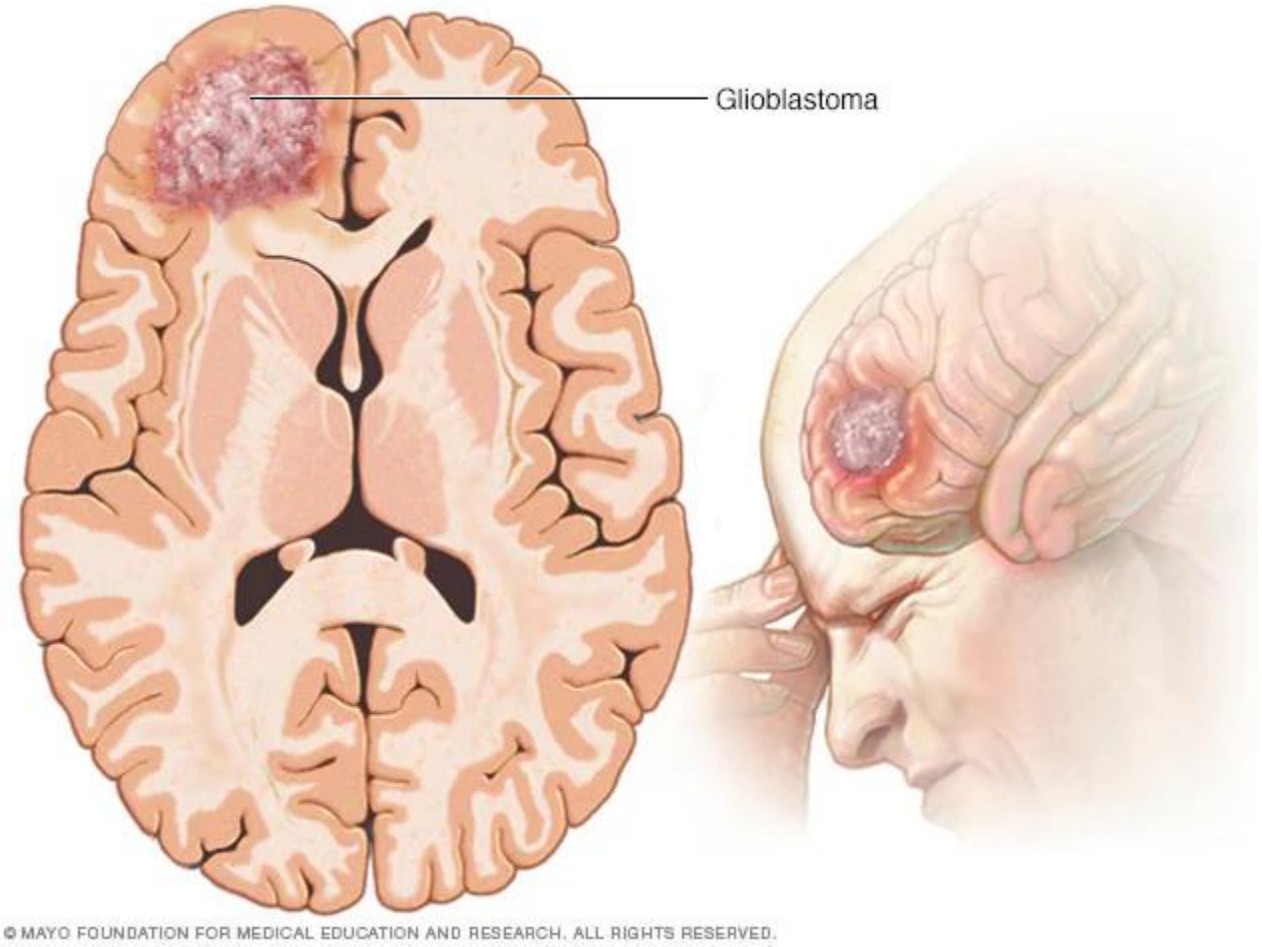
Neuro-Oncology



Dr. Pouria Adeli
Radio oncologist

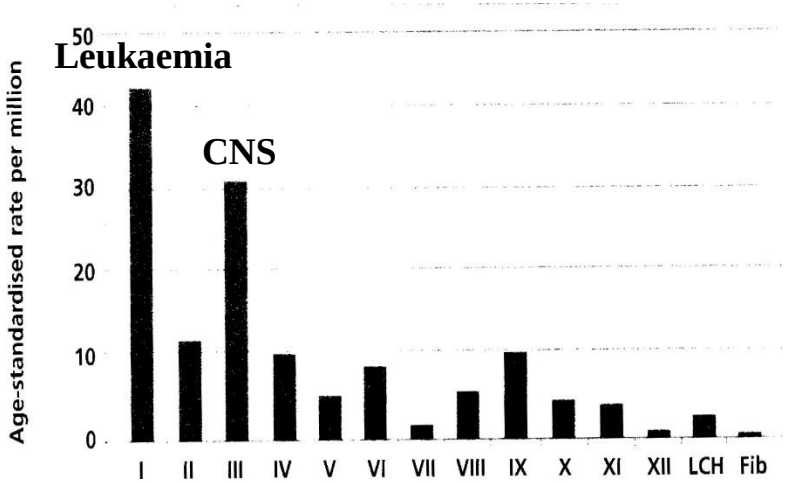
Neuro-Oncology

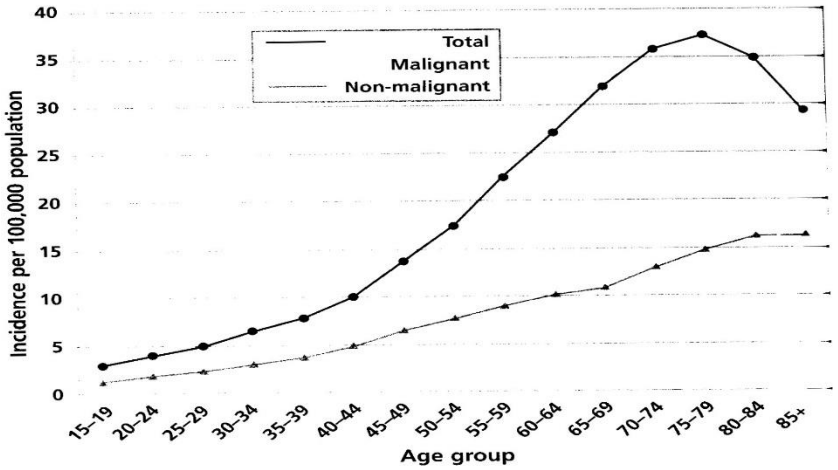
- Primary CNS tumours
- Metastatic disease
- Primary PNS tumours
- CNS complications of cancer treatment
