Open Journal of Clinical & Medical Images

www.jclinmedimages.org

ISSN: 2833-2725

Research Article

Open Access, Volume 6

Introduction of stereotactic ablative radiotherapy as a safe and feasible treatment option for patients with hepatocellular carcinoma

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Received: Mar 04, 2026
Accepted: Apr 30, 2026
Published: May 07, 2026
Archived: www.jclinmedimages.org

Keywords: Stereotactic ablative radiotherapy; Hepatocellular carcinoma; Liver cancer.

Abstract

Background: Stereotactic Ablative Body Radiotherapy (SABR) is a highly focused radiation treatment that delivers an intense dose of radiation to a tumour whilst limiting exposure of surrounding tissues. SABR has been associated with improvement in survival and good rates of local control in non-surgical candidates with Hepatocellular Carcinoma (HCC). The aim of this study was to evaluate the outcomes of HCC patients treated with SABR after its introduction in a tertiary referral hepatobiliary centre. **Methods:** A total of 32 patients (median age 73 years {47 to 85}, 78% male) who received SABR for HCC liver lesions between July 2020 and August 2022 were retrospectively analysed. Patient, treatment and follow-up details were obtained from online patient records and imaging. **Results:** Overall Survival rate was 78% at a median follow-up of 12 months (range 4 to 30). Local control was achieved in 72%, while progression occurred in 31%. Median time to progression was 6 months (range 3 to 31). The rate of progression-free survival at 12 months was 62.5%. Only 31% reported toxicities. No patients in the study group experienced any Grade ≥ 3 toxicities. **Conclusion:** Our experience suggests SABR is a viable, well-tolerated and effective treatment option for patients with HCC .

Introduction

Hepatocellular Carcinoma (HCC) is the most common type of primary liver cancer and the fourth most common cause of cancer-related death worldwide [1]. Over the past three decades, primary liver cancer mortality rates have more than tripled in the United Kingdom (UK) [2,3]. The rise in incidence of HCC can be explained by a rise in underlying liver cirrhosis [4]. Cirrhosis can be due to several aetiologies including chronic hepatitis B or C infection, alcoholic liver disease, and Non-Alcoholic Fatty Liver Disease (NAFLD) [5].

Treatment of HCC is informed by the size and location of liver lesions as well as underlying liver function and medical comorbidities [6]. Patients with HCC frequently present with advanced disease on a background of hepatic decompensation, limiting treatment options. Criteria such as Child-Pugh (CP) [7] classification and Eastern Cooperative Performance Status (PS) [8] have been developed to estimate treatment tolerance and risk of liver decompensation in order to guide treatment choice and avoid futile interventions.

The Barcelona Clinic Liver Cancer (BCLC) staging system uses a set of criteria (CP, PS and radiological tumour extent) to guide the management of patients with HCC [9,10]. Patients presenting at very early stage or early stage (BCLC stage 0 and A) are offered radical therapy; either liver transplantation or resection (if presenting with a single tumour in the absence of portal hypertension or significant underlying liver dysfunction). Non-surgical candidates with lesions relatively distant from major vessels or bile ducts may be offered percutaneous Radiofrequency Ablation (RFA) or Microwave Ablation (MWA) [11]. Patients with multifocal disease (BCLC stage B) may be offered therapies such as trans arterial embolisation or chemoembolisation (TAE or TACE). Systemic chemotherapy such as oral tyrosine kinase inhibitors can be used for palliative treatment in patients with macrovascular invasion (BCLC stage C) whilst patients unsuitable for these treatments for anatomical reasons, or those with disease progression following ablation or TACE, may be suitable for Stereotactic Ablative Body Radiotherapy (SABR). SABR is a highly focused radiation treatment that delivers an intense dose of radiation to a tumour whilst limiting exposure of surrounding tissues. Technological advances in the delivery of SABR and an increasing body of literature establishing high rates of Local Control (LC) with low rates of toxicity have led to SABR emerging as a novel and important treatment modality in the management of both early and more advanced HCC [12-16].

