UNIVERSITY of MARYLAND
SCHOOL OF MEDICINE

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

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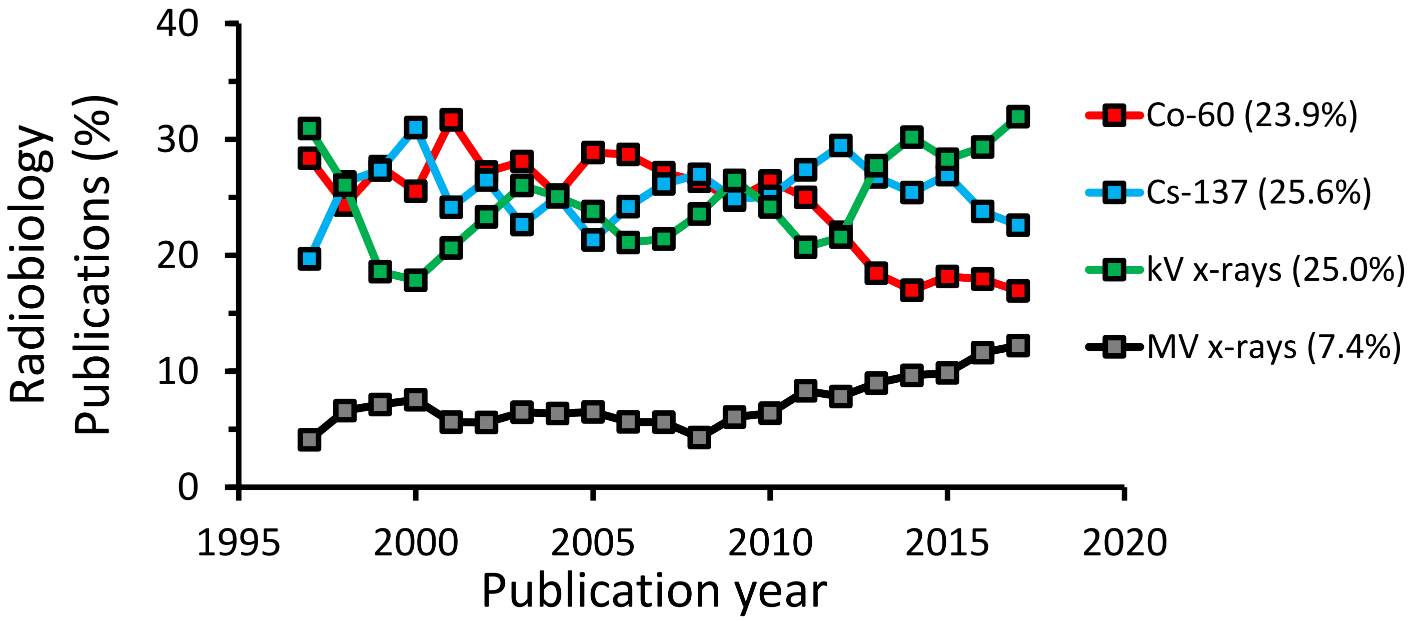
Background – kV irradiators on the rise in rad biology research

- ~**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 <u>expected to rise</u>



Unpublished; data from **E Draeger** et al, *"A Dose of Reality: How 20 years of incomplete physics and dosimetry reporting in radiobiology studies may have contributed to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.

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

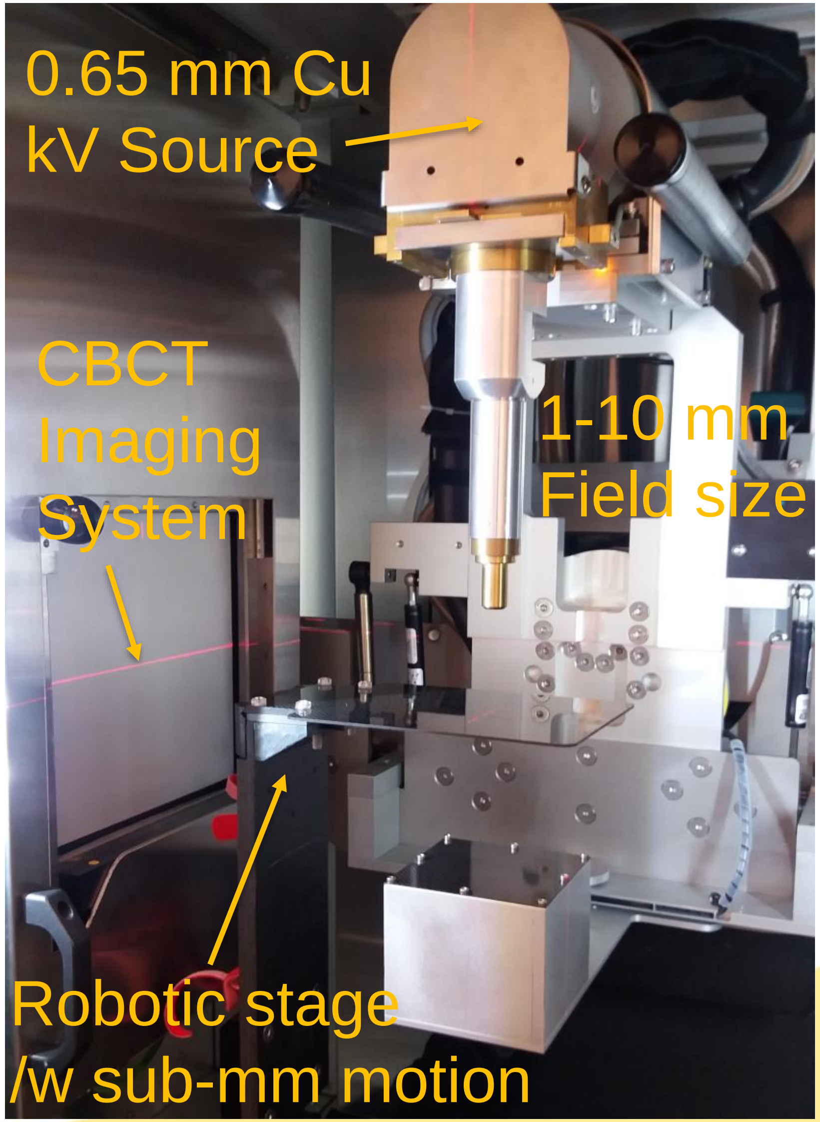
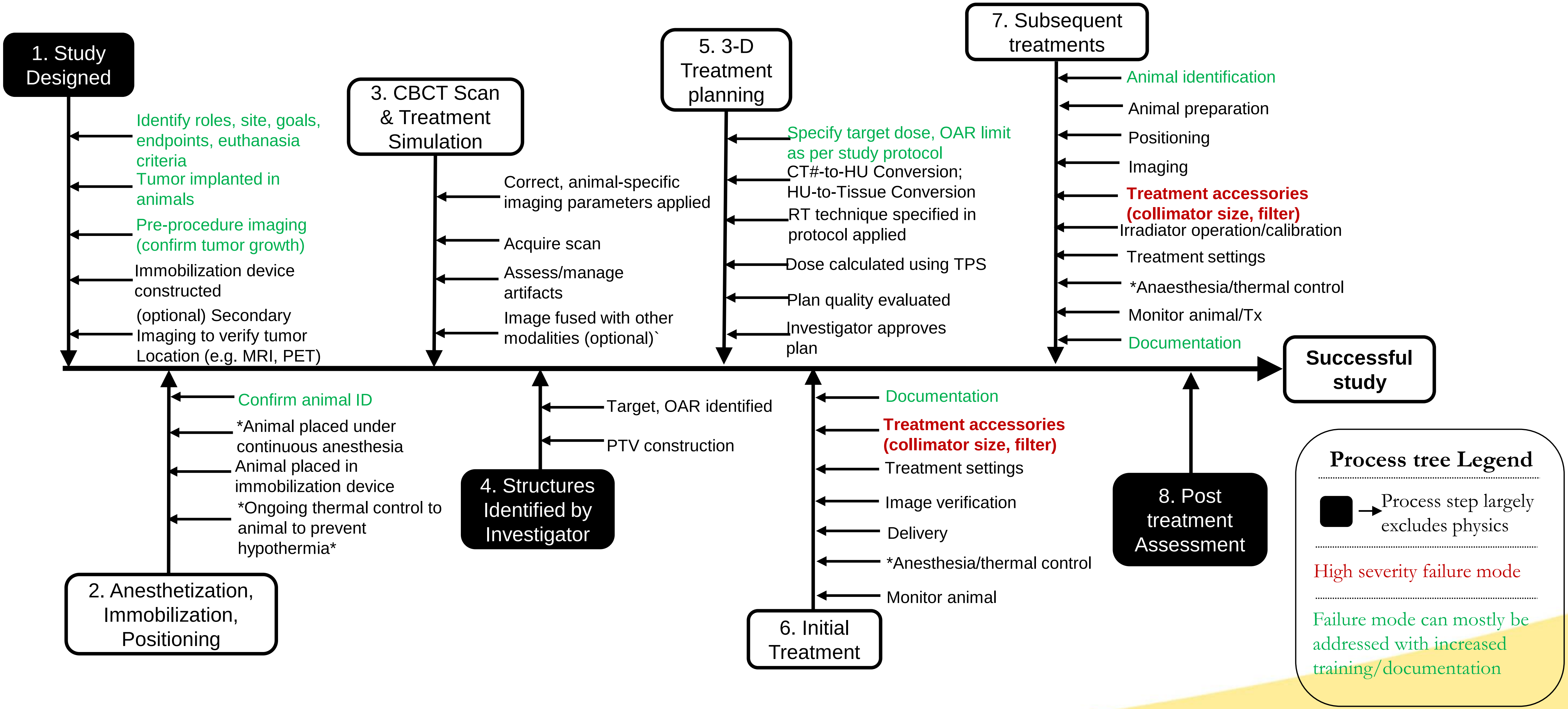


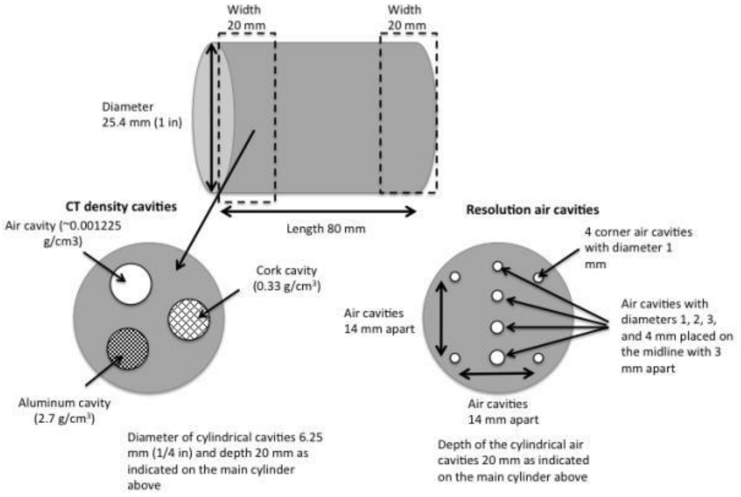
Image-guided small animal irradiation process tree



Y Poirier et al, *"A Failure Modes and Effects Analysis Quality Management Framework for Image-Guided Small Animal Irradiators: A change in paradigm for radiation biology"* Med Phys **47**(4), 2013-2022, 2020.

