

# Vaginal morphology and position associated with prolapse recurrence after vaginal surgery: a secondary analysis of the DEMAND study

Shaniel T. BOWEN<sup>1</sup>, Pamela A. MOALLI<sup>2</sup>, Steven Abramowitch<sup>2</sup>, Douglas Luchristt<sup>3</sup>, Isuzu MEYER<sup>4</sup>, Charles Rardin<sup>5</sup>, Heidi S. HARVIE<sup>6</sup>, Michael E. HAHN<sup>7</sup>, Donna MAZLOOMDOOST<sup>8</sup>, Pooja IYER<sup>9</sup>, Benjamin CARPER<sup>10</sup>, and Marie G. GANTZ<sup>10</sup>

<sup>1</sup>University of Pittsburgh Swanson School of Engineering

<sup>2</sup>University of Pittsburgh Department of Bioengineering

<sup>3</sup>Duke University Department of Obstetrics and Gynecology

<sup>4</sup>The University of Alabama at Birmingham Heersink School of Medicine

<sup>5</sup>Brown University Warren Alpert Medical School

<sup>6</sup>University of Pennsylvania Perelman School of Medicine

<sup>7</sup>University of California San Diego Department of Radiology

<sup>8</sup>National Institute of Child Health and Human Development

<sup>9</sup>PPD Incorporated

<sup>10</sup>RTI International Social Statistical and Environmental Sciences Unit

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## Abstract

**Objective:** To identify postoperative vaginal morphology and position factors associated with prolapse recurrence following vaginal surgery. **Design:** Secondary analysis of MRIs of the Defining Mechanisms of Anterior Vaginal Wall Descent cross-sectional study. **Setting:** Eight clinical sites in the US Pelvic Floor Disorders Network. **Population:** Women who underwent vaginal mesh hysteropexy (hysteropexy) with sacrospinous fixation or vaginal hysterectomy with uterosacral ligament suspension (hysterectomy) for symptomatic uterovaginal prolapse between April 2013 and February 2015. **Methods:** MRIs (rest, strain) obtained 30-42 months after surgery, or earlier for participants with recurrence who desired reoperation prior to 30 months, were analyzed. Prolapse recurrence was defined as prolapse beyond the hymen at strain on MRI. Vaginal segmentations (at rest) were used to create 3D models placed in a morphometry algorithm to quantify and compare vaginal morphology (angulation, dimensions) and position between groups. **Main Outcome Measures:** Vaginal angulation (upper, lower, and upper-lower vaginal angles in the sagittal and coronal plane), dimensions (length, maximum transverse width, surface area, volume), and position (apex, mid-vagina) at rest. **Results:** Of the 82 women analyzed, 12/41 (29%) in the hysteropexy group and 22/41 (54%) in the hysterectomy group had prolapse recurrence. After hysteropexy, recurrences had a more laterally deviated upper vagina ( $p=0.02$ ) at rest than successes. After hysterectomy, recurrences had a more inferiorly (lower) positioned vaginal apex ( $p=0.01$ ) and mid-vagina ( $p=0.01$ ) at rest than successes. **Conclusions:** Vaginal angulation and position were associated with prolapse recurrence and indicative of vaginal support mechanisms related to surgical technique and unaddressed anatomical defects. Future prospective studies in women before and after prolapse surgery may distinguish these two factors. **Funding:** Eunice Kennedy Shriver National Institute of Child Health and Human Development-sponsored Pelvic Floor Disorders Network (Grant/Award Number: U10 HD054214, U10 HD041267, U10 HD041261, U10 HD069013, U10 HD069025, U10 HD069010, U10 HD069006, U10 HD054215, U01 HD069031); National Institutes of Health Office of Research on Women's Health; Boston Scientific Corporation; National Academies of Sciences, Engineering, and Medicine's Ford Foundation Predoctoral Fellowship

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Vaginal morphology and position associated with prolapse recurrence after vaginal surgery: a secondary analysis of the DEMAND study

**LIST OF AUTHORS:**

Shaniel T. BOWEN, MS<sup>1\*</sup>; Pamela A. MOALLI, MD, PhD<sup>1,2\*</sup>; Steven D. ABRAMOWITCH, PhD<sup>1</sup>; Douglas H. LUCHRISTT, MD, MPH<sup>3</sup>; Isuzu MEYER, MD, MSPH<sup>4</sup>; Charles R. RARDIN, MD, FACOG, FACS<sup>5</sup>; Heidi S. HARVIE, MD, MSCE, MBA<sup>6</sup>; Michael E. HAHN, MD, PhD<sup>7</sup>; Donna MAZLOOMDOOST, MD, FACOG<sup>8</sup>; Pooja IYER, MPH<sup>9</sup>; Benjamin CARPER, MS<sup>10</sup>; Marie G. GANTZ, PhD<sup>10</sup>; for the NICHD PELVIC FLOOR DISORDERS NETWORK

**AUTHOR AFFILIATIONS:**

<sup>1</sup>Department of Bioengineering, University of Pittsburgh, Pittsburgh, PA

<sup>2</sup>Department of Obstetrics, Gynecology & Reproductive Sciences, University of Pittsburgh Medical Center, Magee Women's Research Institute, Pittsburgh, PA

