TIME- AND DOSE-DEPENDENT, RADIATION CYSTITIS-INDUCED ALTERATIONS TO BLADDER WALL MECHANICAL BEHAVIOR

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Background

Following radiation treatment for pelvic organ cancer, patients can develop a debilitating disease of the urinary bladder, called radiation cystitis (RC). This can cause bleeding, pain, and kidney disease, limiting a cancer patient's ability to fully recover. To create a deeper understanding of the development of this disease, we have examined the effects of RC on the mechanics of the urinary bladder following radiation.

Methods

At 8 weeks, of age, C57BL female mice were subjected to varying doses of bladder-centered radiation treatment. The doses were: 1x40Gy, 2x28Gy, or 3x22Gy (multiple doses separated by two weeks). Along with age-matched controls, the mice were euthanized at either 3 months or 6 months after treatment, and their urinary bladders isolated (sample sizes in **Figure 1**). Each bladder was decellularized, sliced into circumferential rings, and subjected to a uniaxial stress-strain test. The resulting stress-strain curve and stiffness at an estimated "micturition" point (based on bladder capacity and geometry) were calculated.

Results

From the stress-strain curves, at 3 months, the 1x40Gy dose was slightly less distensible ($P < 0.1$) than the control group, **Figure 1**. At 6 months, no irradiated bladders showed differences from the controls, though the 3x22Gy was less distensible ($P < 0.05$) at mid-level stresses than the 1x40Gy. There were no time-related differences in the stress-strain curves. The stiffness at micturition was significantly higher ($P < 0.05$) for 1x40Gy and 2x28Gy (as well as the compiled irradiated data) than the controls, at 3 months following treatment, **Figure 1**. These significantly increased stiffnesses returned to control levels at 6 months.

Conclusions

Though differences between doses, controls, and time points were limited in the stress-strain curves, there were several significant differences in the stiffness at micturition. Namely, at 3 months, two radiation doses showed a significantly higher stiffness, which decreased by the 6-month time point. Overall, this study suggests the possibility of a dose-dependent increased bladder stiffness as a response to radiation, followed by a time-dependent recovery.

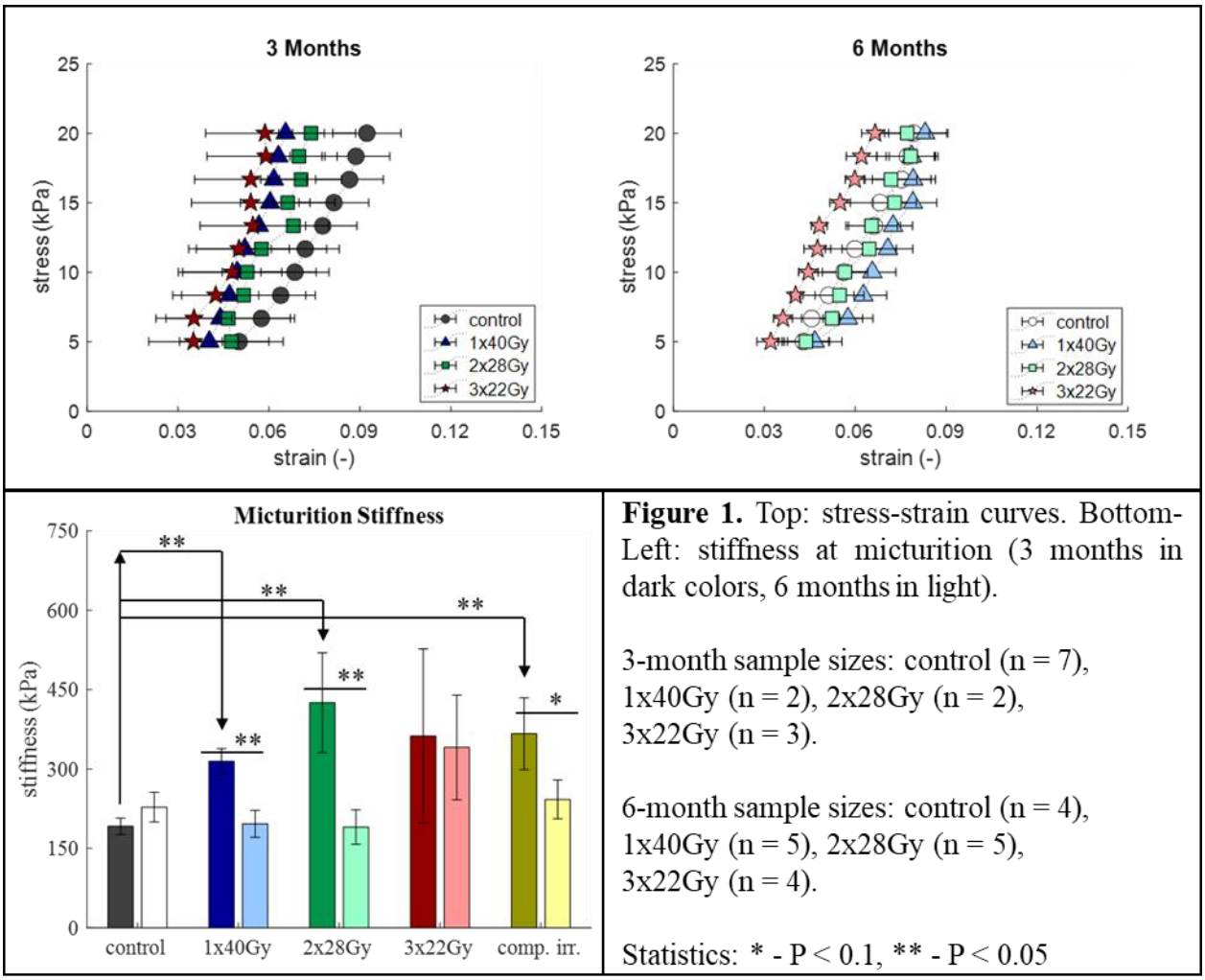

Figure 1. Top: stress-strain curves. Bottom-Left: stiffness at micturition (3 months in dark colors, 6 months in light).

3-month sample sizes: control (n = 7), 1x40Gy (n = 2), 2x28Gy (n = 2), 3x22Gy (n = 3).

6-month sample sizes: control (n = 4), 1x40Gy (n = 5), 2x28Gy (n = 5), 3x22Gy (n = 4).

Statistics: * - $P < 0.1$, ** - $P < 0.05$