

NNE in Non-Specialized Centers: 1:29.4

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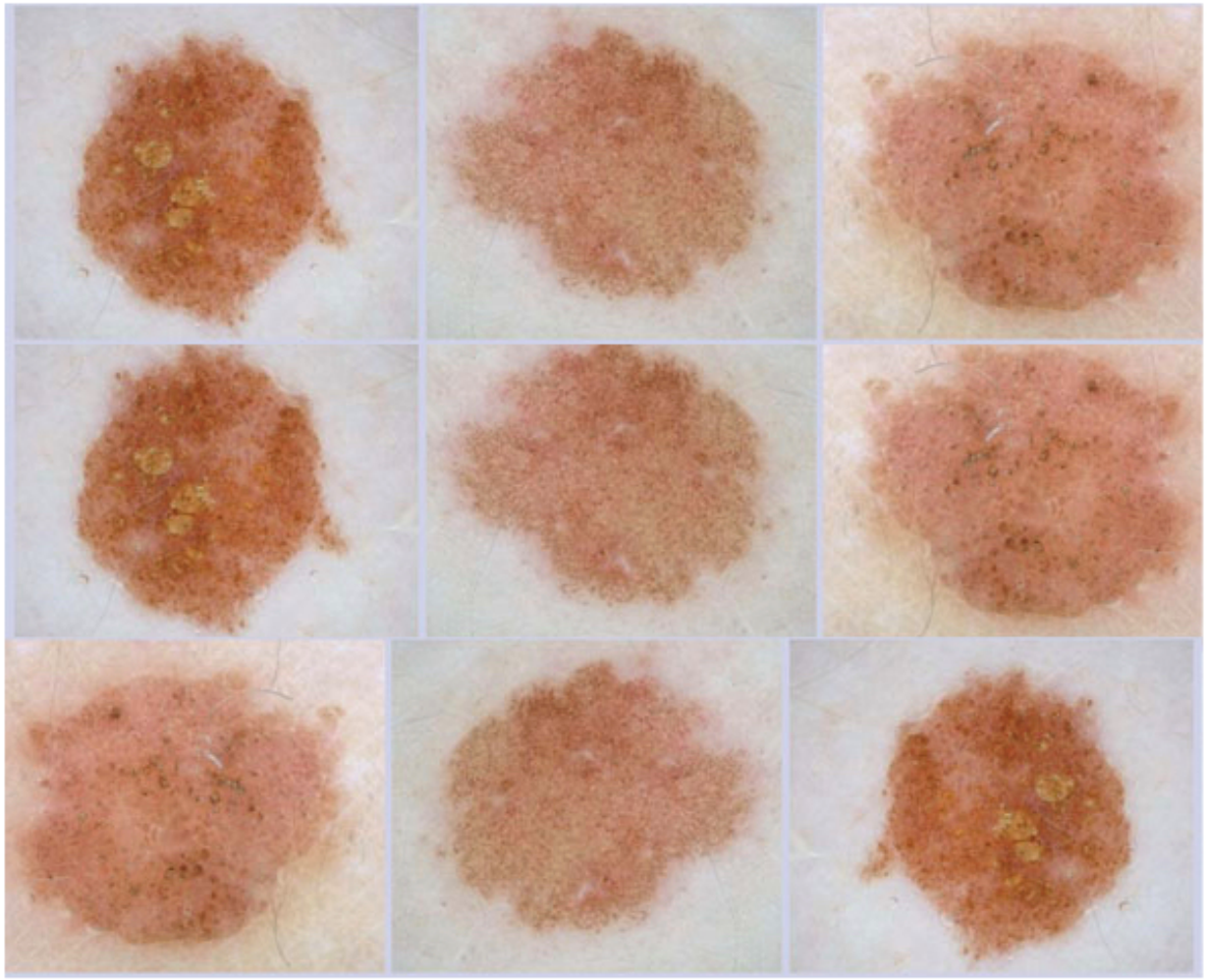

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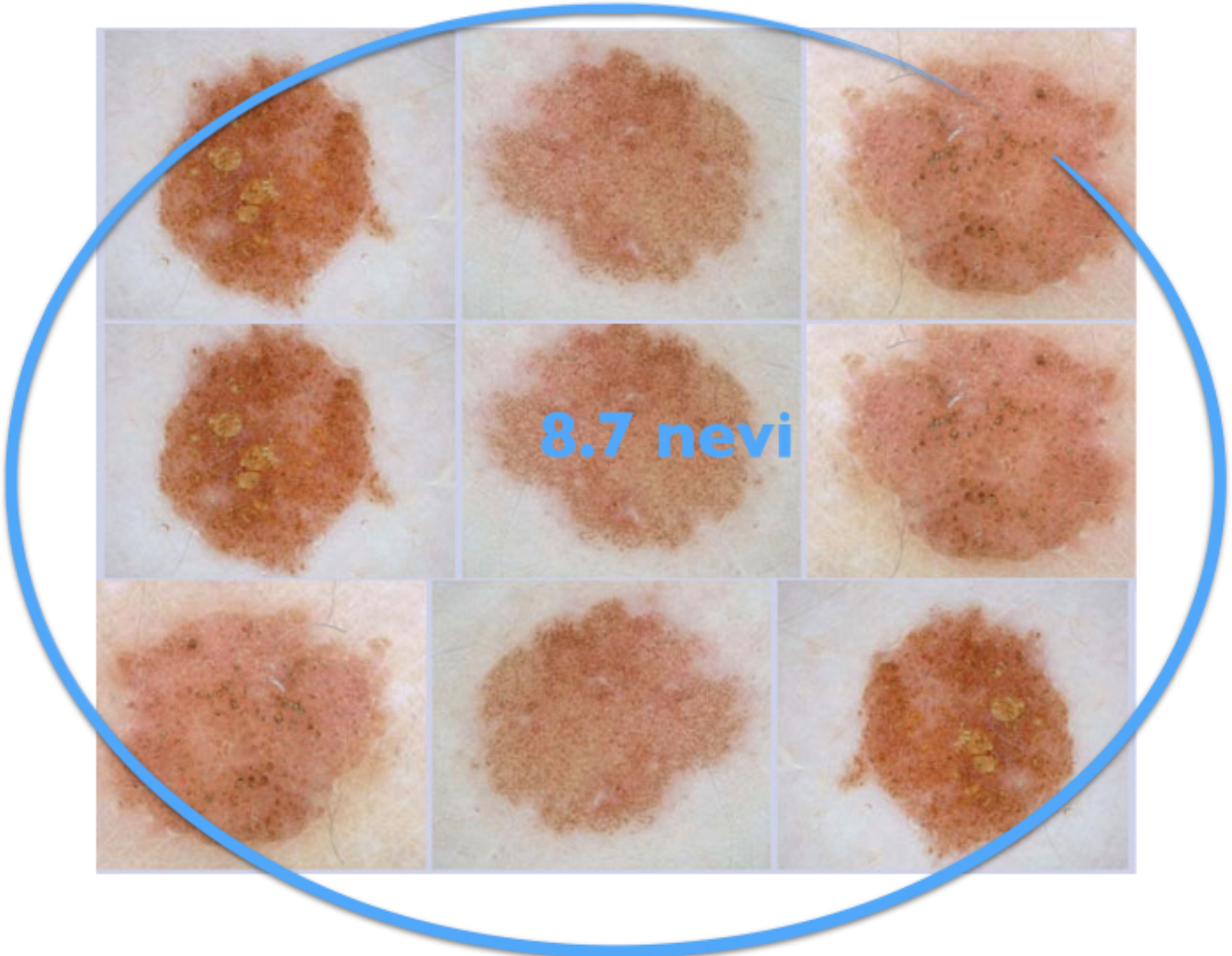

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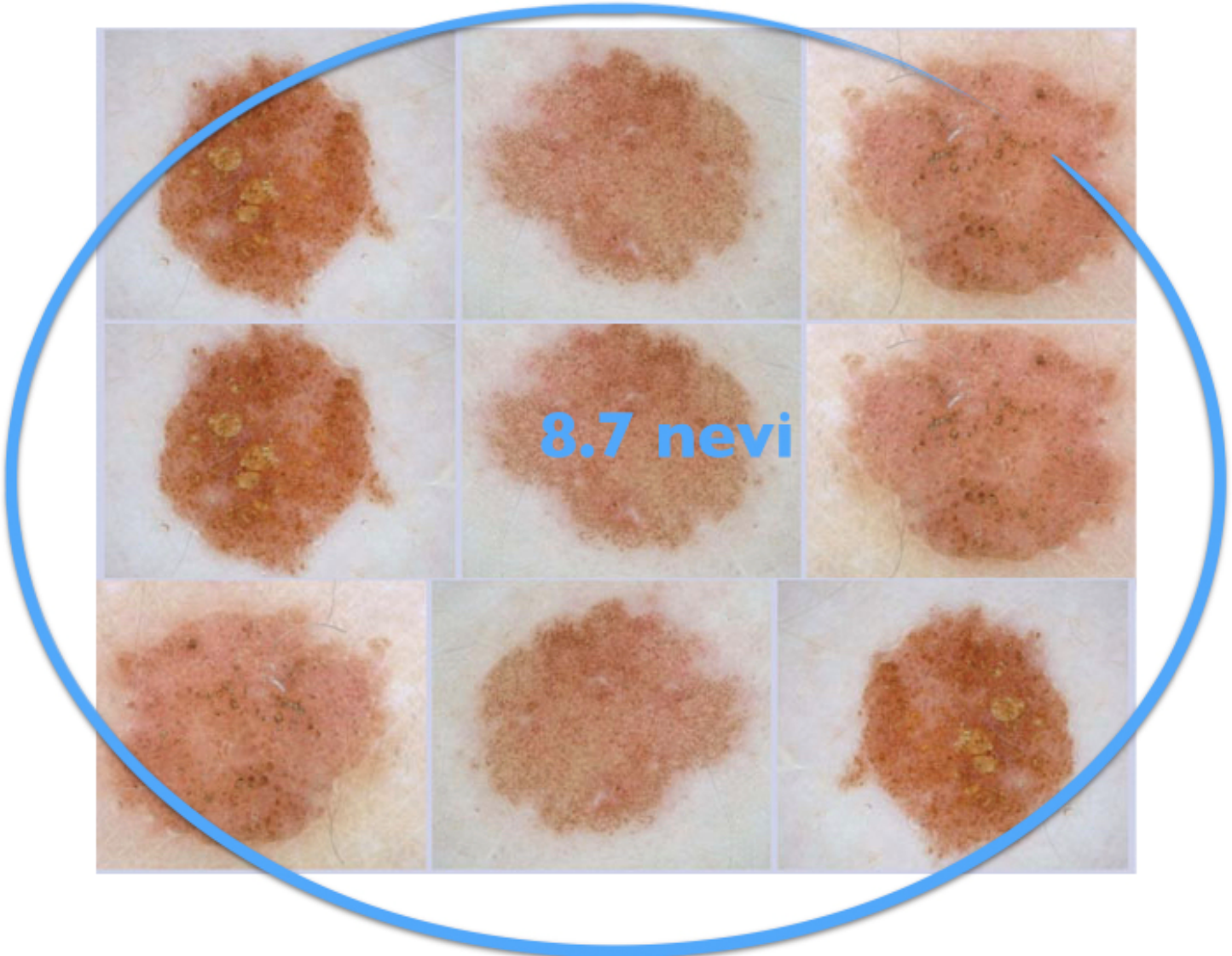

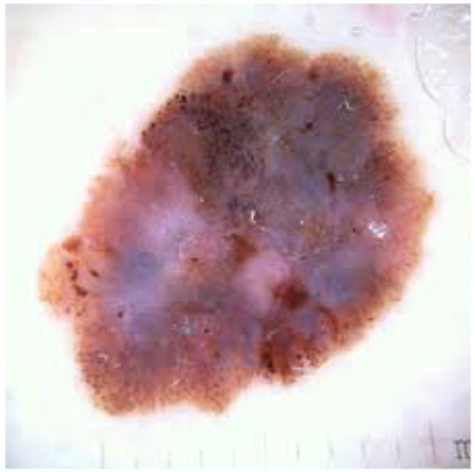

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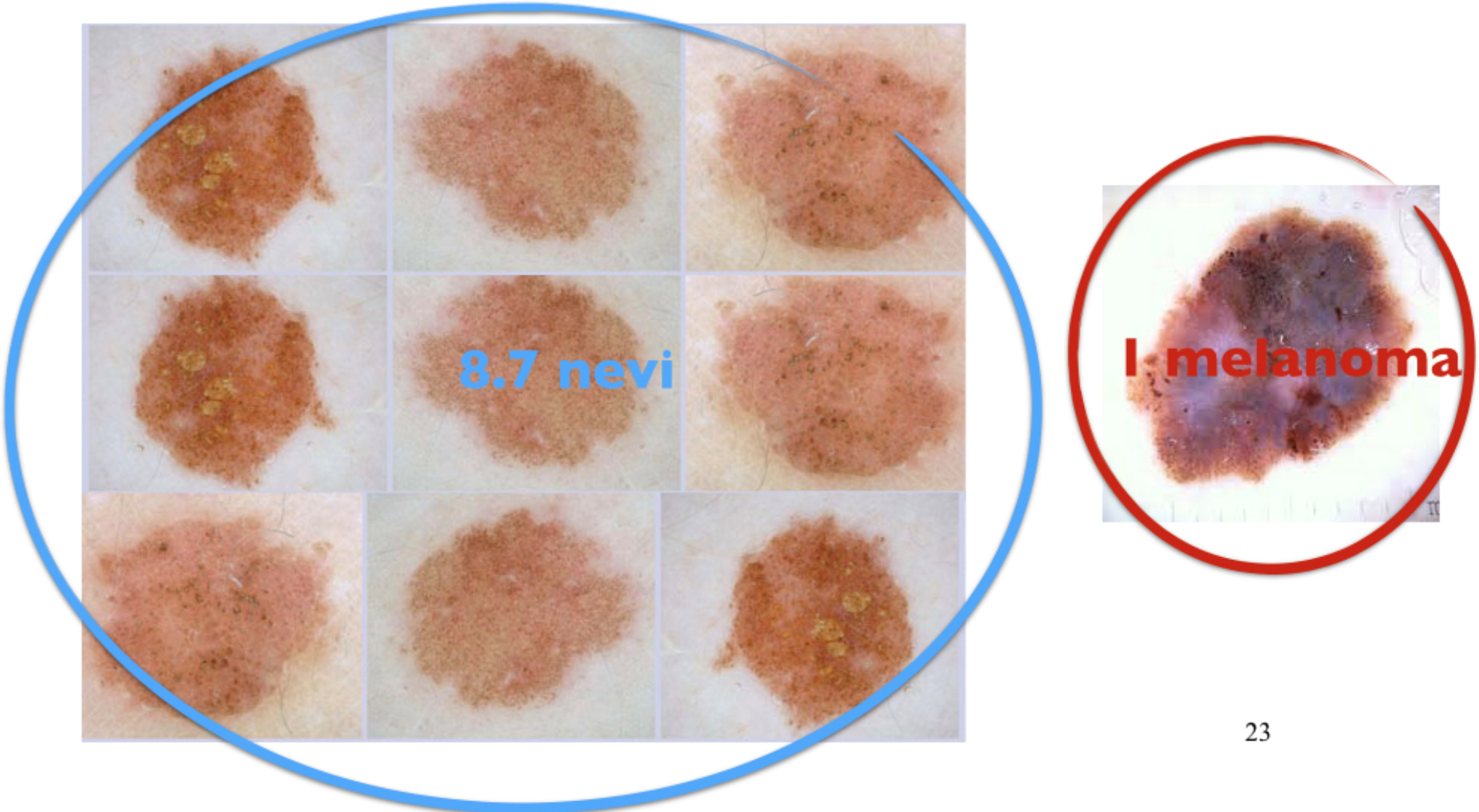

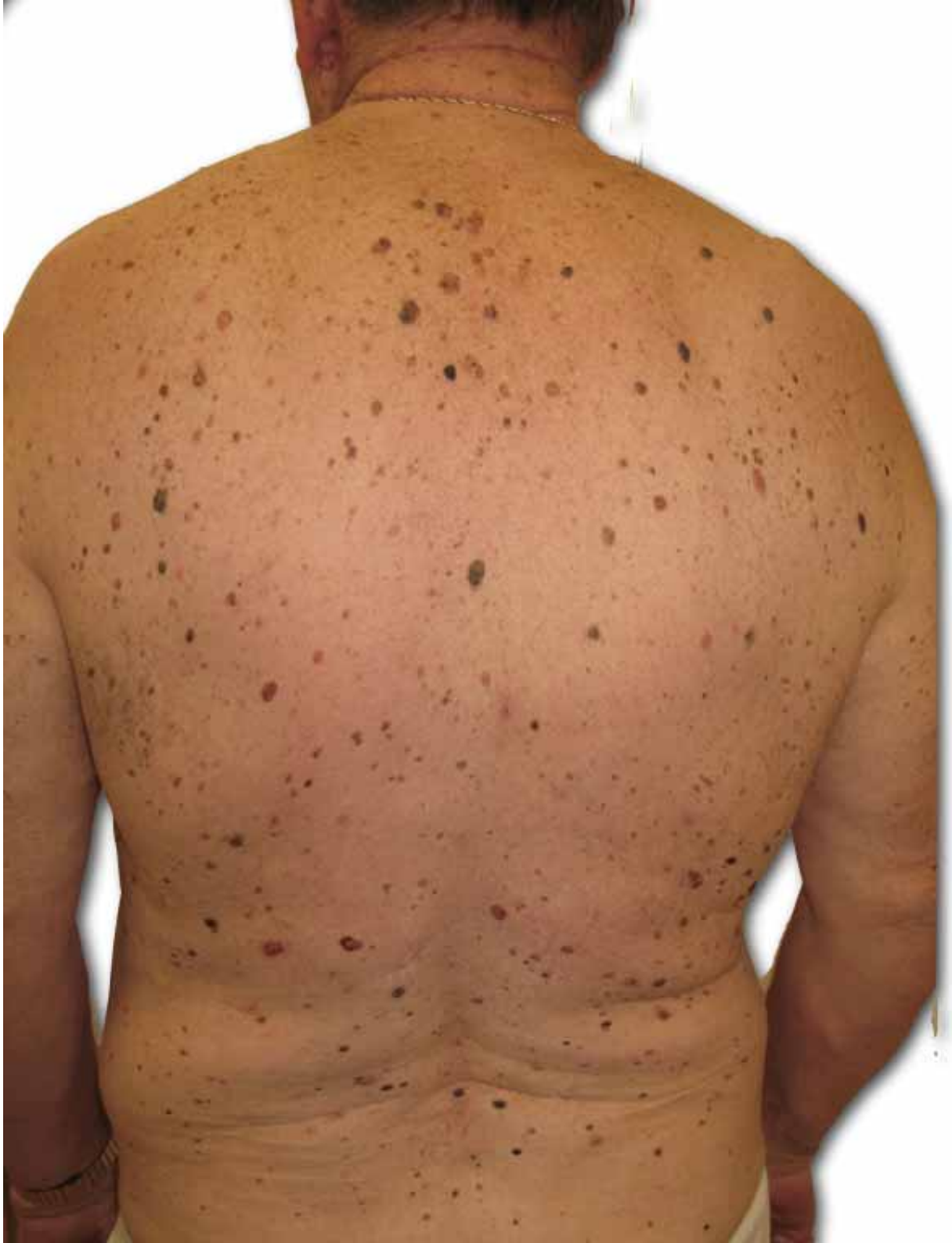

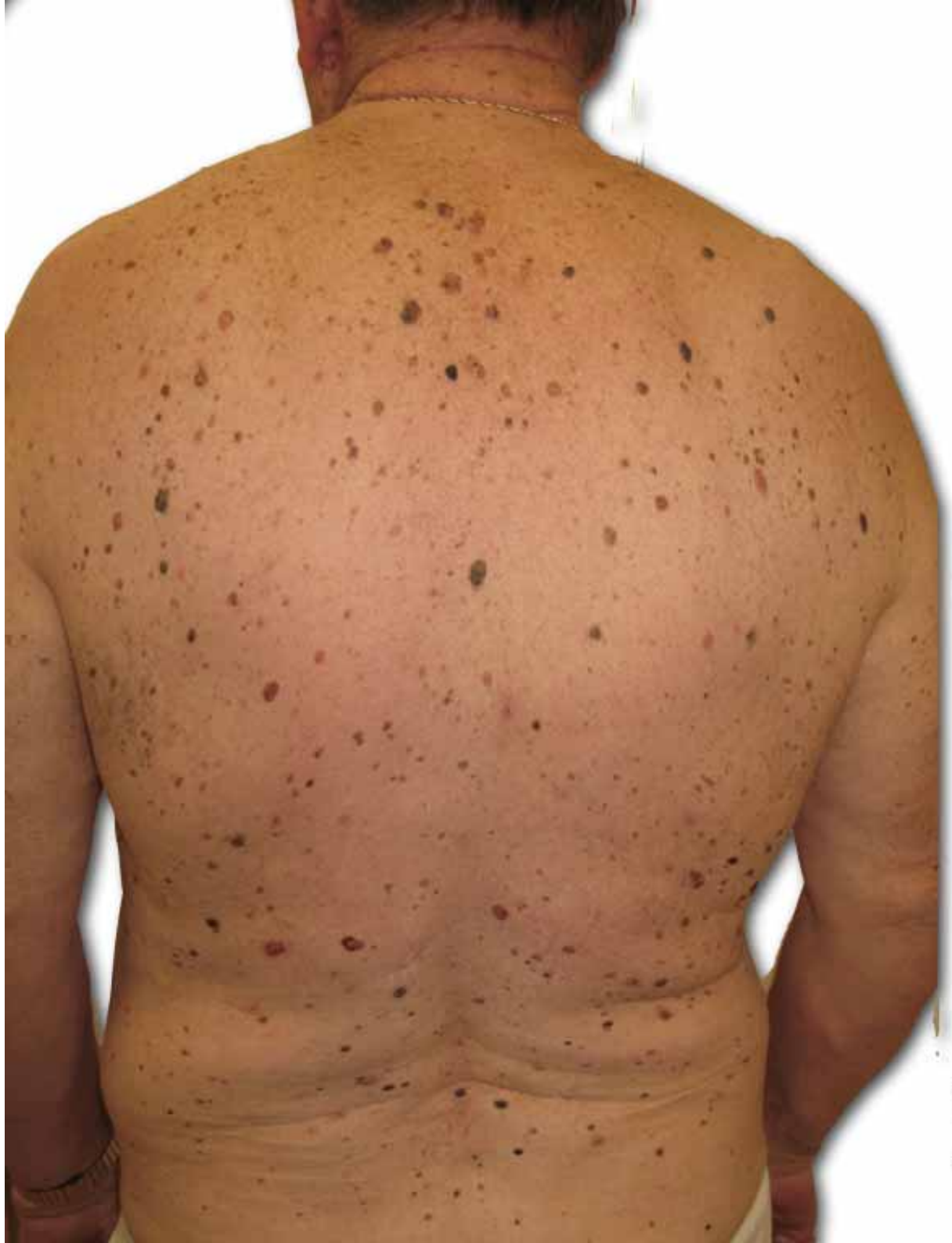

Digital Dermoscopy

DIGITAL DERMOSCOPY MONITORING

ELSEVIER

Clinics in Dermatology • 2002;20:297–304

Follow-up of Melanocytic Skin Lesions with Digital Total-Body Photography and Digital Dermoscopy: A Two-Step Method

JOSEP MALVEHY, MD
SUSANA PUIG, MD

The increase of the treatment threshold is accompanied by a **loss of sensitivity** and a **gain in specificity**.

The utility of this technique depends on the experience in the interpretation of follow-up images and on the **patient's compliance** with follow-up.

