Using stereotactic radiation therapy to treat oligometastasis

What is oligometastasis?

- Oligometastatic disease has been described as an intermediate state of cancer spread between localised disease and widespread metastases[1,2]

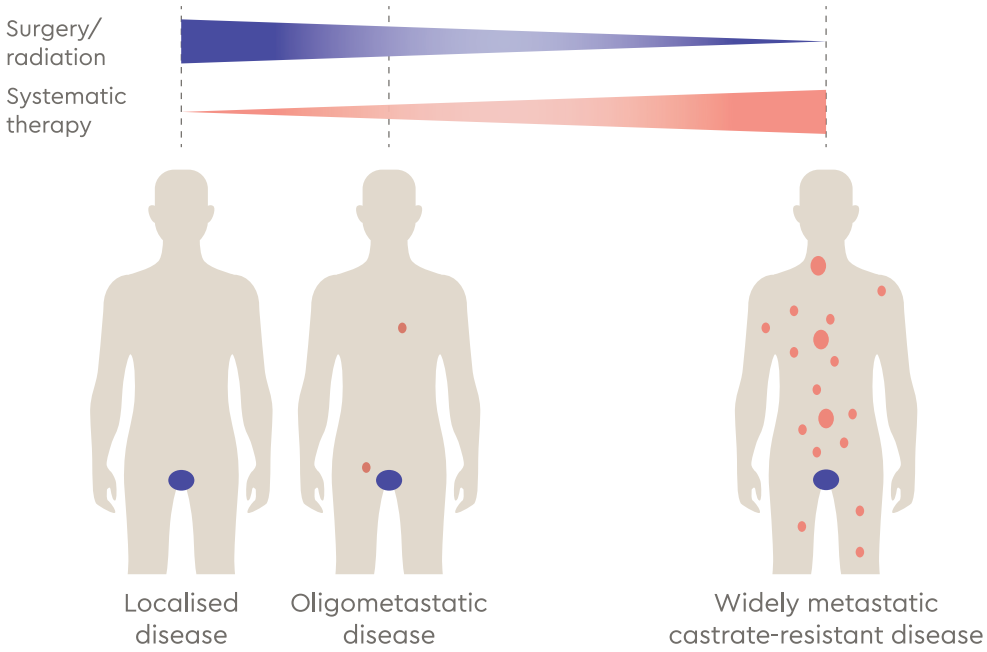


Figure 1: Example of oligometastatic disease in prostate cancer[3]

- Metastatic tumours are conventionally treated with palliative intent, as they are usually deemed incurable[4]
- There is good evidence to suggest improved disease-free survival if all lesions are eradicated using aggressive local therapy[4]
- Stereotactic radiation therapy is a viable non-invasive treatment option for patients with one to five metastases at multiple organ locations[5,6]
- A review of stereotactic body radiation therapy (SBRT*) used to treat patients with one to five extracranial oligometastases showed better progression free survival (PFS) and overall survival (OS) with ≤3 compared to 4–5 metastases[6]
- SBRT has also been used to treat various sites of oligometastases (mainly liver, lung and lymph nodes) in a wide variety of primary tumours with a median overall survival rate of 2.4 years and the survival rates are shown in **Table 1**[7]

Table 1:

Survival rates	
1 year	80%
3 years	39%
5 years	23%
7.5 years	12%

Univariate analysis of survival in the total cohort[7]

Covariate categories (n)	Median OS years (95% CI)	HR (95% CI)	p-value
Cancer type			
Colorectal (201)	2.4 (2.0 - 2.7)	0.84 (0.63 - 1.11)	0.22
Lung (32)	1.5 (1.2 - 2.5)	-	-
Renal (17)	2.4 (1.1 - 3.1)	-	-
Breast (12)	6.1 (1.5 - 9.6)	-	-
Others (59)	-	-	-
Number of metastases			
1 metastasis (162)	2.5 (1.9 - 3.2)	0.81 (0.61 - 1.06)	0.12
2-6 metastases (159)	2.3 (2.0 - 2.6)		

*Throughout this paper, the use of stereotactic body radiation therapy (SBRT) is interchangeable with stereotactic ablative body radiation therapy (SABR).

Local consolidative therapy versus maintenance therapy or observation for patients with oligometastatic non–small-cell lung cancer[8]

- Local consolidative therapy ± maintenance therapy improved PFS in NSCLC patients with ≤3 metastases vs maintenance therapy alone (median PFS 14.2 vs 4.4 months; HR 0.57, P = 0.022)[8]
- The median time to appearance of new lesions was 14.2 months in the LCT group (95% CI, 5.7 to 24.3 months) versus 6.0 months in the MT/O group (95% CI, 4.4 to 8.3 months; P = 0.11)[8]
- The median OS time for all patients was 37.7 months (95% CI, 16.6 to 41.2 months). OS time was significantly longer in the LCT group (median, 41.2 months; 95% CI, 18.9 months to not reached) than in the MT/O group (median, 17.0 months; 95% CI, 10.1 to 39.8 months; P = .017)[8]

NB: This trial had mixed RT dose/fractionations also including conventional external beam radiation therapy.

