

Non-Melanoma Cutaneous Malignancies

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***No Related Financial Disclosures
or
Conflicts of Interest***



The Changing Face of Skin Cancer



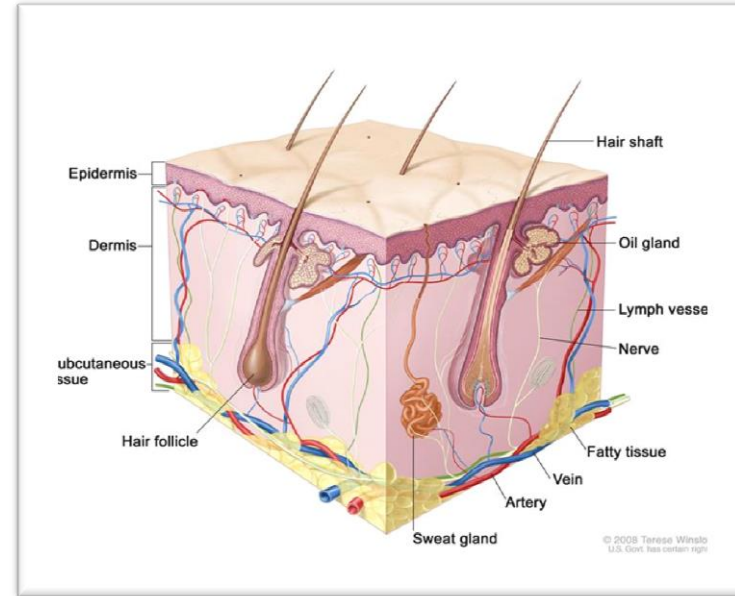
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The Changing Face of Skin Cancer



Overview

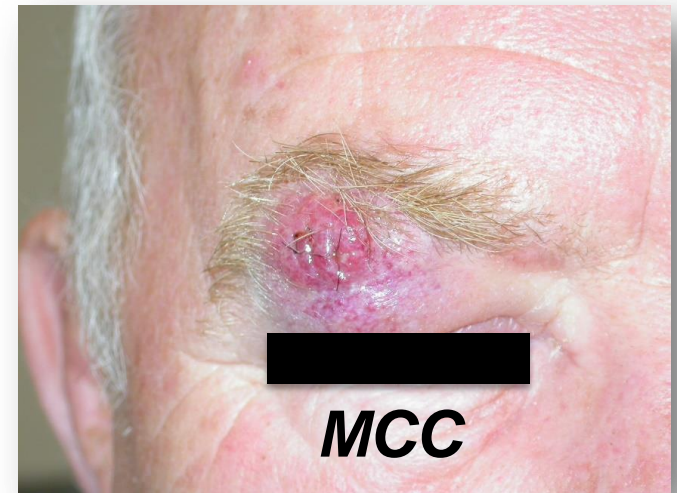
- **Skin Cancer Epidemiology**
 - **Cost**
 - **Tanning Booths**
- **Basal Cell Carcinoma (BCC)**
- **Squamous Cell Carcinoma (cSCC)**
- **Merkel Cell Carcinoma (MCC)**



Non-Melanoma Skin Ca (NMSC)

> 80 different histologic types

- Basal Cell Carcinoma (70 - 75%)
- Squamous Cell Ca (20%)
- Merkel Cell Ca (5%)



NMSC incidence

- **BCC**
Most common cancer
2.8 million cases year
- **SCC**
700,000 cases per year
Incidence increased 200% over past 30 yrs
(Karia PS, et al. J Am Acad Derm. 2013; 68(6):957)
- **40 – 50% Americans will have at least one SCC or BCC by age 65** *(NCI Cancer Trends 2009/2010)*

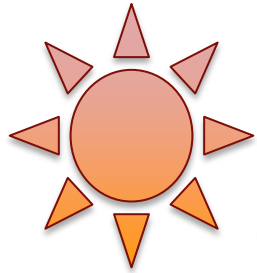


Non-Melanoma Skin Cancer (NMSC)

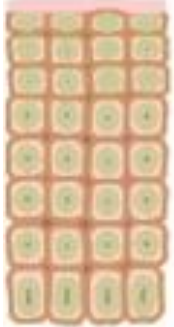
- Overall excellent prognosis
90% 5-yr overall survival
- Subset of aggressive NMSC
10% locally recurrent
3-5% regional metastasis
2,500 deaths per year
- Prospective NMSC registries generally lacking



cSCC Tumor Progression



UV-B Radiation



Basement Membrane



Normal

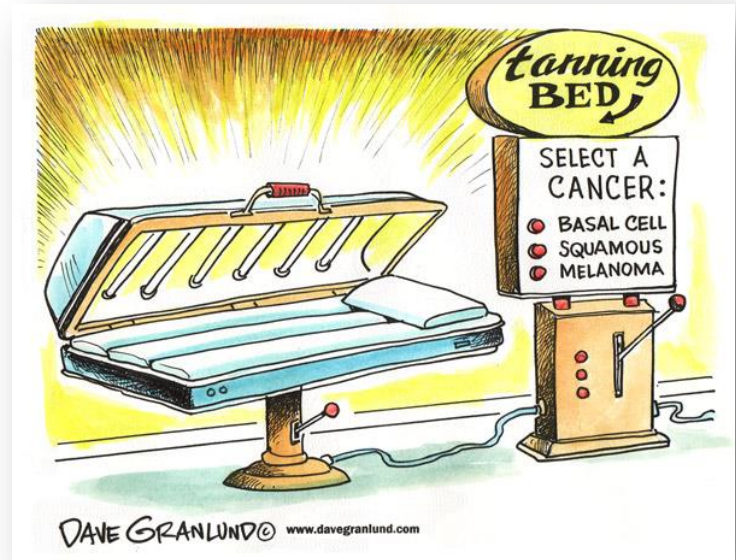
**Pre-cancerous
(Actinic Keratosis)**

**cSCC
*in situ***

**Invasive
cSCC**

Tanning Booths

- Ultraviolet Radiation (UVR) = Carcinogen
Exceeds risk of Lung CA from smoking
- 1,957 ER visits from tanning bed burns
- Skin cancers from Tanning Beds
 - 245,000 ~ BCC
 - 168,000 ~ SCC
 - 6,200 ~ Melanoma



Tanning Booths

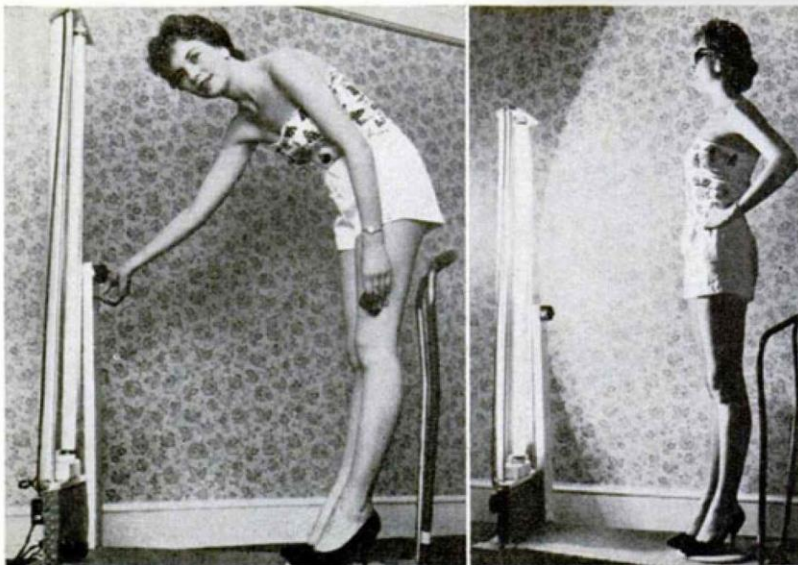
- 21 yr old: Tanned 4-5 times per wk
- 1 tanning session
 - SCC risk increases 67%
 - BCC risk increases 29%
 - Melanoma risk inc. 75%
- Outlawed in Brazil, Australia, and New South Wales



Circa 1947



Circa 1960



Coin dropped in slot . . .

. . . turns on sun lamp . . .

Give a June tan for Christmas



ALL-PURPOSE GIFT
For tanning, styling or drying hair and more. The Westinghouse Sun Lamp costs only **\$1.10** Regular, **\$0.95** for Red Bell.

VACATION GLAMOUR for every woman (and many on your list). For every compliment, they'll thank you for your Westinghouse Sun Lamp gift.

WESTINGHOUSE SUN LAMP
ONLY **\$8.50**
ACCEPTED BY AMERICAN MEDICAL ASSOCIATION as a safe and effective lamp for general use by the public.

This Christmas, give her the suntan she had in June. Give her the look of "just back from Bermuda"—the healthy look of a summer tan. For like the sun, this ultra violet Westinghouse Sun Lamp is a source of Vitamin D. It beats the sun, because you can turn the lamp on at will. It needs only a socket in any lamp that's handy and can be aimed. In a pin-up bracket over the bathroom mirror, you'll tan while shaving. A few minutes of the lamp each day on your children will keep their cheeks from looking pale this winter. Give a Westinghouse Sun Lamp, and you'll give benefits worth more than its cost of only \$8.50.

