NEUROGENIC AND AGONIST-EVOKED CONTRACTIONS ARE NEGATIVELY IMPACTED BY IN VIVO IRRADIATION IN THE MOUSE BLADDER

Hypothesis / aims of study
Patients undergoing radiotherapy for pelvic malignancies experience adverse effects on bladder function. The cellular basis of radiation-induced bladder dysfunction is incompletely understood and may represent pathologies in several cell types. We previously reported that ex vivo irradiation of guinea-pig bladder tissue attenuated spontaneous and neurogenic contractions (1). The purpose of the present study was to investigate the effect of in vivo pelvic irradiation on mouse bladder neurogenic and agonist-evoked contractions.

Study design, materials and methods
C57BL mice underwent pelvic irradiation in accordance with local ethics approval. Animals were sacrificed 1h or 1wk post-irradiation. Full thickness and detrusor (mucosa removed) tissue strips were studied with in vitro myography and electrical field stimulation (EFS).

Results
Neurogenic contractions, evoked by EFS in full thickness or detrusor strips (0.5Hz–16Hz) one-hour post-irradiation were not significantly different from controls (at 16Hz, 1.18±0.18g vs 1.38±0.15g; both data sets n=10; N=5; p=0.4). However, full-thickness bladder strips from animals one-week post-irradiation had smaller neurogenic contractions at all frequencies tested (n=10, N=5; at 16Hz, 1.18±0.18g in control vs 0.62±0.11g post-irradiation; p=0.012). This effect was not seen in detrusor strips (at 16Hz, 1.03±0.19g control vs 1.2±0.08g, p=0.44).

Carbachol-evoked contractions were reduced in irradiated full thickness strips (0.89±0.12g in control vs 0.31±0.06g irradiated, n=10 N=5, p=0.0005) 1 week post-irradiation. Similarly, ATP-responses were reduced 1 week following irradiation (0.37±0.09g vs 0.12±0.02g, n=10; N=5, p=0.014). Interestingly, in detrusor strips, there was no difference in carbachol or ATP responses after irradiation (p=0.42 and p=0.40, respectively).

Receptor-independent contractions evoked by high external K+ solution was also reduced in full thickness strips (n=10; N=5) one-week post-irradiation (1.02±0.11g vs 0.64±0.09g, p=0.018); an effect not seen in detrusor strips (n=10, N=5; p=0.78), indicating that the ability of the detrusor smooth muscle to contract per se was not affected by irradiation.

Interpretation of results
In summary, in vivo pelvic irradiation reduced neurogenic, agonist, and high external K+-evoked contractions in full thickness bladder strips, one week after irradiation. These differences were not found in detrusor strips, indicating that radiation may impact the cells of the mucosal layer.

Concluding message
Neurogenic, agonist, and high external K+-evoked contractions in full thickness bladder strips were negatively impacted one week post-irradiation. Our findings indicate that cells of the mucosal layer may be more sensitive to irradiation than detrusor smooth muscle.

References

Disclosures
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