University of CINCINNATI

Acquiring Remnant Tissue for Research Purposes

Thursday, May 16th, 2024

University of CINCINNATI

Compliance Corner

Recently updated Clinical Research SOPs:

- **UCH-OCR-OPS-SOP-017- Linking in EPIC for Clinical Research**

All OCR SOPs are accessible at the following link.
And from the UC Health intranet home page utilizing the Policy Portal Search function or reach out to the Office of Clinical Research with any questions or concerns.

OCR CRP First Friday June 2024

Overview of the Center for Clinical & Translational Science & Training (CCTST)

Dr. Achala Vagal, MD
Co-Chair CCTST
Executive Vice Chair and Vice Chair of Research, Radiology

Dr. Jeffrey Strawn, MD
Co-Chair CCTST
Professor & Associate Vice Chair of Research, Psychiatry & Behavioral Neuroscience

UC / UC Health
Clinical Research Orientation and Training (CRO&T)

Thursday, June 13th, 2024

9:00 am - 3:00 pm

IN PERSON presentation

MSB Room 6051

The last day of registration is

Friday, June 7th, 2024

Register **Here**

Please reach out to Nate Harris,
harrisnl@ucmail.uc.edu for any questions

UC/UCH Clinical Research Professional

OTR Stillhouse
2017 Branch St, Cincinnati, OH 45214

Thursday, June 13th, 2024
5:00pm – 8:00pm

next
lives
here

University of
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Today's Presentation:

Acquiring Remnant Tissue for Research Purposes

In this session representatives from the Department of Pathology will provide an overview of the preferred procedure for acquiring remnant human tissue for research purposes.

The discussion will focus on the process by which a human tissue specimen procured for the purposes of clinical management is determined to be remnant prior to the release of the tissue or any portion of the tissue for research purposes.

The intent is to ensure that tissue specimens are collected for research in a manner that does not compromise the diagnostic integrity of a specimen or the ability of the pathologist to determine pathologic stage or other prognostic features.

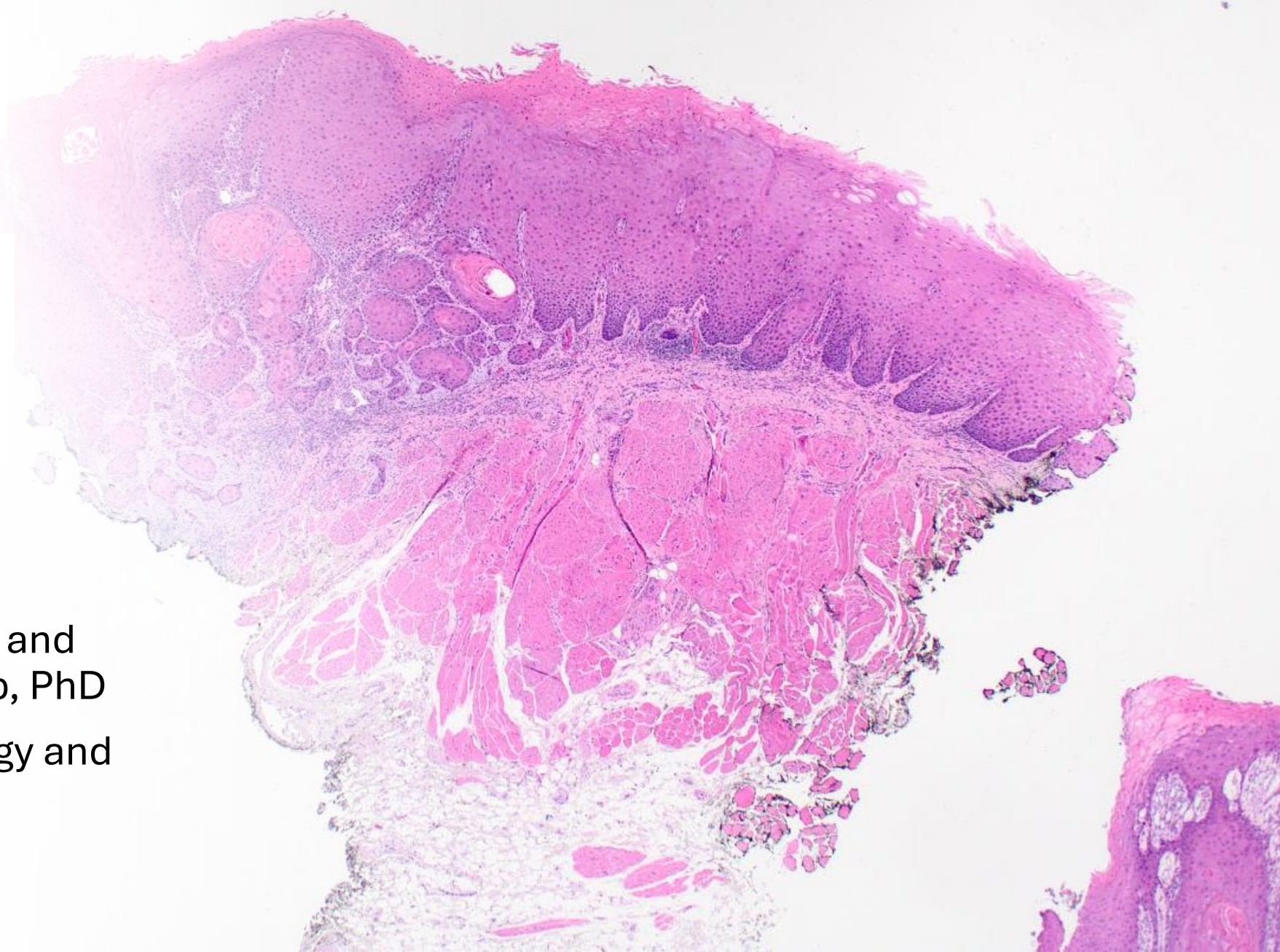
Dr. Kelsey Dillehay McKillip, PhD
Director, University of Cincinnati Biorepository
Technical Director, UC Histopathology Core Laboratory
Pathology & Laboratory Medicine
University of Cincinnati College of Medicine
Department of Biomedical Informatics

