

**OPEN MAGNETIC RESONANCE IMAGING:
APPLICATION OF NEW TECHNOLOGY TO IMPROVE THE
EVALUATION OF PELVIC ORGAN PROLAPSE IN WOMEN**

by

Marwa Mohammed Abdulaziz

B.Sc., University of King Abdulaziz, 2004

M.Sc., University of King Abdulaziz, 2010

A THESIS SUBMITTED IN PARTIAL FULFILLMENT OF
THE REQUIREMENTS FOR THE DEGREE OF

DOCTOR OF PHILOSOPHY

in

THE FACULTY OF GRADUATE AND POSTDOCTORAL STUDIES
(EXPERIMENTAL MEDICINE)

THE UNIVERSITY OF BRITISH COLUMBIA

(Vancouver)

January 2019

© Marwa Mohammed Abdulaziz, 2019

Committee Page

The following individuals certify that they have read, and recommend to the Faculty of Graduate and Postdoctoral Studies for acceptance, the dissertation entitled:

Open magnetic resonance imaging: Application of new technology to improve the evaluation of pelvic organ prolapse in women

submitted by Marwa Mohammed Abdulaziz in partial fulfilment of the requirements for

the degree of Doctor of Philosophy

in Experimental Medicine

Examining Committee:

Lynn Stothers, Urologic Sciences
Supervisor

Aziz Ghahary, Experimental Medicine
Supervisory Committee Member

Andrew Macnab, Urologic Sciences
Supervisory Committee Member

Kourosh Afshar, Urologic Sciences
University Examiner

Ismail Laher, Anesthesiology, Pharmacology and Therapeutics
University Examiner

Abstract

Background: Weakness or damage to the pelvic floor muscles results in pelvic organ prolapse (POP), which affects 50% of women >50 years old. Posture and gravity impact organ position and symptom severity. Current limitations of clinical examination and restriction to imaging in the supine position impact accurate diagnosis and disease staging. Open upright magnetic resonance imaging (MRO), allows images of patients sitting, standing, and supine. In this dissertation it is hypothesized that MRO images will allow improved detection of the presence and extent of prolapse.

Methods: A Paramed Medical Systems 0.5 T upright Open MRI scanner (MRO) was used to obtain axial and sagittal T2-weighted pelvic scans in women when supine, sitting, and standing. Symptomatic women with POP and asymptomatic controls were studied. The protocol developed obtains good quality images efficiently in all three positions. Validated reference lines were used to identify where POP was present in the same patient in different positions and to grade its severity. A manual segmentation methodology was developed using Analyze 12.0 software to construct 3D models of the female pelvis from 2D images to enhance the visualization of complex pelvic anatomy.

Results: Forty women (20 with POP and 20 asymptomatic controls) were studied. Detection of POP in standing versus supine images in symptomatic women was 50% vs. 5% for cystocele and 35% vs. 25% for vaginal prolapse, indicating improved visualization of gravity-dependent POP with MRO standing imaging. Image comparison indicated that the extent of prolapse is best evaluated in the standing position using the pubococcygeal reference line. These images better identify

downward movement in the anterior and posterior compartments. No appreciable benefit was afforded by seated images.

Conclusion: The findings support the hypothesis that MRO imaging of POP patients is relevant to improving the detection and quantification of POP. The MRO protocol developed for standing images in women with POP demonstrated feasibility allowing supine, sitting, and standing imaging of changes in pelvic floor anatomy in upright positioning. When compared with supine images, standing images better identify the presence and extent of POP. 3D image modeling allows more comprehensive visualization of complex female pelvic anatomy.

Lay Summary

Pelvic organ prolapse (POP) occurs in more than 50% of women over 50 because the supporting pelvic floor muscles are weak or damaged. Symptoms include bladder, bowel, and sexual problems. Clinical evaluation is difficult because POP is often made worse by upright posture. It is problematic that imaging is currently only able to be done with patients lying supine. My research goal was to use upright open MRI (MRO), which allows imaging of patients sitting or standing, to improve diagnostic accuracy by detecting where posture and gravity affect POP. I developed a protocol for MRO imaging of the female pelvis, improved diagnostic accuracy by adding established reference lines to standing MRO images, and created 3D models from 2D MRO images to enable clinicians and patients to better visualize the interplay of the pelvic structures, to improve the diagnosis and staging of POP severity on which correct treatment planning depends.

Preface

The work presented in this thesis has already been published in peer-reviewed journals or has been submitted and is under peer review. I am the first author of all of the publications shown below.

Dr. Lynn Stothers was the Principal Investigator for the research project presented here. The research ideas and approach were developed by her.

Dr. L. Stothers and Dr. A. Macnab provided the necessary financial support grant from the Vancouver Coastal Health Research Institute (VCHRI) and additional support came from the Saudi Cultural Bureau (SACB) for utilizing the Open Magnetic Resonance Imaging machine. The University of British Columbia's Clinical Research Ethics Board (CREB) provided approval for the research project "New MRI System to Quantify and Stage Pelvic Organ Prolapse in Women". The CREB identification number for this project H14-03507, was approved by Vancouver Coastal Health and included a number of supportive scientists (including but not limited to Dr. Darren Lazare, Dr. Andrew Macnab, and Dr. Denise Pugash) in addition to the principal investigator Dr. Lynn Stothers.

Distribution of the work is as follows:

A part of Chapter 1 has been published as Marwa Abdulaziz, Lynn Stothers, Andrew Macnab. Effects of posture and gravity on pelvic organ prolapse, Pelvic Floor Disorders, 2018, ISBN 978-1-78923-245-5. I was responsible for writing the complete manuscript. Drs. L. Stothers and A. Macnab supervised the project, provided guidance on near final drafts of the manuscript, contributed edits on all versions of the manuscript, and reviewed it prior to submission.

Chapter 2: A version of Chapter 2 has been published as Marwa Abdulaziz, Lynn Stothers, Darren Lazare, Andrew Macnab. An integrative review and severity classification of complications related to pessary use in the treatment of female pelvic organ prolapse. *Can Urol Assoc. J* 2015. 9(5-6). In this work Dr. L. Stothers conceived and generated the review outline. I was responsible for writing the manuscript, conducting the systematic review, data collection and its analysis. Dr. L. Stothers and Dr. A. Macnab supervised the project and assisted with manuscript review, and editing was contributed by Dr. D. Lazare.

