Cleveland Clinic

Obstetrics, Gynecology & Women's Health Institute

3RD ANNUAL

# Research Day

**May 23, 2018**

Intercontinental Hotel &
Conference Center

3RD ANNUAL

# Obstetrics, Gynecology & Women's Health Institute

## RESEARCH DAY

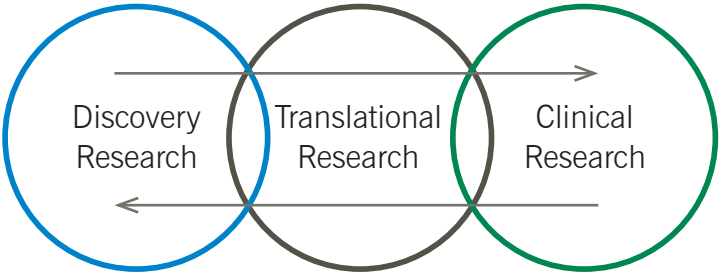
**May 23, 2018**

Intercontinental Hotel & Conference Center

Ballroom A & B

This event and research is supported in part by the donation made by two generous donors.

Cleveland Clinic




**Key Note Address & Lecture**

Maureen Phipps, MD, MPH
Chair, Department of Obstetrics and Gynecology
Women and Infants
Assistant Dean for Teaching and Research on Women's Health
at Alpert Medical School, Providence, RI

**Judges (Oral Presentations)**

Maureen Phipps, MD, MPH

Rosanne Kho, MD

Chad Michener, MD

Tommaso Falcone, MD

**Judges (Poster Presentations)**

Mark Dassel, MD

Mark Walters, MD

Beri Ridgeway, MD

Uma Perni, MD

# Agenda

| | |
|---|---|
| **7–7:30 am** | **Registration and Continental Breakfast** |
| **7:30–7:40 am** | **Introduction & Welcome**<br>Ruth Farrell, MD, MA |
| **7:40–8:40 am** | **Key Note Address**<br>***U.S. preventive services task force recommendations for women's health***<br>Maureen Phipps, MD, MPH |

| **8:40–9:10 am** | **Graduating Fellow Oral Presentations** |
|---|---|
| 8:40 am | ***Long-term pelvic organ prolapse and mesh-related outcomes following sacrocolpopexy***<br>Tonya N. Thomas, MD<br>Fellow, Female Pelvic Medicine & Reconstructive Surgery |
| 8:55 am | ***An avatar model prospectively guides the therapy of a recalcitrant cancer***<br>Roberto Vargas, MD<br>Fellow, Gynecologic Oncology |

| 9:10–9:45 am | Ballroom Foyer | Refreshment Break & PGY2 Resident Poster Presentations |
|---|---|---|

9:20 am — ***Understanding risk factors and trends in vaginal cuff dehiscence***
Dee Das, MD

9:25 am — ***Does immediate post-abortion LARC decrease rates of repeat elective abortion***
Sarah Hershman, MD

9:30 am — ***Association between hemoglobin A1c and preeclampsia diagnosis in pregestational Type 2 diabetics***
Emily Holthaus, MD

9:35 am — ***PCOS and Infertility: Is weight loss being discussed with patients?***
Christine Hur, MD

9:40 am — ***Gynecology Oncology physician barriers and perceptions of palliative care and hospice services***
Erica Newlin, MD

| 9:45–11:15 am | PGY3 Resident Oral Presentations |
|---|---|

9:45 am — ***Predictors of lynch syndrome and clinical outcomes among universally screened endometrial cancer patients***
Caitlin Carr, MD

10:00 am — ***Effects of myomas and myomectomy on assisted reproductive technology outcomes***
Chelsea Fortin, MD

| | |
|---|---|
| 10:15 am | ***Predicting embryo morphokinetic annotations from time-lapse video using convolutional neural networks***<br>Julian Gingold, MD, PhD |
| 10:30 am | ***Endometrial Fluid Profiling as a noninvasive diagnostic approach to endometriosis***<br>Natalia Llarena, MD |
| 10:45 am | ***Maternal-fetal and diagnostic characteristics of antenatal myelomeningocele: a prenatal and postnatal evaluation***<br>Jessian Munoz, MD, PhD |
| 11:00 am | ***Use of prophylactic antibiotic treatment after obstetrical anal sphincter injury: an opportunity for quality improvement***<br>Katherine Woodburn, MD |

| **11:15 am – 12:15 pm** | **Ballroom A & B** | **Innovations in Ob/Gyn Lecture** |
|---|---|---|

| | |
|---|---|
| 11:15 am–<br>12:15 pm | ***Prevention of cervical cancer in low resource settings – an opportunity to make a difference***<br>Miriam Cremer, MD, MPH |
| 12:15 pm | Presentation of Certificate to Maureen Phipps, MD, MPH |
| 12:20 pm | Foyer Group Picture – Presenters, mentors, judges, discussants, Program Directors, Drs. Farrell, Falcone, Reed and Ridgeway. |
| 12:30 pm | Adjourn |

