Confocal Application in Practice Everyday (CAPE)  
AAD NYC 7/2017  
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Why this is important?  
• Skin cancer epidemic  
  – Patients do not consider biopsies trivial!  
• New available technology to help dx skin cancers in vivo & reduce unnecessary biopsies  

Devices currently available to enhance clinical dx of melanoma  
• Full body photography  
• Dermoscopy  
  - NNT (# needed to treat or # pig lesions bx’d to dx MM):18→4.3  
  - Skin Ca Ctr using dermoscopy: 76,783 nevi excised to dx 9,910 MMs  
• Reflective confocal microscopy (RCM)  

Confocal microscope is a high resolution, non-invasive imaging device  
Visualization on a cellular level comparable to histopathology:  
• Epidermis  
• Dermo-epidermal junction  
• Dermis  

RCM in Dermatology: Fundamentals and Clinical Application. Editor: S. Gonzalez. 2011  

Biopsy is performed  
Histopathology
**Histopathology**

Skin is sectioned in a vertical plane: allows for evaluation <2% of lesion

**RCM**

More of the lesion is able to be evaluated!

Horizontal sectioning: optical images with a field of view up to 8X8 mm

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**Technical Principles of RCM**

RCM uses a diode laser (830nm)

- penetration into the skin illuminating a tiny point inside the tissue.

**Technical Principles of RCM**

- Reflected light then passes through a pinhole.
- Light collected by the detector is converted to pixels to form an image.

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**In-Vivo Confocal vs. H&E Horizontal sections**

Rajadhyaksha M. JID 1999

- Melanin back scattered the light= bright cells

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- Relies on inherent diff refractive index of structures: melanocytes, keratinocytes... Psaty, Halpern. Clinics in Dermatology 2009;27:35
- Max depth of imaging 200-300 um usually @ level of papillary dermis

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**Stratum Corneum** (surface)

**Dermal-Epidermal Junction**

**Superficial Dermis**
**Stratum Corneum**
Keratinocytes: 10 to 30µm bright polygonal structures w/ dark outlines

**Stratum Granulosum**
15-20 µm below skin surface: Keratinocytes 25 to 35µm in diameter w/ bright, granular cytoplasm & dark oval nuclei → Honeycombed pattern

**Stratum Spinosum**
20-100 µm below stratum corneum: Honeycombed pattern c/o 15 to 25µm cells w/ bright cytoplasm & dark oval-round nuclei

**Suprabasalar Layer**
50-100 µm below stratum corneum (location depends on epidermis thickness): Single layer of refractive cells corresponds to horizontal sectioning @ suprapapillary plates

**Patterns of cells in Sup Epid = Honeycombed**
- **Typical Honeycombing**: polygonal cells w/ dark nuclei & bright & thin cytoplasm
- Spinous & Granular layers: well-demarcated cellular outlines form grid → resemble honeycomb
- Cells diminish in size in deeper layers of epid
**Atypical honeycombing**

- Cell size irregular & contour is thicker than normal.

**Cobblestone Pattern:**
- Aggregates of small polygonal cells w/bright cytoplasm (= normal pig'd basal keratinocytes) separated by less refractive outline in the epidermis.

**Cobblestone pattern**

**Atypical Cobblestoning:** irregularity in cell size, shape, &/or refractivity; may present with multiple small nucleated cell pattern.

**Disarranged pattern:**
- Absence of honeycomb or cobblestone pattern.
- Disarray of normal architecture of sup layers w/ unevenly distributed bright granular particles & cells.

**Patterns formed by cells in the Superficial Layers**
**Pattern formed at the DEJ**

*Edged papilla*
- Demarcated rim of bright confluent basal cells
- Dark holes in epidermis = opening of dermal papillae

**Pattern formed at the Dermo-epidermal Junction**

*Non-edged papillae*
- Dermal papilla w/o demarcated rim of bright cells but separated by a series of large reflecting cells.

