

Standardized MRI Protocol for Brain Tumor Clinical Trials

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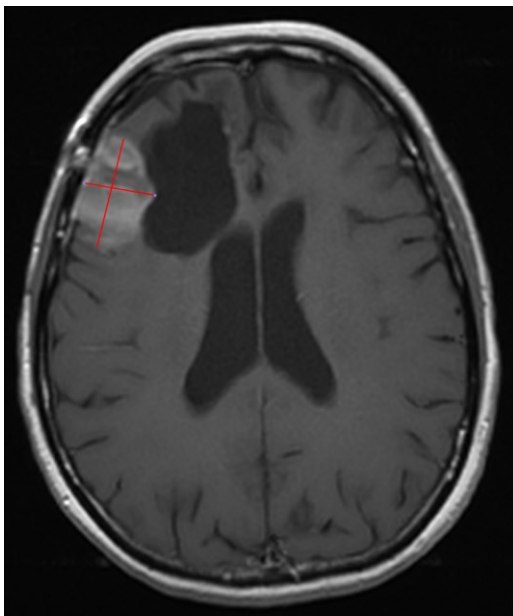
Standardized MRI Protocol for Therapeutic Studies

- **FDA Meeting in January 2014 highlighted the need to standardize MRI acquisition protocol**
 - Needed to increase the FDA confidence in using imaging response as a surrogate for drug efficacy in brain tumors
 - Most clinical MRI sequences are T1 or T2 “weighted”
 - Lesion contrast is highly dependent on sequence parameters
 - Lesion size is subjective due to ability for reader (or algorithm) to generalize across levels of image quality
 - Comparisons and pooling across studies, drugs, etc.
 - Ethically important to limit number of patients on ineffective drugs

Why do we need Image Standardization?

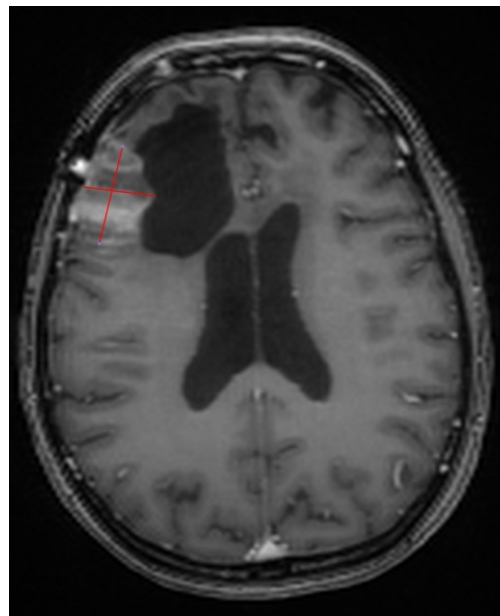
- **Reduce measurement variability due to protocol differences**
 - *Minor differences in hardware or sequence timing (e.g. TE/TR) can result in significant changes in image contrast*

Bidim=7.53



TE=13ms; TR=560ms
2D Fast Spin Echo

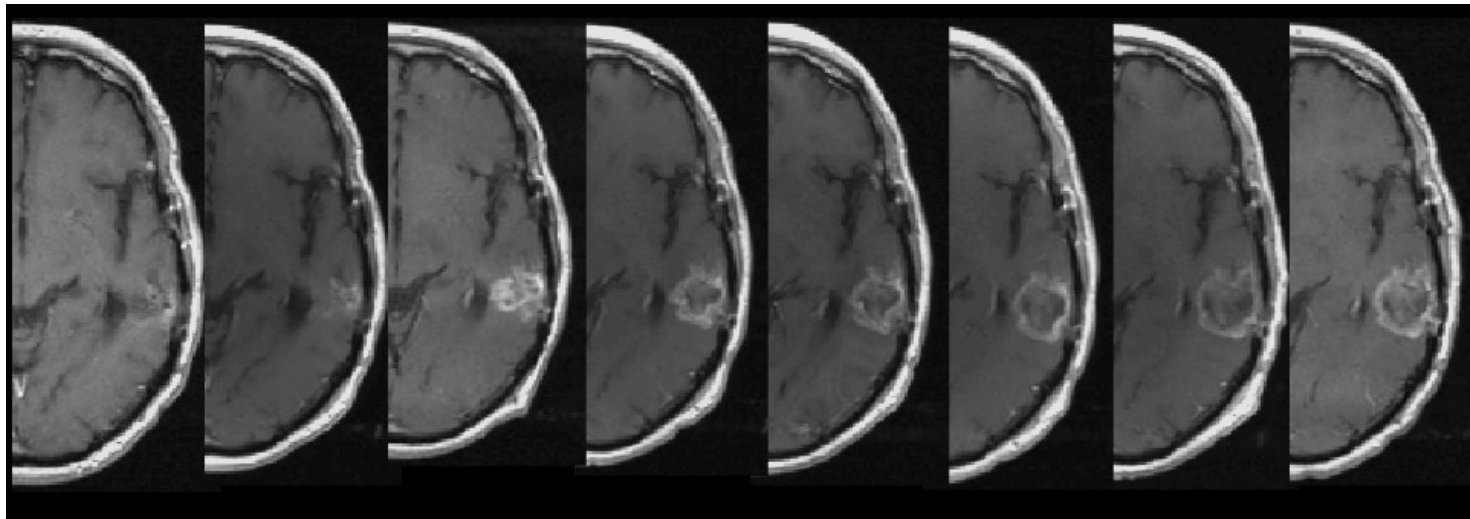
Bidim=7.05



TE=3ms; TR=10ms
3D IR Gradient Echo

Why do we need Image Standardization?

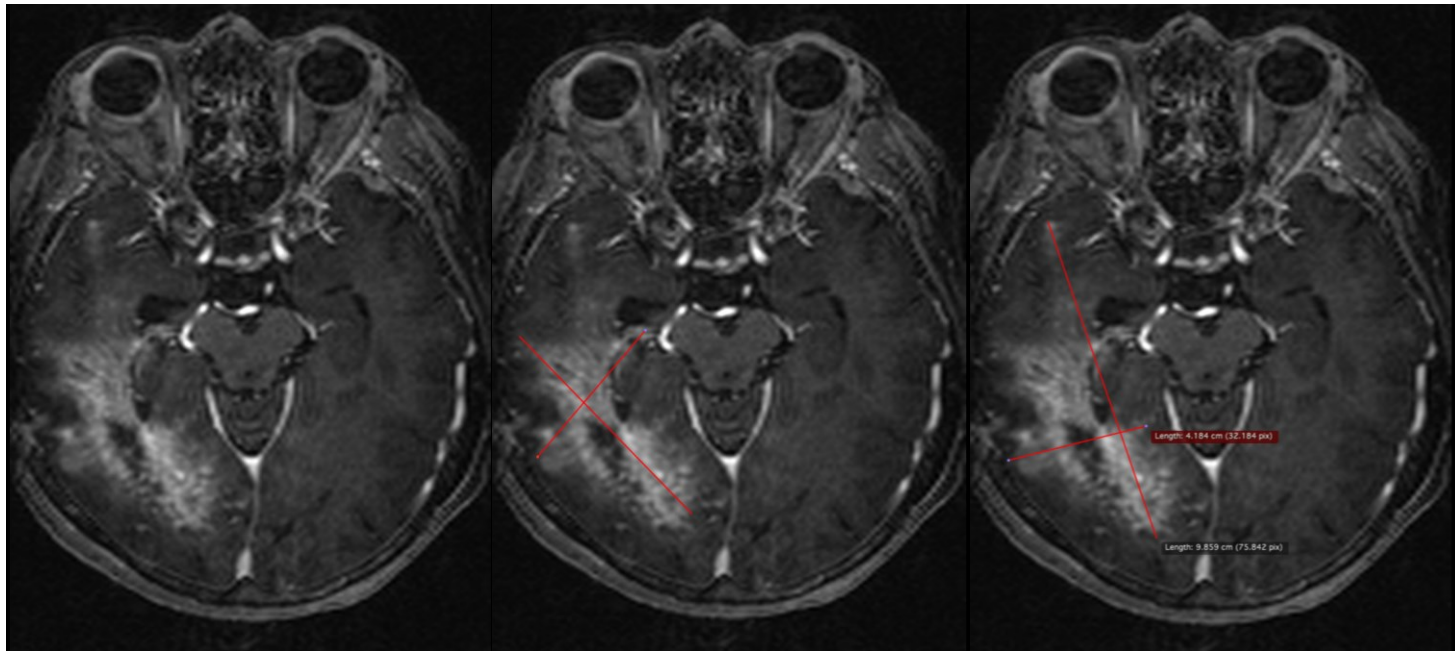
- **Reduce variability due to contrast timing**
 - *Time between injection and imaging affects contrast enhancement*
 - Contrast agent type, dose, and timing (4-8 min after admin is optimal (Akeson, Acta Radiol, 1997b))



Time →

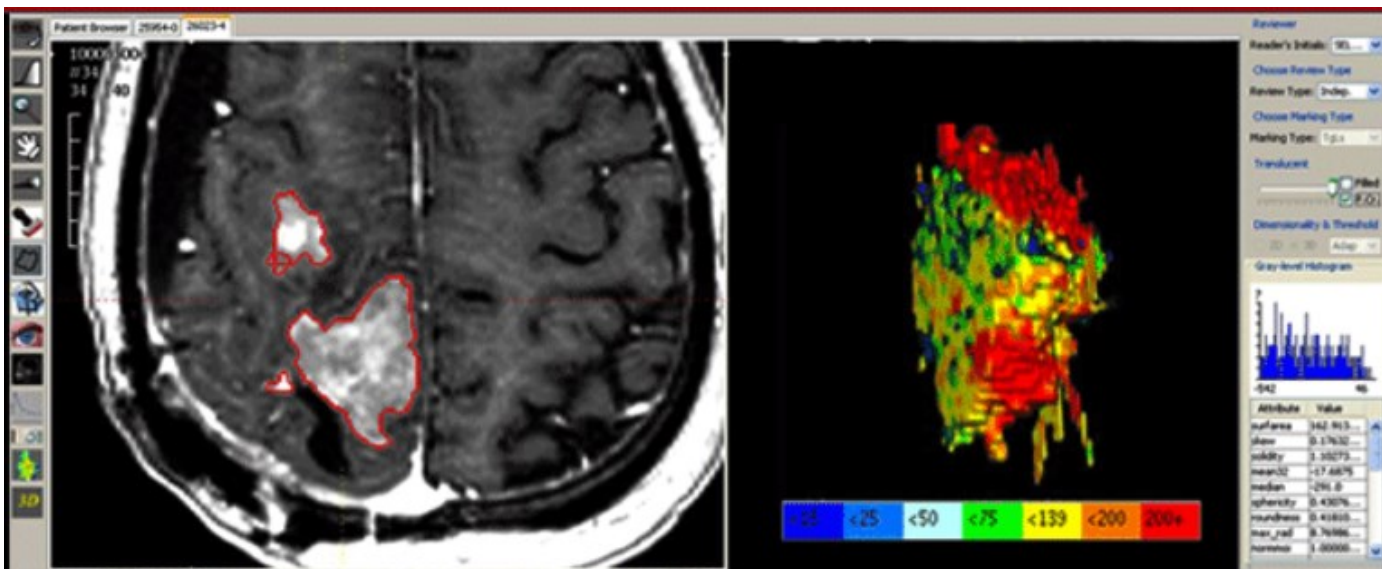
Why do we need Image Standardization?

- **Automated Volumetric Segmentation & Feature Extraction**
 - *Difficulty in defining the exact margins and identifying the largest diameter or perpendicular diameter* (Fornage, Radiology, 1993)



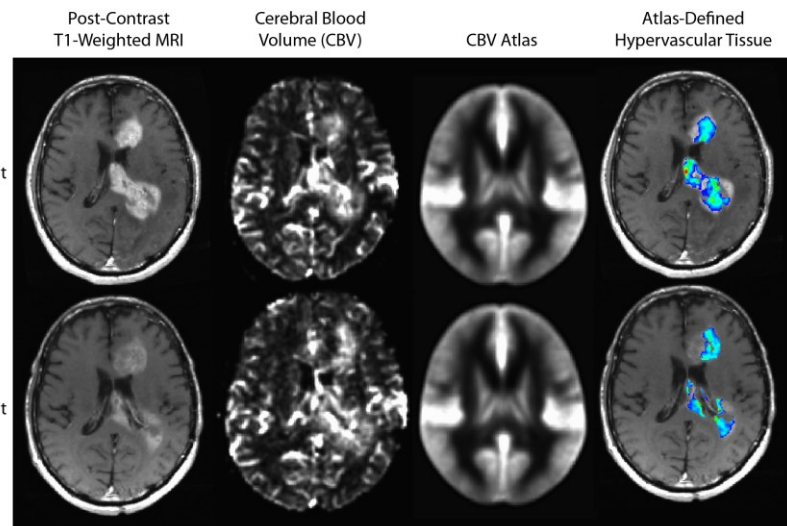
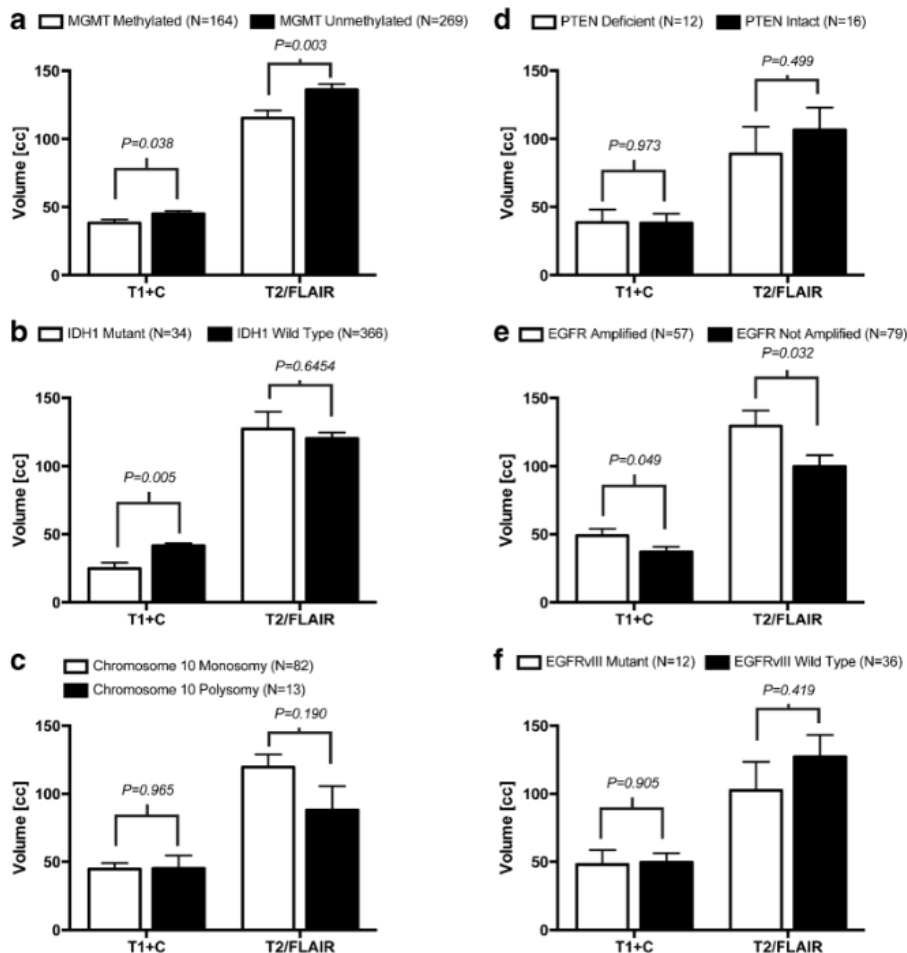
Why do we need Image Standardization?

