# PERCORSO DIAGNOSTICO TERAPEUTICO

# DELLE LESIONI SURRENALICHE NELLA PROVINCIA DI FERRARA

Sabato 3 dicembre 2022 - Aula Magna Nuovo Arcispedale S. Anna

## Quadri anatomo-patologici

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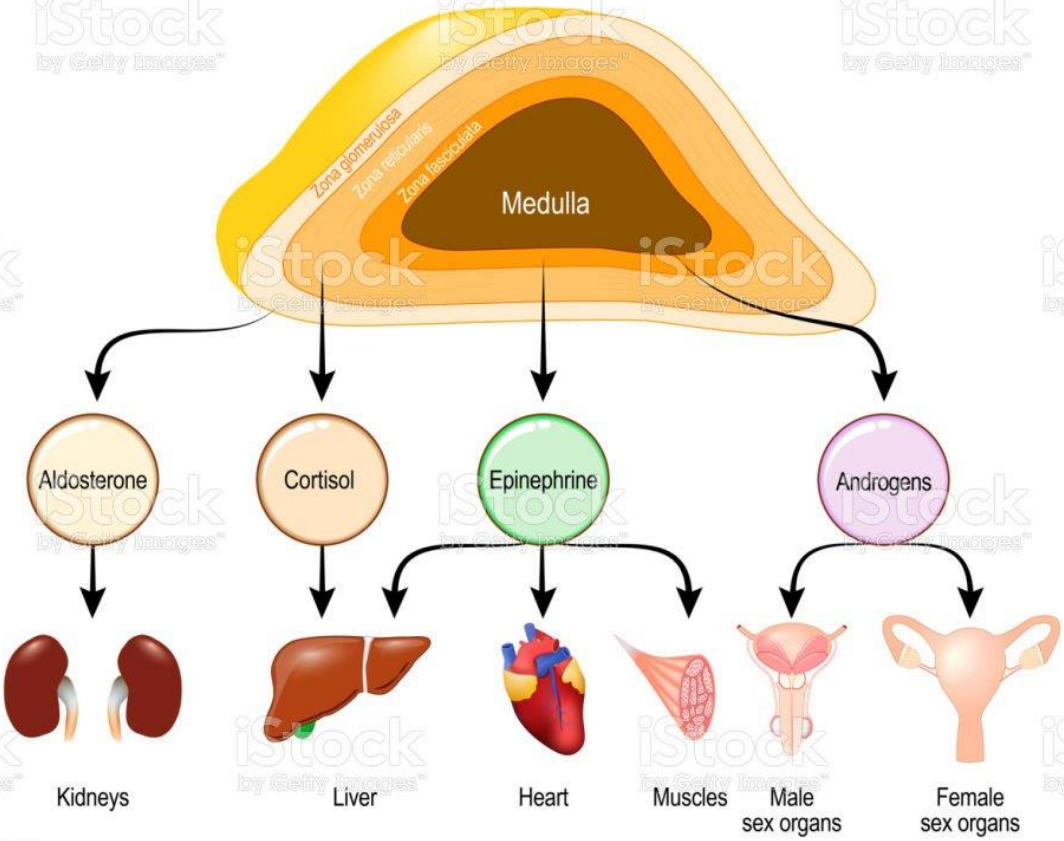
**Direttore Prof. G. Lanza**

# Adrenal gland
## (hormones)

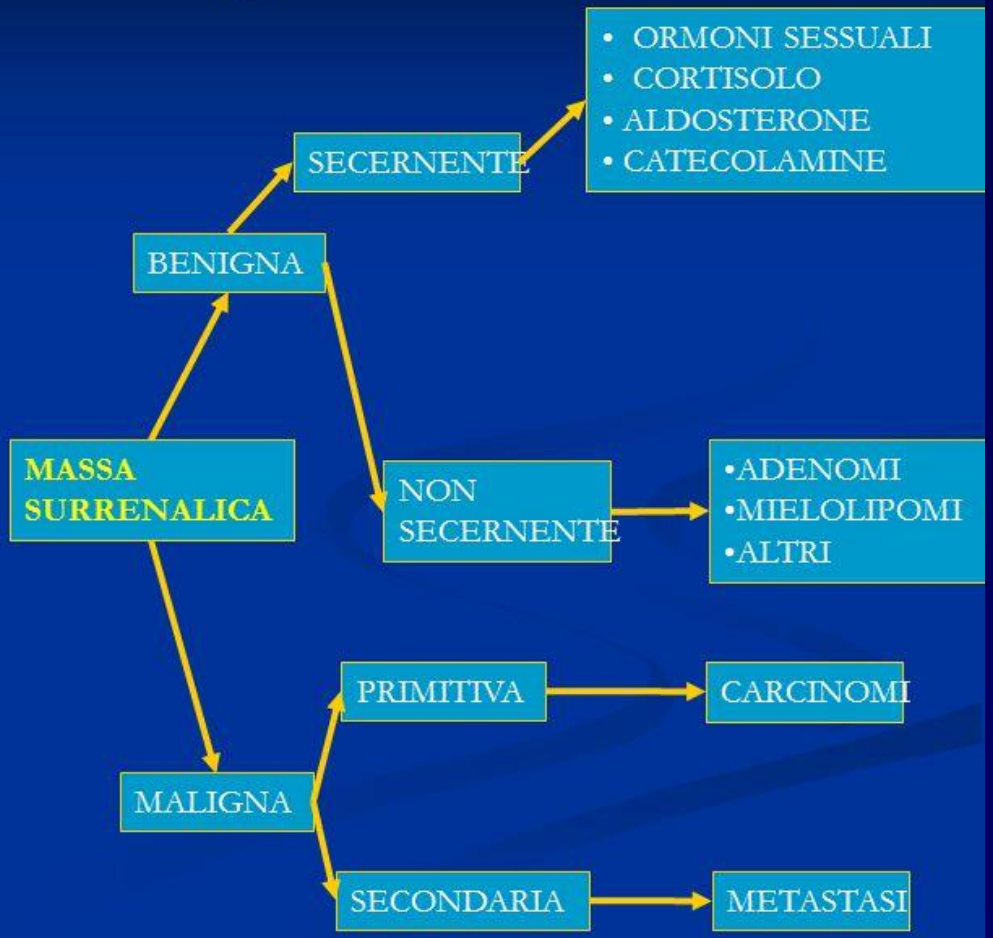


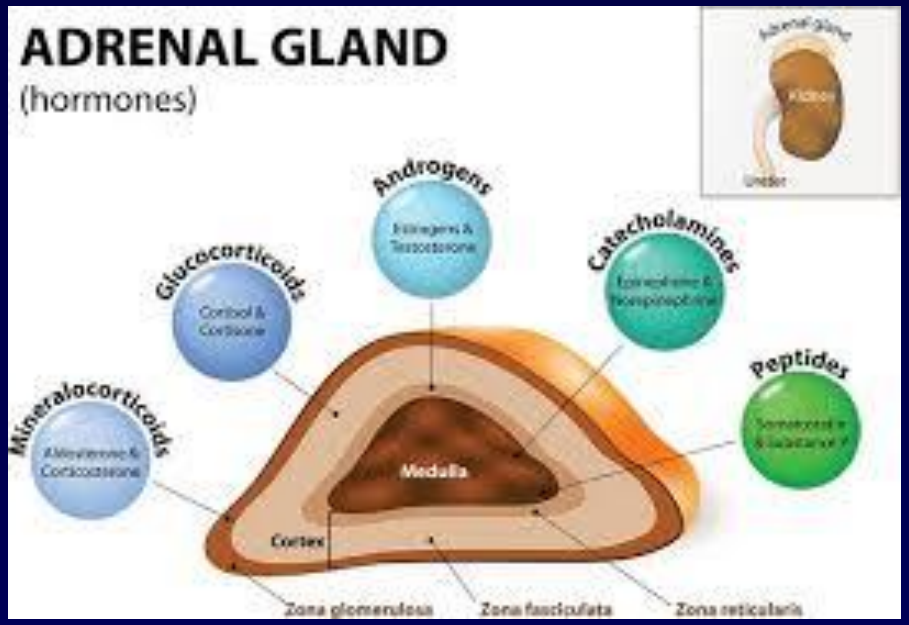

dreamstime

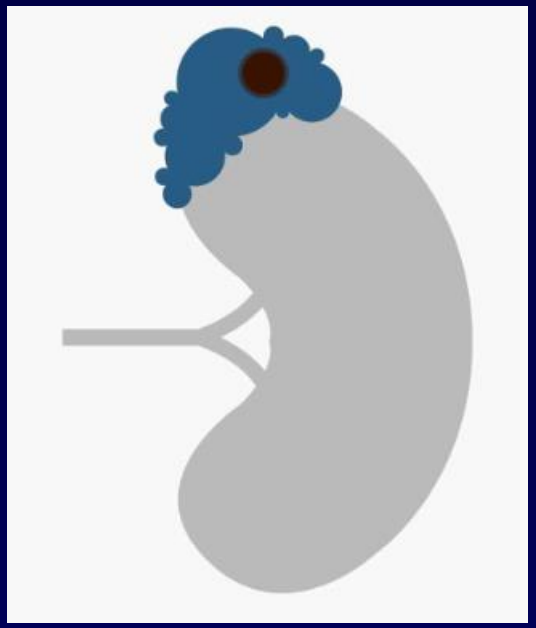
# Patologia chirurgica del surrene

- Patologia tumorale benigna e maligna
- Patologia iperplastica

distinta in base a:
- biologia (benigno/maligno)
- increzione ormonale





Nearly all studies done on the subjects have shown that no single parameter short of detection of metastases discrimenated sharply between bening and malignant tumors

