Sensitivity and Specificity of Emerging Technologies for Noninvasive Diagnosis of Melanoma

Jordon K. March[1], Austin J. Christensen[1], Ryan M. Dudley[1]

[1] School of Medicine, University of Nevada, Reno, NV, USA

INTRODUCTION

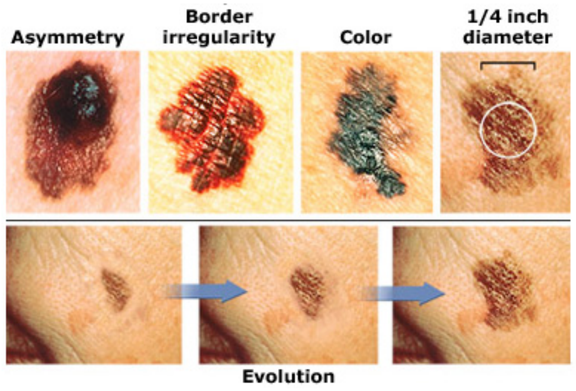
Biopsy remains the gold standard for establishing a melanoma diagnosis; however, many benign lesions are needlessly biopsied, which unnecessarily increases the healthcare costs and patient morbidity. The majority of melanomas can be easily detected by visual inspection, but some lesions (e.g., ambiguous pigmented lesions) can be much more difficult to identify and correctly diagnose. Therefore, there is a need for new technologies to assist in the clinical examination of pigmented lesions and detection of melanoma. This study examined the efficacy of several emerging technologies in the detection of melanoma.

POPULATION AT RISK

Melanoma has the highest mortality of all skin cancers and can affect individuals beginning as early as 19 years of age.[1,2] Melanoma is currently the 2nd most common cancer in individuals 19-25 years of age, while being the 5th most common new cancer diagnosis in men in the U.S. and 7th most common new cancer diagnosis in women in the U.S.[1,2] Incidence and mortality of melanoma in the United States is highest amongst Caucasians. The incidence of melanoma in 2011 for white individuals was 25-30/100,000 individuals and a mortality of 3.0-3.25/100,000. The 2nd most affected group with melanoma was Hispanics. Hispanic melanoma incidence was 2.5-5/100,000 and a mortality 0.25-0.5/100,000.[1] Risk factors for melanoma include fair skin (4 fold), red hair and blue eyes (2 fold), long periods of sun exposure (2 fold), multiple nevi, family history of melanoma, and blistering sunburns at a young age.[1,26]

METHODS

An exhaustive literature review was performed using the NCBI PubMed database. Search terms utilized were melanoma, electrical impedance, skin cancer, multi-spectral imaging, infrared imaging, dermatology mobile apps, teledermatology, SIAscopy, MelaFind, Nevisense, telehealth, and dermoscopy. No additional filters were used to aid in the review and no specific date range was used as criteria for inclusion. All studies that involved the detection or diagnosis of melanoma were noted. A large number of studies were reviewed, of which 23 studies were deemed relevant and were used in our analysis. Of the 23 studies, 6 analyzed mobile device applications, 10 analyzed devices that used multispectral imaging, and 7 examined electrical impedance spectroscopy. All studies included were clinical trials and thus are relevant and valid in addressing our hypothesis.



https://www1.ghc.org/html/public/specialties/cancer/melanoma-diagnosis.html

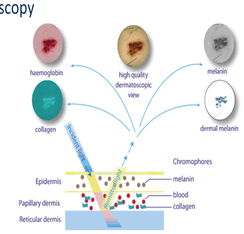
RESULTS

Table I. Noninvasive technologies and their performance in melanoma detection.

