College of American Pathologists Cancer Data Summit
October 18, 2024

It's All About the Data: Perspectives on Structured Data Across the Cancer Patient Care Continuum

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Co-Leader, MD Anderson Melanoma Moon Shot

Chair, AJCC Executive Committee. & Version 9 Melanoma Expert Panel

Vice-Chair, AJCC

THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center
Making Cancer History®

Disclosures

- Merck – consultant/advisory board

- I am not a pathologist, but continue to enjoy a very close partnership with our MD Anderson pathologists and longstanding collaboration with pathology colleagues worldwide

Special Thanks

Martin Madera, MA, CPHIMS
Senior Manager, AJCC

AJCC Mission Statement

- The AJCC provides worldwide leadership in the development, promotion, and maintenance of evidence-based systems for the classification and management of cancer in collaboration with multidisciplinary organizations dedicated to cancer surveillance and to improving care.

AJCC - 22 Member Organizations

- American Association of Pathologists' Assistants
- American Cancer Society
- American College of Physicians
- American College of Radiology
- American College of Surgeons
- American Head and Neck Society
- American Society for Radiation Oncology
- American Society of Clinical Oncology
- American Society of Colon and Rectal Surgeons
- American Urological Association
- Canadian Partnership Against Cancer
- Centers for Disease Control and Prevention
- College of American Pathologists
- International Collaboration on Cancer Reporting
- National Cancer Database
- National Cancer Institute
- National Cancer Registrars Association
- National Comprehensive Cancer Network
- North American Association of Central Cancer Registries
- Society of Gynecologic Oncologists
- Society of Surgical Oncology
- Society of Urologic Oncology

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Classification and Staging of Cancer

- **Principal communication tool** – common language facilitates worldwide consistency
  - Cancer care - clinician–patient & clinician–clinician
  - Surveillance/registry reporting: state/province, national, international, etc.
- Risk stratification defines patient groups → staging/prognosis
- Treatment recommendations → often stage-based
- Informs clinical trial eligibility, stratification, analysis
- AJCC/UICC – TNM structure (de facto constrained) → incorporation of evidence-based non-anatomic factors
- Informs clinical/translational/correlative science

American College of Surgeons - Cancer Programs

AJCC
American Joint Committee on Cancer

Commission on Cancer®

Commission on Cancer®
NATIONAL ACCREDITATION PROGRAM FOR RECTAL CANCER

NAPBC®
NATIONAL ACCREDITATION PROGRAM FOR BREAST CENTERS

CANCER RESEARCH PROGRAM™
Program of the American College of Surgeons and the Alliance for Clinical Trials in Oncology

Cancer Surgery Standards PROGRAM

NATIONAL CANCER DATABASE

American Joint Committee on Cancer
American College of Surgeons

AJCC Content and CAP Protocols

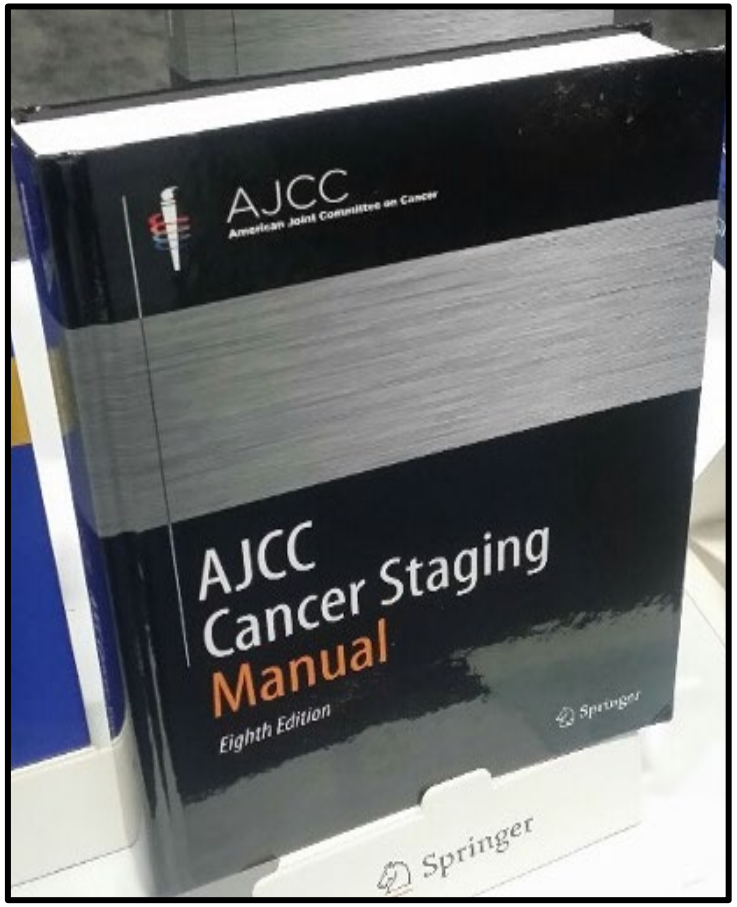
AJCC Cancer Staging Manuals

AJCC
American Joint Committee on Cancer
Validating science. Improving patient care.

Source of Cancer Staging for Decades → 8 Editions

1st - 1977
2nd - 1983
3rd - 1988
4th - 1992
5th - 1997
6th - 2002
7th - 2010
8th - 2017

8th Edition



1st – 7th Editions

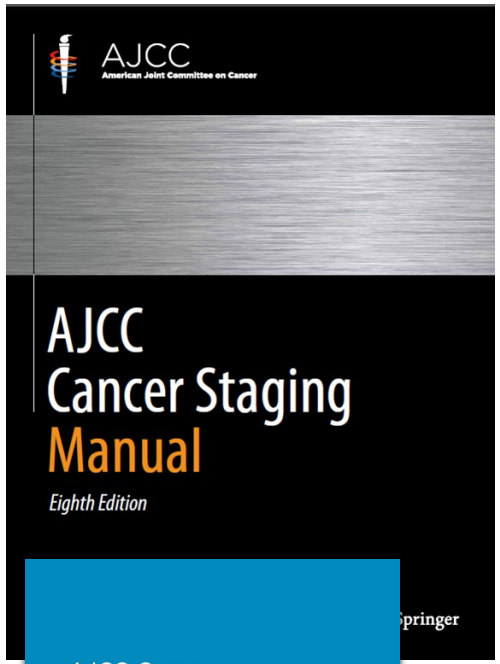
Presented by Jeff Gershenwald

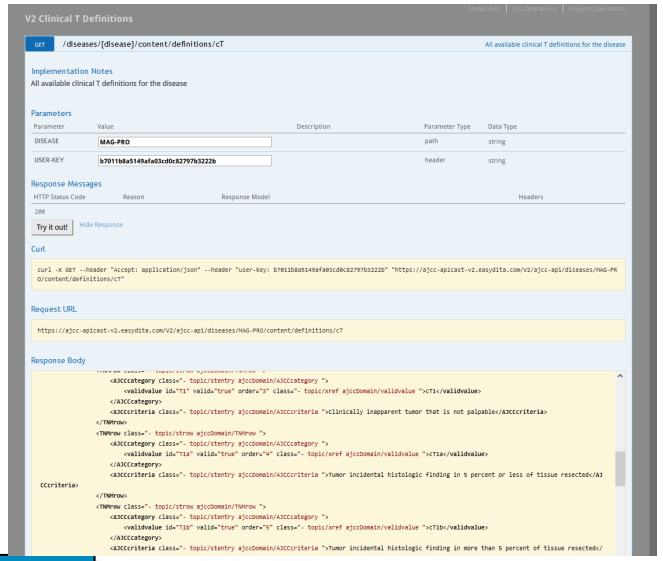
Evolution of Cancer Staging

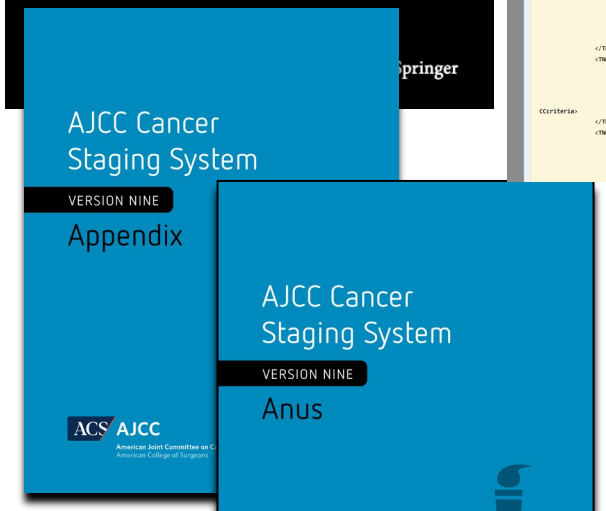
- Cancer Staging ***Manual*** → rebranded as Cancer Staging ***System***
- Goal → Continue to ensure cancer staging is current, evidence-based, and meets needs of clinical care and surveillance communities

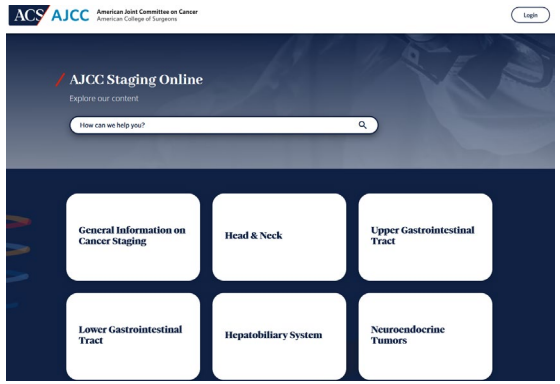
8th Edition	Version 9
Hardcopy book	Leverages Content Management infrastructure to support multiple products
Chapters	Protocols for each disease site (Cervix released in 2020)
Published every 5-7 years	AJCC will release 1-5 protocols each year
Entire manual (all chapters) published simultaneously	Protocols published disease site by disease site based on needs of clinical care & surveillance communities and in coordination with WHO Blue Book update cycle
Print manual → "static"	Electronic platform facilitates rapid integration of updated staging information into EHR and cancer registry software as well as other products

Work Products





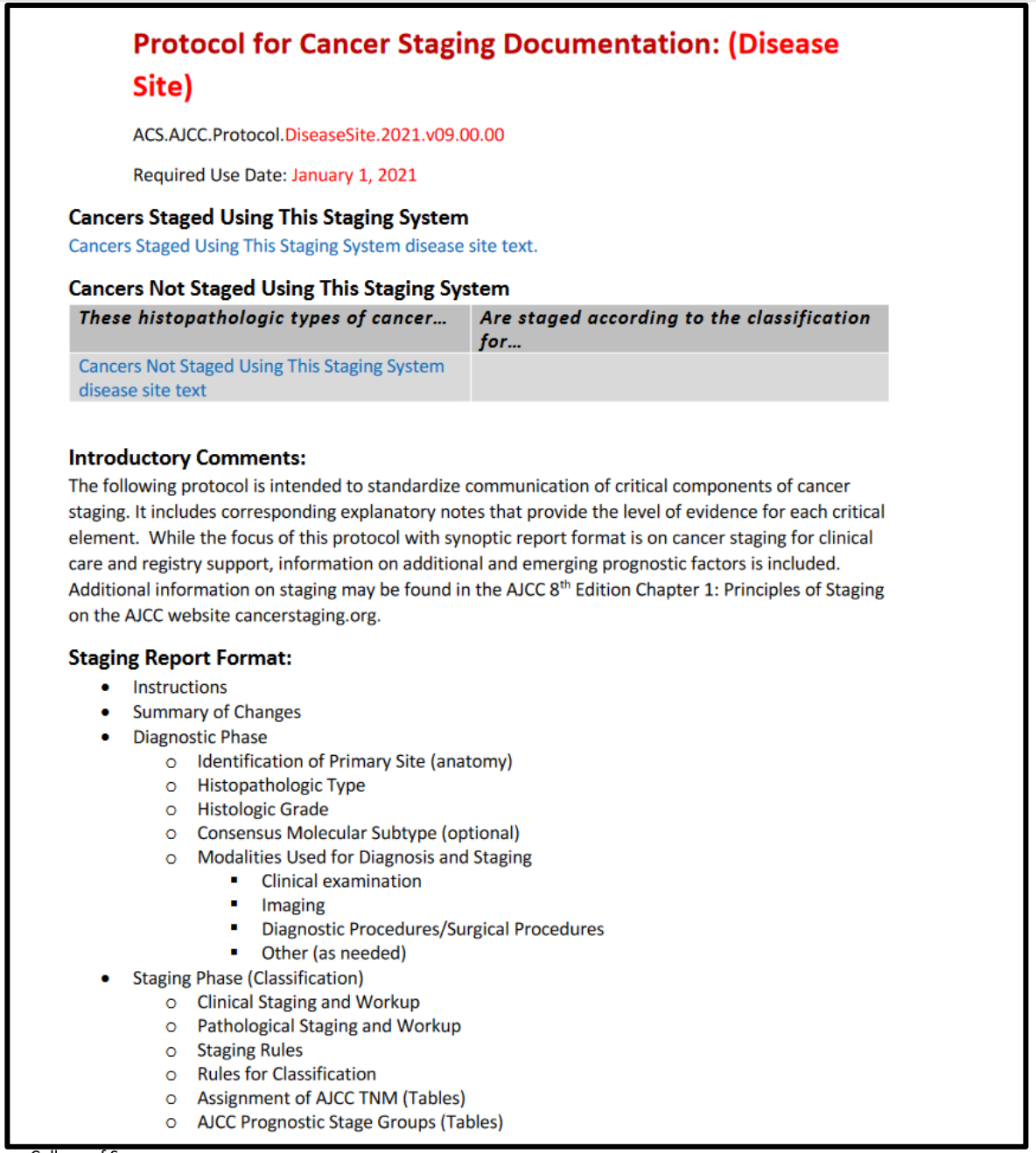




- 8th Edition Cancer Staging Manual
- 8th Edition e-Book on Amazon Kindle
- Version 9 releases of site specific protocols
- AJCC API Portal
- Cancer Surveillance DLL
- Educational Resources
  - Disease-site webinars
  - Journal articles
- AJCC Staging Online

Version 9 – Protocol Structure

- Version control to clearly indicate Version 9, and allow for minor corrections (typos and other errata)
- Clear indication of effective date for implementation
- Standardized format with required and optional sections
- Clear indications of cancers covered in Protocol and those not staged
- Outline of Staging Report Format to orientate reader



Protocol for Cancer Staging Documentation: (Disease Site)

ACS.AJCC.Protocol.DiseaseSite.2021.v09.00.00

Required Use Date: January 1, 2021

Cancers Staged Using This Staging System

Cancers Staged Using This Staging System disease site text.

Cancers Not Staged Using This Staging System

These histopathologic types of cancer…	*Are staged according to the classification for…*
Cancers Not Staged Using This Staging System disease site text	

Introductory Comments:

The following protocol is intended to standardize communication of critical components of cancer staging. It includes corresponding explanatory notes that provide the level of evidence for each critical element. While the focus of this protocol with synoptic report format is on cancer staging for clinical care and registry support, information on additional and emerging prognostic factors is included. Additional information on staging may be found in the AJCC 8th Edition Chapter 1: Principles of Staging on the AJCC website cancerstaging.org.

Staging Report Format:

- Instructions
- Summary of Changes
- Diagnostic Phase
  - Identification of Primary Site (anatomy)
  - Histopathologic Type
  - Histologic Grade
  - Consensus Molecular Subtype (optional)
  - Modalities Used for Diagnosis and Staging
    - Clinical examination
    - Imaging
    - Diagnostic Procedures/Surgical Procedures
    - Other (as needed)
- Staging Phase (Classification)
  - Clinical Staging and Workup
  - Pathological Staging and Workup
  - Staging Rules
  - Rules for Classification
  - Assignment of AJCC TNM (Tables)
  - AJCC Prognostic Stage Groups (Tables)

AJCC Version 9 Protocols

Protocol for Cancer Staging Documentation: Anus

ACS.AJCC.Protocol.Anus.2022.v09.00.00
Required Use Date: January 1, 2023

Cancers Staged Using This Staging System

All carcinomas arising in the anal canal, including high-grade neuroendocrine carcin
neuroendocrine carcinoma and large cell neuroendocrine carcinoma), and carcinom
anorectal fistulas and those arising in the perianal area are staged using this system

Cancers Not Staged Using This Staging System

These histopathologic types of cancer…	*Are staged according to the cla*
Sarcomas	Soft tissue sarcoma of the abdo visceral organs
Mucosal melanoma of the anus	No AJCC staging system
Well-differentiated neuroendocrine tumors	No AJCC staging system
Premalignant lesions [i.e., LSIL, HSIL, anal intraepithelial neoplasia (AIN) Paget's disease, Bowen's disease]	Not part of AJCC staging system

Introductory Comments:

The following protocol is intended to standardize communication of critical compor
staging. It includes corresponding explanatory notes that provide the level of evider
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    - Clinical examination
    - Imaging
    - Diagnostic Procedures/Surgical Procedures
- Staging Phase (Classification)

*Definition of Primary Tumor (T) (Note T)

	T Category	*T Criteria*
___	TX	Primary tumor not assessed
___	T0	No evidence of primary tumor
___	T1	Tumor less than or equal to 2 cm in greatest dimension
___	T2	Tumor greater than 2 cm but less than or equal to 5 cm in greatest dimension
___	T3	Tumor greater than 5 cm in greatest dimension
___	T4	Tumor of any size invading adjacent organ(s), such as the vagina, urethra, or bladder

Primary Tumor Suffix
___ (m) Multiple synchronous primary tumors

*Definition of Regional Lymph Nodes (N) (Note N)

	N Category	*N Criteria*
___	NX	Regional lymph nodes cannot be assessed
___	N0	No tumor involvement of regional lymph node(s)
___	N1	Tumor involvement of regional lymph node(s)
___	N1a	Tumor involvement of Inguinal, mesorectal, superior rectal, internal Iliac, or obturator lymph node(s)
___	N1b	Tumor involvement of external Iliac lymph node(s)
___	N1c	Tumor involvement of N1b (external iliac) with any N1a node(s)

Regional Lymph Nodes Suffix
___ (sn) Sentinel node procedure
___ (f) FNA or core needle biopsy

*Definition of Distant Metastasis (M) (Note M)

	M Category	*M Criteria*
___	cM0	No distant metastasis
___	cM1	Distant metastasis
___	pM1	Microscopic confirmation of distant metastasis

Prognostic Factors Required for Stage Grouping

Beyond the factors used to assign T, N, or M categories, no additional prognostic factors are required for stage grouping.

the radiologist provide important staging information, and may provide important T-, N-, and/or M-related information, stage is defined ultimately from the synthesis of an array of patient history and physical examination findings supplemented by imaging and pathology data.

Survival Data

ata from the National Cancer Data Base (NCDB) for 2010 to
each of the stage groups per Version 9 are as follows: Stage
5.5%; Stage IIB (*n* = 5,750), 69.3%; Stage IIIA (*n*
C (*n* = 1,782), 51.1%; Stage IV (*n* = 3,454), 20.5%
ival and Figure Anus-Survival.

e Grouping 2- and 5-year Unadjusted Survival

-year Overall urvival (%)	5-year Overall Survival (%)	Media (mont
2.2	83.5	191.74
7.5	75.5	165.22
4.1	69.3	155.70
5.7	59.2	96.00
1.5	55.4	83.32
9.5	51.1	63.44
9.	20.5	16.53

erall Survival Curves, 2010-2017

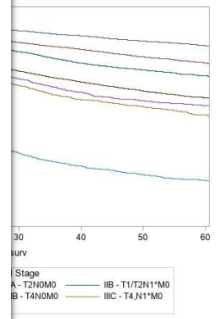


FIGURE ANUS-N1a. N1a is defined as tumor involvement of
rectal, internal iliac, or obturator lymph nodes.

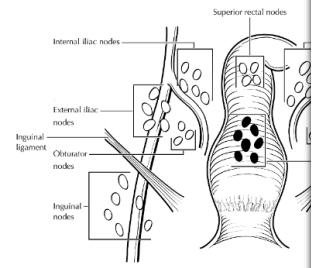


FIGURE ANUS-N1b. N1b is defined as tumor involvement of

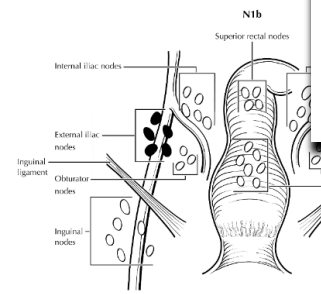
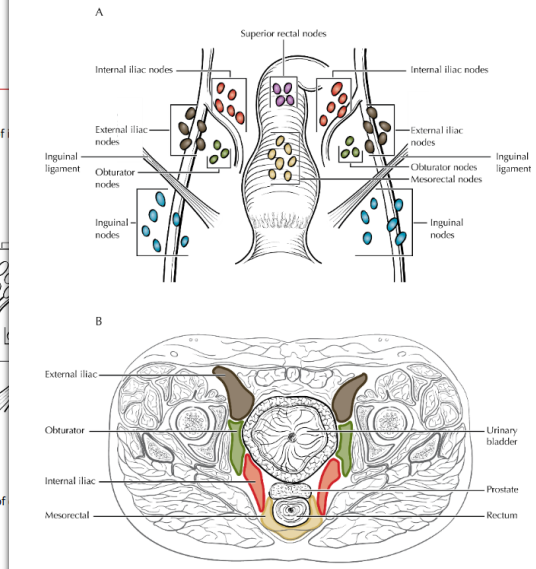


FIGURE ANUS-NODAL MAP. Schematic of regional draining lymph nodes for tumors of the anus, coronal view (A). Depiction of cross-sectional imaging of regional lymph nodes in the pelvis (B).



