

# MELA<sup>TM</sup>

Sciences

## MelaFind® Package Insert.

### By Prescription Only

**CAUTION:** Federal (USA) law restricts this device to sale by or on the order of a licensed dermatologist. Before using MelaFind®, thoroughly read the following information, as well as the MelaFind® User guide.

### DEVICE DESCRIPTION

MelaFind is a multi-spectral, non-invasive and automated (objective) computer-vision system that captures images of pigmented skin lesions and classifies them based upon degree of 3-dimensional morphological disorganization: MelaFind Positive (high degree of morphological disorganization) or MelaFind Negative (low degree of morphological disorganization). MelaFind consists of:

- A hand-held imager that for every skin lesion acquires 10 multi-spectral [from 430 nm (blue) to 950 nm (near infrared)] digital images (1280 × 1024 pixels) using 91% isopropyl alcohol for refractive index matching;
- A password-protected computer connected to the imager;
- A monitor for displaying multi-spectral and reconstructed Red Green Blue (RGB) digital images of clinically atypical pigmented skin lesions and MelaFind results;
- A removable media for storing acquired images and MelaFind results;
- Fixed algorithms for automatic image analysis:
  1. **calibration algorithms** that reduce noise and artifacts in the images and determine the diffuse reflectance (the fraction of the incident light that is reflected) of skin and lesions relative to a target of known reflectance;
  2. **image quality control algorithms** that automatically detect problems (overexposure, underexposure, lesion too big, lesion too small, too much hair on the lesion, too many bubbles on the lesion, motion of the hand-held imager during imaging, etc) and, when appropriate, request the operator to re-image the lesion; only images that pass these algorithms are accepted for further processing and are considered evaluable;
  3. **lesion segmentation algorithm** that identifies image pixels that belong to the lesion;
  4. **feature extraction algorithms** that compute parameters characterizing lesions;
  5. **lesion classification algorithm** that differentiates lesions with high level of 3-dimensional morphological disorganization (MelaFind Positive) from lesions with low level of disorganization (MelaFind Negative).

MELA Sciences conducted pre-pivotal studies designed to develop a classification algorithm that would have a high sensitivity to the positive class of lesions (malignant melanoma and high grade) with a high biopsy specificity. These algorithms were tested prospectively in pivotal clinical study, Protocol 20061.

## INDICATIONS FOR USE

MelaFind is intended for use on clinically atypical cutaneous pigmented lesions with one or more clinical or histological characteristics of melanoma, excluding those with a clinical diagnosis of melanoma or likely melanoma. MelaFind is designed to be used when a dermatologist chooses to obtain additional information for a decision to biopsy. MelaFind should NOT be used to confirm a clinical diagnosis of melanoma.

MelaFind is only for use by physicians trained in the clinical diagnosis and management of skin cancer (i.e., dermatologists) who have also successfully completed a training program in the appropriate use of MelaFind.

The MelaFind result is one element of the overall clinical assessment. MelaFind Positive lesions (which may include malignant melanoma, melanoma *in situ*, high grade dysplastic nevi and atypical melanocytic proliferation/hyperplasia) should be considered for biopsy; the biopsy decision of a MelaFind Negative lesion should be based on the remainder of the entire clinical context. Lesions that are “non-evaluable” by MelaFind should be carefully re-evaluated for biopsy.

MelaFind is indicated only for use on lesions with a diameter between 2 mm and 22 mm, lesions that are accessible by the MelaFind imager, lesions that are sufficiently pigmented (i.e. not for use on non-pigmented or skin-colored lesions), lesions that do not contain a scar or fibrosis consistent with previous trauma, lesions where the skin is intact (i.e., non-ulcerated or non-bleeding lesions), lesions greater than 1 cm away from the eye, lesions which do not contain foreign matter, and lesions not on special anatomic sites (i.e., not for use on acral, palmar, plantar, mucosal, or subungual areas). MelaFind is not designed to detect pigmented non-melanoma skin cancers, so the dermatologist should rely on clinical experience to diagnose such lesions.

## CONTRAINDICATIONS

None

## WARNINGS

- **DO NOT USE MELAFIND FOR SCREENING** - MelaFind is not a screening device. MelaFind should be used in conjunction with dermatological clinical expert assessment. See Indications for Use section.
- A MelaFind Negative reading does not eliminate the possibility that the lesion might be or evolve into a melanoma. See Clinical Studies section.
- In pivotal study (Protocol 20061), 3 of 175 pathologically confirmed lesions including melanoma, melanoma *in situ*, high grade dysplastic nevi and atypical melanocytic proliferation / hyperplasia were classified by MelaFind as MelaFind Negative. There is a potential for MelaFind to not detect all malignant or high grade lesions.
- In MelaFind training, non-melanoma skin cancers are classified as MelaFind Negative. Therefore, MelaFind Negative lesions must be evaluated appropriately in order to rule out non-melanoma skin cancers.
- Careful clinical reassessment should be given to those lesions that are non-evaluable by MelaFind as to whether the lesion should be biopsied.
- MelaFind use data represent thin melanomas (*in situ* or thinner than 1 mm), not thicker or ulcerated melanomas (T2 – T4).

## PRECAUTIONS

- Safety and effectiveness of MelaFind use has not been assessed or established in the following:
  - The lesion is not pigmented;
  - The lesion pigmented area diameter is < 2 mm or > 22 mm;
  - The lesion is not clinically atypical;
  - The patient has a known allergy to isopropyl alcohol;
  - The lesion has been previously biopsied, excised, or traumatized;
  - The lesion and surrounding skin are not intact (e.g., open sores, ulcers, bleeding);
  - The lesion is within 1 cm of the eye;
  - The lesion is on mucosal surfaces (e.g., lips, genitals);
  - The lesion is on the palms or soles;
  - The lesion is on or under the nails;
  - The lesion is located on or near an area of visible scarring;
  - The lesion contains foreign matter (e.g., tattoo, splinter, marker);
  - The lesion is inaccessible to the MelaFind imager;
  - In practices with management that includes option for lesion follow-up as well as biopsy;
  - With repeated MelaFind use on the same lesion within any time interval or by any user; or
  - In patients with Fitzpatrick Skin Type 5 and 6.
- Use of the MelaFind device is restricted to physicians trained in the clinical diagnosis and management of skin cancer who have also successfully completed a training program in the appropriate use of MelaFind.
- There is a potential for MelaFind Positives to include benign lesions as malignant or high grade.
- MelaFind requires periodic monitoring to verify system functionality through a mandatory self-test. If MelaFind does not pass the scheduled self-test, it will not permit further evaluation of clinically atypical pigmented skin lesions until it successfully passes the self-test. In the event of an unsuccessful self-test, any lesions evaluated with MelaFind during the period following the last successful self-test that were not biopsied should be considered for re-examination by the dermatologist.
- The 91% isopropyl alcohol used for lesion preparation and imaging procedures may cause skin irritation.
- There is a potential for nicking the skin if shaving is used in preparation for imaging. This could produce blood in the intended imaging site that would interfere with MelaFind imaging.

## SUMMARY OF CLINICAL STUDIES

MelaFind was developed, trained, and tested in six clinical studies, which enrolled a total of 9439 images of 9078 lesions from 6931 patients, including 630 melanomas, at 40 clinical study sites in the United States and broad over seven years. Five of these – Protocols 20011, 20012, RCP2007-05, 20031-A, and 20031-B – were e-pivotal clinical studies to develop the automatic MelaFind image analysis algorithms. The last, Protocol 20061, was the pivotal trial to evaluate the safety and effectiveness of MelaFind.

