

## Pigmented Lesions Clinic for Early Detection of Melanoma: Preliminary Results

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### Abstract

**Background:** Early detection of malignant melanoma of the skin is the most important factor in patient survival. Naked-eye diagnostic sensitivity and specificity are low. Patients with multiple nevi are at high risk to develop melanomas and the clinical follow-up of such patients is difficult, resulting in missed melanomas on the one hand and unnecessary biopsies on the other.

**Objectives:** To describe the set-up of a special clinic aimed at early detection of melanoma and follow-up of high risk patients and preliminary results from 20 months of operation.

**Methods:** We established a pigmented lesions clinic based on a digital photography studio enabling documentation and comparison over time of full body photography and dermoscopy.

**Results:** In the first 20 months of work, 895 patients were seen, 206 of them for follow-up visits. A total of 29,254 photos were taken. Altogether, 236 lesions were suspicious (either clinically or dermoscopically) and the patients were advised to excise them. Seven melanomas were found in this initial examination (which did not include long-term follow-up).

**Conclusions:** With multimode photographic cutaneous surveillance, early detection of melanoma in high risk patients has been reported. Our clinic utilizes the same techniques and diagnostic algorithm as other leading clinics throughout the world, thus enabling us to deliver better follow-up for those patients.

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Malignant melanoma incidence is increasingly rising in Caucasian populations all over the world. The American Cancer Society estimates that 62,190 people (34,260 men and 27,930 women) will be diagnosed with invasive melanoma of the skin and 7910 men and women will die of melanoma of the skin in 2006 [1]. The rates are rising faster than those of any other cancer [2,3]. The lifetime risk of invasive melanoma developing in the United States was 1 in 1500 during 1930; it is currently 1 in 74 [2,3]. In Israel, 1000 new cases are diagnosed every year – one-third of them non-invasive melanoma and two-thirds invasive melanoma [4]. The incidence of melanoma in Israel is among the highest in the world: In Israeli-born males, the annual standard rate of melanoma is 33/100,000, i.e., the lifetime risk to develop melanoma (both superficial and invasive) is 1:40.

