

Management of Primary Malignant Melanoma

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Malignant Melanoma: A Clinical Overview

- The melanoma now is the 5th most common cancer in the US
- Only 4-5% of all skin cancers
- Majority of deaths from skin malignancies (>75%).
- In the year 2013, an estimated
 - 76,690 new cases of melanoma
 - 9,480 patients will die of the disease in the US
- Increasing in men more rapidly than any other malignancy and, in women more rapidly than any other malignancy except lung cancer.

Malignant Melanoma: A Clinical Overview

- The incidence of melanoma is increasing at a rate of 3% per year- remains the largest annual percent change for any malignancy in the US.
- Disease of Caucasians – incidence is 29 per 100,000 Caucasians compared to 1 per 100,000 non-Caucasians.
- Medial age of diagnosis is 61.
- It is also one of the most frequent cancers found in adolescents and young adults
- The most common malignancy in women ages 20-30.

Malignant Melanoma: Epidemiology and Risk Factors

- Disease of whites
- Less common in Asian and black populations
- M>F
- Prognosis better for women
- Anatomic distribution
 - * men – trunk, head, neck
 - * women – lower extremity
 - * dark skin – palms, soles, nailbed
- > 95% originate in the skin
- 3%-10% present with metastatic disease with no clinically visible primary melanoma on the skin

Malignant Melanoma: Risk Factors

- Blue eyes; Red/Blonde hair; Fair Complexion
- Eastern Europe; Russia; Former USSR; Irish/Scottish background
- Exposure to sunlight

*severe blistering sunburn in childhood is a significant risk factor

- Prior history of MM (5%)
- Family history of MM (5-10%)
- Genes linked to familial melanoma – CDK, CDKN2A, CDK4, MC1R, BRAF oncogene
- Single dysplastic nevus (5x risk)
- Dysplastic nevus syndrome (10-15%)
- Large congenital nevus (10%)
- Spitz nevi

Dysplastic Nevus

- Dysplastic nevus
 - 1 clinical DN: 2 x incidence
 - 10 clinical DN: 12 x incidence



- Acquired moles
 - Small: <5mm
 - Symmetric
 - Defined borders

- Dysplastic nevus
 - >5mm (6-15mm)
 - Flat, ill-defined borders
 - Brown-tan
 - Mottled
 - Most common on trunk



- Asymmetry, variations of color, black → biopsy

Malignant Melanoma: Histology

- Superficial spreading melanoma 70%
- Nodular melanoma 15%
- Lentigo maligna melanoma 10%
- Acral lentiginous melanoma 5%
- Desmoplastic melanoma 1.7% – 4%

Superficial Spreading Melanoma

- Most common (70%)
- Not necessarily a/w sun-exposed skin
- Flat, pigmented
- Grow in a radial pattern
- Arise near or from a pre-existing brown junctional nevi
- Multicolored: black and blue



Nodular Melanoma

- 15% cases
- Do NOT arise from pre-existing nevi
- Darker than SSM
- Uniform coloration
- Raised with sharp notched borders
- Worst prognosis



Lentigo Maligna Melanoma

- ~10%
- Older people
- Sun-damaged skin
- Flat, irregular borders
- Large (>3cm)
- Flat with lacy perimeter
- Looks like a brown stain of the skin



Acral Lentiginous Melanoma

- 2-8% of cases
- 35-60% of cases in dark-skinned patients
Black, Hispanic, Asian
- 7th decade
- Majority of the soles
- Large (>3cm)
- Irregular, flat lesions with variegated color (brown)
- Poor prognosis



Desmoplastic Melanoma

- First described by Conley in 1971
- Accounts for 1.7%-4% of all melanomas
- Male gender
- Extensive sun exposure
- Different behavioral patterns
- Local recurrence rate as high as 50%
- Rate of nodal metastases less than 10%

Malignant Melanoma: Clinical Features

- **CHANGING** pigmented skin lesion
 - A** Asymmetry
 - B** Borders are irregular
 - C** Color variation
 - D** Diameter > 6 mm
 - E** Elevation

Malignant Melanoma: Principles of Biopsy

- **Excisional biopsy**
 - preferred
 - 2-3 mm margin
 - avoid wider margin to permit accurate subsequent lymphatic mapping
 - primary closure
- **Incisional or punch biopsy**
 - full thickness of the clinically **thickest** portion

Malignant Melanoma: Principles of Biopsy

- Plan for definitive surgery
- Longitudinal on extremities
- Transverse of trunk



Wrong



Correct

Malignant Melanoma: Pathology Report

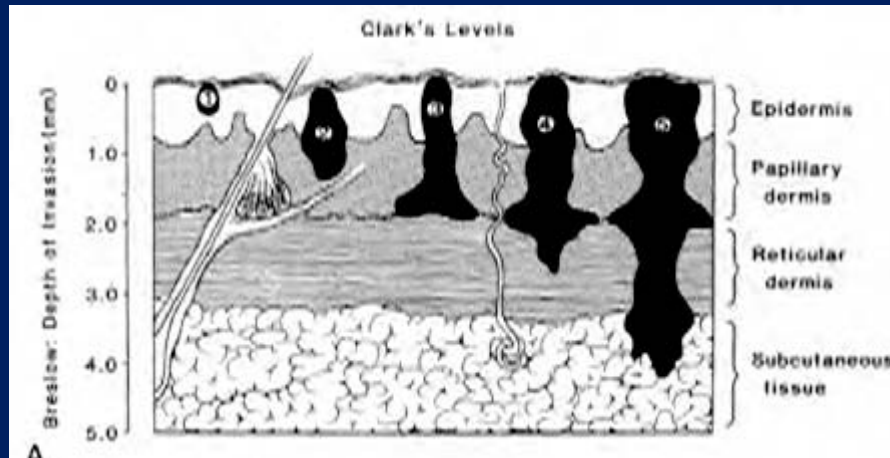
- Breslow thickness (mm)
- Histologic Ulceration
- Mitotic rate
- Clark level
- Peripheral and deep margin status
- Microsatelitosis if present, should be presented

