Updates In Orbital and Ocular Adnexal Oncology

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Practice Locations

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Get Directions

Appointment Information

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Medical Specialties

- Ophthalmology
- Surgery

Clinical Focus

- Oculoplastics

Board Certifications

- American Board of Ophthalmology - Ophthalmology

Special Training

- 2016 - Orbital Oncology and Oculoplastic Surgery Fellowship
  Fellowship - Univ. of Texas MD Anderson Cancer Center
- 2014 - Ophthalmic Pathology
  Fellowship - University of Wisconsin
- 2013 - Ophthalmology
  Residency - University of Arkansas for Medical Sciences
- 2010 - Internship
  Other Special Training - University of Arkansas

Education

- 2009 - University of Arkansas College of Medicine - MD

Topics for Discussion

- Oncology in ophthalmology
- The growing use of immunomodulators for cancer treatment
  - Orbital inflammation
  - Trichomegaly
  - Secondary malignancies
- Non-surgical management of complex basal cell carcinoma
- Acceptance and adoption of the AJCC staging system for ocular adnexal tumors
- Considerations for complex surgical reconstruction

Oncology in Ophthalmology

Or vice versa

Oncology in Ophthalmology

- Obviously, there is the unique, yet small, niche of ophthalmologists known as ophthalmic oncologists
  - Uveal melanoma, retinoblastoma, and mostly other retinal/choroidal tumors
- But what about the rest of us?

How Ophthalmology Has Played a Role

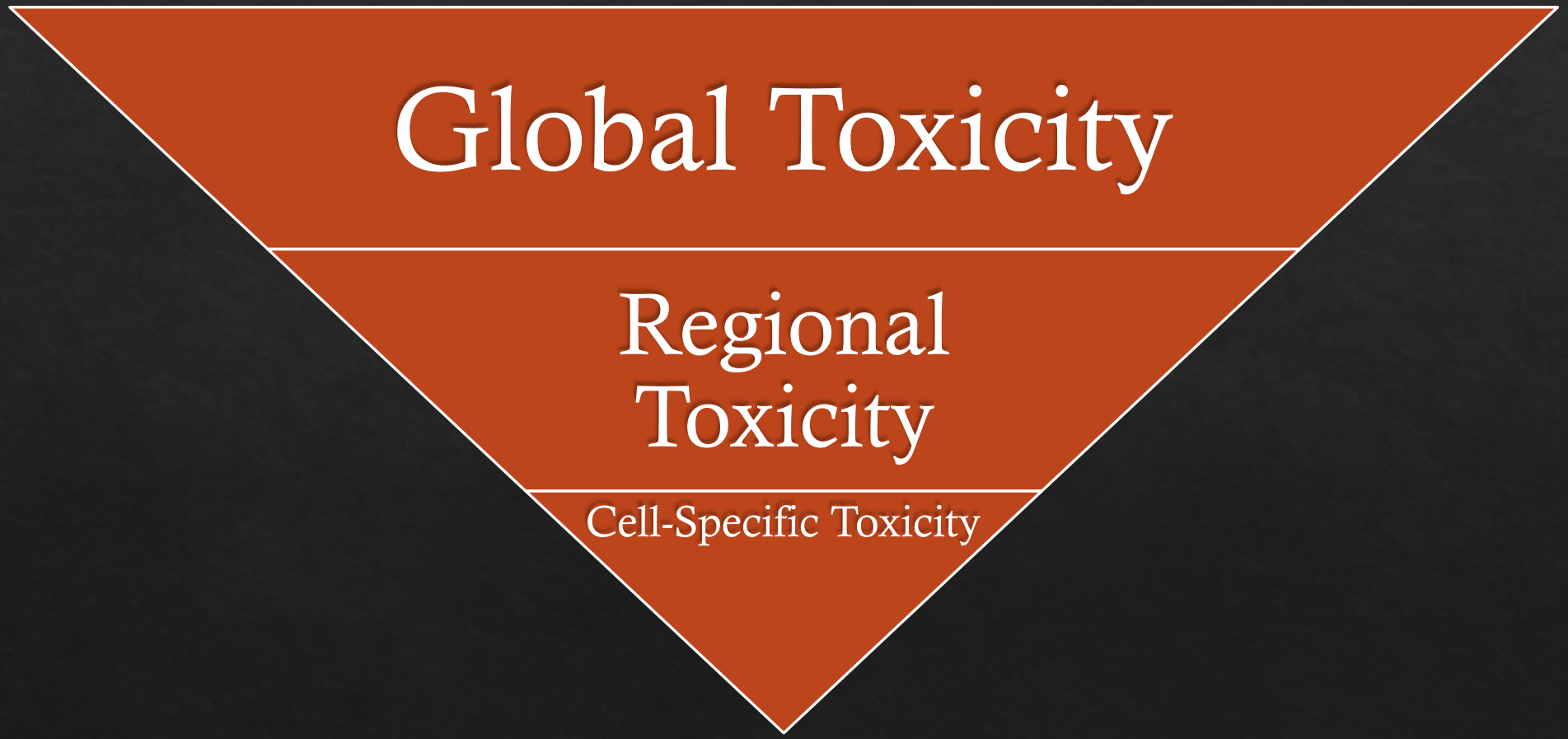
- Management of ocular/orbital metastases
- Management of ophthalmic disease as a result of systemic side effects
  - i.e. hemorrhagic disease in the setting of thrombocytopenia, infection, etc.
- Management of local ocular/orbital side effects

How Ophthalmology Has Played a Role

- Blurry Vision - Platins
- Epiphora – Platins, doxorubicin
- Dacryostenosis – 5-FU, docetaxel, mitomycin-C, RAI
- Conjunctivitis – Ifosfamide, rituximab
- Keratitis – Chlorambucil
- Cataract – Tamoxifen, steroids
- Retinopathy – Carmustine
- Macular Edema – Methotrexate, steroids, MEK inhibitors
- Papilledema/Optic Neuritis/Neuropathy – Platins, vincristine, steroids

How can the ophthalmic effects be minimized?

The Overarching Goal



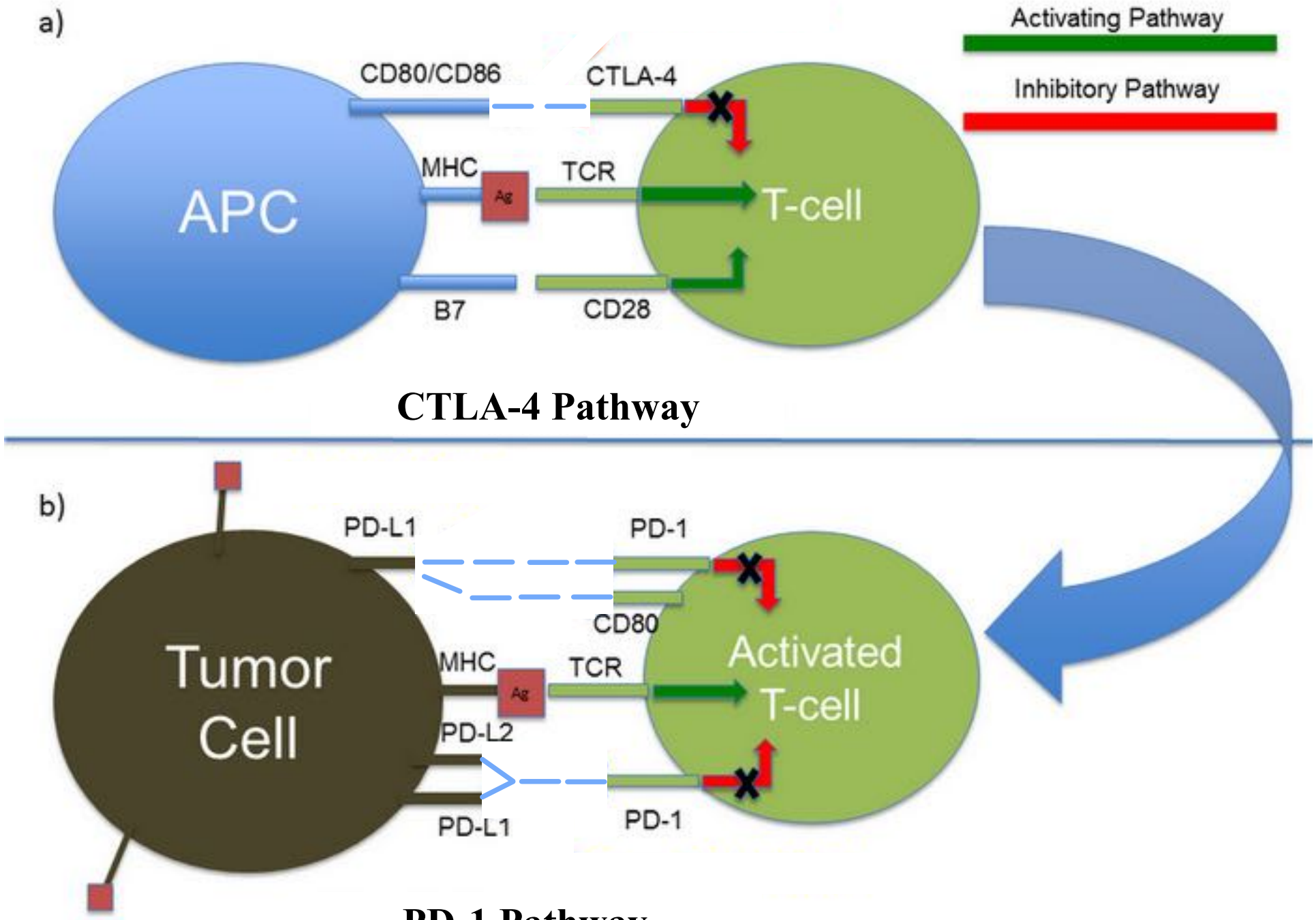
Maximal Toxicity

Minimal/No Toxicity

Making the target even smaller. . .

