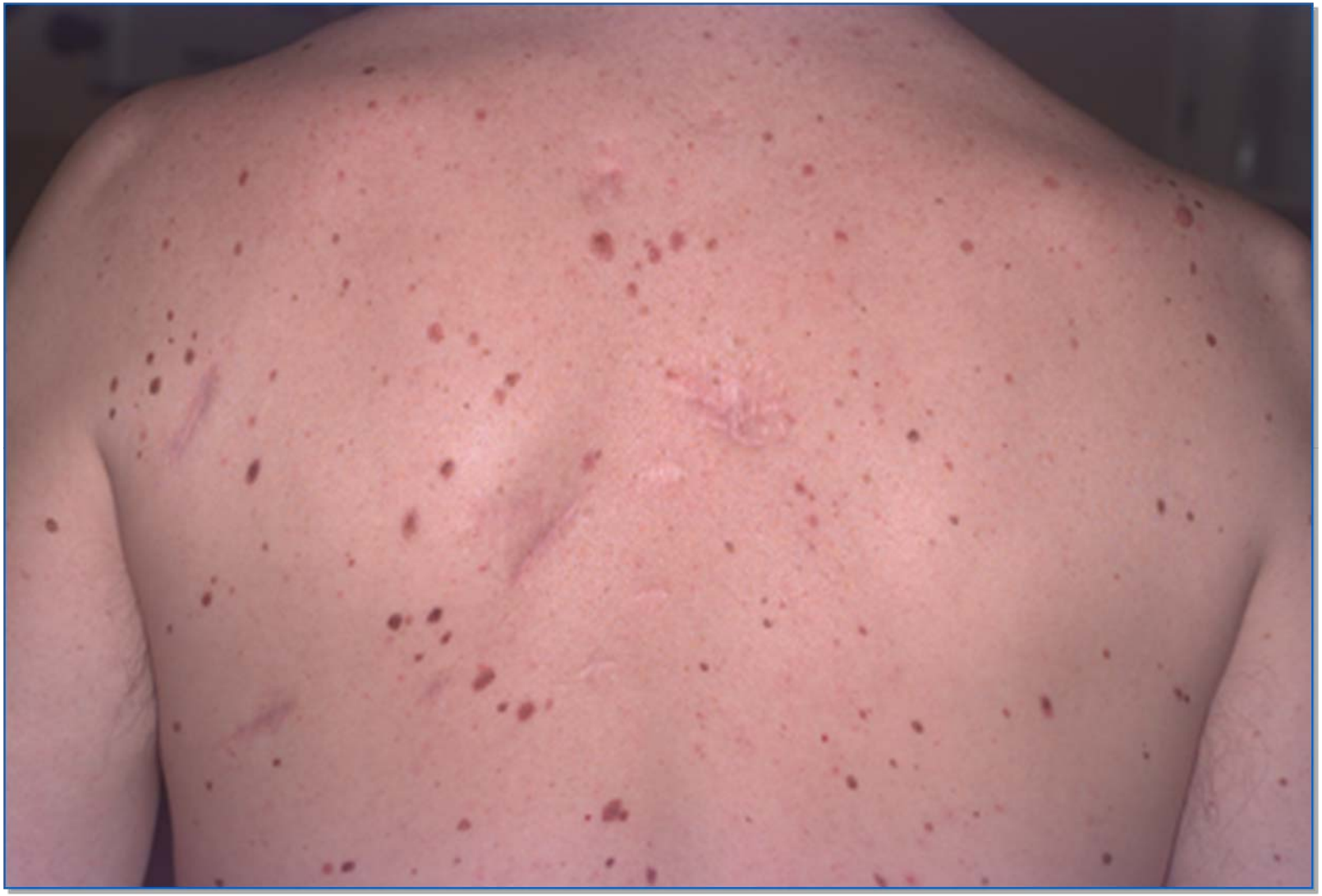


What should we do in a person with dysplastic nevus syndrome ?

Surgical Prophylaxis of Malignant Melanoma

MAX H. COHEN, M.D., PH.D., F.A.C.S., BARRY J. COHEN, M.D., JANE D. SHOTKIN, R.N., and PAULA T. MORRISON, R.N.

A review of a 14-year experience with prophylactic pigmented skin lesion removal is presented. Data obtained during a 4-year interval of this 14-year experience is analyzed specifically. During this 4-year interval, 250 patients with melanoma were seen. Of these patients, 75 with a history of stage I (localized) melanoma

From the Department of Surgery, Washington Hospital Center, the Washington Hospital Center Cancer Institute, the Mid-Atlantic Pigmented Lesion Clinic, and the George Washington University School of Medicine, Washington, D.C.

Ann Surg 1991:213:308-14

JDDG Journal of the German Society of Dermatology

DOI: 10.1111/j.1610-0387.2009.07095.x

Dysplastic nevus syndrome with development of multiple melanomas. A surgical concept for prophylaxis

Corinna Brod, Wilfried Schippert, Helmut Breuninger
Department of Dermatology, University of Tübingen, Germany