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



Performance	Tests	Tolerance
Output consistency	Measure dose-rate the at isocenter using an appropriately calibrated ion chamber	± 1%
Image resolution consistency / Object representation	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.	± 0.2 mm for resolution ± 0.5 mm for distances ± 1.0 mm for object size representation
Accuracy of image-guided target localization	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 mm^2 collimator at gantry angles 0° and 90°.	± 0.5 mm
Dose calculation consistency	Calculate a four-field 10 × 10 mm^2 treatment plan for 10 Gy on a reproducible isocenter in the imaging phantom and record the treatment times.	± 2 s (± 3%) per treatment field

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.

Current proposals for QA methodologies for IGSAI - Verhaegen

- Description of commissioning tests by *Verhaegen* et al.
- Most tests require specialized equipment and software

Supplementary materials

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

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

Table S3: Recommendations when commissioning and using small animal TPS

Recommendation	Comments
Determine comprehensive benchmarking data set (relative dosimetry)	Use large reference field (e.g. 4x4 cm²) Compare measured and calculated depth dose and lateral profiles at several depths in a suitable phantom, e.g. stack of solid water slabs Compare measured and calculated output factors for all fixed-field collimators (normalized to reference field) Compare measured and calculated output factors for a sub-set of fields for a variable field collimator (normalized to reference field),
Establish a link to absolute dosimetry (calibration of irradiator)	Convert absolute dose units of TPS to absolute dose in Gy/mAs. This requires a conversion factor per kV 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 XRAD device, a single conversion factor is used for each x-ray tube energy, and additionally correction factors are employed for the smallest collimators (≤5mm).
Determine focal spot size of irradiator	Dose calculations are sensitive to focal spot size and position, in particular for small fields Focal spot may also drift spatially over time, which may alter dosimetry
Coordinate systems	Check coordinate systems of images, irradiator and TPS
Spatial accuracy	Check spatial accuracy with a test object
Predefine material types	Make sure all needed tissue types and other materials are available in the TPS, this may include the treatment table
Establish conversion of CT images into electron or mass density	Obtain a calibration curve, HU to mass/electron density from a CT image of a small heterogeneous phantom Need to assign various HU intervals to various materials Be aware of imaging artifacts (e.g. beam hardening, streaks, ...) which may influence tissue assignment and dose calculations
Set-up dose reporting system	Dose-to-water-in-medium / dose-to-medium-in-medium, the latter is current standard but both should be available Dose-to-water-in-water is not recommended for kV x-rays
Validate image transfer and image registration functionality	TPS may handle imaging modalities other than CT, e.g. for targeting (PET, BLI, ...). Proper registration between the images is crucial.
Minimize motion effects	Motion may severely degrade the dose calculation in a static CT phantom. Currently no animal TPS can handle this.
Transfer of treatment plan	Check transfer of treatment plan to irradiator by verifying dose calculations under different conditions (single beam, arc, variable collimators, variable couch angles)
Establish periodic quality assurance	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

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.
[2]**M Desrosiers** et al. "*The Importance of Dosimetry Standardization in Radiobiology*", J Res Natl Inst Stand Technol (118): 403-418 (2013).
[3]**K Pedersen** et al, "*Radiation Biology Dose Verification Survey*", Radiation Research 185, 163-168 (2016).
[4]**T Seed** et al. "*An interlaboratory comparison of dosimetry for a multi-institutional radiobiological research project: Observations, problems, solutions and lessons learned*", Int J Radiat Biol 92;59-70 (2016).
[5]**J Zoetlief** et al, "Protocol for x-ray dosimetry in radiobiology", Int J Radiat Biol 77; 817-935(2001).

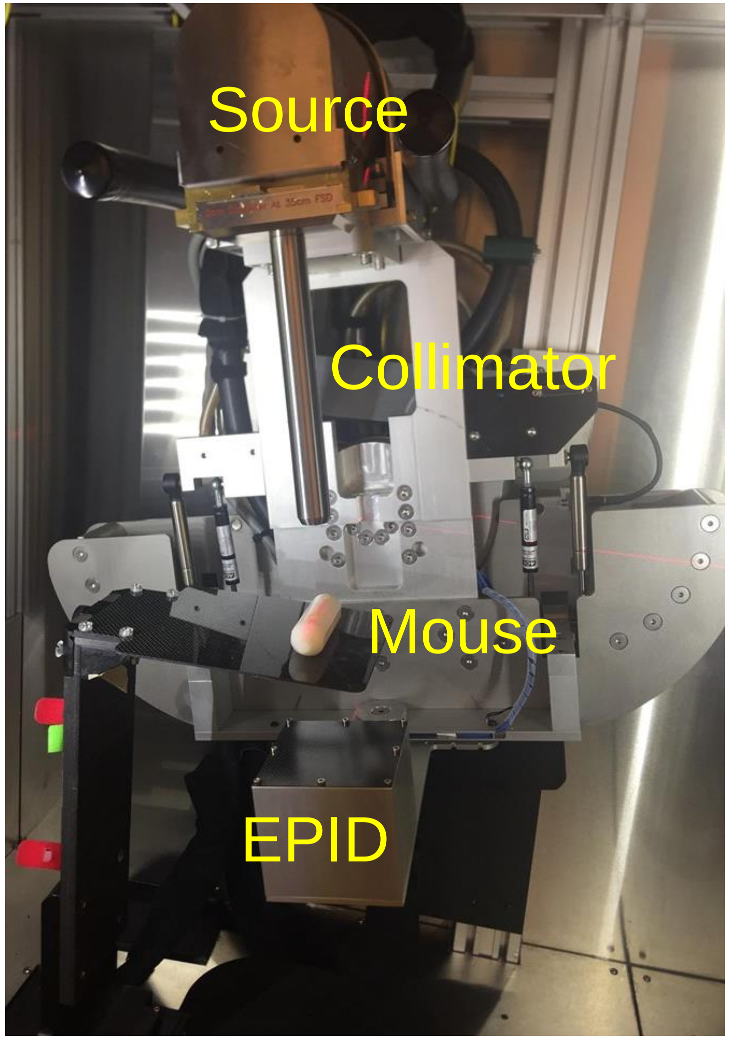
Implementation and Validation of EPID as a kV Dosimeter

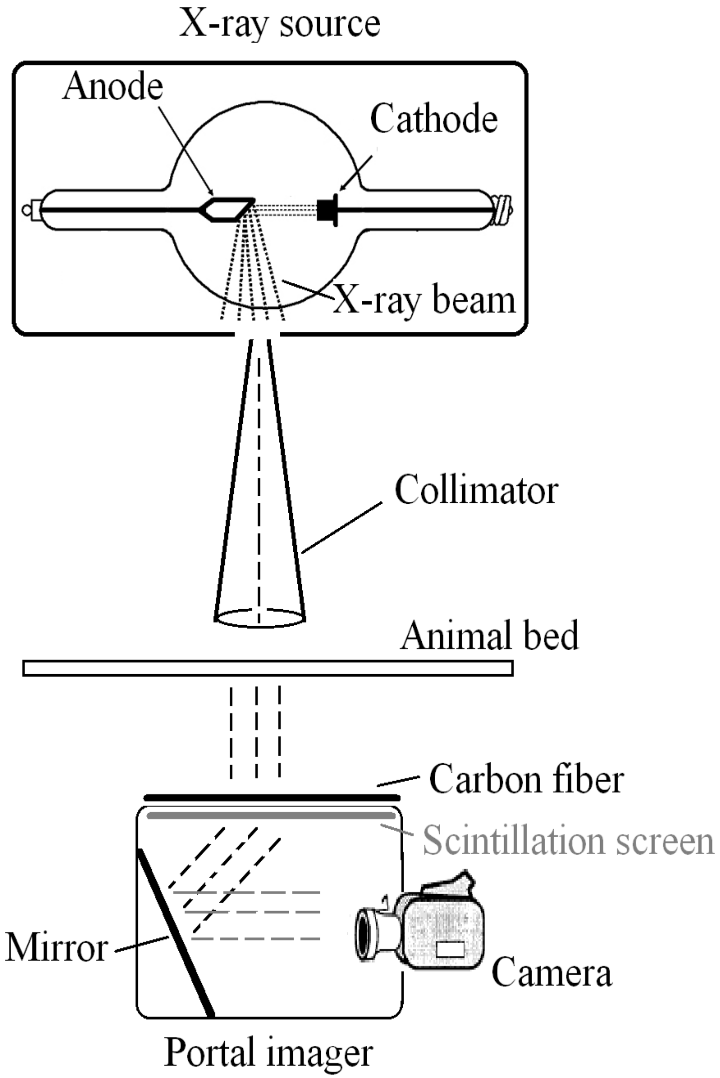
- Compared to other detectors like ion chambers and film, EPIDs are **standard** to the SARRP and the **analysis** could be largely **automated**

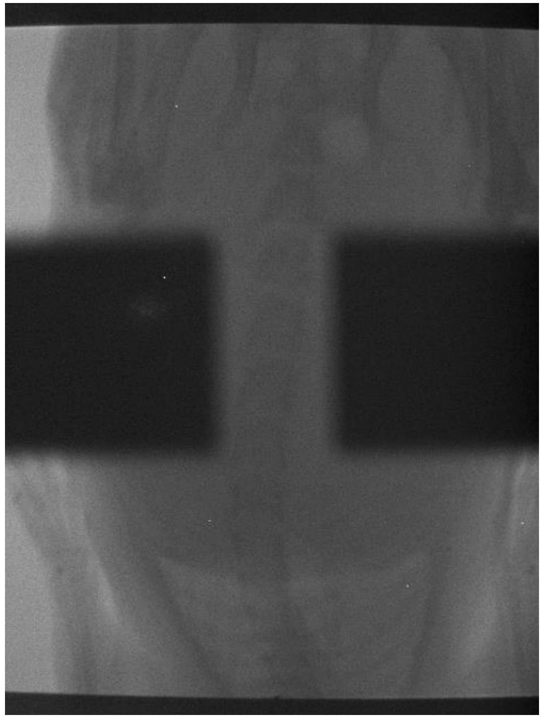
- Potential for QA framework not reliant on **specialized physics knowledge** or access to **specialized equipment**