Workup Tables & Illustrations

Clinical Staging and Workup

This table is a simplified algorithm of the investigations and procedures utilized to generate appendiceal cancer clinical TNM staging information.

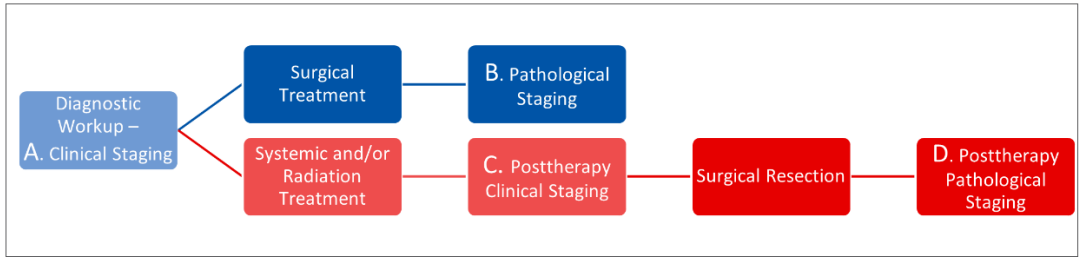
Its purpose is to provide clarity regarding appropriate modalities to use in determining the individual categories of the appendiceal cancer clinical TNM staging.

Disclaimer: *The table represents common approaches to staging and work up for this cancer. Some or all of these tests are used in staging the cancer and are provided as a reference. The table is not a guideline for treatment and should not be used in this manner but instead utilized to identify how each of these tests contribute to the determination of T, N, M categories and Stage.*

DIAGNOSTIC WORKUP	DESCRIPTION	SPECIFIC CONTRIBUTION TO TNM CATEGORY
Clinical exam		
Medical history and physical examination	Non-contributory before surgery	None
Colonoscopy	In certain cases, can provide histological diagnosis	None
Exploratory laparotomy with diagnostic appendectomy (not definitive treatment)	Intraoperative identification of extent of tumor; assessment of peritoneal spread with microscopic confirmation	T1-T4, N1, M1
Exploratory laparotomy without colectomy	Intraoperative identification of extent of tumor; assessment of peritoneal spread with microscopic confirmation	T1-T4, N1-N2, M1
Imaging		
CT	Chest/abdomen/pelvis – define extent of local disease, nodal involvement, metastases (Note: for localized LAMN or HAMN chest imaging may not be indicated)	T4, N1-N2, M1

Staging Rules for Appendix

Information to help guide staging is shown in the figure below and described in the treatment scenarios. For metastatic patients, diagnostic workup can result in pM1 which can be used in both a clinical stage and a pathological stage if there is no surgical resection. Depending on the appendiceal histology, an appendectomy can represent a diagnostic workup procedure or a definitive surgical treatment (e.g. an appendectomy is definitive surgical treatment for a LAMN).



Common staging scenarios (Note CSS):

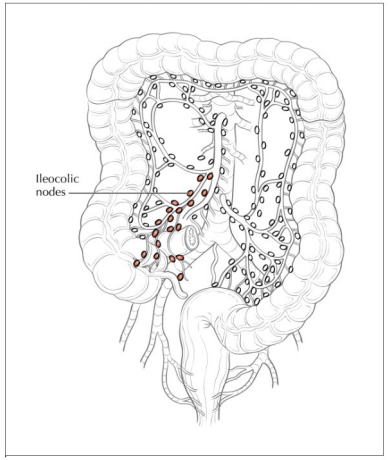
1. Unsuspected cancer in an appendectomy specimen

The most common way that appendiceal cancer is diagnosed and staged is by pathological examination of an appendectomy specimen, often in a patient presenting with signs and symptoms of acute appendicitis in whom appendiceal cancer is not suspected preoperatively. Pathological staging (B in figure above) is assigned by the managing physician for this incidental finding. There is no clinical staging.

2. Detection by imaging or colonoscopy prior to or without appendectomy

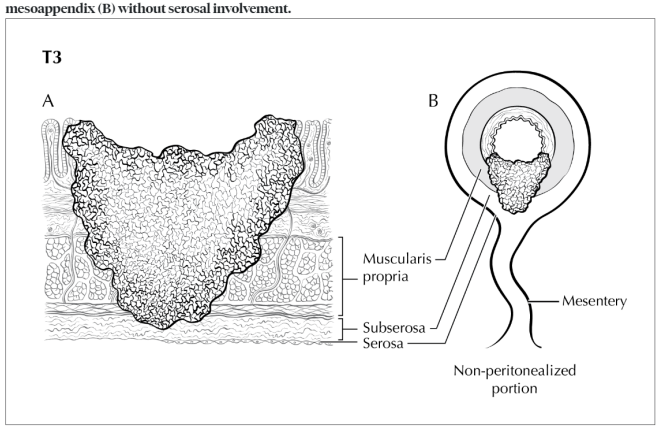
Less commonly appendiceal cancer is identified on imaging or as a lesion at the appendiceal origice upon colonoscopy. Clinical staging (A in figure above) cT, cN, and cM/pM are assigned based on imaging findings. The pathologist assigns pT, pN, and pM (when metastases are sampled) based on the

FIGURE APPENDIX-NODAL MAP. Regional lymph nodes of the appendix.



Lymph node involvement is classified as N1 or N2 according to the number of nodes involved v
is pN1 (Figure Appendix-N1), and the presence of four or more nodes involved with tumor met
examination of a right hemicolectomy specimen ordinarily includes 12 or more lymph nodes. If

FIGURE APPENDIX-T3. T3 is defined as tumor that invades through the muscularis propria into the subserosa (A) or the mesoappendix (B) without serosal involvement.



Evolution of Cancer Staging - II

- AJCC Version 9 disease site protocol releases will replace relevant existing Eighth edition chapters over next several years
- 8th edition Cancer Staging Manual content will continue to be used for staging and cancer surveillance until new Version 9 disease site protocol available
- Ongoing communication efforts in coordination with partners, vendors, physicians and registrars for smooth transition

Discover AJCC Staging Online

With Version 9 updates

New website provides access to the entire AJCC Cancer Staging System, with all the latest Version 9 updates available to individual users for just $49.99 per year.

ACS AJCC
American Joint Committee on Cancer
American College of Surgeons

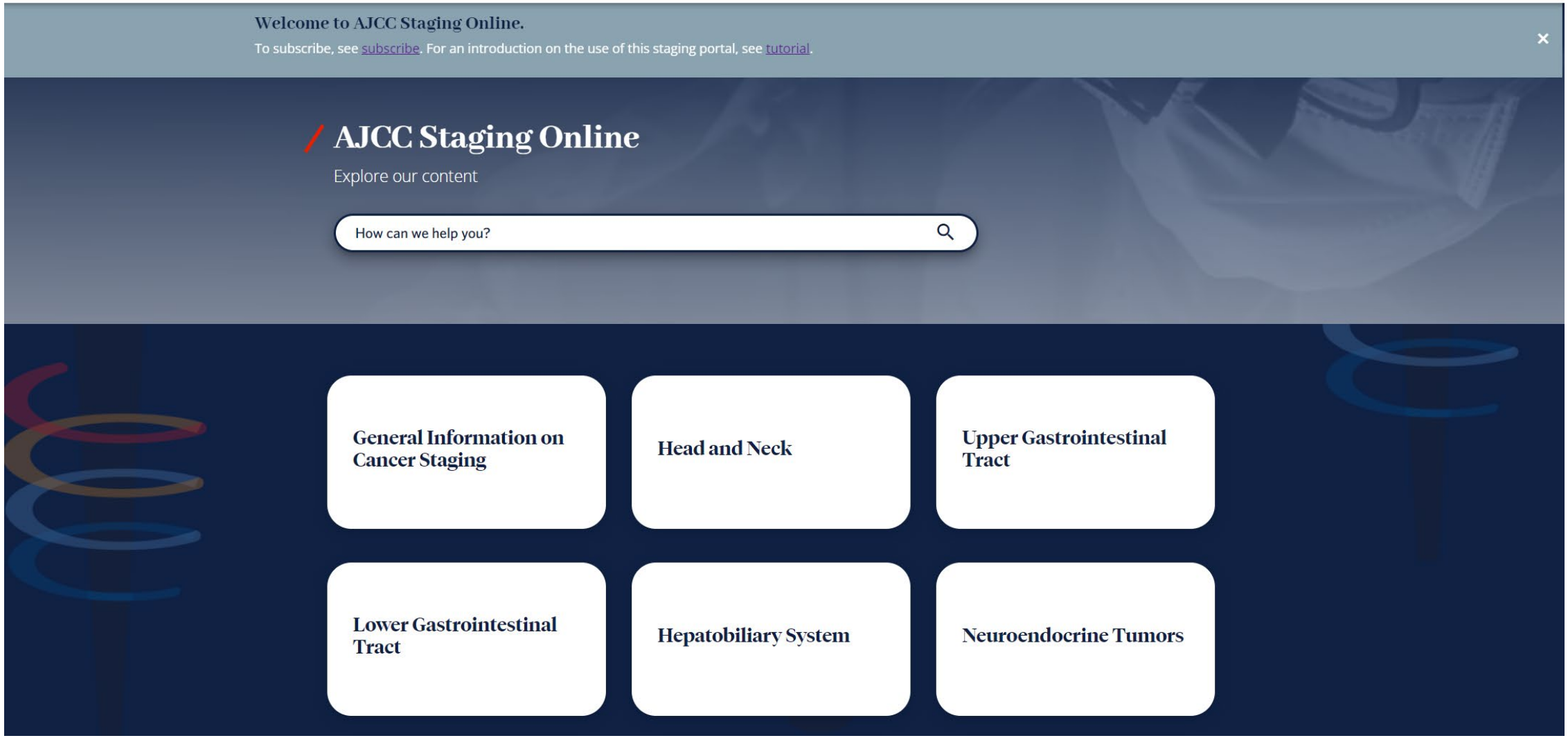
facs.org/ajcconline

AJCC Staging Online Released June 13, 2024

ACS AJCC American Joint Committee on Cancer
American College of Surgeons

Source of truth for Staging

given_name



All updated AJCC Content in one place

Version: 2024 V9

Appendix Staging - Quick Reference

*Definition of Primary Tumor (T) (Note T)

T Category	T Criteria
TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
Tis	Carcinoma *in situ* (intramucosal carcinoma; invasion of the lamina propria or extension into but not through the muscularis mucosae)
Tis(LAMN)	Low-grade appendiceal mucinous neoplasm confined to the muscularis propria; Acellular mucin or mucinous epithelium may invade into the muscularis propria. T1 and T2 are not applicable to LAMN; Acellular mucin or mucinous epithelium that extends into the subserosa or serosa should be classified as T3 or T4a, respectively.

American Joint Committee on Cancer
American College of Surgeons

AJCC Content in the CAP Protocols

AJCC Move from Chapters to Protocol Format

New Process for updating the Cancer Staging System

- In 2020, AJCC made first Version 9 update (protocol) for Cervix Uteri
- Stand alone Protocol format similar to CAP Protocol Structure
- Designed for consistent structure across diseases
- Approximately 3-7 disease sites updated each year

Coordination with CAP

- CAP licenses use of AJCC content in CAP Protocols
- AJCC provides CAP updated content prior to publication for use in development of protocols

*Prognostic Factors Required for Stage Grouping (Note PFR)

	G	*G Definition*
___	GX	Grade cannot be assessed
___	G1	Well differentiated
___	G2	Moderately differentiated
___	G3	Poorly differentiated

Note: In rare cases of discordance in primary and metastatic histological grade, the grade of metastatic disease is utilized for stage group assignment.

Assignment of AJCC TNM

AJCC data elements required for staging are identified with an asterisk (*).

***Stage classification based on time frame and criteria (see Supplemental Information)**

____ c (clinical)
____ p (pathological)
____ yc (posttherapy clinical)
____ yp (posttherapy pathological)

***Definition of Primary Tumor (T) (Note T)**

	T Category	*T Criteria*
___	TX	Primary tumor cannot be assessed
___	T0	No evidence of primary tumor
___	Tis	Carcinoma *in situ* (intramucosal carcinoma; invasion of the lamina propria or extension into but not through the muscularis mucosae)
___	Tis(LAMN)	Low-grade appendiceal mucinous neoplasm confined to the muscularis propria; Acellular mucin or mucinous epithelium may invade into the muscularis propria T1 and T2 are not applicable to LAMN; Acellular mucin or mucinous epithelium that extends into the subserosa or serosa should be classified as T3 or T4a, respectively
___	T1	Tumor invades the submucosa (through the muscularis mucosa but not into the muscularis propria)
___	T2	Tumor invades the muscularis propria
___	T3	Tumor invades through the muscularis propria into the subserosa or the mesoappendix
___	T4	Tumor invades the visceral peritoneum, including acellular mucin or mucinous epithelium involving the serosa of the appendix or mesoappendix, and/or directly invades adjacent organs or structures
___	T4a	Tumor invades the visceral peritoneum, including acellular mucin or mucinous epithelium involving the serosa of the appendix or serosa of the mesoappendix
___	T4b	Tumor directly invades or adheres to adjacent organs or structures

Histologic Grade# (Note D)

 # The grade of the appendiceal and peritoneal tumors is concordant in most instances but can be discordant in some cases. In case of discordance of grades, the final grade should be assigned based on the peritoneal metastasis. (Note D)

___ G1, well differentiated
___ G2, moderately differentiated
___ G3, poorly differentiated
___ Other (specify): _____
___ GX, cannot be assessed: _____
___ Not applicable: _____

Tumor Size

___ Greatest dimension in Centimeters (cm): _____ cm
+Additional Dimension in Centimeters (cm): ____ x ____ cm
___ Cannot be determined (explain): _____

Tumor Deposits (Note E)

___ Not identified
___ Present
Number of Deposits
___ Specify number: _____
___ Other (specify): _____
___ Cannot be determined (explain): _____
___ Cannot be determined: _____

Tumor Extent (Note I) (select all that apply)

___ Tumor invades lamina propria or muscularis mucosa
___ Acellular mucin invades submucosa
___ Tumor invades submucosa
___ Acellular mucin invades muscularis propria
___ Tumor invades muscularis propria
___ Acellular mucin invades subserosa or mesoappendix but does not extend to serosal surface
___ Tumor invades through muscularis propria into subserosa or mesoappendix but does not extend to

American Joint Committee on Cancer
American College of Surgeons

CAP Protocols and Commission on Cancer (CoC) Standards

Commission on Cancer (CoC) Background

Partnership with Pathology

- 2004- Accreditation Standards of CoC require CAP data items must be in the pathology reports.

> ***Standard 4.6 - The guidelines for patient management and treatment currently required by the CoC are followed***.
>
> *The CoC requires that 90 percent of pathology reports that include a cancer diagnosis will contain the scientifically validated data elements outlined on the surgical case summary checklist of the College of American Pathologists (CAP) publication, Reporting on Cancer Specimens.*

Commission on Cancer (CoC) Background

Partnership with Pathology

- July 2008- Standards updated to require CAP data items in their pathology report use a synoptic format, such as CAP Protocols

> ***Standard 4.6 - The guidelines for patient management and treatment currently required by the CoC are followed.***
>
> *CAP Protocols For Compliance, the surveyor will evaluate the pathology reports for a random sample of eligible analytic cases for the last complete year, and the current year, of abstracting to confirm that 90% of the reports include all of the **scientifically validated data items defined by the protocols**. A maximum of 25 pathology reports will be reviewed. For Commendation the surveyor will confirm that 90% of the pathology reports include all of the scientifically validated data items defined by the protocols and **90% of the reports use a synoptic format**.*

Commission on Cancer (CoC) Today

Standard 5.1: College of American Pathology (CAP) Synoptic Reporting

Measure of compliance each calendar year, the cancer program fulfills the compliance criteria:

An internal audit is conducted confirming ninety percent **(90%) of the eligible cancer pathology reports are structured using synoptic reporting format as defined by the College of American Pathologist (CAP) cancer protocols,** including containing all core data elements within the synoptic format. If the ninety percent (90%) compliance rate is not met, the cancer program has implemented a corrective action plan addressing all barriers affecting the required synoptic reporting format for all eligible cancer pathology"

Cancer Surgery Standards Program (CSSP)*

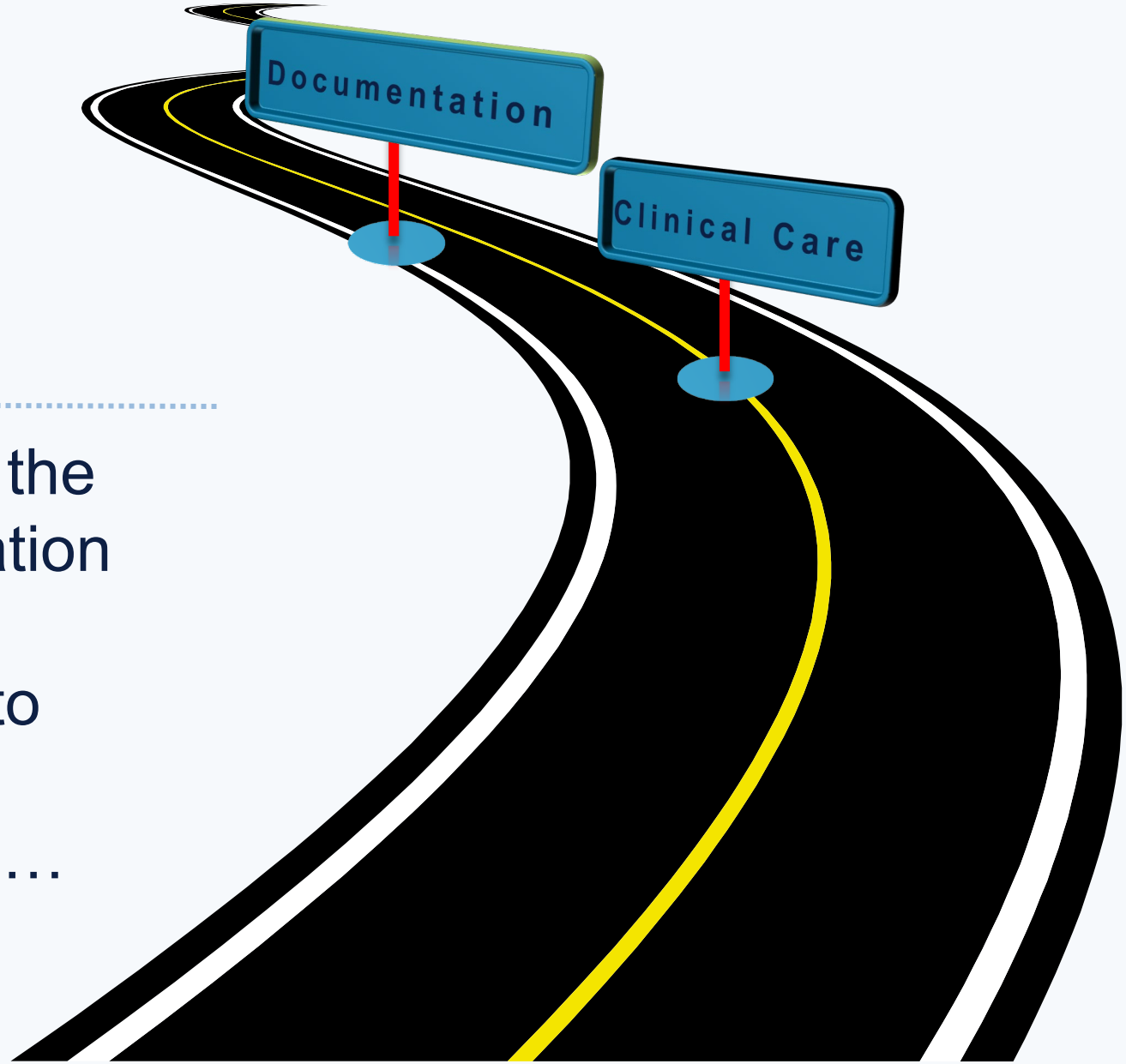
- **Mission**
  - **To improve the quality of surgical care for persons with cancer**

- **Goals**
  - *Develop **standards for the technical conduct of oncologic surgery***
  - Disseminate **resources and tools that support implementation** of **and adherence** to those standards
  - **Improve communication** regarding cancer surgery to facilitate appropriate (downstream) multidisciplinary care
  - **Educate** and train surgeons, trainees, staff