JDDG; 2009 · 7 Submitted: 23. 1. 2009 | Accepted: 16. 3. 2009

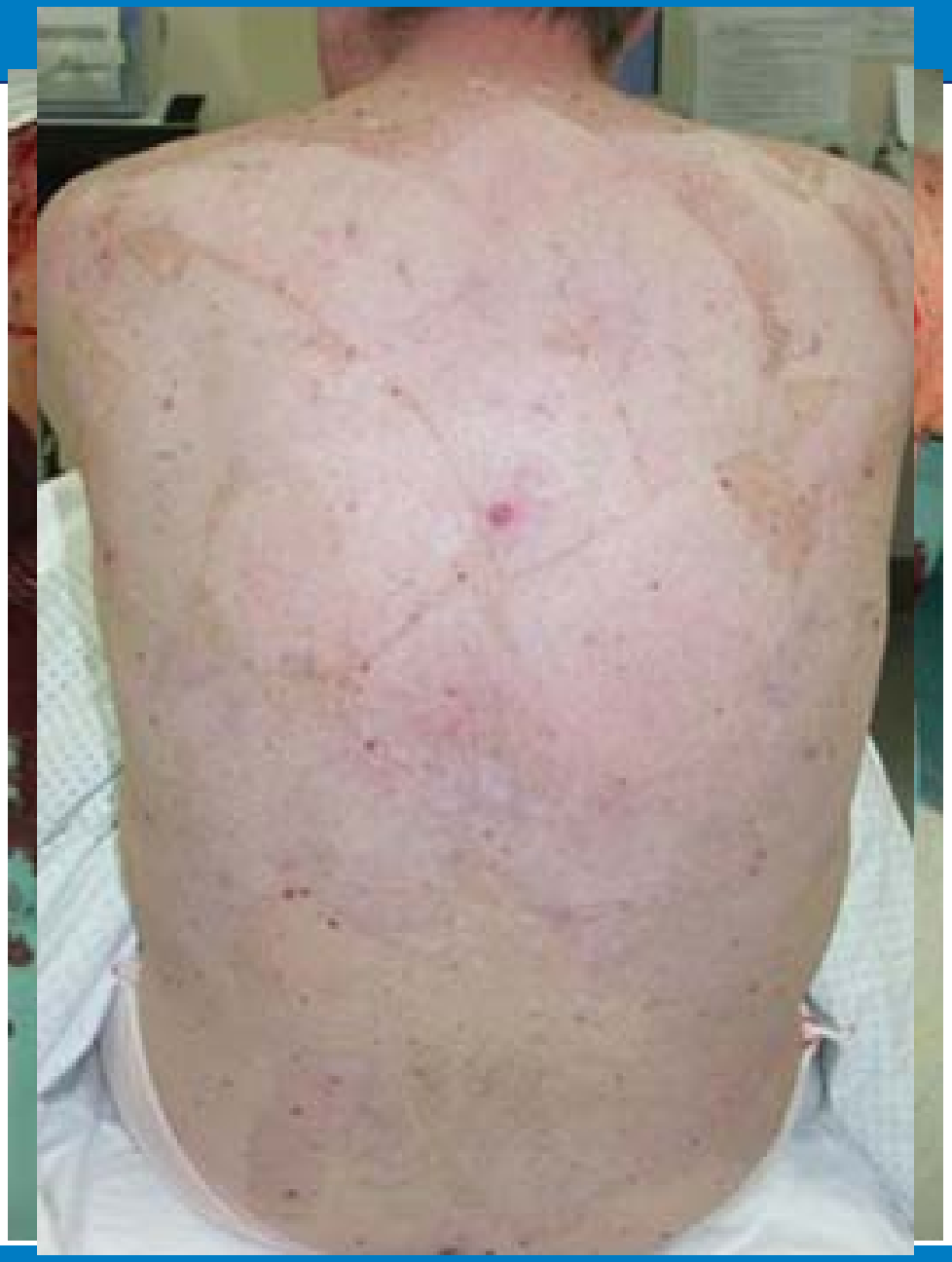
Case report

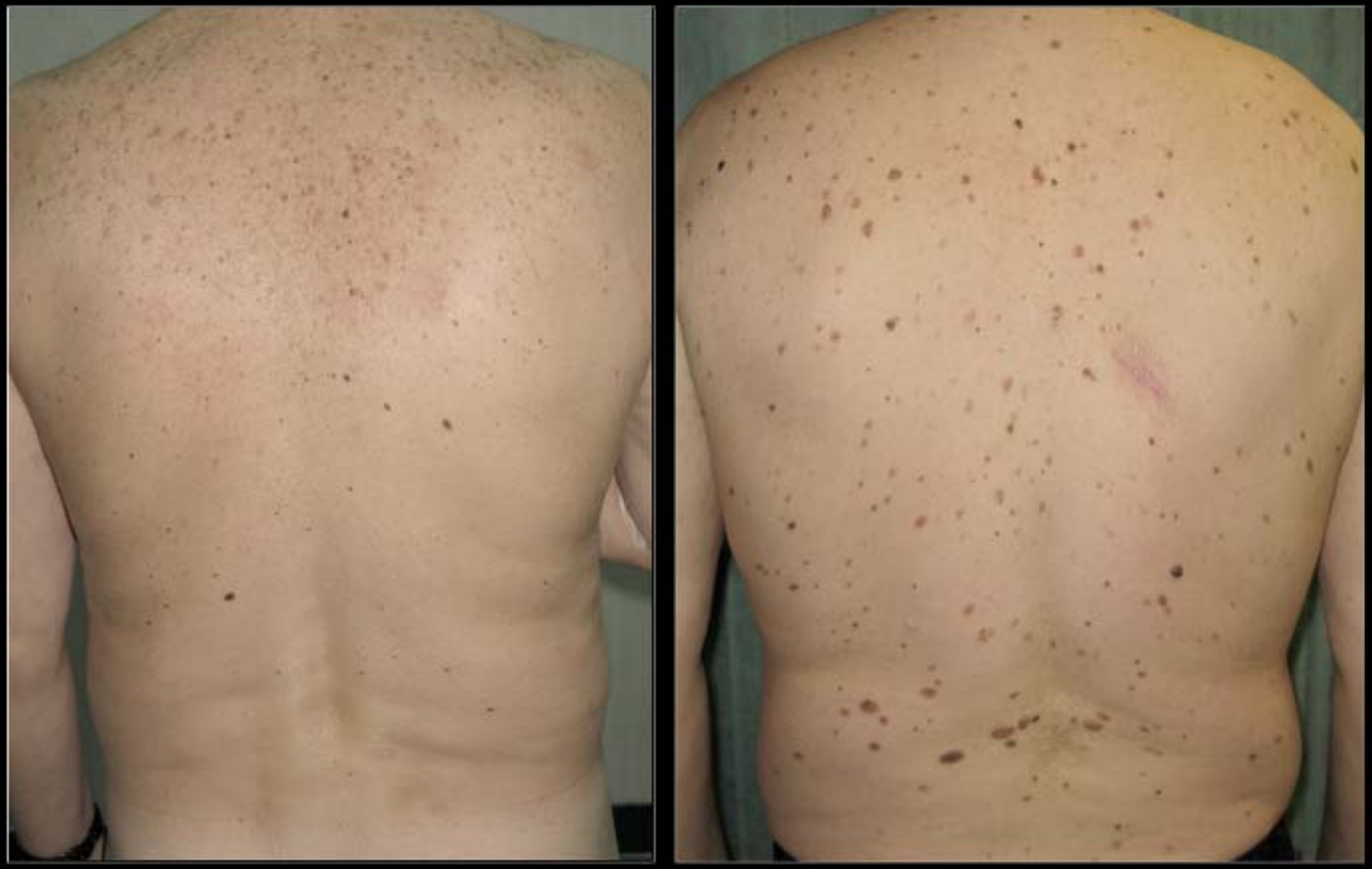
History

A 58-year-old man with hereditary dysplastic nevus syndrome had several hundred nevocellular nevi, at least 300–400, of which far more than 100 were clinically atypical (Figure 1). Externally multiple excisions of melanocytic and dysplastic nevi had been performed. In 2001 three melanomas on the back and breast 0.3–0.9 mm in thickness had been excised elsewhere. The patient was then referred to us for the first time for re-excision with safety margin.

Clinical findings

In 2001 about 300–400 melanocytic nevi were found with emphasis on the back and upper arms but also disseminated on the anterior chest and legs, of which about 100 were clinically and dermatoscopically atypical melanocytic





Individual Lesions

- Clinical
- Dermoscopy
- Digital dermoscopy monitoring
- Reflectance confocal microscopy
- Histopathology

Dysplastic Nevus Syndrome

- Total body examination (TBE) & SSE
- TBE with dermoscopy
- Total body photography (TBP)
- Digital dermoscopy monitoring (Fotofinder, MoleMax)
- TBP & digital dermoscopy monitoring (Melanographer – MoleMap)

TBP in melanoma detection

- 278 patients with ≥5 DN
- 20 patients (7%) developed MM
- MM diagnosed at earlier stage
  - 45% of MM were in-situ (vs. 33% for population)
  - Median thickness of invasive MM= 0.4 mm in cohort (vs. 1.4 mm for population)
- 2/3 of MM were de-novo – futility of "prophylactic excisions" of nevi

Kelly JW et al. Med J Aust 1997

An alternative to removal of nevi?

- 844 melanoma-prone family members followed at the NIH (the highest risk group with lifetime risk of MM approaching 80 to 100%)
- No MM related deaths have occurred in pts followed

- What was the key? PHOTOGRAPHY

Tucker et al. A natural history of melanomas and dysplastic nevi. Cancer 2002:94:3192-209

STUDY

Incidence of New and Changed Nevi and Melanomas Detected Using Baseline Images and Dermoscopy in Patients at High Risk for Melanoma

Jeremy P. Banky, MBBS; John W. Kelly, MDBS; Dallas R. English, PhD; Josephine M. Yeatman, MBBS, FACD; John P. Dowling, MBBS, FRCPA

Objective: To determine the incidence of new, changed, and regressed nevi and melanomas in a cohort of patients at high risk for melanoma using baseline total body photography and dermatoscopy.

Design: Cohort study of patients at high risk for melanoma who underwent baseline cutaneous photography between January 1, 1992, and December 31, 1997, and had at least 1 follow-up visit by December 31, 1998.

Setting: Private practice rooms of 1 dermatologist in conjunction with a public hospital-based, multidisciplinary melanoma clinic in Victoria, Australia.

Patients: A total of 309 patients who had at least 1 of the following risk factors for melanoma: personal history, family history, 100 or more nevi, or 4 or more dysplastic nevi.

Main Outcome Measures: Number of new, changed, and regressed nevi and melanomas detected and excised during the study interval.

Results: The incidence of new, changed, and regressed nevi decreased with increasing age ($P<.001$), whereas the incidence of melanomas increased ($P=.05$). The number of dysplastic nevi at baseline was positively associated with the incidence of changed nevi ($P<.001$) and melanomas ($P=.03$). The use of baseline photography and dermatoscopy was associated with low biopsy rates and early detection of melanomas. The development of melanoma in association with a preexisting nevus was not directly correlated with a change in a preexisting lesion monitored by baseline photography.

Conclusions: Nevi are dynamic, and only a small percentage of all new and changed melanocytic lesions are melanomas. Patients younger than 50 years had a lower incidence of melanomas and a higher rate of new, changed, and regressed nevi when compared with patients older than 50 years. A new or changed pigmented lesion is more likely to be a melanoma in patients older than 50 years.

Arch Dermatol. 2005;141:998-1006

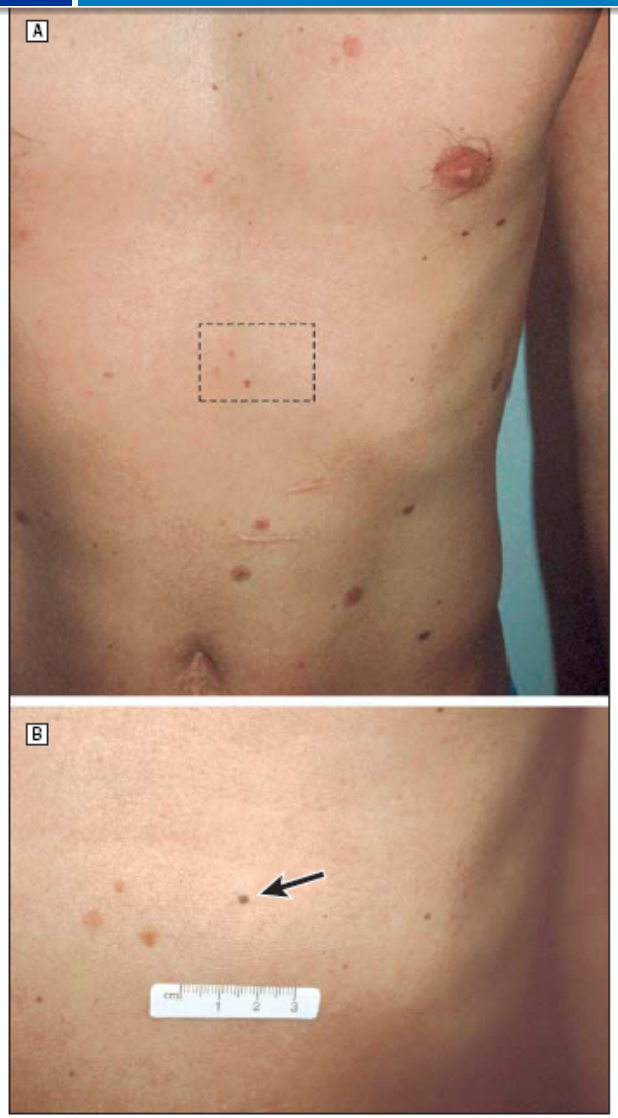


Figure 3. Photographs of the abdomen. A, View of the abdomen of the patient at the initial visit (baseline photograph). B, Close-up view of a new pigmented lesion (arrow) appearing on the midabdomen.

Table 1. Number of Patients With Risk Factors for Developing Melanoma

Risk Factors	No. of Patients
No. of nevi at first visit	
≤100	54
>100	255
No. of dysplastic nevi at first visit	
≤10	144
11-20	113
≥21	52
Family history of melanoma	
No	222
Yes	87
Personal history of melanoma	
No	219
Yes	90

Table 2. Histopathologic Diagnosis of All Changed and New Pigmented Lesions That Were Considered Suggestive of Melanoma and Excised

Histopathologic Diagnosis	No. of Changed Pigmented Lesions	No. of New Pigmented Lesions
Melanoma	14	4
Dysplastic nevus	25	5
Spitz nevus	1	2
Common benign nevus	9	2
Pseudomelanoma	1	0
Other	3	5
Total	**53**	**18**

creased with increasing age. Histologically, Lund and Stobbe[22] demonstrated that with increasing age, nevi become less active and more mature so that fewer changes and less regression occur.