## Past Research Day Award Winners

**Resident Poster Presentation – 1st Place**

2017 Caitlin Carr, MD
2016 Laura Moulton, DO

**Resident Oral Presentation – 1st Place**

2017 Laura Moulton, DO
2016 Jamie Stanhiser, MD

**PGY3 Resident Oral Presentation – 1st Place**

2016 Lisa Caronia Hickman, MD

**Fellow Oral Presentation – 1st Place**

2017 Kathryn Maurer, MD
2016 Linnea Goodman, MD

# Key Note Address & Lecture

## Maureen Phipps, MD, MPH

Chair, Department of Obstetrics and Gynecology, Women and Infants

Assistant Dean for Teaching and Research on Women's Health

Alpert Medical School, Providence, RI

**Maureen G. Phipps, MD, MPH,** holds the Chace-Joukowsky professorship, is chair of the Department of Obstetrics and Gynecology, and is assistant dean for Teaching and Research in Women's Health at Alpert Medical School. She is also the Executive Chief of Obstetrics and Gynecology for the Care New England Health System. She has led numerous initiatives at Brown, Women & Infants Hospital, and in Rhode Island including leading the effort for the Brown/Women & Infants Hospital National Center of Excellence in Women's Health and the Rhode Island Task Force on Preterm Birth. Her research and academic activities involve collaborations across departments, hospitals, and state agencies.

Phipps has been the principal investigator or co-investigator in numerous projects and programs funded through the National Institutes of Health and other agencies, including the Brown University National Children's Study; Women's Reproductive Health Research Scholars Program; the Children's Environmental Health Formative Center; ESCUCHE-a program to improve health and science literacy; FIT for Delivery; Project REACH, a study to prevent postpartum depression in adolescent mothers; and several other projects related to women's health in vulnerable population.

*(continued)*

Nationally, Dr. Phipps has been chair of the American College of Obstetrics and Gynecology (ACOG) Committee on Health Care for Underserved Women, is an associate editor for the American Journal of Obstetrics & Gynecology, is currently serving on the US Preventive Services Task Force, is a member of the advisory panel for ACOG's Women's Preventive Service Initiative and is a member of the Board of Directors for The American Board of Obstetrics & Gynecology (ABOG) and the Exxcellence Foundation.

Phipps has been recognized on numerous occasions as an outstanding teacher and mentor, including being recognized nationally with the ACOG Mentor Award for District I, the Council on Residency Education in Obstetrics and Gynecology Excellence in Teaching Award and the Association of Professors of Gynecology and Obstetrics Excellence in Teaching Award.

Phipps' broad interest in women's health has been geared toward improving the health of underserved women. In addition to excellence in clinical care and research, she is dedicated to training the next generation of women's health providers.

# Oral and Poster Presentation Judges

## Judges (Oral Presentations)

**Maureen Phipps, MD, MPH**
Chair, Obstetrics and Gynecology – Women and Infants
Assistant Dean for Teaching and Research on Women's Health
Alpert Medical School,
Providence, RI

**Chad Michener, MD**
Associate Professor of Surgery
Vice Chair, Gynecology
Staff, Gynecologic Oncology
Obstetrics, Gynecology & Women's Health Institute
Cleveland Clinic

**Rosanne Kho, MD**
Associate Professor of Surgery
Section Head, Benign Gynecologic Surgery
Obstetrics, Gynecology & Women's Health Institute
Cleveland Clinic

**Tommaso Falcone, MD**
Professor of Surgery &
Chair, Obstetrics, Gynecology and Women's Health Institute
Cleveland Clinic

# Oral and Poster Presentation Judges

## Judges (Poster Presentations)

**Mark Dassel, MD**
Director, Minimally Invasive Gynecologic Surgery
Obstetrics, Gynecology & Women's Health Institute
Cleveland Clinic

**Mark Walters, MD**
Professor of Surgery & Staff
Obstetrics, Gynecology & Women's Health Institute
Cleveland Clinic

**Beri Ridgeway, MD**
Assistant Professor of Surgery &
Vice Chair, Regional Ob/Gyn
Obstetrics, Gynecology & Women's Health Institute
Cleveland Clinic

**Uma Perni, MD**
Associate Professor of Surgery & Staff, Maternal Fetal Medicine
Obstetrics, Gynecology & Women's Health Institute
Cleveland Clinic

Obstetrics, Gynecology & Women's Health Institute
Graduating Fellows

# Oral Presentations

# Long-term pelvic organ prolapse and mesh-related outcomes following sacrocolpopexy

*Tonya N. Thomas, MD*

**Objective:** To describe and compare the objective and subjective prevalence of recurrent pelvic organ prolapse (POP) and mesh-related complications after open, robotic, and laparoscopic sacrocolpopexy and to describe patient-reported post-operative outcomes.

