

Merkel Cell Carcinoma And Dermatofibrosarcoma Protuberans



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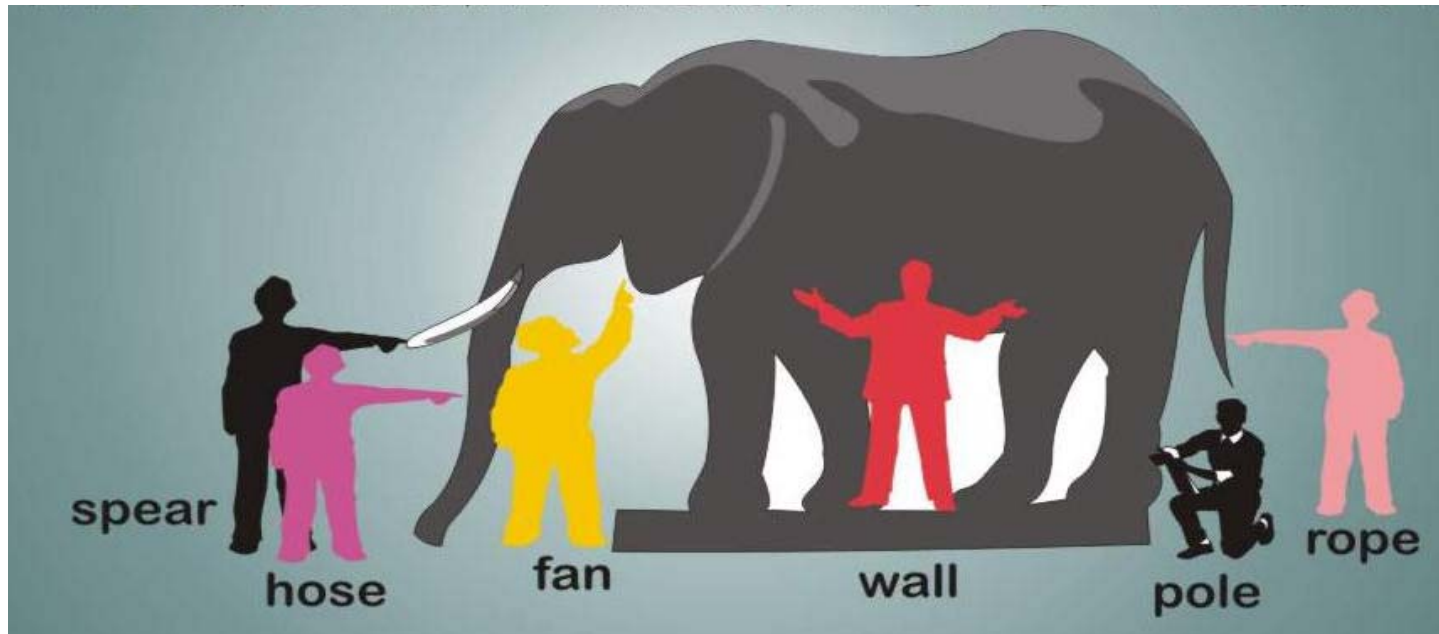
H. Lee Moffitt Cancer Center
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Cutaneous Oncology Program

Merkel Cell Carcinoma

Different People See A Different Beast!

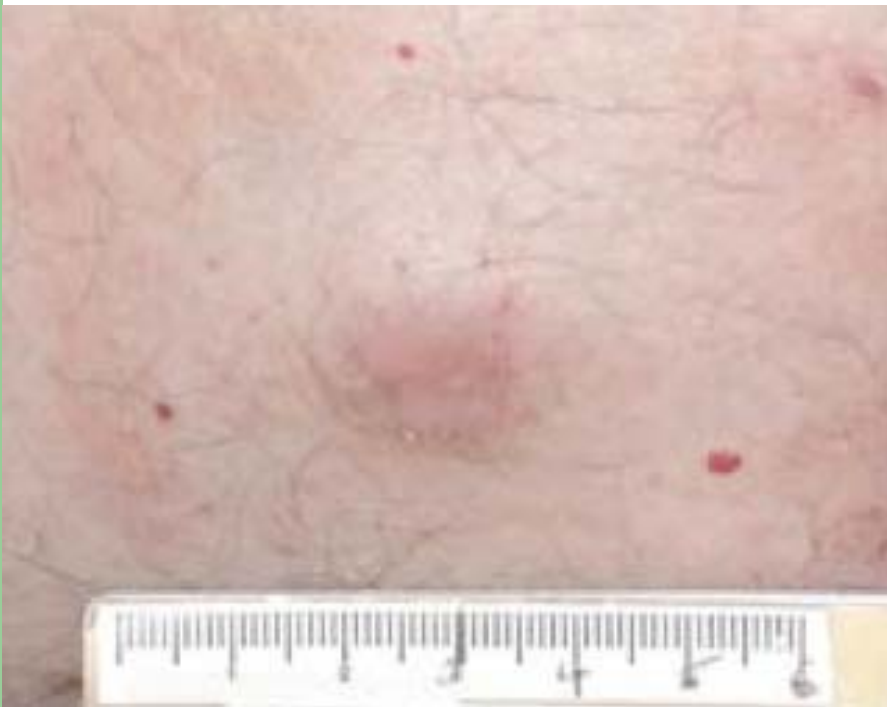


Merkel Cell Carcinoma

Different People See A Different Beast!



Merkel Cell Carcinoma Different People See A Different Beast!



Images courtesy of Paul Ngiehm, MD
University of Washington

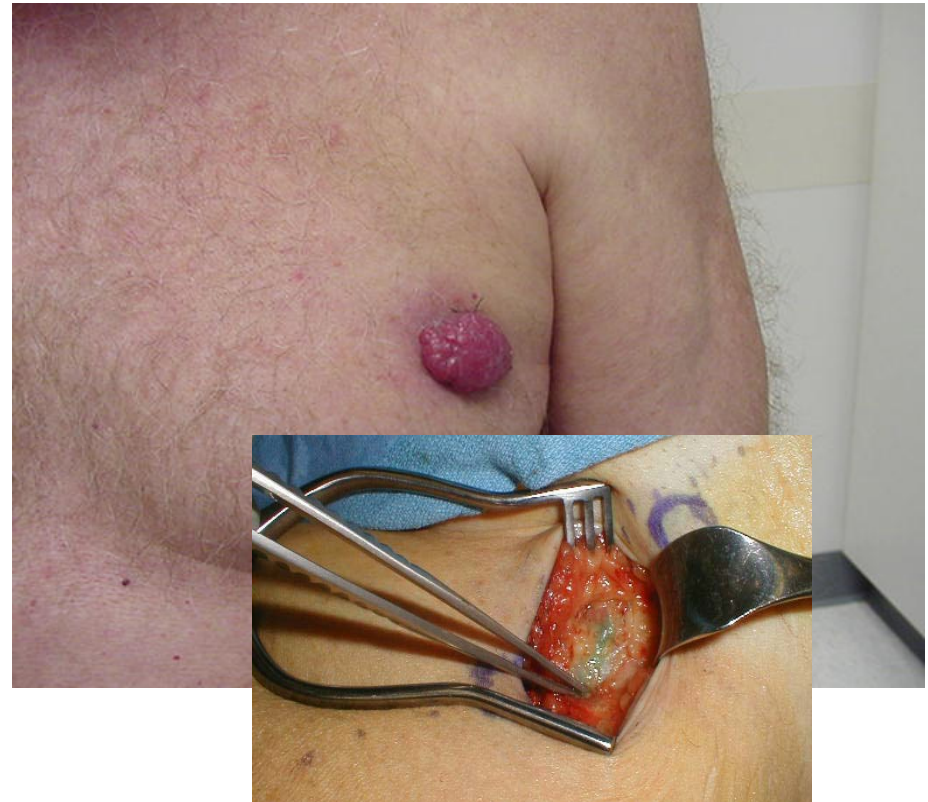


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Merkel Cell Carcinoma

What Is It?

- Merkel cell carcinoma is a aggressive neuroendocrine cutaneous neoplasm with a propensity to spread to regional lymph nodes.
- A standardized approach to performing a SLNB does not exist.
- In addition, definitive regional therapy after a positive sentinel lymph node has not been defined



Merkel Cell Carcinoma A Great Masquerader Revealed!

