A review of treatment planning for precision image-guided photon beam pre-clinical animal radiation studies

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Abstract

Recently, precision irradiators integrated with a high-resolution CT imaging device became available for pre-clinical studies. These research platforms offer significant advantages over older generations of animal irradiators in terms of precision and accuracy of image-guided radiation targeting. These platforms are expected to play a significant role in defining experiments that will allow translation of research findings to the human clinical setting. In the field of radiotherapy, but also others such as neurology, the platforms create unique opportunities to explore e.g. the synergy between radiation and drugs or other agents.

To fully exploit the advantages of this new technology, accurate methods are needed to plan the irradiation and to calculate the three-dimensional radiation dose distribution in the specimen. To this end, dedicated treatment planning systems are needed. In this review we will discuss specific issues for precision irradiation of small animals, we will describe the workflow of animal treatment planning, and we will examine several dose calculation algorithms (factorization, superposition-convolution, Monte Carlo simulation) used for animal irradiation with kilovolt photon beams. Issues such as dose reporting methods, photon scatter, tissue segmentation and motion will also bediscussed briefly.

Eine Übersicht der Photonen-Bestrahlungsplanung für präzise, bildgesteuerte, präklinische Tierstudien

Zusammenfassung

Seit Kurzem stehen Präzisions-Bestrahlungsgeräte mit einer integrierten, hoch auflösenden Röntgen-CT-Bildgebung für präklinische Studien zur Verfügung. Diese Forschungsplattformen bieten erhebliche Vorteile gegenüber Tier-Bestrahlungsgeräten der älteren Generationen hinsichtlich der Genauigkeit der bildgeführten, gezielten Strahlentherapie. Diese Plattformen werden wahrscheinlich eine entscheidende Rolle bei der Entwicklung von Experimenten spielen, welche die Übertragung von Forschungsergebnissen in klinische Situationen zum Ziel haben. Innerhalb des Fachgebietes Strahlentherapie, aber auch in anderen Bereichen wie zum Beispiel der Neurologie, bieten diese Geräte einzigartige Möglichkeiten, unter anderen Substanzen die Synergie zwischen Bestrahlung und Medikamenten oder anderen Agentien zu erforschen.

Um die Vorteile dieser neuen Technologie voll ausschöpfen zu können, sind genaue Methoden notwendig, um die Bestrahlung planen und die dreidimensionale Dosisverteilung im Organismus berechnen zu können.

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Spezielle, hierfür entworfene Bestrahlungsplanungssysteme sind hierbei essentiell. In dieser Übersichtsarbeit erörtern wir die spezielle Situation der Präzisionsbestrahlung von Kleintieren, wir beschreiben die Arbeitsweise der Bestrahlungsplanung bei Tieren, und wir untersuchen verschiedene Algorithmen zur Dosisberechnung (Ray Tracing, Superposition-Konvolution, Monte-Carlo-Simulation), die für die Tierbestrahlung mittels Kilovolt-Photonen verwendet werden. Des Weiteren werden Punkte, wie zum Beispiel Methoden der Dosismeldung, Photonenstreuung, Gewebesegmentation und Bewegung kurz angerissen.

Keywords: Small animal, precision irradiation, image-guidance, treatment planning system, dose calculation, photon scatter

Schlüsselwörter: Kleintier, Präzisionsbestrahlung, Bildführung, Bestrahlungsplanungssystem, Dosisberechnung, Photonenstreuung

1 Introduction

The technical capabilities in human radiotherapy have reached a high level of sophistication with e.g. intensity modulated radiotherapy and volumetric modulated arc therapy whereby the photon fluence is modulated while a medical accelerator irradiates the tumor with a crossfire of beams from several directions [1,2]. Radiation dose distributions can now be sculpted intricately with techniques such as dose painting e.g. to preferentially target hypoxic tumor regions [3]. This degree of sophisticated beam delivery requires an equally complex level of planning and dose calculation which is nowadays available in clinical treatment planning systems (TPS). Arguably the next progress in radiation delivery comes in the form of hadron beams such as protons and carbon ions [4] where also sophisticated treatment planning methods are being developed [5].

Most progress in radiotherapy, real or perceived, has come from technological developments, and not from knowledge derived e.g. from animal irradiation experiments [6]. The latter were mostly performed with irradiation technology which bears little resemblance to modern radiotherapy equipment. The recent development of many animal tumor models has enabled the detailed study of the tumor micro environment and the interaction of radiation with tumors. Improved models of normal tissue response are also needed to assess optimal radiotherapy strategies.

The recent literature [6–8] has described some novel technology which, for the first time, allows precision image guided radiotherapy for pre-clinical studies in radiotherapy. It combines narrow radiation beams of photons which may be aimed precisely at tumorous or healthy tissues with the aid of x-ray imaging equipment. It is expected that this new technology may lead to meaningful translation of novel forms of cancer therapy, e.g. by exploiting the synergy between radiation and drugs or other agents.

In a recent review paper on the novel animal technology [6] it was explained why small animal precision irradiation with photons is preferably done with kilovolt (kV) instead of megavolt (MV) photons. The main rationale is to avoid extensive dose buildup regions near medium interfaces, and to avoid wide beam penumbras, sometimes encompassing the whole animal. Many animal studies done in the past didn't employ a TPS and usually no imaging was available. Using a human TPS for animal studies is not really advisable, at least not without precautions. Human TPS employ calculation models unsuitable for small beams (<3 cm field size). One of the few animal studies accurately modelling small beams of high energy photon beams with a dedicated TPS is [9] where rats were irradiated with small beams of ^{60}Co photons from a GammaKnife device. A human TPS may not be suited to handle the animal voxel phantoms from e.g. a CT or MRI scan with commonly a large number of very small voxels. There is also no human TPS that can reliably calculate dose distributions in heterogeneous phantoms irradiated by kV photon energies.

Recently, dedicated photon dose calculation methods for small animals have been proposed from relatively simple pencil beam type calculations to Monte Carlo simulations. The latter has the potential of being the most accurate dose calculation technique available for a wide range of conditions [10], provided accurate models are used. This review discusses several of these methods with an emphasis on the technical capabilities and not on treatment planning studies themselves. Sometimes precision proton [11] or hadron beams [12] are used for pre-clinical studies; treatment planning for these is not included in this review. Treatment planning for radiotherapy for pet animals is also excluded from the review.