

# 19<sup>th</sup> EADO CONGRESS

April 20<sup>th</sup>-22<sup>nd</sup>, 2023



## Challenging cases in patients with multiple nevi

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Barcelona. Spain



# 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



**What means multiple nevi ?**





54 years old



2/27/2023











## Nevus genes

- SNPs have been significantly associated with increasing (IRF4) or decreasing (PARP1, CDK6 and PLA2G6) naevus count in multivariate shrinkage analyses with all SNPs included in the model; TERT, CDKN1B, MTAP and PARP1 were associated with either globular or reticular dermoscopic patterns ( $P < 0.05$ ). (Orlow I et al)
- MTAP rs10757257, PLA2G6 rs132985 and IRF4 rs12203592 (Kvaskoff M et al)



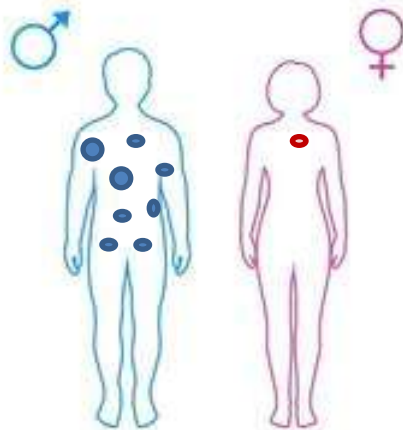
Kvaskoff M, Whiteman DC, Zhao ZZ, Montgomery GW, Martin NG, Hayward NK, Duffy DL. Polymorphisms in nevus-associated genes MTAP, PLA2G6, and IRF4 and the risk of invasive cutaneous melanoma. *Twin Res Hum Genet.* 2011 Oct;14(5):422-32. doi: 10.1375/twin.14.5.422. PMID: 21962134; PMCID: PMC3266856.

Orlow I, Satagopan JM, Berwick M, Enriquez HL, White KA, Cheung K, Dusza SW, Oliveria SA, Marchetti MA, Scope A, Marghoob AA, Halpern AC. Genetic factors associated with naevus count and dermoscopic patterns: preliminary results from the Study of Nevi in Children (SONIC). *Br J Dermatol.* 2015 Apr;172(4):1081-9.

## Common genetic variants associated with melanoma risk or naevus count in patients with wildtype *MC1R* melanoma

Neus Calbet-Llopart <sup>1,2</sup>, Marc Combalia <sup>1</sup>, Anil Kiroglu <sup>1</sup>, Miriam Potrony <sup>2,3</sup>, Gemma Tell-Marti <sup>1,2</sup>,  
Andrea Combalia <sup>1</sup>, Albert Brugués <sup>3</sup>, Sebastian Podlipnik <sup>1</sup>, Cristina Carrera <sup>1,2</sup>, Susana Puig <sup>1,2</sup>,  
Josep Malvehy <sup>1,2</sup> and Joan Anton Puig-Butillé <sup>2,4</sup>

- The rs3798577 ESR1 variant was significantly associated with lower TNC (OR 0.79, 95% CI 0.67–0.92; adjusted P = 0.003).
  - the association was maintained among women (OR 0.71, 95% CI 0.57–0.88; adjusted P = 0.002)
  - and not among men (adjusted P = 0.28).

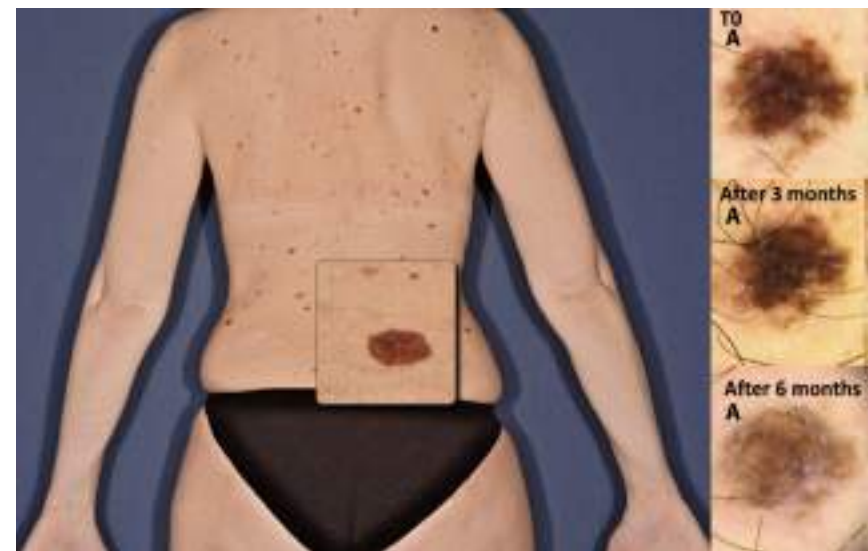




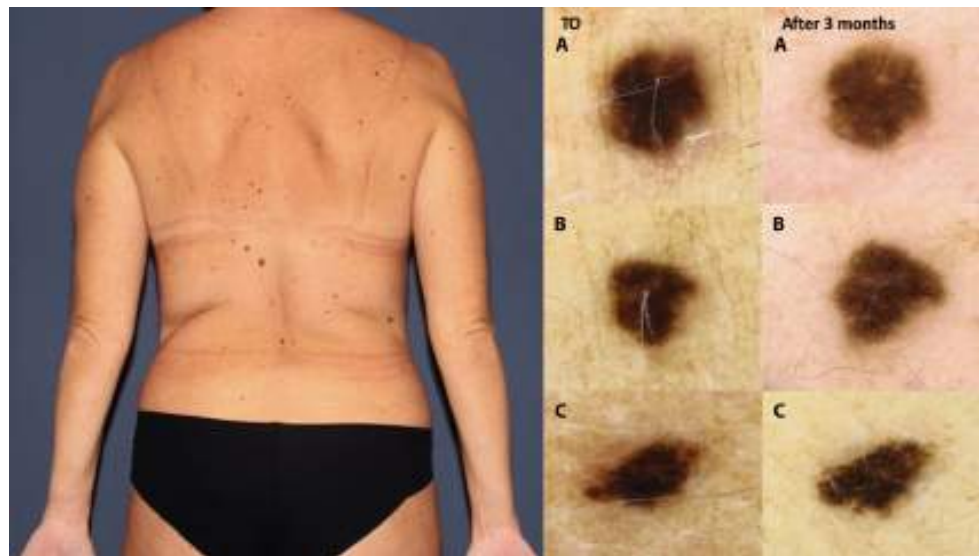
## Indications for Digital Monitoring of Patients With Multiple Nevi: Recommendations from the International Dermoscopy Society.

The results of the second round allowed us to propose the following five indications for digital monitoring in the third round:

1. Patients with more than 60 melanocytic nevi.
2. Patients with a *CDKN2A* mutation or other rarer high-risk melanoma genetic variants.
3. Patients with more than 40 melanocytic nevi and a personal history of melanoma.
4. Patients with more than 40 melanocytic nevi and red hair and/or a *MC1R* mutation
5. Patients with more than 40 melanocytic nevi and a history of organ transplantation.

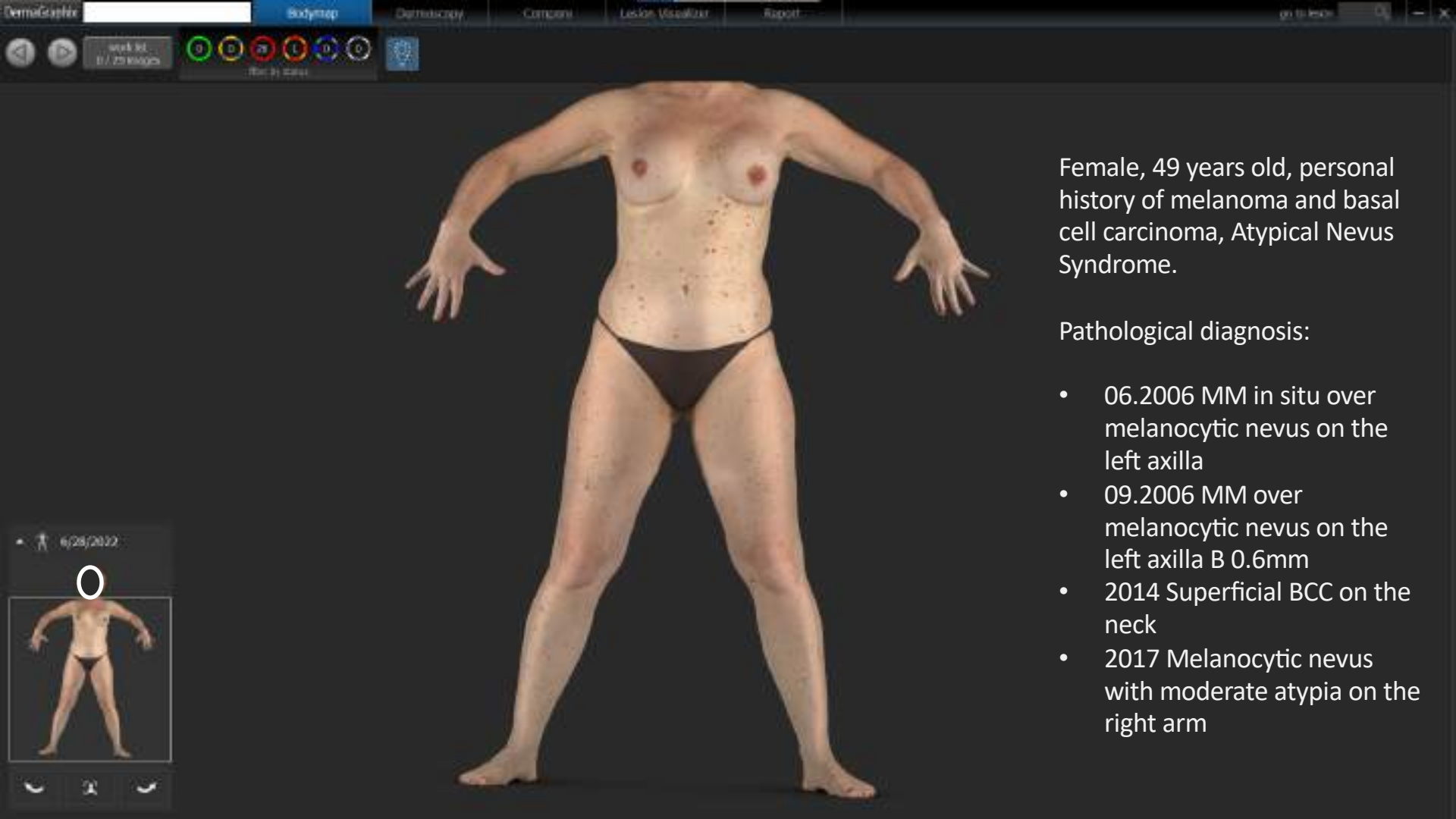


**Figure 1.** Patient with more than 60 nevi. Side by side comparison of 3 lesions (A, B, C) during follow-up. The structures over time of the first lesion (A) on the left, which was therefore excised and diagnosed as a melanoma in situ.



**Figure 2.** Patient with more than 40 nevi and previous melanoma. Lesion C showed remarkable change in the lesion after 3 months of follow-up and was therefore excised and confirmed to be a melanoma in situ, while lesion A and B did not show significant modifications.

# Case 1



Female, 49 years old, personal history of melanoma and basal cell carcinoma, Atypical Nevus Syndrome.

Pathological diagnosis:

- 06.2006 MM in situ over melanocytic nevus on the left axilla
- 09.2006 MM over melanocytic nevus on the left axilla B 0.6mm
- 2014 Superficial BCC on the neck
- 2017 Melanocytic nevus with moderate atypia on the right arm



Back 1st 11 / 23 Images

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Back to start



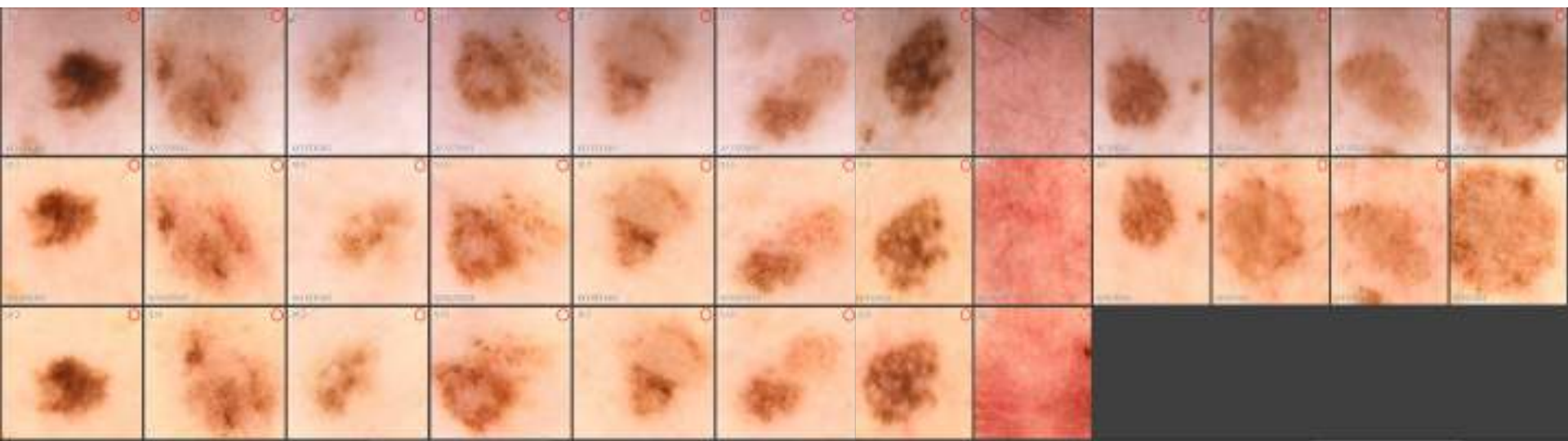
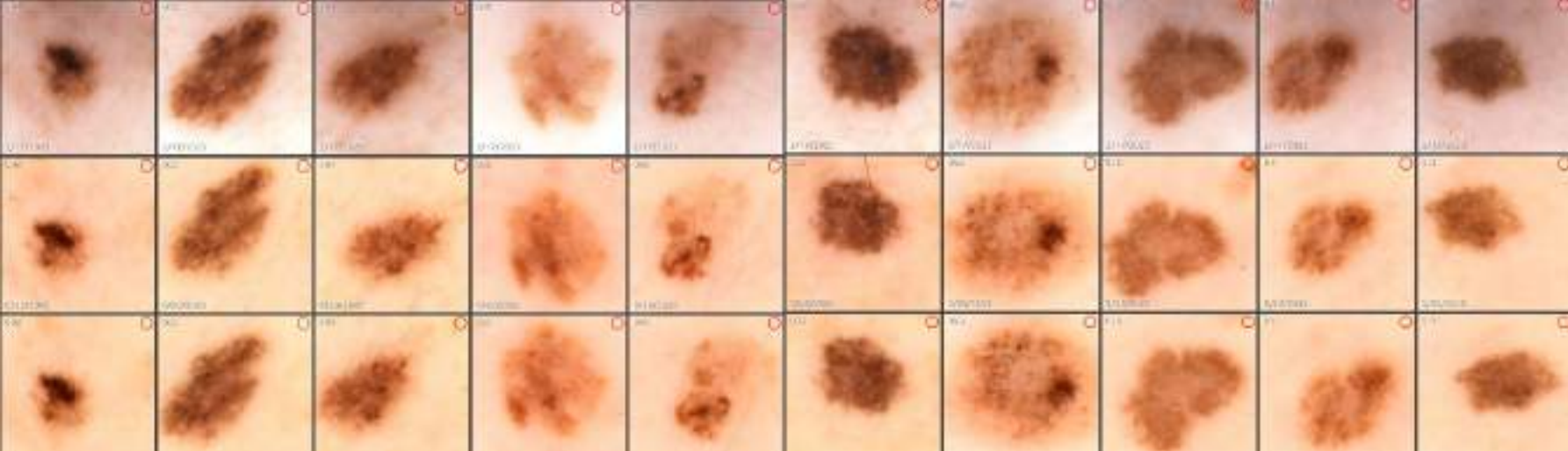
6/28/2022

Navigation icons: a left arrow, a person icon, and a right arrow.