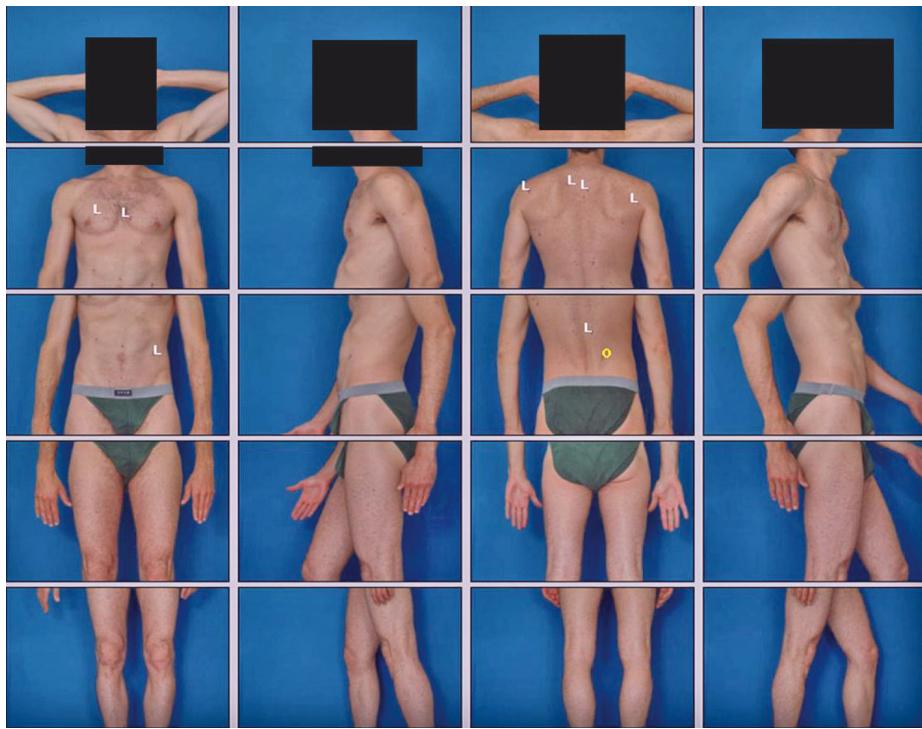
### Risk factors for melanoma

Risk factors include multiple nevi, dysplastic/atypical nevi, freckles, personal or family history of melanoma, fair complexion (skin types 1-2, blond/red hair, green/blue/gray eyes), multiple sunburns (especially during childhood), large congenital nevi, and immunosuppression. Epidemiological studies have consistently shown that the total number of melanocytic nevi on the body is the strongest risk factor for the development of cutaneous melanoma [5]. For example, analysis of the above-mentioned independent risk factors using logistic regression analysis revealed a maximum relative risk of 587 for men with more than 20 common nevi, some freckling, more than three atypical nevi and more than three episodes of sunburn [5]. The relative risks for increased number of nevi alone is 3–10 for > 20 common nevi, 4–17 for > 50 nevi and 7–46 for > 100 nevi. For atypical nevi, the relative risk to develop melanoma is 2–3 for two atypical nevi, and 3–24 for more than two atypical nevi. For freckling, the relative risk is 2–7 [5].

Unfortunately, invasive melanoma is still a disease with a grave prognosis: While superficial (*in situ*) melanoma carries a 100% 10 year survival, only 3% of stage IV patients survive for 10 years [6]. Therefore, diagnosis and treatment of melanoma during the earliest stages of its evolution is of critical importance for patient survival.

### Methods for the clinical diagnosis of melanoma

Currently, most dermatologists rely solely on the naked eye to diagnose pigmented skin lesions. However, many studies have documented that the diagnostic accuracy of such examination is only around 60% [7,8]. In 1985, the “ABCD” acronym (**a**symmetry, **b**order irregularity, **c**olor variegation, **d**iameter > 6 mm) was coined to help primary care physicians to better differentiate melanoma from benign nevi [9]. However, up to 38% of melanomas are small-diameter melanoma [10], and therefore the “D” criterion is constantly under debate. Also, nodular melanomas do not often respond to the A, B, and C criteria. Conversely, a huge number of seborrheic keratosis or so-called atypical nevi fulfill most of the ABCD criteria. In recent years, “E” was added to the “ABCD” rule: evolution. Since melanoma, like all cancers, is a



**Figure 1.** Full body imaging. The letters mark the places of selected lesions.

dynamic process, a benign lesion that becomes malignant will change. Another important change/evolution is the appearance of a new pigmented lesion, especially in patients over 50 years old. Many articles have documented the role of change as an important indicator differentiating benign from malignant lesions [9,11-13]. However, most changes are self-detected by patients (or close family members) and not by dermatologists [14,15]. Due to the importance of the change phenomenon, it has been shown that the history of change (relayed by the patient) is an important factor influencing dermatologists' differentiation of melanoma from benign nevi [14].

The pursuit to improve the diagnostic accuracy and sensitivity for melanoma while decreasing unnecessary biopsies has,

in part, led to the development of new, non-invasive, *in vivo*, optical as well as other, imaging technologies. Those technologies include the use of a magnifying lens, Wood's light, individual lesions photography, total cutaneous photography (total body photography), magnetic resonance imaging, dermoscopy, high frequency ultrasound, optical coherence tomography, and confocal scanning laser microscopy [16].

Comparison of an individual's baseline total cutaneous photographs with their periodic follow-up cutaneous screening examinations is currently the only modality that can help clinicians detect objectively the evolution phenomenon and direct them to the lesions of concern. The other techniques mentioned above are designed to help clinicians further evaluate individual lesions deemed to be suspicious by visual inspection. From those techniques, dermoscopy

is the modality that most increases the diagnostic accuracy in melanoma.

