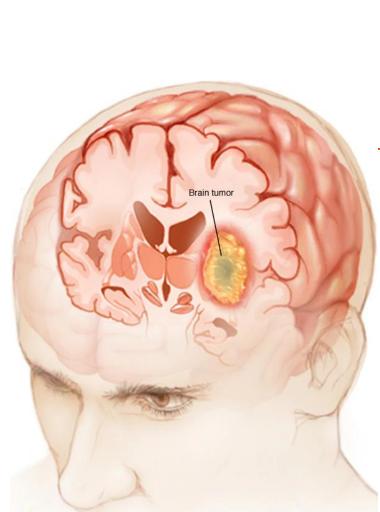


Department of Surgery Neurosurgery Teaching Unit



SEMINAR: BRAIN TUMOURS 34484 Pathology of the nervous system

Neurosurgery

Prof. Vicente Vanaclocha Prof. Pedro Roldan Prof. Guillermo García-March Prof. José María Gallego Prof. Ricardo Prat Prof. Francisco Verdú <u>vivava @uv.es</u> pedro.roldan @uv.es



Key concepts

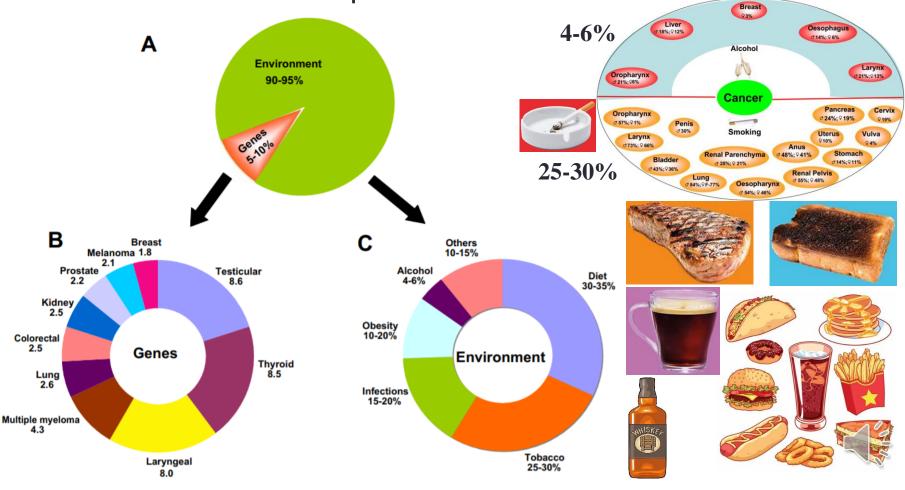
- Cancer
- Brain tumours
- Brain metastases
- Gliomas
- Meningiomas
- Schwannomas
- Pituitary tumours
- Craniopharyngioma
- Primary brain lymphoma
- Meningeal carcinomatosis





Causes of cancer

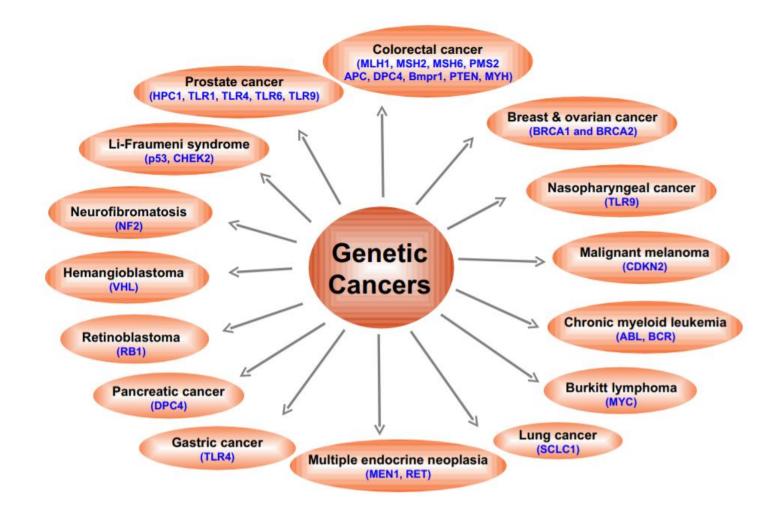
- Genetic <10%
- Environment >90% = preventable



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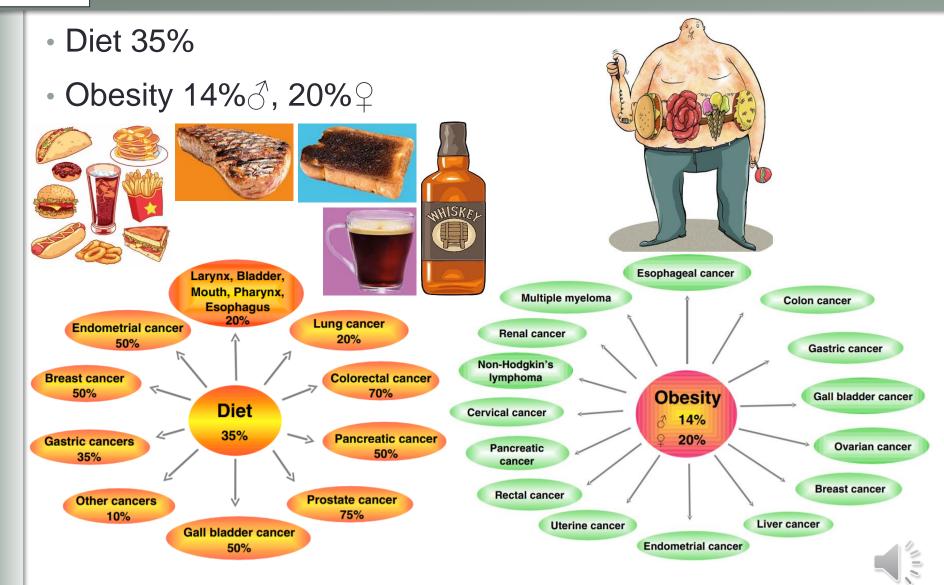
Cancer genetic abnormalities

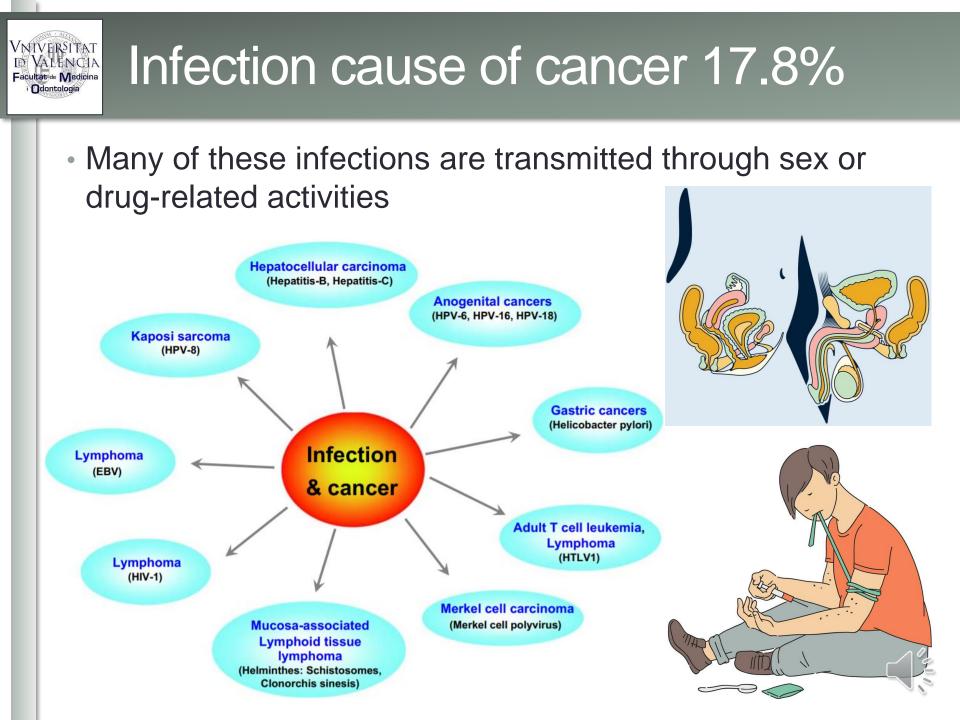
Enhanced by environmental chemical compounds





Preventable cancer causes

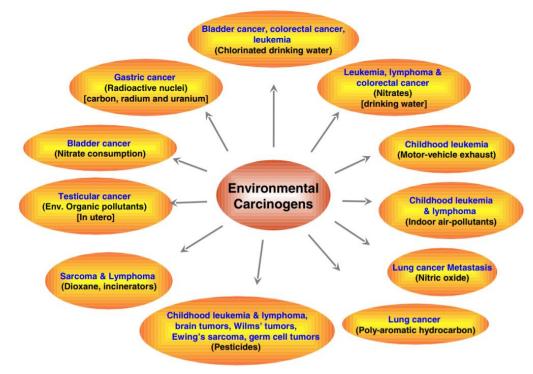






VNIVERSITAT D VALENCIA Facultative Medicina Environmental (95%)

- Many related to professional exposure
 - Often relaxed prevention measures (pesticide & herbicide exposure, saw dust, building workers, ...)
- Usually controlled legislation











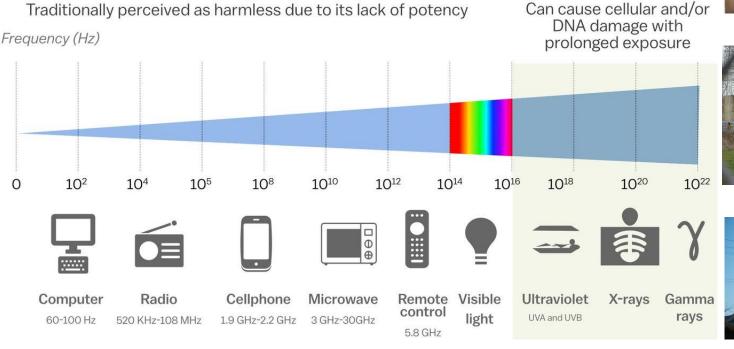


Electromagnetic waves cause cancer?

IONIZING RADIATION

- Mobile telephones = no proven relationship
- Electric power stations & high voltage electric lines possible relationship with leukaemia and pineal tumours

NON-IONIZING RADIATION



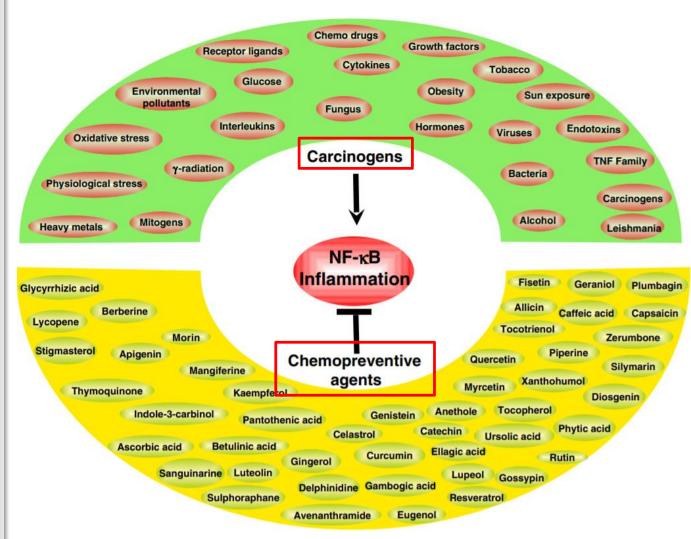






Can we prevent cancer?

• Our habits change the equilibrium for better or worse

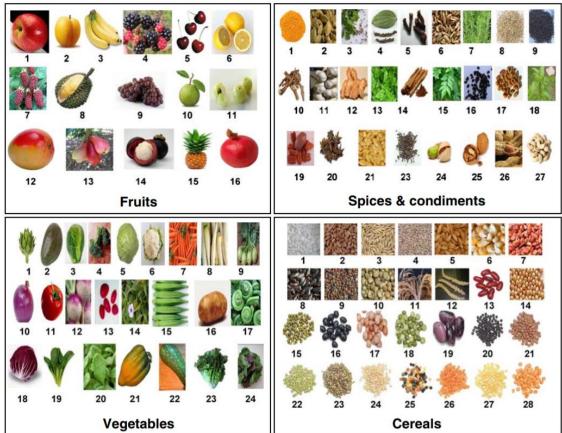






How to prevent cancer?

- Most fruits, spices, vegetables & cereals prevent cancer = adequate diet!
 - ↓roasted meat
 - ↓fried potatoes
 - Cooking by boiling healthier than roasting, frying or microwaving

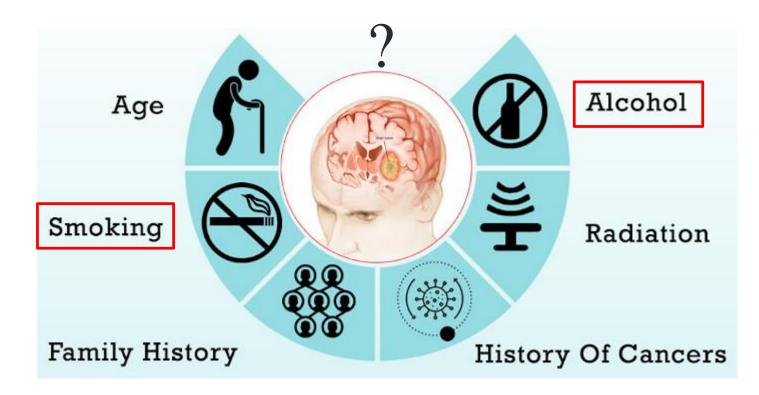


Fruits, vegetables, spices, condiments and cereals with potential to prevent cancer. Fruits include 1 apple, 2 apricot, 3 banana, 4 blackberry, 5 cherry, 6 citrus fruits, 7 dessert date, 8 durian, 9 grapes, 10 guava, 11 Indian gooseberry, 12 mango, 13 malay apple, 14 mangosteen, 15 pineapple, 16 pomegranate. Vegetables include 1 artichoke, 2 avocado, 3 brussels sprout, 4 broccoli, 5 cabbage, 6 cauliflower, 7 carrot, 8 daikon 9 kohlrabi, 10 onion, 11 tomato, 12 turnip, 13 ulluco, 14 water cress, 15 okra, 16 potato, 17 fiddle head, 18 radicchio, 19 komatsuna, 20 salt bush, 21 winter squash, 22 zucchini, 23 lettuce, 24 spinach. Spices and condiments include 1 turmeric, 2 cardamom, 3 coriander, 4 black pepper, 5 clove, 6 fennel, 7 rosemary, 8 sesame seed, 9 mustard, 10 liquorice, 11 garlic, 12 ginger, 13 parsley, 14 cinnamon, 15 curry leaves, 16 kalonji, 17 fenugreek, 18 camphor, 19 pecan, 20 star anise, 21 flax seed, 22 black mustard, 23 pistachio, 14 walnut, 25 peanut, 26 cashew nut. Cereals include 1 rice, 2 wheat, 3 oats, 4 rye, 5 barley, 6 maize, 7 jowar, 8 pearl millet, 9 proso millet, 10 foxtail millet, 11 line millet, 12 barnyard millet, 13 kidney bean, 14 soybean, 15 mung bean, 16 black bean, 17 pigeon pea, 18 green pea, 19 scarlet runner bean, 20 black beluga, 21 brown Spanish pardine, 22 green, 23 green (eston), 24 ivory white, 25 multi-coloured blend, 26 petite crimson, 27 petite golden, 28 red chief.



Cause of brain tumours

- Metastases = primary tumour prevention
- Primary brain tumours = some known causes
 - Most carcinogenic agents also act in the brain
 - Which are stopped by the blood brain barrier?

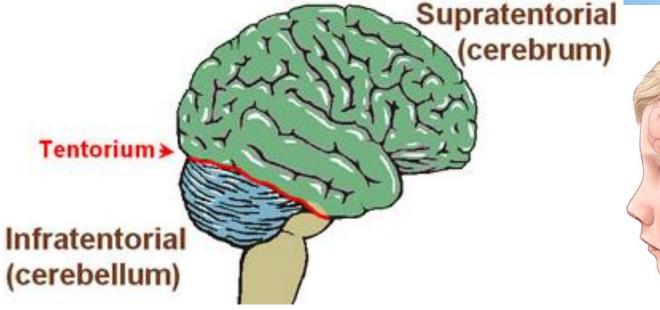


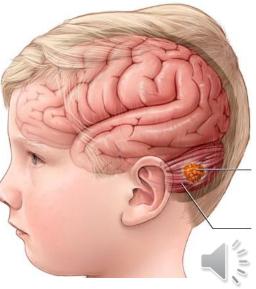


BRAIN TUMOURS: incidence & location

- Incidence: 10-17 / 100,000 inhabitants
- Location
 - Children: posterior fossa
 - 20% childhood malignant tumours
 - Adults: cerebral hemispheres 80%



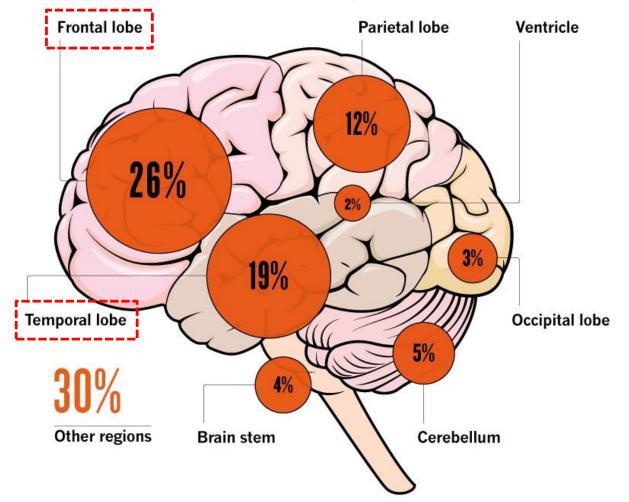






BRAIN TUMOUR: distribution

• Frontal & temporal lobes mostly affected







CLINICAL PRESENTATION

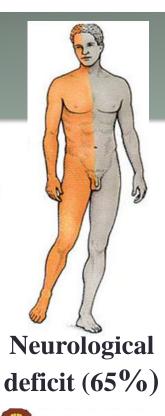


Headache (50%)



Nausea / vomiting (24%)

Epileptic seizures (15%)













Emotional disturbance Enlarged sella turcica Moon facies Osteoporosis Cardiac hypertrophy (hypertension Buffalo humo Obesity Adrenal tumor or hyperplasia Thin, wrinkled ski Abdominal stria menorrhea Muscle weakness Purpura Skin ulcers (poor wound healing) Hormon²

disorders (8%)

Depression, personality changes,(25%)

Cerebral haemorrhage (1%)

Vision loss (9%)

Hearing loss (2%)



BRAIN TUMORS: types

- Gliomas: • Astrocytoma
 - Oligodendroglioma
 - Ependymoma
- Neuronal tumours
- Poorly differentiated tumours:
 - Medulloblastoma
- Other parenchymal tumours
 - Primary brain lymphoma
 - Germ cell tumour
 - Pineal gland tumours

Meningioma

- Hemangioblastoma
- Pituitary tumours
- Nerve sheath tumours of the peripheral nervous system:
 - Schwannoma
 - Neurofibroma
- Metastatic tumours

REMEMBER?



BRAIN TUMOURS: diagnosis

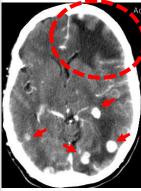
- Clinical features
- Physical examination
 - Neurological examination
 - Weight loss
 - Skin lesions
- Neuroimaging tests
 - CT scan
 - Cerebral
 - Thorax-abdomen-pelvic
 - Brain MRI
 - Spectroscopy
- PET
 - Cerebral
 - Total body



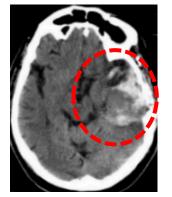


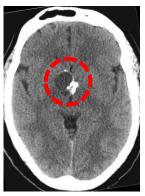
Neuroimaging: CT scan

- Diagnoses the tumour not its nature
 - Possible confusion with benign lesions

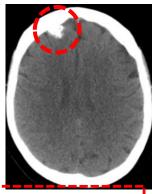




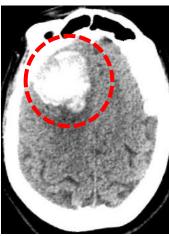




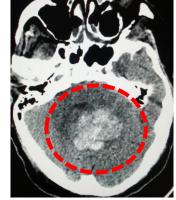


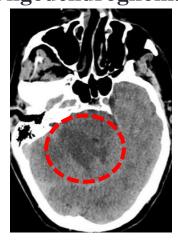


Glioblastoma Craniopharyngioma Oligodendroglioma Calcification











Metastasis

Meningioma

Cystic astrocytoma

Medulloblastoma Astrocytoma



Searching for the primary tumour

- Plain chest x-ray not very useful
- CT thorax-abdomen-pelvis finds most primary tumours
 - Also helps to rule out other metastases
 - Melanomas request clinical inspection of WHOLE body



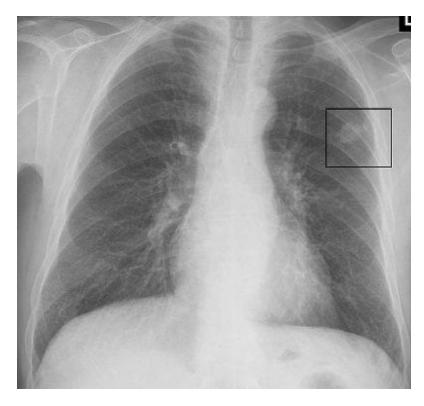


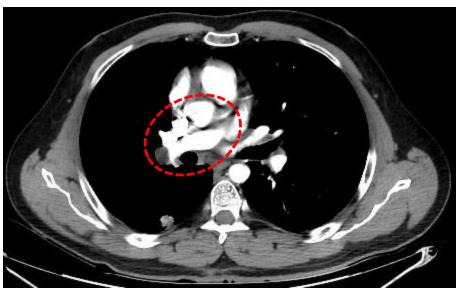




Chest plain x-ray

- Requested on a regular basis on pre-operative tests
- Poor diagnostic performance
 - Findings MUST be confirmed with CT scan





Lung cancer





CT thorax-abdomen-pelvis

- Detects most primary tumours & their metastases
- In 15% primary not found = PET scan needed



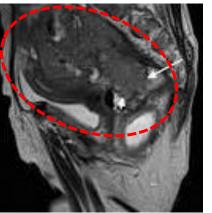


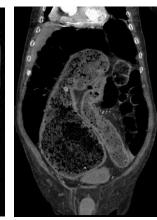


Lung cancer

Breast cancer

Retroperitoneal tumour

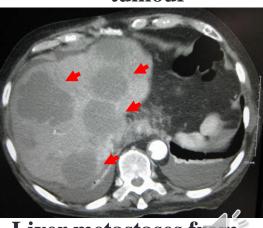




Rectum neoplasm + intestinal obstruction



Prostate neoplasm

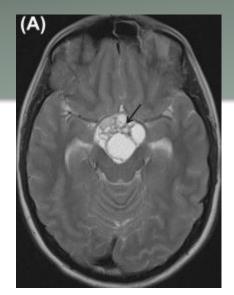


Liver metastases from colon neoplasm



Neuroimaging: MRI

- Better anatomical detail than CT
- Several different series
 - Each depicts different tumour characteristics
- Shows lesion + edema + infiltration
- Calcifications better seen on CT
- Spectroscopy = biochemical markers
- Tractography
 - Shows if tumour displaces or destroys tracts
 - Helps decide if removal is possible and the path to take
- Eloquent brain area location
 - Essential for surgical planning



