Morphological Characterization of Female Rat Genitourinary Tissues Following Pelvic Radiation

Pelvic radiation-induced pathological changes observed in rats mimic what is seen in cancer patients undergoing radiotherapy.

Julia Quirin
Mentor: Dr. Johanna Hannan
Department of Physiology

Julia L. Quirin and Johanna L. Hannan
[1]Department of Physiology, Brody School of Medicine, East Carolina University, Greenville, United States.

@Hannan_Lab @JuliaQuirin

BACKGROUND/INTRODUCTION

Background

- Pelvic radiotherapy (RT): Treatment of GI, prostate, and gynecological cancers
- Induction of histological changes → Post-irradiation dysplasia
- Most cancer survivors report sexual dysfunction; gynecological cancer survivors cite 16 distinct types of physical sexual dysfunction post-RT
- Current interventions for post-RT vaginal adhesion and stenosis: low adherence and limited data supporting efficacy

Need for animal model of pelvic RT:
Develop model → evaluate preclinical therapies → facilitate progression of successful interventions to clinical studies → novel therapies for cancer survivors

Hypothesis

We predicted that pelvic radiation will:

- increase vaginal epithelial atrophy
- decrease vaginal blood flow

Additionally, we sought to characterize the cervical and clitoral tissue of female rats.

Methods

Animals: Female Sprague-Dawley rats. RT rats were randomly assigned to 4 week and 9 week post-RT evaluation groups (n=8/group). Control group (n=6) did not undergo RT.
Radiation therapy: 0 or 25 Gy single-dose pelvic radiation was administered to anesthetized rats via MultiRad350 small animal irradiator.
Histological analysis: Vaginal, cervical, and clitoral tissues were fixed and embedded in paraffin. Tissue sectioned (6 µm) and stained with Masson's Trichrome to assess fibrosis. Quantitative image analysis was used to determine epithelial changes.
Blood flow: Vaginal blood flow was measured in vitro using a laser Doppler probe following pelvic nerve stimulation.

RESULTS

Vaginal epithelium exhibited significant atrophy at 4 and 9 weeks post-RT

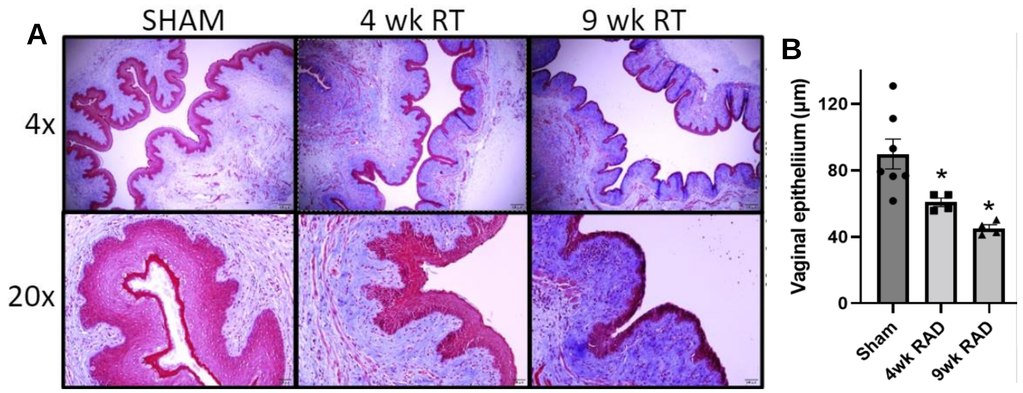


Figure A. Histologic sections of vaginal mucosa stained with Masson trichrome show decreased epithelial layer in radiation groups at 4 and 9 weeks post-RT compared to sham group. **Figure B.** Quantitative image analysis of epithelial atrophy in the vaginal mucosa at sham group and 4 and 9 week post 25 Gy RT.

