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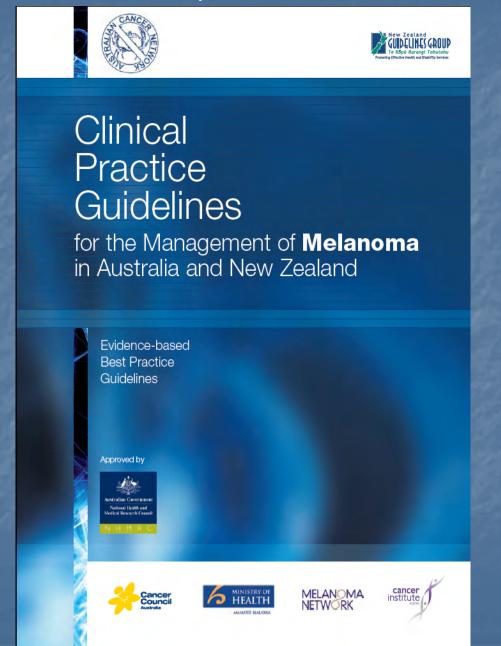
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Melanoma Update

Richard Bloom

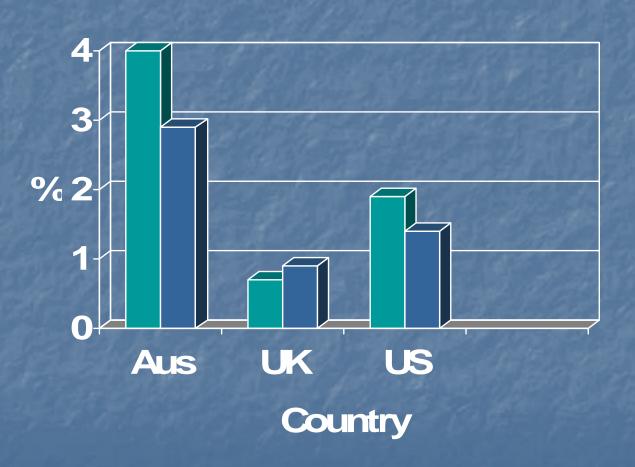
http://www.cancer.org.au/File/HealthProfessionals/ClinicalPracticeGuideline s-ManagementofMelanoma.pdf



Melanoma Update

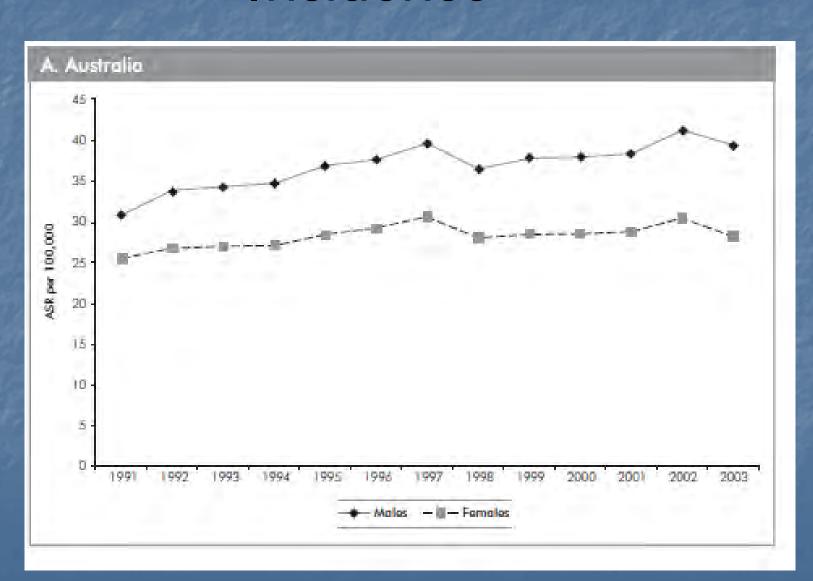
- Risk Factors
- Margins
- SNB
- Surveillence

