

Table S1. Genes and primers on microfluidic low-density arrays in RT-PCR assays of the gene signature.

Gene	Primer
<i>TOMM70A</i>	Hs00207896_m1
<i>MCF2</i>	Hs00180467_m1
<i>RAD52 homolog</i>	Hs00172536_m1
<i>MCM2</i>	Hs00170472_m1
<i>C18B11</i>	Hs00398863_m1
<i>SEC13L</i>	Hs00229687_m1
<i>SLC25A5</i>	Hs00854499_g1
<i>PLSCR1</i>	Hs00275514_m1
<i>TXNRD1</i>	Hs00182418_m1
<i>RAD50</i>	Hs00194871_m1
<i>INPPL1</i>	Hs00155533_m1
<i>PBX2</i>	Hs00855025_s1
<i>SSBP1</i>	Hs00268409_m1
<i>HSPCB</i>	Hs00607336_gH
<i>PDGFRA</i>	Hs00183486_m1
<i>ACOT4</i>	Hs00745041_s1
<i>DDOST</i>	Hs00193263_m1
<i>IGHA1</i>	Hs00733892_m1
<i>S100P</i>	Hs00195584_m1
<i>FAT</i>	Hs00170627_m1
<i>FGF2</i>	Hs00960934_m1
<i>INSM1</i>	Hs00357871_s1
<i>IRF5</i>	Hs00158114_m1
<i>SMARCD2</i>	Hs00161987_m1
<i>MAP2K2</i>	Hs00360961_m1
<i>HMBS</i>	Hs00609297_m1
<i>GAPDH</i>	Hs99999905_m1
<i>18S</i>	Hs99999901_s1
<i>IPO8</i>	Hs00183533_m1

SEER description ICD-O-3

A cohort of patients diagnosed with primary breast cancer was retrieved from the Surveillance Epidemiology and End Results (SEER) database. The SEER database is an aggregate of registry data from specific geographic areas covering approximately 26 percent of the U.S. population and contains clinical, demographic, treatment, and follow-up information for a variety of cancers. The requirements for inclusion in this breast cancer study included a diagnosis of papillary carcinoma NOS (ICD-O-3 8050/3), spindle cell sarcoma (ICD-O-3 8801/3), carcinoma NOS (ICD-O-3 8010/3), infiltrating duct mixed with other types of ca. (ICD-O-3 8523/3), mucinous adenocarcinoma (ICD-O-3 8480/3), infiltrating duct carcinoma NOS (ICD-O-3 8500/3), or infiltrating lobular mixed with other types of ca. / infiltrating duct and lobular carcinoma / lobular carcinoma NOS (ICD-O-3 8524/3, 8522/3 and 8520/3) between the years 1988 and 2007, as well as available data on AJCC T-N-M (or tumor extend, nodes, size) information, tumor grade, survival, and treatment. A total of 400,978 patients met the inclusion criteria.

Table S2. Clinical characteristics of breast cancer patients in our patient cohorts and SEER database.

	Our Study (n = 60)	SEER Database (n = 400,978)
Patient Age:		
Median	60	61
Range	36-86	17-106
Pathologic Characteristics:		
Tumor Stage		
1	10 (16.67%)	214,474 (53.49%)
2	31 (51.67%)	157,177 (39.20%)
3	12 (20%)	23,942 (5.97%)
4	4 (6.67%)	1,304 (0.33%)
Missing info	3 (5%)	4,081 (1.02%)
Tumor Grade		
1	5 (8.33%)	67,661 (16.87%)
2	23 (36.67%)	183,857 (45.85%)
3	33 (55%)	149,460 (37.27%)
Missing info	0	0
Histology:		
Papillary carcinoma, NOS	1 (1.67%)	672 (0.17%)
Carcinoma, NOS	1 (1.67%)	1521 (0.38%)
Infiltrating duct mixed with other types of ca.	2 (3.33%)	7,771 (1.94%)
Mucinous adenocarcinoma	3 (5%)	8,766 (2.19%)
Infiltrating lobular mixed with other types of ca. / Infiltrating duct and lobular carcinoma / Lobular carcinoma, NOS	6 (10%)	58,448 (14.58%)
Infiltrating duct carcinoma, NOS	47 (78.33%)	323,800 (80.75%)