Dr. Benjamin Hinrichs, MD
Director of Surgical Pathology
Pathology & Laboratory Medicine
University of Cincinnati College of Medicine

Acquiring Remnant Tissue for Research Purposes

Benjamin Hinrichs, MD and
Kelsey Dillehay McKillip, PhD

Department of Pathology and
Laboratory Medicine



UC Health

- [X] UCH/ENTERPRISE
- [ ] UCMC
- [ ] WCH
- [ ] DRAKE – LTCH
- [ ] DRAKE – BWP
- [ ] DRAKE – SNF
- [ ] DRAKE – OUTPATIENT
- [ ] AMBULATORY/UCPC
- [ ] LEGAL/COMPLIANCE
- [ ] MEDICAL STAFF
- [ ] MEDICATION MGMT
- [ ] OTHER

STANDARD OPERATING PROCEDURE

SOP #	UCH-OCR-REV-SOP-008-04
SOP NAME	Determination of Human Tissue as Remnant Specimen for Approved Research Purposes
ORIGINATION DATE	11/08/2018
SPONSORED BY	Nathaniel L. Harris Clinical Research Administrator, Office of Clinical Research
SPONSORED BY	Kelsey Dillehay McKillip, PhD Department of Pathology and Laboratory Medicine
ADMINISTRATIVE APPROVAL	Maria Stivers, MS Senior Director, Office of Clinical Research
LAST REVIEW/ REVISION DATE	12/07/2023 NEXT REVIEW DATE 12/07/2025

I. STANDARD OPERATING PROCEDURE

- [ ] Administrative
- [X] Interdepartmental
- [ ] Departmental
- [ ] Unit Specific

This document details the procedures for the acquisition of remnant human tissue produced from clinical procedures performed in UC Health facilities for research purposes. This is a system-wide standard operating procedure that applies to clinical research conducted in the facilities of UC Health, LLC, University of Cincinnati Physicians Company (UCPC), LLC, affiliated facilities, and all UC Health associates that conduct clinical research in these facilities.

PURPOSE

- This SOP defines the process by which a human tissue specimen that is procured for purposes of clinical management is determined to be remnant prior to the release of the tissue or any portion of the tissue for research purposes.

- The intent is to ensure that tissue specimens are collected for research in a manner that does not negatively impact patient care. The collection of tissue samples for research should never compromise the diagnostic integrity of a specimen or the ability of the pathologist to determine pathologic stage or other prognostic features

REGULATORY CONSIDERATIONS

- Collection and storage of tissue specimens and/or data for research purposes usually meet the definition of research involving human subjects and may therefore require IRB review and approval. Informed consent and HIPAA authorization for use of data that includes PHI may also need to be obtained prior to the collection and use of tissue specimens for research purposes.

- Documentation of IRB approval or Not Human Subjects Research determination must be provided upon request to the Department of Pathology and Laboratory Medicine, Department of Surgery, UCCC Biospecimen Shared Resource, etc. in order to obtain remnant human tissue for research purposes.

DEFINITIONS AND SCOPE

- **Remnant/Leftover Specimen:** Any remaining portion of a specimen obtained for clinical purposes that is no longer needed for its original purpose and that would otherwise be discarded.
- Human tissues collected specifically for research purposes are **not** within the scope of this policy. Examples of this include but may not be limited to:
    1. Biopsy procedures performed for research (e.g., as part of participation in a clinical trial).
    2. Additional biopsy passes performed specifically for research at the time of a standard of care procedure.

