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Melanoma screening with serial whole body photographic change detection using Melanoscan® technology

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ABSTRACT

The use of an automated, whole-body, diffusely lit digital imaging enclosure to produce serial images, which were then compared, using an astrophysics image display method, enabled a private practice dermatologist to detect melanoma at significantly thinner Breslow depths compared to all other clinical detection paradigms examined in this study. The patients were triaged to scanning using a melanoma risk survey system. The system employed a 24 camera semicircular imaging wall, with front and back views. 10,000 whole body photographic scans were obtained. Privacy was maintained with 128-bit image encryption and off-line storage. Image to image comparison of whole body digital photography was combined with a whole body skin exam in order to sensitize a clinical dermatologist to skin changes in individuals at risk for melanoma. Mean depths (Breslow scores) were compiled from six distinct melanoma biopsy cohorts segregated and based on different clinical screening paradigms. The Breslow depth of invasive lesions of the serial screening cohort was significantly less (by at least 0.050 mm) compared to three other clinical screening groups (patient self -detection 0.55 mm, p=0.007; referred by outside non-dermatologist physician 0.73 mm, p=0.03; and serial dermatologic evaluation 0.23 mm, p=0.03) as well as two pathology laboratory cohorts (community hospital laboratory 1.45 mm, p=0.003; dermatopathology laboratory 0.18, p=0.0003). This approach provides a quick and effective method for detection of early melanomas with a significant reduction in the skin area required for lesion examination.

INTRODUCTION

The point of origin for cutaneous melanoma is highly visible; in fact, it produces the most superficial, colorful cancer on a volume basis of all human cancers. It is hypothesized that melanoma screening will be improved by automatic analysis of pigmented lesion growth patterns. The foundation for such a system was tested using a change detection screening system for melanoma employing the eye of an experienced dermatologist in assessing change.

Melanomas are traditionally sought and discovered by distinct morphological characteristics [1]. A dramatic fall in mortality rates from melanoma may come from early detection of melanoma based on cutaneous color change patterns. Life saving melanoma skin cancer interventions may be summarized as primary prevention (reduction in case numbers), screening (public health methods for the detection of disease), and treatment. Primary prevention has been ineffective; melanoma has been the fastest growing type of cancer for the last 70 years. The incidence increases from 3 percent to 7 percent yearly [2, 3]. Melanoma incidence has increased fifteen-fold in 40 years, the greatest increase in incidence recorded for any malignancy [4]. Progress in early detection of melanoma has not kept pace with the increasing incidence and mortality of this deadly skin cancer. Melanoma mortality appears to be increasing, with one-fifth of those affected developing metastatic disease, and one in five of those affected dying from this malignancy [5, 6]. Although melanoma is the least common of the three major types of skin cancer, it is the most lethal and costly [7, 8, 9]. In the United States alone, one person dies from melanoma every hour [10]. In young adults, melanoma is among the most common of malignancies, with women preferentially affected [11].

Public health screening of high-risk skin regions for thin, curable melanomas holds tremendous promise for achieving dramatic reductions of morbidity and mortality [12, 13]. Diagnosis of an early-stage melanoma (<1 mm Breslow depth) results in a cure rate of over 90%). Efforts to optimize

prevention and earlier diagnosis include public education campaigns, referral to dermatologists, identification and more careful scrutiny of groups at-risk, as well as adjuncts to clinical diagnosis, such as photography, dermoscopy, telespectrophotometry, and confocal laser microscopy [14-31].

