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Patterns of care and outcome of liver SBRT: results from a multicentre National quality project

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Abstract

Background Stereotactic body radiotherapy (SBRT) is applied for both primary liver tumours and liver metastases. Within a national project, we investigated patterns of care for liver SBRT and factors influencing local control (LC) and overall survival (OS).

Methods Patients treated with SBRT were prospectively registered within a quality assurance project. Patient- and tumour-related factors, and data on use of markers, personalised immobilisation, image guidance and radiotherapy techniques were collected. OS and LC were evaluated by Kaplan-Meier analysis and Cox proportional hazard models.

Results From August 2013 to December 2019, fourteen centres treated 352 patients with SBRT for a total of 408 lesions (66 primary, 342 metastases). Colorectal adenocarcinoma was the most common primary cancer ($n = 170$, 42%). A gradual uptake of SBRT and increasing prescription dose were observed over time. One, 2- and 5- year OS probabilities were 74.3%, 49.7% and 19.4%. LC data were available for 354 lesions. LC probabilities at 1-, 2- and 5-years were 69.9%, 52.2% and 32.4%. Better OS and LC were found for patients with smaller PTV volumes and higher BED10. Patients with better performance status had a better OS. A better LC was observed in patients who were not priorly treated with systemic therapy.

Conclusions We observed an increase in liver SBRT uptake and a reasonable LC and OS. Higher BED10 and smaller PTV volumes translated into high local tumour control and survival. After correction of patient case-mix, none of the technical parameters showed a significant association with outcome.

Trial registration Not applicable, this is a retrospective analysis of data that were prospectively registered as part of a national quality assurance programme of the Belgian Cancer Registry.

Keywords Stereotactic body radiotherapy, Liver metastases, Hepatocellular carcinoma, National registry

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Background

The liver is a common site for metastatic spread of various tumours. A retrospective registry study demonstrated that 5.14% of cancer patients present with liver metastases at initial diagnosis, with the highest incidence in pancreatic and colorectal cancer [1]. Since Hellman and Weichselbaum changed the historical concept of metastatic disease as an incurable state proposing an intermediate stage of 'oligo-metastatic disease', therapeutic approaches have shifted from systemic and palliative to more aggressive local therapies [2, 3]. Recent prospective trials indeed demonstrated a benefit of metastasis-directed therapies in low-volume metastatic disease [4, 5]. Resection remains the gold standard local treatment for liver metastases, but only 10–20% of patients are candidates for surgery due to comorbidities, unfavourable liver involvement, uncontrolled primary or extrahepatic disease [6]. Local therapies for patients who are not candidates for resection include local ablation, irreversible electroporation, HIFU, TACE and radioembolisation. Percutaneous ablation techniques such as radiofrequency ablation and microwave ablation are generally not recommended for lesions larger than three centimeters or in close proximity of main bile ducts or large vessels as their proximity can lead to severe biliary toxicity or reduce the effectiveness of ablation due to the heat-sink effect of the circulating blood.

Stereotactic body radiotherapy (SBRT) is a non-invasive therapeutic option for patients with metastases that are more challenging to reach percutaneously (i.e. subcapsular, perihilar, periampullary) and for large lesions adjacent to hollow organs, bile ducts and vasculature [7]. The highly conformal dose distribution with a rapid dose drop-off spares large portions of the liver while allowing dose escalation without increasing the risk of radiation induced-liver disease. Given the precarious liver function of patients with hepatocellular carcinoma (HCC), SBRT is a particularly interesting treatment option for patients with localised HCC for whom standard modalities such as surgery (resection and transplantation) or ablation are deemed unsuitable [8–10]. Patients with a high risk of local failure after ablation due to the location of the lesion are also good SBRT candidates. SBRT yields local control of HCC at rates as high as 90% [11].

Over the past few years, growing evidence supports SBRT as an effective treatment option for liver metastases of various primary tumours and for liver-confined hepatocellular carcinoma. However, in 2011, uncertainties regarding its clinical benefit and cost-effectiveness blocked the request to the National Institute for Health and Disability Insurance (NIHDI) to include SBRT into the Belgian radiotherapy reimbursement system. After a multistakeholder dialogue, a nationwide coverage with evidence development (CED) project was set up to assess clinical and technical patterns of care and to monitor survival of patients treated with SBRT for various primary tumours and oligometastatic disease [12]. The programme was a close collaboration between the NIHDI, the Belgian Cancer Registry (BCR), and radiation oncology professionals under the auspices of the College for Physicians of Radiation Oncology Centres. As of 2020, stereotactic radiotherapy was formally included in the Belgian radiotherapy reimbursement system. However, relevant questions remain regarding optimal patient selection, radiation dose and fractionation, and technical parameters.

Within this study, we aim to gain insights into the patterns of care for liver SBRT in Belgium. Oncological outcome in terms of local control and overall survival and their influencing factors were investigated.

