NHS England

# Clinical Commissioning Policy: The use of Stereotactic Ablative Radiotherapy (SABR) as a treatment option for patients with Hepatocellular carcinoma or Cholangiocarcinoma

**Reference: NHS England: 16022/P**

| NHS England INFORMATION READER BOX | | |
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| **Directorate** | | |
| Medical | Operations and Information | **Specialised Commissioning** |
| Nursing | Trans. & Corp. Ops. | Commissioning Strategy |
| Finance | | |

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| **Publications Gateway Reference:** | **05527s** |
| **Document Purpose** | Policy |
| **Document Name** | Clinical Commissioning Policy 16022/P |
| **Author** | Specialised Commissioning Team |
| **Publication Date** | 13 July 2016 |
| **Target Audience** | CCG Clinical Leaders, Care Trust CEs, Foundation Trust CEs , Medical Directors, Directors of PH, Directors of Nursing, NHS England Regional Directors, NHS England Directors of Commissioning Operations, Directors of Finance, NHS Trust CEs |
| **Additional Circulation List** | |
| **Description** | Not Routinely Commissioned - NHS England will not routinely commission this specialised treatment in accordance with the criteria described in this policy. |
| **Cross Reference** | This document is part of a suite of policies with Gateway Reference 05527s. |
| **Superseded Docs** (if applicable) | N/A |
| **Action Required** | N/A |
| **Timing / Deadlines** (if applicable) | **N/A** |
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# Clinical Commissioning Policy: The use of Stereotactic Ablative Radiotherapy (SABR) as a treatment option for patients with Hepatocellular carcinoma or Cholangiocarcinoma

First published: July 2016

**Prepared by NHS England Specialised Services Clinical Reference Group for Radiotherapy**

Published by NHS England, in electronic format only.

# Contents

## Policy Statement

NHS England will not routinely commission the use of Stereotactic Ablative Radiotherapy (SABR) as a treatment option for patients with Hepatocellular carcinoma or Cholangiocarcinoma in accordance with the criteria outlined in this document. In creating this policy NHS England has reviewed this clinical condition and the options for its treatment. It has considered the place of this treatment in current clinical practice, whether scientific research has shown the treatment to be of benefit to patients, (including how any benefit is balanced against possible risks) and whether its use represents the best use of NHS resources. This policy document outlines the arrangements for funding of this treatment for the population in England.

## Equality Statement

Throughout the production of this document, due regard has been given 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 in under the Equality Act 2010) and those who do not share it.

## Plain Language Summary

The proposal aims to confirm NHS England's approach to the use of Stereotactic Ablative Radiotherapy (SABR) as a treatment option for:

- a type of liver cancer called ‘hepatocellular carcinoma’; and
- cancer of the bile duct, which is called ‘cholangiocarcinoma’.

**About SABR treatment**

Stereotactic Ablative Radiotherapy (SABR) is a highly targeted radiation therapy which aims to target a tumour with radiation beams from different angles at the same time so that:

- The tumour receives a high dose of radiation
- The tissues around the tumour receive a low dose

There are usually between 1 and 8 treatments, called ‘fractions’.

**What we have decided**

NHS England has carefully reviewed the evidence to treat hepatocellular carcinoma and cholangiocarcinoma with Stereotactic Ablative Radiotherapy (SABR). We have concluded that there is not enough evidence to make the treatment available at this time.

# 1 Introduction

This document describes the evidence that has been considered by NHS England in formulating a proposal to not routinely commission Stereotactic Ablative Radiotherapy in the treatment of patients with hepatocellular carcinoma or cholangiocarcinoma. For the purpose of this policy Stereotactic Ablative Radiotherapy (SABR) refers to hypo-fractionated treatment of not more than 8 fractions.

Commissioning arrangements for fractionated treatments utilising a larger number of fractions are beyond the remit of this policy. This policy concerns the use of SABR to treat hepatoceullar carcinoma or cholangiocarcinoma.

# 2 Definitions

**Stereotactic Ablative Radiotherapy (SABR)** refers to the precise irradiation of an image defined extra cranial lesion and is associated with the use of a 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 surrounding healthy normal tissues.

**Stereotactic radiation therapy** has been used for benign and malignant lesions in the brain for many years. Stereotactic radiosurgery (SRS) is a single fraction of stereotactic directed radiation of a limited volume in the brain or other structure of the skull base, whereas stereotactic radiotherapy (SRT) has been defined as a fractionated stereotactic directed radiation of a limited volume in the brain. Stereotactic Ablative radiotherapy (SABR) refers to the use of stereotactically directed radiation therapy to structures outside the brain and skull.

**Extra-cranial malignant disease** is a catch all term for all malignancies excluding cerebral metastases, which is the subject of a separate policy.

# 3 Aims and Objectives

This policy considers whether there is sufficient robust evidence of clinical and cost-effectiveness and safety to support the use of SABR to treat patients with hepatocellular carcinoma or cholangiocarcinoma.

The objective was to identify whether the evidence is sufficiently robust and what criteria should be used to identify suitable patients to be considered for SABR.

# 4 Epidemiology and Needs Assessment

Primary tumours in the liver are much less common than ones which have metastasised there from elsewhere. The commonest primary liver tumour is hepatocellular carcinoma, which often develops from liver cells affected by chronic liver disease such as cirrhosis or hepatitis. Cholangiocarcinoma is less common, and arises from the cells lining the bile ducts.

Hepatocellular carcinoma can be treated with surgical resection, liver transplantation, trans-catheter arterial chemo-embolisation, percutaneous ablation, systemic drug treatment, and external beam or stereotactic radiotherapy.

Cholangiocarcinoma can be treated with surgery in less advanced cases, and with radiotherapy. Chemotherapy may also be used.