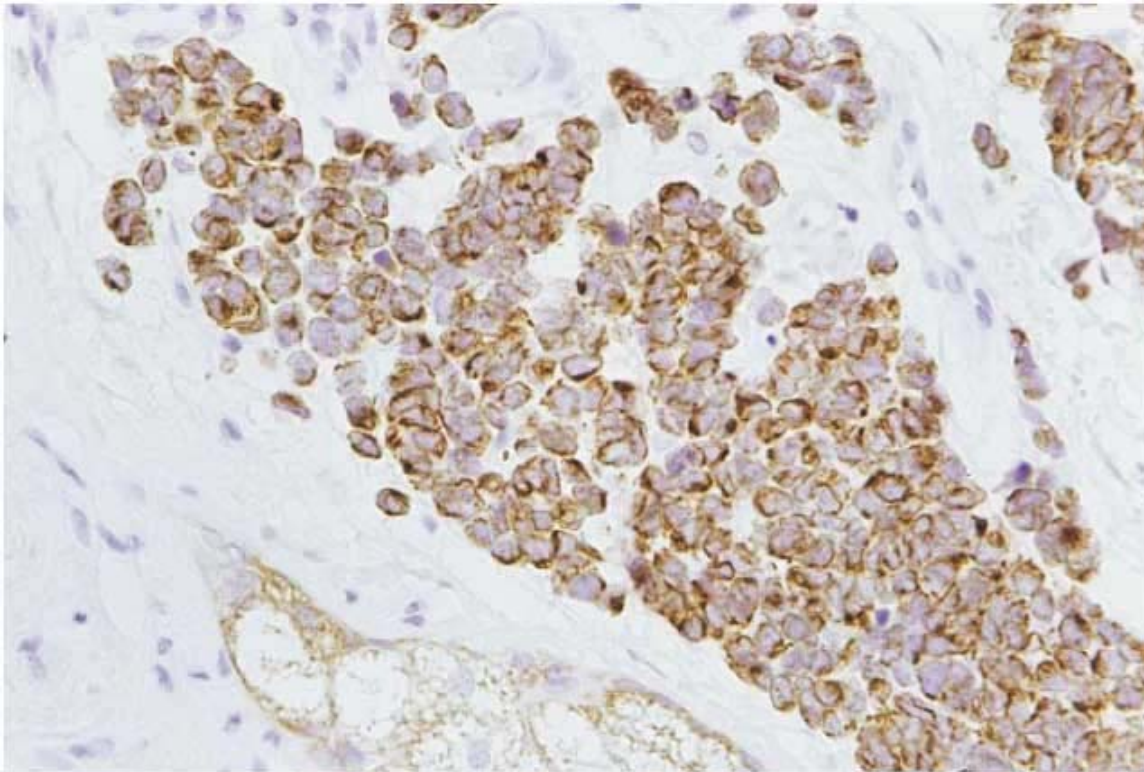
Biopsy Characteristics for MCC and Tumors Resembling MCC

Tumor	Stain					
	CAM5.2 or AE1/AE3	CK20	NSE	CK7 or TTF-1	LCA	S100
MCC	+	+	+	-	-	-
SCLC	+	-	+	+	-	-
Lymphoma	-	-	-	-	+	-
Melanoma	-	-	+	-	-	+

SCLC = small cell lung cancer



Merkel Cell Carcinoma A Great Masquerader Revealed!



Perinuclear
dot-like
positivity
Cytokeratin 20



Merkel Cell Carcinoma More lethal than melanoma?

**Table 8.2–1. COMPARISON OF SKIN CANCERS:
INCIDENCE AND MORTALITY IN THE UNITED STATES**

Tumor	Annual US Incidence	Deaths	Fatality Rate
Merkel cell carcinoma*	400	130	1 in 4
Melanoma	42,000	8,000	1 in 5
Squamous cell carcinoma	100,000	2,000	1 in 50
Basal cell carcinoma	850,000	< 80	< 1 in 10,000



Merkel Cell Carcinoma and Melanoma

How Do They Compare?

- Merkel cell carcinoma is more radiosensitive than melanoma, and it is known that radiation can effectively treat microscopically positive nodal basins.
- Therefore, if reliable parameters can be found to identify sentinel node positive patients who have a low likelihood of positive non-sentinel node (NSLN), radiation alone would be an option.
- In melanoma, SLN positivity correlates with thickness of the primary. It is unclear if this holds true in Merkel cell carcinoma.



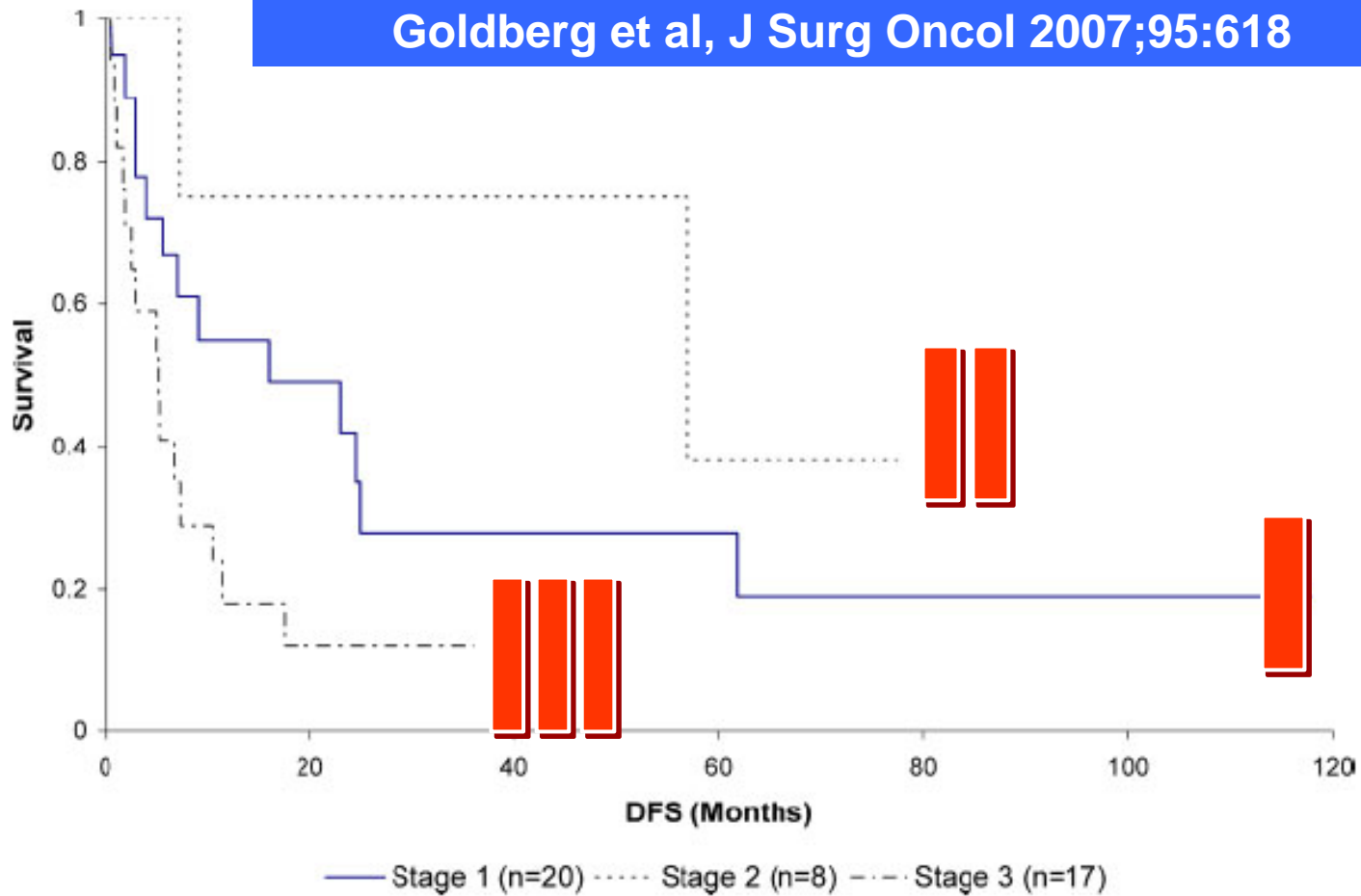
Current Staging Systems for Merkel Cell Carcinoma

Stage			
AJCC		MSKCC	Description
I		IA	Localized disease < 2 cm in diameter
II		IB	Localized disease \geq 2 cm in diameter
III		II	Involvement of regional lymph nodes
IV	IV	III	Metastatic disease