Lifetime risk of Melanoma

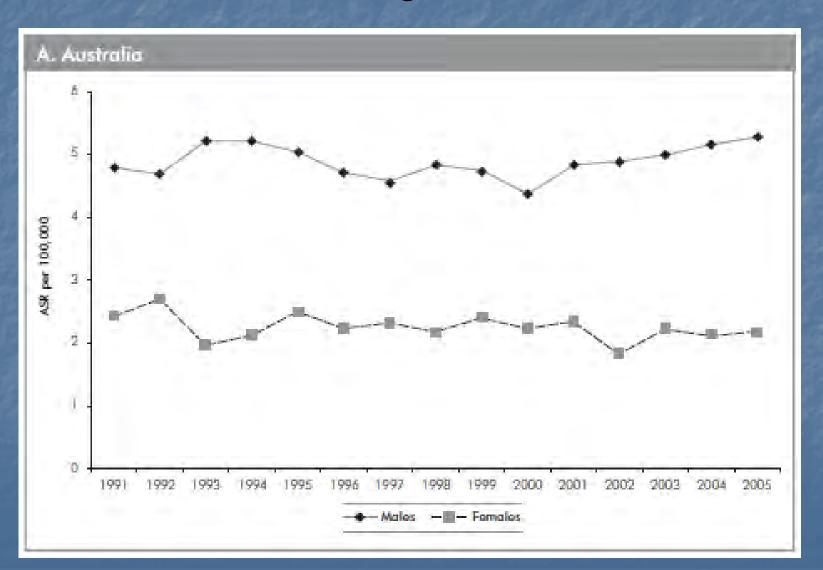


- Males
- □ Female

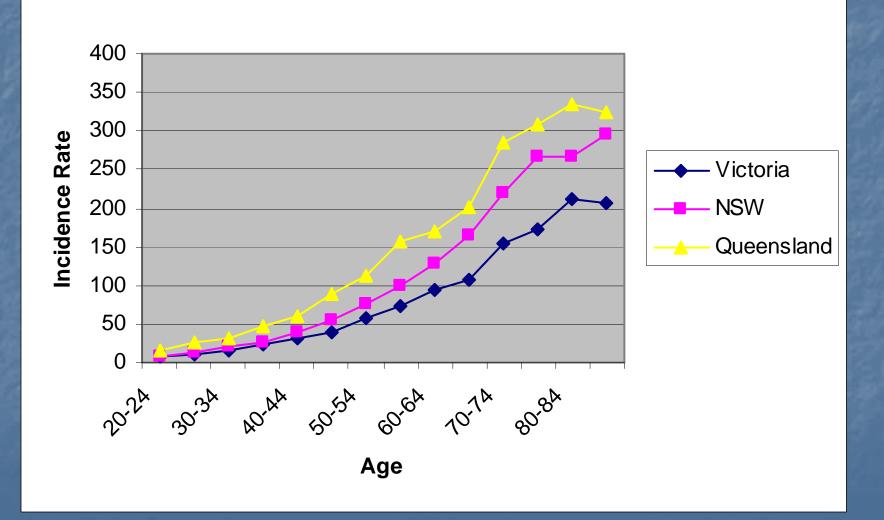
Incidence



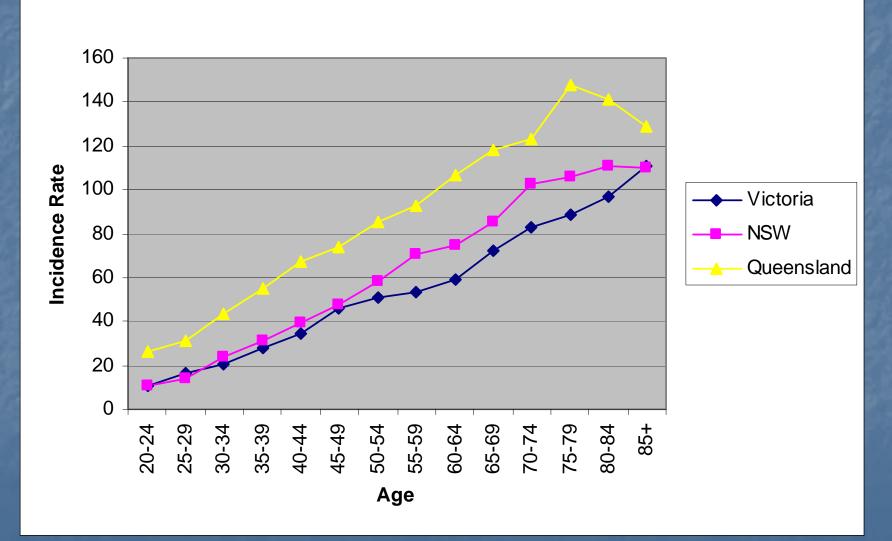
Mortality rates



Melanoma Incidence Males



Melanoma Incidence Females



Risk Factors

http://www.cancer.gov/melanomarisktool/

History of Margins

1907	Handley recommended a liberal
	resection of skin

- 1962 Petersen advocated a 5cm margin
- 1977 Breslow related prognosis to thickness
- 1988 Early results from Veronesi's study
- 1991 WHO trial: 1 Vs 3cm for thin melanoma