Skin Cancer Healthcare Costs

\$8.1 Billion Dollars per year

\$4.8 Billion NMSC

\$3.3 Billion Melanoma



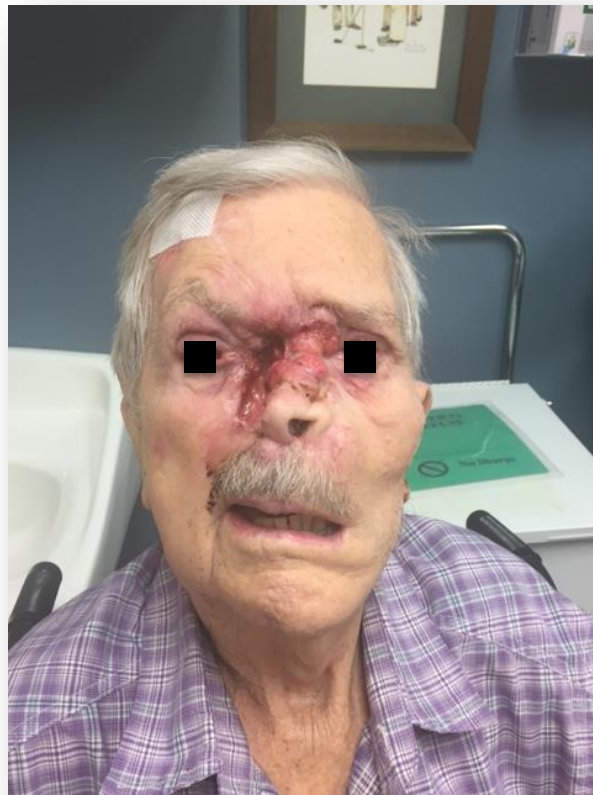
By hikingArtist.com



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Guy GP, et al. Am J Prev Med. 2014; 104(4):e69.

I. Management of the Basal Cell Carcinoma (BCC)



BCC/SCC: Risk Stratification

	LOW RISK	HIGH RISK
Location/Size	< 20mm L Zone	≥ 20mm L Zone
	< 10mm M Zone	≥ 10mm M Zone
	< 6mm H Zone	≥ 6mm H Zone
Borders	Well Defined	Poorly Defined
History	Primary Tumor	Recurrent Tumor
Immunosuppression	No	Yes
Prior Radiation	No	Yes
Pathology		<u>BCC</u> : micronodular; infiltrative; sclerosing; morpheophorm
		<u>SCC</u> : adenoid; adenosquamous; desmoplastic
Perinervial /Vascular Invasion	No	Yes



Work-up: BCCA

- **Complete history & physical**
Full body exam
- **Biopsy**
If more than superficial, inclusion of deep reticular dermis preferred
- **Imaging studies as indicated for extensive disease**

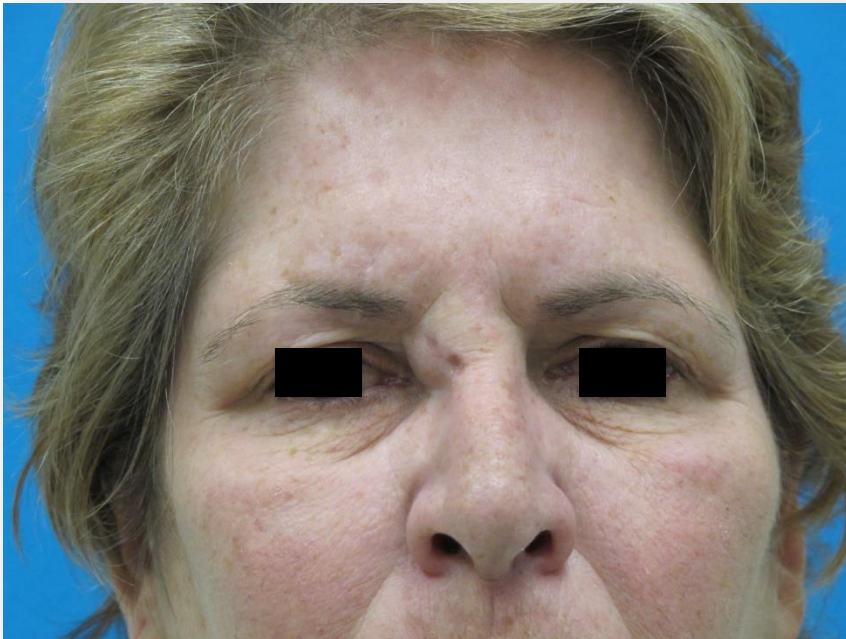


High Risk BCC Treatment

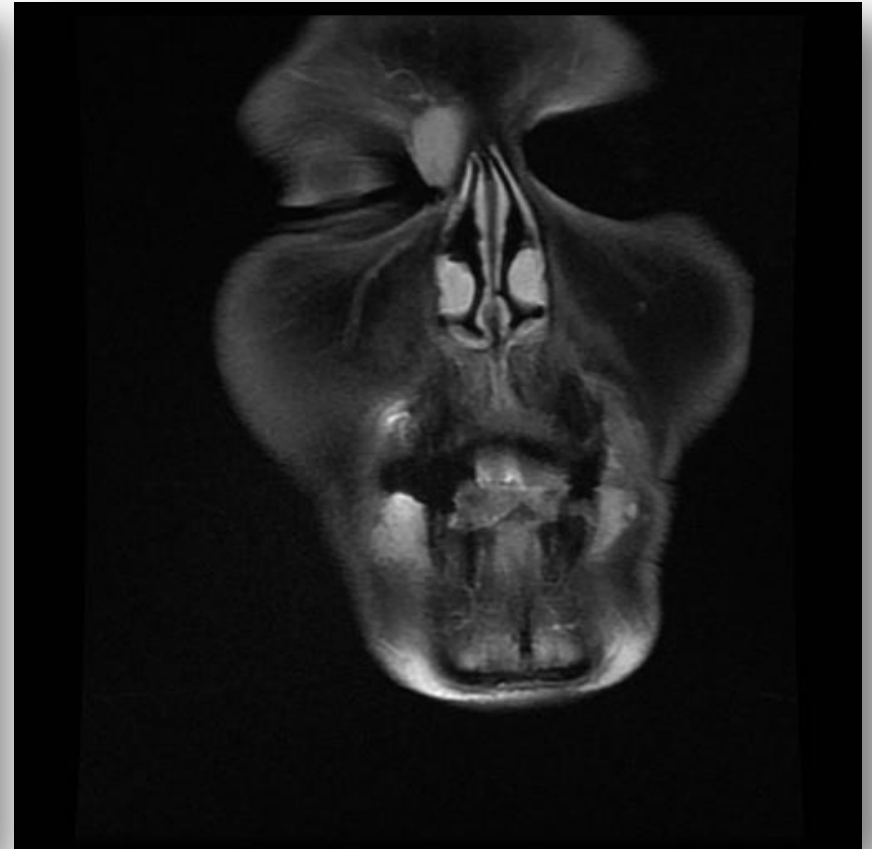
- **High-Risk**
 - Primary Excision (1 cm margin)**
 - MOHS**
 - Primary XRT**
 - **Non-surgical Candidates**
 - **Level 2B evidence**



I. Management of the Basal Cell Carcinoma (BCC)



BCC: MRI – T2



BCC: CT Orbit



S/P MOHS: All Margins Clear



Local Advancement & FTSG



Advanced Basal Cell Carcinoma (BCC)



Hedge Hog (Hh) Inhibitor

Vismodegib (Erivedge)

Indications

- Metastatic BCC
- Locally advanced BCC recurring a/f surgery
- Patients who are not surgical/XRT candidates



Baseline



Week 8



Week 20



Vismodegib: Side Effects (150 mg PO QD)

- Arthralgia
 - Muscle Cramping
 - Alopecia
 - Diarrhea
 - Fatigue
 - Dysguesia/loss appetite/weight loss
 - Teratogen****
- } Hyponatremia

