## Stereotactic radiosurgery for managing brain metastases in Victoria, 2012–2017

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he conventional treatment for brain metastases is whole brain radiotherapy (WBRT).<sup>1</sup> But there has been a gradual move to managing limited brain metastases with stereotactic radiosurgery (SRS),<sup>2</sup> and delaying or avoiding WBRT because of its effects on cognition and quality of life. Data on contemporary SRS practice for managing brain metastases in Australia are, however, very limited.<sup>3</sup>

We performed a population-based linkage study, analysing data from the Victorian Cancer Registry and the Victorian Radiotherapy Minimum Data Set (VRMDS). We included all patients with solid tumours (ICD-10 codes C00–C80), but excluding primary central nervous systems malignancies (ICD-10 codes C69–72), who received brain radiotherapy in Victoria between 1 January 2012 and 31 December 2017.

The primary outcome was the proportion of patients treated with SRS. Although SRS refers to large single fraction radiotherapy, patients treated with fractionated "stereotactic radiotherapy" were also classified as receiving SRS. In addition, because of potential coding inconsistencies, patients who had no more than four fractions of radiotherapy and were treated with "volumetric

modulated arc therapy" or "intensity modulated radiation therapy" were also classified as receiving SRS. Differences in factors of interest by SRS use were assessed in Pearson  $\chi^2$  (categorical variables) and Student t or Mann–Whitney U tests (continuous variables). Temporal changes were assessed with the Cochran–Armitage test for trend. Factors associated with SRS use were assessed by logistic regression, with year as an ordinal categorical variable; variables for which P < 0.10 in univariate analyses were included in the multivariate model. The study was approved by the Austin Health Human Research Ethics Committee (reference, LNR/18/Austin/34).

A total of 3961 patients who received radiotherapy for brain metastases were included, of whom 1116 (28%) received SRS. The proportion of patients receiving SRS increased from 27% (105 of 388) in 2012 to 35% (287 of 821) in 2017 (for trend: P < 0.001). The mean age of patients who received SRS (63.5 years; standard deviation [SD], 12.5 years) was lower than for those who did not (65.2 years; SD, 12.5 years). Factors that influenced SRS use included socio-economic status, primary cancer type (about half the patients with melanoma received SRS, and about one-quarter

## Baseline characteristics of 3961 patients who received radiotherapy for brain metastases, Victoria, 2012–2017 Stereotactic radiosurgery

	Stereotactic radiosurgery			
	Received	Not received	<ul> <li>Multivariable analysis: odds ratio (95%CI)</li> </ul>	P
Number of patients	1116 (28%)	2845 (72%)		
Age at first treatment for brain metastases (years)				
< 55	266 (33%)	543 (67%)	1	
55–59	157 (32%)	331 (68%)	1.11 (0.86–1.44)	0.42
60-64	161 (28%)	419 (72%)	0.89 (0.69-1.14)	0.35
65–69	177 (26%)	502 (74%)	0.85 (0.67–1.08)	0.19
70-74	153 (25%)	448 (75%)	0.88 (0.68-1.14)	0.33
75 or more	202 (25%)	602 (75%)	0.78 (0.62-0.99)	0.045
Mean (SD)	63.5 (12.5)	65.2 (12.5)	_	_
Sex				
Men	528 (28%)	1373 (72%)	_	_
Women	588 (29%)	1472 (71%)	_	_
Primary cancer type				
Lung	419 (24%)	1344 (76%)	1	
Breast	203 (28%)	512 (72%)	1.24 (1.00–1.53)	0.05
Melanoma	252 (47%)	277 (52%)	2.89 (2.32–3.59)	< 0.001
Gastrointestinal	93 (28%)	235 (72%)	1.37 (1.03–1.80)	0.028
Genitourinary	73 (28%)	189 (72%)	1.33 (0.97–1.80)	0.07
Other	76 (21%)	288 (79%)	0.80 (0.60–1.06)	0.12

