19th EADO CONGRESS
April 20th–22nd, 2023

Total body imaging and sequential dermatoscopy

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DISCLOSURE OF CONFLICTS OF INTEREST

SPEAKER: Almirall, BMS, ISDIN, La Roche Posay, Leo, Novartis, Pierre Fabre, Roche, Sanofi

HONORARIA OR CONSULTATIONS FEES : Almirall, BMS, Biofrontera, GSK, ISDIN, La Roche Posay, Leo, Novartis, Polychem, Dermavision, Pierre Fabre.

GRANTS & RESEARCH SUPPORT: Almirall, Amgen, BMS, Biofrontera, Canfield, Cantabria, Fotofinder, GSK, ISDIN, La Roche Posay, Leo, Mavig, Nevisense, Novartis, Polychem, Roche, Dermavision

Spouse/partner: Almirall, Amgen, BMS, Biofrontera, Canfield, Cantabria, Fotofinder, GSK, ISDIN, La Roche Posay, Leo, Mavig, Nevisense, Novartis, Pierre Fabre, Polychem, Roche

Other support (please specify): Abbie (educational activities), Lilly (educational activities), Novartis Co-Founder of Athena Tech.

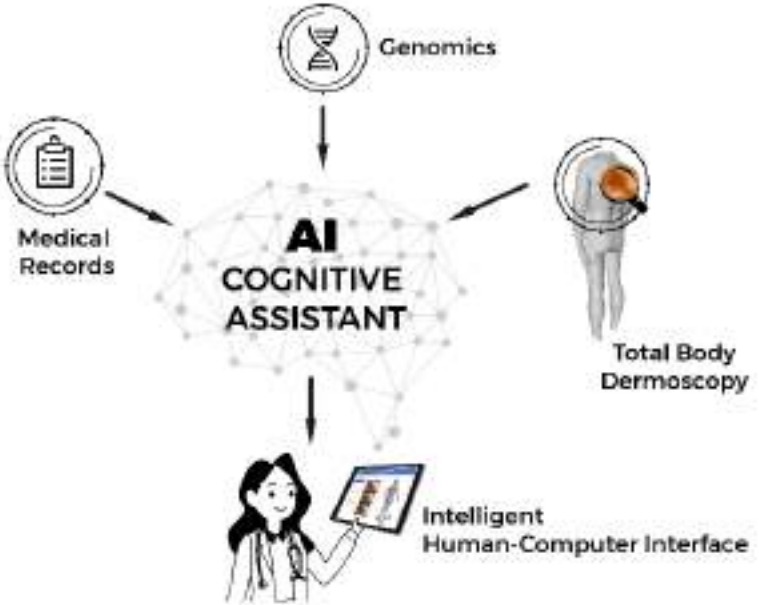
RESEARCH AND INNOVATION GRANTS

M-Skip

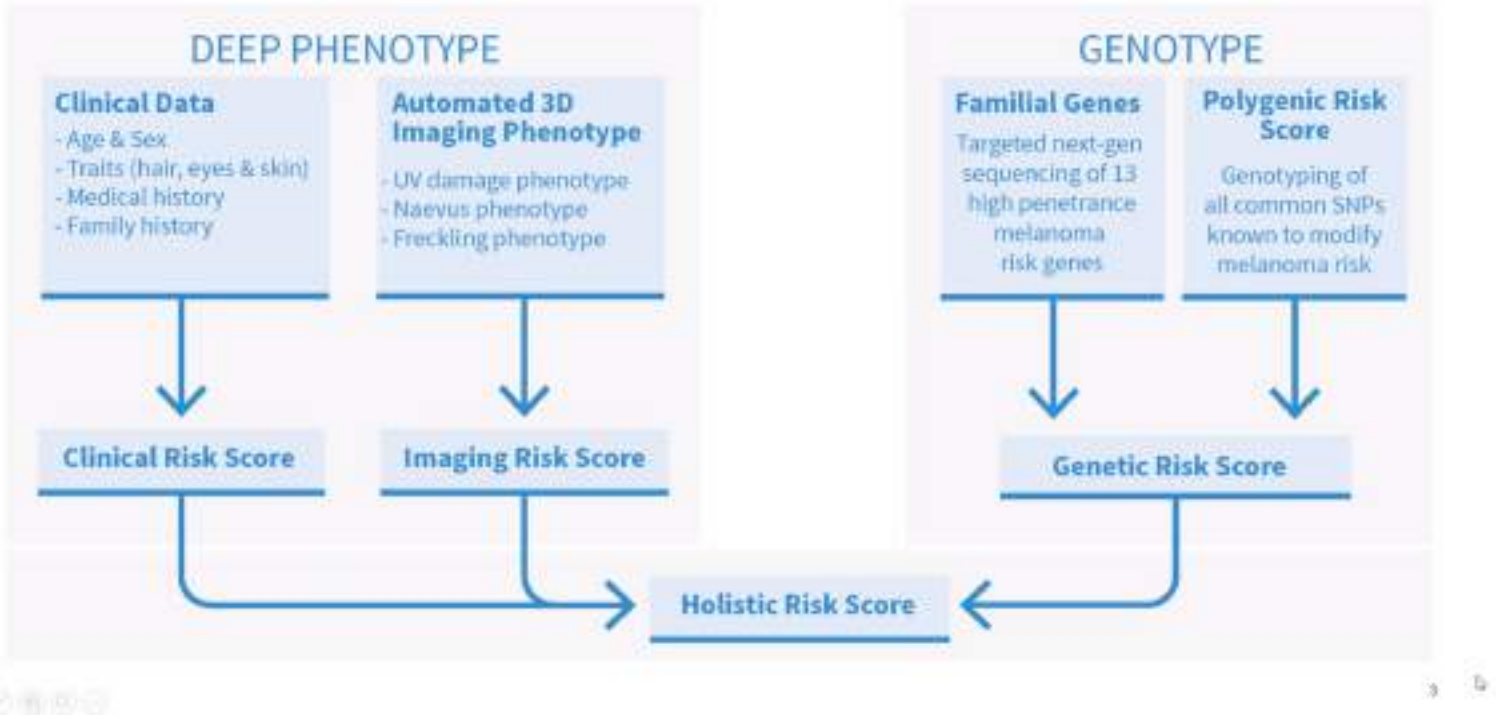
ITOBOS: INTELLIGENT TOTAL BODY SCANNER FOR EARLY DETECTION OF MELANOMA (EU H2020)

iToBOS

- **New diagnostic tool** for the early detection of melanoma, exploiting **all the available information** of the patient.
- This **holistic assessment tool** should understand the specific characteristics of every patient in order to enable a **personalised, early detection of melanoma**.



HOLISTIC RISK STRATIFICATION FOR MELANOMA

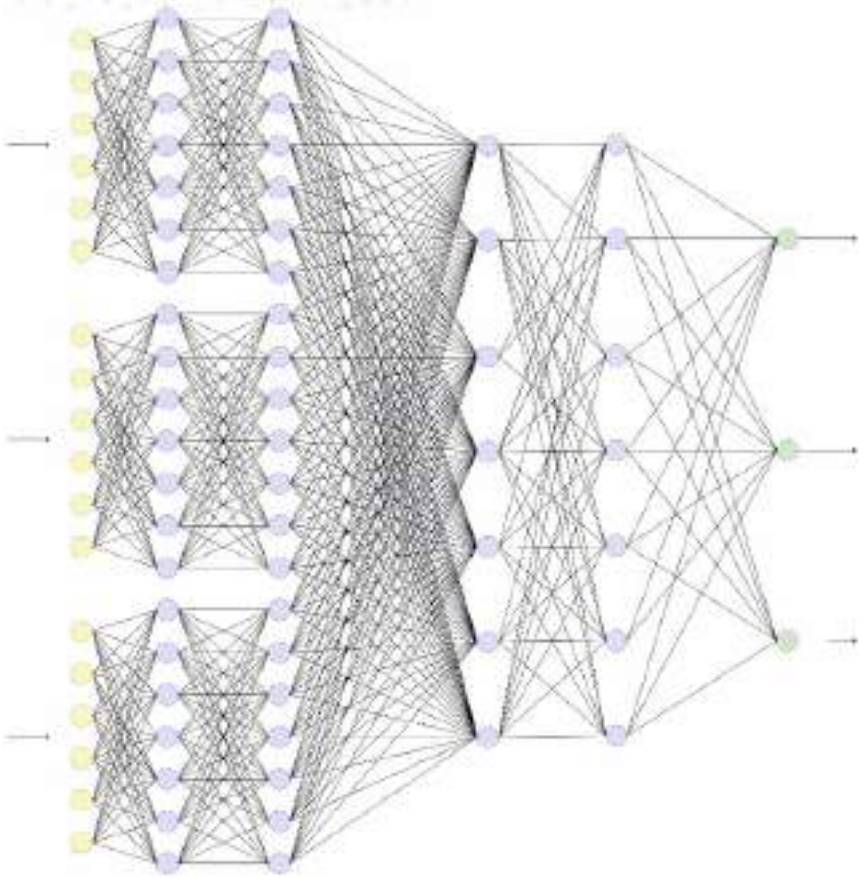


Lee KJ, Betz-Stablein B, Stark MS, Janda M, McInerney-Leo AM, Caffery LJ, Gillespie N, Yanes T, Soyer HP. The Future of Precision Prevention for Advanced Melanoma. Front Med (Lausanne). 2022 Jan 17;8:818096.

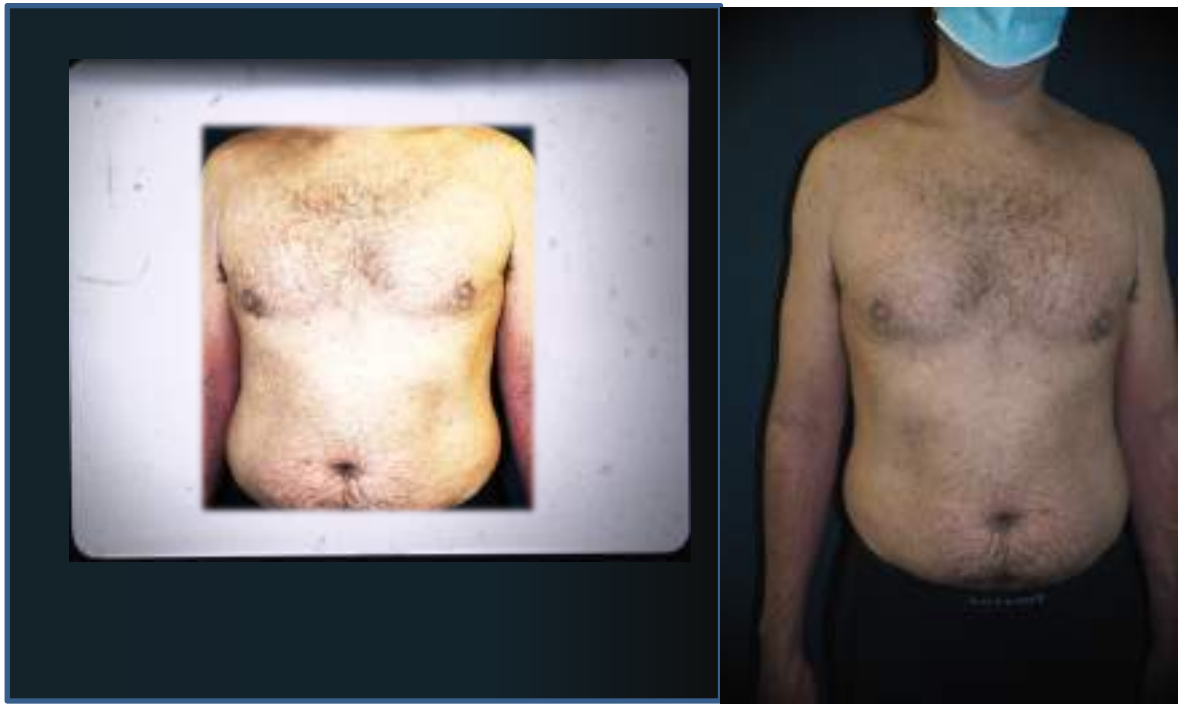
Image

Medical Records

Genomics



Pigmented lesions Clinic (1980 in US)

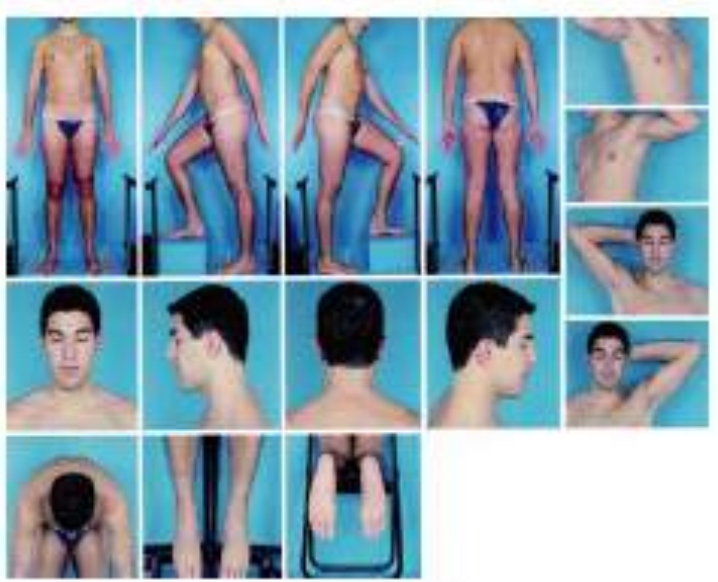


Monitoring of patients using slides with base line total body photography photos projected in real time side by side with the patient during the follow-up

Pigmented lesions Clinic (1980 in US)

Total Body Photography

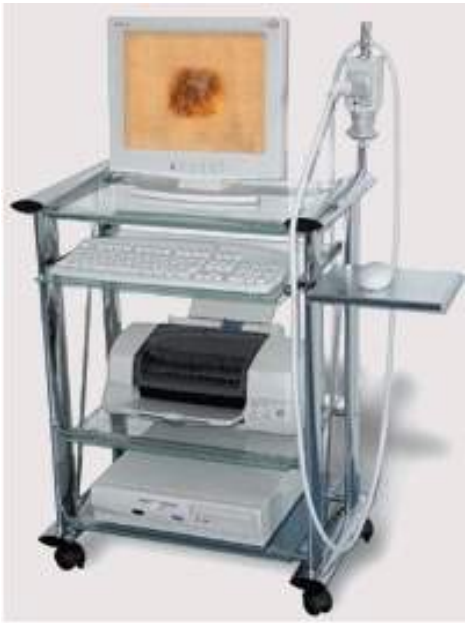
- Detection of new lesions and changes in moles
- More stablished in US
- Evidence Level III
- Type I method (patient) /III (specialized centers)



Terushkin V, Oliveria SA, Marghoob AA, Halpern AC. Use of and beliefs about total body photography and dermatoscopy among US dermatology training programs: an update. J Am Acad Dermatol. 2010

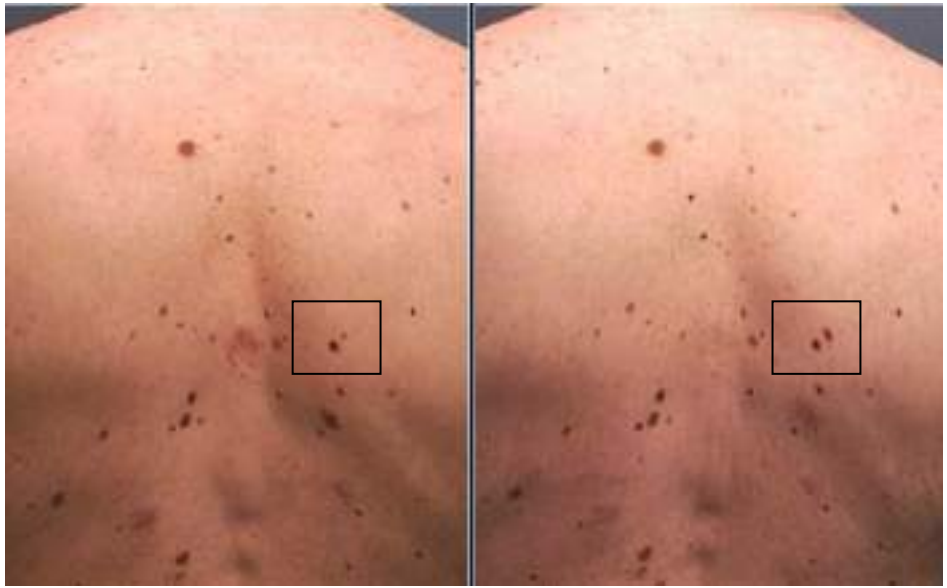
Slue W, Kopf AW, Rivers JK. Total-body photographs of dysplastic nevi. Arch Dermatol. 1988 Aug;124(8):1239-43.