Malignant Melanoma: Pathology Report

- Encourage reporting of these additional factors (AAD Task Force):
 - Location
 - Regression
 - Tumor infiltrating lymphocytes (TIL)
 - Vertical growth phase (VGP)
 - Angiolymphatic invasion

Malignant Melanoma: Clark's Classification

Level	Description	T Stage
I	Limited to epidermis	Tis
II	Into papillary dermis	T1
III	Fill the papillary dermis	T2
IV	Into reticular dermis	T3
V	Into subcutaneous tissue	T4



Breslow Microstaging System

Thickness

0-1 mm
1-2 mm
2-4 mm
> 4 mm

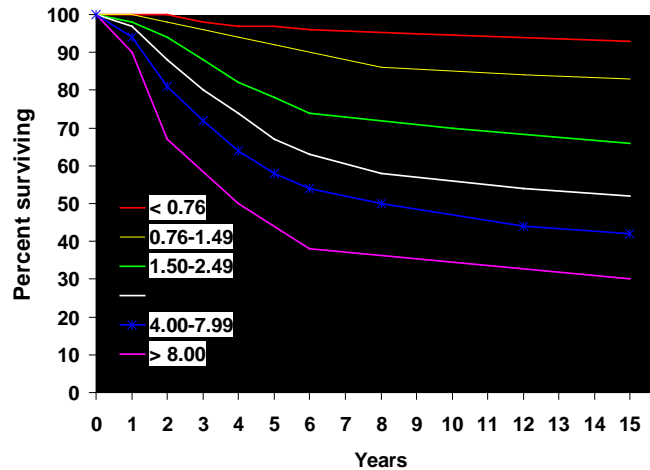
Description

Thin
Intermediate
Intermediate
Thick

T Stage

T1
T2
T3
T4

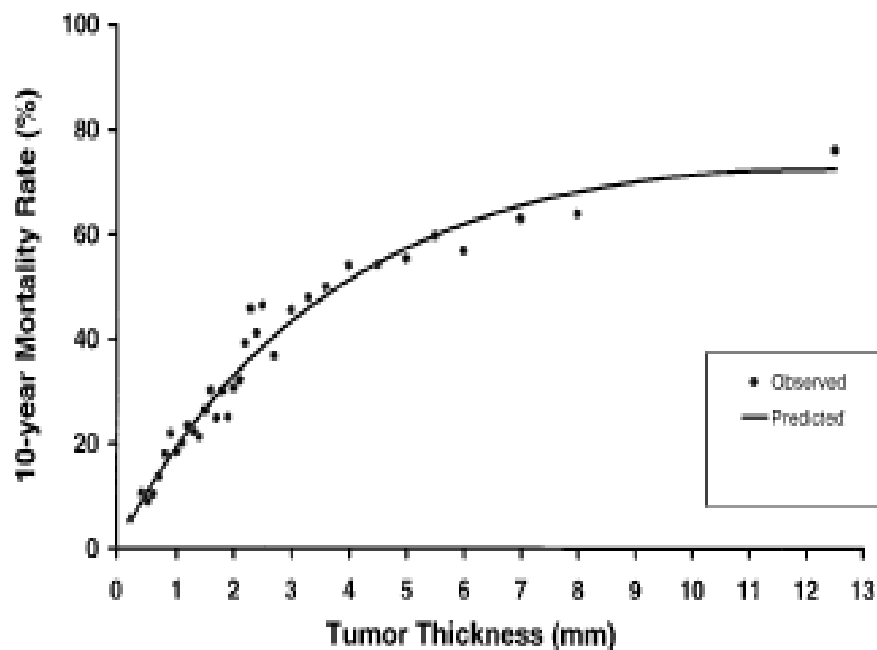
SURVIVAL BY THICKNESS (STAGE I AND II)



Prognostic Factors: Tumor Thickness is Highly Correlated with Mortality

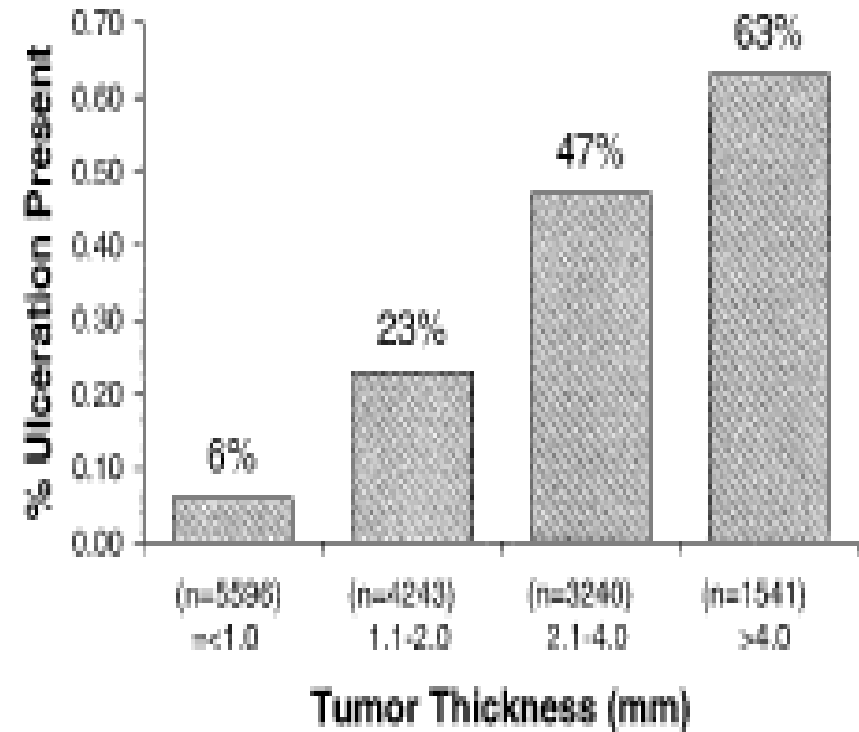
- 10-year mortality of 15,320 patients with clinically localized melanoma
- **Thickness** is the most important prognostic factor for melanoma-specific survival in node negative patients

