EFFICACY AND SAFETY OF STEREOTACTIC BODY RADIOTHERAPY FOR UNRESECTABLE LIVER METASTASES

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INTRODUCTION

• Liver Metastases Burden: <20% of liver metastases patients are eligible for curative surgical resection at initial presentation.

• Role of SBRT: Technical advancements in respiratory motion management (4DCT, ABC) and linear accelerator (IGRT, high-definition MLC) enable ablative dose delivery while sparing adjacent liver parenchyma.

• Clinical Context: SBRT remains underutilized in regional workflows relative to systemic therapy, requiring dedicated local efficacy and prognostic validation.

OBJECTIVES

• Primary Objective: Local Control (LC) and Overall Survival (OS) rates

• Secondary Objective: Treatment safety and toxicities

• Exploratory Objective: Independent clinical/radiological prognostic factors

MATERIALS & METHODS

• Study Cohort: Patients with unresectable liver metastases treated across Prince of Wales Hospital and Queen Mary Hospital (Jan 2015 – Dec 2023).

• Treatment Planning & Delivery: Varian Eclipse TPS; 4DCT simulation, motion management (ABC, compression, or shallow breathing); Varian TrueBeam with coplanar VMAT arcs; daily CBCT.

• Data Collection: Radiotherapy plan details were collected directly from the Varian Eclipse Treatment Planning System. Patients' demographics, disease information, and clinical notes were collected from the Clinical Management System.

•Statistics: Kaplan-Meier survival curves for LC/OS rates; Cox proportional hazards model for subgroup analysis.

53 Patients with 72 treated liver metastases

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Inclusion Criteria

1. Any histologically confirmed malignancy with liver metastases. While histological confirmation via direct biopsy of the liver lesions was not necessary, secondary diagnostic investigations, such as PET/CT and MRI, were required to confirm the diagnosis of liver metastases.
2. Treatment plans should be discussed in a multidisciplinary team meeting which consensus designated the metastases as unresectable.

Exclusion Criteria

1. Previously received other kinds of local therapy for liver metastases, for example, surgery, radiofrequency ablation, and microwave ablation

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RESULTS

A total of 52 patients with 71 treated liver metastases were included.

Treatment Efficacy

• Local Control (LC): Median LC duration was 24.5 months (range: 1–125 months). 1-Year LC: 77.0% | 2-Year LC: 67.3%.

• Overall Survival (OS): Median OS duration was 26.0 months (range: 3–125 months). 1-Year OS: 84.6% | 2-Year OS: 61.5%.

• Failure Patterns: In-field local recurrence in 15 (28.8%); out-field intrahepatic failure in 21 (40.4%); extrahepatic progression in 34 (65.4%).

Treatment Safety (RTOG CRITERIA)

• Low-Grade Events: Grade 1 Nausea / Vomiting: 8 (15.4%) | Grade 1 Fatigue: 5 (9.6%) | Grade 2 Gastritis: 1 (1.9%).

• High-Grade Toxicity: 0% Grade 3 or Grade 4 toxicities across the entire cohort.

Parameter	Value [Median (Range) / N (%)]
Age	64 years (40–88 years)
Gender Distribution	Male: 25 (48.1%) | Female: 27 (51.9%)
Primary Cancer Types	Colorectal: 16 (30.8%) | Breast: 11 (21.2%) | Lung: 10 (19.2%) | NPC: 4 (7.7%) | Others: 11 (21.1%)
Simultaneous Metastases	Lymph Node: 47 (90.4%) | Bone: 18 (34.6%) | Lung: 11 (21.2%) | Adrenal: 4 (7.7%)
Lesions Treated per Patient	1 lesion: 39 (75.0%) | 2 lesions: 9 (17.3%) | ≥ 3 lesions: 4 (7.7%)
GTV Volume	8.185 cm^3 (0.03 – 268.19 cm^3)
PTV Volume	28.955 cm^3 (3.84 – 762.65 cm^3)
Prescribed Dose / BED10	Prescribed Dose: 45 Gy (27.5–50 Gy) BED10: 100 Gy (37.5–112.5 Gy)
Fractionation	3 fractions: 32 (61.5%) 5 fractions: 20 (38.5%)
Systemic Treatment	Prior: 44 (84.6%) Subsequent: 33 (63.5%)

