Advances in Imaging Technology for Melanoma Diagnosis

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DISCLOSURE OF RELEVANT RELATIONSHIPS WITH INDUSTRY

NYU receives compensation from MoleSafe for my telemedicine dermoscopic diagnoses.
Imaging Technologies for Melanoma Diagnosis

• Total body photography
  – Automated machines
  – 3D photography

• Sequential digital dermoscopic imaging
  – Combined with total body photography

• More sophisticated imaging devices
  – Confocal imaging
  – Electrical impedance spectroscopy (Nevisense)
  – Optical coherence tomography
  – Multiphoton microscopy

• Artificial intelligence
Total Body Photography for Melanoma Detection

• Allows identification of new or changing lesions in patients with atypical nevi for melanoma detection

  – Slue et al Arch Dermatol 1988
  – Rivers et al Cancer 1990
  – Shriner et al Cutis 1992
  – Marghoob et al Arch Dermatol 1994
Total Body Photos Reduce Biopsy Rates

- Risser et al J Am Acad Dermatol 2007 – didn’t show reduction, only 1 year follow-up (time of highest biopsy rate)
- Truong et al JAAD 2016 – did show 3.8 fold reduction in biopsy rates after total body photos
- Reviewed all patients from 2 pigmented lesion clinics who received TBP and had 2 or more follow-up visits over a period of 2 years or longer
TBPs Decrease Cancer Worry

• Moye et al JAMA Dermatol Feb 2015
• 137 patients with atypical mole syndrome at Emory and U of Arizona completed questionnaire about worry before and after TBPs
• Low level of cancer-related worry (similar to other cancers in high risk patients)
• TBPs decreased cancer worry to negligible
• Hay JAMA Dermatol Feb 2015 – Worry About Developing Melanoma in the PLC Does it Warrant a Solution?
• Controversy over whether cancer worry facilitates or hinders screening
TBPs Aid Self-Skin Exam

- 50 patients (3167 moles)
- Created or altered existing moles with eyeliner (10% of moles in each patient)
- Sensitivity of detecting change without / with photos = 60.2% vs 72.4%
- Specificity 96.2% vs 98.4%
- Patients with TBP reported more frequent SSE
- Give patients a copy of their photos
- Oliveria et al Arch Dermatol 2004
# Automated Total Body Photography Machines

<table>
<thead>
<tr>
<th>Machine</th>
<th>Available soon</th>
<th>Price</th>
</tr>
</thead>
<tbody>
<tr>
<td>Melanoscan</td>
<td>$50K</td>
<td></td>
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<tr>
<td>Fotofinder</td>
<td></td>
<td>$62K</td>
</tr>
<tr>
<td>DermSpectra</td>
<td></td>
<td>$125-150K</td>
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<tr>
<td>Vectra 360</td>
<td></td>
<td>$245K</td>
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</tbody>
</table>

Some have computerized technology to highlight differences, still emerging

Approximate list prices
Vectra WB360 – 3D Photography

• Automated 3D Total Body Photography
• Creates a patient avatar that can be rotated in space
• Can annotate with dermoscopic photos
Sequential Digital Dermoscopic Imaging (SDDI)

• Take digital dermoscopic image

• Short term (3 month) monitoring – look for any change
  – 10% will be melanoma

• Routine monitoring – look for marked changes

  ▪ Caveats:
    ▪ You have to trust that the patient will come back
    ▪ Need a reliable patient recall system
    ▪ Patient comes back sooner than 3 months if change
      is noted at home

Altamura et al Arch Dermatol. 2008
Evidence for Total Body Photography with Digital Dermoscopic Monitoring

- Moloney et al JAMA Dermatol 2014 (Sydney)
- Salerni et al JAAD 2012 (Barcelona)
- Banky et al Arch Derm 2005 (Victoria)
- Rademaker and Oakley J Prim Health Care 2010 (New Zealand)

- Low biopsy rate
- Melanomas are detected earlier than without imaging
TBP/ Sequential Dermoscopic Surveillance

• 618 high risk patients 1999-2008 – monitored 11,396 lesions (18.44 / patient), 1152 lesions, 1.86 per patient, were excised

• 98 melanomas (8.5% of excised lesions) were diagnosed in 78 patients (12.6%)
  – 53 melanomas were in situ (53.3%),
  – invasive (45); all <1 mm (median 0.5 mm); none ulcerated

• 311 high risk patients 2006-2009 – monitored 1697 lesions

• Benign to malignant ratio – 1.6:1 for all lesions, 4.4:1 for melanocytic: melanoma, median thickness of MM during study period was MMIS

• In a selected high risk population → early detection of melanomas with a low rate of excisions

