

Laboratory for Quantitative Medicine
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Validation: Size+Nodes Equation

This report presents results demonstrating the validity and accuracy of the Size+Nodes equation.

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I. Introduction

This report summarizes all verification and validation studies that have been performed on the Size+Nodes equation, for breast cancer. The data is grouped and permuted in multiple ways, showing that the Size+Nodes equation is extremely accurate. Because the Size+Nodes equation adds another layer of information to the SizeOnly equation, we should expect that accuracy is improved over using the SizeOnly equation alone. Indeed, this is shown through all the various measures of accuracy.

The parameter of Qs (refer to Technical Report #2: Equation Parameters) was derived using the SEER dataset. Section III verifies that this derived value indeed provides accurate results over a wide range of data stratification strategies. Section IV then validates this in an entirely separate dataset, using the Partners Healthcare Breast Cancer Database.

II. Datasets

SEER Dataset (Breast Cancer)

Breast cancer data was extracted from the US Surveillance, Epidemiology, and End Results (SEER) dataset, which is provided by the National Cancer Institute. It consists of 17 regional registries across the US, with data from 1973 to 2004. An extensive effort was made to clean the data, for example by considering only first malignant primary tumors. Also, analysis is restricted to patients with 1-50 mm tumors and 0-7 positive lymph nodes. These patients total 362,491.

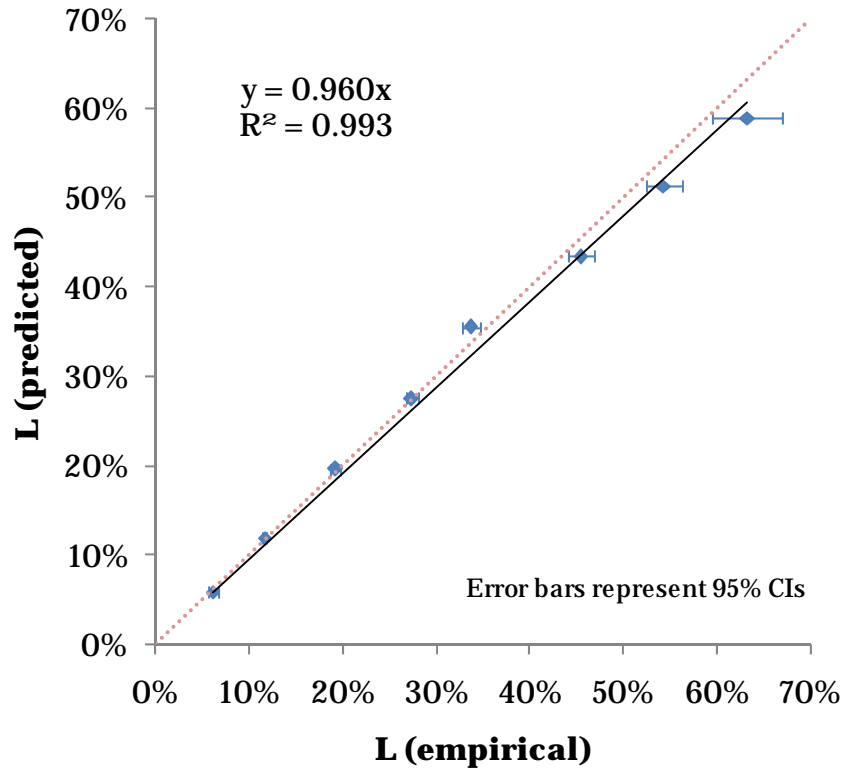
Partners Healthcare Breast Cancer Database

This database consists of 24,771 breast cancer patients diagnosed at the Massachusetts General Hospital or the Brigham and Women's hospital between 1968 and 2007. Analysis is restricted to patients with 1-50 mm tumors and 0-7 positive lymph nodes, a subset with 7,907 patients.