Dedicated systems for digital monitoring (1998)

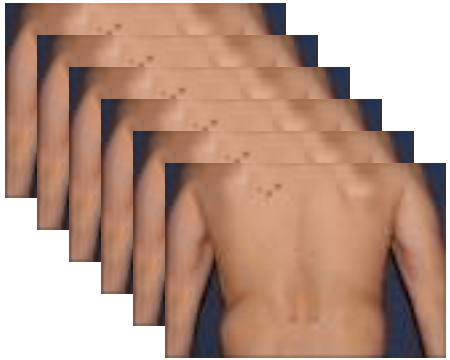


TBP and sequential digital drmoscopy

TBP-SDD can help identify new or changing melanocytic lesions through comparison of base- line images with subsequent images over time

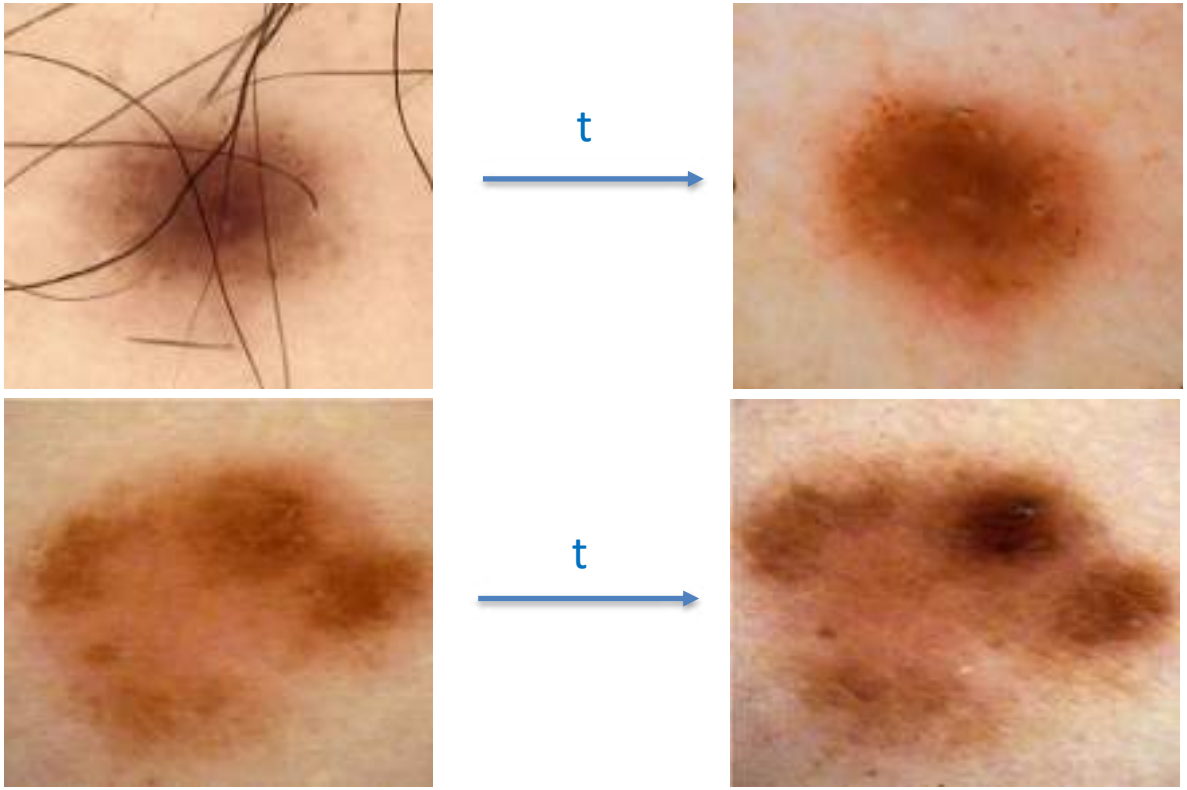


- 2D TBP /3D TBP / Standard photography vs polarised light TBP
- TBP vs digital Dermoscopy follow-up

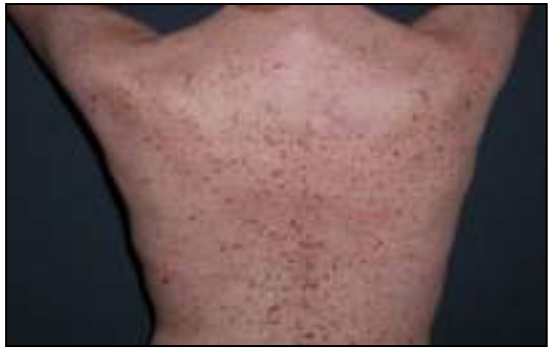


Digital follow-up (Dermoscopy)

Digital follow-up (Dermoscopy)

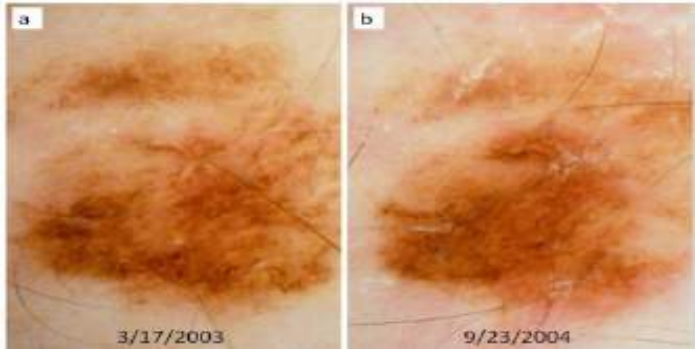


Total Body Photography



24 Photos per patient (15-56)

Digital Dermoscopy



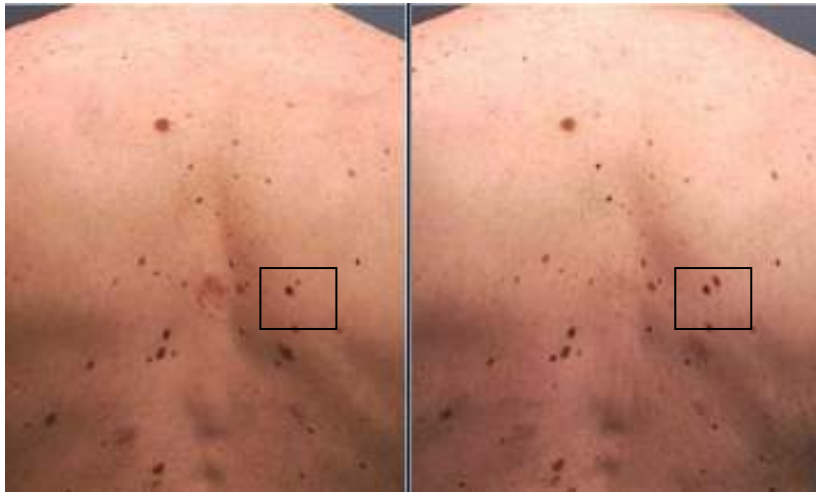
18.44 lesions /patient (15-25)

“Two steps method of digital follow-up”

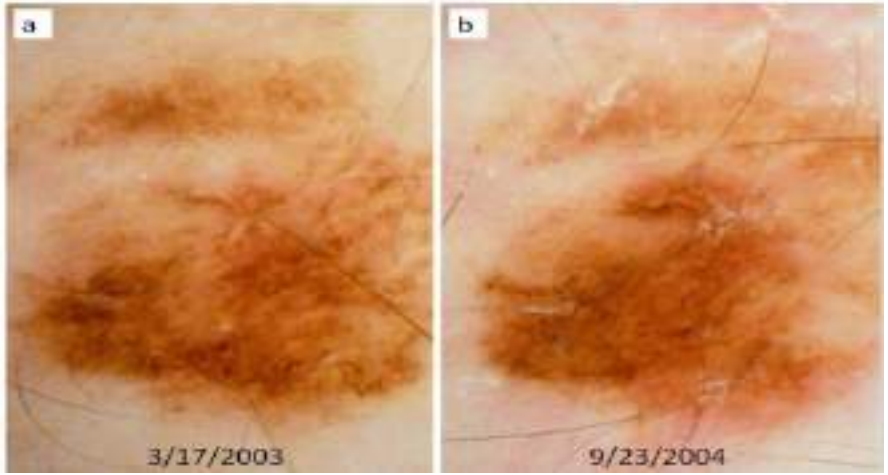
J Malvehy, S Puig, R Martí, et al. Follow-up of melanocytic skin lesions with digital total-body photography and digital dermoscopy: a two steps method. Clinics in Dermatol 2002

30% of lesions were excised because changes in Total Body Photography

40% of the new MMs



70% excised because changes in digital dermoscopy /60% of the new MMs



Salerni G, et al. Benefits of total body photography and digital dermatoscopy ("two-step method of digital follow-up") in the early diagnosis of melanoma in patients at high risk for melanoma. JAAD 2012

What do we know about TBP-SDD?

- **Improved detection of thin melanomas**.
- Useful in **high risk melanoma patients** by providing confirmation that **suspicious lesions remain stable**
- Reduce **patient anxiety** regarding melanoma recurrence.
- Reduce the **number of biopsies per patient**, which can reduce patient anxiety and waiting times.

- **Fewer biopsies in all patient cohorts ?**
- **Diagnostic accuracy for melanoma** ?
- Improved **overall survival**?
- **Cost efficiency**?

Metanalyses of TBP-SDD (Salerni G, Terán T, Puig S, Malvehy J, Zalaudek I, Argenziano G, Kittler H. Meta-analysis of digital dermoscopy follow-up of melanocytic skin lesions: a study on behalf of the International Dermoscopy Society. J Eur Acad Dermatol Venereol. 2013 Jul;27(7):805-14)

Second primary melanomas in a cohort of 977 melanoma patients within the first 5 years of monitoring

Aimilios Lallas, MD, PhD, MSc,[a] Zoe Apalla, PhD,[b] Athanassios Kyrgidis, PhD,[c] Chryssoula Papageorgiou, MD,[a] Ioannis Boukovinas, MD,[d] Mattheos Bobos, PhD,[e] George Efthimiopoulos, MD,[f] Christina Nikolaidou, MD,[g] Andreas Moutsoudis, MD,[a] Theodosia Gkentsidi, MD,[a] Konstantinos Lallas, MD,[a] Elizabeth Lazaridou, PhD,[h] Elena Sotiriou, PhD,[a] Efstratios Vakirlis, PhD,[a] and Dimitrios Ioannides, PhD[a]
Thessaloniki, Greece

Am Acad Dermatol 2020;82:398-406

- 17.3% of melanomas diagnosed by Clin/derm
- 48.1% of melanomas diagnosed by TBP
- 34.6% of melanomas diagnosed by Digital Dermoscopy

JAMA Dermatology | Original Investigation

Efficiency of Detecting New Primary Melanoma Among Individuals Treated in a High-risk Clinic for Skin Surveillance

Pascale Guitera, MD, PhD; Scott W. Menzies, MB, BS, PhD; Elliot Coates, MB, BS; Anthony Azzi, MB, BS; Pablo Fernandez-Penas, MB, BS, PhD; Alister Lilleyman, MB, BS; Caro Badcock, MApplStat, AStat; Helen Schmid, MPH; Caroline G. Watts, PhD; Helena Collgros, MB, BS; Rose Liu, MB, BS; Cathelijne van Kemenade, MPH; Graham J. Mann, MB, BS, PhD; Anne E. Cust, MPH(Hons), PhD

JAMA Dermatol. 2021;157(5):521-530. doi:10.1001/jamadermatol.2020.5651

- 31.6% of melanomas diagnosed by TBP
- 29.2% of melanomas diagnosed by Digital Dermoscopy

- 11% of melanomas diagnosed by TBP
- 89% of melanomas diagnosed by Digital Dermoscopy

Median of number of lesions monitored per patient = 38

Hôpital Saint-Louis, Paris, France

Usefulness of the 'two-step method' of digital follow-up for early-stage melanoma detection in high-risk French patients: a retrospective 4-year study

DOI: 10.1111/bjd.18006

Dear Editor, Dermatoscopy has proven more accurate than naked-eye examination,[1] and sequential digital dermatoscopic imaging (SDDI) superior to dermatoscopy alone for melanoma detection.[2] SDDI combined with total-body photography (TBP),[3] namely the 'two-step method' of digital follow-up (DFU), seems at present the best surveillance strategy for high-risk patients.[4,5]

With the aim to endorse the usefulness of this method, we retrospectively studied 148 high-risk patients with DFU at the Dermato-Oncology Unit of Hôpital Saint-Louis between 2014 and 2018. Risk characteristics included atypical mole syndrome (AMS), personal and family history of melanoma, personal history of at least two melanomas, confirmed gene mutation of *CDKN2A* or *CDK4*, and other cancer risk conditions. DFU was performed by an expert dermatoscopist with FotoFinder (FotoFinder Systems GmbH, Bad Birnbach, Germany). Baseline TBP comprised about 16 photographs of the patient's skin surface. Clear-cut malignant lesions[1,2] were excised. SDDI of atypical melanocytic lesions was performed, with short-term (3 months) or medium-term (6 months) follow-up according to the dermatoscopist's grade of suspicion. At each DFU, scheduled every 6 or 12 months, the patient's body surface was compared with baseline TBP. *De novo* lesions displaying criteria for melanoma were excised. All new or not previously registered atypical lesions were referred for SDDI. SDDI was performed for previously registered lesions, and those showing substantial modifications over time[1,2,4,5] were excised.

