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Role of Reflectance Confocal Microscopy in Skin Inflammations

Babar K. Rao, MD, FAAD

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Babar K. Rao, MD, FCAP

- 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
- Member of the CAP's In Vivo



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Disclosure

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

Atlas of Confocal Microscopy in Dermatology

Clinical, Confocal, and Histological Images



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Malignant

Webinar series-3

Chapter 5: Non- Melanocytic Lesion-
Benign

Chapter 6: Non- Melanocytic Lesion-
Malignant

Webinar series-4

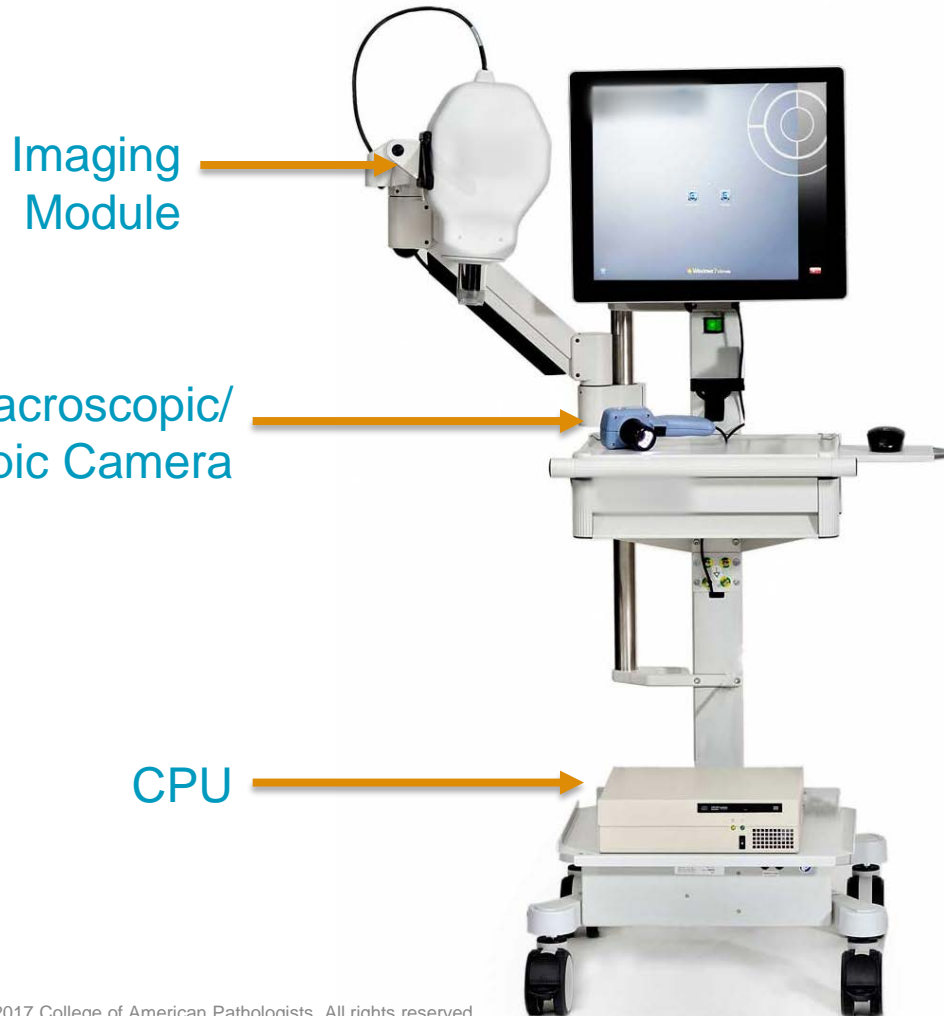
Chapter 7: Inflammation

Reflectance Confocal Microscopy



Non invasive, harmless and quick way of diagnosing skin lesions using a laser (830nm) based scope.

Clinical Confocal Microscope

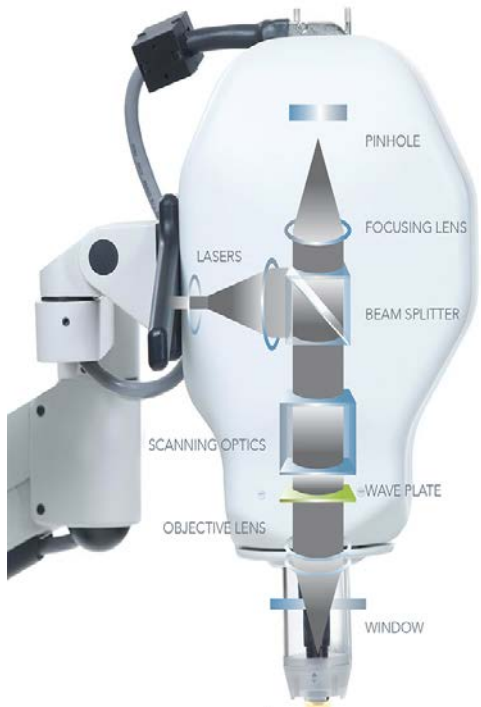


Commercially available RCM Systems:

- FDA 510(k) Cleared
- Class I Laser Device
- No goggles required
- Class II medical device
- No adverse events reported in over 500 clinical studies

CM is a real-time, non-invasive and painless approach to tissue diagnosis

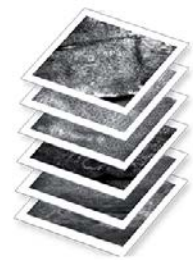
830nm
(laser)



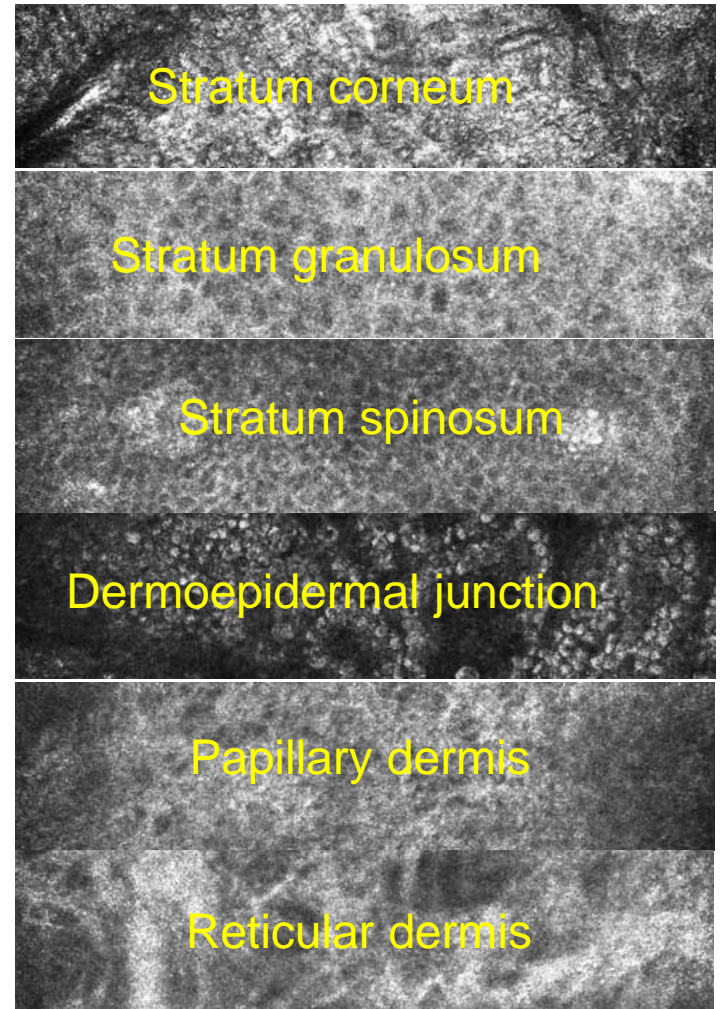
Cross section
of skin



=



Confocal
image stack

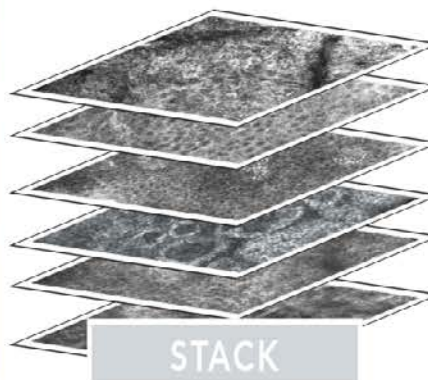
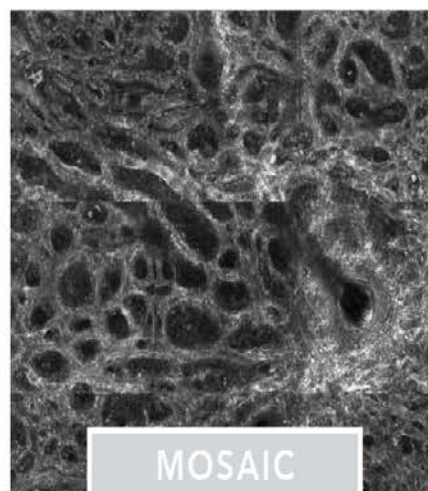


1 EXAM

2 DERMOSCOPY

3 CONFOCAL IMAGING

4 EVALUATE



Inflammatory Skin Lesions

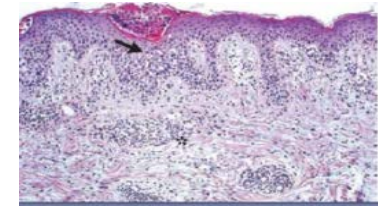
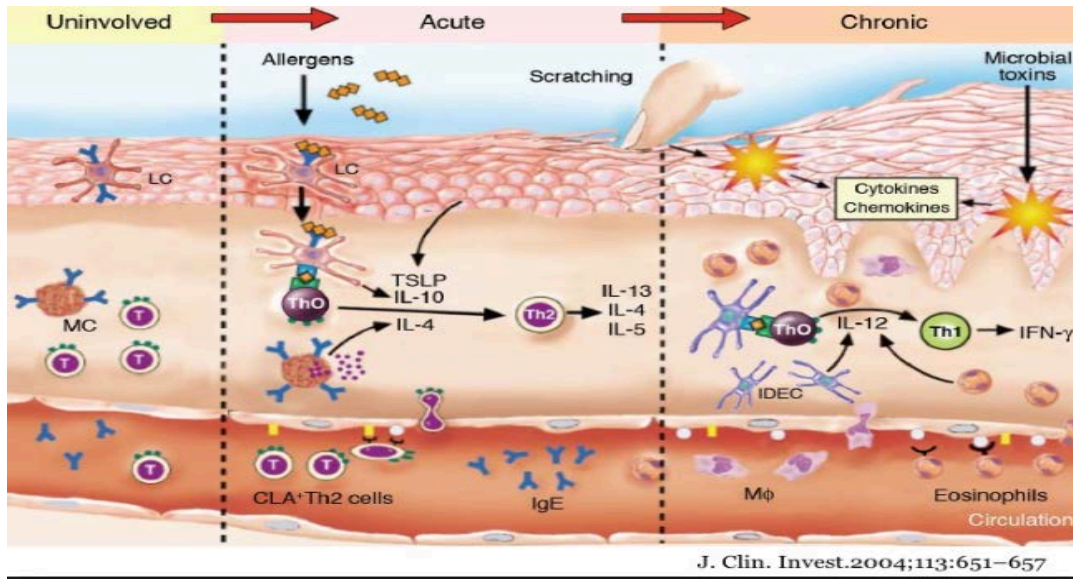
- **Common skin inflammatory conditions include:**
- **Psoriasis**
- **Eczema**
- **Lichen planus**
- **Herpes**

Diagnosis is based on history, clinical exam, and biopsy.

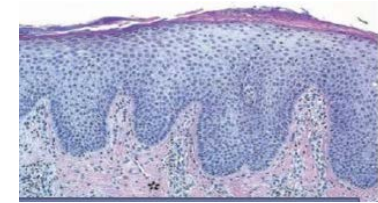
Challenge: Skin inflammation pathophysiology varies based on lesion age.