**SUMMARY OF PIVOTAL CLINICAL STUDY: PROTOCOL 20061**

**Design:** Protocol 20061 was a prospective pivotal clinical study designed for enrollment to proceed until at least 3 eligible and evaluable histologically confirmed melanomas were enrolled among lesions receiving dermatological diagnosis of either “melanoma cannot be ruled out” or “not melanoma”, with a minimum total number of lesions of 1200 for evaluating sensitivity and specificity to determine safety and effectiveness of MelaFind.

**Procedure:** Complete clinical histories, including risk factors for melanoma, were obtained. A lesion was included if the lesion was pigmented (i.e., contains melanin, keratin, or blood), the pigmented area diameter was between 2 and 22 mm, the lesion was accessible to the MelaFind imager, the examining dermatologist clinical management decision was to either biopsy *in toto* or follow-up in 3 months, and the patient signed the Informed Consent to participate in this study. A lesion was excluded if the lesion was on skin that was not intact (e.g., open sores, ulcers, bleeding), within 1 cm of the eye, on mucosal surfaces (e.g., lips, genitals), on palmar hands, on plantar feet, under nails, or on an area of visible scarring, previous biopsy, excision, trauma or containing foreign matter (e.g., tattoo, splinter, marker). Three high resolution digital photographs of the lesions were obtained – two clinical views (from 21 inches and 8 inches away) and a dermoscopic image – using standard cameras. Enrolled lesions were assessed by MelaFind as (1) Positive or (0) Negative and by dermatologists masked to MelaFind output, based upon clinical and dermoscopic (if performed) pre-biopsy diagnosis as definite melanoma - F2 cohort (100% likely melanoma), melanoma cannot be ruled-out - F3 cohort (likely melanoma, 67-99%; possible melanoma, 34-66%; and unlikely melanoma, 1-33%), and not melanoma - F4 cohort (0% likely melanoma) and by dermatopathologists with histologic diagnosis of biopsy specimens using the schema described in Figure 1.

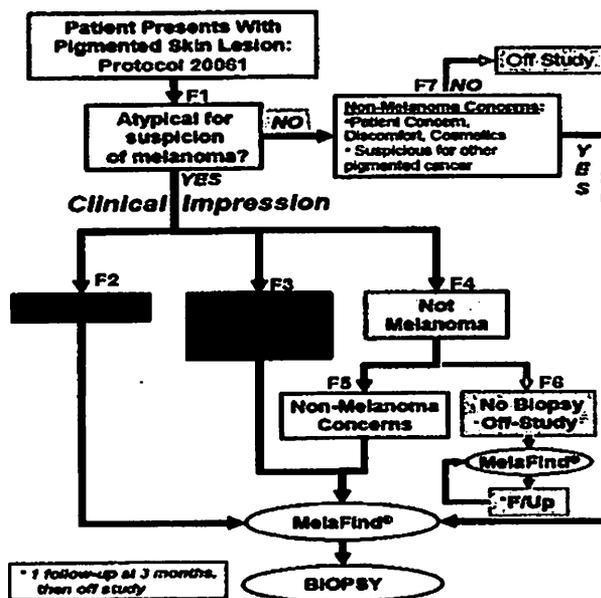


Figure 1: Population Schema

All study lesions were biopsied; no study lesions were followed to assess lesion change with time (evolution). Biopsies were reviewed by at least two central dermatopathologists; the positive class of lesions consisted of melanomas (*in situ* and invasive), and high grade lesions (high grade dysplastic nevi, atypical melanocytic proliferation/hyperplasia). Breslow thicknesses of invasive melanomas were recorded.

**Outcomes:** A total of 1831 pigmented skin lesions from 1383 patients (age: 7 to 97 years, median 47 years; gender: 638 male and 745 female) were enrolled at 7 clinical (3 academic and 4 community) geographically

diverse sites in the US with 21 board certified dermatologists and 2 physician assistants. Lesion accounting is in Table 1.

Table 1. Protocol 20061: Lesion Accounting

<b>Total Lesion Registration</b>		<b>1835</b>
<b>Mis-Registrations</b>		<b>4</b>
	Demo lesion enrolled as real patient – Invalid data point	2
	Wrong lesion imaged – Invalid data point	1
	Duplicate lesion registration – Invalid data point	1
<b>Lesions Enrolled</b>		<b>1831</b>
	Patient withdrew from Study	1
<b>Lesions Enrolled and Not Withdrawn</b>		<b>1830</b>
<b>Determined to be ineligible due to violation of inclusion/exclusion criteria</b>		<b>3</b>
	Patient did not sign Informed Consent Form	2
	Lesion was previously biopsied excised or traumatized	1
<b>Determined to be ineligible during central dermatohistopathology</b>		<b>14</b>
	Lesion biopsied but biopsy not in toto	1
	Lesion was not pigmented	1
	Lesion biopsied but biopsy not in toto; Lesion was not pigmented	1
	Lesion contained dermal scar/fibrosis consistent with previous trauma	11
<b>Eligible Lesions</b>		<b>1813</b>
<b>Determined to be non-evaluable due to CRF or dermatohistopathology</b>		<b>19</b>
	Slides not received, or received late	16
	Slides not received, or received late; MelaFind image not acquired	1
	Slides not received, or received late; Image disqualified by MelaFind quality control algorithms	1
	Inadequate histology – poorly prepared slide not prepared	1
<b>Eligible Lesions with CRF and Reference Standard (RefStd)</b>		<b>1794</b>
<b>Determined to be non-evaluable due to unsuccessful imaging attempts</b>		<b>162</b>
	Irretrievable electronic data loss – eCRF, MelaFind images, clinical images	4
	MelaFind image not acquired	9
	Phantom self-test failure	7
	Phantom self-test failure; Image disqualified by MelaFind quality control algorithms	2
	Image disqualified by MelaFind quality control algorithms	14
		0
<b>Eligible and Evaluable</b>		<b>1632</b>

Of the 1831 lesions enrolled, 1632 lesions considered to be eligible and evaluable for analysis. Table 2 presents lesion demographics for Protocol 20061.

Table 2. Protocol 20061: Lesion Demographics

Demographics		All Enrolled Subject Population			
		Atypical			All Pigmented Lesions
		Melanoma (F2)	Melanoma Cannot Be Ruled Out (F3)	Not melanoma (F4)	All Populations ***
<b>N, Lesions from Patients Enrolled</b>		25	1702	103	1831
<b>Gender*</b>	Female	11	920	61	993
	Male	14	782	42	838
<b>Age*</b>	< 21 years	0	102	5	107
	21 - 55 years	13	1082	46	1142
	> 55 years	12	518	52	582
<b>Anatomic Location*</b>	Face	1	51	7	59
	Posterior Torso	7	745	34	787
	Anterior Torso	0	358	18	376
	Extremity: Arm/ Leg	16	491	30	537
	Neck	0	32	8	40
	Scalp	1	25	6	32
<b>Fitzpatrick Skin Type*</b>	I	3	112	2	117
	II	11	897	73	981
	III	8	610	24	642
	IV	3	75	3	82
	V	0	5	1	6
	VI	0	3	0	3
<b>Geographic Sites**, Patients*</b>	US - sun belt	22	1349	88	1459
	US - non-sun belt	3	353	15	372
	Non - US	0	0	0	0

\*Table presents total lesion counts. Patients who contributed more than one lesion to the study are represented in more than one population when those lesions occur in more than one population.

\*\*Geographic sites were tabulated based on clinical study site. US - sun belt included Alabama, California, Florida, and North Carolina. US - non-sun belt included Pennsylvania and Illinois. All clinical study sites were in the US.

\*\*\*Total eligible and evaluable lesions include 1 lesion from the Not Atypical for suspicion of Melanoma (F7)

Prevalence of clinical and historical characteristics of melanoma among eligible and evaluable lesions in the pivotal study is shown in Table 3. Classic characteristics such as ABC (asymmetry, border irregularity, and color variegation) have high sensitivities (over 80%) to positive lesions (melanoma and high-grade). About 30% of positive and 60% of negative lesions were small (diameter < 6 mm). Three melanomas were identified only as “ugly ducklings”, i.e., these melanomas had no ABCDE characteristics. Eleven of 1632 lesions did not have any of these characteristics and these were all benign.