The patients' mean age was 46·4 ± 11·5 years; 66 (44·6%) were male and 82 (55·4%) female. Overall 109 patients (73·6%) had a history of melanoma at baseline, 64 (43·2%) were affected by AMS and 82 (55·4%) had moderate-to-severe photodamage. In total 6788 lesions were monitored, with a median of 38 [interquartile range (IQR) 28·8–55·5] per patient, over a median of 20 months (IQR 12–27, range 6–47), with a median of 3 DFUs per patient (IQR 2–4·25, range 2–9). Overall, 279 lesions (4% of monitored lesions) were excised, with a median of 2 (IQR 0–3) per patient. The melanoma detection rate was 7·9%. Twenty-two melanomas (7·9% of excised lesions) were diagnosed in 20 (13·5%) patients (Table 1). Four melanomas were detected at baseline, with two (11%) *de novo* detected by TBP and 16 (89%) by SDDI.

Melanoma detection by SDDI required a median of 2 (range 1–4) imaging follow-ups and 4 months (range 1–28). Seven melanomas (32%) were *in situ*, and 15 (68%) invasive, with a median Breslow thickness of 0·4 mm (IQR 0·2–0·6, range 0·15–2·55); 95% of melanomas were < 1 mm in Breslow thickness. The pT3b melanoma was diagnosed at baseline. Three were thin slow-growing nonlentigo maligna melanomas, with 0·15, 0·17 and 0·2 mm Breslow thickness, diagnosed after long-term SDDI of 28, 18 and 18 months, respectively. Overall 201 melanocytic naevi, mean 2 per patient, were excised, with 15·9% presenting dysplasia. Twenty-three basal cell carcinomas, 12 actinic keratoses and one Bowen disease were also excised. The number needed to

Table 1 Characteristics of melanomas detected during digital dermatoscopic follow-up (*n* = 22)

Breslow thickness (mm)[a]	
Median (IQR)	0·4 (0·2–0·6)
Range	0·15–2·55
Tis *in situ*	7 (32)
pT1a, < 0·8 mm without ulceration	12 (55)
pT1b, 0·8–1·0 mm without, or < 1·0 mm with ulceration	2 (9)
pT3b	1 (5)
Histopathological subtype	
Superficial spreading melanoma	18 (82)
Lentigo maligna	1 (5)
Invasive, not histopathologically classified	3 (14)
Body site	
Trunk	10 (45)
Lower limbs	6 (27)
Upper limbs	4 (18)
Head and neck	2 (9)
Detection modality	
Detection time (months), median (IQR)	7·1 (3·0–8·8)
Baseline	4 (18)
Total-body photography	2 (9)
SSDI	16 (73)
Short term (≤ 3 months)	6 (27)
Medium term (3–12 months)	7 (32)
Long term (≥ 12 months)	3 (14)

Data are given as *n* (%) unless stated otherwise. IQR, interquartile range; SDDI, sequential digital dermatoscopic imaging.
[a]According to the American Joint Committee on Cancer 8th edition, 2018.

Nelson KC, Swetter SM, Saboda K et al. Evaluation of the number- needed-to-biopsy metric for the diagnosis of cutaneous melanoma: a systematic review and meta-analysis. JAMA Dermatol 2019; 155:1167–74.

Study (year)	Patients receiving TBP	Total number of biopsies	Mean biopsies per patient	True positives	False positives	Number needed to biopsy	Naevus : melanoma ratio	MIS : MM ratio
Drugge (2020)[12]	218	225	2·0	67	158	3·36	2·36	1·91
Feit (2004)[5]	567	77	6·4	27	50	2·85	1·85	3·50
Goodson (2010)[7]	1076	548	0·6	28	520	19·57	18·57	1·15
Greenwald (2020)[20]	36832	1571	1·1	260	1311	6·04	5·04	2·81
Lallas (2020)[13]	977	121	NS	52	69	2·33	1·33	2·06
Mintsoulis (2016)[21]	114	267	2·3	14	253	19·10	18·07	NA
Moloney (2014)[22]	311	770	NS	82	688	9·39	8·39	NA
Risser (2007)[11]	64	53	1·9	0	53	NE	NA	NA
Salerni (2012)[19]	618	1152	1·9	98	1054	11·76	10·76	1·18
Truong (2016)[8]	926	1419	1·6	93	1326	15·26	14·26	0·98
Total	41703	6203	NA	721	5482	NA	NA	NA
Range			0·6–6·4			2·33–19·6	1·33–18·57	0·98–3·50
Weighted mean			1·6			8·6	7·6	1·68

MIS, melanoma *in situ*; MM, malignant melanoma; NA, not applicable; NE, not estimable. Values were calculated from source study data when not directly provided in the manuscript. Mean biopsies per patient = number of lesions biopsied/number of patients biopsied. True positives (MIS or MM on histopathology), false positives (neither MIS nor MM on histopathology), and number needed to biopsy (lesions biopsied for one MIS or MM) are shown for combined MIS and MM.

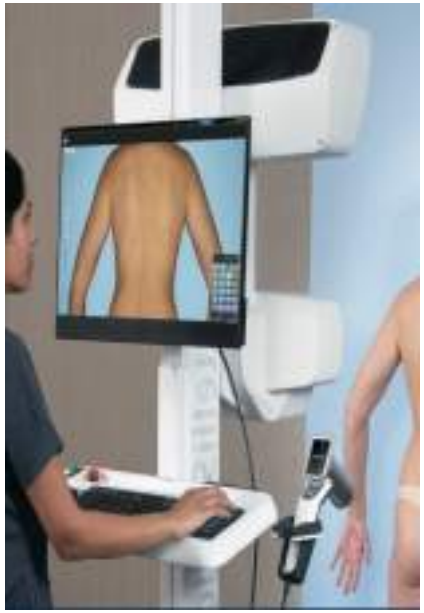
455 496 biopsies and 29 257 melanomas from 46 studies, assessed the accuracy of clinicians diagnosing melanoma. Mean 4–12% of lesions biopsied demonstrated melanoma; NNB of 14,8

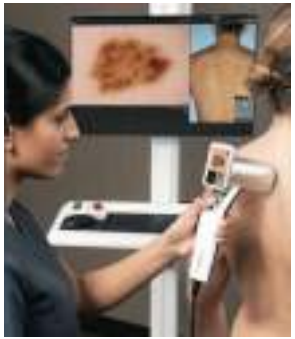
Diagnostic accuracy

1. Based on previous studies, **the sensitivity of TBP+SDD** is very low in the first visit (<25%) and increase to 100% in subsequent visits (1,2,3...) since we can assume that every MM can be detected when the tumor grows and exhibits a significant change.
2. However **benign lesions can change** as well, and this fact determines a **specificity** in this population that is very low (i.e. NNT= 1:12-14).

Metanalyses of TBP-SDD (Salerni G, Terán T, Puig S, Malvehy J, Zalaudek I, Argenziano G, Kittler H. Meta-analysis of digital dermoscopy follow-up of melanocytic skin lesions: a study on behalf of the International Dermoscopy Society. J Eur Acad Dermatol Venereol. 2013 Jul;27(7):805-14)

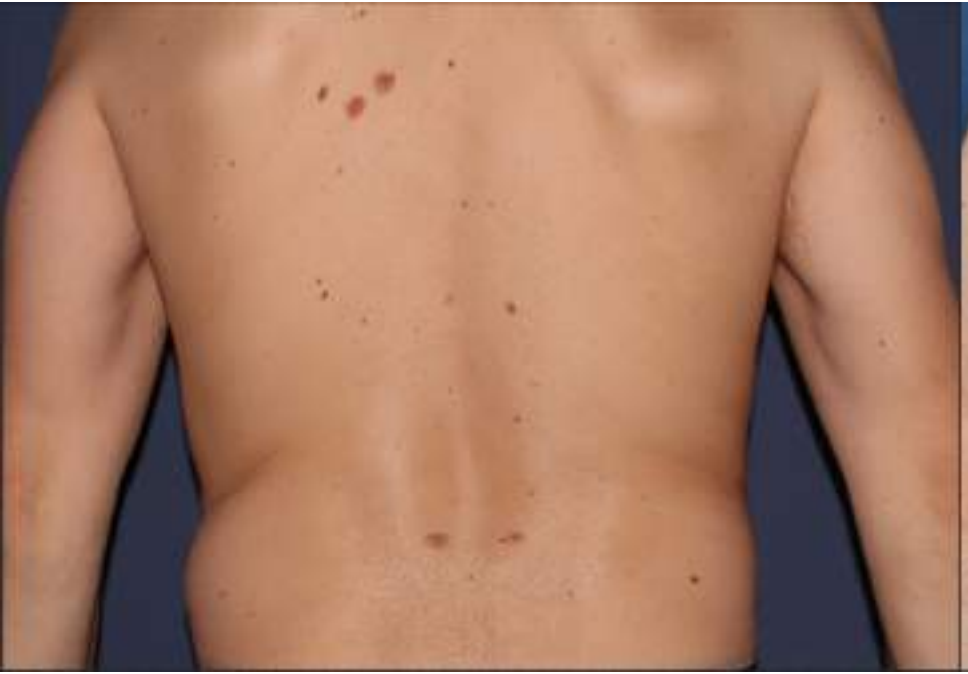
2D TBP with polarized light and high-resolution



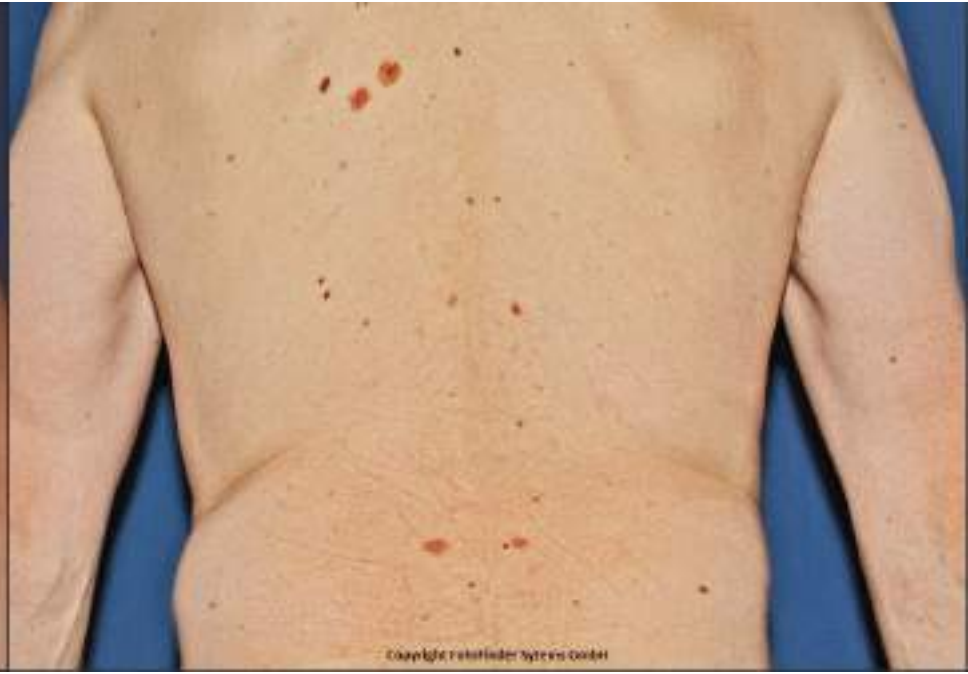


Automatic identification of lesions; detection of changes; lesion risk assessment; faster examination

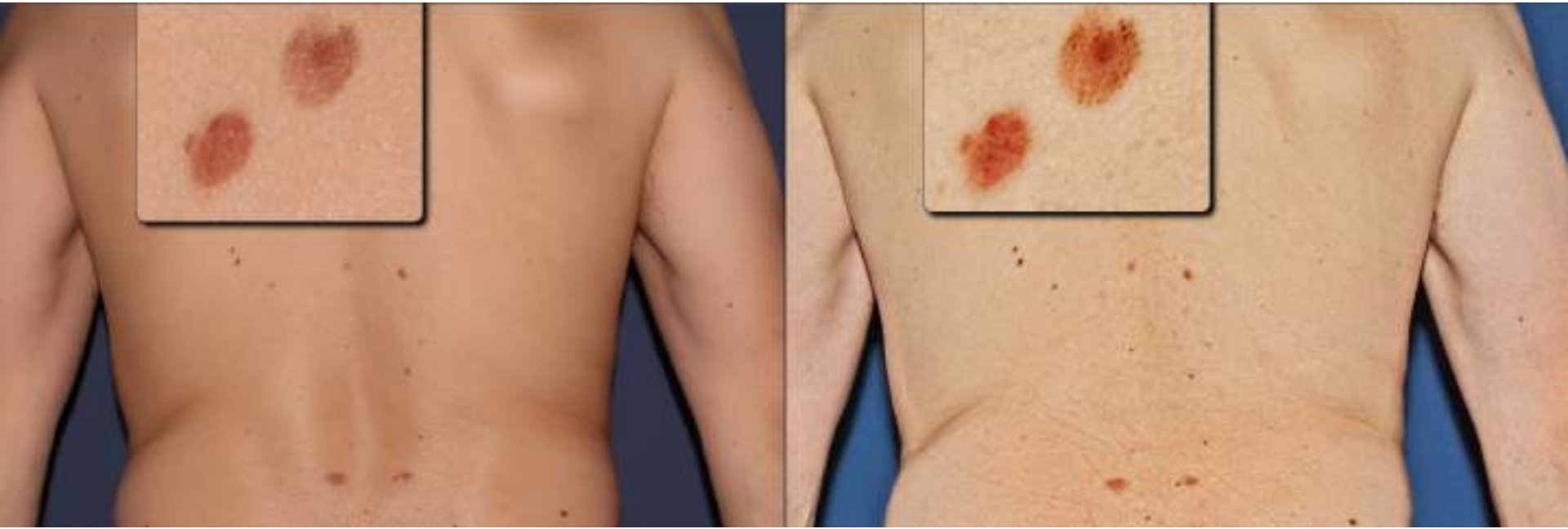
Next Gen TBM: cross-polarised light and higher resolution



Non polarized image (EOS 700D)