Age of Inflammatory Lesions:

- Day 1- Early
- Day 5-7- Intermediate
- Day greater than 7- Late



“Histological changes of early Inflammation”



“Histological changes of late Inflammation”

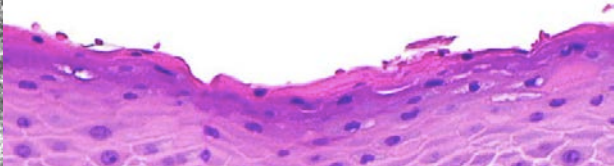
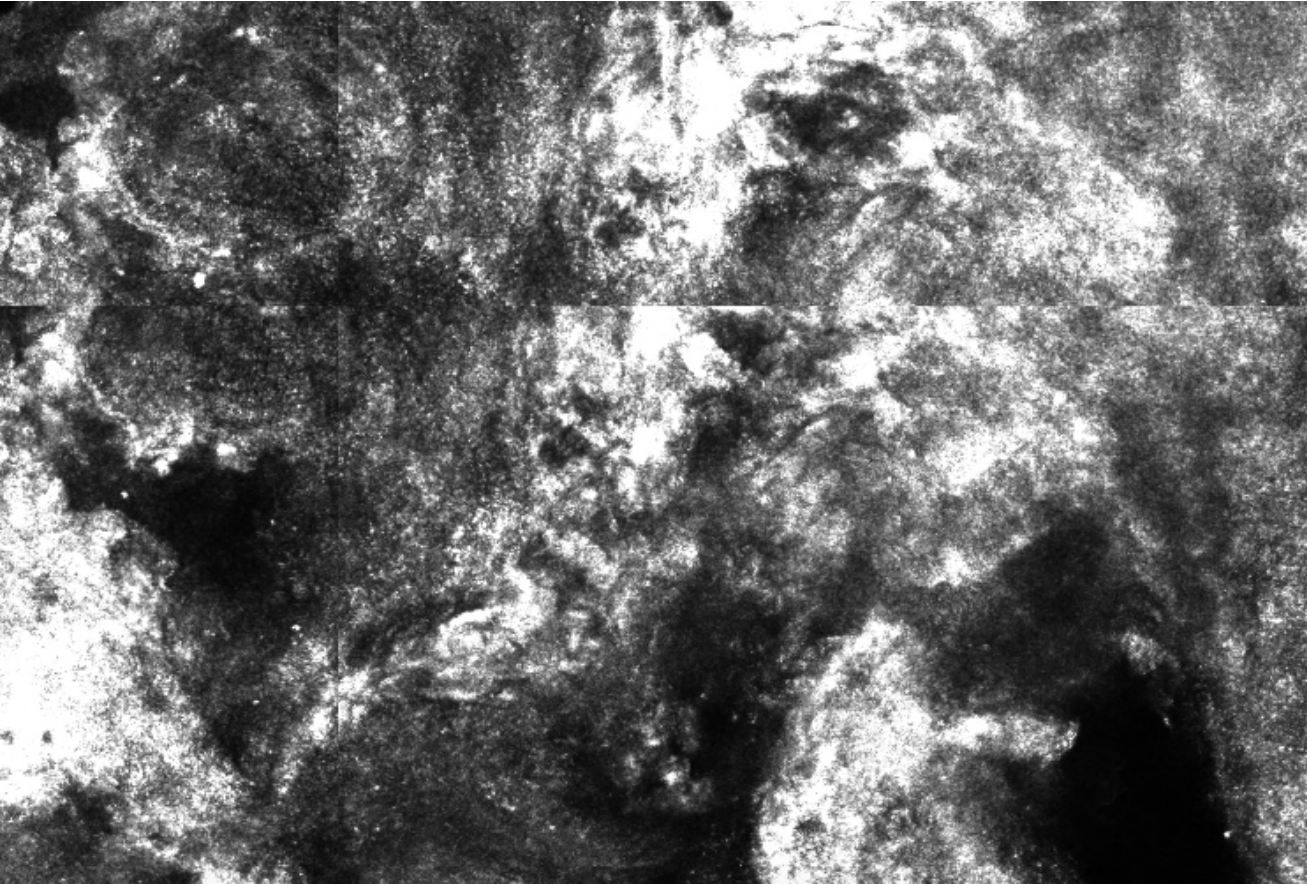
Objective

- **Describe the characteristic confocal features of common skin inflammation**
- **Clinico- Histo-confocal correlation**
- **Discuss the role of RCM in monitoring skin inflammation**

“Understanding Confocal Terms used to Diagnose Inflammatory Skin Lesions”