Chapter 3: A version of Chapter 3 has been accepted for publication in November 2018 online issue of the *Canadian Urological Association Journal*: Marwa Abdulaziz, Alex Kavanagh, Lynn Stothers, Andrew Macnab. Relevance of Open Magnetic Resonance Imaging Position (sitting and standing) to Quantify Pelvic Organ Prolapse in Women. Dr. Stothers generated the hypothesis and conceived the study design. Drs. L. Stothers and A. Kavanagh provided the recruited patients from their urogynecology clinic. I was responsible for data collection (Centre for Hip Health and Mobility), analyzed the MRO assessment scans, conducted the statistical analyses, and drafted the manuscript. Dr. A. Macnab provided detailed feedback and conducted edits on all versions of the manuscript. Drs. L. Stothers and A. Macnab supervised the project, provided guidance on near final drafts of the manuscript, contributed to the study design, edited all versions of the manuscript, and reviewed it prior to submission.

Chapter 4: A version of Chapter 3 has been published: Marwa Abdulaziz, Lynn Stothers, Andrew Macnab. Methodology for 3D image reconstruction of the female pelvis from upright open MRI (MRO) 2D imaging. *Biomedical Spectroscopy and*

Imaging, April 2018, IOS Press DOI: 10.3233/bsi-180178. Dr. L. Stothers generated the hypothesis and conceived the study designed. I was responsible for data collection (Centre for Hip Health and Mobility), generated a 3D model of the female pelvis, analyzed the MRO assessment scans, and drafted the manuscript. Dr. A. Macnab provided detailed feedback, contributed in drafting the manuscript and conducted edits on all versions of the manuscript. Honglin Zhang taught me how to use Analyze 12.0 software. Drs. L. Stothers and A. Macnab supervised the project, provided guidance on near final drafts of the manuscript, contributed to the study design, edited all versions of the manuscript, and reviewed it prior to submission.

Table of Contents

Abstract	iii
Lay Summary	v
Preface	vi
Table of Contents	ix
List of Tables	xii
List of Figures	xiii
List of Acronyms and Abbreviations	xv
Acknowledgements	xvii
Chapter 1. Introduction	1
1.1. Pelvic floor anatomy	1
1.2. Pelvic diaphragm	1
1.3. Urogenital diaphragm	3
1.4. Perineal body	4
1.5. Anterior compartment	4
1.6. Middle compartment	7
1.7. Posterior compartment	8
1.8. Description of pelvic organ prolapse	10
1.9. Description of functional POP symptoms	11
1.9.1. Urinary symptoms	11
1.9.2. Bowel symptoms	11
1.9.3. Sexual symptoms	12
1.9.4. Local symptoms	12
1.9.5. Quality of life	13
1.10. Pelvic organ prolapse staging	13
1.11. Early POP grading systems	14
1.12. Pelvic organ prolapse quantification system POP-Q	15
1.13. Limitation of the POP-Q system	17
1.14. A new simplified POP classification system	18
1.15. Surgery	18
1.16. Surgical procedures	19
1.16.1. Sacral colpopexy (open, robotic, and laparoscopic)	19

1.16.2. McCall culdoplasty	20
1.16.3. Sacrospinous ligament fixation	21
1.16.4. Uterosacral ligament suspension.....	22
1.16.5. Iliococcygeus fascia suspension.....	23
1.16.6. Vaginal mesh to augment apical suspension.....	24
1.17. Pessary	24
1.17.1. History of pessary	24
1.17.2. Indication for pessary usage	26
1.17.3. Types of pessaries.....	26
1.17.3.1. Support pessaries.....	27
1.17.3.2. Space-filling pessaries.....	28
1.17.3.3. Inflatable pessary.....	28
1.17.4. Pessary maintenance and follow-up.....	29
1.17.5. Guidelines for pessary fitting.....	29
1.17.6. Effectiveness of pessary usage	30
1.18. Current imaging techniques	31
1.18.1. Ultrasound.....	31
1.18.2. Computerized tomography (CT)	32
1.18.3. Magnetic resonance imaging (MRI).....	33
1.18.3.1. Upright open MRI (MRO).....	35
1.18.3.2. Reference lines.....	37
1.19. Rationale	39
Chapter 2. An Integrative Review and Severity Classification of Complications Related to Pessary Use in the Treatment of Female Pelvic Organ Prolapse	41
2.1. Introduction.....	41
2.2. Methods.....	42
2.2.1. Systematic review search strategy	42
2.2.2. Analytic process.....	43
2.3. Results	43
2.4. Discussion	48
2.5. Conclusions.....	52
Chapter 3. Relevance of Open Magnetic Resonance Imaging Position (Sitting and Standing) to Quantify Pelvic Organ Prolapse in Women.....	53

3.1. Introduction.....	53
3.2. Materials and methods	55
3.2.1. Reference lines	59
3.2.2. Anatomical landmarks and clinical measurement points	62
3.2.3. Image analysis	62
3.3. Results	63
3.4. Discussion	71
3.5. Conclusion.....	75
Chapter 4. Methodology for 3D Image Reconstruction of the Female Pelvis from Upright Open MRI (MRO) 2D Imaging	76
4.1. Introduction.....	76
4.2. Methods.....	79
4.2.1. Upright open MRI.....	79
4.2.2. Subjects	79
4.2.3. Image acquisition.....	80
4.2.4. Generation of 3D models	81
4.2.5. Surface rendering	83
4.2.6. Image interpretation and grading of POP severity	85
4.3. Results	86
4.4. Discussion	89
4.5. Conclusions	98
Chapter 5. Discussion and Conclusion.....	99
5.1. Summary and discussion	99
5.1.1. Posture and gravity dependence of POP.....	101
5.1.2. MRO protocol development	102
5.1.3. MRO and POP staging	103
5.1.4. 3D modeling methodology	106
5.2. Limitations	107
5.3. Significance	109
5.4. Future studies.....	110
References	111