Balch et al., J Clin Oncol, 2001



Prognostic Factors: Incidence of Ulceration Correlates With Tumor Thickness

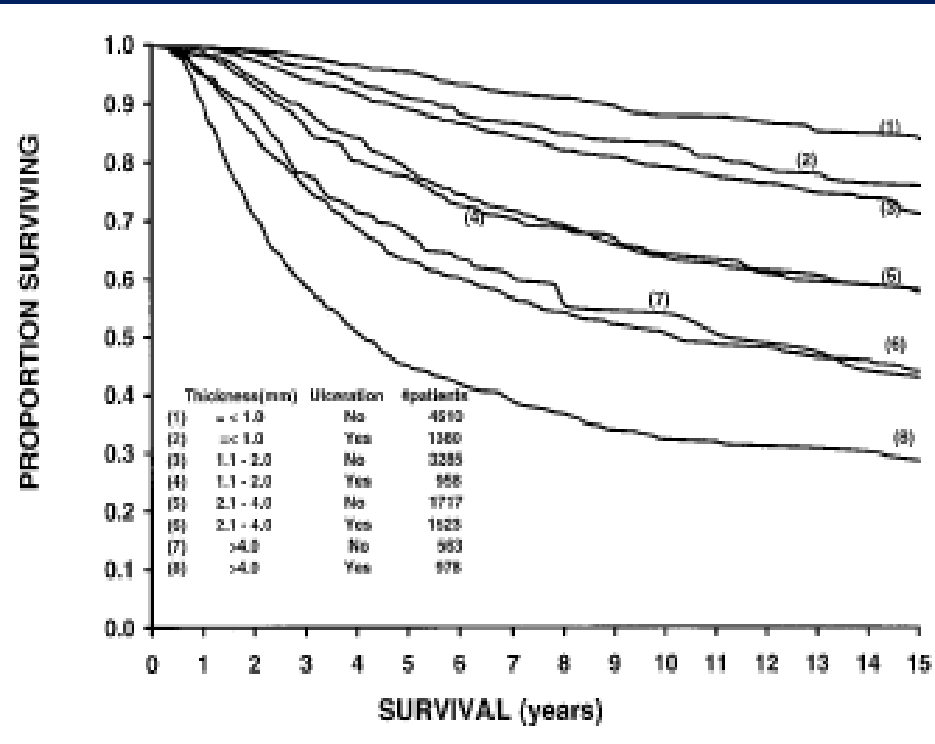
- **Ulceration** is the second most important prognostic factor for melanoma-specific survival



- *Balch et al., J Clin Oncol, 2001*

Prognostic Factors: Ulceration Influences Survival for Melanoma

- Survival curves of 14,914 patients with localized melanoma stratified for lesion thickness and ulceration



Balch et al., *J Clin Oncol*, 2001

The Importance of Mitotic Rate as a prognostic Factor for Localized Cutaneous Melanoma

- Mitotic rate is an indicator of tumor proliferation and is measured as the number of mitoses per mm².
- *Barnhill et al* compared the relative importance of mitotic rate vs ulceration as major prognostic factors in localized melanoma
 - 650 consecutive invasive CMM cases
 - in a multivariate analysis
 - 1) tumor thickness
 - 2) moderate mitotic rate (1-6)
 - 3) mitotic rate >6