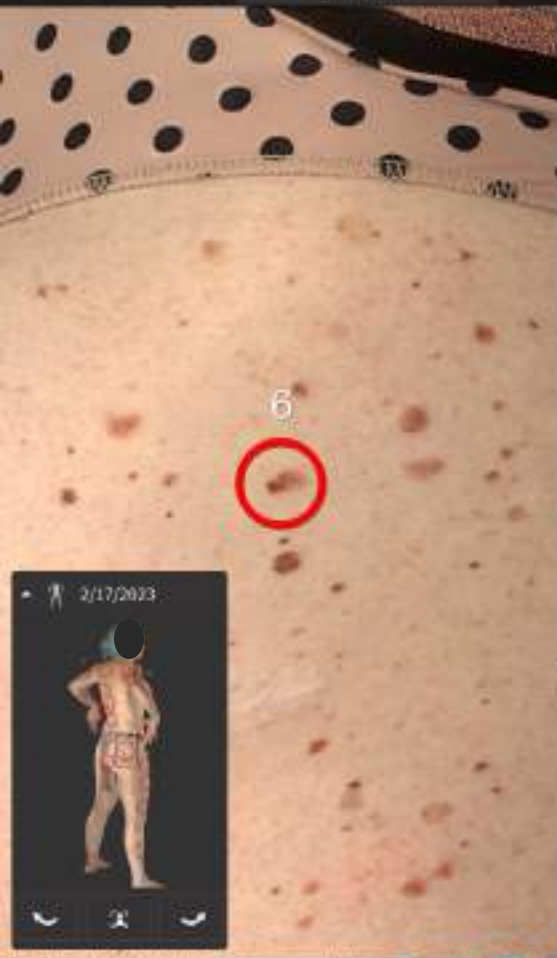












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[6] 1/17/2023 11:00:39 AM - 11:00:39 AM  
Set lesion 6 status to Following.  
[6] 1/17/2023 11:00:39 AM - 11:00:39 AM  
Set lesion 6 status to No Remark.  
Set lesion name as 6.

2/17/2023 9:00:57 AM  
[undo] [redo] [copy] [paste] [delete] [refresh] [help]

Live View



DermaStation
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Lesion 6
2/17/2023
Following

6

15X light polarization

15X light polarization

2/17/2023 11:26:10 AM

**Risk assessment**

**2.1**

**Asymmetry** 5.1

**Border** 2.1

**Color** 6.2

**Structure** 3.0mm

2/17/2023 4:02:37 AM

**Risk assessment**

**9.2**

**Asymmetry** 3.0

**Border** 2.0

**Color** 4.0

**Structure** 3.4mm

2/17/2023 11:26:10 AM - **Following**  
Set lesion 6 status to Following.

2/17/2023 4:02:37 AM - **No Remark**  
Set lesion 6 status to No Remark.  
See lesion history on R.

Live View

4/18/2023

← → 1/31 images 0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46 47 48 49 50 51 52 53 54 55 56 57 58 59 60 61 62 63 64 65 66 67 68 69 70 71 72 73 74 75 76 77 78 79 80 81 82 83 84 85 86 87 88 89 90 91 92 93 94 95 96 97 98 99 100

Lesion 24  
 6/18/2022  
 Followup

🗑️ 🖨️ ⬇️ 📷



2/17/2023

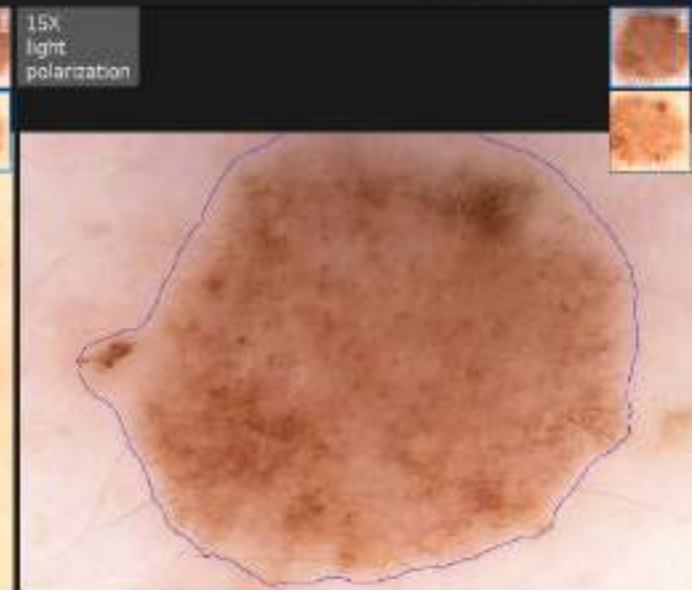
6.1 15X 6.1 15X 7M P3 📧 🔍 ⌂ ☰

- 📄 6/18/2022 11:49:51 AM - 6/18/2022 11:49:51 AM  
 Set lesion 24 status to Followup.
- 📄 6/18/2022 11:49:51 AM - 6/18/2022 11:49:51 AM  
 Set lesion 24 status to No Remark.  
 Set lesion name as 24.

Live View

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Lesson 24  
 6/18/2022  
 Followup



6/18/2022 11:49:44 AM

Max assessment: **0.1**  
 Extended grayscale  
 Asymmetry: 2.2  
 Border: 1.0  
 Color: 3.3  
 Diameter: 12.6mm

2/17/2023 9:13:17 AM

Max assessment: **0.1**  
 Extended grayscale  
 Asymmetry: 2.0  
 Border: 1.0  
 Color: 3.1  
 Diameter: 13.2mm

6/18/2022 11:49:44 AM - 6/18/2022 11:49:44 AM  
 Set lesion 24 status to Followup.

6/18/2022 11:49:44 AM - 6/18/2022 11:49:44 AM  
 Set lesion 24 status to No Remark.  
 Set lesion number to 24.

Live View

dermographix
Bodymap
Dermoscopy
Lesion Viewer
Report
go to lesion

work for 0 / 31 images
view for device
take image
split stack
flow mode
Lesion 8
2/8/2023
followup

Sort by
Relative Change
1838 LESIONS
New Lesions 39
Resolved Lesions 0
Avg. Diameter 4.31265

8

2/17/2023

Total Change
Relative Change
Lesion Diameter Growth
Contrast
Border Irregularity
Color Variance
Fluor
Seven Landmarks
Asymetric Size
Tracking Status
Use Inspector

10
13

The screenshot displays the Dermographix software interface. On the left, a large dermoscopy image shows a skin lesion circled in red and labeled '8'. Below it is a bodymap showing the location of the lesion on a human torso. The right side of the interface features a grid of lesion images, with the 10th and 13th images in the second row highlighted in red. The top navigation bar includes tabs for 'Bodymap', 'Dermoscopy', 'Lesion Viewer', and 'Report'. The top right corner has a 'go to lesion' button. The top center shows 'Lesion 8' and '2/8/2023'. The top right corner also displays '1838 LESIONS', 'New Lesions 39', 'Resolved Lesions 0', and 'Avg. Diameter 4.31265'. The left sidebar contains various analysis tools and filters, including 'Total Change', 'Relative Change', 'Lesion Diameter Growth', 'Contrast', 'Border Irregularity', 'Color Variance', 'Fluor', 'Seven Landmarks', 'Asymetric Size', and 'Tracking Status'. The bottom left corner shows a date '2/17/2023' and a small bodymap icon.

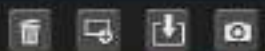


Lesion 8

2/17/2023

-

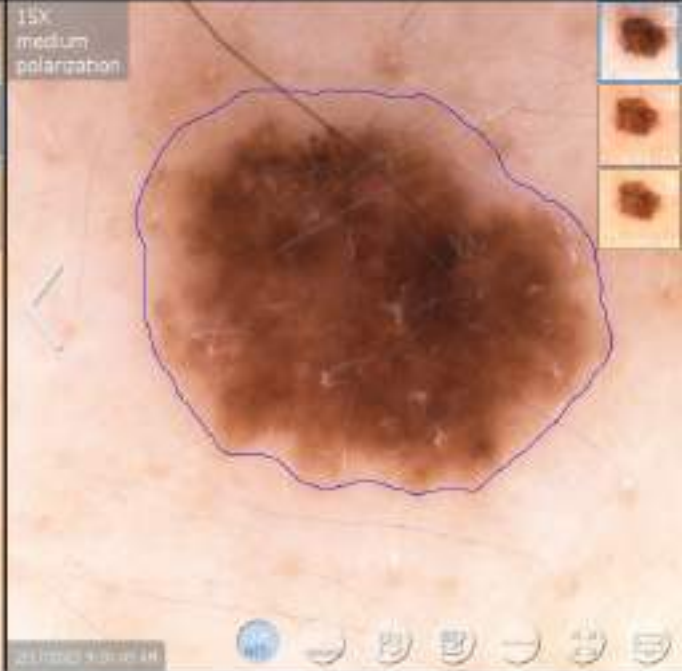
Following



-  2/17/2023 11:20:26 AM - 11:20:26 AM  
Set lesion 8 status to Following.
-  2/17/2023 11:20:46 AM - 11:20:46 AM  
Set lesion 8 status to No Remark.  
Set lesion name as 8.



Lesion 8  
2/17/2023  
Followup



Risk assessment: **0.9**

Asymmetry: 2.4  
Border: 1.3  
Color: 4.2  
Diameter: 6.7mm

Risk assessment: **1.4**

Asymmetry: 2.0  
Border: 0.8  
Color: 4.0  
Diameter: 7.8mm

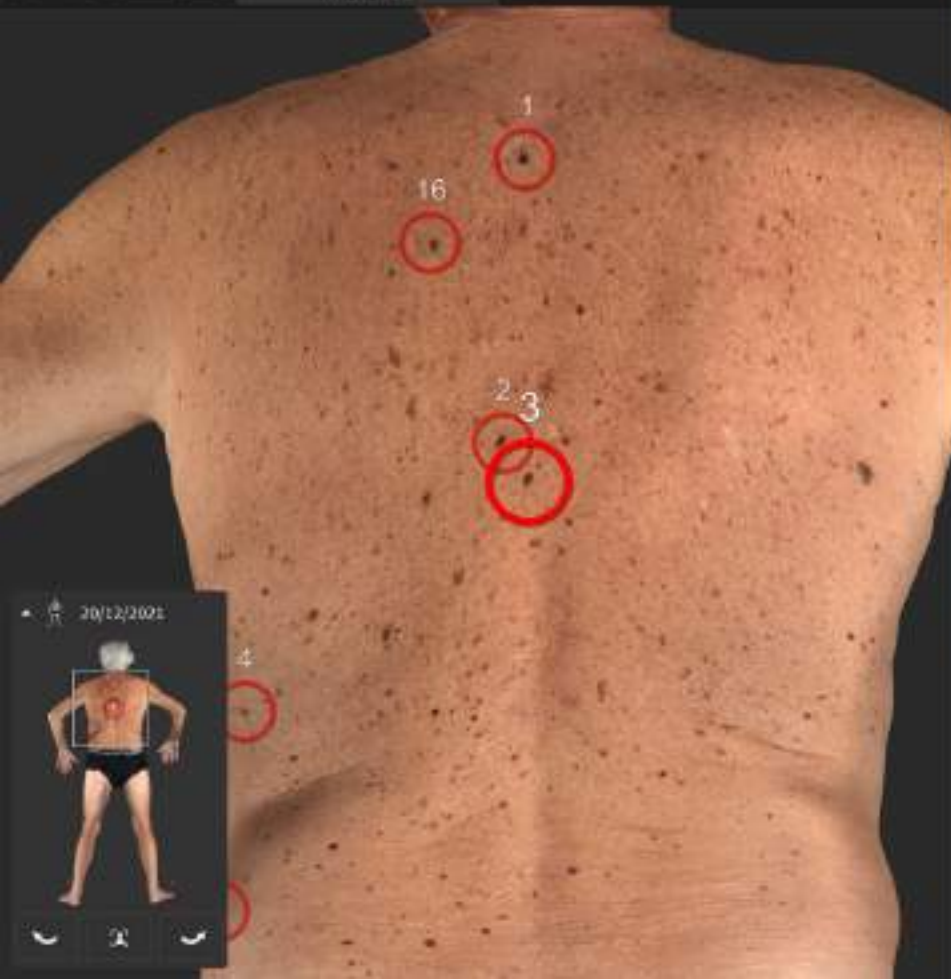
2/17/2023 11:02:00 AM - 11:02:00 AM  
Set lesion 8 status to Followup.

2/17/2023 11:02:00 AM - 11:02:00 AM  
Set lesion 8 status to No Remark.  
Get lesion remark on 8

SSMM in situ

Live View

## Case 2

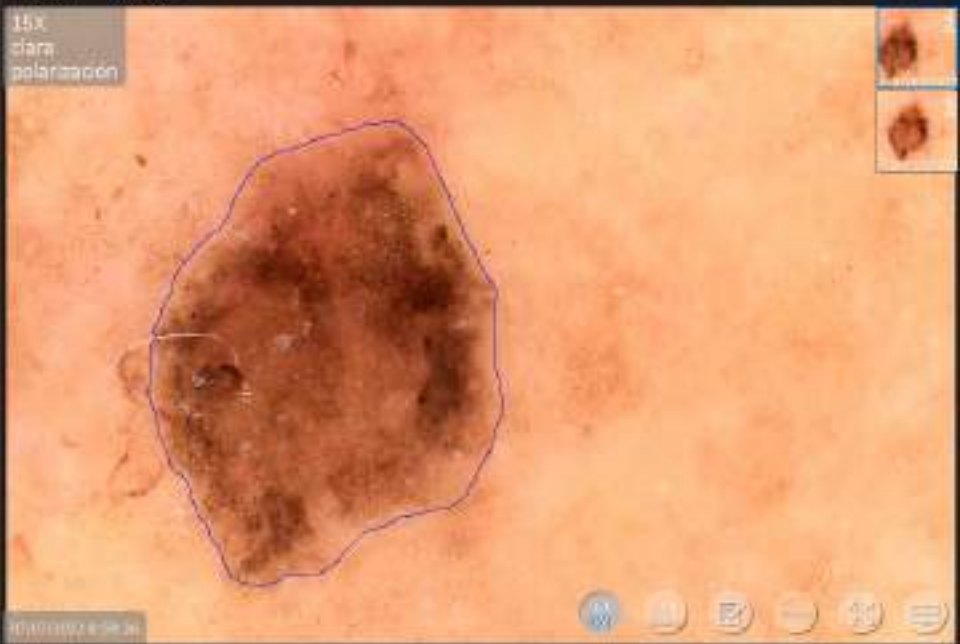
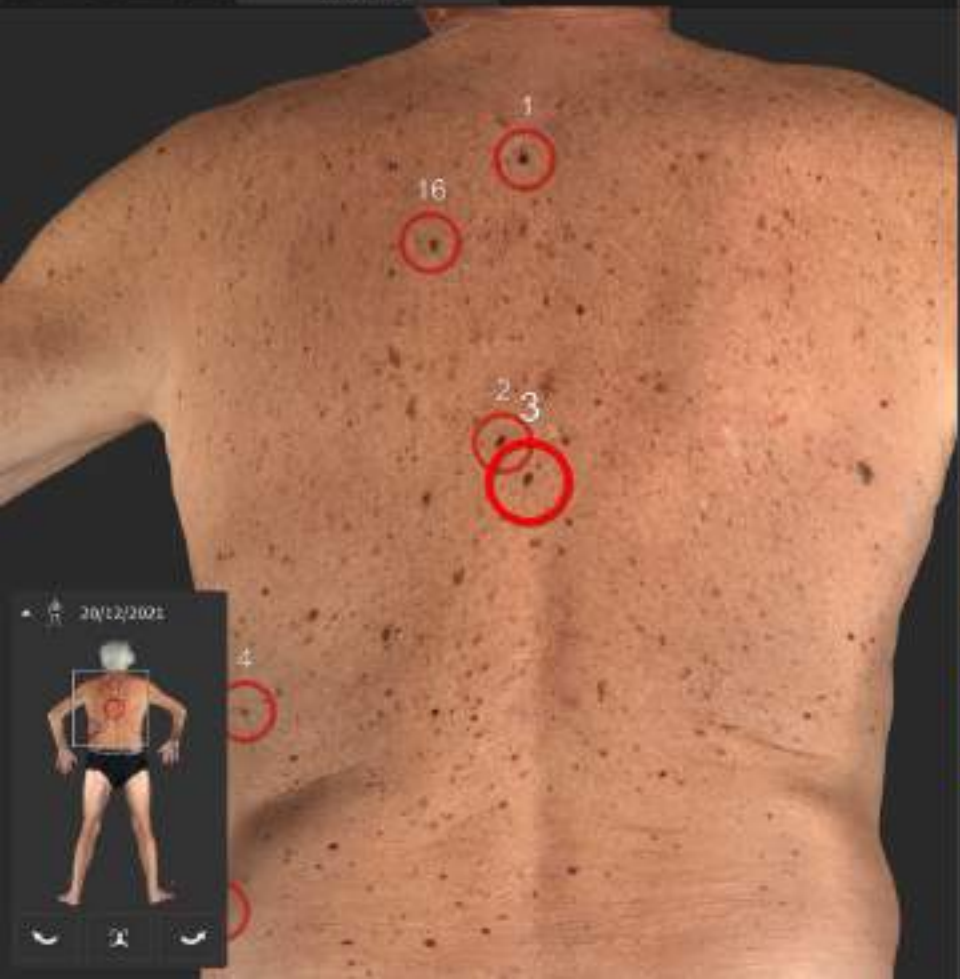