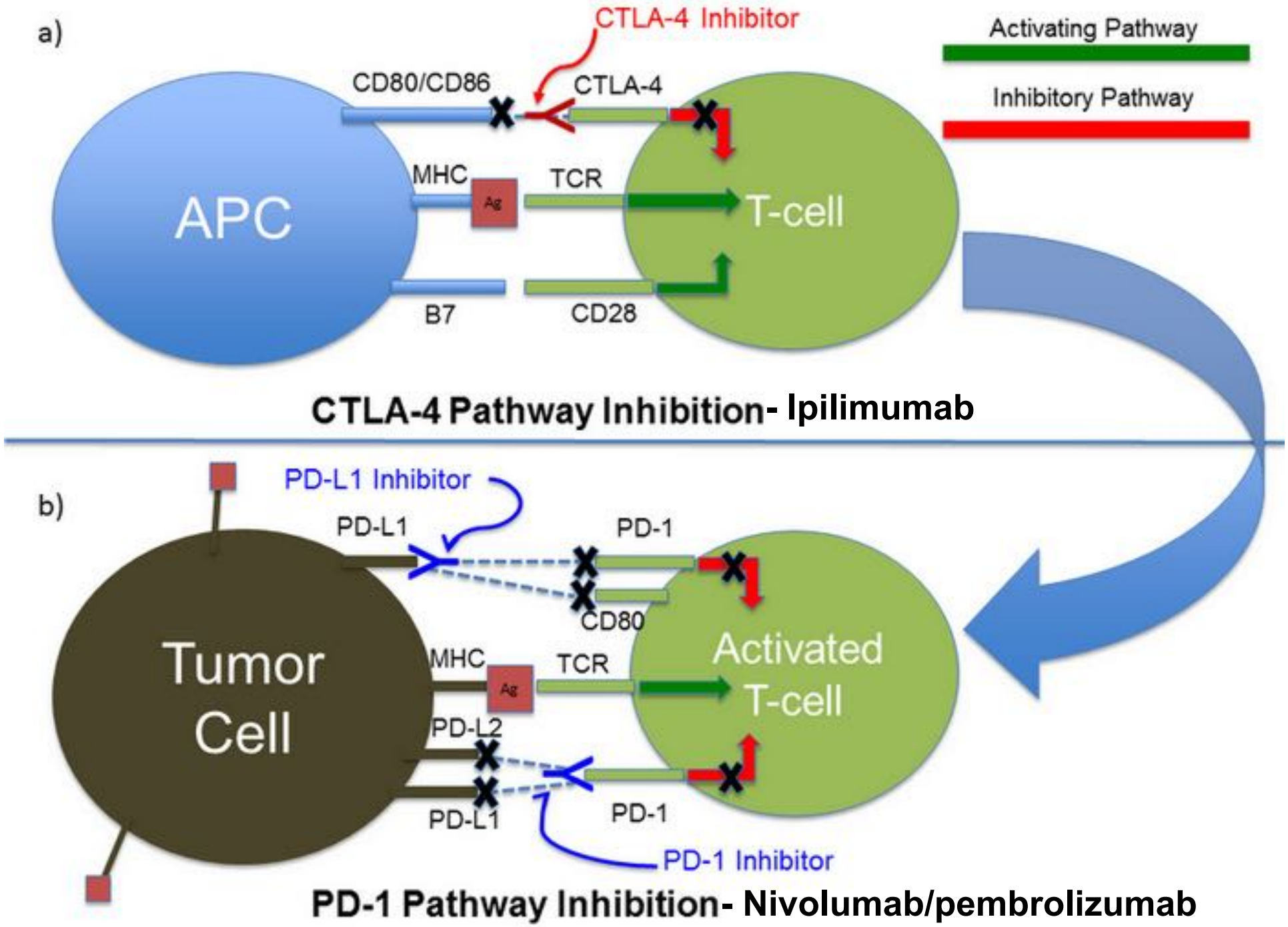
Immune Checkpoint Inhibitors

- Disrupt the normal inhibitory signals in immune system regulation
- Results in an expanded population of active T-cells with increased anti-tumor activity
- Have been particularly useful in the treatment of metastatic melanoma, but have also been used in renal cell carcinoma, bladder carcinoma, colorectal cancer, lung cancer, head and neck cancer, etc.



CTLA-4 Pathway

PD-1 Pathway

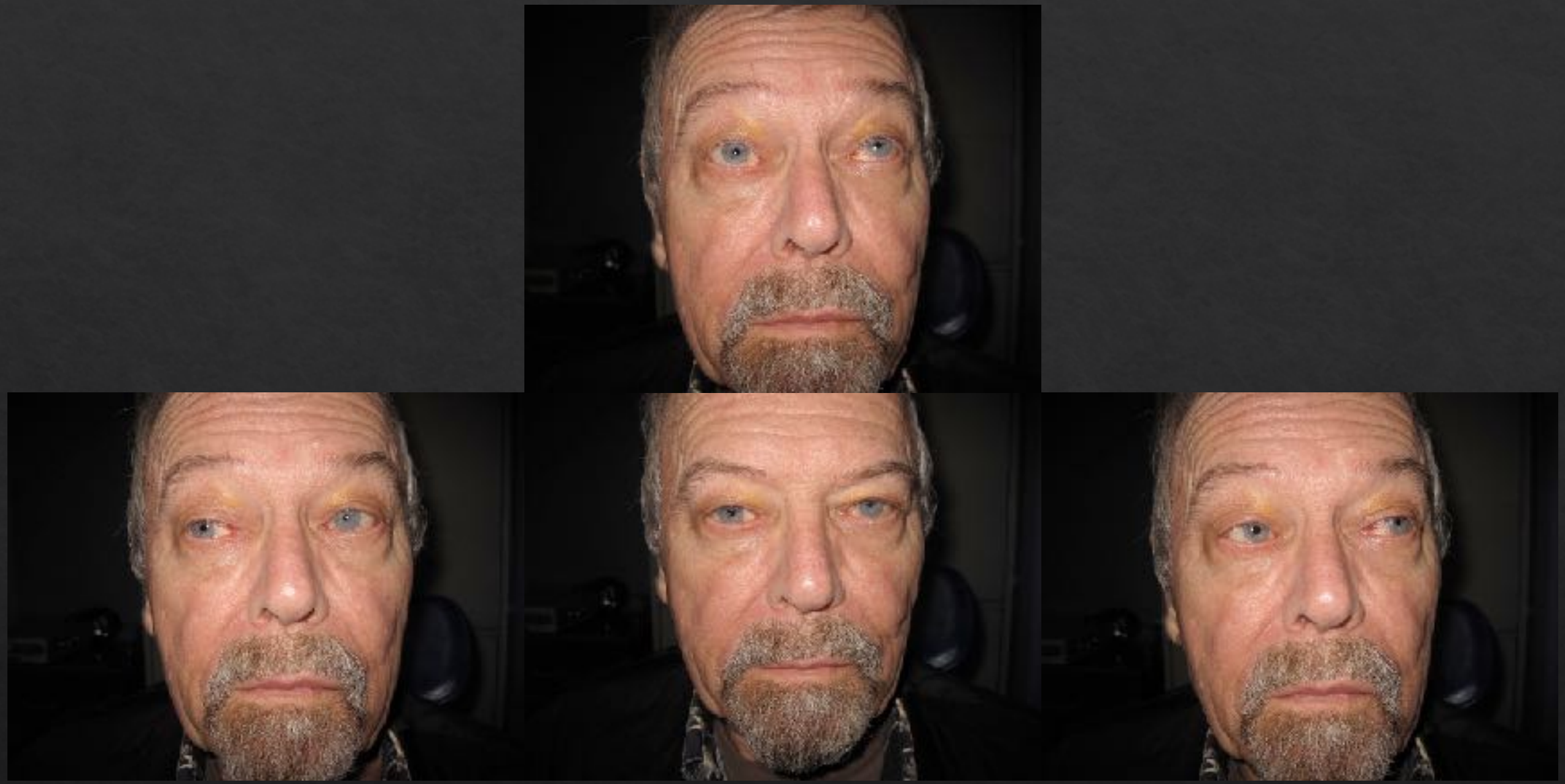

a)
CTLA-4 Inhibitor
Activating Pathway
Inhibitory Pathway
CD80/CD86
CTLA-4
APC
MHC
Ag
TCR
T-cell
B7
CD28
CTLA-4 Pathway Inhibition- Ipilimumab
b)
PD-L1 Inhibitor
PD-L1
PD-1
CD80
Tumor Cell
MHC
Ag
TCR
Activated T-cell
PD-L2
PD-L1
PD-1
PD-1 Inhibitor
PD-1 Pathway Inhibition- Nivolumab/pembrolizumab