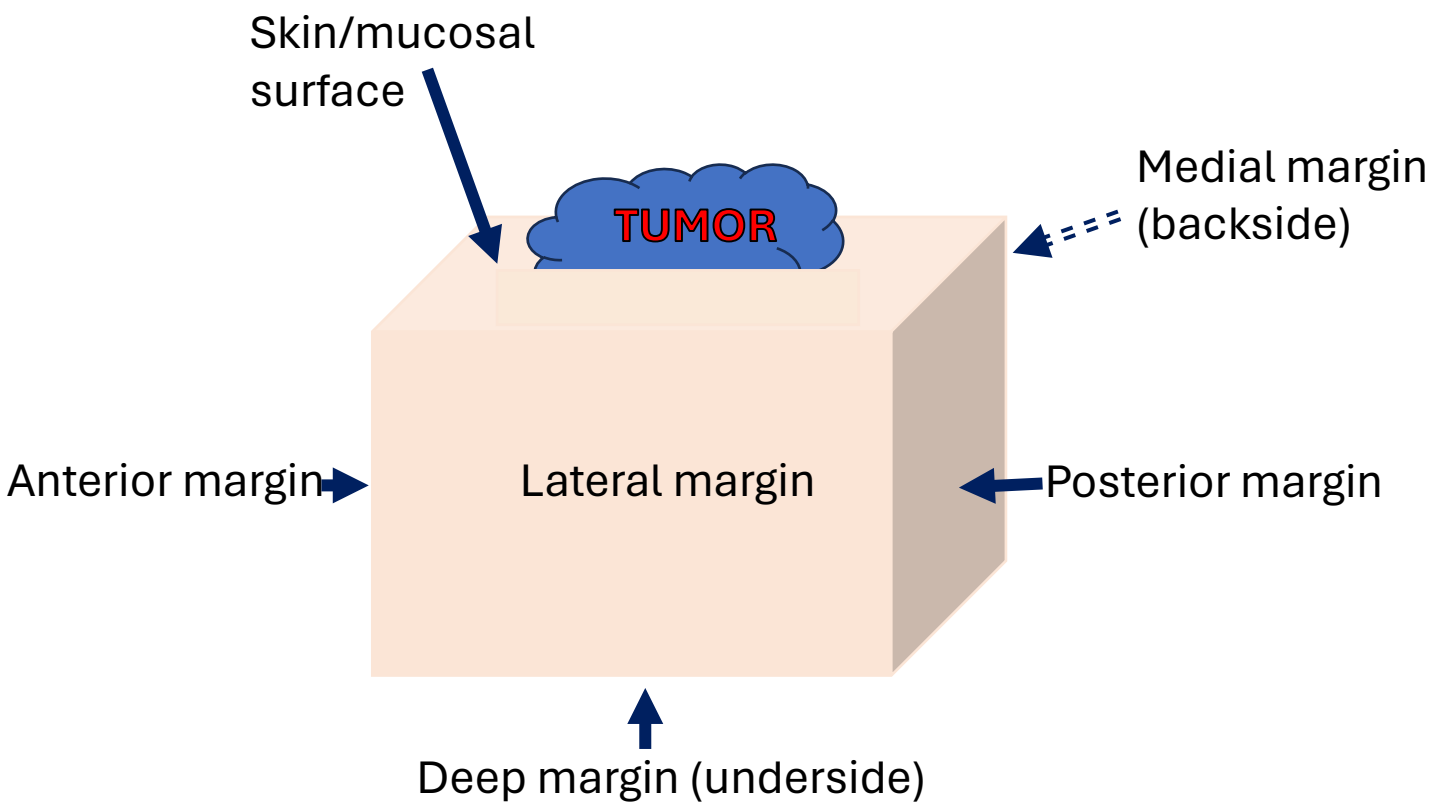
CASE REVIEW

- Patient who was enrolled in a research protocol had surgery as part of their standard of care.
- Specimen was removed from patient and oriented with stitches.
- Communication between surgeon and circulating nurse: conclusion was that the whole specimen was placed in container and then sent to research lab.
- Specimen was dissected/sectioned by research team to obtain a sample of tumor for the research protocol and placed in formalin.
- Remainder of the specimen was discarded in biohazardous waste.

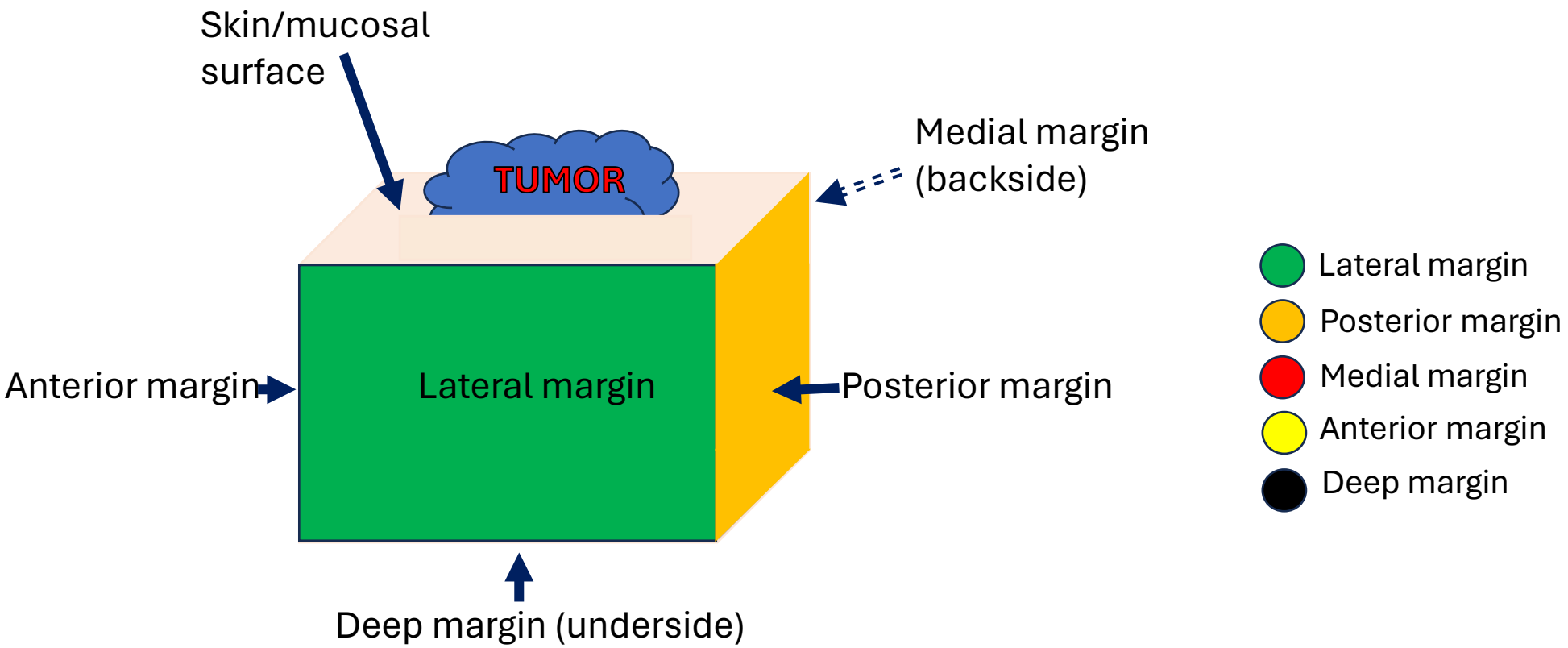
CASE REVIEW

- The day after surgery, staff in pathology accession several specimens for this patient obtained during the same surgery (biopsy of margins and lymph nodes).
- When no main tumor specimen was received, pathology staff contact pathologist covering OR frozen sections that week.
- Pathologist calls surgeon to indicate missing main tumor specimen.
- Surgeon communicates with research lab, who communicates that the specimen has been cut into multiple pieces.
- Surgeons determine that assessment of margins not possible.
- Conclude also that specimen not suitable for pathologic assessment because specimen was placed into “research media”.
- Specimen in formalin as well as from biohazardous waste retrieved from research lab and processed by pathology.