**Ring Pattern**
- Histopathology: junctional nevi with a lentiginous proliferation of melanocytes
- Bright peripheral rim = single melanocytes & small nests at DEJ
- Holes = dermal papillae

**Meshwork Pattern**
- Round & oval shaped structures = melanocytic nests located at tips of rete (junctional nests)
- Junctional thickening = elongated rete ridges filled with melanocytes
Dermis

W/in dermis diff structures can be visualized:
• Nests
• Bright cells
• Collagen fibers
• Blood vessels

Junctional nest

nests connected w/ epidermal basal cell layer & bulge into dermal papillae

Dermis: Nest (cluster or clod)

• Dermal melanocytic nests w/in papillae w/o connection to epidermis
• Oval to round bright aggregate w/ well-defined borders, c/o clustered cells, freq large & highly refractive

Dermis: Plump Bright Cells

• Irregularly shaped, w/ ill-defined borders
• No visible nucleus
• = melanophages

Collagen

• Bright elongated fibrillar structures/bundles w/ no cellular component, no visible nucleus, & no visible movement
• Distributed side by side thru out dermis

Collagen

Distributed as coils or rings in papillary dermis

Distributed as parallel bundles in reticular dermis
Blood vessels

Linear or canalicular vessels parallel to horizontal plane

Vessels traversing thru papillae perpendicular to horizontal plane

Why Confocal?
The Future is NOW

• Help w/ DDX
• Confocal makes me better at dermpath: horizontal sections \(\rightarrow\) see more of lesion!
• Convince resistant patient of need for surgery
• Avoid bx & go directly to Rx
  – Pts do not consider a skin bx trivial!
    At UCONN we spare \(\sim60\%\) of our pts bxs
  – Cosmetic sites, sites w/ delayed healing (legs)
• ID lesion to bx in pt w/ many atypical nevi
• ID site for surgery after bx

Confocal Near: At the Bedside

• Obtain image at exam table & evaluate while obtaining image or immed after
• Immediate answer \(\rightarrow\) avoid bx if benign or proceed to definitive therapy if malignant

Remote Reading

Image captured by confocalist \& read at bedside or transmitted electronically to dermatopathologist for sign out

Home Screen: Patient list

Lists completed \& uncompleted evaluations

Select patient case
Access to clinical information
• Access to all images as thumbnails (dermoscopy \& RCM)
• Each can be clicked \& expanded for evaluation
Does it Work?  
**RCM Diagnostic Accuracy**

- 340 lesions: 2 readers, 1 on site & 1 distal
- 1 reader highly experienced but other less experienced
- Sensitivity >90%, Specificity 60%.
- All malig lesions except 1 SCC recommended for excision


Others Experience with RCM

- RCM sensitivity for melanocytic lesions:
  - 68-99% sensitivity
  - 66-99% specificity
  - Positive predictive value of 97.5%
  - Negative predictive value of 99%
  - Rare but not impossible to miss melanoma

### ARTICLES

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<tr>
<th>LEISON</th>
<th>SENSITIVITY</th>
<th>SPECIFICITY</th>
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<td>Nori, et al. JAAD 2004;51:923</td>
<td>BCC</td>
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<td>Guitera, et al. JID 2012;132:2386 (Reduced 68% of bx’s)</td>
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<td>Guitera, et al. JAMA Derm 2013; 149:692</td>
<td>MM</td>
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<td>Pellacani, et al. BJD 2014;171:1044</td>
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<td>Farretani, et al. JAMA Derm 2015;151:1075</td>
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<td>Borsari, et al JAMA Derm 2016;152:1093</td>
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<td>Menge, et al. JAAD 2016;74:1114</td>
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<tr>
<td>Song, Grant-Kels, et al. JAAD 2016;75:1187 (Reduced 60% of bx)</td>
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<td>85.7%</td>
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### UCONN Experience

- Prospective study: RCM Vs MDSLA
  - Multispectral digital skin lesion analysis
- Pts scheduled for bx of clinical &/or dermoscopically atypical pigmented lesions but NOT obviously MM
- Lesions evaluated w/ RCM & MDSLA prior to bx
- 55 lesions evaluated:
  - MDSL Sensitivity 71% Specificity 25%
  - RCM Sensitivity 86% Specificity 67%
- RCM recommended bx for 22 lesions (40%)
  - Path: 4 MMIS, 3 severely DN, 4 Atypical mel lesions
- 60% of cases spared bx bc RCM benign!

