Tumor Board: Case based learning

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Memorial Sloan Kettering Cancer Center

International Dermoscopy Society

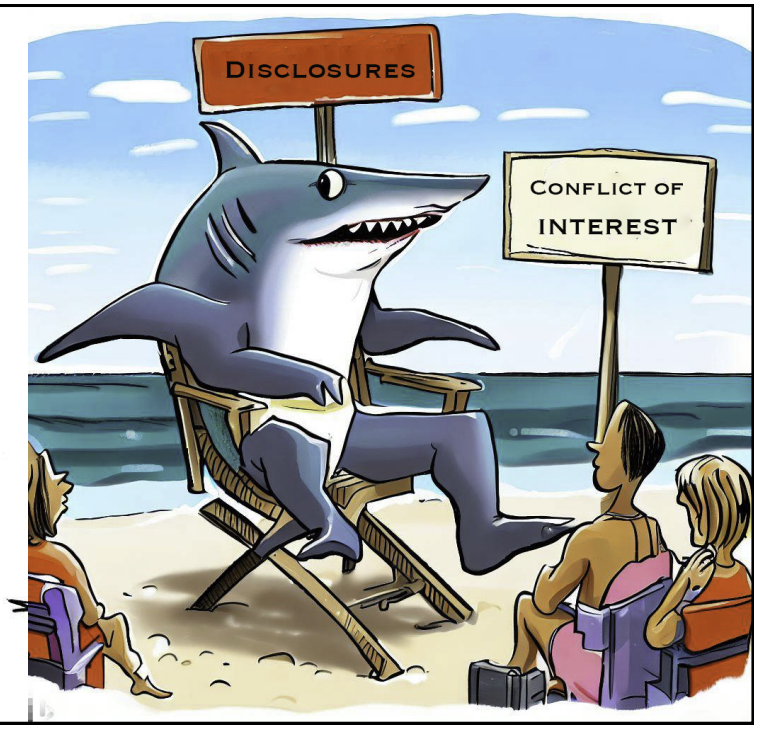
Welcome to dermoscopedia

AMERICAN DERMOSCOPY MEETING

1

Disclosures

- Canfield
- DermLite
- Heine
- FotoFinder
- Casio



Microsoft Bing AI image generator (no need for copyright)

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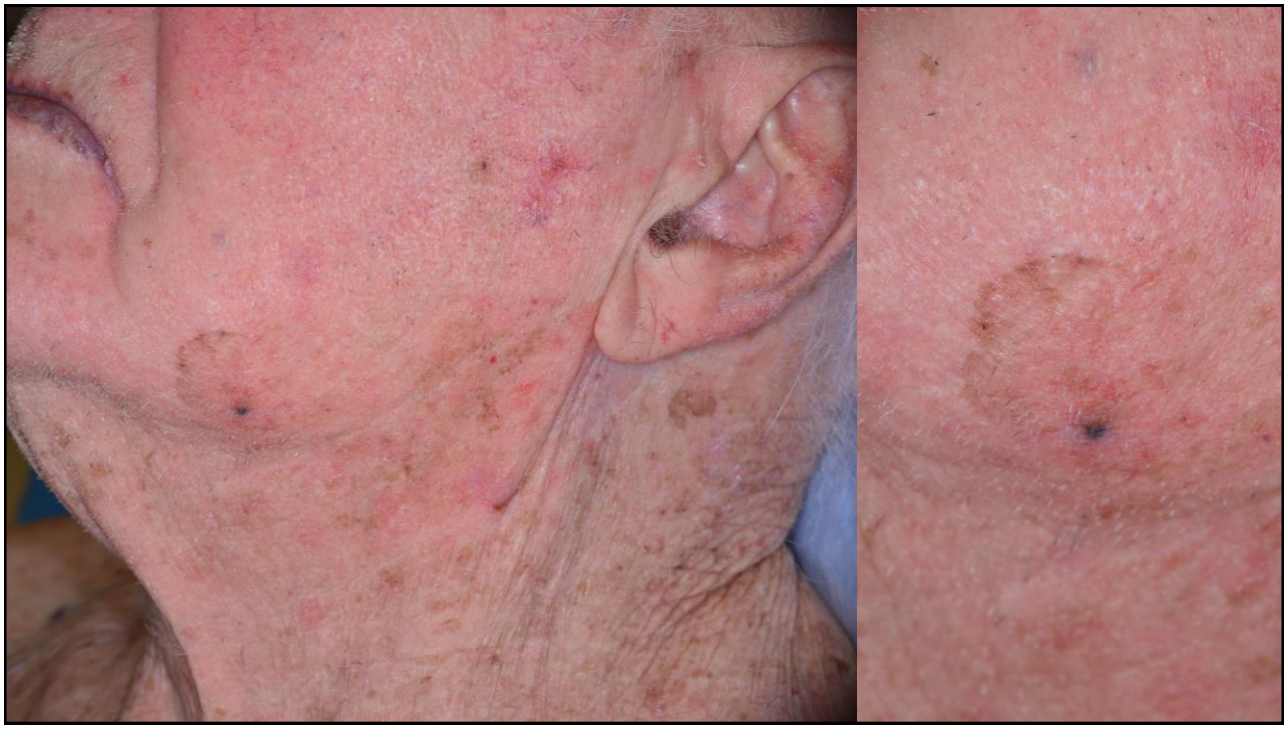
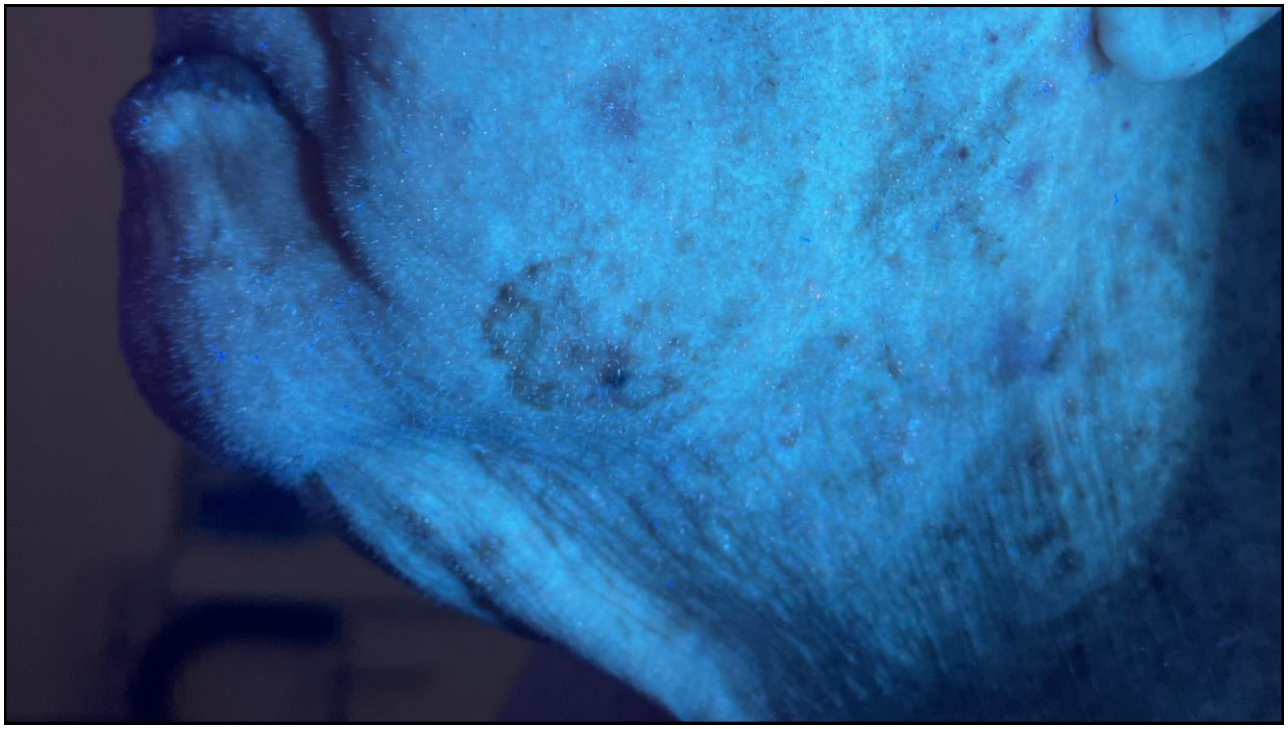


3


An 80+ yo patient with a personal history of skin cancer presents for follow-up skin cancer surveillance exam.
This asymptomatic lesion was noted on his jaw line.
This lesion was not selected or tagged by AI (TBP) as a lesion of concern. Wood's light examination…