- Paraneoplastic conditions

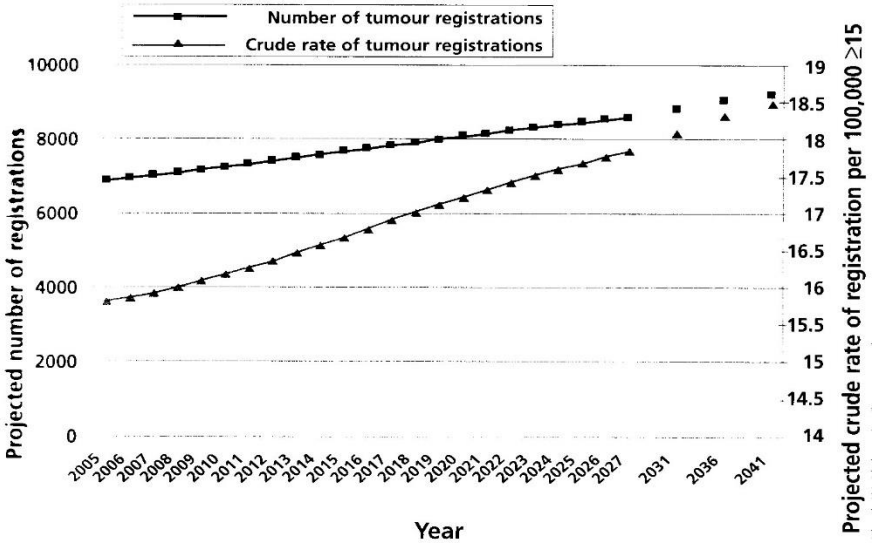
Neuro-Oncology

‘Brain Tumour’ is **not** a diagnosis

Primary CNS Tumours - Who?





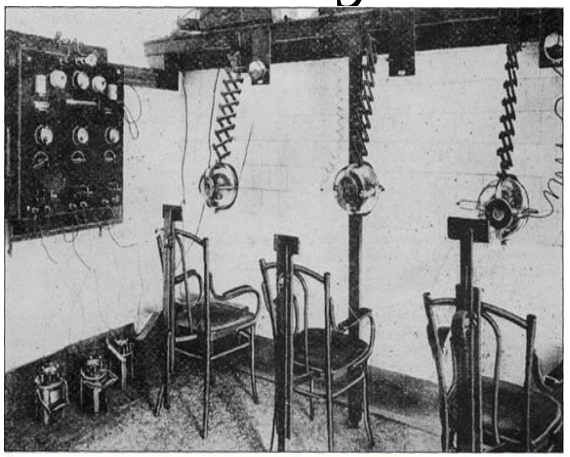


- **Uncommon, not rare**
- **~5% of all ‘cancers’**
- **Underestimated in cancer registries**
- **Increasing in incidence**