emerged as the most important independent prognostic factors

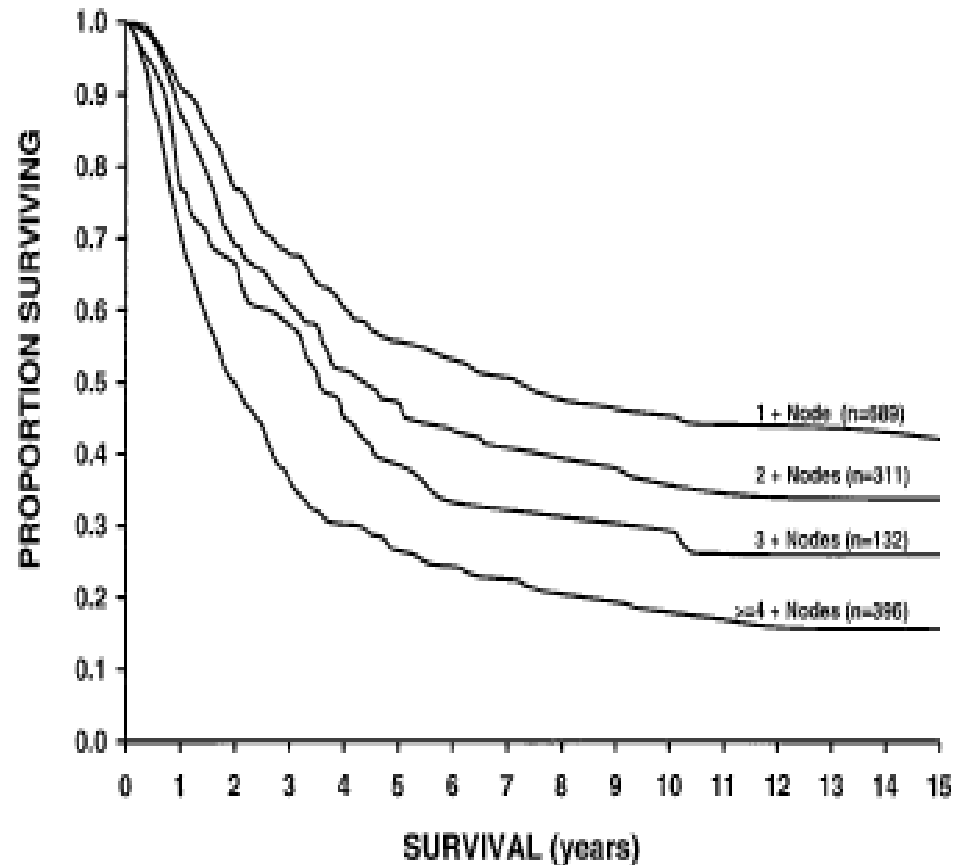
Barnhill et al, J Cutan Pathol, 2005

The Importance of Mitotic Rate as a prognostic Factor for Localized Cutaneous Melanoma – Barnhill et al

Variable	Relative Risk	95%CI	P value
Breslow thickness (per mm)	1.5	1.3-1.9	<0.01
Ulceration	1.7	0.8-3.6	<0.21
Mitotic Index (0-6.0)	8.3	2.4-28.7	<0.01
Mitotic Index (>6)	11.6	3.0-44.6	<0.01

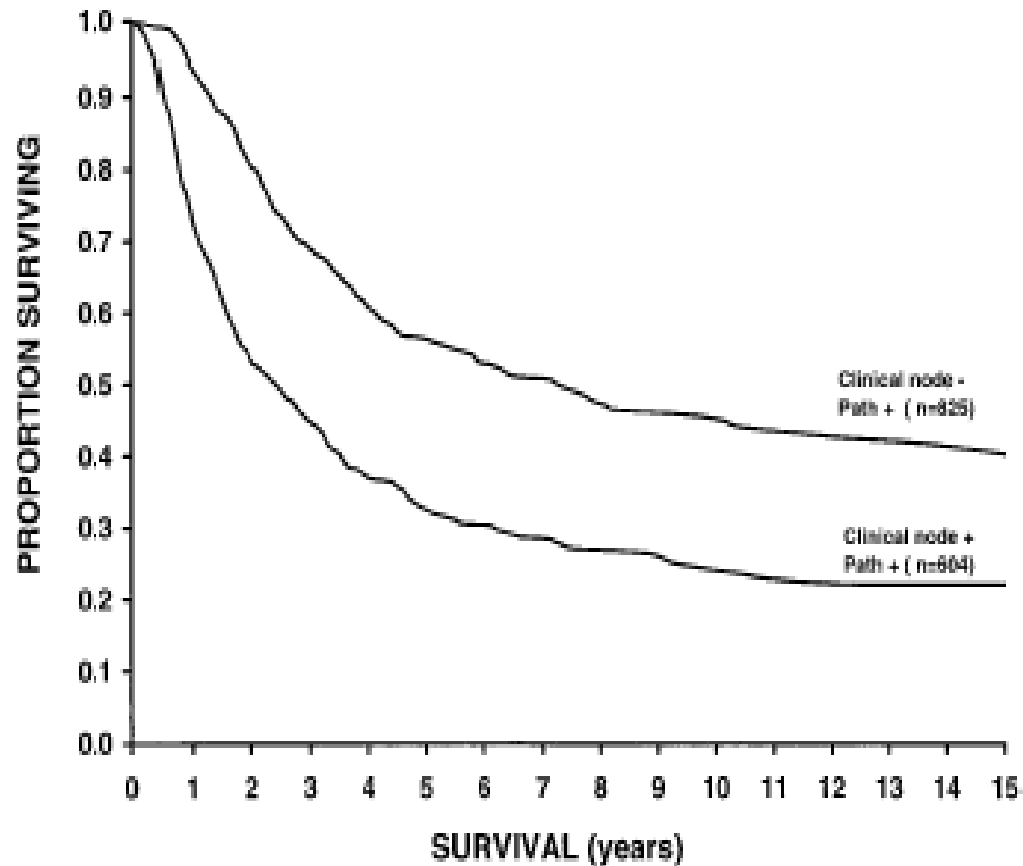
Prognostic Factors: Number of Lymph Nodes Correlates with Melanoma Survival

- Survival curves of 1,528 melanoma patients by the number of metastatic lymph nodes
- This is the most important prognostic factor for N staging:
 - N1 1
 - N2 2-3
 - N3 > 4
- *Balch et al., J Clin Oncol, 2001*



Prognostic Factors: Regional Lymph Node Tumor Burden Correlates with Melanoma Survival

