



Wilson, T. G., Robinson, T., MacFarlane, C., Spencer, T., Herbert, C., Wade, L., Reed, H., & Braybrooke, J. P. (2020). Treating brain metastases from breast cancer: outcomes after stereotactic radiosurgery. *Clinical Oncology*. Advance online publication. <https://doi.org/10.1016/j.clon.2020.02.007>

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[10.1016/j.clon.2020.02.007](https://doi.org/10.1016/j.clon.2020.02.007)

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			Overall	ER+/HER2-	ER+/HER2+	ER-/HER2+	TNBC
<b>Patients</b>			91	31	14	30	16
<b>Median Age</b>			51	50.5	49.5	53	53.5
<b>Patients with systemic treatment data</b>			60	21	10	17	12
<b>Treatment prior to SRS</b>	Neo-Adjuvant	Taxane	5	1	1	3	0
		Anthracycline	8	2	1	3	2
		Other	1	1	0	0	0
	Adjuvant	Taxane	15	3	2	4	6
		Anthracycline	30	9	5	8	8
	Metastatic	Taxane	27	7	4	12	4
		Anthracycline	4	1	2	0	1
		Capecitabine	12	7	1	2	2
		Other	12	6	1	3	2
	Endocrine treatment	Adjuvant	20	15	5		
		Metastatic	15	12	3		
	Anti-HER2 therapy	Adjuvant	17		5	12	
		Metastatic	17		6	11	
	Lines of Metastatic chemotherapy	1	24	8	4	7	5
		2	8	1	3	4	0
3		5	1	0	2	2	
<b>Treatment post SRS</b>	Taxane		6	1	3	1	1
	Anthracycline		0	0	0	0	0
	Capecitabine		18	2	3	8	5
	Other		25	9	2	9	5
	No Chemotherapy		22	9	5	3	5
	Endocrine treatment		13	9	4		
	Anti-HER2 therapy		19		7	12	
	No Treatment		13	5	1	2	5
	Lines of Metastatic chemotherapy	1	29	9	3	13	4
		2	7	2	2	2	1
3		2	0	1	1	0	

Table 1 – Patient demographics including systemic treatments given prior to SRS treatment and post SRS treatment

Receptor Subgroup	Number of Patients (%)	Patients alive at time of analysis (%)	Median age (Range)	Presence of systemic disease at SRS (%)	Controlled systemic disease at SRS (%)	Median No. of BM treated (Range)	Median BM Volume treated in cm <sup>3</sup> (Range)
<b>ER+/HER2-</b>	31 (34)	2 (6.5)	50.5 (23-76)	27/31 (87)	7/27 (26)	2 (1-15)	2.4 (0.3-17.5)
<b>ER+/HER2+</b>	14 (15.4)	4 (28.6)	49.5 (31-70)	12/14 (86)	7/12 (58)	2 (1-8)	3.8 (0.5-16.2)
<b>ER-/HER2+</b>	30 (33)	6 (20)	53 (30-78)	23/30 (77)	16/23 (70)	2 (1-21)	3.5 (0.1-17.4)
<b>TNBC</b>	16 (14)	0 (0)	53.5 (30-76)	9/16 (56)	3/9 (33)	1 (1-16)	7.9 (0.1-19.9)
<b>Overall</b>	91	12 (13.2)	51 (23-78)	71/92 (77)	33/71 (46)	2 (1-21)	3.8 (0.1-24.5)

Table 2 – Patient demographics split by receptor subtype

Molecular Subgroup	Number of Patients	Time from diagnosis to develop brain metastases			Overall survival following SRS			
		Median (months)	Interquartile range (months)	Significant differences	Median OS (months)	Interquartile range (months)	Compared to TNBC pts	Compared to ER+HER2-pts
<b>ER+/HER2-</b>	31	79.3	39.9 – 135.8	p=0.036 (v TNBC)	13.8	7.0 – 22.6	p=0.025	NA
<b>ER+/HER2+</b>	14	68.6	25.1 – 114.8	p=0.045 (v TNBC)	21.4	9.4 – 34.9	P=0.0011	p=0.0499
<b>ER-/HER2+</b>	30	39.3	22.0 – 58.8		20.4	11.6 – 27.4	p=<0.0001	p=0.0242
<b>TNBC</b>	16	23.8	17.7 – 58.8		8.5	4.0 – 12.0	NA	p=0.025
<b>Overall</b>	91	45.7	23.4 – 91.9		15.9			

Table 3 - Time from diagnosis to development of brain metastases and overall survival following SRS treatment, split by receptor subtype