In order to maximize earlier clinical detection of melanoma and thereby reduce the morbidity and mortality attendant to this malignancy, the medical research community needs to evaluate the efficacy of various screening tools and introduce appropriate standardized paradigms for the evaluation of melanoma. Several studies from the United States, Australia, the United Kingdom, and Scandinavia suggest that mortality may be on the decrease as a result of improved public awareness and better screening [11, 32, 33]. Patients who are as a result of improved public awareness and better screening [11, 32, 33]. Patients who are at high risk for melanoma followed up with periodic surveillance have been proven to have significantly thinner and less invasive melanomas compared with patients whose tumors are diagnosed at first encounter [34]. Baseline photography, as an adjunct to traditional, clinical examination of patients, appears to improve the accuracy and early detection of melanomas [35, 36, 37, 38, 39]. In a prior study, baseline digital photographic evaluation of at-risk individuals has shown significant advantages; earlier and more specific diagnoses of melanoma have been demonstrated.[40]. It has been postulated that small tumors might otherwise be overlooked in the absence of baseline photography [41]. In general, small diameter tumors are more likely to be thinner or *in situ* when compared with larger diameter skin cancers [42, 43, 44]. Photographic changes provide evidence of growth and have been used to advantage in combination with dermoscopic features to classify and follow pigmented skin lesions for development of malignancy [45]. Serial dermoscopy in 80 evidence of growth and have been used to advantage in combination with dermoscopic features to classify and follow pigmented skin lesions for development of malignancy [45]. Serial dermoscopy in 80 pigmented skin lesions helped to discriminate melanoma from benign lesions [46]. However, this is the first study of serial whole body photography (Melanoscan®) for the detection of melanoma. Improved machine vision capable of overcoming problems such as scene memory may minimize change blindness. We hypothesize that flickering the presentation of serial images from reproducible perspectives of patient positioning in a camera light matrix reveals the presence of early melanoma to the human eye.

A lack of standardization as well as the significant cost of the procedure, as currently noticed, both limitations with respect to serial photographic evaluation of patients at risk for melanoma. In this study we examined the efficacy of a rapid, digital, automated, low-cost, whole-body photographic instrument in patients at-risk for melanoma. We compared mean Breslow depths of melanomas diagnosed using the automated scanner with the mean Breslow depths of melanomas obtained by other currently practiced methods of melanoma detection.

METHODS

Image Capture

Patients were scanned with the use of a serial, automated, digital whole-body photographic imaging instrument, Melanoscan®, a technology developed by a research team headed by the first author, Rhett J. Drugge, M.D. The software used for image processing and analysis was also developed by Dr. Drugge's team. Total body capture produces 48 images that can be viewed separately or as a mosaic (Fig. 1).

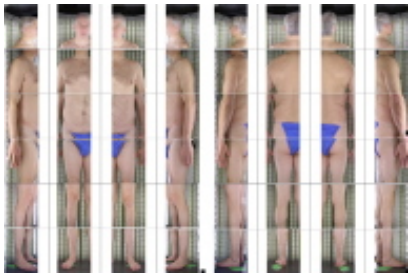

Figure 1. Mosaic of front and back Melanoscan® Images.

Image to image comparison of the whole body digital photography was combined with whole body skin exam in order to sensitize a clinical dermatologist to skin changes in individuals at risk for melanoma. Changes in lesion characteristics were evaluated as demonstrated in Figure 2. Dermatologists' time cost for image analysis was estimated at 10 minutes per scan review (Fig. 3).

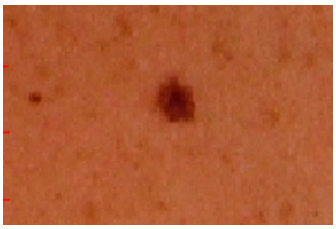

Figure 2. Time-lapse melanoma images.

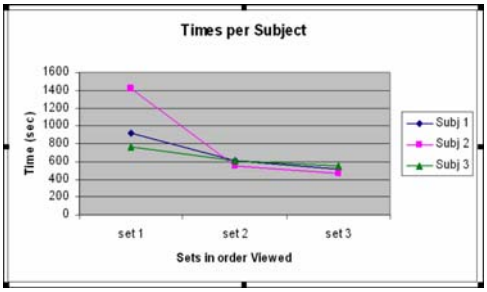

Figure 3. Simulated melanoma lesions were added to three sets of patient images to determine the time required to process the images.

