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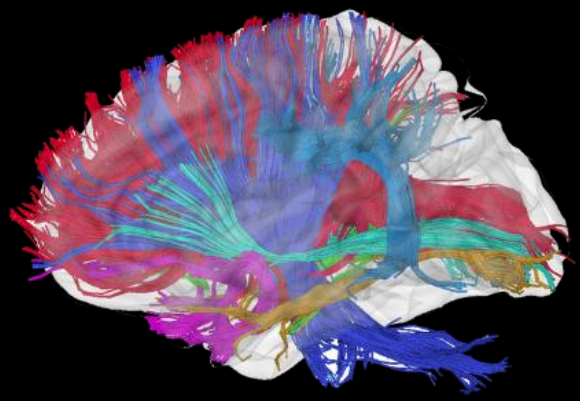
Importance of neuroanatomical subsites in defining patterns of infiltration and recurrence in Glioblastoma

Challenging uniform margin expansion for RT target volume delineation.



A/Prof Michael Back

Sydney Australia

EANO Oct2025

NORTHERN SYDNEY CANCER CENTRE

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No disclosures to report

A/Prof Michael Back

Sydney Australia

EANO Oct2025

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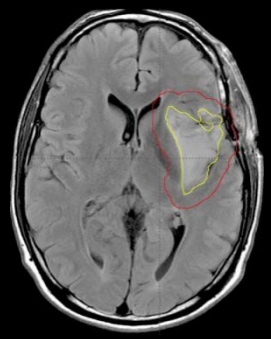
RT TARGET DELINEATION

DEFINING TUMOUR

1. MRI Gold Standard

T1 gad / T2 FLAIR

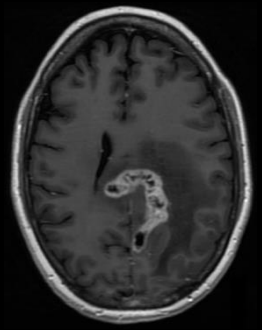
2. FET-FDG PET Imaging



PREDICTING SPREAD

1. Patterns of Infiltration

2. Patterns of Relapse



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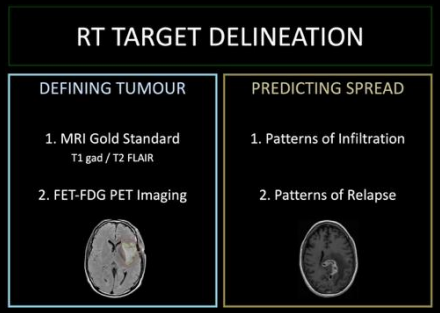
RT TARGET DELINEATION



OPTIMAL MARGIN EXPANSION

DETECT NON-ENHANCING TUMOUR

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RT TARGET DELINEATION

Radiotherapy and Oncology 184 (2023) 109663

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

Original Article

ESTRO-EANO guideline on target delineation and radiotherapy details for glioblastoma

Maximilian Niyazi [a,b,c,*], Nicolaus Andratschke [d], Martin Bendszus [e], Anthony J Chalmers [f], Sara C Erridge [g], Norbert Galldiks [h,i,j], Frank J Lagerwaard [k], Pierina Navarria [l], Per Munck af Rosenschöld [m], Umberto Ricardi [n], Martin J van den Bent [o], Michael Weller [p], Claus Belka [a,b,c], Giuseppe Minniti [q,r]

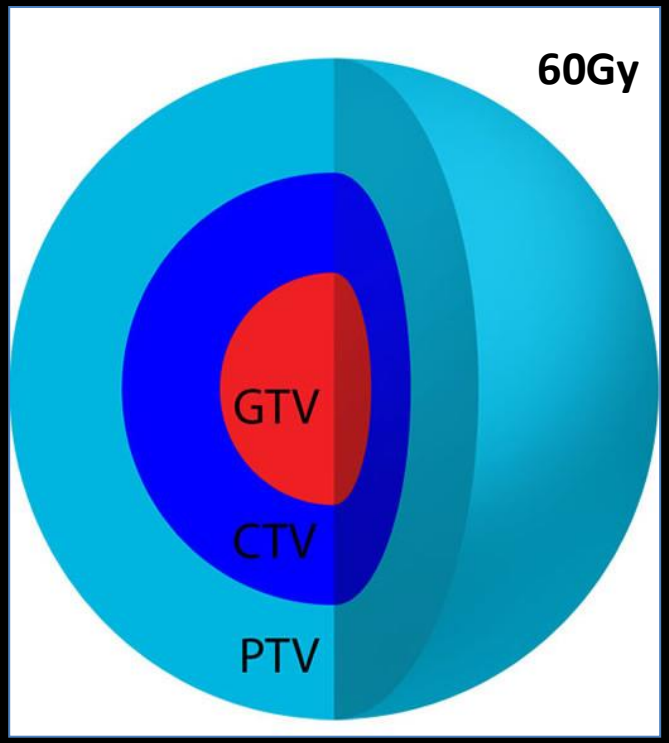
RT TARGET DELINEATION

OPTIMAL MARGIN EXPANSION

DETECT NON-ENHANCING TUMOUR

GTV defined as T1 contrast-enhancing tumour (for biopsy only patients) and/or resection cavity plus residual contrast-enhancing tumour, if present

A 15 mm margin around the GTV should be applied in three dimensions to generate the CTV, edited to take account of anatomical barriers to tumour spread



Radiotherapy and Oncology 184 (2023) 109663

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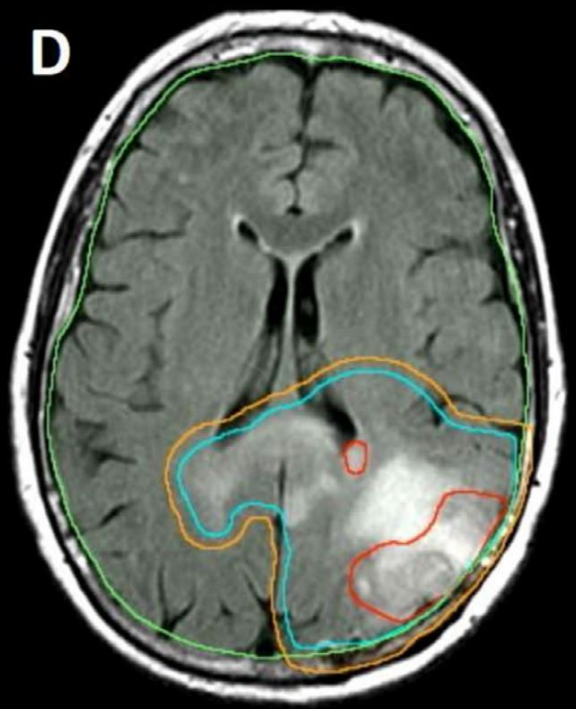
RT TARGET DELINEATION

OPTIMAL MARGIN EXPANSION

DETECT NON-ENHANCING TUMOUR

Inclusion of T2 abnormalities (oedema) within CTV is not advised

Non-enhancing areas may represent a component of glioblastoma, as defined in the new WHO brain tumour classification; in such cases, consideration should be given to including regions of high T2/FLAIR signal intensity within the GTV in addition to contrast enhancing tumour, and to adapting or decreasing GTV to CTV margins



Radiotherapy and Oncology 184 (2023) 109663

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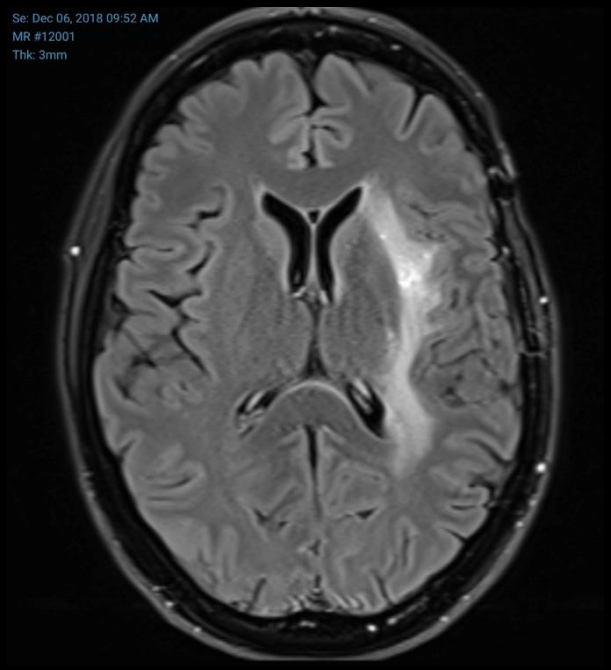
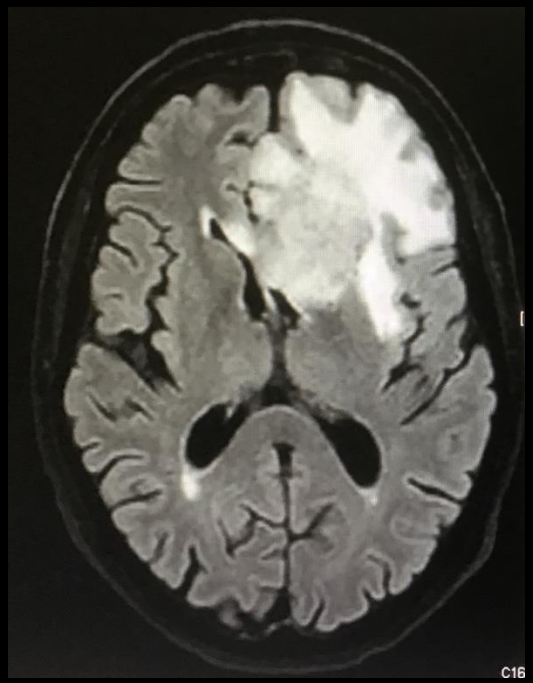
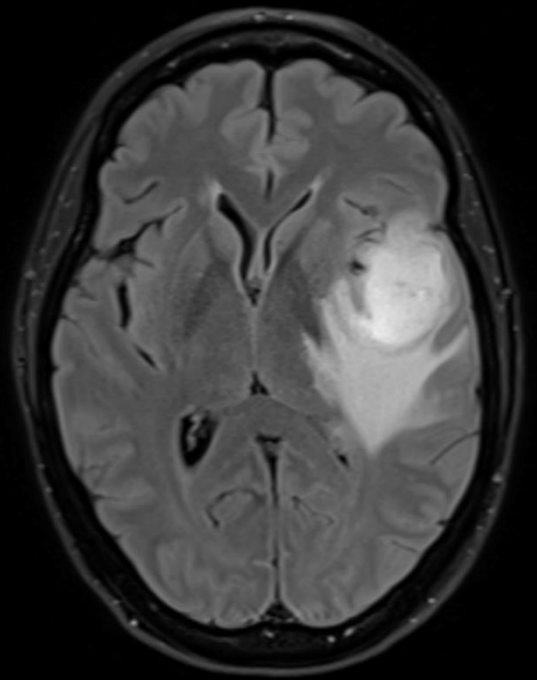
NORTHERN SYDNEY CANCER CENTRE

