F006 – Imaging in Dermatology
Melanocytic Neoplasia
Clinical-Confocal-Pathological-Correlations

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No Conflicts of Interest
Goals

• Learn how in vivo Reflectance Confocal Microscopy (RCM) compares to histopathology for the evaluation of melanocytic neoplasms

• Develop a basic understanding of which melanocytic features are better observed and why on RCM vs histopathology and vice versa

• Understand for which melanocytic tumors RCM provides reliable data and for which biopsy is needed to exclude melanoma

• Review how to safely use RCM to evaluate melanocytic neoplasms
RCM: Horizontal B&W Images to Depth of ~0.150-0.250 mm
Histopathology: H&E (IHC, PAS, etc) Stained Vertical Sections

**RCM Mosaic** Image:
Several images captured in same horizontal plane to create one large (up to 8mm x 8mm) image
*Mosaic imaging not yet commercially available for hand-held device*

**Stack Capture:**
Multiple individual images up & down a vertical axis
Direct Dermoscopy-RCM Correlations
RCM Bridges Dermoscopy and Histopathology

Correlation of Dermoscopy With In Vivo Reflectance Confocal Microscopy of Streaks in Melanocytic Lesions
Alice Sogo, MD; Melissa Gill, MD; Cristiane Reverso-Azevedo, MD; Allen C. Halpern, MD; Salvador Gonçalves, MD, PNG; Adria A. Murphy, MD

Arch Dermatol. 2007;143:727-734
How to Use RCM as a Diagnostic Aid

• RCM is indicated for lesions that remain unclear after both clinical and dermoscopic exam, but where suspicion for melanoma is low to moderate.

• If there is a high concern for melanoma prior to RCM, the lesion should be biopsied NO MATTER WHAT, and RCM would only be useful if it could help determine best location or technique for biopsy.

• RCM should be used with caution in raised or ulcerated lesions, due to risk of non-representative sampling.

• Before deciding biopsy is NOT NEEDED, make sure you reconcile RCM findings with clinical/dermoscopic findings and your diagnosis makes sense!
Limitations of RCM

• **Resolution:** Distinction between cell types can be challenging on RCM, and ancillary studies (IHC) are not available. Certain cytologic features, such as chromatin quality, nucleolar detail and mitotic figures, cannot be visualized on RCM.

• **Depth of imaging:** *Akin to shave biopsy*, dermal-based features of importance, such as vertical maturation, vertical contour, and location/number of mitoses may not be present for review.

• **Cellular Resolution Decreases with Increasing Imaging Depth:** Dermal RCM features, both stromal and melanocytic, do not reliably correlate with histology.
Cellular Resolution

Dendritic Pagetoid Cells: Langerhans Cells vs Dendritic Melanocytes

Langerhans cells and melanocytes share similar morphologic features under in vivo reflectance confocal microscopy: a challenge for melanoma diagnosis

Pantea Hashemi, MD, Melissa P. Pulitzer, MD, Alon Scope, MD, Ivanka Kovalyshyn, DO, Allan C. Halpern, MD, and Ashfaq A. Marghoob, MD

Cellular Resolution

Hyporeflective Round Pagetoid Cells/Nests: Paget’s Cells or Melanocytes

Reflectance confocal microscopy for diagnosis of mammary and extramammary Paget’s disease


JEADV 2013, 27, e24–e29

Hyporeflective pagetoid cells: a new clue for amelanotic melanoma diagnosis by reflectance confocal microscopy

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British Journal of Dermatology (2014) 171, pp48–54
Depth of Imaging: Flat Lesion Misclassification

Example: Blue nevus arising in background lentiginous skin being misclassified as solar lentigo

Pitfall:
• Dermal-based lesion too deep to visualize on RCM
• As flat, RCM could be misinterpreted as solar lentigo

Solution:
• Correlation with clinical and dermoscopic images to avoid misclassification
Depth of Imaging: Palpable Lesion Misclassification