Opportuno follow-up

Il quadro morfologico complessivo fa prendere in considerazione come prima ipotesi la diagnosi di adenoma cortico-surrenalico.
Le atipie riscontrate consigliano comunque follow-up prudenziale.

# Istologia

- **lo strato corticale esterno**

  distinto dall'esterno all'interno:

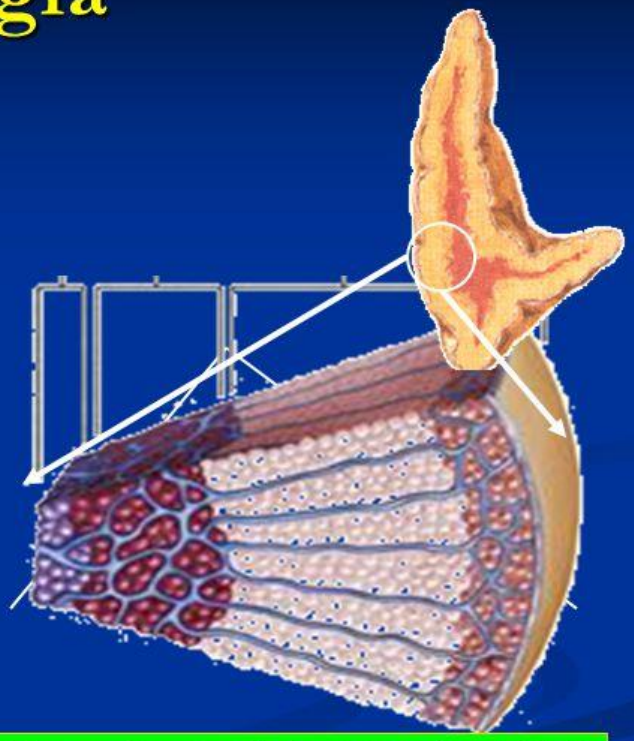
  - Glomerulare ( mineralcorticoidi )
  - Fascicolare ( glucocorticoidi )
  - Reticolare ( androgeni )

- **la regione midollare,**

  costituita da

  - cell. postgangliari (adrenalina e noradren.)

  stimolo da fibre pregangl. nervi splancnici.



Glomerulare Fascicolare Reticolare Midollare

# WHO 2022

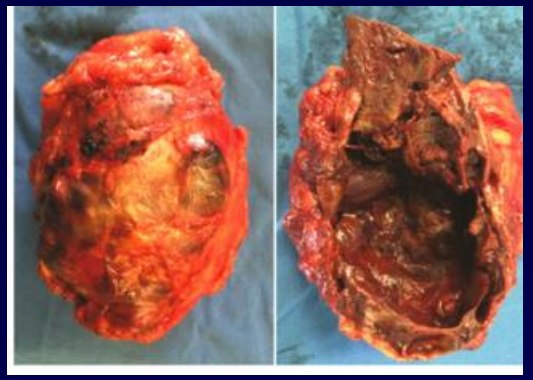
## Adrenal cortex

- Adrenal rests
- Adrenal cysts
- Adrenal myelolipoma
- Adrenal cortical tumours
- Congenital adrenal hyperplasia
- Adrenocortical nodular disease
- Adrenal cortical adenoma
- Adrenal cortical carcinoma
- Sex cord stromal and other tumours
- Adrenal sex cord stromal tumour
- Adenomatoid tumour
- Adrenal melanoma

## Adrenal medulla

- Neuroblastic tumours
- Neuroblastoma
- Ganglioneuroblastoma, intermixed
- Ganglioneuroblastoma, nodular
- Ganglioneuroma
- Paraganglioma and pheochromocytoma
- Phaeochromocytoma
- Sympathetic paraganglioma
- Parasympathetic paraganglioma
- Composite paraganglion tumours
- Composite phaeochromocytoma and paraganglioma

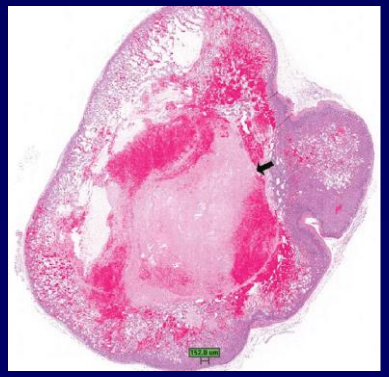
# CISTI

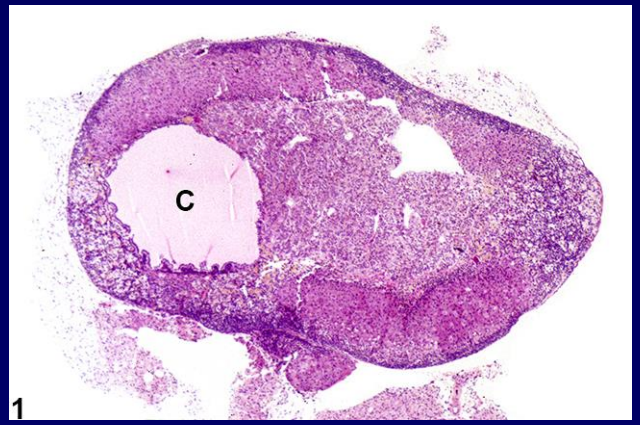


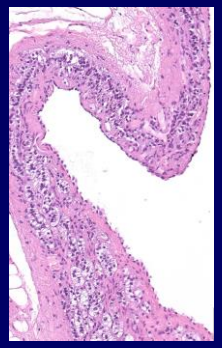
- 4% delle masse surrenaliche
- Prevalentemente PSEUDOCISTI (39-78%)
- Uniloculari
- Postraumatiche, infettive, parassitarie, post emorragiche, endoteliali (trombotiche), mesoteliali
- DD Necrosi !!

The differential diagnosis includes cystic degeneration in adrenocortical neoplasms, cystic pheochromocytoma, vascular tumours or malformations, cystic renal cell carcinoma and

ectopic thyroid



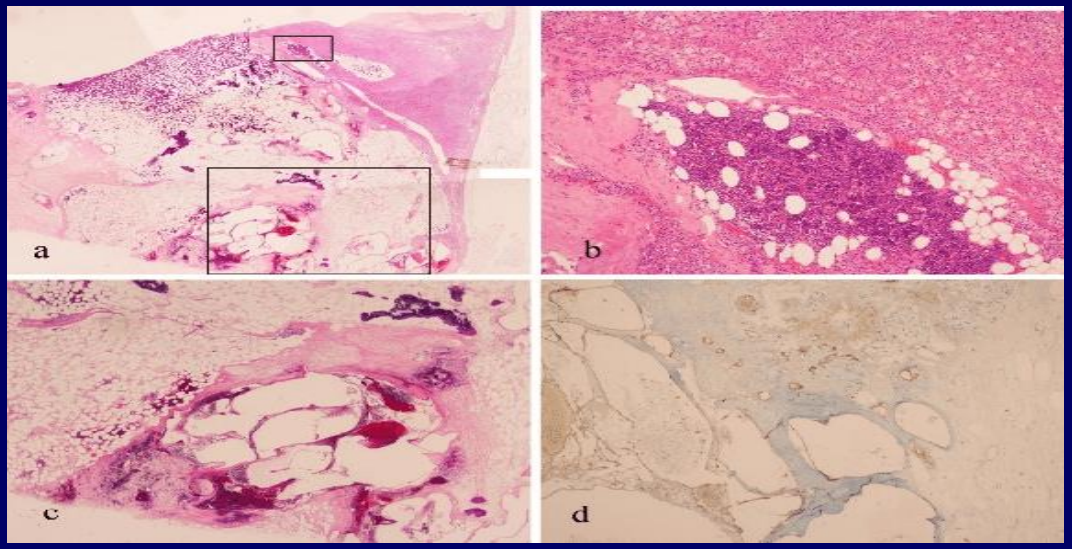


Neoplasia surrenalica capsulata, con aree calcifiche e pressochè completa degenerazione necrotico-emorragica, riccamente vascolarizzata (emangioma like), con aspetti di organizzazione. Residua minima componente cellulare, marginalmente rappresentata, costituita da rari elementi dissociati, privi di pattern architetturale, ad abito oncocitario, con evidenti atipie citologiche ed elevato indice di attività proliferativa, non ulteriormente definibili.

