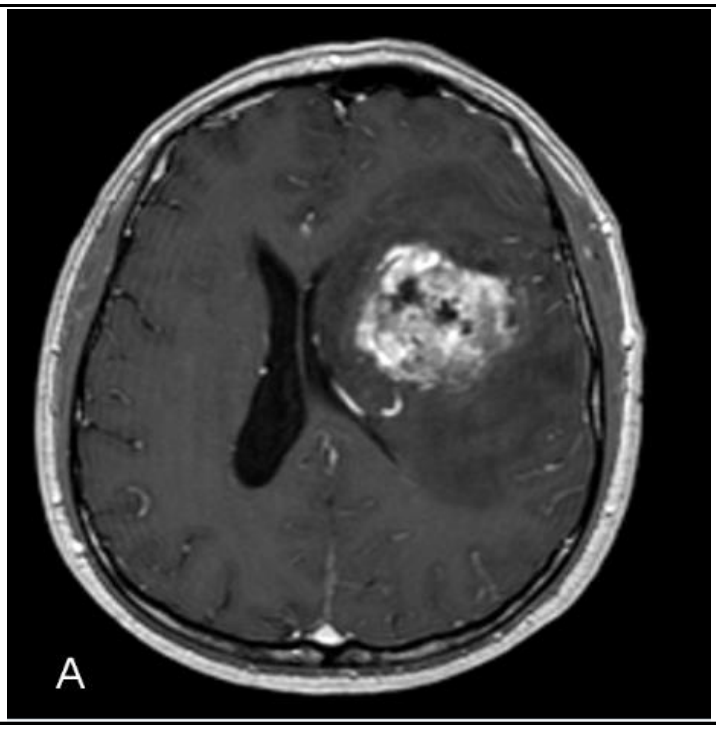
Medico-Legal Issues in Neurosurgery & Neurological Disease

28 February 2018, 7 Bedford Row, London

Cranial surgery

- Common tumour types
- Signs and symptoms
- Imaging procedures employed
- Surgical treatments
- Consequences of the delay in diagnosis

Mr Richard Kerr, Consultant Neurosurgeon, Oxford University Hospitals NHS



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REVIEW

The 2016 World Health Organization Classification of Tumors of the Central Nervous System: a summary

David N. Louis[1] · Arie Perry[2] · Guido Reifenberger[3,4] · Andreas von Deimling[4,5] · Dominique Figarella-Branger[6] · Webster K. Cavenee[7] · Hiroko Ohgaki[8] · Otmar D. Wiestler[9] · Paul Kleihues[10] · David W. Ellison[11]

WHO classification of tumours of the central nervous system

Diffuse astrocytic and oligodendroglial tumours

Diffuse astrocytoma, IDH-mutant	9400/3
Gemistocytic astrocytoma, IDH-mutant	9411/3
Diffuse astrocytoma, IDH-wildtype	9400/3
Diffuse astrocytoma, NOS	9400/3
Anaplastic astrocytoma, IDH-mutant	9401/3
Anaplastic astrocytoma, IDH-wildtype	9401/3
Anaplastic astrocytoma, NOS	9401/3
Glioblastoma, IDH-wildtype	9440/3
Giant cell glioblastoma	9441/3
Gliosarcoma	9442/3
Epithelioid glioblastoma	9440/3
Glioblastoma, IDH-mutant	9445/3*
Glioblastoma, NOS	9440/3
Diffuse midline glioma, H3 K27M-mutant	9385/3*
Oligodendroglioma, IDH-mutant and 1p/19q-codeleted	9450/3
Oligodendroglioma, NOS	9450/3
Anaplastic oligodendroglioma, IDH-mutant and 1p/19q-codeleted	9451/3
Anaplastic oligodendroglioma, NOS	*9451/3*
Oligoastrocytoma, NOS	*9382/3*
Anaplastic oligoastrocytoma, NOS	*9382/3*

Other astrocytic tumours

Pilocytic astrocytoma	9421/1
Pilomyxoid astrocytoma	9425/3
Subependymal giant cell astrocytoma	9384/1
Pleomorphic xanthoastrocytoma	9424/3
Anaplastic pleomorphic xanthoastrocytoma	9424/3

Ependymal tumours

Subependymoma	9383/1
Myxopapillary ependymoma	9394/1
Ependymoma	9391/3
Papillary ependymoma	9393/3
Clear cell ependymoma	9391/3
Tanycytic ependymoma	9391/3
Ependymoma, *RELA* fusion-positive	9396/3*
Anaplastic ependymoma	9392/3

Other gliomas

Chordoid glioma of the third ventricle	9444/1
Angiocentric glioma	9431/1
Astroblastoma	9430/3

Choroid plexus tumours

Choroid plexus papilloma	9390/0
Atypical choroid plexus papilloma	9390/1

Neuronal and mixed neuronal-glial tumours

Dysembryoplastic neuroepithelial tumour	9413/0
Gangliocytoma	9492/0
Ganglioglioma	9505/1
Anaplastic ganglioglioma	9505/3
Dysplastic cerebellar gangliocytoma (Lhermitte–Duclos disease)	9493/0
Desmoplastic infantile astrocytoma and ganglioglioma	
Papillary glioneuronal tumour	
Rosette-forming glioneuronal tumour	
Diffuse leptomeningeal glioneuronal tumour	
Central neurocytoma	
Extraventricular neurocytoma	
Cerebellar liponeurocytoma	
Paraganglioma	

Tumours of the pineal region

Pineocytoma	
Pineal parenchymal tumour of intermediate differentiation	
Pineoblastoma	
Papillary tumour of the pineal region	

Embryonal tumours

Medulloblastomas, genetically defined	
Medulloblastoma, WNT-activated	
Medulloblastoma, SHH-activated and *TP53*-mutant	
Medulloblastoma, SHH-activated and *TP53*-wildtype	
Medulloblastoma, non-WNT/non-SHH	
Medulloblastoma, group 3	
Medulloblastoma, group 4	
Medulloblastomas, histologically defined	
Medulloblastoma, classic	
Medulloblastoma, desmoplastic/nodular	
Medulloblastoma with extensive nodularity	
Medulloblastoma, large cell / anaplastic	
Medulloblastoma, NOS	
Embryonal tumour with multilayered rosettes, C19MC-altered	
Embryonal tumour with multilayered rosettes, NOS	
Medulloepithelioma	
CNS neuroblastoma	
CNS ganglioneuroblastoma	
CNS embryonal tumour, NOS	
Atypical teratoid/rhabdoid tumour	
CNS embryonal tumour with rhabdoid features	

Tumours of the cranial and paraspinal nerves

Schwannoma	
Cellular schwannoma	

Melanotic schwannoma	9560/1
Neurofibroma	9540/0
Atypical neurofibroma	9540/0
Plexiform neurofibroma	9550/0
Perineurioma	9571/0
Hybrid nerve sheath tumours	
Malignant peripheral nerve sheath tumour	9540/3
Epithelioid MPNST	9540/3
MPNST with perineurial differentiation	9540/3

Meningiomas

Meningioma	9530/0
Meningothelial meningioma	9531/0
Fibrous meningioma	9532/0
Transitional meningioma	9537/0
Psammomatous meningioma	9533/0
Angiomatous meningioma	9534/0
Microcystic meningioma	9530/0
Secretory meningioma	9530/0
Lymphoplasmacyte-rich meningioma	9530/0
Metaplastic meningioma	9530/0
Chordoid meningioma	9538/1
Clear cell meningioma	9538/1
Atypical meningioma	9539/1
Papillary meningioma	9538/3
Rhabdoid meningioma	9538/3
Anaplastic (malignant) meningioma	9530/3

Mesenchymal, non-meningothelial tumours

Solitary fibrous tumour / haemangiopericytoma**	
Grade 1	8815/0
Grade 2	8815/1
Grade 3	8815/3
Haemangioblastoma	9161/1
Haemangioma	9120/0
Epithelioid haemangioendothelioma	9133/3
Angiosarcoma	9120/3
Kaposi sarcoma	9140/3
Ewing sarcoma / PNET	9364/3
Lipoma	8850/0
Angiolipoma	8861/0
Hibernoma	8880/0
Liposarcoma	8850/3
Desmoid-type fibromatosis	8821/1
Myofibroblastoma	8825/0
Inflammatory myofibroblastic tumour	8825/1
Benign fibrous histiocytoma	8830/0
Fibrosarcoma	8810/3
Undifferentiated pleomorphic sarcoma / malignant fibrous histiocytoma	8802/3
Leiomyoma	8890/0
Leiomyosarcoma	8890/3
Rhabdomyoma	8900/0
Rhabdomyosarcoma	8900/3
Chondroma	9220/0
Chondrosarcoma	9220/3
Osteoma	9180/0
Osteochondroma	9210/0
Osteosarcoma	9180/3

Melanocytic tumours

Meningeal melanocytosis	8728/0
Meningeal melanocytoma	8728/1
Meningeal melanoma	8720/3
Meningeal melanomatosis	8728/3

Lymphomas

Diffuse large B-cell lymphoma of the CNS	9680/3
Immunodeficiency-associated CNS lymphomas	
AIDS-related diffuse large B-cell lymphoma	
EBV-positive diffuse large B-cell lymphoma, NOS	
Lymphomatoid granulomatosis	9766/1
Intravascular large B-cell lymphoma	9712/3
Low-grade B-cell lymphomas of the CNS	
T-cell and NK/T-cell lymphomas of the CNS	
Anaplastic large cell lymphoma, ALK-positive	9714/3
Anaplastic large cell lymphoma, ALK-negative	9702/3
MALT lymphoma of the dura	9699/3

Histiocytic tumours

Langerhans cell histiocytosis	9751/3
Erdheim–Chester disease	9750/1
Rosai–Dorfman disease	
Juvenile xanthogranuloma	
Histiocytic sarcoma	9755/3

Germ cell tumours

Germinoma	9064/3
Embryonal carcinoma	9070/3
Yolk sac tumour	9071/3
Choriocarcinoma	9100/3
Teratoma	9080/1
Mature teratoma	9080/0
Immature teratoma	9080/3
Teratoma with malignant transformation	9084/3
Mixed germ cell tumour	9085/3

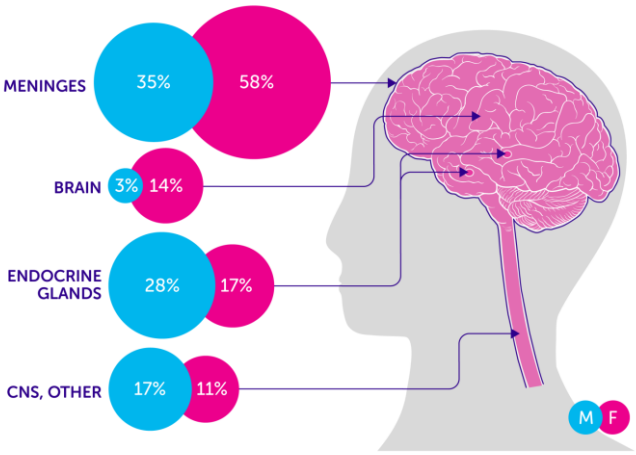
Tumours of the sellar region

Craniopharyngioma	9350/1
Adamantinomatous craniopharyngioma	9351/1
Papillary craniopharyngioma	9352/1
Granular cell tumour of the sellar region	9582/0
Pituicytoma	9432/1
Spindle cell oncocytoma	8290/0

Metastatic tumours

The morphology codes are from the International Classification of Diseases for Oncology (ICD-O) (*7*4*2*4). Behaviour is coded */0* for benign tumours; */1* for unspecified, borderline, or uncertain behaviour; */2* for carcinoma in situ and grade III intraepithelial neoplasia; and */3* for malignant tumours. The classification is modified from the previous WHO classification, taking into account changes in our understanding of these lesions.
*These new codes were approved by the IARC/WHO Committee for ICD-O.
Italics: Provisional tumour entities. **Grading according to the 2013 *WHO Classification of Tumours of Soft Tissue and Bone*.