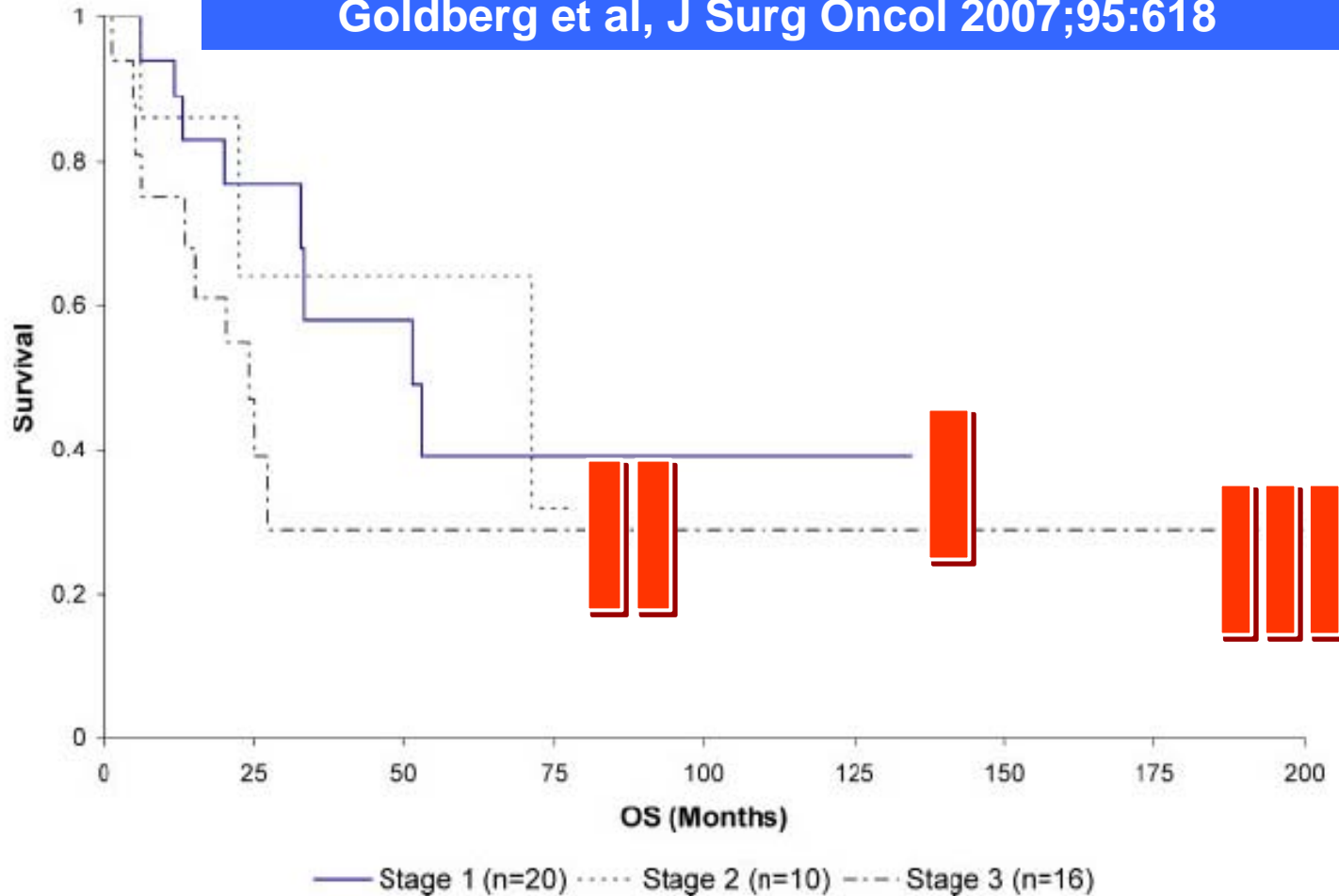
Lack of Correlation Between AJCC Stage and Outcome

Goldberg et al, J Surg Oncol 2007;95:618



Lack of Correlation Between AJCC Stage and Outcome

Goldberg et al, J Surg Oncol 2007;95:618

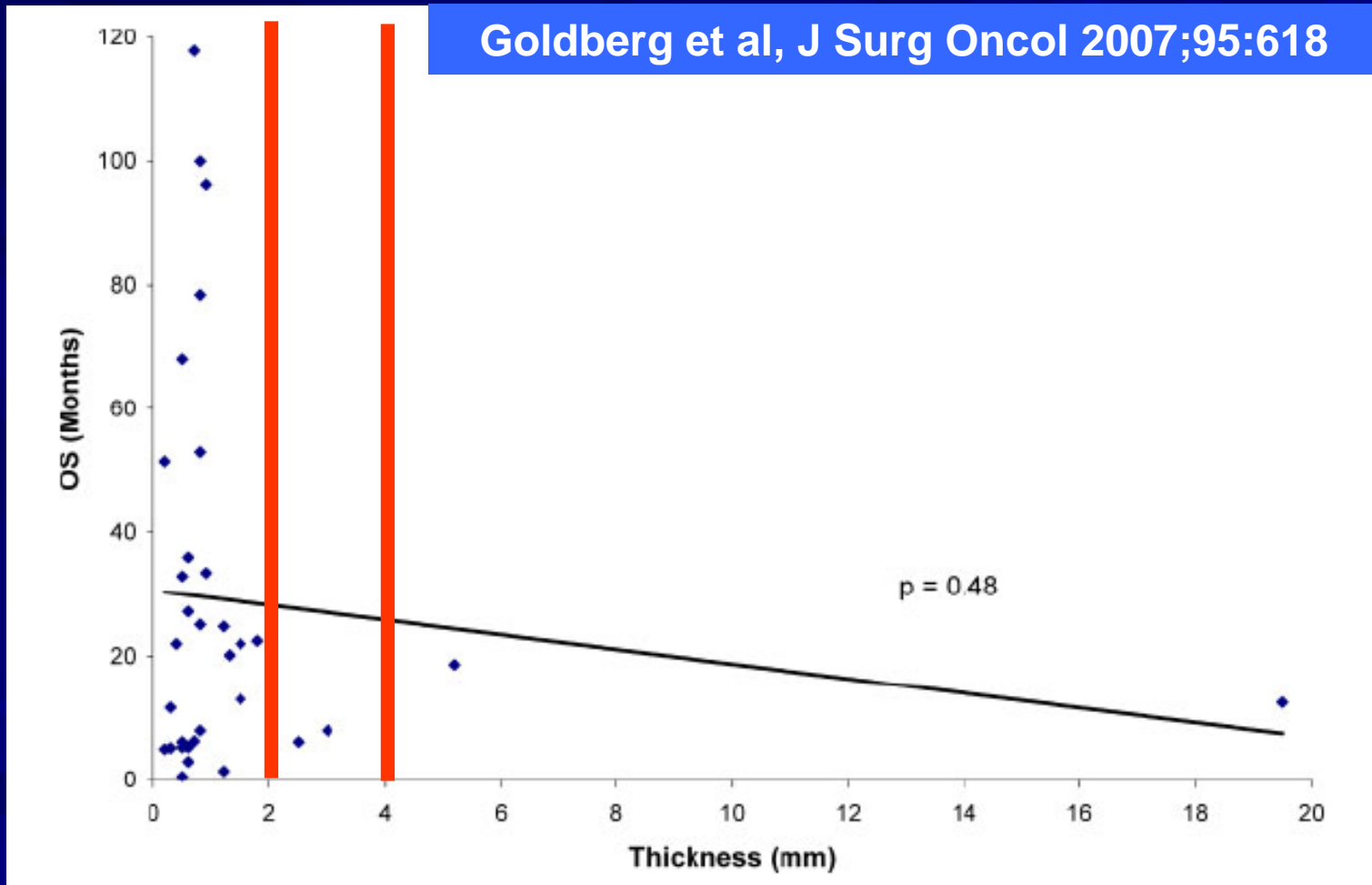


Would Thickness Be a Better Prognostic Factor Than Size in Merkel Cell Carcinoma?

- Melanoma staging is based on thickness and there is a direct correlation between tumor thickness and SLN positivity, and between SLN status and outcome.
- SLN status could serve as a surrogate for identifying prognostic factors in primary localized Merkel cell carcinoma.
- Staging of Merkel cell carcinoma is based on diameter of the lesion, however the relationship between tumor diameter and SLN positivity is currently unclear.



Lack of Correlation Between Thickness and Outcome?



Would Thickness Be a Better Prognostic Factor Than Size in Merkel Cell Carcinoma?

