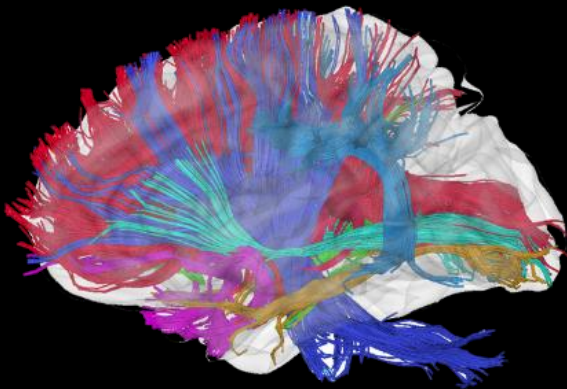


Improving Radiation Therapy outcomes in High Grade Glioma

*Importance of white matter tract pathways for
RT target volume delineation.*



A/Prof Michael Back

Sydney Australia

ASNO August 2024



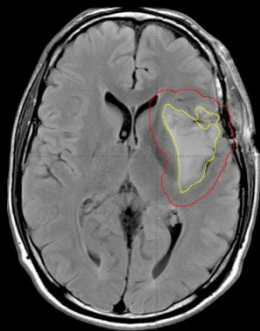
RT TARGET DELINEATION

DEFINING TUMOUR

1. MRI Gold Standard

T1 gad / T2 FLAIR

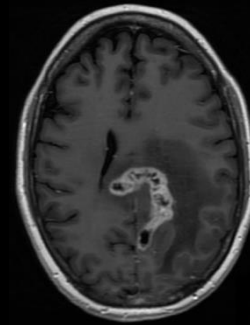
2. FET-FDG PET Imaging



PREDICTING SPREAD

1. Patterns of Infiltration

2. Patterns of Relapse



RT TARGET DELINEATION

RT TARGET DELINEATION

DEFINING TUMOUR

1. MRI Gold Standard
T1 gad / T2 FLAIR
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PREDICTING SPREAD

1. Patterns of Infiltration
2. Patterns of Relapse



OPTIMAL MARGIN EXPANSION
DETECT NON-ENHANCING TUMOUR

RT TARGET DELINEATION

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PREDICTING SPREAD

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2. Patterns of Relapse



OPTIMAL MARGIN EXPANSION
DETECT NON-ENHANCING TUMOUR



AVOID
GEOGRAPHICAL MISS

REDUCTION
NORMAL BRAIN DOSE

RT DOSE
ESCALATION

RT TARGET DELINEATION



Radiotherapy and Oncology 184 (2023) 109663



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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}

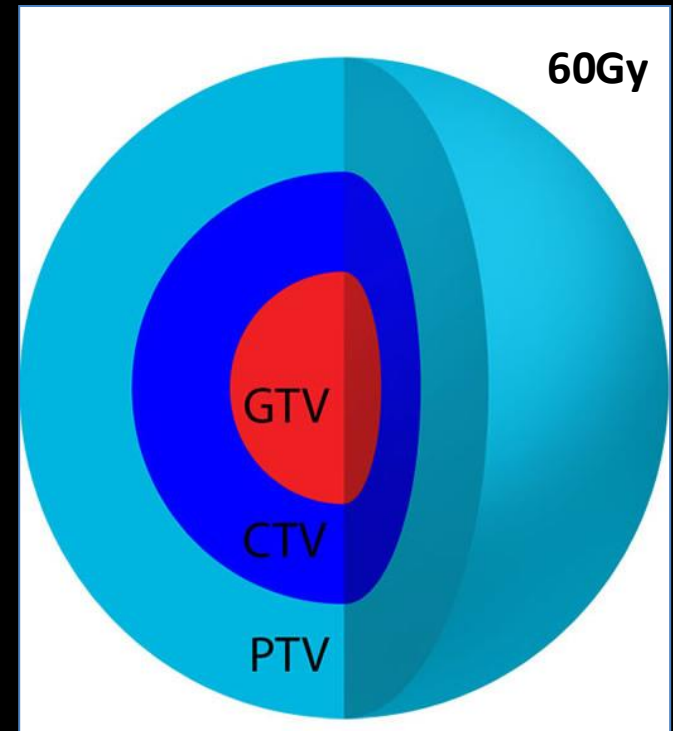
RT TARGET DELINEATION



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



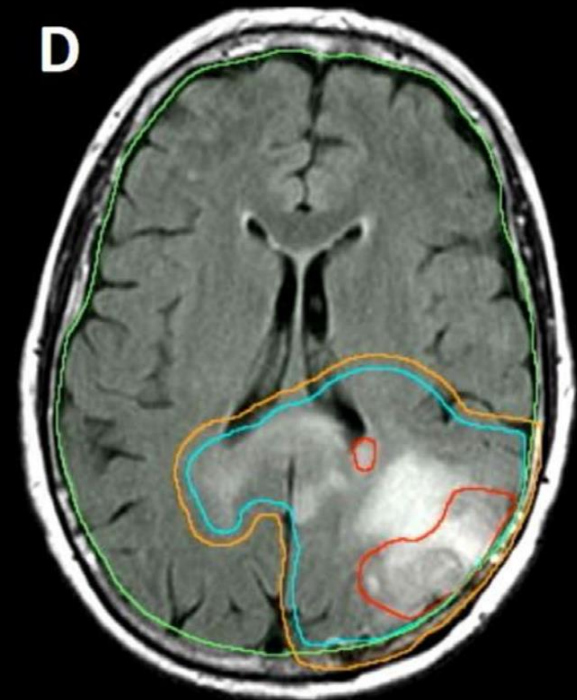
RT TARGET DELINEATION



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



RT TARGET DELINEATION



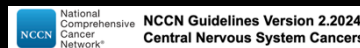
National Comprehensive
Cancer Network®

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)

Central Nervous System Cancers

Version 2.2024 — July 25, 2024

[NCCN.org](https://www.nccn.org)



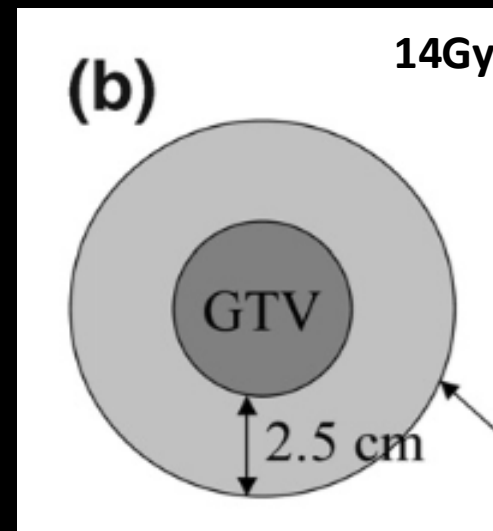
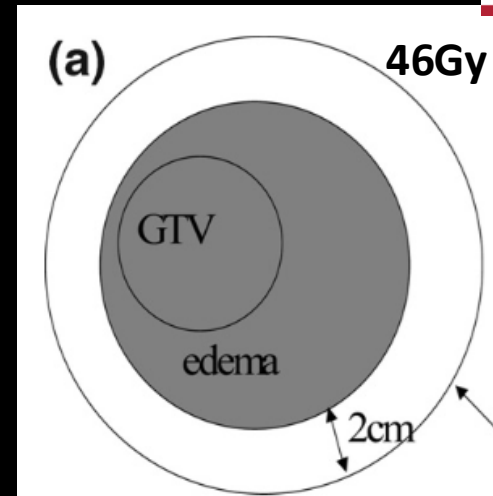
RT TARGET DELINEATION