Follow-up of Melanocytic Skin Lesions with Digital Total-Body Photography and Digital Dermoscopy: A Two-Step Method

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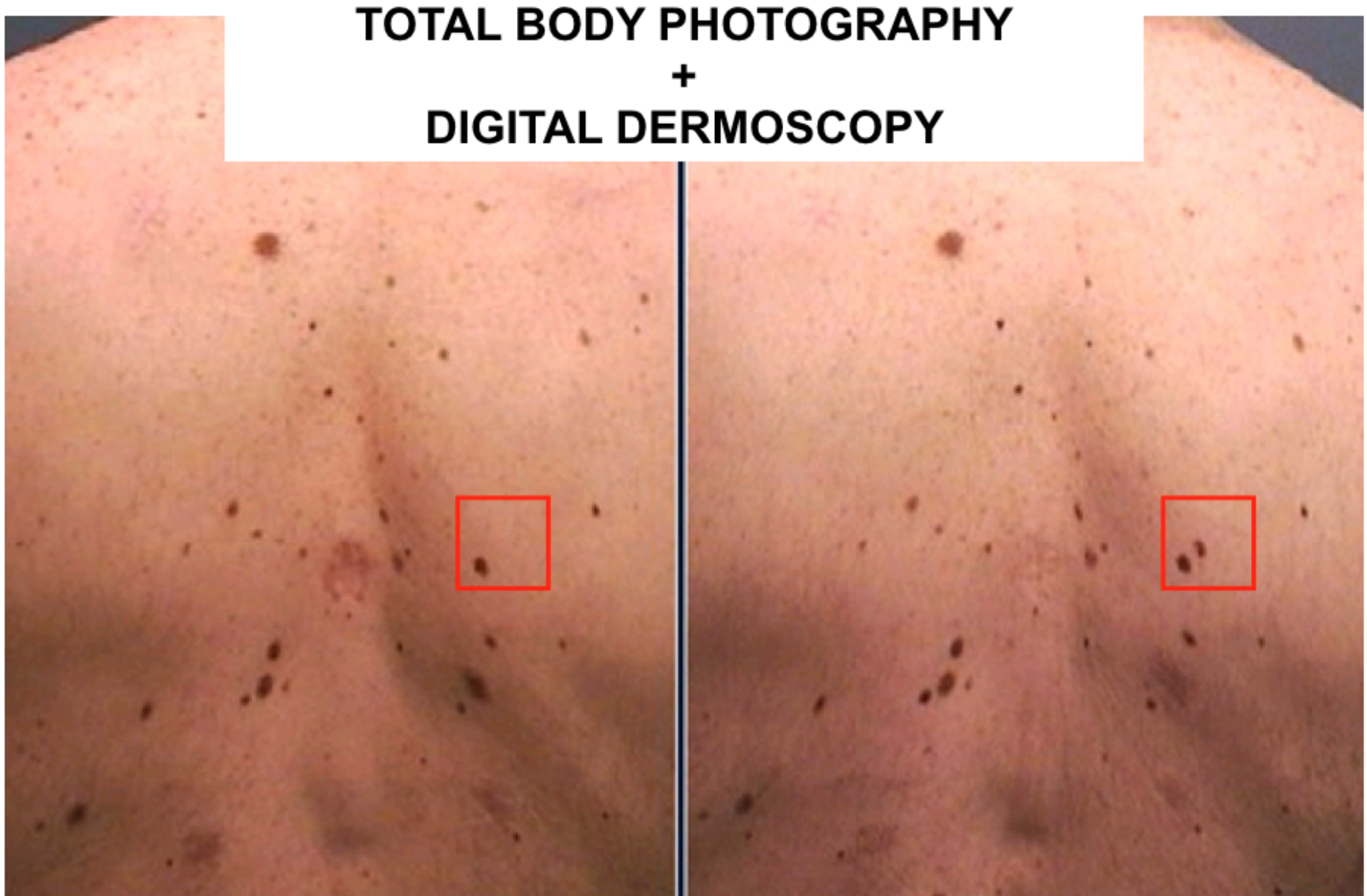

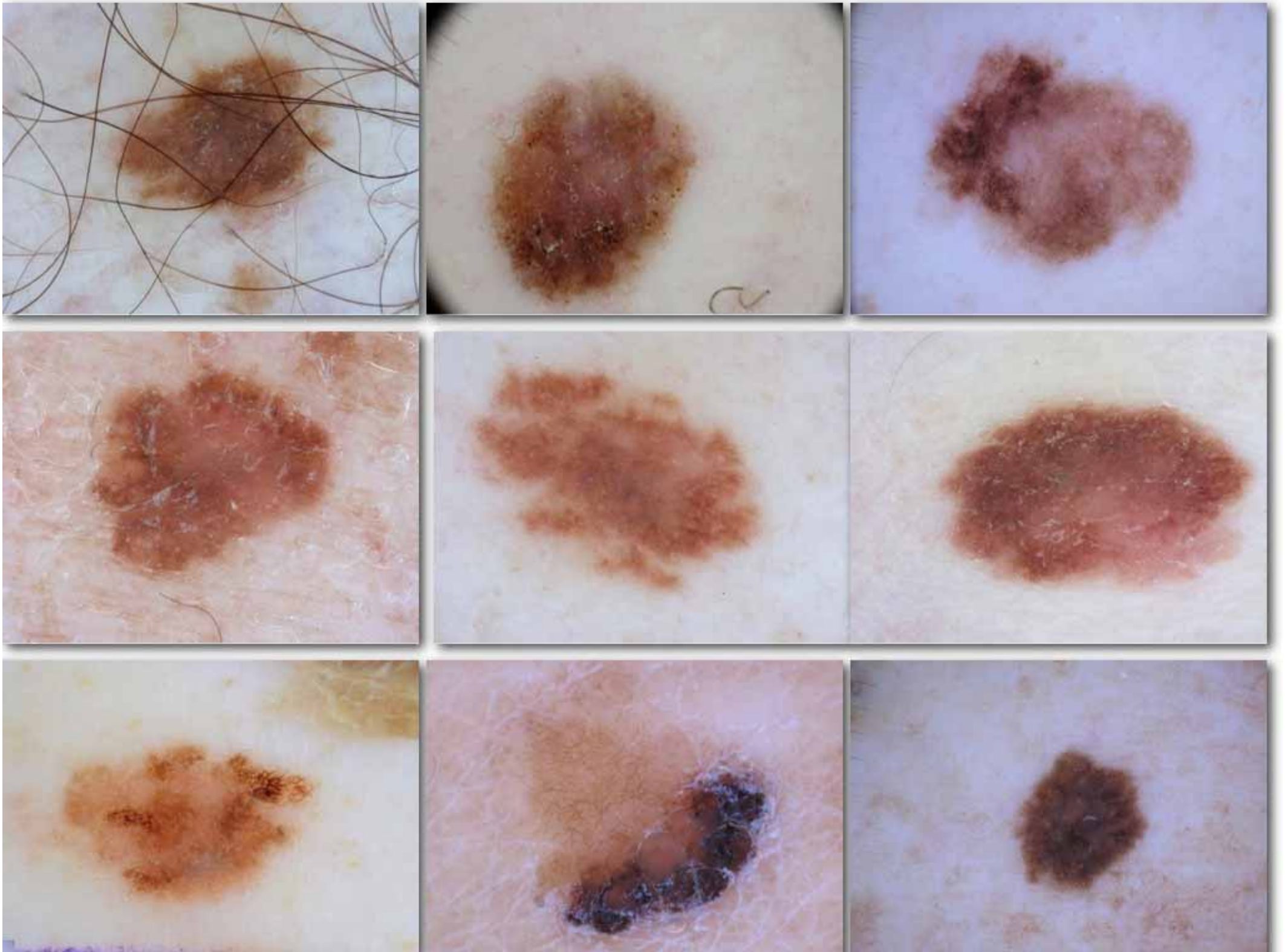

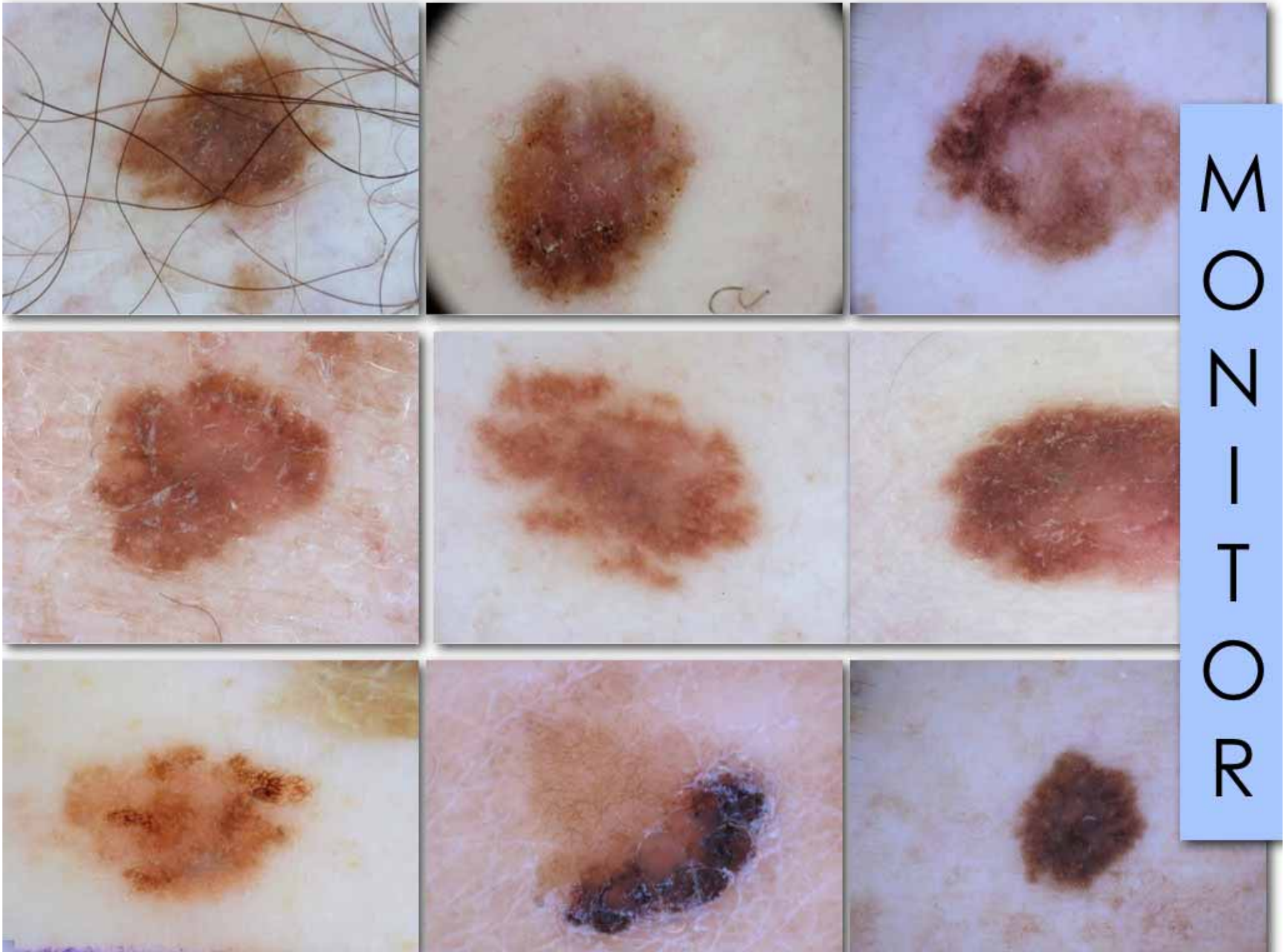
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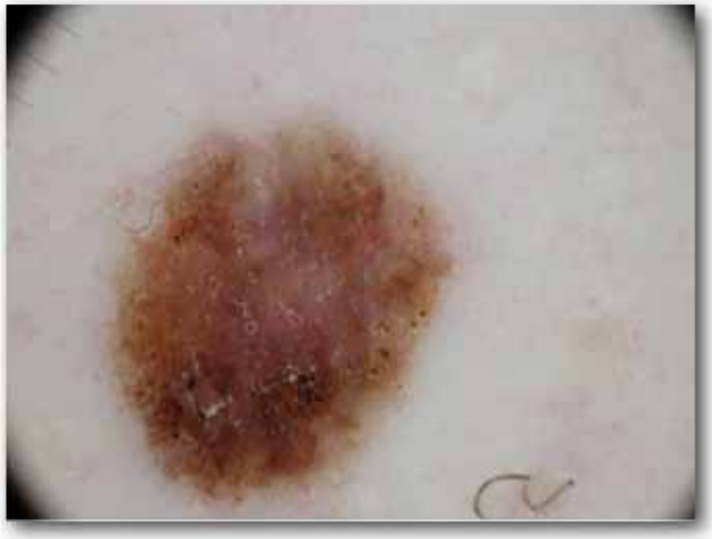
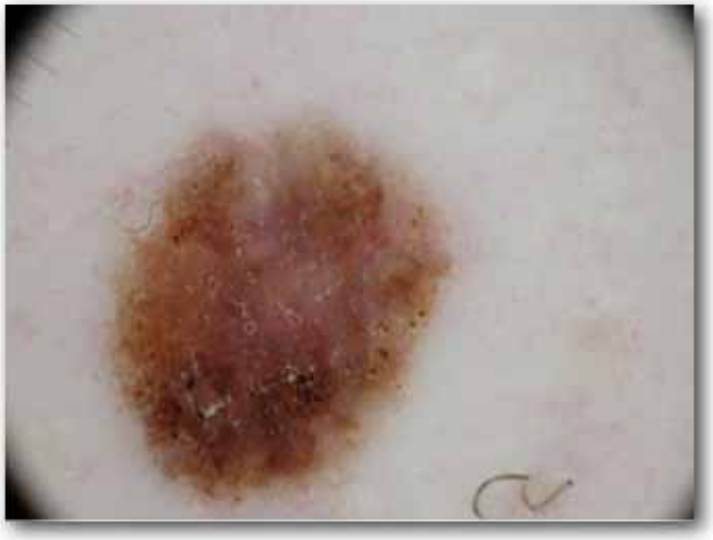
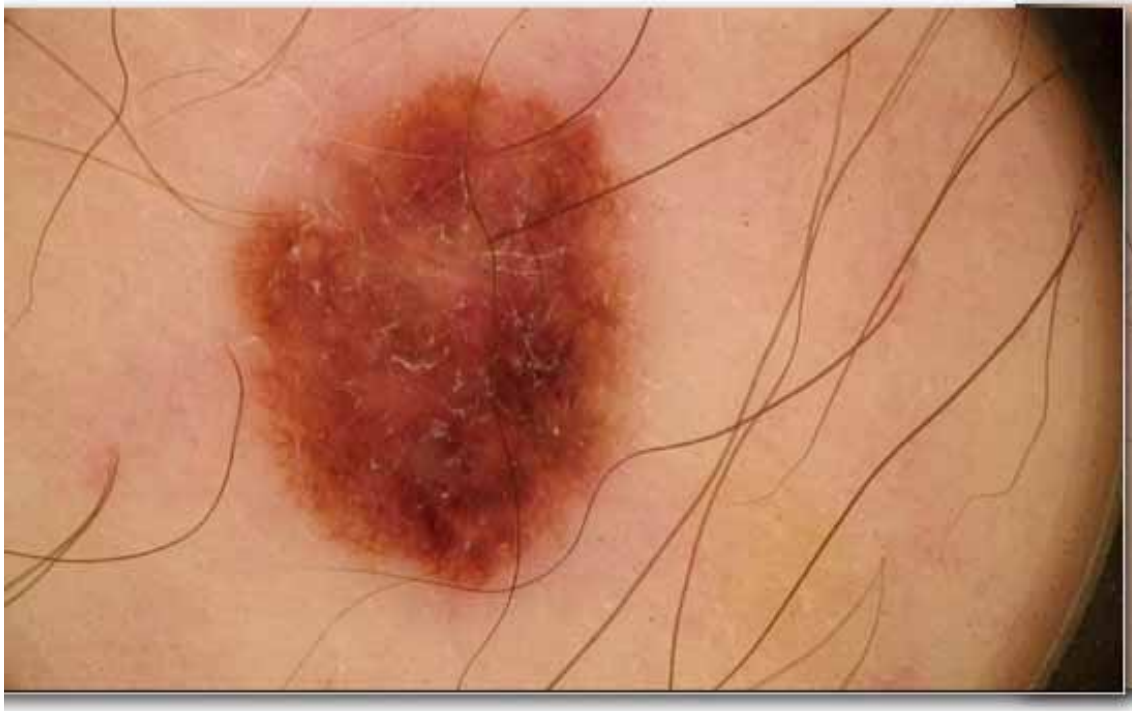
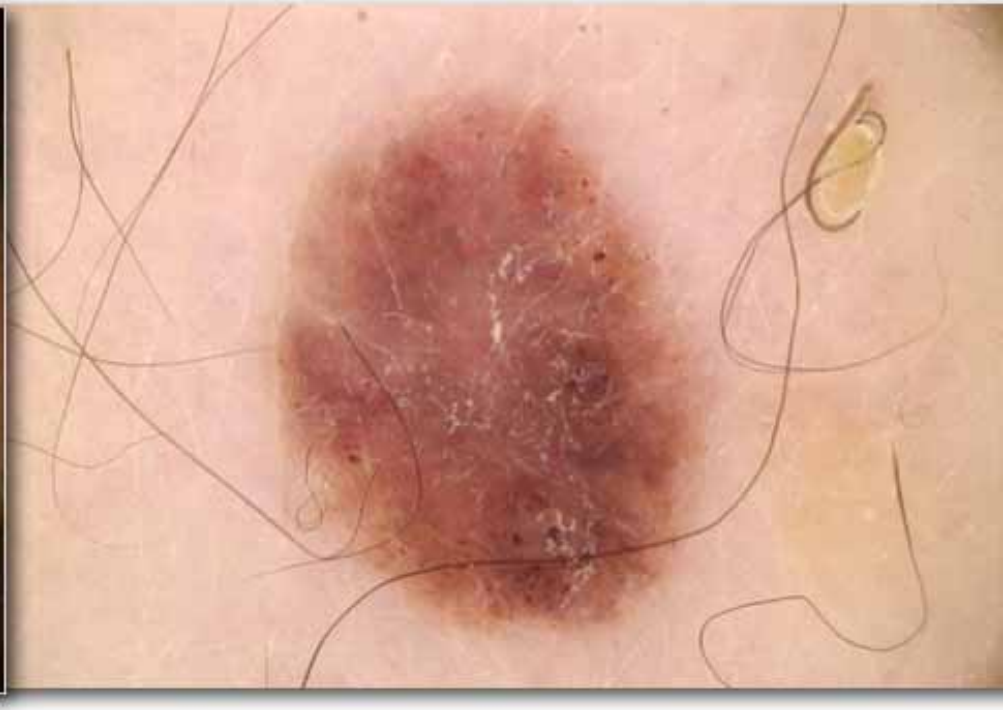




2011



2014



DOI: 10.1111/jdv.12032

REVIEW ARTICLE

Meta-analysis of digital dermoscopy follow-up of melanocytic skin lesions: a study on behalf of the International Dermoscopy Society

G. Salerni,[1,*] T. Terán,[2] S. Puig,[3,4] J. Malvehy,[3,4] I. Zalaudek,[5,6] G. Argenziano,[6] H. Kittler[7]

	FU strategy	
	Short-term FU	Medium/long-term FU
No. of studies	2	14
Mean patients per study (range)	1052 (245, 1859)	334.8 (100–688)
Mean lesions per study (range)	1460 (318, 2602)	4529 (272–11 396)
Mean lesions per patient (range)	1	14 (2–35)
Mean No. of melanoma detected per study (range)	44 (7, 81)	27 (0–98)

DOI: 10.1111/jdv.12032

JEADV

2012

REVIEW ARTICLE

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G. Salerni,[1,*] T. Terán,[2] S. Puig,[3,4] J. Malvehy,[3,4] I. Zalaudek,[5,6] G. Argenziano,[6] H. Kittler[7]

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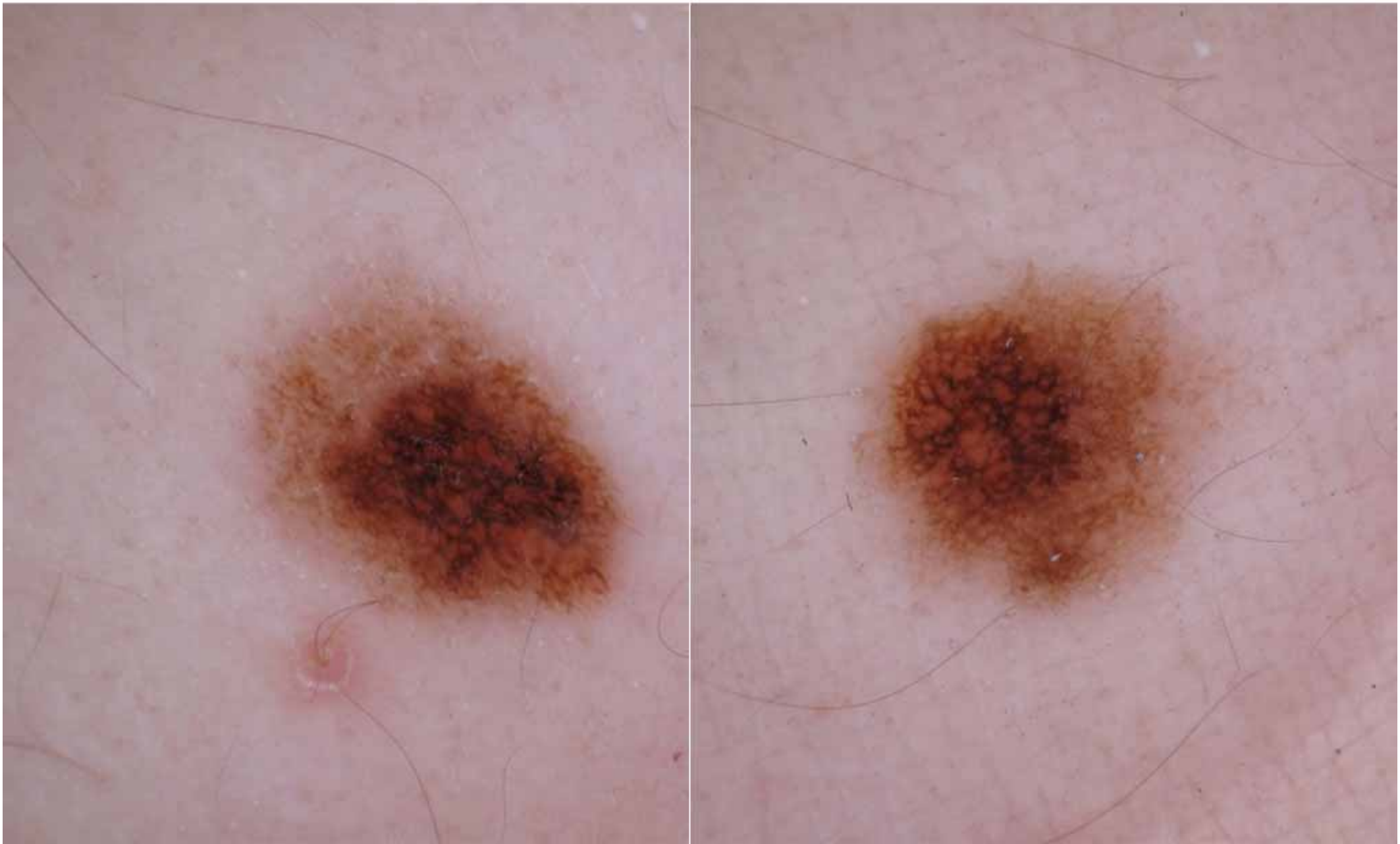
4.1% of patients (1.1% of lesions) will be diagnosed MELANOMA during the FOLLOW-UP

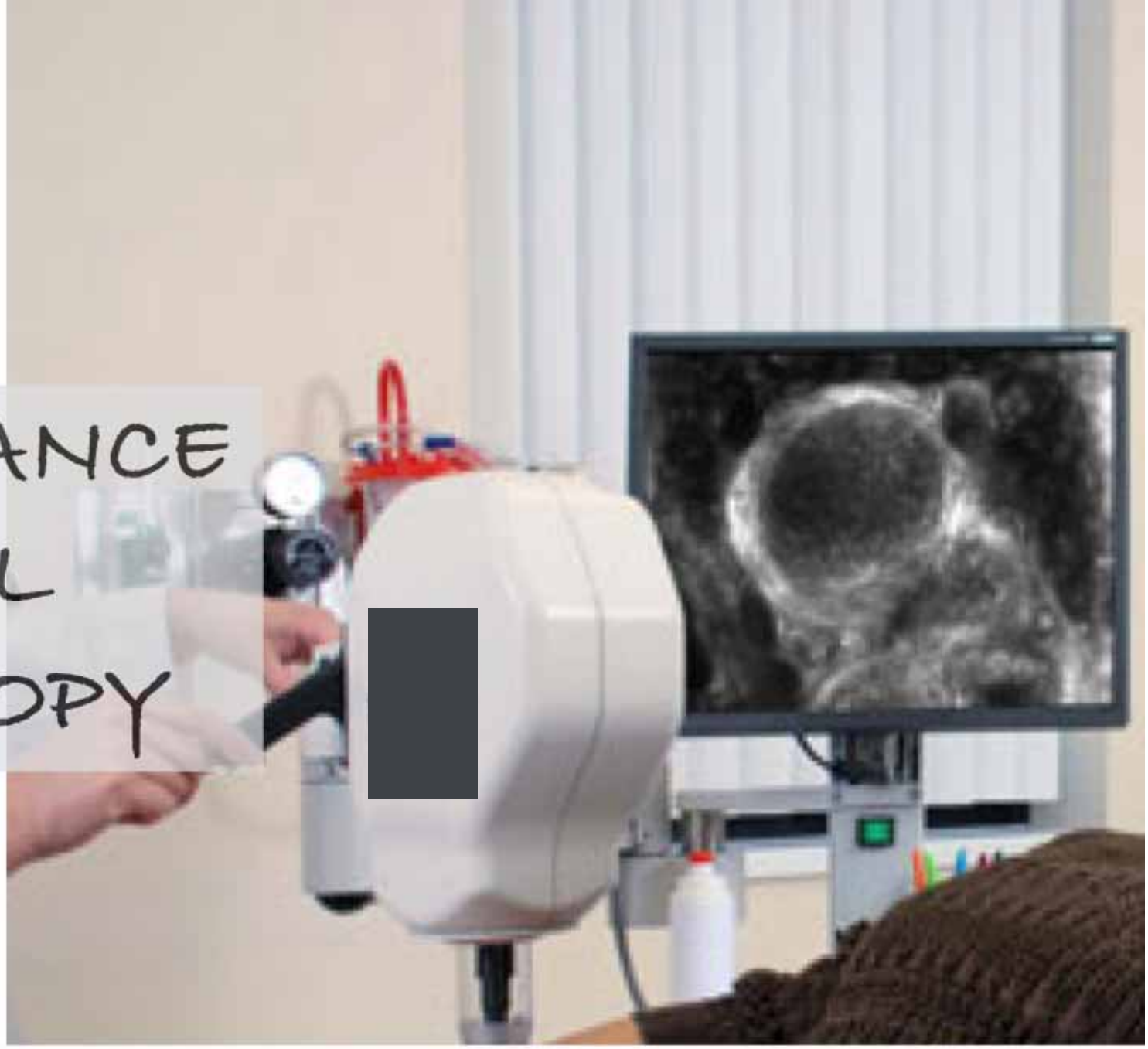
1992——————————————————2004

"FALSE TWINS"



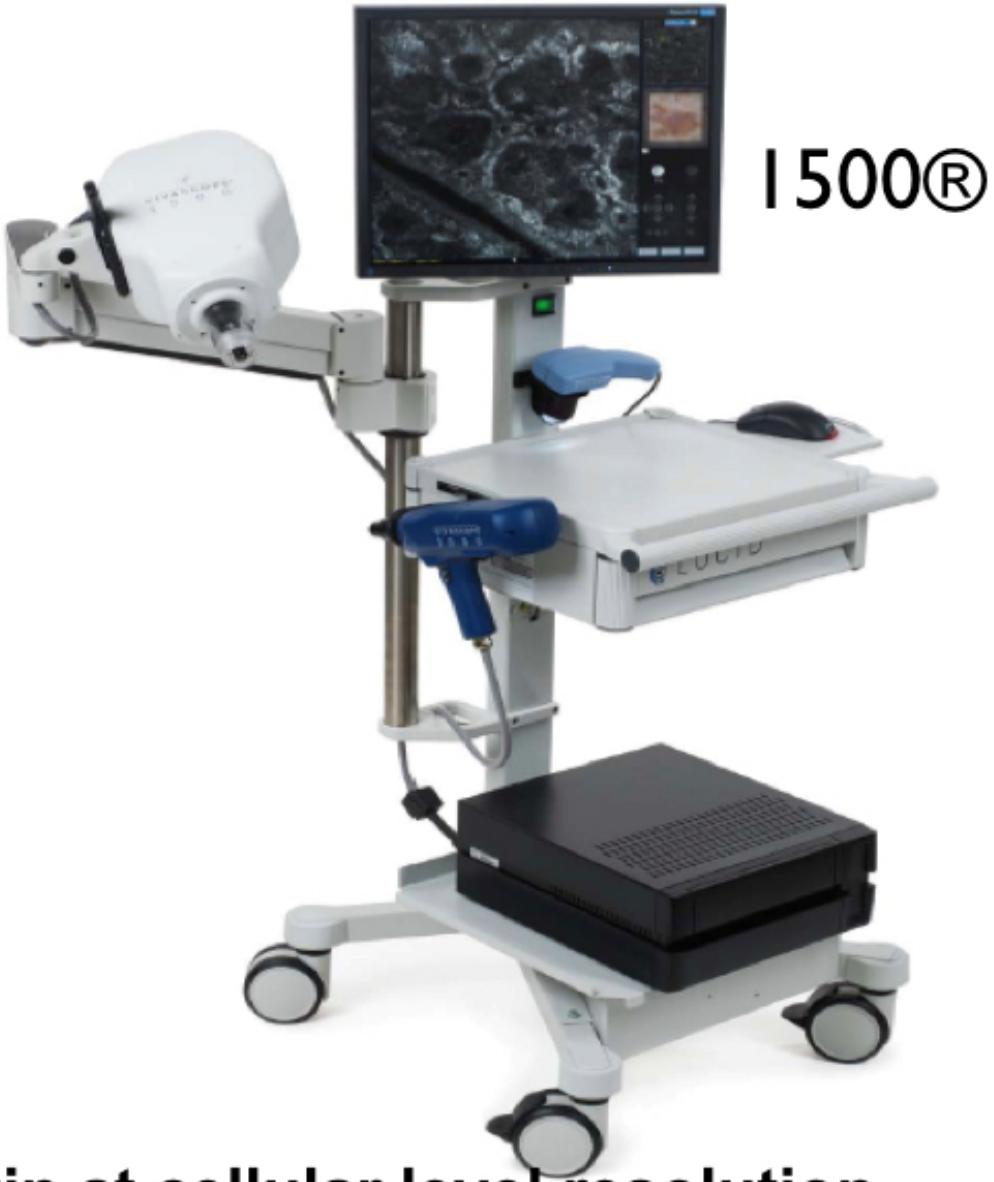
"FALSE TWINS"