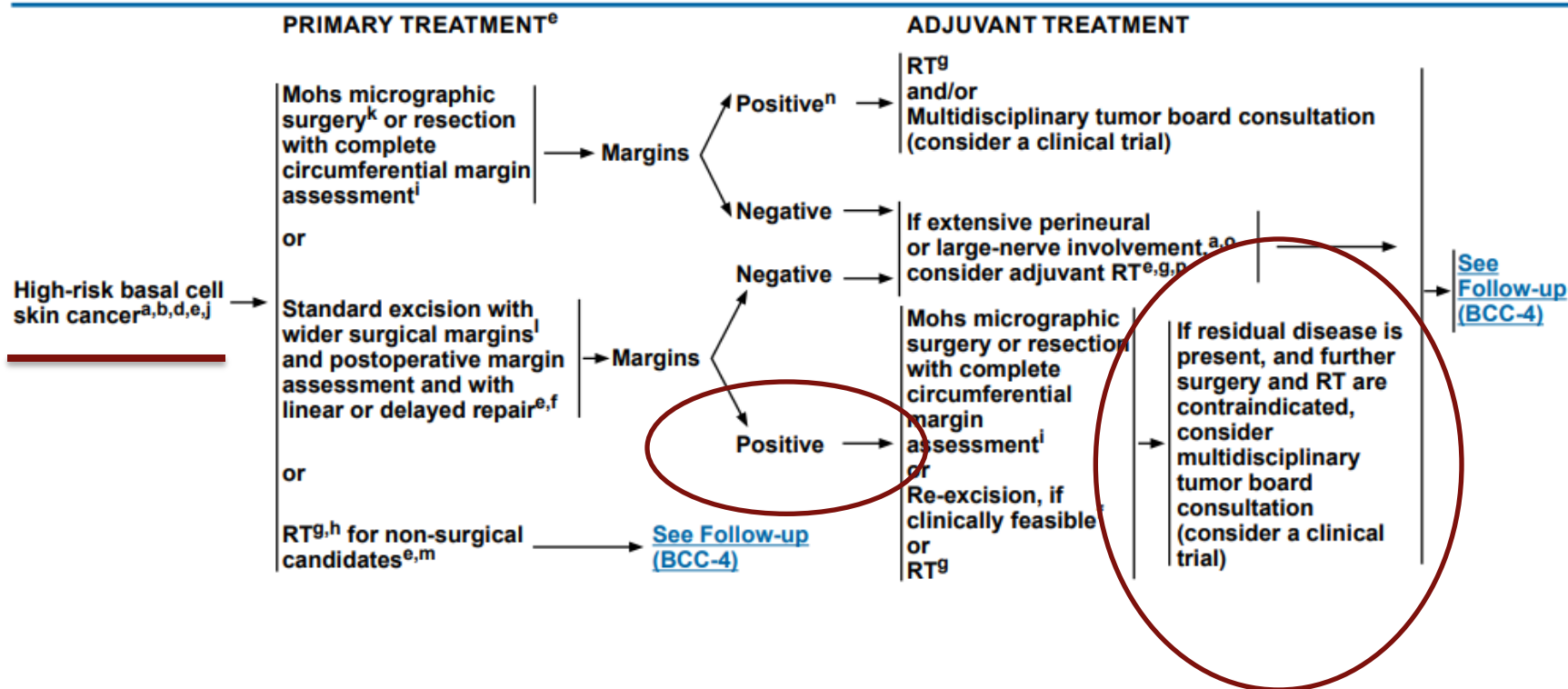


HHg Inhibitor: Indications



National
Comprehensive
Cancer
Network®

NCCN Guidelines Version 1.2019 Basal Cell Skin Cancer



HHg Inhibitor: Indications



National
Comprehensive
Cancer
Network®

NCCN Guidelines Version 1.2019 Basal Cell Skin Cancer

FOLLOW-UP

- H&P
 - ▶ Including complete skin exam every 6–12 mo for first 5 years, and then at least annually for life
- Patient education:
 - ▶ Sun protection
 - ▶ Self-examination

RECURRENCE

Local

[Follow Primary Treatment Pathways \(BCC-1\)](#)

Nodal or
distant metastases

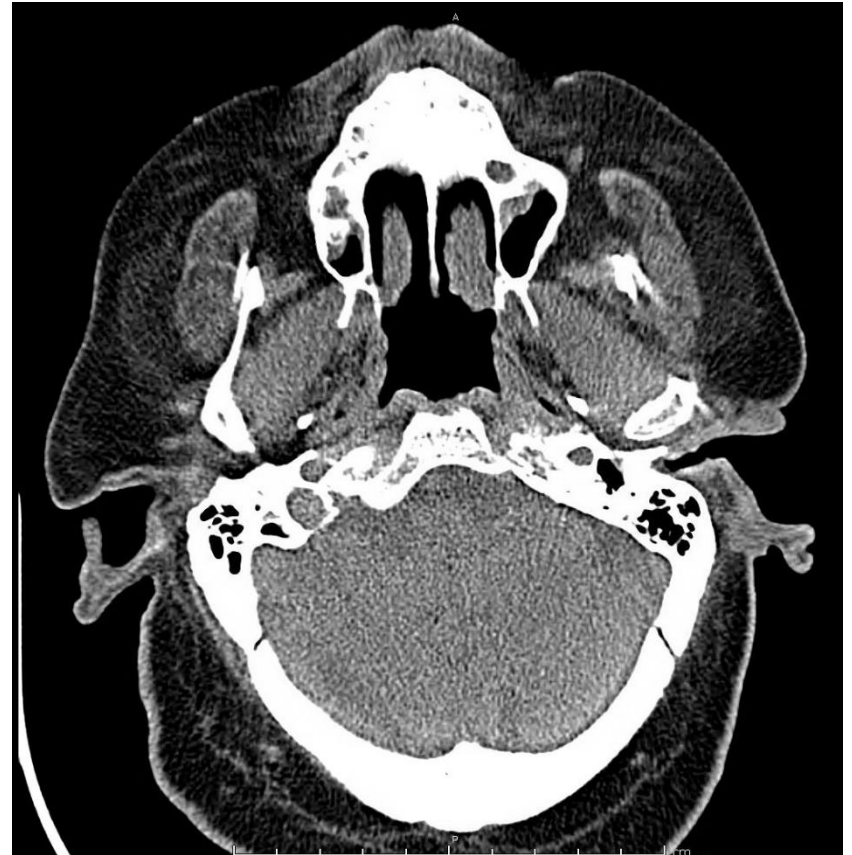
Surgery and/or RT^m
Multidisciplinary tumor board consultation
(consider a hedgehog pathway inhibitor^P or clinical trials)



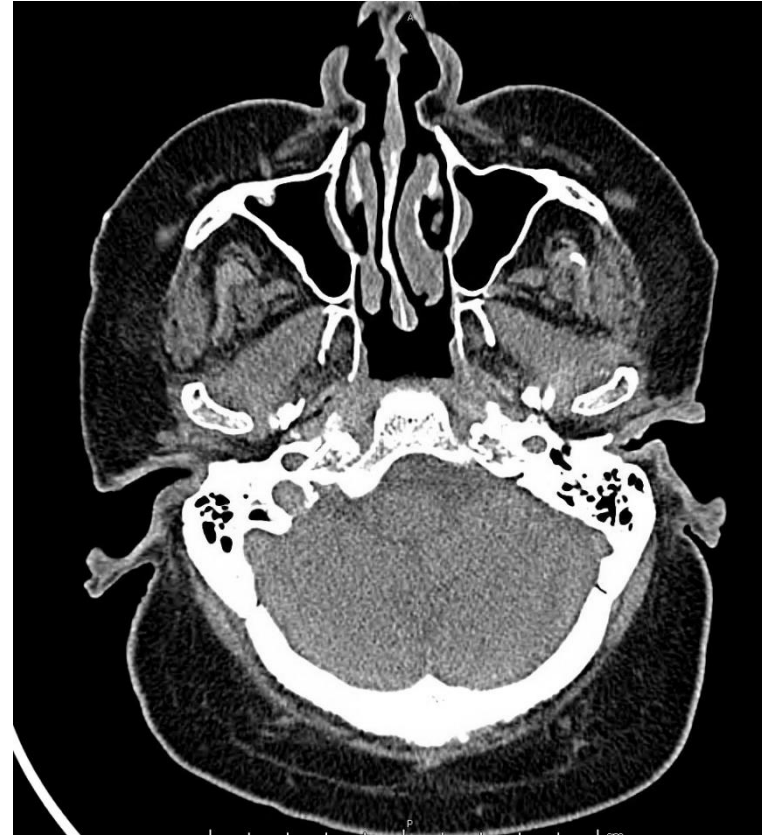
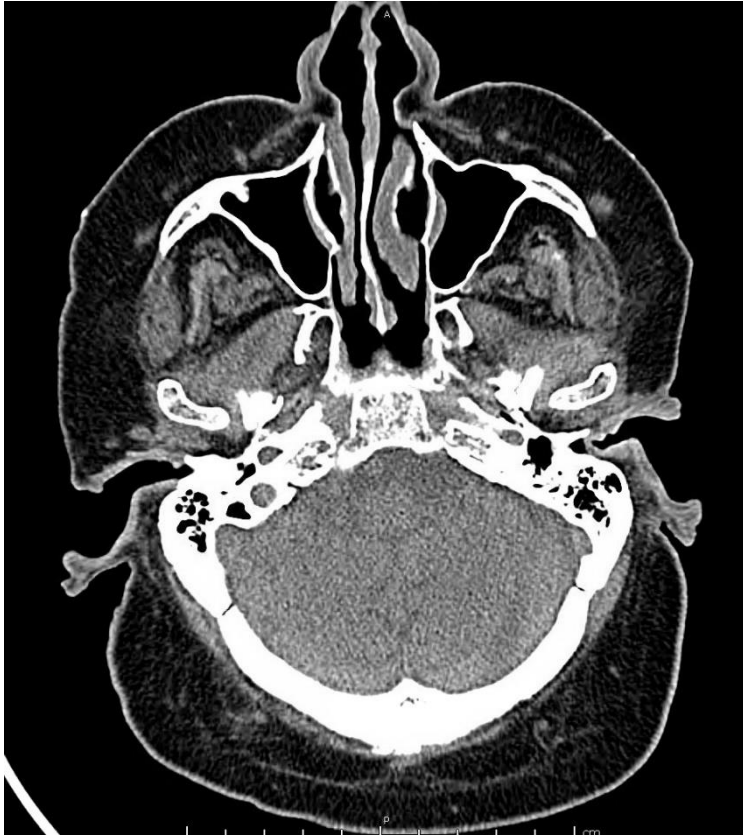


*78 y.o. demented
male presents
with biopsy
proven advanced
BCC
(present for > 3
yr)*





