Brain Tumour UK Neuro-oncology Research Centre and brain tumour research at the University of Wolverhampton

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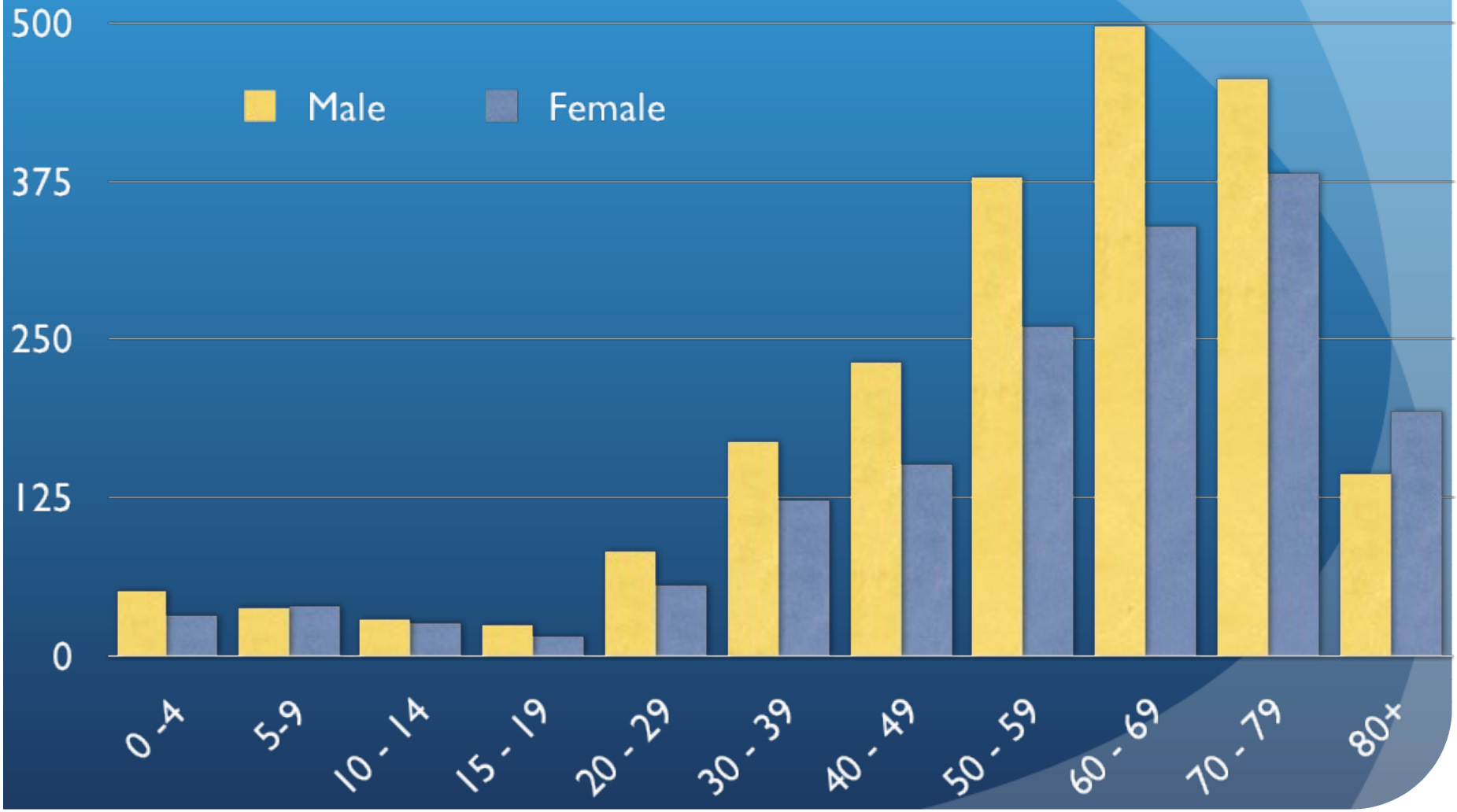
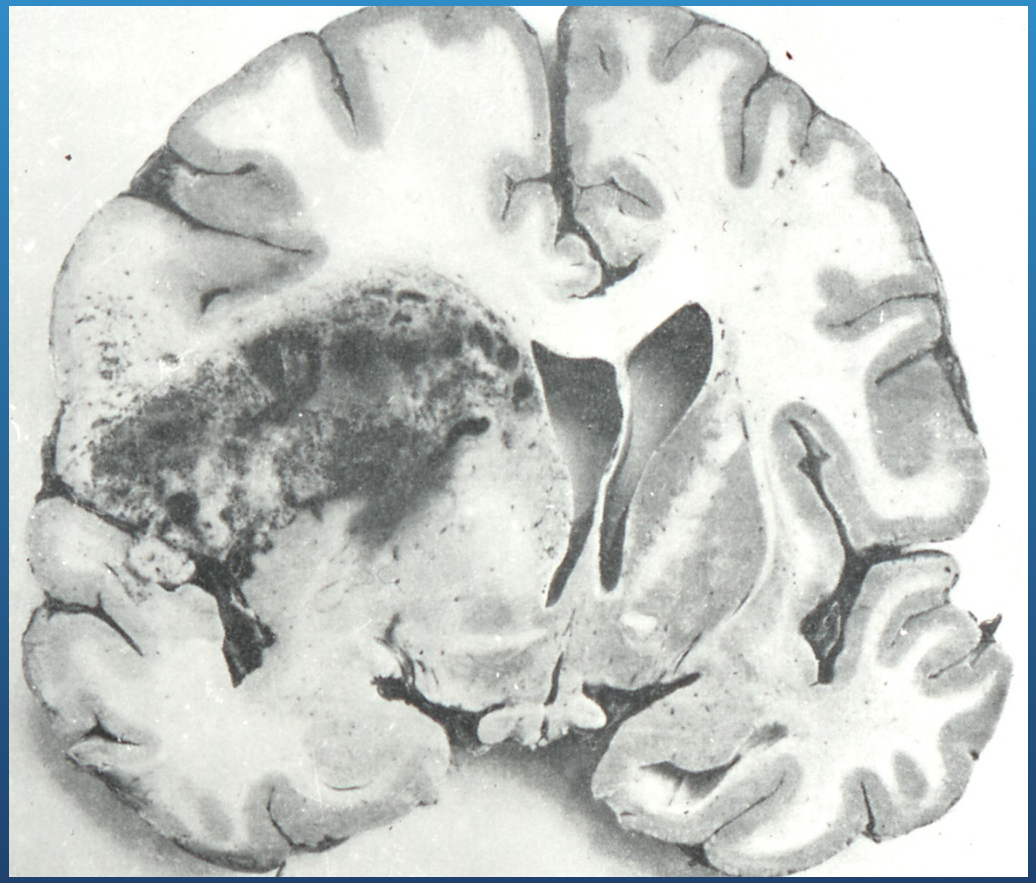
Brain Tumours