The aim of this study was to evaluate the outcomes of HCC patients selected for treatment with SABR during its introduction in a tertiary referral Hepatobiliary (HPB) centre in the UK. The primary outcomes were Overall Survival (OS) and safety (toxicity). Secondary outcomes were LC, Progression-Free Survival (PFS) and feasibility of SABR as a treatment for HCC.

Materials and Methods

All patients who received SABR for HCC liver lesions between July 2020 and August 2022 were retrospectively analysed. Eligibility for SABR was determined via the weekly HPB cancer Multidisciplinary Team meeting (MDT). Patient characteristics, PS and CP were obtained from online patient records [7,8]. Charlson Comorbidity Index (CCI) was calculated using the HPB MDT referral data [17].

Imaging

Computed tomography (CT) or Magnetic Resonance Imaging (MRI) for each patient was reviewed by an experienced investigator specialised in liver radiology (MC) to determine tumour location, number and size of lesions. Follow-up imaging was further reviewed to determine LC or disease progression. Progression was defined using modified Response Evaluation Criteria in Solid Tumors (mRECIST) as: an increase in the sum of maximum tumour diameters of at least 20% or the development of any new lesions [18]. LC was defined as freedom from local progression by mRECIST.

Treatment details

Patients were positioned supine with their arms above their head using the Elekta WingSTEP wingboard. Knee and ankle supports were used to improve comfort. The Elekta Active Breathing co-ordinator was used to minimise motion artefact. To define the targeted lesions for Gross Tumour Volume (GTV) delineation, the multiphase contrast-enhanced CT or MRI images were imported into the planning system and fused with the images from planning CT (Figure 1). A planning three-dimensional CT scan with intravenous contrast was acquired in exhale breath hold with 2 mm slices. The planning target volume (PTV) was determined by adding an internal margin and a setup margin to the GTV to compensate for the internal organ movement and positional uncertainties, namely 8 mm superior and inferior and 6 mm in all other planes. Dosimetry plans were calculated on Raystation and a Volumetric Modulated Arc Therapy (VMAT) plan generated. Normal tissue constraints were derived from the national UK SABR consortium guidelines [19]. Treatment was delivered on Elekta Versa HD linear accelerator with daily cone beam CT.

Follow-up

Patients were aimed to be followed up at three months, six months and then at six-monthly intervals until two years with liver function tests, AFP estimation and CT/MRI imaging as appropriate. Reported toxicities were obtained either from clinic follow-up documentation, hospital admission or General Practitioner (GP) records where available. Toxicities were graded using the toxicity criteria of the radiation therapy oncology group [20]; Grade 1: mild toxicity, Grade 2: moderate toxicity, Grade 3: severe toxicity, Grade 4: life-threatening toxicity. The OS, defined as the number of months from the start of treatment to date of death from any cause, or censorship if still alive at follow-up (6th July 2023), was calculated. PFS was defined as the number of months from the start of treatment, to first imaging at which progression was evident, or death from any cause.

Ethical approval

The study was registered with and approved by the institutional ethical review board (HEPSUR/CA/2023-24/02).

Results

Thirty-two patients received SABR over the study period with a median age of 73 years (range 47 to 85, Interquartile Range {IQR} 13). Table 1 shows the demographics of the study cohort. There were 25 male (78%) and seven female patients (22%). Median BMI was 29 (range 23.8 to 40, IQR 6).

Clinical details

HCC was diagnosed on surveillance imaging of known liver lesion, cirrhosis or post HCC in the majority of cases (n=25/32, 78%). Three patients presented symptomatically with abdominal pain and/or deranged liver function tests while in four cases HCC was an incidental finding. Overall, 47% (15/32) of patients had undergone previous liver-directed therapies for HCC: Five patients had previously undergone liver resection, nine previous TACE and four previous MWA. Of these, one patient underwent both a resection and TACE, and a further two had both TACE and MWA.