• Moloney et al JAMA Dermatol 2014 (Sydney), Salerni et al JAAD 2012 (Barcelona), Banky et al Arch Derm 2005 (Victoria), Rademaker and Oakley J Prim Health Care 2010 (New Zealand)
The MoleMap / MoleSafe System – Remote Surveillance

- Combines Total Body photography with dermoscopy of atypical skin lesions
- Trained nurse “Melanographers” perform skin exams and image patients
  - Low threshold for dermoscopic imaging of atypical lesions
- Dermoscopy-trained Dermatologists review all images and complete the diagnosis using a secure internet telemedicine application
- MoleSafe reports and follow up instructions sent to patient and referring physician
Pros and Cons of Total Body Photography

Cons
• Cost (patient)
• Time (patient and visit)
• Patient discomfort
• Privacy issues / storage
  – Don’t store TBPs in the general electronic health record
    (Lakdawala et al J Am Acad Dermatol 2013)

Pros
• Helps to monitor for new / changing lesions
• Decreases biopsies
• Aids in self exam
• Decrease patient worry
• Good for patients who have trouble keeping track of moles

Can be useful in the management of high risk patients
When to use TBP vs Sequential Digital Dermoscopic Imaging

• Patients with many but dermoscopically “easy” nevi may benefit more from TBPs

• Patients with few but dermoscopically “complex” nevi may benefit more from SDDI

• Total body photography can be used in combination with sequential digital imaging
Simplified Digital Photography for the Practicing Dermatologist

• If all the moles are on the back, take a good back photo
• Digital dermoscopy with your iphone into your EMR
• Inexpensive connector to magnetically attach your dermatoscope to a smartphone or ipad
• Dedicated SLR camera with dermoscopic lens
Cell phone imaging

• Cell phone camera
• Molely backs
• Patient monitoring at home
• Selfie Skin Examination (Criscito and Stein JAAD 2016)
MoleMapper: DIY Mole Mapping App from OHSU

- Free downloadable iPhone app
- Patients can take regional photos of their body
- Add photos of individual moles
- Use at home or in the office visit
- Can consent to use data for research study
- Webster et al Sci Data 2017

Currently no reliable mobile app for MM diagnosis – Rat et al J Med Internet Res 2018
Confocal Imaging

• In vivo imaging with cellular detail at 30x magnification
• Like an US, but with laser light at 830nm instead of sound
• Can image up to an 8 x 8 mm area
• It is able to penetrate to a depth of papillary dermis
• Confocal provides in vivo “quasi” histology
• Melanin and melanosomes provide strong contrast
• Numerous publications showing efficacy
Confocal Workflow

• Image acquisition takes about 5 minutes, can be done by staff member
• Image can be read by you or can be read remotely
• You can read other people’s images
Dermoscopy vs RCM to Diagnose Lentigo Maligna
Cinotti et al JEADV 2018

• Compared dermoscopy to RCM
• Diagnostic accuracy of both was good and equal– AUC of 0.86, 0.89
• RCM was more sensitive (80% vs 61%) and higher sensitivity for hypomelanotic and recurrent LM/LMM
• RCM had higher inter-investigator agreement and confidence level than dermoscopy
• Dermoscopy was more specific (92% vs 81%)
RCM for Definition of Lentigo Maligna Margins

• Pellicani et al JEAHV 2018, University of Modena and Reggio Emilia ($n = 17$) and Melanoma Institute Australia ($n = 6$)
  – Dermoscopy predicted tumor border in 26% cases, RCM predicted border in 91% cases

• Yelamos et al JAMA Dermatol 2017 (MSKCC)
  – Handheld RCM identified LM beyond clinical margin 43.4% of 23 cases – 9 false positive from photodamage
Confocal vs Multispectral Digital Skin Lesion Analysis

• Song et al JAAD 2016

• Lower sensitivity of MDSLA than prior studies (71% sens and 25% spec)

• RCM had sensitivity and specificity than MDSLA (86% sens and 67% spec)
Sounds like a great technique, but how do you convince your chair / boss / yourself to buy you a confocal?

- List price = 89K
- Annual maintenance = about 5K
- Leasing available
- Confocal imaging / interpretation now have reimbursable CPT codes (thanks to Jane Grant-Kels, Harold Rabinovitz and Dan Siegel)
- Estimate to break even – image and interpret about 2-3 cases / day
Reimbursement for Confocal Imaging, rates are approximate based on 2018 Medicare rates