OPTIMAL MARGIN EXPANSION
DETECT NON-ENHANCING TUMOUR

Although trials in glioblastoma have historically used CTV expansion in the range of 2 cm, smaller CTV expansions are supported in the literature

NCCN National Comprehensive Cancer Network
NCCN Guidelines Version 2.2024
Central Nervous System Cancers



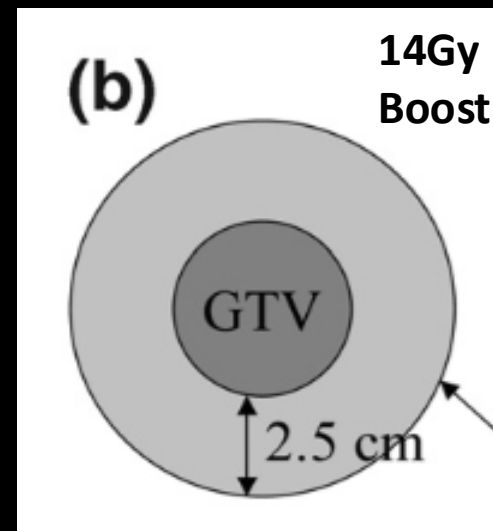
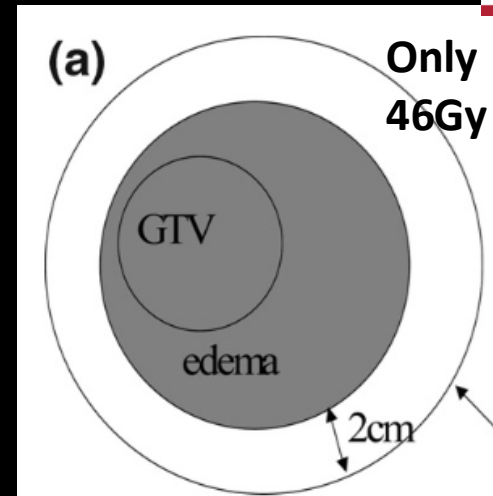
RT TARGET DELINEATION



OPTIMAL MARGIN EXPANSION
DETECT NON-ENHANCING TUMOUR

When edema as assessed by T2/FLAIR is included in the initial phase of treatment, fields are usually reduced for the last phase of treatment (boost). The boost target volume will typically encompass only the gross residual tumor and the resection cavity.

NCCN National Comprehensive Cancer Network
NCCN Guidelines Version 2.2024
Central Nervous System Cancers



RT TARGET DELINEATION

RT TARGET DELINEATION

DEFINING TUMOUR

1. MRI Gold Standard
T1 gad / T2 FLAIR
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PREDICTING SPREAD

1. Patterns of Infiltration
2. Patterns of Relapse



The challenge for Target Volume Delineation

OPTIMAL MARGIN EXPANSION

DETECT NON-ENHANCING TUMOUR

RT TARGET DELINEATION

RT TARGET DELINEATION

DEFINING TUMOUR

1. MRI Gold Standard
T1 gad / T2 FLAIR
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PREDICTING SPREAD

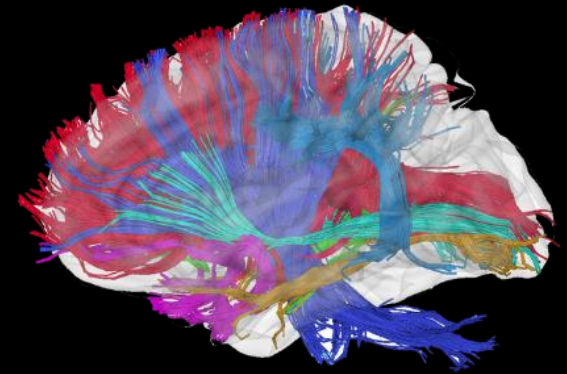
1. Patterns of Infiltration
2. Patterns of Relapse



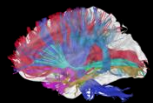
The challenge for Target Volume Delineation

OPTIMAL MARGIN EXPANSION

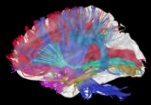
DETECT NON-ENHANCING TUMOUR



Understanding White Matter Tract Pathways

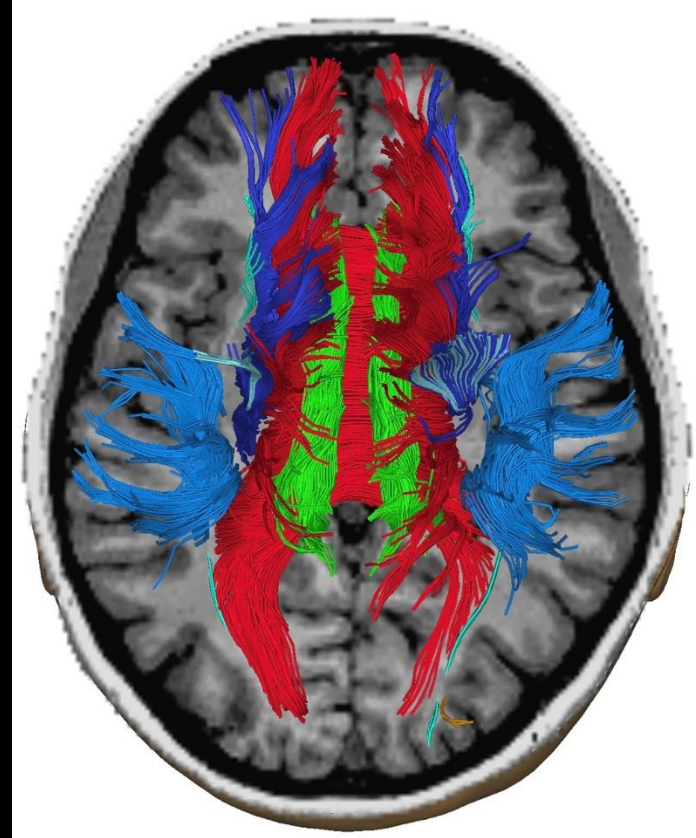
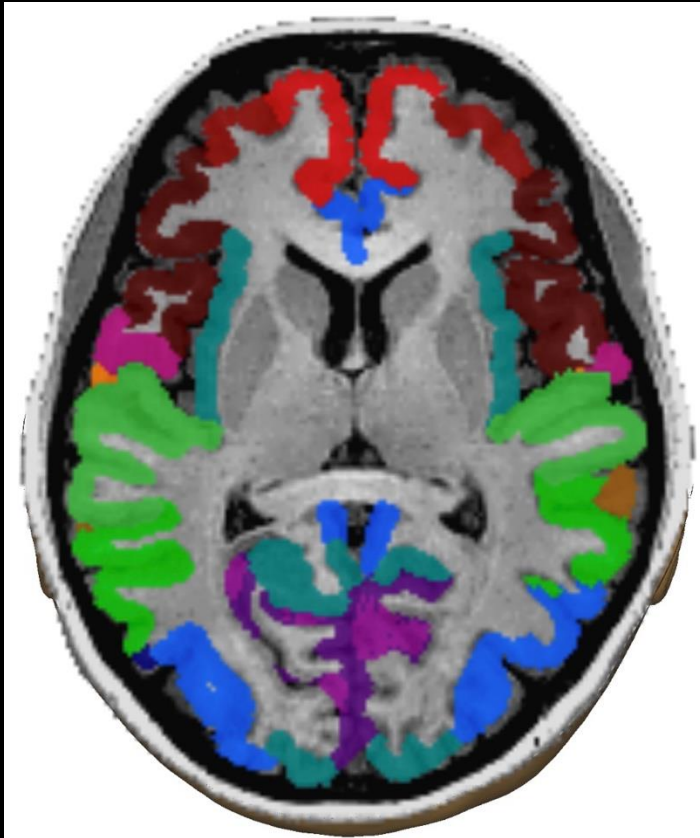