Veronesi¹

- 612 patients
- 1cm Vs 3cm margin for CM < 2mm
- No difference in OS, DFS or LR
- Follow up 8 years
- LR rate very low

Swedish Study²

- 769 patients
- 2cm Vs 5cm for Melanoma <2mm</p>
- No difference in LR, OS or RFS
- LR rate very low

[2] Cohn-Cedermark et al Long term results of a randomized study by the Swedish Melanoma study group on 2cm versus 5cm resection margins for Patients with cutaneous melanoma with a tumor thickness of 0.8-2.0mm. Cancer. 2000;89:1495-501

Intergroup³

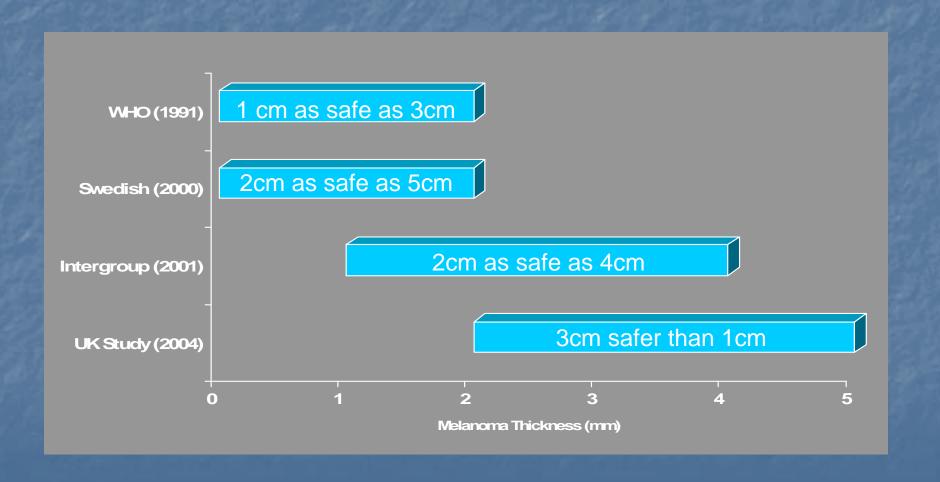
- 486 patients
- 2 Vs 4cm margin for Melanomas 1-4mm
- No difference in OS or locoregional recurrence
- LR rare
- Ulceration is a poor indicator for recurrence

[3] Balch CM et al. Long-term Results of a Prospective Surgical Trial Comparing 2cm vs. 4cm Excision Margins for 740 Patients with 1-4mm Melanomas. *Annals Surg Oncology*.8(2):101-108

UK Study⁴

- 900 patients
- 1cm Vs 3cm for melanoma > 2cm
- Locoregional higher in 1cm group
- LR low in both groups
- No difference in death from melanoma

Summary



Melanoma Guidelines

Recommendations	
	Grade
 After initial excision biopsy; the radial excision margins, measured clinically from the edge of the melanoma, be: 	
1. (pTis) melanoma in situ: margin 5mm	С
2. (pT1) melanoma < 1.0mm: margin 1cm	В
3. (pT2) melanoma 1.0-2.0mm: margin 1-2cm	В
4. (pT3) melanoma 2.0-4.0mm; margin 1-2cm	В
5. (pT4) melanoma > 4.0mm: margin 2cm	В
 Caution be exercised for melanomas 2–4mm thick, because evidence concerning optimal excision margins is unclear. Where possible, it may be desirable to take a wider margin (2cm) for these tumours depending on tumour site and surgeon/patient preference 	В
 Acral lentiginous and subungual melanoma are usually treated with a minimum margin as set out above, where practicable, including partial digital amputation usually incorporating the joint immediately proximal to the melanoma 	D

Food for thought

- Local recurrence
 - Rate is very low
 - More likely stage IV disease than residual
- Ulceration
 - Consider wider margin

