



The Eyes of March:
Mohs Micrographic Surgery &
Periocular Malignancies


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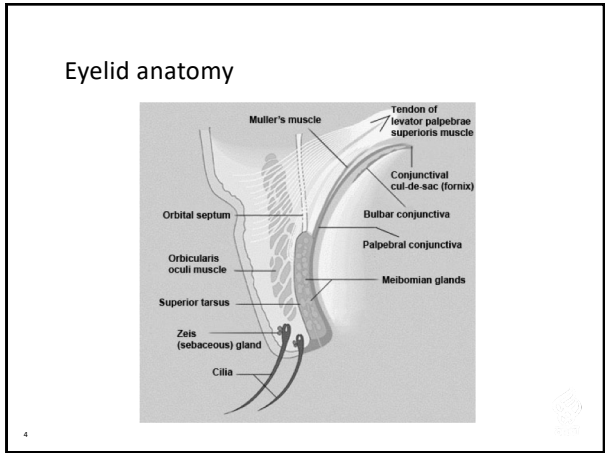



QAO POST GRADUATE CONVENTION
MARCH 9th, 2019

No conflicts of interest



- ### Objectives
- Review common benign and malignant cutaneous eyelid neoplasms
 - Discuss management of high-risk cutaneous SCC, BCC, melanoma
 - Highlight the Mohs Micrographic Surgery technique and it's application in margin assessment
- 



- ### Tumor origin
- Cutaneous
 - Epithelial
 - Malignant: Basal cell carcinoma, Squamous cell carcinoma, actinic keratosis (pre-malignant)
 - Benign: Seborrheic keratosis, squamous papilloma, inverted follicular keratosis, verruca vulgaris
 - Melanocytic
 - Malignant: Melanoma
 - Benign: Ephelis (freckles), lentigines, nevi, nevi of ota
 - Adnexal
 - Malignant: Sebaceous carcinoma
 - Benign: Follicular cysts (EIC), hydrocystoma, syringomas
 - Stromal tumors, other inflammatory conditions mimicking tumors
- 



Seborrheic keratosis



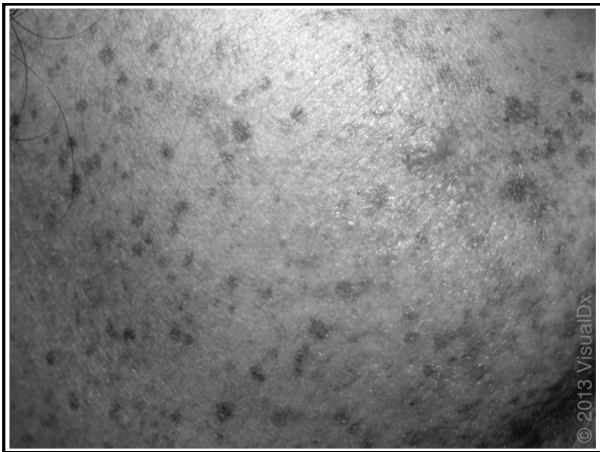
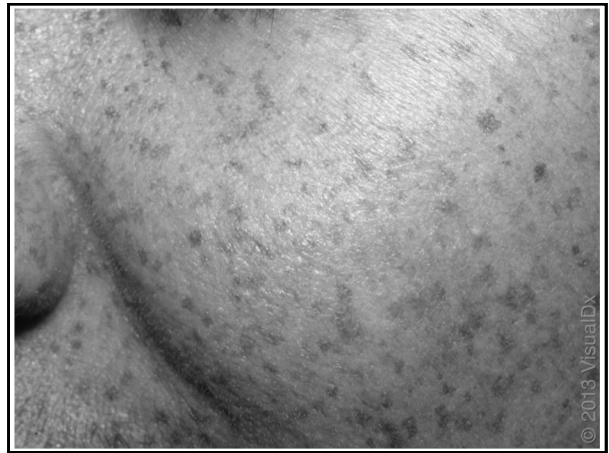
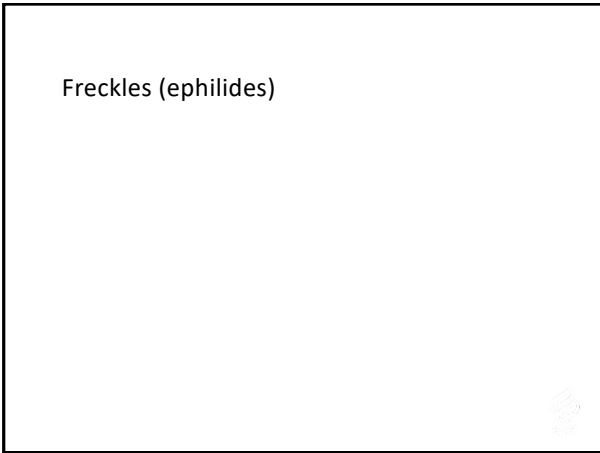
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Seborrheic keratosis

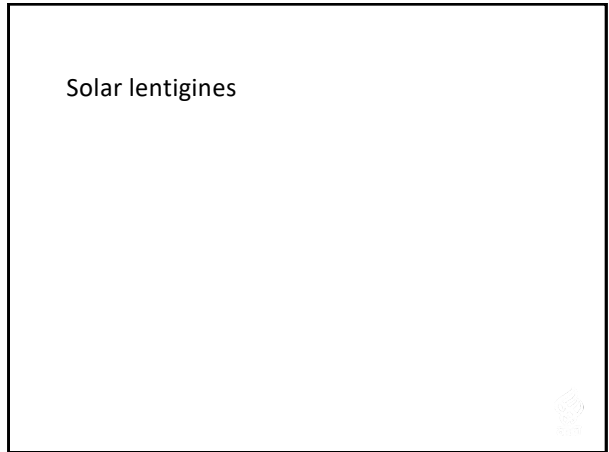


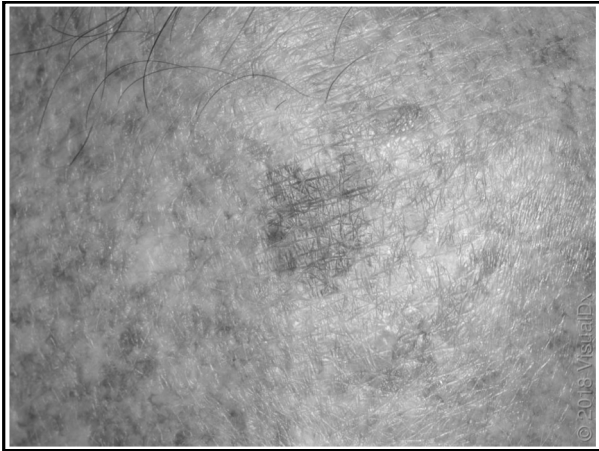
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Freckles (ephelides)