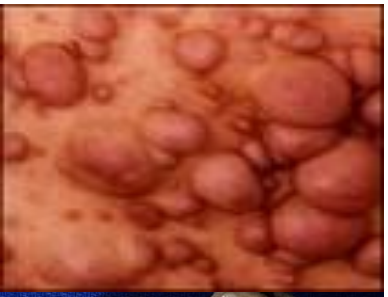
- **What is ‘benign & malignant’?**

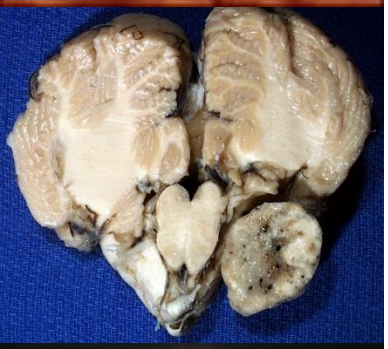
Primary CNS Tumours - Why?

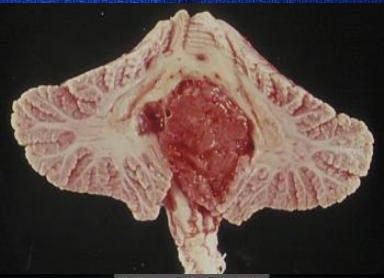
- Majority are ‘sporadic’
- Link to ionising radiation
- Link to immunosuppression in PCNSL
- Link to familial cancer syndromes

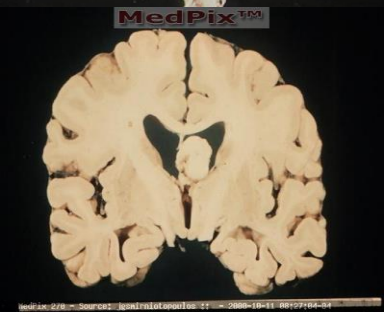


Primary CNS tumours – genetic predisposition [The majority of tumours are sporadic]





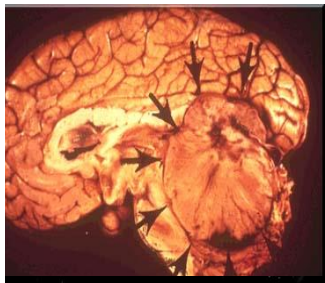


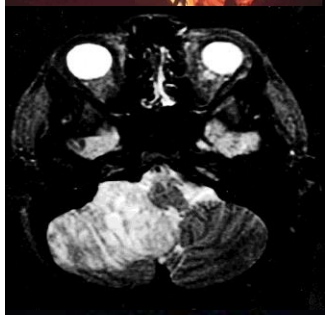


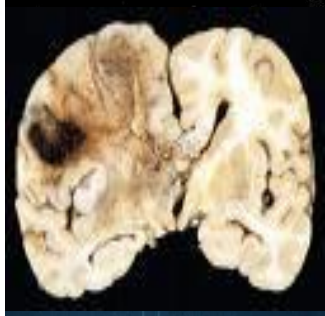
Syndrome	Gene	Chromosome	Nervous system
Neurofibromatosis type 1	NF1	17q11	Neurofibromas, malignant nerve sheet tumour, optic nerve gliomas, astrocytoma
Neurofibromatosis type 2	NF2	22q12	Bilateral acoustic schwannomas, multiple meningiomas, astrocytomas, glial hamartomata
von Hippel–Lindau Syndrome	VHL	3p25	Haemangioblastomas
Tuberous sclerosis	TSC1 TSC 2	9q34 16p13	Subependymal giant cell astrocytoma, cortical tubers
Li–Fraumeni	p53	17p13	Astrocytomas/primitive neuroectodermal tumour
Cowden's disease	PTEN	10q23	Dysplastic gangliocytoma of the cerebellum
Turcot's syndrome	APC HMLH1 HPSM2	5q21 3p21 7p22	Medulloblastoma Glioblastoma
Naevoid basal cell carcinoma syndrome (Gorlin syndrome)	PTCH	9q22	Medulloblastoma