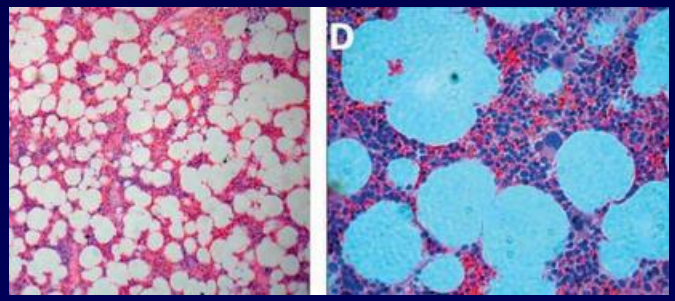
Caratterizzazione fenotipica: INIBINA-/ CROMOGRANINA-/ HMB45-.

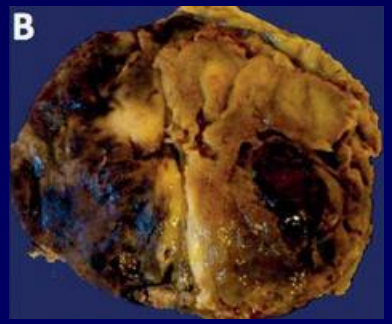
Opportuno follow-up.



# MIELOLIPOMA

- 3-6.5% dei tumori surrenalici
- solitario (bilaterale CAH)
- asintomatico (emorragie)
- Adipociti maturi + tutte le filiere ematopoietiche
- Può associarsi a un tumore corticale funzionante nella CAH
- Può associarsi a ganglioneuroma, hibernoma



# Tumori della Corticale

## ADRENOCORTICAL NODULAR DISEASE

Proliferazioni nodulari benigne della corticale

SOTTOTIPI:

- Sporadic nodular adrenocortical disease (unilaterale/bilaterale)

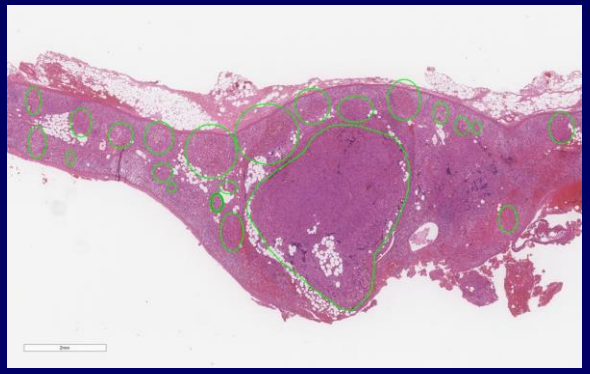
Incidentaloma; noduli <10 mm

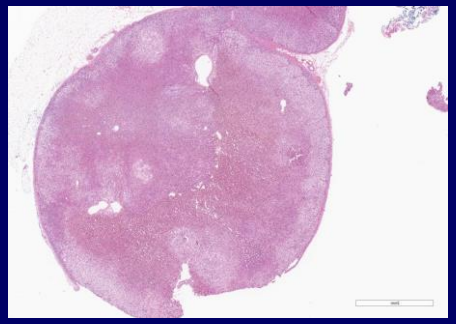
- Bilateral micronodular adrenocortical disease
- a) Isolated micronodular adrenocortical disease (i-MAD)
- b) Primary Pigmented Nodular Adrenocortical Disease (PPNAD)

Carney complex

- Bilateral macronodular adrenocortical disease

associati a Cushing





Sporadic small adrenal cortical nodules may be clonal and thus the term “sporadic nodular adrenal cortical disease” has replaced “cortical nodular hyperplasia” for incidental nonfunctional cortical nodules

With the exception of size, sporadic nodular adrenocortical disease is indistinguishable from non-functional adrenocortical adenomas.

There can be more than one nodule per gland and both adrenal glands may be involved.

When they occur in adrenals from patients with functional adenomas, their distinction from subcentimeter functional adrenal cortical adenomas requires the use of steroidogenic enzyme immunohistochemistry

# ADENOMA CORTICOSURRENALICO

Definizione: tumore epiteliale BENIGNO della corticale del surrene (!!)

Il più comune tumore della corticale

5% della popolazione generale

Solo raramente bilaterale e multifocale

Funzionante (ormonalmente attivo) / silente

MACROSCOPICA

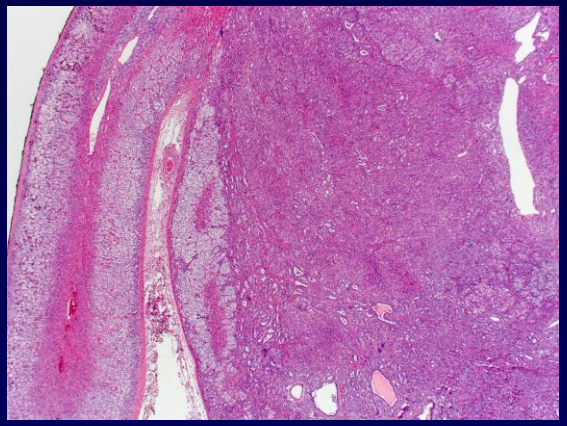
Ben circoscritto (integrità del pezzo operatorio)

Giallastro, aranciato o bruno

Normalmente < 50 mm, può mostrare aree emorragiche, necrosi e degenerazione cistica

# ADENOMA CORTICOSURRENALICO

## ISTOLOGIA

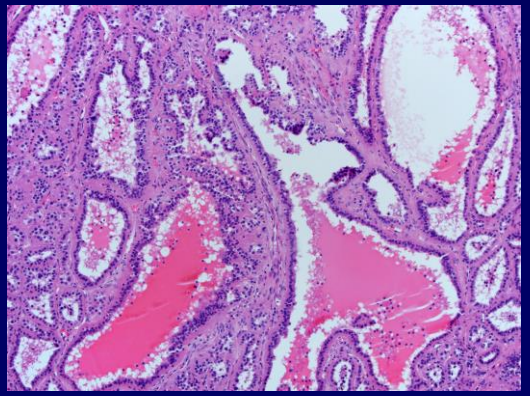


Cellule lipidic rich (zona fascicolata)
Cellule lipidic poor (zona reticolare)
Cellule zona glomerulosa-like
Cellule oncocitarie (spesso non funzionanti)

Attività mitotica bassa o assente (no mitosi atipiche)
Aree mixoidi, mielolipomatose, lipomatose, presenza di lipofuscina

NON dovrebbe mostrare caratteristiche di malignità:

- Necrosi
- Alto grado nucleare
- Attività mitotica elevata
- Mitosi atipiche
- Angioinvasione
- Pattern di crescita invasivo



# DIAGNOSI DIFFERENZIALE

- Carcinoma corticosurrenalico
- Feocromocitoma
- Pecoma (elementi oncocitari)

Algoritmi:

- WEISS
- LIN-WEISS-BISCEGLIA (per neoplasie oncocitarie)
- ALGORITMO FREMEWORK RETICOLARE
- HELSINKY SCORING SYSTEM
- AFIP (neoplasie pediatriche)

N.B le neoplasie mixoidi restano molto difficili da classificare: non è del tutto possibile escluderne il comportamento maligno

# The WEISS Scoring System

| Parameter | Score |
|---|---|
| High Fuhrman nuclear grade (III or IV) | 1 |
| Mitotic count >5 per 10mm$^2$ (50 high power fields of 0.2 mm$^2$) | 1 |
| Atypical mitosis | 1 |
| Necrosis | 1 |
| Diffuse architecture >30% of tumour volume | 1 |
| Clear cells ≤25% of the tumour volume | 1 |
| Capsular invasion | 1 |
| Venous invasion (vascular invasion) | 1 |
| Sinusoidal (lymphatic) invasion | 1 |
| Total score<br>**A score of ≥3 indicates malignancy** | 9 |