Vaginal blood flow was unchanged long-term by pelvic RT

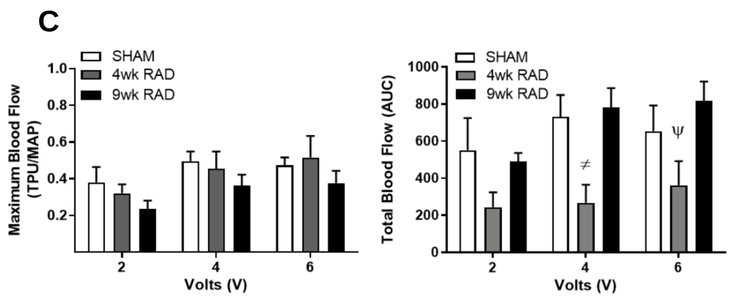
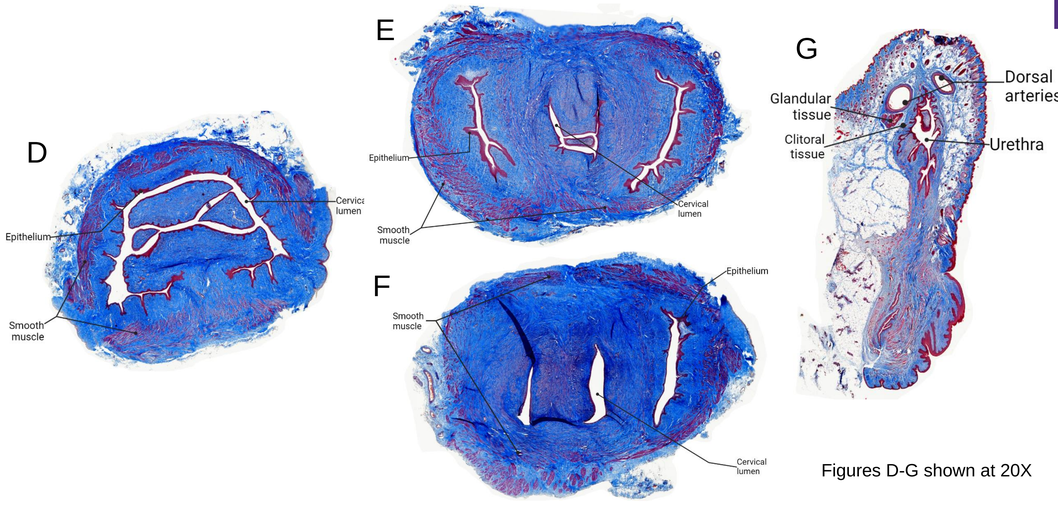


Figure C. Maximal vaginal blood flow (normalized to MAP) was not significantly affected at 4 weeks or 9 weeks post-RT. Total vaginal blood flow was decreased at 4 weeks but recovered by 9 weeks post-RT.

Novel characterization of rat cervix and clitoris tissue



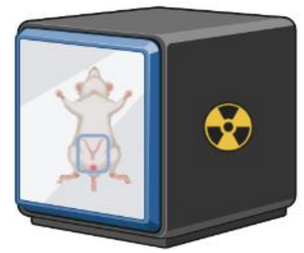
Figures D-G shown at 20X

Figure D. 6 µm Masson's Trichrome stained section of 4 week control cervix. **Figures E and F.** 6 µm Masson's Trichrome stained section of 4 week RT (Figure E) and 9 week RT (Figure F) cervix. **Figure G.** 6 µm Masson's Trichrome stained section of control clitoris.

CONCLUSION

Pelvic radiotherapy at a 25 Gy dose:

- Induces fibrosis and atrophy of vaginal tissue
- Causes increased contractility of vaginal tissue
- Produces pathological outcomes characteristic of clinical pelvic radiotherapy used for treatment of cancer
- Can be utilized to evaluate RT-induced changes in newly-characterized rat genitourinary tissues



FUTURE DIRECTIONS

1. **Complete evaluation of effects of pelvic radiation on clitoral tissue**
2. **Determine bioadhesive properties and confirm in vivo application safety of intravaginal hydrogel developed at Mt. Sinai**
3. **Evaluate the efficacy of intravaginal hydrogel in preventing radiation-induced genitourinary pathologies**