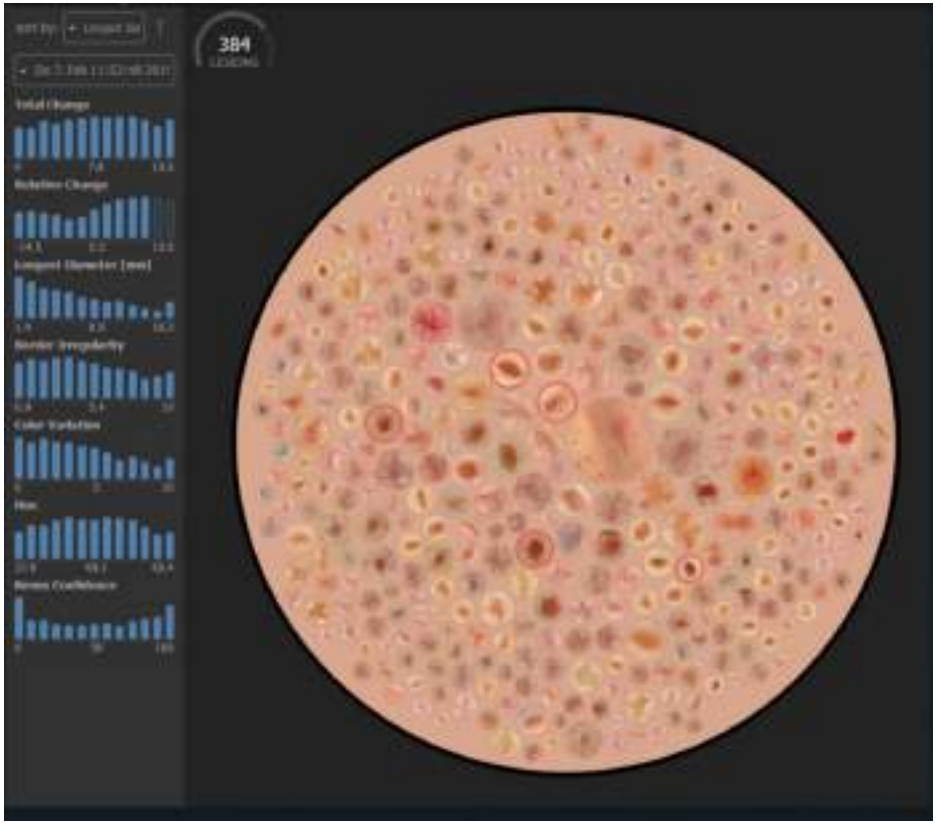
RAW processed image (full frame DSLR)



Non polarized image (EOS 700D)

RAW processed image (full frame DSLR)

3D TBP with polarized light and high ressolution



DESCRIPTION OF IMAGES OF TBP AND D-DERMOSCOPY

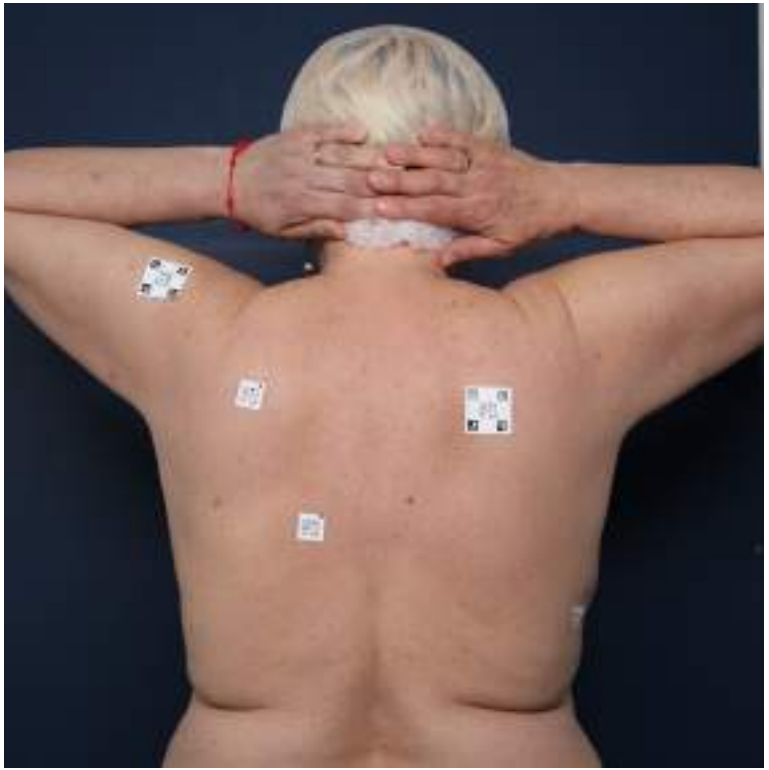
Number of Line Pairs / mm in USAF Resolving Power Test Target 1951

	Group Number											
Element	-2	-1	0	1	2	3	4	5	6	7	8	9
1	0.250	0.500	1.00	2.00	4.00	8.00	16.00	32.0	64.0	128.0	256.0	512.0
2	0.281	0.561	1.12	2.24	4.49	8.98	17.96	35.9	71.8	143.7	287.4	574.7
3	0.315	0.630	1.26	2.52	5.04	10.08	20.16	40.3	80.6	161.3	322.5	645.1
4	0.354	0.707	1.41	2.83	5.66	11.31	22.63	45.3	90.5	181.0	362.0	724.1
5	0.397	0.794	1.59	3.17	6.35	12.70	25.40	50.8	101.6	203.2	406.4	812.7
6	0.445	0.891	1.78	3.56	7.13	14.25	28.51	57.0	114.0	228.1	456.1	912.3

1951 USAF resolution test chart widely used in optical engineering laboratory work to analyze and validate imaging systems.

- Koren 2003: Norman Koren's updated resolution chart better suited for computer analysis

DESCRIPTION OF IMAGES OF TBP AND D-DERMOSCOPY



1951 USAF resolution test chart widely used in optical engineering laboratory work to analyze and validate imaging systems.

DESCRIPTION OF IMAGES OF TBP AND D-DERMOSCOPY

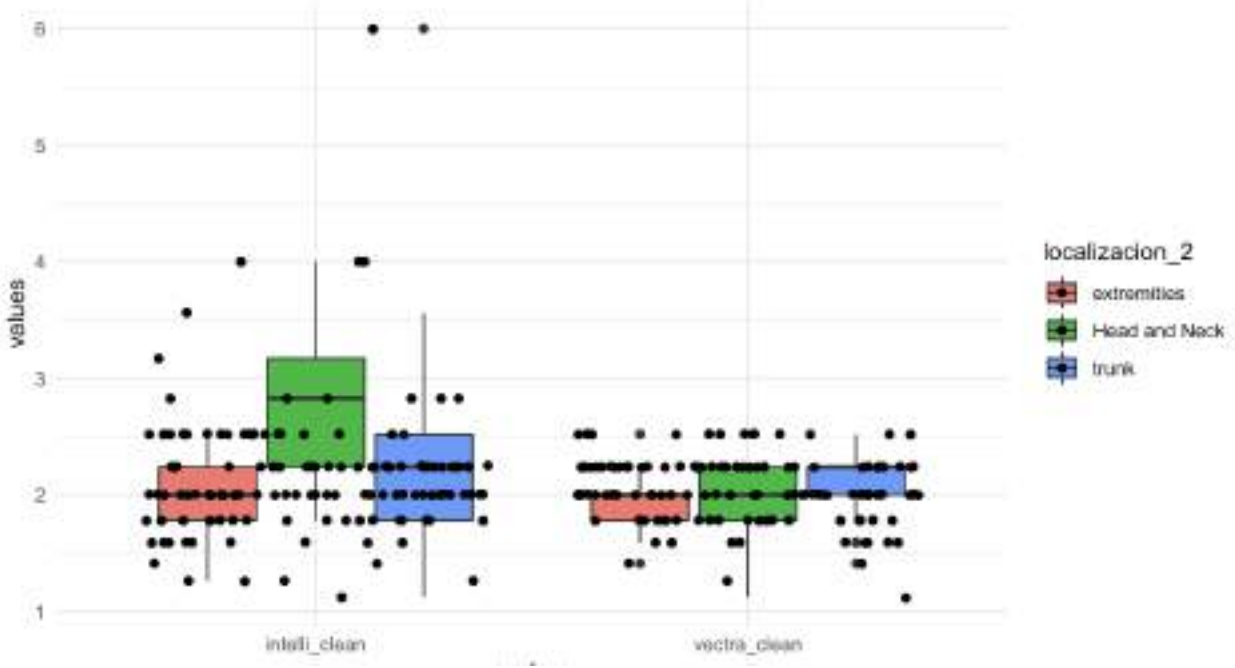


Figure 7 Graphic of 1951 USAF test mediums comparison according to body site

TBP
1951 USAF (25 cm) = 3.56 lp/mm.
1951 USAF (150 cm)= 1 lp/mm.

Cross-polarized manual dermatoscope
USAF 1951 >14.3 lp/mm.

- Better ressolution for fase with 2D TBP compared to 3D TBP due to the different focal lengths*.
- The 2D TBP ffor ace image have focal length of 85mm, while images from the lower parts of the body have a focal length of 45mm.
- These data are provided by the manufacturer but the clinical value had never been assessed before.

*Focal length is an optical property of lenses and describes their angle of view. Larger focal length produce better resolution for shorter field of view, subjects appear larger with it; on the other hand, the lower focal lengths are good to represent larger fields of view.

DESCRIPTION OF IMAGES OF TBP* / D-DERMOSCOPY

- **Dermoscopic features of skin cancer not visible in TBM* polarised images**: pigment network, streaks, dots, vessels, small globules, white-shiny streaks.

- **Dermoscopic features of skin cancer visible in TBM images**: pseudo-reticular pattern of the face in (2D TBP>3DTBP), hyperpigmentations-hypopigmentation, changes in diameter, changes in pigmentation.

Conclusions:

- TBP polarised is a technology that allows detecting changes, but cannot replace Dermoscopy.
- Both technologies should be associated.

* VECTRA 360^{R} and Intellistudio^{R} (Canfield) uses polarised light with different cameras and lighting

CLINICAL PROTOCOL HOSPITAL CLINIC OF BARCELONA

Inclusion criteria of patients

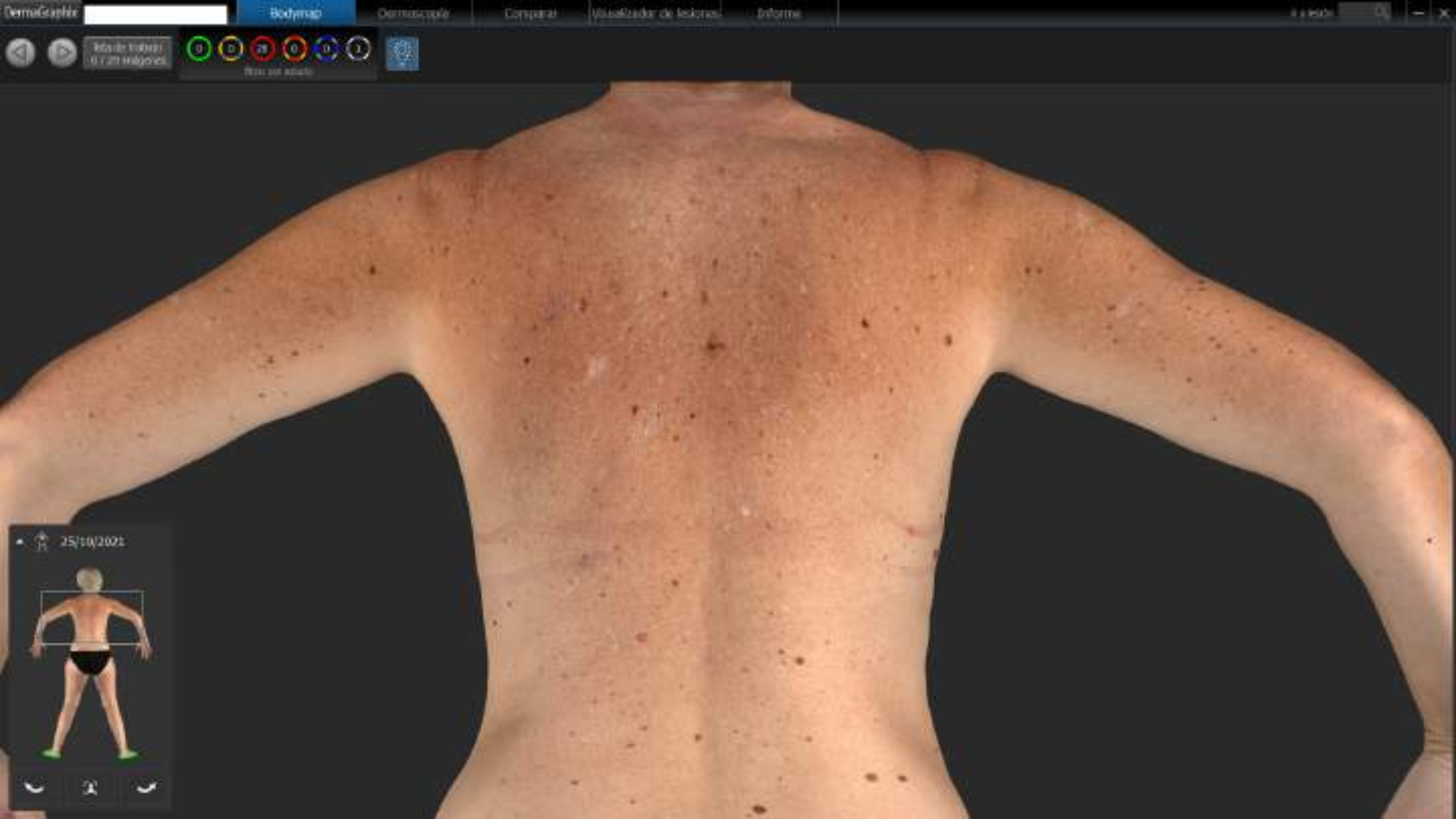
1. high-risk for melanoma due to multiple atypical melanocytic lesions +/- personal or familial melanoma +/- genetic sindromes