List of Tables

Table 2.1. Nature of complications of pessary use and frequency of reporting classified by type of report].....	45
Table 2.2. Reported complications of individual pessary type.....	46
Table 2.3. Classification of complications using the Clavien-Dindo system based on management strategies reported in the literature	47
Table 3.1. Summary of clinical data on the 20 symptomatic subjects	64
Table 3.2. Comparison of data from pelvic reference line length (cm) between subjects symptomatic for POP and the control group obtained in the standing position ...	66
Table 3.3. Comparison of data from pelvic reference line length (cm) between subjects symptomatic for POP and the control group obtained in the supine position.	67
Table 3.4. Comparison of data from pelvic reference line length (cm) between subjects symptomatic for POP and the control group obtained in the sitting position	68
Table 3.5. Detection of POP in MRO standing images from the symptomatic subjects using reference line parameters	70
Table 3.6. Detection of POP in MRO supine images from the symptomatic subjects using reference line parameters	70
Table 4.1. Presence and extent of pelvic organ prolapse (by distance below the pubococcygeal reference line of the bladder and vagina) in supine MRO imaging in 13 symptomatic subjects.....	88
Table 4.2. Presence and extent of pelvic organ prolapse (by distance below the pubococcygeal reference line of the bladder and vagina) in standing MRO imaging in 13 symptomatic subjects	89

List of Figures

Figure 1.1. 27-year-old asymptomatic woman without pelvic floor defect	2
Figure 1.2. A 70-year-old patient with pelvic organ prolapse	6
Figure 1.3. Comparison of the three-validated pelvic organ prolapse grading systems and a current simplified POP grading system.....	15
Figure 1.4. Points and landmarks used for POP-Q system examination	177
Figure 1.5. The scheme used for enrollment of the nine points [51]	17
Figure 1.6. The vagina is fixed by two pieces of mesh.....	20
Figure 1.7. McCall stitches from internal and external (from Baggish and Karram [59]).....	211
Figure 1.8. Intraperitoneal suite of sutures in a cross-section of the pelvic floor.....	23
Figure 1.9. Treatment by Polybus of vaginal prolapse	25
Figure 1.10. Varieties of vaginal pessary types used [80]	27
Figure 1.11. Shows how the pelvic reference lines will be drawn	39
Figure 2.1. Flowchart of citation review and inclusion strategy	44
Figure 3.1. Open magnetic resonance imaging.....	58
Figure 3.2. A patient in the standing position of open magnetic resonance imaging (MRO) examination with a compression cuff around each leg	59
Figure 3.3. Sagittal T2-weighted midline views of the female pelvis in a 51-year-old symptomatic subject demonstrating evidence of POP when the patient is imaged standing	61
Figure 3.4. Sagittal MRO midline views of the female pelvis obtained in the supine position.	66
Figure 3.5. Sagittal MRO midline views of the female pelvis obtained in the supine position.	68
Figure 3.6. Sagittal MRO midline views of the female pelvis obtained in the sitting position	69
Figure 3.7. The perpendicular distances from the pubococcygeal reference line (PCL) to the bladder base, vaginal apex, and anorectal junction.....	70
Figure 4.1. A flowchart of the image analysis method to convert 2D MRO images into 3D models of the female pelvis using the software Analyze 12.0.....	82
Figure 4.2 (A) Axial T2-weighted MR image of the female pelvis as exported to Analyze 12. (B) Once “segmentation” is complete, colored markings are drawn manually slice by slice around the structures of interest.....	83

Figure 4.3. Examples of three-dimensional models generated of the female pelvis	84
Figure 4.4. An example of a 3D model being generated	85
Figure 4.5. Bar graphs of the percentage of symptomatic subjects with mild POP evident in supine MRO imaging	87
Figure 4.6. Bar graphs of the increased percentage of symptomatic subjects with mild, moderate, and severe POP evident in standing MRO imaging .. Error! Bookmark not defined.	
Figure 4.7. T2-weighted sagittal MRO images of the same patient:.....	92
Figure 4.8. T2-weighted sagittal MRO images of the same 24-year-old patient	93
Figure 4.9. 3D models, and the 2D MRO supine and standing images from which they were generated, in two different patients with symptomatic POP	966

List of Acronyms and Abbreviations

2D	two dimensional
3D	three dimensional
ARJ	anorectal junction
ASC	abdominal sacral colpopexy
AUGS	American Urogynecologic Society
BMI	body mass index
CCD	colpocystodefecography
CT	computerized tomography
D&C	dilation and curettage
FOV	field of view
FSE	fast spin-echo
GFE	gradient field echo
GH	genital hiatus
HL	H line
HMO	H line, M line, organ prolapse
HRQOL	health-related quality of life
HRT	hormone replacement therapy
ICG	iliococcygeus fascia suspension
ICS	International Continence Society
IUGA	International Urogynecology Association
LH	levator hiatus
ML	M line

MPL	mid-pubic line
MRI	magnetic resonance imaging
MRO	open magnetic resonance imaging
NEX	number of excitations
PC	pubococcygeal
PCL	pubococcygeal line
PFM	pelvic floor muscles
PL	perineal line
POP	pelvic organ prolapse
POP-Q	POP quantification
PP	pubopromontoreal line
QOL	quality of life
SCIPP	sacrococcygeal–inferior pubic point
SGS	Society of Gynecologic Surgeons
SSLF	sacrospinous ligament fixation
TE	echo time
TR	repetition time
UI	urinary incontinence
USLS	uterosacral ligament suspension
UTI	urinary tract infection
VCHRI	Vancouver Coastal Health Research Institute
VVFs	vesicovaginal fistulas

Acknowledgements

This dissertation would not have been possible without the many people who helped me in different ways I would like to express my sincerest thanks to my supervisors and to the members of my advisory committee, Dr. Lynn Stothers, Dr. Aziz Ghahary, and Dr. Andrew Macnab. I am fortunate to have spent the past five years learning from you; it has been a truly fulfilling journey.

I would like to express my deepest gratitude especially to my supervisor, Dr. Lynn Stothers, who believed in me and opened the door that was the first step to achieving my dream. I cannot speak highly enough about my experience under her tutelage. Her abundant humanity in dealing with my situation and her wholehearted support and care helped me overcome setbacks and stay focused on my goals; her encouragement, guidance, and spot-on feedback have inspired and motivated me. I would also thank her for providing me the independence and flexibility to develop and work in my own time. I will forever be indebted to you.

