ACRIN 6684
MRI Imaging Parameters

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ACRIN 6684 MRI PARAMETERS

All MRI scans must be completed on a 1.5 or 3.0 Tesla scanner, and 3.0 Tesla is preferred. To ensure the reproducibility of images, sites MUST scan study participants on the same ACRIN-approved MRI scanner for which trial qualification scans were performed and using the same protocol-specific parameters consistently at each time point.
The following MRI and MRS sequences are mandatory across all scanner models for each study participant:

Scout -use methods that can produce scan to scan reproducibility

T1 Pre Contrast Spin Echo	Plane	TR	TE		FOV	Phase FOV%	Slice Thickness	Gap	Matrix	Phase	NEX / NSA
	Axial	400-600	min. (≤15)		220-240	75%	5mm	1mm	256x192	R-L	1

3D T2 Slab	Plane	TR	TE	Echo Train	FOV	Phase FOV%	Slice Thickness	Gap	Matrix	Phase	NEX / NSA
	Axial	3200	428	944	256	100	1mm	0mm	256x256	A-P	1

Siemens (SPACE) **GE (CUBE)**

FLAIR	Plane	TR	TE	TI	FOV	Phase FOV%	Slice Thickness	Gap	Matrix	Phase	NEX / NSA
	Axial	10000	70-130	2500	220-240	75%	5mm	1mm	256x192	R-L	1

BOLD 2D-EPI 450 measurements	Plane	TR	TE	Flip Angle	FOV	Phase FOV%	Slice Thickness	Gap	Matrix	Phase	NEX / NSA
	Axial	2000-3000	20-30	90	220	100	8mm	0mm	256x192	A-P	1

T1 Mapping 3D- T1 GRE	Plane	TR	TE	Flip Angle	FOV	Phase FOV%	Slice Thickness	Gap	Matrix	Phase	NEX / NSA
	Axial	4-6	min	2,10,15, 20,30	256	75-100	3-5mm	0mm	256x128 to 256	R-L	2

DCE-MRI **---First Injection---** **Injection takes place after 10 baseline frames are obtained.**

DCE 3D- T1 GRE	Plane	TR	TE	Flip Angle	FOV	Phase FOV%	Slice Thickness	Gap	Matrix	Phase	NEX / NSA
	Axial	4-6	min	20	256	75-100	3-5mm	0mm	256x128 to 256	R-L	1

Diffusion DWI / DTI 2D EPI	Plane	TR	TE	B Value	# of Directions	FOV	Phase FOV%	Slice Thickness	Gap	Matrix	Phase	NEX / NSA
	Axial	7500-8000	Min 80-85	~0,700 -1000	6-100	220-240	100%	5mm	1.5mm	128x128 minimum	A-P	1

DSC - Perfusion-MRI

---2nd Injection--- **Inject bolus of Gad at time point 60(35 minimum)**
Continue to collect to achieve a total of 120 points

	Plane	TR	TE	Flip Angle	FOV	Phase FOV%	Slice Thickness	Gap	Matrix	Phase	NEX / NSA
DSC 2D EPI	Axial	1000-1500ms	30-40(GE) 70-105(SE)	70-90	220-240	75-100	3-5mm	0-2.5 mm	128 to 128	A-P	1

	Sagittal Plane	TR	TE	TI	Flip Angle	FOV	Phase FOV%	Slice Thick	Gap	Matrix	Phase	NEX / NSA
T1 Post Contrast 3D SPGR (MPRAGE)	(Siemens)	2530	3.44(min)	1100	7°	256	100%	1.3mm	0mm	256x256	A-P	1
	(GE)	~10	~2.8	450	20°	25	100%	1.3mm	0mm	256x256	A-P	1-2

	Plane	TR	TE		FOV	Phase FOV%	Slice Thickness	Gap	Matrix	Phase	NEX / NSA
T1 Post Contrast Spin Echo*	Axial	400-600	min. (<15)		220-240	75%	5mm	1mm	256x192	R-L	1

The post-contrast imaging must be performed in at least the plane of the pre-contrast imaging

	Plane	TR	TE	k-space	FOV	Sat Bands	Slice Thickness	Flip	Matrix	Phase	NEX / NSA
3D Volumetric Spectroscopy ~6min Siemens	Axial*	1140	144	Elliptical	>160mm	6 bands	>40mm	default	12x12x8	A-P	1

Spectroscopy power point presentation located on the ACRIN website

	Plane	TR	TE	k-space	FOV	Sat Bands	Slice Thickness	Flip	Matrix	Phase	NEX / NSA
3D Volumetric Spectroscopy ~10min GE	Axial*	1140	144	Elliptical	>160mm	6 bands	>40mm	default	12x12x8	A-P	0.5

Spectroscopy power point presentation located on the ACRIN website

MR Imaging Procedures for Advanced Imaging

Choose slice locations for the advanced imaging sequences (DCE, DSC, BOLD and MRS) so that the same volume of tissue (6cm) is imaged for each sequence. For DCE, DSC and BOLD sequences, be sure as much as possible that the same slice locations are imaged.

