Challenges in the Management of Advanced Cutaneous Malignancies of the Head and Neck

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Ear, Nose & Throat Institute

BEST HOSPITALS U.S.News & WORLD REPORT EAR, NOSE & THROAT 2022-23

Ranked #17 in the nation and Best in Ohio

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Disclosures

- None

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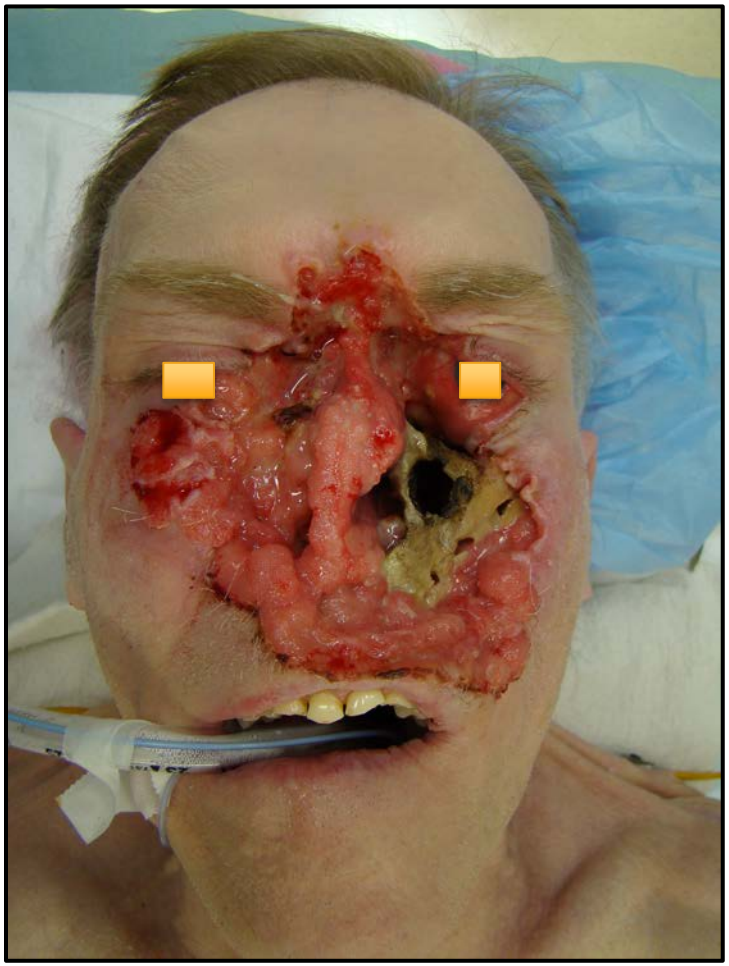
Outline

- Overview of the problem
- Treatment strategies
  - Non-surgical
    - Radiation
    - Systemic (Immunotherapy)
  - Surgical
- Challenges (Diagnosis, Medical Co-morbidities)
- Case presentations
- Future directions

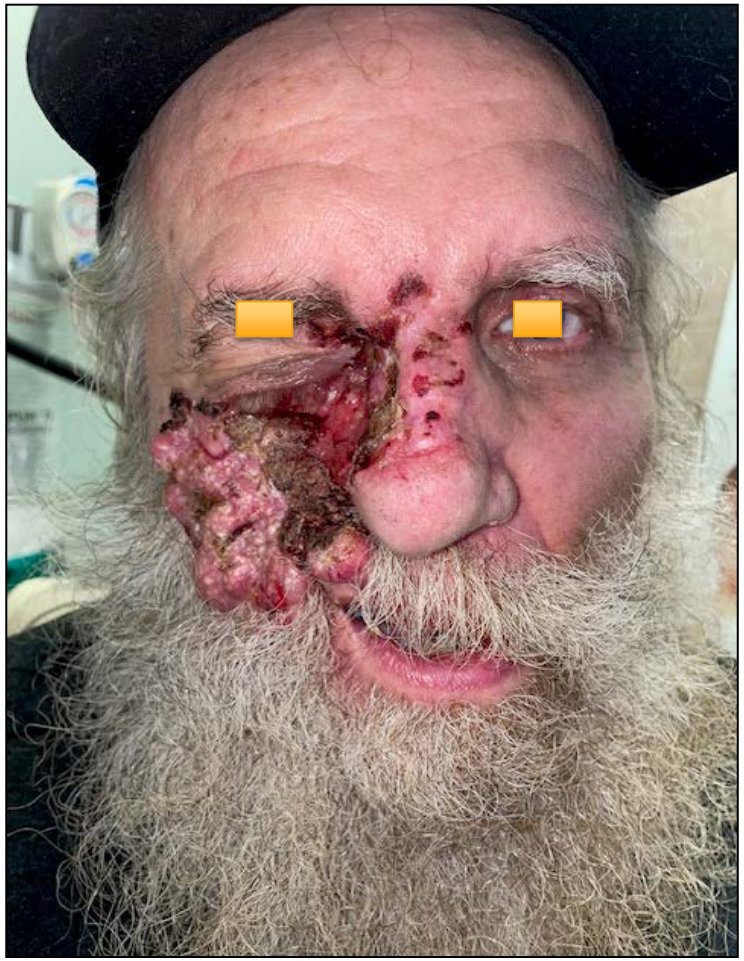
General Considerations

- Multidisciplinary Team approach
  - Surgeon
  - Medical oncologist
  - Radiation oncologist
  - Advanced Practice Providers
  - Nursing support
  - Social work
  - Nutritional support
  - Psychological support
  - Physical therapy
  - Speech Therapy
  - Mohs surgeons/Dermatologists