Table 1: Patient Demographic & Treatment Characteristics (N = 52)

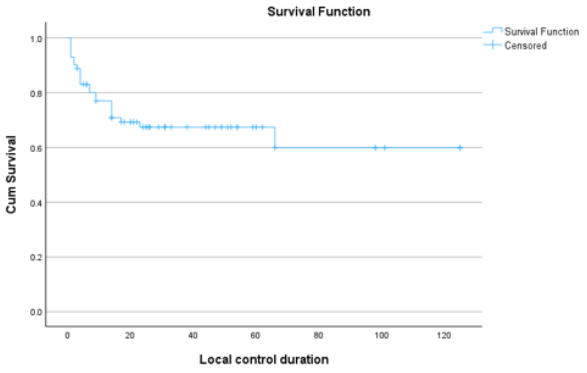


Figure 1: Kaplan-Meier Survival Curve: Local Control

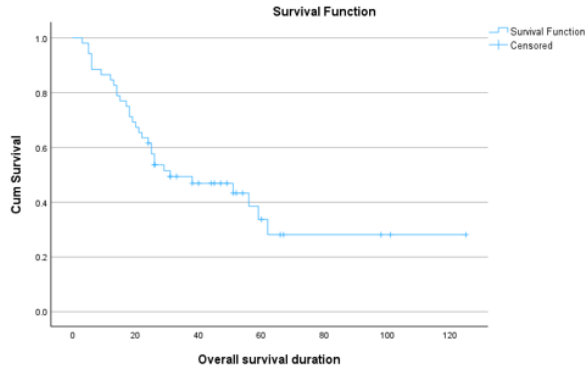


Figure 2: Kaplan-Meier Survival Curve: Overall Survival

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RESULTS

- Local Control (LC) Predictors: GTV volume was significant on univariate analysis (p = 0.019) but failed to maintain independent significance in the multivariate analysis (p = 0.068, HR = 1.007, 95% CI: 0.999–1.016).
- Overall Survival (OS) Predictors: Primary cancer type overall p = 0.057. Primary breast cancer demonstrated a statistically significant survival benefit compared to colorectal cancer (p = 0.032, HR = 0.087, 95% CI: 0.009–0.812).

Univariate and multivariate analyses for local control

	Univariate analysis		Multivariate analysis	
Variable	p-value	HR	95% CI	p-value
Age at treatment	0.517	-	-	-
Primary cancer type	0.587	-	-	-
Colorectal vs Breast	-	-	-	-
Colorectal vs Lung	-	-	-	-
Colorectal vs Others	-	-	-	-
Simultaneous extrahepatic metastasis	0.132	1.832	0.777-4.318	0.167
Site of tumour (Liver segment)	0.561	-	-	-
Affected liver side	0.578	-	-	-
Systemic therapies prior to SBRT	0.897	-	-	-
GTV	0.019	1.007	0.999-1.016	0.068
PTV	0.480	-	-	-
BED_{10}	0.727	1.006	0.988-1.025	0.487
Subsequent systemic therapies after SBRT	0.433	0.774	0.321-1.868	0.569

Abbreviations: CI, confidence interval; SBRT, stereotactic body radiotherapy; GTV, gross tumour volume; HR, hazard ratio; PTV, planning target volume; BED, biologically effective dose

Table 2: Univariate and Multivariate Analysis for Local Control

Univariate and multivariate analyses for overall survival

	Univariate analysis		Multivariate analysis	
Variable	p-value	HR	95% CI	p-value
Age at treatment	0.016	1.025	0.980-1.073	0.275
Primary cancer type	0.042	-	-	0.057
Colorectal vs Breast	-	0.087	0.009-0.812	0.032*
Colorectal vs Lung	-	1.290	0.320-5.211	0.720
Colorectal vs Others	-	0.458	0.136-1.536	0.206
Simultaneous extrahepatic metastasis	0.891	1.156	0.373-3.585	0.802
Number of liver metastases	0.667	-	-	-
Site of tumour (Liver segment)	0.961	-	-	-
Affected liver side	0.930	-	-	-
Systemic therapies prior to SBRT	0.128	1.141	0.352-3.702	0.826
GTV	0.303	-	-	-
PTV	0.024	1.002	0.998-1.006	0.249
BED_{10}	0.145	0.993	0.979-1.008	0.350
Subsequent systemic therapies after SBRT	0.050	0.598	0.249-1.439	0.251

