

ZONE-SPECIFIC DIFFERENCES IN THE SPONTANEOUS CONTRACTILITY OF THE HUMAN PROSTATE GLAND

Hypothesis / aims of study

An increase in smooth muscle tone is a major component implicated in Benign Prostatic Hyperplasia (BPH); the most common benign neoplasm in men, resulting in lower urinary tract symptoms (LUTS) which severely affect the quality of life of patients. BPH occurs in the transition zone (TZ), as opposed to the peripheral zone (PZ). However, the aetiology of BPH remains poorly understood, and the fundamental reason there is an increase in prostatic smooth muscle tone remains unknown. Our overall hypothesis is that changes in the mechanisms regulating spontaneous activity of the prostate gland, significantly contribute to the pathogenesis of BPH. This study focuses on understanding the basic physiology, to ultimately identify a novel therapeutic target that targets the origins and underlying mechanisms of spontaneous activity to potentially treat BPH. In this study, we characterised the spontaneous contractile activity in TZ and PZ prostatic specimens from men.

Study design, materials and methods

Prostate tissue was obtained from consenting patients undergoing radical prostatectomy, and placed into ice-cold RPMI medium supplemented with 5% fetal calf serum and antibiotics (penicillin at 300 units/ml, streptomycin at 300 µg/ml and amphotericin at 1 µg/ml). A resected benign TZ and PZ specimen (10 mm x 15 mm) was collected, with original tissue retained to confirm pathology. Subsequent recordings were made from prostatic preparations (3 mm x 10 mm) using conventional tension recording experiments (1).

Results

All specimens from the TZ, displayed spontaneous contractions at $2.2 \pm 0.4 \text{ min}^{-1}$, with an average amplitude of $0.20 \pm 0.03 \text{ N}\cdot\text{g}^{-1}$ (n=18). Spontaneous contractions in all PZ specimens were significantly more frequent (Student's paired t-test, $P < 0.01$), significantly larger in amplitude and significantly shorter in duration (Student's paired t-test, $P < 0.05$), occurring at $4.5 \pm 0.3 \text{ min}^{-1}$, with an amplitude of $0.41 \pm 0.07 \text{ N}\cdot\text{g}^{-1}$ and duration of $6.7 \pm 0.3 \text{ s}$, in comparison to the spontaneous contractions in the TZ from the same patients (n=8), occurring at $1.8 \pm 0.3 \text{ min}^{-1}$, with an amplitude of $0.21 \pm 0.03 \text{ N}\cdot\text{g}^{-1}$ and duration of $10.5 \pm 1.4 \text{ s}$. The TZ had an increased resting basal tension of $3.70 \pm 0.53 \text{ mN}$, in comparison to the PZ with a resting basal tension of $2.72 \pm 0.63 \text{ mN}$. Application of neurotransmission blockers, 1 µM tetrodotoxin (n=5), 1 µM guanethidine (n=4), and 1 µM atropine (n=6), had no significant effects on spontaneous contractile activity parameters in the TZ of the human prostate gland (Student's paired t-test, $P > 0.05$). Preliminary results using 1 µM tetrodotoxin, significantly reduced the resting basal tension from $2.51 \pm 0.53 \text{ mN}$ to $2.15 \pm 0.51 \text{ mN}$ in the PZ of the human prostate gland (Student's paired t-test, $P < 0.05$, n=4).

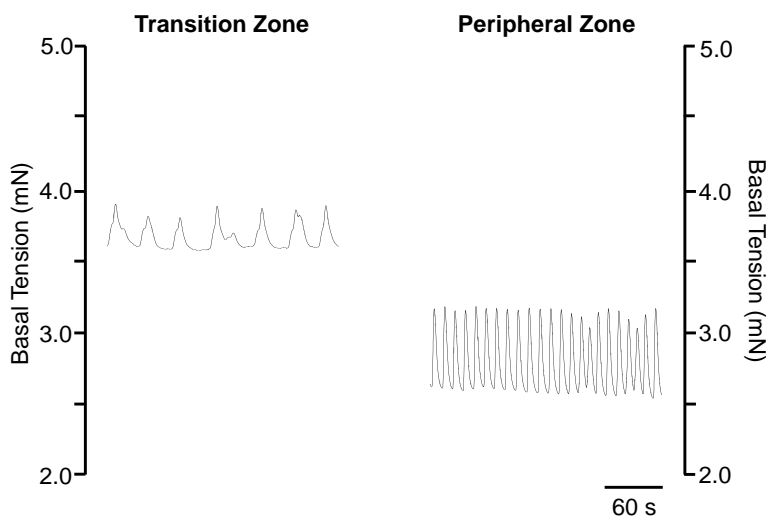


Figure 1. An increased resting basal tension in TZ, in comparison to the PZ, demonstrates an increased smooth muscle tone in the region where BPH occurs. There are significant differences in contractility profiles for the TZ and PZ. Spontaneous contractions in the TZ are significantly less frequent, longer in duration, and smaller in amplitude.

Interpretation of results

All specimens from the TZ and PZ of the human prostate gland exhibit regular spontaneous contractions that are different. An increased resting basal tension in the TZ, in comparison to the PZ, demonstrates an increased smooth muscle tone in the region where BPH commonly occurs. The differences in the parameters that contribute to spontaneous contractility in the TZ and PZ, demonstrate that there are significant differences in contractility profiles in the anatomically defined regions of the human prostate gland. Differences in the effects of neurotransmission blockers in the TZ and PZ of the human prostate gland, further suggest zone-specific differences in the generation of spontaneous contractions.

Concluding message

The TZ of the human prostate gland is where BPH occurs, and has an increased smooth muscle tone in comparison to the PZ. The lack of effects of neurotransmission blockers on spontaneous contractions in the TZ suggests contractions are myogenic, as opposed to spontaneous contractions in the PZ which are more likely to be neurogenic. The results from this study provide novel insight into the basic physiology of the human prostate gland, which may provide alternative approaches in treating and managing the LUTS associated with BPH.

References

1. DEY, A., KUSLJIC, S., LANG, R. J. & EXINTARIS, B. 2010. Role of connexin 43 in the maintenance of spontaneous activity in the guinea pig prostate gland. Br J Pharmacol, 161, 1692-707.

Disclosures

Funding: NONE **Clinical Trial:** No **Subjects:** HUMAN **Ethics Committee:** Cabrini Human Research Ethics Committee Epworth HealthCare Human Research Ethics Committee La Trobe Regional Hospital Human Research Ethics Committee Monash University Research Ethics Committee **Helsinki:** Yes **Informed Consent:** Yes