4



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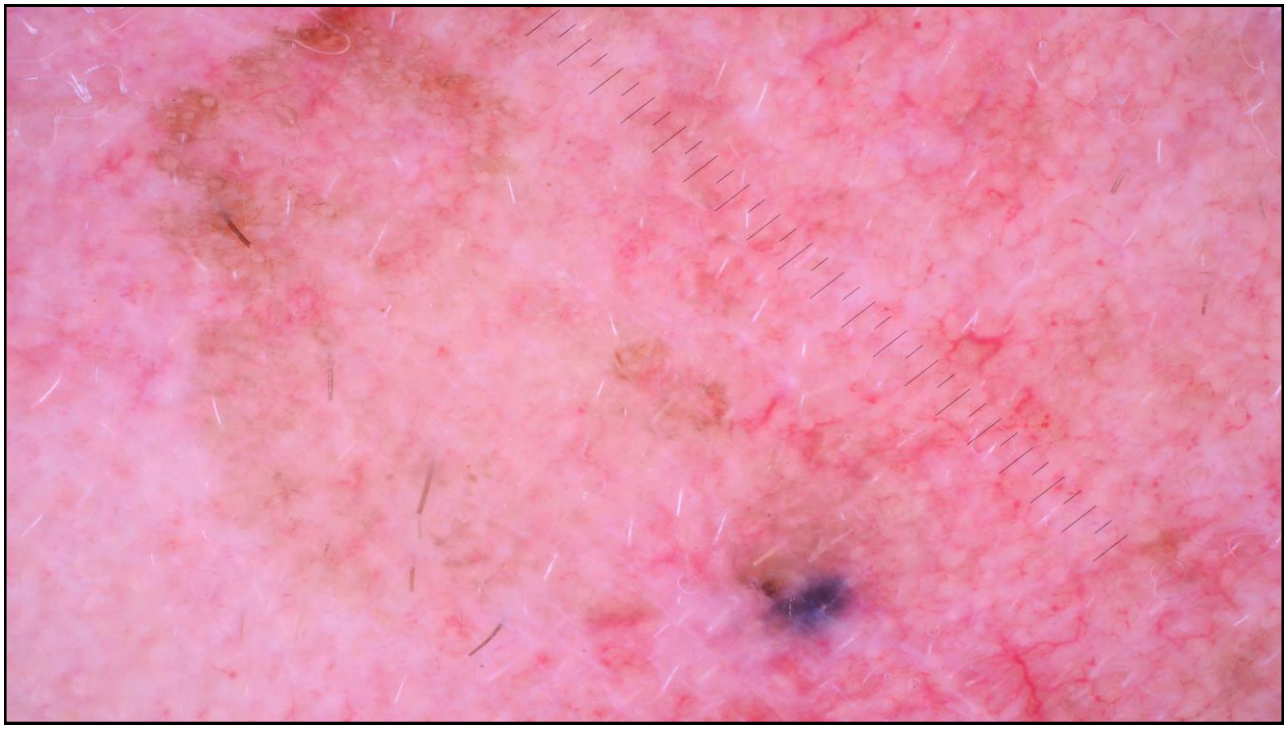

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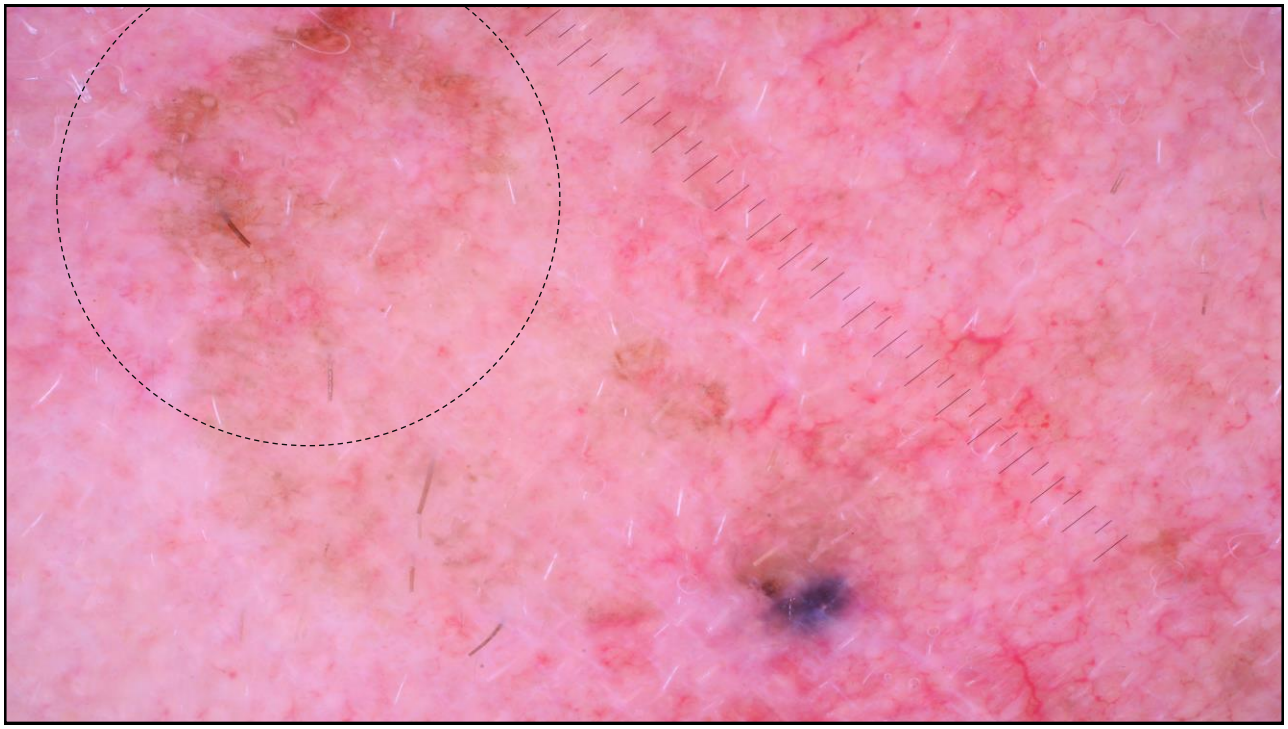

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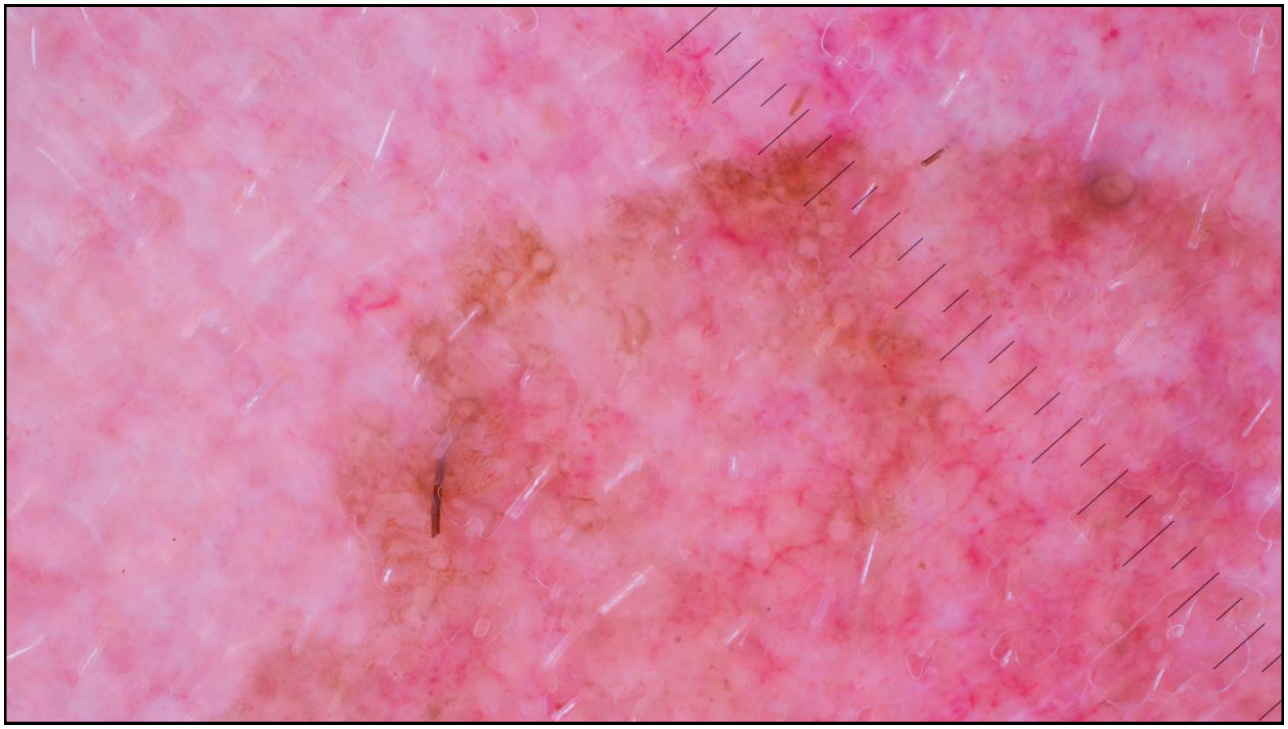

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What is your diagnosis?
a) Lentigo
b) AIMP
c) Lentigo maligna (MMIS)
d) Lentigo maligna melanoma

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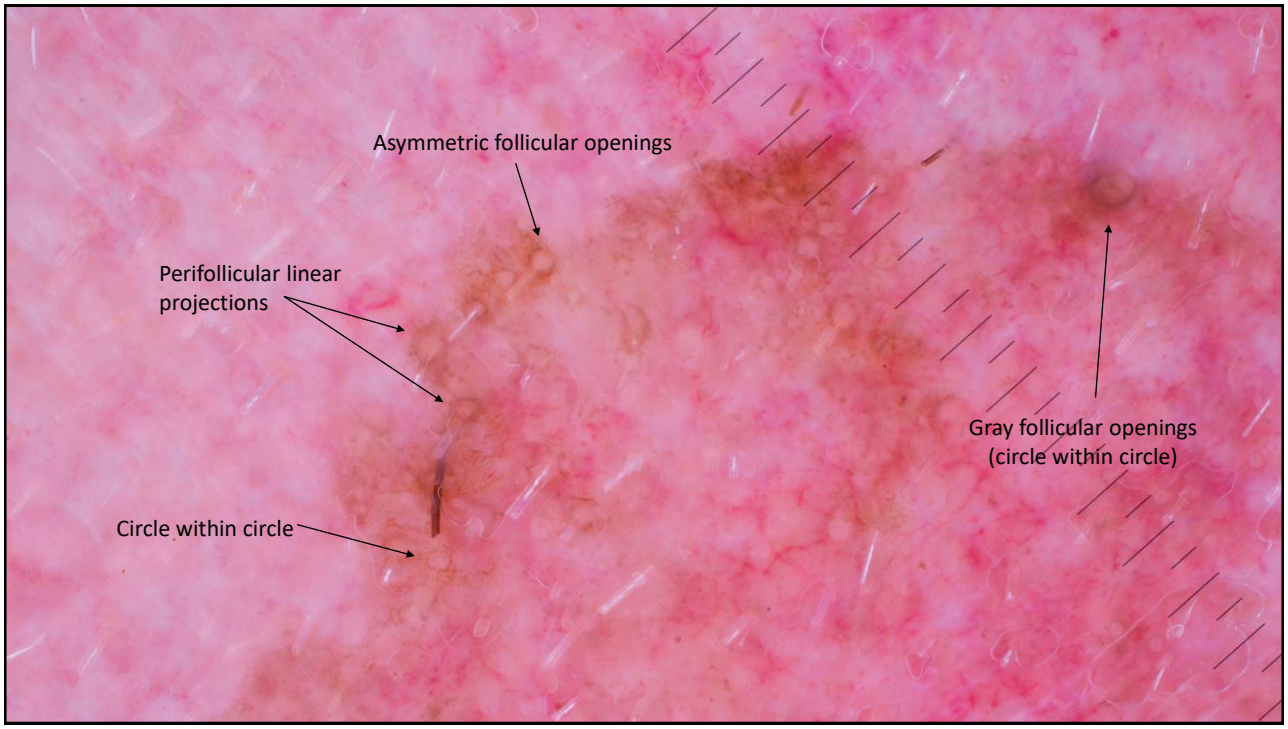
Asymmetric follicular openings
Perifollicular linear projections
Gray follicular openings (circle within circle)
Circle within circle

