ORIGINALARBEIT

Magnetic resonance imaging for precise radiotherapy of small laboratory animals

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Abstract

Aims: *Radiotherapy of small laboratory animals (SLA) is often not as precisely applied as in humans. Here we describe the use of a dedicated SLA magnetic resonance imaging (MRI) scanner for precise tumor volumetry, radiotherapy treatment planning, and diagnostic imaging in order to make the experiments more accurate.*

Methods and materials: *Different human cancer cells were injected at the lower trunk of pfp/rag2 and SCID mice to allow for local tumor growth. Data from cross sectional MRI scans were transferred to a clinical treatment planning system (TPS) for humans. Manual palpation of the tumor size was compared with calculated tumor size of the TPS and with tumor weight at necropsy. As a feasibility study MRI based treatment plans were calculated for a clinical 6 MV linear accelerator using a micro multileaf collimator (μMLC). In addition, diagnostic MRI scans were used to investigate animals which did clinical poorly during the study.*

Results: *MRI is superior in precise tumor volume definition whereas manual palpation underestimates their size.*

Magnetresonanzbildgebung zur präzisen Strahlenbehandlung kleiner Labortiere

Zusammenfassung

Ziele: *Strahlentherapeutische Behandlungen von kleinen Labortieren (SLA) werden häufig nicht so präzise durchgeführt wie bei Menschen. In diesem Artikel wird beschrieben, wie dedizierte Kleintier-Magnetresonanztomographen (MRT) zur präzisen Tumorvolumetrie, Bestrahlungsplanung und diagnostischen Bildgebung eingesetzt werden können, um die Experimente akkurater zu gestalten.*

Methoden und Materialien: *Unterschiedliche humane Tumorzellen wurden im Bereich der Flanke von pfp/rag2 und SCID-Mäusen injiziert, um einen lokalen Primärtumor zu bilden. Die MRT-Schnittbilder wurden an ein klinisches Bestrahlungsplanungssystem für Menschen (TPS) übertragen. Die manuell palpierten Tumorgrößen wurden mit den vom TPS berechneten Werten sowie den Tumorgewichten bei Sektion verglichen. Als Machbarkeitsstudie wurden MRT-basierte Bestrahlungspläne für einen klinischen*

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Cross sectional MRI allow for treatment planning so that conformal irradiation of mice with a clinical linear accelerator using a μMLC is in principle feasible. Several internal pathologies were detected during the experiment using the dedicated scanner.

Conclusion: *MRI is a key technology for precise radiotherapy of SLA. The scanning protocols provided are suited for tumor volumetry, treatment planning, and diagnostic imaging.*

Keywords: Magnetic resonance imaging, small animal irradiation, treatment planning, tumor volumetry

6MV-Linearbeschleuniger mit einem Mikro-MLC (μMLC) berechnet. Zusätzlich wurden mit MRT Tiere untersucht, die eine klinische Belastung während der Studie zeigten.

Ergebnisse: *Die MRT-Bildgebung ermöglichte eine präzise Tumorvolumetrie, wohingegen die manuelle Palpation die Tumorgrößen eher unterschätzt. Die MRT-Schnittbilder ermöglichten eine konformale Bestrahlungsplanung, so dass SLA prinzipiell auch mit einem klinischen Linearbeschleuniger mit μMLC präzise bestrahlt werden können. Darüber hinaus konnte die MRT-Bildgebung diverse innere Mauspathologien entdecken.*

Schlussfolgerungen: *MRT ist eine Schlüsseltechnologie für eine präzise Strahlenbehandlung von SLA. Die vorgestellten Protokolle sind sowohl für die Tumorvolumetrie als auch eine Bestrahlungsplanung und diagnostische Bildgebung geeignet.*

Schlüsselwörter: Magnetresonanztomographie, Kleintierbestrahlung, Bestrahlungsplanung, Tumorvolumetrie

Objective

Modern cancer therapies combine surgery, radiotherapy, chemotherapy, and immunotherapy. For a better understanding of single and combined therapies and their influence on metastases formation small laboratory animal models are required. A large variety of spontaneous xenograft models for various human tumor entities in immunodeficient mice exist. In order to simulate the clinical situation as closely as possible, cross sectional imaging should be used for radiotherapy treatment planning for small laboratory animals as well. Particularly magnetic resonance imaging (MRI) helps to mimic the clinical situation [1,2].

We already implemented a cost effective way for partial body irradiation of mice with an industrial X-ray tube [3]. It was now our goal to further improve our radiation experiments with mice to approximate treatment modalities used in clinical medicine. We used a dedicated small animal MRI scanner to acquire cross sectional images. In a first step we imported all data into our human treatment planning system. The software provided us a tool for precise tumor volumetry and visualization so that we could compare these results with manual palpation and weighing of the tumors at necropsy.

The next step was a feasibility study: We wanted to investigate whether a clinical linear accelerator equipped with a micro multileaf collimator could in principle be used for further radiation experiments. All treatment planning was done on the MRI data.

Chemo- and radiotherapy in our experiments also required adequate monitoring of the animals. For this reason it was another aim of this study to establish a routine imaging concept providing whole body cross sectional imaging for diagnostic purposes as well. Besides monitoring the tumor burden of our animals we wanted to detect unexpected tumor masses without invasive manipulation of the animal.

Methods and materials

Xenograft mouse tumor models

Our MRI experiments were a part of a much bigger series of experiments analyzing the influence of local tumor therapy on metastases development. Our experiments comply with German animal experimentation licensing act. For this MRI study we used the prostate cancer cell lines PC3 and LNCaP in combination with male pfp/rag2 mice (B6-129S6-Pfp^{tmlClrk}-Rag2^{tmlFwa}N12; Taconic, One Hudson City Centre, Hudson, NY 12534, USA) [4] as well as OH1 and H69 small cell lung cancer cells in combination with SCID mice (CB17/Icr-Prkdc^{scid}/IcrIcoCrl; Charles River Laboratories International Inc., 251 Ballardvale Street, Wilmington, MA 01887, USA) as previously described [5]. For each of the animals 1×10^6 tumor cells were injected subcutaneously over the right lower trunk of the mice so that they could form a local tumor in the pelvic/leg region of the mice. The mice were approximately 8 cm in length and had an average weight of 25 g. MRI was performed for a small subgroup of mice only: 1 mouse bearing H69 tumor cells, 1 mouse bearing OH1 tumor cells, 2 mice bearing PC3, 20 mice bearing LNCaP (for precise tumor volumetry), and 3 mice without prior injection of tumor cells.