5 Months Vismodegib



Neoadjuvant Vismodegib

June 4, 2014

**Newly
Diagnosed
Advanced BCC**

**Pts not
surgical/XRT
candidates**



Sept 10, 2014

**4 wks
Neoadjuvant
Vismodegib**



Oct. 29, 2014

**11 wks
Neoadjuvant
Vismodegib**



Nov. 19, 2014

**14 wks
Neoadjuvant
Vismodegib**

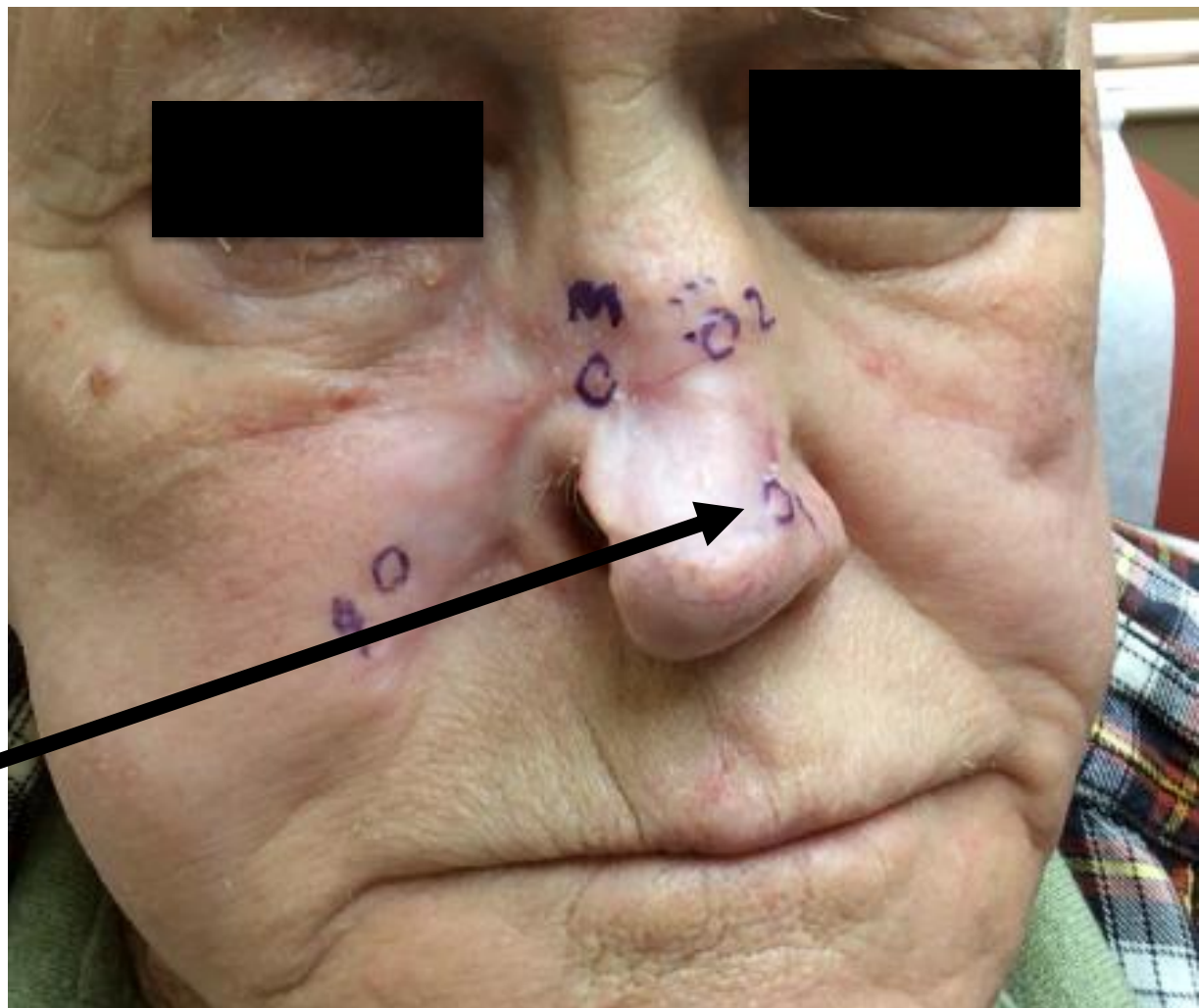


Jan 28, 2015

**24 wks
Neoadjuvant
vismodegib**

**#2, #3, #4 -
Scar**

#1 BCC



March 10, 2015

**30 weeks
(7.5 mons)
Neoadjuvant
Vismodegib**

**Day of
Cheek MOHS**



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Courtesy: Evans Bailey, MD, PhD

March 10, 2015

MOHS:
**Cleared in 1
stage of Mohs**

Perm Section
pathology:
No BCC



MAY 13, 2015

**39 wks
Neoadjuvant
Vismodegib**

**Day Nasal
MOHS**



May 13, 2015

MOHS:
Cleared in 4
stages of Mohs

Perm Section
pathology:
Central Focus
BCC



June 17, 2015



Pre-Vismodegib



**7.5 months
Post-Vismodegib**



March 10, 2015

MOHS:
**Cleared in 1
stage of Mohs**

Perm Section
pathology:
No BCC

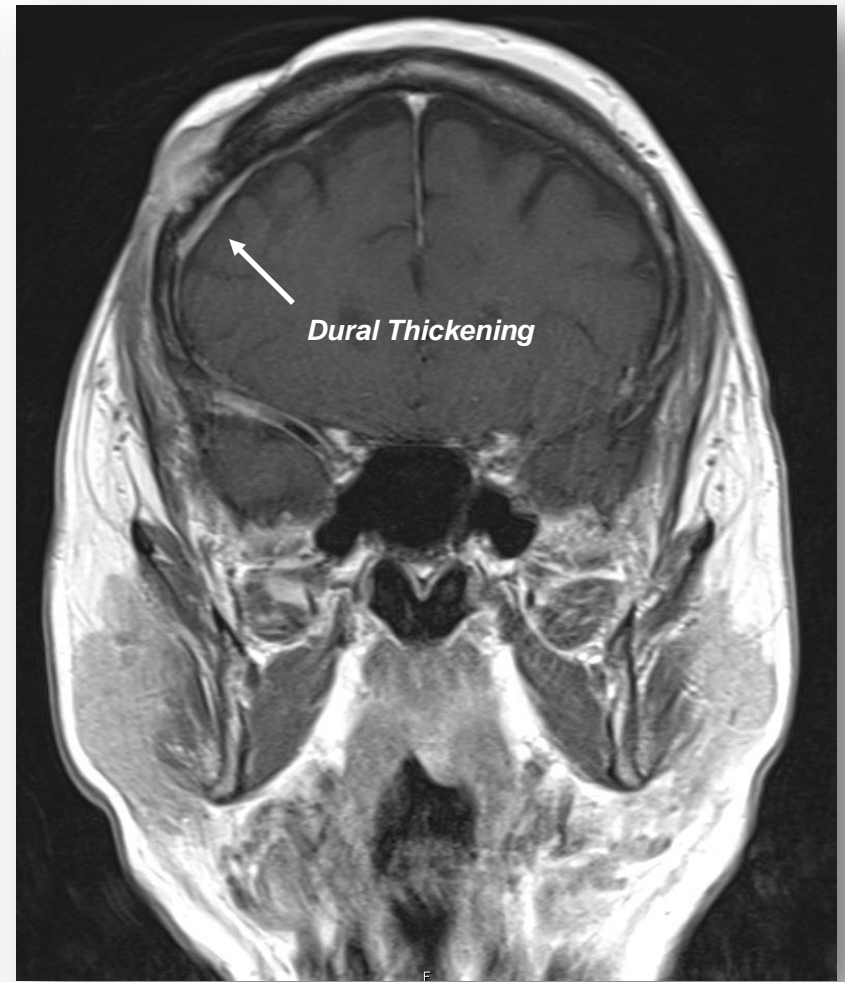
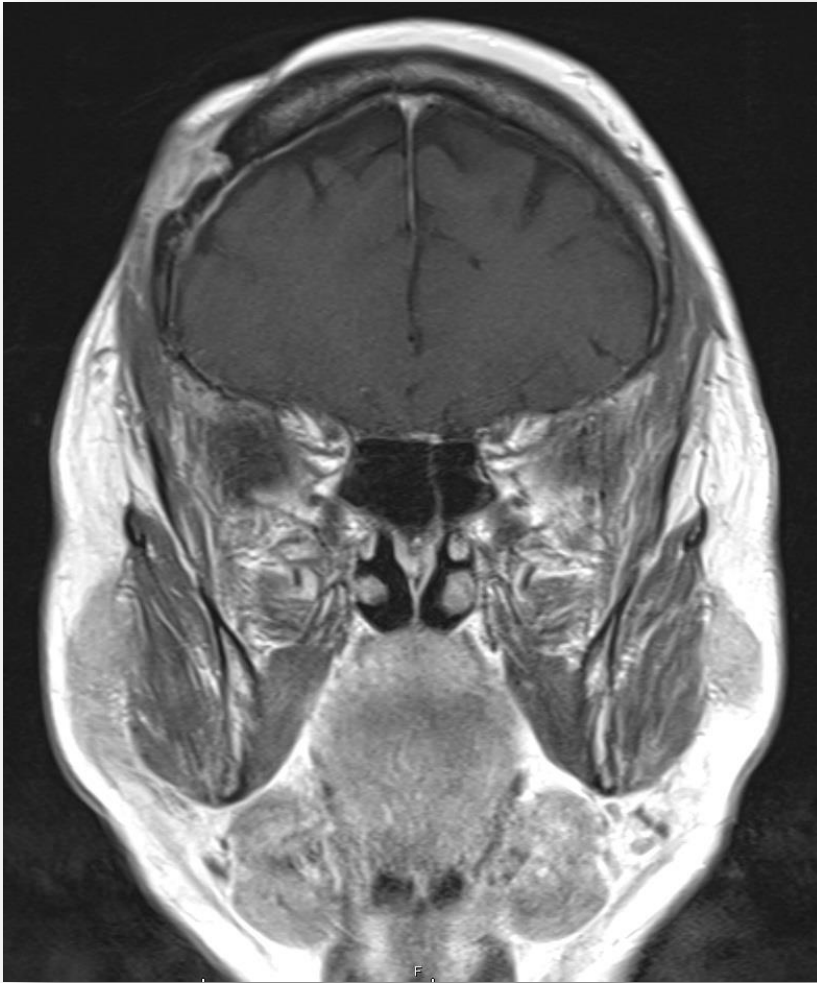




