

Human bladder tissue (neurogenic patients)

Advantages over bladder tissues from control patients:

- In vitro investigation of human bladder function in pathophysiological conditions.
- Useful to investigate the effect of drugs targeting neurogenic detrusor overactivity but also overactive bladder whatever its etiology.
- Increase in occurrence of spontaneous phasic contractions in detrusor from neurogenic patients when compared to detrusor from control patients.
- Suitable model for the evaluation of the ability of drugs at modulating spontaneous detrusor phasic contractile activity which represents an in vitro modelling of detrusor overactivity.
- Evaluation of the ability of drugs at modulating detrusor smooth muscle tone can be performed:
 - on cholinergic contractile response elicited by muscarinic pharmacological stimulation (carbachol) or by electrical field stimulation (EFS) which stimulates efferent nerve terminals present in the tissue.
 - on β -adrenergic relaxant response induced by pharmacological agents (norepinephrine).
 - on KCl response.
 - on others non adrenergic non cholinergic responses (purinergic, nitrenergic...)
- Evaluation of the influence of urothelium on the detrusor contractility.
- Evaluation of mRNA by RT-PCR or protein expression, by immunohistochemistry (IHC) or western-blot (WB), in parallel of organ bath studies.

Source of human tissues:

- Human bladder tissues are obtained from patients who suffer from neurogenic bladder due to damage caused by spinal cord injury, multiple sclerosis or other neurological disease and who underwent partial or total cystectomy. According to their medical chart, patients had urodynamically proven neurogenic detrusor overactivity.

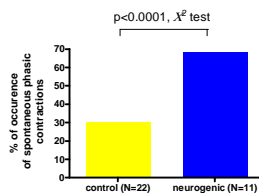


Figure 1: Occurrence and characterization of spontaneous phasic contractile activity in detrusor from neurogenic patients when compared to detrusor from control patients. Oger, S. et al. J Urol Abstract (AUA, 2008) : 179(4) : 352

Myogenic origin of spontaneous contractile activity of detrusor from neurogenic patients

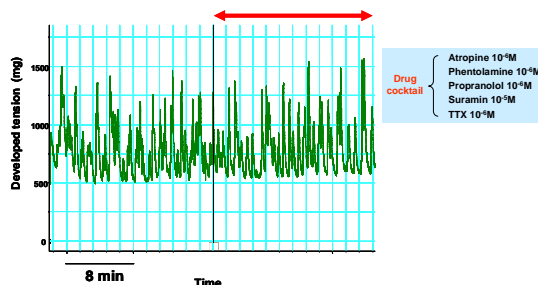


Figure 2: Original recording of myogenic contractile activity developed by human bladder strip from neurogenic patient: atropine (1 μ M), muscarinic antagonist; phentolamine (1 μ M), α -adrenergic antagonist; propranolol (1 μ M), β -adrenergic antagonist; suramin (10 μ M), purinergic antagonist; tetrodotoxin (1 μ M), neuronal Na⁺ channel blocker. (Pelvipharm, internal data)

Typical representative tracing of spontaneous phasic contractions of detrusor strip from neurogenic patients

Endpoints:

- Evaluation of the capacity of a drug to inhibit detrusor smooth muscle contractions or detrusor phasic contractile activity in **human pathophysiological condition**.
- Determination of potency (**EC₅₀**) and efficiency (**Emax**) of a drug.
- Determination of the affinity (**pA₂**) of a drug for a human bladder receptor.
- Evaluation of the influence of the urothelium.

Related Pelvipharm bibliography:

Oger, S. et al. *BJU Int* (2011) : 108(4):604-11
 Oger, S. et al. *Basic & Clinical Pharmacology & Toxicology*, 107 (Suppl. 1), 192 (WorldPharma 2010)
 Oger, S. et al. *Eur Urol Suppl* Abstract: 9(2) : 112(EAU, 2010)
 Oger, S. et al. *Eur Urol Suppl* (2008) : 7(3):183 (EAU, 2008)
 Oger, S. et al. *J Urol* (2008) : 179(4):352 (AUA, 2008)
 Oger, S. et al. *Neurourol Urodyn* (2007) : 26(5) (ICS, 2007)

Links to applicable experimental skills

- Organ bath studies (EFS / Pharmacological studies)

- * Human tissues
- **Biochemistry (Plasma / Urine / Tissue)**
 - * Spectrophotometric assays
 - * Protein expression and activity

- Histology

- * Histomorphology
- * Histomorphometry
- * Oxidative fuorescence

- Immunohistology / Confocal microscopy

- * Protein expression – immunohistochemistry / immunofluorescence
- * Confocal microscopy