10/10/2021 8:29 AM

- 20120001 Lesión 3 - seguimiento  
Configurar estado de lesión 3 a Follow-up
- 20120001 Lesión 3 - seguimiento  
Configurar estado de lesión 3 a No renovar
- 20120001 Lesión 3 - seguimiento  
Configurar nombre de lesión como 1

Vista en vivo





01/01/2022 8:58:34

Info assessment **1.1**

Knowledgebase

asymmetry 3.2  
border 1.3  
color 4.0  
structure 7.9mm

DEXI

- 20/12/2021 09:01 - Configuración estado de lesión 3 a Follow-up.
  - 20/12/2021 10:02 - Configuración estado de lesión 3 a No remark.
  - 20/12/2021 10:02 - Configuración estado de lesión 3 a No remark.
- [Vista en vivo](#)





20/12/2021 18:04:05

- 20/12/2021 18:04:05 - Configuración  
Configurar estado de lesión 5 a Follow-up
- 20/12/2021 18:04:05 - Configuración  
Configurar Asocia de lesión 5 a His renals.  
Configurar nombre de lesión como 5.

Vista en vivo

20/12/2021



1.1

Knowledgebase

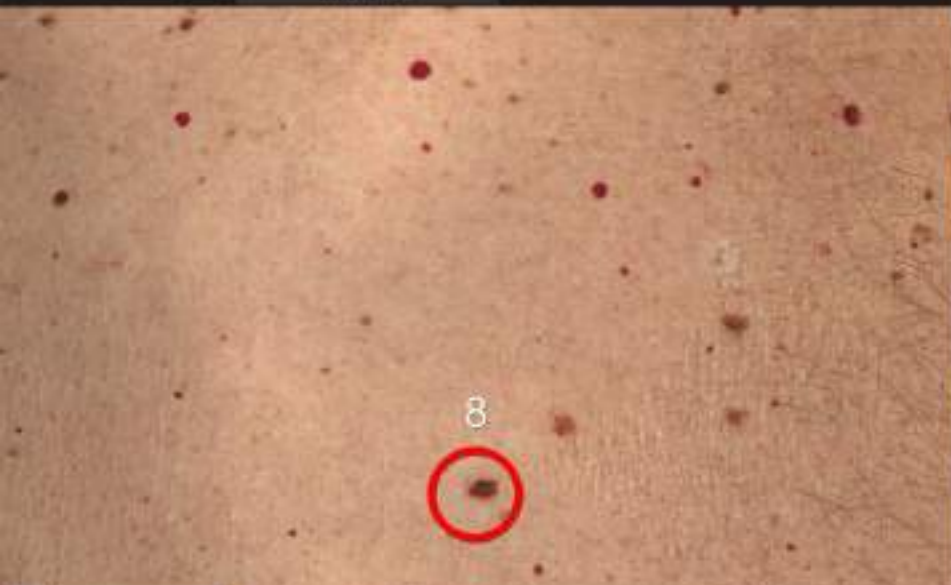
asymmetry	2.5
border	1.3
color	3.4
diameter	5.2mm

DEXI

- 30/12/2021 08:47 - [Historial de cambios](#)  
Configurar estado de lesión 5 a Follow-up.
  - 30/12/2021 12:54 - [Historial de cambios](#)  
Configurar estado de lesión 5 a No remark.  
Configurar nombre de lesión contra 5.
- Vista en vivo

20/12/2021





20/12/2021

Navigation icons: back, home, forward

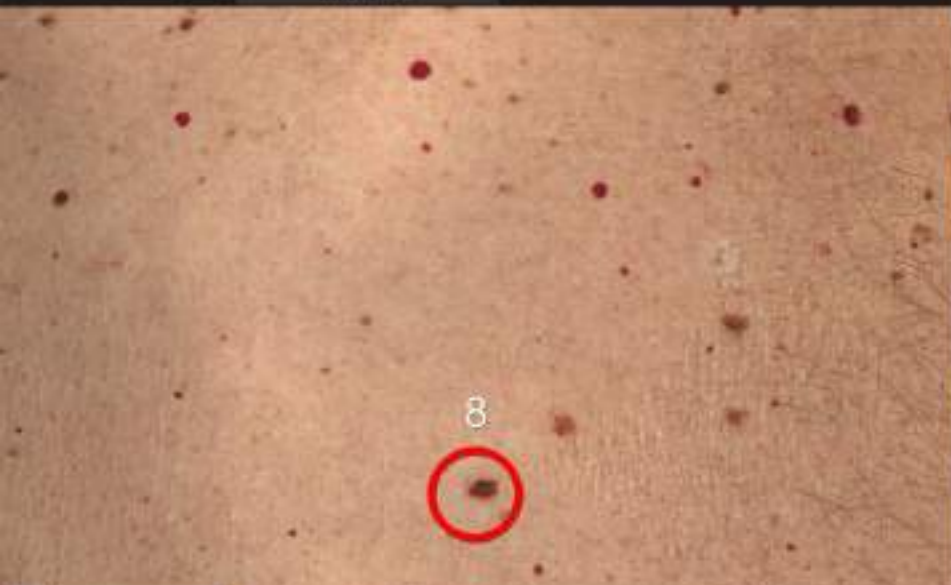


20/12/2021 05:04:34

Configurar estado de lesión 8 a Follow-up

20/12/2021 05:04:34 Configurar Asocia de lesión 8 a Ris renal. Configurar nombre de lesión como 8.

Vista en vivo



02/12/2021 8:04:34

0.8

Knowledgebase

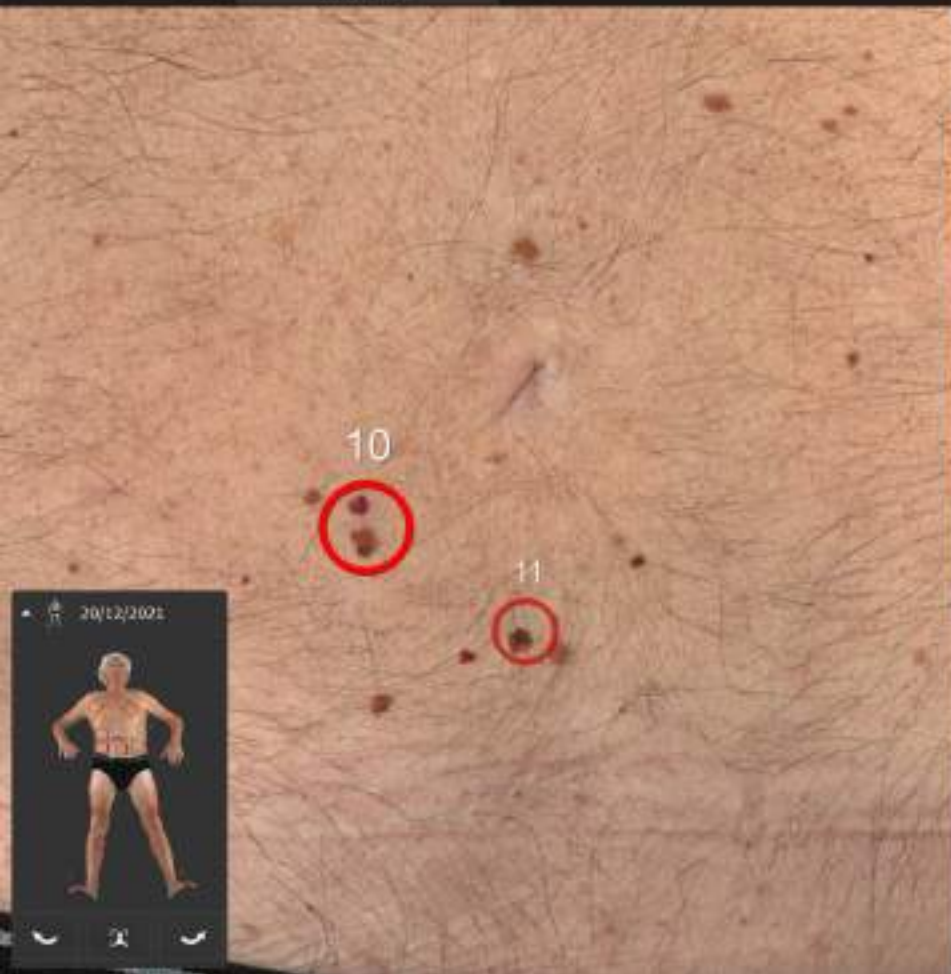
asymmetry	2.8
border	1.2
color	4.3
diameter	6.2mm

DEXI

- 20/12/2021 8:04:34 - 02/12/2021 8:04:34 Configurar estado de lesión 8 a Follow-up.
  - 20/12/2021 8:04:34 - 02/12/2021 8:04:34 Configurar estado de lesión 8 a No remark. Configurar nombre de lesión como 8.
- Vista en vivo







20/12/2021 10:52:21

Integración de contenidos  
Configurar estado de lesión 10 a follow-up.

20/12/2021 10:52:21  
Configurar estado de lesión 10 a no remark.  
Configurar nombre de lesión como 10.

Vista en vivo



0000002850211

0.8

Knowledgebase

asymmetry	2.8
border	1.1
color	4.0
diameter	4.0mm

DEXI

- 30/12/2021 10:51 - 0000002850211  
Configurar estado de lesión 10 a Follow-up.
  - 30/12/2021 10:54 - 0000002850211  
Configurar estado de lesión 10 a No remark.  
Configurar nombre de lesión como 10.
- Vista en vivo





20/12/2021

Bodymap navigation icons: back, forward, home, search, etc.



Historial de lesiones

- 09/07/2021 - 09/07/2021 Configuración estado de lesión 14 a follow-up.
- 09/07/2021 - 09/07/2021 Configuración estado de lesión 14 a fin remark. Configuración nombre de lesión como 14.

Vista en vivo



20/12/2021

Navigation icons: back, forward, home, search, etc.

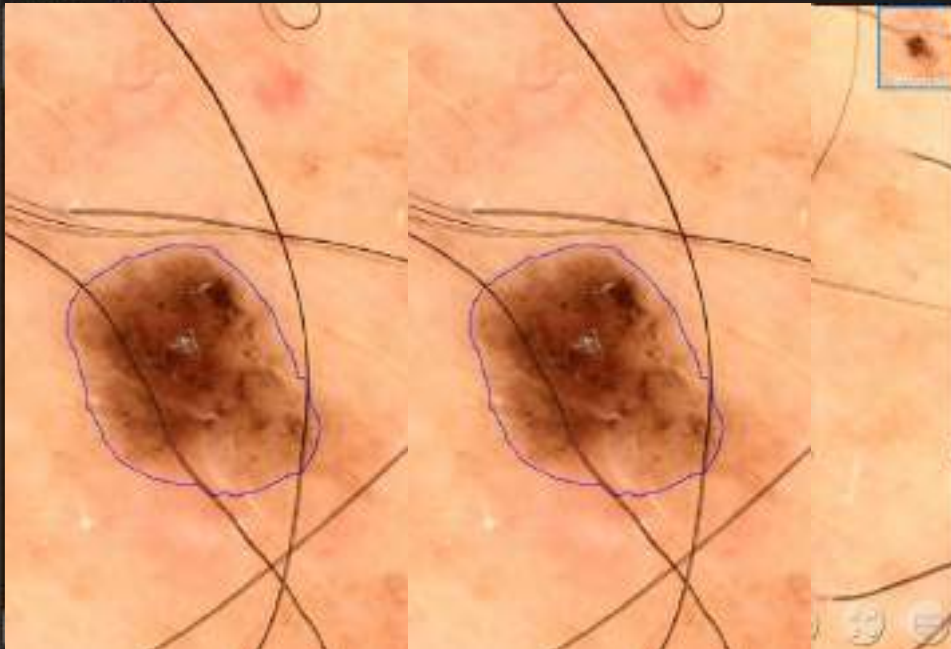


3.8

Asimetría 3.5  
Estructura 1.2  
Color 5.7  
Grosor 4.2mm

- 09/07/2021 09:31 - 09/07/2021  
Configurar estado de lesión 14 a Follow-up.
- 09/07/2021 09:32 - 09/07/2021  
Configurar estado de lesión 14 a No remark.  
Configurar nombre de lesión como 14.

Vista en vivo



20/12/2021. [Body map thumbnail showing a human figure with a red box on the back indicating the lesion location.]

3.8 [Color scale bar]. Dermoscopia. [Color calibration icons: R, G, B, W, A]. [Metrics: asymmetry 3.5, border 1.2, color 5.7, diameter 6.2mm]. DEXI logo.

- [Icon] 09/07/2021 09:03:11 [Info] Configurar estado de lesión 14 a Follow-up.
- [Icon] 09/07/2021 09:03:11 [Info] Configurar estado de lesión 14 a No remark. Configurar nombre de lesión como 14.

