SABR in the UK: Current status and developments

Further advancements in planning such as the use of volumetric arc therapy (VMAT) allow increased conformity of dose to the tumour and hence better sparing of OARs (figures 2a and 2b). The introduction of flattening filter free (FFF) linear accelerators with high dose rate delivery means that SABR treatments can be delivered as quickly as standard conventional radiotherapy. This is clearly beneficial and more comfortable for patients and means there are fewer concerns regarding patient stability during radiation delivery.

SABR doses for NSCLC aim to deliver between 54 and 60 Gy in three to eight fractions delivered on an alternate day basis, depending on proximity of OARs (figures 2a and 2b). Where the tumour is close to the chest wall patients are treated with five fractions to reduce the risk of late rib fractures and chest wall toxicity. Tumours close to the vertebral column, brachial plexus and major vessels are usually treated with eight fractions with the three fraction regimen mainly used for tumours surrounded by lung parenchyma only with no concerns of radiation toxicity to other OARs. Tumours that lie within 2 cm of the main airways are presently not routinely treated with SABR due to increased toxicity seen in the dose escalation studies by Timmerman.

Development of SABR in the UK

The UK SABR Consortium was formed in 2008 by interested centres active in lung cancer radiotherapy, with the aim of achieving a consensus on how best to develop, implement and research SABR in the UK. In the presence of varying dose fractionation, different planning, image guidance systems and linear accelerators the first task of the SABR Consortium was to draw up generic guidelines for treatment of early inoperable non-small cell lung carcinoma (NSCLC). These stated the minimum standards required for departments to build local protocols which would allow them to work within their existing infrastructure but have similarities with respect to delivered dose fractionation and high standards of radiation planning and delivery using image guidance to ensure safe implementation of SABR across centres.

In 2011 the National Radiotherapy Implementation Group (NRIG) report also acknowledged that SABR had become the standard of care for the management of early-stage medically inoperable peripheral NSCLC. It also tasked the UK SABR Consortium to maintain evidence-based prospective treatment protocols for all body sites and to produce a common data set to allow meaningful analysis of treatment outcomes. The report also emphasised the importance of developing high quality clinical trials to investigate the use of emerging radiotherapy technology, in addition to improving patient outcomes and experience.

With recent changes within the NHS and establishment of commissioning/tariffs for radiotherapy, a main focus of the consortium is to work closely with NHS England to ensure that centres are reimbursed appropriately for SABR delivery to reflect the complexities in treatment planning and delivery. The QA subgroup of the consortium was originally involved in mentoring new departments to set up SABR services with guidance from more established centres. The QA subgroup is now working on delivering a robust national quality assurance programme for the centres providing SABR services. This would ensure access for patients to SABR treatments locally as more and more centres are able to offer this technology.

Introduction

Stereotactic ablative body radiotherapy (SABR), also known as stereotactic body radiotherapy (SBRT), as defined by the American Society of Radiation Oncology and the American Society of Radiology is an external beam radiation therapy method used to very precisely deliver a high dose of radiation to an extracranial target within the body, using either a single dose or a small number of fractions. The UK National Radiotherapy Implementation Group (NRIG) report defines SBRT as the precise irradiation of an image-defined extracranial lesion, using a high total radiation dose delivered in a small number of fractions (hypofractionation).

The most evidence for SABR in extracranial sites is available in early lung cancer where systematic reviews have shown two-year survival rates and local control as high as 70% and 90% respectively. Even with the increasing number of scientific publications on SABR, phase III evidence against surgery and conventional radiotherapy is limited. Despite this SABR is now a recognised standard of care in early inoperable lung cancer due to its ability to produce local control rates similar to surgery, its low toxicity and patient convenience as a result of reduced number of visits required for treatment when compared to conventionally fractionated radiotherapy. There is also an increasing evidence base/clinical experience for SABR in other sites such as prostate, pancreas, spinal metastases and oligometastatic disease.