Solar lentigines



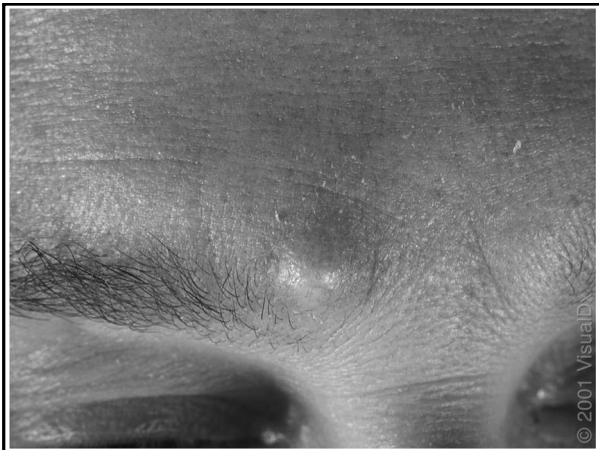


Nevi



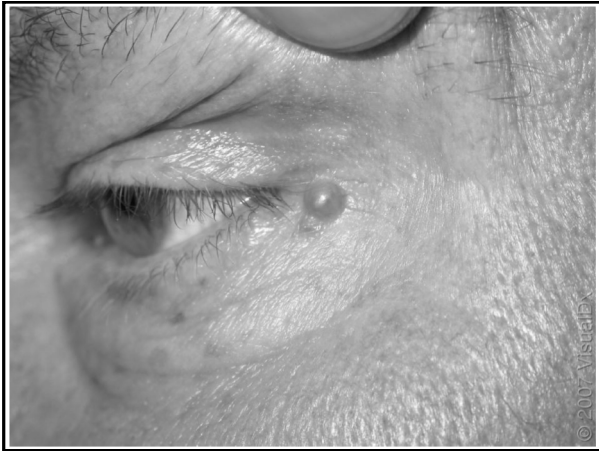


Follicular cyst/epidermoid cyst/sebaceous cyst





Hidrocystoma

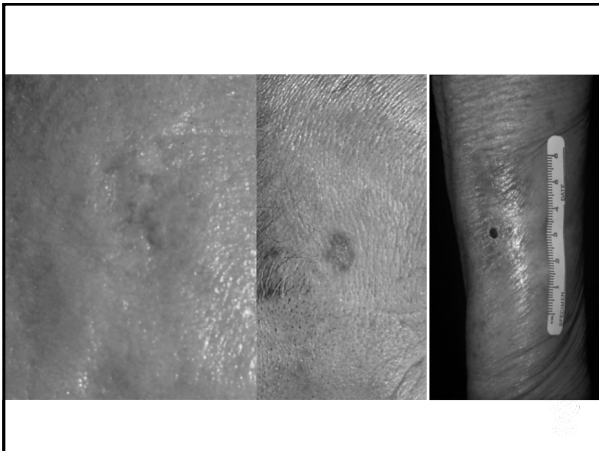


Syringoma





The Big 3: Skin Cancer



Cancer Incidence in US

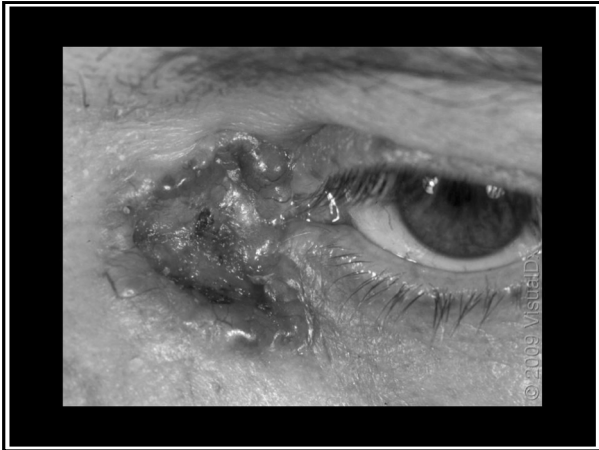
Cancer type	Annual incidence
• Non-Melanoma Skin Cancer (NMSC)	• 5,400,000 (1mil SCC)
• Prostate	• 394,000
• Breast	• 372,000
• Lung	• 193,000
• Colorectal	• 126,000

CDC - National Program of Cancer Registries – 2015 Estimates

2019 Skin Cancer Estimates


- Basal Cell Carcinoma
 - 4.4 million cases / year
- Squamous Cell Carcinoma
 - 1 million cases / year
- Malignant Melanoma
 - 137,000 new cases / year
 - 63,000 melanoma in-situ
 - 74,000 invasive melanoma

Basal Cell Carcinoma




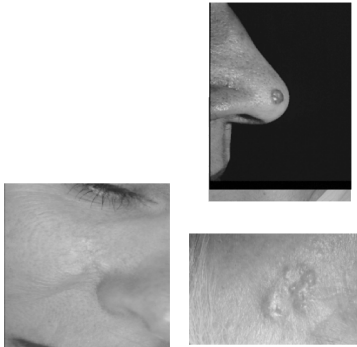
Basal Cell Carcinoma

- Arises and mimics the appearance of basal keratinocytes of the epidermis
- "Pearly" appearance
- Fair-skinned individuals in sun exposed areas
- Usually slow growing




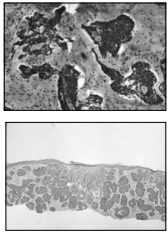
Basal Cell Carcinoma

- Nodular
- Pigmented
- Superficial
- Infiltrative
- Micronodular
- Sclerotic (morpheaform)


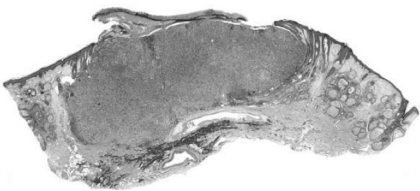


Basal Cell Carcinoma (BCC)


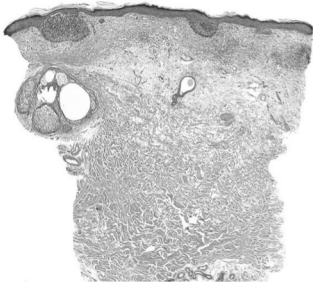
- Histopathology
 - Dark purple staining basal cells in mass
 - Peripheral palisading
 - Retraction




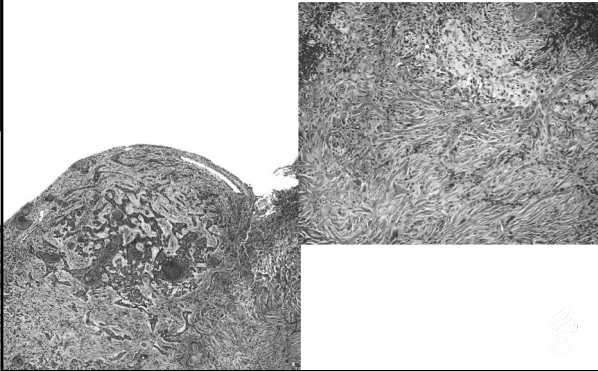
Basal Cell Carcinoma – Nodular Type



Basal Cell Carcinoma – Superficial Type



Basal Cell Carcinoma – Sclerosing Type



Hedgehog Signaling Pathway

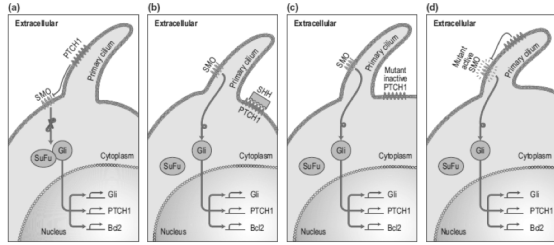


Figure 1 Hedgehog signaling pathway.¹⁸ (a) In the absence of Hedgehog (Hh), PATCHED1 (PTCH1) constitutively inhibits the activity of Smoothened (SMO) (b) Upon binding to soluble protein Hh (SHH), PTCH1 is unable to suppress SMO, and SMO goes on to activate the Hh signaling cascade (c) The majority of BCCs possess PTCH1-inactivating mutations (d), and a minority possess SMO-activating mutations
Liu and Colegio, International Journal of Dermatology 2013, 52, 654-665

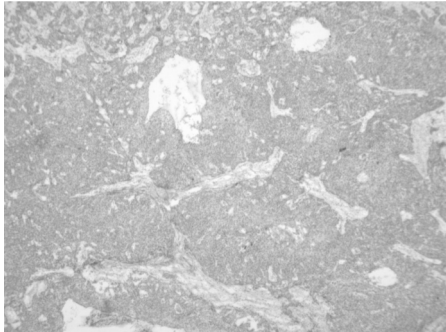
6 months after starting vismodegib



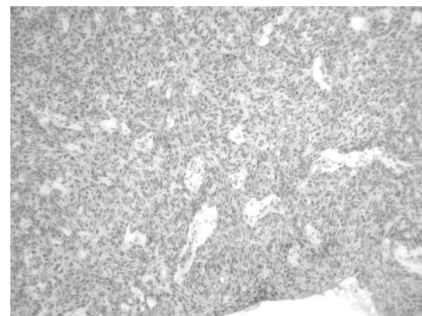
- Side effects
 - Severe muscle cramps
 - Dysgeusia, nausea
 - 60 lb weight loss
 - Hair loss
- Stopped Vismo, proceeded with Mohs surgery

- Frozen histology
 - Not typical basal cell appearance
 - Tumor revealed squamoid appearance with spindled differentiation, possibly related to Vismodegib treatment

SCC transformation

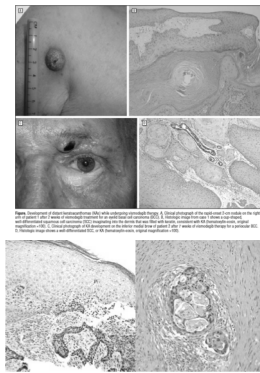


SCC transformation

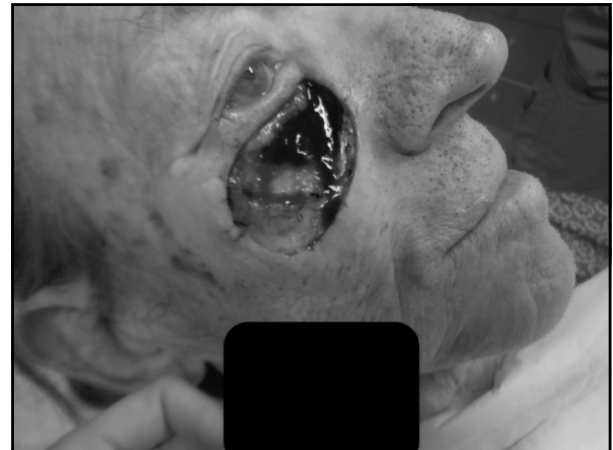


Vismodegib induction of SCC/KA

- Archives Feb. 2013
 - Developed KA within BCC plaque on eyelid
 - Distant KA after 2 weeks
- JAAD July 2013
 - 61 yo with metastatic BCC of the shoulder skin to left axillary nodes
 - Nodal histology consistent with BCC
 - Lymphadenectomy --> recurrence
 - Tx with vismodegib, initial response of primary and nodes, then progression of axillary node
 - Histology c/w SCC (+p63, -BerEP4)
 - Conclusion : residual or progressive tumor after vismo may not be BCC



Aasi et al. *JAMA Dermatol.* 2013;149(2):242-243
Iarrobino et al. *J Am Acad Dermatol.* 2013 Jul;69(1):e33-4



Neoadjuvant Vismodegib Before Mohs: Lack of Tissue Sparing and Squamous Differentiation of Basal Cell Carcinoma in a Patient With Chronic Lymphocytic Leukemia

Oral hedgehog pathway inhibitors, such as vismodegib, offer the potential of shrinking large, neglected, locally advanced or metastatic basal cell carcinoma (BCC) tumors. The neoadjuvant therapeutic promise may facilitate clearance with Mohs micrographic surgery (MMS) by yielding a smaller

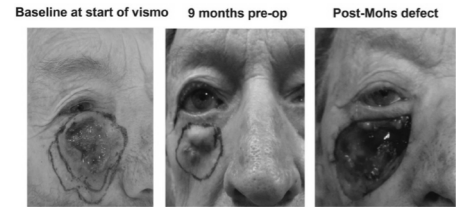
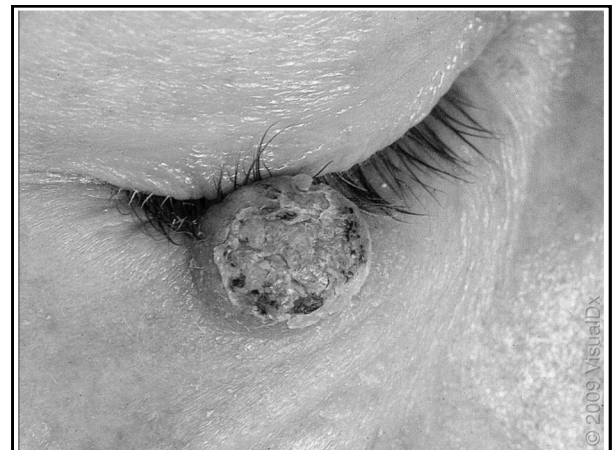


Figure 1. Clinical recession of basal cell carcinoma tumor during the months of vismodegib therapy and resultant post-operative defect following Mohs Micrographic Surgery clearance of the tumor.

