



## Clinical Commissioning Policy

### Stereotactic Ablative Radiotherapy (SABR) for Hepatocellular Carcinoma (Adults) [URN: 1913]

#### Commissioning Position

##### Summary

A final decision as to whether stereotactic ablative radiotherapy (SABR) will be routinely commissioned will be made by NHS England following a recommendation from the Clinical Priorities Advisory Group. The proposal is: stereotactic ablative radiotherapy (SABR) is recommended to be available as a treatment option through routine commissioning for hepatocellular carcinoma in adults within the criteria set out in this document.

The policy is restricted to certain age groups as there is insufficient evidence to confirm safety and/or it is not recommended to be used in those age groups not included in the policy.

#### Executive Summary

##### Equality statement

Promoting equality and addressing health inequalities are at the heart of NHS England's values. Throughout the development of the policies and processes cited in this document, we have:

- Given due regard to the need to eliminate discrimination, harassment and victimisation, to advance equality of opportunity, and to foster good relations between people who share a relevant protected characteristic (as cited under the Equality Act 2010) and those who do not share it; and
- Given regard to the need to reduce inequalities between patients in access to, and outcomes from healthcare services and to ensure services are provided in an integrated way where this might reduce health inequalities

#### Plain language summary

##### About Hepatocellular Carcinoma

Hepatocellular carcinoma (HCC) is the most common type of primary liver cancer. This type of liver cancer develops from the main liver cells called hepatocytes. The disease is more likely to develop in men than women and becomes more common in older people (Cancer Research UK, 2018).

There are approximately 5,000 new diagnoses of hepatocellular carcinoma per year in England and the number of diagnoses is increasing due to people living with obesity, viral hepatitis and alcohol excess. These things cause damage and scarring of the liver (known as cirrhosis), which increases the likelihood of hepatocellular carcinoma developing.

##### About current treatment

Treatment for hepatocellular carcinoma depends on the stage the condition is at and a number of patient factors including liver function, co-morbidities, fitness and patient choice. If diagnosed

early, then it may be possible to completely remove the tumour using surgical techniques such as resection or transplantation.

However, most people are diagnosed when the cancer has spread too far to be removed or completely destroyed. In these cases, treatments are used to slow down the spread of the cancer and relieve symptoms such as pain and discomfort, and can include:

- Chemotherapy directly into the liver and cutting off the blood supply to the tumour (known as transarterial chemoembolisation or TACE).
- Radiofrequency ablation (RFA), a procedure which uses heat made by radio waves to destroy cancer cells.
- Systemic cancer treatments, using drugs to treat the whole of the body.

## About stereotactic ablative radiotherapy

Stereotactic ablative radiotherapy (SABR) is a highly targeted form of radiotherapy which targets a tumour with radiation beams from different angles at the same time. The treatment is delivered in a fewer numbers of treatments (hypofractionation) than conventional radiotherapy using one, three, five or eight fractions. The aim of treatment with SABR is to ensure that the tumour receives a high dose of radiation whilst the tissues close to the tumour receive a lower dose of radiation sparing the surrounding healthy normal tissues.

It is thought that SABR could be an additional treatment option for people with hepatocellular carcinoma confined to the liver (referred to as localised disease) who are unable to have any of the current available treatments. In addition, SABR may also be an alternative treatment option for some people currently eligible for treatment with either radiofrequency ablation or systemic cancer treatments.

## What we have decided

NHS England has carefully reviewed the evidence to treat hepatocellular carcinoma with stereotactic ablative radiotherapy (SABR) in adults. We have concluded that there is enough evidence to make the treatment available at this time in line with the criteria set out in this document.

## Links and updates to other Policies

This document updates:

- [Clinical Commissioning Policy: The use of Stereotactic Ablative Radiotherapy \(SABR\) as a treatment option for patients with hepatocellular carcinoma or cholangiocarcinoma.](#)  
NHS England. 2016.