BENIGN BRAIN, OTHER CNS AND INTRACRANIAL TUMOURS: PERCENTAGE DISTRIBUTION BY ANATOMICAL SITE



LET'S BEAT CANCER SOONER
cruk.org/cancerstats

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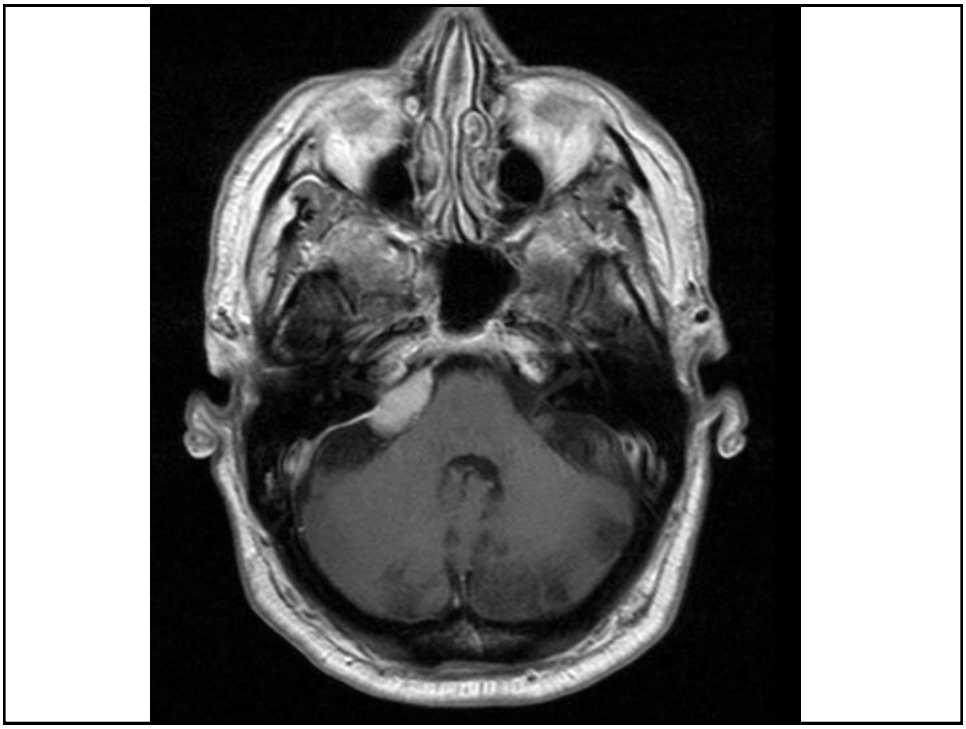
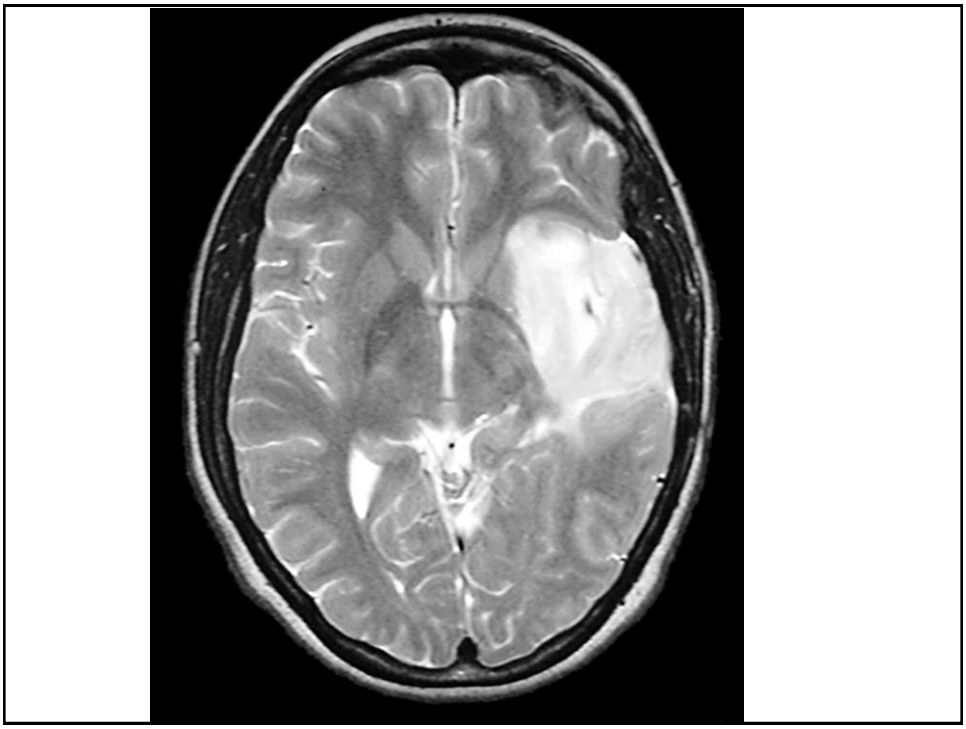
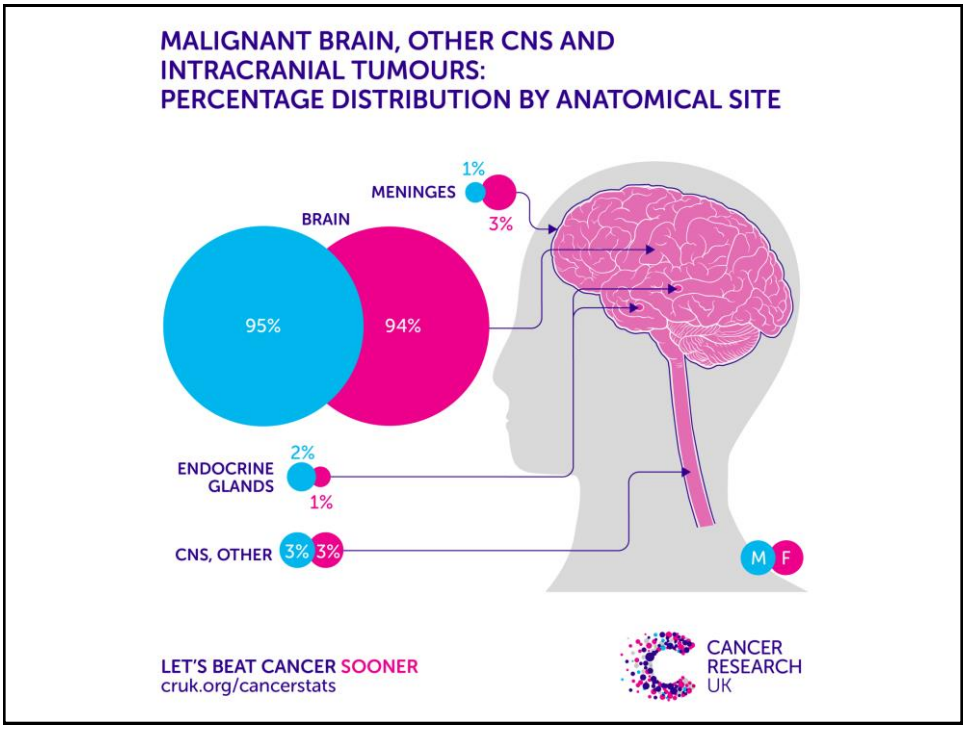
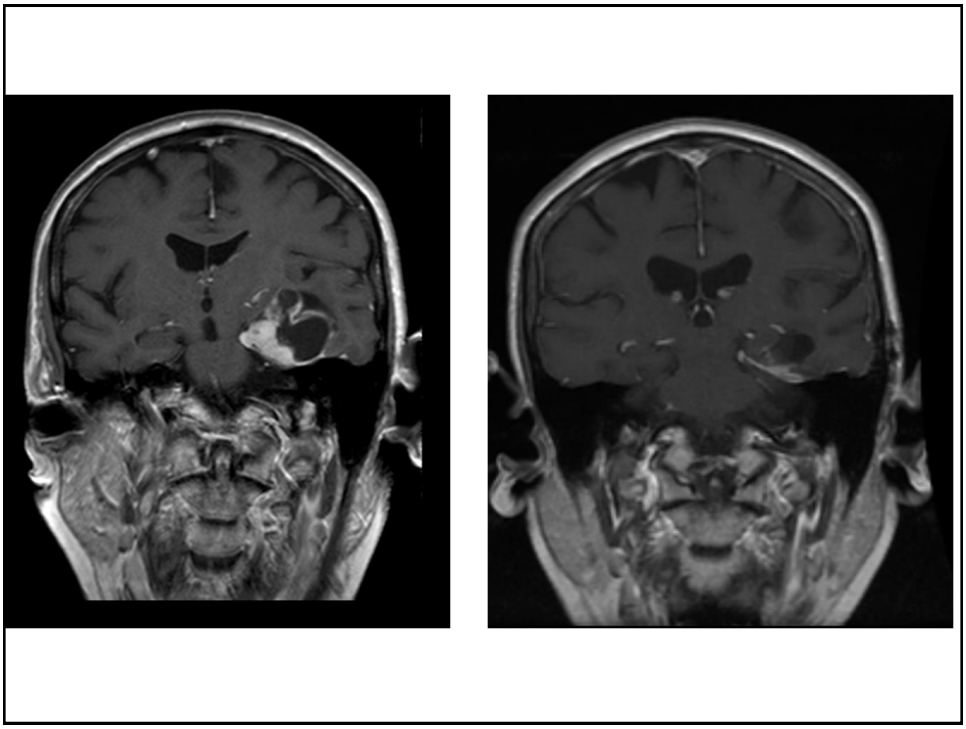
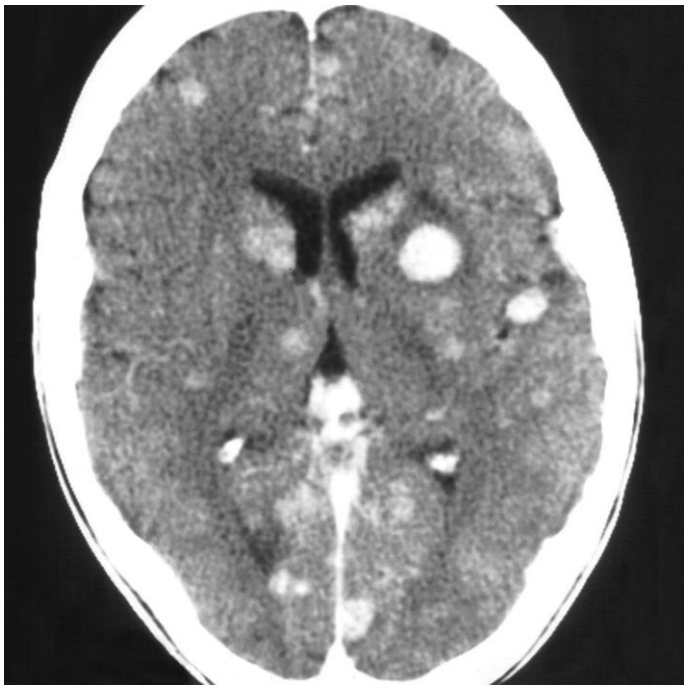





MALIGNANT BRAIN, OTHER CNS AND INTRACRANIAL TUMOURS: PERCENTAGE DISTRIBUTION BY ANATOMICAL SITE
MENINGES
1%
3%
BRAIN
95%
94%
ENDOCRINE GLANDS
2%
1%
CNS, OTHER
3%
3%
M
F
LET'S BEAT CANCER SOONER
cruk.org/cancerstats
CANCER RESEARCH UK

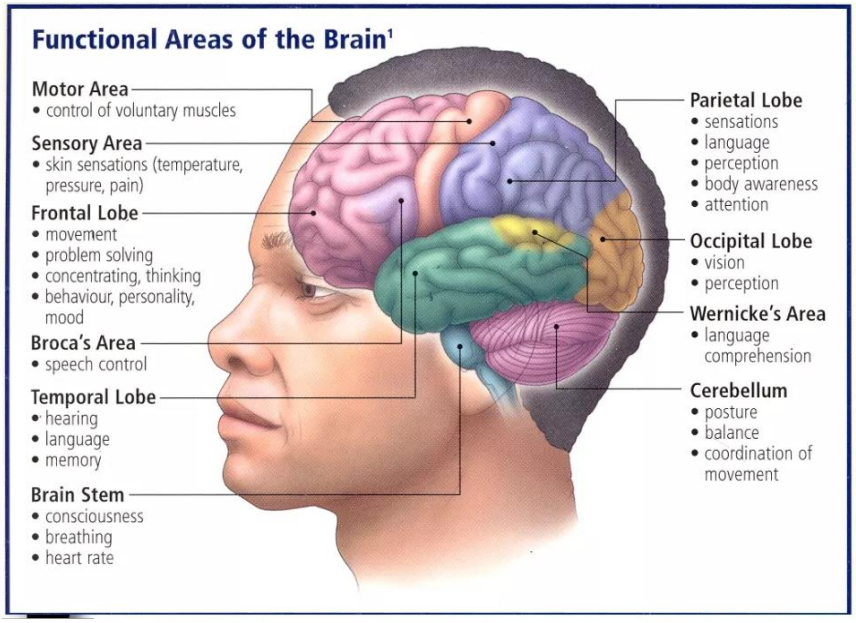




What symptoms do brain tumours cause?

