



Influencers (drugs, pregnancy, phototherapy, etc)

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Conflicts of interest

- None

Nevi modifiers

- Melanocytic lesions have distinct dermoscopic patterns
 - Benign patterns
 - Melanoma patterns
- Occasionally, patterns are influenced by external variations
- Most of these nevi changes/modifiers overlap with melanoma features
 - Benign nevus → melanoma mimicker on dermoscopy

Agenda

- Drugs:
 - Chemotherapy-ICI-targeted therapies (pembrolizumab, nivolumab)
 - Others (GLP-1, melanocyte stimulators)
- Pregnancy:
 - Larger nevus
 - Darker nevus
- Laser hair removal
- UV-exposure/PUVA/nbUVB

Agenda

- **Drugs:**
 - **Chemotherapy-ICI-targeted therapies (pembrolizumab, nivolumab)**
 - **Others (GLP-1, melanocyte stimulators)**
- **Pregnancy:**
 - Larger nevus
 - Darker nevus
- **Laser hair removal**
- **UV-exposure/PUVA/nbUVB**

Drugs on nevi

- Most drugs have no influence on nevi
- Drugs that have direct stimulation over nevogenesis/evolution of nevi
- Drugs that target the melanocyte stimulation axis might affect nevi
- Drugs that target the immune system might also affect nevi

Research Letter

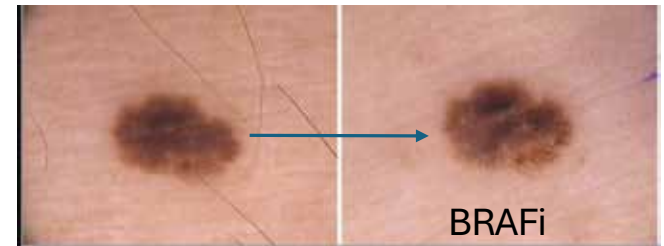
FREE

Dermoscopic Evaluation of Melanocytic Nevi Changes With Combined Mitogen-Activated Protein Kinase Pathway Inhibitors Therapy for Melanoma

Marie Perier-Muzet, MD¹; Amélie Boespflug, MD¹; Nicolas Poulalhon, MD²;
Julie Caramel, PhD¹; Anne-Laure Breton, MD²; Luc Thomas, MD, PhD²; Stephane Dalle, MD, PhD²

> Author Affiliations | Article Information

- Target blockade: BRAF and MEK
- BRAFi monotherapy: hyperpigmentation
- BRAFi+MEKi →
 - Less changes in preexisting melanocytic lesions compared with BRAFi alone
 - different dermoscopic modification patterns
 - Mainly hypopigmentation
 - Might show regression



JAMA Dermatol 2016 Oct 1;152(10):1162-1164.
Dermatol Pract Concept. 2023 Jan 1;13(1):e2023022

A Patient 4



B Patient 7



C Patient 13

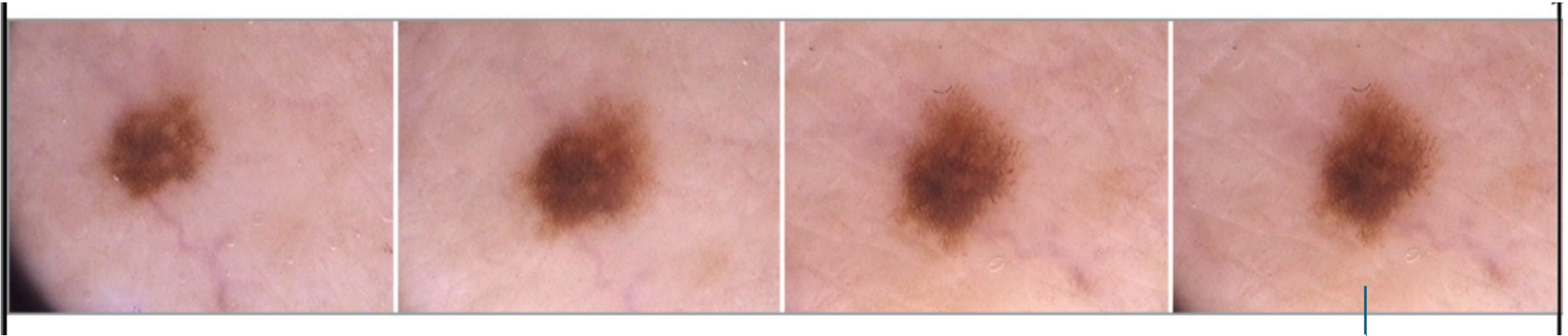


Baseline

BRAF+MEKi

BRAF+MEKi

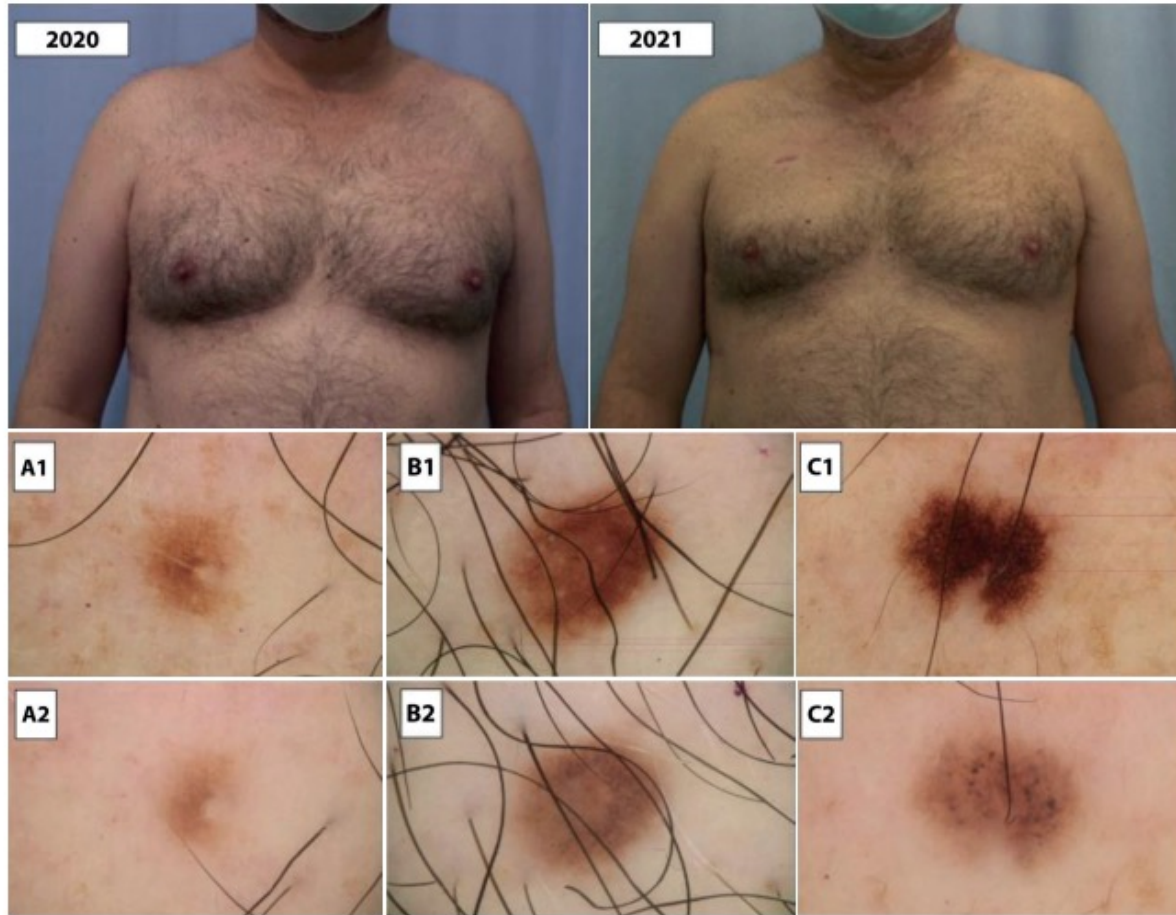
BRAF+MEKi



MEKi
withdrawn



Patient
receiving
BRAFi+MEKi



Hypopigmentati
on and
regression

Figure 1. Clinical images of patient 1: 2020 (left) and 2021 (right). Three examples of lesions registered in digital monitoring of patient 1. (A1-C1) First row shows these benign melanocytic in 2020. (A2-C2) Second row shows the same lesions one year later in 2021, 6 months after starting treatment with nivolumab.

Immune checkpoint inhibitors

- Immune checkpoint inhibitors can also produce changes in nevi
- **Dermoscopy:**
 - Diffuse “bleaching”
 - Loss of reticular pattern
 - **Regression**
 - **Halo reaction**
- Under immunotherapy regression/halo might translate into specific immune response of melanocytes → Good prognosis
- Changes might mimic melanoma

Mauzo SH, Tetzlaff MT, Nelson K, et al. Regressed melanocytic nevi secondary to pembrolizumab therapy: an emerging melanocytic dermatologic effect from immune checkpoint antibody blockade. *Int J Dermatol.* 2019 Sep;58(9):1045-1052.

Baeza-Hernández G, Rubio-Aguilera RF, et al. Regression of Multiple Melanocytic Nevi in Two Patients on Nivolumab for Metastatic Melanoma. *Dermatol Pract Concept.* 2023 Jan 1;13(1):e2023022.



68-year-old Female
Melanoma history
Pembrolizumab



GLP-1 agonists and nevi

- Glucagon-like peptide-1 receptor (GLP-1R) agonists (GLP-1RAs) are approved for type-2 diabetes and obesity, with well-established metabolic benefits
- GLP-1R are expressed in multiple tissues—including pancreas, kidney, and brain— significance of their presence in human skin is unclear → expressed in mice
- GLP-1 agonists not associated with melanoma

Unpublished data, Submitted manuscript
Diabet Med. 2024, 41:e15248.