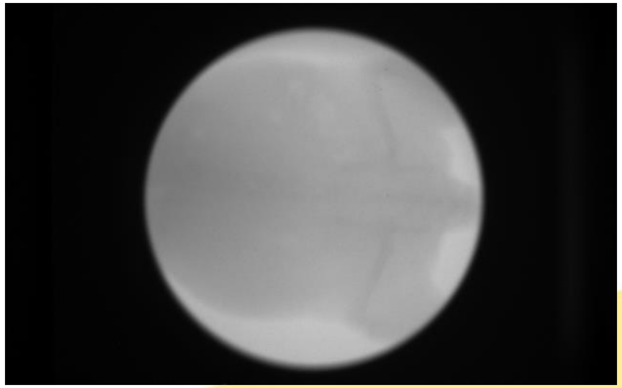
- Based on the publications of Akbar Anvari
  - **A Anvari**, Y Poirier, A Sawant, *Development and implementation of EPID-based quality assurance tests for the small animal radiation research platform (SARRP)*, Med Phys **45**(7), 3246–3257 (2018).
  - **A Anvari**, Y Poirier, A Sawant, *Kilovoltage transit and exit dosimetry for a small animal image-guided radiotherapy system using built-in EPID*, Med Phys **45**(10), 4642–4651 (2018).
  - **A Anvari**, Y Poirier, A Sawant, *A comprehensive geometric quality assurance framework for preclinical microirradiators*, Med Phys **46**(14): 1840–1851 (2019).
  - **A Anvari**, A Modiri, R Pandita, J Mahmood, A Sawant, *On-line dose delivery verification in small animal image-guided radio therapy*, Med Phys **47**(4) 1871-1879 (2020)

SARRP System and built-in EPID





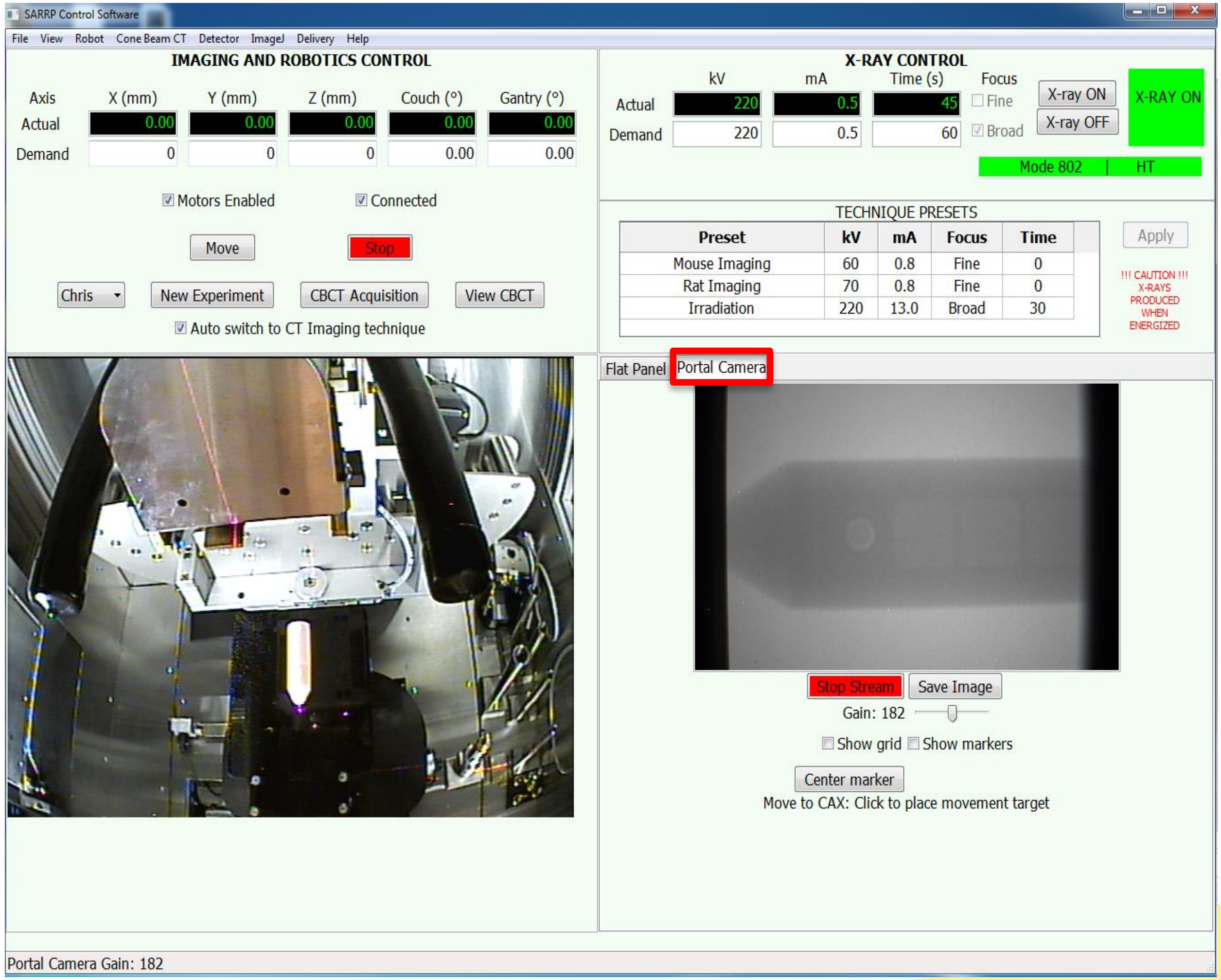




Left & Right- Unpublished Data. Middle - Figure 1, **A Anvari** et al, *"Kilovoltage transit and exit dosimetry for a small animal image-guided radiotherapy system using built-in EPID"* Med Phys **45**(10), 4562-45610, 2018.

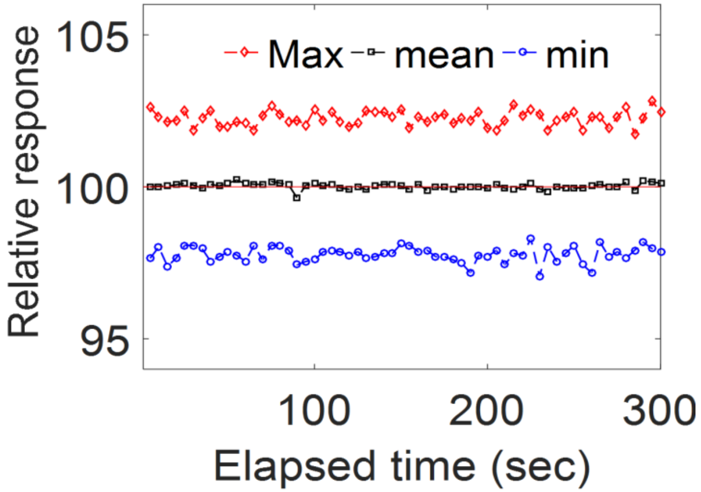
Promise of EPID lies in its **Potential Automatization**

- 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)