***73 y.o. Vismodegib, WLE
with drilling of calvarium
and regional flap, + deep
margin and restarted on
Vismodegib***



MRI with Gadolinium: BCC





Cranial Erosion



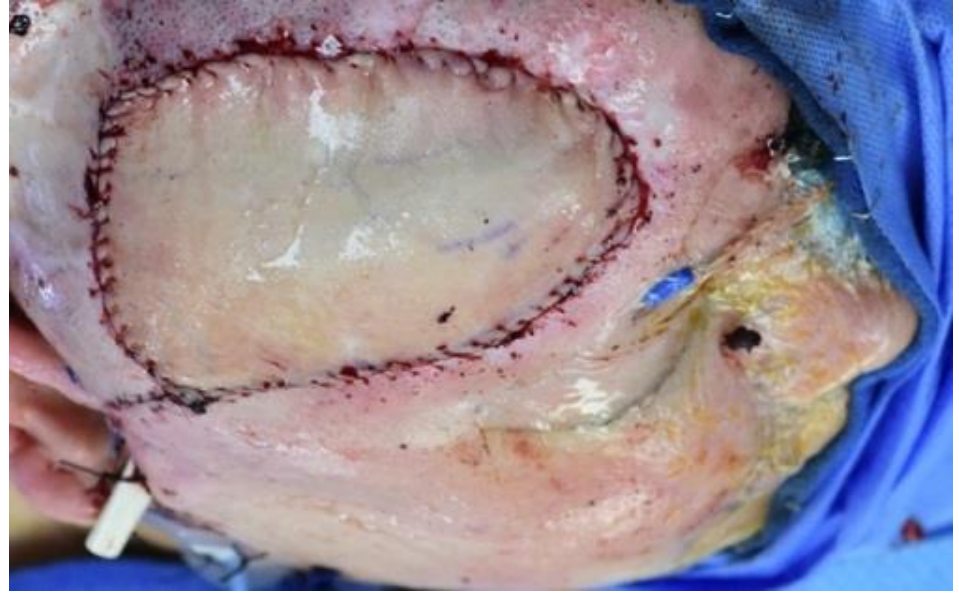
Dural Involvement



Dural Resection



Mesh & RFFF



3 weeks post-op



9 weeks post-op



II. Management of the Squamous Cell Carcinoma (SCC)

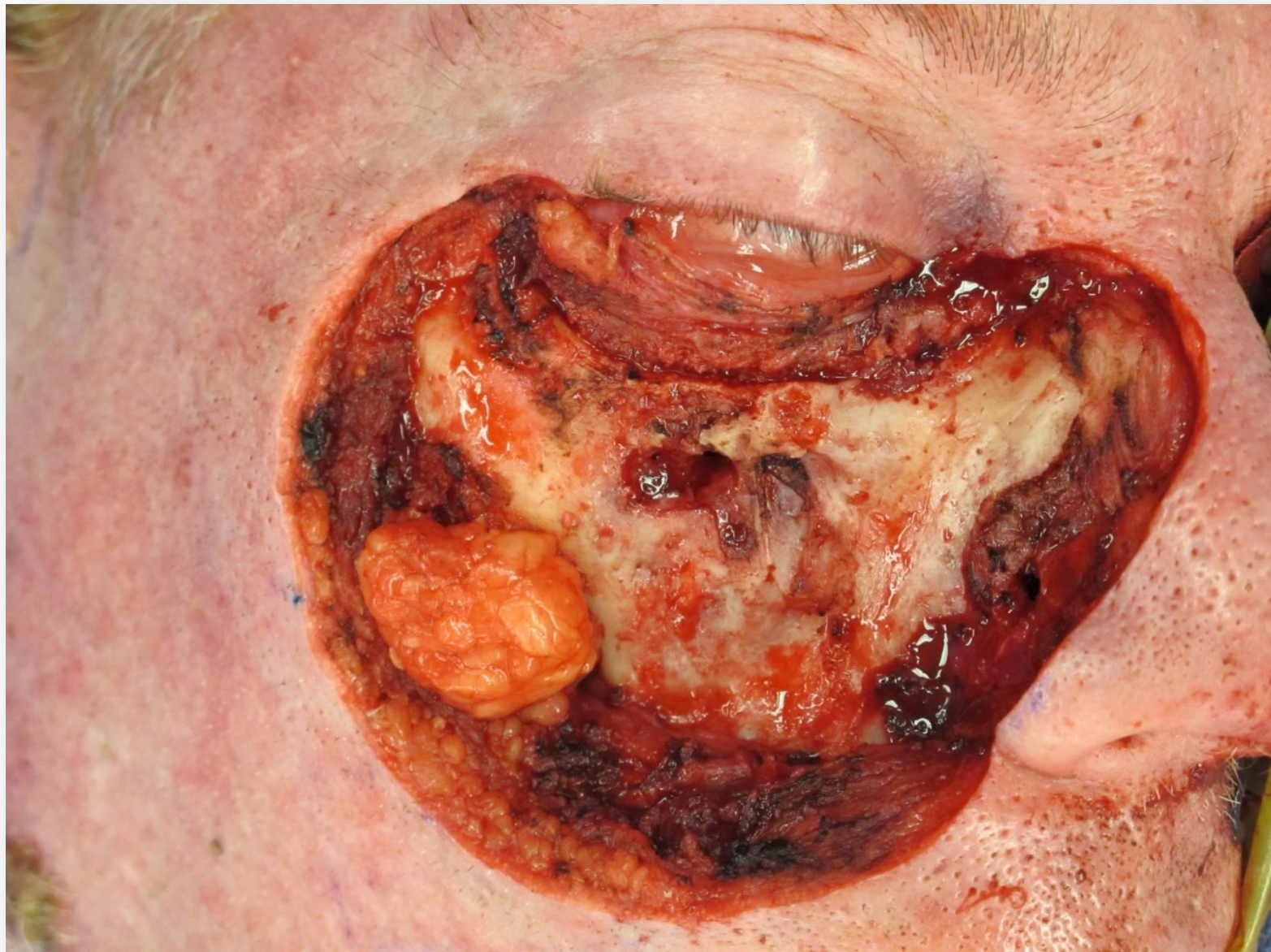


Advanced cSCC



Surgical Management

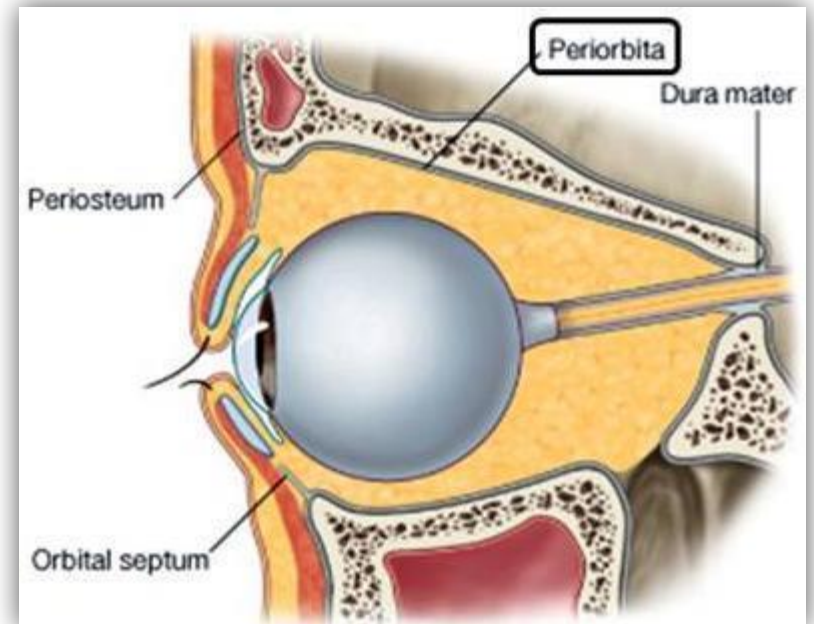


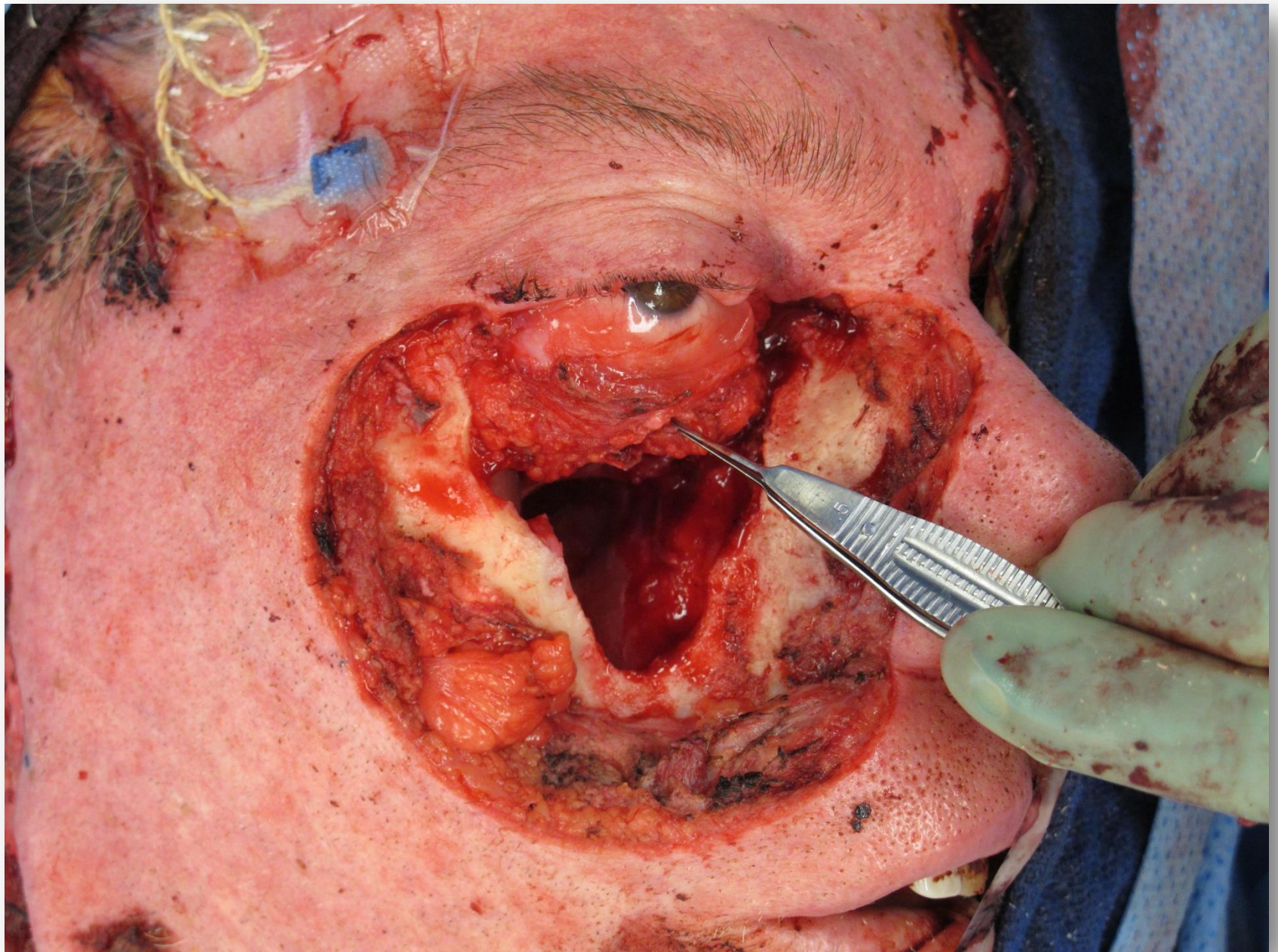


When do you Exenterate?

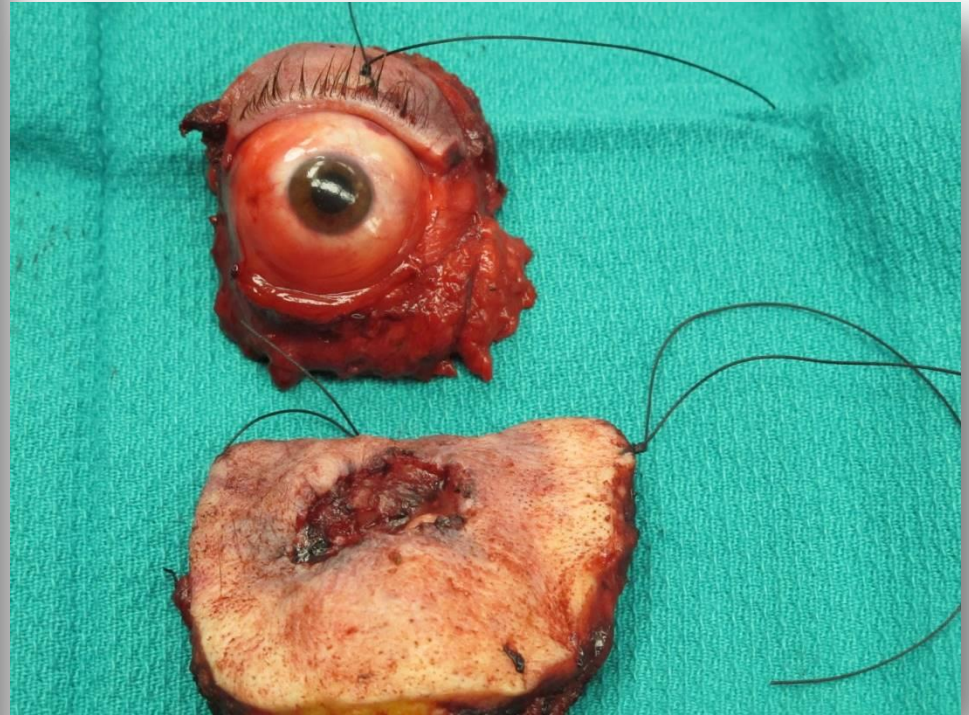
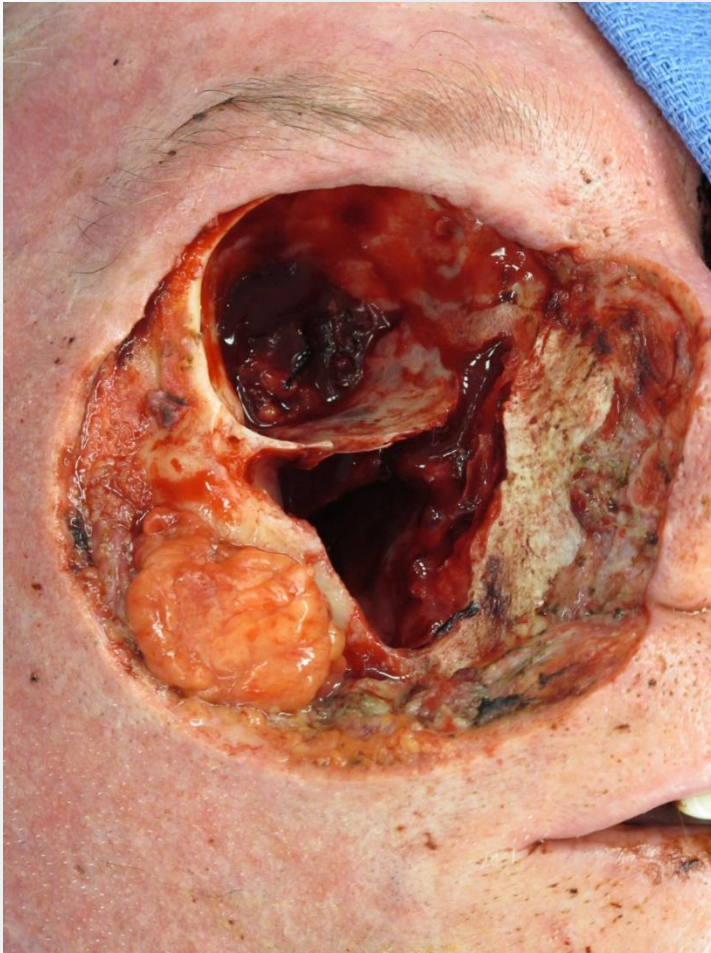
- Intraoperative decision based on FS
- Only when Periorbital FAT is directly invaded.
- Periorbital involvement is not an indication

*Perry et al. Preservation of the eye in
paranasal sinus cancer surgery.
Arch Otolaryn Head Neck Surg.
1988. Jun; 114(6):632*





Orbital Exenteration



ALT FF



Final Pathology

- **Invasive cutaneous SCCA (3.3 x 2 cm)**
- **Perineural invasion**
- **+ Peri-orbital Fat**
- **All margins negative**
- **Intra-parotid LN (0/1) negative**
- **2 + cervical LN, one with ECS**



SCCA Adjuvant Therapy

Primary Tumor XRT

- Positive Margin
- Perineural spread
- Large (named) nerve involvement

Regional Disease

- | | |
|--------------------------|-----------------|
| • 1LN \leq 3cm; no ECS | <i>Optional</i> |
| • ≥ 2 LN | XRT |
| • 1 LN $>$ 3cm | XRT |
| • ECS | XRT +/- Chemo |
| • Incomplete excision | XRT +/- Chemo |