Vista en vivo

← → 0 1 18 0 0 0 0 0

Foto de referencia: 0 / 17 imágenes Ver foto de referencia

Lesión 4 21/12/2021 Follow-up
🗑️ 🖨️ ⬇️ 📷



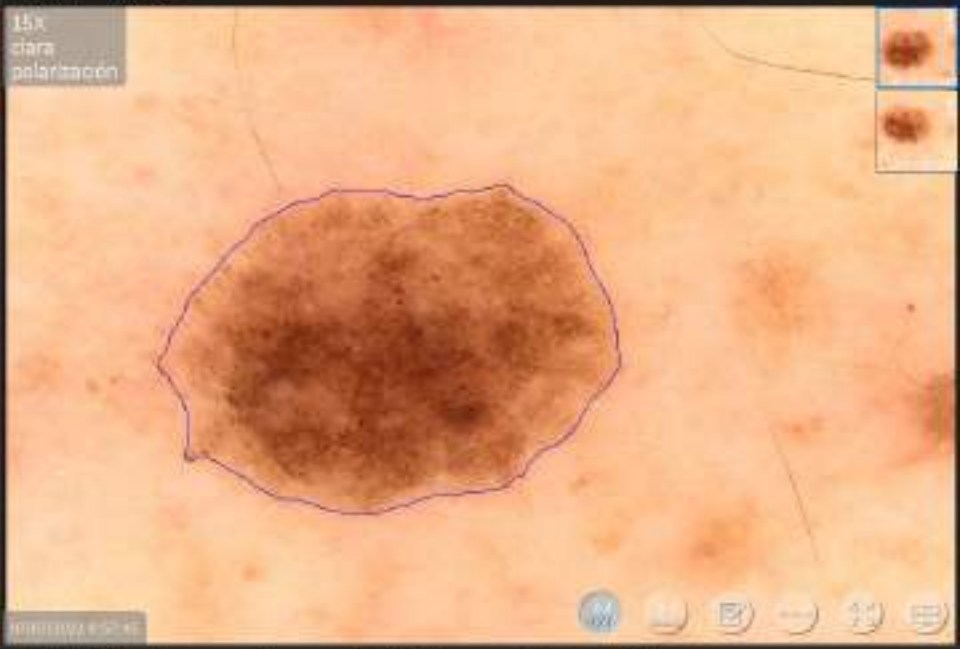
20/12/2021

20/12/2021 20/12/2021

20/12/2021 20/12/2021

Configuración de estado de lesión 4 a Follow-up  
 Configuración de estado de lesión 4 a Follow-up  
 Configuración de estado de lesión 4 a Follow-up  
 Configuración nombre de lesión como 4

Vista en vivo



0.2

Knowledgebase

asymmetry	2.5
border	0.9
color	9.1
diameter	7.9mm

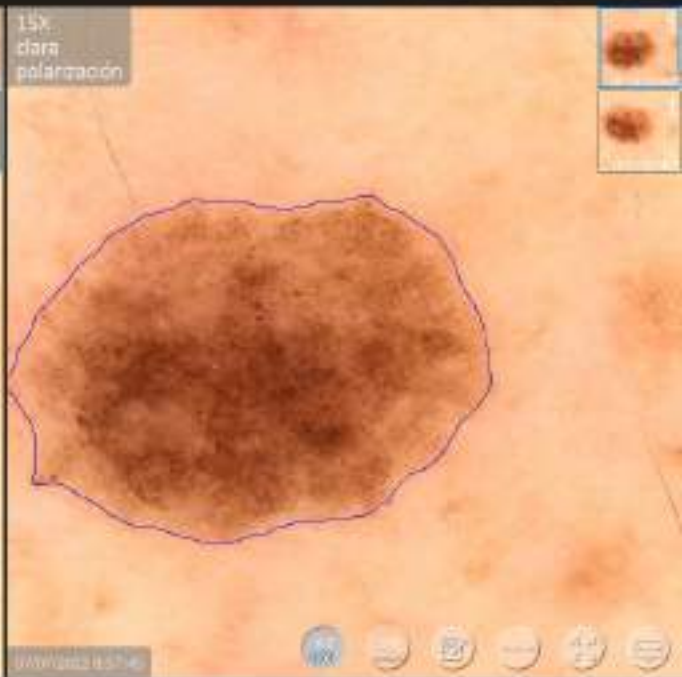
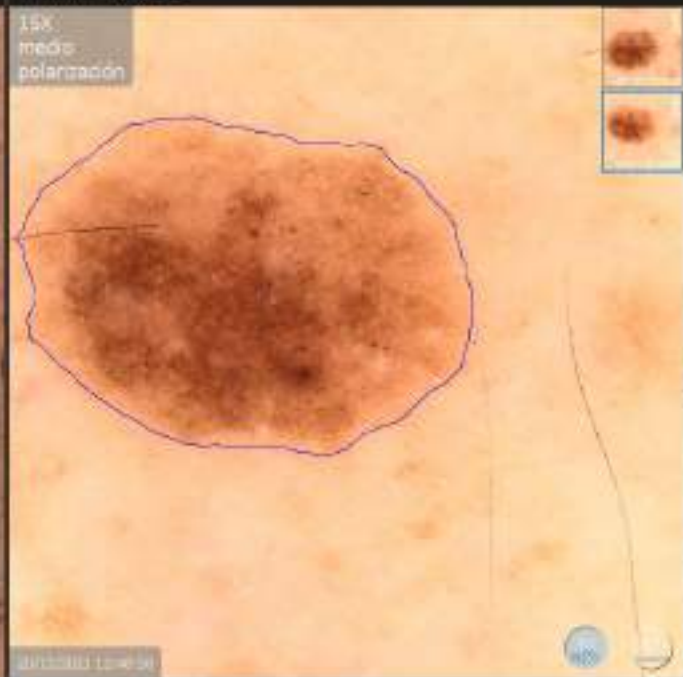
DEXI

- 20/12/2021 07:41 - 18/12/2021 - 18/12/2021  
Configurar estado de lesión 4 a Follow-up.
  - 20/12/2021 10:02 - 18/12/2021 - 18/12/2021  
Configurar estado de lesión 4 a No remark.  
Configurar nombre de lesión contra 4.
- Vista en vivo



0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 mejores

Lesión 4



0.1 


 geometry: 2.0  
 border: 0.5  
 color: 4.0  
 diameter: 7.5mm

0.2 


 geometry: 2.5  
 border: 0.9  
 color: 4.1  
 diameter: 7.9mm

Configurar estado de lesión 4 a Polbe-up.

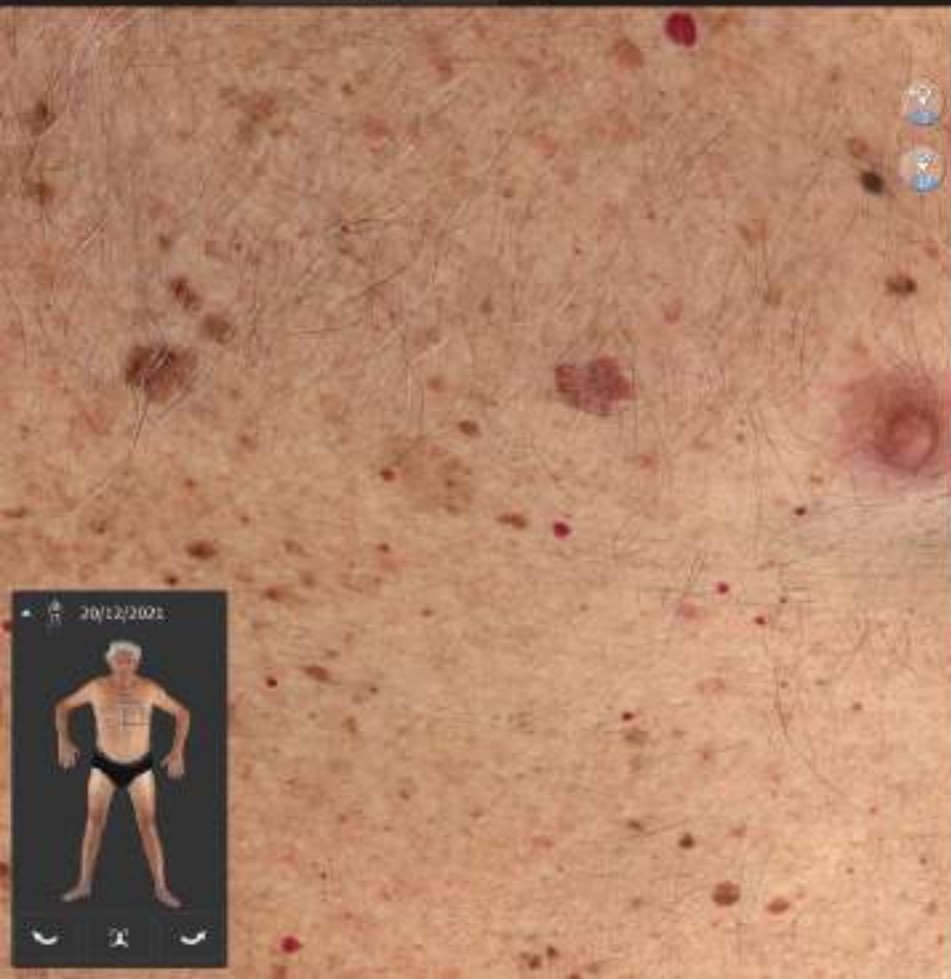
Configurar estado de lesión 4 a No remark.