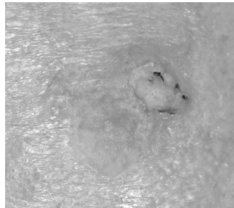
Guo, D, Kosintseva, I & J.I. Leitenberger. *Dermatol Surg.* 2016 Jun;42(6):780-3.

Squamous Cell Carcinoma






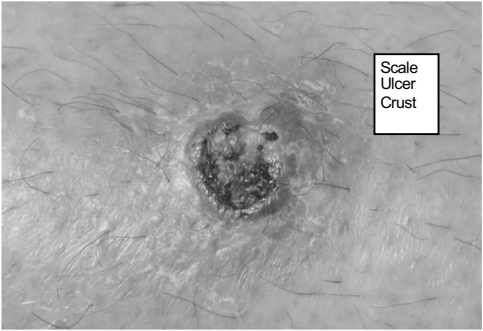
Squamous Cell Carcinoma




Scale



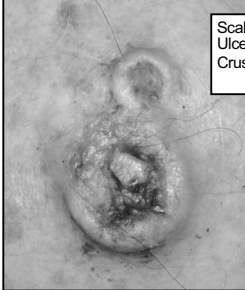
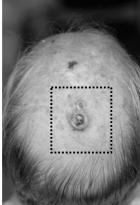
Squamous Cell Carcinoma




Scale
Ulcer
Crust

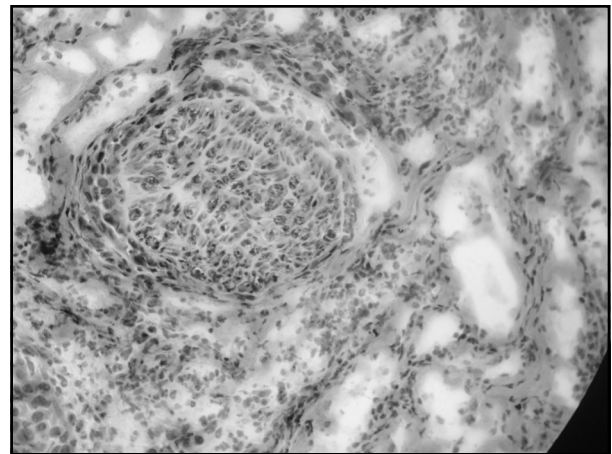
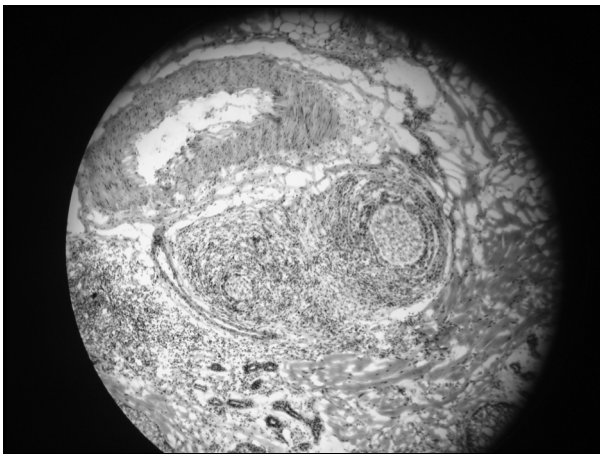
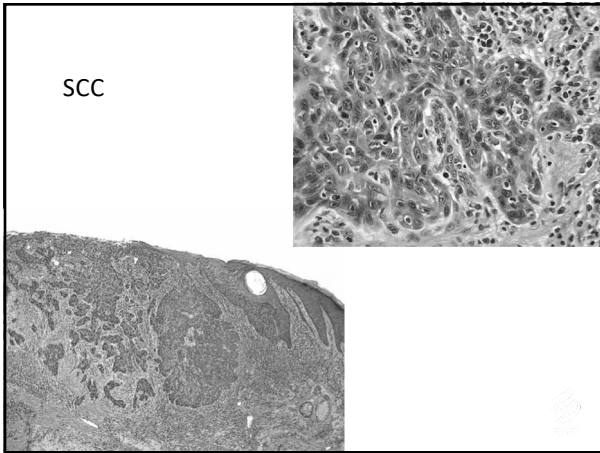
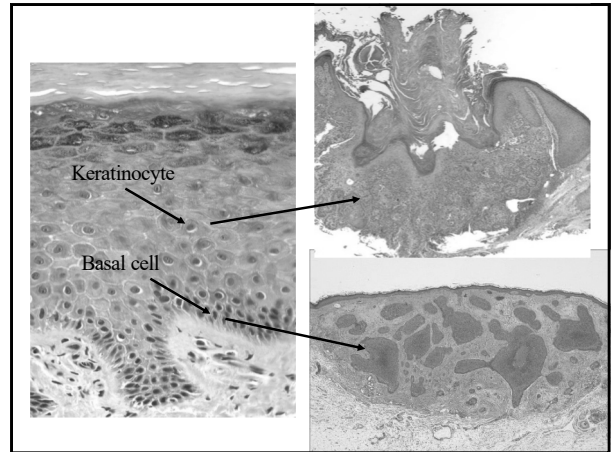
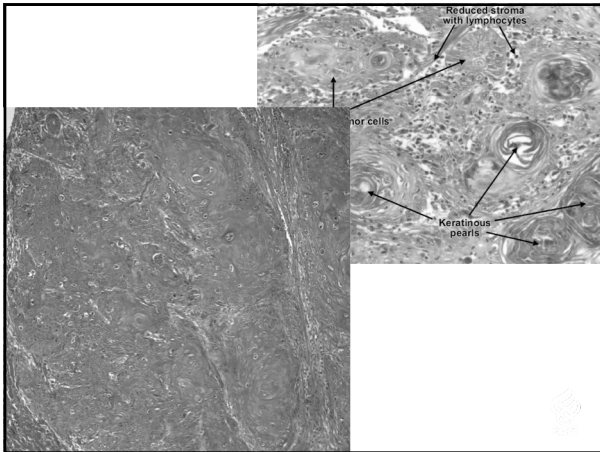


Squamous Cell Carcinoma



Scale
Ulcer
Crust







HIGH RISK CUTANEOUS SCC

Brigham and Women's Alternative T Staging for Cutaneous SCC

- T0 : Squamous cell carcinoma in-situ
- T1: 0 risk factors
- T2a: 1 risk factor
- T2b: 2-3 risk factors
- T3: 4 risk factors or invasion to bone

- Risk factors:
 1. Tumor \geq 2 cm in diameter
 2. Depth beyond subcutaneous fat
 3. Poorly differentiated histology
 4. Perineural invasion (PNI)

Stage T2b tumors accounted for 72% of nodal metastases and 83% of deaths from CSCC.

Jambusaria et al. JAMA Dermatol. 2013;149(4):402-410.



EVOLVING PARADIGM FOR HIGH-RISK SCC MANAGEMENT

- BWH T2b (19% of the cohort) had significantly higher incidences of all end points of interest (18% LR, 37% NM, 20% DSD, and 47% all cause death)
- Since stage T2b tumors are relatively uncommon but account for the bulk of poor CSCC outcomes, this group (in addition to the very rare stage T3 cases) may be the target of future studies of high-risk CSCC treatment.

Jambusaria et al. JAMA Dermatol. 2013;149(4):402-410.