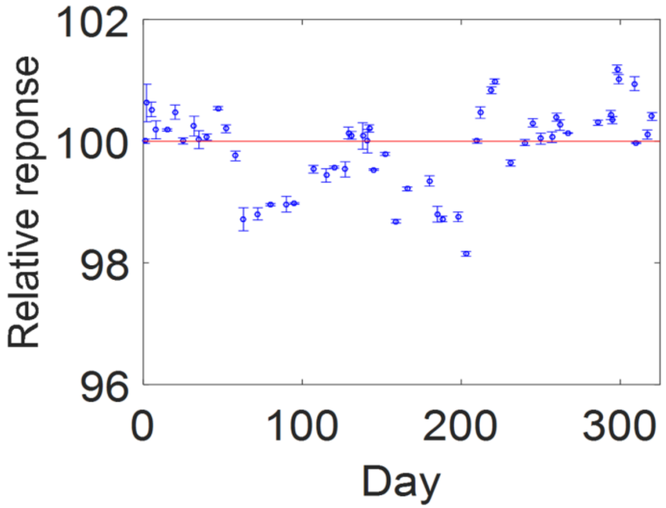


Characterization of the EPID at kV energies - Reproducibility

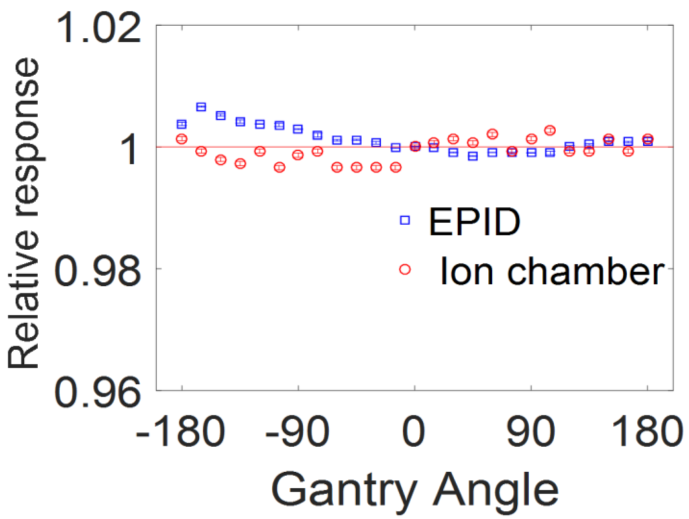
Short-term Reproducibility



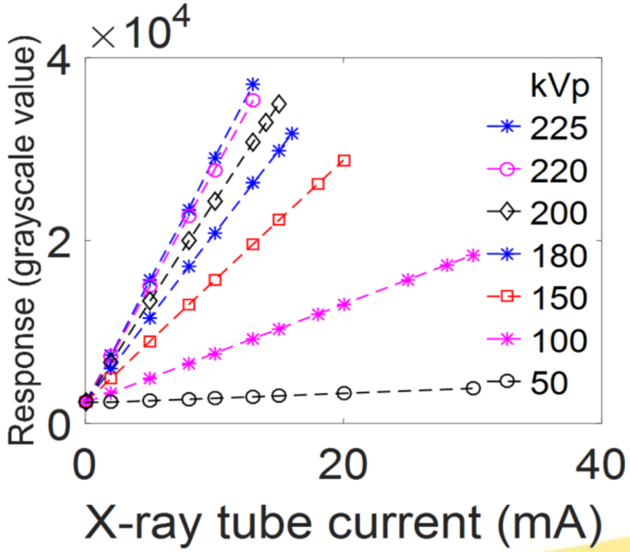
Long-term Reproducibility



Gantry Angle Reproducibility



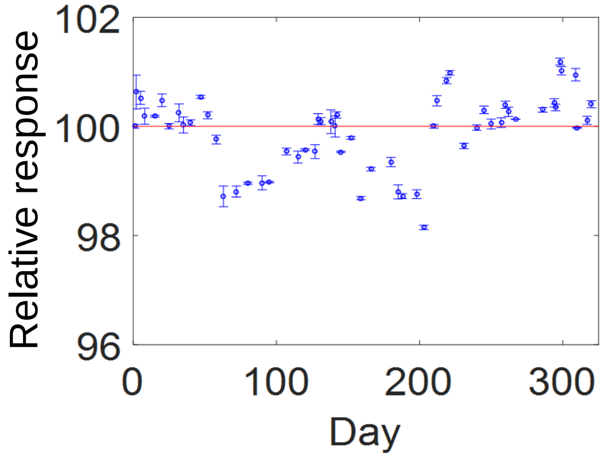
Beam Current /Beam Energy

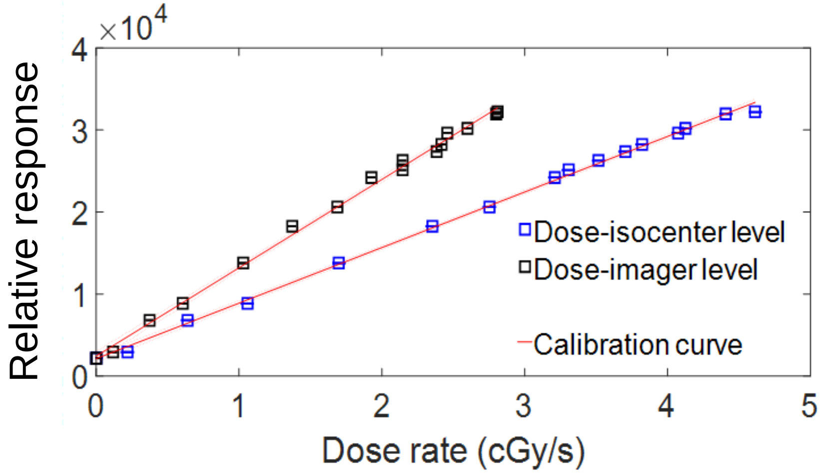


Figures 3,5,6,8; **A Anvari** et al, “*Development and implementation of EPID-based quality assurance tests for the small animal radiation research platform (SARRP)*" Med Phys **45**(7), 3246-3257, 2018.

Possible EPID Dosimetric Tests

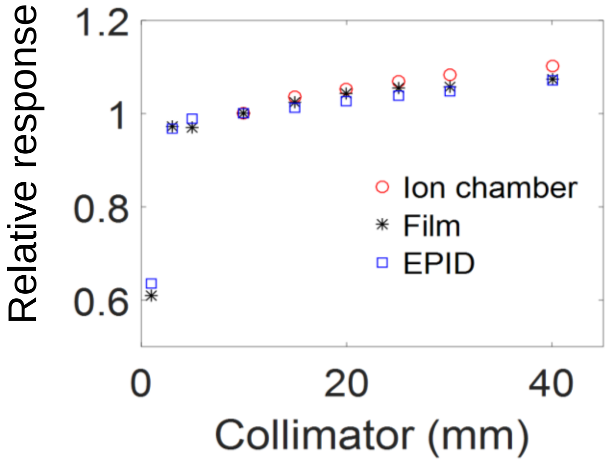
Daily output test

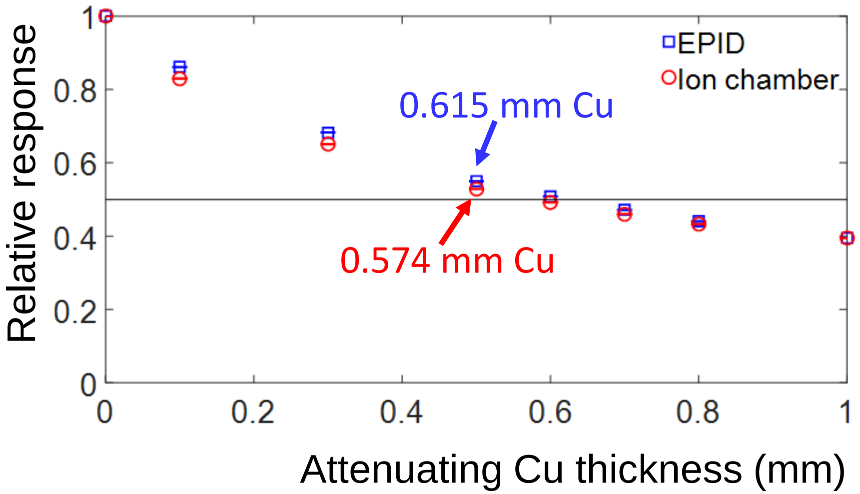




Daily Output Test (projected to iso)

Output factor tests



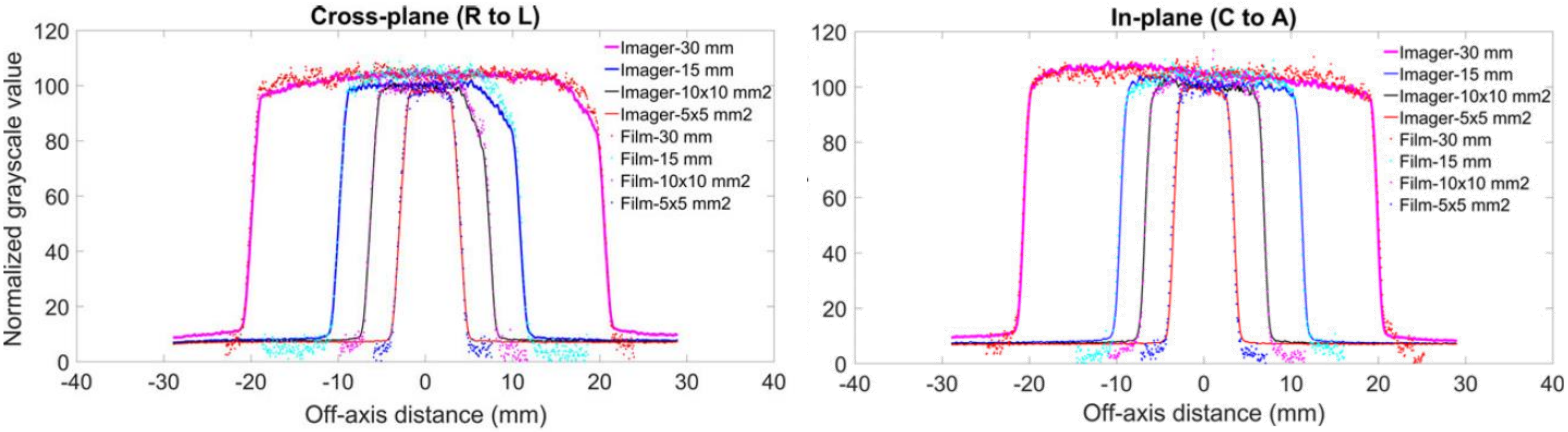


Half-value Layer (HVL) Constancy

7.1% difference,
0.1% 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.

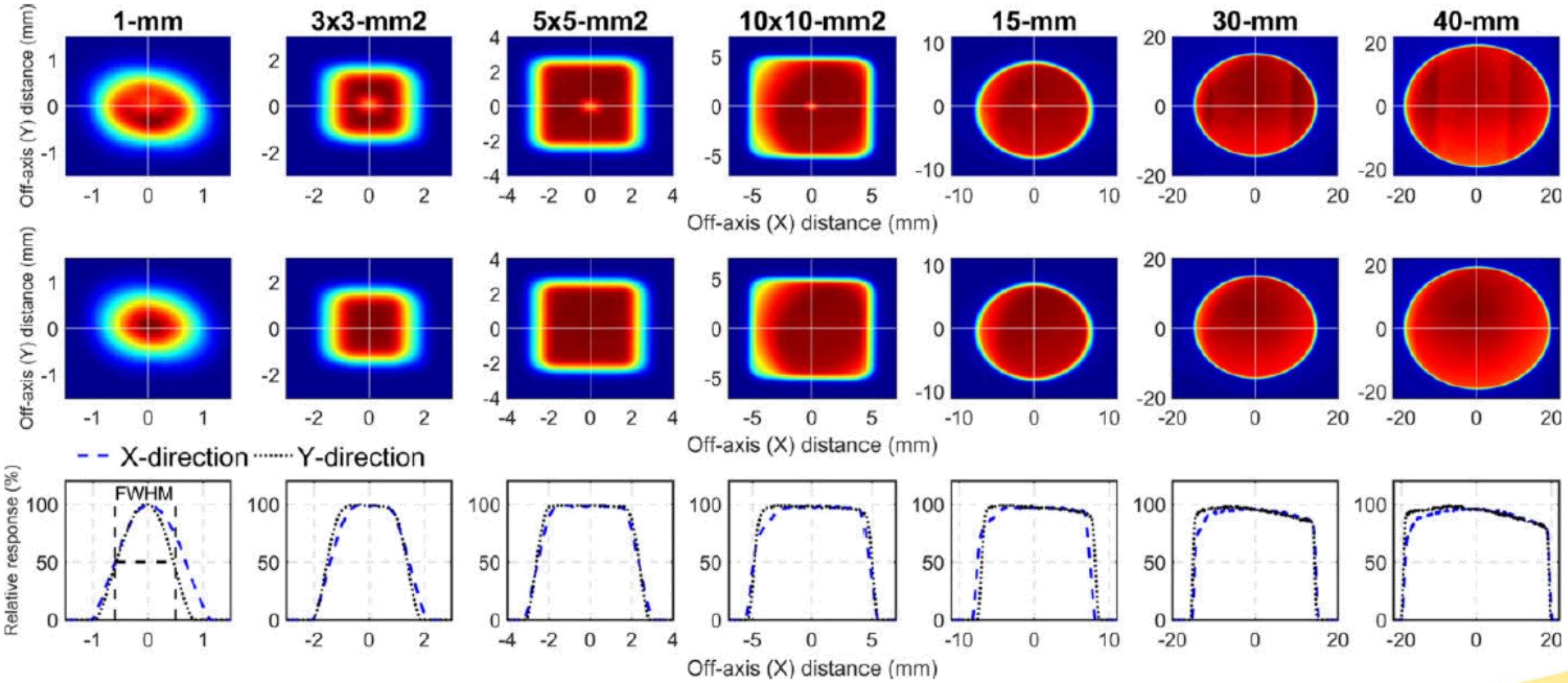
Using the EPID for Profile Measurements



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

Figures 14, **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.