**Table 3. Protocol 20061: Prevalence of Clinical and Historical Characteristics of Melanoma Among Eligible and Evaluable Lesions**

Lesion ABCDEPRU Criteria	Atypical						Not Atypical	
	Melanoma (F2)		Melanoma Cannot Be Ruled Out (F3)		Not melanoma (F4)		Non-atypical pigmented lesion (F7)	
N, Eligible and Evaluable Lesions	20		1528		83		1	
ABCDEPRU n (# recorded); N (# pt = # lesion) % = n / N	n	%	n	%	n	%	n	%
Asymmetry: when one half of the mole does not match the other half	19	95% (19/20)	1202	78.7% (1202/1528)	36	43.4% (36/83)	0	0% (0/1)
Border: when the edges of the mole are ragged or irregular	19	95% (19/20)	1142	74.7% (1142/1528)	35	42.2% (35/83)	0	0% (0/1)
Color: when the color of the mole varies throughout	18	90% (18/20)	1188	77.8% (1188/1528)	45	54.2% (45/83)	0	0% (0/1)
Diameter: if mole's diameter is larger than a pencil eraser (> 6mm)	17	85% (17/20)	620	40.6% (620/1528)	40	48.2% (40/83)	0	0% (0/1)
Evolving: changing size, shape or color over a short period of time	14	70% (14/20)	487	31.9% (487/1528)*	39	47% (39/83)	0	0% (0/1)
Patient concern	11	55% (11/20)	481	31.5% (481/1528)	69	83.1% (69/83)	0	0% (0/1)
Regression: areas of hypo- or depigmentation, sometimes resulting in scar-like white or blue grey areas	4	20% (4/20)	85	5.6% (85/1528)	1	1.2% (1/83)	0	0% (0/1)
Ugly duckling: distinct from other nevi on the same patient	14	70% (14/20)	693	45.4% (693/1528)	27	32.5% (27/83)	0	0% (0/1)
Number of ABCDEPRU criteria per patient lesion)								
1	0	0% (0/20)	72	4.7% (72/1528)	14	16.9% (14/83)	0	0% (0/1)
2	2	10% (2/20)	180	11.8% (180/1528)	12	14.5% (12/83)	0	0% (0/1)
3	0	0% (0/20)	392	25.7% (392/1528)	16	19.3% (16/83)	0	0% (0/1)
4	2	10% (2/20)	403	26.4% (403/1528)	16	19.3% (16/83)	0	0% (0/1)
5	2	10% (2/20)	243	15.9% (243/1528)	15	18.1% (15/83)	0	0% (0/1)
6	6	30% (6/20)	147	9.6% (147/1528)	3	3.6% (3/83)	0	0% (0/1)
7	6	30% (6/20)	67	4.4% (67/1528)	7	8.4% (7/83)	0	0% (0/1)
8	2	10% (2/20)	14	0.9% (14/1528)	0	0% (0/83)	0	0% (0/1)
0	0	0% (0/20)	10	0.7% (10/1528)	0	0% (0/83)	1	100% (1/1)

Table 4 is a summary table of biopsy sensitivity and specificity based on Protocol 20061.

Table 4. Summary of Pivotal Trial Demonstrating the Safety and Effectiveness of MelaFind®

	MelaFind®	Dermatologists
<b>Biopsy Sensitivity</b> (n = 175 melanomas <sup>a</sup> and high grade lesions <sup>b</sup> )	172/175 - 98.3% (95.1% lcb) <sup>c</sup>	NA <sup>d</sup>
<b>Biopsy Specificity</b> (n = 1457 negative lesions)	<i>Overall Pooled<sup>e</sup></i>	
	157/1457 (10.8%)	82/1457 (5.6%)
	p = NA <sup>e</sup>	
	<i>Average</i>	
	9.9%	3.7%
<b>Biopsy Ratio (false positives : true positives)</b>	1300:172 = 7.6:1	1375:175 = 7.9:1
	p < 0.01 <sup>f</sup>	
<sup>a</sup> 127 melanomas (57 <i>in situ</i> ; 70 invasive – median Breslow thickness 0.36 mm, range 0.12 to 1.2 mm) <sup>b</sup> 48 high grade lesions (43 high grade dysplastic nevi; 5 atypical melanocytic proliferation/hyperplasia) <sup>c</sup> Statistical significance at > 95% lcb (lower confidence bound) <sup>d</sup> Dermatologist sensitivity cannot be measured since only lesions selected for biopsy by the investigating dermatologist were enrolled and does not include all possible candidate lesions per subject. <sup>e</sup> Overall pooled biopsy specificity is the sum of true negative lesions divided by the sum of all negative lesions (true negatives + false positives) for all investigators; p < 0.0001 assumes the same specificity across investigators <sup>f</sup> 75 fewer false positives for MelaFind®		

Based upon dermatopathology, Protocol 20061 evaluated the performance of MelaFind based on all eligible and evaluable lesions selected for biopsy by the investigating dermatologist, which does not include all possible candidate lesions per subject. Sensitivity of MelaFind to detect melanomas (*in situ* and invasive), and high grade lesions (high grade dysplastic nevi, atypical melanocytic proliferation/hyperplasia) in the population of study lesions was 98.3% (172/175) with a two-sided 95% lower confidence bound of 95.1%. One melanoma *in situ*, one invasive melanoma (Breslow thickness 0.28 mm) and one high grade lesion were not detected by MelaFind. MelaFind correctly identified 157/1457 (10.8%) dermatopathology negative lesions compared to dermatologist investigators who correctly identified 82/1457 (5.6%) negative class lesions; the difference was statistically significant (p < 0.01).

Of the 1632 eligible and evaluable lesions, 175 were dermatopathologically positive lesions (melanoma or high grade), 1457 were dermatopathologically negative lesions. Of the 1632 eligible and evaluable lesions, 1472 were MelaFind Positive and 160 were MelaFind Negative. Of the 1472 MelaFind Positive lesions, 172 were positive by dermatopathology - 56 melanomas *in situ*, 70 invasive melanomas with a median Breslow thickness of 0.36 mm (range 0.12 to 1.2 mm), and 42 high grade dysplastic nevi and 4 atypical melanocytic proliferation/hyperplasia). Table 5 presents MelaFind output among all eligible and evaluable lesions in Protocol 20061 according to lesion characteristics sub-divided by the initial study dermatologist's pre-biopsy diagnosis of definite melanoma (F2), melanoma cannot be ruled-out (F3), and not melanoma (F4). Lesions categorized as F2 and F3 are considered dermatologist positive and F4 as dermatologist negative.