Example: Congenital nevus with area of trauma containing recurrent nevus over-called as melanoma rising in congenital nevus on RCM

Histo: Compound Congenital Nevus with Focal Area of Trauma and Recurrent nevus

Pitfalls:
- RCM misdiagnosed lesion as invasive melanoma using DN algorithm
- Underlying scar and maturing nevus not present for review to provide context
- Vertical contour, maturation and lack of mitotic figures in recurrent nevus not visualized

In vivo confocal microscopy for detection and grading of dysplastic nevi: A pilot study

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Cellular Resolution Decreases with Increased Imaging Depth

Non-invasive *in vivo* dermatopathology: identification of reflectance confocal microscopic correlates to specific histological features seen in melanocytic neoplasms

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- Epidermal and junctional features showed great correlations between histology and RCM.
- RCM was very good at identifying the presence of a histological dermal component, but the qualitative descriptions of the dermal component did not correlate well.
- Stromal features did not show good correlations between histology and RCM.
Cellular Resolution and Depth of Imaging: Example: Dense and Sparse Nests on RCM

Histologic features poorly seen on RCM:

**Intradermal Nevus:**
- Maturing melanocytes arranged as solitary units, cords, and small nests
- No cytologic atypia, but heavy pigmentation of superficial melanocytes

**Melanoma:**
- Dermal nests with no maturation, internal discohesion, and cytologic atypia

*JEADV* 2014, 28, 1069–1078
Cellular Resolution and Depth of Imaging:
Example: Balloon Cell Change on RCM

Pitfall:
• RCM identifies dermal non-homogenous dense and sparse clusters. The presence of large epithelioid cells with pleomorphic nuclei was concerning for melanoma.
Limitations of Histopathology

• **SAMPLING! SAMPLING! SAMPLING!**

• **Vertical sectioning** does not allow for evaluation of the entire lesional area resulting in the following types of **sampling errors**:
  • under-calling asymmetry (concerning feature)
  • over-calling peripheral rim of nests (reassuring feature)
  • missed areas of concern or melanoma arising in a nevus

• **Shave biopsy, akin to in vivo RCM**, may prevent evaluation of underlying dermal-based features of importance, such as vertical maturation, vertical contour, and location/number of mitoses as they are not sampled.

3D image courtesy of Kivanc Kose
Asymmetry and Peripheral Rim of Nests

Histopathology: JDN moderate atypia
Symmetry and peripheral rim of nests
NOT REPRESENTATIVE OF ENTIRE lesion!

RCM: Asymmetry and zonal absence of peripheral rim of nests on RCM

37 yo M with H/O MM; 5 mm flat irregular brown lesion on chest w/ reticular-globular pattern, central network and peripheral globules, suggesting growing lesion

Images from:
RCM easily identifies asymmetry and zonal loss of peripheral rim of nests which are missed on histopathology.
Asymmetry with Heterogenous Zones of Concern

40 yo F, chest, 4 mm asymmetric light & dark brown macule w/ atypical pigmented network, streaks & dots

Elongated junctional thickenings extending across breadth of lesion

Haphazardly distributed pleomorphic atypical cells trailing off at periphery

Case courtesy of Joseph Malvehy and Francesca Perino
Asymmetry with Heterogenous Zones of Concern

Histopathology: CDN with mild to moderate atypia
Focal bridging by small nests, solitary junctional melanocytes, cytological atypia and focal dermal nests
NOT REPRESENTATIVE OF ENTIRE LESION!
Get Levels!