Table S3. Genes whose ΔC_T has a significant correlation ($p < 0.05$) with SEER patient survival. Correlations were obtained from SEER patients within three treatment groups (both surgery and radiation, surgery only and radiation only)

Both surgery and radiation group (n = 195,717):						
Gene	20-year survival		10-year survival		5-year survival	
	correlation	p-value	correlation	p-value	correlation	p-value
MCM2	0.539	0.017	0.573	0.010	0.618	0.005
RAD52	0.692	0.001	0.676	0.001	0.600	0.007
S100P	0.415	0.077	0.477	0.039	0.501	0.029
SMARCD2	0.584	0.009	0.651	0.003	0.670	0.002
PSMC3IP	0.427344	0.127	0.491	0.074	0.542	0.045
IGHA1	0.528	0.020	0.369	0.120	0.337	0.159
Surgery only group (n = 204,434):						
Gene	20-year survival		10-year survival		5-year survival	
	correlation	p-value	correlation	p-value	correlation	p-value
RAD52	0.610	0.006	0.592	0.008	0.510	0.026
SMARCD2	0.486	0.035	0.581	0.009	0.574	0.010
Radiation only group (n = 827):						
Gene	20-year survival		10-year survival		5-year survival	
	correlation	p-value	correlation	p-value	correlation	p-value
MCM2	0.501	0.029	0.500	0.029	0.557	0.013
RAD52	0.371	0.118	0.427	0.068	0.480	0.037
S100P	0.533	0.019	0.545	0.016	0.615	0.005
SMARCD2	0.423	0.071	0.448	0.054	0.544	0.016
PLSCR1	0.284	0.238	0.312	0.193	0.510	0.026
TOMM70A	0.308	0.199	0.283	0.241	0.476	0.039
TXNRD1	0.390	0.099	0.379	0.109	0.531	0.019

Table S4. Hazard ratio and 95% confidence interval of RAD52 and PBX2 in both overall survival univariate Cox model and recurrence-free univariate Cox model.

Hazard Ratio in Overall Survival Model:			
<i>Protein</i>	<i>IHC Score</i>	<i>Hazard Ratio</i>	<i>95% Confidence Interval</i>
RAD52	1	9.571	[1.321, 69.33]
	2	91.652	[1.745, 4806.652]
Hazard Ratio in Recurrence-Free Survival Model:			
<i>Protein</i>	<i>IHC Score</i>	<i>Hazard Ratio</i>	<i>95% Confidence Interval</i>
RAD52	1	3.471	[1.390, 8.668]
	2	12.049	[1.932, 75.134]
PBX2	1	1.704	[1.056, 2.750]
	2	2.903	[1.115, 7.563]
	3	4.946	[1.178, 20.797]
	4	8.428	[1.244, 57.191]

Table S5. SMARCD2 overall survival and recurrence-free survival IHC protein level COX results. *Warning message after Cox model: In fitter(X, Y, strats, offset, init, control, weights = weights, : Loglik converged before variable 1 ; beta may be infinite.

	OS coef	OS <i>p</i> -value	RFS coef	RFS <i>p</i> -value
SMARCD2	*19.7852351511077	*1	0.112586	0.85