CASE REVIEW - SPECIMEN MARGINS



CASE REVIEW - SPECIMEN MARGINS



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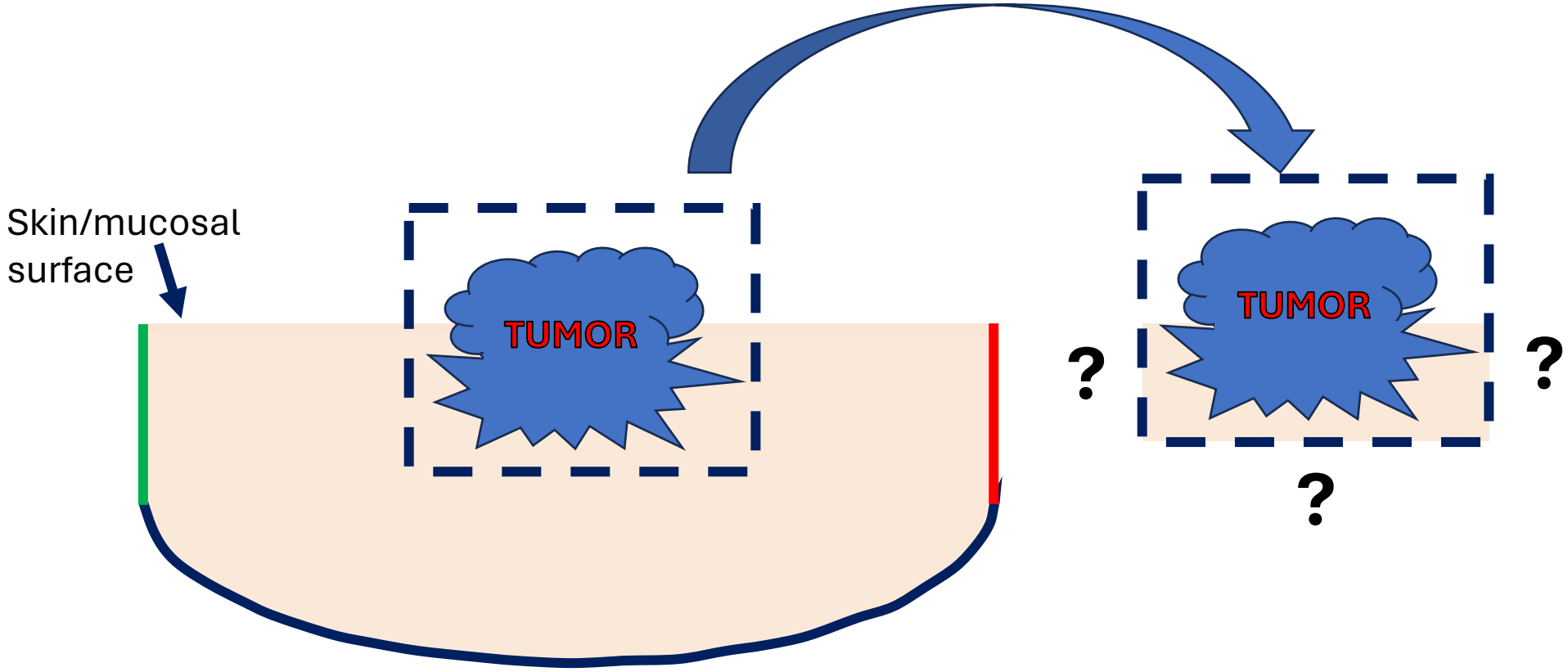
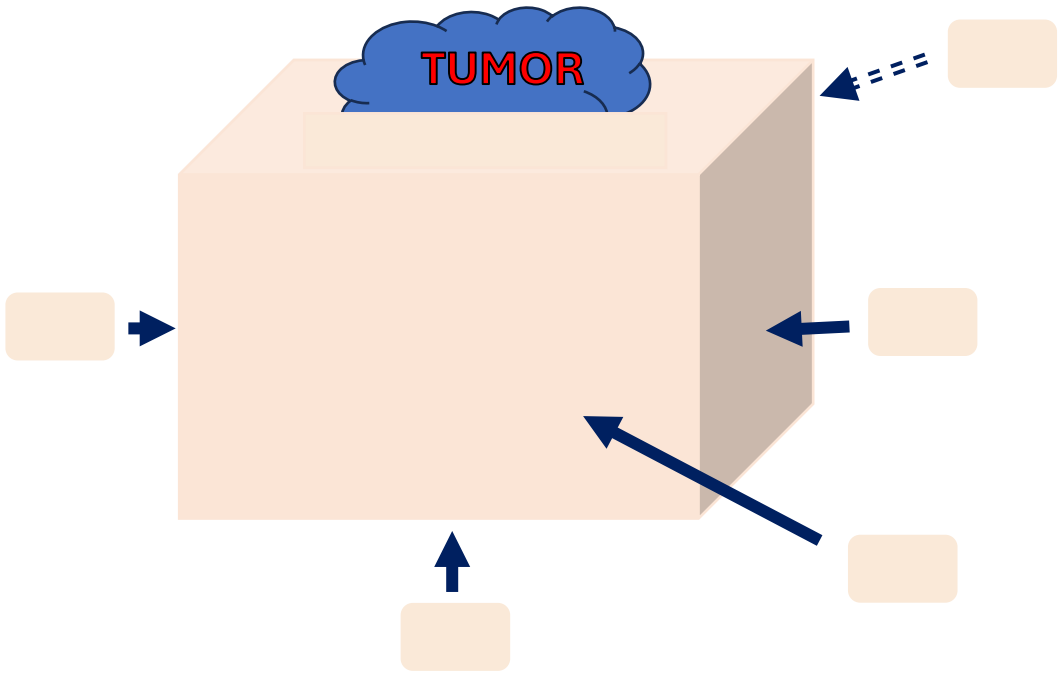