Abbreviations: CI, confidence interval; SBRT, stereotactic body radiotherapy; GTV, gross tumour volume; HR, hazard ratio; PTV, planning target volume; BED, biologically effective dose

Table 3: Univariate and Multivariate Analysis for Overall Survival

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DISCUSSION & LIMITATIONS

• Technological Impact: Literature using rigid motion control (CyberKnife Synchrony, MR-guided online adaptive and intra-fraction monitoring) reports higher LC rates (82–94%) compared to the present study. It may indicate that the implementation of state-of-the-art radiotherapy technologies improves local tumor control by delivering ablative radiation doses precisely to the target while sparing surrounding normal tissues.

• Prognostic Driver: Given that the present study illustrated that SBRT achieves consistent local control efficacy regardless of primary cancer type, the OS advantage observed in the breast cancer cohort suggests that OS is governed by the underlying systemic tempo of the disease and the efficacy of systemic treatments.

• Limitations: The single-arm retrospective design prevents causal claims; the modest sample size limits statistical power to detect subtle multivariate predictors.

Study	Mahadevan et al, 2018	Anstadt et al, 2019	Ugurluer et al, 2021	Voglhuber et al, 2021	Choi et al, 2023	Seyfried et al, 2025	Present study
Number of patients	427	42	21	115	31	76	52
Number of liver metastases	568	81	24	150	NR	101	71
Age, median (range)	67 (31-91)	65 (39-87)	62 (42-86)	65 (34-86)	66 (48-81)	66 (32-93)	64 (40-88)
Primary cancer type	Mixed	Mixed	Mixed	Mixed	Mixed, majority colorectal	Mixed	Mixed
Prescription	12-60 Gy in 1-5 fractions	14-20 Gy in 3 fractions	40-60 Gy in 3-8 fractions	12-60 Gy in 2-16 fractions	24-48 Gy in 3/6 fractions	30-66 Gy in 3-12 fractions	27.5-50Gy in 3/5 fractions
Median BED10	100 Gy	NR	100 Gy	59.5 Gy	76.8 Gy	84.38 Gy	100 Gy
1-year LC rate	84%	86%	89.70%	82%	94%	82.50%	77%
2-year LC rate	72%	80%	64.60%	77%	55%	82.50%	67.30%
1-year OS rate	74%	72%	93.30%	72%	89.60%	74.10%	84.60%
2-year OS rate	49%	62%	NR	45%	57.10%	NR	61.50%
≥ grade 3 toxicities	0	0	0	10 patients (cholestasis, cholangitis, subileus, esophageal stenosis, liver abscess)	0	3 patients (cholestasis, fivefold elevation in transaminases, superinfection)	0
Radiotherapy technique	CyberKnife Stereotactic Radiosurgery System with Synchrony Respiratory Motion Tracking System	CyberKnife Stereotactic Radiosurgery System with Synchrony Respiratory Motion Tracking System	Stereotactic MR-guided online adaptive radiation therapy. Real-time MR imaging for intra-fraction monitoring and gating.	Image guided stereotactic body radiotherapy with abdominal compression	Image guided stereotactic body radiotherapy with abdominal compression or ABC	Image guided stereotactic body radiotherapy combined with iBH using a surface-guided RT (SGRT) system.	Image guided stereotactic body radiotherapy with voluntary shallow breathing, ABC or abdominal compression.

Table 4: A comparative synthesis against established literature

CONCLUSION

• Clinical Conclusion: SBRT is an effective and safe liver-directed therapy, achieving high local control and overall survival with an outstanding safety profile (0% ≥ Grade 3 toxicity).

• Future Research: Exploratory subgroup findings highlight the need for larger prospective randomized trials integrating SBRT with modern systemic regimens.

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