*Launched 2020

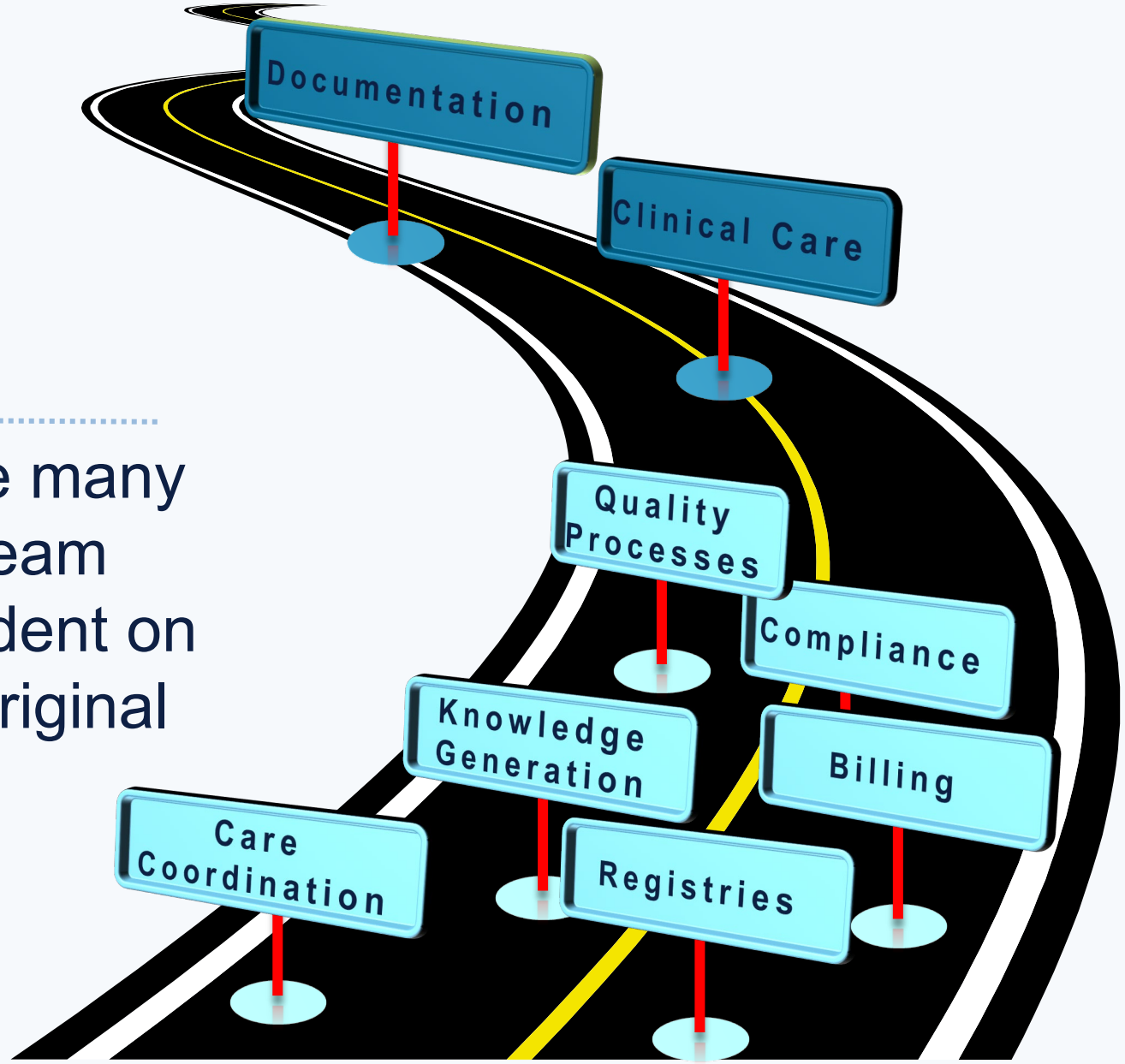
Documentation Considerations

We often focus on the ***task*** of documentation and having an immediate record to assist with postoperative care…



Documentation Considerations

…yet records have many important downstream roles, each dependent on the quality of the original documentation



Challenges Breed Opportunities!

Currently…a garbage-in/garbage-out problem that has direct impact on ***quality, delivery of care, and costs***.

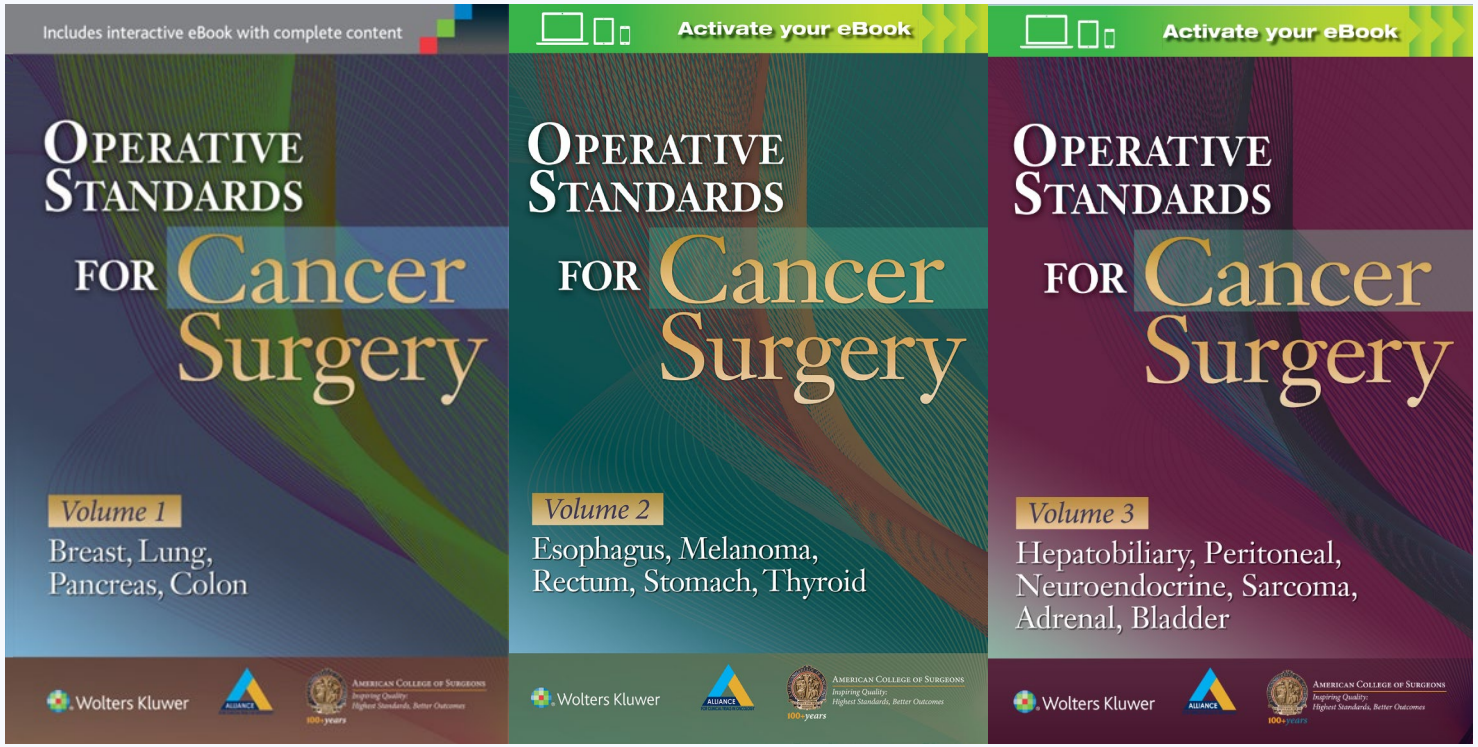
Standardizing operative reports are a mechanism by which we can address it.

Stogryn et al., 2019

Oncology Standards

- Legacy focus - medical management and institutional care processes
- Operative standards are *assumed* (although highly variable)
- Measurement of outcome metrics after surgery (e.g. number of lymph nodes in a resection specimen)…
- …however, lack of defined **standards** for the actual **cancer operation**
- Historically, surgery has been the only component of care that can be curative!

Operative Standards for Cancer Surgery Manuals



2015 2018 2022

- Describe critical steps of the major cancer operations for key disease sites
- Promote surgical uniformity for clinical trials (and pt care)
- Highlight evidence-based best practices in surgical oncology
- Establish surgical checklists
- Gap analysis for future research
- Inform protocol standards

Narrative Reporting vs. Synoptic Reporting

Narrative reporting…

- May be constructed using pre-determined data fields and pre-determined responses
- Constructed by dictation, free text, smarttext, etc.
- May use standardized terminology
- Presented in a **prose** format
- Prone to **omission** of necessary data and **inconsistencies** in language and formatting
- May allow for discrete data capture

Synoptic reporting…

- **Always** constructed using pre-determined data fields and pre-determined responses
- Typically created using a **tool**
- **Always** uses standardized terminology
- Presented in **checklist** format
- **Always** allows for discrete data capture
  - Information is formatted so it can be collected, stored, and is easily retrievable for data repositories
  - Can automatically populate data from the EHR

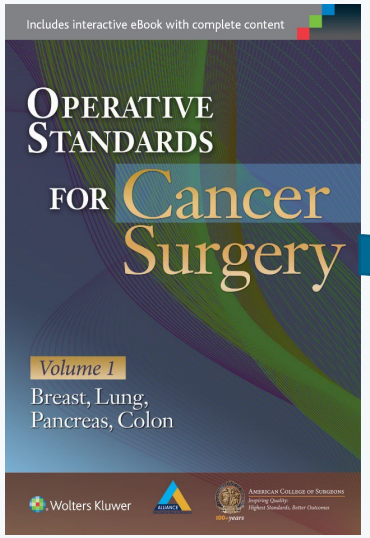
A note may (ideally?) be a combination of the two!

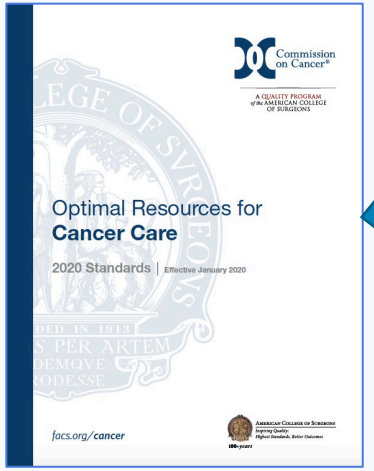
What is the value of Synoptic Operative Reporting?

- Improve accuracy of documentation and communication across multidisciplinary team
- Place focus on the critical elements of surgery
- Reinforce education: emphasize “critical elements” of oncologic operations
- Improve efficiency of data entry and facilitate data abstraction
- Enhance research, QI, compliance, demonstration of value
- Reduce variability in care
- **…Improve patient satisfaction and quality of cancer care***

*Smith TJ, Hillner BE. Ensuring quality cancer care by the use of clinical practice guidelines and critical pathways. *J Clin Oncol* 2001 Jun 1;19(11):2886-97

The CoC Operative Standards



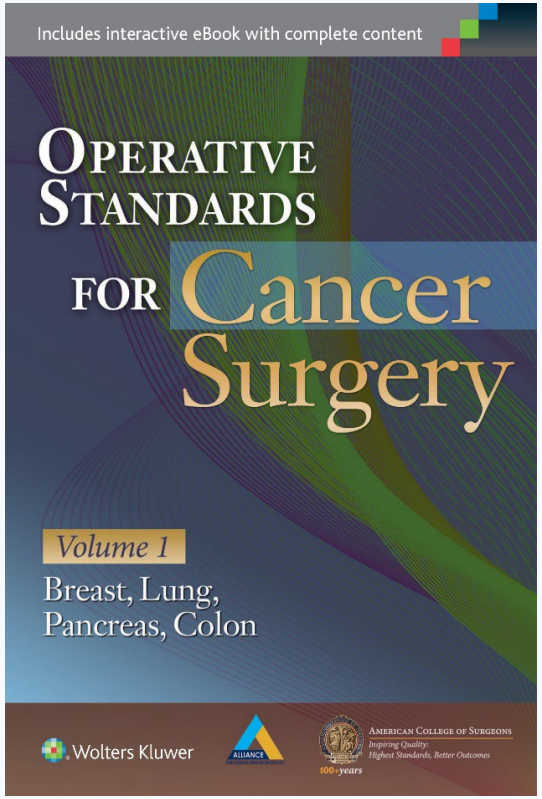


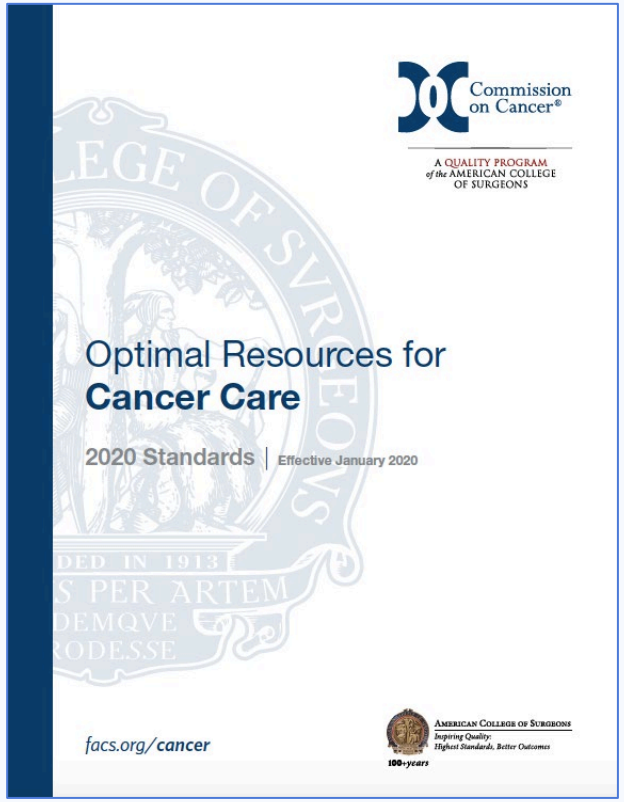
Standard	Disease Site	Procedure	Documentation
5.3	Breast	Sentinel node biopsy	Operative report
5.4	Breast	Axillary dissection	Operative report
5.5	Melanoma	Wide local excision	Operative report
5.6	Colon	Colectomy (any)	Operative report
5.7	Rectum	Mid/low resection (TME)	Pathology report (CAP)
5.8	Lung	Lung resection (any)	Pathology report (CAP)

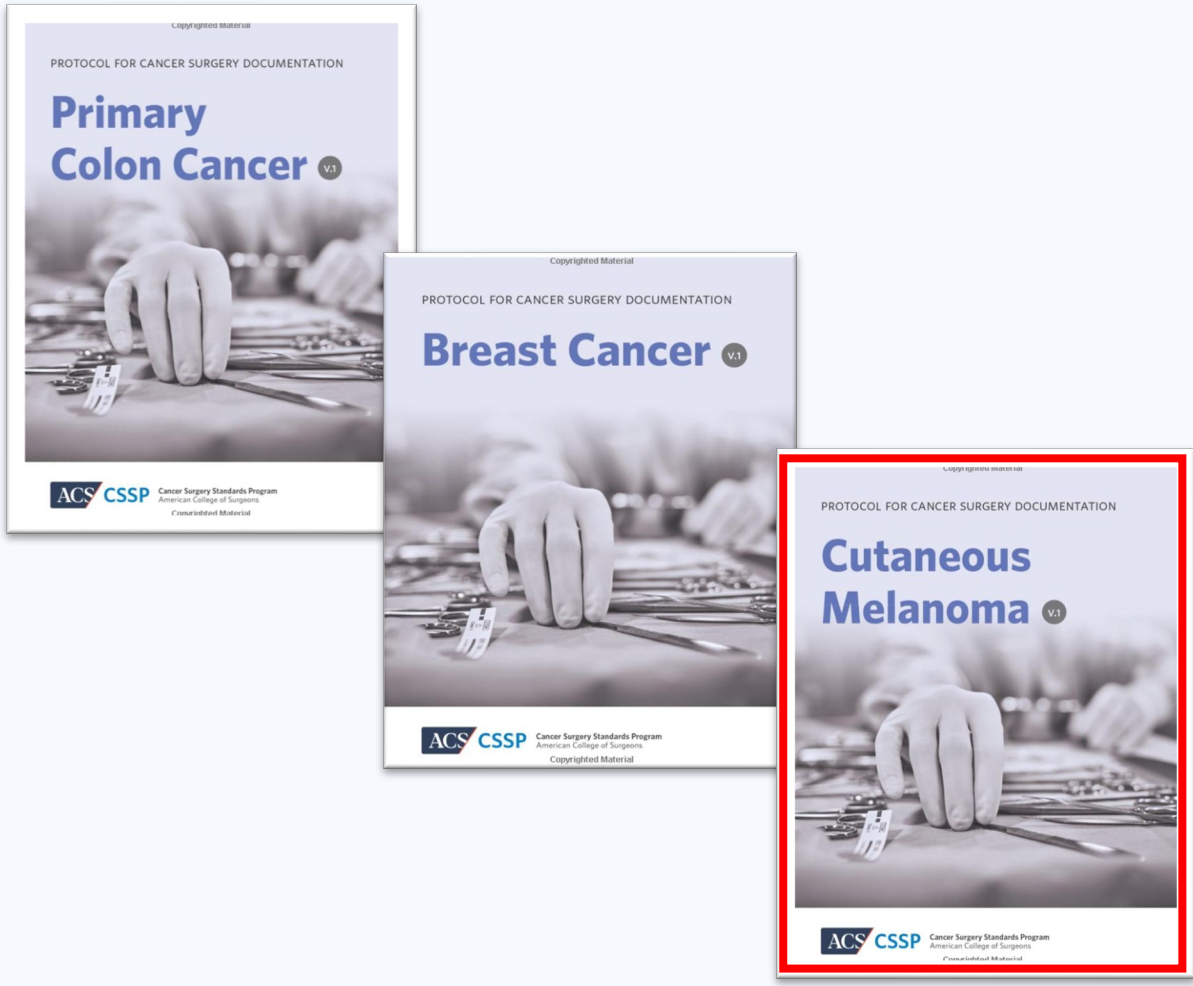
Operative Standards Evolution

Synoptic Operative Report & Knowledge Platform →

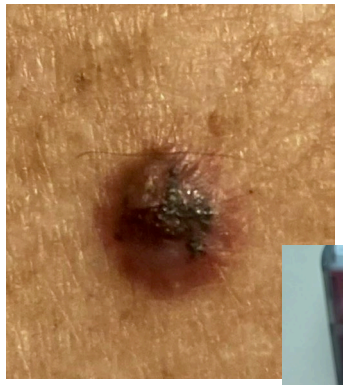
Cancer Surgery Protocol

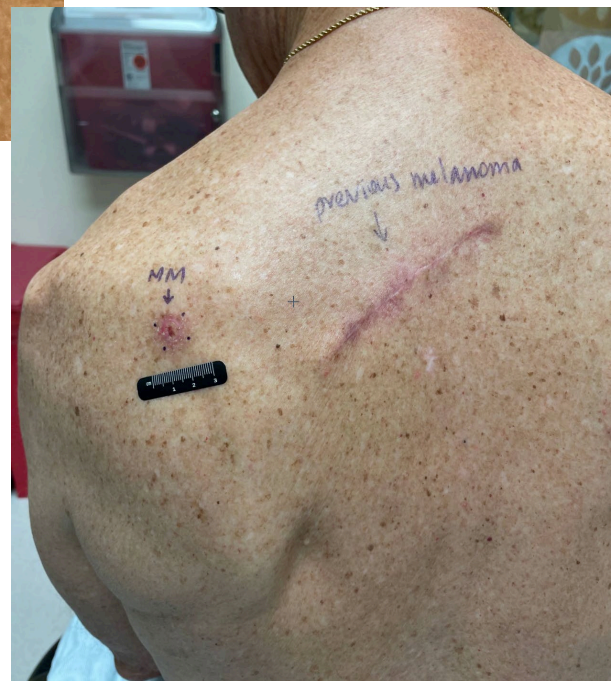






Case study – 71 yo male with prior h/o melanoma (6 years ago)…presents to dermatologist with suspicious pigmented lesion





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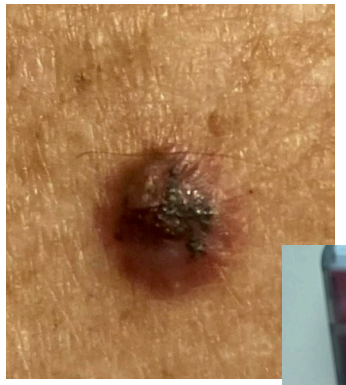
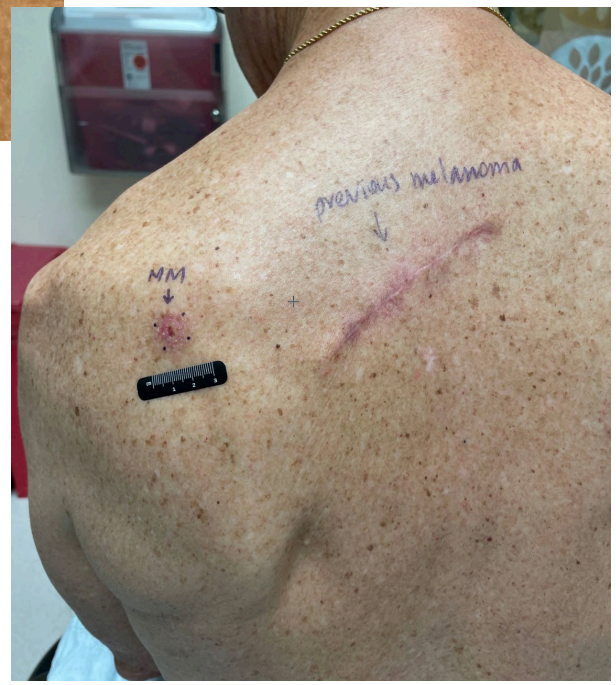
Management of Primary Cutaneous Melanoma

- Surgical approach to the primary melanoma (i.e., wide excision)
- Approach to the regional nodal basin
- Adjuvant therapy?