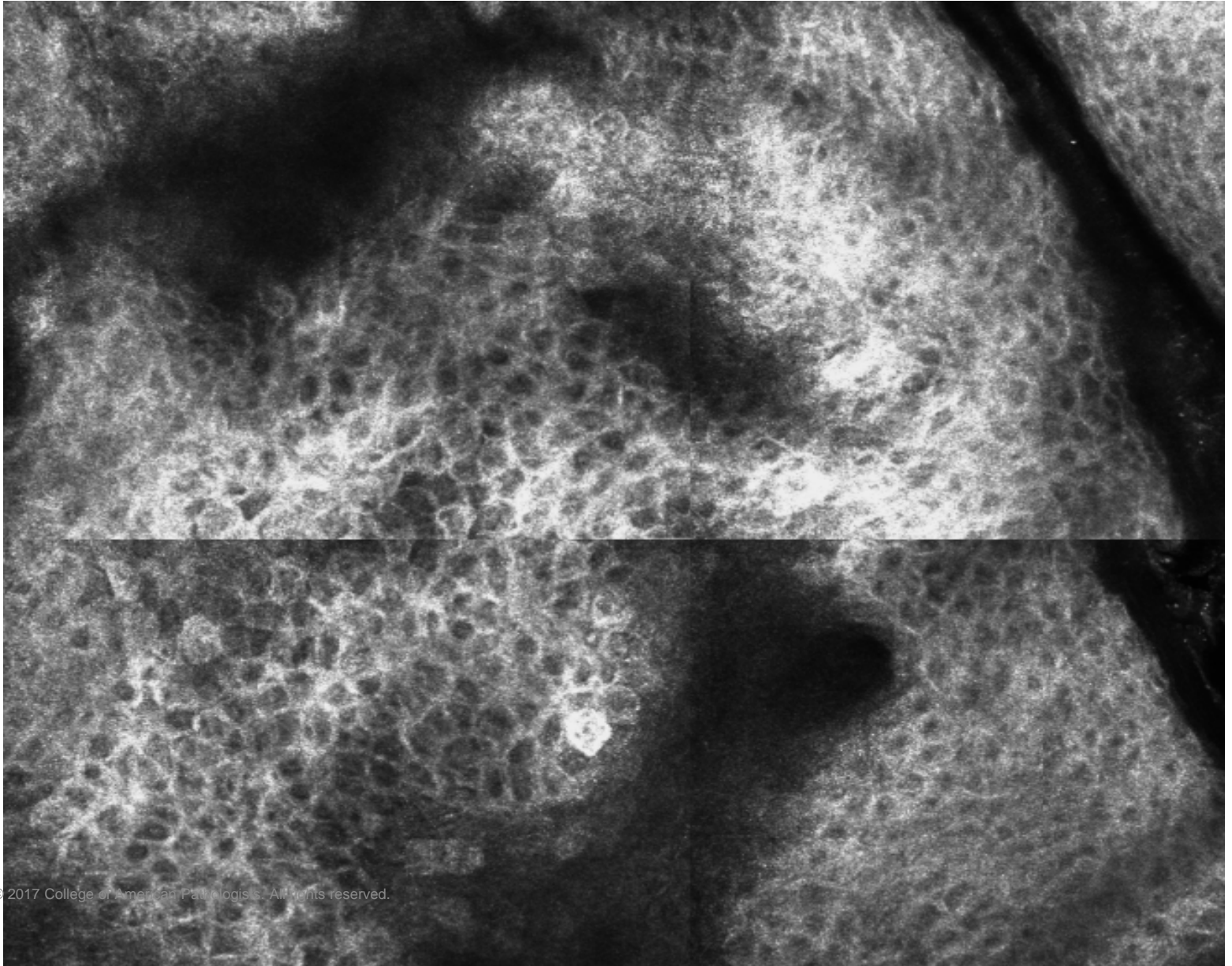
Parakeratosis



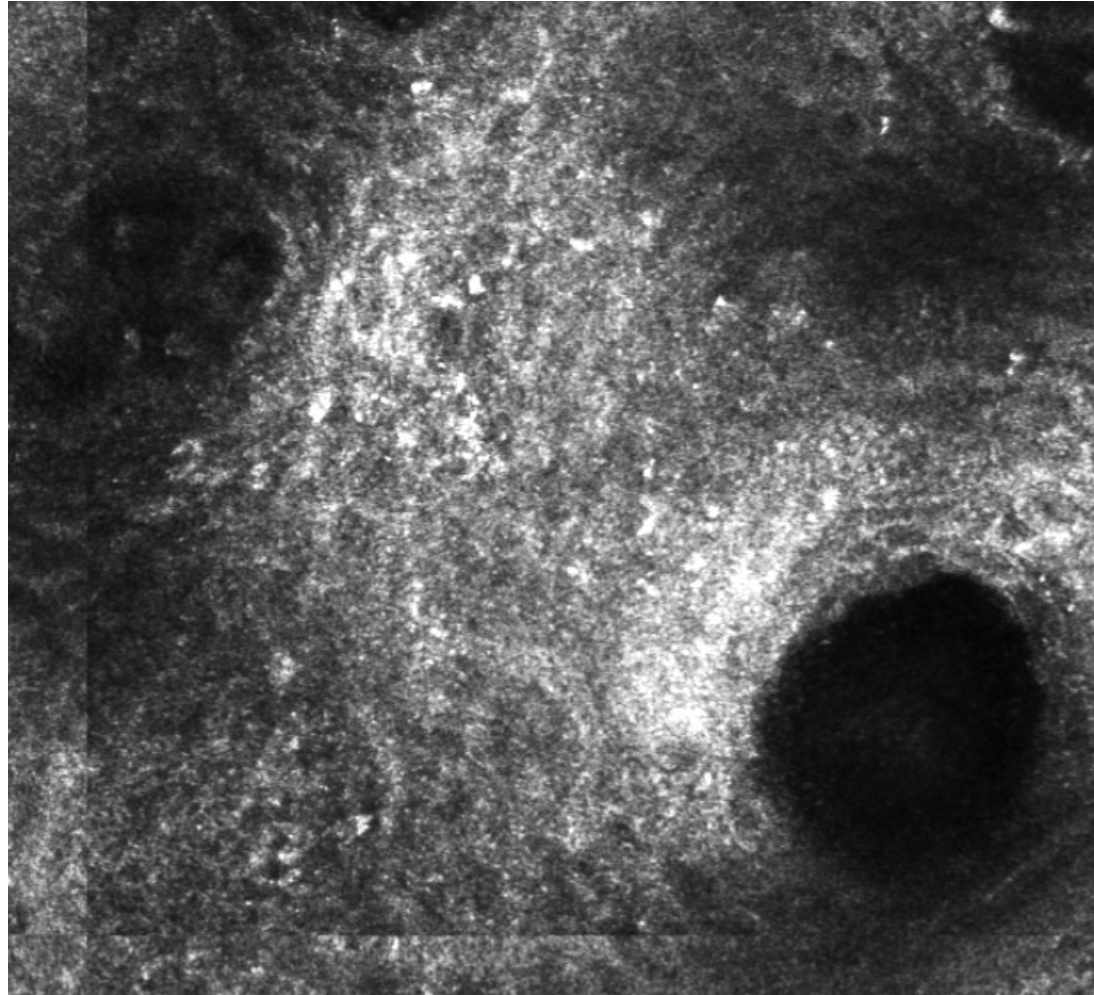
10 micrometer



Spongiosis

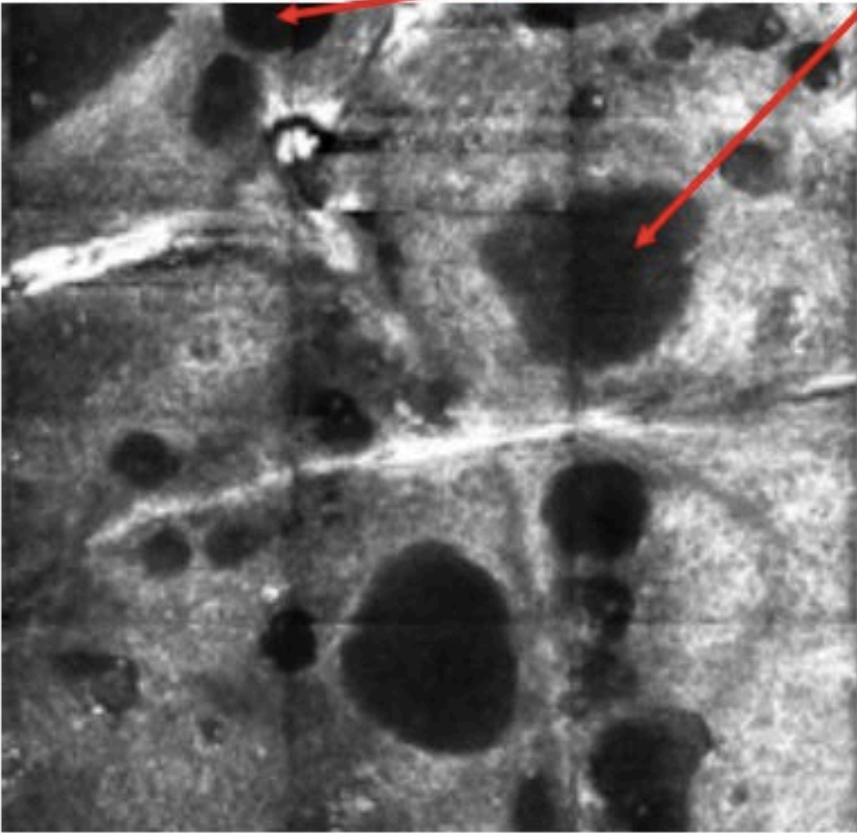


Inflammatory infiltrates

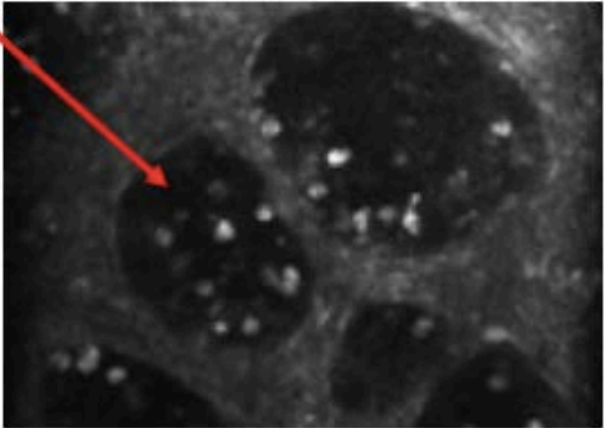


Vesicle Formation

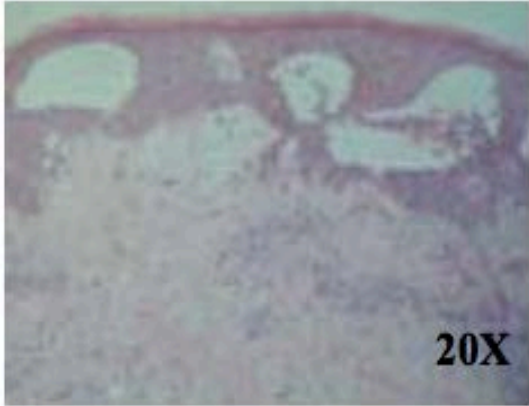
vesicles



250µm

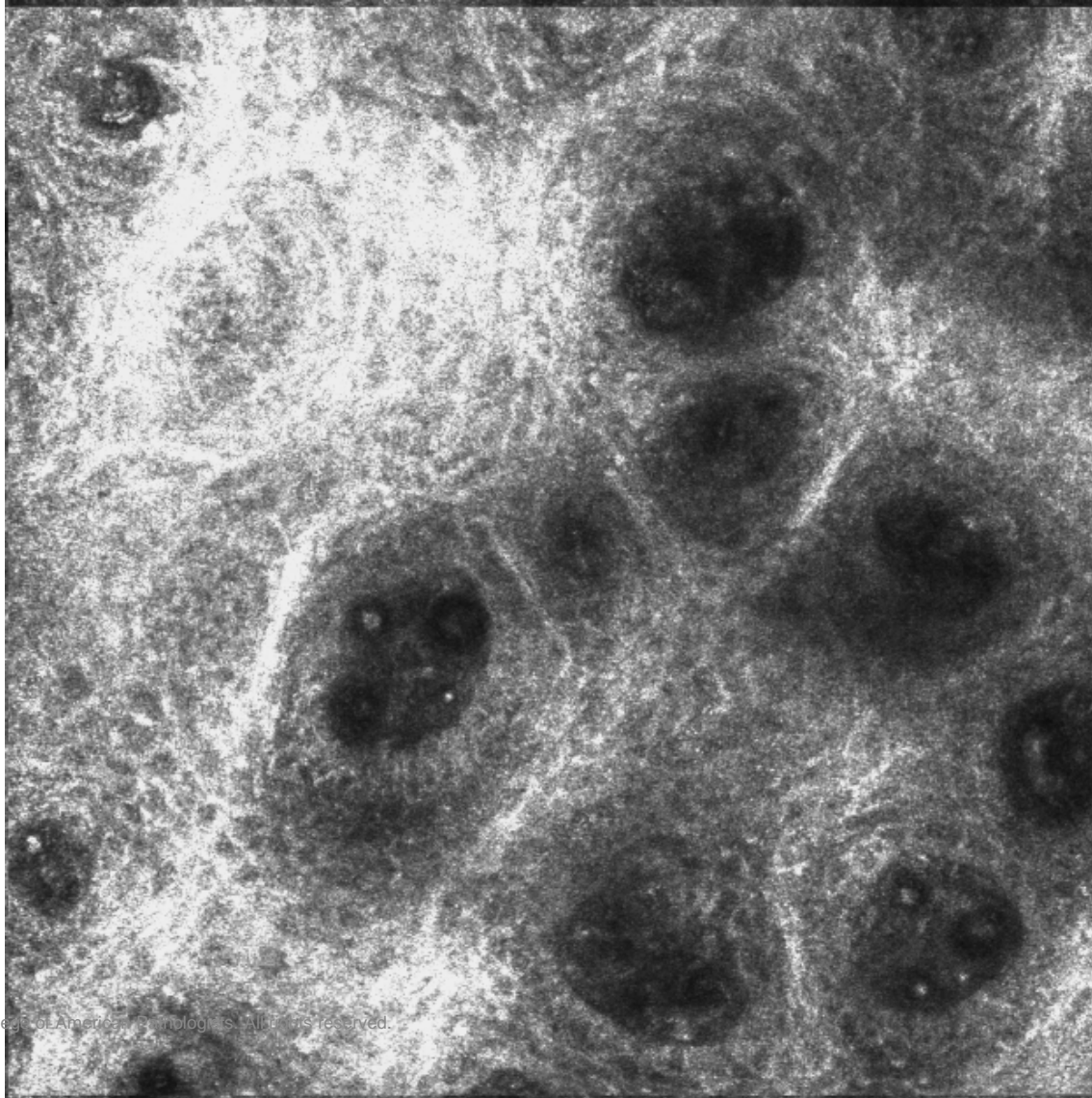


250µm

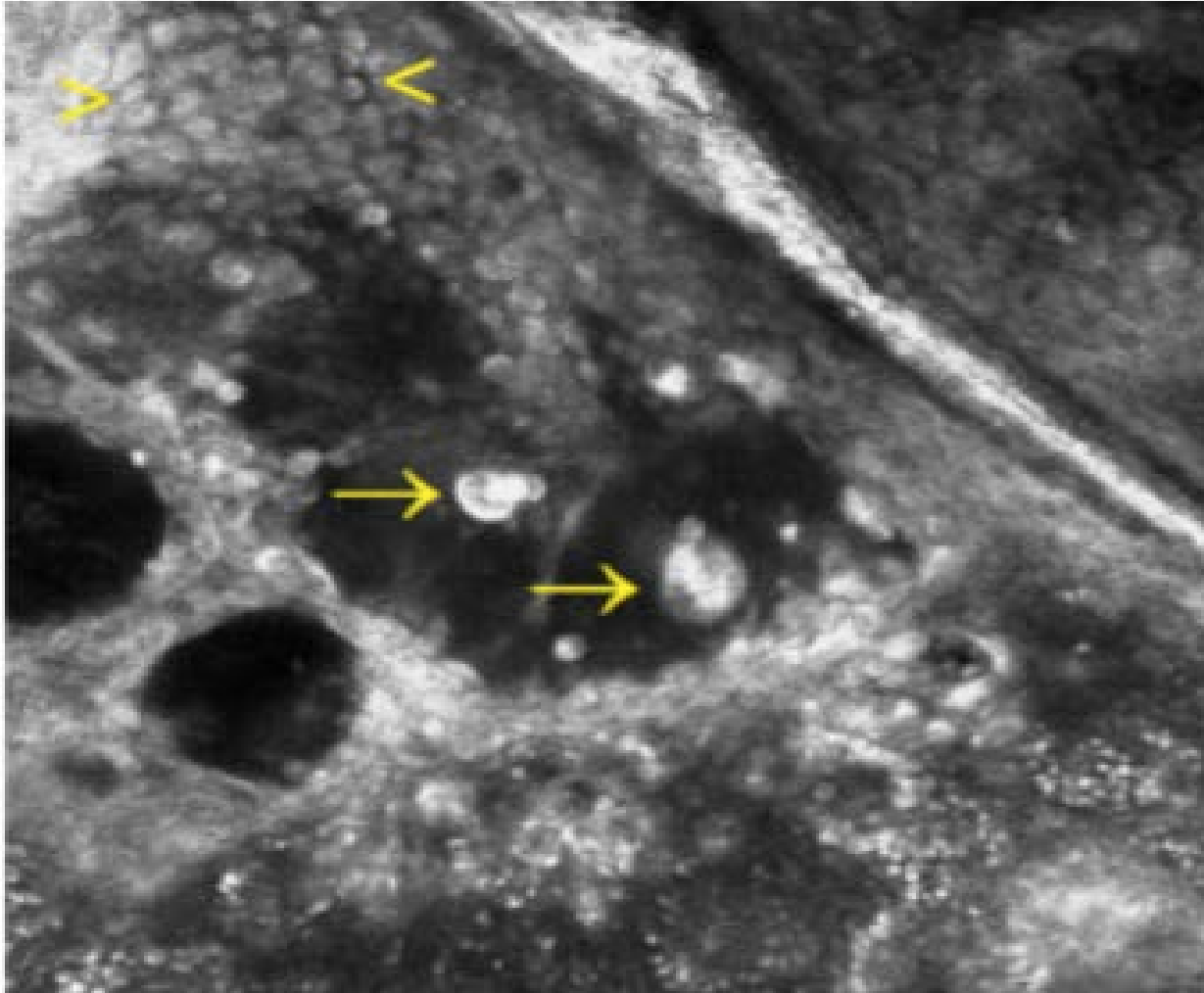


20X

Capillary dilatation



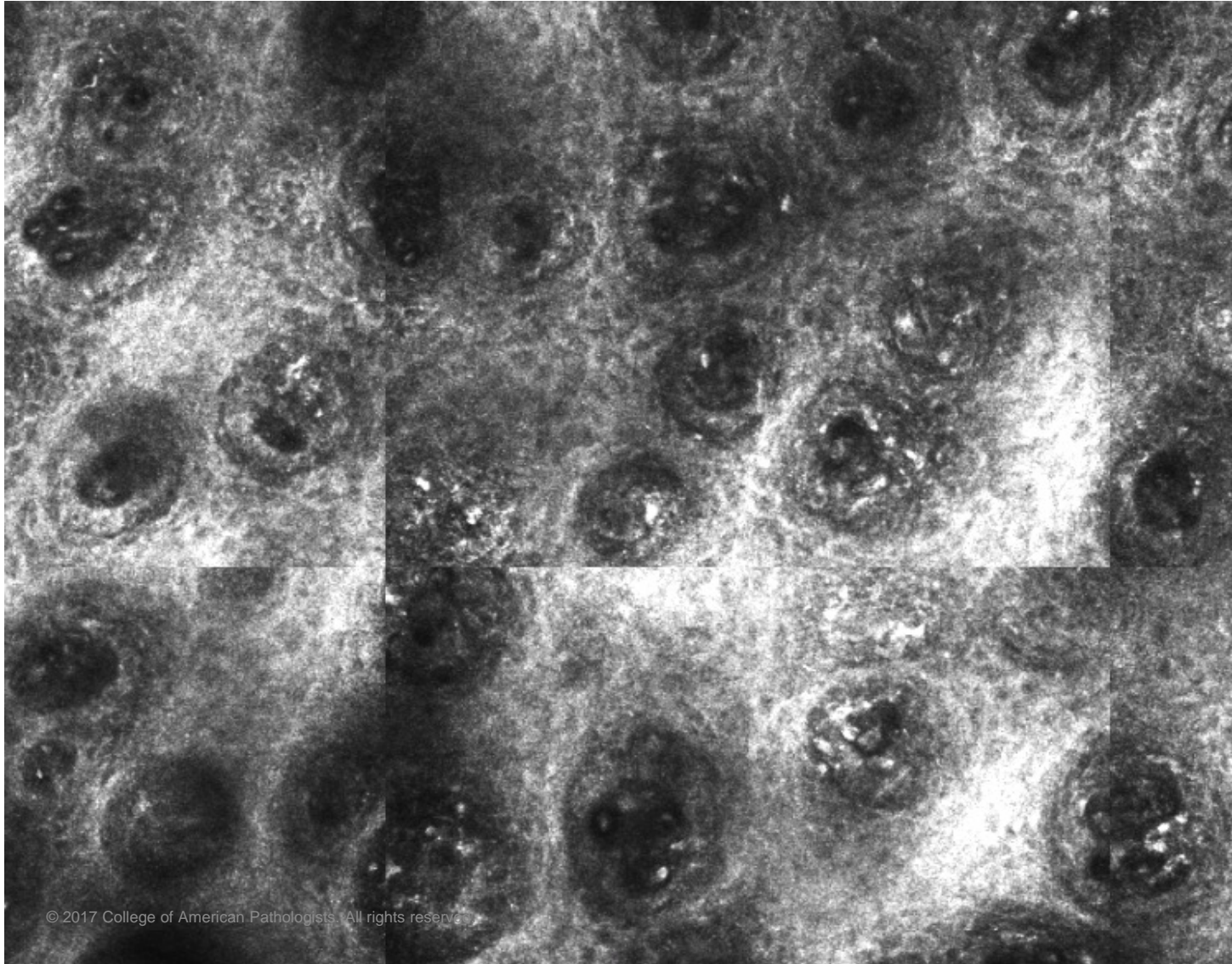
Multinucleated giant cells



Herpes zoster. RCM examination of an erythematous area shows multiple intraepidermal vesicles containing bright acantholytic keratinocytes (arrowheads), giant cells, expression of ballooning degeneration (arrows), and inflammatory cells, appearing as small bright particles.