# Modified Weiss System

| Parameter | Score |
|---|---|
| | |
| Mitotic count >5 per 10mm$^2$ (50 high power fields of 0.2 mm$^2$) | 1 |
| Atypical mitosis | 1 |
| Necrosis | 1 |
| | |
| Clear cells ≤25% of the tumour volume | 1 |
| Capsular invasion | 1 |
| | |
| | |
| Total score<br>**A score of ≥3 indicates malignancy** | |

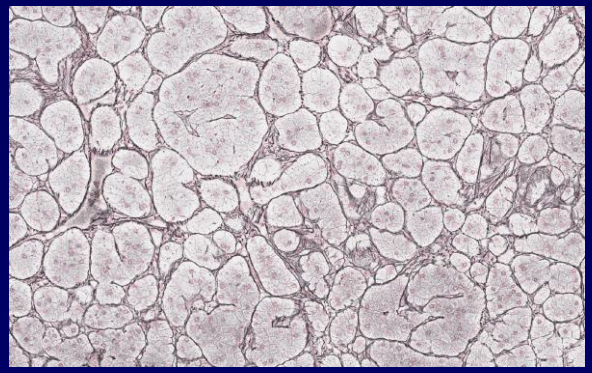
# LIN-WEISS- BISCEGLIA per neoplasie oncocitarie

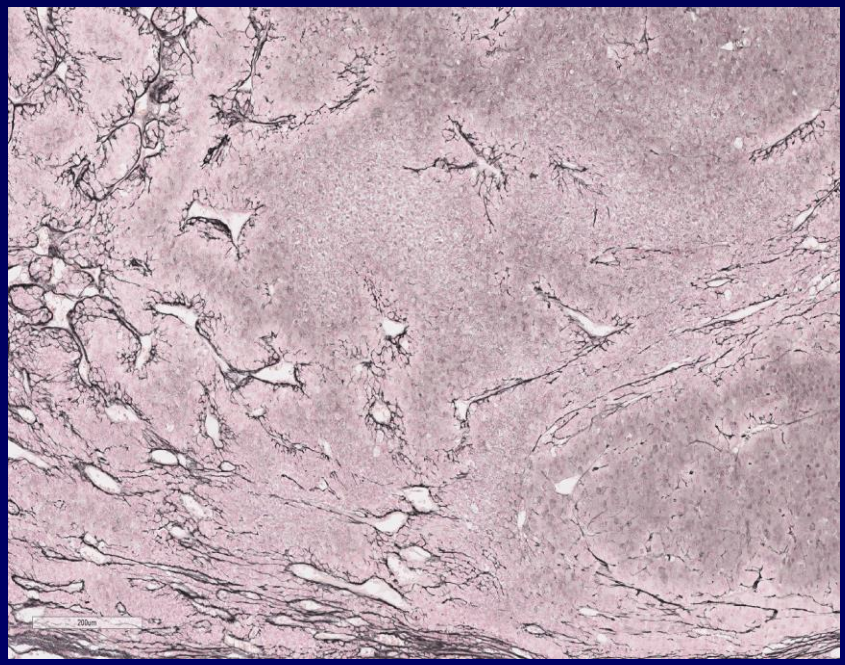
| **CRITERI MAGGIORI** | |
|---|---|
| | |
| Conta Mitotica >5 per 10mm$^2$ (50 high power fields of 0.2 mm$^2$) | |
| Mitosi atipiche | |
| Invasione venosa | |
| **CRITERI MINORI** | |
| grandezza (>100mm) | |
| Invasione capsulare | |
| Necrosi | |
| Invasione sinusoidi | |
| Maligno: almeno un criterio maggiore<br>Incerto: almeno un criterio minore<br>Benigno: assenza di criteri maggiori e minori | |

# ALGORITMO FRAMEWORK RETICOLARE

**Altered reticulin framework in association with one of the following features indicates malignancy:**

- Mitotic count >5 per 10mm2 (50 high power fields of 0.2 mm2)
- Tumor necrosis
- Vascular invasion





# HELSINKY SCORING SYSTEM

| Parameter | Score |
|---|---|
| | |
| Mitotic count >5 per 10mm$^2$ (50 high power fields of 0.2 mm$^2$) | 3 |
| | |
| Necrosis | 5 |
| | |
| Ki67 proliferation index | Numeric value from the highest proliferative area |
| | |
| | |
| | |
| Total score<br>**Score 0-8.5: benigno**<br>**Score >8.5: maligno**<br>**Score > 17 prognosi avversa** | |

# WIENEKE /AFIP

## per neoplasie pediatriche

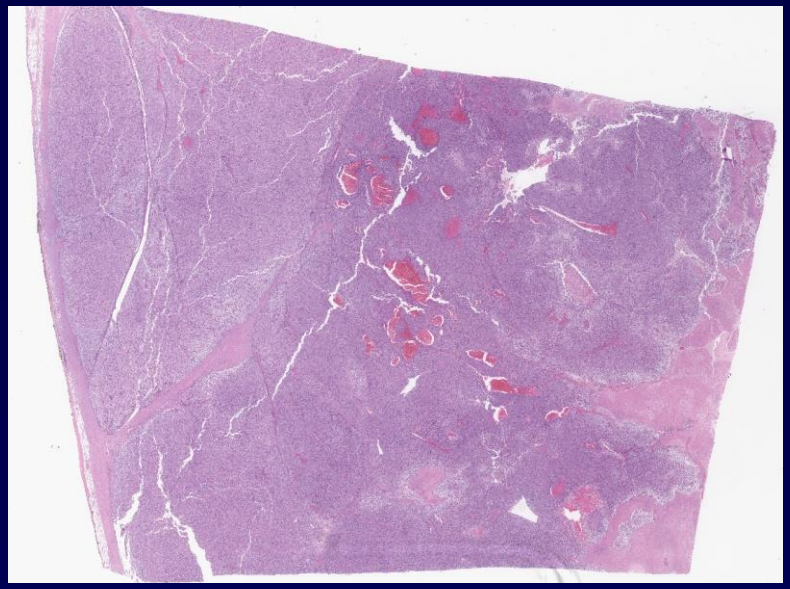
| **Parameter** |
| --- |
| Peso >400gr |
| Grandezza >105 mm |
| Estensione a organi adiacenti o tessuto periviscerale |
| Invasione vena cava |
| Invasione vascolare |
| Necrosi |
| Invasione capsula |
| Mitosi >15 X4 $mm^2$ |
| Mitosi atipiche |
| Maligno/ prognosi peggiore: ≥ 4<br>Incerto potenziale: 3<br>Benigno: ≤ 2 |

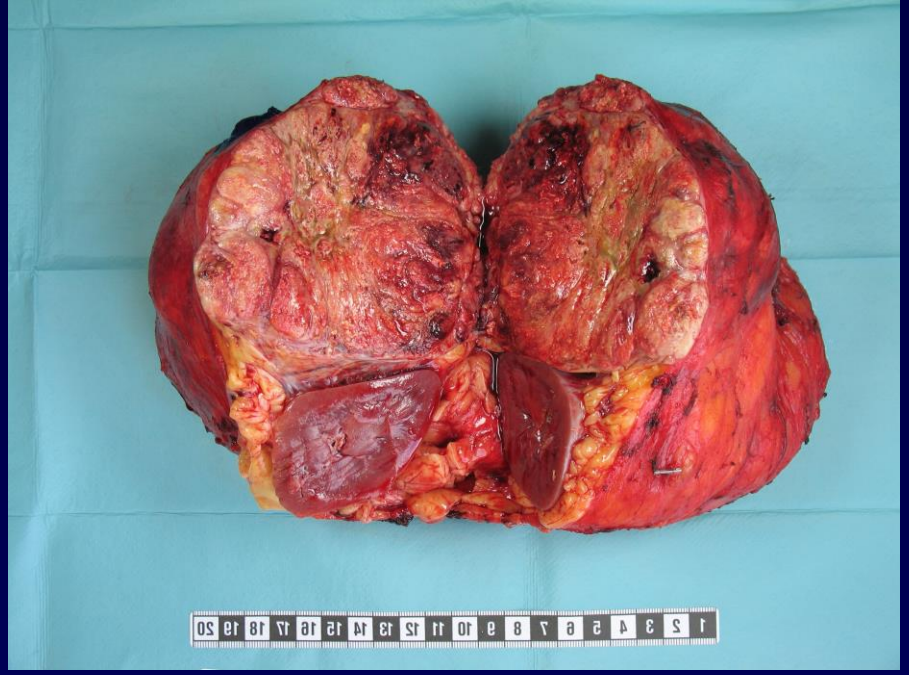
Neoplasia cortico-surrenalica con pattern di crescita alveolare prevalente, costituita da cellule a citoplasma eosinofilo commiste ad elementi a citoplasma chiaro, microvacuolato (>25%), grado II secondo Fuhrmann.
Sono presenti occasionali atipie, anche con vistosa anisonucleosi.
Non si osserva significativa attività mitotica (< 1/10HPF), nè si evidenziano mitosi atipiche.
Attività proliferativa valutata mediante Ki67: 2% circa.
Pattern reticolare conservato.
Assenza di necrosi.
Capsula, ove riconoscibile, indenne.
Presenza di trombosi venosa neoplastica capsulare.
Margini di resezione indenni.
Valutazione secondo WEISS System: <3
**Neoplasia corticosurrenalica a incerto potenziale maligno.**
Opportuno follow-up.
Profilo immunoistochimico: INIBINA+ / SINAPTOFISINA +/ MELAN A+/ CROMOGRANINA -