REFLECTANCE CONFOCAL MICROSCOPY



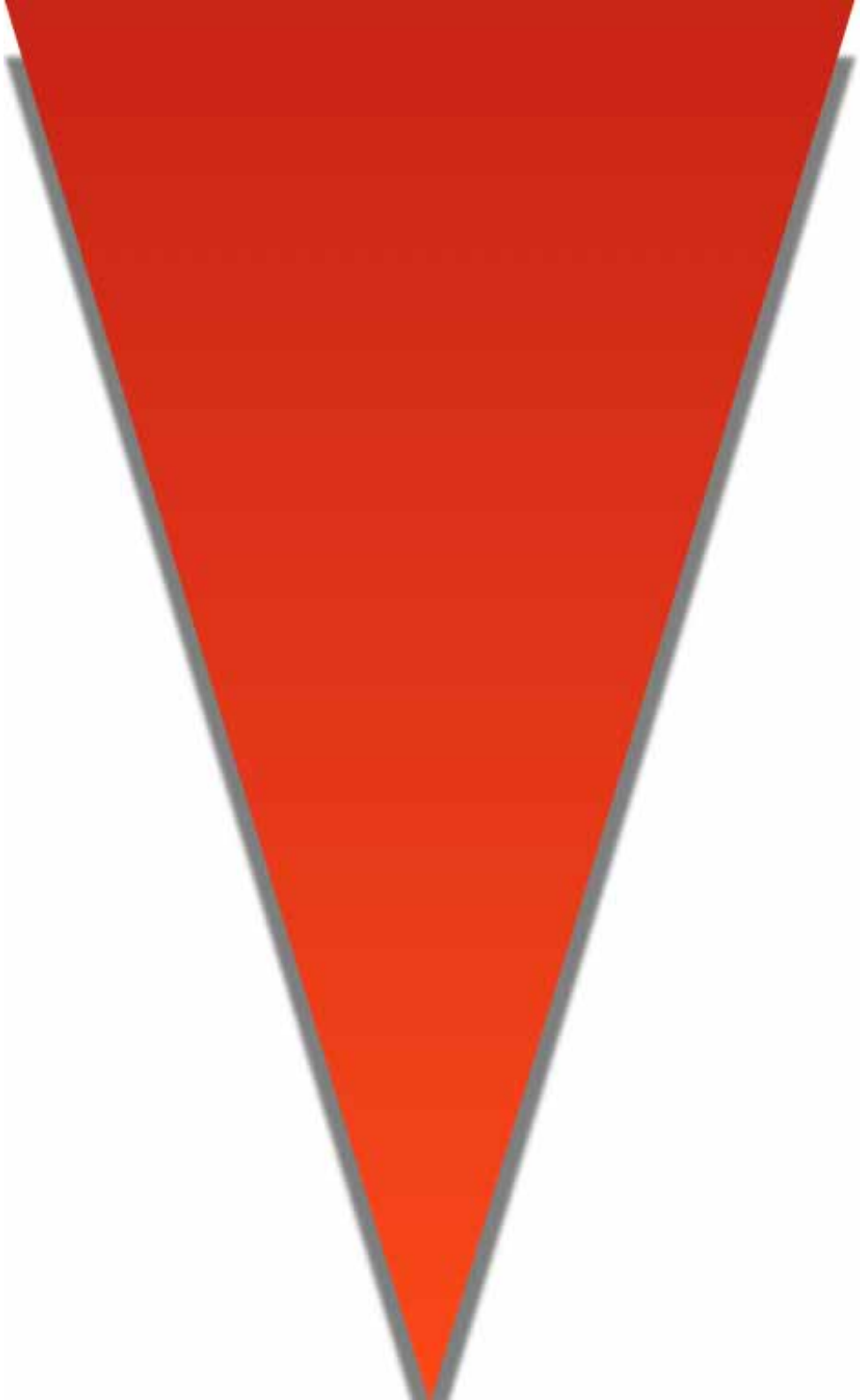
2004————————————————2016

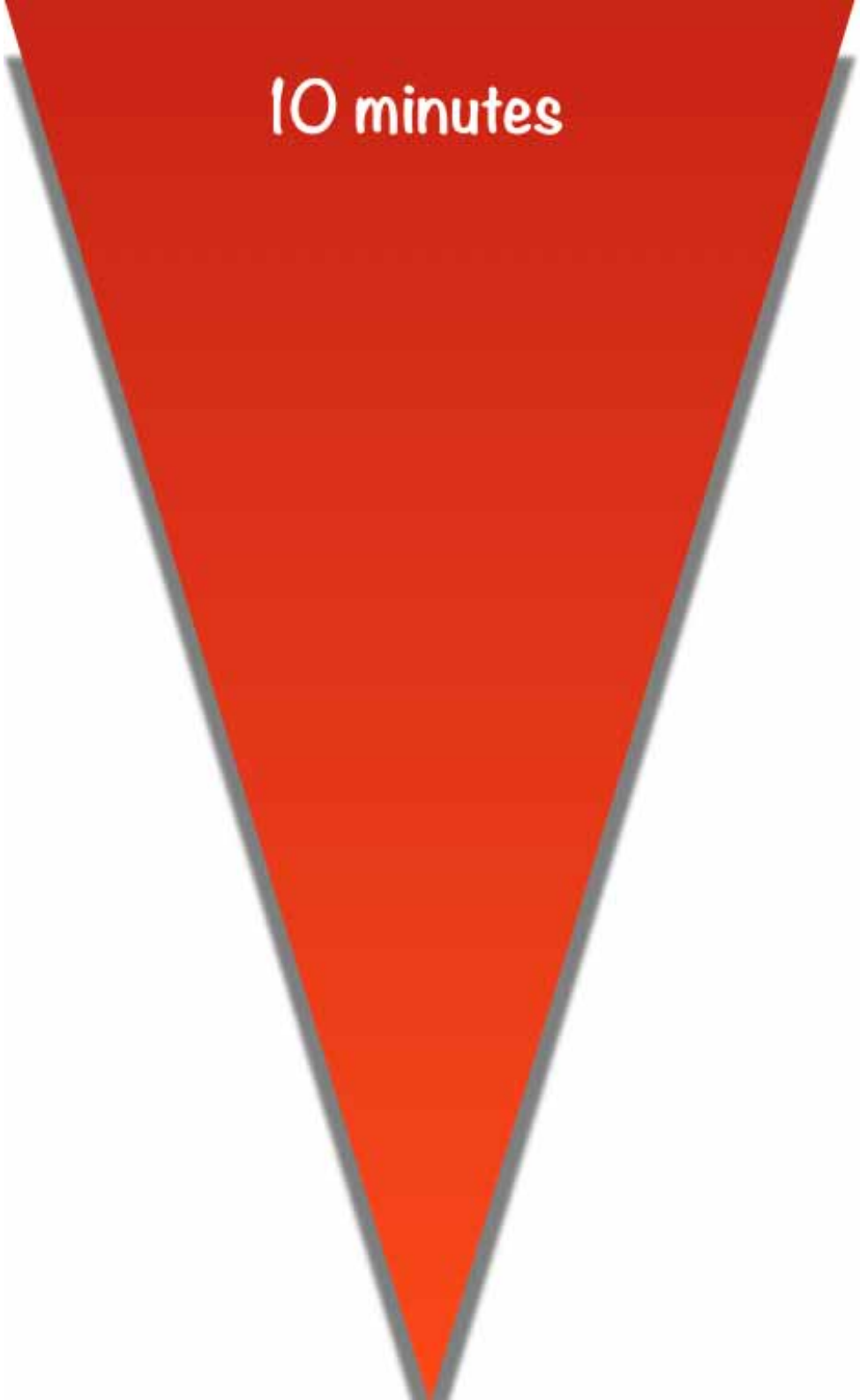
Reflectance Confocal Microscopy



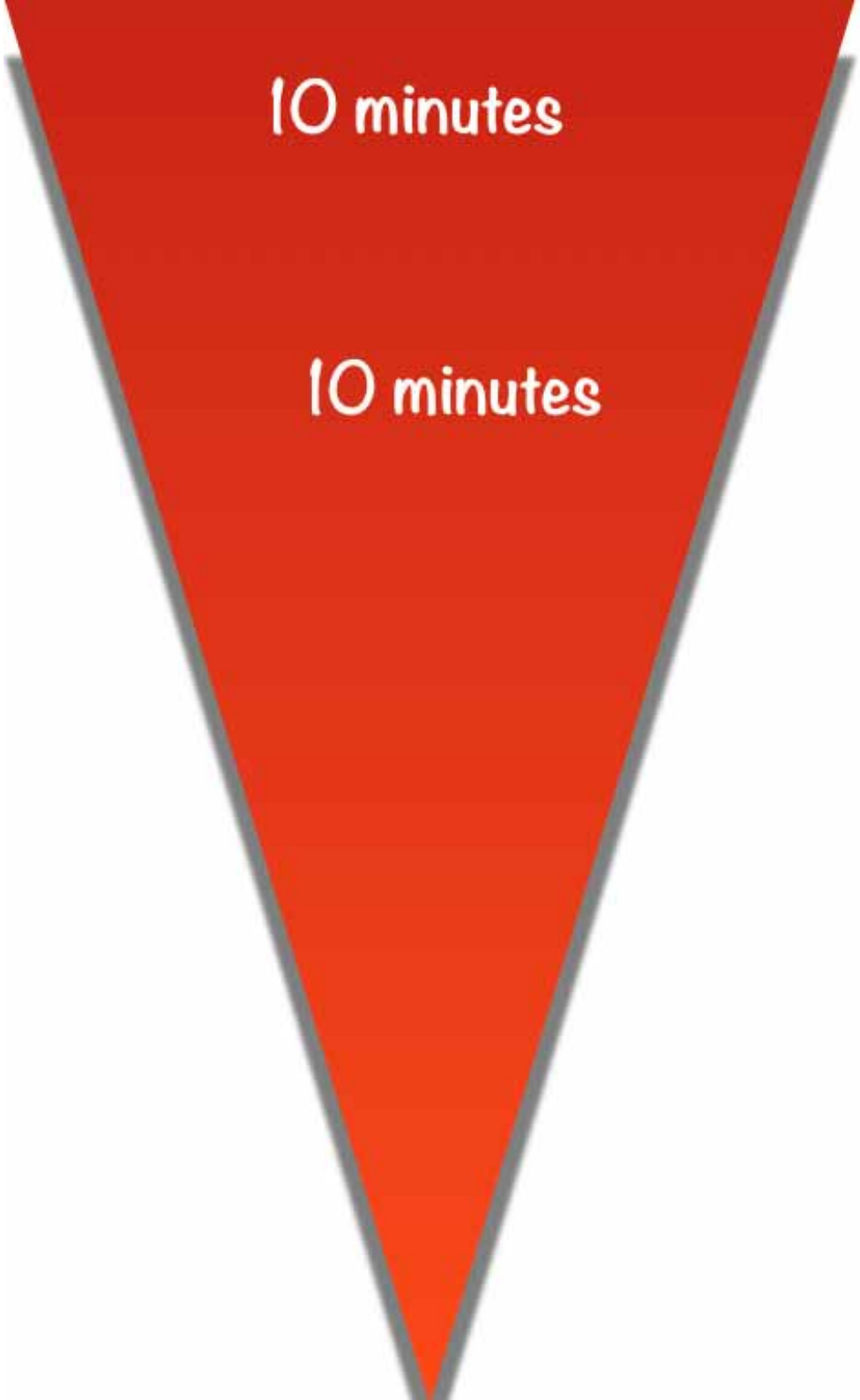
Light: Diode Laser 830 nm
max power 35 mW
Resolution: Lateral (X-Y) 0.5-1 μm
Axial (Z) 3-4 μm
Max depth: 300 μm

***in vivo* imaging of the skin at cellular level resolution**
horizontal sections of the skin



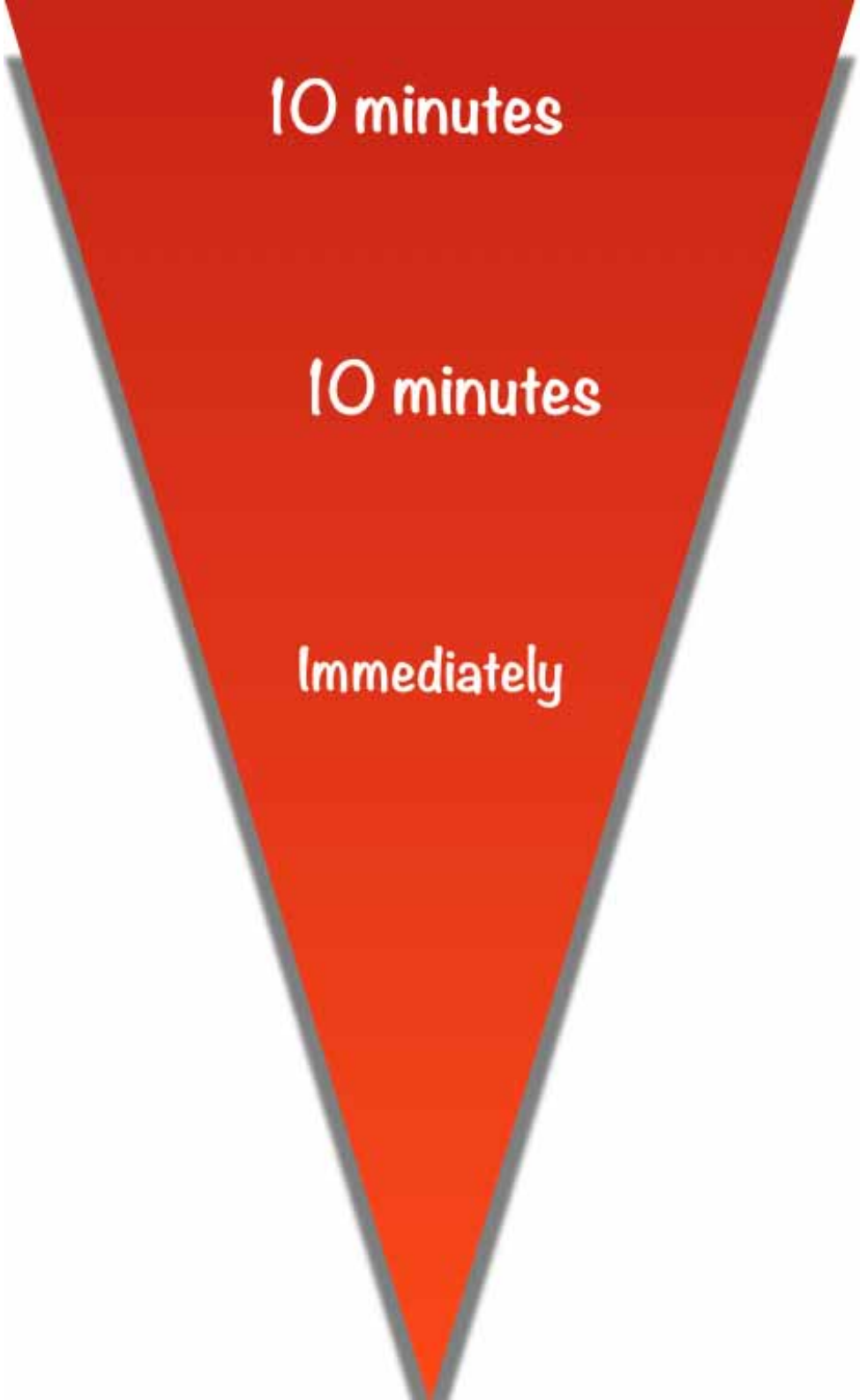


"virtual" biopsy



"virtual" biopsy

Diagnosis



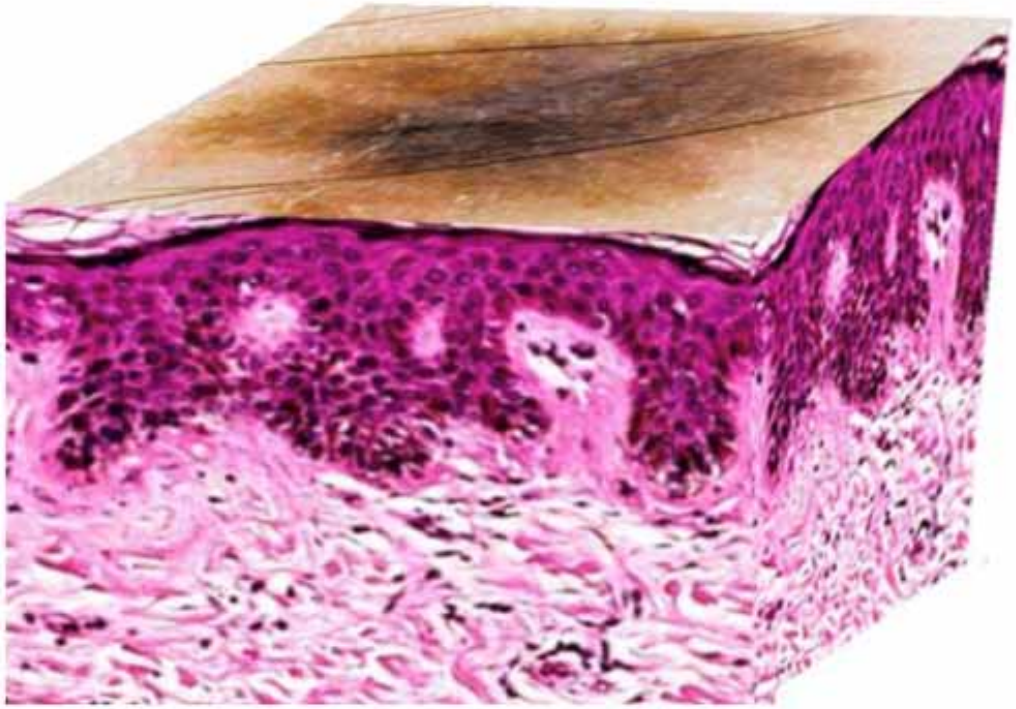
"virtual" biopsy

Diagnosis

Patient's treatment

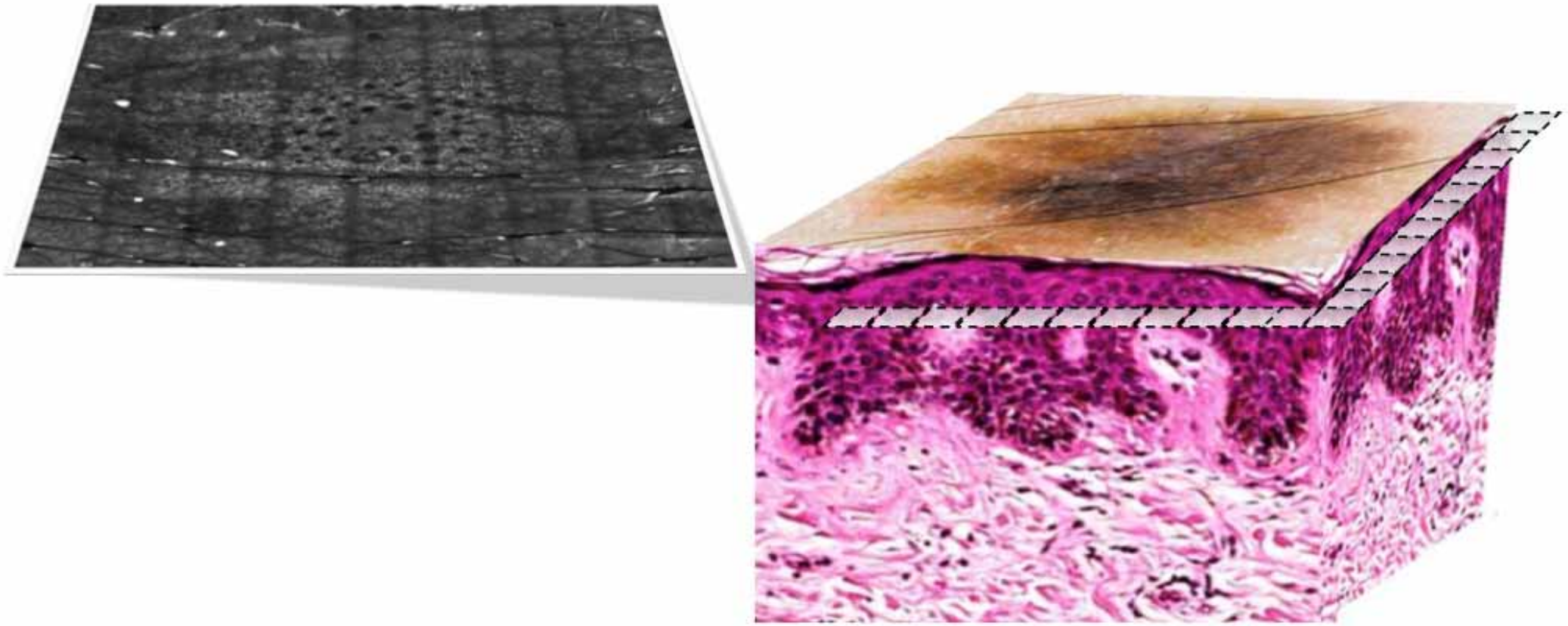
Confocal Technology

MOSAIC: composite image formed by consecutive confocal frames and mounted together in order to form a horizontal section of an area up to 8 by 8 mm



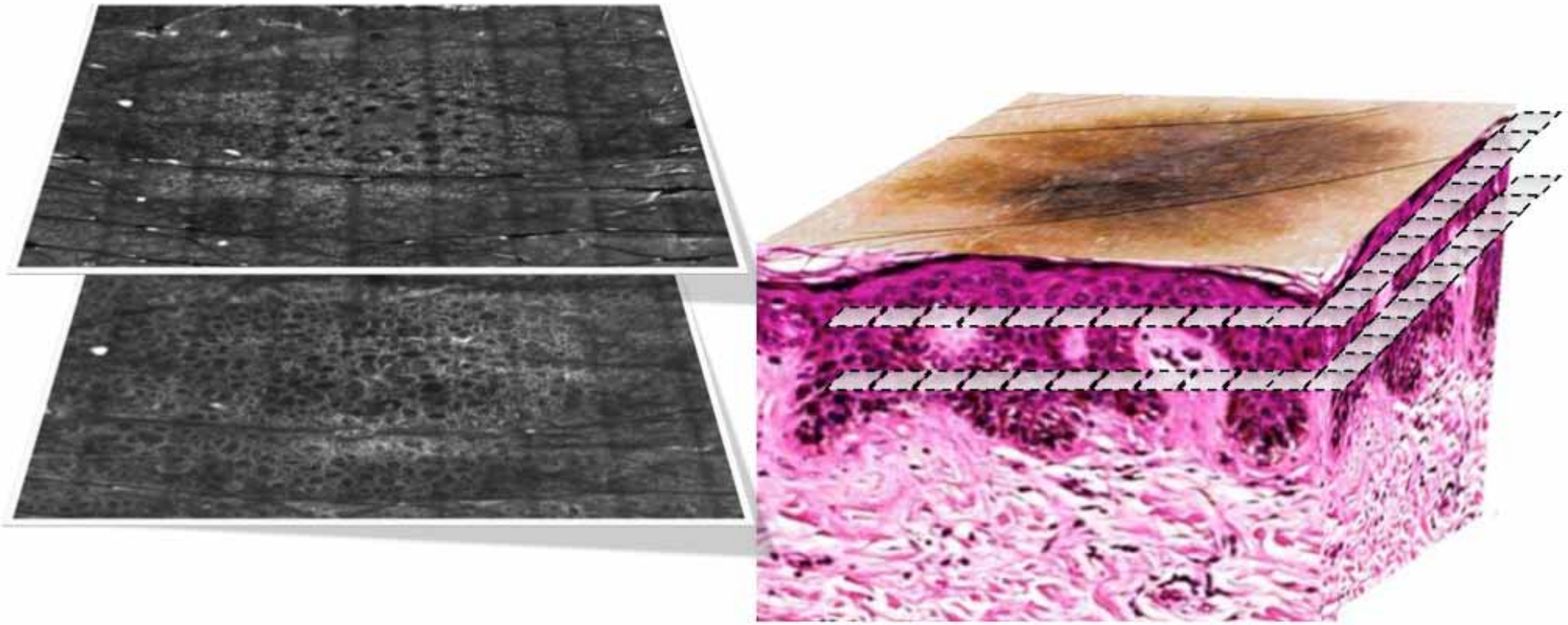
Confocal Technology

MOSAIC: composite image formed by consecutive confocal frames and mounted together in order to form a horizontal section of an area up to 8 by 8 mm