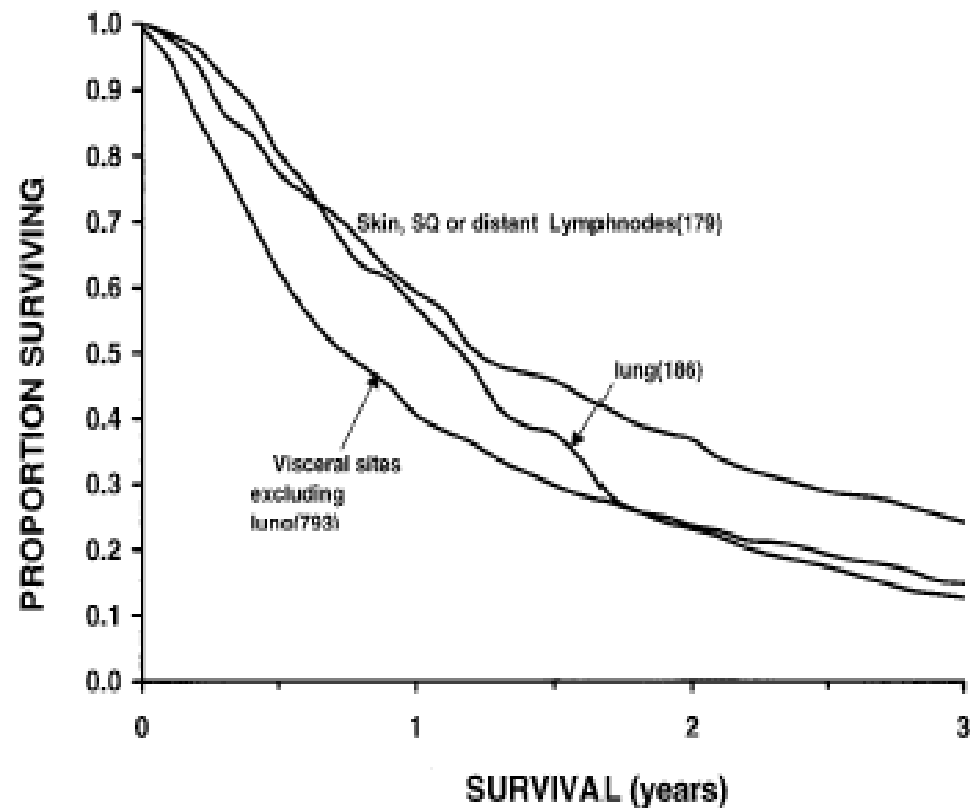
- Survival curve of 1,429 patients with nodal disease
- Macroscopic disease influences survival



Balch et al., *J Clin Oncol*, 2001

The Site of Metastatic Disease Correlates with Survival

- 3-year survival curves of 1,158 patients with metastatic melanoma
- Skin and soft tissue lesions are better than lung ($P=.003$) and other visceral sites ($P<.0001$)



Balch et al., *J Clin Oncol*, 2001

American Joint Committee on Cancer (AJCC) TNM staging System for Melanoma (7th ed., 2010)

<i>T classification</i>	<i>Thickness (mm)</i>	<i>Ulceration/Status/Mitoses</i>
T1	< 1.0	a: w/o ulceration and mitosis <1/mm ² b: with ulceration or mitoses >1/mm ²
T2	1.01-2.0	a: w/o ulceration b: with ulceration
T3	2.01-4.0	a: w/o ulceration b: with ulceration
T4	>4	a: w/o ulceration b: with ulceration

American Joint Committee on Cancer (AJCC) TNM staging System for Melanoma (7th ed., 2010)

Regional Lymph Nodes (N)

NX Cannot be assessed

N0 No regional metastases detected

<i>N Classification</i>	<i>No. of Metastatic</i>	<i>Nodal Metastatic Mass</i>
N1	1 node	a:micrometastases b:macrometastases
N2	2-3 nodes	a:micrometastases b:macrometastases c:in transit met(s)/satelite(s) w/o metastatic nodes
N3	4 or more nodes, or matted nodes, or in transit met(s)/satelite(s) with metastatic nodes	

American Joint Committee on Cancer (AJCC) TNM staging System for Melanoma (7th ed., 2010)

Distant Metastases

- M0** No detectable evidence of distant metastases
- M1a** Metastases to skin, subcutaneous, or distant lymph nodes
- M1b** Metastases to lung
- M1c** Metastases to all other visceral sites or distant metastases to any site combined with an elevated serum LDH

American Joint Committee on Cancer (AJCC) TNM staging System for Melanoma (7th ed., 2010)

Stage	Pathologic
0	Tis
IA	T1a
IB	T1b
	T2a
IIA	T2b
	T3a
IIB	T3b
	T4a
IIC	T4b

American Joint Committee on Cancer (AJCC) TNM staging System for Melanoma (7th ed., 2010)

Stage IIIA	T1-4a	N1a or N2a	
Stage IIIB	T1-4b	N1a or N2a	
	T1-4a	N1b or N2b	
	T1-4a	N2c	
Stage IIIC	T1-4b	N1b or N2b	
	T1-4b	N2c	
	Any T	N3	
Stage IV	Any T	Any N	M1

Malignant Melanoma: Preoperative Workup

- **Stage I, IIA**
H&P
- **Stage IIB-IIC**
CXR is optional
- **Stage III (Sentinel node positive)**
CXR, CT+/- PET, MRI (distant metastases 0.5-3.7%)
- **Stage III (Clinically positive node/s)**
FNA or LN biopsy
CXR, CT +/-PET, MRI (distant metastases 4-16%)
CT pelvis if inguinofemoral nodes positive
- **Stage III in-transit**
FNA or biopsy
CXR, CT+/-PET, MRI
- **Stage IV**
FNA or biopsy
LDH
CT C/A/P, MRI brain, and/or PET as clinically indicated

Body CT for Staging Asymptomatic Patients with Stage III Melanoma

Institution	N	True Positive Percent	False Positive Percent	New Primary Percent
MDACC	89	6.7	22.4	0
MSKCC	136	4.4	8.4	1.4
University of Michigan	127	16	12	0.7

Treatment of Primary Melanoma: Wide Local Excision

- In 1987, William Norris recommended surgery “not only to remove the disease, but to cut away some of the healthy parts”.
- The concept became known as WLE and remains the standard for surgical management of melanoma today.
- Historically, 5 cm margins were the goal causing substantial morbidity from WLE.
- Beginning in 1990s, multiple prospective, randomized, controlled trials began to challenge the necessary margins needed for adequate surgical resection.