Methods

Patient population

Patients with liver lesions treated within a nationwide CED programme on SBRT were analysed. Various patient-, tumour- and treatment related characteristics were prospectively collected via an online registration module. Additionally, radiation oncology centres were contacted for individual patient data on primary tumour histology, local control, use of follow-up imaging, prior liver-directed therapies, gross tumour volume (GTV) and planning target volume (PTV) volumes and doses. If primary histology was unknown to the treating physician, it was retrieved by linkage to registered primary cancers in the BCR database.

Endpoints

Survival status was retrieved up to November, 2022 by linkage with the Belgian Crossroads Bank for Social Security. Survival time started from the day of last SBRT fraction up to the date of death or up to the last date confirmed alive in which case the patient was treated as censored.

Local control was predefined as absence of major progression (>20% according to RECIST) of the treated lesions or absence of confirmed minor growth during follow-up imaging. Radiological reports were reviewed and radiation oncologists were encouraged to assess the images, eventually in collaboration with a radiologist. Local control time started from the day of the last SBRT fraction up to the date of imaging showing local progression (event) or the date of the last imaging available

showing local control of the treated lesion (censor). In case of uncertainty of local control (e.g. region of progression not specified and imaging not available), the date of imaging where progression of the lesions was uncertain was used.

To calculate biologically effective doses (BED), the following linear quadratic formalism was used: BED = n x d x (1 + d/(α/β)) with *n* being the number of fractions, *d* the daily single fraction and using an *α/β* for tumour tissue of 10 Gy (BED10).

Data were collected and stored at the Belgian Cancer Registry and pseudonymised for further analyses.

Statistics

Local control and overall survival were calculated using the Kaplan-Meier method [13]. Local control was analysed at the individual lesion level while overall survival was calculated at the patient level. Univariable and multivariable analysis of prognostic factors were performed using Cox proportional hazard models. Because of the small groups per histology, Cox proportional hazards models were performed for all histology groups combined. P-values of < 0.05 were considered statistically significant. Results were stratified according to various patient-, tumour- and treatment-related characteristics. Statistical analyses were performed in SAS 9.4 (SAS institute, Cary, NC, USA).

Ethical considerations

This study was performed within the legal framework of BCR. Based on the Coordinated Law of 10 May 2015 (art. 138), BCR has a legal task to collect data on cancer, subject it to quality control, process and analyze it, encrypt and store it, report on it, make it accessible for research and protect it. Within the boundaries of this legal framework BCR is allowed to act without Ethical Committee approval. BCR processes the data in accordance with GDPR and is exempt from the obligation to disclose information to the persons whose data are processed since notification to the data subject is impossible or takes disproportionate effort due to the large number of data subjects, in particular when data are processed for statistical purposes or for historical or scientific research (cfr. Art. 14.5, b. GDPR EU 2016/67).

Results

Patient characteristics

From August 2013 to December 2019, fourteen centres treated 352 patients with SBRT for a total of 408 liver lesions. The number of lesions treated per centre varied between 2 and 116.

SBRT was applied for 66 primary liver lesions and 342 liver metastases. The majority of the patients received prior systemic therapy, including antihormonal therapy ($n = 244$). Median age at the start of SBRT was 70 years (range 22–93). Median time between diagnosis of the primary tumour and the start of liver SBRT was 28.3 months (range 0.8–357). Colorectal adenocarcinoma was the most common primary tumour histology ($n = 170$), followed by breast cancer ($n = 42$). In most patients, only one lesion was treated. Median GTV and PTV volumes were 17 cc and 74 cc respectively. Maximally 3 lesions were treated simultaneously. SBRT plans consisted of a median of 5 fractions (range 2–15) delivering a median BED10 of 105 Gy (range 23.8–180 Gy). During the entire project, a gradual uptake in liver SBRT and a higher dose prescription were observed (Fig. 1). Patient, tumour and treatment characteristics are summarised in Tables 1 and 2.