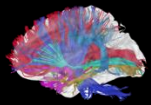
Understanding White Matter Tract Pathways



Understanding White Matter Tract Pathways

Neuroanatomical Regions



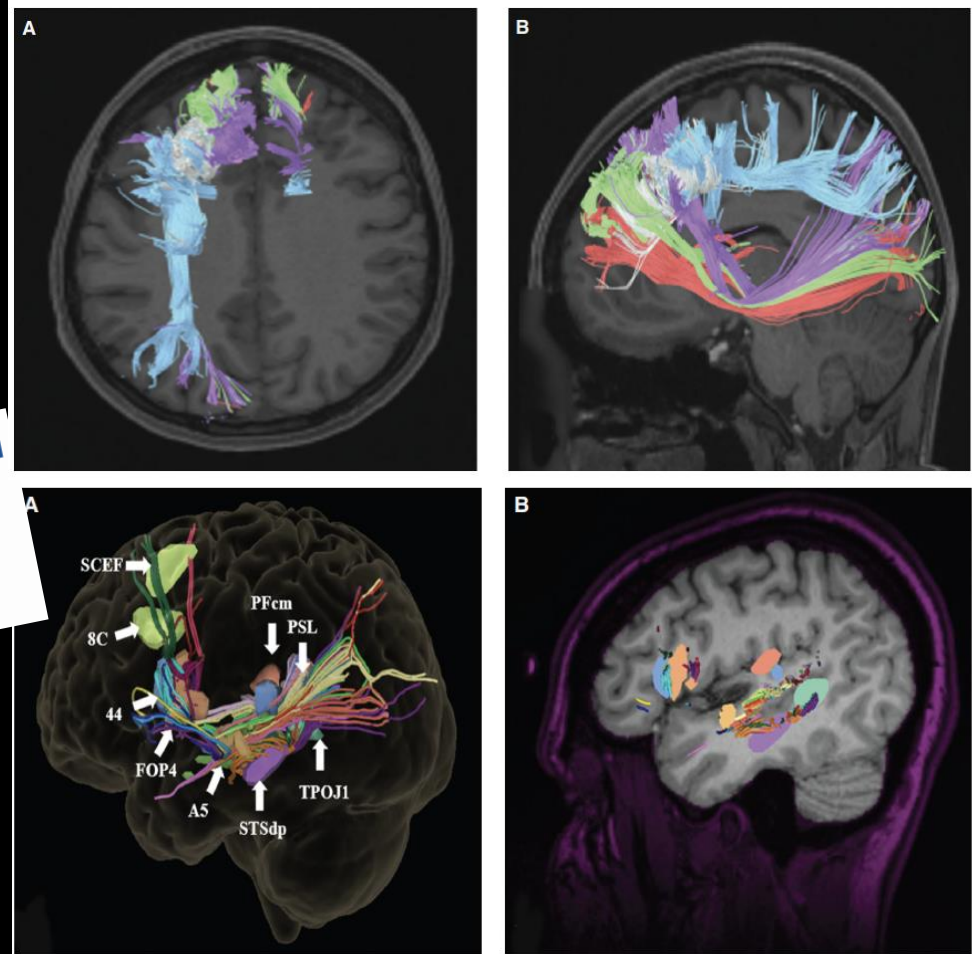


Understanding White Matter Tract Pathways

Connectomes

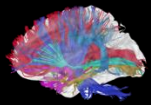
A CONNECTOMIC ATLAS OF THE HUMAN CEREBRUM SUPPLEMENT

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



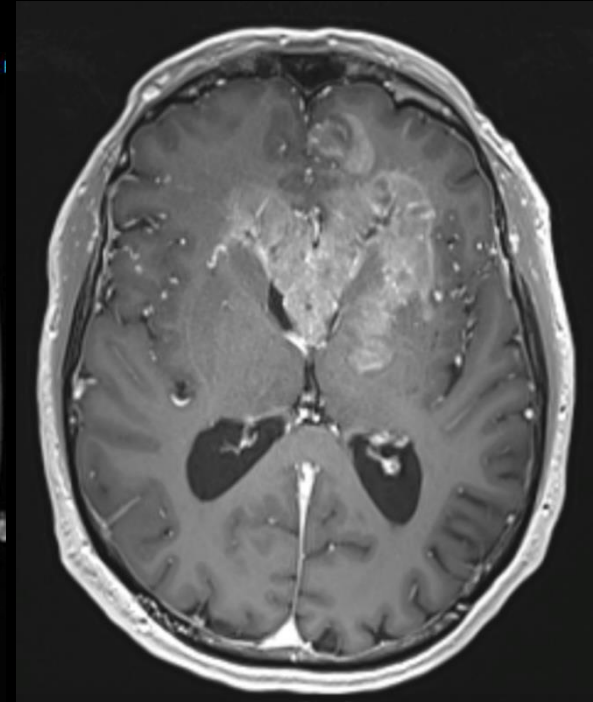
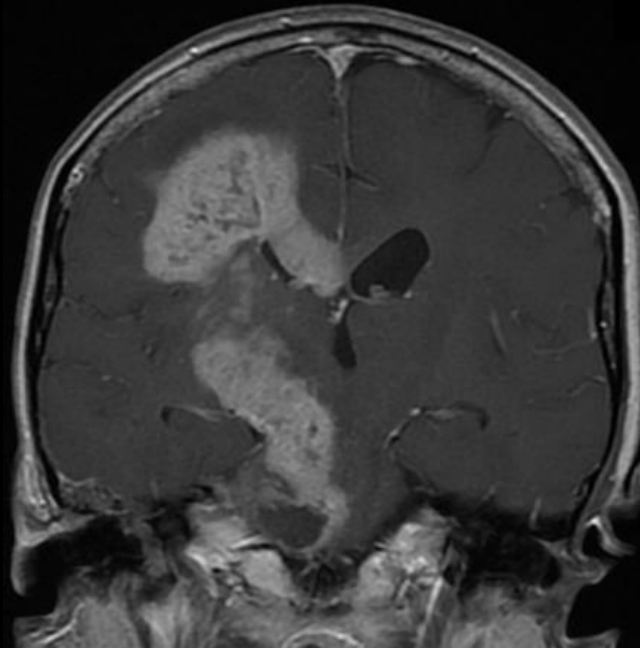
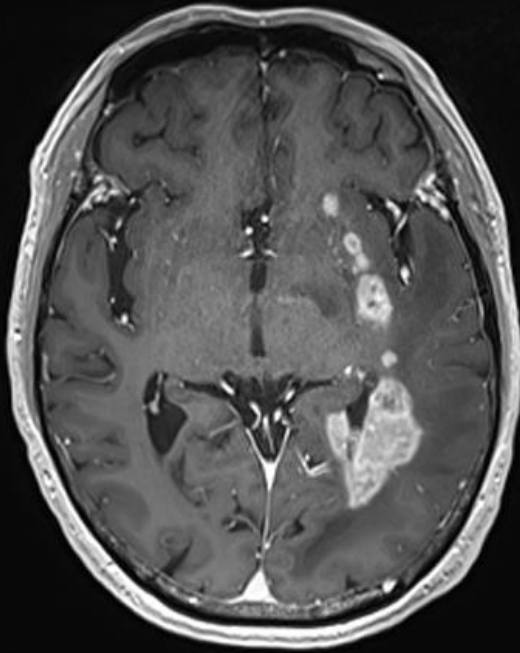
Michael E. Sughrue, MD,