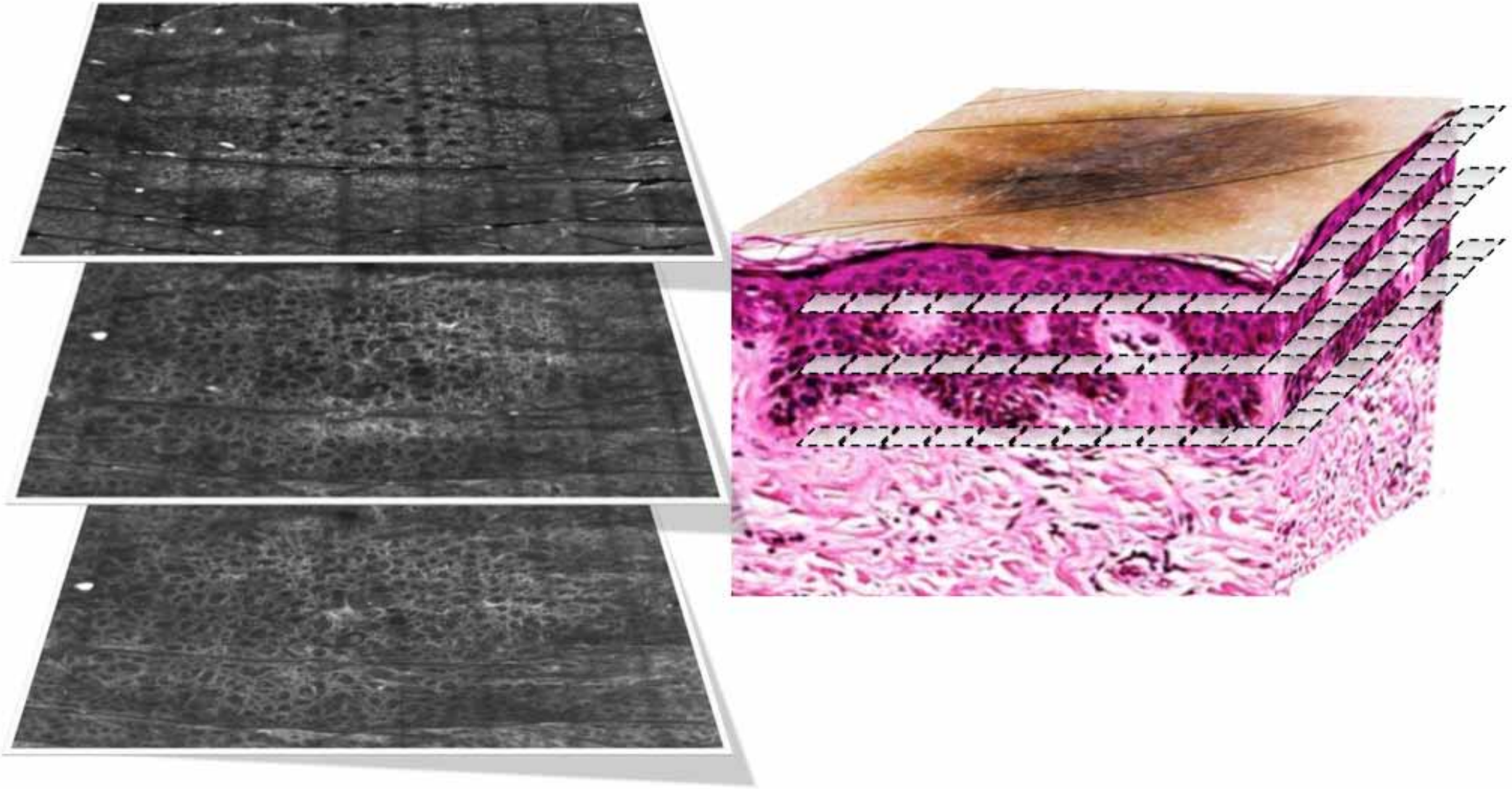
Confocal Technology

MOSAIC: composite image formed by consecutive confocal frames and mounted together in order to form a horizontal section of an area up to 8 by 8 mm

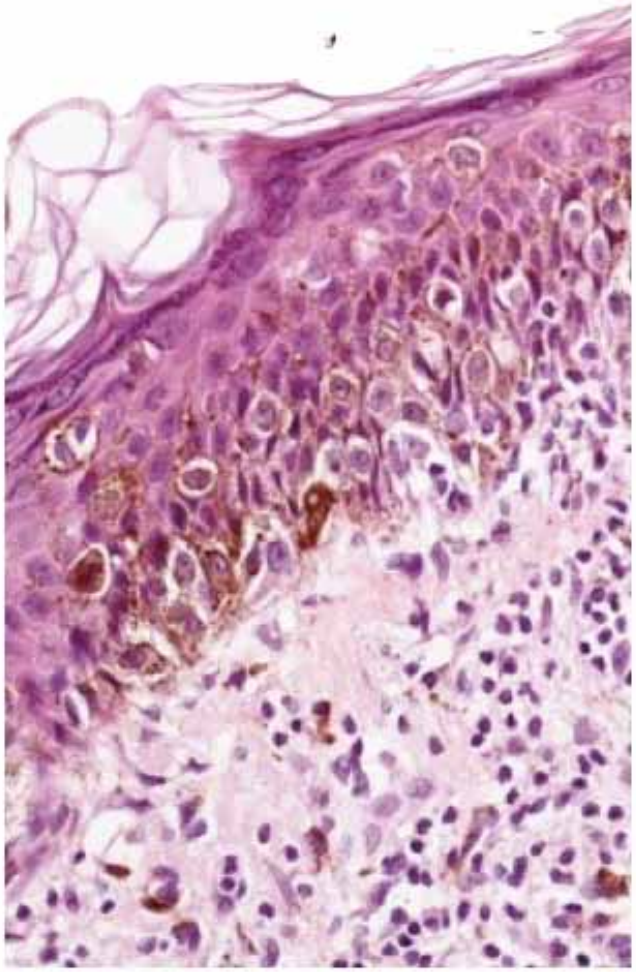


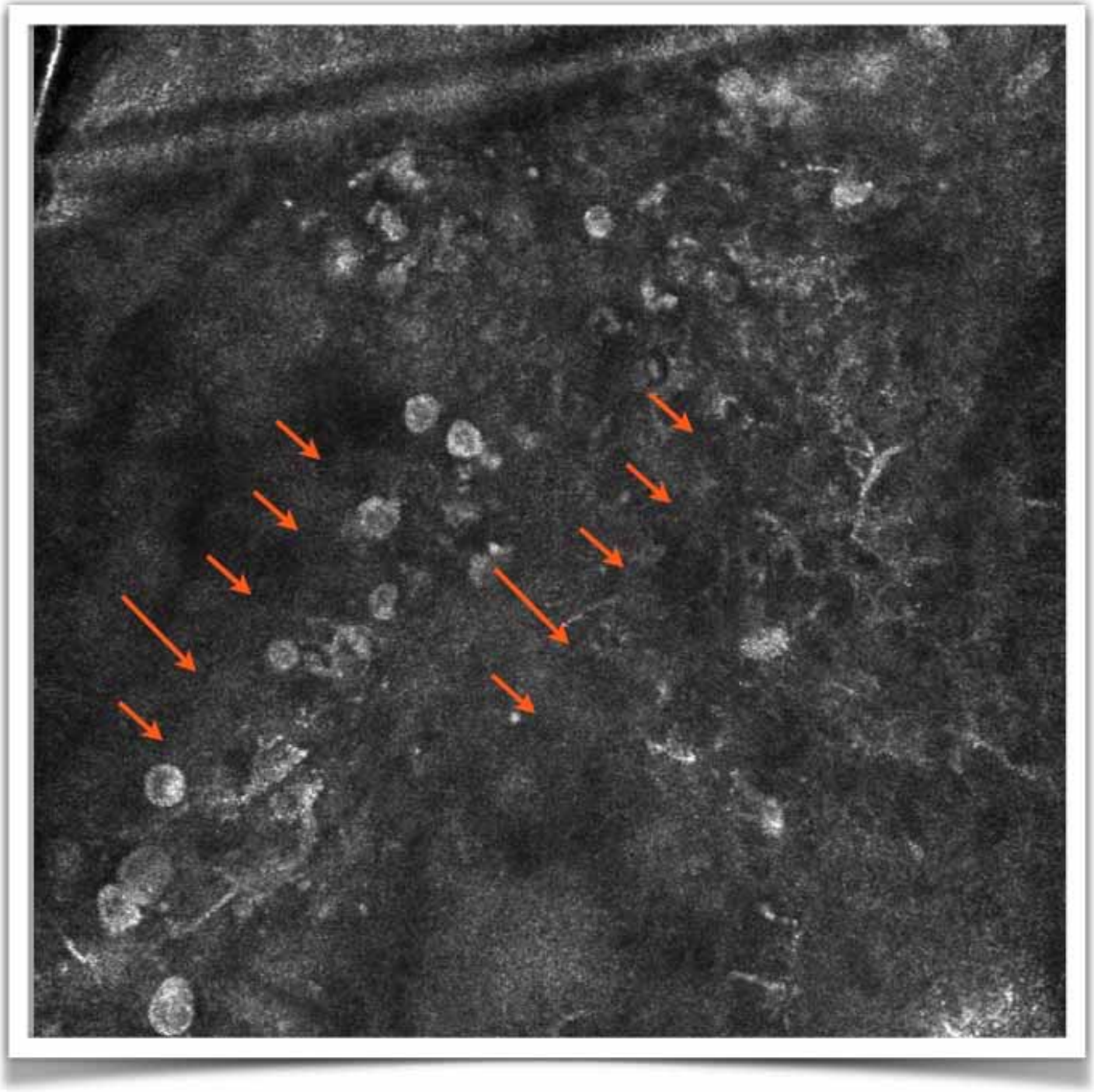
Confocal Technology

MOSAIC: composite image formed by consecutive confocal frames and mounted together in order to form a horizontal section of an area up to 8 by 8 mm



MELANOMA





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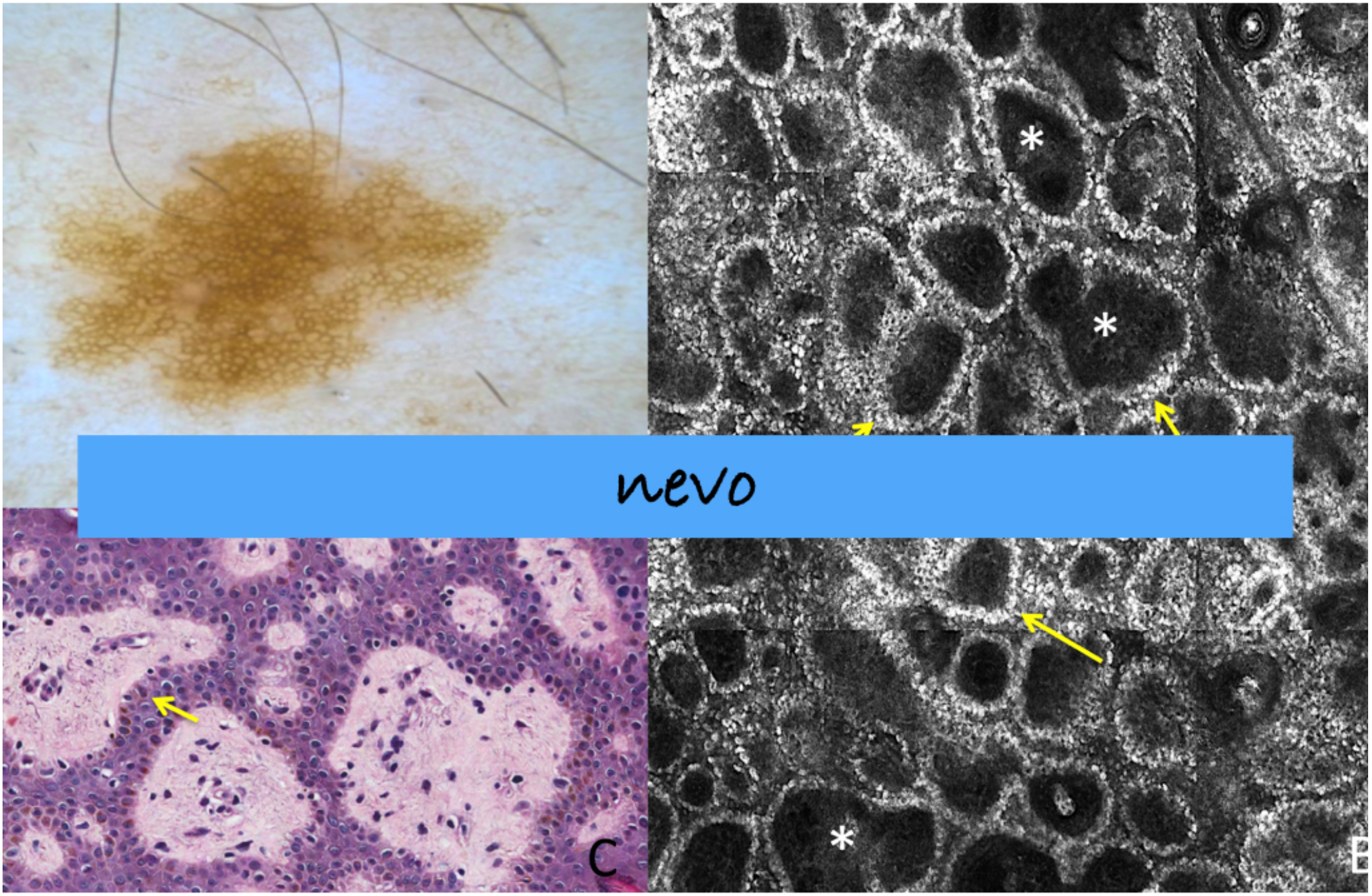

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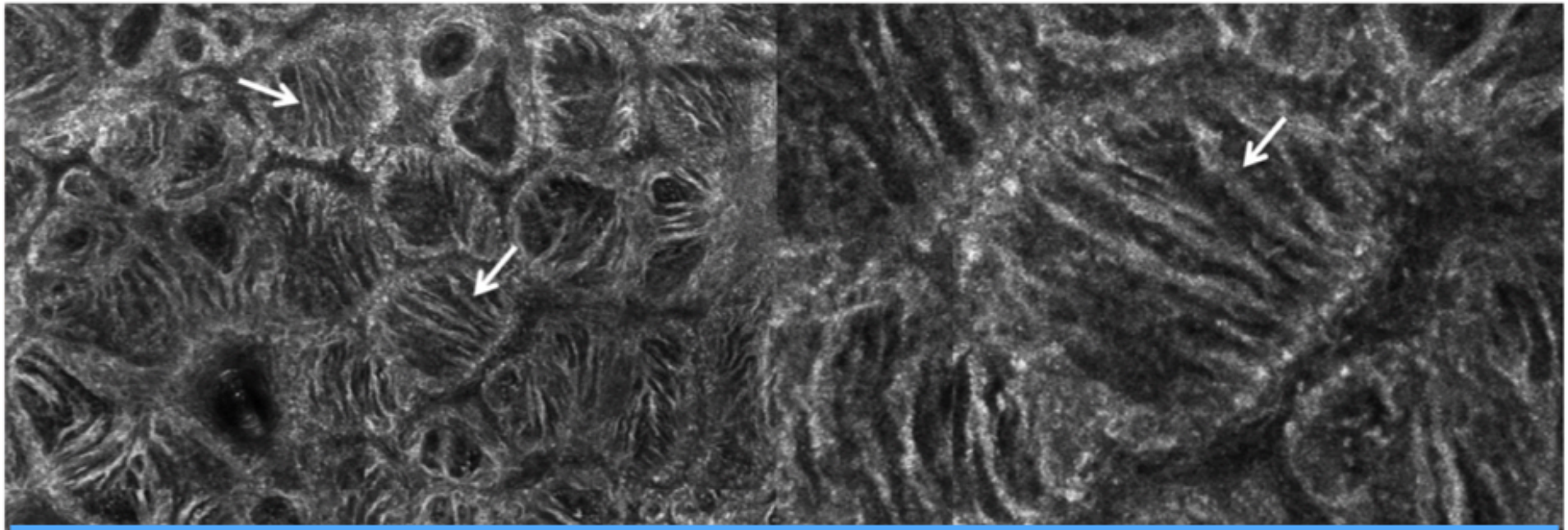
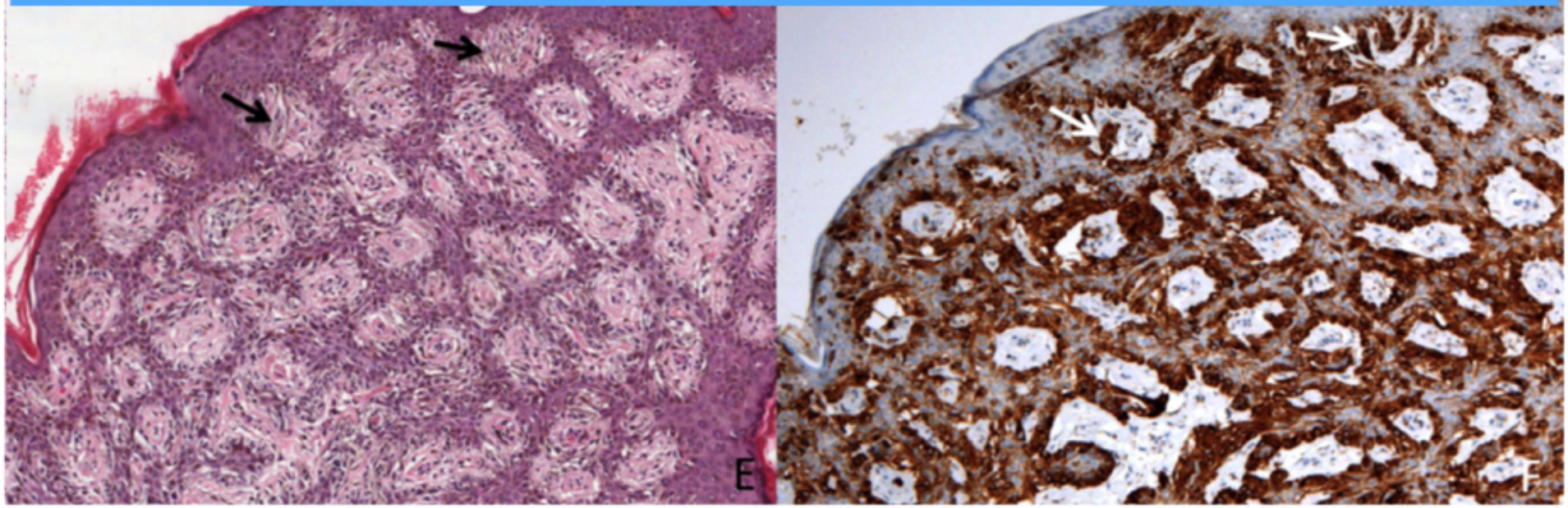
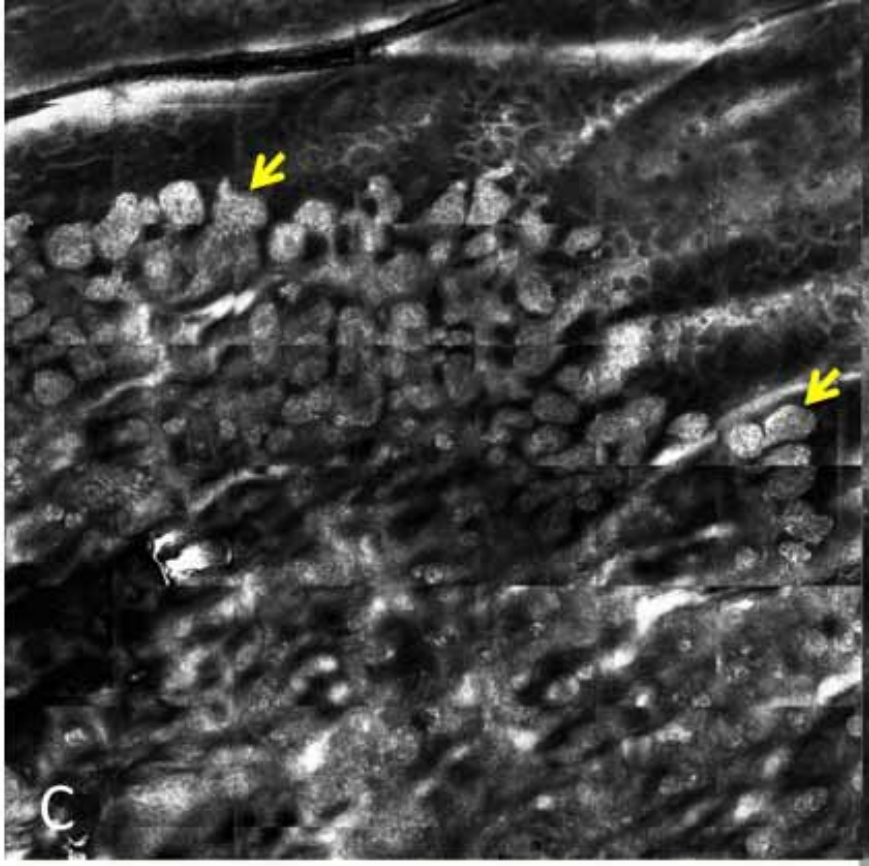


melanoma

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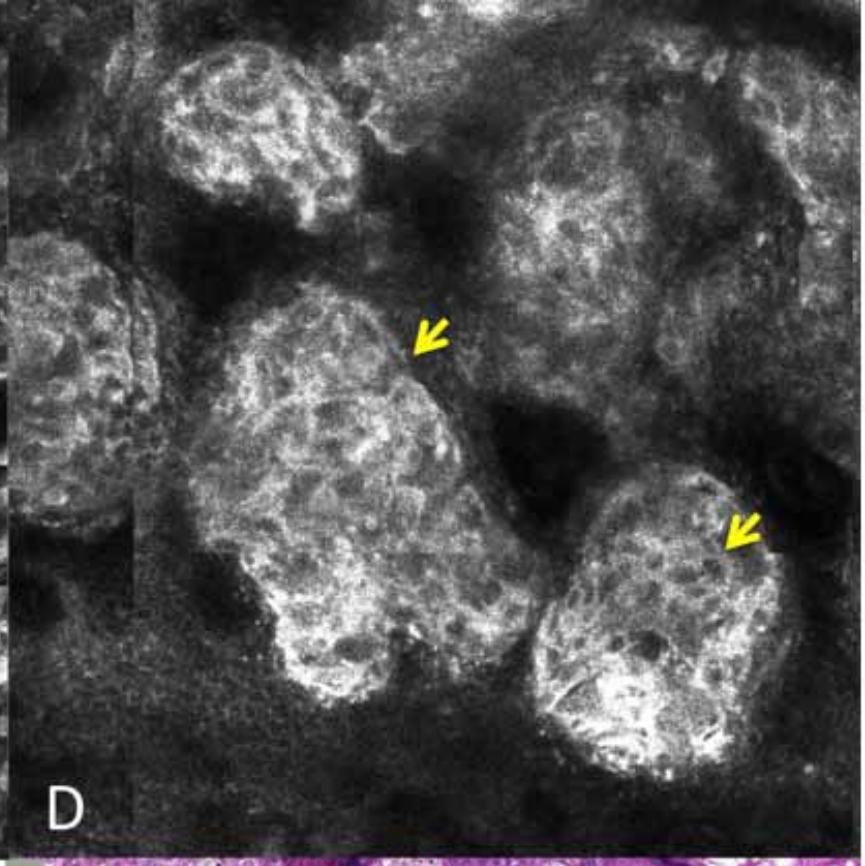
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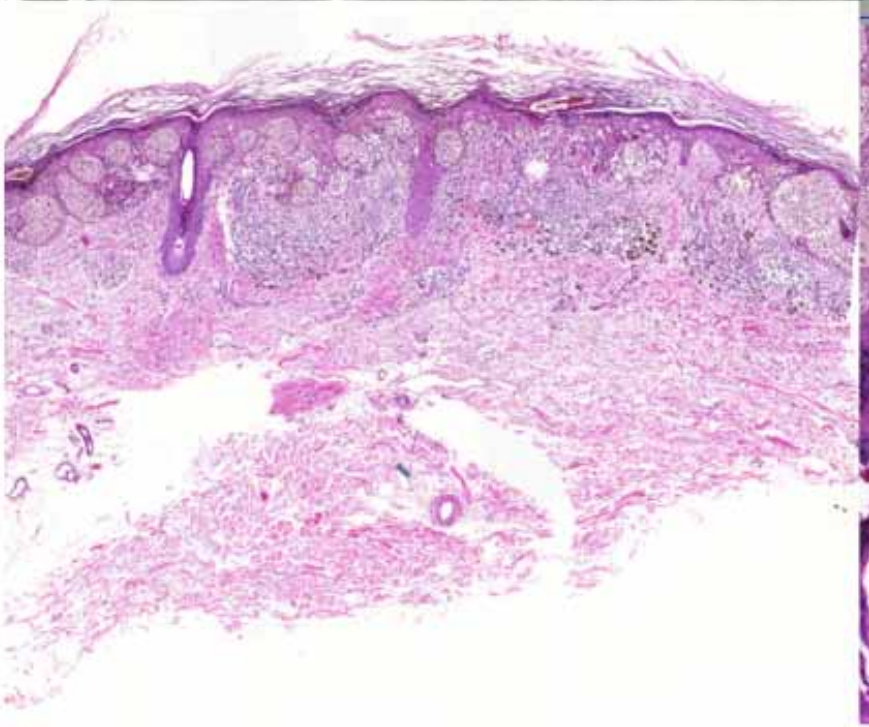