Brain tumours present in three main ways:

1. Headaches – this is due to an increase in the pressure within the skull caused by the expanding tumour and any swelling associated with it. These headaches are often worse at night, in the early hours of the morning and may sometimes be associated with vomiting or visual disturbance.
2. Changes in function – due to damage to, or pressure on, certain areas of the brain. For example, a tumour in the right hemisphere might cause weakness of the left side of the body. Tumours in the frontal lobes might cause changes in personality or behaviour.
3. Seizures (fits or epilepsy) – due to irritation of certain areas of the brain causing neurones to fire-off uncontrollably. These may be focal (partial) fits causing a jerking or twitching of one or more limbs, which is commonly followed by a period of paralysis in the affected limb (which then recovers). There may also be generalised fits (often termed an epileptic fit) in which there is loss of consciousness, twitching of all the limbs and often tongue biting and incontinence.



New presentation of Brain Tumour

- Neuro-oncology MDT

  Intrinsic tumours, Meningiomas, Lymphoma, metastatic tumours

- Skull Base MDT

  All tumours involving skull base

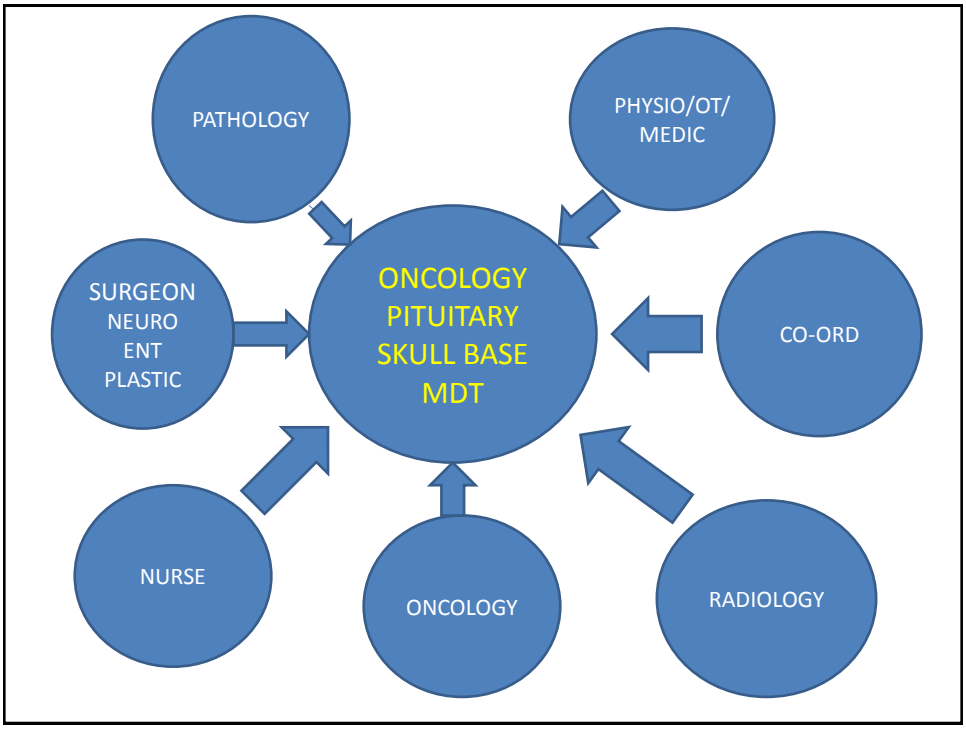
- Pituitary MDT

  All pituitary and Para pituitary disease

DH Department of Health

Improving Outcomes: A Strategy for Cancer

January 2011



ABC2 Brain Cancer Breakthroughs

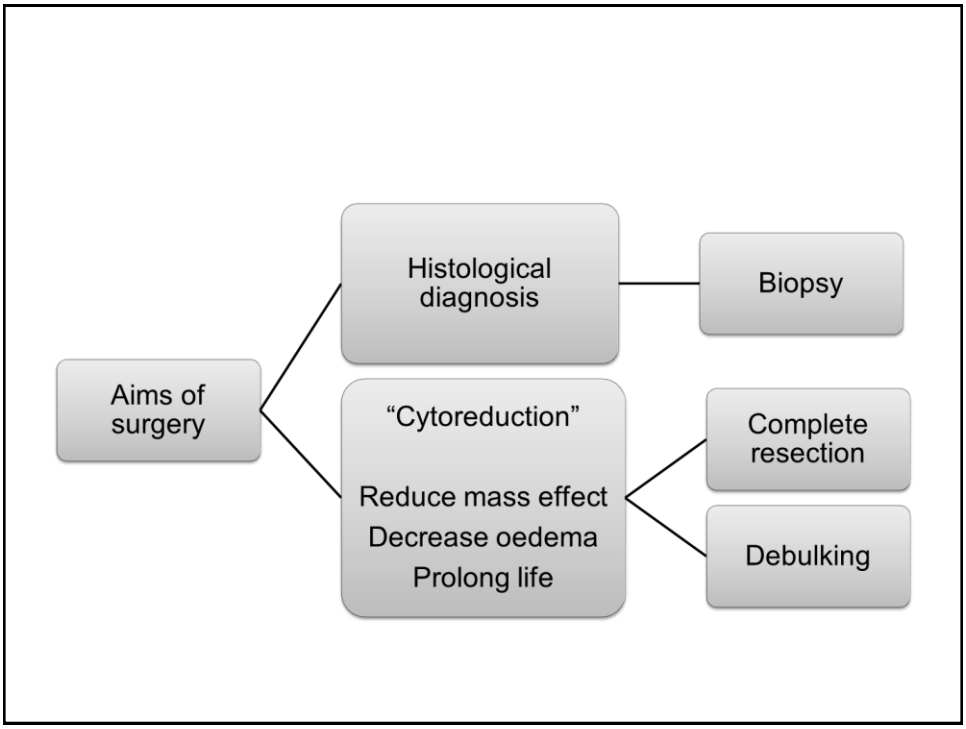
Treatments

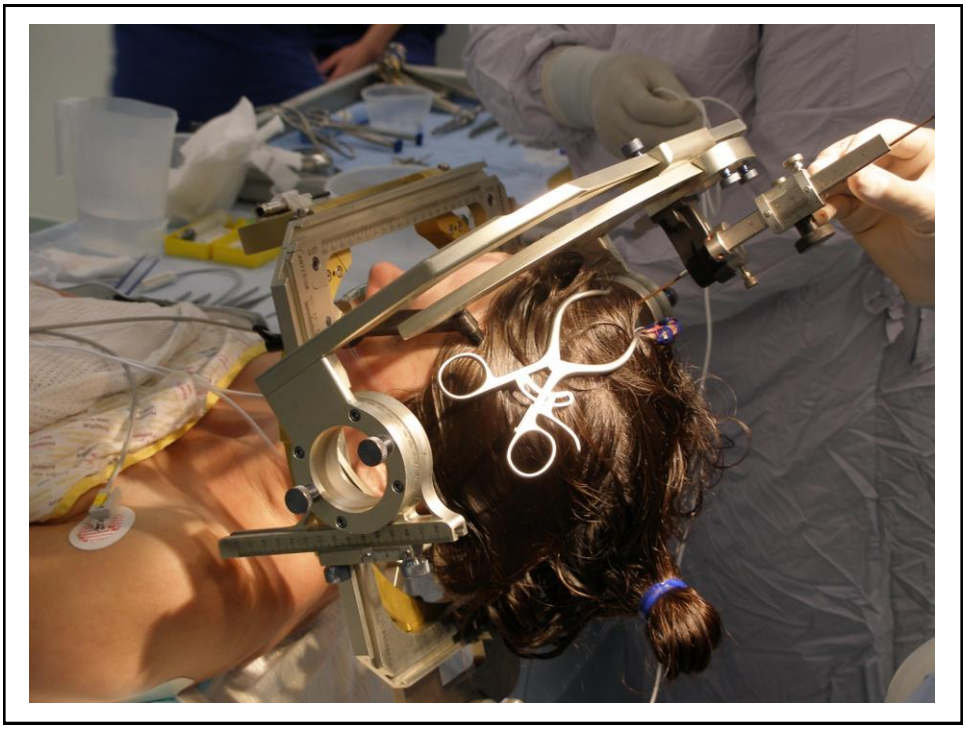
People with brain tumors have several treatment options. The options are surgery, radiation therapy, and chemotherapy. Many people get a combination of treatments. The choice of treatment depends mainly on the following:

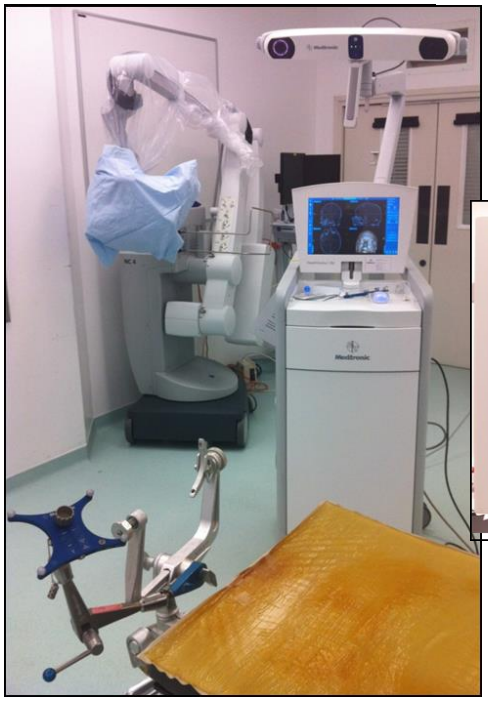
- The type and grade of brain tumor
- Its location in the brain
- Its size
- Your age and general health

But not mentioned……..

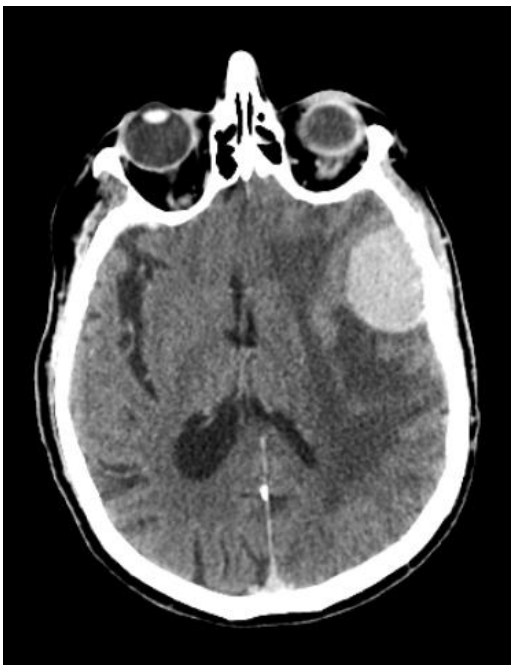
- The importance of Personal choice
- The Option of no treatment and accept the natural history

