Micro Irradiator / Animals

**Advanced Applications of 3D Dosimetry and 3D Printing in Radiation Therapy.**
Devin Miles 2016 DUKE Master Thesis

Pre-clinical animal studies are used as a conventional means of translational research, as a midpoint between in-vitro cell studies and clinical implementation. However, modern small animal radiotherapy platforms are primitive in comparison with conventional linear accelerators. This work also investigates a series of 3D printed tools to expand the treatment capabilities of the X-RAD 225Cx orthovoltage irradiator, and applies them to a feasibility study of hippocampal avoidance in rodent whole-brain radiotherapy.

As an alternative material to lead, a novel 3D-printable tungsten-composite ABS plastic, GMASS, was tested to create precisely-shaped blocks. Film studies show virtually all primary radiation at 225 kVp can be attenuated by GMASS blocks of 0.5cm thickness. A state-of-the-art software, BlockGen, was used to create custom hippocampus-shaped blocks from medical image data, for any possible axial treatment field arrangement. A custom 3D printed bite block was developed to immobilize and position a supine rat for optimal hippocampal conformity. An immobilized rat CT with digitally-inserted blocks was imported into the SmART-Plan Monte-Carlo simulation software to determine the optimal beam arrangement. Protocols with 4 and 7 equally-spaced fields were considered as viable treatment options, featuring improved hippocampal conformity and whole-brain coverage when compared to prior lateral-opposed protocols. Custom rodent-morphic PRESAGE dosimeters were developed to accurately reflect these treatment scenarios, and a 3D dosimetry study was performed to confirm the SmART-Plan simulations. Measured doses indicate significant hippocampal sparing and moderate whole-brain coverage.

**Investigating the accuracy of microstereotactic-body-radiotherapy utilizing anatomically accurate 3D printed rodent-morphic dosimeters.**
Bache, S.T., Juang, T., Belley, M.D., (...), Kirsch, D.G., Oldham, M.

Sophisticated small animal irradiators, incorporating cone-beam-CT image-guidance, have recently been developed which enable exploration of the efficacy of advanced radiation treatments in the preclinical setting. Microstereotactic-body-radiation-therapy (microSBRT) is one technique of interest, utilizing field sizes in the range of 115 mm. Verification of the accuracy of microSBRT treatment delivery is challenging due to the
lack of available methods to comprehensively measure dose distributions in representative phantoms with sufficiently high spatial resolution and in 3 dimensions (3D). This work introduces a potential solution in the form of anatomically accurate rodent-morphic 3D dosimeters compatible with ultrahigh resolution (0.3 mm3) optical computed tomography (optical-CT) dose read-out. Methods: Rodent-morphic dosimeters were produced by 3D-printing molds of rodent anatomy directly from contours defined on x-ray CT data sets of rats and mice, and using these molds to create tissue-equivalent radiochromic 3D dosimeters from Presage. Anatomically accurate spines were incorporated into some dosimeters, by first 3D printing the spine mold, then forming a high-Z bone equivalent spine insert. This spine insert was then set inside the tissue equivalent body mold. The high-Z spinal insert enabled representative cone-beam CT IGRT targeting. On irradiation, a linear radiochromic change in optical-density occurs in the dosimeter, which is proportional to absorbed dose, and was read out using optical-CT in high-resolution (0.5 mm isotropic voxels). Optical-CT data were converted to absolute dose in two ways: (i) using a calibration curve derived from other Presage dosimeters from the same batch, and (ii) by independent measurement of calibrated dose at a point using a novel detector comprised of a yttrium oxide based nanocrystalline scintillator, with a submillimeter active length. A microSBRT spinal treatment was delivered consisting of a 180° continuous arc at 225 kVp with a 20?10 mm field size. Dose response was evaluated using both the Presage/optical-CT 3D dosimetry system described above, and independent verification in select planes using EBT2 radiochromic film placed inside rodent-morphic dosimeters that had been sectioned in half. Results: Rodent-morphic 3D dosimeters were successfully produced from Presage radiochromic material by utilizing 3D printed molds of rat CT contours. The dosimeters were found to be compatible with optical-CT dose readout in high-resolution 3D (0.5 mm isotropic voxels) with minimal artifacts or noise. Cone-beam CT image guidance was possible with these dosimeters due to sufficient contrast between high-Z spinal inserts and tissue equivalent Presage material (CNR ∼10 on CBCT images). Dose at isocenter measured with optical-CT was found to agree with nanoscintillator measurement to within 2.8%. Maximum dose in line profiles taken through Presage and film dose slices agreed within 3%, with FWHM measurements through each profile found to agree within 2%. Conclusions: This work demonstrates the feasibility of using 3D printing technology to make anatomically accurate Presage rodent-morphic dosimeters incorporating spinal-mimicking inserts. High quality optical-CT 3D dosimetry is feasible on these dosimeters, despite the irregular surfaces and implanted inserts. The ability to measure dose distributions in anatomically accurate phantoms represents a powerful useful additional verification tool for preclinical microSBRT.
A small animal image guided irradiation system study using 3D dosimeters.

