



COLLEGE of AMERICAN
PATHOLOGISTS

Confocal Microscopy for Pigmented Lesions

Babar K. Rao, MD, FAAD

4/25/2017

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Babar K. Rao, MD, FAAD

- Board certified Dermatologist, Dermatopathologist, and Mohs Surgeon
- Acting Chairman and Associate Clinical Professor of Dermatology and Dermatopathology of the Department of Dermatology at the Rutgers – Robert Wood Johnson Medical School
- Associate Clinical Professor of Dermatology at Weill Cornell Medical College at Cornell University
- Author of Atlas of Confocal Microscopy in Dermatology
- Committee member of the CAP's In Vivo Microscopy Committee



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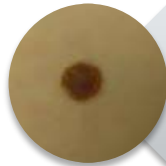
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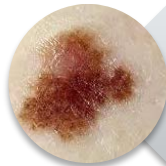
Disclosure

- Consultant for **CALIBER ID** (maker of Vivascope)

Pigmented Skin Lesions



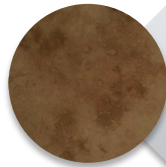
Benign Melanocytic Nevus



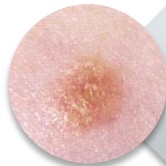
Melanocytic Nevi with atypia



Melanoma



Lentigo

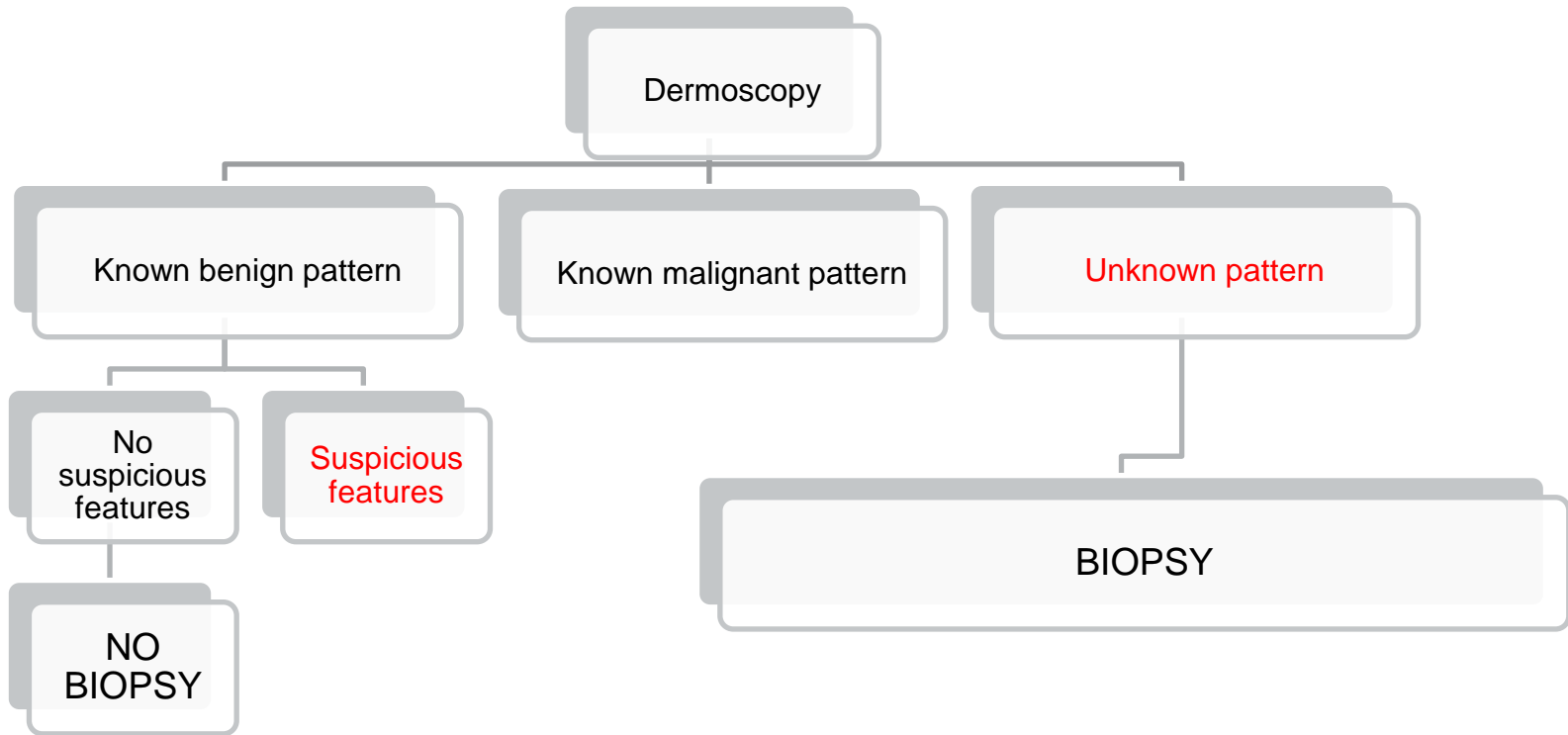


Spitz Nevi



Blue Nevi

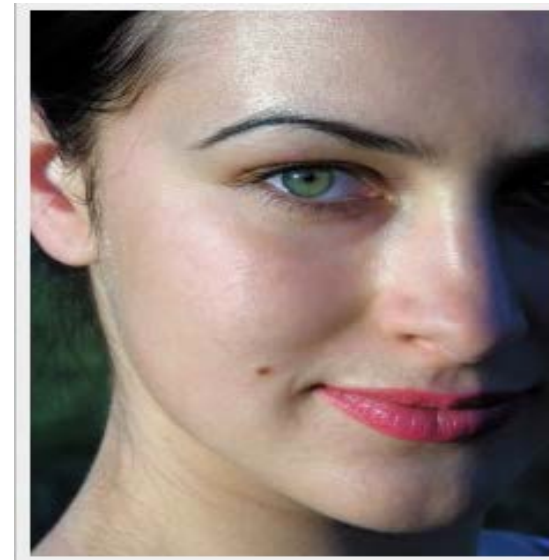
Management of Pigmented skin lesions



Difficult lesions/unknown pattern/suspicious lesions on Dermoscopy → Reflectance confocal microscopy (RCM)

Biopsy

- **Not feasible in ALL cases of pigmented skin lesions**



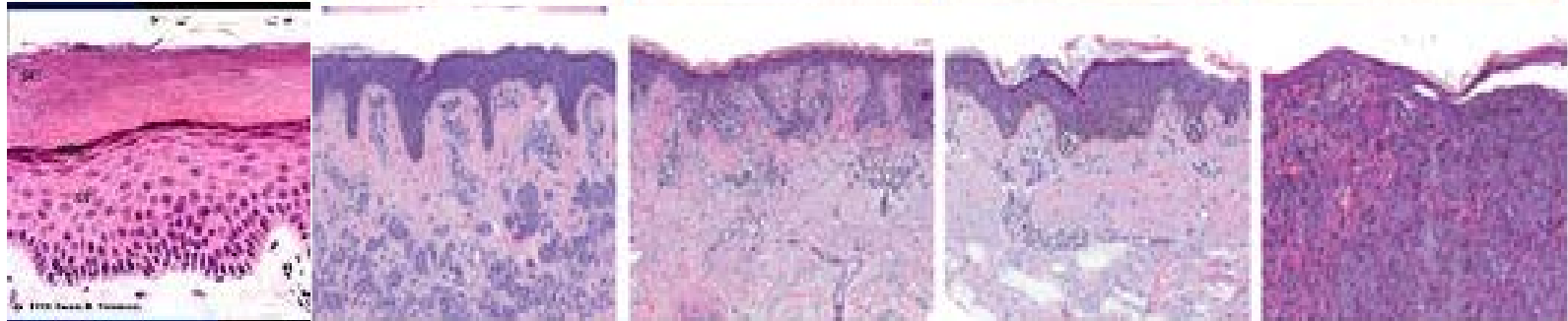
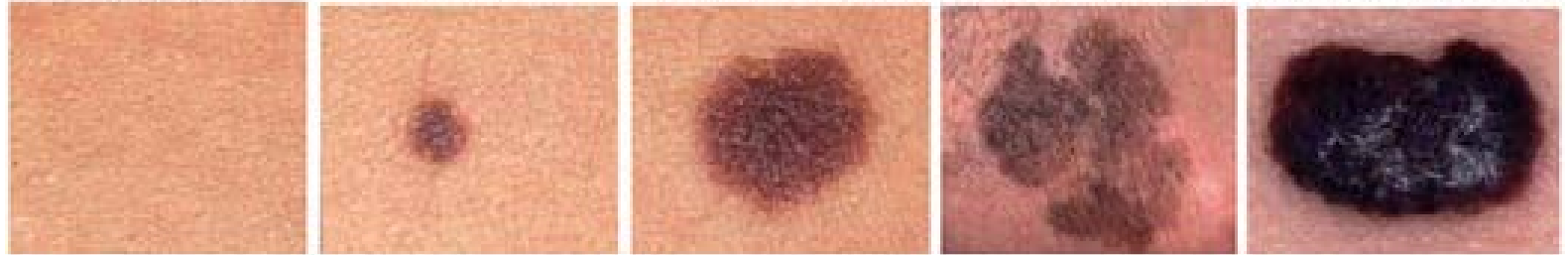
Confocal Microscopy

- **What is confocal microscopy?**

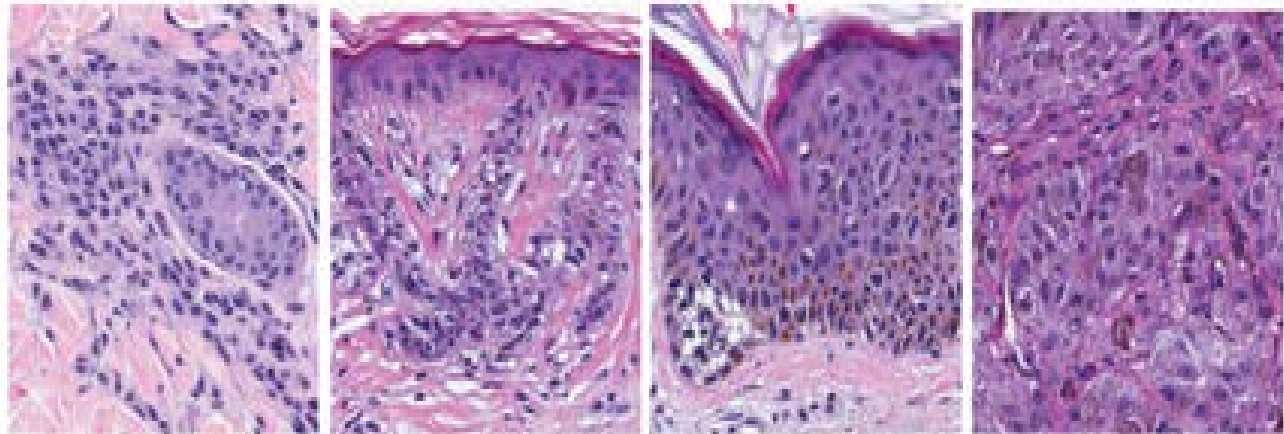


Histology Reviews

a Normal skin Naevus Dysplastic naevus Melanoma in situ Invasive melanoma

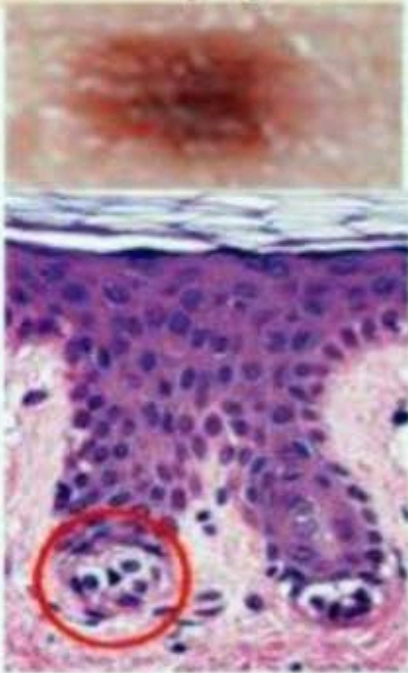


50µm

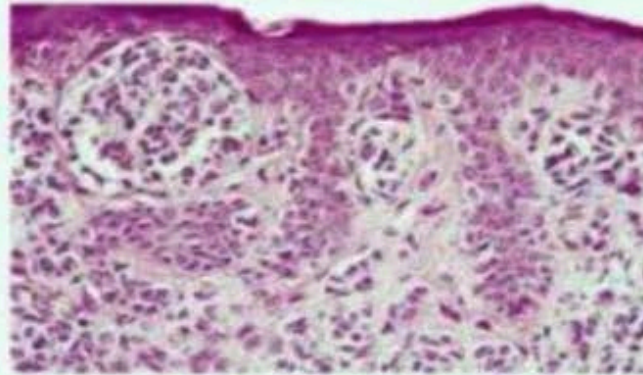


Histology Review

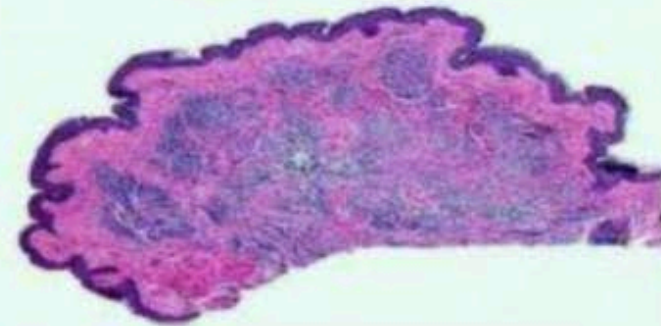
**Junctional
Maculopapular**



**Compound
Papule**



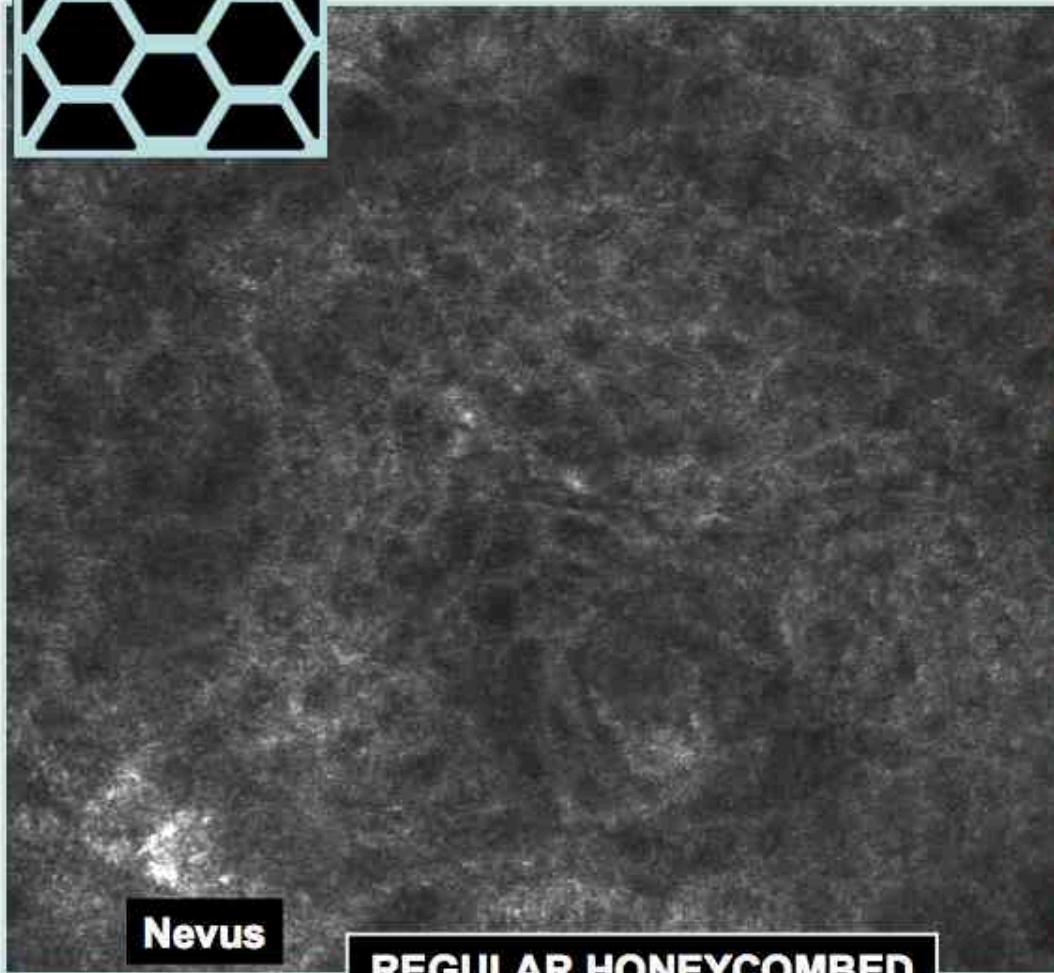
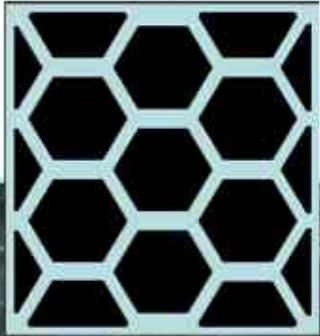
**Intradermal
Nodule**



“Understanding Confocal Terms used to Diagnose Pigmented Skin Lesions”

