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## ESTROGEN SIGNIFICANTLY INFLUENCES DETRUSOR CONTRACTILITY IN FEMALE RATS

### Hypothesis / aims of study
Lower urinary tract dysfunctions that occur after menopause, such as detrusor overactivity, stress urinary incontinence and detrusor underactivity, are thought to be due in part to estrogen deficiency. It is therefore hypothesized that estrogen replacement therapy may be useful for stress incontinence and detrusor overactivity. However, little attention has focused on detrusor underactivity and the possibility that estrogen deficiency may concern this condition. If detrusor contractility is impaired in elderly female, the management of bladder dysfunction would be more complicated.
 The role of estrogen in bladder function has been studied using the ovariectomized animal models. Although many studies have shown that ovariectomy alters the contractile responses of detrusor muscle to carbachol, ATP, KCl and electric nerve stimulation, no studies have evaluated the effects of estrogen on contractility itself (the contraction strength) which is defined as the mechanical power generated by detrusor contraction.
 Thus, in the present study, we evaluate whether the contraction strength of detrusor decreases after estrogen depletion by ovariectomy and reverses from this decrease upon estrogen replacement.

### Study design, materials and methods
A total of 30 female Sprague-Dawley rats (16 weeks old) were divided into three groups including sham operated (SHAM), bilateral ovariectomy (OVX) and bilateral ovariectomy plus estrogen replacement (OVX+E). The OVX+E group was treated with estradiol at 3mg/kg/week subcutaneously. At 4 weeks after surgery, detrusor strips were taken from the bladder and suspended in a organ bath. Transmural electrical stimulation (15V, 0.5msec duration, 50Hz) was applied to detrusor strips in order to induce contraction. The shortening responses to electrical stimulation under various loads (4.9 mN to 19.6 mN) were recorded using an isotonic transducer. At each contraction, the applied load was regarded as force generated (F), and velocity of shortening (V) was calculated from the shortening curve of a muscle strip. The relation between F and V was analyzed using a computer (Microsoft Excel Solver) to investigate whether F / V plots were governed by the Hill equation. The strength of contraction was defined as the total mechanical power (P) produced in each detrusor strip, which is given by the following Hill equation; $P = FV + aV + bF = bFiso$, where a and b are parameters characteristic of the muscle, and Fiso was an isometric force (i.e., under this load the strips were never shorten). After the contraction study, wet weight of each strip was measured.

