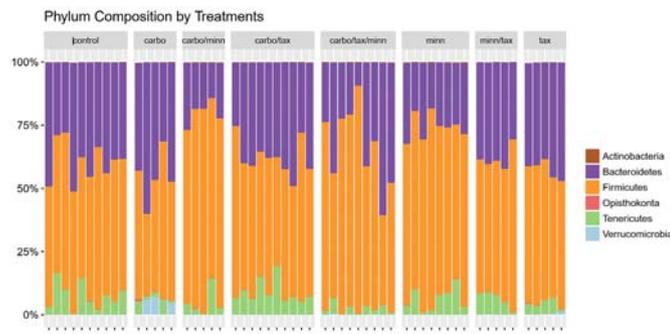


emergence of Verrucomicrobia. Further studies are underway to delineate the role of the microbiome observed.



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Poster #3

Whole genome CRISPR/Cas9 screen identifies established and novel genes required for ovarian cancer dissemination

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Objectives: A majority of high-grade serous ovarian cancers (HGSOC) arise from the exfoliation of transformed cells from the fimbriated end of the fallopian tube, indicating that these cells must escape anoikis to disseminate. Our aim was to identify novel genes and pathways critical for HGSOC dissemination.

Methods: We performed a CRISPR/Cas9 whole genome screen of HGSOC cells grown in adherent and suspension settings. 19,050 genes were targeted with at least 6 guide RNAs (gRNA) per gene totaling 123,411 gRNAs. We conducted principal component and differential gRNA expression analyses, as well as Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway and gene ontology (GO) analyses. We completed next generation sequencing of cells grown in adherent and suspension (RNA-seq). Known databases, including Protein Atlas, Oncomine, and The Cancer Genome Atlas, were utilized to refine gene list. We validated a subset of candidate genes, using small hairpin RNA (shRNA) knockdown and cell viability studies. Student t-test was used with threshold of < 0.05 for significance.

Results: CRISPR/Cas9 screen of cells grown in adherent compared to suspension settings identified 15,636 differentially expressed guide RNAs (gRNAs) (adj. $p < 0.05$), mapping to 11,571 genes. 3,395 genes had ≥ 2 targeting gRNAs, suggesting greater significance. RNA-seq analysis of the cells grown in adherent compared to suspension setting identified 804 differentially regulated genes ($p < 0.0001$).

CRISPR/Cas9 and RNA-Seq overlap analysis found 444 genes, representing a 3.2-fold enrichment. Of these genes, 108 had ≥ 2 gRNAs with similar directionality. KEGG pathway analysis of these 108 genes revealed enriched pathways including dorso ventral axis formation (NOTCH signaling), TGFbeta and calcium signaling. GO for biological processes showed enrichment for regulation of cell differentiation and positive regulation of development. In two independent ovarian cancer datasets, Oncomine analysis of the 108 genes revealed a significant enrichment in metastatic associated genes. Utilizing The Protein Atlas, 13 genes predominantly expressed in ovarian cancer were selected for further validation and elucidation of their role in anoikis. All 13 genes were significantly upregulated in suspension cells.

Cross-referencing the 108 genes with TCGA we found the expression of eight genes were significantly correlated with overall survival (Log Rank, $p < 0.05$). Notably, most had not been previously correlated with survival.

Conclusions: CRISPR/Cas9 and RNA-seq uncovered numerous regulators of anoikis escape. Known pathways, including NOTCH and TGFbeta were identified, increasing confidence in our findings. We also found novel regulators of anoikis escape that correlated with overall survival and metastatic disease. This genomic-based endeavor highlights potential new markers and therapeutic targets in HGSOC dissemination.

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Poster #4

Complications and costs of minimally invasive versus open radical hysterectomy for early stage cervical cancer

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Objectives: Recent results suggest that when compared to open (ORH), a minimally invasive (MIS) approach to radical hysterectomy, results in worse overall survival. Herein, we evaluate the effects of surgical approach on perioperative outcomes including complications and costs. **Methods:** We performed an observational retrospective cohort analysis of 2,830 women cervical cancer recorded in the 2010-2015 Premier database (Premier, Inc.) to evaluate complications and costs. Premier is a comprehensive electronic healthcare database which provides U.S. hospital-based, service-level, all-payer data, in the form of ICD-9 procedure and diagnosis codes and billing data. Premier was used to compare complications, length of stay (LOS), readmission, and costs between surgery types among propensity score matched patients. All p values were 2 sided.