		<b>Number of Patients</b>	<b>Median OS (months)</b>	<b>Interquartile range (months)</b>	<b>Significant differences</b>
<b>Status of systemic disease at SRS</b>	<b>Intra-cranial disease only</b>	17	13.1	5.7 – 25.0	
	<b>Stable extra-cranial disease (SD)</b>	33	11.4	5.3 – 19.7	p=0.0011 (v PD)
	<b>Progressive extra-cranial disease (PD)</b>	30	20.1	10.2 – 31.2	p=0.0011 (v SD)
<b>Age</b>	<b>&lt;65 years old</b>	66	16.3	8.4 – 25.1	
	<b>&gt;65 years old</b>	25	11.4	5.1 – 20.3	
<b>Number of lesions treated</b>	<b>1</b>	39	18.1	8.6 – 27.3	
	<b>2 – 5</b>	33	10.1	5.4 – 22.9	
	<b>&gt;6</b>	19	18.3	8.1 – 23.4	
<b>Volume of lesions treated (cm<sup>3</sup>)</b>	<b>&lt;1</b>	24	22.6	15.7 – 27.4	p=<0.0001 (v >10)
	<b>1 - 5</b>	29	16.3	7.7 – 26.2	p=0.0015 (v >10)
	<b>5 - 10</b>	23	15.7	8.4 – 26.9	p=0.0023 (v >10)
	<b>&gt;10</b>	15	9.2	3.9 – 11.6	

Table 4 - Overall survival post-SRS split by status of systemic disease, age at the time of treatment and the total number and volume of cerebral metastases treated

Study	No. of patients	Median OS post-SRS (Months)	Positive predictive factors of improved OS post-SRS
<b>Kasad [9] 2009</b>	176	16	Age <50 years old (p=0.015), Karnofsky performance score >70 (p=0.021), ER+ (p=0.032) or HER2+(p=0.037) receptor status
<b>Jaboin [10] 2013</b>	100	12.3	Age <65 years old (p=0.01), Less than 3 brain metastases treated (p=<0.01)
<b>Vern-Gross [11] 2012</b>	154	8 (HER2-) 17 (HER2+)	HER2+ receptor status (p=0.007)
<b>Akywek [12] 2007</b>	49	19	Karnofsky performance score ≥90 (p=0.02), ER+ receptor status (p=0.04)
<b>Muacevic [13] 2004</b>	151	10	Karnofsky performance score ≥70 (p=0.04)
<b>Combs [14] 2004</b>	62	6.5	Age <40 years old (p=0.04)
<b>Firlik [15] 2000</b>	30	13	1 treated brain metastasis only (p=0.01)
<b>Mohammadi [16] 2016</b>	896 (166 Breast patients)	14.9	Tumours <1cm (p<0.001), Additional whole brain radiotherapy (p=0.001)
<b>Kondziolka [17] 2010</b>	350	11.2	Fewer brain metastases, Smaller total tumour volume treated, Smaller number of brain metastases treated, Higher Karnofsky performance score
<b>Karam [18] 2011</b>	441	4.5	Recursive partitioning analysis (RPA) which includes Karnofsky performance score and age (p=<0.001), 1 treated brain metastasis only (p=<0.001)
<b>Caballero [19] 2012</b>	310 (90 Breast patients)	8.4	Age <50 years old (p=0.002), Smaller total tumour volume treated (p=0.042), Higher Karnofsky performance score (p=<0.001)
<b>Yang [20] 2014</b>	136	17.6	Controlled extra-cranial disease (p=0.0007), ER+ or HER2+ receptor status (p=0.006), 1 treated brain metastasis only (p=0.02)
<b>Cho [21] 2015</b>	131	15.7	ER+ or HER2+ receptor status (p=0.022)
<b>Xu [22] 2012</b>	103	16 (Non-TNBC) 6 (TNBC)	ER+ or HER2+ receptor status, Higher Karnofsky performance score (p=0.053)

Table 5 – Summary of literature looking at factors affecting survival in metastatic breast cancer patients treated with stereotactic radiosurgery.