**Methods:** This is a retrospective cohort study with a cross-sectional, prospective survey. Participants were identified by Current Procedural Terminology code for open or minimally invasive colpopexy performed between January 2004 and December 2014. The electronic medical record was queried for demographic, perioperative, and follow-up data. Consenting participants were surveyed concerning complications, treatments, and symptoms.

**Results:** Seven hundred nine participants met inclusion criteria. Of the participants, 183, 173, and 353 underwent open, robotic, and laparoscopic sacrocolpopexy, respectively. Median time from sacrocolpopexy to last follow-up visit for all participants was 0.5 years (2 days-13.4 years). 11.6% (n=80) experienced stage 2 or greater recurrent POP, and 4.7% (n=33) underwent retreatment with pessary (n=4) or surgery (n=29). 15% (n=104) experienced recurrent stage 2 or greater POP or retreatment, with higher prevalence in the robotic group (n=35, 21.1%; p=0.03) due to higher retreatment (n=15, 8.7%; p=0.01). 5.2% (n=37) of participants experienced mesh and/or suture exposure (mesh n=19, suture n=10, mesh and suture n=8) with no significant difference between groups (open n=14, 7.7%; robotic n=6, 3.5%, laparoscopic n=17, 4.8%; p=0.19). 29.7% (n=11) required office excision, and 64.9% (n=24) required surgical treatment. Six cases involved erosion of mesh (n=3) and/or permanent suture (n=5) into the bladder. Survey response rate was 41.7% (n=296). Survey outcomes are shown in the table. Median time from sacrocolpopexy to survey completion was 6.5 (1.6-13.4) years. 88% (n=258) of respondents reported improvement since surgery. 37.5% (n=109) reported complications or problems related to surgery, and 8.4% (n=25) and 4.4% (n=13) reported complications related to recurrent POP or mesh exposure, respectively. 9.2% (n=27) reported evaluation or treatment for recurrent POP. 6.9% (n=20) reported evaluation or

treatment for mesh exposure. 5 respondents reported reoperation for POP, and 12 reported reoperation for mesh exposure.

**Conclusions:** This initial analysis shows that excision of an endometrioma does significantly alter the levels of circulating pro-inflammatory cytokines. This leads to an increase in cytokines which can activate a diffuse inflammatory response which could have potential negative implications on ovarian function and egg quantity.

**Survey Outcomes**

| | All Survey Respondents (N=296) | Open (N=50) | Robotic (N=80) | Laparo-scopic (N=166) | P value |
|---|---|---|---|---|---|
| Time from surgery to survey (years) | 6.5 (1.6-13.4) | 10.1 (2.5-13.4) | 5.4 (2.0-10.8) | 6.4 (1.6-13.0) | <0.0001† |
| Patient Global Impression of Improvement Scale Missing N=3 | | | | | 0.44‡ |
| Very much better | 131 (44.7) | 15 (30.0) | 35 (44.3) | 81 (49.4) | |
| Much better | 92 (31.4) | 19 (38.0) | 23 (29.1) | 50 (30.5) | |
| A little better | 35 (11.9) | 10 (20.0) | 9 (11.4) | 16 (9.8) | |
| No change | 19 (6.5) | 4 (8.0) | 6 (7.6) | 9 (5.5) | |
| A little worse | 5 (1.7) | 1 (2.0) | 3 (3.8) | 1 (0.6) | |
| Much worse | 8 (2.7) | 1 (2.0) | 2 (2.5) | 5 (3.1) | |
| Very much worse | 3 (1.0) | 0 | 1 (1.3) | 2 (1.2) | |
| Looking back, would have surgery again Missing N=5 | 271 (93.1) | 48 (98.0) | 70 (89.7) | 153 (93.3) | 0.20‡ |
| Any surgical complication or problem Missing N=5 | 109 (37.5) | 18 (36.0) | 31 (39.2) | 60 (37.0) | 0.92‡ |
| POP recurrence complication | 25 (8.4) | 4 (8.0) | 8 (10.0) | 13 (7.8) | 0.84‡ |
| Mesh exposure complication | 13 (4.4) | 3 (6.0) | 1 (1.3) | 9 (5.4) | 0.27‡ |
| Evaluated or treated for POP Missing N=4 | 27 (9.2) | 3 (6.3) | 10 (12.5) | 14 (8.5) | 0.44‡ |