MRI

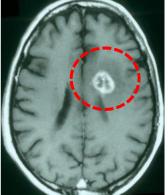


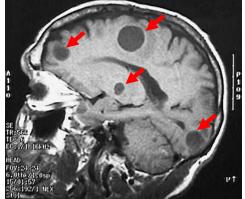
Craniopharyngio



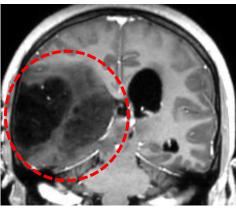
MRI: better anatomical detail

Helps to identify the tumour type

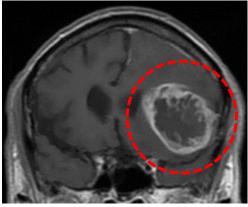




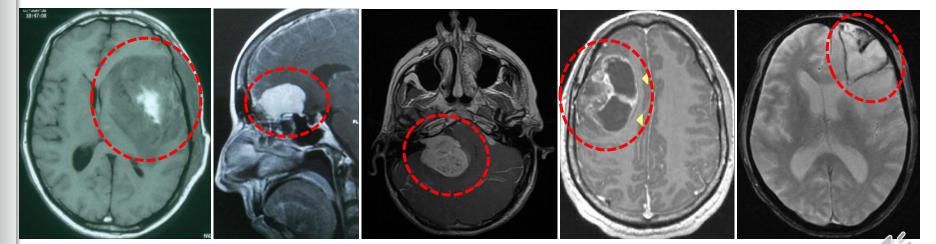
Single metastasis Multiple metastases







Glioblastoma



Low grade glioma & Meningioma malignant evolution

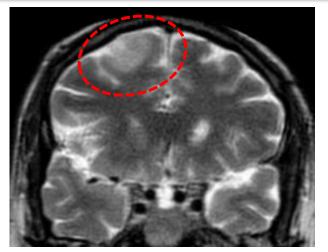
Vestibular schwannoma Oligodendrolioma

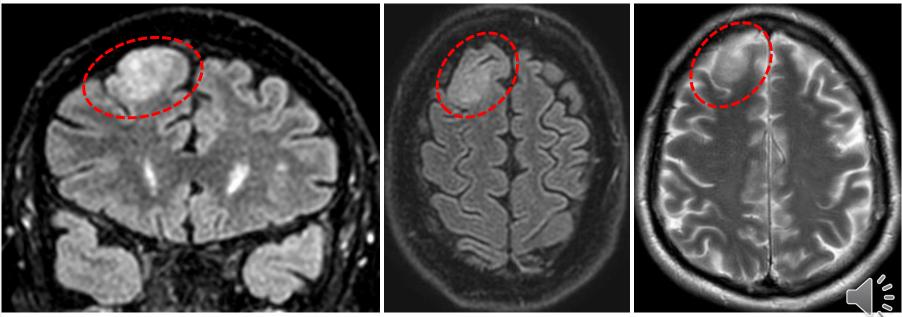
Brain abscess



MRI: different series = different tumour characteristics

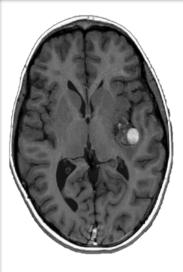
- Helps differentiate between tumour types
- Shows infiltrative patterns
- Allows surgery planning



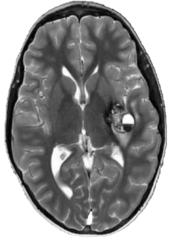




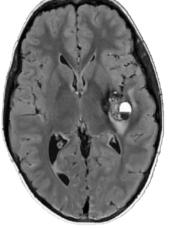
MRI: different series show different tumour characteristics



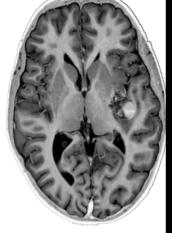
T1w



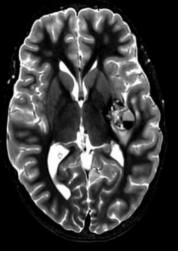
T2w



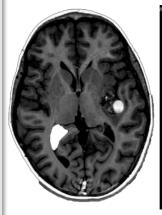
T2 FLAIR*

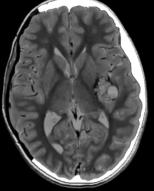


PSIR

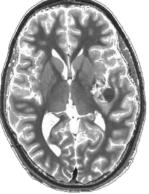


STIR





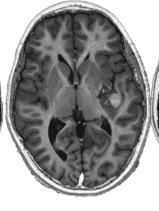
PD



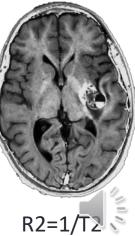
T1



T2



R1=1/T1



T1 FLAIR



Brain lipoma

Typical MRI features



Sagittal T1 brain MRI

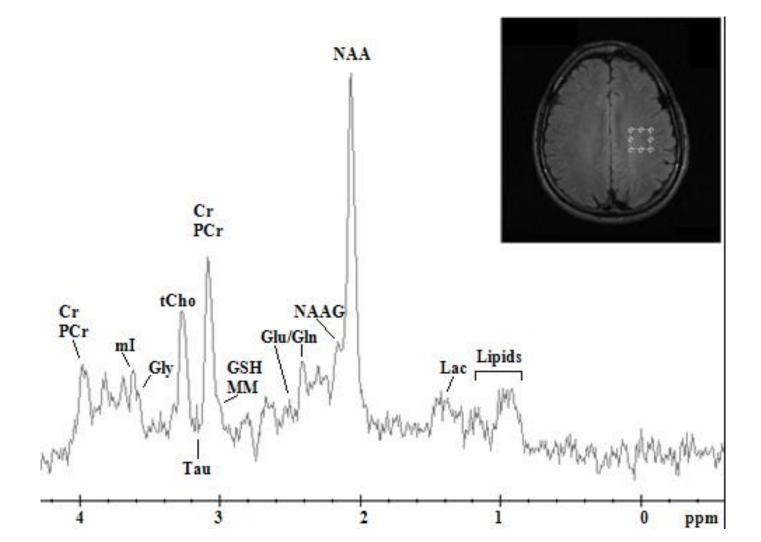
Sagittal fat saturation brain MRI

110



MRI spectroscopy: normal brain

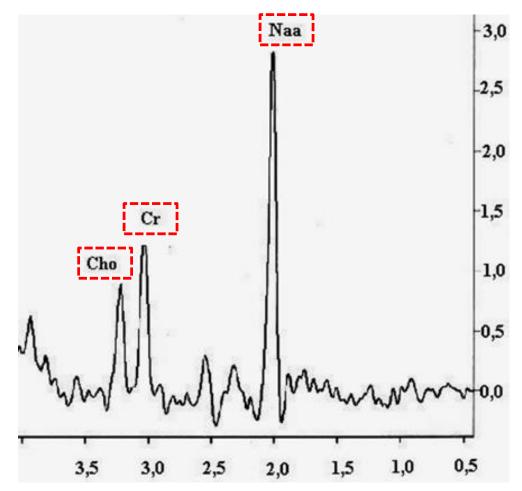
Analyses the tissular biochemical compounds





MRI spectroscopy: normal brain

- Most important to remember
 - NAA (N-acetyl-aspartate)
 - Cr (creatinine)
 - Cho (choline)

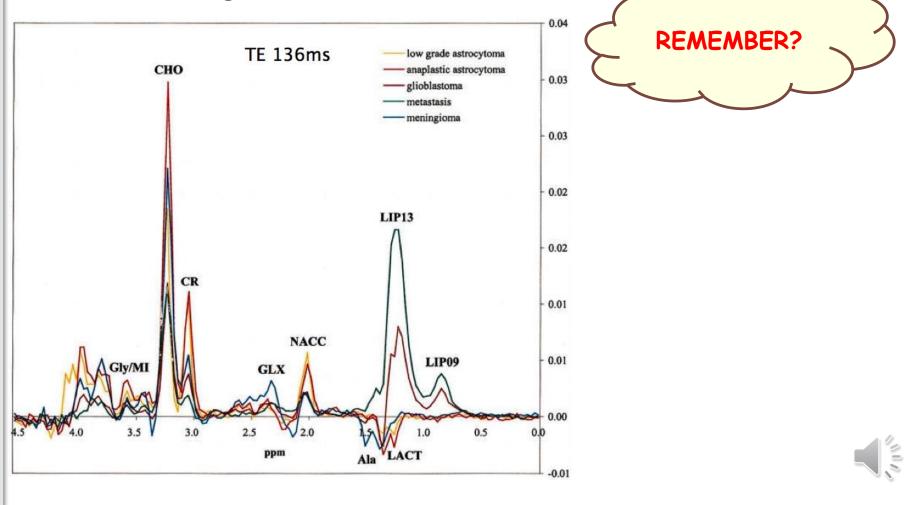






MRI spectroscopy: brain tumours

 Different patterns between different tumours = NONinvasive diagnosis





MRI spectroscopy: brain tumours

Brain biopsy may still be necessary

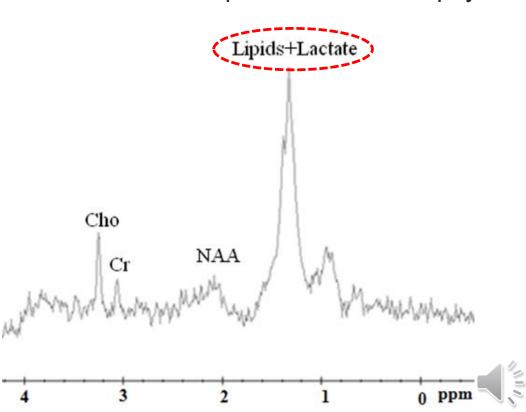
normal brain mel anom a metastasis lung metastasis lung metastasis grade 2 glioma grade 2 glioma grade 3 glioma grade 3 glioma center of grade 4 gliom grade 4 gliom a grade 4 glioma grade 4 glioma



MRI spectroscopy: brain metastases

- Lipids + lactate peak
- Different between different metastases
 - Not enough to decipher primary tumour
 - If primary NOT found in CT thorax-abdomen-pelvis \rightarrow brain biopsy

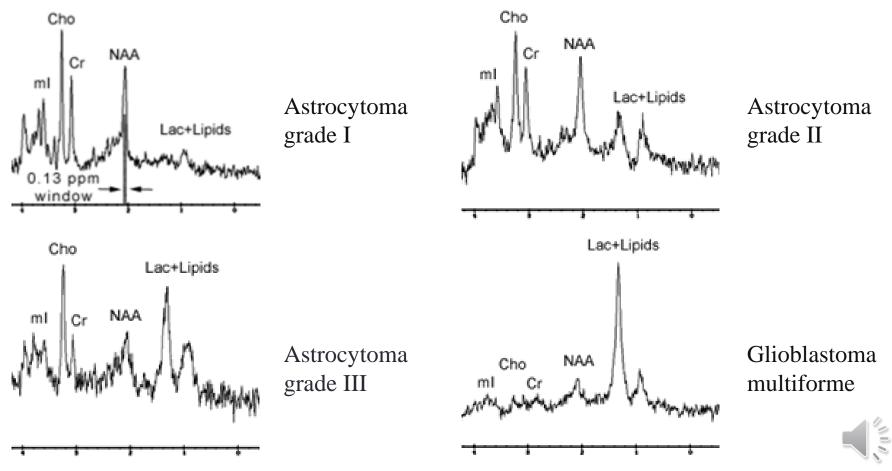


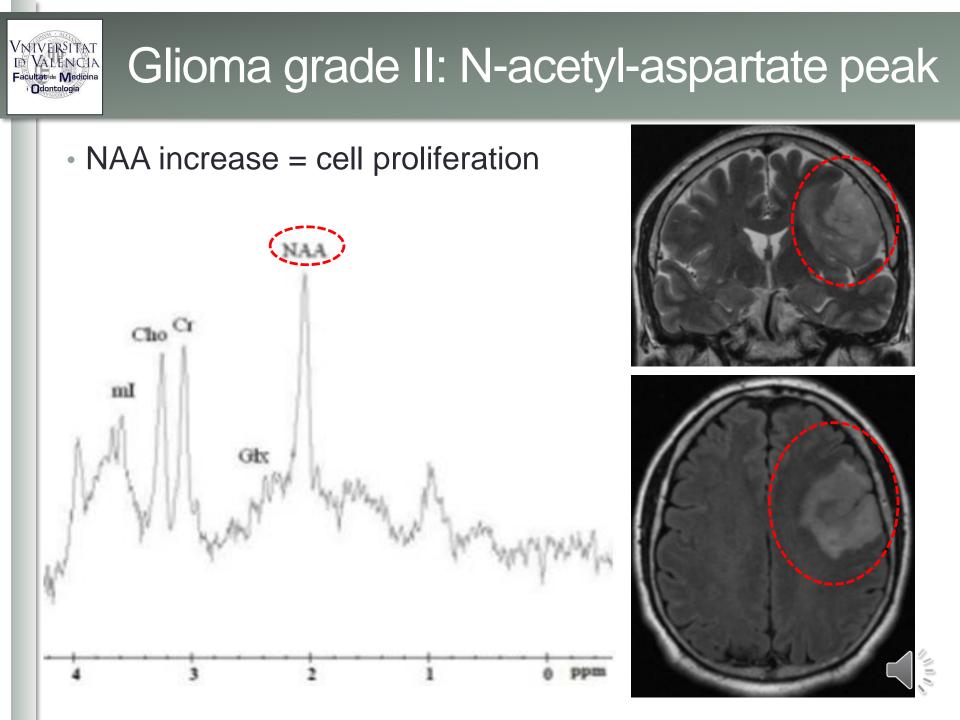


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MRI spectroscopy: gliomas

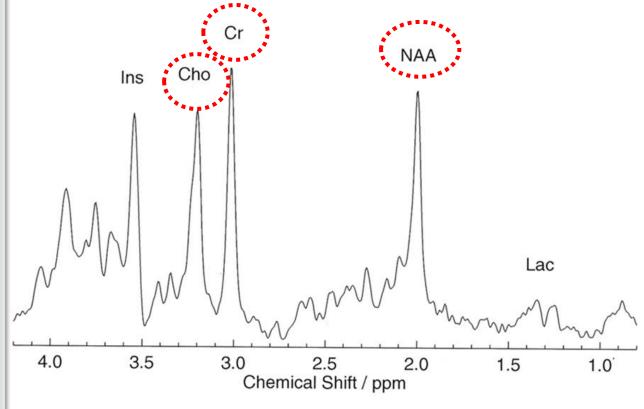
- NAA = cell proliferation
- Lactate + lipids = anaerobic metabolism = malignant

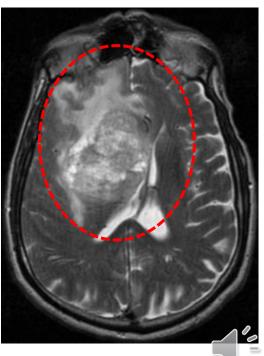




Glioblastoma: choline + creatinine + Nacetyl-aspartate peak

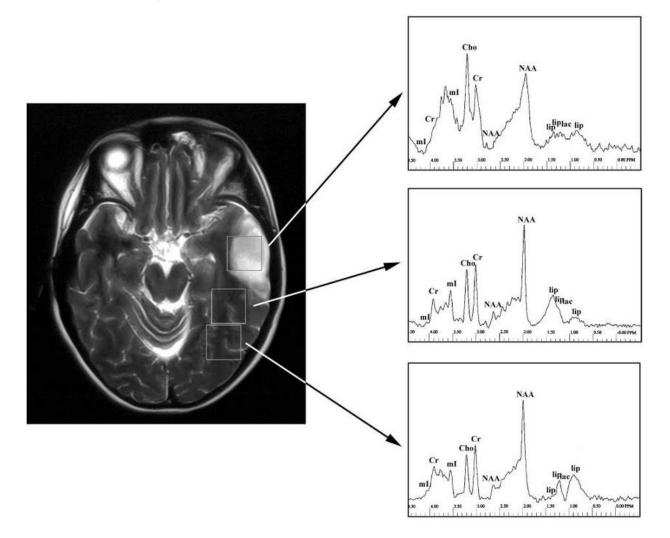
- Cr = index of mitochondrial energy production = malignity
- Cho = involved in pathways of phospholipid synthesis and degradation = cell membrane







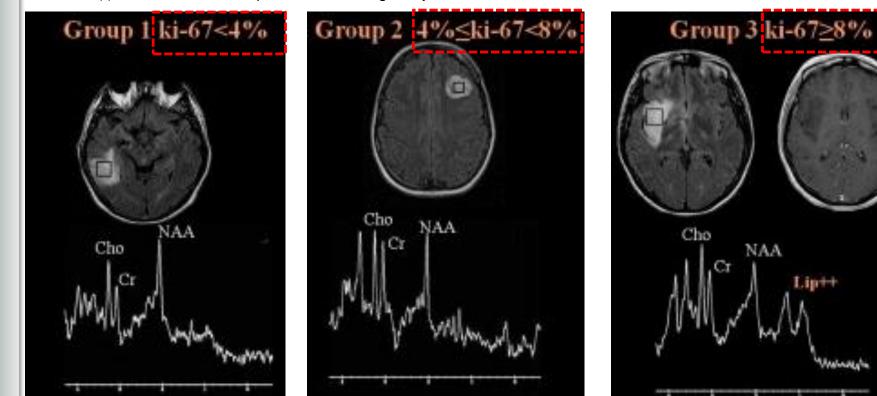
Helps identify infiltration pattern



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MRI spectroscopy gliomas: malignity

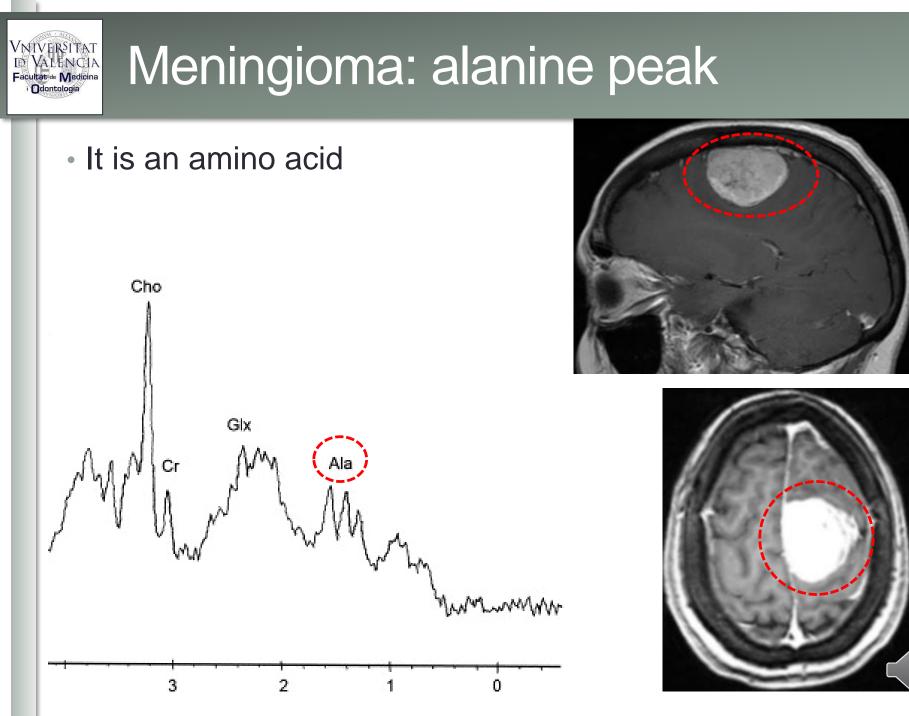
- Does not substitute histological examination!
- Ki-67 protein in cells ↑ increases as they divide
 - $\uparrow\uparrow$ cells with Ki-67 = rapid division= malignancy



Absence lipids + lactate

Presence lipids + absence lactate

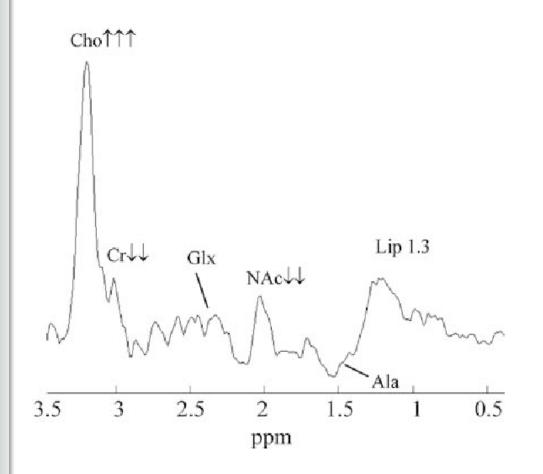
Presence lipids +

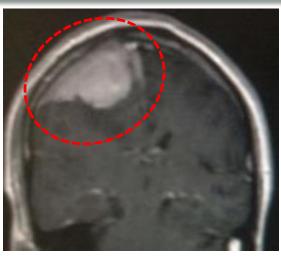




Atypical meningioma

- Other signs of malignancy
 - ↑↑↑ Choline

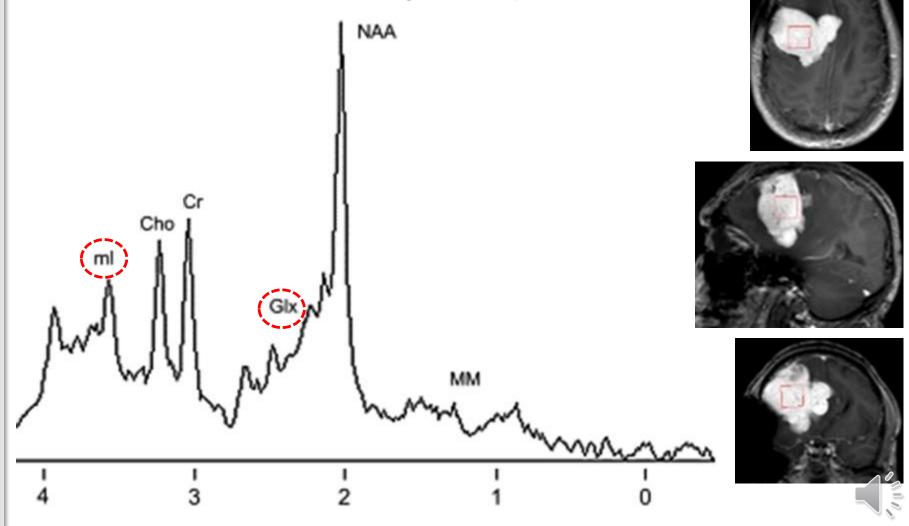






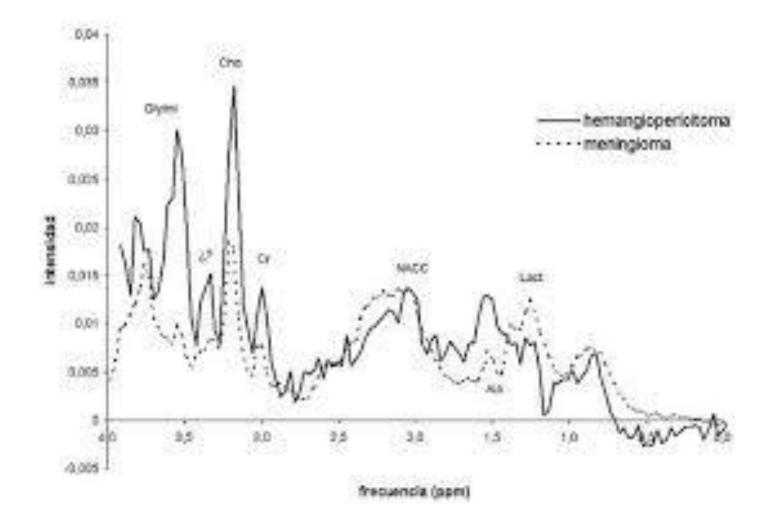
Fibrous solitary tumour: peak myoinositol (ml) & glycine (Glx)

Known before as hemangiopericytoma



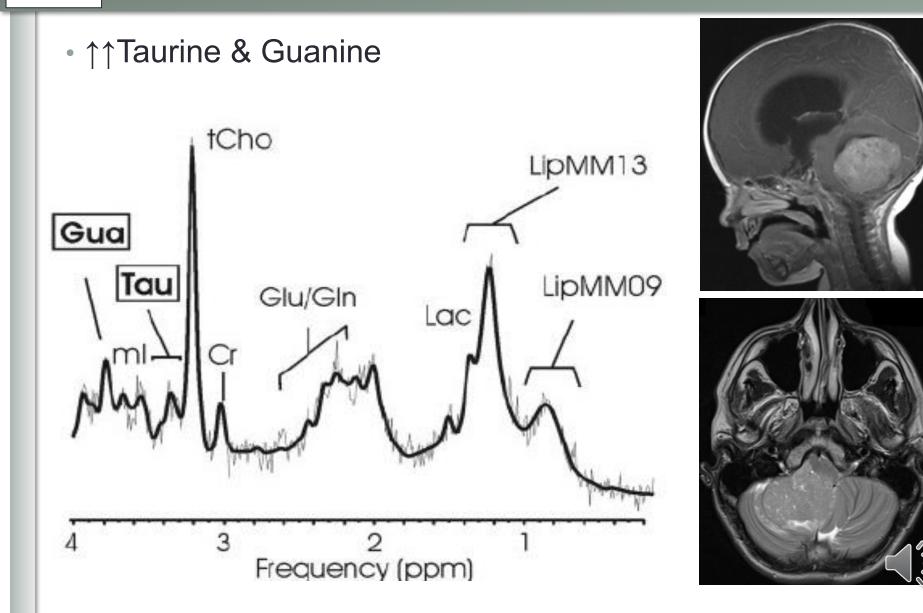
Differential diagnosis meningioma / fibrous solitary tumour

