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Impact and Future Opportunities in Translational Radiobiology by Translational Imaging

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Abstract

Background and goal to offer a scoping overview of studies that have been published employing small animal irradiators and to draw attention to the advancements made possible by these platforms in preclinical radiation research since their creation and commercialization in 2007. Materials and procedures 359 small animal RT trials were included in the analysis after 907 studies were found by screening using manufacturer data and PubMed searches. To detect trends in the preclinical RT research landscape, these publications were divided into subgroups based on research objectives, experimental models, and other criteria and classed as contributions from the fields of biology or physics. Results Between 2007 and 2021, biology contributions made up the majority of articles that were published, while physics contributions made up 38% of publications. In physics papers, dosimetry and calibration treatment were the primary study fields. The developments in small animal irradiator-based preclinical RT research are covered in this study from 2007 to 2021. Our findings indicate a rise in the number of preclinical RT investigations being conducted in crucial fields of biology and physics research that might help guide the translation of those findings into clinical trials.

Keywords: Radiotherapy; Preclinical models; Preclinical radiotherapy; Small animal irradiators

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Introduction

Cancer patients have liver transplants. Technology advancements are largely driving the continued evolution of RT, but sophisticated preclinical studies using small animal irradiators are making it possible to conduct more in-depth research, which is leading to a better understanding of radiobiological reactions at the cell, tissue, and whole-organism levels [1]. Small animal RT response models are crucial tools for bridging the gap between in vitro principles and clinic translation [2]. Clinical translation is frequently seen as a two-step process that involves both the translation of in vitro data to preclinical animal models and the transfer of preclinical animal model information to clinical practise [3]. How well preclinical models represent actual disease characteristics and treatment responses, however, is a crucial concern. Traditional radiobiology research these restrictions have mostly been overcome by small-scale beam geometries, cone beam CT image guiding, and customised TPSs in small animal irradiators [4]. Several tiny animal irradiators with revolving or stationary gantries and CBCT detectors or micro-CT device conversions have been created. Two systems, the X-Rad small animal radiotherapy system from Precision X-ray Inc., originally developed at Princess Margaret Hospital, and the small animal radiotherapy research platform SARRP, Strahler Life Sciences), have been commercialised and extensively established into research laboratories across the globe [5]. Small animal irradiators' foundational ideas and technological advancements have already been covered in a number of studies [6]. We sought to present a scoping overview of the preclinical RT research literature in this work [7]. Shows the article screening and exclusions. Only papers that were published between 2007 and December 2021 were included in this review [8]. Studies had their titles, abstracts, and methodologies carefully checked for relevance. Studies that did not use small animal image-guided sources including clinical sources and preclinical

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non-image guided studies were identified for further review [9]. These studies excluded review articles, poster conference abstracts, technical notes, studies using companion animals, studies using internal sources of radiation brachytherapy, and studies using internal sources of radiation [10]. This review was limited to peer-reviewed research publications that used image-guided irradiators on small animals to offer unique experimental findings [11]. PubMed searches using the terms "small animal image-guided radiation," "small animal irradiator," and "preclinical image-guided radiotherapy" were used to find articles initially [12]. Both "normal tissue radiation preclinical model" and "tumour radiotherapy preclinical model" are used. In order to add papers that were overlooked during the original search, articles were then cross-referenced with manufacturer records that were requested from the databases of Strahler and Precision X-ray Inc [13]. There were 907 studies in all that were found. The identified publications' abstracts, methodologies, and any additional material that was necessary were carefully reviewed. Each article's goal was used to determine whether it was a contribution to biology or physics, and they are organised by year in According to the primary research topic, experimental models employed, and study methodology, the publications were sub classified [14]. Dosimetry and calibration, treatment planning and simulation, imaging, platform development, new detectors, phantom development, and in vivo dosimetry were listed as research fields for physics investigations [15]. The claimed radioactivity Size of the collimator, imaging technique, and model utilised In vivo small animal models, computer simulations, or phantom in-house and commercial models were listed as the research models employed. Studies in biology were divided among those that were focused on normal tissue or tumours. By target tissue or tumour model, as described in the techniques, both tumour and normal tissue types were categorised. Studies that included different tumour types in the same investigation were added to a separate class called "multiple."