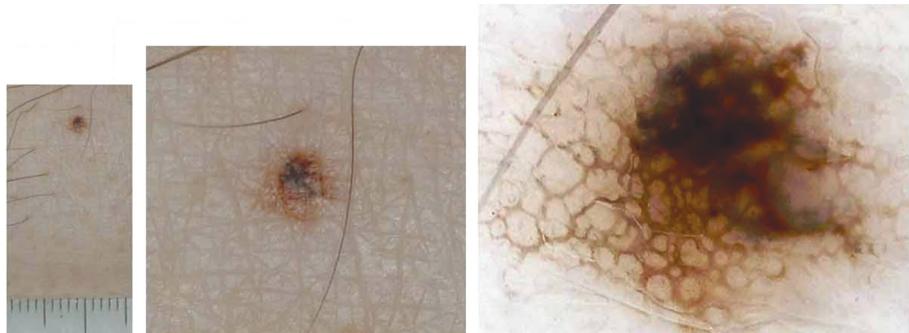
Dermoscopy, also known as epiluminescence microscopy, *in vivo* cutaneous surface microscopy, incident light microscopy, magnified oil immersion diascopy and dermatoscopy, is an *in vivo*, non-invasive technique that has revealed a new dimension to the clinical morphological features of pigmented skin lesions using incident light magnification systems with either immersion oil or polarized light at the skin-microscope interface. The purpose of this method is to obtain the visualization of numerous morphological features that are not visible to the naked eye, which enhance the clinical diagnosis of nearly all pigmented skin lesions. These morphological features seen by dermoscopy examination have specific, rather well-defined histopathological correlates [7,16]. By knowing the histopathological equivalent of such structures, the investigators are able to increase *in vivo* diagnostic accuracy of melanocytic versus non-melanocytic pigmented skin lesions and, in particular, benign vs. malignant lesions. Many studies have documented that dermoscopy can increase diagnostic sensitivity of melanoma from 60% by naked-eye examination to 90% in experienced hands [17,18].

### Screening for melanoma

The recognition of numerous banal nevi and dysplastic nevi as important risk markers for melanoma has permitted the identification of a high risk cohort to be targeted with efforts in prevention and early detection. The goal of early detection is to identify evolving melanoma in its earliest stages when it can be fully cured by simple outpatient limited excision. The prevailing



**Figure 2.** Close-up view of chest, with three marked nevi.

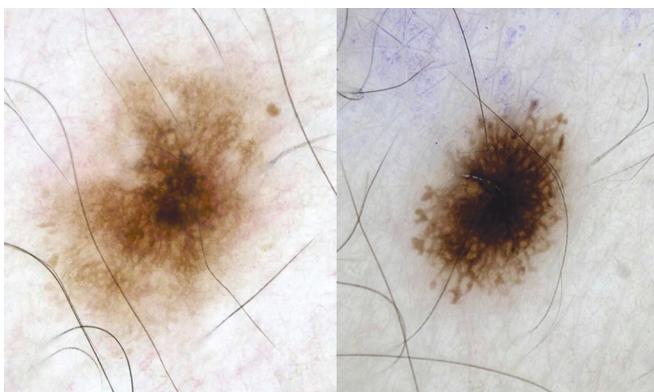


**Figure 3.** Close-up images of a small lesion (diameter 2.5 mm. Lesion #3 from Figure 2) (left and center). Dermoscopic image (right) was suspicious for melanoma. Pathological report: malignant melanoma *in situ*.

strategy to accomplish this is total body skin examination for the detection of atypical pigmented lesions that manifest the "ABCDs" of melanoma. Applying this strategy to individuals with floridly expressed dysplastic nevi proves problematic. Setting a low threshold for excision in this group will lead to an impractical number of excisions with significant associated morbidity and expense. On the other hand, setting a high threshold for excision may result in failure to recognize early melanomas before they have acquired significant potential for metastasis.