- We retrospectively reviewed charts from 101 patients with diagnosis of Merkel cell carcinoma who underwent sentinel lymph node biopsy between 1994-2007.
- We recorded for each patient:
 - ❖ Age
 - ❖ Tumor location
 - ❖ Tumor thickness
 - ❖ Tumor diameter
 - ❖ SLN metastasis



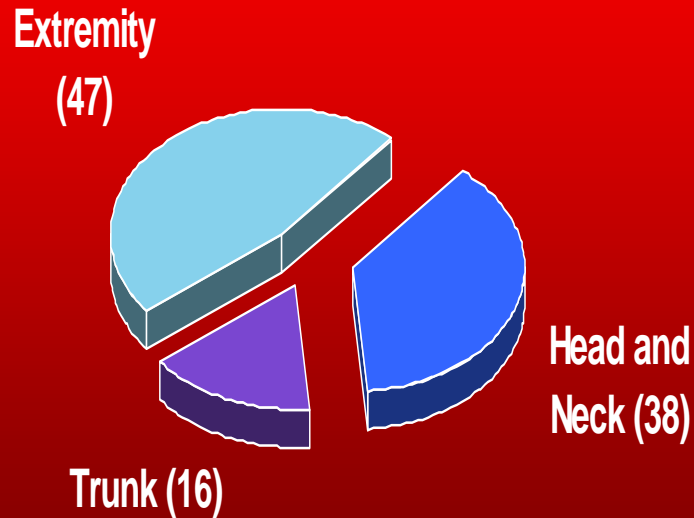
Patient Characteristics by Sentinel Lymph Node Status

	SLN + (n=29)	SLN - (n=72)
Mean Age	75.4	72.5
Median Thickness (Range, 0.4-22.8)	7.0 mm	4.5 mm
Median Diameter (Range, 0.2-9.5)	2.0 cm	2.0 cm

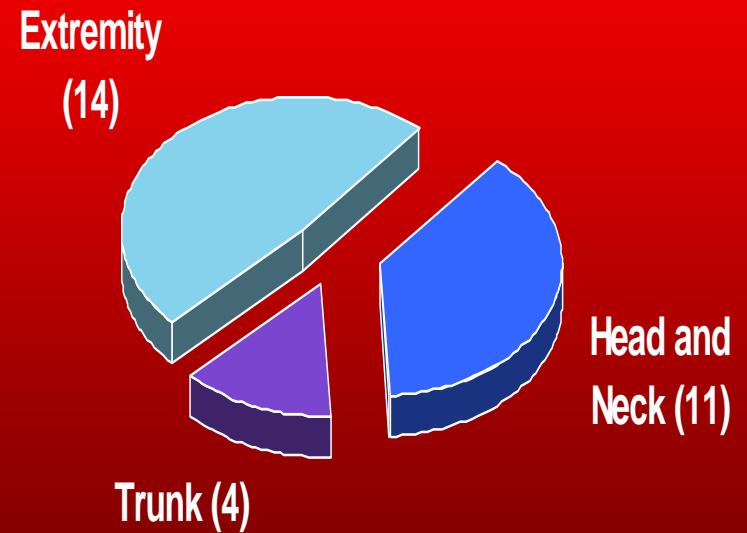


Tumor Location

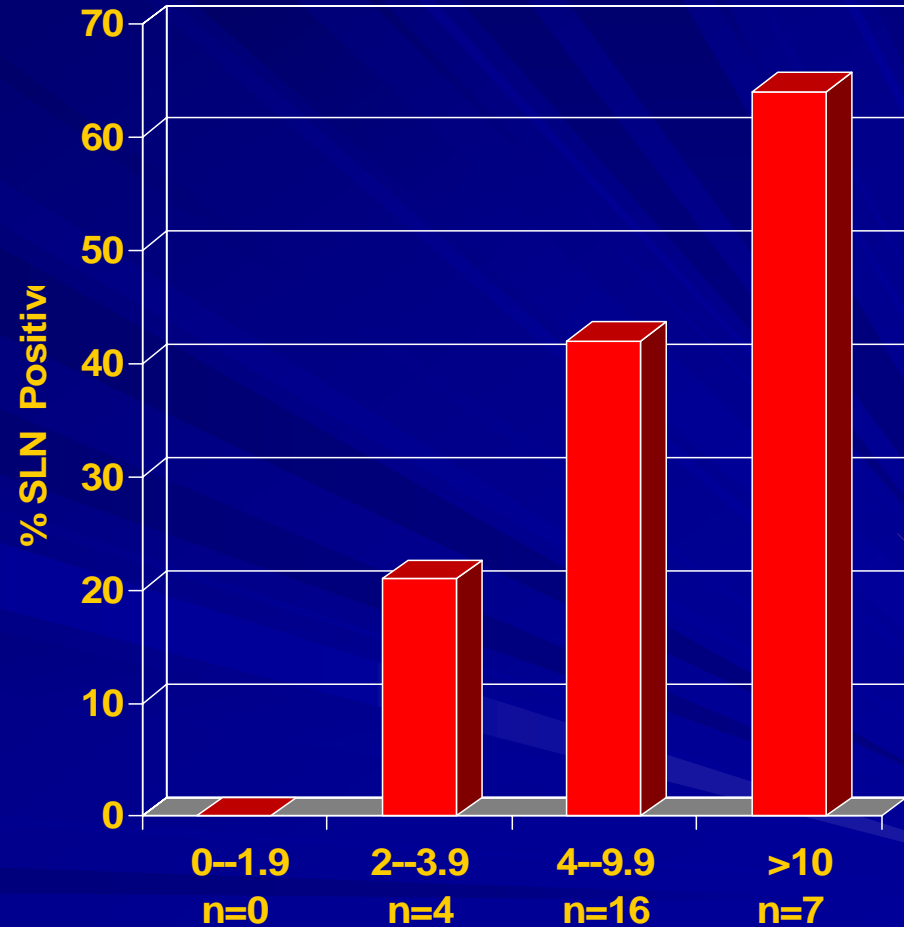
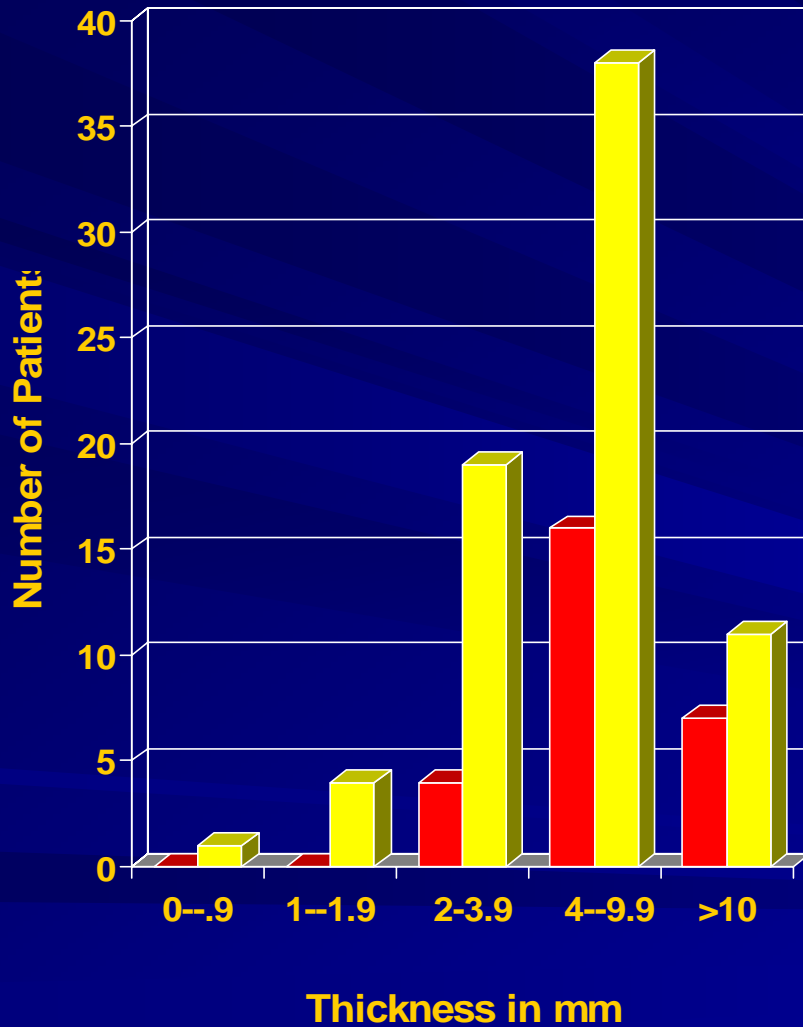
All Patients (n=101)



SLN Positive Patients (n=29)