Case study – 71 yo male with prior h/o melanoma (6 years ago)…presents to dermatologist with suspicious pigmented lesion





Left upper back, skin shave (1xH&E: CLRC):

MELANOMA, INVASIVE, SUPERFICIAL SPREADING TYPE
CLARK LEVEL: AT LEAST IV
BRESLOW THICKNESS: 1.15 MM
RADIAL (NON-TUMORIGENIC) GROWTH PHASE: PRESENT
VERTICAL (TUMORIGENIC) GROWTH PHASE: PRESENT
MITOTIC FIGURES/mm^2: 2
ULCERATION: NOT IDENTIFIED
REGRESSION: NOT IDENTIFIED
VASCULAR INVASION: NOT IDENTIFIED
PERINEURAL INVASION: NOT IDENTIFIED
MICROSCOPIC SATELLITOSIS: NOT IDENTIFIED
TUMOR-INFILTRATING LYMPHOCYTES: PRESENT, NON-BRISK
ASSOCIATED MELANOCYTIC NEVUS: NOT IDENTIFIED
PREDOMINANT CYTOLOGY: EPITHELIOID
TISSUE EDGES: INVASIVE MELANOMA PRESENT AT DEEP TISSUE EDGE; MELANOMA IN SITU PRESENT AT PERIPHERAL TISSUE EDGE.

Victor G. Prieto, MD
MD Anderson

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MD Anderson Cancer Center

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Discordance in Diagnosis of Melanocytic Lesions and Its Impact on Clinical Management

A Melanoma Referral Center Experience With 1521 Cases

Guideline-based treatment recommendation based on the cancer center diagnosis: more extensive in 5.9% (89 of 1521) and less extensive in 5.0% (76 of 1521) of pts

N=1521 melanocytic lesions
Histopathological dx compared between referring institution & MD Anderson dermpath

Concordance rates:

- Dysplastic nevus – 75%
- Melanoma in situ – 91%
- Invasive melanoma – 96%
- Metastatic melanoma – 99.6%

Extent of discordance:

Major – 20%

Minor – 49%

Definition of Primary Tumor (T) - AJCC 8th Edition

T Category	Thickness	Ulceration status
Tis (melanoma *in situ*)	Not applicable	Not applicable
T1	≤1.0 mm	Unknown or unspecified
T1a	<0.8 mm	Without ulceration
T1b	<0.8 mm 0.8–1.0 mm	With ulceration With or without ulceration
T2	>1.0–2.0 mm	Unknown or unspecified
T2a	>1.0–2.0 mm	Without ulceration
T2b	>1.0–2.0 mm	With ulceration
T3	>2.0-4.0 mm	Unknown or unspecified
T3a	>2.0–4.0 mm	Without ulceration
T3b	>2.0–4.0 mm	With ulceration
T4	>4.0 mm	Unknown or unspecified
T4a	>4.0 mm	Without ulceration
T4b	>4.0 mm	With ulceration

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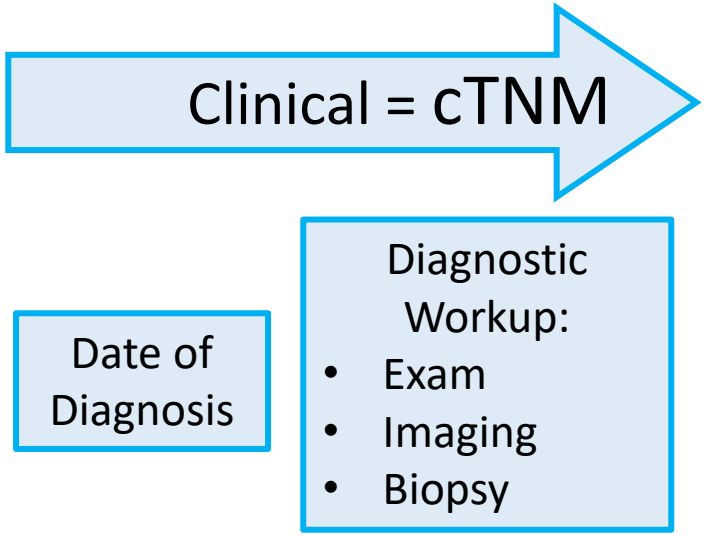
Gershenwald, Scolyer, et al. Melanoma. In AJCC Cancer Staging Manual. 8th Ed. New York: Springer; 2017

AJCC Classification schema



Adapted and expanded from Byrd, Brierley, Baker, Sullivan, Gress. CA CANCER J CLIN 2021;71:140–148

Management of Primary Cutaneous Melanoma

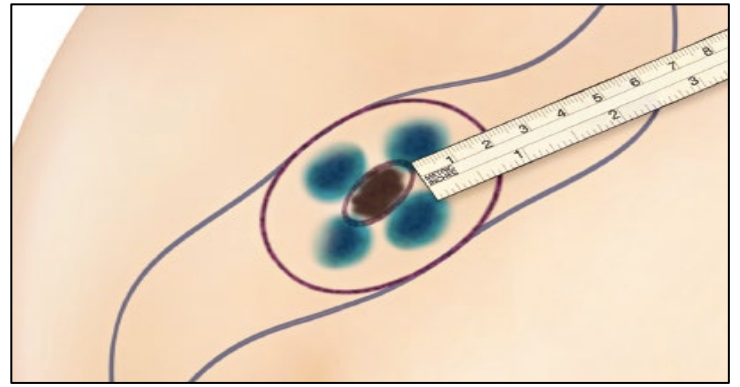
- Wide excision of the primary melanoma
  - Margins appropriate for tumor thickness
- Approach to the regional nodal basin
- Adjuvant therapy?

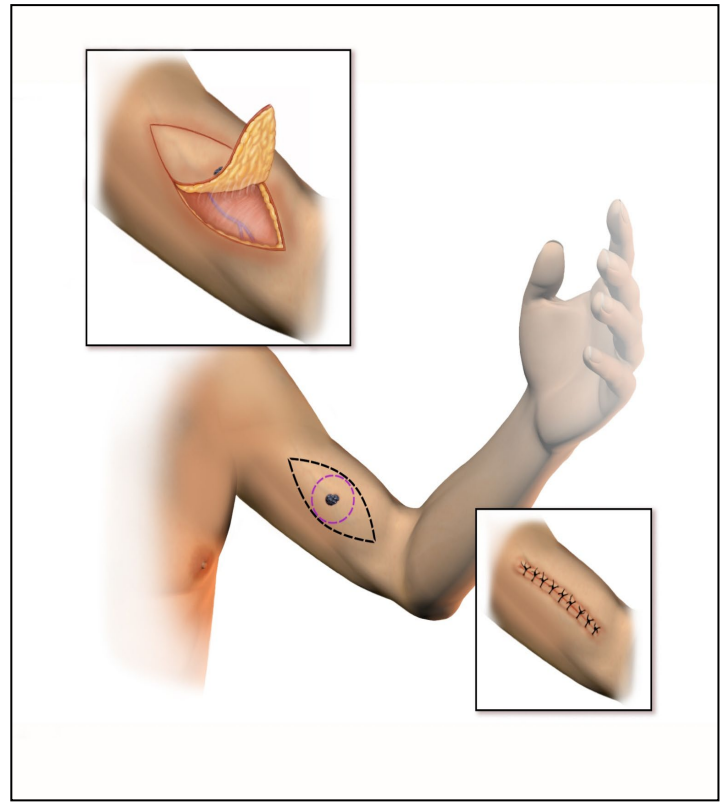
National Comprehensive Cancer Network®

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)

Melanoma: Cutaneous

Guideline-based Exicsion Margin Recommendations - Invasive Melanoma





Recommended Excision Margin

Tumor Thickness	USA (NCCN v3.2024)	European* (2022)	Australia** (2020 wiki)
<=1 mm	1 cm	1 cm	1 cm
1 mm – 2 mm	1 or 2 cm	1 cm	1 or 2 cm
2 mm – 4 mm	2 cm	1 or 2 cm	1 or 2 cm***
>4 mm	2 cm	2 cm	2 cm

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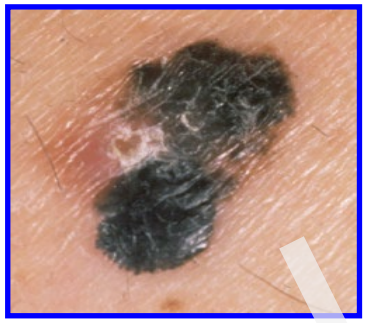
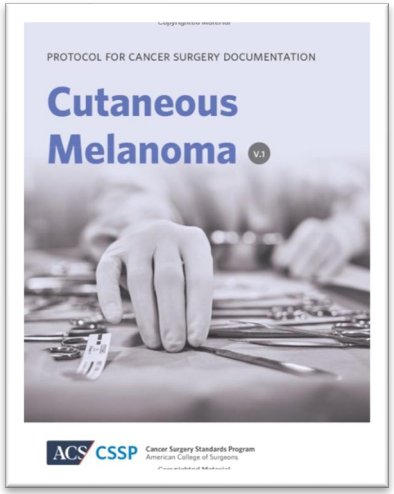
*Eur J Cancer. 2022 Jul;170:256-284. – a safety margin should be performed

**https://wiki.cancer.org.au/australia/Guidelines:Melanoma – wide excision (category 1)

***Caution should be exercised for melanomas 2.01–4.00 mm thick

Knowledge Platform - Melanoma





Wide Local Excision (Note I)

*** Clinical Margin Width** (Note J)
Select single best answer, measuring from edge of the lesion or the prior excision scar.
A response to this question is required to fulfill CoC Standard 5.5, which applies to curative-intent wide local excisions of primary cutaneous melanoma lesions. Mucosal, ocular, and subungual melanomas are excluded.
__ 0.5 cm
__ 1 cm
__ 2 cm
__ Other: __ cm due to cosmetic/anatomic concerns
__ Other [*Narrative box*]

*** Depth of Excision** (Note K)
Select single best answer.
A response to this question is required to fulfill CoC Standard 5.5, which applies to curative-intent wide local excisions of primary cutaneous melanoma lesions. Mucosal, ocular, and subungual melanomas are excluded.
__ Full-thickness skin/subcutaneous tissue down to fascia (melanoma)
__ Only skin and superficial subcutaneous fat (melanoma in situ)
__ Other [*Narrative box*]

gin Width (Wide Local Excision)

nts: In melanoma, the recommended margin width (radial margin) for wide local excision is slow thickness of the primary melanoma. The margin is a clinical one, measured from the edge of mor (pigment) or from the edge of the previous biopsy. For a melanoma <1mm in thickness, a 1cm d. For a 1-2mm thick melanoma, a 1-2cm margin is recommended, and for a melanoma >2mm recommended. Proper measurement of a 2cm margin is shown in Figure 1. For melanoma in situ, a is recommended. Although the above recommendations for margin width applies to melanoma of utation of all or part of the digit may be necessary to achieve the appropriate margin (see Note O).

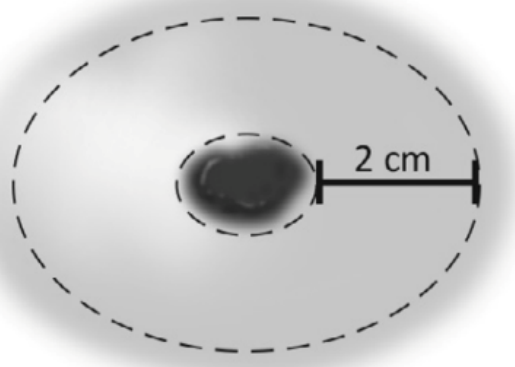
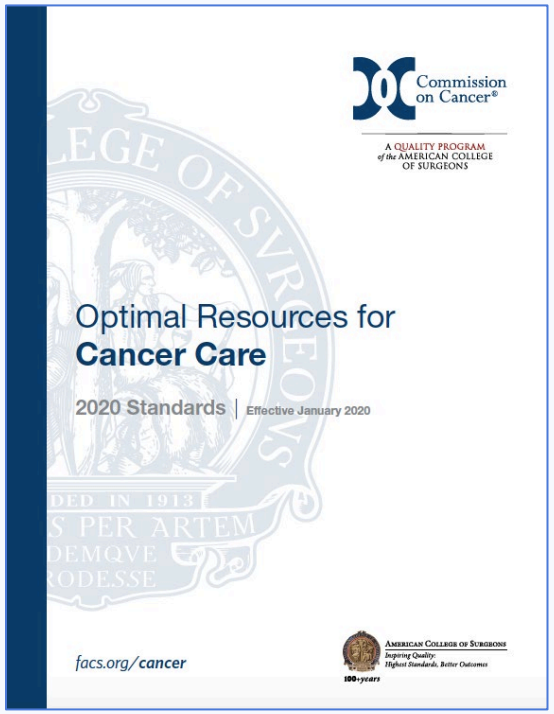


Figure 1. Wide local excision clinical margin width of 2 centimeters, measured from the edge of any visible residual tumor or from the edge of the previous biopsy.

The CoC Operative Standards



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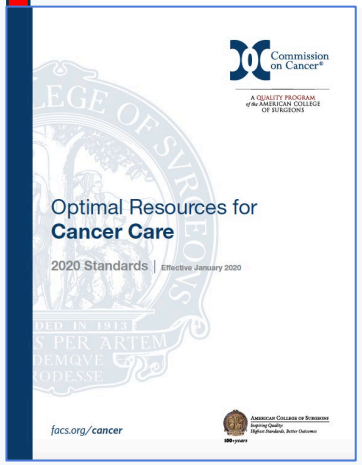
5.8	Lung	Lung resection (any)	Pathology report (CAP)

Standard 5.5: Wide Local Excision for Primary Cutaneous Melanoma

Measures of Compliance

- Wide local excisions for melanoma **include the skin and all underlying subcutaneous tissue down to the fascia** (for invasive melanoma) or **the skin and the superficial subcutaneous fat** (for in situ disease). **Clinical margin width** is selected based on original Breslow thickness:
  - 1 cm for invasive melanomas less than 1 mm thick.
  - 1 to 2 cm for invasive melanomas 1 to 2 mm thick.
  - 2 cm for invasive melanomas greater than 2 mm thick.
  - At least 5 mm for melanoma in situ.
- Operative reports for wide local excisions of primary cutaneous melanomas **document the required elements in synoptic format**.

Element	Response Options
Operation performed with curative intent	Yes; No.
Original Breslow thickness of the lesion	Melanoma in situ (MIS); _._ mm *(to the tenth of a millimeter).*
Clinical margin width *(measured from the edge of the lesion or the prior excision scar)*	0.5 cm; 1 cm; 2 cm; Other: __ cm due to cosmetic/anatomic concerns; Other *(with explanation).*
Depth of excision	Full-thickness skin/ subcutaneous tissue down to fascia (melanoma); Only skin and superficial subcutaneous fat (melanoma in situ); Other *(with explanation).*



Cancer-specific data and technical details in synoptic format

CoC Standard 5.5
Wide excision for primary cutaneous melanoma
"Smartphrase"

Commission on Cancer standard 5.5 - wide excision for primary cutaneous melanoma:
Operation performed with curative intent? YES NO
Original primary tumor (Breslow) thickness: primary tumor Breslow thickness
Surgical/Clinical margin width: surgical resection margin
Depth of excision: depth of wide excision to fascia
Overall clinical/surgical wide excision margin width summary: wide excision margin summary
was was not performed

Commission on Cancer standard 5.5 - wide excision for primary cutaneous melanoma:
Operation performed with curative intent? yes
Original primary tumor (Breslow) thickness: 1.2 mm (to the tenth of a mm)
Surgical/Clinical margin width: 1 cm
Depth of excision: Full-thickness skin/subcutaneous tissue down to fascia (melanoma).
Overall clinical/surgical wide excision margin width summary: 1 to 2 cm margin for melanomas 1 to 2 mm thick was performed

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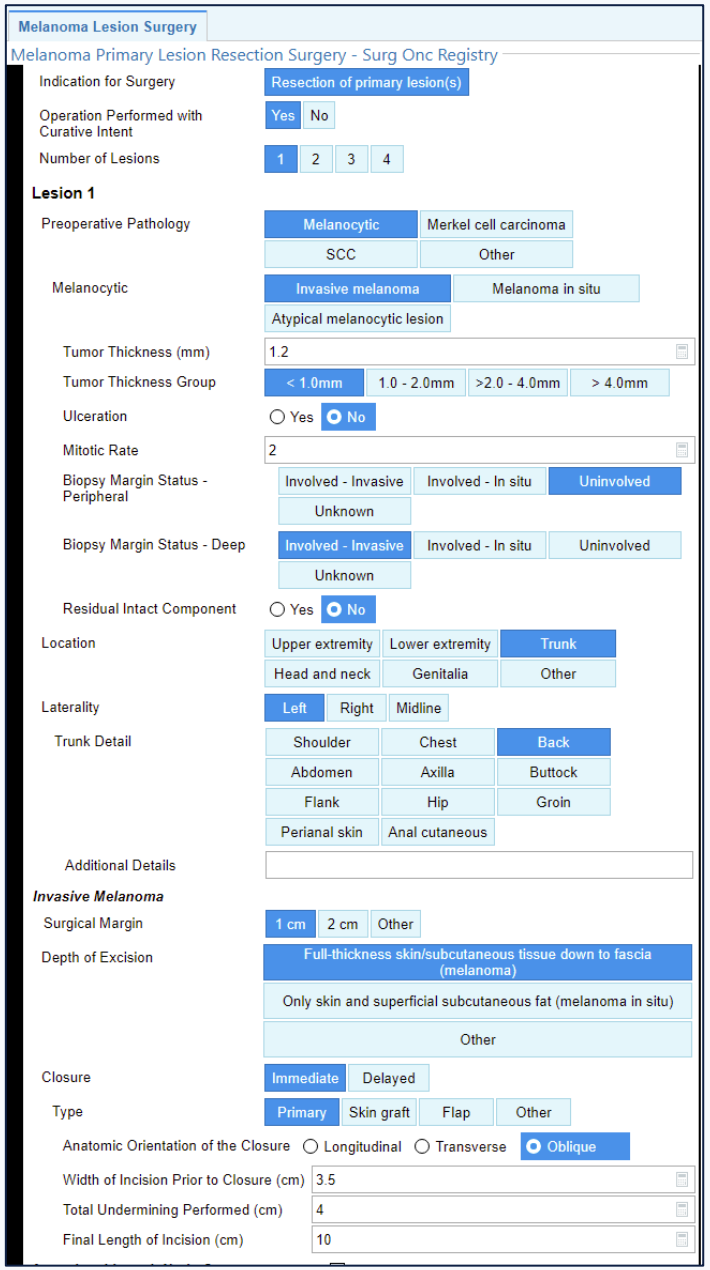
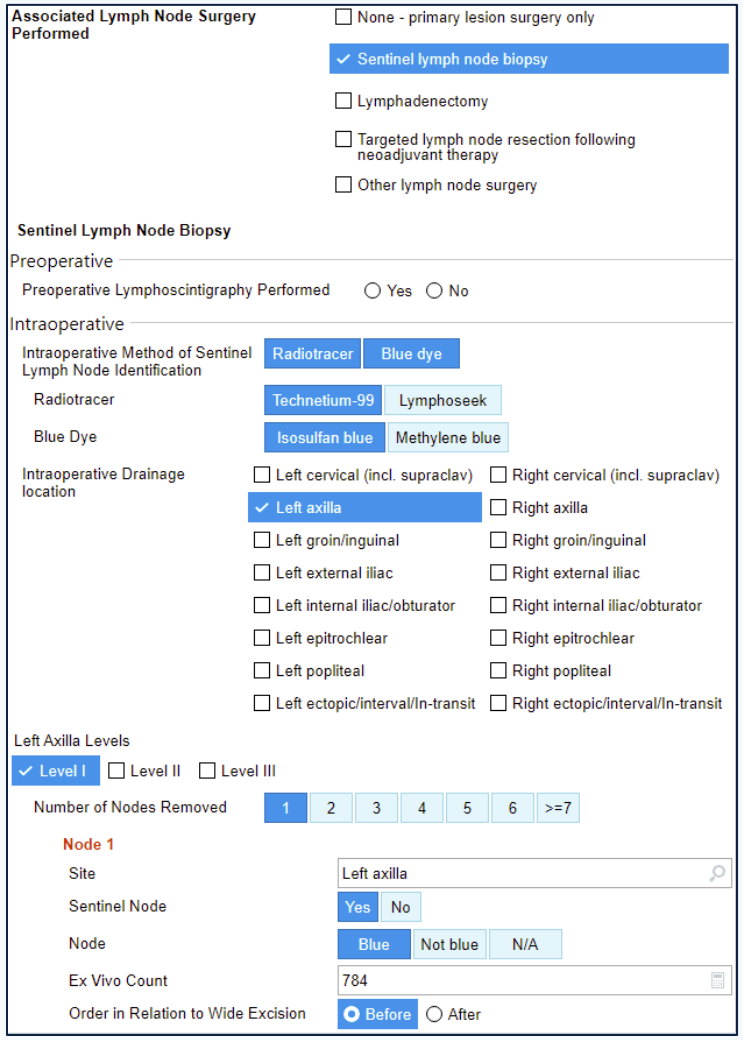
MD Anderson Synoptic Operative Report v1.0