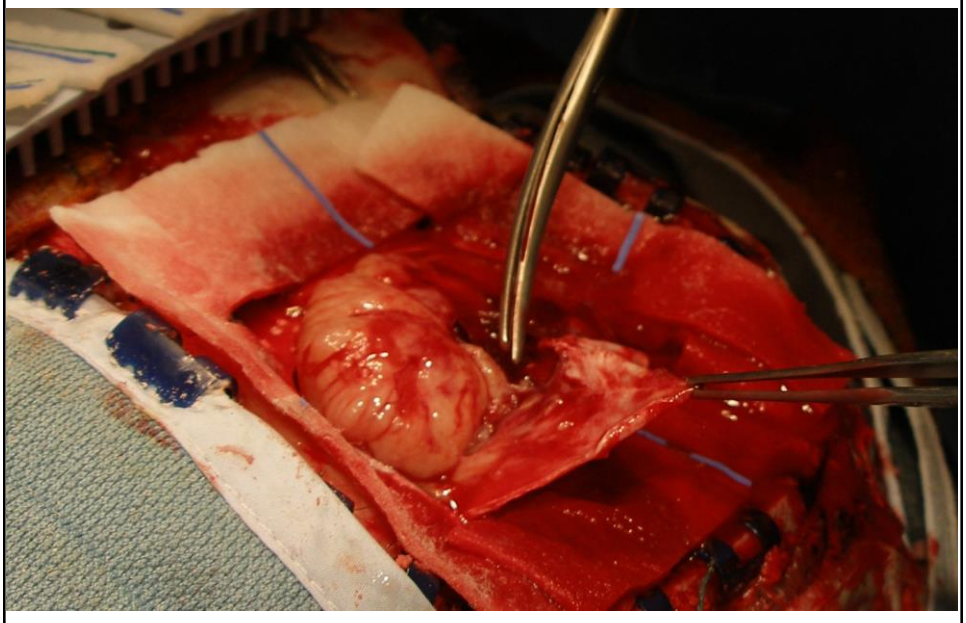

Aims of surgery
Histological diagnosis
Biopsy
"Cytoreduction"
Reduce mass effect
Decrease oedema
Prolong life
Complete resection
Debulking

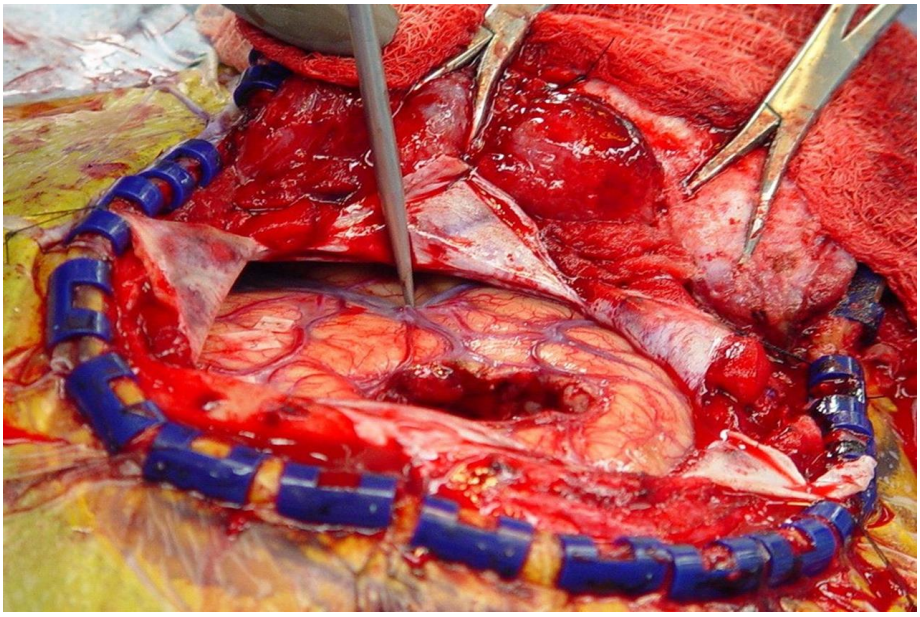


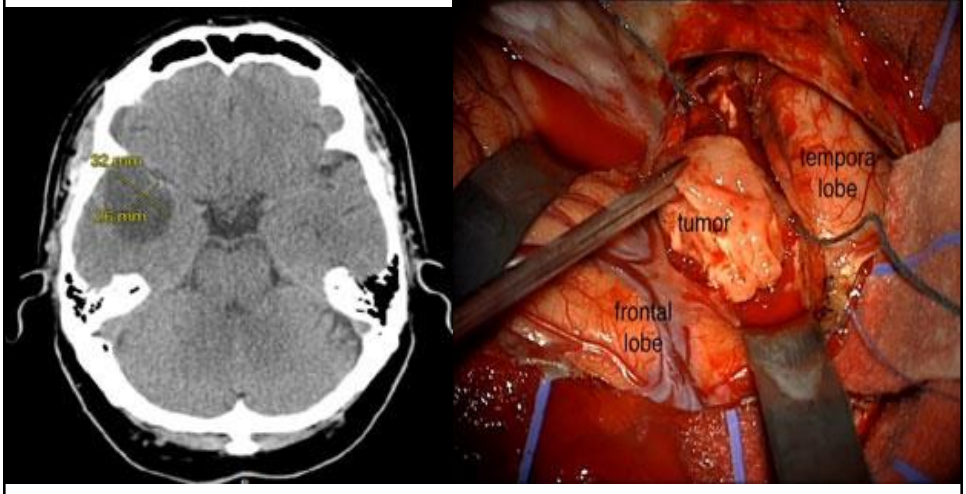

Medtronic

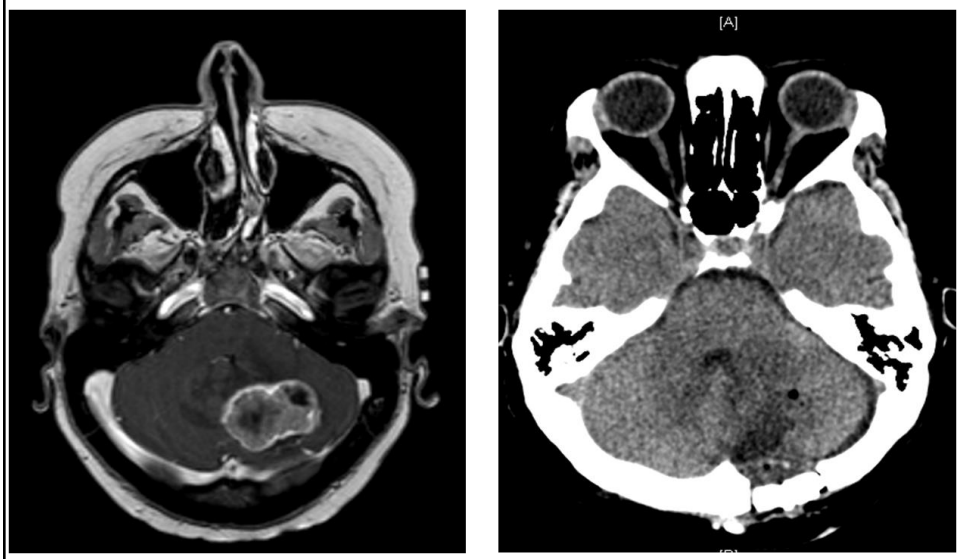

Medtronic



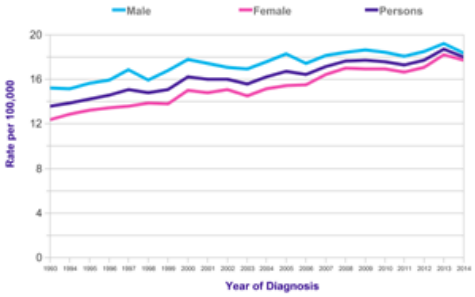





32 mm
26 mm
tempora
lobe
tumor
frontal
lobe


[A]

Brain, Other CNS and Intracranial Tumours (C70-C72, C75.1-C75.3, D32-D33, D35.2-D35.4, D42-D43, D44.3-D44.5): 1993-2014
European Age-Standardised Incidence Rates per 100,000 Population, by Sex, UK



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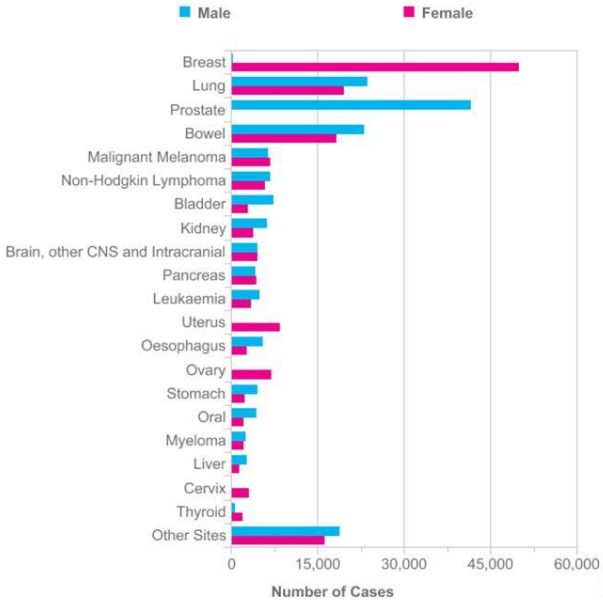
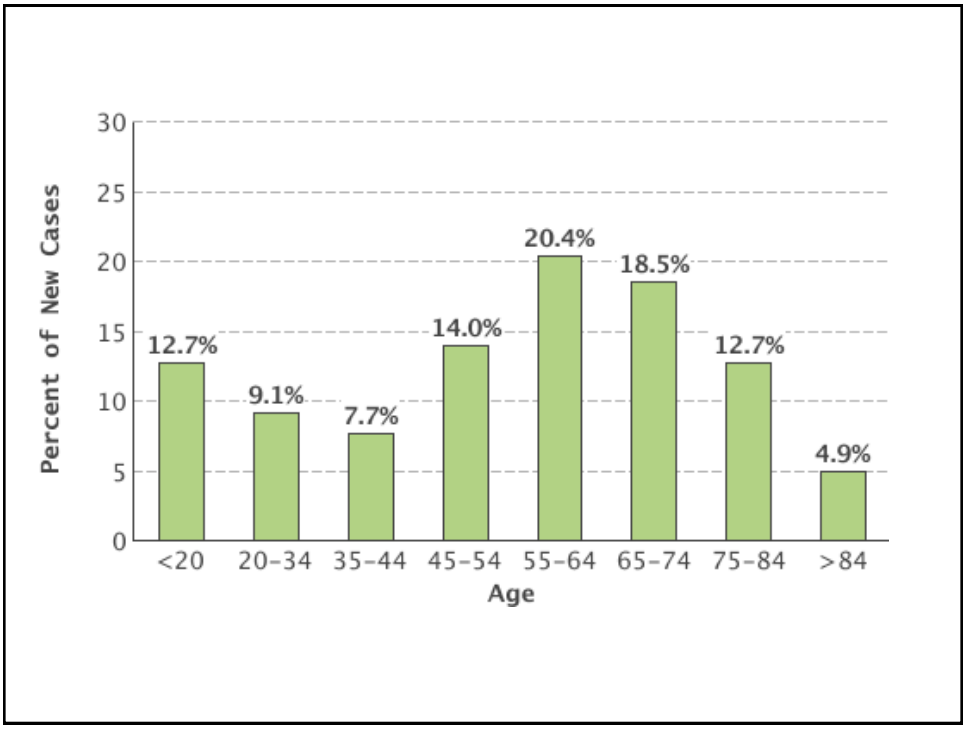
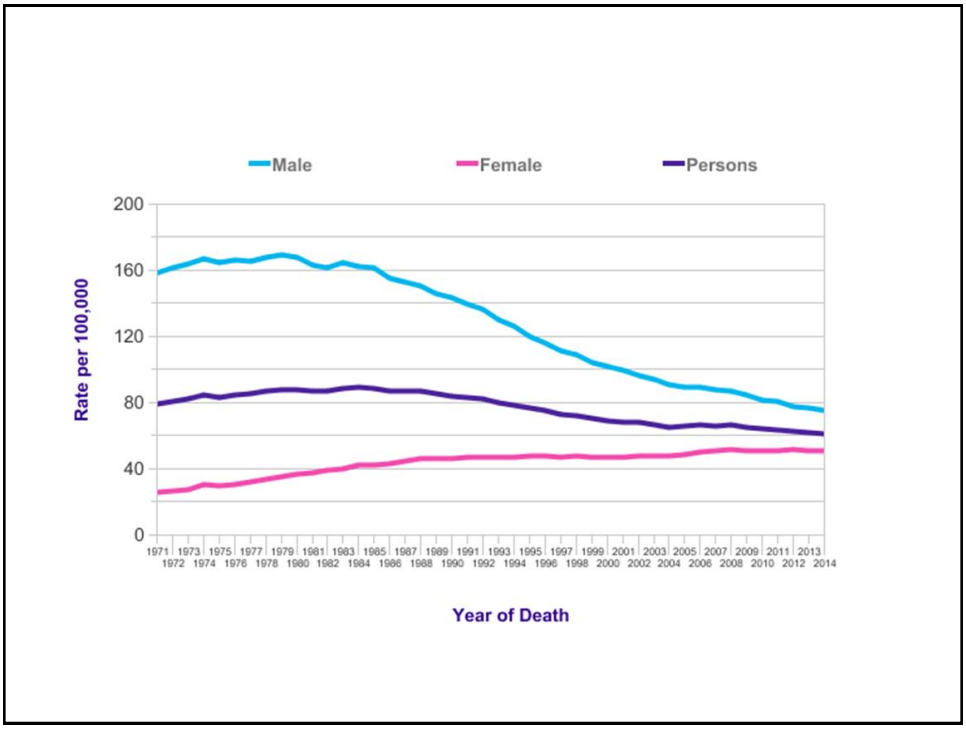