I wish to sincerely thank Dr. Aziz Ghahary who graciously and continually provided his time. His wisdom provided me the greatest opportunity to complete this journey.

I am particularly grateful to Dr. Andrew Macnab, who was always there for me, despite his many academic and professional commitments. I truly appreciate his endless support, assistance and kind words of encouragement. His expertise, invaluable attention to the detail, editing, and thought-provoking discussions were critical to this dissertation.

I owe deep gratitude to Dr. Vincent Duronio for his kind support and encouragement during the past 5 years. Also, I would like to acknowledge the academic and technical support of the University of British Columbia and the Department of Medicine, especially the Experimental Medicine Program.

I gratefully acknowledge the funding sources that made my Ph.D. possible; I thank Saudi Cultural Bureau (SACB) over the past five years and Vancouver Coastal Health Research Institute (VCHRI) for their financial support.

Most importantly, none of this would have been possible without the endless love, support, and patience of my beloved my husband and to my little angels. Words fail me to as I try to express my deepest feelings of gratitude and indebtedness. I especially wish to thank my husband, Jameel Metwalli. Jameel is my best friend, my support system, and the one person who constantly picks me up when I fall. He has seen the worst and best of me during the past five years, and I thank him; what we have accomplished together over the past five years is nothing short of incredible. With the end of this experience I look forward to new beginnings, wherever life may take us.

Chapter 1. Introduction¹

1.1. Pelvic floor anatomy

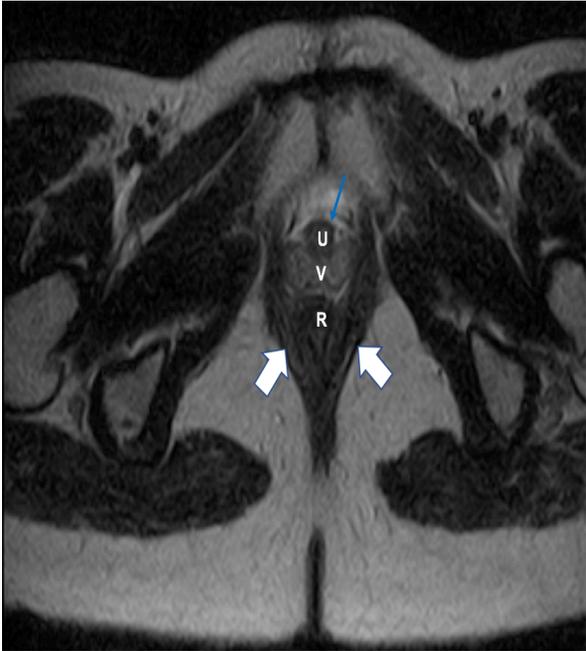
The essential supportive structures of the pelvis are made up of the pelvic fascia (passive) and pelvic floor musculature (active). The fascial structure components are of two types, parietal and visceral (endopelvic). Parietal fascia covers the pelvic skeletal muscle and binds muscles to the bony pelvis. Visceral endopelvic fascia exists throughout the pelvis as a framework that provides support for the internal pelvic organs in the center of the pelvis and maintains their relationship with each other. The skeletal muscles of the pelvic floor consist of the levator ani muscles, the coccygeus muscle, the external anal sphincter, the striated urethral sphincter, and the superficial perineal muscles [1].

1.2. Pelvic diaphragm

The pelvic diaphragm is a sheet of muscles that arise from the anterior pelvis at the posterior portion of the symphysis pubis and connect to the ischial spine and coccyx. The pelvic diaphragm consists of the levator ani, which is a combination of three muscles, pubococcygeus, iliococcygeus, puborectalis, and coccygeus, with various insertions (Fig. 1.1). The puborectalis muscle originates from the posterior surface of pubic rami and arcus tendineus levator ani pass posteriorly to form a sling around the vagina, rectum, and the perineal body. The pubococcygeus has an identical origin and ends in the midline on the anococcygeal raphe. The iliococcygeal muscle attaches along the arcus tendineus levator ani and then on the anococcygeal raphe to make up the levator plate [1].

¹ Part of the text in Chapter 1 will be published: "Imaging techniques to demonstrate the effects of posture and gravity on pelvic organ prolapse". In: *Pelvic Floor Disorders*, ISBN 978-953-51-5767-0.

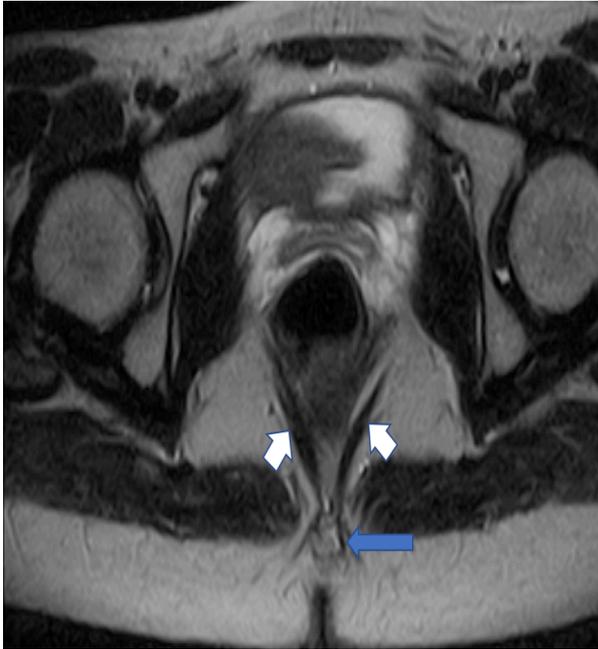
Figure 1.1. 27-year-old asymptomatic woman without pelvic floor defect. Axial T1-weighted fast spin-echo images show a normal pelvic diaphragm. (A) The puborectalis muscles (white arrow) surrounding the urethra, vagina, and rectum and the periurethral ligament (blue arrow) spanning anteriorly to the urethra among the levator ani. Note that the H-shape of the vagina determines the symmetric attachments. Note normal urethra (U), normal vagina (V), and normal rectum (R). (B) Axial T1-weighted image shows the pubococcygeus m. part (white arrow) of the levator m. and the coccyx (blue arrow). (C) Axial image shows the iliococcygeus m. part (white arrows) of the levator and the coccyx (blue arrows). (Original images from source subjects).