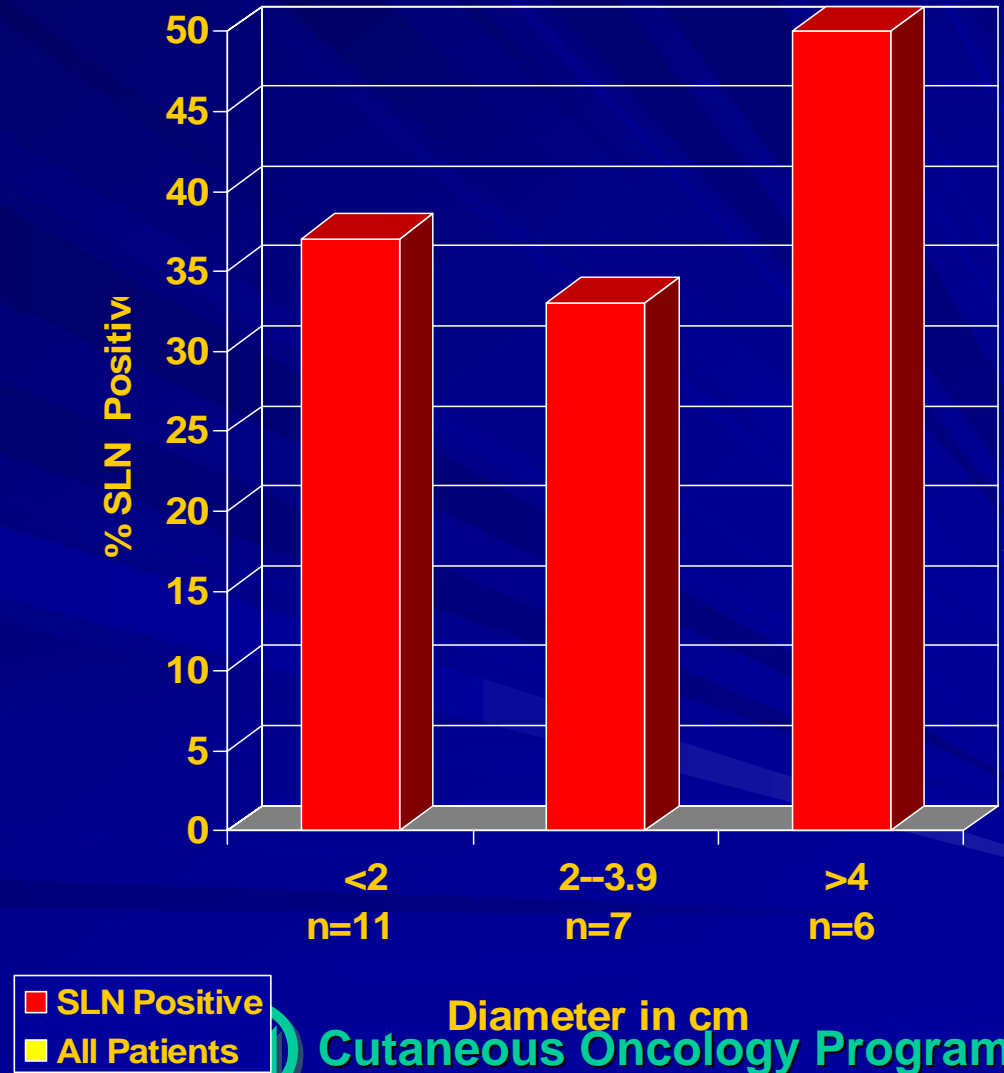
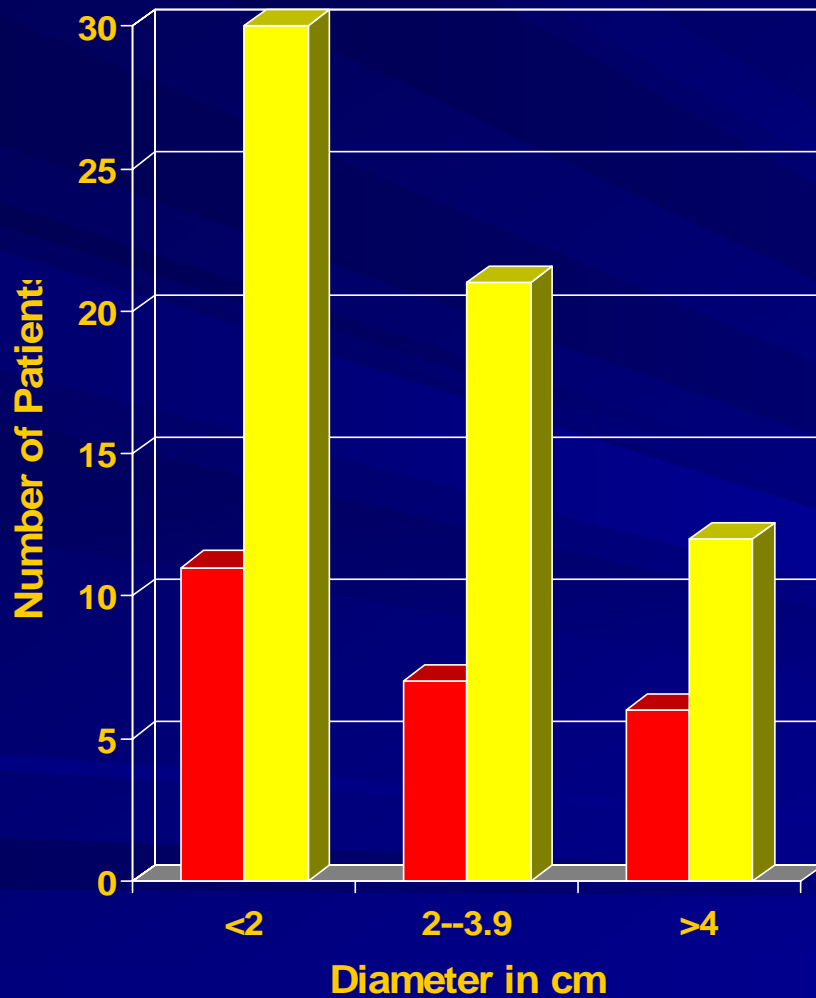
Tumor Thickness and SLN Positivity



■ SLN Positive
■ All Patients

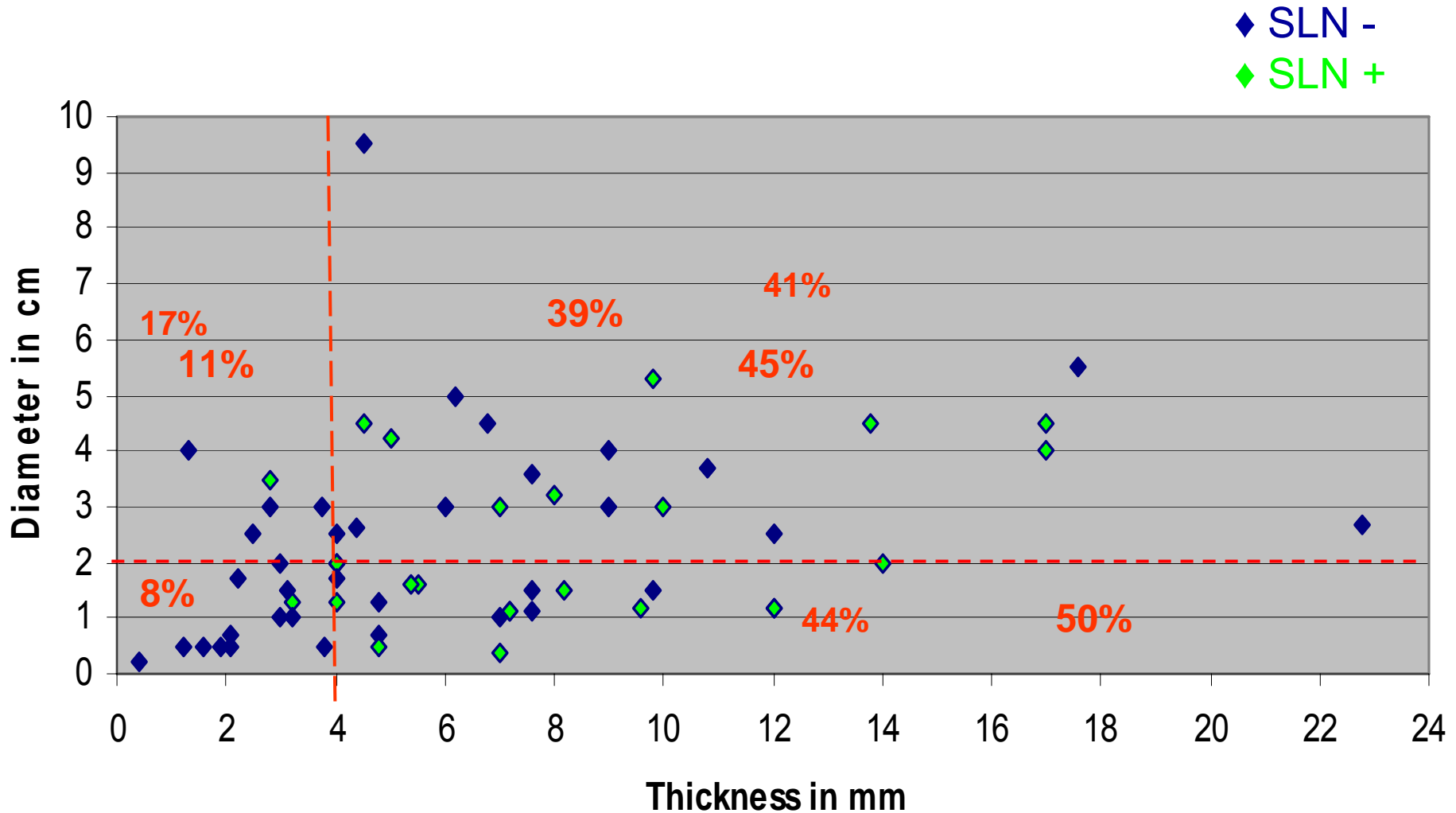
Thickness in mm
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Tumor Diameter and SLN Positivity