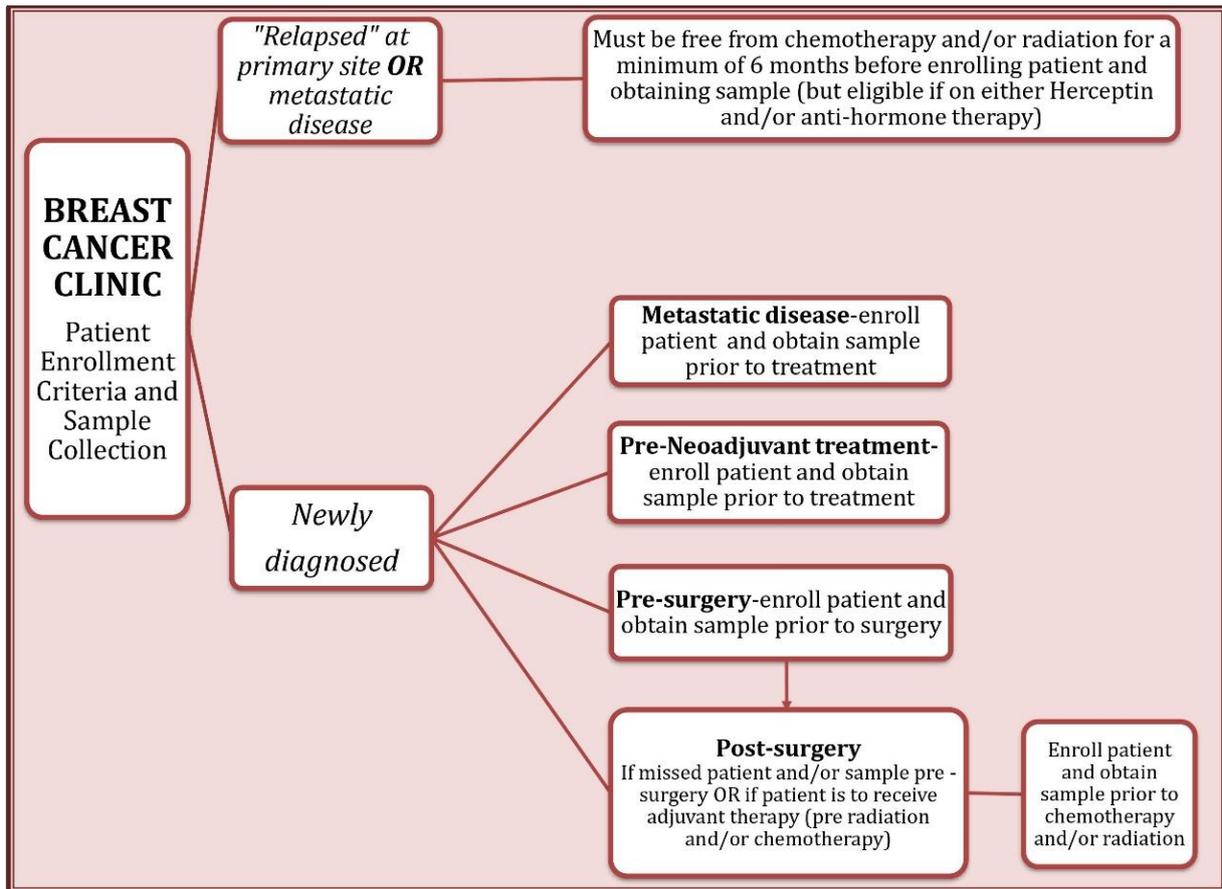


Figure S1. Breast cancer patient enrollment criteria.

