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NOTE

A survey of dosimetry quality assurance practice at UK small animal radiation research platform (SARRP) facilities

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Abstract

Introduction: Improvements in preclinical radiation research have been made to better mimic the equipment and techniques implemented in the clinic. The development of dedicated small animal radiation units facilitates such advances by combining treatment planning, image guidance and conformal delivery. One area significantly behind its clinical equivalent are standardised dosimetry quality assurance (QA) protocols, hampering the translatability of results into the development of clinical interventions. *Approach*: The aim of the study described herein was to summarise the current QA procedures implemented at several institutions on Small Animal Radiation Research Platforms (SARRPs), the system used by the six institutions surveyed, and to determine the barriers to implementing a standard dosimetry protocol. Participants at UK research institutions were invited to complete a questionnaire to ascertain their current preclinical QA practice. *Main results*: All participants involved undertake regular dose output measurements and most perform image guidance QA measurements. Consistency in QA procedures differed when more complex plan verification or end-to-end testing was discussed. *Significance*: This survey demonstrates that, although improvements are being made in the awareness of the importance of regular dosimetry tests, there is still a way to go to standardise the procedures with regards to more complex verifications. Incorporating robust QA procedures and strict dose constraints would ensure the reliability and ethical integrity of experiments involving small animals. This approach not only protects the welfare of the animals but also enhances the quality and reproducibility of the preclinical results.

Introduction

The development of preclinical irradiators has significantly impacted the use of small animal models in radiation research, particularly over the last decade when small animal image-guided radiotherapy (IGRT) platforms became commercially available [1]. The Small Animal Radiation Research Platform (SARRP, Xstrahl), the most common preclinical IGRT system in the UK, was designed to mimic clinical radiotherapy systems

with on-board image guidance and treatment planning capabilities. Rather than the higher energy megavoltage x-rays used to treat humans, the SARRP source of radiation produces x-rays in the kilovoltage (kV) medium-energy range which manifests in more appropriate dose distributions and a reduction of hotspots and scatter when irradiating such small samples. Using kV energies also permits the combination of irradiation and imaging using the same source [2]. Cone beam computed tomography (CBCT) scans are captured on the SARRP platform and, in combination with treatment planning software (TPS), allows small animals to be treated using an IGRT approach [1]. With gantry and couch rotations of 360°, high quality conformal preclinical radiotherapy plans can be delivered on such platforms to an accuracy of 0.2 mm and 5% of the dose prescribed [1]. The motorised stage allows accurate positioning and is equipped for various set ups and immobilisation requirements [1]. To increase throughput, an adapted couch with acrylic dividers could be commissioned and used to facilitate immobilisation and positioning of multiple subjects [3].

Considering the complex designs of the small animal irradiators, robust quality assurance (QA) methods and appropriate dose tolerances have yet to be established and widely adopted within the UK [4]. It is recommended that preclinical devices operate under QA programs as comprehensive as those implemented on their counterpart clinical linear accelerators [5, 6]. Lack of medical physics support at this level prevents the design and implementation of such QA programs, considering that preclinical radiotherapy units are often found in biological discovery-focused research institutions. Furthermore, the small size of the animals makes it difficult to use standard dosimetry equipment, which may not be sensitive enough for accurate measurements. While there are various methods currently being developed to address the small volume challenges, different dosimetry modalities are still being used across the UK [7]. Moreover, research groups may use varying protocols for irradiation, leading to challenges in reproducibility and standardisation. The absence of dosimetry standards impacts the accuracy, reproducibility and overall quality of results produced [8].

There are many potential sources of error that may impact the accuracy of the dose delivered such as: incorrect external filter or tertiary collimator used, misalignment of the focal spot with the collimation system, positional errors of the motorised stage and animal motion between the acquisition of the planning image and the beam delivery [9]. Machine QA alone may be unable to detect some of the possible errors, and therefore local plan/technique-specific QA and external audits introduce another line of defence to ensure reliability. In relation to independent dose verifications, a previous dosimetry audit of conventional irradiators recorded differences of between 0.9% to 42% between the planned and thermoluminescent dosimeter-measured doses across 12 radiobiology centres [10]. More recently, and for image-guided irradiations, two UK audits by Biglin *et al* [11] and Silvestre Patallo *et al* [12] showed differences of $<$10% and $<$7%, respectively, between the planned and alanine-measured doses.

