- In vitro investigation of human or animal prostate function in normal or in pathophysiological conditions.
- Unrestricted amount of tissue with animal models.
- Useful to investigate the effect of drugs developed to improve the dynamic component of prostatic lower urinary tract symptoms associated with benign prostatic hyperplasia (BPH).
- Evaluation of the ability of drugs at modulating prostatic smooth muscle tone can be performed:
  - on adrenergic contractile response elicited by alpha-adrenergic pharmacological stimulation (phenylephrine/norepinephrine) or by electrical field stimulation (EFS) which stimulates efferent nerve terminals present in the tissue
  - on KCl response
  - on others relevant physiological precontracted states (endothelin-1, thromboxane agonist…)
- Evaluation of mRNA by RT-PCR or protein expression, by immunohistochemistry (IHC) or western-blot (WB), in parallel of organ bath studies.

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 sample

- **Human normal prostate** samples are obtained from patients undergoing cystoprostatectomy for infiltrating bladder cancer.
- **Human BPH samples** are obtained from patients diagnosed clinically for BPH and undergoing adenomectomy.

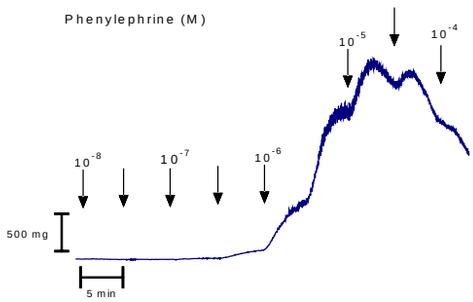


Figure 1: Original tracing showing the effect of cumulative addition of increasing concentrations of phenylephrine (M) on human prostatic tissue from BPH patient. (Pelvipharm, internal data)

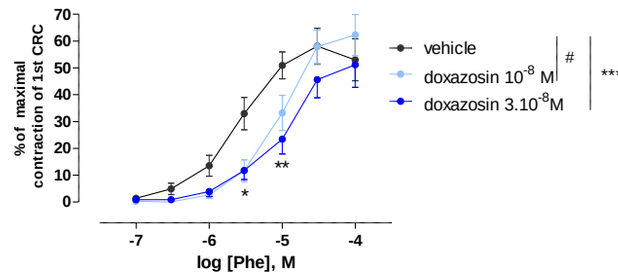


Figure 2: Effect of doxazosin on phenylephrine-induced contractions on human prostatic tissue from control patient. (From Oger et al., 2009)

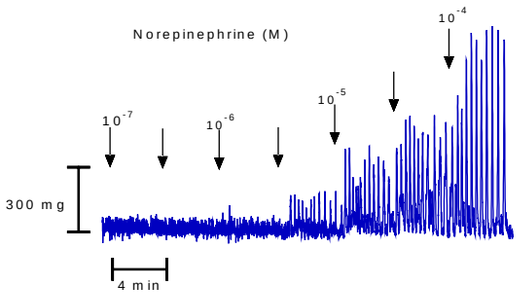
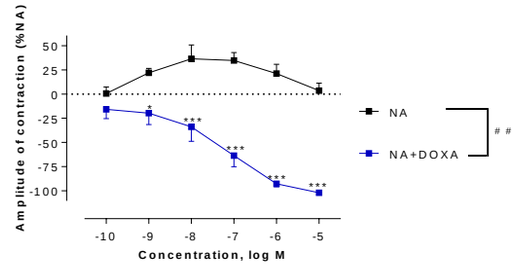


Figure 3: Recording of CRC to norepinephrine on prostatic strip of guinea-pig.



p<0.001 Two-Way ANOVA
*p<0.05, ***p<0.001 Bonferroni's complementary analysis

Figure 4: Concentration-response curves to doxazosin in pre-contracted prostatic strip of guinea-pig. Results are expressed as a % of relaxation compared to the initial developed tension obtained with NE (3.10-5 M) (Pelvipharm, internal data)

Endpoints

- Evaluation of the capacity of a drug to inhibit prostatic smooth muscle contractions.
- Determination of potency **(EC50)** and efficiency **(Emax)** of a drug.
- Determination of the affinity **(pA2)** of a drug for a human or animal prostatic receptor.

Related Pelvipharm bibliography:

Oger, S. et al. **Eur Urol** (2010):57(4):699-707
Oger, S. et al. **J Sex Med** (2009):6(3):836-847
Giuliano, F. et al. **J Urol** (2009):181(4):693 (AUA, 2009)

NB: Pelvipharm will gladly study the feasibility to fit this experimental model to its client's needs.