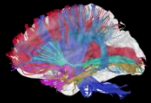
Operative Neurosurgery 15:S245–S294, 2018



Understanding White Matter Tract Pathways

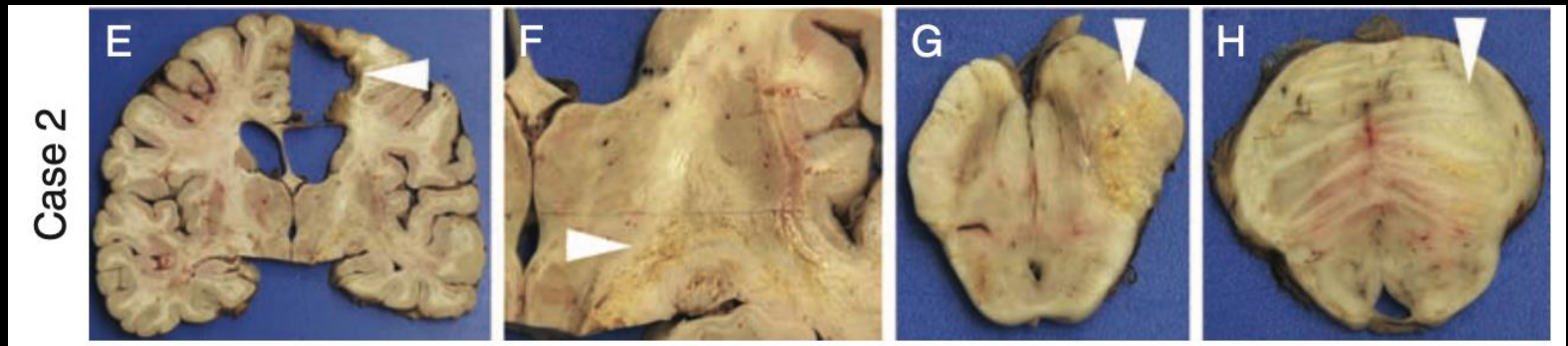
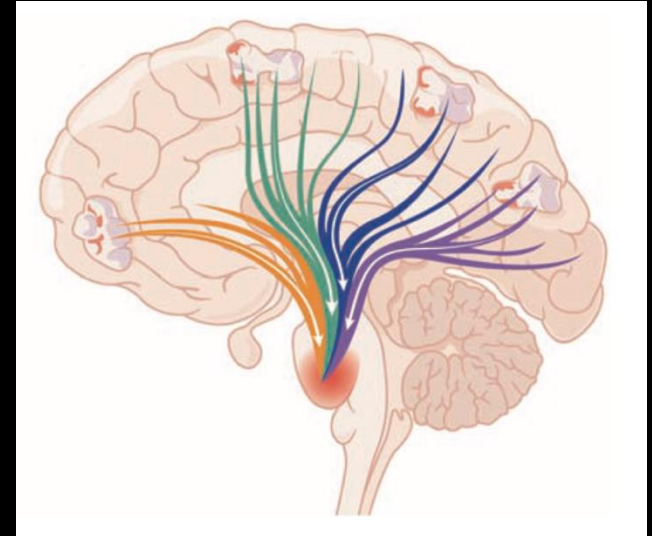
Relapse Patterns

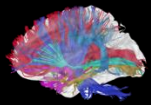




Understanding White Matter Tract Pathways

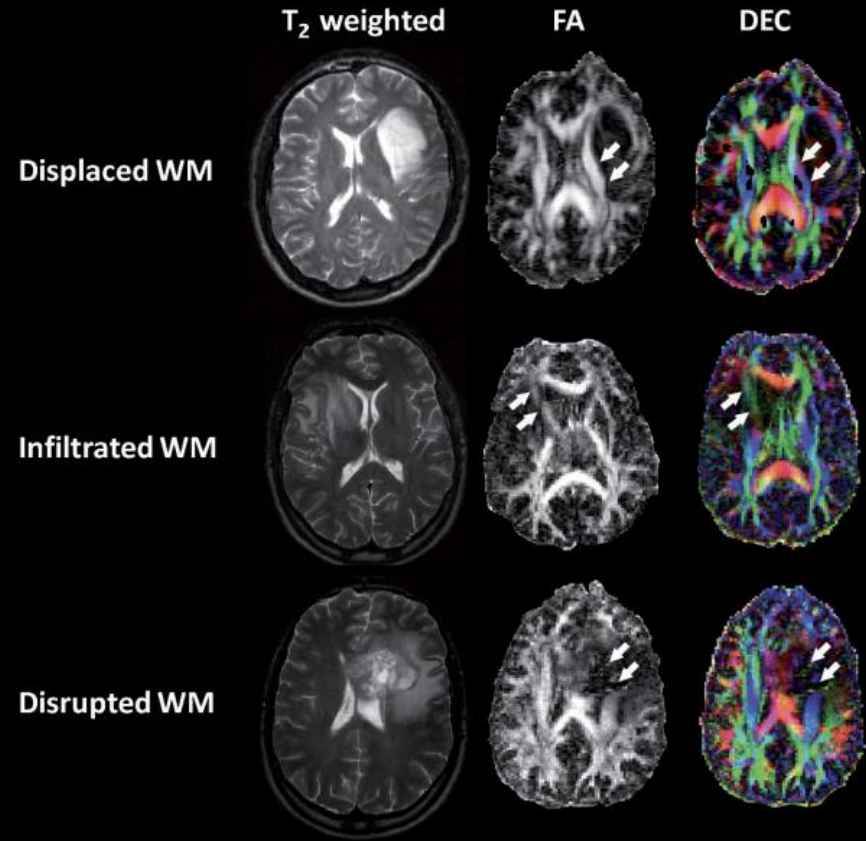
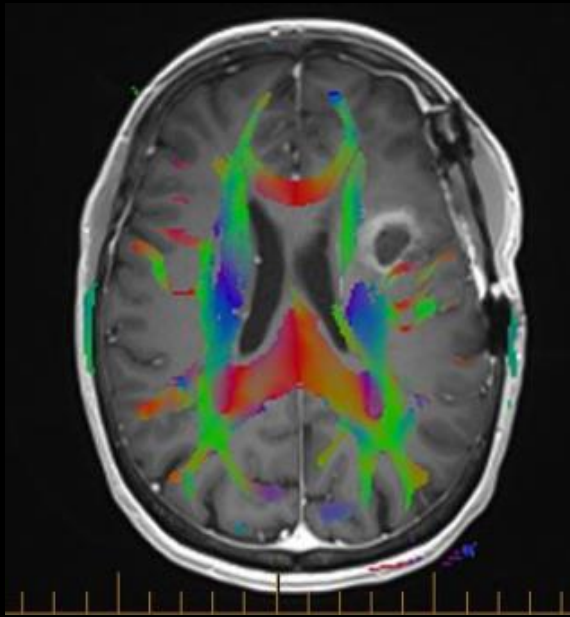
Autopsy Series