- The brain is the 11th most common site to develop cancer in men and the 14th most common site in women
- The commonest brain tumours in adults are highly aggressive tumours known as “glioblastoma multiforme”. Untreated patients usually survive about 12 weeks from diagnosis and even with optimal treatment rarely survive longer than about 12-15 months
- Brain tumours are the second commonest cause of death in children in the developed world
- The cause is unknown an no change of behavior is known to reduce risk

Brain Tumour Registrations in England, 2000



Malignant Astrocytoma
Glioblastoma multiforme

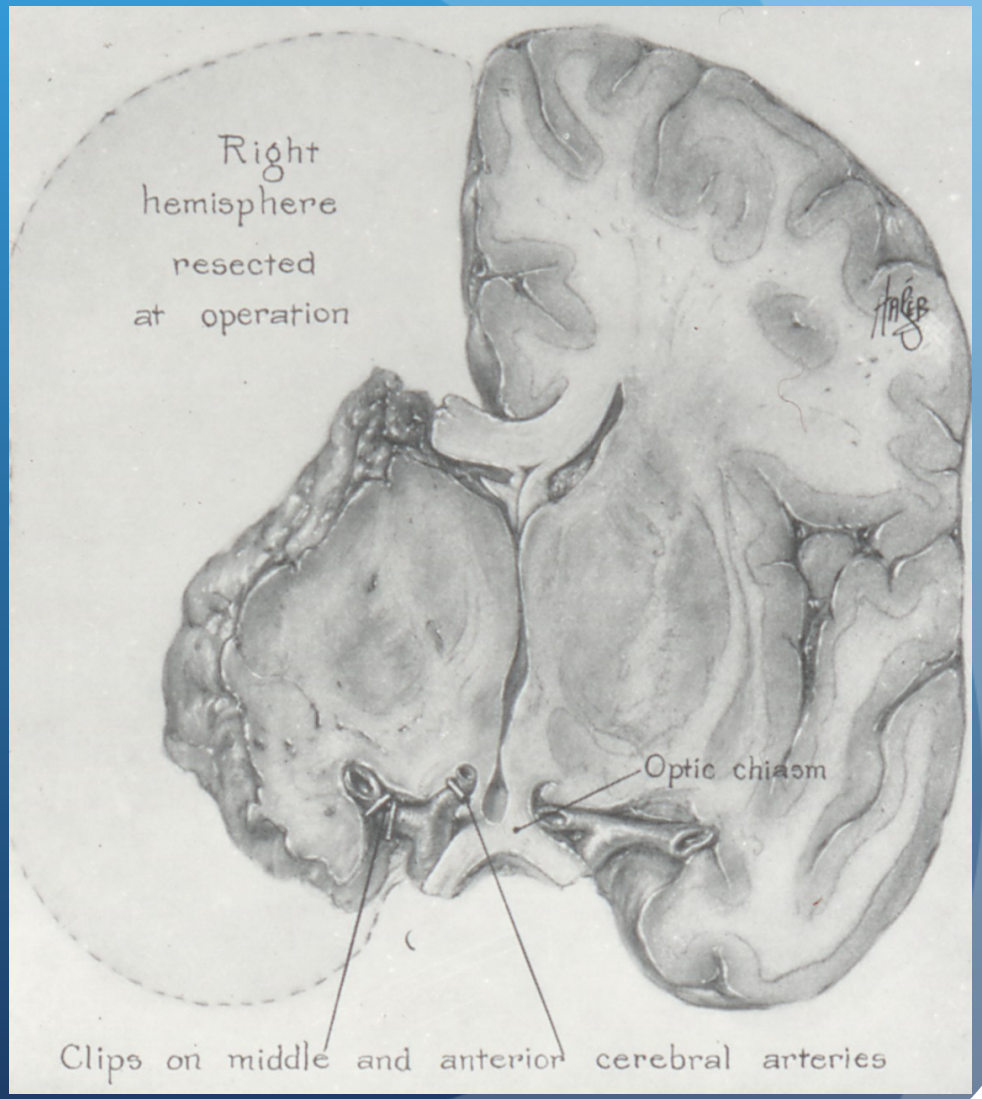


Treatment

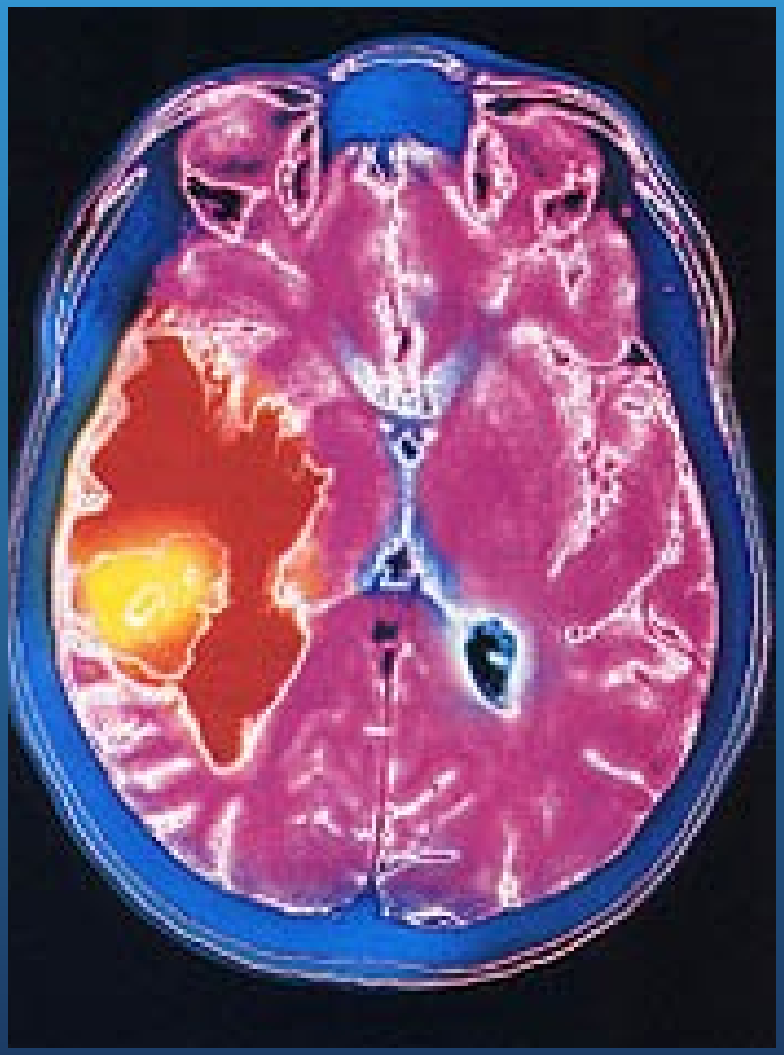
- Surgery
  - Provides definitive diagnosis
  - Almost always improves neurological signs and symptoms
  - Provides time for other modalities to be given
  - For malignant tumours, surgery is almost never curative because of local invasion
- Radiotherapy
  - Is effective in increasing median survival, but the brain is a radio-sensitive organ which limits dose
- Chemotherapy
  - Is effective in increasing median survival and long-term survival
  - Small number of effective drugs
  - Limited by blood-brain barrier