In a high resolution image-guided small animal irradiation platform, a cone beam computed tomography (CBCT) is integrated with an irradiation unit for precise targeting. Precise quality assurance is essential for both imaging and irradiation components. The conventional commissioning techniques with films face major challenges due to alignment uncertainty and labour intensive film preparation and scanning. In addition, due to the novel design of this platform the mouse stage rotation for CBCT imaging is perpendicular to the gantry rotation for irradiation. Because these two rotations are associated with different mechanical systems, discrepancy between rotation isocenters exists. In order to deliver x-ray precisely, it is essential to verify coincidence of the imaging and the irradiation isocenters. A 3D PRESAGE dosimeter can provide an excellent tool for checking dosimetry and verifying coincidence of irradiation and imaging coordinates in one system. Dosimetric measurements were performed to obtain beam profiles and percent depth dose (PDD). Isocentricity and coincidence of the mouse stage and gantry rotations were evaluated with starshots acquired using PRESAGE dosimeters. A single PRESAGE dosimeter can provide 3-D information in both geometric and dosimetric uncertainty, which is crucial for translational studies.


Micro-beam Radiation Therapy (MRT) is an experimental radiation therapy with provocative experimental data indicating potential for improved efficacy in some diseases. Here we demonstrated a comprehensive micro-beam verification method utilizing high resolution (50pm) PRESAGE/Micro-Optical-CT 3D Dosimetry. A small PRESAGE cylindrical dosimeter was irradiated by a novel compact Carbon-Nano-Tube (CNT) field emission based MRT system. The Percentage Depth Dose (PDD), Peak-to-Valley Dose Ratio (PVDR) and beam width (FWHM) data were obtained and analyzed from a three strips radiation experiment. A fast dose drop-off with depth, a preserved beam width with depth (an averaged FWHM across three beams remains constant (405.3um, sigma=13.2um) between depth of 3.0~14.0mm), and a high PVDR value (increases with depth from 6.3 at 3.0mm depth to 8.6 at 14.0mm depth) were discovered during this verification process. Some operating procedures such as precise dosimeter mounting, robust mechanical motions (especially rotation) and stray-light
artifact management were optimized and developed to achieve a more accurate and
dosimetric verification method.

**Investigating end-to-end accuracy of image guided radiation treatment delivery using a micro-irradiator**

By Rankine L J; Newton J; Bache S T; Das S K; Adamovics J; Kirsch D G; Oldham M. From Physics in medicine and biology (2013), 58(21), 7791-801.