Photographically assisted follow-up is based on the premise that change in a pigmented lesion is a sensitive sign of early melanoma, and stability of a lesion speaks against a diagnosis of melanoma. By using baseline photographs for comparison the examiner attempts to identify new pigmented lesions, lesions that are undergoing significant focal change, and lesions that are growing at a distinctly faster pace than the remainder of the patient's nevi. Several teams have documented that with this approach approximately a third of the prospectively diagnosed melanomas are recognized on the basis of change in comparison to baseline photographs [19].

This article describes the establishment of the first pigmented lesions clinic in Israel dedicated for early detection of melanoma and details some preliminary data from the clinic's first 20 months of operation.



**Figure 4.** Change in a nevus detected by dermoscopy (Left picture taken 6 months after the picture on the right).

## Methods

After a comprehensive literature review and personal visits to pigmented lesions clinics abroad, it was clear that we need a system that fulfills the following principles:

- The main "target audience" are patients at high risk for melanoma: namely, patients with multiple (more than 20) common acquired nevi or multiple freckles, patients with multiple dysplastic nevi, patients with personal or family history of melanoma, and children with congenital nevi.
- The hardware should enable the clinician to capture high quality, reproducible, digital images of the whole body and of selected lesions (both close-up and dermoscopic images).
- The use of existing, "off the shelf" software and hardware.
- The software and hardware should use open standards, enabling us to add future devices and methods through commercially available interfaces.

Based on those principles, we built a professional studio that included a high-end 12MP digital SLR (single lens reflex) camera used for full body photography and macro images, and 7MP digital camera attached to a polarized light dermoscope (DermLite Photo System, 3Gen LLC, Dana Point, CA, USA) for dermoscopic images. All photos are archived in a dedicated body mapping program.

On the first visit, the patient undergoes complete skin examination by a dermatologist using the naked eye and dermoscopy for all pigmented lesions. Suspicious or borderline lesions are numbered sequentially with a marker on the body. Full body photography is performed using a standard set of 20 photos to document as much skin as possible [Figures 1 and 2]. Occasionally, more pictures are added to document a specific body area. Each marked lesion is then photographed by a close-up lens with a scale and by a dermoscopic camera [Figure 3]. When the patient returns after 1–2 weeks, he/she is given a detailed report of what was found as well as a compact disk with all the photos. This CD is then used by the patient for a total body self-check every 1–2 months. We instruct the patient that any significant change in a pigmented lesion or the appearance of a new one must be evaluated by a dermatologist [Figure 4]. If any lesion warrants a biopsy or excision, the patient is operated in our clinic or is given a letter to the dermatologist or primary care physician, detailing what lesion is suspicious, along with a color printout of the body region with the suspicious lesion clearly marked. Most patients are then rescheduled for a follow-up once a year, although for some patients, short-term mole monitoring – as described by Menzies et al. [20] – is recommended every 3 to 6 months.

CD = compact disk

At the yearly follow-up visits, the above process is repeated, with specific emphasis on detecting changes from previous sessions. Patients diagnosed with melanoma are transferred to the melanoma team where their full treatment regimen and follow-up is discussed and defined.

## Results

During 20 months of work (1 January 2005 – 30 August 2006), 895 patients (M:F = 494:401) visited the pigmented lesions clinic, 206 (23%) of them for more than 1 session (i.e., follow-up). Patients' age ranged from 0 to 82 years (mean 35.9, median 34.0 years). Fifty-nine patients (6.6%) were under the age of 18 years, and 14 of these were between the ages of 0 to 3 (sent for evaluation of congenital nevi).

Overall, 29,254 photos were taken, 4715 of them were dermoscopic and 4602 macro images. Altogether, 236 lesions (5.1%) were suspicious (either clinically or dermoscopically) and excision was recommended. Seven of these lesions were malignant melanomas (one patient had two melanomas at the same time).

