The Potential of Automated QA in Radiation Biology Using Comprehensive EPID-Based QA Tools for Image-Guided Small Animal Irradiators

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Small Animal Radiotherapy: What’s New?

WE-C-TRACK 3-1
Learning objectives

• Current challenges in developing QA programs in radiation biology, particularly for image-guided small animal irradiators

• Description of the Xstrahl SARRP’s EPID & characterization as a dosimeter with potential for automatization

• Review possible QA tests using EPID and its advantages over other dosimeters and QA methodologies
Background – kV irradiators on the rise in rad biology research

- ~1/3 of all published radiation biology research in 2017-2018
- About ~1/3 of these are orthotopic/flank irradiations which would benefit from modern irradiators
- Image-guided irradiators made up ~5% of all radiation research performed with kV irradiators since 2013, but this is expected to rise

Increased complexity of image-guided small animal irradiators

- Soft kV source introduces energy dependency in most detectors
- Small field sizes introduce volume averaging effects (e.g. like SRS)
- Sub-mm motion by robotic stage, gantry and couch rotation
- CBCT imaging system
- TPS introduces even more uncertainties

Each of these moving parts introduce potential failure modes
Current proposals for QA methodologies for IGSAI - Brodin

- Prescriptive QA methodology proposed by Brodin et al.
- Requires specialized equipment / knowledge
  - Ion chamber / Correction factors
  - Imaging phantom / CBCT analysis
  - BB Phantom / Dose computation

<table>
<thead>
<tr>
<th>Performance</th>
<th>Tests</th>
<th>Tolerance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Output consistency</td>
<td>Measure dose-rate the at isocenter using an appropriately calibrated ion chamber</td>
<td>± 1%</td>
</tr>
<tr>
<td>Image resolution consistency / Object representation</td>
<td>Use a CBCT scan of the imaging phantom to derive diameters of all resolution air cavities by vertical and horizontal line profiles. Derive distances between cavities from the same line profiles. Check the length and diameter of the imaging phantom in a sagittal slice.</td>
<td>± 0.2 mm for resolution, ± 0.5 mm for distances, ± 1.0 mm for object size representation</td>
</tr>
<tr>
<td>Accuracy of image-guided target localization</td>
<td>Locate a well-defined target using the high-CT density BB phantom and then verify that its location identified on the CBCT coincides with the radiation isocenter using the 5 × 5 mm² collimator at gantry angles 0° and 90°.</td>
<td>± 0.5 mm</td>
</tr>
<tr>
<td>Dose calculation consistency</td>
<td>Calculate a four-field 10 × 10 mm² treatment plan for 10 Gy on a reproducible isocenter in the imaging phantom and record the treatment times.</td>
<td>± 2 s (± 3%) per treatment field</td>
</tr>
</tbody>
</table>

Figure 2 & Table 1: P Brodin et al, “Proposal for a Simple and Efficient Monthly Quality Management Program Assessing the Consistency of Robotic Image-Guided Small Animal Radiation Systems" Health Phys 109 (3 Supl 3), S190-9, 2015.
• Description of commissioning tests by Verhaegen et al.

• Most tests require specialized equipment and software

Table S1: Recommendation for commissioning and ongoing operation of small animal Image guided irradiators