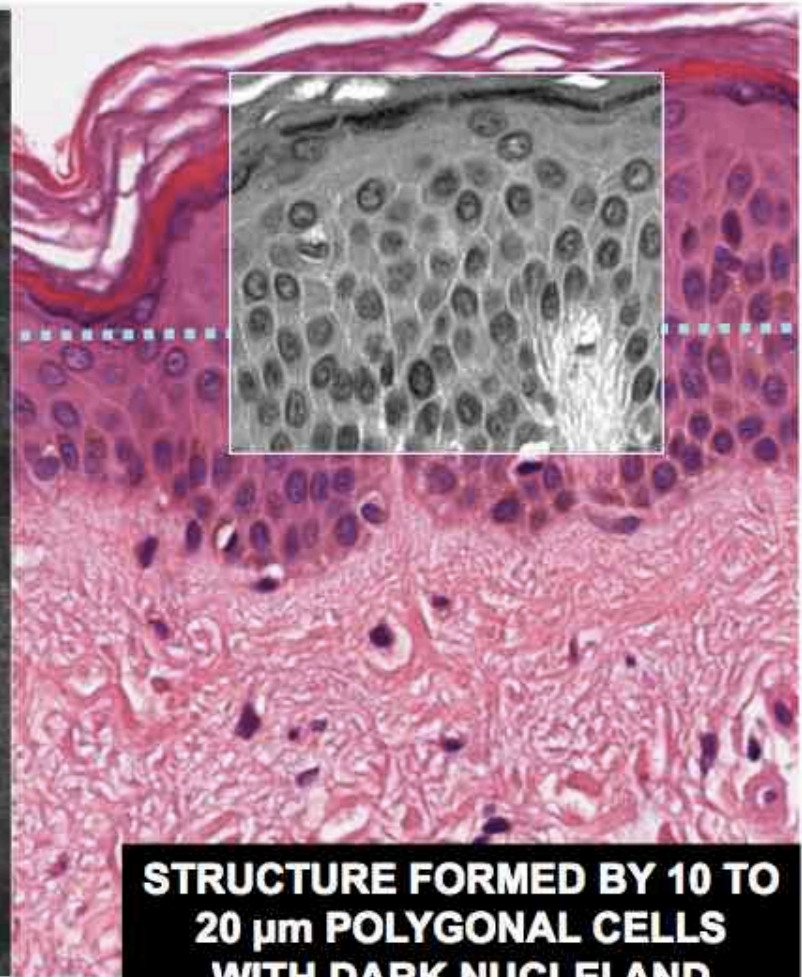


Normal epidermis

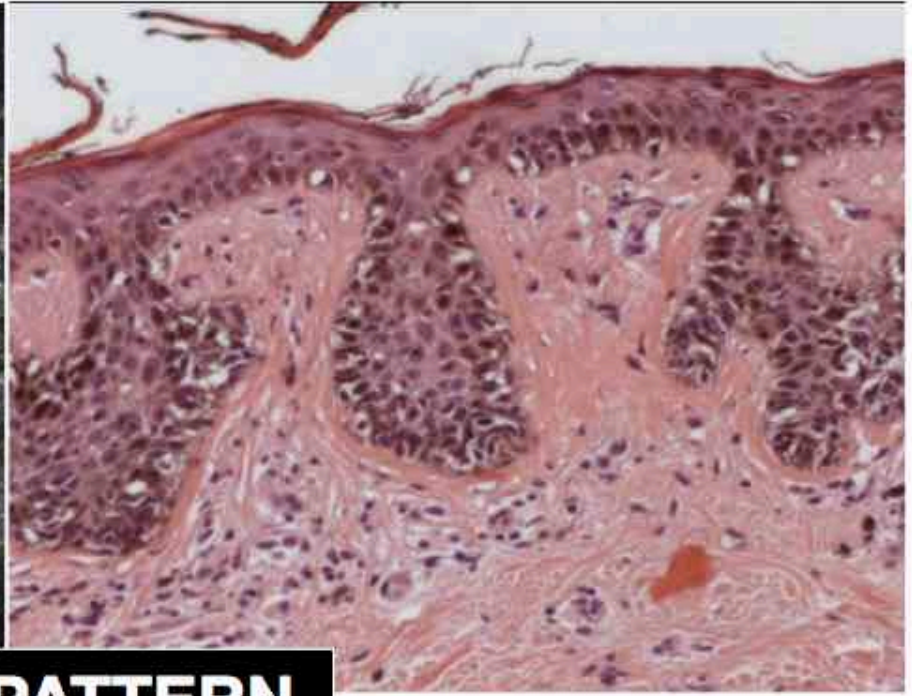
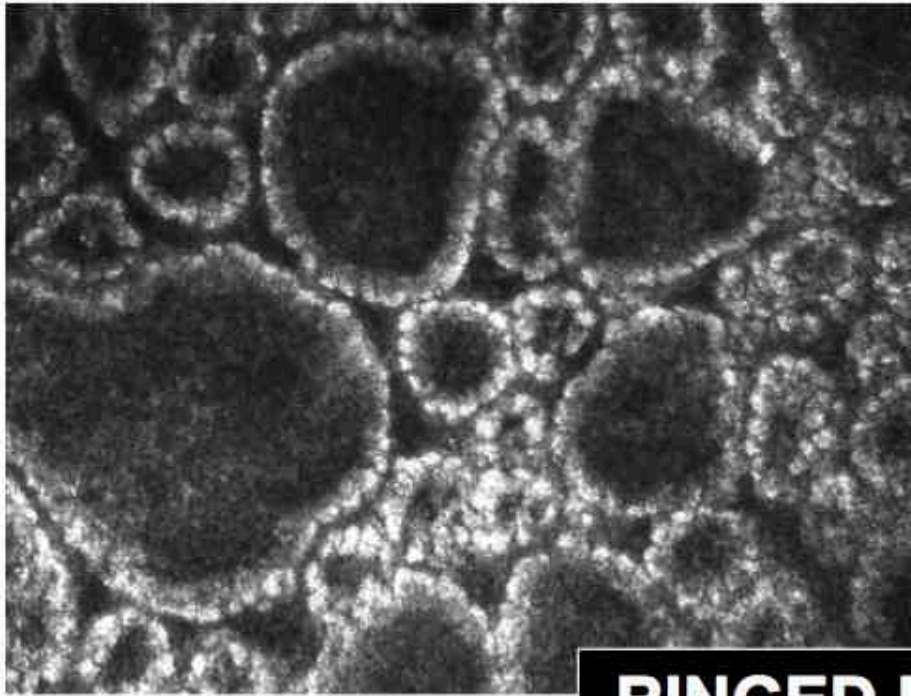
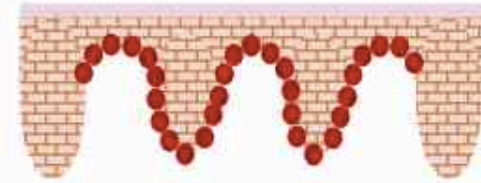
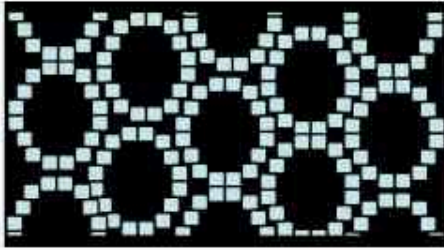


Nevus

REGULAR HONEYCOMBED

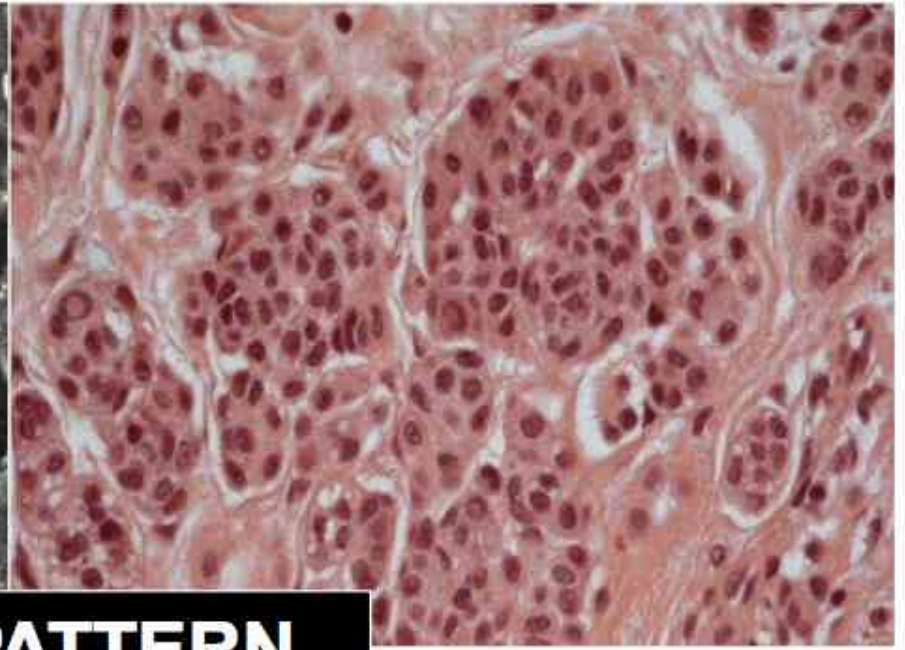
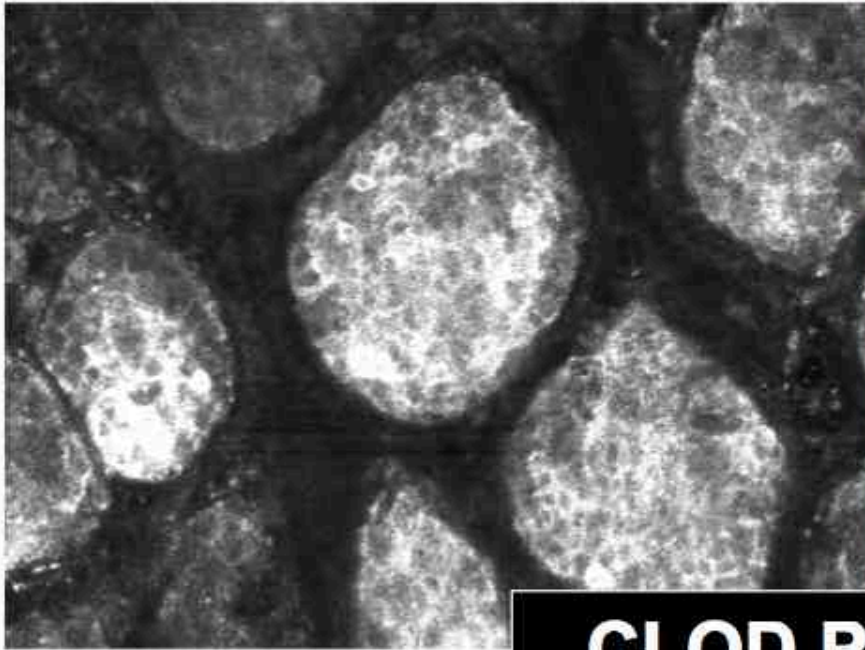
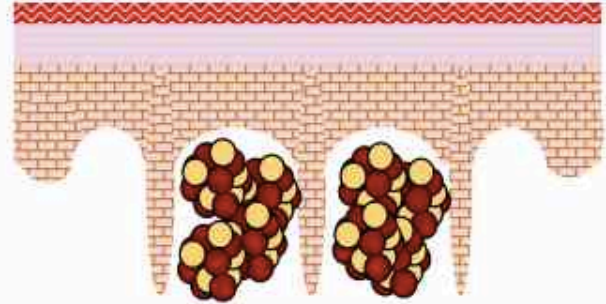
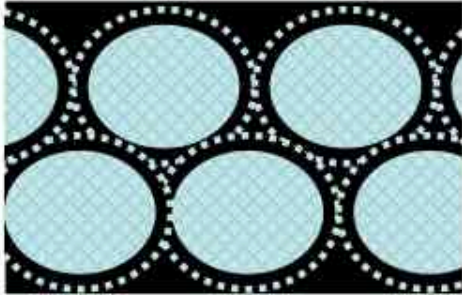


STRUCTURE FORMED BY 10 TO 20 μm POLYGONAL CELLS WITH DARK NUCLEI AND BRIGHT THIN CYTOPLASM



RINGED PATTERN

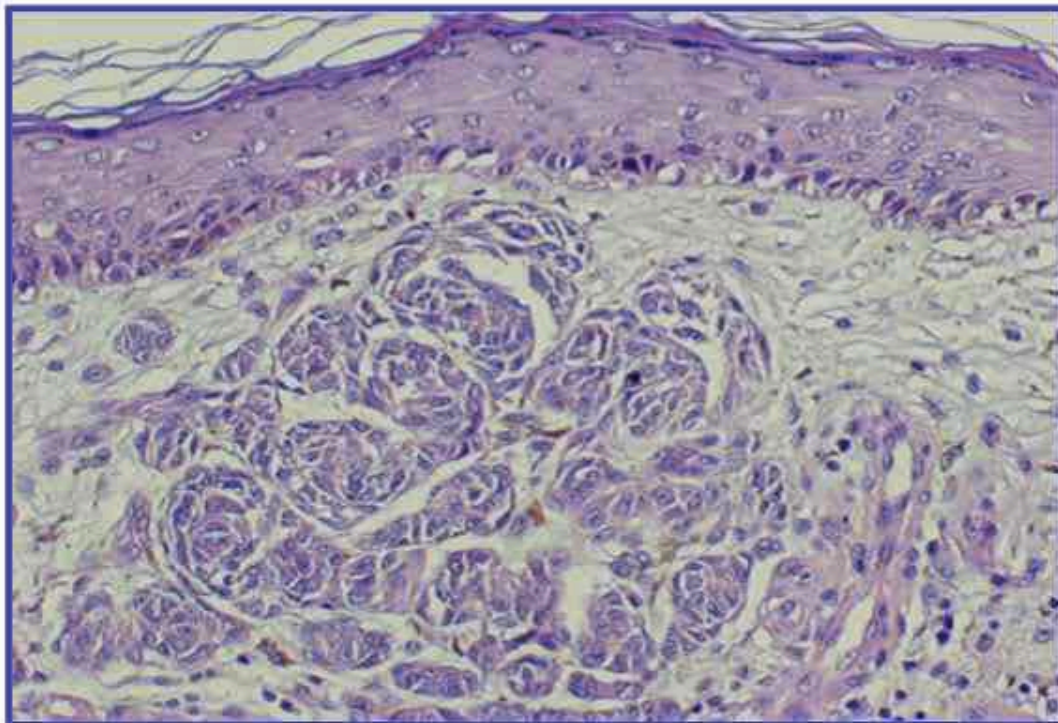
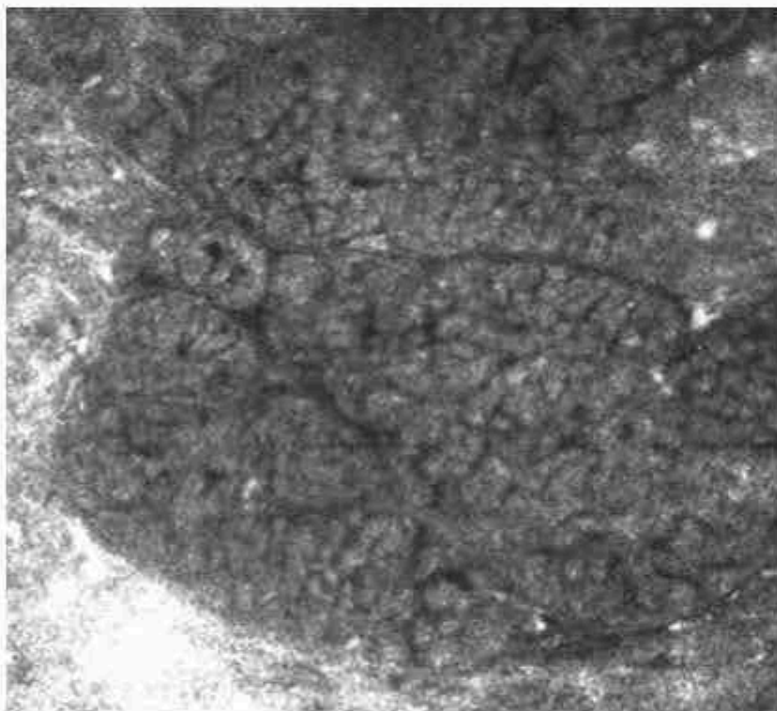
Predominance of edged papillae at DEJ, corresponding to dermal papillae surrounded by a rim of small bright cells, appearing as bright rings sharply contrasting with the dark background.



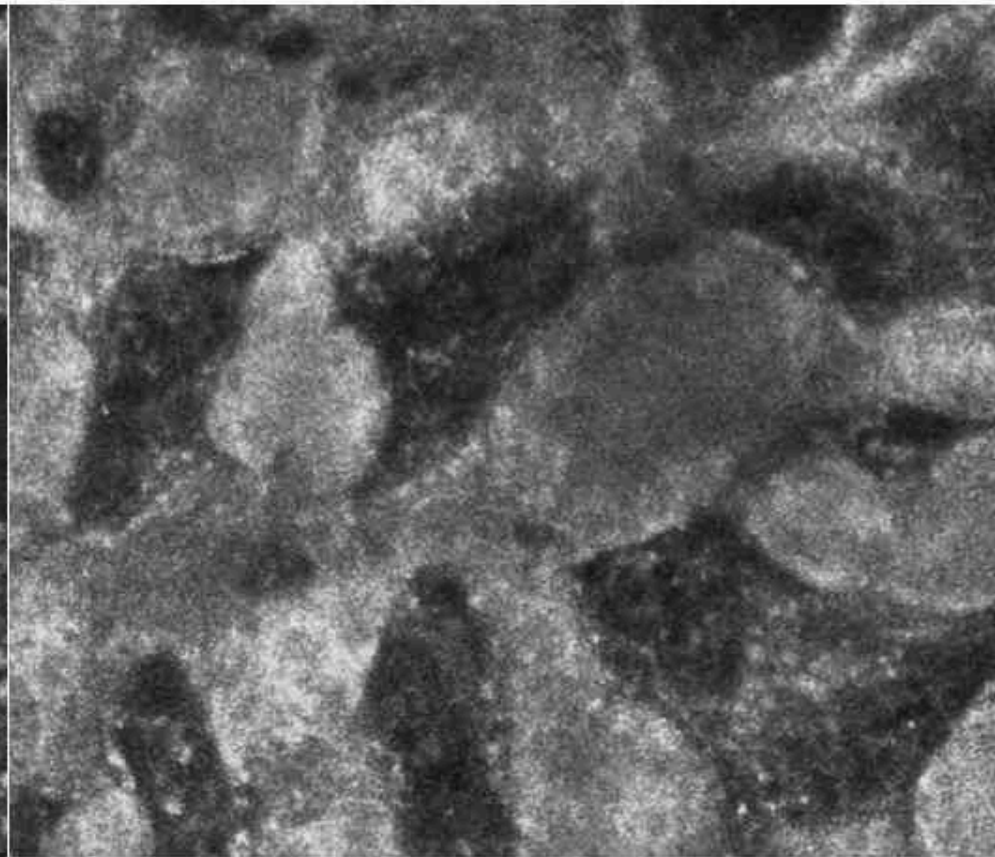
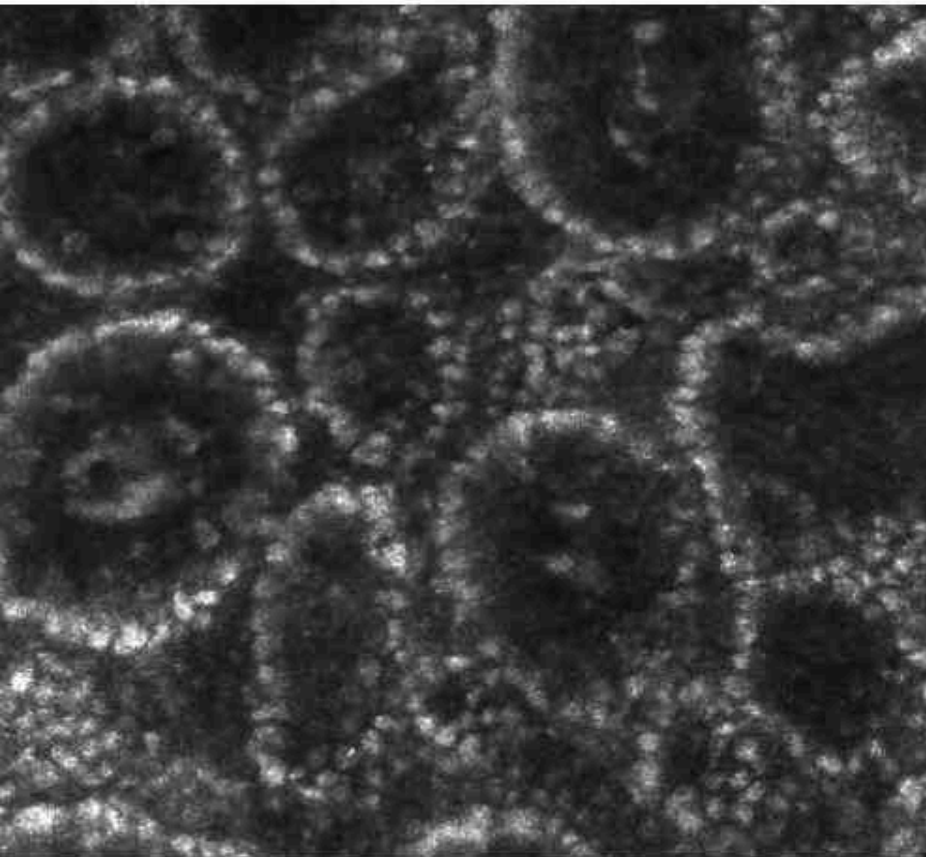
CLOD PATTERN

Dense compact clusters of melanocytes within dermal papillae.