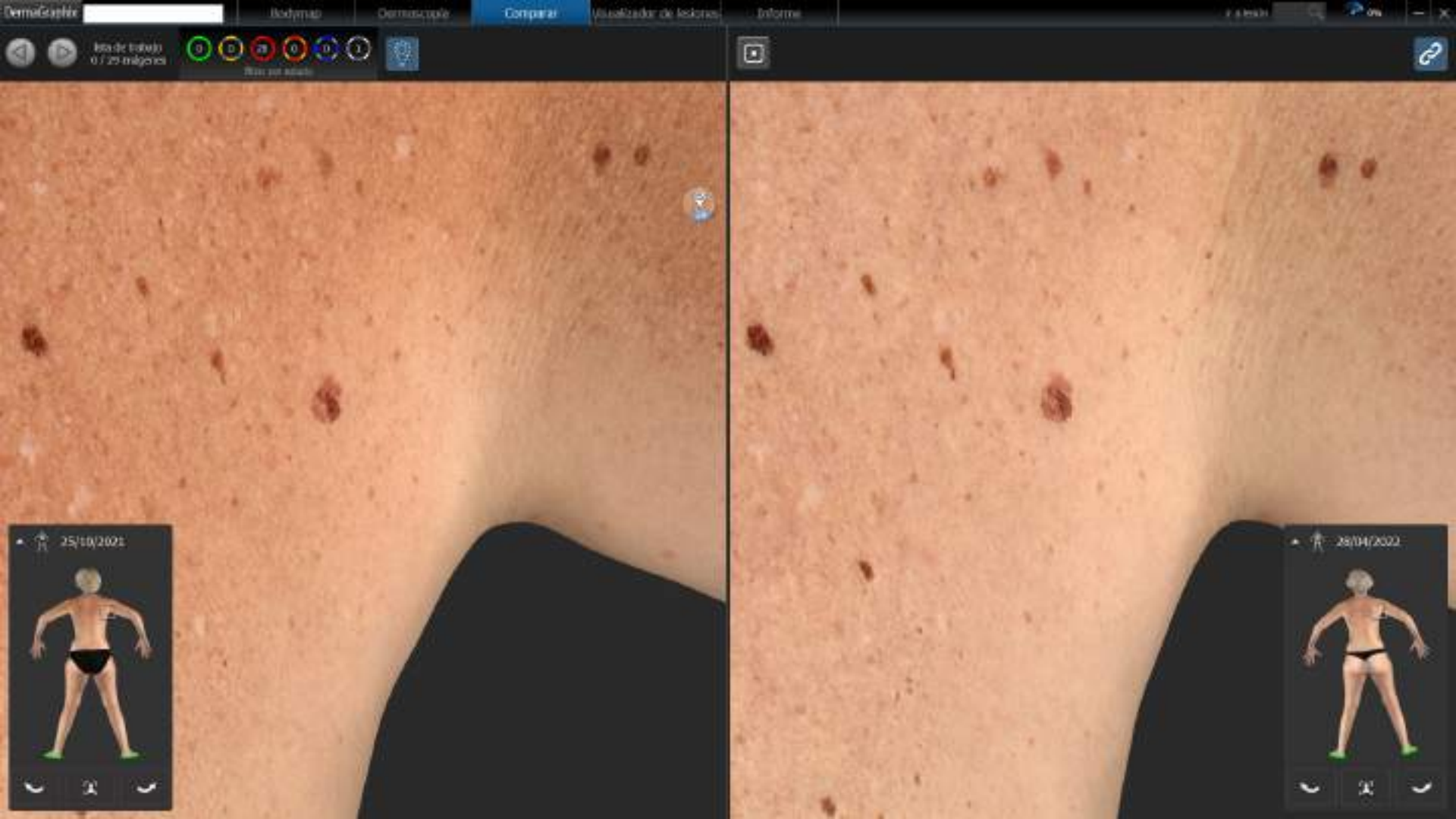
Schedule

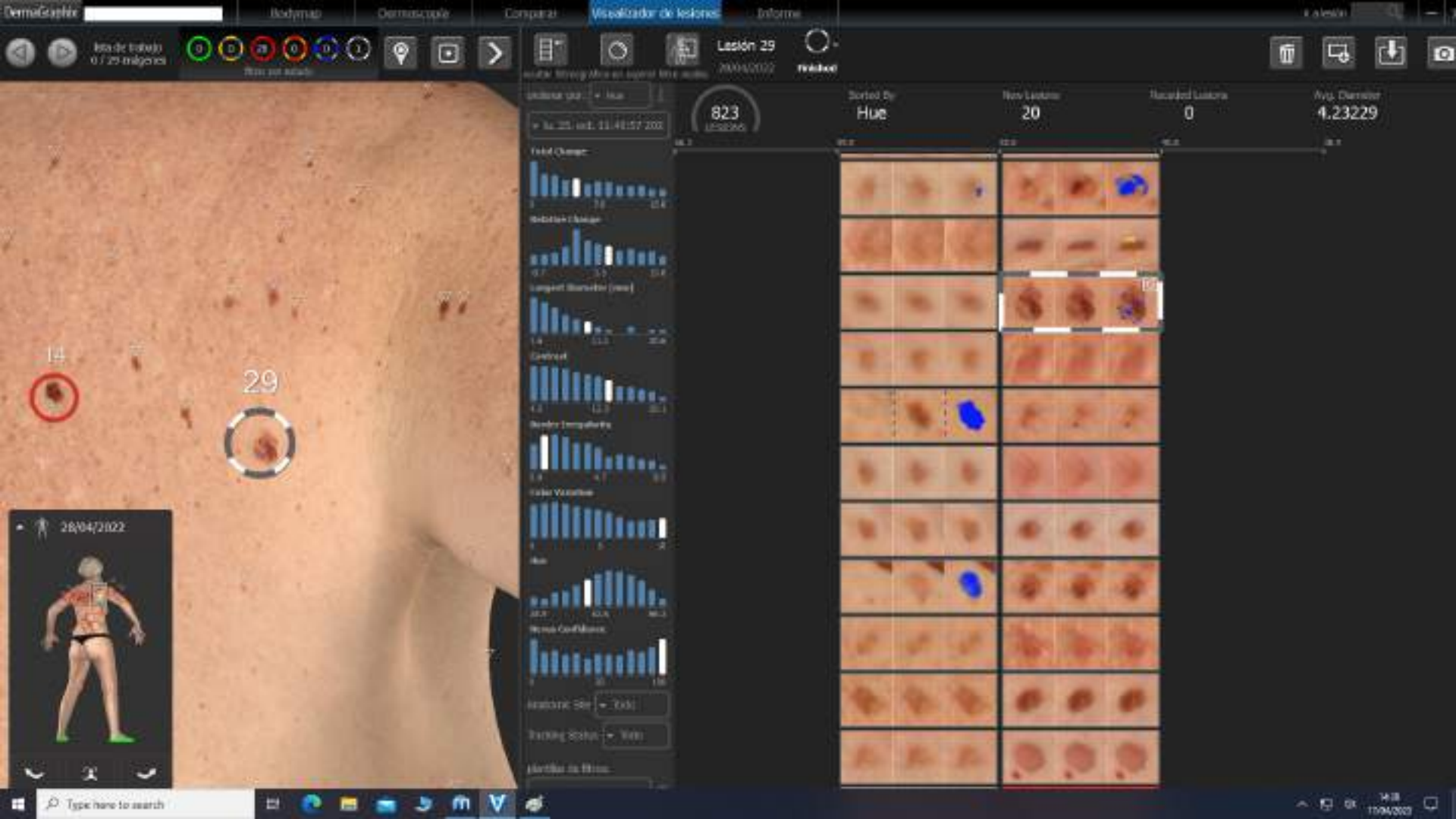
1. Base line with full body exam +Dermoscopy-TBP+SDD
2. Follow-up: Imaging (detection of changes)- full body exam with Dermoscopy

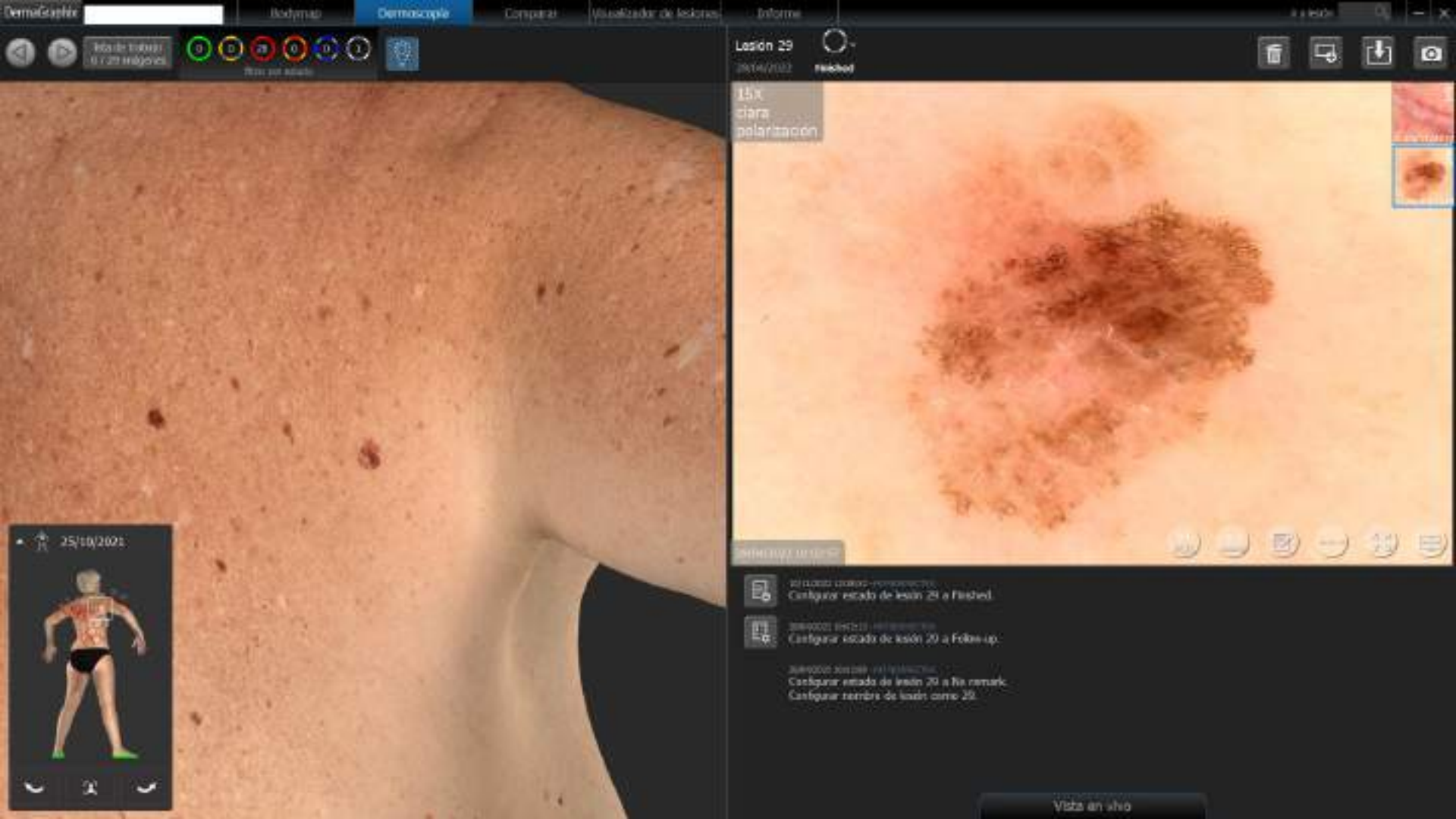
Selection of lesions for Dermoscopy image

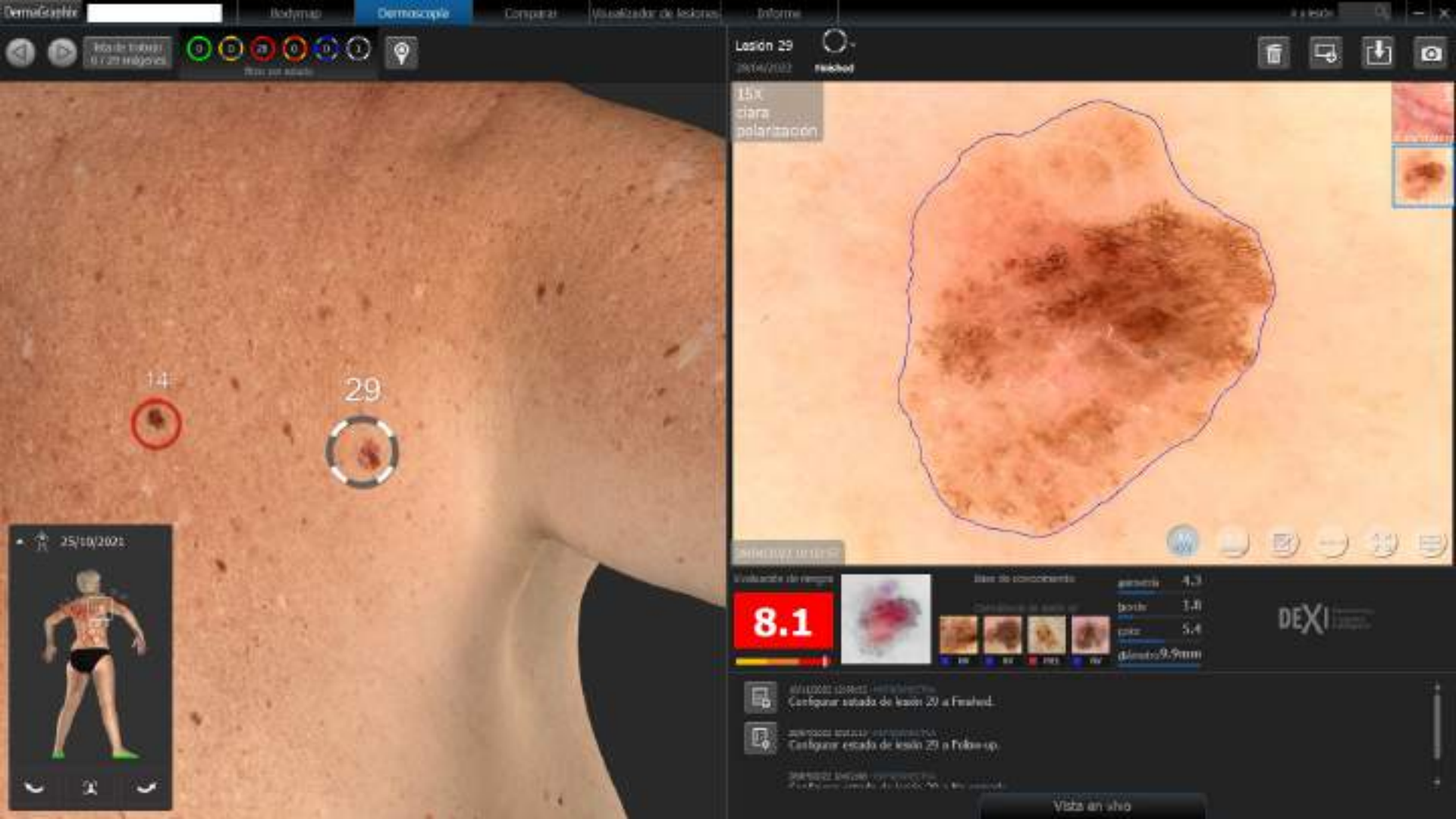
- Any lesion considered for excision;
- Lesions considered for follow-up with one or more of the following dermoscopic criterio: asymmetry, multicomponent pattern, negative of the pigmented network, regression structures, streaks, ring of globules or atypical vessels


DermaGraphir
Bodymap
Dermoscopia
Compara
Visualizador de lesiones
Informe
25/10/2021


