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

- Melanoscan
  - Available soon
  - $50K

- Fotofinder
  - $62K

- DermSpectra
  - $125-150K

- Vectra 360
  - 3D images
  - $245K

Some have computerized technology to highlight differences, still emerging
Vectra WB360 – 3D Photography

- Automated 3D Total Body Photography
- Creates a patient avatar that can be rotated in space
- Can annotate with dermoscopic photos

Rayner et al Front Med 2018 - Queensland
Sequential Digital Dermoscopic Imaging (SDDI)

• Take digital dermoscopic image
• Short term (3 month) monitoring – look for any change
  – Lentigo maligna may need 6 month follow-up
• Routine monitoring – look for marked changes
TBP/ Sequential Dermoscopic Surveillance

• 618 high risk patients 1999-2008 – only excised 1.86 per patient
• 98 melanomas
  – 53 melanomas were in situ (53.3%),
  – invasive (45); all <1 mm (median 0.5 mm)
• 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

Salerni et al JAAD 2012 (Barcelona), Moloney et al JAMA Dermatol 2014 (Sydney), 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”** image patients (total body and dermoscopy)
  - 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

• Numerous publications showing efficacy
• 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
Confocal Workflow

1. Exam
2. VIVACAM Dermoscopy
3. Confocal Imaging
4. Evaluate

- Image acquisition takes about 5 minutes, can be done by staff member
- Image can be read by you or can be read remotely
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 J EADV 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 can improve diagnostic confidence and management of equivocal lesions

- Yelamos et al JAAD 2019 (MSKCC and Barcelona)
- 272 lesions from 226 patients were examined by 7 dermatologists
- After RCM, diagnostic confidence increased from 6.2 to 8.1 (P<.001) – scale 0 - 10
- Management changed in 33.5% cases to observation in 51 cases, to biopsy in 31
- Number needed to excise was 1.2
- Sensitivity and specificity for malignancy increased after RCM
  - Sens increased from 78.2% to 85.1%, spec from 78.8% to 80%
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)

<table>
<thead>
<tr>
<th>Calculation 1</th>
<th>Gold Standard</th>
<th></th>
<th>Calculation 2</th>
<th>Gold Standard</th>
</tr>
</thead>
<tbody>
<tr>
<td>MDSLA</td>
<td>+ 2</td>
<td>39</td>
<td>MDSLA</td>
<td>+ 5</td>
</tr>
<tr>
<td></td>
<td>- 2</td>
<td>12</td>
<td></td>
<td>- 2</td>
</tr>
<tr>
<td>Sensitivity: 50.0%</td>
<td>Specificity: 23.5%</td>
<td></td>
<td>Sensitivity: 71.4%</td>
<td>Specificity: 25.0%</td>
</tr>
</tbody>
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| RCM           | + 3           | 19              | RCM           | + 6           | 16              |
|               | - 1           | 32              |               | - 1           | 32              |
| Sensitivity: 75.0% | Specificity: 62.7% | | Sensitivity: 85.7% | Specificity: 66.7% |

Calculation 1 = MM
Calculation 2 = MM plus atypical lesions needing re-excision
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>
</tr>
</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</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
- How Google recommends YouTube videos
- 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
HAMM and meta-analysis

- [https://www.thelancet.com/journals/lanonc/article/PIIS1470-2045(19)30333-X/fulltext](https://www.thelancet.com/journals/lanonc/article/PIIS1470-2045(19)30333-X/fulltext)
- Tschandl et al Lancet Oncology 2019

- JAMA Dermatology Accuracy of Computer-Aided Diagnosis of Melanoma: A Meta-Analysis
- *JAMA Dermatol* 2019 Jun 19;[EPub Ahead of Print], V Dick, C Sinz, M Mittlböck, H Kittler, P Tschandl
Computer challenge – sponsored by ISBI / ISIC

• International Symposium on Biomedical Imaging (ISBI) Challenge hosted by International Skin Imaging Collaboration (ISIC)
• 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 > mean receiver operating characteristic area of dermatologists (0.86 vs. 0.71, $P = .001$) – better than some, not all dermatologists
• ISIC 2017; ISIC 2018; ISIC 2019
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

Haenssle et al Ann Oncol 2018
CNN for Acral Melanoma Dermoscopic Diagnosis

- 724 acral MM
- 374 nevi
- Split the set into 2 groups (train in one, test in other)
- Google Inception-V3
- CNN performed similarly to experts, better than non-experts

Yu et al PLOS One 2018
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 included metadata with patient demographics – age, skin type, anatomic location, etc
- Variability in photographic technique (lighting, areas)
Cazzaniga et al JAAD July 2019

• 56 lesions were classified as suspicious from the online assessment
• On direct clinical exam, 14 of those (25%) were confirmed as suspicious
• One lesion (0.5%) was classified as non-suspicious online was considered suspicious in person
• All clinically suspicious were biopsied
• 6 melanomas (2.6%) were confirmed as melanomas (0.4 mm mean thickness - +/- 0.2mm), 2 pigmented BCC
• Diagnostic accuracy of online compared with direct exam was 81% - sensitivity was 92.9%, spec 80.3%, PPV 23.2%, NPV 99.4%
• 70% participants said they would not have seen a dermatologist without the program
• “Was expensive and time consuming”
• Biased toward young people, concerned about health and familiar with technology
Humans WITH Machines

https://dermachallenge.meduniwien.ac.at/ham10000/
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
Thank You!

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