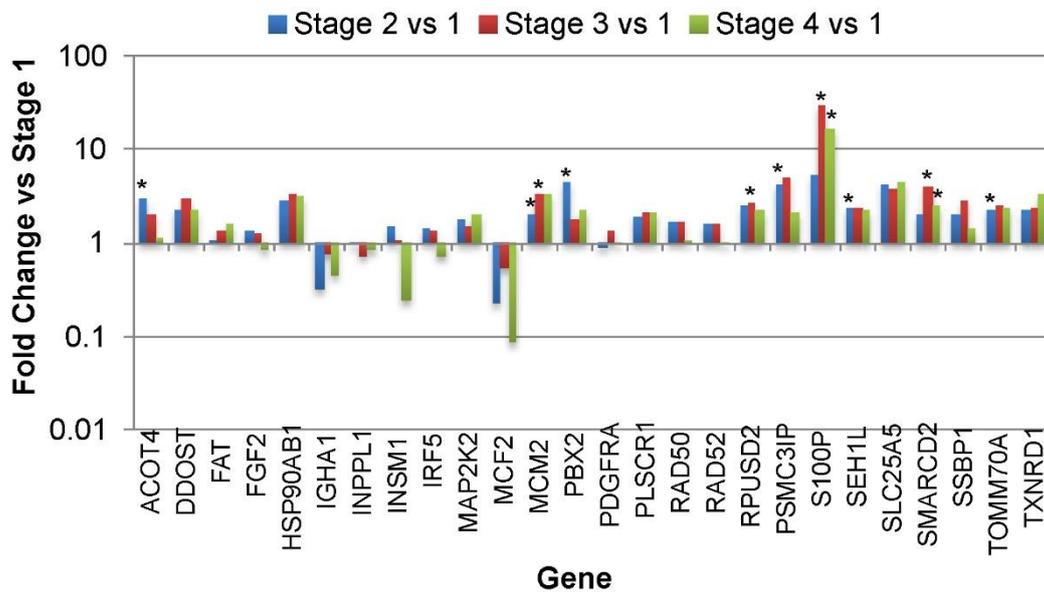


Figure S2. Stage fold change calculated with *HMBS* plate-wise. The average expression of *HMBS* in each plate was used as a house keeping gene measurement in the analysis. * $p < 0.05$ in two-sample t -tests.

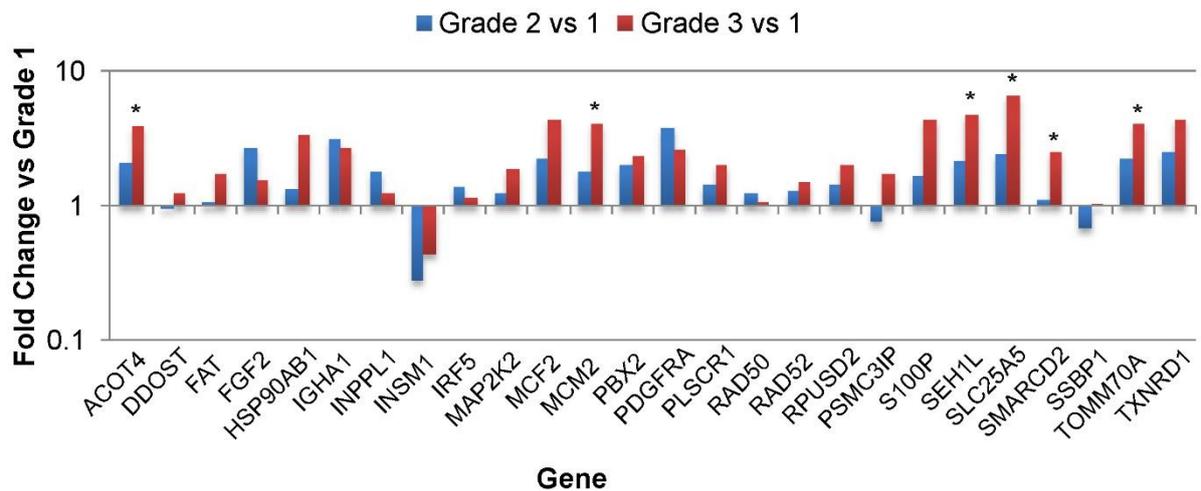


Figure S3. Grade fold change calculated with *HMBS* plate-wise. The average expression of *HMBS* in each plate was used as a house keeping gene measurement in the analysis. * $p < 0.05$ in two-sample *t*-tests.