10

Progression Model for LM-LMM

P. Schiffner, et al.
J.Am.Acad.Dermatol.
2000

Improvement of early recognition of lentigo maligna using dermatoscopy

Roman Schiffner, MD,[a] Julia Schiffner-Rohe, MSc,[a] Thomas Vogt, MD,[a] Michael Landthaler, MD,[a]
Uwe Wlotzke, MD,[a] Armand B. Cognetta, MD,[b] and Wilhelm Stolz, MD[a]

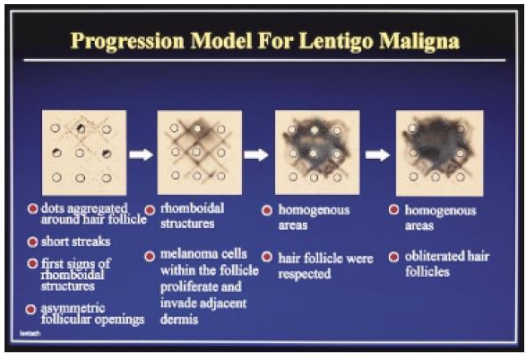

Fig. 6. Progression growth model of LM. *Circles* represent hair follicles.

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Melanocyte stem cells: Biology and current aspects

Monika Gola, Rafał Czajkowski, Anna Bajek, Aleksander Dura, Tomasz Drewa

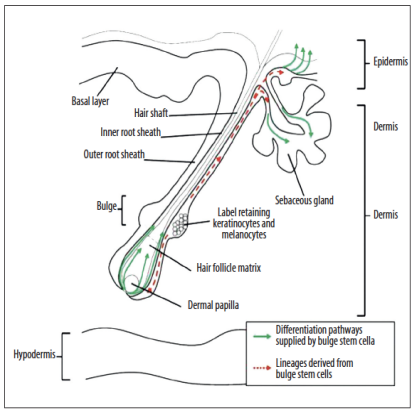

Figure 1. Hair follicle and the localization of melanocyte and keratinocyte stem cells. As depicted in this picture, melanocyte stem cells reside in the lower part of the hair bulge (a niche, where also occur epidermal stem cells) among of the matrix keratinocytes. Dividing keratinocytes give rise to the keratinized hair shaft. During the transition from telogen to anagen, activation of a melanocyte stem cell leads to development of melanocyte progenitors, after all to differentiated melanocytes which produce melanin pigment. Packets of melanin are transferred to adjacent keratinocytes, which confers color to the hair shaft [39].

EDITORIALS

Three Roots of Melanoma

SEGURA ET AL.[1] DESCRIBE MORPHOLOGIC FEATURES of melanomas with a nodular component using in vivo reflectance-mode confocal microscopy (RCM) and correlate these RCM findings with histopathologic findings. The most striking observation made by the investigators is the remarkable difference in epidermal

See also page 1311

involvement between nodular melanoma (NM) and superficial spreading melanoma (SSM) with a nodular component. At RCM, SSMs frequently showed epidermal disarrangement and pagetoid infiltration, whereas NMs exhibited a preserved epidermal pattern and few pagetoid cells.[1] This new observation provides fertile ground for revisiting the conventional concept of melanoma development. We propose an alternative hypothesis based on recent observations made in stem cell research and demonstrate how this hypothesis can better account for the observed clinical and epidemiologic differences between melanoma subtypes.

Many clinicians and researchers subscribe to the theory that all cutaneous melanomas arise from transformed epidermal melanocytes. The malignant cells are thought to initially proliferate along the basal layer (melanoma in situ). After a variable period, which can range from months to decades, the malignant melanocytes may acquire the capacity to not only proliferate radially but also invade

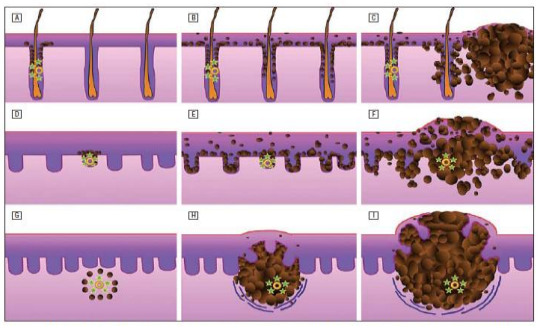

Figure 1. Schematic model shows the origin of lentigo maligna, nodular melanoma, and superficial spreading melanoma from melanoma stem cells of the hair follicle, the dermis, and the epidermal basal layer, respectively. Melanoma stem cells (yellow concentric ring) produce progenitor cells (green stars) that drive proliferation and progression of melanoma cells (brown circles). A-C, Lentigo maligna deriving from stem cells of the outer sheet of the facial hair follicle. D-F, Superficial spreading melanoma deriving from stem cells in the epidermal basal layer. G-I, Nodular melanoma deriving from dermal stem cells.

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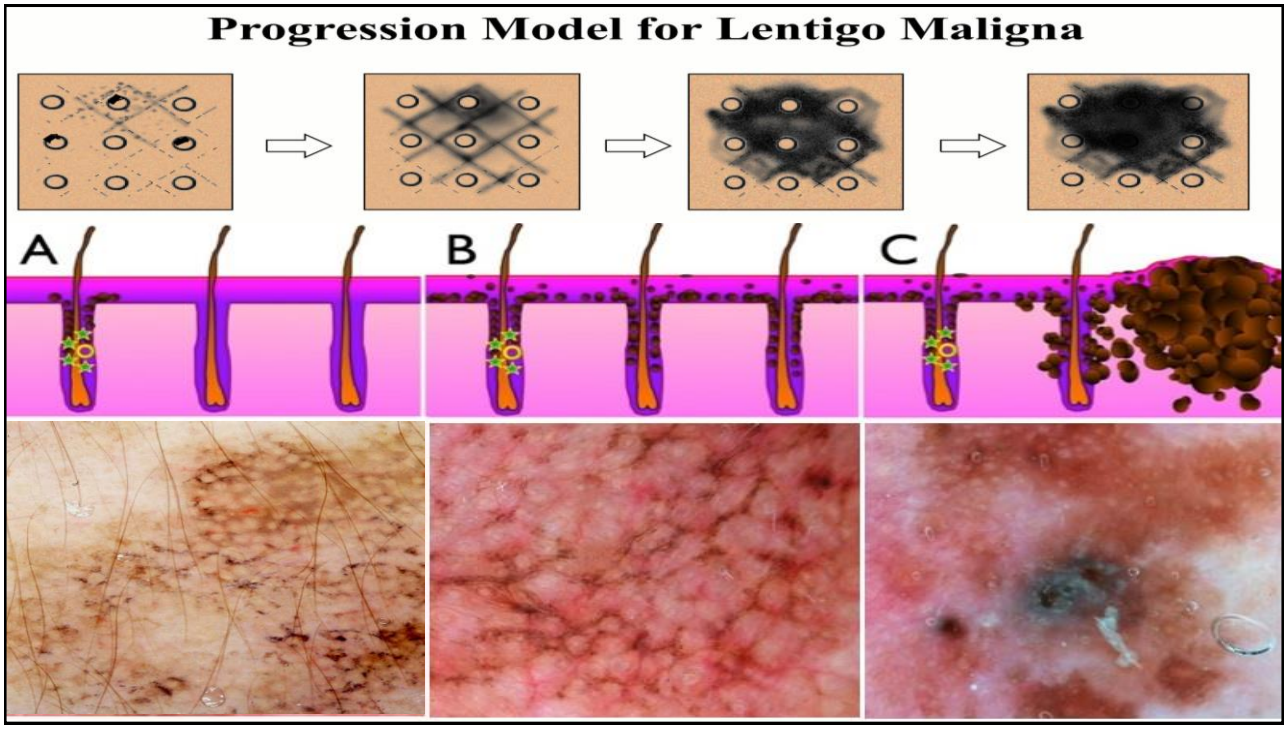