Study Design

An assessment of mean depth (Breslow scores) was compiled from six distinct melanoma biopsy cohorts. The cohorts were segregated based on different clinical screening paradigms. The test cohort included patients at risk for melanoma who were serially screened at regular intervals utilizing the Melanoscan®. Two cohorts represented melanoma biopsies obtained from separate pathology laboratories. The other three cohorts were derived from the following sources: (1) outside non-dermatologist physician-referrals, (2) patients who were self-referred, and (3) a cohort of patients followed by a dermatologist but without serial photographic screening. The total number of melanoma biopsies analyzed was 1854, with 1752 biopsy results obtained from the two pathology laboratories and 102 biopsy results obtained from the four clinical screening groups.

Cohort 1. Serial scanning cohort (SSC)

These melanoma biopsy samples were obtained from at-risk patients in a single dermatology practice. Patients were monitored with the use of the Melanoscan® in addition to traditional clinical examination by a dermatologist. Patients were determined to be at-risk for melanoma based on scores obtained by a patient questionnaire risk-assessment tool [47]. Individuals who were felt to be at-risk based on answers to the risk assessment tool were placed in the serial scanning cohort, and scanned at yearly intervals. Patients were instructed on monthly self-examination and were able to opt in to receive monthly email reminders. The scans tool were placed in the serial scanning cohort, and scanned at yearly intervals. Patients were instructed on monthly self-examination and were able to opt in to receive monthly email reminders. The scans were reviewed by a dermatologist and a complete clinical skin exam was performed on each follow-up visit.

Cohort 2. Patient self-referral (PSR)

Melanoma biopsies from this cohort resulted from visits to a dermatologist by self-referred patients who had noticed and were concerned about a pigmented lesion on their skin. Many of these individuals had also received self-examination instructions and monthly email reminders.

Cohort 3. MD referred (MDR)

Physician referred (MDR) refers to melanoma biopsies obtained from patients who had been referred by non-dermatologist MDs to a dermatologist, because of a suspicious, pigmented lesion.

Cohort 4. Followed by dermatologist (FBD)

Melanoma biopsies in Cohort 4 were obtained from individuals who were established patients of a dermatologist and who were seen on a yearly basis for total body skin exams. After year 2000 all of these patients deemed at risk for melanoma were offered free scans but opted for traditional clinical examination or had received only a single Melanoscan®.

Cohort 5. Community pathology laboratory (CPL)

All melanoma biopsies submitted to this local community hospital pathology laboratory since 1996 were included in this cohort. These biopsies were interpreted by general pathologists and were submitted by a variety of different physician specialties.

Cohort 6. Dermatopathology laboratory (DPL)

Dermatopathology laboratory (DPL) is a regional referral dermatopathology laboratory. The majority of the biopsies processed at this laboratory originated from dermatologists based in either private practice or academic medicine.

Sample collection

Biopsies were obtained for the following reasons: (1) suspicious, pigmented lesion found on traditional clinical skin examination, according to ABCDE criteria; (2) suspicious, new pigmented lesion detected on serial photographic exam; (3) suspicious enlargement in a pigmented lesion previously identified on serial photographic examination; (4) other suspicious change in previously identified pigmented lesion seen in serial photographic exam.

Breslow scores (vertical depth penetration in millimeters of tumor beyond the granular layer of the stratum granulosum) were collected from a total of 1858 biopsy reports. Biopsies were obtained from six different cohorts between 1996 and 2005. All biopsy reports utilized were serially collected within the cohort over the specified time period.Care was taken to assure that the same melanoma biopsies were not represented in more than one cohort.

Melanoma biopsies were excluded from this study for any of the following reasons: (1) Characterization as amelanotic melanoma, (2) Palmar or plantar melanomas, (3) Recurrent scar melanoma, (4) Shave biopsies in which tumor extended beyond the margin of the biopsy.