Understanding White Matter Tract Pathways

Patterns of T2F Abnormality are asymmetrical and vary for different sites







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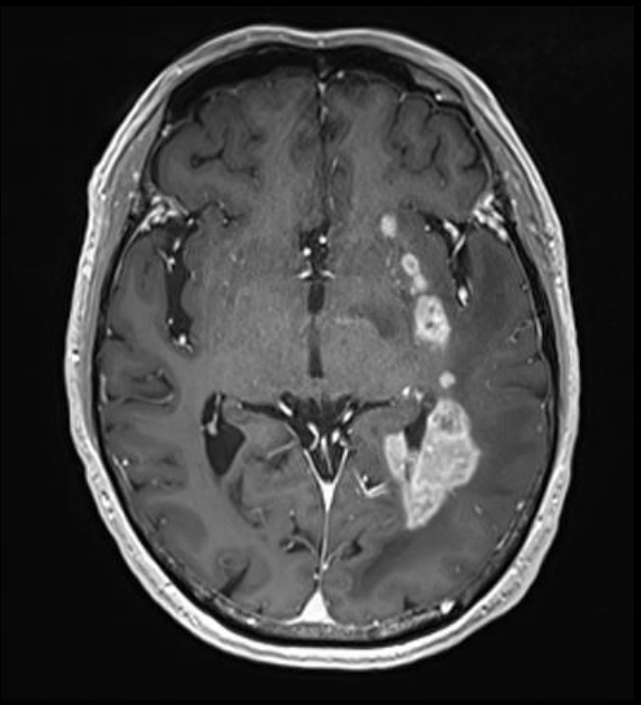
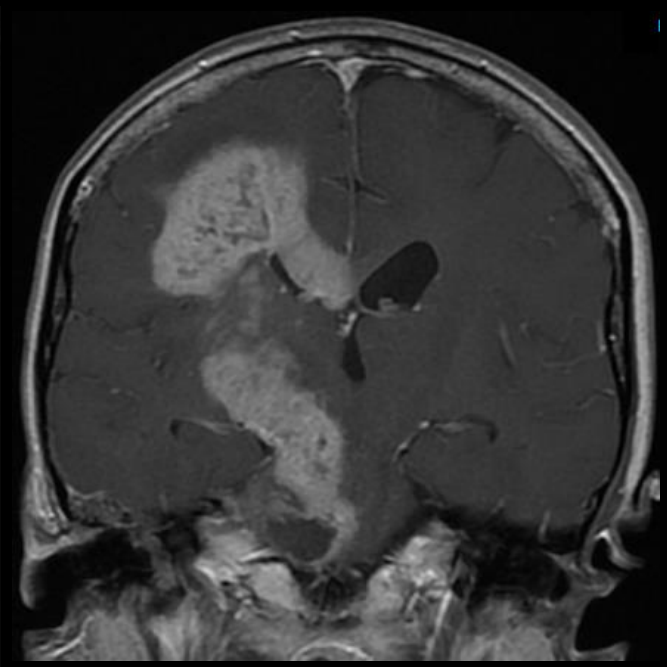
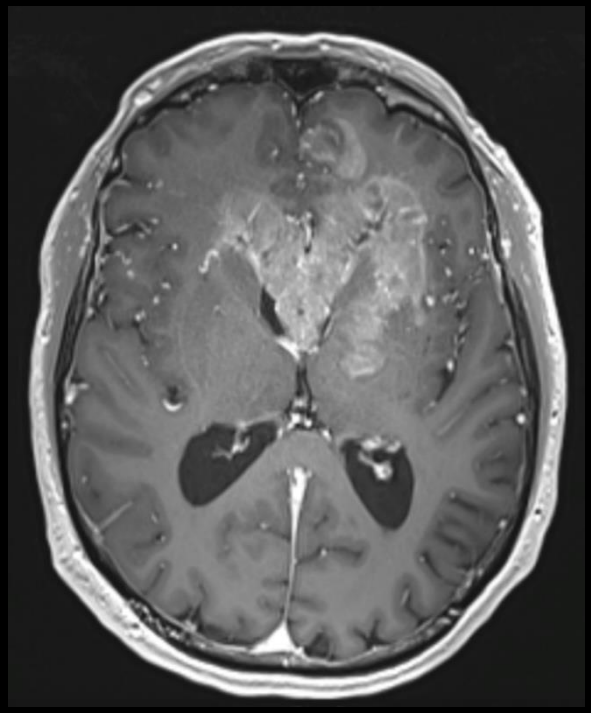
NORTHERN SYDNEY CANCER CENTRE

Understanding White Matter Tract Pathways

Relapse Patterns are asymmetrical and vary for different sites







Understanding White Matter Tract Pathways

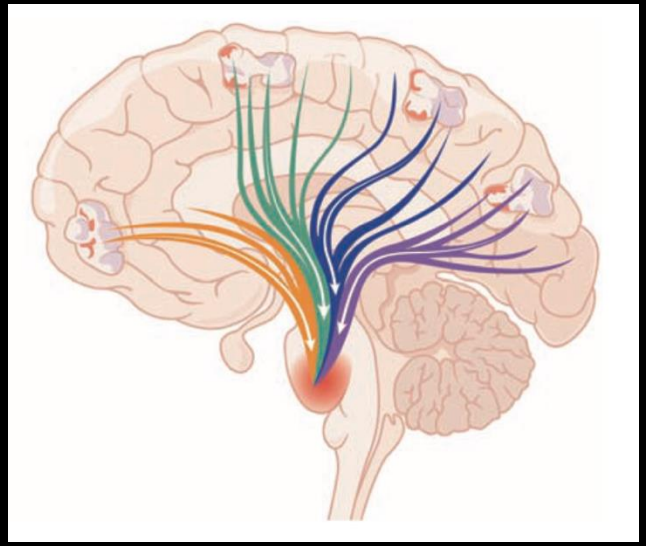
Autopsy Series show non-isotropic infiltration patterns

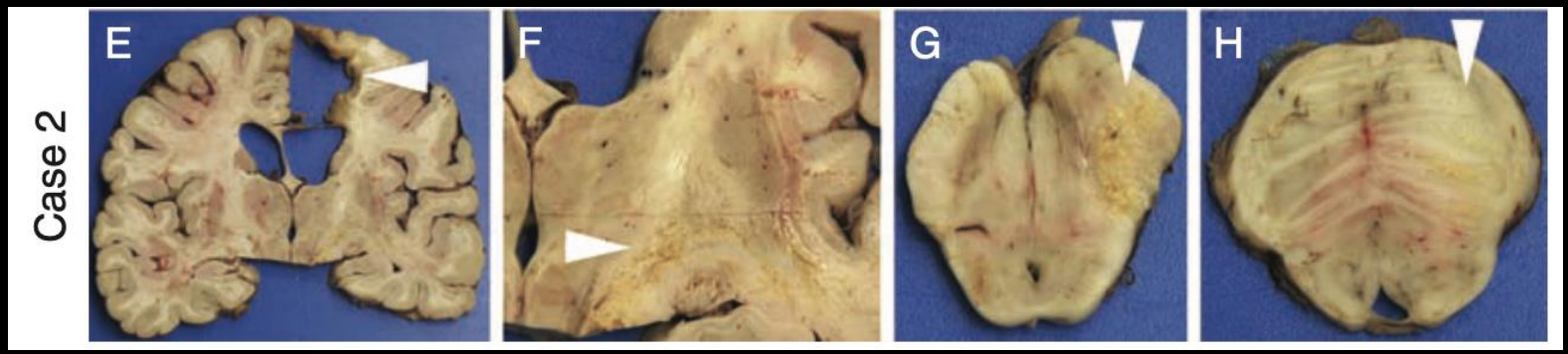
Neuro-Oncology
22(4), 470–479, 2020 | doi:10.1093/neuonc/noz216 | Advance Access date 10 November 2019