Overall survival

Overall survival data could be retrieved for all patients. Median overall survival was 24 months for the entire patient population. The median follow-up period was 23.6 months. One year-, 2 year-, and 5 year- overall survival probabilities for the entire patient population were 74.3%, 49.7% and 19.4% respectively (Fig. 2). 1 year-, 2 year-, and 5 year- overall survival probabilities were 74.3%, 49.8% and 18.6% versus 75.4%, 49,1% and 23.8% for metastatic and HCC lesions respectively. In univariable analysis, a superior overall survival was found for patients with a better performance status (PS) at diagnosis (PS 2 + vs. PS 0; HR 2.260 [1.35, 3.79], 95% CI, $p = 0.002$), prior liver surgery (HR 0.762 [0.58, 0.99], 95% CI, $p = 0.044$), use of MRI (HR 0.749 [0.59, 0.95], 95% CI, $p = 0.017$) or PET-CT (HR 0.715 [0.56, 0.90], 95% CI, $p = 0.005$) during follow-up, image fusion for target delineation (no vs. yes HR 1.547 [1.04, 2.30], 95% CI, $p = 0.032$), higher BED10 (BED10 ≥ 100 Gy vs. BED10 < 100 Gy HR 0.734 [0.58, 0.93], 95% CI, $p = 0.010$) and smaller PTV volume (PTV > 130 cc vs. <45 cc HR 2.048 [1.47, 2.85], 95% CI, $p < 0.001$) (Suppl. Table 1). After multivariable analysis, a higher overall survival was observed for patients with better PS (PS 2 + vs. PS 0 h 2.679 [1.54, 4.66], 95% CI, $p < 0.001$), a smaller PTV volume (PTV>130 cc vs. PTV<45 cc HR 1.972 [1.40, 2.78], 95% CI, $p < 0.001$) and a higher BED10 (BED10 ≥ 100 Gy vs. BED10 < 100 Gy HR 0.734 [0.56, 0.96], 95% CI, $p = 0.0239$) (Table 3).

Local control

Local control data could be retrieved for 354 lesions. Median duration of local control was 2,2 years for the