Table 5. Protocol 20061: Eligible and Evaluable Lesion Population

Lesion Assessment per Dermatologists, MelaFind Dermatopathology		Population									
		Atypical						All Pigmented Lesions			
		Melanoma (F2)	Melanoma Cannot Be Ruled Out (F3)		Not melanoma (F4)		All Populations				
N, Lesions Enrolled		25	1702		103		1831				
N, Lesions Biopsied		25	1702		103		1831				
N, Eligible and Evaluable Lesions		20	1528		83		1632				
N <sup>3</sup>	DP	MelaFind Result <sup>1</sup> =	1	0	1	0	1	0	Total <sup>2</sup>		
		By Dermatologist (MD)	20	0	1528	0	0	83	1632		
		By MelaFind (MF)	20	0	1383	145	68	15	1632		
		By Dermatopathology (DP)	14	6	159	1369	2	81	1632		
		MM <sup>4</sup> Type	in situ	4	NA	52	NA	1	NA	57	
				Invasive	9	NA	61	NA	0	NA	70
			Breslow Thickness	< 1 mm	8	NA	60	NA	0	NA	68
				1 - 2 mm	1	NA	1	NA	0	NA	2
				2.1 - 4 mm	0	NA	0	NA	0	NA	0
		> 4 mm	0	NA	0	NA	0	NA	0		
		HGDN	1	NA	41	NA	1	NA	43		
		AMP/AMH	0	NA	5	NA	0	NA	5		
		Dysplastic nevi, low grade	NA	5	NA	978	NA	15	998		
		Other nevi	NA	0	NA	189	NA	28	218		
		Non-melanoma skin cancers	NA	0	NA	23	NA	10	33		
		Other non-melanocytic lesions	NA	1	NA	179	NA	28	208		
		by DP & MD & MF		NA	0	NA	0	NA	15	15	
by DP & MD & not MF		NA	0	3	0	NA	66	70			
by DP & MF & not MD		NA	0	NA	142	NA	0	142			
by DP & not MF & not MD		NA	6	NA	1227	NA	0	1233			
by DP & MD		NA	0	NA	0	NA	81	82			
by DP & MF		14	0	156	142	2	15	329			

<sup>1</sup> MelaFind 1 = MM/HGDN/AMP/AMH, MelaFind 0 = Not MM/HGDN/AMP/AMH  
<sup>2</sup> Total eligible and evaluable lesions include 1 lesion from the Not Atypical for suspicion of Melanoma (F7)  
<sup>3</sup> Number of lesions, <sup>4</sup> Melanomas

Of the 1831 enrolled lesions, 162 lesions were deemed to be non-evaluable. Dermatopathology identified 205 of the total enrolled lesions as melanoma and high grade of which 30 were found non-evaluable by MelaFind. Lesion non-evaluability was due to investigator, operator, and MelaFind errors which are shown in Table 6. Overall, 30 (14.6%) of positive lesions and 132 (8.3%) of negative lesions were not evaluable.

Table 6. Protocol 20061: Non-Evaluable Lesions

Reason for Non-Evaluability	Melanomas and high grade lesions Number of cases (% of all cases = 205)	Other lesions Number of cases (% of all cases = 1589)
Investigator errors (non-eligible lesions)	6 (2.9%)	30 (1.9%)
Operator errors (bubble, hair, etc)	11 (5.4%)	60 (3.8%)
MelaFind errors (images not acquired, etc)	13 (6.3%)	42 (2.6%)
All errors	30 (14.6%)	132 (8.3%)

Table 7 reports specific dermatopathology for eligible and evaluable melanomas, including melanomas *in situ*.

Table 7. Protocol 20061: Eligible and Evaluable Melanomas

Melanoma Type (N = 127)		
Melanoma invasive	n = 70	55.1%
Superficial Spreading	60	85.7%
Lentigo Maligna Melanoma	7	10.0%
Nodular	2	2.9%
Unclassified	1	1.4%
Melanoma in situ	n = 57	44.9%
Superficial Spreading	31	54.4%
Lentigo Maligna	25	43.9%
Unclassified	1	1.8%

Table 8 summarizes data on Breslow thickness of eligible and evaluable invasive melanomas in the pivotal study. Almost all melanomas in the pivotal clinical study were early lesions that can be successfully treated with surgical excision, but may be difficult to differentiate from benign look-alikes.

Table 8. Protocol 20061: Eligible and Evaluable Invasive Melanoma – Breslow Thickness

Breslow Thickness	n = 70
Mean	0.41 mm
Std. Deviation	0.20 mm
Median	0.36 mm
Range	0.12 – 1.2 mm
Number of Lesions <1 mm	68 (97.1%)
Number of lesions 1 - 2 mm	2 (2.9%)
Number of lesions 2.1 – 4 mm	0
Number of lesions >4 mm	0

Table 9 compares dermatological categorization and the histological reference standard for all eligible and evaluable lesions. Most histologically verified melanomas were diagnosed prior to biopsy as “Melanoma cannot be ruled out”; about a third of melanomas were considered unlikely (likelihood between 1 and 33%). Study investigators enrolled these lesions based upon inclusion/exclusion criteria including management plan for lesion excision *in toto*. Inclusion/exclusion criteria were not based upon dermatologist categorization of the likelihood of lesion to be melanoma (*in situ*, invasive), high grade dysplastic nevus or atypical melanocytic proliferation or hyperplasia.

Table 9. Protocol 20061: Eligible and Evaluable Lesions by Dermatological and Histological Diagnoses

Dermatological Diagnosis	Histological Diagnosis		
	MM	HGDN*	OTHER
Melanoma	13	1	6
Melanoma Can Not Be Ruled Out			
Likely melanoma (67-99%)	30	4	46
Possible melanoma (34-66%)	44	14	471
Unlikely melanoma (1-33%)	38	27	827
Not Melanoma			
Clinical concern (dermoscopy only)	1	1	27
Non-melanoma skin cancer	0	0	13
Patient’s concern	1	1	55
Physical discomfort	0	0	8
Cosmetic purposes	0	0	4
<b>Total</b>	<b>127</b>	<b>48</b>	<b>1457</b>
*Also includes AMP and AMH			

Of the 1632 eligible and evaluable lesions, 645 had dermoscopic evaluations. Table 10 reports prevalence of dermoscopic characteristics of these 645 lesions.

**Table 10. Protocol 20061: Eligible and Evaluable Lesions, Dermoscopic Characteristics Prevalence by Dermatopathology**

Dermoscopic Characteristic	Histological Diagnosis		
	Any (n = 645)	MM/HGDN* (n = 88)	Non- MM/HGDN* (n = 557)
<b>Multicomponent pattern</b>	184 (28.5%)	29 (33.0%)	155 (27.8%)
<b>Streaks/pseudopods</b>	41 (6.4%)	11 (12.5%)	30 (5.4%)
<b>Blue-white veil</b>	34 (5.3%)	6 (6.8%)	28 (5.0%)
<b>Branched streaks</b>	59 (9.1%)	11 (12.5%)	48 (8.6%)
<b>Asymmetry</b>	395 (61.2%)	62 (70.5%)	333 (59.8%)
<b>Multiple colors</b>	430 (66.7%)	66 (75.0%)	364 (65.4%)
<b>Regression structures/peppering</b>	97 (15.0%)	27 (30.7%)	70 (12.6%)
<b>Atypical dots/globules</b>	162 (25.1%)	24 (27.3%)	138 (24.8%)
<b>Atypical network</b>	242 (37.5%)	41 (46.6%)	201 (36.1%)
<b>Atypical vasculature</b>	40 (6.2%)	8 (9.1%)	32 (5.7%)
<b>Border sharpness</b>	63 (9.8%)	8 (9.1%)	55 (9.9%)
<b>Scar-like depigmentation</b>	37 (5.7%)	12 (13.6%)	25 (4.5%)
<b>*Includes diagnoses of Atypical Melanocytic Proliferation/Hyperplasia (AMP/AMH)</b>			

Melanoma risk factors among patients with eligible and evaluable lesions in the pivotal study are shown in Table 11. Over 30% of patients had a history of dysplastic nevi, 17% had a personal history of melanoma, over 20% had a family history of melanoma, and about 15% had more than 50 nevi. However, of 127 patients with eligible and evaluable melanomas, 57 (45%) had none of these factors.

