NHS England

Draft for

Clinical Commissioning Policy Proposition:

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

Reference: NHS England B01X26

Clinical Commissioning Policy Proposition: The use of Stereotactic Ablative Radiotherapy (SABR) as a treatment option in the management of patients with hepatocellular carcinoma or cholangiocarcinoma.

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1 Executive Summary

Policy Statement

NHS England proposes to not routinely commission Stereotactic Ablative Radiotherapy in the treatment of patients with hepatocellular carcinoma or cholangiocarcinoma.

In creating this policy proposition NHS England has reviewed a number of clinical conditions and the options for 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.

Equality Statement

NHS England has a duty to have regard to the need to reduce health inequalities in access to health services and health outcomes achieved as enshrined in the Health and Social Care Act 2012. NHS England is committed to fulfilling this duty as to equality of access and to avoiding unlawful discrimination on the grounds of age, gender, disability (including learning disability), gender reassignment, marriage and civil partnership, pregnancy and maternity, race, religion or belief, gender or sexual orientation. In carrying out its functions, NHS England will have due regard to the different needs of protected equality groups, in line with the Equality Act 2010. This document is compliant with the NHS Constitution and the Human Rights Act 1998. This applies to all activities for which NHS England is responsible, including policy development, review and implementation.

Plain Language Summary

The policy proposition aims to confirm NHS England's commissioning approach to the use of Stereotactic Ablative Radiotherapy (SABR) as a treatment option in the management of patients with hepatocellular carcinoma or cholangiocarcinoma. Stereotactic body radiotherapy refers to the use of highly targeted radiation therapy to structures outside the brain and skull.

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2 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 consultation NHS England invites views on the evidence and other information that has been taken into account as described in this policy proposition.

A final decision as to whether NHS England will continue to routinely commission SABR as an option in the treatment of patients with hepatocellular carcinoma or cholangiocarcinoma is planned to be made by NHS England by May 2016 following a recommendation from the Clinical Priorities Advisory Group.

3 Proposed Intervention and Clinical Indication

For the purpose of this policy 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 hepatocellular carcinoma or cholangiocarcinoma.

4 Definitions

Stereotactic body 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

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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

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

Hepatocellular carcinoma or Cholangiocarcinoma.

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.

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5 Aims and Objectives

This policy proposition considered:

Whether there is sufficient robust evidence of clinical and cost- effectiveness and safety to support the use of SBRT / SABR to treat patients with hepatocellular carcinoma or cholangiocarcinoma.

The objectives were to:

- To identify whether the evidence is sufficiently robust and what criteria should

be used to identify suitable patients to be considered for SABR.

6 Epidemiology and Needs Assessment

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

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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 realted 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 uncontrooled 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

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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."

7. Evidence Base

The evidence regarding the effectiveness and safety of SBRT / 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 SBRT for this cohort of patients.
This policy will replace the current published clinical commissioning policy statement on this topic.

NHS England commissioned an evidence review (Solutions for Public Health, 2015) in relation to the clinical indication outlined in this policy.

8. Documents That Have Informed This Policy Proposition

National Radiotherapy Implementation Group Report. Stereotactic Body Radiotherapy Guidelines for Commissioners, Providers and Clinicians in England 2011. Available from: http://www.ncat.nhs.uk/sites/default/files/NRIG%20SBRT%20Final%20June%2011.p df. Accessed September 2012.

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National Radiotherapy Implementation Group Report. Stereotactic Body Radiotherapy Clinical review of the evidence for SBRT 2011.

Yorkshire and the Humber commissioning policy
Stereotactic radiosurgery/radiotherapy.

9 Date of Review

This document will lapse upon publication by NHS England of a clinical commissioning policy for the proposed intervention that confirms whether it is routinely or non-routinely commissioned (expected by May 2016).

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Hepatocellular carcinoma or cholangiocarcinoma

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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.

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