The problems we face have not changed over time

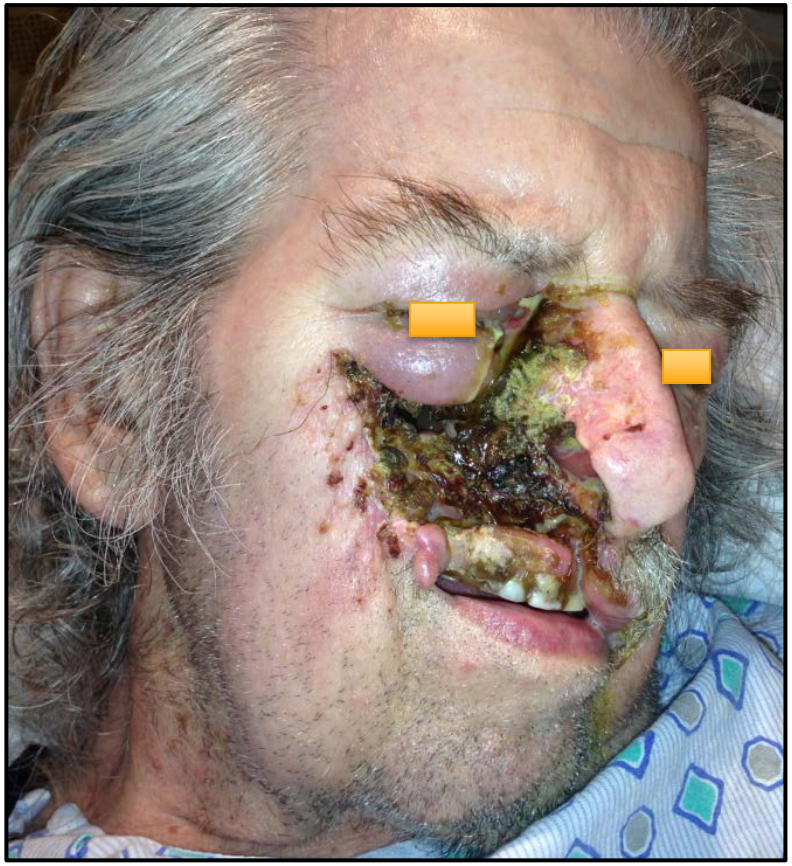


2006



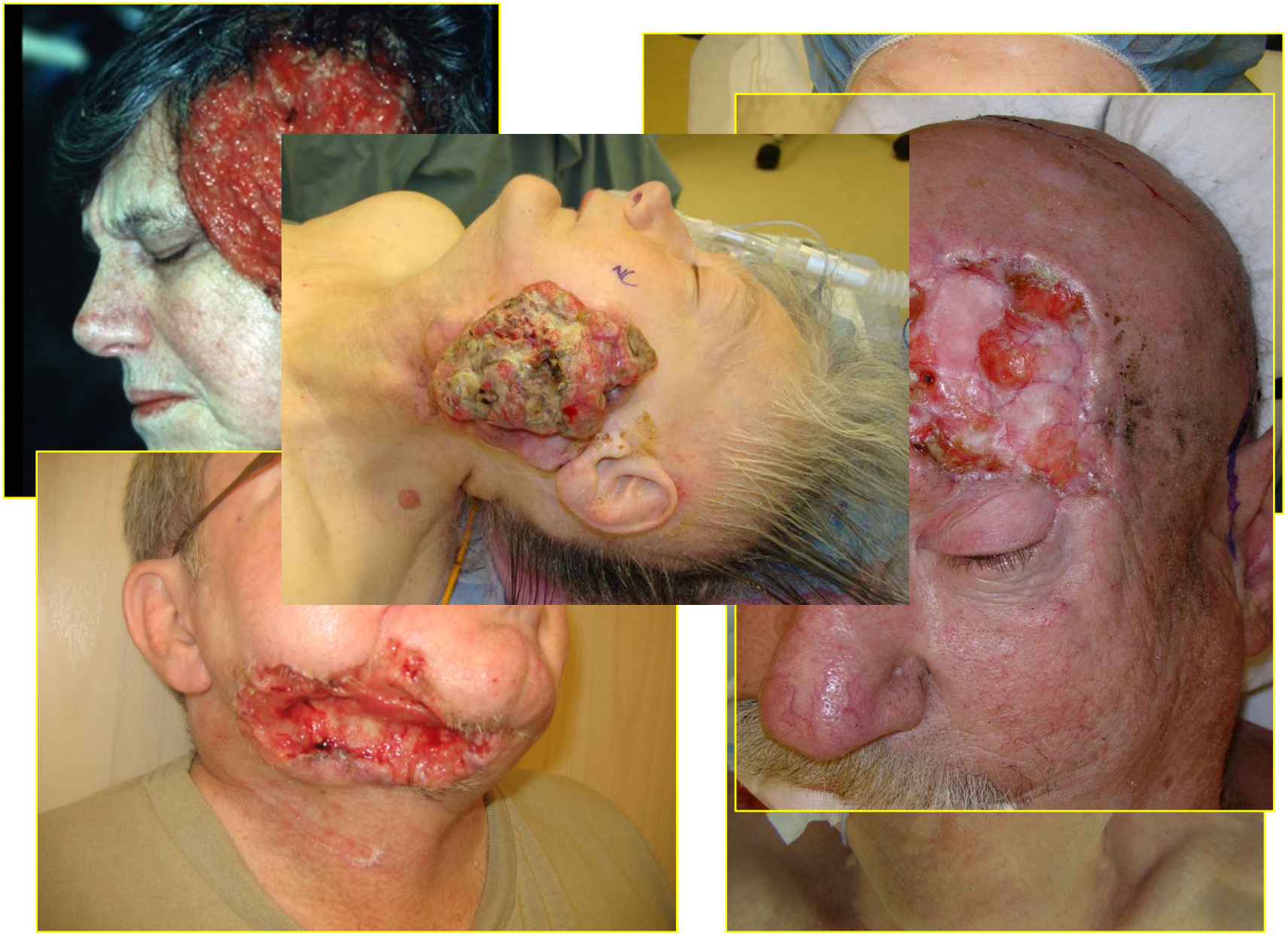
2024

Tools in our surgical and medical arsenals have



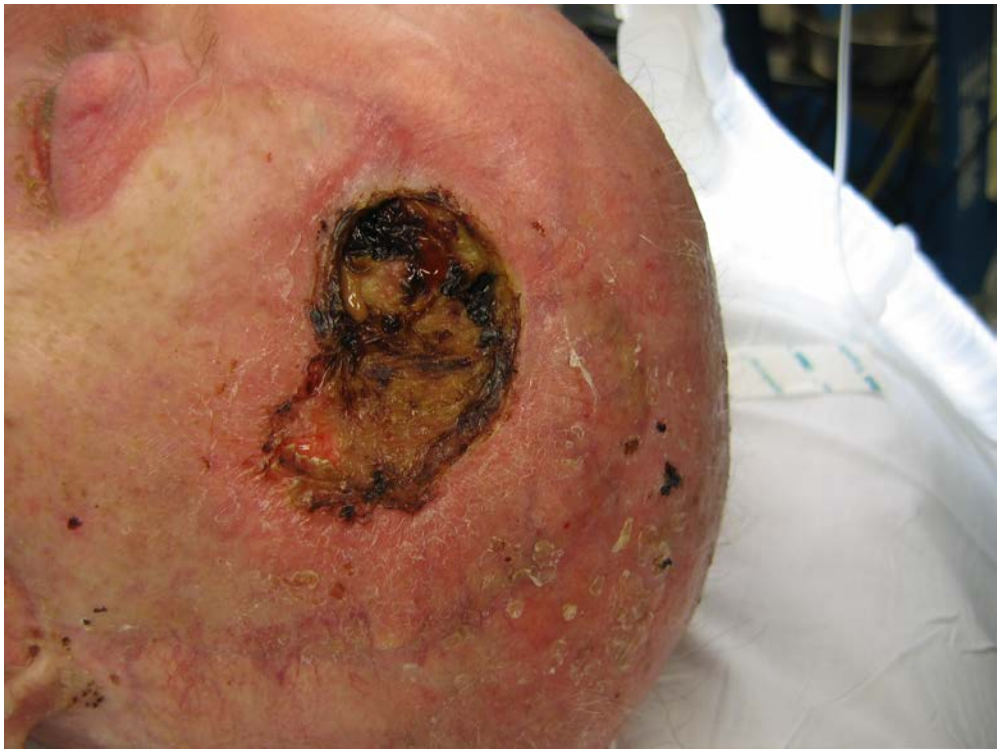
2007

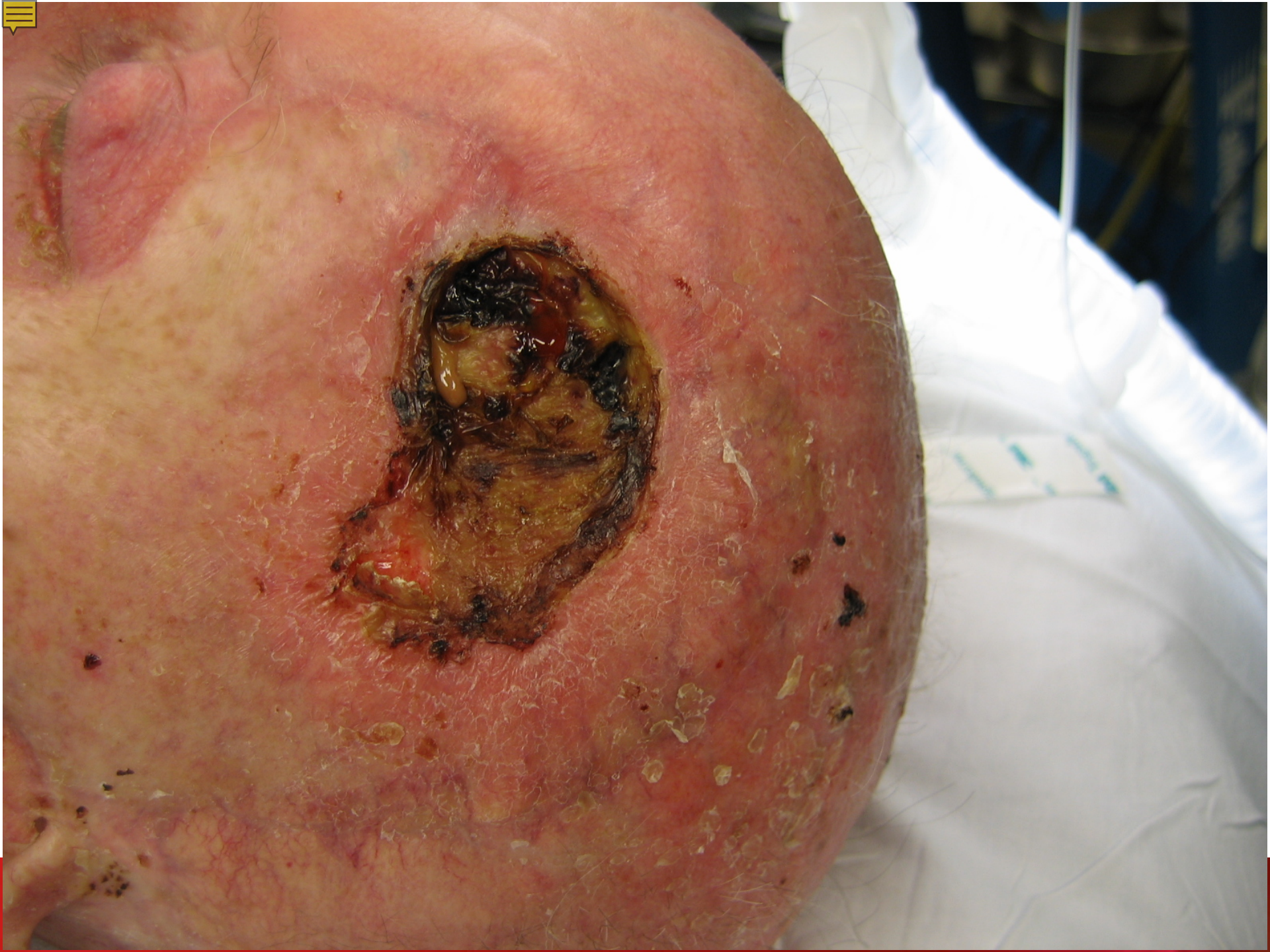
2024

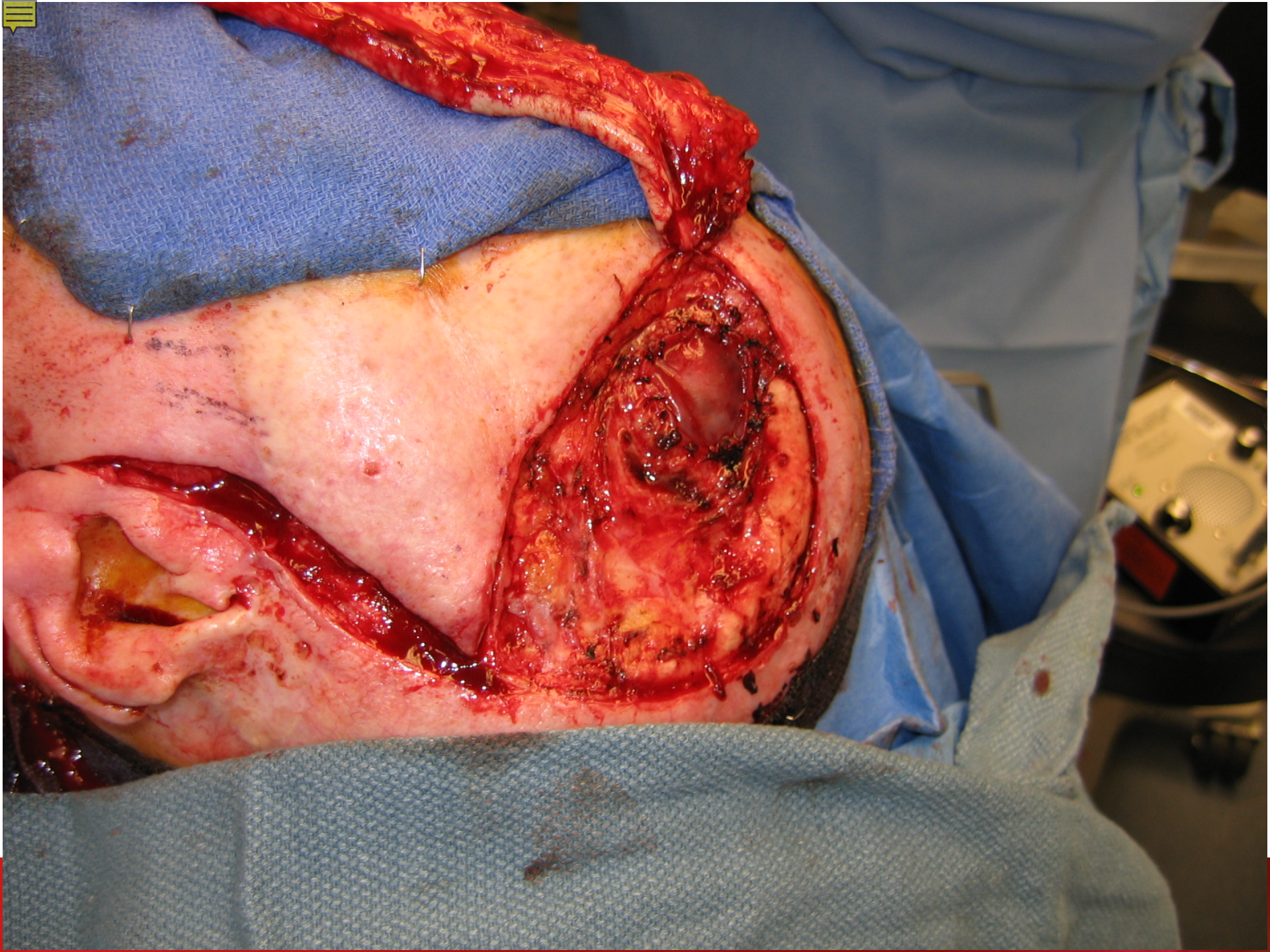


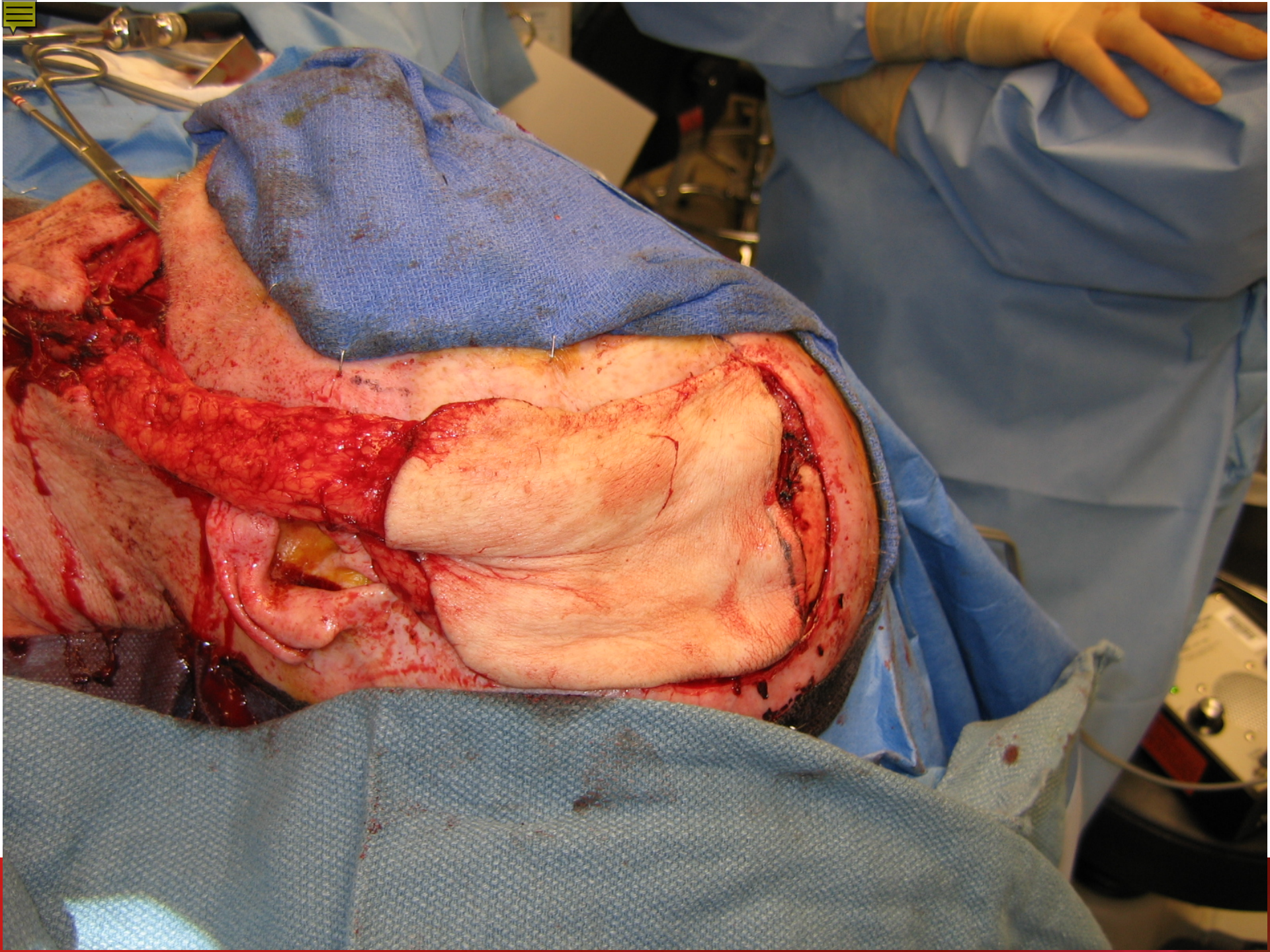
Challenging Case 1

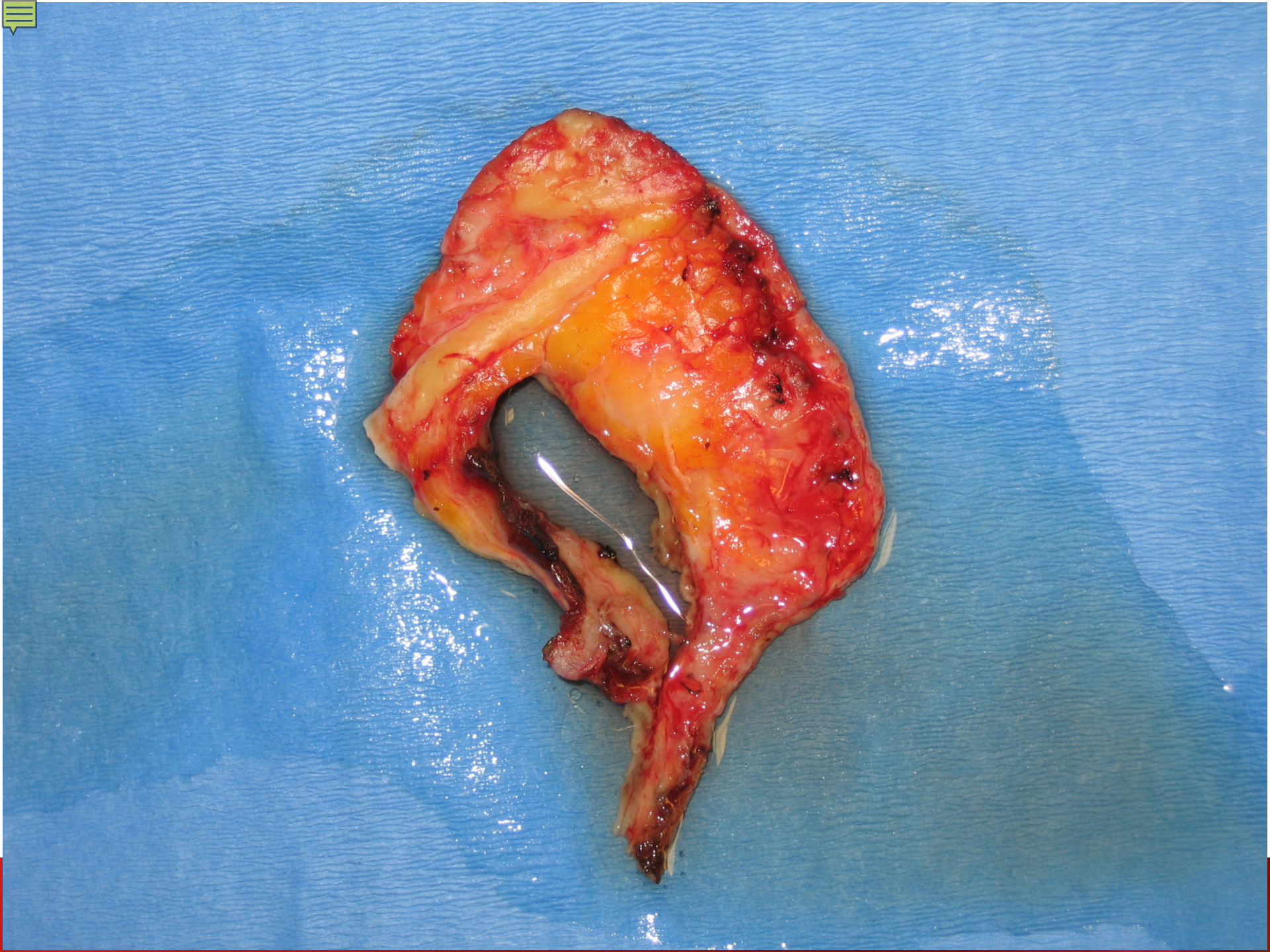
75 y/o farmer
18 yrs s/p renal transplant
Multiple prior cutaneous malignancies
XRT
Chronic wound post XRT
DX: persistence/recurrence/ necrosis
Point: consider repeat bx
?limitations of shave bx

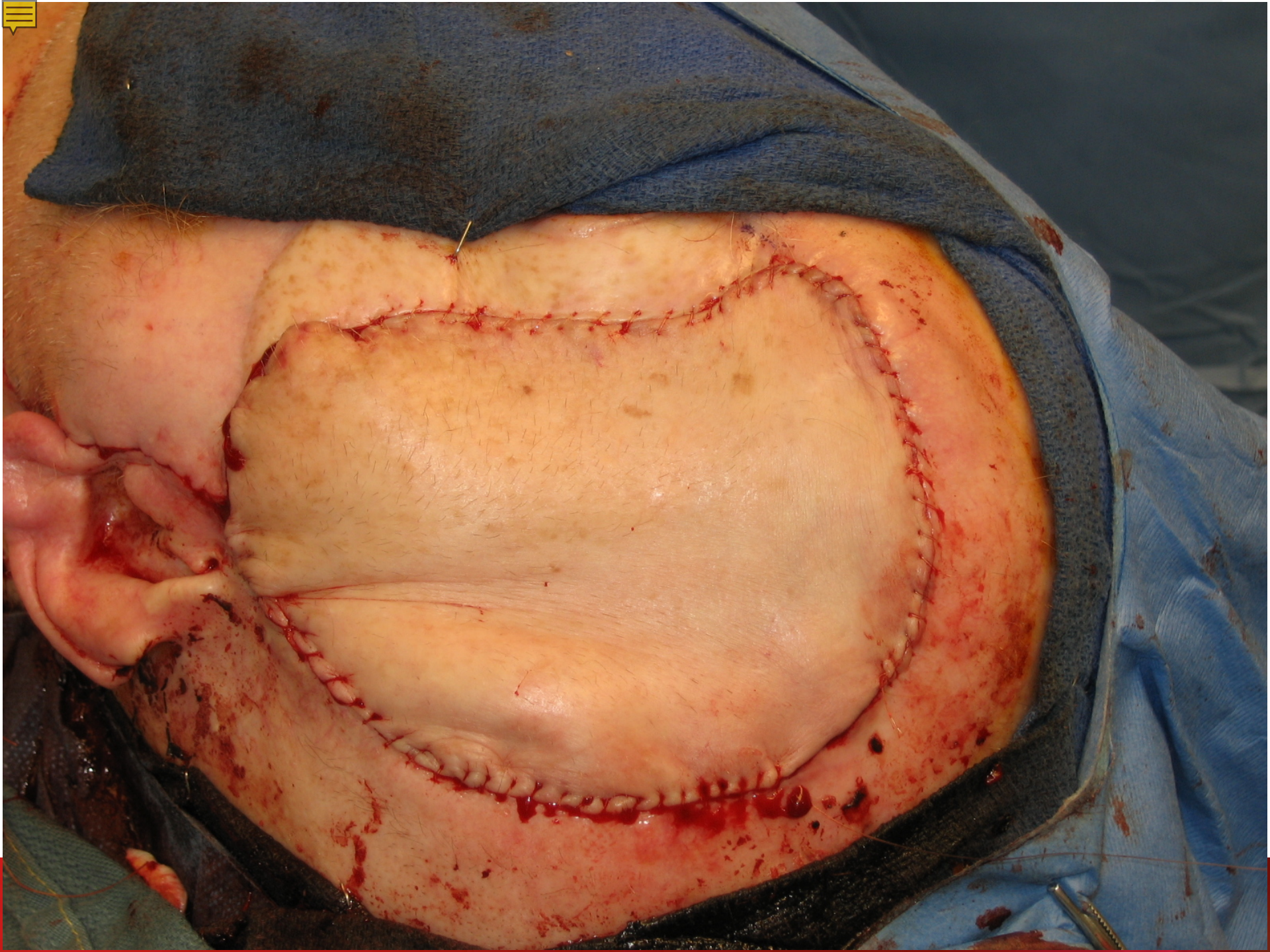


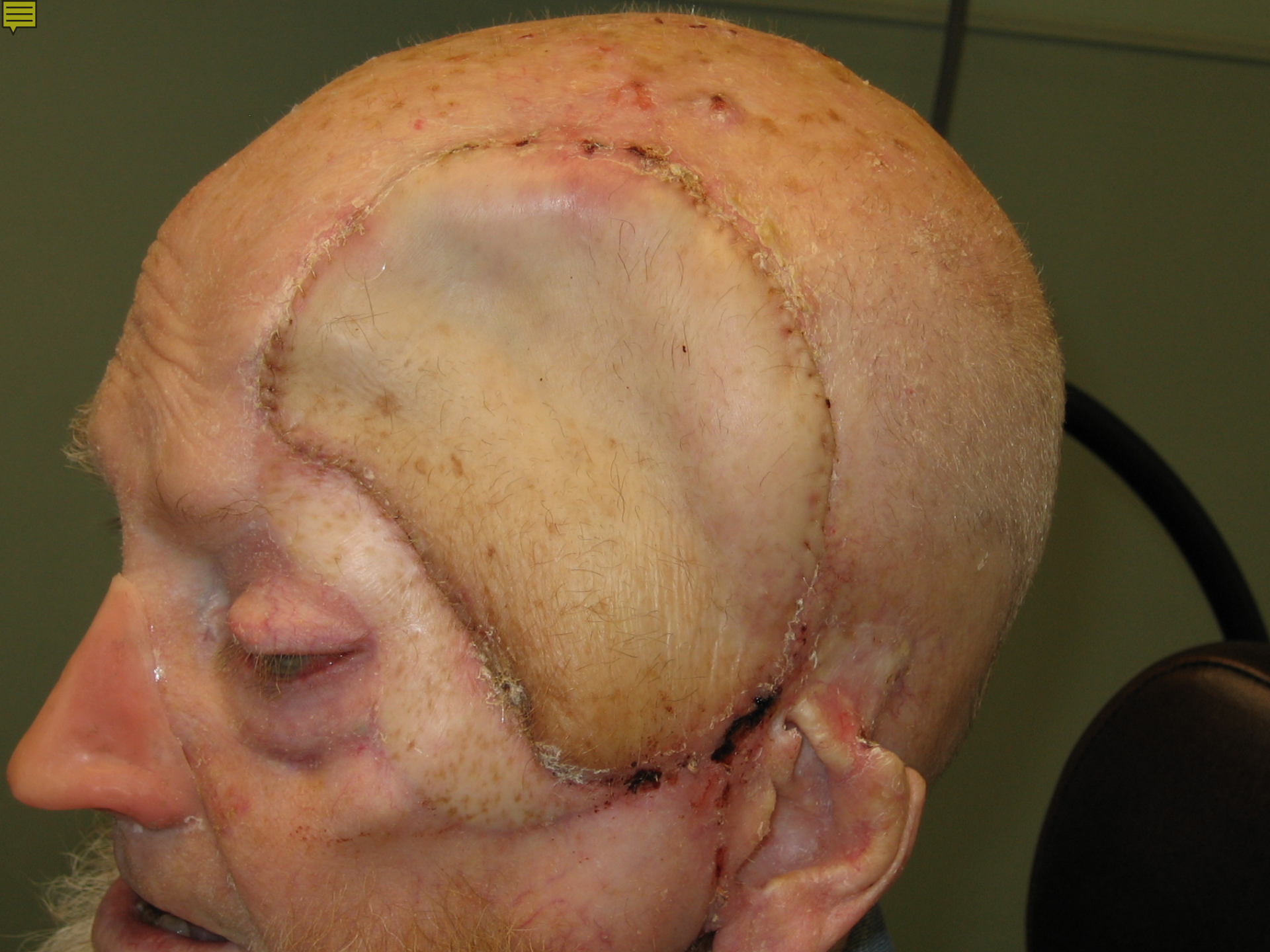












64y/o male 8 yr hx of recurrent right skin lesion bled when he shaved

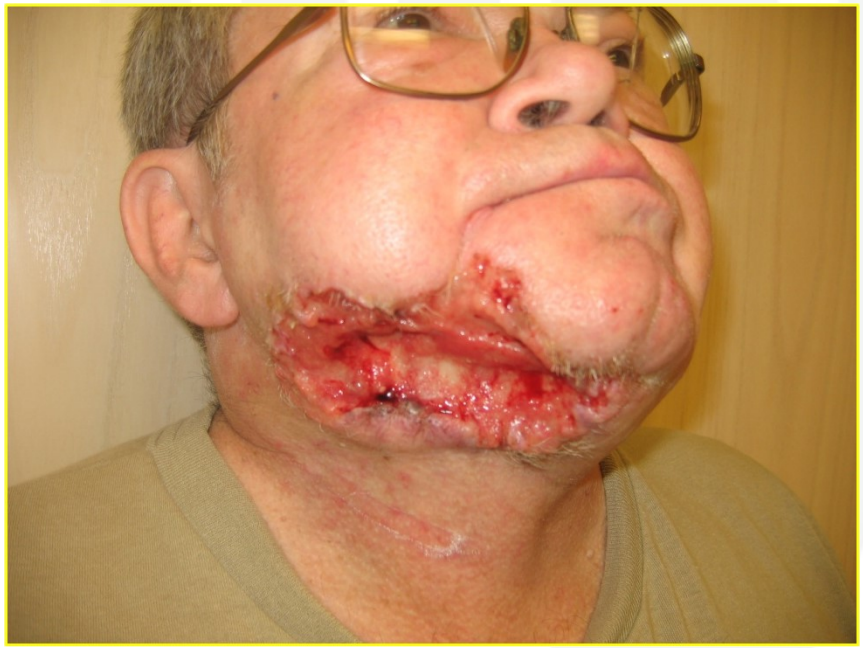
Recurred after curettage

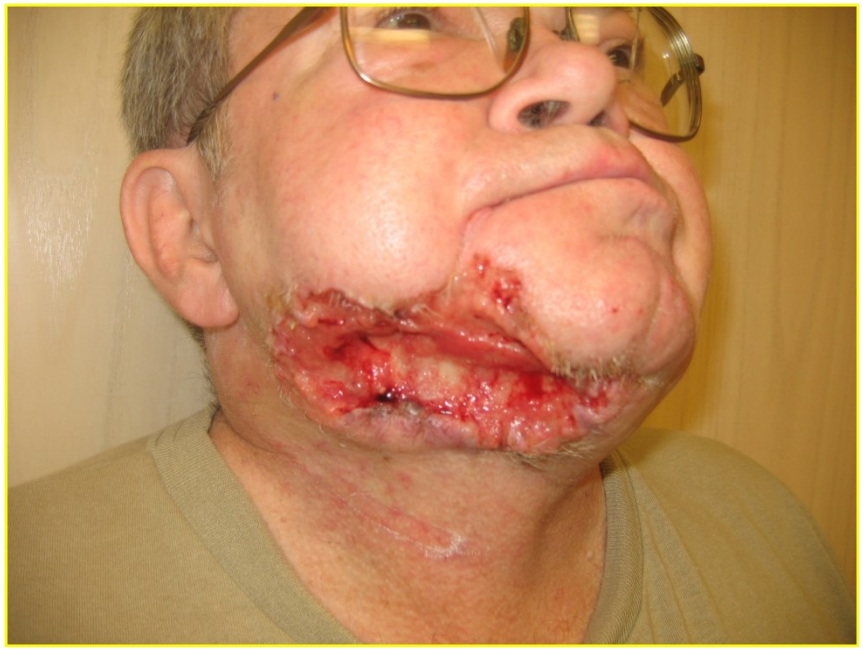
Initial dx: necrotic debris and atypical cell