STAGING IMAGING IN HIGH-RISK CUTANEOUS SCC

- Limited radiologic nodal staging data, explains variability
- Imaging utilized when clinically negative for palpable LAD
 - False negatives – imaging unable to detect micrometastases
 - False positives – result in additional unnecessary procedures
- CT, PET/CT, MRI, Ultrasound +/- guided FNA all have roles
- Optimal staging modality is open to further research
- Encouraging results from US and USgFNA
 - Main limitation of all forms of radiologic is imaging cannot detect lesions < 5 mm in size



ROLE OF SENTINEL LYMPH NODE BIOPSY IN HIGH-RISK cSCC

Table 4. SLN^b by T Stage in Patients With Nonanagenal cSCC In 2 Staging Systems

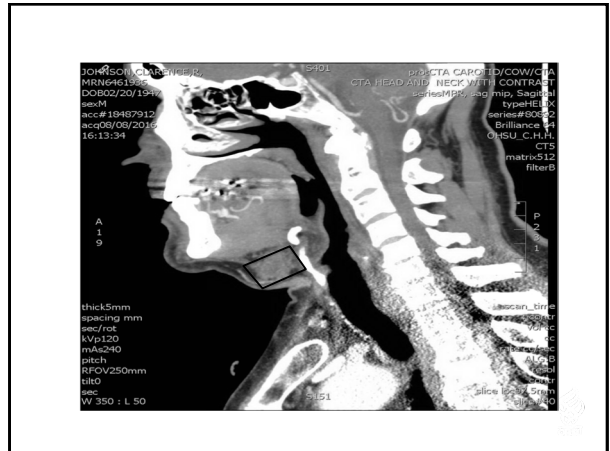
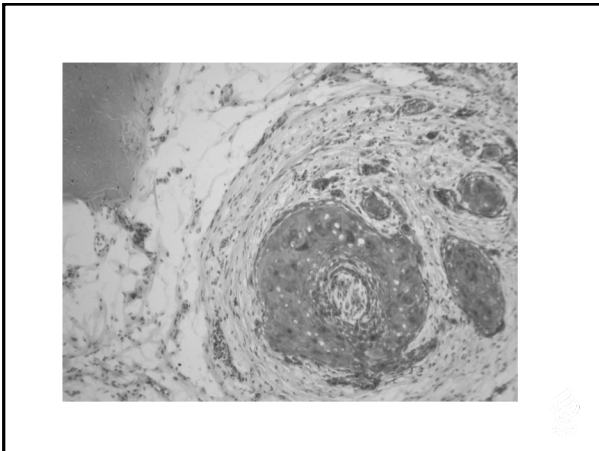
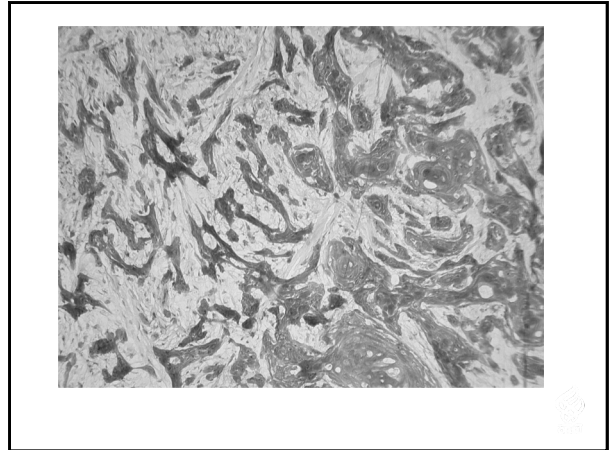
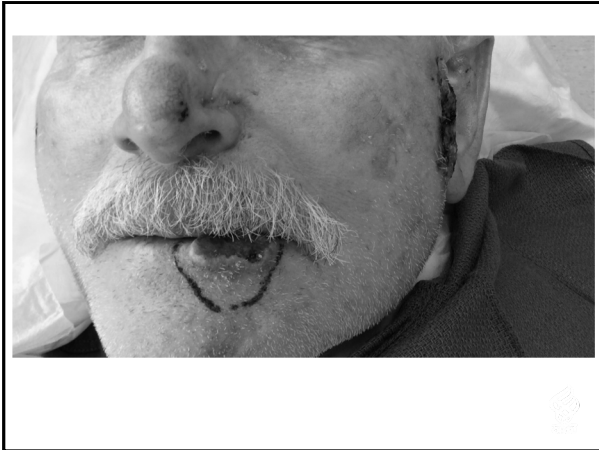
T Stage	No. of SLN ^b Tumors/Total No. of Tumors (%)
AJCC staging system ^a	
T1	0/9
T2	13/16 (81.2)
T3	0/0
T4	3/5 (60.0)
Alternative staging system ^a	
T0	Not included
T1	0/9
T2a	6/85 (7.1)
T2b	5/17 (29.4)
T3	3/6 (50.0)

Abbreviations: AJCC, American Joint Committee on Cancer; cSCC, cutaneous squamous cell carcinoma; SLN^b, positive sentinel lymph node.
^a Described in Table 1, adapted from the seventh edition of the AJCC staging manual.¹⁷
^b Described in Table 2, adapted from Jambusaria-Pahjani et al.¹⁸

- 12.3 % patients with 'high risk SCC' had microscopic nodal metastases
- If we follow the 10% threshold for SLNB findings applied to Melanoma, T2b tumors may warrant SLNB investigation

Schmitt, Brewer, Bordesaux, Baum JAMA Derm 2014 Jan;150(1):19-24



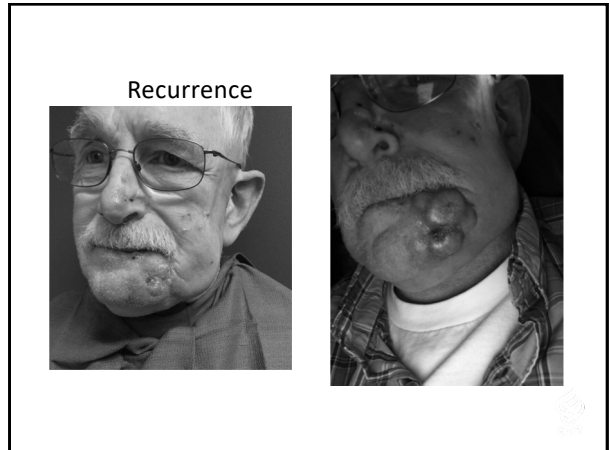


High Risk SCC

Referred to ENT for wide local excision of the SCC on left cheek with superficial parotidectomy and neck dissection. Facial plastics repaired the lip and cheek.

Biopsy of the neck mass revealed SCC.

Clear surgical margins not obtained, XRT postoperatively.





2 cycles of Pembrolizumab

Aggressive Skin Cancers Occurring in Patients Treated With the Janus Kinase Inhibitor Ruxolitinib

Adam B. Blechman MD,^a Christine E. Cabell MD,^b Christine H. Weinberger MD,^c Anna Duckworth MD,^d Justin J. Leitenberger MD,^e Fiona O. Zwald MD,^f and Mark A. Russell MD^g

J Drugs Dermatol. 2017 May 1;16(5):508-511.

Melanoma

Flat surface, irregular outline

Irregular color and surface

Melanoma arising from a nevus

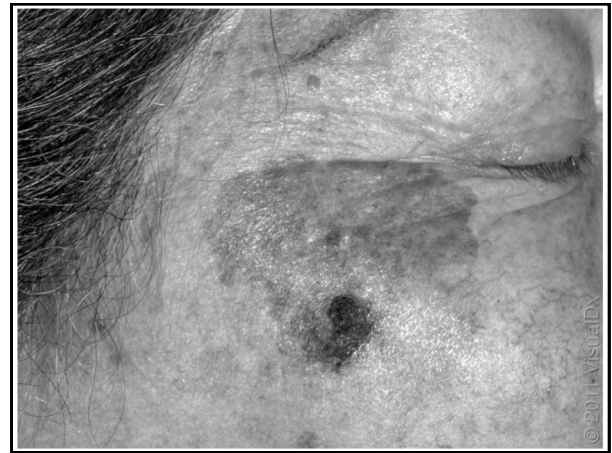
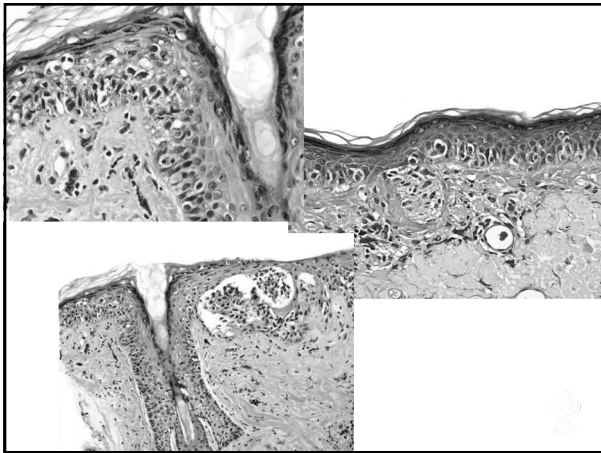
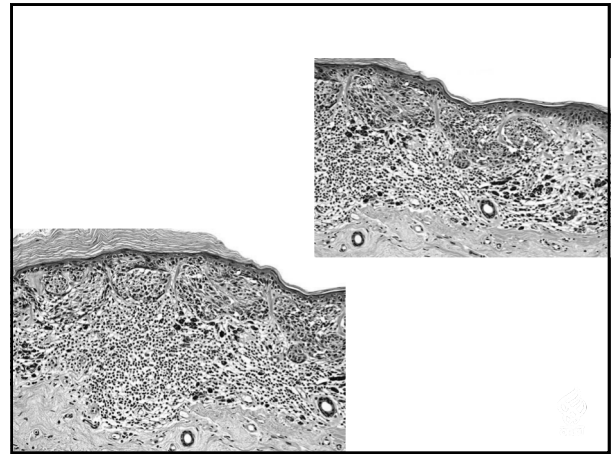
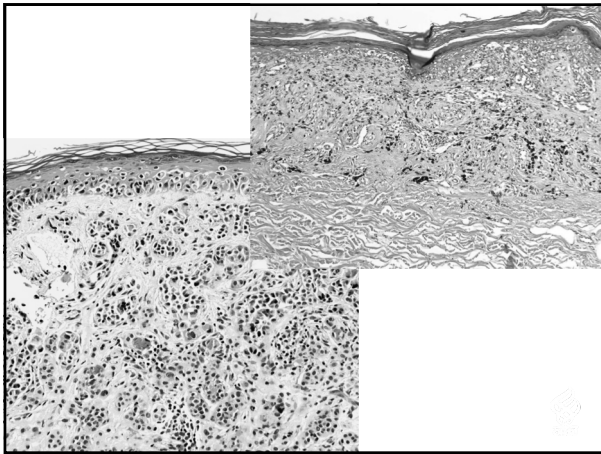
Irregular color and outline

20% of melanomas arise from preexisting mole

What to look for:
ABCDEs

- Asymmetry
- Borders
- Colors
- Diameter
- Evolving

JAMA 2004;292:2771-2776.