Vista en vivo

Lista de trabajos  
0 / 17 trabajos

0 1 18 0 0 0 0

Buscar por nombre

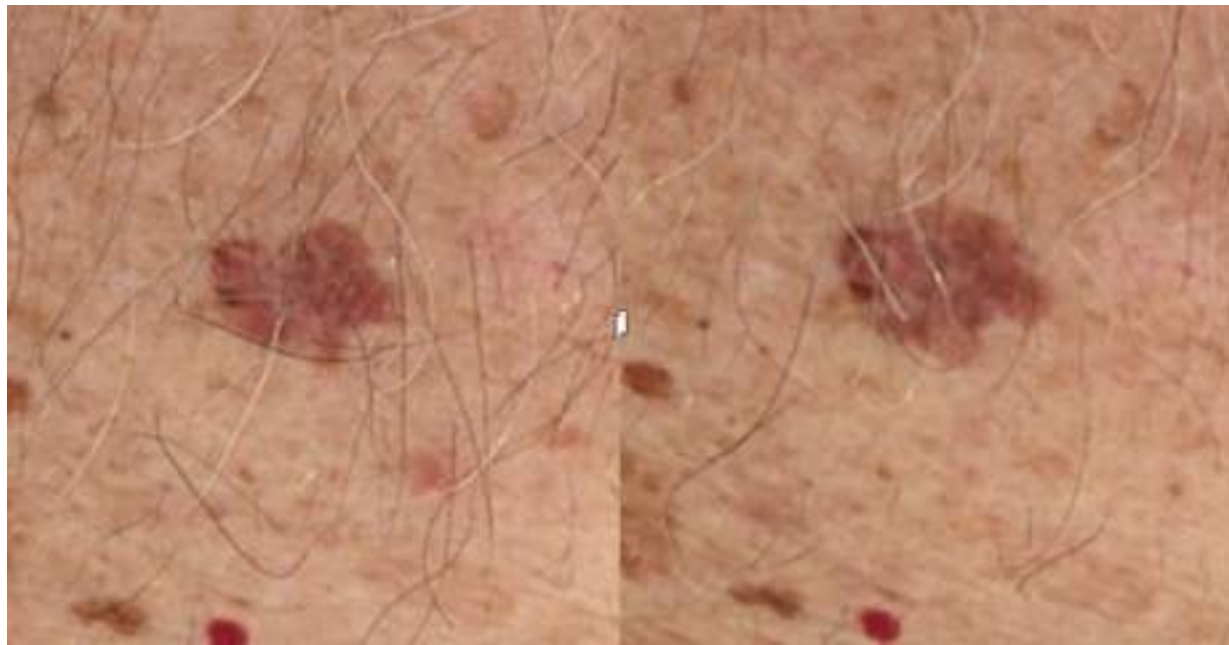


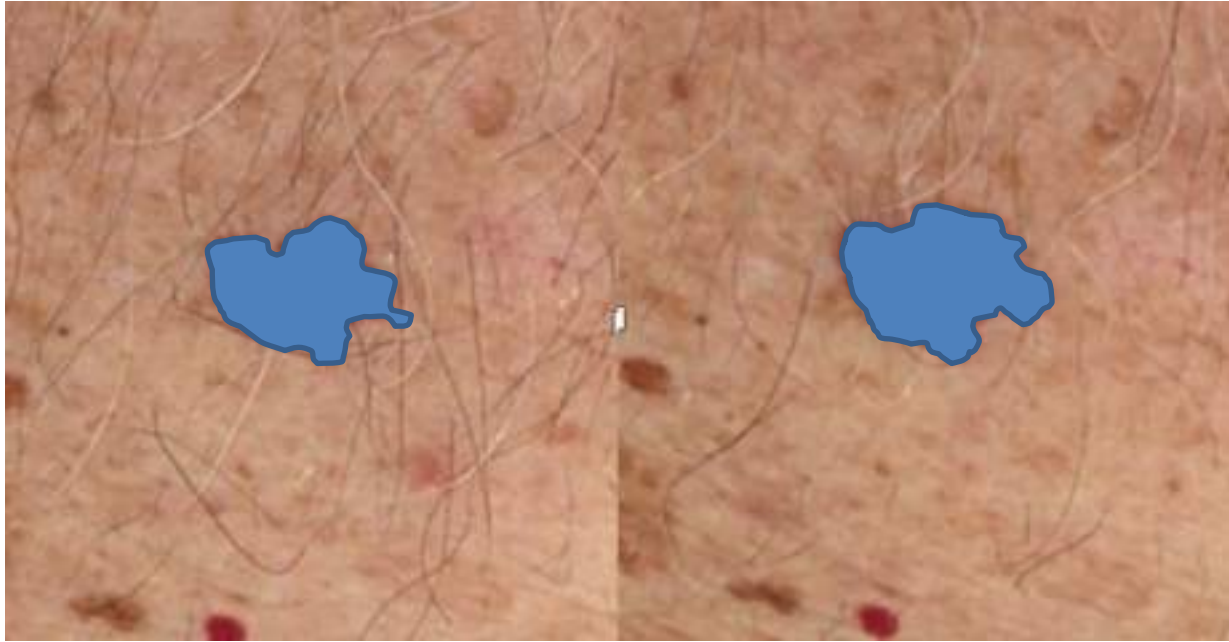
20/12/2021

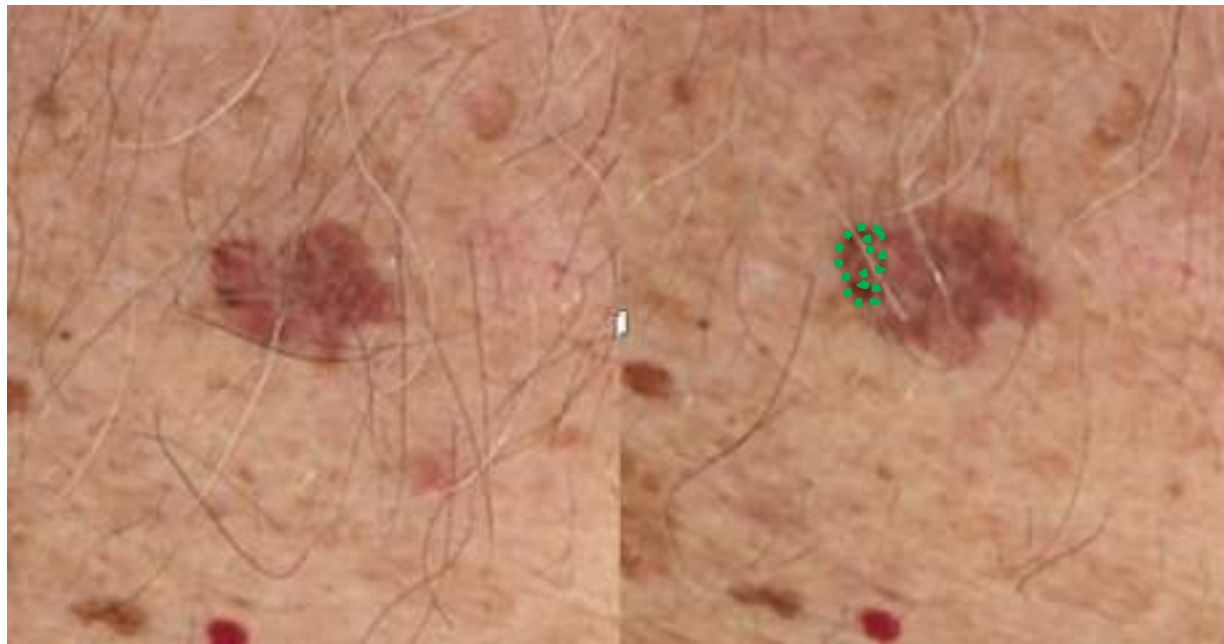
Navigation icons

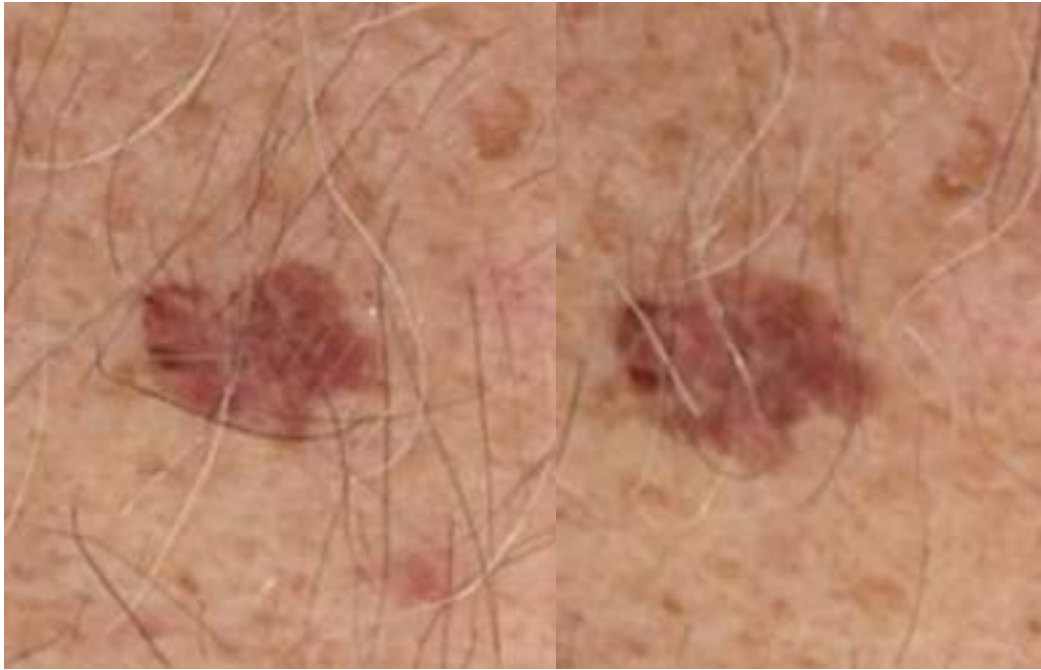
17/07/2022

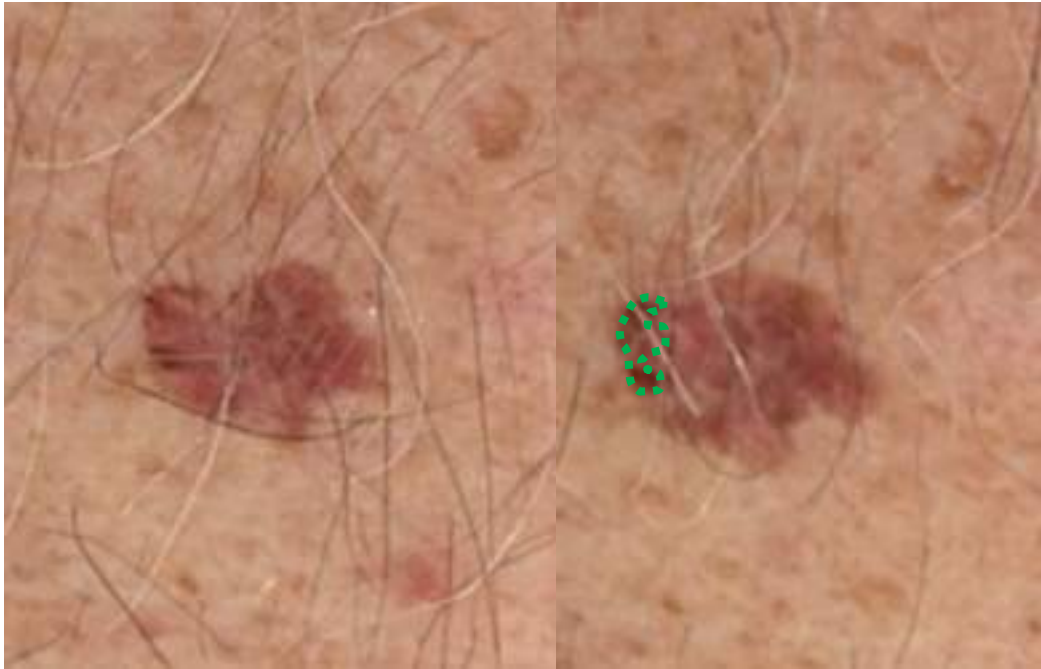
Navigation icons











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10 de 10 fotos
0 / 17 imágenes
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Lesión 15
09/07/2021
Follow-up
🗑️
🖨️
⬇️
📷



20/12/2021

📄 **Historial de imágenes**  
 Configurar estado de lesión 15 a Follow-up.

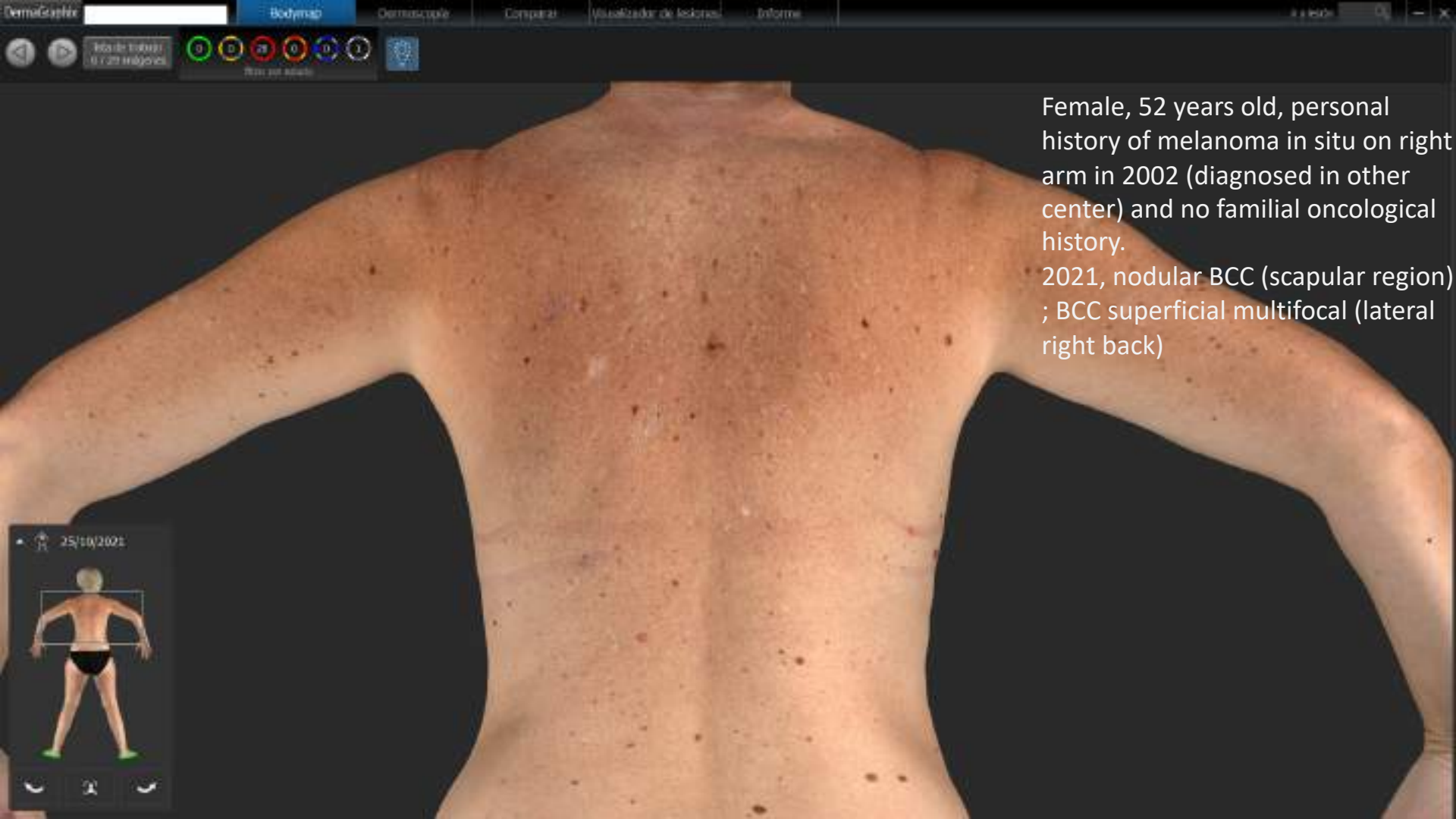
📄 **Historial de imágenes**  
 Configurar estado de lesión 15 a No remak.  
 Configurar nombre de lesión como 15.

Vista en vivo





## Case 3



Female, 52 years old, personal history of melanoma in situ on right arm in 2002 (diagnosed in other center) and no familial oncological history.

2021, nodular BCC (scapular region) ; BCC superficial multifocal (lateral right back)















Lista de trabajos: 0 / 25 trabajos

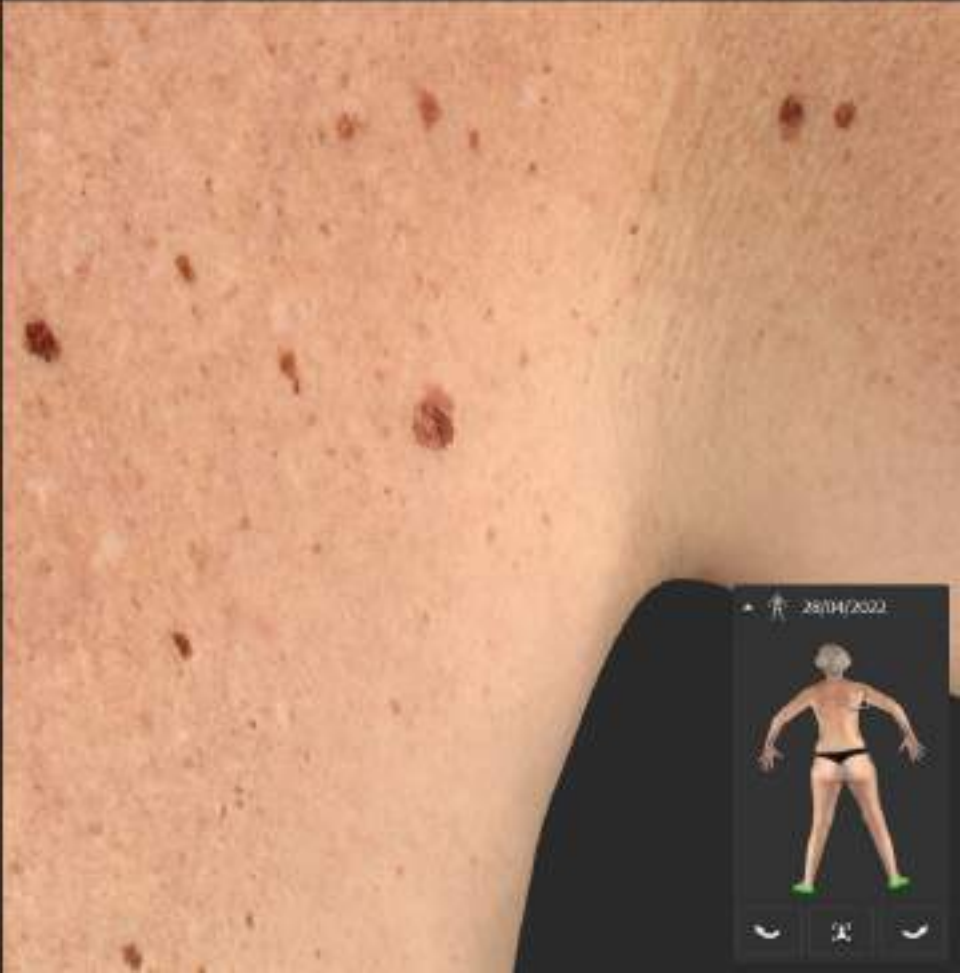
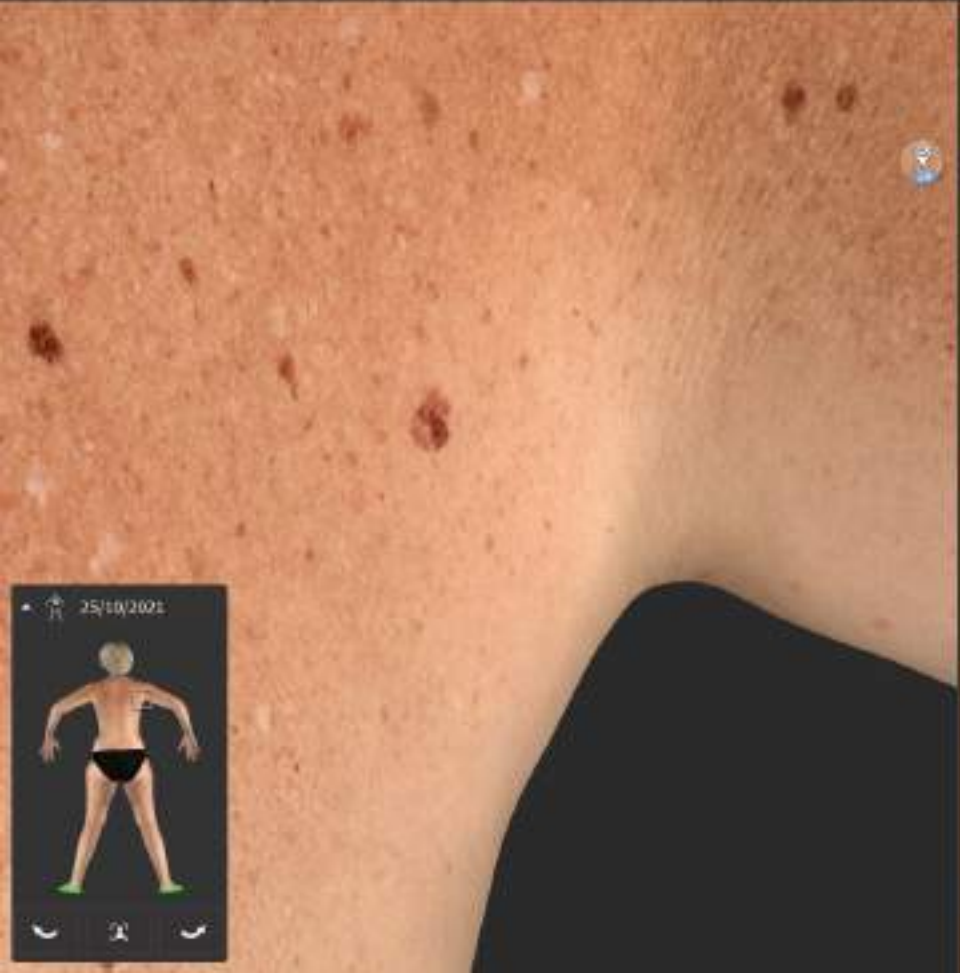
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Mapa del cuerpo

📷

📺

🔗





Localización: Strong Africa en español lista actual

Indicador de: + lista  
28/04/2022 11:48:57 2002

823 LESIONES

Sorted By: Hun  
New Lesions: 20  
Recorded Lesions: 0  
Avg. Diameter: 4.23229

Field Change:



Reddish Change:



Complex Structure (mm):



Ulcerated:



Border Irregularity:



Color Variance:



Blue:



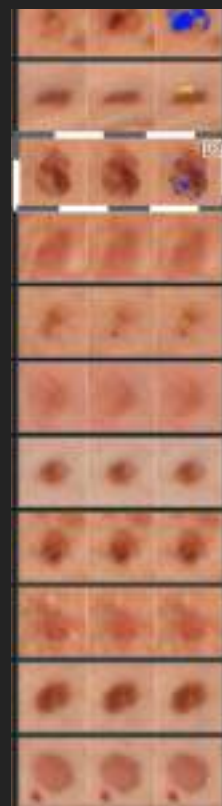
White Cast/Brown:



Anatomic Site: + lista

Tracking Status: + lista

Marked as Photo:







Lesión 29 25/10/2021

15x clara polarización

25/10/2021

Visualizador de tiempo **8.1**

Índice de conocimiento

asimetría	4.3
borde	3.8
color	5.4
diámetro	9.9mm

DEXI

25/10/2021 10:00:00 Configurar estado de lesión 29 a Fresh.

25/10/2021 10:00:00 Configurar estado de lesión 29 a Follow-up.