III. Verification on the SEER dataset

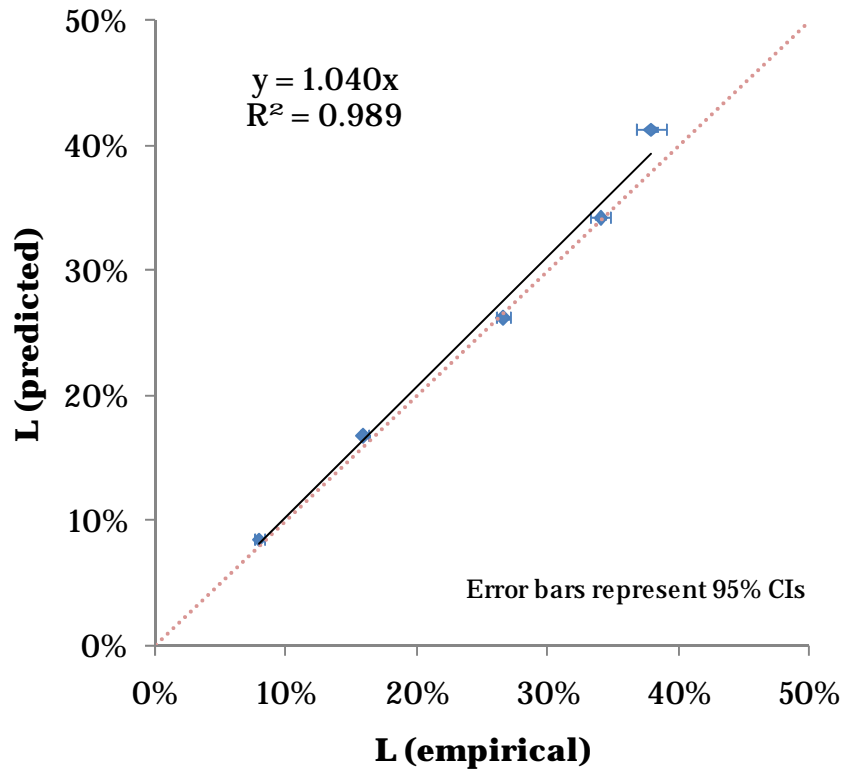
Grouped by 8% predicted lethality bins using the Size+Nodes equation

Group	N	L empirical (SEM)	L predicted (SEM)	Difference (pred – emp)
0-8%	40311	6.13% (0.25%)	5.87% (0.01%)	-0.26%
9-16%	128451	11.63% (0.16%)	11.92% (0.01%)	0.29%
17-24%	85467	19.21% (0.22%)	19.60% (0.01%)	0.39%
25-32%	55879	27.42% (0.30%)	27.55% (0.01%)	0.13%
33-40%	27146	33.71% (0.48%)	35.52% (0.01%)	1.80%
41-48%	14829	45.40% (0.71%)	43.43% (0.02%)	-1.97%
49-56%	8146	54.37% (0.99%)	51.35% (0.03%)	-3.02%
57-63%	2262	63.22% (1.92%)	58.91% (0.04%)	-4.31%
<i>Mean (std. dev.)</i>				-0.87% (2.04%)
<i>Mean weighted by N (std. dev.)</i>				0.15% (0.66%)
<i>Root Mean Square (std. dev.)</i>				2.10% (2.56%)
<i>Root Mean Square weighted by N (std. dev.)</i>				0.63% (0.63%)



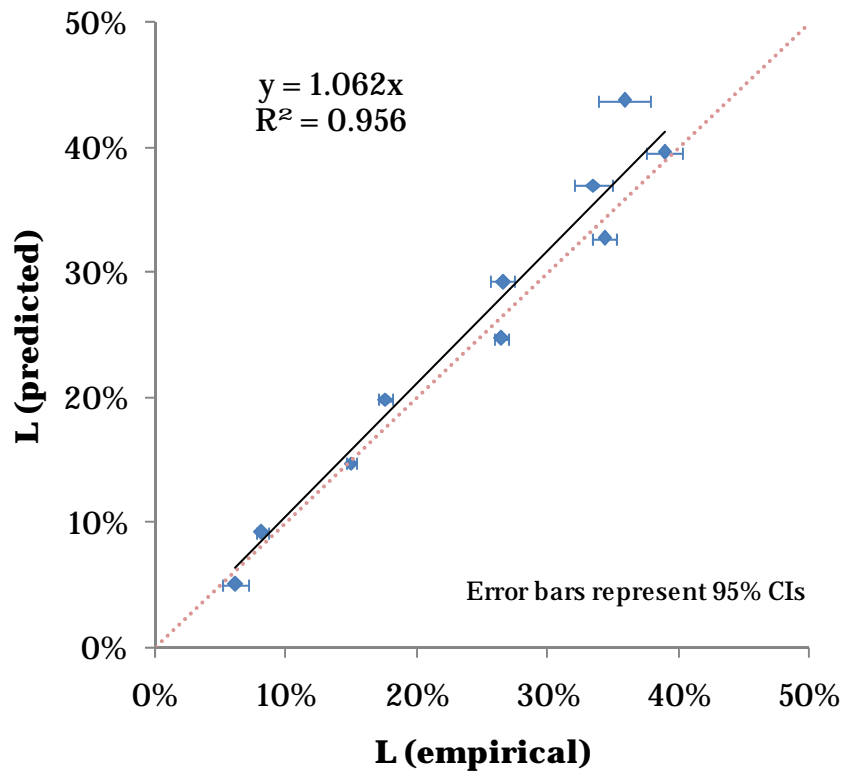
Grouped by 10 mm tumor size bins

Group	N	L empirical (SEM)	L predicted (SEM)	Difference (pred – emp)
1-10 mm	79542	7.89% (0.19%)	8.52% (0.02%)	0.64%
11-20 mm	153328	15.92% (0.16%)	16.79% (0.02%)	0.87%
21-30 mm	81722	26.57% (0.24%)	26.24% (0.03%)	-0.33%
31-40 mm	32763	34.02% (0.39%)	34.21% (0.05%)	0.19%
41-50 mm	15136	37.88% (0.58%)	41.28% (0.07%)	3.40%
<i>Mean (std. dev.)</i>				0.95% (1.44%)
<i>Mean weighted by N (std. dev.)</i>				0.59% (0.83%)
<i>Root Mean Square (std. dev.)</i>				1.60% (2.24%)
<i>Root Mean Square weighted by N (std. dev.)</i>				0.95% (1.18%)