Background

- Historically wide local excision (WLE) has been the standard of care for treating melanoma
- Other treatment options: staged excisions and slow Mohs with rush permanent sections; time intensive and increased patient morbidity

Key points for treatment

Detect microscopic tumor that is not clinically evident

The greater the percentage of the margin that can be evaluated, the more reliable the interpretation of the margin status after excision

Microscopic examination is only reliable if tumor cells are identifiable

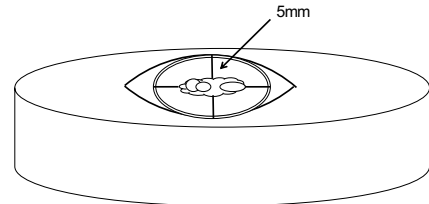
Mohs for melanoma

- Advantages include:
 - Ability to evaluate 100% of the surgical specimen margins
 - Lentigo maligna and lentigo maligna melanoma often have subclinical spread that can be missed with traditional bread loaf sectioning of formalin fixed paraffin embedded tissue (FFPE)
 - Breadloaf sections of excised melanoma in situ (MIS) specimens at 4 mm intervals have only a 19% chance of detecting a positive margin²
 - Tissue sparing in areas of high anatomic sensitivity and functionality (ie: free margins such as the eyelid and alar rim, hands/fingers)
 - Closure can happen same or following day

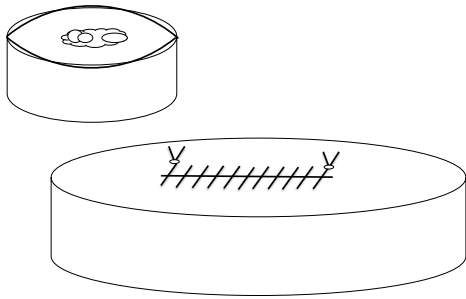
Disadvantages of WLE

- 1 out of 4 conventional wide local excisions of head and neck melanomas has positive microscopic margins³ (ie: occult in situ tumor present)
- Recurrence rates for melanoma in situ on the head and neck with wide local excision range from 8-20%³

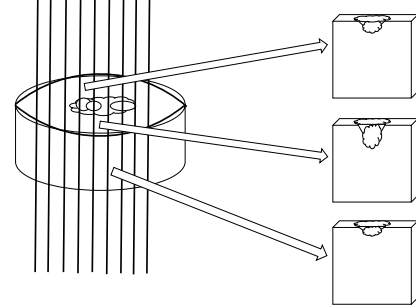
Wide Local Excision



Wide Local Excision



Wide Local Excision



Modified Mohs Surgery

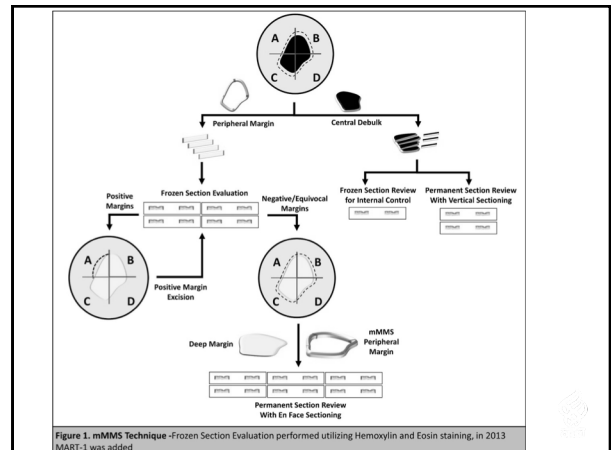
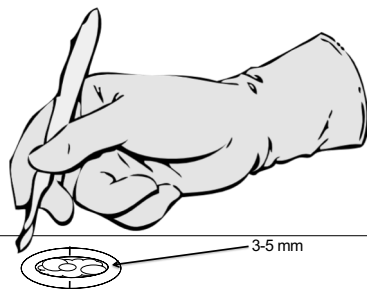
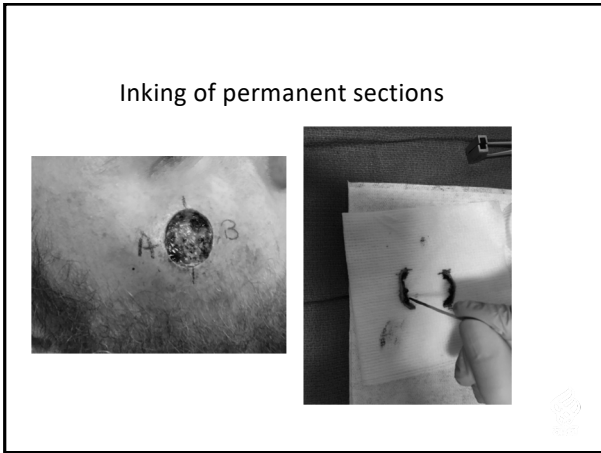
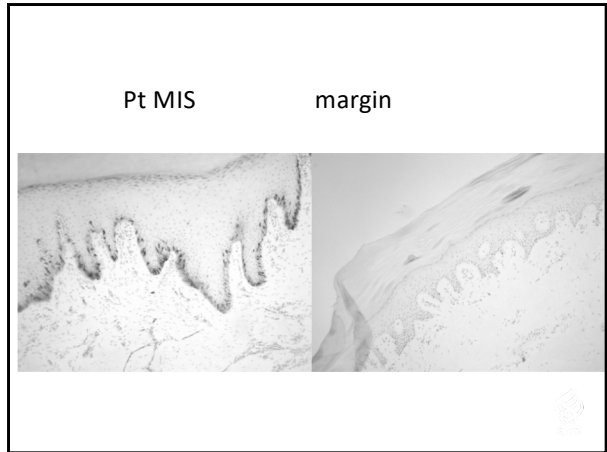
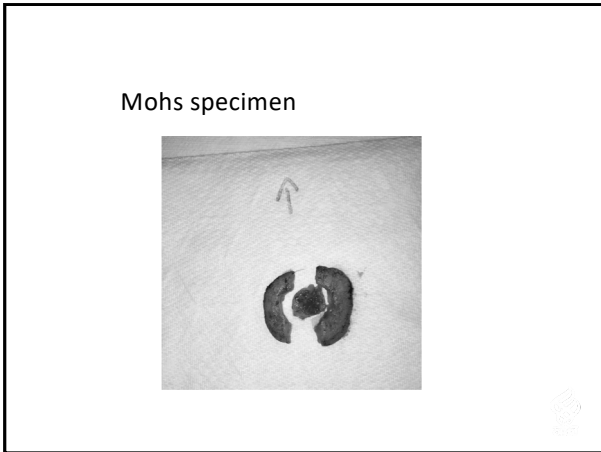
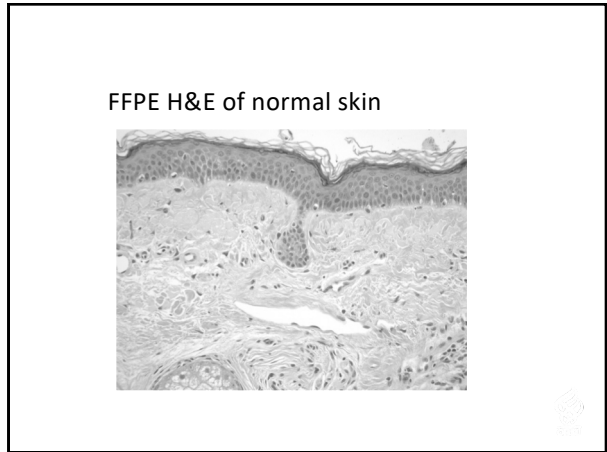
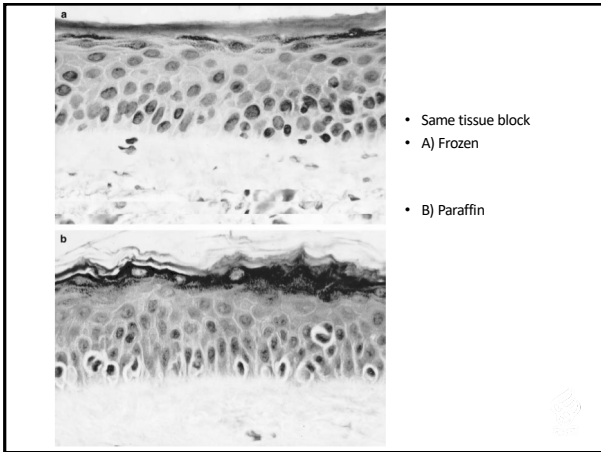