<sup>3</sup>Division of Urogynecology, Department of Obstetrics and Gynecology, Duke University School of Medicine, Durham, NC

<sup>4</sup>Division of Urogynecology and Pelvic Reconstructive Surgery, University of Alabama at Birmingham, Birmingham, AL

<sup>5</sup>Division of Urogynecology, Alpert Medical School of Brown University, Providence, RI

<sup>6</sup> Division of Urogynecology and Pelvic Reconstructive Surgery, Department of Obstetrics and Gynecology, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA

<sup>7</sup>Department of Radiology, University of California, San Diego, La Jolla, California, USA

<sup>8</sup>*Eunice Kennedy Shriver* National Institute of Child Health and Human Development, National Institutes of Health, Bethesda, MD

<sup>9</sup>Biostatistics Division, PPD Incorporated, San Francisco, CA

<sup>10</sup>Social, Statistical, and Environmental Sciences, RTI International, Research Triangle Park, NC

\*co-first authors

**CORRESPONDING AUTHOR:**

Pamela A. Moalli, MD, PhD

Professor of Obstetrics and Gynecology

Division of Urogynecology and Reconstructive Pelvic Surgery

Magee Women's Hospital of the University of Pittsburgh

Magee Women's Research Institute

204 Craft Avenue, A320

Pittsburgh, PA 15213

Phone: 412-641-6052

Fax: 412-641-3580

Email: moalpa@upmc.edu

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**Setting:** Eight clinical sites in the US Pelvic Floor Disorders Network.

**Population:** Women who underwent vaginal mesh hysteropexy (hysteropexy) with sacrospinous fixation or vaginal hysterectomy with uterosacral ligament suspension (hysterectomy) for symptomatic uterovaginal prolapse between April 2013 and February 2015.

**Methods:** MRIs (rest, strain) obtained 30-42 months after surgery, or earlier for participants with recurrence who desired reoperation prior to 30 months, were analyzed. Prolapse recurrence was defined as prolapse beyond the hymen at strain on MRI. Vaginal segmentations (at rest) were used to create 3D models placed in a morphometry algorithm to quantify and compare vaginal morphology (angulation, dimensions) and position between groups.

**Main Outcome Measures:** Vaginal angulation (upper, lower, and upper-lower vaginal angles in the sagittal and coronal plane), dimensions (length, maximum transverse width, surface area, volume), and position (apex, mid-vagina) at rest.

**Results:** Of the 82 women analyzed, 12/41 (29%) in the hysteropexy group and 22/41 (54%) in the hysterectomy group had prolapse recurrence. After hysteropexy, recurrences had a more laterally deviated upper vagina ( $p=0.02$ ) at rest than successes. After hysterectomy, recurrences had a more inferiorly (lower) positioned vaginal apex ( $p=0.01$ ) and mid-vagina ( $p=0.01$ ) at rest than successes.

**Conclusions:** Vaginal angulation and position were associated with prolapse recurrence and indicative of vaginal support mechanisms related to surgical technique and unaddressed anatomical defects. Future prospective studies in women before and after prolapse surgery may distinguish these two factors.

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angulation, dimension, hysterectomy, hysteropexy, MRI, pelvic organ prolapse, position, prolapse recurrence, vagina, vaginal angle, vaginal mesh

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### INTRODUCTION (394/400 words):

Vaginal morphology (angulation, dimensions) and position are key indicators and determinants of pelvic organ support. Restoration of normal vaginal anatomy and apical support is believed necessary for successful repair of pelvic organ prolapse (POP). Normally, the lower vagina is nearly vertical, the upper vagina is more horizontal and directed posteriorly towards the sacral hollow, and the angle between the upper and lower vagina is approximately  $160^\circ$  in older parous women. Surgical repair of POP often abnormally alters vaginal anatomy, which may increase the risk of prolapse recurrence.

Magnetic resonance imaging (MRI) has been used to assess vaginal anatomy following prolapse surgery. However, little is known about how vaginal morphology and position relate to prolapse recurrence after POP repair. In our previous work, the *Defining Mechanisms of Anterior Vaginal Wall Descent (DEMAND)* study, we showed that apical descent and—to a lesser extent—anterior vaginal wall (AVW) elongation were mechanisms of prolapse recurrence following vaginal surgery. Results suggested that these mechanisms may involve postoperative changes in vaginal angulation and position (i.e., posterior-inferior deviation and straightening of the vagina) that can promote vaginal mobility/distensibility by making the AVW more susceptible to descent and elongation—especially with an enlarged genital hiatus (GH).

As the primary DEMAND study and similar works were limited to 2D vaginal analysis, this study assessed vaginal morphology and position in 3D to gain more comprehensive insight into the relationship between vaginal anatomy and prolapse recurrence after vaginal surgery. The primary aim of this study was to identify postoperative vaginal morphology (angulation, dimensions), and position factors associated with prolapse recurrence following one of two vaginal surgeries for uterovaginal prolapse in the DEMAND cohort: vaginal mesh hysteropexy with sacrospinous fixation (hysteropexy) or vaginal hysterectomy with uterosacral ligament suspension (hysterectomy). The secondary aim was to correlate postoperative vaginal morphology and position factors with measures commonly associated with prolapse recurrence: vaginal mobility/distensibility and GH size.