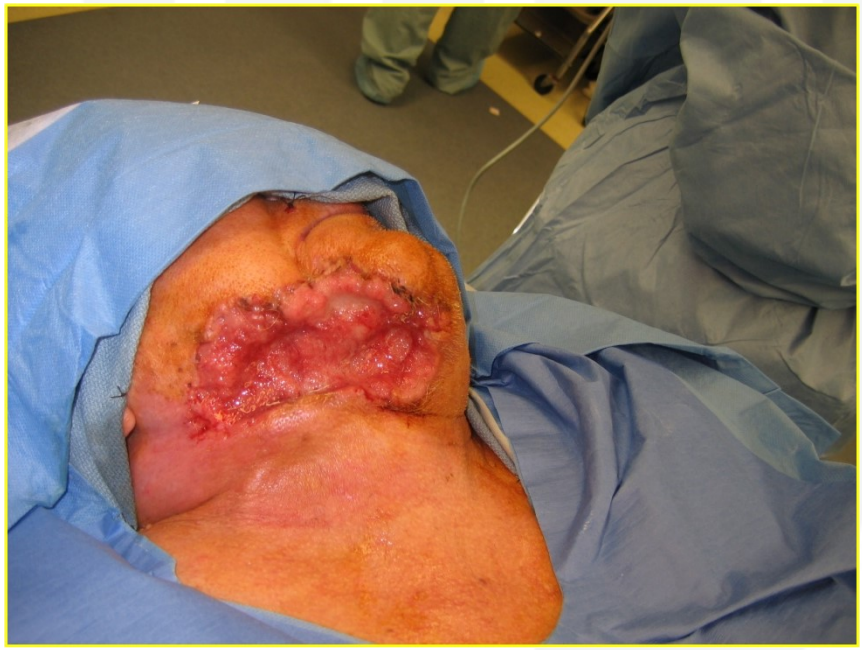
Rx with antibiotics

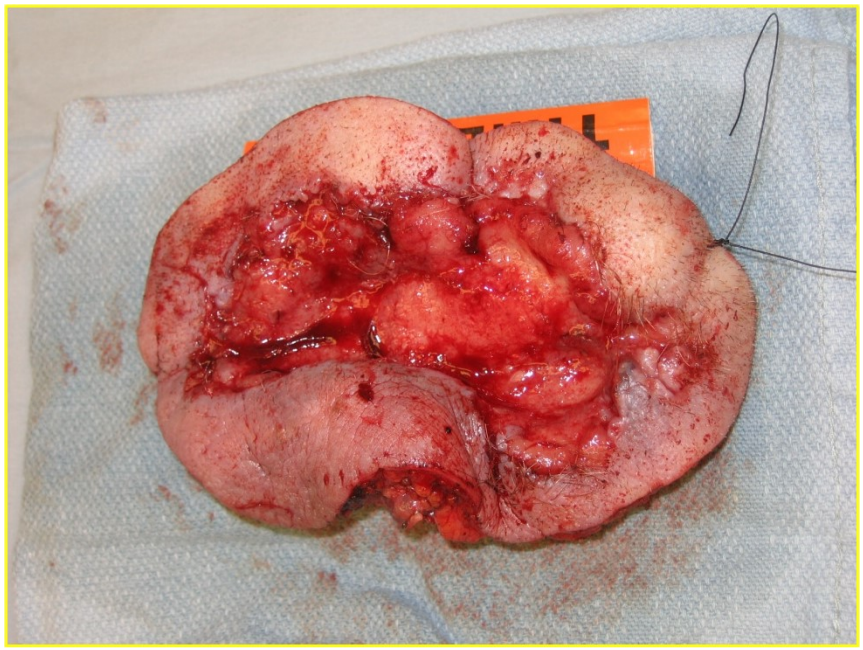
Bx:basosquamous ca

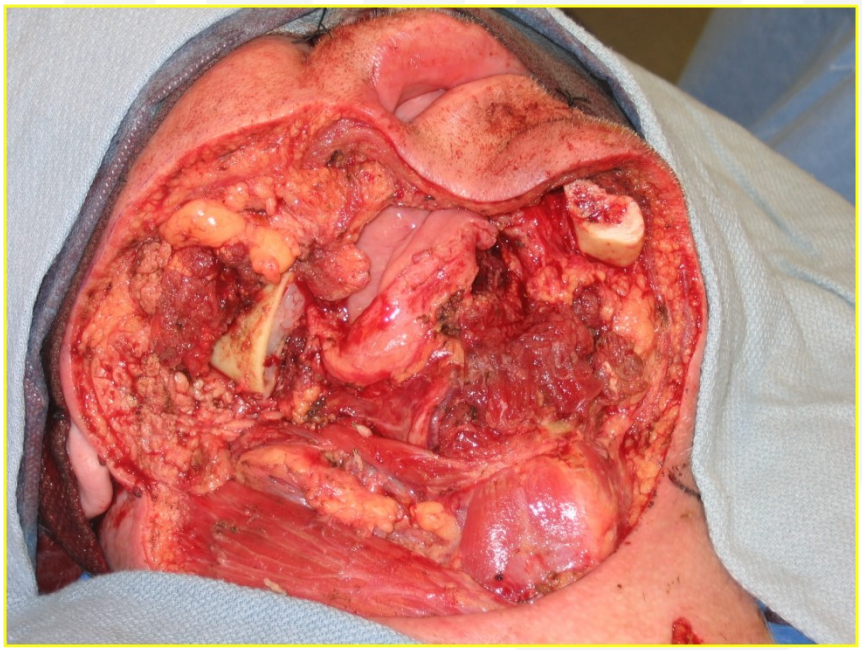
Considerations: PE shows bone, marginal nerve weakness

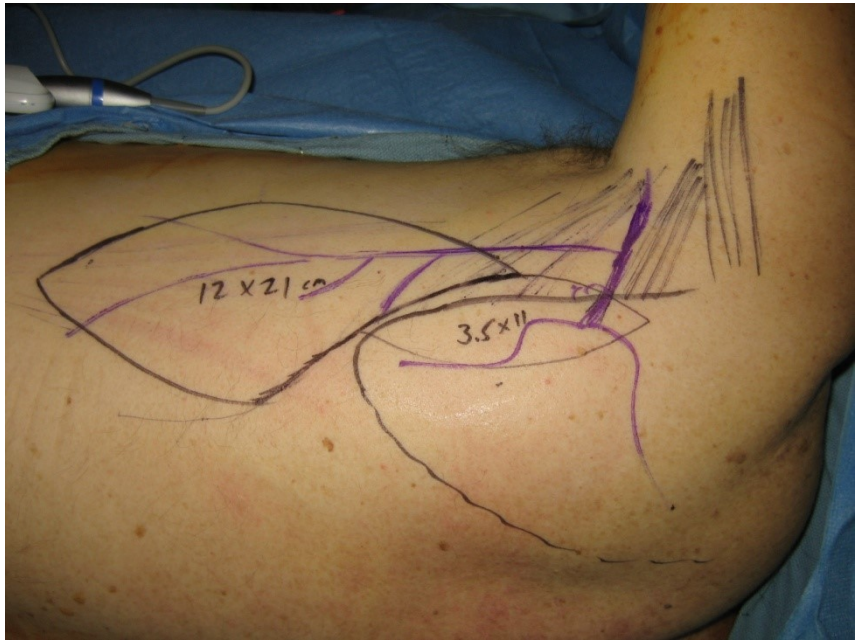


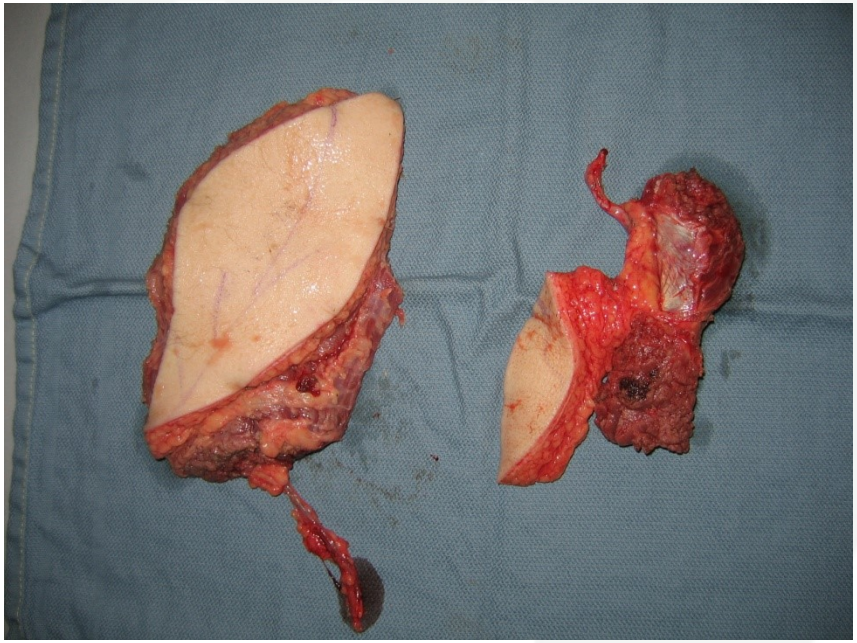


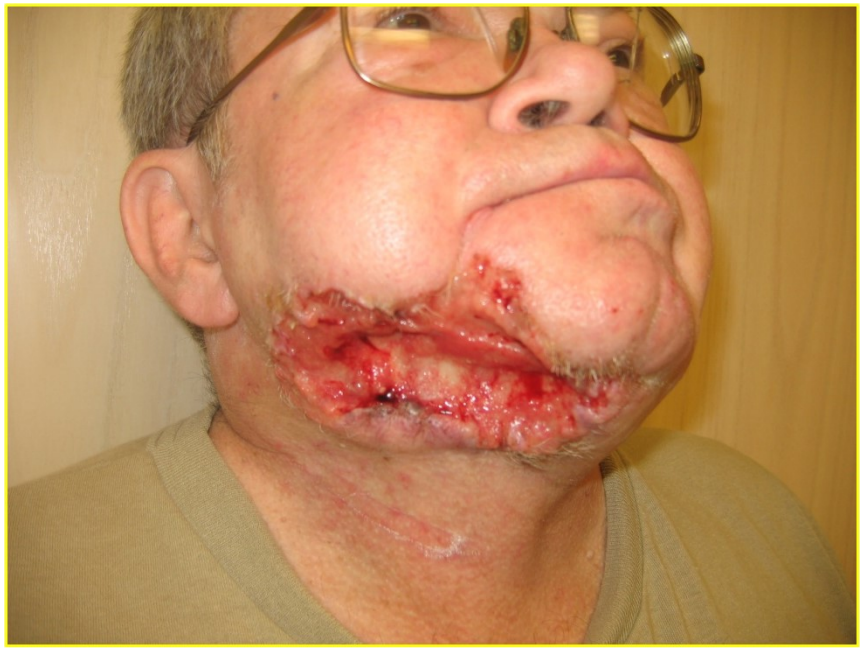


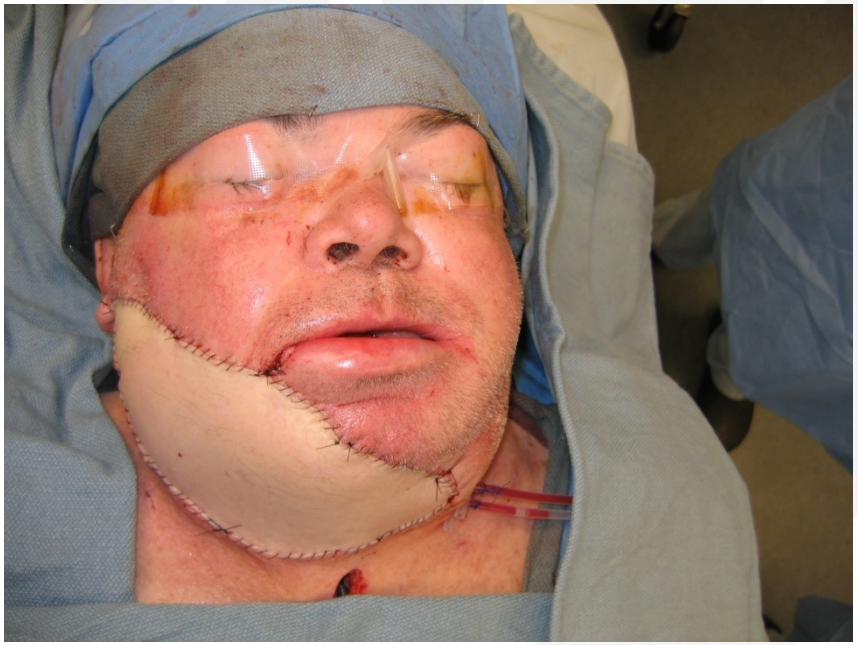












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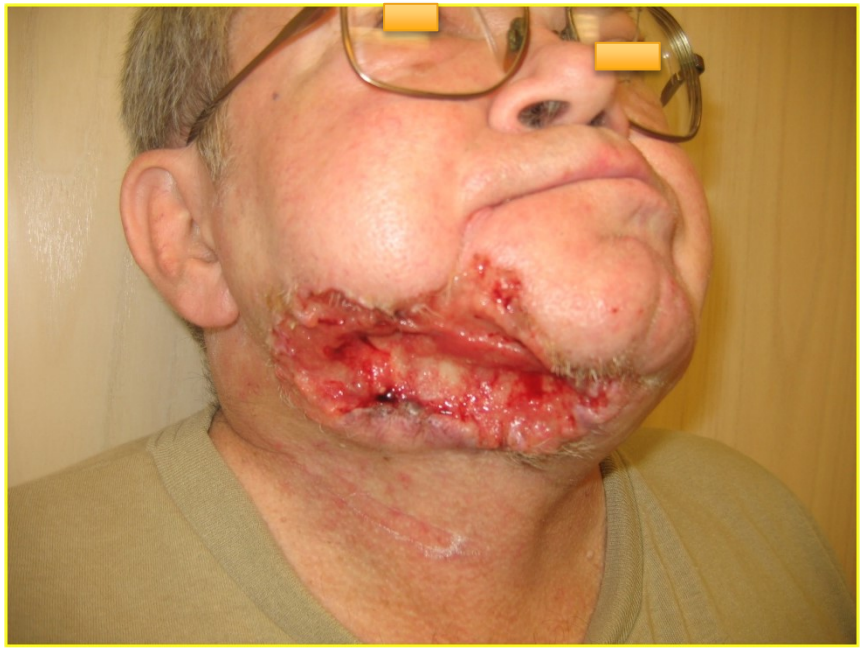