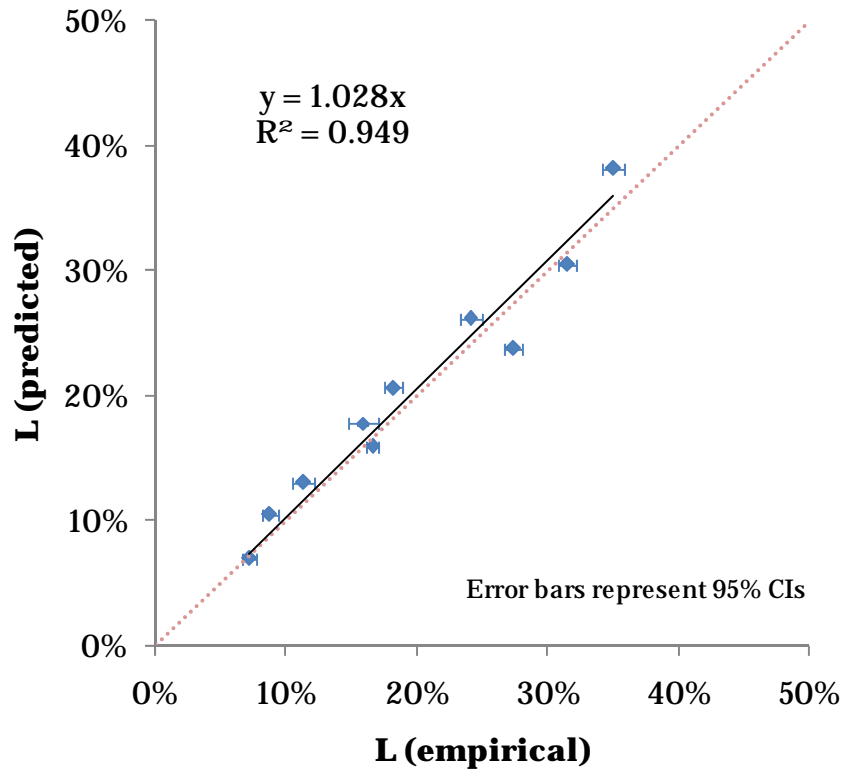
Grouped by 5 mm tumor size bins

Group	N	L empirical (SEM)	L predicted (SEM)	Difference (pred – emp)
1-5 mm	12919	6.08% (0.49%)	5.09% (0.04%)	-0.99%
6-10 mm	66623	8.15% (0.21%)	9.19% (0.02%)	1.04%
11-15 mm	91912	14.89% (0.20%)	14.75% (0.02%)	-0.14%
16-20 mm	61416	17.56% (0.29%)	19.85% (0.03%)	2.29%
21-25 mm	54761	26.43% (0.29%)	24.74% (0.03%)	-1.69%
26-30 mm	26961	26.54% (0.46%)	29.27% (0.05%)	2.73%
31-35 mm	21281	34.31% (0.45%)	32.72% (0.06%)	-1.59%
36-40 mm	11482	33.44% (0.77%)	36.97% (0.07%)	3.53%
41-45 mm	8985	38.90% (0.70%)	39.59% (0.09%)	0.68%
46-50 mm	6151	35.81% (1.04%)	43.76% (0.10%)	7.95%
<i>Mean (std. dev.)</i>				1.38% (2.93%)
<i>Mean weighted by N (std. dev.)</i>				0.63% (1.81%)
<i>Root Mean Square (std. dev.)</i>				3.10% (4.38%)
<i>Root Mean Square weighted by N (std. dev.)</i>				1.83% (2.15%)