Reference: Early diagnosis of Herpes zoster by hand held reflectance confocal microscopy. *JAAD*. 2015; 73(6):e201–e203

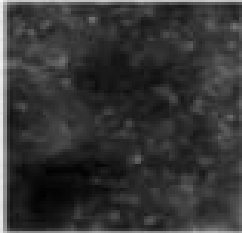
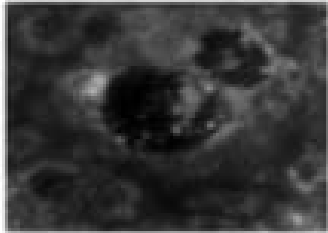

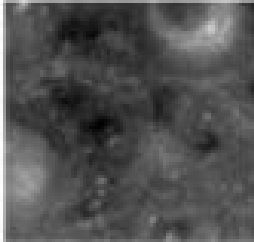
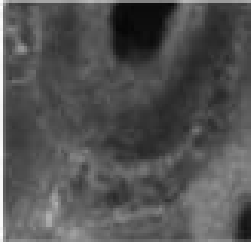
Exocytosis



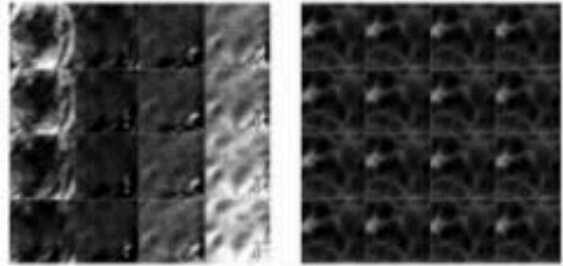
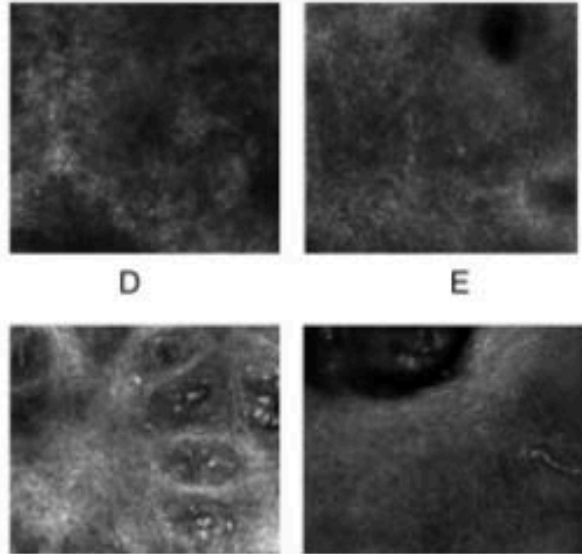
Classification of Skin Inflammation

- **Spongiosis**
- **Interface changes**
- **Psoriasiform changes**
- **Lichenoid infiltrate**
- **Blisters**

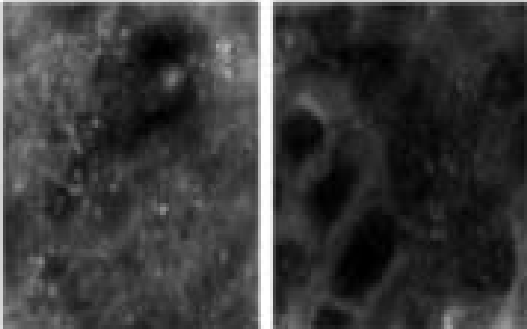
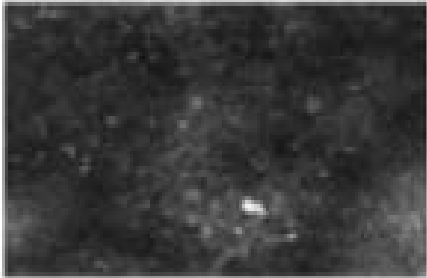
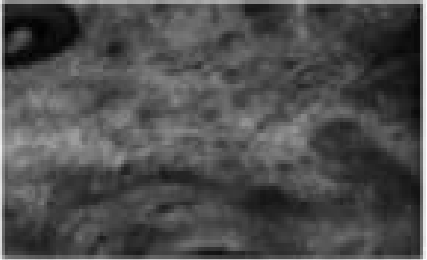
Spongiotic-RCM Diagnostic Criteria

		Spongiotic dermatitis		
Major criteria	<p>Moderte to severe spongiosis & vescicle</p> <p><i>-Dark, round areas fulfilled by bright inflammatory cells at the level of the epidermis</i></p>			
Minor criteria	<p>a) Exocytosis</p> <p><i>Single or aggregates of round to polygonal, refractive cells at the level of the stratum spinosum</i></p> <p>b) Dermal inflammation</p> <p>c) Dilated vessels</p>			
		A	B	C

Psoriasiform-RCM Diagnostic Criteria

	Psoriasiform dermatitis	RCM examples
Major criteria	<p>Stratum corneum and epidermal thickening <i>-Calculated using the viva stack software analysis, counting stack images needed to move from the top of the stratum corneum to the first cellulated epidermal layer</i></p> <p>Acanthosis <i>-Calculated by the number of single frames needed to move from the first cellulated layer of the epidermis to the DEJ</i></p>	 <p>Vertical stack 5 microns step</p>
Minor criteria	<p>d) Parakeratosis <i>-Presence of multiple refractive round to polygonal nucleated structures visible at the top of the stratum corneum</i></p> <p>e) Spongiosis <i>-Presence of multiple bright polygonal cells in the context fo darker epidermal areas</i> <i>-Slight to moderate spongiosis in PP</i> <i>-More prominent spongiosis in SD</i></p> <p>f) Papillomatosis <i>-Up located and enlarged DP separated by thin interpapillary spaces</i> <i>-Diffuse papillomatosis in pp</i> <i>-Irregularly distributed papillomatosis in SD</i></p> <p>f-g) Dilated vessels <i>-Vertically oriented filling DP in PP</i> <i>-Horizontally oriented in SD</i></p>	 <p>D E</p> <p>F G</p>

Interface Dermatitis-RCM Diagnostic Features

	Interface dermatitis	
<p>Major criteria</p>	<p>Interface changes</p> <ul style="list-style-type: none"> -Presence of multiple refractile cells located at the level of the DEJ obscuring DP rimming. -Focal in DLE -Diffused in LP 	
<p>Minor criteria</p>	<ul style="list-style-type: none"> h) Inflammatory cells in the epidermis <ul style="list-style-type: none"> -Single or aggregates of round to polygonal, mildly refractive cells i) Dilated vessels i) Dermal inflammation i) Dermal sclerosis 	<p>H</p>  <p>I</p> 

Lives of lesions study

Role of reflectance confocal microscopy to monitor skin inflammation at various stages (early, intermediate, late).



Methods

Patients with common skin Inflammation (eczema, psoriasis, lichen planus, herpes)



History and physical exam



Reflectance Confocal Microscopy Day 1, 5, 7 or greater than 7



Evaluation of features of Confocal Microscopy



Results compiled to compare features of various skin inflammation at different days of presentation

RCM Features of **Early** Skin Inflammation

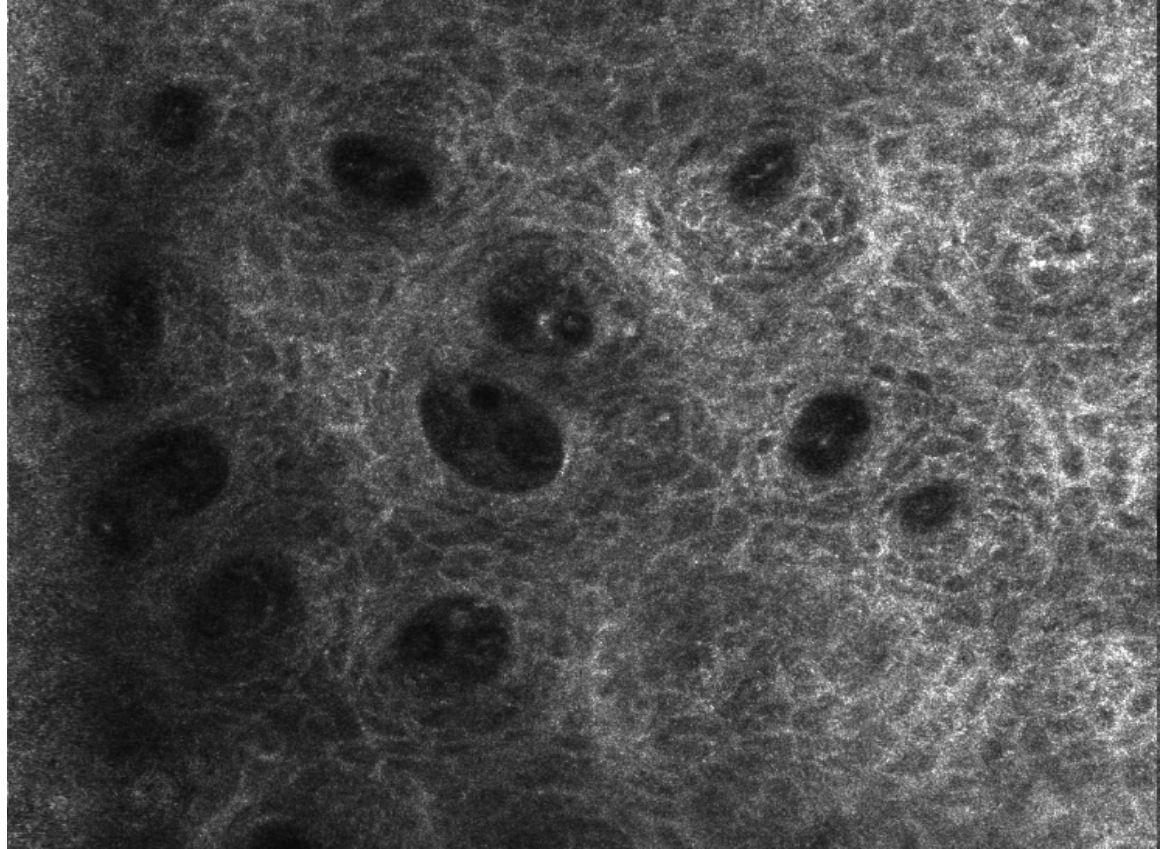
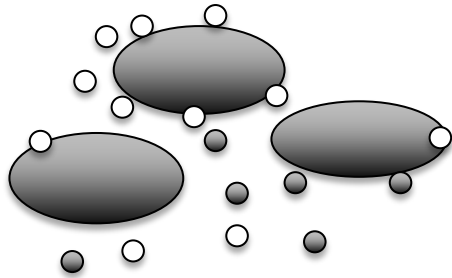


RCM features of Lichen Planus

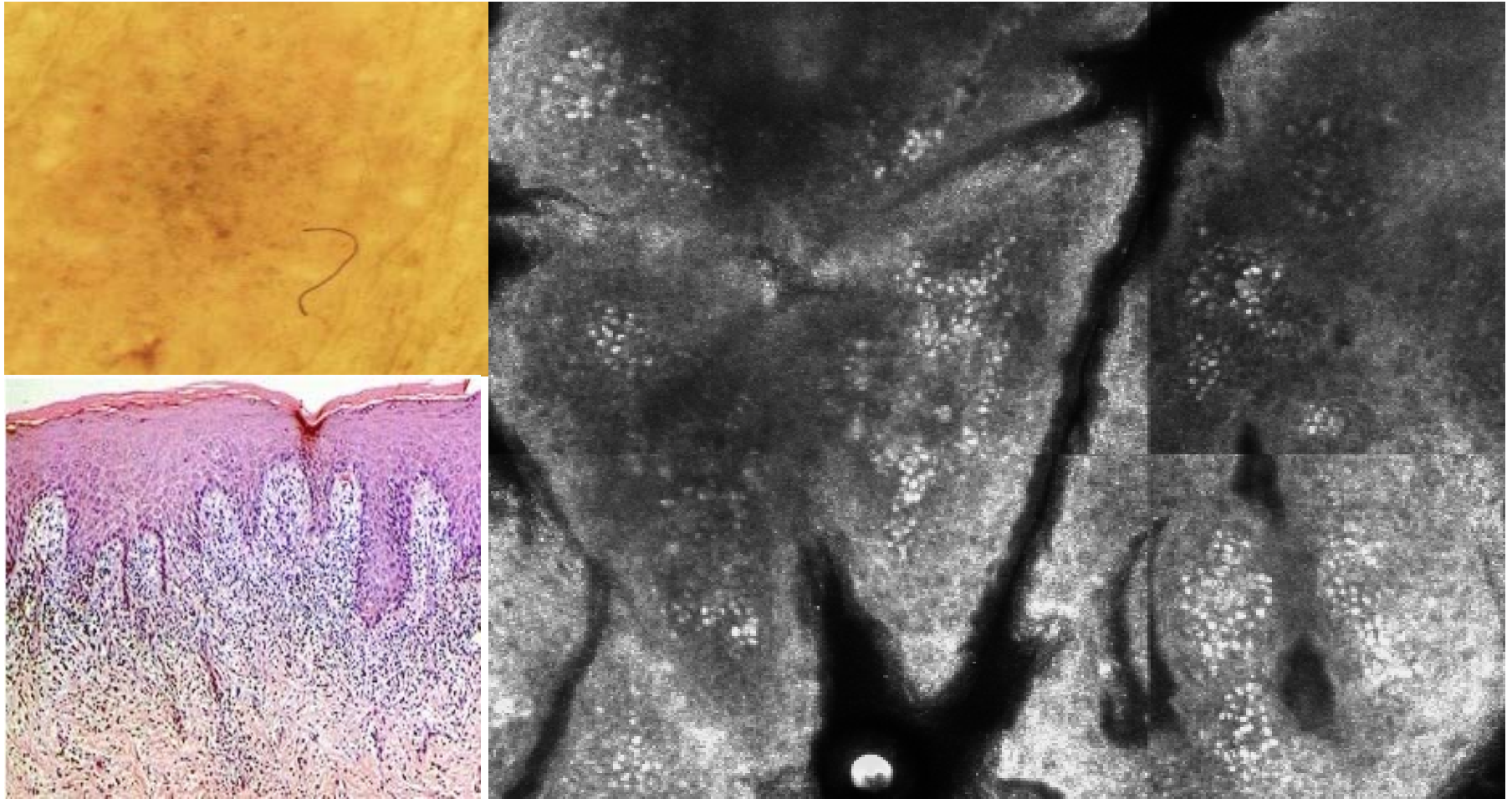
- **Epidermal Disarray**
- **Interface dermatitis**
- **Perivascular inflammatory infiltrates**
- **Dermal Inflammatory infiltrates**