*(continued)*

| | All Survey Respondents (N=296) | Open (N=50) | Robotic (N=80) | Laparo-scopic (N=166) | P value |
|---|---|---|---|---|---|
| POP evaluated or treated by a different provider or hospital Missing N=1 (26/27) | 11 (42.3) | 2 (66.7) | 4 (40.0) | 5 (38.5) | 0.66‡ |
| POP treatments* | | | | | |
| Observation | 12 (44.4) | 2 (66.7) | 4 (40.0) | 6 (42.9) | 0.71‡ |
| Pessary | 3 (11.1) | 0 | 3 (30.0) | 0 | 0.06‡ |
| Surgery | 5 (18.5) | 1 (33.3) | 3 (30.0) | 1 (7.14) | 0.29‡ |
| Evaluated or treated for mesh exposure | 20 (6.9) | 3 (6.0) | 3 (3.9) | 14 (8.6) | 0.38‡ |
| Mesh evaluated or treated by a different provider or hospital Missing N=1 (19/20) | 11 (57.9) | 3 (27.3) | 1 (33.3) | 7 (53.9) | 0.22‡ |
| Mesh treatments* | | | | | |
| Observation | 3 (15.0) | 0 | 2 (66.7) | 1 (7.1) | 0.02‡ |
| Vaginal estrogen | 7 (35.0) | 1 (33.3) | 0 | 6 (42.9) | 0.37‡ |
| Surgery | 12 (60.0) | 3 (100.0) | 1 (33.3) | 8 (57.1) | 0.23‡ |

Data are median (range), or n (%)
*total % may not equal 100 due to multiple treatments or other treatments not listed
†Kruskal-Wallis
‡Pearson chi-square

**Conclusions:** Objective and subjective long-term prevalence of recurrent POP and mesh-related complications are low following sacrocolpopexy by all routes. Participants who underwent robotic sacrocolpopexy may have a higher prevalence of retreatment for recurrent POP.

**Funding:** None

Faculty Mentor: Cecile Unger, MD, MPH

## An avatar model prospectively guides the therapy of a recalcitrant cancer

*Roberto Vargas, MD*

**Objective:** There has been little progress in the use of patient-derived xenografts (PDX) to guide individual therapeutic strategies. Inherent obstacles to their use in clinical care include engraftment time of tumors limiting their applicability to actual patient care, in addition to concerns for tumor fidelity as compared to the human host. A viable model to guide therapy and study tumor evolution in aggressive and highly chemo-resistant tumors, such as clear cell carcinoma, would be invaluable. Our objective was to determine if a 3x1x1 PDX-based model could be used to guide therapy in a concurrent (co-clinical) manner in the setting of stage IV clear cell carcinoma (CCC).

**Methods:** Under an IRB/IACUC approved protocol, processed tumor was injected into NSG mice. Tumors were allowed to grow until 300 mm3 in size, at which time the mice were then randomized into treatment groups. Mice were randomized to receive therapy with gemcitabine (GEM), cisplatin (CDDP), paclitaxel (TAX), nivolumab (NIVO), and/or neratinib (NER) in a longitudinal manner. Mice receiving nivolumab also received injections of peripheral blood lymphocytes. PDX-tumors were harvested and genomic material extracted for DNA/RNA analysis. Paraffin-embedded samples were obtained for hematoxylin-eosin and immunohistochemistry, to confirm morphologic similarity and Her2 expression.

**Results:** Tumor engraftment was noted within 10 days. The donor and PDX tumors were subjected to genome-wide gene expression profiling, which demonstrated high transcriptomic concordance (Pearson r= 0.94). ERBB2 gene amplification was confirmed in the PDX (copy number estimate of 7.9) which correlated with IHC/FISH of the primary tumor. After engraftment, the PDX sample was passaged into four cohorts that received treatment in parallel. Results confirmed CDDP resistance, and activity of single agent GEM, TAX, and NER. The patient ultimately received GEM/NIVO as primary therapy, thus treatment with this combination was continued in the PDX until resistance developed. Treatment-resistant PDX tumors were then randomized to receive TAX, NER, or both. The combination of TAX/NER demonstrated greater tumor

activity than TAX alone. Neratinib was continued in a maintenance fashion with tumor suppression until discontinued. The patient subsequently progressed and received TAX/NER with a partial response in known tumor sites.

**Conclusions:** PDX response correlated with patient response in the first and second line settings and predicted development of resistance to first line therapy before it was observed in the clinical setting. Using next generation sequencing technologies Her2/neu amplification was identified and confirmed to be an actionable target with in-vivo activity. Our model highlights truly personalize cancer therapy with the potential to improve patient outcomes in rare and aggressive disease, with co-clinical PDX-based treatment strategies incorporating genomic data.

