

## 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<sup>+</sup> 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<sup>+</sup>-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<sup>+</sup>-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

1. McDonnell et al, 2012. Proc Physiol Soc 27

### Disclosures

**Funding:** Financial support was received from the European Union, FP7 "INComb" (FP7-HEALTH-2007-B). BMcD is in receipt of a DEL studentship, Queen's University Belfast. **Clinical Trial:** No **Subjects:** ANIMAL **Species:** Mouse **Ethics Committee:** Animal Ethics Committee, Queen's University Belfast