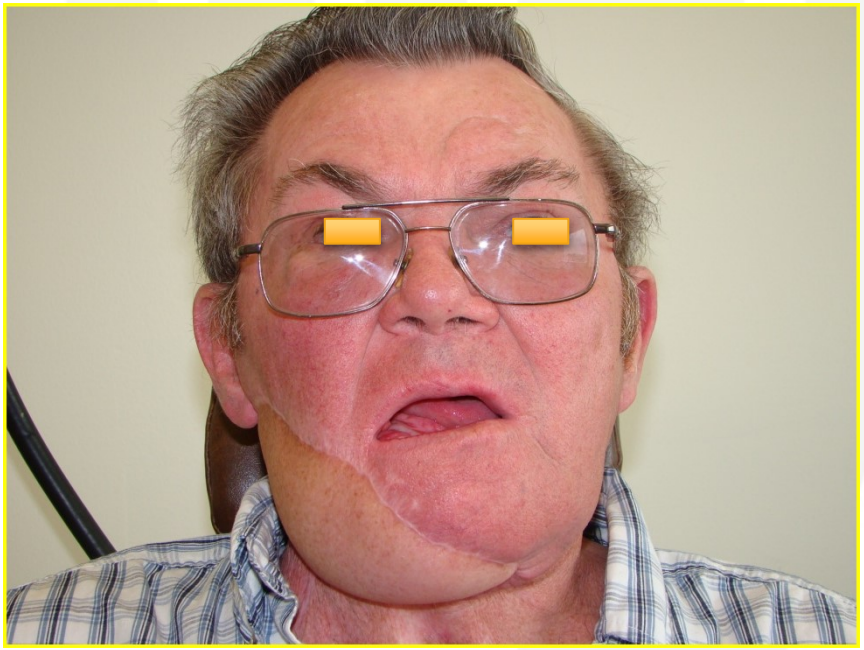

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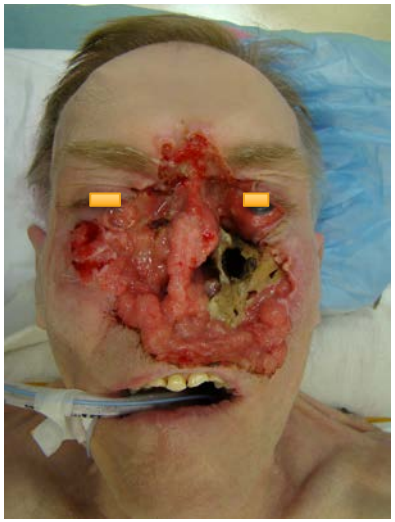
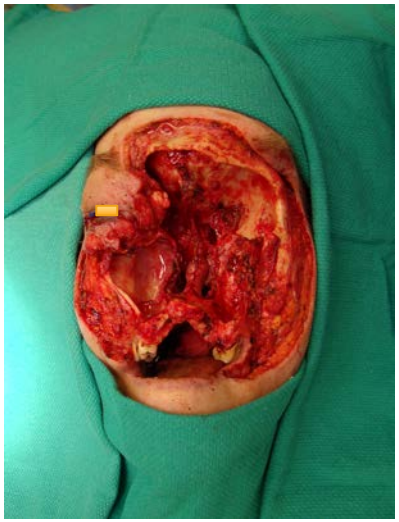
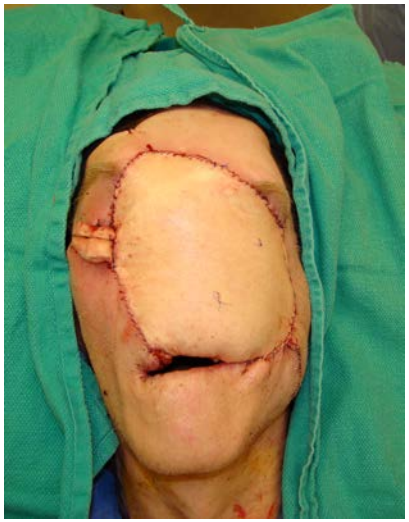
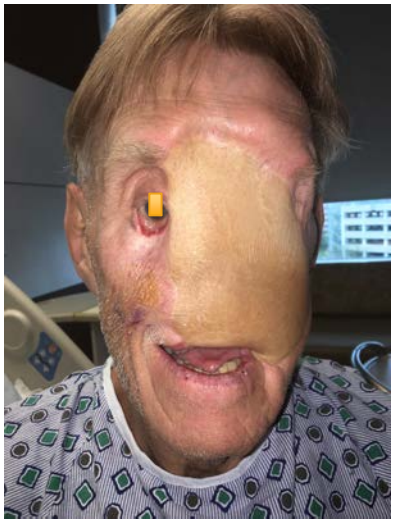
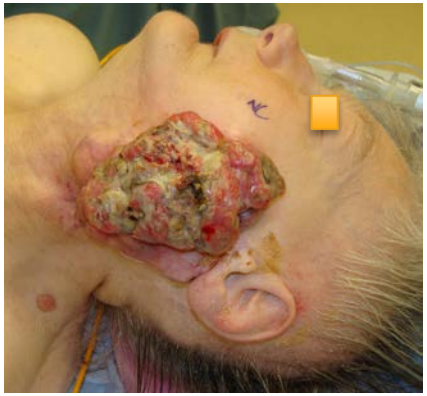
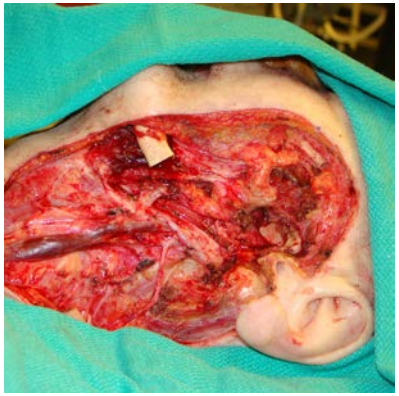
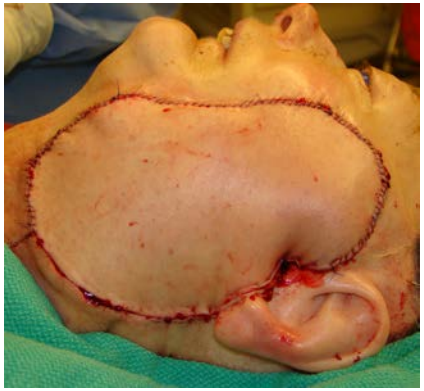
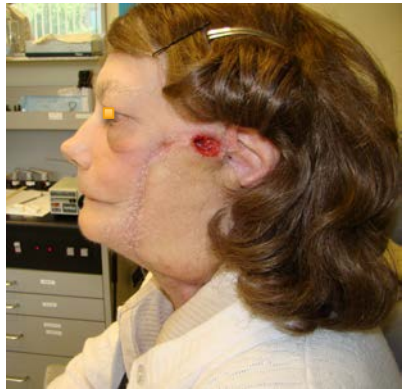
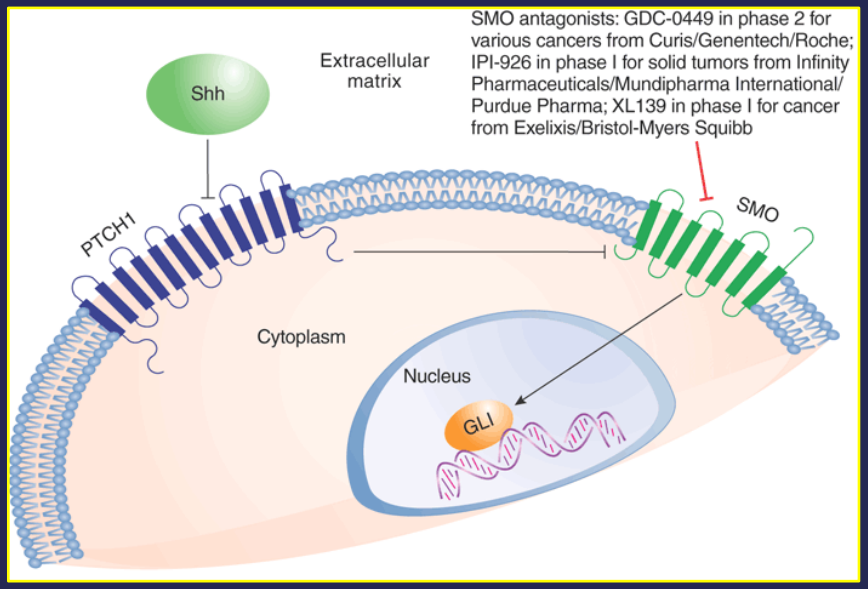
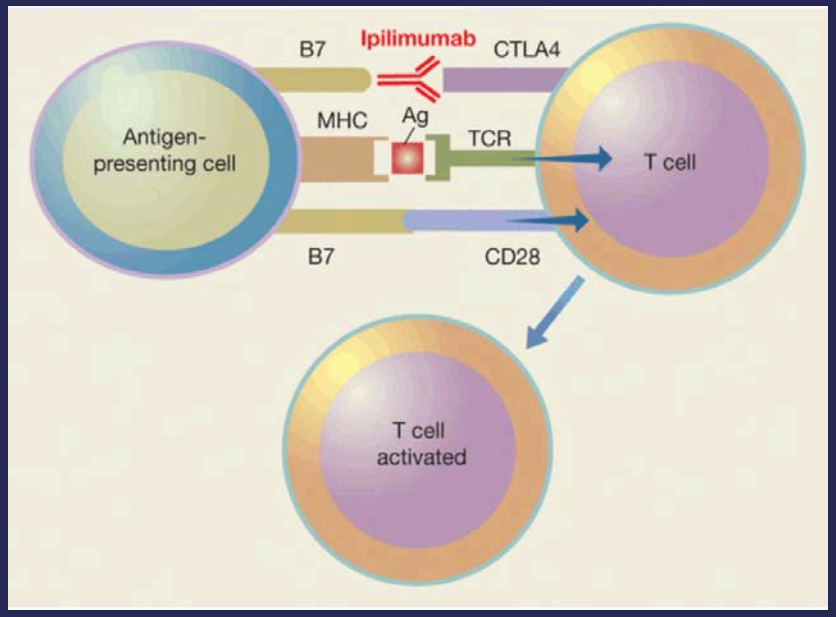
Surgery was main potentially curative option available with post op XRT
New systemic treatment was only on the horizon

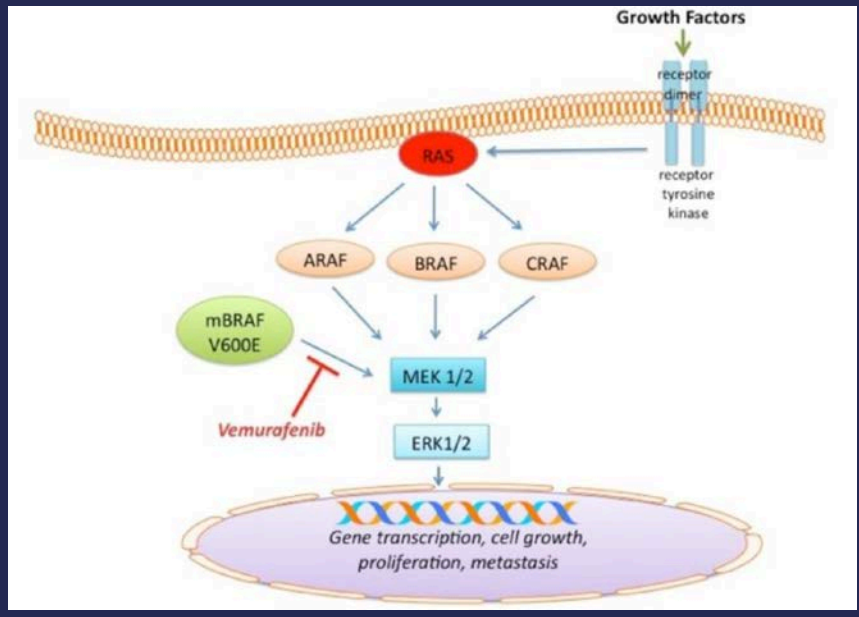









Future Directions

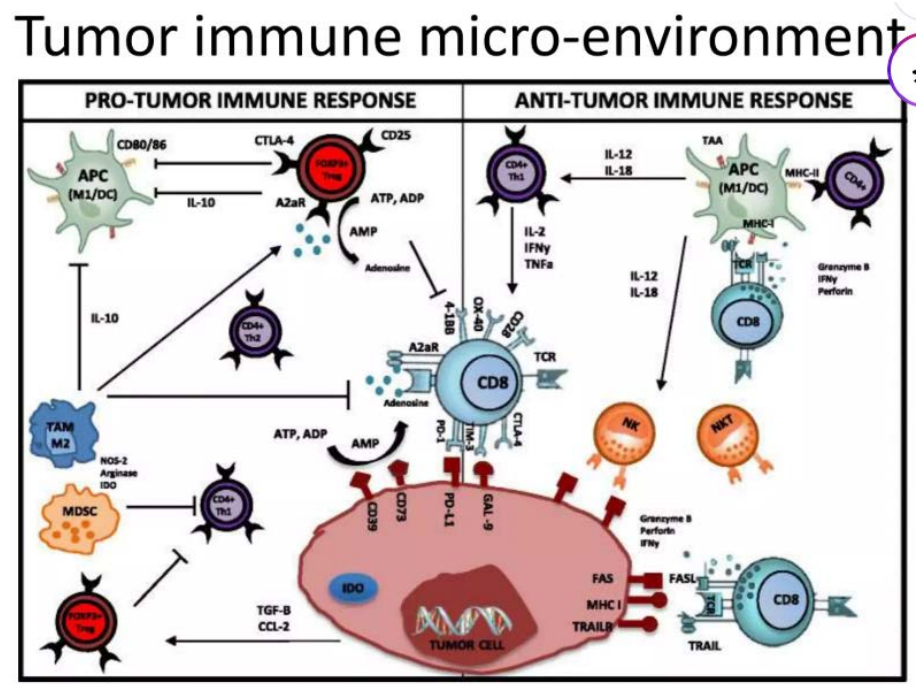
- Targeted Therapy
  - Hedgehog Pathway Inhibition
    - Vismodegib
  - Immunotherapy
    - Ipilimumab
  - BRAF inhibitors
    - Vemurafenib



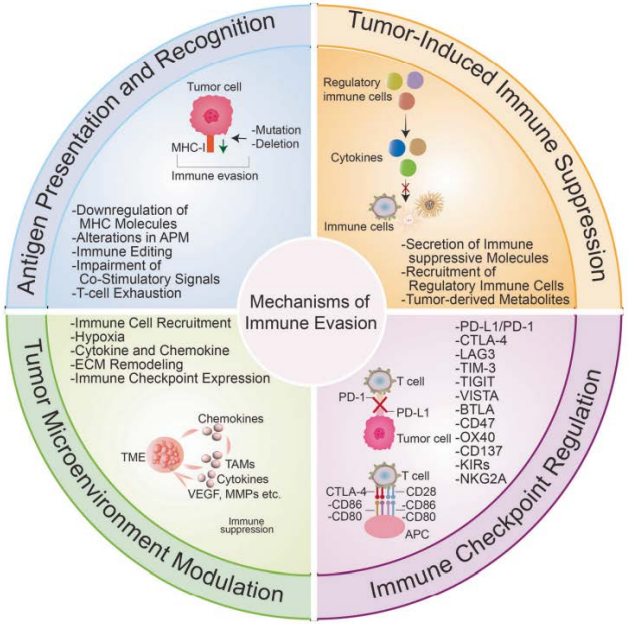




Complex Interaction points between cancer and immune cells



Immune evasion in cancer: mechanisms and cutting-edge therapeutic…
Tufail et al.



Era of Immunotherapy: The Problems and Solutions

- Cancer cells develop an ability ‘hide’ themselves from the immune system
  - via various mechanisms (create a ‘cloak’ around themselves)
  - evade detection (express high levels of proteins like PD-L1)
- Immune system uses T-cells to survey and patrol the body and blood stream for any perceived threat (infection, cancer).
- T cells express proteins like PD-1
- Theory that when a cancer cell binds a PD-L1 protein to a PD-1 protein receptor on a T-cell a ‘don’t attack me’ signal gets created…therefore the tumor cell can grow unchecked

Immunotherapy Concepts

- PD-L1/PD-1 ‘checkpoint’ is one of multiple potential targets for immunotherapy (monoclonal antibodies seek and bind there)
  - When bound the ‘don’t attack me’ signal sent by the tumor cell is diminished/eliminated
  - Now the T-cells can activate/recognize/kill AND then remember the cancer cells (can provide a durable response)

PD-1 Blockade with Cemiplimab in Advanced Cutaneous Squamous-Cell Carcinoma

Authors: Michael R. Migden, M.D., Danny Rischin, M.D., Chrysalyne D. Schmults, M.D., Alexander Guminski, M.D., Ph.D., Axel Hauschild, M.D., Karl D. Lewis, M.D., Christine H. Chung, M.D., +29 , and Matthew G. Fury, M.D., Ph.D.Author Info & Affiliations

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VOL. 379 NO. 4

-Phase 2 study showing promising results in patients with advanced cutaneous SCCA deemed inoperable and not amenable to radiation

-Positives:

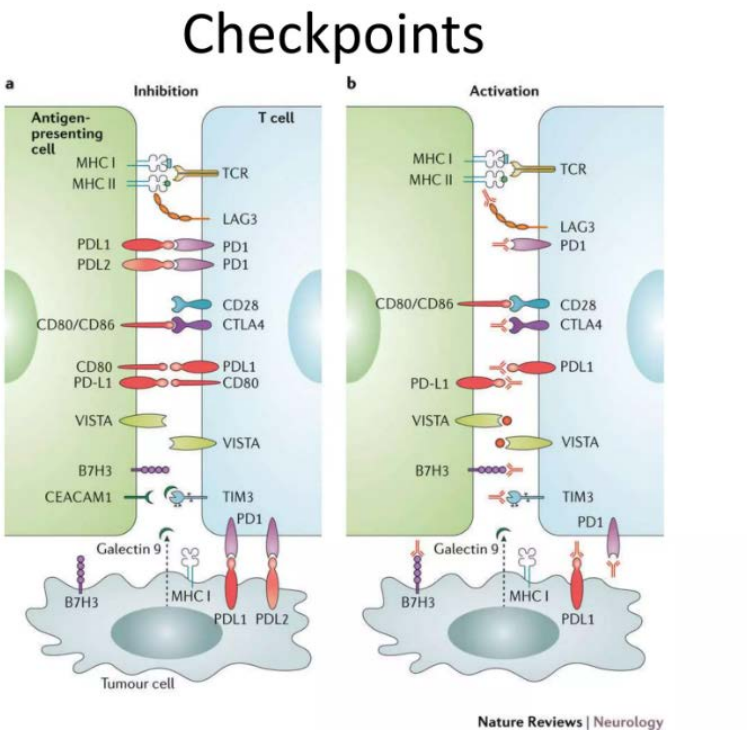
- -reasonable and durable response rates (42% and 82%)
- -manageable and tolerable side effects (typical GI, fatigue, nausea)

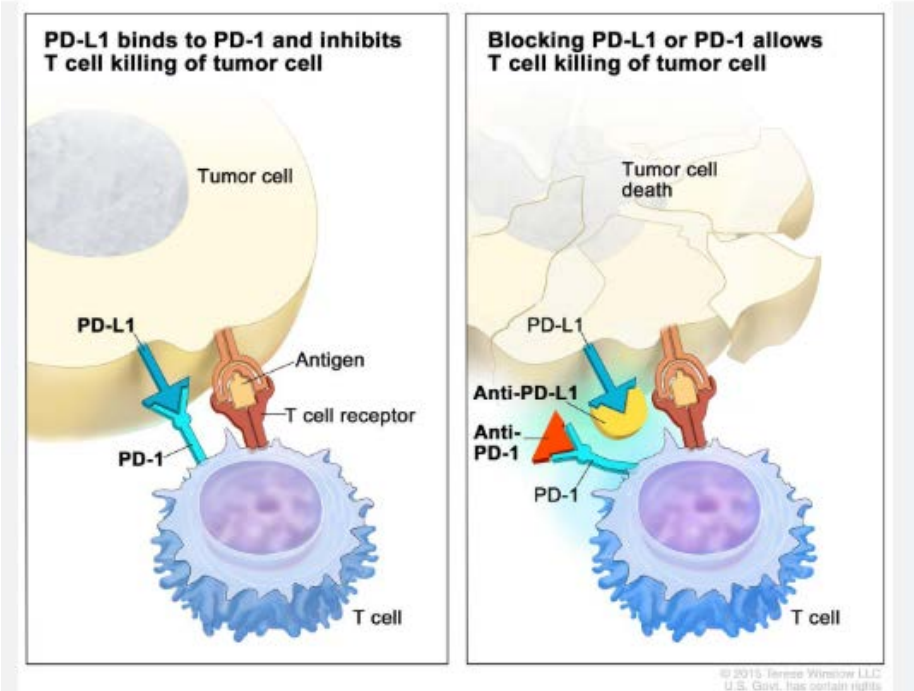
-Negatives

- -non randomized

In 2018, the FDA approved cemiplimab as the first programmed cell death-1 (PD-1) monoclonal antibody for the treatment of patients with metastatic CSCC or locally advanced CSCC who are not candidates for curative surgery or curative radiation

Check point blockade





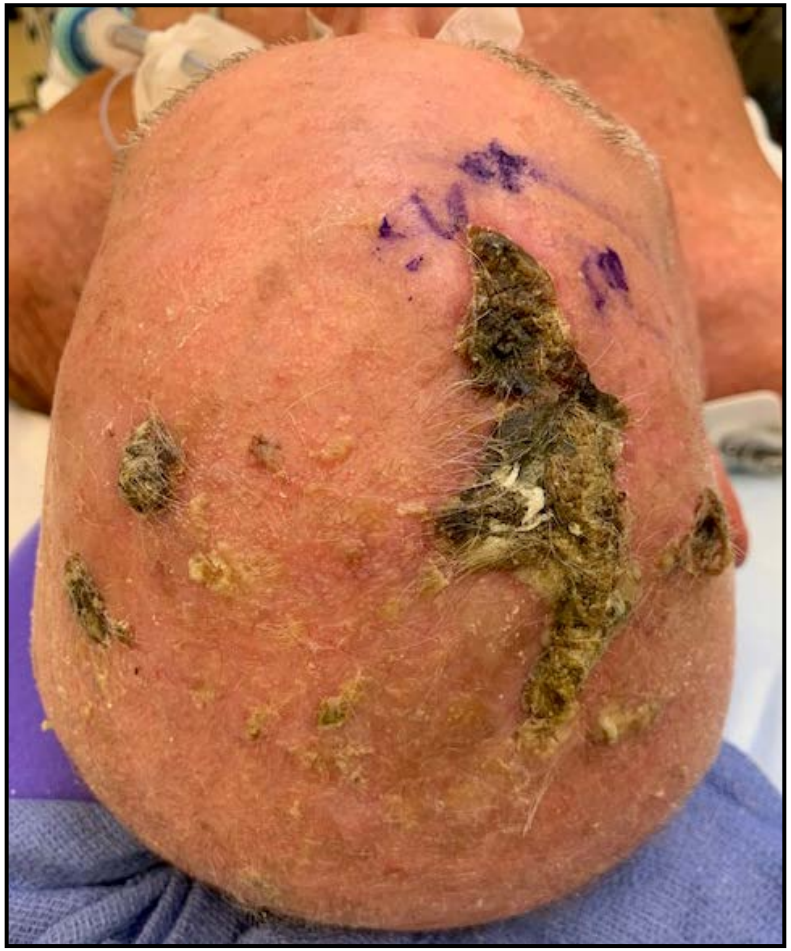
Outline

- Case 1
  - Surgical treatment of advanced scalp SCCA treated with multiple Mohs procedures, XRT and then referred
- Case 2
  - Nonsurgical management of advanced naso/facial/orbital/sinus/anterior skull base BCC
    - Vismodegib (Erivedge)
- Case 3
  - Nonsurgical management of advanced scalp SCCA with sagittal sinus involvement
    - Pembrolizumab (Keytruda)-→Complete clinical and radiographic response
- Case 4
  - Nonsurgical management of recurrent advanced scalp SCCA s/p multiple Mohs, recurrence, XRT, persistent/recurrence in proximity to sagittal sinus
    - Cemiplimab (Libtayo)-→ICU admission with hepatitis and encephalitis with SNF