Table 11. Protocol 20061: Eligible and Evaluable Lesions, Melanoma Risk Factors

Melanoma Risk Factor	Histological Diagnosis						
	Any (n = 1632)		MM/HGDN (n = 175)		Non-MM/HGDN** (n = 1457)		
	Prevalence (%)	No. of Responses	Prevalence (%)	No. of Responses	Prevalence (%)	No. of Responses	
Personal history of basal cell carcinoma	21.0	1612	33.5	173	19.5	1439	
Personal history of squamous cell carcinoma	13.5	1611	26.0	173	12.0	1438	
Personal history of dysplastic nevi	36.0	1567	26.2	172	37.2	1395	
Personal history of melanoma	18.9	1619	24.7	174	18.2	1445	
Family History of Melanoma	25.1	1507	25.3	162	25.1	1345	
Fitzpatrick Skin Type	I	6.5	1632	5.7	175	6.6	11457
	II	53.7		65.7		52.3	
	III	35.2		26.9		36.2	
	IV	4.2		1.7		4.5	
	V	0.2		0.0		0.3	
	VI	0.1		0.0		0.1	
Natural red/blond hair	39.5	1632	49.1	175	38.4	1457	
Blue/Green Eyes	67.8	1632	73.1	175	67.1	1457	
Sunburns prior to age 20	0	13.9	1599	13.6	169	14.0	1430
	1-2	26.5		24.3		26.7	
	3-4	14.6		11.2		15.0	
	≥5	45.0		50.9		44.3	
Sunburns after age 20	0	32.2	1537	34.7	167	31.9	1370
	1-2	33.1		32.9		33.1	
	3-4	12.4		7.2		13.0	
	≥5	22.4		25.1		22.0	
Outdoor summer jobs as a teenager	42.0	1618	43.9	173	41.8	1445	
Nevi ≥ 2mm	0	0.1	1632	0.6	175	0.1	1457
	1-10	37.4		51.4		35.7	
	11-30	30.5		22.3		31.4	
	31-50	14.8		10.9		15.3	
	>50	17.2		14.9		17.5	
Atypical Pigmented Skin Lesions	0	1.2	1632	0.6	175	1.3	1457
	1	47.5		67.4		45.2	
	2	21.4		16.6		22.0	
	3	7.7		4.0		8.1	
	4	4.5		1.7		4.9	
	>4	17.6		9.7		18.5	
Use of Tanning Beds	0	56.3	1632	65.7	175	55.2	1457
	1-10	17.6		11.4		18.3	
	11-24	9.3		10.9		9.1	
	>24	16.8		12.0		17.4	
History of UVA/UVB Treatment	3.7	1632	2.9	175	3.8	1457	

\*Excludes entries of "Unknown" or "n/a"

Anatomic sites for eligible and evaluable lesions in the pivotal study are shown in Table 12. The majority of lesions were from the trunk.

Table 12. Protocol 20061: Eligible and Evaluable Lesions, Anatomic Sites

Anatomic Site	Histologic Diagnosis		
	Any (N = 1632)	MM/HGDN* (N = 175)	Non- MM/HGDN* (N = 1457)
Head/neck	84 (5.1%)	24 (13.7%)	60 (4.1%)
Trunk	1074 (65.8%)	93 (53.1%)	981 (67.3%)
Upper limbs	227 (13.9%)	34 (19.4%)	193 (13.2%)
Lower limbs	247 (15.1%)	24 (13.7%)	223 (15.3%)
*Includes diagnoses of Atypical Melanocytic Proliferation/Hyperplasia			

Age distribution of patients with eligible and evaluable lesions in the pivotal study is shown in Table 13. Majority of melanomas were from adult patients; seven melanomas (all correctly identified by MelaFind) were from pediatric patients, with age ranging from 11 to 20 years. Ninety eight eligible and evaluable lesions in patients under the age of 21, including 7 melanomas, were enrolled; MelaFind detected all 7 melanomas in patients under the age of 21.

Table 13. Protocol 20061: Eligible and Evaluable Lesions, Subject Age Distribution

Age (years)	Histologic Diagnosis		
	Any (N = 1632)	MM/HGDN* (N = 175)	Non- MM/HGDN* (N = 1457)
0 - 20	98 (6.0%)	7** (4.0%)	91 (6.2%)
21 - 64	1268 (77.7%)	106 (60.6%)	1162 (79.8%)
65 +	266 (16.3%)	62 (35.4%)	204 (14.0%)
*Includes diagnoses of Atypical Melanocytic Proliferation/Hyperplasia ** MelaFind correctly identified all 7 melanomas enrolled on patients < 21			

**POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH**

Potential adverse effects for MelaFind are associated with incorrect test results or result interpretations. Failure of this device to perform as expected or failure to correctly interpret results may lead to incorrect diagnoses and subsequently, improper patient management decisions in melanoma cancer biopsy and treatment. False negative results may lead to delays in the timely diagnosis of melanoma cancer and treatment, allowing an undetected condition to worsen and potentially increasing morbidity and mortality. False positive results could lead to patients unnecessarily undergo more frequent screening and potentially invasive procedures such as skin biopsy.

**SUMMARY OF READER STUDIES**

Investigator sensitivity could not be determined on the pivotal trial since all eligible and evaluable lesions were selected for biopsy by the investigating dermatologist, which does not include all possible candidate lesions per subject; therefore, two reader studies were conducted to estimate the biopsy sensitivity of dermatologists.

**Reader studies.** A pilot reader study (Protocol 20081) of 50 randomly-selected pigmented skin lesions from Protocol 20061 with 39 dermatologist readers showed 80% biopsy sensitivity for dermatologists with a kappa score of 0.22. Thereafter, to assess and compare the biopsy sensitivity and specificity of MelaFind, to the average biopsy/referral sensitivity and specificity of expert and general dermatologists as well as primary care physicians who did not participate in the pivotal clinical study under Protocol 20061, a prospective, randomized, and investigator blinded web-based reader study under Protocol 20063 was conducted electronically. In this reader study, randomly-selected Protocol 20061 lesions were evaluated by physicians who recorded their biopsy decisions. One-hundred-thirty lesions (65 melanomas and 65 non-melanomas) were selected randomly from the Protocol 20061 database, maintaining the prevalence of non-melanoma lesion types observed in Protocol 20061. Non-melanomas were matched by age and anatomic site to melanomas. All lesion images underwent review by the principal investigator for image quality. Physicians (pigmented skin lesion experts, general dermatologists, and primary care physicians) were recruited until at least 40 participants from each category completed the study. Physician heterogeneity was assessed using kappa statistics.

**Procedure.** A total of 1690 physicians were invited to participate; 241 agreed and registered for the study. For data to be included in the study, physicians must have completed at least 78 of the 130 cases; 155 of the 241 physicians completed the study. An intake survey was used to assign the physicians to the appropriate caregiver groups. The order in which the cases were presented to the physicians was serially assigned within each caregiver group; the random assignment of cases per 10 different modules was performed in blocks. Reader study physicians reviewed three high resolution digital images taken from standard cameras – clinical images from 21 and 8 inches away from the lesion, and a dermoscopic image. In addition, twenty-four items of information were provided, including clinical history, risk factors for melanoma, and the results of physical examination findings by the Protocol 20061 investigating physician. Reader study physicians answered 6 questions regarding the decision to biopsy or not biopsy the lesion.

**Primary Objective.** The primary objective of the 20063 adjunctive reader study was to test the hypothesis that MelaFind sensitivity to identify melanoma was at least as good as that of investigators using photographs and histories of the same lesions collected by pivotal study investigators by live assessment. Table 14 presents a summary of the Reader Study (Protocol 20063) results.