In our patients, approximately one third had a changing nevus each year. This rate of change is far less than that found by Halpern et al,[20] with 51% of all evaluated nevi in the mean 89-month follow-up showing clinical

Table 6. Melanomas Detected

No.	Type	Clark Level	Thickness, mm	New or Changed According to Photographs	Associated Nevus Histologically	Detection Method	Time to Detection, mo
1	NM	IV	2.45	Changed	Yes	Patient	25
2	SSM	II	0.8	Changed	Yes	Photographs	5
3	SSM	I	. . .	New	Yes	Photographs	46
4	SSM	II	0.45	Changed	Yes	Photographs	24
5	SSM	II	0.3	Changed	Yes	Photographs	37
6	SSM	III	0.55	Changed	Yes	Photographs	21
7	SSM	I	. . .	Changed	No	Photographs	27
8	LM	II	0.35	New	Yes	Photographs	56
9	SSM	III	0.4	New	No	Photographs	56
10	SSM	I	. . .	New	No	Photographs	37
11	SSM	I	. . .	Changed	No	Photographs	46
12	SSM	II	0.2	Changed	No	Photographs	5
13	SSM	II	0.35	Changed	Yes	Photographs	35
14	SSM	III	0.37	Changed	Yes	Photographs	72
15	SSM	I	. . .	Changed	No	Photographs	22
16	LM	I	. . .	Changed	Yes	Photographs	53
17	SSM	I	. . .	Changed	No	Photographs	15
18	SSM	I	. . .	Changed	No	Photographs	23

Abbreviations: LM, lentigo maligna melanoma; NM, nodular melanoma; SSM, superficial spreading melanoma.

A stable lesion is biologically benign

New / changing lesions identify suspicious lesions that should be further assessed

Utility of TBP in melanoma detection

- N=576 high risk patients f/u by TBP
- 12 MM identified
  - 74% of MM were changed lesions, 20% were new lesions
  - Most melanomas lacked the ABCD criteria & were mainly found due to changes noted on comparison to TBP
  - 30% of MM were identified by patient SSE
- 25% of lesions that concerned patients were not biopsied following comparison with baseline TBP

Feit NE, Br J Dermatol 2004

Potential benefits of using TBP

Increase sensitivity for detecting early MM

- Detect subtle melanomas that lack the ABCD criteria

Avoid unnecessary biopsies of benign lesions

- Decrease morbidity
- Decrease healthcare costs

Reassure patient and physician

Aid skin self examination (SSE)

STUDY

Short-term Digital Surface Microscopic Monitoring of Atypical or Changing Melanocytic Lesions

Scott W. Menzies, MBBS, PhD; Alex Gutenev, PhD; Michelle Avramidis, BSc; Andrew Batrac, MSc; William H. McCarthy, MBBS, MEd

Objective: To examine the outcome of short-term digital surface microscopic monitoring of suspicious or changing atypical melanocytic lesions.

Design: Digital surface microscopic (oil epiluminescence microscopy, and dermoscopy) images of clinically melanocytic lesions were taken with a color calibrated 3 CCD video instrument. In general, lesions were moderately atypical, flat or only slightly raised, without a history of change or surface microscopic evidence of melanoma, or were mildly atypical lesions with a history of change. Lesions were monitored during a 2.5- to 4.5-month period (median, 3.0 months). With the exception of overall change in pigmentation consistent with that seen in surrounding skin (solar exposure changes), any morphologic change after monitoring was considered an indication to excise.

Setting: Sydney Melanoma Unit, Sydney, Australia (a referral center).

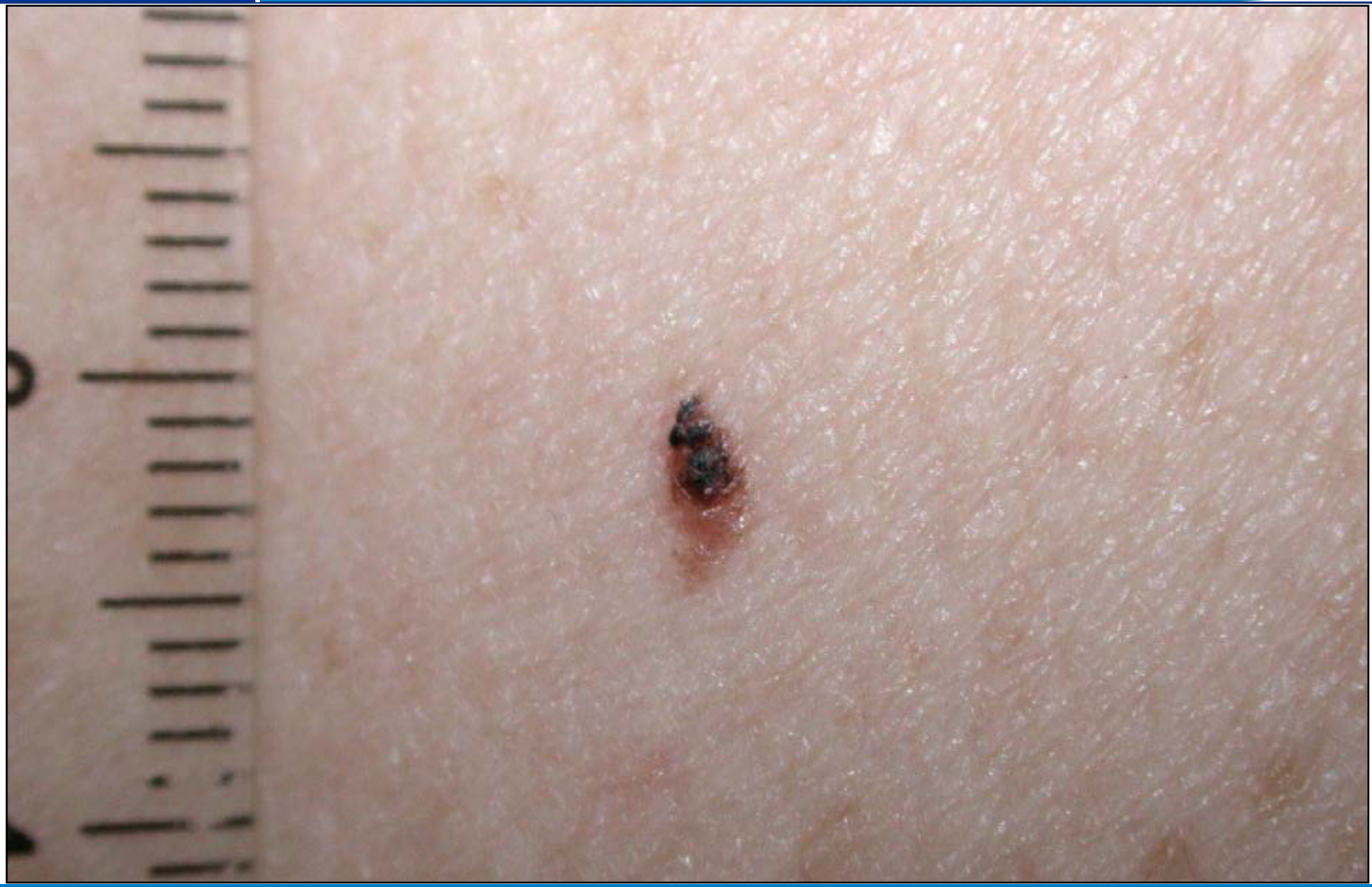
Patients: A consecutive sample of 318 lesions from 245 patients (aged 4-81 years).

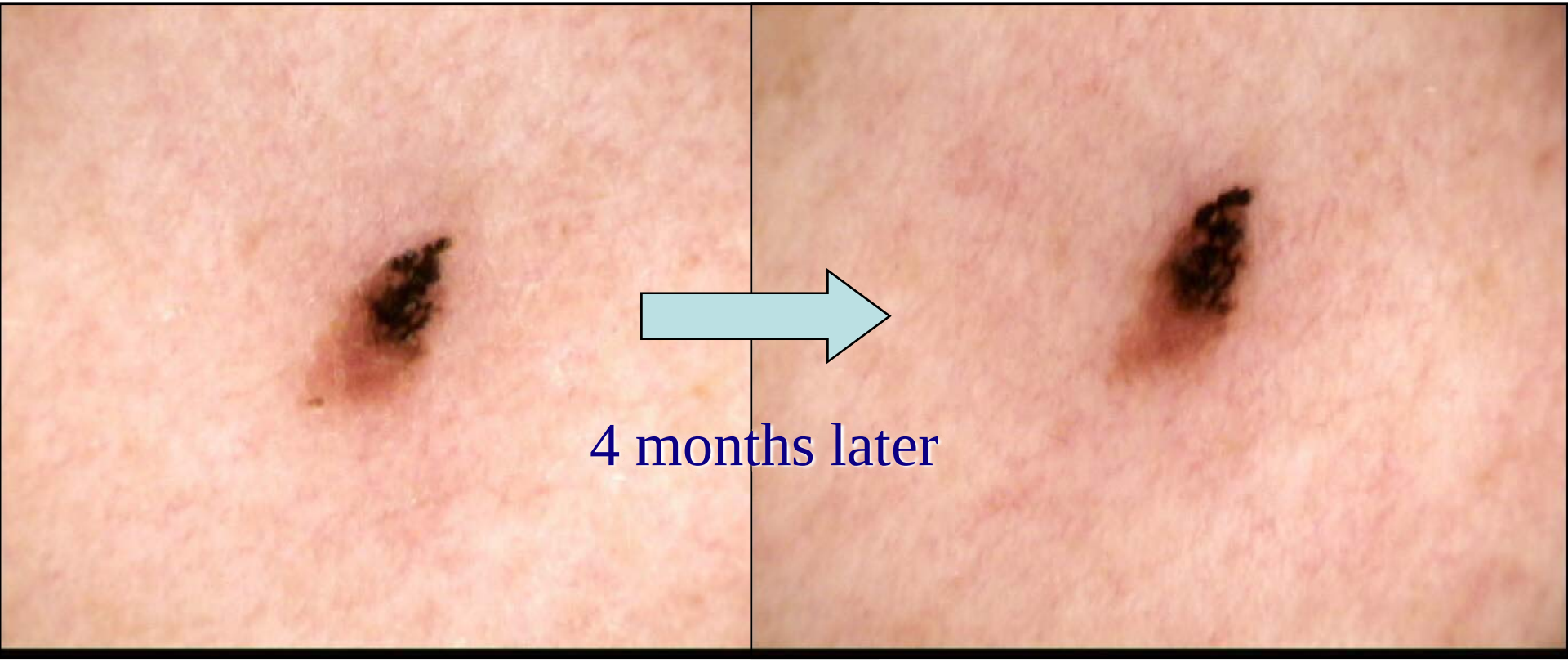
Main Outcome Measure: Specificity for the diagnosis of melanoma.