Data analysis

Data were collected, tabulated and analyzed in spreadsheet form using Excel (Microsoft Corp.). Mean Breslow depths of each cohort were compared using the Student's t-test [48]. Differences between means were determined to be statis-

tically significant if the derived p value was less than 0.05.

RESULTS

The melanomas derived from the CPL, n=24, had a mean Breslow depth of 1.4462 mm (Table 1). All these biopsies were submitted by non-dermatologist physicians. The DPL, n=1728, derived melanomas had a mean Breslow depth of 0.1824 mm. Pathologists interpreting the CPL specimens were general pathologists, whereas specimens from statistically greater than the Breslow depth of melanomas from the SSC (mean PSR depth 0.5528 vs. mean SSC depth 0.048; p=0.0066).

Table 1

Cohort	Melanomas (n)	Depth (mm)
SSC (Serial Scan)	16	0.0480
PSR (Patient Self-Referral)	21	0.5528
MDR (M.D. Referred)	20	0.7285
FBD (Followed by Dermatologist)	49	0.2257
CPL (Community Hosp Lab)	24	1.4460
DPL (Dermatopathology Lab)	1728	0.1824

When the means of Breslow depths of melanomas from the pathology laboratories were compared with the SSC of melanomas, results from both laboratories were statistically greater than melanomas from the SSC (comparison of SSC and CPL mean Breslow depths, p=0.0032; comparison of SSC and DPL mean Breslow depths, p=0.00029, Table 2).

The PSR cohort, n=21, with a mean Breslow depth of 0.5528 mm, were patients who had not been seen by a medical provider for the lesion in question, but presented directly to the dermatologist. The Breslow depth of their melanomas was statistically greater than the Breslow depth of melanomas from the SSC (mean PSR depth 0.5528 vs. mean SSC depth 0.048; p=0.0066). Melanomas from the MDR cohort, n=20, were from patients who had been referred by non-dermatologists to a dermatologist and exhibited a mean Breslow depth of 0.7285, statistically greater than the mean Breslow depth of the SSC (p=0.03219, Table 2).

The largest clinical cohort was comprised of melanomas derived from the same dermatology practice that utilized the serial scanner. These patients comprised individuals diagnosed before the serial scanner was fully operational or who were unable or chose not to take advantage of serial scanner services. This group of patients (FBD) was evaluated in a standard dermatologic fashion, utilizing history, including skin cancer specific risk assessment. Each patient also received a complete skin exam, and, when appropriate, dermoscopy and even a baseline scan; however, this group didn't utilize free annual melanoscans as an adjuvant to physical exams for melanoma. The mean Breslow depth of melanomas in this group (0.2257 mm) was statistically greater than the mean for the SSC patients (p=0.0285).

No statistically significant differences between mean Breslow depths were seen when the FBD cohort was compared with either the MDR cohort or the PSR cohort (FBD vs. MDR, p=0.086; FBD vs. PSR, p=0.0589).

Table 2

Comparison of mean depths	p Value	Significance
SSC vs. PSR	0.0066	Yes
SSC vs. MDR	0.0322	Yes
SSC vs. FBD	0.0285	Yes
SSC vs. CPL	0.0032	Yes
SSC vs. DPL	0.0003	Yes
FBD vs. MDR	0.0860	No
FBD vs. PSR	0.0589	No

DISCUSSION

Given its strong correlation with prognosis, the success of melanoma screening is shown by the ability to identify melanomas at a very thin Breslow thickness. It is imperative that the clinical and research community optimize effective adjuncts to the standard dermatologic evaluation of individuals at risk for melanoma. Our study focuses on improvements in the early diagnosis of melanoma, which can be achieved utilizing serial, automated, whole-body, digital photography. The methodology builds on prior observations of change in-serial dermoscopy imaging of 80 pigmented skin lesions, which was shown to improve both sensitivity and specificity of melanoma diagnosis [46]. Early detection of potentially metastatic skin cancers, especially melanomas, may be facili-

tated by the detection of pigmented lesion changes [46, 49]. The more comprehensive technique of baseline photography with serial clinical comparison tends to be expensive and time -consuming. The serial clinical comparisons between photographs and clinical examinations are often fraught with variability of position, operator, and lighting. The system we tested was designed for cost-effectiveness, speed, consistency and ease of interpretation, via proprietary, software-driven image processing and analysis.