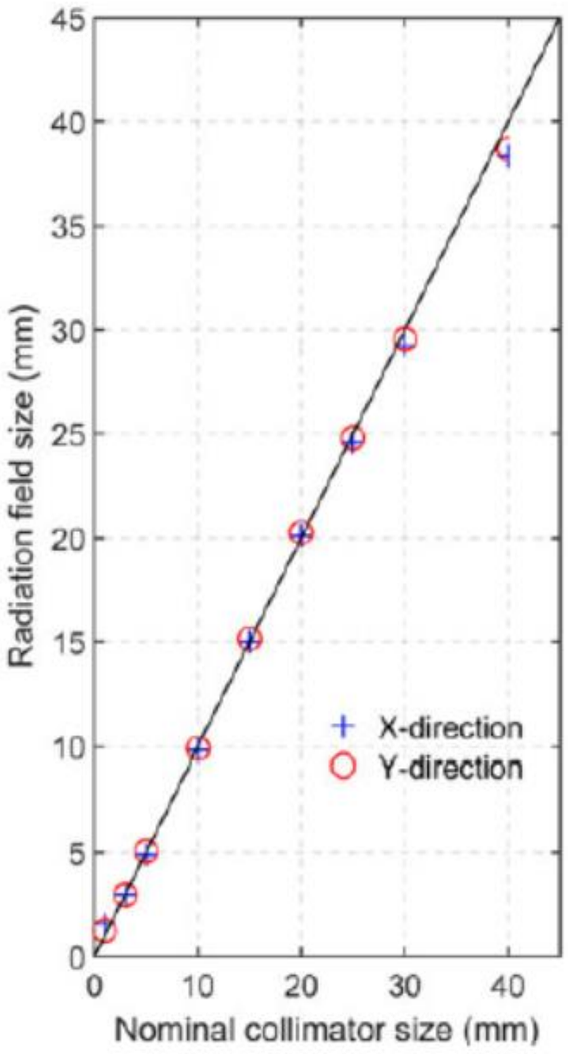
Field size, position, symmetry

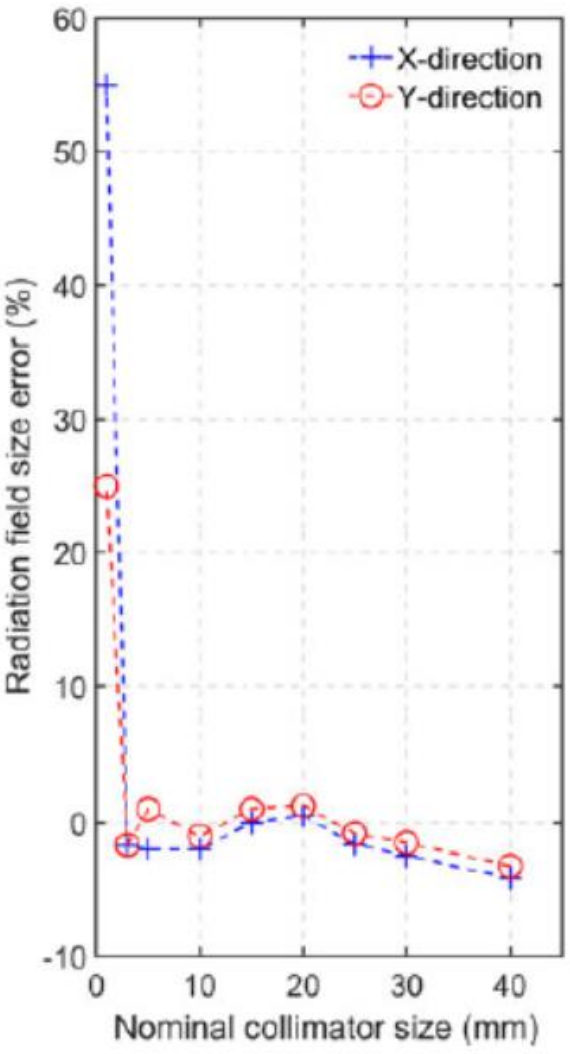


Place BB at centre of 1 mm field, acquire EPID image for all collimators

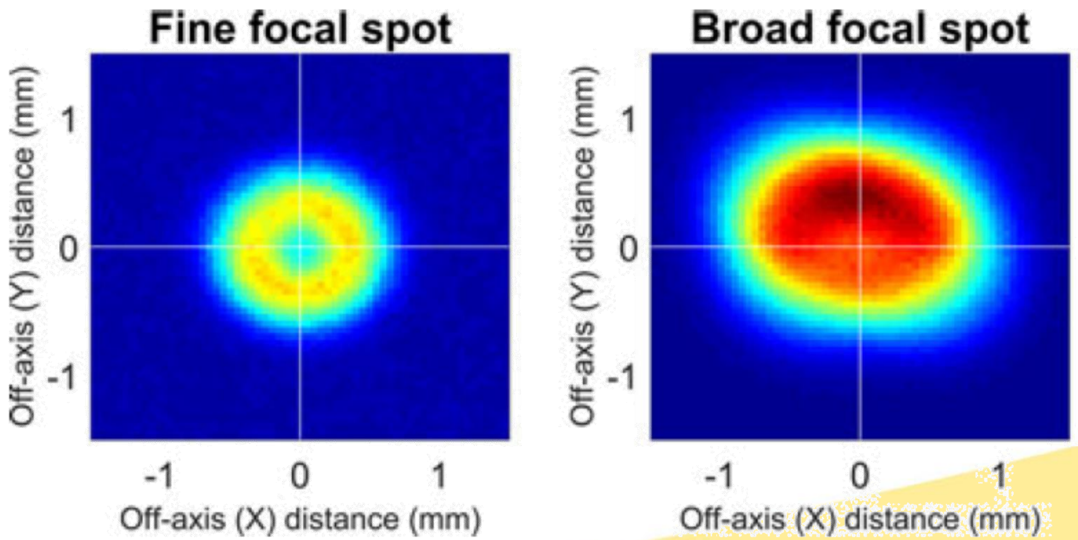
Figure 3, **A Anvari** et al, *"A comprehensive geometric quality assurance framework for preclinical microirradiators"* Med Phys **46**(4), 1840-1851, 2019.

Field size



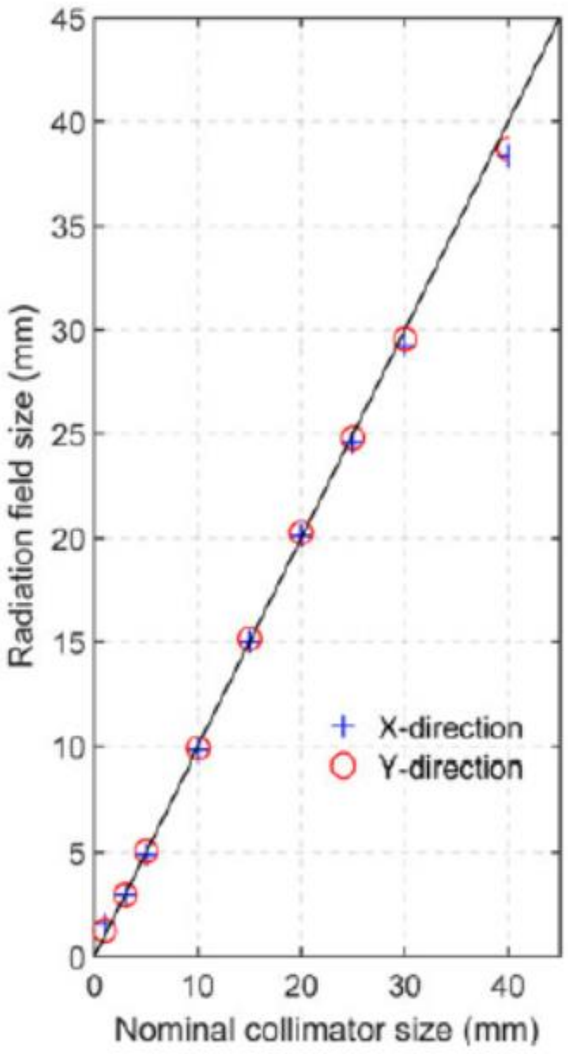


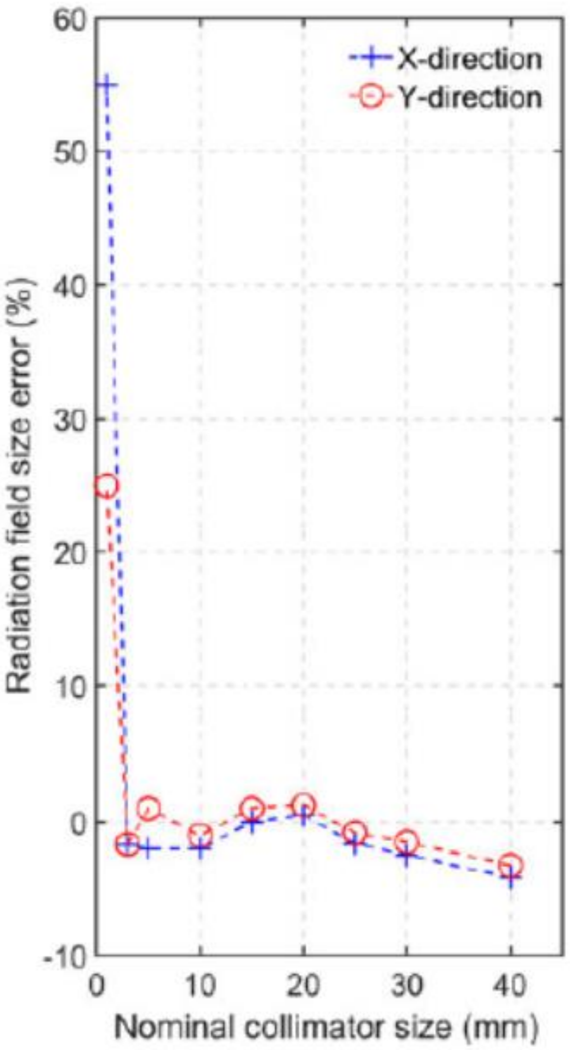
- Radiation field sizes generally correct size
  - 1 mm cone measures 1.55 x 1.25 mm
  - Caused by large geometric penumbra due to broad (3 mm) spot size
  - All others <1% error in size



Figures 4(a+b) + 2, **A Anvari** et al, *"A comprehensive geometric quality assurance framework for preclinical microirradiators"* Med Phys **46**(4), 1840-1851, 2019.