DermaGraphix
Bodymap
Dermoscopia
Comparar
Visualizador de lesiones
Informe
Lista de trabajo
0 / 29 imágenes
Filtro sin aplicar
25/10/2021
28/04/2022

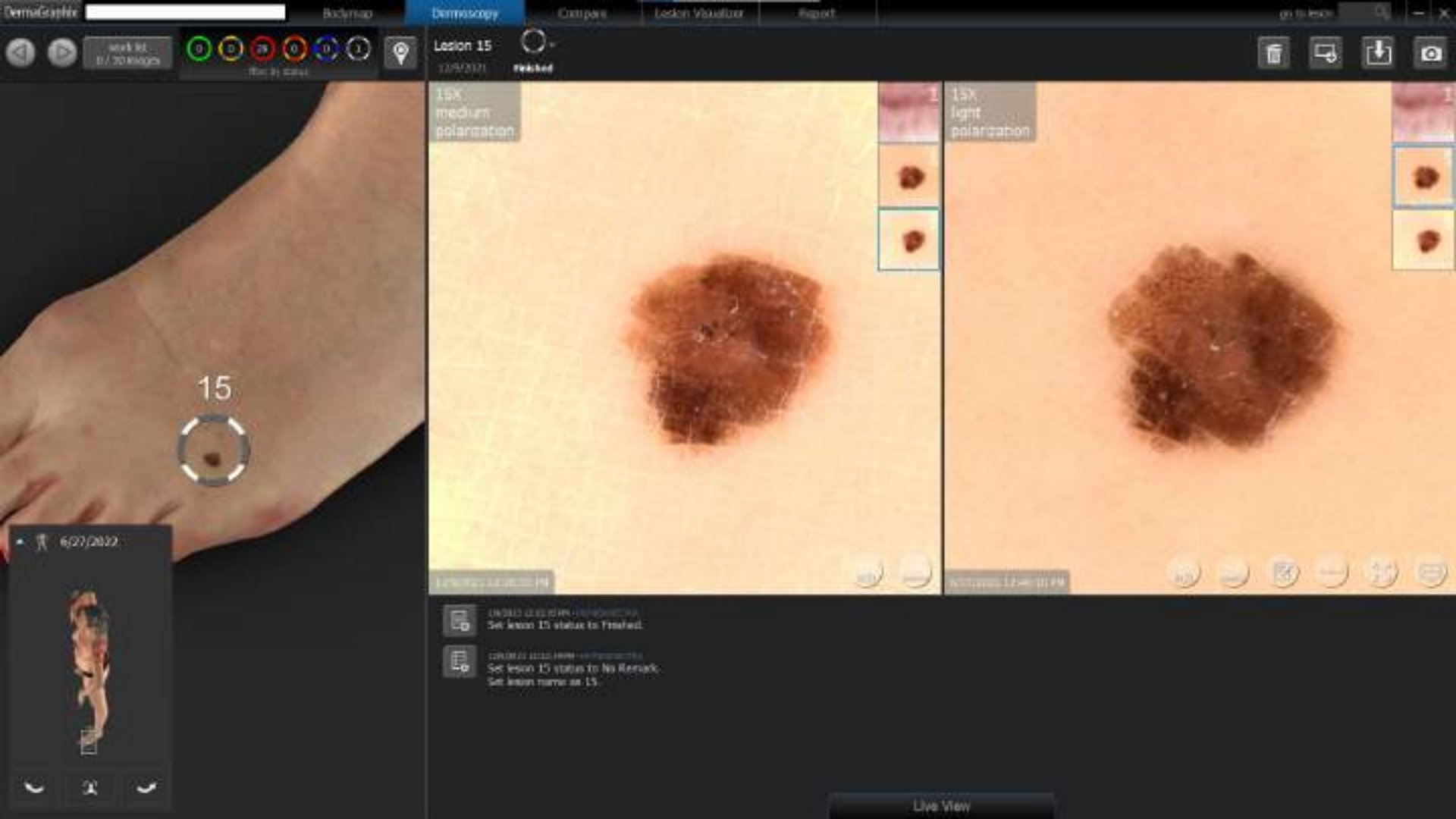

DermaGraphix
Bodymap
Dermoscopia
Comparar
Visualizador de lesiones
Informe
Lesión 29
823
Sorted By
Hue
New Lesions
20
Recorded Lesions
0
Avg. Diameter
4.23229
14
29
28/04/2022

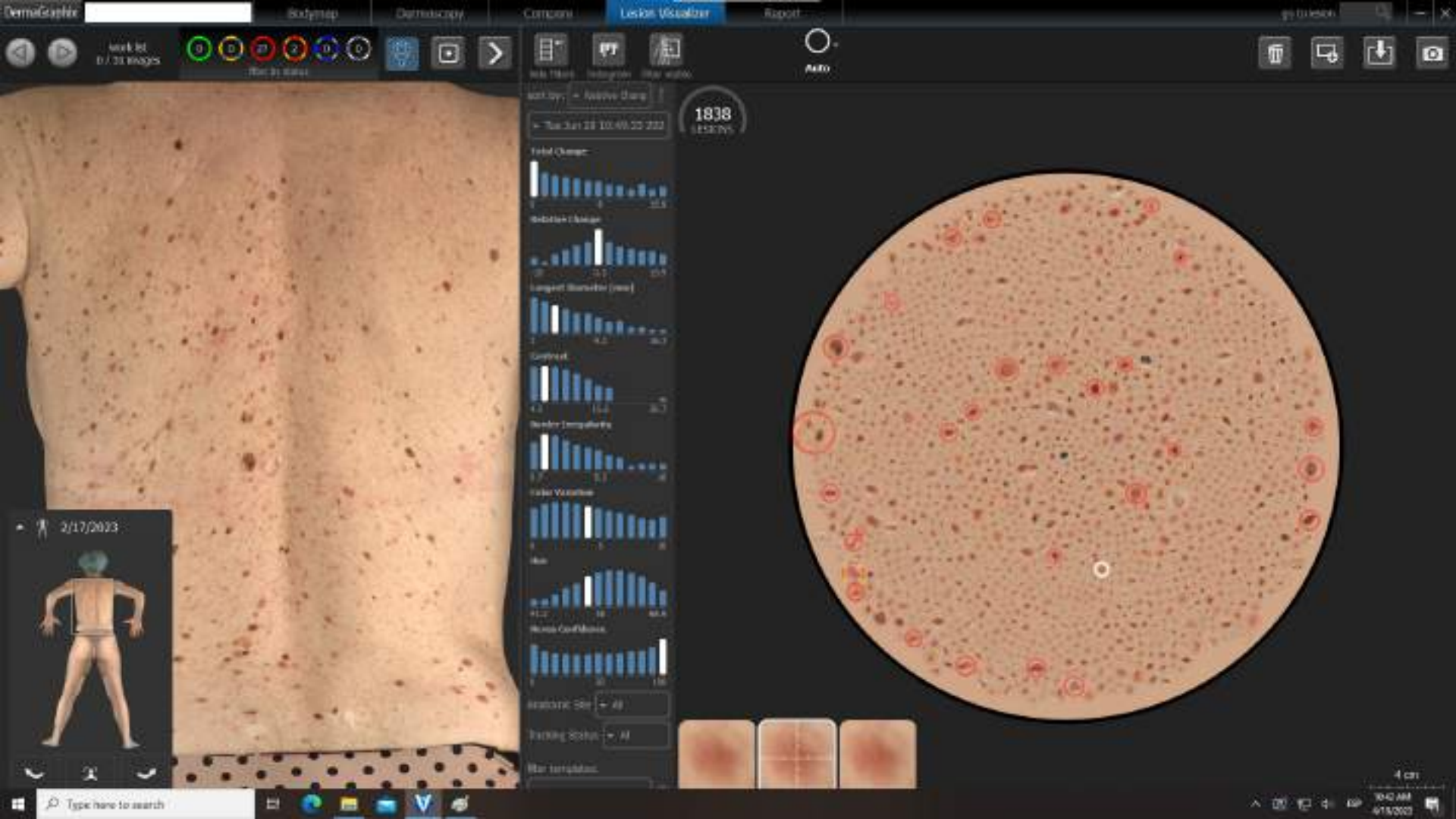

DermaGraphIr
Bodymap
Dermoscopia
Compara
Visualizador de lesiones
Informe
Lesión 29
15x
clara
polarización
Configurar estado de lesión 29 a Finished.
Configurar estado de lesión 29 a Follow-up.
Configurar estado de lesión 29 a No remark.
Configurar nombre de lesión como 29.
Vista en vivo

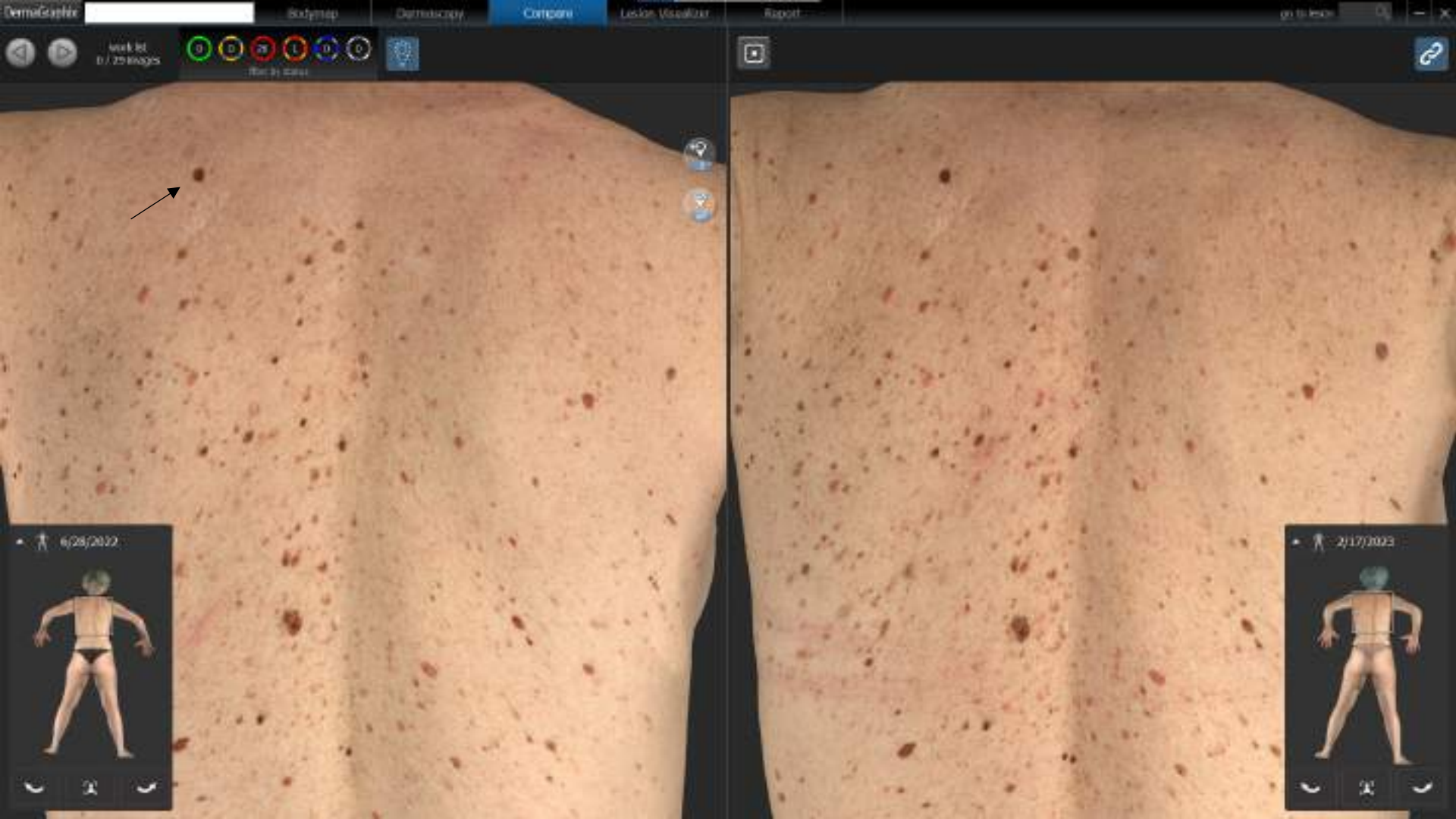

DermaGraphic
Bodymap
Dermoscopia
Compara
Visualizador de lesiones
Informe
Lesion 29
Finished
15x
clara
polarizacion
14
29
25/10/2021
8.1
Configurar estado de lesión 29 a Finished.
Configurar estado de lesión 29 a Follow-up.
Vista en vivo

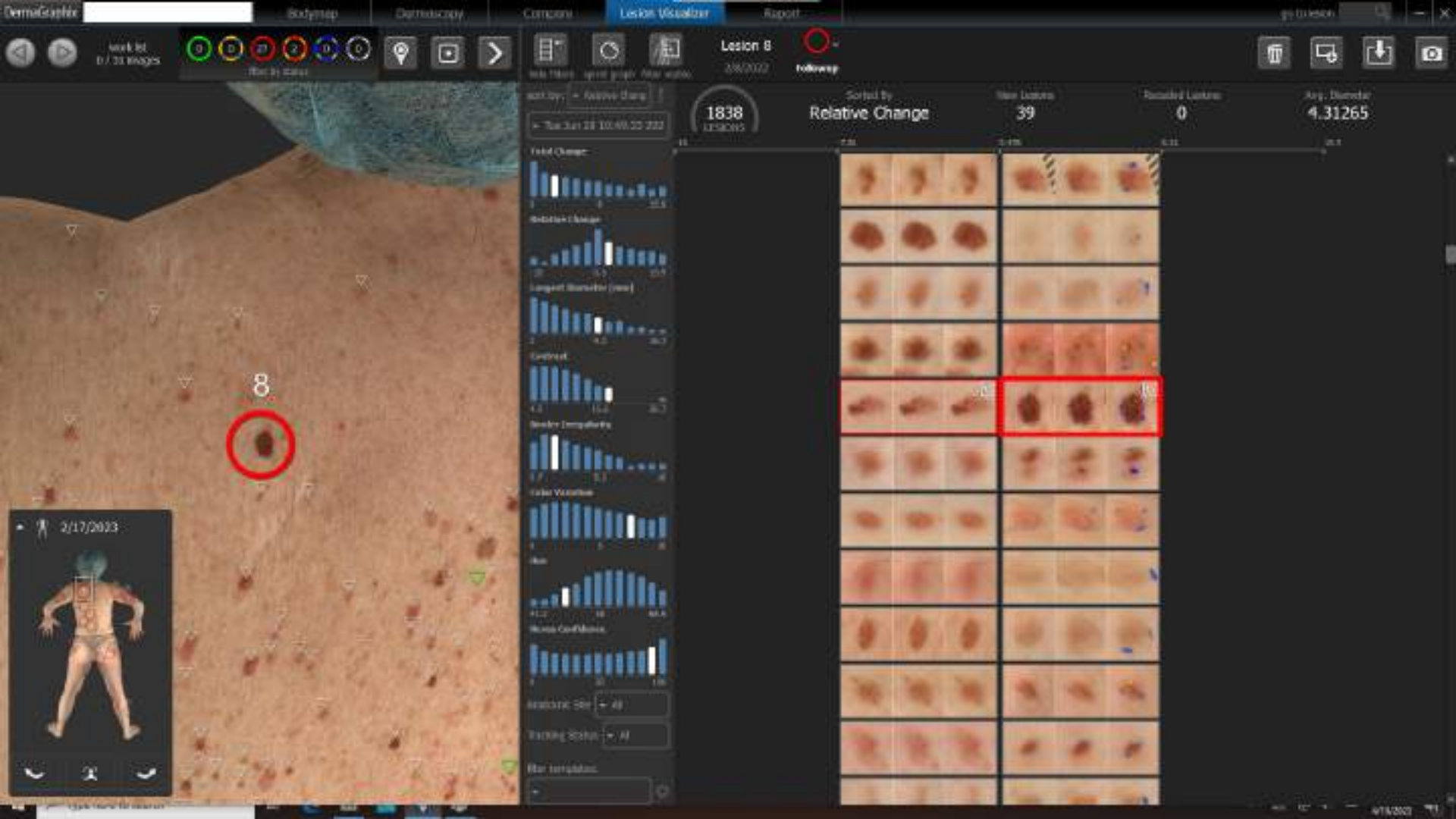

DermaGraphic
Bodymap
Dermoscopy
Compare
Lesion Visualizer
Report
work list
0 / 22 images
6/27/2022
Building Textures.. 74%