GLP-1 agonists and nevi

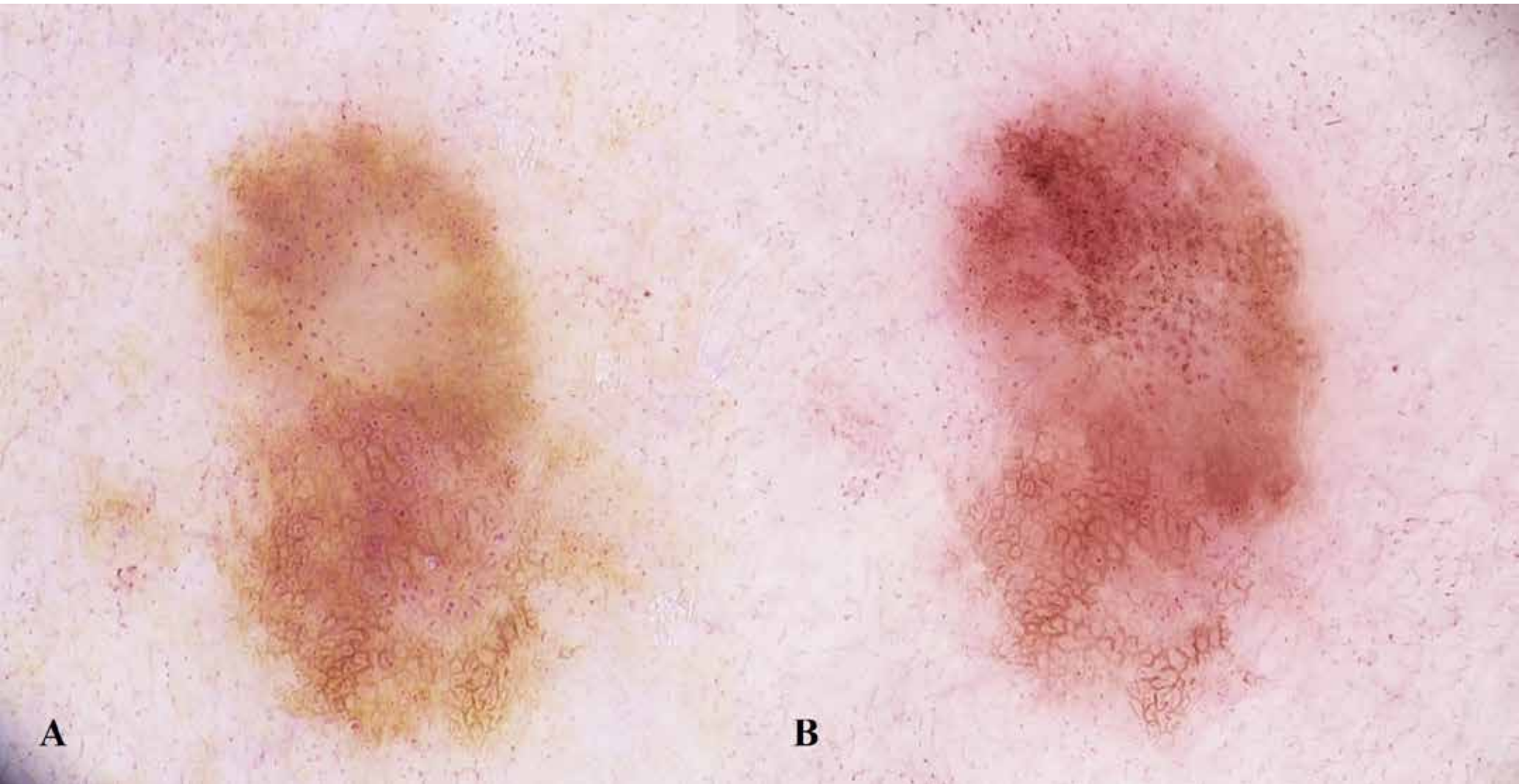
- Study including 91 pts, 18 met inclusion criteria
- Across 83 melanocytic lesions, “increase in size” and “follicular changes” were the only features reaching statistical significance
- Five lesions (6.0%) were biopsied, revealing mild to moderate-to-severely dysplastic nevi or melanocytic proliferation
- Characteristic finding: Follicular changes (p=0.002)
 - Early GLP-1RA-associated effects may involve the hair follicle microenvironment? (Mice GLP-1 in follicles)

Variable	Evaluator results (Yes/No)	% of Total (N=83)
Change		
Evaluator #1 (NJ)	39/41	46.9
Evaluator #2 (CND)	47/36	56.6

Dermoscopic Structures Analysis			
Structure Evaluated	N Evaluable Pairs	P-value*	Cohen's k
Change	80	0.345	0.302
Larger	83	0.031	0.419
Follicular changes	83	0.002	0.193
New dots	83	0.125	0.423
New Globules	83	0.688	0.363
Loss of Pigment	83	0.688	0.363

Unpublished data, Submitted manuscript





ORIGINAL ARTICLE

Dermoscopic changes in melanocytic nevi in patients receiving immunosuppressive and biologic treatments: Results of a prospective case-control study

Gamze Koseoglu, MD,^a Bengu Nisa Akay, MD,^a Orhan Kucuksahin, MD,^b and Cengizhan Erdem, MD^a
Ankara, Turkey

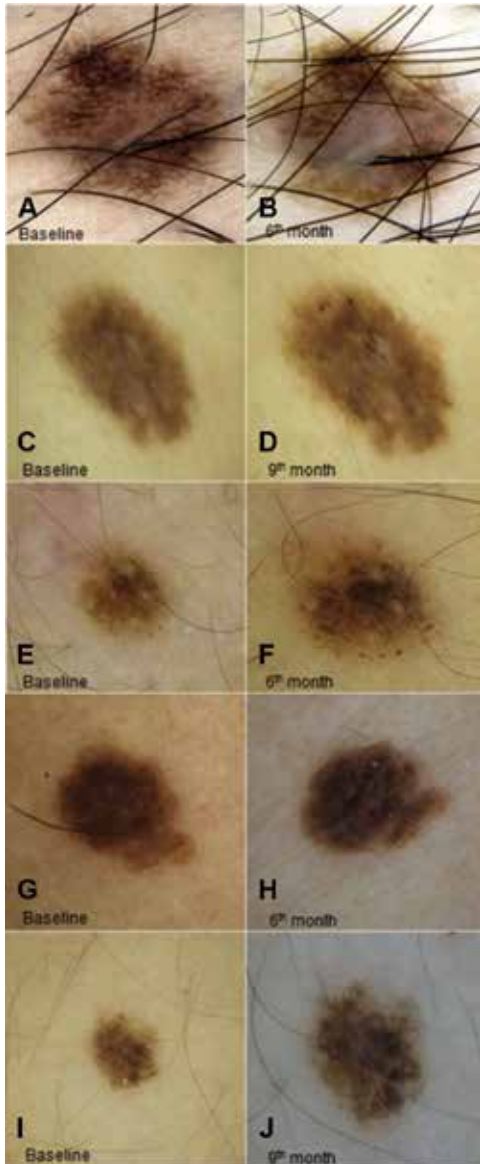
Case control prospective study

103 immunosuppressed pts (trasplant, connective tissue diseases) and **60 healthy controls**

446 lesions (266 in immunossuppressed, 180 in controls) for 12 months

Dermatoscopic evaluation and ABCD

- **Increased in the number of nevi** ($p < .001$), no changes in controls
- **Slight but significant growth in nevi size** in treated patients($p = .046$)
- **42.6%** dermoscopic changes in immunosuppression group vs 0% in controls.
- **10 were excised**, all benign (dysplastic nevus, congenital, blue nevus).
- No melanomas during treatment.