Immune Checkpoint Inhibitors

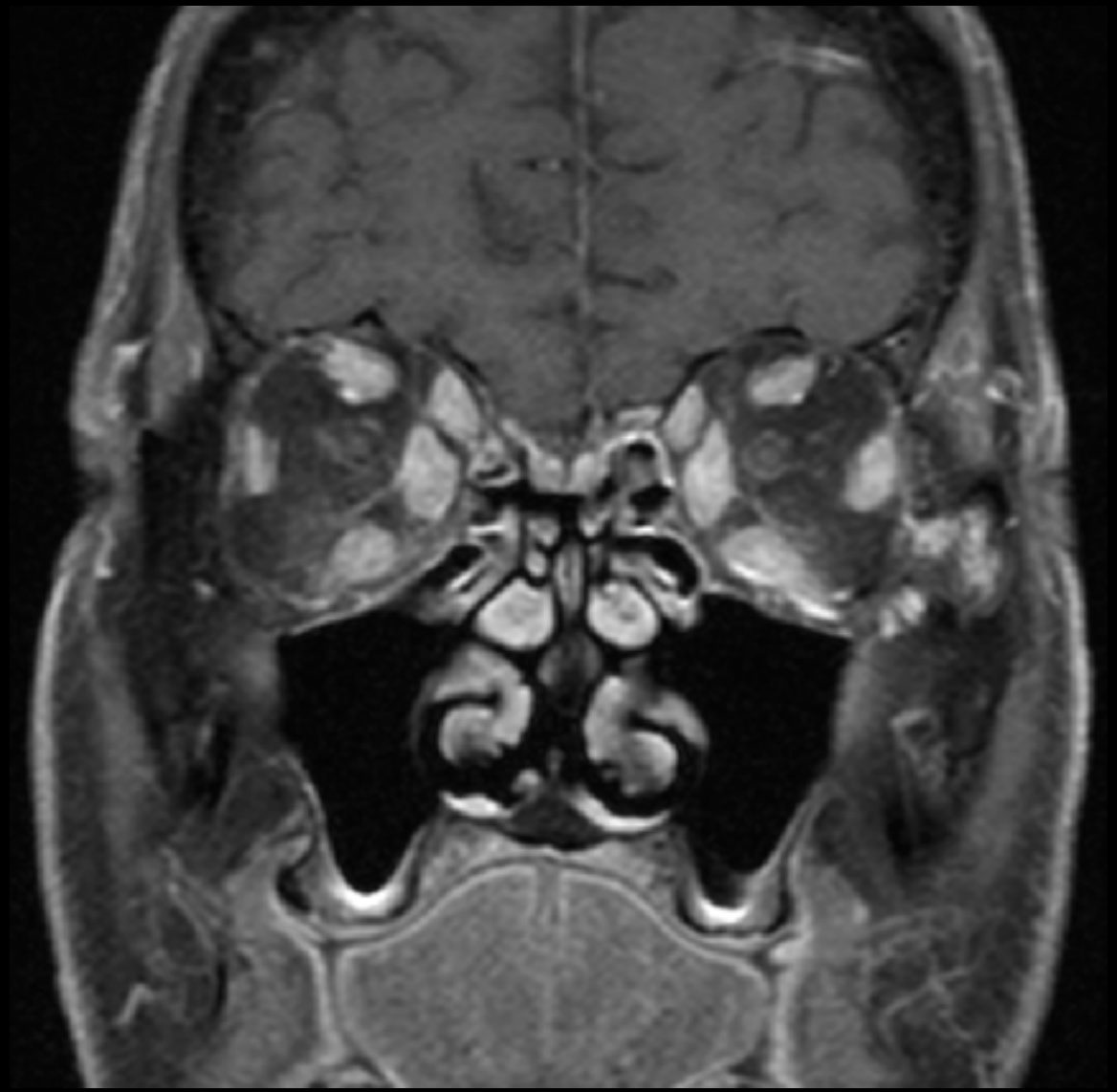
- Result in a spectrum of immune-related adverse events (irAEs)
- Can affect any T-cell-infiltrated organ system
  - Dermatitis
  - Hepatitis
  - Pneumonitis
  - Uveitis
  - Diffuse lymphadenitis

Immune Checkpoint Inhibitors

- Fortunately, most of these side effects can be effectively managed with corticosteroids, or additional agents as necessary
- The use of steroids does not appear to significantly affect the response durability or patient survival



Photos courtesy of Bita Esmaeli, MD



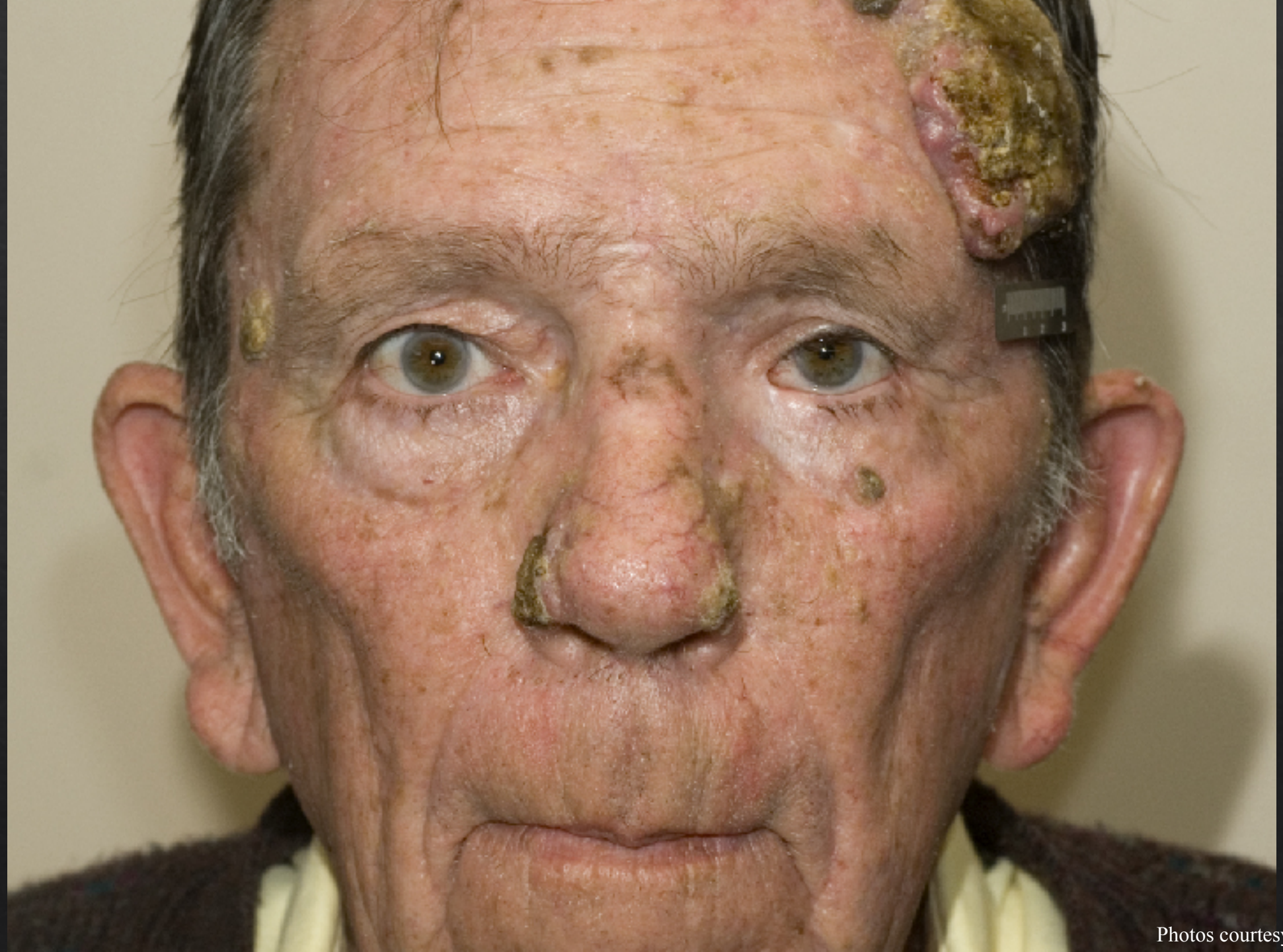
Patient Course

- This patient remarkably improved after a course of IV steroids using the EUGOGO protocol
- Unfortunately, he passed away from progressive metastatic disease since he elected to not resume treatment with ipilimumab/nivolumab

Trichomegaly

- Epidermal growth factor receptor inhibitors
  - Cetuximab, panitumumab
- Tyrosine kinase inhibitors
  - Gefitinib, erlotinib
- Used for many solid tumor diseases
- May be part of the PRIDE syndrome (papulopustules and/or paronychia, regulatory abnormalities of hair growth, itching, and dryness due to EGFR inhibitors) – an indicator of treatment response