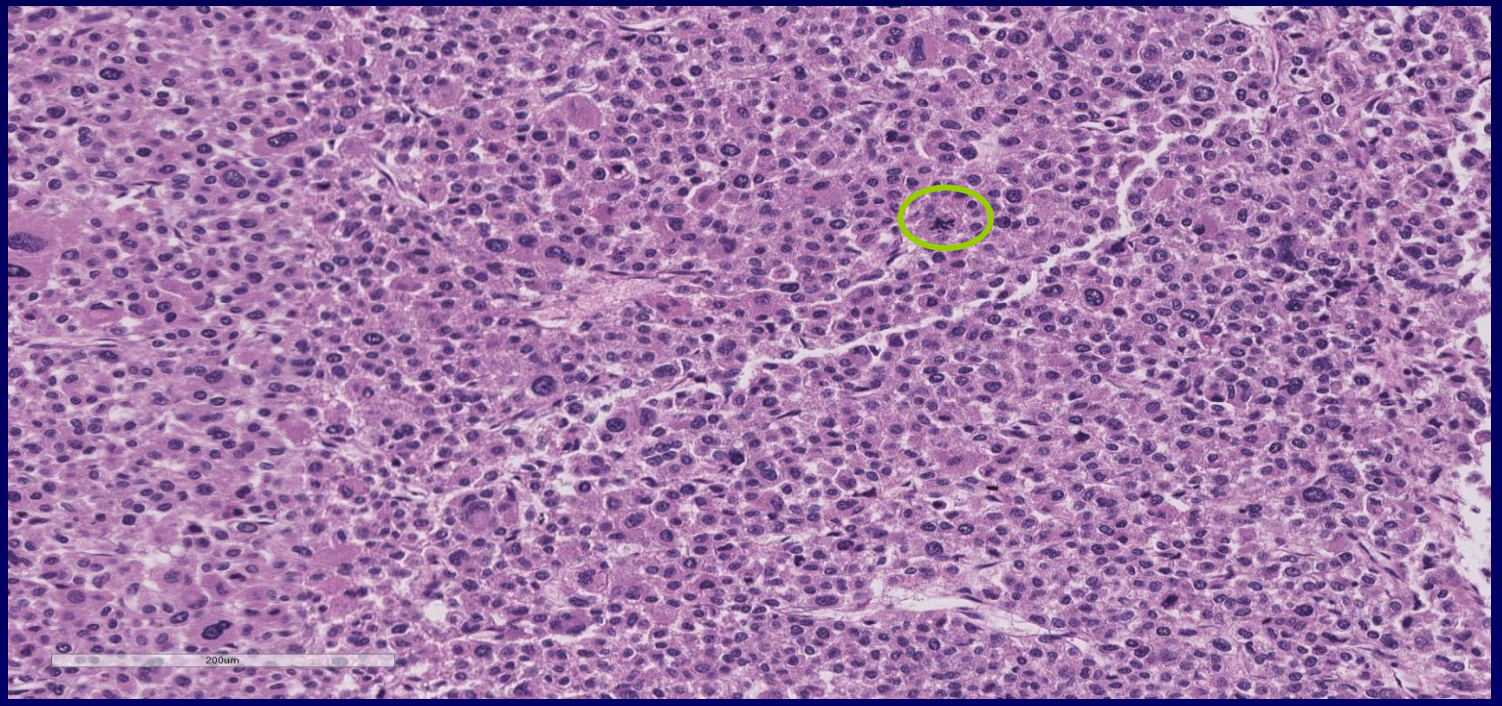
# CARCINOMA CORTICOSURRENALICO

- Unilaterale (anche eterotopico), solitario, grande, Secernente nel 50% dei pazienti/effetto massa
- TP53 mutata in 1/5 dei casi
- Mutinodulare, solido
- Perdita del pattern reticolare
- Necrosi comedonica

- Myxoid carcinomas have abundant extracellular connective tissue mucin
- In myxoid carcinomas, some Weiss parameters such as diffuse growth pattern, lymphatic invasion and nuclear atypia, may be absent or difficult to assess, thus increasing the risk of an under diagnosis of malignancy.