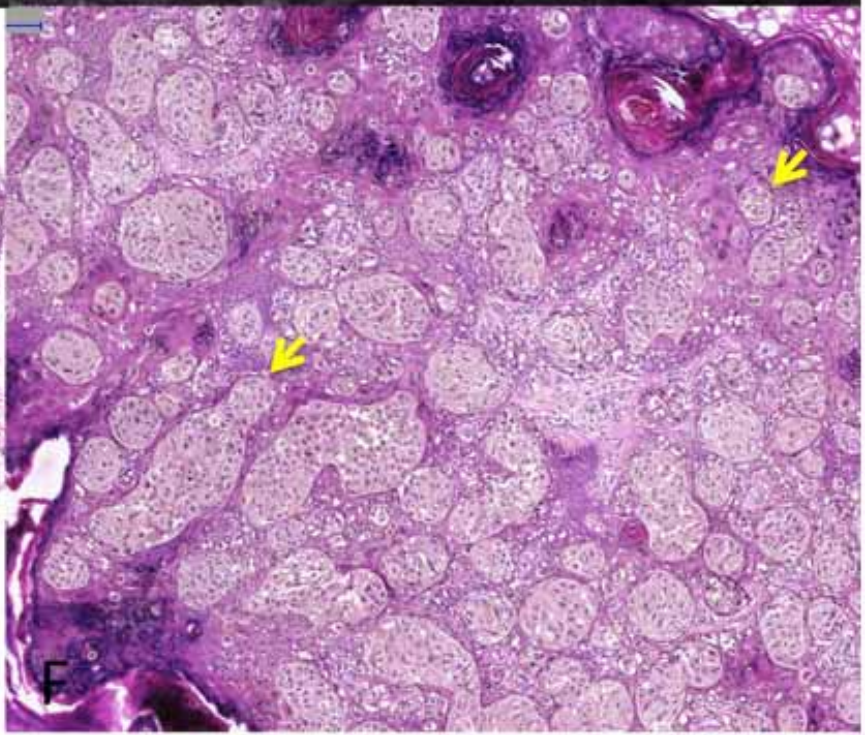
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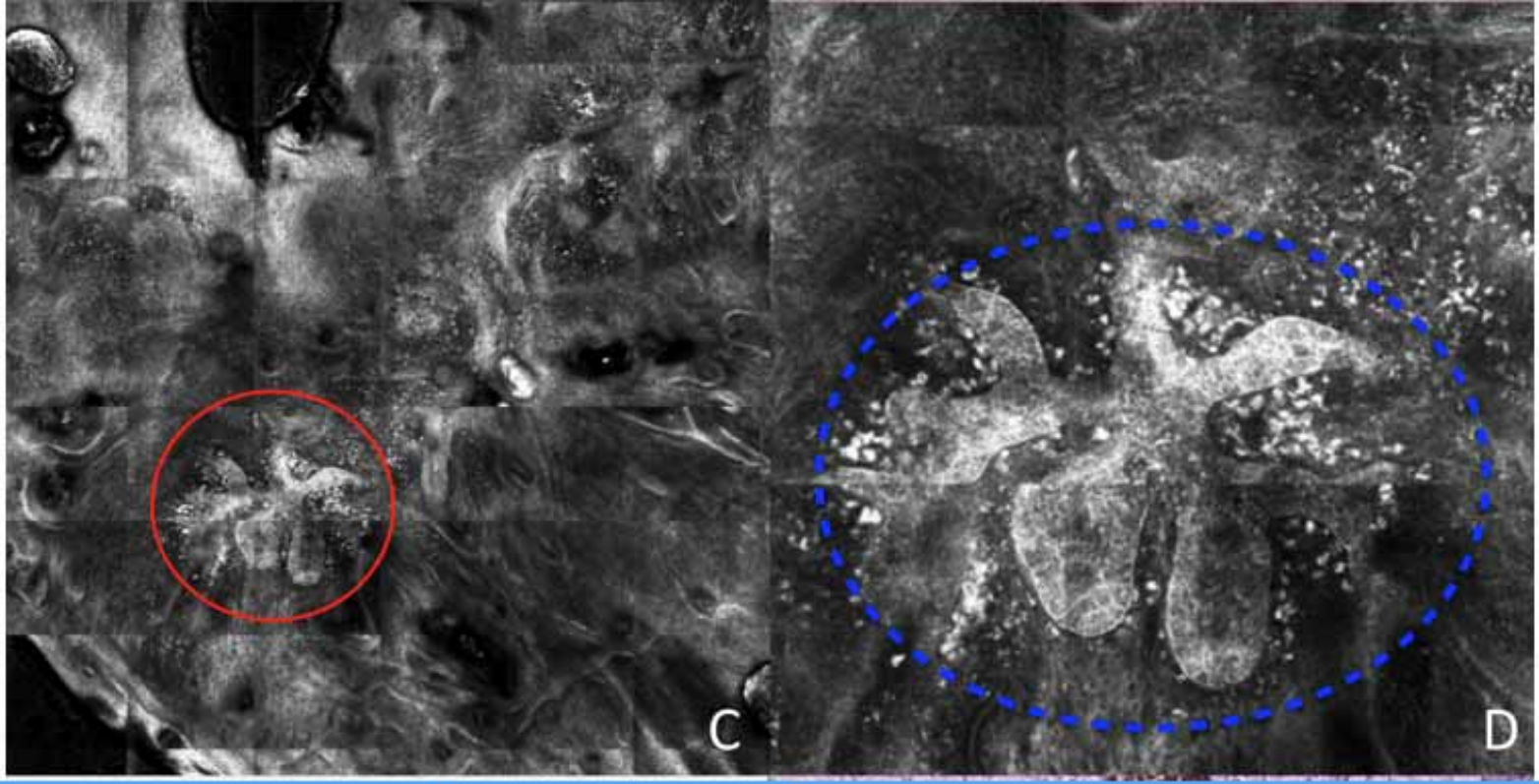
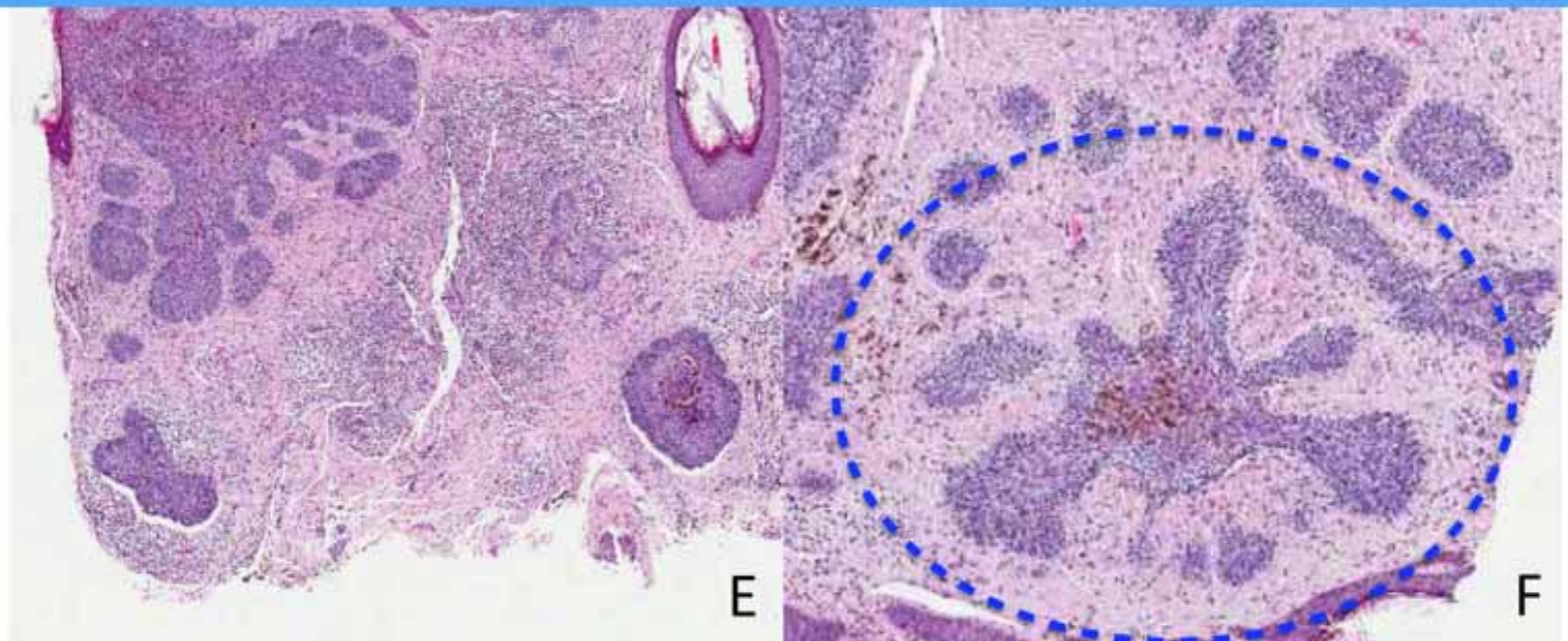


carcinoma basocellulare



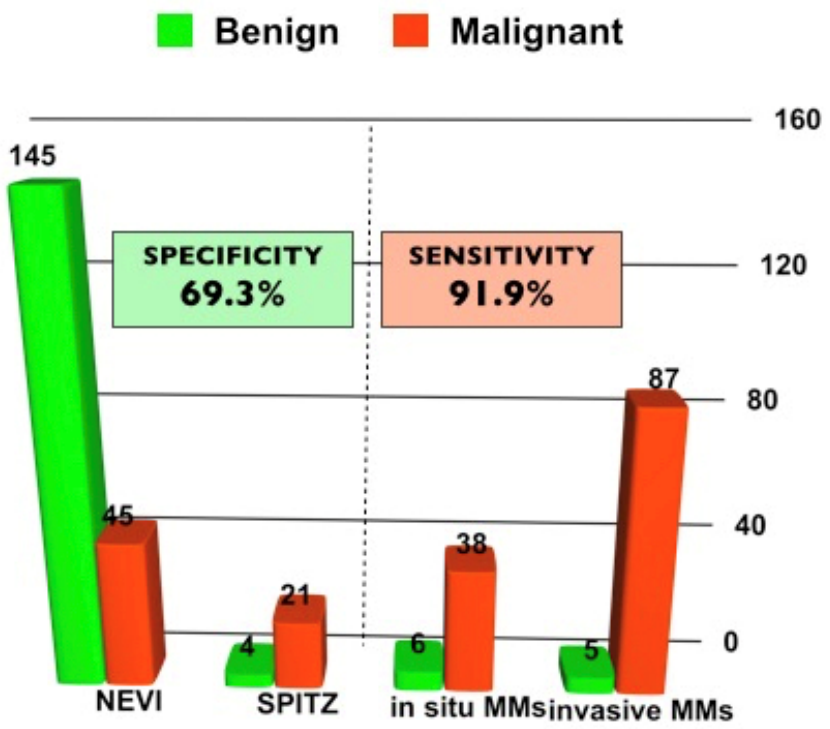
The Impact of *In Vivo* Reflectance Confocal Microscopy for the Diagnostic Accuracy of Melanoma and Equivocal Melanocytic Lesions

Giovanni Pellacani[1], Pascale Guitera[2], Caterina Longo[1], Michelle Avramidis[2], Stefania Seidenari[1] and Scott Menzies[2]

In vivo confocal reflectance microscopy recently showed promising results for melanoma (MM) diagnosis on a limited series. The aim of the study was to evaluate the sensitivity and specificity of confocal features for the diagnosis of MM 351 equivocal melanocytic lesions (136 MMs and 215 nevi) were evaluated for 37 confocal features by two blinded expert observers. χ^2 test, multivariate discriminant analysis and binary logistic regression were performed for the identification of the significant features and for testing newly created diagnostic models. Melanomas were mostly characterized by epidermal disarray and pagetoid cells in the epidermis, non-edged papillae, and cellular atypia at the junction, and atypical nests and bright nucleated cells in the upper dermis. On the other hand, regular dermal-epidermal architecture, and absence of pagetoid infiltration and atypical cells were suggestive of benign lesions. Five out of 136 melanomas, with mildly atypical melanocytes and occasional pagetoid cells at histopathology, were not diagnosed by confocal microscopy. Nevertheless, new diagnostic models showed no significant improvement compared with the previously proposed confocal microscopy algorithm. Owing to the visualization of cellular aspects, confocal microscopy seems useful for second level examination of clinically and dermoscopically equivocal lesions.

Journal of Investigative Dermatology (2007) 127, 2759–2765; doi:10.1038/sj.jid.5700993; published online 26 July 2007

J Invest Dermatol 2007

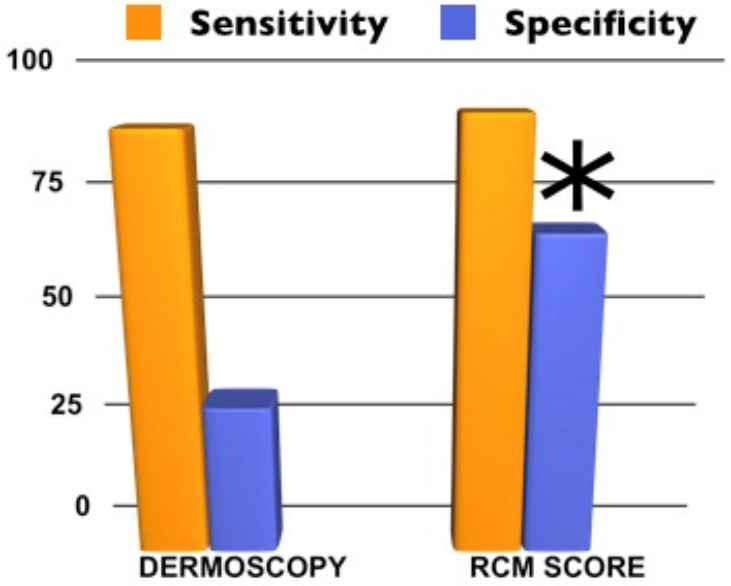


In Vivo Reflectance Confocal Microscopy Enhances Secondary Evaluation of Melanocytic Lesions

Pascale Guitera[1], Giovanni Pellacani[2], Caterina Longo[2], Stefania Seidenari[2], Michelle Avramidis[1] and Scott W. Menzies[1]

We recently described an *in vivo* reflectance confocal microscopy (RCM) method and our aim was to evaluate a possible additive value of this type of analysis in the management of melanocytic lesions. In two referral centers (Sydney and Modena), lesions (203 nevi and 123 melanomas (MMs) with a median Breslow thickness of 0.54 mm) were excised on the basis of clinical suspicion (history, dermoscopy examination, and/or digital monitoring). The RCM method was also trialed on a non-biopsied population of 100 lesions, which were clinically and dermoscopically diagnosed as benign nevi. All RCM and dermoscopy diagnoses were performed blinded to the histopathological diagnosis. Firstly, in the study population, a high interobserver agreement (on a subset of 90 lesions) was seen with the RCM method, which had superior specificity (68%, 95% confidence interval (95% CI): 61.1–74.3) for the diagnosis of MM compared with dermoscopy (32%, 95% CI: 25.9–38.7), while showing no difference in sensitivity (91%, 95% CI: 84.6–95.5, RCM; 88%, 95% CI: 80.7–92.6 dermoscopy). The two techniques had a weak correlation, resulting in only 2.4% of MMs being misclassified by both techniques. Diagnosis of light-colored lesions is improved by RCM (specificity 84%, 95% CI: 66.3–94.5) compared with dermoscopy (specificity 39%, 95% CI: 23.7–56.2). Secondly, the RCM method classified 100% of the non-biopsied control nevi population as benign.

J Invest Dermatol 2009

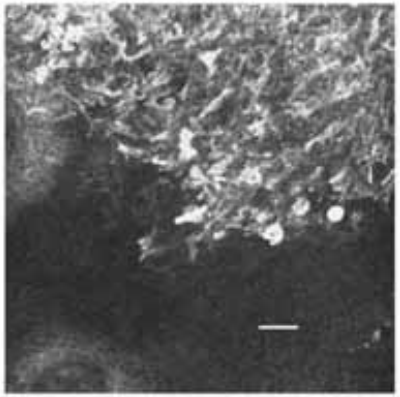


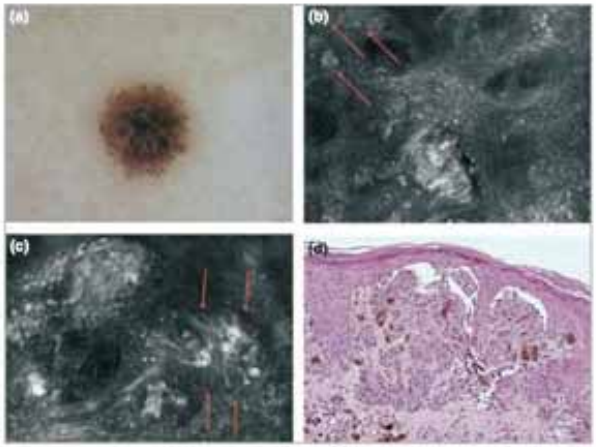
CONFOCAL HELPS IN CLINICAL AND DERMOSCOPIC DIFFICULT SITUATIONS

The Impact of *In Vivo* Reflectance Confocal Microscopy on the Diagnostic Accuracy of Lentigo Maligna and Equivocal Pigmented and Nonpigmented Macules of the Face

Pascale Guitera[1,7], Giovanni Pellacani[2], Kerry A. Crotty[1], Richard A. Scolyer[3,4], Ling-Xi L. Li[3], Sara Bassoli[2], Marco Vinceti[5], Harold Rabinovitz[6], Caterina Longo[2] and Scott W. Menzies[1,7]

JID 2011





CLINICAL AND LABORATORY INVESTIGATIONS

BJD
British Journal of Dermatology

Small-diameter melanocytic lesions: morphological analysis by means of *in vivo* confocal microscopy

G. Pupelli,[1] C. Longo,[2] L. Veneziano,[1] A.M. Cesinaro,[3] G. Ferrara,[4] S. Piana,[5] E. Moscarella,[2] C. Ricci,[2] I. Zalaudek,[2] S. Seidenari,[1] G. Argenziano[2] and G. Pellacani[1]

[1]Department of Dermatology and [3]Department of Pathology, University of Modena and Reggio Emilia, Italy

[2]Dermatology and Skin Cancer Unit and [5]Department of Pathology, Arcispedale Santa Maria Nuova, (Istituto di Ricovero e Cura a Carattere Scientifico-IRCCS), Reggio Emilia, Italy

[4]Department of Oncology, Anatomic Pathology Unit, Gaetano Rummo General Hospital, Benevento, Italy

BJD 2013

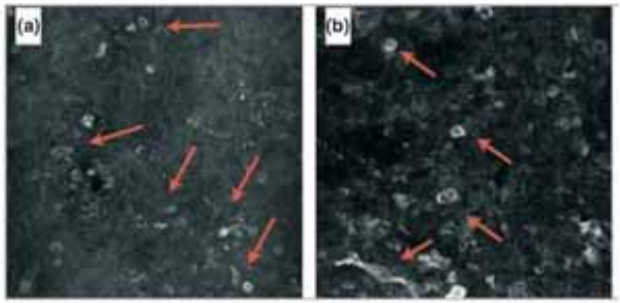
CLINICAL AND LABORATORY INVESTIGATIONS

BJD
British Journal of Dermatology

Is confocal microscopy a valuable tool in diagnosing nodular lesions? A study of 140 cases

C. Longo,[1] F. Farnetani,[2] S. Ciardo,[2] A.M. Cesinaro,[3] E. Moscarella,[1,2] G. Ponti,[4] I. Zalaudek,[1,5] G. Argenziano[1] and G. Pellacani[2]

BJD 2013



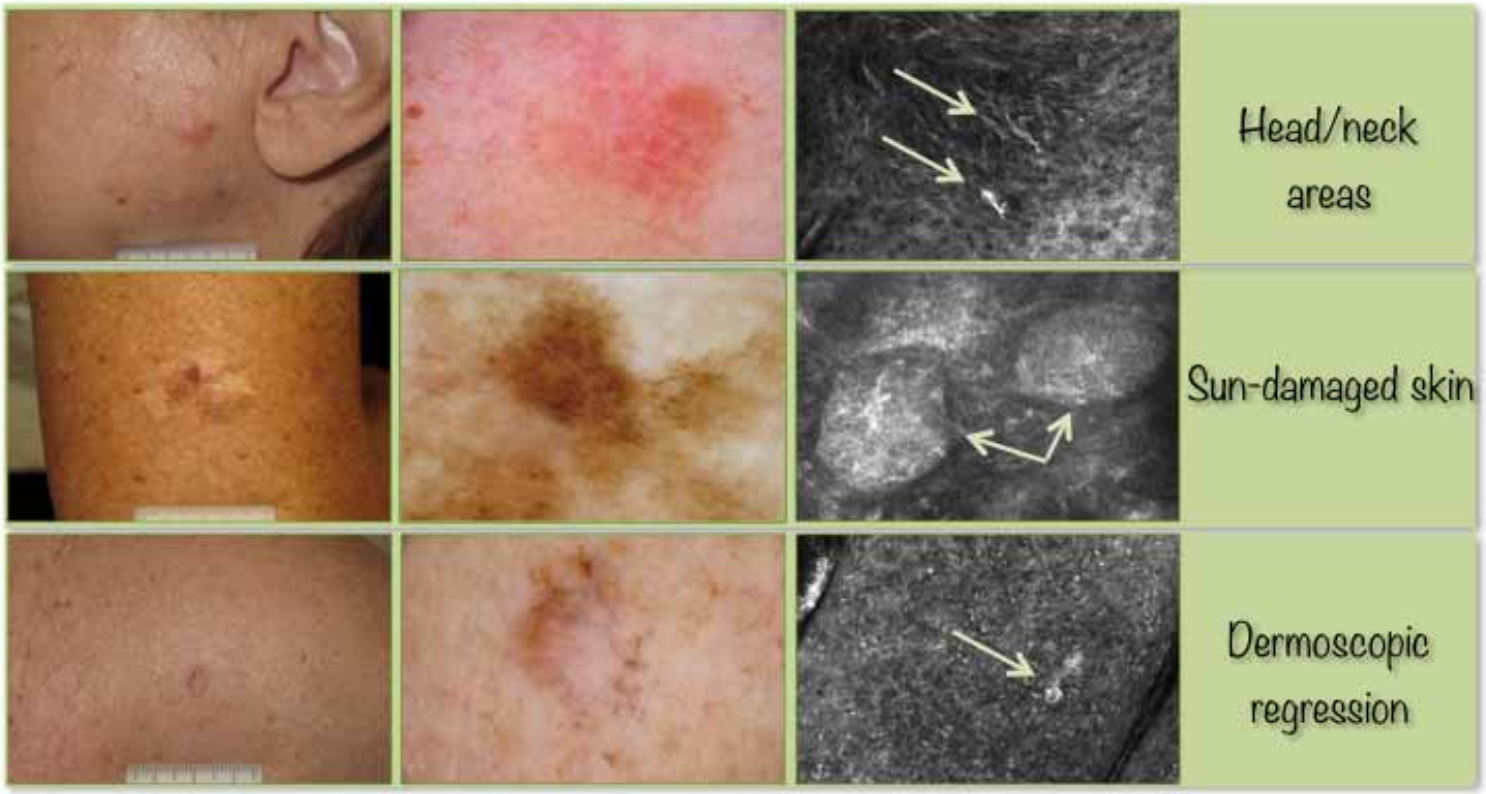
Which are clinical/dermoscopic criteria that predict a good RCM performance?

Which are RCM best indications?

1256 clinically and dermoscopically equivocal lesions

Sensitivity: 95.3% Specificity: 83.9%

Number needed to excise to detect a melanoma (NNE): 2.4



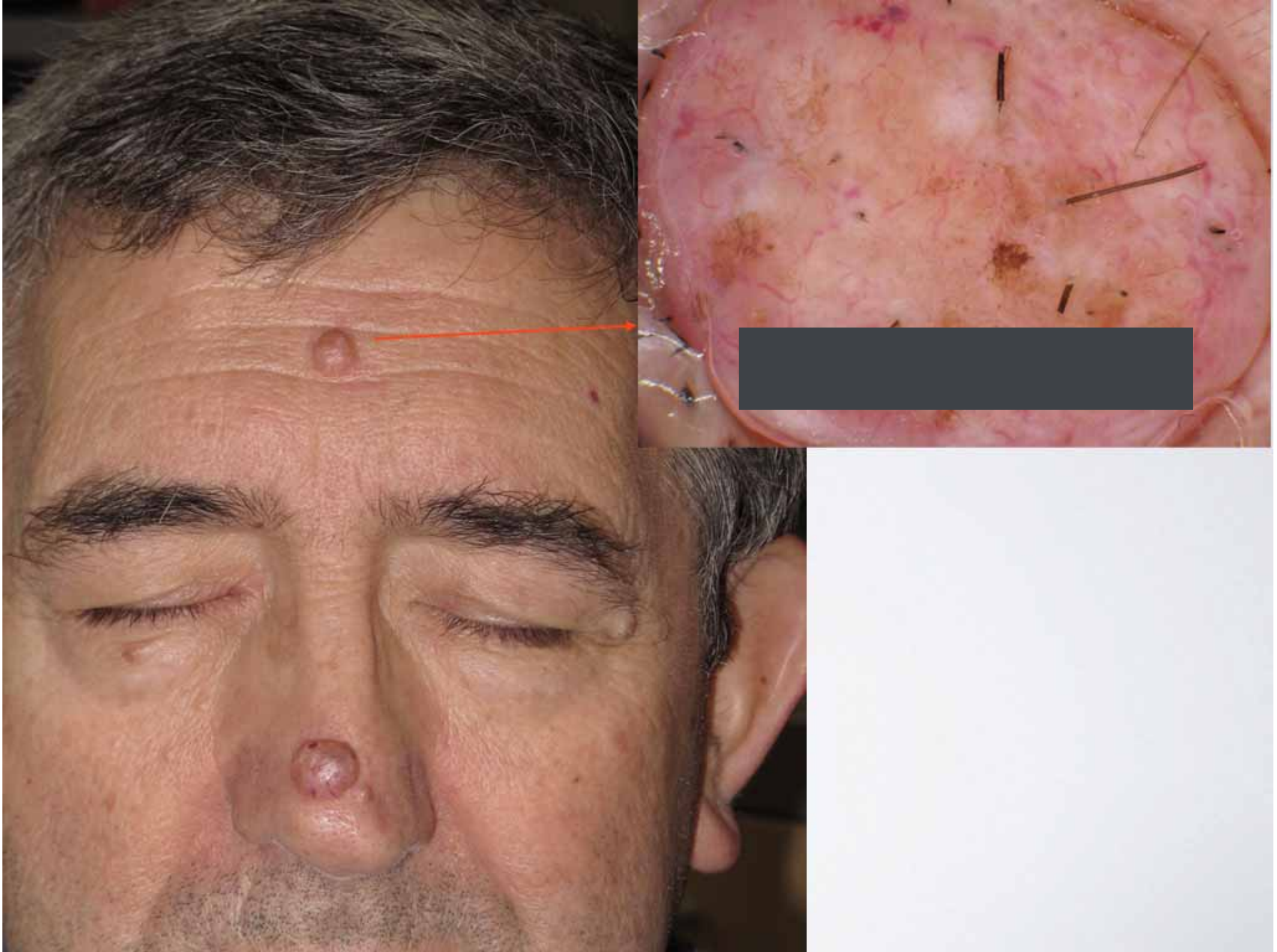
Screening: Clinical and handy dermatoscope

