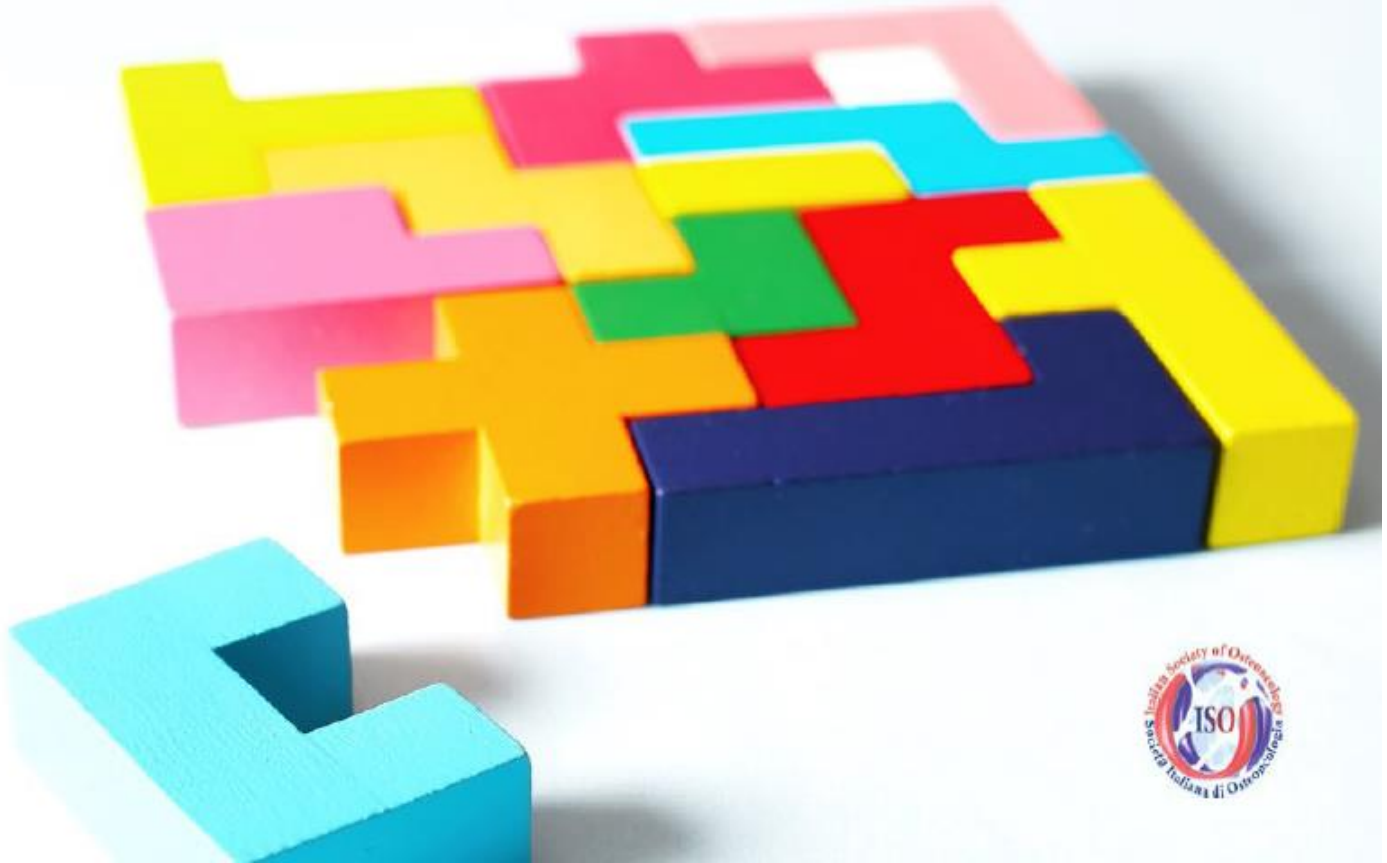
CORSO SOCIETÀ ITALIANA DI OSTEONCOLOGIA - ISO

23 APRILE 2024 ROMA ISTITUTO DI STORIA DELLA MEDICINA

QUALI STRATEGIE TERAPEUTICHE E QUALI NOVITÀ NELLA GESTIONE DELLE METASTASI OSSEE

RESPONSABILI SCIENTIFICI: G. LANZETTA - T. IBRAHIM - D. SANTINI



Limiti della biopsia ossea nell'era dell'Oncologia di Precisione

Giuseppe Perrone

Professore Ordinario di Anatomia Patologica
Direttore UOC Anatomia Patologica
Responsabile UOS Diagnostica Molecolare Predittiva

Fondazione Policlinico Universitario Campus Bio-Medico – Roma
g.perrone@policlinicocampus.it