25/10/2021 10:00:00

Vista en vivo

SSMM Breslow 0,2mm

## Case 4



56 yrs old. Multiple primary melanoma (2008 SSMM Breslow 0,5, MMis). MITF mutation, CDKN2A, CDK4 wt

15/12/2022

Thumbnail image of the full-body scan showing the back view with a red box highlighting the area of interest.



Ver medicación
Bodymap
Dermoscopia
Comparar
Visualizador de lesiones
Informe
1 a 10

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Inicio de sesión
0 / 12 imágenes
10
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29
30

---

15/10/2022

1622
12/0000

Sorted By
Relative Change

New Lesions
23

Recorded Lesions
0

Avg. Diameter
4.31994

Total Change

Relative Change

Lesion Diameter (mm)

Contrast

Lesion Temperature

Color Variance

Area

Lesion Confidence

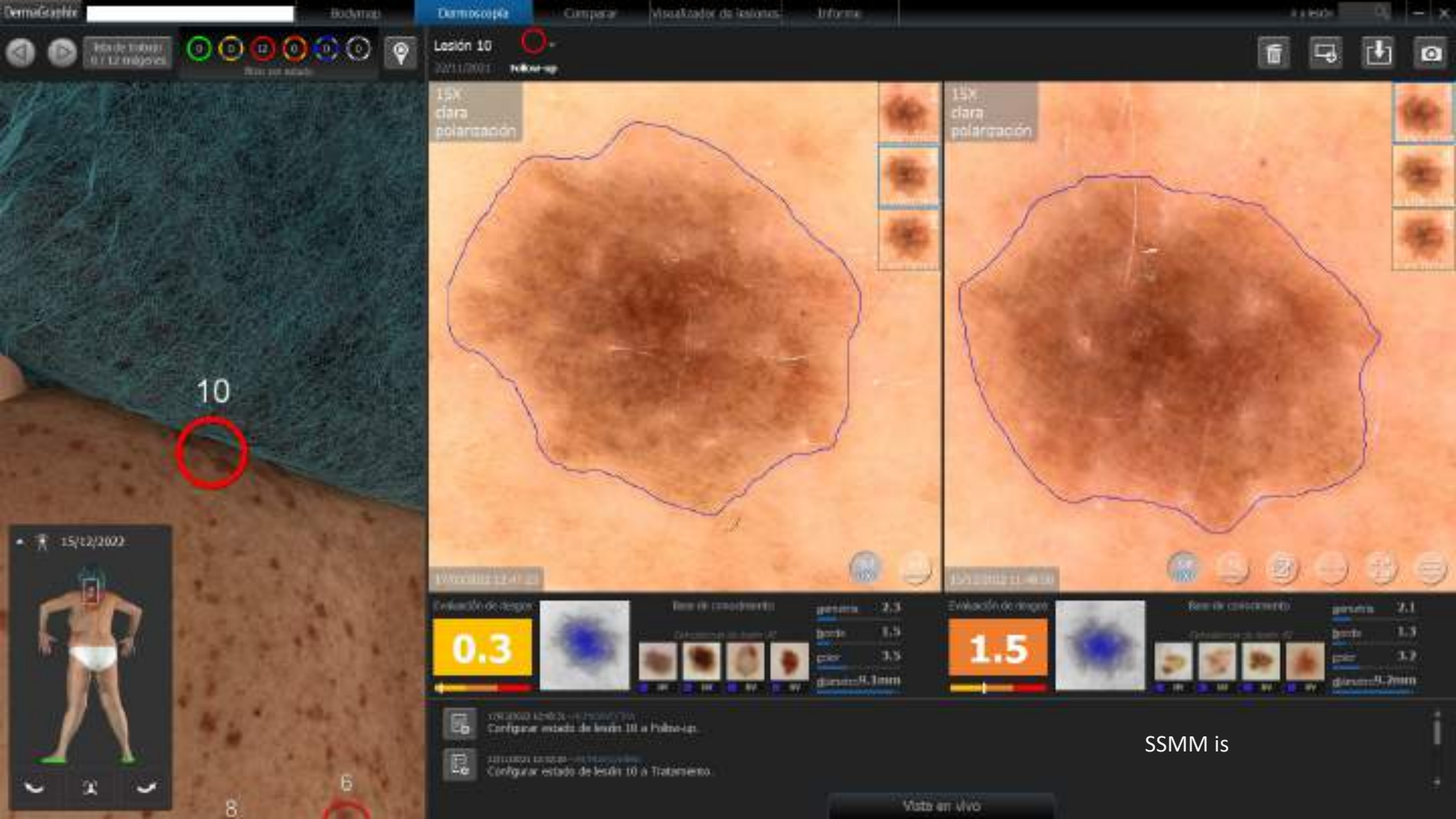
Analysis Size
Full

Tracking Status
Valid

Marked as Blank

Property	Value	Delta
Relative Change	+4.85	-1.25
Lesion Diameter (mm)	6.21	-1.15
Contrast	15.42	-1.15
Area (mm²)	5.36	+2.17
Color Variance	3.30	-1.06
Temp	36.25	-0.13
Area Confidence	98.68	+0.15
Analysis Size	Full	Full
Tracking Status	Valid	Valid





Lección 10  
2021/12/02

15x clara polarización

15x clara polarización

Evaluación de riesgo  
**0.3**

Evaluación de riesgo  
**1.5**

Base de crecimiento  
Densidad de áreas de color

Base de crecimiento  
Densidad de áreas de color

perímetro 2.3  
altura 1.5  
color 3.5  
diámetro 4.2mm

perímetro 2.1  
altura 1.3  
color 3.2  
diámetro 4.2mm

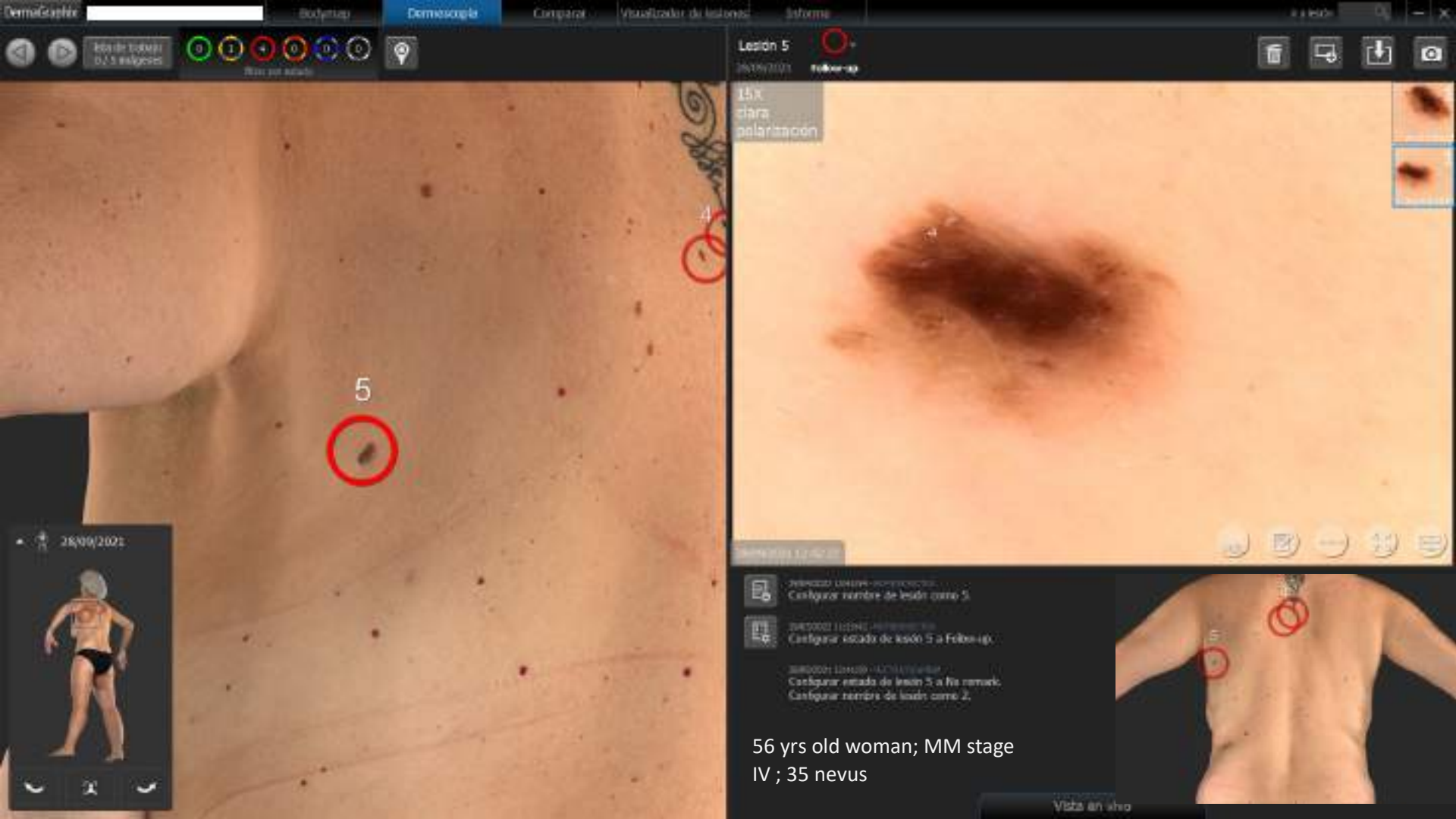
Configurar estado de lesión 10 a Polvo-10.

Configurar estado de lesión 10 a Tratamiento.

SSMM is

Vista en vivo

## Case 6



Lesión 5  
28/09/2021 Follow-up

15x  
para  
polarización

5

28/09/2021

28/09/2021 11:29:40 - INFORME  
Configurar nombre de lesión como 5

28/09/2021 11:29:40 - INFORME  
Configurar estado de lesión 5 a Follow-up

28/09/2021 11:29:40 - INFORME  
Configurar estado de lesión 5 a No removido.  
Configurar nombre de lesión como 2.

56 yrs old woman; MM stage  
IV ; 35 nevus

Vista en vivo



Lesión 5 28/09/2021 Follow-up

15x clara polarización

28/09/2021 12:02:02

100 assessment **2.0**

Evolution

asymmetry	5.2
border	1.0
color	0.0
structure	7.2mm

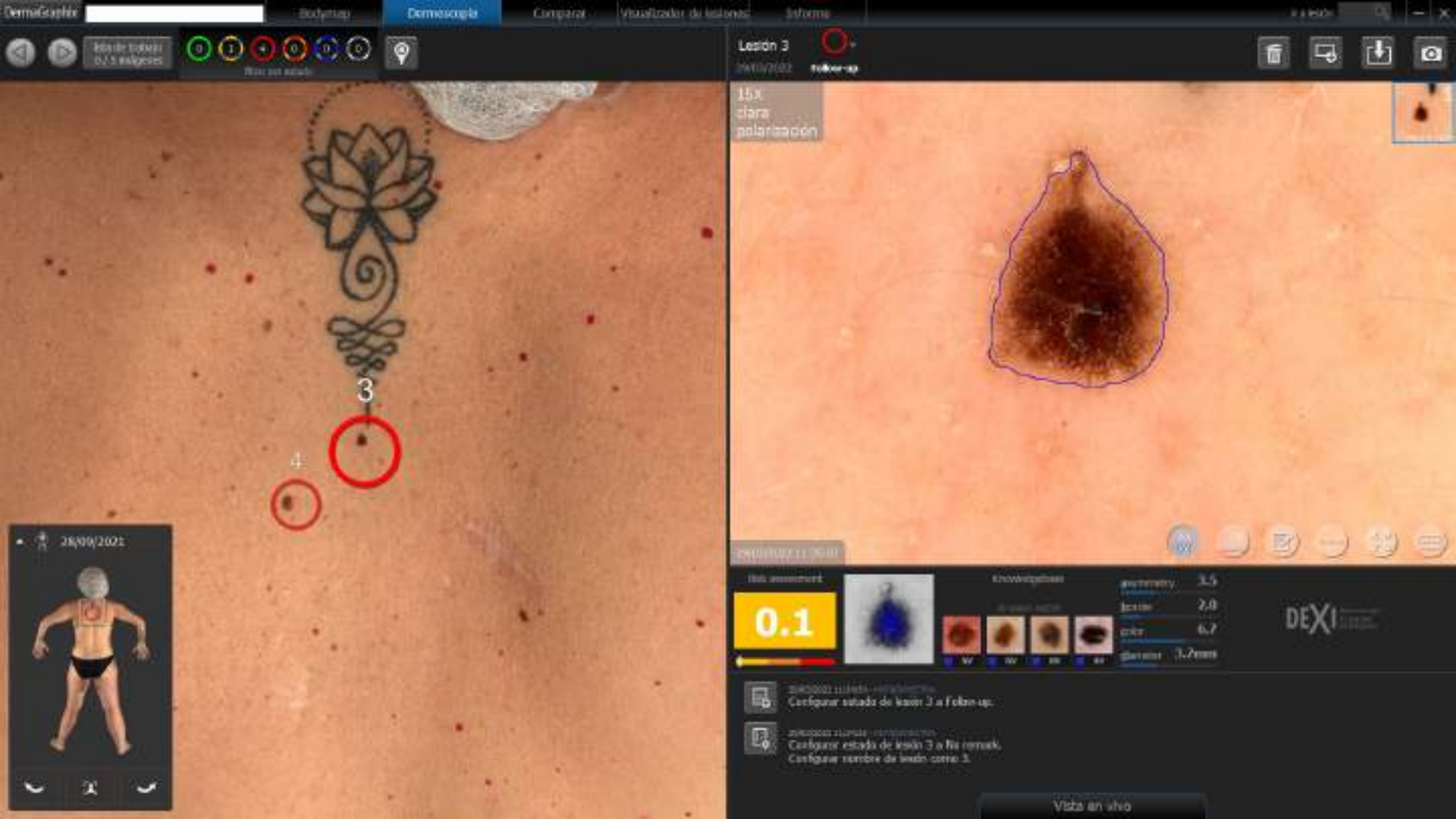
28/09/2021 04:02:04 - 100% seguimiento  
Configurar nombre de lesión como 5.

28/09/2021 12:02:02 - 100% seguimiento  
Configurar estado de lesión 5 a Follow-up.

28/09/2021 12:02:02 - 100% seguimiento  
Pulsar para guardar. 4x. Tamaño: 6 x. No eliminar.