Field size





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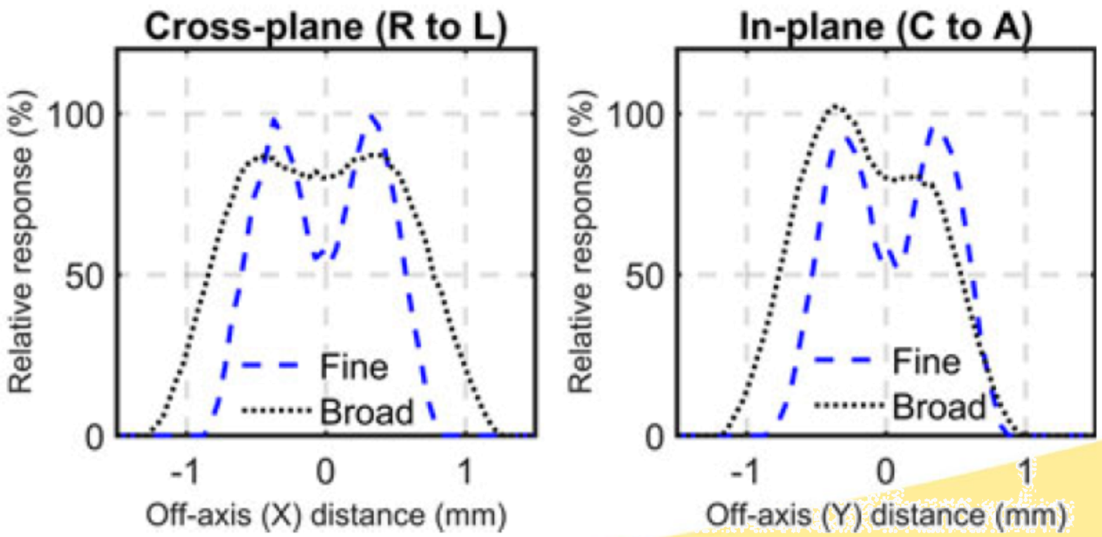
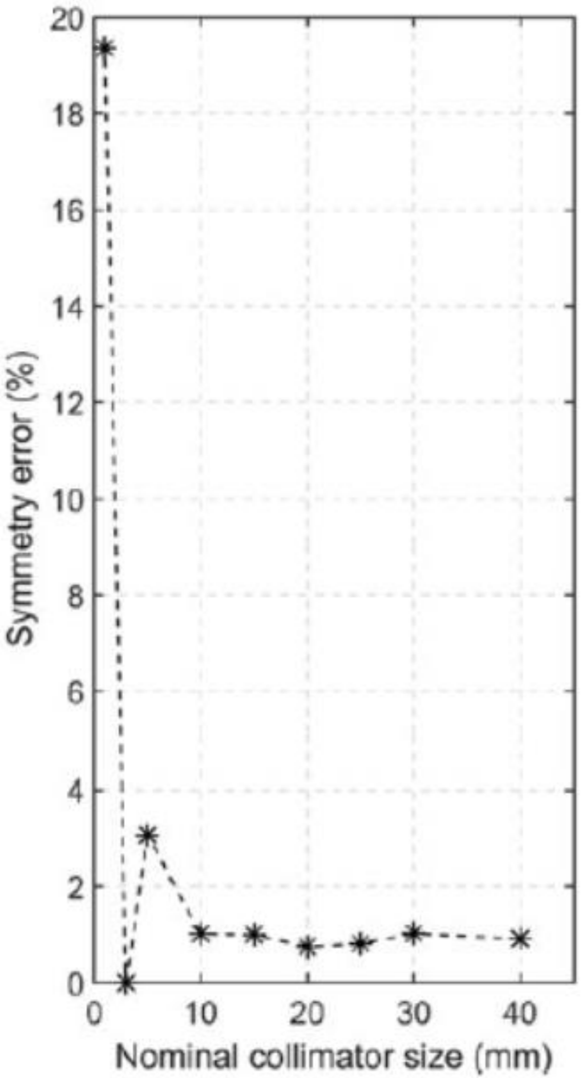
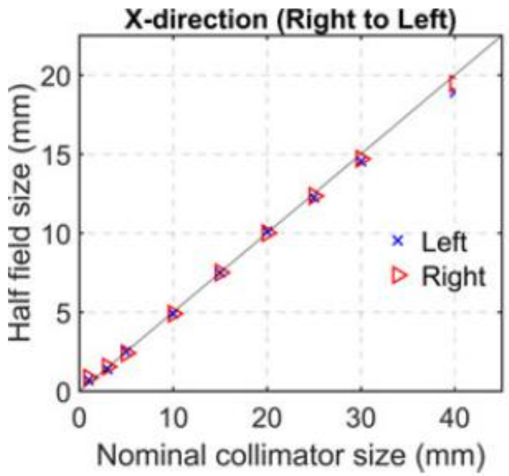
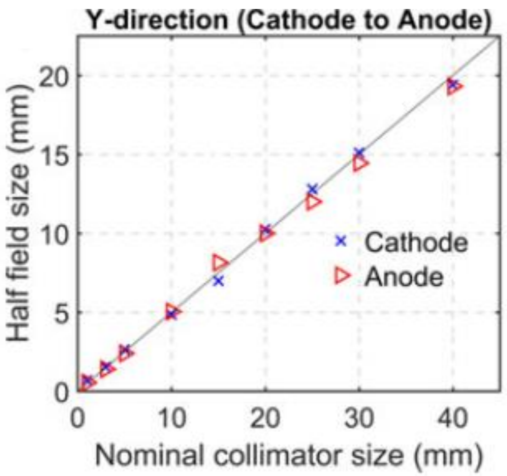


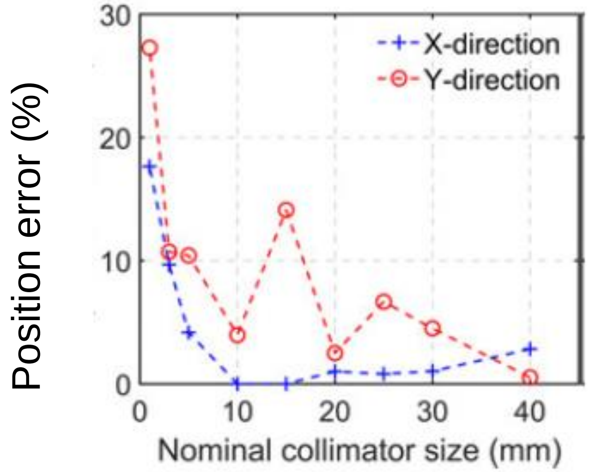
Figures 4(a+b) + 2, **A Anvari** et al, *"A comprehensive geometric quality assurance framework for preclinical microirradiators"* Med Phys **46**(4), 1840-1851, 2019.

Field position and symmetry









❑ Radiation fields generally misaligned

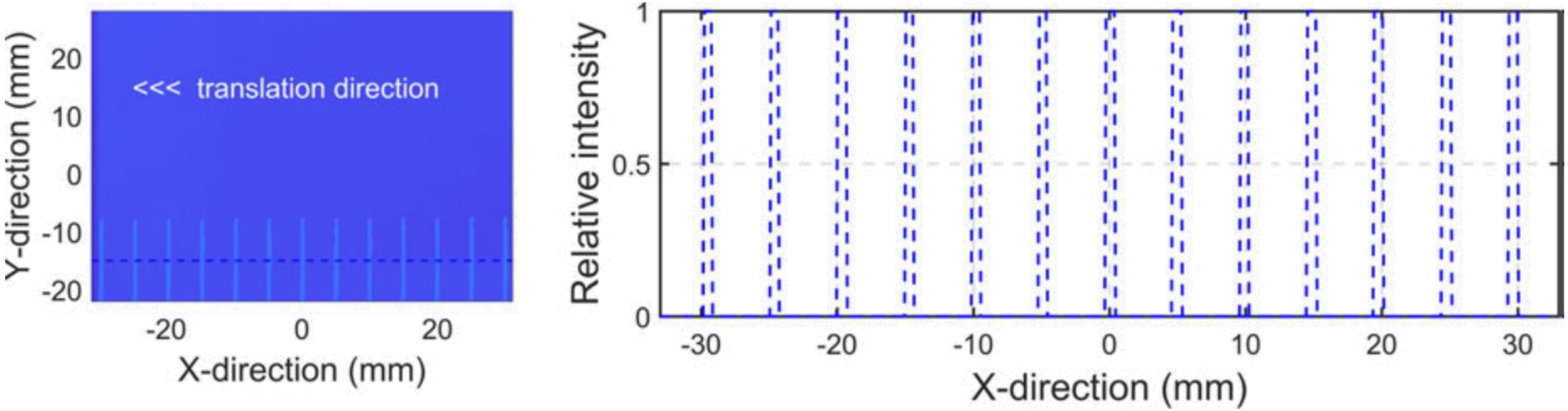
- Symmetry (total Field size X vs Y) within 1% for all fields except 1 mm and 5×5 mm^2 (3%)
- Position (Field size vs BB) error is 10%/16% of field size on average in X/Y direction
- Larger collimators had lower positional errors

Figures 4(c)+5, **A Anvari** et al, *“A comprehensive geometric quality assurance framework for preclinical microirradiators"* Med Phys **46**(4), 1840-1851, 2019.

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)

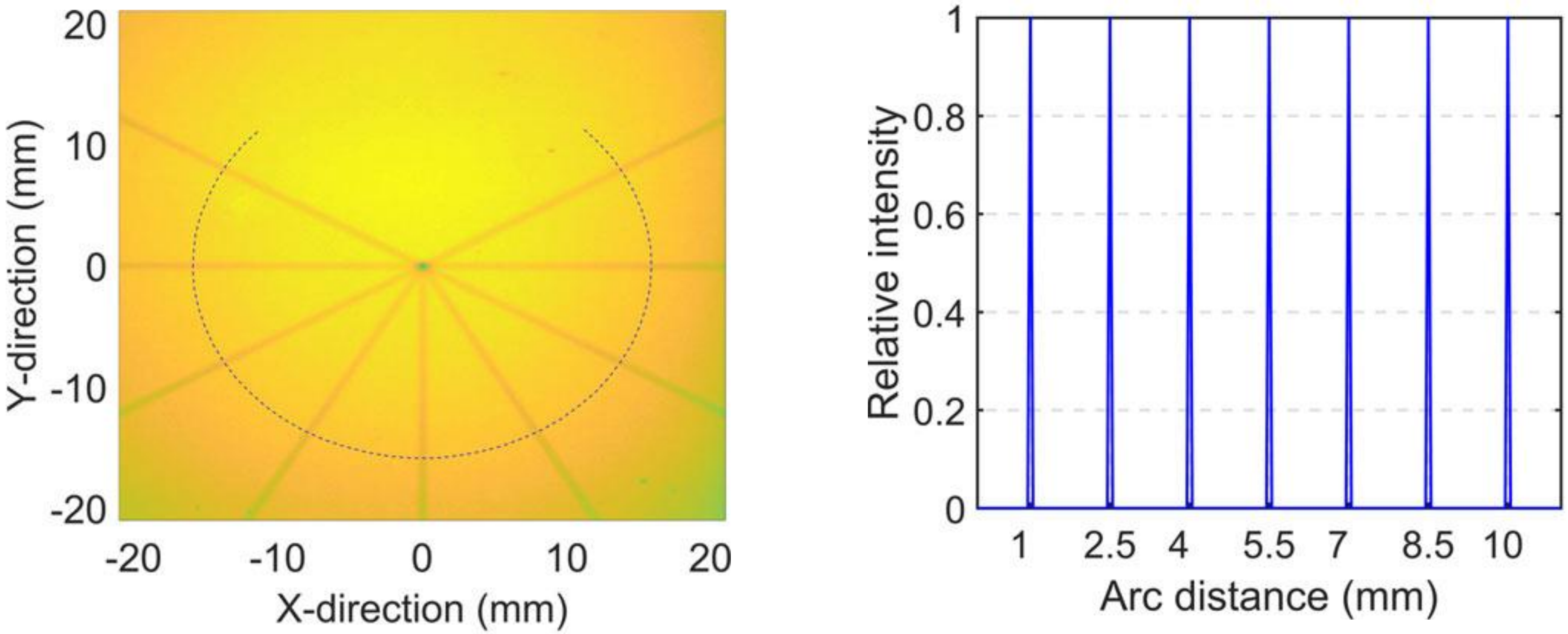


- Accuracy of 0.015, 0.010, and 0.000 mm in the X, Y, Z directions respectively

Figure 8, **A Anvari** et al, *"A comprehensive geometric quality assurance framework for preclinical microirradiators*" 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