DermaGraphix
Bodymap
Dermoscopy
Compare
Lesion Visualizer
Report
work list
0 / 30 images
Lesion 15
1942
Relative Change
Non Lesions
31
Resected Lesions
0
Avg. Diameter
3.58021
15
6/27/2022


DermaGraphix
Bodymap
Dermoscopy
Compare
Lesion Visualizer
Report
Lesion 15
Finished
15X medium polarization
15X light polarization
15
6/27/2022
Set lesion 15 status to Finished
Set lesion 15 status to No Remark
Set lesion name as 15
Live View


DermaGraphix
Bodymap
Dermoscopy
Compare
Lesion Visualizer
Report
work list
0 / 33 images
1838
LESIONS
2/17/2023
4 cm


DermaGraphix
Bodymap
Dermoscopy
Compare
Lesion Visualizer
Report
work list
0 / 29 images
6/28/2022
2/17/2023


DermaGraphix
Bodymap
Dermoscopy
Compare
Lesion Visualizer
Report
Lesion 8
1838
LESIONS
Sorted By
Relative Change
New Lesions
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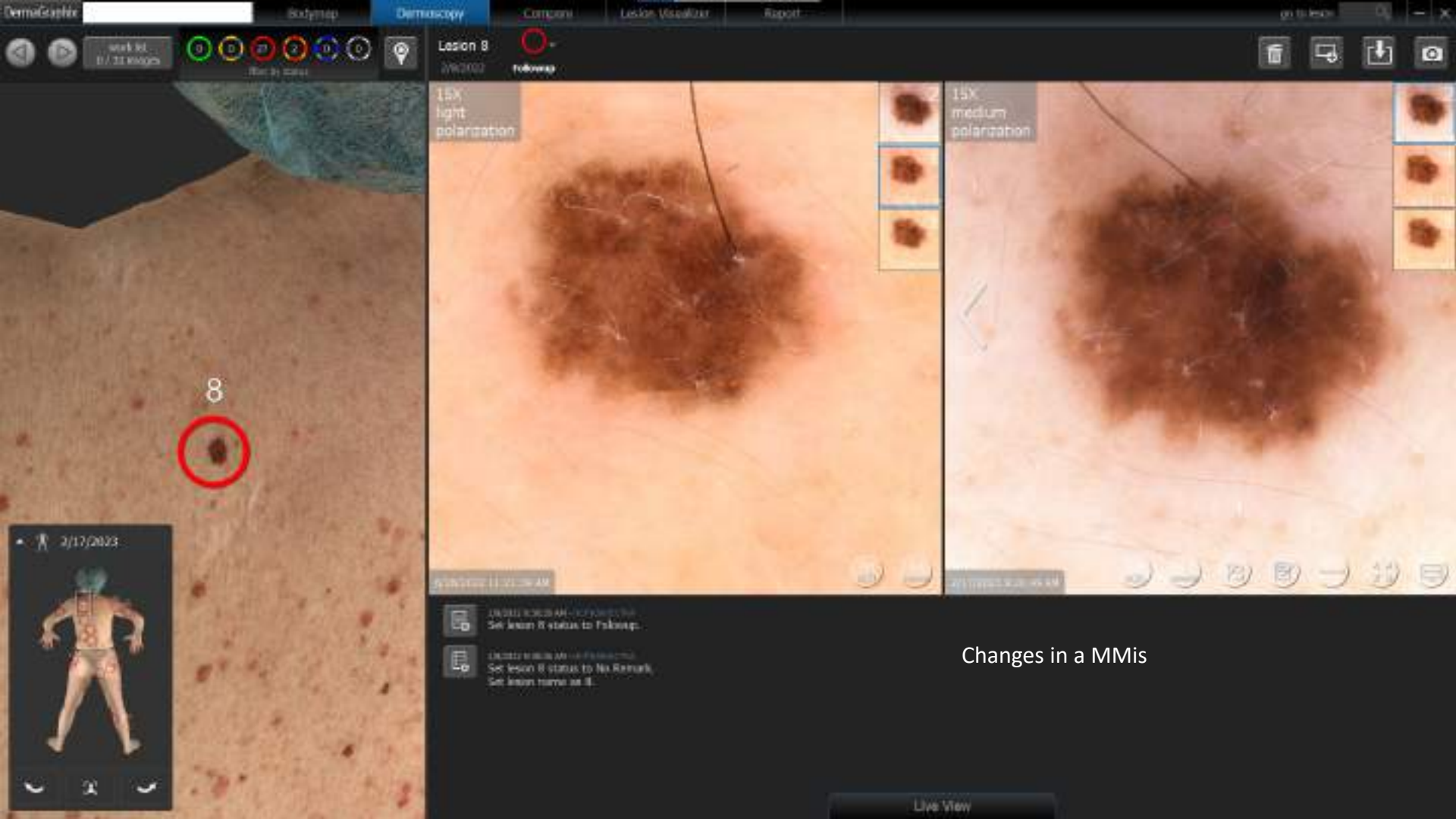
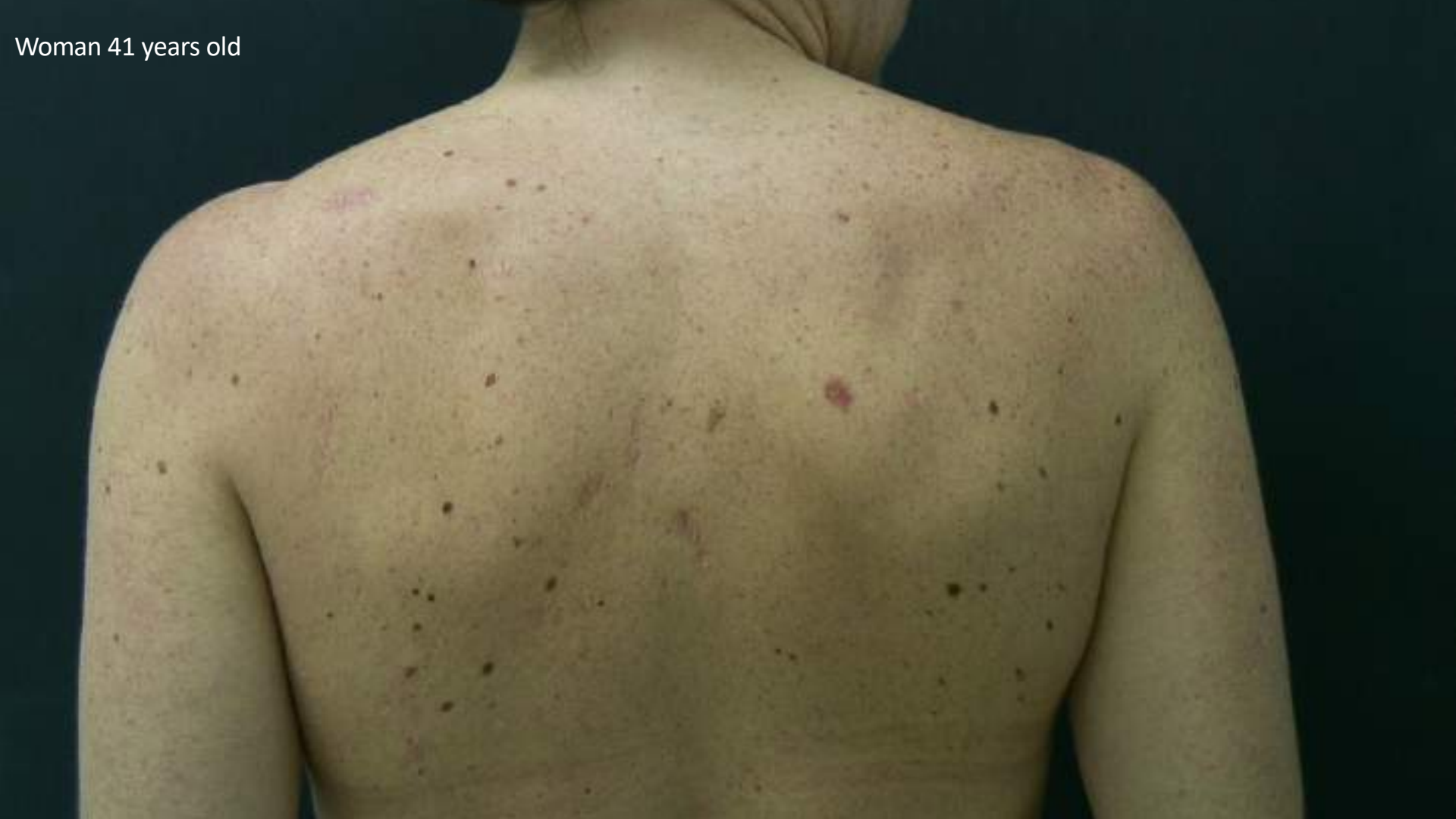
Recorded Lesions
0
Avg. Diameter
4.31265
8
2/17/2023

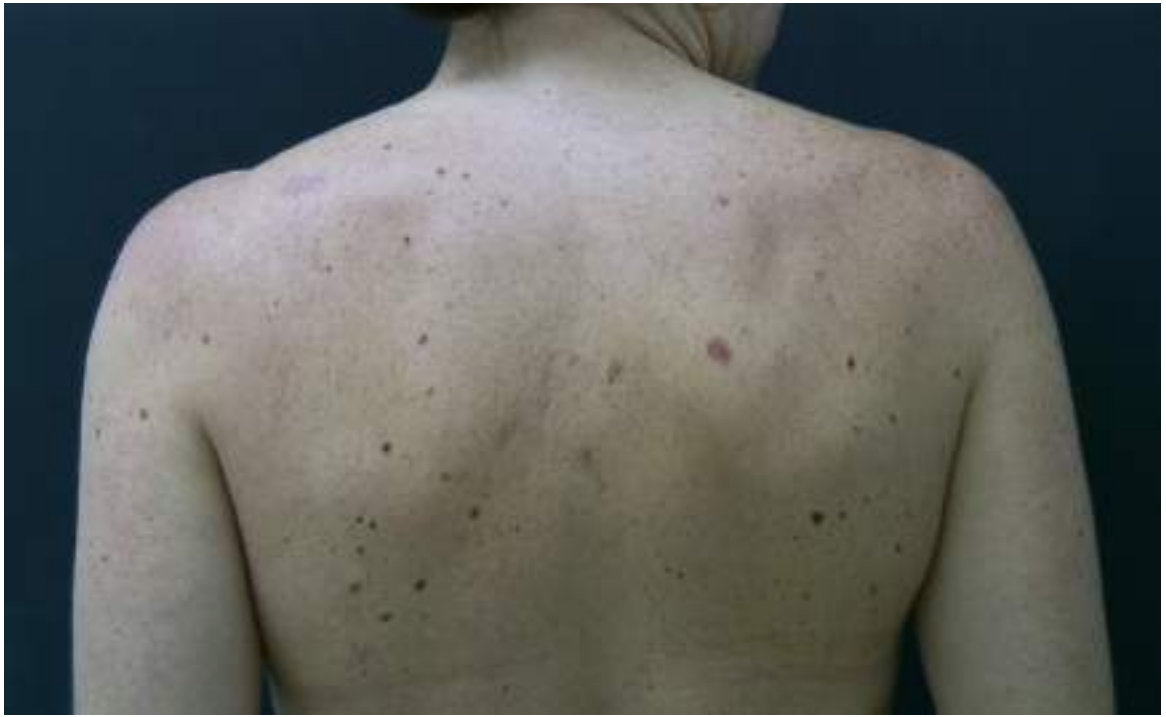


Changes in a MMis

Woman 41 years old



MELANOMA RISK SCORE: DEEP PHENOTYPING



Deep imaging (phenotype)

- Skin type
  - Skin color (spectrophotometry)
  - Hair/eyes color
- Photoaging signature
  - Atrophy
  - Hypertrophy
  - Dyschromia
  - Solar lentigos
  - Field cancerization
- Atypical mole syndrome
  - Number of melanocytic lesions
  - Diameter, color, …
  - Distribution
- Dermoscopic characteristics
  - Pigmentation
  - Pattern: reticular, globular, homogeneous,…
- Other skin lesions

Clinical information

- *45 years old woman*
- *No medications*
- *Previous MM (n=2 ; stage 1A; trunk; 2011,2014)*
- *Familial MM (3 members; Lung Ca, Breast Ca)*

