Technoleg Iechyd Cymru
Health Technology Wales

HEALTH TECHNOLOGY WALES (HTW) GUIDANCE 038 (April 2022)

Stereotactic ablative radiotherapy to treat people with primary kidney cancer

HTW Guidance:

The evidence supports the routine adoption of stereotactic ablative radiotherapy (SABR) to treat people with primary kidney cancer who are not suitable for surgery or other ablative techniques.

The use of SABR provides a treatment option that may improve survival in patients who would otherwise have no other treatment options available. Patient selection for SABR should be undertaken by a cancer multidisciplinary team.

Economic modelling estimates that the use of SABR is cost effective when compared with clinical surveillance, with a cost per quality-adjusted life year (QALY) of £1,675.

Why did Health Technology Wales (HTW) appraise this topic?

Kidney cancer develops when abnormal cells in either of the kidneys start to divide and grow in an uncontrolled way. This appraisal focuses on cancer that has not spread outside of the kidney.

Surgery is currently the standard of care for the treatment of kidney cancer. However, many older patients have comorbidities, which may make them unsuitable for major surgery. Minimally invasive ablative therapies, involving extreme cold or heat to remove the tumour (such as cryotherapy, radiofrequency ablation and microwave ablation), are potential treatment options for patients who are unsuitable for or decline surgery. However, these therapies are limited to smaller kidney tumours distant from vascular structures. Active surveillance (observation) is commonly utilised in elderly, frail people with kidney cancer, with small tumours less than four centimetres. However, active surveillance may require delayed intervention, often triggered by tumour growth.

SABR is a type of external radiotherapy, which uses smaller, thinner beams of radiation than standard radiotherapy. It delivers precise beams of radiation at various intensities guided by sophisticated imaging systems that track the exact three-dimensional location of a tumour. Such precision allows high doses of radiation to be delivered to the tumour while minimising damage to surrounding healthy tissue. SABR can be given with fewer treatments than standard radiotherapy and isa non-invasive treatment option, delivered in the outpatient setting without the need for general anaesthetic, meaning that the patient usually does not need to need to stay in hospital.

This topic was proposed by Dr Jacob Tanguay, Consultant Oncologist, Velindre University NHS Trust.

The status of HTW guidance is that NHS Wales should adopt this guidance or justify why it has not been followed. HTW will evaluate the impact of its guidance.

Evidence Summary

Refer to Evidence Appraisal Report 038 (EAR038) for a full report of the evidence supporting this Guidance.

HTW carried out an evidence review to address the following research question: What is the clinical and cost effectiveness of stereotactic ablative radiotherapy (SABR) to treat people with primary kidney cancer compared to standard care?

HTW's evidence review found two systematic reviews and one meta-analysis investigating the use of SABR in renal cell carcinoma (RCC), but we were unable to use the pooled results from the meta-analysis since some of the included patients had metastatic disease. The majority of the primary evidence we identified came from single-arm retrospective studies.

Local control, commonly defined as the proportion of stable disease or decreased tumour size following treatment, ranged from 75% to 100% in the systematic reviews, and 97.8% to 100% in a multi-centre pooled analysis and retrospective single-arm study.

A number of different survival outcomes were measured. Overall survival was the only outcome which included comparative data, and was reported in two retrospective analyses of the same American cancer database. SABR was associated with an increased overall survival compared with observation, but a worse overall survival compared to partial nephrectomy, cryoablation, radiofrequency ablation or microwave ablation. In the non-comparative systematic reviews, recurrence-free survival with SABR was between 63% and 98%. In a multi-centre pooled analysis study, cancer-specific survival was 91.9% and progression-free survival was 65.4%, both at four-years post SABR.

A multi-centre pooled analysis assessed tumour relapse rate with SABR and reported recurrence rates of between 0% and 8.1%. In addition, the systematic review reported that post-SABR estimated glomerular filtration rate changes ranged from -18 millilitres per minute to +6 millilitres per minute.

The majority of reported adverse events with SABR were mild. Serious adverse events were reported as occurring in between 0 to 19% of patients, including pyelonephritis, fatigue, skin toxicity and chronic kidney disease, with no treatment-related mortality reported in any of the studies. Additionally, quality of life in people with kidney cancer appears to be well-preserved at six-months following SABR.