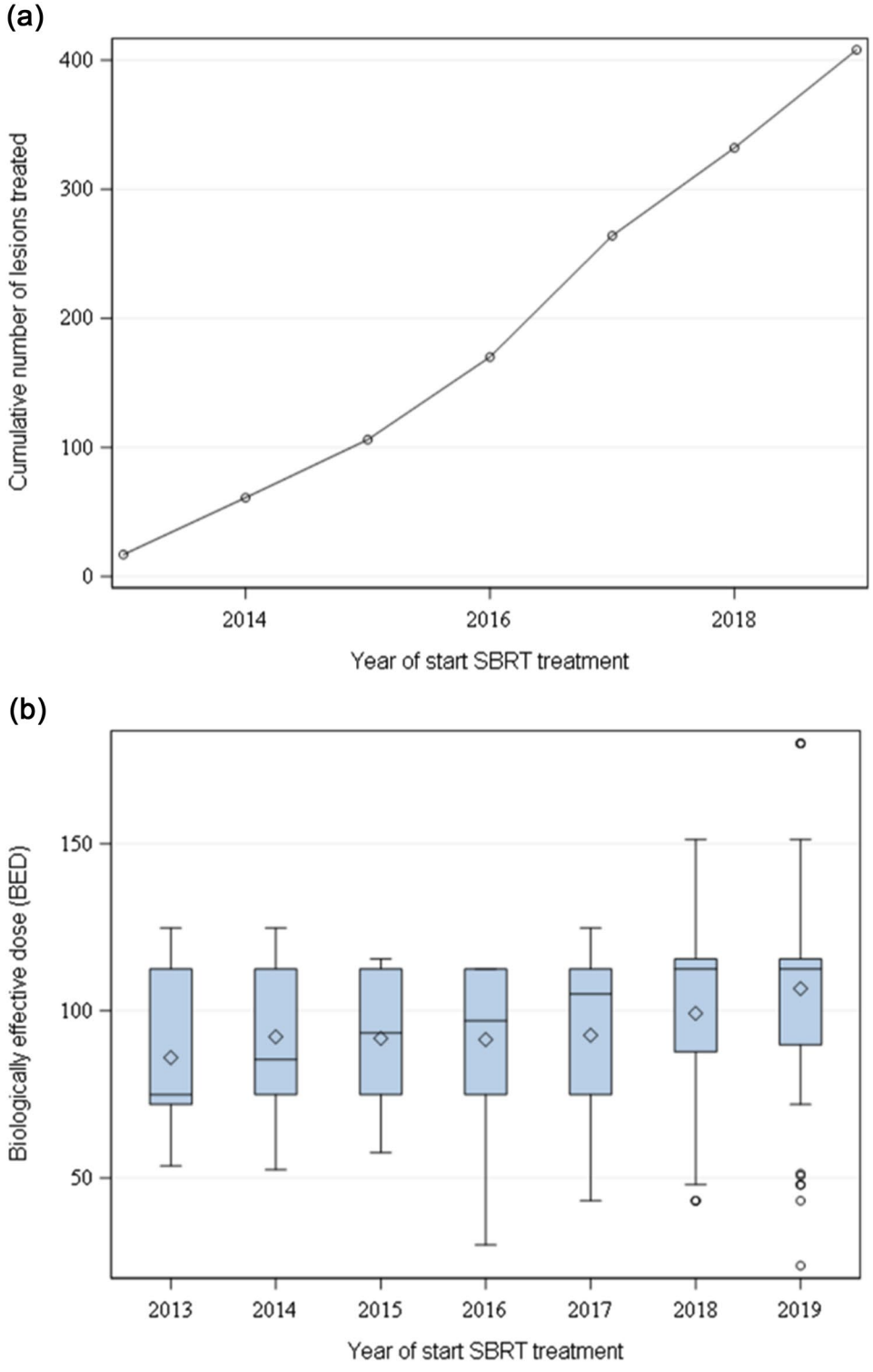

Fig. 1 SBRT uptake (**a**) and dose prescription (**b**) over time

Table 1 Patient and tumour characteristics

	N = 352	%
Median age at diagnosis (years, range): 66.5 (16–92)		
Median age at SBRT (years, range): 70 (22–93)		
Gender		
Male	197	56
Female	155	44
WHO at diagnosis		
0–2	302	86
3–4	3	1
Unknown	48	14
Tumour characteristics (lesion based)	***N* = 408**	**%**
Primary histology		
HCC	66	16
Breast	42	10
Colorectal	170	42
Lung	20	5
Other	110	27
Prior LDT		
Surgery	100	25
MWA/RFA	45	11
Systemic	230	56
RT	19	5
Other	27	7
Follow up		
MRI	192	47
CT	292	72
PET	190	47
US	60	15

Abbreviations: CT: computed tomography; HCC: hepatocellular carcinoma; LDT: liver-directed therapies; MRI: magnetic resonance imaging; MWA: microwave ablation; PET: positron-emission tomography; RFA: radiofrequency ablation; RT: radiotherapy; US= ultrasound

entire group and 2 and 4,1 years for the metastatic lesions and HCC respectively. For all lesions combined, local control rates at one, two and five years were 69.9%, 52.2% and 32.4% respectively (Fig. 3). Local control at one, two and five years were 67.6%, 48.2% and 31% versus 82.8%, 76.2% and 43.6% for metastatic and HCC lesions respectively. In univariable analysis, a better local control was found for HCC and "other histologies" as compared to colorectal metastases (HR 0.417 [0.24, 0.72], 95% CI, $p = 0.002$; HR 0.664 [0.46,0.96], 95% CI, $p = 0.030$) (Suppl. Table 2). A better local control was also observed for lesions in patients who did not receive prior systemic therapy (prior systemic therapy including antihormonal therapy yes vs. no HR 2.168 [1.45, 3.24], 95% CI, $p < 0.001$), lesions treated with robotic SBRT (robotic SBRT vs. 3D-CRT HR 0.478 [0.27, 0.83], 95% Ci, $p = 0.0095$) and lesions treated in sessions using personalised immobilisation (no personalised immobilisation HR 1.545 [1.08, 2.20], 95% CI, $p = 0.016$) (Suppl. Table 2). Targets defined after image fusion had better local control (no image fusion HR 1.711 [1.02, 2.88], 95% CI, $p = 0.043$). Lower local control was found when CT imaging was used for follow-up (HR 1.621 [1.03, 2.55], 95% CI, $p = 0.036$). A higher BED10 (BED10 ≥ 100 Gy vs. BED10 < 100 Gy HR 0.435 [0.31, 0.60], 95% CI, $p < 0.001$) and a smaller PTV volume (PTV>130 cc vs. PTV<45 cc HR 2.337 [1.49, 3.67], 95% CI, $p < 0.001$) were also associated with a superior local control. In multivariable analysis better local control was only found for smaller PTV volumes (PTV>130 cc vs. PTV<45 cc HR 2.051 [1.29, 3.27], 95% CI, $p = 0.003$), higher BED10 (BED10 ≥ 100 Gy vs. BED10 < 100 Gy; HR 0.616 [0.42, 0.89], 95% CI, $p = 0.011$) and for lesions in patients who were not priorly treated with systemic therapy (HR 1.823 [1.16, 2.87], 95% CI, $p = 0.010$) (Table 4). Histology and technical radiotherapy parameters were no longer influencing LC.

Discussion

Within a multicentric project, we collected data on local control and overall survival and we identified factors impacting these outcome parameters. Previous studies have shown that SBRT provides excellent local control with limited toxicity, both for primary lesions and for metastases from various tumours. Recent randomised trials revealed that metastasis-directed therapies, including SBRT, potentially improve survival [4, 5]. Another potential benefit is delaying systemic progression and the need for systemic treatment [14]. As evidence continues to accumulate, an increasing number of centers are adopting SBRT in routine clinical practice. Accordingly, we observed a gradual increase in the use of liver SBRT. As centres became more familiar with SBRT planning and delivery, they increasingly prescribed higher doses. Three large registry studies demonstrated SBRT is a valuable tool to treat liver lesions and recognised that its effectiveness is influenced by factors such as tumour histology, tumour size and radiation dose [15–17]. In contrast with other published registries, we were able to investigate a wide variety of technical parameters. Overall survival rates in our series at 1 year, 2 years, and 5 years were 74.3%, 49.7% and 19.4%. Overall survival data were quite similar between patients with liver metastases and primary liver lesions, except at 5 years where HCC patients had a 5% point higher survival. Our median overall survival reached 24 months, similarly to other registries that reported outcomes with a median overall