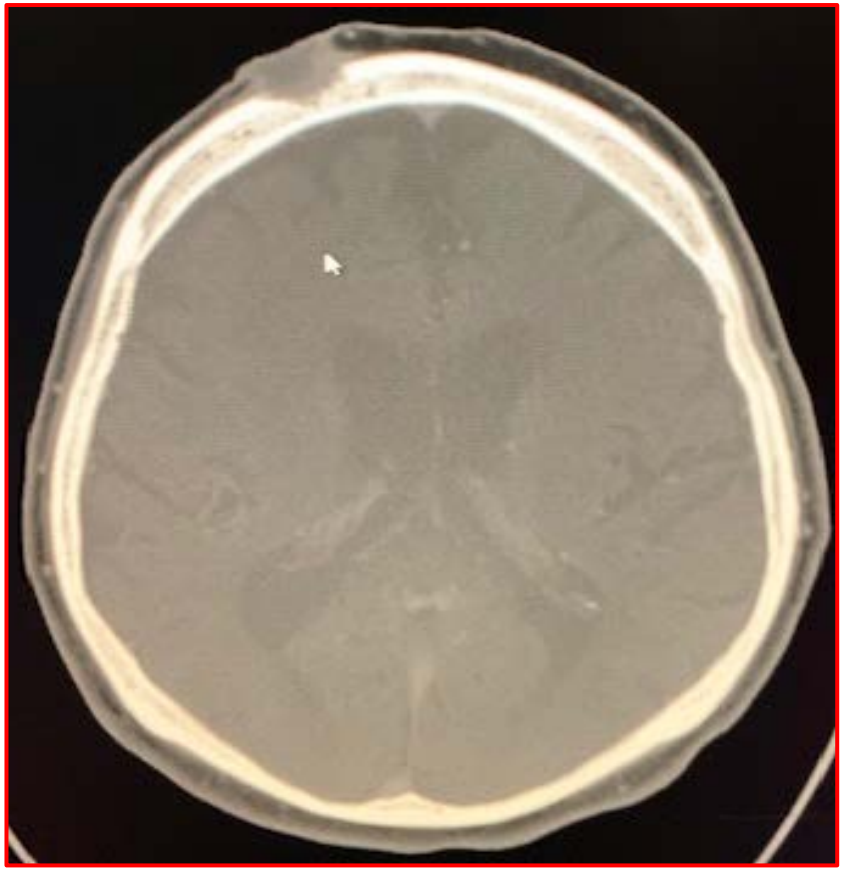
Case 1

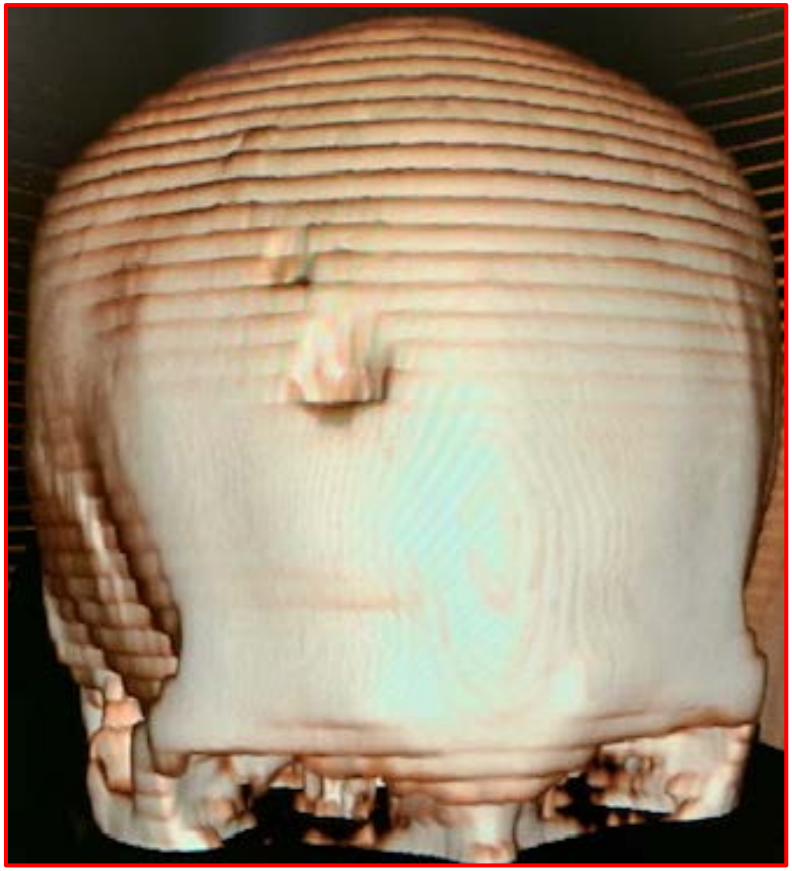
- Ca hx: 67 y/o M hx scalp SCC, multiple prior scalp resections/curretage/XRT
- Exam: BMI 24, diffuse scalp lesions w/ satellitosis, some scalp attachment to underlying bone
- PMHx: liver transplant (1998), kidney transplant (2015) , CAD, MI, stents x 4
- Meds: ASA, prednisone, sirolimus

Extensive, multifocal, locally aggressive, recurrent spindle squamous cell carcinoma



Multi-focal radiographic erosion to level of inner table





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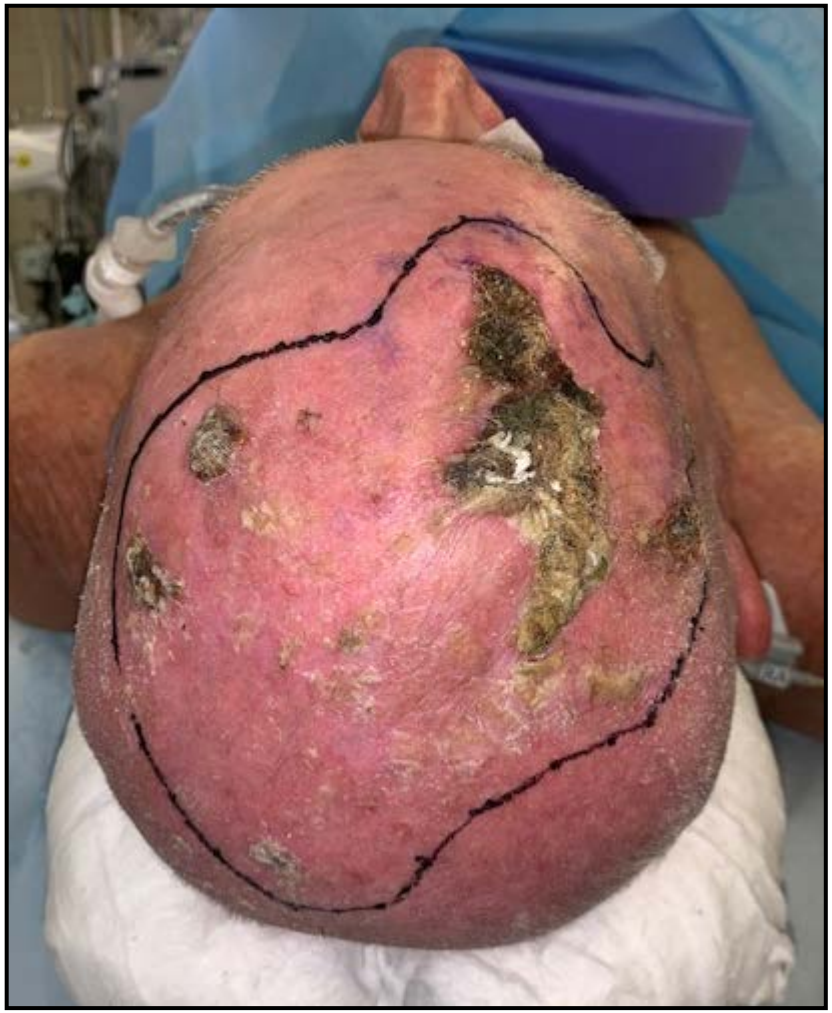
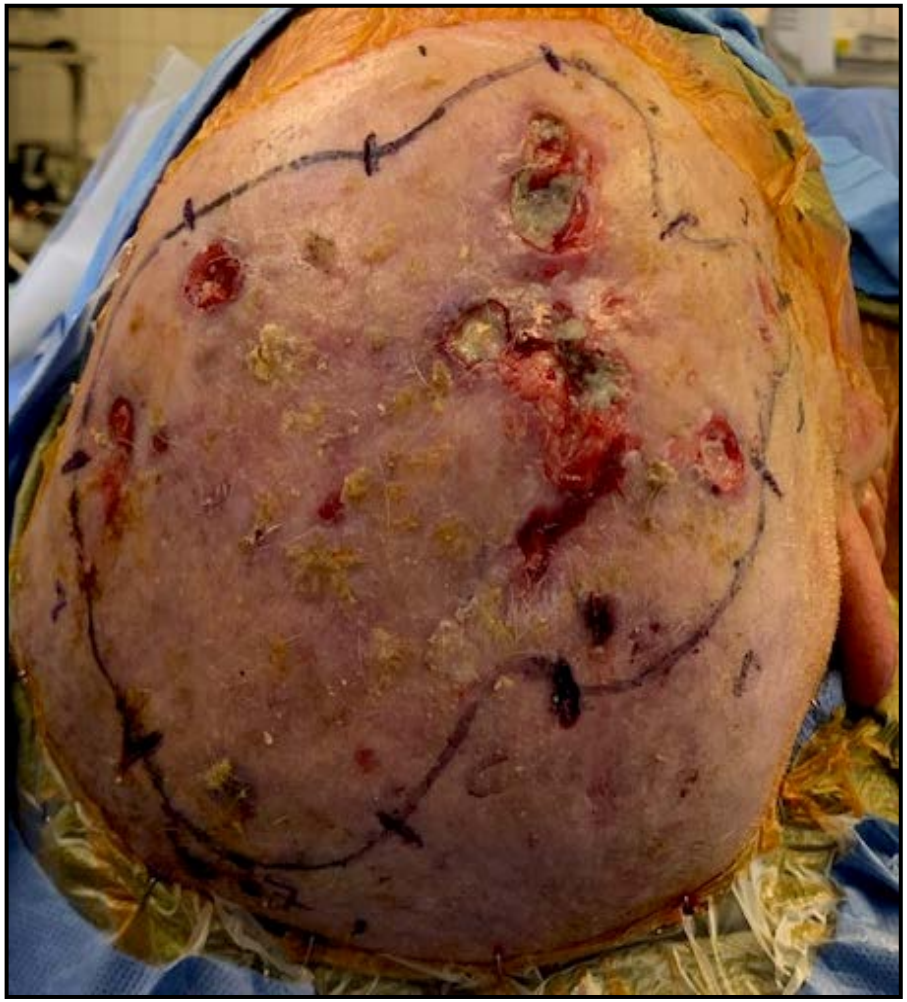
CASE
COMPREHENSIVE CANCER CENTER
A Comprehensive Cancer Center
Designated by the National Cancer Institute

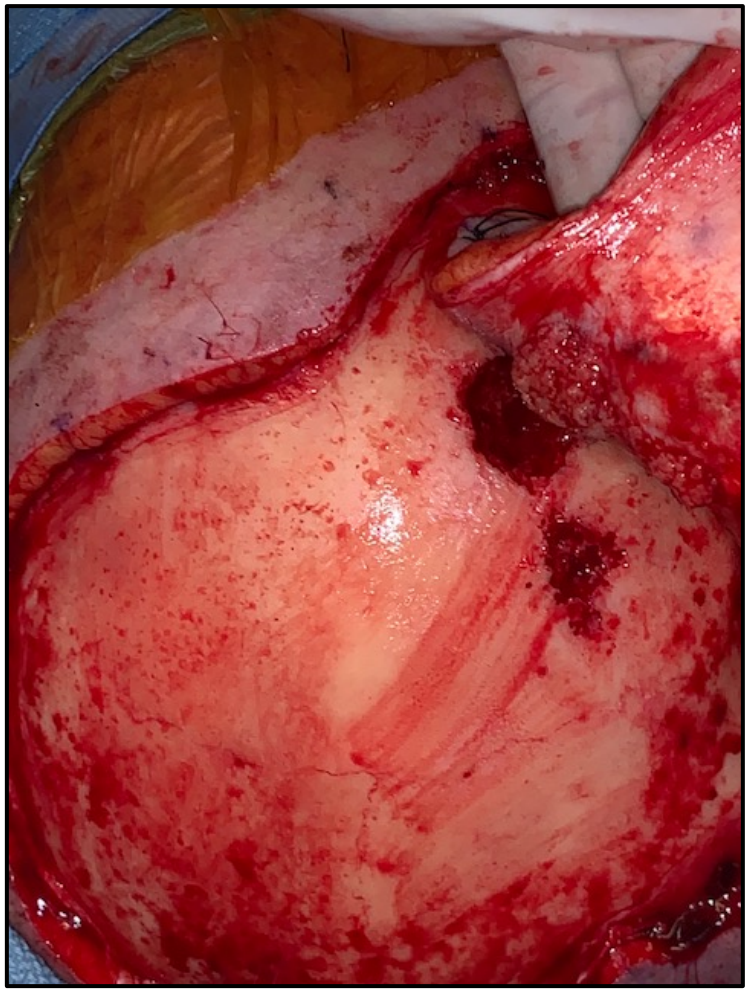
Multidisciplinary TB

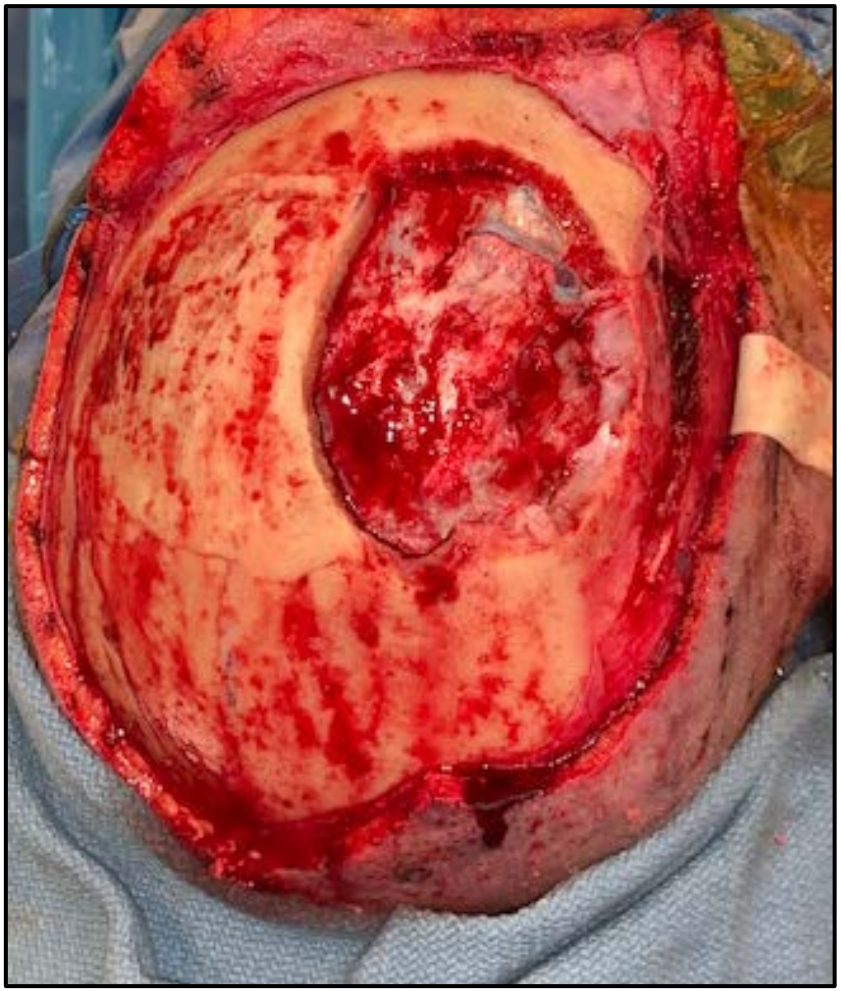
- Surgery
- Consider systemic treatment
- Post operative adjuvant treatment based on pathology and intraop findings
- Patient agreed



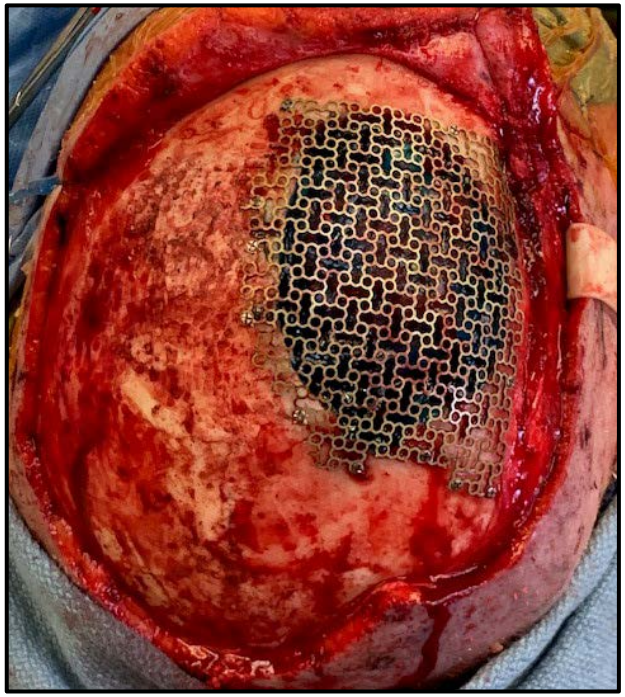


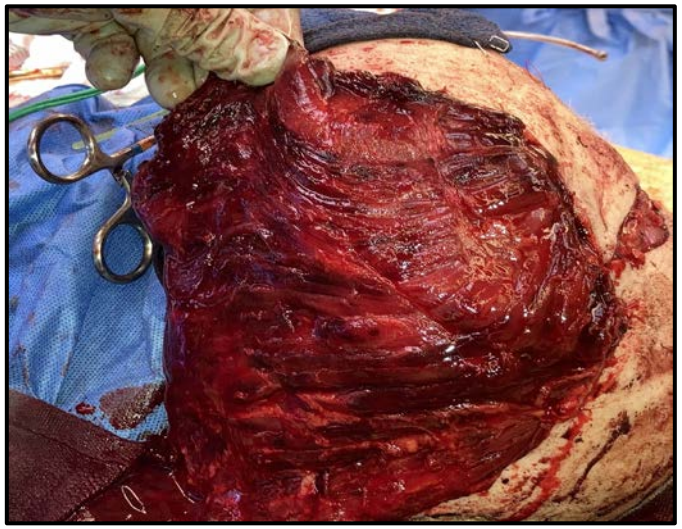
Local skull invasion confirmed—>craniectomy with dural repair