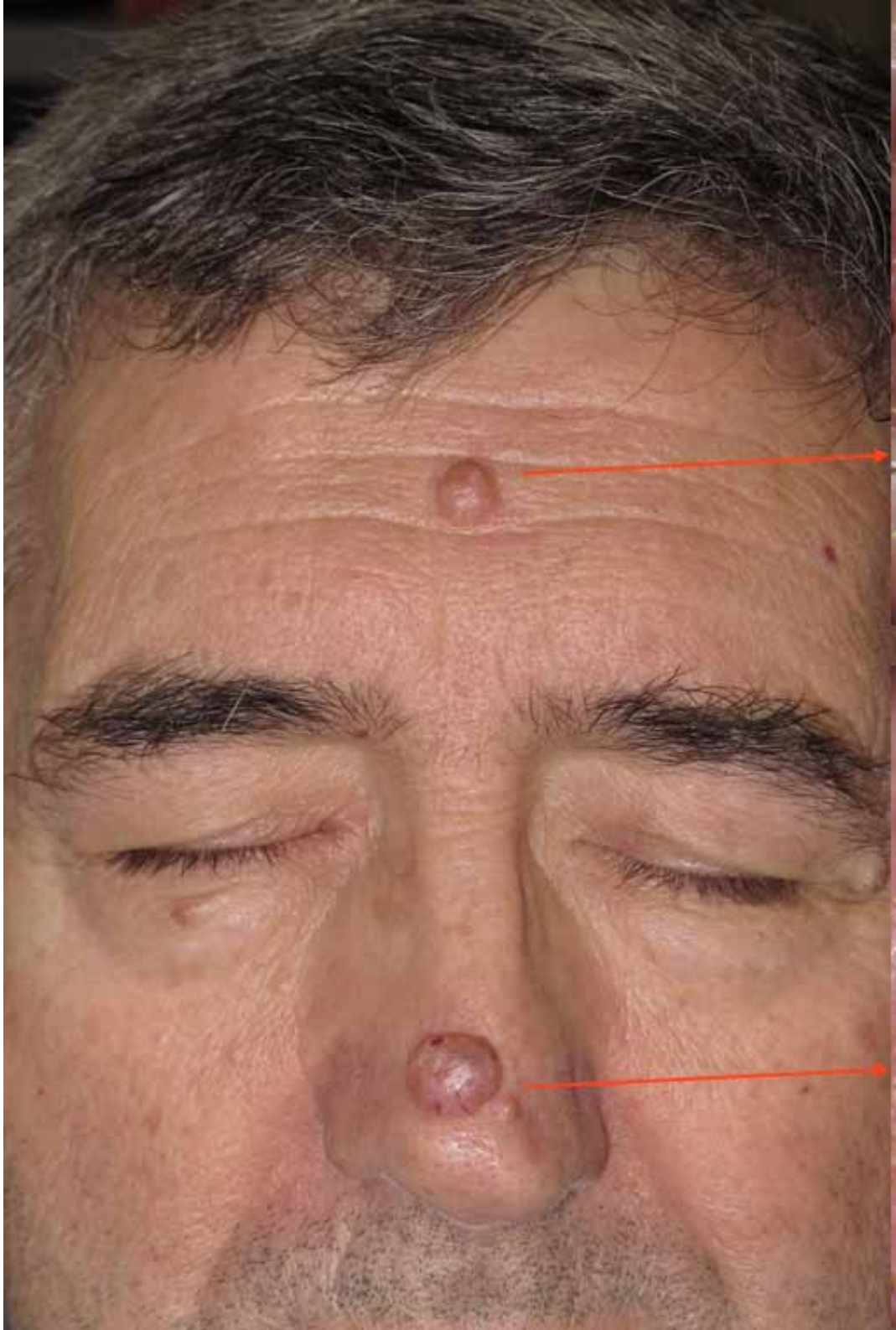
High risk patient: digital dermatoscope

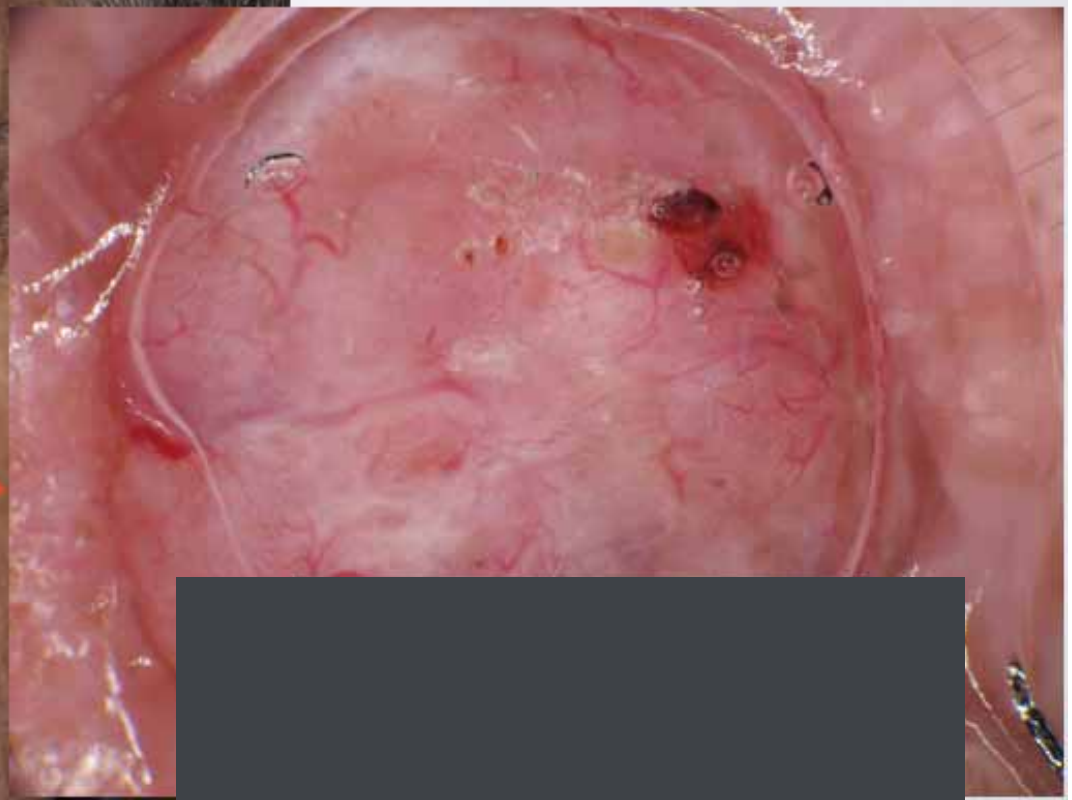
history of skin cancer
multiple nevi
light skin type

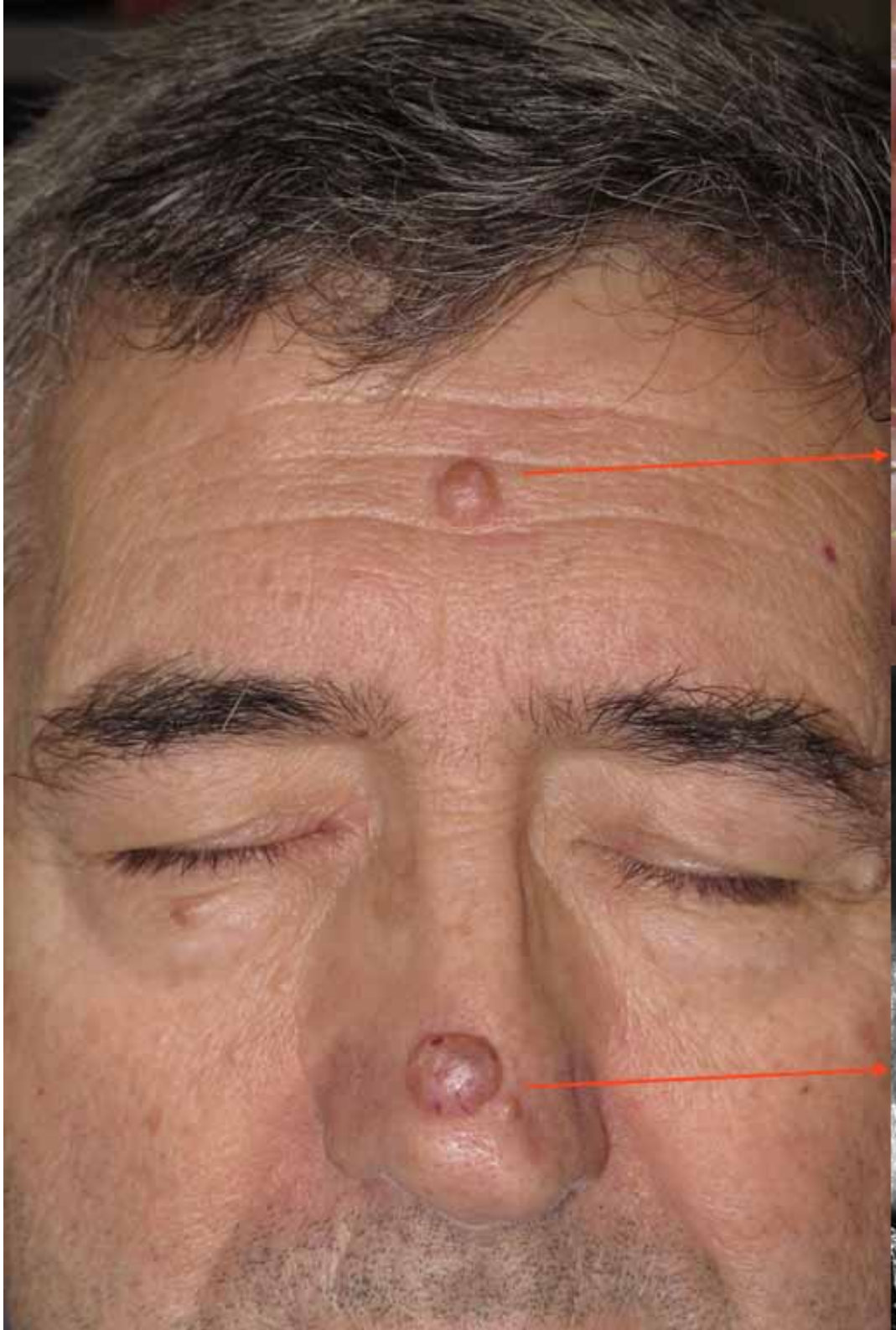
Atypical lesion: reflectance confocal microscopy

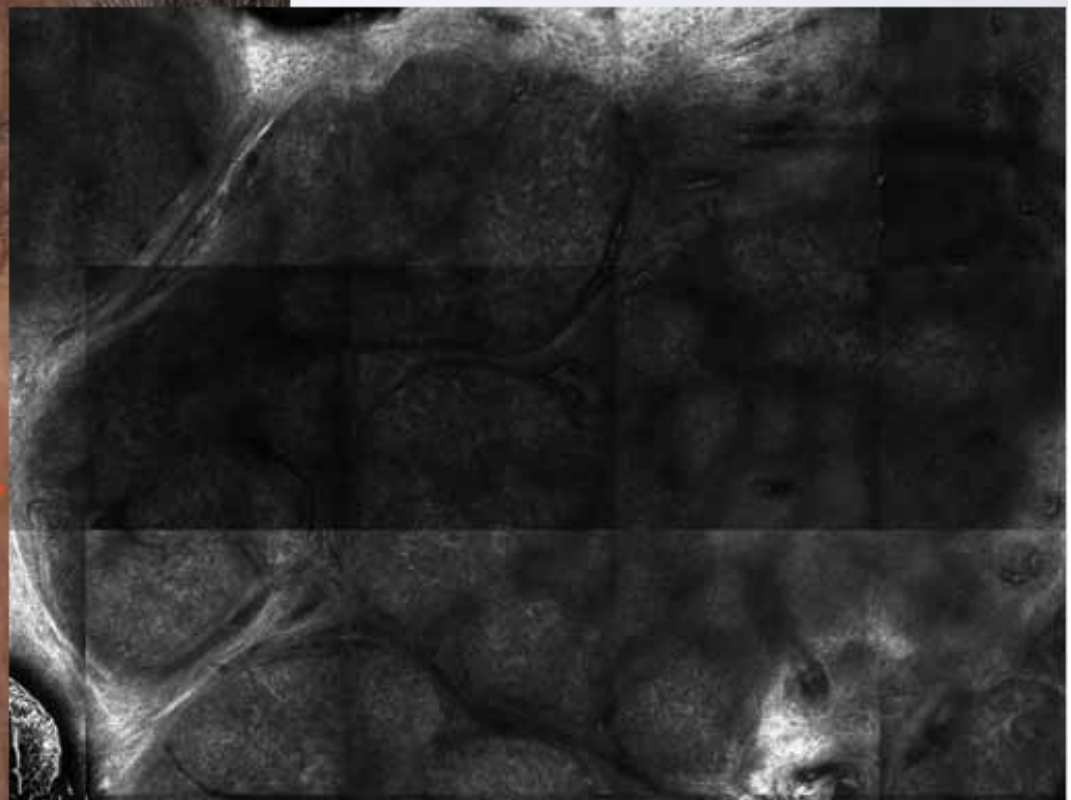
Practical cases...