Table 2 Treatment characteristics

Treatment details	Median	Range
Number of lesions treated with SBRT	1	1–3
Number of fractions delivered	5	2–15
GTV volume (cc)	17,1	0.2–533.0
PTV volume (cc)	74,2	4.19–955.1
Mean PTV dose (cGy)	5047	1910–9198
BED10 (Gy)	105	23.8–180
Time primary diagnosis to start SBRT (months)	29	0.8–360
Technical details	**N**	**%**
Identification tumour motion		
kV fluoroscopy	8	2
4D-CT	276	67
Max inspiration/expiration breath-hold CT	108	26
None or not applicable	15	4
Other	12	3
Tumour motion compensation strategy		
Abdominal compression	184	45
Breath-hold	0	0
Gating	37	9
Tracking	146	36
None or not applicable	50	12
Other	17	4
Imaging modalities treatment planning		
CT	382	94
MR	232	57
PET-CT	171	42
Other	18	4
Image fusion for target delineation		
Yes	371	91
No	37	9
Personalised immobilisation		
Yes	319	78
No	89	22
Markers		
Implanted markers	208	51
External skin sensors	11	3
No markers	196	48
Delivery technique		
3D-CRT	40	10
IMRT	1	0
Rotational IMRT	246	60
Rotation 3D	5	1
Robotic SBRT	116	28
Dose calculation algorithm		
Pencil Beam	0	0
AAA	188	46
CCC	30	8
Monte Carlo	72	18
Other	118	29
Patient specific QA prior to start		
1D	136	33
2D	134	33
3D	130	32
4D	24	6

Table 2 (continued)

Treatment details	Median	Range
None	5	1
Type of IGRT		
CBCT	271	66
EPID	28	7
Exactrac	139	34
No IGRT	0	0
Other	20	5

Abbreviations: CCC: collapsed cone convolution; CT: computed tomography; EPID: electronic portal imaging device; GTV: gross tumour volume; IGRT: image guided radiotherapy; IMRT: intensity modulated radiotherapy; kV: kilo voltage; MRI: magnetic resonance imaging; MWA: microwave ablation; PET: positron-emission tomography; PTV: planning target volume; QA: quality assurance

survival of 22–24 months [15, 16] After multivariable analysis, we found a higher overall survival for patients with a better PS, smaller PTV volumes and higher BED10.

While comparing overall survival data between studies, one must acknowledge the large heterogeneity in patient inclusion (i.e. performance status and severity of extrahepatic disease). Therefore, we believe local control is a more valuable outcome parameter for liver SBRT as compared to OS. In our study, we found a reasonable local control at 1 year, 2 years and 5 years of 69.9%, 52.2% and 32.4% respectively. HCC lesions are known to be radiosensitive and showed higher local control rates as compared to liver metastases. Local control numbers in our series are lower as compared to the previously published registries (76–87% and 56–68% at 1 year and 3 years respectively) [15–17]. Of note, there is a high heterogeneity among studies regarding patient inclusion, prescribed dose and definition of local control. As data on tumour control were not available in the original registration at the BCR, centres were individually contacted to determine local control for each lesion. Local control was defined as the absence of progression of the treated lesions and absence of confirmed minor growth during follow-up imaging. The term "absence of confirmed minor growth" was used to take into account the potential inflammatory changes on imaging early after SBRT. Other studies evaluated local control according to modified RECIST criteria (i.e. defining local progression as a > 20% increase in lesion size and/or the appearance of one or more lesions in the target treatment location [15], or as reappearance after complete remission or regrowth after initial partial response) [16, 17] We included a "minor growth" criterion because when there is confirmed minor growth (< 20%), treating physicians might start other treatments while these lesions technically remain under control according to RECIST, introducing a bias in the local control numbers. Therefore, our local control data might be more realistic than those obtained purely by RECIST definitions. Although retrospectively performed, we believe our local control analysis is representative since it was determined for individual lesions using a predefined definition. Local control data were available for 86% of the lesions. In line with other publications, smaller PTV volumes and higher BED10 (i.e. ≥100 Gy) were found as independent significant variables for LC.[17] Ohri et al. found a better LC for liver metastases treated with BEDs exceeding 100 Gy than for those treated with BED of 100 Gy or less [18]. In his analysis, this dose response was not observed for primary liver tumours. It is known that radiosensitive HCCs do not require highly ablative doses, as shown by the NRG/RTOG 1112 trial [19]. Radiotherapy technique was not found to be a significant factor for local control in multivariable analysis. However, we believe that highly conformal radiotherapy techniques should be used when administering high doses as lower conformality may increase toxicity. Patients who were not priorly treated with systemic therapy experienced better local control. This observation has been found by others and could be explained by the systemic therapy-driven selection of radioresistant clones. Metastases from colorectal cancer are deemed to be relatively resistant to SBRT. The DEGRO analysis demonstrated