Extensive brainstem infiltration, not mass effect, is a common feature of end-stage cerebral glioblastomas

Michael R. Drumm, Karan S Dixit, Sean Grimm, Priya Kumthekar, Rimas V. Lukas, Jeffrey J. Raizer, Roger Stupp, Milan G. Chheda, Kwok-Ling Kam, Matthew McCord, Sean Sachdev, Timothy Kruser, Alicia Steffens, Rodrigo Javier, Kathleen McCortney, and Craig Horbinski

Department of Neurological Surgery, Northwestern University, Chicago, Illinois (M.R.D., A.S., R.J., K.M., C.H.);





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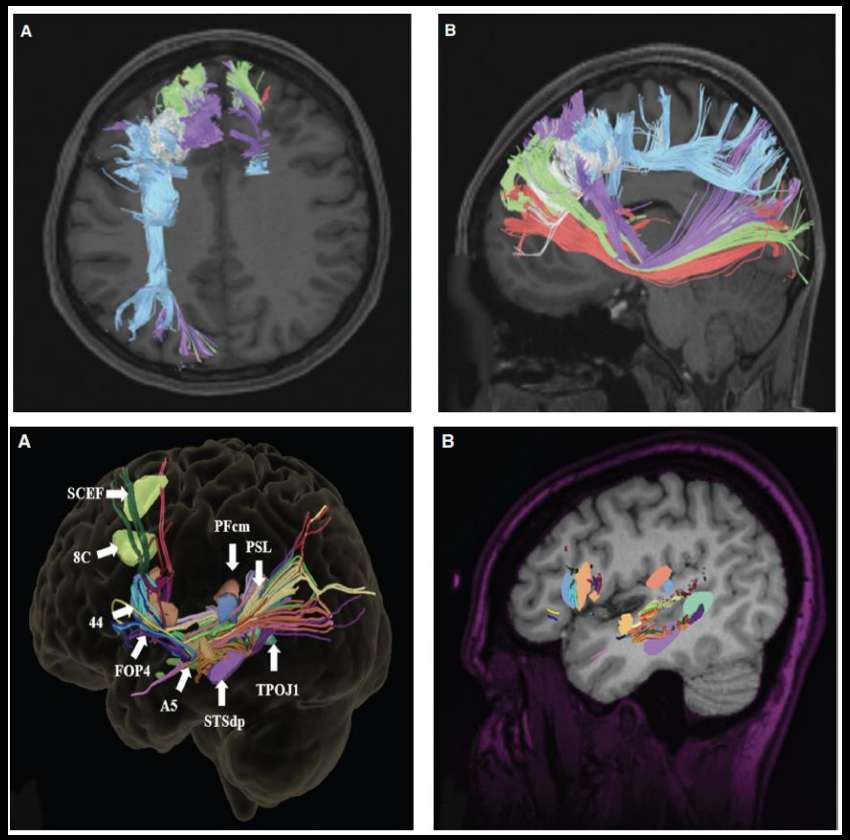
Understanding White Matter Tract Pathways

Connectomes show non-isotropic distribution

A CONNECTOMIC ATLAS OF THE HUMAN CEREBRUM SUPPLEMENT

A Connectomic Atlas of the Human Cerebrum—Chapter 18: The Connectional Anatomy of Human Brain Networks

Operative Neurosurgery 15:S245–S294, 2018



Michael E. Sughrue, MD,

The Brain Cancer Group

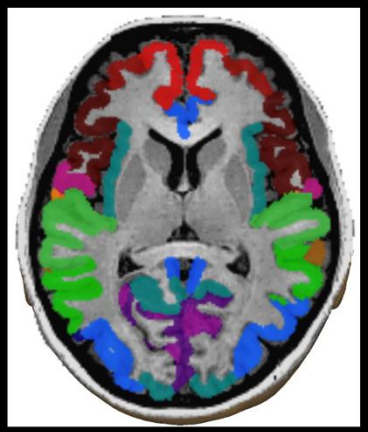
NORTHERN SYDNEY CANCER CENTRE

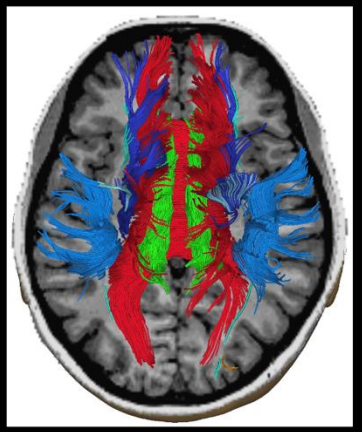
RT TARGET DELINEATION

OPTIMAL TARGET VOLUME DELINEATION MAY NEED TO BE INDIVIDUALISED

NEUROANATOMICAL SUBSITES

WHITE MATTER TRACT PATHWAYS





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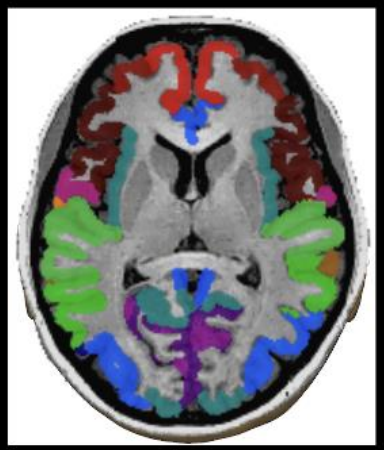
Aims

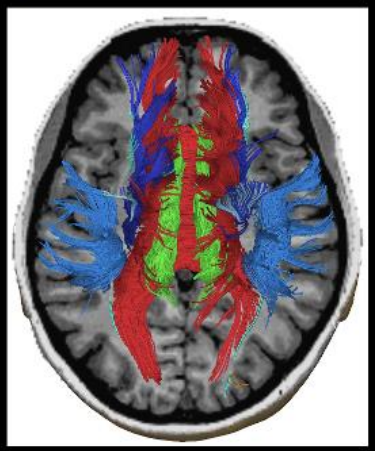
In glioblastoma explore:

- patterns of infiltration
- patterns of relapse

In relation to:

Neuroanatomical subsites
Adjacent white matter tracts





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Methods

Glioblastoma (60Gy TMZ) : 2008-2023

497 patients : medianOS 17.4 months (95%CI: 15.1-19.9mths)

<u>Volumetric Segmentation Project</u>

: 15 neuroanatomical subsites

: Initial gyrus and infiltration detailed

: Relapse site detailed

: Relationship to T1gd, T2, White Matter Tract

: Relapse distant if >20mm from GTV60

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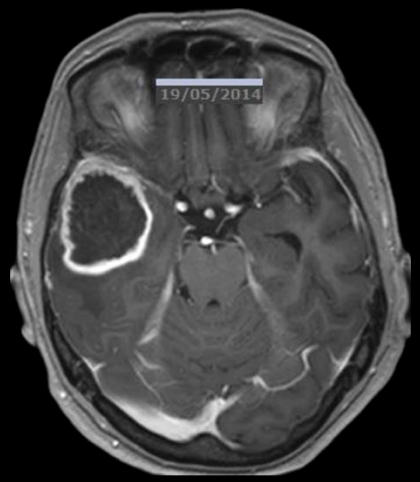
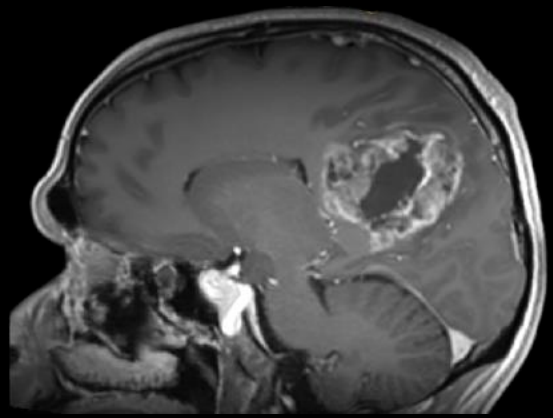
NORTHERN SYDNEY CANCER CENTRE

Methods

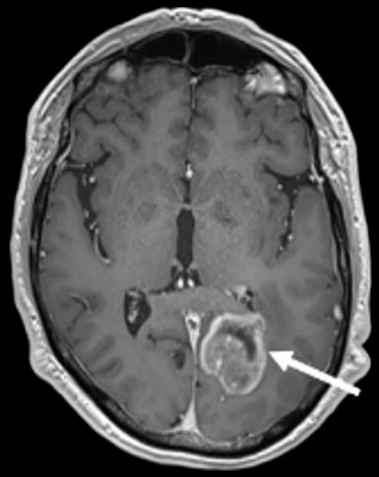
Initial three neuroanatomical subsites



ANT TEMPORAL LOBE



POST PARIETAL



OCCIPITAL

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NORTHERN SYDNEY CANCER CENTRE