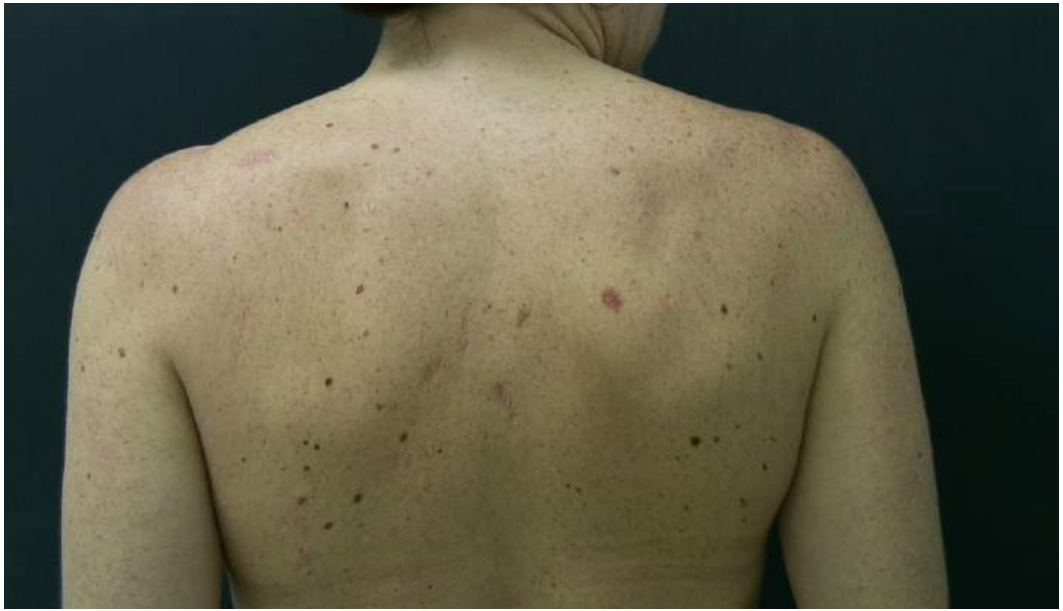
Phenotype

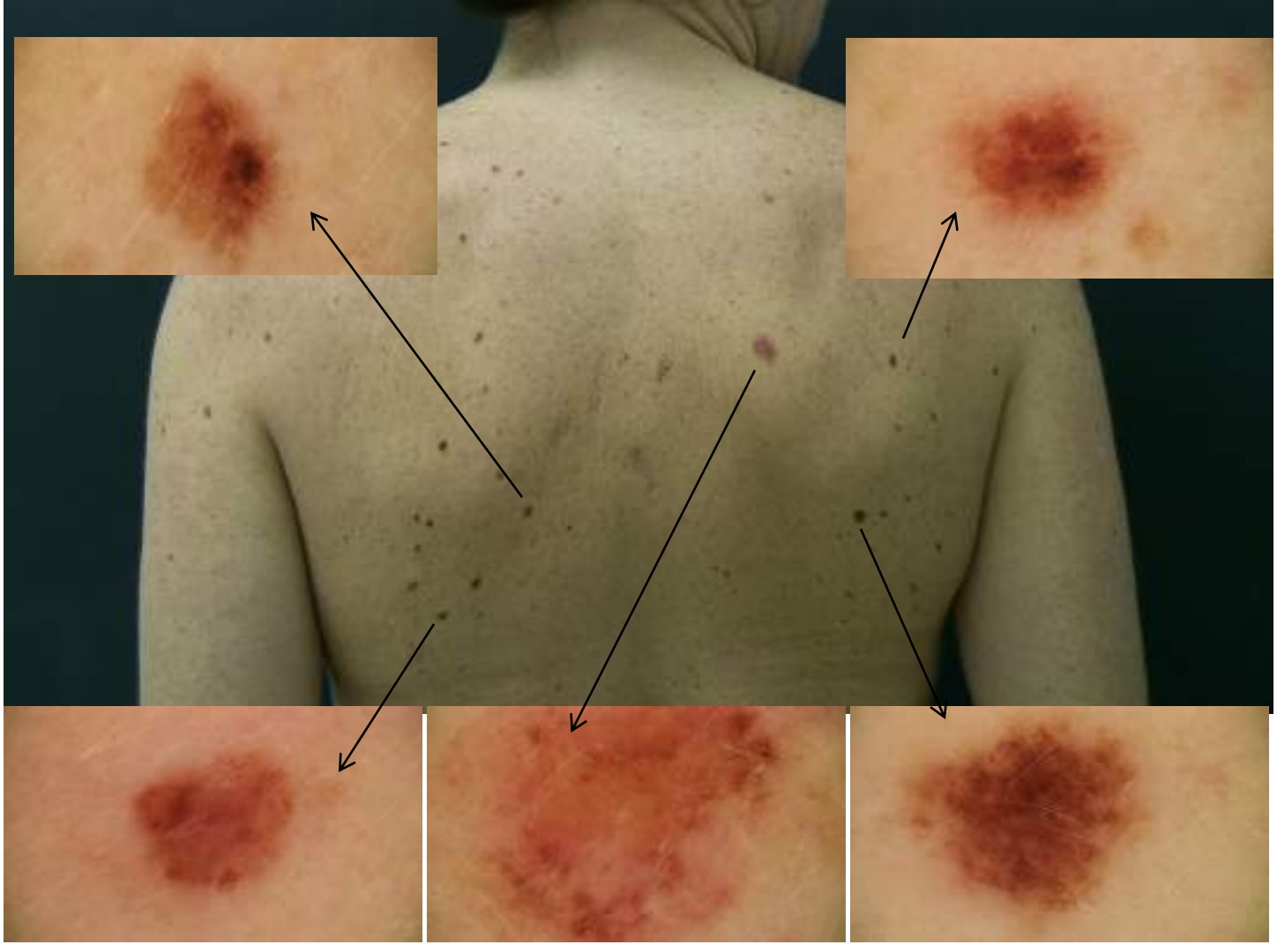
- *Skin color 3*
- *Photodamage= 3*
- *235 skin pigmented lesions*

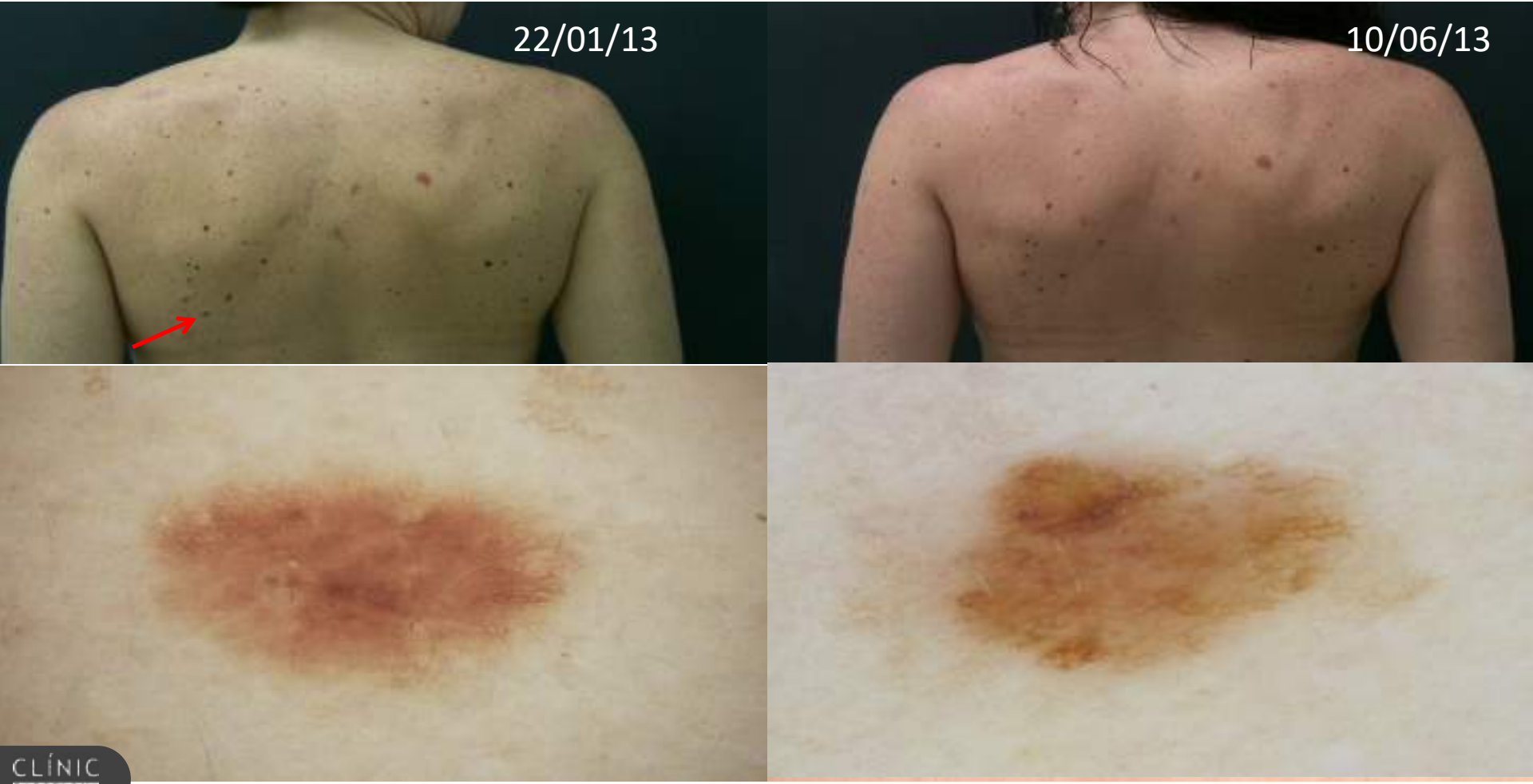
Reticular 70%; homogeneous 25%; Combination patterns 5%; Brown light and dark
Others: seb ker =3; angiomas= 11; Other: 12
Trunk=70%; lower extrem=20%; upper extre=7%;Other=3% ; special sites=0%

Genetics

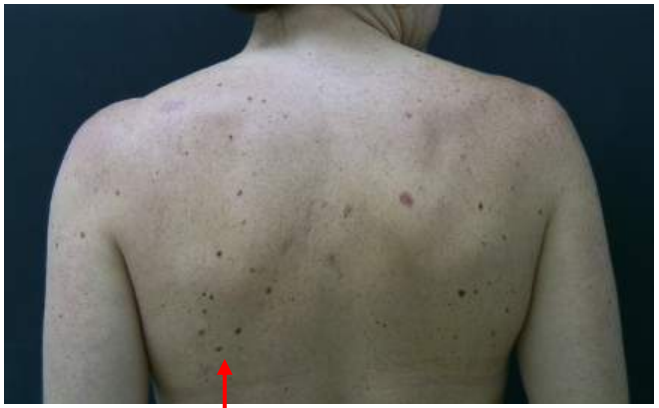
*CDKN2A G*101w
MITF wt, POT-1 wt, TERT wt
MC1R wt
Polygenic risk score= 2,45

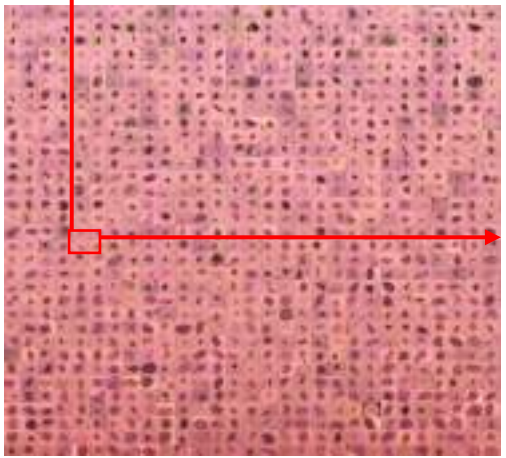


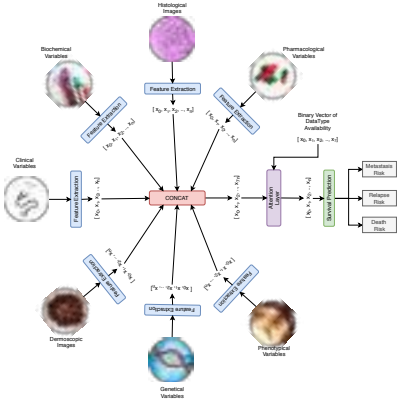



22/01/13
10/06/13

MELANOMA RISK SCORE: DEEP PHENOTYPING







Age, sex, ethnicity, geography
Skin UV damage
Skin type (spectrophotometry)

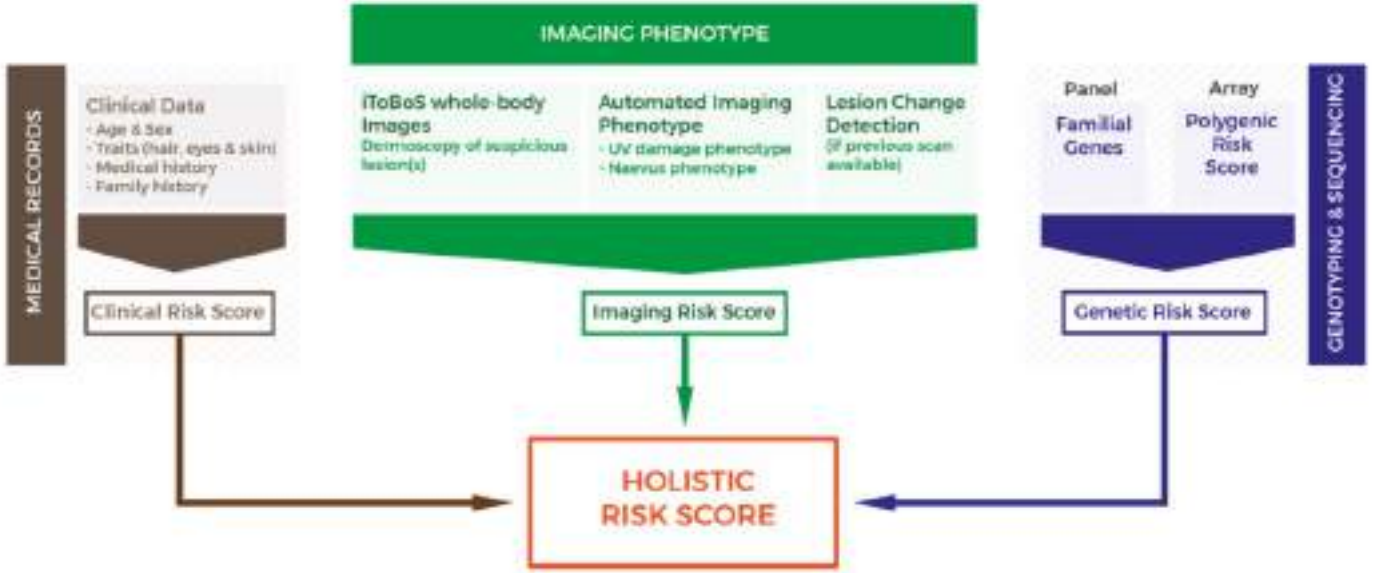
CLINICAL
Clinical background
Previous MM
Familial MM
Medications

GENETIC
*CDKN2A G*101w
MITF wt, POT-1 wt, TERT wt
MC1R wt
Polygenic risk score

DEEP IMAGING
Full body Dermoscopy

CLÍNIC BARCELONA

HOLISTIC MELANOMA RISK STRATIFICATION



Courtesy of P.Soyer

CONCLUSIONS

- Best current estimates suggest that in patients at high risk of melanoma, TBP-SDD has an acceptable NNB, when compared with previous studies using standard clinical examination without TBP.
- New technologies with faster examination and computed aided
- The combination of Deep phenotyping with machine learning can improve detection of skin cancer and risk stratification of patients

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