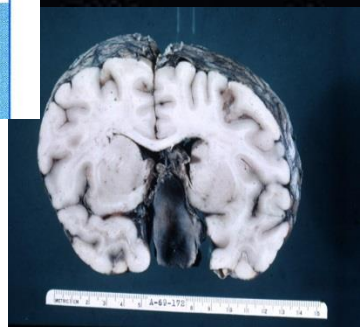
MEN type 1

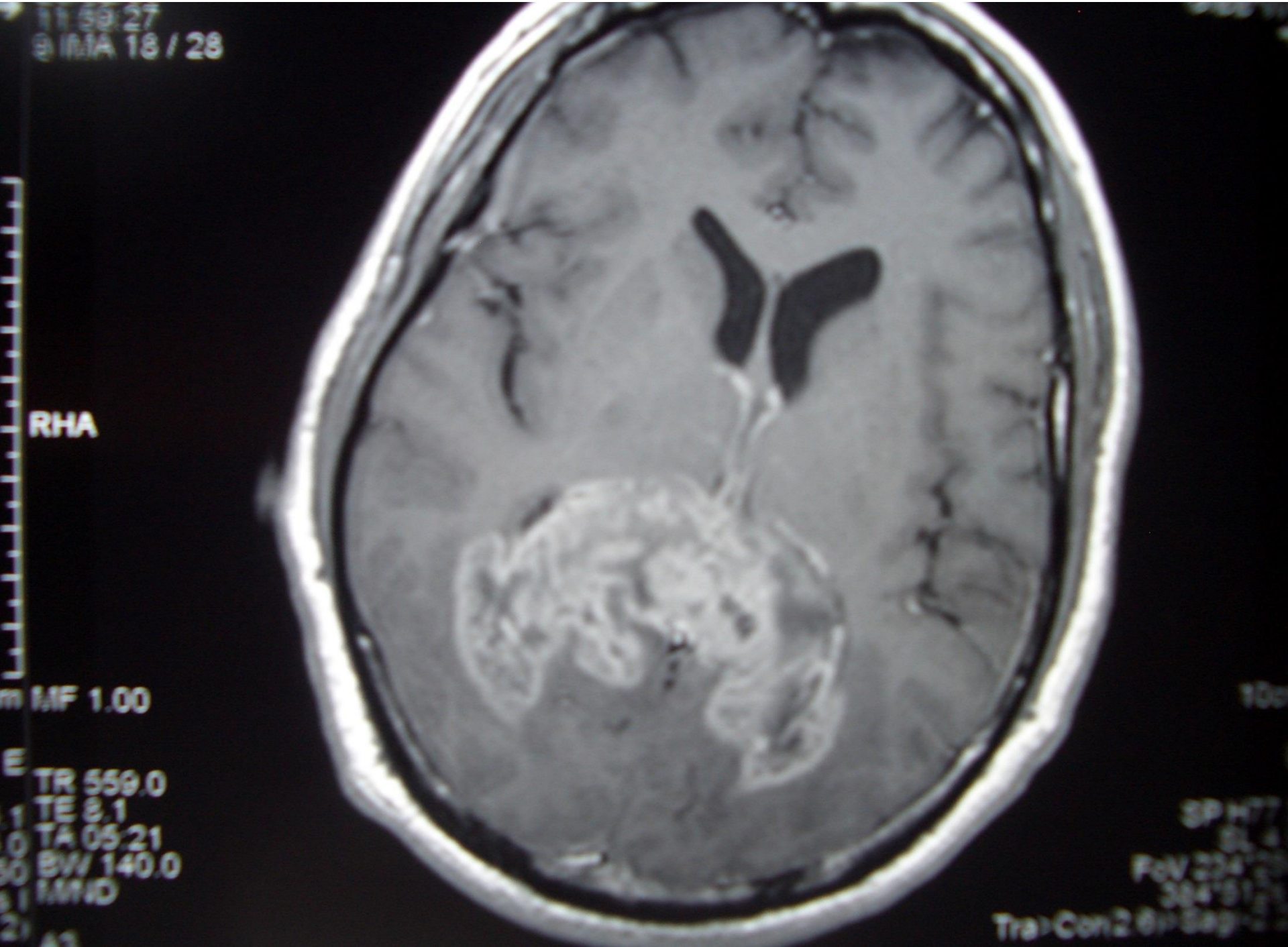
'Brain Tumour Families'