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Tumor Thickness and Diameter By Sentinel Node Status



Treatment

- The 29 sentinel node positive patients received one of three regional treatments based on primary tumor and SLN characteristics as well as the surgeon's discretion
 - Complete lymph node dissection (CLND) without radiation (n=6)
 - Regional radiation (XRT) without CLND (n=6)
 - CLND + XRT (n=14)
- Three patients refused further treatment after a positive sentinel node biopsy and were lost to follow-up



Results By Treatment

- CLND group
 - 6 sentinel lymph node positive patients.
 - 1 of 6 had extracapsular extension in the sentinel node, also found to have positive non-sentinel nodes.
 - There were no regional recurrences or deaths from disease.
- XRT group
 - 6 sentinel lymph node positive patients.
 - None had extracapsular extension.
 - All had concomitant radiation to primary.
 - There were no regional recurrences or deaths from disease.



Results By Treatment

- CLND + XRT
 - 14 SLN positive patients.
 - 6 of 14 had extracapsular extension in the sentinel node and all 6 had evidence of non SLN metastasis.
 - 1 additional patient had non-sentinel nodes with metastases that had extracapsular extension although the sentinel node did not
 - There were 3 regional recurrences, all developed distant metastases and died of disease
 - ❖ 1 patient had extracapsular extension and non sentinel lymph node metastasis.
 - ❖ 2 had no evidence of extracapsular extension, and no evidence of non sentinel lymph node metastasis.
 - **Both <2 cm in diameter but thickness >4 mm**



Conclusion

- In our retrospective study, tumor thickness correlates with SLN metastasis at least as well if not better than diameter.
- Pathologists should measure and report on tumor thickness as well as tumor diameter
- Extracapsular extension in the SLN correlates with the presence of non-sentinel lymph node metastasis.



Conclusion

- In patients with sentinel node positive Merkel cell carcinoma <4mm thick without extracapsular extension, completion node dissection alone or radiation alone is associated with excellent regional control.
- We currently recommend complete lymph node dissection and postoperative radiation to patients with sentinel node positive tumors ≥ 4 mm or if the sentinel nodes show extracapsular extension.



Cutaneous Sarcomas

What are they?

- Frequent or rare?
 - **Not as rare as you'd think!**
- Indolent or aggressive?
 - **Both, and in between as well**
- A disease of the old or young?
 - **Both, and in between as well**
- Simple to treat or complicated?
 - **Somewhere in between**



Dermatofibrosarcoma protuberans



Dermatofibrosarcoma protuberans



Dermatofibrosarcoma protuberans

- A very indolent disease of all ages, with a poorly defined risk of fibrosarcomatous transformation
- Now the most common cutaneous sarcoma, and the second most common cutaneous malignancy, in my clinic!
- **CONTROVERSIES**
 - The role of Mohs surgery
 - The role of radiation therapy
 - The role of Gleevec



Dermatofibrosarcoma protuberans

The role of Mohs surgery

- Popularized in the dermatology literature, with very low recurrence rates compared to “historical” surgical series having recurrences of 30% or more
- Taught us that DFSP grows in a very asymmetric fashion, with small roots that may grow far from the visible tumor
- In most anatomic sites, no advantage for Mohs surgery over surgical excision with careful evaluation of peripheral margins

❖ Dubay et al, Cancer 2003



Dermatofibrosarcoma protuberans

The role of the pathologist

- **The pathologist cures DFSP, not the surgeon!**
- **To achieve optimally low recurrence rates, the entire peripheral margin should be examined histologically**
- **Frozen section sometimes useful intraoperatively but not reliable**
- **Immunochemical staining may be helpful**
- **Reexcision is indicated for positive margins whenever possible**



Dermatofibrosarcoma protuberans

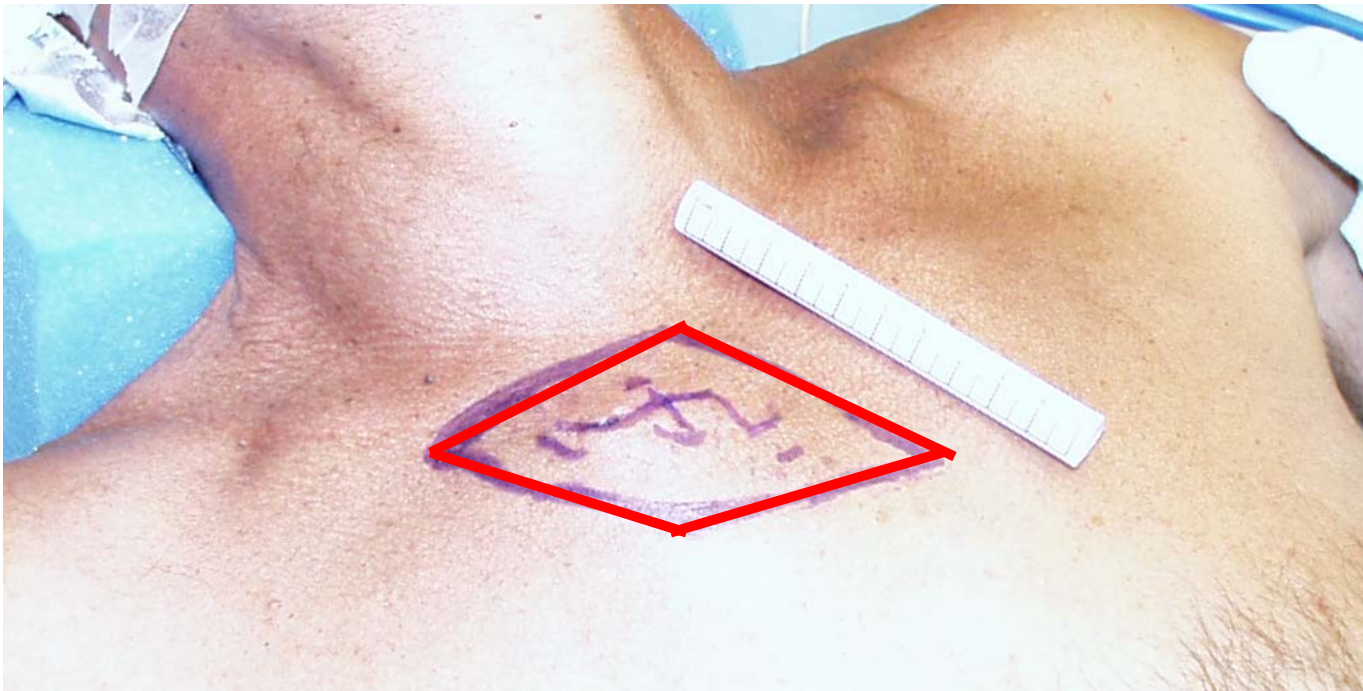
The role of radiation therapy

- The addition of radiation increases local control in difficult situations, however it should only be used in cases where further reexcision of positive margins is not feasible or if fibrosarcomatous transformation has taken place