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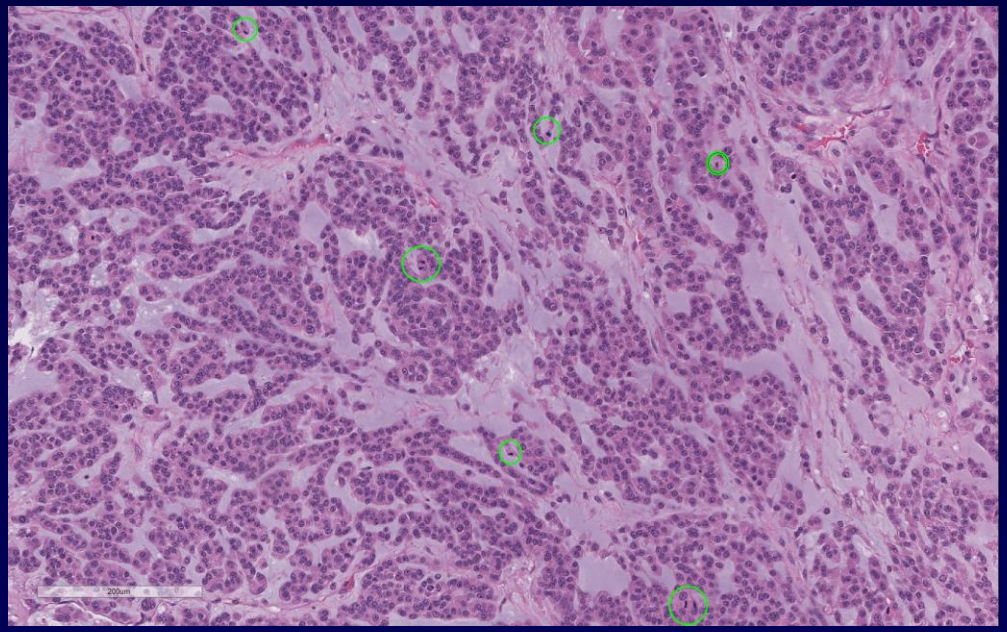
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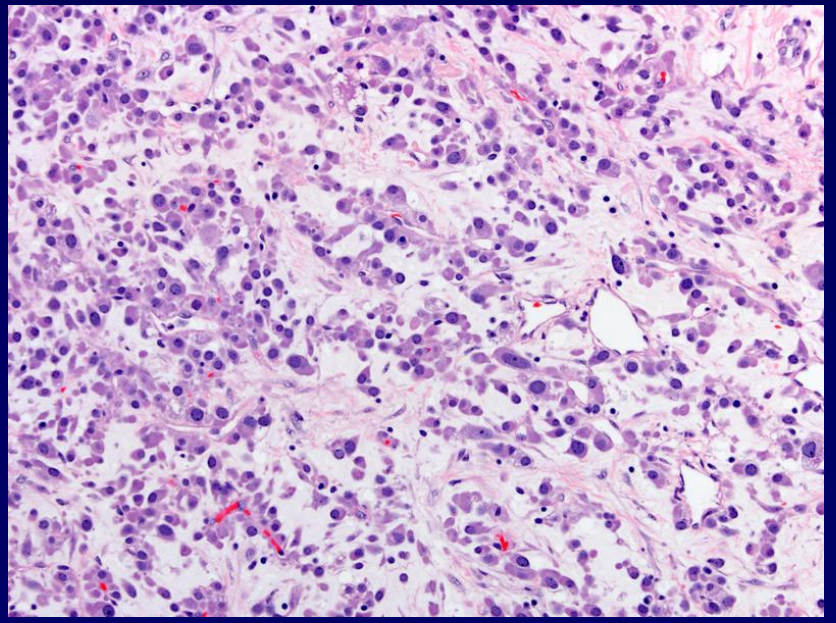
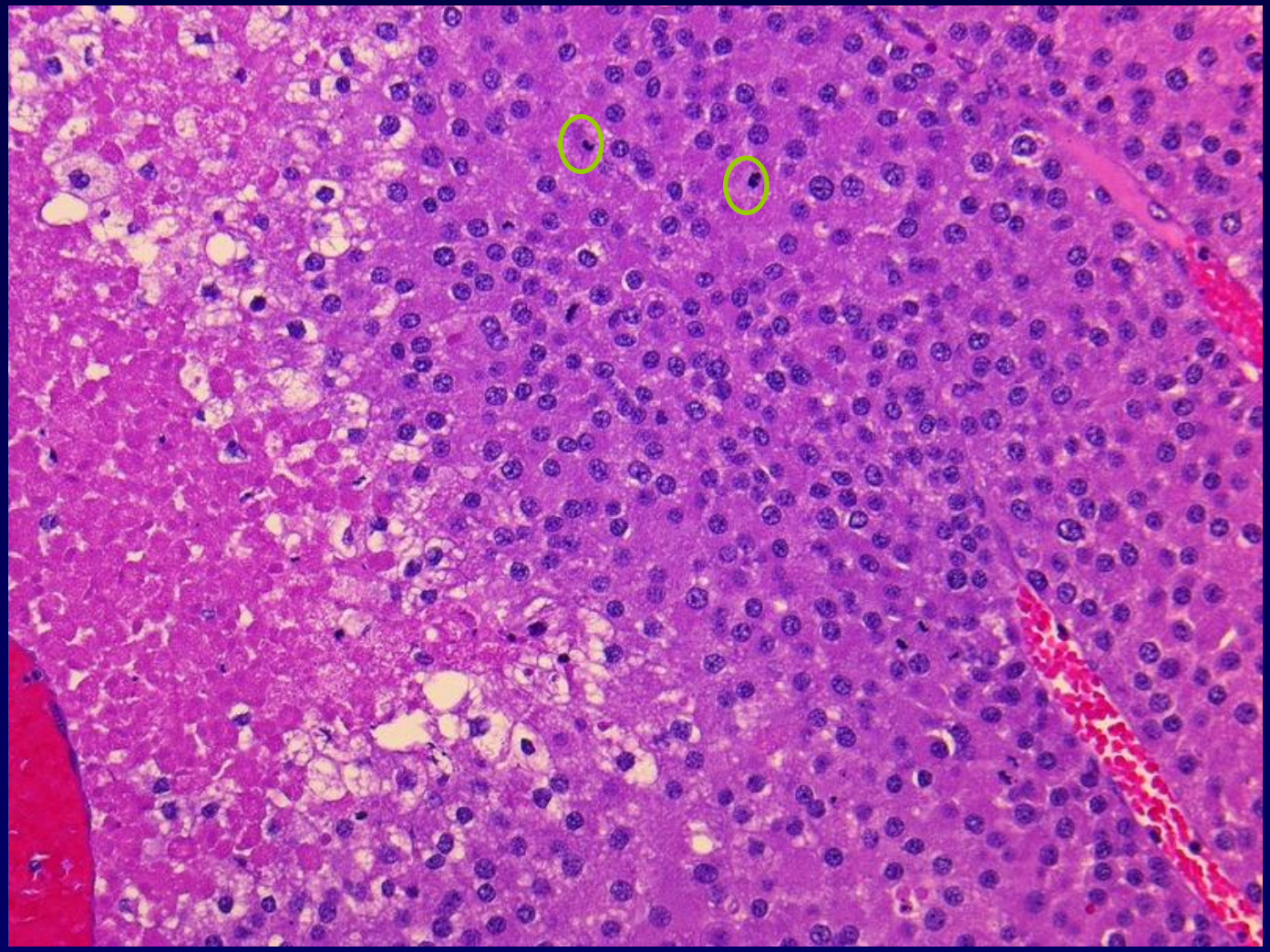
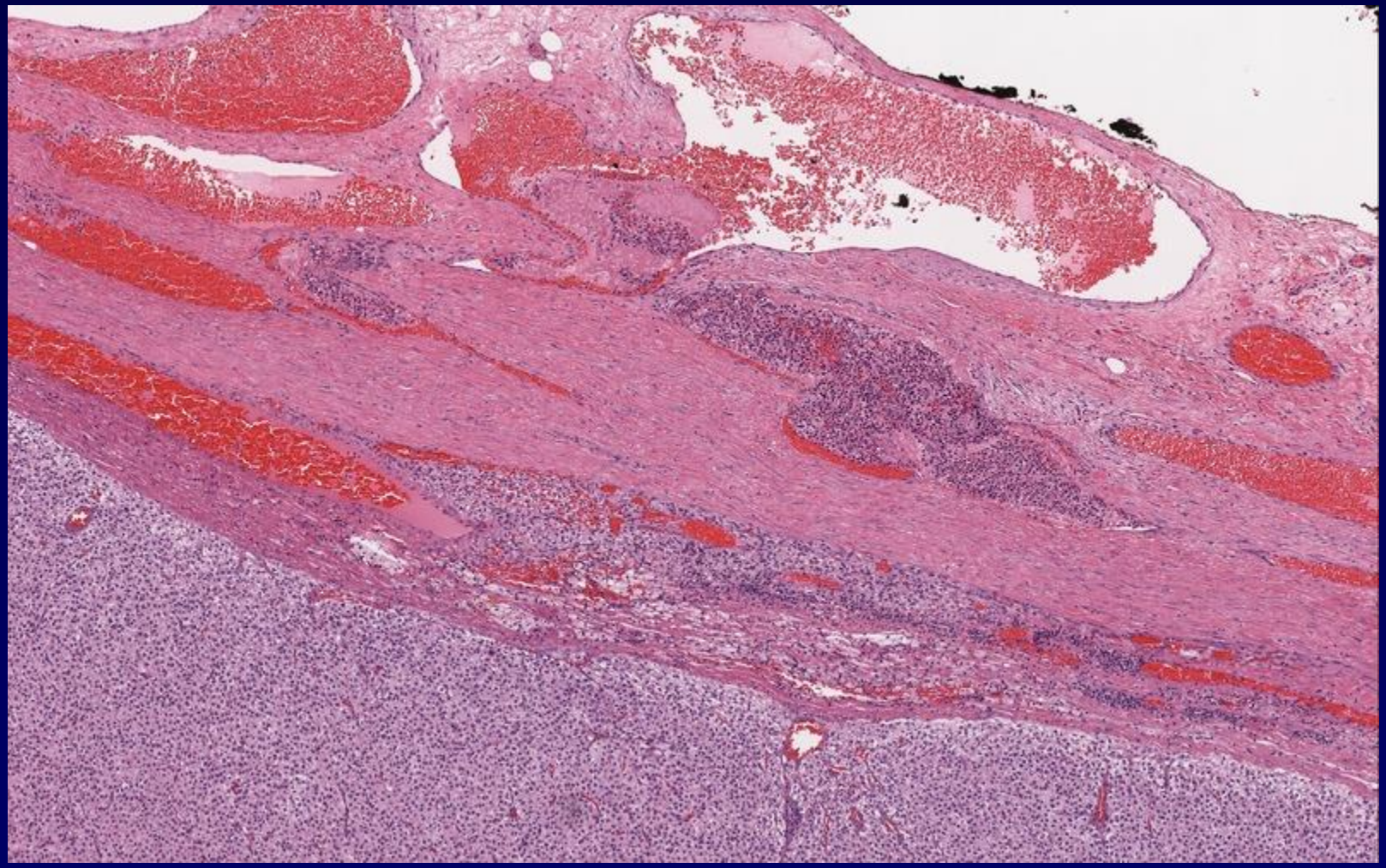
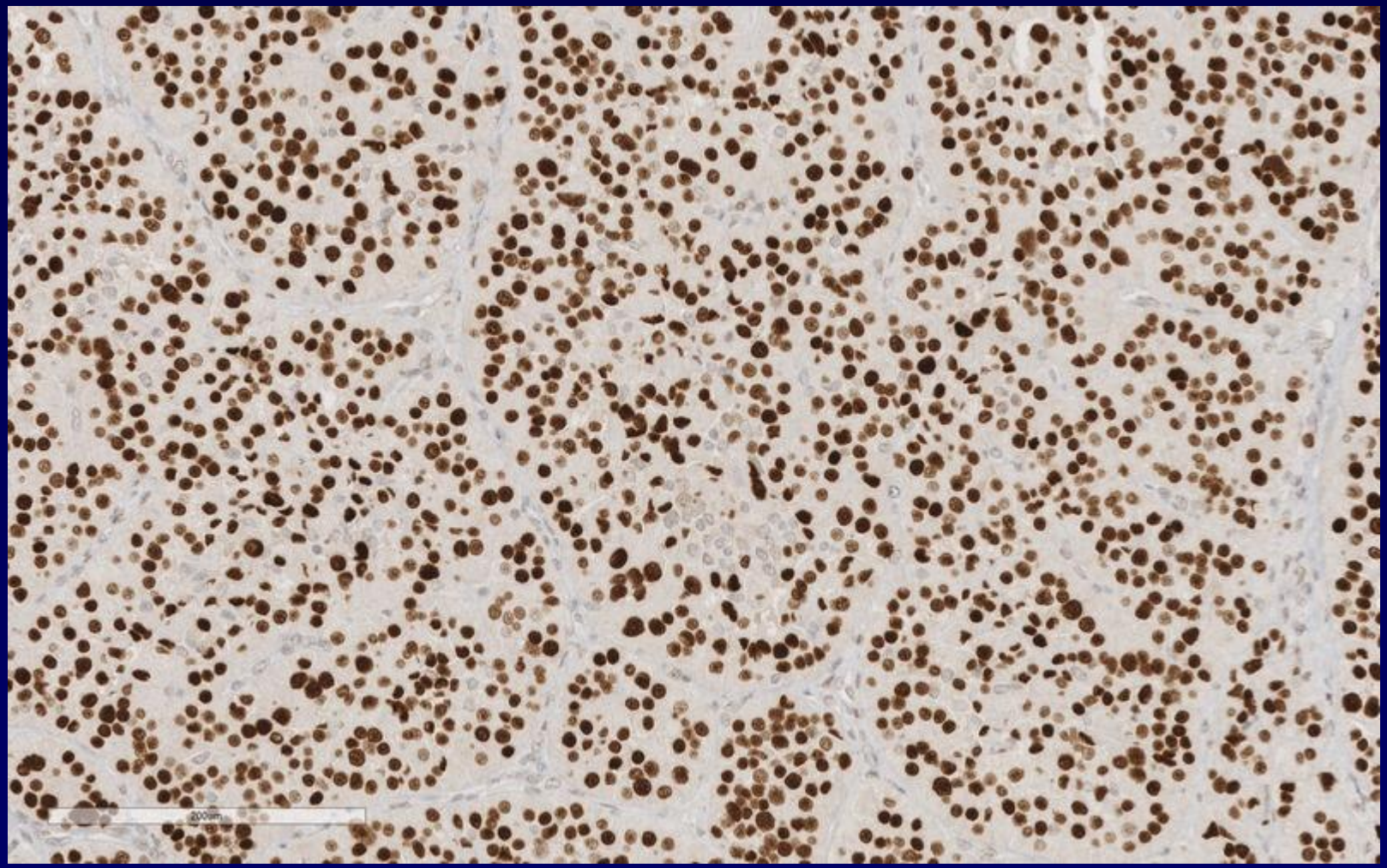






