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## Guidelines

## UK Consensus on Normal Tissue Dose Constraints for Stereotactic Radiotherapy

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## Abstract

Six UK studies investigating stereotactic ablative radiotherapy (SABR) are currently open. Many of these involve the treatment of oligometastatic disease at different locations in the body. Members of all the trial management groups collaborated to generate a consensus document on appropriate organ at risk dose constraints. Values from existing but older reviews were updated using data from current studies. It is hoped that this unified approach will facilitate standardised implementation of SABR across the UK and will allow meaningful toxicity comparisons between SABR studies and internationally.

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**Key words:** Constraints; normal tissue; OAR; SABR; SBRT; stereotactic radiotherapy

## Introduction

Stereotactic ablative radiotherapy (SABR or SBRT) is routinely used for the treatment of early stage peripheral lung cancer and is increasingly used to treat other primary or metastatic tumour sites [1–9]. There are currently a number of UK studies open to recruitment (of which three are randomised trials) investigating the utility of SABR in the treatment of oligometastatic disease (breast, lung and

prostate), lung, prostate, pancreas and hepatobiliary primary malignancies [10–13]. These are supported by Cancer Research UK and further studies are in development. In addition, a National Health Service Commissioning through Evaluation programme was started in 2015 to evaluate SABR in situations where clinical trials are not available [14].

The focus of many of these studies is the use of SABR in the treatment of oligometastatic disease. Inherent in the delivery of SABR to oligometastatic sites at any location in the body is an understanding of the local normal tissue dose constraints. It is recognised that as SABR is a relatively new treatment technique, definitively established dose constraints that directly correlate to the risk of toxicity are rare. However, in order to standardise protocols and the associated radiotherapy planning, members of the various trial management groups collaborated to generate a consensus

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document on appropriate organ at risk (OAR) dose constraints associated with the various common SABR fractionations.

There are numerous publications that report toxicity after SABR at various sites. These have been summarised in a number of reports or reviews [15–18]. The most comprehensive of these reviews is the AAPM-101 report [16], but this is now over 5 years old, and newer data are available. Rather than conduct a primary systemic review, the values contained within the AAPM-101 report were revised where appropriate, by taking into consideration any updated or more robust data on a given dose constraint value in the opinion of the panel, as described below.

## General Principles of Dose Constraint Selection and Application to Clinical Trials or Routine Practice

In choosing the most appropriate dose constraints for UK SABR treatments, the following principles in selecting and applying these dose constraints have been used:

- (1) Both optimal and mandatory dose constraints were included, where appropriate.
- (2) For body (extra-cranial) dose constraints, except for the spinal cord/canal, a near-point maximum dose volume of 0.5 cm<sup>3</sup> should be used across sites. This represents a volume that is both clinically realistic and comparable when calculated across different planning systems. For cranial regions, and the spinal canal as a surrogate for cord dose in most cases, a near-point maximum dose volume of 0.1 cm<sup>3</sup> should be used. It should be noted that where the area to be treated abuts the spinal cord, the spinal cord should be explicitly defined on both computed tomography and magnetic resonance

imaging and a margin for set-up errors added based on local specification.

- (3) There are differences in the ways dose constraints are reported for serial and parallel organs. Care should be taken to distinguish between these and the key principles are listed in Figure 1.
- (4) For the purpose of these guidelines, single fraction treatment should not be given extra-cranially. Three or five fraction regimens are recommended, together with eight fractions for selected thoracic lesions.
- (5) Radiation Therapy Oncology Group (RTOG) normal tissue atlases should be used for the delineation of OARs [19]. Specifically it is recommended to follow the RTOG guidance by contouring the spinal canal based on the bony limits of the spinal canal. The spinal cord should be contoured starting at the level just below the cricoid (or at the level of the base of skull for tumour of the lung apex) and continuing on every computed tomography slice to the bottom of L2. Neural foraminae should not be included.
- (6) The dose constraints described in this document are only applicable for patients receiving SABR alone. For patients who have received recent or are receiving concomitant systemic therapy (and in particular anti-angiogenic agents and other biological agents) there may be an enhanced risk of normal tissue toxicity.
- (7) These dose constraints are not applicable to re-irradiation of the same organ using SABR, except where another part of the organ (e.g. lung or liver) has incidentally previously received standard fractionation radiotherapy on a previous occasion.
- (8) Where two separate gross tumour volumes are being treated in the same organ (e.g. two separate lung metastases) during the same treatment course, then the summed dose to both lesions and associated OARs should not usually exceed the given dose constraints.

Organ type	Principle of Dose Constraint Descriptor	Example
Serial	Dose constraints are typically described as a threshold dose or higher that can be given to a small volume of the organ which receives the highest doses, but the remaining volume must be spared below the threshold dose.  (N.B. For cumulative dose-volume histograms, this is equivalent to the maximum volume of the organ that can receive a threshold dose or higher).	The minimum dose to the 5cc volume of small bowel receiving the highest dose should be lower than 25.2Gy ( $D_{5cc} < 25.2Gy$ ).  (equivalent to $V_{25.2Gy} < 5cc$ )
Parallel (Entire organ) (e.g. liver, kidneys and lungs)	Dose constraints are typically described as a maximum percentage volume of the organ that can receive a threshold dose or higher.	The volume of lung receiving a dose of 20Gy or higher should be less than 10% of the total lung volume ( $V_{20Gy} < 10\%$ ).
Parallel (Minimum critical volume of an organ) (e.g. liver, kidneys and lungs)	For these, the constraint is typically described as a minimum critical volume of the organ which must be spared from receiving a threshold dose (or higher).	At least 200cc of kidney should receive a dose of 16Gy or lower ( $Dose\ to\ \geq 200cc \leq 16Gy$ ).

Fig 1. Description of dose constraint types.

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