(A)



(B)



(C)

1.3. Urogenital diaphragm

The urogenital diaphragm exists over the anterior pelvic outlet under the pelvic diaphragm. However, there is debate over whether this structure consists of a transverse sheet of muscle continuing across the pubic arch (deep transverse perineal muscle) among superior and inferior fascia [2] or comprises three contiguous striated muscles (compressor urethrae, sphincter urethrae, and urethra-vaginalis) and an inferior fascial layer known as the perineal membrane [3, 4].

The most superficial ischiocavernosus and bulbocavernosus muscles, as well as the thin slips of the superficial transverse perinei [4], continue the inferior aspect of the urogenital diaphragm. The structure extends across the gap between the inferior pubic rami bilaterally and the perineal body. It closes the urogenital (levator) hiatus. It adds support and has a sphincter-like impact at the distal part of the vagina, and due to its connection to periurethral striated muscles, contributes to continence. It also supplies

structural support for the distal urethra. At the posterior triangle encircling the anus there is an identical diaphragm or membrane. The ischioanal fossae are the areas lateral to the anus under the pelvic diaphragm [2].

1.4. Perineal body

The perineal body, situated between the vagina and anus, is a focal element among the urogenital and anal triangles of the perineum. A mass of interlocking muscular, fascial, and fibrous components between the vagina and anorectum [5], it is integral for continence and vulnerable to injury from episiotomy or tears during vaginal delivery. It is the focal point for insertion of the muscles of the deep transverse perineal muscle, which originates from the perineal body to the ischial tuberosity, the superficial muscles of the perineal membrane, the external sphincter urethrae, and the external anal sphincter, which passes posteriorly and is inserted onto the coccyx and the levator ani. The importance of the perineal body is as an attachment point for the anorectum and vagina and as a means of preventing stretching of the urogenital hiatus. The urogenital hiatus is the U-shaped hiatus in the levator ani muscles through which the urethra, vagina, and rectum pass [1].

1.5. Anterior compartment

Support of the urethra comes from the pelvic muscles and fasciae. The endopelvic fascia condensations supply ligamentous support for the urethra. In a study of the urethral support ligaments using high-resolution MRI and an endourethral MR coil by Macura et al. [6], three groups of urethral support ligaments were defined in females: the periurethral ligaments originate from the puborectalis muscle and pass ventral to the urethra, the paraurethral ligaments originate from the lateral wall of the urethra to the

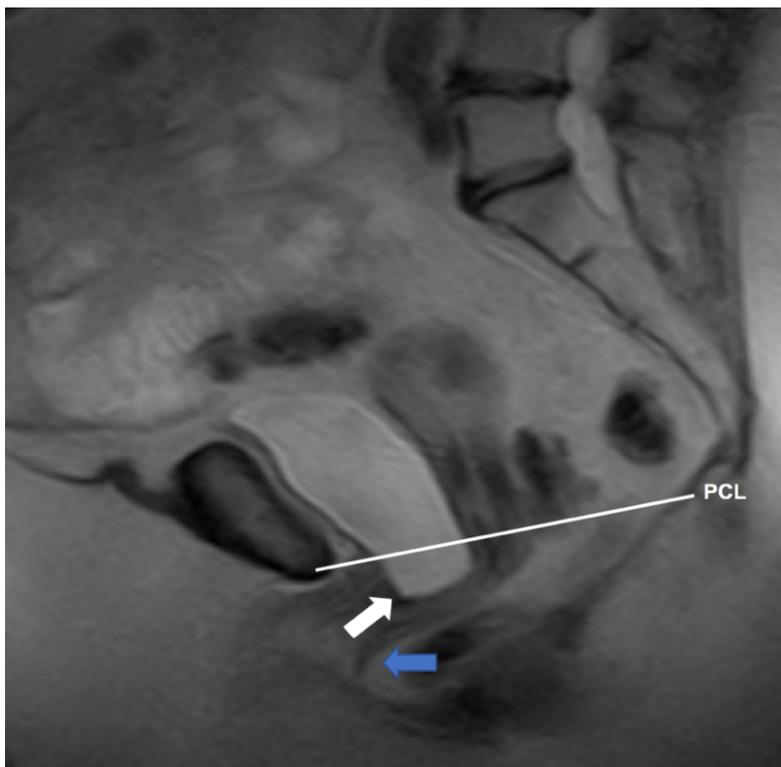
periurethral ligaments, and the pubourethral ligaments. This group of ligaments and the anterior vaginal wall give a hammock-like support to the urethra. These support mechanisms, with the pelvic diaphragm, which raises the urinary bladder and prolongs the urethra, all play a significant role in preserving urinary continence in women [3]. Several studies have reported that disorders of this hammock-like support component are closely associated with the beginning of stress urinary incontinence [7, 8].

Yang et al. [9] demonstrated that the normal vertical location of the bladder neck at strain should be less than 1 cm from the pubococcygeal line (PCL). The distal part of the urethra is correlative with the anterior vaginal wall. In women with stress urinary incontinence, the anterior vaginal wall support is diminished. Raised intraabdominal pressure causes a downward motion of the bladder neck below the PCL and prolapse of the urinary bladder out of the anterior vaginal wall, resulting in a cystocele (Fig. 1.2). Because the bladder neck and proximal urethra are mobile, downward motion of the bladder neck during straining can cause clockwise rotational displacement of the bladder neck and proximal urethra. If the proximal urethra rotates more than 30°, urethral hypermobility exists and may result in kinking of the proximal urethra that can make stress urinary incontinence disappear [10]. In a study by Kim et al. [11], disruption of the periurethral and paraurethral ligamentous supports were recurrently observed in patients with stress urinary incontinence; they propose that a dysfunction of attachment among the urethra and the puborectalis sling is one of the main reasons for urethral hypermobility [10].