Treatment of Primary Melanoma: Wide Local Excision

➤ WHO

- 612 patients
- < 2mm thickness
- 1cm vs 3cm
- median follow-up 90 months
- LR, DFS and OS were similar

Veronesi et al., Arch Surg, 1991

Veronesi et al., N Engl J Med, 1988

Treatment of Primary Melanoma: Wide Local Excision

➤ National Intergroup Trial

- 468 patients
- 1.0-4.0 mm thickness
- 2cm vs 4 cm margins
- median follow-up 10 years
- LR, DFS and OS no differences

Balch et al., Ann Surg Oncol, 2001

Balch et al., Ann Surg, 1993

Treatment of Primary Melanoma: Wide Local Excision

➤ Thomas et al

- >2mm thickness
- 1 cm vs 3 cm
- no improvement in LR alone or in DSS

➤ Systemic review and meta-analysis

- surgical excision margins **no more than 2cm** are adequate
- surgical margins should **not be less than 1 cm** around primary melanoma

Thomas et al., N Engl J Med, 2004

Haigh et al., Can J Surg, 2003

Treatment of Primary Melanoma: Wide Local Excision

- **NCCN Guidelines:**

Tumor Thickness (mm)	Clinical Margins ² (cm)
In-situ	0.5 cm
<1.0 mm	1.0 cm
<hr/>	
1.0-4.0 mm	2.0 cm
>4.0 mm	2.0 cm

² Clinical margins do not need to correlate with final histologic margins

Panel recognizes that 1-2 cm margins might be acceptable in anatomically difficult areas

Treatment of Primary Melanoma: Wide Excision

- WLE can be performed under local anesthesia in most cases
- The appropriate margins of excision is measured radially from the edge of the lesion or from the previous biopsy scar.
- WLE should involve removal of the skin and subcutaneous tissue down to the muscular fascia.
- Majority of incisions can be closed primarily
- Skin grafts or complex tissue flaps maybe necessary for melanomas located in areas with cosmetically important or immobile skin









Treatment of Primary Melanoma: Sentinel Lymph Node Biopsy

- Since its original description by Morton, thousands of articles have been published validating the SLN hypothesis in a variety of malignancies, and SLN biopsy has become a standard method of staging the regional lymph nodes in both melanoma and breast cancer
- SLNB is the single most important prognostic factor in melanoma patients without clinical evidence of nodal metastases.
- SLNB is a minimally invasive procedure that usually involves removal of only 1-3 lymph nodes.

Treatment of Primary Melanoma: Sentinel Lymph Node Biopsy

- **Thin melanomas (1.00 mm or less)**
 - Incidence of +SLNB is **2-5%**
 - Factors predicting increased probability of a +SLN:
 - * increasing Breslow thickness
 - <0.75 mm 1-4% incidence of SLN metastases
 - >0.75 mm 6-8 % incidence of SLN metastases
 - * increasing Clark level
 - * higher mitotic rate
 - * younger age

Thompson et al., Surg oncol Clin N Am, 2007

Treatment of Primary Melanoma: Sentinel Lymph Node Biopsy

- **Thick melanoma (4 mm or greater)**
 - Probability of +SLNB is 30-40%
 - SLN status is a strong independent predictor of outcome in these patients

Ferrone et al., Ann Surg Oncol, 2002

Gershenwald et al., Ann Surg Oncol, 2007

Gutzmer et al., J Dtsch Dermatol ges, 2008

Treatment of Primary Melanoma: Sentinel Lymph Node Biopsy

- NCCN Recommendations:

- ***Should be considered***

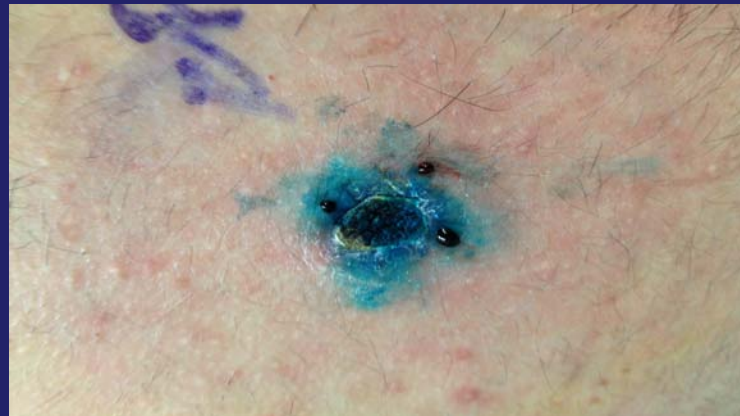
- **Stage IA** (1.0 mm or less) with **adverse** features:
 - * **thickness > 0.75 mm**
 - * **positive** deep margins
 - * **lymphovascular invasion**
 - * **young age**
- **Stage III** – resectable solitary in-transit disease

- ***Should be discussed and offered***

- **Stage IB - II**

Technical Aspects of SLNB

- All patients should undergo preoperative lymphoscintigraphy
- Technetium-99 sulfur colloid is injected into the *dermis*, *raising a wheel*
- Once in the operating room, a vital blue dye (eg, isosulfan blue or methylene blue) is injected into the dermis around the melanoma site
- The SLNB is identified in 99% of patients when performed correctly.