FONDAZIONE
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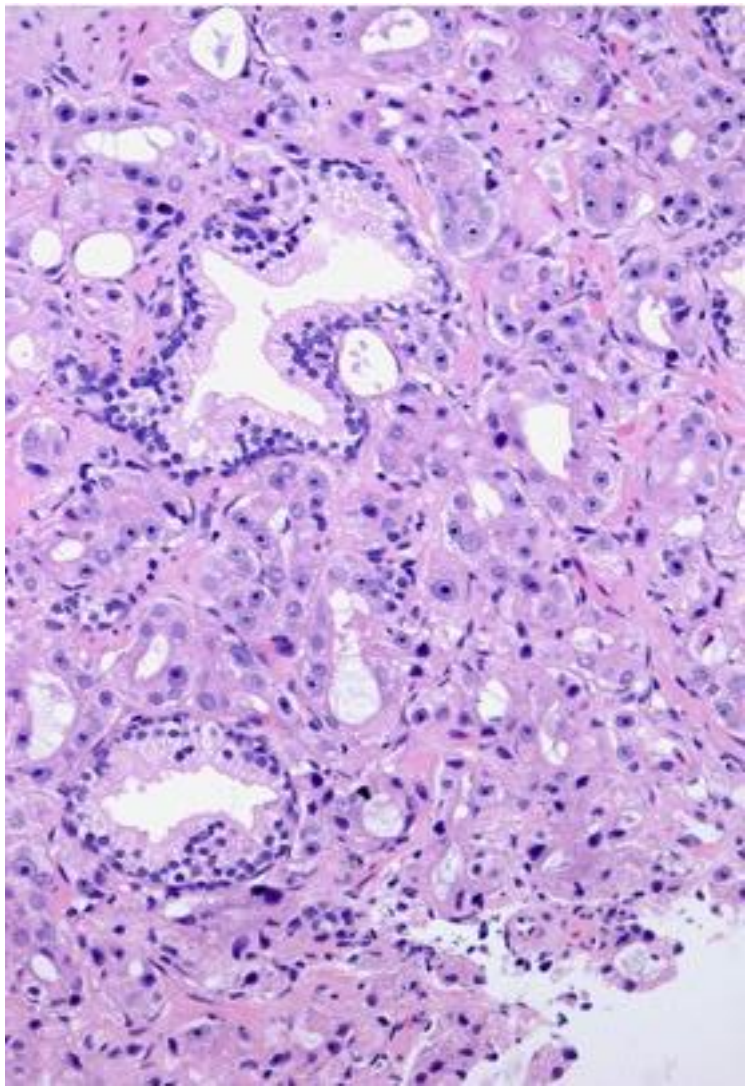
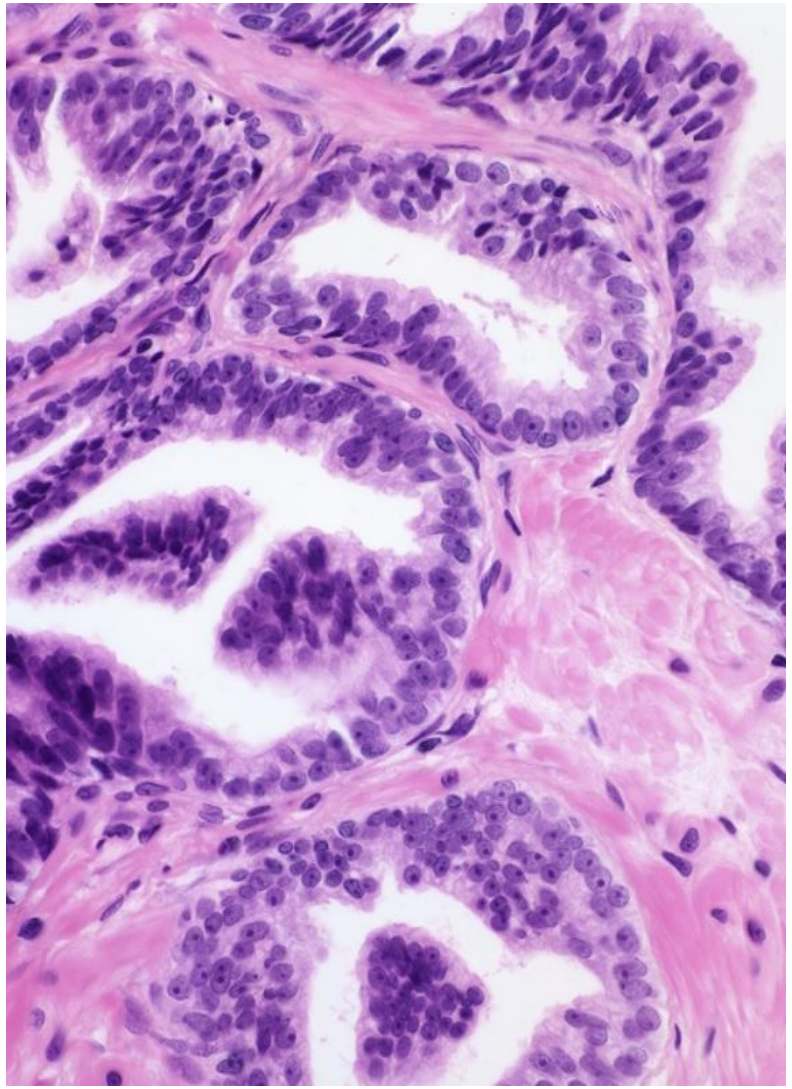
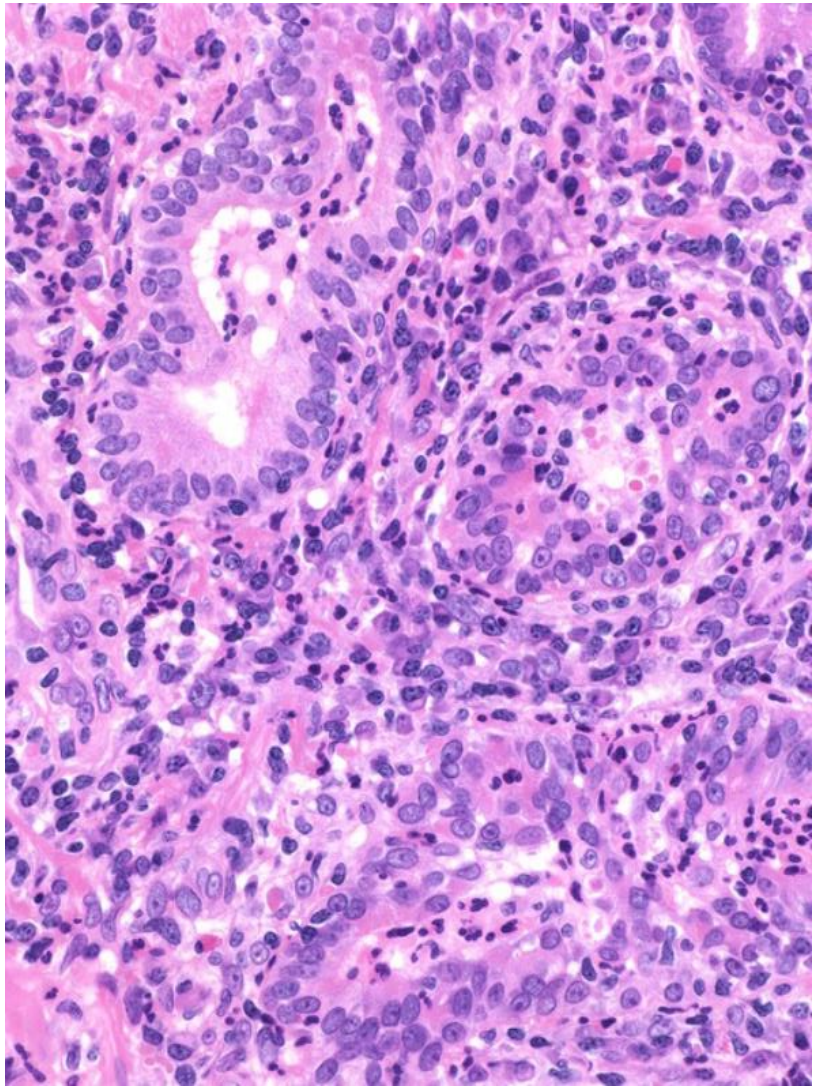
Diagnostica anatomopatologica







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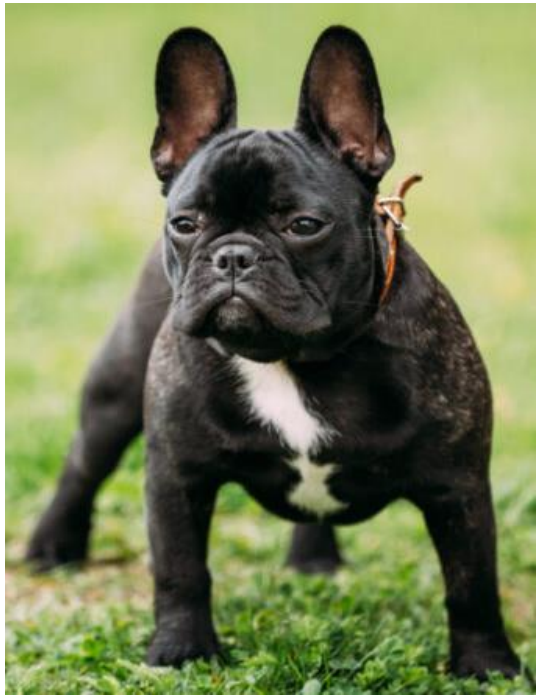