Because apical descent was the dominant mechanism of prolapse recurrence in the DEMAND cohort, our primary hypothesis was that, within each surgery group, women with prolapse recurrence had a more inferiorly positioned (lower) vagina with an angulation distinct from that seen in women with success. We further hypothesized that within the recurrence and success groups, the same associations would be observed with hysterectomy and hysteropexy. Our secondary hypothesis was that a lower, straighter vagina would be associated with greater vaginal mobility/distensibility and larger GH.

### METHODS:

#### Study Design:

This was a secondary analysis of MRI data from the DEMAND study, a multisite prospective supplementary study of the *Study of Uterine Prolapse Procedure s-Randomized (SUPeR)* trial, designed to identify anatomic mechanisms and correlates of prolapse recurrence based on MRI evaluation among a subset of SUPeR participants randomized to either (1) vaginal mesh hysteropexy with sacrospinous fixation (hysteropexy) or (2) vaginal hysterectomy with uterosacral ligament suspension (hysterectomy). DEMAND and SUPeR were performed through the Pelvic Floor Disorders Network. Institutional review board approval and participants' written informed consent were obtained at all study sites. Detailed study protocol and 3-year outcomes for both studies are published.

#### Study Population:

The study population included a subset of 88 DEMAND participants who underwent pelvic MRI between June 2014 and May 2018. A full list of inclusion and exclusion criteria has been published. Additional exclusion criteria were failure to capture the full vagina, poor demarcation of the vaginal borders, incomplete MRIs, and MRIs taken after reoperation. Patient characteristics—demographics, medical history, and Pelvic Organ

Prolapse Quantification (POP-Q) measurements—from SUPeR were obtained at baseline (preoperative) and follow-up (i.e., SUPeR study visit date closest to MRI examination date).

### **MRI Protocol:**

The MRI methods have been reported. Briefly, participants were trained to perform maximal straining prior to MRI examination. Supine, multi-planar, T2-weighted images were collected with a 3T system and a pelvic phased array coil at rest (with prolapse fully reduced), maximal strain, and recovery (rest period following strain without prolapse reduced). The first rest scan provided a common reference configuration of the vagina across all participants to obtain more reliable baseline (rest) and dynamic (rest to strain) vaginal measurements. The final rest (recovery) scan provided the physiological configuration of the vagina. MRI scans were imported into 3D Slicer v4.10.0 ([www.slicer.org](http://www.slicer.org)) to (1) build a 3D pelvic coordinate system (PCS) and (2) generate 3D vaginal models to compare vaginal morphology and position across all participants while accounting for differences in position in the MRI scanner.

### **Establishment of the 3D Pelvic Coordinate System:**

A PCS was established to quantify vaginal angulation and position in 3D space while accounting for differences in patient position in the MRI scanner. The medio-lateral (X) axis was defined by the line connecting the ischial spines, where its midpoint provided the origin of the PCS. The anterior-posterior (Y) axis was given by the line orthogonal to the X-axis starting from the origin to the point one-third along the inferior-superior length of the pubic symphysis. The superior-inferior (Z) axis was the cross product of the X- and Y-axes. The Y-Z plane defined the midsagittal plane.

### **Vaginal Segmentation and 3D Reconstruction:**

The vagina was manually segmented (with the lumen excluded) from axial recovery MRI scans using 3D Slicer. Segmentations of multiple MRI slices were stacked to reconstruct aliased (i.e., jagged edges of an object) 3D surface models of the vagina with zero thickness. Vaginal models were exported to Blender v2.83.2 (Blender Foundation, Amsterdam, The Netherlands) to remove aliasing (sharp edges) by interpolating segmentations between adjacent slices via a smoothing algorithm. As described in a previous work, the smoothing algorithm allows unbiased, global smoothing of aliased geometries while preserving their original shape and volume. A diagram of the 3D reconstruction technique is shown in **Figure 1a**.

### **3D Vaginal Position and Morphology Analysis:**

Smoothed 3D vaginal models were imported into Mathematica v12.2.0 (Wolfram Research, Champaign, IL) to quantify vaginal morphology and position via computational morphometry—an algorithmic technique that performs automated measurements of anatomical structures by detecting and extracting anatomical landmarks from 3D models (**Figure 1b**). All 3D-model-based vaginal position and morphology parameters were static measures assessed at recovery (rest period following strain without prolapse reduced).

#### **Vaginal Position:**

From the distal to proximal direction, each 3D vaginal surface model was iteratively sliced along the axial plane at 1.5 mm intervals (i.e., half of the MRI slice thickness), where for each vaginal slice (represented as a thin ribbon), the centroid and lateral edges were calculated. The centroidal and lateral edge points computed through this iterative process defined the centerline and lateral margins of the vagina, respectively. Using the centerline, the following vaginal position parameters were measured with respect to the 3D PCS (**Figure 2a**): (1) vaginal apex position, the 3D coordinates of the most proximal point on the centerline and (2) mid-vagina position, the 3D coordinates of the midpoint of the centerline.