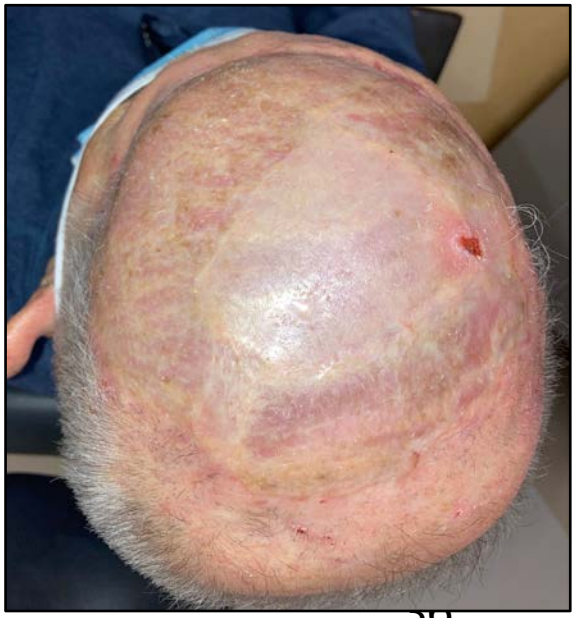




Reconstruction





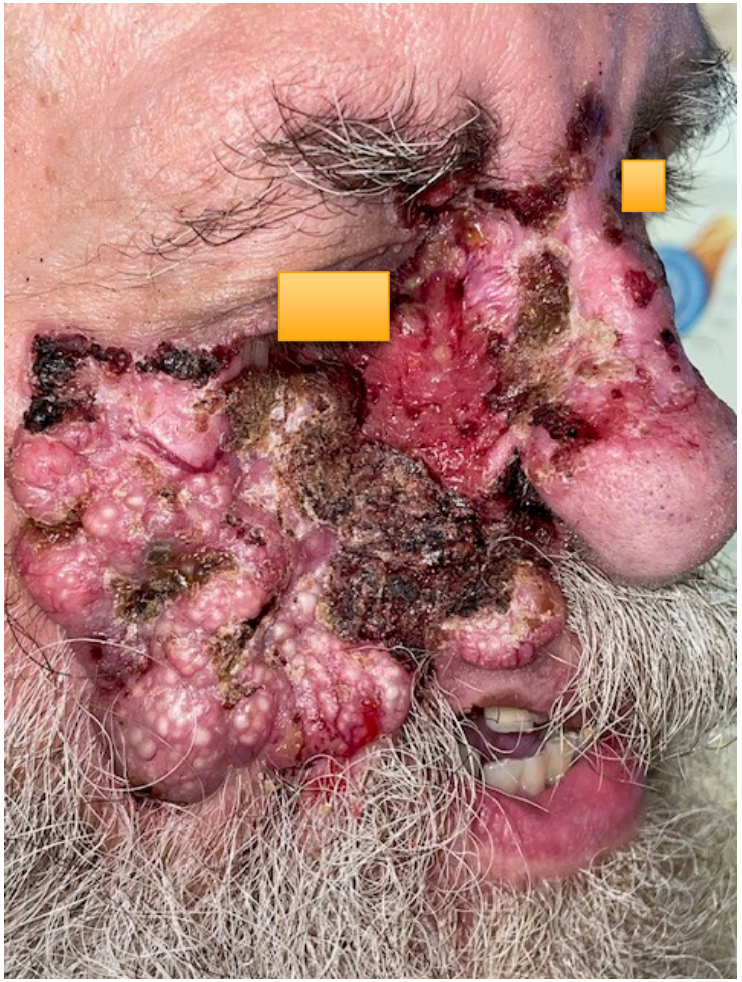


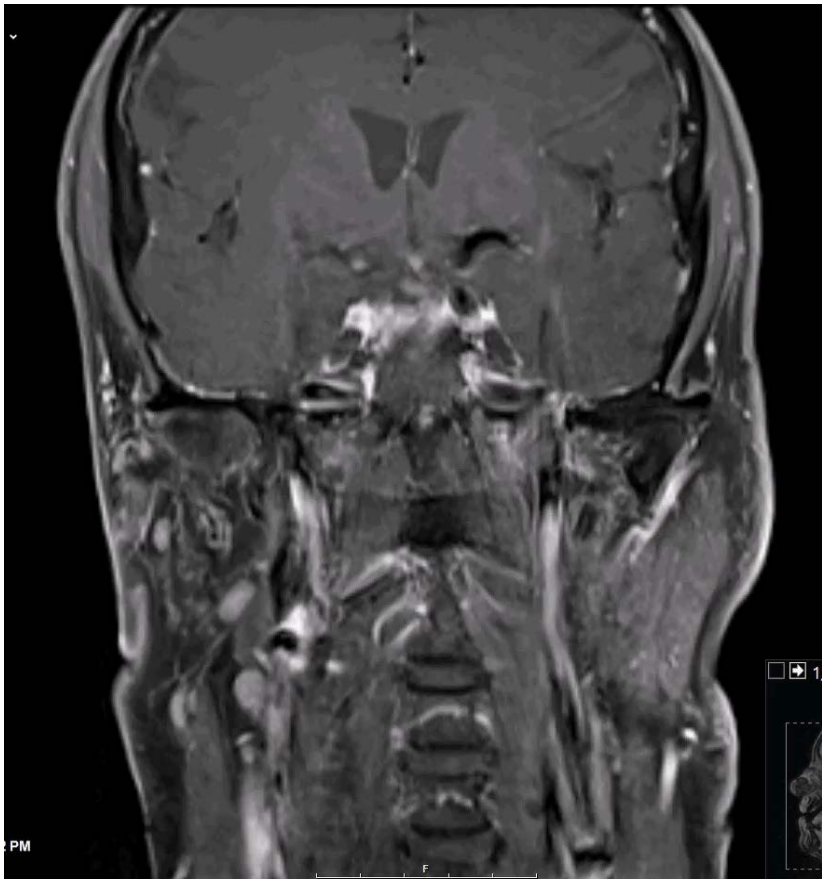
Questions to consider

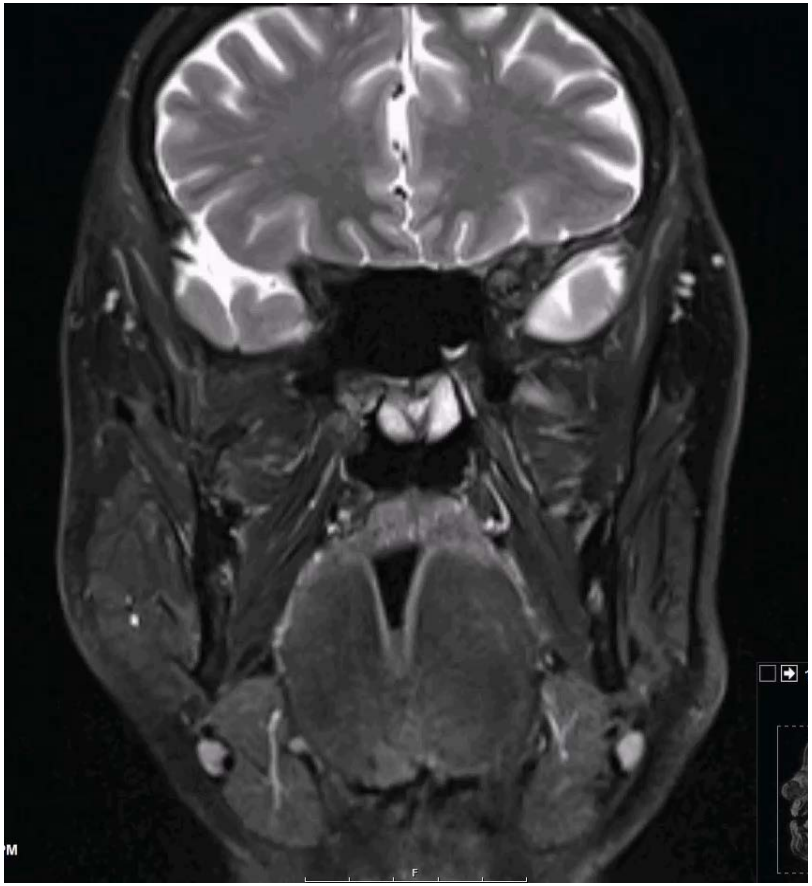
- Role of Mohs
  - Primary
    - Extent of lesion, fixation, etc.
  - Recurrent
  - Preop to determine margins
- Role of XRT
  - After Mohs failure?
  - Post op?
  - Re-irradiation
    - Type?
- Transplant History
  - Role of immunotherapy?

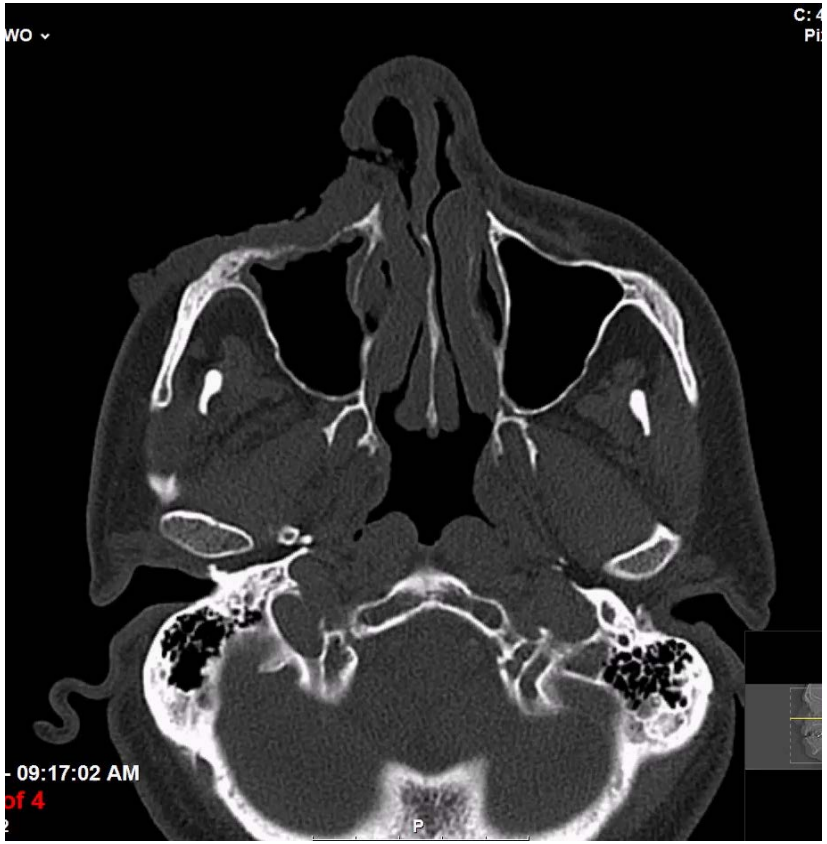
Case 2: Advanced Basal Cell Carcinoma

- 75 y/o male with several year history of right facial lesion
- Initially thought to be a ‘boil’
- Treated conservatively
- Insurance challenges prevented seeking care
- Biopsy--→ BCC
- TB discussion: surgery vs systemic tx





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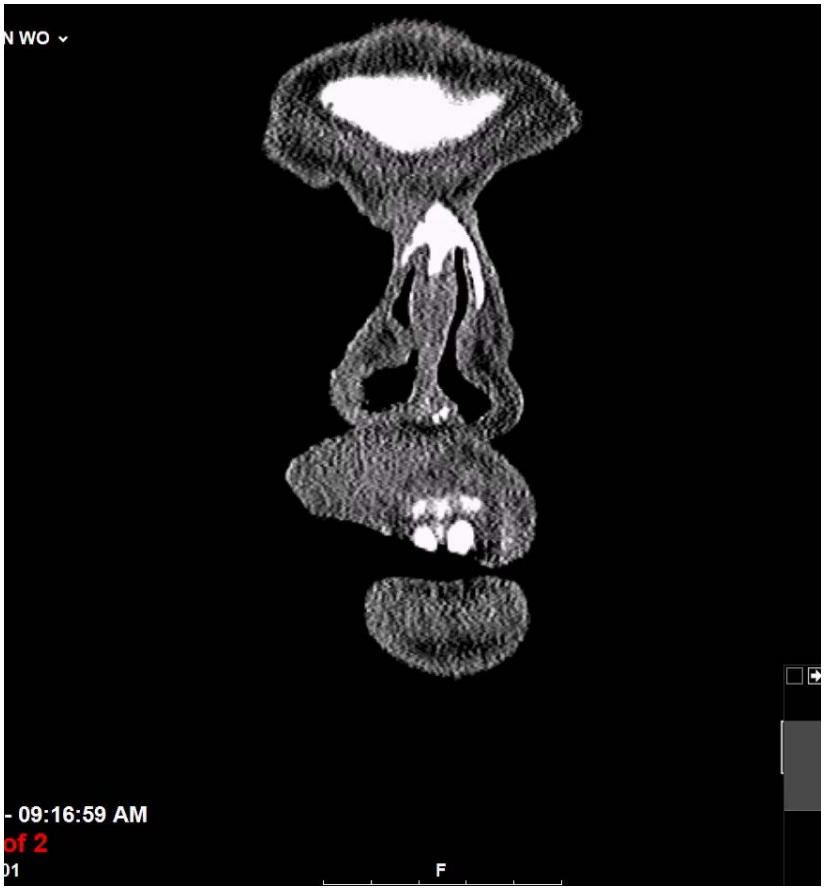
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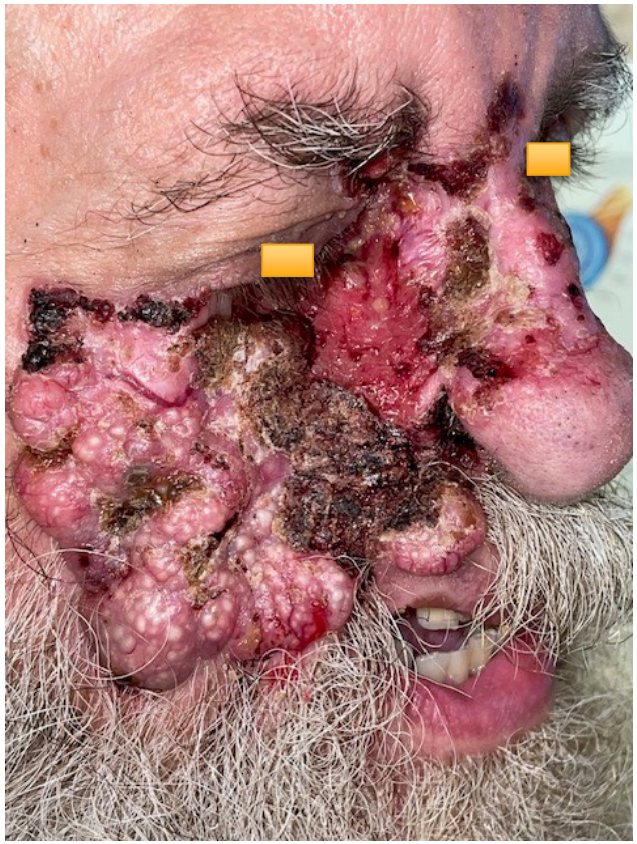
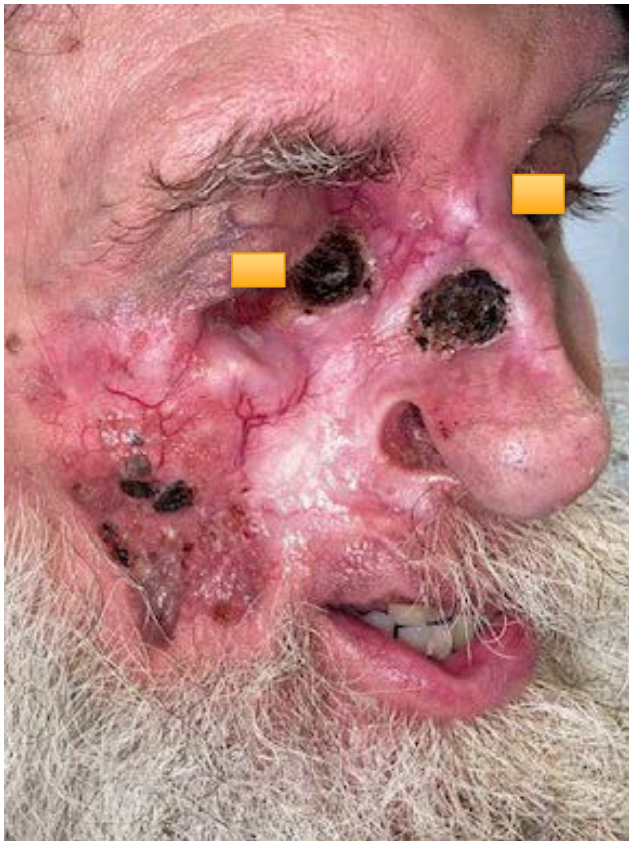
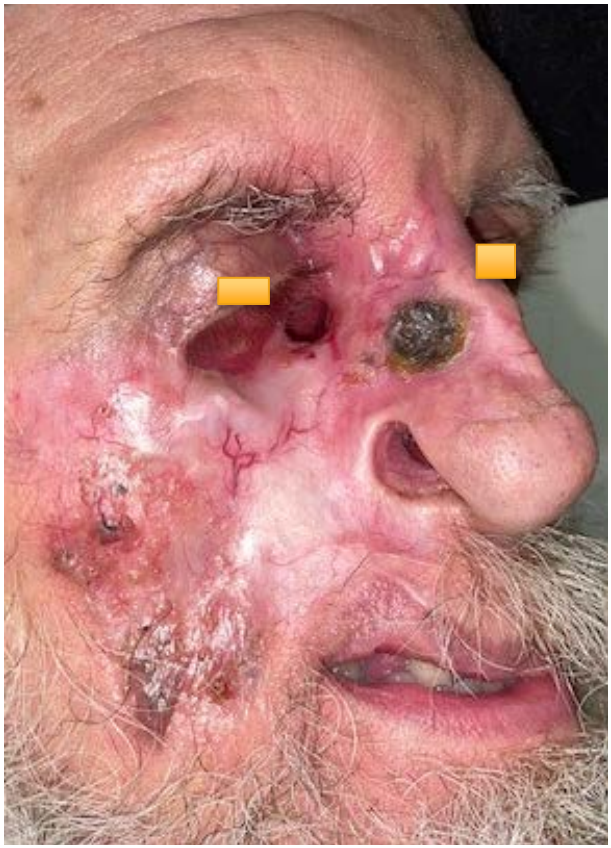
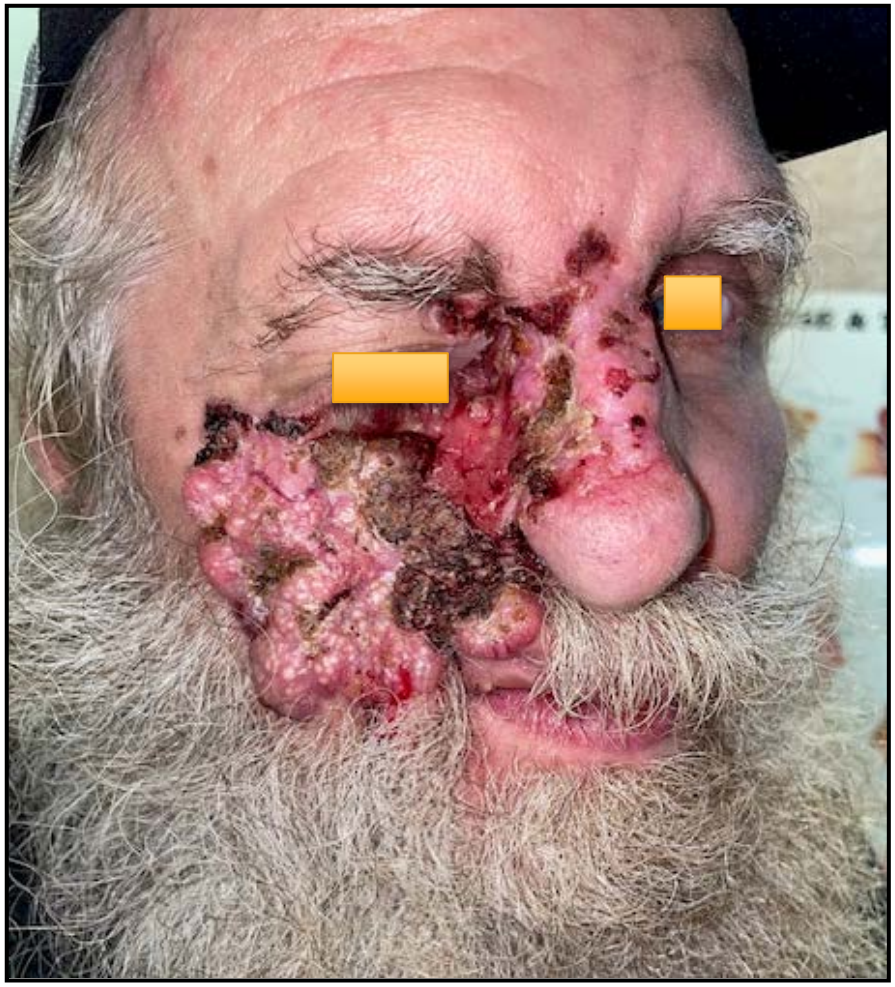
Vismodegib (Erivedge)