- **Automated Volumetric Segmentation & Feature Extraction**
 - *Low Reproducibility in 1D/2D Measurements* (Hopper, 1996; Lavin, 1980; Quijox, 1988; Thiesse, 1997; Warr, 1993)
 - *High Reproducibility in Volume Measurements*
 - Kaus, Radiology, 2001 – Interobserver COV = 2% (automated segmentation) and 13.6% (manual segmentation)
 - Salman, J Biomed Sci Eng, 2009 – Interobserver COV = 2.5%-10% (automated)
 - Shah, Neuro Oncol, 2006 – 99.4% intraobserver correlation and 88.9% interobserver correlation (N=50 patients)



Why do we need Image Standardization?

- **Automated Volumetric Segmentation & Feature Extraction**
 - Imaging Genomics & Atlas-Based Approaches for Response Characterization



Leu, Cancer Imaging, 2014

Ellingson, Curr Neurol Neurosci Rep, 2015

Standardized MRI Protocol for Therapeutic Studies

- **Large variety of imaging capabilities for large clinical trials:**
 - Small Outpatient Clinics & Imaging Centers – Minimal Capabilities
 - Community Medical Centers – Basic Capabilities
 - Academic Medical Centers – Advanced Capabilities
- **Need for 3 different & synergistic imaging protocols:**
 - Minimal Standardized MRI Protocol
 - Designed for the small outpatient clinics and community imaging facilities
 - Large throughput, fast protocol, minimal chance for error (< 30 min)
 - Basic Standardized MRI Protocol
 - Designed to work for most community medical centers and most sites
 - Standard throughput, typical protocol (< 30 min)
 - Advanced Standardized MRI Protocol + Optional “Modules”
 - Designed for academic centers with expertise in advanced imaging
 - Optional “modules” allow for flexibility depending on needs for the trial

Consensus Recommendations for a

Standardized Brain Tumor Imaging Protocol (BTIP) in Clinical Trials

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[§] Representative of the Ivy Consortium for Early Phase Clinical Trials

[¥] Representative of the American College of Radiology Imaging Network (ACRIN)

^β Representative of the European Organisation for Research and Treatment of Cancer (EORTC)

[‡] Representative of the Alliance for Clinical Trials in Oncology

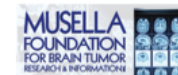
^æ Representative of the RSNA Quantitative Imaging Biomarker Alliance (QIBA)

^Ω Representative of the American Society of Neuroradiology (ASNR)

[‡] Representative of the American Society of Functional Neuroradiology (ASFNR)

[‡] Representative of the Radiation Therapy Oncology Group (RTOG)

Jumpstarting Brain Tumor Drug Development Coalition

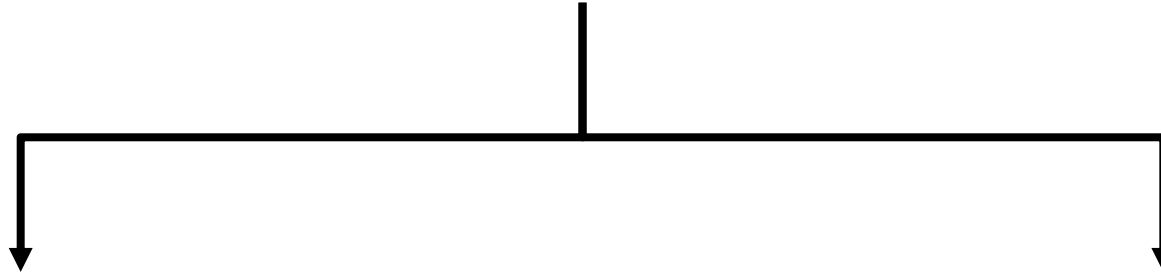


Standardized MRI Protocol for Therapeutic Studies

- **Designed to be aligned with the EORTC, ACRIN, Alliance, and ABTC**
- **Designed to work with almost all community medical centers and most sites in ACRIN, EORTC, and the Alliance**
- **Standard throughput, similar to “basic” EORTC protocol**
 - Under 1 hour set up to take down (<30 min), little expertise necessary, no special equipment (e.g. power injector)

Balance Between Maximizing Compliance & Data Quality

Philosophical Questions Regarding Goals of MRI
Standardization in Brain Tumor Clinical Trials



Maximizing Compliance
*Parameters reflect the range
of values that 100% of centers use*

Maximizing Data Quality
*Parameters reflect the range
of values that >80% of centers use*

Minimum Standard 1.5T & 3T MRI Protocol

| | 3D T1w Pre ^b | Ax 2D FLAIR ^j | Ax 2D DWI | Contrast Injection ^a | Ax 2D T2w ^{h,i} | 3D T1w Post ^b | |
|--|--------------------------------------|--------------------------------|--|---------------------------------|---------------------------------|--------------------------------------|-----------------------|
| Sequence | MPRAGE ^{e,f} | TSE ^c | SS-EPI ^g | | | TSE ^c | MPRAGE ^{e,f} |
| Plane | Sagittal/ Axial | Axial | Axial | | | Axial | Sagittal/ Axial |
| Mode | 3D | 2D | 2D | | | 2D | 3D |
| TR [ms] | 2100 ^m | >6000 | >5000 | | | >2500 | 2100 ^m |
| TE [ms] | Min | 100-140 | Min | | | 80-120 | Min |
| TI [ms] | 1100 ⁿ | 2000-2500 ^k | | | | | 1100 ⁿ |
| Flip Angle [Degrees] | 10-15 | 90/≥160 | 90/180 | | | 90/≥160 | 10-15 |
| Frequency | ≥172 | ≥256 | ≥128 | | | ≥256 | ≥172 |
| Phase | ≥172 | ≥256 | ≥128 | | | ≥256 | ≥172 |
| NEX | ≥1 | ≥1 | ≥1 | | | ≥1 | ≥1 |
| Frequency Direction | A/P | A/P | R/L | | | A/P | A/P |
| FOV | 256mm | 240mm | 240mm | | | 240mm | 256mm |
| Slice Thickness | ≤1.5mm | ≤4mm ^l | ≤4mm ^l | | | ≤4mm ^l | ≤1.5mm |
| Gap/Spacing | 0 | 0 | 0 | | | 0 | 0 |
| Diffusion Options ^p | | | $b = 0, 500, 1000 \text{ s/mm}^2$ ≥3 directions | | | | |
| Parallel Imaging | Up to 2x | Up to 2x | Up to 2x | | Up to 2x | Up to 2x | |
| Scan Time (Approx) [Benchmarked on 3T Skyra] | 5-10 min [5:49 for 1mm isotropic] | 4-8 min [3:22 for 2D FLAIR] | 2-4 min [1:22 for 3 direction DWI and 3 b-values] | | 4-8 min [5:10 for dual echo] | 5-10 min [5:49 for 1mm isotropic] | |

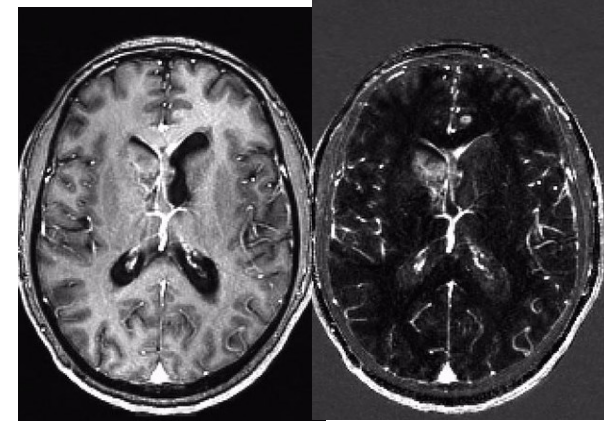
Minimum Standard 1.5T & 3T MRI Protocol

- *MPRAGE Pre- and Post*
- *1-1.5mm isotropic*
- *Can be reformatted to 3mm slices (axial, sagittal, or coronal)*
- *Can be used for RANO*
- *Allows for T1 subtraction*
- *Allows for longitudinal registration*
- *Available from all 3 major vendors as part of ADNI*

| | 3D T1w Pre ^b | Ax 2D FLAIR ^j | Ax 2D DWI | Contrast Injection ^a | Ax 2D T2w ^{h,i} | 3D T1w Post ^b | |
|--|--------------------------------------|--------------------------------|--|---------------------------------|---------------------------------|--------------------------------------|-----------------------|
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| Plane | Sagittal/ Axial | Axial | Axial | | | Axial | Sagittal/ Axial |
| Mode | 3D | 2D | 2D | | | 2D | 3D |
| TR [ms] | 2100 ^m | >6000 | >5000 | | | >2500 | 2100 ^m |
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| Gap/Spacing | 0 | 0 | 0 | | 0 | 0 | |
| Diffusion Options ^p | | | <i>b</i> = 0, 500, 1000 s/mm ² ≥3 directions | | | | |
| Parallel Imaging | Up to 2x | Up to 2x | Up to 2x | | Up to 2x | Up to 2x | |
| Scan Time (Approx) [Benchmarked on 3T Skyra] | 5-10 min [5:49 for 1mm isotropic] | 4-8 min [3:22 for 2D FLAIR] | 2-4 min [1:22 for 3 direction DWI and 3 b-values] | | 4-8 min [5:10 for dual echo] | 5-10 min [5:49 for 1mm isotropic] | |

T1+C

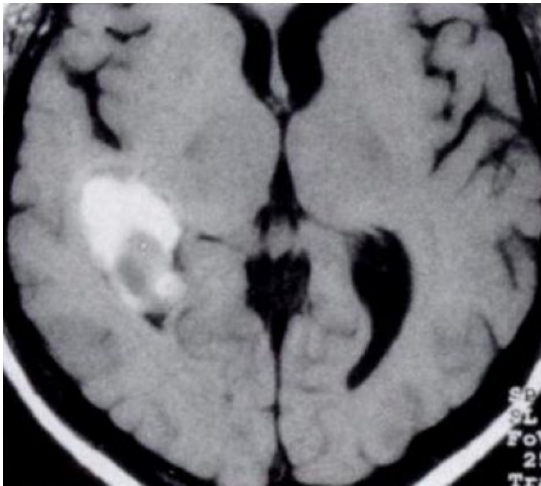
T1 Subt.



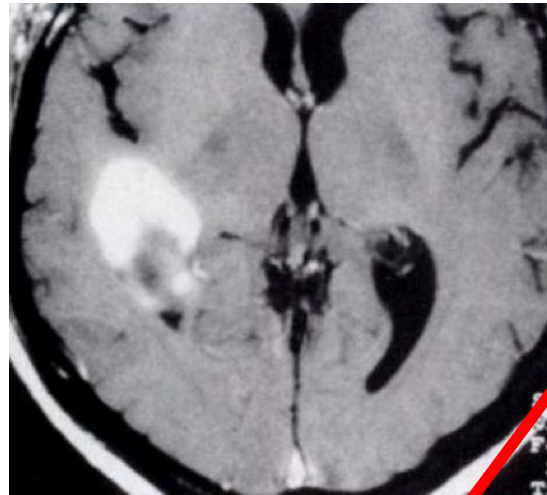
T1 Subtraction

- **Suto, Comput Assist Tomogr, 1989** – Subtracted synthetic images on Gd-DTPA enhanced MRI
- **Lloyd, Br J Radiol, 1993** – Subtraction Gd-enhanced MR for head/neck imaging
- **Lee, AJR, 1996** – Digital subtraction for brain lesions or hemorrhage
- **Gaul, AJNR, 1996** – Enhancing brain lesions vs. hemorrhage
- **Melhem, JMRI, 1999** – Enhancing brain lesions

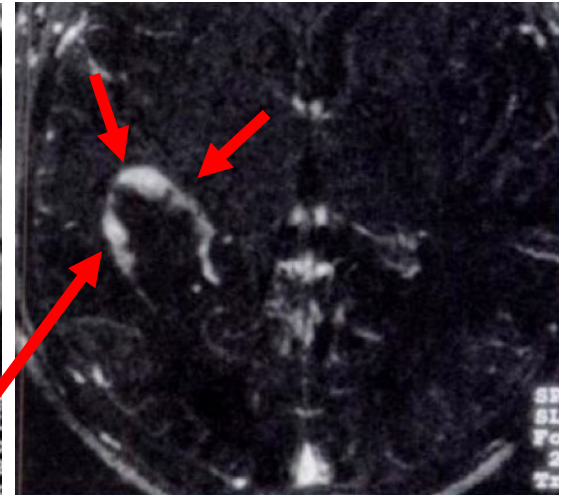
Pre-Contrast T1



T1+C



T1 Subtraction



59 y.o. Female with Thyroid Carcinoma + Headaches

Ring Enhancing Lesion
Adjacent to Ventricle

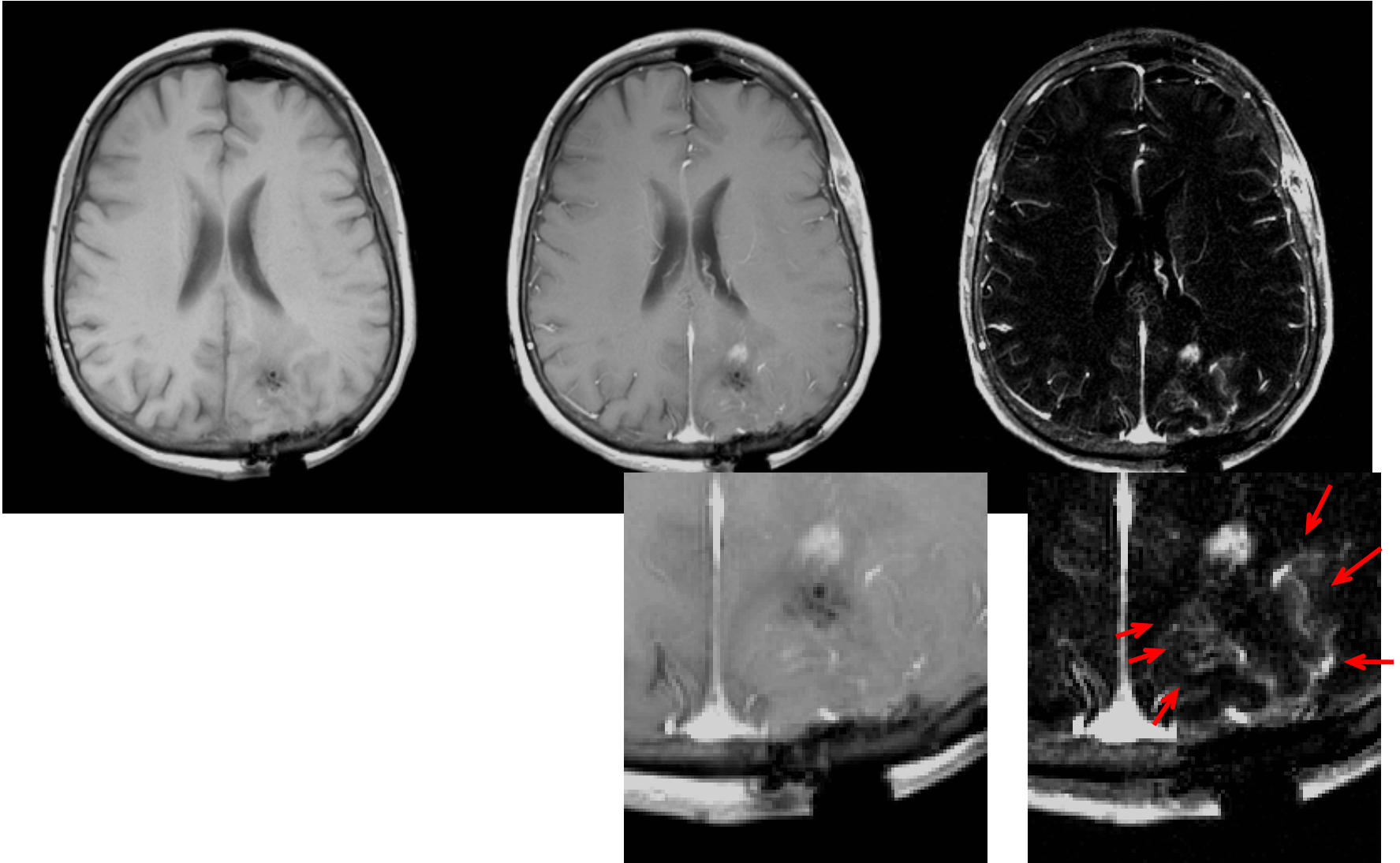
T1 Subtraction

- Extent of Resection

Pre-Contrast T1w

Post-Contrast T1w

T1 Subtraction Map



T1 Subtraction

- Phase II, Multicenter Trial of Bev vs. Bev+CPT11 in Recurrent GBM (BRAIN Trial)