#### **Vaginal Angulation:**

The vaginal centerline points were divided into proximal and distal halves to demarcate the upper and lower vagina. A line of best fit was computed for each set of points to define the upper and lower vaginal axes. From these axes, the following vaginal angulation parameters were calculated with respect to the 3D PCS

**(Figure 2b):** (1) upper vaginal sagittal angle, the angle between the upper vaginal and anterior-posterior axes; (2) lower vaginal sagittal angle, the angle between the lower vaginal and anterior-posterior axes; (3) upper-lower vaginal sagittal angle, the angle between the upper and lower vaginal axes in the sagittal plane; (4) upper vaginal coronal angle, the angle between the upper vaginal and superior-inferior axes; (5) lower vaginal coronal angle, the angle between the lower vaginal and superior-inferior axes; and (6) upper-lower vaginal coronal angle, the difference between the upper and lower vagina coronal angles (i.e., a measure of the overall lateral orientation of the vagina). A more horizontal sagittal angle (towards the sacrum) is given by smaller values and a more vertical sagittal angle is given by larger values. A more medial coronal angle (aligned with the midline) is given by values closer to zero and a more lateral coronal angle (tilted to the left or right) is given by values further away from zero.

#### Vaginal Dimensions:

Using the vaginal centerline, lateral margins, and surface model, the following vaginal dimension parameters were quantified (**Figure 2c**): (1) vaginal length, the length of the vaginal centerline; (2) maximum transverse vaginal width, the largest pairwise straight-line distance between the vaginal lateral margins across all vaginal slices; (3) vaginal surface area, the surface area of the vaginal model; and (4) vaginal volume, the volume enclosed by the vaginal surface.

#### Vaginal Mobility/Distensibility and Genital Hiatus Measures:

Measurements of vaginal mobility/distensibility and GH size were obtained from the primary DEMAND study by methods previously described. In short, rest (with prolapse fully reduced) and strain sagittal MRIs were co-registered in 3D Slicer using the 3D PCS. The superior-inferior and anterior-posterior axes defined the midsagittal plane. In this plane, the anterior and posterior vaginal walls were outlined. A line was drawn between the posterior margin of the external urethral meatus and anterior margin of the perineal body (PB) to approximate the vaginal introitus length, GH size, and the level of the hymen (i.e., hymenal line). The position of the vaginal apex, AVW (i.e., point along the AVW wall corresponding to its half-length), and PB (i.e., the posterior margin of the GH) were identified. Using these landmarks, the following measurements commonly associated with prolapse recurrence were obtained: vaginal mobility (displacement of the vaginal apex, AVW, and PB from rest to strain); vaginal distensibility (elongation of the AVW and vaginal introitus from rest to strain); and GH size (at recovery and strain). Vaginal mobility/distensibility parameters are dynamic measures, where displacement is the straight-line distance between the rest and strain position and elongation is the difference in length between rest and strain. The GH size parameters are static measures assessed at recovery and strain.

#### Definition of Prolapse Recurrence:

Prolapse recurrence was defined as prolapse beyond the level of the hymen at strain on MRI. Using the midsagittal trace of the vaginal wall and hymenal line in the strain MRI, vaginal protrusion past the hymenal line indicated prolapse recurrence.

#### Statistical Analysis:

Descriptive statistics of demographic and medical history information were calculated and stratified by recurrence or success within each surgery group. Linear models including surgery group, recurrence/success, and their interaction were fit to each vaginal morphology and position measure. Model-estimated means and standard errors were calculated for each combination of surgery group and recurrence/success. Model-estimated differences and 95% confidence intervals were calculated for the difference between success and recurrence within each surgery group and for the difference between surgery groups within recurrence and success. The association between (1) vaginal morphology/position parameters and (2) vaginal mobility/distensibility and GH measures was analyzed using Pearson correlation. All statistical tests were two-sided and evaluated at a significance level of 0.05. Due to the exploratory nature of the analysis, no adjustment for multiple comparisons was performed. All statistical analyses were performed using SAS software v9.4 (SAS Institute Inc, Cary, NC).

## RESULTS:

### Study Population:

Of the 88 women from the primary DEMAND study, 82 met analysis inclusion criteria (41 hysteropexy, 41 hysterectomy). Of those, 75 (38 hysteropexy, 37 hysterectomy) were imaged at 30-42 months, six (2 hysteropexy, 4 hysterectomy) were imaged prior to 30 months, and one (hysteropexy) was imaged at 48 months. Full baseline and 30–42-month follow-up characteristics of the study cohort are given in **Table 1**. The population primarily consisted of white (81.7%), older ( $65 \pm 8$  years), postmenopausal (97.6%) women. Based on MRI criteria, 34 (41%) women had recurrence, with 12/41 (29%) in the hysteropexy group and 22/41 (54%) in the hysterectomy group.

### Physiological Vaginal Morphology and Position

Model-estimated group differences in physiological vaginal characteristics related to morphology (angulation, dimensions) and position are provided in **Table 2**.

#### Recurrence versus Success

After hysteropexy, women with recurrence had larger upper-lower and upper vaginal coronal angles oriented  $-9.5^\circ$  ( $p=0.009$ ) and  $-7.4^\circ$  ( $p=0.02$ ) farther towards the left side of the body (more laterally deviated) whereas women with success had smaller upper-lower and upper vaginal coronal angles nearly aligned with the midline of the body (closer to  $0^\circ$ ). Following hysterectomy, the vaginal apex and mid-vagina were  $-8.7$  mm ( $p=0.01$ ) and  $-6.1$  mm ( $p=0.02$ ) more inferiorly positioned (lower) in the recurrence group than in the success group.

