THE EFFICACY AND SAFETY OF POLYLACTIC ACID (PLA) MICROSPHERES AND ADIPOSE-DERIVED STROMAL VASCULAR FRACTION (SVF) CELLS ON URETHRAL FUNCTION IN A RAT MODEL OF STRESS URINARY INCONTINENCE.

Hypothesis / aims of study
The aim of this study is to evaluate whether polylactic acid (PLA) microspheres and adipose-derived stromal vascular fraction (SVF) cells could increase the leak point pressure (LPP) over long term in a rat model of stress urinary incontinence.

Study design, materials and methods
36 female Sprague-Dawley rats (2-week-old) were randomized into 3 groups: saline-injected (S) (n=12), PLA injected (P) (n=12), PLA+SVF cells injected (PS) (n=12). In S, P and PS groups, the pudendal nerve was transected bilaterally via a ventral incision in order to denervate the external urethral sphincter and 0.05ml of saline, PLA microsphere suspension and PLA microsphere suspension mixed with PKH26-labelled SVF cells were injected into both sites of proximal urethra, respectively. At 2, 8, 16, 24 weeks of injection, Urethral functions of 3 rats in each group were evaluated using urodynamic leak point pressure (LPP) measurement and they were sacrificed. The urethral tissues including implants were analysed and compared grossly and histologically between groups. The distant organs including the liver, kidney, spleen and lung were also harvested and examined histologically to determine migration of PLA microspheres.

Results
Compared with the S group, LPP in P and PS groups were significantly higher at all times and there was no significant difference in LPP between P and PS group (Fig.). There was no evidence of complications including swelling or erythema at the injection sites. In histological analyses, injected PLA microspheres were localized in muscular layer of urethra without infiltration into adjacent layer. From 2-16 weeks of injection, hybrid tissues contained collagen and actin were observed between PLA microspheres and these findings were more clear in group PS. PKH26-labelled SVF cells were identified by fluorescence microscopy at all time points. There was no migration of PLA microspheres to other organs and no abnormality in weight gain and hematologic values.

Interpretation of results
At 24 weeks of PLA implantation, reasonable maintenance of LPP and hybrid tissue growth in injection site were observed and hybrid tissue formation may be improved with SVF cells.

Concluding message
These results suggest the possibility of PLA microspheres as a potentially useful bulking agent in stress urinary incontinence and further investigation is needed to know synergic effect of SVF cells.

Fig. The leak point pressure in the saline-injected (S), PLA injected (P) and PLA+SVF cells injected (PS) group at each time point.

Disclosures
Funding: None Clinical Trial: No Subjects: ANIMAL Species: Rat Ethics Committee: Hallym University Ethics Committee