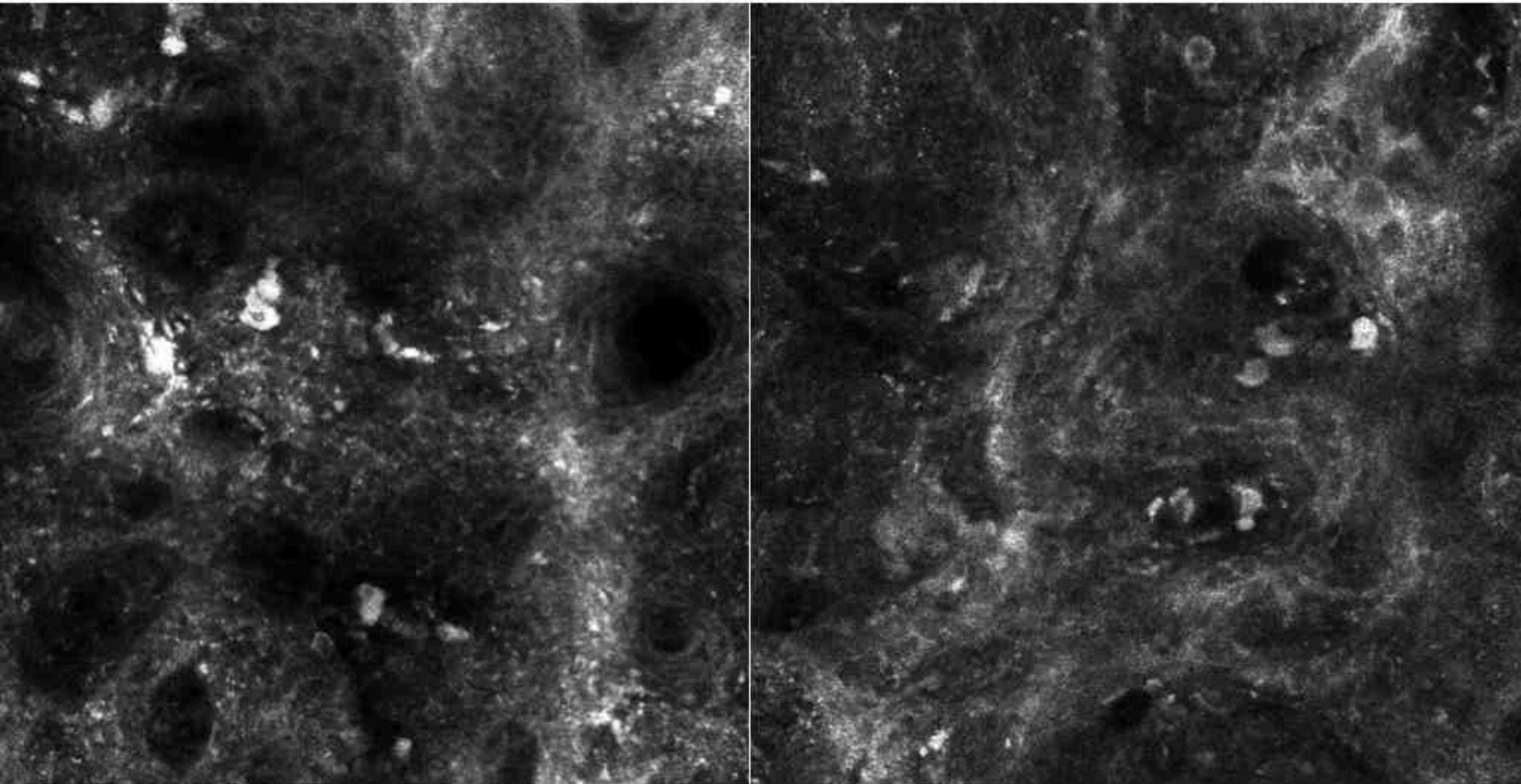
DERMAL NESTS – CEREBRIFORM



EDGED PAPILLAE

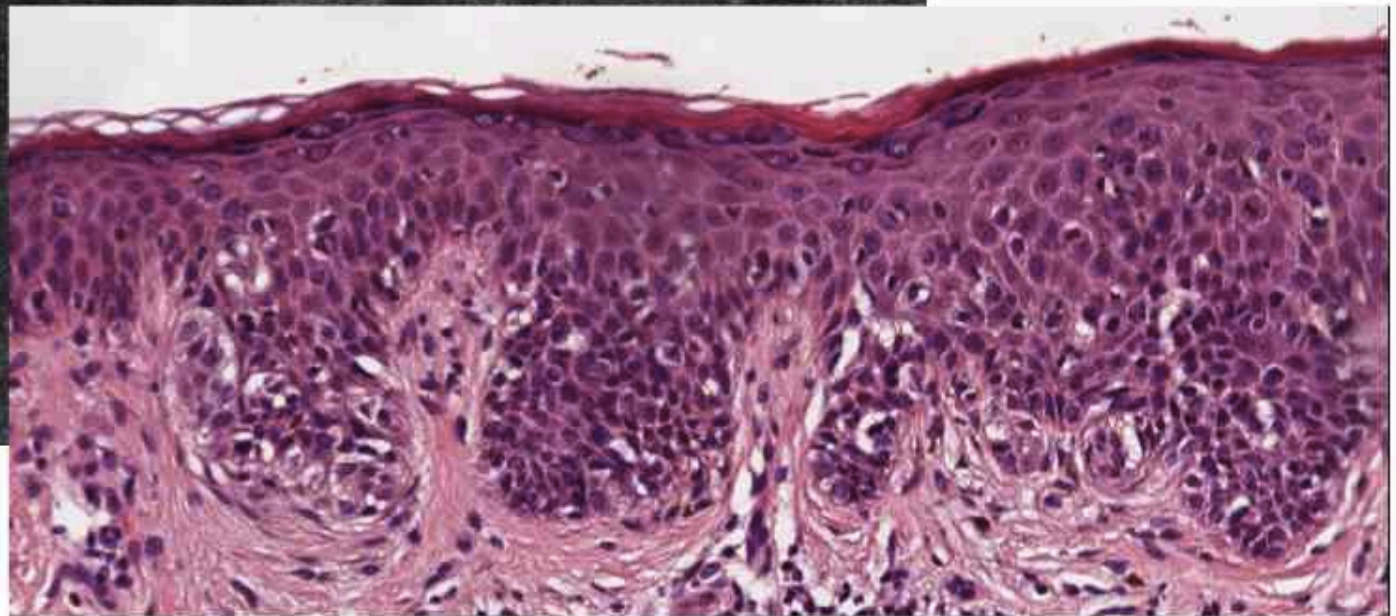
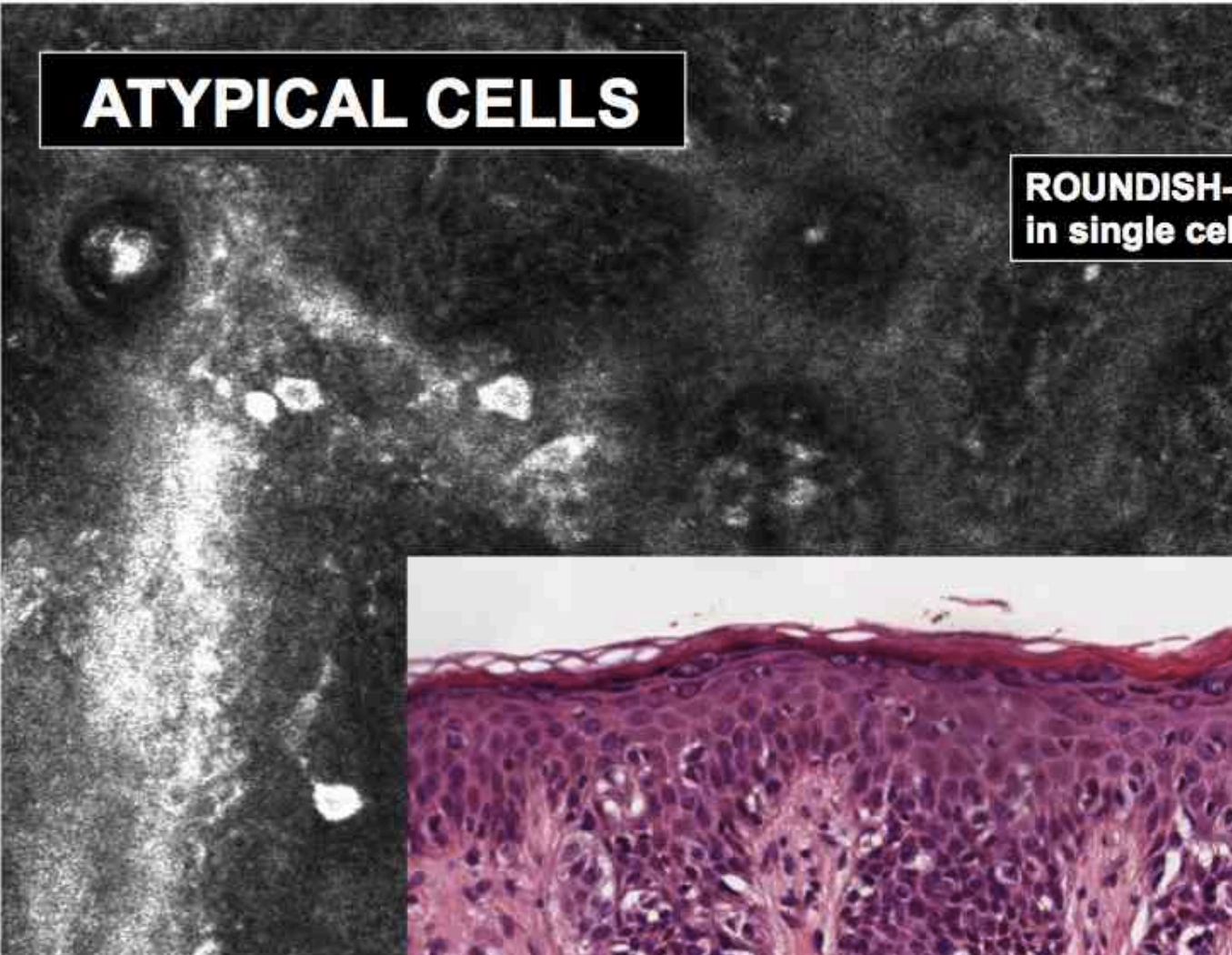


NON-EDGED PAPILLAE

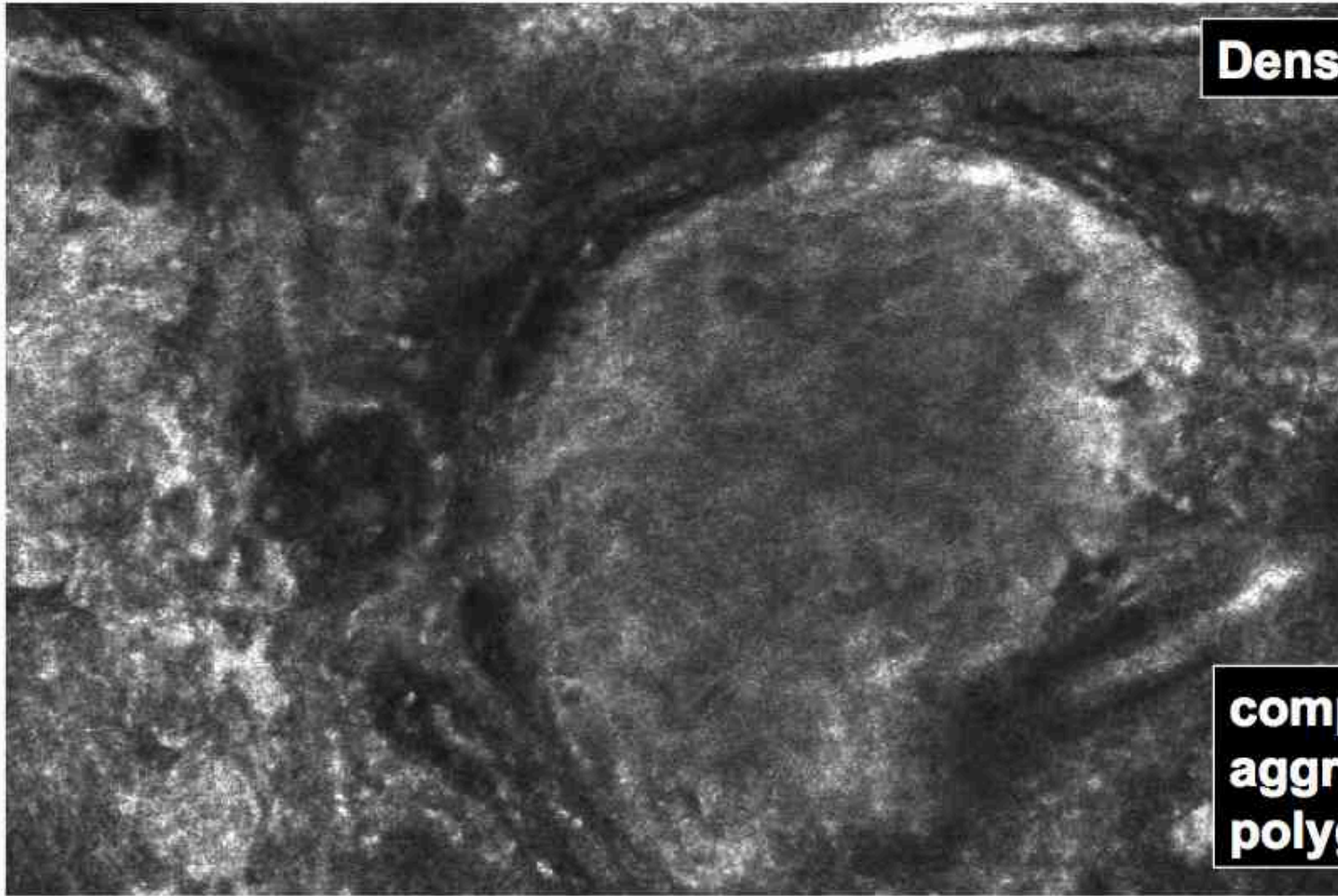


ATYPICAL CELLS

ROUNDISH-POLYGONAL
in single cells and in small nests



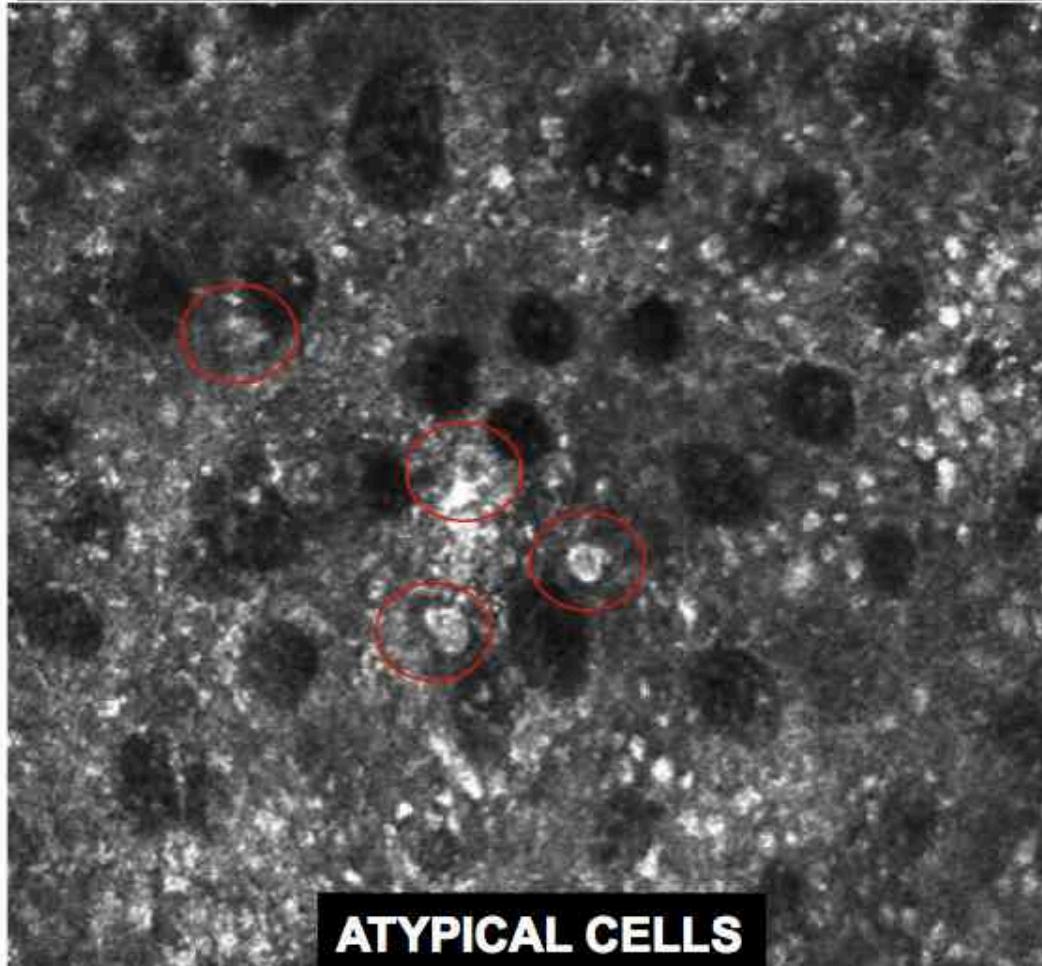
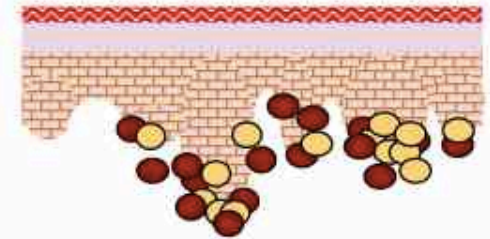
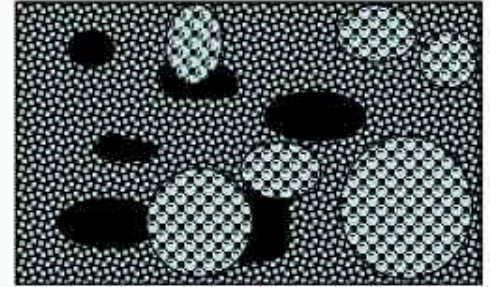
DERMAL NESTS - DENSE



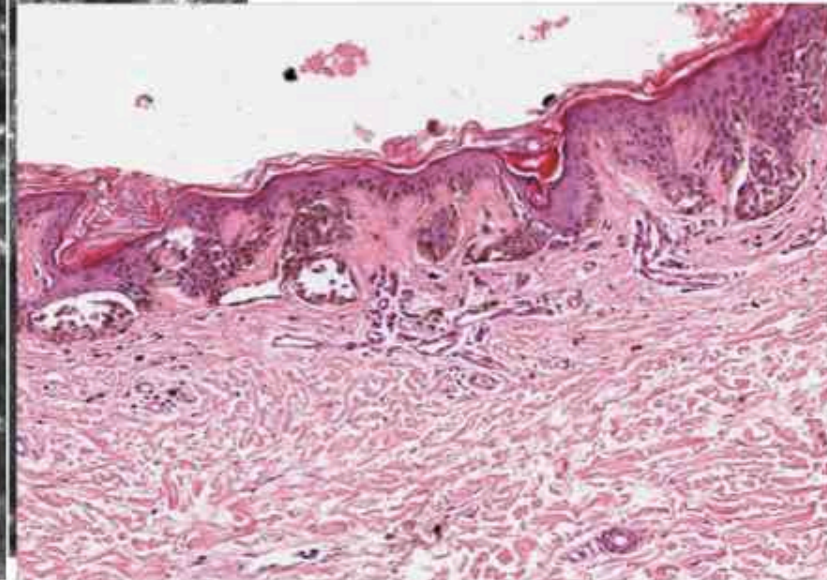
Dense nests

**compact
aggregates of
polygonal cells**

NON SPECIFIC PATTERN



ATYPICAL CELLS



Regression

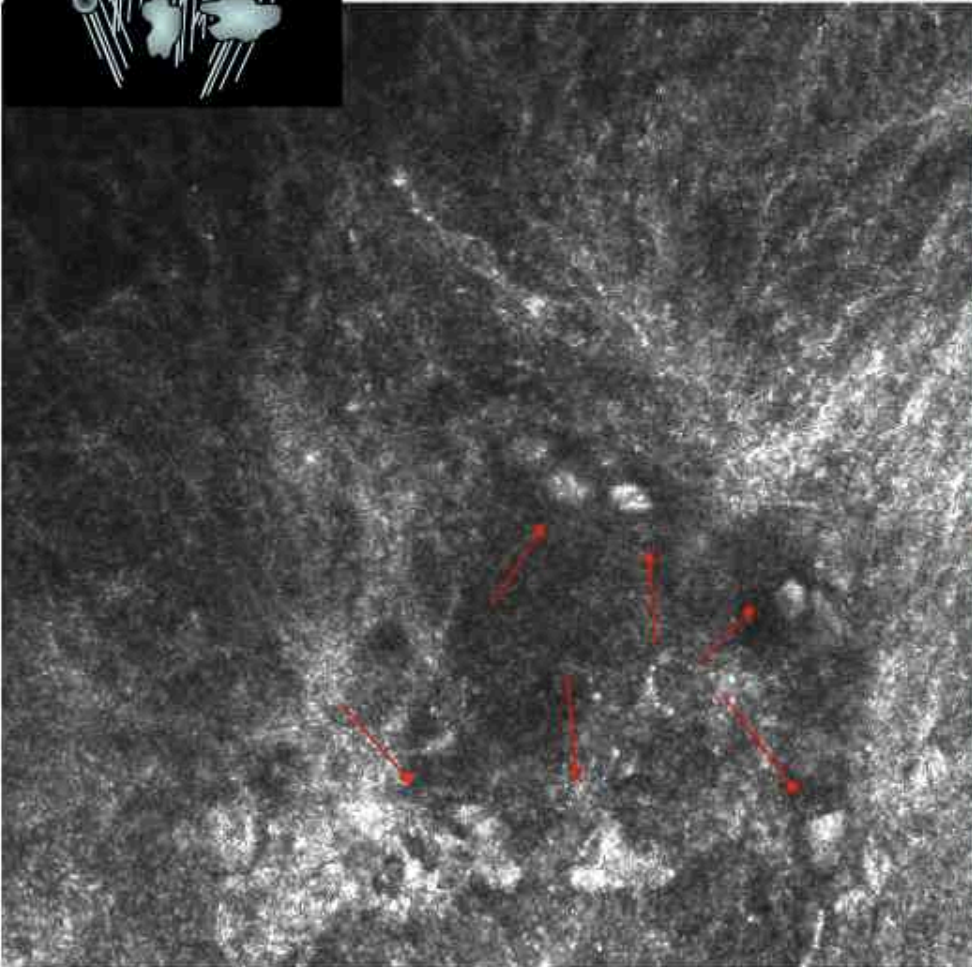


Table I. Frequency of in vivo reflectance-mode confocal laser microscopy features and odds ratio values observed at superficial layers in benign and malignant melanocytic lesions

	MM (37)	Nevi (49)	Spitz/Reed (16)	Total (102)	OR (CI 95%)
General aspect of superficial layers:					
Honeycombed	17* (45.9%)	36 (73.5%)	12 (75%)	65 (63.7%)	0.30 (0.13-0.71)
Cobblestone	14 (37.8%)	24 (49%)	6 (37.5%)	44 (43.1%)	NS
Disarranged	15* (40.5%)	0 (0%)	1 (6.3%)	16 (15.7%)	43.6 (5.4-349.8)
Pagetoid infiltration:					
Presence of pagetoid cells	32* (86.5%)	3 (6.1%)	4 (25%)	39 (38.2%)	53.0 (15.6-180.7)
Numerous cells	16* (43.2%)	0 (0%)	1 (6.3%)	17 (16.7%)	48.8 (6.1-390.1)
Roundish cells	31* (83.8%)	2 (4.1%)	2 (12.5%)	35 (34.3%)	78.8 (20.7-300)
Dendritic cells	18* (48.6%)	2 (4.1%)	4 (25%)	24 (23.5%)	9.32 (3.2-26.8)
Pleomorphism	27* (73%)	2 (4.1%)	2 (12.5%)	31 (30.4%)	41.2 (11.9-142.9)
Widely diffused cells	21* (56.8%)	0 (0%)	1 (6.3%)	22 (21.6%)	84.0 (10.5-672.1)
Extension to the stratum corneum	26* (70.3%)	2 (4.1%)	2 (12.5%)	30 (29.4%)	36.1 (10.5-123.7)

CI, Confidence interval; MM, melanoma; NS, not significant; OR, odds ratio.