Methods

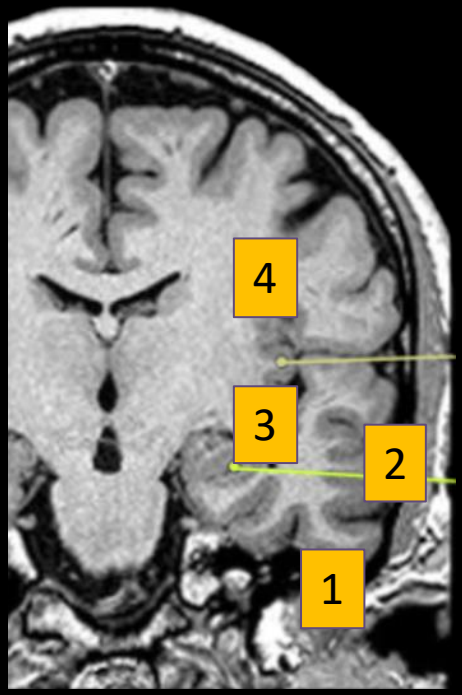
Designation of Infiltration Zones

Define neuroanatomical subsite

Adjacent sites designated as Zones

Zones extending deeper in brain

Neuroradiological subsites in each zone



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NORTHERN SYDNEY CANCER CENTRE

Methods

Designation of Infiltration Zones

Define neuroanatomical subsite

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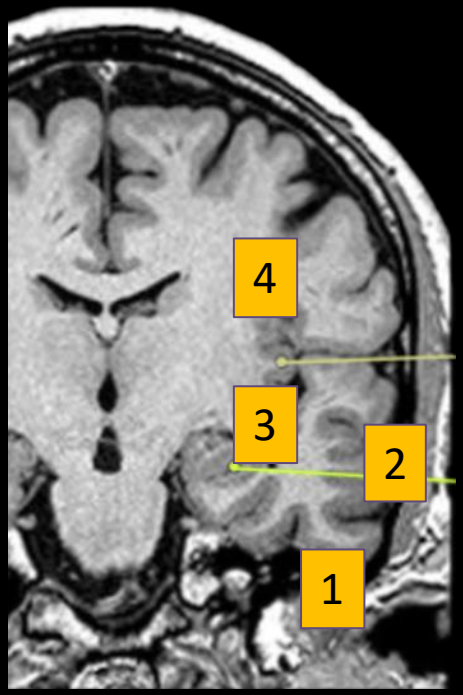

Analyse Zone involvement:

- At Diagnosis
- At Initial Relapse

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NORTHERN SYDNEY CANCER CENTRE

Methods

Designation of Infiltration Zones

Define neuroanatomical subsite

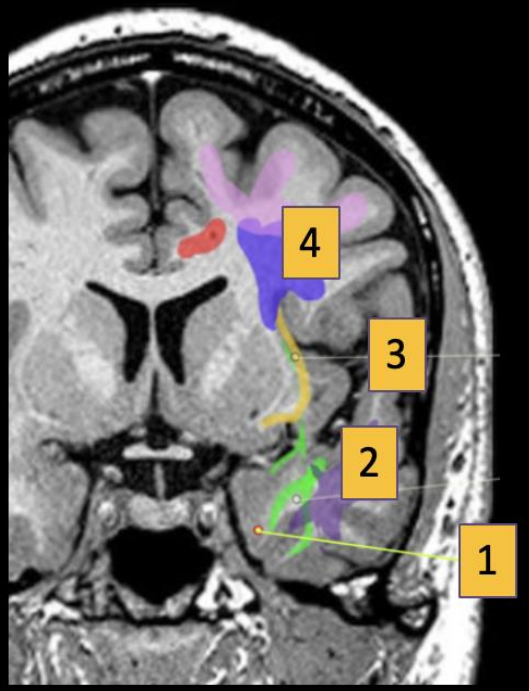
Adjacent sites designated as Zones

Zones extending deeper in brain

Neuroradiological subsites in each zone

Analyse Zone involvement:

- Relationship to White Matter Tract



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NORTHERN SYDNEY CANCER CENTRE

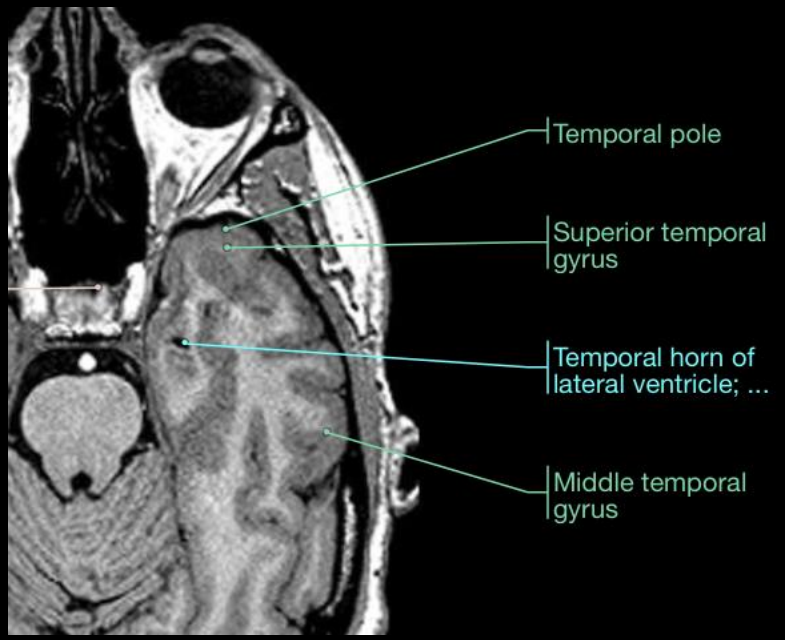
Methodology: Ant Temp Lobe Example

Define Neuroanatomical Site

Anterior Temporal Lobe

Region bound by the:

1. Middle cranial fossa (ANT-INF-LAT)
2. Lat Ventricle Ant Horn (POST)
3. Lateral sulcus (SUP)



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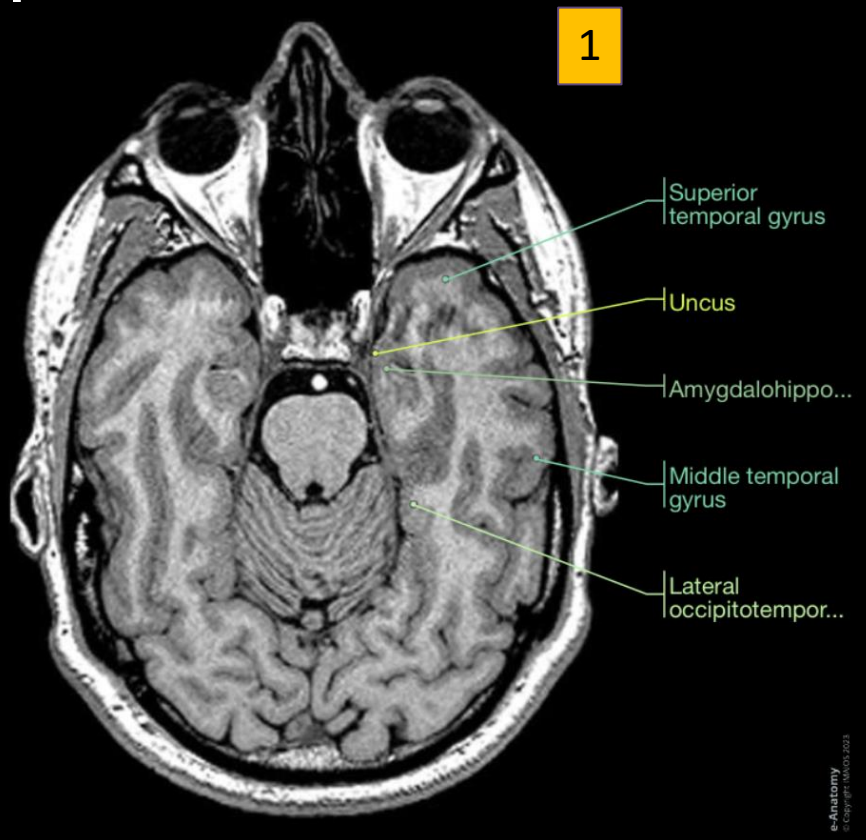
Methodology: Ant Temp Lobe Example

Categorising Infiltration / Relapse Sites

ZONE 1:

1. Sup Temporal Gyrus
2. Middle Temporal Gyrus
3. Lat Occipito-Temp Gyrus
4. Amydala
5. Uncus



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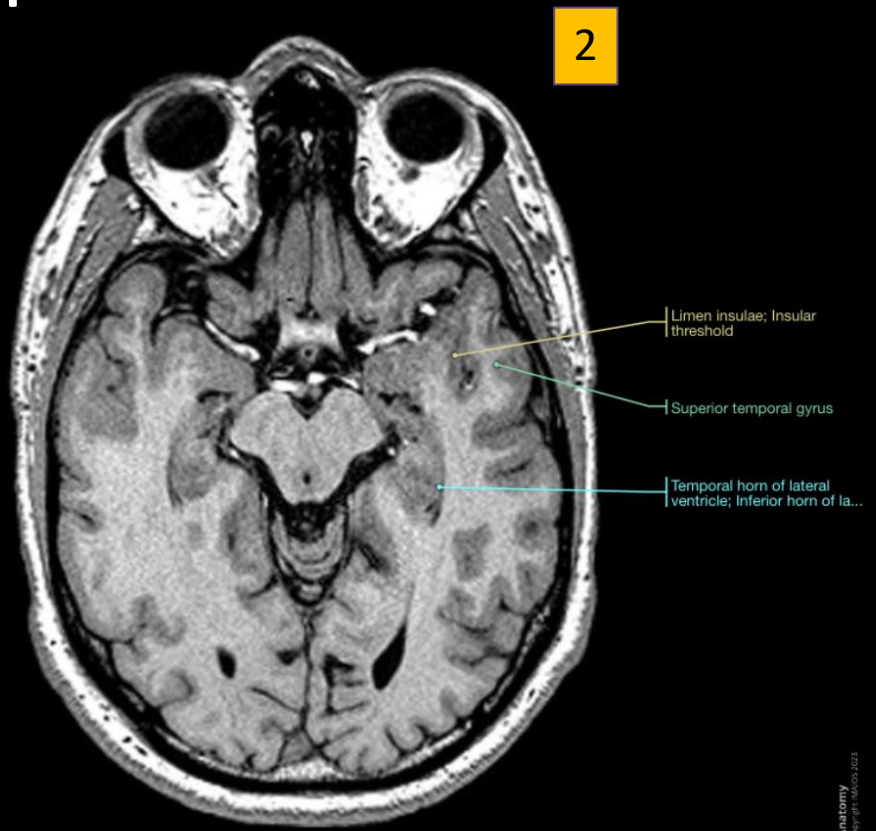
Methodology: Ant Temp Lobe Example