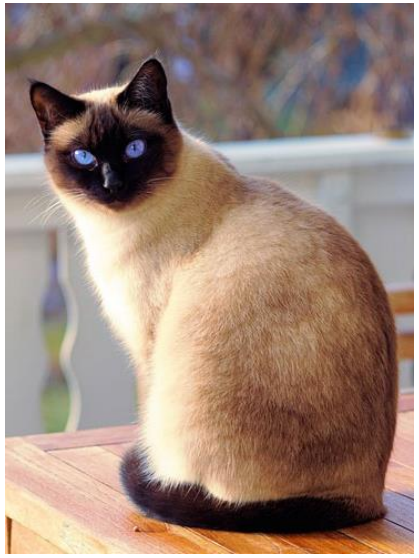

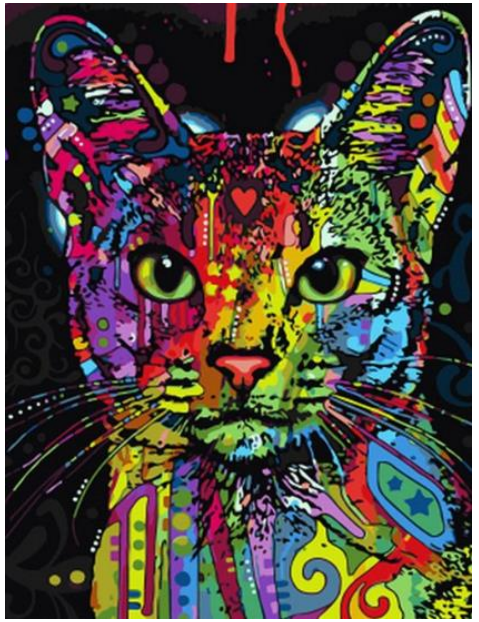

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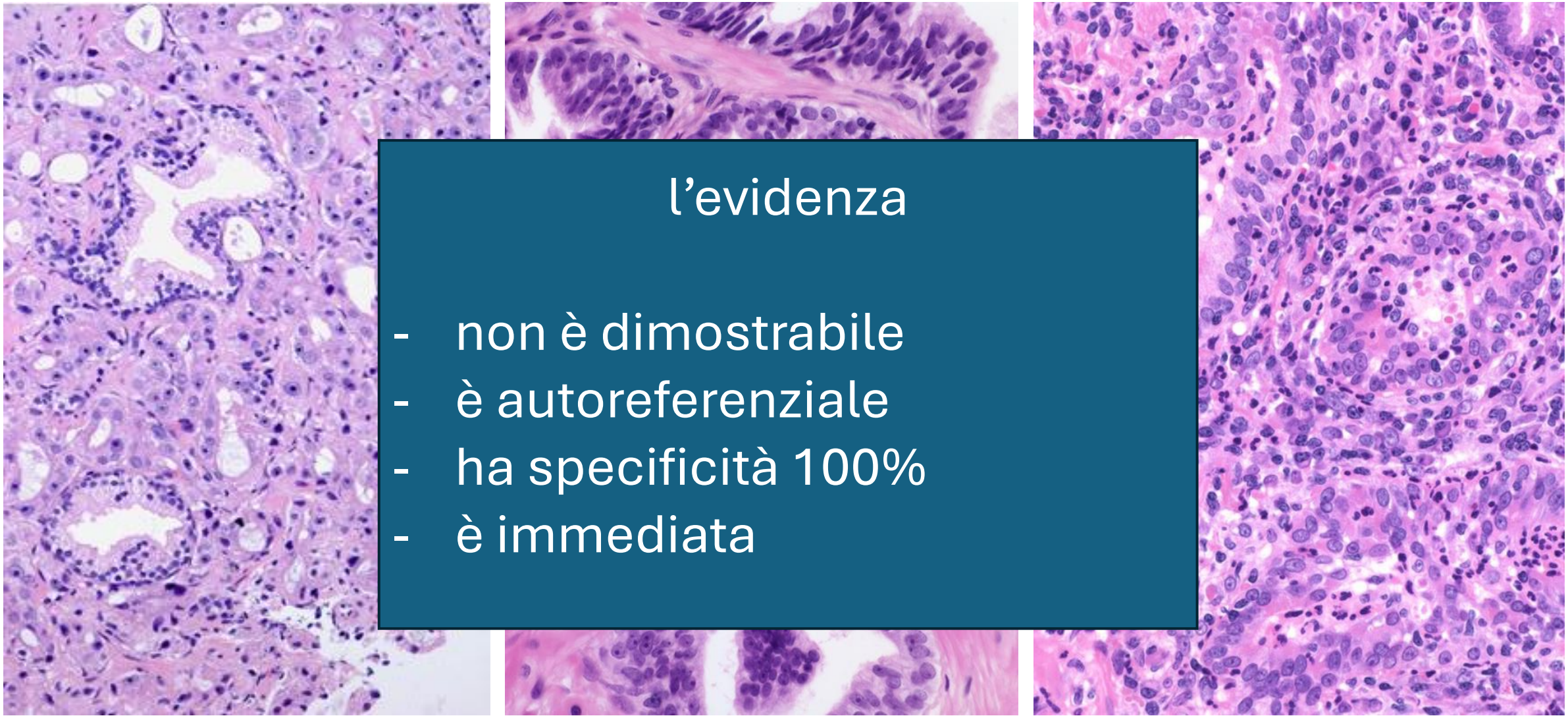
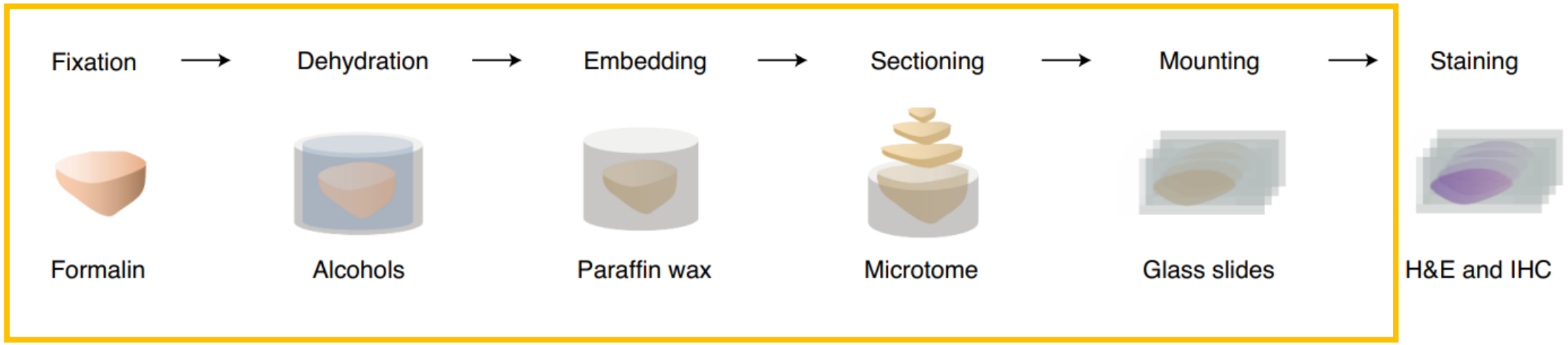
Diagnostica anatomopatologica



l'evidenza

- non è dimostrabile
- è autoreferenziale
- ha specificità 100%
- è immediata


Fixation
Dehydration
Embedding
Sectioning
Mounting
Staining
Formalin
Alcohols
Paraffin wax
Microtome
Glass slides
H&E and IHC

Hernandez et al. BMC Cancer (2018) 18:44
DOI 10.1186/s12885-017-3922-0

BMC Cancer

RESEARCH ARTICLE Open Access

Incidence of bone metastases in patients with solid tumors: analysis of oncology electronic medical records in the United States

Rohini K. Hernandez[1], Sally W. Wade[2], Adam Reich[3], Melissa Pirolli[3], Alexander Liede[5*] and Gary H. Lyman[4]

Methods: Electronic medical records (OSCER, Oncology Services Comprehensive Electronic Records, 569,000 patients, 52 US cancer centers) were used to identify patients ≥18 years with a solid tumor diagnosis recorded between 1/1/2004 and 12/31/2013, excluding patients with hematologic tumors or multiple primaries. Each

Table 2 1-, 2-, 5-, and 10-year incidence of bone metastases by tumor type

Tumor type	Incidence of bone metastases (%)			
	1-year (95% CI)	2-year (95% CI)	5-year (95% CI)	10-year (95% CI)
All tumor types combined (*N* = 382,733)	4.8 (4.7–4.8)	5.6 (5.5–5.6)	6.9 (6.8–7.0)	8.4 (8.3–8.5)
Breast (*N* = 137,720)	3.4 (3.3–3.5)	4.2 (4.1–4.3)	6.0 (5.8–6.1)	8.1 (7.9–8.3)
Prostate (*N* = 22,801)	18.0 (17.5–18.5)	20.4 (19.9–20.9)	24.5 (23.9–25.1)	29.2 (28.3–30.1)
Lung (*N* = 59,344)	10.4 (10.2–10.7)	11.5 (11.3–11.8)	12.4 (12.1–12.7)	12.9 (12.6–13.2)
Colorectal (*N* = 46,832)	1.0 (0.9–1.1)	1.4 (1.3–1.5)	2.1 (2.0–2.3)	2.7 (2.5–2.9)
Gastrointestinal (*N* = 32,874)	2.3 (2.1–2.5)	2.7 (2.6–2.9)	3.2 (3.0–3.4)	3.6 (3.3–3.8)
Gynecological (*N* = 21,075)	1.1 (0.9–1.2)	1.3 (1.2–1.5)	1.9 (1.7–2.1)	2.4 (2.1–2.7)
Malignant melanoma (*N* = 12,152)	1.6 (1.4–1.8)	2.0 (1.7–2.2)	2.5 (2.2–2.8)	3.0 (2.6–3.4)
Renal (*N* = 17,717)	5.8 (5.5–6.2)	6.9 (6.6–7.3)	8.4 (8.0–8.9)	9.9 (9.3–10.5)
All other tumors (*N* = 32,218)	2.0 (1.8–2.1)	2.5 (2.3–2.7)	3.2 (3.0–3.4)	3.9 (3.5–4.2)

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Breast Cancer

Version 2.2024 — March 11, 2024

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National Comprehensive Cancer Network®

NCCN Guidelines Version 2.2024
Breast Cancer

The section on management of recurrent/Stage IV breast cancer was updated on 03/06/20.

Recurrent/Stage IV Breast Cancer

Staging and Workup for Recurrent and Stage IV Breast Cancer

The staging evaluation of patients who present with recurrent or stage IV breast cancer includes history and physical exam; the performance of a complete blood count, liver function tests, chest diagnostic CT, bone scan, and radiographs of any long or weight-bearing bones that are painful or appear abnormal on bone scan; diagnostic CT of the abdomen (with or without diagnostic CT of the pelvis) or MRI scan of the abdomen; and biopsy documentation of first recurrence if possible. The NCCN Panel generally discourages the use of sodium fluoride PET or PET/CT scans for the evaluation of patients with recurrent disease. There is limited evidence (mostly from retrospective studies) to support the use of PET/CT scanning to guide treatment planning through determination of the extent of disease in select patients with recurrent or metastatic disease.[109,110,464,465] In general, the non-diagnostic CT scans used for PET under-evaluate the lungs and the liver compared with contrast-enhanced diagnostic CT scans.

allows for biomarker determination and selection of appropriate treatment. Soft tissue tumor biopsy is preferred over bone sites unless a portion of the biopsy can be protected from harsh decalcification solution to preserve more accurate assessment of biomarkers.

