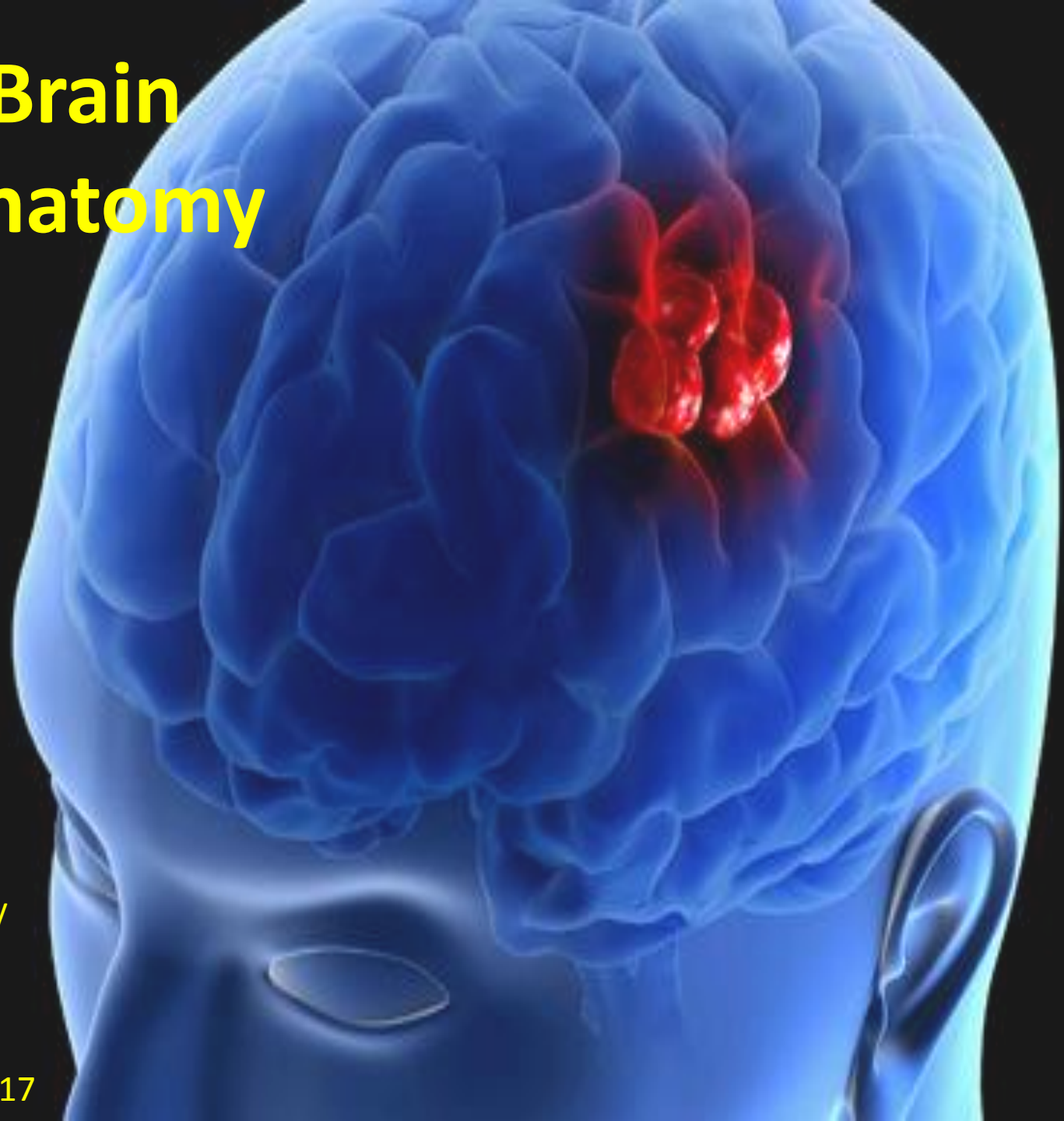
An Introduction to Brain Tumours and Neuroanatomy



Dr. Ruman Rahman
Assistant Professor of Molecular Neuro-Oncology
University of Nottingham

ruman.rahman@nottingham.ac.uk

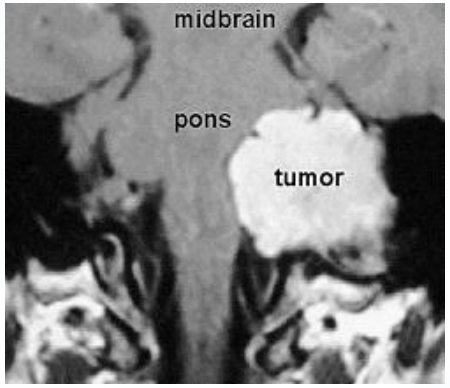
BTC Nurse & AHP Study Day – Birmingham, 19.05.17

Key Learning Objectives

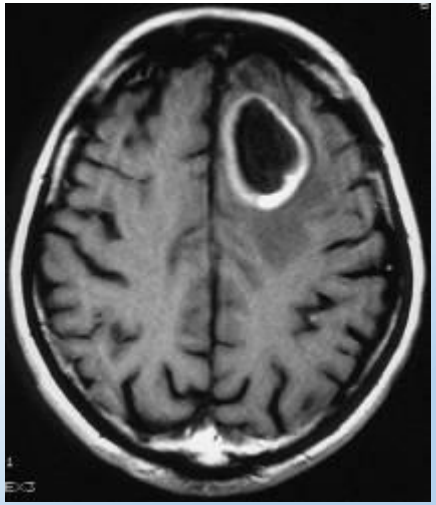
- Be able to describe the common clinical presentations of intra-cranial tumours.
- Describe the most common primary brain tumours, their relevant neuroanatomy and their prognoses.
- List the common tumours (from outside the brain) which metastasise to the brain

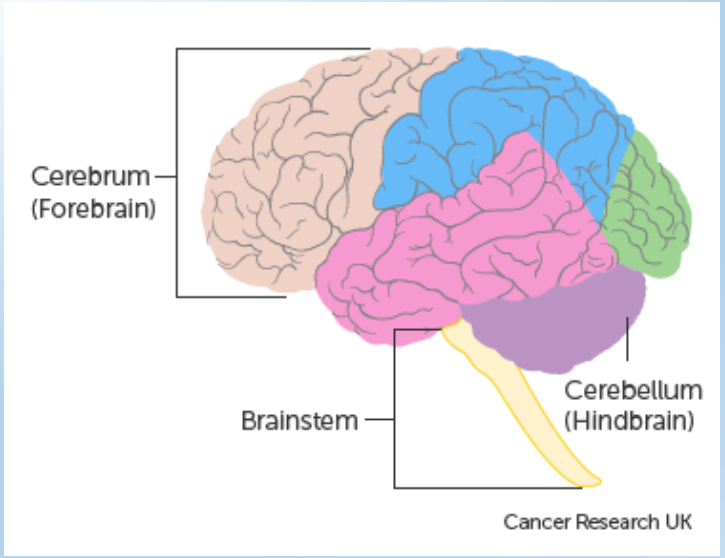
Tumours affecting the CNS

- EXTRINSIC
  - Primary tumours arise from bone, meninges (dura), nerve.
  - May be metastatic from malignancy elsewhere



- INTRINSIC
  - Primary tumours arise from cells normally comprising the brain or spinal cord



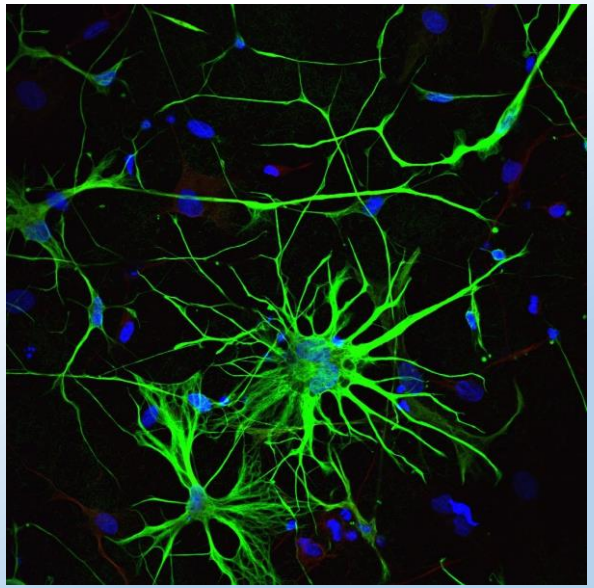


CNS Neural Cell Types (gives rise to intrinsic CNS tumourS)