# 5 Evidence Base

The evidence regarding the effectiveness and safety of Stereotactic Ablative Radiotherapy (SABR) for treating patients with hepatocellular carcinoma or cholangiocarcinoma has been used as a basis for this commissioning policy. The evidence base indicates that there is insufficient evidence to routinely commission SABR for this cohort of patients.
This policy will replace the current published clinical commissioning policy statement on this topic.

Three systematic reviews were identified relating to the use of SABR in hepatocellular carcinoma:

- Tao and Yang (2012) reviewed studies of SABR for hepatocellular carcinoma and hepatic metastases (search date 2011). The authors found no randomised trials or other controlled research. They included four uncontrolled studies of SABR for hepatocellular carcinoma. They did not meta-analyse the studies, but reported overall one-year survival rates of 33% to 100% after SABR. Tao and Yang contrasted these rates with those of 50% to 70% reported after other treatments such as resection, radiofrequency ablation and chemo-embolisation. However, the relevance of this comparison is uncertain, as SABR is sometimes used when other treatments are not feasible.

- The second systematic review was by Qi et al (2015) These authors included studies of people with hepatocellular carcinoma treated with photon therapy (including SABR), charged particle (proton and carbon ion) therapy or combined photon therapy and charged particle therapy. Qi et al found no controlled studies comparing charged particle therapy with photon therapy. They found twenty uncontrolled studies of charged particle therapy including a total of 1627 participants, thirty studies of SABR with 1473 participants and twenty-three studies of conventional radiotherapy with 2104 participants.

There were important differences between the three sets of participants in median age, tumour size, severity of cirrhosis and duration of follow-up. The authors also reported a high degree of heterogeneity within all three groups of studies, but nevertheless meta-analysed them. Overall survival, progression-free survival and locoregional control were similar in people treated with charged particle therapy and SABR, both of which were reportedly superior to conventional radiotherapy. The frequency of adverse effects of treatment was also similar, except that there was significantly more late toxicity in the SABR group than in the charged particle therapy group.

The third systematic review related to safety of SABR, Ibarra et al (2012):

- The authors included studies of the SABR for liver tumours which reported a dose-volume constraint and liver toxicity; they used these to standardise doses and thereby to make studies more comparable.

- There were eight suitable studies, only four of which included participants with hepatocellular carcinoma. They did not meta-analyse the results but reported that, of 65 people treated for hepatocellular carcinoma with SABR, four developed grade 5 radiation-induced liver disease (the most severe) and two developed grade 4 disease. This led them to recommend that SABR should only be used with caution or in a clinical trial.

Other studies also considered toxicity and safety related to SABR. Kopek et al (2010) reported that six of the 27 participants (22%) in their study developed “severely symptomatic” duodenal ulcers with bleeding, anaemia and either admission and/or transfusion. Three patients developed duodenal stenosis.

Bujold et al (2013) report seven deaths in their study of 102 people with cholangiocarcinoma “at least possibly related to treatment.” Five had liver failure, of whom two also had massive tumour thrombosis; the other two had cholangitis and duodenal haemorrhage.

For cholangiocarcinoma six uncontrolled studies of SABR were identified, four studies were excluded due to low numbers of participants (n<10). Two studies have been appraised in relation to this policy, there are:

- Kopek et al (2010) which reported the results of SABR in 27 people with unresectable cholangiocarcinoma. Median follow-up was more than five years, longer than is usual for studies of this type. Median progression-free survival was less than seven months and median overall survival was less than eleven months. The authors concluded that the survival results in their study “appear no better than the survival outcomes achieved with external beam

> radiotherapy … despite the use of a dose schedule of very high radiobiological potency."

Ibarra et al (2012) also treated participants with hepatocellular carcinoma and cholangiocarcinoma at three hospitals in the north-eastern United States. The eleven people with cholangiocarcinoma were followed for a median of less than five months. Only a third of patients showed a response to treatment, and median survival was less than a year. The authors concluded that "randomised controlled trials are needed to further define the role of [SABR] in the treatment of primary liver tumours."

# 6 Documents which have informed this Policy

National Cancer Action Team. National Radiotherapy Implementation Group Report Stereotactic Body Radiotherapy Guidelines for Commissioners, Providers and Clinicians in England 2011. Available from: Accessed September 2012.

National Cancer Action Team. National Radiotherapy Implementation Group Report Stereotactic Body Radiotherapy Clinical Review of the Evidence for SBRT 2011.

Yorkshire and the Humber Specialised Commissioning Group. Commissioning Policy Stereotactic radiosurgery/radiotherapy.

# 7 Date of Review

This document will be reviewed when information is received which indicates that the policy requires revision.

# References

Bujold A, Massey CM, Kim JJ, et al. Sequential phase I and II trials of stereotactic body radiotherapy for locally advanced hepatocellular carcinoma. J Clin Oncol 2013; 31: 1631-39.

Kopek N, Holt MI, Hansen AT, Høyer M. Stereotactic body radiotherapy for unresectable cholangiocarcinoma. Radiother Oncol 2010; 94: 47-52.

Ibarra RA, Rojas D, Snyder L, et al. Multicenter results of stereotactic body radiotherapy (SBRT) for non-resectable primary liver tumors. Acta Oncol 2012; 51: 575-83.

Tao C, Yang LX. Improved radiotherapy for primary and secondary liver cancer: stereotactic body radiation therapy. Anticancer Res 2012; 32: 649-55.

Qi WX, Fu S, Zhang Q, Guo XM. Charged particle therapy versus photon therapy for patients with hepatocellular carcinoma: A systematic review and meta-analysis. Radiother Oncol 2015; 114: 289-95.