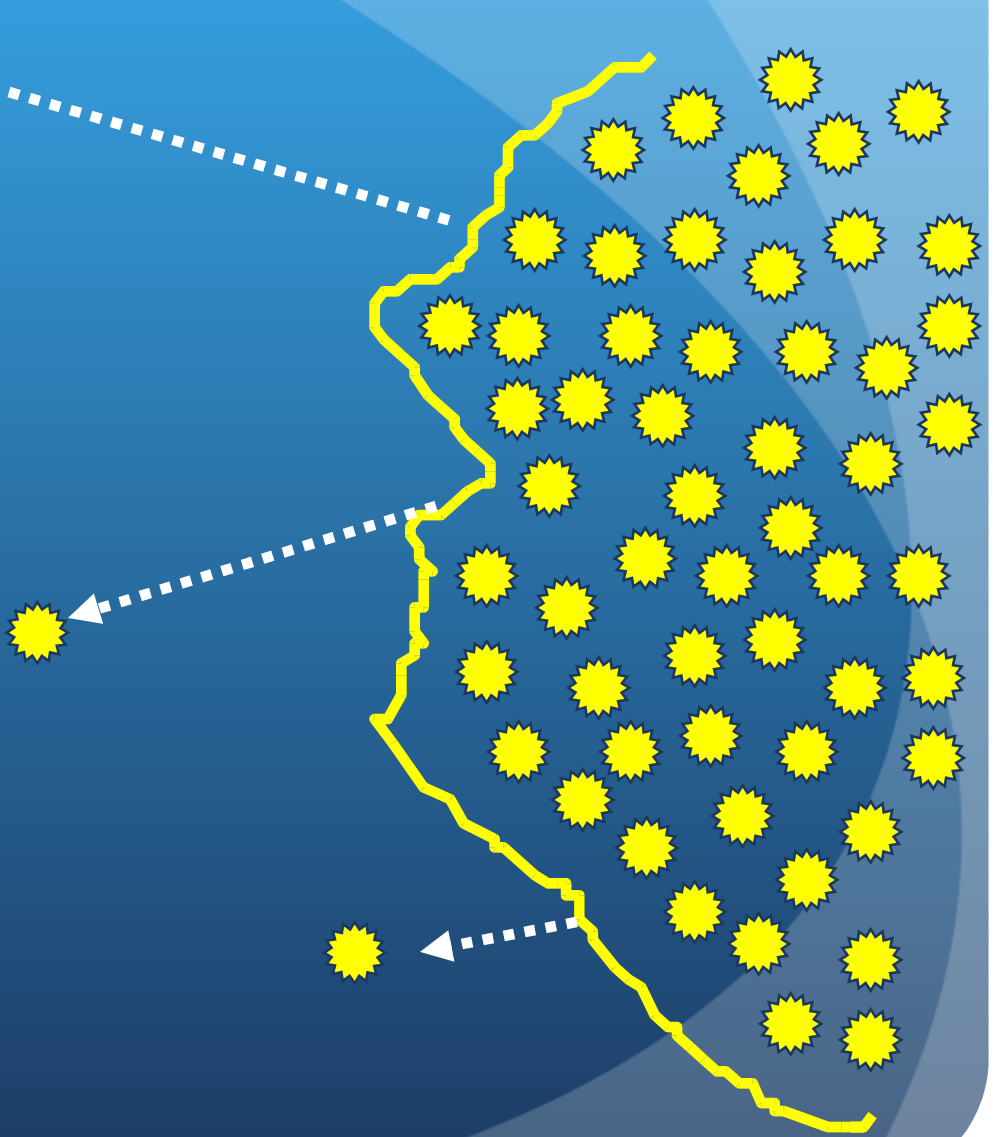
Walter Dandy

Walter Dandy (left) and Harvey Cushing (right) taken in February 1921 at Jekyll Island, Georgia



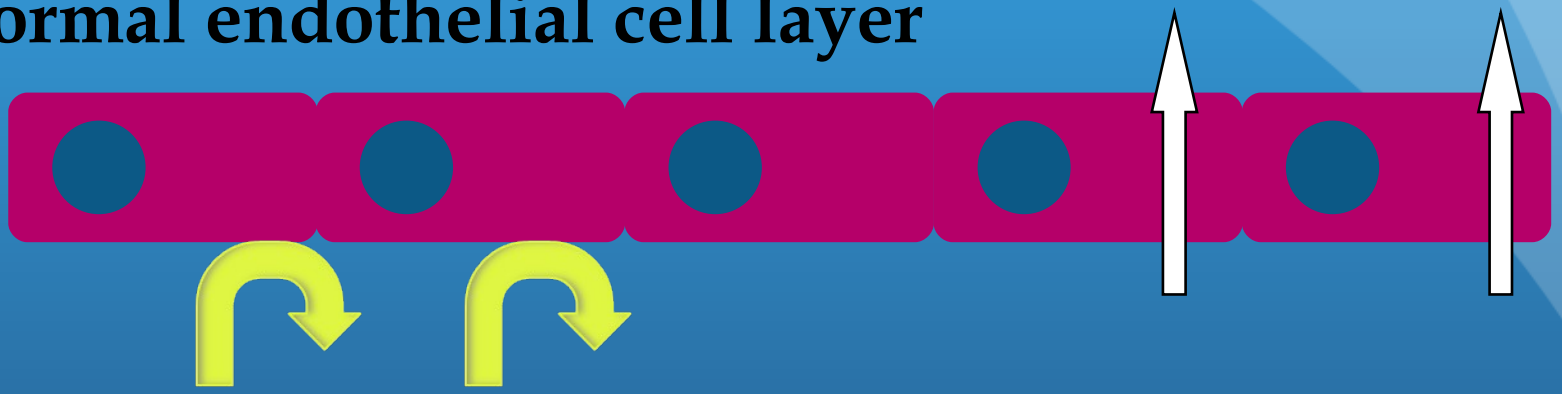
Where is the edge of the tumour?