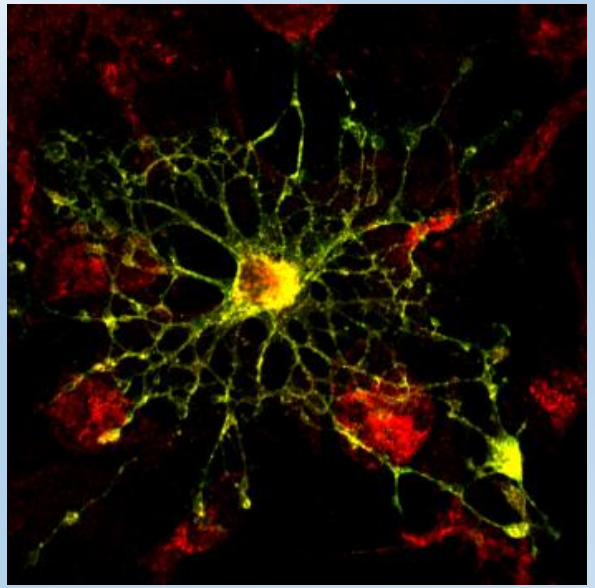
Neurons

Glia

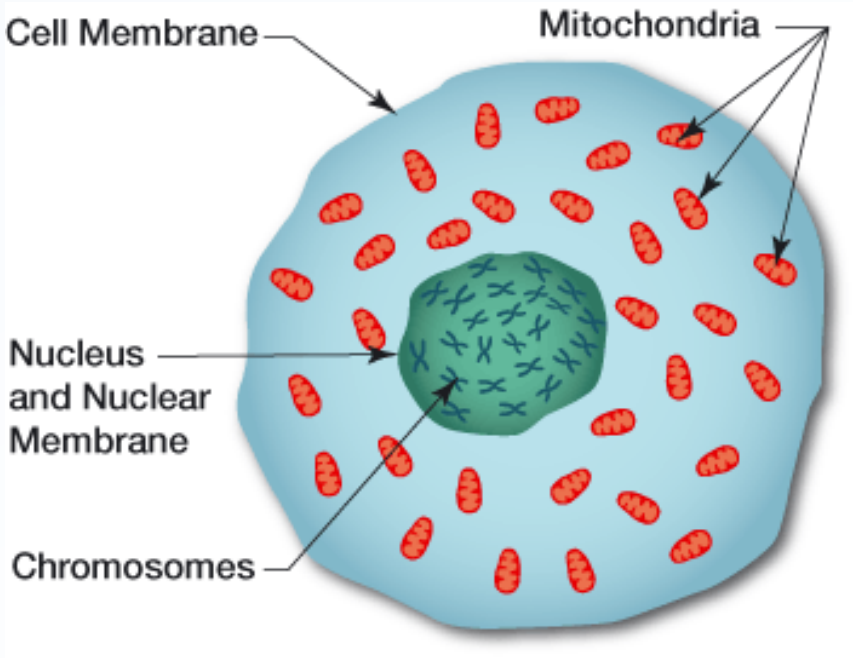
Astrocytes

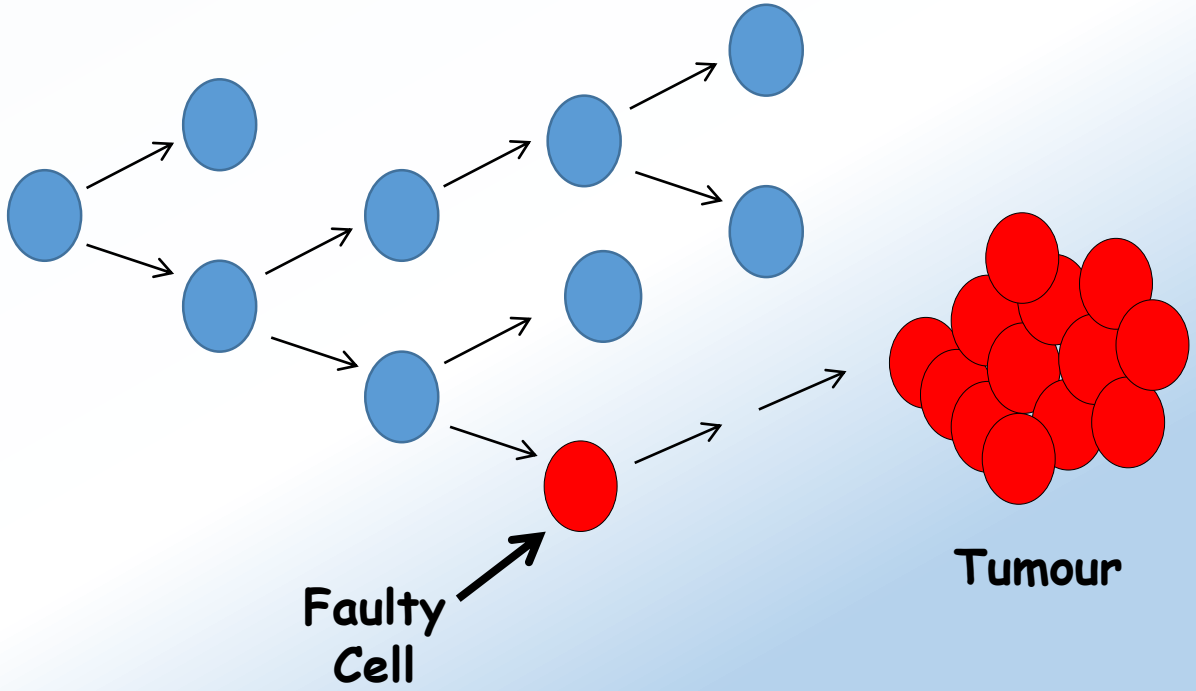


Oligodendrocytes



Brain cell



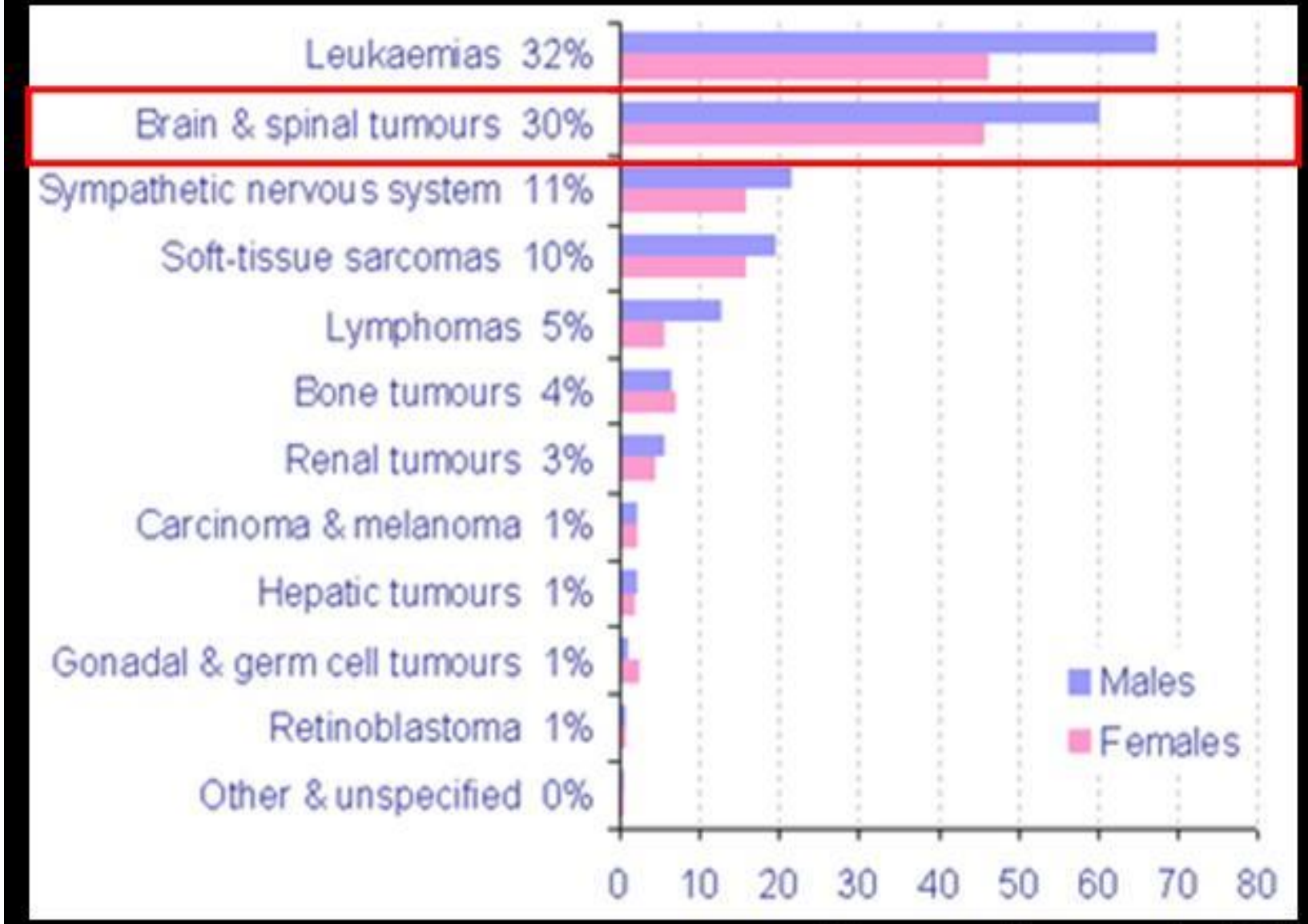


In cancer, one brain cell becomes faulty (sufficient number of mutations) and grows out of control to produce a tumour

Not as rare as you think.....

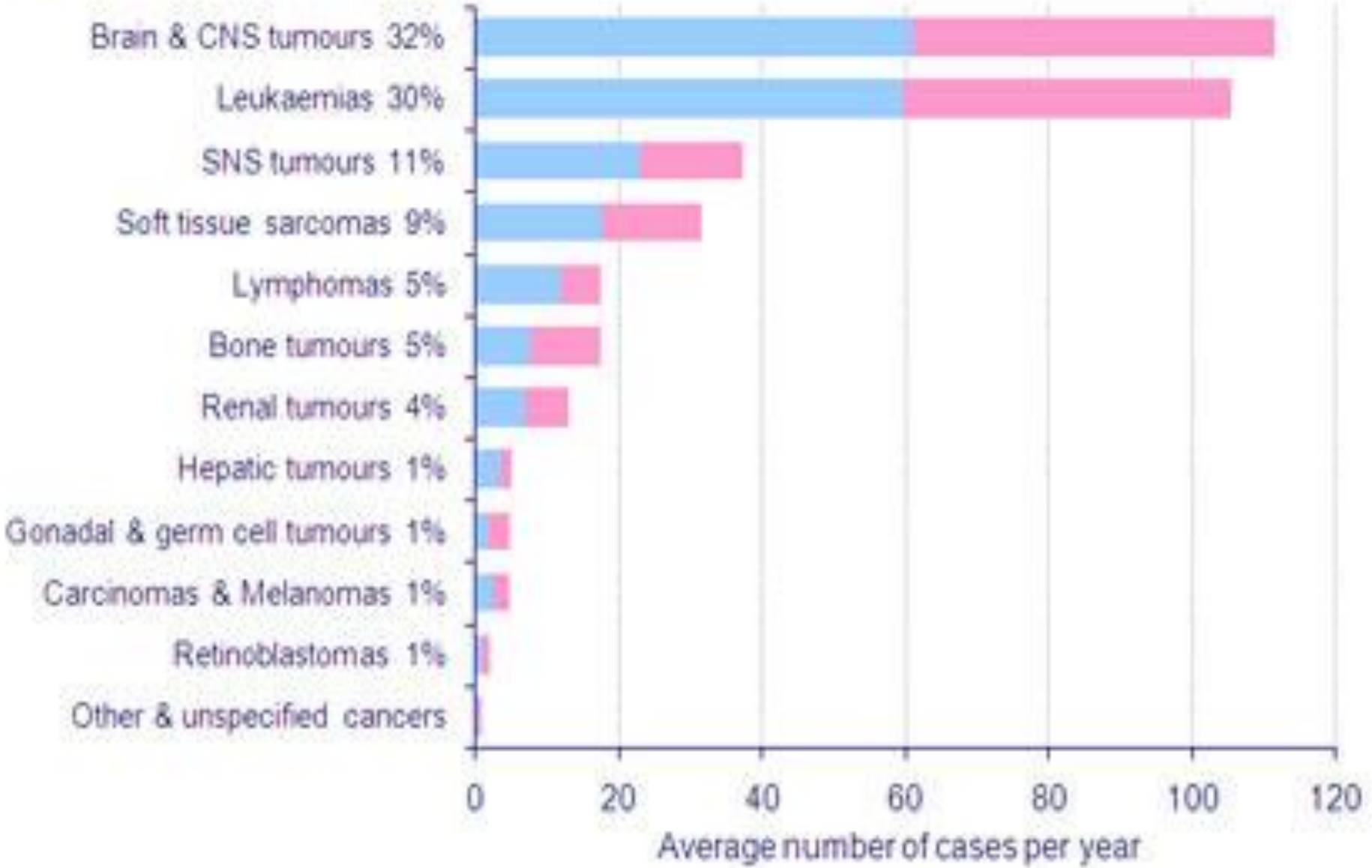
- Increasing incidence – 10 000 primary tumours per year in UK
- 5000 people per year die in the UK
- Second commonest group of tumours after leukaemias in children, leading cause of death
- Sixth commonest group of tumours in adult
- 10.7% of cancer deaths under 45yrs
- 13% of patients dying from cancer have CNS involvement