Skin Cancer as a Result of Immunosuppression



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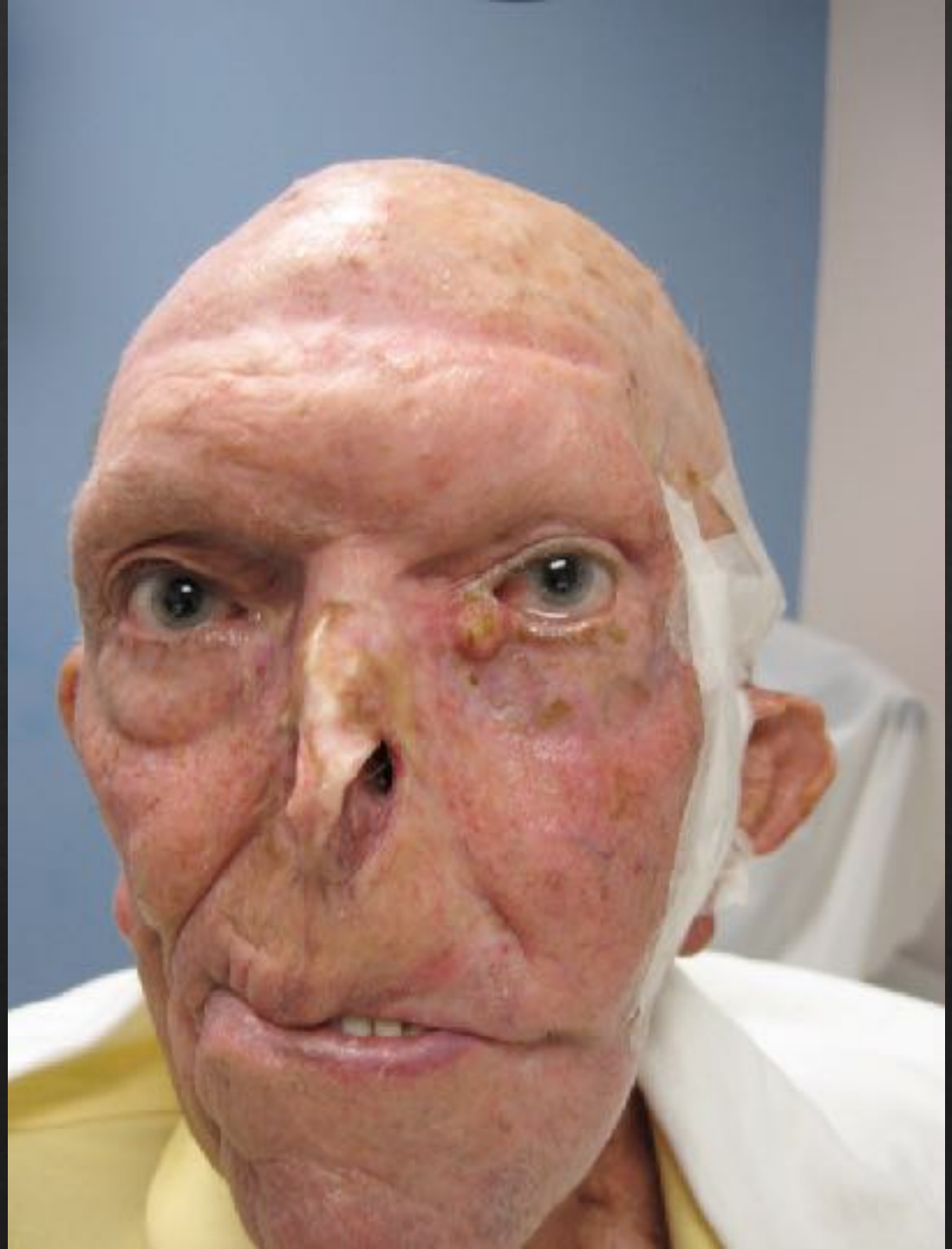
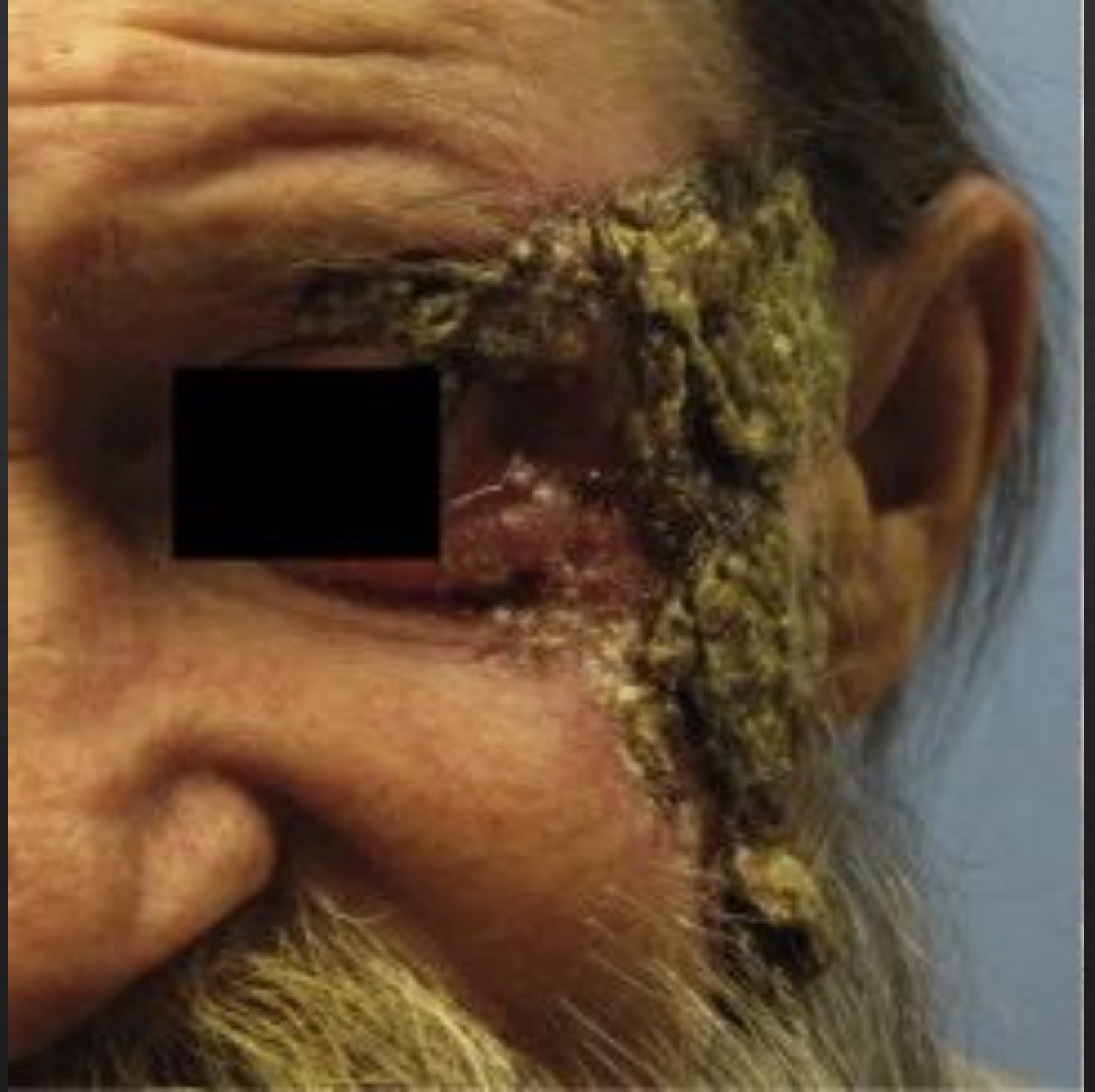


Photos courtesy of Bita Esmaeli, MD

Basal Cell Carcinoma

- Suppose this patient came into your office. . .



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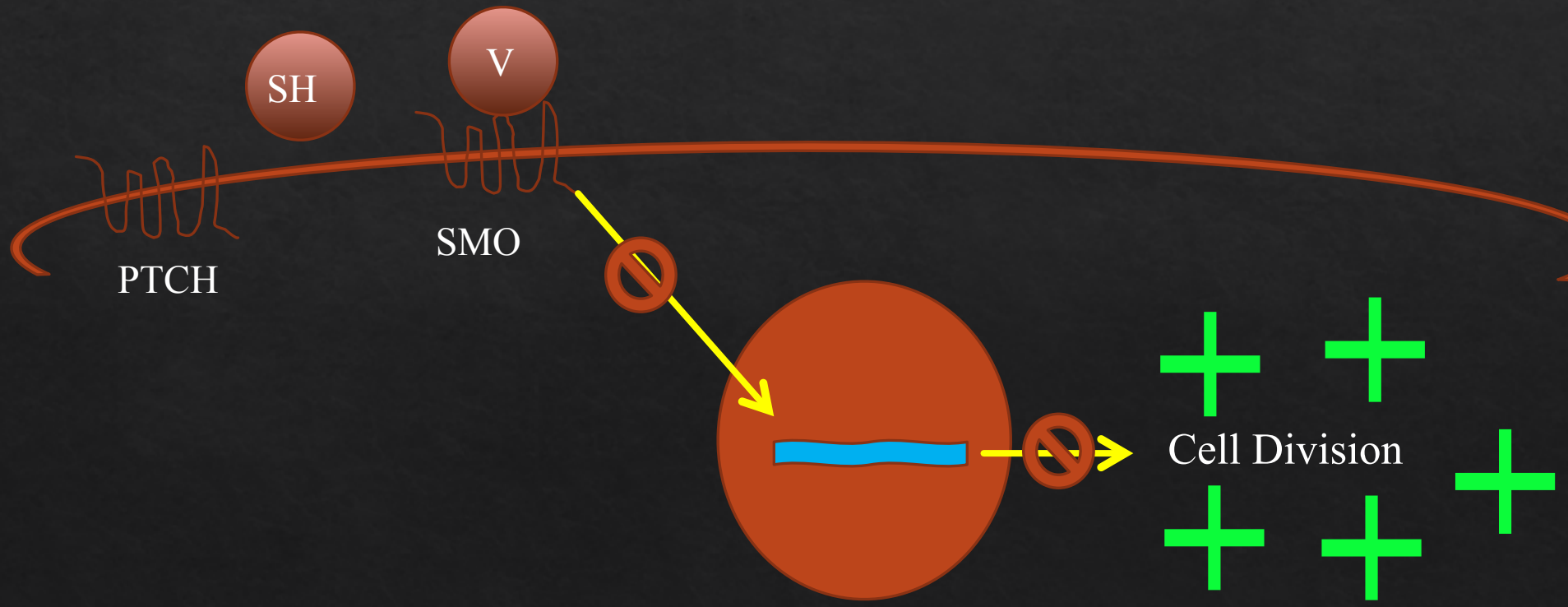
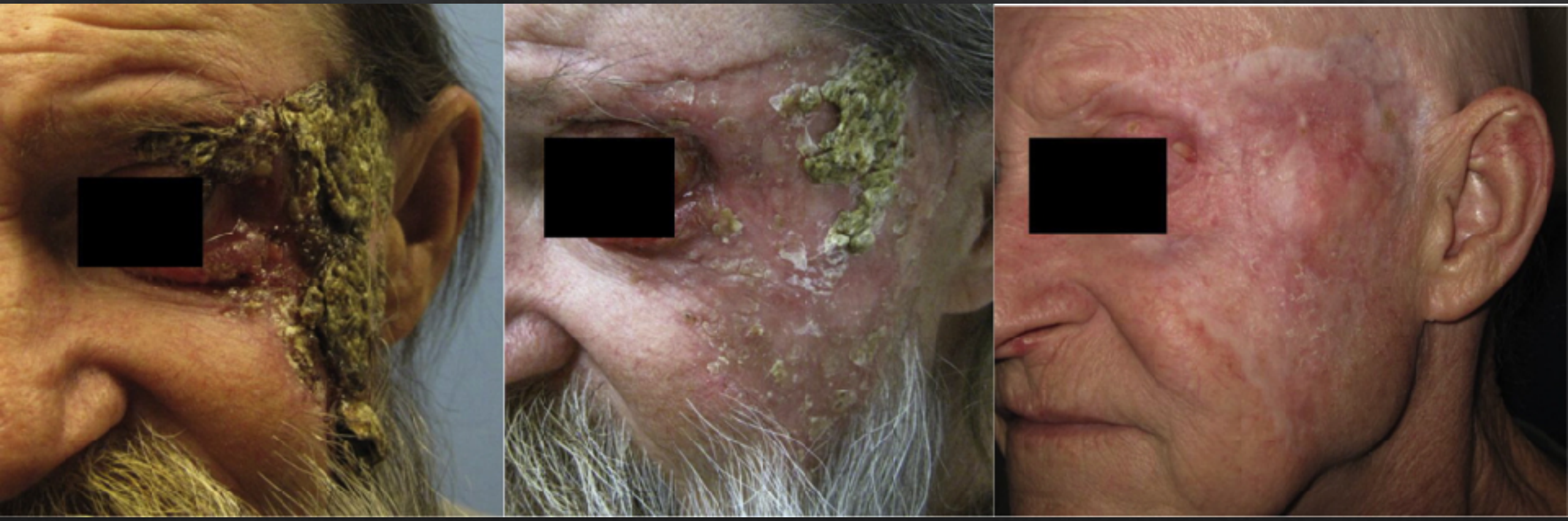
When Surgery for BCC is Not Optimal