(Ellingson, *Radiology*, 2014)

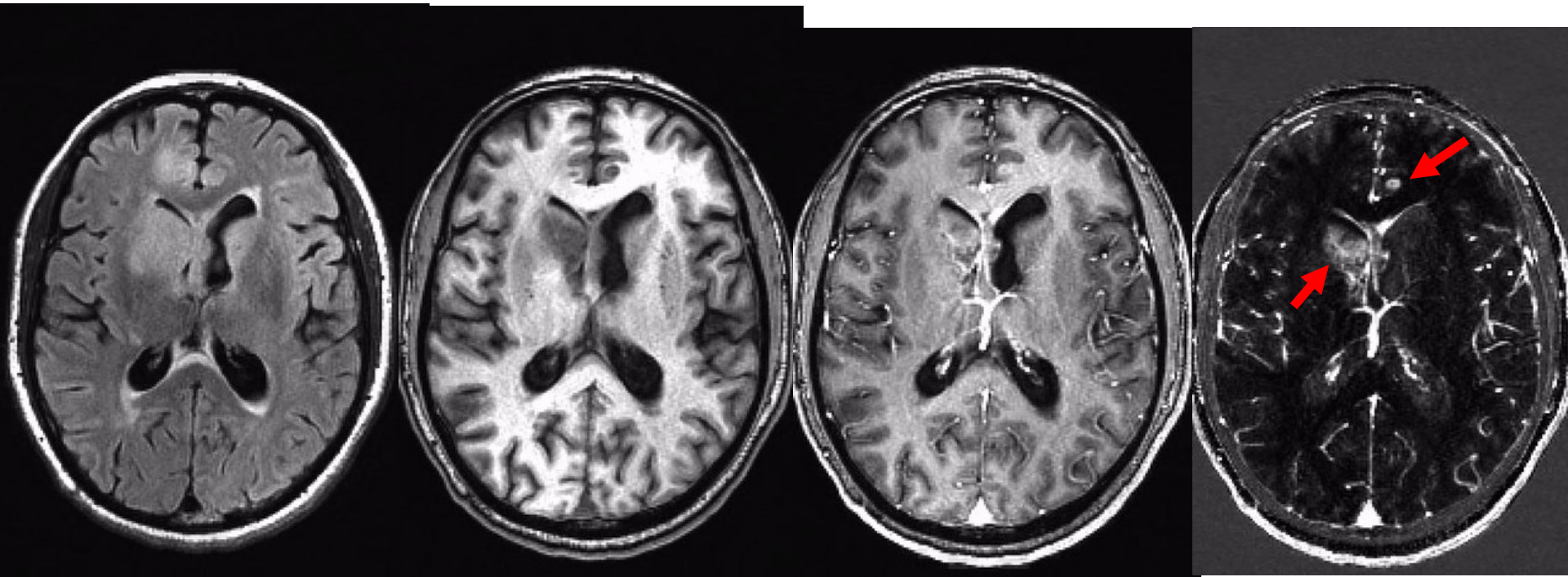
FLAIR

T1w

Post-Bev

T1+C

CE- Δ T1w Map



T1 Subtraction

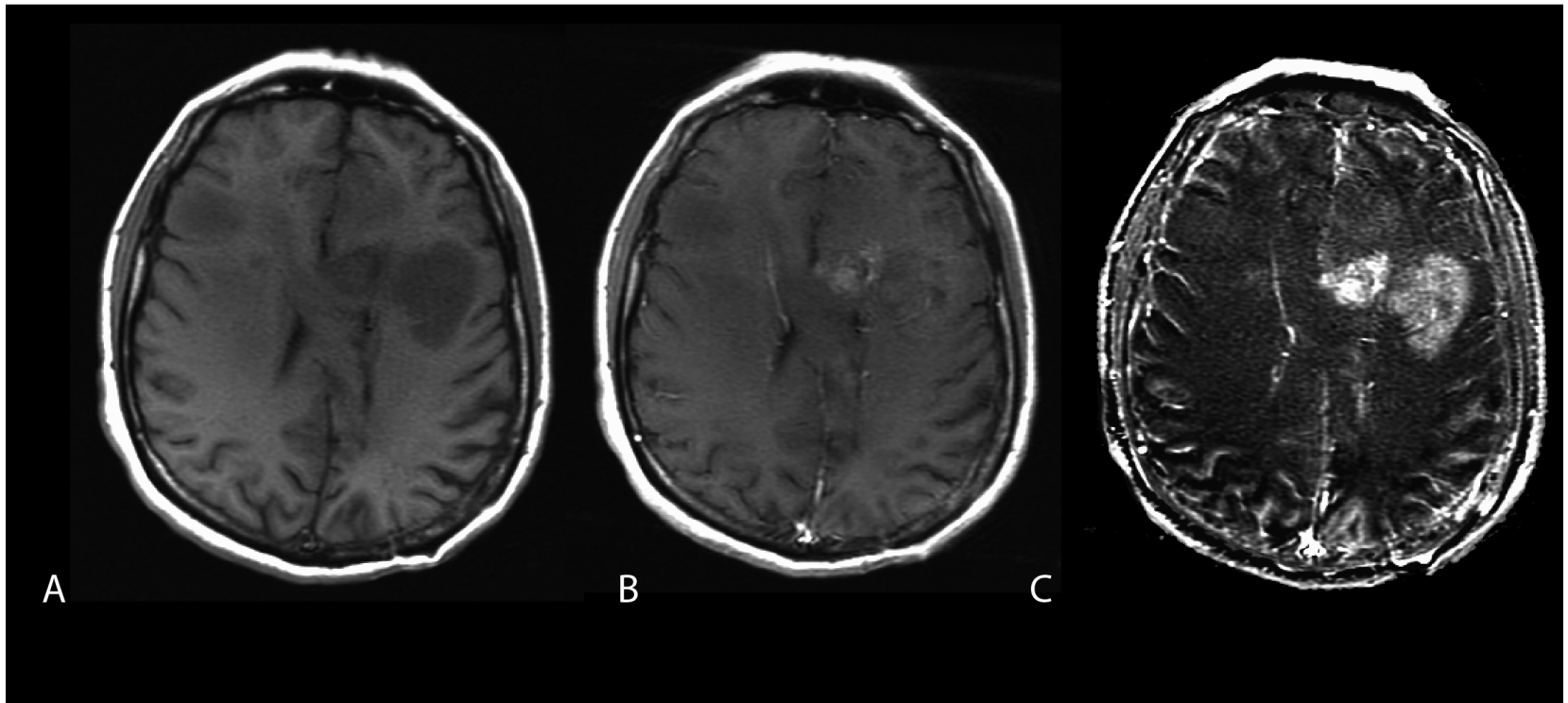
- Phase II, Multicenter Trial of Bev vs. Bev+CPT11 in Recurrent GBM (BRAIN Trial)

(Ellingson, *Radiology*, 2014)

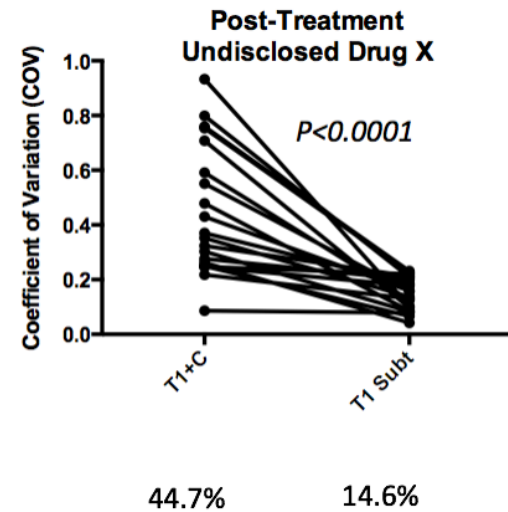
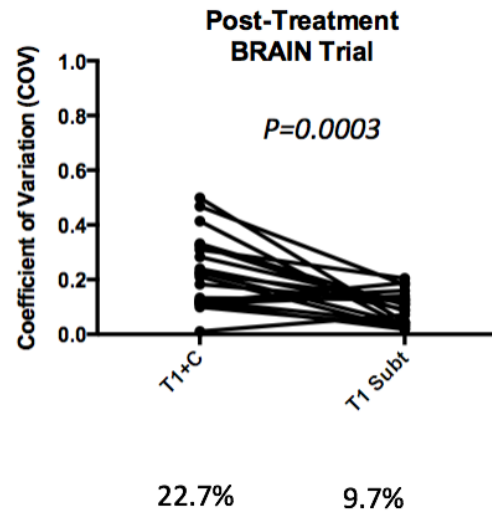
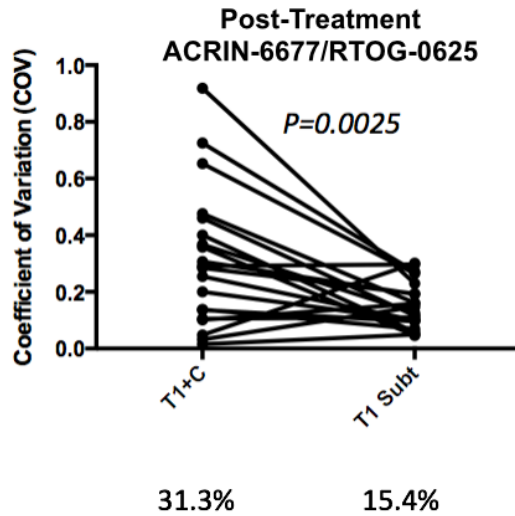
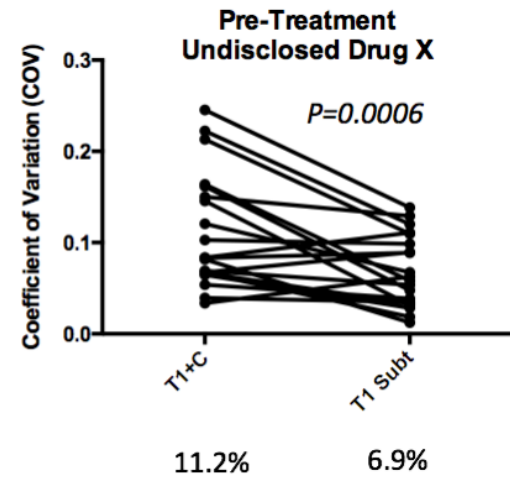
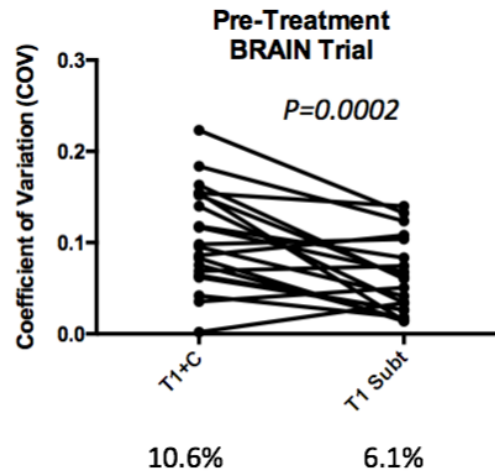
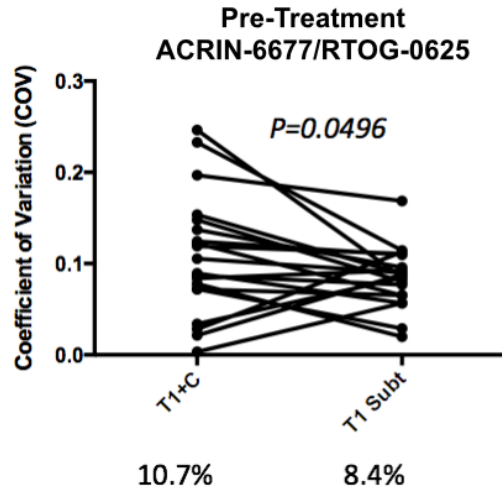
Pre-Contrast
T1w MRI