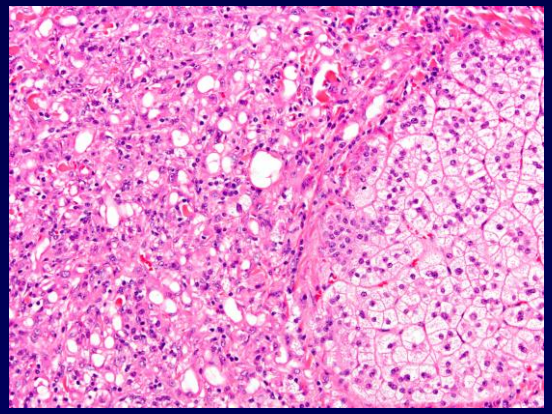
# p53

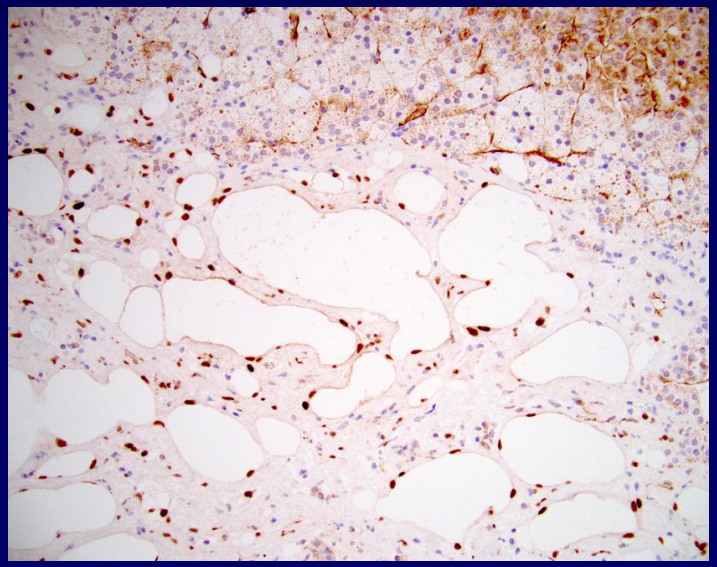


# Sex Cord Stromal Tumours

## TUMORE ADENOMATOIDE

- Raro (50 casi)
- mesoteliale
- No atipie, mitosi, necrosi
- Cellule cubiche disposte in tubuli, canali e spazi cistici
- Stroma fibroso con con aggregati linfatici
- Benigno dopo escissione



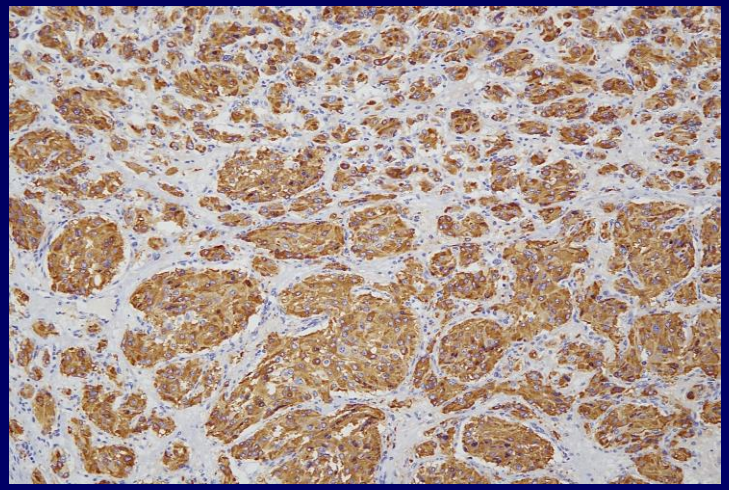


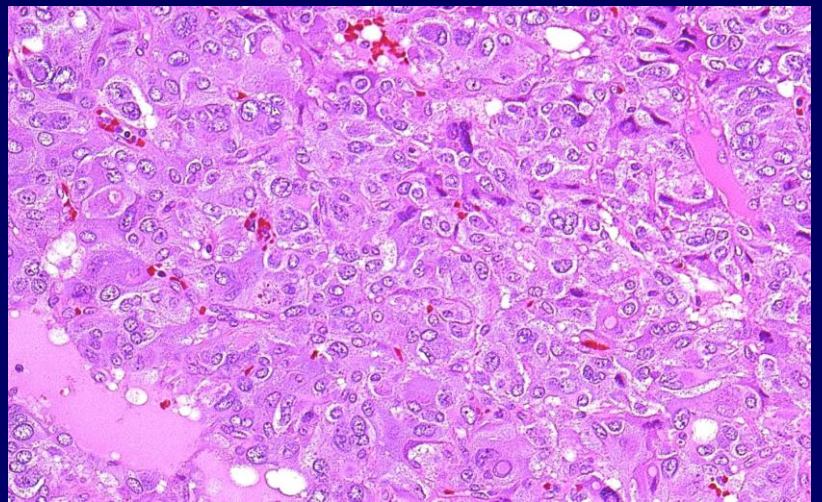
# MIDOLLARE

The previous edition of the WHO Classification of endocrine and neuroendocrine tumours addressed the fact that all phaeochromocytomas and paragangliomas should be considered malignant. This is continued in the new edition. Consequently the adjectives benign and malignant are no longer recommended and can be replaced by a **concept of risk stratification.** While several systems have been proposed to predict the risk of metastasis, no individual system is endorsed for routine use.