Melanoma Primary Lesion Resection Surgery:
Indication for Surgery: **Resection of primary lesion(s)**
Operation Performed with Curative Intent: **Yes**
Number of Lesions: **1**

Lesion 1
Preoperative Pathology: **Melanocytic**
Melanocytic: **Invasive melanoma**
Tumor Thickness (mm): **1.2**
Tumor Thickness Group: **< 1.0mm**
Ulceration: **No**
Mitotic Rate: **2**
Biopsy Margin Status - Peripheral: **Uninvolved**
Biopsy Margin Status - Deep: **Involved - Invasive**
Residual Intact Component: **No**
Location: **Trunk**
Laterality: **Left**
Trunk Detail: **Back**
Invasive Melanoma:
Surgical Margin: **1 cm**
Depth of Excision: **Full-thickness skin/subcutaneous tissue down to fascia (melanoma)**
Closure: **Immediate**
Type: **Primary**
Anatomic Orientation of the Closure: **Oblique**
Width of Incision Prior to Closure (cm): **3.5**
Total Undermining Performed (cm): **4**
Final Length of Incision (cm): **10**

Associated Lymph Node Surgery Performed: **Sentinel lymph node biopsy** ***Intraoperative***
Intraoperative Method of Sentinel Lymph Node Identification: **Radiotracer and Blue dye**
Radiotracer: **Technetium-99**
Blue Dye: **Isosulfan blue**
Intraoperative Drainage location: **Left axilla**

Left Cervical Levels:	Right Cervical Levels:
Left Axilla Levels: **Level I**	Right Axilla Levels:
Please Explain Left ectopic/interval/In-transit:	Please Explain Right ectopic/interval/In-transit:

Number of Nodes Removed: **1**
Node 1
Site: **Left axilla**
Sentinel Node: **Yes**
Node: **Blue**
Ex Vivo Count: **784**
Order in Relation to Wide Excision: **Before**

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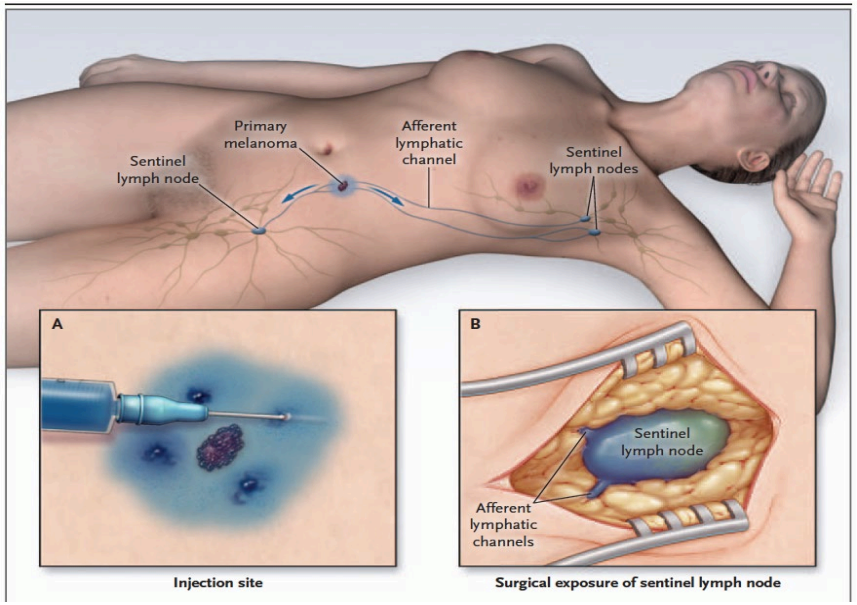
Management of Primary Cutaneous Melanoma

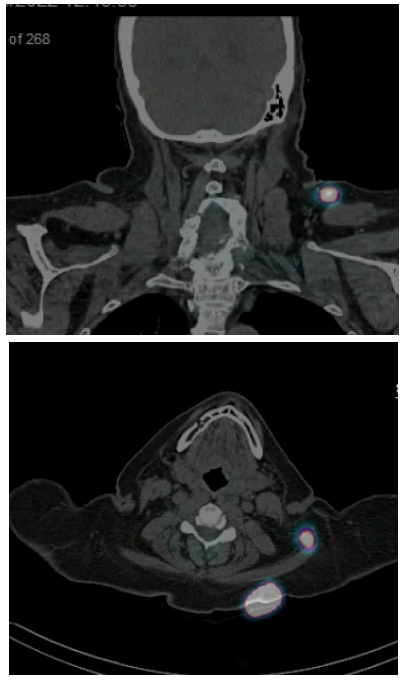
- Wide excision of the primary melanoma
  - Margins appropriate for tumor thickness
- Approach to the regional nodal basin
- Adjuvant therapy?

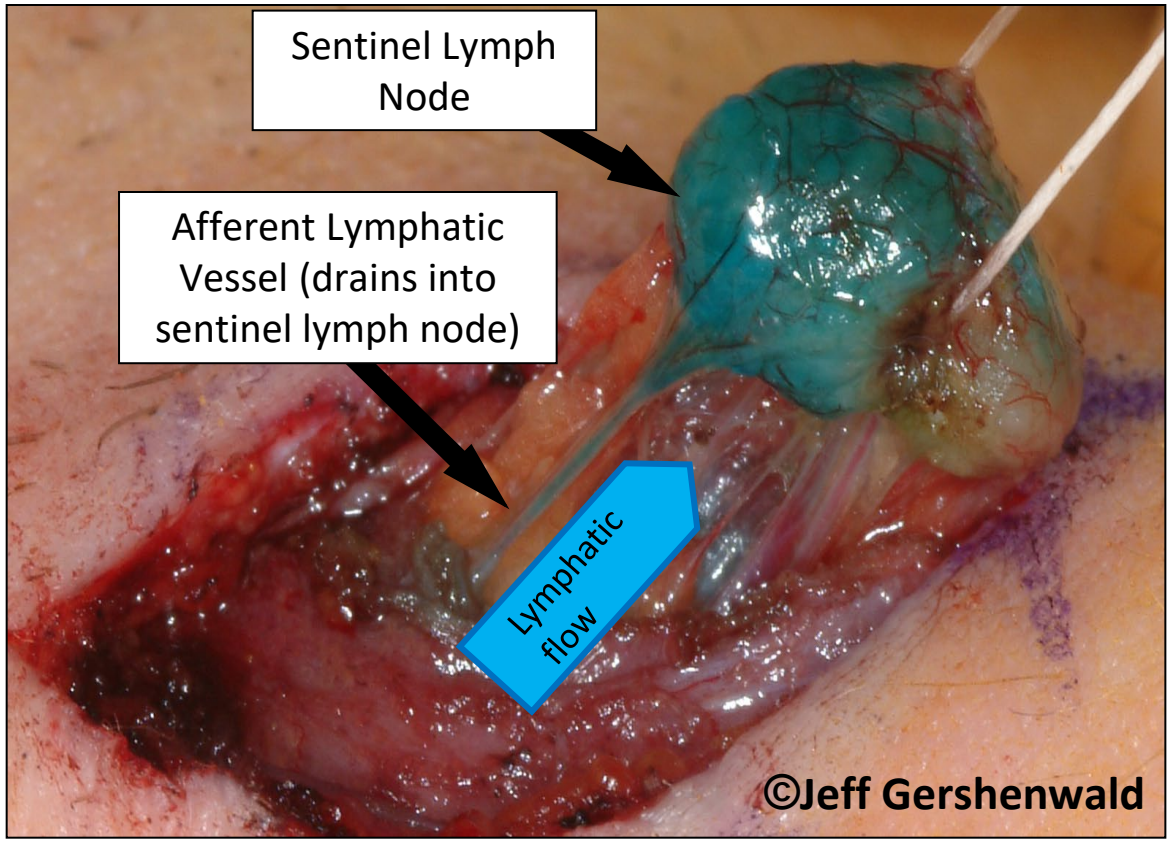
Lymphatic Mapping & Sentinel Node Biopsy

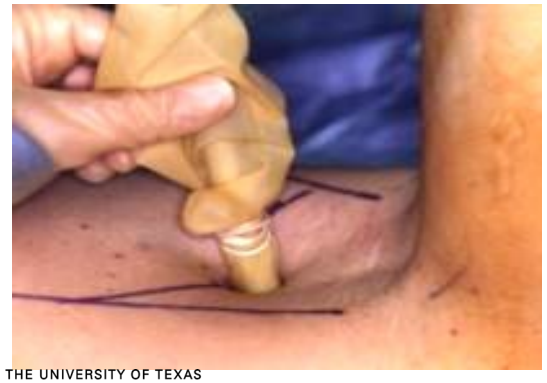
Identify patients with tumor-involved regional nodes

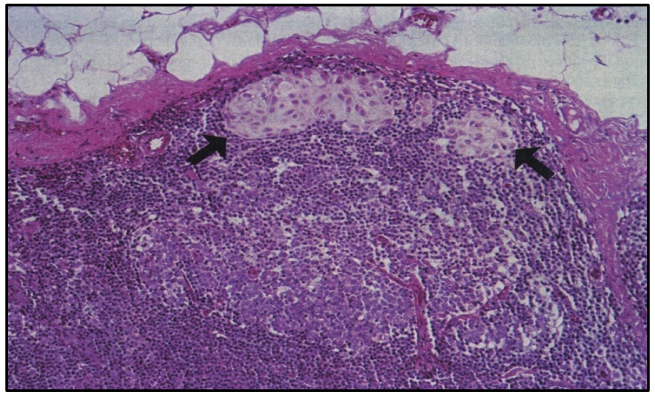


Gershenwald and Ross, N Engl J Med 2011;364:1738-45.









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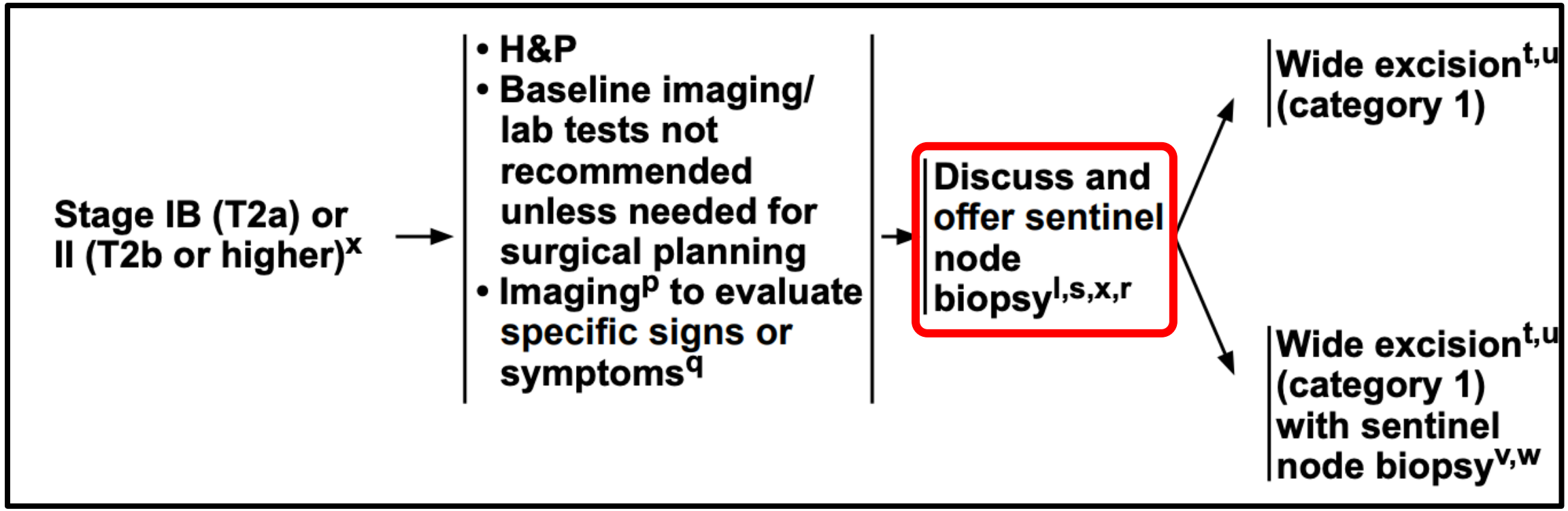
NCCN (v2.2024)
23 September 2024

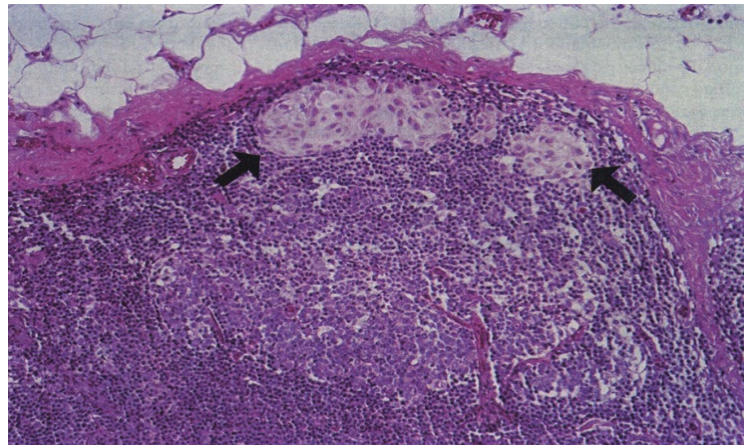
National Comprehensive Cancer Network®



Case study → Patient undergoes wide excision and concomitant lymphatic mapping & SLN biopsy

Diagnosis

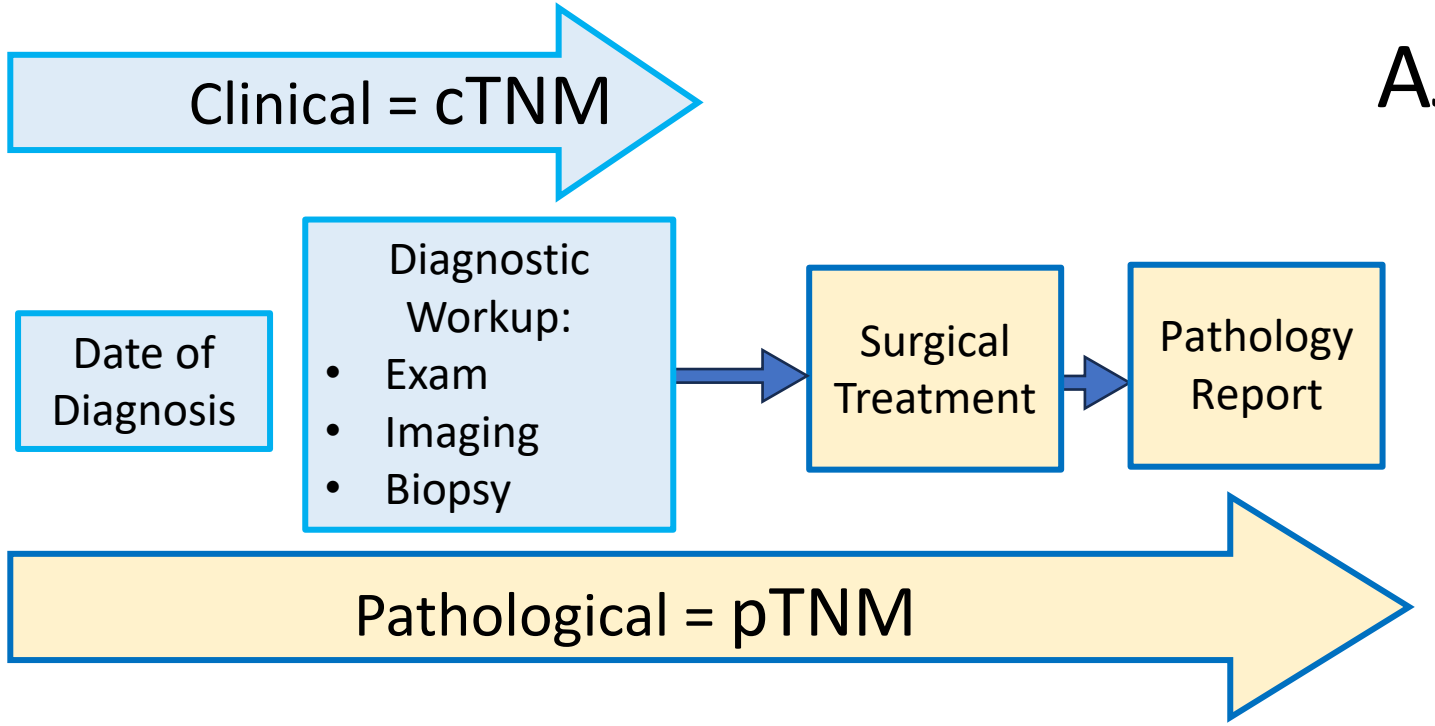
A: Lymph node, left axilla, sentinel lymph node #1, blue, counts: 784, lymphadenectomy:
MELANOMA, METASTATIC TO ONE OF ONE LYMPH NODE (1/1).
Largest tumor deposit size: 5.3 x 0.2 mm
Location: Subcapsular
Extracapsular extension: Not identified
See comment.



B: Skin, left back, scapular region, ellipse:
Skin and subcutis with healing surgical wound/scar.
Melanoma not identified.
Margins are free of in situ and invasive melanoma.
Background focal reactive melanocytic hyperplasia.
INCIDENTAL MELANOCYTIC NEVUS, PREDOMINANTLY JUNCTIONAL TYPE, WITH MODERATE ARCHITECTURAL DISORDER AND MILD CYTOLOGIC ATYPIA OF MELANOCYTES (“DYSPLASTIC”), MARGINS ARE FREE.

Gershenwald et al., J Clin Oncol, 1999

AJCC Classification schema



Presented by Jeff Gershenwald

Adapted and expanded from Byrd, Brierley, Baker, Sullivan, Gress. CA CANCER J CLIN 2021;71:140–148

AJCC 8th Edition N-category criteria

N Category	Number of tumor-involved regional lymph node	Presence of in-transit, satellite, and/or microsatellite metastases
N0	No regional metastases detected	No
N1	One tumor-involved node or in-transit, satellite, and/or microsatellite metastases with no tumor-involved nodes	
N1a	One clinically occult (i.e., detected by SLN biopsy)	No
N1b	One clinically detected	No
N1c	No regional lymph node disease	Yes
N2	Two or three tumor-involved nodes or in-transit, satellite, and/or microsatellite metastases with one tumor-involved node	
N2a	Two or three clinically occult (i.e., detected by SLN biopsy)	No
N2b	Two or three, at least one of which was clinically detected	No
N2c	One clinically occult or clinically detected	Yes
N3	Four or more tumor-involved nodes or in-transit, satellite, and/or microsatellite metastases with two or more tumor-involved nodes, or any number of matted nodes without or with in-transit, satellite, and/or microsatellite metastases	
N3a	Four or more clinically occult (i.e., detected by SLN biopsy)	No
N3b	Four or more, at least one of which was clinically detected, or presence of any number of matted nodes	No
N3c	Two or more clinically occult or clinically detected and/or presence of any number of matted nodes	Yes

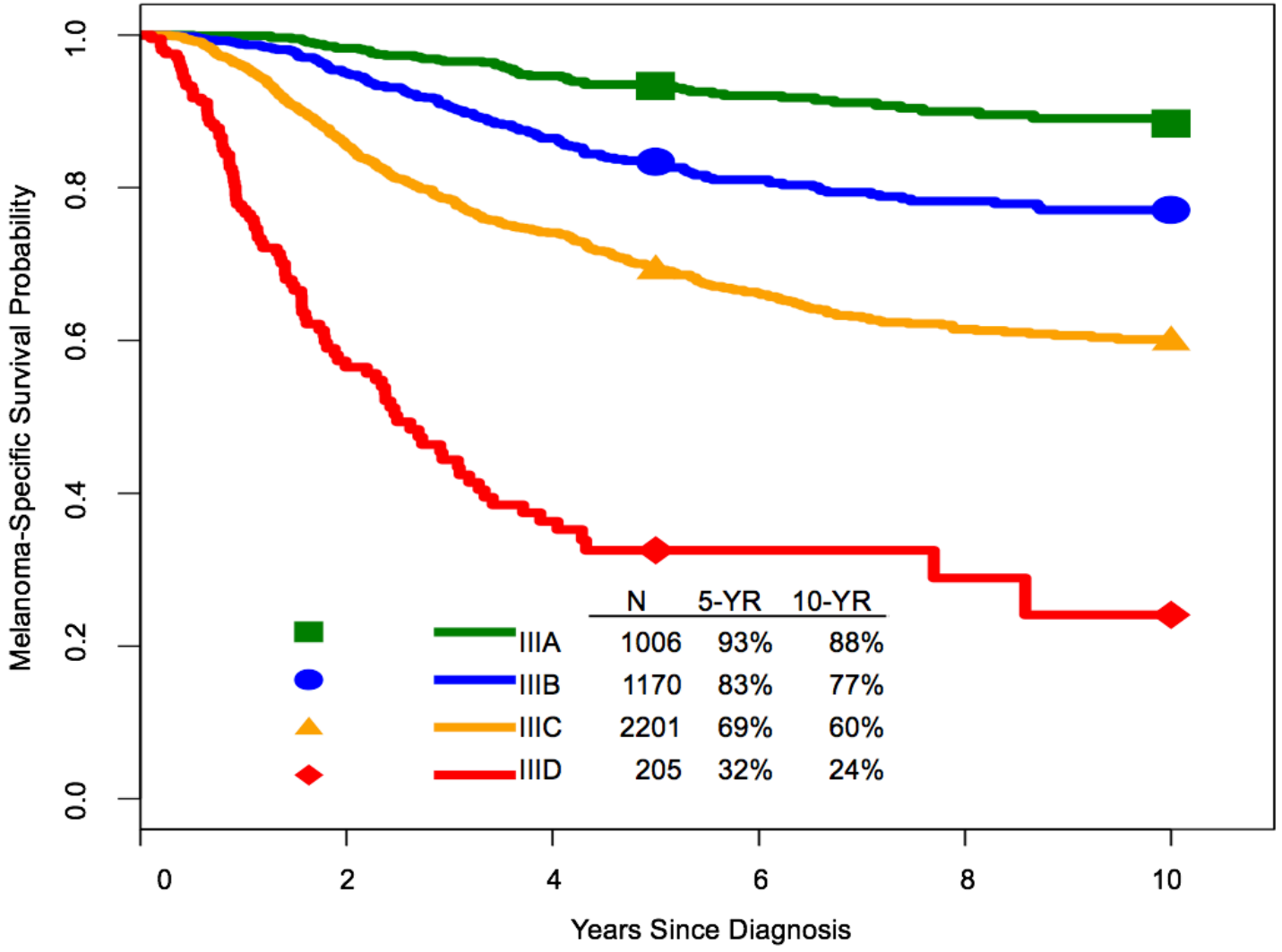
Gershenwald, Scolyer, et al. Melanoma. In Amin, M.B., Edge, S.B., Greene, F.L., et al. (Eds.) AJCC Cancer Staging Manual. 8th Ed. New York: Springer; 2017