BOLD Imaging Protocol

We recommend running the simultaneous BOLD and ASL sequence, which gives us BOLD and flow images at the same time.
Total scan time is ~15 min
The oxygen breathing procedure described below is to be performed the BOLD imaging sequence:

1. Room air for 8 minutes
2. 100% FiO2 hyperoxia for 4 minutes
3. Room air for 2 minutes

A 0-75 L/min high precision flow meter is to be attached to the oxygen wall outlet, to deliver oxygen at flow rates of 40 to 45 L/min. Wide-bore plastic tubing must be used to minimize gas draft with a simple face mask.

Dynamic Contrast-Enhanced (DCE)- MRI Protocol

Description

The DCE-MRI consists of five 3D pre contrast short series used for T1 mapping, followed by the 3D multi-phase dynamic contrast enhanced T1 weighted series. The dynamic series is a "multiphase" technique with images acquired before, during, and after intravenous injection of gadolinium (Gd)-based contrast agent.

Platform/scheduling

Patients must be imaged on the same scanner for all MRI studies.

General technique

- Prescan calibration should be completed prior to the T1 mapping series and should not be repeated until after the dynamic series is completed (if needed).
- The slice locations and positioning for the T1 mapping and the dynamic series should be identical.
- For all series, do not use normalization filters such as SCIC or PURE.
- If magnets and multichannel head coils are available to perform parallel imaging, speed factors for ASSET or IPAT of 2 can be used. Do not use higher speed factors.
- If parallel imaging techniques are used, identical parallel imaging techniques must be used on all series.
- If parallel imaging techniques are not available, sites can use zero-filled interpolation in the phase and frequency direction "Zip x 2."
- Images should be acquired as axial; do not acquire as oblique.
- 3 to 5 mm slices thickness - yielding a 6 cm slab of effective coverage.
- A contrast agent power injector should be used for contrast administration in this study. The power injector should be set up per standard protocol.

- Enough contrast agent should be loaded for both the DCE scan and the additional contrast agent used for the DSC-MRI sequence.
- The rate of injection should be 3 to 5 cc/sec, followed by a saline flush at the same rate.

T1 mapping series technique

- The repetition time (TR) must be identical for all flip angles.
- The lowest flip angle should be 2 degrees. ACRIN can provide source code to compile to run this sequence, if needed.

- **For the baseline study**
  - If prior studies are available, center the slice locations (in the z-direction) for T1 mapping series on the area with the largest enhancing abnormality.
  - If no prior studies are available, center slice locations on the area with largest abnormality on T2-weighted images.
  - Note that if the largest abnormality is near the top or bottom of the brain, it is acceptable for the highest or lowest slice locations (respectively) to be outside of the brain or outside of coil coverage.
- **For subsequent studies**
  - Center the slice locations for subsequent studies to match those of the baseline study.

Dynamic series technique

- Allowable contrast agents are: Magnevist, Omniscan, Dotarem, ProHance, and Gadovist. Please **do not use MultiHance.**
- The contrast agent should be administered using a power injector. Patients will require a heparin lock or other similar device for the administration of contrast agent during the dynamic sequence with the patient in the scanner.
- The frame rate of the multiphase acquisition should be acquired in 6 seconds or less such that each volume should be completely sampled every six seconds or more frequently, if possible.
- Injection takes place after 10 baseline frames are obtained.
- The total imaging time should be 5.5 minutes. This amounts to 55 to 95 frames, depending upon the acquisition time. The total number of slices acquired should be 660 to 1,900, depending on the number of slices in each frame.

  For example: *If your time per phase works out to 5 seconds per phase, then:*

  5 seconds x 66 phases = 330 seconds (5.5 minutes)
  66 phases x 10 slices per phase = 660 slices
  Inject at 50 seconds (5 seconds x 10 frames)

- Contrast agent administration is 0.1 mmol/kg via power injector (3 to 5 cc/sec), followed by a flush with 20 cc of normal saline at the same rate.

Dynamic Susceptibility Contrast (DSC)- MRI Protocol

Description

The DSC-MRI protocol consists of administering a preload of a Gad (the Gad used for the DCE exam), followed by the collection of echo planar imaging (EPI) data before, during, and after administration of an additional bolus of Gad contrast agent. The DSC acquisition is started 5 to 10 min after the DCE acquisition.