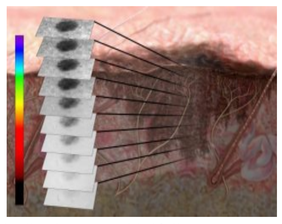
Technology	Approach	Study	Lesions	Melanomas	Sensitivity	Specificity	Level of evidence
Mobile apps							
	AA	Robson et al[3]	35*	2	50%	58%	Small sample size Image database Unable to analyze 40%
	AA	Ferrero et al[4]	93	93	11%	-	Small sample size Image database Unable analyze 10%
		Wolf et al[5]	188	60			
	AA				70%	40%	
	AA				69%	37%	
	AA				6.8%	94%	
	TD				98%	30%	
	TD	Massone et al[6]	18	2	100%	94%	Small sample size No mobile dermascope
	TD	Kroemer et al[7]	104	6	100%	97%	No mobile dermascope
	TD	Borve et al[8]	69	12	61%**	-	Small sample size Mobile dermascope No control for face-to-face
Multispectral Imaging							
SIAscopy							
		Moncrieff et al[9]	348	52	83%	80%	
		Haniffa et al[10]	881	31	87%	91%	No control
		Glud et al[11]	83	12	100%	59%	Small sample size
		Tomatis[12]	1391	184	80%	76%	Multi-center study
		Carrera[13]	1966	287	88%	80%	
MelaFInd							
		Elbaum et al[14]	246	63	95%	68%	Multi-center study
		Friedman et al[15]	99	49	98%	44%	Small sample size Reader study 10 expert dermatologists
		Monheit et al[16]	1632	127	98%	11%	39 dermatologists Failed to report on controls
		Wells et al[17]	47	23	96%	8%	Small sample size Reader study Always recommends biopsy
		Hauschild et al[18]	130	65	96%	9%	Reader study 130 dermatologists
Electrical Impedance Spectroscopy							
Nevisense							
		Glickman et al[19]	178	12	92%	67%	
		Har-Shal et al[20]	449	69	91%	64%	Failed to detect on head and neck
		Aberg et al[21]	511	16	100%	75%	
		Aberg et al[22]	99	13	92%	80%	Small sample size
		Aberg et al[23]	210	62	95%	49%	
		Mohr et al[24]					
	Algorithm 1		780	103	98%	24%	
	Algorithm 2		715	162	99%	25%	
		Malvehy et al[25]	1946	265	97%	34%	Multi-center study

AA, Automated analysis; TD, teledermatology. (*) Fourteen of 35 lesions could not be analyzed by the app. (**) Presented as diagnostic accuracy rather than sensitivity.

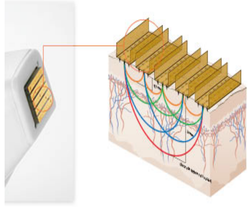
http://southernbeautyblog.com/tag/skin-care-2/



http://www.medxhealth.com/about-siascopy/



http://www.hautarzt-messer.de/melafind.htm



http://scibase.se/en/the-nevisense-product/the-eis-method/

CONCLUSIONS

Multiple emerging technologies have been developed to assist in the noninvasive diagnosis of malignant melanoma, which could potentially reduce the morbidity associated with biopsy. Detecting melanoma with some of the new technologies appears feasible, with teledermatology, MoleMate, and Nevisense holding the most promise. However, the current devices have significant limitations to their utilization. Additional randomized, controlled, clinical studies are suggested to further understand the limitations of each technology and to develop a strategy to overcome these barriers to clinical implementation. Until further studies are conducted, physicians should use noninvasive technologies with caution and continue to rely on biopsy as the "gold standard" for establishing a melanoma diagnosis.

Table II. Comparison of new generation non-invasive imaging devices

	MoleMate	MelaFind	Nevisense
Technology	MSI	MSI	EIS
Sensitivity	80-100% (μ = 87.6%)	95-98% (μ = 96.6%)	92-100% (μ = 95.5%)
Specificity	59-91% (μ = 77.2%)	8-68% (μ = 28%)	24-75% (μ = 52.25%)
Speed*	< 1 min	1-2 min	5-10 min
Approval	US, EU, and Canada	US and EU	EU and Australia
Cost	$6,000	Lease**	N/A

Note: Mole mate, MelaFInd, and Nevisense are trademarks of their respective manufacturers.
EU, European Union; N/A, not available; US, United States
* Approximate time to evaluate single lesion.
** 2013 leasing agreement stipulates $10,000 installation and training fee, $2000 annual renewal fee, plus charges per lesion or patient session.