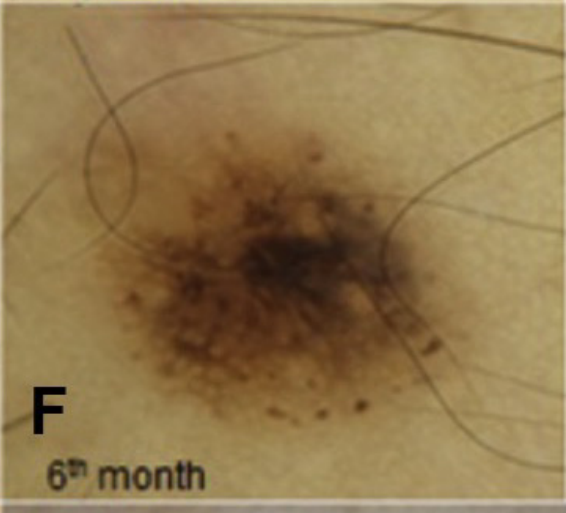
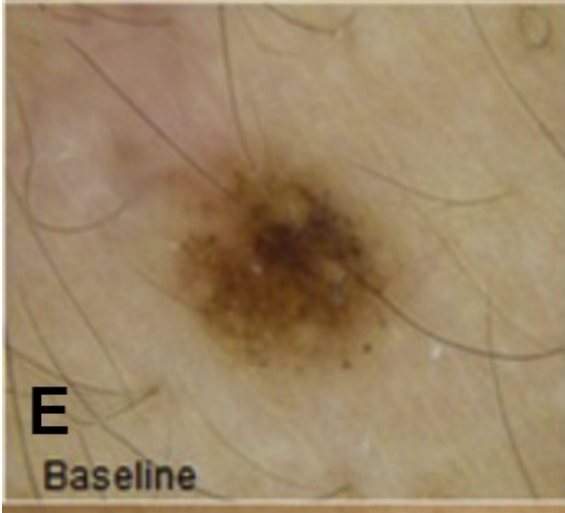
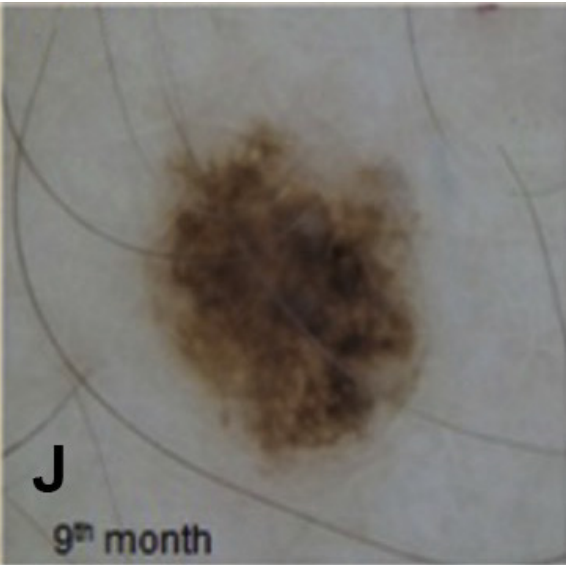
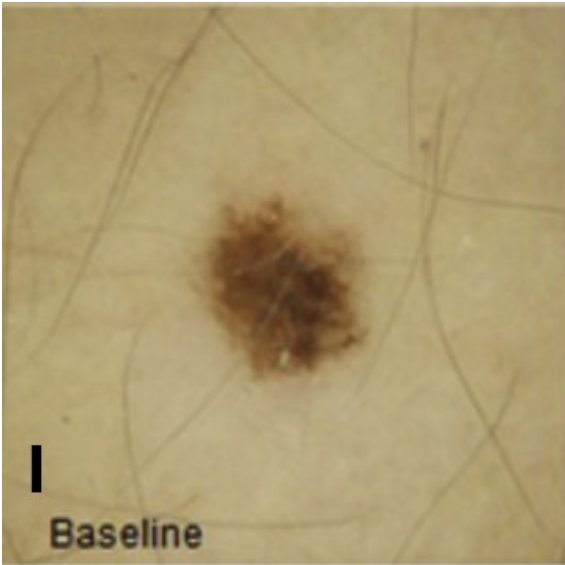
Dermoscopic changes in melanocytic nevi in patients receiving immunosuppressive and biologic treatments: Results of a prospective case-control study

Gamze Koseoglu, MD,^a Bengu Nisa Akay, MD,^a Orhan Kucuksahin, MD,^b and Cengizhan Erdem, MD^a
Ankara, Turkey

Table IV. Evaluation of dermoscopic changes in nevi at the 12th month

	Anti-TNF-alfa	Methotrexate	Cyclosporine	Azathioprine	All therapies ^a	Healthy control group ^a
No change	35 (49.3%)	40 (51.9%)	22 (59.5%)	51 (69.8%)	148 (57.4%)	180 (100.0%)
Minor change	29 (40.8%)	35 (45.5%)	12 (32.4%)	19 (26.0%)	95 (36.8%)	0 (0.0%)
Moderate change	6 (8.5%)	1 (1.3%)	3 (8.1%)	1 (1.4%)	11 (4.3%)	0 (0.0%)
Major change	1 (1.4%)	1 (1.3%)	0 (0.0%)	2 (2.8%)	4 (1.5%)	0 (0.0%)
Total	71 (100%)	77 (100%)	37 (100%)	73 (100%)	258 (100%)	180 (100.0%)

There was no statistically significant difference among each therapy in terms of dermoscopic changes in nevi ($P = .065$) when compared with baseline.



Agenda

- Drugs:
 - Chemotherapy-ICI-targeted therapies (pembrolizumab, nivolumab)
 - Others (GLP-1, melanocyte stimulators)
- **Pregnancy:**
 - **Larger nevus**
 - **Darker nevus**
- Laser hair removal
- UV-exposure/PUVA/nbUVB

Pregnancy and nevi

- Pregnancy is associated with multiple changes in the woman body
 - Hormonal
 - “Stretching”
- Few studies
- Some of these changes might affect the way nevi are seen under dermoscopy
- Some of these might mimic melanoma



***Melanoma and pregnancy

Pregnancy and the Use of Hormones
in Melanoma Patients

Alexandra Gangi, Robyn Saw, and Vernon K. Sondak

- Melanoma is the most common malignancy encountered during pregnancy (30-35% of cases)
 - 19,000 women with melanoma only 0.9% were diagnosed during their actual pregnancy
- Data does not support a clear link between pregnancy and an increased risk of development of cutaneous melanoma.
- Women with higher parity (≥ 5 live births) had a slightly lower risk of melanoma when compared to nulliparous women (RR 0.76, 95% CI 0.5–1.0).
- Prognosis? → Unaffected *per sé* but might be associated to delayed diagnosis
- Risk of transplacental transmission very low

Balch, editor, Cutaneous Melanoma Book
Cancer Causes Control 17:11–19.
Int J Obstet Gynaecol 119:1572–1582.
J Eur Acad Dermatol Venereol 29:1457–1466.
J Clin Oncol 21:2179–2186.



Total Body Photography and Sequential Digital Dermoscopy in Pregnant Women

Gabriela M. Martins-Costa¹, Renato Bakos^{1,2}

Table 1. Clinical Characteristics of New Lesions During Total Body Photography

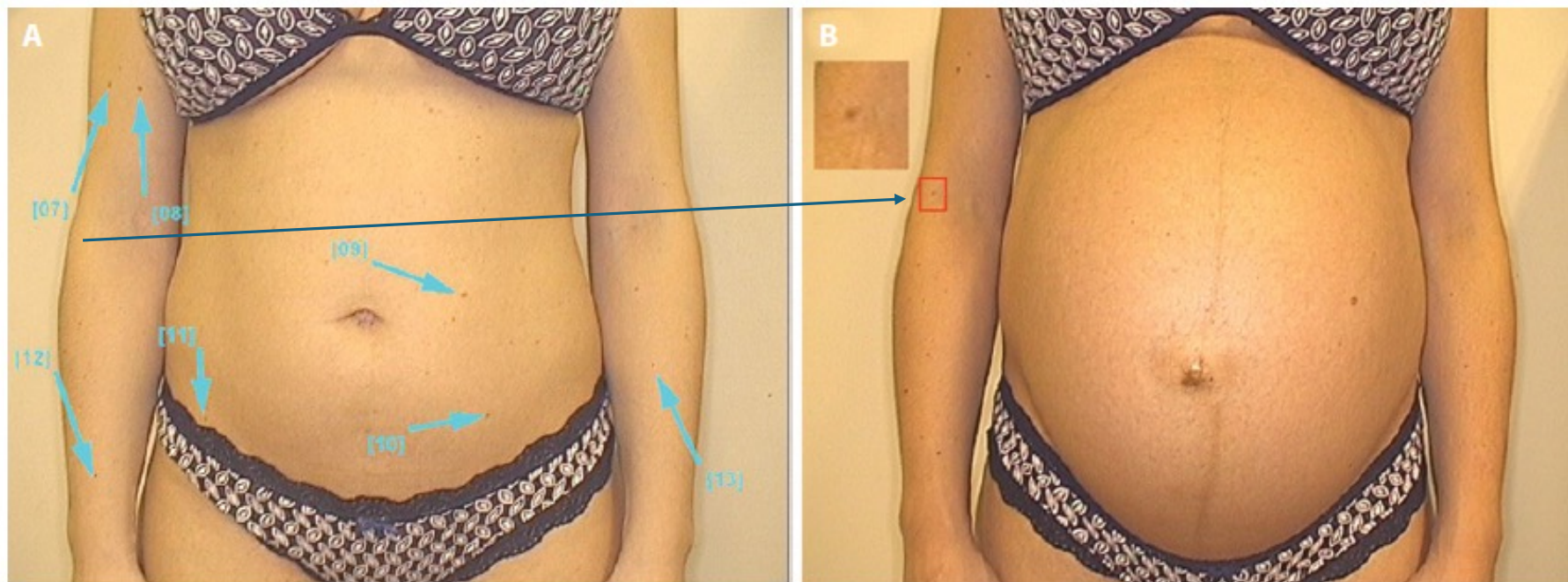
Clinical Characteristics	n (%)
Patients with new lesions	8 (44.4)
No. of new lesions per patient	
1 lesion	2 (11.0)
2 lesions	2 (11.0)
≥ 3 lesions	4 (17.0)
Location of new lesions (n = 21)	
Upper limbs	8 (100.0)
Chest	3 (37.5)
Abdomen	3 (37.5)
Lower limbs	3 (37.5)
Back	2 (25.0)
Head	1 (12.5)
Neck	1 (12.5)

- **Prospective study: 18 women (703 nevi)**
- **Age 28-44 años (mean: 33 años)**
- **Digital dermoscopy follow up - 1º to 3º trimester**

1° trimester

3° trimester

New lesion



Courtesy of Renato Bakos, MD



Courtesy of Renato Bakos, MD

Table 2. Frequencies of Dermoscopic Changes Between First and Third Trimester Observed in 703 Melanocytic Nevi

Dermoscopic Aspects	n (%)
Enlargement	387 (55.6)
Pigmentation	
Hyperpigmentation	73 (10.4)
Hypopigmentation	41 (5.8)
Dermoscopic structures	
Network changes	163 (23.2)
New dots/globules	87 (12.4)
New vascular structures	23 (3.2)
New streaks	12 (1.7)
New structureless areas	7 (1.0)

Table 3. Association of Nevus Enlargement With Body Location, Skin Type, Melanoma Risk, Presence of Dermoscopic Structures, and Age Group (n = 703)

	n (%)	P Value
Body location		
Abdomen	88/101 (87.1)	<0.001
Back	100/178 (56.2)	
Anterior chest	79/146 (54.1)	
Lower limbs	58/114 (50.9)	
Neck	19/39(48.7)	
Face	10/28 (35.7)	
Upper limbs	29/93 (31.2)	
Skin type		
IV	32/54 (59.3)	
II	142/255 (55.7)	0.959
III	213/394 (54.1)	
High-risk patients for melanoma ^a	99/220 (45.0)	0.019
Dermoscopic structures		
Network changes	105/387 (27.1)	0.014
Globules/dots formation	62/387 (16.0)	<0.001
Streaks	6/387 (1.6)	0.765
Age group (n = 18)		
<30 yrs old	1/2 (50.0)	0.867
>30 yrs old	9/16 (56.3)	

^aPatients presenting with personal or family history of melanoma in first-degree relatives.