No relevant health economic studies were identified in the literature review. An economic analysis was developed by HTW to consider the cost-effectiveness of SABR in people who cannot be managed with either surgery or invasive ablative techniques. The results showed SABR to be more effective but more costly than observation. The resulting ICER of £1,675 per quality adjusted life year (QALY) is below the commonly accepted threshold of £20,000 per QALY, indicating that SABR is cost effective compared to clinical surveillance. The conclusion of the analysis did not change in any of the alternative scenarios modelled within sensitivity analysis. In probabilistic sensitivity analysis, SABR was found to have a 100% probability of being cost effective at a threshold of £20,000 per QALY.

The appropriate mechanism for patient engagement was determined and the patient perspective was considered where possible.

Appraisal Panel considerations

- The Appraisal Panel heard from patient and public involvement representatives about the benefits that SABR could bring to patients and their families. SABR could be potentially curative for patients who do not have any other treatment options; could improve quality of life and long-term local tumour control but be associated with limited adverse events. Patient and public involvement representatives did describe some potential limitations of SABR, including the fact that some patients may be unable to lie flat to receive the treatment. On the other hand, experts commented that, in their experience, the majority of patients have been able to tolerate SABR. Experts confirmed that the safety profile of SABR reported in clinical trials reflected their own experiences of using SABR for other types of cancer but that a single fraction of SABR has been associated with an increased rate of nausea compared to multiple fractions.

- The Appraisal Panel were informed by clinical experts that active surveillance is sometimes adopted for patients with kidney cancer, especially those who are not suitable for surgery and have small tumours. Under these circumstances, there is, however, a risk that the cancer might become more aggressive and progress. The uncertainty of active surveillance can therefore have a negative psychological impact on some patients who often prefer to be considered for active treatment if possible. The experts explained that SABR provides an option for people who are not suitable for conventional treatments and would rather have active treatment than surveillance..

- Experts described how SABR is a non-invasive treatment option, which can be given in one to three fractions in the outpatient setting. It was noted by the Appraisal Panel that this may be particularly advantageous to many people across Wales, especially those living in remote rural communities. Panel members noted that whilst there are no objective measurements of the carbon footprint of SABR as compared with other therapies, a lower number of hospital visits is likely to be environmentally advantageous because of a reduction in travelling, fuel consumption and therefore carbon emissions.

- The Appraisal Panel were advised by experts that the people most likely to receive SABR for kidney cancer are be those that are unsuitable for surgery or ablative treatments as well as those who develop locally progressive disease. These people are usually elderly and frail and often have co-morbidities that increase the risk of anaesthesia, surgery and invasive treatments. In addition, the Appraisal Panel were informed by the experts about the details of clinical scenarios when SABR would be most likely to be beneficial compared to invasive ablative techniques:

    - Experts noted that SABR is particularly considered for kidney tumours greater than four centimetres in size since these are unlikely to be appropriate for ablation and are most likely to progress following active surveillance.. Experts explained that invasive ablative techniques, such as radiofrequency ablation, microwave ablation and cryotherapy, are less likely to achieve local control in larger tumours and are often not considered safe since these tumours are likely to be near important vascular structures which might be damaged with energy dissipation.

    - The Appraisal Panel were advised by experts about the important anatomical factors that are taken into account when considering SABR. They explained that it is more difficult to treat people with SABR when the primary kidney cancer is anterior and therefore adjacent

to the bowel since the dose needs to be adjusted to avoid surrounding bowel injury. On the other hand, SABR is more applicable to treating kidney tumours that are posterior and may also be considered for those that are near the renal hilum and major vessels, since these are more difficult to treat with invasive ablative techniques.

- Experts described other clinical scenarios when SABR may be considered. For example in people on anticoagulants who may be at risk of increased risk of bleeding with surgery or of thrombosis if the anticoagulant has to be stopped. Another scenario could be patients who develop cancer in a single functioning kidney in whom the objective is to maintain renal function after treatment and avoid the need for dialysis.