CASE REVIEW - SPECIMEN MARGINS



FINAL DIAGNOSIS:

A. [redacted] right anterior, biopsy:
- Skeletal muscle
- Negative for malignancy

B. [redacted] right posterior, biopsy:
- Skeletal muscle
- Negative for malignancy

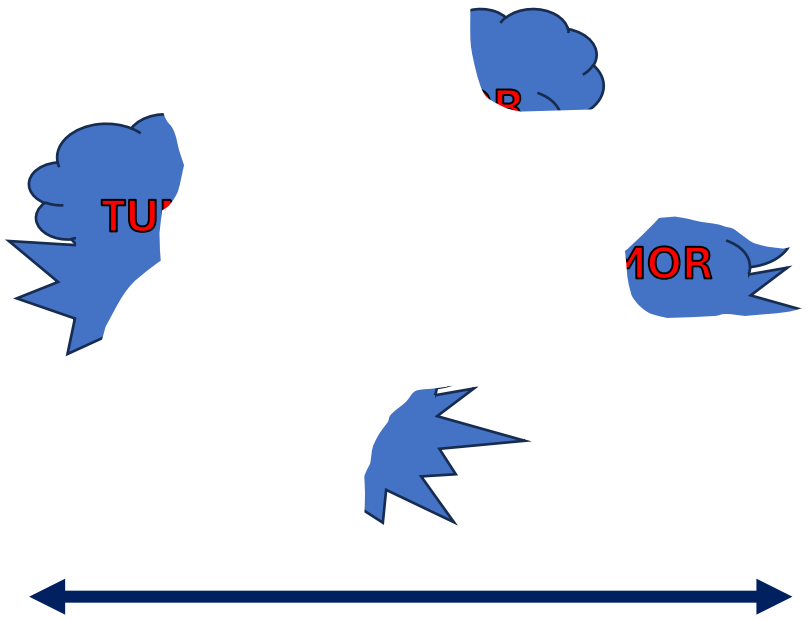
C. [redacted] right dorsal, biopsy:
- Squamous mucosa and underlying skeletal muscle
- Negative for high-grade dysplasia or malignancy

D. [redacted] right ventral, biopsy:
- Squamous mucosa and underlying skeletal muscle
- Negative for high-grade dysplasia or malignancy

E. [redacted] right deep, biopsy:
- Skeletal muscle, negative for malignancy

Surgeon took biopsies of margins at time of surgery

CASE REVIEW - TUMOR SIZE



Tumor size?

pT Category

Superficial erosion alone of bone / tooth socket by gingival primary is not sufficient to classify a tumor as T4.
DOI is depth of invasion and not tumor thickness.

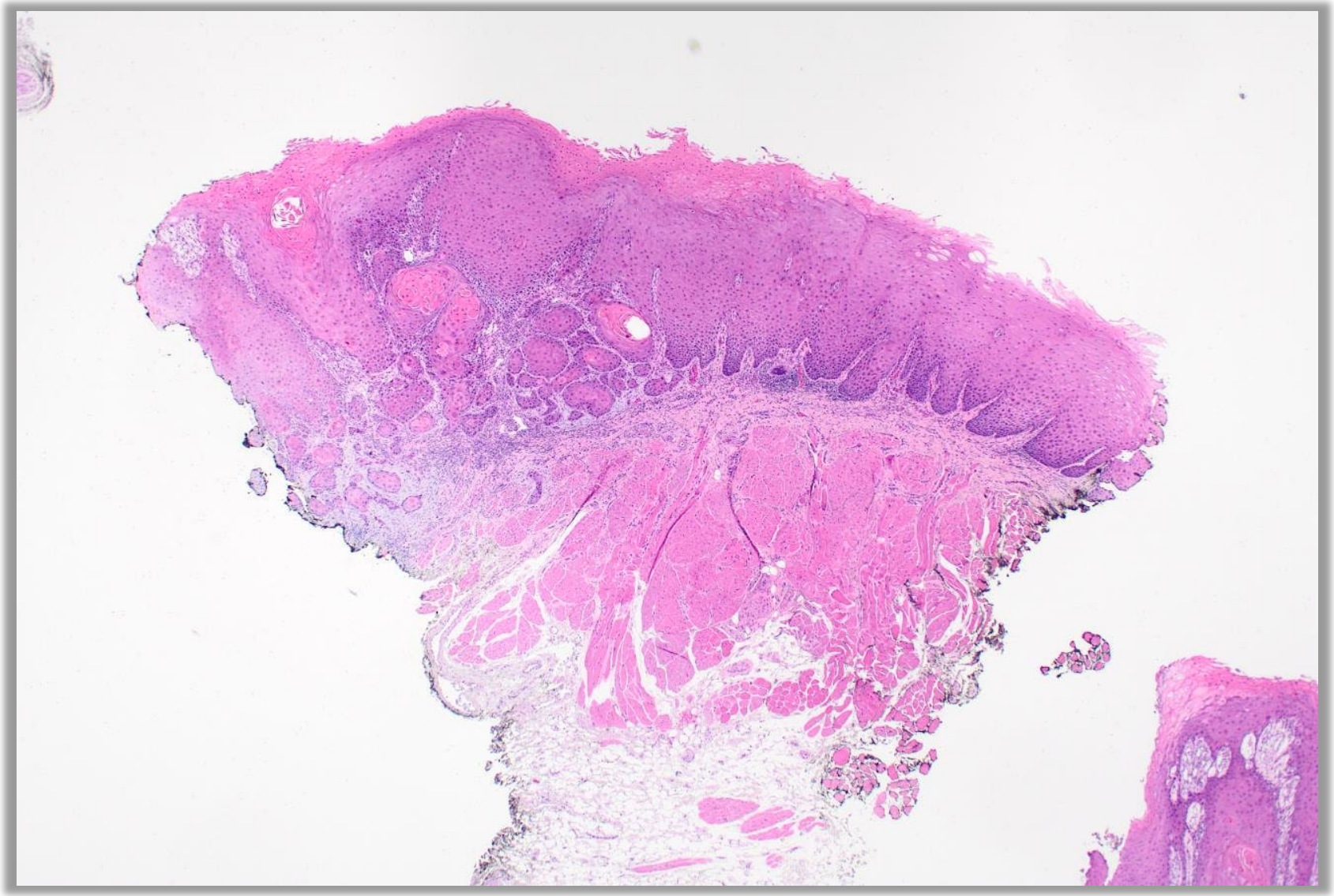
___ pT not assigned (cannot be determined based on available pathological information)
___ pTis: Carcinoma *in situ*
___ pT1: Tumor less than or equal to 2 cm with depth of invasion (DOI) less than or equal to 5 mm
___ pT2: Tumor less than or equal to 2 cm with DOI greater than 5 mm or tumor greater than 2 cm and less than or equal to 4 cm with DOI less than or equal to 10 mm
___ pT3: Tumor greater than 2 cm and less than or equal to 4 cm with DOI greater than 10 mm or tumor greater than 4 cm with DOI less than or equal to 10 mm