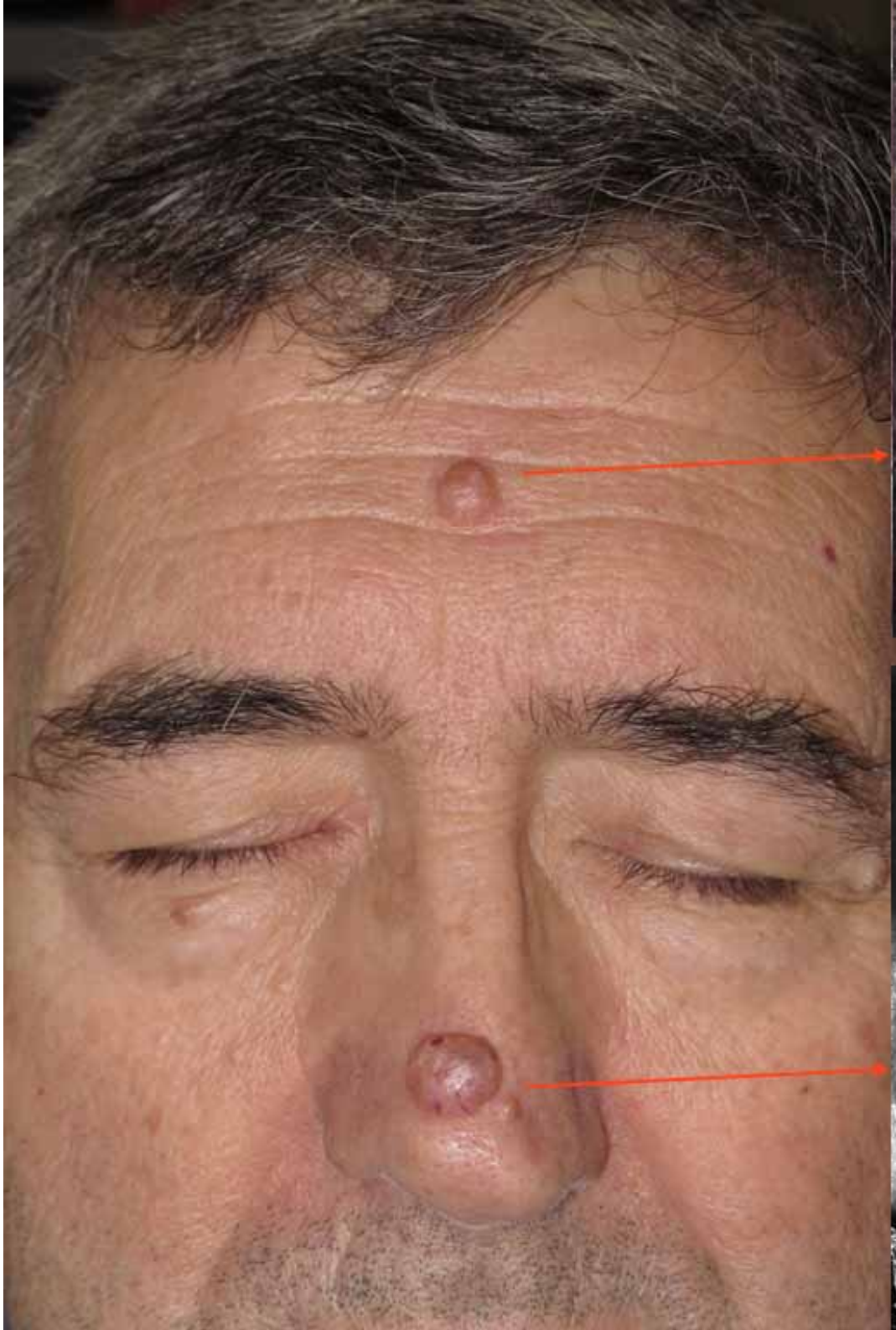


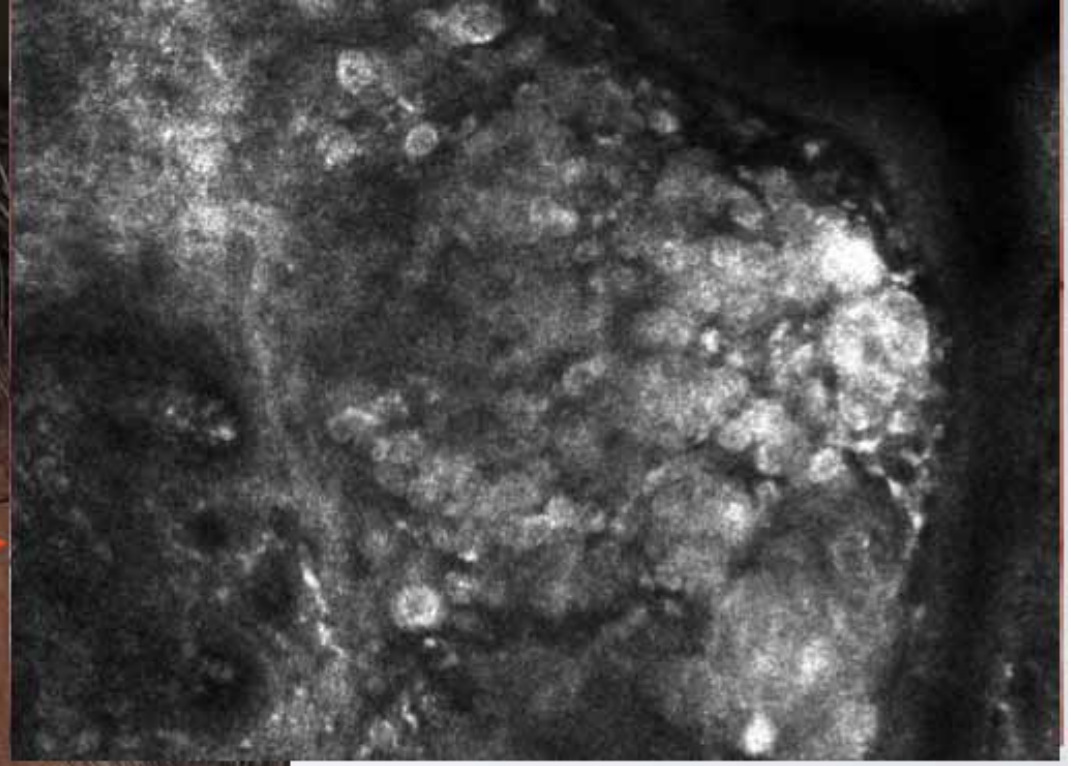


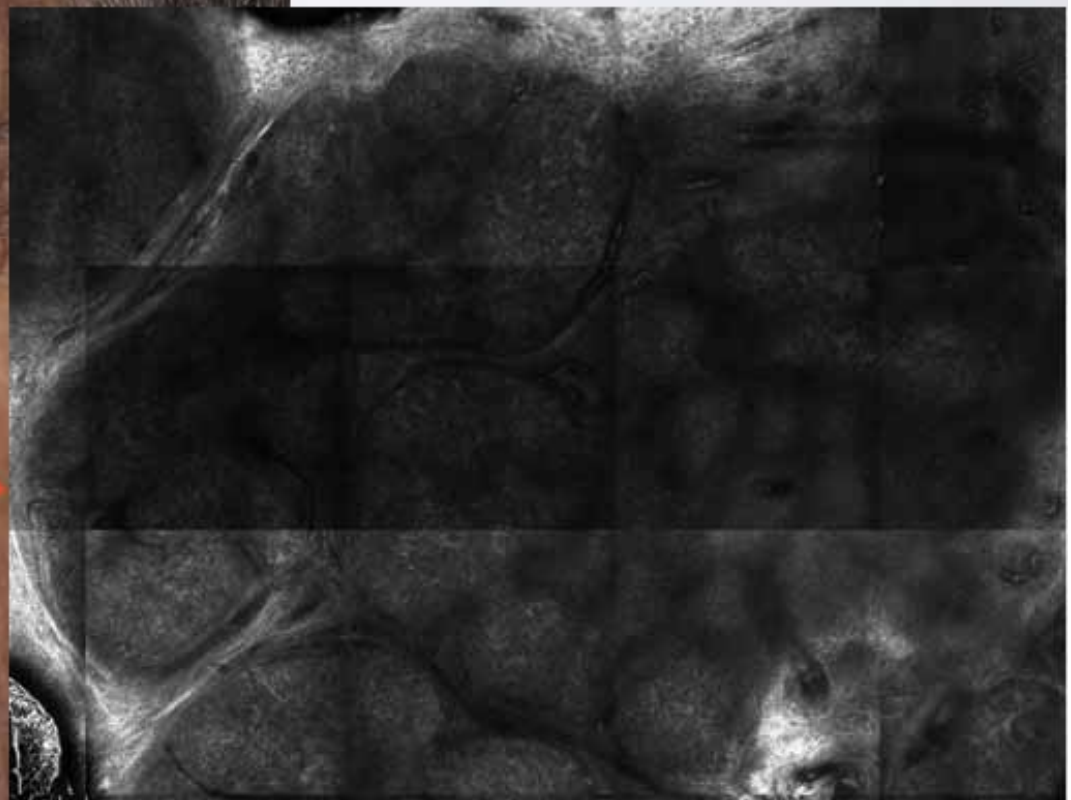


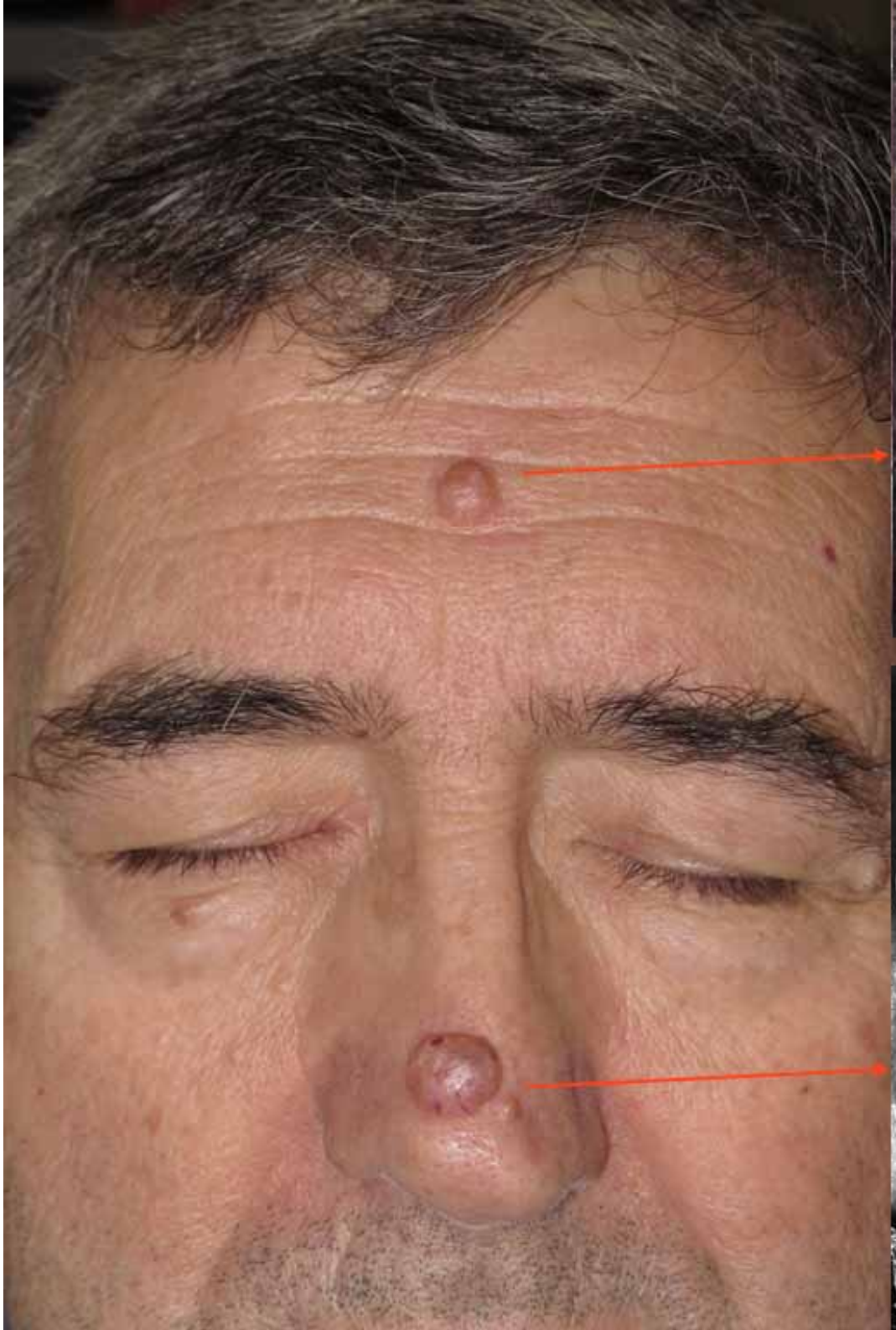


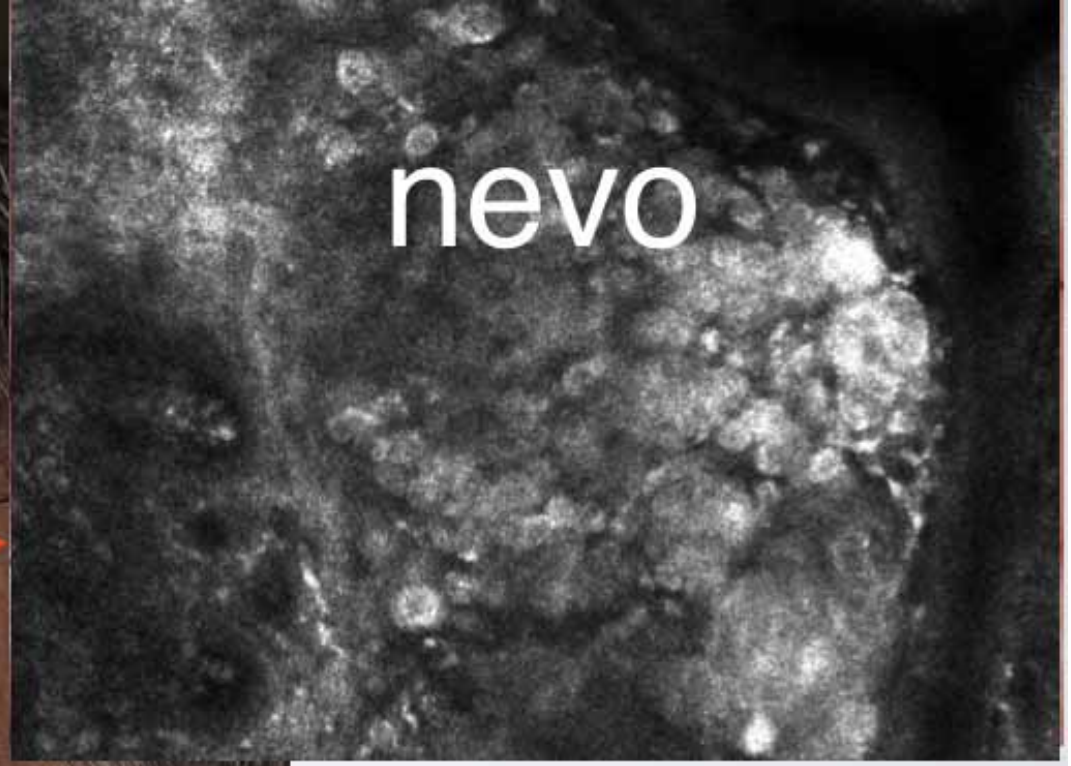








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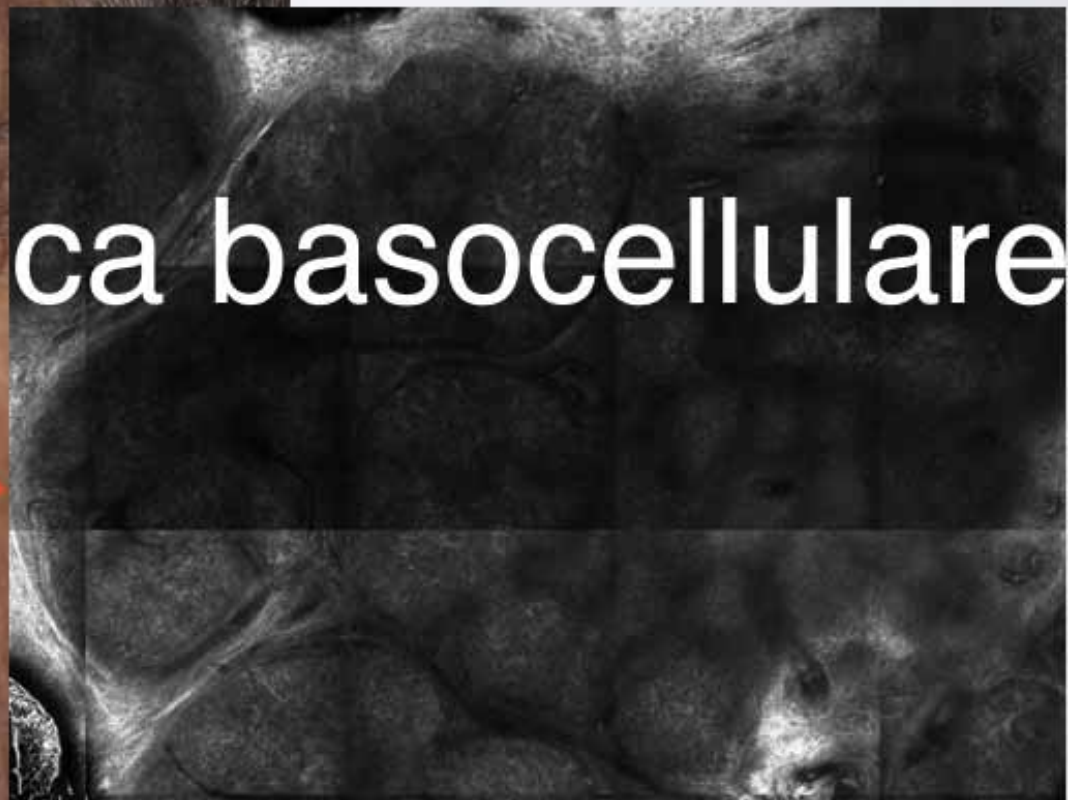
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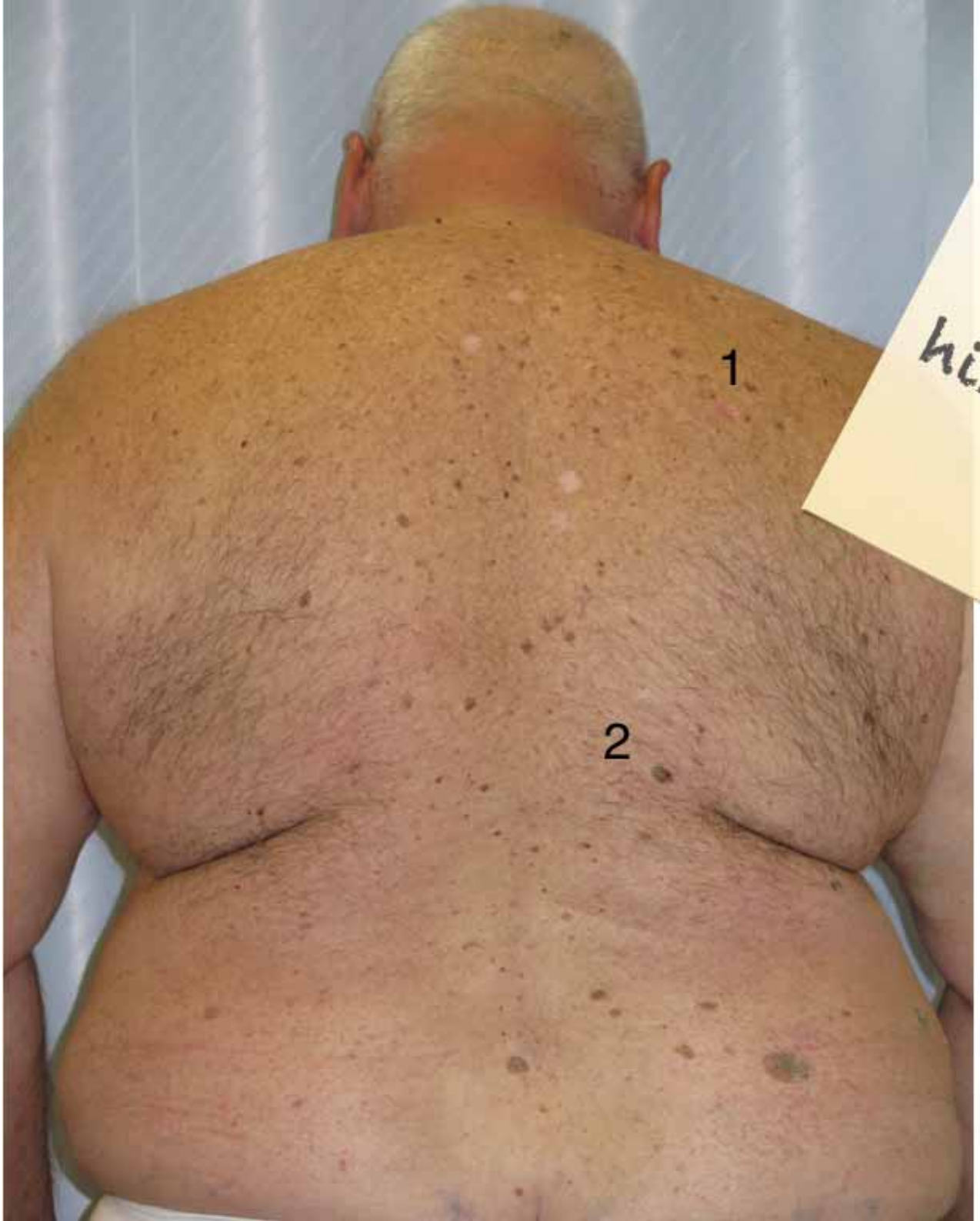
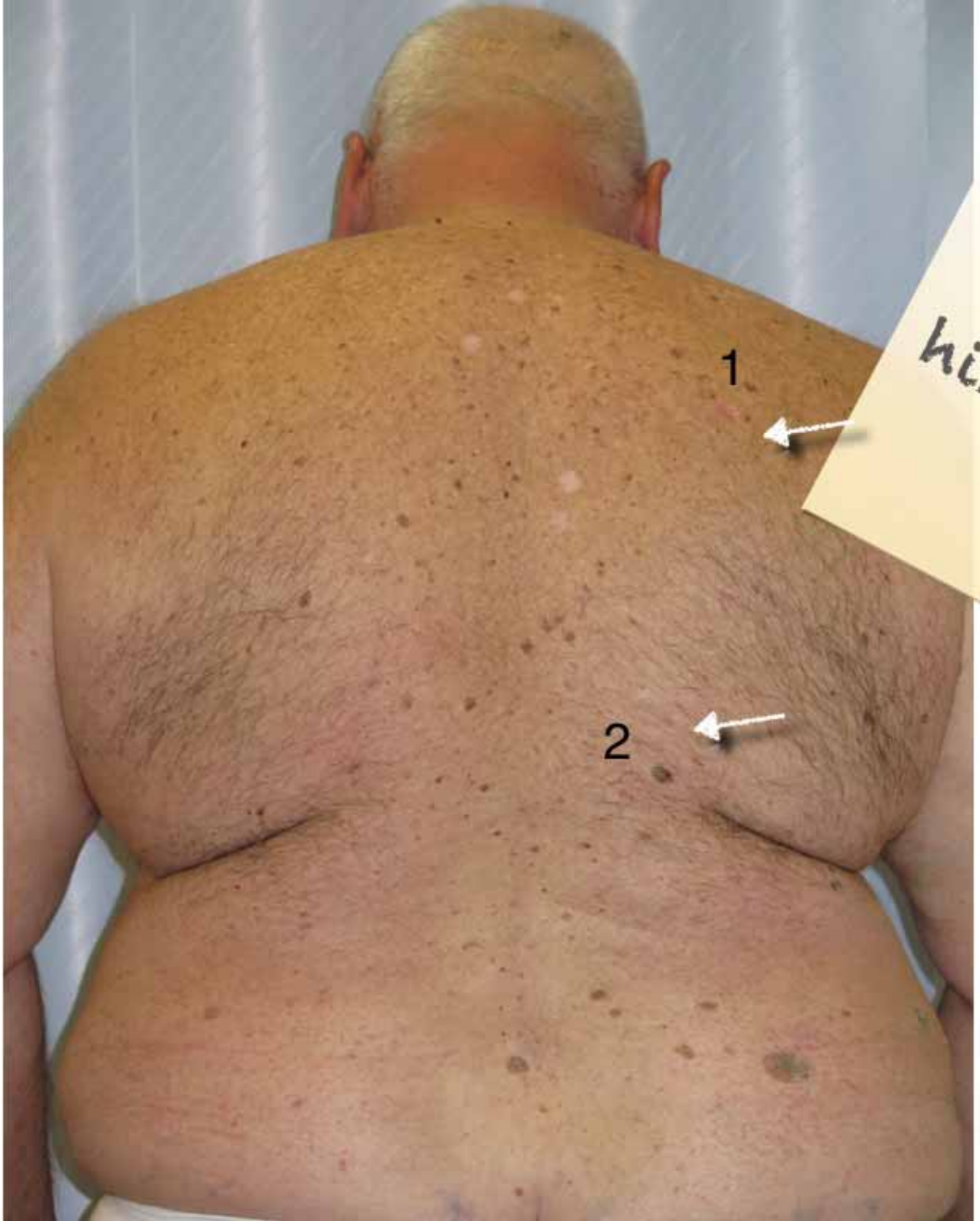


73 y.o.
back
2 lesions
history of BCCs and
AKs



73 y.o.
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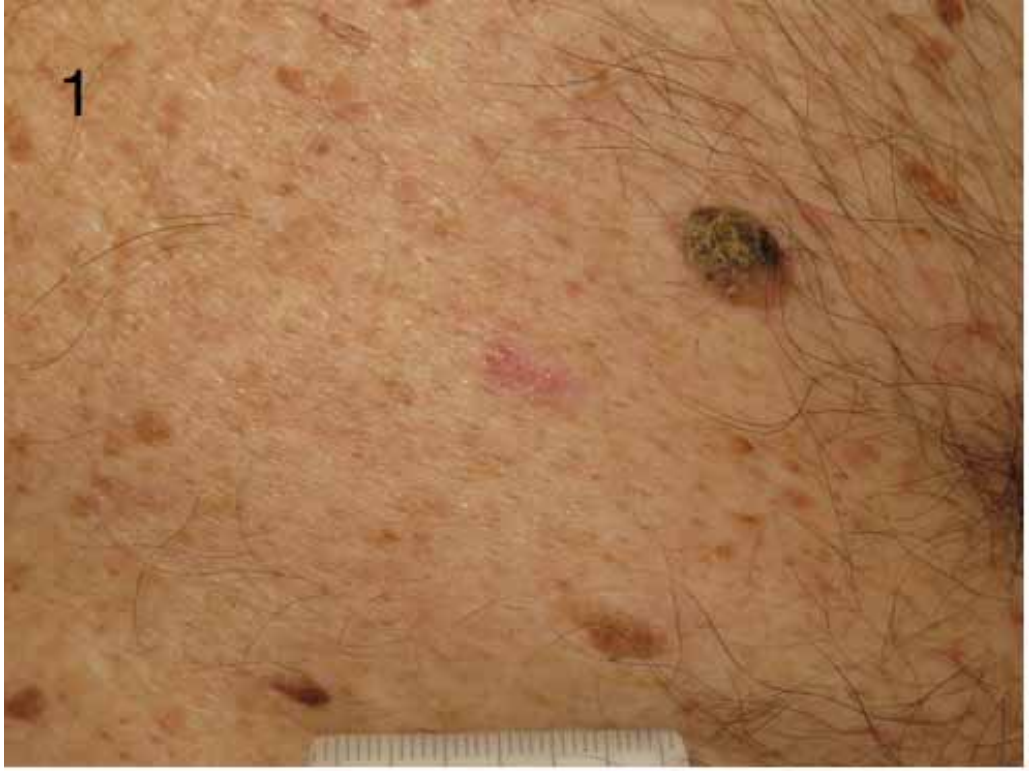
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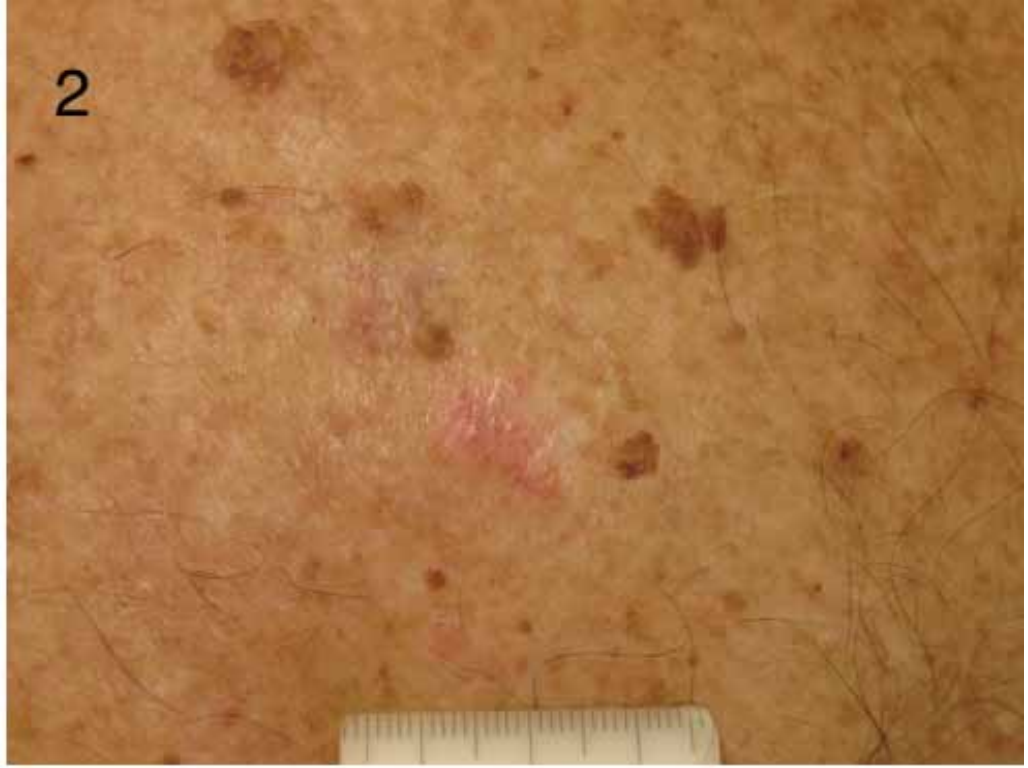
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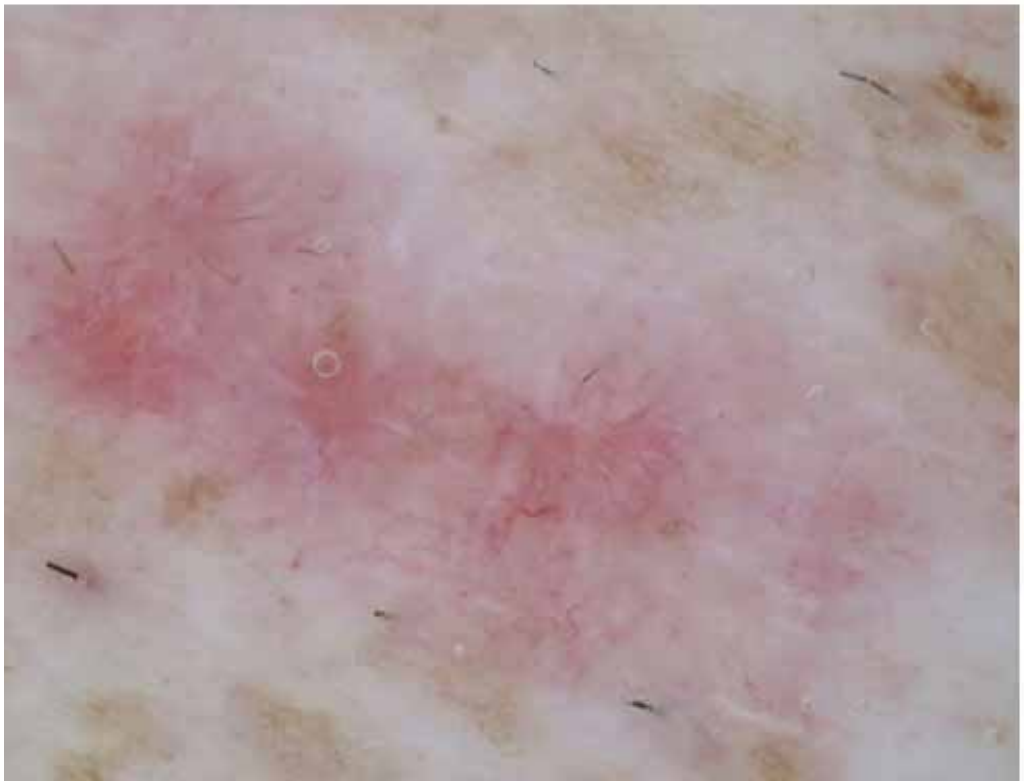