Post-Contrast
T1w MRI

Normalized
Raw Subtraction Map

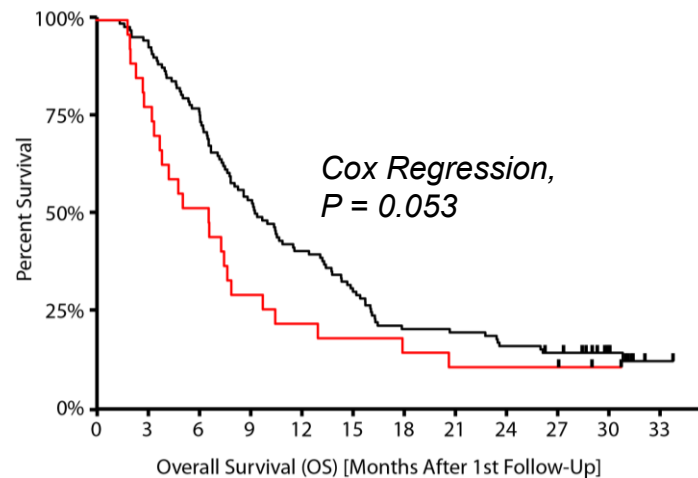
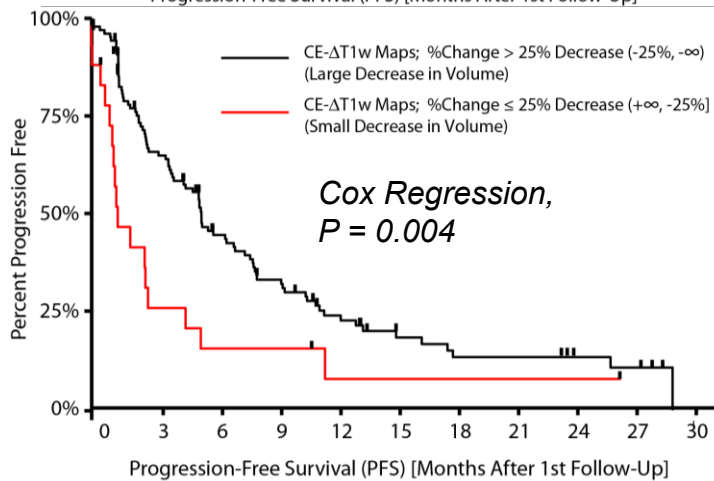
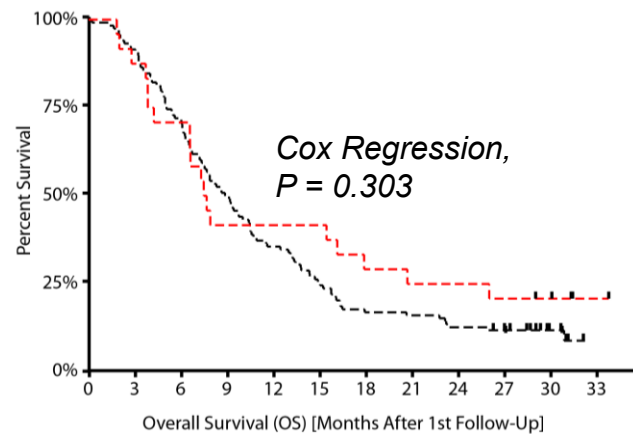
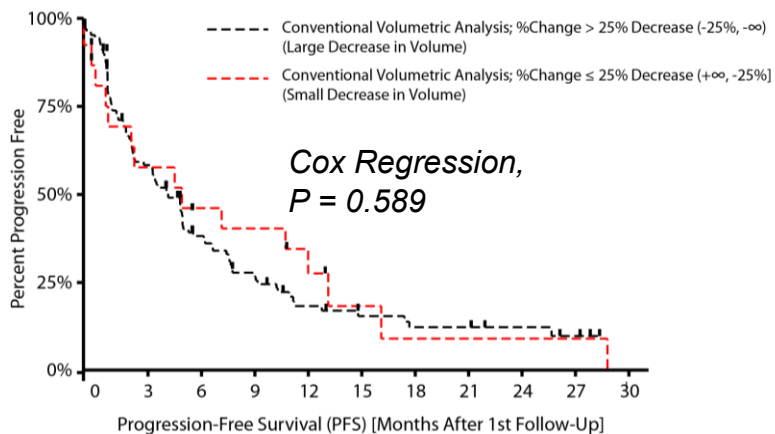
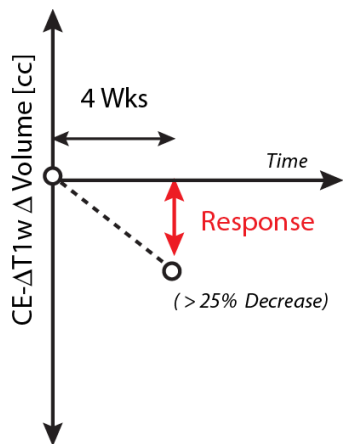


T1 Subtraction



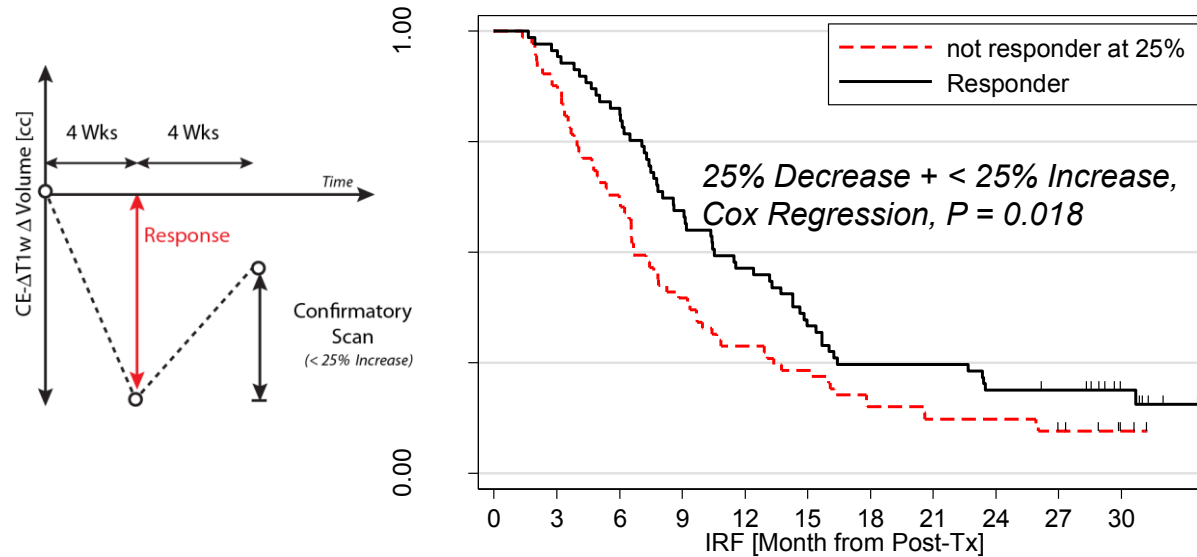
T1 Subtraction

- BRAIN Trial (Ellingson, *Radiology*, 2013)



T1 Subtraction

- BRAIN Trial (Ellingson, *Radiology*, 2013)
- Further improved by “confirmatory scan”



| | 0 | 3 | 6 | 9 | 12 | 15 | 18 | 21 | 24 | 27 | 30 |
|----------------|----|----|----|----|----|----|----|----|----|----|----|
| Number at risk | 73 | 64 | 45 | 29 | 21 | 17 | 11 | 9 | 9 | 6 | 2 |
| non-responder | 69 | 66 | 57 | 41 | 32 | 23 | 17 | 17 | 13 | 12 | 6 |
| responder | | | | | | | | | | | |

p=0.018 by log rank test

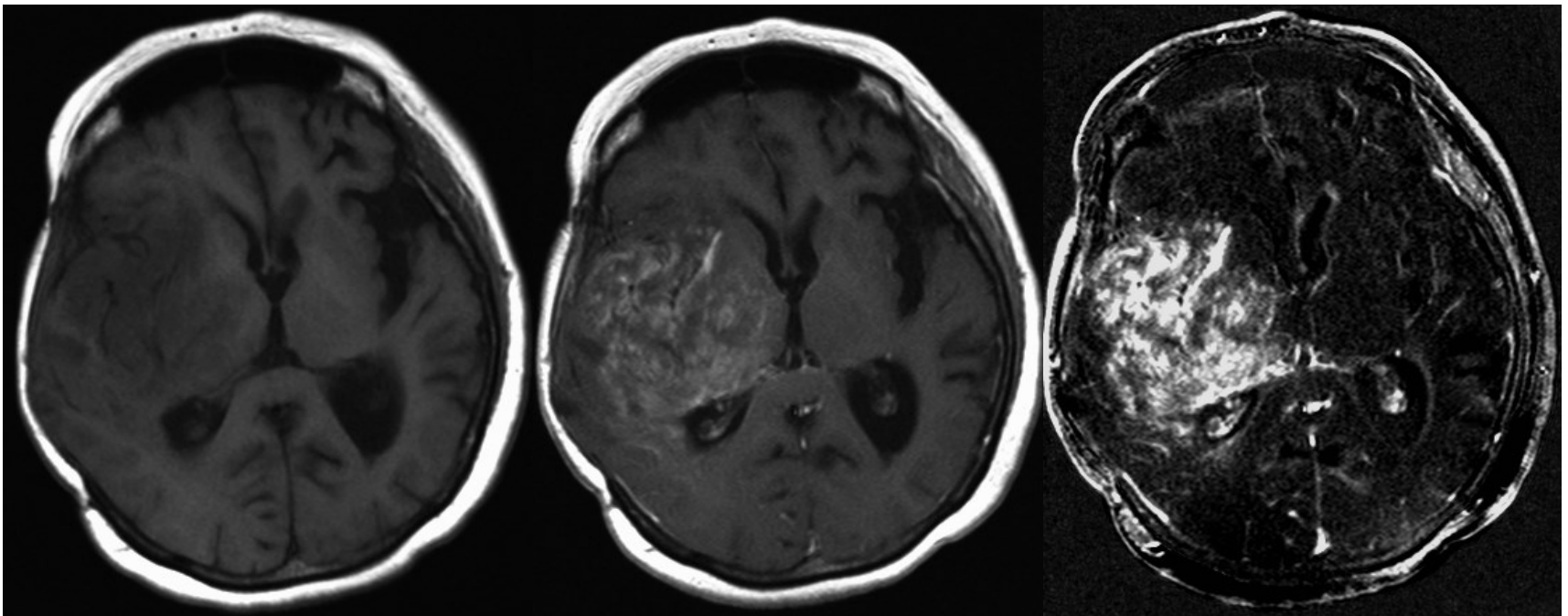
T1 Subtraction

- Phase III, Multicenter Trial of TMZ+RT+Bev vs. TMZ+RT in Newly Diagnosed GBM (AVAglio Trial)

Pre-Contrast T1

T1+C

T1 Subtraction



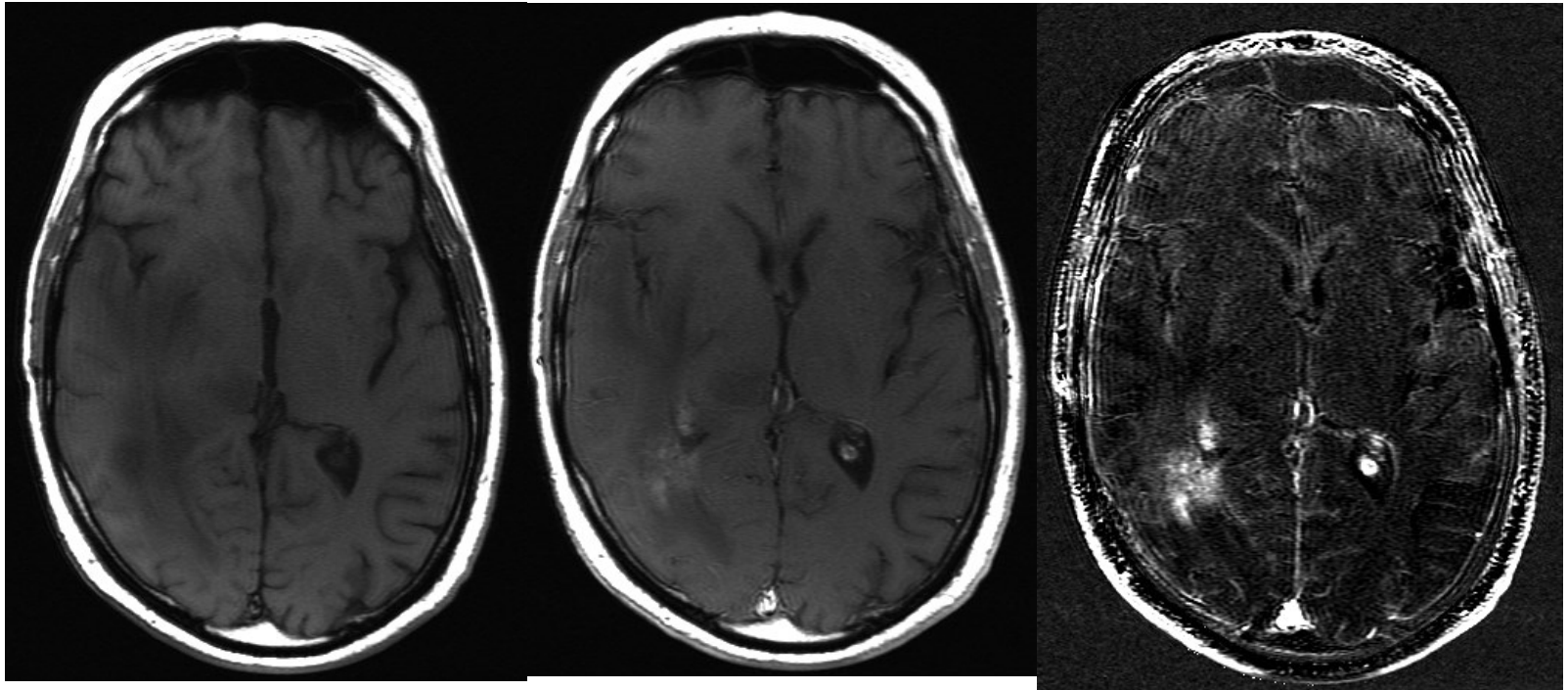
T1 Subtraction

- Phase III, Multicenter Trial of TMZ+RT+Bev vs. TMZ+RT in Newly Diagnosed GBM (AVAglio Trial)

Pre-Contrast T1

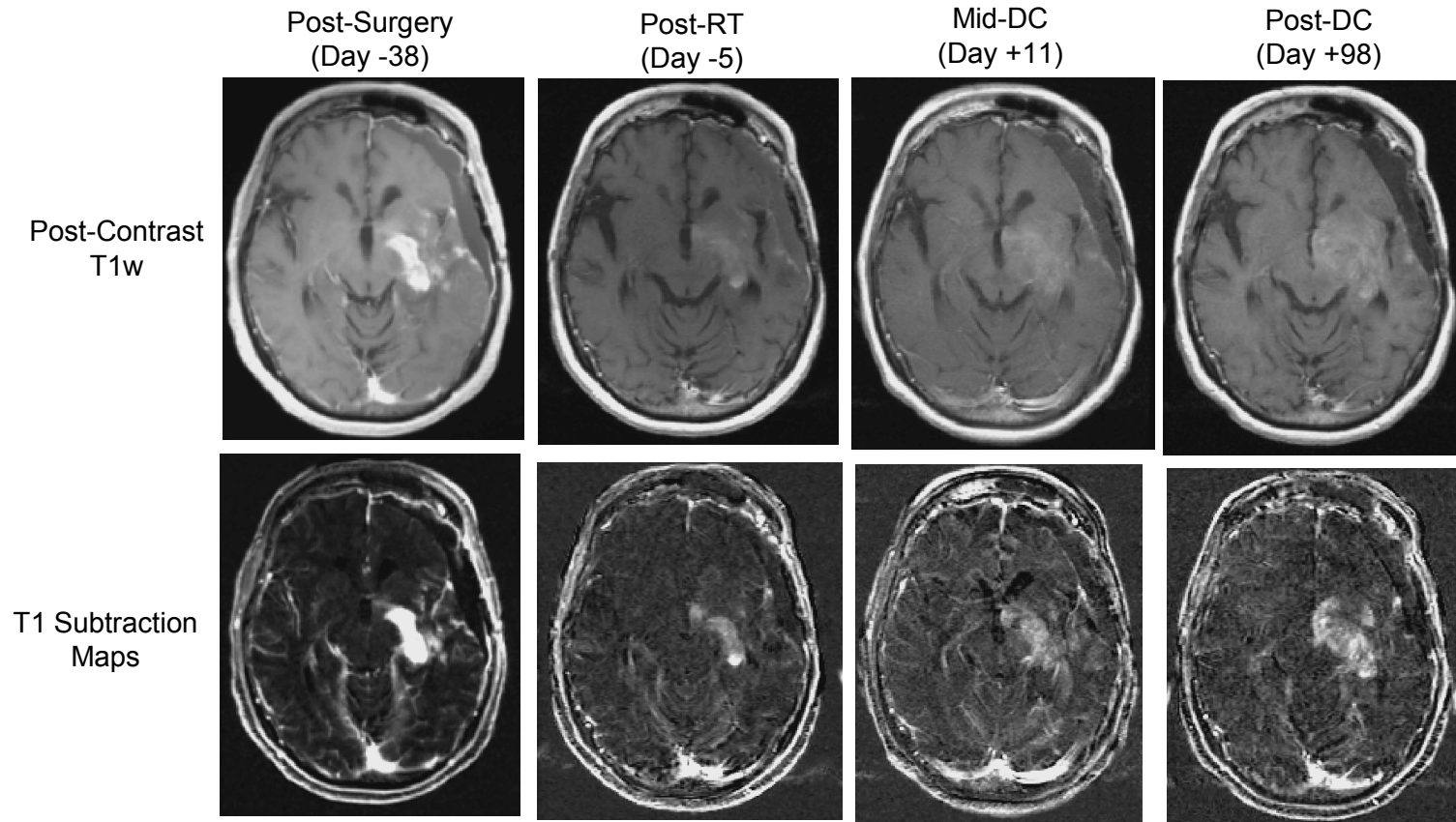
T1+C

T1 Subtraction



T1 Subtraction

- Phase III, Newly Diagnosed GBM with DC Vaccination



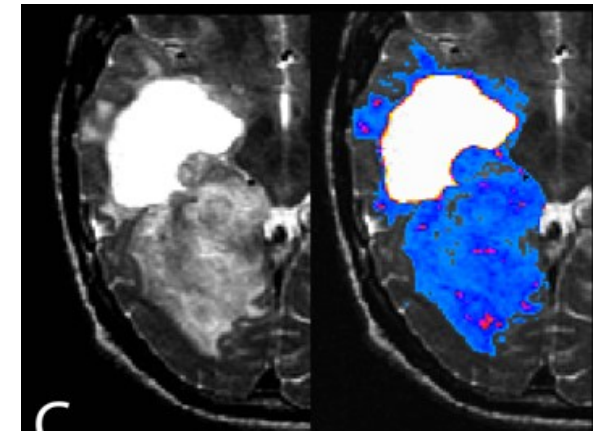
Minimum Standard 1.5T & 3T MRI Protocol

- 2D T2w TSE (Dual Echo PD/T2 TSE Recommended)
- Can be used for current RANO evaluations
- Available on all scanners as part of ADNI
- Part of ACR scanner accred.
- Allows for quantification of T2 within clinically feasible scan times