*Significant ($P < .05$) compared with benign lesions (acquired nevi + Spitz nevi).

Reference:

Pellacani et al. Reflectance-mode confocal microscopy of pigmented skin lesions -- improvement in melanoma diagnostic specificity. *J Am Acad Dermatol.* 2005; 53(6): 979-985.



Table II. Frequency of in vivo reflectance-mode confocal laser microscopy features and odds ratio values observed at basal layers and dermoepidermal junction in benign and malignant melanocytic lesions

	MM (37)	Nevi (49)	Spitz (16)	Total (102)	OR (CI 95%)
Dermal papilla feature:					
Edged papilla	5* (13.5%)	34 (69.4%)	5 (31.3%)	44 (43.1%)	0.10 (0.04-0.30)
Nonedged papilla	35* (94.6%)	16 (32.7%)	12 (75%)	63 (61.8%)	23.1 (5.1-104.4)
Junctional nest features:					
Junctional clusters	15 (40.5%)	18 (36.7%)	10 (62.5%)	43 (42.2%)	NS
Junctional thickenings	16 (43.2%)	23 (46.9%)	6 (37.5%)	45 (44.1%)	NS
Cell aspects:					
Large cell	32* (86.5%)	3 (6.1%)	4 (25%)	39 (38.2%)	53.0 (15.6-180.7)
Presence of cellular atypia	36* (97.3%)	13 (26.5%)	11 (68.8%)	60 (58.8%)	61.5 (7.9-477.6)
Typical cell	1* (2.7%)	36 (73.5%)	5 (31.3%)	42 (41.2%)	-
Mild atypia	15 (40.5%)	13 (26.5%)	8 (50%)	36 (35.3%)	-
Marked atypia	21* (56.8%)	0 (0%)	3 (18.8%)	24 (23.5%)	-
Stretches of cells	24* (64.9%)	1 (2%)	1 (6.3%)	26 (25.5%)	58.2 (12.2-277.1)

CI, Confidence interval; MM, melanoma; NS, not significant; OR, odds ratio.

*Significant ($P < .05$) compared with benign lesions (acquired nevi + Spitz nevi).

Reference:

Pellacani et al. Reflectance-mode confocal microscopy of pigmented skin lesions -- improvement in melanoma diagnostic specificity. *J Am Acad Dermatol.* 2005; 53(6): 979-985.



Table III. Frequency of in vivo reflectance-mode confocal laser microscopy features and odds ratio values observed at papillary dermis in benign and malignant melanocytic lesions with dermal component

	Invasive MM (33)	Compound nevi (28)	Compound Spitz/Reed (13)	Total (74)	OR (CI 95%)
Melanocytic nest features:					
Dense clusters	21 (63.6%)	26 (92.8%)	11 (84.6%)	58 (78.4%)	NS
Sparse cell clusters	6* (18.2%)	1 (3.6%)	1 (9.1%)	8 (10.8%)	NS
Cerebriform clusters	7* (21.2%)	0 (0%)	0 (0%)	7 (9.5%)	Not evaluable
Isolated cells within papillary dermis:					
Nucleated cells	15* (45.5%)	1 (3.6%)	1 (9.1%)	17 (23.0%)	16.3 (3.4-78.7)

CI, Confidence interval; MM, melanoma; NS, not significant; OR, odds ratio.

*Significant ($P < .05$) compared with benign lesions (acquired nevi + Spitz nevi).

Reference:

Pellacani et al. Reflectance-mode confocal microscopy of pigmented skin lesions -- improvement in melanoma diagnostic specificity. *J Am Acad Dermatol.* 2005; 53(6): 979-985.

Major Criterion to diagnose MM on RCM

The two major criteria corresponded to

- **the presence of cytologic atypia**
- **nonedged papillae at basal layer**

Reference:

Pellacani et al. Reflectance-mode confocal microscopy of pigmented skin lesions -- improvement in melanoma diagnostic specificity. *J Am Acad Dermatol.* 2005; 53(6): 979-985.



Minor Criterion to Diagnose MM on Confocal Microscope

The 4 minor criteria were represented by the

- presence of roundish cells in superficial layers spreading upward in a pagetoid fashion,
- pagetoid cells widespread throughout the lesion
- cerebriform clusters in the papillary dermis
- nucleated cells within dermal papilla

Reference:

Pellacani et al. Reflectance-mode confocal microscopy of pigmented skin lesions -- improvement in melanoma diagnostic specificity. *J Am Acad Dermatol.* 2005; 53(6): 979-985.



Confocal diagnosis of MM

- **“The Presence of two major criteria OR the presence of one major and one minor criterion is essential for the diagnosis of melanoma”**

Reference:

Pellacani et al. Reflectance-mode confocal microscopy of pigmented skin lesions -- improvement in melanoma diagnostic specificity. *J Am Acad Dermatol.* 2005; 53(6): 979-985.



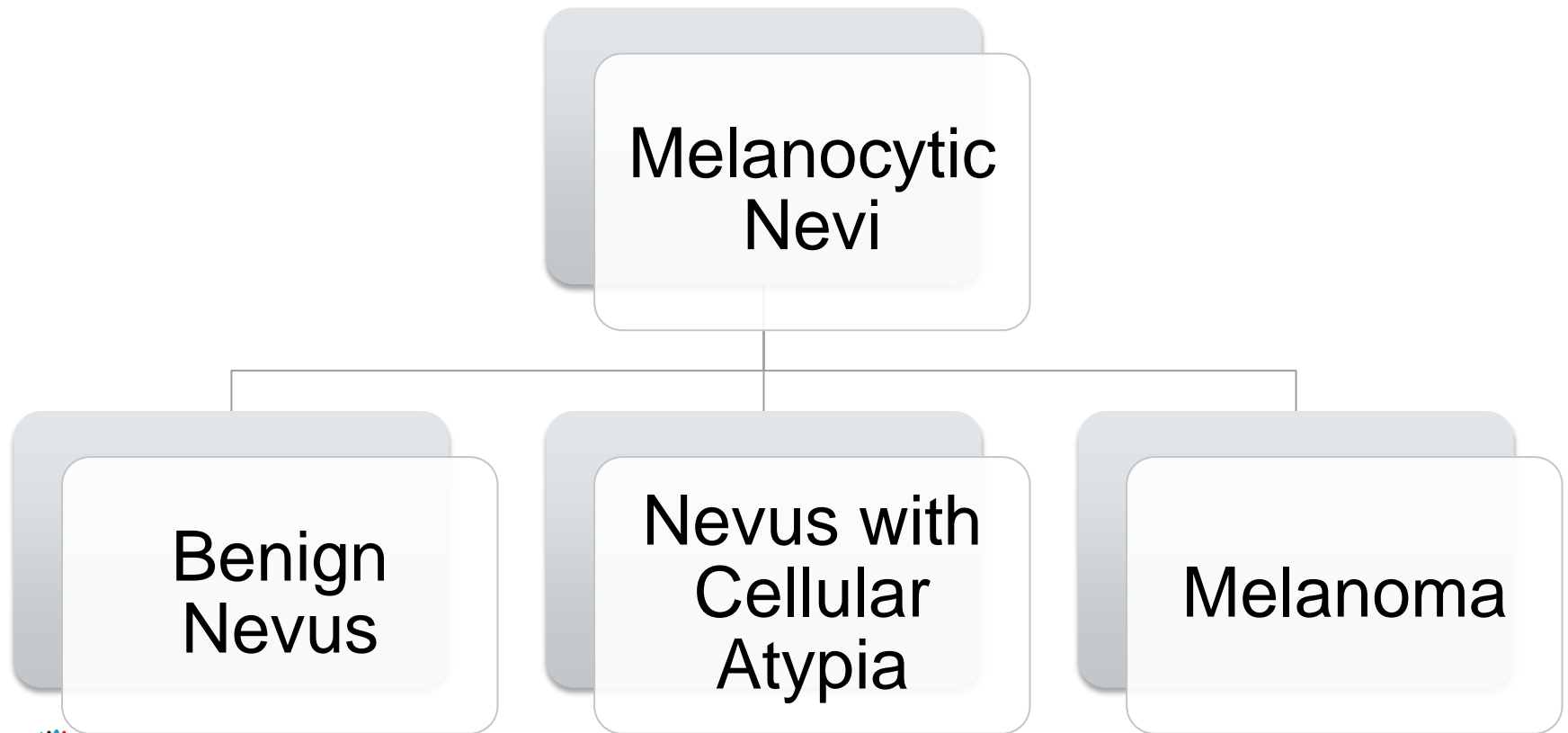
Accuracy of Diagnosis

- **Sensitivity:**
 - = $TP / TP + FN$
 - = $38 / 38 + 0$
 - = **100%**
- **Specificity: (scenario 2)**
 - = $TP / TP + FN$
 - = $TN / TN + FP$
 - = $(75 + 629) / (75 + 629) + 6$
 - = $704 / 704 + 6$
 - = **99.2%**

Reference:

Rao B et al. The diagnostic accuracy of in vivo confocal microscopy in clinical practice. *J Am Acad Dermatol.* 2015;73(2):317-319.

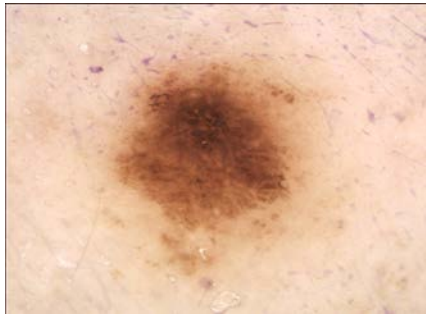
“Confocal Microscopy Features of Pigmented Lesions”



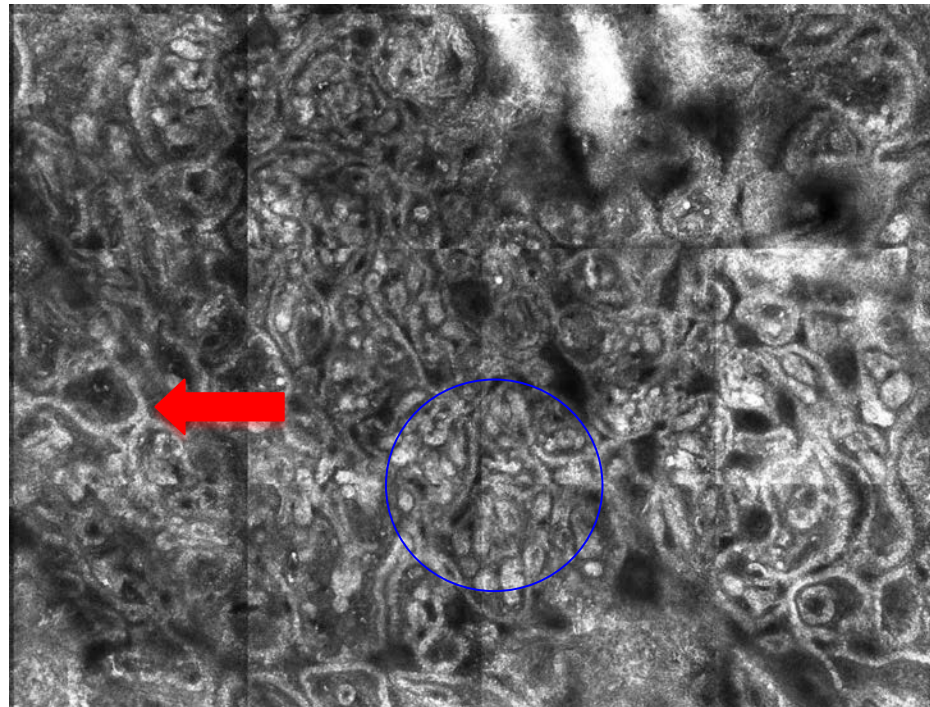
Benign Melanocytic Nevus

- **Diagnostic Confocal Features**
 - **Symmetric architecture**
 - **Regular honey comb pattern**
 - **Edged Papillae**
 - **Dermal nests with monomorphous cells**
- **Types:**
 - **Junctional Nevi**
 - **Compound Nevi**
 - **Dermal Nevi**

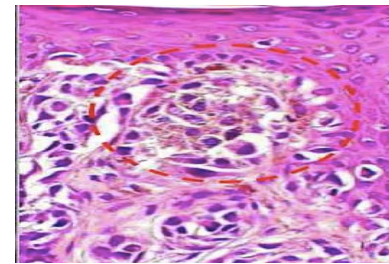
Benign Melanocytic Nevus



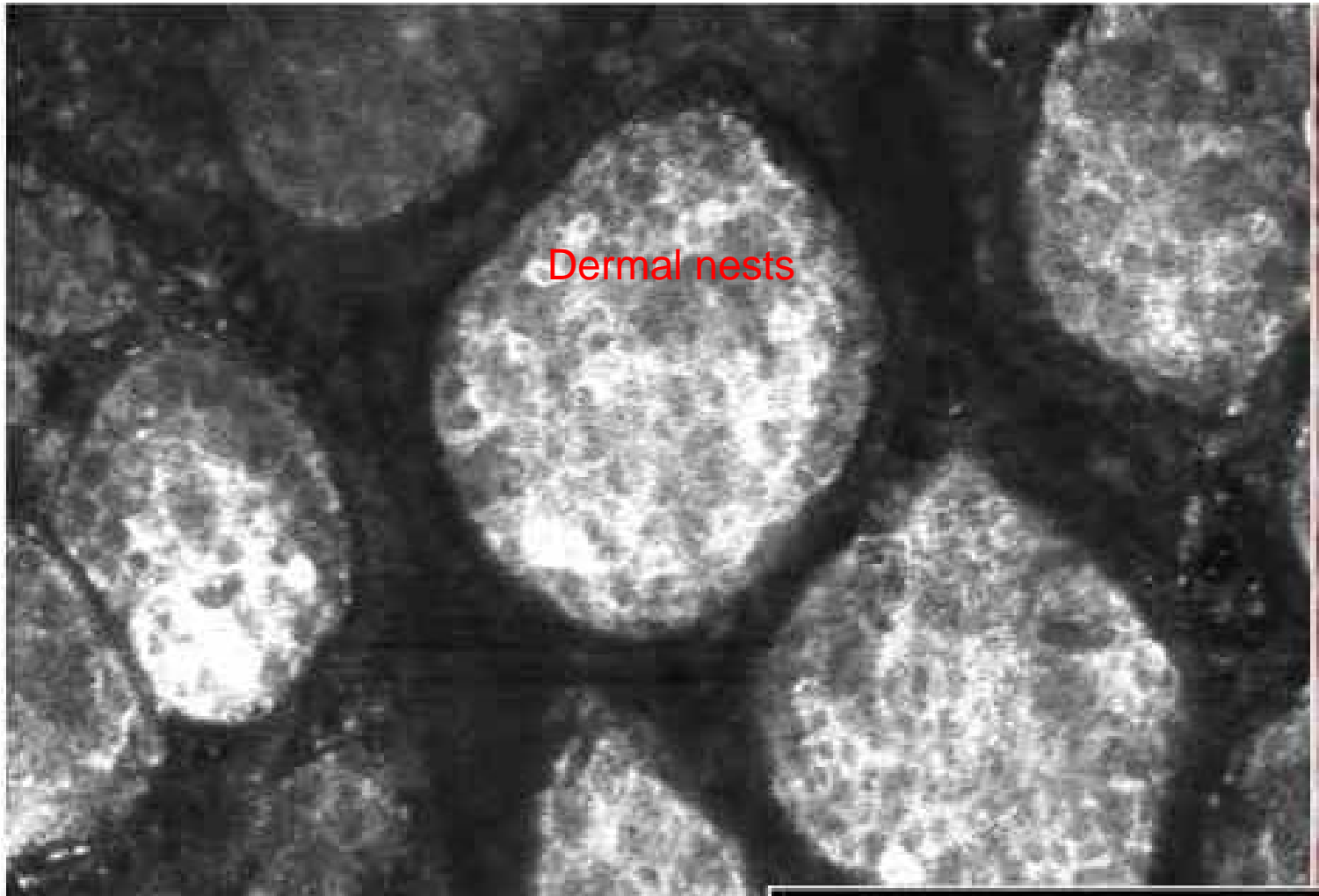
Clinical



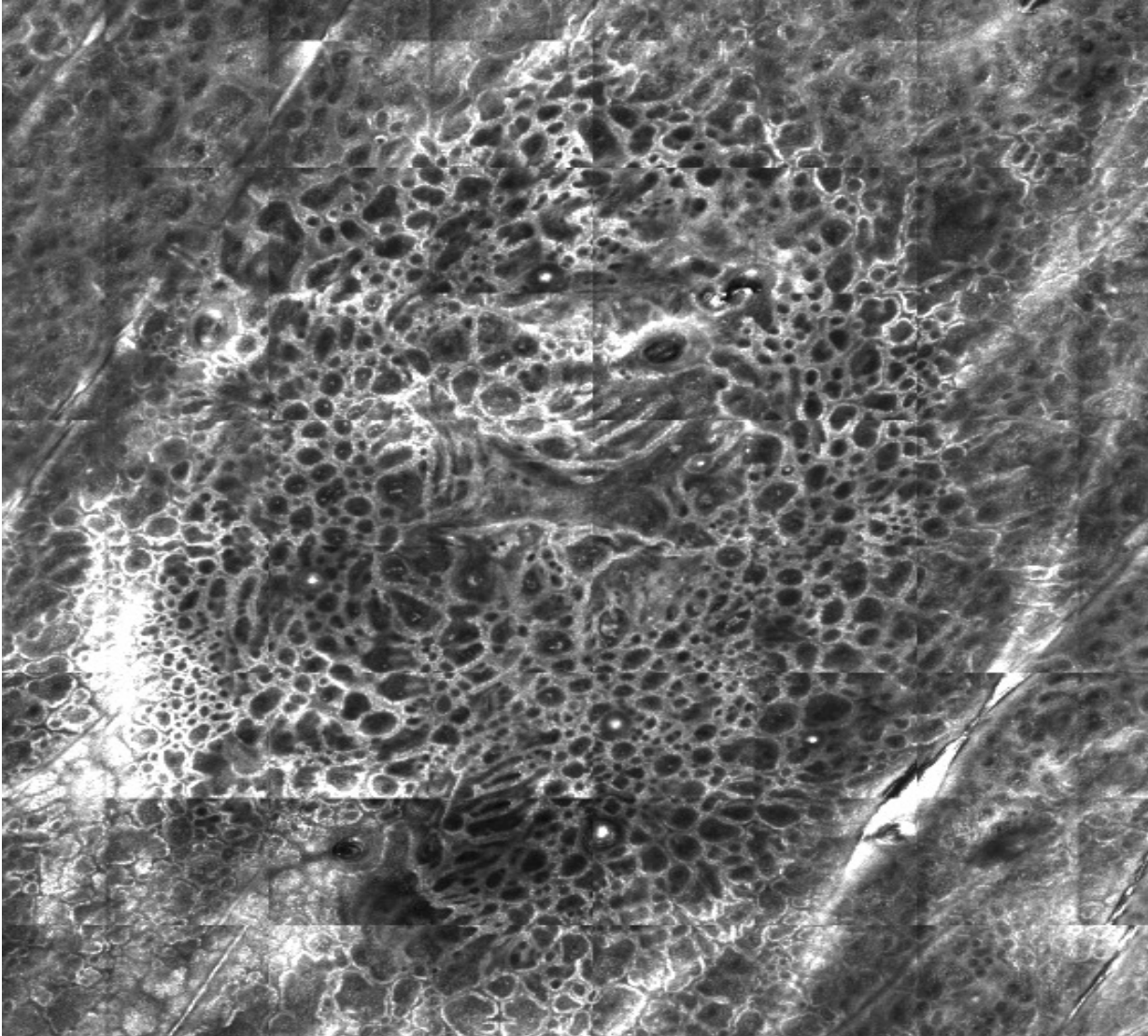
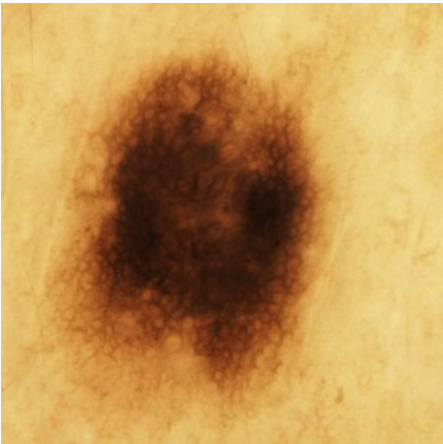
Confocal