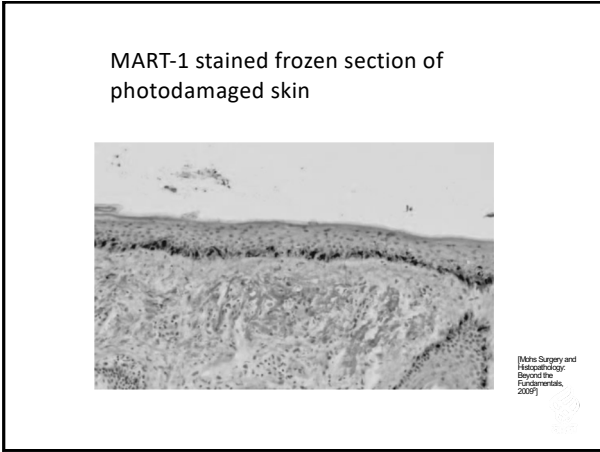
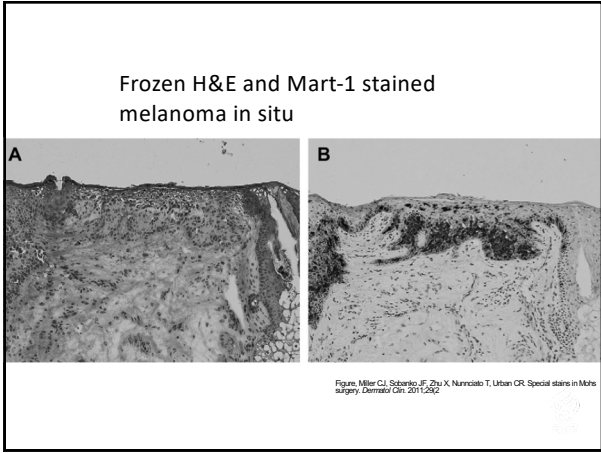
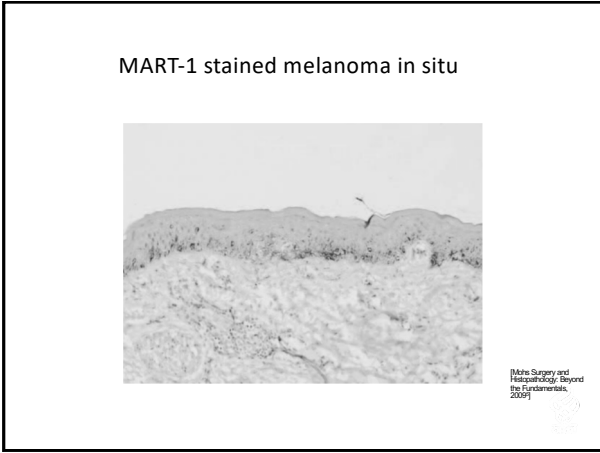
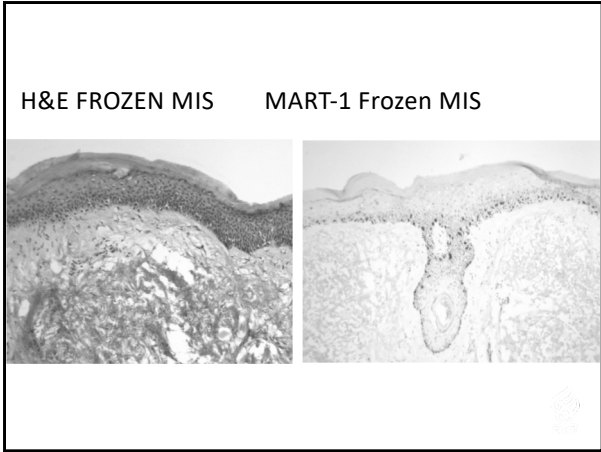
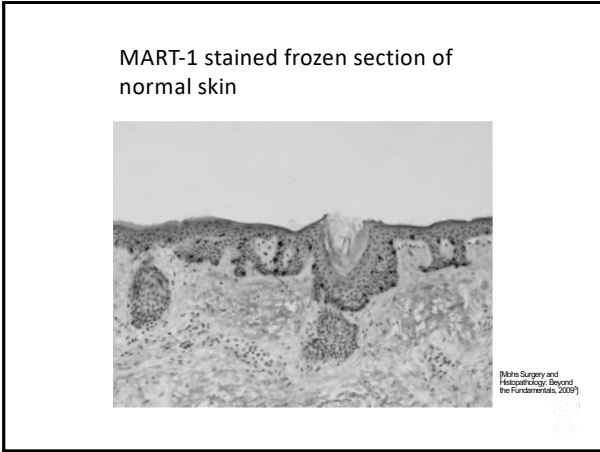
Figure 1. mMMS Technique -Frozen Section Evaluation performed utilizing Hemoxilyn and Eosin staining, in 2013 MART-1 was added



Outcomes of Mohs Micrographic Surgery using MART-1

- Nazario et al(2016)²: retrospective review of 2,114 patients
 - 0.5% recurrence rate for primary MIS (4/863) treated with MMS
 - 1.3% recurrence rate for primary invasive melanoma (7/556) treated with MMS
 - 9-20% recurrence rate for primary MIS in control group treated with WLE
 - 2.8-7.5% recurrence rate for primary invasive melanoma treated with WLE
- Miller et al(2015)⁴: retrospective review of 577 patients
 - 0.34% recurrence rate for melanoma in situ only (2/597) treated with MMS



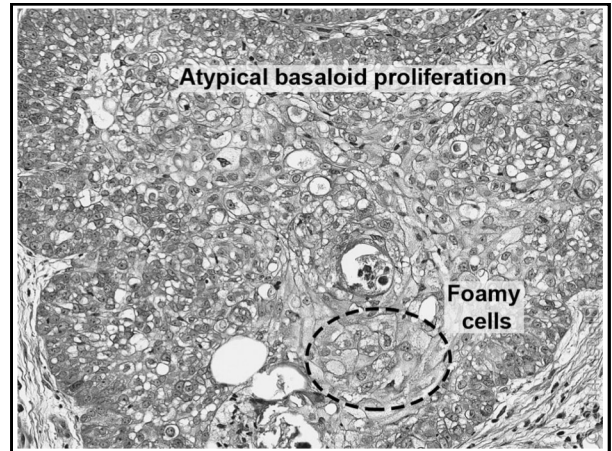
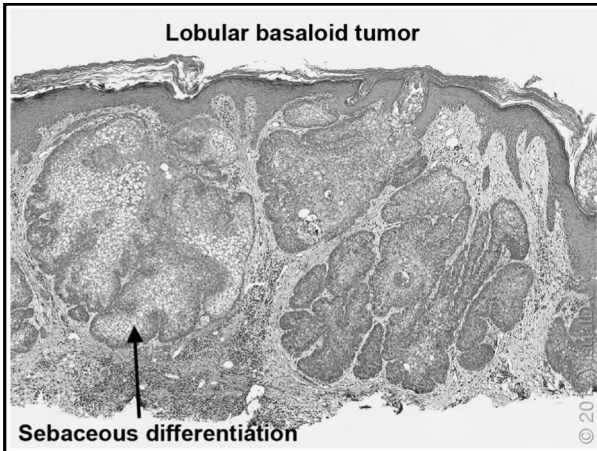
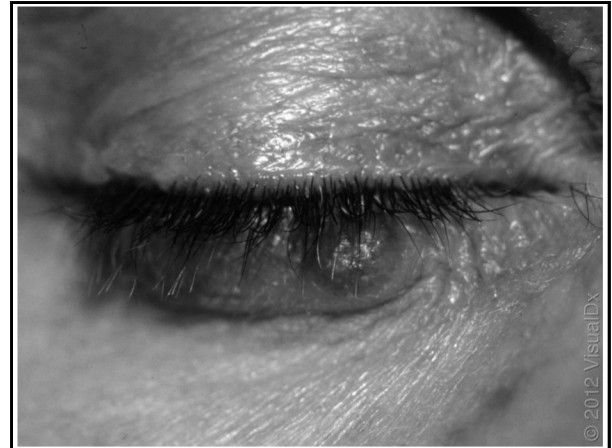


Mohs and Melanoma

- Traditional Mohs
- Mohs with immunostaining
- Mohs with additional permanent sections
- Best suited for Melanoma in situ on the Head & Neck (severely sun-damaged skin)

Sebaceous Carcinoma

- 1-2 : 100,000 incidence
- Common on the head and neck/eyelid skin, but may arise anywhere
- Elderly
- Caucasian predominance
- Asian/Pacific Islanders (periocular)