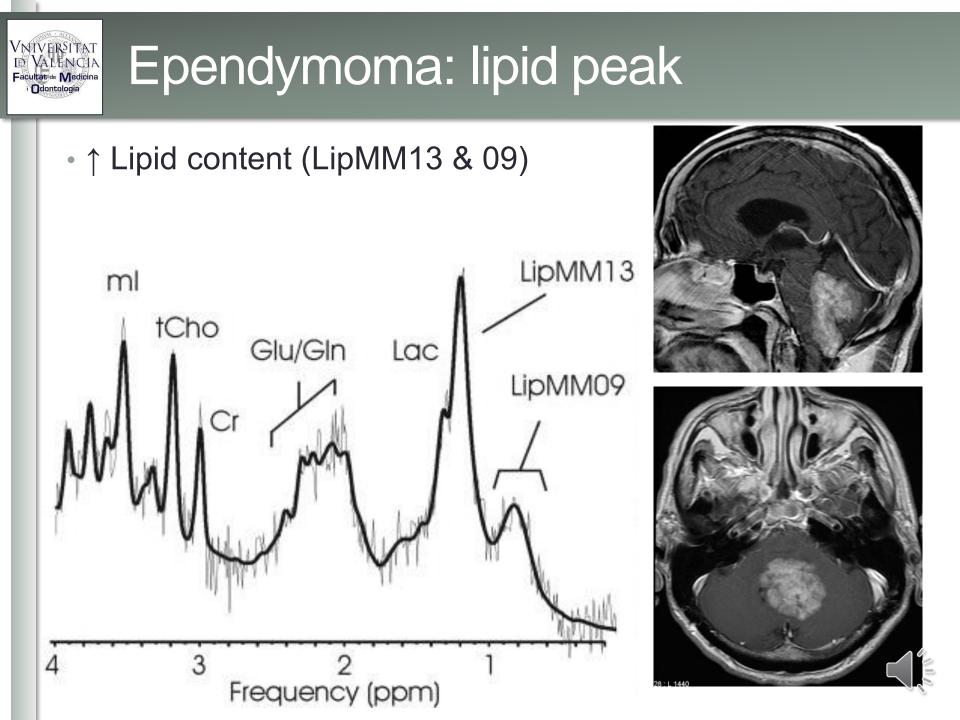
Not 100% accurate but useful





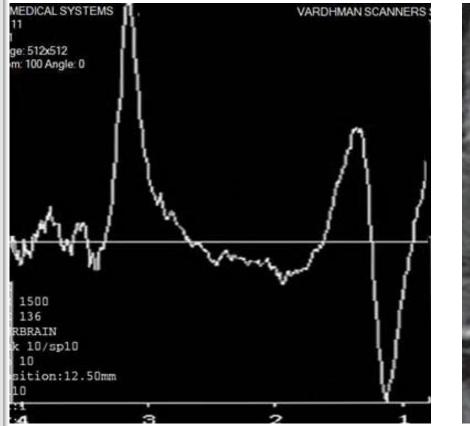
Medulloblastoma







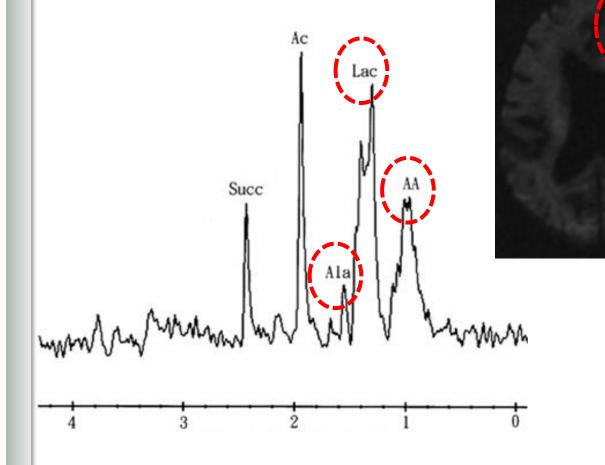
Chordoma

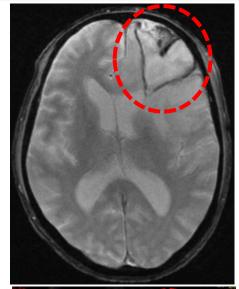




Brain abscess: lactate & amino acid peak

Reflect anaerobic glycolysis
 + unusual metabolites



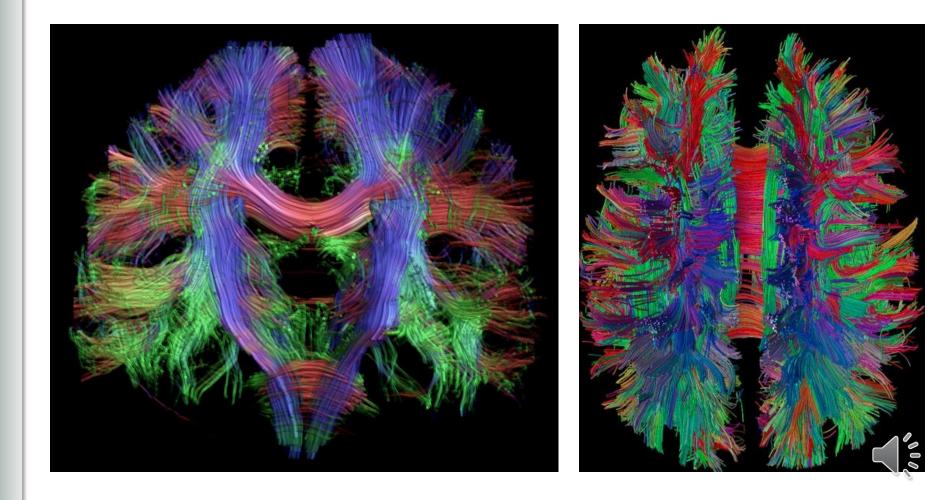






MRI tractography (1)

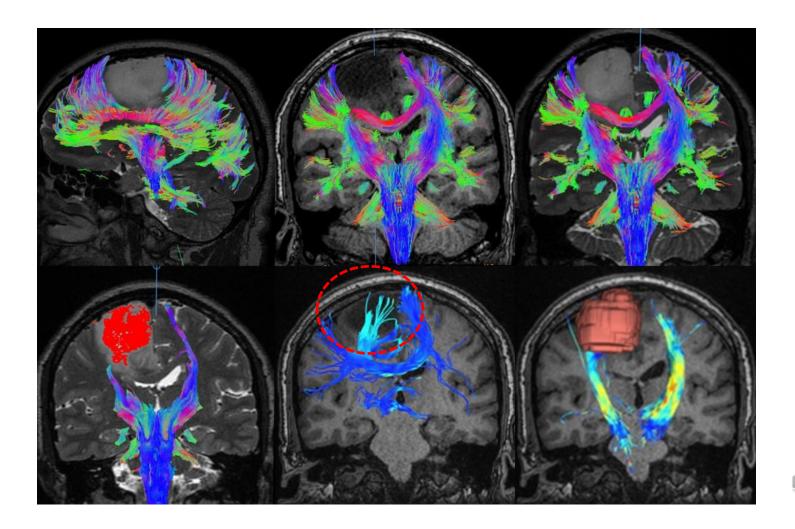
Allows pathway identification





MRI tractography (2)

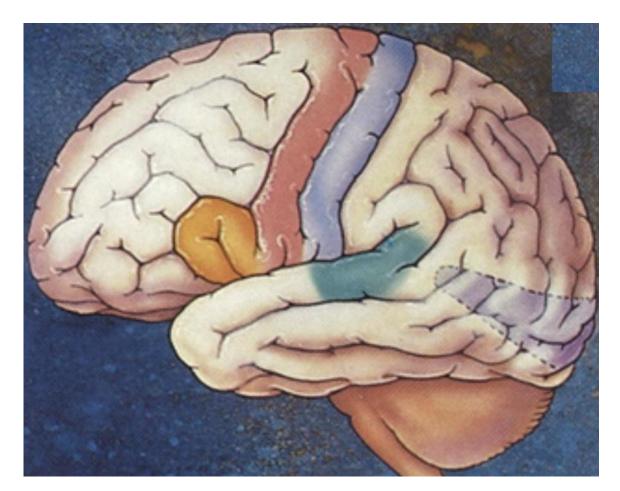
Allows identification pathways / tumour relationships





Functional MRI: eloquent brain areas

 There are no mute brain areas, there are areas for which WE are still deaf!



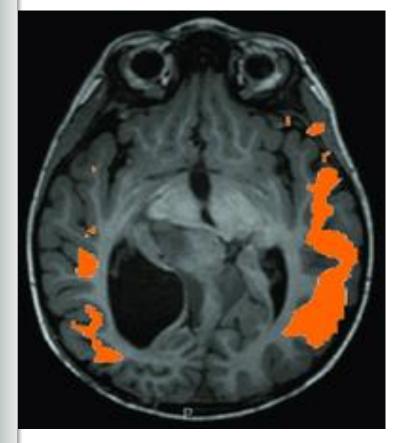
Brain eloquent areas

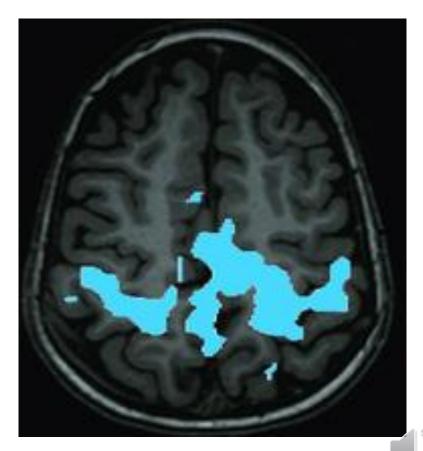




Functional MRI: identification of brain eloquent areas

 No precise anatomical detail = intraoperative neurostimulation essential





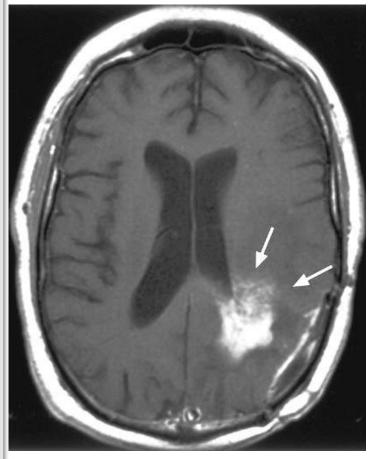
Language

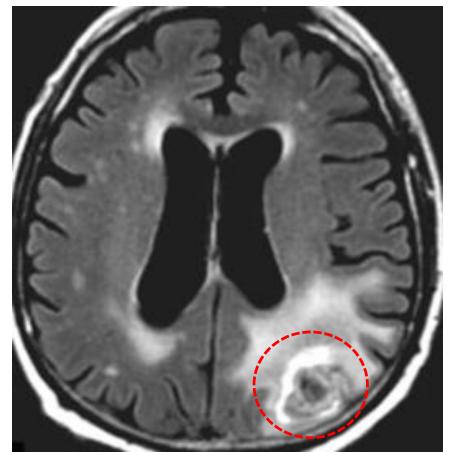




Positron emission tomography (PET) (1)

Distinguishes tumour progression versus radionecrosis





MRI images of brain tumour /radionecrosis





Brain PET (2)

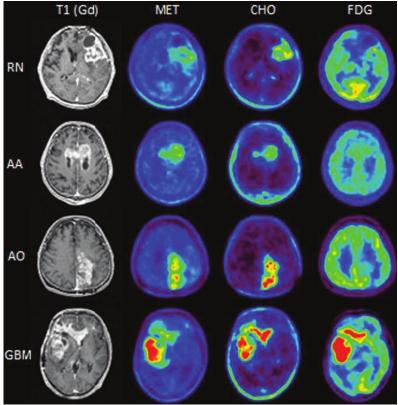
- Markers
 - Methionine (MET) = protein synthesis
 - Choline (Cho) = cell membrane synthesis
 - Fluorodeoxyglucose (FDG) = glucose consumption

Radionecrosis

Astrocytoma

Anaplastic oligodendroglioma

Glioblastoma

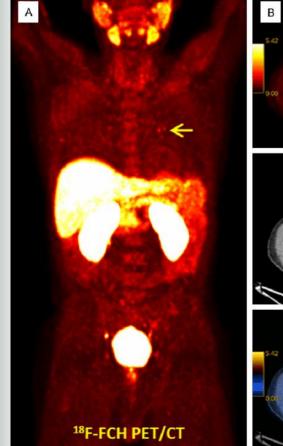


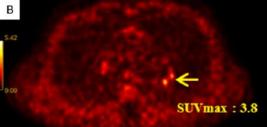




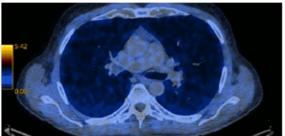
PET body: primary tumours & other metastases

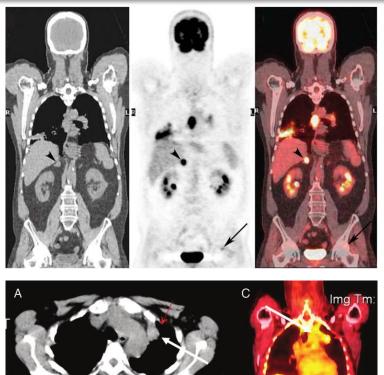
Little anatomical definition

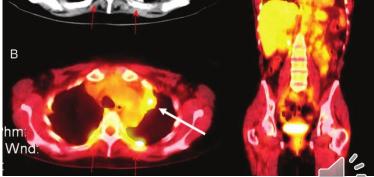














Primary tumour



Karnofsky scale & average survival

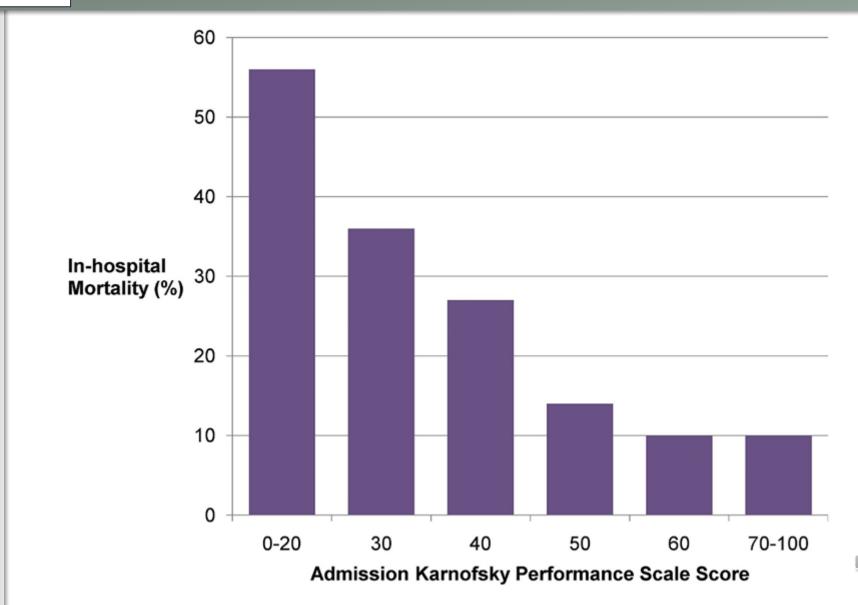
%	Ambulation	Activity Level Evidence of	Self-Care	Intake	Level of Consciousness	Estimated Median Survival In Days		
		Disease				(0)	(b)	(c)
100	Full	Normal No Disease	Full	Normal	Full			
90	Full	Normal Some Disease	Full	Normal	Full	N/A	N/A	
80	Full	Normal with Effort Some Disease	Full	Normal or Reduced	Full			
70	Reduced	Can't do normal job or work Some Disease	Full	As above	Full	145		108
60	Reduced	Can't do hobbles or housework Significant Disease	Occasional Assistance Needed	As above	Full or Confusion	29 4		
50	Mainly sit/lie	Can't do any work Extensive Disease	Considerable Assistance Needed	As above	Full or Confusion	30 11		41
40	Mainly in Bed	As above	Mainly Assistance	As above	above Full or Drowsy or Confusion 18		8	
30	Bed Bound	As above	Total Care	Reduced	As above	8	5	
20	Bed Bound	As above	As above	Minimal	As above	4	2	
10	Bed Bound	As above	As above	Mouth Care Only	Drowsy or Coma	1	1	6
0	Death		-		-			

(a) Survival postadmission to an inpatient palliative unit
all diagnoses (Virik 2002). (b) Days until inpatient death following admission to an acute hospice unit diagnoses not specified (Anderson 1996). (c) Survival post admission to an inpatient palliative unit
cancer patients only (Morita 1999).





Karnofsky scale & in-hospital mortality





General treatment



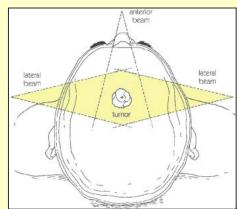
Surgical

- Stereotactic brain biopsy
- Surgical resection

Skull

Adjuvant

- Radiotherapy
- Chemotherapy

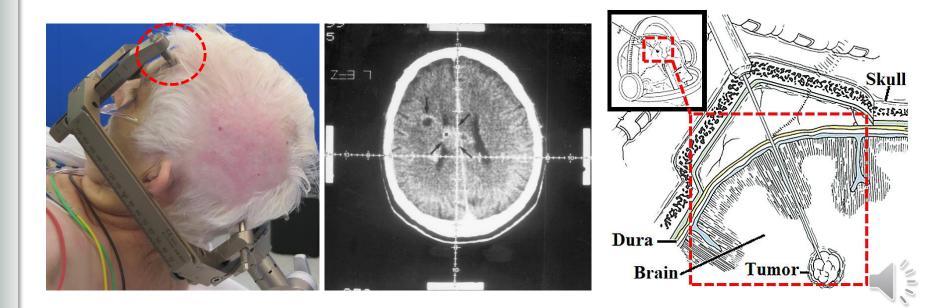






Tumour removal not advisable = stereotaxic brain biopsy for histological confirmation

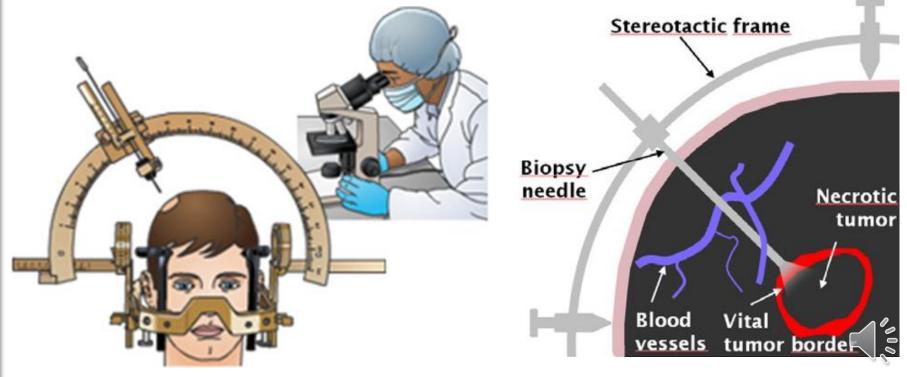
- Stereotactic frame
 - MUST be fixed to skull with screws = painful
 - Frameless systems available but LESS accurate
- Preop CT scan & MRI needed for coordinate calculation
- A devoted neuropathologist recommended





Stereotaxic biopsy

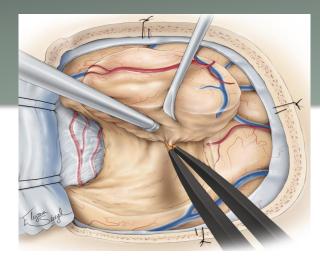
- Small samples
 - Inhomogeneity in tumor cell distribution ⇒ possibility of error
 - Especially in gliomas
 - NO molecular nor genetic studies
- Results DEPENDING ON WHERE BIOPSY IS TAKEN





Surgical treatment

- Extent of tumour resection direct relationship with survival
 - Even in malignant gliomas
 - LIMITATION: avoid inducing new neurological deficits
- Complex and expensive equipment required
 - Thorough preoperative preparation with tractography & functional MRI
 - Drug administration to improve intraoperative visualisation of residual tumour
 - Neuronavigation
 - Neurophysiological monitoring
 - Intraoperative MRI







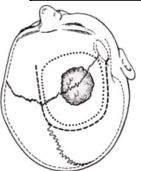


Meningiomas: Simpson grade =

recurrence rate

- The dural tail & infiltrated bone are also tumours

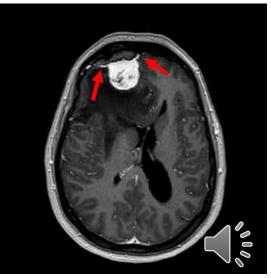
Simpson	Definition	10-Year		
grade		recurrence		
		rate		
1	Macroscopic gross-total	9%		
	resection with excision of dura			
	, sinus ,and bone .			
2	Macroscopic gross-total	19%		
	resection with coagulation of			
	dural attachment.			
3	Macroscopic resection without	29%		
	resection or coagulation of			
	dural attachment.			
4	Subtotal resection.	40%		
5	Biopsy.	Not available		







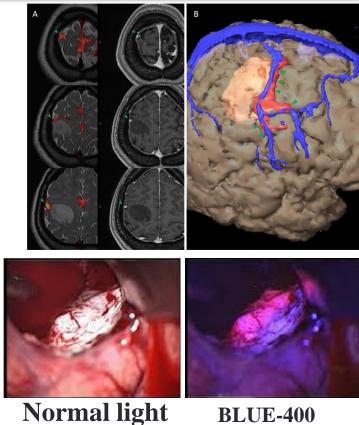






How to improve safely tumour excision?

- Thorough preoperative preparation
- Preop δ-aminolevulinic acid administration
- Neurophysiological monitoring
- Neuronavigation
- Intraoperative tumour identification
- Intraoperative MRI

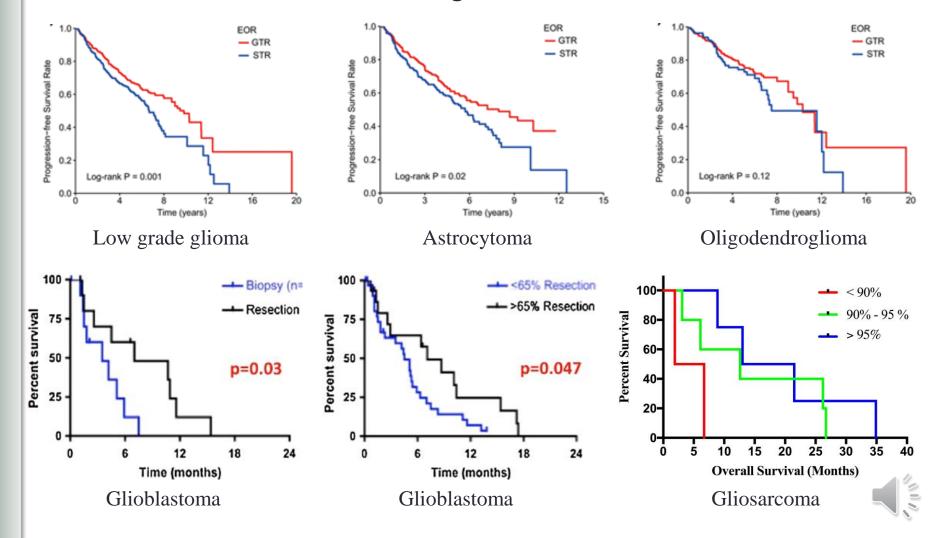






Gliomas: extent of resection & survival

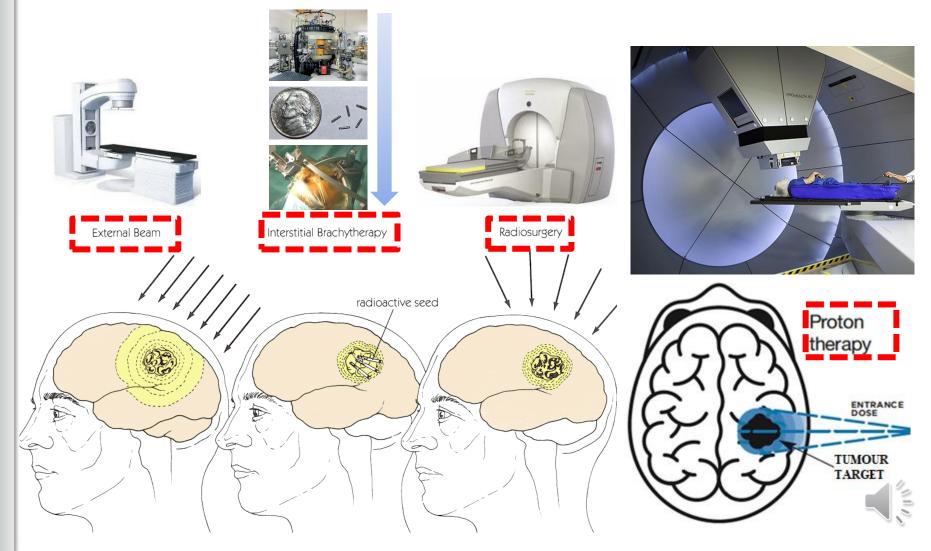
More radical removal = longer survival





Ionizing radiation treatment: types

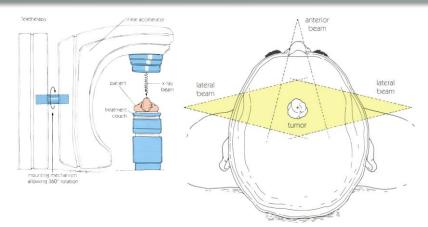
Each has advantages and disadvantages & costs