Melanoma Re-excision – CAP protocol
pT2apN1a(sn)M0 = **AJCC stage IIIA**

MELANOMA OF THE SKIN: Excision, Re-Excision 8th Edition - Protocol posted: 11	MELANOMA OF THE SKIN: EXCISION, RE-EXCISION - All Specimens
SPECIMEN	
Procedure	Excision Sentinel node(s) biopsy
Specimen Laterality	Left
TUMOR	
Tumor Site	Skin of trunk: left back scapular region/left upper back
Histologic Type	Superficial spreading melanoma (low-cumulative sun damage (CSD) melanoma)
Maximum Tumor (Breslow) Thickness (Millimeters)	1.15 mm
Macroscopic Satellite Nodule(s)	Not identified
Ulceration	Not identified
Anatomic (Clark) Level	IV (Melanoma invades reticular dermis)
Mitotic Rate	2 mitoses per mm2
Microsatellite(s)	Not identified
Lymphovascular Invasion	Not identified
Neurotropism	Not identified
Tumor-Infiltrating Lymphocytes	Present, nonbrisk
Tumor Regression	Not identified
MARGINS	
Margin Status for Invasive Melanoma	All margins negative for invasive melanoma
Margin Status for Melanoma in situ	All margins negative for melanoma in situ
REGIONAL LYMPH NODES	
Regional Lymph Node Status	Tumor present in regional lymph node(s)
Total Number of Lymph Nodes with Tumor	1
Number of Sentinel Lymph Nodes with Tumor	1
Nodal Site(s) with Tumor	Subcapsular
Size of Largest Sentinel Node Metastatic Deposit	5.3 x 0.2 mm
Size of Largest Nodal Metastatic Deposit	N/A
Extranodal Extension	Not identified
Matted Nodes	Not identified
Total Number of Lymph Nodes Examined	1
Number of Sentinel Nodes Examined	1
PATHOLOGIC STAGE CLASSIFICATION (pTNM, AJCC 8th Edition)	Classification assigned in this report includes information from a prior procedure: X23-028229
pT Category	pT2a
pN Category	pN1a

MSS according to Stage III Groups
8th Edition international melanoma database

- Stage group stratification based on both T- and N-category criteria
  - Tumor thickness
  - Ulceration
  - LN #, SLN(+) or clinically evident regional LNs
  - Microsatellite/ITM/satellites
- Recursive partitioning → final = 4 stage groups
- Significant heterogeneity



Gershenwald, Scolyer, Hess, Sondak et al. CA Cancer J Clin. 2017 Oct 13. doi: 10.3322/caac.21409. [Epub ahead of print]

MSS according to Stage III Groups
8th Edition international melanoma database

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center
Making Cancer History®

- Stage group stratification based on both T- and N-category criteria
  - Primary tumor thickness
  - Ulceration
  - # LNs
  - Microsatellite/ITM/s
- Significant heterogeneity

AJCC Eighth Edition Melanoma Stage III Subgroups

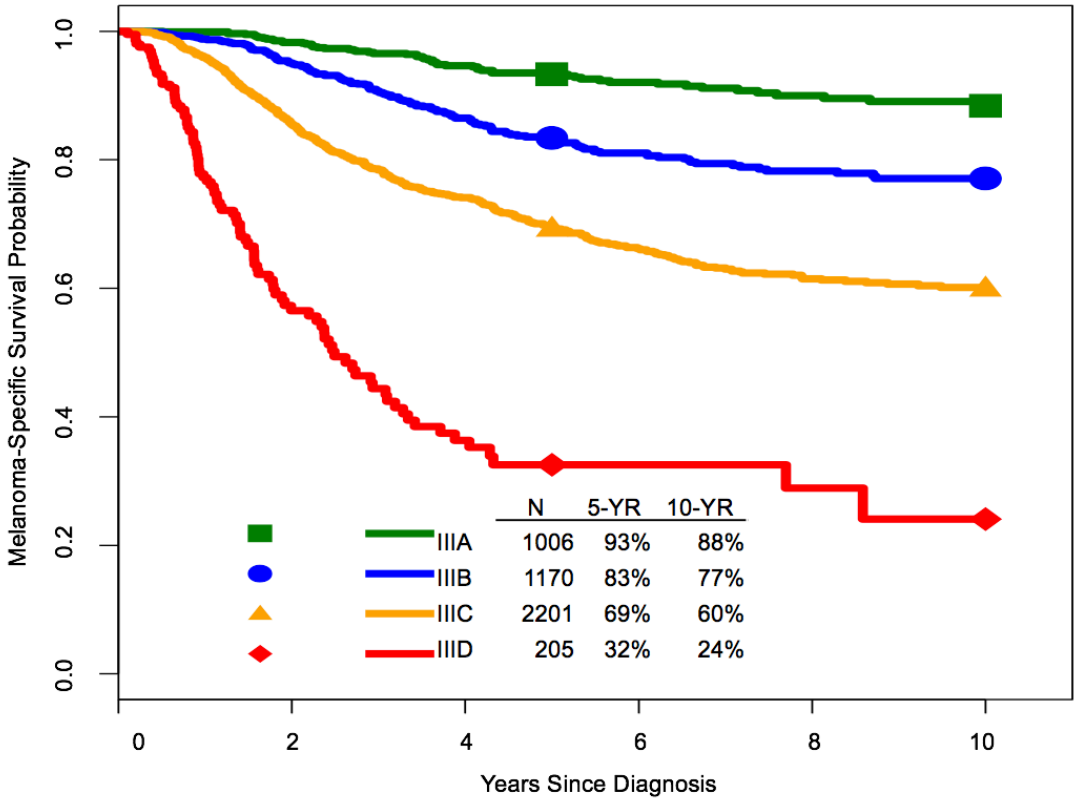
N Category	T Category								
	T0	T1a	T1b	T2a	T2b	T3a	T3b	T4a	T4b
N1a	N/A	A	A	A	B	B	C	C	C
N1b	B	B	B	B	B	B	C	C	C
N1c	B	B	B	B	B	B	C	C	C
N2a	N/A	A	A	A	B	B	C	C	C
N2b	C	B	B	B	B	B	C	C	C
N2c	C	C	C	C	C	C	C	C	C
N3a	N/A	C	C	C	C	C	C	C	D
N3b	C	C	C	C	C	C	C	C	D
N3c	C	C	C	C	C	C	C	C	D

Instructions
(1) Select patient's N category at left of chart.
(2) Select patient's T category at top of chart.
(3) Note letter at the intersection of T&N on grid.
(4) Determine patient's AJCC stage using legend.

N/A=Not assigned, please see manual for details. REF

Legend

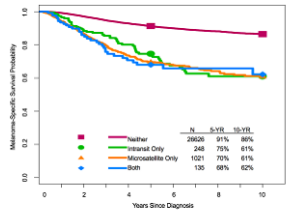
A	Stage IIIA
B	Stage IIIB
C	Stage IIIC
D	Stage IIID



Gershenwald, Scolyer, Hess, Sondak et al. CA Cancer J Clin. 2017 Oct 13. doi: 10.3322/caac.21409.

AJCC 8th Edition N-category

- Regional nodes
- Non-nodal regional disease
  - In-transits (ITM)
  - Satellites
  - Microsatellites
- Microsatellites/satellites/ITM grouped together for staging purposes



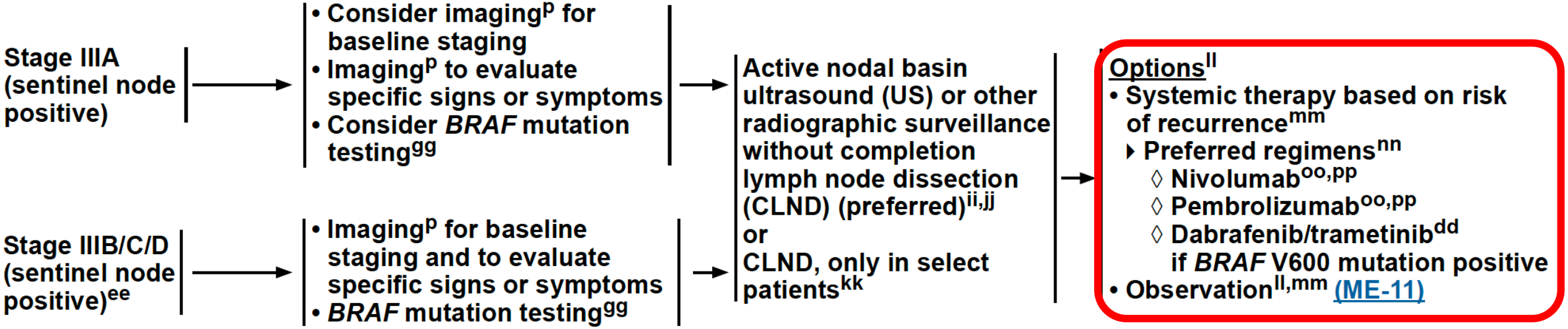
Gershenwald, Scolyer, et al. Melanoma. In Amin, M.B., Edge, S.B., Greene, F.L., et al. (Eds.) AJCC Cancer Staging Manual. 8th Ed., 2017
Gershenwald, Scolyer, Hess, Sondak et al. CA Cancer J Clin. 2017

Management of Primary Cutaneous Melanoma

- Wide excision of the primary melanoma
- Approach to the regional nodal basin
- Adjuvant therapy?

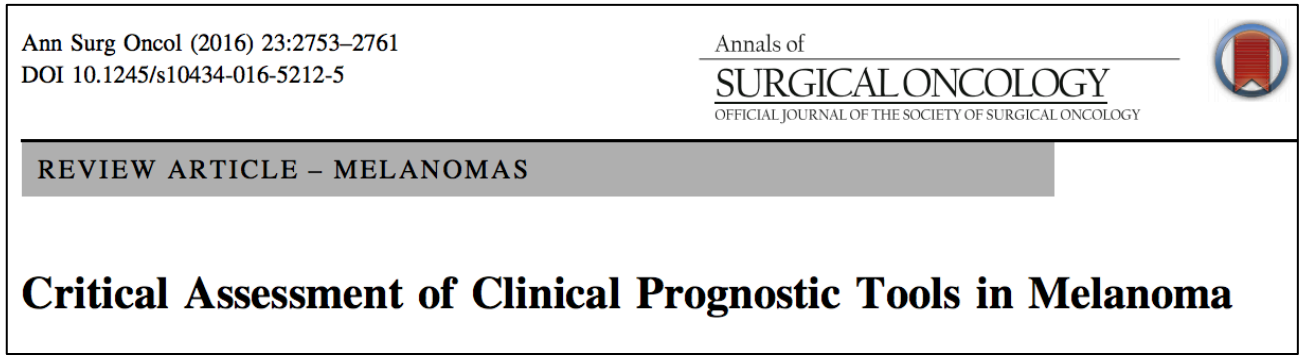
v1.2024 12 February 2024

National Comprehensive Cancer Network®



[mm] **In patients with very-low-risk stage AJCC8 IIIA disease (T1a/b–T2a/N1a or N2a), the toxicity of adjuvant therapy may outweigh the benefit.** Patients with T1b–T2a/ N1a or N2a pathologic stage IIIA melanoma and SLN tumor deposits ≥0.3 mm in maximum dimension are at higher risk of disease progression and may benefit from adjuvant systemic therapy. Stage IIIA patients with SLN deposits <0.3 mm in maximum dimension demonstrate 5-year melanoma-specific survival similar to those with pathologic stage IB (T2aN0) melanoma, with consideration for less intensive radiologic surveillance and follow-up (Moncrieff MD, Lo SN, Scolyer RA, et al. J Clin Oncol 2022;40:3940-3951).

Towards an era of individualized prognostic assessment in melanoma



Ann Surg Oncol (2016) 23:2753–2761
DOI 10.1245/s10434-016-5212-5

Annals of SURGICAL ONCOLOGY
OFFICIAL JOURNAL OF THE SOCIETY OF SURGICAL ONCOLOGY

REVIEW ARTICLE – MELANOMAS

Critical Assessment of Clinical Prognostic Tools in Melanoma

COMMENTARY

CA CANCER J CLIN 2016;00:0

American Joint Committee on Cancer Acceptance Criteria for Inclusion of Risk Models for Individualized Prognosis in the Practice of Precision Medicine

Michael W. Kattan, PhD[1]; Kenneth R. Hess, PhD[2]; Mahul B. Amin, MD[3]; Ying Lu, PhD[4]; Karl G.M. Moons, PhD[5]; Jeffrey E. Gershenwald, MD[6]; Phyllis A. Gimotty, PhD[7]; Justin H. Guinney, PhD[8]; Susan Halabi, PhD[9]; Alexander J. Lazar, MD, PhD[10]; Alyson L. Mahar, MSc[11]; Tushar Patel, MD[12]; Daniel J. Sargent, PhD[13]; Martin R. Weiser, MD[14]; Carolyn Compton, MD, PhD[15]; members of the AJCC Precision Medicine Core

- We are entering an era where *decisions regarding therapy will be based on individualized risk models that incorporate a multitude of clinicopathological …and ultimately… molecular and immune factors*
- Conventional staging will likely continue to inform, but will not be a sole criterion

Ann Surg Oncol. 2016 Sep;23(9):2753-61.
Kattan MW et al. CA Cancer J Clin. 2016 Sep;66(5):370-4.

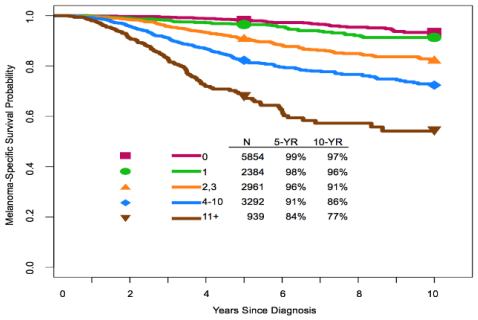
Presented by Jeff Gershenwald

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center
Making Cancer History®

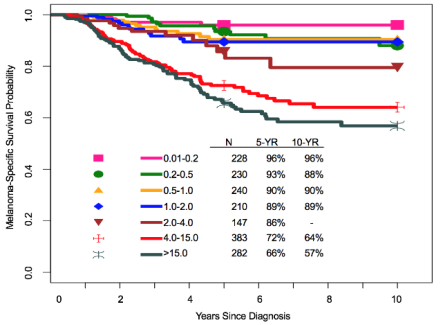
How Do We Leverage Contemporary Analyses to Improve Melanoma Staging and Prognosis?

- New statistical models & contemporary analytic approaches that better inform:
  - Use of *multiple characteristics & continuous* variables
    - Mitotic rate across tumor thickness strata
    - SLN tumor burden
  - Conditional Probability
    - Estimate survival *after treatment and at any time during f/u*
  - Enhanced ability to combine prognostic features to better estimate cancer-specific survival in *individual patient settings*
- Molecular targets/profiles will undoubtedly serve as new prognostic and/or predictive factor(s) → Is clinical value added?

Mitotic rate



SLN tumor burden



Presented by Jeff Gershenwald

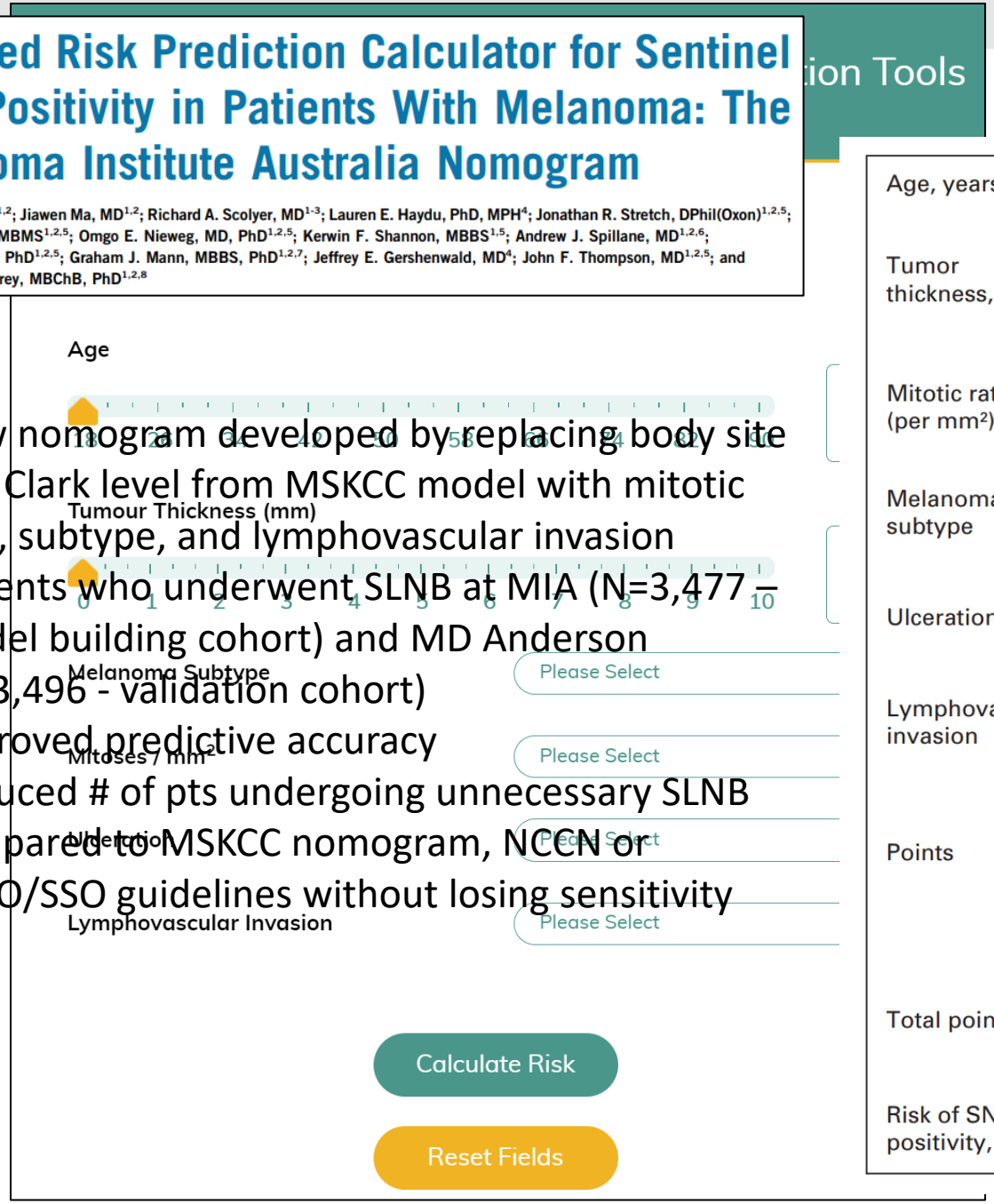
Gershenwald, Scolyer, et al. CA Cancer J Clin. 2017
Gershenwald, Scolyer, et al. Melanoma. In Amin, M.B., et al. (Eds.) AJCC Cancer Staging Manual. 8th Ed. New York: Springer; 2017