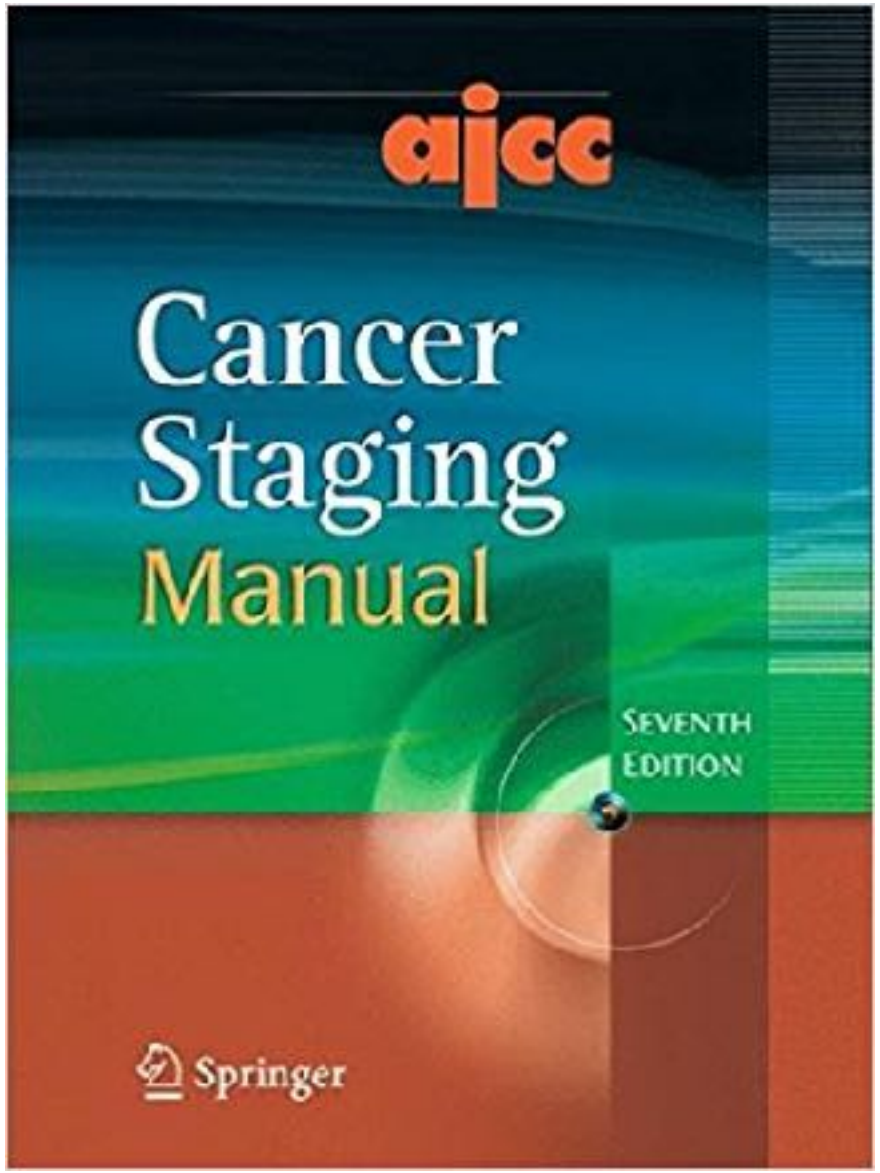
- Sonic hedgehog pathway

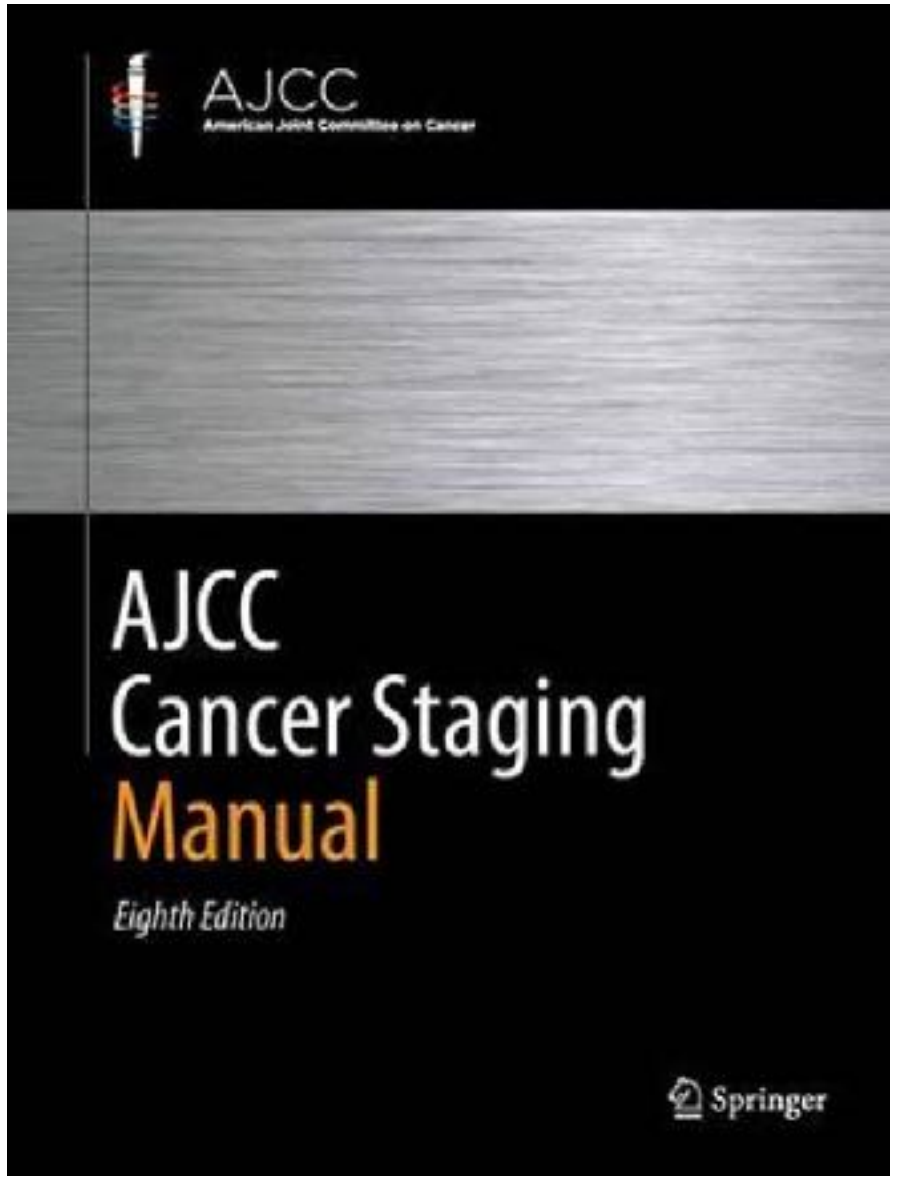




Photos courtesy of Bita Esmaeli, MD

Adoption of AJCC for Use in Ophthalmology


ajcc
Cancer
Staging
Manual
Seventh
Edition
Springer


AJCC
American Joint Committee on Cancer
AJCC
Cancer Staging
Manual
Eighth Edition
Springer

AJCC CANCER STAGING 7TH EDITION
FOR ORBITAL AND OCULAR ADNEXAL TUMORS

DOB: PATIENT INFO HERE/other data
Date of Diagnosis:
□ right □ left □ bilateral / □ recurrent

Histology –

Other orbital tumors –

Other interesting oncologic conditions –

CARCINOMA LACRIMAL GLAND

□ TX - Primary tumor cannot be assessed
□ T0 - No evidence of primary tumor
□ T1 - Tumor ≤ 2 cm in greatest dimension, w/o or w/o extraglandular extension into orbital soft tissue
□ T2 - Tumor > 2 cm but not > 4 cm in greatest dimension*
□ T3 - Tumor > 4 cm in greatest dimension
→T4 - Tumor invades periosteum or orbital bones or adjacent structures
□ T4a - Tumor invades periosteum
□ T4b - Tumor invades orbital bone
□ T4c - Tumor invades adjacent structures (brain, sinus, pterygoid, base temporal tissue)

*As the maximum size of the lacrimal gland is 3cm, T2 and greater tumors will usually extend into the orbital soft tissue

□ NX – regional lymph nodes cannot be assessed
□ N0 – no regional lymph node metastasis
□ N1 - Regional lymph node metastasis

□ M0 – no distant metastasis
□ M1 – distant metastasis

ORBITAL SARCOMA

□ TX - Primary tumor cannot be assessed
□ T0 - No evidence of primary tumor
□ T1 - Tumor ≤ 15 mm in greatest dimension
□ T2 - Tumor >15 mm in greatest dimension w/o invasion of globe or bony wall
□ T3 - Tumor of any size w/ invasion of orbital tissues and/or bony walls
□ T4 - Tumor invasion of globe or paraorbital structures, such as eyelids, temporal fossa, nasal cavity, and paranasal sinuses, and/or central nervous system

□ NX – regional lymph nodes cannot be assessed
□ N0 – no regional lymph node metastasis
□ N1 - Regional lymph node metastasis
□ M0 – no distant metastasis
□ M1 – distant metastasis

OCULAR ADNEXAL LYMPHOMA

□ Lower Eyelid □ Upper Eyelid □ Periorbital
□ Bulbar Conjunctiva □ Non Bulbar Conjunctiva
□ Orbit □ Lacrimal Gland