Results: Of the 318 lesions, 81% remained unchanged. Of the 61 lesions that showed morphologic changes, 7 (11% of changed and 2% of total lesions) were found to be early melanoma (5 in situ and 2 invasive with a Breslow thickness of 0.25 mm and 0.28 mm, respectively). None of these melanomas developed any classic surface microscopic features of melanoma and therefore could be identified only by morphologic change. The specificity for the diagnosis of melanoma by means of short-term digital monitoring was 83%.

Conclusion: On the assumption that all melanoma will change during the monitored period, surface microscopy digital monitoring is a useful adjunct for the management of melanocytic lesions.

Arch Dermatol. 2001;137:1583-1589




4 months later

Identification of Clinically Featureless Incipient Melanoma Using Sequential Dermoscopy Imaging

Harald Kittler, MD; Pascale Guitera, MD; Elisabeth Riedl, MD; Michelle Avramidis, MD; Ligia Teban, MD; Manfred Fiebiger, MD; Rickard A. Weger, MD; Markus Dawid, MD; Scott Menzies, MBBS, PhD

"After 3-6 months changes are very subtle. Criteria for melanoma appear after 6-12 months or more"

Objectives: To examine the role of sequential dermoscopy imaging in detecting incipient melanoma and to elucidate the impact of length of follow-up on the relevance of observed changes.

Design: Baseline and follow-up images of melanomas and melanocytic nevi excised only because of changes across time were inspected on a computer screen and assessed according to prospectively defined criteria. Lesions were stratified into 3 groups according to the length of follow-up.

Setting: Three hospital-based referral centers in Europe and Australia.

Patients: Four hundred sixty-one patients selected for digital dermoscopy monitoring.

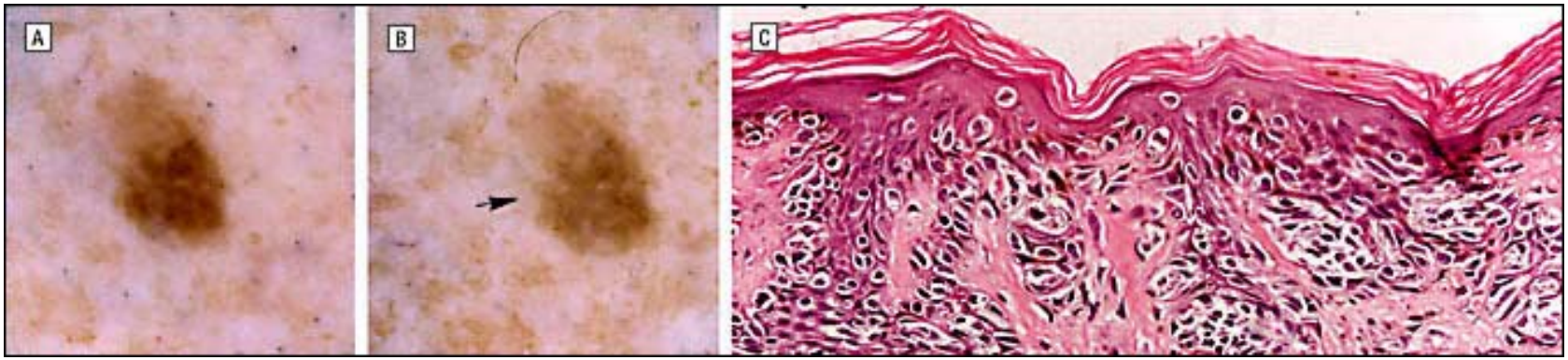
Main Outcome Measures: Description and comparison of dermoscopy features and changes in melanomas and melanocytic nevi at baseline and after follow-up.

Results: We inspected baseline and follow-up images of 499 melanocytic skin lesions from 461 patients. The histopathologic diagnosis was melanoma in 91 cases and melanocytic nevus in 408. Most melanomas (58.2%; n=53) were in situ, and the median thickness of invasive melanomas was 0.38 mm. Dermoscopy features of melanomas and nevi did not differ significantly at baseline. After follow-up of 1.5 to 4.5 months, 61.8% of the melanomas showed no specific dermoscopy features for melanoma. This value declined to 45.0% after follow-up of 4.5 to 8.0 months and to 35.1% after more than 8.0 months. We could not differentiate melanomas and changing nevi by means of observed changes or dermoscopy features when follow-up was shorter than 4.5 months. With longer follow-up, melanomas tended to enlarge asymmetrically with architectural and color changes, and nevi tended to enlarge symmetrically without architectural and color changes.

Conclusions: Sequential dermoscopy imaging detects incipient melanomas when they are still featureless. Interpretation of changes observed during follow-up depends on the length of follow-up.

Arch Dermatol. 2006;142:1113-1119

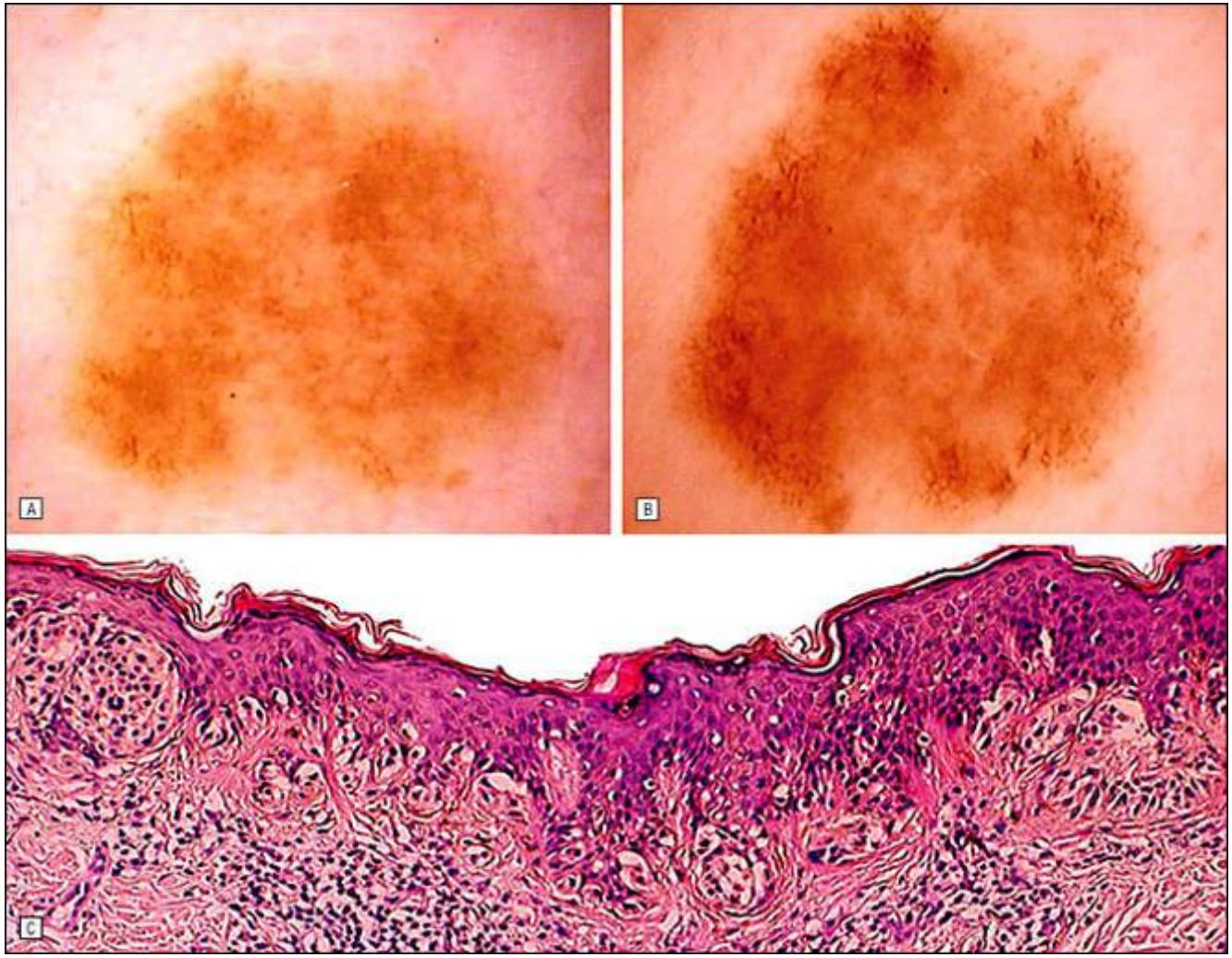
Melanoma in situ identified by short-term (3-month) monitoring



Kittler, H. et al. Arch Dermatol 2006;142:1113-1119.

Figure 1. Melanoma in situ identified by short-term (3-month) monitoring. A, Baseline image of inconspicuous lesion without dermoscopic features of melanomas. B, The follow-up lesion image shows an asymmetrical increase in size (arrow), with scattered areas of architectural change. C, The histopathologic study shows melanocytes arranged in irregular nests and as single cells, some of them disposed in higher layers of the epidermis (hematoxylin-eosin, original magnification x40). Histopathologic diagnosis: melanoma in situ.

Melanoma in situ identified by long-term (16-month) follow-up in a patient with multiple melanocytic nevi



Kittler, H. et al. Arch Dermatol 2006;142:1113-1119.

Figure 2. Melanoma in situ identified by long-term (16-month) follow-up in a patient with multiple melanocytic nevi. A, The baseline image. B, The follow-up image shows an asymmetrical increase in size and the appearance of a pigment network at the periphery. C, The histopathologic study shows melanocytes arranged in irregular nests and as single cells, some of them disposed in higher layers of the epidermis (hematoxylin-eosin, original magnification x40). Histopathologic diagnosis: melanoma in situ.