For dosimetry tests, measurements of the reference dose output are typically performed using an ionisation chamber within a solid water phantom, typically following AAPM TG61 [13]. The solid water phantom should have a material density that guarantees its water equivalence in the medium-energy x-ray range. The ionisation chamber and the charge/current measurement equipment is recommended to have calibrations traceable to primary standard dosimetry laboratories. In geometrical and imaging quality tests, a specifically designed ball bearing phantom is used for the analysis of the imaging and targeting accuracy. Independent end-to-end type of dose verification tests are mostly performed with phantoms that mimic the mouse anatomy, combined with the utilisation of small-volume detectors. Some centres choose to test their procedures by inserting the detectors directly in euthanized mice. In this approach, researchers are able to verify both simple and complex irradiation beam arrangements [14]. Further advances in technology are being reflected in the development of realistic dosimetry phantoms, where more sophisticated geometries, are replacing the use of basic cylindrical shapes [15]. The increasing popularity of 3D printing in this field is continuously raising the bar [16–20]. Sophisticated murine phantoms facilitate end-to-end testing of the experimental pathway, including animal imaging, treatment planning system (TPS) calculations, evaluation of complex dose distributions and radiation delivery. While small animal irradiators represent a valuable tool for preclinical research, addressing the limitations in dosimetry and QA is crucial for enhancing the reliability of experimental outcomes. This study aims to assess the current QA practices across a selection of UK centres.

Methods

In 2023, 6 UK-based institutions which actively undertake preclinical radiation research using SARRPs were surveyed. Each participant was sent a series of questions relating to their routine QA practice, more complex dosimetry procedures and what resources would be useful to make QA more accessible. The full list of questions can be found in the supplementary material.

Results

The first part of the survey enquired about the equipment used for machine QA, and how often it is performed. All centres used an ionisation chamber in solid water for

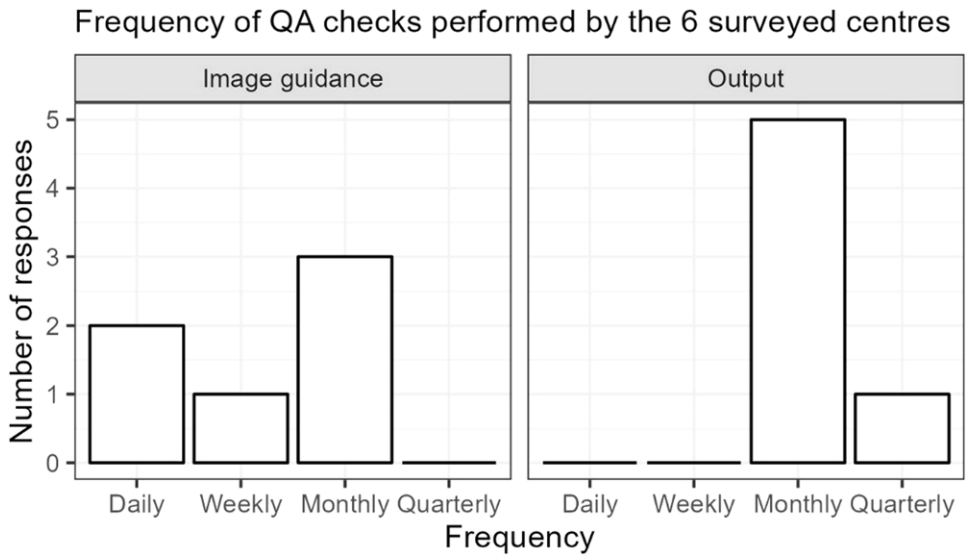

Figure 1. Frequency of QA checks performed by the 6 surveyed centres.

Table 1. Equipment routinely used for plan/technique verification and end-to-end dosimetry.

	Phantom type		Detector type			No routine approach
	3D printed mouse phantom	Solid-water block	Farmer ionisation chamber	Gafchromic EBT3 film	Alanine	
Institution 1						y
Institution 2			y	y		
Institution 3	y				y	
Institution 4	y			y		
Institution 5	y	y		y	y	
Institution 6		y				

Table 2. Frequency of plan/technique verification and end-to-end dosimetry.