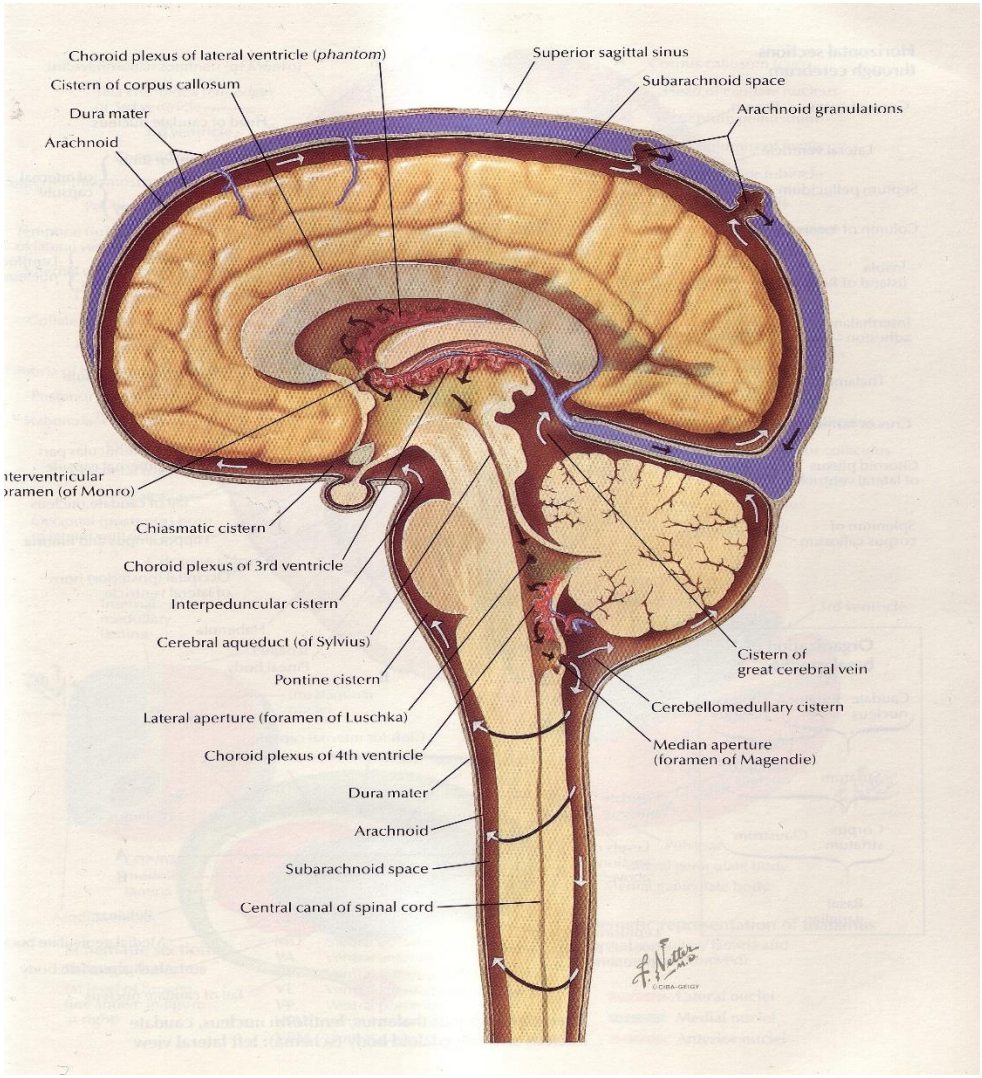



IMA 18 / 28
RHA
MF 1.00
TR 559.0
TE 8.1
TA 05:21
BW 140.0
MMD

Neuro-Oncology
Metastatic Disease

- Leptomeningeal Metastases
- Brain Metastases
- Spinal Cord [& cauda equina] compromise

Leptomeningeal Disease
‘Malignant Meningitis’



Neuro-Oncology
Leptomeningeal Disease

- PRIMARY TUMOURS OF CNS

  PNETs, GCTs, Ependymoma, Oligodendroglioma, GBM

- SECONDARY INVOLVEMENT

  Leukaemia / Lymphoma
  Melanoma
  Lung Cancer [esp small cell]
  Breast Cancer*
  Prostate Cancer*

Neuro-Oncology
Leptomeningeal Disease

- Symptoms can be non-specific and variable
- Mainly due to effects of tumour on nerve roots, direct infiltration of cord & brain or hydrocephalus
- Most have symptoms/signs at more than one site

  Headache

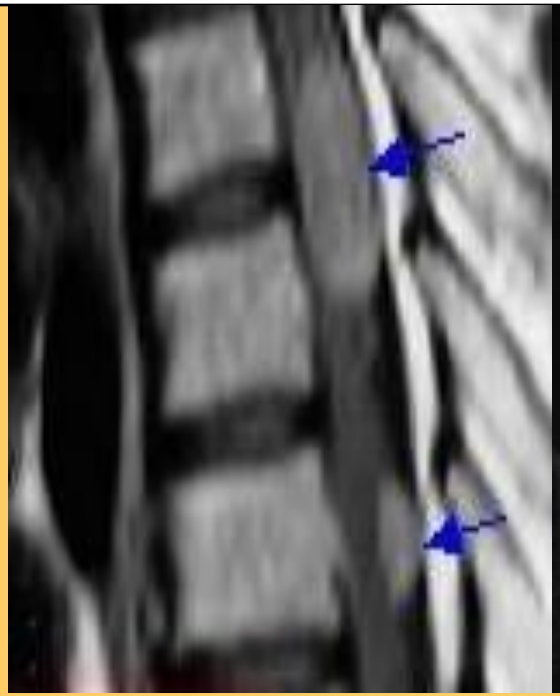
  Cranial or spinal nerve pain/dysfunction