Digital Dermoscopy Follow-up of Atypical Nevi

- 7001 atypical nevi in 530 patients were followed-up for a median of 32.2 months
- 53 melanomas were detected among 637 excised lesions
- 18 of the 53 melanomas were exclusively identified by dermoscopy monitoring

Haenssle HA et al. J Invest Dermatol 2006: 126; 980

MoleMap
by Dermatologists

MoleMap

A comprehensive melanoma surveillance programme utilizing a tele-dermatology infrastructure.

- Low cost point of care imaging systems in standalone imaging clinics staffed by melanographers (nurses)
- Uses well proven digital dermoscopic techniques, clinical imaging, total body photography combined with a comprehensive set of data collected during the procedure
- Connects to a network of dermatologists highly experienced in the identification of melanoma – ***DERMOSCOPISTS***

The MoleMap Solution

Image and Data Capture

- RN Melanographer trained and mentored by Dermatologists
- Dermatologist developed protocols to guide the imaging procedure – regular clinical auditing and mentoring
- Digital camera specifically designed for dermatology with a dermoscopic light and lens

Diagnosis – Dermatologist

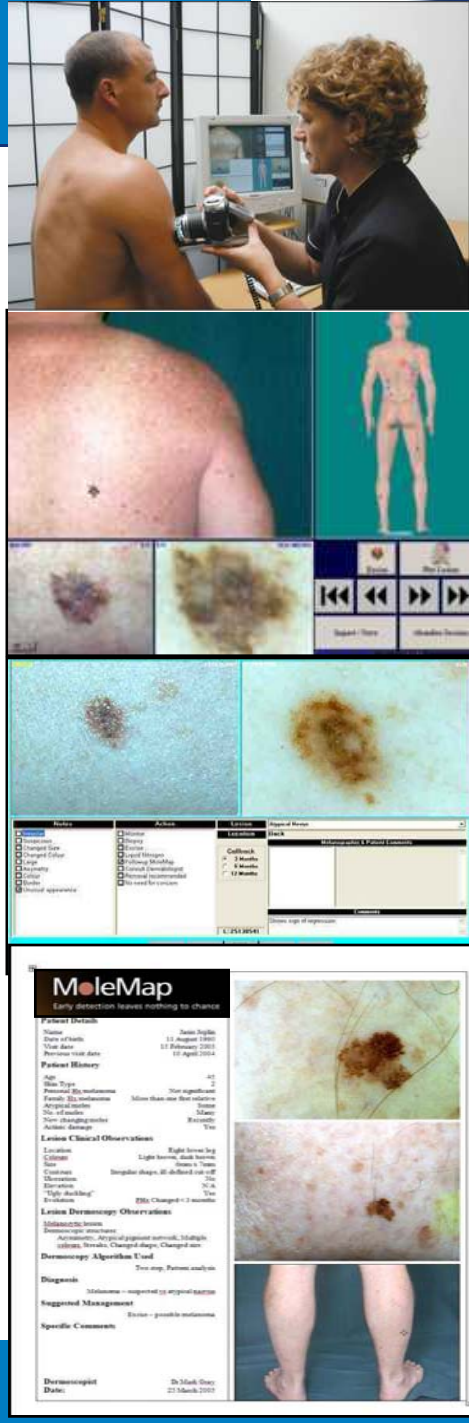
- Electronic receipt of data and images analysed and reported on through an expert interface
- Dermoscopy trained Dermatologists complete the diagnosis

Distributed Database – Electronic Medical Record

- Secure transfer and storage of digital images and patient data via peer to peer network – privacy compliant
- Historical monitoring to detect changes

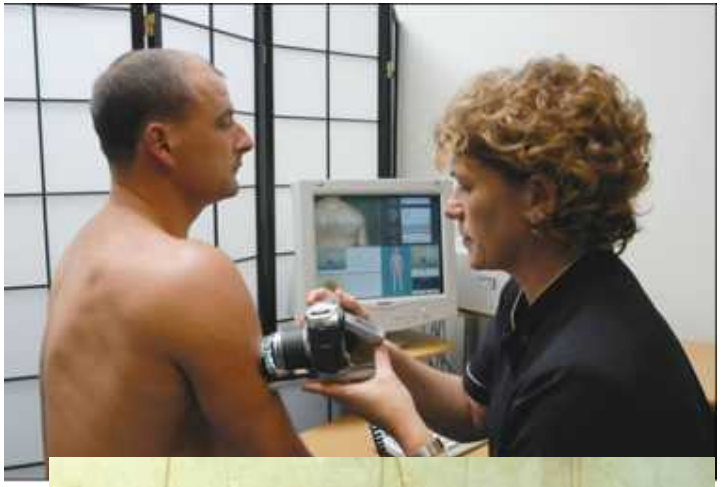
Report

- Sent to GP and patient
- GP remains manager of patient treatment

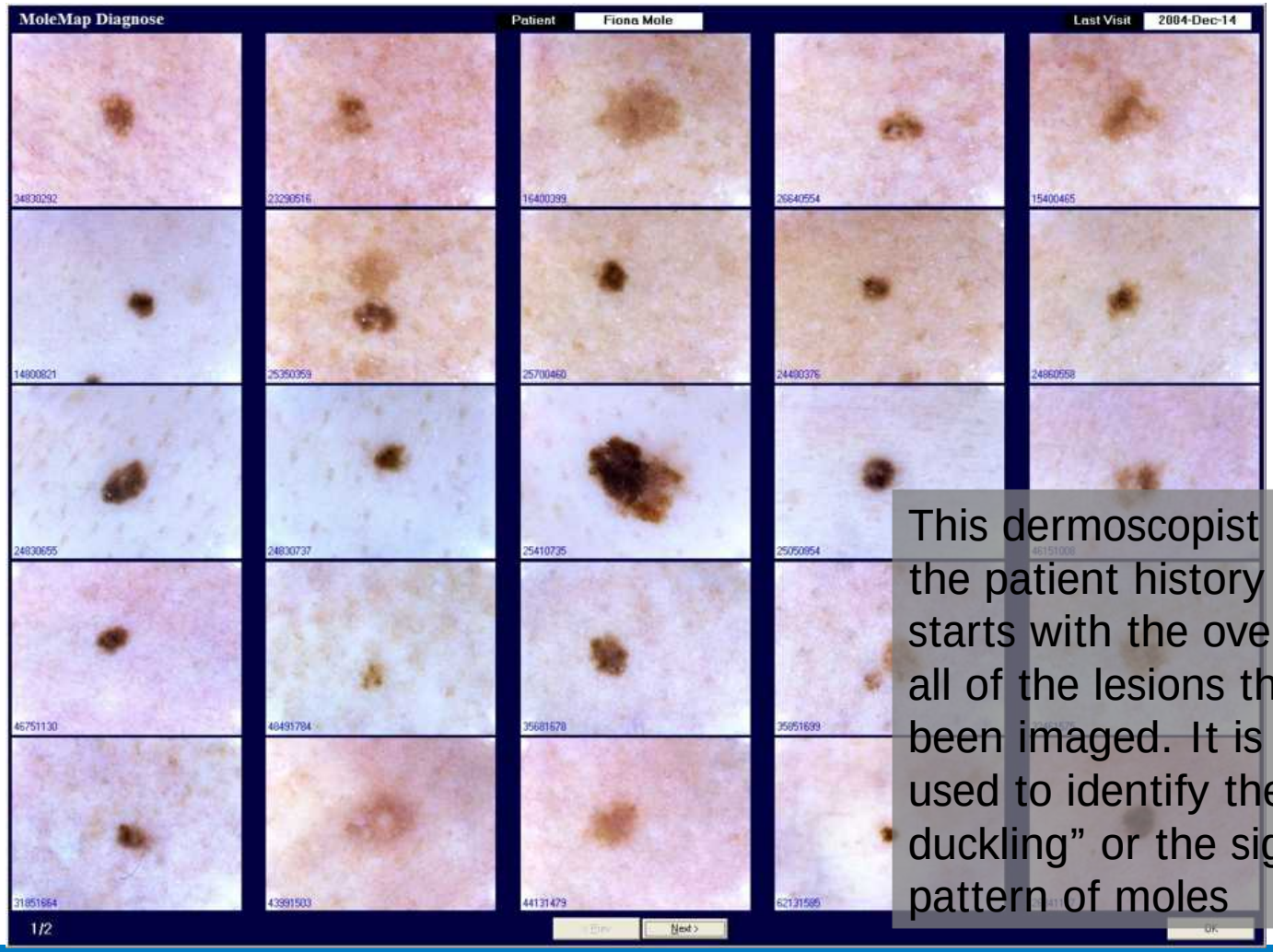


MoleMap Point of Care Clinics

- Customised digital camera with dermoscopic and clinical lighting units
- Standardised total body photography configuration
- Nurse driven for cost effectiveness and to provide a new level of patient care – melanographer
- Follows dermatologist developed and supervised protocols to guide the melanographer through the imaging procedure