**Table 14. Summary of Adjunctive Reader Study (Protocol 20063) Supporting Safety and Effectiveness of MelaFind**

	<b>MelaFind®</b>	<b>Dermatologists</b>
<b>Biopsy Sensitivity</b> (n = 65 melanomas <sup>a</sup> )	97% (63/65) <sup>b</sup>	72% <sup>c</sup> (47/65)
	p < 0.0001 <sup>d</sup>	
<b>Biopsy Specificity</b> (n = 65 negative <sup>e</sup> lesions)	9%	51%
	p = 0.0001 <sup>d</sup>	
<b>Biopsy Specificity (when Biopsy Sensitivity ≥ 95%)</b> (n = 4 of 110 dermatologists)	9%	10%
<b>Kappa Score</b>	NA	0.29 ± 0.01 (Fair Agreement)
<sup>a</sup> 65 melanomas (29 in situ; 36 invasive – median Breslow thickness 0.39 mm, range 0.12 to 1.2 mm) <sup>b</sup> Two melanomas not detected by MelaFind® were not detected by 71% (invasive, Breslow thickness 0.28 mm) and 21% (in situ) of the dermatologist readers <sup>c</sup> Trend (p = 0.33) for lower biopsy sensitivity to melanoma <i>in situ</i> (69%) versus invasive (74%) <sup>d</sup> Statistical significance at p < 0.05 <sup>e</sup> 60% - low grade dysplastic nevi		

Tables 15 and 16 provide study outcomes. MelaFind sensitivity was 97%, which was statistically significantly superior to that of 110 dermatologists who, on the average, missed (i.e., elected not to biopsy) 28% of melanomas in this electronic study (p-value < 0.0001).

**Table 15. Protocol 20063: ANOVA Results for Biopsy/Referral Sensitivity and Specificity with 95% CI**

	<b>Sensitivity</b>	<b>Std. Dev.</b>	<b>CI</b>	<b>Specificity</b>	<b>Std. Dev.</b>	<b>CI</b>
<b>All Derms</b>	0.72	0.03	(0.66, 0.78)	0.51	0.04	(0.43, 0.58)
<b>MelaFind</b>	0.97	0.15	(0.90, 0.99)	0.09	.19	(0.04, 0.19)
<b>Difference</b>	0.25	0.03	(0.18, 0.32)	-0.41	0.05	(-0.51, -0.31)

Inter-reader variability for biopsy decisions in the reader study was evaluated using kappa statistics (shown in Table 16) and indicates variability in biopsy decisions of dermatologists (kappa: 0.313) and primary care physicians (kappa: 0.200).

**Table 16. Protocol 20063: Kappa Statistics for Biopsy/referral for Melanoma**

	<b>Lesions</b>	<b>Mean readers per lesion</b>	<b>Kappa</b>	<b>SE0</b>
<b>Overall</b>	130	154.1	0.256	0.001
<b>Melanomas</b>	65	154.1	0.204	0.001
<b>Non-melanomas</b>	65	154.1	0.235	0.001
<b>PCPs</b>	130	45.0	0.200	0.003
<b>General dermatologists</b>	130	45.6	0.313	0.003
<b>PSL experts</b>	130	63.6	0.276	0.002

Figure 2 shows 39 reader-dermatologist assessments from Protocol 20081 reader study compared to 23 average live dermatologist assessments (solid diamond), that is, variability between reader study investigators and live vital study assessment. Figure 3 shows biopsy decisions by the 155 physicians participating in the Protocol 2063 reader (web-based lesions assessment; open symbols) study compared to MelaFind (black circle), that is, variability between reader study investigators and MelaFind. Figures 2 (solid diamond) and Figure 3 (solid circle) show MelaFind and live assessment.

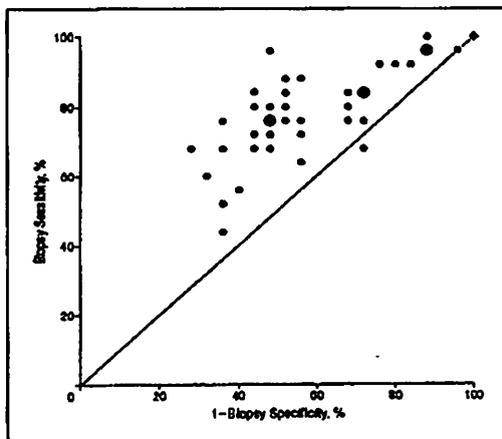


Figure. Biopsy decisions by 39 dermatologists participating in the pilot reader study. Small black circles represent individual readers; big black circles, pairs of readers; and the diamond, examining clinicians in the clinical trial on the same set of lesions.

Figure 2. 39 Reader-Dermatologists assessments compared to 23 average live dermatologist assessments

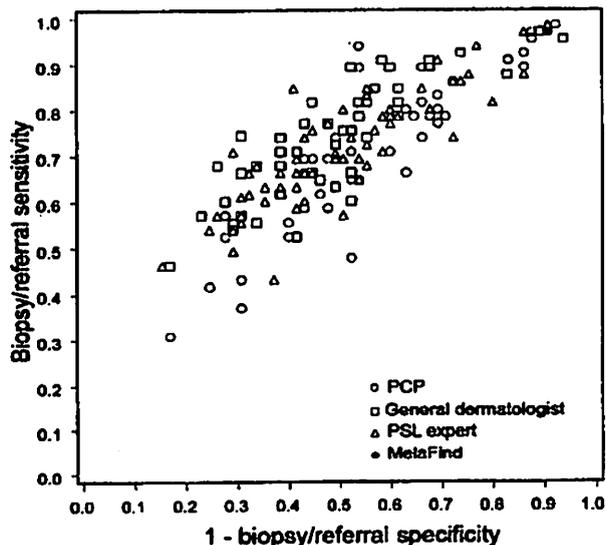


Figure 3. 155 reader-dermatologist assessments compared to average MelaFind assessment.

This data is based upon the 130 lesions randomly selected from 124 patients (age: 11 to 97 years, median 58 years; gender: 60 male and 64 female) in Protocol 20061 and matched as per study design description. Of the 65 melanomas, 29 were *in situ* and 36 were invasive with a median Breslow thickness of 0.39 mm (range 0.12 mm to 1.2 mm). Of the 65 non-melanomas, 60% were low grade dysplastic nevi. The results from 155 physicians were included in the analysis – 64 pigmented skin lesion experts, 46 general dermatologists, and 45 primary care physicians. The median years in practice of the physicians were 10, 12 and 15 years, respectively. Forty-five percent of physician readers were female and 55% were male. The average biopsy sensitivity of the dermatologists-readers was 72%, which was not statistically significantly different than the average biopsy sensitivity for primary care physician-readers (71%). The biopsy sensitivity of MelaFind was 97% ( $p < 0.0001$ ).

versus dermatologists). On average, the dermatologist-readers detected 47 of 65 melanomas and MelaFind detected 63/65 melanomas; the invasive (Breslow thickness 0.28 mm) and *in situ* melanomas not detected by MelaFind were missed by 71% and 21% of the dermatologist-readers, respectively. The kappa score of the dermatologist-readers was 0.29, indicating only “fair agreement.” There was a trend toward lower sensitivity of dermatologists for *in situ* versus invasive melanomas (69% versus 74%,  $p = 0.33$ ). The biopsy specificity of the dermatologists was 51% versus 9% for MelaFind ( $p < 0.0001$ ). Four dermatologist-readers had biopsy sensitivities at or above the 95% threshold for MelaFind in the Pivotal Trial (98%, 97%, 97%, and 95%; average 97%); the average biopsy specificity of these four dermatologist readers was 10% (9%, 11%, 14% and 6%, respectively).

## INSTRUCTIONS FOR USE OF MELAFIND

Please refer to the MelaFind® User Guide for detailed instructions for use. The User Guide also provides complete descriptions, images, and technical specifications of the system’s components, as well as all information about how MelaFind is supplied and how it should be handled and stored.

### Summary of MelaFind Workflow Steps

The outline below provides a list of steps that would occur during a typical MelaFind workflow session after a dermatologist examines a patient and determines if a given lesion is appropriate for imaging according to the Indications for Use:

1. Operator logs in to MelaFind with assigned login ID and password
2. Patient and physician information are entered for the session
3. Location of lesion(s) selected by physician is entered using body map
4. Lesion is prepared for imaging
5. Lesion is imaged with MelaFind hand-held imager
6. Images are sent to computer
7. MelaFind evaluates lesion
8. Images and results are displayed on monitor (depending on display settings, results can either display immediately, or only upon request of the operator or physician). Steps 4 thru 7 are repeated for each lesion indicated for MelaFind Use.

