

X-ray skeleton imaging in conjunction with bioluminescence imaging does not alter pancreatic tumors

Christopher G. England, M.S.¹, Shanice V. Hudson, M.S.², Justin Huang, B.S.², Wenyuan Yin², Hermann B. Frieboes, Ph.D.^{1,3}, and Lacey R. McNally, Ph.D.^{1,2}

¹ Dept. of Pharmacology & Toxicology, University of Louisville, ² Dept. of Medicine, University of Louisville, ³Dept. of Bioengineering, University of Louisville

ABSTRACT

Purpose: The technology for bioluminescence imaging allows for noninvasive study of biological processes in small animals. Since mammalian tissues have low intrinsic bioluminescence, images are obtained with incredibly high signal-to-noise ratio. The ease of use, along with capabilities to monitor disease progression, has prompted bioluminescence imaging as an excellent methodology for cancer research. Recently, detection of mouse skeleton via X-Ray, has become popular as a method for providing anatomical context of bioluminescence signals. Because repeated X-ray can cause DNA damage, upregulate radiation sensitive proteins, and induce cell stress, our goal was to evaluate the potential damage resulting from repeated X-ray exposure in conjunction with bioluminescence imaging.

Methods: Mice were orthotopically implanted with either S2VP10L or MiaPaCa2A cells containing a luciferase reporter. Mice were imaged ten times on consecutive days using bioluminescence imaging in conjunction with either High Resolution X-ray or Low Resolution X-ray using an Advanced Molecular Imager 1000X. A dosimeter was placed inside the AMI 1000-X along with each group of mice. Total radiation was measured via dosimeter. Bioluminescence signals were compared for both groups. At the end of 10 days, Rad51, H2AX, and TUNEL were evaluated on tumor and liver sections.

Results: The radiation dose for the High Resolution was 15.6mGy while the Low Resolution was 10.7 mGy. S2VP10 and MiaPaCa2 tumors did not have higher levels of double strand breaks in comparison to control tumors. Additionally, immunohistochemistry did not demonstrate a statistical difference in radiation sensitive proteins.

Conclusion: Overall, radiation exposure obtained during animal imaging does not increase DNA damage, up-regulate radiation sensitive markers, or induce cell stress.

METHODS

Cell Culture: S2VP10 and MiaPaCa2 cell were cultured as previously described.

Human Pancreatic Xenograft Model: Mice were orthotopically with S2VP10 cells, and imaged as described.

XRT-radiation control for Histology: A separate set of mice were treated with 5Gy to induce cell damage within pancreatic tumors to serve as radiation controls.

Histology: Tumor xenografts were harvested at 17 days after cell injection, formalin fixed, and processed into paraffin blocks using standard methods.

RESULTS

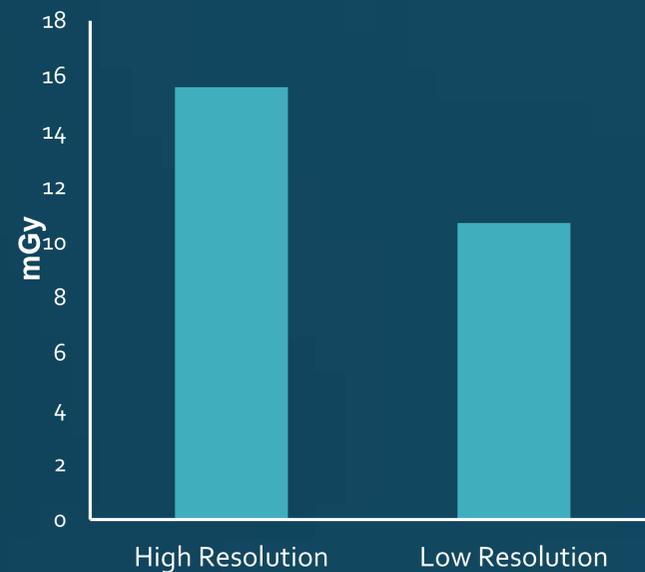


Figure 1: Evaluation of Radiation Dose when utilizing XRT imaging in conjunction with bioluminescence imaging. Dosimeters were placed into the AMI 1000-X immediately adjacent to mice bearing S2VP10L or MiaPaCa2 tumors. Mice were imaged once daily using either the High Resolution XRT or Low Resolution XRT. Mice were imaged for 10 consecutive days. Total radiation levels (including all 10 time-points) were 15.6 mGy and 10.7mGy respectively.