<table>
<thead>
<tr>
<th></th>
<th>Biopsy (11100, 11101)</th>
<th>RCM Image Acquisition Only (96932, 96935)</th>
<th>RCM Interpretation Only (96933, 96936)</th>
<th>RCM Imaging and Interpretation (96931, 96934)</th>
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</thead>
<tbody>
<tr>
<td>RVU First Lesion</td>
<td>2.93</td>
<td>2.92</td>
<td>1.28</td>
<td>4.51</td>
</tr>
<tr>
<td>RVU each additional lesion</td>
<td>0.93</td>
<td>0.98</td>
<td>1.22</td>
<td>2.32</td>
</tr>
<tr>
<td>Medicare Payment Rate – First Lesion</td>
<td>104.82</td>
<td>124.89</td>
<td>41.75</td>
<td>172.03</td>
</tr>
<tr>
<td>Medicare Payment – Each Additional</td>
<td>33.27</td>
<td>35.63</td>
<td>39.95</td>
<td>75.58</td>
</tr>
</tbody>
</table>

adapted from J Grant-Kels, based on 2018 Medicare rates
The Future? – Artificial Intelligence / Deep Convolutional Neural Networks (CNN)
What is a CNN?

• Convolutional Neural Network – form of deep learning
• Computer system designed to work like a human brain
• Trainable to recognize anything you like
• Play Go, how Google recommends YouTube videos, voice recognition software
• Teach it to recognize images - cats or skin cancer
Deep Convolutional Neural Networks (CNN) - Melanoma

• Esteva et al Nature 2017 (Stanford)
• Trained 129,450 clinical images
• GoogleNet Inception v3
• Comparable performance to group of board certified dermatologists
International Symposium on Biomedical Imaging (ISBI) Challenge hosted by International Skin Imaging Collaboration (ISIC)

- [https://isic-archive.com](https://isic-archive.com) – public archive of 20K images
- Results of the 2016 Challenge - Marchetti et al JAAD 2018
- 1270 MM and 1031 nevi / lentigines - chosen from ISIC archive
  - Randomly divided into 900 images for training / 379 for testing
- 25 teams participated, compared to 8 experienced derms from 4 countries
- The top fusion algorithm was greater than the mean receiver operating characteristic area of dermatologists (0.86 vs. 0.71, $P = .001$) – better than some, not all dermatologists
- ISIC 2017 – in preparation – see ISIC website - Codella et al
- ISIC 2018 – deadline was yesterday, results will be announced tomorrow- stay tuned!
Google’s Inception v4 CNN Outperformed Most Derms

- Haenssle et al Ann Oncol 2018 – used Google's Inception v4 CNN
- Large international group of 58 dermatologists, including 30 experts
- Most dermatologists were outperformed by the CNN
- ROC AUC of 0.79
- Similar to top 3 winners of the 2016 ISBI challenge
CNN for Acral Melanoma Dermoscopic Diagnosis

Yu et al PLOS One 2018

• 724 acral MM
• 374 nevi
• Split the set into 2 groups (train in one, test in other)
• Inception-V3
• CNN performed similarly to experts, better than non-experts
A Publicly Available CNN with Good Performance

- Han et al JID 2018
- Used deep learning algorithm - Microsoft ResNet-152, made it publicly available
- Used multiple datasets, different skin types
- Superior performance than the dermatologists in the diagnosis of BCC in one dataset and nevi in another
Lower Performance in Different Population

• Navarrete-Dechent et al JID 2018 – Automated Dermatological Diagnosis: Hype or Reality

• Independently tested the publicly available algorithm from Han et al JID 2018 on 100 sequentially biopsied melanomas (37), BCC (40), SCC (23) from the International Skin Imaging Collaboration Archive (ISIC)

• 29 / 100 matched the diagnosis – sensitivity is considerably lower when applied to a different patient population

• Modifying their images (zooming, altering contrast) gave different diagnoses

• Authors suggest datasets should include metadata with patient demographics – age, skin type, anatomic location, etc

• Variability in photographic technique (lighting, areas)
# MSDL A Testing vs Real World Performance

<table>
<thead>
<tr>
<th>Publication</th>
<th>Screening MDs</th>
<th>N</th>
<th>Sn</th>
<th>Sp</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elbaum et al JAAD 2001</td>
<td>“skin cancer specialists”</td>
<td>CREATED DATASET 246 pigmented lesions • 63: mm • 183: nevi</td>
<td>100%</td>
<td>85%</td>
</tr>
<tr>
<td>Monheitt et al Arch Derm 2011</td>
<td>Academic dermatologists</td>
<td>PROSPECTIVE DATA SET 1632 • 114: mm • 995: low grade DN • 244 non-melanocytic</td>
<td>98%</td>
<td>9.5%</td>
</tr>
</tbody>
</table>

From Kelly Nelson, MD

JAAD 2001;44:207-218; Arch Dermatol 2011;147:188.
Is AI going to replace us?

• Not yet
• When??
• Potentially use AI for screening patients with poor access to dermatologist
• AI to assist in triaging / identifying higher risk lesions
• Refer to dermatology for treatment

Mar and Soyer Ann Oncol 2018
Thank You!

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