Perifollicular inflammatory infiltrates- Lupus

Interface dermatitis

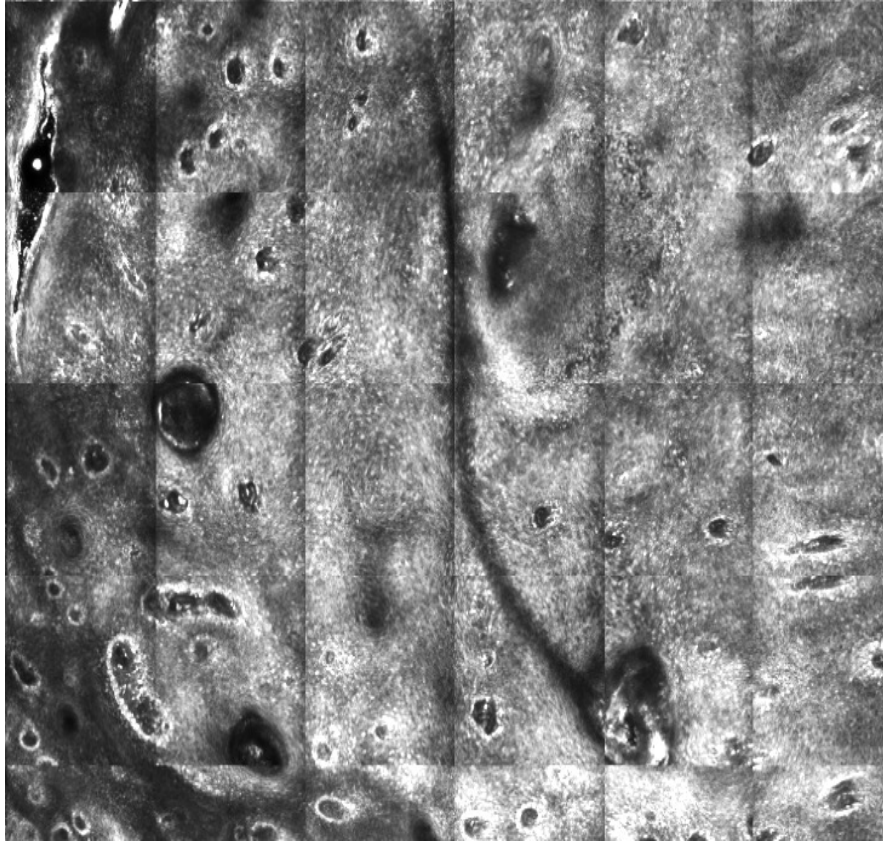


Lichen Planus

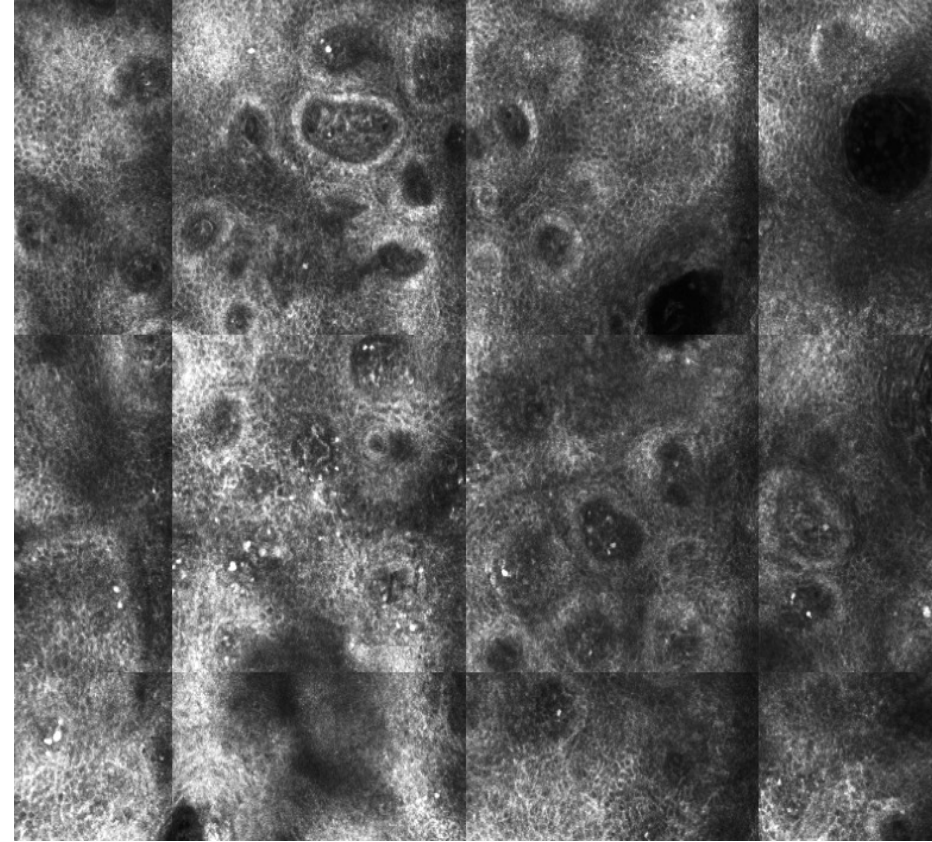


 **Lichen Planus** (a)dermoscopy (b)histology (c) RCM Features –
Interface dermatitis

Interface Dermatitis- Higher Power

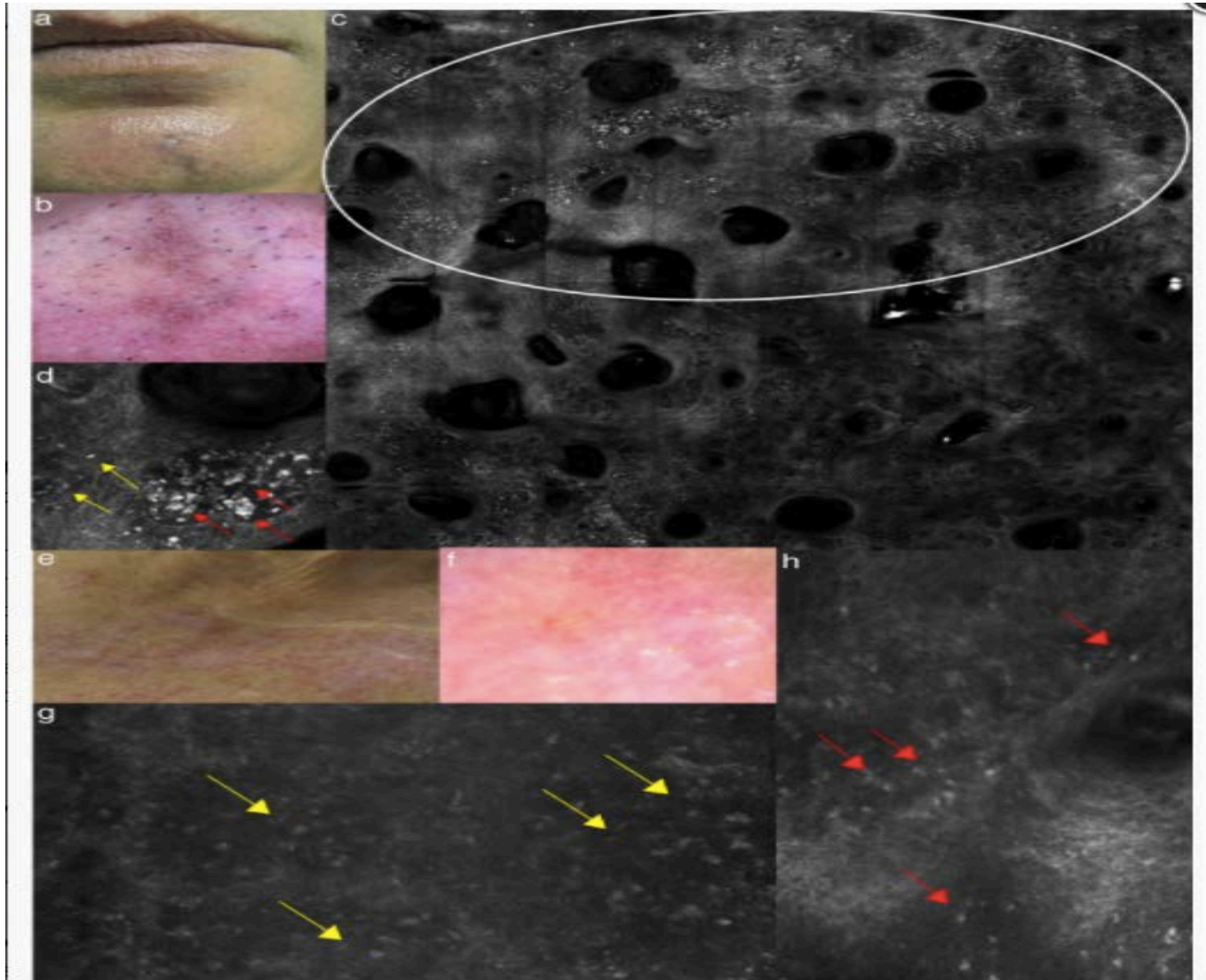


Lupus



Lichen planus

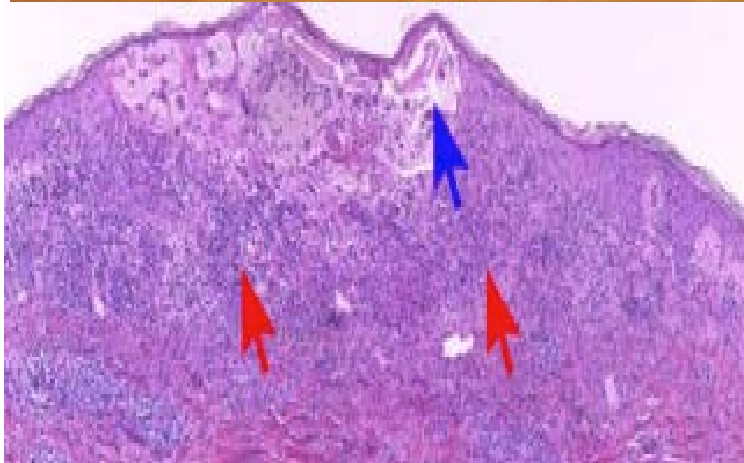
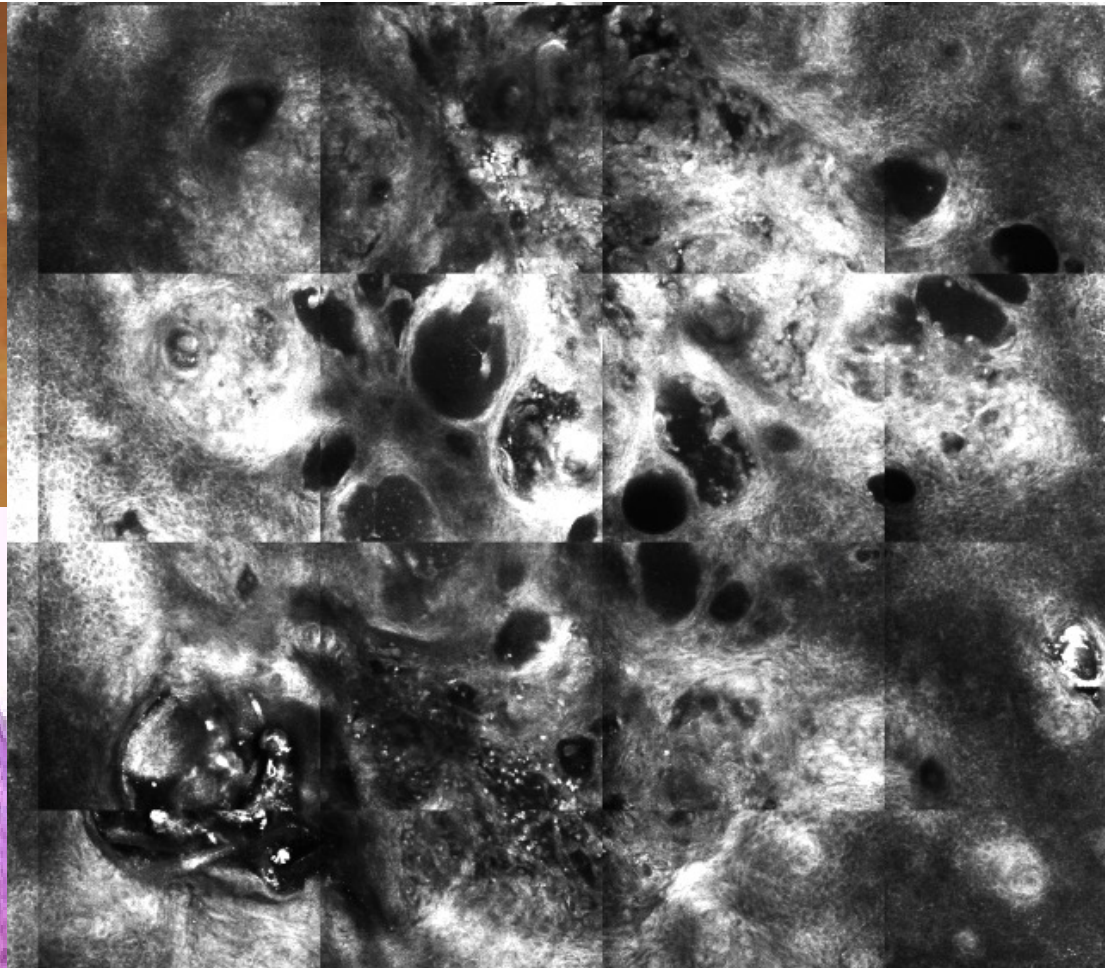
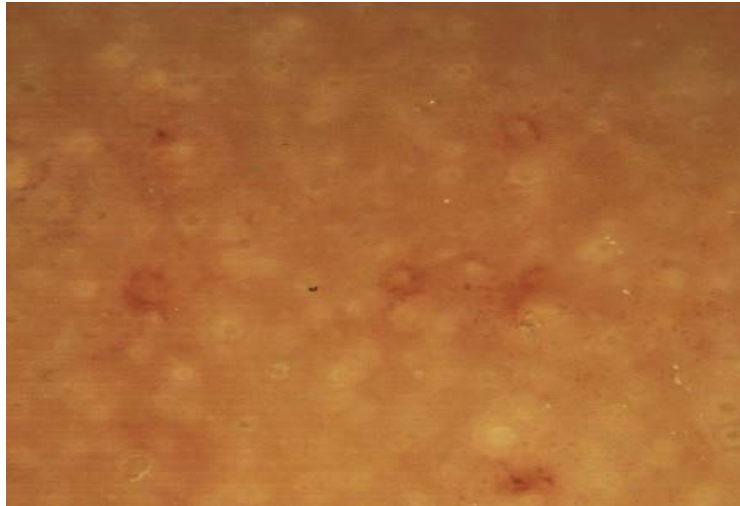
RCM – Lichen Planus