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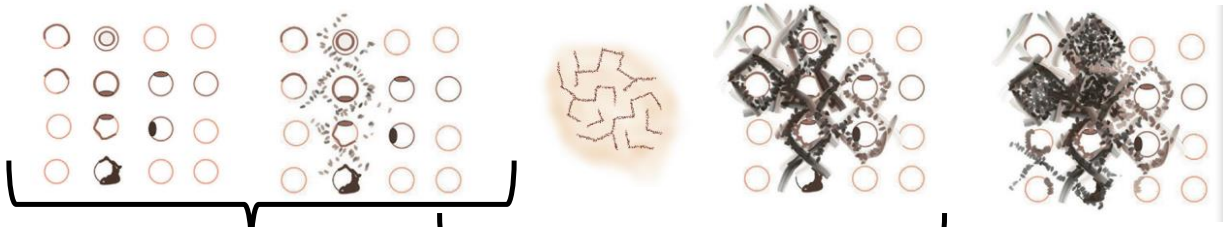
CLINICAL AND LABORATORY INVESTIGATIONS
BJD
British Journal of Dermatology

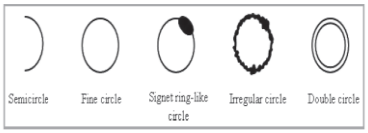
Dermoscopy of lentigo maligna melanoma: report of 125 cases

P. Pralong,[1] E. Bathelier,[1] S. Dalle,[1] N. Poulalhon,[1] S. Debarbieux[1] and L. Thomas[1]

Progression model



Annular-granular pattern



Interfollicular pattern:
-Angulated lines (polygons)
-Perifollicular linear projections

Blotch pattern:
-preserved follicular openings
-obliteration of follicular openings

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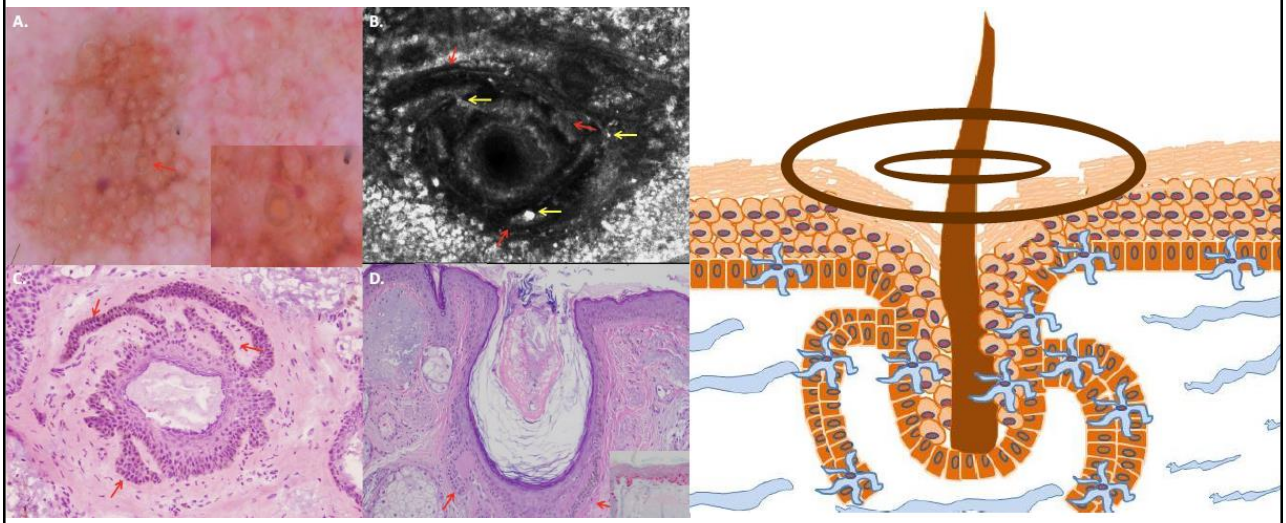
Circle within a circle (isobar)



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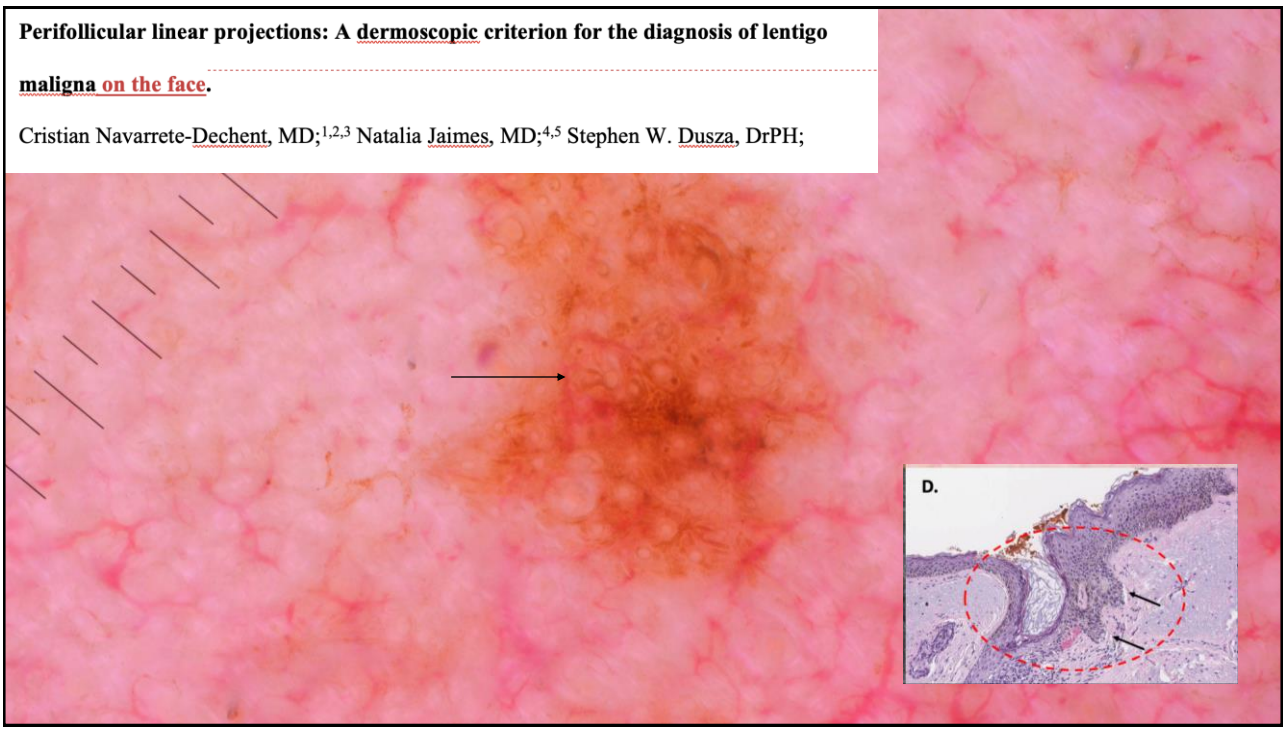
Perifollicular linear projections: A dermoscopic criterion for the diagnosis of lentigo maligna on the face.

Cristian Navarrete-Dechent, MD;[1,2,3] Natalia Jaimes, MD;[4,5] Stephen W. Dusza, DrPH;



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Perifollicular Linear Projections (PLP)

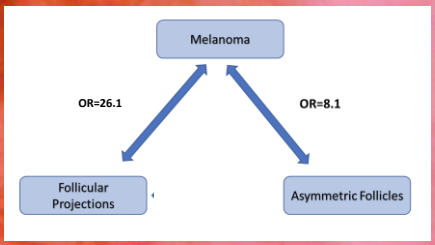
Study in progress:

Sensitivity = 61.8%

Specificity = 96.02%

PPV = 87.04%

6.6% of LM had PLP w/o any other MM-specific structures



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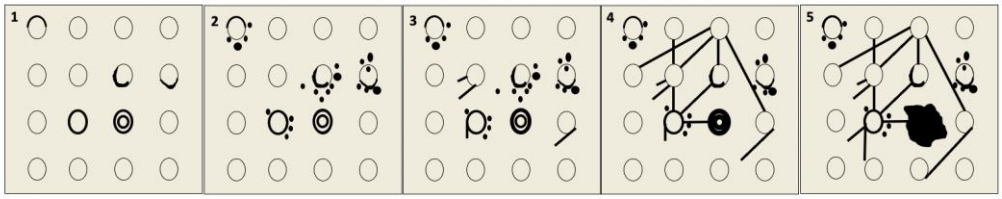

Updated Lentigo Maligna dermoscopic criteria

1. Asymmetric pigmentation of the hair follicles, circle within circle
2. Annular granular pattern
3. Peri Follicular projections
4. Rhomboidal structures
5. Obliteration of hair follicles

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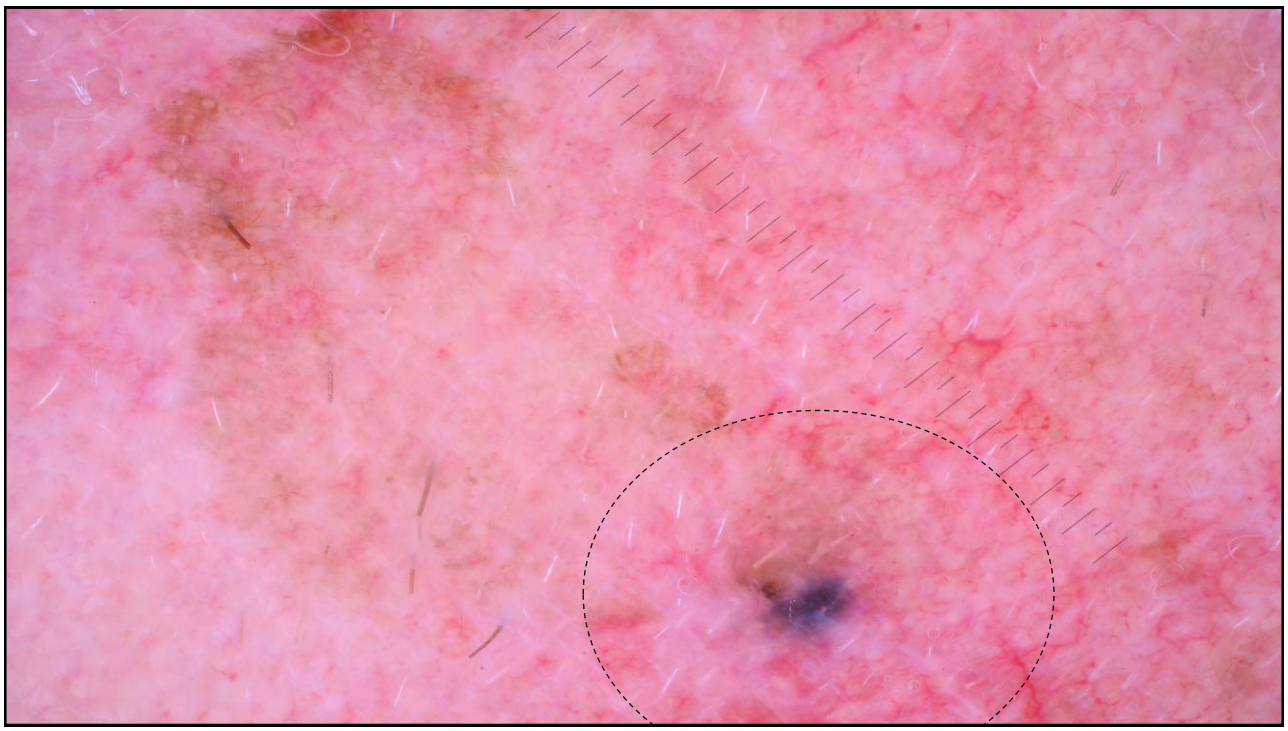