# FEOCROMOCITOMA

- Tumore secernente catecolamine
- Raramente ectopico – paraganglioma
- Markers neuroendocrini
- Hereditary disease /germline mutation





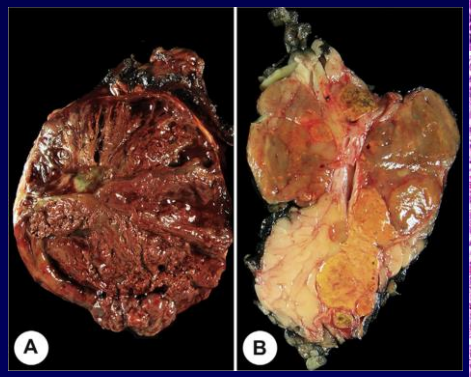
# FEOCROMOCITOMA

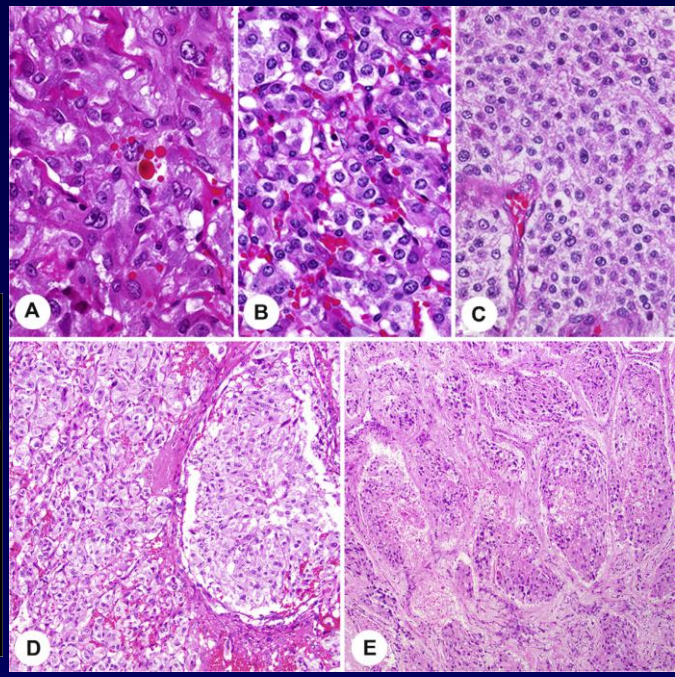
## MACROSCOPICA

- Circoscritto ma non capsulato 30-50mm
- Comprime la corticale che ne diviene la capsula
- Micronoduli accessori nelle sindromi ereditarie (MEN 2)

## ISTOLOGIA

- Architettura variegata
- Zellballen, trebecolare, diffuso
- Pseudoinclusi nucleari  e globuli PAS+
- Nucleoli, atipie nucleari,pleomorfismo
- Rare mitosi (ki67<10%)




- All patients with phaeochromocytomas are currently considered to have a lifelong risk of metastases and therefore conceptually they are all considered ‘malignant’.
- The risk of metastasis ranges from ~5 to 15%.
- There is no single histological finding or biomarker to reliably predict metastatic disease, and multiparameter scoring systems have been proposed.

# PASS (2002)

Pheochromocytoma of the Adrenal Gland Scaled Score (PASS) to Separate Benign From Malignant Neoplasms

A Clinicopathologic and Immunophenotypic Study of 100 Cases

Lester D. R. Thompson, M.D.

**TABLE 1.** *Pheochromocytoma of the Adrenal Gland Scoring Scale (PASS)*

| Feature | Score if present (no. of points assigned) |
|---|---|
| Large nests or diffuse growth (>10% of tumor volume) | 2 |
| Central (middle of large nests) or confluent tumor necrosis (not degenerative change) | 2 |
| High cellularity | 2 |
| Cellular monotony | 2 |
| Tumor cel spindling (even if focal) | 2 |
| Mitotic figures >3/10 HPF | 2 |
| Atypical mitotic figure(s) | 2 |
| Extension into adipose tissue | 2 |
| Vascular invasion | 1 |
| Capsular invasion | 1 |
| profound nuclear pleomorphism | 1 |
| Nuclear hyperchromasia | 1 |
| **Total** | **20** |

HPF = high-power field.

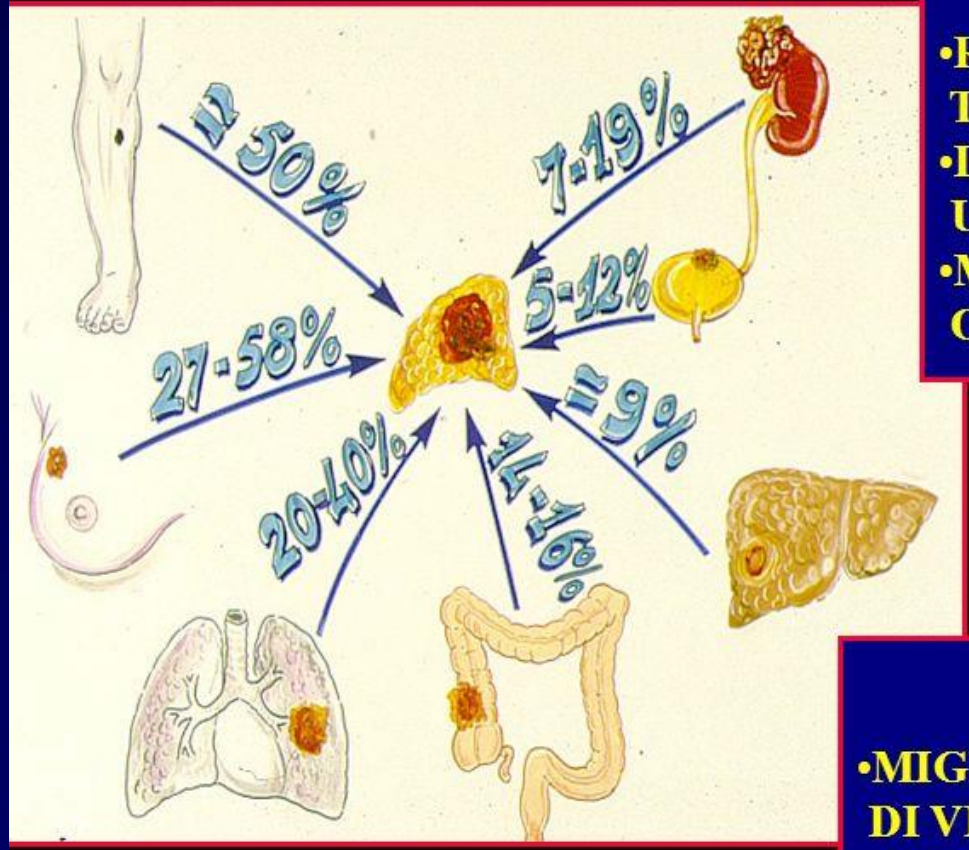
Tumore potenzialmente
- aggressivo PASS>=4
- benigno PASS<4

## ICCR Pheochromocytoma and Paraganglioma dataset

**Table 1** Core and non-core elements for pathology reporting of pheochromocytoma and paraganglioma.

| Core elements | Non-core elements |
|---|---|
| Clinical information | Tumor dimensions |
| Operative procedure | Additional dimensions (largest tumor) |
| Specimen(s) submitted | Margin status |
| Tumor focality | Distance of the tumor to the closest ma |
| Tumor site | Closest margin, specify if possible |
| Specimen integrity | Lymph node status |
| Tumor dimensions | Extranodal extension (ENE) |
| Medullary hyperplasia | Adverse features |
| Histological tumor type | Ancillary studies |
| Extent of invasion | |
| Lymphovascular invasion | |
| Margin status | |
| Proliferative fraction | |
| Lymph node status | |
| Histologically confirmed distant metastases | |
| Pathological staging | |

# METASTASI SURRENALICHE




## INDICAZIONI

- RESEZIONE TUMORE PRIMITIVO
- LOCALIZZAZIONE UNICA
- METASTASI SINTOMATICA O COMPLICATA

## FINALITA'

- MIGLIORAMENTO QUALITA' DI VITA
- AUMENTO SOPRAVVIVENZA (?)


DON'T FORGET TO
Follow Up!


TAKE CARE OF YOUR ADRENAL GLANDS
1 REDUCE STRESS
2 TAKE ADRENAL-BOOSTING SUPPLEMENTS
3 EAT RIGHT
4 TAKE VITAMIN C
5 GET PLENTY OF SLEEP