| | 3D T1w Pre ^b | Ax 2D FLAIR ^j | Ax 2D DWI | Contrast Injection ^a | Ax 2D T2w ^{h,i} | 3D T1w Post ^b | |
|--|--------------------------------------|--------------------------------|--|---------------------------------|---------------------------------|--------------------------------------|-----------------------|
| Sequence | MPRAGE ^{e,f} | TSE ^c | SS-EPI ^g | | | TSE ^c | MPRAGE ^{e,f} |
| Plane | Sagittal/ Axial | Axial | Axial | | | Axial | Sagittal/ Axial |
| Mode | 3D | 2D | 2D | | | 2D | 3D |
| TR [ms] | 2100 ^m | >6000 | >5000 | | | >2500 | 2100 ^m |
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| Frequency Direction | A/P | A/P | R/L | | A/P | A/P | |
| FOV | 256mm | 240mm | 240mm | | 240mm | 256mm | |
| Slice Thickness | ≤1.5mm | ≤4mm ^l | ≤4mm ^l | | ≤4mm ^l | ≤1.5mm | |
| Gap/Spacing | 0 | 0 | 0 | | 0 | 0 | |
| Diffusion Options ^p | | | $b = 0, 500, 1000 \text{ s/mm}^2$ ≥3 directions | | | | |
| Parallel Imaging | Up to 2x | Up to 2x | Up to 2x | | Up to 2x | Up to 2x | |
| Scan Time (Approx) [Benchmarked on 3T Skyra] | 5-10 min [5:49 for 1mm isotropic] | 4-8 min [3:22 for 2D FLAIR] | 2-4 min [1:22 for 3 direction DWI and 3 b-values] | | 4-8 min [5:10 for dual echo] | 5-10 min [5:49 for 1mm isotropic] | |

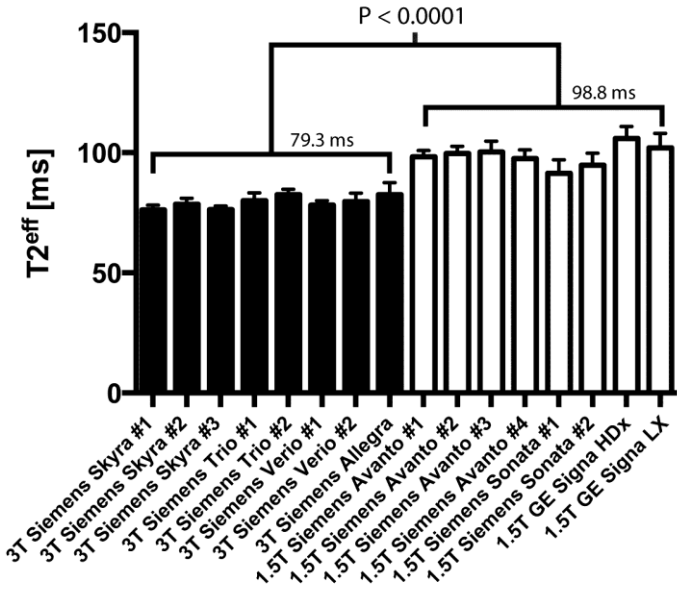
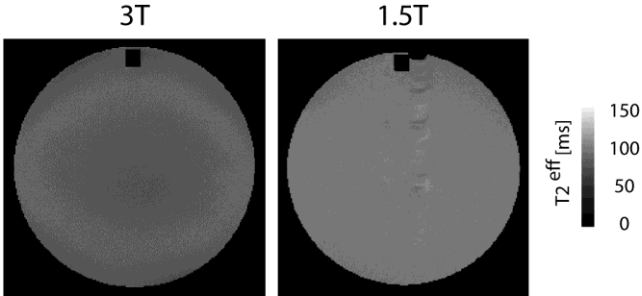
T2w

T2^{eff} Map



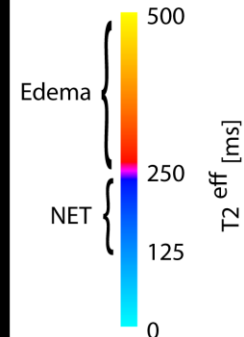
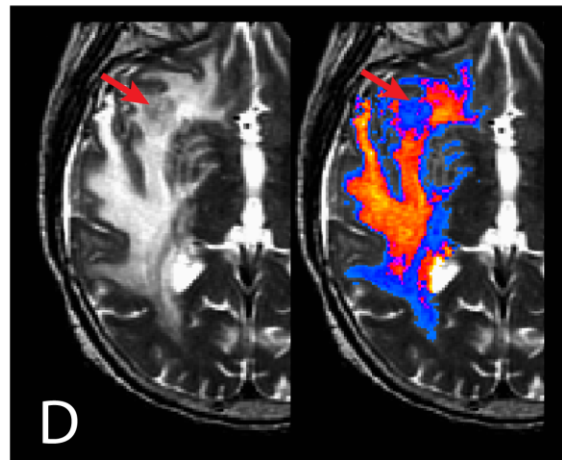
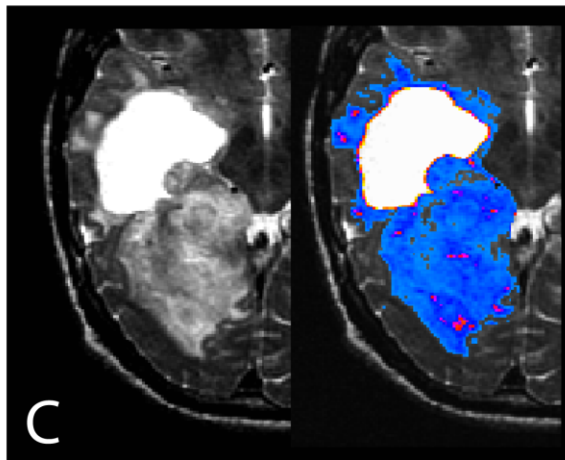
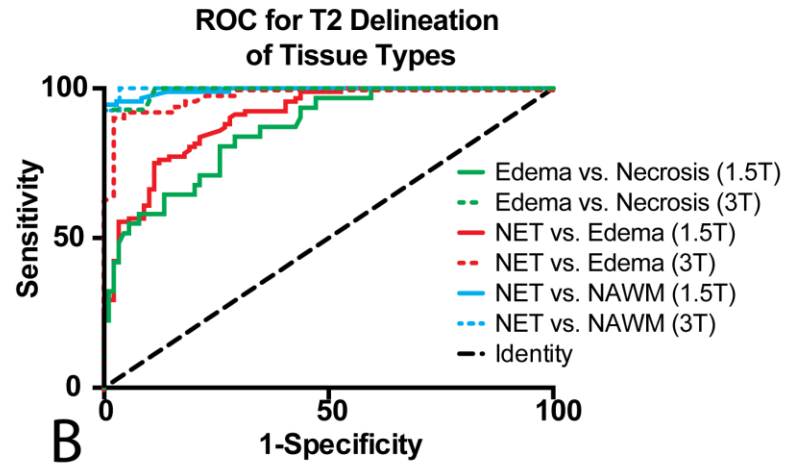
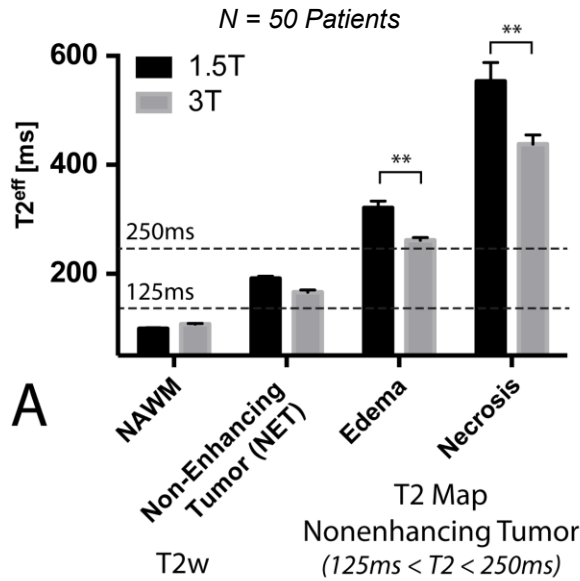
Dual Echo Turbo Spin Echo MRI

3-5% Variability Across Scanner Measurements of T_2^{eff}



Dual Echo Turbo Spin Echo MRI

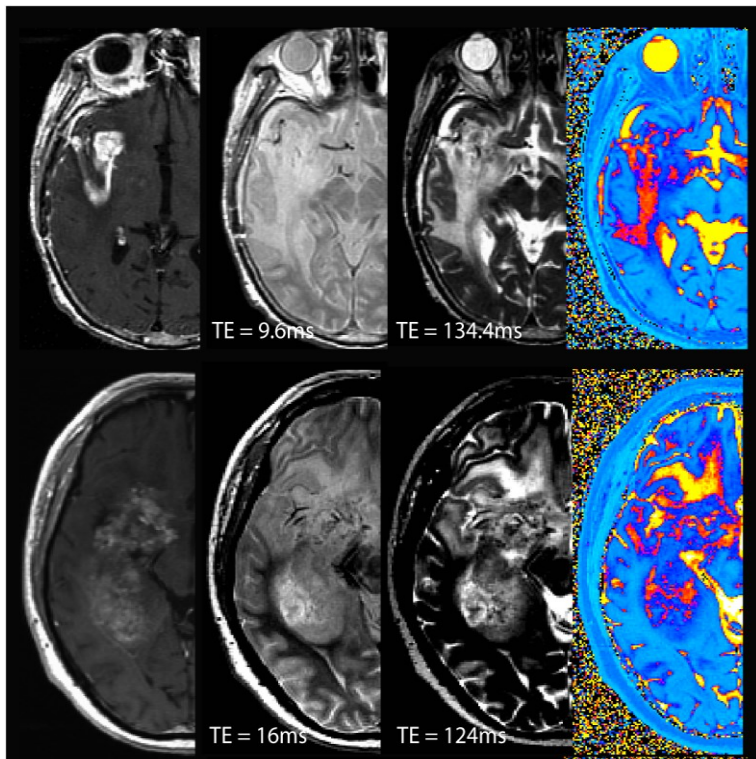
$125\text{ms} < T_2^{\text{eff}} < 250\text{ms}$ has 60-70% sensitivity and 80-90% specificity for containing NET



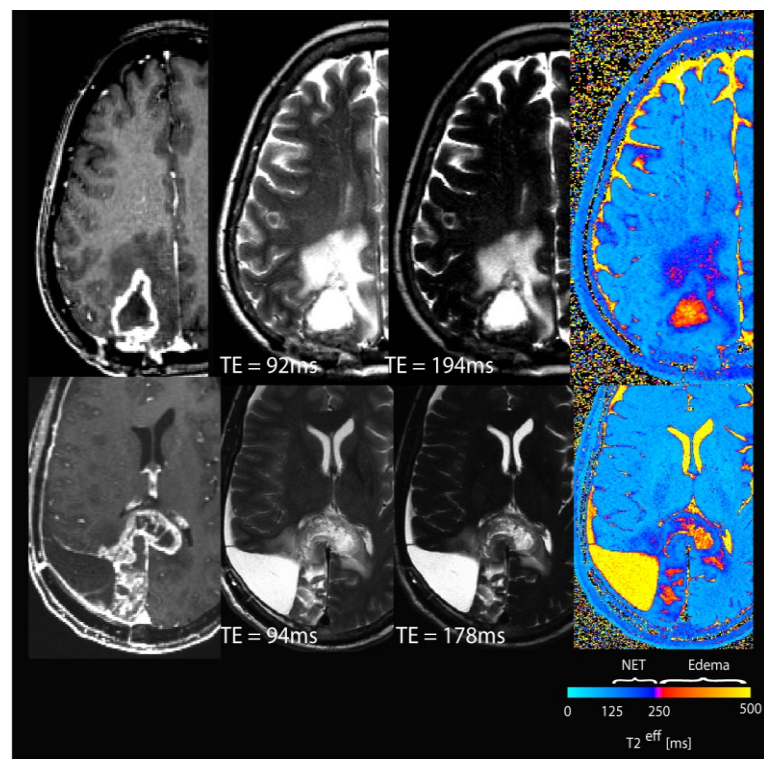
Dual Echo Turbo Spin Echo MRI

$125\text{ms} < T_2^{\text{eff}} < 250\text{ms}$ has 60-70% sensitivity and 80-90% specificity for containing NET

Post-Contrast T1w Dual Echo T2w
(Echo #1) (Echo #2) T2 Map

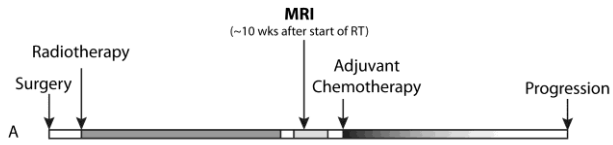


Post-Contrast T1w Dual Echo T2w
(Echo #1) (Echo #2) T2 Map

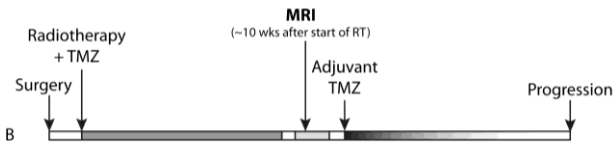
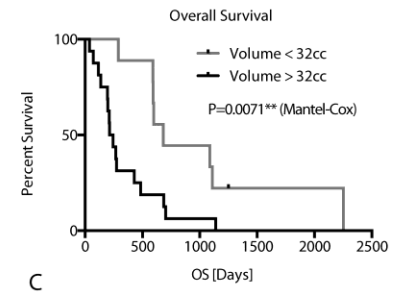
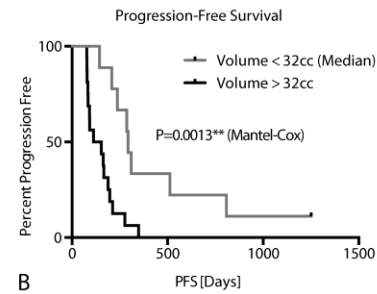
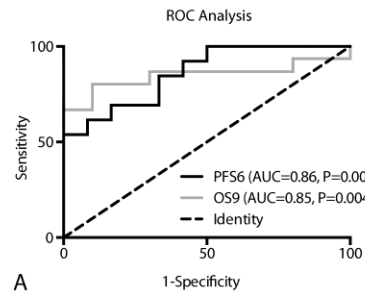