## Committee discussion

The Clinical Priorities Advisory Group are asked to consider the evidence and the policy proposition. See the committee papers (link) for full details of the evidence.

## The condition

Hepatocellular carcinoma (HCC) is the most common type of primary liver cancer arising from hepatocytes. It is more common in people with cirrhosis, hence, the rising incidence of obesity, alcohol use and viral hepatitis is driving an epidemic in HCC in both Western and Far Eastern populations.

## Current treatments

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There are many available treatment options for HCC and the choice of treatment depends on a number of factors including: (i) the stage of the disease at diagnosis; (ii) patient co-morbidities; (iii) liver function; and (iv) patient choice.

Surgical resection and liver transplant are available choices to treat early stage disease. However, most people present with either severe co-morbidities or advanced disease meaning that treatment with surgery and liver transplant is not always possible.

For people unsuitable for surgery or transplant, local ablative treatments such as radiofrequency ablation (RFA) can be offered. TACE is also another possible treatment option, however, the treatment is associated with cumulative toxicity imposing a limit on the amount times a patient can undergo TACE.

Systemic chemotherapy, using an oral tyrosine kinase inhibitor called sorafenib (National Institute for Health and Care Excellence (NICE) Technology Appraisal TA474) can be used with palliative intent to improve local control.

### **Proposed treatments**

The policy considers whether SABR, a form of hypofractionated radiotherapy, should be routinely offered for the treatment of localised HCC. The use of SABR in this indication is thought to stop further growth of the lesion (or cancer), supporting the management of any associated symptoms of the disease; this is referred to as local control.

The use of SABR in this indication would offer an additional treatment option for people unsuitable for any of current treatments but would also offer an alternative treatment option for people currently eligible for treatment with either RFA or systemic treatments such as sorafenib, delaying or avoiding the use of these treatments.

### **Epidemiology and Needs Assessment**

HCC is the most common form of primary liver cancer. The disease is more common in males than females and the risk of developing the disease increases with age, with the peak rate of incidence being in people aged between 75 – 85 years of age (Cancer Research UK, 2019). Liver cancer incidence rates are projected to rise by 38% in the UK between 2014 and 2035 and this includes a larger increase for males than for females (Cancer Research UK, 2019).

In 2016, there were 4,925 cases of liver cancer in England (Cancer Research UK, 2019). Of the 4,925 approximately 20% of people are estimated to be suitable for surgical intervention, equating to 985 cases per year. The remainder of patients will be treated with non-curative treatments. The Policy Working Group estimated that between 100 – 150 people with HCC would be eligible for SABR treatment per year in England in line with the criteria set out in this document.

### **Evidence summary**

NHS England has concluded that there is sufficient evidence to support a proposal for the routine commissioning of this treatment for the indication.

#### Evidence Review

Following a systematic search of medical databases, 7 studies were identified which met the inclusion criteria for this review. These included:

- 5 retrospective comparative cohort studies: one comparing SABR with sorafenib ((Bettinger et al., 2018)- 1023 patients) and 4 comparing SABR with radiofrequency

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ablation (RFA) ((Wahl et al., 2016, Rajyaguru et al., 2018, Parikh et al., 2018, Kim et al., 2019)- 224, 796, 64 and 773 patients respectively).

- 1 systematic review and meta-analysis of non-comparative studies ((Rim et al., 2019)- 1950 patients).
- 1 non-comparative prospective cohort study ((Klein et al., 2015)- 205 patients).
- There was no evidence that compared SABR with either standard fractionated radiotherapy or no treatment/best-supportive care.

All five included comparative studies were selected because they used at least one statistical method to account for baseline imbalances between the two groups.

One of the included studies compared SABR with sorafenib reporting that SABR resulted in superior overall survival (OS) in comparison to sorafenib with a median OS of 17.0 (95% CI 10.8-23.2) months compared to 9.6 (95% CI 8.6-10.7) months, respectively (Bettinger et al. 2018). Progression-free survival (PFS) was a secondary outcome in patients with metastatic HCC. After propensity score matching, patients treated with SABR had an improved progression-free survival compared to patients treated with sorafenib (9.0 vs. 6.0 months).