Sentinel Node Biopsy

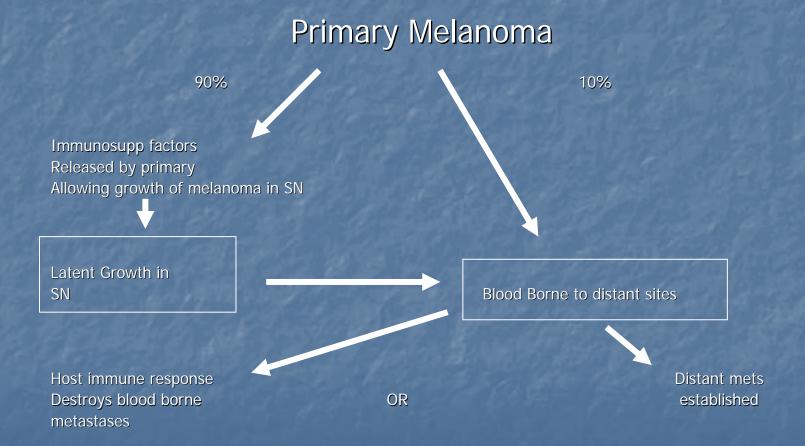
Introduction

- Background
- Theory
- Technique
- **SNB**
- MSLT-1
- MSLT-2

SNB – Hypothesis

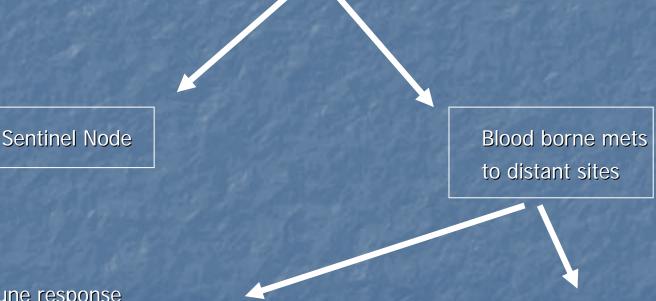
- Lymphatic metastasis is orderly
- Predictable by lymphatic mapping
- SN is the first regional node in lymphatic drainage pathway from the PM
- SNB detects occult mets
- Tumour status of SN accurately reflects tumour status of the basin
- SN status allows prediction of regional nodal status and who may benefit from early CLND

Incubator Theory



Marker Hypothesis

Primary Melanoma



Host immune response
Destroys blood borne mets

Establishes distant mets

ELND

- 20% of patients with Intermediately thick melanomas have nodal mets at time of PCM
- **3** RCT
 - Intergroup (Balch 1996)
 - WHO Melanoma Trial 14 (Cascinelli 1998)
 - WHO Melanoma Trial 1 (Veronesi 1982)
- No overall survival benefit
 - Subset analysis showed some benefit for non ulcerated, PCM 1.0 2.0mm, <60 years</p>
- Complication rate 71% Serpell ANZ JS 2003

Technique

- Performed at time of WLE
- Lymphoscintography on day of surgery
- Patent blue intradermal injection
- Gamma probe intraoperatively

Morton DL, Wen DR, Wong JH, et al. Technical details of intraoperative lymphatic mapping for early stage melanoma. Arch Surg 1992;127:392-9.



Patent blue injection



- Positive node
 - Blue
 - Radioactive count
 - 97% accurate (Morton)

SNB

Incidence of micrometastases in SLN

■ PCM < 0.75mm 1%

□ PCM 0.76 – 1.5mm 8.3%

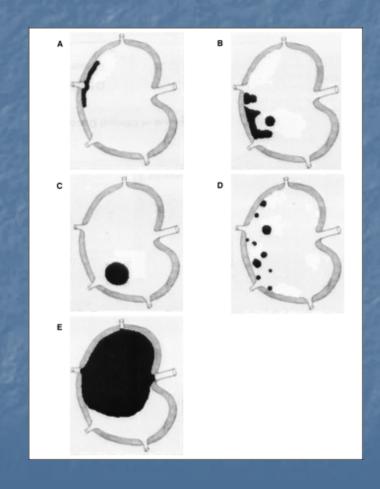
■ PCM 1.51- 4.0mm 22.7%

□ PCM >4.0mm 35.5%

Lens MB, Dawes M, Newton-Bishop JA, Goodacre T. Tumour thickness as a predictor of occult lymph node metastases in patients with stage I and II melanoma undergoing sentinel lymph node biopsy. Br J Surg 2002; 89(10):1223–1227.