REFERENCES

1. http://www.cancer.gov/researchandfunding/progress/snapshots/melanoma
2. http://www2.epa.gov/sites/production/files/documents/nv_facts_web.pdf
3. Robson Y, Blackford S, Roberts D. Caution in melanoma risk analysis with smartphone application technology. Br J Dermatol. 2012;167:703-704.
4. Ferrero NA, Morrell DS, Burkhart CN. Skin scan: a demonstration of the need for FDA regulation of medical apps on iPhone. J Am Acad Dermatol. 2013;68: 515-516.
5. Wolf JA, Moreau JF, Akilov O, et al. Diagnostic inaccuracy of smartphone applications for melanoma detection. JAMA Dermatol. 2013;149:422-426.
6. Massone C, Hofmann-Wellenhof R, Ahlgrimm-Siess V, Gabler G, Ebner C, Soyer HP. Melanoma screening with cellular phones. PLoS One. 2007;2:e483.
7. Kroemer S, Fruhauf J, Campbell TM, et al. Mobile teledermatology for skin tumour screening: diagnostic accuracy of clinical and dermoscopic image tele-evaluation using cellular phones. Br J Dermatol. 2011;164:973-979.
8. Borve A, Terstappen K, Sandberg C, Paoli J. Mobile teledermoscopy-there's an app for that!. Dermatol Pract Concept. 2013;3:41-48.
9. Moncrieff M, Cotton S, Claridge E, Hall P. Spectrophotometric intracutaneous analysis: a new technique for imaging pigmented skin lesions. Br J Dermatol. 2002;146:448-457.
10. Haniffa MA, Lloyd JJ, Lawrence CM. The use of a spectrophotometric intracutaneous analysis device in the real-time diagnosis of melanoma in the setting of a melanoma screening clinic. Br J Dermatol. 2007;156:1350-1352.
11. Glud M, Gniadecki R, Drzewiecki KT. Spectrophotometric intracutaneous analysis versus dermoscopy for the diagnosis of pigmented skin lesions: prospective, double-blind study in a secondary reference centre. Melanoma Res. 2009;19:176-179.
12. Tomatis S, Carrara M, Bono A, et al. Automated melanoma detection with a novel multispectral imaging system: results of a prospective study. Phys Med Biol. 2005;50:1675-1687.
13. Carrara M, Bono A, Bartoli C, et al. Multispectral imaging and artificial neural network: mimicking the management decision of the clinician facing pigmented skin lesions. Phys Med Biol. 2007;52:2599-2613.
14. Elbaum M, Kopf AW, Rabinovitz HS, et al. Automatic differentiation of melanoma from melanocytic nevi with multispectral digital dermoscopy: a feasibility study. J Am Acad Dermatol. 2001;44:207-218.
15. Friedman RJ, Gutkowicz-Krusin D, Farber MJ, et al. The diagnostic performance of expert dermoscopists vs a computer-vision system on small-diameter melanomas. Arch Dermatol. 2008;144:476-482.
16. Monheit G, Cognetta AB, Ferris L, et al. The performance of MelaFind: a prospective multicenter study. Arch Dermatol. 2011;147:188-194.
17. Wells R, Gutkowicz-Krusin D, Veledar E, Toledano A, Chen SC. Comparison of diagnostic and management sensitivity to melanoma between dermatologists and MelaFind: a pilot study. Arch Dermatol. 2012;148:1083-1084.
18. Hauschild A, Chen SC, Weichenthal M, et al. To excise or not: impact of MelaFind on German dermatologists' decisions to biopsy atypical lesions. J Dtsch Dermatol Ges. 2014;12: 606-614.
19. Glickman YA, Filo O, David M, et al. Electrical impedance scanning: a new approach to skin cancer diagnosis. Skin Res Technol. 2003;9:262-268.
20. Har-Shai Y, Glickman YA, Siller G, et al. Electrical impedance scanning for melanoma diagnosis: a validation study. Plast Reconstr Surg. 2005;116:782-790.
21. Aberg P, Nicander I, Hansson J, Geladi P, Holmgren U, Ollmar S. Skin cancer identification using multifrequency electrical impedanceea potential screening tool. IEEE Trans Biomed Eng. 2004;51:2097-2102.
22. Aberg P, Geladi P, Nicander I, Hansson J, Holmgren U, Ollmar S. Non-invasive and microinvasive electrical impedance spectra of skin cancer - a comparison between two techniques. Skin Res Technol. 2005;11:281-286.
23. Aberg P, Birgersson U, Elsner P, Mohr P, Ollmar S. Electrical impedance spectroscopy and the diagnostic accuracy for malignant melanoma. Exp Dermatol. 2011;20: 1392 648-652.
24. Mohr P, Birgersson U, Berking C, et al. Electrical impedance spectroscopy as a potential adjunct diagnostic tool for cutaneous melanoma. Skin Res Technol. 2013;19: 1395 75-83.
25. Malvehy J, Hauschild A, Curiel-Lewandrowski C, et al. Clinical performance of the Nevisense system in cutaneous melanoma detection: an international, multi-centre, prospective and blinded clinical trial on efficacy and safety. Br J Dermatol. 2014;171:1099-1107.
26. Goodson AG, Grossman D. Strategies for early melanoma detection: approaches to the patient with nevi. J Am Acad Dermatol. 2009;60:719-735.