**Funding:** None

Faculty Mentor: Mohamed Abazeed, MD, PhD

PGY2 Obstetrics & Gynecology Residents

# Poster Presentations

### Understanding risk factors and trends in vaginal cuff dehiscence

Faculty Mentor: Chad Michener, MD

*Deepanjana Das, MD*

### Does immediate post-abortion LARC decrease rates of repeat elective abortion?

Faculty Mentor: Mitchell Reider, MD

*Sarah Hershman, MD*

### Association between hemoglobin A1c and Preeclampsia diagnosis in pregestational Type 2 diabetics

Faculty Mentor: Katherine Singh, MD

*Emily Holthaus, MD*

### PCOS and Infertility: Is weight loss being discussed with patients?

Faculty Mentor: Rebecca Flyckt, MD

*Christine Hur, MD*

### Gynecology Oncology physician barriers and perceptions of palliative care and hospice services

Faculty Mentor: Chad Michener, MD

*Erica Newlin, MD*

PGY3 Obstetrics & Gynecology Residents

# Oral Presentations

# Predictors of Lynch syndrome and clinical outcomes among universally screened endometrial cancer patients

*Caitlin Carr, MD*

**Objective:** To determine the clinicopathologic characteristics associated with a probable diagnosis of Lynch syndrome (LS) among patients undergoing universal LS screening.

**Methods:** (Study design, participants, outcome measures, and, in the case of a negative study, statistical power): IRB approved single institution prospective analysis. From August 2012 to August 2015, all patients diagnosed with EC underwent screening for LS using immunohistochemistry (IHC) staining for MMR proteins: MLH1, PMS2, MSH2, and MSH6. Tumors with lack of expression of PMS2 or MLH1 were assessed for MLH1 promotor methylation. Tumors were classified as MMR-I (intact expression of MMR proteins), MMR-DM (MMR-deficient due to MLH1 methylation), and MMR-DU (MMR-deficient without MLH1 methylation). Patients with MMR-DU were offered genetic counseling, and germline genetic testing was conducted at a commercial laboratory where appropriate. Clinical and pathologic factors predictive of MMR-DU were evaluated using univariate and multivariate analysis. Overall survival (OS) and progression-free survival (PFS) were assessed using Cox proportional hazards for patients with at least 2 years of follow-up.

**Results:** Among 723 patients who underwent universal screening, 522 (72.2%) were MMR-I and 168 (23.2%) were MMR-DM. A total of 33 patients (4.6%) had MMR-DU. Of 27 patients who underwent genetic testing, 12 (44.4%) were confirmed to have LS. On multivariate analysis, clinical factors independently associated with MMR-DU included younger age (OR = 0.97, CI 0.92–1.01, P < 0.0008) and lower BMI (OR = 0.89, CI 0.84–0.95, P = 0.0017). In addition, MMR-DU tumors were more likely to be grade 3 or grade 2 versus grade 1 (OR = 4.67, CI 1.51–14.5; OR = 79.25, CI 18.42–340.98, respectively, P < 0.0001), endometrioid histology (OR = 1.51, 0.92–2.50, P = −0.046), <50% myometrial invasion (OR = 6.65, CI 1.56–28.3, P = 0.037), and <2 cm tumor size (OR = 2.18, CI 0.80–5.89, P = 0.014). Family history, menopausal status, race, lymphovascular space invasion, and stage were not predictive of

MMR-DU status. There was no difference in overall survival or progression-free survival based on MMR or LS status (P = NS).

**Conclusions:** Application of clinical and pathologic criteria may help stratify patients at highest risk for LS among those undergoing universal screening. These factors may be used to develop a risk prediction model to guide clinical counseling and genetic testing

**Funding:** None

Faculty Mentor: Miriam AlHilli, MD
Disscussant: Laura Moulton, DO

## Effects of myomas and myomectomy on assisted reproductive technology outcomes

*Chelsea Fortin, MD*

**Objective:** To determine the effects of fibroids, and their removal, on assisted reproductive technology (ART) outcomes.

**Methods:** Single institution retrospective cohort study of infertility patients who underwent myomectomy prior to initiation of either in vitro fertilization (IVF) or intrauterine insemination (IUI) between August 2006 and October 2015 (N=49). Two separate control groups were established: 1) women with fibroids left in situ during the ART process (N=76), and 2) women with no fibroids (N=103). Women met inclusion criteria if they were ≤45 years old and undergoing ART with at least 18 months of follow-up with attempts to conceive. The study was powered to detect a difference between a 42%, 11%, and 25% live birth rate in the myomectomy, fibroids in situ, and no fibroids groups at $p<0.05$.