### Results
The force (F) / velocity (V) plots obtained from the isotonic contraction study were well fitted to the Hill equation (Fig.1). Thus, contraction power (P), isometric force (Fiso), a and b for each strip could be determined. As shown in Fig.2, the contraction power (per unit tissue weight) of OVX group (mean $\pm$ SD) was $3.24 \pm 0.19$ mwatt/g and significantly lower than that of SHAM group ($5.37 \pm 0.28$ mwatt/g). However, the contraction power of OVX + E group was approximately the same as that of SHAM group (Fig.2).
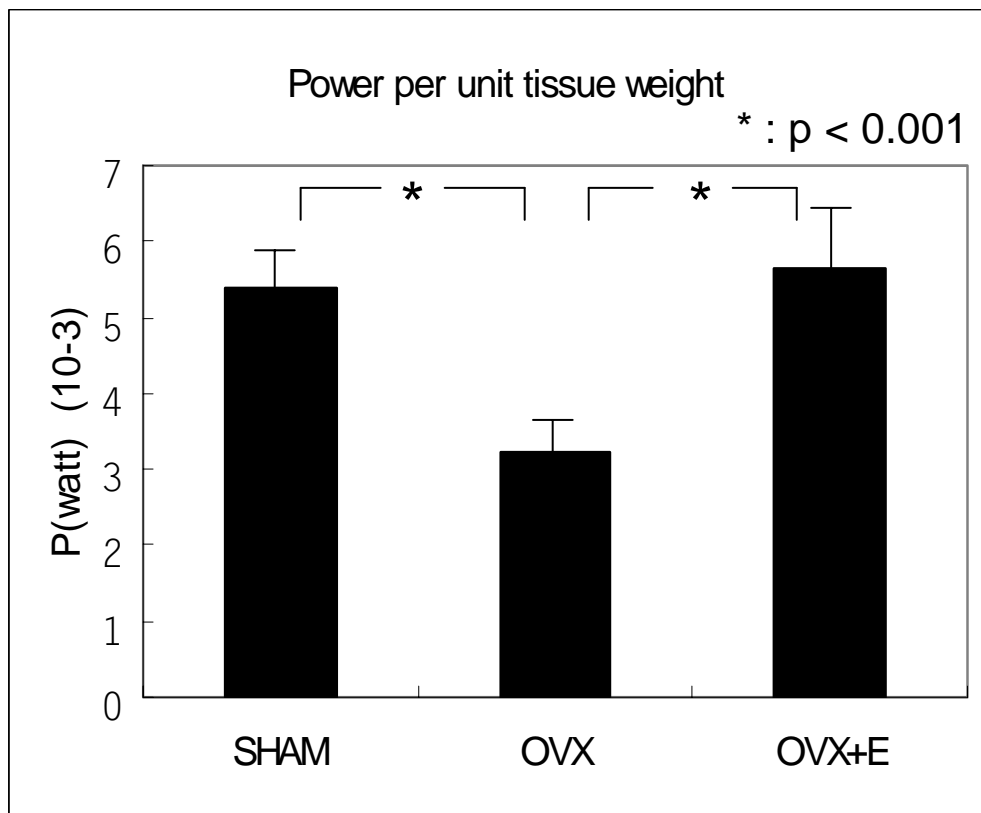
### Concluding message
The results of this study showed that ovariectomy decreased the contraction power in rat detrusor muscle, and the estrogen replacement improved it. This may suggest that estrogen plays a role in maintaining detrusor muscle power. The mechanism by which estrogen influences detrusor contractility remains unclear. As recent studies suggest, it may be speculated that estrogen modulates the expression of contractile proteins or protects the bladder against collagen formation. A clinical implication from our study is that estrogen replacement may be beneficial for treating postmenopausal detrusor underactivity.
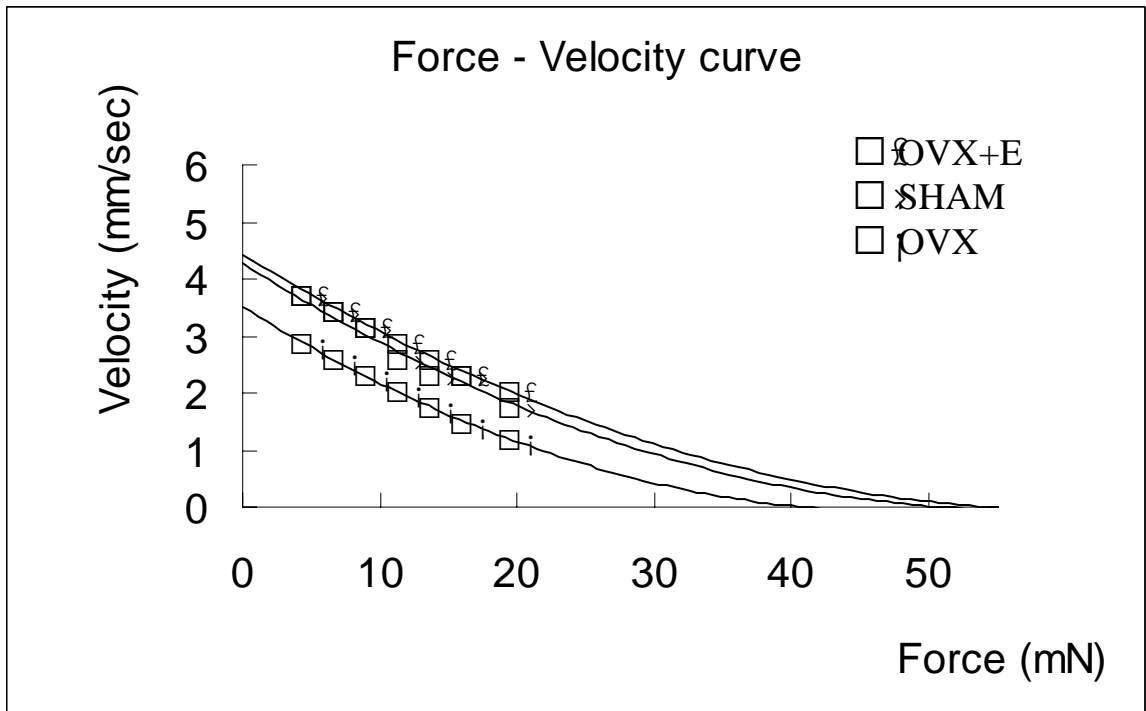
(Fig.1)
The force / velocity curve was determined from one detrusor strip.



(Fig.2)