Method: Genomic data from established endometrial cancer cell lines from the Cancer Cell Line Encyclopedia (CCLE) were analyzed. Cell lines were profiled for radiation response in triplicate by using a validated high-content platform. Area under the curve (AUC) after irradiation was calculated for each cell line. A novel exon/intron junctional CRISPR/Cas9 methodology was used to knock out TP53 in targeted cell lines while maintaining the ability to complement with wildtype (exonic) TP53. Knockout was confirmed via Western blots of monoclonal isolates prior to radiation profiling. ANOVA was performed to compare AUC of knockout and complement cell lines.

Results: In total, 23 established cell lines were profiled for radiation response. Increasing SCNA were positively correlated with AUC for radiation response ($R^2 = 0.26$, $P = 0.01$). TP53 mRNA expression was not statistically different between cell lines (R^2 0.02, $P = 0.4$). In SCNA low cell lines with wildtype TP53, knockout of TP53 AUC was between 43% and 53% ($P = 0.002$). Conversely, in SCNA high cell lines containing TP53 missense mutations, knockout did not appear to alter AUC ($P > 0.5$). Complementation of wildtype restored the radiosensitive phenotype of SCNA low cell lines, but only partially conferred sensitivity in SCNA high cell lines.

Conclusion: High SCNA levels and TP53 status affect radiation response. Assessing the impact of the cancer genome on radiotherapy outcomes may create an information capability to guide individualized radiotherapy dose prescriptions.

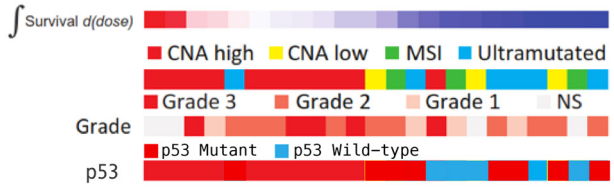

Fig. 1.

doi:10.1016/j.ygyno.2020.05.333

446 - Poster Session

From prognostication to prediction: Copy-number alterations predict poor response to radiotherapy in endometrial cancer

R. Vargas, M. Kuznicki, R. DeBernardo, M. Abazeed. *Cleveland Clinic, Cleveland, OH, USA*

Objective: Endometrial cancers with high levels of somatic copy-number alterations (SCNA) represent a poor prognostic group, frequently comprising high-grade carcinomas. To date, no studies have demonstrated a correlation between SCNA burden and response to genotoxic therapies. Herein, we examine whether high SCNA status is associated with significantly worse outcomes after radiotherapy compared to an unirradiated population, potentially indicating that SCNA is predictive of radiotherapeutic efficacy.

Method: De-identified clinical data from The Cancer Genome Atlas (TCGA) endometrial cancer cohort were analyzed. Only patients with information including stage, histology, somatic copy-number burden, and exposure to radiotherapy or chemoradiotherapy (CRT) were included. Patients who received CRT were analyzed separately from those receiving radiotherapy. SCNA values were abstracted from the fraction of genome altered estimates. ANOVA was performed to test for differences in SCNA burden between groups. Kaplan-Meier analyses were performed to determine overall survival (OS) and progression-free survival (PFS) for each cohort, stratified by median SCNA values.

Results: In total, 66 patients had genomic and treatment data available for analysis. The mean SCNA for the no therapy, radiotherapy, and CRT groups was 0.24, 0.3, and 0.31, respectively ($P = 0.62$), indicating no significant difference in SCNA burden between each cohort. In patients who received radiotherapy, high SCNA was associated with a worse PFS (HR = 0.14, $P = 0.006$) and OS (HR = 0.07, P <0.001). Similarly, patients with high SCNA receiving CRT had a worse PFS (HR = 0.12, $P = 0.04$). A difference in OS did not reach statistical significance in the CRT cohort (HR = 0.15, $P = 0.11$). Importantly, in the no treatment cohort, OS and PFS were not significantly different when comparing SCNA groups. See **Figure 1**.

Conclusion: These data indicated that SCNA burden is predictive of poor outcomes after radiotherapy, in turn explaining the poor prognosis observed in these groups. This summary genomic marker could inform the treatment of patients with endometrial cancer. Additional work to determine a biological basis for these findings is pending.