Dual Echo Turbo Spin Echo MRI

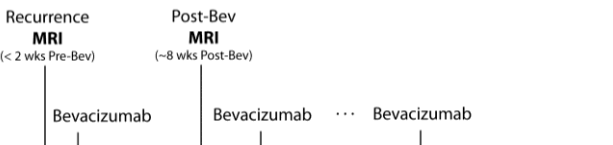
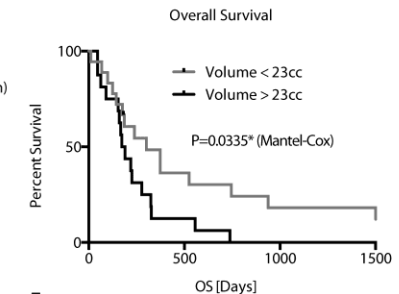
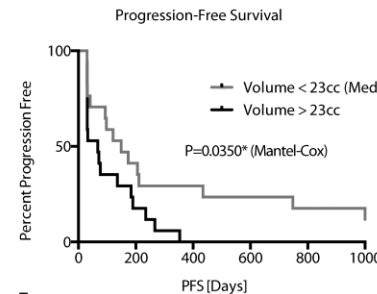
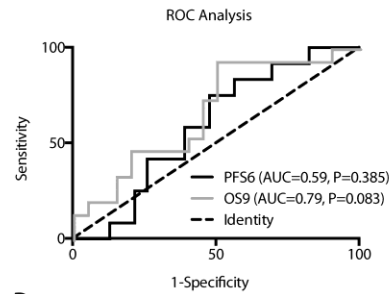
T_2^{eff} –defined NET volume is predictive of PFS and OS After Radiation Therapy (new GBM), Radiation Therapy and Concurrent Temozolomide (new GBM), and Bevacizumab (recurrent GBM)



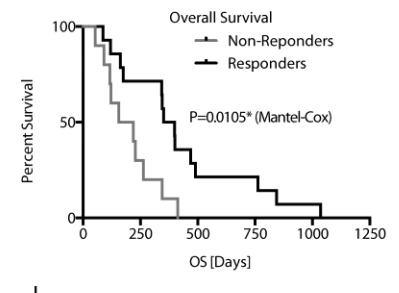
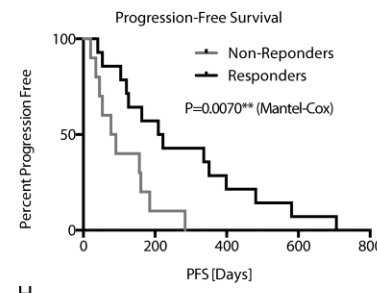
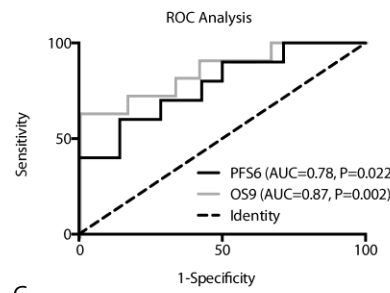
RADIOTHERAPY IN NEW GBM



RADIOTHERAPY + CONCURRENT TEMOZOLOMIDE IN NEW GBM



BEVACIZUMAB IN RECURRENT GBM



Minimum Standard 1.5T & 3T MRI Protocol

- *Timing of Contrast & T2*
- *Timing between pre- and post-contrast T1w images is critical to ensure extravasation*

| | 3D T1w Pre ^b | Ax 2D FLAIR ^j | Ax 2D DWI | Contrast Injection ^a | Ax 2D T2w ^{h,i} | 3D T1w Post ^b | |
|--|--------------------------------------|--------------------------------|--|---------------------------------|---------------------------------|--------------------------------------|-----------------------|
| Sequence | MPRAGE ^{e,f} | TSE ^c | SS-EPI ^g | | | TSE ^c | MPRAGE ^{e,f} |
| Plane | Sagittal/ Axial | Axial | Axial | | | Axial | Sagittal/ Axial |
| Mode | 3D | 2D | 2D | | | 2D | 3D |
| TR [ms] | 2100 ^m | >6000 | >5000 | | | >2500 | 2100 ^m |
| TE [ms] | Min | 100-140 | Min | | | 80-120 | Min |
| TI [ms] | 1100 ⁿ | 2000-2500 ^k | | | | | 1100 ⁿ |
| Flip Angle [Degrees] | 10-15 | 90/≥160 | 90/180 | | | 90/≥160 | 10-15 |
| Frequency | ≥172 | ≥256 | ≥128 | | | ≥256 | ≥172 |
| Phase | ≥172 | ≥256 | ≥128 | | | ≥256 | ≥172 |
| NEX | ≥1 | ≥1 | ≥1 | | | ≥1 | ≥1 |
| Frequency Direction | A/P | A/P | R/L | | | A/P | A/P |
| FOV | 256mm | 240mm | 240mm | | | 240mm | 256mm |
| Slice Thickness | ≤1.5mm | ≤4mm ^l | ≤4mm ^l | | | ≤4mm ^l | ≤1.5mm |
| Gap/Spacing | 0 | 0 | 0 | | | 0 | 0 |
| Diffusion Options ^p | | | <i>b</i> = 0, 500, 1000 s/mm ² ≥3 directions | | | | |
| Parallel Imaging | Up to 2x | Up to 2x | Up to 2x | | Up to 2x | Up to 2x | |
| Scan Time (Approx) [Benchmarked on 3T Skyra] | 5-10 min [5:49 for 1mm isotropic] | 4-8 min [3:22 for 2D FLAIR] | 2-4 min [1:22 for 3 direction DWI and 3 b-values] | | 4-8 min [5:10 for dual echo] | 5-10 min [5:49 for 1mm isotropic] | |

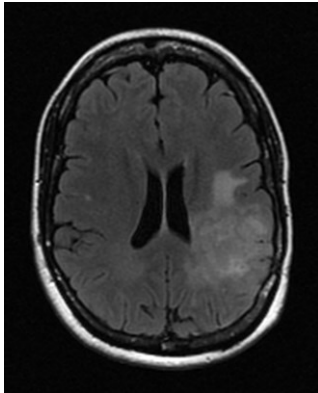
Minimum Standard 1.5T & 3T MRI Protocol

- *T2w FLAIR*
- *Used for RANO evaluations*
- *Similar to ACRIN, EORTC, and Alliance Protocols*
- *3D FLAIR is optional*

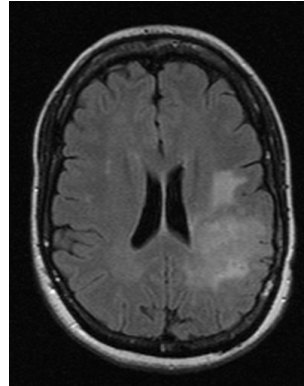
| | 3D T1w Pre ^b | Ax 2D FLAIR ^j | Ax 2D DWI | Contrast Injection ^a | Ax 2D T2w ^{h,i} | 3D T1w Post ^b | |
|--|--------------------------------------|--------------------------------|--|---------------------------------|---------------------------------|--------------------------------------|-----------------------|
| Sequence | MPRAGE ^{e,f} | TSE ^c | SS-EPI ^g | | | TSE ^c | MPRAGE ^{e,f} |
| Plane | Sagittal/ Axial | Axial | Axial | | | Axial | Sagittal/ Axial |
| Mode | 3D | 2D | 2D | | | 2D | 3D |
| TR [ms] | 2100 ^m | >6000 | >5000 | | | >2500 | 2100 ^m |
| TE [ms] | Min | 100-140 | Min | | | 80-120 | Min |
| TI [ms] | 1100 ⁿ | 2000-2500 ^k | | | | | 1100 ⁿ |
| Flip Angle [Degrees] | 10-15 | 90/≥160 | 90/180 | | | 90/≥160 | 10-15 |
| Frequency | ≥172 | ≥256 | ≥128 | | | ≥256 | ≥172 |
| Phase | ≥172 | ≥256 | ≥128 | | | ≥256 | ≥172 |
| NEX | ≥1 | ≥1 | ≥1 | | | ≥1 | ≥1 |
| Frequency Direction | A/P | A/P | R/L | | A/P | A/P | |
| FOV | 256mm | 240mm | 240mm | | 240mm | 256mm | |
| Slice Thickness | ≤1.5mm | ≤4mm ^l | ≤4mm ^l | | ≤4mm ^l | ≤1.5mm | |
| Gap/Spacing | 0 | 0 | 0 | | 0 | 0 | |
| Diffusion Options ^p | | | <i>b</i> = 0, 500, 1000 s/mm ² ≥3 directions | | | | |
| Parallel Imaging | Up to 2x | Up to 2x | Up to 2x | | Up to 2x | Up to 2x | |
| Scan Time (Approx) [Benchmarked on 3T Skyra] | 5-10 min [5:49 for 1mm isotropic] | 4-8 min [3:22 for 2D FLAIR] | 2-4 min [1:22 for 3 direction DWI and 3 b-values] | | 4-8 min [5:10 for dual echo] | 5-10 min [5:49 for 1mm isotropic] | |

FLAIR and T2 TSE @ 3mm for 1.5T & 3T

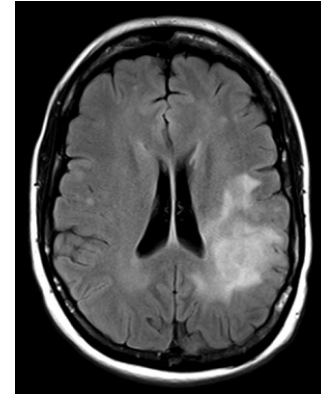
GE 1.5T Signa
3mm no skip



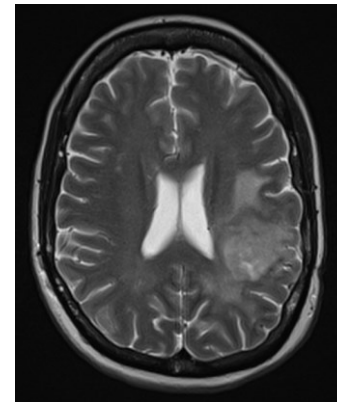
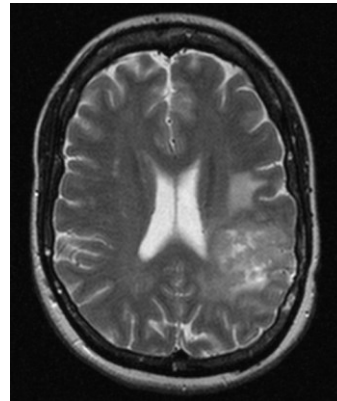
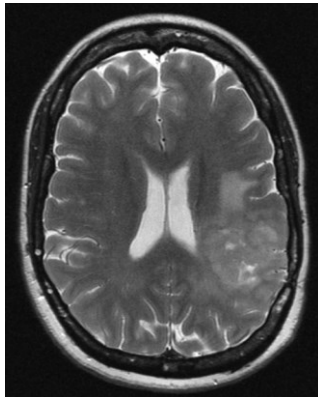
Siemens 1.5T Sonata
3mm no skip



Siemens 3T Trio
3mm no skip



FLAIR



T2w

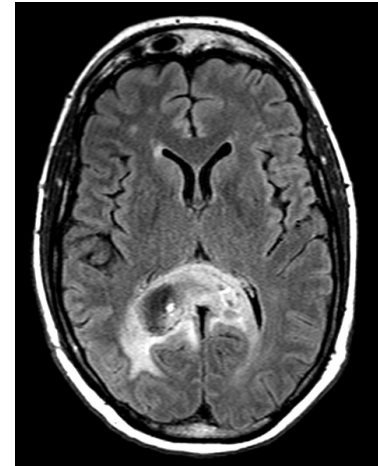
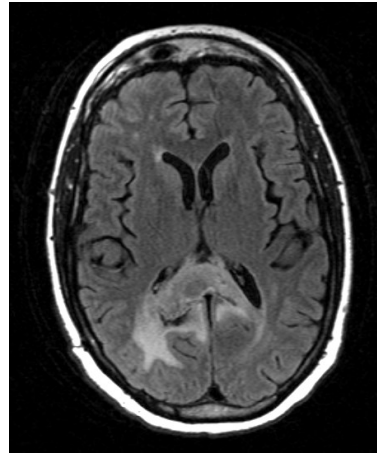
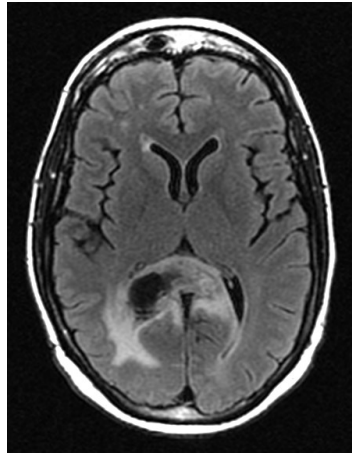
FLAIR and T2 TSE @ 3mm for 1.5T & 3T

GE 1.5T Signa
3mm no skip

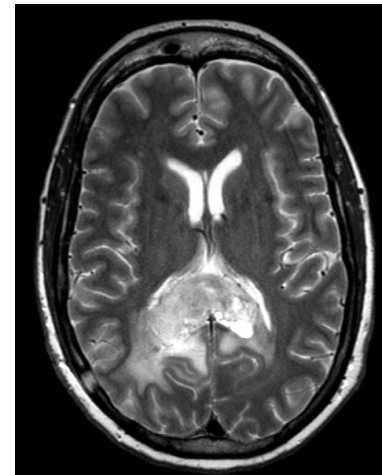
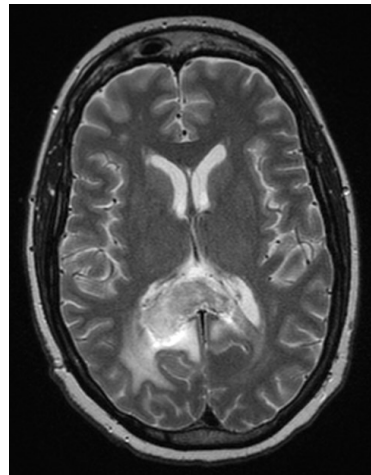
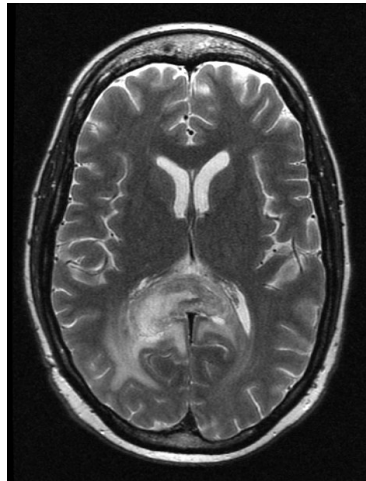
Siemens 1.5T Avanto
3mm no skip