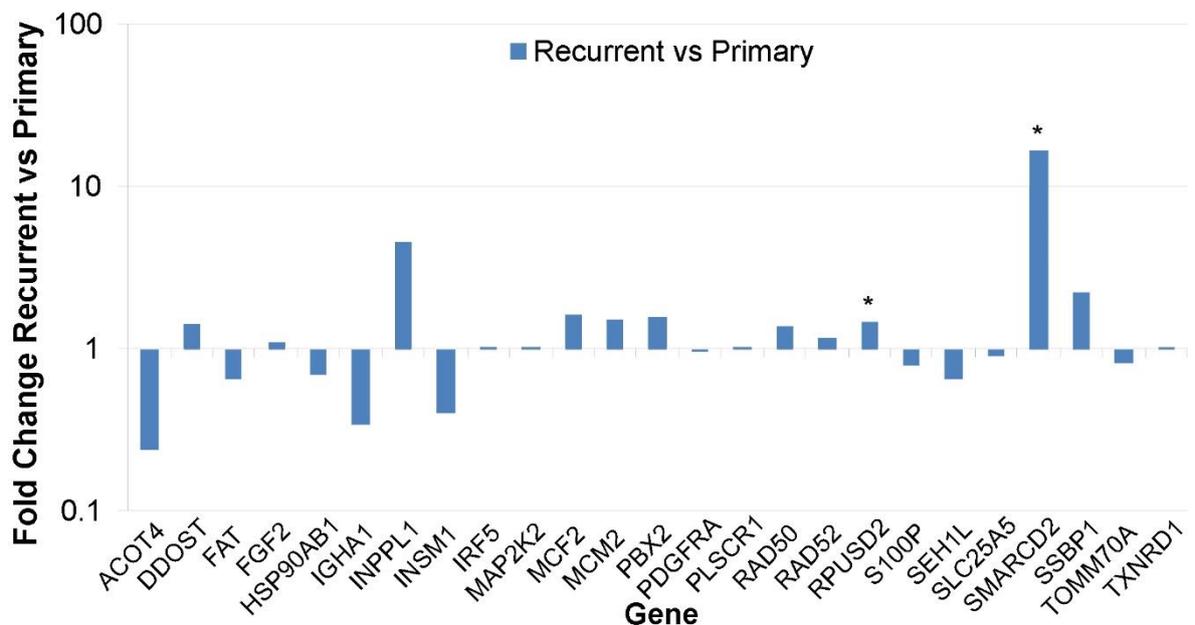


Figure S4. Fold change recurrent vs primary breast cancer for grade 3 samples (25 genes) calculated with *HMBS* sample-wise normalization. The average expression of *HMBS* in each sample was used as a house keeping gene measurement in the analysis. *PSMC3IP* was not included, since it was only measured in recurrent samples. Sample wise normalization was used since the recurrent samples were in different plates. There were 4 recurrence cancers with grade 3; 33 primary cancers with grade 3. * $p < 0.05$ in two-sample *t*-tests.