**Results:** Women in the no fibroids group were significantly younger and more likely to be Caucasian than those in the myomectomy or in situ groups (36.3 years vs. 37.6 years vs. 37.2 years, $p= 0.026$; Caucasian 97.1% vs. 46.8% vs. 76.3%, $p<0.001$). There were no significant differences in IVF cycle parameters between groups. Fibroids that were either submucosal or intramural

with associated cavity distortion were significantly more likely to be removed. Amongst women undergoing IVF, the cumulative incidence of clinical pregnancy (CP) was significantly higher in the myomectomy group than the in situ or no fibroids groups. Women who underwent pre-IVF myomectomy also achieved CP more quickly. Cumulative LB rates did not differ significantly amongst women undergoing IVF. CP and LB rates per cycle were similar between myomectomy, in situ, and no fibroids groups (CP 49% vs. 37.5% vs. 54.4%, p=0.21; LB 41.7% vs. 27.1% vs. 43.9%, p=0.17). These outcomes remained similar after adjusting for confounding variables.

**Conclusions:** IVF outcomes appear to be improved by judicious removal of clinically significant fibroids. Further prospective studies are required to confirm the role of fibroids, and their removal, on ART outcomes before advocating for routine myomectomy amongst women with fibroids undergoing ART.

**Funding:** None

Faculty Mentor: Tommaso Falcone, MD
Discussant, Emily Nacy, MD

## Predicting embryo morphokinetic annotations from time-lapse video using convolutional neural networks

*Julian Gingold, MD, PhD*

**Objective:** To identify morphokinetic parameters of developing human embryos with neural networks trained on time-lapse video.

**Methods:** We performed a retrospective cohort study with IRB approval on 1309 embryos from 113 patients undergoing in vitro fertilization from 2014-2016 at the Cleveland Clinic Fertility Center.

Embryos were imaged from 18-140 hours post-fertilization every 15 minutes using an EmbryoScope® incubator. An embryologist recorded the earliest time an embryo met each developmental milestone, including beginning of

observation (tStart), breakdown of the pronuclei (tPN), appearance of 2 cells (t2), 3 cells (t3), 4 cells (t4), 5 cells (t5), 8 cells (t8), partially compacting embryo (t9+), morula (tM), start of blastulation (tSB), blastulation (tBL), expanded blastocyst (tEB) and hatching blastocyst (tHB). Annotations for frames between transition times were interpolated.

Models were divided as training/validation/test sets with 93/10/10 patients, respectively. A convolutional neural network was trained on the first 70 hours of each embryo to predict the first 6 morphokinetic stages (remaining stages condensed to t4+) using a ResNet architecture. Monotonicity of progression through developmental stages was enforced through a dynamic programming (DP) postprocessing step. Additional models incorporating surrounding video frames (early fusion) or more distant frames (late fusion) as well as time post-fertilization were constructed. Per frame accuracy of predictions, mean absolute error (MAE) and root mean squared error (RMSE) were computed for each model variation.

**Results:** Video frames were distributed across classes as 10.3%, 5.3%, 19.4%, 4.5%, 19.8%, and 40.7% for tStart through t4+, respectively. A per-frame ResNet model successfully classified frames into the appropriate developmental stage with 82% accuracy. After incorporating a late fusion model including the 14 surrounding frames, we achieved 84% accuracy, which improved to 87% following DP postprocessing (MAE 8.594, RMSE 24.334).

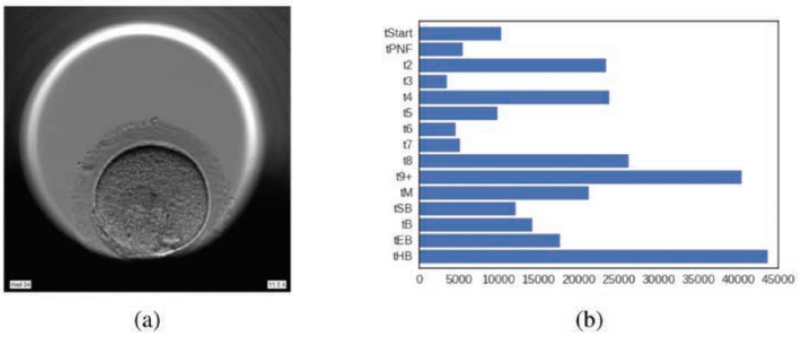



***Figure 1.*** *Left (a) sample frame from an EmbryoScope (public image), and right b) summary statistics on the number of frames assigned to each stage of development in human annotations.*