Non SLN status

- Microanatomiclocation of metastaticmelanoma
 - Subcapsular no nonSLN mets 0/38 patients
 - Combined subcapsular and parenchymal
 - Parenchymal
 - Multifocal
 - Extensive



Non SLN status

Micromorphometric features

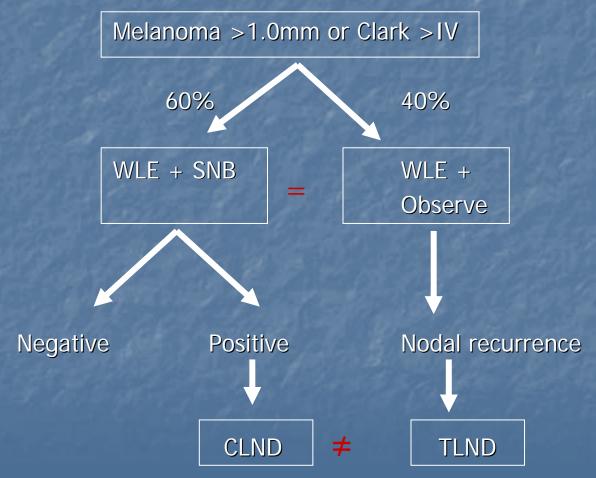
- Tumour penetrative depth >2mm
- Deposit size >10mm²
- Presence of melanoma in perinodal lymphatic vessels
- Effacement of nodal architecture by metastatic melanoma cells

American Journal of Clinical Pathology Vol 122, 2004

Argument against SNB

- No proven adjuvant Rx for pts with +ve SNB
- No proven benefit of survival CLND following +ve SNB
- Ample prognostic information provided from tumour thickness, level, ulceration
- No benefit from ELND in 3 prospective, randomised, trials
- Is CLND post SNB just an ELND?

MSLT 1



Morton DL, Thompson JF, Cochran AJ, Mozzillo N, Elashoff R, Essner R et al. Sentinel-node biopsy or nodal observation in melanoma. N Engl J Med 2006; 355(13):1307–1317.

MSLT -1

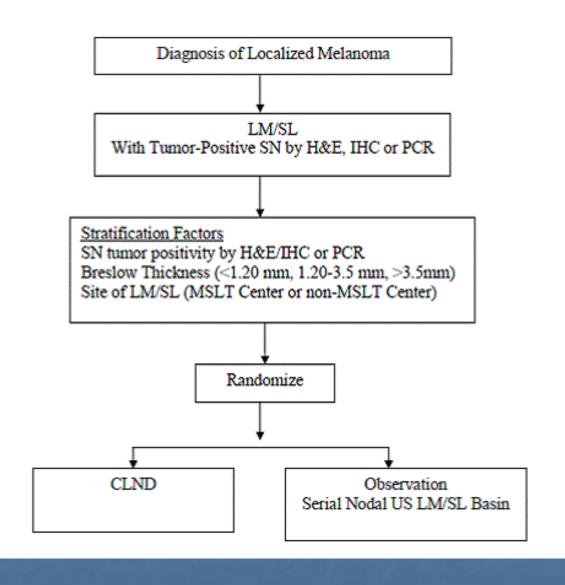
- 5 YSR between WLE group and SNB were similar
- Status of the SNB provides important prognostic information
- Decreased distant mets for SNB patients
- Potential survival advantage for melanomas 1.2-3.5mm thick

MSLT - II

- Does removal of a positive SN alone improve survival?
- Is CLND necessary?

Is CLND necessary

- 1 study at least has shown retrospectively
 - No difference in Nodal recurrence or DSS



Current Guidelines

Evidence summary	Level	References
Sentinel lymph node status provides accurate prognostic information for disease-free and overall survival for melanomas stage T1b ¹⁰ or greater	1	1,3
To date, the MSLT-1 study shows no overall survival benefit	11	4,5
Patients undergoing SLNB have a significantly lower rate of distant metastasis compared with wide local excision and observation	И	5
The interim results of the MSLT-1 study shows a potential survival benefit to patients with 1.2–3.5mm thick melanomas with positive sentinel lymph nodes who undergo immediate completion lymphadenectomy compared to those in the control group who undergo clinical observation and develop nodal recurrence	111-2	4
Sentinel node biopsy can be technically demanding and requires specialised expertise and resources	111-1	2

Recommendations

	Grade
 Patients with a melanoma greater than 1.0mm in thickness be given the opportunity to discuss sentinel lymph node biopsy to provide staging and prognostic information 	С
 SLNB be performed only, following a full discussion of the options with the patient, in a unit with access to appropriate surgical, nuclear medicine and pathology services 	С

Monitoring