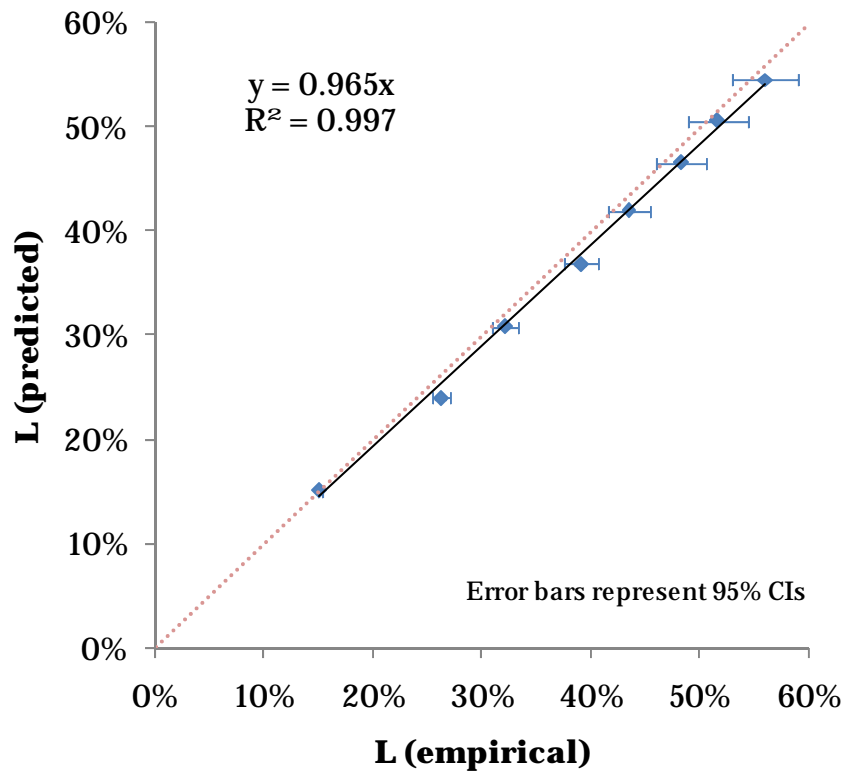
Grouped by 10% tumor size percentiles

Group	N	L empirical (SEM)	L predicted (SEM)	Difference (pred – emp)
1-8 mm	44510	7.16% (0.25%)	6.98% (0.02%)	-0.18%
9-10 mm	35032	8.76% (0.30%)	10.47% (0.03%)	1.72%
11-13 mm	36804	11.29% (0.39%)	13.04% (0.03%)	1.75%
14-15 mm	55108	16.59% (0.24%)	15.90% (0.03%)	-0.70%
16-17 mm	16894	15.81% (0.58%)	17.79% (0.05%)	1.97%
18-20 mm	44522	18.15% (0.33%)	20.63% (0.03%)	2.48%
21-23 mm	30854	27.40% (0.35%)	23.79% (0.04%)	-3.61%
24-27 mm	29468	24.07% (0.44%)	26.19% (0.05%)	2.12%
28-33 mm	33673	31.44% (0.37%)	30.46% (0.04%)	-0.98%
34-50 mm	35626	34.96% (0.41%)	38.13% (0.05%)	3.17%
<i>Mean (std. dev.)</i>				0.77% (2.08%)
<i>Mean weighted by N (std. dev.)</i>				0.70% (1.98%)
<i>Root Mean Square (std. dev.)</i>				2.12% (2.05%)
<i>Root Mean Square weighted by N (std. dev.)</i>				2.00% (1.98%)



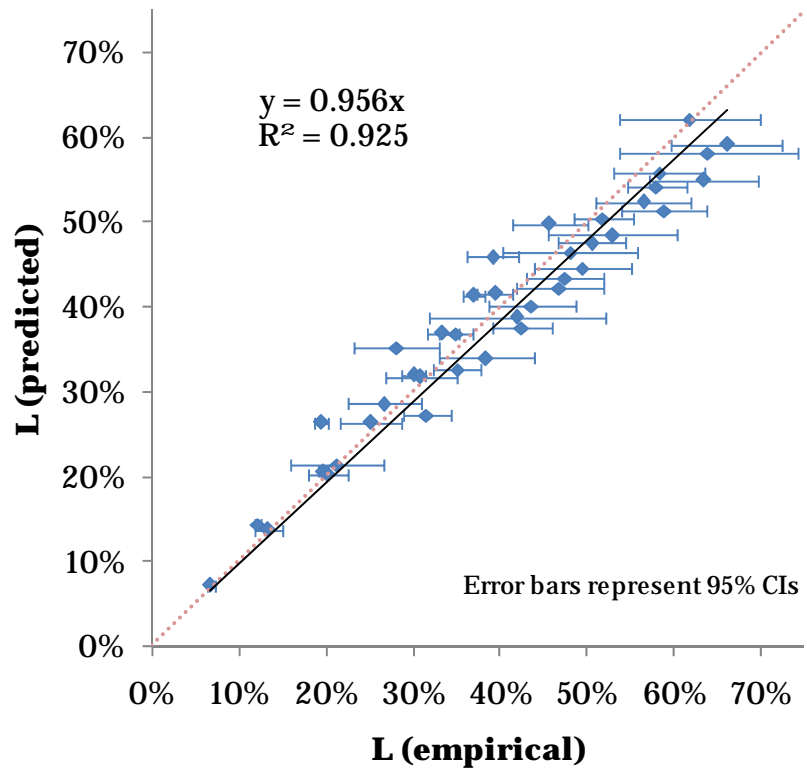
Grouped by number of positive lymph nodes