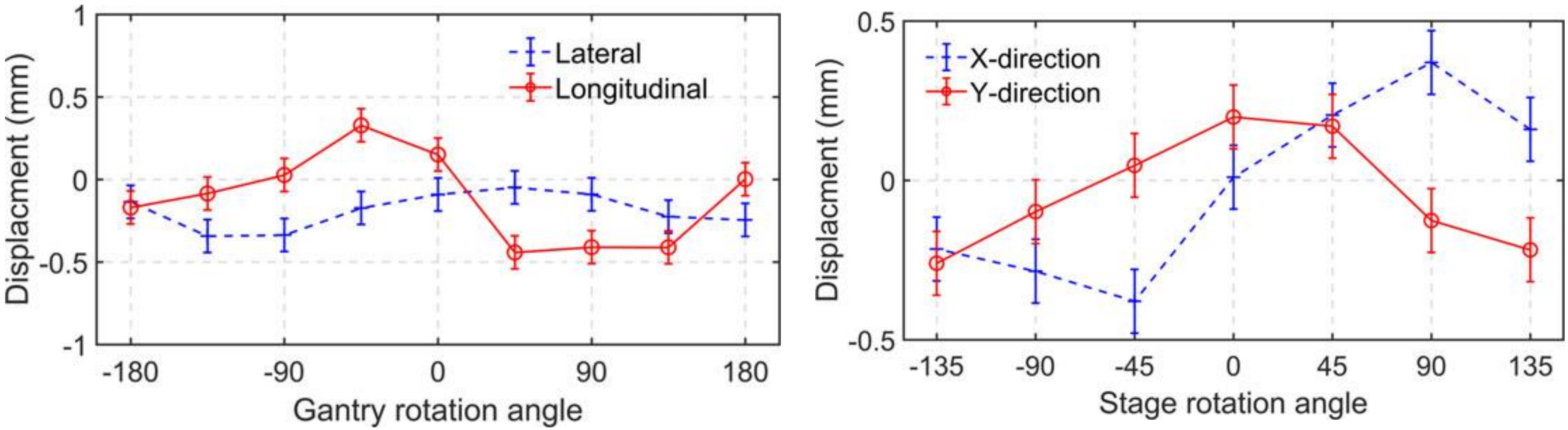


- Negligible error

Figure 11, **A Anvari** et al, *“A comprehensive geometric quality assurance framework for preclinical microirradiators*" Med Phys **46**(4), 1840-1851, 2019.

Winston-Lutz / Gantry-Collimator runout

- Place object (BB) at isocenter, rotate gantry/robotic stage in 45° increments, measure motion on EPID

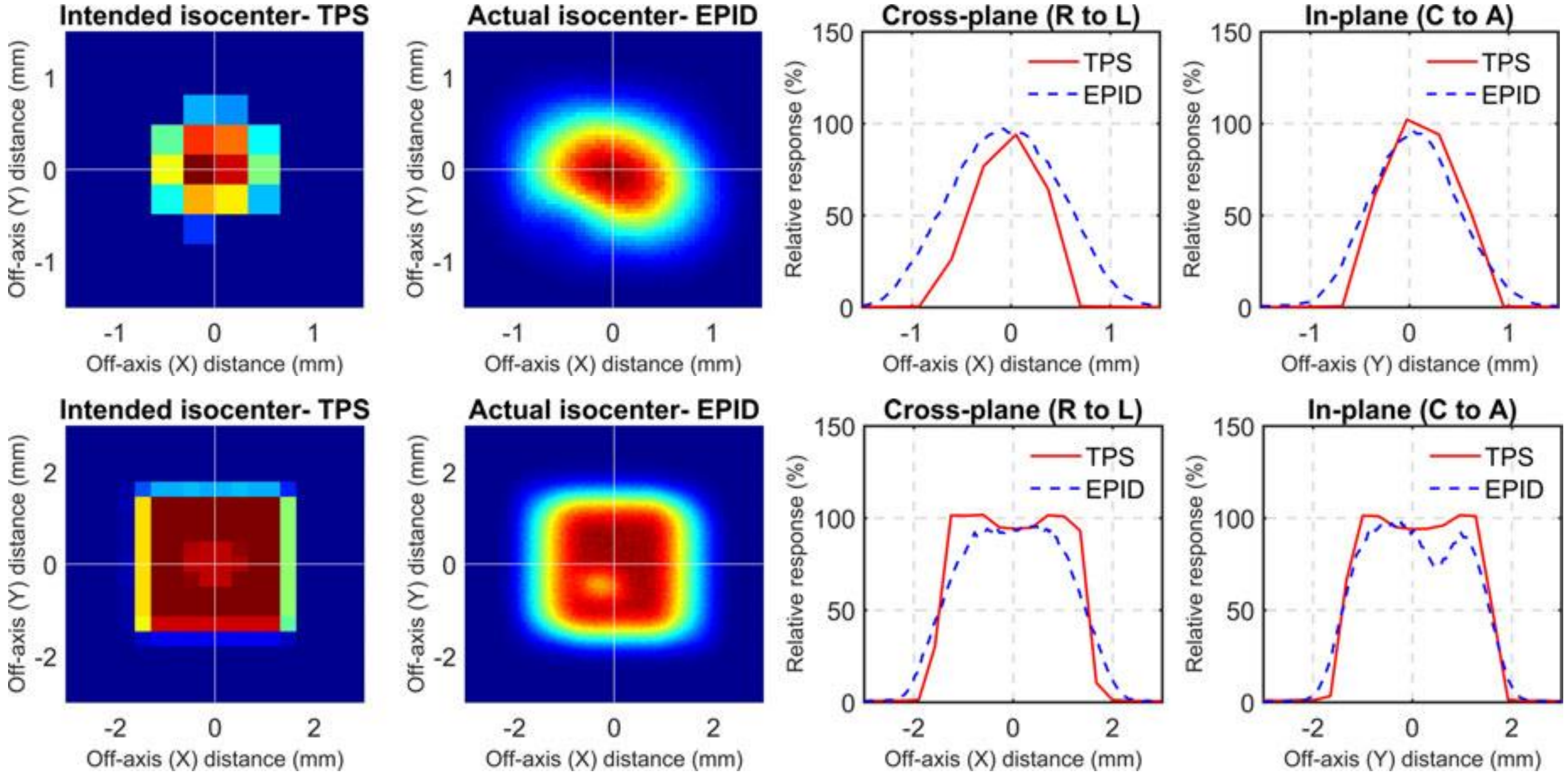


- Error ~±0.5 mm for Gantry and stage rotation alike.

Figures 7+14, **A Anvari** et al, *"A comprehensive geometric quality assurance framework for preclinical microirradiators*" Med Phys **46**(4), 1840-1851, 2019.

End-to-end testing

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

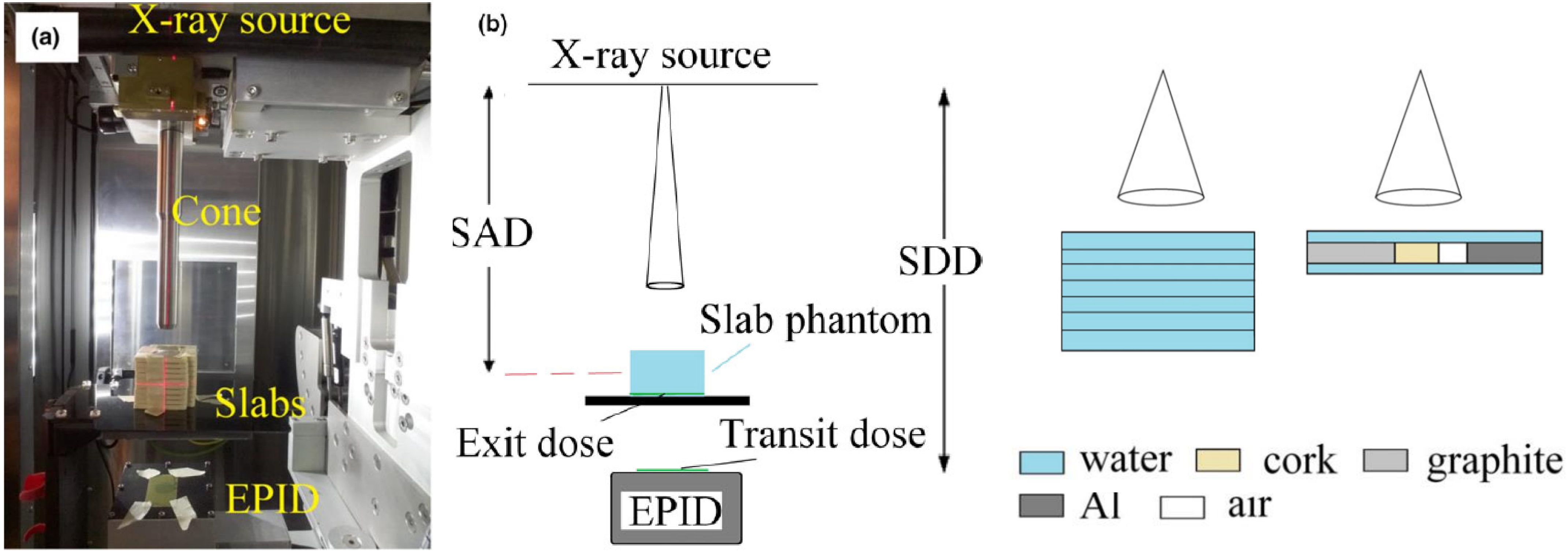


- Displacement error of 0.24 ± 0.10, 0.12 ± 0.62, and 0.12 ± 0.42 mm in X, Y, Z

Figures 13+14, **A Anvari** et al, *"A comprehensive geometric quality assurance framework for preclinical microirradiators*" Med Phys **46**(4), 1840-1851, 2019.