  Nausea/Vomiting

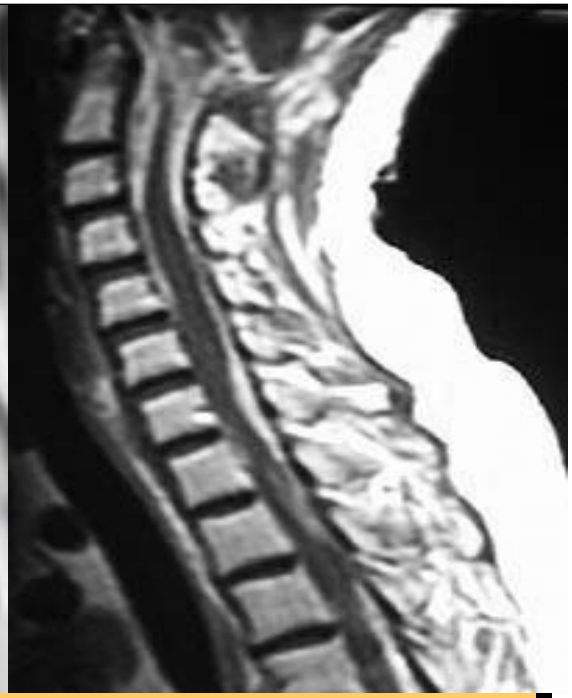
  Weakness
- Early recognition important

Neuro-Oncology
Leptomeningeal Disease

- Imaging shows



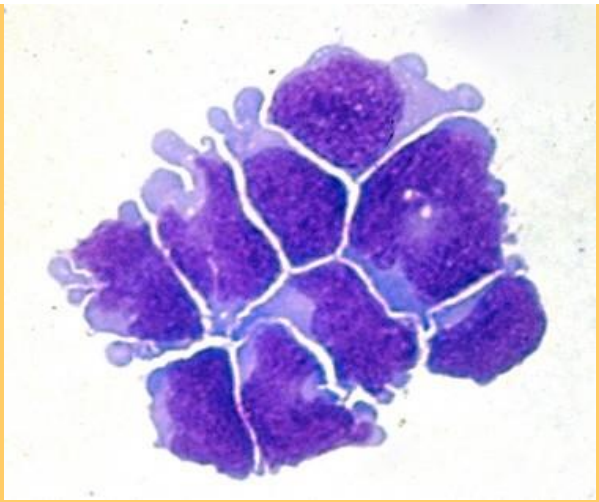
Subarachnoid masses



zuckerguss

Neuro-Oncology
Leptomeningeal Disease

CSF Cytology



LP not always safe [or appropriate]

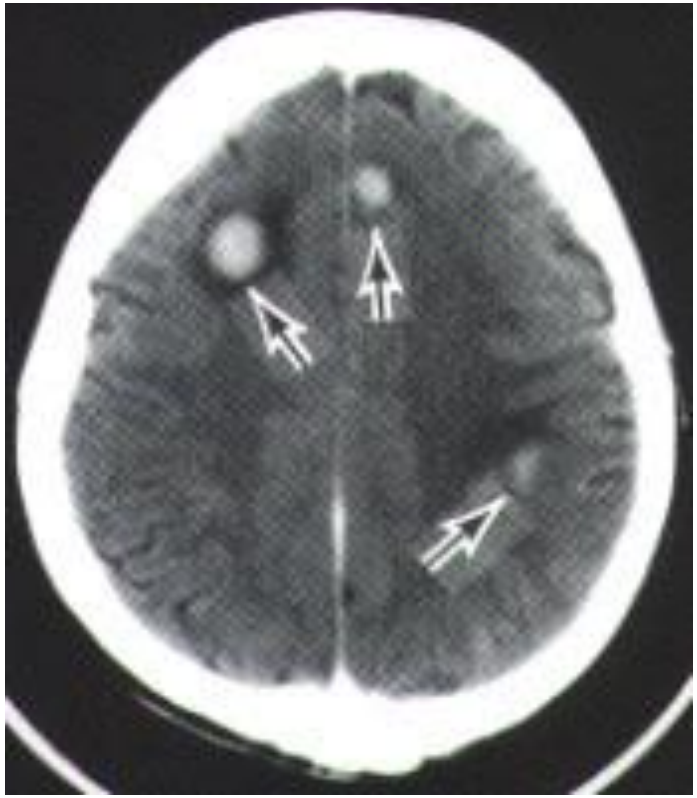
Only ~50% pickup with 1 sample [high false negative]