Categorising Infiltration / Relapse Sites

ZONE 2:

1. Pre-Insular Region
2. Mid Temp Gyrus Sup
3. Temporal Horn of ventricle



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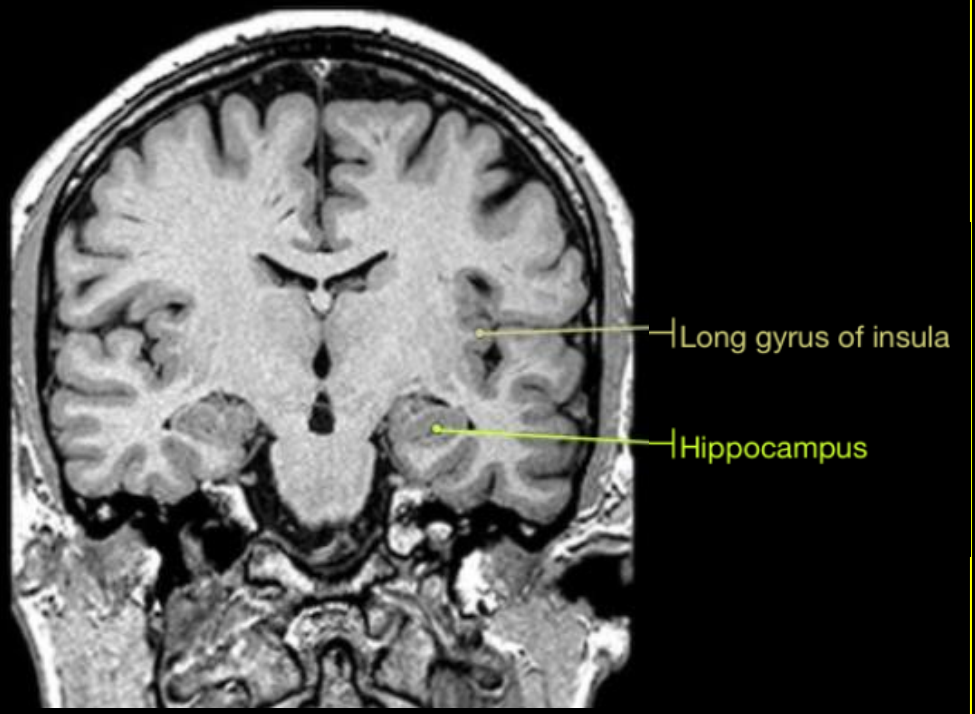
Methodology: Ant Temp Lobe Example

Categorising Infiltration / Relapse Sites

3

ZONE 3:

1. Insular Gyri
2. Parahippocampal/HG



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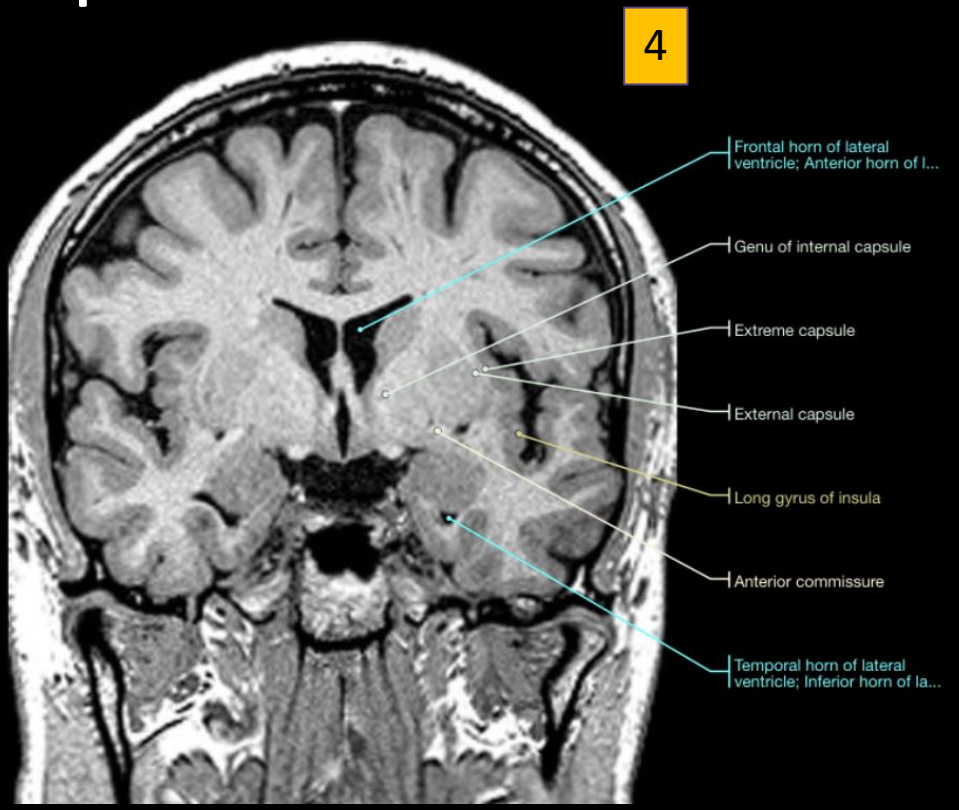
Methodology: Ant Temp Lobe Example

Categorising Infiltration / Relapse Sites

ZONE 4:

1. Ext / Extreme Capsule
2. Internal capsule
3. Ant Commissure
4. Frontal Horn of Ventricle
5. Vent Trigone



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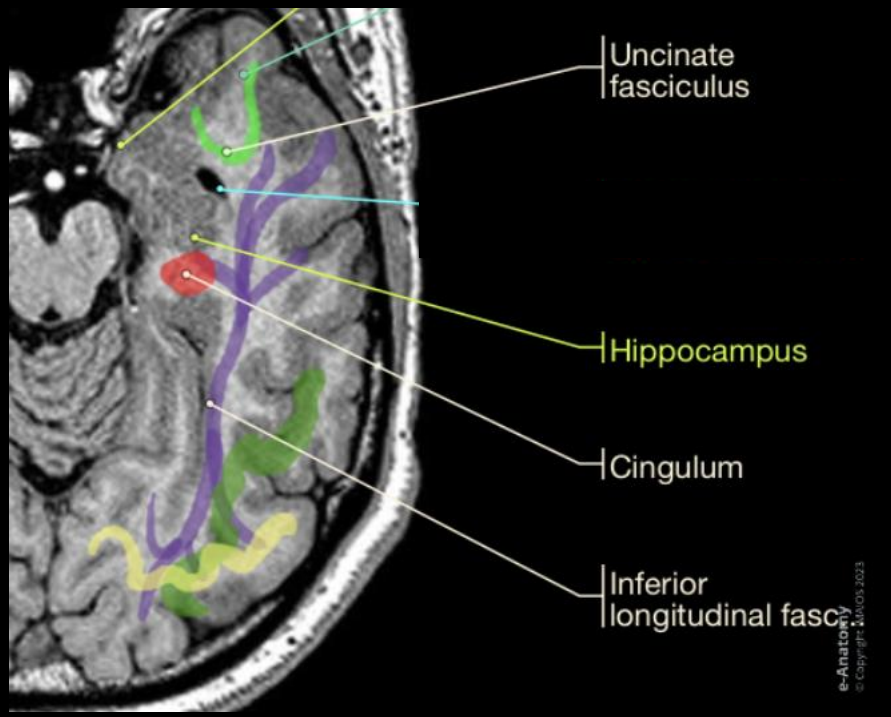
Methodology: Ant Temp Lobe Example

Adjacent White Matter Tracts

1. Uncinate Fasciculus / IFOF
2. PHG-HG (Cingulum/ Fornix)
3. Inf Longitudinal Fasciculus



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Results: Ant Temporal Lobe

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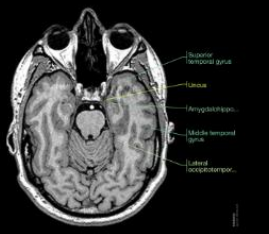
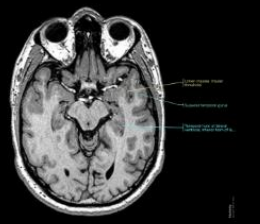
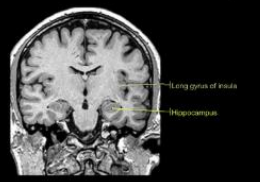
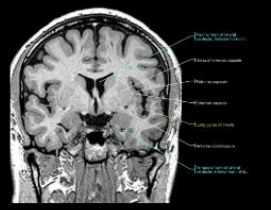
NORTHERN SYDNEY CANCER CENTRE

