NHS England

Clinical Commissioning Policy: The use of Stereotactic Ablative Radiotherapy (SABR) in the treatment of oligometastatic disease

Reference: NHS England: 16032/P

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Finance		

Publications Gateway Reference:	**05527s**
Document Purpose	Policy
Document Name	Clinical Commissioning Policy 16032/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Superseded Docs (if applicable)	N/A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**
Contact Details for further information	england.specialisedcommissioning@nhs.net

Document Status

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Clinical Commissioning Policy: The use of Stereotactic Ablative Radiotherapy (SABR) in the treatment of Oligometastatic disease

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 stereotactic ablative radiotherapy (SABR) in the treatment of oligometastatic disease 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

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

The proposal aims to confirm NHS England's approach to the use of Stereotactic Ablative Radiotherapy (SABR) as a treatment option for 'oligometastatic disease'. This is a type of cancer that has spread but only to a small number of other places, often near to the main ('primary') tumour.

About SABR treatment

Stereotactic body radiotherapy (SABR) is a highly targeted radiation therapy which targets a tumour with radiation beams from different angles at the same time:

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

SABR is delivered in between 1 and 8 treatments (called ‘fractions’).

What we have decided

NHS England has carefully reviewed the evidence to treat oligometastatic disease with Stereotactic body radiotherapy. 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 oligometastatic disease. 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 in the treatment of oligometastatic disease.

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. SABR refers to the use of stereotactically directed radiation therapy to structures outside the brain and skull.

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 in the treatment of patients with oligometastatic disease.

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

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.

Oligometastatic disease

If not treated in time, malignant tumours often spread by means of distant metastases. In 1995, Hellman and Weichselbaum coined the term oligometastatic disease, hypothesising that some patients enter a transitional state between localised disease and widespread, incurable metastatic spread. During this period, patients have a limited number of clinically detectable metastases, removal or ablation of which may prolong survival or even be curative. An alternative hypothesis is that patients with apparently oligometastatic disease often also harbour many occult deposits which will progress and limit life expectancy, whatever local treatments are used for the manifest disease.

Neither of these views is universally accurate. There are patients in both these categories, though it is difficult to separate them prospectively. Oncologists are more likely to treat metastases with curative intent in patients whose primary tumour has been treated with apparent success, whose metastases appear small and few in number and whose prognosis would be materially improved by treating them. Other relevant factors are the patient's age, comorbidity and performance status.

Treatments for metastases include surgical excision, radio-frequency or microwave ablation, locally delivered chemotherapy and external beam radiotherapy. Another treatment option is SABR.

5 Evidence Base

The evidence regarding the effectiveness and safety of SABR for treating patients with oligometastatic disease 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.

Four systematic reviews were identified in relation to oligometastatic disease:

- Florescu and Thariat (2014) systematically reviewed published evidence about the treatment of metastatic head and neck cancer (search date 2012). The review contained only limited information on how it was carried out.

The authors found 12 studies of the use of SABR, with a variety of durations, treatment regimens, inclusion and exclusion criteria and follow-up. This made it impossible to meta-analyse the results or even to draw general conclusions. None of the studies was randomised. All but two were uncontrolled, and so provide no information on the benefits for patients of SABR versus other treatment options.

Of the controlled studies, the first evaluated pulmonary metastasectomy, with SABR as a treatment for participants less suitable for surgery (Widder et al 2013). Survival was similar after the two treatments. The other controlled study included participants with brain metastases who received surgery, whole brain radiotherapy, surgery plus whole brain radiotherapy, radiosurgery (i.e. SABR) or supportive care (Maclean et al 2013). No conclusive results about the effectiveness of SABR emerged from this study.

Florescu and Thariat's review provides no reliable information on the outcomes of SABR versus other treatments for metastatic head and neck cancers.

- Ashworth et al (2013) published a systematic review of the treatment of oligometastatic non-small cell lung cancer (search date 2012). The authors included studies of people with tumours of that histological type and fewer than

six metastases. Studies were included whether or not the primary was controlled. The review was rigorously carried out and thoroughly reported.

Ashworth et al found no randomised trials, and none of the studies was apparently controlled. They found five studies of SABR, but do not report details of the regimes or the results according to the mode of treatment. They do report a wide range of outcomes among the studies of all interventions, with five-year survival ranging from 8.3 to 86 percent. Half of the participants in the studies progressed within a year.

- Gunjar et al (2014) reviewed systematically the treatment of tumours metastatic to the adrenal gland (search date 2012).They included studies regardless of the extent of control of the primary or the number of metastases.