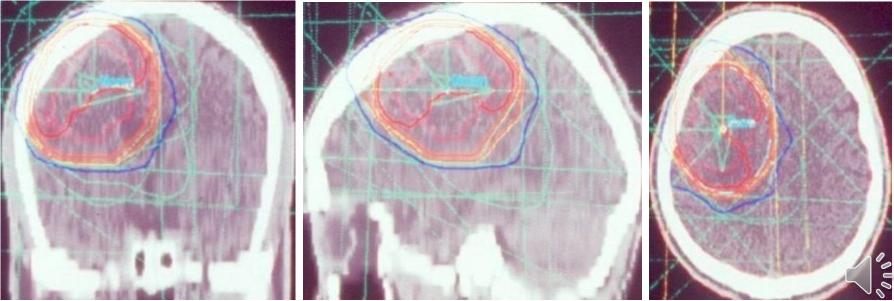


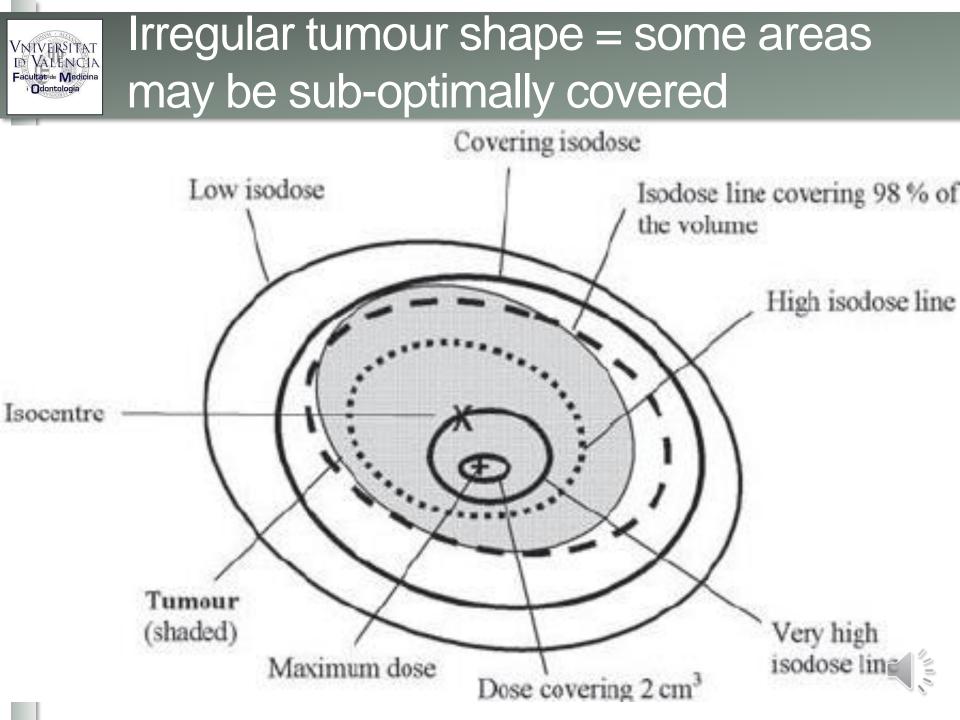


Conventional radiotherapy

- Extensive areas of non-tumoral brain radiated
- Glial & vascular damages = progressive neurological / cognitive deficit in survivors
- Can only be administered once



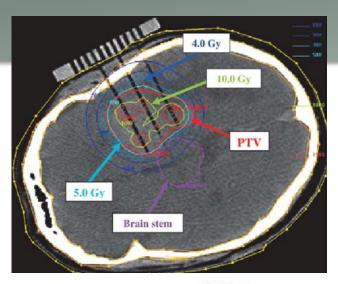


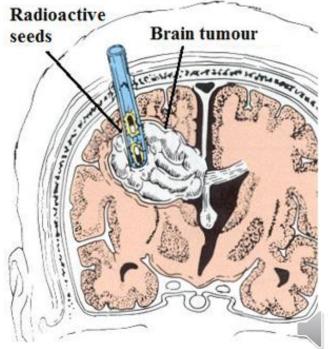




Brachytherapy

- Radioactive seeds inserted surgically inside the tumour
 - Must be flown from Canada
- Stereotactic frame needed
- Seeds MUST be removed when radiation dose is administered
- Higher doses possible as nearby brain spared
- Difficult to cover irregular shape tumours
- Can be used after conventional radiotherapy

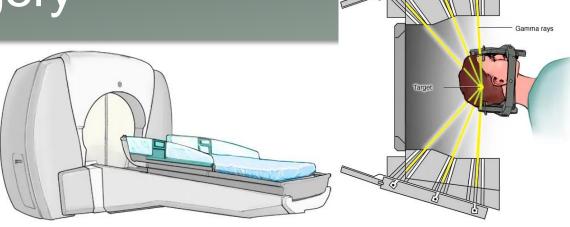


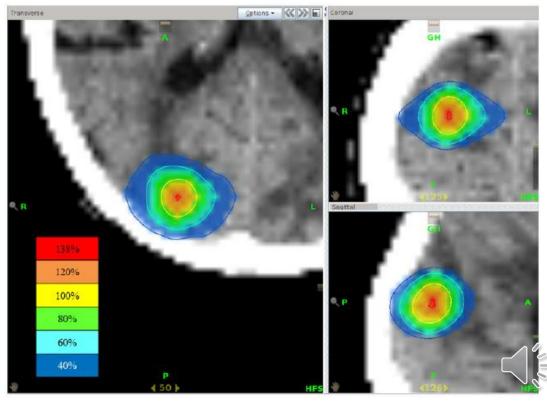




Radiosurgery

- Multiple thin radiation beams converging at target
- Maximal dose to tumour and minimal to brain
- Possible to treat multiple lesions
- Lesion size <3cm in \varnothing
- Particularly useful in metastases

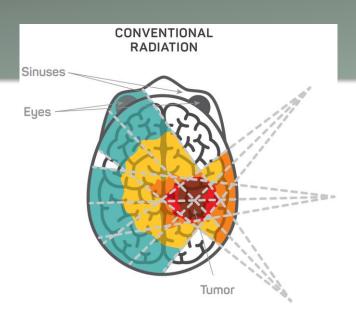




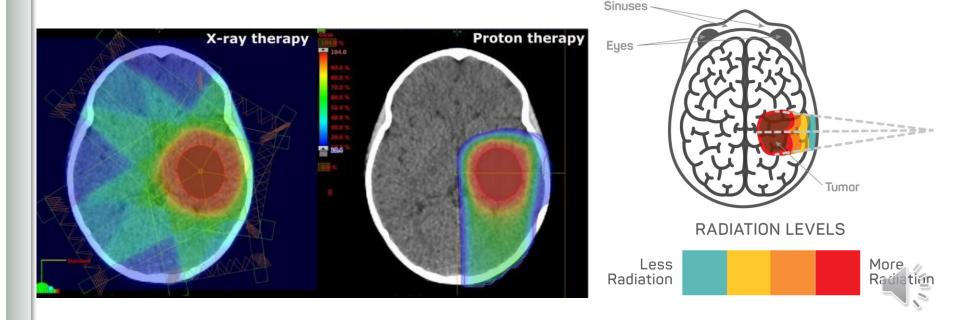


Proton beam

- More precise dose administration
 - Higher effectiveness
 - Less surrounding brain damage
- Very costly equipment



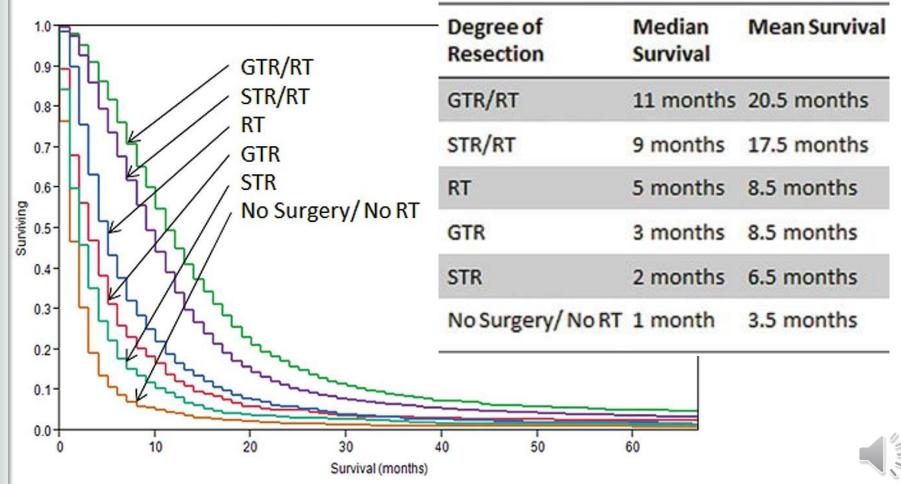
PROTON THERAPY



VNIVERSITAT D VALENCIA Facultate de Medicina i Odontología

Surgical removal + radiotherapy glioblastoma survival

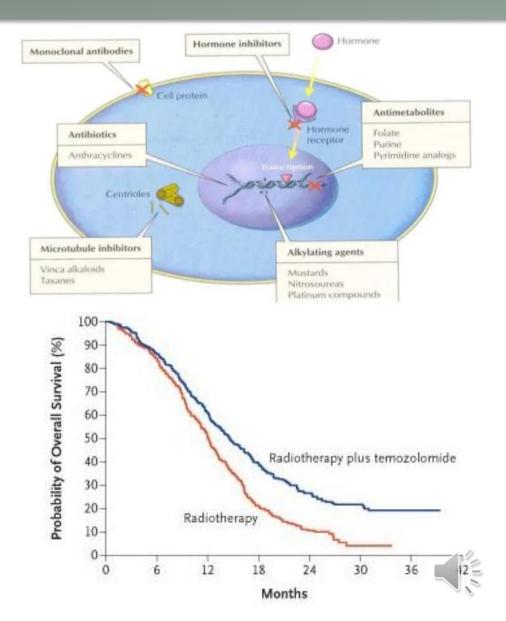
 Therapeutic combinations = longest survivals in malignant brain tumours





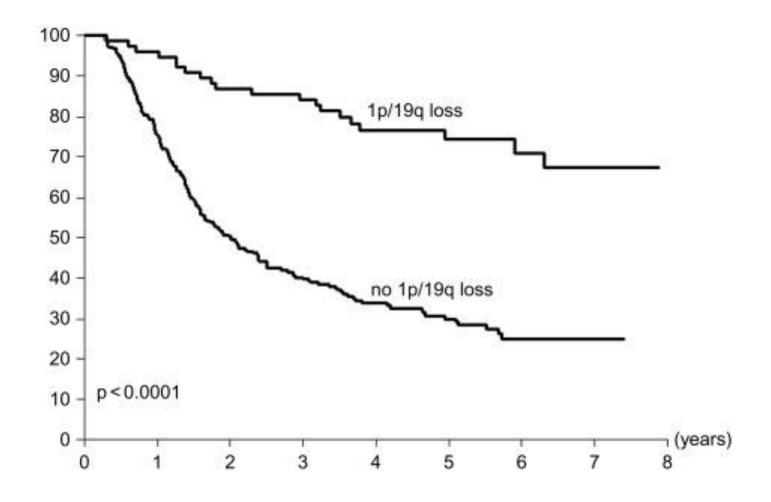
Chemotherapy for brain tumours

- Resistant tumour cells survive → recurrence
- Best combining different action chemotherapeutic agents
- Some enhance radiation therapy effects (Temozolomide)



Codeletion 1p 19q prolongs Oligodendroglioma survival

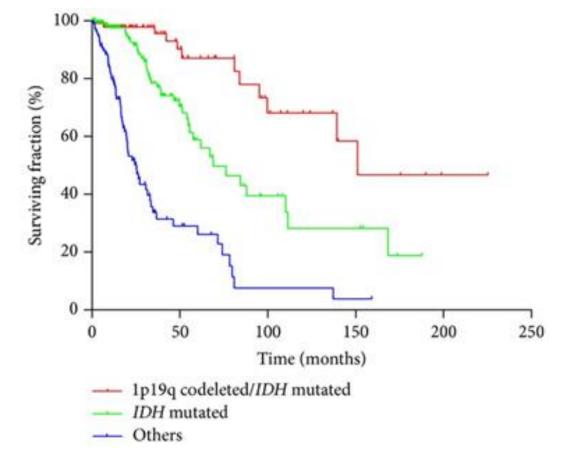
Prolongs survival significantly



Low grade gliomas: markers and VNIVERSITAT ENCIA Facultat de Medicina survival rate (1)

Adontologia

 Codeletion 1p 19q versus IDH mutation and others prolong survival most





Low-grade gliomas: markers and survival rate (2)

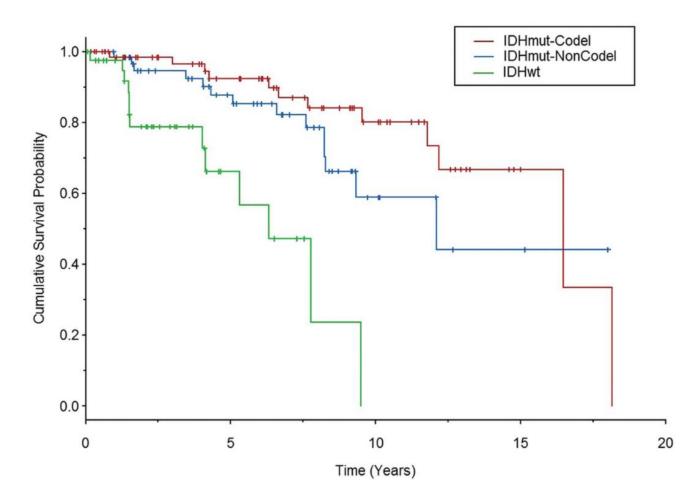
IDH mutation = longer survival

VNIVERSITAT

Odontologia

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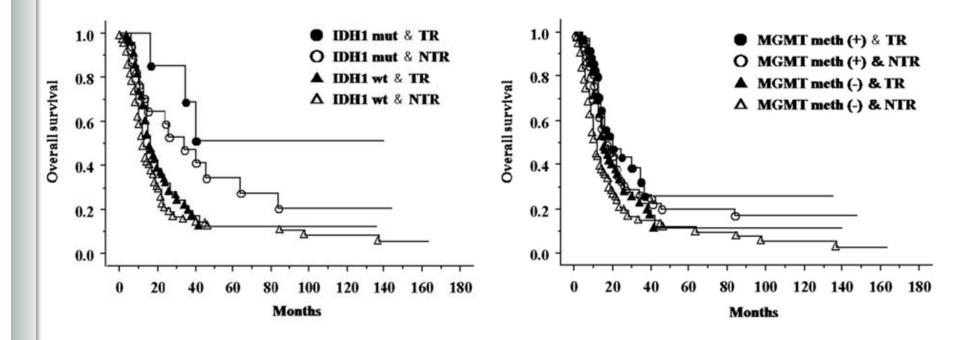
Codeletion 1p 19q = increases survival rate





Anaplastic astrocytoma: markers and survival rate

 Total resection with IDH1 mutated & MGMT methylated = longer survival

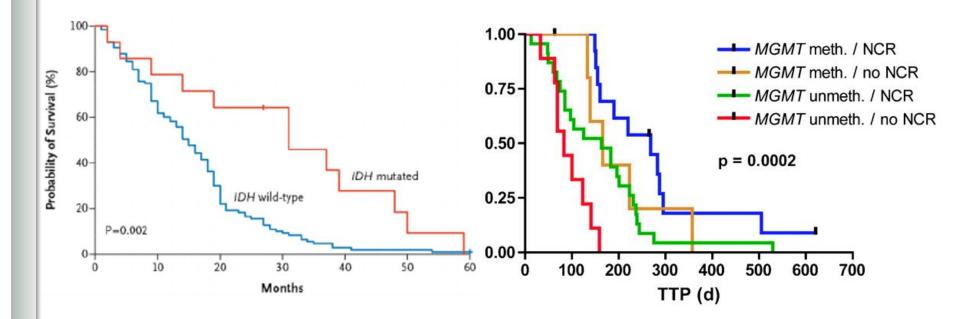






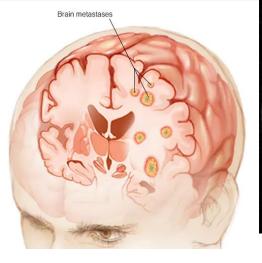
Glioblastoma: markers and survival rate

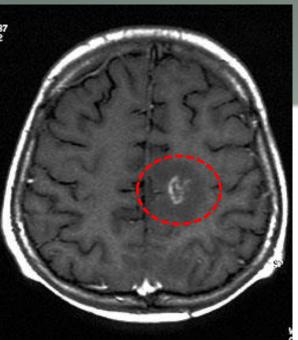
 Prolonged with IDH mutated and MGMT methylation with near-complete tumour removal (NCR)



BRAIN METASTASES

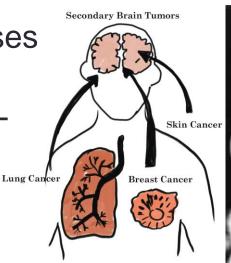
- > 50% brain tumours
- 15-30% primary ⇒
 brain metastases
- 15% metastasis ⇒
 first symptoms
 unknown primary

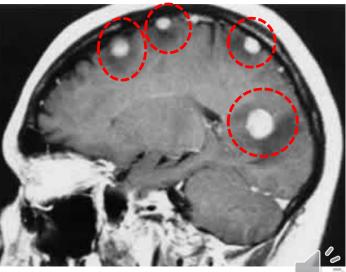




30% single

- 70% brain metastases are multiple
- 6% lesions are NOT neoplastic = vital stereotaxic biopsy



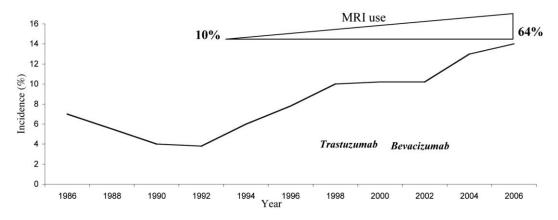


70% multiple



Brain metastases: incidence

- Improved diagnostic capabilities
 - CT
 - RM
 - Bone scan
 - PET
- Many chemotherapeutic agents Ø cross bloodbrain barrier
- Chemotherapy alters blood-brain barrier







Metastases pathways

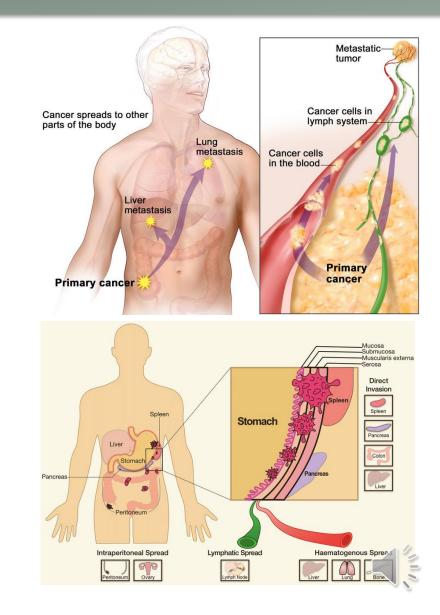
Hematogenous

- Through regular venous/ arterial system
- Through Batson's venous plexus

Lymphatic

Transceolomic

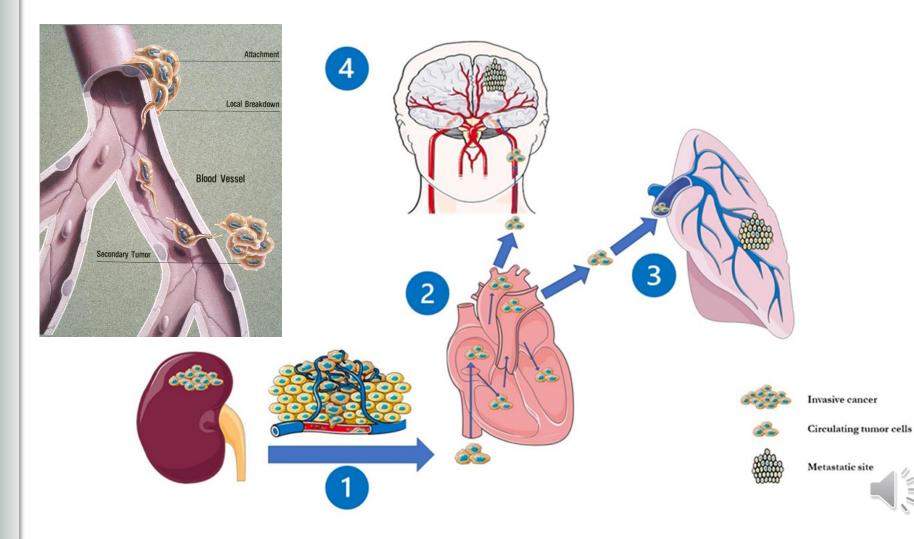
- Peritoneal or pleural cavity
- Meningeal carcinomatosis
- Air borne
- Pyknotic vesicles
- Retrograde growth through peripheral nerves





Hematogenous metastases

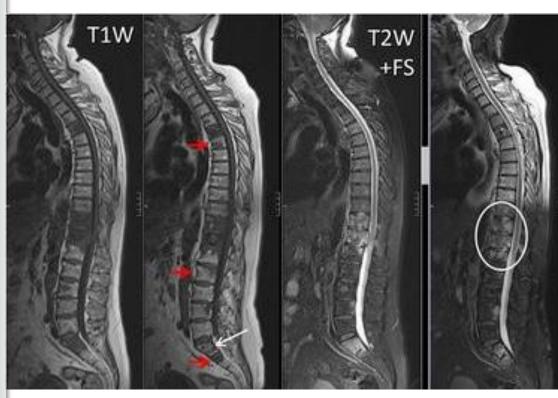
The most common pathway

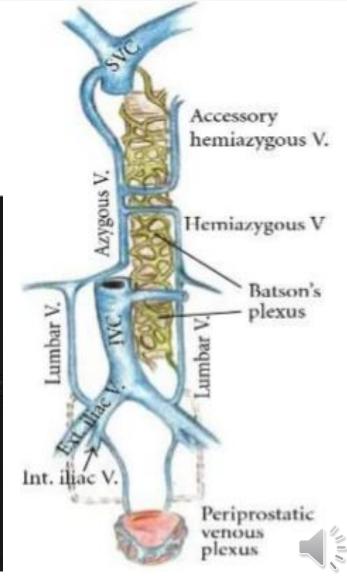


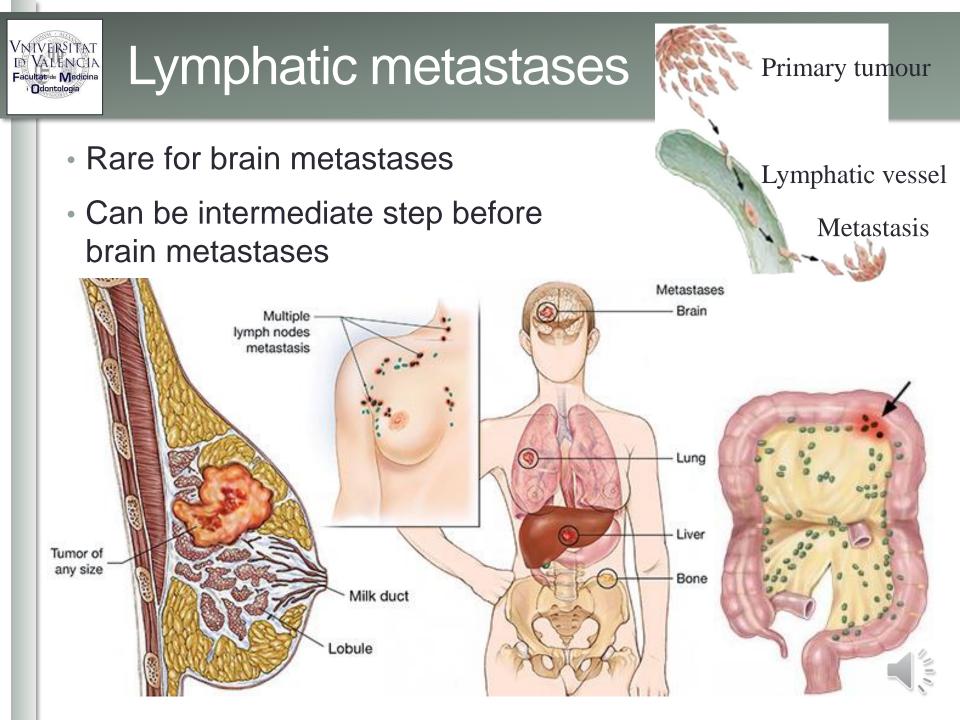


Hematogenous metastases through Batson's venous plexus

- Uncommon pathway
- Induces spinal metastases
- Typical of prostate cancer









Transceolomic



Ovarian cancer

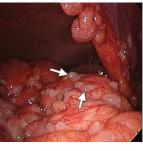


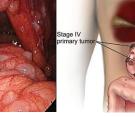
Dura mater

Pia mater

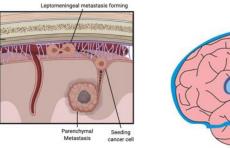
Subarachnoid space

Arachnoid mater

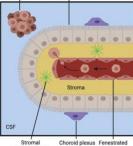




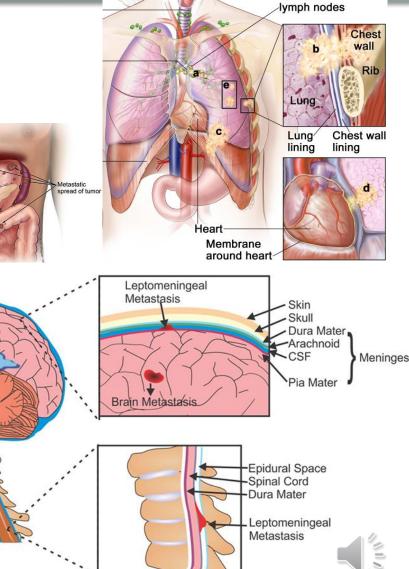




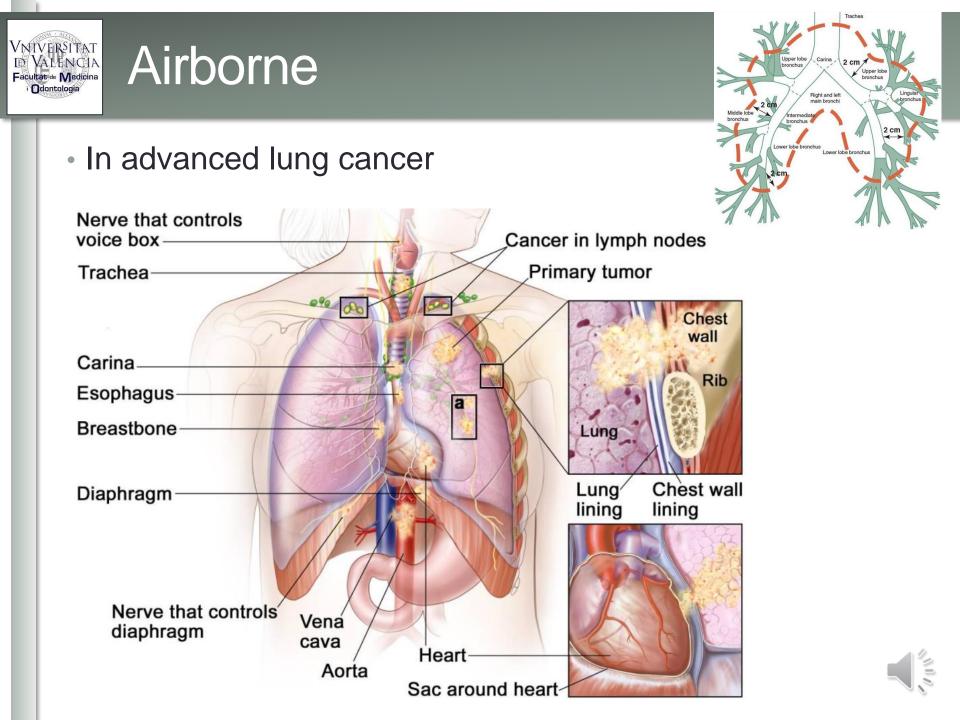
Leptomeningeal Choroid plexus Metastasis epithelial cells