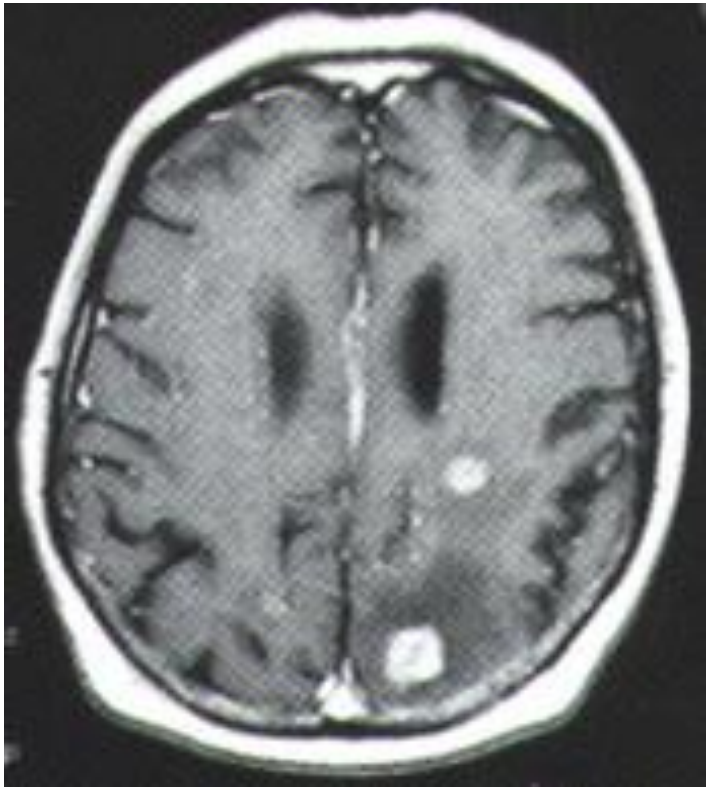
Complementary to MR imaging

Neuro-Oncology
Leptomeningeal Disease

- Treatment depends on patient & tumour factors
- Traditionally a terminal event in solid tumours
- Can still be cured in some chemo/radiosensitive tumours
- Will be seen increasingly in younger patients without evidence of systemic disease as newer agents control disease outside of the blood brain barrier i.e. sanctuary site disease

Neuro-Oncology
Brain Metastases



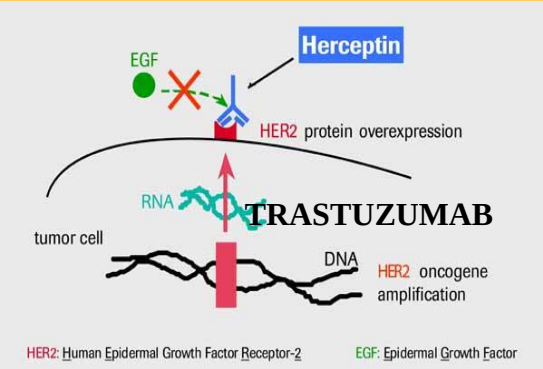


Neuro-Oncology
Brain Metastases

- ~ 10X more common that primary CNS tumours
- Most common in terminal phase of disease
- Historically steroids +/- whole brain RT
- Can be presenting feature [5%+] of cancer – 50% of time primary found [usually lung]
- Again changing natural history – are we starting to see a new group of patients?

Neuro-Oncology
Brain Metastases

The Herceptin 'problem'



- Increase in symptomatic brain mets since Herceptin
- 35% systemic disease stable or still responding
- Unmasking of brain mets that would have remained silent prior to death from systemic disease
- Cohort of young women who are otherwise well, of good performance status & no active disease outside of CNS
- Is palliative whole brain RT good enough?

Neuro-Oncology
Brain Metastases

Usual suspects [in descending order]

- Lung
- Breast
- Melanoma
- Renal
- Colorectal

Neuro-Oncology
Brain Metastases

Symptoms

- About 2/3 symptomatic at some point
- Typically slow, but can be acute e.g. bleed
- Seizures uncommon < 20%
- Raised ICP – headache, confusion, vomiting, lethargy
- Focal features – hemiparesis,visual field defects, ataxia

Neuro-Oncology
Brain Metastases

Investigations

- CT
- MR [20% solitary lesions on CT are multiple]
- Systemic investigations [if unknown primary]
- Biopsy if indicated

Neuro-Oncology
Brain Metastases

Treatment

- Patient factors
- Tumour factors
- Usually palliative

Neuro-Oncology
Brain Metastases

Treatment

- Resection
- Radiosurgery
- Adjuvant whole brain RT [prophylactic in SCLC]
- Whole Brain RT
- Best Supportive Care
- ? Chemotherapy

Neuro-Oncology
Brain Metastases

Treatment

- Resection of solitary [1 – 3] metastasis
  - Large symptomatic metastasis/metastases causing mass effect or hydrocephalus
  - May improve survival – studies show +ve benefit, overview no overall advantage over WBRT, but fewer neurological deaths, increased time patient remains independent, no significant additional toxicity
  - Risk of bleeding/bleeding e.g.melanoma
  - Radio resistant tumours e.g. melanoma, renal cell & colorectal
  - Selected patients only
  - Beware post fossa mets – some strong suggestions of increased leptomeningeal mets – up to 35%