Group	N	L empirical (SEM)	L predicted (SEM)	Difference (pred – emp)
0	263544	15.09% (0.12%)	15.09% (0.01%)	0.00%
1	44002	26.21% (0.42%)	23.98% (0.03%)	-2.23%
2	21367	32.06% (0.59%)	30.81% (0.05%)	-1.25%
3	12319	39.05% (0.80%)	36.86% (0.06%)	-2.19%
4	7934	43.40% (0.98%)	41.98% (0.07%)	-1.41%
5	5699	48.28% (1.17%)	46.53% (0.07%)	-1.75%
6	4296	51.63% (1.38%)	50.63% (0.08%)	-1.00%
7	3330	55.99% (1.53%)	54.58% (0.08%)	-1.41%
<i>Mean (std. dev.)</i>				-1.41% (0.71%)
<i>Mean weighted by N (std. dev.)</i>				0.50% (0.71%)
<i>Root Mean Square (std. dev.)</i>				1.56% (1.32%)
<i>Root Mean Square weighted by N (std. dev.)</i>				0.83% (1.27%)



Permutations of 10 mm tumor size bins and number of positive lymph nodes

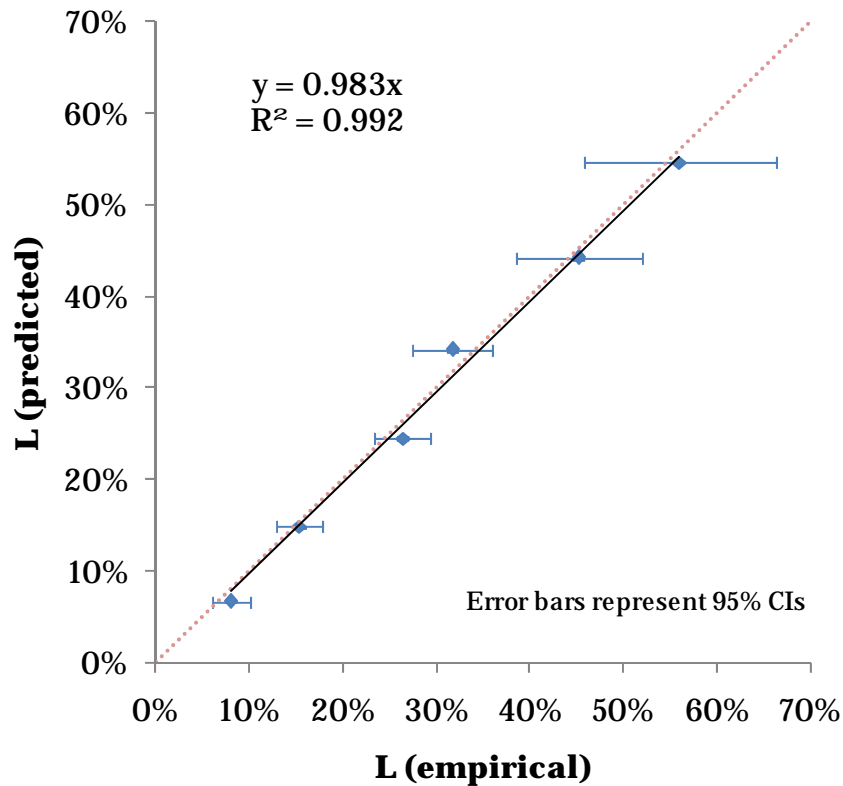
Group Size	Nodes	N	L empirical (SEM)	L predicted (SEM)	Difference (pred – emp)
1-10 mm	0	70435	6.77% (0.19%)	7.14% (0.01%)	0.37%
1-10 mm	1	5482	12.14% (0.17%)	14.30% (0.01%)	2.16%
1-10 mm	2	1806	19.64% (0.27%)	20.57% (0.01%)	0.93%
1-10 mm	3	740	19.39% (0.45%)	26.38% (0.02%)	6.99%
1-10 mm	4	453	30.01% (0.69%)	31.89% (0.03%)	1.87%
1-10 mm	5	285	34.87% (0.96%)	36.75% (0.02%)	1.88%
1-10 mm	6	208	37.00% (0.63%)	41.35% (0.02%)	4.34%
11-20 mm	0	115490	13.33% (0.82%)	13.66% (0.02%)	0.32%
11-20 mm	1	19148	20.12% (1.15%)	20.28% (0.03%)	0.16%
11-20 mm	2	8321	25.12% (1.81%)	26.27% (0.04%)	1.15%
11-20 mm	3	4188	30.86% (2.10%)	31.76% (0.03%)	0.91%
11-20 mm	4	2464	33.37% (0.97%)	36.83% (0.02%)	3.46%
11-20 mm	5	1623	39.40% (1.04%)	41.50% (0.02%)	2.10%
11-20 mm	6	1210	39.12% (1.49%)	45.84% (0.03%)	6.72%
11-20 mm	7	883	45.67% (2.21%)	49.76% (0.05%)	4.09%
21-30 mm	0	51410	21.24% (2.73%)	21.35% (0.05%)	0.11%
21-30 mm	1	12198	31.52% (1.40%)	27.20% (0.03%)	-4.32%
21-30 mm	2	6651	35.02% (1.41%)	32.54% (0.03%)	-2.48%
21-30 mm	3	4143	42.47% (1.78%)	37.49% (0.04%)	-4.98%
21-30 mm	4	2668	46.79% (2.56%)	42.12% (0.05%)	-4.67%
21-30 mm	5	2034	48.02% (3.95%)	46.37% (0.06%)	-1.66%
21-30 mm	6	1487	51.78% (1.76%)	50.34% (0.03%)	-1.44%
21-30 mm	7	1131	57.92% (1.74%)	54.06% (0.03%)	-3.86%
31-40 mm	0	18375	26.62% (2.16%)	28.52% (0.04%)	1.90%
31-40 mm	1	4997	38.34% (2.77%)	33.88% (0.06%)	-4.46%
31-40 mm	2	3096	41.88% (5.17%)	38.69% (0.07%)	-3.19%
31-40 mm	3	2157	47.38% (2.31%)	43.28% (0.04%)	-4.09%
31-40 mm	4	1501	50.48% (1.97%)	47.45% (0.03%)	-3.04%
31-40 mm	5	1082	58.78% (2.49%)	51.23% (0.05%)	-7.55%
31-40 mm	6	850	63.31% (3.18%)	54.82% (0.06%)	-8.49%
31-40 mm	7	705	63.84% (5.23%)	58.09% (0.08%)	-5.75%
41-50 mm	0	7833	28.03% (2.49%)	35.09% (0.04%)	7.05%
41-50 mm	1	2177	43.63% (2.51%)	40.07% (0.04%)	-3.55%
41-50 mm	2	1493	49.39% (2.83%)	44.47% (0.05%)	-4.93%
41-50 mm	3	1091	52.85% (3.81%)	48.42% (0.06%)	-4.43%
41-50 mm	4	848	56.40% (2.81%)	52.26% (0.04%)	-4.15%
41-50 mm	5	675	58.22% (2.67%)	55.74% (0.04%)	-2.48%
41-50 mm	6	541	66.03% (3.25%)	59.10% (0.05%)	-6.94%
41-50 mm	7	478	61.68% (4.14%)	62.01% (0.06%)	0.34%
<i>Mean (std. dev.)</i>					-1.02% (4.01%)
<i>Mean weighted by N (std. dev.)</i>					0.04% (1.87%)
<i>Root Mean Square (std. dev.)</i>					4.09% (4.28%)
<i>Root Mean Square weighted by N (std. dev.)</i>					1.84% (2.83%)