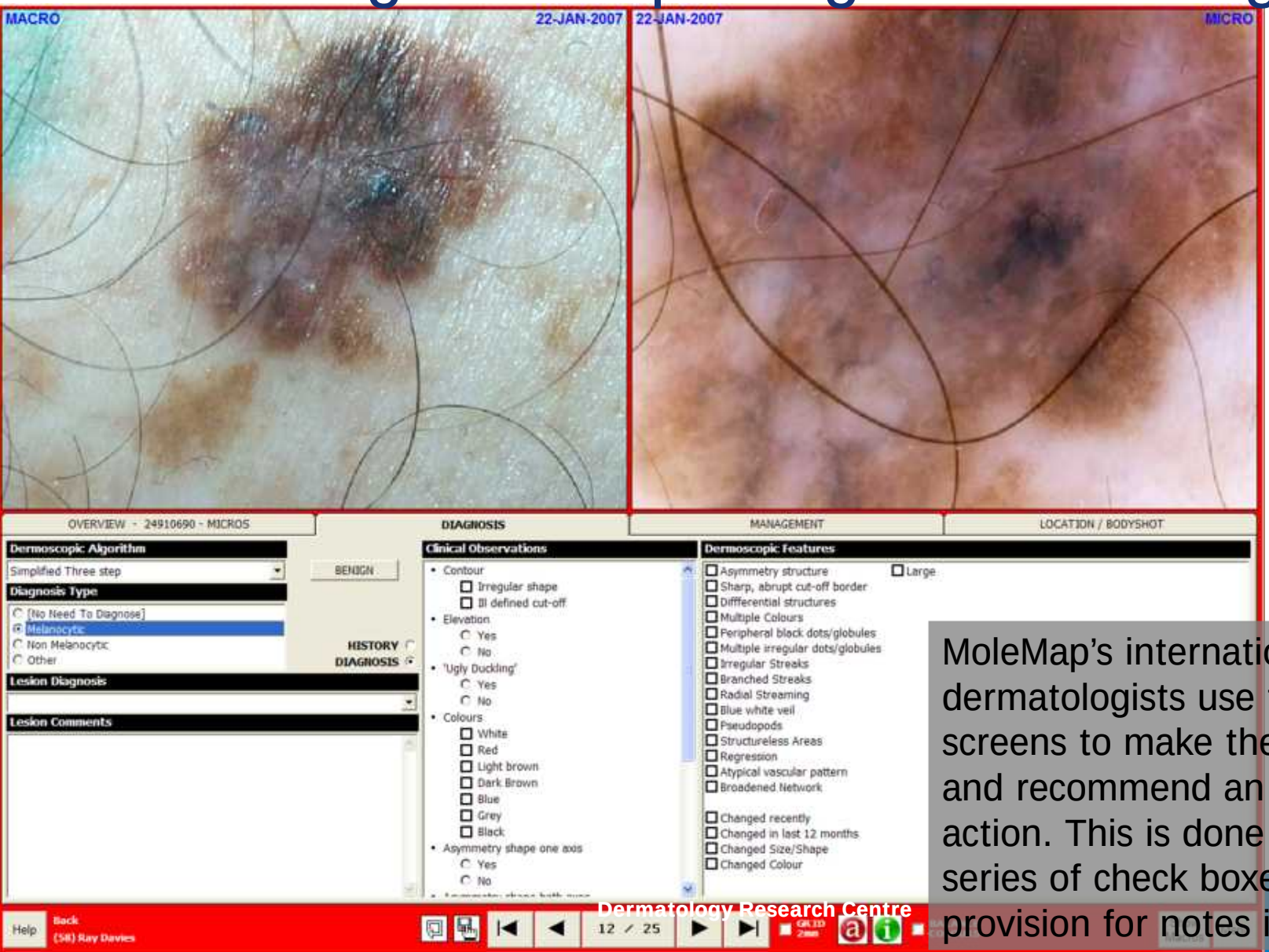


Point of Diagnosis Reporting – Lesion Overview



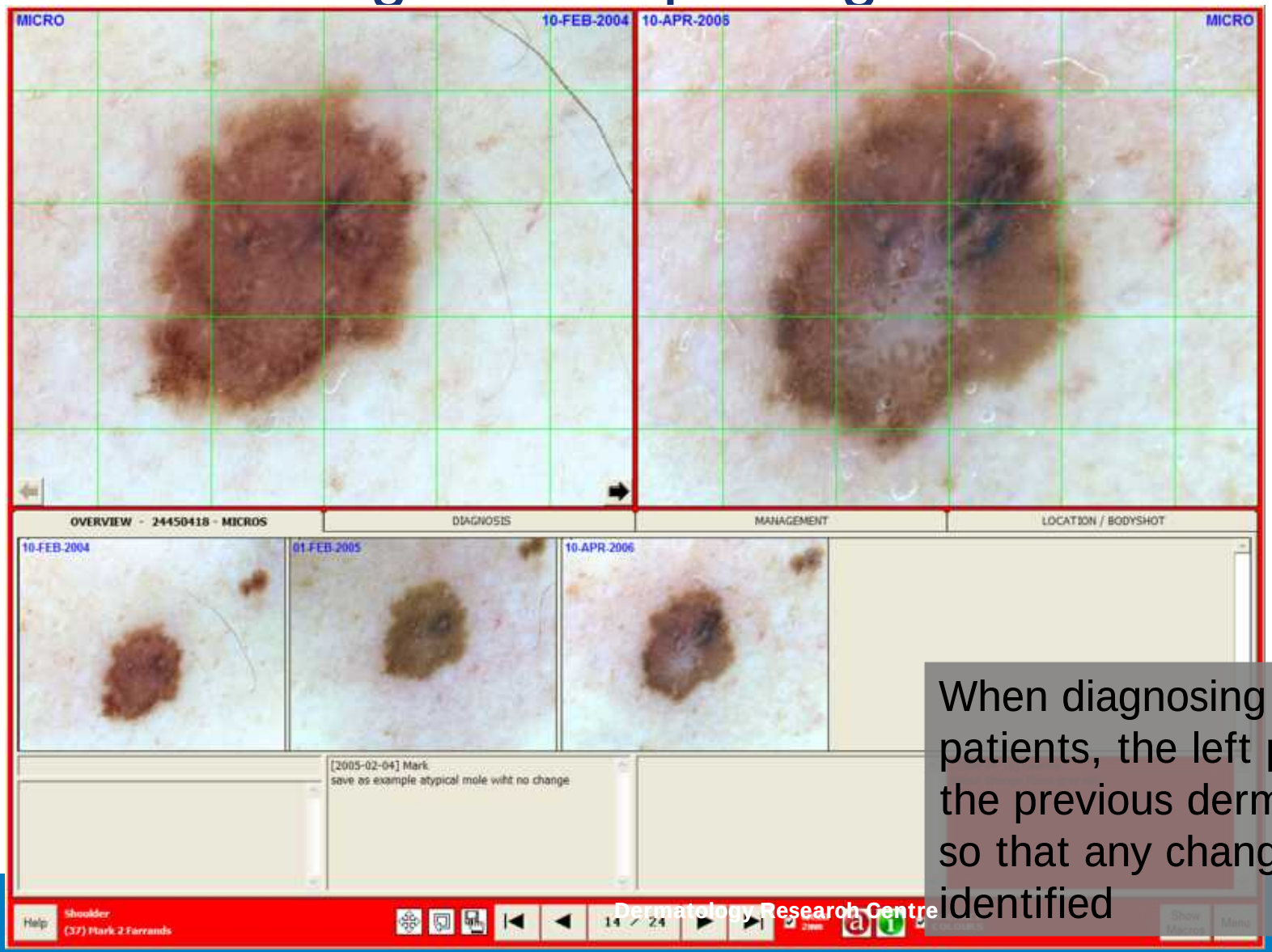
This dermoscopist reviews the patient history and then starts with the overview of all of the lesions that have been imaged. It is generally used to identify the “ugly duckling” or the signature pattern of moles

Point of Diagnosis Reporting – Lesion Diagnosis



MoleMap's international panel of dermatologists use these screens to make the diagnosis and recommend an appropriate action. This is done through a series of check boxes with the provision for notes if required

Point of Diagnosis Reporting – Serial Monitoring



When diagnosing follow-up patients, the left panel shows the previous dermoscopy view so that any changes can be identified

Lesions requiring attention

Any lesions that require further investigation are reported through this standardised dermoscopy report that is sent to the patient's doctor

Patient report and associated images are sent to appropriate doctor(s) for treatment or monitoring

Patient file is available on CD for self monitoring or dermatologist clinical follow-up

Electronic hyperlink can link to the report and relevant images. This can be used for imbedding into an electronic record

MoleMap
early detection avoids the risks of melanoma

Patient Details

Name	Patient 4
Date of birth	11 August 1954
Visit date	20 March 2006
Previous visit date	

Patient History

Age	51
Skin Type	2
Personal Hx melanoma	No
Family Hx melanoma	No
Atypical moles	Some
No. of moles	Some
New changing moles	Recently
Actinic damage	Yes

Lesion Clinical Observations

Location	Shoulder
Colours	Light brown, dark brown, black, red
Size	12mm x 17mm
Contours	Irregular shape, ill-defined cut-off
Ulceration	No
Elevation	N/A
"Ugly duckling"	Yes
Evolution	PHx Changed < 12 months

Lesion Dermoscopy Observations

Melanocytic lesion
Dermoscopic structures:

Asymmetry, Irregular Borders, Irregular structure, Multiple Colours, Large, Globules/Dots, Blue grey veil, Changed, Changed Size/Shape, Regression