pT4: Moderately advanced or very advanced local disease

___ pT4a: Moderately advanced local disease. Tumor greater than 4 cm with DOI greater than 10 mm or tumor invades adjacent structures only (e.g., through cortical bone of the mandible or maxilla or involves the maxillary sinus or skin of the face)
___ pT4b: Very advanced local disease. Tumor invades masticator space, pterygoid plates, or skull base, and / or encases internal carotid artery
pT4 (subgroup cannot be determined)

From CAP protocol templates: https://www.cap.org/protocols-and-guidelines/cancer-reporting-tools/cancer-protocol-templates

CASE REVIEW - PATHOLOGY



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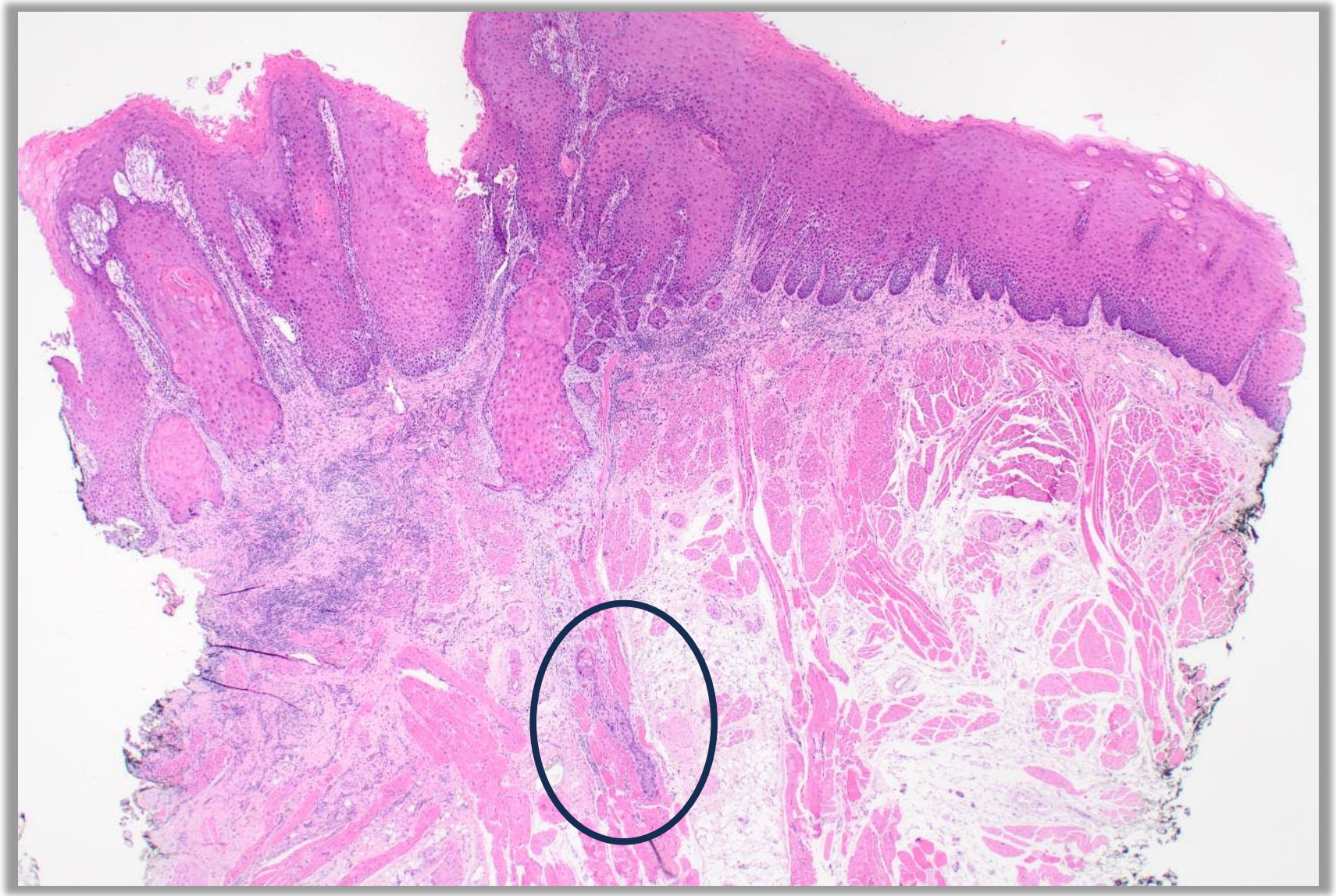