Vista en vivo





Botón de navegación (izquierda)

Botón de navegación (derecha)

Botón de navegación (centro)

Botón de navegación (centro)

Botón de navegación (centro)

Botón de navegación (centro)

Botón de navegación (centro)

Botón de navegación (centro)

Botón de navegación (centro)

Botón de navegación (centro)

Botón de navegación (centro)

Botón de navegación (centro)

Botón de navegación (centro)

Botón de navegación (centro)

Botón de navegación (centro)

Botón de navegación (centro)

Botón de navegación (centro)

Botón de navegación (centro)

Botón de navegación (centro)

Botón de navegación (centro)

Lesión 3

28/09/2021

Follow-up

Botón de eliminación

Botón de impresión

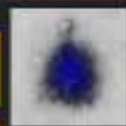
Botón de descarga

Botón de cámara

15x  
clara  
polarización

0.1000021126001

0.1



asymmetry	3.5
border	2.0
color	6.7
diameter	3.2mm

DEXI

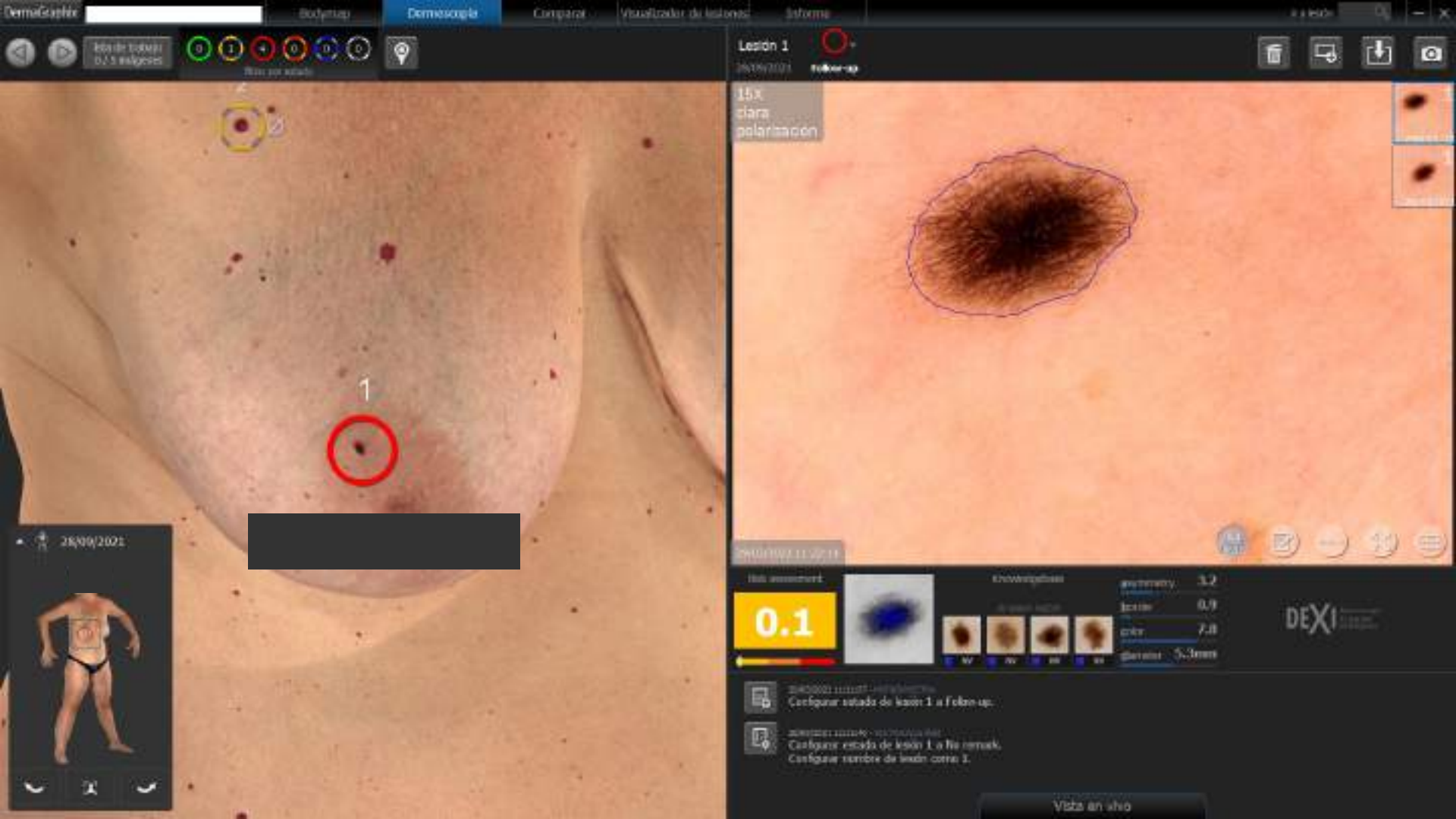
28/09/2021 11:50:02 - 11:50:02  
Configurar estado de lesión 3 a Follow-up.

28/09/2021 11:50:02 - 11:50:02  
Configurar estado de lesión 3 a No remark.  
Configurar nombre de lesión con 3.

Vista en vivo

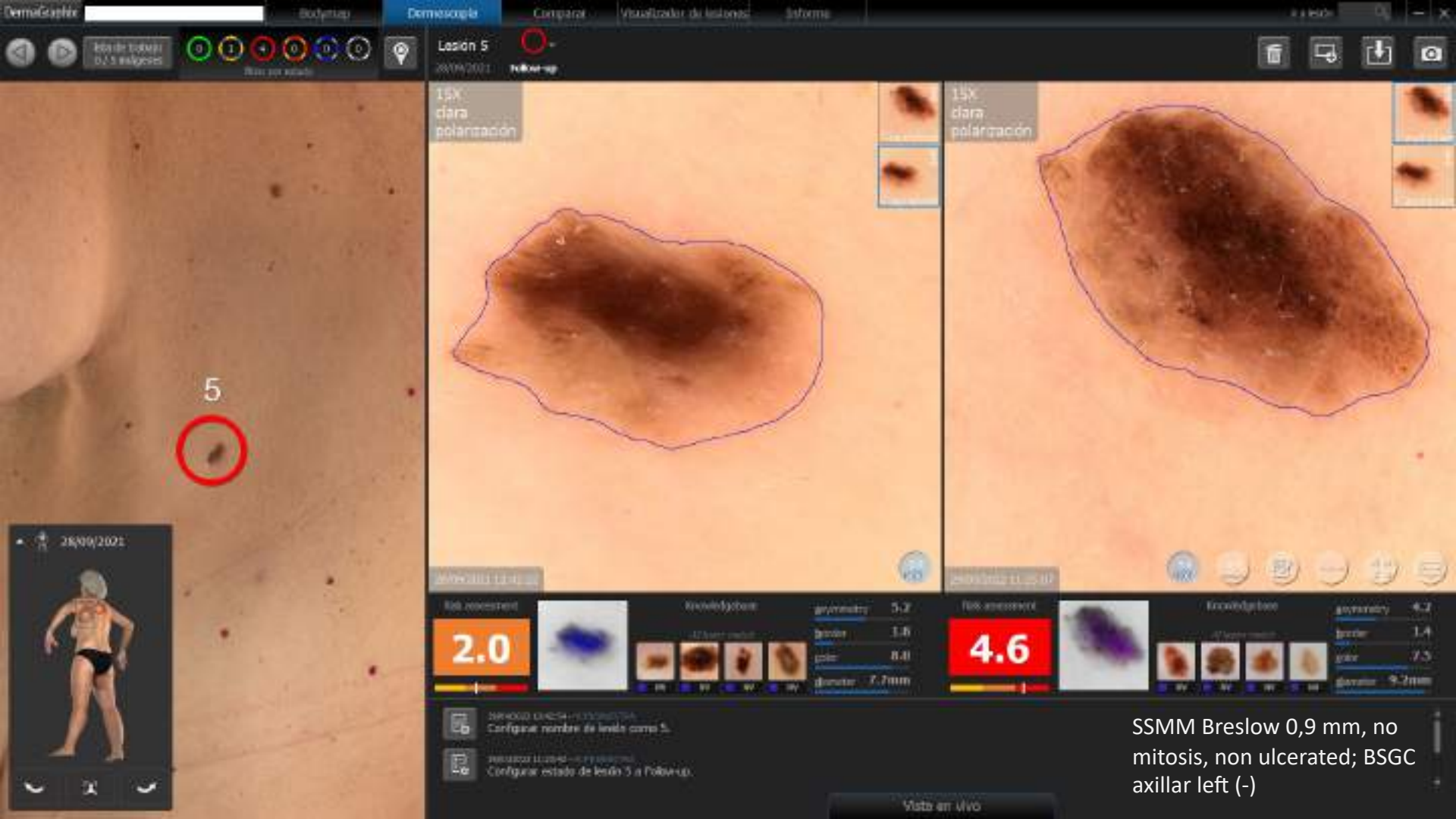
28/09/2021











5

Lesión 5

28/09/2021 Follow-up

15x  
clara  
polarización

15x  
clara  
polarización

28/09/2021 Lesión 5

28/09/2021 Lesión 6

Risk assessment

2.0

Knowledgebase

asymmetry 5.2

border 1.8

color 8.8

diameter 7.7mm

Risk assessment

4.6

Knowledgebase

asymmetry 4.2

border 1.4

color 7.5

diameter 9.2mm

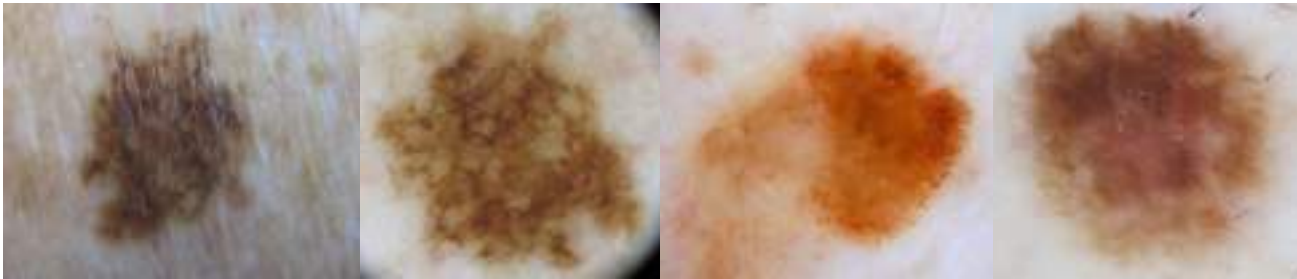
REVISAR LESIÓN PERSONALITARIA.  
Configurar nombre de lesión como 5.

REVISAR LESIÓN - CATEGORÍA.  
Configurar estado de lesión 5 a Follow-up.

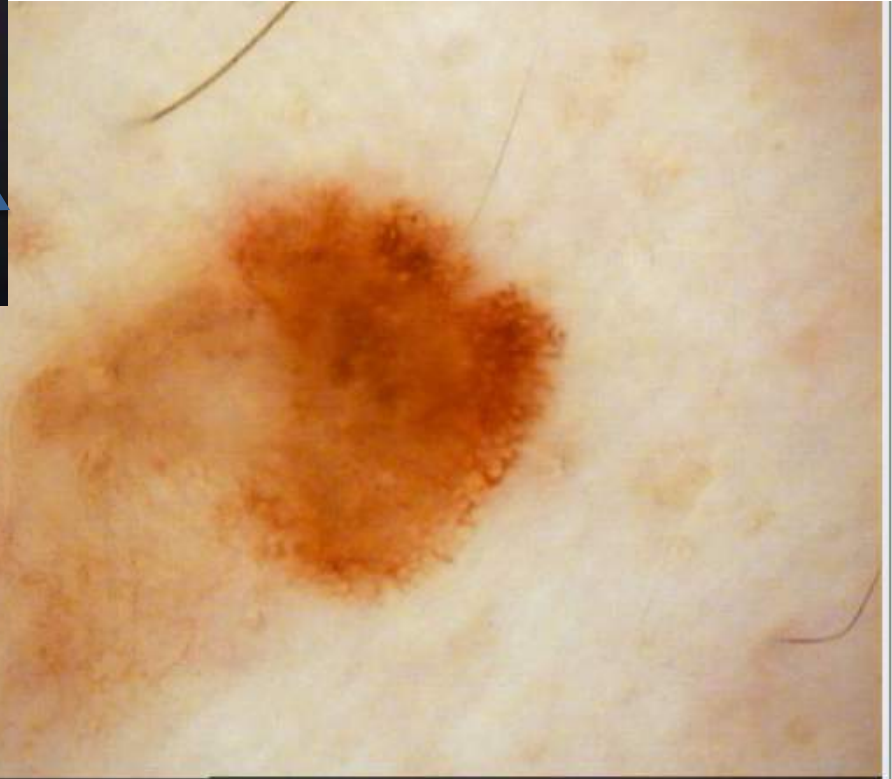
SSMM Breslow 0,9 mm, no mitosis, non ulcerated; BSGC axillar left (-)

Vista en vivo

Are slow growing melanomas  
“benign” melanomas?

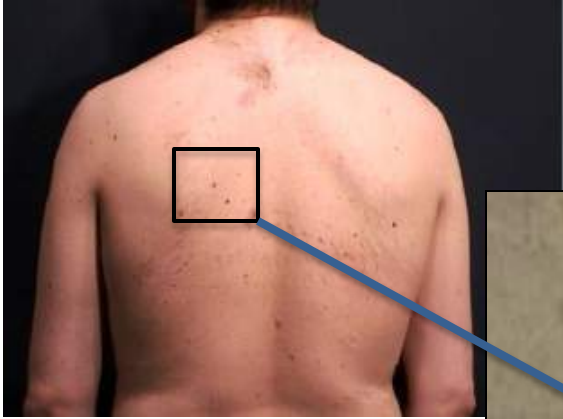


# Case 7



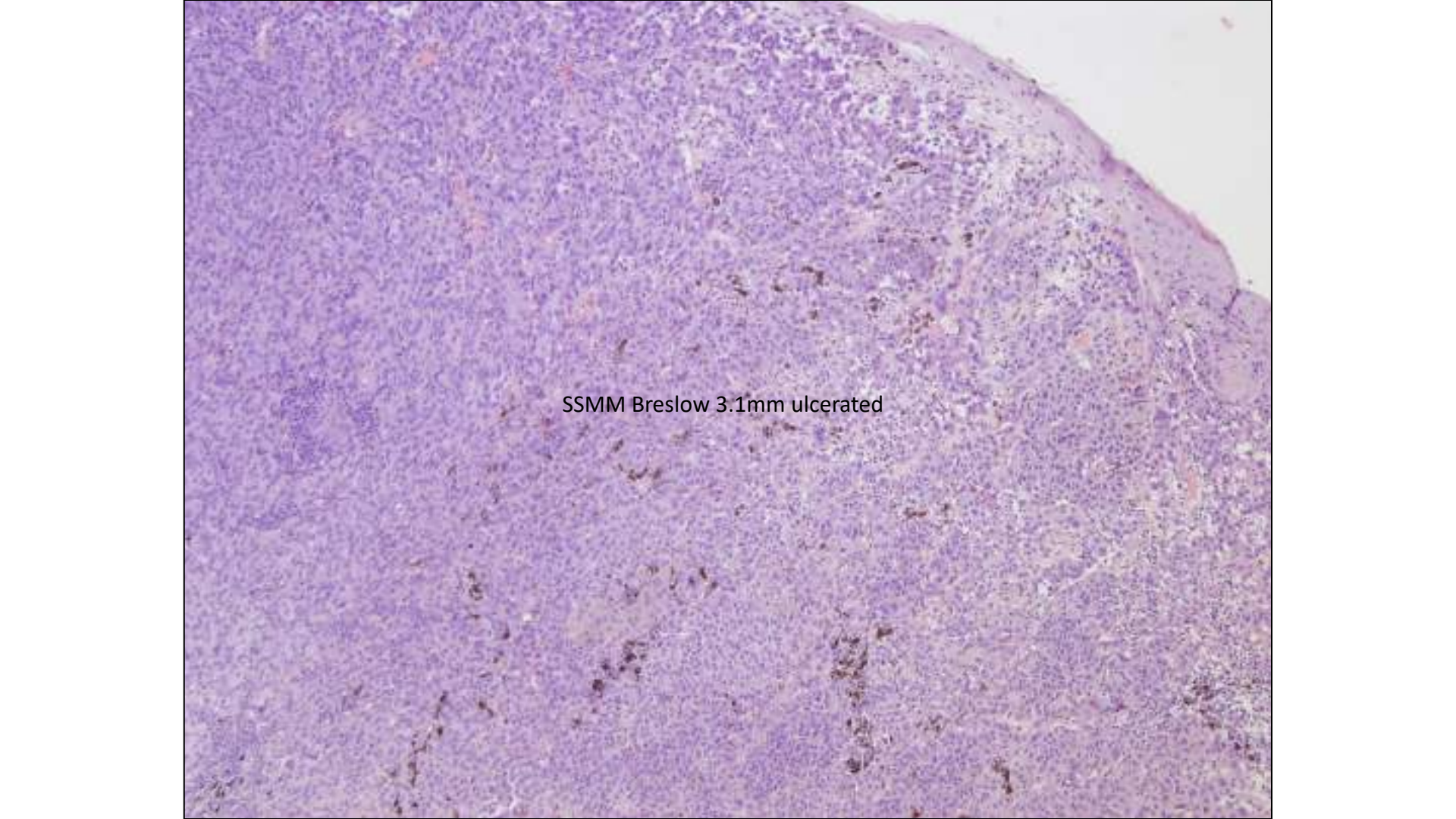
MM  
FAMMMsd (mother MM)

August 2010: after 6 years....