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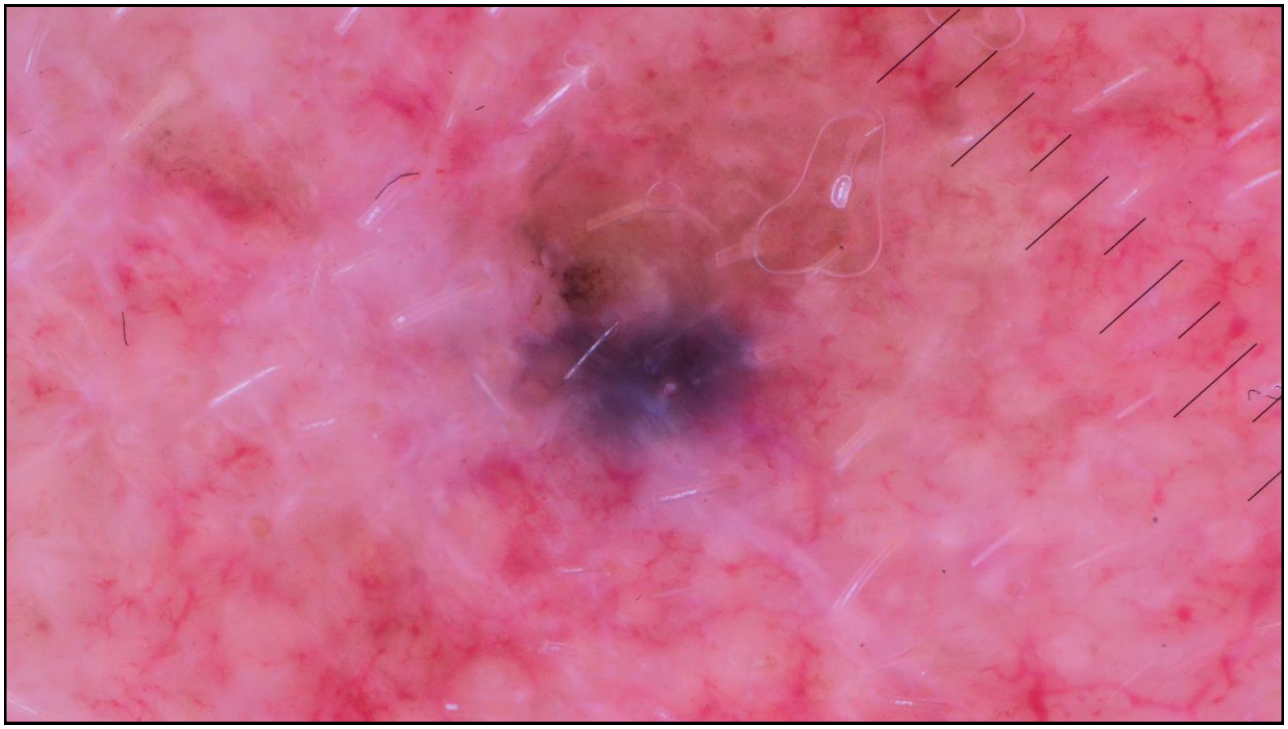

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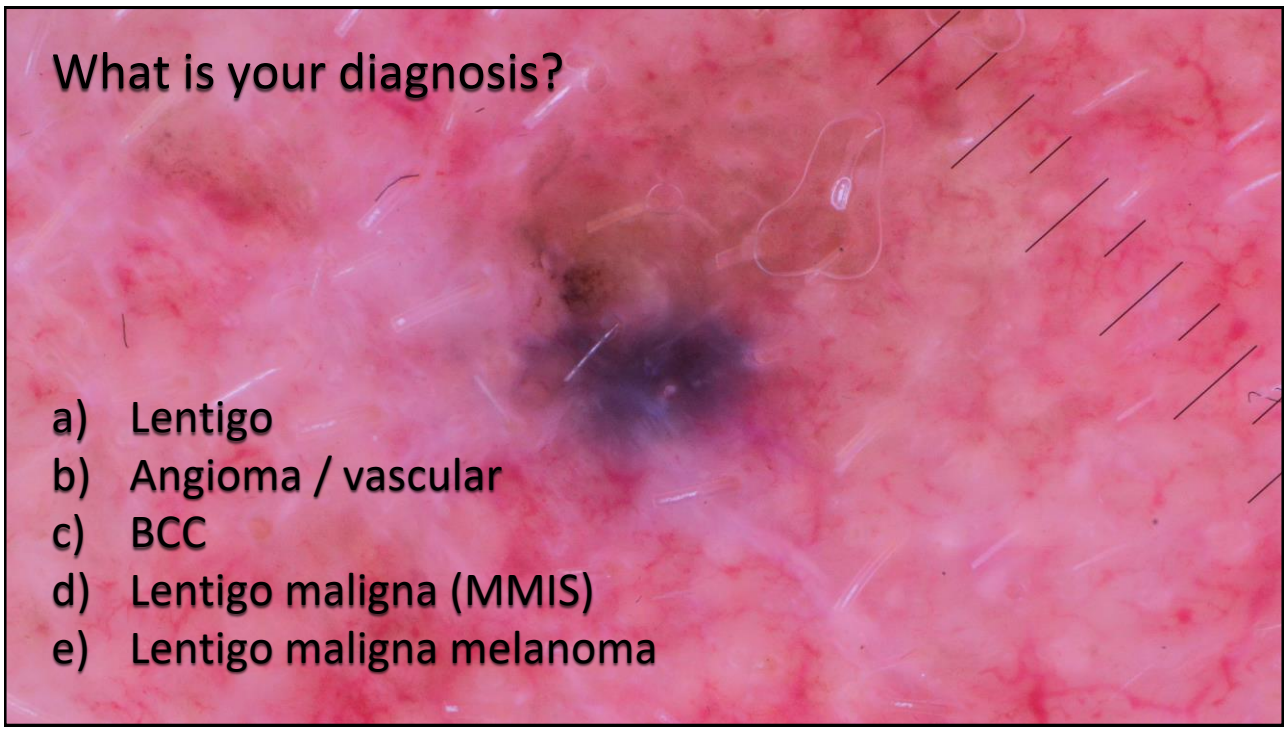
What is your diagnosis?
a) Lentigo
b) Angioma / vascular
c) BCC
d) Lentigo maligna (MMIS)
e) Lentigo maligna melanoma

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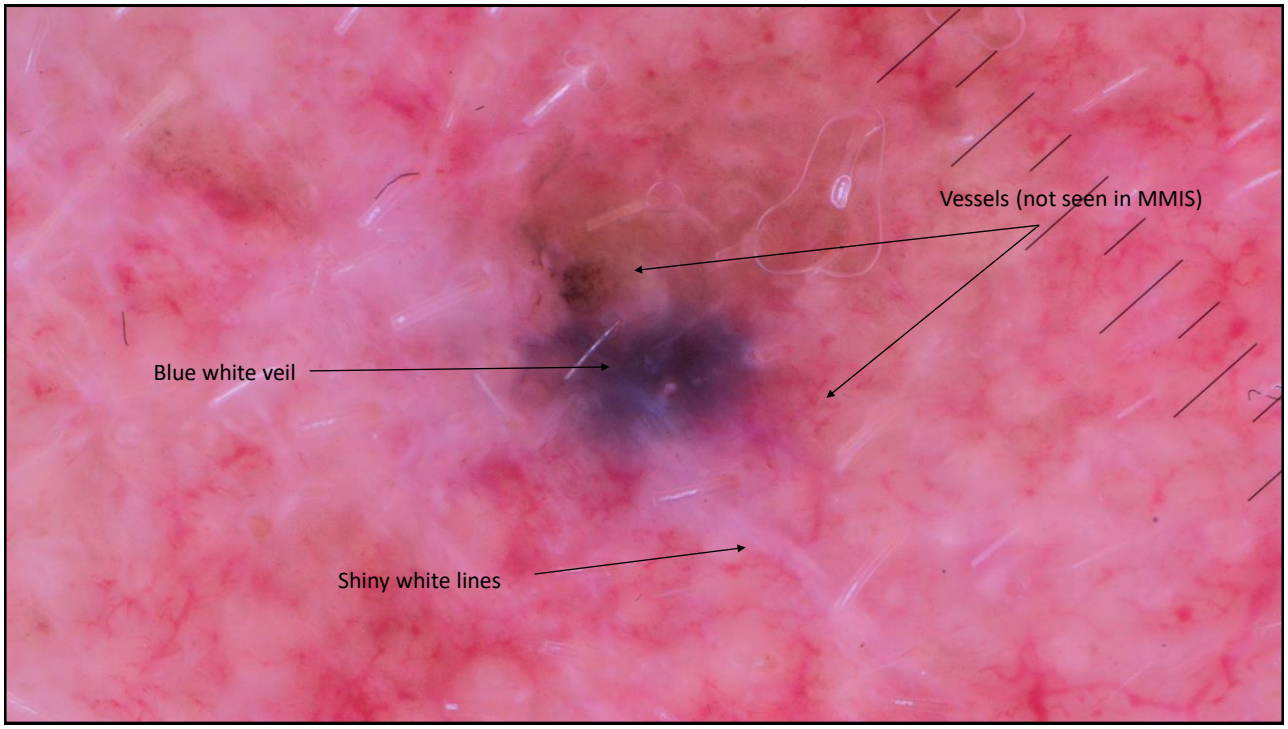