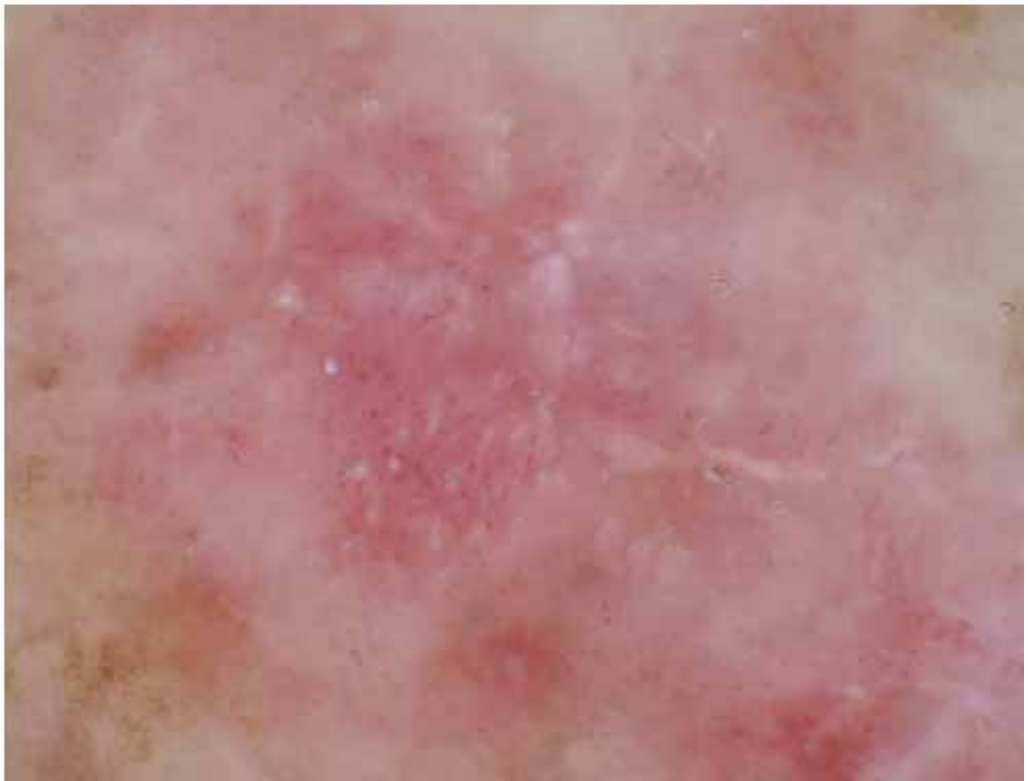

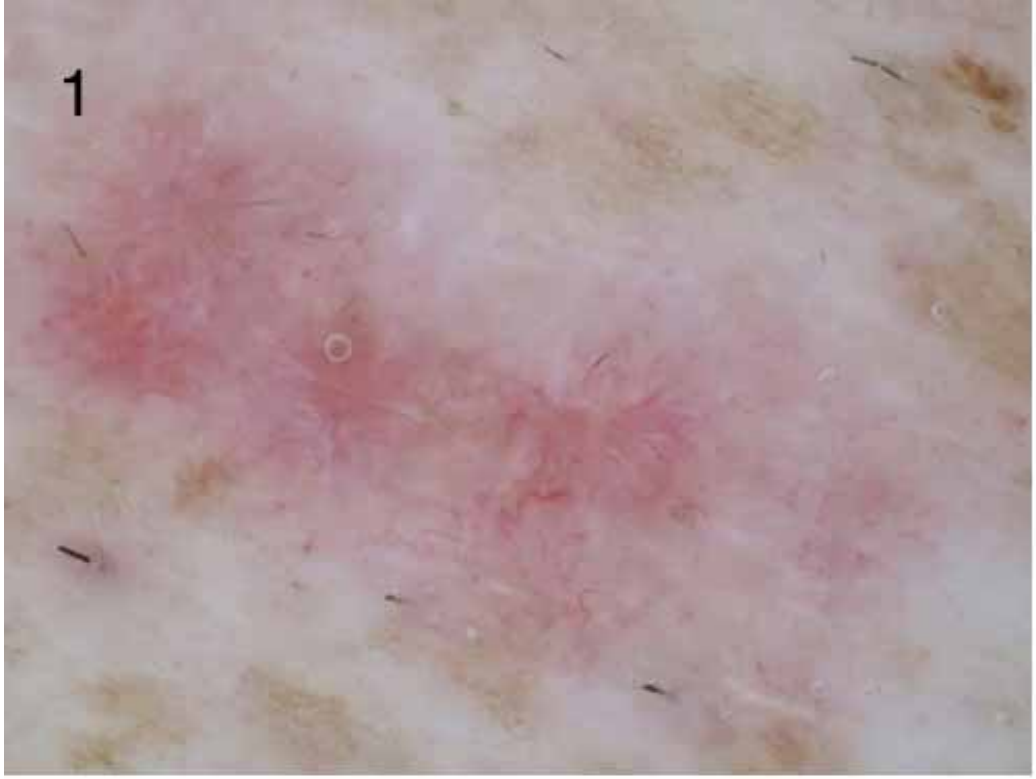
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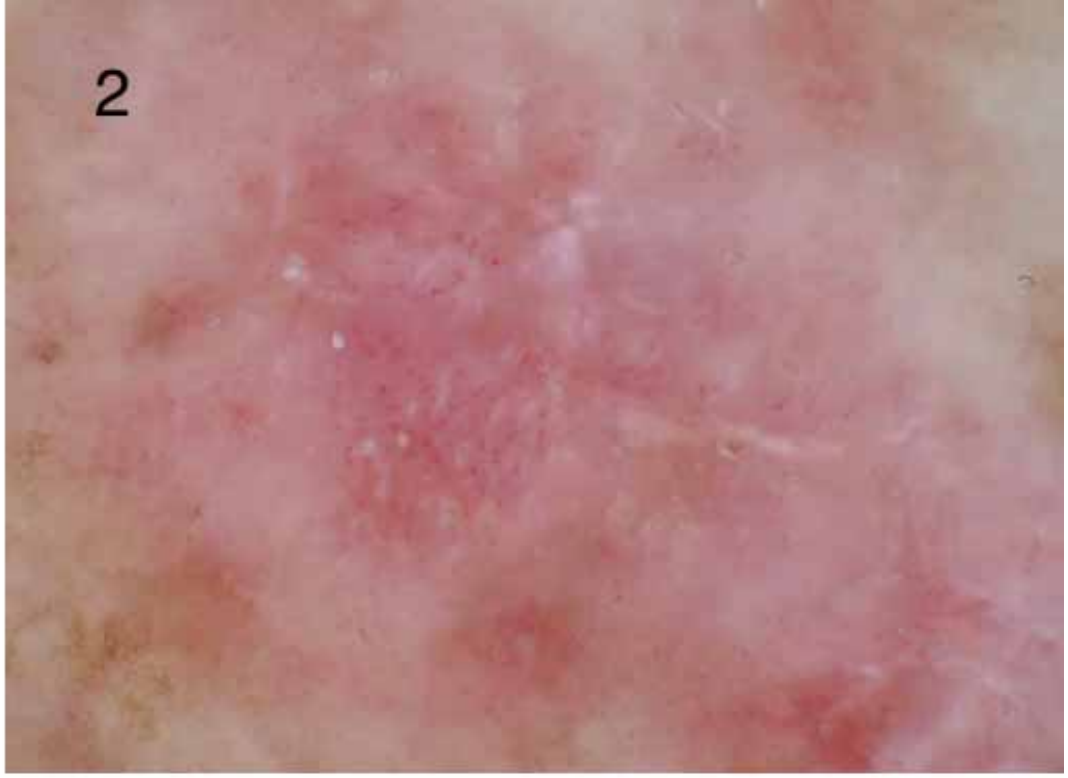
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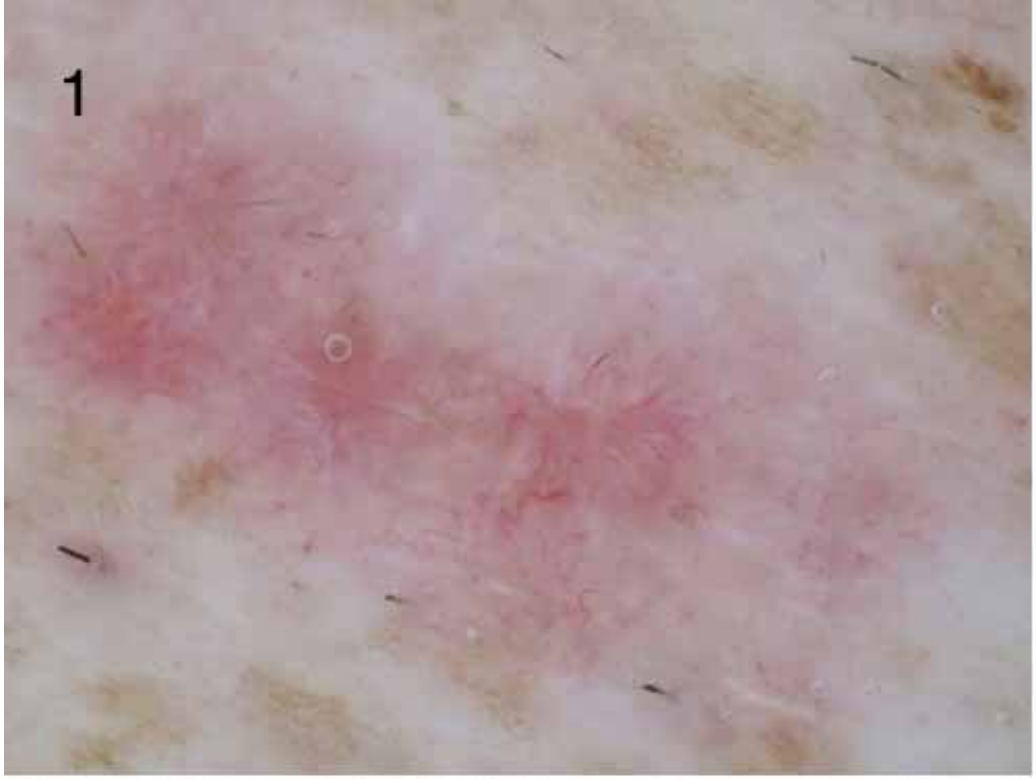
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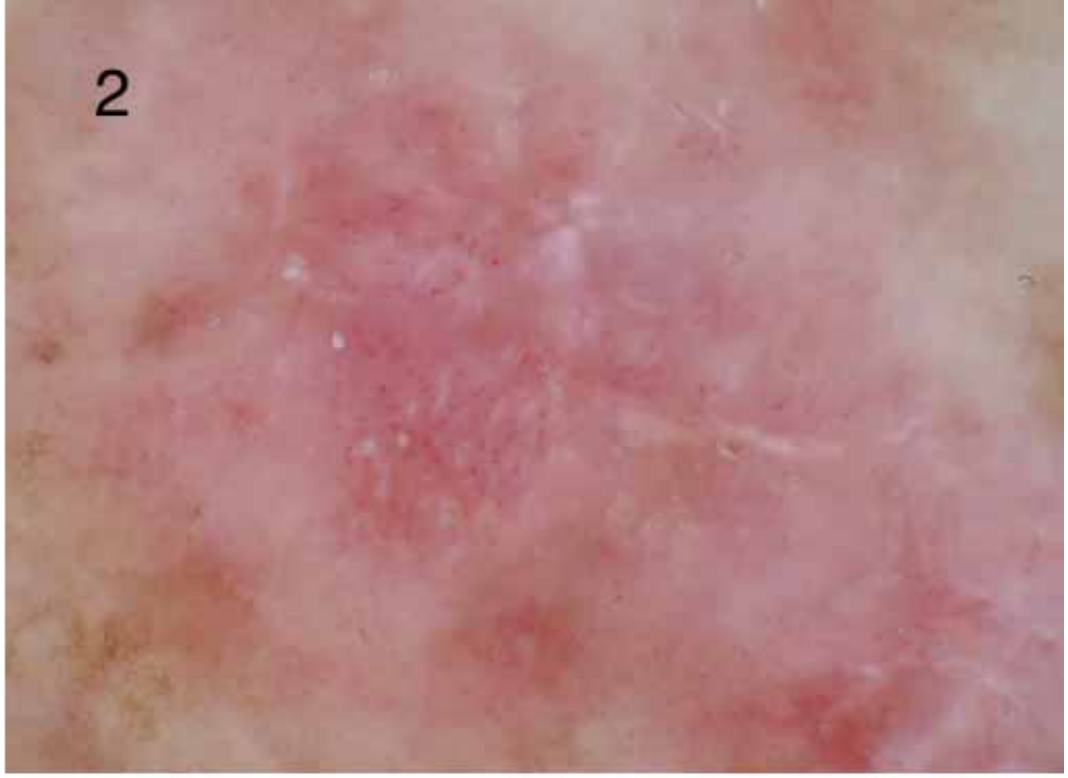
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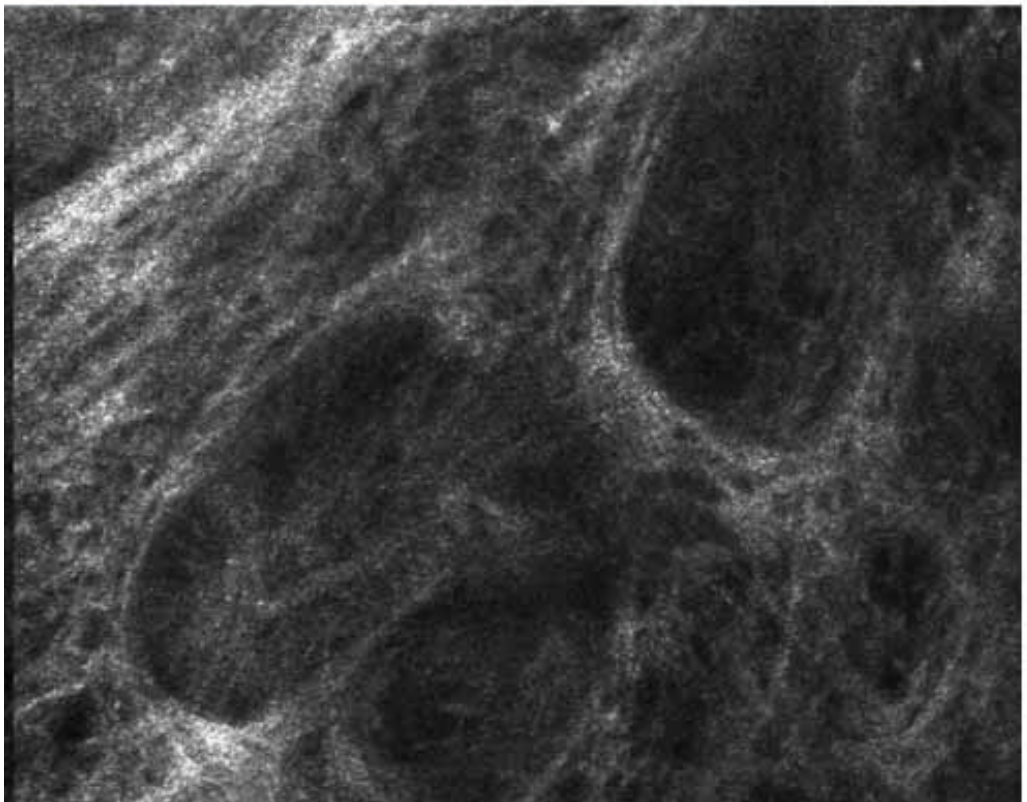

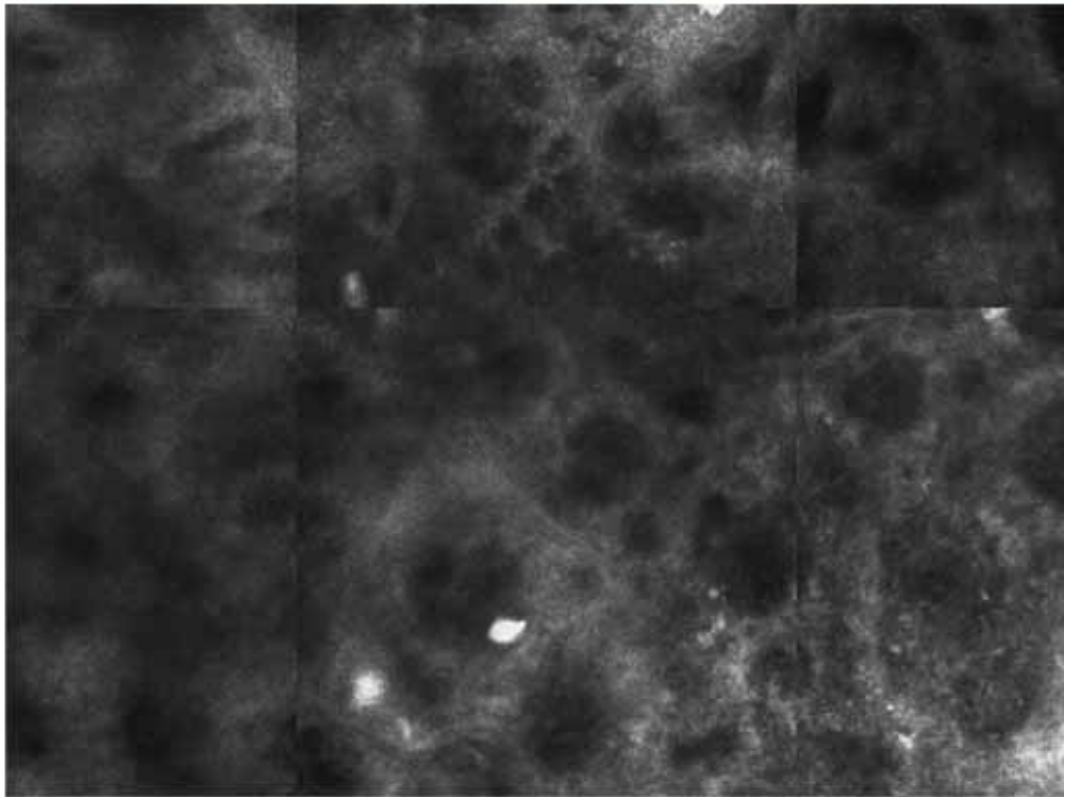

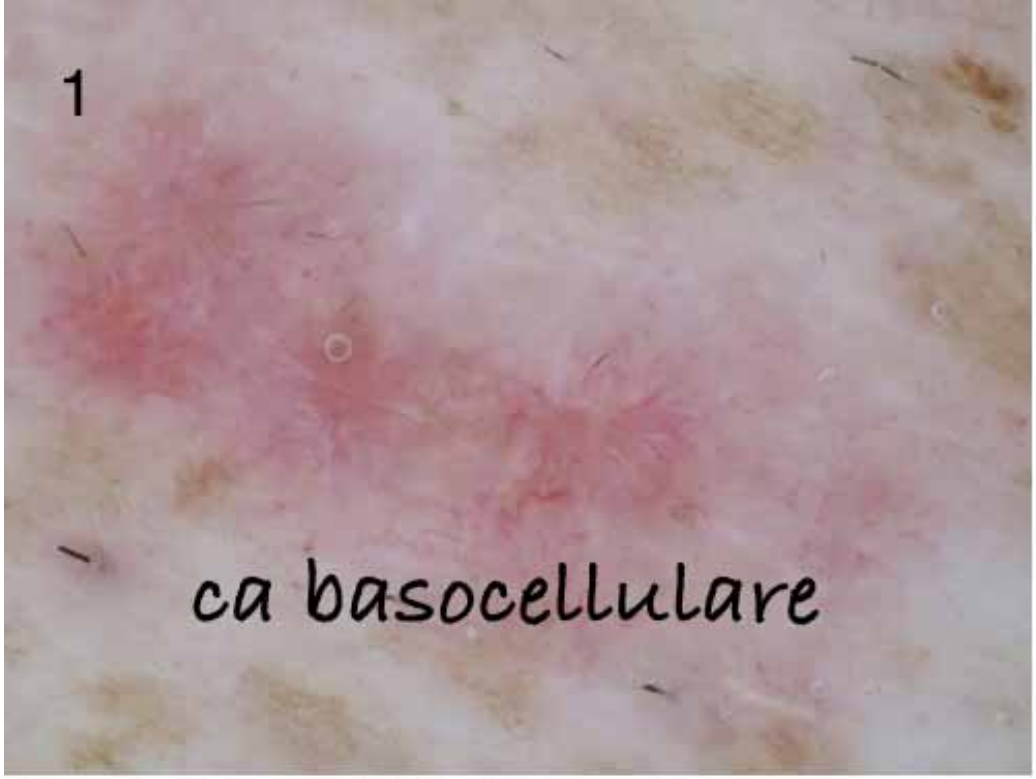
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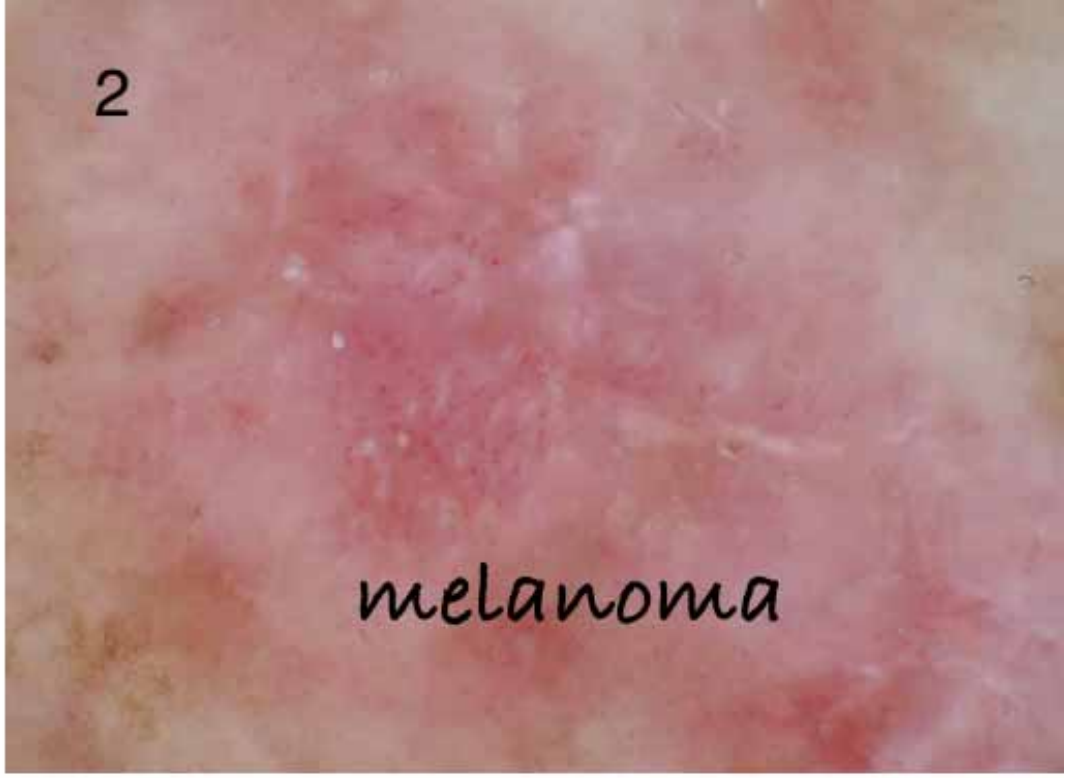
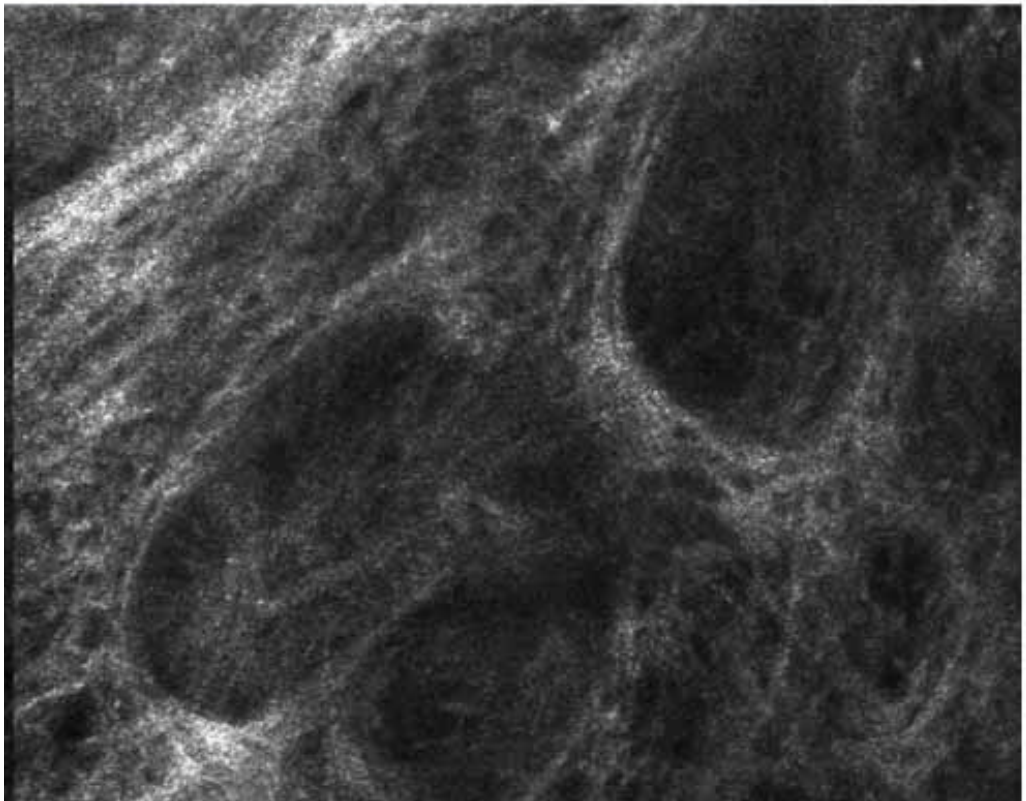
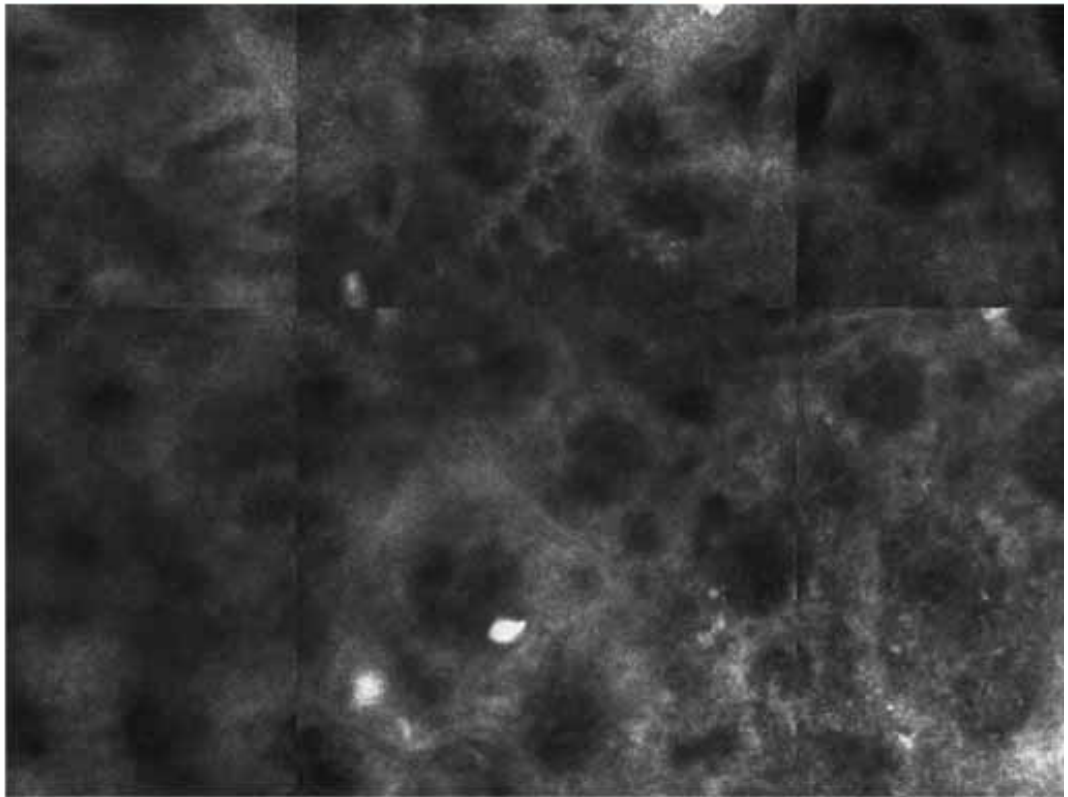
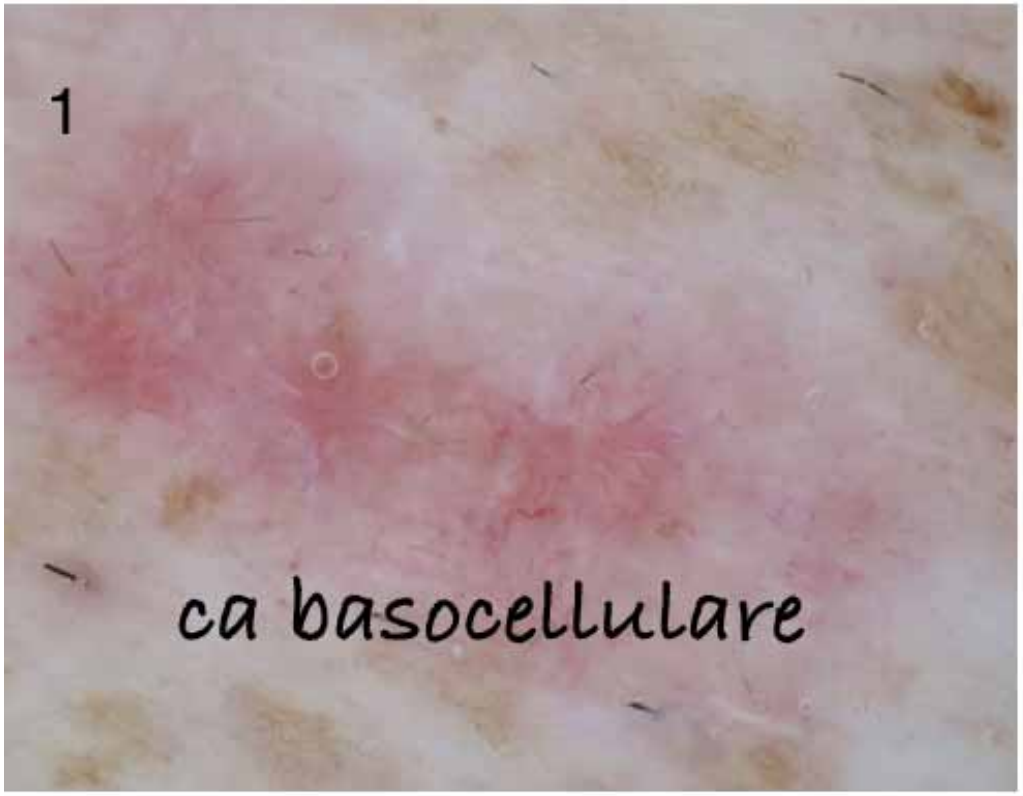
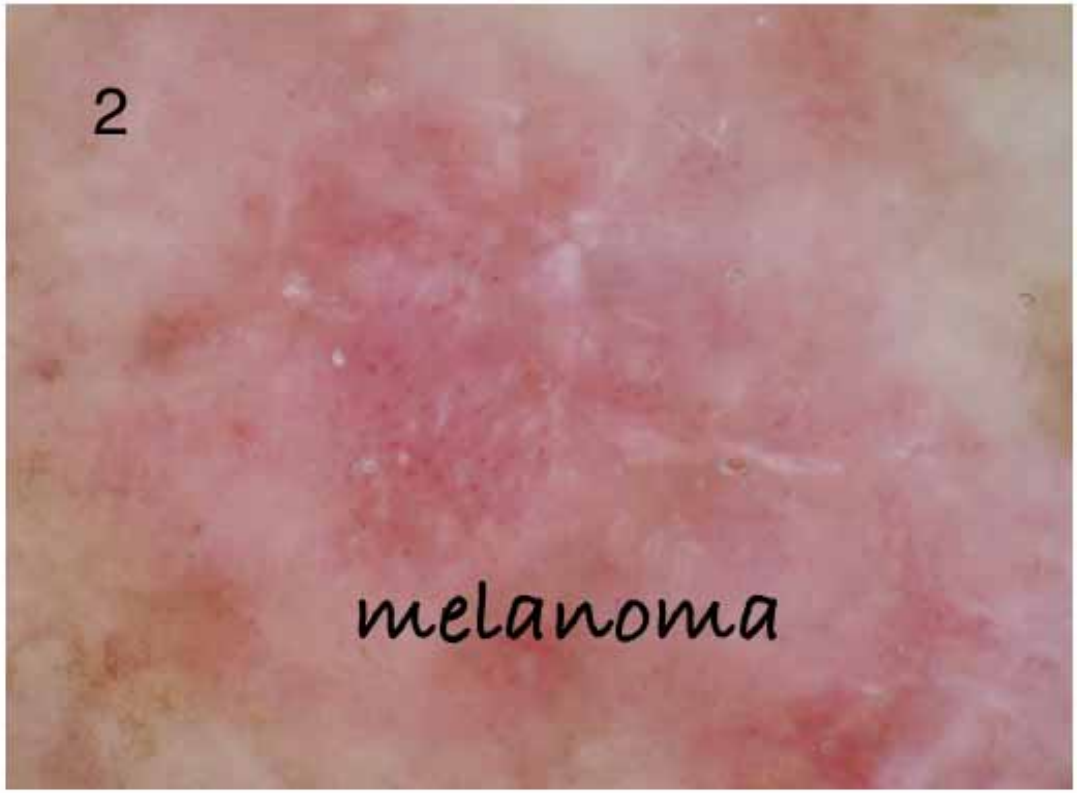

2
melanoma





Practical implications...





cryotherapy
or scheduled surgery

prompt surgical excision

FUTURE CHALLENGE: INTEGRATION OF DERMOSCOPY AND RCM FOR EARLY/SMALL SKIN CANCER DIAGNOSIS

HIGH SENSITIVITY (NOT MISS MELANOMA)
ESPECIALLY "THICK/NODULAR" ONES

↓

SCREENING OF A LARGE NUMBER OF PATIENTS
RULE OUT POSSIBLE "KILLERS"
IDENTIFY AT RISK POPULATION

SECONDARY PREVENTION
EARLY DIAGNOSIS OF MM (INCREASE IN SENSITIVITY)

↓

MONITORING SELECTED HIGH RISK PATIENTS

REDUCTION OF COSTS FOR NOT NECESSARY EXCISIONS (INCREASE IN SPECIFICITY)

↓

DIGITAL FOLLOW-UP AND CONFOCAL MICROSCOPY IN SPECIALIZED CENTERS

BENEFICIAL POPULATION

MASS (CHEAP AND FAST) APPROACH

SCREENING
INFORMATION
CAMPAIN
TRIAGE DECISION

MD SPECIALISTS AND TOOLS FOR SELECTED PATIENTS

HIGHLY SPECIALIZED CENTERS AND MDs

TOOLS FOR SELECTED PATIENTS AND LESIONS