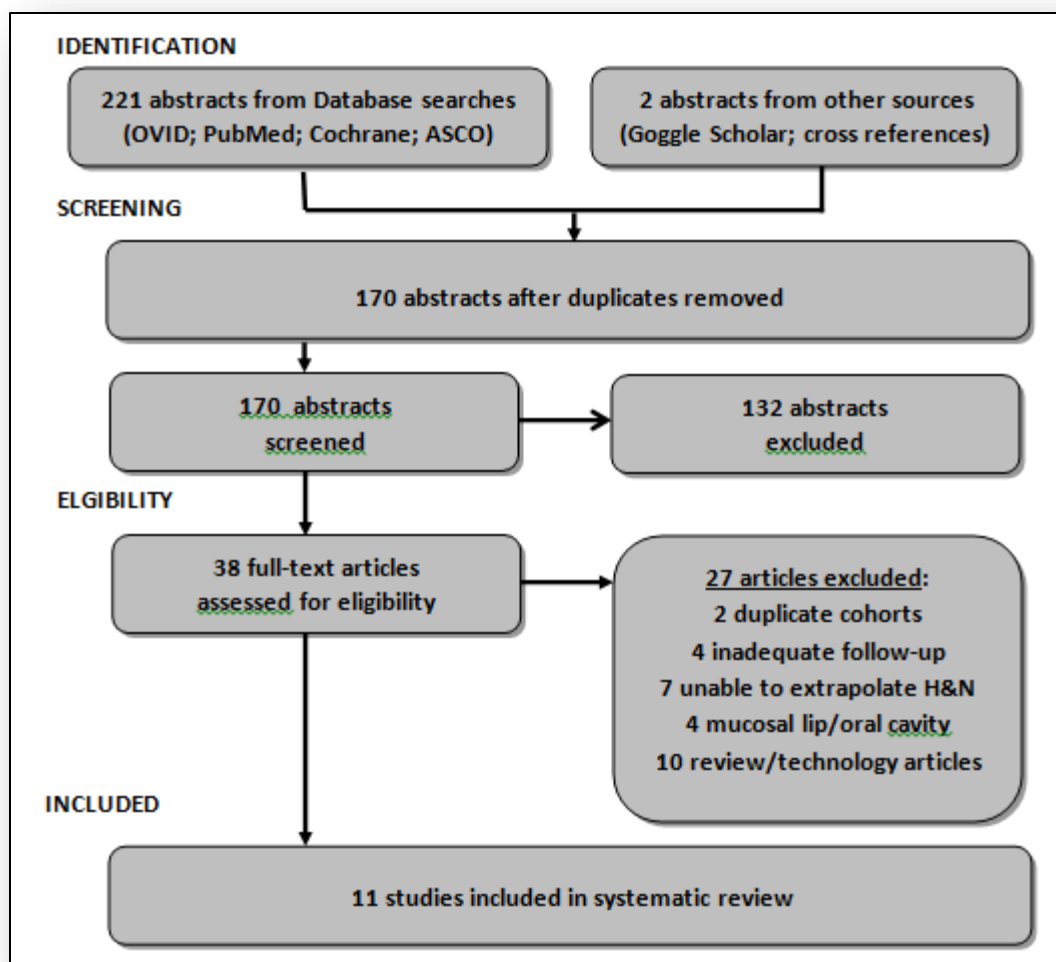


High Risk cSCC Patient

- Poorly defined borders
- Recurrent tumor
- Prior radiation
- Chronic inflammation
- Rapid growth
- Neurologic symptoms
- Pathology
 - Adenoid subtype
 - Desmoplastic subtype
 - Adenosquamous subtype (mucin)
 - Perivascular invasion



Utility of SLNB for cSCC



Utility of SLNB for cSCC

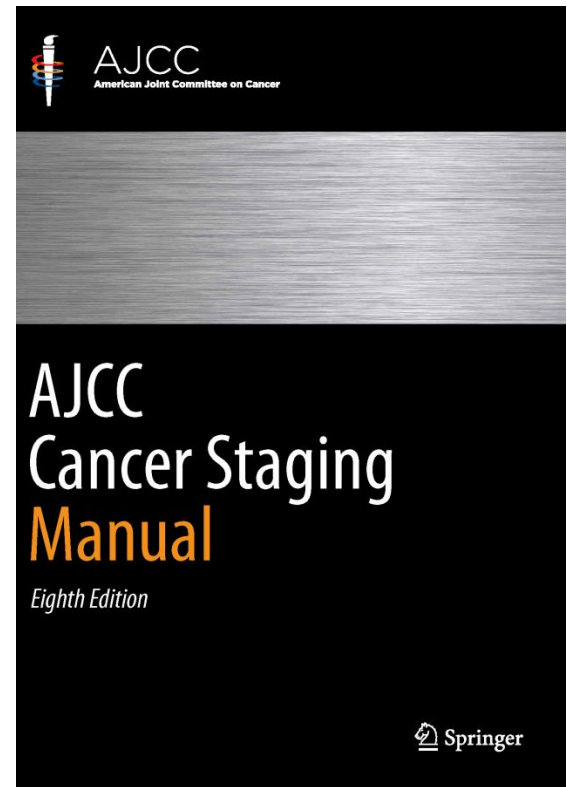
Author/Year	Country	No. Pts	No. +SLN Pts	Rate of False Omission* (No. Pts; %)	Median Follow-up (mon.)	SLN Technique [£]
Michl (2003) ¹²	Germany	5	0	0	29	Colloid
Reschly (2003) ¹³	USA	4	1 (25%)	0	14.5	Colloid + Dye
Wagner (2004) ⁸	USA	5	2 (40%)	1 (33%)	14	Colloid + Dye
Nouri (2004) ¹⁴	USA	8	1 (12.5%)	0	18	Colloid
Cecchi (2005) ¹⁵	Italy	2	0	0	22	Colloid + Dye
Civantos (2006) ¹⁶	USA	15	2 (13%)	0	16	Colloid
Sahn (2007) ¹⁷	USA	4	0	0	27.5	NS
Resendez (2007) ¹⁸	Mexico	11	3 (27%)	0	21	Colloid + Dye
Rastrelli (2011) ¹⁹	Italy	11	1 (9%)	2 (20%)	24	Colloid + Dye
Kwon (2011) ²⁰	USA	2	0	0	13.65	Colloid
Demir (2011) ²¹	Turkey	14	0	0	38.5	Colloid
Total		73	10	3 (4.76%)	21.5	



8th Ed AJCC Staging

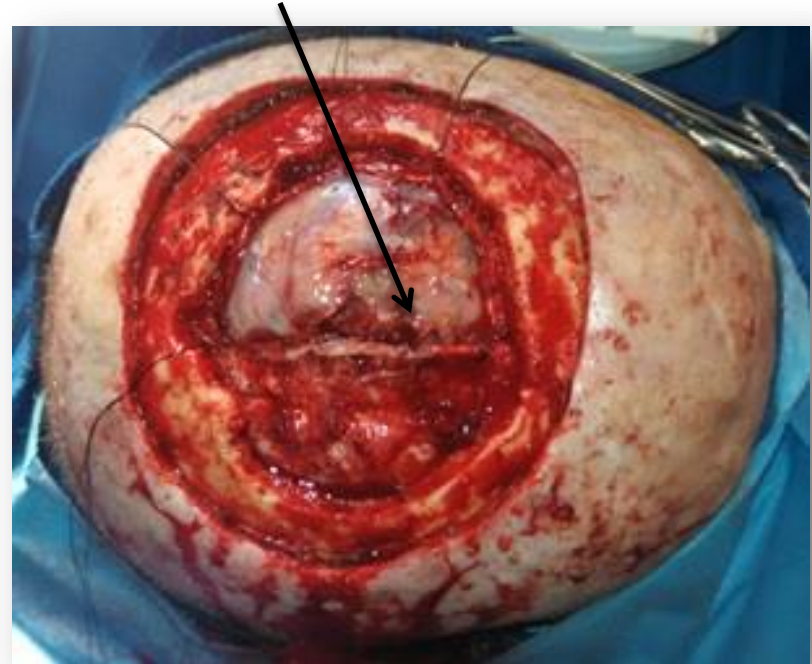
January 2018

- **cSCC AJCC Task Force disbanded**
 - cSCC now a subcategory in Head & Neck
 - Only applies to H&N
- **TNM staging unchanged**
 - Tumor diameter
 - Adjacent structure invasion
 - Risk Factors removed



Organ Transplant: Risk Increases x 250

Sagittal Sinus Invasion

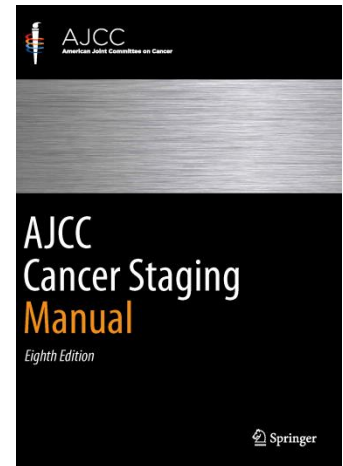


8th Ed AJCC Staging

January 2018

Strong consideration was given toward including immunosuppression as a risk factor

- Only a single study demonstrated an independent association between poor outcome and immunosuppression
- Call for prospective cancer registry [1]