In order to deliver ablative doses of radiotherapy to tumours, it is necessary to accurately identify both the target and the surrounding organs at risk (OAR), in addition to accommodating inter- and intra-fraction movement of both. The three key components required to achieve this involve patient immobilisation, on-treatment image guidance, and on-treatment patient motion management. With the use of 4D CT scanning for planning the tumour and image guidance with CBCT during treatment delivery, uncertainties/errors have been reduced significantly increasing the confidence in delivering hypofractionated radiation, especially in early lung cancers which can exhibit considerable amounts of respiratory motion.
Current use of SABR in the UK

SABR is now well established in the UK in patients with early stage NSCLC who are medically inoperable due to comorbidity. There are several centres in the UK that now routinely offer SABR, and this has certainly increased from the previous audit undertaken by the consortium three years ago. However, due to the resources required in terms of equipment and manpower many centres in the UK are still unable to deliver this technique locally. Centres that are up and running are therefore taking external referrals from nearby centres. In Leeds we have now treated over 1,000 patients with SABR. Preliminary analysis of the first 300 patients shows local control in excess of 95% in keeping with published literature.

The majority of the SABR treatments being delivered in UK are in early NSCLC. The use of SABR in other extracranial sites is also being developed, with liver and prostate being the next commonly treated sites. The majority of these are within a research setting as phase III evidence suggesting routine use is lacking. In localised prostate cancer, pooled case series and single arm phase I and II trials have demonstrated consistent results, with outcome of biochemical relapse-free survival at five years of 95%, 84% and 81% for low, intermediate and high risk disease respectively.

Oligometastatic disease has been defined as an extension of locally advanced disease, with a certain number of metastatic sites of disease (between one and six), and therefore potentially curable. The state can be thought of as a point on a linear line between local disease and widespread metastatic disease. A number of studies have demonstrated efficacy and safety of the potential use of SABR to eradicate metastatic disease in various sites (lung, spine, liver, lymph nodes, adrenal glands), as well as multiple metastatic deposits within the lungs and liver. However, further data from robust trials would be required before widespread SABR use in the UK in this diverse group of patients.

SBRT treatment in locally advanced pancreatic cancer has recently been put into the limelight. Induction chemotherapy followed by chemoradiotherapy (CRT) in inoperable patients has shown an improvement in overall survival when compared to chemotherapy or CRT alone. Case series have reported acceptable rates of acute toxicity, but have reported higher rates of significant late bowel toxicity. A recent review of SBRT in pancreatic cancer reported a 75% local control rate at 25.1 months with 75Gy BED (biologically effective dose), with no improvement seen with increasing doses in addition to more toxicity. Furthermore, SBRT in combination with neoadjuvant chemotherapy and CRT has also been shown to increase R0 resection and has potential efficacy.

Upcoming trials for SABR in the UK

Presently there are at least eight planned research studies exploring SABR in several extracranial sites (Table 1). Commissioning through evaluation is aiming to establish SABR outside research studies in the setting of other oligometastatic disease such as sarcomas, benign spinal conditions such as AVM, meningioma, schwannoma, benign hepatomas and pelvic recurrence for gynaecological and urological malignancies.

Summary

The NRIG has encouraged the use of SABR and investment in radiotherapy. Development and emerging clinical trials utilising SABR will hopefully provide evidence showing improvement in patient outcomes and overall experience. The safety profile of SABR in various tumour sites has been shown to be acceptable, although more follow-up data is required to monitor late toxicity. The potential benefits of SABR clinically, economically and in patient experience of lower treatment fractions make a compelling rationale for increasing its use in the UK. However, this must be tempered with good quality evidence from appropriately powered clinical trials. There will also be a significant increase in resource demand in planning, dosimetry and physics quality assurance, and a multidisciplinary approach to continued development and safety of delivery of SABR in the UK is required.

References


Proposed trial | Site
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SABR TOOTH | Early NSCLC, borderline for surgery, randomised phase II trial of SABR against surgery
PACE | Prostate – surgery vs SBRT/SBRT vs EBRT
SARON | Lung cancer with lung metastatic disease
ABC-07 | Addition of SBRT to systemic chemotherapy in locally advanced biliary tract cancers
SPARC | Phase I SBRT pre-operatively for borderline resectable pancreatic cancer
Lung Tec | SABR for central early lung tumours (phase II)
Core | SABR for oligometastatic disease from lung, prostate and breast primary tumours
HALT | SABR for oligometastatic disease in oncogene driven tumours

Table 1
Figure 1
Selected axial and coronal images demonstrating dose distribution in a peripheral lung cancer treated by SABR.

Figure 2a
Tumour not close to chest wall and suitable for 54Gy in three fractions.

Figure 2b
Tumour close to chest wall and suitable for 55Gy in five fractions.