Overall, 22 (69%) patients underwent SABR because they were deemed medically unfit for surgery, nine (28%) because treatment alternatives weren't technically possible. One was

due to patient choice. Median CCI was 7 (range 3 to 10, IQR 2) and PS 1 (range 0 to 2) (Table 1). The majority of patients had underlying liver disease classed as CP A (n=21/32, 66%); two patients CP B (n=2/32, 6%), four had steatohepatitis without cirrhosis (n=4/32, 12%) and five had no evidence of underlying liver cirrhosis (n=5/32, 16%). The most common aetiology of underlying liver disease was NAFLD (11/32) followed by chronic hepatitis C infection (6/32) and alcoholic liver disease (5/32).

Tumour features

Median number of lesions treated was one (range 1 to 3) with 36 lesions treated in total. A single lesion was treated in 91% (n=29/32) of cases, two lesions were treated in 6% (n=2/32) and three lesions in 3% (n=1/32) of cases. Median tumour size was was 30 mm (range 11 to 43 mm, IQR 16). Location of liver lesions were liver segment 8 (n=11/36), 7 (n=4/36), 6 (n=3/36), 5 (n=6/36), 4 (n=3/36), 3 (n=4/36) and 2 (n=5/36).

Treatment details

Median time to treatment from time of diagnosis was one month (range 0 to 9, IQR 1). Delays of more than six months (n=3) were due to hospitalisation with other acute medical conditions. The median treatment dose was 50 Gy, (range 40 to 50 Gy, IQR 5) delivered over five fractions in the majority of cases (24/32, 75%), and three fractions in the remaining cases (8/32, 25%). Median treatment duration was one week (range 0 to 2, IQR 1). Planning scan (Figure 1).

Safety, feasibility

Overall, 10 patients reported Grade 1 or 2 toxicities (10/32, 31%). Of these, six reported gastrointestinal symptoms (nausea, diarrhoea), five reported fatigue and three reported localised rib discomfort. No patients in the study cohort reported any Grade ≥ 3 toxicities.

Radiological outcomes

Median follow-up was 12 months (range 4 to 30). Overall 72% (n=23/32) achieved LC, while progression occurred in 31% (n=10/32) of patients. Median time to progression was 6 months (range 3 to 31). A total of 60% of patients with disease progression received further liver-directed therapies. Treatment of progression was with TACE (n=3/10), transplant (n=1/10), MWA (n=1/10) or systemic therapy (n=1/10). The remaining patients either passed away before they were able to receive further treatment (n=3/10) or were kept under active surveillance (n=1/10). Of the patients who received previous liver-directed therapies prior to treatment with SABR (n=15/32), LC was achieved in 80% (n=12/15), while local progression occurred in the remaining three cases.

Survival

Median OS was 15 months (range 4 to 35, IQR 10). Rate of OS was 78% (n=25/32) at 12 months. A total of seven patients died at a median of 9 months post SABR (range 4 to 19 months, IQR 3). Rate of PFS at 12 months was 62.5% (20/32).

Discussion

Here we present the results of a single-centre experience of the introduction of SABR for HCC. These data suggest SABR is safe in this setting, without severe toxicities (Grade ≥3) reported and just one in three patients experiencing mild toxicities. SABR is a suitable treatment option in patients who had previously received liver-directed therapies, as was the case in half of