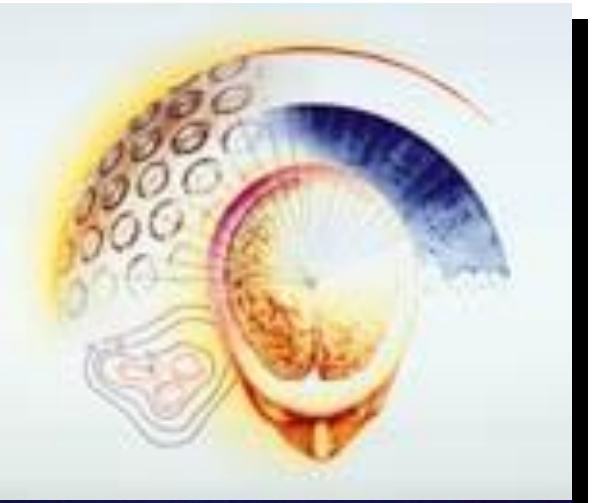
Neuro-Oncology
Brain Metastases

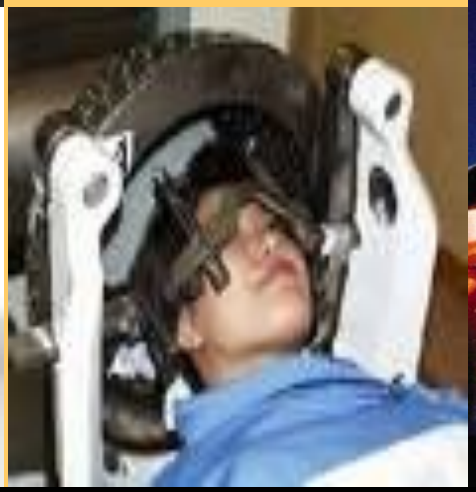
Treatment

- Radiosurgery
  - Single metastasis [1 – 8]
  - Never tested head to head with surgery, but considered same efficacy
  - Care with post-treatment oedema

Skull base tumours
Gamma Knife

4,8,14 or 18mm





Skull base tumours
LinAc-based SRS

Neuro-Oncology
Brain Metastases

Treatment

- Adjuvant whole brain RT – after surgery/radiosurgery?
- EORTC trial closed end of 2007
  - 1-3 mets surgery/SRS
  - Stable systemic disease & good PFS
  - Not brainstem/leptomeningeal/SCLC/lymphoma/leukaemia/myeloma
  - Max diam 3.5cm single [2.5cm multiple]
  - Randomised to no further treatment or 30/10 WBRT
  - Primary outcome survival, but significant QOL data

Neuro-Oncology
Brain Metastases

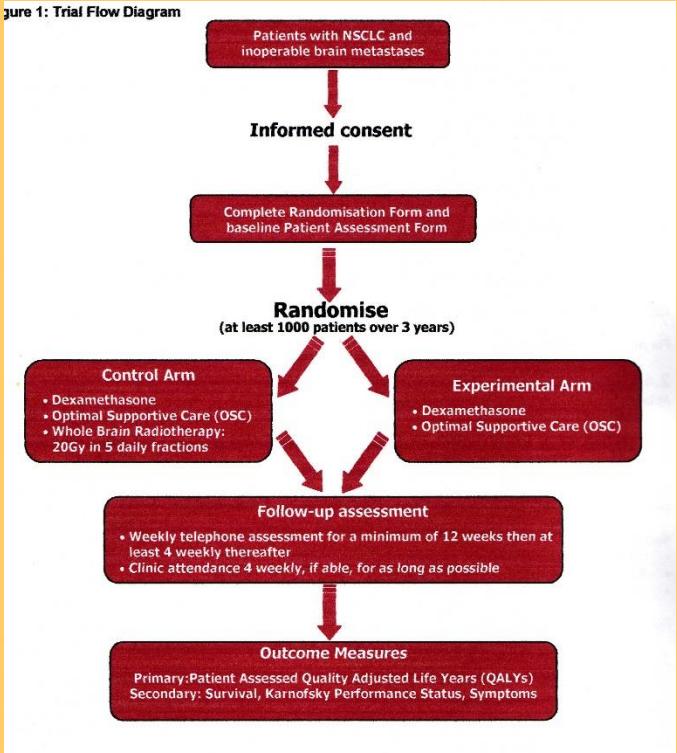
Treatment

- Prophylactic whole brain RT in SCLC
  - LSD [since 1999] 60% brain mets > 30% @ 3 yrs
    OS 21% v 15% @ 3 yrs
  - ESD [EORTC 2007] 40% > 14% @ 1 year
    OS 27% v 13% @ 1 year

Neuro-Oncology
Brain Metastases

Treatment

- Whole Brain RT v Best Supportive Care in NSCLC [QUARTZ] LU24



Neuro-Oncology
Brain Metastases

Conclusions [from my bit….]

- Likely increasing numbers of patients with metastatic CNS disease
- Younger & fitter [& more demanding] than before
- Need better strategies for treatment i.e. optimise therapeutic ratio [max control v min effect on QOL]