Siemens 3T Trio
3mm no skip

FLAIR



T2w



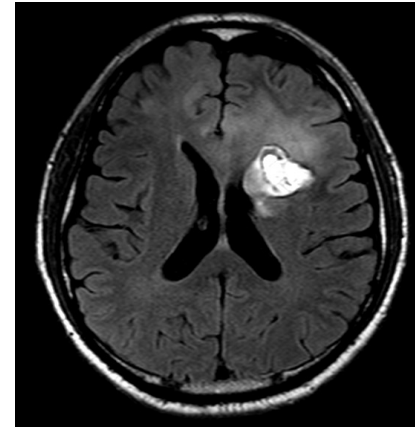
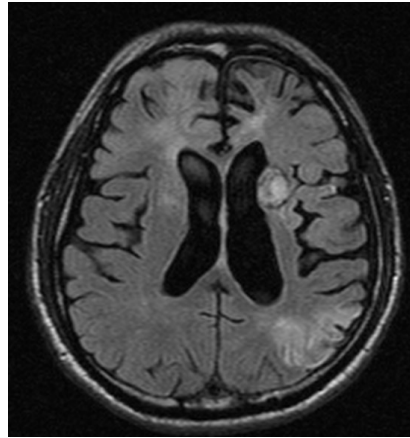
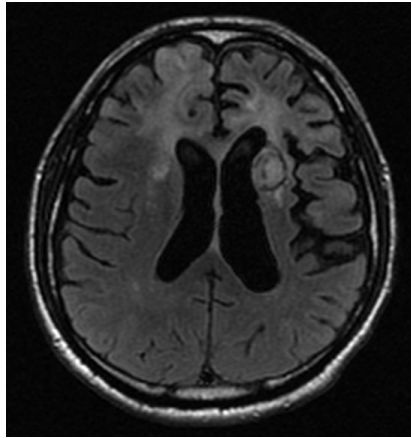
FLAIR and T2 TSE @ 3mm for 1.5T & 3T

GE 1.5T Signa
3mm no skip

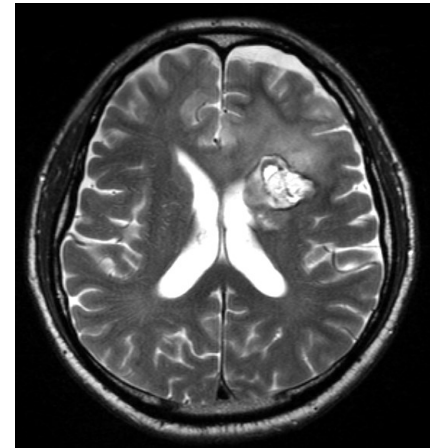
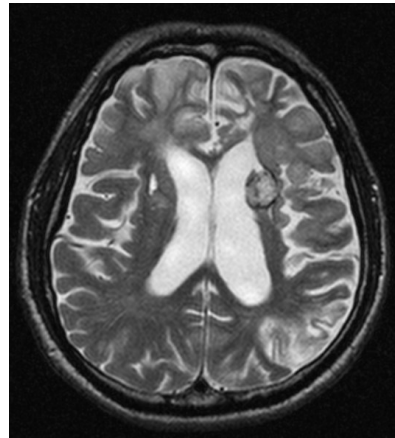
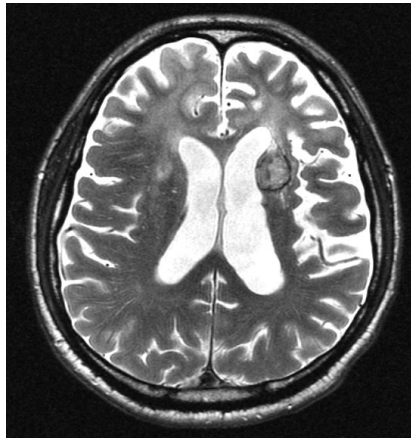
Siemens 1.5T Sonata
3mm no skip

Siemens 3T Trio
3mm no skip

FLAIR



T2w



Minimum Standard 1.5T & 3T MRI Protocol

- *Diffusion Weighted Imaging*
- *Uses recommendations by the ISMRM/NCI Diffusion Consensus Mtg. 2008*
- *3 b-values (0, 500, 1000 s/mm²) are recommended*

| | 3D T1w Pre ^b | Ax 2D FLAIR ^j | Ax 2D DWI | Contrast Injection ^a | Ax 2D T2w ^{h,i} | 3D T1w Post ^b |
|--|-----------------------------------|-----------------------------|--|---------------------------------|-----------------------------------|--------------------------|
| Sequence | MPRAGE ^{e,f} | TSE ^c | SS-EPI ^g | | TSE ^c | MPRAGE ^{e,f} |
| Plane | Sagittal/ Axial | Axial | Axial | | Axial | Sagittal/ Axial |
| Mode | 3D | 2D | 2D | | 2D | 3D |
| TR [ms] | 2100 ^m | >6000 | >5000 | | >2500 | 2100 ^m |
| TE [ms] | Min | 100-140 | Min | | 80-120 | Min |
| TI [ms] | 1100 ⁿ | 2000-2500 ^k | | | | 1100 ⁿ |
| Flip Angle [Degrees] | 10-15 | 90/≥160 | 90/180 | | 90/≥160 | 10-15 |
| Frequency | ≥172 | ≥256 | ≥128 | | ≥256 | ≥172 |
| Phase | ≥172 | ≥256 | ≥128 | | ≥256 | ≥172 |
| NEX | ≥1 | ≥1 | ≥1 | ≥1 | ≥1 | |
| Frequency Direction | A/P | A/P | R/L | A/P | A/P | |
| FOV | 256mm | 240mm | 240mm | 240mm | 256mm | |
| Slice Thickness | ≤1.5mm | ≤4mm ^l | ≤4mm ^l | ≤4mm ^l | ≤1.5mm | |
| Gap/Spacing | 0 | 0 | 0 | 0 | 0 | |
| Diffusion Options ^p | | | <i>b = 0, 500, 1000 s/mm² ≥3 directions</i> | | | |
| Parallel Imaging | Up to 2x | Up to 2x | Up to 2x | Up to 2x | Up to 2x | |
| Scan Time (Approx) [Benchmarked on 3T Skyra] | 5-10 min [5:49 for 1mm isotropic] | 4-8 min [3:22 for 2D FLAIR] | 2-4 min [1:22 for 3 direction DWI and 3 b-values] | 4-8 min [5:10 for dual echo] | 5-10 min [5:49 for 1mm isotropic] | |

Minimum Standard 1.5T & 3T MRI Protocol

^a 0.1 mmol/kg dose injection with a Gadolinium chelated contrast agent. Use of a power injector is desirable at an injection rate of 3-5cc/sec.

^b Post-contrast 3D T1-weighted images should be collected with equivalent parameters to pre-contrast 3D T1-weighted images

^c TSE = turbo spin echo (Siemens & Philips) is equivalent to FSE (fast spin echo; GE, Hitachi, Toshiba)

^d FL2D = two-dimensional fast low angle shot (FLASH; Siemens) is equivalent to the spoil gradient recalled echo (SPGR; GE) or T1- fast field echo (FFE; Philips), fast field echo (FastFE; Toshiba), or the radiofrequency spoiled steady state acquisition rewind gradient echo (RSSG; Hitachi). A fast gradient echo sequence without inversion preparation is desired.

^e MPRAGE = magnetization prepared rapid gradient-echo (Siemens & Hitachi) is equivalent to the inversion recovery SPGR (IR-SPGR or Fast SPGR with inversion activated or BRAVO; GE), 3D turbo field echo (TFE; Philips), or 3D fast field echo (3D Fast FE; Toshiba).

^f A 3D acquisition without inversion preparation will result in different contrast compared with MPRAGE or another IR-prepped 3D T1-weighted sequences and therefore should be avoided.

^g In the event of significant patient motion, a radial acquisition scheme may be used (e.g. BLADE [Siemens], PROPELLER [GE], MultiVane [Philips], RADAR [Hitachi], or JET [Toshiba]); however, this acquisition scheme can cause significant differences in ADC quantification and therefore should be used only if EPI is not an option. Further, this type of acquisition takes considerable more time.

^h Dual echo PD/T2 TSE is optional for possible quantification of tissue T2.

ⁱ Advanced sequences can be substituted into this time slot, so long as 3D post-contrast T1-weighted images are collected between 4 and 8 min after contrast injection.

^j 3D FLAIR is an optional alternative to 2D FLAIR, with sequence parameters as follows per EORTC guidelines: 3D TSE/FSE acquisition; TE=90-140ms; TR=6000-10000ms; TI=2000-2500ms (chosen based on vendor recommendations for optimized protocol and field strength); GRAPPA \leq 2; Fat Saturation; Slice thickness \leq 1.5mm; Orientation Sagittal or Axial; FOV \leq 250 mm x 250 mm; Matrix \geq 244x244.

^k Choice of TI should be chosen based on the magnetic field strength of the system (e.g. TI \approx 2000ms for 1.5T and TI \approx 2500ms for 3T).

^l In order to ensure comparable SNR older 1.5T MR systems can use contiguous (no interslice gap) images with 5mm slice thickness or increase NEX for slice thickness \leq 4mm.

^m For Siemens and Hitachi scanners. GE, Philips, and Toshiba scanners should use a TI = 400-450ms for similar contrast.

ⁿ For Siemens and Hitachi scanners. GE, Philips, and Toshiba scanners should use a TR = 5-15ms for similar contrast.

^p Older model MR scanners that are not capable of >2 *b*-values should use *b* = 0 and 1000 s/mm².

Acronyms:

Ax = Axial; ADC = apparent diffusion coefficient. FLAIR = fluid attenuated inversion recovery; DWI = diffusion-weighted imaging; 3D = three dimensional; TSE = turbo spin echo; EPI = echo planar imaging; SS-EPI = single-shot echo planar imaging; GE-EPI = gradient echo echo planar imaging; 2DFL = two-dimensional FLASH (fast low angle shot) gradient recalled echo; MPRAGE = magnetization prepared rapid gradient-echo; A/P = anterior to posterior; R/L = right to left; NEX = number of excitations or averages; FOV = field of view; TE = echo time; TR = repetition time; TI = inversion time; PD = proton density; DSC = dynamic susceptibility contrast

Minimum Standard 1.5T & 3T MRI Protocol

^a 0.1 mmol/kg dose injection with a Gadolinium chelated contrast agent. Use of a power injector is desirable at an injection rate of 3-5cc/sec.

^b Post-contrast 3D T1-weighted images should be collected with equivalent parameters to pre-contrast 3D T1-weighted images

^c TSE = turbo spin echo (Siemens & Philips) is equivalent to FSE (fast spin echo; GE, Hitachi, Toshiba)

^d FL2D = two-dimensional fast low angle shot (FLASH; Siemens) is equivalent to the spoil gradient recalled echo (SPGR; GE) or T1- fast field echo (FFE; Philips), fast field echo (FastFE; Toshiba), or the radiofrequency spoiled steady state acquisition rewind gradient echo (RSSG; Hitachi). A fast gradient echo sequence without inversion preparation is desired.

^e MPRAGE = magnetization prepared rapid gradient-echo (Siemens & Hitachi) is equivalent to the inversion recovery SPGR (IR-SPGR or Fast SPGR with inversion activated or BRAVO; GE), 3D turbo field echo (TFE; Philips), or 3D fast field echo (3D Fast FE; Toshiba).

^f A 3D acquisition without inversion preparation will result in different contrast compared with MPRAGE or another IR-prepped 3D T1-weighted sequences and therefore should be avoided.

^g In the event of significant patient motion, a radial acquisition scheme may be used (e.g. BLADE [Siemens], PROPELLER [GE], MultiVane [Philips], RADAR [Hitachi], or JET [Toshiba]); however, this acquisition scheme can cause significant differences in ADC quantification and therefore should be used only if EPI is not an option. Further, this type of acquisition takes considerable more time.

^h Dual echo PD/T2 TSE is optional for possible quantification of tissue T2.

ⁱ Advanced sequences can be substituted into this time slot, so long as 3D post-contrast T1-weighted images are collected between 4 and 8 min after contrast injection.

^j 3D FLAIR is an optional alternative to 2D FLAIR, with sequence parameters as follows per EORTC guidelines: 3D TSE/FSE acquisition; TE=90-140ms; TR=6000-10000ms; TI=2000-2500ms (chosen based on vendor recommendations for optimized protocol and field strength); GRAPPA \leq 2; Fat Saturation; Slice thickness \leq 1.5mm; Orientation Sagittal or Axial; FOV \leq 250 mm x 250 mm; Matrix \geq 244x244.

^k Choice of TI should be chosen based on the magnetic field strength of the system (e.g. TI \approx 2000ms for 1.5T and TI \approx 2500ms for 3T).

^l In order to ensure comparable SNR older 1.5T MR systems can use contiguous (no interslice gap) images with 5mm slice thickness or increase NEX for slice thickness \leq 4mm.

^m For Siemens and Hitachi scanners. GE, Philips, and Toshiba scanners should use a TI = 400-450ms for similar contrast.

ⁿ For Siemens and Hitachi scanners. GE, Philips, and Toshiba scanners should use a TR = 5-15ms for similar contrast.

^p Older model MR scanners that are not capable of >2 *b*-values should use *b* = 0 and 1000 s/mm².

Acronyms:

Ax = Axial; ADC = apparent diffusion coefficient. FLAIR = fluid attenuated inversion recovery; DWI = diffusion-weighted imaging; 3D = three dimensional; TSE = turbo spin echo; EPI = echo planar imaging; SS-EPI = single-shot echo planar imaging; GE-EPI = gradient echo echo planar imaging; 2DFL = two-dimensional FLASH (fast low angle shot) gradient recalled echo; MPRAGE = magnetization prepared rapid gradient-echo; A/P = anterior to posterior; R/L = right to left; NEX = number of excitations or averages; FOV = field of view; TE = echo time; TR = repetition time; TI = inversion time; PD = proton density; DSC = dynamic susceptibility contrast

Recommended 3T Protocol

| | 3D T1w Pre | Ax 2D FLAIR | Ax 2D DWI | Contrast Injection ^a | Ax 2D T2w | 3D T1w Post ^b | |
|----------------------------|-----------------------|------------------|--|---------------------------------|-----------|--------------------------|-----------------------|
| Sequence | MPRAGE ^{d,e} | TSE ^c | EPI ^f | | | TSE ^c | MPRAGE ^{d,e} |
| Plane | Sagittal/Axial | Axial | Axial | | | Axial | Axial/Sagittal |
| Mode | 3D | 2D | 2D | | | 2D | 3D |
| TR [ms] | 2100 ^g | >6000 | >5000 | | | >2500 | 2100 ^g |
| TE [ms] | Min | 100-140 | Min | | | 80-120 | Min |
| TI [ms] | 1100 ^h | 2500 | | | | | 1100 ^h |
| Flip Angle | 10-15 | 90/≥160 | 90/180 | | | 90/≥160 | 10-15 |
| Frequency | 256 | ≥256 | 128 | | | ≥256 | 256 |
| Phase | 256 | ≥256 | 128 | | | ≥256 | 256 |
| NEX | ≥1 | ≥1 | ≥1 | | ≥1 | ≥1 | |
| Frequency Direction | A/P | A/P | R/L | | A/P | A/P | |
| FOV | | 240mm | 240mm | | 240mm | 256mm | |
| Slice Thickness | 1mm | 3mm | 3mm | | 3mm | 1mm | |
| Gap/Spacing | 0 | 0 | 0 | | 0 | 0 | |
| Diffusion Options | | | <i>b</i> = 0, 500, and 1000 s/mm ² ≥3 directions | | | | |
| Parallel Imaging | Up to 2x | Up to 2x | Up to 2x | | Up to 2x | Up to 2x | |
| Scan Time (Approx) | 5-8 min | 4-5 min | 3-5 min | | 3-5 min | 5-8 min | |

^a 0.1 mmol/kg or up to 20cc (single, full dose) of MR contrast.