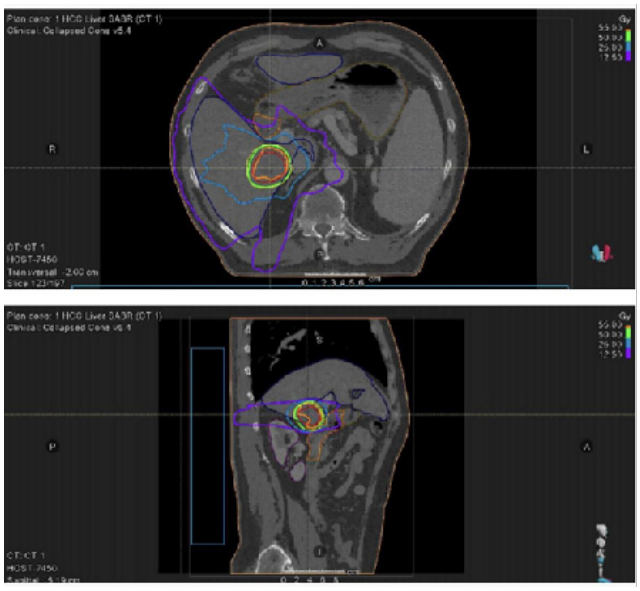

Figure 1: SABR planning CT abdomen and pelvis. Transverse view above, sagittal view below. In red, the planning target volume (obtained by adding an 8mm superior and 6mm margin in all other planes to the GTV) receiving maximum dose of 55 Gy.

Table 1: Demographics and treatment details of the study cohort (n=32).

Median age, years (range)	73 (47 to 85)
Sex	
Male, n (%)	25 (78)
Female, n (%)	7 (22)
Median BMI, kg/m^2 (range)	29 (24 to 49)
Performance status, n(%)	
0: Fully active	11 (34)
1: Restricted in physically strenuous activity	14 (44)
2: Unable to carry out work activities	7 (22)
Median CCI (range)	7 (3 to 10, 2)
Child-Pugh Score, n(%)	
A:	21 (66)
B:	2 (6)
Underlying liver disease, n(%)	
NAFLD	11 (34)
HCV	6 (19)
Alcoholic liver disease	5 (15)
Median tumour size mm (range)	30 (11 to 43)
Median treatment dose, Gy (range)	50 (40 to 50)
Median fractionations n (range)	5 (3 to 5)

Table 2: Outcomes of patients treated with SABR after previous liver-directed therapies (n=15).

Median age, years (range)	75 (47 to 85)
Previous liver directed therapy:	
Liver resection	5(33)
TACE	9 (60)
MWA	4 (27)
Outcomes n(%):	
LC	12 (80)
Progression	3 (20)
OS	10 (66%)
Median OS (months)	10
PFS (months)	10
Grade 3 toxicity:	0 (0)

the patients in this cohort. We show SABR remained effective, with three-quarters of patients still alive at 12 months post-treatment and seven out of 10 patients free from disease at this stage. Despite this, one in three patients developed disease progression.

Shanker *et al.* published a systematic review of 48 observational studies involving 2846 patients who underwent SABR for HCC [12]. The pooled rate of 1-year OS was 78%. Our results are consistent with this and other published work [13,21]. Rim *et al.* found a pooled LC rate at 12 months of 85.7%, though published rates of LC range more widely from 72.5% to 95% [13,15,16,22,23]. Size of lesion, dose of radiation delivered and degree of underlying liver dysfunction have all been found to affect LC and OS rates [12,13]. Patients with more advanced underlying disease are likely to receive lower doses, and patients often have significant competing risks for mortality including recurrence outside of the treatment field and progression of underlying liver disease.

Radical therapy with transplantation or resection remains first line for BCLC 0 and A. Ablative therapies with RFA or MWA have proven reasonable alternatives for lesions < 30 mm although there are reports suggesting a decreased OS and PFS compared with surgery [24].

There are several limiting factors even in the BCLC 0 and A group making above mentioned therapies unsuitable strategies. Overall only 30-40% of HCC patients are suitable for radical therapy at time of diagnosis [25]. The combination of age, BMI, degree of underlying liver disease; CP and presence of portal hypertension, can make patients unsuitable candidates for major surgery. Limiting factors for ablation are often the proximity of lesions to major vessels, giving so called heat sink effect which decreases the effectiveness of the applied energy. Although this effect is higher in RFA compared to MWA [26,27]. Anatomical proximity of tumours to the diaphragm or biliary tree, mean many of the patients in this series are unsuited to more radical treatment modalities, purely due to technical restraints. Another limiting factor for ablation is size of the lesion. Currently, HCC >30 mm is considered unsuitable for RFA or MWA when following the latest update of the BCLC guidelines [10]. Some centres are proposing expanding the size criteria for ablation using a more complex stereotactic approach [28]. However, this remains a challenging technique not suitable for all patients or centres.