The comparison of SABR and RFA showed that the two modalities result in equivalent 1- and 2-year OS of 70-80% and 40-50%, respectively. Higher OS rates for both SABR and RFA were reported by Kim et al. (2019). This finding suggests that differences in OS are mostly driven by patient characteristics and not due to the treatment effect. The results reported by the four studies examining this comparison (Wahl et al., 2016, Rajyaguru et al., 2018, Parikh et al., 2018, Kim et al., 2019) are in agreement with the pooled non-comparative results for SABR reported in the systematic review by Rim et al. (2019).

The strongest evidence from non-comparative studies on OS, LC and safety came from the Rim et al. (2019) systematic review which reported the analysis of 32 studies including 1950 patients with HCC and found that SABR resulted in 1-, 2-, and 3-year OS rates of 72.6% (95% CI 65.7-78.6), 57.8% (95% CI 50.9-64.4), and 48.3% (95% CI 40.3-56.5), respectively. The pooled analysis of LC rates, using random effects analyses, showed 1-, 2-, and 3-year LC rates of 85.7% (95% CI 80.1-90.0%), 83.6% (95% CI 77.4-88.3%), and 83.9% (95% CI 77.6-88.6%), respectively.

One non-comparative prospective cohort study reported quality of life (QoL) with SABR (Klein et al., 2015). The study included patients with HCC, intrahepatic cholangiocarcinoma, and liver metastases but presented separate results for the three cohorts. Treatment with SABR did not significantly affect QoL.

The meta-analysis reported toxicity rates from 23 of 33 included studies. The most commonly reported complications of grade  $\geq 3$  were gastrointestinal (GI) or hepatic toxicities with a pooled rate of 3.9% (95% CI 2.6-5.6%) for the former and 4.7% (95% CI 3.4-6.5%) for the latter. An association between Child-Pugh score and toxicity was found but not with either tumour size or radiation dose.

The meta-analysis also looked at separately the results of the three studies that reported high rates of grade  $\geq 3$  toxicity. The authors concluded that considering the pooled rates of complications and the fact that complications at high rates were mostly due to transient liver enzyme elevation and possibly caused by chronic liver disease, the use of SABR to treat patients with HCC was safe.

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There are severe limitations to the evidence for SABR in people with HCC, with the evidence base mainly composed by retrospective non-comparative studies and high levels of heterogeneity in the included patient population and study designs. The inherent bias of retrospective comparisons cannot be completely addressed with statistical methods as evident by the Rajyaguru et al. (2018) study where failure to capture all important baseline characteristics during propensity-score matching resulted in wrong conclusions subsequently disproved by the literature.

### Commissioning through Evaluation (CtE) Report

Between 2015 and 2018, the CtE scheme collected outcomes from 91 patients recruited from 7 centres nationally. The mean age of patients was 72 years, and most (72.5%) were men. The cohort was mainly comprised of patients with a single lesion. The majority of the patients (95%) were treated with a standard linear accelerator<sup>1</sup>. Most patients were treated with 5 fractions of radiotherapy receiving a median dose of 45 Gy of radiation in total. Cone beam CT (CBCT) image guidance was the most commonly used technique to assist treatment delivery in this patient cohort.

The data analysis reported overall survival (OS) of 76.5% (95% CI: 62.4 to 85.9%) at 1 year and 41.7% at 2 years (95% CI: 22.4 to 60.0%). The 95% confidence interval of the CtE data contains the survival target set at the beginning of the SABR CtE scheme (2-year target = 50%). The findings of the CtE scheme on the effect of SABR in OS of patients with HCC is supported by low quality evidence from the literature. The main evidence comes from a systematic review and meta-analysis (Rim et al. 2019) that included 32 observational single-arm studies involving 1950 patients with HCC who underwent SABR. Pooled 1-, 2-, and 3-year OS rates were 72.6% (95% CI 65.7-78.6), 57.8% (95% CI 50.9-64.4), and 48.3% (95% CI 40.3-56.5), respectively. Although the meta-analysis included studies with heterogeneous patient populations and study designs, the pooled result resulted in a patient cohort with similar characteristics to the CtE scheme.