	Following system commissioning	Following any system changes	Quarterly	When requested for a study	Following technique commissioning
Institution 1	y				
Institution 2			y		
Institution 3				y	
Institution 4				y	y
Institution 5		y			y
Institution 6	y				

reference output QA, and a ball-bearing phantom for imaging QA. The frequency of machine QA reported by the six institutions is summarised in figure 1.

The first question of the survey enquired into the frequency of routine quality assurance (QA) checks examining the accuracy of the Small Animal Radiation Research Platform's (SARRP's) on-board imaging capabilities and a measurement of the dose output. Participants were given the option of answering daily, weekly, monthly, quarterly or never.

The next series of questions asked each participant about plan/technique-specific QA, and the inclusion of end-to-end tests. End-to-end tests involve the complete evaluation of all aspects of an experiment; imaging, treatment planning, radiation delivery and detector analysis. The equipment in use for these tasks and the frequency at which they were performed are shown in tables 1 and 2. The resources available for end-to-end dosimetry are summarised in figure 2. Each institution was then asked to prioritise which parts of the QA process they believe should be verified in an end-to-end test. Validating the dose delivered to the target was ranked as the top priority, followed by validation of the positional accuracy and finally, measurement of the dose outside of the target area that may affect surrounding organs-at-risk.

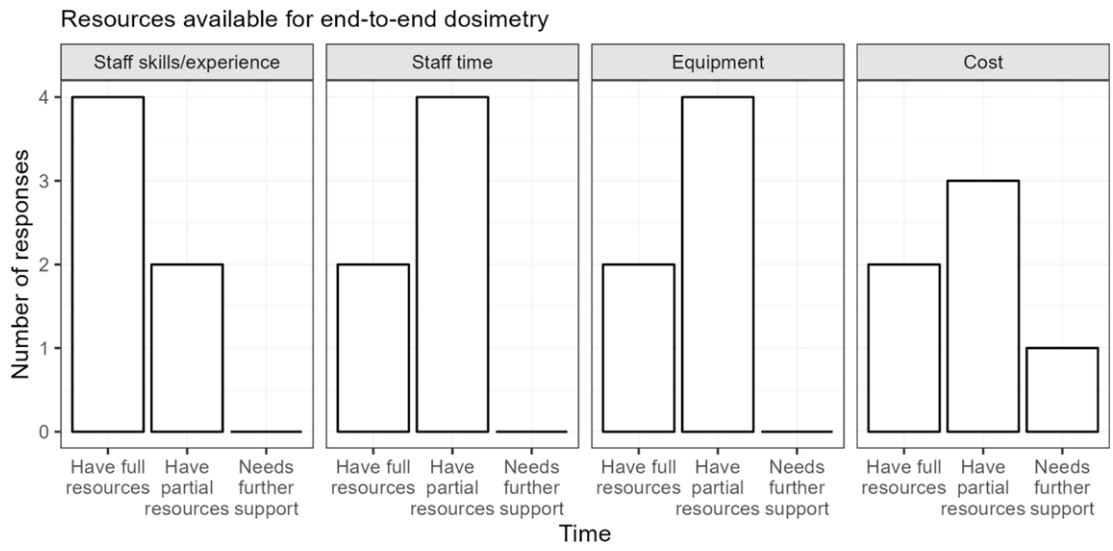

Figure 2. Resources available for end-to-end dosimetry.

To undertake consistent and accurate quality assurance (QA) testing staff need access to adequate training, time, equipment and funding. Each participant was asked to describe the current levels of these resources at their institution, categorised as access to the full resource, partial resource or need support in this area.

Finally, each institution was asked about the level of resources and/or equipment they would find most useful to enable or improve their end-to-end dosimetry verification processes. The most common request was for dosimetry equipment that allowed a direct read-out. Other suggestions included murine phantoms, access to traceable alanine dosimetry and guidance on free or reasonably priced dosimetry software. Four institutions noted that they would do more end-to-end dosimetry verification if suitable resources were more readily available.