Discussion

Radio sensitizers, model creation, imaging, delivery method, radio protectors, and fiducial markers were the six key study areas into which the contributions from biology were split. During screening, precise information on any drug + RT combinations, imaging contrast agents, fiducial markers, or studies was noted. Tumor models were divided into three categories and visualising. These research fields have made it possible for the contributions to biology to expand exponentially, and they are crucial for the creation and quality assurance of preclinical RT setups. Due to the extremely small size of the target areas in comparison to the known techniques in the clinic, novel detectors, phantom construction, and in vivo dosimetry constitute hard preclinical RT features that require additional research. Only 18% of the overall physics contributions came from these fields. From 2007 to 2021, 359 papers reporting on the usage of small animal irradiators were examined. In studies published between 2007 and 2010, contributions from physics predominated. A consistent increase in the number of physics and biology papers was seen after commercialization and the early use of small animal irradiators, and ever since We selected six primary study fields from a total of publications on biology, including the evaluation of novel radio sensitizers, model creation, imaging innovative delivery mechanism, evaluation radio protectors, and assessment of fiducial marker. In publications on radio sensitizers, all medication + RT combinations are included, and these combinations are evaluated utilising tumour trials. Studies using radio sensitizers are within the category of immunotherapies. Chemotherapy using nanoparticles or other molecularly targeted substances. The breakdown of articles in various regions is displayed in from 2013 through 2021, more than half of therapeutic agent research projects targeted immune modulators or immunotherapy drugs. Studies on the construction of models used tissue targeting, GEMMs, orthotropic delivery, and dosage regimens. These publications were distributed very evenly between investigations on tumour and normal tissue. In order to establish more complicated delivery schedules, preclinical models have also experimented with various imaging techniques (21%) and delivery mechanisms. Fiducial markers were by far the least reported in studies on radio protectors, barely accounting for 4% of all published studies. This diagram displays the distribution of various tumour locations and models. Allograft and xenograft cell-line derived tumour models make up the majority of tumour research (82%) and are reported across all tumour types due to their versatility and simplicity.

Conclusion

These included the injection of human or mouse tumour cells into syngeneic immunocompetent animals. Subcutaneous tumour models were not included in the study as these frequently demand higher field sizes for targeting and have no proximal adjacent organs at risk. Irradiation field sizes were recorded for studies targeting orthotic cancers and displayed in The measured radio chromic film output for circular collimators is shown in 18% of the articles reviewed used collimators of mm and are thus at risk of underdoing if output correction was not performed used the less severely impacted 3mm collimator whereas the other 6% are at risk of severe dose overestimation, which could have a significant impact on the study reliability and reproducibility. No research employed the 0.5 mm collimator in orthotropic tumour models, which may be an indication of the significant degree of dosimetry uncertainty linked to fields this size. A more therapeutically applicable method for enhancing the translational power of preclinical models of RT response has been made available by small animal irradiators. We evaluated the primary contributions of small animal irradiators based on a study of all recognised articles from to give a comprehensive picture of the present preclinical RT environment. According to our statistics, there are more papers employing small animal irradiators. These publications, which mostly covered physics research between 2007 and 2010, reflected the need for reliable dosimetry, imaging, etc. The amount of contributions from biology then started to rise after that. The greater use of the systems during this period can be attributed to these improvements. Additionally, this is consistent with the "Lesson Learned from Radiation Oncology" paper. Physics contributions were mostly carried out utilising phantoms and focused on the development and quality assurance of these platforms by evaluating dosimetry, treatment planning,

and imaging. Multi-tissue density phantoms have taken the role of relatively basic phantom models in an effort to enhance dose assessments for diverse irradiation geometries. Dosimetry and QA are essential components of preclinical RT research that are essential to understanding why studies have poor repeatability. Additionally, we demonstrated that 18% of orthotropic tumour studies that reported collimator sizes employed modest field widths of mm. The focus point is obscured by beam collimation when reducing beams to less than around 5 mm in diameter at discounter. This occlusion of the focus point is difficult to replicate since the focal spot is very diverse, hence measurement is preferred if this impact exists.

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None

Conflict of Interest

None

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