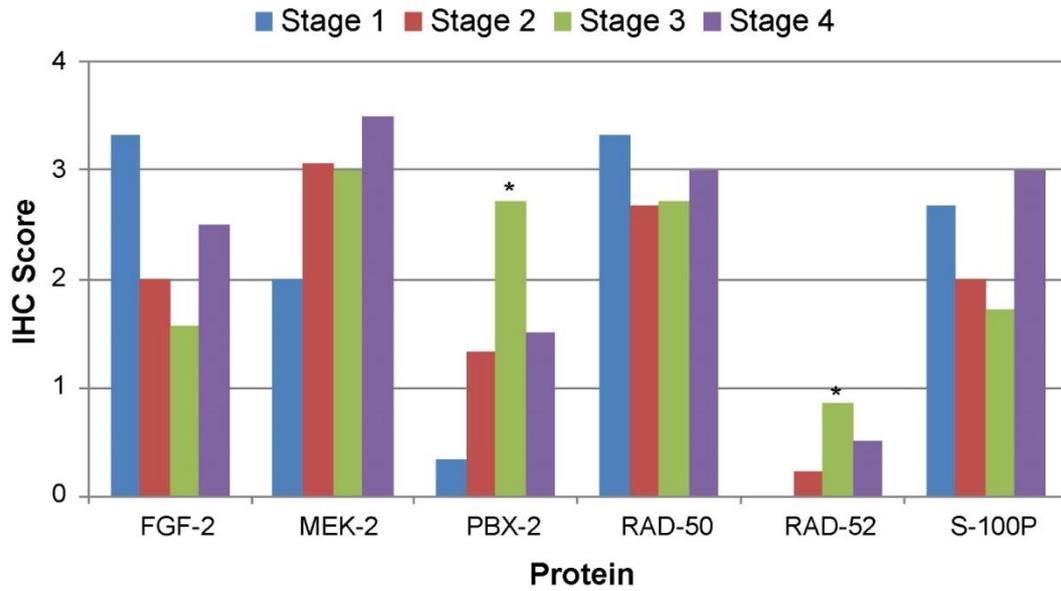


Figure S5. Average protein expression measured with immunohistochemistry (IHC) score in each breast cancer stage. * $p < 0.05$ in ANOVA tests.

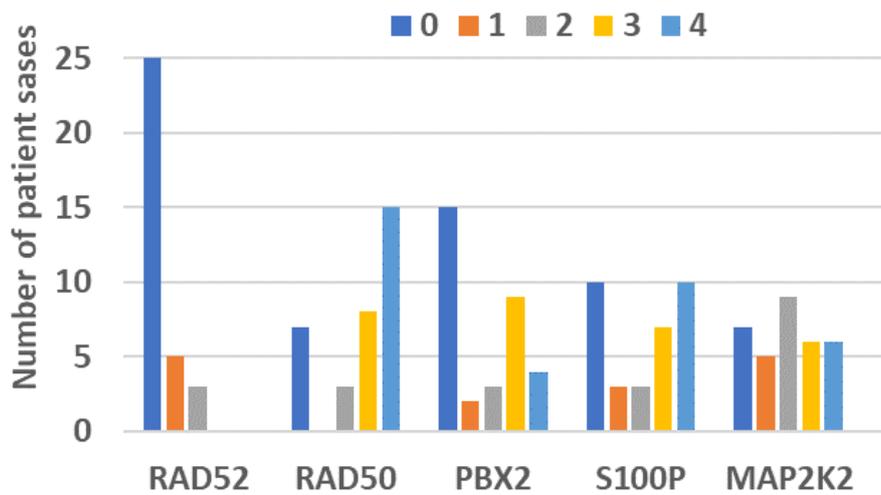


Figure S6. Protein expression levels of RAD52, RAD50, PBX2, S100P, and MAP2K2 scored in immunohistochemistry assays of invasive breast cancer tumor samples ($n=33$). 0 = no staining; 1 = equivocal staining; 2 = weak staining; 3 = moderate staining; 4 = strong staining.

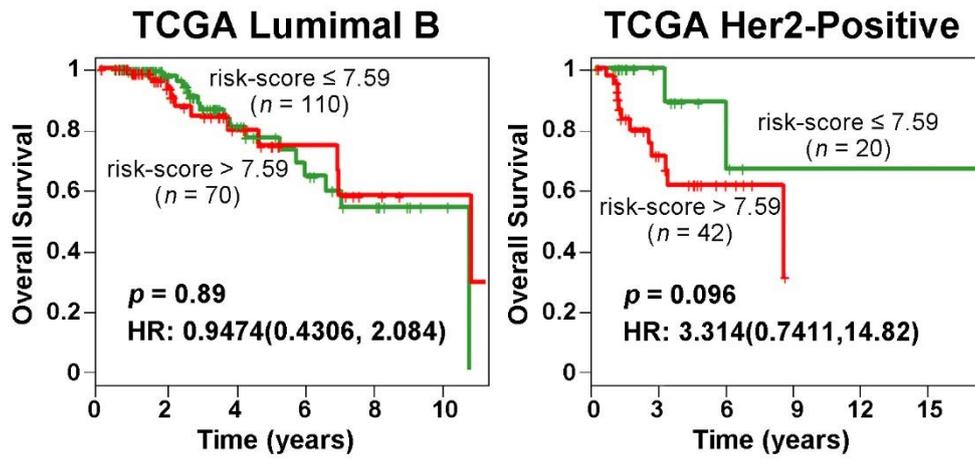


Figure S7. For the subtypes Luminal B and Her2-positive patients in TCGA-BRCA, the low-risk and high-risk patient group did not have significantly different survival. The plots showed the survival outcome of the first 10 years after surgery.