Dermoscopy Algorithm Used

Two step, Pattern analysis

Diagnosis

Melanoma

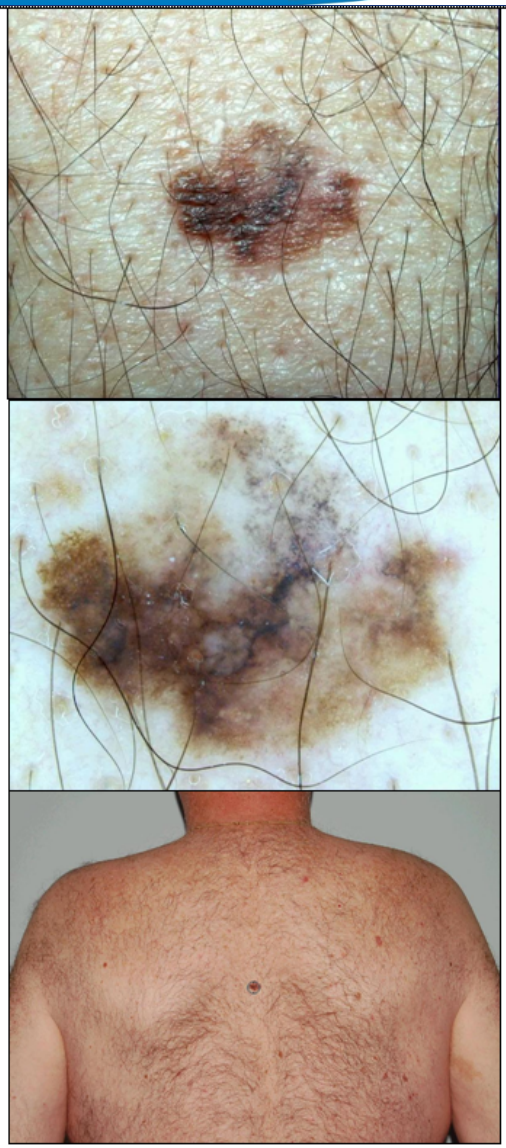
Suggested Management

Excise – probable melanoma

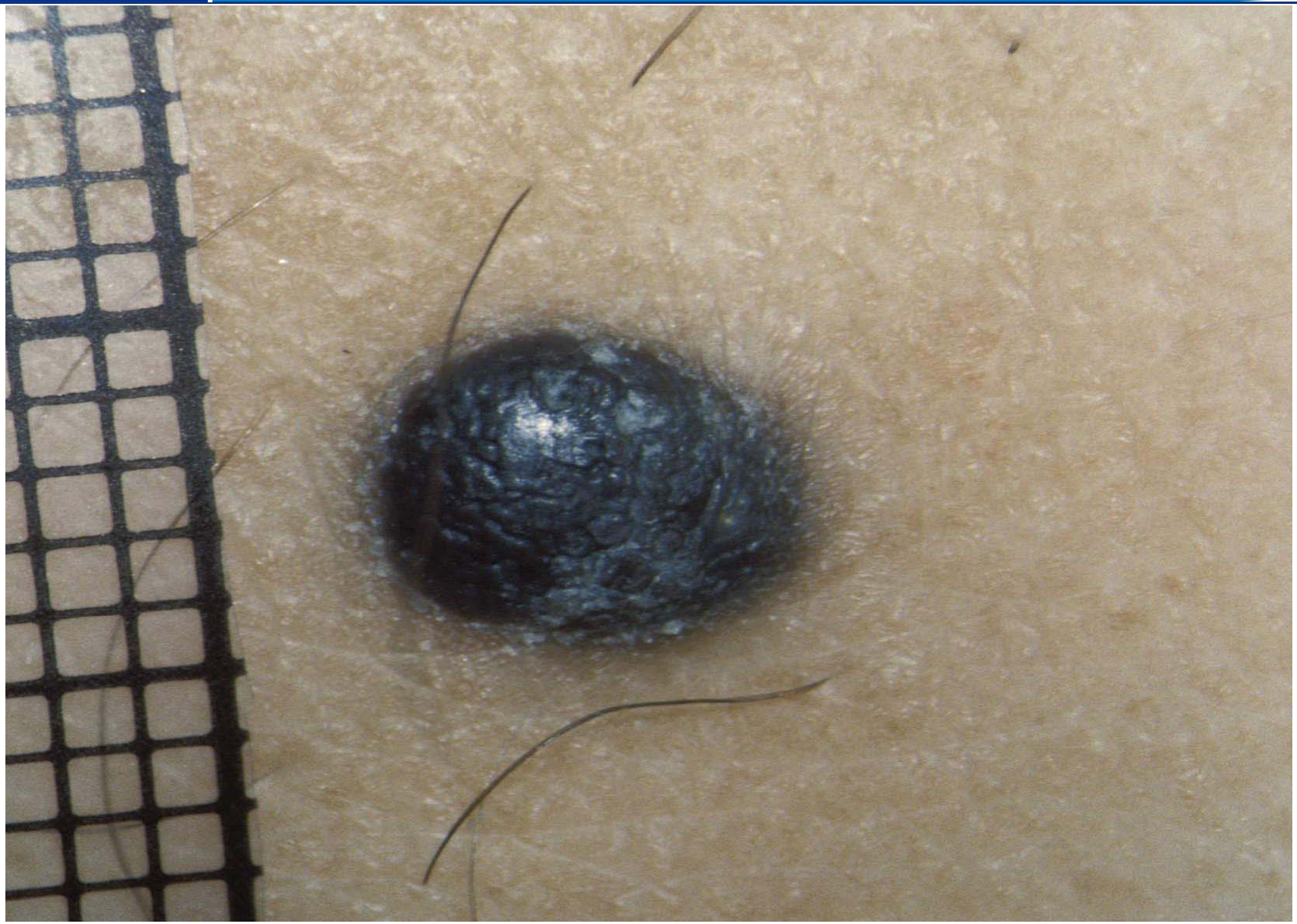
Specific Comments

Very High Risk - Self surveillance with 6 to 12 monthly MoleMap and / or clinical assessment

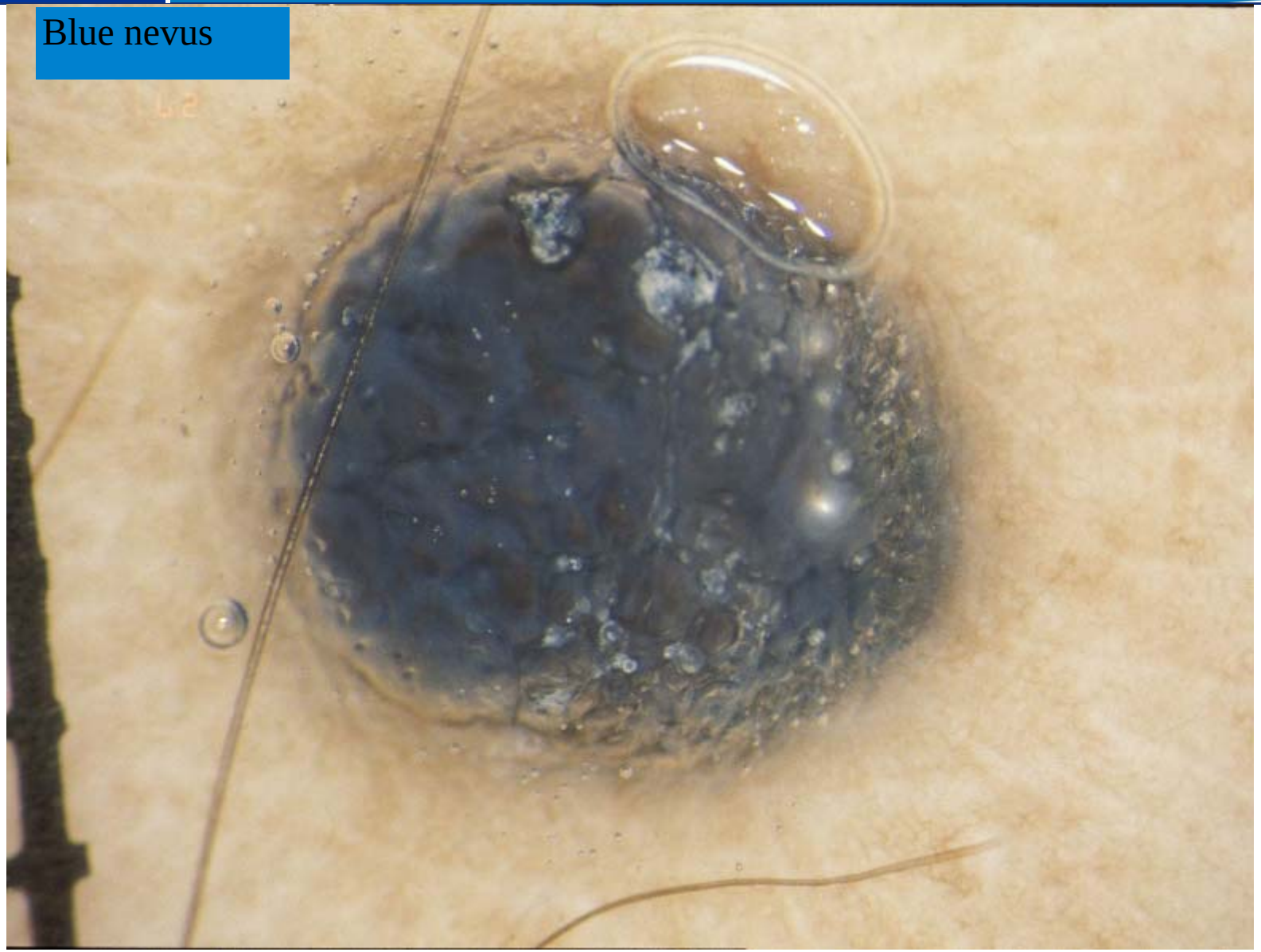
Dermoscopist	Dr Martin Haskett
Date:	21 March 2006