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Set-up absolute dosimetry and dose reporting system</td>
<td>Identify reference standards protocol used</td>
</tr>
<tr>
<td>Specify radiation source</td>
<td>Identify detector type used and traceability to national/international standard</td>
</tr>
<tr>
<td>Establish detailed description of irradiator</td>
<td>Dose reporting; dose to water and possibly in addition, dose to medium</td>
</tr>
<tr>
<td>Establish periodic quality assurance</td>
<td>If radionuclide: type, activity, geometry and &quot;delivery method&quot;</td>
</tr>
<tr>
<td>Acquire beam specific data for the range of collimators available and as a function of SSD</td>
<td>Focal spot size and distribution</td>
</tr>
<tr>
<td>Acquire beam specific data for the range of collimators available and as a function of SSD</td>
<td>Contribution to dose during tube ramp up and timer errors</td>
</tr>
<tr>
<td>Acquire beam specific data for the range of collimators available and as a function of SSD</td>
<td>Detail irradiator geometry and degrees of freedom</td>
</tr>
<tr>
<td>Acquire beam specific data for the range of collimators available and as a function of SSD</td>
<td>Mechanical flex maps during imaging and radiation delivery and accuracy after correction</td>
</tr>
<tr>
<td>Acquire beam specific data for the range of collimators available and as a function of SSD</td>
<td>Beam positioning precision and accuracy exceeded by other reasons than flex</td>
</tr>
<tr>
<td>Acquire beam specific data for the range of collimators available and as a function of SSD</td>
<td>Determine how measurements were made</td>
</tr>
<tr>
<td>Acquire beam specific data for the range of collimators available and as a function of SSD</td>
<td>Collimator details (size &amp; shape at isocentre or specified point)</td>
</tr>
<tr>
<td>Acquire beam specific data for the range of collimators available and as a function of SSD</td>
<td>Depth dose curves in water.</td>
</tr>
<tr>
<td>Acquire beam specific data for the range of collimators available and as a function of SSD</td>
<td>Beam profiles as a function of depth (FWHM, 20-80% penumbrae, flatness, symmetry)</td>
</tr>
<tr>
<td>Acquire beam specific data for the range of collimators available and as a function of SSD</td>
<td>Assessment of out of field dose rate</td>
</tr>
<tr>
<td>Acquire beam specific data for the range of collimators available and as a function of SSD</td>
<td>Beam/collimator targeting alignment</td>
</tr>
<tr>
<td>Acquire beam specific data for the range of collimators available and as a function of SSD</td>
<td>Imaging and irradiation Winston-Lutz test</td>
</tr>
<tr>
<td>Acquire beam specific data for the range of collimators available and as a function of SSD</td>
<td>Dose rate measurements to assess tube stability with time</td>
</tr>
<tr>
<td>Acquire beam specific data for the range of collimators available and as a function of SSD</td>
<td>Beam quality measurements (e.g. AID, or PDD) to assess stability with time</td>
</tr>
<tr>
<td>Acquire beam specific data for the range of collimators available and as a function of SSD</td>
<td>If real-time dosimetry is desired use of small dosimeters, e.g. optical fibers or microdetectors can be considered.</td>
</tr>
<tr>
<td>Acquire beam specific data for the range of collimators available and as a function of SSD</td>
<td>Use of the on-board imaging panel may also be considered for real-time dosimetry.</td>
</tr>
</tbody>
</table>

