Stereotactic ablative body radiotherapy for renal cancer

Questions to be addressed

1. What is the clinical effectiveness of stereotactic ablative body radiotherapy for inoperable renal cancer, compared to best standard care?

2. What is the cost effectiveness of stereotactic ablative body radiotherapy for inoperable renal cancer, compared to best standard care?

Summary

Background

- Stereotactic ablative body radiotherapy (SABR) is a targeted mode of radiation therapy. It can be used to treat renal cancer, but there is uncertainty about the clinical and cost effectiveness of this approach.

Clinical effectiveness

- We found no studies restricted to people with inoperable renal cancer, the area of uncertainty that we were asked to address. We therefore widened our search to include all studies of SABR for renal cancer.
- We found no randomised controlled trials.
- We found one systematic review of SABR for renal cancer. The authors found ten papers reporting a total of 126 participants; three studies were prospective and seven retrospective. None of the studies were controlled. Technique and dose fractionation varied widely, with three-, four- and five-fraction regimes most commonly reported. The most common total dose was 40 Gy.
- After follow-up ranging from nine to fifty-eight months, local control rates varied from 84% to 100%. Without testing for heterogeneity, the authors calculated average rates of 93% for overall local control and 93% for local control at two years.
- Survival was inconsistently reported. Six of the ten studies did not report survival, while the results from the remaining four were varied widely. They reported respectively median survival of “58+” months, a five-year survival rate of 74%, median survival of 32 months and that four of nine participants were still alive when the study closed.
- We found no studies published since Siva et al’s search date, nor any published before that date which they did not include.

Cost effectiveness

- We found no studies of the cost effectiveness of SABR for renal cancer.

Activity and cost

- No cost or activity data were available.
Equity issues

- We identified no specific equity issues.

1 Context

1.1 Introduction

Stereotactic ablative body radiotherapy (SABR) is a targeted mode of radiation therapy.

1.2 Existing national policies and guidance

We found no national policies or guidance based on systematic reviews of the evidence.

2 Epidemiology

Renal cell carcinoma is a malignancy that originates in the lining of the proximal convoluted tubule of the kidney. The condition, usually described as renal carcinoma or renal cancer, is the most frequent malignant disorder of the kidney in adults, but is uncommon, accounting for only about 3% of cancers in the United Kingdom; its annual incidence is about 13 per 100,000. The incidence is apparently rising, but this probably reflects the incidental detection of radiological abnormalities in the kidney when patients are scanned for other reasons. This has led to annual increases in the detection of renal cancers of about three percent, with the incidence of small renal tumours increasing at a faster rate. Lesions detected in this way may have a more favourable prognosis than those which present with symptoms.

Initial treatment is most commonly a radical or partial nephrectomy. Where the tumour is confined to the renal parenchyma, the five-year survival rate is 60% to 70%, but it is much lower when metastasis has occurred. Small tumours may be treated non-invasively with cryotherapy and radio-frequency ablation, both of which are the subject of guidance from the National Institute for Health and Care Excellence.[1][2][3] Renal cancer is relatively resistant to radiation therapy and chemotherapy, but sunitinib, temsirolimus, bevacizumab and other forms of immunotherapy can have some effect.

3 The intervention

Stereotactic ablative body radiotherapy (SABR) is a targeted mode of radiation therapy. It involves the use of radiation delivered from numerous angles so that only a small volume of tissue is exposed to the full dose. It can be delivered either as a single dose or in up to five fractions. It is an alternative to surgery or other forms of radiotherapy, especially in patients who cannot undergo surgery and for tumours that are hard to reach, located close to vital structures or subject to movement within the body.

4 Findings

In March 2015, we searched for evidence about the clinical and cost effectiveness of SABR for the treatment of renal cancer.
The search strategy is in the Appendix.

4.1 Evidence of effectiveness

We found no studies restricted to people with inoperable renal cancer, the area of uncertainty that we were asked to address. We therefore widened our search to include all studies of SABR for renal cancer.

We found no randomised controlled trials.

We found one systematic review of SABR for renal cancer (search date 2012).[4] The authors, Siva et al, found ten papers reporting a total of 126 participants; three studies were prospective and seven retrospective. None of the studies were controlled. Technique and dose fractionation “varied widely”, with three-, four- and five-fraction regimes most commonly reported. The most common total dose was 40 Gy. Little further information is available, for example on the median ages of the participants or the use of other treatments. There is no information on whether the tumours were biopsied before treatment – this is not always the case with renal tumours, and some tumours are treated as malignant despite being histologically benign.