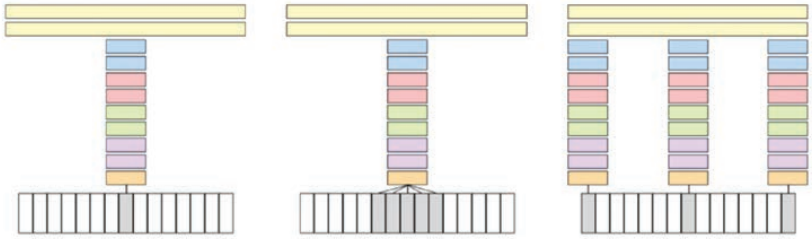


***Figure 2.*** *Model architectures: single (left), early-fusion (center), late-fusion (right).*

| | | | DP: label likelihood s.t. monotonicity | | | DP: earthmover's distance s.t. monotonicity | | |
|---|---|---|---|---|---|---|---|---|
| **Model** | **Frames** | **Raw Acc.** | **Accuracy** | **MAE** | **RMSE** | **Accuracy** | **MAE** | **RMSE** |
| ResNet50 | 1 | 0.8200 | 0.8460 | 11.225 | 29.650 | 0.8368 | 11.115 | 28.899 |
| Early Fusion | 3 | 0.8237 | 0.8448 | 10.555 | 27.370 | 0.8397 | 10.687 | 27.962 |
| Early Fusion | 9 | 0.8252 | 0.8423 | 10.927 | 29.400 | 0.8362 | 10.808 | 28.375 |
| Early Fusion | 15 | 0.8182 | 0.8456 | 10.935 | 27.719 | 0.8364 | 11.242 | 27.756 |
| Early Fusion + time | 9 | 0.8343 | 0.8430 | 11.152 | 26.231 | 0.8388 | 11.068 | 25.979 |
| Early Fusion + time | 15 | 0.8420 | 0.8446 | 10.761 | 26.849 | 0.8411 | 10.904 | 26.701 |
| Late Fusion | 15 | **0.8479** | 0.8676 | 8.963 | 24.756 | **0.8708** | **8.594** | **24.334** |

***Table 1.*** *Quantitative results for various architectures and output decoding schemes*

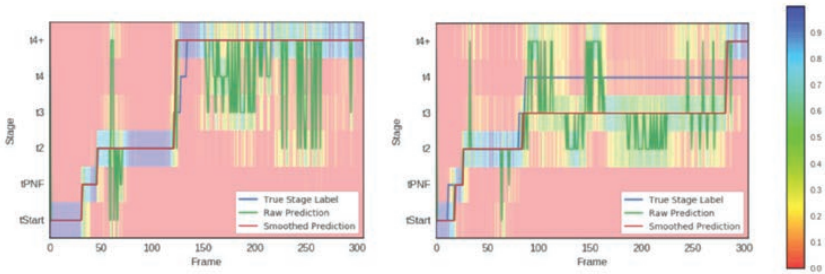



***Figure 3.*** *DP decoders smooth predictions. On left, smoothing significantly reduces the error caused by the model's uncertainty in later stages.*

**Conclusions:** Convolutional neural networks can predict morphokinetic annotations of early embryo development directly from time-lapse video with high frame-level accuracy. Future work will refine these models to predict later developmental annotations as well as implantation potential.

**Funding:** None

Faculty Mentor: Nina Desai, PhD, HCLD
Discussant, Alex Kotlyar, MD

## Endometrial fluid profiling as a noninvasive diagnostic approach to endometriosis

*Natalia Llarena, MD*

**Objective:** To compare growth factor and cytokine profiles in endometrial secretions of patients with and without endometriosis to determine whether a particular protein profile may be predictive of the disease.

**Methods:** This study included 58 premenopausal patients undergoing abdominal or laparoscopic gynecologic surgery for benign indications. Prior to surgery, 0.5 mL of endometrial fluid were aspirated with a Wallace catheter. Multiplex immunoassay was used to quantify 7 cytokines and growth factors. During surgery, each patient was staged according to the American Society for Reproductive Medicine staging system for endometriosis. Patients were divided into two groups: no disease or stage 1-2 endometriosis, and stage 3-4 disease. Cytokines and growth factors were evaluated using Student's t-test and 1-way ANOVA for normally distributed continuous data, and the Mann Whitney and Kruskal-Wallis tests for non-normally distributed data. Combinations of cytokines were evaluated using logistic regression analysis.

**Results:** Endometrial fluid was aspirated from 58 patients. 29 patients had none or stage I-2 endometriosis, and 14 had stage 3-4 disease. There were no significant differences in demographic factors between groups. All 7 cytokines were detected in endometrial fluid samples. IL-1B was found to be significantly elevated in the endometrial secretions of women with stage 3-4 endometriosis compared to women with none – stage 2 endometriosis (17 + 25.8 pg/mL

versus 2.4 + 6.2 pg/mL, p = 0.004). A receiver operating curve was generated demonstrating an area under the curve of 0.78. Using a threshold value of IL-1B greater than 1.6 pg/mL, the presence of IL-1B in endometrial secretions has a sensitivity of 75% and specificity of 79% for the diagnosis of stage 3-4 endometriosis.