Table S3: Recommendations when commissioning and using small animal TPS

<table>
<thead>
<tr>
<th>Recommendation</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Determine comprehensive benchmarking data set (relative dosimetry)</td>
<td>Use large reference field (e.g. 4x4 cm²)</td>
</tr>
<tr>
<td>Determine comprehensive benchmarking data set (relative dosimetry)</td>
<td>Compare-measured and calculated depth dose and lateral profiles at several depths in a suitable phantom, e.g. stack of solid water slabs</td>
</tr>
<tr>
<td>Determine comprehensive benchmarking data set (relative dosimetry)</td>
<td>Compare-measured and calculated output factors for all field size collimators (normalized to reference field)</td>
</tr>
<tr>
<td>Determine comprehensive benchmarking data set (relative dosimetry)</td>
<td>Compare-measured and calculated output factors for a sub-set of fields for a variable field irradiation (normalized to reference field)</td>
</tr>
<tr>
<td>Establish a link to absolute dosimetry (calibration of irradiator)</td>
<td>Convert absolute dose units of TPS to absolute dose in Gy/gray. This requires a conversion factor per x-ray energy. In the SARRP device a conversion factor is required for each collimator, and for each x-ray tube energy (but most users use only a single x-ray energy). In the XRadio device, a single conversion factor is used for each x-ray tube energy, and additionally correction factors are employed for the smallest collimators (0.5mm).</td>
</tr>
<tr>
<td>Determine focal spot size of irradiator</td>
<td>Dose calculations are sensitive to focal spot size and position, in particular for small fields</td>
</tr>
<tr>
<td>Coordinate systems</td>
<td>Focal spot may also drift spatially over time, which may alter dosimetry</td>
</tr>
<tr>
<td>Spatial accuracy</td>
<td>Check coordinate systems of images, irradiator and TPS</td>
</tr>
<tr>
<td>Predetermine material types</td>
<td>Check spatial accuracy with a test object</td>
</tr>
<tr>
<td>Establishe periodic quality assurance</td>
<td>Make sure all needed tissue types and other materials are available in the TPS, this may include the treatment table</td>
</tr>
<tr>
<td>Establish conversion of CT images into electron or mass density</td>
<td>Obtain a calibration curve, HU to mass/electron density from a CT image of a small heterogeneous phantom</td>
</tr>
<tr>
<td>Validate image transfer and image registration functionality</td>
<td>Need to assign various HU intervals to various materials</td>
</tr>
<tr>
<td>Minimize motion effects</td>
<td>Be aware of imaging artifacts (e.g. beam hardening, streaks, ... ) which may influence tissue assignment and dose calculations</td>
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<td>Transfer of treatment plan</td>
<td>Dose to-water-in-medium / dose-to-medium-in-medium, the latter is current standard but both should be available</td>
</tr>
<tr>
<td>Transfer of treatment plan</td>
<td>Dose to-water-in-water is not recommended for x-ray beams and TPS may handle imaging modalities other than CT, e.g. for targeting (PET, MRI). Proper registration between the images is crucial.</td>
</tr>
<tr>
<td>Transfer of treatment plan</td>
<td>Motion may severely degrade the dose calculation in a static CT phantom. Currently no animal TPS can handle this.</td>
</tr>
<tr>
<td>Transfer of treatment plan</td>
<td>Check transfer of treatment plan to irradiator by verifying dose calculations under different conditions (single beam, arc, variable collimators, variable couch angles)</td>
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<tr>
<td>Transfer of treatment plan</td>
<td>Animal TPS require minimal QA but when dosimetric QA on the irradiator shows changes over time, then recalculation of the dose conversion factor may be needed</td>
</tr>
</tbody>
</table>

Table S1 & S3: F Verhaegen et al, “ESTRO ACROP: technology for precision small animal radiotherapy research: optimal use and challenges” Radiother & Oncol 126 (3), 471-478, 2018.
Current state of physics knowledge in radiation biology

- Radiation biology laboratories repeatedly fail to produce **accurate dosimetry** (±5%)
  - University of Wisconsin\(^3\): 5 out of 11 sites
  - NIH\(^4\): 3 out of 7 sites
  - EULAP project\(^5\): 13 out of 15 sites - 6 out of 15 sites delivered within ±10% homogeneity

- The majority of radiation biology studies do not report basic irradiation details such as scattering environment and field sizes\(^1,\,2\)
  - Implication is that these factors are not considered in the dosimetry\(^2\)
  - “Few students or researchers using ionizing radiation in biological research have training in basic radiation physics.”^2
  - Conclusion: There is a need for QA tests which do not rely on specialized knowledge or non-standard equipment.

\(^1\)E Draeger et al, “A Dose of Reality: How 20 years of incomplete physics and dosimetry reporting in radiobiology studies may have contributed to the reproducibility crisis” Int J Radiat Oncol Biol Phys 106(2),243-252, 2020.


Implementation and Validation of EPID as a kV Dosimeter

• Compared to other detectors like ion chambers and film, EPIDs are **standard** to the SARRP and the **analysis** could be largely **automated**

• Potential for QA framework not reliant on **specialized physics knowledge** or access to **specialized equipment**

• Based on the publications of Akbar Anvari
SARRP System and built-in EPID

Left & Right- Unpublished Data. Middle - Figure 1, A Anvari et al, “Kilovoltage transit and exit dosimetry for a small animal image-guided radiotherapy system using built-in EPID” Med Phys 45(10), 4562-45610, 2018.
Promise of EPID lies in its **Potential Automatization**

- EPID image acquisition already integrated in console
- Tests would have to be performed sequentially through pre-set plans with integrated image acquisition
- Analysis can be automated through scripts, automatic edge detection
- Would not require specialized end user knowledge or equipment
- Similar to EPID clinical QA frameworks (e.g. Varian MPC)
Characterization of the EPID at kV energies - Reproducibility