- Most common solid tumour in children



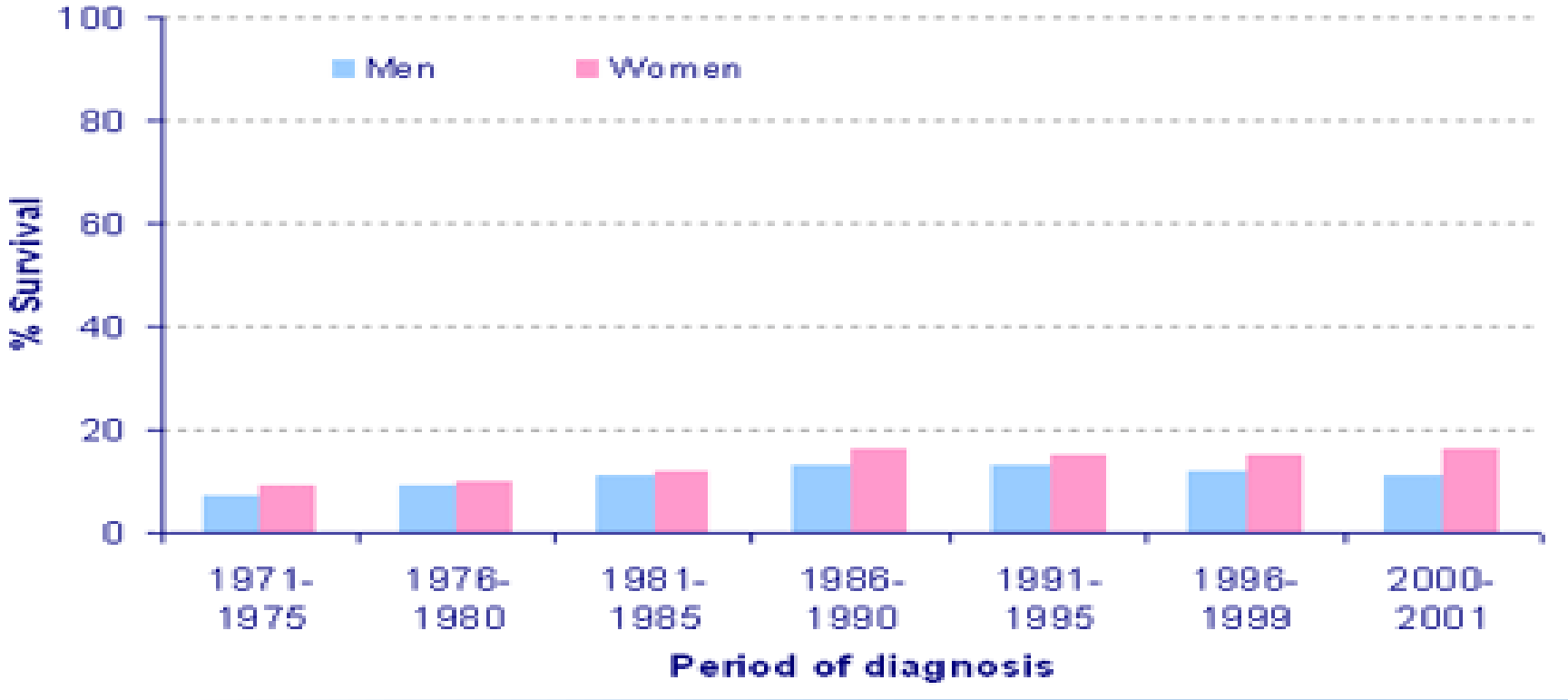
(Cancer Research UK)

Figure 2.1: Average annual number of deaths in children previously diagnosed with cancer, 0-14 years, GB 1996-2005



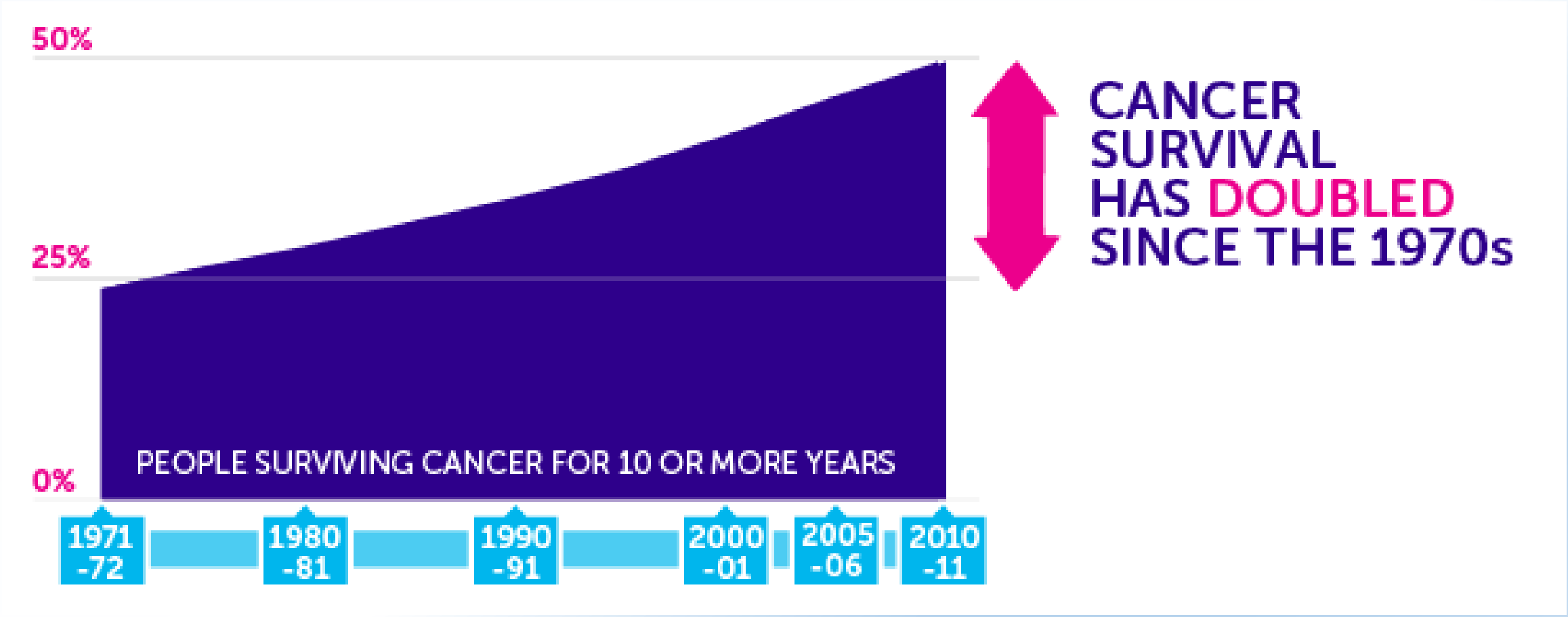
Overall 5-year survival for adult brain cancer is also poor

Figure 3.2: Five-year age-standardised survival for brain cancer by sex for patients diagnosed in England and Wales during 1971-1999

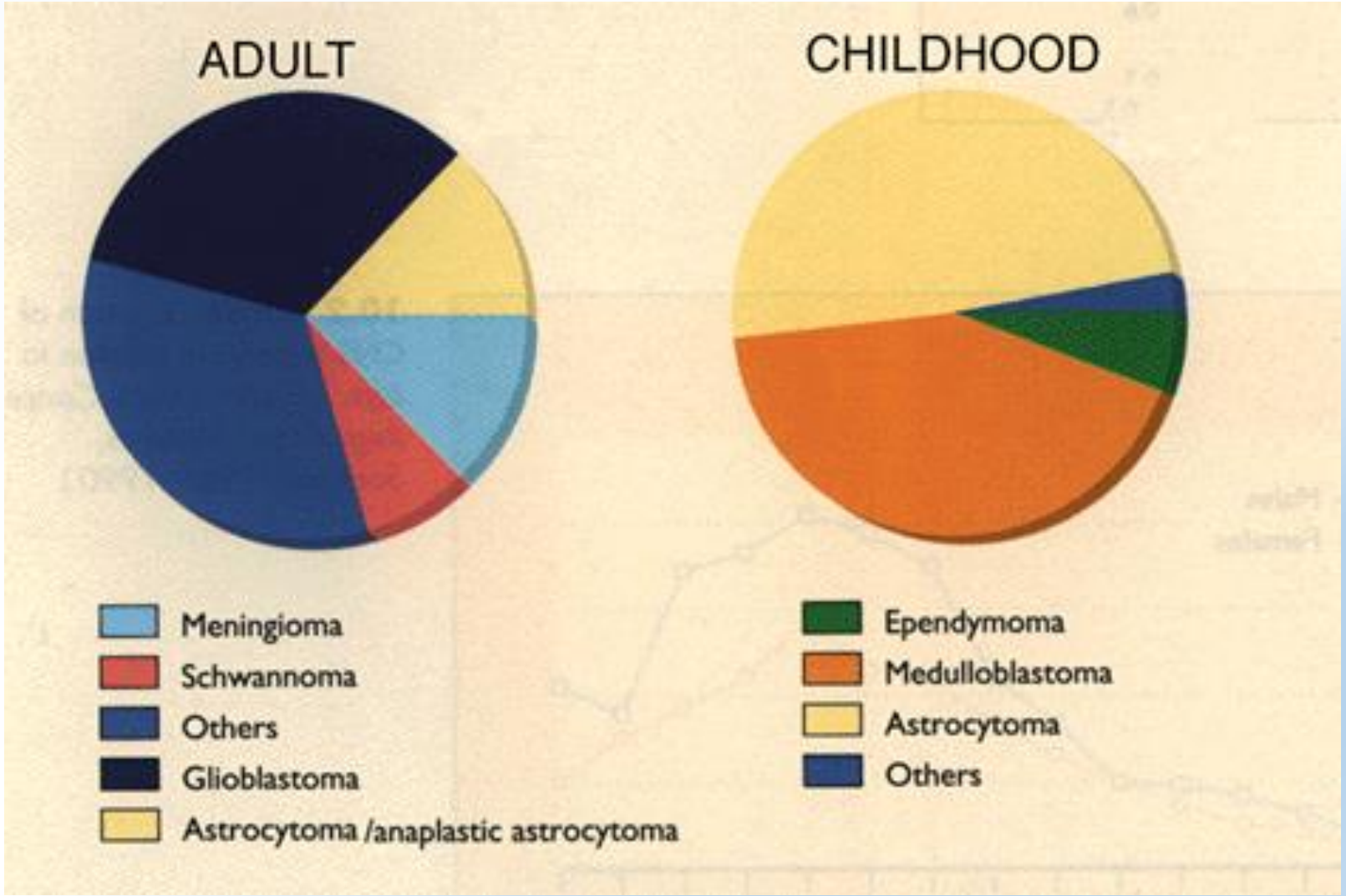


(Cancer Research UK)

But the general trend for all cancers is increased survival



Tumour Incidence



Aetiology

- **<u>Unknown despite considerable research effort</u>**
- Links to mobile phone usage scientifically unproven as yet.
- Childhood Irradiation
- Genetic Factors
  - NF1 and NF2 genes, Von Hippel Lindau syndrome

Childhood brain cancer – a developmental biology disorder

Adult brain cancer – multi-step progression, acquisition of mutations

Fallacy of causation

“The most dangerous job in the United Kingdom is not, as expected, bomb disposal expert, steeplejack, or Formula One racing driver but…..

……having a role in one of the United Kingdom's most well known soap operas.”