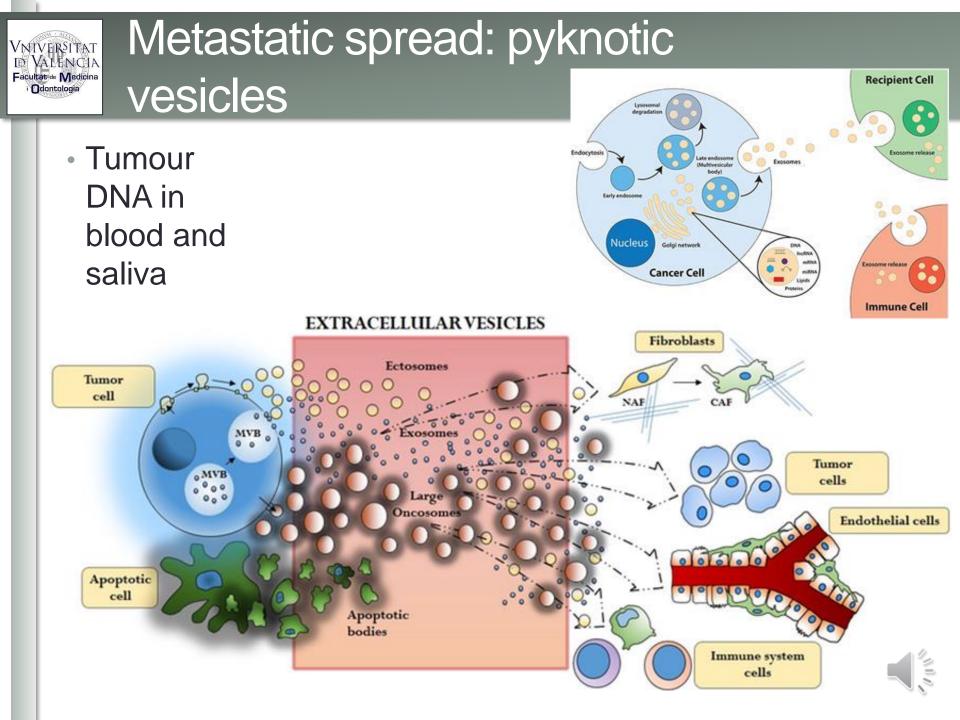


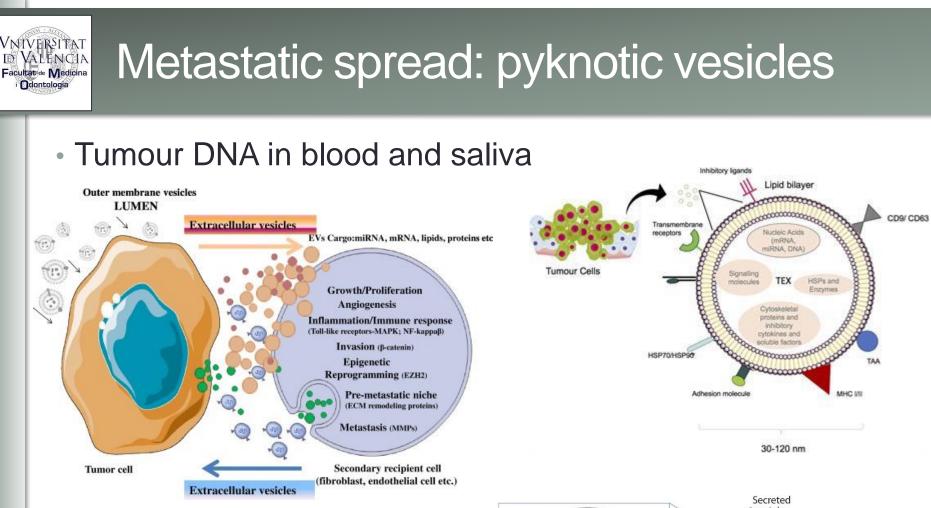
Stromal Choroid plexus Fenestrated dendriritic cell macrophage capillary

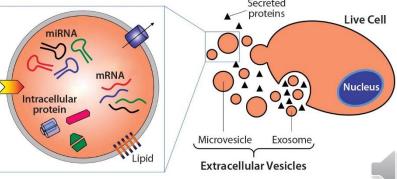


Cancer in



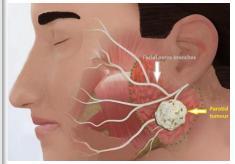


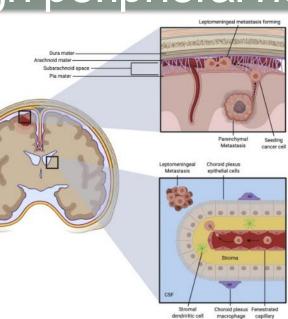


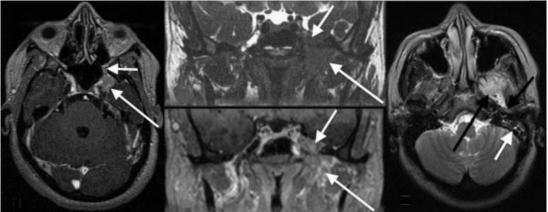


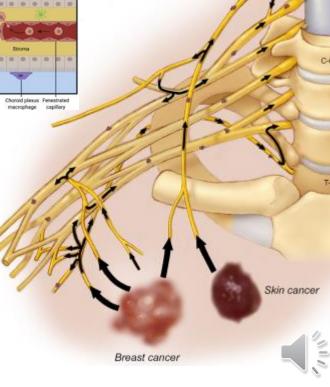
Metastatic pathways: retrograde growth through peripheral nerves

- Typical of parotid tumours
- Cause meningeal carcinomatosis











Clinical examination oncologic patient (1)

Thorough examination compulsory



Basal cell tumour

Melanoma



Upper limb cancer



Parotid tumour

Larynx tumour

Lower limb cancer



Clinical examination oncologic patient (2)

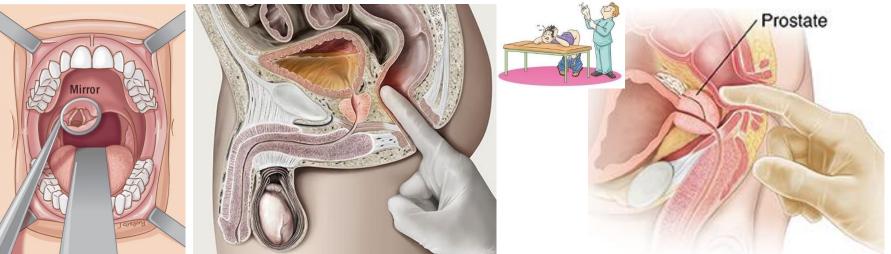
ALL lymphatic ganglia chains MUST be examined



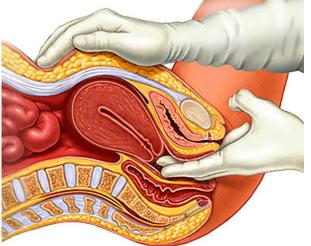


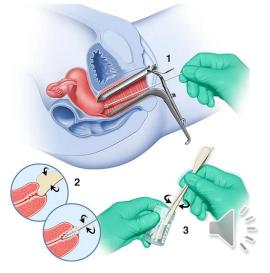
Clinical examination oncologic patient (3)

ALL tumour sources MUST be ruled out



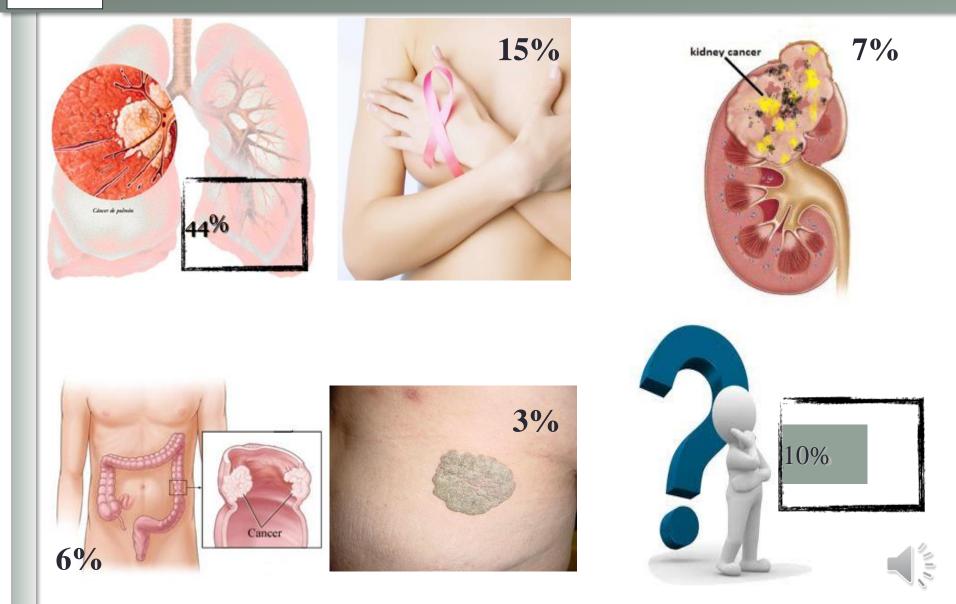








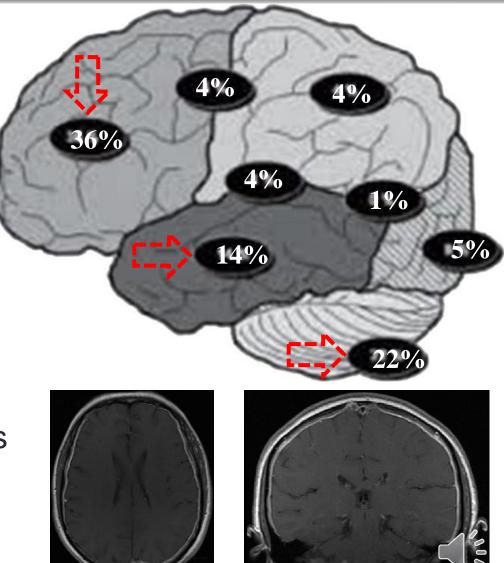
Brain metastases: primary tumour





Brain metastases: location

- Cerebral hemispheres
 78%
 - Cortico-subcortical location
 - Mostly frontal / temporal lobes
- Posterior fossa 22%
 - Cerebellum 16%
 - Single posterior fossa lesion in adults = metastasis until proven otherwise
- Meningeal carcinomatosis
 / Carcinomatous
 meningitis

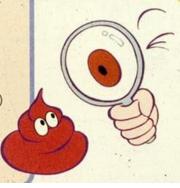




Extension study

Treatment highly dependent on it





Chest x-ray

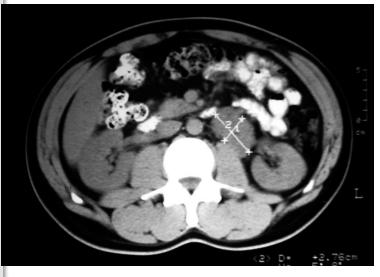
Stool analysis



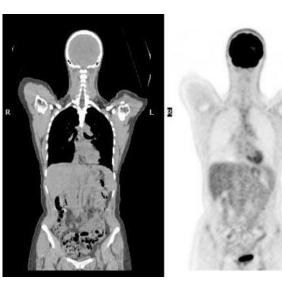
Prostate antigen



Mammography



Thorax-abdomen-pelvis CT scan





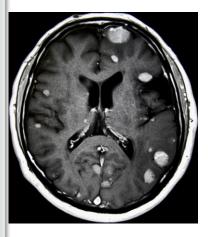
Positron emission tomography (PET)

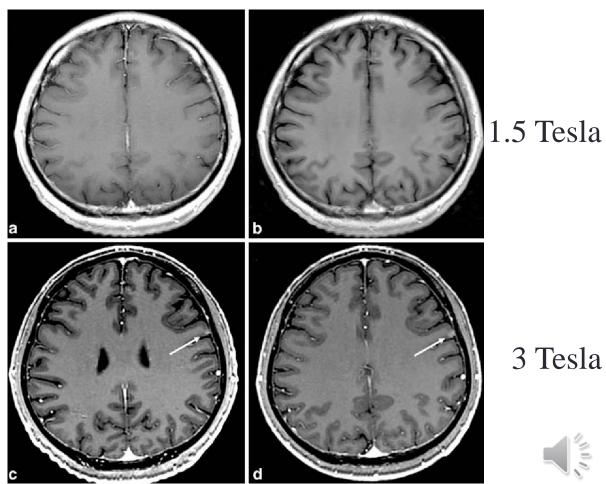


Single versus multiple metastases

- High field MRI needed to see tiny metastases
 - This will decide treatment & prognosis



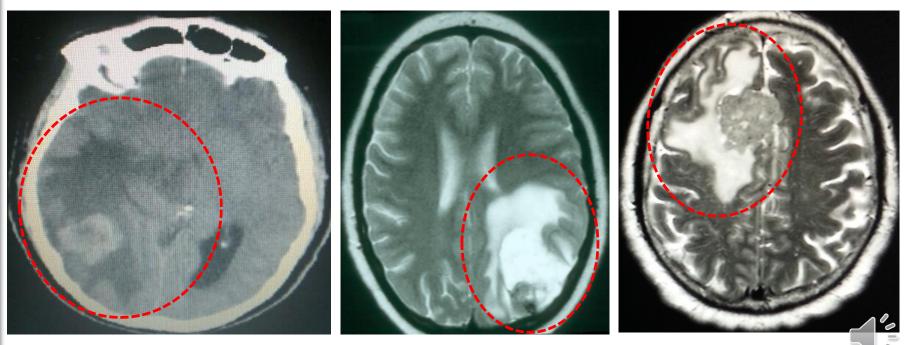






Brain metastases: medical treatment

- Corticosteroids
 - Dexamethasone 10-20mg i.v. / 6mg / 6h
- H₂ antagonists
- Anticonvulsants

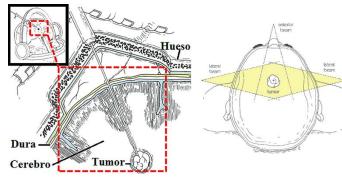


Brain edema around brain metastasis



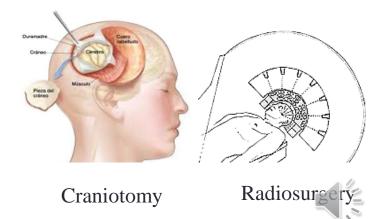
Brain metastases: specific treatment

- Unknown primary or diagnosis
 NOT confirmed = stereotactic
 biopsy
- Primary NOT controlled = No treatment / palliative whole cranial radiotherapy
- Controlled primary (Karnofsky \geq 70)
 - Single = surgery + whole cranial radiotherapy
 - Multiple
 - ≤ 3 = radiosurgery ± whole cranial radiation therapy
 - > 3 = whole cranial radiation therapy



Stereotaxic biopsy

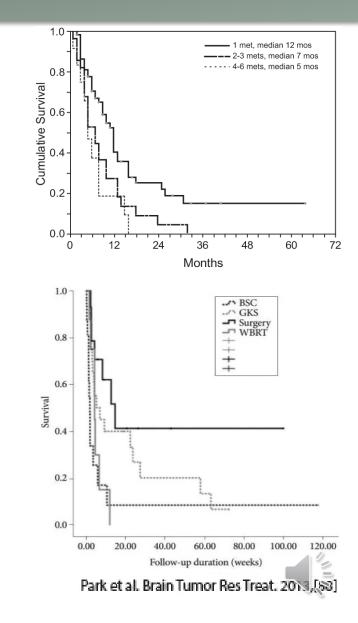
Whole cranial radiotherapy





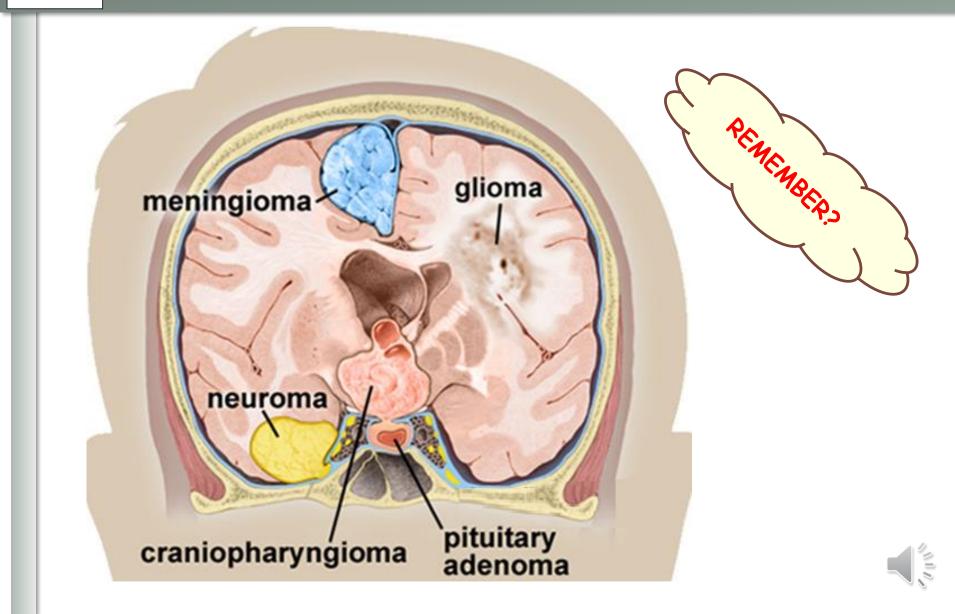
Brain metastases: prognosis

- No treatment ~ 1 month
- Corticosteroids to control oedema ~ 2 months
- Whole cranial radiation
 therapy + corticosteroids
 ~ 3-6 months
- Surgery + whole cranial radiotherapy ~ 8-12 months
- Radiosurgery + whole cranial radiotherapy ~ 12-14 months



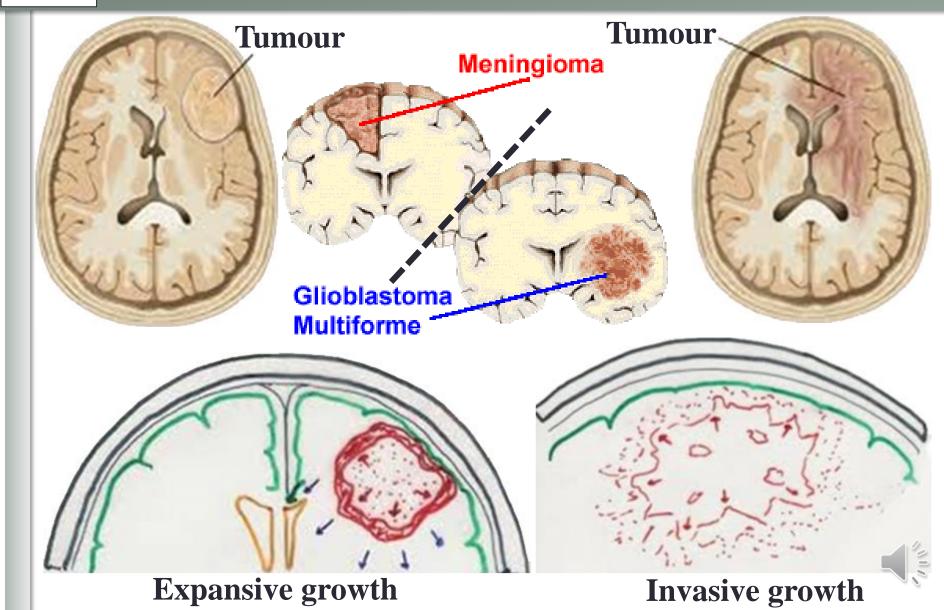


PRIMARY BRAIN TUMOURS



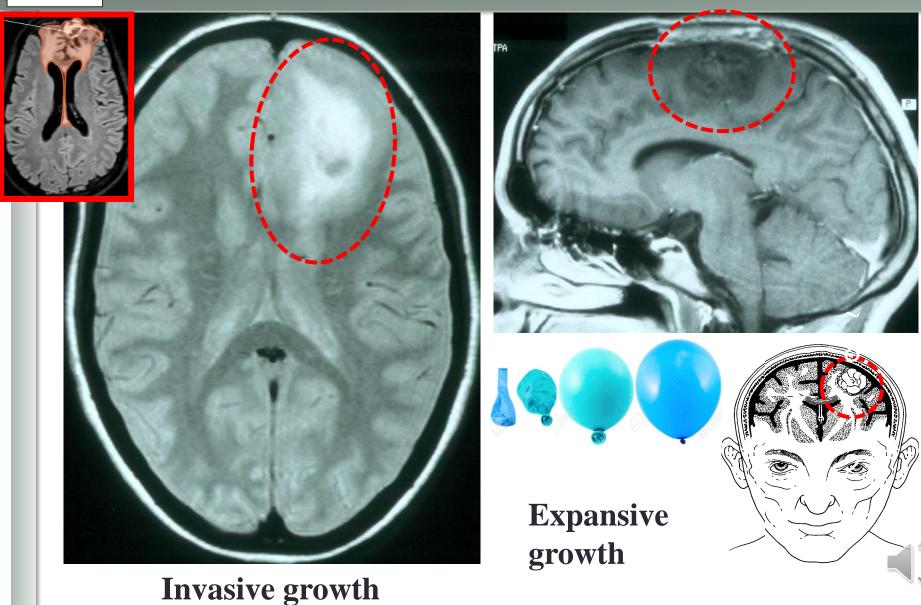


Primary brain tumours: growth patterns





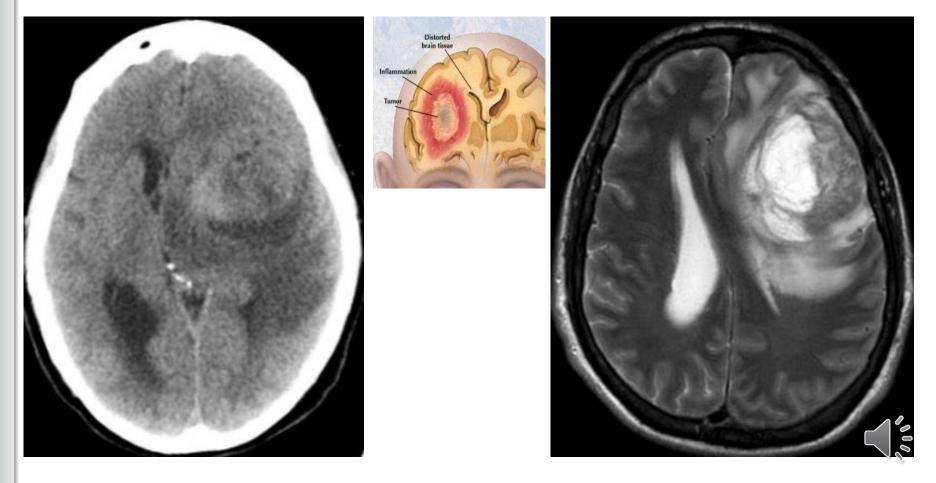
Primary brain tumours: growth patterns





Primary brain tumours: inflammatory reaction

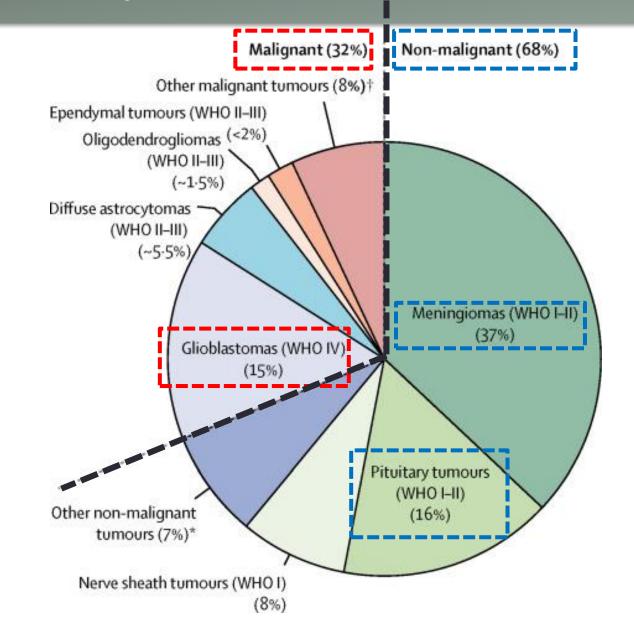
- Worsens the mass effect
- Corticosteroids help control it