After follow-up ranging from nine to fifty-eight months, local control rates varied from 84% to 100%. Without testing for heterogeneity, Siva et al crudely weighted the control rates according to the studies’ sizes, and calculated average rates of 93.1% for overall local control and 92.9% for local control at two years. A more sophisticated approach would have been to include studies’ duration in the weighting, though the heterogeneity of the studies casts doubt on the appropriateness of pooling the results at all.

Siva et al note the inconsistent reporting of survival after treatment. Six of the ten studies did not report survival at all, while the results from the remaining four varied widely. They reported respectively median survival of “58+” months, a five-year survival rate of 74%, median survival of 32 months and that four of nine participants were still alive when the study closed.

We found no studies published since Siva et al’s search date, nor any published before that date which they did not include.

4.2 Trials in progress

We searched clinicaltrials.gov and found one randomised controlled trial and five uncontrolled studies:

- A randomised trial of SABR versus radiofrequency ablation in people with small renal cell carcinomas is now recruiting in Michigan and is expected to complete in 2019 (NCT02138578).
- An uncontrolled study of SABR for the treatment of small renal tumours is recruiting in Texas and is expected to complete in 2018 (NCT02141919).
- An uncontrolled study of the safety and efficacy of SABR in renal cell carcinoma in medically inoperable patients and/or patients who refuse surgery is recruiting in New York and expected to complete in 2017 (NCT02410174).
• An uncontrolled study of SABR cancers of the kidney or isolated adrenal metastases is recruiting in Melbourne, Australia, and expected to complete in 2015 (NCT01676428).
• An uncontrolled study in Ohio is recruiting people with renal cancer for SABR, with completion also due in 2015 (NCT00458484).

4.3 Evidence of cost-effectiveness
We found no studies of the cost effectiveness of SABR for renal cancer.

4.4 Safety
Siva et al report that the most common adverse effects of SABR for renal cancer are fatigue and nausea, followed by radiation dermatitis and enteritis. The crudely weighted average rate of minor adverse effects was 21%. More severe toxicity was rare, with an average rate of 4%.

4.5 Summary of section 4
Evidence to support the effectiveness on SABR for renal cancer is scanty. We found no controlled studies, and the uncontrolled studies had a total number of reported participants of only 126. From this we can conclude that the treatment is feasible, and that severe adverse effects are apparently uncommon. We cannot gauge the effect of SABR on symptoms or on the quality or duration of life, and have no information on how it compares with other minimally invasive approaches to the treatment of small renal tumours.

5 Cost and activity
No cost or activity data were available.

6 Equity issues
We identified no specific equity issues.

7 Discussion and conclusions
Siva et al conclude that “there is only limited scientifically rigorous prospective evidence” about SABR for renal disease. Since they made that observation in 2012, no further research has apparently been published, and the world literature still consists of only 126 people, reported in uncontrolled studies. These provide some information about the subsequent clinical course of people with renal cancer treated with SABR, but not about the treatment’s effect on symptoms, quality of life or survival. We cannot tell from this research whether, or to what extent, SABR altered the natural history of these tumours, nor whether another form of treatment would have produced better results.

There are other approaches to the treatment of renal cancer. Surgery is widely used. For patients unable or unwilling to undergo open or laparoscopic resection of their tumour,
other minimally invasive ablative treatments are available, including cryotherapy and radiofrequency ablation. Since these procedures have been more thoroughly evaluated than SABR and are subject to guidance from the National Institute for Health and Care Excellence, clinicians and policy-makers may think it prudent to offer them in preference to SABR, unless evidence emerges that SABR is superior. No such evidence exists at present.

1. What is the clinical effectiveness of stereotactic ablative body radiotherapy for inoperable renal cancer, compared to best standard care?

The evidence that we found is too limited to provide a reliable answer to this question. No studies have compared SABR with more widely used alternative treatments, and it is unclear what difference, if any, SABR makes to patients’ prognosis.

2. What is the cost effectiveness of stereotactic ablative body radiotherapy for inoperable renal cancer, compared to best standard care?