Discussion

QA procedures are an extension of the commissioning process with daily, monthly and annual tests of the imaging, dosimetry and TPS components [4]. A report by Chen *et al* [21] found large calibration errors caused by incorrect procedures and omission of correction factors by the vendor upon installation, highlighting the importance of independent checks following the commissioning procedure. This is further complicated by the differences between the dose measured in reference and experimental conditions when working with kV x-ray radiation [22]. Dosimetry errors are widely regarded as a significant concern as they have the potential to affect every experiment in a laboratory [22]. Most of the institutions surveyed undertake comprehensive end-to-end dosimetry evaluations at least once after the installation of their system, followed by regular dose output checks. Undertaking a comprehensive QA routine efficiently means organising these tests in a tiered manner, considering both the importance of the parameter being tested and the likelihood of it changing over time [23]. The most important checks i.e. those relating to the dose output should be assessed monthly, followed by reviewing other components of dose delivery and targeting quarterly. Image quality, TPS dose calculation and field profiles, which are less likely to deviate over time, should be checked biannually. Finally, complete end-to-end tests should be performed annually [23]. Guidelines for dosimetry in radiobiology experiments tailored for both biologists and medical physicists are currently under development [24].

While these more sophisticated units are able to produce more conformal dose deliveries, they require stringent QA procedures with one of the main challenges related to the need to perform measurements in very small fields (down to 0.5 mm diameter) [7]. Logistically, the main challenges to implement these procedures highlighted in this survey are time and access to appropriate equipment, closely followed by funding. To encourage QA uptake, Jermoumi *et al* [25] presented a comprehensive QA system that encompassed radiation, geometrical and image quality tests by adapting the SARRP commissioning phantom to include different tissue equivalent materials and several detector types. This combination allowed the evaluation of different beam parameters (e.g. field size, penumbra flatness, etc), the CBCT system (spatial resolution, noise, etc) and the accuracy of the CT number calculations and Hounsfield unit (HU) conversion for different materials with one set-up. Another proposed 4-step QA protocol measuring the output, image resolution, image guidance and dose calculation consistency using process familiar to the platform users. This protocol required knowledge of

MATLAB for efficient read-out, however proved effective for long-term dosimetry [26]. Developments in artificial intelligence, already being proposed for QA in the clinical setting, could create real-time monitoring tools for assessing dose output and distributions, beam profile, stage and gantry movement, image quality and alignment [27]. There could also be scope to develop tools for predictive maintenance, scheduling in different QA tests when they would likely be needed based on historical measurements.

High quality data allows for more informed decisions regarding the progression of research, such as moving from preclinical to clinical studies. Small dose errors in the preclinical setting can have significant impacts on the radiobiological outcome [22]. QA procedures help ensure compliance with ethical guidelines, promoting humane treatment and reducing unnecessary suffering. Implementing QA allows for better planning of pilot studies to assess feasibility before full-scale experiments and encourages ongoing evaluation and refinement of experimental protocols leading to more effective study designs. The implementation of regular QA tests will reduce the numbers of animals required to counteract the uncertainties associated with dose which represents a major source of noise in experimental data [28]. Sample size calculation studies in dose response studies suggest a reduction in animals of up to 60%, based on excluding very high doses for which tumour control is assumed (>90% tumour control probability) or very low doses where tumour control or tumour growth delay is not likely to occur. However, these assumptions can only be made if the resultant dose–response curves are trustworthy [28].

Conclusions

This report describes the results of a survey among the UK preclinical radiobiology community to examine the status of QA procedures at this level. Over the last decade, the advances in technology in and out of the laboratory has encouraged the development of an irradiation device that can mimic all aspects of a clinical linear accelerator: CBCT image-guidance, treatment planning capabilities and the delivery of arc-based radiotherapy plans. The lack of standardised QA protocols in preclinical radiation research impacts the scientific quality of the experimental results which could lead to questioning the ethical production of such research if the results are not fit for purpose or able to progress into clinical trials. Enhanced documentation practices lead to better reporting of methods and results, fostering transparency and trust in the research community.

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Conflict of interests

None.

Data availability statement

The data that support the findings of this study are available upon reasonable request from the authors.

Author contributions

All authors were involved in designing the survey and provided the anonymous responses from their institutions. AHA and AM collated the data. ERB and AHA drafted the manuscript. ISP, TLL, MGP and GS provided vital feedback. All authors reviewed and approved the manuscript.

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