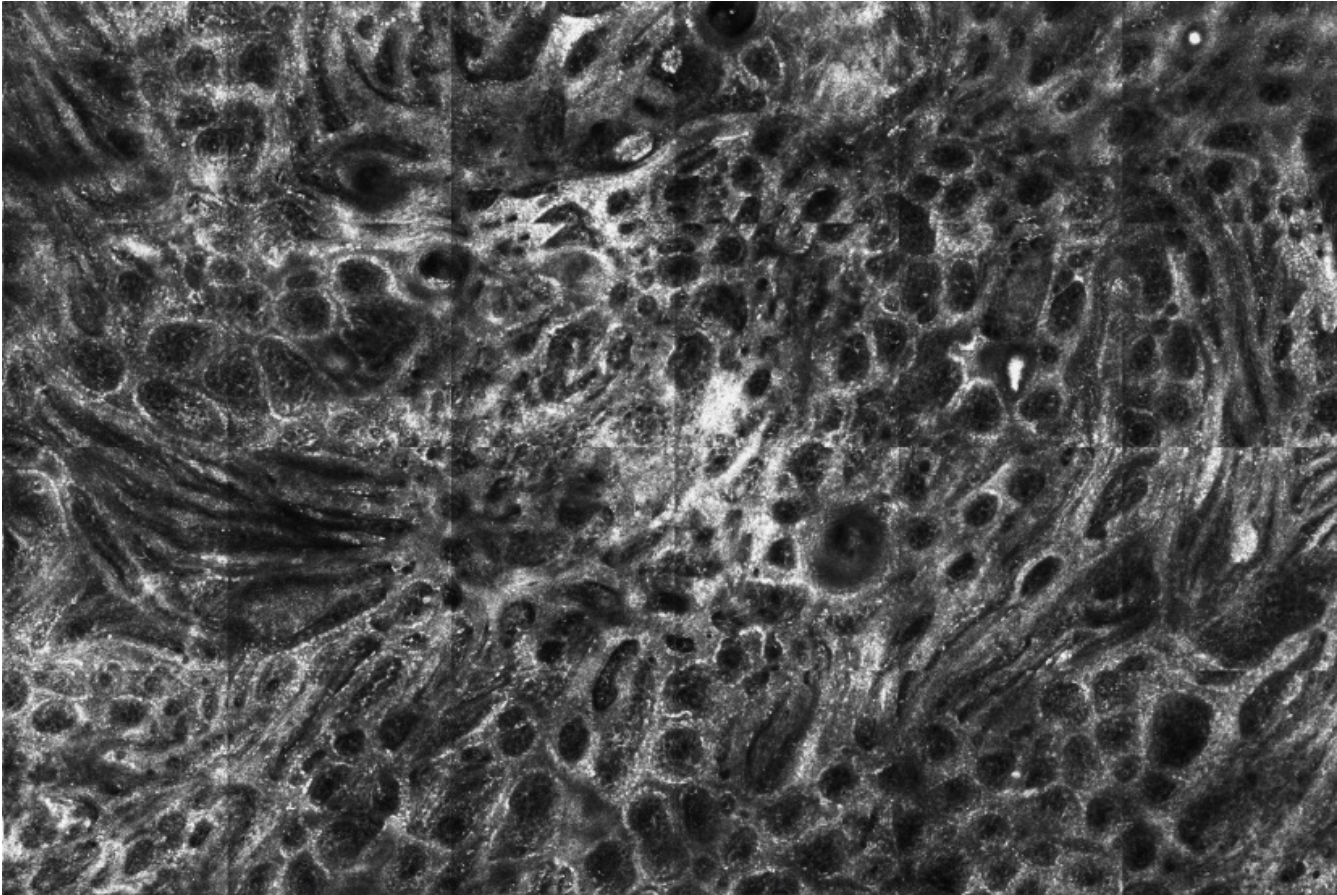
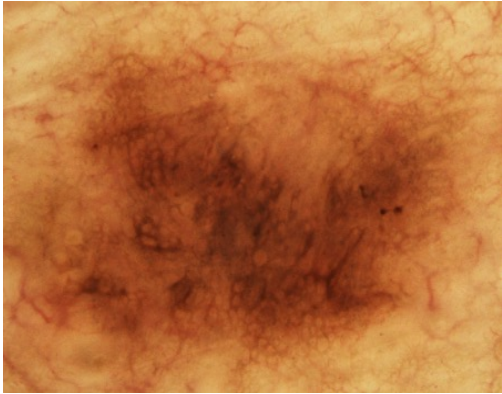
Histology



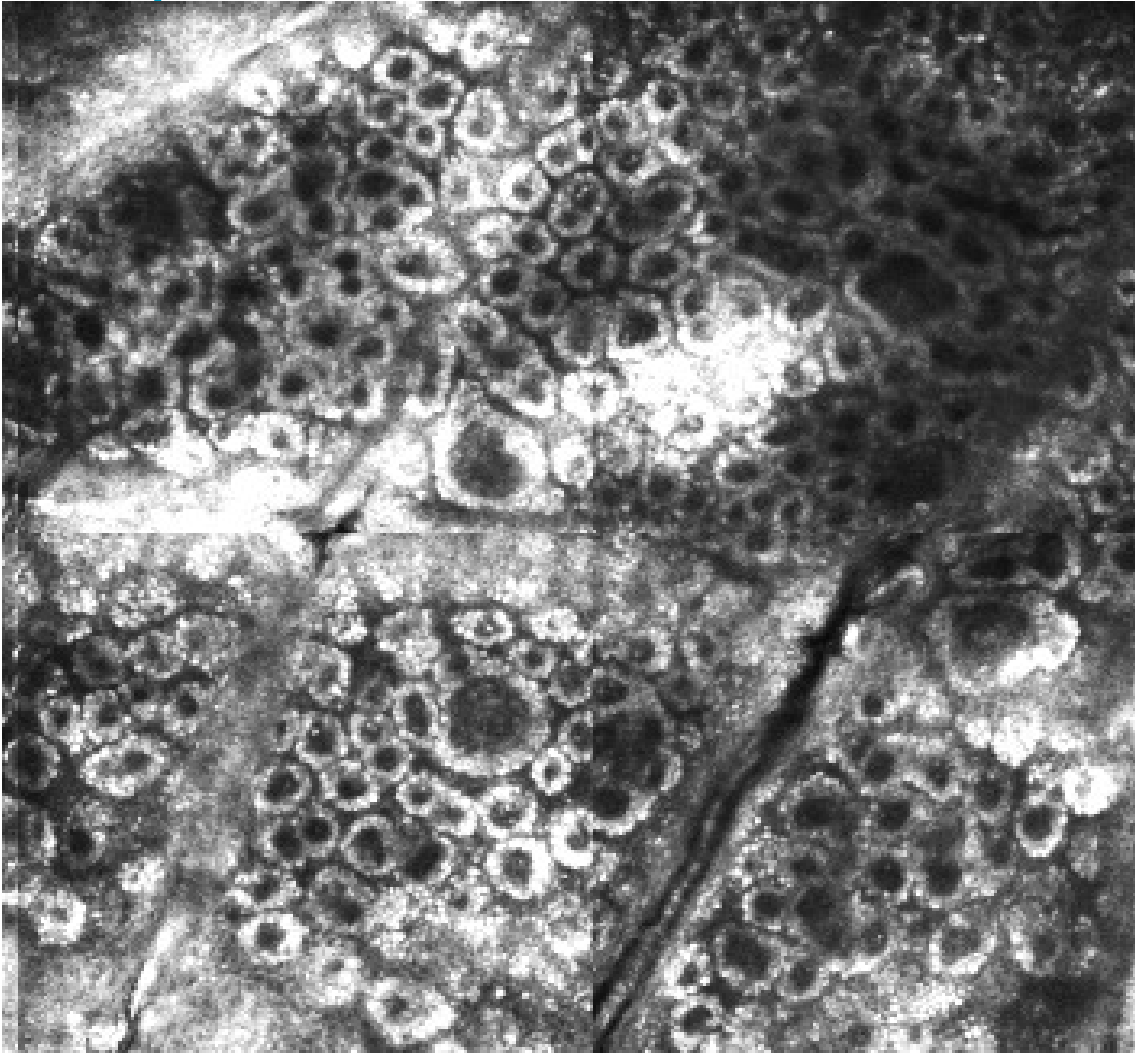
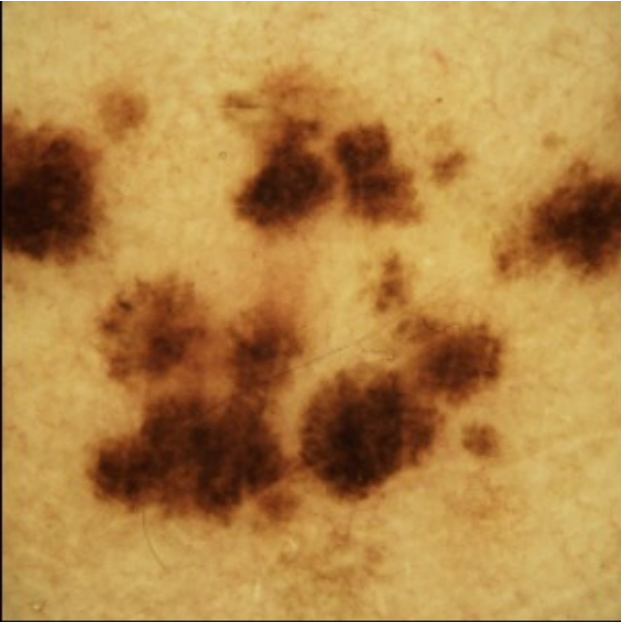
Benign melanocytic Nevus



Benign melanocytic Nevus



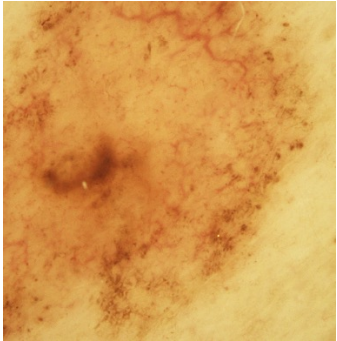
Benign melanocytic Nevus



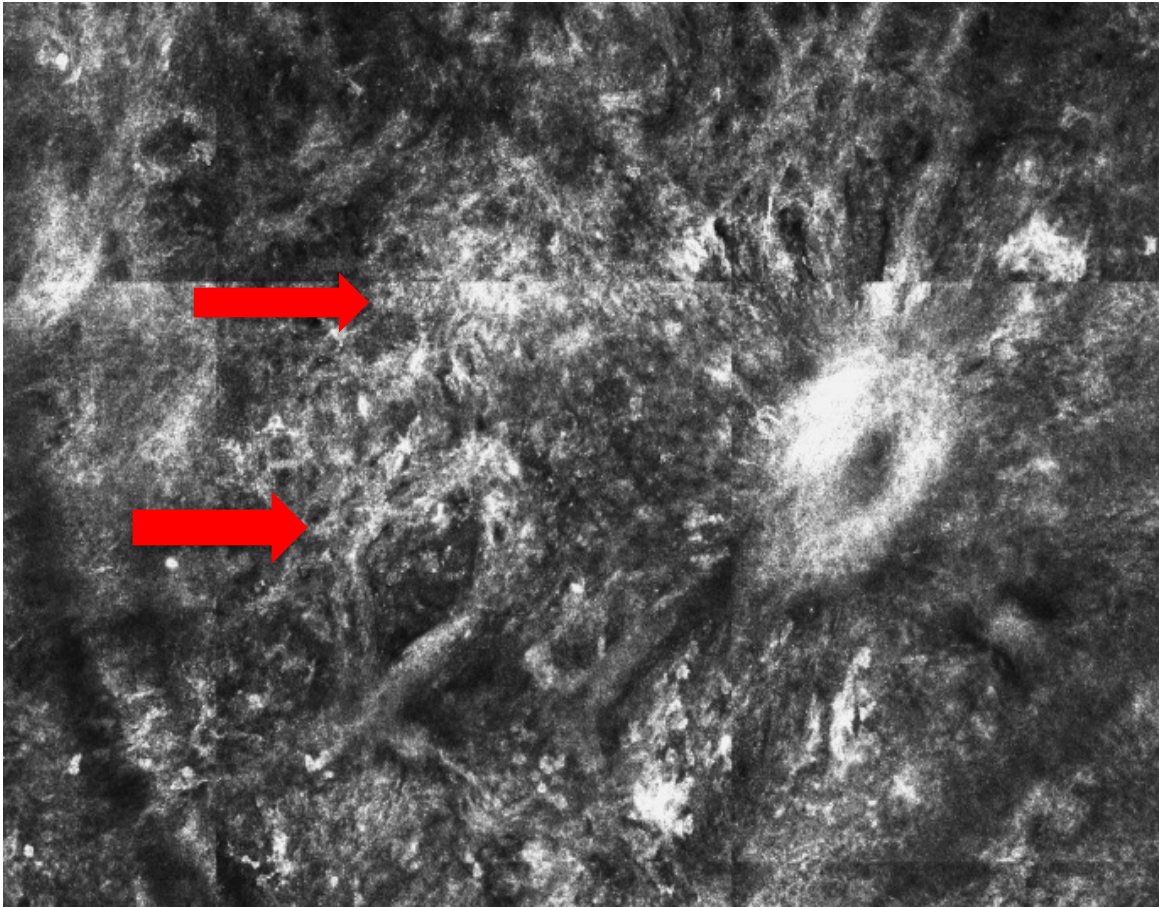
Nevus with Cellular Atypia

- **Diagnostic Confocal Features**
 - Irregular honeycomb pattern
 - Few atypical cells (melanocytes)
 - Edged and non edged papillae
 - Borders poorly defined

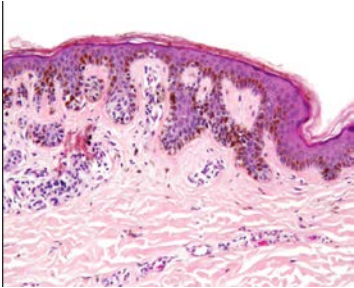
Nevus with Cellular Atypia



Clinical



Confocal



Histology

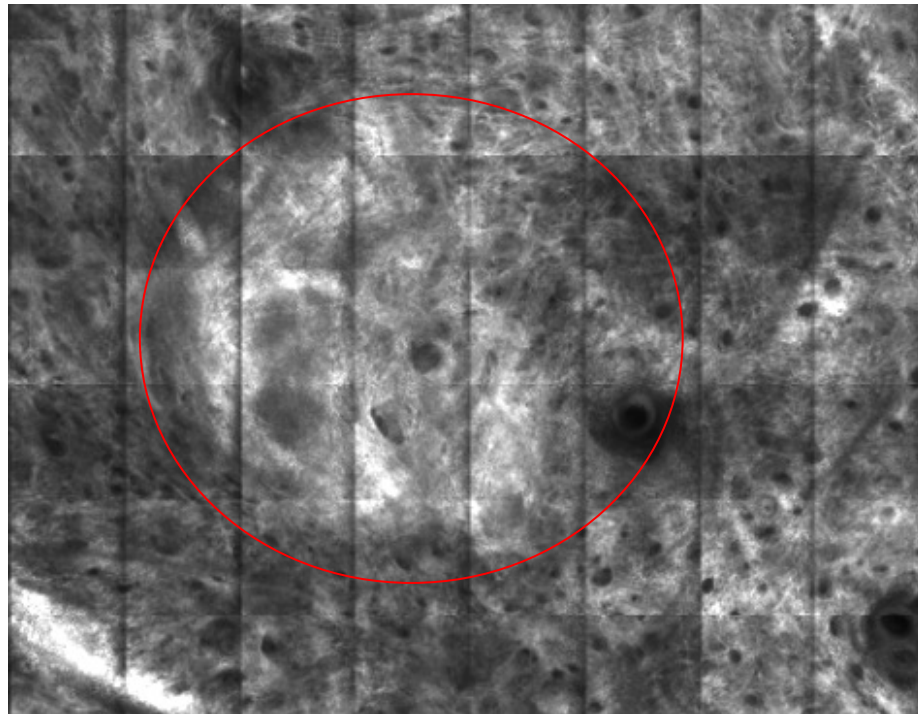
Blue Nevus

- **Diagnostic Confocal Features**
 - **Regular honeycomb pattern**
 - **Edged papillae**
 - **Dermis shows small bright round or dendritic nucleated cells**
 - **Polygonal and plump bright non nucleated cells**

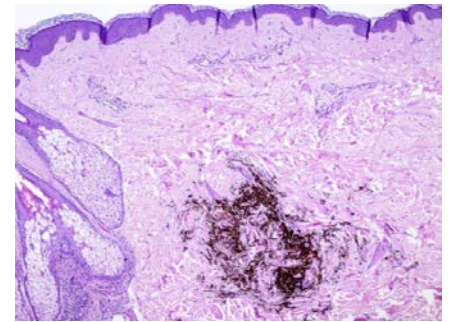
Blue Nevus



Clinical

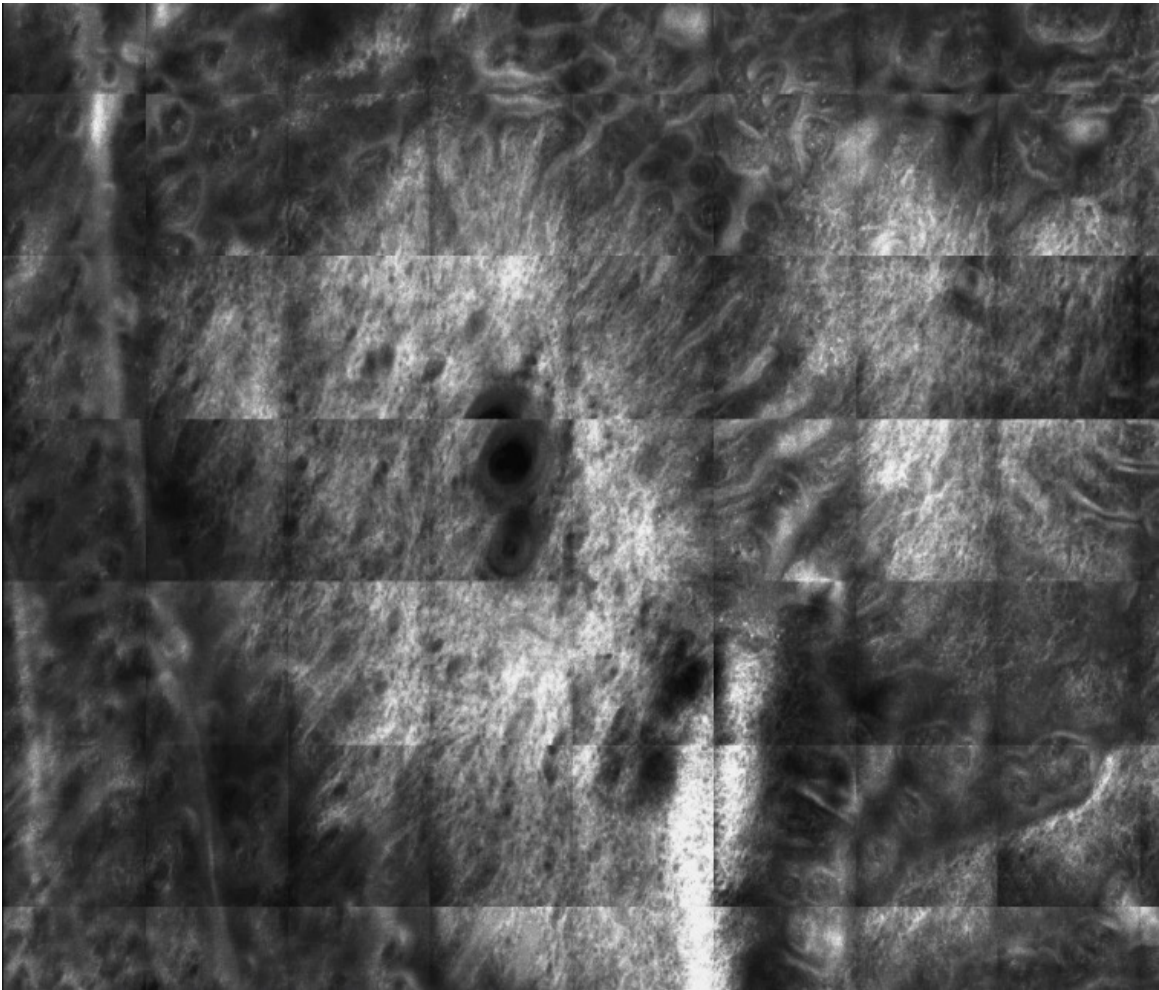
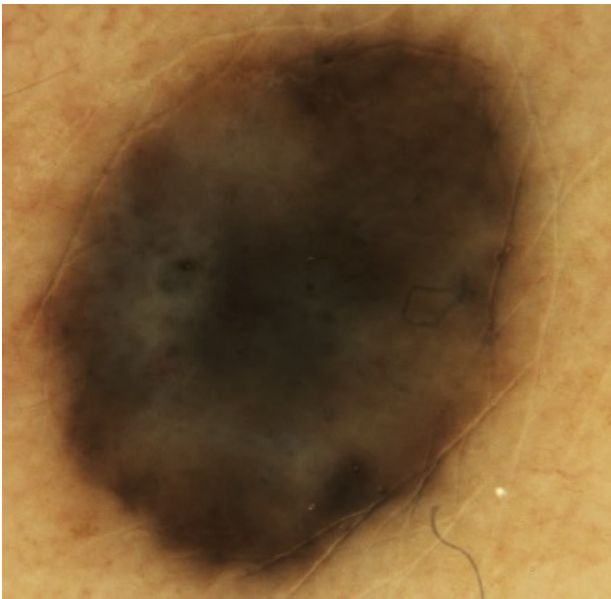