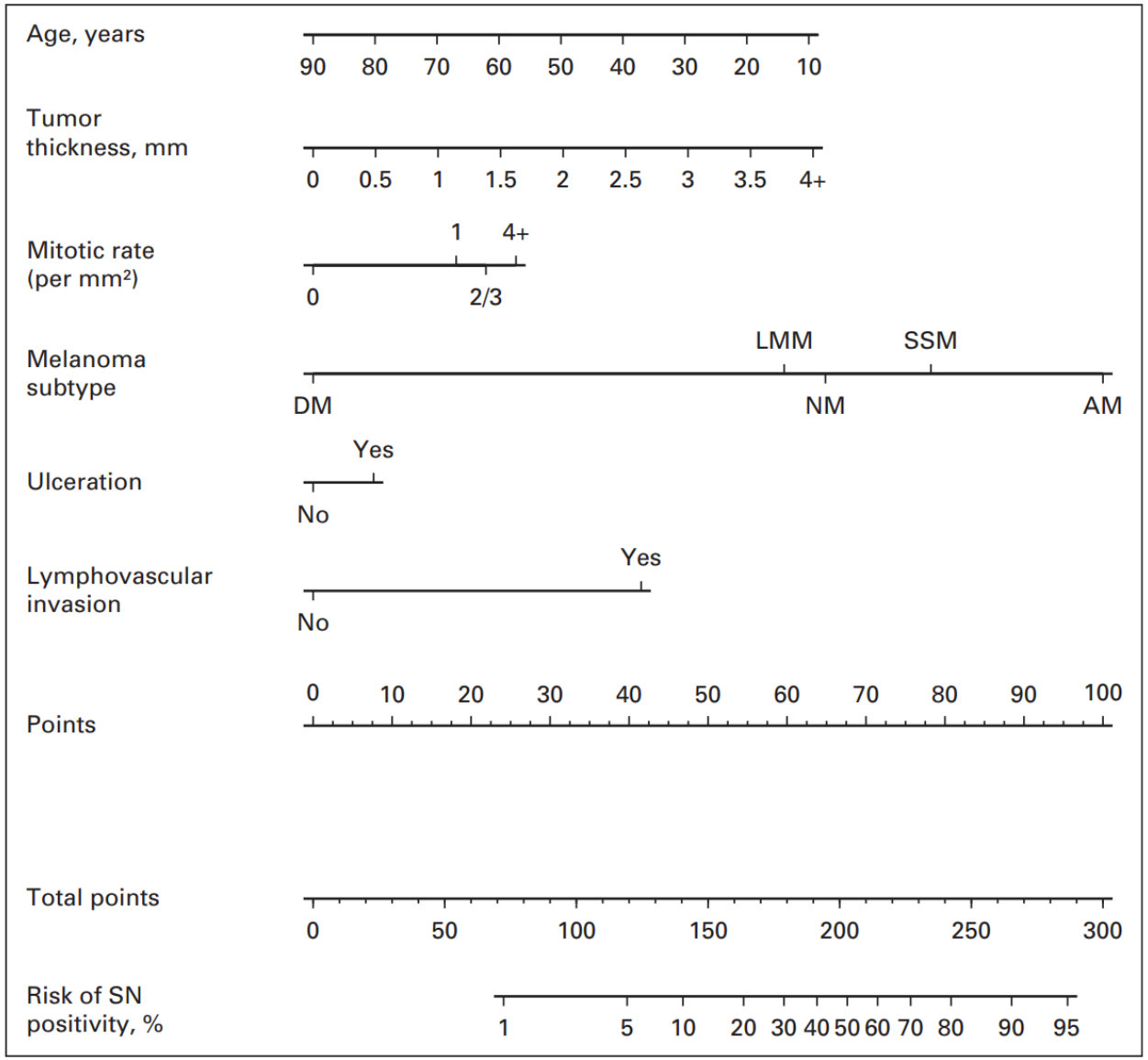
THE UNIVERSITY OF TEXAS MD Anderson Cancer Center

Improved Risk Prediction Calculator for Sentinel Node Positivity in Patients With Melanoma: The Melanoma Institute Australia Nomogram

Serigne N. Lo, PhD[1,2]; Jiawen Ma, MD[1,2]; Richard A. Scolyer, MD[1-3]; Lauren E. Haydu, PhD, MPH[4]; Jonathan R. Stretch, DPhil(Oxon)[1,2,5]; Robyn P. M. Saw, MBMS[1,2,5]; Omgo E. Nieweg, MD, PhD[1,2,5]; Kerwin F. Shannon, MBBS[1,5]; Andrew J. Spillane, MD[1,2,6]; Sydney Ch'ng, MD, PhD[1,2,5]; Graham J. Mann, MBBS, PhD[1,2,7]; Jeffrey E. Gershenwald, MD[4]; John F. Thompson, MD[1,2,5]; and Alexander H. R. Varey, MBChB, PhD[1,2,8]

- New nomogram developed by replacing body site and Clark level from MSKCC model with mitotic rate, subtype, and lymphovascular invasion
- Patients who underwent SLNB at MIA (N=3,477 – model building cohort) and MD Anderson (N=3,496 - validation cohort)
- Improved predictive accuracy
- Reduced # of pts undergoing unnecessary SLNB compared to MSKCC nomogram, NCCN or ASCO/SSO guidelines without losing sensitivity





Lo et al. J Clin Oncol 38:2719-2727 (2020).

https://melanomarisk.org.au/SNLForm

Sentinel Node Metastasis Risk

Enter the patient's primary melanoma details below:

Age

18 26 34 42 50 58 66 74 82 90

25

Tumour Thickness (mm)

0 1 2 3 4 5 6 7 8 9 10

2

Melanoma Subtype Superficial spreading

Mitoses / mm^2 3

Ulceration No

Lymphovascular Invasion No

Calculate Risk

Reset Fields

Sentinel Node Metastasis Risk

33%

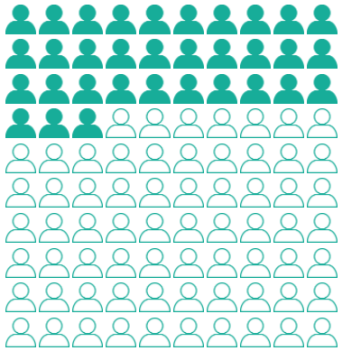
95% Confidence Interval: 30-36%

These results are based on:

Age	25
Thickness	2.0mm
Subtype	Superficial Spreading
Mitoses	3/mm^2
Ulceration	No
LV Invasion	No

Results Interpretation

The following information may be useful for clinicians when discussing with patients



The probability of having spread of melanoma to the lymph nodes is 33%. In other words, 33 out of 100 people with melanoma and the same risk factors as your patient will have spread of the melanoma to the lymph nodes.

Typically a sentinel node biopsy is recommended for patients with a risk greater than 10% and may be considered for those with a risk between 5% and 10%.

Where indicated, sentinel node biopsy should be done at the same time as wide local excision of the primary melanoma is undertaken.

Edit Inputs

New Test

https://melanomarisk.org.au/SNLForm

Sentinel Node Metastasis Risk

Enter the patient's primary melanoma details below:

Age

18 26 34 42 50 58 66 74 82 90

65

Tumour Thickness (mm)

0 1 2 3 4 5 6 7 8 9 10

2

Melanoma Subtype Superficial spreading

Mitoses / mm^2 3

Ulceration No

Lymphovascular Invasion No

Calculate Risk

Reset Fields

Sentinel Node Metastasis Risk

14%

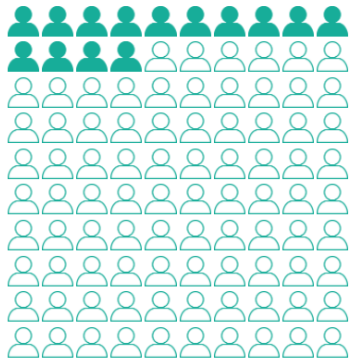
95% Confidence Interval: 12-16%

These results are based on:

Age	65
Thickness	2.0mm
Subtype	Superficial Spreading
Mitoses	3/mm^2
Ulceration	No
LV Invasion	No

Results Interpretation

The following information may be useful for clinicians when discussing with patients



The probability of having spread of melanoma to the lymph nodes is 14%. In other words, 14 out of 100 people with melanoma and the same risk factors as your patient will have spread of the melanoma to the lymph nodes.

Typically a sentinel node biopsy is recommended for patients with a risk greater than 10% and may be considered for those with a risk between 5% and 10%.

Where indicated, sentinel node biopsy should be done at the same time as wide local excision of the primary melanoma is undertaken.

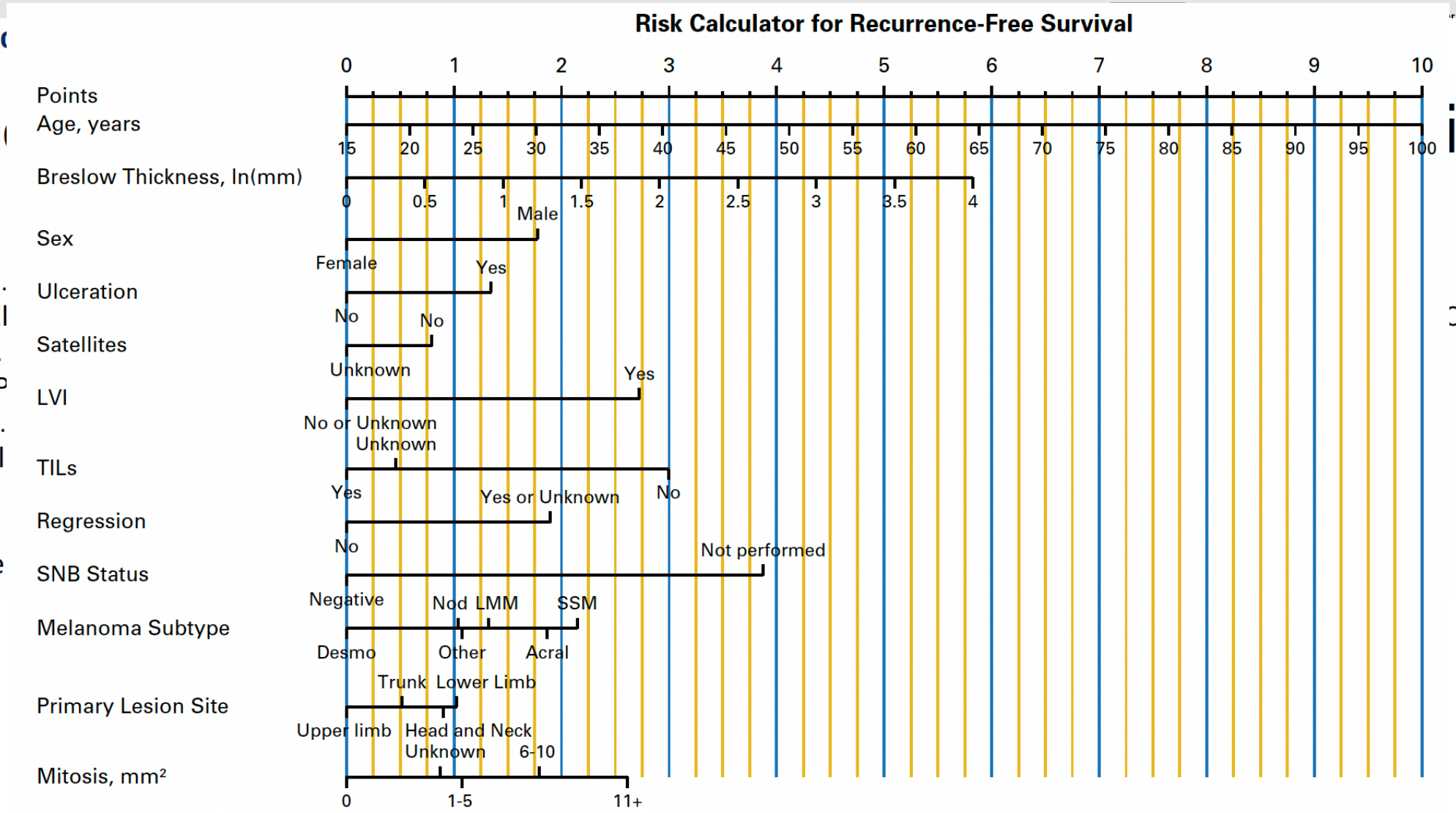
Edit Inputs

New Test

https://melanomarisk.org.au/SNLForm

Predi With ients

Alexander H.
Mary-Ann El
Robyn P.M.
Thomas E. P
Jonathan R.
Ryan J. Sull
Paul J. van
Georgina V.
and Serigne



- Online tool allows easy calculation of 5-year and 10-year RFS and OS
- Multivariable models based on standard clinicopathological parameters
- Includes predictions for pts who have had SLNB (or not)

J Clin Oncol 00:1-12 © 2024 by ASCO. ***Published online 5 February 2024***

Melanoma Institute Australia

Risk Prediction Tools

Stage II Survival Prediction

Recurrence-free Survival

5 Year	10 Year
90%	84%
95% CI: 85 - 93%	95% CI: 77 - 89%

Overall Survival

5 Year	10 Year
94%	88%
95% CI: 92 - 95%	95% CI: 84 - 91%

These results are based on:

Age	31	Mitoses (/mm^2)	0
Breslow Thickness (mm)	2.1	Satellites	No
Gender	Female	LVI	No
Primary Lesion Site	Upper Limb	TILS	Yes
Melanoma Subtype	SSM	Regression	No
Ulceration	No	SNB Status	Negative

Results Interpretation

The following information may be useful for clinicians when discussing with patients

Recurrence-free Survival

The probability of being alive and recurrence-free at five years after the initial diagnosis of melanoma is 90%. Therefore, 90 out of 100 people with initial Stage II melanoma and the same risk factors as your patient are expected to be alive and relapse-free at 5 years. Similarly, at ten years after the initial diagnosis of melanoma, 84 out of 100 people are expected to be alive and recurrence-free.

Overall Survival

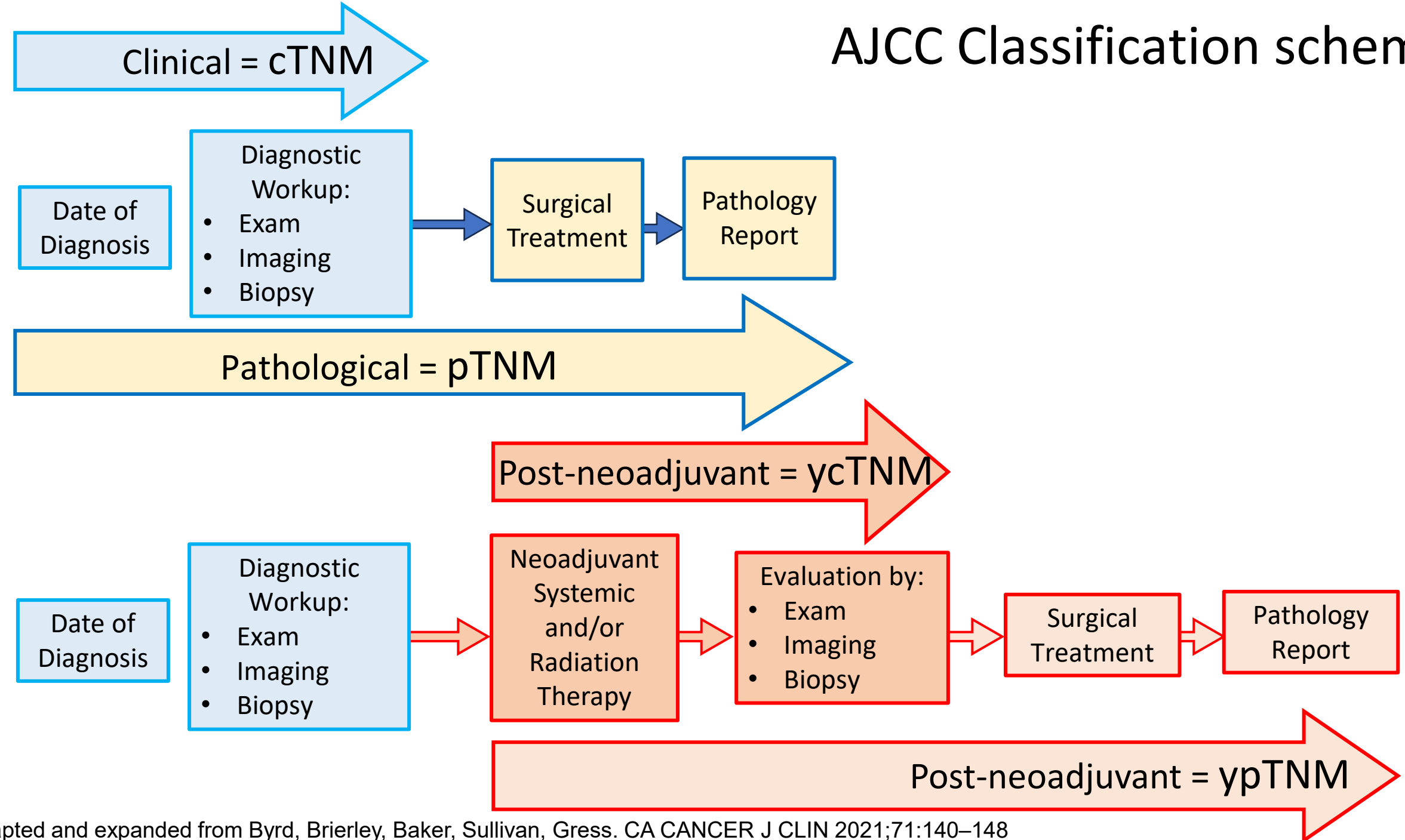
The probability of being alive at five years after the initial diagnosis of melanoma is 94%. Therefore, 94 out of 100 people with initial Stage II melanoma and the same risk factors as your patient are expected to be alive at five years. Similarly, at ten years after the initial diagnosis of melanoma, 88 out of 100 people are expected to be alive.

Edit Inputs

New Test

https://melanomarisk.org.au/Stage2Form

AJCC Classification schema



Adapted and expanded from Byrd, Brierley, Baker, Sullivan, Gress. CA CANCER J CLIN 2021;71:140–148

Treatment Effect - Mapped to CAP Protocols

Colon and Rectum

COLLEGE of AMERICAN PATHOLOGISTS

Protocol for the Examination of Resection Specimens From Patients With Primary Carcinoma of the Colon and Rectum

Version: 4.3.0.0
Protocol Posting Date: December 2023
CAP Laboratory Accreditation Program Protocol Required Use Date: September 2024

Treatment Effect (Note I)

___ No known presurgical therapy
___ Present, with no viable cancer cells (complete response, score 0)
___ Present, with single cells or rare small groups of cancer cells (near complete response, score 1)
___ Present, with residual cancer showing evident tumor regression, but more than single cells or rare small groups of cancer cells (partial response, score 2)
___ Present (not otherwise specified)
___ Absent, with extensive residual cancer and no evident tumor regression (poor or no response, score 3)
___ Cannot be determined: _____

I. Treatment Effect

Neoadjuvant chemoradiation therapy in rectal cancer is associated with significant tumor response and downstaging.[1] Because eradication of the tumor, as detected by pathologic examination of the resected specimen, is associated with a significantly better prognosis,[2] specimens from patients receiving neoadjuvant chemoradiation should be thoroughly sectioned, with careful examination of the tumor site. Minimal residual disease has been shown to have a better prognosis than gross residual disease.[3] A modified Ryan scheme is suggested for scoring of tumor response, and has been shown to provide good interobserver reproducibility of prognostic significance.[4] Several other systems have been studied and can be chosen to report the tumor regression score.

Modified Ryan Scheme for Tumor Regression Score[2]

Description	Tumor Regression Score
No viable cancer cells (complete response)	0
Single cells or rare small groups of cancer cells (near complete response)	1
Residual cancer with evident tumor regression, but more than single cells or rare small groups of cancer cells (partial response)	2
Extensive residual cancer with no evident tumor regression (poor or no response)	3

Tumor regression should be assessed only in the primary tumor; lymph node metastases should not be included in the assessment.

Treatment Effect - Mapped to CAP Protocols

Carcinoma of the Breast

Treatment Effect in the Breast (Note K)

The largest contiguous focus of residual tumor, if present, is used to determine ypT category. Treatment-related fibrosis in the tumor bed adjacent to foci of residual invasive carcinoma is not included in determining ypT dimension.

___ No known presurgical therapy
___ No definite response to presurgical therapy in the invasive carcinoma
___ Probable or definite response to presurgical therapy in the invasive carcinoma
___ No residual invasive carcinoma is present in the breast after presurgical therapy

Treatment Effect in the Lymph Nodes (required if nodes are submitted and it is known that the patient had presurgical therapy)

The largest contiguous focus of residual tumor in the lymph nodes, if present, is used to determine ypN category. Treatment-related fibrosis adjacent to residual nodal deposits is not included in determining ypN dimension.