TACE, proposed in the BCLC guidelines for BCLC B lesions, also has technical limitations. These include issues surrounding vascular access as well as variations in effectiveness which are less well understood but could be related to tumour phenotype and genotype [29]. In cases where TACE is possible, there might be a role for SABR. Some papers report an augmented effect from the combination of TACE and radiotherapy, though this is beyond the scope of this paper [30,31].

SABR as a treatment modality has logistical benefits. SABR is commonly performed for <2 weeks and is non-invasive, making it an attractive low-risk alternative to the treatments mentioned above [14].

HCC patients treated with SABR have been found to have no statistically significant reduction in quality of life and in fact showed a trend towards improvement as measured by quality of life outcome measures [32]. We found low rates of toxicity post SABR, despite significant comorbidities and underlying liver dysfunction. Reported toxicities from SABR include gastroduodenitis, increase in CP status without disease progression, and radiation-induced liver disease. Published rates of severe (grade ≥3) toxicity post SABR range from 3.9% for gastrointestinal to 4.7% for liver toxicities, these being the most common [13]. Degree of underlying liver disease (CP status), size of lesion and radiation dose have been correlated with risk of hepatic toxicity from SABR [12,13]. Despite this, SABR has been successfully used to treat patients with underlying CP B or C disease [33]. Lower dose-volumes are advised in these patients to reduce risk of toxicity [23]. Of note, in the UK SABR is currently only commissioned for CP A disease [34]. Compared to liver resection, SABR has significantly lower rates of treatment complications and no requirement for hospitalisation. Compared to other non-surgical treatment modalities, SABR has been shown to compare favourably to RFA with statistically more likely LC and OS in HCC ≥ 30 mm in size [35,36]. Other studies in advanced HCC have shown improved OS and lower reported toxicities from SABR compared to systemic therapy with Sorafinib [37].

Another role for SABR is that it can be used on lesions that have previously been treated by other means, for instance after local recurrence post resection, which might pose technical challenge for re-do surgery. It can also be used in patients that have recurrence or residual disease in previously ablated lesions and even in patients that have been previously treated with TACE. Other literature in the field predominantly reports on SABR as first treatment for HCC. Half the patients in our series had received previous treatment for HCC (TACE, ablation and/or liver resection) and the majority of patients with progression received further liver-directed treatment. There is increasing evidence to suggest the combination of SABR with other treatment modalities such as TACE, resection or systemic agents might be beneficial [13]. Other studies have suggested the use of SABR not only as definitive treatment in non-surgical candidates, but also as bridging to transplant [38]. Increasingly, SABR has become a key treatment modality in the management of HCC. Further randomised control trials are required to further assess combination treatments and their impact on clinical outcomes of patients with HCC.

Limitations include our relatively small sample size, which remains respectable compared to other single-centre observational studies [35,39,40]. The retrospective nature of the study means toxicities may be under-reported. However, with access to hospital attendance and GP records, we would assume that no high-grade toxicities were missed. Furthermore, our toxicity rates are comparable to previously published data [12,24,41].

Conclusion

SABR is an effective treatment option for non-surgical candidates or as additional palliative treatment for patients with HCC. SABR can be delivered over a short period of time with low levels of toxicity even after previous liver-directed therapies and despite significant comorbidity. Subsequent liver-directed therapies remain feasible after SABR. These data are paramount for clinicians and MDT guiding HCC treatment decision-making. Further research is warranted to examine the clinical benefits of combination treatment with SABR and other treatment modalities to maximise disease control in patients with both early and advanced HCC.