Blood-Brain Barrier

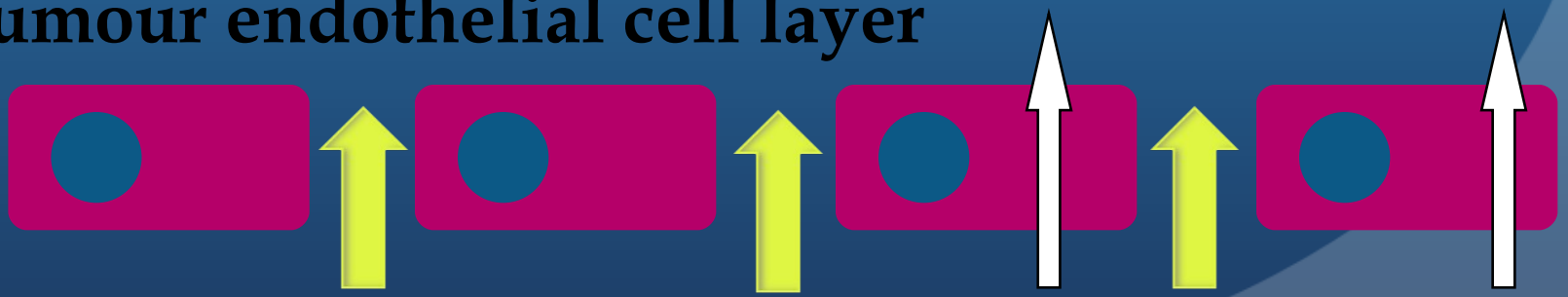
Normal endothelial cell layer



Large molecular weight lipid insoluble drugs

Small molecular weight lipid soluble drugs

Tumour endothelial cell layer



Conventional Drugs

- Small molecular weight
- Lipid soluble
- Non-ionised at physiological pH
- Effective throughout the cell cycle
- Little or no systemic toxicity

BTUK Brain Tumour Neuro-oncology Research Centre

- understanding the genetic mechanisms driving tumour development;
- identifying robust predictive markers of clinical outcome, including malignant progression, tumour recurrence, response to therapy and overall patient survival;
- understanding the molecular basis of chemotherapeutic resistance;
- identifying novel therapeutic targets for clinical intervention.

Why do some patients with GBM do much better than others?