Death rates of characters in soap operas on British television: is a government health warning required?
BMJ 1997

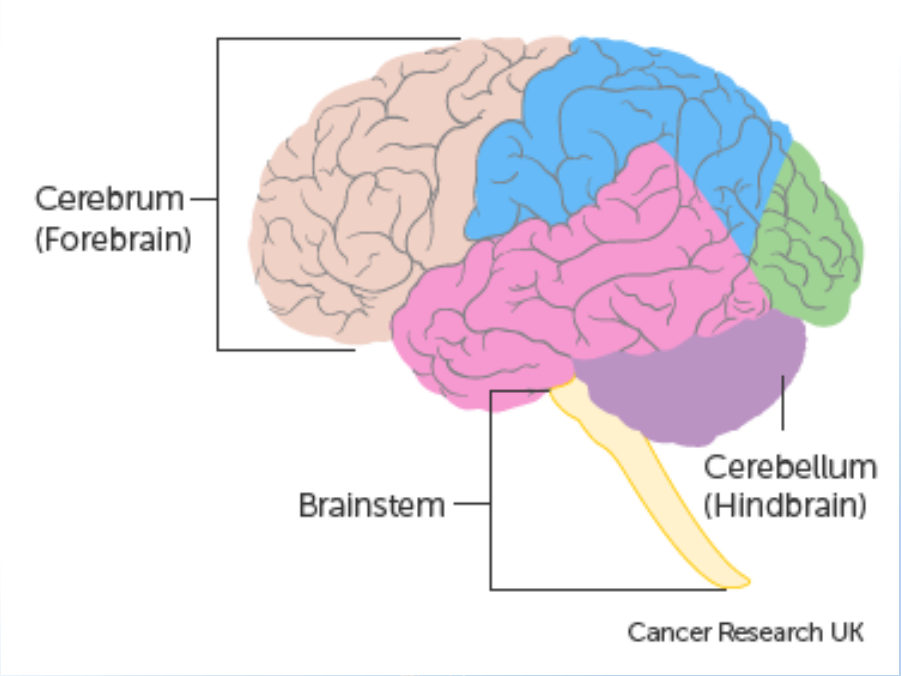
Clinical Symptoms - extrinsic

- Extrinsic tumours compress underlying brain or spinal cord – focal neurological signs

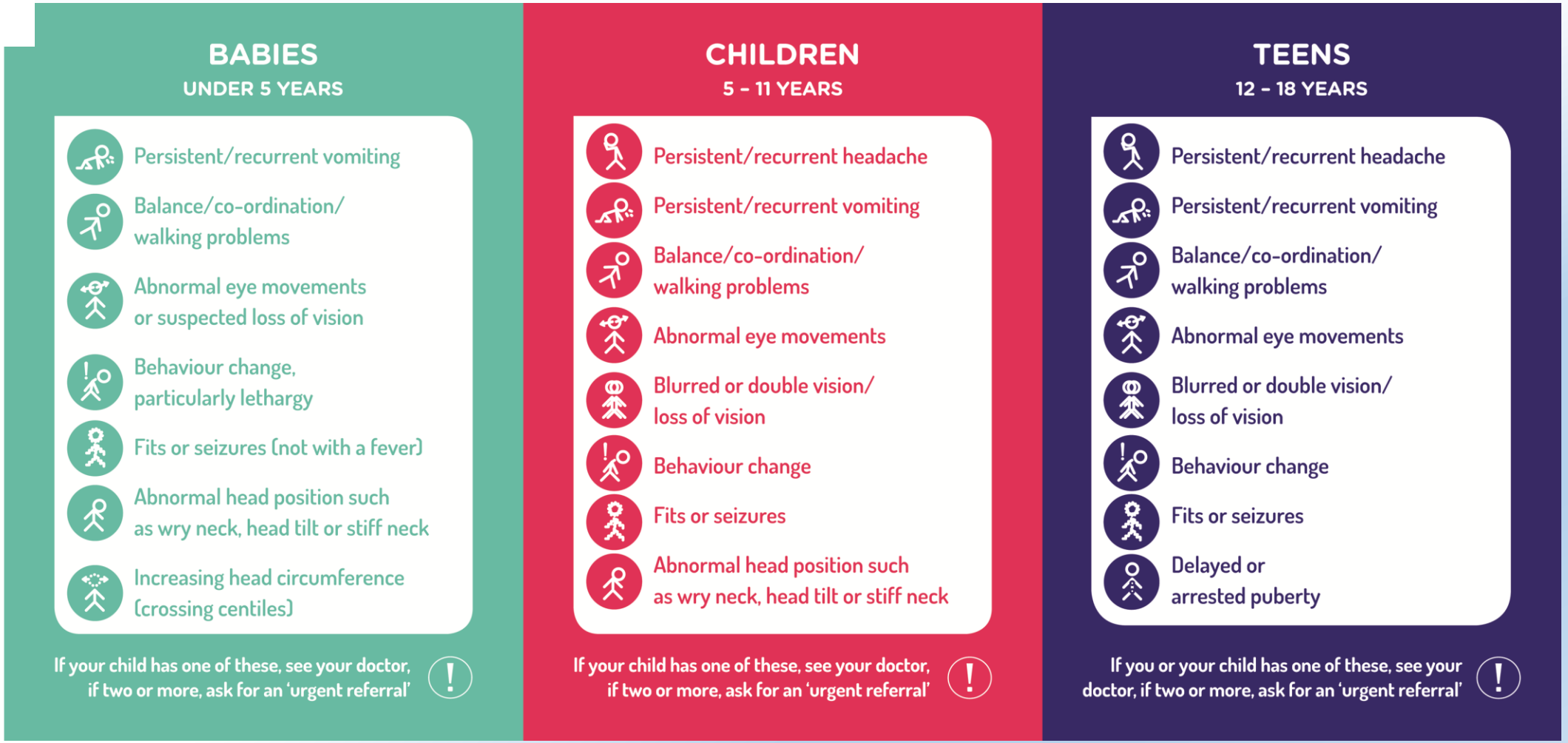
- Extrinsic brain tumours cause symptoms of raised intracranial pressure

Clinical Symptoms - intrinsic

- Infiltration of brain or spinal cord
- Focal neurology depending on site of involvement
- Intrinsic brain tumours cause brain swelling and lead to symptoms of raised intracranial pressure



Helping to diagnose childhood brain tumours earlier



https://www.headsmart.org.uk/

Clinical Presentation

- **Low grade tumours** – brain can accommodate growth and slow pressure rise, so more likely to present with seizures or focal neurology

- **High grade tumours** – brain struggles with rapid pressure rise; more likely to present with pressure symptoms

Common Brain Tumours

- Secondary = metastases

- Primary –
- Astrocytoma / Glioma – High and low grade
- Meningioma

- Rarer – Ependymoma, Medulloblastoma/PNET, Choroid Plexus tumours Pineal

Metastases

- The most common type of brain tumour
- Most likely to come from breast, lung, bone, melanoma or renal. Others can spread to the brain but rarely
- Can be single or multiple tumours
- Treatment options are palliation, surgery, stereotactic radiosurgery or whole brain radiotherapy

Metastases

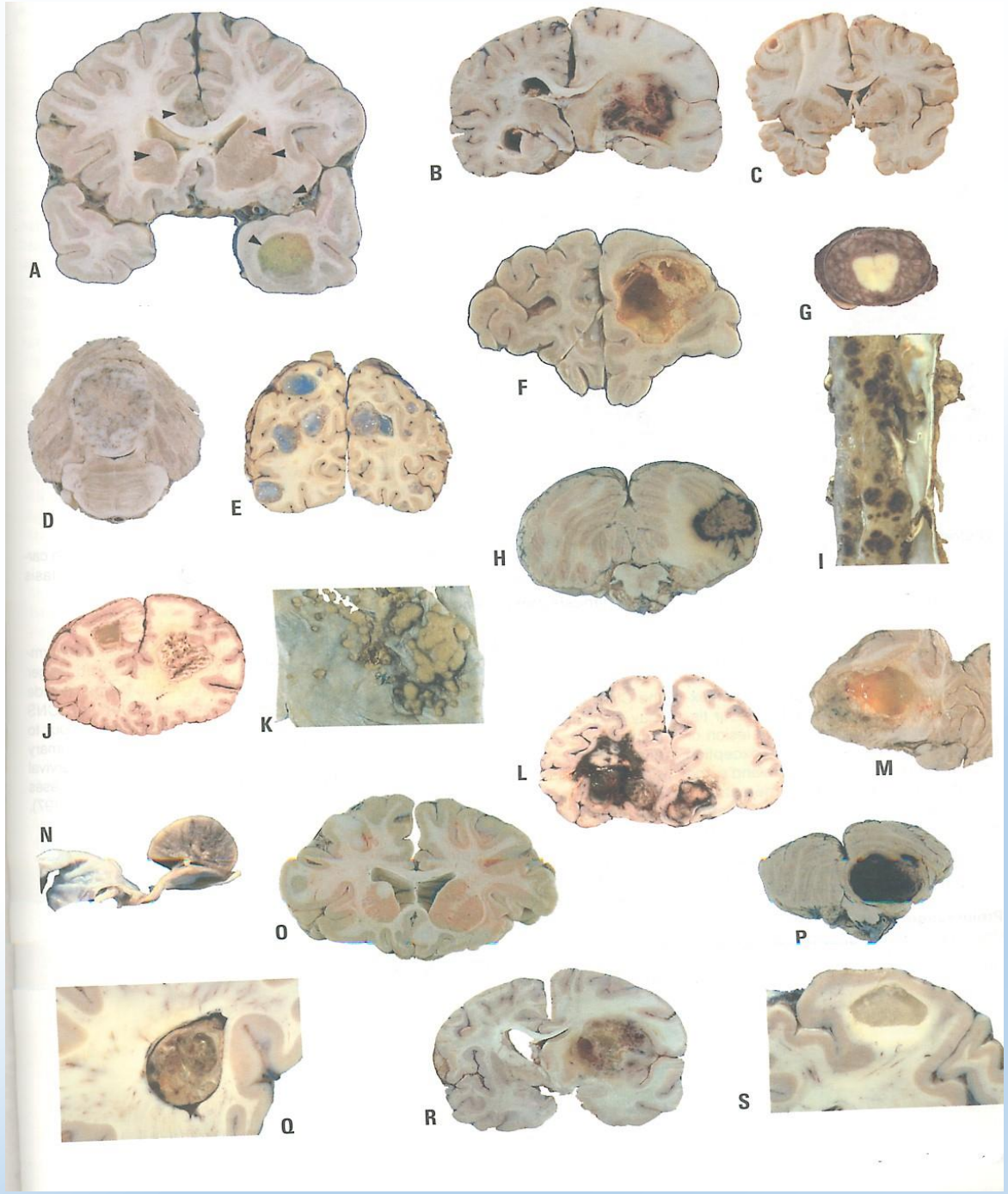
~30% of brain tumours

Spherical masses often at grey-white junction or in cerebellum (hindbrain).

Often multiple

Lung	60%
Breast	15%
Kidney	10%

Untreated median survival is only 1-2 months.

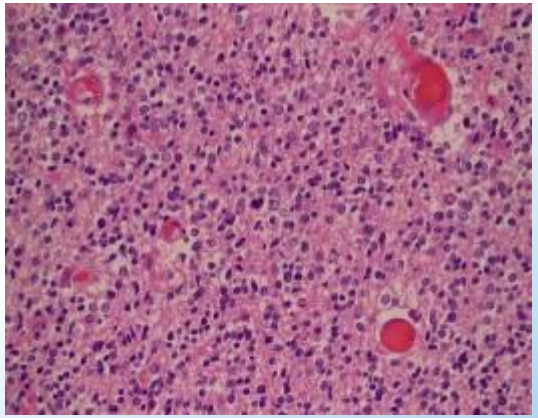


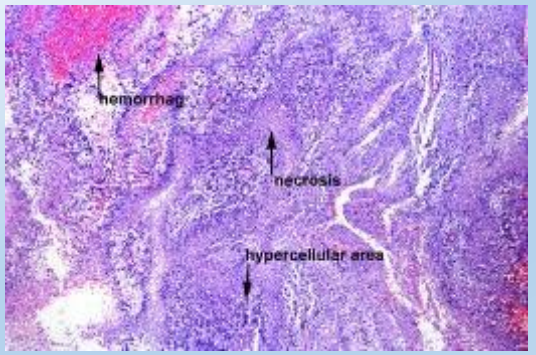
Primary Brain Tumours

High Grade Astrocytoma
Low Grade Astrocytoma
Meningioma

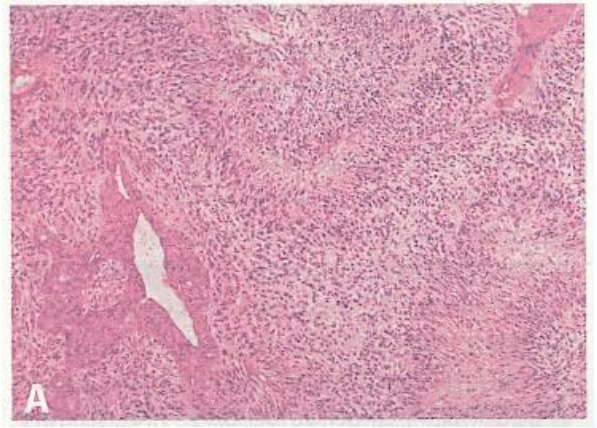
Tumour nomenclature & WHO grading

- **Histogenesis** – what is the cell of origin
- **Malignancy grade** – pleomorphism, mitoses, microvascular proliferation, necrosis
- Grade 1: low grade – curative with surgery
- Grade 2: astrocytoma (low grade)
- Grade 3: anaplastic astrocytoma
- Grade 4: high grade – death within one year of diagnosis





Histological grading of Astrocytomas



Grade of Glioma	Name	Histology
1	Pilocytic Astrocytoma	Low proliferation, -children / young adults
2	Diffuse Astrocytoma	Low cellularity, minimal atypia – young adults
3	Anaplastic Astrocytoma	Anaplasia, mitotic activity – 30 to 60 years
4	Glioblastoma multiforme (GBM)	Microvascular proliferation, necrosis – 50-70 years

No predictive biomarker for progression. Difficult to communicate to patient.