Cancer Incidence (CRUK)

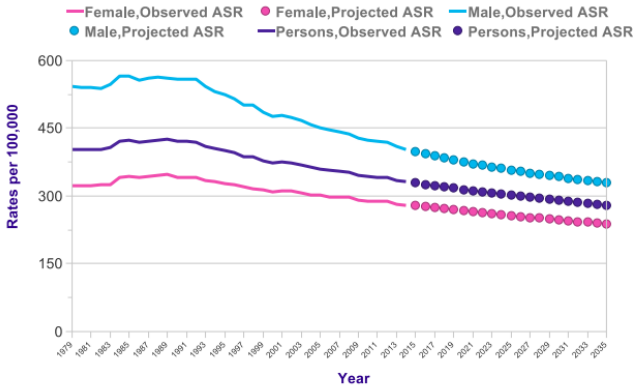
The Nottingham Oncology Group


Percent of New Cases
30
25
20
15
10
5
0
12.7%
9.1%
7.7%
14.0%
20.4%
18.5%
12.7%
4.9%
<20
20-34
35-44
45-54
55-64
65-74
75-84
>84
Age


Male
Female
Persons
Rate per 100,000
200
160
120
80
40
0
1971 1972 1973 1974 1975 1976 1977 1978 1979 1980 1981 1982 1983 1984 1985 1986 1987 1988 1989 1990 1991 1992 1993 1994 1995 1996 1997 1998 1999 2000 2001 2002 2003 2004 2005 2006 2007 2008 2009 2010 2011 2012 2013 2014
Year of Death

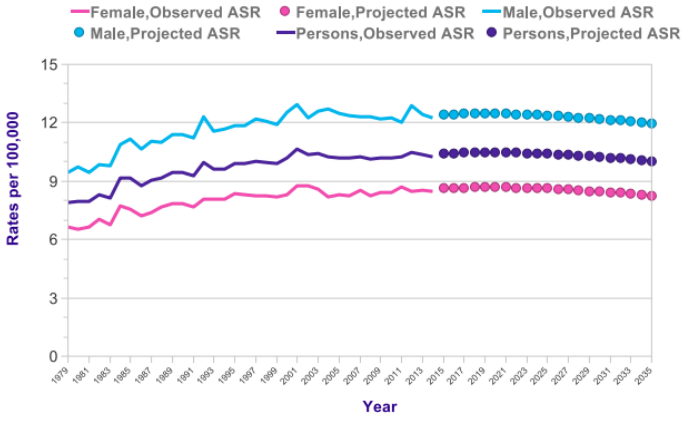
All Cancers Excluding Non-Melanoma Skin Cancer Plus Benign Brain Other CNS and Intracranial Tumours (C00-C97 (Excl. C44) D32-D33 D35.2-D35.4 D42-D43 D44.3-D44.5): 1979-2035

Observed and Projected Age-standardised Mortality Rates, by Sex, UK



Brain, Other CNS and Intracranial Tumours (C70-C72, C75.1-C75.3, D32-D33, D35.2-D35.4, D42-D43, 1979-2035

Observed and Projected Age-standardised Mortality Rates, by Sex, UK



Source: cruk.org/cancerstats

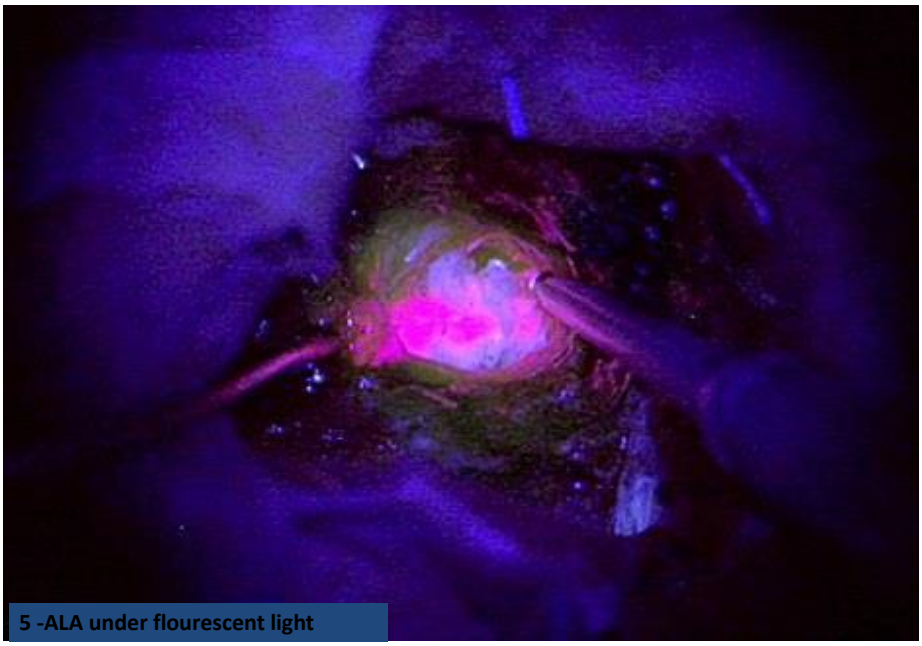
One-, Five- and Ten-Year Net Survival (%), Adults Aged 15-99, England & Wales

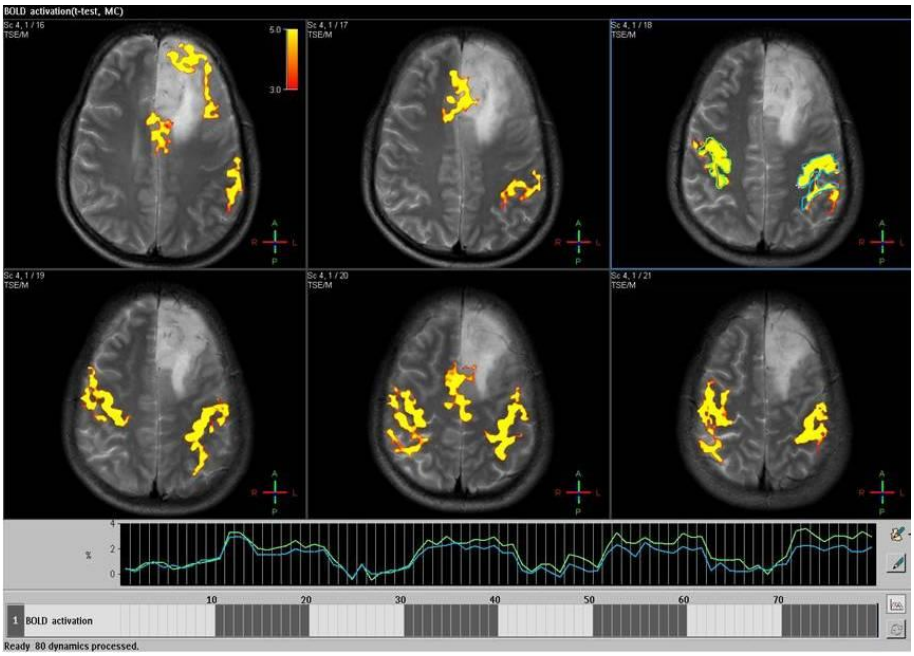
		1-Year Survival (%)	5-Year Survival (%)	10-Year Survival (%)
Men	Net Survival	41.0	17.8	12.8
	95% LCL	40.7	16.3	9.9
	95% UCL	41.4	19.4	16.1
Women	Net Survival	38.8	19.5	14.4
	95% LCL	38.3	17.9	11.5
	95% UCL	39.2	21.1	17.7
Adults	Net Survival	40.1	18.5	13.5
	95% LCL	39.8	17.4	11.4
	95% UCL	40.4	19.6	15.8

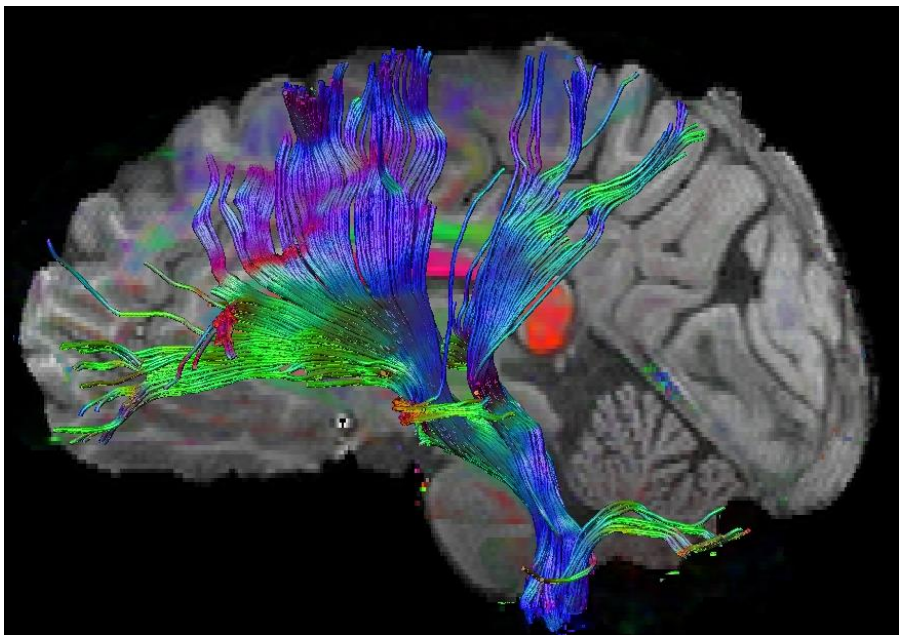
Five- and Ten-year survival has been predicted for patients diagnosed in 2010-2011 (using an excess hazard statistical model)
95% LCL and 95% UCL are the 95% lower and upper confidence limits

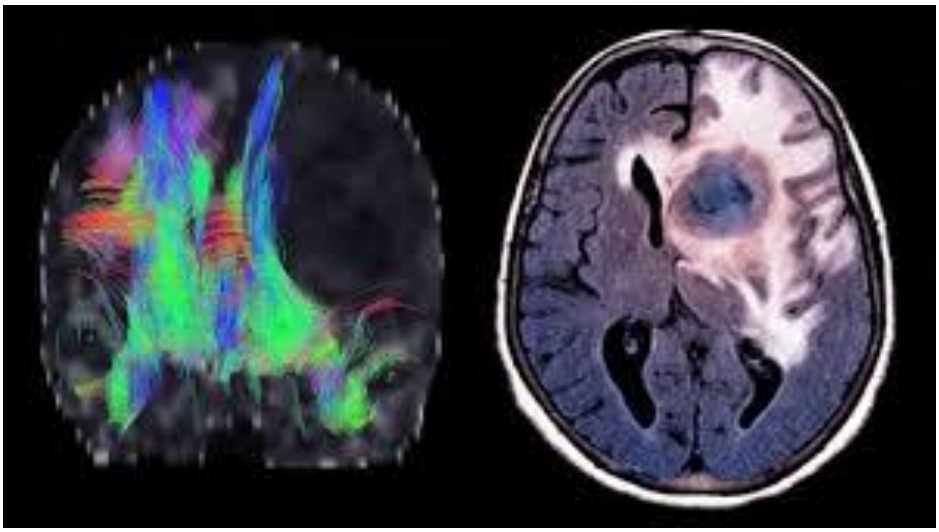
Please include the citation provided in our Frequently Asked Questions when reproducing this chart:
http://info.cancerresearchuk.org/cancerstats/faqs/#How
Prepared by Cancer Research UK
Original data sources:
Survival estimates were provided on request by the Cancer Research UK Cancer Survival Group at the London School of Hygiene and Tropical Medicine. http://www.lshtm.ac.uk/eph/ncde/cancersurvival/