1° trimester



3° trimester



Courtesy of Renato Bakos, MD



1° trimester



3° trimester



Courtesy of Renato Bakos, MD

1° trimester

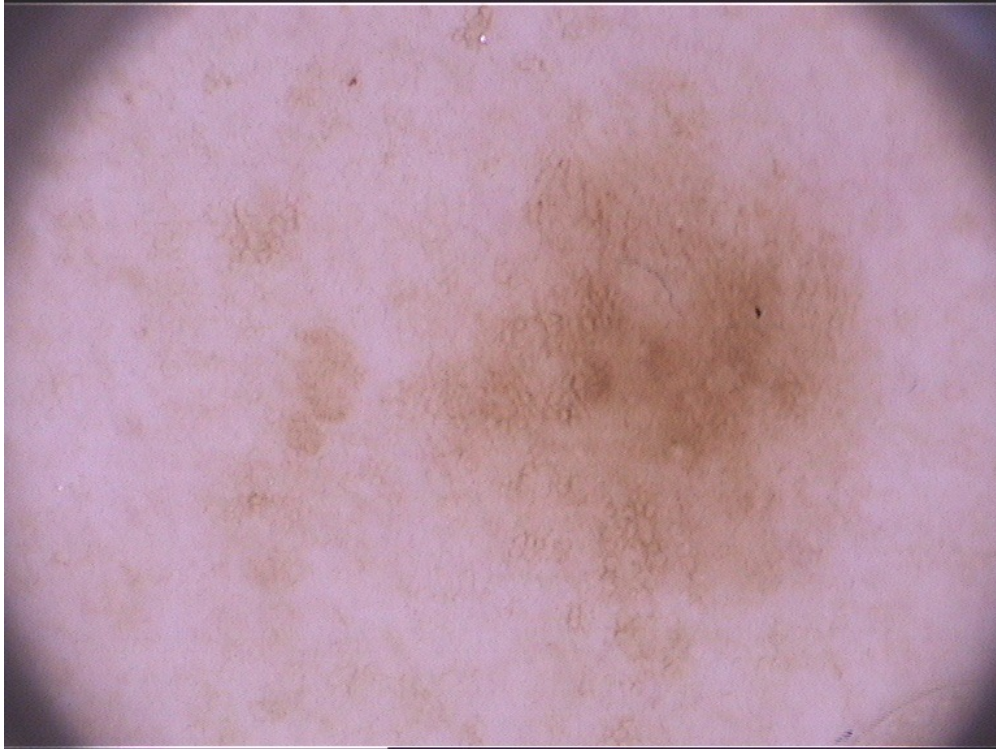


3° trimester



Courtesy of Renato Bakos, MD

1° trimester

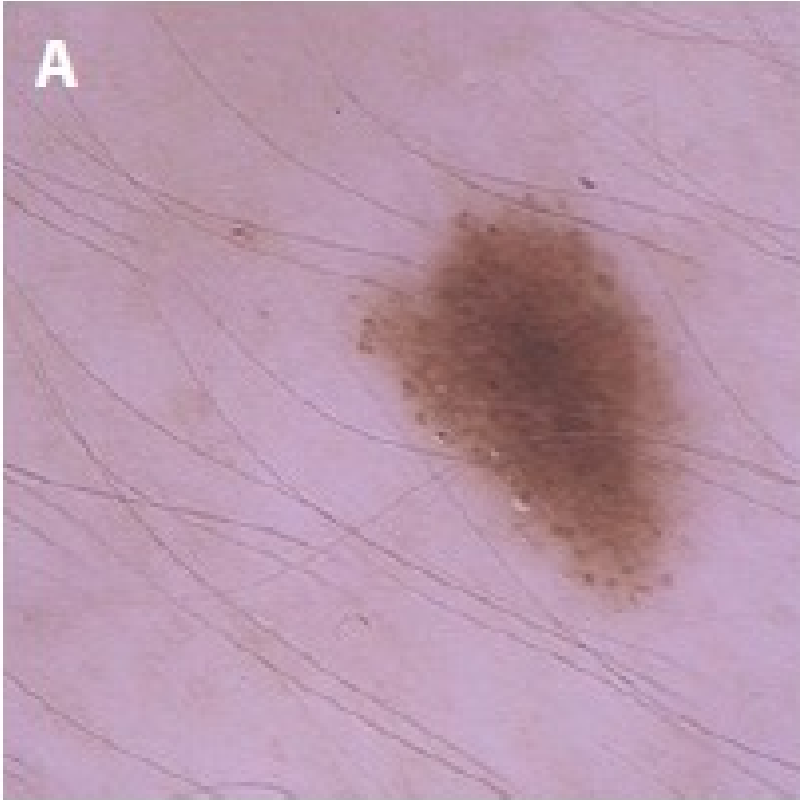


3° trimester

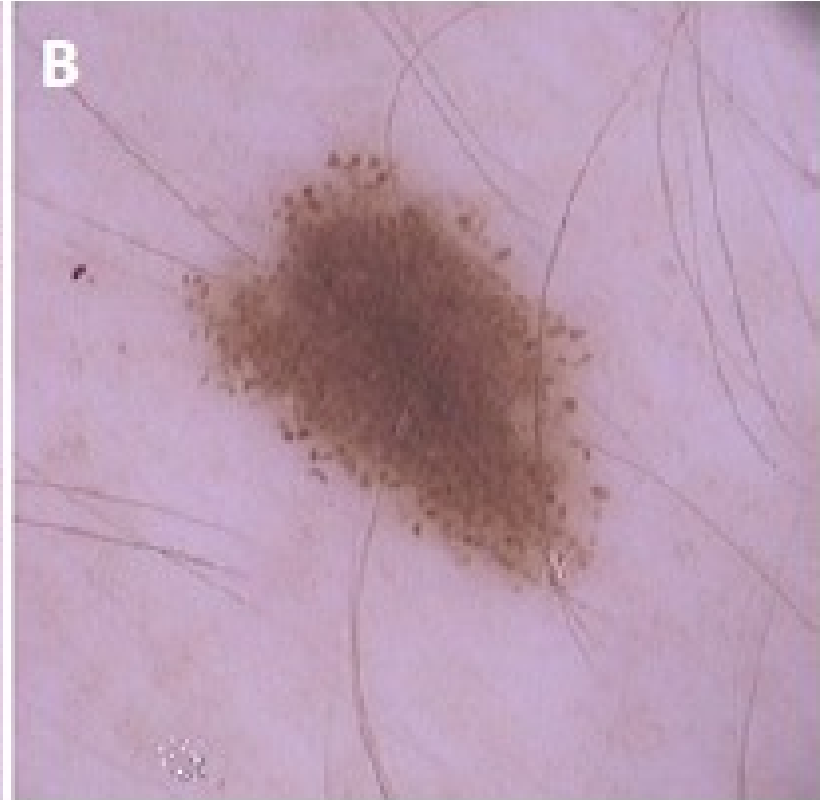


Courtesy of Renato Bakos, MD

1° trimester



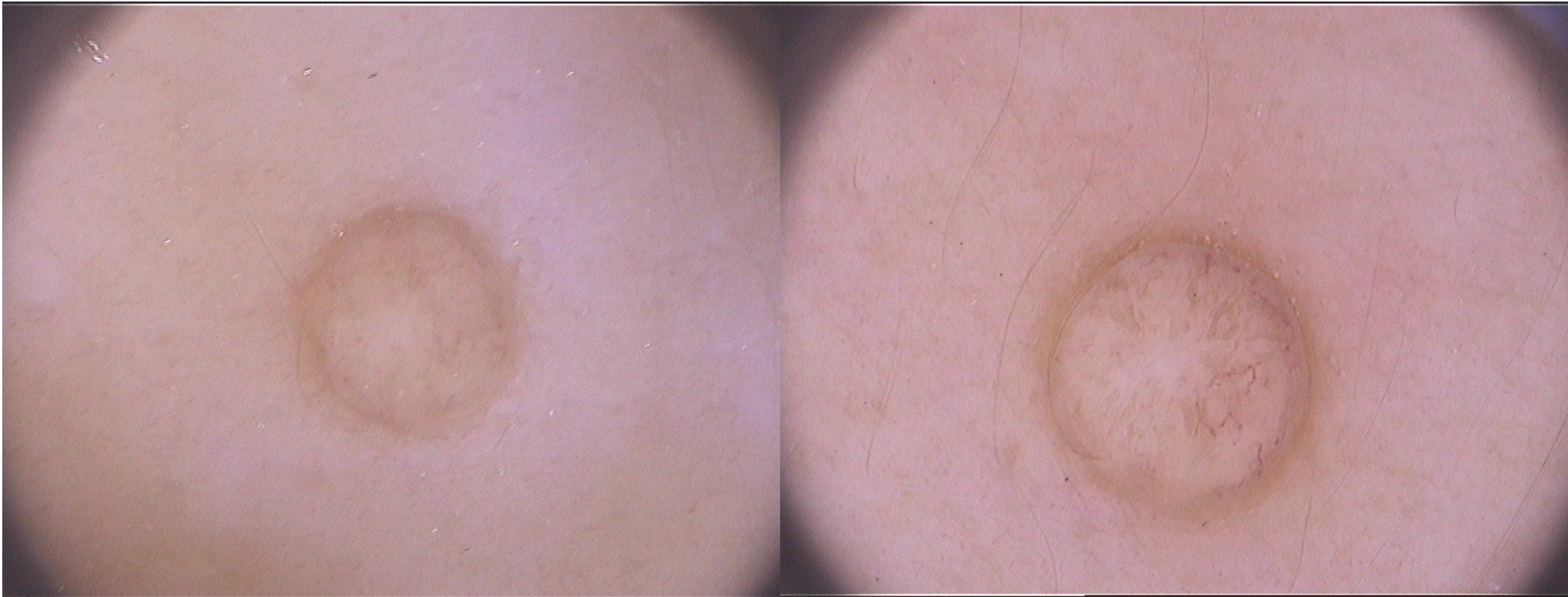
3° trimester



Courtesy of Renato Bakos, MD

1° trimester

3° trimester



Courtesy of Renato Bakos, MD

Transitory vs permanent
changes?