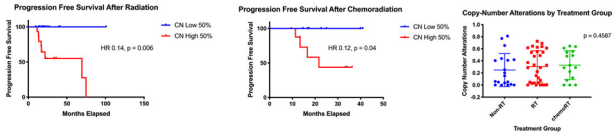

Fig. 1.

doi:10.1016/j.ygyno.2020.05.334

447 - Poster Session

Prediction of endometrial cancer recurrence by using a novel machine learning algorithm

O. Houri[a], Y. Gil[b], O. Raban[c], E. Yeoshoua[d], G. Sabah[d], A. Jakobson-Setton[e], R. Eitan[c]. *[a]Helen Schneider Hospital for Women, Rabin Medical Center, Petah Tikva, Israel, [b]Tel Aviv University, Tel Aviv, Israel, Tel Aviv, Israel, [c]Rabin Medical Center, Petah Tikva, Israel, [d]Rabin Medical Center, Sackler School of Medicine, Tel Aviv University, Petah Tikva, Israel, [e]Chaim Sheba Medical Center, Tel HaShomer, Israel*

Objective: Endometrial cancer is the most common gynecologic malignancy in the Western world. The overall risk of recurrence is associated with traditional risk factors. Their relative significance is under debate, and new molecular signatures are being looked at. We aim to evaluate whether machine learning algorithms can predict recurrence of endometrial cancer.

Method: Machine learning was used to predict recurrence among women who were diagnosed and treated for endometrial cancer between 2006 and 2014 at 1 university-affiliated medical center. Median follow-up was 5 years. The following data were retrieved from the medical records: age, chronic metabolic diseases, family and personal cancer history, hormone replacement therapy use, endometrial thickness, uterine polyp presence, laboratory results at diagnosis, CA-125 level, surgical staging, histology, depth of myometrial invasion, lymphovascular space invasion (LVSI), grade, cytology, lymph nodes metastasis and location, and adjuvant treatment. We used XGBoost algorithm, which fits the training data using decision trees and can also rate the factors according to their influence on the prediction. We assigned a weight to each class (positive/negative) to overcome potential biases due to the unbalanced nature of data. For the machine training phase, 66% of the cohort was randomly selected. We then used the rest of the samples as a test set to evaluate our model's accuracy. The test set

samples' parameters were fed into the trained model, and the predicted outcome was compared to the actual outcome.

Results: A total of 321 women were found, and 60 of them had a recurrent disease at 5 years of follow-up. The incidence outcome of recurrent disease was 18.6% for the whole cohort. On the randomly picked samples used to evaluate our model, the specificity was 75%, and the sensitivity was 89%. The most predictive parameters were white blood count, age, hemoglobin, and CA-125.

Conclusion: A state-of-the-art machine learning algorithm presented promising ability to predict recurrence of endometrial cancer. The algorithm provides an opportunity to identify at-risk patients who may benefit from adjuvant therapy, tighter surveillance, and intervention. We now plan to expand the cohort and evaluate the model in larger numbers.

doi:10.1016/j.ygyno.2020.05.335

448 - Poster Session

What is the clinical significance of grade 2 histology in patients with stage IA endometrial cancer?

D. Nelson[a], A. Nizam[a], K.K. Shih[a], W. Shan[b], B. Bustamante[a], L. dos Santos[a], M. Frimer[a], A.W. Menzin[a], A. Sakaris[a], J.S. Whyte[a], G.L. Goldberg[a]. [a]*Zucker School of Medicine at Hofstra/Northwell, New Hyde Park, NY, USA,* [b]*Hofstra - North Shore Long Island Jewish School of Medicine, Manhasset, NY, USA*

Objective: In women with FIGO stage 1A endometrioid adenocarcinoma, grade 2 histology represents an equivocal prognostic indicator. There is debate about the need for adjuvant therapy. Despite the increasing prevalence of early-stage endometrial cancer, there is ongoing uncertainty regarding the difference in outcomes of a 3-tiered histologic grading system.

Method: An Institutional Review Board-approved study identified all patients with FIGO stage 1A endometrioid adenocarcinoma treated between January 2011 and February 2019. Uterine serous and clear cell carcinomas were excluded. Demographics and outcome measures were abstracted from the medical records and tumor registry. Cox proportional hazard models, log rank tests, and comparisons of means were used to calculate significance ($P < 0.05$).