**Conclusions:** Aspiration of endometrial fluid is a safe and effective approach for evaluating the endometrial profile of women with endometriosis. The presence of IL-1B in endometrial secretions is a predictor of stage 3-4 endometriosis and may have potential as a screening tool for the diagnosis of moderate to severe endometriosis.

**Funding:** None

Faculty Mentor: Rebeca Flyckt, MD
Discussant, Thanh Ha Luu, MD

## Maternal-fetal and diagnostic characteristics of antenatal myelomeningocele: A prenatal and postnatal evaluation

*Jessian Munoz, MD, PhD*

**Objective:** In this study we aimed to identify maternal, fetal and diagnostic characteristics associated with pregnancy and pediatric outcomes.

**Methods:** A retrospective cohort analysis was performed with patients who had presented to the Cleveland Clinic Fetal Care Center between2005-2017. Infants were followed up at an interdisciplinary myelomeningocele pediatrics clinic.

**Results:** Our data showed 40% of patients with antenatal diagnosed Myelomeningocele elected for second trimester terminations vs. 60% who chose to continue their pregnancy and deliver either by cesarean section or vaginal delivery. Maternal body mass index was significantly higher in those who continued pregnancies (p=0.036). In addition, the fetal diagnostic methods chosen by patients was significantly different. Those who elected to terminate were more likely to pursue amniocentesis instead of MRI characterization of the fetus (p=0.030). MRI and Ultrasound varied in

correlation with physical exam at time of birth and surgery.

**Conclusions:** While no differences were detected in demographics, pregnancy outcomes or pediatric outcomes, it was noted the majority of patients developed neurogenic bladders irrespective of lesion level. In our cohort, pregnancies complicated by MMC did not vary in morbidity and pediatric outcomes remain similar regardless of level of lesion. This data provides additional information for the counseling of patients when faced with this antenatal diagnosis.

**Funding:** None

Faculty Mentor: Katherine Singh, MD
Discussant, Sarah Steele, MD

## Use of prophylactic antibiotic treatment after obstetrical anal sphincter injury: An opportunity for quality improvement

*Katherine Woodburn, MD*

**Objective:** To describe the rate of prophylactic antibiotic usage in obstetrical anal sphincter injury in the Cleveland Clinic system and determine risk factors for patients not receiving appropriate antibiotic prophylaxis.

**Methods:** This is a retrospective chart review of all patients who delivered vaginally within the Cleveland Clinic system between July 2016 and December 2017 with a documented obstetric anal sphincter injury. Patients were identified by EMR documented 3$^{rd}$ or 4$^{th}$ degree lacerations. Delivery details and patient demographics were analyzed.

**Results:** 216 patients met inclusion criteria, with 47 (21.8%) receiving a dose of postpartum antibiotics for OASIS. 112 patients (51.9%) received at least 1 dose of antibiotics during labor or in the postpartum period for any reason.

Comparing patients who received OASIS prophylaxis to those who did not, there were no statistical differences between location of delivery, maternal age, gestational age at delivery, maternal BMI, parity, duration of second stage or fetal birth weight. Patients who received OASIS prophylaxis had a higher average estimated blood loss (400 to 350, $p<0.001$) and a repair more likely

to be done in the delivery room (OR 9.6 (2.4, 38.9) $p<0.001$). The higher degree the laceration, the greater likelihood patients received OASIS prophylaxis [3C/4th OR 9.2 (3.7,23.3) and 3B OR 4.9 (2.0, 11.9)) $p<0.001$].

Though not statistically significant, patients undergoing TOLAC (OR 1.5 (0.44,4.9)), a shoulder dystocia (OR 1.7 (0.56,5.2)), or postpartum hemorrhage (OR 1.06 (0.48,2.3)), were more likely to receive OASIS prophylaxis. Patients delivered at night (OR1.1(0.60,2.2)) or on a holiday (OR1.2(0.12,11.8)) were also more likely to receive OASIS prophylaxis, but this was not statistically significant. Patients who had an episiotomy (OR 0.93 (0.35, 2.4)) or an operative delivery (OR 0.71 (0.35, 1.5)) were not more likely to receive OASIS prophylaxis. Patients with midwife involvement in delivery were more likely to receive OASIS prophylaxis (OR 2.0 (0.83,4.8)) while resident involvement showed no benefit (OR 0.89 (0.47, 1.7).

**Conclusions:** The most recent guidelines by ACOG recommend, with Grade A evidence, the administration of a single dose of antibiotic at the time of repair for OASIS. Our institution is compliant with this recommendation in less than one quarter of the time. Using trends seen in appropriate OASIS prophylaxis over the past 2 years, we may be able to increase our compliance through simple but high yield interventions.

**Funding:** None

Faculty Mentor: Kenneth Edelman, MD and Ruth Farrell, MD, MA
Discussant, Sarah Steele, MD

2016–2017

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