Gunjar et al found nine published studies of SABR for adrenal metastases, reporting 178 participants. All studies were uncontrolled, and there were a wide range of total radiation doses (from 10 to 60 Gy) delivered in one to eighteen fractions. Sixty-eight percent of patients had lung cancer.

The authors apparently carried out no tests for heterogeneity but nevertheless pooled the results. At two years, the rate of local control was 63%, and overall survival was 19%. The results from the studies of adrenalectomy were better – 84% and 46% respectively. Although the studies of the two treatments were not comparable, Gunjar et al concluded that “surgery appears to be the most reasonable option, given the large body of retrospective data … and the apparently acceptable complication rates.”

The heterogeneity of the studies in Gunjar et al’s review casts doubt on the appropriateness of pooling the studies, but their results provide no basis for a conclusion that SABR is a better alternative to surgery.

- Siva et al (2010) carried out a similar review of the treatment of pulmonary metastases (search date 2009). The authors included six studies of unfractionated treatment reporting a total of 148 participants, and 13 studies of fractionated treatment, in 334 people. All studies were uncontrolled, and they

varied widely in dosage regimens, lesion size, maximum number of metastases, duration of follow-up and reported outcomes.

As undeterred by this heterogeneity as Gunjar et al, Siva et al pooled the results. The unfractionated studies reported a weighted two-year local control rate of 79% (range 48% to 91%) and a two-year overall survival rate of 50% (range 33% to 73%). The corresponding figures for fractionated treatment are 78% (67% to 96%) and 54% (33% to 89%).

Again, these pooled results must be treated with caution because of the studies' heterogeneity.

One randomised controlled trial was identified. Lim et al (2014) randomised 105 people with non-small cell lung cancer and cerebral metastases to either stereotactic radiosurgery followed by chemotherapy or chemotherapy alone. Overall survival and progression-free survival for cranial disease were similar in the two groups.

33 uncontrolled studies of SABR for oligometastatic disease were identified. The review for this policy included those reporting at least 75 participants; including further uncontrolled studies would have not provided any further information on the effectiveness of SABR relative to other treatments. There were seven such studies:

- Comito et al (2014) studied 82 people with one to three colorectal metastases in the liver or lung. Median overall survival was 32 months, with 43% of participants surviving to 3 years. Rates of local control were higher than overall survival, suggesting that occult metastases were often responsible for participants' deaths.

- Fumagalli et al (2012) reported a series of 90 heavily pre-treated participants with five or fewer hepatic or pulmonary metastases. Most had a single metastasis. Seventy-two per cent of tumours showed a response to SABR, and local control was maintained at two years in two-thirds of participants. However, the effect on longevity was modest: median disease-free survival was less than seven months and only one in ten participants was alive and disease-free at two years.

- Jereczek-Fossa et al's (2013) study included 95 people with up to five metastases in a wider range of organs, mainly brain, bone and lymph nodes. Thirty-one percent of lesions were primary tumours. Despite a bias in the ascertainment of response rates likely to inflate them, only 46% of lesions responded to SABR. Over three years, more than four out of five patients progressed despite treatment, and more than two-thirds died.

- Navarria et al (2014) reported 76 participants treated for no more than five lung metastases. These authors used higher doses of radiation than Jereczek-Fossa et al, and reported better survival. Sixty per cent of lesions showed a complete response to treatment, and a further 29% had a partial response. Despite this, median survival was only 20 months. The reported rates of local control (89%), progression-free survival (70%) and overall survival (73%) were the same at two and at three years. It is likely that some patients with metastatic cancer would experience loss of local control, progression or death in the third year after treatment. Perhaps these results were based on small numbers of potentially unrepresentative longer-term survivors, and may therefore be statistically unstable and less reliable.

- Milano et al's (2012) cohort had a high proportion of women with metastatic breast cancer. All the participants had a maximum of five metastases. The results for the breast cancer participants were better, with 47% survival to six years, compared with only 9% for the other primary sites. Milano et al investigated several other potentially important prognostic factors but none significantly affected outcomes.

- Milano et al (2010) published a separate study of 77 patients from the above cohort whose metastases were confined to a single organ. After median follow-up of 23 months, 47 (61%) had died.

Wang et al (2012) reported results from 149 people with mechanically stable, non-cord-compressing spinal metastases. The number reporting no pain from bone metastases increased from 26% before treatment to 54% six months after treatment.

6 Documents which have informed this Policy

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7 Date of Review

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

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