Declarations

Author contributions: Conceptualization, Boris Wagner, Stephen Falk and Stijn van Laarhoven; Data curation, Boris Wagner and Mark Callaway; Investigation, Boris Wagner, Mark Callaway, Reyad Abbadi, Gautham Appanna, Jonathan Rees, James Skipworth and Stijn van Laarhoven; Methodology, Boris Wagner, Stephen Falk, Mark Callaway and Stijn van Laarhoven; Supervision, Stephen Falk, Jonathan Rees and Stijn van Laarhoven; Writing – original draft, Boris Wagner; Writing – review & editing, Stephen Falk, Reyad Abbadi, Gautham Appanna, Jonathan Rees, James Skipworth and Stijn van Laarhoven. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Institutional review board statement: The study was conducted in accordance with the Declaration of Helsinki, and approved by the Institutional Review Board of University Hospitals Bristol and Weston NHS Foundation Trust (HEPSUR/CA/2023-24/02 approved 15/08/2023).

Informed consent statement: Informed consent for treatment was obtained from all subjects involved in the study. / Not applicable.

Acknowledgments: For the purpose of open access, the author has applied a Creative Commons Attribution (CC BY) license to any author accepted manuscript arising from this submission.

Conflicts of interest: The authors declare no conflict of interest.

References

1. Fitzmaurice C, Allen C, Barber RM, Barregard L, Bhutta ZA, Brenner H, et al. Global, regional, and national cancer incidence, mortality, years of life lost, years lived with disability, and disability-adjusted life-years for 32 cancer groups, 1990 to 2015: a systematic analysis for the Global Burden of Disease Study. JAMA Oncol. 2017; 3: 524-48.
2. Burton A, Tataru D, Driver RJ, Bird TG, Huws D, Wallace D, et al. Primary liver cancer in the UK: incidence, incidence-based mortality, and survival by subtype, sex, and nation. JHEP Rep. 2021; 3: 100232.
3. Cancer Research UK. Liver cancer statistics. 2023. Available from: https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/liver-cancer#heading-One
4. Parikh ND, Marshall VD, Green M, Lawrence TS, Razumilava N, Owen D, et al. Effectiveness and cost of radiofrequency ablation and stereotactic body radiotherapy for treatment of early-stage hepatocellular carcinoma: an analysis of SEER-Medicare. J Med Imaging Radiat Oncol. 2018; 62: 673-81.
5. Fattovich G, Stroffolini T, Zagni I, Donato F. Hepatocellular carcinoma in cirrhosis: incidence and risk factors. Gastroenterology. 2004; 127: S35-50.
6. Bruix J, Sherman M. Management of hepatocellular carcinoma: an update. Hepatology. 2011; 53: 1020-2.
7. Child CG, Turcotte JG. Surgery and portal hypertension. Major Probl Clin Surg. 1964; 1: 1-85.
8. Oken MM, Creech RH, Tormey DC, Horton J, Davis TE, McFadden ET, et al. Toxicity and response criteria of the Eastern Cooperative Oncology Group. Am J Clin Oncol. 1982; 5: 649-55.
9. Llovet JM, Fuster J, Bruix J. The Barcelona approach: diagnosis, staging, and treatment of hepatocellular carcinoma. Liver Transpl. 2004; 10: S115-S20.
10. Reig M, Forner A, Rimola J, Ferrer-Fàbrega J, Burrel M, Garcia-Criado Á, et al. BCLC strategy for prognosis prediction and treatment recommendation: the 2022 update. J Hepatol. 2022; 76: 681-93.
11. Curley SA, Stuart KE, Schwartz JM, Carithers R. Nonsurgical therapies for localized hepatocellular carcinoma: radiofrequency ablation, percutaneous ethanol injection, thermal ablation, and cryoablation. UpToDate. 2012.