Understanding White Matter Tract Pathways

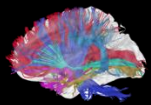
Diffusion Tensor Imaging



Imaging biomarkers of brain tumour margin and tumour invasion

¹S J PRICE, PhD, FRCS(NEURO.SURG) and ²J H GILLARD, MD, FRCR

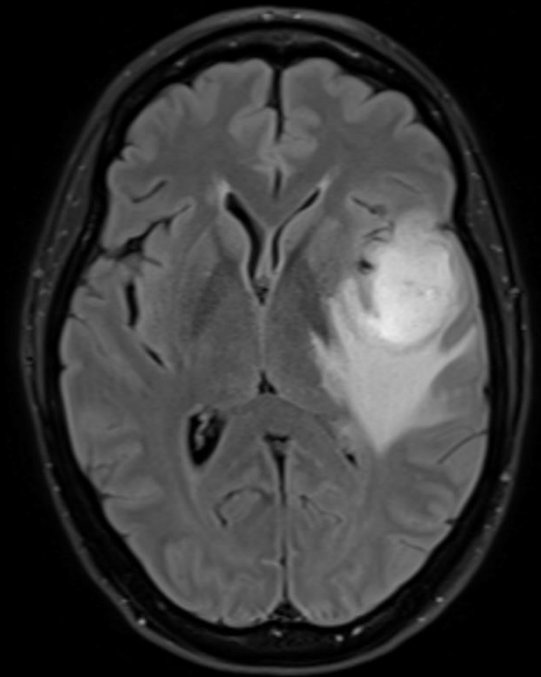
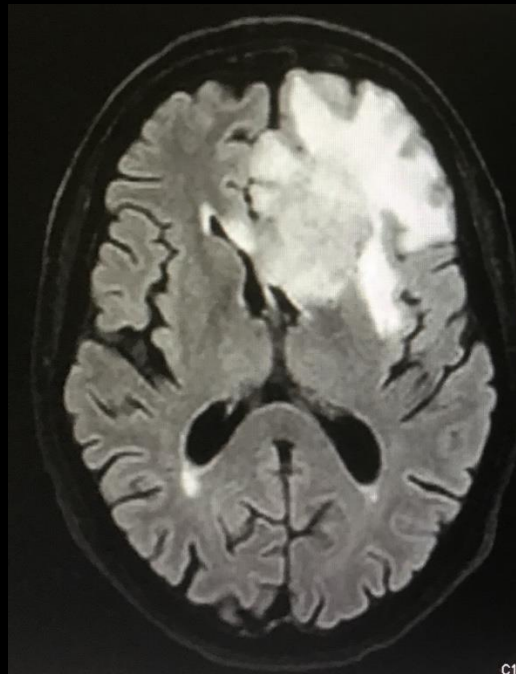
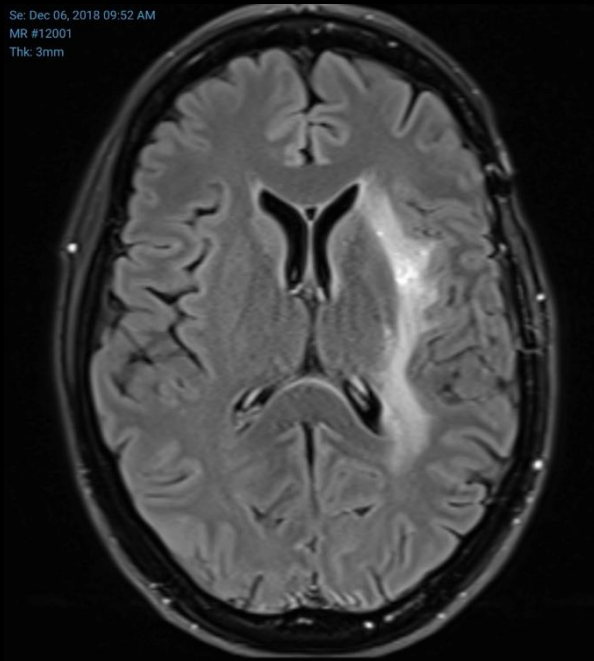
¹Academic Neurosurgery Division, Department of Clinical Neuroscience, and ²University Department of Radiology, Addenbrooke's Hospital, Cambridge, UK



Understanding White Matter Tract Pathways

Pattern of T2F Abnormality

Se: Dec 06, 2018 09:52 AM
MR #12001
Thk: 3mm



WMT Exploratory Audit

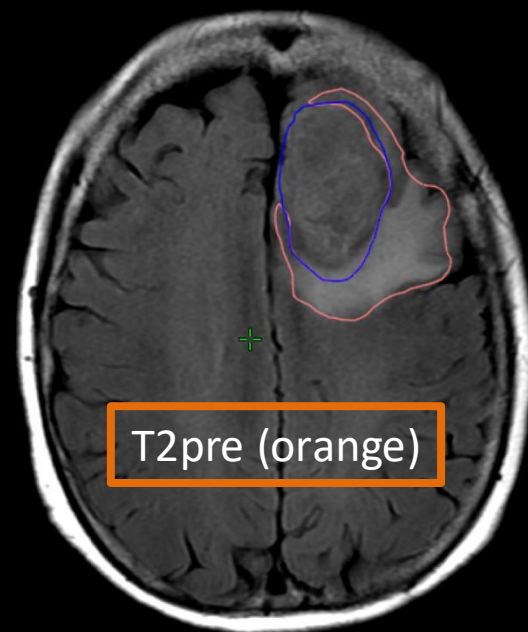
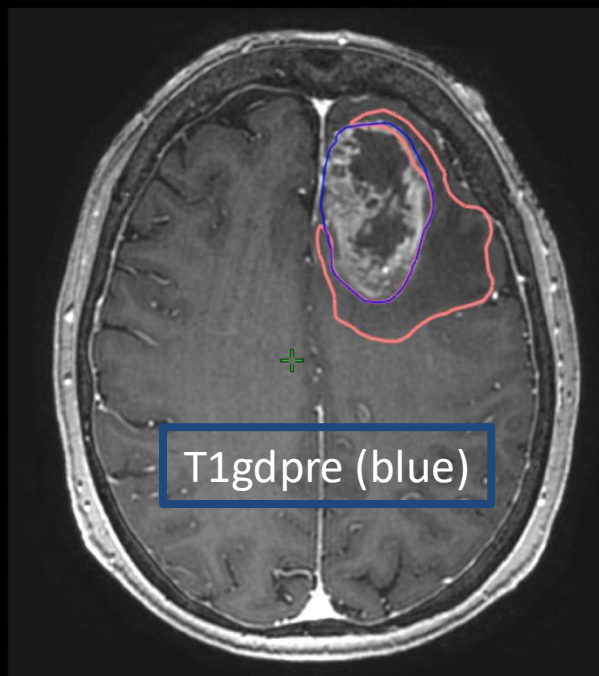
GBM (60Gy TMZ) : 2016-2020