In the serial scanning cohort, standardization of the evaluation process in at-risk patients was an important factor. Patients entering into, or referred to the dermatology practice utilizing the serial scanner automatically filled out a risk assessment questionnaire as part of their new patient intake. At-risk patients were automatically entered into a serial scanning program, with follow-up reminders mailed to the patients at appropriate intervals. This standardization of process would help to minimize the variation in methods of patient assessment characteristic to current-day dermatology practices [50].

Whereas dermatologist referral, patient self-examination, and use of adjunct tools such as dermoscopy have been shown to allow the diagnosis of thinner melanomas, there is broad variability in the implementation and level of competency of these interventions. As currently practiced, dermoscopy is limited to 4 cm^2 of skin per observation making the ergonomics and mapping of the technique a challenge. Potential benefits from pointed spot specific image enhancement will be hampered by significant productivity issues prompting underutilization. In addition, the limits of adjuncts such as dermoscopy are well-known [51]. Similarly, it is well-known that the sensitivity of experienced dermatologists in recognizing early melanoma is limited [52]. With these factors in mind, it behooves the dermatology community to rely to a greater degree on comprehensive surface imagery in the management of skin diseases, especially regarding the earlier diagnosis of melanomas.

There were no statistically significant differences in depth means when the non-serial scan clinical subsets (PSR, MDR, and FBD) were compared with one another. Based on this, the statement could be made that patient self-examination was as effective, in this dataset, as physician evaluation. It is likely that the self-referred cohort were better educated and therefore more motivated regarding the risks of melanoma. The mean depth of serial scan melanomas was, however, statistically superior to all the clinical as well as laboratory cohorts examined. This may indicate that thinner melanomas had a more benign appearance, lacking the ABCDE or "ugly duckling" characteristics normally considered to be suspicious for melanoma.

This may indicate that thinner melanomas had a more benign appearance, lacking the ABCDE or "ugly duckling" characteristics normally considered to be suspicious for melanoma. Not infrequently, new or changed pigmented lesions detected by the serial scanner that turned out to be melanoma, had an otherwise benign appearance when evaluated by the dermatologist. A subsequent study of the dermoscopy characteristics of these lesions is underway.

Statistically significant differences were observed between mean depths of the community hospital laboratory and the dermatopathology laboratory. This trend may reflect the lack of experience of non-dermatologist physicians in the clinical detection of melanoma. Generally, the majority of dermatologists utilize a dermatopathologist to evaluate suspicious pigmented lesions. The thin depth of the melanomas from the dermatopathology laboratory also reflects an expert referral base, comprised of academic and private practice dermatologists with expertise in skin cancer.

Dermatologists are encountering an ever-increasing number of subjects with multiple atypical nevi that are at elevated risk for melanoma. Following these patients is difficult, but novel digital photographic techniques have the potential for facilitating the task of monitoring these people.

In conclusion, using the Melanoscan® to obtain high-speed serial whole body imagery, serial dermatologic evaluation for melanoma is enhanced. Melanomas are discovered at the thinnest depth reported in any study to date. We recommend that serial melanoscans become a standard of care intervention for patients at risk for melanoma. The new approach sets the stage for a dramatic reduction in the area of skin that requires individual lesion examination. In this study, the serial use of an automated, whole-body, photographic system in at-risk individuals resulted in detection of melanoma at significantly thinner Breslow depths compared to all other clinical detection paradigms.

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