Low grade diffuse Astrocytoma (Grade 2)

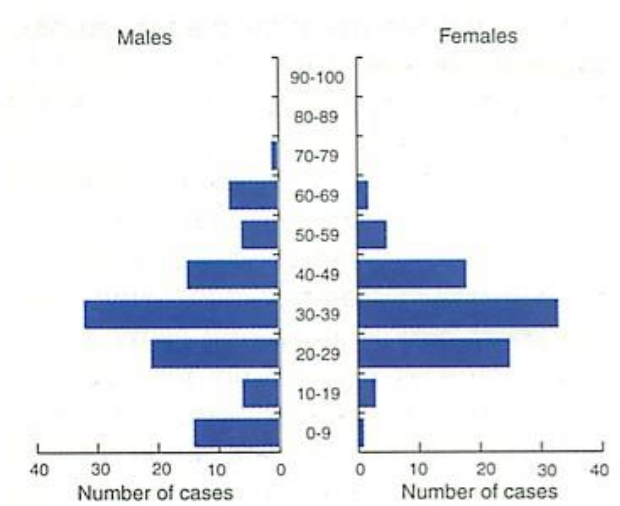
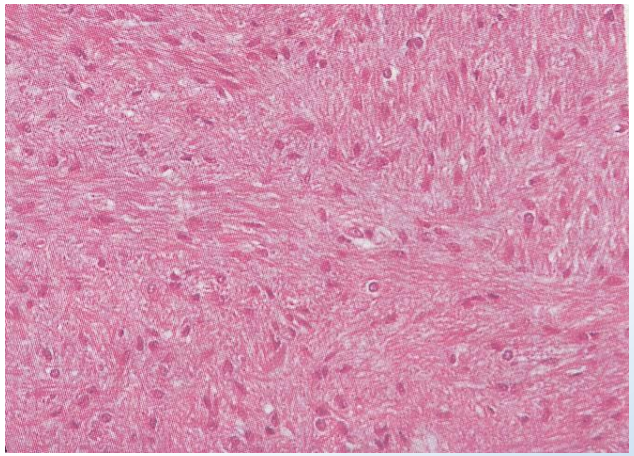
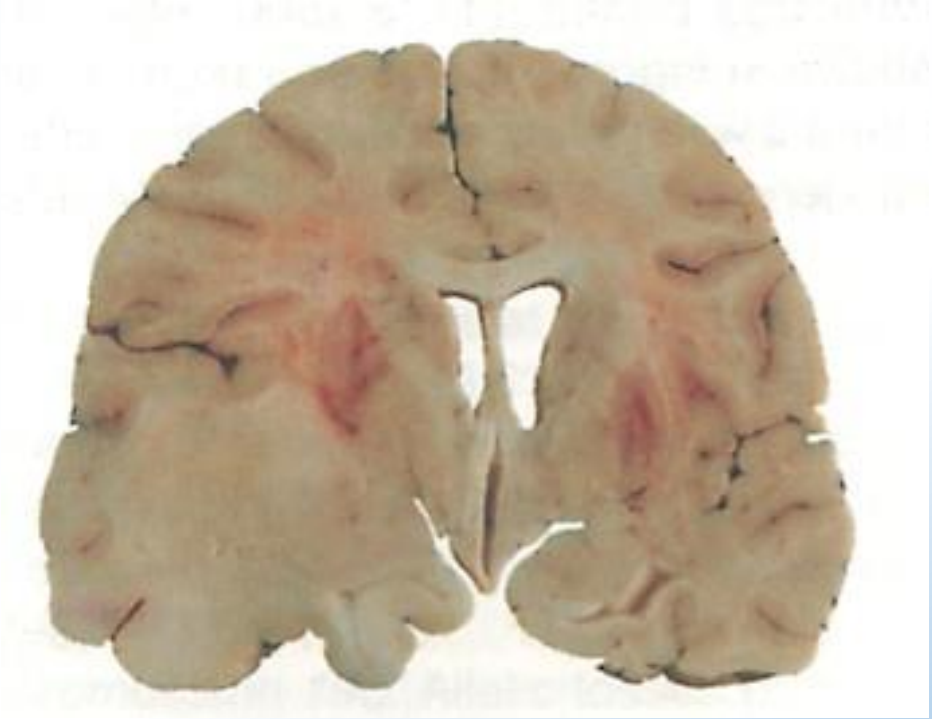


Fig. 1.7 Age distribution of low-grade diffuse astrocytomas, based on biopsies of 190 patients treated at the University Hospital, Zurich.





May be long history, seizures, relatively well, younger age group

Anaplastic Astrocytoma (Grade 3)

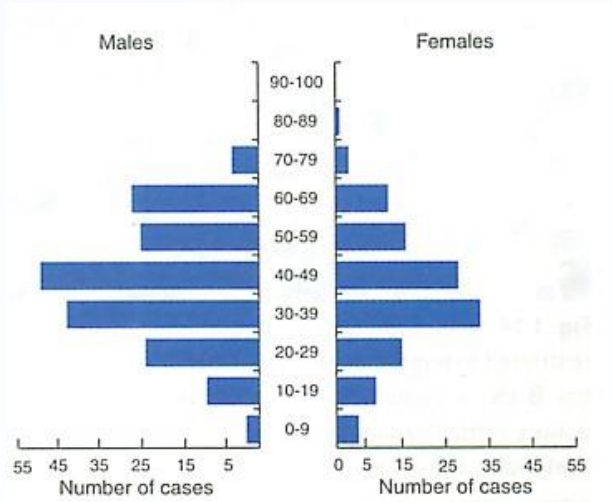
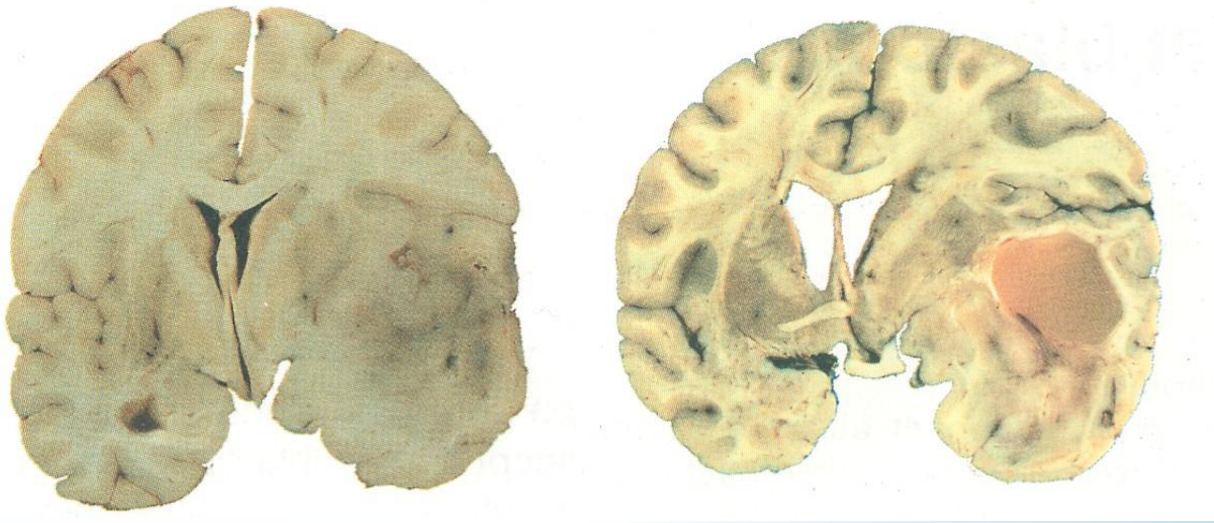
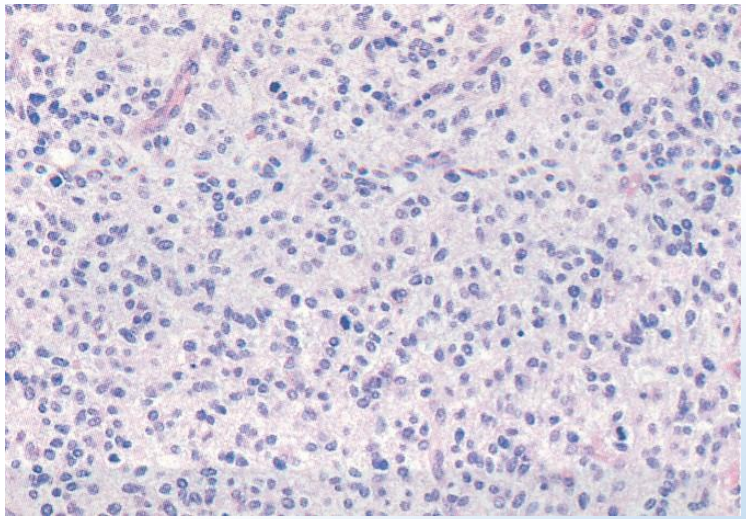


Fig. 1.15 Age distribution of anaplastic astrocytomas, based on biopsies of 319 patients treated at the University Hospital, Zurich.





May be more unwell, shorter history, slightly older.
Some will have progressed from known Grade 2 tumour.