#### Hysteropexy versus Hysterectomy

Within the recurrence group, women treated with hysteropexy had an upper-lower vaginal coronal angle oriented  $-7.7^\circ$  ( $p=0.04$ ) farther to the left side of the body while women treated with hysterectomy had an upper-lower vaginal coronal angle aligned with the midline of the body ( $0^\circ$ ). In addition, with recurrence, the hysteropexy group had a  $5.8$  mm ( $p=0.02$ ) wider transverse vaginal width and  $12.1$  cm<sup>2</sup> ( $p=0.04$ ) larger vaginal surface area than the success group. Within the success group, women treated with hysteropexy had a smaller upper vaginal sagittal angle oriented  $-6.4^\circ$  ( $p=0.04$ ) more horizontally towards the sacrum compared to women treated with hysterectomy. Additionally, within successes, the vaginal apex and mid-vagina were  $-8.8$  mm ( $p=0.005$ ) and  $-5.2$  mm ( $p=0.03$ ) more posteriorly positioned (closer to the sacrum) in the hysteropexy group than in the hysterectomy group.

#### Relationship with Vaginal Mobility/Distensibility and GH Size

None of the correlations exceeded  $\pm 0.4$  (moderate correlation) (**Table S1**). Of the vaginal mobility measures, greater AVW displacement correlated with a smaller transverse vaginal width ( $r=-0.24$ ,  $p=0.03$ ). Regarding vaginal distensibility, greater vaginal introitus elongation correlated with a more posterior vaginal apex ( $r=-0.26$ ,  $p=0.02$ ) and greater AVW elongation correlated with a lower vaginal apex ( $r=-0.26$ ,  $p=0.02$ ) and mid-vagina ( $r=-0.34$ ,  $p=0.002$ ), larger (more horizontal) lower vaginal sagittal angle ( $r=0.27$ ,  $p=0.01$ ), and more obtuse (straighter) upper-lower vaginal sagittal angle ( $r=0.29$ ,  $p=0.008$ ). In addition, elongation of the vaginal introitus correlated with a more posterior vaginal apex ( $r=-0.26$ ,  $p=0.02$ ). Lastly, a larger GH at rest correlated with a lower mid-vagina ( $r=-0.28$ ,  $p=0.01$ ), larger (more vertical) upper vaginal sagittal angle ( $r=0.24$ ,  $p=0.03$ ), and more obtuse upper-lower vaginal sagittal angle ( $r=0.23$ ,  $p=0.04$ ).

## DISCUSSION:

### Main Findings:

After hysteropexy, a more laterally oriented vagina, particularly the upper vagina, was associated with prolapse recurrence. After hysterectomy, a lower vaginal apex and mid-vagina were associated with prolapse recurrence. Among recurrences, women treated with hysteropexy had a more laterally deviated vagina, wider transverse vaginal width, and larger vaginal surface area compared to women treated with hysterectomy.

Among successes, the hysteropexy group had a more horizontal upper vagina and more posteriorly positioned vaginal apex and mid-vagina (pulled towards the sacrum) compared to the hysterectomy group.

Weak correlations were observed between (1) physiological vaginal morphology and position factors and (2) vaginal mobility/distensibility and GH size measures, where only the superior-inferior position of the mid-vagina explained >10% of the variation in AVW elongation. Most notably, a lower (more inferiorly positioned) mid-vagina and straighter (more obtuse) upper-lower vaginal sagittal angle were both correlated with greater AVW elongation and larger physiological rest GH.

In the primary DEMAND study, assessment of vaginal morphology with respect to prolapse recurrence and vaginal surgery was limited to midsagittal (2D) MRI measurements of vaginal length. By expanding the vaginal analysis to 3D, this study was able to distinguish differences in lateral orientation and position of the vagina in recurrences versus successes within the hysteropexy and hysterectomy group, respectively. Furthermore, the current study identified vaginal angulation and position factors correlated with vaginal mobility/distensibility and GH measures found to be associated with prolapse recurrence in the primary DEMAND study.

### **Interpretation:**

Regardless of prolapse surgery type or outcome, the mean postoperative upper-lower vaginal sagittal angle across groups ( $\sim 171^\circ$ - $177^\circ$ ) was larger than its normal value ( $160^\circ$ ) for women of similar age and vaginal parity. Thus, normal vaginal anatomy was not maintained postoperatively—a key goal of many pelvic reconstructive procedures for POP. Studies have shown that prolapse surgeries often straighten the vagina, resulting in an irregular vaginal angulation and position that may predispose to prolapse recurrence.

It is speculated that there are two key vaginal support structures for maintaining vaginal angulation and position, the uterosacral ligaments (USLs) and levator ani muscles (LAM). The USLs pull the upper vagina horizontally and posteriorly, positioning it above the levator plate and towards the sacral hollow. Detachment, elongation, or injury of the USLs can lead to anterior tilt and loss of horizontal-posterior orientation of the upper vagina. This allows the upper vagina to displace anteriorly past the levator plate and inferiorly towards the GH, increasing the risk of vaginal descent and POP. This anterior and inferior deviation of the upper vagina has been observed in prolapse surgeries like hysterectomy which involve disruption of the USLs and was also seen in the hysterectomy group of this study. With mesh-augmented prolapse surgery, these vaginal angulation and position changes would involve loosening or lengthening of the mesh arms.