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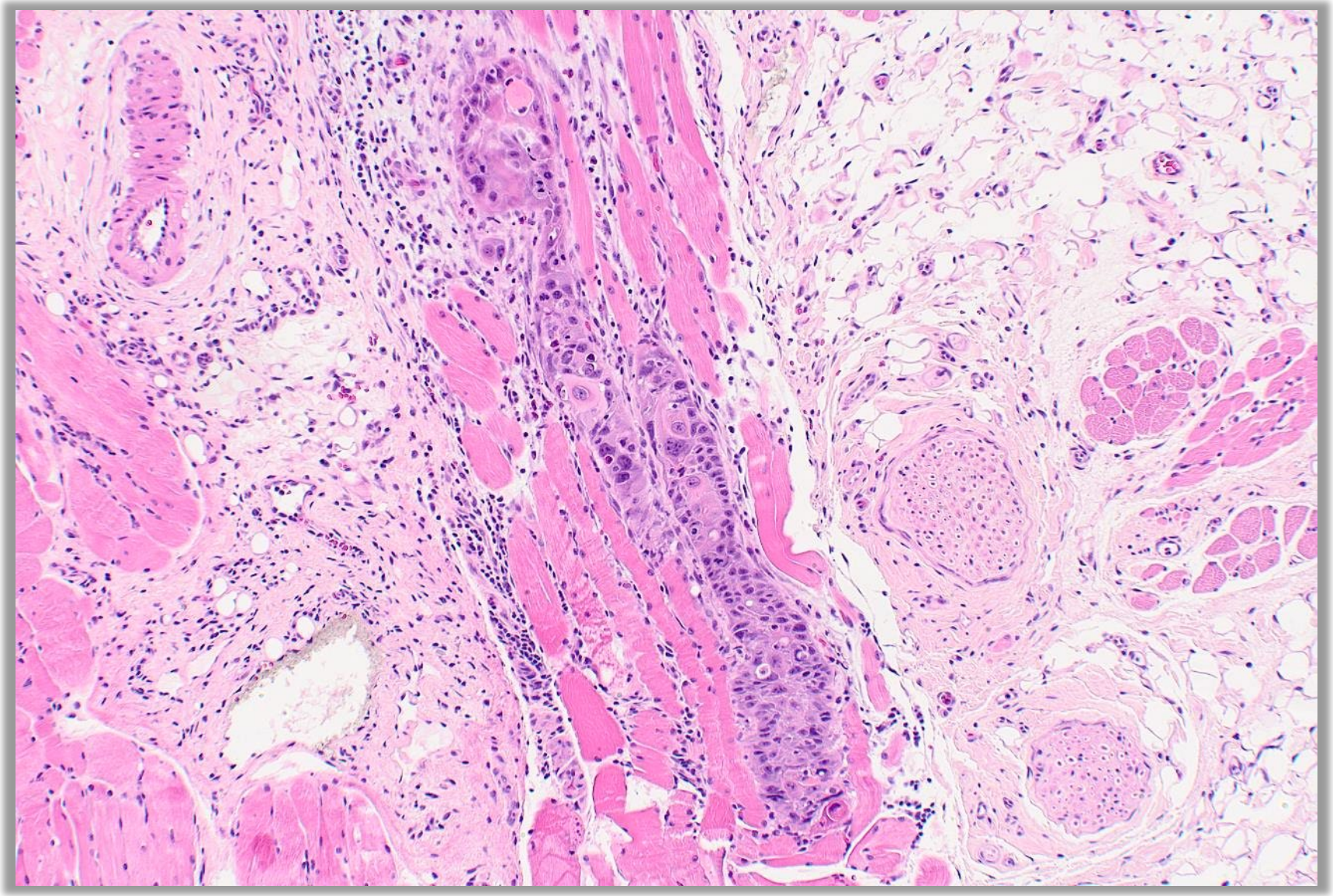

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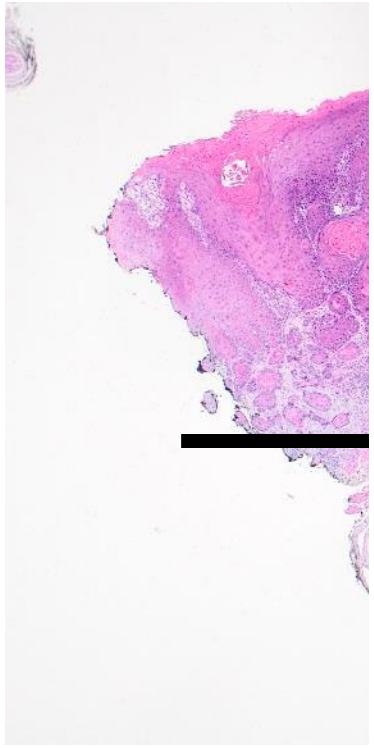

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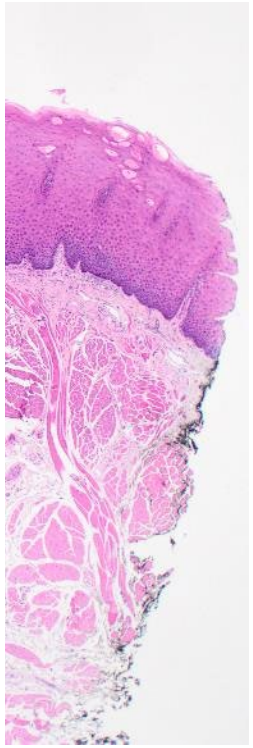

CASE REVIEW - PATHOLOGY REPORT

FINAL DIAGNOSIS:

[redacted]

- **Invasive squamous cell carcinoma, keratinizing, moderately differentiated.**
- **Depth of invasion: 3 mm**
- **No lymph-vascular or perineural invasion identified.**
- **Background squamous mucosa showing extensive dysplasia, mostly moderate.**
- **See comment.**

Comment: This specimen was received disrupted and therefore an accurate tumor size or accurate surgical resection margins cannot be determined. Based on microscopic slide review, the mass appears to be approximately 1 cm or less in size, and would correspond to a pT1. The case is prospectively reviewed within the department.