Short-term Reproducibility

Long-term Reproducibility

Gantry Angle Reproducibility

Beam Current /Beam Energy

Figures 3,5,6,8; A Anvari et al, “Development and implementation of EPID-based quality assurance tests for the small animal radiation research platform (SARRP)” Med Phys 45(7), 3246-3257, 2018.
Possible EPID Dosimetric Tests

Daily output test

Output factor tests

Daily Output Test (projected to iso)

Half-value Layer (HVL) Constancy

Figures 5,7,10,11; A Anvari et al, "Development and implementation of EPID-based quality assurance tests for the small animal radiation research platform (SARRP)" Med Phys 45(7), 3246-3257, 2018.
Using the EPID for Profile Measurements

- EPID Can be used to measure radiation profile constancy ≤1.8%
  - Can detect shifts in focal spot position

Field size, position, symmetry

Place BB at centre of 1 mm field, acquire EPID image for all collimators

Figure 3, A Anvari et al, “A comprehensive geometric quality assurance framework for preclinical microirradiators” Med Phys 46(4), 1840-1851, 2019.
Radiation field sizes generally correct size

- 1 mm cone measures 1.55 x 1.25 mm
- Caused by large geometric penumbra due to broad (3 mm) spot size
- All others <1% error in size

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Radiation fields generally misaligned

- Symmetry (total Field size X vs Y) within 1% for all fields except 1 mm and 5×5 mm² (3%)
- Position (Field size vs BB) error is 10%/16% of field size on average in X/Y direction
- Larger collimators had lower positional errors

Stage motion accuracy - translation

- Position thin object (needle) on couch, take EPID image, translate couch in 5 mm increments, measure distance
- Repeat for other directions (Y, Z)

- Accuracy of 0.015, 0.010, and 0.000 mm in the X, Y, Z directions respectively

Figure 8, A Anvari et al, “A comprehensive geometric quality assurance framework for preclinical microirradiator” Med Phys 46(4), 1840-1851, 2019.
Stage motion accuracy rotation

- Similar: Position thin object (needle) on couch, take EPID image, rotate couch in 45° increments, measure angle

- Negligible error

Figure 11, A Anvari et al, “A comprehensive geometric quality assurance framework for preclinical microirradiators” Med Phys 46(4), 1840-1851, 2019.
Place object (BB) at isocenter, rotate gantry/robotic stage in 45° increments, measure motion on EPID

Error \(\sim \pm 0.5\) mm for Gantry and stage rotation alike.

End-to-end testing

- Place object (BB) at isocenter per CBCT, shift robotic stage, deliver dose, compare to TPS prediction

- Displacement error of $0.24 \pm 0.10$, $0.12 \pm 0.62$, and $0.12 \pm 0.42$ mm in X, Y, Z

Transmission Exit Dosimetry

- Characterized Epid can be used to measure exit dose through phantom or animal

- Validated with EBT3 Gafchromic film and ionization chamber

Figure 2, A Anvari et al, “Kilovoltage transit and exit dosimetry for a small animal image-guided radiotherapy system using built-in EPID” Med Phys 45(10), 4562-45610, 2018.
Transmission Exit Dosimetry - Results

- Agreement within 5% in profiles

Figures 4 (left) and 11+12 (right), A Anvari et al, "Kilovoltage transit and exit dosimetry for a small animal image-guided radiotherapy system using built-in EPID" Med Phys 45(10), 4562-45610, 2018.
Animal transit/exit dosimetry applied to verify accuracy of TPS

Conclusion

- Radiation biology in need of simple detectors
  - Lack of physics training and equipment is largest obstacle to overcome

- EPID detector can be used to achieve most standard QA tests
  - Reproducible, high-resolution, linear detector
  - Instant readout - no post-processing or specialized equipment required
  - Dosimetric tests: Output, HVL constancy, Profile constancy
  - Geometric tests: Field size and positioning, robotic stage translation and rotation accuracy
  - Winston-lutz test, transit dosimetry

- Promise of EPID lies in its **Potential Automatization** using a minimum of specialized phantoms and equipment
Thank you!