### Medical Device Patient Labeling is available for MelaFind

Protected by the following Issued United States Patents: 6,081,612; 6,208,749; 6,626,558; 6,657,798; 6,710,947; 7,102,672; 7,127,094; D613,866; and D613,867; as well as the following U.S. Patent Applications: 11/500,197 (to be issued mid-January 2011); 11/681,345; 11/761,816; 12/204,247; 11/956,918; 12/512,775; 12/512,895; 61/280,386; 12/852,195; and 12/876,549.

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MELA Sciences, Inc.  
 M113-MN-002 Rev. B, 10-31-11

# **MelaFind<sup>®</sup>**

## **Medical Device Patient Label**

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## Glossary

<b>Term</b>	<b>Definition</b>
Atypical skin lesion	A skin lesion that has unusual or irregular appearance
Biopsy	A removal of tissue for examination by pathologists
Clinically atypical skin lesion	A skin lesion that has unusual or irregular appearance when examined with the naked eye
Computer-vision system	A device that captures images and uses its computer to analyze them
Dermoscope	A device for visualization of skin structures not seen with the unaided eye.
Dermatologist	A doctor who specializes in the care of diseases of the skin, hair, and nails. MelaFind is for use by dermatologists who undergo training in the use of the device.
False negative rate	Proportion of cases with disease identified as having no disease
Imager	A device that captures images, such as a camera or a hand-held imaging device
Invasive melanoma	Melanoma that is present in the inner layers of the skin
Keratinocytes	Most common cells in the outer layer of the skin.
MelaFind Positive	A result from a MelaFind reading that indicates that a lesion has a very disorganized structure. It does not mean that you have melanoma.
MelaFind Negative	A result from a MelaFind reading that indicates that a lesion does not have a very disorganized structure. Your dermatologist makes the final decision on whether or not to biopsy. MelaFind is not 100% accurate.
Melanocyte	A skin cell that produce a pigment melanin, which is mostly responsible for skin color and pigmentation.
Melanoma	Cancer of skin pigment cells that is the most dangerous type of skin cancer.
Melanoma <i>in situ</i>	Melanoma that is present only in the outer layer of the skin and is almost 100% curable by surgical removal
Mole	A type of skin lesion that is usually pigmented and may be raised or flat

Non-Melanoma skin cancer	These are types of skin cancers that are not melanoma. These include basal cell skin cancer and squamous cell skin cancer. The MelaFind device cannot diagnose these skin cancers.
Pathologist	A physician who examines tissues under a microscope and makes diagnoses
Pigmented skin lesion	A skin lesion that has different color from the surrounding skin
Pivotal clinical study	A study conducted with patients to establish the safety and effectiveness
Reader study	A study in which images and patient information are presented to physicians who have not physically examined patients in order to determine safety effectiveness in a broader group of physicians
Sensitivity	Proportion of correctly identified cases with disease
Skin lesion	A patch of skin that looks different from the surrounding skin
Specificity	Proportion of correctly identified cases without disease

## *What Is Melanoma?*

Melanoma is the most dangerous type of skin cancer, in which some skin pigment cells (melanocytes) grow out of control. It is the leading cause of death from skin disease. On the surface of the skin, a melanoma may look like other harmless, benign moles or skin lesions to an untrained person. When such a mole or lesion is removed by your dermatologist for a biopsy, pathologists, who are doctors trained in diagnosing disease in tissue, examine it to determine whether it is a skin cancer.

Melanoma is a cancer of melanocytes. Non-melanoma skin cancers such as basal cell or squamous cell carcinoma, are cancers of keratinocytes, which are cells mostly found in the outermost part of the skin.

If detected early and treated properly by complete removal, melanomas of the skin can be curable. But, melanomas can be deadly if caught too late. Currently, there is no effective treatment for late stage melanoma.

You are at an increased risk for melanoma if you have many irregular (also called atypical) moles, a personal or a family history of melanoma or other skin cancers, a history of severe sunburns, or if you have frequently used tanning beds. However, some people who develop melanoma have NO known risk factors. You should have your skin examined regularly by your dermatologist.

## *What Is a Skin Lesion That Is Atypical Due to at Least One Clinical or Historical Characteristic of Melanoma?*

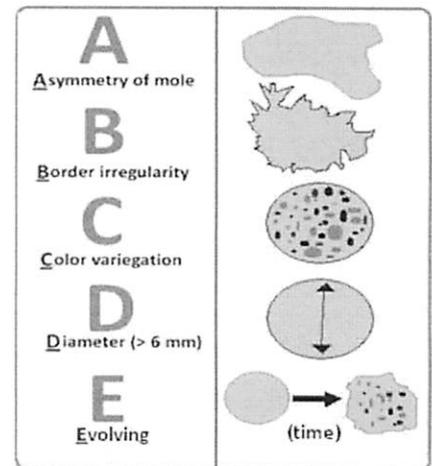
An atypical skin lesion is a mole that has at least one of the known visual characteristics of melanoma. These characteristics are often called the ABCDE's of melanoma:

- A = Asymmetry: one half of the lesion is different from the other
- B = Border Irregularity: uneven, fuzzy, notched or scalloped edges
- C = Color variegation: multiple colors within the lesion
- D = Diameter: greater than 6 mm or larger than the width of a pencil eraser
- E = Evolving: lesion changing over time

In addition to the ABCDE's, the following items are also considered characteristic of melanoma:

- P = Patient's concern: you express concern that a lesion might be melanoma
- R = Regression: lesion has areas that look scar-like white or blue-gray
- U = Ugly Duckling: a lesion that has a markedly different appearance than other lesions on a patient

Dermatologists use un-aided visual examination (i.e., examination with the naked eye) and aided visual examination (i.e., with a dermoscope) to examine lesions and decide which ones to biopsy. A dermoscope is a hand-held magnifier that illuminates the skin allowing dermatologists to see structures just below the surface of the skin such as blood vessels and pigmentation.

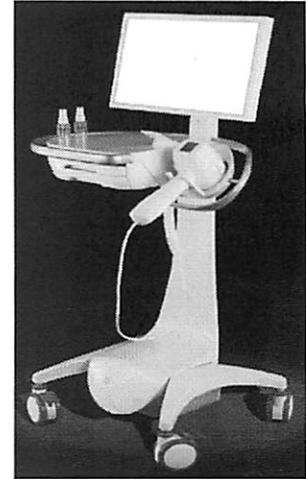


## *Description of MelaFind*

MelaFind® is a non-invasive, automated computer-vision system that captures, displays, and stores images of atypical pigmented skin lesions. MelaFind takes these images using light of different colors (from blue through red to near infrared). MelaFind then uses its computer to analyze these images and generate a result – MelaFind Positive or MelaFind Negative. This result is meant to help your dermatologist in making a decision on whether to biopsy or not. A MelaFind Positive reading does not mean that you have melanoma.

## *FDA Approved Indication for Use*

MelaFind is intended for use on clinically atypical cutaneous pigmented lesions with one or more clinical or historical characteristics of melanoma, excluding those with a clinical diagnosis of melanoma or likely melanoma. MelaFind is designed to be used when a dermatologist chooses to obtain additional information for a decision to biopsy. MelaFind should NOT be used to confirm a clinical diagnosis of melanoma.



MelaFind is only for use by physicians trained in the clinical diagnosis and management of skin cancer (i.e., dermatologists) who have also successfully completed a training program in the appropriate use of MelaFind.