The main evidence from the literature for the effect of SABR in comparison with radiofrequency ablation (RFA) comes from two retrospective propensity matched cohort studies (Wahl et al. 2016, Parikh et al. 2018). They reported equivalent OS results between SABR and RFA with 1-year OS of approximately 70-80% and a 2-year OS of 50%. The combined findings from the published literature and the CtE scheme provide low quality evidence that SABR treatment in patients with HCC results in similar OS in comparison with RFA. There is additional low quality evidence from one retrospective, propensity matched cohort study that the OS following treatment with SABR is better than sorafenib. SABR resulted in superior OS in comparison to sorafenib with a median OS of 17.0 (95% CI 10.8-23.2) months compared to 9.6 (95% CI 8.6-10.7), respectively (Bettinger et al. 2018).

The CtE data analysis also reported a local control (LC) rate of 72.3% (95% CI 57.9-82.5%) at 1 year and 52.4% (95% CI: 25.2-73.9%) at 2 years. The 95% confidence interval of the CtE data contains the LC target set at the beginning of the SABR CtE scheme (1-year target = 80%). The findings of the CtE scheme on the effect of SABR on LC is partially supported by the findings of the meta-analysis by Rim et al. (2019). Pooled 1-, 2-, and 3-year LC rates from the meta-analysis were 85.7% (95% CI 80.1-90.0), 83.6% (95% CI 77.4-88.3), and 83.9% (95% CI 77.6-88.6), respectively. Only the 1-year and not the 2-year LC rate of the CtE is within the 95% confidence interval reported by Rim et al. (2019).

Contrary to the rest of the studies, the CtE has not used RECIST to calculate LC. Therefore, the results are not easily comparable. The combined findings from the published literature and the CtE provide low quality evidence that SABR achieves high LC rates.

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The CtE data analysis reported a grade 3/4 adverse event rate of 12.1% (95% CI 6.8-20.7) and a grade 4 adverse event rate of 3.3% (95% CI 1.1-9.9%), above and within the proposed targets of 15% and 10%, respectively. No grade 5 adverse events were reported. Longitudinal analysis of the adverse events rates showed that a high proportion of patients (57%) reported symptoms consistent with CTCAE grade 1 and above adverse events at baseline before SABR treatment started. The most frequently reported adverse event was fatigue. Other frequently recorded adverse events were associated with increased blood levels of alanine aminotransferase (ALT) and bilirubin. Longitudinal analysis of these results suggests that the abnormal liver function test results were not treatment related.

The main evidence from the literature on the safety of SABR is provided by the meta-analysis by Rim et al. (2019). The most commonly reported grade 3+ adverse events observed following SABR treatment were gastrointestinal (GI) or hepatic. For GI adverse events, the grade 3+ event rate was less than 5% in 16 of 17 included studies. It was 15% in one study and was not reported in 6 of the studies. The combined event rate from all studies for grade 3+ GI adverse events using random effects analysis was 3.9% (95% CI 2.6-5.6%). For hepatic adverse events, the rates of grade 3+ events were <10% in 23 of 24 cohorts. The pooled rate was 4.7% (95% CI 3.4-6.5%). Meta-regression analysis showed that Child-Pugh (CP) class was significantly correlated with hepatic complications of grade 3+ ( $p = 0.013$ ). With the exception of ALT and bilirubin, the analysis of the CtE adverse events did not take into account the timing of the event. It is therefore not possible to separate acute and late adverse events. The combined findings from the CtE and the published literature, provide low quality evidence that SABR does not result in high rates of adverse events in this patient cohort.