□ TX - Lymphoma extent not specified
□ T0 - No evidence of lymphoma
→T1 - Lymphoma involving the conjunctiva alone w/o orbital involvement
□ T1a - Bulbar conjunctivae only
□ T1b - Palpebral conjunctiva ± fornix ± caruncle
□ T1c - Extensive conjunctival involvement
→T2 - Lymphoma with orbital involvement ± any conjunctival involvement
□ T2a - Anterior orbital involvement (± conjunctival involvement)
□ T2b - Anterior orbital involvement (± conjunctival + lacrimal involvement)
□ T2c - Posterior orbital involvement (± conjunctival involvement ± anterior involvement ± any extraocular muscle involvement)
□ T2d - Nasolacrimal drainage system involvement (± conjunctival involvement but not including nasopharynx)
□ T3 - Lymphoma with pre-septal eyelid involvement (defined above) ± orbital involvement ± conjunctival involvement
→T4 - Orbital adnexal lymphoma extending beyond orbit to adjacent structures such as bone and brain
□ T4a - Involvement of nasopharynx
□ T4b - Osseous involvement (including periosteum)
□ T4c - Involvement of mucoliobacial, ethmoidal and/or frontal sinuses
□ T4d - Intracranial spread

□ NX – regional lymph nodes cannot be assessed
□ N0 – no regional lymph node metastasis
□ N1 – involvement of ipsilateral regional lymph nodes
□ N2 – involvement of contralateral or bilateral regional lymph nodes
□ N3 – involvement peripheral lymph nodes not draining ocular adnexal region
□ N4 – involvement of central lymph nodes

*the regional lymph nodes excluded preauricular (parotid), submandibular, and cervical

□ M0 – no evidence of involvement of other extranodal sites
□ M1a – noncontiguous involvement of tissues or organs external to the ocular adnexa
□ M1b – lymphomatous involvement of the bone marrow
□ M1c – both M1a and M1b involvement

CARCINOMA OF CONJUNCTIVA

□ Bulbar Conjunctiva □ Non Bulbar Conjunctiva

□ TX – Primary tumor cannot be assessed
□ T0 – No evidence of primary tumor
□ Tis – Carcinoma in situ
□ T1 – Tumor ≤ 5mm in greatest dimension
□ T2 – Tumor > 5 mm in greatest dimension, w/o invasion of adjacent structures
□ T3 – Tumor invades adjacent structures (excluding orbit)
→T4 – Tumor invades the orbit w/ or w/o further extension
□ T4a – Tumor invades orbital soft tissues, w/o bone invasion
□ T4b – Tumor invades bone
□ T4c – Tumor invades adjacent paranasal sinuses
□ T4d – Tumor invades brain

□ NX – regional lymph nodes cannot be assessed
□ N0 – no regional lymph node metastasis
□ N1 – Regional lymph node metastasis

□ M0 – no distant metastasis
□ M1 – distant metastasis

CARCINOMA OF EYELID

□ Lower Eyelid □ Upper Eyelid □ Eyebrow
□ Medial Canthus □ Lateral Canthus

□ TX - Primary tumor cannot be assessed
□ T0 - No evidence of primary tumor
□ Tis – Carcinoma in situ
□ T1 – Tumor ≤ 5 mm in greatest dimension, not invading the tarsal plate or eyelid margin
□ T2a - Tumor > 5 mm, but not > 10 mm in greatest dimension, or any tumor that invades tarsal plate or eyelid margin
□ T2b - Tumor > 10 mm, but not > 20 mm in greatest dimension or involves full thickness of eyelid.
□ T3a - Tumor > 20 mm in greatest dimension or any tumor that invades adjacent ocular or orbital structures. Any tumor with perineural invasion
□ T3b - Tumor complete resection requires exenteration, eyeball resection or bone resection.
□ T4 - Tumor not resectable due to extensive invasion of ocular, orbital, craniofacial structures or brain.

□ NX – regional lymph nodes cannot be assessed
□ N0 (-) – no regional lymph node metastasis, based upon clinical evaluation or imaging
□ N0 (+) – no regional lymph node metastasis, based upon lymph node biopsy
□ N1 - Regional lymph node metastasis

□ M0 – no distant metastasis
□ M1 – distant metastasis

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FOR ORBITAL AND OCULAR ADNEXAL TUMORS

DOB: PATIENT INFO HERE/other data
Date of Diagnosis:
□ right □ left □ bilateral / □ recurrent

MERKEL CELL CARCINOMA

□ Lower Eyelid □ Upper Eyelid □ Periorbital

□ TX - Primary tumor cannot be assessed
□ T0 - No evidence of primary tumor
□ Tis - (in situ) primary tumor
□ T1 - ≤ 2 cm maximum tumor dimension
□ T2 - > 2 cm but ≤ 5 cm maximum tumor dimension
□ T3 - > 5cm maximum tumor dimension
□ T4 - Primary tumor invades bone, muscle, fascia, or cartilage

□ NX – regional lymph nodes cannot be assessed
→N0 – no regional lymph node metastasis
□ cN0 – nodes negative by clinical exam (no pathologic node exam performed)
□ pN0 – based upon lymph node biopsy
→N1 - metastasis in regional lymph node(s)
□ N1a – micrometastasis
□ N1b – macrometastasis
□ N2 – in transit metastasis

□ M0 – no distant metastasis
→M1 – includes beyond regional lymph nodes
□ M1a – metastasis to skin, subcutaneous tissues or distant lymph nodes
□ M1b – metastasis to lung
□ M1c – metastasis to all other visceral sites

MELANOMA OF THE SKIN

□ Lower Eyelid □ Upper Eyelid □ Periorbital
□ Medial Canthus □ Lateral Canthus

□ TX – Primary tumor cannot be assessed
□ T0 – No evidence of primary tumor
□ Tis – Melanoma in situ
→T1 - Melanomas ≤ 1.0 mm in thickness
□ T1a – w/o ulceration & mitosis <1/mm²
□ T1b – w/ ulceration or mitoses ≥ 1/mm²
→T2 - Melanomas 1.01 – 2.0 mm
□ T2a – w/o ulceration
□ T2b – w/ ulceration
→T3 - Melanomas 2.01 – 4.0 mm
□ T3a – w/o ulceration
□ T3b – w/ ulceration
→T4 - Melanomas > 4.00 mm
□ T4a – w/o ulceration
□ T4b – w/ ulceration

□ NX – regional lymph nodes cannot be assessed
□ N0 – no regional lymph node metastasis
→N1 – 1node
□ N1a – micrometastasis*
□ N1 b – macrometastasis**
→N2 – 2-3 nodes
□ N2a – micrometastasis*
□ N2b – macrometastasis**
□ N2c – in transit mets(s)/satellite(s) without metastatic nodes
□ N3 clinical - ≥ 1 node with in transit met(s)/satellite(s)
<pN3 4 or more metastatic nodes, or matted nodes, or in transit met(s)/satellite(s) with metastatic nodes(s)

□ M0 – no metastasis
□ M1a – metastasis to skin, subcutaneous tissues or distant lymph nodes
□ M1b – metastasis to lung
□ M1c – metastasis to all other visceral sites or distant metastases to any site combined with an elevated serum LDH

MALIGNANT MELANOMA OF THE CONJUNCTIVA

□ Bulbar Conjunctiva □ Non Bulbar Conjunctiva

Quadrants are defined by clock hour, starting at the limbus (e.g. 6,9,12 & 3) extending from the central cornea to and beyond the eyelid margin. This will bisect the caruncle.
□ TX- Primary tumor cannot be assessed
□ T0 - No evidence of primary tumor
□ Tis - Melanoma confined to the conjunctival epithelium*
→T1 - Malignant conjunctival melanoma of the bulbar conjunctiva
□ T1a - ≤ to 1 quadrant
<pT1a - Melanoma of the bulbar conjunctiva not > 0.5 mm in thickness w/ invasion of the substantia propria
□ T1b - > 1 but ≤ to 2 quadrants
<pT1b - Melanoma of the bulbar conjunctiva > 0.5mm but ≤ 1.5 mm in thickness w/ invasion of the substantia propria
□ T1c - > 2 but ≤ to 3 quadrants
<pT1c - Melanoma of the bulbar conjunctiva > 1.5 mm in thickness w/ invasion of the substantia propria
□ T1d - > than 3 quadrants
→T2 - Malignant conjunctival melanoma of the non- bulbar (palpebral, fornicial caruncular)
□ T2a - Non-caruncular, ≤ to 1 quadrant
<pT2a - Melanoma of the palpebral, fornicial or caruncular conjunctiva not > 0.5 mm in thickness w/ invasion of the substantia propria
□ T2b - Non-caruncular, > 1 quadrant
<pT2b - Melanoma > 0.5 but not > 1.5 mm in thickness w/ invasion of the substantia propria
□ T2c - Any caruncular, ≤ to 1 quadrant
<pT2c - Melanoma of the palpebral, fornicial caruncular conjunctiva > 1.5 mm in thickness w/ invasion of the substantia propria
□ T2d - Any caruncular, > 1 quadrant
→T3 - Any malignant conjunctival melanoma w/ local invasion
<pT3 - Melanoma invades the eye, eyelid, nasolacrimal system, sinuses or orbit
□ T3a - Globe
□ T3b - Eyelid
□ T3c - Orbit
□ T3d - Sinus
□ T4 - Tumor invades the central nervous system
<pT4 - Melanoma invades the central nervous system

*pTis (Melanoma in situ (includes the term primary acquired melanosis) w/ atypia replacing > 75% of the normal epithelial thickness, with diffuse lesions of epithelioid cells, including abundant cytoplasm, vesicular nuclei or prominent nucleoli, another presence of intraepithelial nests of atypical cells.