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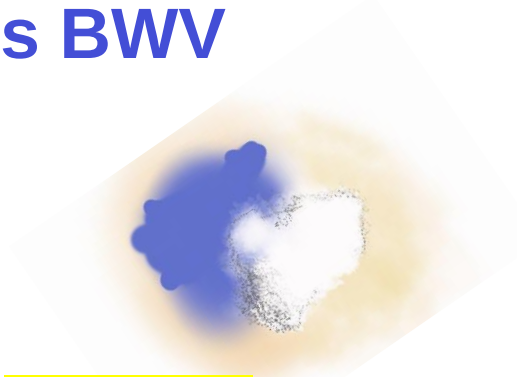
Difference between BWV seen in regression vs BWV

- Palpable / raised
- The whitish veil is more conspicuous with NPD
- With PD the area with the BWV will often reveal SWS



- Flat non palpable
- At perimeter of BWV-like area one can often see focal granularity
- Not associated with SWL

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waning sign melanoma

Bing Image Creator | 1024 × 1024 jpg | Created now

The co-presence of shiny white structures (PD) & vessels in a lesion with a BWV should raise suspicion for invasive melanoma

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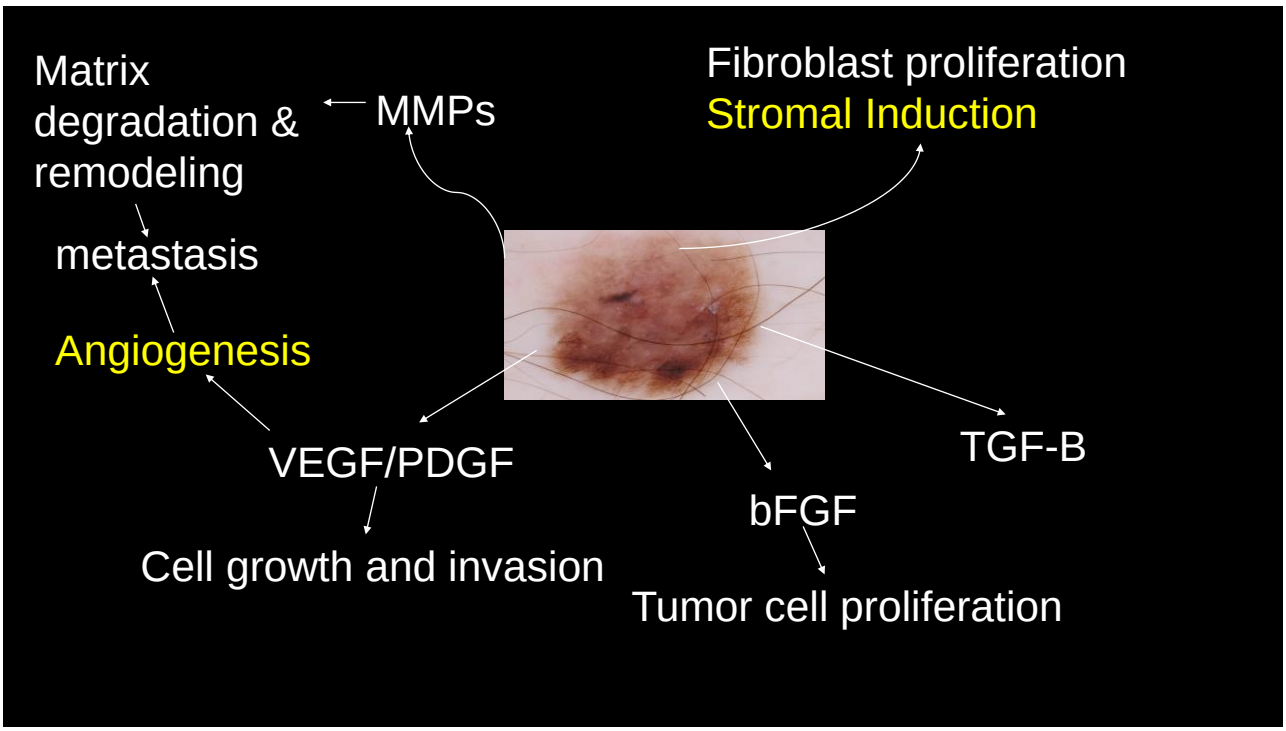

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Tissue mobility – early vertical growth

Leon vanKempen & Dirk Ruiter' work

- Type I collagen synthesis by fibroblasts is modulated by growth factors and cytokines produced by melanoma (i.e., desmoplastic MM).
- Collagen expression during early MM development contributes to the formation of a melanoma-associated vasculature (neo-angiogenesis).
- Type I collagen synthesis by fibroblasts and the angiogenic response primarily occurs in the papillary dermis.
- Once MM travels along collagen into the reticular dermis it no longer exerts a stromal response. It is now free to move around on its own without the need for a collagen scaffold.

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The significance of crystalline/chrysalis structures in the diagnosis of melanocytic and nonmelanocytic lesions

Yevgeniy Balagula, MD,[a] Ralph P. Braun, MD,[b] Harold S. Rabinovitz, MD,[c] Stephen W. Dusza, DrPH,[a] Alon Scope, MD,[a,d] Tracey N. Liebman, BA,[a] Ines Mordente, MD,[e] Katherine Siamas, MD,[f] and Ashfaq A. Marghoob, MD[a]

Brooklyn and New York, New York; Zurich, Switzerland; Plantation, Florida; Tel Aviv, Israel; and Naples, Italy

Background: Crystalline/chrysalis structures (CS) are white shiny streaks that can only be seen with polarized dermatoscopy.

Objectives: We sought to estimate the prevalence and assess the clinical significance of CS in melanocytic and nonmelanocytic lesions.

Methods: This was a prospective observational study in which dermatoscopic assessment of lesions was recorded in consecutive patients examined during a 6-month period. In addition, a data set of biopsy-proven melanomas was retrospectively analyzed.

Results: In all, 11,225 lesions in 881 patients were prospectively examined. Retrospectively, 229 melanomas imaged with polarized dermatoscopy were analyzed. In the prospective data set, a median of 12.7 lesions (range, 1-54) were evaluated per patient. None of clinically diagnosed Clark nevi (n = 9750, 86.8%) demonstrated CS. Overall, CS were observed in 206 (1.8%) lesions, most commonly dermatofibromas and scars among nonbiopsied lesions. A total of 265 (2.4%) lesions were biopsied, including 20 melanomas and 36 nevi. Among biopsied malignant lesions, CS were most commonly observed in basal cell carcinoma (47.6%) and invasive melanomas (84.6%). Melanomas were more likely to have CS than biopsied nevi (odds ratio = 9.7, 95% confidence interval 2.7-34.1). In the retrospective data set, CS were more commonly observed among invasive melanomas (41%) compared with in situ melanomas (17%) (odds ratio = 3.4, 95% confidence interval 1.9-6.3, $P < .001$). The prevalence of CS correlated with increased melanoma thickness ($P = .001$).

Limitations: Biopsied lesions represent a small percentage of the total number of lesions evaluated.

Conclusion: Among biopsied malignant lesions, CS are most commonly observed in basal cell carcinoma and invasive melanomas and rarely seen in nevi. In melanoma, CS may reflect increased tumor thickness and progression. (J Am Acad Dermatol 2012;67:194.e1-8.)

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229 consecutively diagnosed "melanomas" (retrospective review)

-65 of 110 (41%) invasive MMs had SWL
-20 of 119 (17%) in situ MMs had SWL

P<0.001, OR 3.4

Invasive melanomas with SWL were significantly thicker as compared to those without SWL (0.68 vs. 0.43mm)

P<0.001

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The association between SWL (crystalline) structures and the presence of vessels

	Vascular structures			
	No vessels seen	Monomorphous pattern	Polymorphous pattern	Total
SWL Absent	117 (88%) 12% of MM without SWL had vessels	26 (67%)	21 (37%)	164 (72%)
SWL Present	16 (12%) 88% of MM with SWL had vessels	13 (33%) 33% of these had one vessel morphology	36 (63%) 63% of these had a polymorphous pattern (dotted & serpentine)	65 (28%)
Total	133 (100)	39 (100)	57 (100)	229 (100)
	referent	3.6 (1.6-8.5), p=0.003	12.5 (5.9-26.5), p<0.001	