Data on quality of life (QoL) were available for 88 patients (97%) at baseline. According to the summary analysis, the proportion of patients reporting no problems, some problems and severe problems remained stable for the mobility and anxiety/depression outcomes. There was a small increase in the proportion of patients reporting problems with their self-care, usual activities, and pain/discomfort between baseline and 12 months follow-up. It should be noted, however, that the small number of patients with follow-up beyond 12 months increases the uncertainty of these results. The CtE QoL results are supported by 1 observational study that reported no significant impact in most QoL outcomes following SABR treatment in patients with liver cancer. The combined findings from the CtE scheme and the published literature provide low quality evidence that SABR does not significantly affect QoL in this patient cohort.

Data on pain scores were available for 90 patients (99%) at baseline. According to the summary analysis, the majority of patients (87%) did not report any pain at baseline or during follow-up. There was an increase in the number of patients who report severe pain, from 1% at baseline to 9% and 19% at 12 and 18 months, respectively. This finding is in agreement with the analysis of the QoL pain/discomfort dimension that reported a small increase in the number of people reporting worsening symptoms between baseline and follow-up (from 0% to 6% at 18 months).

For both QoL and pain scores, the analysis assumed that missing data have a random distribution and do not introduce bias. Based on the providers' feedback, however, missing data are often associated with a decline in the patient's performance status and clinical condition. There is, therefore, a lot of uncertainty about the QoL and pain conclusions and the results should be interpreted with caution. According to the patient experience questionnaire, 87% of CtE HCC cohort were extremely likely or likely to recommend the SABR service to their friends and family.

The main limitation of the current evidence (including the analysis of the CtE data) is that the majority comes from non-comparative (often retrospective) observational studies. These studies include heterogeneous patient populations, and study designs that limit the generalisability of the results. The evidence from retrospective comparative studies that used propensity score

matching to account for baseline differences between SABR and RFA, and SABR and sorafenib, also suffer from the same limitations as the inherent biases of retrospective design, such as patient selection bias, lack of information on important baseline clinical characteristics and adverse events outcomes, which cannot be fully addressed by statistical methods. Finally, the small size of the CtE scheme cohort and the small number of patients with more than 12 months follow-up, increases the uncertainty around any conclusions drawn for this cohort.

The objective of the economic evaluation in the CtE scheme was to determine whether SABR is a cost-effective intervention compared with radiofrequency ablation (RFA) and surgery for patients with resectable HCC. Despite entry criteria for the CtE scheme excluding patients whose HCC was suitable for treatment by surgery or RFA, these interventions were considered potential alternatives to SABR if the use of SABR is to be expanded in the future. Therefore, they were selected by the data working group as comparators to SABR. The cost-effectiveness analysis found that for adult patients with resectable HCC who may be candidates for surgery, SABR is the most cost-effective intervention. There was considerable uncertainty surrounding this finding and the results were sensitive to assumptions on the cost of SABR and RFA and the impact of treatment modality on mortality. The results are limited by the lack of a control group in the CtE data; it is likely that comparisons with data from the literature on survival and progression rates are confounded by differences in patient characteristics. A randomised trial might provide the robust data required to conclusively assess the cost-effectiveness of treatments for HCC.

## Implementation

All patients with cancer should have their care managed by a variety of different specialists working together as part of a tumour specific cancer multi-disciplinary team (MDT). For people with HCC, the hepato-biliary and pancreatic (HBP) MDT is responsible for radiotherapy case selection and should take into consideration patient comorbidities, potential adverse events and likely outcomes of treatment.