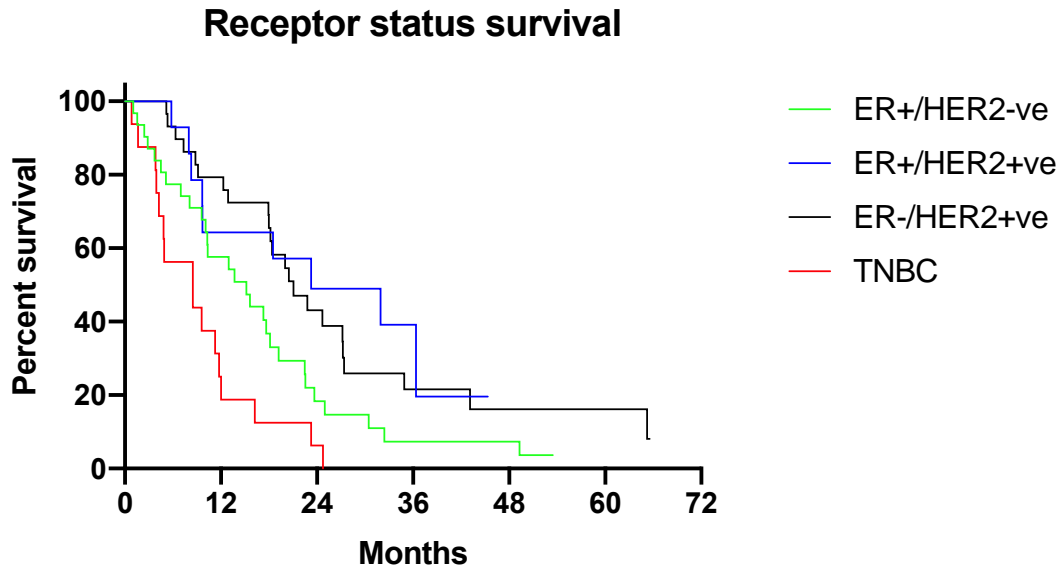


Figure 1 – Kaplan-Meier survival curve of patients post-SRS by receptor subtype

### Effect of extracranial disease on survival at time of SRS

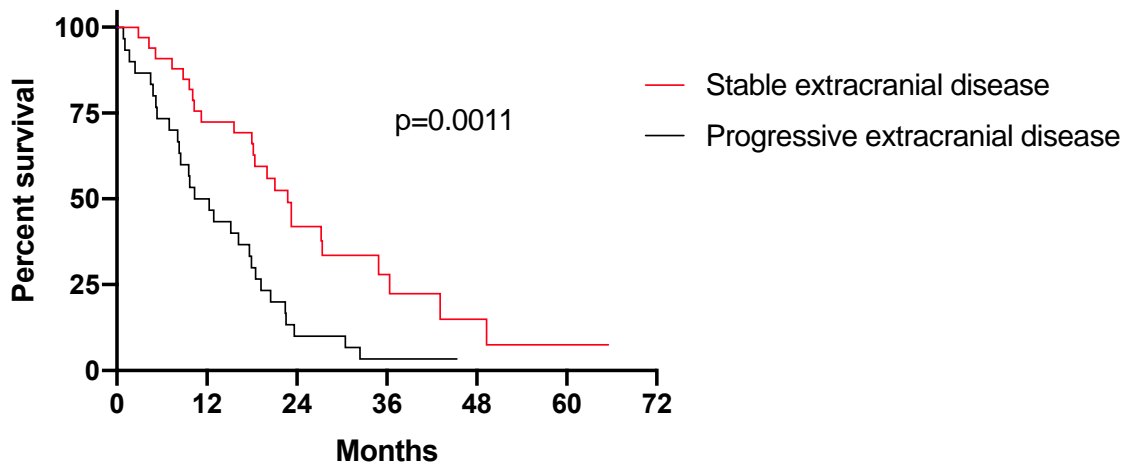


Figure 2 – Kaplan-Meier survival curve of patients post-SRS by disease status at the time of SRS treatment

### Survival and total volume of brain metastases

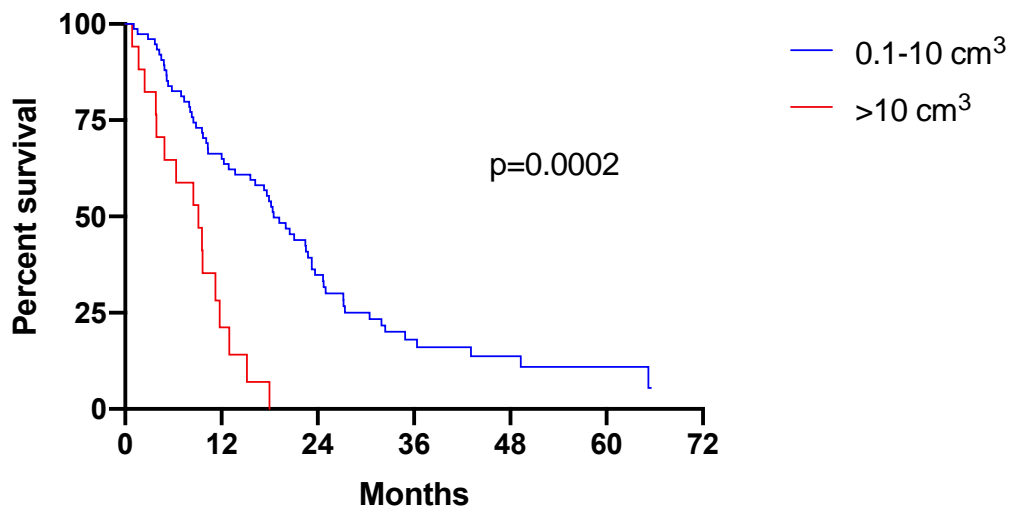


Figure 3 – Kaplan-Meier survival curve of patients post-SRS by the total volume of brain metastases treated