Technical Aspects of SLNB

- A sentinel node is defined as
 - the most radioactive node in the nodal basin
 - any node that is blue
 - any node that has a radioactive count greater than 10% of the most radioactive node in that basin
 - or any node that is palpably suspicious for tumor
- On average, 2 sentinel nodes are identified per nodal basin
- All SLNs should be sent for permanent section histopathology with immunohistochemical staining for specific melanoma markers (eg, S-100 and HMB-45);

Treatment of Primary Melanoma: Sentinel Lymph Node Biopsy

MSLT-I is the largest trial to address the role of lymphatic mapping with SLNB in determining prognosis and its impact on survival

- 1269 patients with intermediate thickness 1.2-3.5 mm randomly assigned to
- WLE+SLNB (and CLND if +SLNB)

vs

- WLE+nodal observation (delayed therapeutic lymphadenectomy if necessary)
- No significant improvement in DSS rates
- The mean 5 year survival rate after WLE alone, 86.6%, was almost identical to that after WLE+SLNB, 87.1%
- Improvement in the estimated 5-year DFS in the SLNB group (78% vs 73%, $p=0.009$)
- All patients with nodal metastases
 - higher survival rate (72% vs 52%) in patients with immediate CLND after +SLNB vs patients with delayed LND for clinical disease

Treatment of Primary Melanoma: Sentinel Lymph Node Biopsy

- SLNB is a useful staging tool
- Its impact on OS is unclear
- The decision NOT to perform SLNB maybe be based on significant patient comorbidities or individual patient preference

Treatment of Primary Melanoma: Lymph Node Dissection

- An anatomically complete dissection of involved nodal basin required
 - anatomic boundaries of LND should be described in the operative report
- **Positive SLNB**
 - additional positive non-sentinel nodes in 15-20%
- **Iliac and obturator LND if:**
 - clinically positive superficial nodes
 - > 3 positive superficial nodes
 - Cloquet's node is positive
 - pelvic CT positive
- **Clinically positive nodes**

Coit DG, Surg Clin North Am, 1992

Coit DG, Brennan MF, Arch Surg, 1989

Shen et al., Cancer J, 2000

Cascinelli et al., J Clin Oncol, 2006

Lee et al., J Clin Oncol, 2004

Malignant Melanoma: Adjuvant Radiotherapy

- **Nodal irradiation appears to improve local control**
 - * rates of recurrence in previously dissected nodal basin ranges from 14 to 30%
 - * adjuvant radiotherapy following complete LND have reported lower recurrence rates, ranging from 5 to 20%
 - * lymphedema is the most common complication (10%)
- **Impact on survival is less clear**

Bastiaannet et al., 2005

Lee et al., 2000

White et al., 2002

Ballo et al., 2004

Malignant Melanoma: Adjuvant Radiotherapy

Factor	Rate of Recurrence	P Value
LN location		
Cervical	43%	.008
Axillary	28%	
Inguinal	23%	
Extracapsular Extension		
Present	63%	<.0001
Absent	23%	
Number +LNs		
1 to 3	25%	.0001
4 to 10	46%	
>10	63%	
Size of largest involved LN		
<3cm	25%	<.001
3 to 6cm	42%	
>6cm	80%	

MONTEFIORRE

Malignant Melanoma: Adjuvant Radiotherapy

- **Most appropriate patients for adjuvant XRT**
 - * extracapsular extension
 - * > 4 involved LNs
 - * LN > 3 cm in size
 - * cervical LN location
 - * recurrent nodal disease

Treatment of Metastatic Melanoma

- Stage III: In-transit metastases
 - small number of in-transit metastases
 - * complete surgical excision with histological negative margins if feasible
 - multiple in-transit metastases not suitable therapies
 - * ILP and ILI



Metastatic Disease: Resection with Curative Intent

- **Skin, soft tissue, distant lymph node metastases:**
 - * **MS** after complete resection is **24 mos**
 - * solitary metastases confined to the dermal or subcutaneous tissue – **8 year survival 80%** after complete resection
- All efforts should be made to perform **complete resection** of skin, soft tissue, and lymph node metastases

Metastatic Disease: Resection with Curative Intent

- **Pulmonary Metastases**

- * multiple nodules and bilateral disease are not definite contraindications to resection if the patient can be rendered free of disease
- * Harpole, 1992
 - 98 patients, MS 20 mos, 5-year OS 20%
- * Tafra, 1995
 - 106 patients, MS 18 mos, 5-year OS 27%
- * Leo, 2000
 - 282 patients, MS 19 mos, 5-year OS 22%
- Aggressive surgical approach is justified if there is a reasonable probability to obtain tumor-free margins while insuring a quality postoperative functional status

Metastatic Disease: Resection with Curative Intent

- Liver Metastases

- * MS 4 to 6 months

- * John Wayne Cancer Institute and the Sydney Melanoma

- Unit experience:

- 1,750 patients with liver metastases

- 34 patients underwent exploration

- 24 patients were resected

- MS for patients resected was 28 mos vs 4 mos for patients who underwent exploration only

- * Hepatic metastases not amenable to surgical resection:

- RFA – MS 25 months (Amersi et al, 2006)

Metastatic Disease: Resection with Curative Intent

- Intracranial metastases
 - * very poor prognosis
 - * MS 7 to 10 months after resection
 - * main role of surgery is palliation
- Splenic metastases
 - * MS 23 mos for completely resected vs 4-5 mos for incompletely resected or no operative intervention
- Adrenal Metastases
 - * MS 26 to 59 mos after complete resection vs 9 to 15 mos for patients with unresectable disease

de Wilt et al, 2003

Branum et al, 1991;