Transmission Exit Dosimetry

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

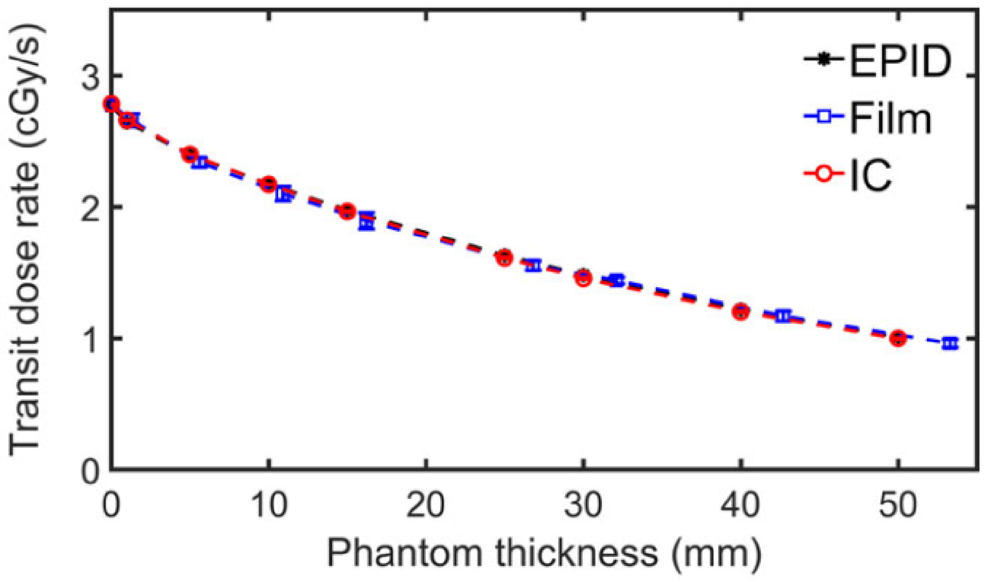


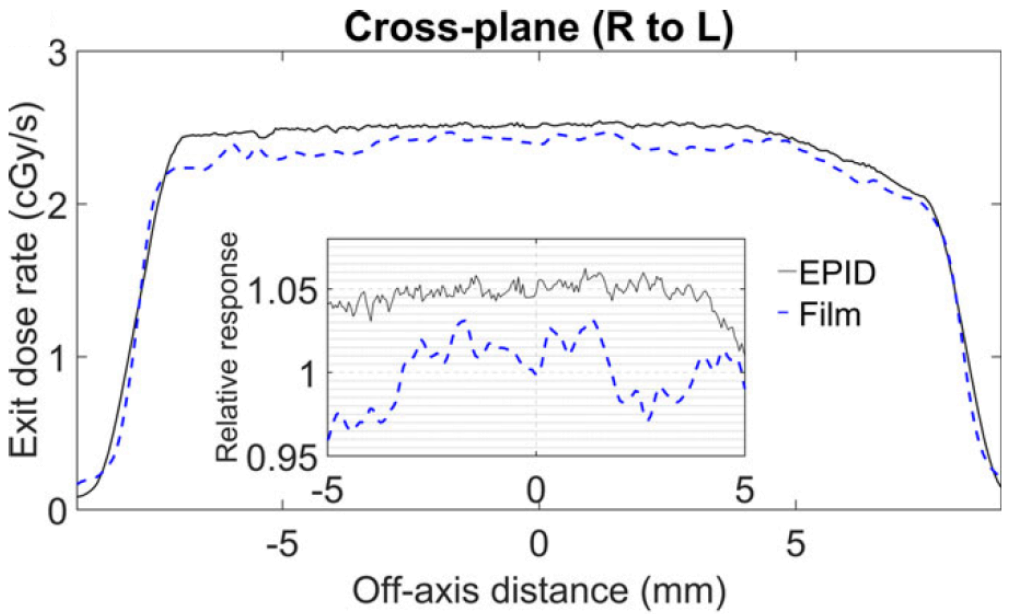
- Validated with EBT3 Gafchromic film and ionization chamber

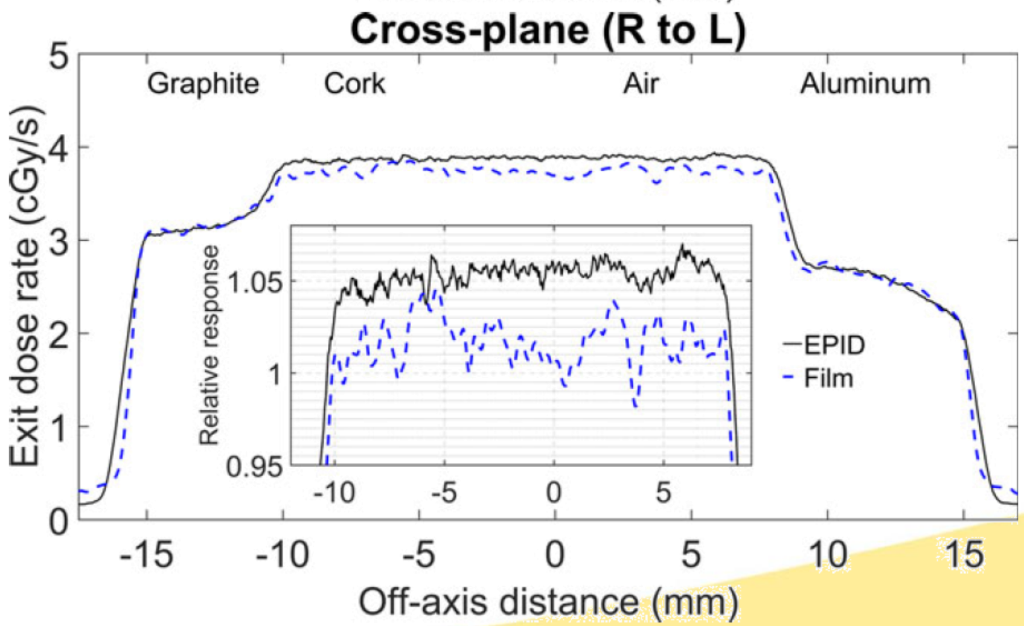
Figure 2, **A Anvari** et al, "*Kilovoltage transit and exit dosimetry for a small animal image-guided radiotherapy system using built-in EPID*" Med Phys **45**(10), 4562-45610, 2018.

Transmission Exit Dosimetry - Results

- Agreement within 5% in profiles

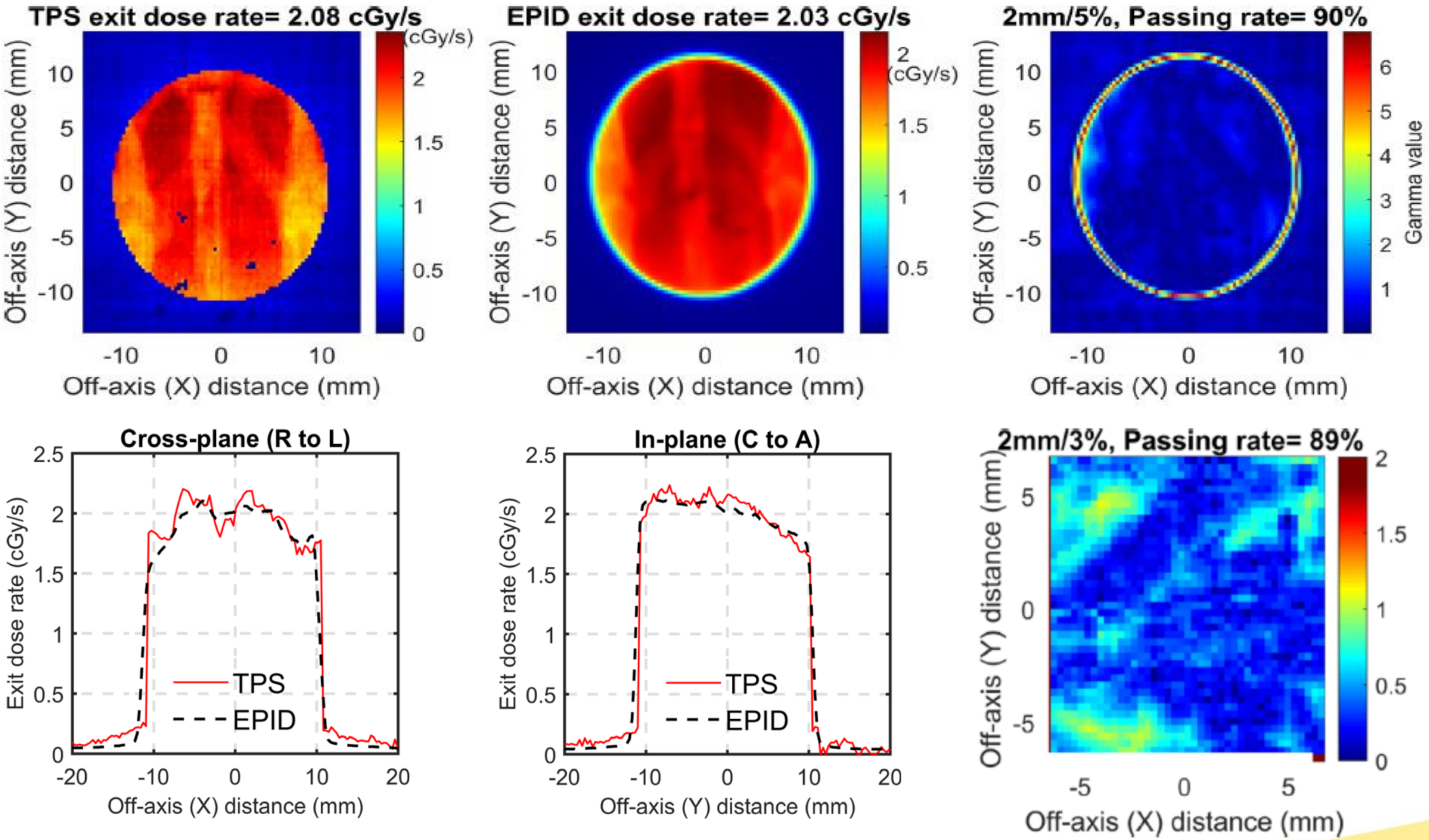






Figures 4 (left) and 11+12 (right), **A Anvari** et al, *"Kilovoltage transit and exit dosimetry for a small animal image-guided radiotherapy system using built-in EPID"* Med Phys **45**(10), 4562-45610, 2018.

Animal transit/exit dosimetry applied to verify accuracy of TPS



Figures 8+9, **A Anvari** et al., *On-line dose delivery verification in small animal image-guided radio therapy*, Med Phys **47**(4) 1871-1879 (2020)

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!