Interestingly, this study showed that the upper vagina was displaced laterally in women with prolapse recurrence after hysteropexy, particularly towards the patients' left side. In these cases, the right mesh arm appeared loose and wave-like compared to the left mesh arm on MRI, suggesting consistent asymmetrical loss of support. Clinically, the right sacrospinous ligament is believed to be more easily identifiable and accessible during sacrospinous fixation, mainly by right-handed surgeons. Thus, it is plausible that this preference may account for the disproportionate "failure" of the right mesh arm (potentially due to asymmetrical tensioning and subsequent gradual lengthening) that leads to a laterally displaced upper vagina towards the patient's left side. This study also demonstrated that among successes, hysteropexy was better able to preserve a more horizontally and posteriorly oriented upper vagina than hysterectomy.

The effects of apical support loss are amplified with the presence of LAM defects, where the levator plate is responsible for upper vaginal support. When defective, the LAM is less able to pull the lower vagina towards the pubic bone and reflexively contract to stabilize the upper vagina in response to increased intrabdominal pressure. As a result, the levator plate is straighter and more dorsally oriented, which places abnormal loading and strain on the USLs and accounts for their elongated and hypertrophic appearance seen clinically. Loss of levator plate angulation is often indicative of LAM defects and accompanied with an enlarged GH, both of which have been associated with prolapse recurrence.

Though it is unclear which is the result or cause of the other, defective apical vaginal support (ligaments, mesh) and distal vaginal support (pelvic floor muscles) can result in a straighter vagina that leaves the

AVW more susceptible to elongate and descend with intraabdominal pressure. Similar observations were noted in this study, where a larger upper-lower vaginal sagittal angle and lower mid-vagina correlated with greater AVW elongation and larger recovery GH, and another study that reported that a lower mid-vagina correlated with a larger strain GH and prolapse recurrence. Longitudinal randomized clinical trials that radiographically assess vaginal anatomy before and after prolapse surgery are needed to distinguish the causative mechanisms of abnormal postoperative vaginal angulation and position—surgical technique versus anatomical defects—and their individual role in prolapse recurrence.

### **Strengths and Limitations:**

This study prospectively evaluated vaginal anatomy after vaginal surgery in a well-characterized cohort of women from a randomized clinical trial. A major strength of this work was that the vagina was analyzed in 3D using computational morphometry. Previous studies have been limited to 2D (planar) and manual vaginal measurements. The computational methods of this study allowed evaluation of the full vaginal geometry relative to a coordinate system which minimized subjectivity and variability of vaginal measurements through 3D modeling and automation.

A major limitation of this study was that the MRI sequences used for the analysis were obtained in the supine position. Thus, the ability to capture the full extent of prolapse was dependent on patient effort and proper performance of straining. To address this, participants underwent training on how to properly maximally strain prior to imaging and were required to perform multiple attempts to achieve maximal strain during the MRI examination. Only about half of SUPeR participants enrolled in DEMAND. Thus, the DEMAND cohort was not a random sample of SUPeR patients. However, when comparing women enrolled versus not enrolled in DEMAND, baseline patient characteristics were similar. Another limitation of this study was the absence of controls (preoperative MRI, immediate/short-term postoperative MRI) which made it difficult to isolate the individual impact of surgery versus POP on vaginal anatomy.

### **CONCLUSION:**

Following hysterectomy, women with prolapse recurrence have a more laterally deviated vagina compared to women with success. After hysterectomy, women with prolapse recurrence have a lower vaginal apex and mid-vagina than women with success. A lower mid-vagina and straighter upper-lower vaginal sagittal angle correlated with greater AVW elongation and larger recovery GH. Findings provide considerations for prolapse surgeries suggesting that postoperative changes in vaginal anatomy that result in a straighter, more inferiorly positioned vagina may predispose to prolapse recurrence, particularly with an enlarged GH. Future studies will assess 3D shape variation of the vagina and pelvic floor muscles after hysterectomy versus hysteropexy to investigate the relationship between pelvic floor muscle and vaginal morphology with respect to prolapse surgery, prolapse recurrence, and LAM defects.

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- *Magee-Women's Hospital, Dept. of OB/GYN & Reproductive Sciences, Pittsburgh, PA*: Michael Bonidie, Judy Gruss, Jonathan Shepherd, Gary Sutkin, Halina M. Zyczynski.
- *Cleveland Clinic Foundation, Cleveland, OH*: Matthew Barber, Annette Graham, Marie Fidela R. Paraiso, Cecile Ferrando.
- *Albany Medical College, Albany, NY*: Rebecca G. Rogers
- *RTI International, Research Triangle Park, NC*: Kate Burdekin, Michael Ham, Amaanti Sridhar, Dennis Wallace, Ryan Whitworth, Taylor Swankie.

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- *Dr. Moalli* reported serving as a consultant to Hologic Inc and receiving research support from the NICHD.
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- No other disclosures were reported.