IV. Validation on the Partners dataset

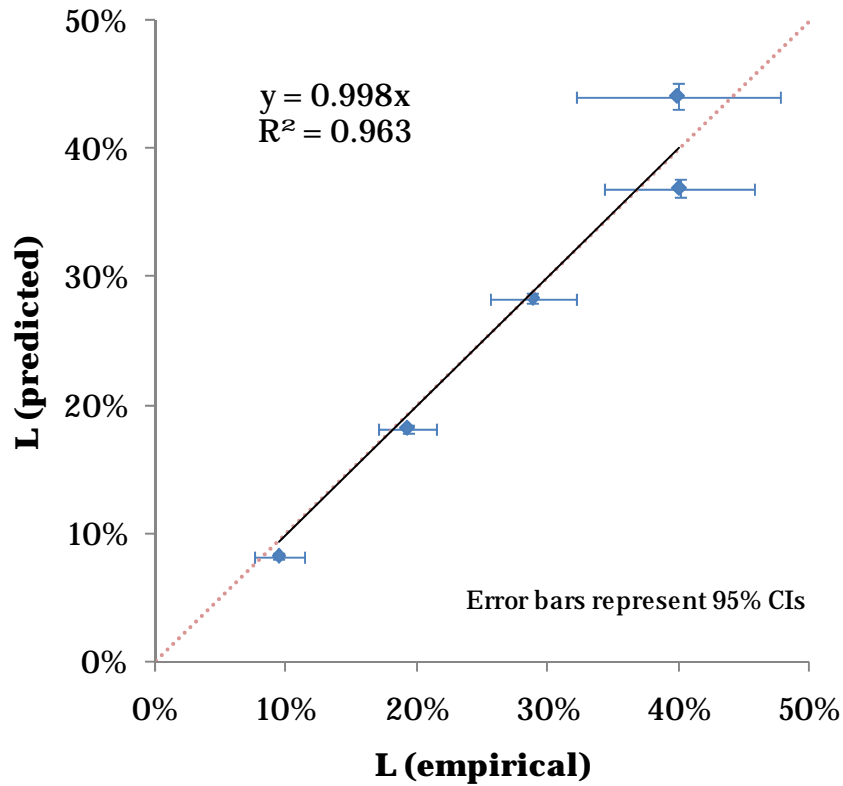
Grouped by 10% predicted lethality bins using the Size+Nodes equation