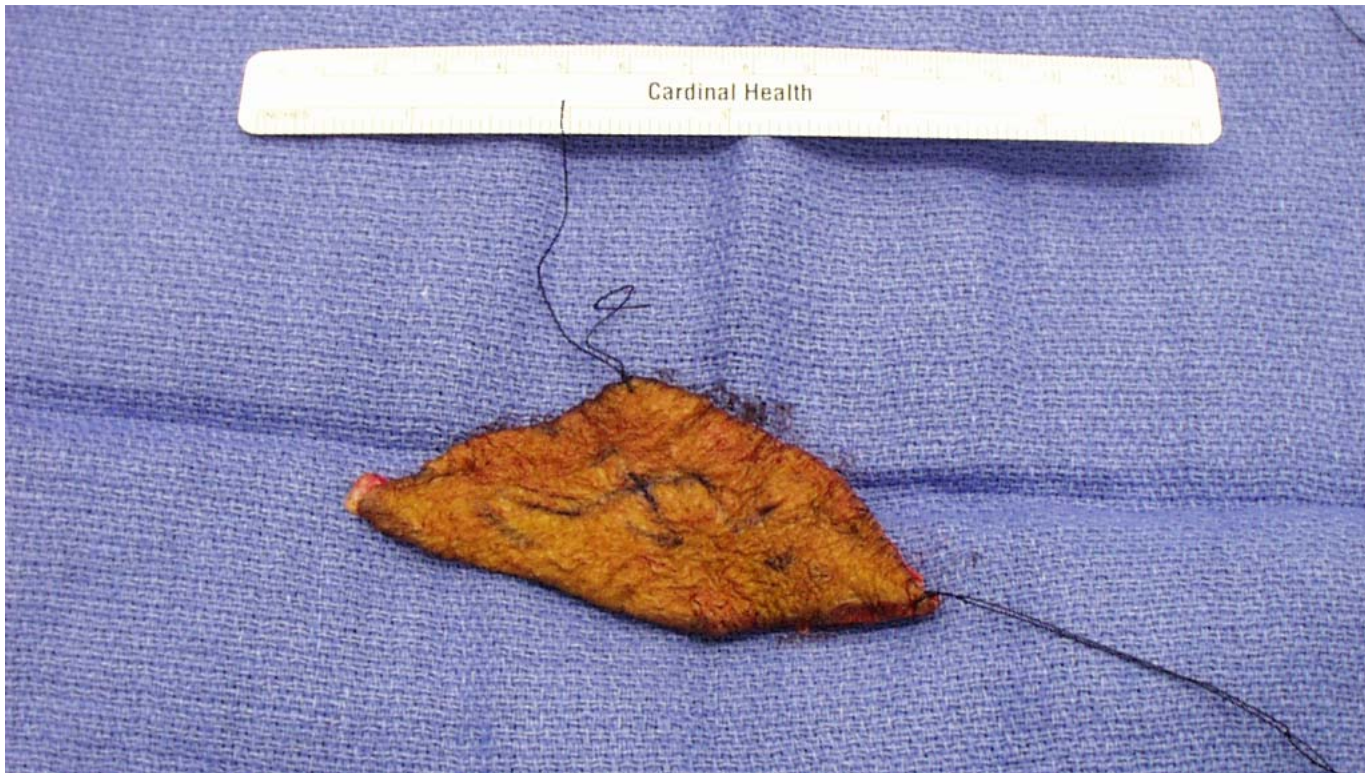
Dermatofibrosarcoma protuberans

Wide excision with margin analysis



Dermatofibrosarcoma protuberans

Wide excision with margin analysis



Dermatofibrosarcoma protuberans

Wide excision with margin analysis



Dermatofibrosarcoma protuberans

Wide excision with margin analysis



Dermatofibrosarcoma protuberans

Wide excision with margin analysis

- **Reexcision is required for positive margins in less than 20% of cases; 80% are adequately treated with a 1 or 2 cm excision margin**
- **Mohs surgery reserved for DFSP on the face or other situations where maximal tissue conservation is required**



Dermatofibrosarcoma protuberans

Results of a modern approach

- In our series, now over 200 consecutive DFSPs treated since 1998 using wide excision with careful peripheral margin control:
 - No patient with a nontransformed DFSP was unresectable
 - Radiation used in <3% of nontransformed cases
 - Local recurrence rate 0
 - 1 patient developed pulmonary metastases



Dermatofibrosarcoma protuberans

The role of Gleevec

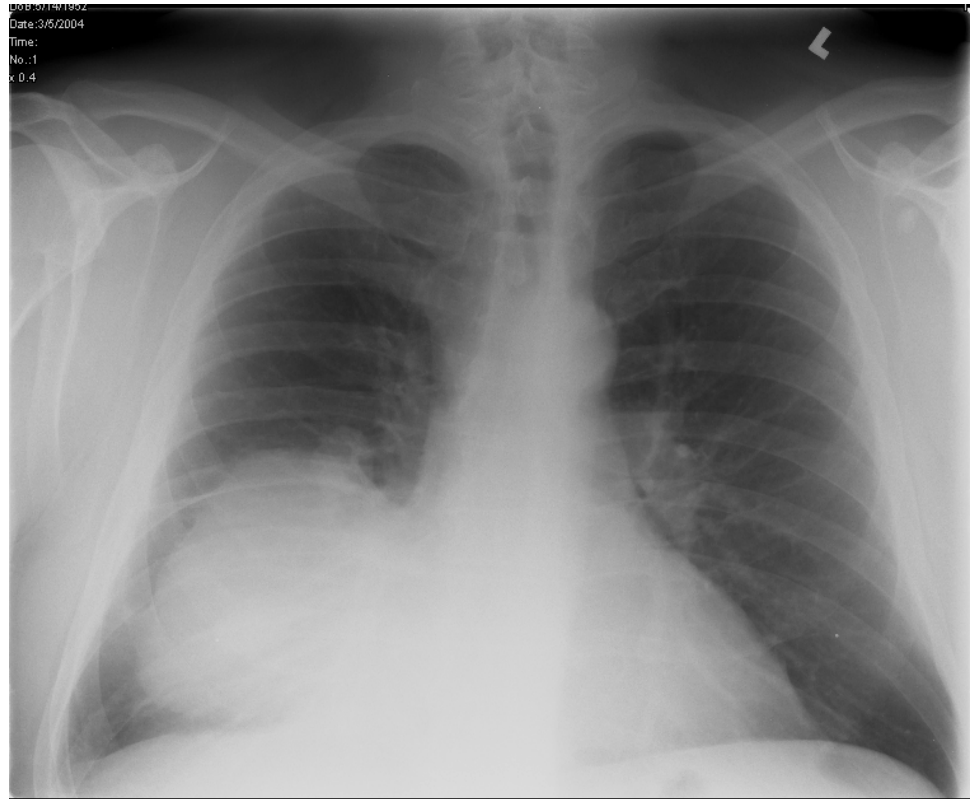
- DFSP is characterized by a chromosomal translocation [t(17:22)(q22;q13)] that results in a fusion protein of the collagen-1A1 promoter with the Platelet-derived Growth Factor Receptor-B gene
- Gleevec (imatinib mesylate) inhibits PDGFR as well as Kit, BCR-Abl
- The drug of choice for metastatic nontransformed DFSP, but its role in locally advanced tumors and transformed sarcomas is much less clear