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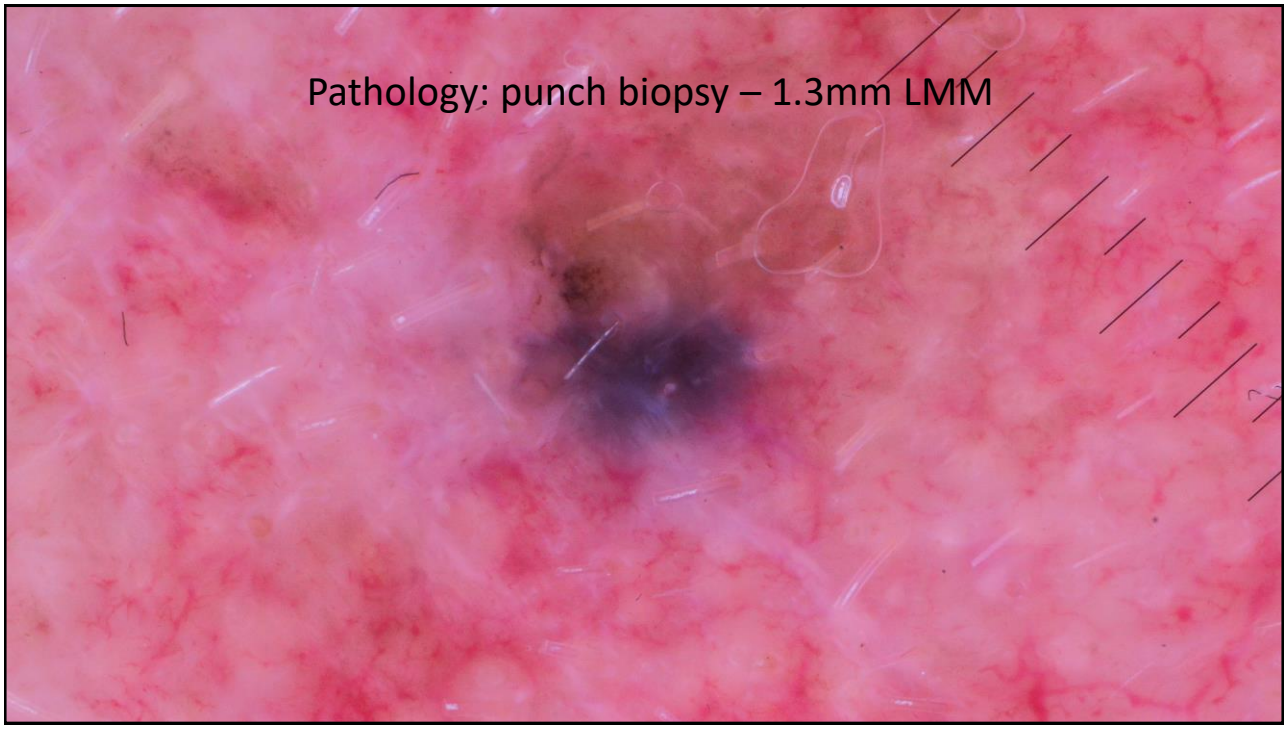
Pathology: punch biopsy – 1.3mm LMM

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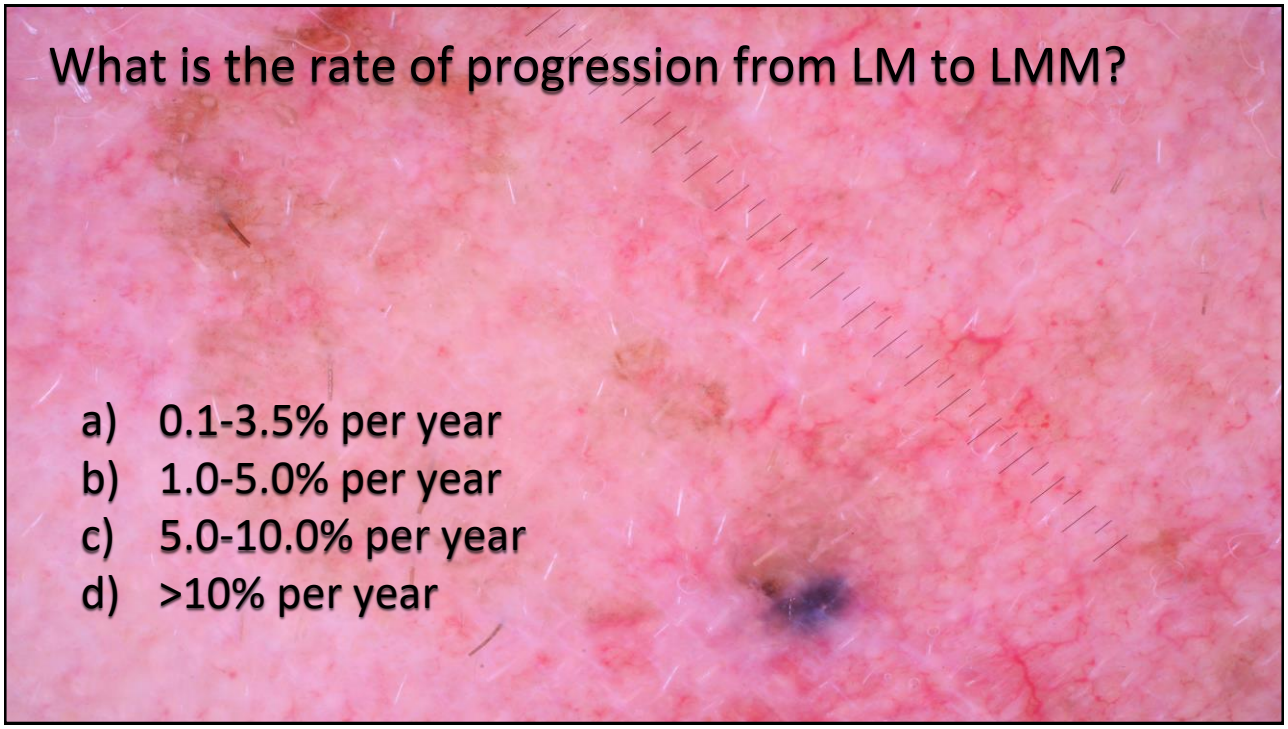
What is the rate of progression from LM to LMM?
a) 0.1-3.5% per year
b) 1.0-5.0% per year
c) 5.0-10.0% per year
d) >10% per year

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British Journal of Dermatology (1987) **116**, 303–310.

The risk of progression of lentigo maligna to lentigo maligna melanoma

M.A.WEINSTOCK AND A.J.SOBER

TABLE 5. Estimate of annual risk of malignant transformation in lentigo maligna

Age (years)	Risk estimate (%)	95% confidence interval* (%)
1–44	0·03	0·01–0·10
45–64	0·13	0·06–0·30
65–74	0·14	0·09–0·22

The annual risk of developing invasive melanoma in a patient with lentigo maligna was calculated using the formula:

$$\frac{(\text{case fraction of LMM among all melanomas}) \times (\text{annual incidence of melanoma})}{\text{prevalence of LM}}.$$

This estimate was calculated separately for each of three age groups (i.e. 1–44, 45–64 and 65–74

TABLE 6. Estimate of melanoma risk in patients with lentigo maligna at ages 45 and 65

Age (years)	Estimate of risk by the age of 75 (%)	Estimate of lifetime risk (%)	Life expectancy (years)*
45	3·3	4·7	33
65	1·2	2·2	11

dence of all invasive melanoma from the Surveillance, Epidemiology and End Results program. From this data, the authors presented an age-stratified risk of progression some 25–116 times lower than in our study (annual risk of progression of only 0.03% (95% CI: 0.01–1.0) at ages <45 years and 0.14% (95% CI: 0.09–0.22) in older people (65–74 years).

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Estimated risk of progression of lentigo maligna to lentigo maligna melanoma

Scott W. Menzies[a,c], Sakitha Liyanarachchi[a], Elliot Coates[a], Annika Smith[d], Claire Cooke-Yarborough[e], Serigne Lo[d], Bruce Armstrong[c,f], Richard A. Scolyer[b,c] and Pascale Guitera[a,c,d]

maligna was (18 months, 0–665) ($P = 0.972$). The estimated risk of progression of lentigo maligna to lentigo maligna melanoma was 3.5% per year (95% confidence interval: 2.5–5.0). This equates to an average time for lentigo maligna to progress to lentigo maligna melanoma of 28.3 years (95% confidence interval: 20.0–40.5) in this population

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Estimated risk of progression of lentigo maligna to lentigo maligna melanoma

Scott W. Menzies[a,c], Sakitha Liyanarachchi[a], Elliot Coates[a], Annika Smith[d], Claire Cooke-Yarborough[e], Serigne Lo[d], Bruce Armstrong[c,f], Richard A. Scolyer[b,c] and Pascale Guitera[a,c,d]

Of note, there was no significant difference in the age at diagnosis or time present on the skin of LM compared to LMM. This may suggest that instead of a constant risk per annum of all LM progressing to LMM, where it may be expected that LMM would have been present for a significantly longer period on the skin than its precursor, only a subset of diagnosed LM have the biological ability to invade. Such a proposal has been made by others, who provided different histopathological criteria for LM that are likely to progress (which they called in situ LM) and LM that are unlikely to progress (which they called just LM) [13].

Task ahead:

Elucidate the characteristics of LM (*morphology, molecular*) that will progress vs. those that will remain indolent.

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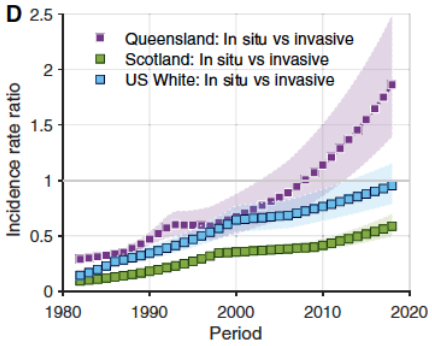
Incidence of in Situ vs Invasive Melanoma: Testing the "Obligate Precursor" Hypothesis

Catherine M. Olsen, PhD [1,2] Nirmala Pandeya, PhD [1,2] Philip S. Rosenberg, PhD [3] David C. Whiteman, MBBS, PhD [1,2,*]

LM is not an obligate precursor to LMM



D) in situ to invasive melanoma incidence rate ratios. ASR =

invasive melanomas overall and stratified by sex and anatomic site. **Results:** In all 3 populations, the in situ to invasive incidence rate ratio increased statistically significantly from less than 0.3 in 1982 to 1.95 (95% confidence interval [CI] = 1.88 to 2.02) in Queensland, 0.93 (95% CI = 0.90 to 0.96) in the US White population, and 0.58 (95% CI = 0.54 to 0.63) in Scotland in 2018. The mean age at diagnosis of in situ melanomas was the same or higher than invasive melanomas for almost all time periods among men and women and on all body sites except the lower limbs. **Conclusions:** The increasing ratio of in situ to invasive melanoma incidence over time, together with the high (and increasing) mean age at diagnosis of in situ melanomas, is consistent with more indolent lesions coming to clinical attention than in previous eras.