**Song, Grant-Kels, Swede, et al. JAAD 2016;75:1187-92.**

### Imaging Mode: Mosaic

Images can be scanned horizontally, with small quadratic fields-of-view forming a square mosaic of contiguous 500 μm by 500 μm images: the RCM mosaic

### Imaging Mode: stack

Field of view: 500 μm by 500 μm

### Case 1

60 yo had 4mm red brown papule on left cheek of unknown duration

Pigmented follicular openings

Gray dots/granules
Mosaic at the spinous granular level

Honeycomb pattern visualized

Honeycomb pattern poorly visualized with bright cells infiltrating the epidermis

Numerous spindle shaped cells and round nucleated cells

Sheets of pleomorphic cells

Case 2

60 yo woman with 3 mm irregular macule of unknown duration

Streaks or leaf like structures: suggest possible BCC

Gray brown dots/granules: suggest melanocytic lesion

Large round bright cells infiltrating the epidermis

Sheets of dendritic cells infiltrating junctional thickenings and within the interpapillary spaces

1. Atypical melanocytic hyperplasia?
2. Sun damaged skin?
3. Melanoma in situ?
4. I am not sure but not a BCC!
Confocal Images & DP: The Future is NOW

Real Life Cases

- Confocal dx’d MM in situ more definitively than pathology sections!
- Pt can be sent for definitive surgery (spared bx) or Rx’d w/ topical imiquimod & spared surgery altogether
- FU can be monitored by repeat confocal avoiding repeat bx’s to determine Rx response

Case 3

69 yo man w/ pigmented lesion on nose. Refuses bx!

DDX:
Melanoma
LPLK
Pigmented AK

Melanoma on sun damaged skin
Confocal Images & DP: The Future is NOW
Real Life Cases

- Confocal established dx in pt who refused bx on face

Cases 4 & 5: Tale of White Lesions

48 yo woman w/ multiple scars & white plaque on back

Mosaic of the DE junction level

Dark silhouettes

Coiled and thickened reticulated collagen

Multiple tumor islands

Serpentine branched vessels

Fine brown dots

Milky white appearance

Features of BCC
55 yo woman & hypopigmented plaque of chest

Serpentine branched vessels

Milky white appearance

Features of morpheaform BCC

Multiple cords and bulbous projections

Coiled and reticulated collagen with a "cotton appearance" (Actinic elastosis)

White lesions

Confocal Images & DP: The Future is NOW Real Life Cases

- Confocal established dx in both pts
- Patient with chest lesion avoided surgery and risk of hypertrophic scar!
Case 6: Tale of which lesion to bx

44 yo w/ many atypical nevi & previous bxs: one mole slightly darker than others. Does it merit bx?

Confocal Images & DP: The Future is NOW Real Life Cases

- Patient with many atypical nevi
- Hates coming to derm because always getting biopsied
- Confocal helps identify which lesions need to be excised & helps avoid unnecessary biopsies!

Melanoma

Nucleated cells

Multiple colors

Atypical network

RCM 1500 Codes
3 Scenarios Possible

- 96931 & 96934: YOUR staff capture the image & you read it
- 96932 & 96935: YOUR staff capture the image & someone else reads it.
- 96933 & 96936: Someone else captures it & YOU read it.

Thanks to AAD RUC team, Dan Siegel & Harold Rabinovitz
2017 Medicare National Payment Rates

<table>
<thead>
<tr>
<th>Procedure</th>
<th>RVU First Lesion</th>
<th>RVU Each Additional Lesion</th>
<th>Medicare National Payment Rate $ First Lesion</th>
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*These rates are adjusted for cost-of-living variances, so your actual payment may be different from this number.

The Handheld RCM 3000

- Introduced to clinical practice in 2011
- Small, portable & more accessible for application on curved facial surfaces
- A faster procedure
- Imaging of several lesions is simple
- No CPT code yet

Vivascope 3000

- Handheld RCM
  - ~10 minutes
  - Field of view = 0.9mm
  - VivaStack capability
  - No mosaics
  - No CPT code

Vivascope 1500

- Traditional RCM
  - ~25-30 minutes
  - Field of view = 8X8mm
  - Viva stack capability
  - Mosaic formation
  - CPT code

Accuracy of in vivo confocal microscopy for dx of BCC: comparative study between handheld & wide-probe confocal imaging


58 yo man w/ hx of NMSC had Mohs' surgery performed on this area approximately 6 yrs ago.
Bottom Line

Thank you for your attention &
Thanks to Harold &
Maggie!

For More Information, Visit: www.ijwdonline.org