The MelaFind result is one element of the overall clinical assessment. MelaFind Positive lesions (which may include malignant melanoma, melanoma *in situ*, high grade dysplastic nevi and atypical melanocytic proliferation/hyperplasia) should be considered for biopsy; the biopsy decision of a MelaFind Negative lesion should be based on the remainder of the entire clinical context. Lesions that are “non-evaluable” by MelaFind should be carefully re-evaluated for biopsy.

MelaFind is indicated only for use on lesions with a diameter between 2 mm and 22 mm, lesions that are accessible by the MelaFind imager, lesions that are sufficiently pigmented (i.e. not for use on non-pigmented or skin-colored lesions), lesions that do not contain a scar or fibrosis consistent with previous trauma, lesions where the skin is intact (i.e., non-ulcerated or non-bleeding lesions), lesions greater than 1 cm away from the eye, lesions which do not contain foreign matter, and lesions not on special anatomic sites (i.e., not for use on acral, palmar, plantar, mucosal, or subungual areas). MelaFind is not designed to detect pigmented non-melanoma skin cancers, so the dermatologist should rely on clinical experience to diagnose such lesions.

## *How is MelaFind Used?*

MelaFind is used on clinically suspicious skin pigmented lesions when your dermatologist chooses to obtain additional information for a decision to biopsy. MelaFind should not be used for lesions that the dermatologist is certain are melanomas and has already decided to biopsy. Your dermatologist successfully completed a training program in the appropriate use of the MelaFind device.

MelaFind Positive lesions should be considered for biopsy to rule out melanoma. Lesions that MelaFind cannot evaluate, i.e., non-evaluable lesions, should be carefully further evaluated by the dermatologist for biopsy.

MelaFind is not designed to detect pigmented non-melanoma skin cancers, so your dermatologist should rely on clinical experience to diagnose such lesions.

### *When should MelaFind Not be Used?*

MelaFind should **not** be used if the lesion

- is not pigmented;
- is not clinically atypical;
- has been previously biopsied, excised, or traumatized;
- and surrounding skin are not intact (e.g., open sores, ulcers, bleeding);
- is within 1 cm of the eye;
- is on mucosal surfaces (e.g., lips, genitals);
- is on the palms or soles;
- is on or under the nails;
- is located on or near an area of visible scarring;
- contains foreign matter (e.g., tattoo, splinter, marker); or
- is inaccessible to the MelaFind imager.

### *What are the Warnings for MelaFind Use?*

- DO NOT USE MELAFIND FOR SCREENING - MelaFind is not a screening device. MelaFind should be used in conjunction with dermatological clinical expert assessment. See Indications for Use section.
- A MelaFind Negative reading does not eliminate the possibility that the lesion might be or evolve into a melanoma. See Clinical Studies section.
- In pivotal study (Protocol 20061), 3 of 175 pathologically confirmed lesions including melanoma, melanoma *in situ*, high grade dysplastic nevi and atypical melanocytic proliferation / hyperplasia were classified by MelaFind as MelaFind Negative. There is a potential for MelaFind to not detect all malignant or high grade lesions.
- In MelaFind training, non-melanoma skin cancers are classified as MelaFind Negative. Therefore, MelaFind Negative lesions must be evaluated appropriately in order to rule out non-melanoma skin cancers.
- Careful clinical reassessment should be given to those lesions that are non-evaluable by MelaFind as to whether the lesion should be biopsied.
- MelaFind use data represent thin melanomas (*in situ* or thinner than 1 mm), not thicker or ulcerated melanomas (T2 – T4).

### *What are the Precautions for MelaFind Use?*

- Use of the MelaFind device is restricted to physicians trained in the clinical diagnosis and management of skin cancer who have also successfully completed a training program in the appropriate use of MelaFind.
- There is a potential for MelaFind Positives to include benign lesions as malignant or high grade.

- MelaFind requires periodic monitoring to verify system functionality through a mandatory self-test. If MelaFind does not pass the scheduled self-test, it will not permit further evaluation of clinically atypical pigmented skin lesions until it successfully passes the self-test. In the event of an unsuccessful self-test, any lesions evaluated with MelaFind during the period following the last successful self-test that were not biopsied should be considered for re-examination by the dermatologist.
- The 91% isopropyl alcohol used for lesion preparation and imaging procedures may cause skin irritation.
- There is a potential for nicking the skin if shaving is used in preparation for imaging. This could produce blood in the intended imaging site that would interfere with MelaFind imaging.
- Safety and effectiveness of MelaFind use has not been assessed or established in the following conditions:
  - In practices with management that includes option for lesion follow-up as well as biopsy.
  - With repeated MelaFind use on the same lesion within any time interval or by any user.
  - In patients with Fitzpatrick Skin Type 5 and 6

### *MelaFind Procedure*

The entire procedure, including preparation, takes 1-5 minutes (or longer when imaging more than one lesion). If appropriate, the hair on and around the lesion will be trimmed or shaved. After cleaning the skin and contact glass of the MelaFind imager with 91% isopropyl alcohol, the MelaFind imager will be positioned over the lesion and lowered into contact with the skin surface. Once the computer indicates that the imager is ready, the operator will acquire lesion images. If images are of good quality, the computer will analyze them and provide a MelaFind result – either Positive or Negative – that the dermatologist may use to help decide whether or not he/she will biopsy the lesion.

If the lesion image cannot be analyzed by MelaFind, the system will indicate to your dermatologist that it is not evaluable by MelaFind, and your dermatologist will use his/her clinical judgment in making a decision whether or not to biopsy the lesion. In the study demonstrating the safety and effectiveness of MelaFind, 9% of lesions were non-evaluable (could not be analyzed) by MelaFind.

The MelaFind system does not save patient data onto its system except for a unique patient ID, and the system maintains strict user access control (i.e., username and password) in order to operate the software.

### *What Was the Clinical Study that Supports MelaFind Use?*

In the pivotal clinical study, among all enrolled and evaluable lesions that were selected by dermatologists, MelaFind correctly identified 172 out of 175 (98.3%) melanomas and high-grade lesions of those that it could read. Also, MelaFind correctly categorized 157 of 1457 (10.8%) benign lesions while dermatologists correctly categorized 82 of 1457 (5.6%) benign lesions. MelaFind also incorrectly identified some lesions as melanomas that were not melanomas.

From this study, MelaFind was determined to provide some benefit in providing additional information to dermatologists for making a biopsy decision in those lesions that could be read and were not already thought to be highly suspicious for melanoma by that dermatologist.

### *Additional Study*

In a web-based image diagnosis reader study, primary care physicians and dermatologists who had not participated in the pivotal study were shown high quality images of 130 lesions and case history information from the pivotal study for each lesion. Then, these physicians were asked whether or not they would biopsy the lesion on the picture. The results of this study showed that dermatologists missed an average of 18 of the 65 melanomas reviewed, in comparison to MelaFind that correctly identified 63 of the 65 melanomas. Data indicated variability in the decision to biopsy amongst dermatologists and primary care physicians as well as between these groups when looking at pictures of lesions.

### *What Should I Expect from MelaFind Use?*

Your dermatologist will examine all of the relevant lesions on your skin if you have scheduled a full body skin exam. Or, if you have a particular lesion that you would like to have checked, she or he will focus on that. If your dermatologist has a very high level of suspicion that a lesion might be melanoma, he or she will be biopsy this lesion right away. However, if the lesion is clinically atypical (unusual but not obviously or highly suspicious for a melanoma), your dermatologist may use MelaFind to help determine if a biopsy is needed.

**If MelaFind indicates that your lesion is MelaFind Positive, it does not necessary mean that the lesion is a melanoma. You should follow-up with your dermatologist and review the biopsy results with him or her.**

### *Your Dermatologist Makes the Determination*

Your dermatologist will exercise his or her clinical judgment and rely on his or her training and experience to determine when to use MelaFind and how to use the MelaFind result in making biopsy decisions.

### **For Further Information**

Please visit [www.melafind.com](http://www.melafind.com) for more information.

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