Determination of HR status (ER and PR) and HER2 status should be repeated in all cases when diagnostic tissue is obtained. ER and PR assays may be falsely negative or falsely positive, and there may be discordance between the primary and metastatic tumors.[466,467] The reasons for the discordance may relate to change in biology of disease, differential effect of prior treatment on clonal subsets, tumor heterogeneity, or imperfect accuracy and reproducibility of assays.[467] Discordance between the receptor status of primary and recurrent disease has been reported in a number of studies. The discordance rates are in the range of 3.4% to 60% for ER-negative to ER-positive; 7.2% to 31% for ER-positive to ER-negative; and 0.7% to 11% for HER2.[468-477]

The NCCN Panel recommends that re-testing the receptor status of recurrent disease be performed, *especially* in cases when it was

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Trastuzumab Deruxtecan in Previously Treated HER2-Low Advanced Breast Cancer

S. Modi, W. Jacot, T. Yamashita, J. Sohn, M. Vidal, E. Tokunaga, J. Tsurutani, N.T. Ueno, A. Prat, Y.S. Chae, K.S. Lee, N. Niikura, Y.H. Park, B. Xu, X. Wang, M. Gil-Gil, W. Li, J.-Y. Pierga, S.-A. Im, H.C.F. Moore, H.S. Rugo, R. Yerushalmi, F. Zagouri, A. Gombos, S.-B. Kim, Q. Liu, T. Luo, C. Saura, P. Schmid, T. Sun, D. Gambhire, L. Yung, Y. Wang, J. Singh, P. Vitazka, G. Meinhardt, N. Harbeck, and D.A. Cameron, for the DESTINY-Breast04 Trial Investigators*

Table 2. Overall Efficacy in All Cohorts.*

Variable	Hormone Receptor–Positive Cohort		All Patients		Hormone Receptor–Negative Cohort	
	Trastuzumab Deruxtecan	Physician's Choice of Chemotherapy	Trastuzumab Deruxtecan	Physician's Choice of Chemotherapy	Trastuzumab Deruxtecan	Physician's Choice of Chemotherapy
Progression-free and overall survival						
No. of patients evaluated	331	163	373	184	40	18
Median progression-free survival (95% CI) — mo	10.1 (9.5–11.5)	5.4 (4.4–7.1)	9.9 (9.0–11.3)	5.1 (4.2–6.8)	8.5 (4.3–11.7)	2.9 (1.4–5.1)
Hazard ratio for disease progression or death (95% CI)	0.51 (0.40–0.64)		0.50 (0.40–0.63)		0.46 (0.24–0.89)	
P value	<0.001		<0.001		—	
Median overall survival (95% CI) — mo	23.9 (20.8–24.8)	17.5 (15.2–22.4)	23.4 (20.0–24.8)	16.8 (14.5–20.0)	18.2 (13.6–NE)	8.3 (5.6–20.6)
Hazard ratio for death (95% CI)	0.64 (0.48–0.86)		0.64 (0.49–0.84)		0.48 (0.24–0.95)	
P value	0.003		0.001		—	

DOI:
10.1056/NEJMoa2203690

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ESTABLISHED IN 1812 JULY 7, 2022 VOL. 387 NO. 1

Trastuzumab Deruxtecan in Previously Treated HER2-Low Advanced Breast Cancer

S. Modi, W. Jacot, T. Yamashita, J. Sohn, M. Vidal, E. Tokunaga, J. Tsurutani, N.T. Ueno, A. Prat, Y.S. Chae, K.S. Lee, N. Niikura, Y.H. Park, B. Xu, X. Wang, M. Gil-Gil, W. Li, J.-Y. Pierga, S.-A. Im, H.C.F. Moore, H.S. Rugo, R. Yerushalmi, F. Zagouri, A. Gombos, S.-B. Kim, Q. Liu, T. Luo, C. Saura, P. Schmid, T. Sun, D. Gambhire, L. Yung, Y. Wang, J. Singh, P. Vitazka, G. Meinhardt, N. Harbeck, and D.A. Cameron, for the DESTINY-Breast04 Trial Investigators*

Routinely processed, formalin-fixed, paraffin-embedded (FFPE) tissues were considered suitable for use with the VENTANA HER2 (4B5) and INFORM HER2 Dual ISH assays, however, because pre-analytical variables (eg, time and type of fixation) may affect the results for all receptor assays, including HER2-low results, to be eligible for HER2 testing, specimens had to have been fixed in 10% neutral buffered formalin (6 to 72 hours fixation recommended). Serial sections (approximately 4-µm thick) of the FFPE specimens were mounted on glass microscope slides. Unstained slides were stored at 2°C–8°C or room temperature (15°C–25°C) for no more than 4 months before staining with the VENTANA HER2 (4B5) assay or for no more than 18 months before staining with the INFORM HER2 Dual ISH assay. Central pathologist review of 1 slide stained with hematoxylin and eosin had to confirm that the specimen contained sufficient tumor tissue for interpretation, i.e., the stained area of the slide had to contain at least 50 viable tumor cells with associated stroma. Specimens lacking sufficient tumor tissue were excluded from testing. Fine needle aspirates and other cytological specimens were also excluded from testing, as were decalcified bone metastases.

MODERN PATHOLOGY (2016) 29, 1460–1470

Influence of decalcification procedures on immunohistochemistry and molecular pathology in breast cancer

Willemijne AME Schrijver[1], Petra van der Groep[1,2,3], Laurien DC Hoefnagel[1,3], Natalie D ter Hoeve[1], Ton Peeters[1], Cathy B Moelans[1] and Paul J van Diest[1]

[1]Department of Pathology, University Medical Center Utrecht, Utrecht, The Netherlands and [2]Cancer Center, University Medical Center Utrecht, Utrecht, The Netherlands