Sebaceous Carcinoma

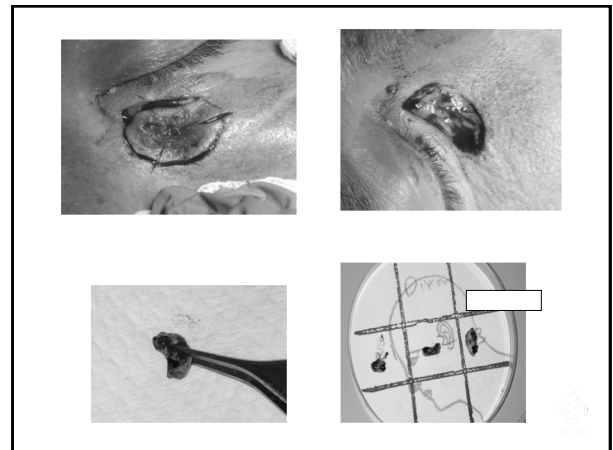
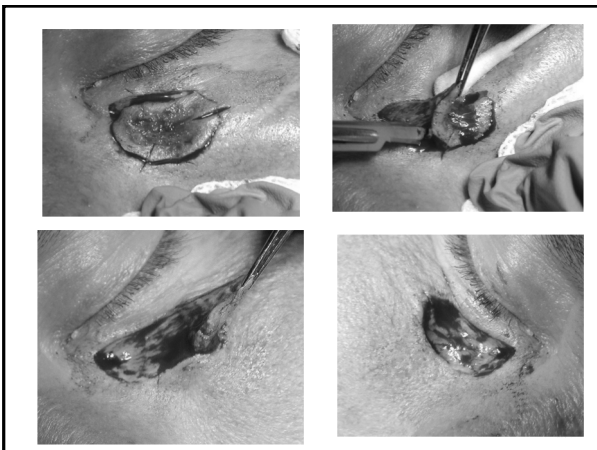
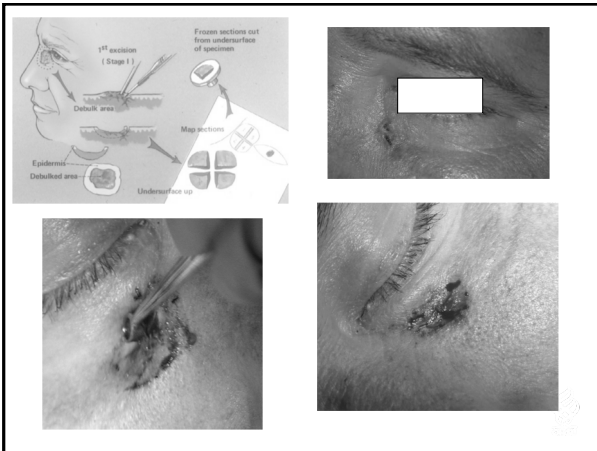
- A deep biopsy is required to accurately diagnose sebaceous carcinoma. Special tissue stains can differentiate sebaceous carcinoma from similar appearing cancers.
- Sebaceous carcinoma is best treated by surgery that analyzes the surrounding and deep edges of the tissue removed -- Mohs micrographic surgery or "complete circumferential peripheral and deep margin assessment". Conjunctival mapping biopsies may assist in surgical planning when the tumor is present on the eyelid.
- Radiation is considered for nerve involvement or treatment of lymph node spread. It does not replace surgery, except in surgery ineligible or in palliative cases.
- Patients should be seen by a physician familiar with sebaceous carcinoma every 6-12 months for the first 5 years after treatment.
- The treatment of metastatic sebaceous carcinoma is poorly understood.

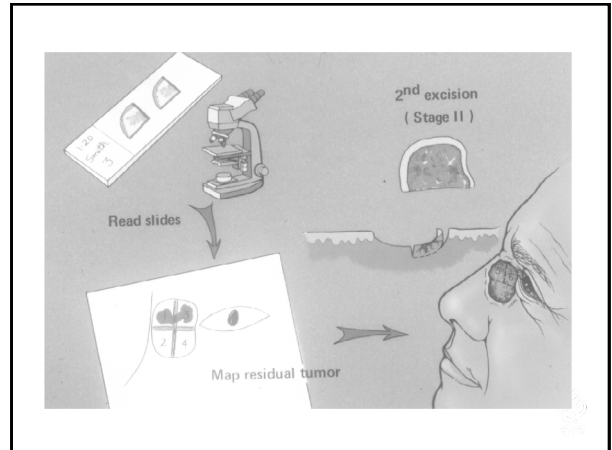
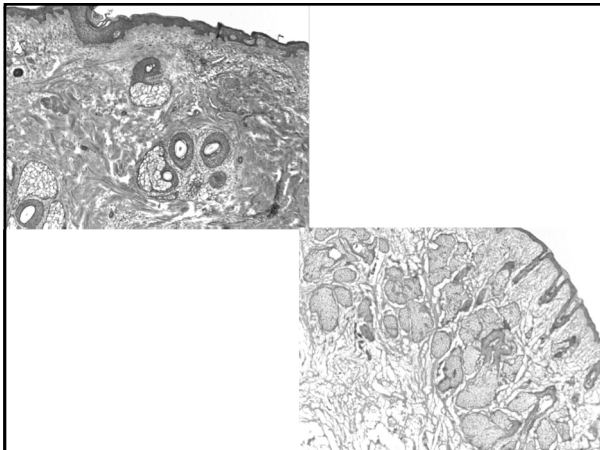
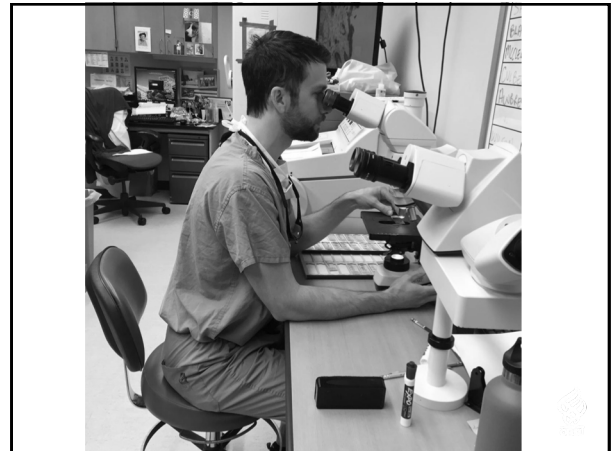
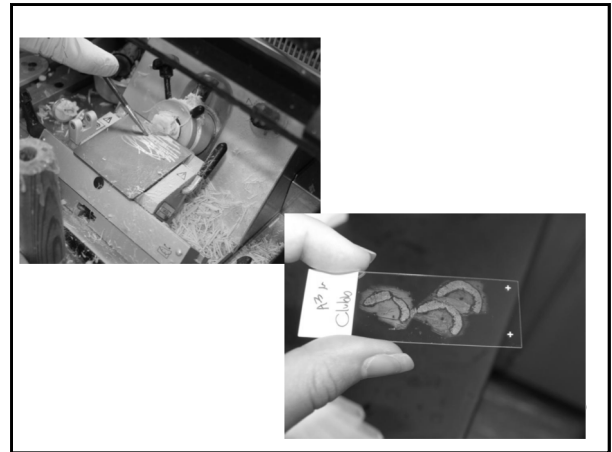
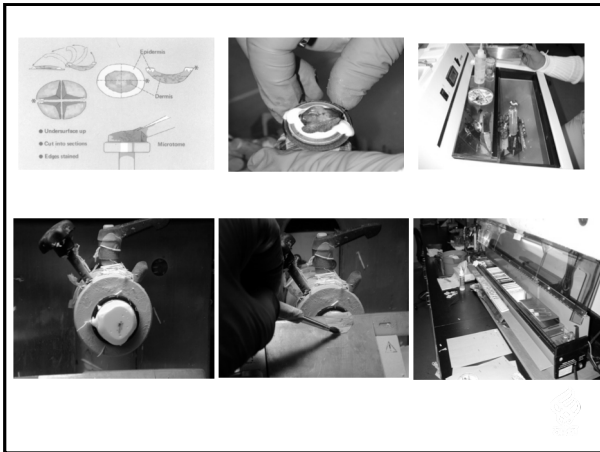
Mohs Micrographic Surgery

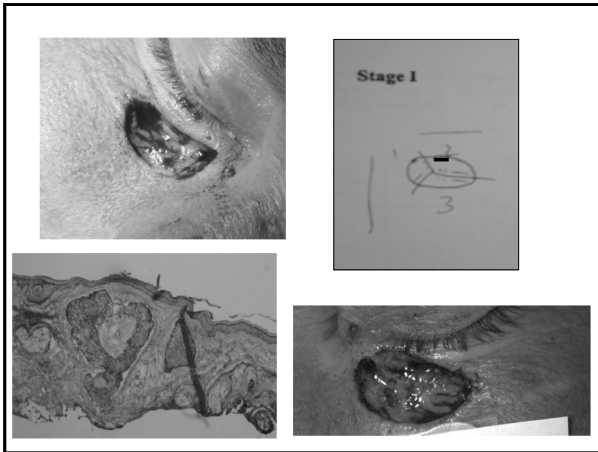
- Skin cancer surgery
- Dr. Fredrick E. Mohs
- "Micro" - microscopic examination
- "graphic" - tissue orientation is mapped

Mohs Micrographic Surgery

- Tangential Excision
- Tissue specimen mapped
- Frozen section
- 100% of tumor margin examined
- Surgeon is the pathologist







Checking Surgical Margins

Top View

Medial Lateral

Side View
(section on slide)

Epidermis
Medial Margin
Deep Margin
Lateral Margin

Top View
(sections on slide)

1 2
3 4

Side View

Epidermis
Medial Margin
Deep Margin
Lateral Margin

Traditional Vertical Sections

Mohs Horizontal Sections

Adapted from Rapini, JAAD

Mohs Surgery Advantages

- All of peripheral & deep margin examined
 - Less than 1% examined in standard vertical sections

Standard "breadloafing" of tissue is only small sample

Mohs Surgery Advantages

- Rapid frozen section evaluation
- Tissue conservation
- Highest cure rate
- Low recurrence rate
- Low complications