The naturalistic butterfly shape of the vagina can also be changed by a reduction in the paravaginal ligamentous support. The vagina can have a flattened appearance

because the vaginal wall will descend posteriorly as a consequence of defect of paravaginal attachments. The loss to the paravaginal ligaments will debilitate support to the urethra because the middle and distal thirds of the urethra are closely connected to and supported by the anterior vaginal wall. The loss of the normal shape of the vagina is therefore an important sign of paravaginal tears in women with urinary incontinence. This finding will be relevant to the surgeon because repair of the cystocele alone will be inadequate, and fascial repair might also be required [12].

Figure 1.2. A 70-year-old patient with pelvic organ prolapse. Sagittal FSE T2-weighted image in the standing position shows prolapse of the bladder neck (white arrow) below the pubococcygeal line (PCL) and outpouching of the anterior rectal wall (blue arrow). (Original images from source subjects).



1.6. Middle compartment

The middle compartment of the pelvic floor includes the reproductive structures, i.e., the uterus, the cervix, and the vagina. Studies by DeLancey [7] defined vaginal support as having three levels. The cephalic 2- to 3-cm part of the vagina, noted as level 1, is suspended from the pelvic side wall by the parametrium and paracolpium, condensations of the endopelvic fascia. Level 3 is noted as the level that begins at the hymen ring and extends 2–3 cm cephalad to it, and level 2 is between levels 1 and 3. Level 2 of the vagina is linked to the arcus tendineus, although level 3 is directly fused anteriorly to the urethra, laterally to the levator ani muscles, and posteriorly to the perineal body, instead of being attached to or suspended from the pelvic walls. The distal third of the vagina has a different embryologic origin from the proximal two thirds of the vagina.

Prolapse of the middle compartment in patients with hysterectomy is also known as “apical prolapse” and is due to the descent of the vaginal apex. When the patient has had a hysterectomy, the paracolpium is supplied as support to the vaginal apex, and the vaginal apex should maintain at least 1 cm over the pubococcygeal line at strain [9]. Dysfunction of the paracolpium may then lead to apical prolapse.

Although loss of the normal butterfly shape of the vagina is widely noted to indicate a defect of the paravaginal ligaments, loss of the normal shape on MRI may also be observed in nulliparous asymptomatic women and in the absence of symptoms. Consequently, the diagnosis of loss of vaginal support should not be made only on the basis of loss of vaginal shape [1].

The parametrium, a component of the uterosacral and cardinal ligaments, suspends the uterus and cervix from the pelvic side walls. On midsagittal MRI, downward movement of the uterus in addition to downward movement of the cervix and vagina often suggests a defect of the uterosacral or cardinal ligaments. The horizontal H and M lines can lengthen. On axial images, the transverse dimension of the levator hiatus can be widened, the vagina may also be flattened or the symmetric butterfly shape diminished. The size of the urogenital hiatus in the levator muscles, a length that is defined clinically by physical examination, has been seen to be larger in patients with pelvic organ prolapse [13].

1.7. Posterior compartment

The distal part of vagina is fused with the perineal body, which separates the vagina from the rectum. The perineal body is a significant anchoring structure for the muscles and ligaments of the urogenital diaphragm. The rectovaginal fascia, which is a condensation of the endopelvic fascia that is connected to the perineal body, also acts as a support diaphragm, avoiding posterior prolapse. The iliococcygeus muscle, which is a flat horizontally oriented shelf within the rectovaginal fascia, forms a diaphragm supporting the pelvic organs, particularly those in the posterior compartment. The puborectalis muscle tightens the urogenital hiatus and keeps the pelvic organs in position by forming a U-shaped sling between the pubis and the anus. An episiotomy during vaginal childbirth can result in damage to the perineal body. Separation of the perineal body or damage of the rectovaginal fascia or the iliococcygeus muscle may permit the bowel and peritoneal contents to protrude inferiorly out of the posterior vaginal wall, causing posterior prolapse.

The levator plate, the midline raphe of the iliococcygeus muscle, is easily recognized on midsagittal MR images. In normal women it should be parallel to the PCL [10]. Caudal angulation of the levator plate on the MRI image by more than 10° with respect to the PCL is an indication of a pelvic floor defect [12].

One of the main reasons for the presence of posterior vaginal bulge is anterior rectocele, which happens by herniation of the anterior wall of the rectum into the posterior vaginal wall as a consequence of weakness from defects in the rectovaginal fascia. Rectoceles are measured as the depth of wall protrusion beyond the expected margin of the normal anorectal wall, and they are clinically significant when the bulge exceeds 2 cm during evacuation [14-18]. A rectocele is distinguished by a rectal bulge of more than 3 cm, which is the distance measured between the anal canal and the tip of the rectocele [19]. An anterior rectal bulge of up to 3 cm can happen in women without creating a disruption deformity. The superior soft-tissue contrast of MRI permits the posterior compartment to be clear images, with good details, such as the hyperintense fluid-filled small-bowel loops in enteroceles, the hyperintense T2 bright peritoneal fat in peritoneoceles, and the hyperintense gel-filled rectum or sigmoid colon in rectoceles or sigmoidoceles [20].

Prolapse of peritoneal contents occurs because of dysfunction of the ligaments providing support and the iliococcygeus muscle resulting in widening of the rectovaginal space. In normal women, the rectovaginal space caudal to the upper third of the vagina is closely apposed [20]. Widening of this space can permit inferior herniation of the peritoneal fat, small bowel, sigmoid colon, and fluid in the pouch of Douglas. A hysterectomy may result in disruption of the rectovaginal fascia and a high risk of

enterocele occurrence [21]. A large enterocele can hide an existing cystocele or rectocele owing to the narrow space in the pelvic floor. Enteroceles are measured as mild, moderate, or severe when they extend 3 cm, 3–6 cm, or greater than 6 cm, respectively, below the PCL [20]. Reduction of the enterocele can be required before evaluation of the other compartments of the pelvic floor. Conversely, a constantly large rectocele or incomplete evacuation of the rectal contents in a large rectocele can also hide an enterocele or a cystocele [22]. Appropriate evacuation of the rectal contents prior to the MR examination is needed to fully evaluate the pelvic floor [10].