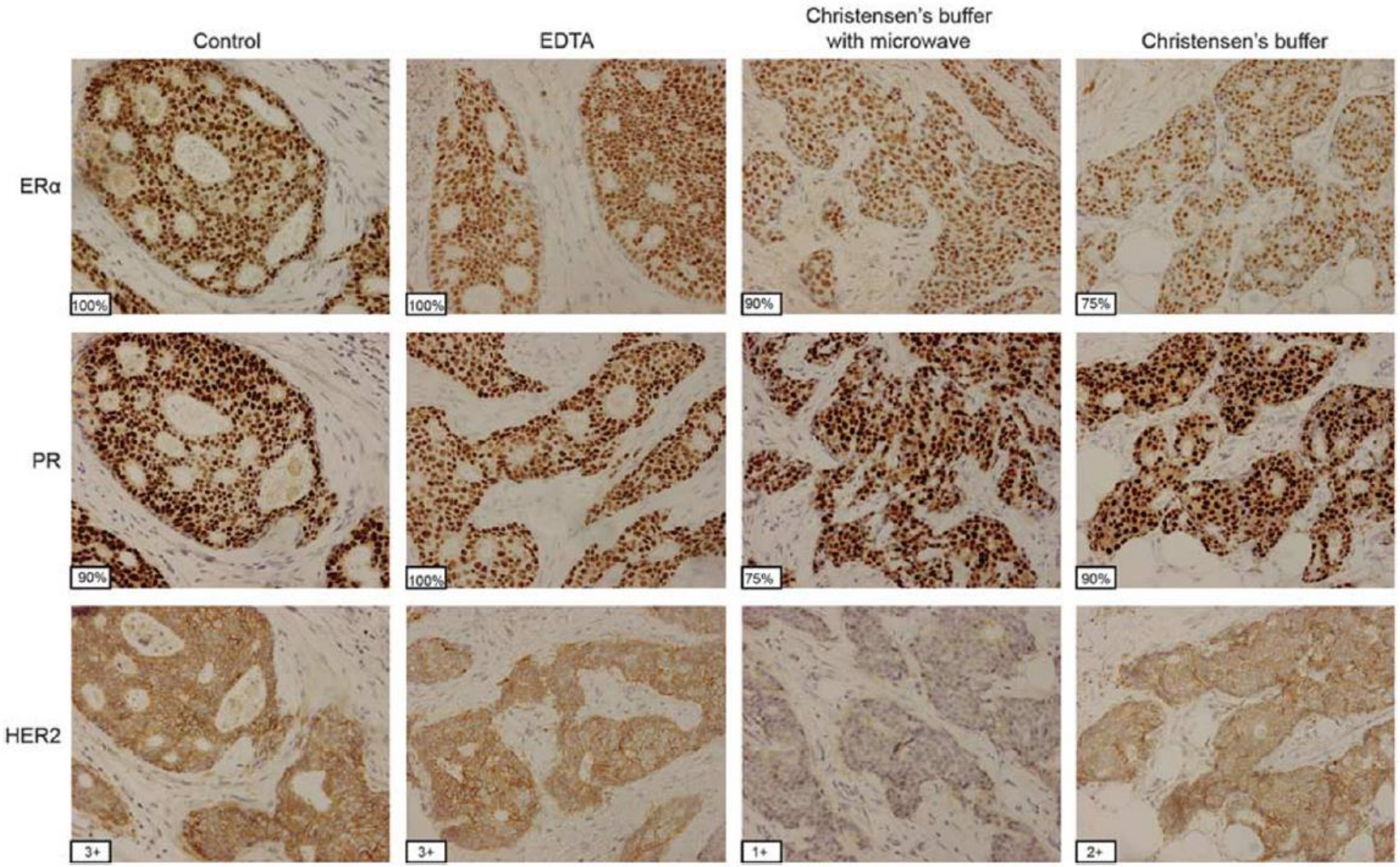
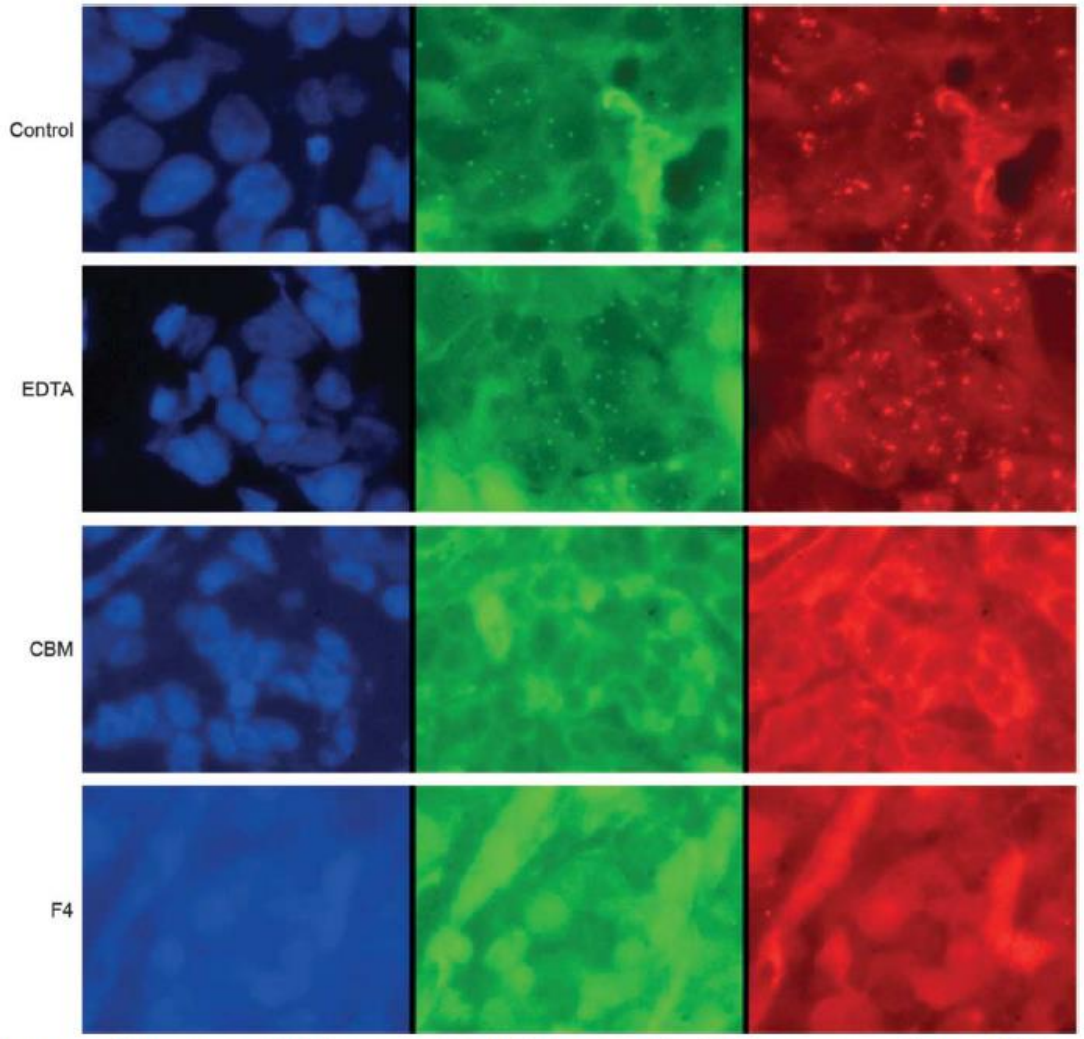


Figure 2 Immunohistochemical stainings for ERα, PR and HER2 on tumor tissue from patient #5 after decalcification in EDTA and Christensen's buffer with and without microwave. $\times 20$ magnification.



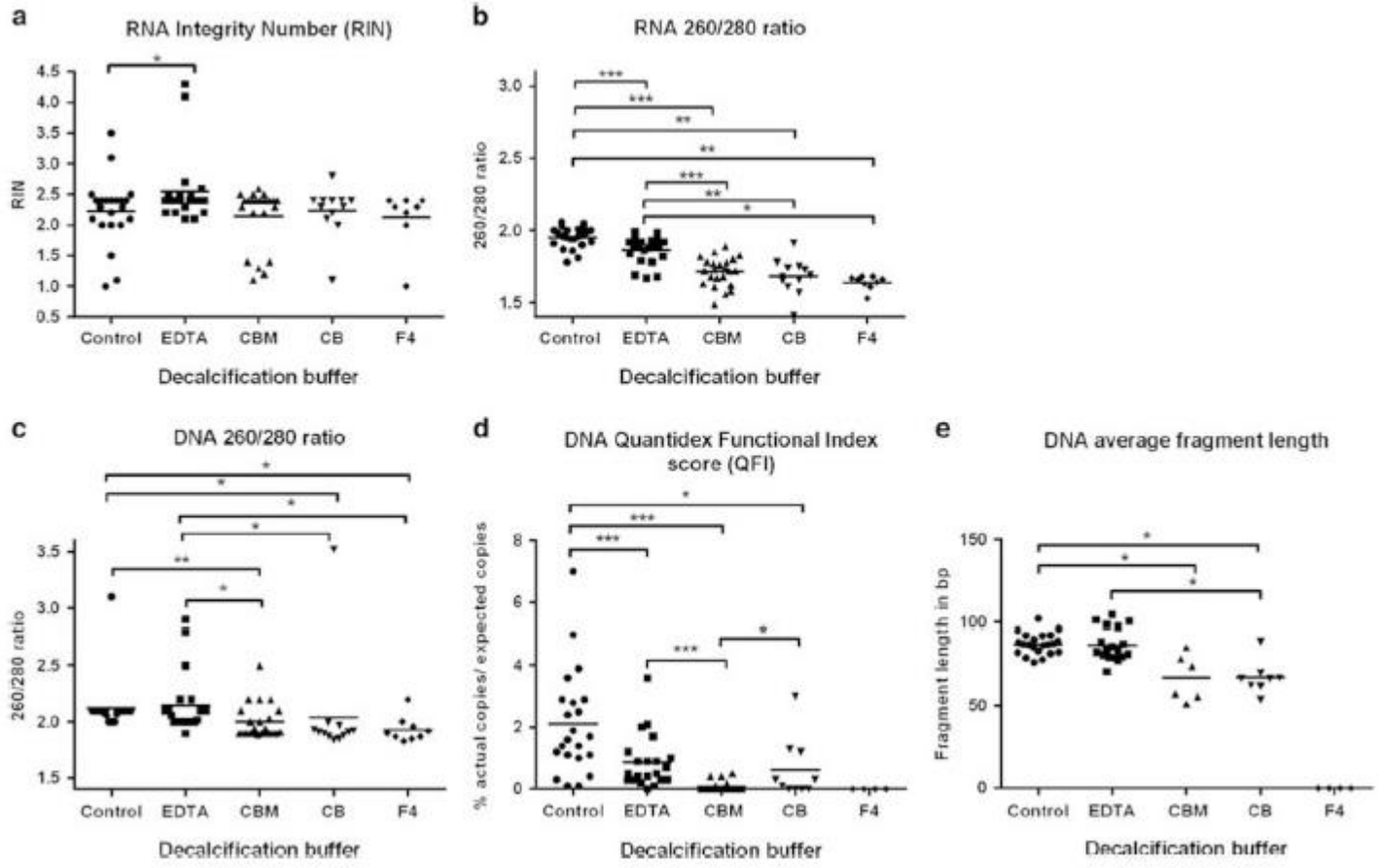


Figure 3 HER2 fluorescence *in situ* hybridization on tumor tissue from patient #16 after decalcification in EDTA, Christensen's buffer with (CBM) and without microwave (CB) and Formical-4 (F4). × 100 magnification is used.