#### **CONTRIBUTION TO AUTHORSHIP :**

MGG, PI, and BC had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

- PAM, DM, and MGG were involved in project administration and supervision.
- PAM, SDA, DHL, IM, CRR, HSH, MEH, and MGG had a role in conceptualization, methodology, and funding acquisition.
- PAM, STB, SDA, DHL, IM, CRR, HSH, MEH, PI, BC, MGG contributed to the data collection and analysis.
- All contributing authors were involved in drafting, revising, and final approval of the manuscript.

#### **DETAILS OF ETHICS APPROVAL:**

The primary study was approved by the institutional review board at each clinical site and the data coordinating center. The secondary analysis was approved by the University of Pittsburgh Institutional Review Board (no. 13110579). Initial approval date: 2 February 2014. Final approval date: 6 November 2019.

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#### **PRESENTATION INFORMATION:**

The work was presented at the Pelvic Floor Disorders Week 2021, Phoenix, AZ, October 12-15, 2021.

#### **REFERENCES:**

#### **TABLE/FIGURE CAPTION LIST:**

##### **Table 1. Comparison of patient characteristics between groups.**

Data presented as mean (standard deviation) or number/total number (percentage), unless otherwise indicated. Patient postoperative characteristics were assessed primarily at 30 or 36 months (N=75), with six prior to 30 months, and one at 48 months.

*BMI* , body mass index; *GH* , genital hiatus; *PB* , perineal body; *POP-Q* , Pelvic Organ Prolapse Quantification; *SD*, standard deviation; *TVL*, total vaginal length

<sup>a</sup> Recurrence is defined as prolapse beyond the hymen with strain.

<sup>b</sup> Pulmonary disease includes any the following: asthma, chronic obstructive pulmonary disease, acute respiratory distress syndrome, or emphysema.

<sup>c</sup> Cardiovascular disease includes any the following: angina, congenital heart failure/heart disease, heart attack, stroke or transient ischemic attack, and peripheral vascular disease.

##### **Table 2. Model-estimated differences in physiological vaginal characteristics between groups.**

Data presented as mean (standard error). All estimates are derived from linear models featuring surgery group, outcome, and their interaction. Significant p-values are indicated in bold.

*CI*, confidence interval; *SE* , standard error

<sup>a</sup> Recurrence is defined as prolapse beyond the hymen with strain.

<sup>b</sup> A more medial position is given by values closer to zero and a more lateral position is given by values further away from zero.

<sup>c</sup> A more anterior position is given by more positive or larger values and a more posterior position is given by more negative or smaller values.

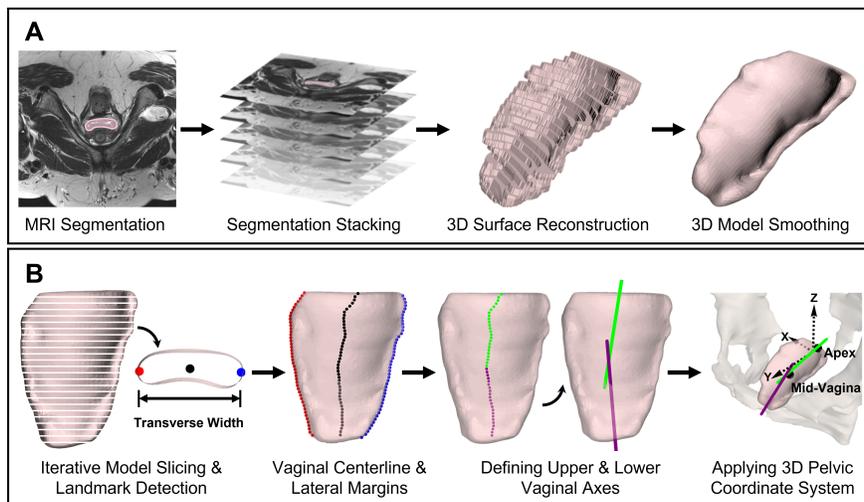
<sup>d</sup> A more superior position is given by more positive or larger values and a more inferior position is given by a more negative or smaller values.