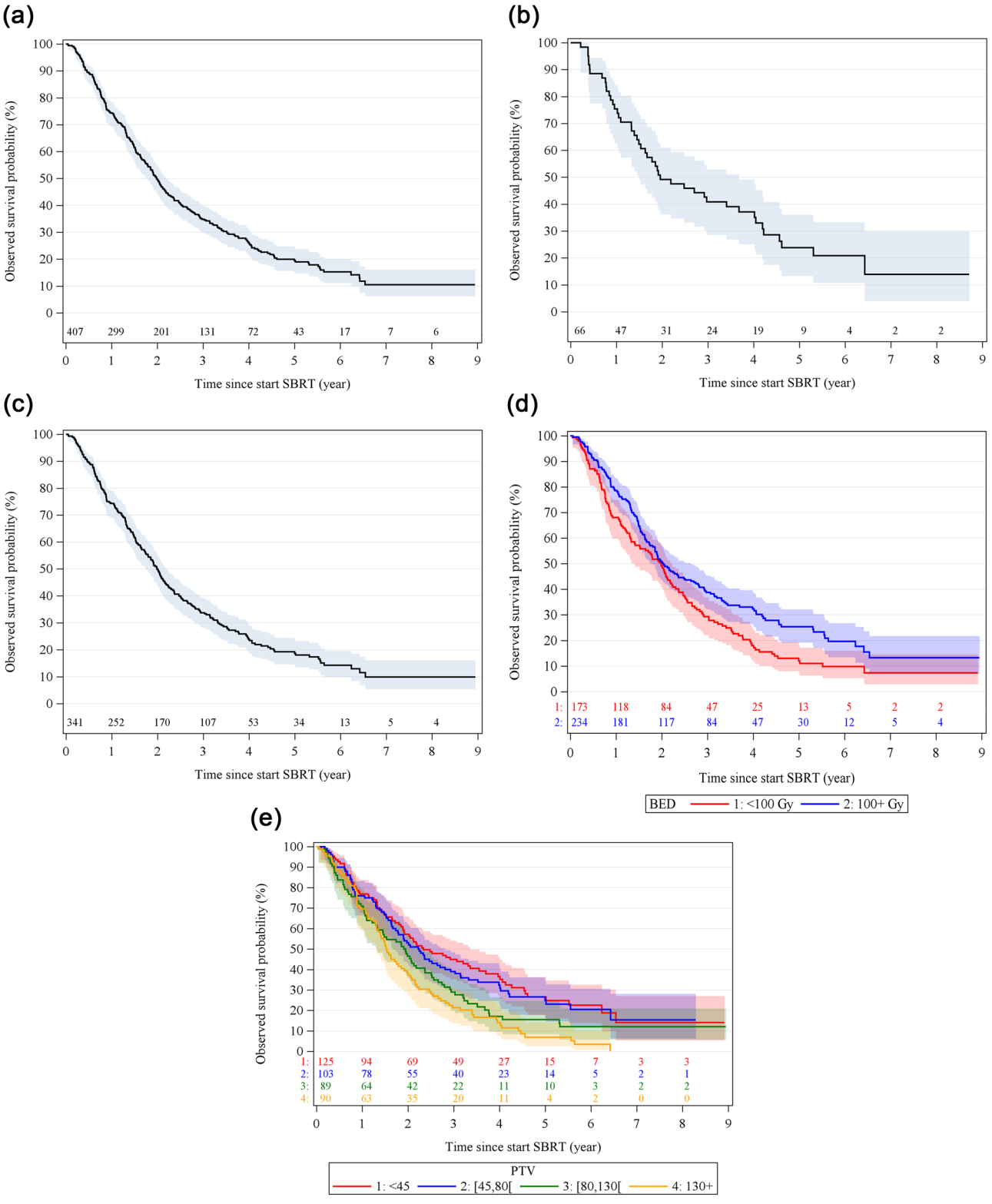

Fig. 2 Observed survival. Observed survival probability since end SBRT (**a**) all patients, (**b**) HCC patients, (**c**) patients with liver metastases. Observed survival (**d**) per BED10, (**e**) per PTV volume