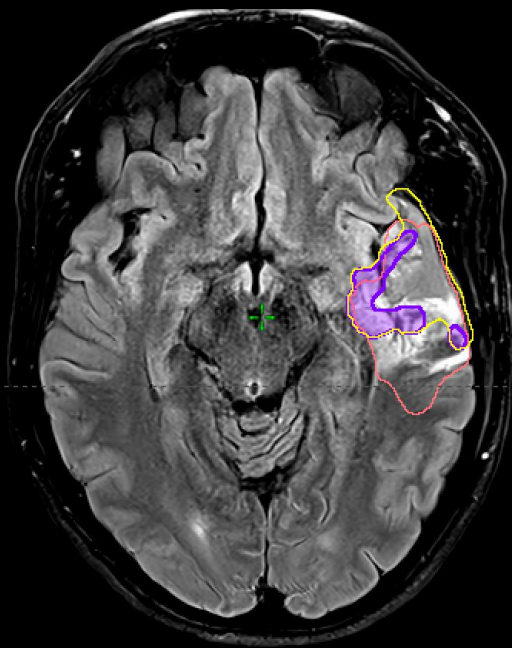
Volumetric Study

- : Volume of Preop T1gd and T2
- : Initial gyrus and infiltration detailed
- : Relapse site detailed
- : Relationship to T1gd, T2, White Matter Tract
- : Relapse distant if >20mm from GTV60

WMT Exploratory Audit

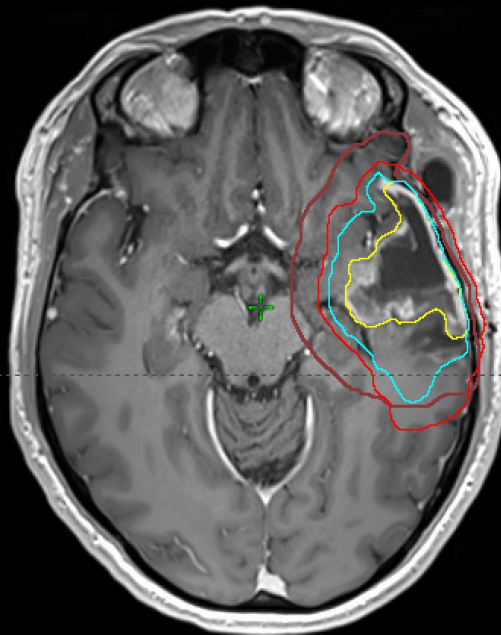
GBM 2016-2020 Volumetric Study





GTV60 (yellow) =

- Cavity +
- T1gdpost +
- Non-Enh tumour

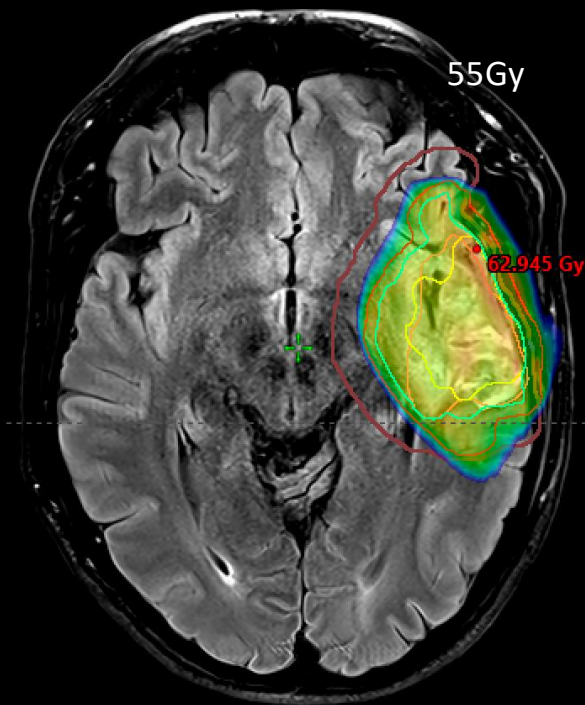


CTV60 (blue) =

- GTV60 x 5mm +
- T2post

PTV60 (red) =

- CTV60 x 3mm

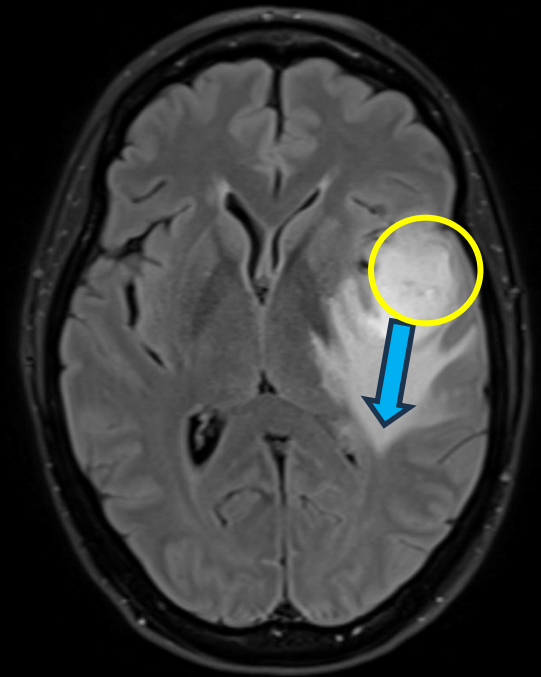
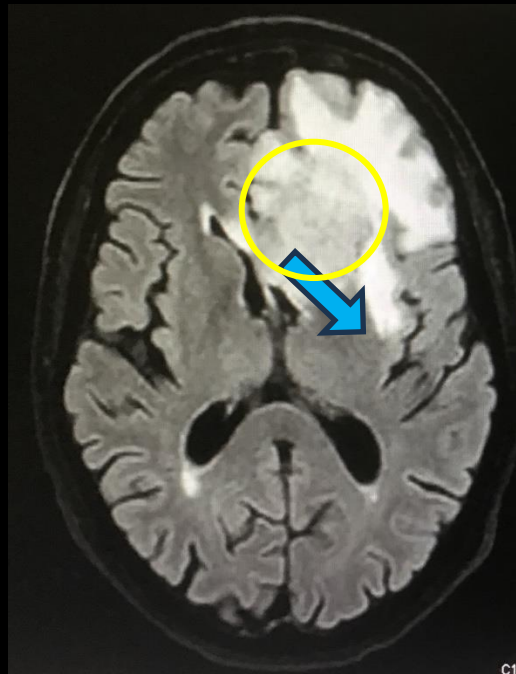
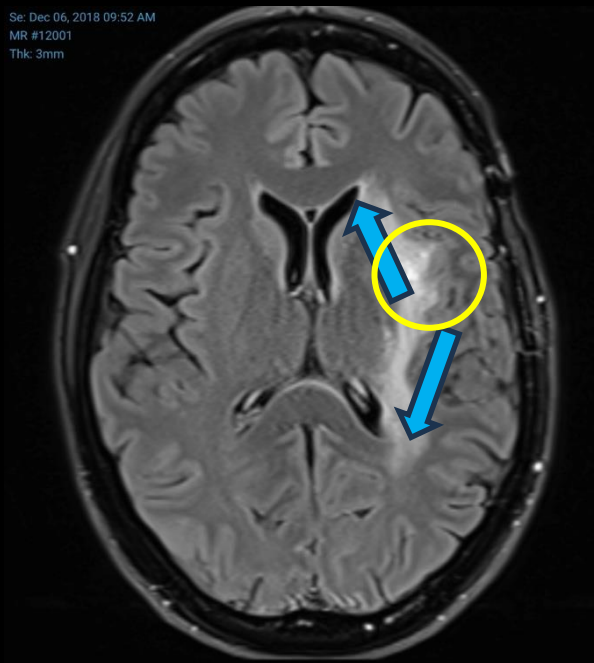