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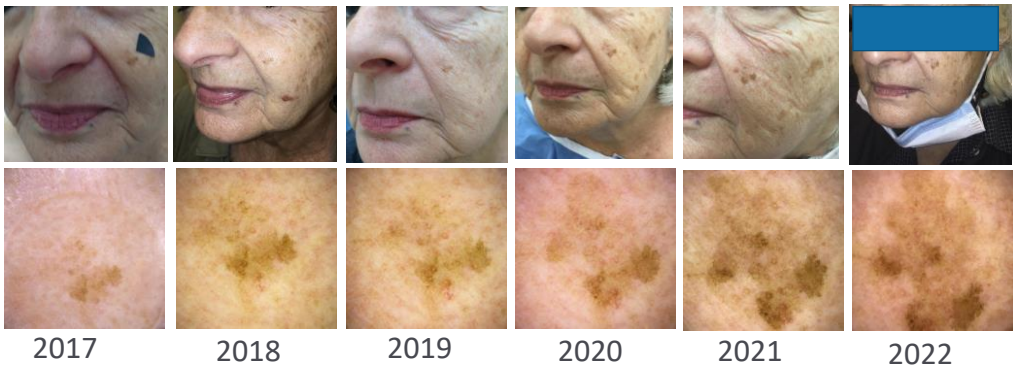
LM is not an obligate precursor to LMM



83-year-old patient (in 2017) elected to monitor the MM (morphology of MM based on dermoscopy and RCM criteria and biology shows growth)

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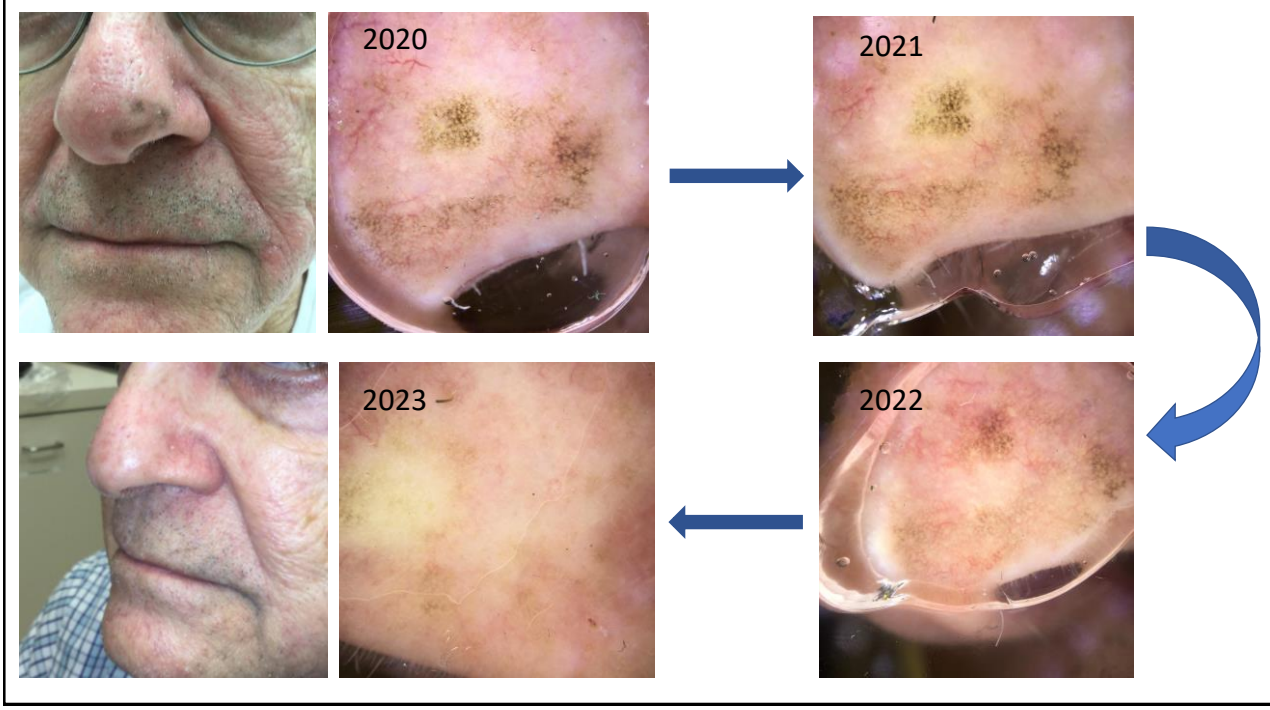

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However, invasion, metastasis & death from LMM does occur

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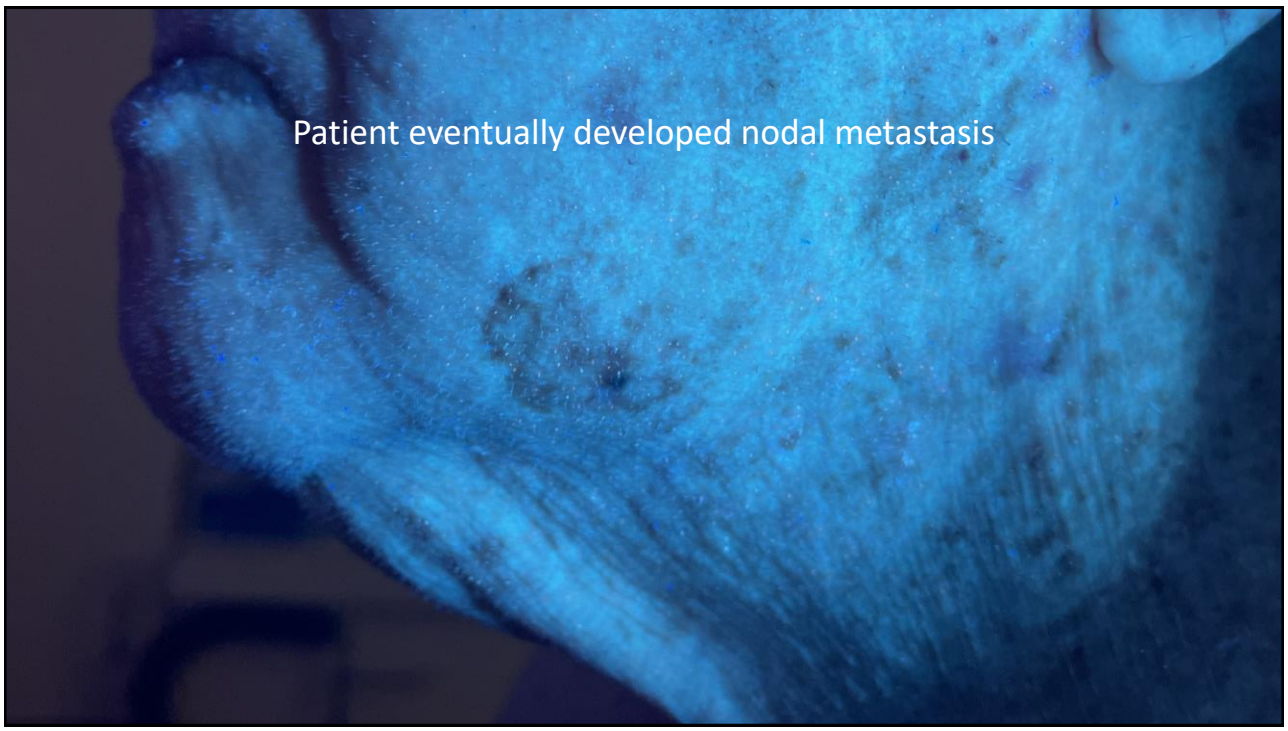

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We need better predictors of which LM will progress

Progression to Invasive Melanoma From Malignant Melanoma In Situ, Lentigo Maligna Type

ZEINA S. TANNOUS, MD, LISA H. LERNER, MD, LYN M. DUNCAN, MD, MARTIN C. MIHM, JR, MD, AND THOMAS J. FLOTTE, MD

We have previously hypothesized that lesions currently classified as lentigo maligna include 2 categories of lesions.[14] The first is a putative precursor lesion characterized histologically by atypical melanocytic hyperplasia. We have termed this lesion *lentigo maligna*. In addition to atypical melanocytic hyperplasia, the second category of lesions is characterized by pagetoid spread, confluence, and nesting of atypical melanocytes. We have designated this subset as malignant melanoma in situ, lentigo maligna type. We and others additionally

In our study, we found that all of the cases of invasive melanoma, lentigo maligna type were associated with melanoma in situ, lentigo maligna type in the epidermis overlying the invasive tumor in the dermis.

TABLE 1. Comparison of Lentigo Maligna and Malignant Melanoma In Situ, Lentigo Maligna Type

	Lentigo Maligna	Melanoma In Situ	*P* Value*
Pagetoid spread			
+	11	27	NS
−	0	0	
Nesting			
+	0	21	.00001
−	11	6	
Confluence			
+	0	25	<.00001
−	11	2	

promising. The apparent lower risk of progression to invasive melanoma from lentigo maligna than from lentigo maligna melanoma in situ may allow patients and their physicians to make informed decisions about less aggressive therapy for lentigo maligna. However,

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We need technology

GEP, multispectral imaging, electrical impedance……..

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