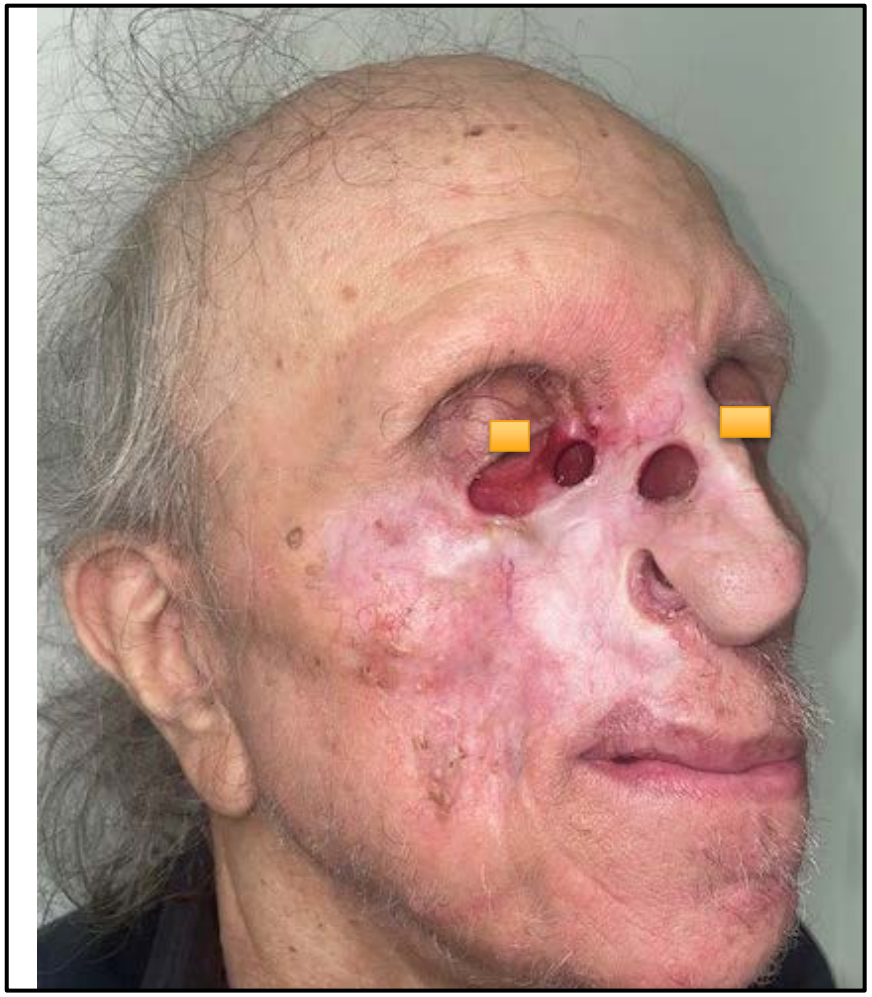




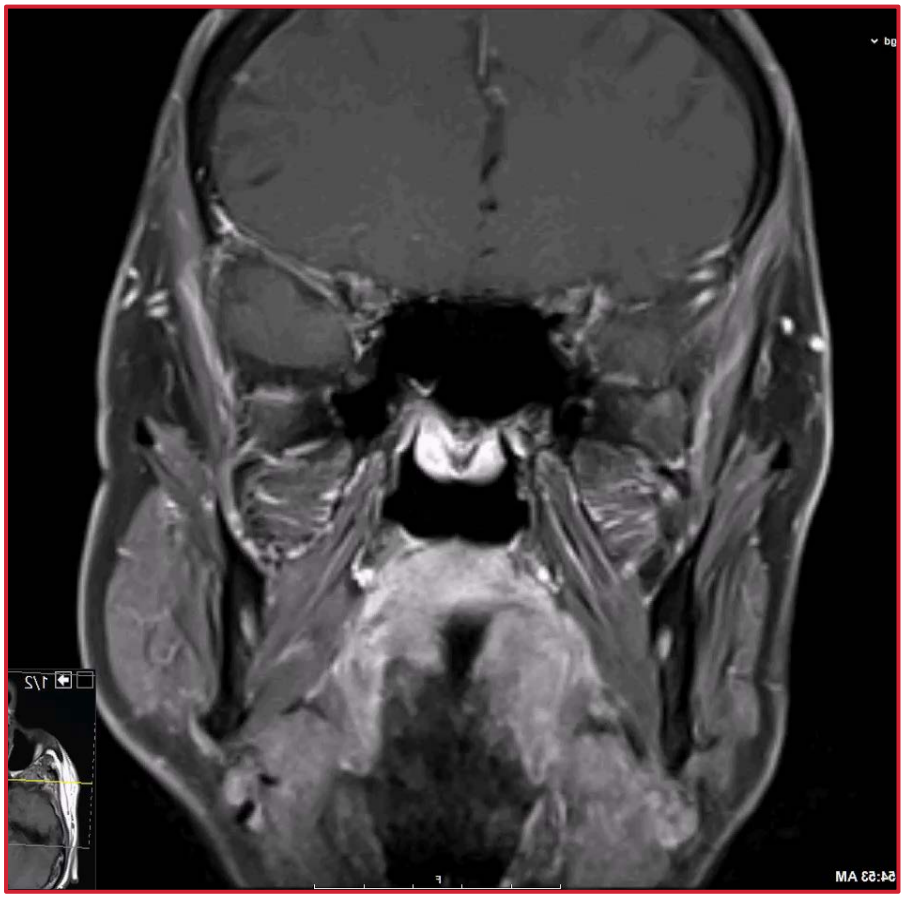


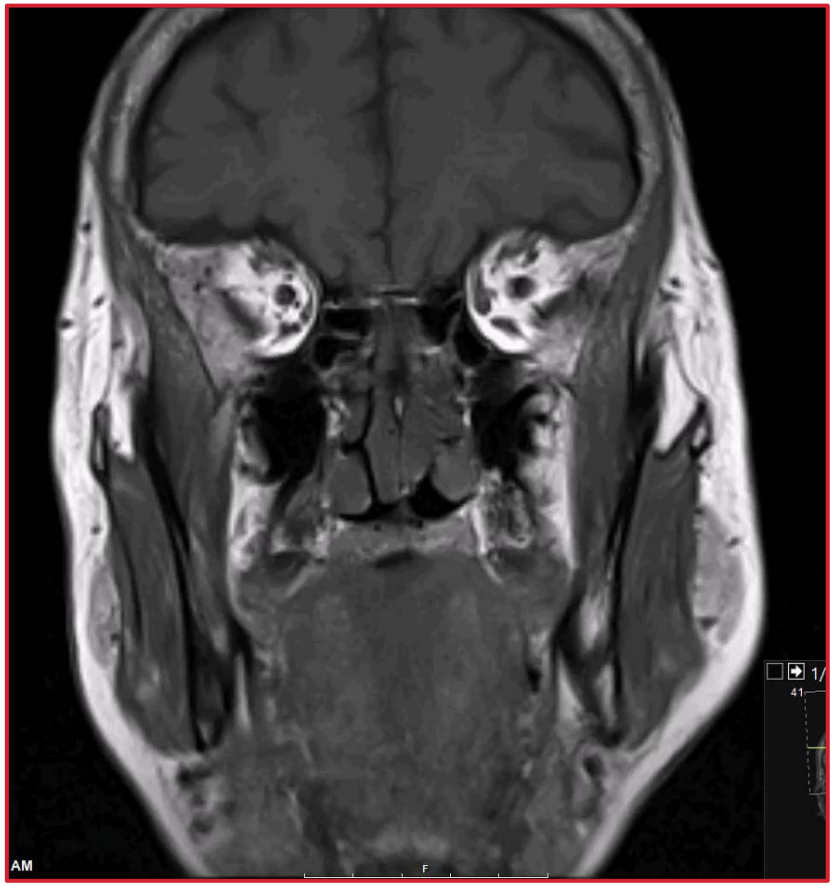
12 months





12 month scans



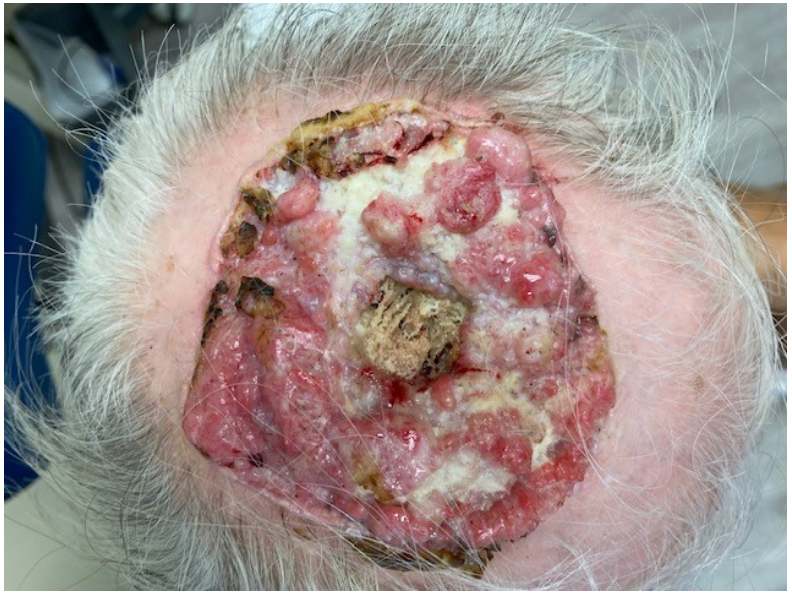


Questions to consider

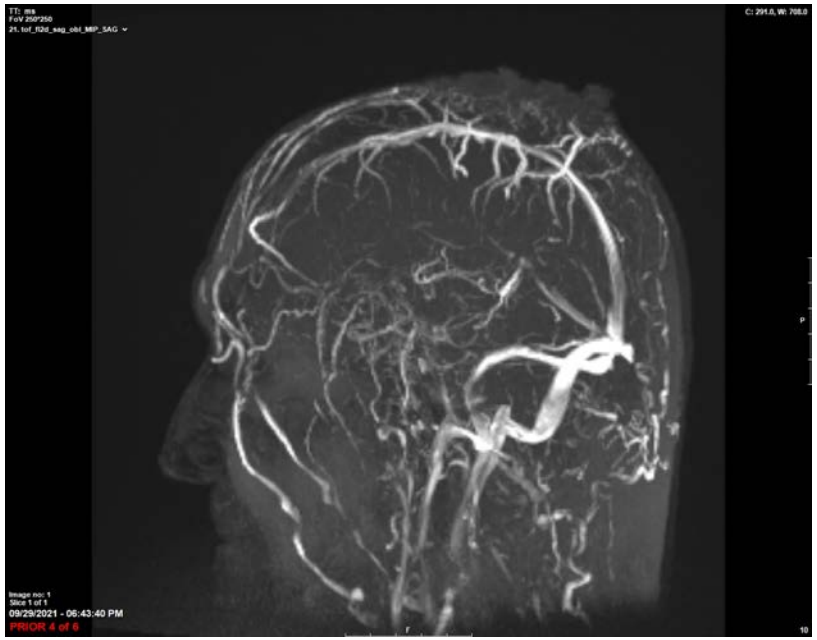
- Duration of treatment?
- Management of toxicities?
  - Fatigue, MSK pain, weight loss, alopecia, GI, etc
- Cost?
  - Patient approved for compassionate use
- Frequency and type of imaging?
- Role and timing of surgery?
- Role of biopsy?
  - Concentric regression vs residual nests

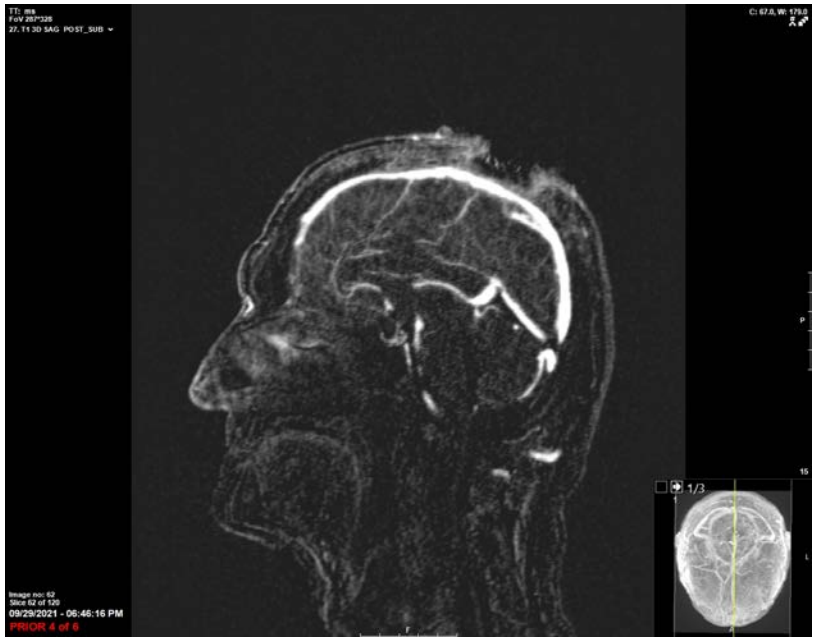
Case 3: Advanced SCC scalp with Sagittal Sinus Involvement

- 73 y/o male with 9 month hx of enlarging friable lesion of the scalp. Referred my Mohs surgeon for evaluation of resection
- PMHx: HTN, High Cholesterol, CAD/MI
- PSHx: CABG
- Presented at Cutaneous Oncology Tumor Board