Results: Four hundred eighty-four women were identified and were eligible for evaluation; 354 (73.3%) were grade 1, 91 (18.8%) grade 2, and 38 (7.87%) grade 3. Women with grade 2 were significantly older than those with grade 1 (66 years vs 62 years, $P < 0.05$). There was no difference in age between the grade 2 and the grade 3 patients (66 years vs 66 years, $P > 0.05$). Sixteen (17.6%) patients with grade 2 pathology met standard criteria for adjuvant therapy. Sixty-nine (75.8%) patients with grade 2 pathology underwent minimally invasive surgical staging compared to 307 with grade 1 (86.8%) and 28 with grade 3 (73.7%) ($P < 0.05$). Seven (7.7%) women with grade 2 recurred within 5 years of surgical staging with 4 vaginal recurrences. Grade 2 patients have a significantly worse progression-free survival (PFS) and overall survival (OS) than grade 1 patients ($P < 0.05$) and a significantly improved PFS and OS when compared to grade 3 patients (**Figure 1**).

Conclusion: Our cohort demonstrates that patients with stage IA grade 2 endometrial cancer have a significantly different outcome profile than grade 1 and grade 3 patients. Given the differences between grade 1 and grade 3, further studies are needed to determine the relation between grade 2 and high-intermediate risk endometrial endometrioid cancer.

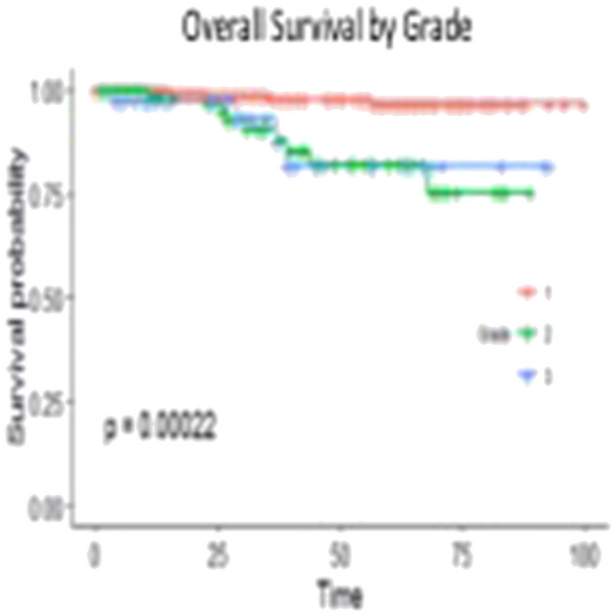

Fig. 1.

doi:10.1016/j.ygyno.2020.05.336

449 - Poster Session

What is the clinical significance of stage II endometrial cancer?

D. Nelson[a], A. Nizam[a], K.K. Shih[a], W. Shan[b], B. Bustamante[a], L. dos Santos[a], M. Frimer[a], A.W. Menzin[a], A. Sakaris[a], J.S. Whyte[a], G.L. Goldberg[a]. [a]*Zucker School of Medicine at Hofstra/Northwell, New Hyde Park, NY, USA,* [b]*Hofstra - North Shore Long Island Jewish School of Medicine, Manhasset, NY, USA*

Objective: Stage II endometrial cancer represents a dilemma for the choice of optimal management and adjuvant therapy. The prevalence of stage II endometrial cancer is much lower than both early- and more advanced-stage disease. There is a need for clear guidelines for the management of women with stage II endometrial cancer.

Method: An Institutional Review Board-approved study identified all patients with surgically staged FIGO stage II endometrial cancer treated between January 2011 and February 2019. All histologic subtypes were included. Demographics and outcome measures were abstracted from medical records and the tumor registry. Cox proportional hazard models, log rank tests, and comparisons of means were used to calculate significance ($P < 0.05$).

Results: Forty-seven (47) women were identified and were eligible for evaluation. All patients were treated with total hysterectomy, bilateral salpingo-oophorectomy, and lymph node sampling. Two patients (4.26%) declined adjuvant therapy; 5 patients (10.6%) received chemotherapy alone; 32 (68.1%) patients received radiation therapy; and 8 (17.0%) patients received both chemotherapy and radiation. Fourteen (29.8%) women recurred within the study period with the most common recurrence site being an abdominal mass or bone metastases with 3 recurrences at each of these sites. Radiation therapy and chemotherapy with radiation improved progression-free survival (PFS) and overall survival (OS) when compared to no adjuvant treatment and to chemotherapy alone ($P < 0.05$, **Figure 1**). Increasing age at time of diagnosis was an independent risk factor for PFS ($P < 0.05$). Age, grade, and race had no significant effect on OS ($P > 0.05$).

Conclusion: Our cohort demonstrates that patients with stage II endometrial cancer treated with radiation therapy or chemotherapy