Table 3 Multivariable analysis for overall survival

Characteristic	Adjusted HR for all-cause death			Type III *p*-value
	Estimate	95% CI	*p*-value	
Age at end SBRT treatment				0.2307
<55 (ref)	1.000			
55–64	1.176	[0.75, 1.85]	0.4848	
65–74	1.241	[0.80, 1.92]	0.3292	
75+	1.500	[0.97, 2.31]	0.0661	
WHO at diagnosis				0.0060
missing	1.365	[0.88, 2.11]	0.1600	
0 (ref)	1.000			
1	1.286	[0.93, 1.78]	0.1261	
2+	2.679	[1.54, 4.66]	0.0005	
Primary tumour localisation				0.0825
Colorectum (ref)	1.000			
Breast	1.042	[0.67, 1.63]	0.8558	
Hepatocellular carcinoma	0.932	[0.64, 1.36]	0.7154	
Other	1.411	[1.05, 1.90]	0.0240	
PTV volume				0.0003
<45 (ref)	1.000			
[45,80]	1.168	[0.81, 1.67]	0.3977	
[80,130]	1.661	[1.17, 2.36]	0.0047	
130+	1.972	[1.40, 2.78]	0.0001	
BED10				0.0239
<100 Gy (ref)	1.000			
100 + Gy	0.734	[0.56, 0.96]	0.0239	

Abbreviations: BED: biologically effective dose; HR: hazard ratio; PTV: planning target volume

a lower 1-year local control rate for metastases from colorectal cancer (67%) as compared to breast cancer (91%), NSCLC (88%) or other histologies (80%).[17] Primary tumour histology was not found to be a predictive factor for local control in our analysis. A possible explanation is the different number of colorectal metastases (42 vs. 48.1% in the DEGRO registry) or variation in other tumour histologies. A recent systematic review showed robotic SBRT yields excellent responses and low toxicity in patients with liver metastases [20]. Although significantly associated with better local control in univariable analysis, the use of robotic SBRT was not withheld as influencing factor on local control in multivariable analysis.

Strengths of our study include the prospective inclusion of all liver SBRT treatments performed in Belgium during the trial period, as registration was required for reimbursement, and that extensive technical details were collected in this registry. Furthermore, we believe our definition of local control is more realistic than those using purely RECIST criteria. Shortcomings are that the analysis is based on a prospective registration on liver SBRT, but data on local control were retrospectively collected. Toxicity data are lacking as they were not available in the original project. However, there is ample data demonstrating SBRT liver is well-tolerated when performed according to established guidelines. Lastly, although the registry included data on both primary liver lesions and liver metastases, the limited number of HCC lesions restricted in-depth analyses on HCC lesions.

Conclusions

We observed a steady increase in liver SBRT uptake over time and reasonable local control and overall survival. Both local control and overall survival depended on BED10 and PTV volume. Prior systemic therapy was associated with reduced local control. After multivariable analysis, none of the technical parameters significantly influenced outcome. Future studies should focus on optimising patient selection, refining planning and dosing strategies, and exploring the combination of SBRT with systemic therapies to enhance tumour control, long-term survival and quality of life.