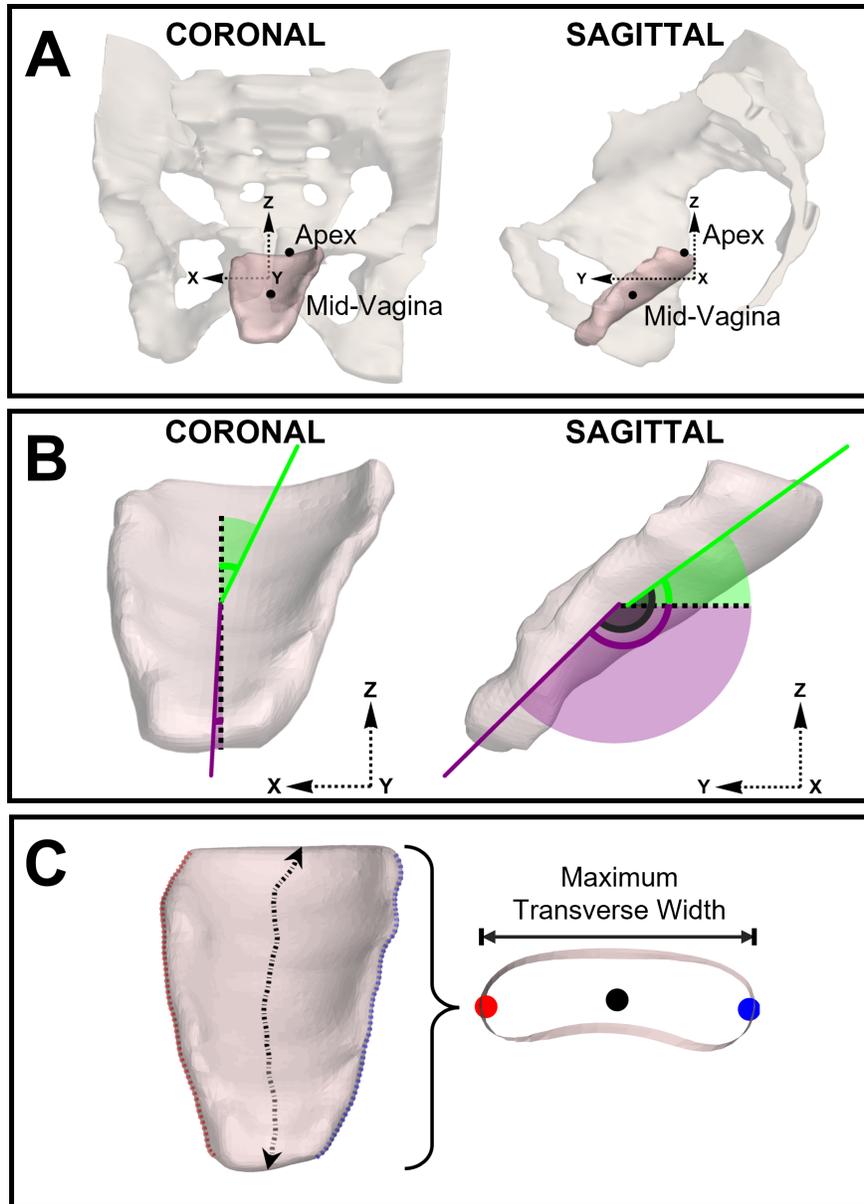
<sup>e</sup> A more horizontal (more acute) sagittal angle (towards the sacrum) is given by smaller values and a more vertical (straighter or obtuse) sagittal angle is given by larger values.

<sup>f</sup> A more medial coronal angle (aligned with the midline) is given by values closer to zero and a more lateral coronal angle (tilted to the left or right) is given by values further away from zero.

**Figure 1.** Illustration of the data processing steps of the vaginal analysis. **(A)** Axial magnetic resonance (MRI) scan of the participant at recovery (rest period following strain without prolapse reduced). The vagina was manually segmented with the lumen excluded. Vaginal segmentations across multiple MRI slices were stacked to reconstruct a 3D surface model of the vagina with zero thickness. To remove aliasing (sharp edges) from the 3D vaginal model, a non-biased smoothing algorithm was applied such that the model’s original shape and volume was preserved. **(B)** The 3D vaginal model was then placed in a morphometry algorithm to perform model-based vaginal measurements through anatomical landmark detection. First, the 3D model was iteratively sliced in the axial direction every 1.5 mm (half of the MRI slice thickness). For each 3D vaginal slice (represented as a thin ribbon), the right (red point) and left (blue point) lateral edges were extracted and the centroid (black point) of the vaginal slice was calculated. The straight-line distance between the lateral edges defined the transverse width of the vaginal slice. This iterative process was used to find the maximum transverse width and establish the right (red points) and left (blue points) lateral margins and centerline (black points) of the vagina. The vaginal centerline points were split in half to represent the upper (green points) and lower (purple) vagina. A line of best fit was calculated for each set to define the upper (green line) and lower (purple) vaginal axes. The pelvic coordinate system (PCS, dashed arrows) was then applied to calculate physiological vaginal position (black points) and morphology (angulation, dimension) measures in 3D space.

**Figure 2.** Visualization of the vaginal position and morphology (angulation, dimension) measures. **(A)** Vaginal position measures. Position (black points) of the vaginal apex and mid-vagina in the coronal and sagittal plane with respect to the 3D pelvic coordinate system (PCS). The X-, Y-, and Z-coordinates of each point correspond to the medial-lateral, anterior-posterior, and superior-inferior position, respectively. The orientation of the axes PCS indicates the positive direction. **(B)** Vaginal angle measures. Angles of the upper (green angle) and lower (purple angle) vagina in the coronal and sagittal plane. The coronal angles are with respect to the Z- (superior-inferior) axis and the sagittal angles are with regard to the Y- (anterior-posterior) axis. The upper-lower vaginal coronal angle is the difference between the upper and lower vaginal coronal angles. The upper-lower vaginal sagittal angle is the sum of the upper and lower vaginal sagittal angles. **(C)** Vaginal dimension measures. The vaginal length (black dotted double arrow) is given by the length of the vaginal centerline. The maximum transverse width (solid black double arrow) is given by the largest straight-line distance between the right (red point) and left (blue point) lateral margin of the vagina across all vaginal slices along the total vaginal length. The vaginal surface area and volume are given by the surface area and the amount of space enclosed by the surface of the 3D vaginal model, respectively.





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