Before pregnancy



3° trimester

Courtesy of Renato Bakos, MD



Before pregnancy



3^o trimester



6 months after pregnancy

Courtesy of Renato Bakos, MD

3^o trimester



2 Years after pregnancy



Courtesy of Renato Bakos, MD

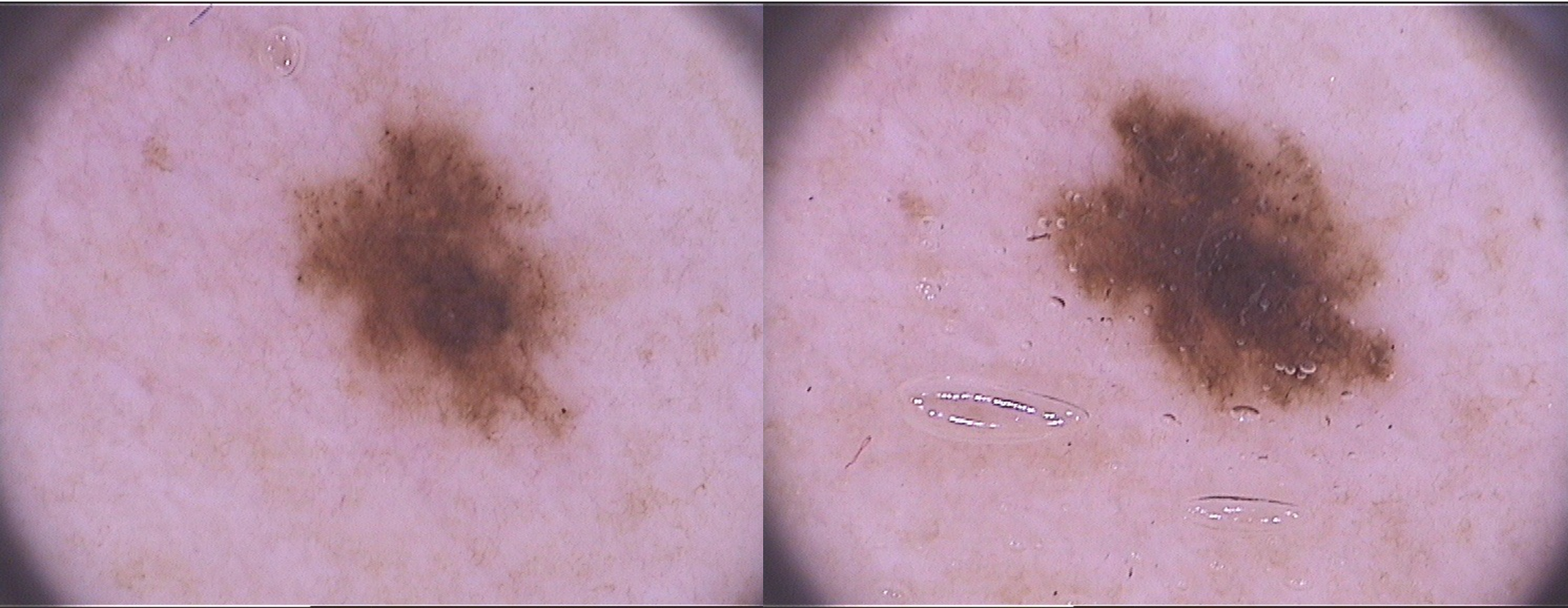
Lesions for excisions?

Melanoma?

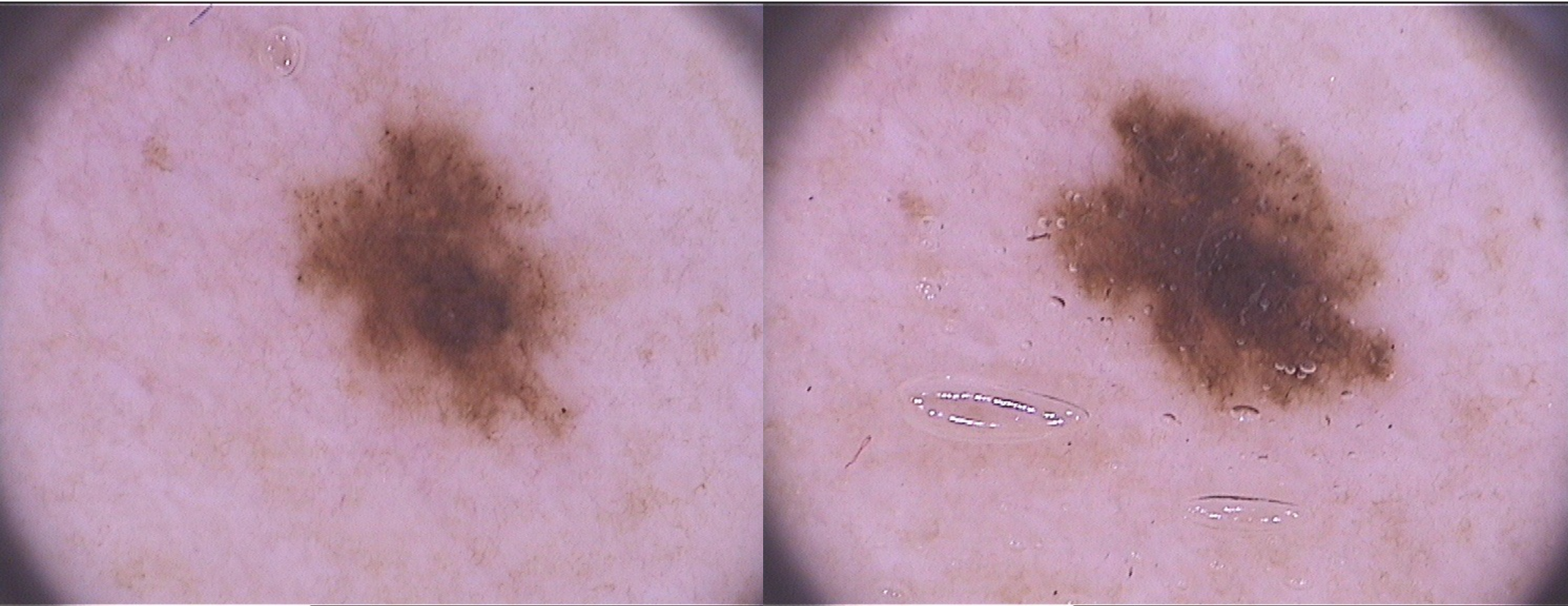


Melanoma *in situ*

Courtesy of Renato Bakos, MD



Courtesy of Renato Bakos, MD



Dysplastic nevus

Courtesy of Renato Bakos, MD



Courtesy of Renato Bakos, MD



Courtesy of Renato Bakos, MD



Dysplastic nevus

Courtesy of Renato Bakos, MD

Melanoma in situ in association with a compound nevus



Courtesy of Renato Bakos, MD

Pregnancy and nevi summary

- Recognize normal changes vs worrisome changes
 - Increase in size
 - Darkening
 - Atypical changes?
- Change in young patients vs pregnancy induced changes?

Agenda

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 - Chemotherapy-ICI-targeted therapies (pembrolizumab, nivolumab)
 - Others (GLP-1, melanocyte stimulators)
- Pregnancy:
 - Larger nevus
 - Darker nevus
- **Laser hair removal**
- UV-exposure/PUVA/nbUVB

Nevi and laser hair removal

- Melanoma is more common on the legs in Women
- Nevi on the legs can have special morphologies
 - Shaving, trauma, etc
 - Laser hair removal
- Laser hair removal: increasing use worldwide
 - It typically targets melanin which is present in nevi
 - Can produce worrisome changes on nevi
 - European Society for Laser Dermatology (ESLD) guidelines recommend avoiding laser on nevi by covering them with white adhesive tape

Gan SD, Graber EM. Dermatologic Surgery. 2013 Jun;39(6):823–38
Borkenhagen, A., et. Col.. Journal of Cosmetic Dermatology. 2020.
Dermatol Surg. 2015;31(12):2005–12.