RCM Features of Herpes

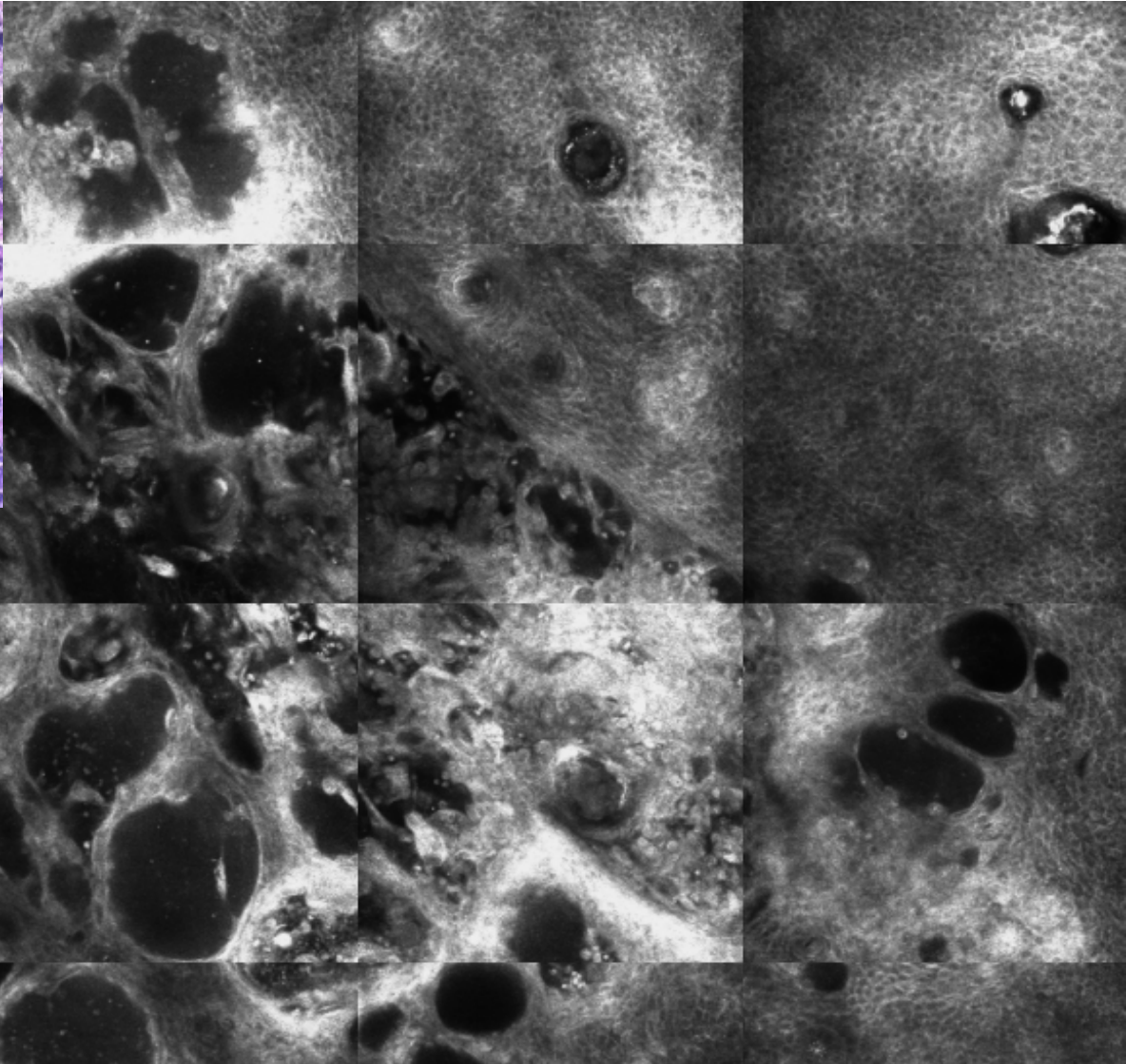
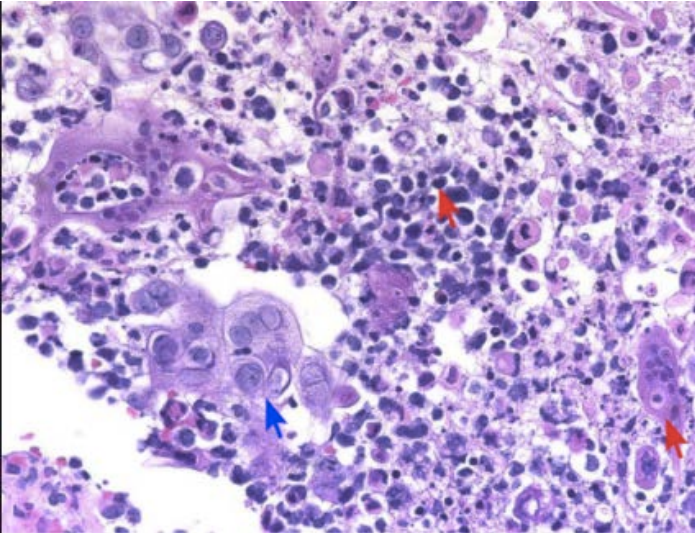
- **Epidermal Disarray**
- **Epidermal inflammations**
- **Necrotic keratinocytes**
- **Multinucleated giant cells**

Herpes Zoster

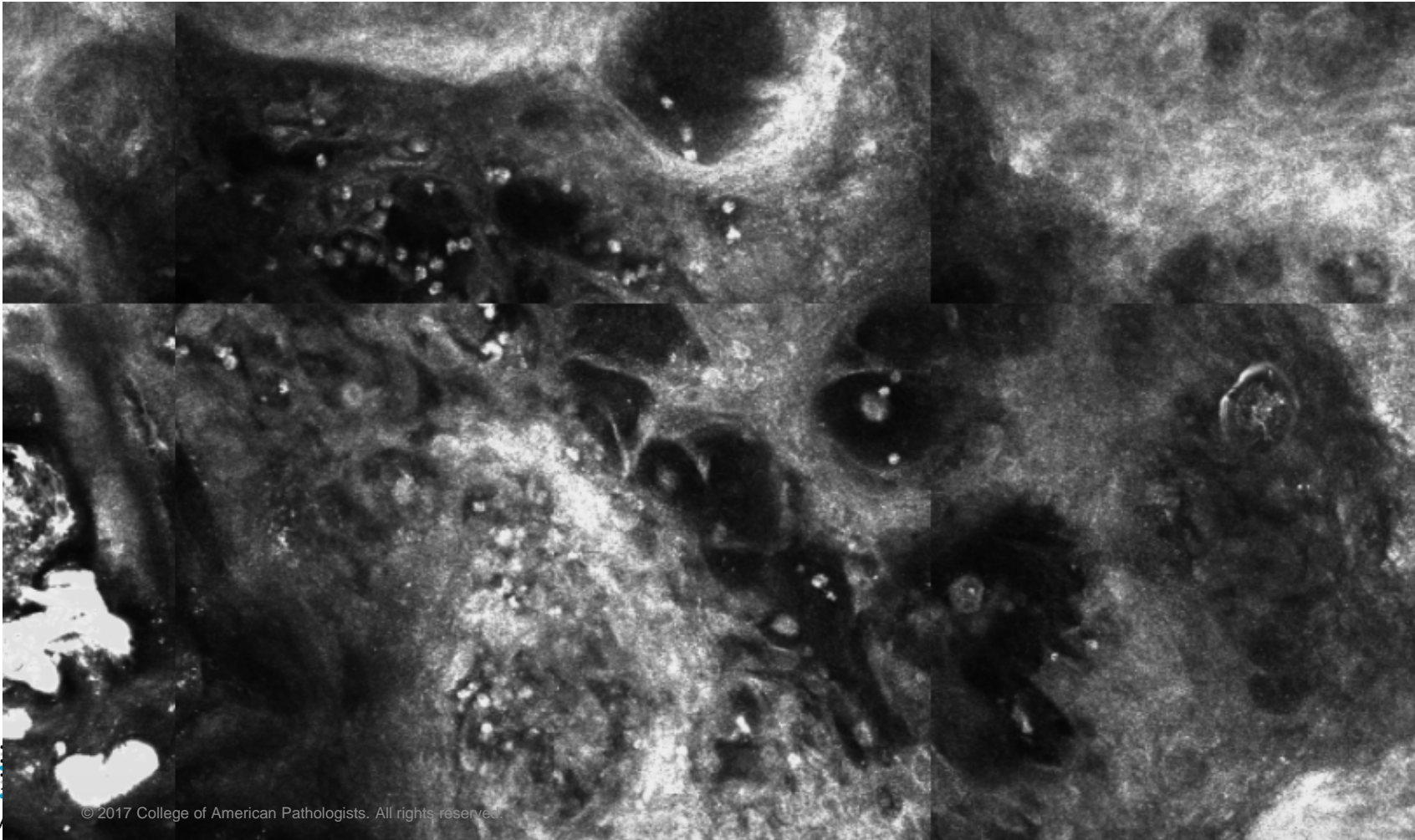


Herpes Zoster. (a) dermoscopy (b) histology (c) RCM Features- multinucleated cells, intraepidermal vesicles. Inf. infiltrates and necrotic keratinocytes