Malignant Glioma – Glioblastoma (Grade 4)

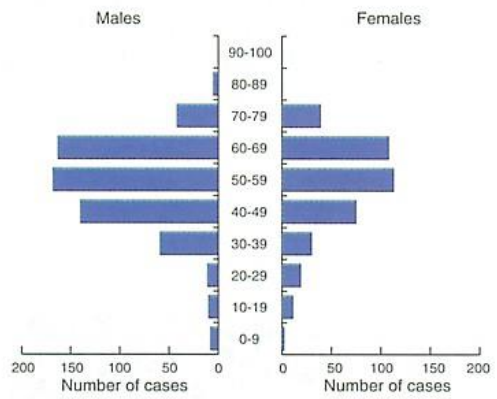
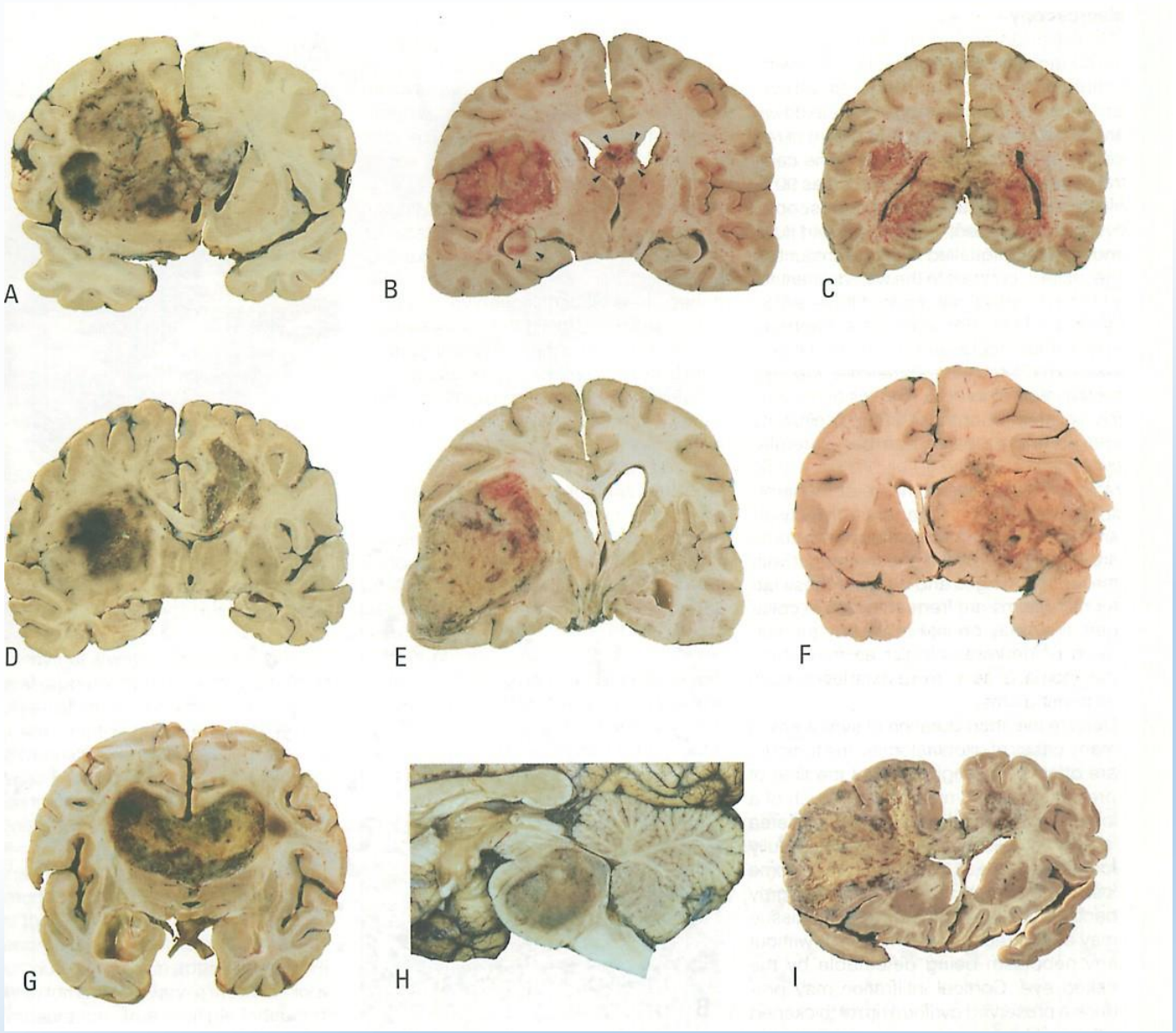
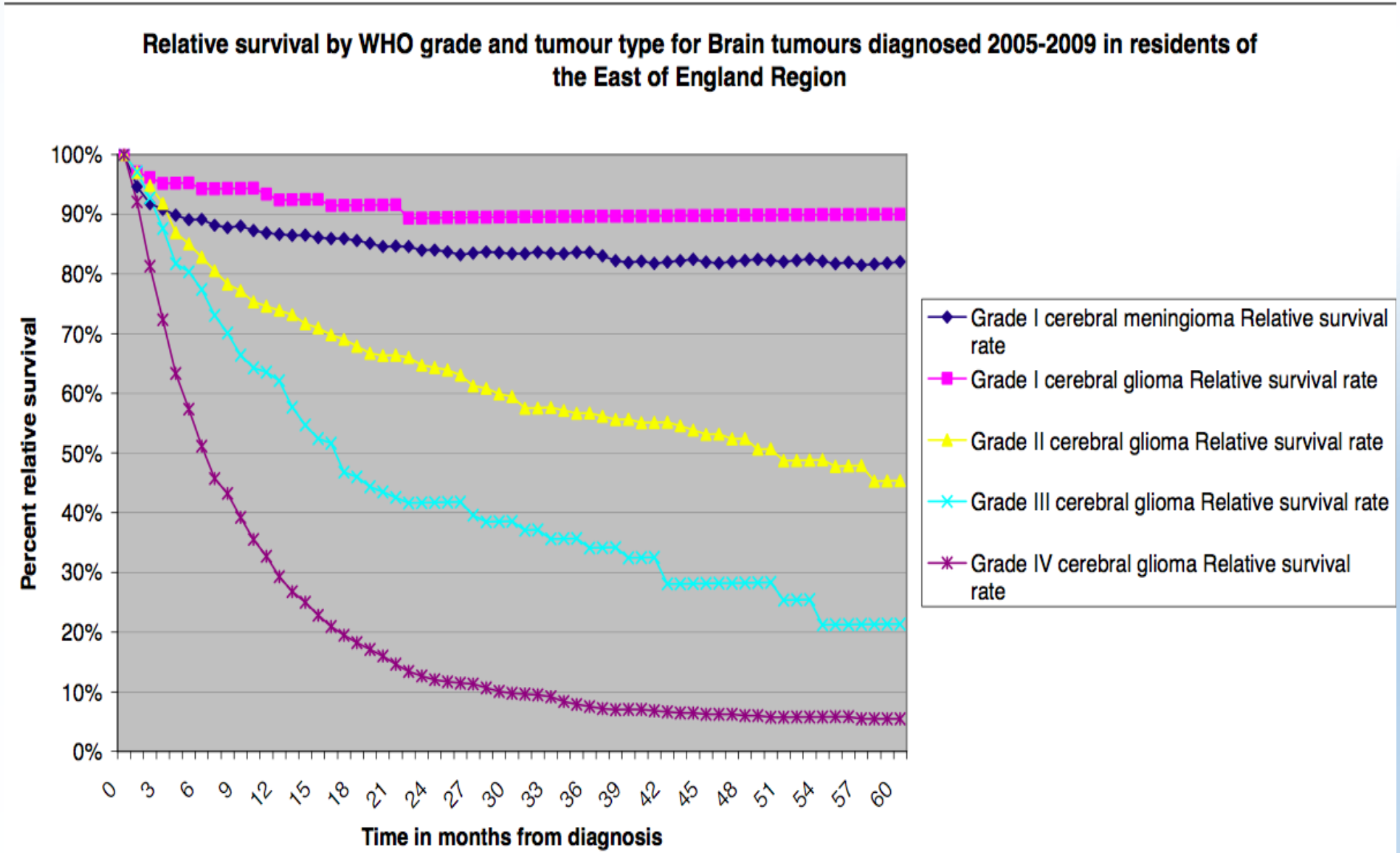


Fig. 1.18 Age distribution of glioblastomas, based on biopsies of 1003 patients treated at the University Hospital, Zurich.

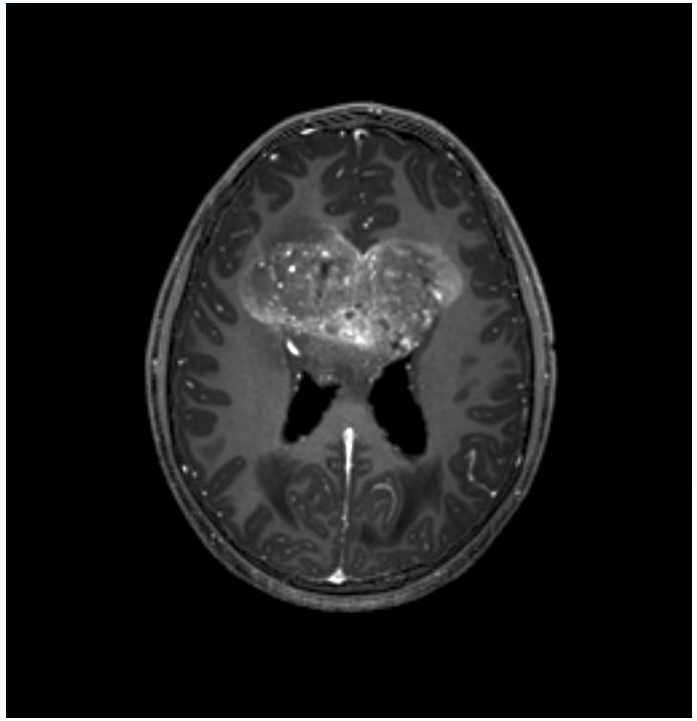
Usually short history (<3 months) especially of headache and personality change

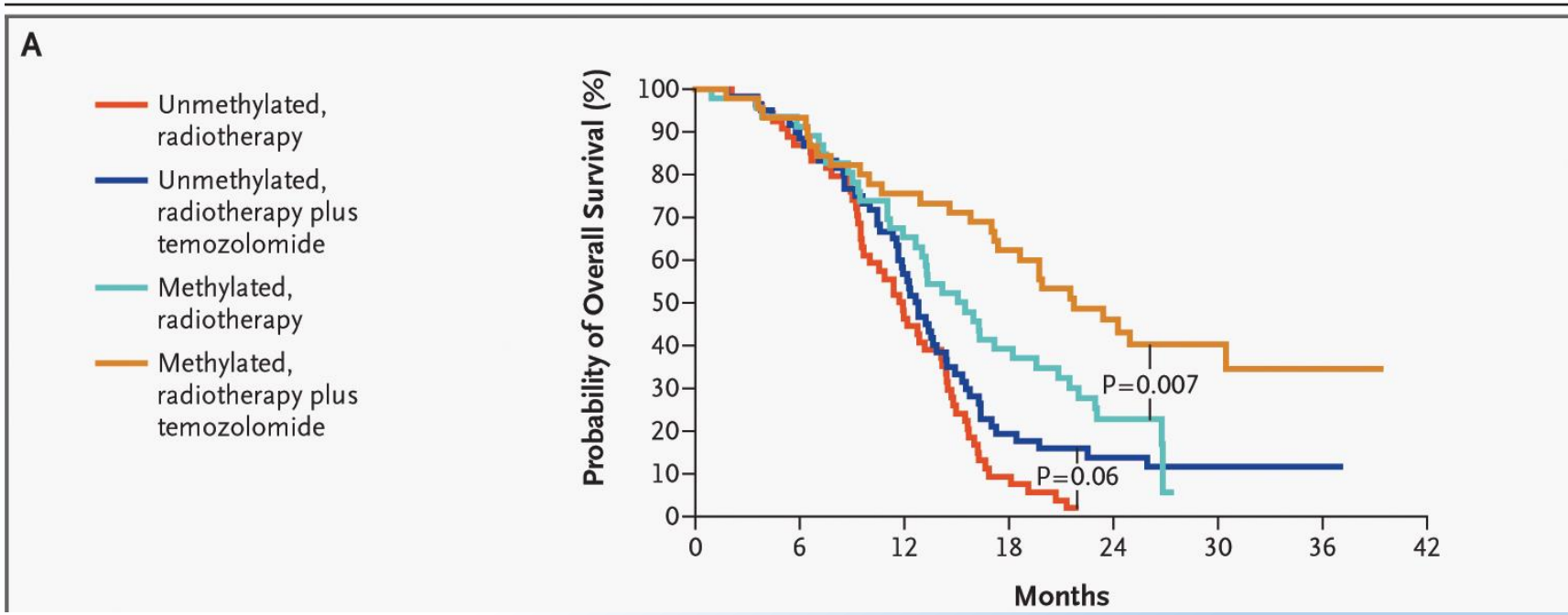


Prognosis


Relative survival by WHO grade and tumour type for Brain tumours diagnosed 2005-2009 in residents of the East of England Region
Percent relative survival
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
0 3 6 9 12 15 18 21 24 27 30 33 36 39 42 45 48 51 54 57 60
Time in months from diagnosis
Grade I cerebral meningioma Relative survival rate
Grade I cerebral glioma Relative survival rate
Grade II cerebral glioma Relative survival rate
Grade III cerebral glioma Relative survival rate
Grade IV cerebral glioma Relative survival rate

Glioblastoma multiforme (GBM) prognosis remains dismal





GBM is a WHO Grade IV astrocytoma (glial).