Two 50 year old men with R frontal GBMs and a Karnofsky score >70

Complete radiological response

Survives 4 years

Surgery Radiotherapy Chemotherapy

Debulking surgery

60 Gy DXT

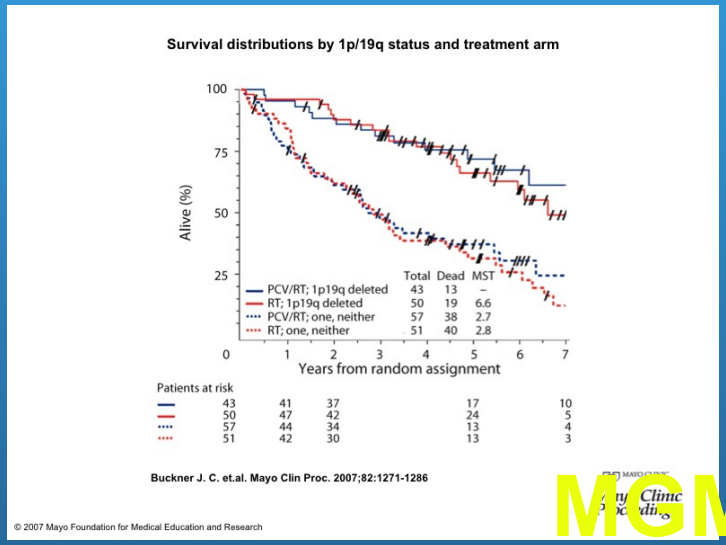
12 cycles of PCV chemotherapy

Surgery Radiotherapy Chemotherapy

Progressive disease

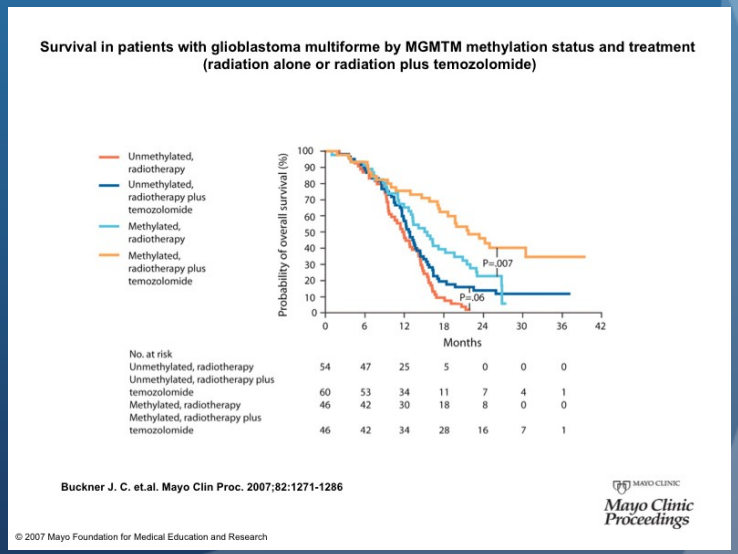
Survives 3 months

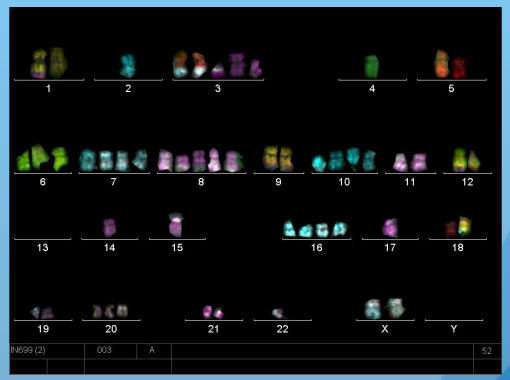
Molecular markers associated with survival and treatment response



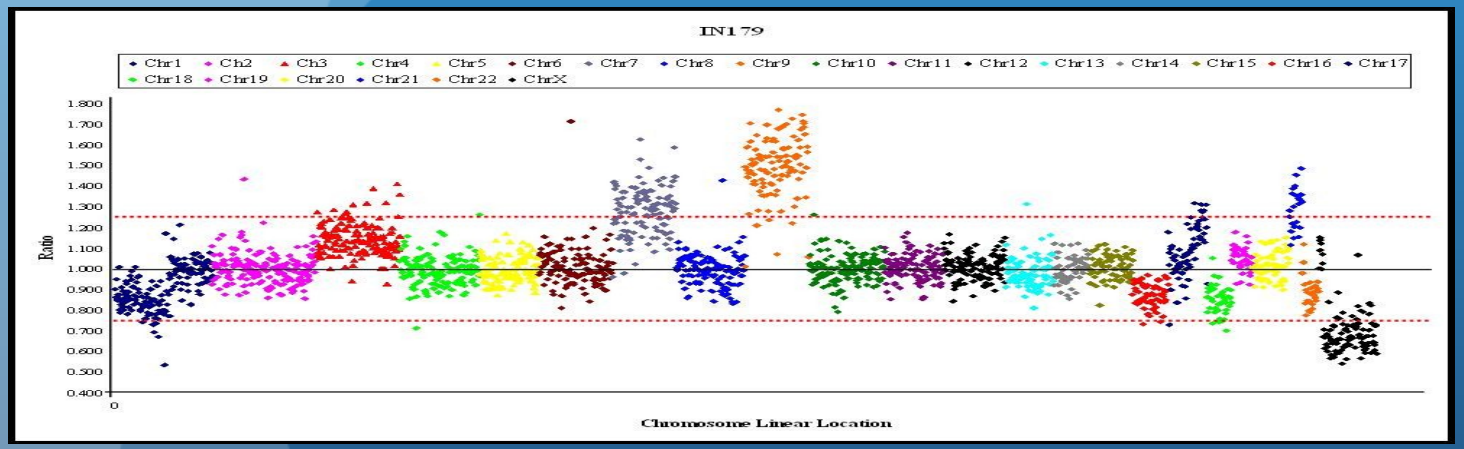
1p and 19q loss in oligodendroglioma

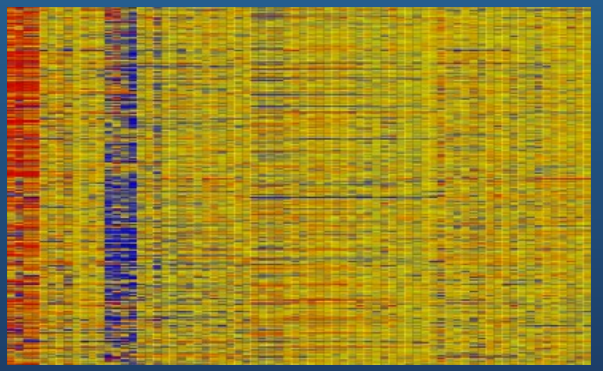
MGMT methylation status in malignant astrocytoma