Herpes



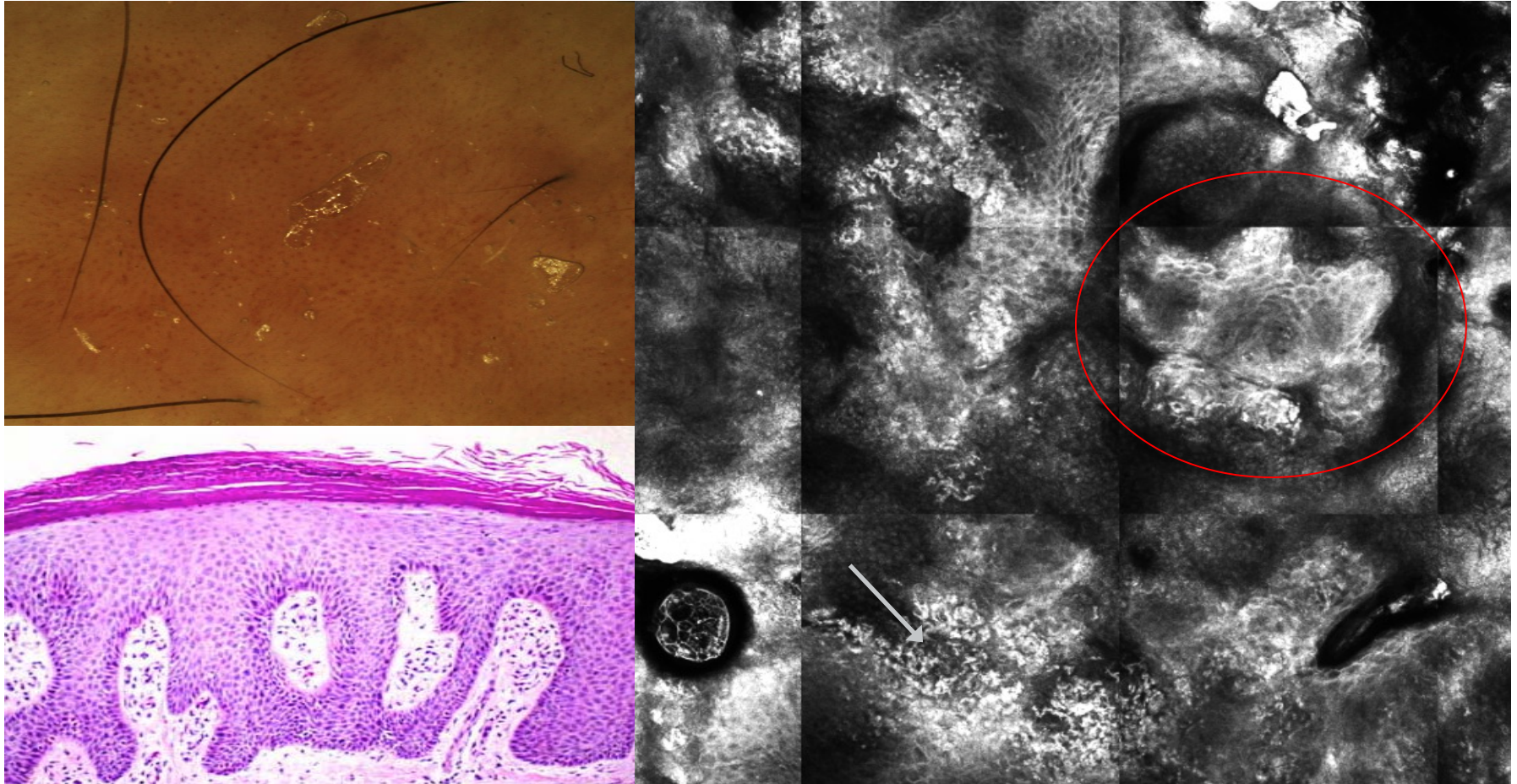
Herpes- High power



RCM Features of Psoriasis

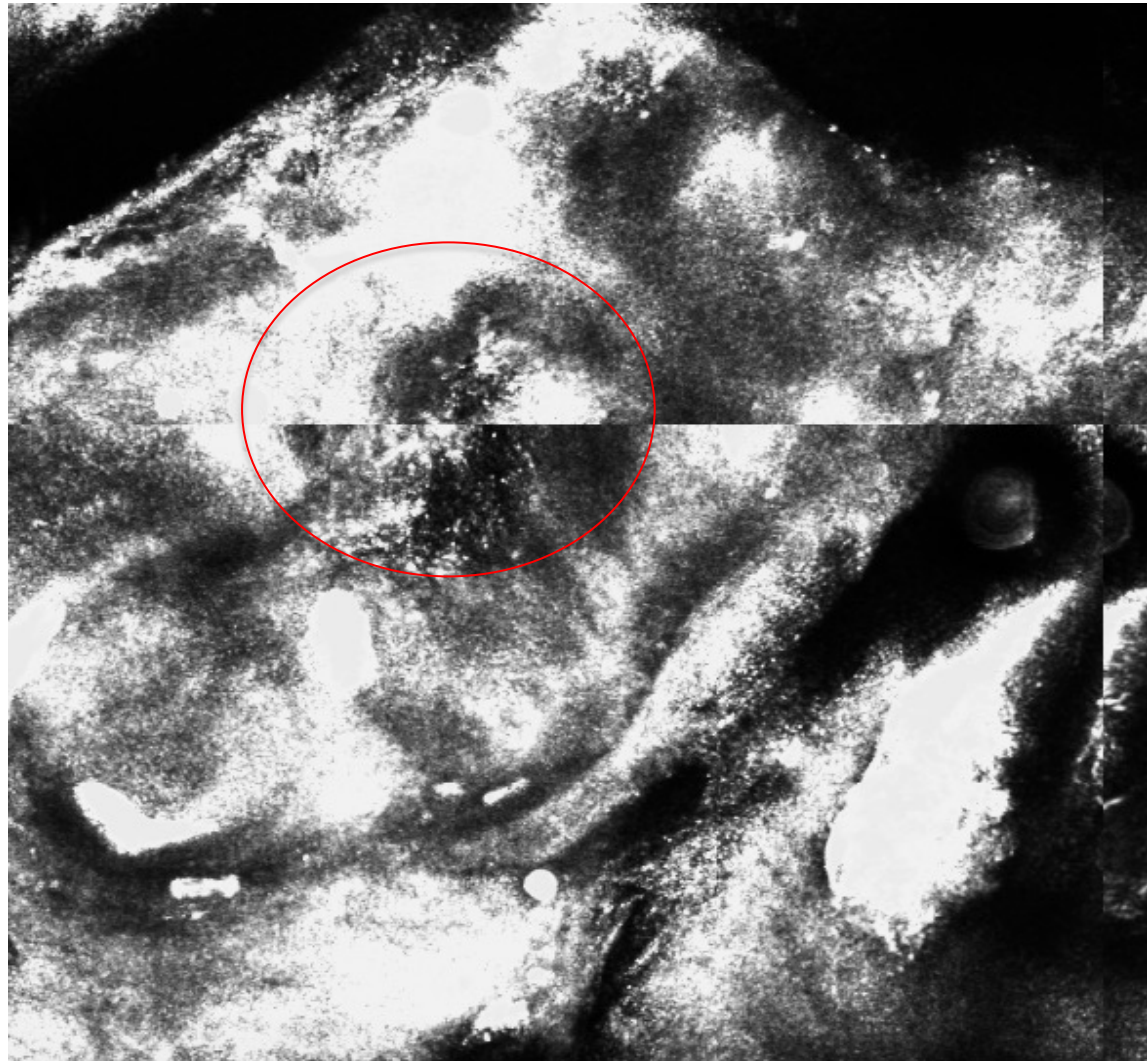
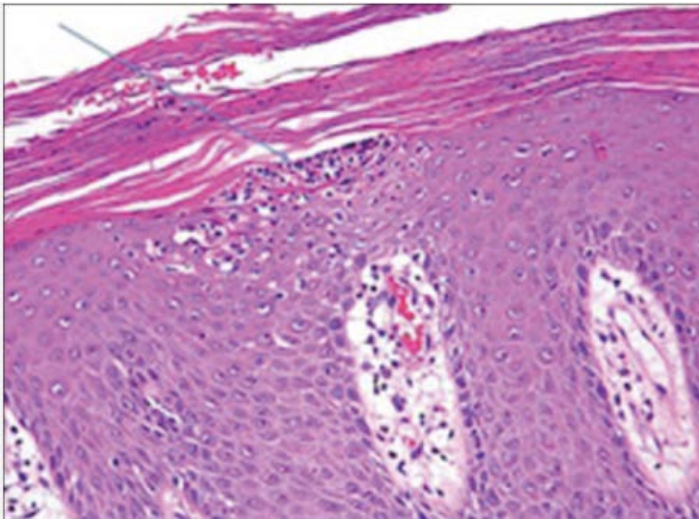
- **Spongiosis**
- **Epidermal inflammatory infiltrates**
- **Dermal inflammatory infiltrates**
- **Dilated vessels**
- **Hyperkeratosis**
- **Papillomatosis**
- **Munro abscesses**

Psoriasis



Psoriasis. (a)dermoscopy (b) histology (c) RCM Features – Papillomatosis, epidermal infiltrates (blue arrow)

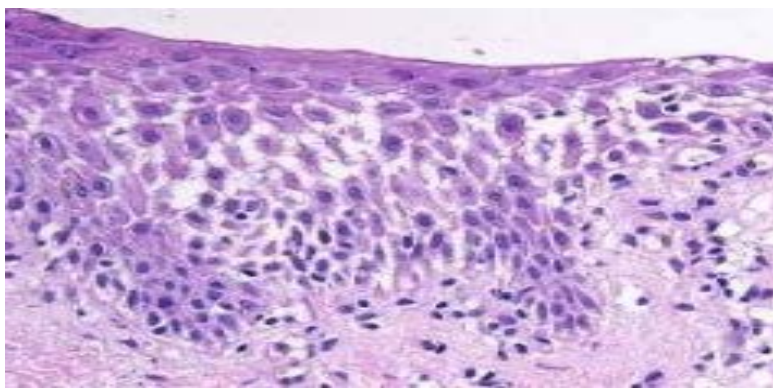
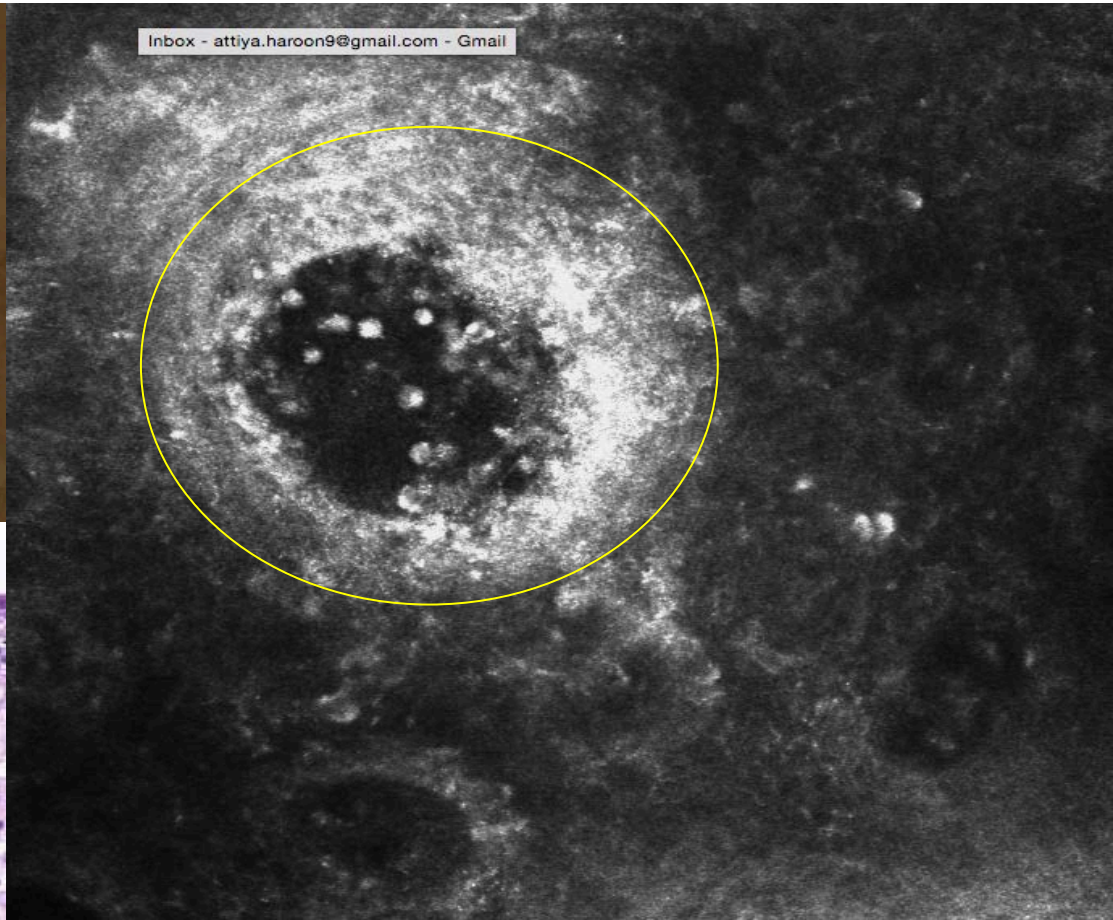
Neutrophil Microabscess-Stratum corneum



RCM Features of Eczema

- **Hyperkeratosis**
- **Spongiosis**
- **Epidermal disarray**
- **Epidermal inflammatory infiltrates**

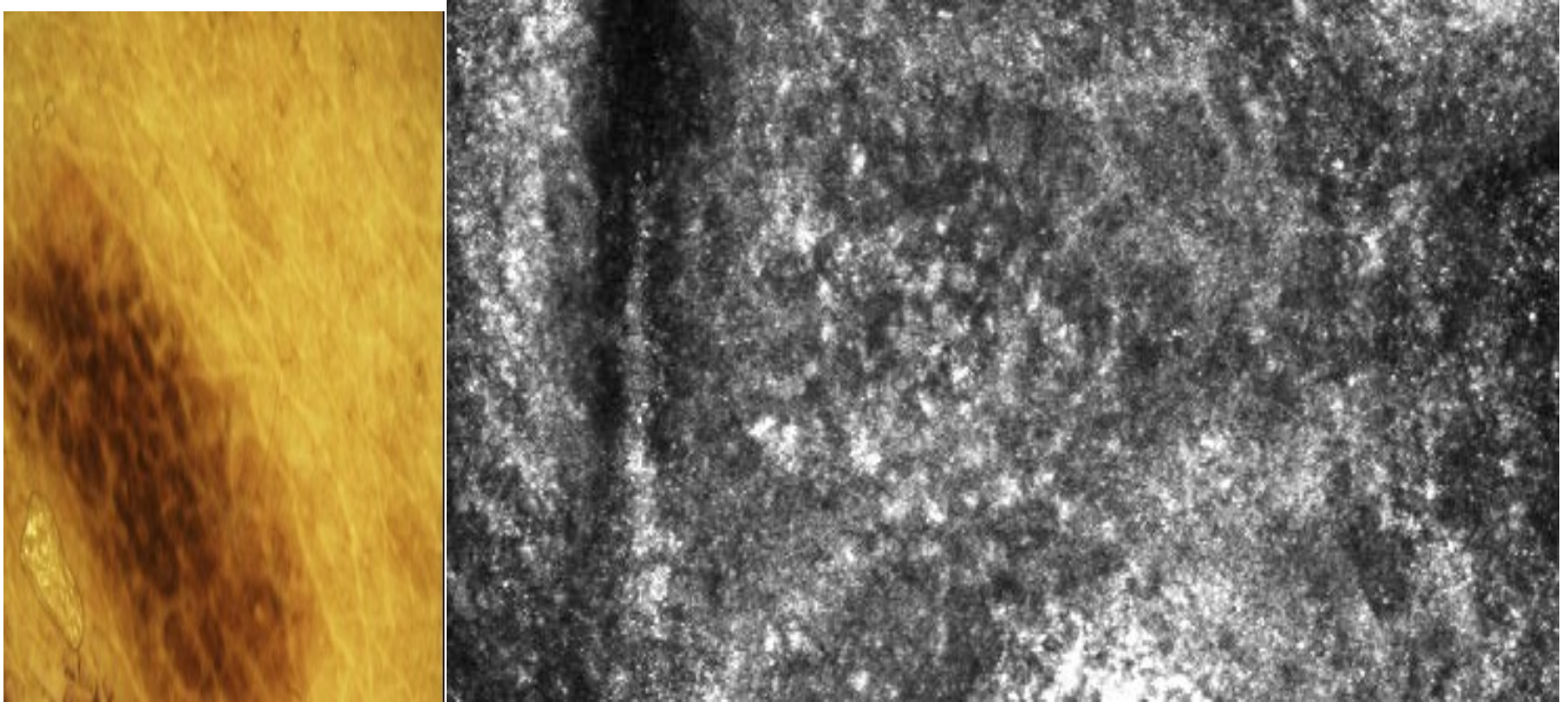
Eczema



Eczema. (a) dermoscopy (b) histology (c) RCM Features – vasodilation, inflammatory infiltrates and spongiosis.