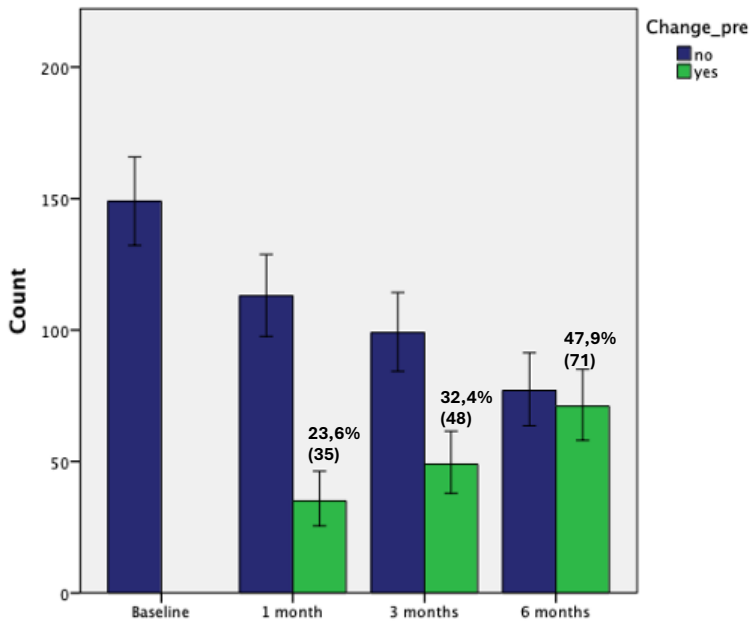
Lesions on the legs after laser:



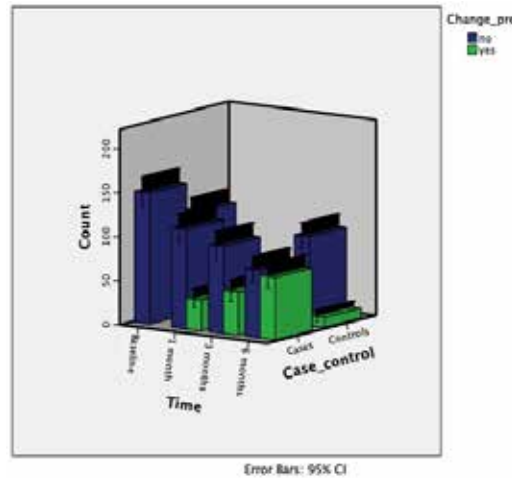
CLINICAL REPORTS

Clinical and dermoscopic evaluation of melanocytic nevi changes during diode laser hair removal: A prospective study

Renata Aclé MD¹ | María José Zambrano-Mericq MD¹ |
 Cristian Navarrete-Dechent MD^{1,2} | Pablo Uribe MD, PhD^{1,2} | Álvaro Abarzúa-Araya MD^{1,2}

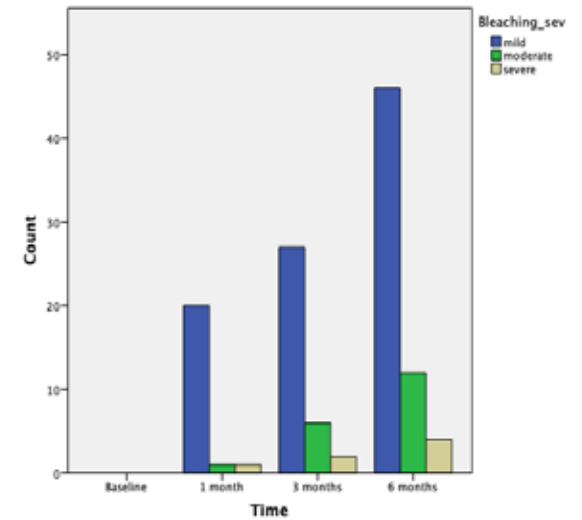


Any change (cases) seen in 31%



47.9% (71/148) nevi on the legs compared with 9.8% (11/112) on the arms (p< 0.001): OR 8.4

34 patients with a total of 148 nevi on the legs and 112 nevi on the arms (controls).



Bleaching was the most common change in 41.9%

Clinical and dermoscopic evaluation of melanocytic nevi changes during diode laser hair removal: A prospective study

Renata Acle MD¹ | María José Zambrano-Mericq MD¹ |
Cristian Navarrete-Dechent MD^{1,2} | Pablo Uribe MD, PhD^{1,2} | Álvaro Abarzúa-Araya MD^{1,2}

- Melanoma-specific features
 - “Irregular hyperpigmented areas” seen in 18% overall, persisting in 5% of the cases at the sixth session
 - “Regression structures” in 5% overall, persisting in 5% of nevi at the sixth session