12. Shanker MD, Moodaley P, Soon W, Liu HY, Lee YY, Pryor DI. Stereotactic ablative radiotherapy for hepatocellular carcinoma: a systematic review and meta-analysis of local control, survival and toxicity outcomes. J Med Imaging Radiat Oncol. 2021; 65: 956-68.
13. Rim CH, Kim HJ, Seong J. Clinical feasibility and efficacy of stereotactic body radiotherapy for hepatocellular carcinoma: a systematic review and meta-analysis of observational studies. Radiother Oncol. 2019; 131: 135-44.
14. Takeda A, Sanuki N, Eriguchi T, Kobayashi T, Iwabutchi S, Matsunaga K, et al. Stereotactic ablative body radiotherapy for previously untreated solitary hepatocellular carcinoma. J Gastroenterol Hepatol. 2014; 29: 372-9.
15. Kang JK, Kim MS, Cho CK, Yang KM, Yoo HJ, Kim JH, et al. Stereotactic body radiation therapy for inoperable hepatocellular carcinoma as a local salvage treatment after incomplete transarterial chemoembolization. Cancer. 2012; 118: 5424-31.
16. Bujold A, Massey CA, Kim JJ, Brierley J, Cho C, Wong RK, et al. Sequential phase I and II trials of stereotactic body radiotherapy for locally advanced hepatocellular carcinoma. J Clin Oncol. 2013; 31: 1631-9.
17. Quan H, Li B, Couris CM, Fushimi K, Graham P, Hider P, et al. Updating and validating the Charlson comorbidity index and score for risk adjustment in hospital discharge abstracts using data from 6 countries. Am J Epidemiol. 2011; 173: 676-82.
18. Lencioni R, Llovet JM. Modified RECIST (mRECIST) assessment for hepatocellular carcinoma. Semin Liver Dis. 2010; 30: 52-60.
19. Stereotactic UK Consortium. Stereotactic ablative body radiation therapy (SABR): a resource. The Royal College of Radiologists. 2019.
20. Cox JD, Stetz J, Pajak TF. Toxicity criteria of the Radiation Therapy Oncology Group (RTOG) and the European Organization for Research and Treatment of Cancer (EORTC). Int J Radiat Oncol Biol Phys. 1995; 31: 1341-6.
21. Cárdenes HR, Price TR, Perkins SM, Maluccio M, Kwo P, Breen TE, et al. Phase I feasibility trial of stereotactic body radiation therapy for primary hepatocellular carcinoma. Clin Transl Oncol. 2010; 12: 218-25.
22. Lo CH, Yang JF, Liu MY, Jen YM, Lin CS, Chao HL, et al. Survival and prognostic factors for patients with advanced hepatocellular carcinoma after stereotactic ablative radiotherapy. PLoS One. 2017; 12: e0177793.
23. Lasley FD, Mannina EM, Johnson CS, Perkins SM, Althouse S, Maluccio M, et al. Treatment variables related to liver toxicity in patients with hepatocellular carcinoma, Child-Pugh class A and B enrolled in a phase 1-2 trial of stereotactic body radiation therapy. Pract Radiat Oncol. 2015; 5: e443-e9.

24. Qi X, Tang Y, An D, Bai M, Shi X, Wang J, et al. Radiofrequency ablation versus hepatic resection for small hepatocellular carcinoma: a meta-analysis of randomized controlled trials. J Clin Gastroenterol. 2014; 48: 450-7.

25. Llovet JM, Fuster J, Bruix J. Intention-to-treat analysis of surgical treatment for early hepatocellular carcinoma: resection versus transplantation. Hepatology. 1999; 30: 1434-40.

26. Luerken L, Haimerl M, Doppler M, Uller W, Beyer LP, Stroszczynski C, et al. Update on percutaneous local ablative procedures for the treatment of hepatocellular carcinoma. Rofo. 2022; 194: 1075-86.