## Inclusion Criteria

Patients meeting **all** of the following criteria will be eligible for treatment with SABR:

- Confirmed diagnosis of localised HCC (primary, recurrent or progressive disease) by at least one criterion listed below:
  - Pathologically (histologically or cytologically) proven diagnosis of HCC.
  - At least one solid liver lesion or vascular tumour thrombosis (involving portal vein, IVC and/or hepatic vein) > 1 cm with arterial enhancement and delayed washout on multiphasic Computed-Tomography (CT) or Magnetic Resonance Image (MRI) in the setting of cirrhosis or chronic hepatitis B or C without cirrhosis.
- No evidence of extrahepatic metastases or malignant nodes (that enhance with typical features of HCC) > 3.0 cm in sum of maximal diameters.
- Unsuitable for surgical resection or transplant.
- Unsuitable or refractory to TACE.
- History/physical examination including examination for encephalopathy, ascites, and Eastern Cooperative Oncology Group (ECOG) Performance Status 0-1.
- Adequate haematological and liver function.
- Childs-Pugh Class A only.
- Maximum dimension of any lesion 5 cm.
- Life expectancy greater than six months.

SABR should be considered as an alternative treatment in people currently eligible for systemic treatments (such as sorafenib) and/or local ablative treatments.



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Any patients suitable for SABR must have recovered from the effects of previous surgery, radiotherapy or chemotherapy with a minimum of 4 weeks break prior to treatment with SABR.

### Exclusion criteria

Treatment with SABR is unsuitable in people with:

- Active hepatitis or clinically significant liver failure (encephalopathy, oesophageal varices, portal hypertension);
- Prior abdominal radiotherapy precluding SABR, that is any previous radiation therapy in which a mean dose to the liver of 15 Gray (Gy) in conventional fractionation was delivered or previous doses to critical normal structures that would make re-irradiation unsafe. Prior pelvic radiation is permitted, as long as there is no overlap between pelvic and liver radiation fields;
- Clinically apparent ascites;
- Any one hepatocellular carcinoma > 6 cm;
- More than 5 discrete intrahepatic parenchymal foci of HCC;
- Direct tumour extension into the stomach, duodenum, small bowel or large bowel;
- Evidence of extrahepatic metastases or malignant nodes (that enhance with typical features of HCC) > 3.0 cm in sum of maximal diameters (e.g. 2 lung lesions >2 cm); or
- Prior liver transplant.

### Dose and fractionation

It is expected that prescription doses of 40-50 Gray (Gy) in 5 fractions of SABR should be delivered in the treatment of HCC.

### Patient Pathway

Radiotherapy is part of an overall cancer management and treatment pathway. Decisions on the overall treatment plan should relate back to an MDT discussion and decision. Patients requiring radiotherapy are referred to a clinical oncologist for assessment, treatment planning and delivery of radiation fractions. Each fraction of radiation is delivered on one visit, usually as an outpatient basis.

### Governance Arrangements

The Service Specification for External Beam Radiotherapy (NHS England Reference: 170091S) describes the governance arrangements for this service. It is imperative that the radiotherapy service is fully compliant with this Service Specification and in particular, with the Ionising Radiation (Medical Exposure) Regulations (IR(ME)R) 2017.

Clinical governance systems and policies should be in place and integrated into the organisational governance with clear lines of accountability and responsibility for all clinical governance functions. Providers should produce annual clinical governance reports as part of the NHS clinical governance reporting system. Providers must have an externally accredited quality management system (e.g. BSI) in place.

All providers must be compliant with Radiotherapy Quality Assurance (RTTQA) for contouring and outlining. A national approach to regular peer review of patient eligibility and treatment plans will be required.

In addition, all providers of treatment with SABR must:

- Be compliant with the Improving Outcomes Guidance (IOG) for liver cancer and have a HBP MDT in place;
- Ensure all patients treated are subject to an MDT approach to patient selection and treatment including discussion at the HBP MDT and SABR planning group;



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- Have an adequate technical multi-professional radiotherapy SABR team present and able to deliver SABR radiotherapy; and
- Have minimum of two subspecialist clinical oncologists with experience in treating SABR patients.

### Mechanism for funding

Radiotherapy planning and delivery is reimbursed through national prices included within the National Tariff Payment System.