Confocal



Histology

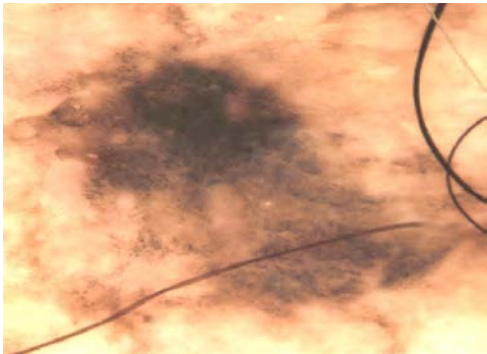
Blue Nevus



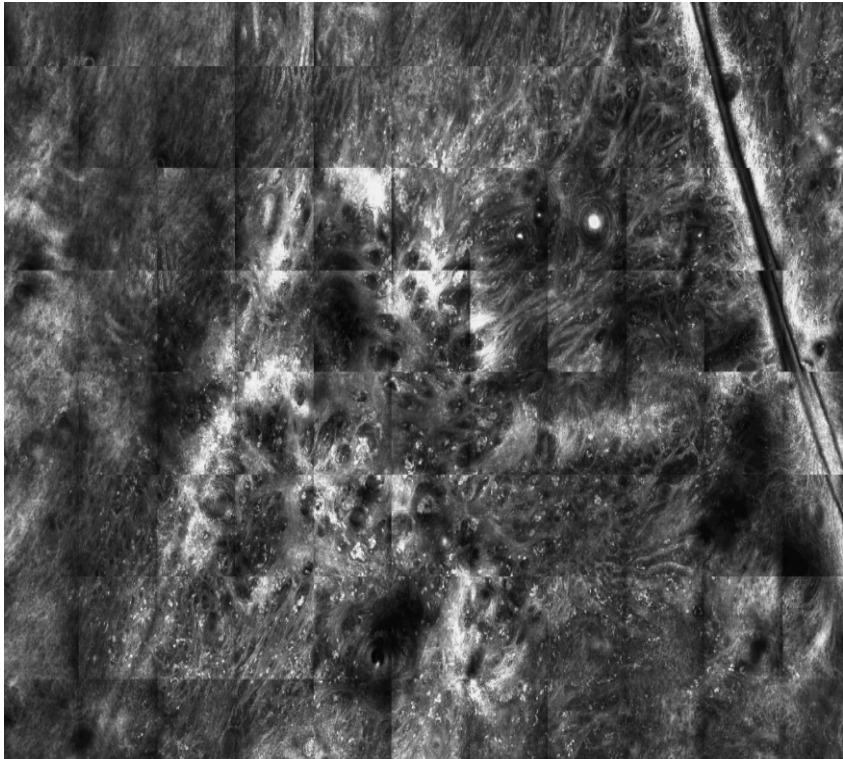
Melanoma in Situ

- **Diagnostic Confocal Features**
 - **Irregular honeycomb pattern**
 - **Pagetoid cells**
 - **Disorganized ringed pattern**
 - **Uneven clusters and atypical cells**

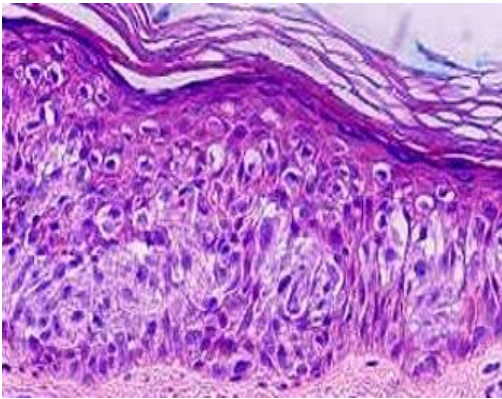
Melanoma in Situ



Clinical

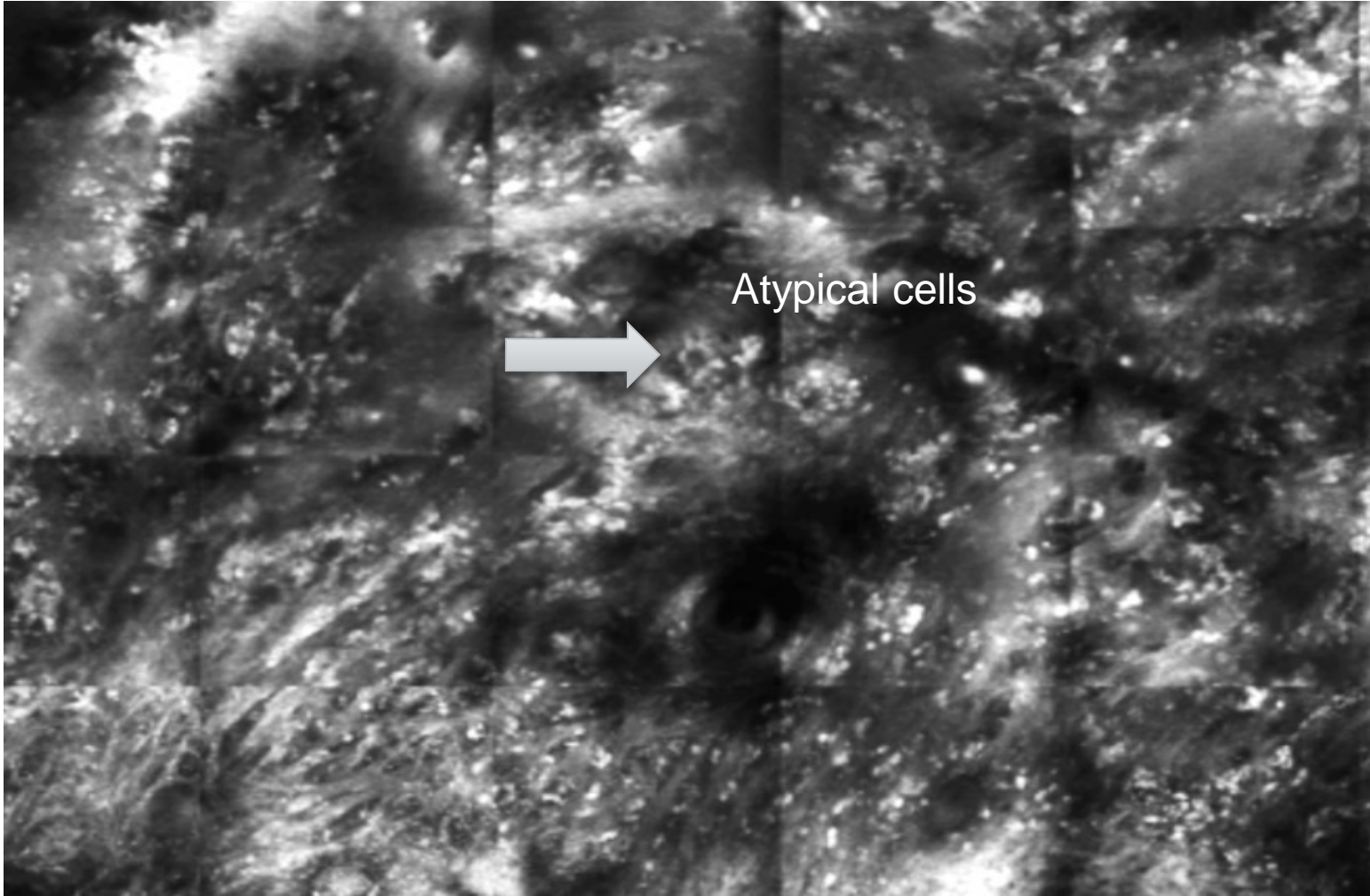


Confocal



Histology

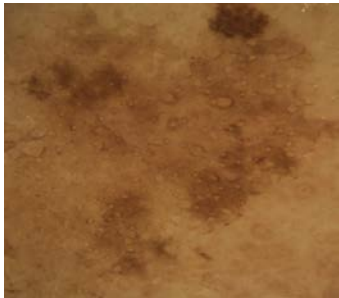
Invasive Melanoma



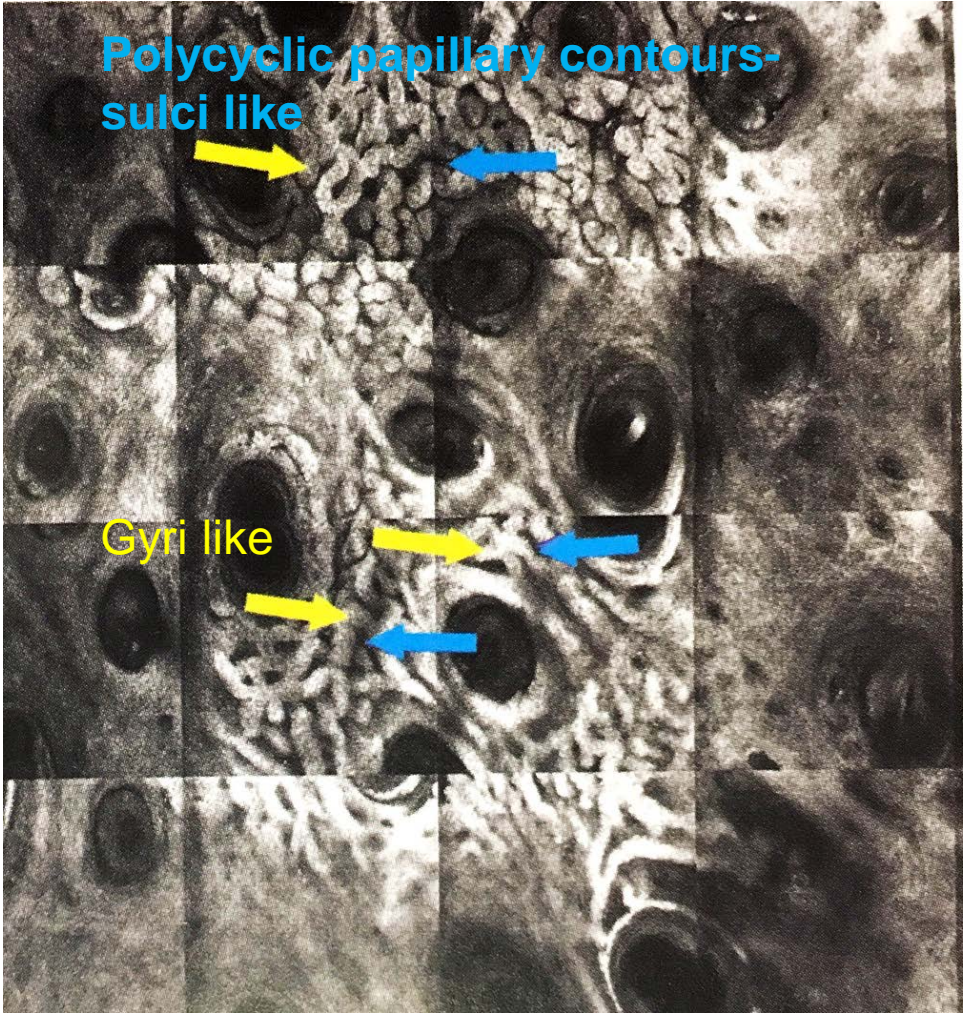
Lentigo Simplex

- **Confocal diagnostic Features**
- **Epidermis**
 - Regular honeycomb pattern
- **Dermis**
 - Polycyclic papillary contours-(Sulci and gyri like)
 - Increase in the density of dermal papillae surrounded by monomorphic layers of cells
 - Cord like rete ridges and polymorphous edged papillae

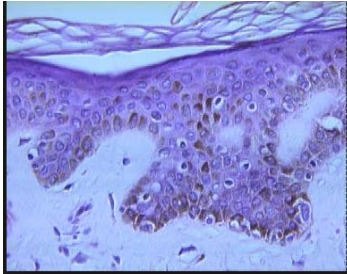
Lentigo Simplex



Clinical



Confocal

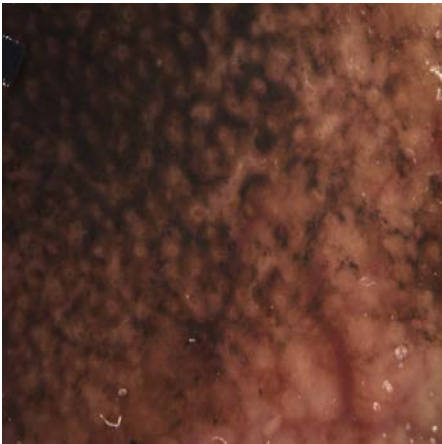


Histology

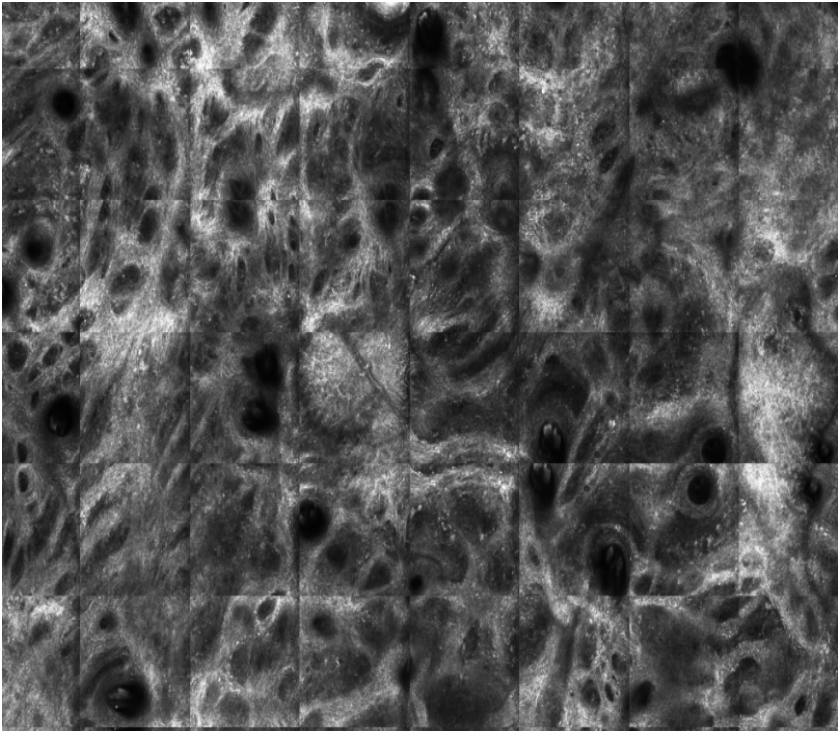
Lentigo Maligna

- **Diagnostic Confocal Features**
 - Irregular honeycomb pattern
 - Multiple large round pagetoid cells
 - Non edged papillae
 - Junctional thickening
 - Atypical; cells may be present around the hair follicle
 - Large nucleated cells may be present within dermal papillae

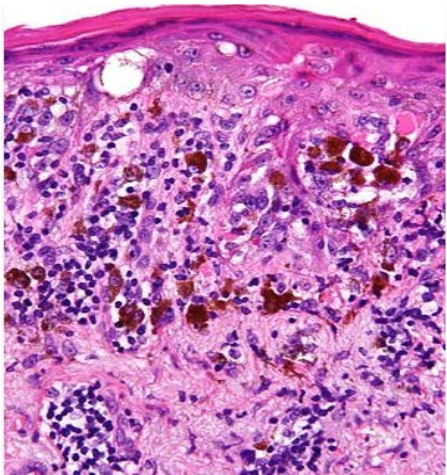
Diagnostic Confocal Features- Lentigo Maligna