Baseline



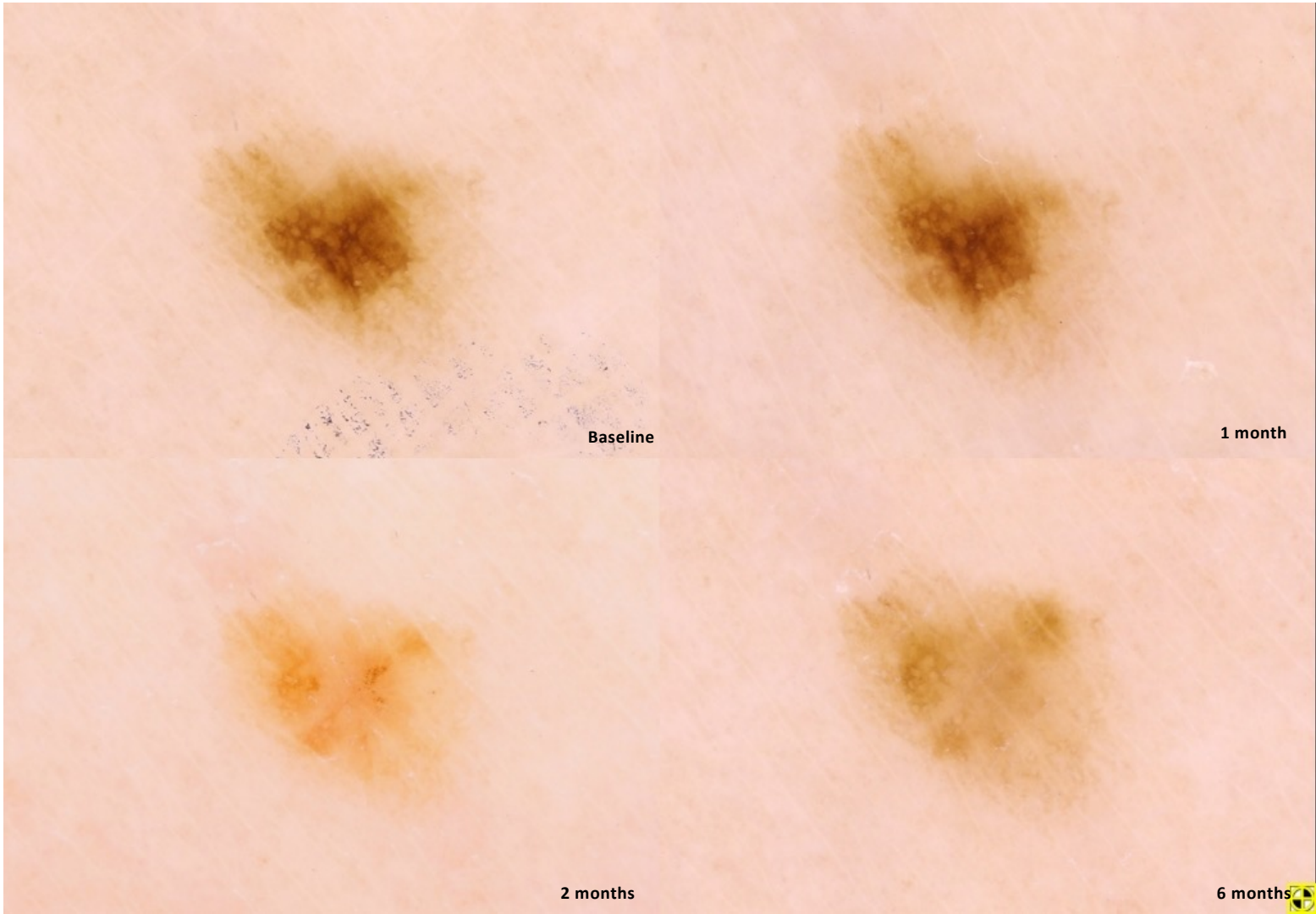
1 month

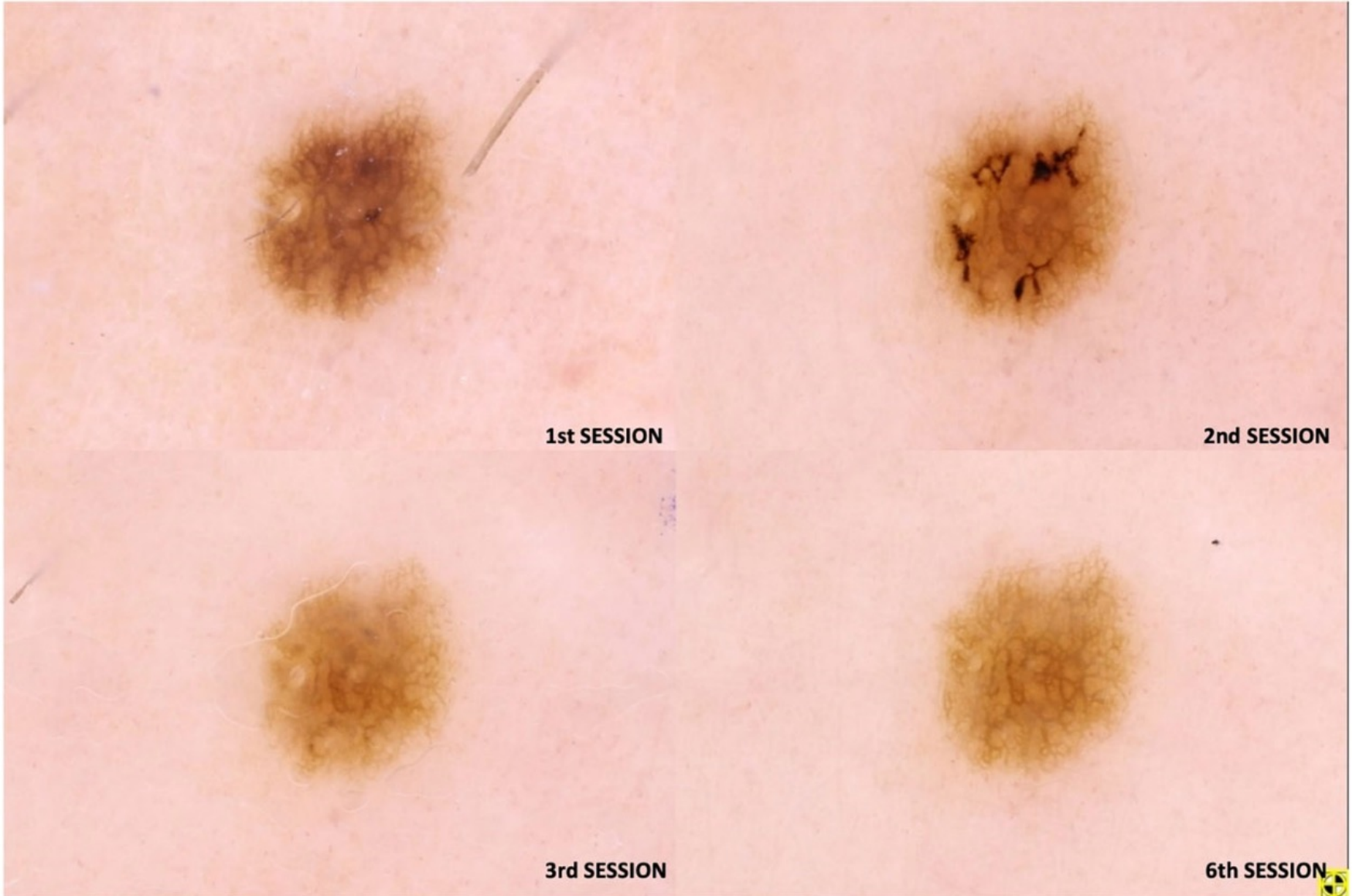


2 months



6 months





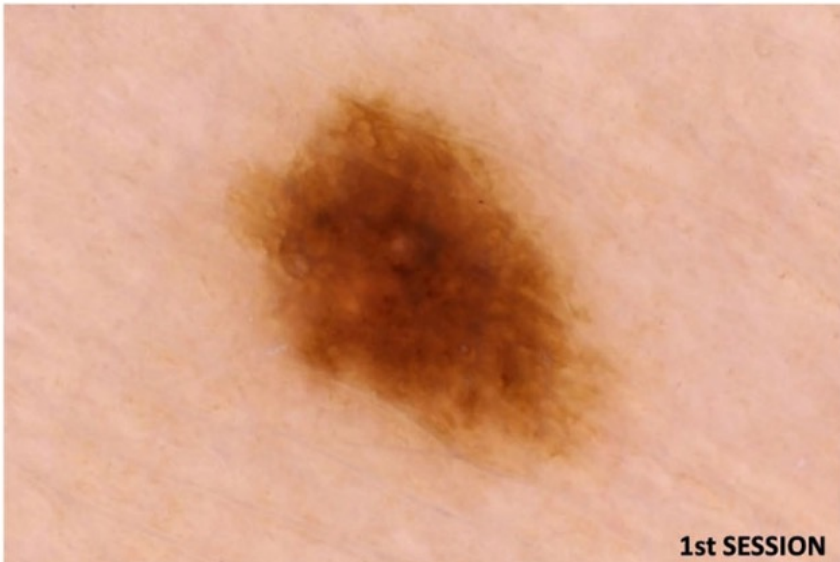
1st SESSION

2nd SESSION

3rd SESSION

6th SESSION

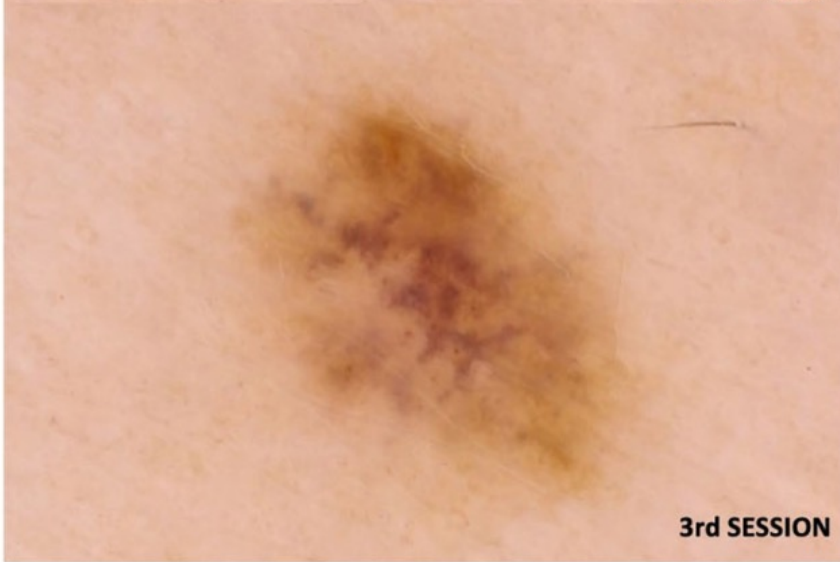




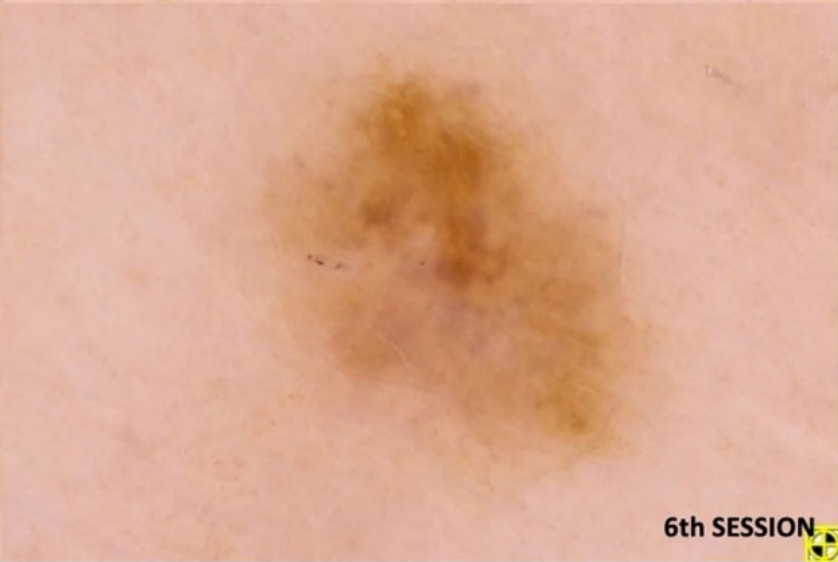
1st SESSION



2nd SESSION



3rd SESSION



6th SESSION

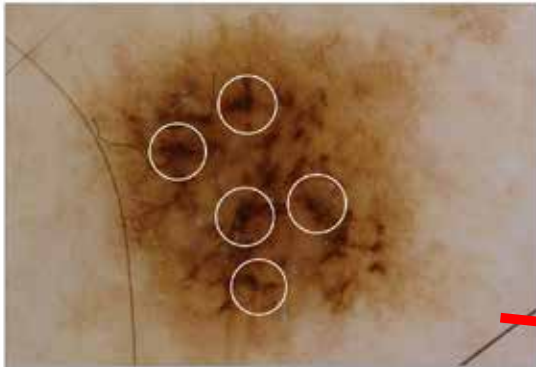


Accuracy of Dermoscopic Criteria for the Diagnosis of Melanoma In Situ

Aimilios Lallas, PhD; Caterina Longo, PhD; Marco Manfredini, MD; Elisa Benati, MD; Graziella Babino, MD; Chiara Chinazzo, MD; Zoe Apalla, PhD; Chryssoula Papageorgiou, MD; Elvira Moscarella, MD; Athanassios Kyrgidis, PhD; Giuseppe Argenziano, PhD