Understanding the genetic changes that occur in malignant brain tumours





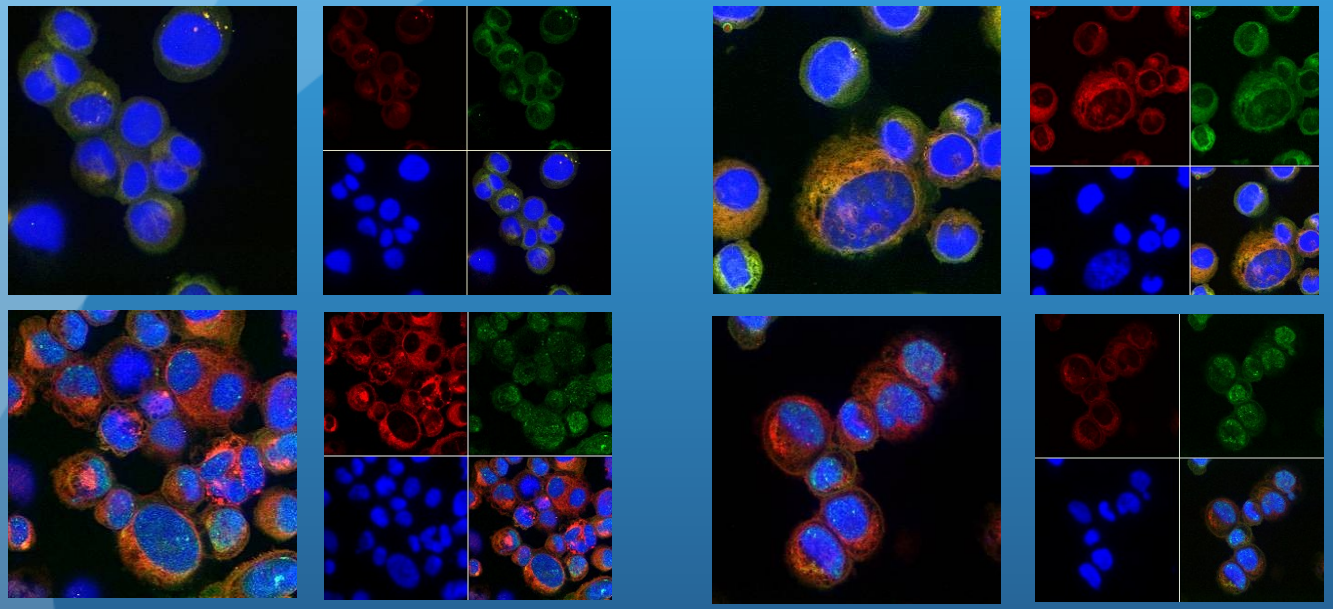
Brain Tumour Stem Cells

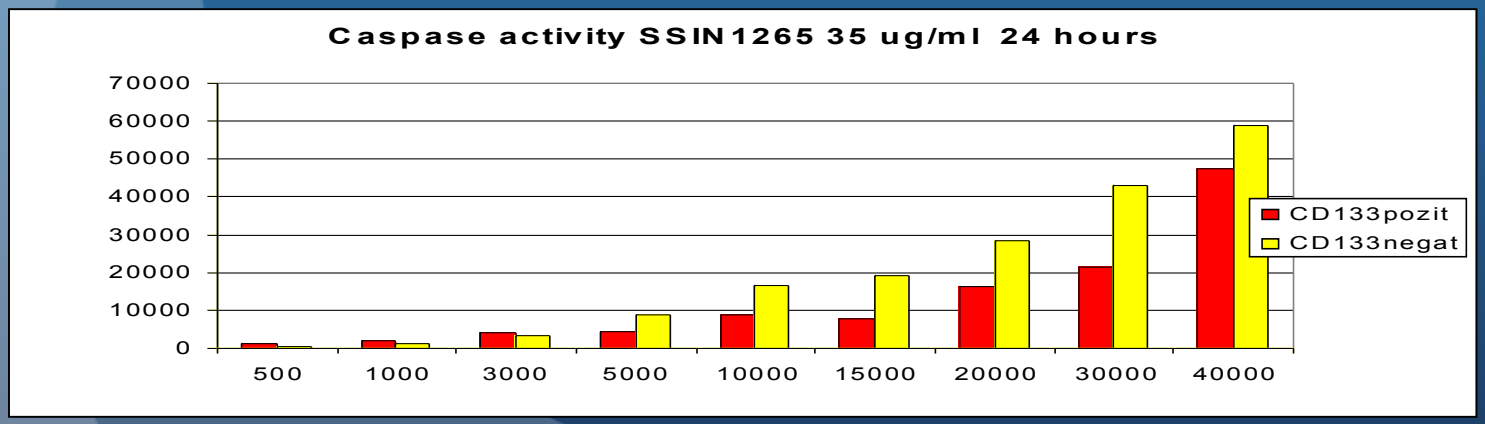
CD133 -

CD133 +

CD133/1, CD133/2

Nestin, Bmi-1





What about new drugs?