General technique

- The EPI sequence should be set up to collect at least 120 points with a TR between 1.0 and 1.5 seconds. A GRE-EPI, SE-EPI, or a simultaneous GRE/SE-EPI sequence can be used:
    - For GRE-EPI, echo time (TE) should equal 30 to 40 milliseconds.
    - For SE-EPI, TE should equal 70 to 105 milliseconds.
    - If using a combined GRE/SE-EPI sequence, use the minimum TE for SE, which will likely be slightly longer than the 70 to 105 milliseconds range listed above.

Specific DSC-MRI acquisition

1. Start the DSC-MRI sequence. After collecting 60 (35 minimum) baseline points, inject the bolus of contrast agent (0.1 mmol/kg). Continue collecting the data so that at least 120 points are collected per slice.

Examples of the DSC-MR images collected and time course from a single voxel are shown below in Figure 1. Note the transient darkening of the image and the decrease in signal as the contrast agent passes through the tissue.

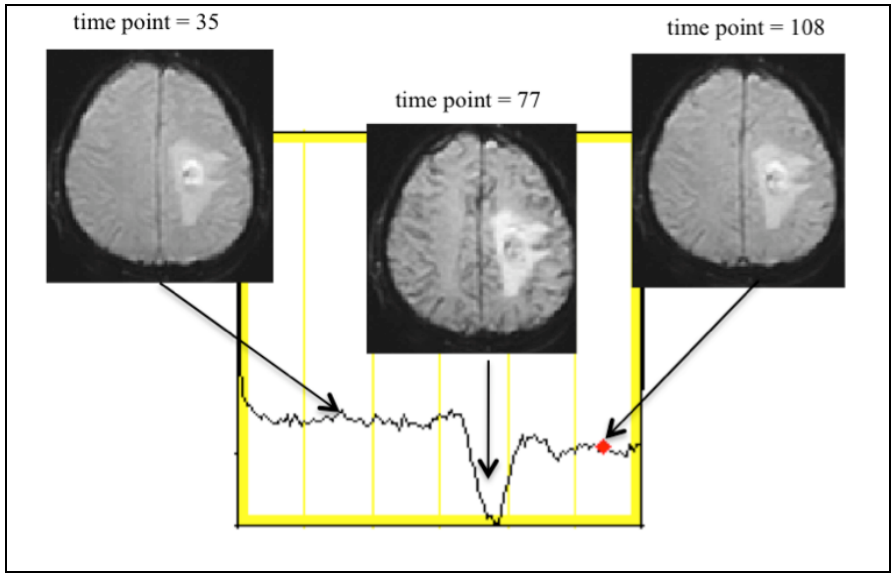

Figure 1. Example images and signal time course collected during a DSC study.
Shown are GRE-EPI images collected at three different time points, before, during and after the bolus injection of contrast agent, along with an example signal time course from one voxel. Notice that the image and voxel signal intensity transiently decrease as the bolus of contrast passes through the tissue.

MRI Collection Time Points/Visits

All patients will undergo baseline ^{18}F-FMISO PET and MRI studies 2 to 4 weeks after initial debulking surgery and prior to radiotherapy (XRT) (T0). Additionally, imaging will be performed after 3 weeks of radiotherapy (T1) and 4 weeks after the radiation is complete, before the second cycle of temozolomide (TMZ) (T2).

Important Note: Please work with the RA and persons responsible for scheduling the PET and MRI scans *to accommodate study participants' preference* for either undergoing the MRI and PET scans on the same day OR for scheduling the scans on separate days, but not longer than 2 days apart per the protocol.

Table 1. TREATMENT AND IMAGING

	Visit 2	Chemoradiation Begins		**Visit 3** *(3-5 weeks after initiation of treatment)*				**Visit 4**
		Wk 1	Wk 2	Wk 3	Wk 4	Wk 5	Wk 6	**3-5 weeks post XRT**
TMZ (mg/m^2/day)		75	75	75	75	75	75	
Radiation Therapy		•	•	•	•	•	•	
FMISO PET Scan†	**Baseline**			**Scan 2**				**Scan 3**
Brain MRI With Contrast‡	**Baseline**			**Scan 2**				**Scan 3**

† The first 15 participants will have two baseline ^{18}F-fluoromisonisazole (FMISO) PET scans performed 1 to 7 days apart for test/retest analysis (see protocol section 9.2.1 for details of visit 2A); both scans must be completed prior to initiation of chemoradiation.

‡ All MRIs (with or without contrast) and CTs performed as standard of care during participant follow up should be submitted to ACRIN (see protocol section 10.4, "Image Submission Criteria," for details).