Most prevalent and aggressive malignant brain tumour.

Incidence 2-3 per 100,00 in Europe/N.America.

Median survival
~ 14.6 months

Treatment - Glioblastoma

- Radical surgery & steroids (dexamethasone)
- Radiotherapy – 60Gy in 30 fractions
- Chemotherapy – Temozolomide (some patients respond)

History

Bennett AH, Godlee RJ

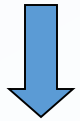
“Excision of a tumour from the brain”

Lancet **1884**

Surgery for Brain Tumours

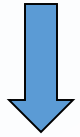
Nothing at all

*Unfit, elderly, risky **eloquent** areas*

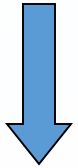


Biopsy

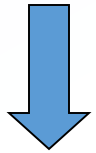
Small deep lesions, eloquent areas



Debulking



Macroscopic Resection



Resection with margins

To control intra-cranial pressure symptoms from larger tumours, cytoreduction

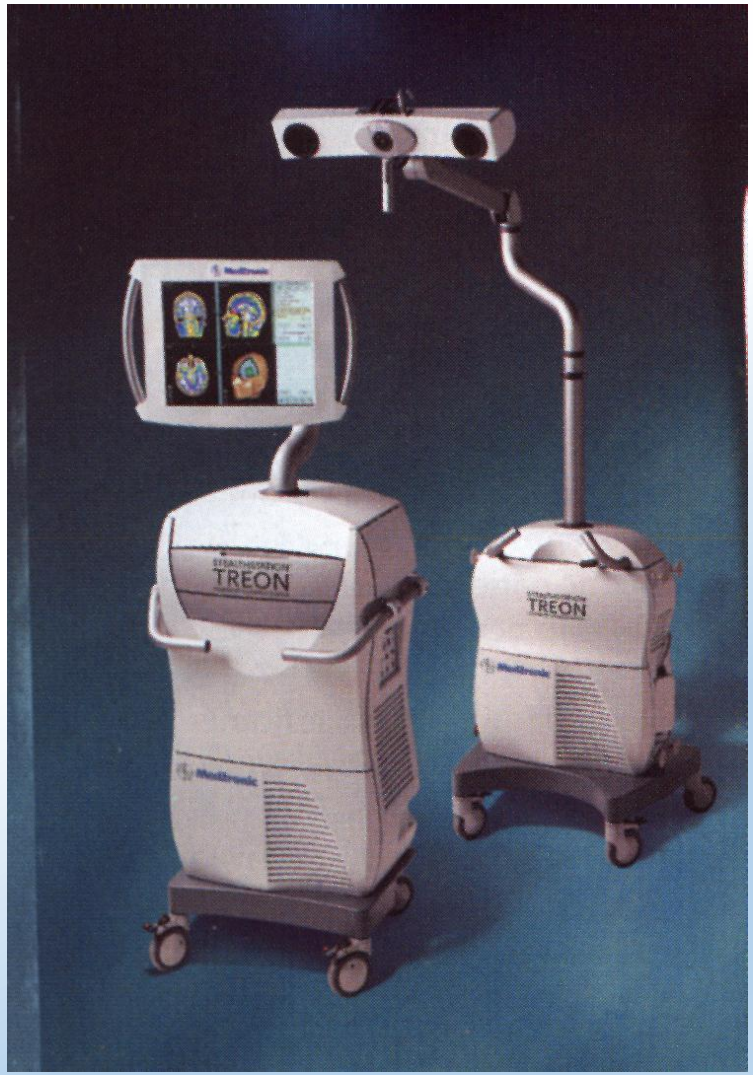
Image Guidance - StealthStation

CT / MRI scans of patients uploaded to StealthStation.

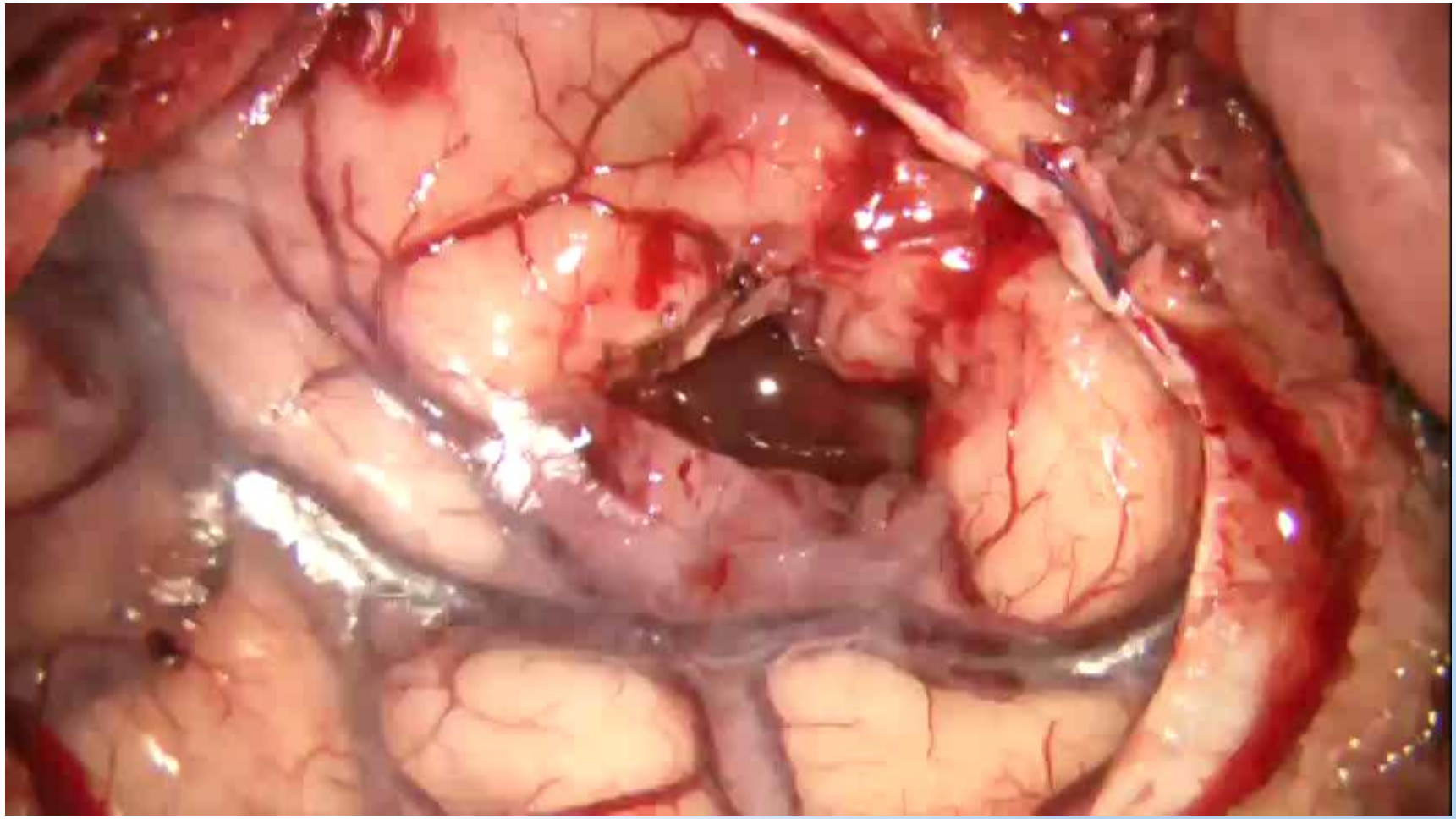
Fix patient's head and register position of head (Pixar technology)

Neurosurgeon can decide where to remove fragment of skull and where to locate tumour using real-time feedback.