□ NX – regional lymph nodes cannot be assessed
□ N0a (biopsied) – no regional lymph node metastasis, biopsy performed
□ N0b (not biopsied) – no regional lymph node metastasis, biopsy not performed
→ N1 - Regional lymph node metastasis
□ N1a – micrometastasis
□ N1b – macrometastasis

□ M0 – no distant metastasis
□ M1 – distant metastasis

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DOB:
Date of Diagnosis:
□ right □ left □ bilateral □ recurrent

PATIENT INFO HERE\other data

UVEAL MELANOMA

ALL
□ TX - Primary tumor cannot be assessed
□ T0 - No evidence of primary tumor

IRIS
→T1 – Tumor limited to iris
□ T1a – ≤ 3 clock hours in size
□ T1b - > 3 clock hours in size
□ T1c - limited to iris w/ secondary glaucoma
□ T2 – Tumor confluent with or extending into the ciliary body, choroid, or both
□ T2a – w/ secondary glaucoma
□ T3 - Tumor confluent with or extending into the ciliary body, choroid, or both w/ scleral extension
□ T3a - w/ secondary glaucoma
→T4 – Tumor w/ extrascleral extension
□ T4a – extrascleral extension ≤ 5 mm in diameter
□ T4b – extrascleral extension > 5 mm in diameter

*Note: In clinical practice, the largest tumor basal diameter may be estimated in optic disc diameters (DD, average: 1 dd = 1.5 mm). Tumor thickness may be estimated in doddles (average: 2.5 diopters = 1 mm). However, techniques such as ultrasonography and fundus photography are used to provide more accurate measurements. Ciliary body involvement can be evaluated by the slit lamp, ophthalmoscopy, gonioscopy, and transillumination. However, high-frequency ultrasonography (ultrasound biomicroscopy) is used for more accurate assessment. Extension through the sclera is evaluated visually before and during surgery, and with ultrasonography, computed tomography, or magnetic resonance imaging.

** Note: When histopathologic measurements are recorded after fixation, tumor diameter and thickness may be underestimated because of tissue shrinkage.

*** Note: Iris melanomas originate from, and are predominantly located in, this region of the eyes. If less than half of the tumor volume is located within the iris, the tumor may have originated in the ciliary body, and consideration should be given to classifying it accordingly.

CILIARY BODY & CHOROID
Primary ciliary body and choroid melanomas, as defined in Figure 51.1, are classified according to the four tumor size categories below:
→T1 – Tumor size category 1
□ T1a – w/o ciliary body involvement and extraocular extension
□ T1b – w/ ciliary body involvement
□ T1c – w/o ciliary body involvement but w/ extraocular extension ≤ 5 mm in diameter
□ T1d – w/ ciliary body involvement and extraocular extension ≤ 5 mm in diameter
→T2 – Tumor size category 2
□ T2a – w/o ciliary body involvement and extraocular extension
□ T2b – w/ ciliary body involvement
□ T2c – w/o ciliary body involvement but w/ extraocular extension ≤ 5 mm in diameter
□ T2d – w/ ciliary body involvement and extraocular extension ≤ 5 mm in diameter
→T3 – Tumor size category 3
□ T3a – w/o ciliary body involvement and extraocular extension
□ T3b –w/ ciliary body involvement
□ T3c – w/o ciliary body involvement but w/ extraocular extension ≤ 5 mm in diameter
□ T3d –w/ ciliary body involvement and extraocular extension ≤ 5 mm in diameter
→T4 – Tumor size category 4
□ T4a – w/o ciliary body involvement and extraocular extension
□ T4b –with ciliary body involvement
□ T4c – w/o ciliary body involvement but w/ extraocular extension ≤ 5 mm in diameter
□ T4d – w/ ciliary body involvement and extraocular extension ≤ 5 mm in diameter
□ T4e – Any tumor size category with extraocular extension > 5 mm in diameter

□ NX – regional lymph nodes cannot be assessed
□ N0 – no regional lymph node metastasis
□ N1 – regional lymph node metastasis

□ M0 – no metastasis
→ M1 – distant metastasis
□ M1a – largest diameter of the largest metastasis ≤ 3 cm
□ M1b – largest diameter of the largest metastasis 3.1 – 8.0 cm
□ M1c – largest diameter of the largest metastasis > 8 cm

RETINOBLASTOMA

□ TX – Primary tumor cannot be assessed
□ T0 – No evidence of primary tumor.
→T1 – Tumors ≤ 2/3 the volume of the eye with no vitreous or subretinal seeding.
□ T1a – No tumor in either eye > 3 mm in largest dimension or located closer than 1.5 mm to the optic nerve or fovea.
□ T1b – At least one tumor > 3 mm in largest dimension or located closer than 1.5 mm to the optic nerve or fovea. No retinal detachment or subretinal fluid beyond 5 mm from the base of the tumor.
□ T1c – At least one tumor > 3 mm in largest dimension or located closer than 1.5 mm to the optic nerve or fovea. With retinal detachment or subretinal fluid beyond 5 mm from the base of the tumor.
→T2 – Tumors ≤ 2/3 the volume of the eye with vitreous or subretinal seeding. Can have retinal detachment.
□ T2a – Focal vitreous and/or subretinal seeding of fine aggregates of tumor cells is present, but no large clumps or "snowballs" of tumor cells.
□ T2b – Massive vitreous and/or subretinal seeding is present, defined as diffuse clumps or "snowballs" of tumor cells.
→T3 – Severe intraocular disease
□ T3a – Tumor fills > 2/3 of the eye
□ T3b – One or more complications present, which may include tumor-associated neovascular or angle closure glaucoma, tumor extension into the anterior segment, hyphema, vitreous hemorrhage or orbital cellulitis.
→T4 – Extraocular disease detected by imaging studies.
□ T4a – Invasion of optic nerve.
□ T4b – Invasion into the orbit.
□ T4c – Intracranial extension not past chiasm.
□ T4d – Intracranial extension past chiasm.

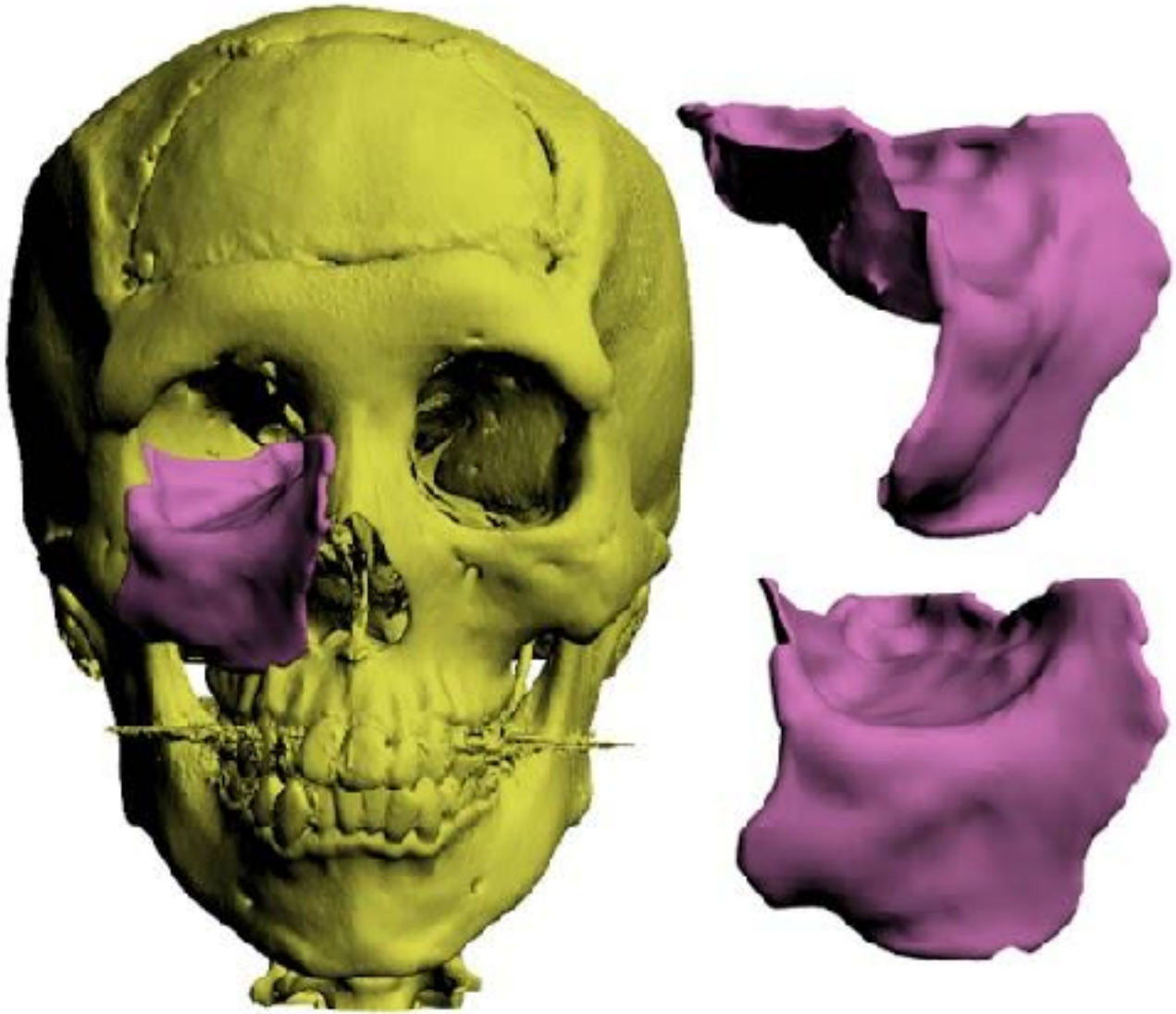
□ NX – Regional lymph nodes cannot be assessed
□ N0 – No regional lymph node involvement
□ N1 – Regional lymph node involvement (preauricular, cervical, submandibular)
□ N2 – Distant lymph node involvement

□ M0 – No metastasis
→M1 – Systemic metastasis
□ M1a – Single lesion in sites other than CNS
□ M1b – Multiple lesions in sites other than CNS
□ M1c – Trilateral retinoblastoma (pineal gland)
□ M1d – Multifocal CNS lesion(s)
□ M1e – Leptomeningeal and/or CSF involvement