CASE REVIEW - PATHOLOGY REPORT

[redacted] dissection:

- Thirteen lymph nodes, negative for malignancy (0/13)

[redacted] dissection:

- Sixteen lymph nodes, negative for malignancy (0/16)

CASE REVIEW - OUTCOME

- Risks of obtaining tissue for research without assessment by qualified pathology personnel include, but are not limited to:
  - Inability to determine margin status for one or more tissue resection margins.
  - Inability to accurately assess tumor stage:
    - If oversampling of the tumor leads to an inability to accurately determine tumor size (of greater concern in smaller tumors).
    - If tumor depth of invasion is no longer able to be accurately assessed due to tissue disruption.
    - If the tissue is disrupted before proper pathologic assessment leading to loss of important staging landmarks or leading to artifactual spread of tumor to uninvolved tissue surfaces.

PREFERRED PROCEDURE

- Investigators interested in obtaining remnant human tissue specimen for research purposes should contact the Department of Pathology and Laboratory Medicine or the UCCC Biospecimen Shared Resource to facilitate the collection, handling, and dispensing of remnant tissue specimens.

- Tissue resected for the purposes of clinical management is deemed remnant by qualified pathology personnel (e.g., Pathologist or Pathologists' Assistant) prior to being dispensed for research purposes. Tissue provided for research prior to Pathology review could negatively affect patient care.

PROCEDURE – OPERATING ROOM

- The excised and intact tissue(s) is placed in a specimen container by operating room staff per standard procedures. **Never place tissue intended for research purposes in formalin.**
- The fresh tissue is delivered to the frozen section room as soon after excision as possible.
- Pathology or UCCC Biospecimen Shared Resource personnel transport the specimen(s) to Surgical Pathology where it is examined by qualified pathology personnel.

PROCEDURE – SURGICAL PATHOLOGY

- Pathology personnel will assess the specimen as follows:
  1. Application of any ink necessary for designation of surgical margins, areas of interested designated by the surgeon, etc.
  2. Sectioning in routine fashion.

- Remnant tissue may be provided for research purposes if enough tumor/area of interest for the Pathologists' clinical examination exists and if a sufficient additional amount of tumor/area of interest remains.

- In order to qualify as a remnant tissue, the portion procured for research must not:
  1. Compromise assessment of a surgical margin.
  2. Prevent an adequate amount of tumor/area of interest to be submitted for clinical examination (generally 1 paraffin block per centimeter of tumor/area of interest).

PROCEDURE – SURGICAL PATHOLOGY

- If pathology personnel determine that there is not enough tissue available for research purposes the entire tissue specimen is submitted and processed as a clinical specimen for patient care.

- Neither this tissue specimen, nor any portion of it, will be used for research purposes except in the event that there is sufficient tissue remaining after all clinical examinations (e.g., gross and microscopic examinations) and ancillary procedures (e.g., additional stains, flow cytometry, molecular pathology, ultrastructural examination, and other procedures) have been performed and a final pathology report is issued.

- For example, sufficient tissue may be present in the resulting diagnostic formalin-fixed paraffin embedded tissue block to allow for recuts to be obtained for research purposes.

PROCEDURE – DISTRIBUTION PRIORITIZATION

- Distribution of remnant tissue for research will be prioritized as follows:
  1. Clinical trials (when required to meet objectives of the clinical trial)
  2. Investigator-initiated studies
     - Note: This includes investigator-initiated studies managed through the UCCC Biospecimen Shared Resource
  3. UCCC Biospecimen Shared Resource (biobanking)
  4. Outside biobanks (including biobanks associated with clinical trials)

SECONDARY PROCEDURE

- For a limited number of research studies collection of tissue from the operating room may be required. In such instances, the corresponding IRB protocol and informed consent document should clearly communicate the risks associated with acquiring tissue for research prior to pathological evaluation.
- In order to qualify as a remnant tissue, the portion procured and dispensed for research prior to review by qualified pathology personnel must not:
    1. Compromise assessment of a surgical margin.
    2. Prevent an adequate amount of tumor/area of interest to be submitted for clinical examination (generally 1 paraffin block per centimeter of tumor/area of interest).

RESPONSIBILITES

Tasks	Responsible Staff
Ensuring that all human tissue specimens procured for the purposes of clinical management are submitted per standard procedures for pathology assessment.	Physicians and staff procuring the specimen
Examining and qualifying human tissue specimen as remnant. Providing remnant tissue to designated personnel.	Pathologist, Pathologists' Assistant, Physicians
Coordinating the collection, processing, and dispensing of remnant human tissues for research purposes.	Pathology and UCCC Biospecimen Shared Resource personnel

SUMMARY

- Tissue should be deemed remnant by qualified pathology personnel prior to being collected and distributed for research purposes.
- Acquiring tissue for research prior to pathological evaluation may compromise the diagnostic integrity of the specimen.
- Procedures being performed specifically for research purposes and/or additional biopsy passes to collect specimens specifically for research are outside the scope of this procedure.
- Contact the UCCC Biospecimen Shared Resource and/or the Department of Pathology and Laboratory Medicine for assistance with acquiring remnant tissue for research purposes.