Figure 2:

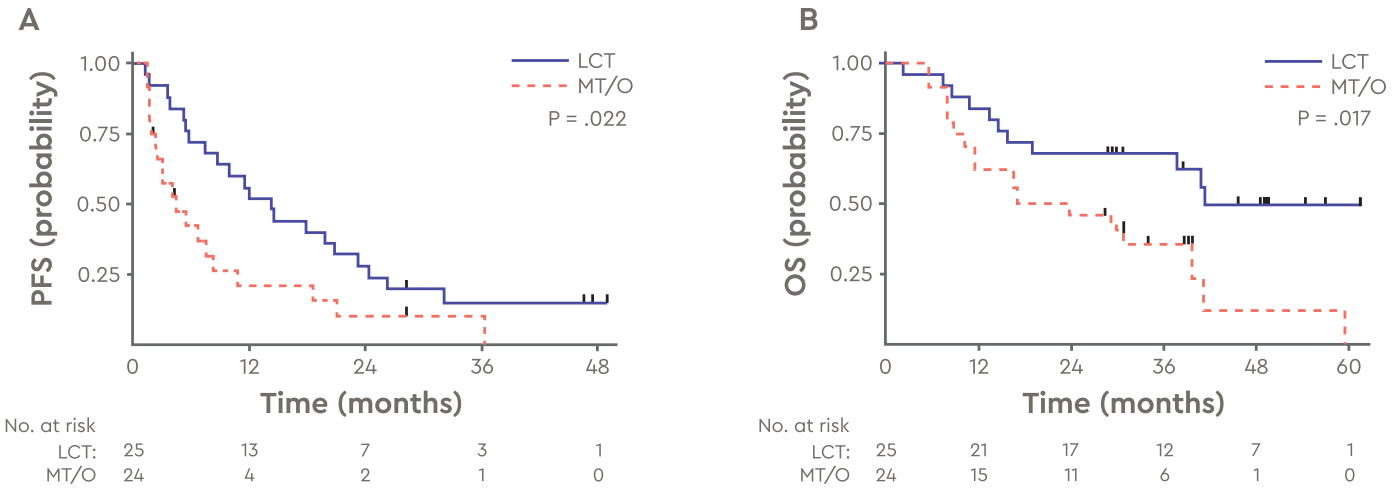


Figure 2: (A) Progression-free survival (PFS) and (B) overall survival (OS) in patients given local consolidative therapy (LCT) or maintenance therapy observation (MT/O) for oligometastatic non-small-cell lung cancer[8]

SBRT in lung oligometastases[9]

- SBRT is being increasingly used for patients with pulmonary oligometastases. Numerous single institution case series and cohort studies have been published and more recently a systematic review of 29 publications from 20 institutions of either single dose SBRT or fractionated SBRT for lung metastases was undertaken by Siva and colleagues[9]

Results were as follows:

	Comparative arms	2-year local control	2-year overall survival	Grade 3 toxicity
Single dose SBRT	n = 154	78.6%	50.3%	2.6%
Fractionated SBRT	n = 334	77.9%	53.7%	4%

- It was concluded that despite insufficient evidence to recommend a consensus view for optimal tumour parameters, dose fractionation and technical delivery of treatment, high local control rates that could potentially lead to a survival benefit justified the consideration of stereotactic radiotherapy for patients with limited pulmonary oligometastases[9]

Subsequent reviews of SBRT for oligometastatic cancer and pulmonary oligometastases suggest the following:

Local control and overall Survival[10]

Patients treated with SBRT typically achieve similar results to those with pulmonary metastatectomy:

- **2-year local control** 94% vs 90%
- **5-year overall survival** 49% vs 41%

SBRT indications complementary to surgery[4]

Deep parenchymal tumours: SBRT may be complementary or preferred to surgical resection.

Reduce the risk of intrapulmonary metastases: Patients may benefit from receiving SBRT upfront, with surgery reserved as salvage.

Synchronous bilateral pulmonary metastases: A hybrid approach using SBRT for one side and surgery for the other can be considered.