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Non-Small Cell Lung Cancer

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Non-Small Cell Lung Cancer

NCCN Guidelines Index
Table of Contents
Discussion

PRINCIPLES OF PATHOLOGIC REVIEW

- **Pathologic Evaluation**
  - **The purpose of the pathologic evaluation of NSCLC will vary depending on whether the sample 1) is a biopsy or cytology specimen intended for initial diagnosis in a case of suspected NSCLC; 2) is a resection specimen; or 3) is obtained for molecular evaluation in the setting of an established NSCLC diagnosis.**
    - **In small biopsies or cytology specimens intended for initial diagnosis, the primary purpose is a) to make an accurate diagnosis using the 2021 WHO classification; and b) to preserve the tissue for molecular studies, especially if the patient has advanced-stage disease.**
    - **In small biopsies of poorly differentiated carcinomas, the terms "non-small cell carcinoma (NSCC)"[1] or "non-small cell carcinoma not otherwise specified (NSCC-NOS)" should be used as little as possible and only when a more specific diagnosis is not possible by morphology and/or special staining.**
    - **The following terms are acceptable: "NSCC favor adenocarcinoma" and "NSCC favor squamous cell carcinoma." "NSCC-NOS" should be reserved only for cases in which immunohistochemical testing is uninformative or ambiguous (see section on *Immunohistochemistry*).**
    - **Preservation of material for molecular testing is critical. Efforts should be undertaken to minimize block reorientation and the number of immunohistochemistry (IHC) stains for cases that cannot be classified on histologic examination alone (see section on *Immunohistochemistry*).**
  - **In resection specimens, the primary purpose is a) to classify the histologic type; and b) to determine all staging parameters, as recommended by the American Joint Committee on Cancer (AJCC), including tumor size, extent of invasion, adequacy of surgical margins, and presence or absence of lymph node metastases.**
    - **The number of involved lymph node stations should be documented since it has prognostic significance (AJCC 8th ed). Direct extension of the primary tumor into an adjacent lymph node is considered as nodal involvement.**
    - **All lobectomy specimens should be extensively dissected to search for involved lymph nodes.**
  - **In small biopsies or cytology specimens—obtained for molecular testing in the context of an established diagnosis after progression on targeted therapies—the primary purpose is a) to confirm the original pathologic type with minimal use of tissue for IHC only in suspected small cell carcinoma transformation or a different histology; and b) to preserve material for molecular analysis.**
- **Formalin-fixed paraffin-embedded (FFPE) material is suitable for most molecular analyses, except bone biopsies that were previously treated with acid decalcifying solutions. Non-acid decalcification approaches may be successful for subsequent molecular testing. While many molecular pathology laboratories currently also accept cytopathology specimens such as cell blocks, direct smears, or touch preparations, laboratories that do not currently do so are strongly encouraged to identify approaches to testing on non-FFPE cytopathology specimens.**

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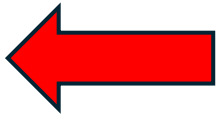
Diagnostica molecolare su lesioni ossee
2022 - 2023

Biopsie osse			
	Totali	Inadeguati	% di insuccesso
BRCA	6	3	50,00%
FISH HER2	44	3	6,80%
EGFR	41	5	12,20%
FUSIONI (RNA)	26	3	11,50%
MSI	5	0	0,00%
Totali	116	11	9,50%



1) istologico 12/2020, molecolare 04/2022
2) istologico 11/2021, molecolare 03/2023
3) istologico esterno 2020, molecolare 12/2023

lunedì 19/04/2021 15:54

Perrone Giuseppe

BRCA pz [redacted]

A Fabio Calabro'; f.calabro@scf.gov.it

Cc Daniela Righi (D.Righi@unicampus.it)

Caro Fabio,
mi è arrivata una tua richiesta per BRCA1/2 per il pz in oggetto.
Solo per avvisarti che il materiale pervenuto NON è risultato idoneo per l'analisi (si tratta di una biopsia epatica con scarso materiale residuo) … ci abbiamo provato, ma senza successo.

Ti informo in anticipo così, se lo ritieni opportuno, puoi organizzare eventuale approfondimento genetico

Un saluto
Giuseppe

Da: Perrone Giuseppe <G.Perrone@unicampus.it>
Inviato: venerdì 14 maggio 2021 17:36:59
A: Fabio Calabro'
Oggetto: [redacted]

Caro Fabio,
per avvisarti che non è stato possibile estrarre DNA adeguato per BRCA dal materiale che ci è pervenuto del paziente in oggetto.
Potrebbe essere opportuno verificare BRCA su sangue.
Saluti

GP

giovedì 04/11/2021 17:54

Perrone Giuseppe

I: Referti BRCA pz. [redacted]

A Fabio Calabro'

Cc Daniela Righi (D.Righi@unicampus.it); Sabarese Giovanna

Caro Fabio,
in allegato i referti del pz. [redacted]
Purtroppo il DNA non è risultato adeguato per completare la valutazione.

Un caro saluto
Giuseppe

venerdì 05/11/2021 16:38

Sabarese Giovanna

[redacted] **BRCA**

A Fabio Calabro'

Cc Perrone Giuseppe; Righi Daniela

[redacted]_2021-M-02420_01.pdf
419 KB

[redacted]_2021-M-02421_01.pdf
418 KB

Gent.mo dott. Calabrò,
in allegato i referti del pz. [redacted]
Purtroppo il DNA non è risultato adeguato per completare la valutazione.
Cordiali saluti,
Giovanna Sabarese

Giovanna Sabarese, PhD

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lunedì 15/11/2021 08:11

Fabio Calabro' <FCalabro@scamilloforlanini.rm.it>

A Perrone Giuseppe

L'utente ha risposto al messaggio in data 15/11/2021 21:12.

Buongiorno Giuseppe, spero tutto bene.

Nonostante non abbiamo mandato moltissimi pazienti con carcinoma prostatico per la determinazione di BRCA2, mi sono accorto che in una alta percentuale dei casi, lo stato di conservazione del materiale non ha permesso la estrazione del DNA per consentire la valutazione.

Ti chiedo quindi se tui credi che questo sia un problema di preparazione del materiale da parte nostra e se esiste una modalità per migliorare questo dato.