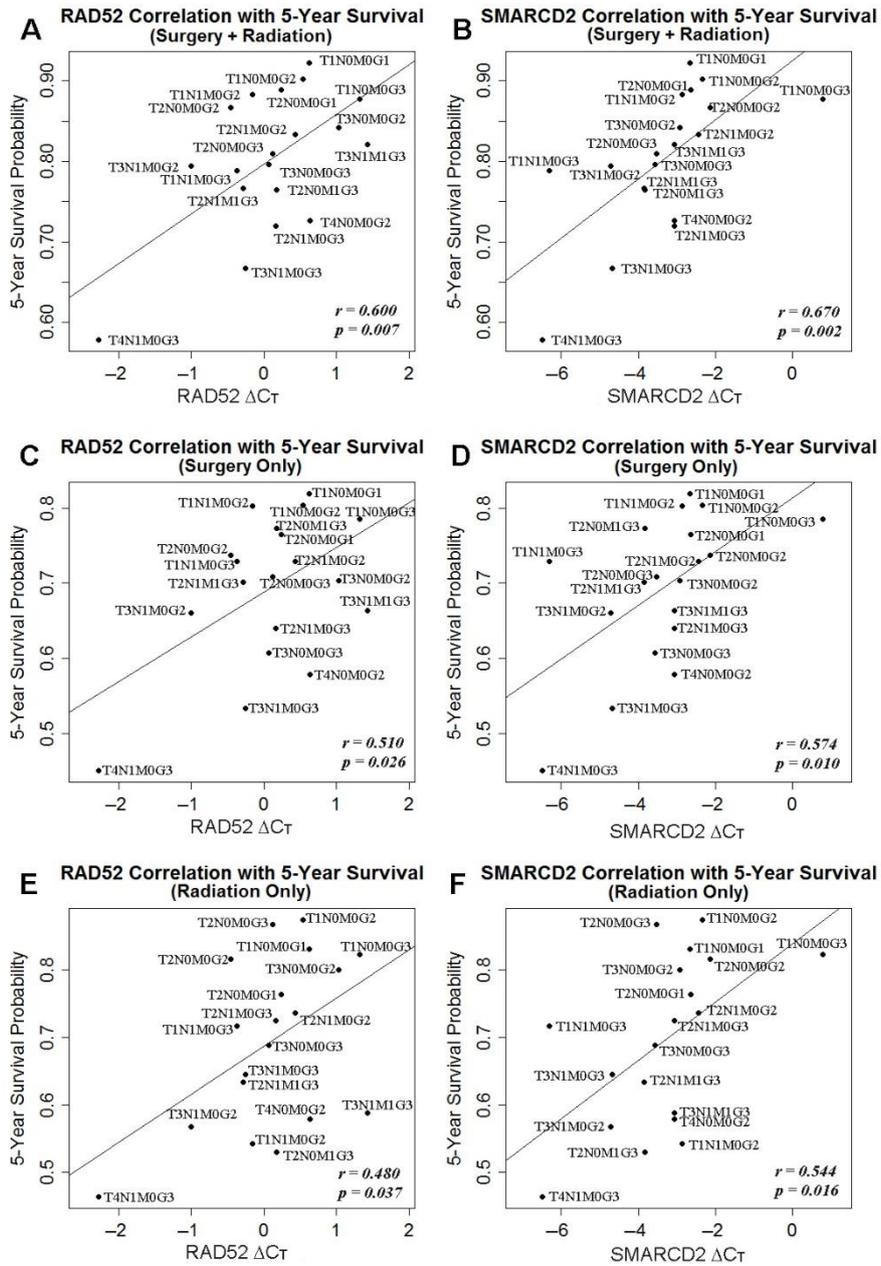


Figure S8. Correlations between gene (RAD52 and SMARCD2) ΔC_T and 5-year survival in the three treatment groups (both surgery and radiation, surgery only and radiation only). The T-N-M-grade category is labeled beside each data point.