Results: Ant Temporal Lobe

47 patients

9.5% of patients

Infiltration could be superiorly into frontal regions or medially along medial temporal lobe

ZONE 1		• Sup Temporal Gyrus • Middle Temporal Gyrus • Lat Occipito-Temp Gyrus • Amygdala • Uncus
ZONE 2		• Pre-Insular Region • Mid Temp Gyrus Sup • Temporal Horn of ventricle
ZONE 3		• Insular Gyri • Parahippocampal/HG
ZONE 4		• External / Extreme Capsule • Internal capsule • Ant Commissure • Frontal Horn of Ventricle • Vent Trigone

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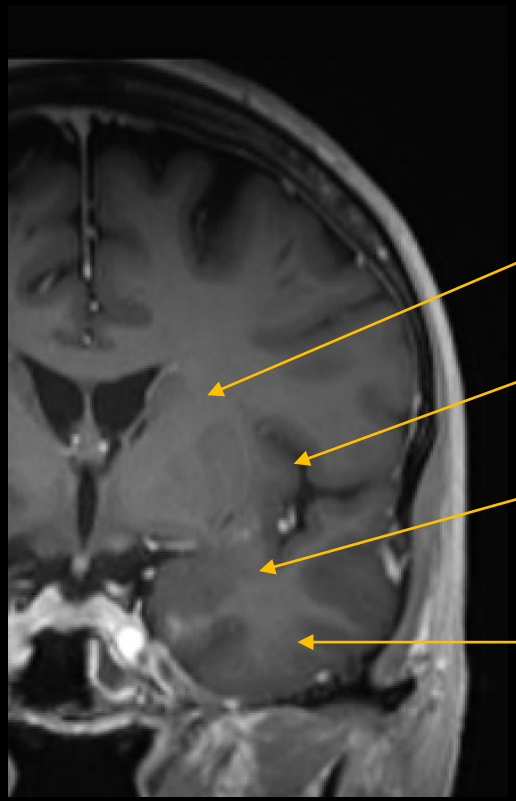
NORTHERN SYDNEY CANCER CENTRE

Results: Ant Temporal Lobe

INITIAL INFILTRATION (T1gd)



Zone 4: 25%
(Ext Cap in 15%
Front Horn in 13%)

Zone 3: 60%
(Insular in 57%
PHG-HG in 4%)

Zone 2: 91%
(Pre-insular in 85%)

Zone 1: 96%
(STG/MTG in 87%
Amygdala in 45%)

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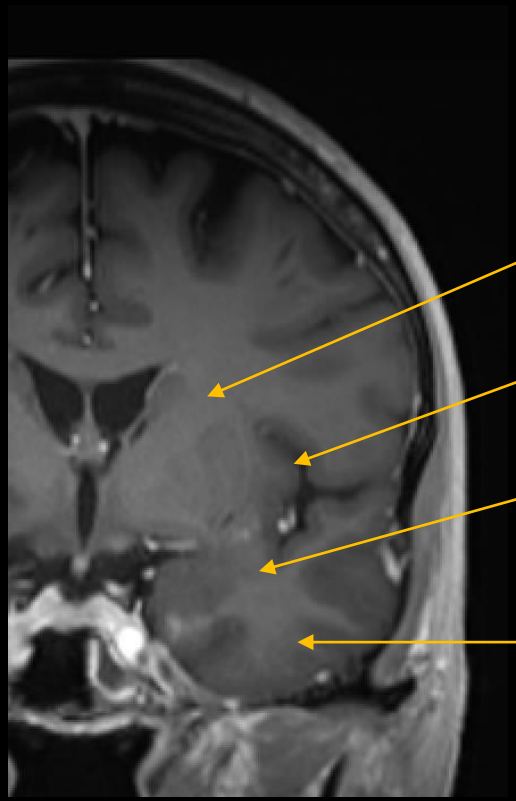
Results: Ant Temporal Lobe

RELAPSE SITES (T1gd)



Zone 4: 73%
(Front Horn in 36%
Ext/Extre Cap in 29%)

Zone 3: 64%
(Insular in 44%
PHG-HG in 22%)

Zone 2: 78%
(Pre-insular in 58%)

Zone 1: 61%
(Amygdala in 44%)

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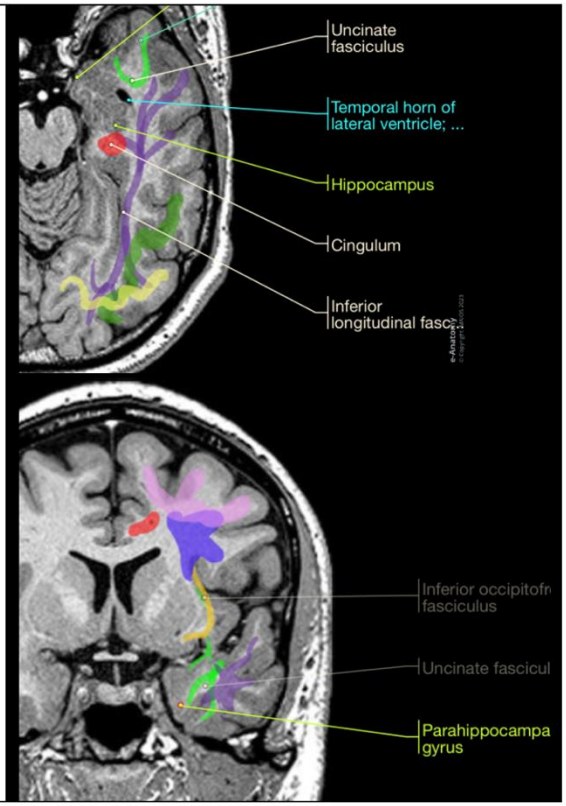
Results: Ant Temporal Lobe

ADJACENT WHITE MATTER TRACTS

- Uncinate Fasciculus / IFOF
- HP-PHG (-Cingulum/ Fornix)
- Inf Longitudinal Fasciculus



Relapse in White Matter Tract Pathway

Uncinate/IFOF : 71%
PHG-HG : 19.5%
Inf Longitudinal: 0%

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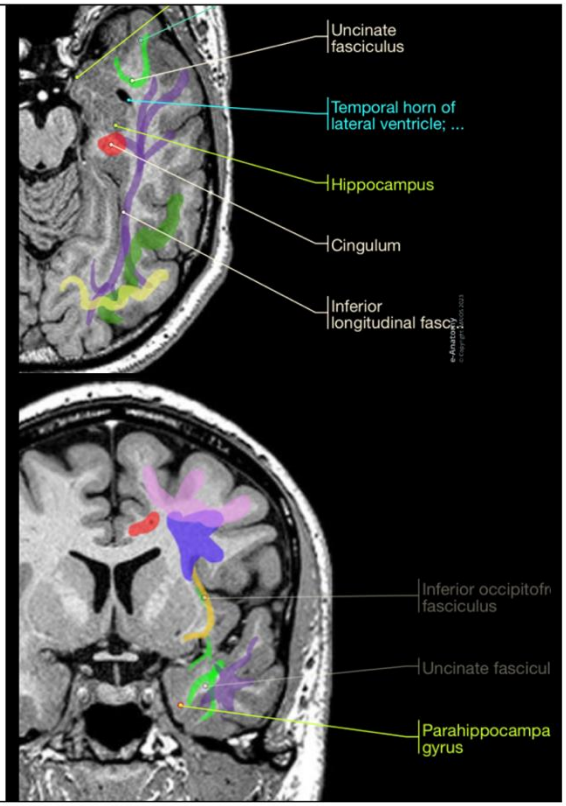
NORTHERN SYDNEY CANCER CENTRE

Results: Ant Temporal Lobe

ADJACENT WHITE MATTER TRACTS

- Uncinate Fasciculus / IFOF
- HP-PHG (-Cingulum/ Fornix)
- Inf Longitudinal Fasciculus



Predicted by Initial T2

None of the isolated Uncinate/IFOF WMT relapses had initial T2 in PHG-HG Pathway.

All Eight Relapses in PHG-HG WMT had initial T2 in PHG-HP Pathway.