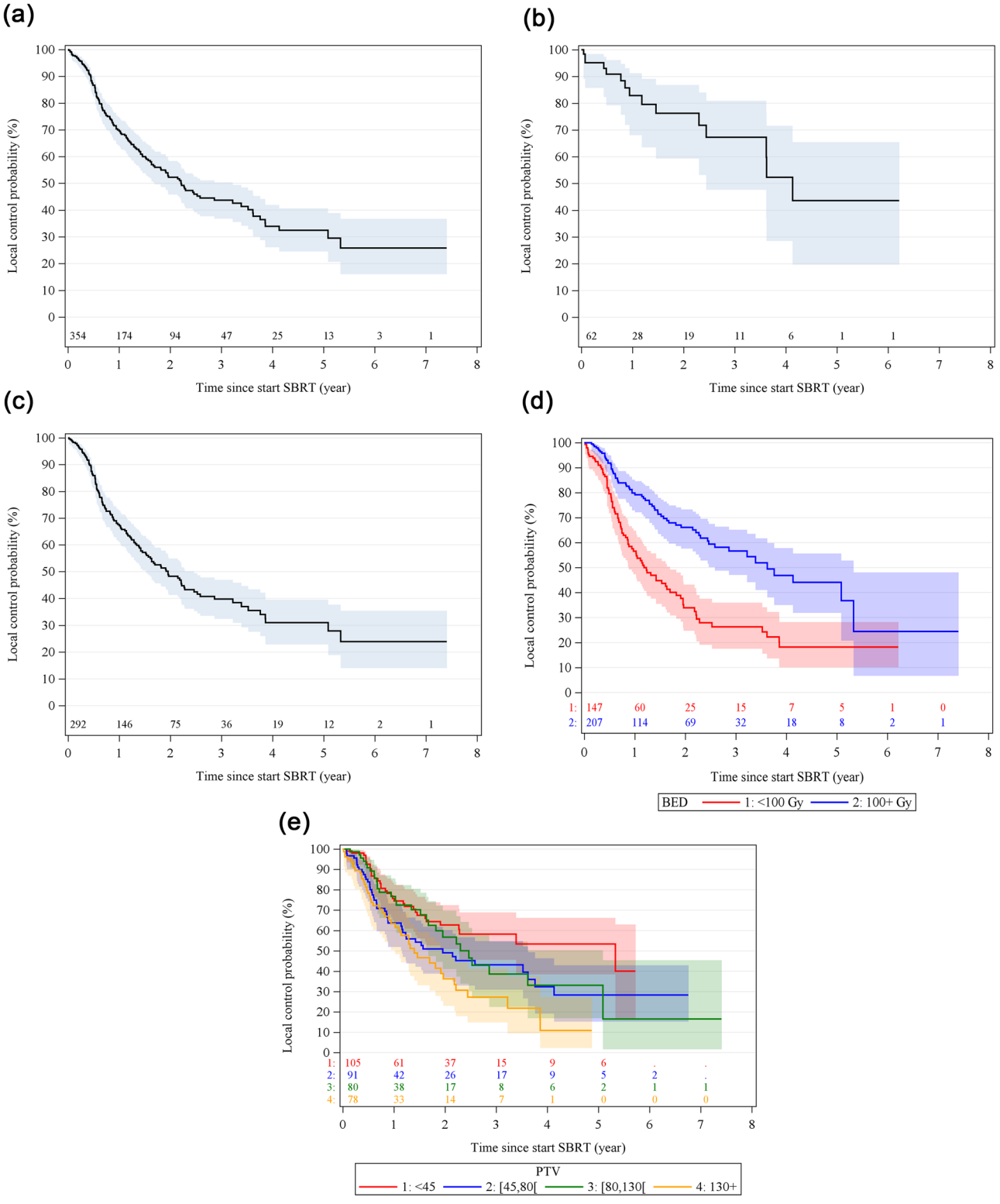

Fig. 3 Local control. Local control probability (**a**) all lesions, (**b**) HCC, (**c**) liver metastases. Local control (**d**) per BED10, (**e**) per PTV volume

Table 4 Multivariable analysis for local control

Characteristic	Adjusted HR for local failure			Type III *p*-value
	Estimate	95% CI	*p*-value	
Primary tumour localisation				0.0954
Colorectum (ref)	1.000			
Breast	0.575	[0.32, 1.04]	0.0693	
Hepatocellular carcinoma	0.672	[0.36, 1.24]	0.2033	
Other	0.686	[0.47, 1.01]	0.0535	
Prior systemic therapy including antihormonal therapy				0.0096
no (ref)	1.000			
yes	1.823	[1.16, 2.87]	0.0096	
CT Imaging used at any point prior to progression for the follow up of the treated lesion				0.7328
no (ref)	1.000			
yes	1.089	[0.67, 1.78]	0.7328	
Personalised immobilisation				0.3350
Yes(ref)	1.000			
No	1.302	[0.76, 2.23]	0.3350	
Image fusion for target delineation				0.0728
Yes (ref)	1.000			
No	1.676	[0.95, 2.95]	0.0728	
PTV volume				0.0206
<45 (ref)	1.000			
[45,80]	1.579	[0.99, 2.51]	0.0533	
[80,130]	1.310	[0.78, 2.20]	0.3056	
130+	2.051	[1.29, 3.27]	0.0026	
BED10				0.0110
<100 Gy (ref)	1.000			
100 + Gy	0.616	[0.42, 0.89]	0.0110	

Abbreviations: BED: biologically effective dose; CT: computed tomography; HR: hazard ratio; PTV: planning target volume

Abbreviations

BCR	Belgian Cancer Registry
BED	Biologically effective dose
GTV	Gross tumour volume
Gy	Gray
HCC	Hepatocellular carcinoma
HR	Hazard ratio
LC	Local control
OS	Overall survival
PTV	Planning target volume
SBRT	Stereotactic body radiotherapy

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s13014-026-02797-x.

Supplementary Material 1

Supplementary Material 2

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Author contributions
PD and IJ were responsible for the conception and design of the study, for the acquisition, analysis and interpretation of the data and for writing the manuscript. GS and NV were responsible for the acquisition of data and statistical analysis. NJ, YL, LM, SV, KV, PB, SD, JR, SB, SC, MD, KH, GV, KS and RW contributed by data acquisition. All authors read and approved the submitted manuscript. All authors agreed to be personally accountable for their own contributions and ensure that questions related to the accuracy and integrity of the work are appropriately investigated and resolved as well as the resolution documented in the literature.

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Data availability
Research data are stored in an institutional repository and can be shared upon request to the corresponding author.

Declarations

Ethics approval and consent to participate
This study was performed within the legal framework of BCR. Within the boundaries of this legal framework BCR is allowed to act without Ethical Committee approval. More details can be found in the manuscript.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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