Grazie sempre per la tua cortesia,
Fabio

dr. Fabio Calabrò
Direttore UOS Oncologia Tumori Genito-urinari
Oncologia Medica
Azienda Ospedaliera San Camillo Forlanini
Roma
Tel 0658704339
Fax 0658704317
email: f.calabro@scf.gov.it

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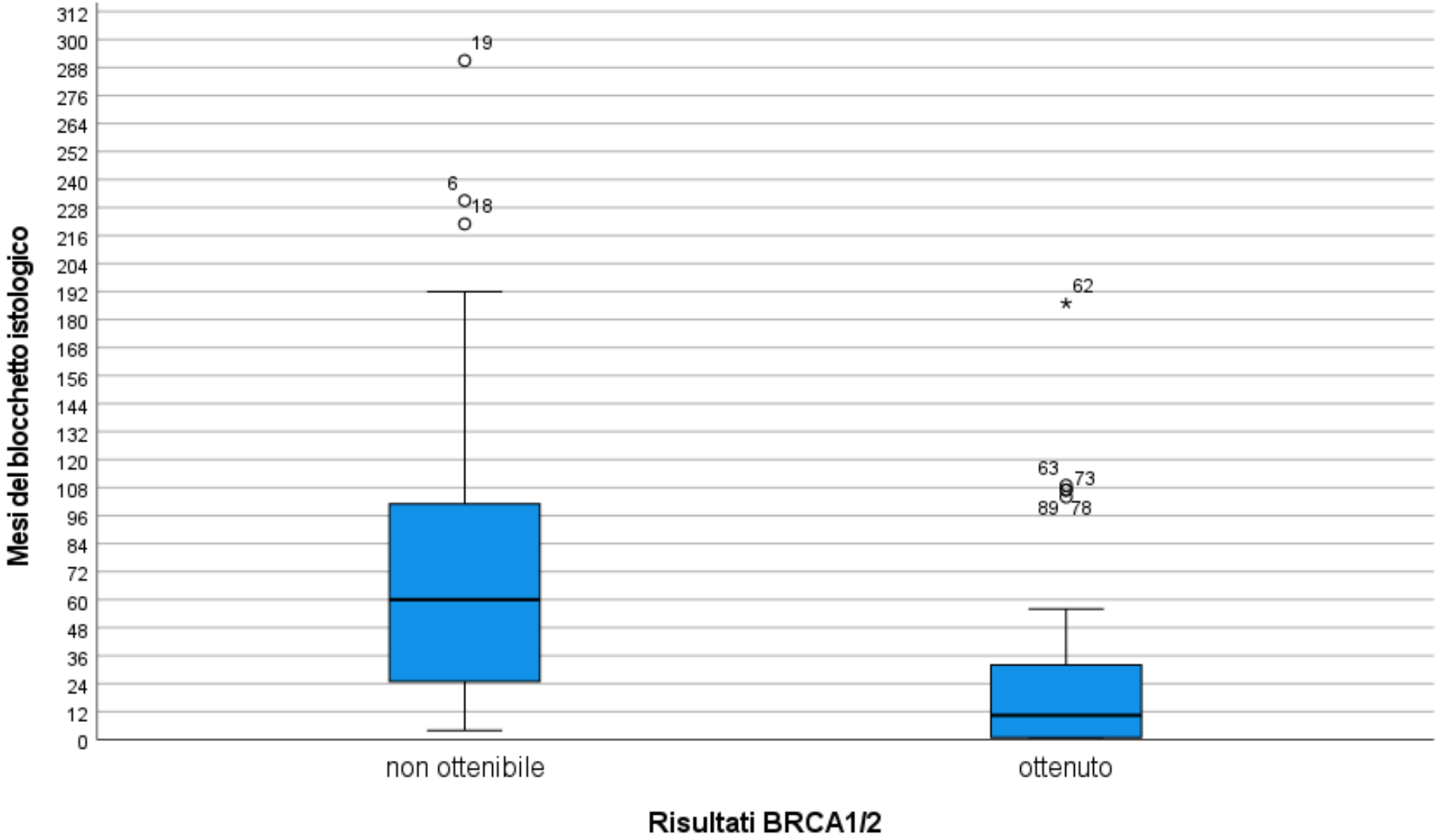
BRCA

1	ARMONIA	Data Analisi	DOB	anno DOB	risultato	CENTRO	Anno intervento
2	2021-M-01122	01/06/2021	24/07/1945	1945	NA	EST	2002
3	2021-M-01474	15/07/2021	03/01/1952	1952	NA	EST	2009
4	2021-M-02324	20/10/2021	13/07/1954	1954	NA	EST	2012
5	2021-M-00945	12/05/2021	03/03/1952	1952	NA	EST	2013
6	2021-M-02199	08/10/2021	10/12/1945	1945	NA	EST	2013
7	2021-M-01787	25/08/2021	15/02/1947	1947	NEG	EST	2017
8	2021-M-02421	29/10/2021	17/06/1962	1962	NA	EST	2017
9	2021-M-00517	23/03/2021	10/05/1976	1976	CNV high BRCA1	CBM	2019
10	2021-M-00589	01/04/2021	01/09/1946	1946	NA	EST	2019
11	2021-M-00770	21/04/2021	21/07/1953	1953	NA	EST	2019
12	2021-M-00587	01/04/2021	23/10/1951	1951	NA	EST	2020
13	2021-M-01026	18/05/2021	23/10/1951	1951	NA	EST	2020
14	2021-M-01177	07/06/2021	14/11/1958	1958	NEG	EST	2020
15	2021-M-00820	27/04/2021	23/09/1943	1943	NEG	EST	2021
16	2021-M-01021	18/05/2021	01/09/1946	1946	NEG	EST	2021
17	2021-M-01366	06/07/2021	27/07/1943	1943	NEG	CBM	2021
18	2021-M-01507	19/07/2021	12/03/1954	1954	CNV LOW BRCA1	CBM	2021
19	2021-M-01667	10/08/2021	18/04/1963	1963	NEG	CBM	2021
20	2021-M-01811	27/08/2021	07/01/1964	1964	NEG	CBM	2021
21	2021-M-01954	09/09/2021	13/08/1955	1955	NEG	CBM	2021

23%

100%

92 BRCA Prostata



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diagnostics

MDPI

Article

Feasibility of Comprehensive Genomic Profiling (CGP) in Real-Life Clinical Practice

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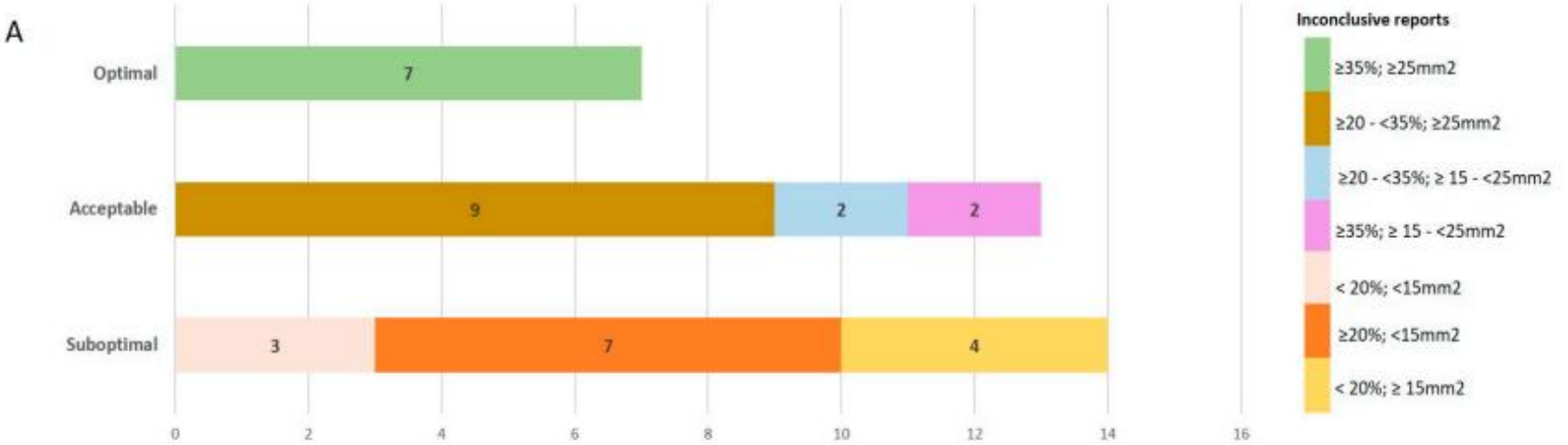
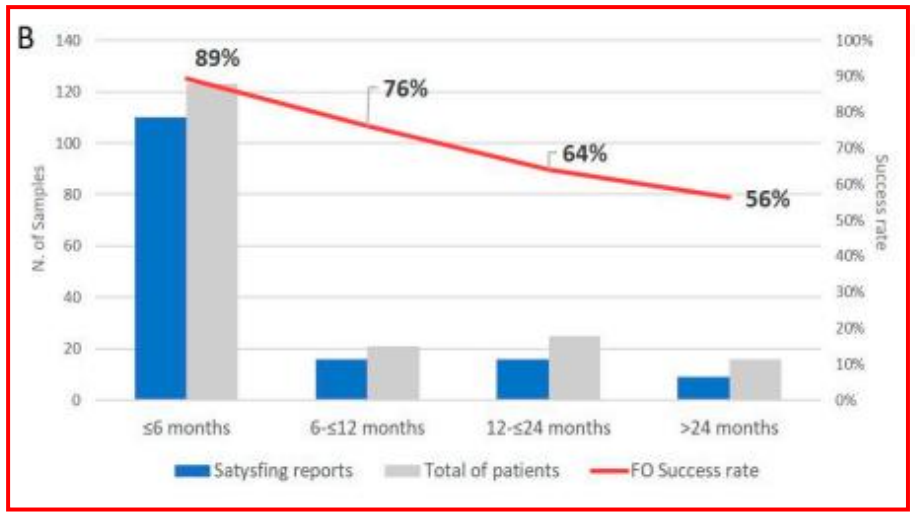
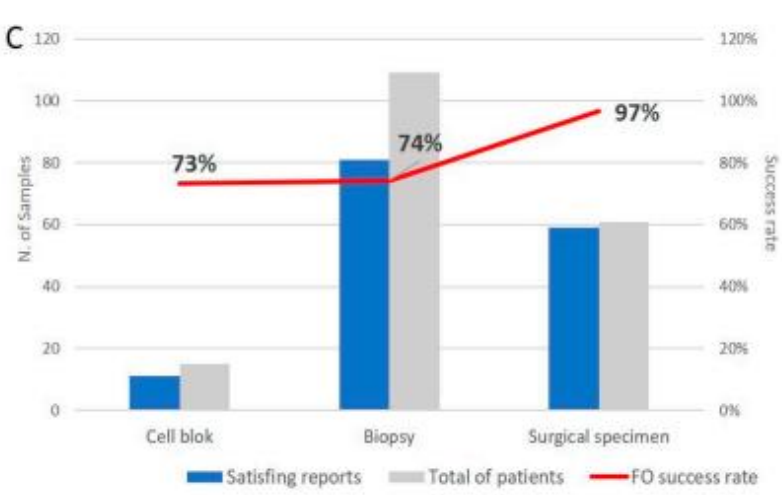
Table 1. Baseline characteristics of patients with solid tumors.