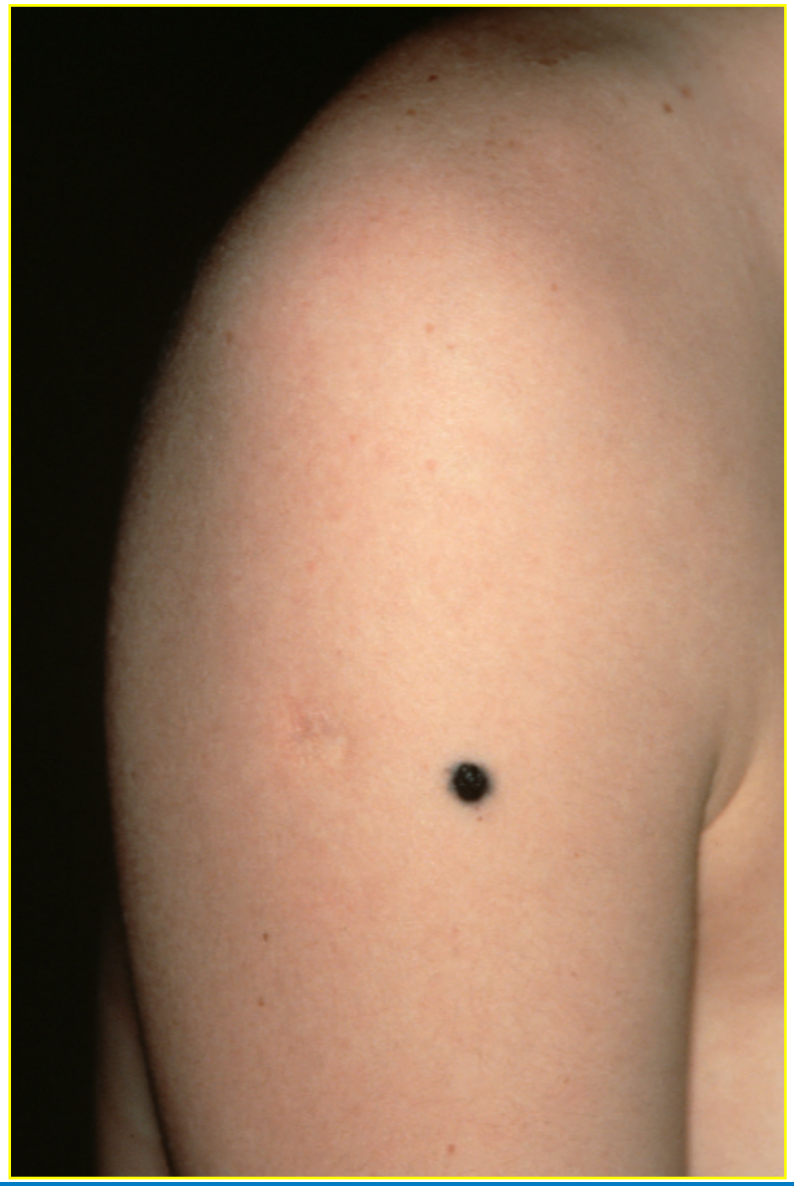


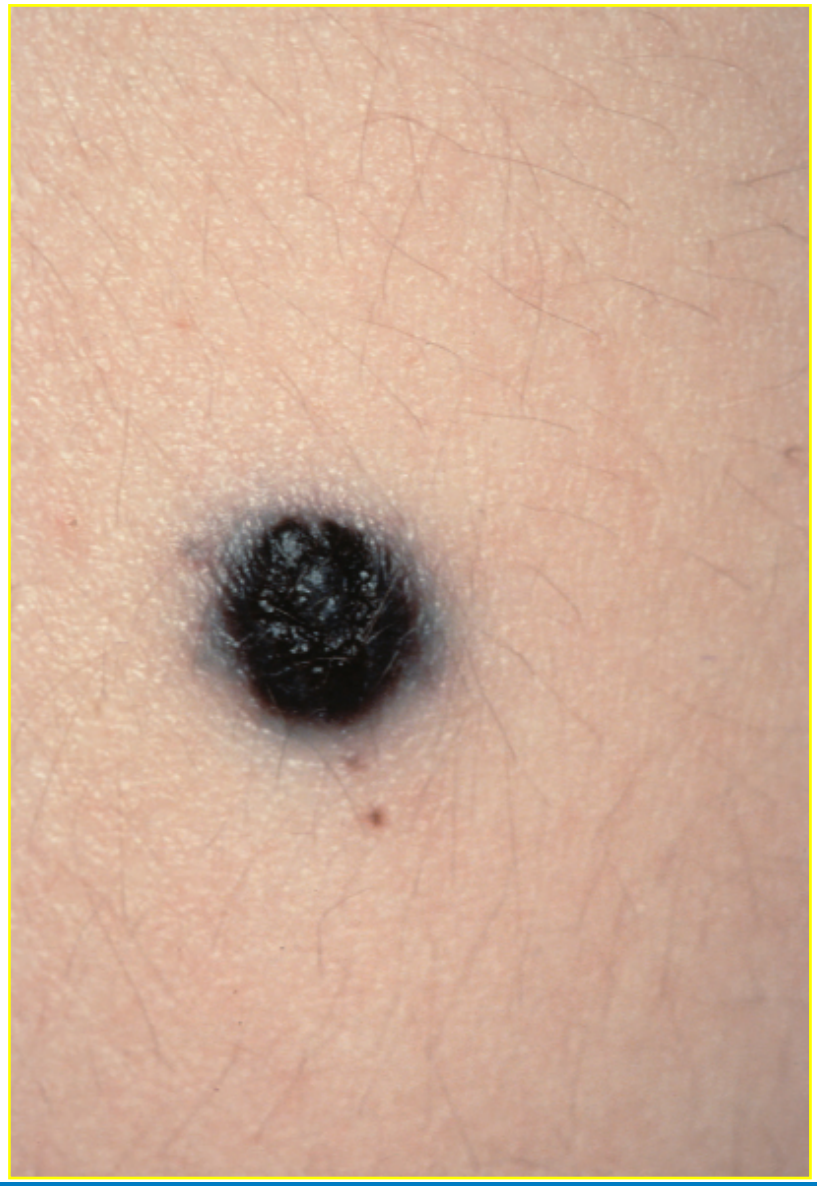
Never follow-up equivocal nodular lesions!!

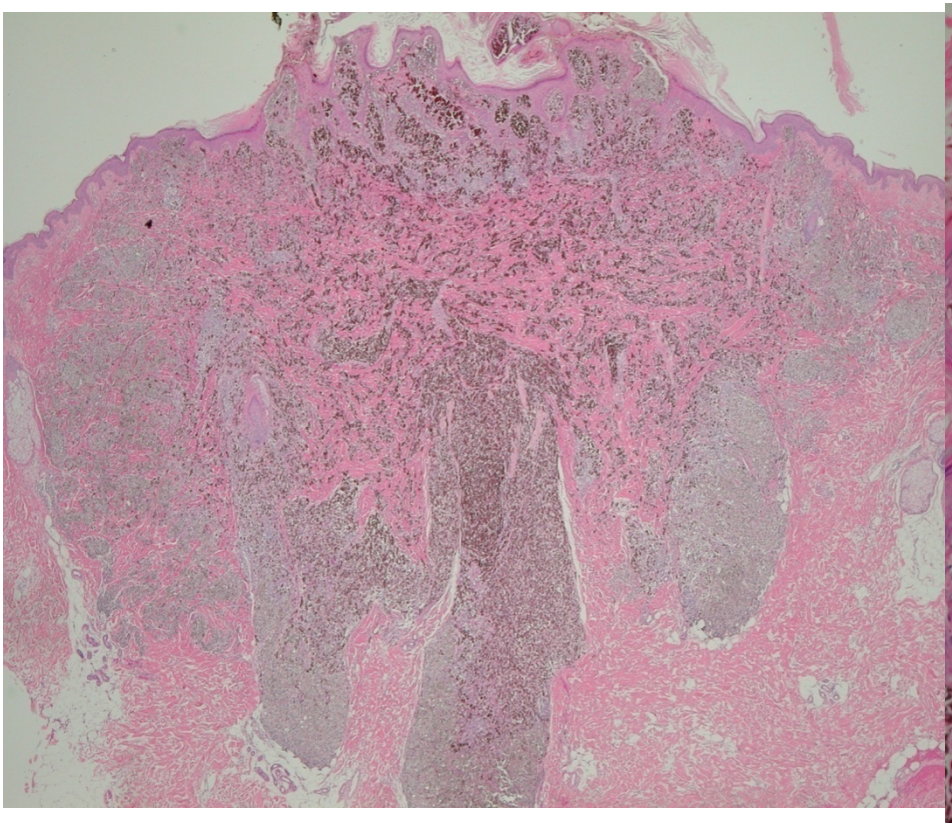


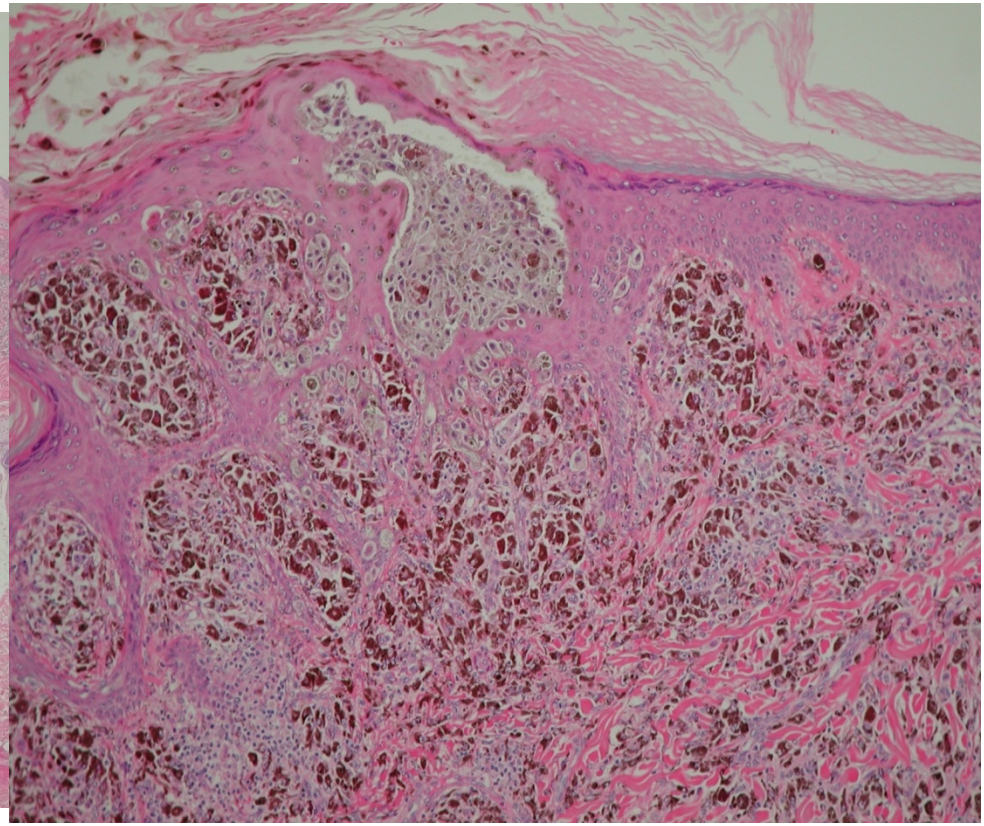
Blue nevus











Conclusion

Excision of suspicious lesions especially if a single atypical lesion (ugly duckling sign)

Follow up in 3 months for slightly atypical, flat lesions especially if numerous “similar” atypical lesions are present

Follow up in 6 months or one year for high risk patients