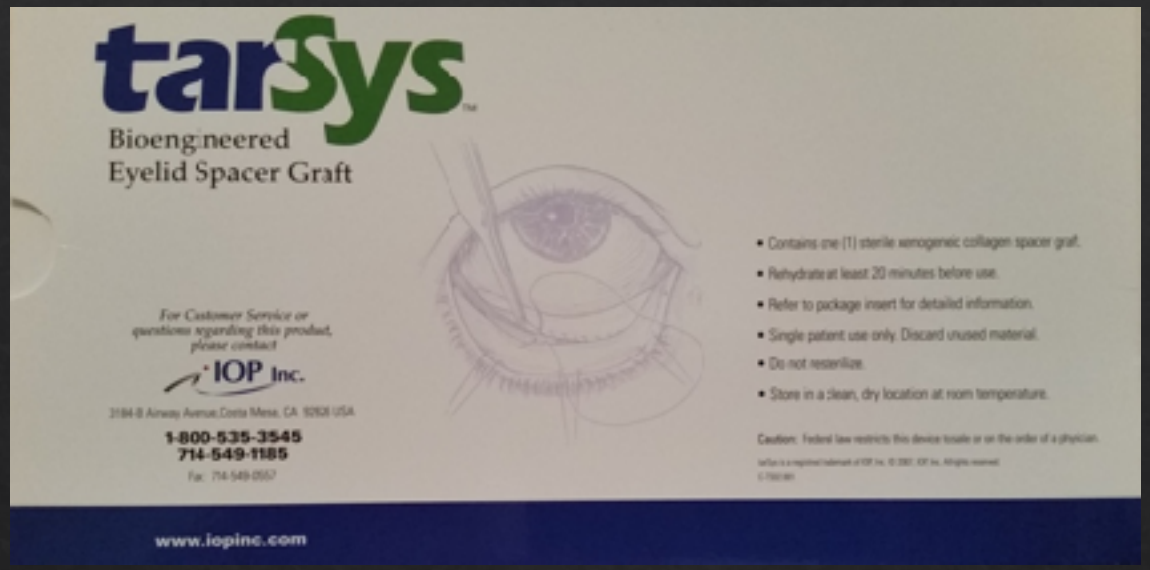
ASOPRS Oncology Database

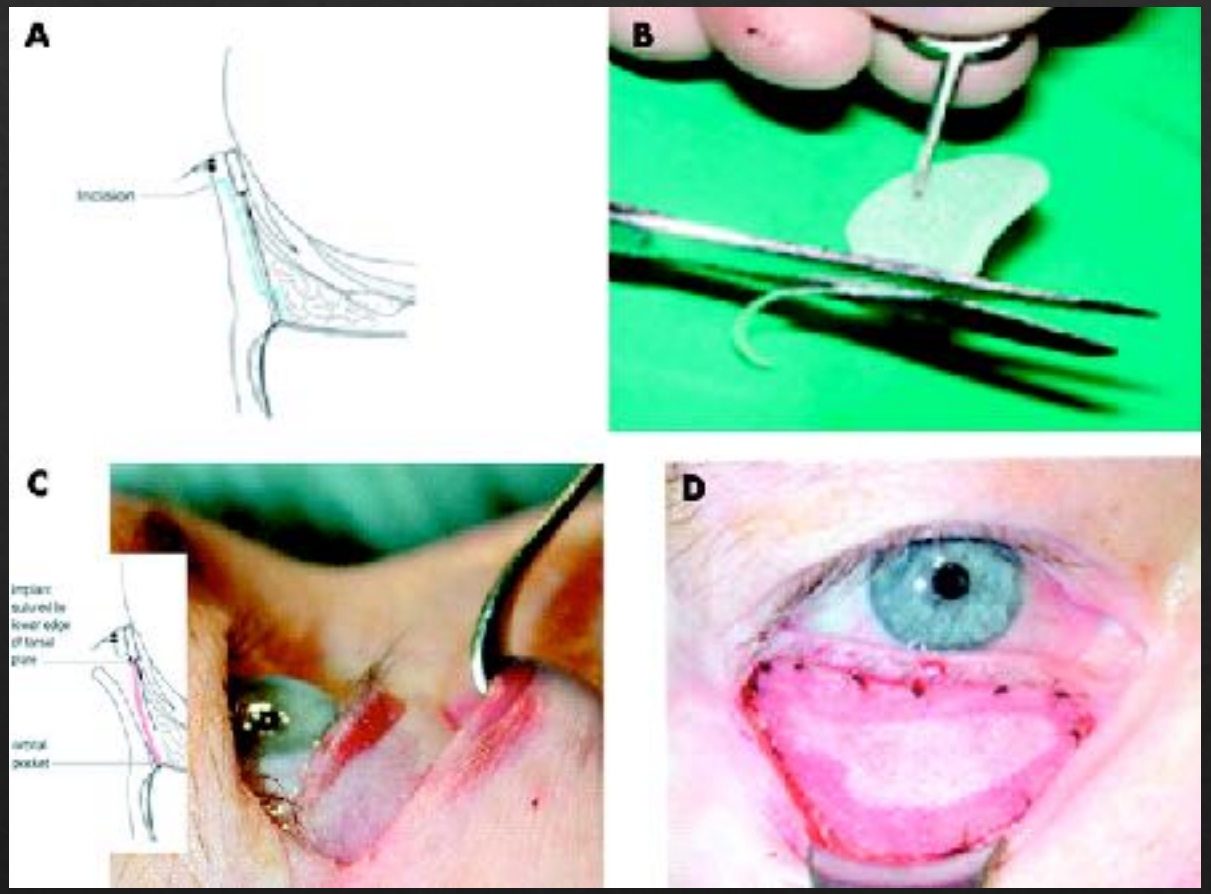
Complex Surgical Considerations

When your own tissue isn't enough. . .



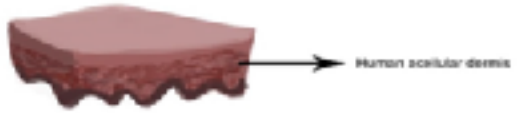
Tarsal Substitutions



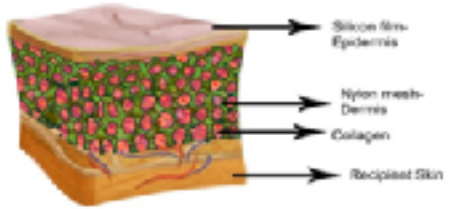


(a) Acellular

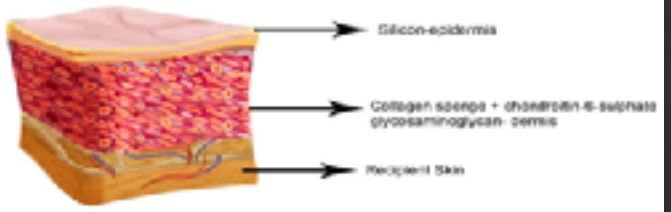
i. Alloderm®



ii. Biobrane®



iii. Integra® DRT

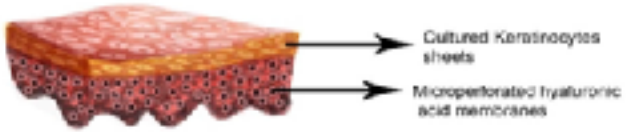


(b) Epidermal Autologous

i. Cell Spray

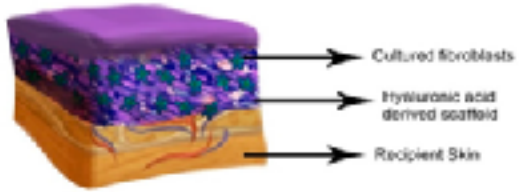
ii. Epicel

iii. Laserskin



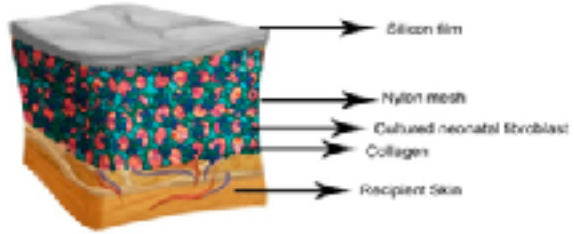
(c) Dermal Autologous

i. Hyalograft 3D

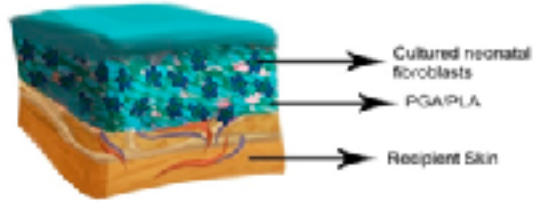


(d) Dermal Allogenic

i.TransCyte



ii. Dermagraft

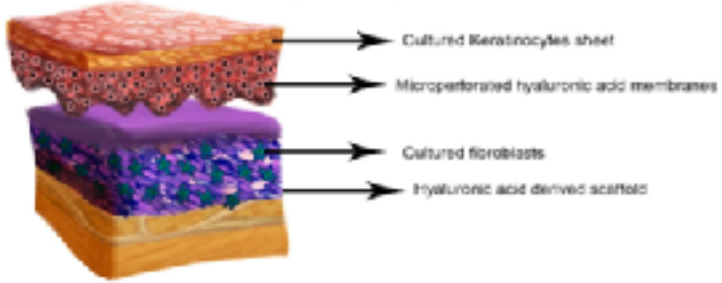


(e) Xenogenic Dermal

i. Permacol

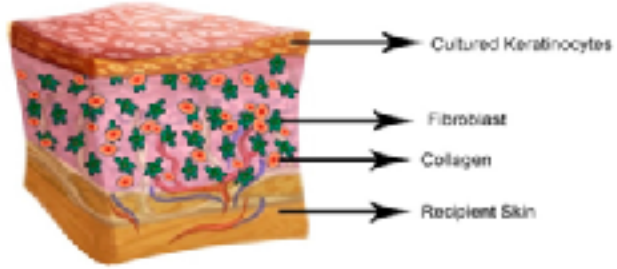
(f) Epidermal/ Dermal (Composite) Autologous

i. Tissue tech autograft system



(g) Epidermal/ Dermal (Composite) Allograft

i. Apligraf



Questions?

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