We do not know. We found no health economic studies of SABR for oligometastases.
### 8 Search Strategy (search date March 2015)

<table>
<thead>
<tr>
<th>Population</th>
<th>Intervention</th>
<th>Comparator</th>
<th>Outcomes</th>
<th>Studies</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Adults (18 years or over) with the following tumours who are not suitable for surgery because of medical co-morbidity or because lesion is technically inoperable.</td>
<td>Stereotactic Ablative Body Radiotherapy (SABR)</td>
<td>Best supportive care</td>
<td>Clinical effectiveness&lt;br&gt;- Survival&lt;br&gt;- Adverse events/complications&lt;br&gt;- No of treatments&lt;br&gt;- Quality of life (including patient self-reported outcome measures)</td>
<td>Meta-analyses&lt;br&gt;Systematic reviews&lt;br&gt;Randomised controlled trials&lt;br&gt;Prospective non-randomised clinical study&lt;br&gt;Other clinical study*&lt;br&gt;Conference abstracts*&lt;br&gt;Health economics studies/models</td>
</tr>
<tr>
<td>Renal cancer</td>
<td></td>
<td></td>
<td>Cost/cost-effectiveness&lt;br&gt;Including resource utilisation, attendances&lt;br&gt;Any other outcomes</td>
<td></td>
</tr>
</tbody>
</table>

1. Lung Neoplasms/
2. (sbrt or sabr).ti,ab.
3. Radiosurgery/
4. (stereotac* adj3 (radiother* or radiat* or irradiat* or radiosurg*)).ti,ab.
5. 2 or 3 or 4
6. Neoplasm Recurrence, Local/ and (Pelvic Neoplasms/ or exp nose neoplasms/ or exp pharyngeal neoplasms/ or exp Spinal Neoplasms/ or exp abdominal neoplasm/ or exp uterine neoplasms/)
7. Retreatment/ and (Pelvic Neoplasms/ or exp nose neoplasms/ or exp pharyngeal neoplasms/ or exp Spinal Neoplasms/ or exp abdominal neoplasm/ or exp uterine neoplasms/)
8. ((retreat* or re-irradiat* or reirradiat*) and ((pelvis or pelvic or nose or nasal or pharynx or pharyngeal or nasopharynx* or spine or spinal or abdomen or abdominal or gynaecolog* or gynecolog* or uter*) adj2 (cancer? or neoplasm? or carcinoma? or tumo?r??))).ti,ab.
9. ((residual or recur*) and ((pelvis or pelvic or nose or nasal or pharynx or pharyngeal or nasopharynx* or spine or spinal or abdomen or abdominal or gynaecolog* or gynecolog* or uter*) adj2 (cancer? or neoplasm? or carcinoma? or tumo?r??))).ti,ab.
10. exp Liver Neoplasms/
11. Cholangiocarcinoma/
12. ((liver or hepatic or hepatocell*) adj2 (cancer? or neoplasm? or carcinoma? or tumor?)).ti,ab.
13. cholangiocarcinoma?.ti,ab.
14. exp Prostatic Neoplasms/
15. ((prostate or prostatic) adj2 (cancer? or neoplasm? or carcinoma? or tumor?)).ti,ab.
16. Spinal Cord/ and Arteriovenous Malformations/
17. Spine/ and Arteriovenous Malformations/
18. Central Nervous System Vascular Malformations/
19. ((spine or spinal or central nervous system or cns) adj3 (arteriovenous malformation? or avm?)).ti,ab.
20. Meningioma/
21. ((spine or spinal or central nervous system or cns) adj3 meningioma?).ti,ab.
22. Neurilemmoma/
23. ((spine or spinal or central nervous system or cns) adj3 schwannoma?).ti,ab.
24. exp Kidney Neoplasms/
25. ((renal or kidney*) adj3 (cancer* or neoplas* or carcinoma* or malignan*)).ti,ab.
26. exp Lung Neoplasms/
27. ((lung or pulmonary) adj3 (cancer? or carcinoma? or neoplasm* or tumor? or malignan*)).ti,ab.
28. 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27
29. 5 and 28
30. limit 29 to (english language and yr="2014 -Current")
31. limit 30 to "reviews (maximizes specificity)"
32. limit 30 to "economics (maximizes sensitivity)" or "costs (maximizes sensitivity)"
33. limit 30 to "therapy (maximizes sensitivity)"
9 References


Competing Interest

All SPH authors have completed the ICMJE uniform disclosure form (www.icmje.org/coi_disclosure.pdf) and declare:

- grants from NHS England to SPH to undertake the submitted work, no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

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