Confocal Application in Practice Everyday (CAPE)

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 bx’s

Lifetime Risk of Developing Invasive MM in US

Changes in annual lifetime risk of developing invasive MM in US: 1930 to 2016


US Annual Deaths From Melanoma

Est’d # of annual deaths from MM in US: 2009 to 2016


Thin Melanoma Mortality
- Greatest # of deaths from MM 1992-2013 from T1 MMs
- Prognosis (risk for death w/in 10 yrs): worse for 0.01-0.25mm thick MMs than from 0.26-0.50mm thick!(not explained by ulceration)
- Prognosis worsened for MM > 0.51mm deep
- EARLY DETECTION (in situ) IS IMPORTANT!

**Skin Cancer Deaths USA**

- **BCC:** 4.3 million cases/yr → 3,000 deaths  
- **SCC:** > 1 million cases/yr → 15,000 deaths


**Devices currently available to enhance clinical dx of melanoma**

- **Full body photography**
- **Dermoscopy**
  - NNT (# pig lesions bx’d to dx MM): 18→4.3  
  
  - Skin Ca Ctr using dermoscopy: 76,783 nevi excised to dx 9,910 MMs  
  
  - **RCM**

**What is confocal microscopy?**

- 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**

Skin is sectioned in a vertical plane: allows for evaluation <2% of lesion
How does RCM Work?

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

ZERO adverse events reported

Technical Principles of RCM

RCM uses a diode laser (830nm)

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

- The image is displayed on a computer monitor in real-time

- Relies on inherent diff refractive index of structures: melanocytes, keratinocytes…


- Max depth of imaging 200-300 μm usually @ level of papillary dermis

Stratum Corneum (surface)

Dermal-Epidermal Junction

Superficial Dermis
**RCM Mosaic**

- Individual 500μm × 500μm images stitched together like a quilt to form a large field-of-view.
- Images captured in a single, horizontal plane.
- Mosaics can be up to 8 mm x 8 mm square.
- Multiple mosaics are captured at different levels in the skin.

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

**Horizontal section**

- Melanin back scattered - light = bright cells.

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**Stratum Corneum**

Keratinocytes:
- 10 to 30μm bright polygonal structures with dark outlines.

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**Stratum Granulosum**

- 15-20 μm below skin surface: Keratinocytes 25 - 35μm in diameter with bright, granular cytoplasm and dark oval nuclei.
- Honeycombed pattern.

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**Stratum Spinosum**

- 20-100 μm below stratum corneum: Honeycombed pattern due to 15 - 25μm cells with bright cytoplasm and dark oval-rounded nuclei.

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**Suprabasalar Layer**

- 50-100 μm below stratum corneum (location depends on epidermal thickness): Single layer of refractive cells corresponds to horizontal sectioning at suprapapillary plates.
**Pattern of cells in Sup Epid = Honeycomb**

- **Typical Honeycomb:** 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 epidermis

**Patterns formed by cells in Superficial Layers**

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

**Atypical Honeycombing:**
- cell size irregular & contour is thicker than nl

**Atypical Cobblestoning:**
- irregularity in cell size, shape, &/or refractivity; may present with multiple small nucleated cell
**Patterns formed by cells in the Superficial Layers**

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

**Patterns formed @ DEJ**

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

**Pattern formed at the DEJ**

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

- Histopath: pred junctional nevi w/ a lentiginous prolif 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 thickening = elongated rete ridges filled w/ melanocytes

**Dermis**

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

**Dermis: Nest (cluster or clod)**

- Dermal melanocytic nests w/in papillae w/o connection to epid
- 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

**Junctional nest**

- Nests connected w/ epidermal basal cell layer & bulge into dermal papillae
Collagen
- Bright elongated fibrillar structures/bundles w/ no cellular component, no visible nucleus, & no visible movement
- Distributed side by side throughout 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 @ DP: horizontal view
- Convince resistant pt of need for biopsy/surgery
- Avoid bx if benign. Go directly to Rx if malignant
  - Pts do not consider a skin bx trivial: @U CONN 60% bxs
  - Cosmetic sites, sites w/ delayed healing (legs)
- ID lesion to bx in pt w/ many atypical nevi
- ID site for surgery after bx

RCM Workflow:
1. Dermoscopy
- Dermoscopic imaging device part of RCM
- Dermoscopy & RCM combined: sensitivity of 98%
- Dermoscopy image 10 x 10 mm

2. RCM Imaging
- After dermoscopy → RCM images acquired: ~4-6 mosaics w/ in epid & sup dermis
- Images reviewed at bedside or transferred via internet for review by remote MD

Confocal Near: At the Bedside

- Obtain image at exam table & evaluate while obtaining image or immed after
- Immed answer → avoid bx if benign or proceed to definitive therapy if malignant

Remote Reading

Image captured by confocalist & read at bedside or transmitted electronically to DP 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 clicked & expanded for SO
Does RCM Work?