Variable	N
Patients	184







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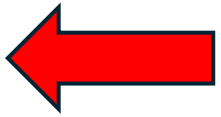
Diagnostica molecolare su lesioni ossee
2022 - 2023

Biopsie osse			
	Totali	Inadeguati	% di insuccesso
BRCA	6	3	50,00%
FISH HER2	44	3	6,80%
EGFR	41	5	12,20%
FUSIONI (RNA)	26	3	11,50%
MSI	5	0	0,00%
Totali	116	11	9,50%



1) istologico 12/2020, molecolare 04/2022
2) istologico 11/2021, molecolare 03/2023
3) istologico esterno 2020, molecolare 12/2023

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Blood-based liquid biopsy in advanced prostate cancer

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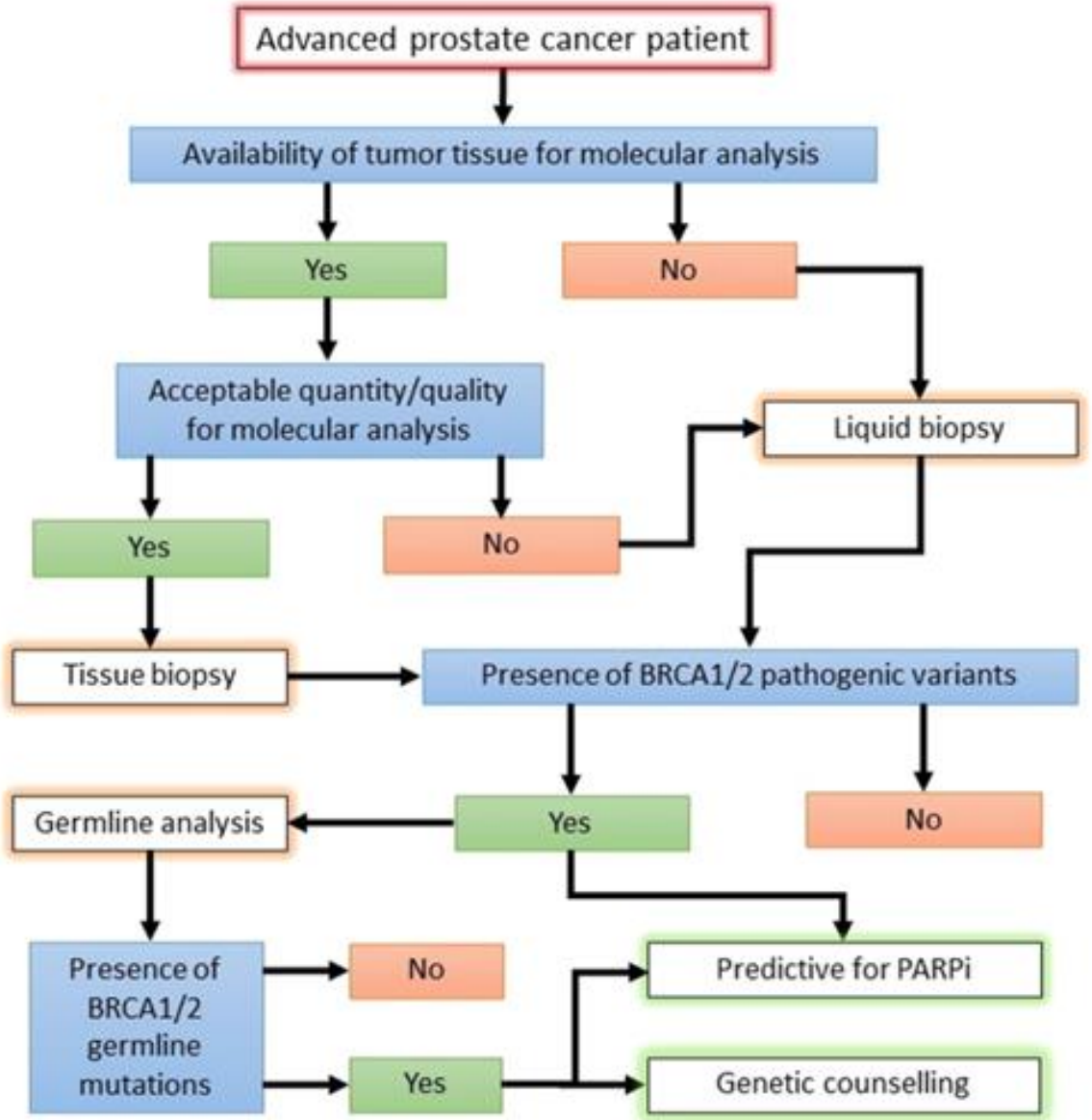

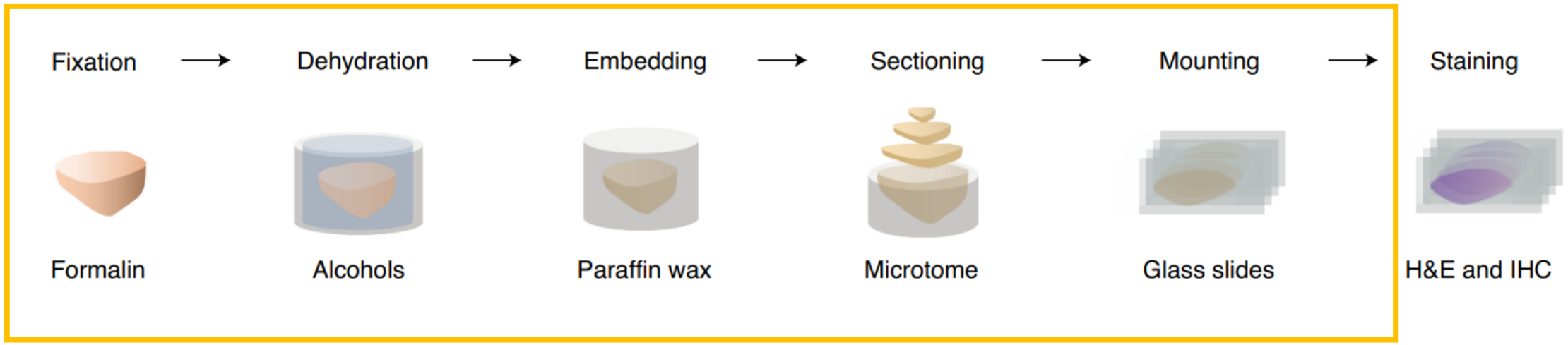
Fixation
Dehydration
Embedding
Sectioning
Mounting
Staining
Formalin
Alcohols
Paraffin wax
Microtome
Glass slides
H&E and IHC

Limiti della Biopsia ossea nell'era dell'Oncologia di Precisione

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