### Melanoma risk factors

In the study group 436 patients (48.8%) had blonde or red hair in their youth, 414 (46%) had bright eyes (blue, gray or green) and 220 (24.6%) had fair skin (Fitzpatrick's type I-II). Furthermore, 116 patients (13%) had the combination of fair skin, light hair color and bright eyes. With regard to place of origin, 569 (88.5%) of the patients were born in Israel. More than three severe sunburns in their childhood were reported by 317 patients (35%).

In 394 patients (44%) at least one previous biopsy of a nevus was found to be benign. A total of 151 patients (17%) had a personal history of melanoma: 1 patient had 4 melanomas before visiting our clinic, 2 patients had 3 melanomas, 12 had 2 melanomas and 136 had one melanoma.

With regard to family history, 109 of the patients (12%) had at least one first-degree relative with melanoma and 56 patients had at least one second-degree relative with melanoma.

More than 50 melanocytic nevi were found in 125 patients (7.2%), of whom 48 had more than 100 nevi over their body (we counted only nevi with diameter > 2 mm). Forty-five patients (3.6%) had > 100 nevi and more than 1 dysplastic nevus, thus forming the "atypical mole syndrome" group. Among them, 27 patients (2.2%) had > 100 nevi and > 10 dysplastic nevi, forming the highest risk group for melanoma.

Personal history of melanoma was statistically associated with previous extended sun exposure ( $P < 0.001$ ), childhood sunburns ( $P = 0.01$ ), sun-sensitive skin ( $P < 0.001$ ), presence of sun-damaged skin (evident by the findings of solar elastosis, cutis rhomboidalis, actinic cheilitis or multiple solar lentigines), freckles, dysplastic nevi count, and the chance of having a lesion considered suspicious and sent for biopsy. No relationship was found in our dataset between personal history of melanoma and total nevi count or atypical mole syndrome.

## Discussion

Cutaneous surveillance has been well described as an effective method for early detection of melanoma. An important aid to this

screening process is baseline cutaneous multimode photography. This was reported to be an efficient method for detecting lesion evolution, which is suggestive of melanoma, and as a means to minimize unnecessary surgery [11]. With photographic cutaneous surveillance, a high incidence of melanoma and early detection of melanoma in high risk patients has been reported. For example, during 120 months of follow-up of patients with classic atypical mole syndrome and high risk non-classic atypical mole syndrome patients in New York University, all melanomas detected were either *in situ* or less than 1 mm in Breslow thickness [21]. By following such patients, new and changed pigmented lesions are detected. Not all of these evolving lesions are melanomas, and along with dermoscopy, many can be managed by further photographic follow-up [11].

One of the most interesting applications of digital follow-up is the evaluation of atypical melanocytic lesions in patients with multiple nevi. Although there is no doubt that all lesions exhibiting features of severe atypia or malignancy must be removed, there is a subset of melanocytic lesions with moderate clinical and/or dermoscopic atypical features. In these cases, excision may not be justified in terms of efficacy, morbidity, and cost. Moreover, evaluation and management of pigmented skin lesions have to be considered in the clinical context of a given patient with a large number of atypical moles. Since dermoscopy provides the clinician with new morphological criteria not visible to the naked eye, the design of standardized procedures combining clinical and dermoscopic images with total body photography for the clinical follow-up of the patient is important [22].

In our clinic, we utilized the surveillance algorithm described by Malvehy and Puig [22] and followed all over the world in pigmented lesions clinics. Those clinics are managed by dermatologists experienced in clinical photography and dermoscopy.

The patients seen at our clinic were mostly young compared to other published series. This reflects the greater awareness of the younger age group to the importance of early detection of melanoma using newer technologies. In our series, about one-third of the patients were diagnosed with a suspicious lesion (mostly based on dermoscopy) and were sent for excisional biopsy. Our preliminary results show a low rate of melanoma found on this initial examination. This reflects the low melanoma rate in young people and the lack of long-time monitoring, which is the main benefit of this system. As time passes and more high risk patients enter the database and will be followed for long periods, it is expected that more melanomas will be found by detecting changed or new pigmented lesions.

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