___ Not applicable
___ No definite response to presurgical therapy in metastatic carcinoma
___ Probable or definite response to presurgical therapy in metastatic carcinoma
___ No lymph node metastases. Fibrous scarring or histiocytic aggregates, possibly related to prior lymph node metastases with pathologic complete response
___ No lymph node metastases and no fibrous scarring or histiocytic aggregates in the nodes

Residual Cancer Burden (RCB) Calculation (for institutions that wish to report treatment effect using the RCB calculator)# (Note K)

 # The RCB calculator can be found at the MD Anderson website: http://www3.mdanderson.org/app/medcalc/index.cfm?pagename=jsconvert3

___ Not reported
___ RCB reported

Primary Tumor Bed

Greatest Dimension of Primary Tumor Bed Area in Millimeters (mm) (involved by residual viable carcinoma): _____ mm

Second Greatest Dimension of Primary Tumor Bed Area in Millimeters (mm): _____ mm

Specify Percentage of Overall Cancer Cellularity (in the area measured above): _____ %

Specify Percentage of Cancer that is in situ Disease: _____ %

Lymph Nodes

Number of Positive Lymph Nodes: _____

Diameter of Largest Nodal Metastasis in Millimeters (mm): _____ mm

RCB Calculations

Residual Cancer Burden: _____

Residual Cancer Burden Class

___ RCB-0 (pCR)
___ RCB-I
___ RCB-II
___ RCB-III

Version: 4.9.0.1
Protocol Posting Date: December 2023
CAP Laboratory Accreditation Program Protocol Required Use Date: March 2024

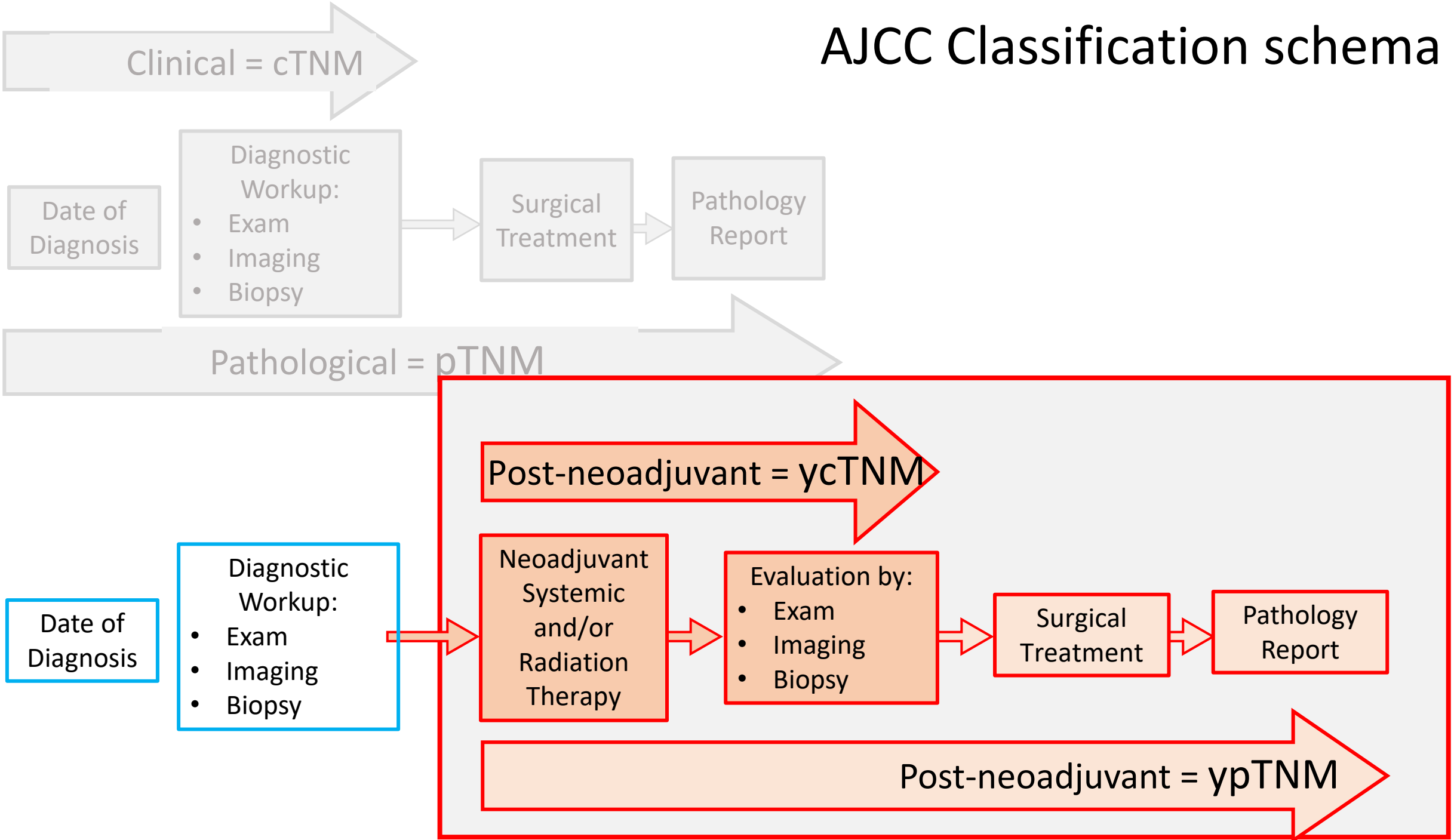
Treatment Effect - Mapped to CAP Protocols

Non-Small Cell Carcinoma, Small Cell Carcinoma, or Carcinoid Tumor of the Lung

Treatment Effect (Note G)
___ No known presurgical therapy
___ Not identified
___ Present
Percentage of Residual Viable Tumor
___ Specify percentage: _____ %
___ Other (specify): _____
___ Cannot be determined: _____
+Percentage of Necrosis
___ Specify percentage: _____ %
___ Other (specify): _____
___ Cannot be determined: _____
+Percentage of Stroma (includes fibrosis and inflammation)
___ Specify percentage: _____ %
___ Other (specify): _____
___ Cannot be determined: _____
___ Cannot be determined: _____

Version: 4.3.0.1
Protocol Posting Date: September 2022
CAP Laboratory Accreditation Program Protocol Required Use Date: March 2023

AJCC Classification schema



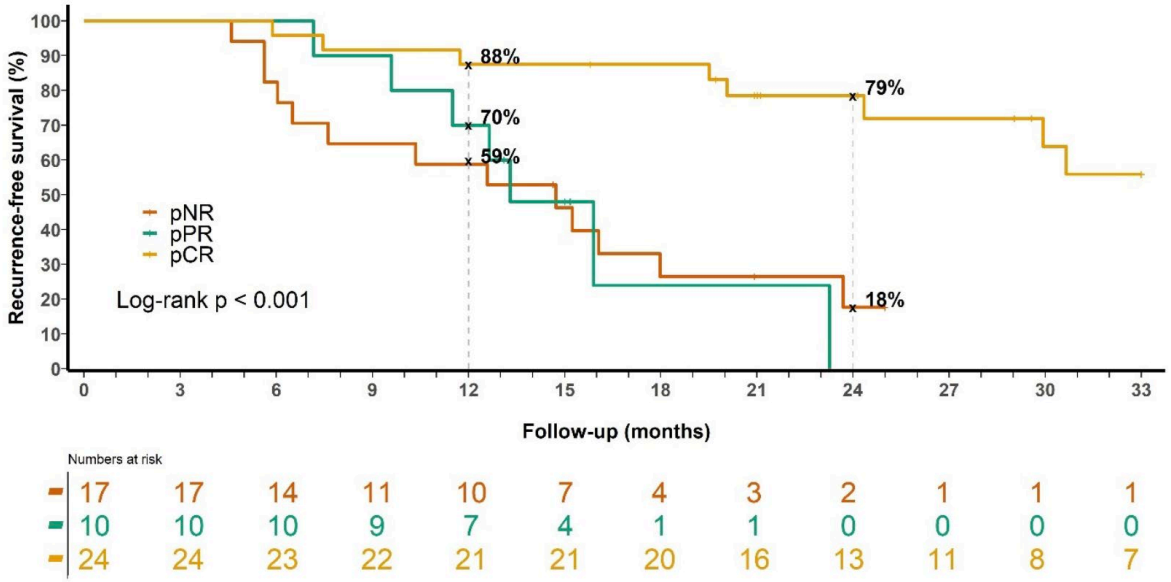
Neoadjuvant Tx Landscape in Melanoma

nature medicine ARTICLES
https://doi.org/10.1038/s41591-020-01188-3
Check for updates

Pathological response and survival with neoadjuvant therapy in melanoma: a pooled analysis from the International Neoadjuvant Melanoma Consortium (INMC)

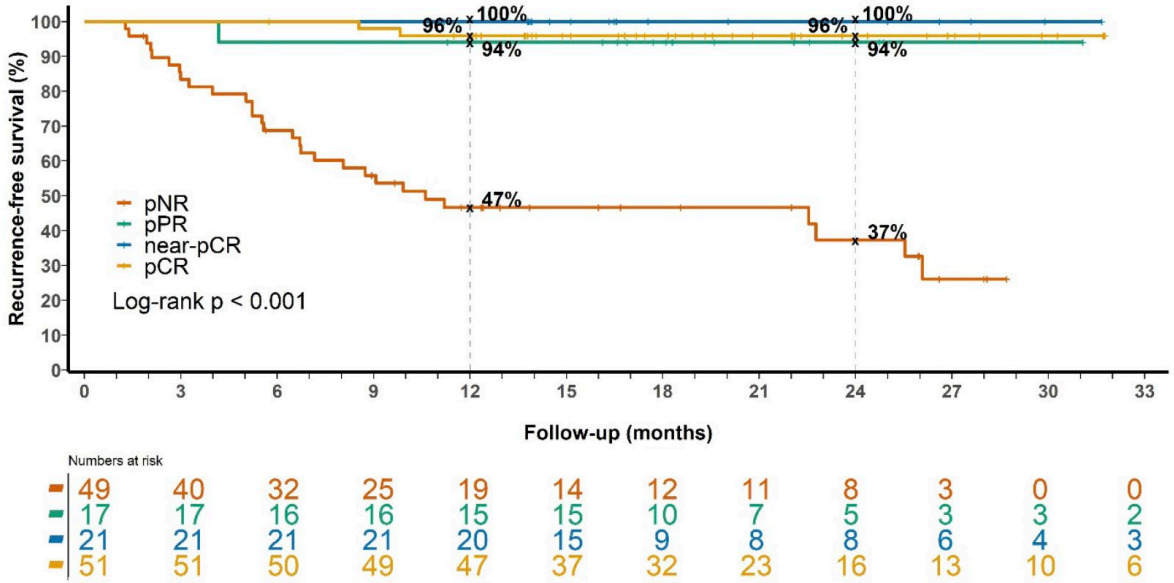
- Patient with stage III (cT4b cN3 cM0) – 3 cycles combo immunotherapy → pCR
- No stage assigned → unable to capture prognostic significance of path CR or indicate agent

Targeted Therapy



*No patient had a near-pCR

Immunotherapy



Menzies AM et al. Pathological response and survival with neoadjuvant therapy in melanoma: a pooled analysis from the International Neoadjuvant Melanoma Consortium (INMC). Nat Med. 2021 Feb;27(2):301-309. doi: 10.1038/s41591-020-01188-3.

Embracing the full spectra of AJCC classification – yc/yp Opportunities in Melanoma and more!

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Neoadjuvant–Adjuvant or Adjuvant-Only Pembrolizumab in Advanced Melanoma

Patel S et al., N Engl J Med 2023; 388:813-823

nature medicine

ARTICLES

https://doi.org/10.1038/s41591-020-01188-3

Check for updates

Pathological response and survival with neoadjuvant therapy in melanoma: a pooled analysis from the International Neoadjuvant Melanoma Consortium (INMC)

Nat Med. 2021 Feb;27(2):301-309.

Current and Future Cancer Staging After Neoadjuvant Treatment for Solid Tumors

David R. Byrd, MD, FACS[1]; James D. Brierley, MB, FRCP, FRCPC [2]; Thomas P. Baker, MD, FCAP[3]; Daniel C. Sullivan, MD[4]; Donna M. Gress, RHIT, CTR[5]

CA CANCER J CLIN 2021;71:140–148

Neoadjuvant Nivolumab and Ipilimumab in Resectable Stage III Melanoma

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Neoadjuvant systemic therapy in melanoma: recommendations of the International Neoadjuvant Melanoma Consortium

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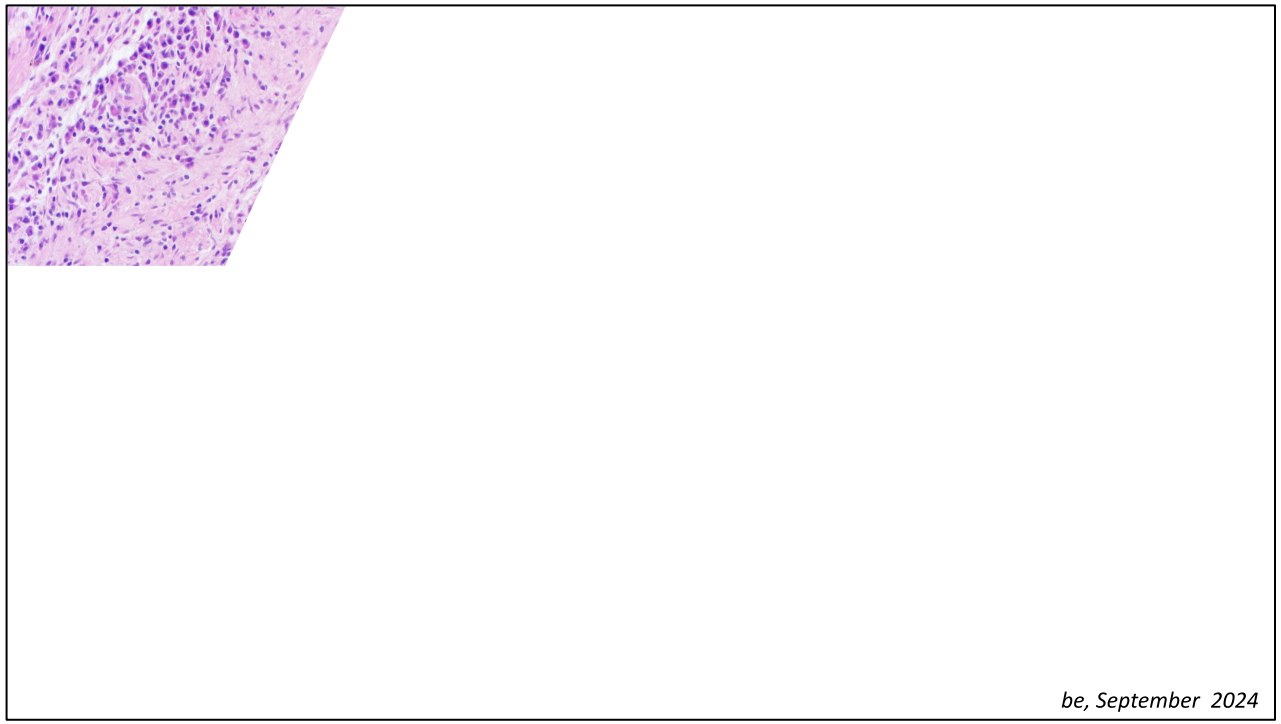
Lancet Oncol 2019; 20: e378–89

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center

Pan-tumor Pathologic Response Reporting Template: Current draft



Assessment of primary tumor components

___Percent Residual Viable Tumor: _____ %
___Percent Necrosis: _____ %
___Percent Regression: _____ %

___Complete Pathologic Response (0% RVT): ____Yes ____No

Assessment of lymph node components

___Percent Residual Viable Tumor: _____ %
___Percent Necrosis: _____ %
___Percent Regression: _____ %

Courtesy of Janis Taube, September 2024

Guiding principle

The theoretical additive value of more detailed, elaborate or disease-specific approaches to scoring will have to be clearly superior with regard to predicting survival outcomes to outweigh the benefits of an efficient, robust and effective pan-tumor system for RVT assessment.

Courtesy of Janis Taube, September 2024

Neoadjuvant “yp/yc” Staging – Melanoma & Beyond

- **What qualifies as Neoadjuvant Therapy?**
  - Agents, duration (minimum?)
  - Era of immunotherapy - toxicity ≠ lack of response, duration not measured in months, etc.

- **How to define, capture, and codify response to neoadjuvant treatment?**
  - Clinical, radiological, pathological response
  - Role of biomarkers

- **Clinical practice registry/surveillance community considerations and harmonization** (eg, NAACR, NPCR, CoC, NCDB, AJCC, NCI, SEER, STORE, SSDI)

- **Disease site agnostic vs disease site specific considerations**

MelCore Database & Laboratory Est 2000

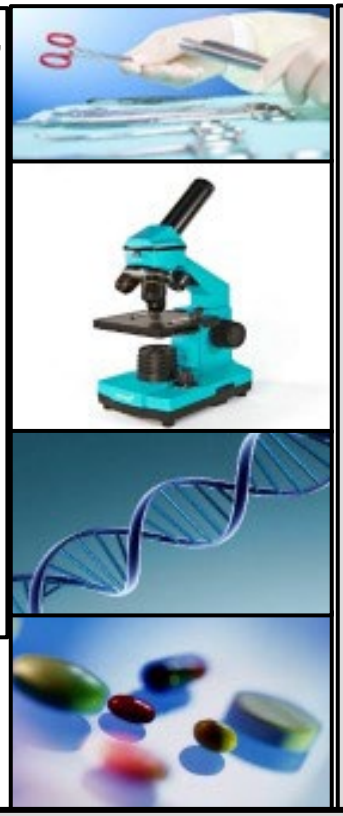
Melanoma Clinical Database, Tissue Resource, and Translational Pathology Core (MelCore)

Diagnosis, Staging,
Surgical Procedures

Primary Pathology,
Lymph Node Tumor Burden,
Metastatic Sites

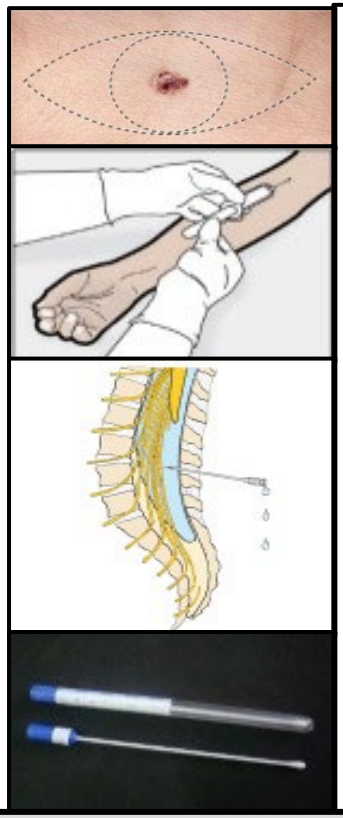
Molecular Testing

Protocols
Treatments
Tumor Measurements



Clinical Data Management

Biospecimen Tracking



Tissue Collections
Fresh
Snap Frozen
Archival FFPE
OCT

Fluid Collections
Ascites, Pleural,
Cerebrospinal fluid
Aqueous Humor

Blood Draws

Microbiome Collections
Fecal, Buccal Swab

Slides
Tissue Microarray

PDX

DNA
RNA
Protein

Single-cell
suspension

CSF
cell suspension
supernatant

Plasma
Sera
PBMCs

Sample Processing

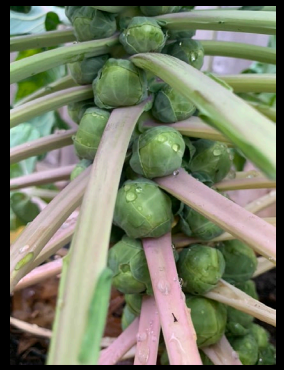
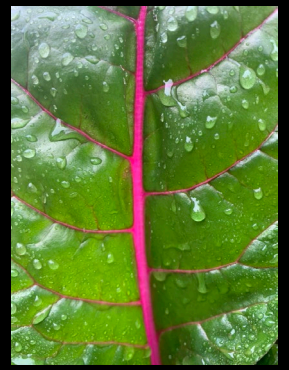
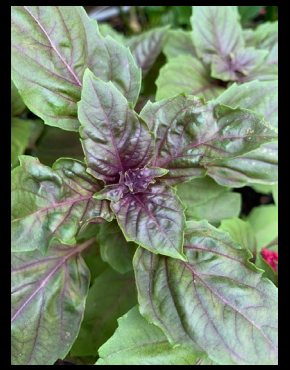
MelCore Clinical Data Team *(Institutional Data Connections)* *(International Data Contributors)*	**Clinical Study Team**	MelCore Biorepository Team Melanoma Translational Pathology Lab Team *(Off-site Storage - Cryogene)*

MAJOR MILESTONE: 10,000th Patient Consented in 2020

THE UNIVERSITY OF TEXAS
MD Anderson
Cancer Center

Summary and Conclusions

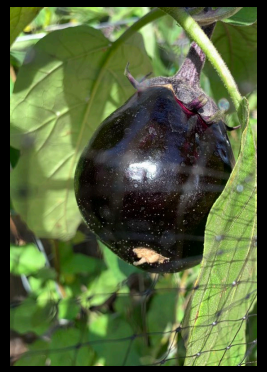
- Classification and staging of cancer → principal communication tool & common language
- Longstanding partnership between AJCC and CAP continues…to expand
- CAP efforts permeate multiple Cancer Programs of the American College of Surgeons
- Lessons learned from CAP's approach to standardized data collection and synoptic reporting have helped to inform interest, development, and implementation of AJCC cancer staging protocols and CSSP synoptic operative reports
- Structured pathology data enables optimal patient care
  - Accurate classification and staging
  - Enhanced decision-making → optimal use of and revisions to evidence-based guidelines
  - Supports ongoing and future efforts to refine care guidelines and inform and validate future prognostic and predictive clinical tools → global advances in precision oncology
- Importance of structured data and synoptic reports across the cancer care continuum









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Thank
you!






GERSHENVVALD FARMS