There is significant interest in delivering precisely targeted small-volume radiation treatments, in the pre-clinical setting, to study dose-volume relationships with tumour control and normal tissue damage. For these studies it is vital that image guidance systems and target positioning are accurately aligned (IGRT), in order to deliver dose precisely and accurately according to the treatment plan. In this work we investigate the IGRT targeting accuracy of the X-RAD 225 Cx system from Precision X-Ray using high-resolution 3D dosimetry techniques. Small cylindrical PRESAGE® dosimeters were used with optical-CT readout (DMOS) to verify the accuracy of 2.5, 1.0, and 5.0 mm X-RAD cone attachments. The dosimeters were equipped with four target points, visible on both CBCT and optical-CT, at which a 7-field coplanar treatment plan was delivered with the respective cone. Targeting accuracy (distance to agreement between the target point and delivery isocenter) and cone alignment (isocenter precision under gantry rotation) were measured using the optical-CT images. Optical-CT readout of the first 2.5 mm cone dosimeter revealed a significant targeting error of $2.1 \pm 0.6$ mm and a cone misalignment of $1.3 \pm 0.1$ mm. After the IGRT hardware and software had been recalibrated, these errors were reduced to $0.5 \pm 0.1$ and $0.18 \pm 0.04$ mm respectively, within the manufacturer specified 0.5 mm. Results from the 1.0 mm cone were $0.5 \pm 0.3$ mm targeting accuracy and $0.4 \pm 0.1$ mm cone misalignment, within the 0.5 mm specification. The results from the 5.0 mm cone were $1.0 \pm 0.2$ mm targeting accuracy and $0.18 \pm 0.06$ mm cone misalignment, outside of accuracy specifications. Quality assurance of small field IGRT targeting and delivery accuracy is a challenging task. The use of a 3D dosimetry technique, where targets are visible on both CBCT and optical-CT, enabled identification and quantification of a targeting error in 3D. After correction, the targeting accuracy of the irradiator was verified to be within 0.5 mm (or 1.0 mm for the 5.0 mm cone) and the cone alignment was verified to be within 0.2 mm (or 0.4 mm for the 1.0 mm cone). The PRESAGE®/DMOS system proved valuable for end-to-end verification of small field IGRT capabilities.
Commissioning a Small Animal Irradiator Using 2D and 3D Dosimetry Techniques
By J. Newton, M. Oldham, Y. Li, J. Adamovics, and S. Das

Purpose: To commission and characterize a novel small animal irradiator, the XRad225cx from Precision X-Ray Inc. This system is capable of delivering both square and circular fields ranging in size from 1mm to 40mm. The combination of very small field size and relatively low energy (225kV) represents a substantial challenge in acquiring accurate dosimetry beam data. This work reports on commissioning studies using 2 independent dosimetry systems: EBT2 radiochromic film and PRESAGE / optical-CT 3D dosimetry.

Methods: Initial measurements were made with 6x8cm pieces of EBT2 radiochromic film. Output factors were determined at 3 depths (0, 0.5 and 2cm) from films irradiated normally resting on the surface or sandwiched in solid water. Percent-depth-dose (PDD) measurements were made from films also sandwiched in solid water and irradiated edge on. Independent 3D dosimetry measurements were obtained using PRESAGE radiochromic dosimeters and imaged with the Duke Large field-of-view Optical-CT Scanner (DLOS). Output factors and PDD’s were obtained using a combination of small fields. Results: The relative output factors and PDD’s obtained from EBT2 and PRESAGE showed agreement below 1 cm depth. For field sizes >1cm, relative output factors were found to be stable (1.00) with differences between PRESAGE and EBT2 <6%. At smaller field sizes the output relative to the 20 mm cone decreased substantially, down to 0.5 for the smallest 1 mm cone. A slightly greater drop was observed in the PRESAGE measurements, which is currently being investigated.

Conclusions: Output factors and PDD curves were successfully obtained for all cones using a combination of EBT2 and PRESAGE. Consistency was observed between both independent measurements after correcting for the lack of exact water equivalence of both the solid water and PRESAGE. The 3D dosimetry system has potential advantages in terms of convenience, efficiency and comprehensiveness when commissioning small fields.