Continues

Continued	Stereotactic radiosurgery			
	Received	Not received	<ul> <li>Multivariable analysis: odds ratio (95%CI)</li> </ul>	P
Socio-economic status (quintile)*				
1st (most disadvantaged)	188 (24%)	612 (77%)	1	
2nd	189 (27%)	501 (73%)	1.12 (0.87–1.44)	0.39
3rd	202 (26%)	572 (74%)	1.02 (0.79–1.30)	0.90
4th	220 (26%)	618 (74%)	0.90 (0.70-1.14)	0.38
5th (least disadvantaged)	317 (37%)	542 (63%)	1.19 (0.94–1.50)	0.14
Remoteness classification <sup>5</sup>				
Major city	780 (29%)	1949 (71%)	_	_
Inner regional	261 (26%)	732 (73%)	_	_
Outer regional/remote/very remote	75 (31%)	164 (69%)	_	_
Treatment institution type				
Public	744 (31%)	1656 (69%)	1	
Private	372 (24%)	1189 (76%)	0.10 (0.07-0.14)	< 0.001
Treatment institution location				
Metropolitan	1071 (34%)	2071 (66%)	1	
Regional	45 (5%)	774 (95%)	0.58 (0.49-0.68)	< 0.001
Year of first brain metastasis treatment				
2012	105 (27%)	283 (73%)	1	
2013	111 (25%)	342 (76%)	1.01 (0.72–1.41)	0.95
2014	147 (25%)	439 (75%)	0.86 (0.63–1.18)	0.35
2015	207 (25%)	633 (75%)	0.79 (0.59–1.06)	0.12
2016	259 (30%)	614 (70%)	1.10 (0.83–1.47)	0.50
2017	287 (35%)	534 (65%)	1.41 (1.06–1.88)	0.017

of patients with other cancer types), treatment institution type (public institutions, 31%; private institutions, 24%), and location (metropolitan centres, 34%; regional centres, 5%). Remoteness of patients' area of residence was not a significant factor. In multivariate analyses, age, primary cancer type, treatment centre type, and location were significant factors for SRS use (Box).

While the VRMDS captures all radiotherapy delivered in Victoria, it does not include data on patients' performance status, numbers of brain metastases, the extent of extracranial disease, and other factors that would allow evaluation of the appropriateness of SRS for individual patients. Another limitation is potential misclassification of radiotherapy classified as "SRS", as the VRMDS did not include data on radiotherapy dose.

As evidence supporting the use of SRS for managing brain metastases grows, we would expect SRS rates to rise. <sup>6,7</sup> While SRS was

less frequently used in regional centres, patients living in regional areas were as likely to receive SRS as patients living in metropolitan areas. It is nevertheless important to ensure easy and convenient access to SRS services for all cancer patients in Victoria.

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- 1 Tsao MN, Xu W, Wong RK, et al. Whole brain radiotherapy for the treatment of newly diagnosed multiple brain metastases. *Cochrane Database Syst Rev* 2018; CD003869.
- 2 Sahgal A, Ruschin M, Ma L, et al. Stereotactic radiosurgery alone for multiple brain metastases? A review of clinical and technical issues. *Neuro Oncol* 2017; 19 (Suppl 2): ii2–ii15.
- 3 Ong WL, Wada M, Ruben J, et al. Contemporary practice patterns of stereotactic radiosurgery for brain metastasis: a review of published Australian literature. J Med Imaging Radiat Oncol 2019; 63: 711–720.
- 4 Australian Bureau of Statistics. 2033.0.55.001.
  Census of Population and Housing: SocioEconomic Indexes for Areas (SEIFA), Australia,
  2016: IRSD. Updated Mar 2018. https://www.
  abs.gov.au/ausstats/abs@.nsf/Lookup/by%20
  Subject/2033.0.55.001-2016~Main%20Features
  ~IRSD~19 (viewed Jan 2020).
- 5 Australian Bureau of Statistics. Australian Statistical Geography Standard. (ASGS). Updated July 2018. https://www.abs.gov.au/websitedbs/ D3310114.nsf/home/Australian+Statistical+Geogr aphy+Standard+(ASGS) (viewed Jan 2020).
- 6 Kann BH, Park HS, Johnson SB, et al. Radiosurgery for brain metastases: changing practice patterns and disparities in the United States. *J Natl Compr Canc Netw* 2017; 15: 1494–1502.
- 7 Halasz LM, Weeks JC, Neville BA, et al. Use of stereotactic radiosurgery for brain metastases from non-small cell lung cancer in the United States. *Int J Radiat Oncol Biol Phys* 2013; 85: e109–e116. ■