^b Post-contrast 3D axial T1-weighted images should be collected with identical parameters to pre-contrast 3D axial T1-weighted images

^c TSE = turbo spin echo (Siemens & Philips) is equivalent to FSE (fast spin echo; GE, Hitachi, Toshiba)

^d MPRAGE = magnetization prepared rapid gradient-echo (Siemens & Hitachi) is equivalent to the inversion recovery SPGR (IR-SPGR or Fast SPGR with inversion activated; GE), 3D turbo field echo (TFE; Philips), or 3D fast field echo (3D Fast FE; Toshiba).

^e A 3D acquisition without inversion preparation will result in different contrast compared with MPRAGE or another IR-prepped 3D T1-weighted sequences and therefore should be avoided.

^f In the event of significant patient motion, a radial acquisition scheme may be used (e.g. BLADE [Siemens], PROPELLER [GE], MultiVane [Philips], RADAR [Hitachi], or JET [Toshiba]); however, this acquisition scheme is can cause significant differences in ADC quantification and therefore should be used only if EPI is not an option.

^g For Siemens and Hitachi scanners. GE, Philips, and Toshiba scanners should use a TR = 5-15ms for similar contrast.

^h For Siemens and Hitachi scanners. GE, Philips, and Toshiba scanners should use a TI = 400-450ms for similar contrast.

Acronyms:

Ax = Axial; ADC = apparent diffusion coefficient. FLAIR = fluid attenuated inversion recovery; DWI = diffusion-weighted imaging; 3D = three dimensional; TSE = turbo spin echo; EPI = echo planar imaging; MPRAGE = magnetization prepared rapid gradient-echo; A/P = anterior to posterior; R/L = right to left; NEX = number of excitations or averages; FOV = field of view

Recommended 1.5T Protocol

| | 3D T1w Pre | Ax 2D FLAIR | Ax 2D DWI | Contrast Injection ^a | Ax 2D T2w | 3D T1w Post ^b | |
|--------------------------------------|-----------------------|------------------|---|---------------------------------|------------------|--------------------------|-----------------------|
| Sequence | MPRAGE ^{d,e} | TSE ^c | EPI ^f | | | TSE ^c | MPRAGE ^{d,e} |
| Plane | Sagittal/Axial | Axial | Axial | | | Axial | Sagittal/Axial |
| Mode | 3D | 2D | 2D | | | 2D | 3D |
| TR [ms] | 2100 ^g | >6000 | >5000 | | | >3500 | 2100 ^g |
| TE [ms] | Min | 100-140 | Min | | | 100-120 | Min |
| TI [ms] | 1100 ^h | 2200 | | | | | 1100 ^h |
| Flip Angle | 10-15 | 90/≥160 | 90/180 | | | 90/180 | 10-15 |
| Frequency | ≥172 | ≥256 | 128 | | | ≥256 | ≥172 |
| Phase | ≥172 | ≥256 | 128 | | | ≥256 | ≥172 |
| NEX | ≥1 | ≥1 | ≥1 | | | ≥1 | ≥1 |
| Frequency Direction | A/P | A/P | R/L | | | A/P | A/P |
| FOV | 256mm | 240mm | 240mm | | | 240mm | 256mm |
| Slice Thickness | ≤1.5mm | ≤4mm | ≤4mm | | | ≤4mm | ≤1.5mm |
| Gap/Spacing | 0 | 0 | 0 | | | 0 | 0 |
| Diffusion Optionsⁱ | | | $b = 0, 500, \text{ and } 1000 \text{ s/mm}^2$ ≥3 directions | | | | |
| Parallel Imaging | Yes-If Available | Yes-If Available | Yes-If Available | | Yes-If Available | Yes-If Available | |
| Scan Time (Approx) | 5-8 min | 4-5 min | 3-5 min | | 3-5 min | 5-8 min | |

^a 0.1 mmol/kg or up to 20cc (single, full dose) of MR contrast.

^b Post-contrast 2D axial T1-weighted images should be collected with identical parameters to pre-contrast 2D axial T1-weighted images

^c TSE = turbo spin echo (Siemens & Philips) is equivalent to FSE (fast spin echo; GE, Hitachi, Toshiba)

^d MPRAGE = magnetization prepared rapid gradient-echo (Siemens & Hitachi) is equivalent to the inversion recovery SPGR (IR-SPGR or Fast SPGR with inversion activated; GE), 3D turbo field echo (TFE; Philips), or 3D fast field echo (3D Fast FE; Toshiba).

^e A 3D acquisition without inversion preparation will result in different contrast compared with MPRAGE or another IR-prepped 3D T1-weighted sequences and therefore should be avoided.

^f In the event of significant patient motion, a radial acquisition scheme may be used (e.g. BLADE [Siemens], PROPELLER [GE], MultiVane [Philips], RADAR [Hitachi], or JET [Toshiba]); however, this acquisition scheme is can cause significant differences in ADC quantification and therefore should be used only if EPI is not an option.

^g For Siemens and Hitachi scanners. GE, Philips, and Toshiba scanners should use a TR = 5-15ms for similar contrast.

^h For Siemens and Hitachi scanners. GE, Philips, and Toshiba scanners should use a TI = 400-450ms for similar contrast.

ⁱ Older model MR scanners that are not capable of >2 b -values should use $b = 0$ and 1000 s/mm^2 .

Examples of Compatible Protocols

Standard Protocol + DCE

| | 3D T1w Pre ^b | Ax 2D FLAIR ⁱ | Ax 2D DWI | Ax 2D T2w ^{h,i} | T1 Map | DCE ^a | 3D T1w Post ^b |
|--|-----------------------------------|-----------------------------|---|------------------------------|------------------|--|-----------------------------------|
| Sequence | MPRAGE ^{e,f} | TSE ^c | SS-EPI ^g | TSE ^c | 3D-FLASH | 3D-FLASH | MPRAGE ^{e,f} |
| Plane | Sagittal/ Axial | Axial | Axial | Axial | Axial | Axial | Sagittal/ Axial |
| Mode | 3D | 2D | 2D | 2D | 3D | 2D | 3D |
| TR [ms] | 2100 ^m | >6000 | >5000 | >2500 | 5 | 5 | 2100 ^m |
| TE [ms] | Min | 100-140 | Min | 80-120 | Min | Min | Min |
| TI [ms] | 1100 ⁿ | 2000-2500 ^k | | | | | 1100 ⁿ |
| Flip Angle [Degrees] | 10-15 | 90/≥160 | 90/180 | 90/≥160 | 5/10/15 /30 | 15 | 10-15 |
| Frequency | ≥172 | ≥256 | ≥128 | ≥256 | 256 | 256 | ≥172 |
| Phase | ≥172 | ≥256 | ≥128 | ≥256 | 192 | 192 | ≥172 |
| NEX | ≥1 | ≥1 | ≥1 | ≥1 | 2 | NEX=1 (130 Repts) 6.5sec/rep (10 baseline points) | ≥1 |
| Frequency Direction | A/P | A/P | R/L | A/P | R/L | R/L | A/P |
| FOV | 256 | 240 | 240 | 240 | 240 | 240 | 256 |
| Slice Thickness | ≤1.5mm | ≤4mm ^l | ≤4mm ^l | ≤4mm ^l | 5mm | 5mm | ≤1.5mm |
| Gap/Spacing | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Diffusion Options ^p | | | <i>b</i> = 0, 500, 1000 s/mm ² ≥3 directions | | | | |
| Parallel Imaging | Up to 2x | Up to 2x | Up to 2x | Up to 2x | Yes-If Available | Yes-If Available | Up to 2x |
| Scan Time (Approx) [Benchmarked on 3T Skyra] | 5-10 min [5:49 for 1mm isotropic] | 4-8 min [3:22 for 2D FLAIR] | 2-4 min [1:22 for 3 direction DWI and 3 b-values] | 4-8 min [5:10 for dual echo] | < 1 min ea | 10 min | 5-10 min [5:49 for 1mm isotropic] |

Examples of Compatible Protocols

Standard Protocol + DTI + DSC Perfusion

| | 3D T1 Pre ^b | Ax 2D FLAIR | Ax DTI | <i>Pre-Load Contrast Injection^b</i> | Dual Echo Ax PD/T2 | DSC Perfusion ⁱ | 3D T1 Post ^b |
|----------------------|------------------------|------------------|--|--|----------------------|---|-------------------------|
| Sequence | MPRAGE ^{e,f} | TSE ^c | SS-EPI ^e | | TSE ^c | GE-EPI | MPRAGE ^{e,f} |
| Plane | Sagittal | Axial | Axial | | Axial | Axial | Sagittal |
| Mode | 3D | 2D | 2D | | 2D | 2D | 3D |
| TR [ms] | 2100 | >6000 | >5000 | | >2500 | < 2000 | 2100 |
| TE [ms] | 5 | 100-140 | Min | | PD=5-50 T2=80-120 | 30 | 5 |
| TI [ms] | 1100 | 2500 | | | | | 1100 |
| Flip Angle [Degrees] | 15 | 90/160 | 90/180 | | 90/160 | 60 | 15 |
| Frequency | 256 | 256 | 128 | | 256 | 128 | 256 |
| Phase | 256 | 256 | 128 | | 256 | 128 | 256 |
| NEX | 1 | 1 | 1 | | 1 | NEX=1 (90 Reps) Inject after 30sec (~15 pts) | 1 |
| Frequency Direction | A/P | A/P | R/L | | A/P | A/P | A/P |
| FOV | 256 | 240 | 240 | | 240 | 240 | 256 |
| Slice Thickness | 1mm | 3mm | 3mm | | 3mm | 5mm | 1mm |
| Gap/Spacing | 0 | 0 | 0 | | 0 | 0mm | 0 |
| Diffusion Options | | | $b_0 = 0$ and 1000 s/mm ² (64 directions) | | | | |
| Parallel Imaging | Up to 2x | Up to 2x | Yes-If Available | | Up to 2x | Up to 2x | Up to 2x |
| Scan Time (Approx) | 5 min | 5 min | 15 min | | 7 min | < 3 min | 5 min |

Examples of Compatible Protocols

Standard Protocol + Site Specific Sequences

| | 3D T1w Pre ^b | Ax 2D FLAIR ^j | Ax 2D DWI | Contrast Injection ^a | Ax 2D T2w ^{h,i} | 3D T1w Post ^b | Ax 2D T1w TSE |
|--|-----------------------------------|-----------------------------|--|---------------------------------|------------------------------|-----------------------------------|----------------|
| Sequence | MPRAGE ^{e,f} | TSE ^c | SS-EPI ^g | | TSE ^c | MPRAGE ^{e,f} | TSE |
| Plane | Sagittal/ Axial | Axial | Axial | | Axial | Sagittal/ Axial | Axial |
| Mode | 3D | 2D | 2D | | 2D | 3D | 2D |
| TR [ms] | 2100 | >6000 | >5000 | | >2500 | 2100 | 500 |
| TE [ms] | Min | 100-140 | Min | | 80-120 | Min | min |
| TI [ms] | 1100 | 2000-2500 ^k | | | | 1100 | |
| Flip Angle [Degrees] | 10-15 | 90/≥160 | 90/180 | | 90/≥160 | 10-15 | 90 |
| Frequency | ≥172 | ≥256 | ≥128 | | ≥256 | ≥172 | ≥256 |
| Phase | ≥172 | ≥256 | ≥128 | | ≥256 | ≥172 | ≥256 |
| NEX | ≥1 | ≥1 | ≥1 | | ≥1 | 1 | ≥1 |
| Frequency Direction | A/P | A/P | R/L | | A/P | A/P | A/P |
| FOV | 256 | 240 | 240 | | 240 | 256 | 240 |
| Slice Thickness | ≤1.5mm | ≤4mm | ≤4mm | | ≤4mm | ≤1.5mm | ≤4mm |
| Gap/Spacing | 0 | 0 | 0 | | 0 | 0 | 0 |
| Diffusion Options | | | <i>b</i> = 0, 500, 1000 s/mm ² ≥3 directions | | | | |
| Parallel Imaging | Up to 2x | Up to 2x | Up to 2x | | Up to 2x | Up to 2x | Up to 2x |
| Scan Time (Approx) [Benchmarked on 3T Skyra] | 5-10 min [5:49 for 1mm isotropic] | 4-8 min [3:22 for 2D FLAIR] | 2-4 min [1:22 for 3 direction DWI and 3 b-values] | | 4-8 min [5:10 for dual echo] | 5-10 min [5:49 for 1mm isotropic] | 2-4 min [2:22] |

Siemens Versions Available for Download

http://www.ellingsonbiomedical.com/Ellingson_Biomedical/MRI_PROTOCOLS.html

STANDARDIZED BRAIN TUMOR MRI PROTOCOLS

| | 3D T1 Pre ^b | Ax 2D FLAIR | Ax DWI | Pre-Load Contrast Injection ^b | Dual Echo Ax PD/T2 | DSC Perfusion ^c | 3D T1 Post ^b |
|----------------------|------------------------|------------------|---------------------------------------|--|----------------------|--|-------------------------|
| Sequence | MPRAGE ^{e,f} | TSE ^c | SS-EPI ^g | | TSE ^c | GE-EPI | MPRAGE ^{e,f} |
| Plane | Sagittal | Axial | Axial | | Axial | Axial | Sagittal |
| Mode | 3D | 2D | 2D | | 2D | 2D | 3D |
| TR [ms] | 2100 | >6000 | >5000 | | >2500 | < 2000 | 2100 |
| TE [ms] | 5 | 100-140 | Min | | PD=5-50 T2=80-120 | 30 | 5 |
| TI [ms] | 1100 | 2500 | | | | | 1100 |
| Flip Angle [Degrees] | 15 | 90/160 | 90/180 | | 90/160 | 60 | 15 |
| Frequency | 256 | 256 | 128 | | 256 | 128 | 256 |
| Phase | 256 | 256 | 128 | | 256 | 128 | 256 |
| NEX | 1 | 1 | 1 | | 1 | NEX=1 (90 Repts) Inject after 30sec (~15 pts) | 1 |
| Frequency Direction | A/P | A/P | R/L | | A/P | A/P | A/P |
| FOV | 256 | 240 | 240 | | 240 | 240 | 256 |
| Slice Thickness | 1mm | 3mm | 3mm | | 3mm | 5mm | 1mm |
| Gap/Spacing | 0 | 0 | 0 | | 0 | 0mm | 0 |
| Diffusion Options | | | b = 0, 500, 1000 s/mm ² | | | | |
| Parallel Imaging | Up to 2x | Up to 2x | Up to 2x | | Up to 2x | Up to 2x | Up to 2x |
| Scan Time (Approx) | 5-10 min | 4-8 min | 2-4 min | | 5-8 min | < 3 min | 5-10 min |

SIEMENS DOWNLOADABLE PROTOCOLS (EDX FILES)

1.5T Siemens Avanto

1.5T Siemens Sonata

3T Siemens Trio

3T Siemens Verio

3T Siemens Skyra

3T Siemens Prisma