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NORTHERN SYDNEY CANCER CENTRE

Results: Post Parietal

NORTHERN SYDNEY CANCER CENTRE

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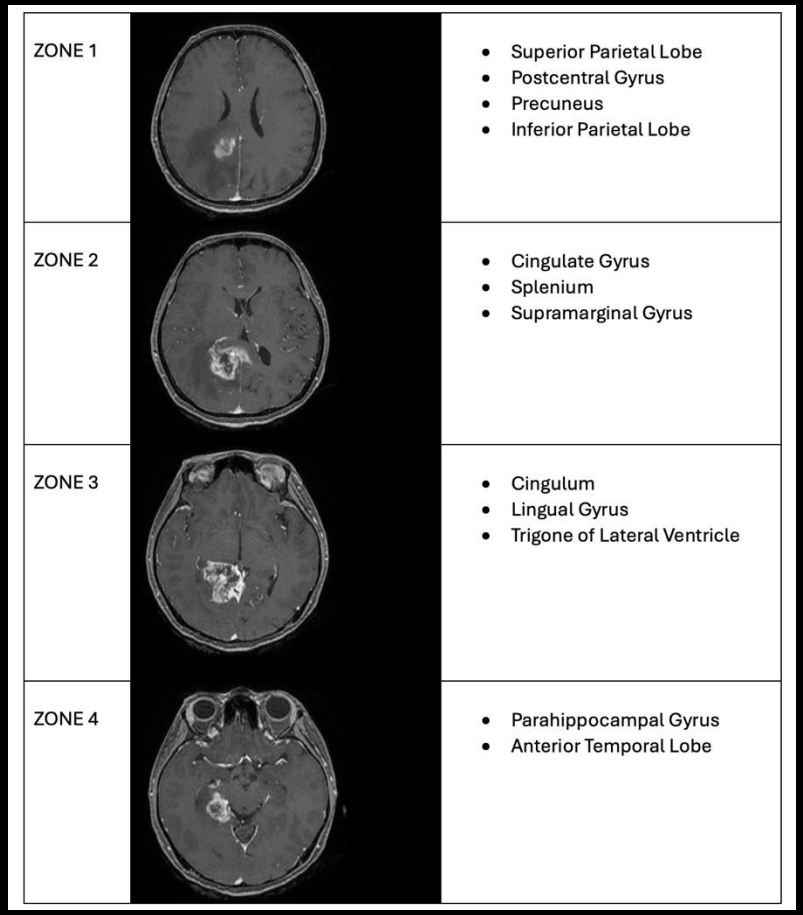
Results: Post Parietal

55 patients

11.0% of patients

Infiltration could be from medial gyri towards splenium or lateral gyri towards trigone of lateral ventricle



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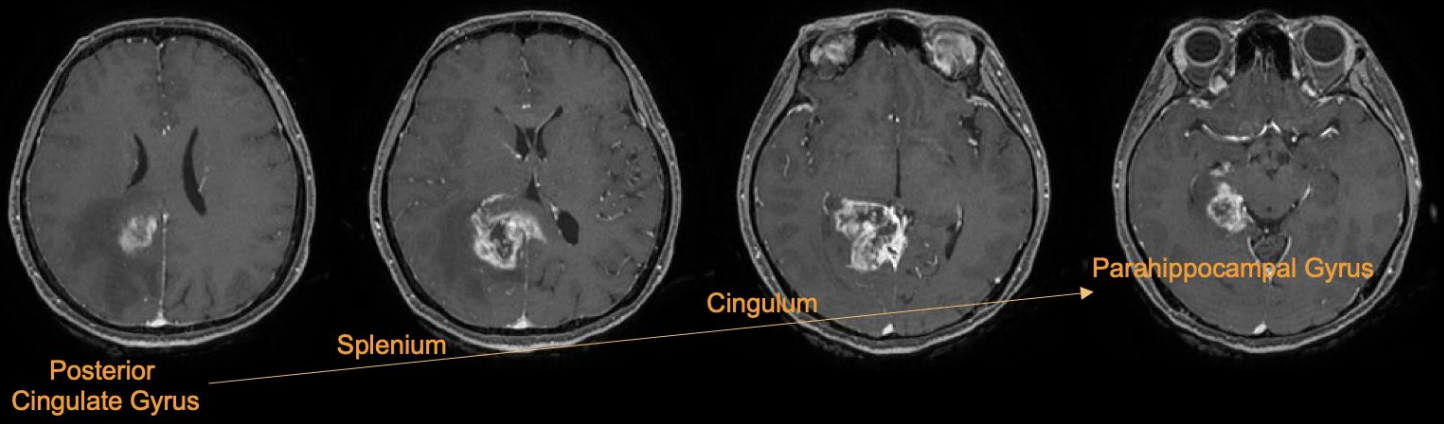
NORTHERN SYDNEY CANCER CENTRE

Results: Post Parietal

INITIAL INFILTRATION (T1gd)

- Post Parietal lobe tumours were based medially in 85%.
- 70% had predictable infiltration down medial structures



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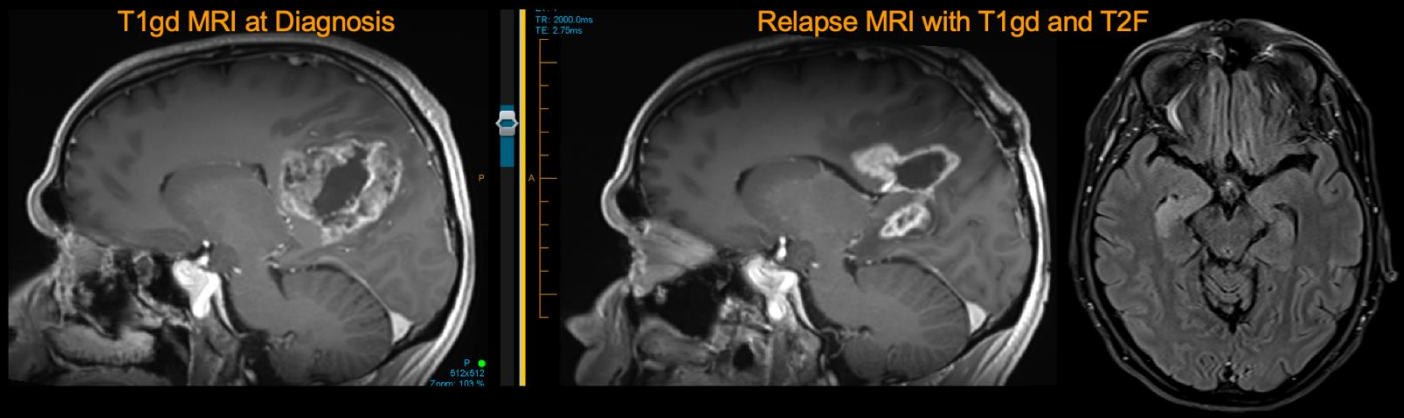
NORTHERN SYDNEY CANCER CENTRE

Results: Post Parietal

RELAPSE SITES (T1gd)

- Relapse was also medial along cingulum pathway
- Distant relapse evident in 53% including both hippocampi



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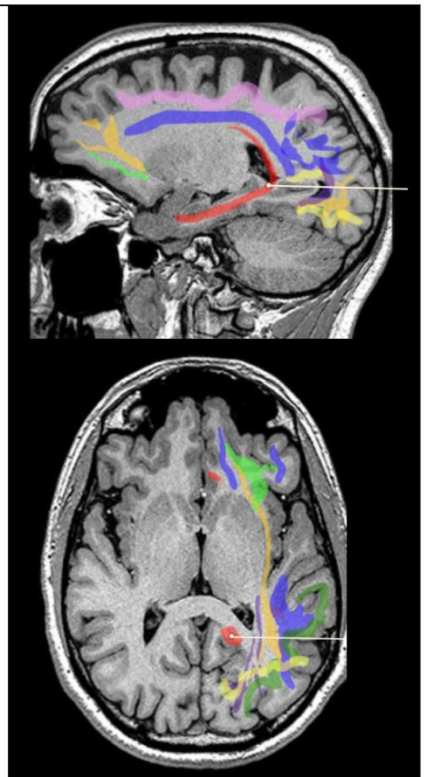
NORTHERN SYDNEY CANCER CENTRE

Results: Post Parietal

ADJACENT WHITE MATTER TRACTS

- Cingulum
- Arcuate Fasciculus
- IFOF



White Matter Tract involvement was determined by initial medial (cingulum) or lateral (Arcuate Fasciculus) sites

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NORTHERN SYDNEY CANCER CENTRE

Results: Occipital

NORTHERN SYDNEY CANCER CENTRE

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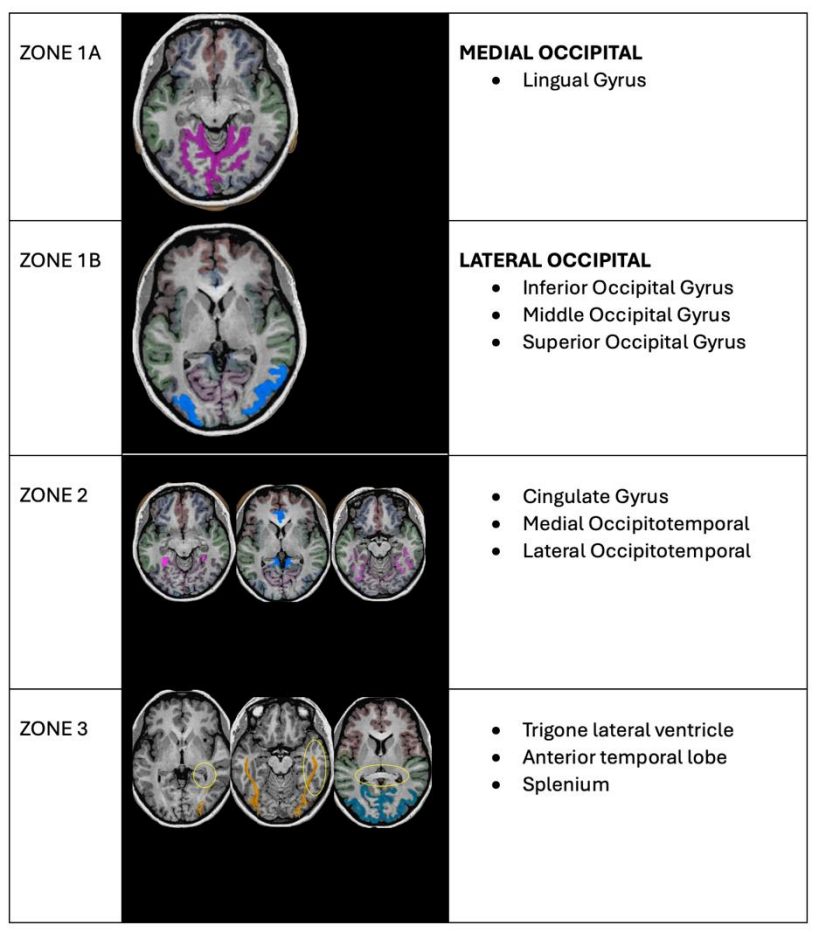
Results: Occipital

46 patients

9.5% of patients

At diagnosis, tumours were localised to either the medial occipital lobe in 20 patients (43.5%) or the lateral occipital lobe in 26 patients (56.5%).