- 748 lesions: 629 cases (84.1%) benign → no bx
- 119 cases (15.9%) bx’d: 
  - 44 concerns of ca: 38 malig & 6 benign
  - 69 for atypical features on RCM: benign w/ atypia
  - 6 due pts’ concerns or cosmetic: all benign
- 75 true neg results: 69 lesions bx’d for atypical RCM features + 6 lesions bx’d bc of pt concerns
- Sensitivity 100%; specificity 92.6%


Others Experience with RCM

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


<table>
<thead>
<tr>
<th>ARTICLES</th>
<th>LESION</th>
<th>SENS</th>
<th>SPECIFICITY</th>
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</thead>
<tbody>
<tr>
<td>Nori, et al. JAAD 2004;51:923</td>
<td>BCC</td>
<td>100%</td>
<td>95.7%</td>
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<tr>
<td>Guitera, et al. JID 2012;132:2386 (Reduced 68% of bx’s)</td>
<td>BCC</td>
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<td>88.5%</td>
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<td>Guitera, et al. JAMA Derm 2013;149:692</td>
<td>MM</td>
<td>97.6%</td>
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<td>Rao, et al. JAAD 2013;69:e295</td>
<td>Mixed</td>
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<td>&gt;60%</td>
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<td>Pellacani, et al. BJD 2014;171:1044</td>
<td>Mixed</td>
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<td>79.3%</td>
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<tr>
<td>Fametani, et al. JAMA Derm 2015;151:1075</td>
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<td>79.3%</td>
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<tr>
<td>Pellacani, et al. JEADV 2016;30:413 (Reduced &gt;70% of bx)</td>
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<td>83.9%</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>
<td>LM</td>
<td>100%</td>
<td>71.4%</td>
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<tr>
<td>Song, Grant-Kels, et al. JAAD 2016;75:1187 (Reduced 60% of bx)</td>
<td>Mixed</td>
<td>85.7%</td>
<td>71.4%</td>
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UCONN Experience

Prospective: RCM Vs MDSL Multispectral digital skin lesion analysis

- Pts scheduled for bx of clinical &/or dermoscopically atypical pigmented lesions but NOT obviously MM
- Lesions evaluated w/ RCM & MDSL prior to bx
- 55 lesions evaluated: MDSL Sens 71% Specificity 25%
  - RCM Sens 86% Specificity 67%
- RCM recommended bx for 22 lesions (40%)
  - Path: 4 MMIS, 3 severely DN, 4 Atypical mel lesions
- 60% spared bx bc RCM benign

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

Reduced 60% of bx

Reduced >70% of bx

Reduced >60% of bx

Reduced 68% of bx’s
Imaging Mode: Mosaic
Images can be scanned horizontally, with small quadratic fields-of-view forming a square mosaic of contiguous 500\(\mu\)m by 500\(\mu\)m images: the RCM mosaic.

Imaging Mode: stack
Field of view: 500 \(\mu\)m by 500 \(\mu\)m

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 2018

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Cut Biopsy 11100</th>
<th>RCM Image Acquisition Only 96932, 96933, 96936</th>
<th>RCM Interpretation Only 96931, 96934</th>
<th>Path PC 88300</th>
<th>RCM Imaging &amp; Interpretation 96931, 96934</th>
<th>Path (TC+PC) 88305</th>
<th>Path TC 88305</th>
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<tr>
<td>RVU First Lesion</td>
<td>2.87</td>
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<tr>
<td>RVU Each Additional Lesion</td>
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<td>Medicare National Payment Rate First Lesion*</td>
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*These rates are adjusted for cost-of-living variances, so your actual payment may be different from this number.

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 simple, faster & simple
• No CPT code yet

Vivascope 1500

Vivascope 3000

Vivascope 1500
Accuracy of in vivo RCM for dx of BCC: Comparative study between handheld & wide-probe RCM

54 BCC imaged with both RCM devices

<table>
<thead>
<tr>
<th>Vivascope 1500</th>
<th>Vivascope 3000</th>
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<tbody>
<tr>
<td>Sensitivity</td>
<td>100%</td>
</tr>
<tr>
<td>Specificity</td>
<td>78%</td>
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