- Experts estimated that there would initially be up to approximately 40 primary kidney cancer patients eligible for SABR in Wales per year, but that this number may increase as experience of using SABR develops. Experts suggested that a cancer multidisciplinary team (MDT) should decide on whether a patient is best suited to SABR or another therapy.

- The Appraisal Panel noted the limitations with the published evidence relating to the use of SABR to treat primary kidney cancer, particularly with regards to the retrospective nature of many of the studies, the lack of comparative data and the relatively small cohorts studied. Experts informed the Appraisal Panel, however, that there are particular challenges in undertaking comparative trials in frail populations, and that SABR is being used on a compassionate basis for kidney cancer in some parts of England. Overall, while acknowledging these limitations, the Appraisal Panel concluded that the evidence suggests that SABR is clinically effective in improving clinical outcomes in patients with localised kidney cancer as compared to clinical surveillance. The Experts reiterated the need for treatment options to be discussed at cancer MDT meetings for all cases of primary kidney cancer that are potentially suitable for SABR since treatment should only be offered to patients who are not suitable for surgery or ablation.

- In considering the economic evidence, the Appraisal panel and experts discussed how the upfront costs of SABR could be offset, at least partially, by delaying time to disease progression and reducing the need for high-cost systemic therapies. This factor, along with a gain in overall survival with SABR as compared with clinical surveillance, was a key consideration in the economic analysis that was developed by HTW, which concluded that SABR is a cost effective intervention.

- The Appraisal Panel were advised by the experts that SABR is not platform-specific and that the insertion of fiducial markers is only relevant to the use of the CyberKnife System. Experts and members of the panel noted that Velindre NHS Trust and Swansea Bay University Health Board have sophisticated image-guidance, which negates the need for fiducial markers.

- The Appraisal Panel recommended the collection of real-world evidence on cancer-related and survival outcomes in people with localised kidney cancer treated with SABR in Wales, for example with a registry or audit.

Responsibilities for consideration of this Guidance

Health Technology Wales (HTW) was established by Ministerial recommendation[1,2] to support a strategic, national approach to the identification, appraisal and adoption of non-medicine health technologies into health and care settings. The HTW Appraisal Panel comprises senior representation from all Welsh boards with delegated authority to produce guidance 'from NHS Wales, for NHS Wales'. The status of HTW guidance is 'adopt or justify'. There is an expectation from Welsh Government that HTW guidance is implemented with adoption regularly audited by HTW.[3]

The guidance in this document is intended to assist Welsh care system decision makers to make evidence-informed decisions when determining the place of health technologies and thereby improve the quality of care services.

The content of this HTW guidance was based upon the evidence and factors available at the time of publication. An international evidence base was reviewed and external topic experts and HTW committee members consulted to contextualise available evidence to Wales. Readers are asked to consider the generalisability of the evidence reviewed to NHS Wales and that new trials and technologies may have emerged since first publication and the evidence presented may no longer be current. It is acknowledged that evidence constitutes only one of the sources needed for decision making and planning.

This guidance does not override the individual responsibility of health professionals to make decisions in the exercise of their clinical judgment in the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

No part of this guidance may be used without the whole of the guidance being quoted in full. This guidance represents the view of HTW at the date noted. HTW guidance is not routinely updated. It may, however, be considered for review if requested by stakeholders, based upon the availability of new published evidence which is likely to materially change the guidance given.

Standard operating procedures outlining HTW's evidence review methods and framework for producing its guidance are available from the HTW website.

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Declarations of interest were sought from all reviewers. All contributions from reviewers were considered by HTW's Assessment Group. However, reviewers had no role in authorship or editorial control and the views expressed are those of Health Technology Wales.

Chair, Health Technology Wales Appraisal Panel

1. National Assembly for Wales, Health and Social Care Committee. Access to medical technologies in Wales. December 2014.
2. Response to Recommendations from the Health & Social Care Committee: Inquiry into Access to Medical Technologies in Wales. February 2015.
3. Gething, V. Letter to all Health Board Chairs re Funding for Sacral Nerve Stimulation in Wales. VG_01655_17. September 2017.