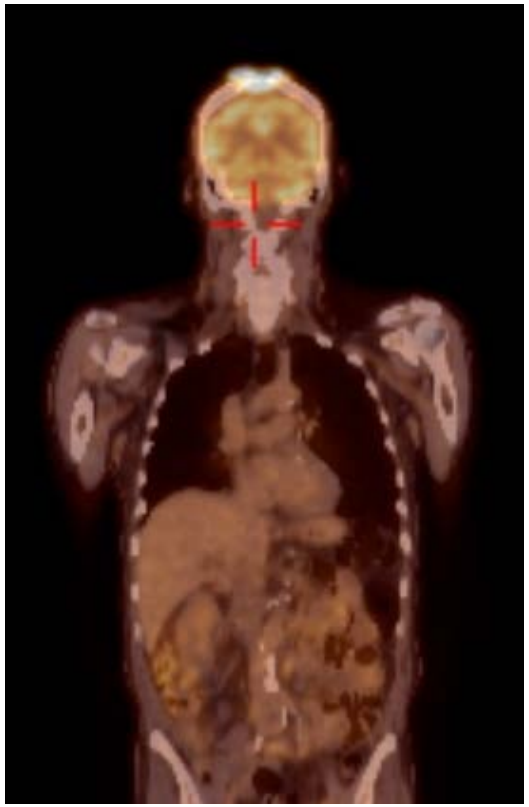


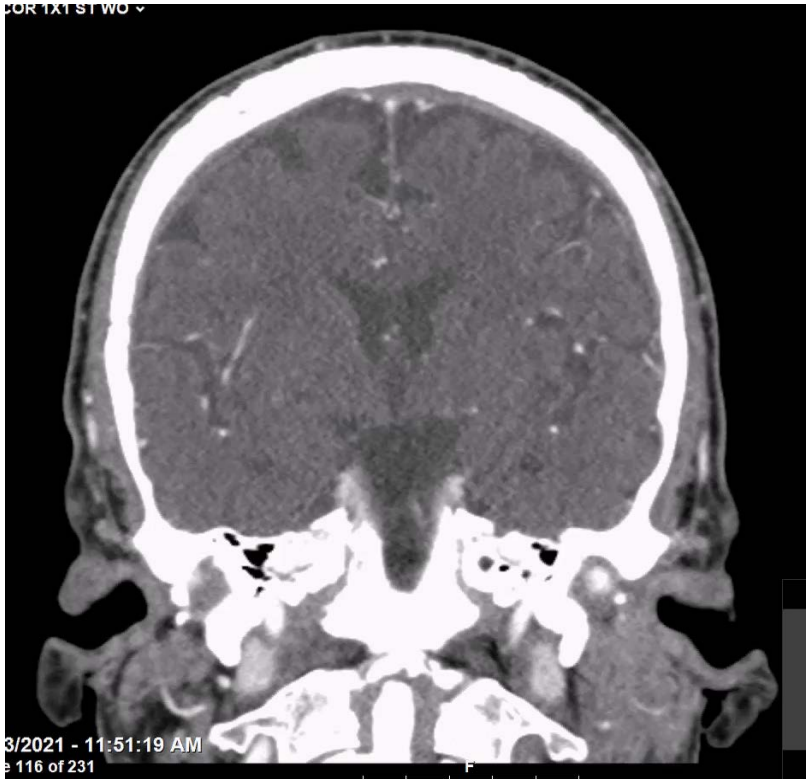
MR Venography



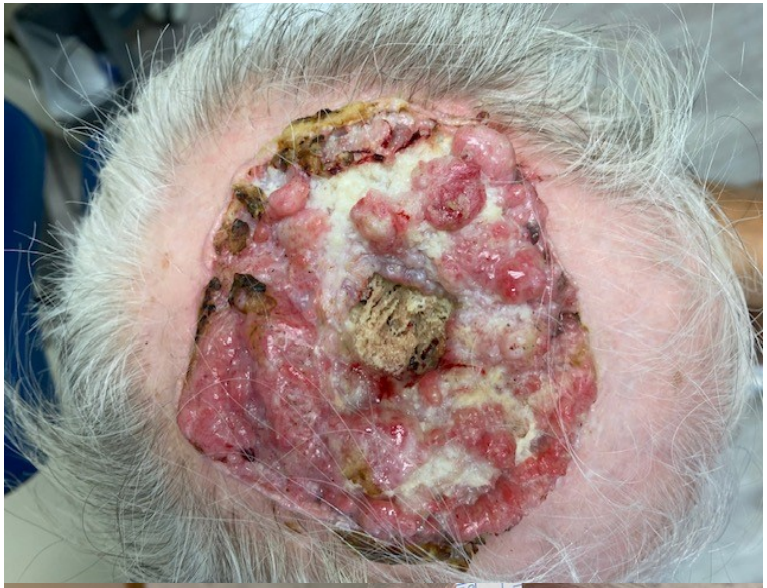


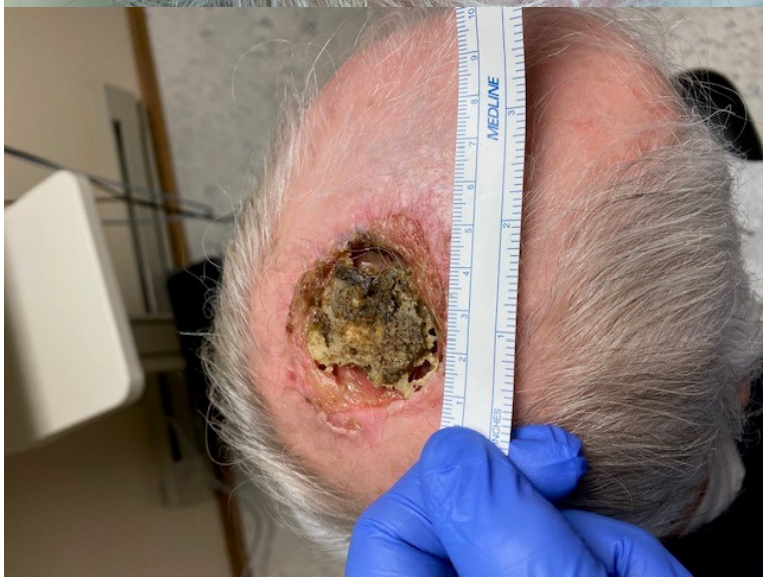
PET/CT Scan





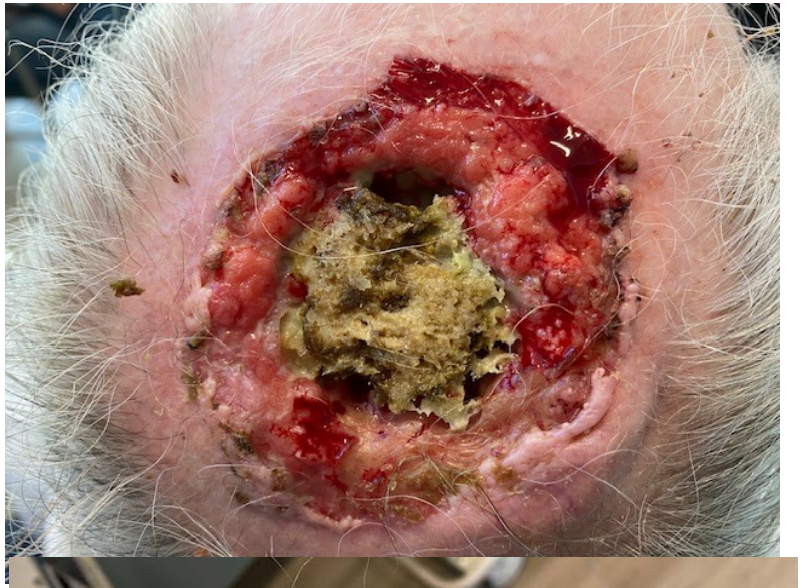
Initial Presentation

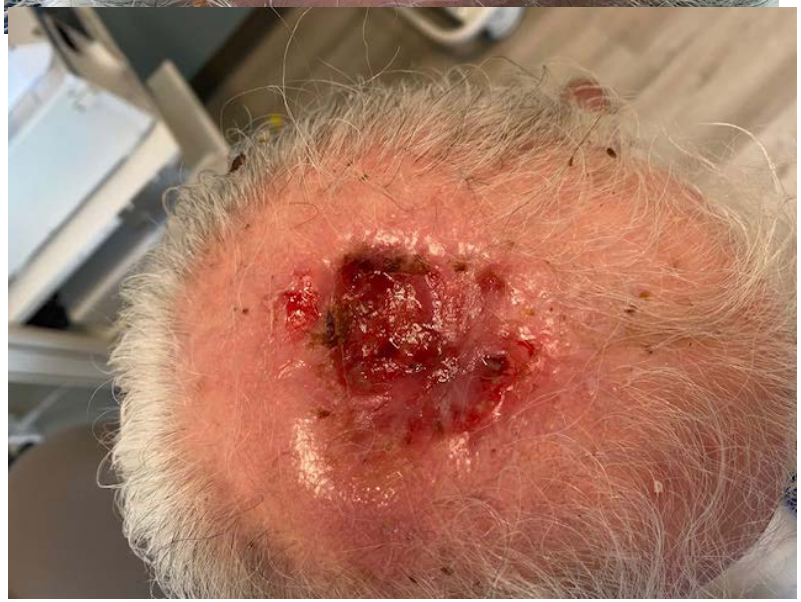




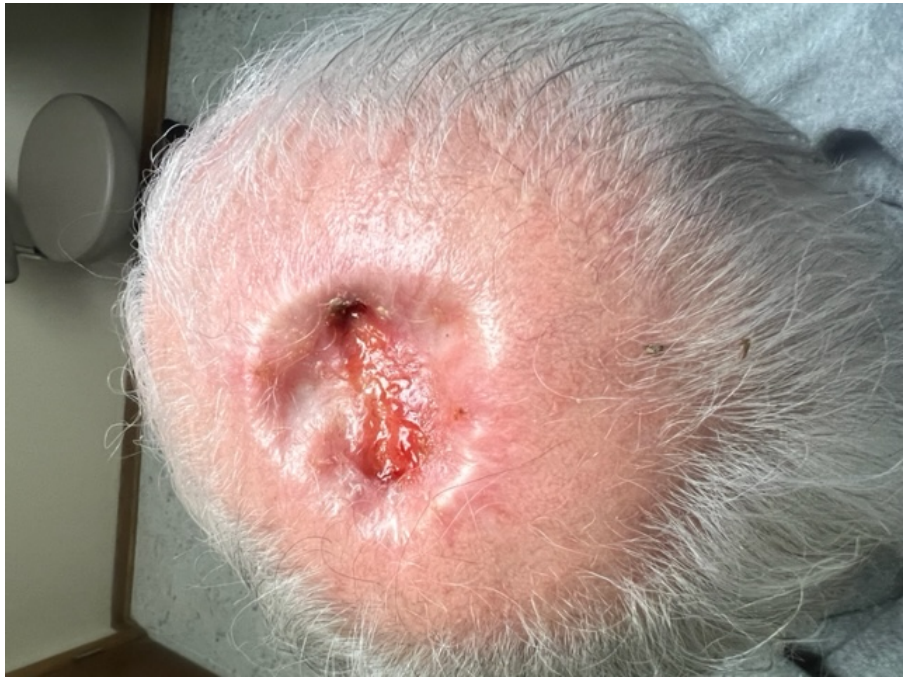
3 cycles

2 cycles pembro

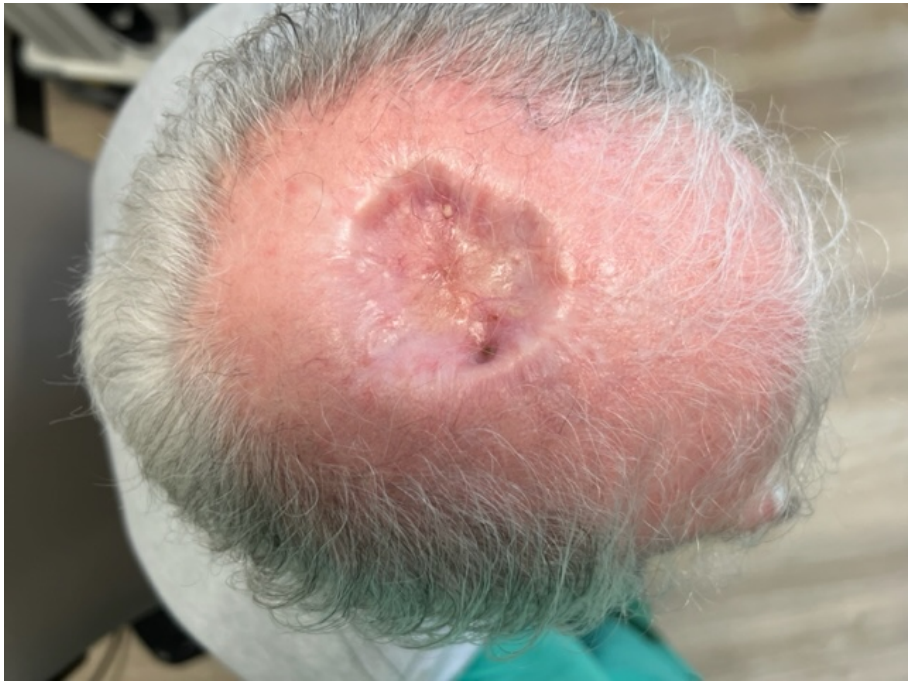




4 cycles

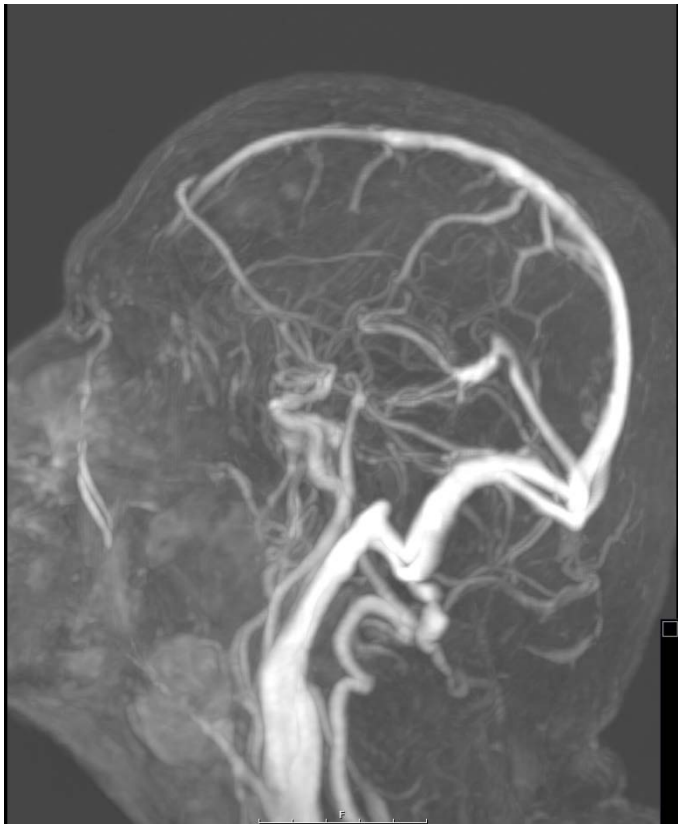


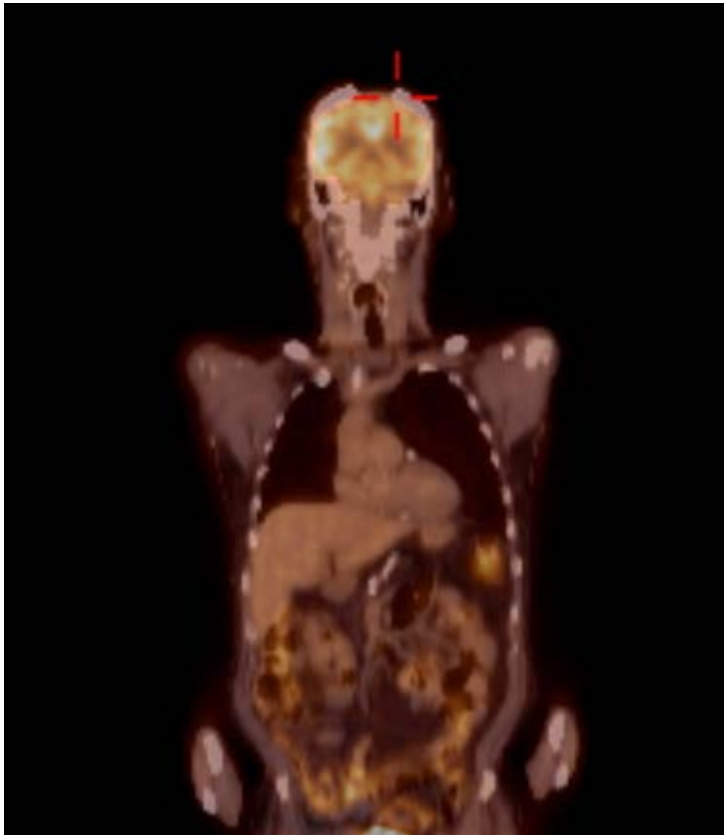
10 cycles



20 cycles

1 year scans





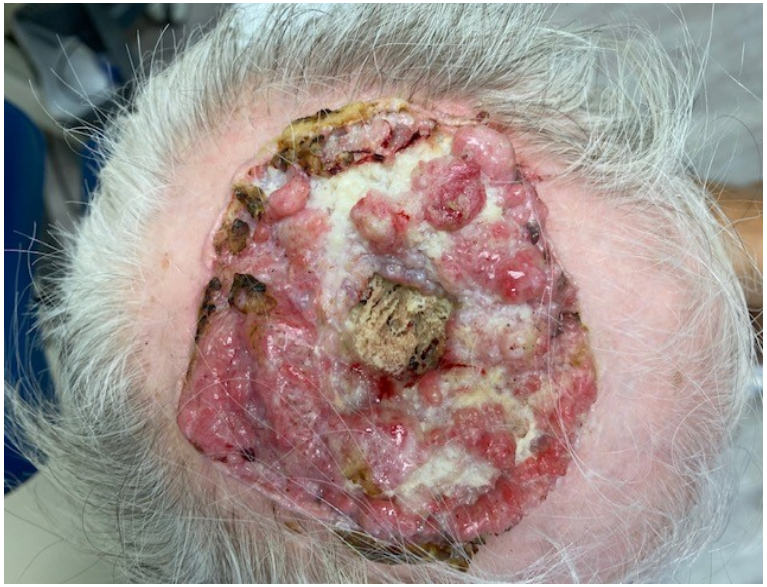
Questions:

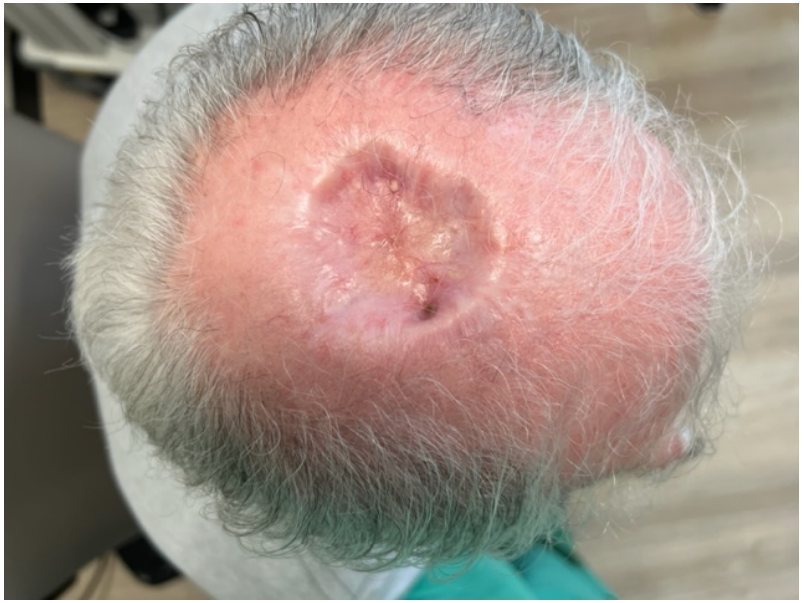
Duration of treatment?

Management of toxicity?

Cost?

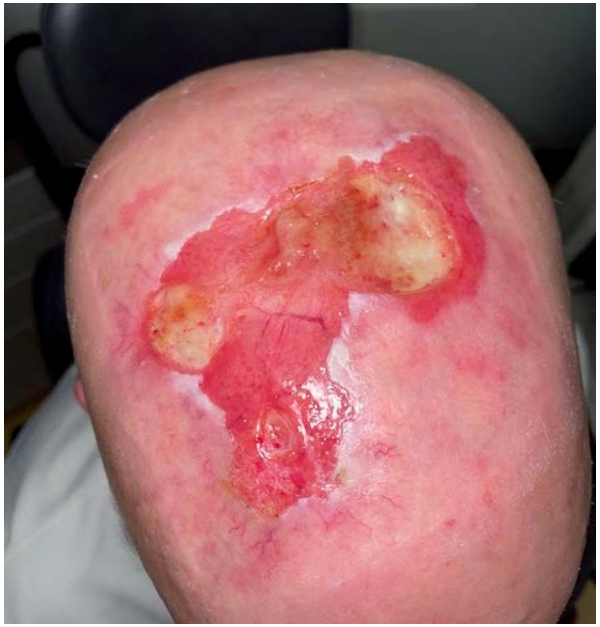
Frequency and type of imaging?

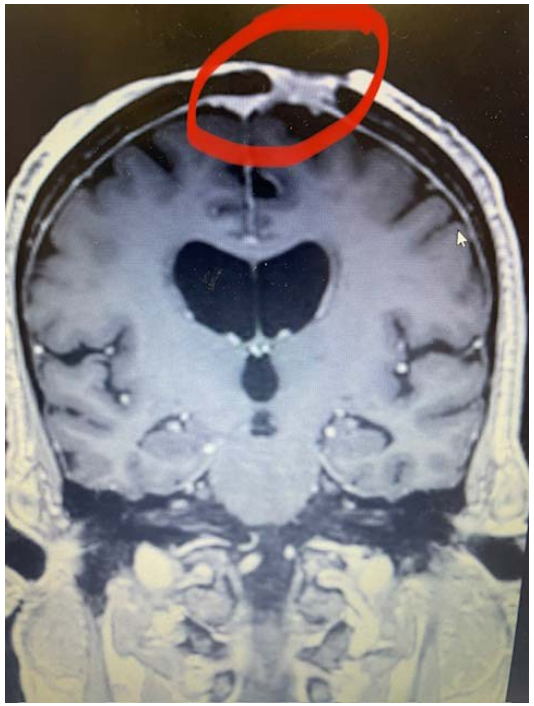




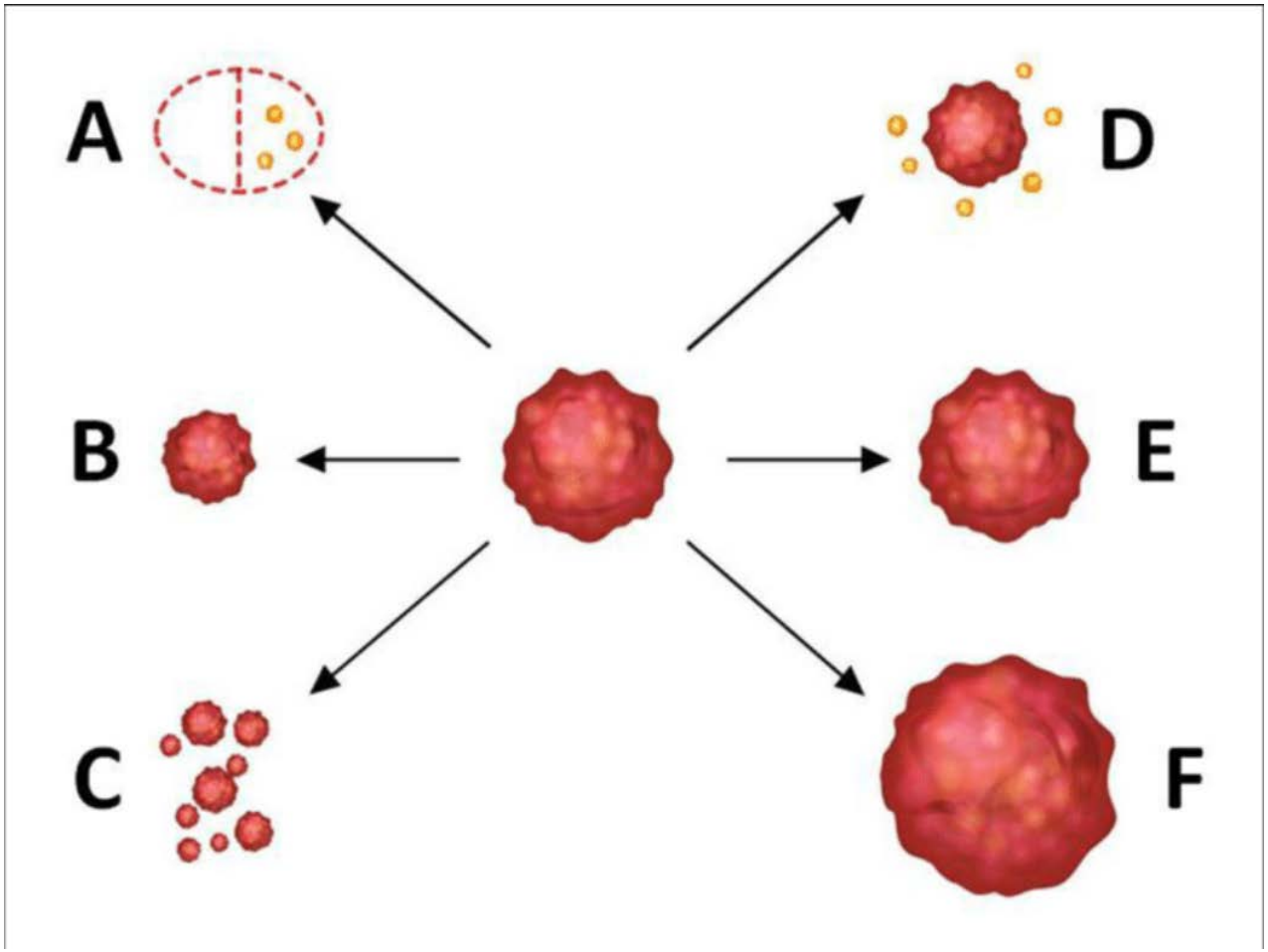
Case 4

- 76 y/o male s/p multiple Mohs procedures for large scalp SCCA, recurrence, XRT, ‘wound issues’ treated with PRP injections, referred for surgical evaluation
- Treated with Cemiplimab
  - ICU admission for hepatitis, encephalitis, colitis, discharged to SNF





Future Directions: Response Adaptive Surgery?



Thank You!