Physica Medica xxx (2017) xxx–xxx

Contents lists available at ScienceDirect

Physica Medica

journal homepage: http://www.physicamedica.com

Review paper

Geometrical and dosimetrical uncertainties in hypofractionated radiotherapy of the lung: A review

Marco Schwarz [a,b,*], Giovanni Mauro Cattaneo [c], Livia Marrazzo [d]

[a] Protontherapy Department, Trento Hospital, Via Al Desert 14, 38123 Trento, Italy
[b] Trento Institute for Fundamental Physics and Applications (TIFPA), National Institute of Nuclear Physics (INFN), Via Sommarive 14, 38123 Trento, Italy
[c] Medical Physics, San Raffaele Scientific Institute, Via Olgettina 60, 20132 Milano, Italy
[d] Medical Physics Unit, Careggi University Hospital, Largo Brambilla 3, 50134 Firenze, Italy

ARTICLE INFO

Article history:
Received 29 September 2016
Received in Revised form 23 December 2016
Accepted 14 February 2017
Available online xxxx

Keywords:
Lung
Radiotherapy
Stereotactic body radiation therapy
SBRT
Hypofractionation
Moving targets

ABSTRACT

The application of high precision hypofractionated regimes (a.k.a. stereotactic body radiotherapy (SBRT)) to the treatment of lung cancer is a 'success story' of radiotherapy. From the technical perspective, lung SBRT is a challenging technique as all aspects of the treatment workflow, from imaging to dose calculation to treatment delivery, should be carefully handled in order to ensure consistency between planned and delivered dose.

In this review such technical aspects are presented and discussed, looking at what has been developed over the years.

The use of imaging techniques such as slow-CT, breath-hold CT, four-dimensional CT and mid-ventilation is reviewed, presenting the main characteristics of each approach but not necessarily to single out 'the best' solution.

Concerning dose calculation, a number of studies clearly separate dose algorithms that should be considered inadequate for lung SBRT (e.g. simple pencil beam algorithms) from approaches such as convolution algorithms, Monte Carlo, and solution of the transport equation, that are much better at handling the combination of small fields and heterogenous geometries that make dose calculation not trivial.

Patient positioning and management of intrafraction motion have been two areas of significant developments, to the point where it is difficult to identify which solution represents the best compromise between technical complexity and clinical effectiveness. The review analyses several of these methods, outlining the residual uncertainties associated with each of them.

Last but not least, two subjects are discussed, adaptive therapy and particle therapy, that may represent in the near future additional tools for the technical improvement of lung SBRT.

Contents

1. Introduction . . . 00
2. The appropriate anatomical model and related uncertainties . . . 00
3. Dose calculation . . . 00
   3.1. Planning studies on phantoms or patients datasets . . . 00
4. Image guidance during treatment, positioning uncertainties and margins . . . 00
   4.1. Interfraction motion . . . 00
   4.2. Intrafraction motion . . . 00
   4.3. Impact of positioning approaches on the PTV margin . . . 00
5. Delivery techniques and related uncertainties . . . 00
   5.1. Intrafractional baseline drifts . . . 00
   5.2. Interplay effects . . . 00

* Corresponding author at: Protontherapy Department, Trento Hospital, Via Al Desert 14, 38123 Trento, Italy.
E-mail address: marco.schwarz@apss.tn.it (M. Schwarz).

http://dx.doi.org/10.1016/j.ejmp.2017.02.011
1120-1797/

Please cite this article in press as: Schwarz M et al. Geometrical and dosimetrical uncertainties in hypofractionated radiotherapy of the lung: A review. Phys. Med. (2017), http://dx.doi.org/10.1016/j.ejmp.2017.02.011

6. Possible future technical developments 00
6.1. Adaptive therapy 00
6.2. Protons and heavy ions 00
References 00

1. Introduction

The first concepts and applications of high precision radiotherapy treatments with high fraction doses to extracranial disease sites are more than 20 years old [1,2]. However, it took more than ten years for hypofractionation to become a routine radiotherapy technique in a large number of centres. It is likely that the current popularity of extracranial hypofractionated regimes, also known as Stereotactic Body RadioTherapy (SBRT) or Stereotactic Ablative Body RadioTherapy (SABR),[1] is caused by the combination of these factors:

1) Widespread availability of soft tissue image guidance tools for accurate patient positioning (e.g. cone beam computed tomography (CBCT));
2) Treatment planning and delivery techniques combining dose conformity and delivery efficiency (e.g. volumetric arc therapy (VMAT));
3) Initial clinical results suggesting safety and efficacy of hypofractionation for specific disease sites and stages [3–6];
4) Development and successful marketing of radiotherapy devices expressly designed or tuned to facilitate hypofractionation via the combination of high mechanical precision, soft tissue image guidance, fast beam delivery (often allowing for gating or tracking), and efficient treatment workflows combining imaging and treatment.