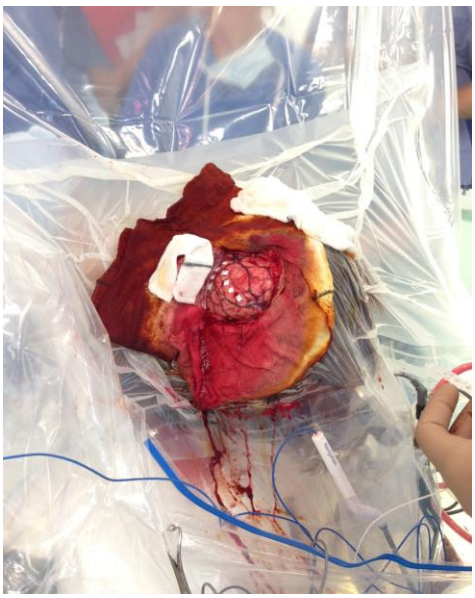
Brain Cancer (C71): 2010-2011



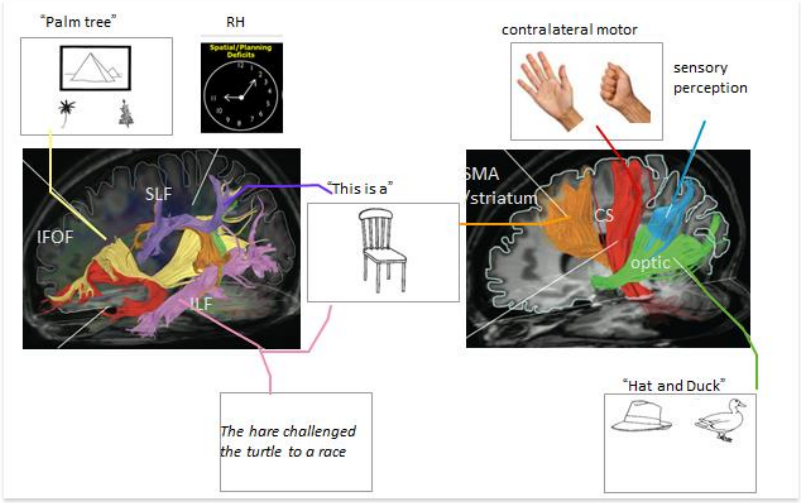

BOLD activation(t-test, MC)
Sc 4, 1 / 16
TSE/M
Sc 4, 1 / 17
TSE/M
Sc 4, 1 / 18
TSE/M
Sc 4, 1 / 19
TSE/M
Sc 4, 1 / 20
TSE/M
Sc 4, 1 / 21
TSE/M
5.0
3.0
%
10
20
30
40
50
60
70
1 BOLD activation
Ready 80 dynamics processed.







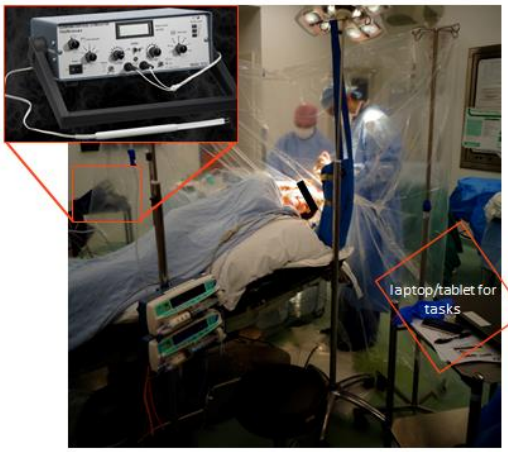
Awake Mapping Tasks



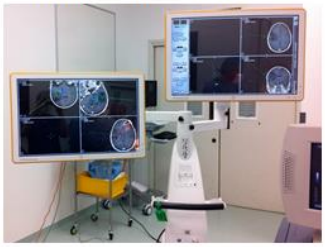
Coello et al., JNS. 2013

Awake Intraoperative set-up

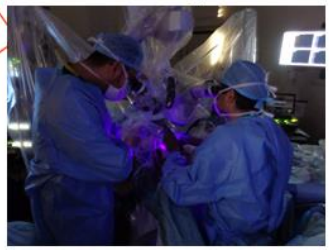
Ojemann stimulator

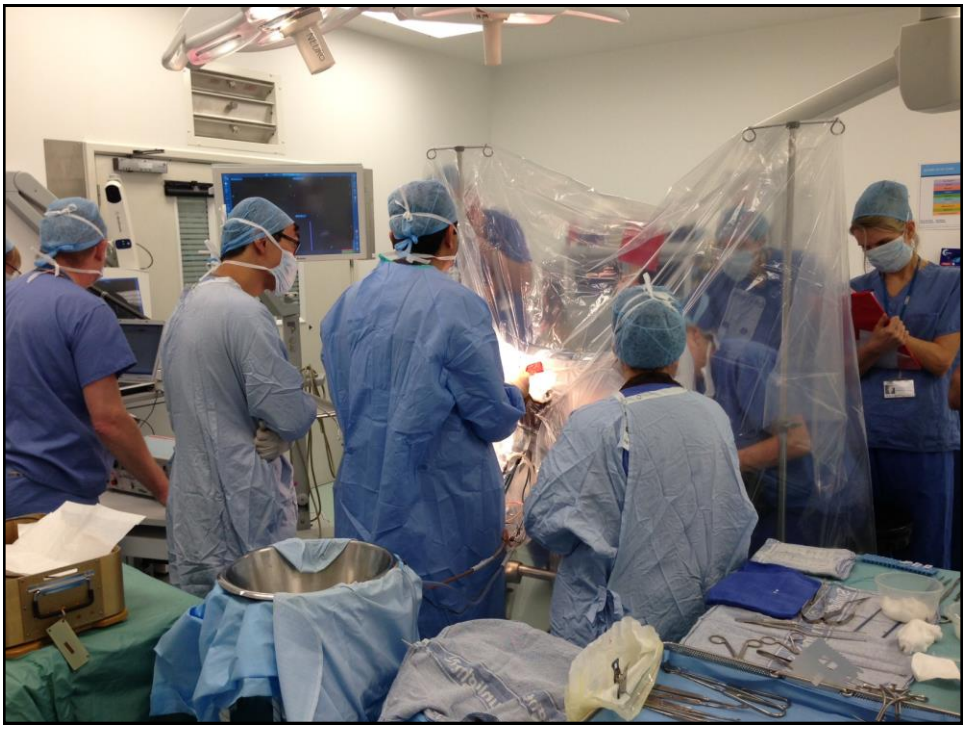


DTI fused with navigation scan

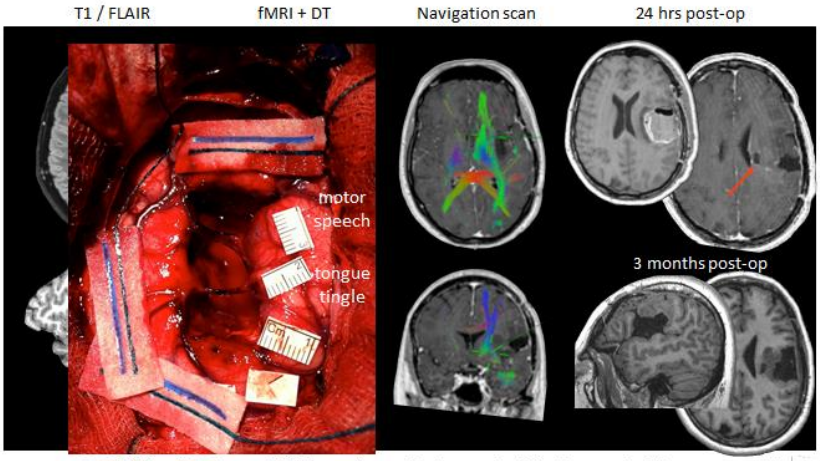


Awake, DTI and 5-ALA guided resection

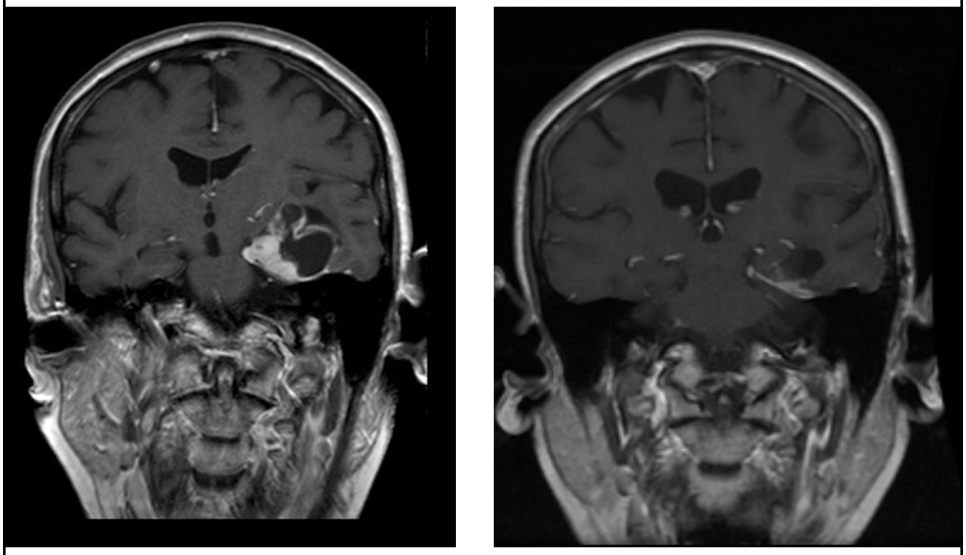




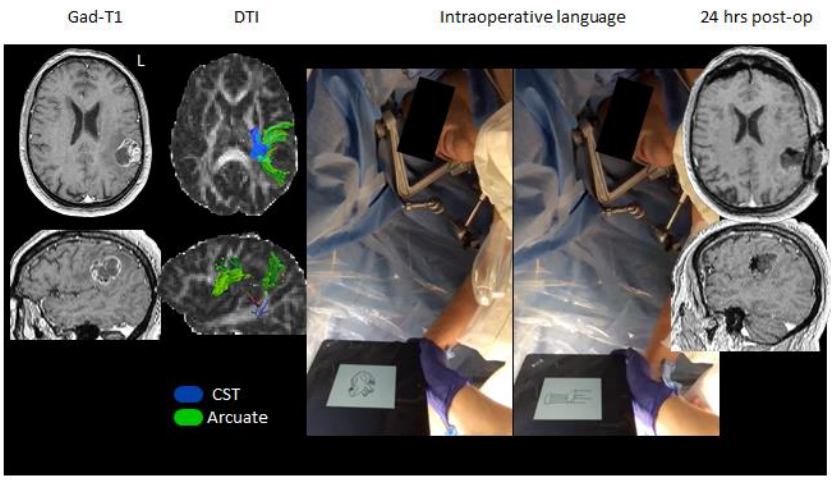
Multi 32 yo R-handed F, swimming instructor. Seizures.



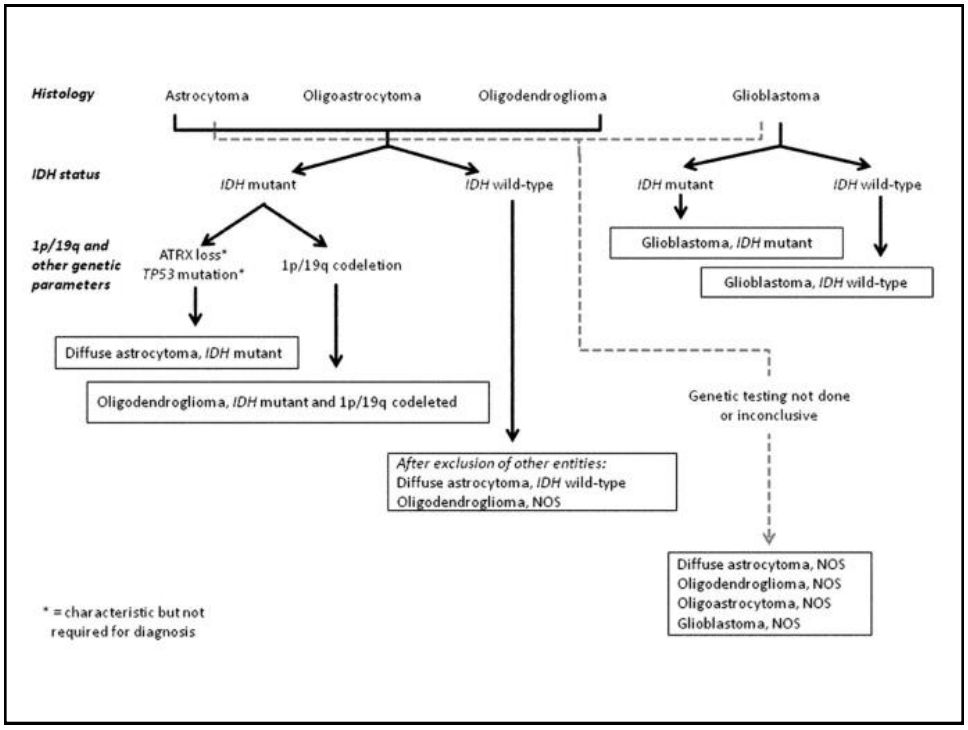
3mA: **CST** hand tingling; ant-inf **IFOF** speech errors. During resection difficulties repeating full sentences, multiple omissions and errors upon stimulation. Progressive difficulties + sudden self-reported drop in fluency.
Intact fluency and naming at 6 months postop. Motor recovery with physiotherapy.