27. Pillai K, Akhter J, Chua TC, Shehata M, Alzahrani N, Al-Alem I, et al. Heat sink effect on tumor ablation characteristics as observed in monopolar radiofrequency, bipolar radiofrequency, and microwave, using ex vivo calf liver model. Medicine (Baltimore). 2015; 94: e580.

28. Bale R, Laimer G, Schullian P, Alzaga A. Stereotactic ablation: a game changer? J Med Imaging Radiat Oncol. 2023.

29. Ebeling Barbier C, Heindryckx F, Lennernäs H. Limitations and possibilities of transarterial chemotherapeutic treatment of hepatocellular carcinoma. Int J Mol Sci. 2021; 22.

30. Huo YR, Eslick GD. Transcatheter arterial chemoembolization plus radiotherapy compared with chemoembolization alone for hepatocellular carcinoma: a systematic review and meta-analysis. JAMA Oncol. 2015; 1: 756-65.

31. Chang Y, Jeong SW, Young Jang J, Jae Kim Y. Recent updates of transarterial chemoembolization in hepatocellular carcinoma. Int J Mol Sci. 2020; 21.

32. Méndez Romero A, Wunderink W, van Os RM, Nowak PJ, Heijmen BJ, Nuyttens JJ, et al. Quality of life after stereotactic body radiation therapy for primary and metastatic liver tumors. Int J Radiat Oncol Biol Phys. 2008; 70: 1447-52.

33. Culleton S, Jiang H, Haddad CR, Kim J, Brierley J, Brade A, et al. Outcomes following definitive stereotactic body radiotherapy for patients with Child-Pugh B or C hepatocellular carcinoma. Radiother Oncol. 2014; 111: 412-7.

34. NHS England. Clinical commissioning policy: the use of stereotactic ablative radiotherapy (SABR) as a treatment option for patients with hepatocellular carcinoma or cholangiocarcinoma (adults). 2020.

35. Kim N, Kim HJ, Won JY, Kim DY, Han KH, Jung I, et al. Retrospective analysis of stereotactic body radiation therapy efficacy over radiofrequency ablation for hepatocellular carcinoma. Radiother Oncol. 2019; 131: 81-7.

36. Cheng PL, Wu PH, Kao WY, Lai YT, Hsu JC, Chiou JF, et al. Comparison of local ablative therapies, including radiofrequency ablation, microwave ablation, stereotactic ablative radiotherapy, and particle radiotherapy, for inoperable hepatocellular carcinoma: a systematic review and meta-analysis. Exp Hematol Oncol. 2023; 12: 37.

37. Bettinger D, Pinato DJ, Schultheiss M, Sharma R, Rimassa L, Pressiani T, et al. Stereotactic body radiation therapy as an alternative treatment for patients with hepatocellular carcinoma compared to sorafenib: a propensity score analysis. Liver Cancer. 2019; 8: 281-94.

38. Andolino DL, Johnson CS, Maluccio M, Kwo P, Tector AJ, Zook J, et al. Stereotactic body radiotherapy for primary hepatocellular carcinoma. Int J Radiat Oncol Biol Phys. 2011; 81: e447-53.

39. Zhang T, Sun J, He W, Li H, Piao J, Xu H, et al. Stereotactic body radiation therapy as an effective and safe treatment for small hepatocellular carcinoma. BMC Cancer. 2018; 18: 451.

40. Hanazawa H, Takahashi S, Shiinoki T, Park SC, Yuasa Y, Koike M, et al. Clinical assessment of coiled fiducial markers as internal surrogates for hepatocellular carcinomas during gated stereotactic body radiotherapy with a real-time tumor-tracking system. Radiother Oncol. 2017; 123: 43-8.

41. Jang WI, Bae SH, Kim MS, Han CJ, Park SC, Kim SB, et al. A phase 2 multicenter study of stereotactic body radiotherapy for hepatocellular carcinoma: safety and efficacy. Cancer. 2020; 126: 363-72.