Actual Histopathology Section Orientation and Location

Optimal Histopathology Section Orientation and Locations
RCM Allows for In Vivo Diagnosis of Dermoscopic Islands

Diagnostic accuracy of reflectance confocal microscopy for lesions typified by dermoscopic island.
• Pagetoid cells and atypical cells at DEJ distinguished melanoma from nevi
• RCM 89.9% sensitive and specific; n=63 (57.1% nevus, 30.2% MMIS, 12.7% invasive MM)

Reflectance confocal microscopy accurately discriminates between benign and malignant melanocytic lesions exhibiting a 'dermoscopic island'.
• RCM 100% sensitive and specific; n=5 (40% nevus, 60% early melanoma)
Case 1: 56 yo F w/ no H/O MM, 8 mm multicolored flat lesion showing irregular border & blue-white veil on upper back

RCM results are compatible with solar lentigo:
- Irregularly shaped small round to elongated dermal papillae surrounded by crisp bright rete ridges creating elongated cords
- The upper epidermal levels show random mild keratinocytic atypia in an otherwise normal cobblestone and honeycomb pattern
- No diagnostic evidence of a melanocytic proliferation
- No significant inflammatory cell infiltrate noted

IS BIOPSY NEEDED?

a) Yes
b) No
Case 1: RCM results are compatible with solar lentigo:

- Irregularly shaped small round to elongated dermal papillae surrounded by crisp bright rete ridges creating elongated cords
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**IS BIOPSY NEEDED?**

a) Yes - RCM fails to explain dermoscopic blue-white veil!!!!

b) No
Case 1: Due to limited imaging depth of RCM, lesion of concern was not visualized.

Histology:
Intradermal nevus, superficial congenital pattern
Possibly a collision between solar lentigo and nevus!
Case 2: 29 yo M w/ an asymmetric 10 mm dark brown papule with focal brown-black pigmentation on the mid back

RCM at the level of the DEJ:
Brown Papule: Organized, fairly uniform dense nests (clods)
Brown-Black Dermoscopic Island: Atypical meshwork pattern with loss of DEJ contours

RCM at the level of the stratum spinosum:
Brown Papule: Tops of organized, fairly uniform dense nests (clods)
Brown-Black Dermoscopic Island: Numerous pleomorphic Pagetoid cells
Case 2: How should this lesion be managed?

a) No biopsy or follow-up
b) 3 month follow-up
c) Shave biopsy
d) Punch biopsy of dark area
e) Excisional biopsy with attached suture and diagram indicating dark area
f) C, D, or E
g) D or E
Case 2: How should this lesion be managed?

a) No biopsy or follow-up
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e) Excisional biopsy w/ attached suture/diagram
f) C, D, or E
g) D or E

Histopathology: Compound nevus, superficial congenital pattern

- This is a high risk lesion for sampling error in histopathology.
- Call the pathologist and ask for levels through the block!
- RCM TRUMPS HISTOPATHOLOGY (HERE)!!!
Summary: RCM Versus Histopathology

• Unlike histopathology, RCM allows for direct correlation of concerning dermoscopic structures.

• RCM provides more complete sampling of epidermal structures, while histopathology provides superior sampling of dermal structures.

• RCM is superior to histopathology at detecting asymmetry, peripheral rim of nests and zonal areas of concern, such as melanoma in situ arising in a nevus.

• Histopathology with IHC can distinguish cell types that represent diagnostic pitfalls on RCM, such as Pagetoid cells and small melanocytes.

• Histopathology (but not shave biopsy!) is needed to diagnose certain melanocytic tumors, such as blue, Spitz, balloon cell, desmoplastic, inflamed, traumatized, in which DDX between nevus and melanoma relies on dermal features that are not (well) visualized with RCM.
Important Take Home Points

- RCM and histopathology provide overlapping, complimentary information, which, if representative, should explain concerning features on dermoscopy.

- Never forget to close the clinical-dermoscopy-RCM-Histopathology loop!
  - If questions after visual inspection, proceed to dermoscopy
  - If questions remain after dermoscopy, proceed to RCM
  - If RCM does not explain concerning feature on dermoscopy, DO A BIOPSY!
  - If histopathology does not explain area of concern on dermoscopy, get levels!
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Questions?