SLF 68 y.o. R-handed M; speech disturbance & parasthesia



@ 4MA, medial / anterior arcuate : neologisms and phonemic errors and slowing.



	IDH-wildtype glioblastoma	IDH-mutant glioblastoma	References
Synonym	Primary glioblastoma, IDH-wildtype	Secondary glioblastoma, IDH-mutant	{1830}
Precursor lesion	Not identifiable; develops de novo	Diffuse astrocytoma Anaplastic astrocytoma	{1827}
Proportion of glioblastomas	~90%	~10%	{1797}
Median age at diagnosis	~62 years	~44 years	{214,1078,1797, 2103}
Male-to-female ratio	1.42:1	1.05:1	{214,1417,1797}
Mean length of clinical history	4 months	15 months	{1797}
Median overall survival			
Surgery + radiotherapy	9.9 months	24 months	{1797}
Surgery + radiotherapy + chemotherapy	15 months	31 months	{2810}
Location	Supratentorial	Preferentially frontal	{1417}
Necrosis	Extensive	Limited	{1417}
TERT promoter mutations	72%	26%	{1801,1830}
TP53 mutations	27%	81%	{1797}
ATRX mutations	Exceptional	71%	{1519}
EGFR amplification	35%	Exceptional	{1797}
PTEN mutations	24%	Exceptional	{1797}

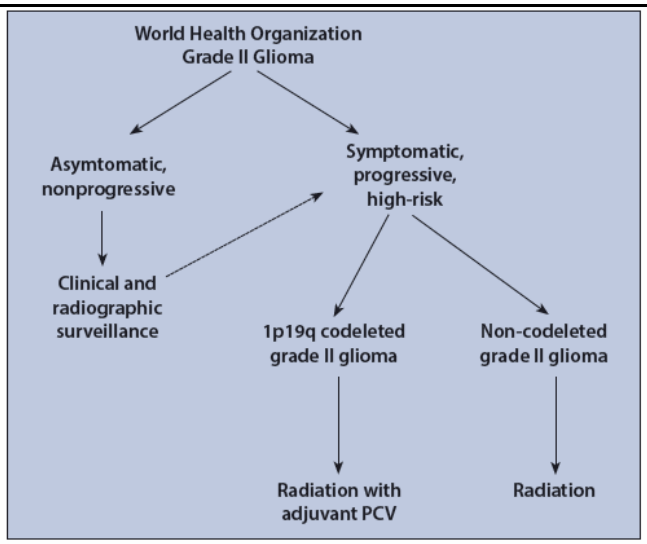


Figure: Suggested Treatment Algorithm for Grade II Gliomas Based on Recent Emerging Data From RTOG 9802—The findings of this study demonstrate the importance of immunohistochemistry and molecular data in guiding treatment selection. Timing of treatment in grade II gliomas is based on clinical symptomatology, radiographic progression, and patient-specific risk. Further reporting of molecular data from the RTOG 9802 trial and ongoing studies will continue to inform this algorithm. RTOG = Radiation Therapy Oncology Group.

Adjuvant therapies

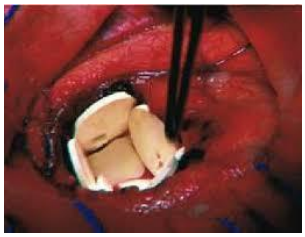
Types of external radiotherapy

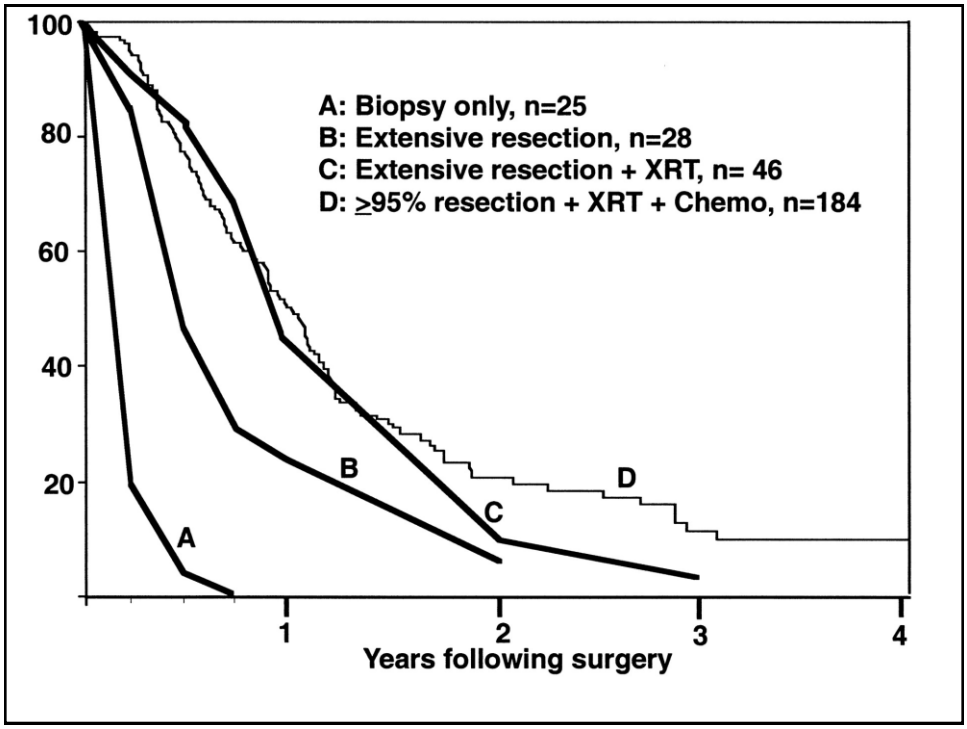
- conformal radiotherapy.
- intensity modulated radiotherapy (IMRT)
- image guided radiotherapy (IGRT)
- 4-dimensional radiotherapy (4D-RT)
- stereotactic radiotherapy and radiosurgery.
- proton therapy.
- electron beam radiotherapy.
- adaptive radiotherapy.

TABLE 1: Chemotherapeutic regimens for gliomas

Regimen	Dose	Route and frequency
Single-agent BCNU		
BCNU	200 mg/m² (maximum cumulative dose, 1,500 mg/m²)	IV q8wk
Single-agent temozolamide		
Temozolamide	150-200 mg/m²	PO on days 1-5
Repeat cycle every 28 days.		
Standard PCV		
CCNU	110 mg/m²	PO on day 1
Procarbazine	60 mg/m²/d	PO on days 8-21
Vincristine	1.4 mg/m² (maximum dose, 2 mg)	IV on days 8 and 29
Repeat cycle every 6-8 weeks, optimally for 6 cycles.		
Intensified PCV[a]		
CCNU	130 mg/m²	PO on day 1
Procarbazine	75 mg/m²/d	PO on days 8-21
Vincristine	1.4 mg/m² (no dose limit)	IV on days 8 and 29
Repeat cycle every 6 weeks.		

[a] Sometimes used in patients with oligodendrogliomas





Currently Recruiting Trials – High Grade Glioma

- **Page last updated October 2, 2017**
- **NEW TRIALS (ADDED HERE IN THE LAST MONTH)**
- *Added September 24, 2017*
  A Phase 1b Study of Toca 511, a Retroviral Replicating Vector, Combined With Toca FC in Patients With Solid Tumors or Lymphoma. Phase 1. University of Miami, Florida. Estimated primary completion date: April 2019. *In the glioma category, only IDH1-mutant or MGMT promoter methylation positive anaplastic astrocytoma and glioblastoma are eligible for this trial.*
  NCT02576665
- **FLUORESCENCE-GUIDED RESECTION AND IMPROVED INTRA-OPERATIVE TUMOUR VISUALIZATION**
- **A Multicenter Study of 5-Aminolevulinic Acid (5-ALA) to Enhance Visualization of Malignant Tumor in Patients With Newly Diagnosed or Recurrent Malignant Gliomas: A Safety, Histopathology, and Correlative Biomarker Study**. Phase II. University of California San Diego CA, New York NY. Estimated primary completion date: December 2017.
  NCT02632370
- **Fluorescence-guided Surgery for Low- and High-grade Gliomas (BALANCE)**. Phase III. Phoenix, Arizona, USA. Estimated primary completion date: January 2018.
  NCT01502280
- **A Phase 1 and 2 Study of 5-aminolevulinic Acid (5-ALA) to Enhance Visualisation and Resection of Malignant Glial Tumors of the Brain**. Springfield, Illinois. Estimated primary completion date: June 2018.
  NCT01128218
- **Quantification of ALA-induced PpIX Fluorescence During Brain Tumor Resection**. Phase I. Dartmouth-Hitchcock Medical Center, Lebanon, New Hampshire. Estimated primary completion date: July 2019.
  NCT02191488
- **5-ALA in Recurrent Glioma**. Phoenix, Arizona, USA. A single-center, non-randomized, single-arm study. Estimated primary completion date: June 2017. *Recurrent only*.
  NCT02119338
- **NEWLY DIAGNOSED**
- **Phase I Study in Humans Evaluating the Safety of Rectus Sheath Implantation of Diffusion Chambers Encapsulating Autologous Malignant Glioma Cells Treated With Insulin-like Growth Factor Receptor-1 Antisense Oligodeoxynucleotide (IGF-1R/AS ODN) in 32 Patients With Newly Diagnosed Malignant Glioma**. Philadelphia PA. Estimated primary completion date: December 2018.
  NCT02507583
- **A Phase I study of neural stem cell based virotherapy in combination with standard radiation and chemotherapy for patients with newly diagnosed malignant glioma**. Chicago IL. Estimated primary completion date: March 2019.
  NCT03072134
- **PROTON RADIATION THERAPY**
- **Proton Radiation Therapy for Low Grade and Favorable Grade 3 Gliomas**. Phase II. The "favorable" descriptor in the title refers to grade III patients with either IDH1 mutation or codeletion of chromosomes 1p and 19q. This is a single-centre study being conducted at the Massachusetts General Hospital in Boston. Proton therapy is a form of radiation which reduces damage to surrounding tissues. Patients receive a total of 54 Gy of radiation over a course of six weeks. Estimated enrollment is 40 patients and estimated primary completion date is May 2017.
  NCT01358058
- **RECURRENT AND PROGRESSIVE**
- **PHOTODYNAMIC THERAPY AND SURGERY**
- **A Phase II Study of Photodynamic Therapy (PDT) With Photofrin® (IND 104,613) For Recurrent High Grade Gliomas in Adults**. Milwaukee USA. Estimated primary completion date: June 2021.
  NCT01966809
- **VACCINES – RECURRENT**
- **Dendritic Cell Vaccine For Relapsed Malignant Glioma and Glioblastoma Multiforme in Adult and Pediatric Subjects**. Phase I. This is a phase I trial conducted by the University of Miami Sylvester Comprehensive Cancer Center. Vaccine preparation involves dendritic cells loaded with tumor lysate. Patients in this trial will also have imiquimod cream (an immune stimulant) applied topically. Patients must have undergone or undergo a surgical resection to obtain tumor material, and also a leukapheresis procedure to obtain dendritic cells from the patients' blood. The trial is open to patients with recurrent high grade gliomas, including patients originally diagnosed with a grade II glioma, but recurrent as a grade III or glioblastoma (grade IV). Estimated primary completion date: July 2018.
  NCT01808820
- **Phase I Study of Safety and Immunogenicity of ADU-623, a Live-attenuated Listeria Monocytogenes Strain (ΔactA/ΔinlB) Expressing the EGFRvIII-NY-ESO-1 Vaccine, in Patients With Treated and Recurrent WHO Grade III/IV Astrocytomas**. Portland, Oregon, USA. Estimated primary completion date: October 2016.
  For patients who have completed the standard of care (ie radiation, chemotherapy).
  NCT01967758
- **VXM01 Phase I Pilot Study in Patients With Operable Recurrence of a Glioblastoma to Examine Safety, Tolerability, Immune and Biomarker Response to the Investigational VEGFR-2 DNA Vaccine VXM01**. Heidelberg, Germany. Estimated primary completion date: August 2017.
  NCT02718443
- **T-CELLS – RECURRENT**
- **Phase I Study of Cellular Immunotherapy Using Central Memory Enriched T Cells Lentivirally Transduced to Express an IL13Rα2-Specific, Hinge-Optimized, 41BB-Costimulatory Chimeric Receptor and a Truncated CD19 for Patients With Recurrent/Refractory Malignant Glioma**. Duarte, California. Estimated primary completion date: December 2018.
  NCT02208362
- **VIROTHERAPY**

So where does it all go wrong…?