1.8. Description of pelvic organ prolapse

Pelvic organ prolapse (POP) is one of the most prevalent and depressing gynecologic conditions and can be hard to measure and relate to symptoms. In the late nineteenth century several attempts at classifying POP were made [23]. It exists when there is a weakness deformity in the pelvic floor supporting structures that keeps the pelvic viscera from displacing. While generally not life threatening, prolapse causes impaired quality of life as it can result in bladder, bowel, and sexual organ deformity [24]. The etiology of pelvic organ prolapse is complicated and multifactorial. Risk factors include pregnancy, childbirth, inherited or acquired connective tissue disruption, hysterectomy, white race, denervation or weakness of the pelvic floor, obesity, smoking, advancing age, estrogen deficiency, and actors related to chronically raised intra-abdominal pressure. Weakening of the main supportive structures of the pelvis, which are composed of the pelvic musculature and fascia, results in stretching and sometimes tearing of the endopelvic fascia and prolapse of the now inadequately supported pelvic organs [6].

It is estimated that 50% of women over the age of 50 years have prolapse, but only 10% to 20% of these women present seek assessment for their condition. [25] A large demographic study by Luber et al. reported that the greatest incidence of symptoms due to prolapse is among ages of 70 and 79, although POP symptoms are still relatively prevalent in younger women [26]. Wu et al. [27] predict that by 2050 the number of women with symptomatic POP in the United States will rise by a minimum of 46% (from 3.3 up to 4.9 million women) and in a “worst-case scenario” up to 200%, which means 9.2 million women will be affected by POP [25].

1.9. Description of functional POP symptoms

Functional abnormalities caused by POP involve four main areas: (1) lower urinary tract, (2) bowel, (3) sexual, (4) local symptoms, and (5) quality of life [28].

1.9.1. Urinary symptoms

Women with POP experience a variety of voiding symptoms, although most have stress or urge incontinence [29-32]; these include stress incontinence, urgency, frequency (diurnal and nocturnal), hesitancy, urge incontinence, weak or prolonged urinary stream, feeling of incomplete emptying, a need for manual reduction of prolapse to begin or complete bladder emptying, or for positional alteration to start or complete voiding [33]. Manual reduction or altered position to urinate is most often needed with large anterior wall prolapse [29, 32]. Prolapse repair may improve or cure both voiding dysfunction, including stress and urge incontinence [33].

1.9.2. Bowel symptoms

There is no internationally accepted definition of fecal incontinence or constipation. It is controversial whether constipation is caused by or an effect of

weakness deformity in the posterior rectovaginal fascia [33]. Symptoms related to POP include urgency of defecation, feeling of incomplete evacuation, incontinence of flatus, incontinence of liquid stool, incontinence of solid stool, fecal staining of underwear, hardness with defecation, inconvenience with defecation, digital manipulation of vagina, perineum, or anus to complete defecation, and rectal protrusion during or after defecation. Defecography is usually used to diagnose and assess defecation problems that cannot be evaluated fully by clinical examination [33].

1.9.3. Sexual symptoms

Dyspareunia is a multifactorial and widespread symptom among elderly women with POP; the feeling of a tight or shortened vagina is common [34, 35]. Other sexual complaints due to urine leakage during intercourse, embarrassment, and vaginal drought are more widespread in those with urinary Incontinence (UI) or POP compared with normal women [36]. Other studies found that vaginal surgery, particularly posterior colporrhaphy, is a risk factor for sexual problems and dyspareunia [34, 35]. It can be hard to differentiate between the capacity to have vaginal intercourse and normal sexual function [28].

1.9.4. Local symptoms

Local symptoms can occur due to the existence of a protrusion or bulge that may be seen or felt [29, 30, 37-39] and include the following: vaginal or perineal pain, feeling of tissue bulge in front of the vagina, vaginal compression or heaviness, abdominal pressure or ache, low back ache, and observation or palpation of a mass [28]. The absence of vaginal bulge symptoms post-surgery is an important element in a patient's evaluation of improvement in quality of life after surgery, whereas anatomical success

alone does not [40]. Clinical assessment includes comprehensive visual inspection and an evaluation of how these symptoms impact quality of life [25].

1.9.5. Quality of life

Quantification of health-related quality of life (HRQOL) may be categorized into two types: generic and condition specific. Generic HRQOL tools are apply to estimate quality of life in a wide range of diseases or populations while condition-specific measurement systems are developed to measure the result of a particular problem on HRQOL. Women with advanced stage POP (stage 3–4) have low generic and condition-specific HRQOL in comparison with women with normal vaginal support [41]. It is recommended that researchers describe the results of POP surgical techniques on HRQOL [25].

1.10. Pelvic organ prolapse staging

Correct staging of POP has an important place in clinical assessment, treatment allocation, and outcome studies. The POP quantification (POP-Q) system [28] was approved by the International Continence Society in 1996; however, other clinical staging systems exist, as currently it remains hard to make a comprehensive diagnosis on clinical examination alone in patients of posterior vaginal wall prolapse and/or a multi-compartment deformity [42]. Problematically, underestimation of POP staging can result in sub-optimal surgery [43], and is one of the causes for the high rate of recurrence and need for repeat procedures after prolapse surgery [44-46]. Currently, the lack of uniformity in staging complicates comparison of published reports and the longitudinal assessment of patients [28].