Clinical

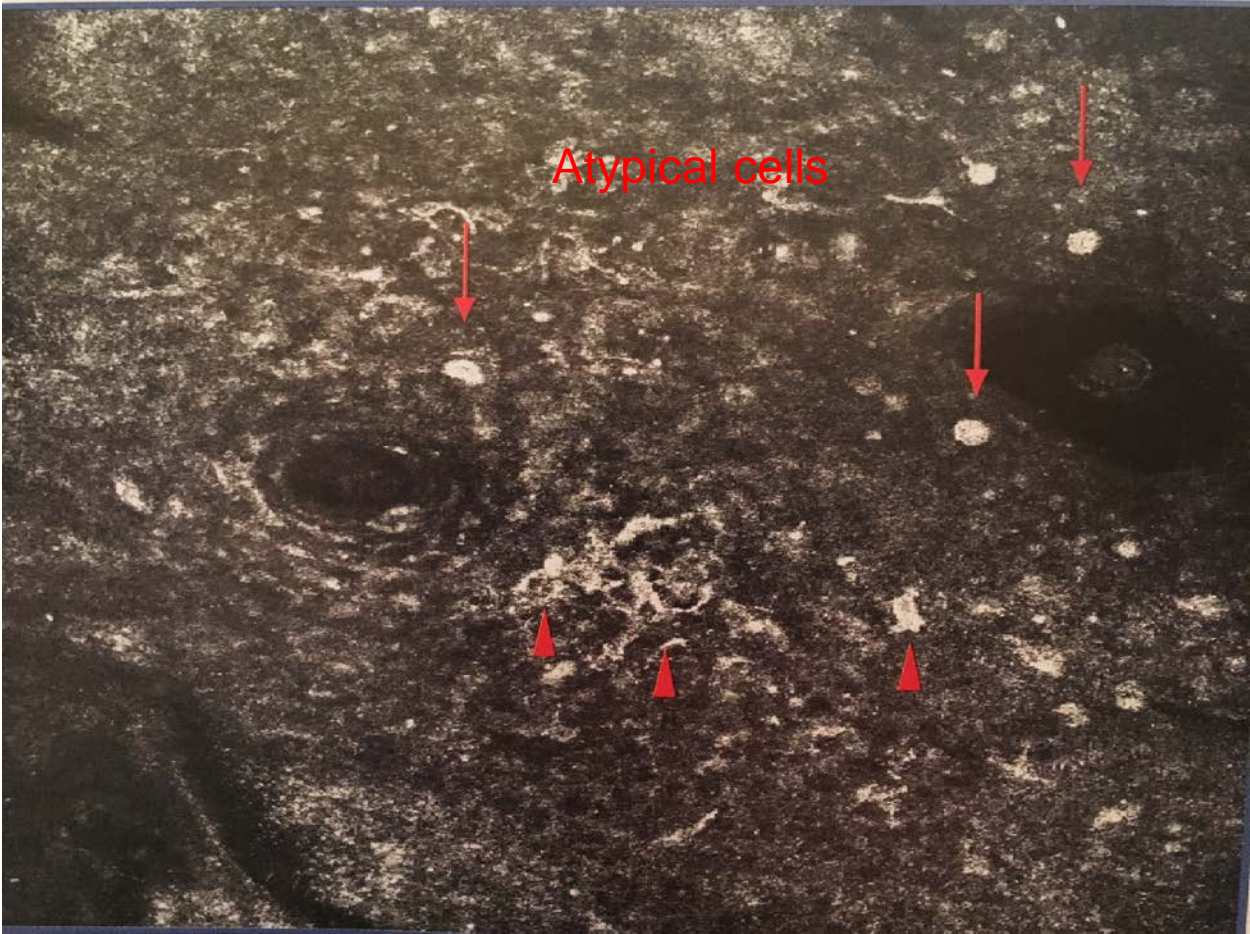


Confocal

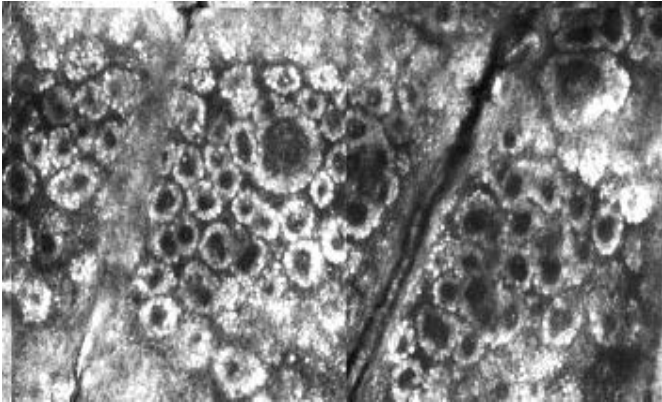


Histology

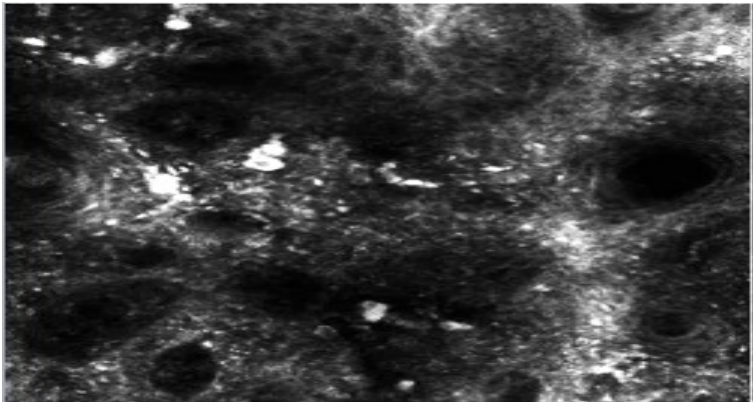
Lentigo Maligna



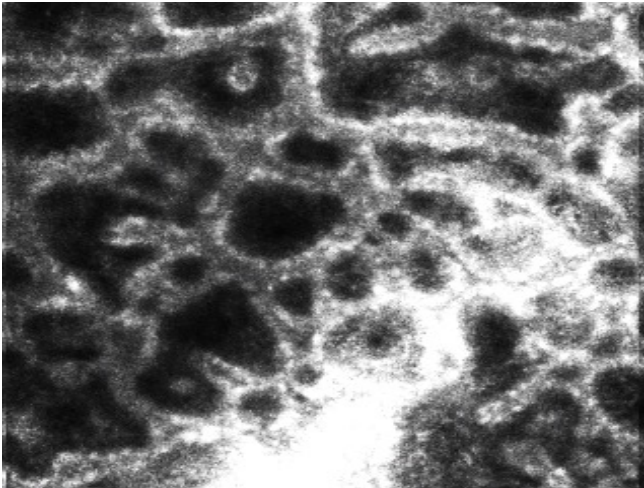
Summary



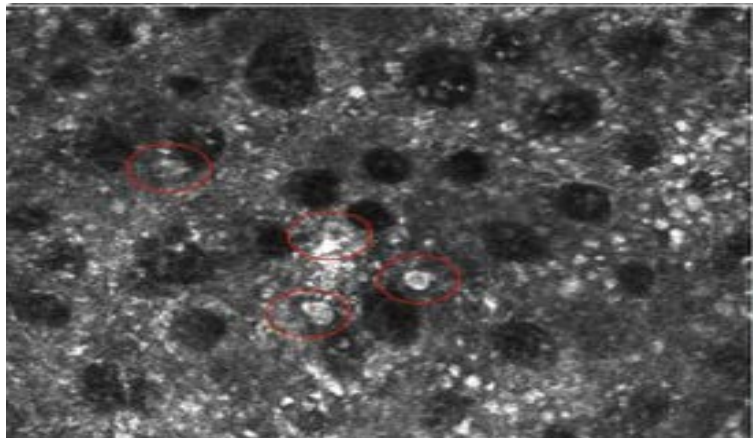
Edged Papillae



Non -Edged Papillae



Monomorphic cells



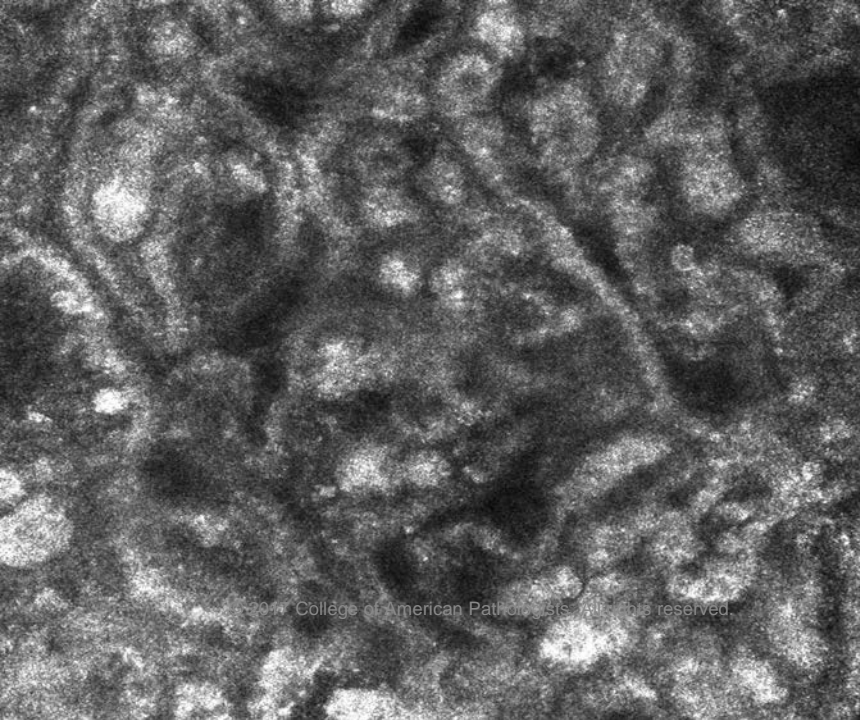
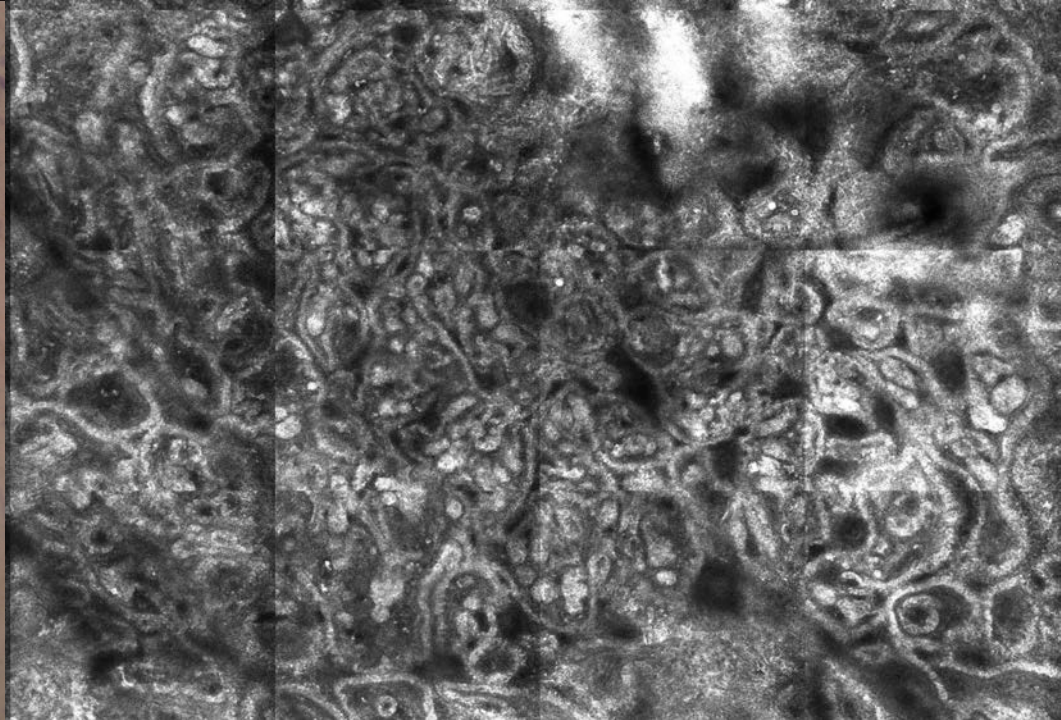
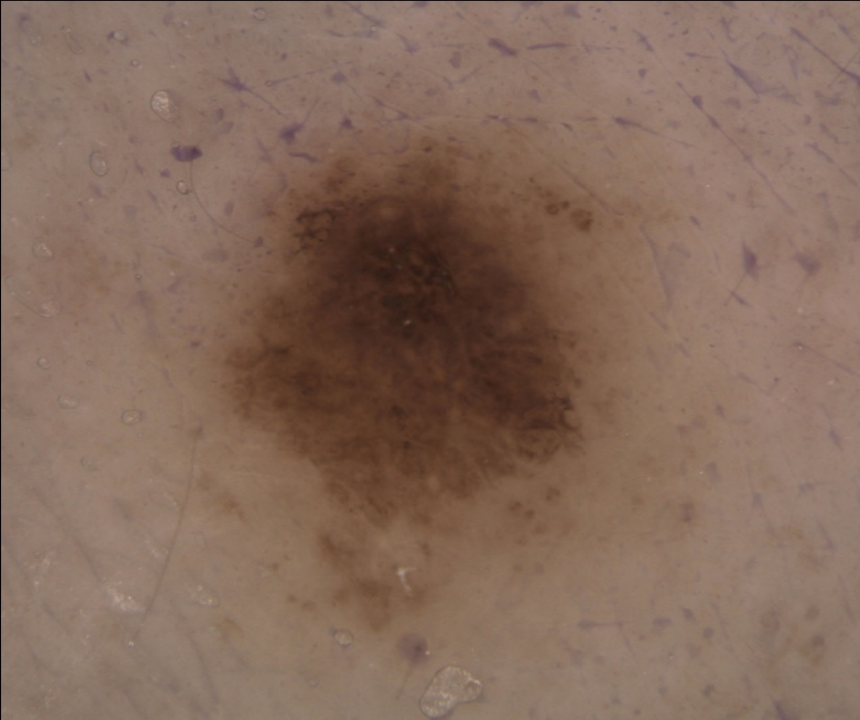
Atypical Cells

**KEEP CALM
IT'S
QUIZ TIME**

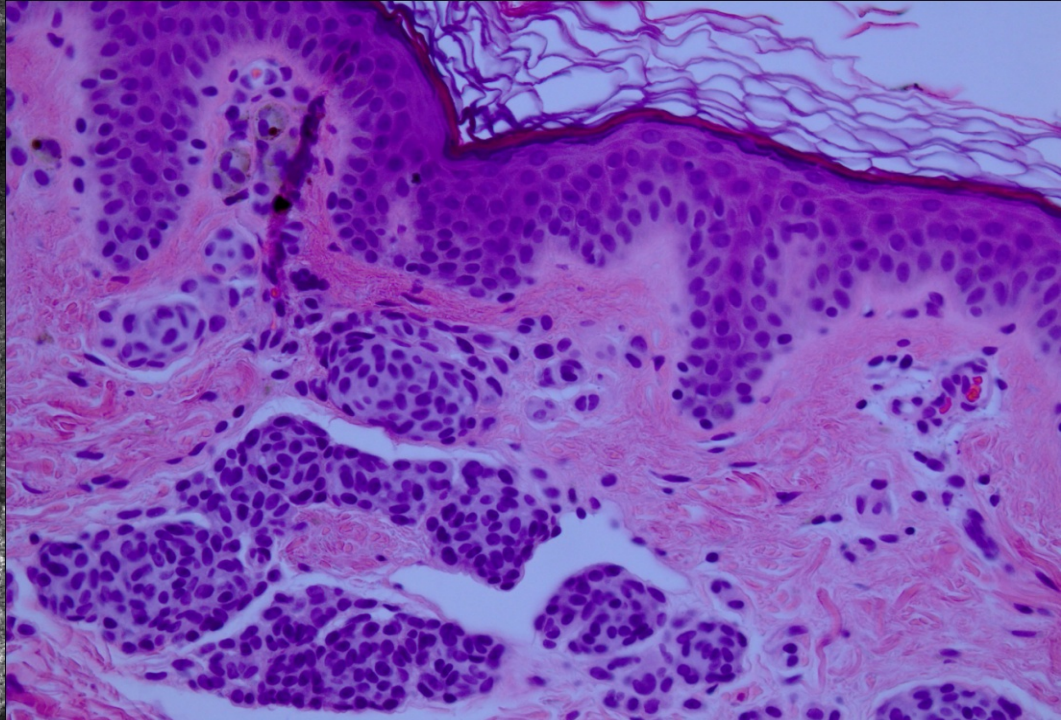
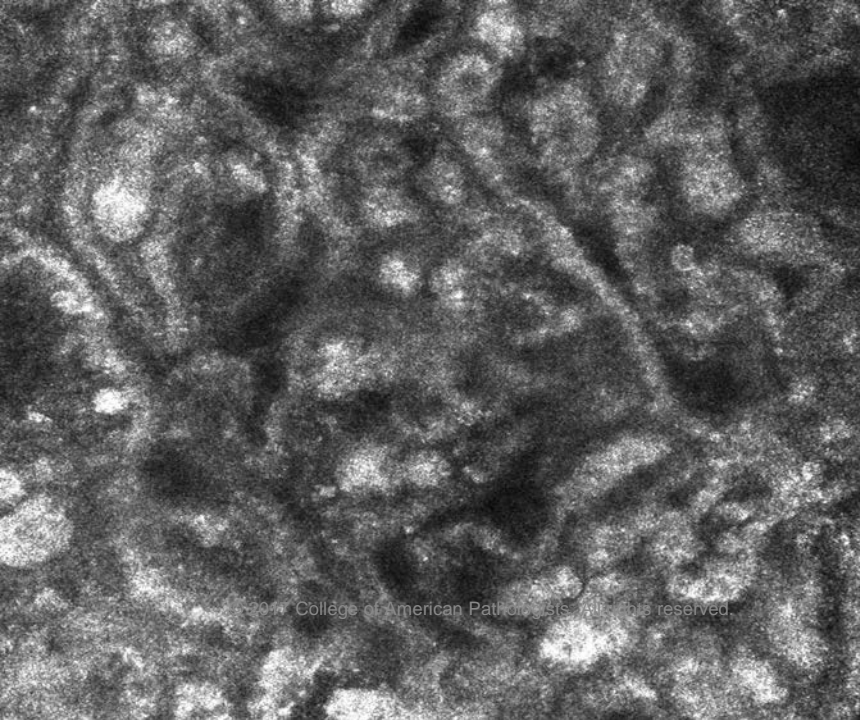
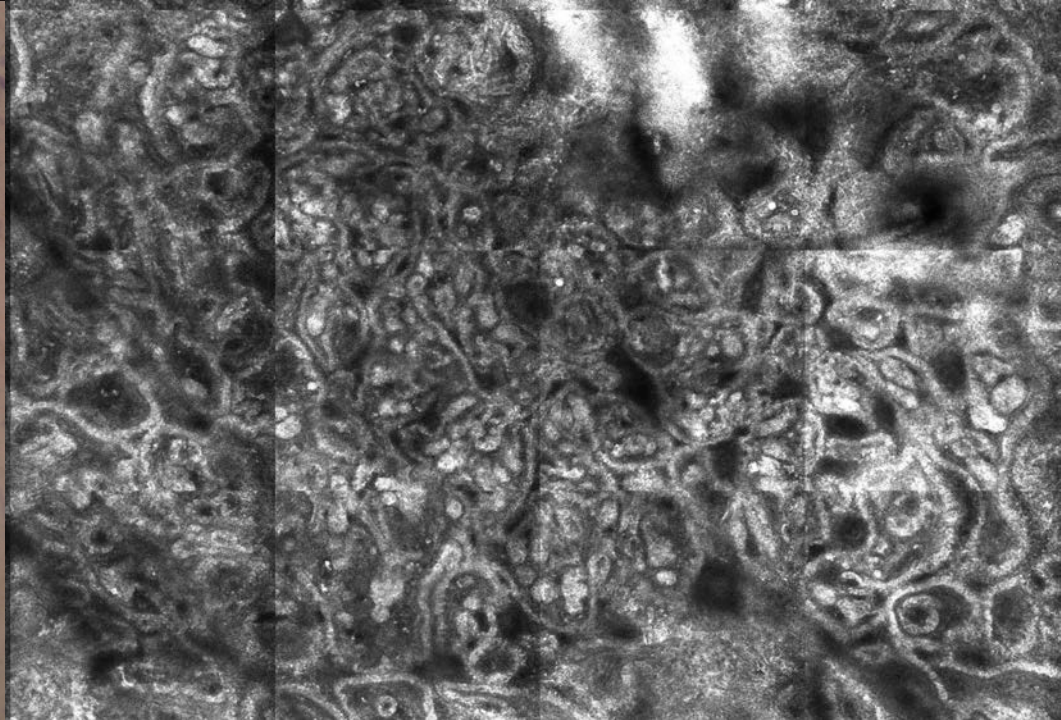
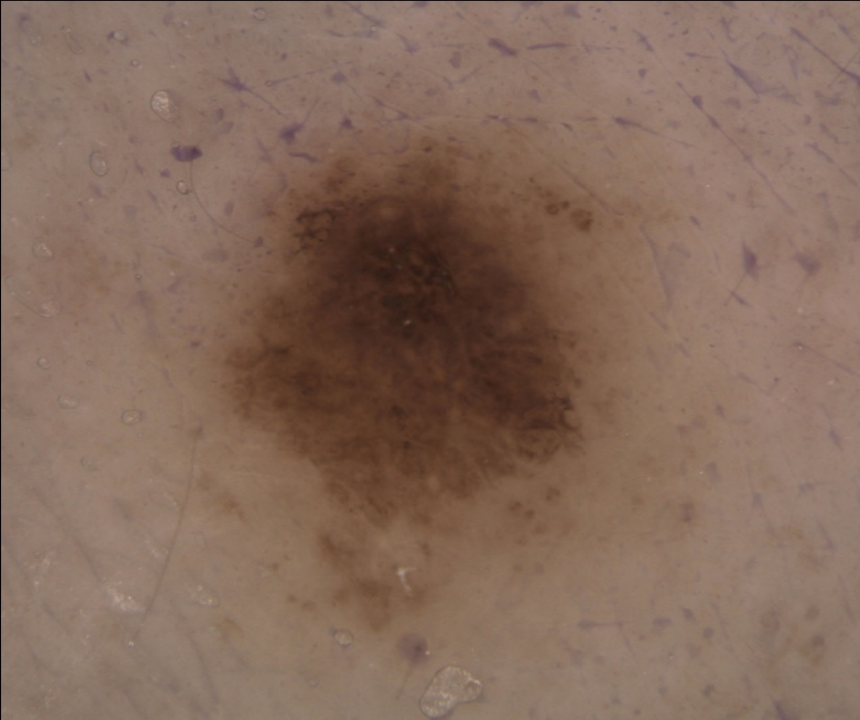