ESTRO-EANO PTV60 15mm margin routinely recorded (brown)

WMT Exploratory Audit

Pattern of T2F Abnormality: *CTV60 non-isotropic expansion down WMT*

Se: Dec 06, 2018 09:52 AM
MR #12001
Thk: 3mm



WMT Exploratory Audit

169 patients : 60Gy TMZ

ECOG PS 0,1: 71%

Near Total Resection: 42%

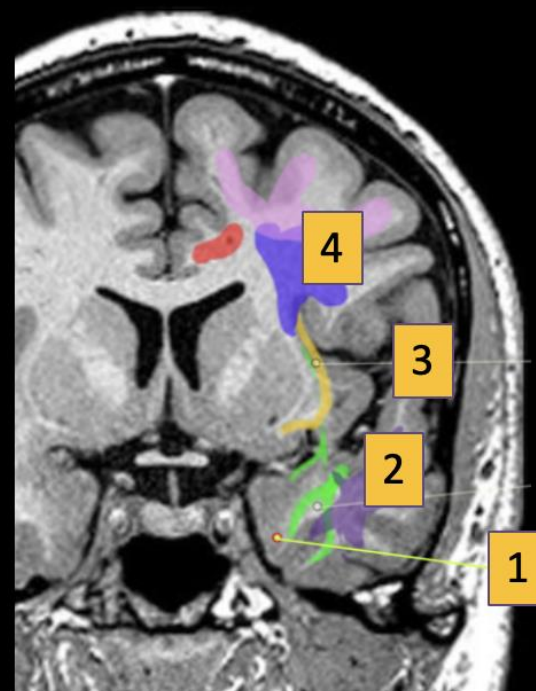
MGMT methylated: 41%

15 Neuroanatomical Sites:

Lat Temp(19%),

Lat Frontal (12%)

Ant Temp(13%),



WMT Exploratory Audit

Infiltration Pattern

Vols Median: T1gd- 18cm³ and T2- 37cm³

83% had white matter tract (WMT) abnormality

34% had T1gd in WMT

49% had only T2 in WMT

These had predictable tract involvement

WMT Exploratory Audit

Infiltration Pattern

83% had white matter tract (WMT) abnormality

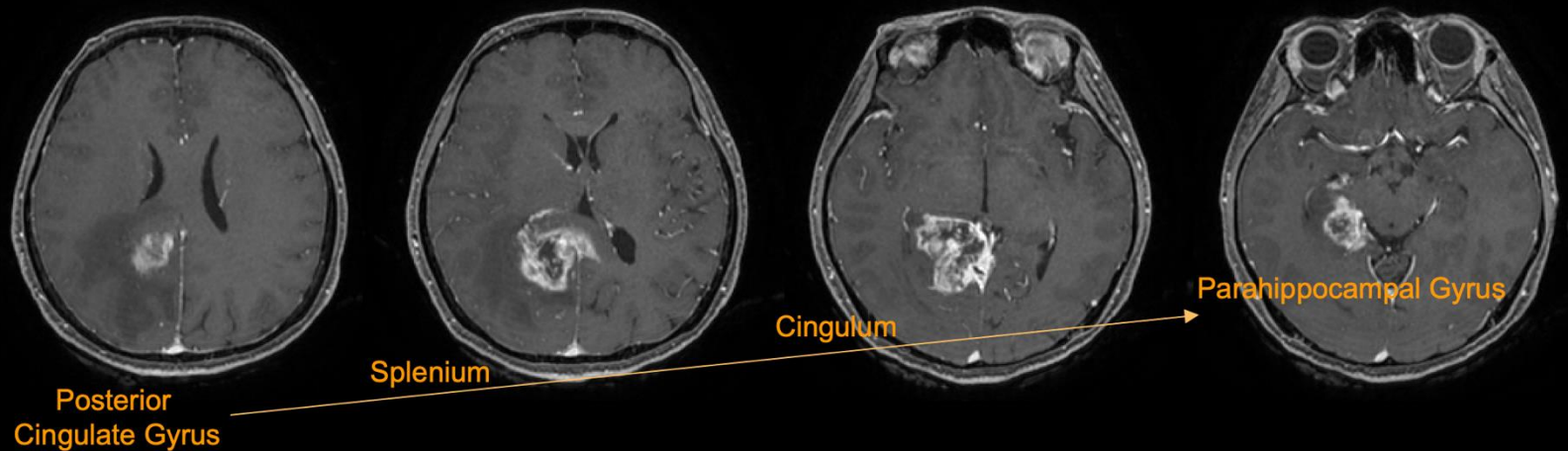


Figure 1: Typical pattern of infiltration with T1gd abnormality along cingulum pathway

WMT Exploratory Audit

Infiltration Pattern

83% had white matter tract (WMT) abnormality

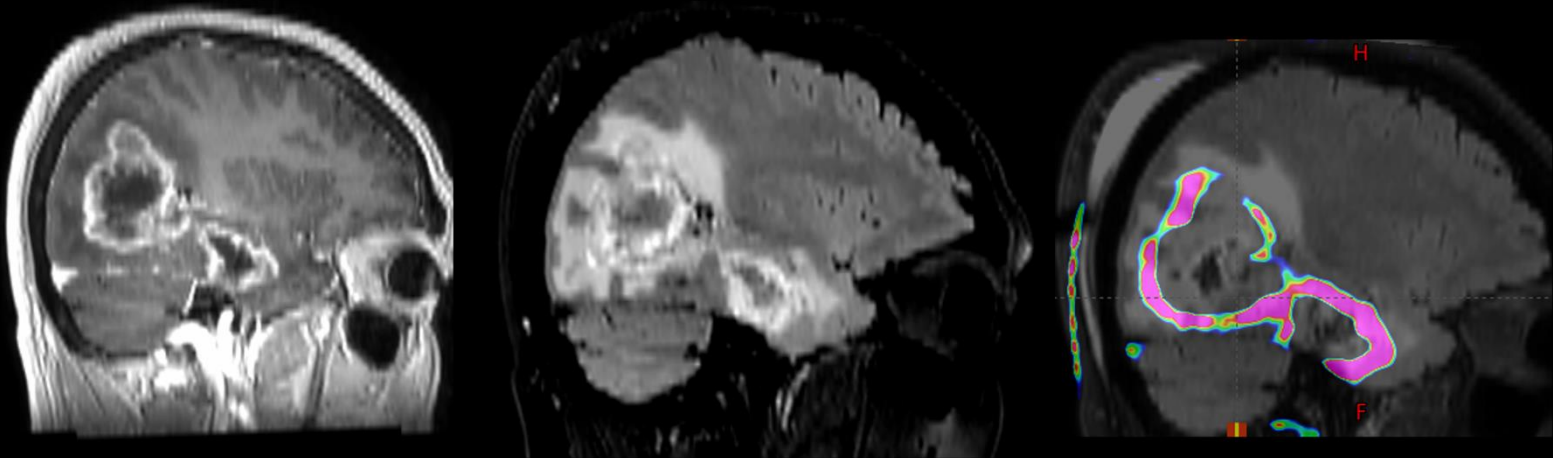


Figure 3: Example of GBM in Rt post cingulate gyrus extending along the cingulum WMT on preop T1gd, T2F and postop FET.