While the seminal paper on the methodology of SBRT showed an example of liver irradiation [1], at the moment (mostly early stage) lung cancer is by far the more popular application of SBRT. Radiotherapy treatment of early stage lung cancer has been for quite some time limited exclusively to patients ineligible for surgery due to medical reasons. Even though some clinical results suggested that conventionally fractionated radiotherapy could be safely delivered to small lung targets even with 3D conformal techniques up to doses in the range of 100 Gy with conventional fractionation [7,8], the number of patients treated at such doses remained very limited. Widespread acceptance of high dose treatment in early stage lung cancer was achieved only after the early results of studies using SBRT such as RTOG 0236 [9] that, building on previous single institute experiences (e.g. [10]), demonstrated safety and effectiveness of lung SBRT in a multicenter trial. Additional factors such as patient convenience and the increase in medically inoperable patients (due to age shift) worked in favor of an increase adoption of lung SBRT. This, in turn, lead to the suggestion that lung SBRT may be competitive with respect to surgery at least for some patient categories [11], possibly even for operable patients [12], and that the large scale application of this technique has actually had an impact on survival of early stage lung cancer patients as a whole [13].

[1] The word 'stereotactic' was initially used to point at a specific reference and positioning system that has now been basically abandoned for extracranial treatments. However, SBRT is still considered a synonymous for 'high precision radiotherapy with hypofractionation in extracranial disease sites', so this acronym will be used in the paper too. A recent definition of SBRT is attempted in [133].

From a technical perspective, the safe delivery of lung SBRT is associated to a number of issues to be addressed ranging from accurate patient modeling via a computed tomography (CT) scan, dose calculation, patient positioning and treatment delivery to a small target affected by breathing motion. Presenting the current status and discussing the remaining open questions on such technical issues is the focus of this review.

In November 2014, a literature search was performed on Medline with the search key "(lung SBRT or lung SABR) AND (geometrical uncertainties OR dose calculation OR patient setup OR motion OR 4D planning)" provided 323 results.

After reading the abstracts, selecting the relevant papers in English, and adding further papers deemed relevant (that were mostly found in the references of the initial set of publications), a total of 327 papers were considered for this review.

2. The appropriate anatomical model and related uncertainties

SBRT is characterized by potent ablative doses and highly conformal dose distributions delivered in a few fractions with a short overall treatment time. While the sources of uncertainty in SBRT are essentially the same as in conventional fractionation, what makes the difference is the increased level of accuracy needed to reliably deliver high doses to the whole target while keeping relatively small safety margins.

Breathing-induced organ motion is a source of uncertainty that may influence the accuracy at all stages of the treatment process. Consequently, a consistent approach is required for full integration in the process of treatment planning and delivery of the temporal changes of the patient's anatomy due to breathing motion.

Tumor motion due to respiration in various locations of the lungs has been widely described with motion amplitudes up to several centimeters; the largest motion was observed in the cranio-caudal direction in lower lobe tumors not attached to rigid structures while the lateral motion appears to be much smaller. The tumors were found to be more stable and spending more time in the exhale phase, and hysteresis has been commonly observed (see e.g.[14,15]).

Several methods have been developed for quantification of breathing motion and for integration of the motion information into the planning and treatment workflow. The most used approaches are: reducing respiratory movement with abdominal compression or breath-holding, motion-encompassing methods to include the entire range of tumor motion at the time of CT acquisition, respiratory-gating and real time tumor tracking [15].

The most common techniques to handle breathing motion during CT imaging are slow-CT, inhale and exhale breath-hold CT and four-dimensional CT (4D-CT).

In slow-CT the scanner acquires images at each couch position for a longer time than the respiratory cycle, so the envelope of multiple respiratory phases are recorded per slice. The blurring of images related to motion reduces the image resolution, so this method is not recommended for lesions close to the mediastinum, chest wall or diaphragm; moreover, when just one single slow scan