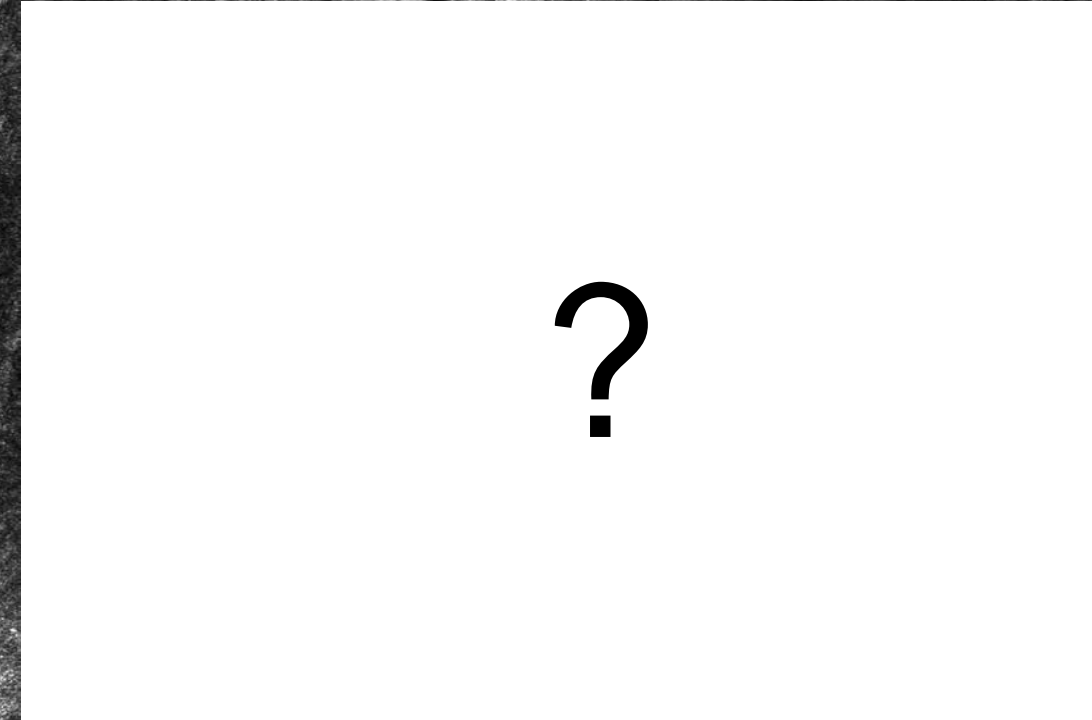
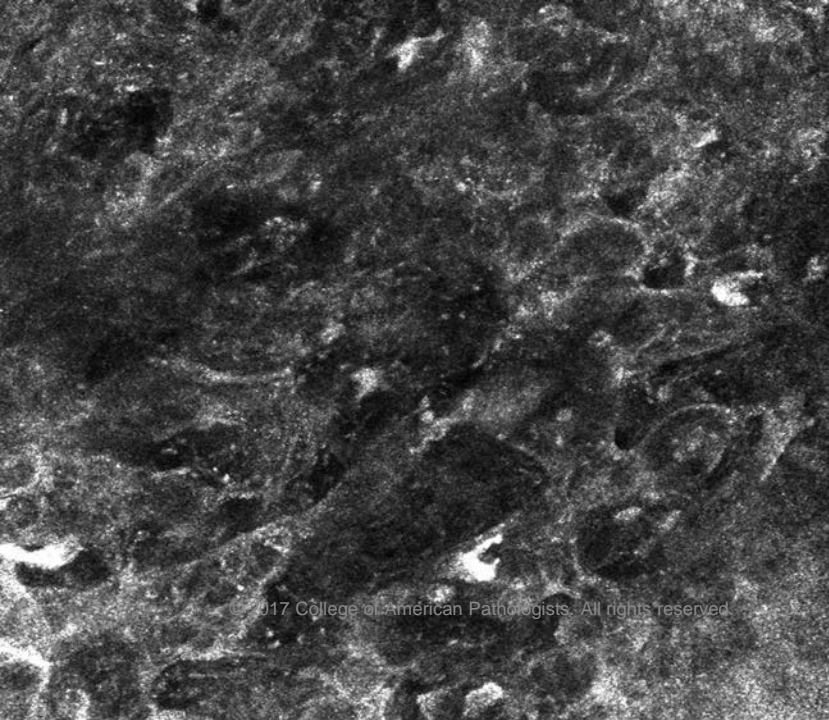
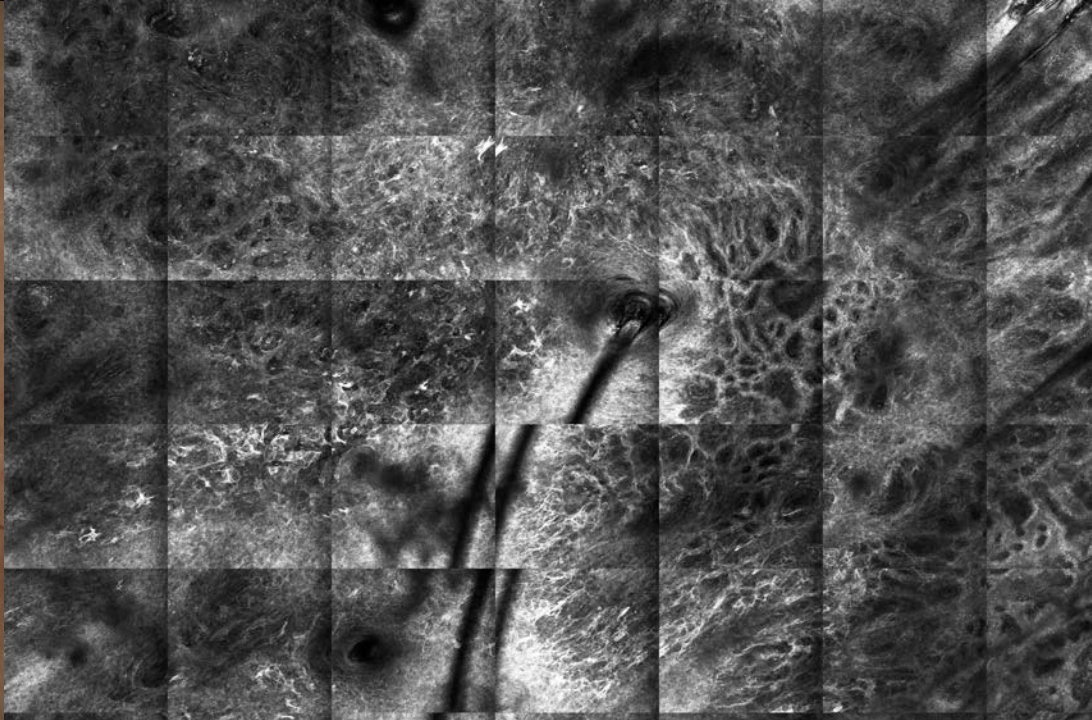
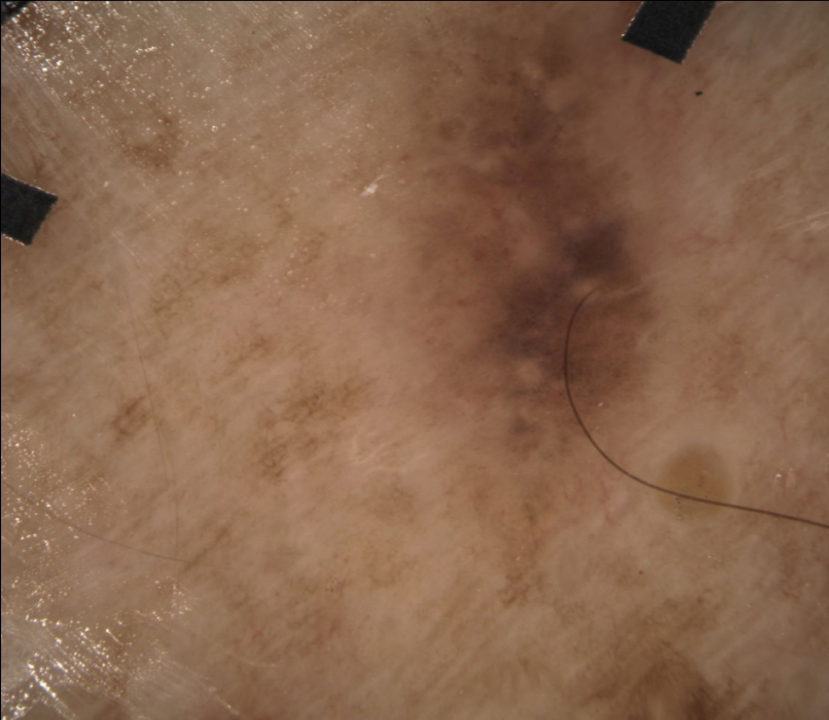
CAP

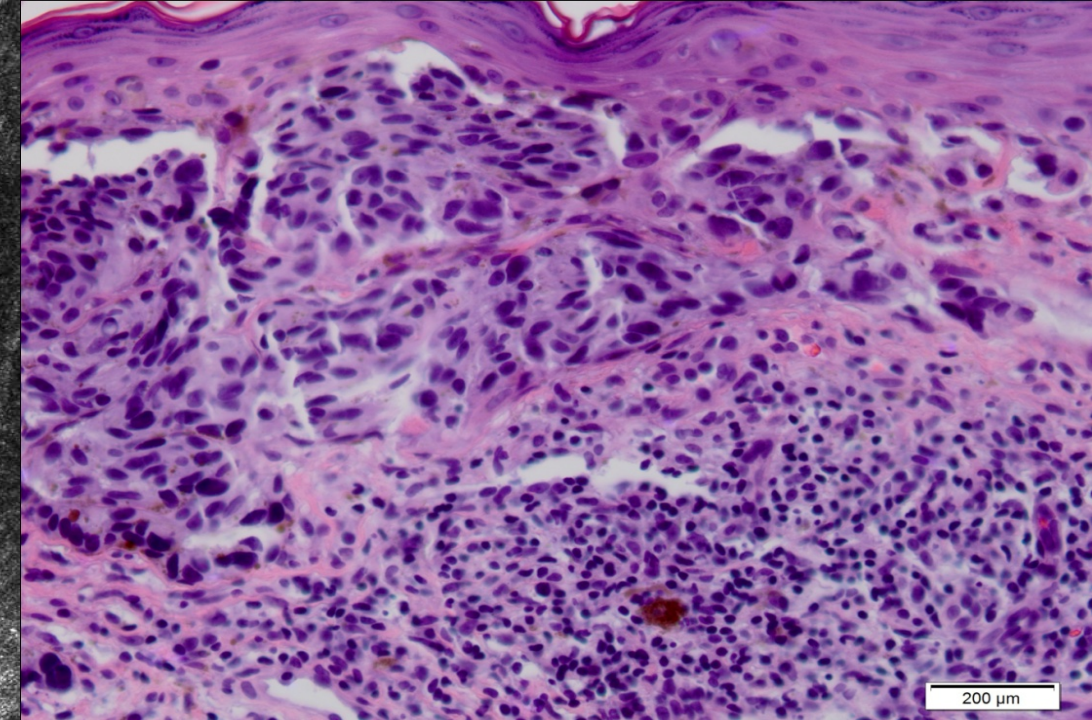
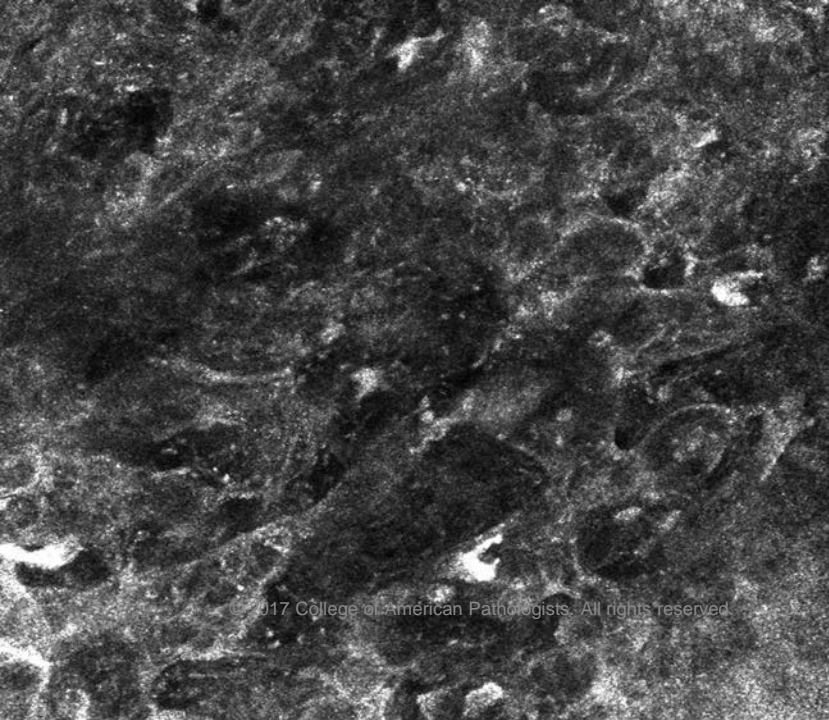
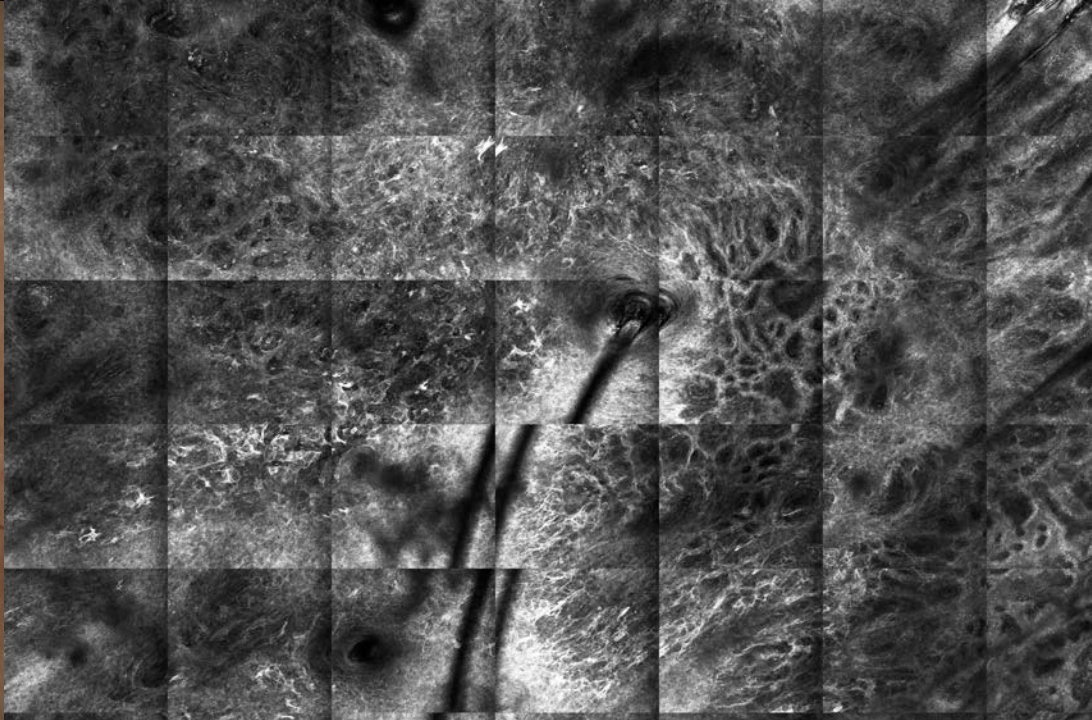
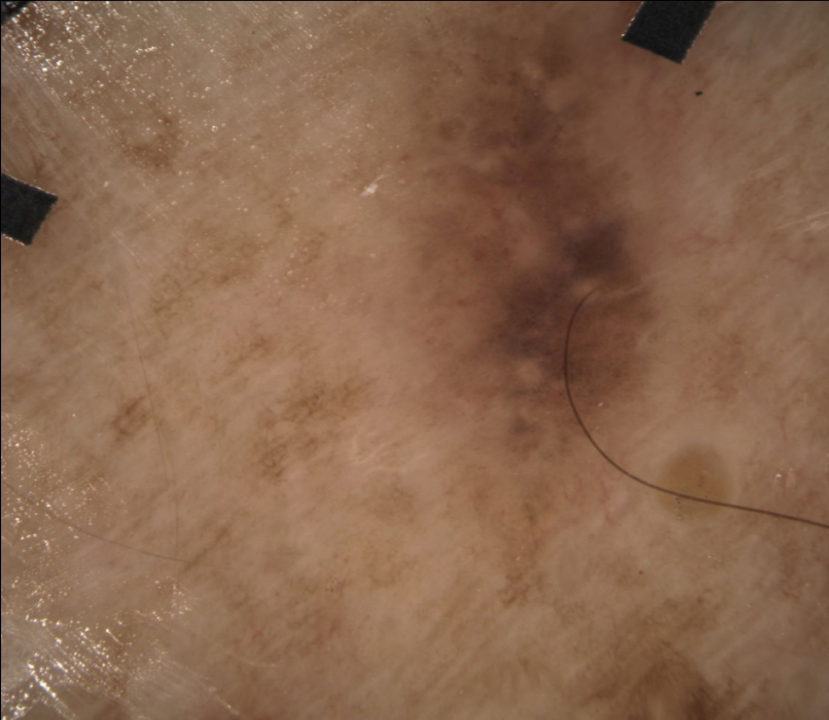
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Acknowledgment

- **Attiya Haroon, MD, PhD**

Thank you

For more information

Contact: attiya.haroon9@gmail.com

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Upcoming Webinars

DATE	TOPIC	SPEAKER(s)
5/30	Creating a successful pathology-engineering collaboration	Nicholas P. Reder, MD, MPH Adam Glaser, PhD Lawrence D. True, MD, FCAP Jonathan T.C. Liu, PhD
8/15	IVM and Skin	Babar Rao, MD, FAAD
10/3	Light-sheet microscopy for 3D pathology	Nicholas P. Reder, MD, MPH Lawrence D. True, MD
11/7	Rapid examination of fresh tissue using light-sheet microscopy	Nicholas P. Reder, MD, MPH

Register for upcoming & archived webinars:
www.cap.org > Calendar > Webinars

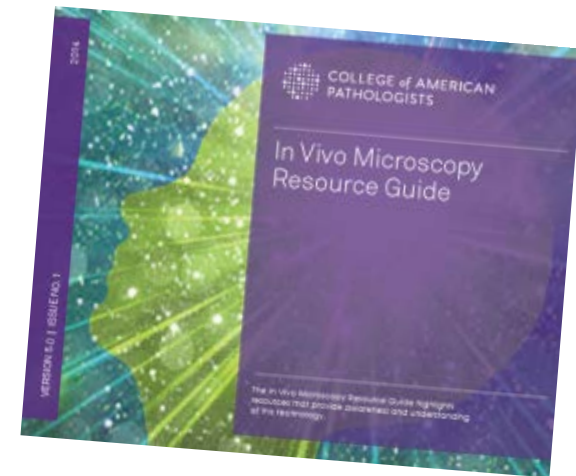


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The CAP In Vivo Microscopy Resource Guide – see handout

- The IVM resource guide highlights current IVM articles and other resources that assist in understanding and potentially adopting IVM and EVM
 - Printed guides are available for members (\$39) and non-members (\$69)
 - The digital copies of all four Resource Guides are a complimentary member benefit
 - Access them www.cap.org > Resources and Publications



IVM Short Presentations on Emerging Concepts (SPECs) – see handout

- IVM SPECs are:
 - Short PowerPoints, created for pathologists
 - Useful for educating pathologists colleagues about IVM and GI specialist on the role and value of pathologists in IVM
- IVM SPEC Topics:
 - In Vivo Microscopy (IVM): A New Role for Pathologists
 - IVM of the GI Tract
 - Ex Vivo Microscopy (EVM): A New Tool for Pathologists **(NEW)**

Access them www.cap.org > Resources and Publications



Introduction to In Vivo Microscopy Interpretation Workshop 2017 – see handout

September 16, 2017, 8-4 pm in Chicago at The James Hotel

- **Complimentary workshop!** Seminar topics:
 - Explain IVM image terminology
 - Demonstrate ex vivo optional imaging for tissue evaluation and surgical pathology practice
 - Explain latest IVM technologies and image acquisition modalities with a focus on GI, skin, and lung
 - Demonstrate familiarity with IVM image interpretation criteria
 - Demonstrate ex vivo optional imaging for tissue evaluation and surgical pathology practice
 - Explain the role of pathologists in IVM programs
 - Explain IVM reimbursement opportunities



CAP

- Register today [surveymonkey.com/r/IVMWorkshop17](https://www.surveymonkey.com/r/IVMWorkshop17)

CAP17 The Pathologists' Meeting – IVM Highlights

- Learn about CAP's in vivo microscopy resources and talk with fellow members who are pioneering these technologies at the **CAP's IVM Committee Booth** in the Exhibit Hall
- Sign up for the complimentary breakfast workshop **“Justifying the Introduction of Emerging Technologies into a Pathology Department: How to Develop a Business Plan”**
- Register at www.cap.org/cap17

IVM Topic Center Page on CAP.ORG

- **Check the IVM Topic Center for continued updates and for all your IVM resources**

www.cap.org > Search for “IVM Topic Center”

THANK YOU!

- Thank you for attending our webinar “**Confocal Microscopy for Pigmented Lesions**” by Babar K. Rao, MD, FAAD
 - For comments about this webinar or suggestions for upcoming webinars, contact ivminfo@cap.org
 - NOTE: There is no CME/CE credit available for today’s complimentary webinar. The pdf of the presentation will be sent out in a week.



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