Results: From Premier, 2,830 women had radical hysterectomy: 45.1% ORH and 54.9% MIS. After propensity score matching, 2,433 patients were selected: 51.2% ORH and 48.8% MIS. ORH was associated with longer LOS than RRH or LRH (days, median (IQR): ORH 3 (3-5); MIS 1 (0-2), $P < 0.001$). ORH also had a higher composite complication rate than RRH or LRH (ORH 52.9%; MIS 25.5%, $P < 0.001$), with increased bowel injuries, urinary tract injuries, vascular injuries, respiratory failure, minor infections, electrolyte or fluid disorders, and ileus (all $P < 0.05$) associated with ORH. Thirty-day readmission rates were similar (ORH 2.4%; MIS 1.3%, $P = 0.078$). Total surgical hospitalization costs favored MIS ($P < 0.001$) with median (IQR) values: ORH \$11,545 (8,622-15,461); MIS \$10,636 (8,023-13,640). Additionally, ORH was associated with additional operations during the surgical admission (ORH: 20.9%; MIS 7.8%, $P < 0.001$) with extra bowel and urinary tract surgeries (all $P < 0.001$) associated with ORH.

Conclusions: MIS hysterectomy is associated with decreased morbidity and costs compared to open radical hysterectomy. Though MIS radical hysterectomy is associated with decreased survival, it may still be a reasonable choice for some women who are deemed lower risk. Patients and physicians should consider morbidity when deciding on surgical approach.

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Poster #5

Assessment of the false negative rate of preoperative imaging in cervical cancer patients undergoing primary radical surgery

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Objectives: Patient selection for primary radical surgery is paramount to avoid the use of adjuvant radiation treatment and its associated adverse effects in cervical cancer. The use of preoperative imaging could help identify those best suited for surgery versus primary radiation; however, no standard of care has been identified. We aim to describe the false negative rate and false positive rate of preoperative imaging at a single institution prior to radical surgery for cervical cancer.

Methods: A retrospective chart review of all patients who underwent radical hysterectomy for early-stage cervical cancer from 1/2010 – 12/2017 at a single tertiary care center was performed. Patient demographics and clinicopathologic information, including imaging, surgery, adjuvant treatment and disease outcomes, were recorded from electronic records. Descriptive statistics were used.

Results: One hundred and nine patients were identified who underwent preoperative imaging. Ninety-four (86%) had no suspicion for metastatic disease, and 15 (14%) had suspicion for metastatic disease on preoperative imaging. Of these 94, 19 (20%) had a false negative study with metastatic disease identified on final surgical pathology with 18 (95%) receiving imaging within 6 weeks of surgery. Regarding imaging modality, 68% (13/19) had PET/CT; 26% (5/19) had an MRI; and one patient had a PET/CT and diagnostic CT. Of the 19 who had false negative imaging, disease was found to be in the pelvic lymph nodes in 11 patients (58%), parametria in 7 (37%), vaginal extension in 3 (16%), and uterine extension in 3 (16%). Sixty-three percent (12/19) underwent conization prior to surgery. Only 1 of these 12 patients (8%) had a tumor >2cm on cone specimen. Only 1 (8%) had positive lympho-vascular space invasion on cone.

Of the 15 with possible metastatic disease on imaging, (60%) had a false positive study with no metastatic disease identified on final surgical pathology.

Conclusions: Preoperative imaging is a commonly utilized tool to help identify cervical cancer patients who are optimal candidates for radical surgery. In this sample, the false negative rate of preoperative imaging was 20%. Further study is needed to explore preoperative testing that may more accurately identify patients who are optimal surgical candidates for cervical cancer treatment.