- **Delays in primary diagnosis**.

  Tumours will progress and become more extensive or more aggressive and thus potentially harder to treat with greater risks.

- **Delays in diagnosis of recurrence of disease**

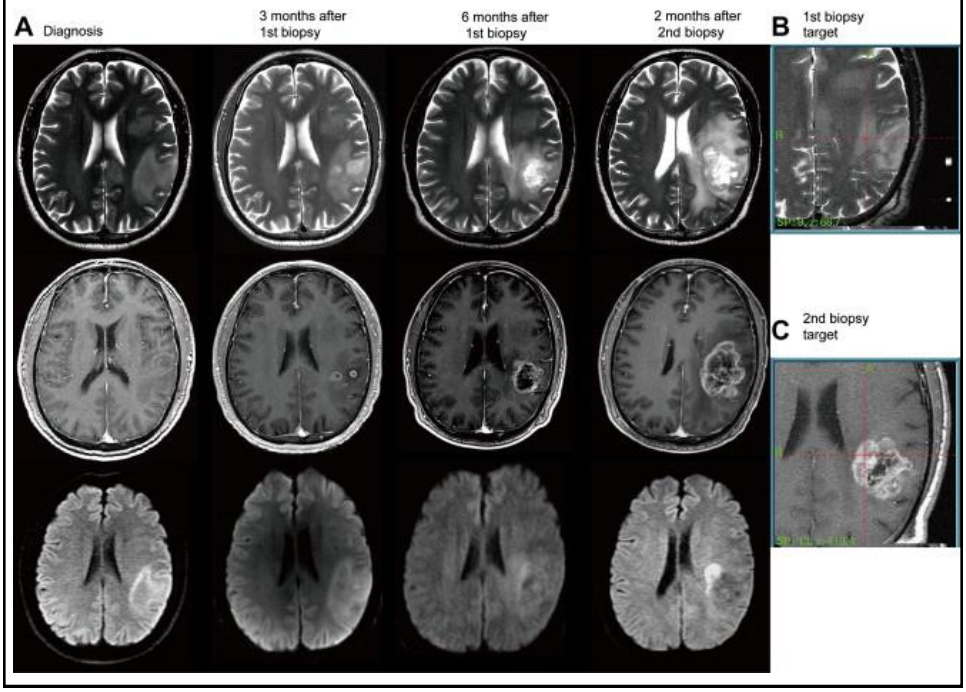
  Disease monitoring over time

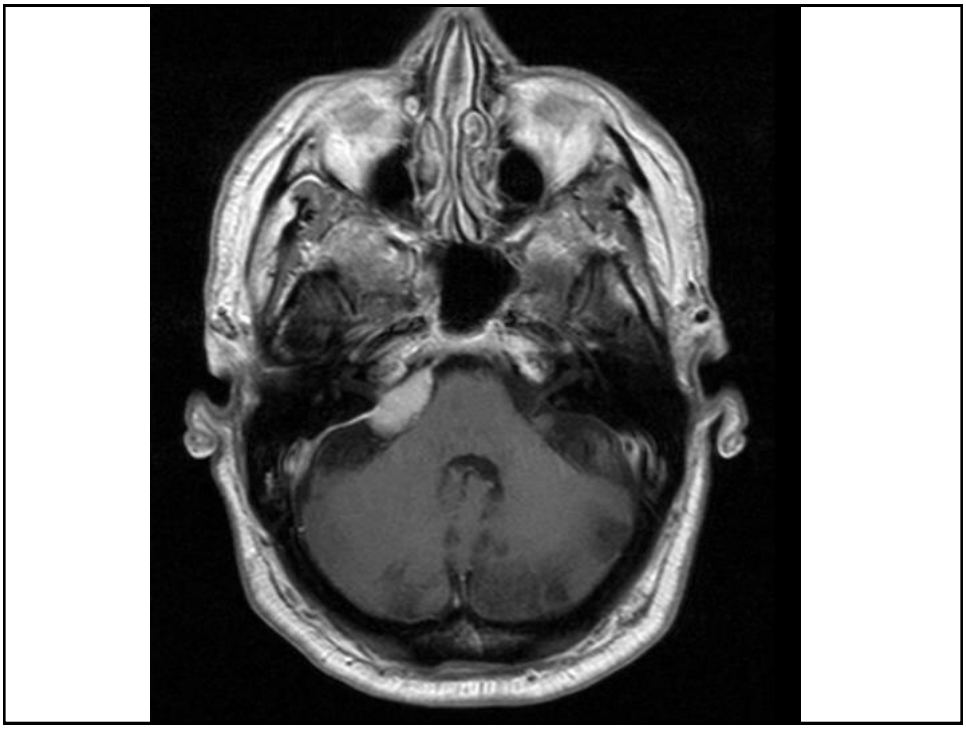
- **Issues around consent / Communication**

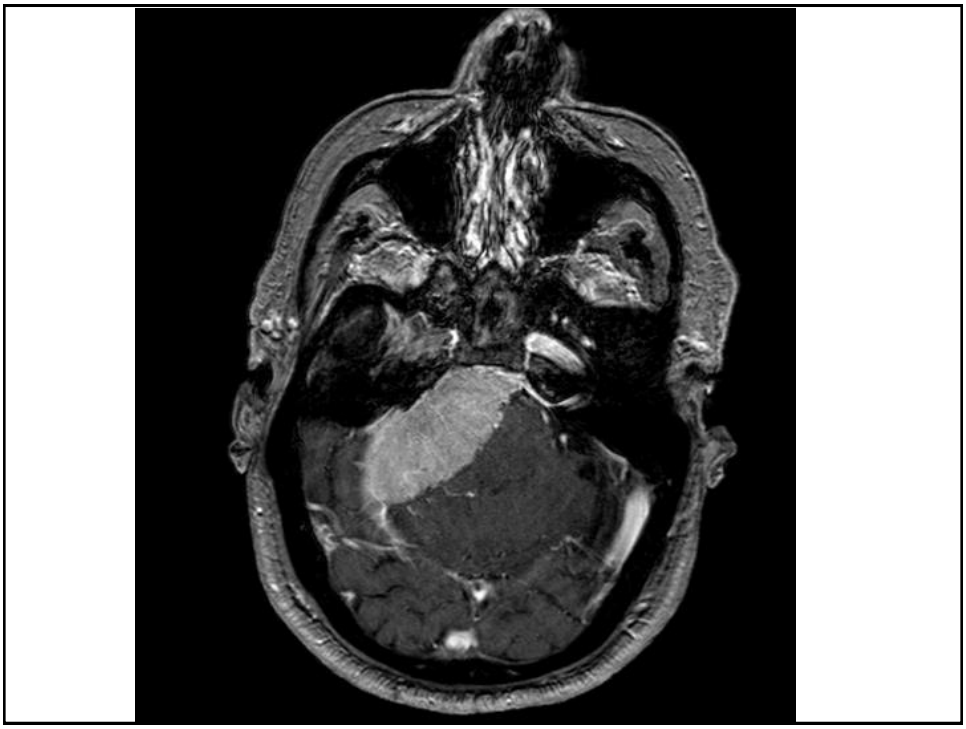
  Treatment options (surgery v radiotherapy)

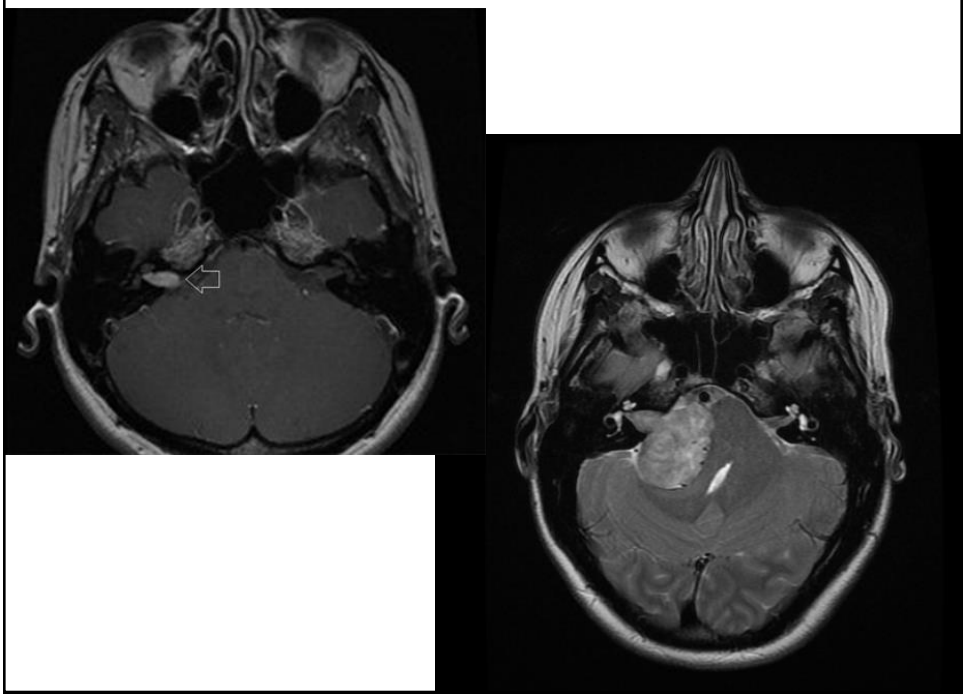
  Risk profile and appreciation of risk

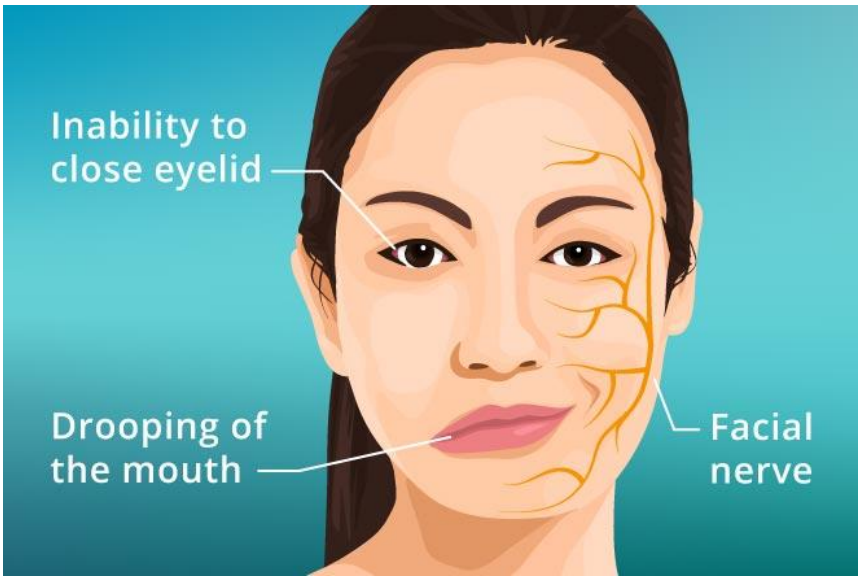
  Patient expectation from therapy










Inability to close eyelid
Drooping of the mouth
Facial nerve


Thankyou