### Audit requirements

Radiotherapy providers must submit their activity to the national Radiotherapy Dataset (RTDS) on a monthly basis. Providers will collect the audit clinical outcome data through their own collection process for all SABR.

Radiotherapy services are subject to regular self-assessment by the national Specialised Commissioning Quality Surveillance. The quality system and its treatment protocols will be subject to regular clinical management and audit as part of the development of radiotherapy networks in England.

The SABR Consortium Guidelines 2019 provide detailed information on each indication contained within this policy and can be found online [here](#).

### Policy review date

This document will be reviewed when information is received which indicates that the policy requires revision. If a review is needed due to a new evidence base then a new Preliminary Policy Proposition needs to be submitted by contacting [england.CET@nhs.net](mailto:england.CET@nhs.net).

Our policies provide access on the basis that the prices of therapies will be at or below the prices and commercial terms submitted for consideration at the time evaluated. NHS England reserves the right to review policies where the supplier of an intervention is no longer willing to supply the treatment to the NHS at or below this price and to review policies where the supplier is unable or unwilling to match price reductions in alternative therapies.

### Definitions

Chemotherapy	The use of a drug to kill or damage cells, most commonly used in cancer treatment.
Child-Pugh score	A scoring system used to assess liver disease. There are three classes: (i) Class A means the liver is working normally; (ii) Class B means there is mild to moderate liver damage; and (iii) Class C means there is severe liver damage.
Cirrhosis	A term used to describe the damage and scarring of the liver. Cirrhosis can be caused by a number of factors including hepatitis infections and excessive alcohol consumption.
Extrahepatic	Outside the liver.
Fraction/Fractionation	The term that describing how the full dose of radiation is divided into a number of smaller doses called fractions. The fractions are

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	given as a series of treatment sessions which make up a radiotherapy course.
Hepatitis	A term used to describe inflammation of the liver. Hepatitis is usually caused as a result of a viral infection or drinking alcohol.
Hepatobiliary and pancreatic (HBP)	The liver, pancreas, gall bladder and bile duct are known as the hepatobiliary and pancreatic system.
Hepatocellular carcinoma (HCC)	The most common form of primary liver cancer, originating from hepatocytes.
Hepatocytes	The most common type of cell in the liver. These cells account for 65 – 75% of the tissue in the liver and are responsible for protein synthesis.
Hypofractionation	Describes a treatment regimen that delivers high doses of radiation using a shorter number of treatments as compared to conventional treatment regimens.
Intrahepatic	Inside the liver.
Local control	Indicates that the cancer has stopped growing and has not increased in size.
Primary liver cancer	Means the cancer started in the liver. It is an uncommon cancer in the UK.
Radiofrequency ablation (RFA)	A cancer treatment that uses heat to destroy cancer cells.
Radiotherapy	The safe use of ionising radiation to destroy cancer cells with the aim of cure or effective palliation.
Refractory	The cancer may be resistant at the beginning of treatment or it may become resistant during treatment.
Stereotactic ablative radiotherapy (SABR)	Refers to the irradiation of an image defined extra cranial lesion and is associated with the use of high radiation dose delivered in a small number of fractions. The technique requires specialist positioning equipment and imaging to confirm correct targeting. It allows sparing of the healthy normal tissues.
Surgical resection	A surgical procedure used to remove the cancer or tumour.
Supportive care	Treatment given to prevent, control, or relieve complications and side effects and to improve the patient's comfort and quality of life.
Systemic treatment	Treatment, usually involving chemotherapy or hormone treatment, which aims to treat the whole body.
Transplant	A surgical procedure in which living tissue or an organ is implanted in another part of the body or in another body.
Trans-arterial chemoembolisation (TACE)	A treatment in which chemotherapy is directly administered into the blood vessel feeding the tumour in the liver and blocking off the blood supply.

Tyrosine kinase inhibitor	A targeted cancer treatment that prevents cancer cells from growing by blocking chemical messengers called tyrosine kinases.
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