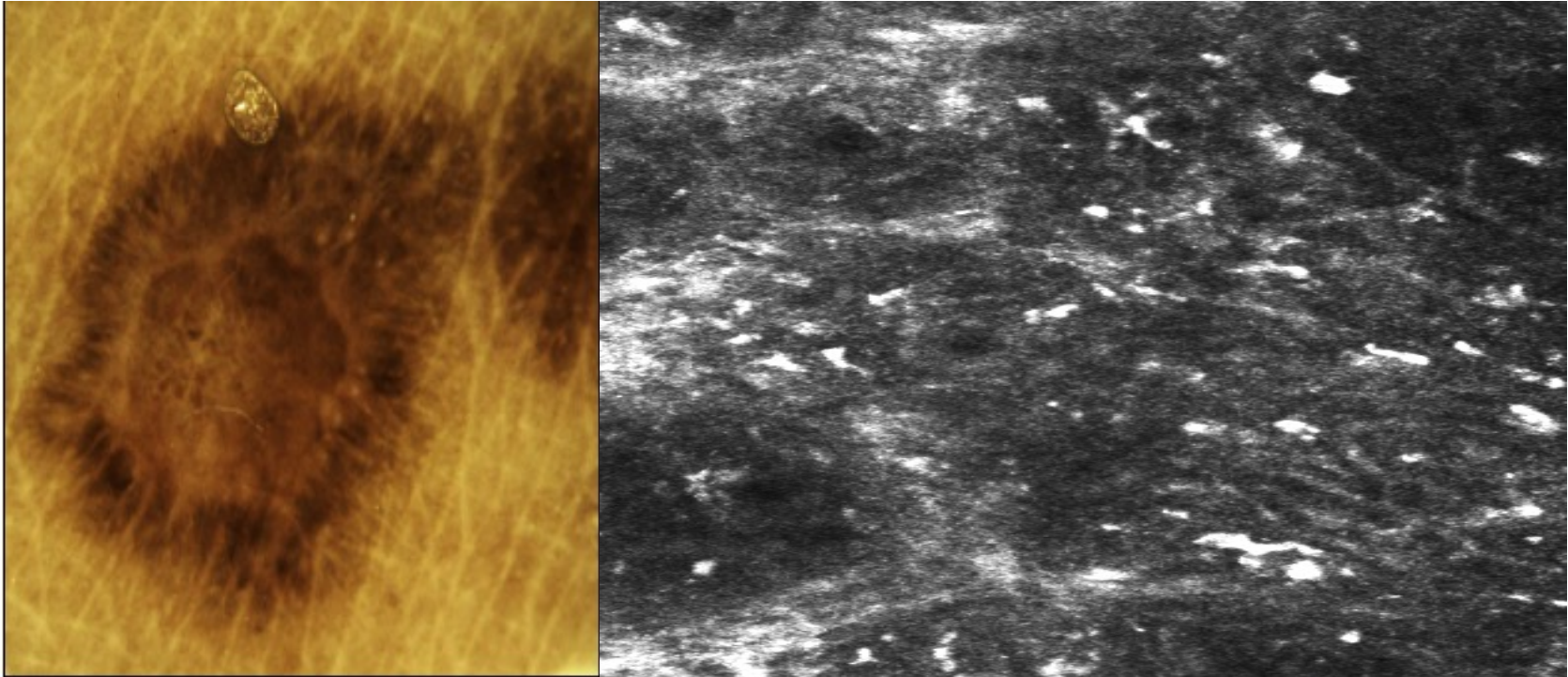
RCM Features of **Intermediate** and **Late** Skin Inflammation

Intermediate-Lichen Planus



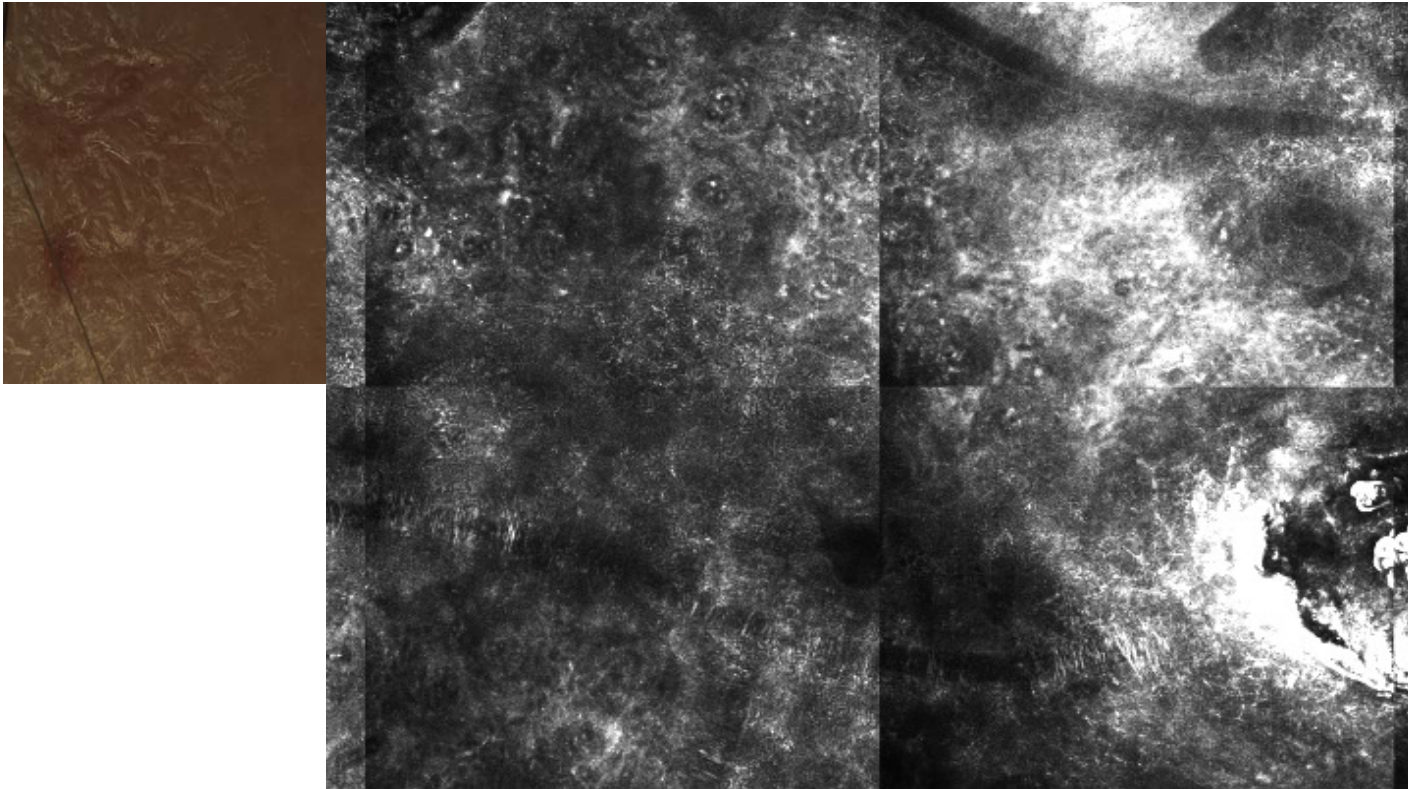
Intermediate lesion- **Lichen Planus** (a) dermoscopy (b) RCM
Features- Parakeratosis, few small bright inflammatory cells.

Late - Lichen Planus



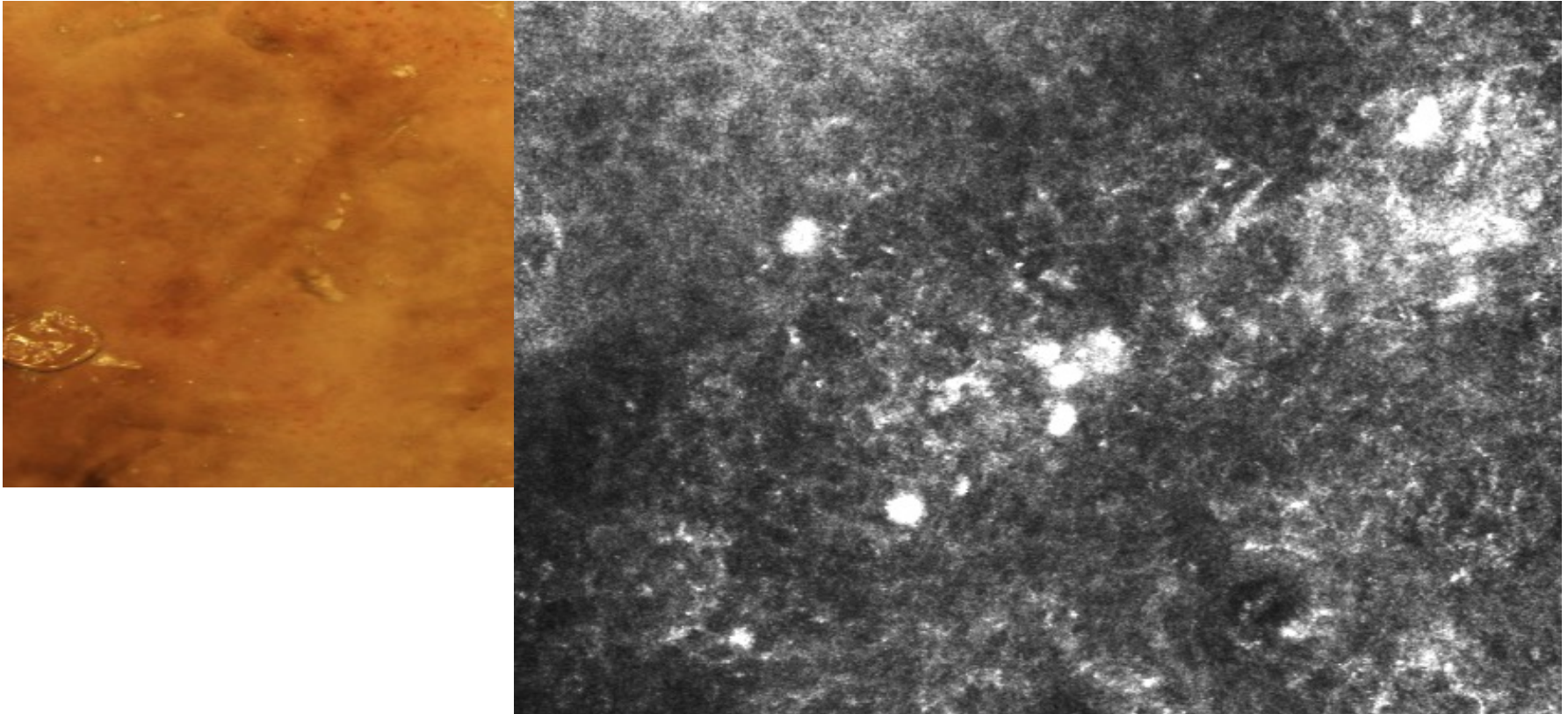
Late lesion- **Lichen Planus**- (a) dermoscopy (b) RCM
Features- Large bright inflammatory cells (yellow arrow)
concentrated around DEJ.

Intermediate - Herpes



Intermediate lesion- **Herpes** (a) dermoscopy (b) RCM
Features- few small bright inflammatory cells.

Late - Eczema



Late lesion-**Eczema** (a) dermoscopy (b) RCM Features- small bright and Large bright inflammatory cells.

Table: Confocal Features of Inflammatory Lesions at Various Ages

RCM Features	Early Lesion	Intermediate Lesion	Late Lesion
Spongiosis	+	-	-
Exocytosis	+	-	-
Hyperkeratosis	-	+	+
Dilated vessels	+	-	-
Parakeratosis	+	+	+
Papillomatosis	-	+	-
Epidermal Disarray	+	-	-
Small bright cells	++	few	-
Large bright cells	-	Start appearing	+
Interface changes	+	-	-
Perivascular infiltration	+	+/-	-

Conclusion

“Confocal microscopy may offer further insight into how best to manage inflammatory skin conditions based on age of the lesion”.

References

1. Aggozino M, Salvador G, Ardigo M, et al. Reflectance confocal Microscopy for Inflammatory Skin Diseases. *Actas Dermosifiliogr.* 2016;107(8):631-9.
2. Ardigo M, Prow T, Aggozino M, et al. The value of in vivo reflectance confocal microscopy in the diagnosis and monitoring of inflammatory and infectious skin diseases: a systematic review. *G Ital Dermatol Venereol.* 2015;150(5):565-73.
3. Kamila BG, Dorota WS, Grzegorz D, Anna WP. The use of reflectance confocal microscopy in selected inflammatory skin diseases. *Pol J Pathol.* 2015; 66 (2): 103-108.

Acknowledgment

Attiya Haroon, MD, PhD

Gina Francisco, MBS, BS

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For more information

Contact: attiya.haroon9@gmail.com

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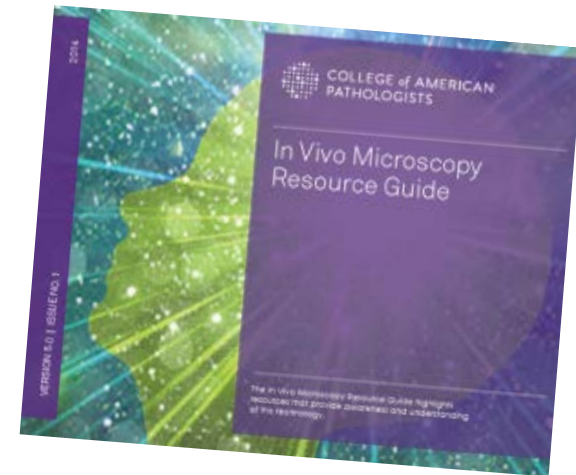
Topic	Speaker
Confocal Microscopy for Pigmented Lesions	Babar Rao, MD
Creating a Successful Pathology-engineering Collaboration	Nicholas P. Reder, MD, MPH
Confocal Microscopy of Non Melanocytic Lesions	Babar K. Rao, MD, FCAP
Light-sheet Microscopy for 3D Pathology	Nicholas P. Reder, MD, MPH; Lawrence True, MD
Rapid Examination of Fresh Tissue Using Light-sheet Microscopy	Nicholas P. Reder, MD, MPH

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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

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