Group	N	L empirical (SEM)	L predicted (SEM)	Difference (pred – emp)
0-10%	2396	8.05% (1.01%)	6.67% (0.05%)	-1.38%
11-20%	2430	15.38% (1.22%)	14.86% (0.05%)	-0.52%
21-30%	1575	26.47% (1.53%)	24.50% (0.07%)	-1.96%
31-40%	906	31.74% (2.18%)	34.16% (0.09%)	2.41%
41-50%	414	45.24% (3.42%)	44.18% (0.14%)	-1.06%
51-63%	186	56.05% (5.26%)	54.64% (0.25%)	-1.41%
<i>Mean (std. dev.)</i>				-0.65% (1.57%)
<i>Mean weighted by N (std. dev.)</i>				-0.78% (1.55%)
<i>Root Mean Square (std. dev.)</i>				1.58% (1.42%)
<i>Root Mean Square weighted by N (std. dev.)</i>				1.61% (1.66%)



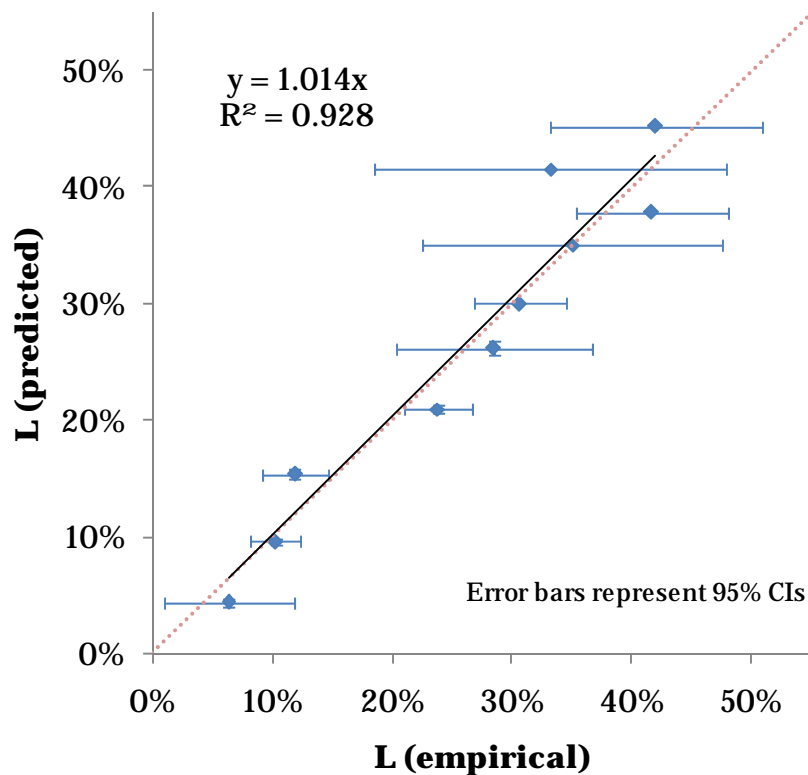
Grouped by 10 mm tumor size bins

Group	N	L empirical (SEM)	L predicted (SEM)	Difference (pred – emp)
1-10 mm	2591	9.41% (0.96%)	8.22% (0.11%)	-1.19%
11-20 mm	3004	19.29% (1.13%)	18.15% (0.15%)	-1.13%
21-30 mm	1499	28.83% (1.68%)	28.34% (0.22%)	-0.50%
31-40 mm	569	40.07% (2.92%)	36.92% (0.36%)	-3.15%
41-50 mm	244	39.91% (3.98%)	44.10% (0.53%)	4.19%
<i>Mean (std. dev.)</i>				-0.36% (2.73%)
<i>Mean weighted by N (std. dev.)</i>				-1.01% (1.14%)
<i>Root Mean Square (std. dev.)</i>				2.47% (2.74%)
<i>Root Mean Square weighted by N (std. dev.)</i>				1.44% (1.42%)