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Poster #6

Rates of ovarian micrometastasis in cervical adenocarcinoma

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Objectives: Rates of ovarian metastases in patients with early stage cervical adenocarcinoma have been reported to be as high as 5% leading to some practitioners to advocate for oophorectomy (BSO) at time of hysterectomy. It is unclear if visual inspection can be used to determine if a BSO is necessary given that no study has differentiated between gross versus microscopic involvement. Our goal is to examine the rates of micro-metastatic disease in cervical adenocarcinoma.

Methods: Patients with a diagnosis of early stage cervical adenocarcinoma who underwent surgical resection between 2007–2016 at a single institution were identified and patient medical records were retrospectively reviewed. Ovarian micro-metastasis was defined as presence of cancer in clinically negative ovaries without contiguous disease. Patient demographics, pathology, treatment, and follow-up information were collected. Logistic regression was performed to assess for predictors of micro-metastatic disease. Survival analysis was performed using Kaplan Meier method utilizing log rank test to determine significance.

Results: Of 271 cases assessed for eligibility, 132 cases were included. The stage distribution for 1A, 1B and 1IA were 25.4%, 72.3% and 2.3%, respectively. Median patient age was 44 (range 25–87), with 75% of patients being age 51 or less, and 10% of patients being 33 years old or younger. Almost half (47.7%) of patients were current or former smokers, average BMI was 26.7 (range 16–45), 7.6% had known HTN, 6% had documented heart disease and 3.8% had DM. The rate of ovarian metastasis was 1.5% (2/132). Of the ovarian metastasis, one of the cases had grossly abnormal ovaries at time of surgery, leaving only one (1/132) identified case of micrometastatic disease to the ovary. The case of micrometastatic disease had associated LVSI, but no stromal or parametrial involvement, and was node negative. Statistical analysis was limited by the few numbers of metastatic cases, but univariate analysis found gross appearance ($p=0.015$), LVSI ($p=0.046$) and corpus invasion ($p=0.031$) to be significantly associated with ovarian metastatic disease. Median overall survival (OS) for patients who underwent oophorectomy was 158 months (range 9–330) with 79.7% of patients alive without evidence of disease at last follow-up. This data was compared to a cohort of 43 patients where ovaries had been conserved. The median OS for this group was not statistically significantly different at 97.5 months (range 12–250) ($p=0.83$) with 88.4% alive without evidence of disease.

Conclusions: This is the first report of the rate of micro-metastatic disease involving the ovaries in cervical adenocarcinomas. This rate was found to be very low at <1% and given that the rate of predisposing factors for osteoporosis and heart disease was high, visual inspection can be considered when deciding if a BSO is appropriate at the time of surgery.

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Poster #7

Highlighting disparities among cervical cancer patients receiving brachytherapy – A National Cancer Database study

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Objectives: Cervical cancer outcomes remain disparate among racial and socio-economic groups. Access to radiation therapy, especially brachytherapy, is critical in the treatment of cervical cancer patients. The aim of this study is to determine if racial minorities and those with sub-optimal insurance receive brachytherapy at the same rate as Non-Hispanic White and privately insured counterparts.

Methods: The National Cancer Database, from 2004 to 2015, includes 53,273 cervical cancer patients who received radiation during their treatment. Of these patients, 25,223 have complete data. A univariate analysis using chi-squared was used to determine covariate association with brachytherapy. A multivariable logistic regression model was used to determine the effect of race/ethnicity (Non-Hispanic White, Non-Hispanic Black, Hispanic, Asian, other) and insurance (private, government, uninsured) on rates of brachytherapy.

Results: Compared to Non-Hispanic White patients, Hispanics are significantly less likely to receive brachytherapy ($P = 0.029$). However, Hispanic and Asian patients receive brachytherapy at similar rates to their white counterparts. Compared to patients with private insurance, those who are uninsured ($P < 0.001$) are less likely to receive brachytherapy.

Conclusions: This study reveals that racial disparities exist for those that receive brachytherapy. Patients that are uninsured or have Medicaid or Medicare insurance also do not receive brachytherapy at the same rate as those with private insurance. These data indicate