Identification of novel targets in glioblastoma
Development of chimeric molecules incorporating cell penetrating peptides (John Howl)

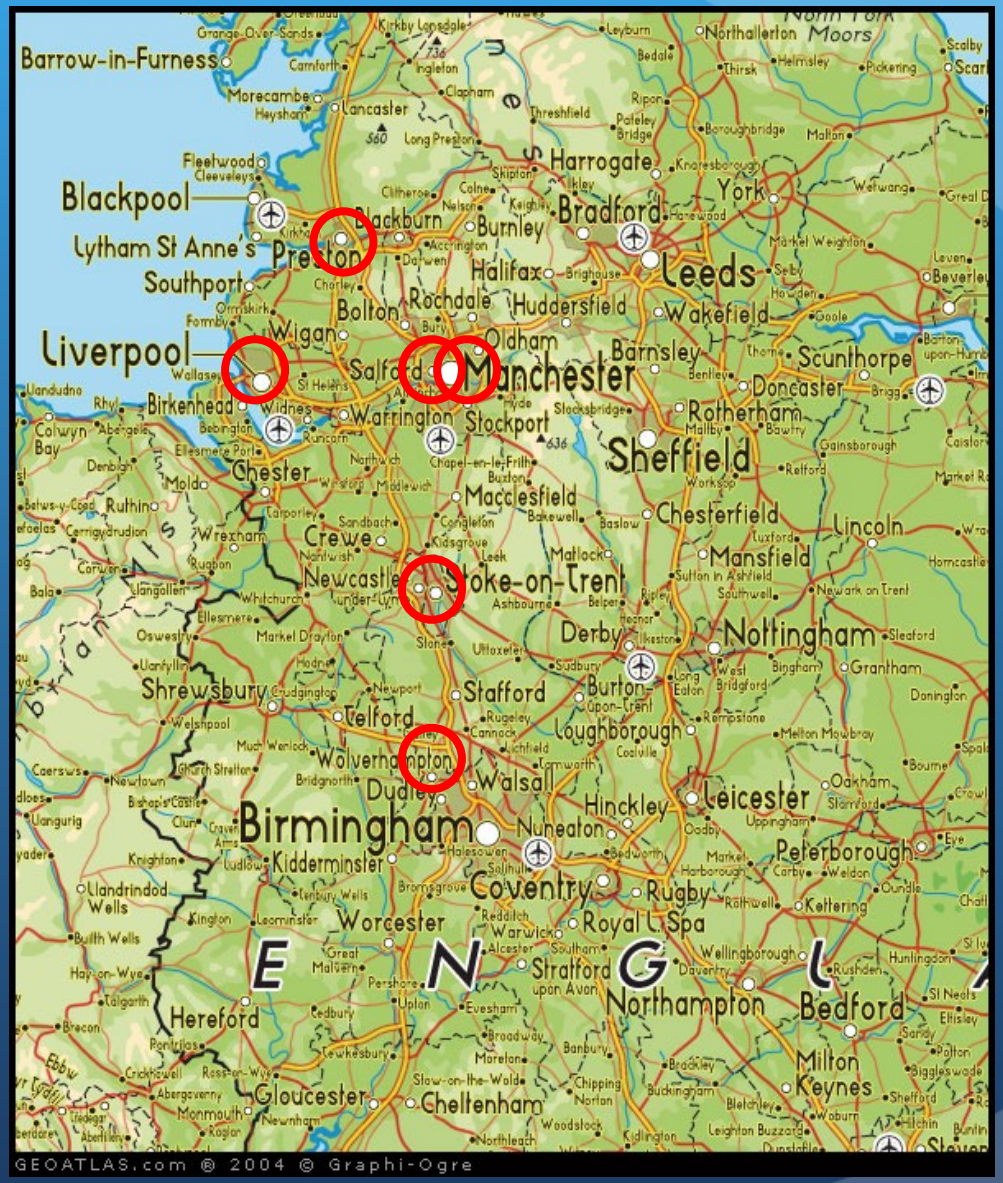
What about using old drugs more intelligently?

Disulfirman and targeting NFkB (Weiguang Wang)
Novel drug delivery methods (James Tang)

How do we get these into clinical practice?

- Regional strategic alliance of brain tumour scientists and clinicians across the north west of England
- Brain Tumour North West
- Avoid duplication of studies
- Maximize the use of equipment, expertise, patient material and other resources
- Develop the ability to deploy large patient/sample cohorts to answer important questions in neuro-oncology quickly and effectively
- Charity funding for Research Coordinator

Brain Tumour North West



BRAIN TUMOUR
NORTH WEST