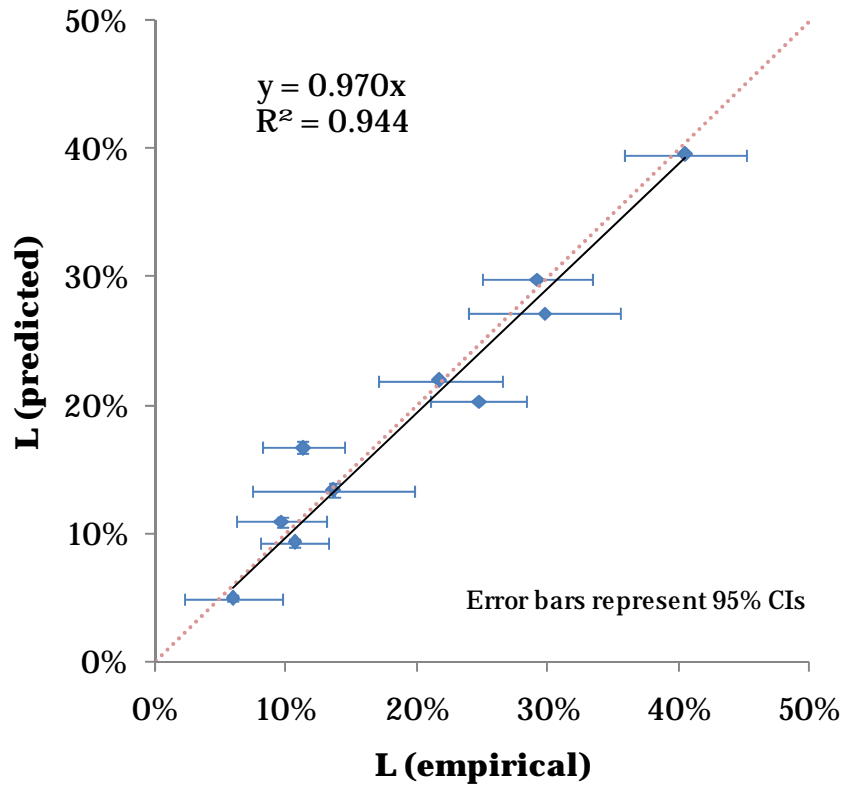
Grouped by 5 mm tumor size bins

Group	N	L empirical (SEM)	L predicted (SEM)	Difference (pred – emp)
1-5 mm	678	6.35% (2.78%)	4.39% (0.18%)	-1.97%
6-10 mm	1913	10.29% (1.06%)	9.58% (0.13%)	-0.71%
11-15 mm	1516	11.88% (1.43%)	15.40% (0.18%)	3.52%
16-20 mm	1488	23.82% (1.48%)	20.96% (0.20%)	-2.86%
21-25 mm	654	28.51% (4.18%)	26.20% (0.31%)	-2.31%
26-30 mm	845	30.66% (1.97%)	29.99% (0.29%)	-0.67%
31-35 mm	189	35.03% (6.37%)	35.00% (0.65%)	-0.04%
36-40 mm	380	41.65% (3.25%)	37.87% (0.42%)	-3.78%
41-45 mm	76	33.20% (7.53%)	41.53% (0.89%)	8.33%
46-50 mm	168	42.04% (4.49%)	45.26% (0.63%)	3.22%
<i>Mean (std. dev.)</i>				0.27% (3.71%)
<i>Mean weighted by N (std. dev.)</i>				-0.50% (3.10%)
<i>Root Mean Square (std. dev.)</i>				3.53% (4.54%)
<i>Root Mean Square weighted by N (std. dev.)</i>				2.98% (3.94%)



Grouped by 10% tumor size percentiles

Group	N	L empirical (SEM)	L predicted (SEM)	Difference (pred – emp)
1.00-6.00 mm	901	5.88% (1.91%)	4.95% (0.15%)	-0.93%
6.01-8.17 mm	979	10.61% (1.31%)	9.28% (0.18%)	-1.33%
8.18-10.00 mm	711	9.61% (1.74%)	10.92% (0.21%)	1.31%
10.01-12.00 mm	580	13.64% (3.15%)	13.36% (0.25%)	-0.28%
12.01-15.00 mm	936	11.28% (1.57%)	16.67% (0.24%)	5.39%
15.01-18.07 mm	909	24.71% (1.86%)	20.32% (0.26%)	-4.39%
18.08-20.00 mm	579	21.75% (2.39%)	21.95% (0.32%)	0.20%
20.01-27.78 mm	816	29.74% (2.96%)	27.15% (0.29%)	-2.58%
27.79-32.00 mm	727	29.16% (2.12%)	29.82% (0.31%)	0.66%
32.01-50.00 mm	769	40.46% (2.40%)	39.53% (0.32%)	-0.92%
<i>Mean (std. dev.)</i>				-0.29% (2.58%)
<i>Mean weighted by N (std. dev.)</i>				-0.32% (2.96%)
<i>Root Mean Square (std. dev.)</i>				2.46% (3.16%)
<i>Root Mean Square weighted by N (std. dev.)</i>				2.82% (3.72%)



Grouped by number of positive lymph nodes

Group	N	L empirical (SEM)	L predicted (SEM)	Difference (pred – emp)
0	5283	14.23% (0.77%)	13.06% (0.11%)	-1.17%
1	1186	25.14% (1.85%)	22.94% (0.22%)	-2.20%
2	597	31.52% (2.80%)	30.29% (0.27%)	-1.23%
3	332	39.37% (4.26%)	36.46% (0.36%)	-2.91%
4	193	44.73% (4.83%)	40.97% (0.44%)	-3.76%
5	124	47.16% (6.13%)	46.89% (0.53%)	-0.27%
6	113	44.52% (6.22%)	49.95% (0.54%)	5.43%
<i>Mean (std. dev.)</i>				-0.87% (3.02%)
<i>Mean weighted by N (std. dev.)</i>				-1.36% (2.04%)
<i>Root Mean Square (std. dev.)</i>				2.92% (3.23%)
<i>Root Mean Square weighted by N (std. dev.)</i>				2.33% (3.35%)