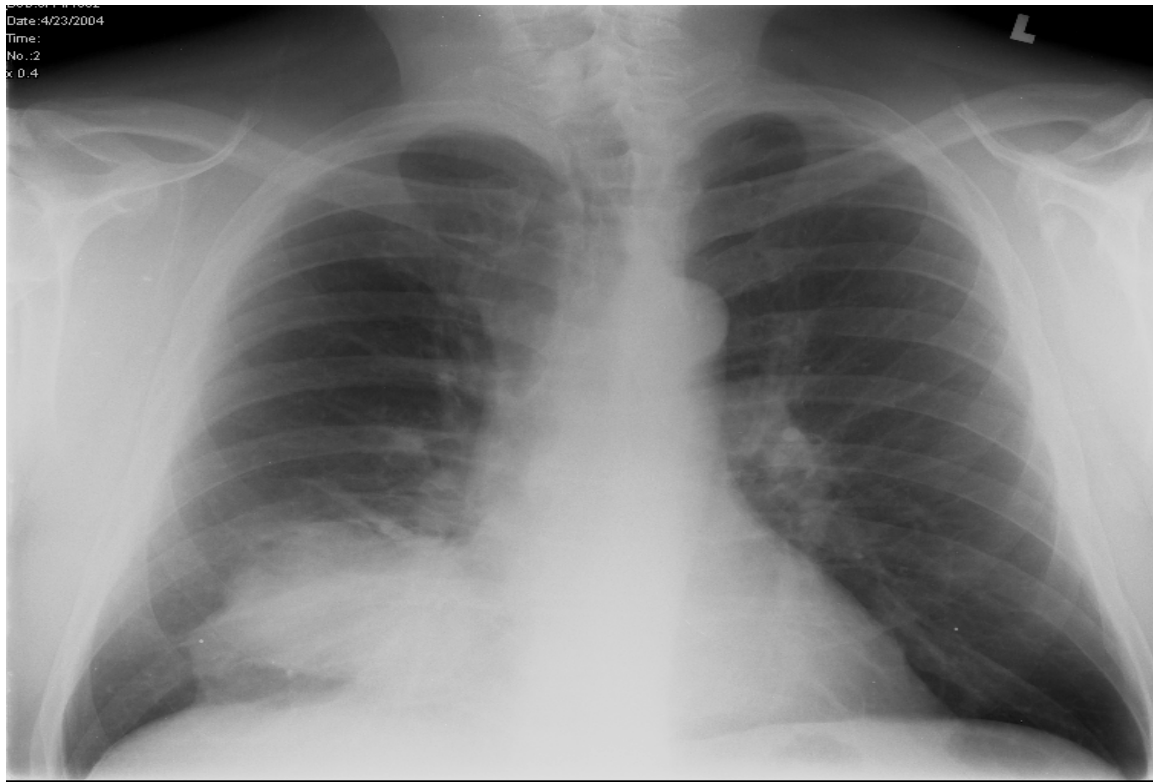
Metastatic DFSP

36 years after initial diagnosis of a scalp DFSP

- 4 operations in the first 18 years, then recurred again 11 years later, treated with surgery and RT
- Lung mass 7 years later with no evidence of local recurrence



Metastatic DFSP After 6 weeks on Gleevec



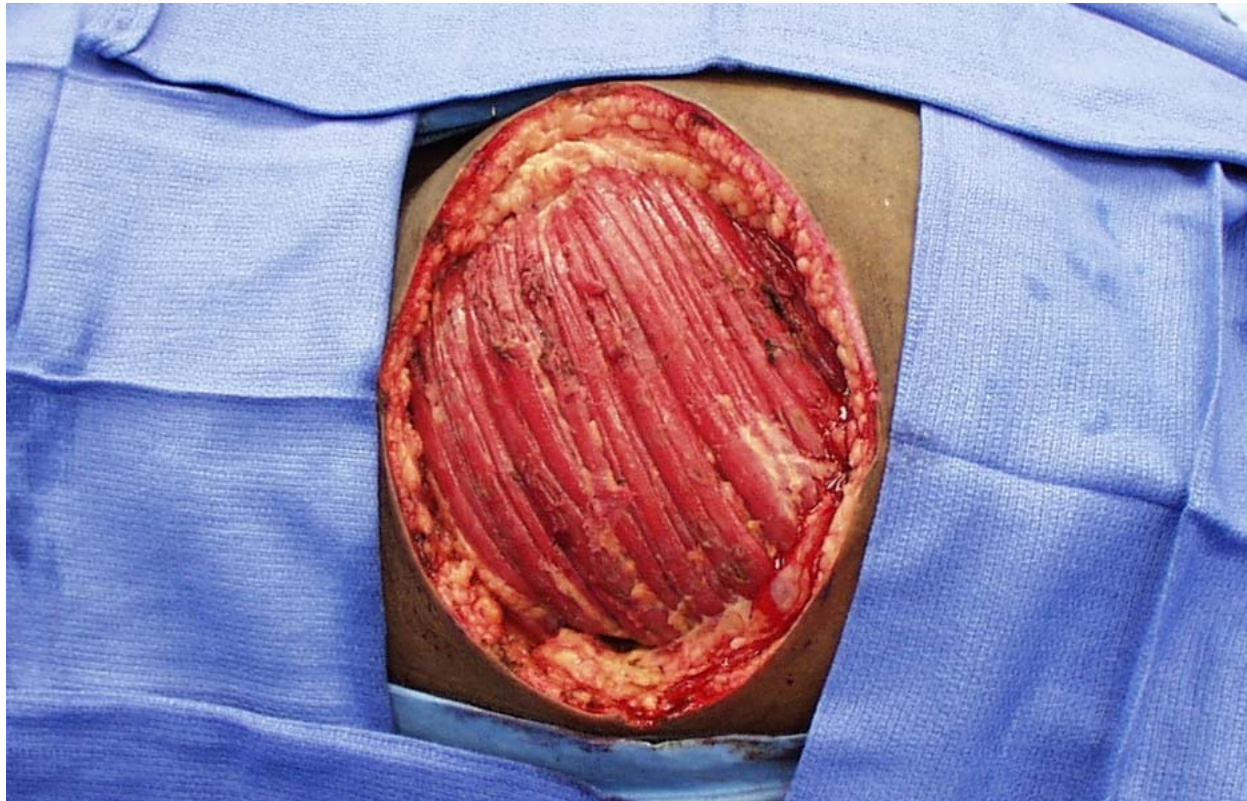
Locally advanced DFSP Gleevec or resection?



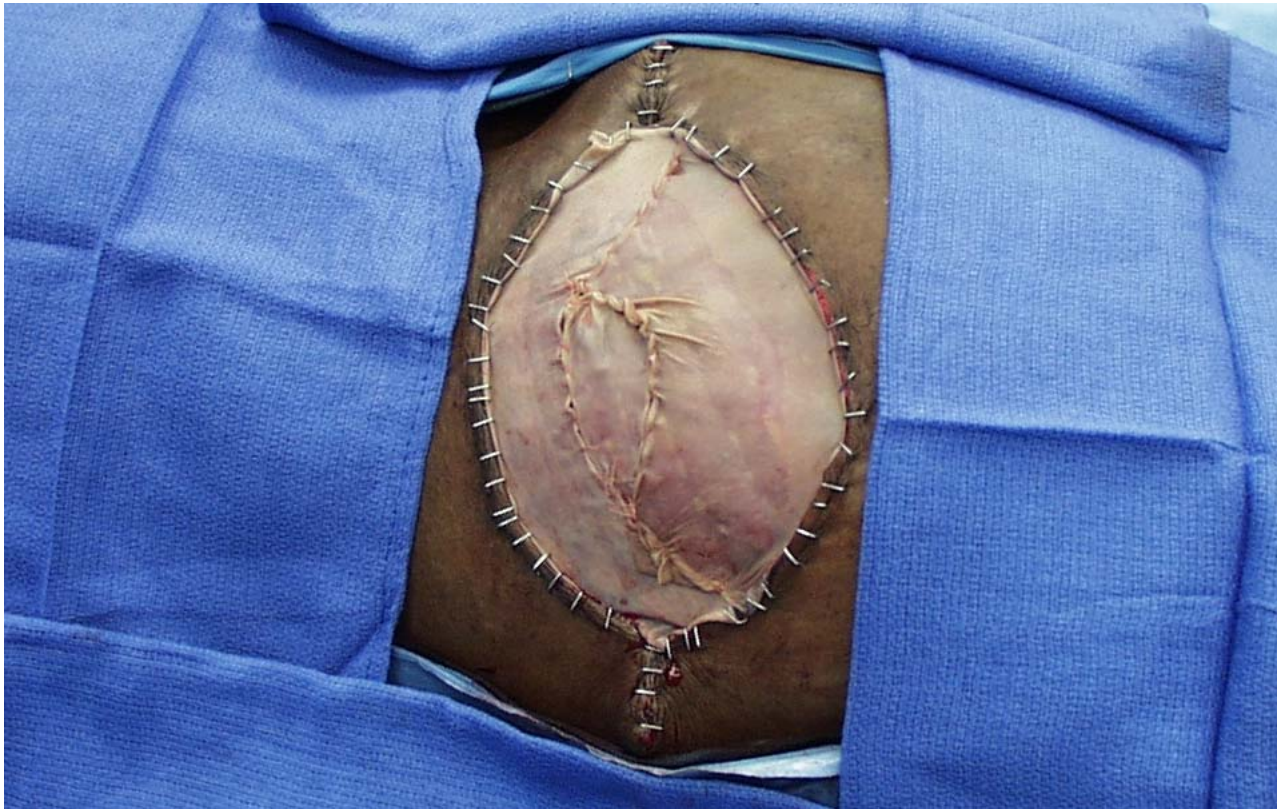
Locally advanced DFSP Gleevec or resection?



Locally advanced DFSP Gleevec or resection?



Locally advanced DFSP Gleevec or resection?



The H. Lee Moffitt Cancer Center Cutaneous Oncology Program



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