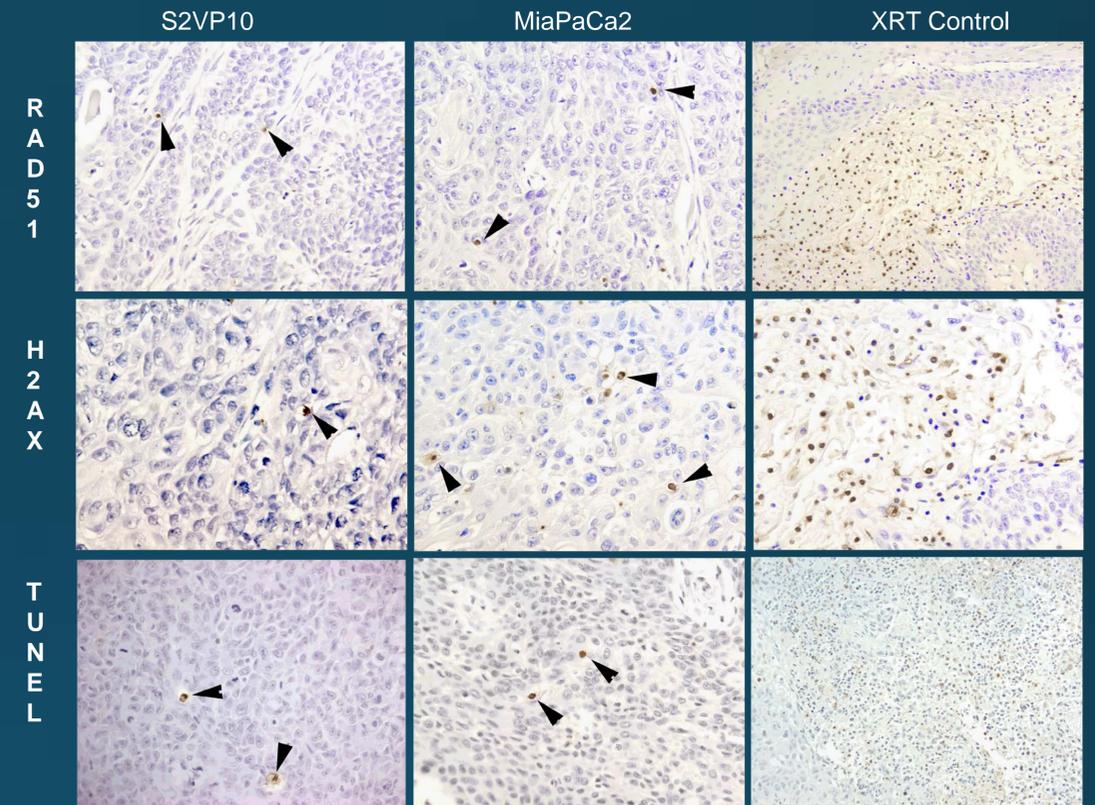


Figure 3: Histology of Pancreatic Adenocarcinoma cell lines, S2VP10 and MiaPaCa2 with x-ray exposure, along with the negative control. For the RAD51, H2AX, and TUNEL, there were no statistical differences between the x-ray exposed samples and control. Arrows illustrates positive staining.

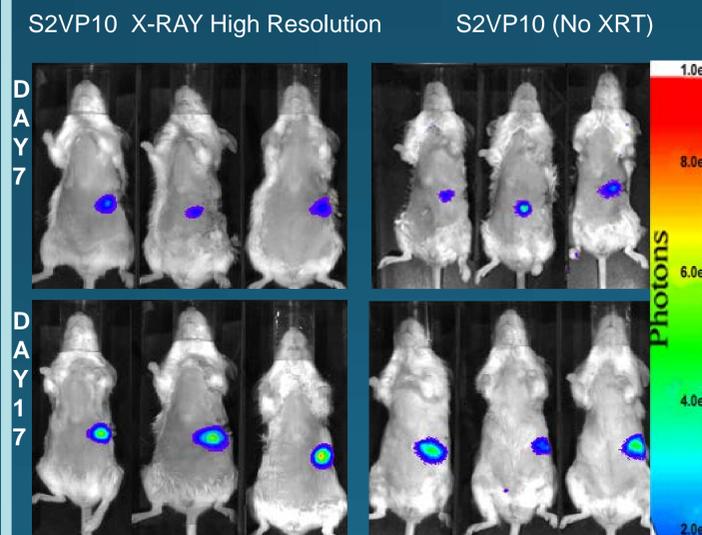


Figure 2: Bioluminescence imaging for Visualization of Pancreatic Cancer. Pancreatic tumors were visualized using bioluminescence imaging with S2VP10 luciferase transfected cells. Mice were imaged for 10 consecutive days (Day 7-17), with increasing tumor size.

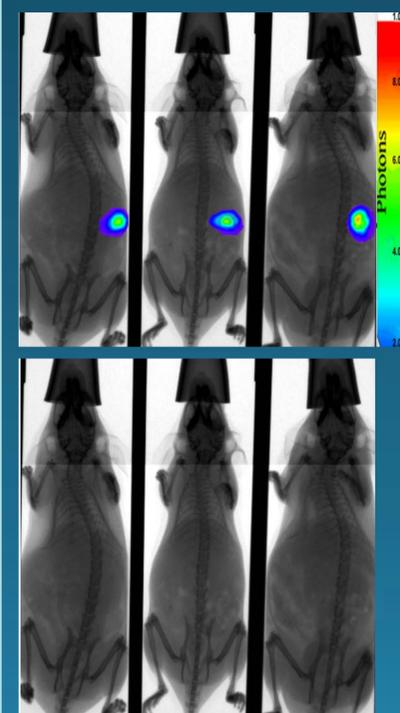


Figure 4: Overlay of Tumor signal (luciferase) with X-Ray image (Top). High Resolution X-Ray image (bottom). Tumor at day 17

CONCLUSION

Exposure to radiation during the imaging of cancer was studied to determine secondary effects. This study found:

- There were no signs of increased DNA damage.
- Tumor size of x-ray exposed mice were statistically similar to control group.
- Immunohistochemistry showed minimal upregulation of radiation-sensitive markers.

ACKNOWLEDGEMENTS

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