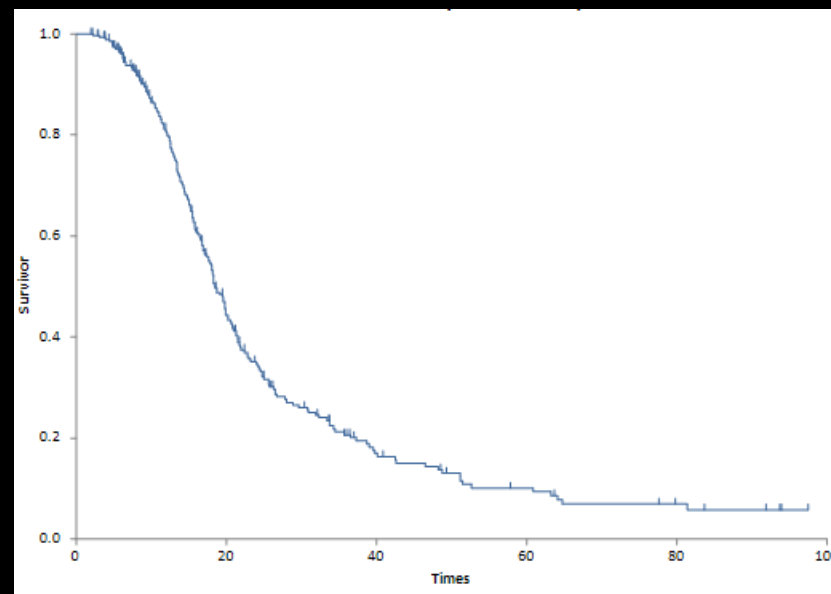
WMT Exploratory Audit

Survival

169 patients : 60Gy TMZ

Median OS : 18.3 months
(95%CI: 16.3-20.3).

Median RFS : 11.9 months
(95%CI: 10.6-13.3).



WMT Exploratory Audit

Infiltration Pattern

Presence of WMT abnormality had worse OS ($p=0.01$).

- No WMT abnormality: : 24.8 months
- T2 WMT abnormality: 19.7months
- T1gd WMT abnormality: 14.8months

The lowest T2/T1 quartile (relatively less T2 WMT abnormality) was associated with better OS ($p=0.04$).

WMT Exploratory Audit

Relapse Pattern

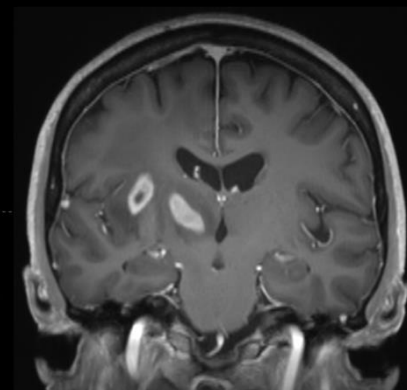
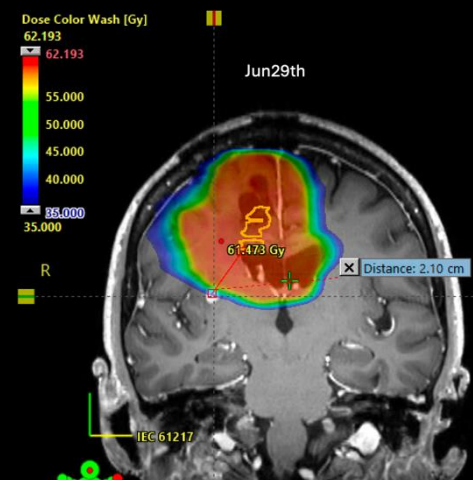
42% distant relapse (28% isolated)

Relapse Site

47% in initial T1gd

71% in initial T2 regions.

77% in adjacent WMT



WMT Exploratory Audit

Patterns of infiltration and relapse of GBM

- vary with neuroanatomical regions
- relate to initial T1gd and 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.

RT TARGET DELINEATION

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



OPTIMAL MARGIN EXPANSION
DETECT NON-ENHANCING TUMOUR



AVOID
GEOGRAPHICAL MISS

REDUCTION
NORMAL BRAIN DOSE

RT DOSE
ESCALATION

RT TARGET DELINEATION

RT TARGET DELINEATION

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PREDICTING SPREAD

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OPTIMAL MARGIN EXPANSION
DETECT NON-ENHANCING TUMOUR



AVOID
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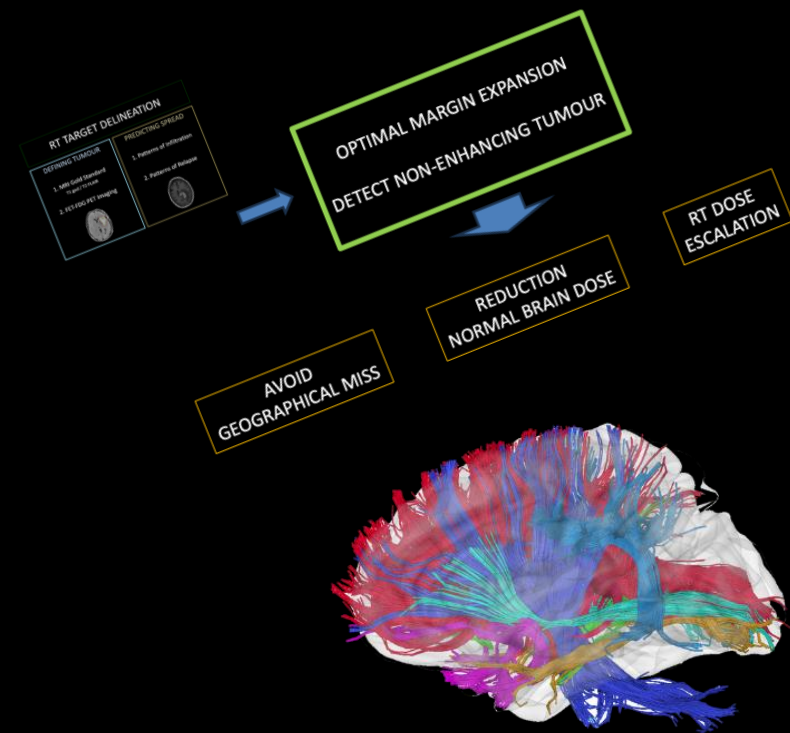
RT DOSE
ESCALATION

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





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