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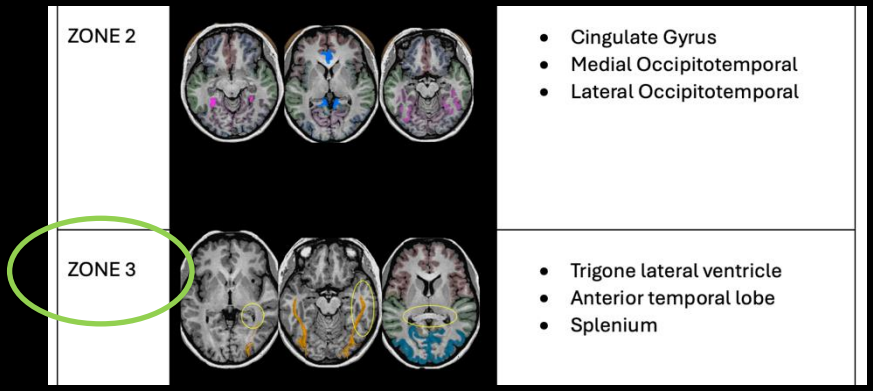
NORTHERN SYDNEY CANCER CENTRE

Results: Occipital

INITIAL INFILTRATION (T1gd)

59% had Zone 3 infiltration



Lateral tumours appeared to involve:

- Trigone (93.8% vs 63.6%. *p*= 0.15) and
- Anterior temporal lobe (18.8% vs 9.1%. *p*=0.62)

Medial tumours involved the splenium (36.4% vs 6.3%. *p*= 0.15).

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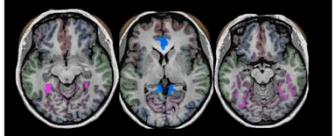
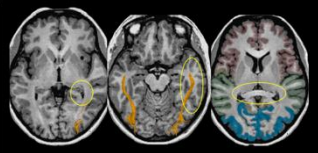
NORTHERN SYDNEY CANCER CENTRE

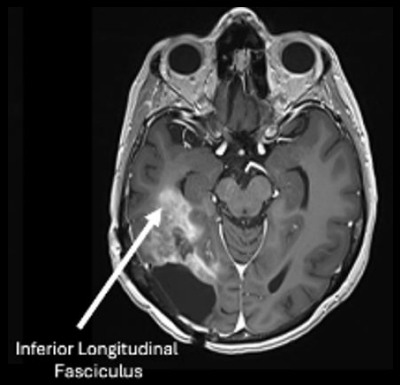
Results: Occipital

RELAPSE SITE (T1gd)

Relapse followed same pattern

ZONE 2		• Cingulate Gyrus • Medial Occipitotemporal • Lateral Occipitotemporal
ZONE 3		• Trigone lateral ventricle • Anterior temporal lobe • Splenium

- **Lateral Tumours** preferentially relapsed in:
  - Trigone (75% vs 52.6%. *p*=0.20)
  - Ant temp region (50% vs 15.8%. *p*=0.03)



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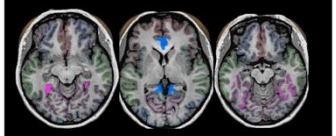
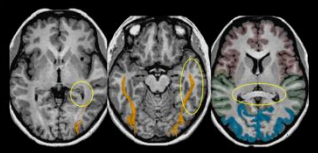
NORTHERN SYDNEY CANCER CENTRE

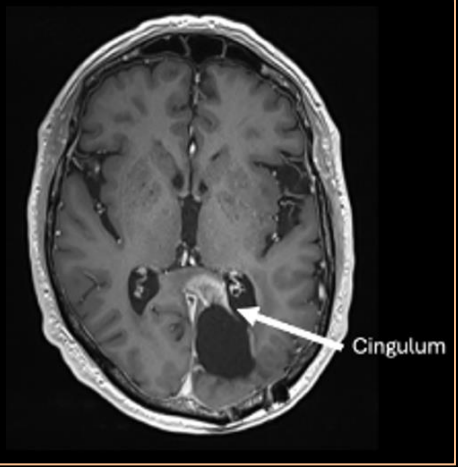
Results: Occipital

RELAPSE SITE (T1gd)

Relapse followed same pattern

ZONE 2		• Cingulate Gyrus • Medial Occipitotemporal • Lateral Occipitotemporal
ZONE 3		• Trigone lateral ventricle • Anterior temporal lobe • Splenium

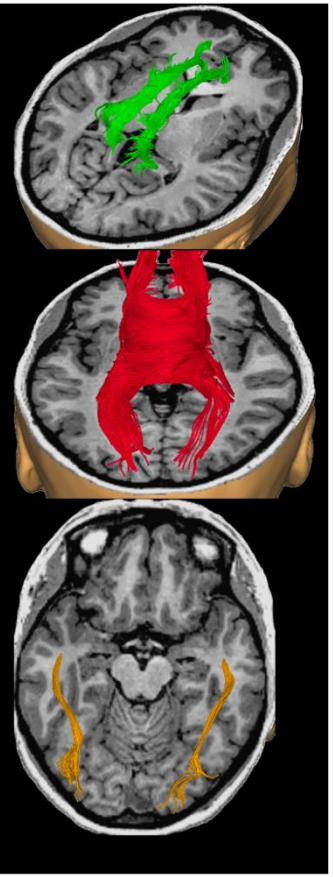
- **Medial Tumours** preferentially relapsed in:
  - Splenium (47.3% vs 16.7%, *p*=0.05)



Results: Occipital

ADJACENT WHITE MATTER TRACTS

- Cingulum
- Corpus Callosum
- Inf Longitudinal Fasciculus



White Matter Tract involvement was also determined by laterality:

- medial tumours (corpus callosum/cingulum) or
- lateral tumours (inf longitudinal fasciculus)

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NORTHERN SYDNEY CANCER CENTRE

Discussion

Patterns of infiltration and relapse of Glioblastoma

- vary with neuroanatomical regions
- relate to initial T2 MRI regions
- relate to adjacent predictable white matter tracts.

This has implication for target volume delineation protocols based on uniform geometrical expansions around T1gd lesion.

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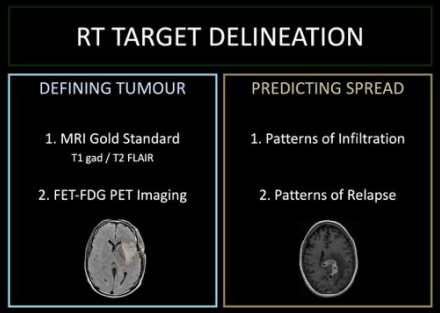
NORTHERN SYDNEY CANCER CENTRE

Discussion



OPTIMAL MARGIN EXPANSION

DETECT NON-ENHANCING TUMOUR

AVOID GEOGRAPHICAL MISS

REDUCTION NORMAL BRAIN DOSE

RT DOSE ESCALATION

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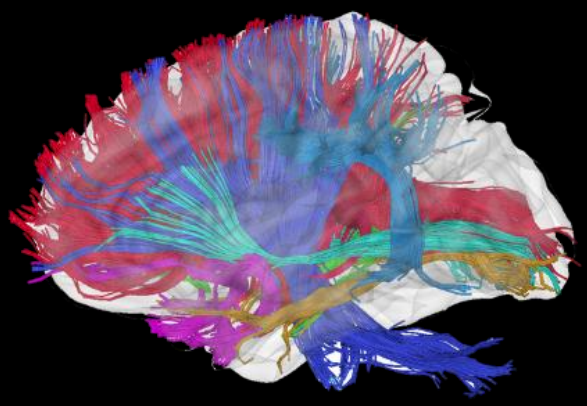
NORTHERN SYDNEY CANCER CENTRE

CONCLUSIONS



Not all tumours and sites in brain act the same way

Infiltration and relapse quite predictable based on neuroanatomical subsites and WMT T2 abnormality

Understanding infiltration/relapse patterns may allow dose escalation

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NORTHERN SYDNEY CANCER CENTRE

The Brain Cancer Group

Northern Sydney Cancer Centre

Neuro-oncology MDT

Dr Helen Wheeler, Dr Adrian Lee, Dr Michael Rodriguez

DR Jamie Drummond, Dr David Brazier, Dr Alison Newey

Dr Geoff Schembri, Prof Dale Bailey, Dr Ed Hsiao

Ms Marina Kastelan, Dr Patrick Horsley

TBCG Brain Cancer Imaging Laboratory

Dr Jamie Drummond, Dr Jackie Yim, Ms Victoria Tung

michael.back@health.nsw.gov.au

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