

## Supplemental Material

**Table S1. Standardized ACRIN 6698 MRI Acquisition Parameters**

Parameter	T2-weighted	DW-MRI	T1-weighted
Sequence type	FSE or STIR	DW SE-EPI	GE
2D or 3D sequence	2D	2D	3D
Slice orientation	Axial or sagittal	Axial	Axial
Laterality	Bilateral	Bilateral	Bilateral
Frequency direction	A/P	A/P	A/P
Phase direction	R/L (axial) S/I (sagittal)	R/L	R/L
*FOV – frequency	260-360 mm (axial) 180-220 mm (sagittal)	260-360 mm	260-360 mm
*FOV - phase	260-360 mm (axial) 180-220 mm (sagittal)	300-360mm	260-360 mm
Matrix – frequency (acquired)	256-512	128-192	384-512
Matrix – phase (acquired)	≥ 256	128-192	≥ 256
Reconstruction Matrix	512 x 512	256 x 256	512 x 512
In-plane resolution	≤ 1.4 mm	1.7 – 2.8 mm	≤ 1.4 mm
Fat-suppression	Active fat-sat recommended	Active fat-sat	Active fat-sat recommended
Repetition Time (TR)	2000-10000 ms	≥ 4,000 ms	4-10 ms
Echo Time (TE)	70-140 ms (STIR 70 ms)	Minimum	Minimum
Echo Train Length	≤ 16	N/A	N/A
Inversion Time (TI; STIR sequence)	170 ms (1.5T) 230 ms (3.0T)	N/A	N/A
Flip Angle	90 degrees	90 degrees	10-20 degrees
Readout Bandwidth (per pixel)	N/A	N/A	Maximum
<i>b</i> -values	N/A	0, 100, 600, 800 s/mm <sup>2</sup>	
Slice thickness (acquired)	≤ 4 mm	4-5 mm	≤ 2.5 mm
Number of slices	Variable; complete bilateral coverage	Variable; complete bilateral coverage	≥ 60; complete bilateral coverage
Slice Gap	≤ 1.0 mm	No gap	No gap
Parallel imaging factor	≤ 2	≥ 2	≤ 2
No. of excitations or averages	≤ 2	≥ 2	≤ 2

<b>k-space ordering</b>	N/A	N/A	-k to +k standard, non- centric
<b>Sequence acquisition time</b>	≤ 7 minutes	≤ 5 minutes	80 sec ≤ scan time ≤ 100 sec
<b>Total post-contrast imaging duration</b>	N/A	N/A	≥ 8 minutes following injection

Abbreviations: FSE = fast spin echo, STIR = short tau inversion recovery, DW = diffusion-weighted, SE = spin echo, EPI = echo planar imaging, GE = gradient echo, 2D = two dimensional, 3D = three dimensional, A/P = anterior-posterior, R/L = right-left, S/I = superior-inferior, FOV = field-of-view, N/A = not applicable

**Table S2. MR imaging systems utilized for the primary analysis and test-retest cohorts.**

	<b>Analysis Set N=210</b>	<b>Test-Retest Set N=71</b>
<b>Vendor</b>	<b>n (%)</b>	<b>n (%)</b>
<b>GE</b>	155 (73.8)	28 (39.4)
<b>Siemens</b>	30 (14.3)	12 (16.9)
<b>Philips</b>	25 (11.9)	31 (43.7)
<b>Field Strength</b>		
<b>1.5 tesla</b>	148 (70.5)	44 (62.0)
<b>3.0 tesla</b>	62 (29.5)	27 (38.0)

### **Sample Size Estimates**

The sample size projection for the ACRIN 6698 trial was designed to achieve 90% power for the primary analysis to test whether the change in tumor ADC from baseline to the early treatment time point is predictive of pathologic complete response. Specifically, the sample size was calculated to detect a difference of 0.15 between the AUC under the null hypothesis of 0.5 and an AUC under the alternative hypothesis of 0.65 using a one-sided Z-test at a significance level of 0.05. It was

assumed that the number of pCR non-responders is approximately 2.7 times greater than the number of complete responders based on the ACRIN 6657 study, requiring a total of 160 analyzable patients (43 responders and 117 non-responders).

We assumed 20% of the cases accrued would not provide usable data for the analysis, for example, having missing MRI scans out of four MRI scans per participant, and assumed a 45% loss rate due to patients who are screened but do not proceed to the treatment phase of I-SPY 2. Additionally, 10% drop out rate is expected. Therefore, target enrollment was set at approximately 404 participants after accounting for the above three conditions.

### **Participating Institutions**

University of California, San Francisco, CA

University of Washington, Seattle, WA

University of California, San Diego, CA

H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL

University of Alabama, Birmingham, AL

University of Texas MD Anderson Cancer Center, Houston, TX

University of Chicago, Chicago, IL

Oregon Health and Science University, Portland, OR

University of Minnesota, Minneapolis, MN

University of Pennsylvania, Philadelphia, PA