Primary brain tumours: rate

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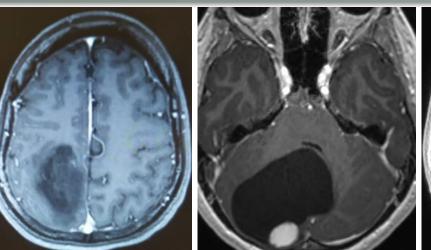


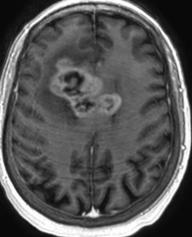




GLIOMAS: most common types

- Low-grade gliomas
- Astrocytoma
- Glioblastoma multiforme
- Oligodendroglioma
- Ependymoma
- Medulloblastoma

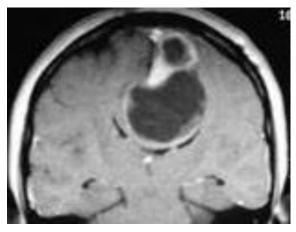




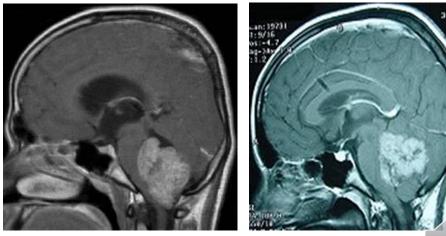
Low grade glioma

a Pilocytic astrocytoma

Glioblastoma



Oligodendroglioma

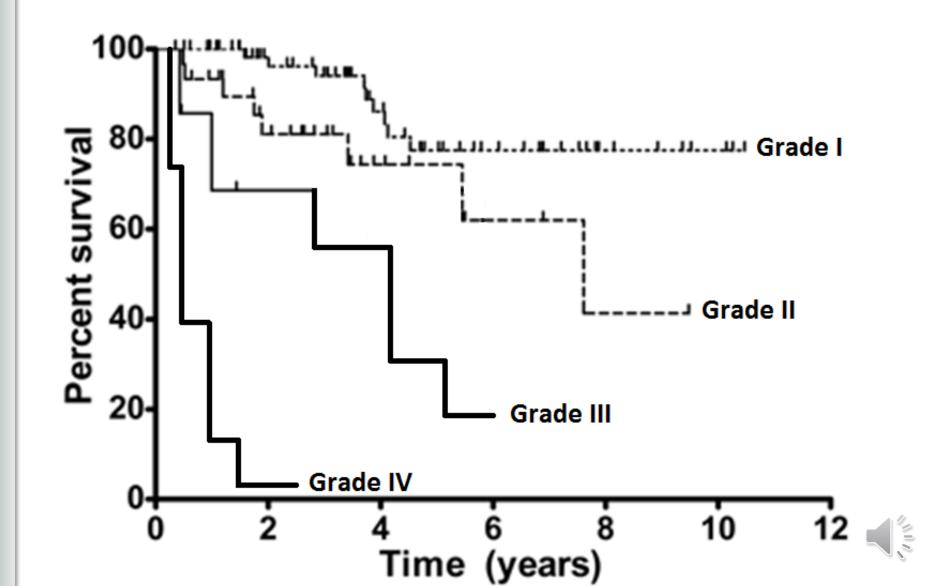


Ependymoma

Medulloblastoma



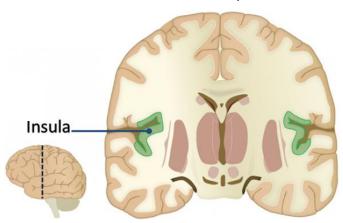
Kaplan-Meier survival curve for gliomas

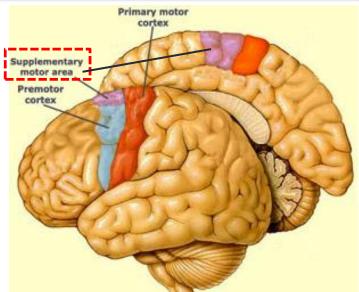


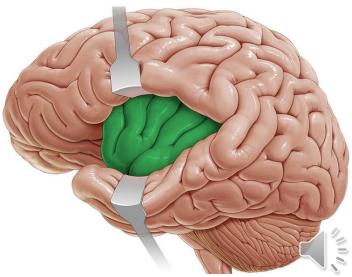


LOW-GRADE GLIOMAS

- 15% primary brain tumours
- Incidence fourth & sixth decades
- Predilection insula + supplementary motor area
- Risk factors
 - Ionizing radiation
 - Hereditary syndromes (Neurofibromatosis, Li-Fraumeni)



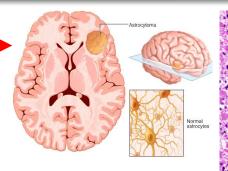


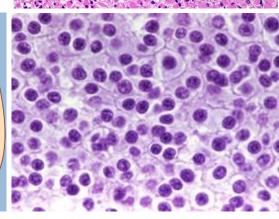


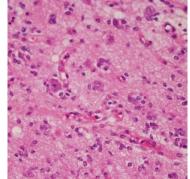


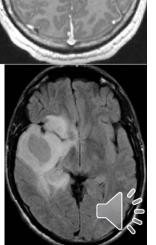
Low-grade gliomas: types

- Astrocytoma -
 - Fibrillar
 - Gemistocytic
 - Protoplasmic
- Oligodendroglioma
- Oligoastrocytoma





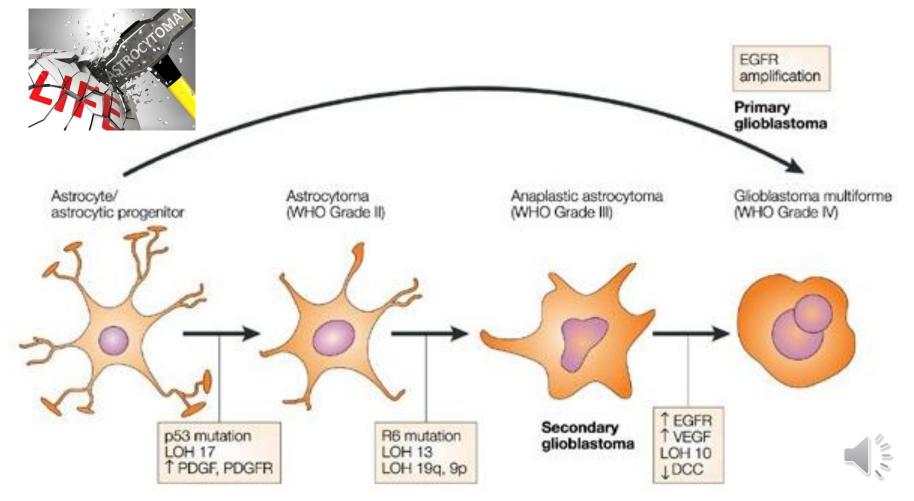






Left untreated low-grade gliomas will become malignant

Low-grade gliomas are not benign but pre-malignant lesions



Vniversitat d Valencia Low-grade gliomas: diagnosis Facultat de Medicina

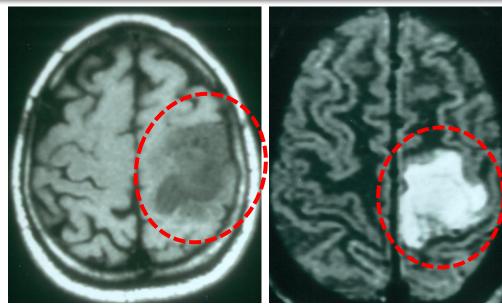
MRI

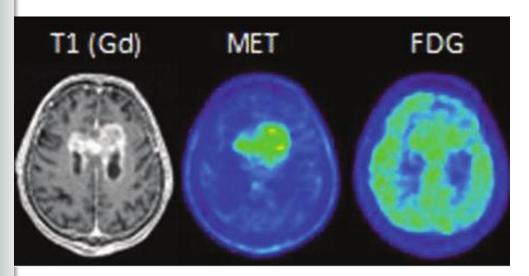
Idontologia

Spectroscopy

• PET/SPECT

- Methionine
- Fluorodeoxyglucose

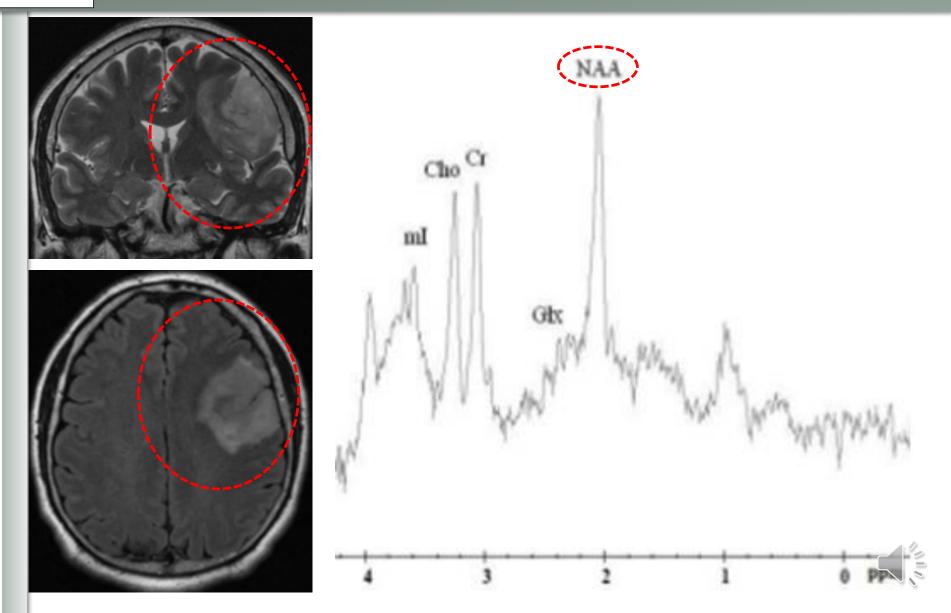








Glioma grade II: peak N-acetylaspartate

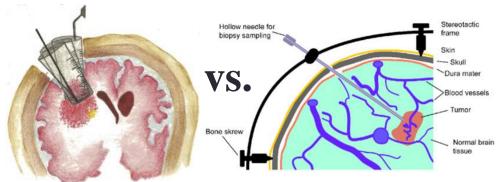




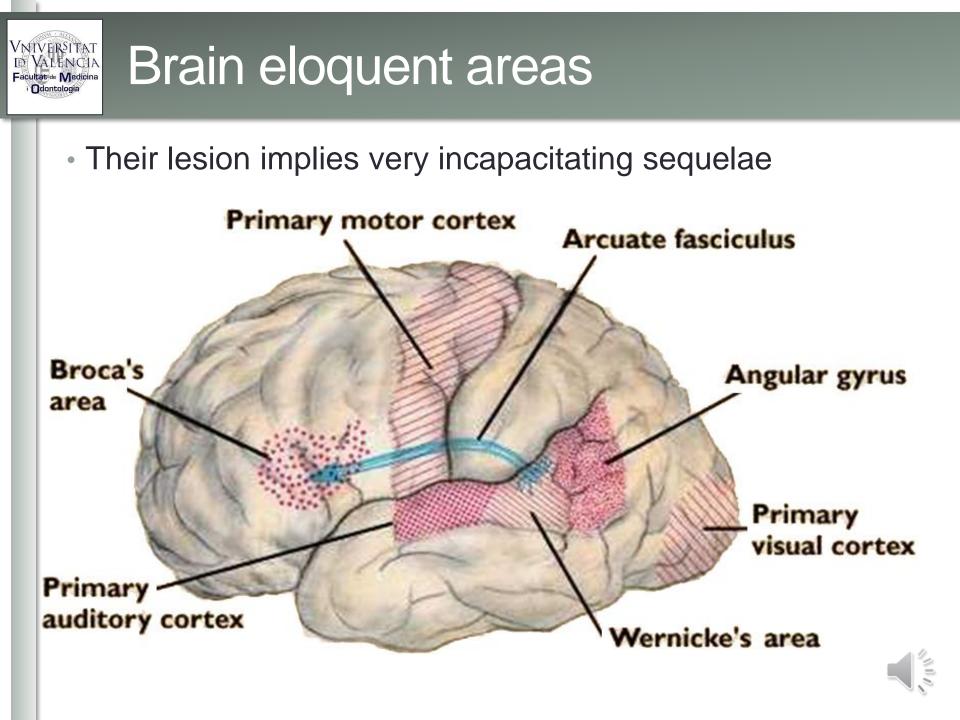
Low-grade glioma treatment: biopsy / resection

- Craniotomy + resection
 - Get histological diagnosis
 - Improve neurological symptoms
 - Eliminate mass effect
 - Cyto-reduction
 - Delay / reduce possibility of malignancy progression
 - Epileptic seizure control
 - Lesions in eloquent areas
 awake craniotomy

- Stereotaxic biopsy
- Diffuse lesions (gliomatosis)
- Location in areas with high risk of post-operative neurological deficits
- Intervention contraindicated for medical reasons

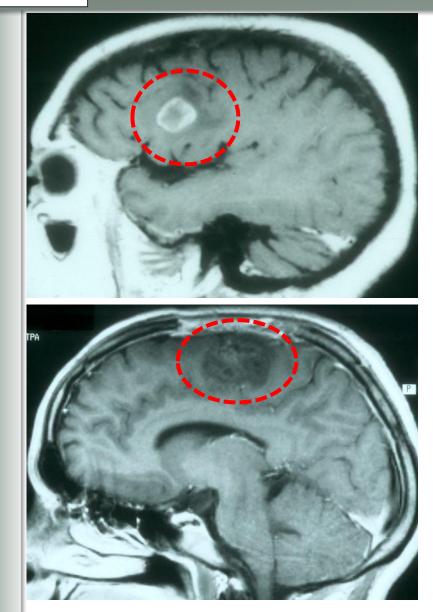


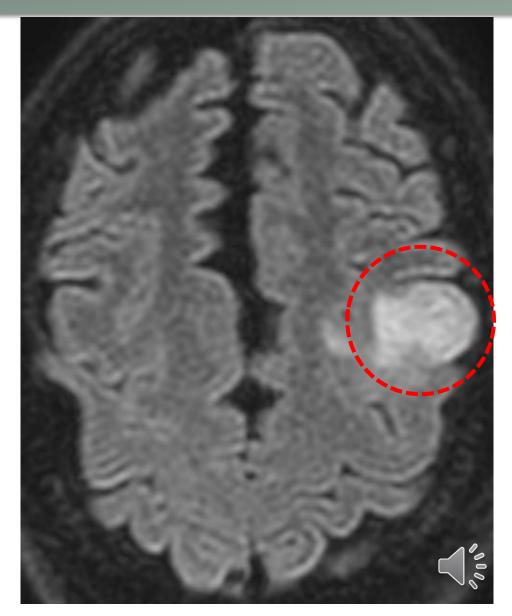
↑ removal = better evolution, ↓ epileptic seizures ↑ time until malignant progression





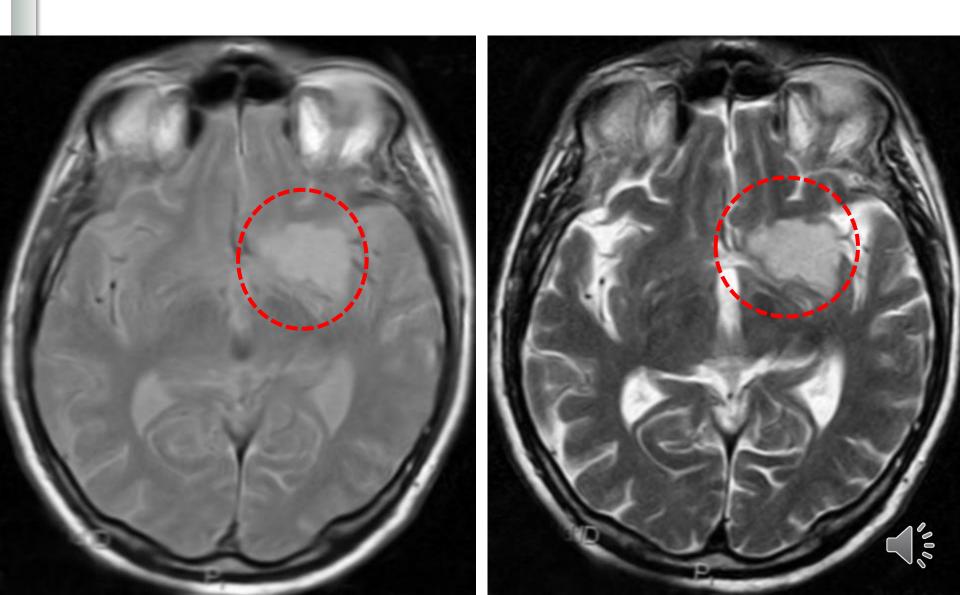
Gliomas in brain eloquent areas





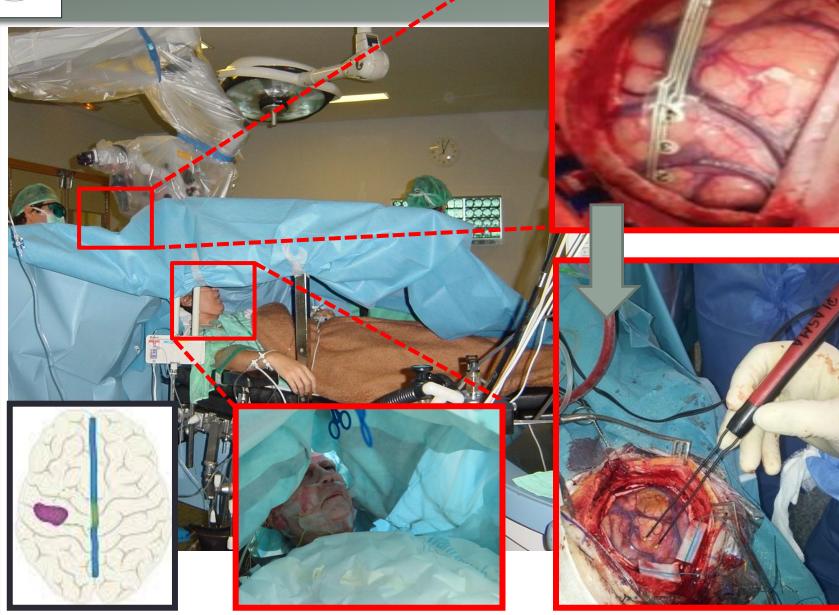


Low-grade glioma in insula





Awake craniotomy





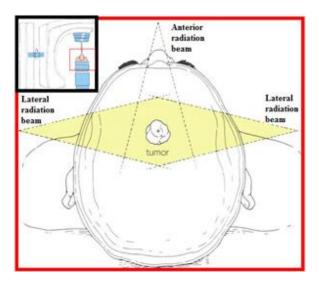
Low-grade gliomas treatment: radiation therapy / chemotherapy

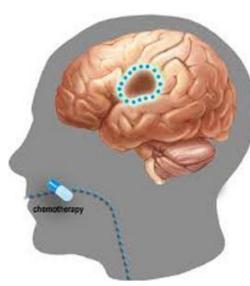
Radiation therapy

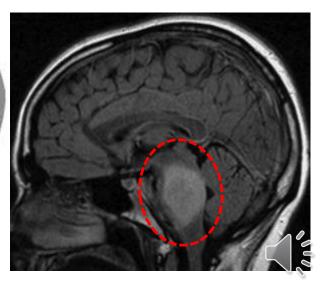
- Subtotal removal
- Recurrence

Chemotherapy

- Subtotal removal
- Recurrence
- Astrocytomas /oligoastrocytomas
- Location in brainstem



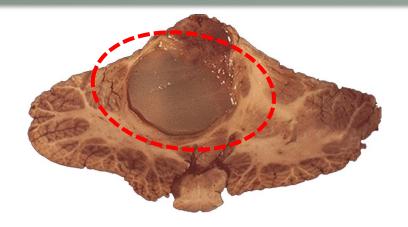


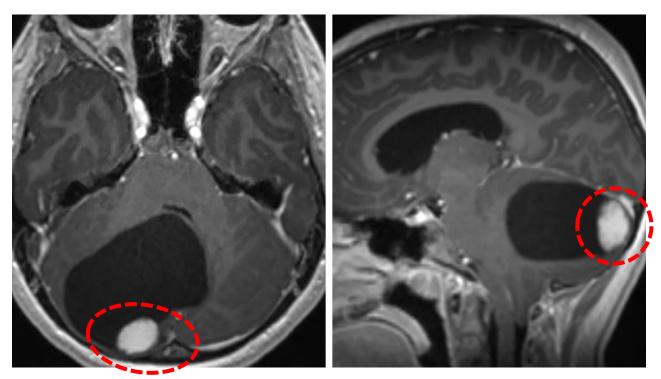




PILOCYTIC ASTROCITOMA

- Children & young adults
- Location: cerebellum > third ventricle > optic nerves
- Cyst with nodule
 - Complete nodule removal = cure

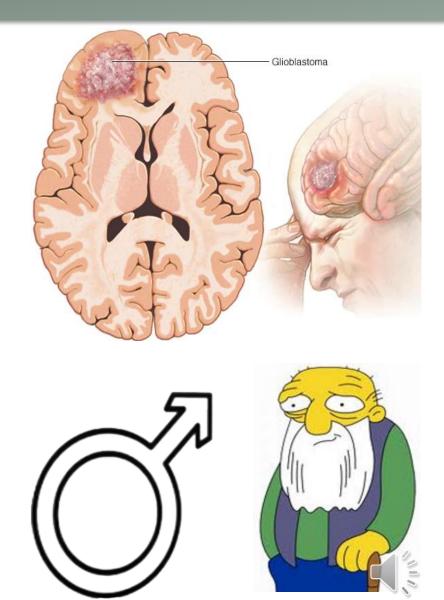






GLIOBLASTOMA MULTIFORME

- Grade IV astrocytoma
- 15% intracranial tumours
- Among primary brain tumours
 - ↑ common (50% of them)
 - ↑ aggressive
- ♂ / ♀ 3: 2
- At any age but incidence ↑ with advanced age

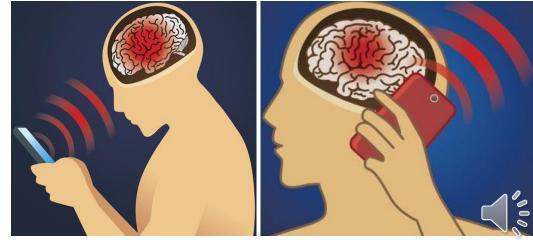




Glioblastoma: etiology

- Unknown cause
- Two development pathways
 - De novo
 - Secondary (from lowgrade gliomas)
- Association with genetic diseases
 - Turcot, Gorlin, ...)
 - Ionizing radiation
 - Electromagnetic waves

