Conclusion/Implications Our team developed a novel 3D printed VIA template that significantly facilitates gynecologic interstitial brachytherapy by simplifying the placement of needles and significantly decreasing procedure time while maintaining excellent dosimetry.

Introduction Cervical cancer is not the only cancer attributable to human papillomavirus (HPV). Of vaginal cancers around 78% and of vulvar cancers around 25% are caused by HPV. The number of these cancers is estimated to grow among younger women as HPV prevalence rises. The world population growth and aging will also increase the burden of these cancers. Our aim was to examine if HPV screening for cervical cancer could have an additional beneficial effect and prevent also vaginal and vulvar cancers. To assess this, we used a long-term follow-up data of the Finnish randomized HPV screening trial.

Methods Between 2003 and 2007, over 236,000 individuals were randomized (1:1) to HPV or to cytology screening in Southern Finland. The median follow-up time was 15 years. To compare the study arms, we calculated the incidence rate ratios for vaginal and vulvar cancers combined using Poisson regression. Analyses were performed with the intention to treat principle.

Results During 3.5 million person-years of follow-up, we detected a total of 51 vaginal or vulvar cancers and 12 cancer deaths in the HPV arm, and 78 cancers and 18 cancer deaths in the cytology arm. The incidence rate ratio for vaginal and vulvar cancers was 0.67 (95% CI 0.47–0.94) in the HPV arm compared to cytology arm.

Conclusion/Implications Based on our results, HPV screening could prevent vaginal and vulvar cancers. The result is promising and suggests that the growing burden of vaginal and vulvar cancers could be reduced by HPV screening. Further research on the topic is needed.

ePoster Viewing

AS01. Basic/Translational science

Introduction The expression of E-cadherin, a crucial cell adhesion molecule, plays a significant role in the progression of various malignancy. However, the role of E-cadherin in cervical cancer has not been elucidated yet. Therefore, we aimed to investigate the expression of E-cadherin in cervical cancer patients and its association with the pERK signaling pathway.

Methods Immunohistochemical analyze E-cadherin and pERK were performed using tissue microarray of cervical cancers and normal cervical epithelial tissues and clinicopathologic
variables were analyzed. Also the functional studies with cervical cancer cell lines were evaluated.

**Results** The expression of E-cadherin was significantly reduced from normal to cancer, and associated with FIGO stage. Furthermore, E-cadherin expression was negatively correlated with pERK expression in cervical cancers. The Kaplan-Meier plots demonstrated that E-cadherin lowexpression was associated with poor DFS and OS, and pERK overexpression was significantly associated with poor DFS and OS. The DFS and OS with expression of low E-cadherin/high pERK was compared with patients with others which revealed a significant difference in DFS and OS. The Cox proportional hazards model revealed that a low E-cadherin/high pERK expression was an independent prognostic factor with respect to overall survival (HR=8.48 [95% CI, 3.36 – 21.37, p<0.01]. In cervical cancer cell lines, the knock down of E-cadherins promoted proliferation in cervical cancer cells and loss of E-cadherin led to EGFR mobility, which may stimulate EGFR dimerization and further boost its activation.

**Conclusion/Implications** Low expression of E-cadherin or combined with pERK is an indicator of poor prognosis in cervical cancer, suggesting their potential utility as prognostic test in clinical assessment.

**EP003/#550** Efficacy of combination chemotherapy and third-generation oncolytic herpes virus therapy for cervical cancer

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**Introduction** Radiotherapy and chemotherapy are the most common treatments for advanced or recurrent cervical cancer, but the prognosis is poor. We have investigated viral therapy with triple mutant herpes simplex virus (T-01) in a mouse model of cervical cancer as a novel therapeutic approach. However, its antitumor effect is not sufficiently effective. In this study, we examined whether the combination of viral therapy and anticaner agents could enhance the antitumor effect.

**Methods** A mouse-derived immortalized cell line TC-1 with HPV16 E6/E7 as tumor antigen was inoculated subcutaneously into the back of C57BL/6 mice to generate cervical cancer model mice. cisplatin (CDDP), etoposide (ETP), fluorouracil (5-FU) from in vitro results, irinotecan (CPT-11), and cyclophosphamide (CPA) were administered to model mice, and anticaner agents that showed antitumor effects were combined with T-01. The combination therapy was evaluated as enhancing the antitumor effect when it exceeded the antitumor effect of viral therapy and chemotherapy.

**Results** The CPT-11, ETP, and 5-FU combination with T-01 groups showed no enhancement of antitumor effect. In contrast, the CDDP and CPA combination with T-01 group showed significant tumor growth inhibition compared to the chemotherapy and T-01 groups. Although there was no significant difference in survival rates between the chemotheraphy and T-01 groups, no mice died during the observation period in either treatment group.

**Conclusion/Implications** The combination of CDDP or CPA and viral therapy exceeded the tumor growth inhibitory effect of viral therapy and chemotherapy, and we concluded that the combination of the two therapies enhanced the anti-tumor effect.