SABR versus standard of care palliative treatment in patients with oligometastatic cancers[11]

- SABR COMET was a randomised phase II trial comparing SABR for oligometastases (defined as 1–5 metastases) versus standard of care in patients with varied primary malignancies[11]
- The predominant primary cancers included breast, colorectal, lung and prostate and 92% of patients treated with SABR had 3 or less metastases[11]
- A significant proportion of the patients in the SABR arm (43%) had lung metastases[11]

Conclusion:

- There was an improvement in median overall survival from 28 to 41 months (p=0.09) and median progression free survival from 6 to 12 months in the SABR arm (p=0.012)[11]
- There were three treatment related deaths (4.5%) including radiation pneumonitis, pulmonary abscess and a subdural haemorrhage after surgery to repair a SABR related perforated gastric ulcer[11]

Figure 3A: overall survival

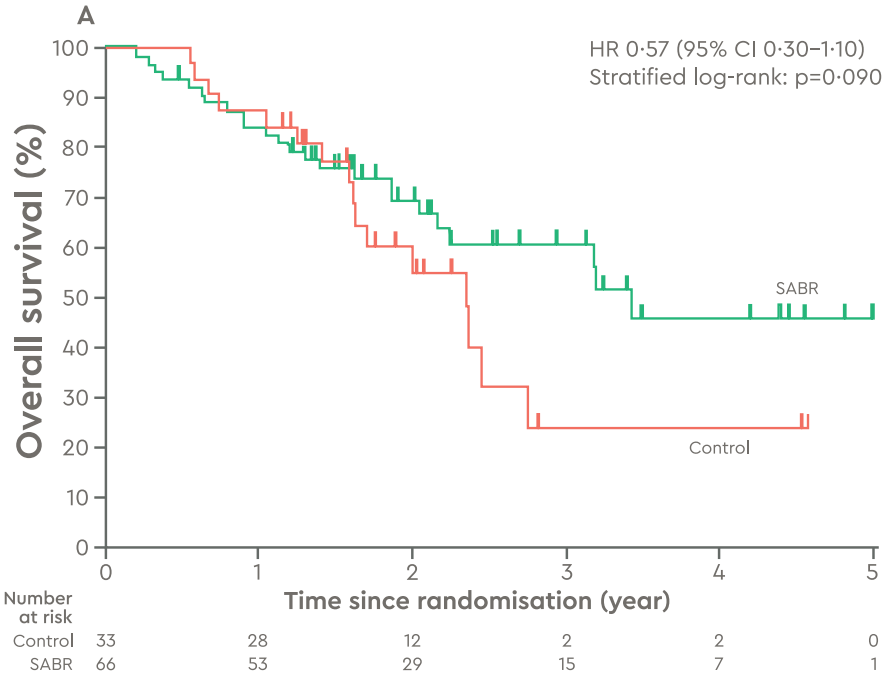
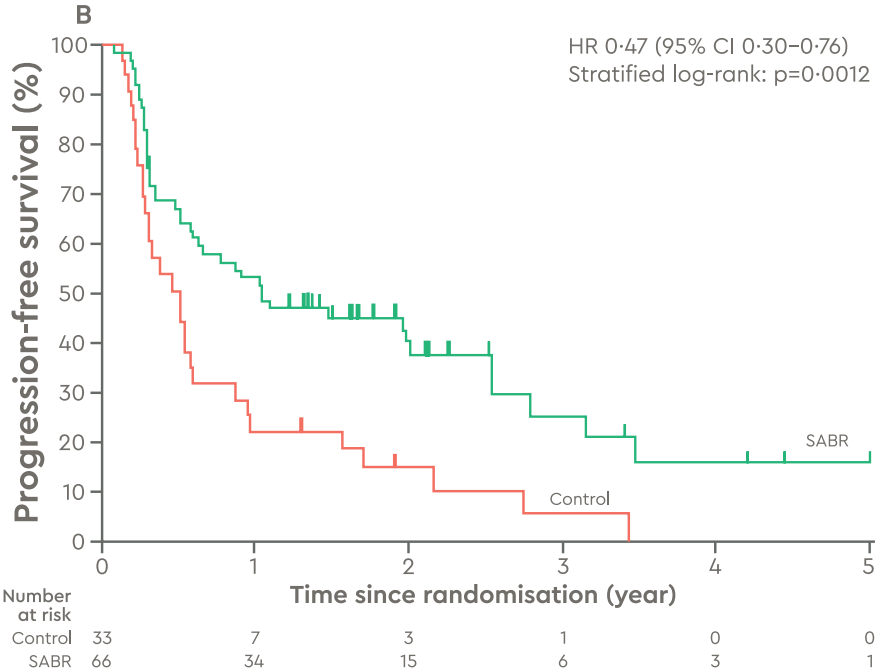


Figure 3B: progression free survival



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