Figure 2. Irregular Hyperpigmented Areas and Blotches

A Irregular hyperpigmented areas



B Irregular hyperpigmented areas

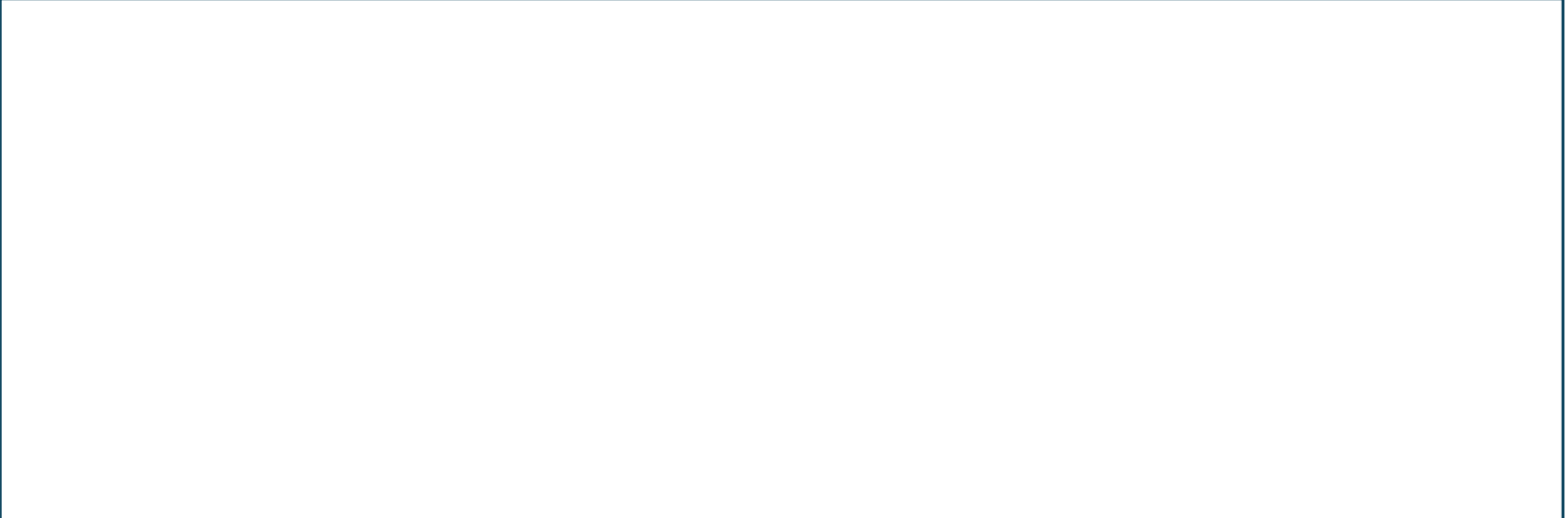


Criterion valid after ruling out prior laser hair removal → follow up

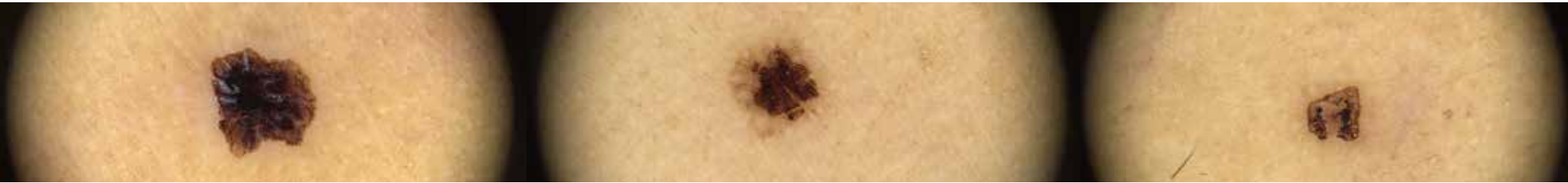


1st SESSION

2nd SESSION







Laser hair removal bottom line

- Patients that underwent LHR experience changes in nevi in 1/3 of cases
- The most common dermoscopic finding is bleaching
- Some nevi can have changes that cannot always be easily distinguished between laser-induced or melanoma.
 - Follow-up, direct interrogation of the patient

Agenda

- Drugs:
 - Chemotherapy-ICI-targeted therapies (pembrolizumab, nivolumab)
 - Others (GLP-1, melanocyte stimulators)
- Pregnancy:
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 - Darker nevus
- Laser hair removal
- **UV-exposure/PUVA/nbUVB**

Phototherapy and nevus

- Phototherapy (nbUVB and PUVA) are used in different dermatologic diseases: psoriasis, vitiligo, MF, etc
- PUVA
 - Increase melanoma risk
 - PUVA lentiginos
- nbUVB:
 - No increase in melanoma risk
 - Might have changes in nevi

Eur J Dermatol 2004;14:230-4.

J Am Acad Dermatol 2008;58:763-8.

J Eur Acad Dermatol Venereol 2007;21:526-31.

Dermoscopic Changes of Melanocytic Nevi after Psoralen-Ultraviolet A and Narrow-Band Ultraviolet B Phototherapy

Hayedeh Ghani-Nejad, Zahra Hallaji, Maede Rayati Damavandi, Vahide Lajevardi, Nessa Aghazadeh, Hooman Moeini, Sara Beigi

- 74 melanocytic nevi of 20 patients, 12 male (60%), with a mean age of 35 years were studied.
 - 54 nevi received NB-UVB while 20 received PUVA
 - 50% of the nevi in each group were exposed to radiation while the remaining nevi were covered.
- Dermoscopic changes were observed in 34/37 (91.8%) of the exposed nevi compared with 16/37 (43.2%) of the covered nevi ($P=0.0001$).
- The most common dermoscopic changes were new dot/globule formation (62.1%), increase in the nevus size (27%), and patchy pigmentation (18.8%).
- The prevalence of overall dermoscopic changes was significantly higher in the PUVA-exposed nevi (100% for PUVA, 88.8% for NB-UVB, P value 0.041).
 - New dot-globule formation was noted in all nevi (100%) exposed to PUVA compared to only 48.1% in the NB-UVB group (P value 0.0056)

Dermoscopic Changes of Melanocytic Nevi after Psoralen-Ultraviolet A and Narrow-Band Ultraviolet B Phototherapy

Hayedeh Ghani-Nejad, Zahra Hallaji, Maede Rayati Damavandi, Vahide Lajevardi, Nessa Aghazadeh, Hooman Moeini, Sara Beigi

Table 2: Changes in the dermoscopic features of exposed and covered melanocytic nevi after receiving UV radiation

Nevi (number)	Dermoscopic features									
	Patchy pigmentation		Overall darkening		New dot and globule formation		Nevus enlargement		Any dermoscopic change	
	N (%)	P value	N (%)	P value	N (%)	P value	N (%)	P value	N (%)	P value
Total (74)										
Covered (37)	1 (2.7)	0.02	3 (8.1)	0.01	7 (18.9)	0.003	1 (2.7)	0.006	16 (43.2)	0.0001
Exposed (37)	8 (18.8)		12 (32.4)		23 (62.1)		10 (27)		34 (91.8)	
PUVA (20)										
Covered (10)	1 (10)	0.58	3 (30)	0.34	5 (50)	0.03	1 (10)	0.3	8 (80)	0.2
Exposed (10)	3 (30)		5 (50)		10 (100)		4 (40)		10 (100)	
NB-UVB (54)										
Covered (27)	0	0.05	0	0.01	2 (7.4)	0.001	0	0.02	8 (29.6)	0.0001
Exposed (27)	5 (18.5)		7 (25.9)		13 (48.1)		6 (22.2)		24 (88.8)	

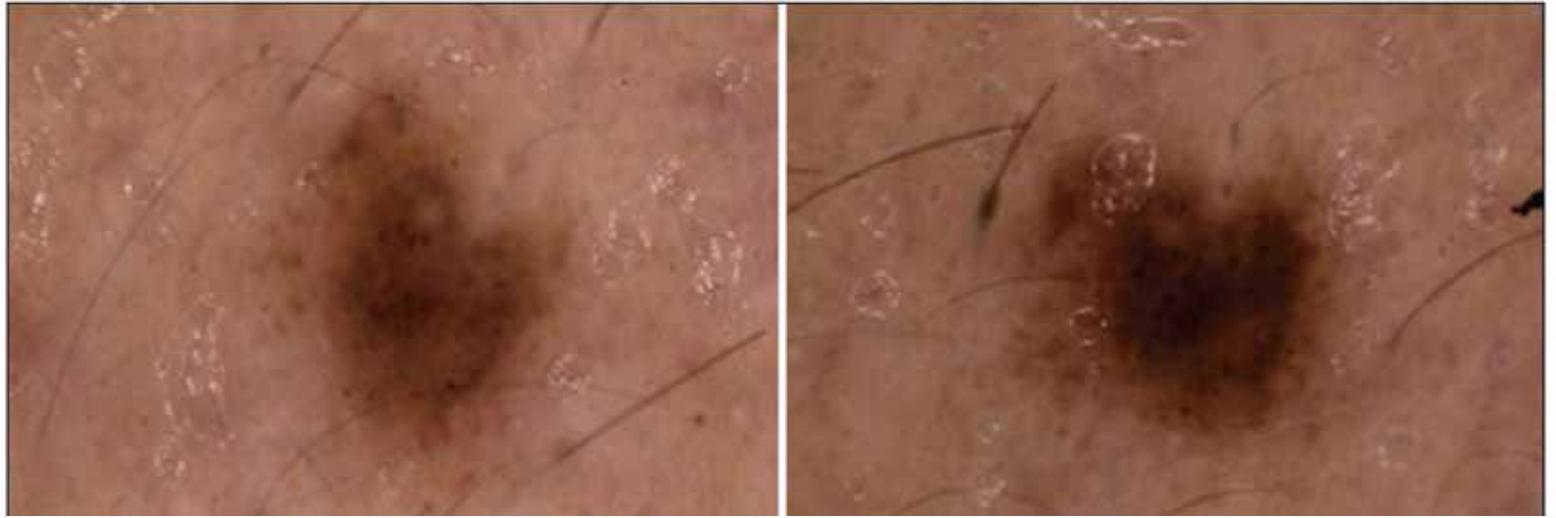
UV: Ultraviolet, PUVA: Psoralen-ultraviolet A, NB-UVB: Narrowband ultraviolet B

Table 3: Comparison of the dermoscopic features of exposed and covered nevi in NB-UVB and PUVA-treated patients

Covered		(%)	P value	Exposed	
				(%)	
Patchy pigmentation	NB-UVB	0	0.2	5 (18.5)	0.65
	PUVA	1 (10)		3 (30)	
Overall darkening	NB-UVB	0	0.5	7 (25.9)	0.23
	PUVA	3 (30)		5 (50)	
New dot/globule formation	NB-UVB	2 (7.4)	0.0092	13 (48.1)	0.0056
	PUVA	5 (50)		10 (100)	
Nevus enlargement	NB-UVB	0	0.2	6 (22.5)	0.42
	PUVA	1 (10)		4 (40)	
Any dermoscopic changes	NB-UVB	2 (7.4)	0.0172	24 (88.8)	0.041
	PUVA	7 (70)		10 (100)	

NB-UVB: Narrowband ultraviolet B, PUVA: Psoralen-ultraviolet A

New dots



Darkening



Take home message

- Many external (and internal) modifiers can affect the morphology of nevi
- Recognizing these modifiers can affect how we approach these lesions
 - Excision vs follow-up
- We reviewed:
 - Drugs
 - Pregnancy
 - Laser hair removal
 - Phototherapy