PROBLEMS – brain size and position shifts leading to inaccuracies



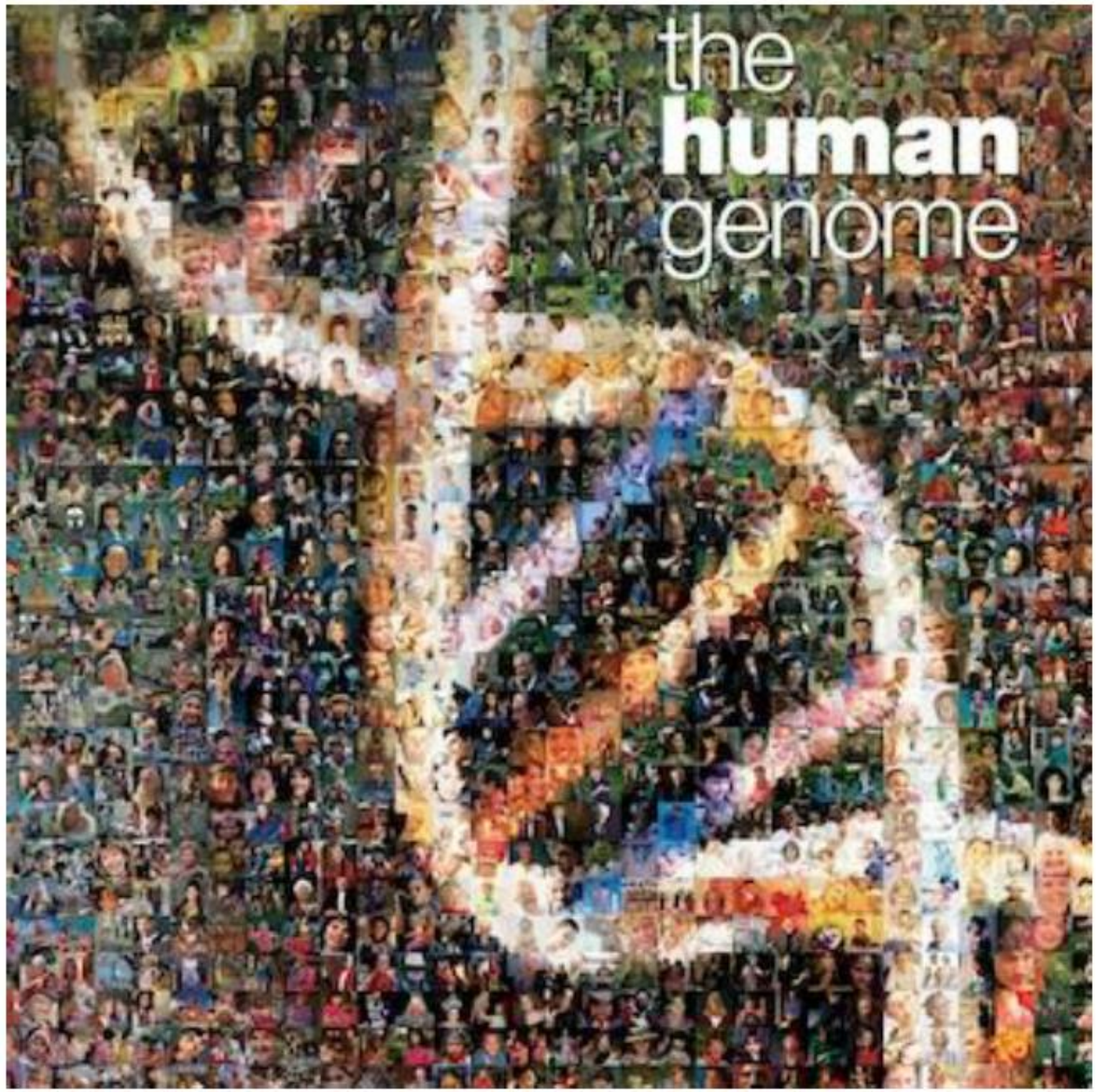
Fluorescence (5ALA)- guided surgery



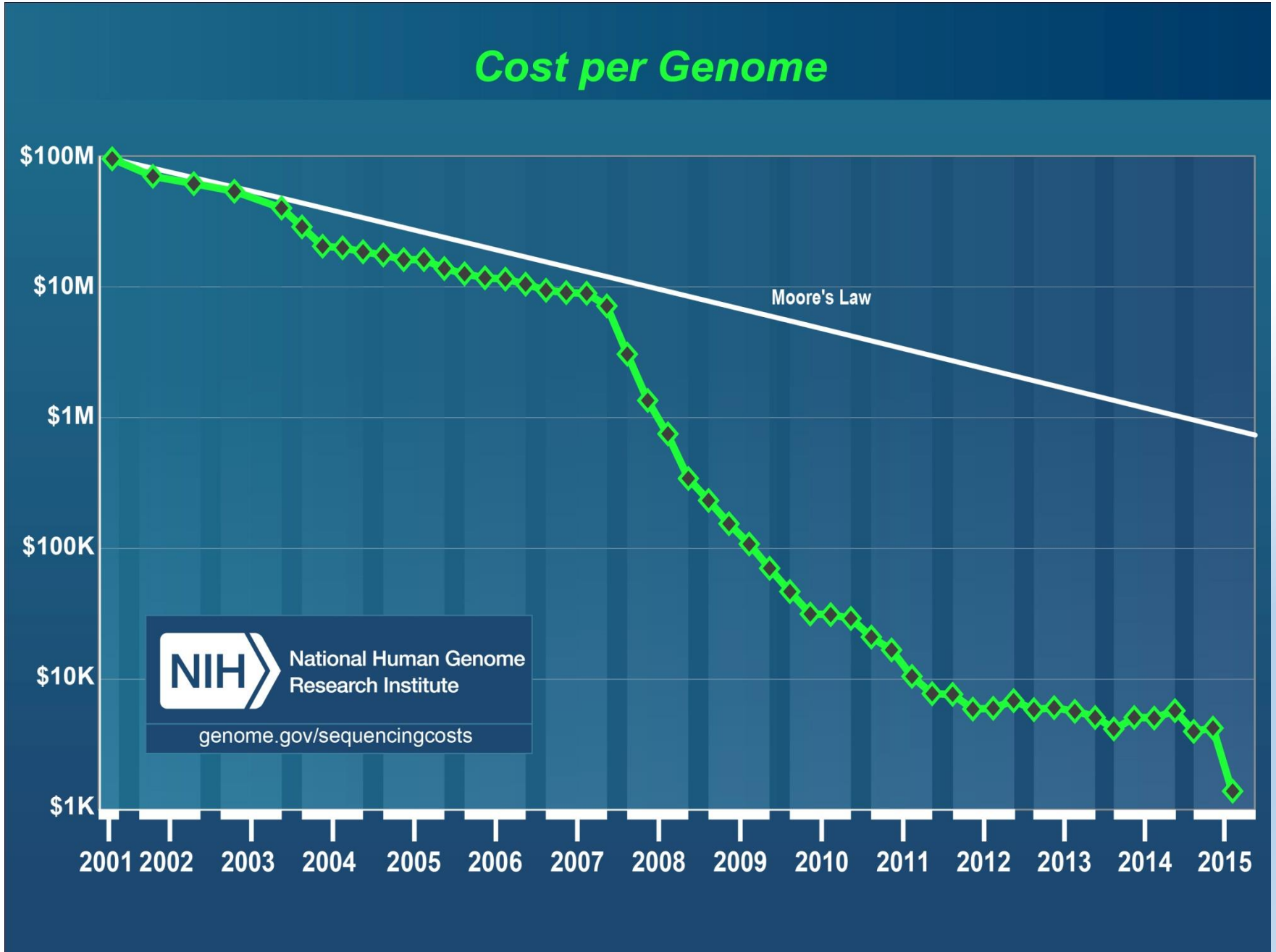
Research

Improving diagnosis (MRI), treatment, prognostic markers, palliative care / survivorship, basic and translational science e.g. molecular biology

Genomic era (1972-2003)

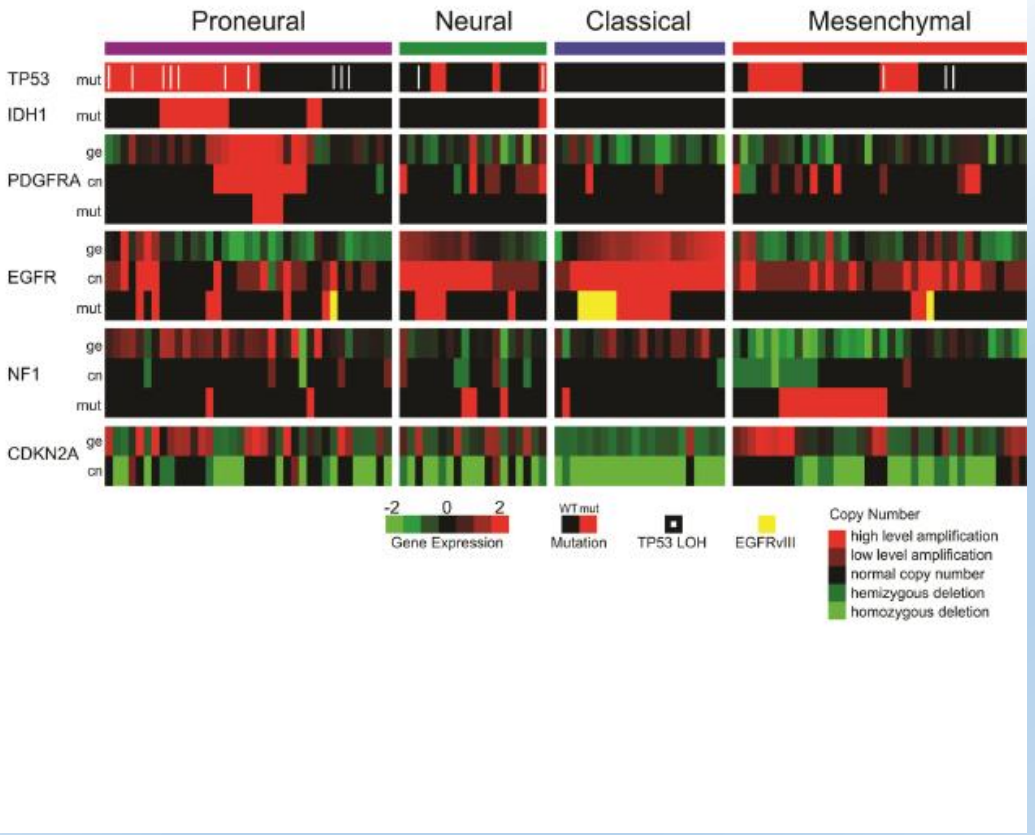


Post-Genomics Era – will soon cost just £100 to sequence your genome!



Chemotherapy tailored to the sub-type of glioblastoma

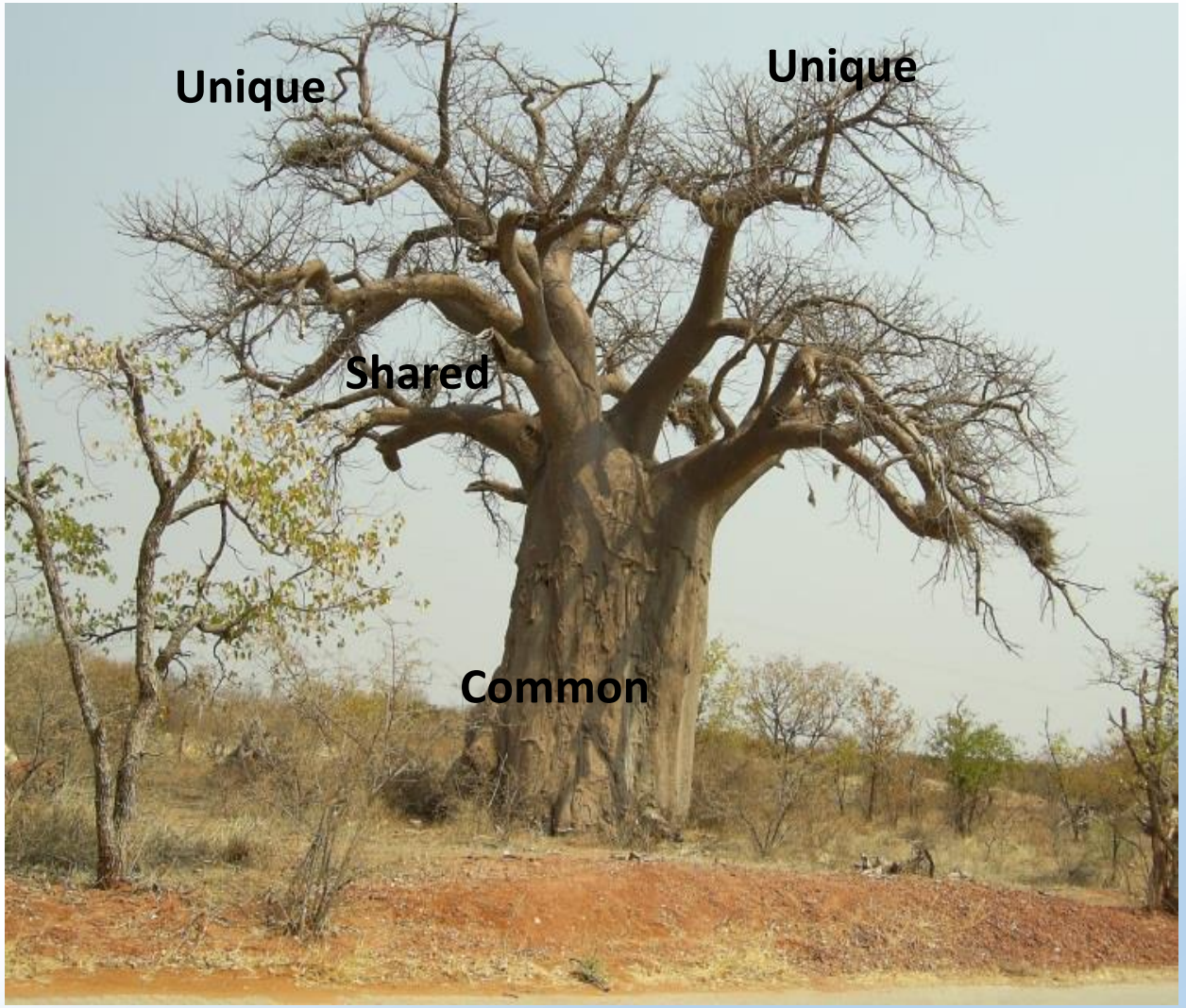
Pro-neural Neural Classical Mesenchymal



No objective response in any phase II clinical trial

Cancer as a process of evolution – implications for therapy

Genetic Mutations



Thank you

Any questions?

ruman.rahman@nottingham.ac.uk