Indication for Mohs Surgery

- Large Size
- Location
- Recurrent Cancers
- Aggressive Histology
- Poorly Defined Borders

Mohs H Zone

Five year Recurrence Rate for BCC
Retrospective study – Literature review since 1945

Method of treatment	Primary	Recurrent
Cryotherapy	7.5%	13% (< 5 yrs)
C & E	7.7%	40%
Excision	10.1%	17.4%
Radiation	8.7%	9.8%
All non-Mohs modalities	8.7%	19.9%
Mohs surgery	1%	5.6%

Adapted from Rowe et al., J Dermatol Surg Oncol 1989

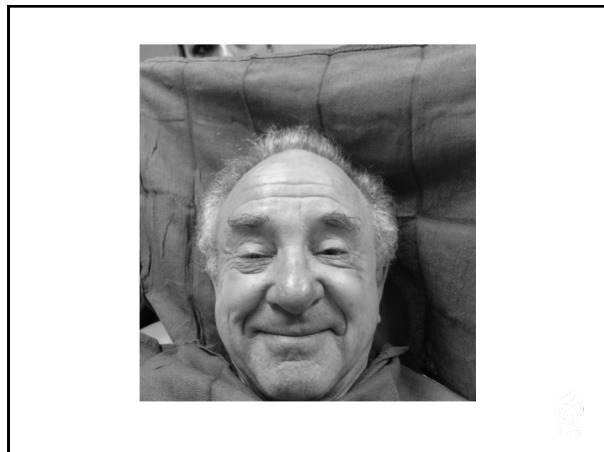
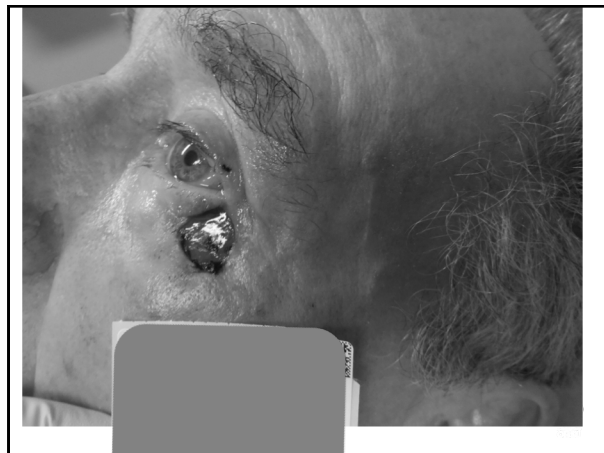
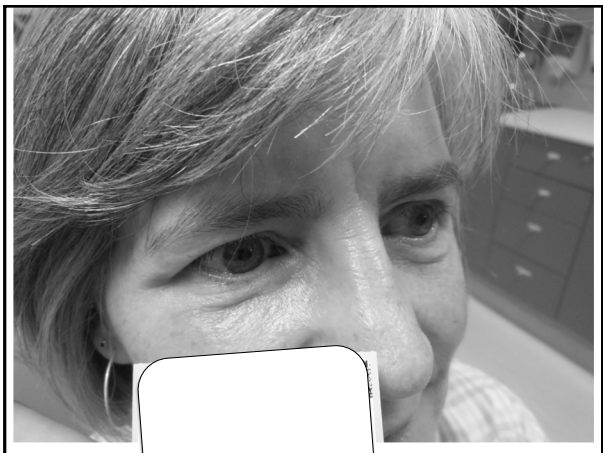
Mohs Micrographic Surgery

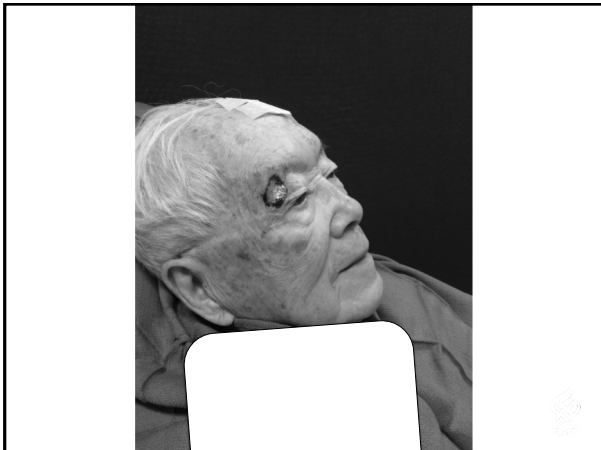
- Other Cutaneous Tumors
 - Dermatofibrosarcoma protuberans (DFSP)
 - Atypical fibroxanthoma (AFX)
 - Sebaceous carcinoma
 - Merkel cell carcinoma
 - Microcystic adnexal carcinoma
 - Verrucous carcinoma
 - Angiosarcoma

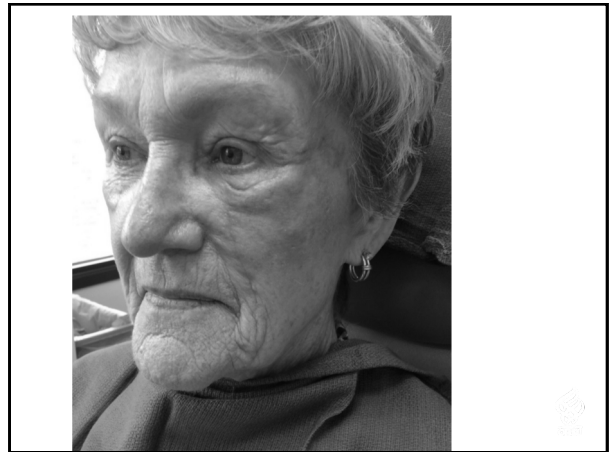
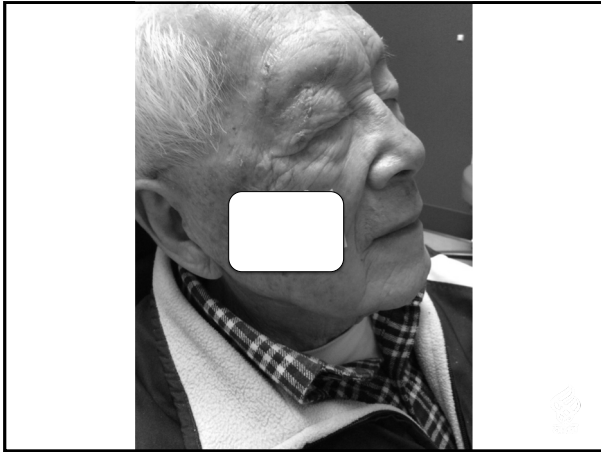
Cases

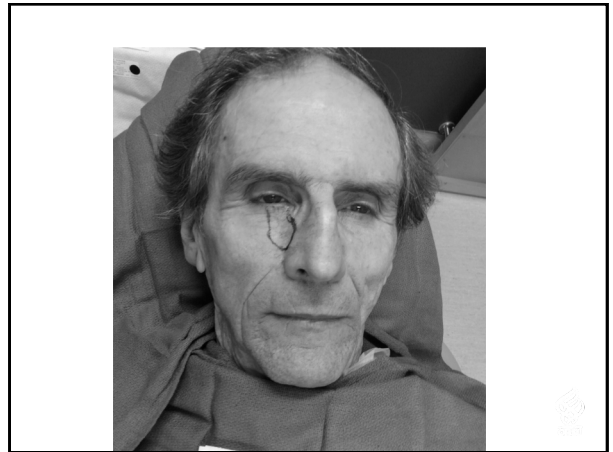
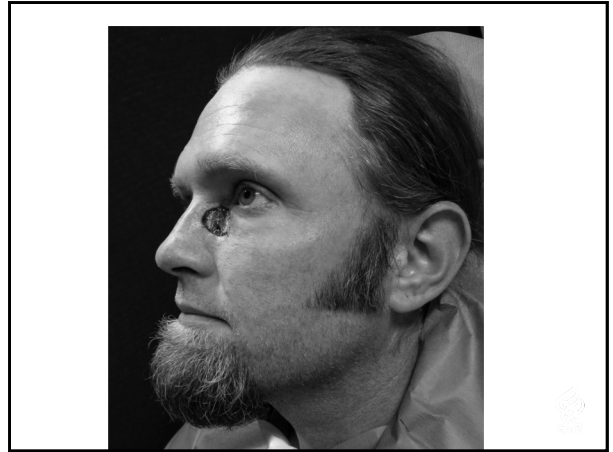
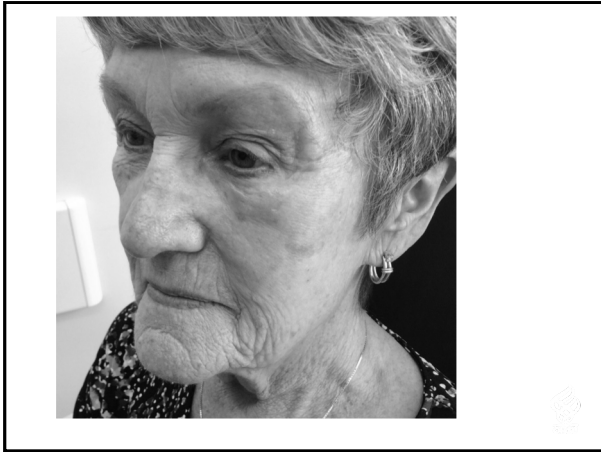


- After repair and some of











What is the moral of the story?

Protect your skin from the sun!!!