III. Merkel Cell Carcinoma (MCC)

- **Rare neuroendocrine tumor**
 - Local recurrence rate of non-melanoma skin ca
 - Regional & distant recurrence of melanoma
 - Mortality rate exceeds melanoma
 - 5-year: 30-64%
- **Elderly**
- **Merkel cell polyomavirus (MCV)**



Merkel Cell Carcinoma

Differential Diagnosis

Merkel Cell Carcinoma

Melanoma

Lymphoma

Neuroblastoma

Carcinoid

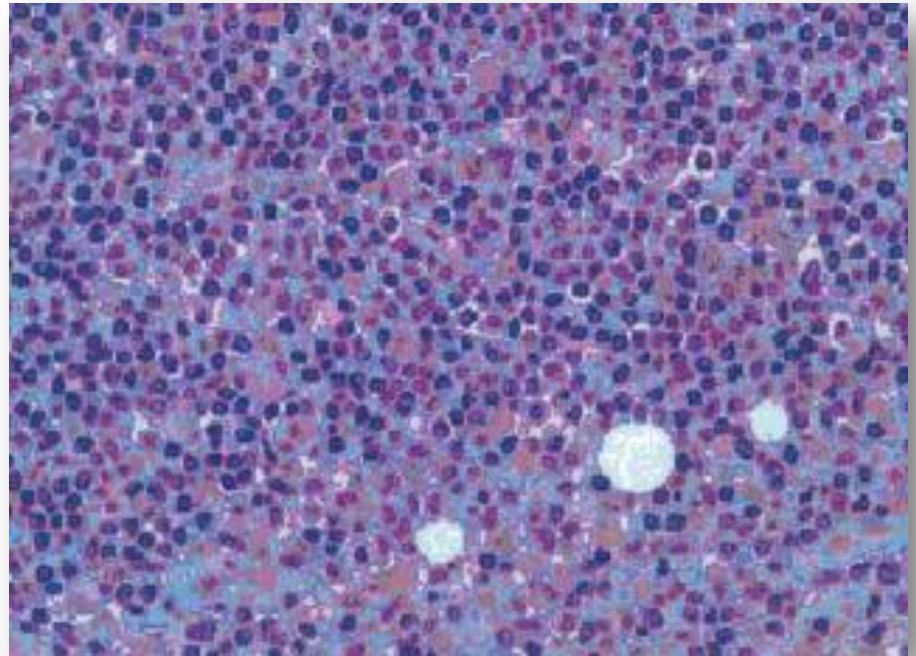
**Metastatic Small Cell Carcinoma of
the Lung**

Rhabdomyosarcoma

Extraskeletal Ewing's Sarcoma

**Primitive Neuroectodermal Tumor
(PNET)**

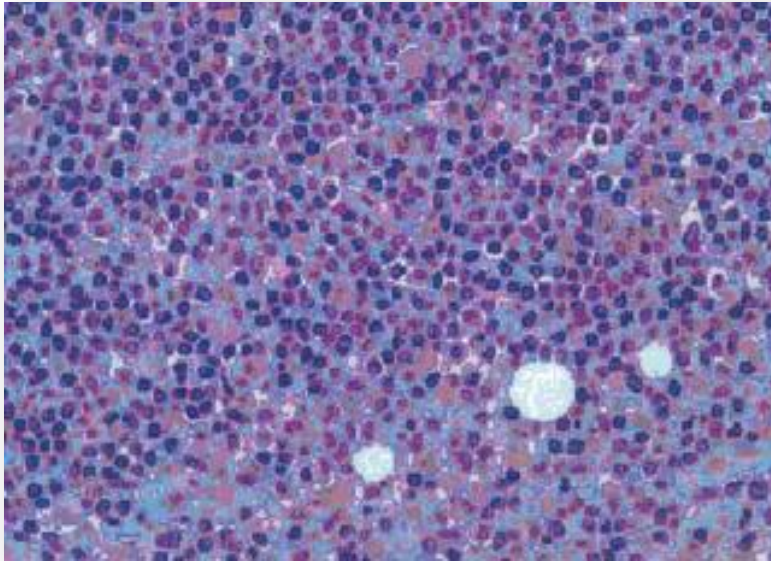
Small Round Blue Cells



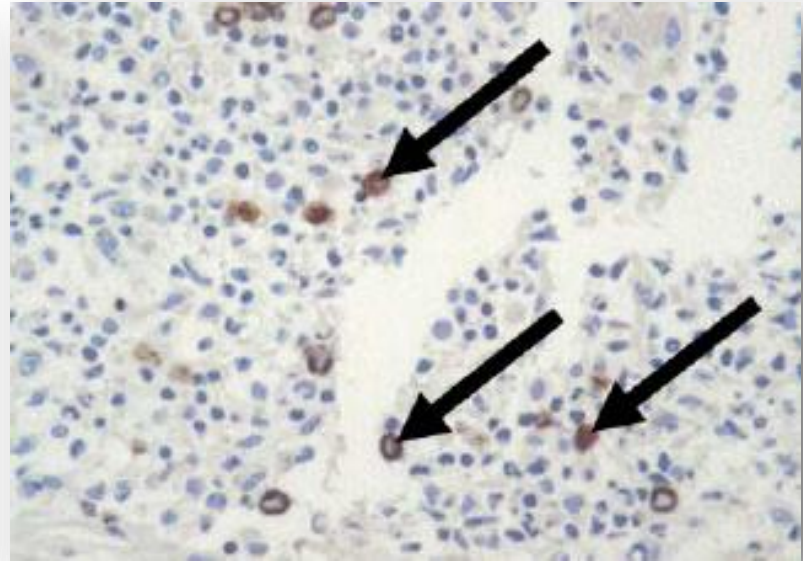
SLN Histologic Evaluation: MCC

H&E Staining

Small Round Blue Cells



CK-20 IHCS



Schmalbach CE, et al. Archives Otolaryngol. 131:610, 2005.



Reliability of SLNB for Regional Staging of H&N MCC

*Schmalbach CE, Lowe L, Teknos TN, Johnson TM, Bradford CR.
Archives Otolaryngol 2005; 131:610*

- 10 patients (1995 – 2003)
- Median F/U: 34.5 months
- SLN identified in 100% Pts (mean: 2.4)
- 2 of 10 pts (20%) had a + SLN
 - Both negative on H&E
 - Occult metastasis only identified with CK-20
- 1 of 8 (12%) – SLN patients recurred regional
 - Rate of false omission = 12%
- SLN technique safe and reliable for MCC



MERKEL CELL CARCINOMA

1.2019

Clinically N-Zero

- ❖ ***WLE***
- ❖ ***Consider SLN biopsy with IHCS***

Considered the most sensitive staging technique

Clinically N-Positive

WLE

- ❖ ***Therapeutic Neck Dissection and/or radiation therapy***
- ❖ ***To consider Chemotherapy***

Distant Metastasis

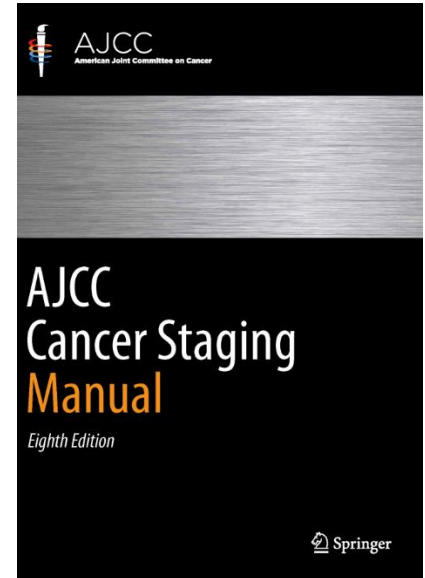
- ❖ ***Supportive Care***
- ❖ ***T/C Surgery, Radiation, and/or Chemotherapy***

8th Ed. MCC Staging (2018)

Primary Tumor Stage Features

- Tx** Tumor cannot be assessed
- T0** No evidence of primary tumor
- Tis** *In situ* primary tumor
- T1** 2 cm in maximum dimension
- T2** > 2 cm but ≤ 5cm in maximum dimension
- T3** > 5cm in maximum dimension
- T4** Tumor invades extracutaneous structures

Fascia; Muscle; Cartilage; Bone



MCC Staging

Regional Lymph Nodes

- Nx Nodes cannot be assessed
- cN0 No regional lymph nodes on clinical or radiographic exam
- pN0 No regional lymph node metastases on pathologic exam
- N1a Micrometastasis (SLNB)
- N1b Macrometastasis
- N2 *In transit* metastasis without LN metastasis
- N3 *In transit* metastasis with LN metastasis

Distant Metastases

- M0 No distant metastasis
- M1a Metastasis to skin, subcutaneous tissues, or distant LN
- M1b Metastasis to lung
- M2b Metastasis to all other visceral sites



Key Pearls

Skin Cancer Epidemic

- Ultraviolet (UV) is a carcinogen

Basal Cell Carcinoma

- Vismodegib for advanced disease

cSCC

- Formal staging disbanded
- Immunosuppressed population behaves differently
- Orbital exenteration for periorbital fat involvement
- SLNB promising but investigational

Merkel Cell Carcinoma

- Elderly; Poor Prognosis
- Small round blue cells (CK-20+; TTF-1 negative)
- SLNB standard of care