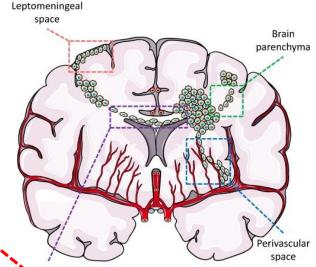




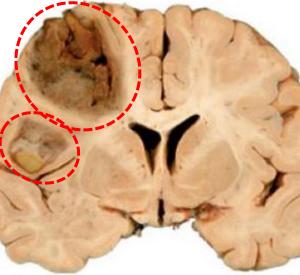


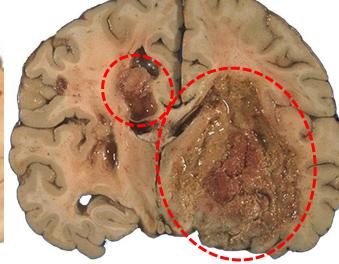
Glioblastoma: infiltrative growth pattern

- Invades nearby brain
- Grows following white matter tracts = contralateral growth
- Meningeal carcinomatosis AFTER surgical removal
- Possible metastases outside brain



White matter tracts: corpus callosum



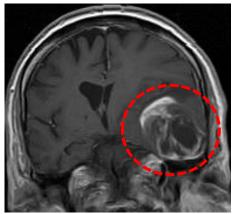






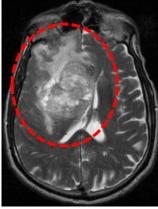
Glioblastoma: MRI

- Ring-like contrast enhancement
- Massive peritumoral oedema
- Invasion of nearby brain
- Distant tumour nodules

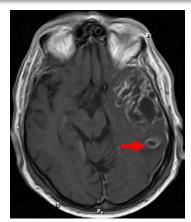


Ring-like contrast

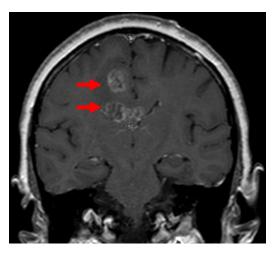
enhancement

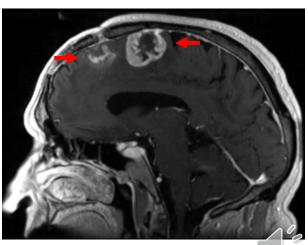






Infiltration nearby brain

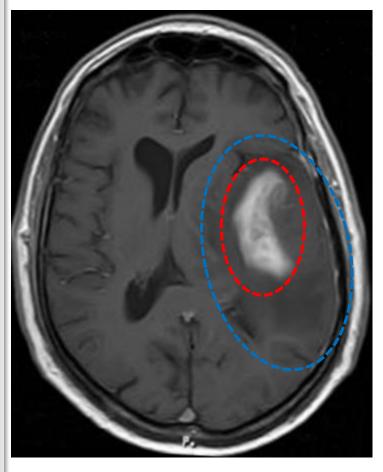


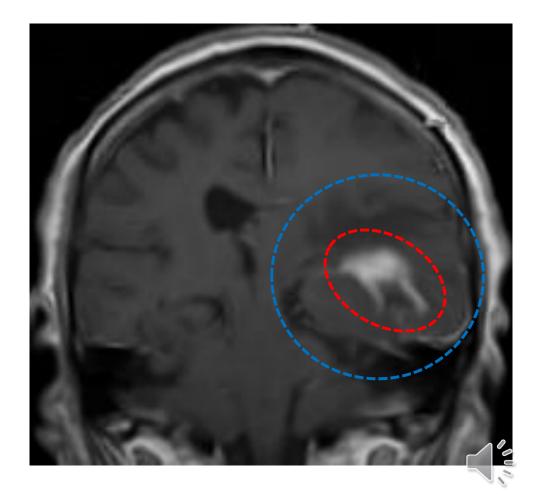


Distant tumour nodules

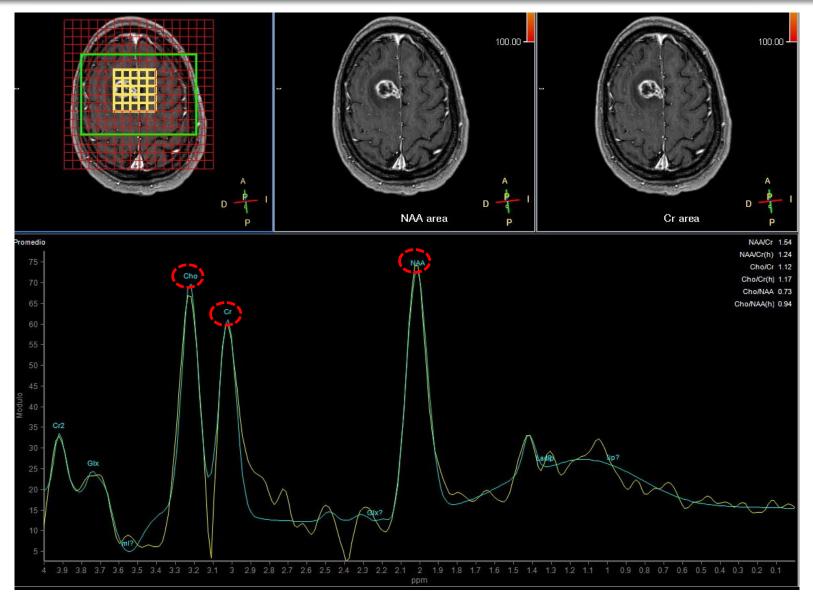
Glioblastoma secondary to low-grade glioma malignant progression

- Remove low-grade gliomas as soon as possible
 - No wait and see attitude





Glioblastoma MRI spectroscopy: peak choline, creatinine and N-acetyl-aspartate

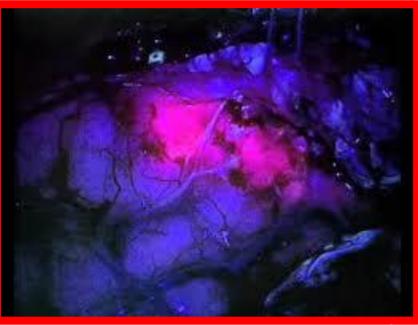




Glioblastoma: treatment

- Resection as radical as possible
 - Preop δ -aminolevulinic acid administration
- Whole cranial radiation therapy
- Chemotherapy
 - BCNU, CCNU
 - Temozolomide
- Average survival 12-14 months
- If excision is NOT possible ⇒ histological confirmation by stereotaxic biopsy





Intraoperative glioblastoma image marked with δ -aminolevulinic acid

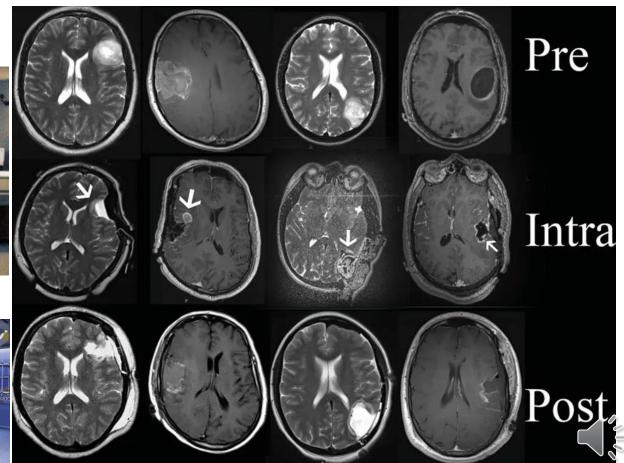


Glioblastoma: intraoperative MRI

- Improves resection
- Improvement in survival still unproved
- Expensive



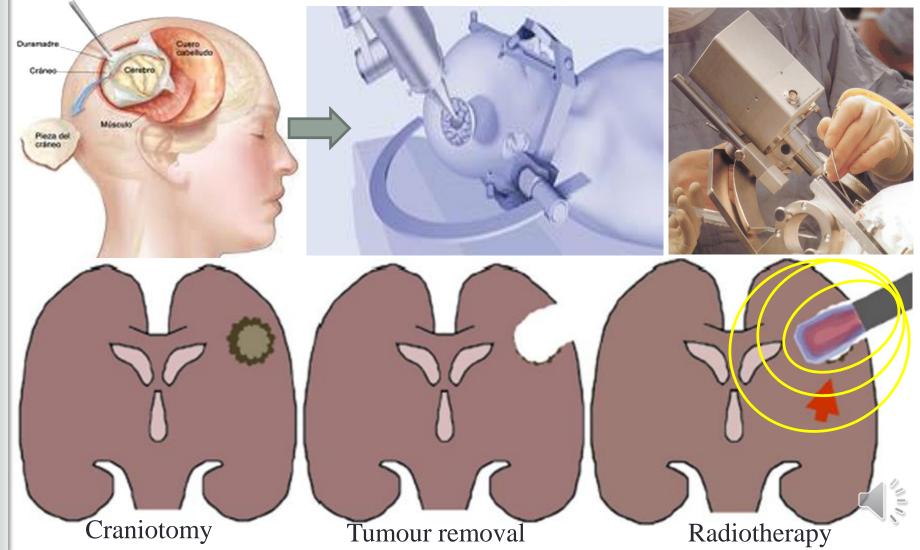






Glioblastoma: intraoperative radiotherapy

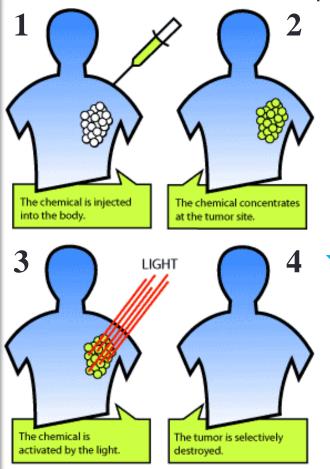
Indication: recurrent tumour with good patient condition



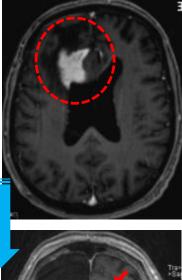


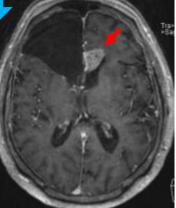
Glioblastoma: photodynamic therapy

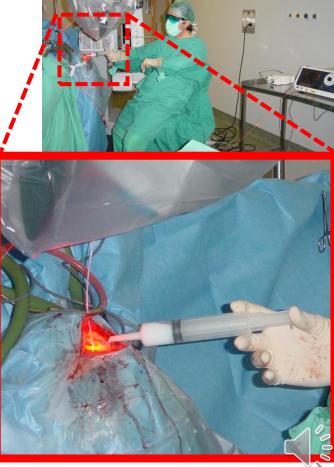
- To kill tumour cells invading 6mm of nearby brain
 - 90% recurrences happen 2cm from resection margins









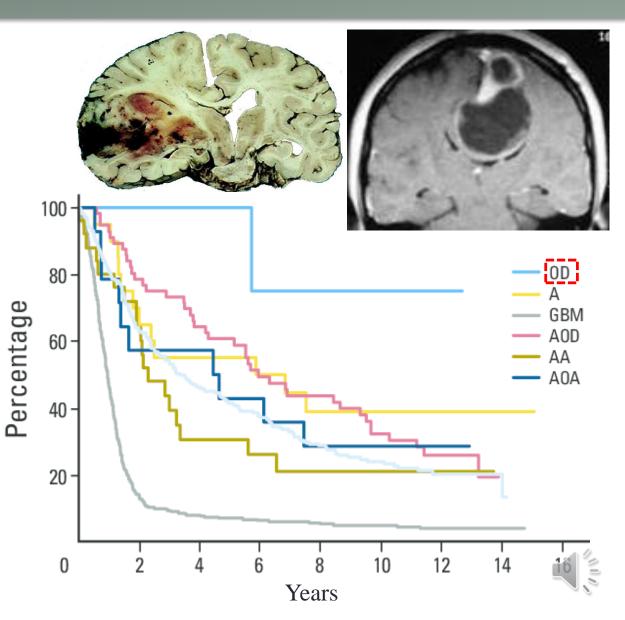


Photodynamic therapy intraop photo



OLIGODENDROGLIOMA

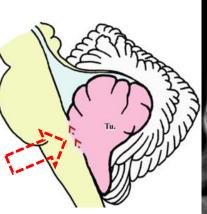
- 3.9% brain tumors
- 4th & 5th decades
- Epileptic seizures common
- Location: cerebral hemispheres
- Better prognosis
 - Good response to chemotherapy (alkylating agents)

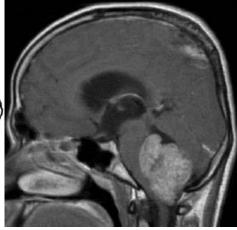




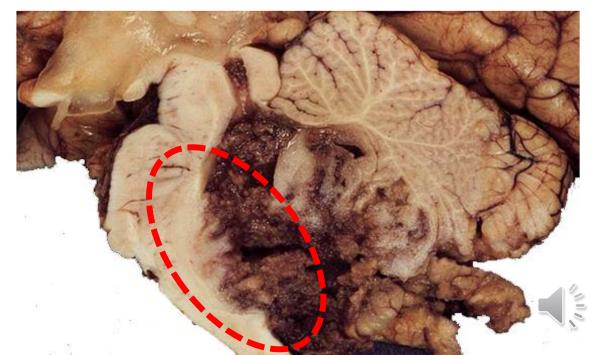
EPENDYMOMA

- Origin: ependyma ventricles & spinal cord
- Incidence in fourth ventricle = hydrocephalus
 - Invades its floor = cranial nerve deficits
- 3% brain tumours
- Spread through CSF pathways = follow-up MRI brain, cervical, dorsal & lumbar
- Surgical removal + radio + chemotherapy
 Bad prognosis





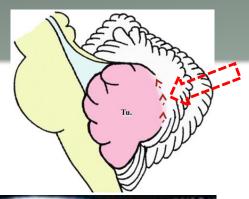






MEDULLOBLASTOMA

- 20% childhood brain tumours
- Location
 - In children: fourth ventricle roof
 - Does not invade floor
 - In adults: cerebellar hemisphere
- Obstructs CSF pathways = hydrocephalus
- Spreads through CSF pathways
 - Horsetail or droplet metastases
- Treatment: radical excision + radio + chemotherapy
 - Bad prognosis



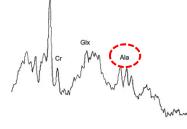




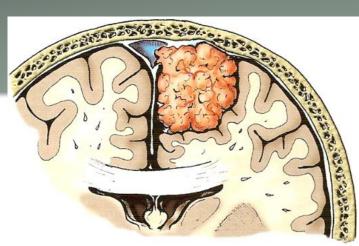
MENINGIOMA

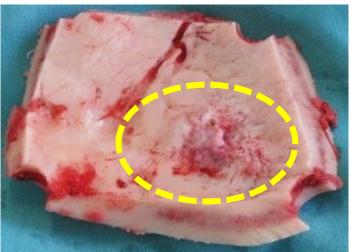
- Origin: arachnoid cells
 - External surface brain & spinal cord and inside ventricles
- 29% primary intracranial tumours
- \uparrow frequent \bigcirc , 5th & 6th decades of life
- 95% benign
 - Encapsulated
 - Slow expansive growth
 - Nerve tissue displacement
 - Possible adjacent bone infiltration
- Spectroscopy = alanine peak
- Histologically EMA marker
- Complete removal = cure





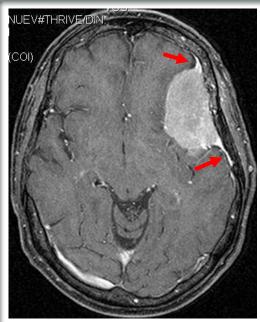








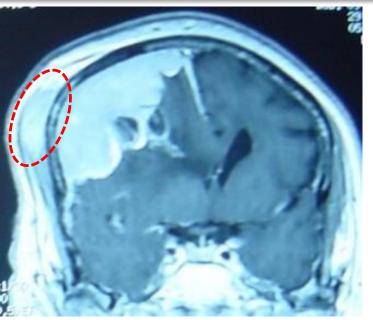
Meningioma: features



Dural tail



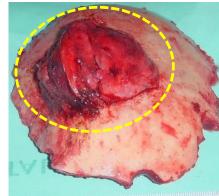
Bone invasion



Extracranial growth



Macroscopic aspect



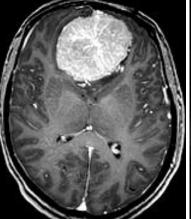
Extracranial growth

Feeding: meningeal arteries

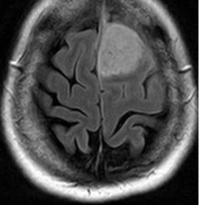


Meningiomas: location





Olfactory grove



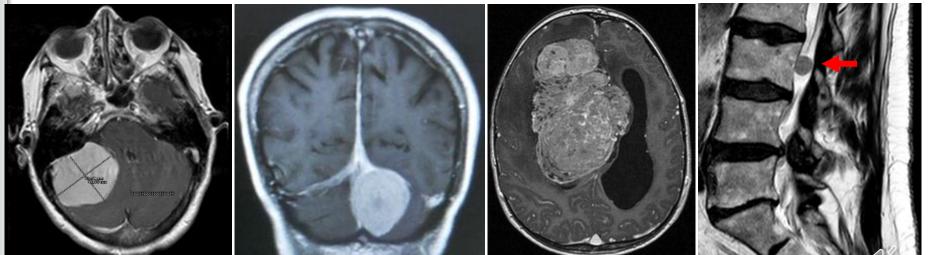
Parasagittal



Sphenoid wing



Temporal fossa



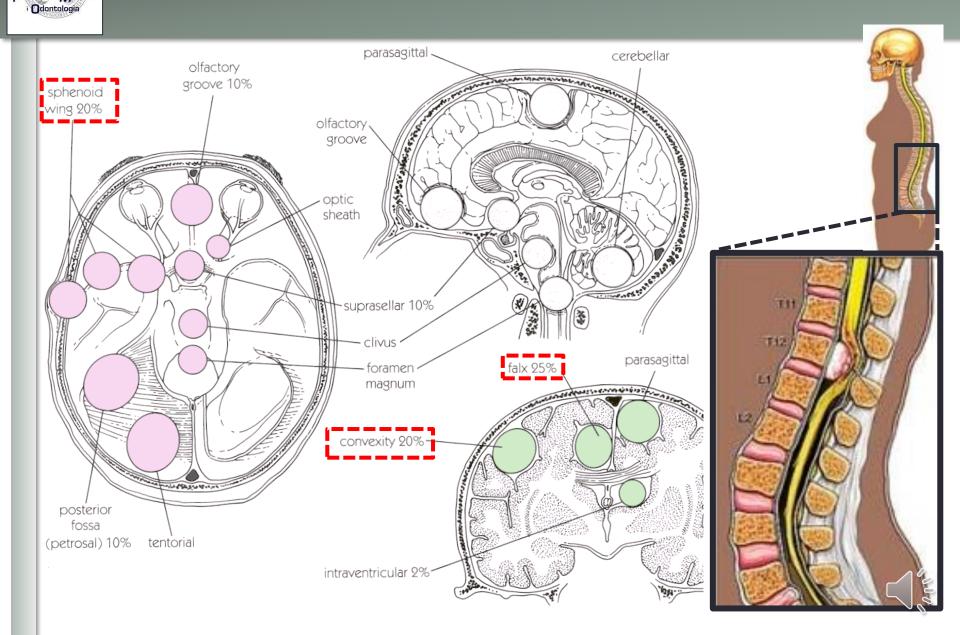
Trautman triangle

Torcula

Intraventricular

Spinal canal

VENTYERSTAT MENINGIOMAS: location / incidence

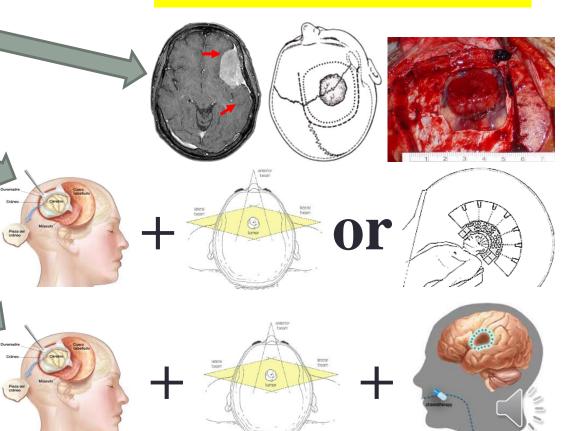


VNIVERSITAT D VALENCIA Facultato de Medicina Odontología

Meningiomas: treatment

- Clinical observation
 - Progressive and linear growth (4.94 cm³ / year)
 - ↑ Ø 0.37cm / year
 - 23% DO NOT grow
- Complete removal (tumour + dura + infiltrated bone)
 - 5-year survival 91%
 - 5-year recurrence 11-15%
- Partial removal = radiation therapy / radiosurgery
 - 5-year recurrence 37-85%
- Atypical (malignant) = radical removal + radiotherapy + chemotherapy
 - Recurrences common
 - Distant metastases possible
 - Prognosis bad

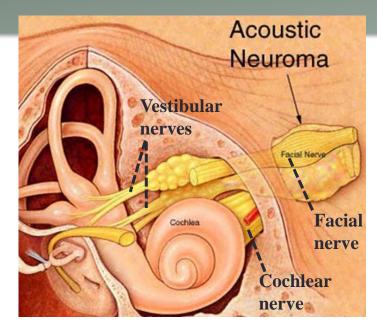
✓ Bad general condition
 ✓ Advanced age
 ✓ < 1 cm & asymptomatic
 ✓ Patient refuses to be operated

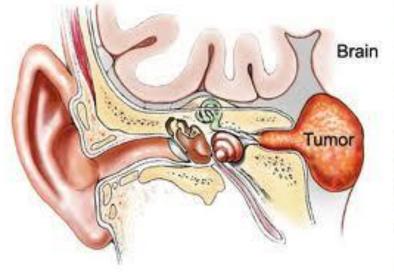




VNIVERSITAT D VALENCIA Facultar or Medicina SCHWANNOMA

- 8-10% intracranial tumors
- Origin: Schwann cells
 - Mostly superior vestibular nerve
- Benign •
- Neurofibromatosis type II (NF2) ↑ Incidence
 - Should be ruled out if bilateral Schwannoma at <40 years age



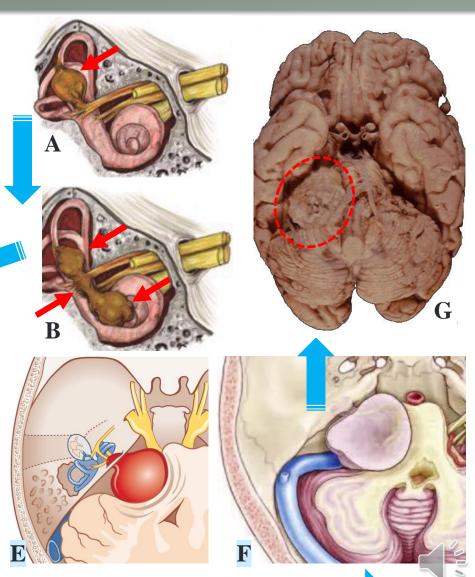


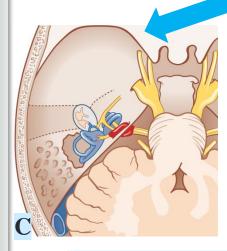


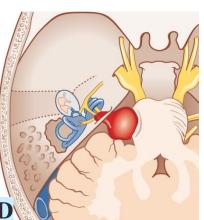


Vestibular schwannoma: clinical features

- Tinnitus 98%
- Sensorineural hearing loss 70%
- Balance disturbances 67%
- Headache 32%
- Facial paresthesia 29%
- Facial paresis 10%
- Diplopia 10%



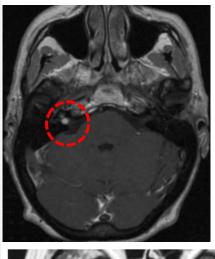






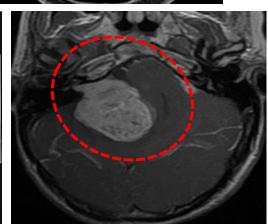
Vestibular schwannoma: MRI

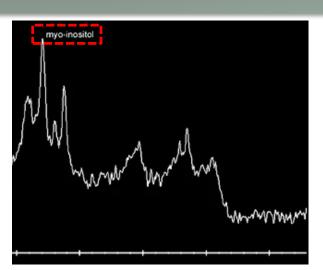
- Typical shape
- Spectroscopy: myo-inositol peak

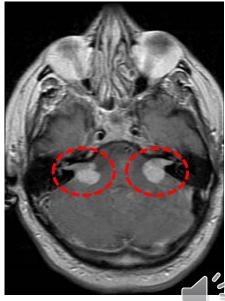










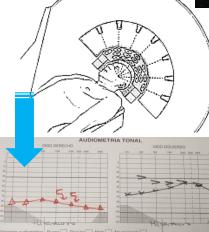


Neurofibromatosis type II



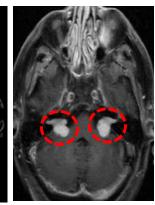
Vestibular schwannoma treatment

- Tumour < 2 cm, asymptomatic & age > 70 years ⇒ wait and see
 - Follow-up MRI monitor growth
- 2-3 cm or bilateral tumours = radiosurgery
- Tumour > 3 cm = surgery
 - Tumour remnant after surgery = radiosurgery
- Inoperable tumours chemotherapy: Bevacizumab