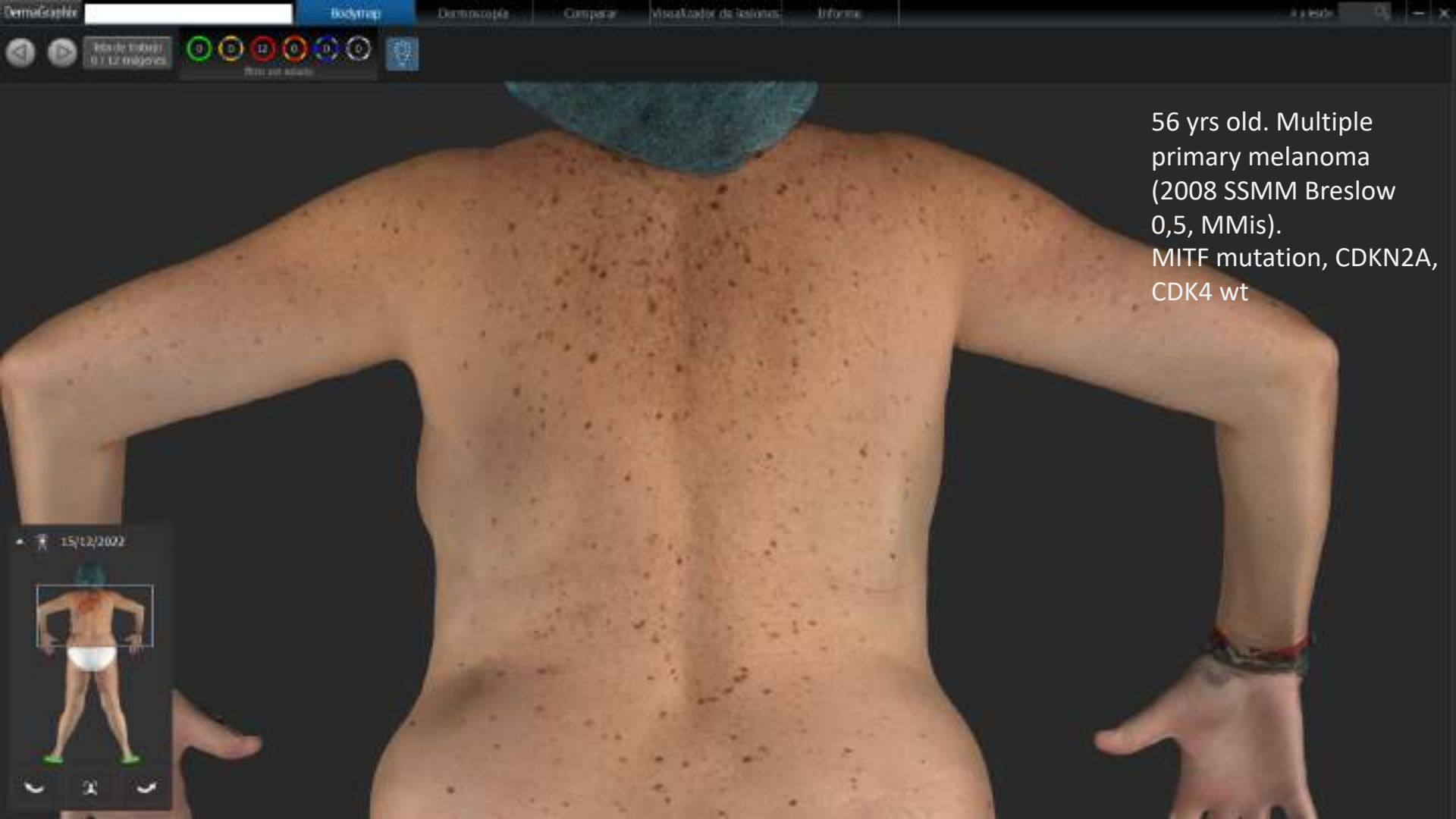




A histological slide of skin stained with hematoxylin and eosin (H&E). The image shows a cross-section of the epidermis and dermis. The epidermis is significantly thickened, and there is a dense population of melanocytes in the basal layer, many of which are heavily laden with dark brown melanin pigment. This is characteristic of severe sunburn-induced melanocyte melaninization (SSMM). The dermis shows some inflammatory infiltrate and areas of ulceration, particularly towards the right side of the image. The overall appearance is that of a severely sunburned skin specimen.

SSMM Breslow 3.1mm ulcerated





56 yrs old. Multiple primary melanoma (2008 SSMM Breslow 0,5, MMis). MITF mutation, CDKN2A, CDK4 wt





Lesión 10  
2021/10/01  
Follow-up

15X  
clara  
polarización

15/10/2022 11:58:54

- 20210001 Lesión 10 - Follow-up  
Configurar estado de lesión 10 a Follow-up.
- 20210001 Lesión 10 - Tratamiento  
Configurar estado de lesión 10 a Tratamiento.
- 20210001 Lesión 10 - Follow-up  
Configurar estado de lesión 10 a Follow-up.
- 20210001 Lesión 10 - Dermacoscopia  
Configurar estado de lesión 10 a la remark.  
Configurar nombre de lesión como 10.

Vista en vivo



Sturm RA, Fox C, McClenahan P, Jagirdar K, Ibarrola-Villava M, Banan P, Abbott NC, Ribas G, Gabrielli B, Duffy DL, Peter Soyer H. Phenotypic characterization of nevus and tumor patterns in MITF E318K mutation carrier melanoma patients. *J Invest Dermatol.* 2014 Jan;134(1):141-149.

## Original Investigation

Prevalence of *MITF* p.E318K in Patients With Melanoma Independent of the Presence of *CDKN2A* Causative Mutations

Miriam Potrony, MSc; Joan Anton Puig-Butillé, PhD; Paula Aguilera, MD; Celia Badenas, PhD; Gemma Tell-Martí, MSc; Cristina Carrera, MD, PhD; Luis Javier del Pozo, MD; Julian Conejo-Mir, MD; Josep Malvehy, MD, PhD; Susana Puig, MD, PhD

**IMPORTANCE** The main high-penetrance melanoma susceptibility gene is *CDKN2A*, encoding p16INK4A and p14ARF. The gene *MITF* variant p.E318K also predisposes to melanoma and renal cell carcinoma. To date, the prevalence of *MITF* p.E318K and its clinical and phenotypic implications has not been previously assessed in a single cohort of Spanish patients with melanoma or in p16INK4A mutation carriers.

**OBJECTIVES** To evaluate the prevalence of *MITF* p.E318K in Spanish patients with melanoma and assess the association with clinical and phenotypic features.

**DESIGN, SETTING, AND PARTICIPANTS** A hospital-based, case-control study was conducted at the Melanoma Unit of Hospital Clinic of Barcelona, with *MITF* p.E318K genotyped in all patients using TaqMan probes. We included 531 patients: 271 patients with multiple primary melanoma (MPM) without mutations affecting p16INK4A (wild-type p16INK4A); 191 probands from melanoma-prone families with a single melanoma diagnosis and without mutations affecting p16INK4A, and 69 probands from different families carrying *CDKN2A* mutations affecting p16INK4A. A population-based series of 499 age- and sex-matched cancer-free individuals from the Spanish National Bank of DNA were included as controls. Patients were recruited between January 1, 1992, and June 30, 2014; data analysis was conducted from September 1 to November 30, 2014.

**MAIN OUTCOMES AND MEASURES** The genetic results of the *MITF* p.E318K variant were correlated with clinical and phenotypic features.

**RESULTS** Among the 531 patients, the prevalence of the *MITF* p.E318K variant was calculated among the different subsets of patients included and was 1.9% (9 of 462) in all melanoma patients with wild-type p16INK4A, 2.6% (7 of 271) in those with MPM, and 2.9% (2 of 69) in the probands of families with p16INK4A mutations. With results reported as odds ratio (95% CI), the *MITF* p.E318K was associated with an increased melanoma risk (3.3 [1.43-7.43];  $P < .01$ ), especially in MPM (4.5 [1.83-11.01];  $P < .01$ ) and high nevi count ( $>200$  nevi) (8.4 [2.14-33.19];  $P < .01$ ). Two fast-growing melanomas were detected among 2 *MITF* p.E318K carriers during dermatologic digital follow-up.

**CONCLUSIONS AND RELEVANCE** In addition to melanoma risk, *MITF* p.E318K is associated with a high nevi count and could play a role in fast-growing melanomas. Testing for *MITF* p.E318K should not exclude patients with known mutations in p16INK4A. Strict dermatologic surveillance, periodic self-examination, and renal cell carcinoma surveillance should be encouraged in this context.

Editorial page 375

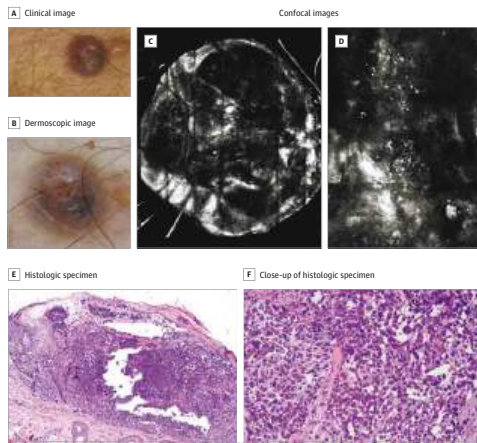
Supplemental content at [jamadermatology.com](http://jamadermatology.com)

**Author Affiliations:** Author affiliations are listed at the end of this article.

**Corresponding Author:** Susana Puig, MD, PhD, Dermatology Department, Hospital Clinic de Barcelona, Universitat de Barcelona, C/ Villarroel, 170, 08036 Barcelona, Spain ([suspui@gmail.com](mailto:suspui@gmail.com)).

*JAMA Dermatology*. 2016;152(4):405-412. doi:10.1001/jamadermatol.2015.4356  
Published online December 9, 2015.

Figure 1. Melanoma



A fast-growing melanoma developed within 3 weeks and was the fourth to occur in patient M0887-01. Clinical picture of a 4-mm-diameter nodular lesion located on the elbow (A). Dermoscopic image of the lesion showing hypopigmentation, asymmetry, unspecific pattern, atypical vessels, and blue-whitish veil (B). Under confocal microscopy, the lesion shows an ulcerated central area (C) with atypical nests in upper dermis with bright roundish nucleated cells in noncohesive nests (D). Histopathologic examination shows an ulcerated nodular melanoma (hematoxylin-eosin, original magnification  $\times 2$ ) (E) and nests of atypical cells and presence of mitosis (hematoxylin-eosin, original magnification  $\times 10$ ) (F).

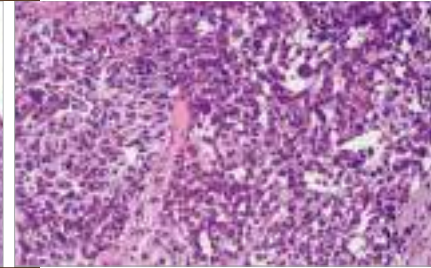
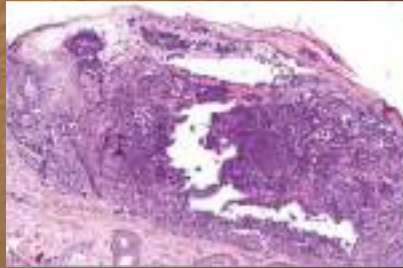
Figure 2. Nevi



The back of patient M3879-01 with 2 previous melanomas and more than 200 nevi. Six dermoscopic images show the predominant pattern, reticulated dark brown.

growing melanomas.<sup>31,32</sup> Until now in our melanoma unit, the only 2 fast-growing melanomas identified by dermatologic digital follow-up in individuals at high risk of melanoma were in *MITF* p.E318K carriers. Fast-growing melanomas are defined by

having a growth rate of greater than 0.4 mm per month; in general, the melanoma growth rate is approximately 0.1 mm per month, and slow-growing melanomas usually have a growth rate of 0.01 mm per month.<sup>33</sup> Furthermore, a high growth rate is



Fast growing melanoma in a patient with 4 primary melanomas carrier of E318K in MITF, MC1R genotype = R/r and p.Gly32Arg in p14arf

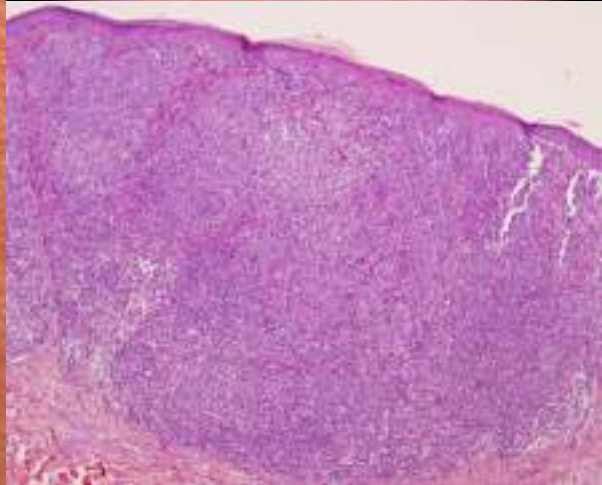


Figure 1: Fast growing Amelanotic melanoma from patient E318K in MITF & MC1R genotype = R/r

# Prevalence of the E318K MITF germline mutation in Italian melanoma patients: associations with histological subtypes and family cancer history

P. Ghiorzo<sup>1,2\*</sup>, L. Pastorino<sup>1,2\*</sup>, P. Queirolo<sup>3</sup>, W. Bruno<sup>1,2</sup>, M. G. Tibiletti<sup>4</sup>, S. Nasti<sup>1</sup>, V. Andreotti<sup>1</sup>, Genoa Pancreatic Cancer Study Group<sup>†</sup>, B. Bressac-de Paillerets<sup>5,6</sup> and G. Bianchi Scarrà<sup>1,2</sup>

1 Department of Internal Medicine and Medical Specialties, University of Genoa, Genoa, Italy 2 Laboratory of Genetics of Rare Hereditary Cancers, IRCCS AOU San Martino-IST, Genoa, Italy 3 Medical Oncology Unit, IRCCS AOU San Martino-IST, Genoa, Italy 4 Unit of Pathology, Department of Human Morphology, University of Insubria-Ospedale di Circolo, Varese, Italy 5 Service de Génétique, Institute de Cancerologie Gustave Roussy, Villejuif, France 6 INSERM, U946, Genetic Variation and Human Disease Unit, Paris, France

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\*These authors equally contributed to the study.

<sup>†</sup>Genoa Pancreatic Cancer Study Group (GPCSG) collaborators: Ghiorzo P, Belli F, Bonelli L, Borgonovo G, De Cian F, Decensi A, Dulbecco P, Filauro M, Fornarini G, Gozza A, Grillo F, Mastracci L, Papadia F, Queirolo P, Romagnoli P, Sacchi G, Savarino V, Sciallero S, Bianchi Scarrà G.

**KEYWORDS** melanoma susceptibility/kidney cancer/MITF/pancreatic cancer

**PUBLICATION DATA** Received 9 October 2012, revised and accepted for publication 13 November 2012, published online 21 November 2012

doi: 10.1111/pcmr.12047

Association with nodular melanoma p=0.018 OR 4.48 IC 95% 1.39-14.43)

## Melanomas in patients with multiple atypical nevi

1. They are more difficult to Dx
2. They can be slow and fast growing tumours
3. Monitoring with TBP +SDD imaging is the Dx best option
4. Susceptibility genes are involved in different phenotypes and the risk of MM
5. Better phenotyping/genotyping can help to improve strategy for follow-up







Hybrid Congress

# 3<sup>rd</sup> World Congress on Confocal Microscopy

June, 1-3, 2023  
Barcelona, Spain

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Susana Puig



# 19<sup>th</sup> EADO CONGRESS

April 20<sup>th</sup>-22<sup>nd</sup>, 2023



## Challenging cases in patients with multiple nevi

Josep Malvehy  
Dermatology Department of Hospital Clinic of  
Barcelona. Spain