Haigh et al, 1999

Malignant Melanoma: Metastatic Disease

• Conclusion

- The limited, currently available systemic therapies for stage IV melanoma patients do not confer the survival advantage of complete metastasectomy
- Surgery as the first option for patients provided a complete metastasectomy can be performed
- **Complete metastasectomy**, regardless of anatomic site, confers survival advantages not seen with the currently available cytotoxic agents.
- Ideal approach would be complete metastasectomy followed by a novel adjuvant therapy that is efficacious and can prolong the 5-year survival beyond that of a surgical resection

Malignant Melanoma: Local Recurrence

- Regional Nodal Recurrence

- Most common site of 1st recurrence after WLE alone

- FNA:

- * if positive - complete resection of nodal basin

- * if negative – excisional biopsy

- Full metastatic workup before CLND

- * CT chest, abdomen, pelvis

- 5 – year survival with single palpable nodal metastases is 40 to 50%

Malignant Melanoma: Local Recurrence

- Local Recurrence

- tumor appearing in skin or subcutaneous tissue within a 2 cm radius of the primary wide excision site
- risk for LR is 13% for melanoma > 4 mm thick
- surgical resection to attain histologically clear margins (WLE guidelines for primary tumors do not apply to local recurrences)
- multiple recurrences
 - * ILI, ILP

Malignant Melanoma: Special Situations

- **Ear**

- wedged excision or partial amputation
- total auricectomy reserved for very locally advanced primary lesions or recurrences
- preserve the upper part of the ear for patients wearing glasses



Malignant Melanoma: Special Situations

• Face

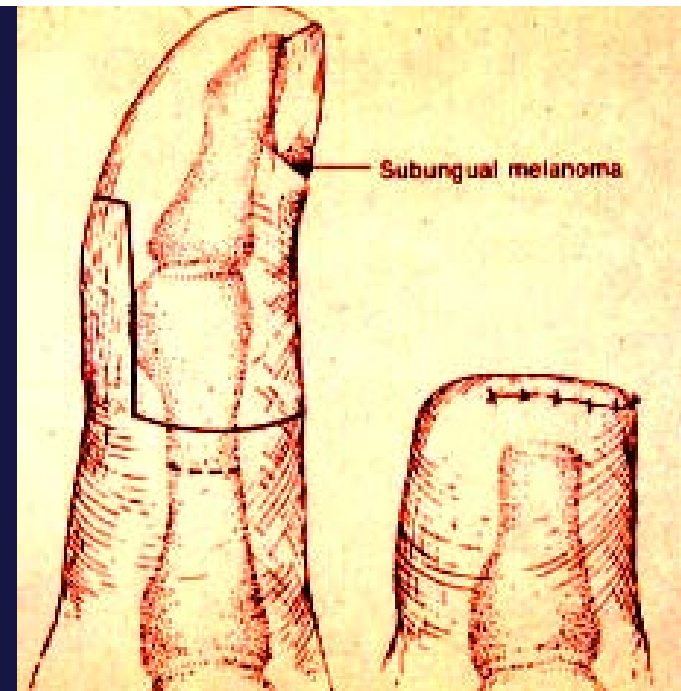
- excisions margins often need to be limited to avoid injury or deformity to the eyes, nose, ears, or mouth
- radiation therapy may be considered to help reduce the risk of local recurrence following the treatment of lesions with very narrow margins
- avoid injury to branches of facial nerve
- regional lymphadenectomy is performed selectively in patients with positive SLNB
- superficial parotidectomy with dissection of all facial nerve branches is recommended for patients with micrometastases in peri-parotid nodes



Malignant Melanoma: Special Situations

• Subungual Melanoma

- Caucasians – 3%
- dark-skinned ethnic groups -15-30%
- great toe and thumb -75%
- amputate proximal to distal interphalangeal joint
- metacarpophalangeal amputation for large lesions or those with satellitosis
- on foot, MCP (ray amputation) causes minimal functional defect





Malignant Melanoma: Special Situations

• Plantar Melanoma

- Caucasians – 2-8%
- dark-skinned ethnic groups – 35-90%
- diagnosed at later stages
- preferred method of biopsy-excisional biopsy
- wound closure:
 - * primary
 - * STSG, FTSG
 - * flaps



Malignant Melanoma: Special Situations

- **Melanoma in Pregnancy**

- 8% of malignancies diagnosed during pregnancy
- one of the most common tumors known to metastasize to placenta and fetus
- no conclusive evidence that pregnancy significantly affects the biologic aggressiveness of a melanoma in terms of increasing the incidence of metastasis or lowering overall survival.

Malignant Melanoma: Special Situations

- **Melanoma in Pregnancy**

- termination of pregnancy of a patient recently diagnosed with melanoma as a therapeutic measure can not be recommended
- because the overwhelming (>75%) majority of melanoma recurrences occur within 2–3 years after treatment of the primary lesion, many women are encouraged to avoid becoming pregnant for that period of time postoperatively

Malignant Melanoma: Special Situations

- **Melanoma in Pregnancy**

- the accuracy and **safety of SLNB** in pregnant patients has **not** yet been studied completely and **confirmed**
- wide and deep excision of the primary melanoma and no treatment of the regional nodes at that time
- regional lymph node dissection may be performed at a later date should palpable nodal metastases become evident or after the completion of pregnancy

Treatment of Primary Malignant Melanoma

- Surgery for localized melanoma and regional lymph node metastases is the standard of care
- SLNB provides precise staging, but has not been reported to affect survival
- The effect of lymph-node dissection on survival is a topic of investigation – MSLT II trial