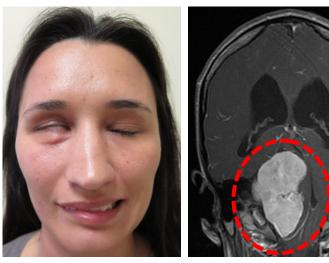


Progressive hear loss



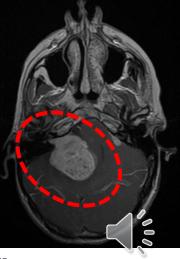


Radiosurgery





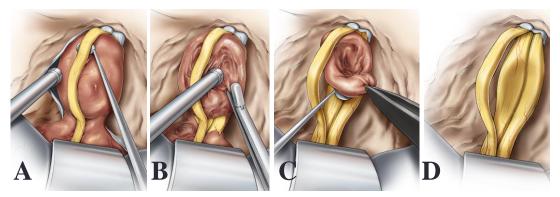
Surgery

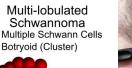




Vestibular schwannoma: hearing preservation

- Conditions
 - Serviceable pre-op hearing
 - Size > 2 cm
 - NOT neurofibromatosis
 type II = cochlear nerve infiltrated
- To allow cochlear implant
- Overgrowth Botryoid (Cluster)
- If contralateral tumour grows
- Brainstem auditory implant
 - For neurofibromatosis type II cases



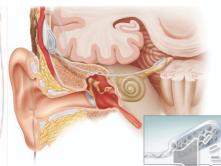






Cochlear implant



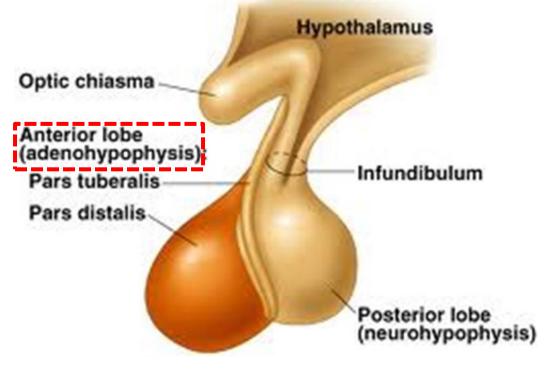


Brainstem auditory implant



PITUITARY TUMOURS

- 10-15% primary brain tumours
- 8.2-14.7 / 100,000 inhabitants
- Incidental finding 25%
- încidence 3rd-6th
 decades
- ↑ incidence
 - Women
 - MEN-1
- 95% adenohypophysis

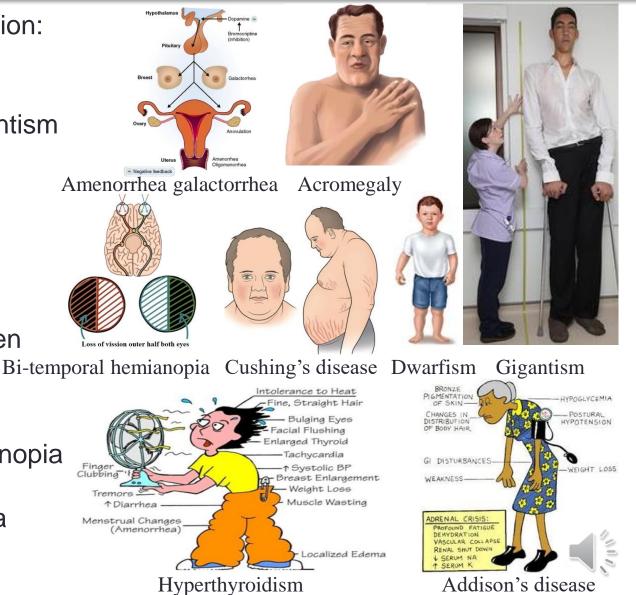


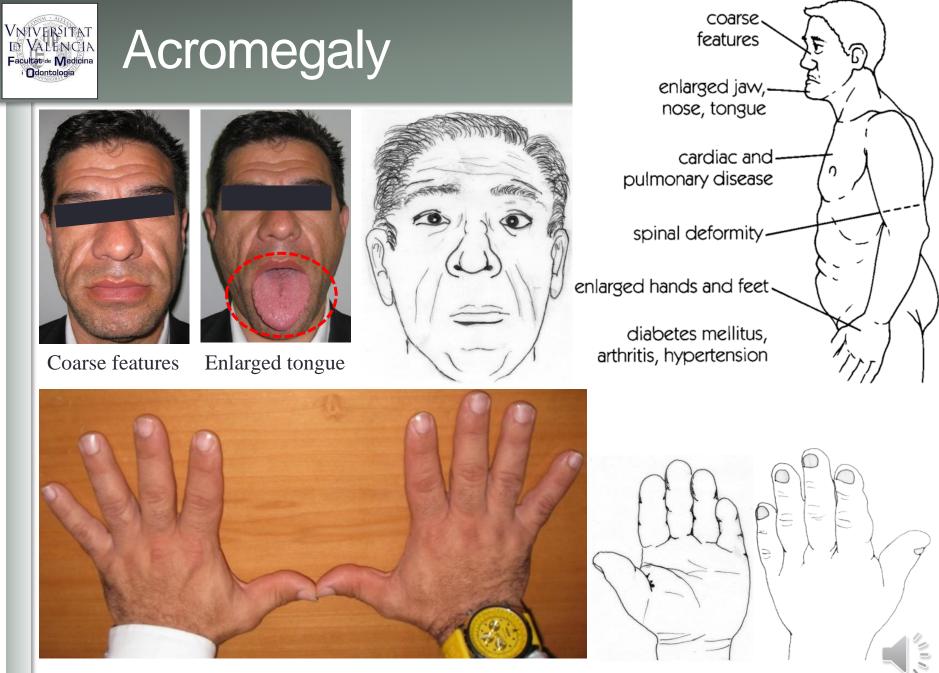




Clinical features

- Hormonal hyperfunction:
 - Amenorrhea and galactorrhea
 - Acromegaly / gigantism
 - Cushing's disease
 - Secondary hyperthyroidism
- Hypopituitarism
 - Addison disease
 - Dwarfism in children
- Mass effect:
 - Headache
 - Bi-temporal hemianopia
 - Moderate hyperprolactinemia (<150ng / ml)





Enlarged hands & feet



Muscle atrophy

Red cheeks

Moon facies

Buffalo hump

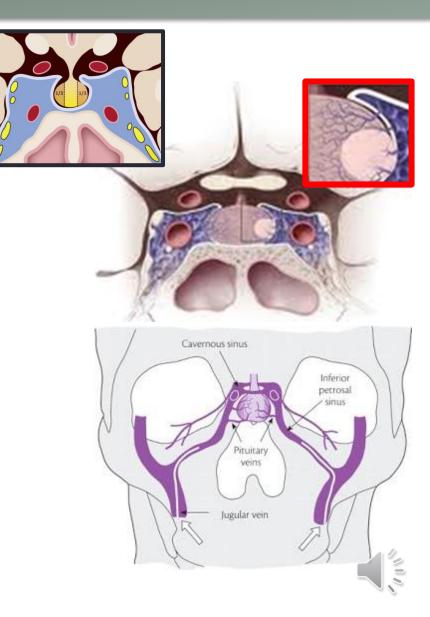
VALENCIA VAL

Types of diagnosis

- Endocrine
 - Baseline hormonal analysis
 - Hormonal dynamic analysis
- Radiological diagnosis (MRI)
 - Tumour size
 - Optic chiasm compression
 - Cavernous sinus invasion
 - Sphenoid sinus involvement
- On the affected side
 - Petrosal sinus catheterization
- Histological

Types of treatment

- Normalise endocrine function
 - Pituitary insufficiency from tumour / surgery
 - Correct excessive hormonal secretion
- Recover or stop visual deterioration
- Prevent recurrences

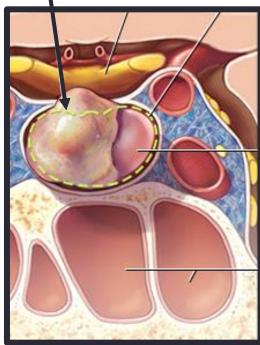


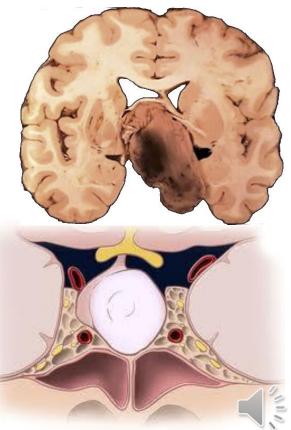


Pituitary tumour according to size

- **Microadenoma** < 1cm = hemi-hypophysectomy = cure
- Adenoma 1 cm = tumour removal = mild hypopituitarism
- Macroadenoma > 1 cm = complete hypopituitarism = full endocrine replacement will be needed
- Invasive adenoma = recurrence to be expected
 Microadenoma





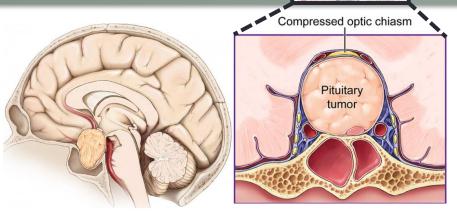


Macroadenoma

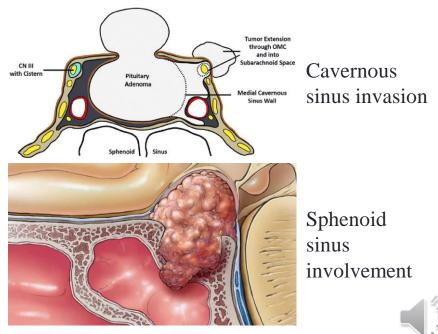


Pituitary tumours: extension

- Chiasm compression = visual loss
- Cavernous sinus invasion = complete tumour removal NOT possible
- Sphenoid sinus involvement = risk CSF leak
- Invasiveness = ↑chance recurrence



Chiasm compression

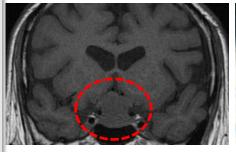


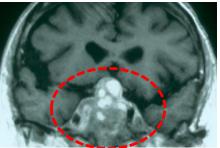


Suprasellar extension

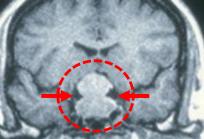
Diaphragm sella turcica

 The sellar diaphragm may make a waist that prevents transsphenoidal removal

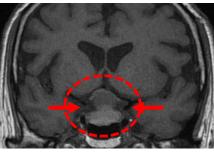




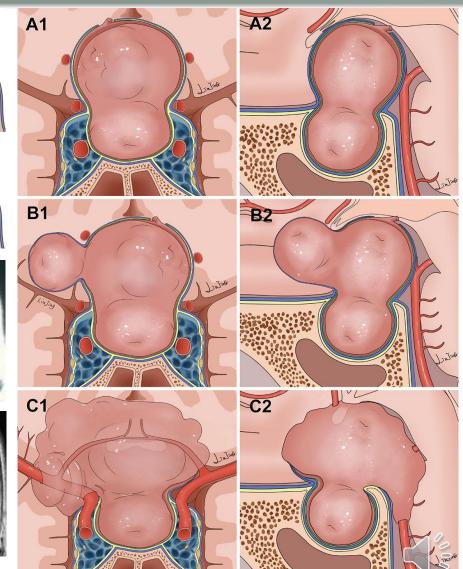
No waist



B



Middle tumour waist





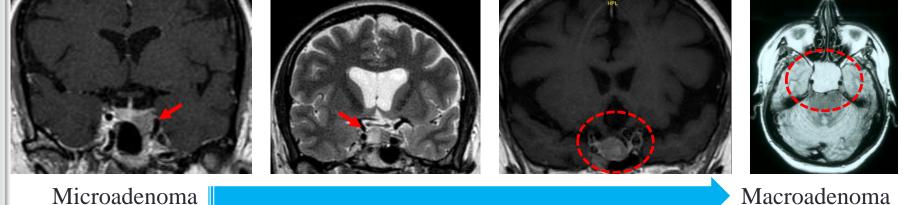
Pituitary tumours: cavernous sinus invasion (Knosp classification)

Grade 1 Grade 0 e longe Grade 2 Grade 3 Grade 4

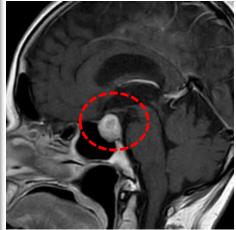


Pituitary tumours: MRI

 Will show size, suprasellar extension, cavernous sinus invasion, remaining pituitary gland, haemorrhages & route surgical removal

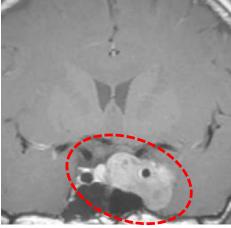


Microadenoma



Suprasellar extension

Sphenoid sinus involvement



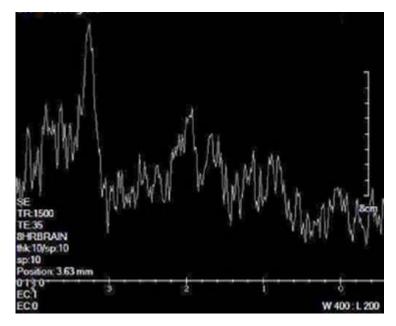
Cavernous sinus invasion





Pituitary tumours: MIR spectroscopy

- Significant reduction NAA & Cr peaks, moderate elevation Cho, and a small lipid and lactate peaks
- Not possible to differentiate between different pituitary tumours
- Helps to rule out craniopharyngioma & chordoma





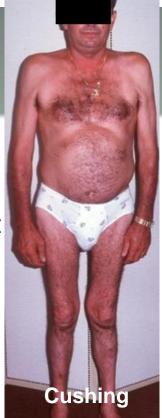


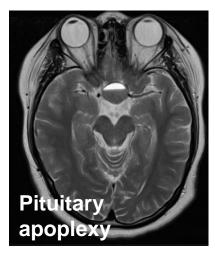
Pituitary tumours: indications surgical treatment

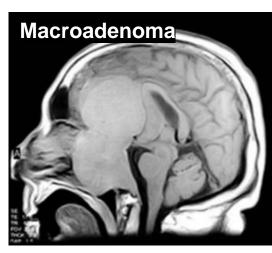
- Pituitary apoplexy → URGENT
- Macroadenoma with progressive mass effect
 - Except prolactinoma: Good response to medical treatment

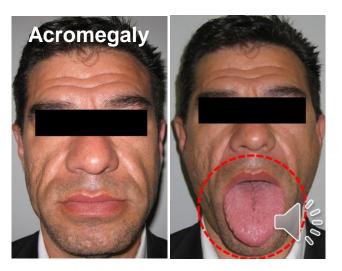
REMEMBER?

- Hyperfunctioning
 - Acromegaly, Cushing, secondary hyperthyroidism
- Medical treatment failure
- To obtain histological diagnosis (non-functioning)







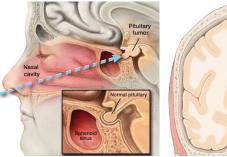


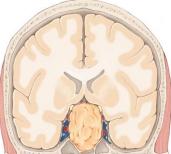


Transsphenoidal vs transcranial removal

Transsphenoidal

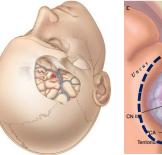
- Microadenomas
 - Hemi-hypophysectomy possible
- Macroadenomas with midline suprasellar growth
- No cavernous sinus invasion
- Better chance vision improvement
- Less aggressive

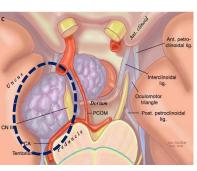


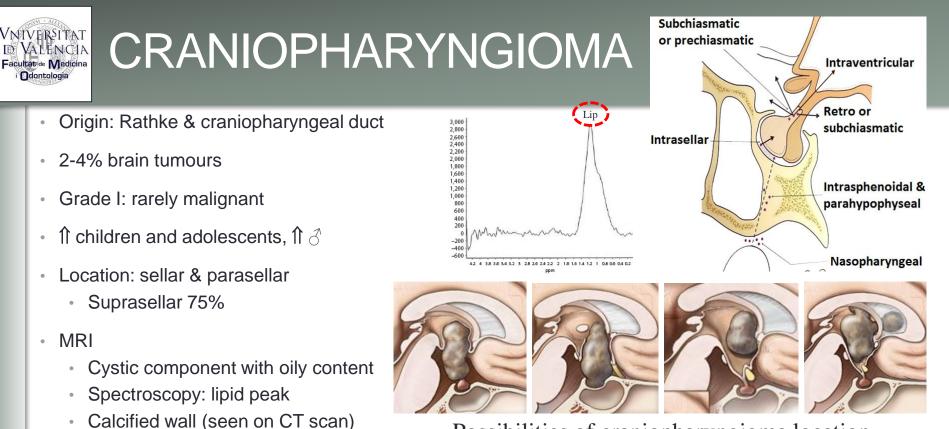


Transcranial

- All tumours, all sizes, all extensions
 - Cavernous sinus invasion
 - Sellar diaphragm waist
- Visual apparatus endangered
- Pituitary function not preserved usually
 - Used for larger tumours
- More aggressive



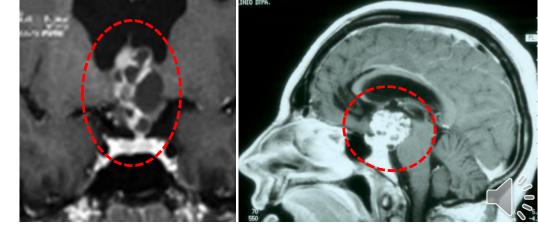




Clinical features

- Neuroendocrine dysfunction
 - Children = short stature + obesity
- Visual field loss
- Hydrocephalus
- Cognitive disorders
- Treatment: surgical
 - Adjuvant radiotherapy / radiosurgery
 - Hormonal replacement

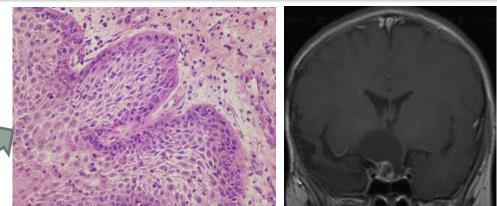
Possibilities of craniopharyngioma location

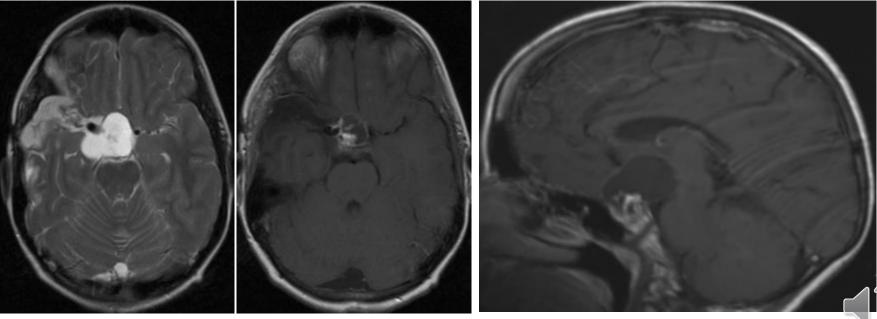




Craniopharyngioma: MRI

- Cysts common
- Pituitary stalk & third ventricle involvement
 - Invade third ventricle walls
 - Surgical removal = severe endocrinological deficits





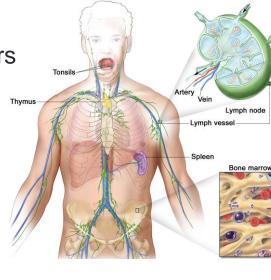


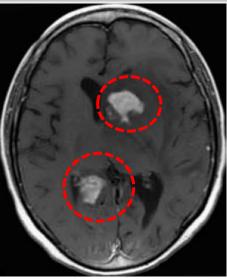
PRIMARY BRAIN LYMPHOMA

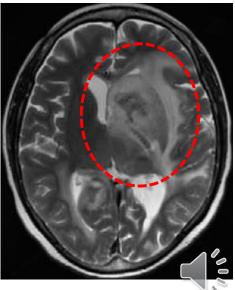
- 2% extra-ganglion lymphomas
- 1% intracranial tumours
- ① common in immunosuppressed patients & AIDS
- Multiple lesions frequent
- Lymph node & bone marrow involvement common
- Incidence ↑ age, peak 50-70 years
- Clinical features
 - Focal neurological deficit 70%
 - Cognitive changes 43%
 - Epileptic seizures 15-20%
 - Eye involvement 5-20%
- Possible origin by malignant cell progression around nerve roots



Ocular involvement in cerebral lymphoma







Bataille B, et al. Primary intracerebral malignant lymphoma: report of 248 cases. J Neurosurg 2000;92:261–266.

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Brain lymphoma: diagnosis & treatment

Diagnosis

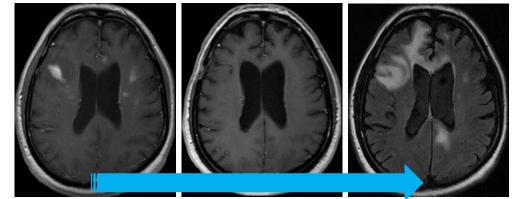
- MRI unspecific patterns
 - Spectroscopy ↑Cho & ↑↑Lip/Lac
- Stereotaxic brain biopsy a MUST
- Bone marrow biopsy to see involvement

Treatment

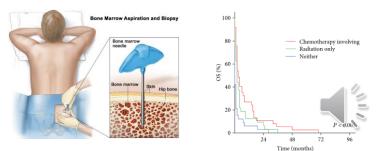
- Corticosteroids = rapid but temporary response
 - Not before biopsy for
 false negatives

Survival

- Ø treatment 1-3 months
- Surgical removal 1-4 months
- 30-50 grey whole cranial radiation therapy 12-18 months
- Chemotherapy + whole cranial radiotherapy 40-60 months



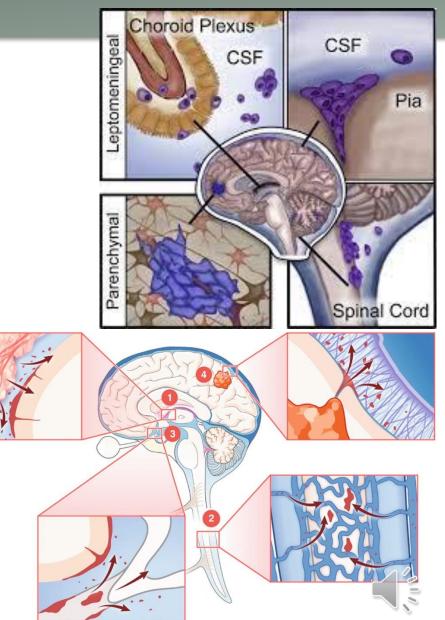
Effect corticosteroid treatment



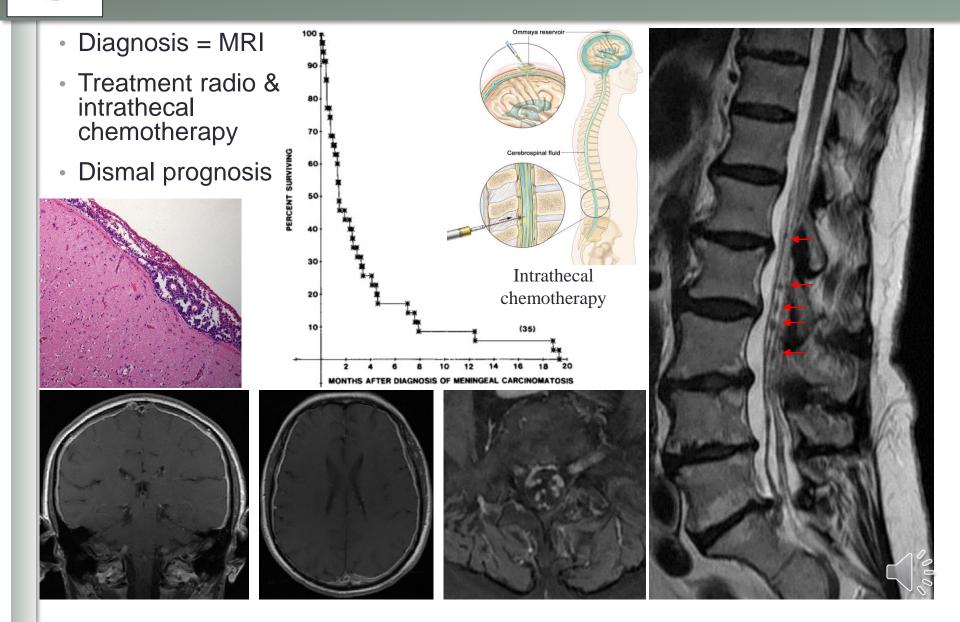
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MENINGEAL CARCINOMATOSIS

- Origin: tumour cells lining dura mater
 - Intracranial tumour metastasizing from CSF
 - Ependymoma, medulloblastoma, post-surgery in 14% malignant gliomas
 - Extracranial tumour that grows retrogradely through nerves and nerve roots
 - Parotid gland tumour
- Clinical features
 - Behavioural changes
 - Hydrocephalus
 - Altered level of consciousness



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