1.11. Early POP grading systems

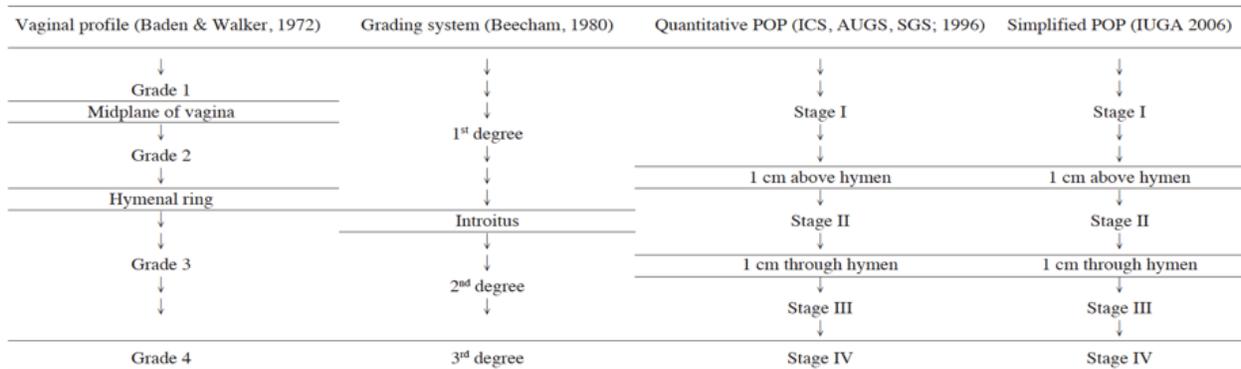
Baden and Walker reported a classification system in 1972 that divides the vagina into three segments: the anterior vaginal wall, the apex, and the posterior vaginal wall, and then additionally subdivides each vaginal segment into two anatomic points, to develop a vaginal profile employing six points, which are designated stages from 0 to 4 [47, 48]. In this classification system, a normal vagina with sufficient support of all six segmentations has a vaginal profile that may be reported as "0-0---0-0---0-0". If an urethrocele protrudes outside the hymen, a cystocele downward to the hymen, and structure components of the superior and posterior segments are without problems, the vaginal profile is described as "3-2---0-0---0-0". Each component is assigned stages 0 through 4. The hymen ring is utilized as a reference point. It is called the "half-way system".

Another widely applied staging system reported by Beecham [49] is also in use. Beecham thought that a urethrocele cannot be considered as a single existence. It can be a portion of a primary cystocele. Most abnormal support of the anterior vaginal point should be considered as a cystourethrocele. Utilizing the introitus as a reference point, he graded the largest of vaginal supporting problem from first to third degree as the following: cystocele, uterine prolapse, enterocele, rectocele, and prolapse of the vaginal apex (Fig. 1.3).

The above two classification systems determine the supporting or suspension anatomical problems as site specific. The patient is assessed during greater straining by using a bidigital method or inserting the speculum or tenaculum inside the vagina. However, these two systems are not fully accepted [47]. Therefore, in 1996 the POP-Q

system was introduced by the Calibration Sub-committee of the International Continence Society (ICS) in cooperation with the American Urogynecologic Society (AUGS) and Society of Gynecologic Surgeons (SGS) [28].

Figure 1.3. Comparison of the three-validated pelvic organ prolapse grading systems and a current simplified POP grading system suggested by the Standardization and Terminology and Research and Development committees of the International Urogynecology Association (IUGA) in 2006 adopted from (Swift S, Morris S, McKinnie V, et al. [50] open access).



1.12. Pelvic organ prolapse quantification system POP-Q

The POP-Q system proposes that the clinical characterization of pelvic floor anatomy should be defined through physical examination of the external genital and vaginal canal. The POP-Q system utilizes segments of the lower reproductive tract to change terms used in the two systems described above, such as cystocele, rectocele, enterocele, or urethrovascular junction [51].

The POP-Q system confirms that the criterion for the end point of the examination and the maximum protruding of the prolapse must be determined. The criteria for defining a full extent of prolapse should involve one or all of the following: protrusion of the vaginal wall becomes narrow during straining by the patient, traction on

the prolapse causes no further descent, the size of the prolapse and the extent of the protrusion are extensive, and a standing, straining examination emphasizes that the maximum extent of the prolapse was seen in different positions [28]. The degree of pelvic organ prolapse can be evaluated sufficiently in the dorsal lithotomy position with the patient doing a maximum Valsalva maneuver. It is not essential to regularly repeat the examination in the standing position [52]. Nine measurements of the defined points comprise two on the anterior side, two on the posterior side, two externally, two superiorly, and the total vaginal length; these should be registered during pelvic examination [51].

Prolapse should be assessed by a standard system relative to obviously determined anatomic points of reference. There are of two types: a fixed reference point and defined points that are situated with respect to this reference [28]. The defined points that are quantified in the POP-Q examination are shown in Figure 1.4, and the grading system of the POP-Q is summarized in Figure 1.5.

Figure 1.4. Points and landmarks used for POP-Q system examination adopted from (Chen G-D, Ng S-C. [51] open access).

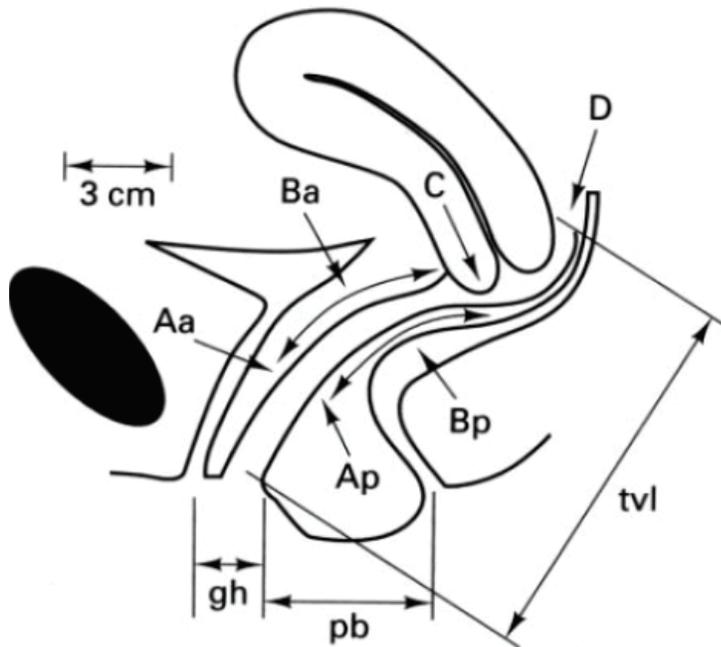


Figure 1.5. The scheme used for enrollment of the nine points adopted from (Chen G-D, Ng S-C. [51] open access).

A point on the anterior vaginal wall, 3 cm proximal to the external urethral meatus Aa	The most dependent point of the upper anterior vaginal wall; from vaginal fornix to Point Aa Ba	Most distal edge of cervix or the leading edge of vaginal cuff C
A point at posterior vaginal wall, 3 cm proximal to the hymen Ap	The most dependent point of the upper posterior vaginal wall; from vaginal fornix to point Ap Bp	A point represent the location of the posterior fornix D
Middle of the external urethral meatus to the posterior midline hymen gh	Posterior margin of the genital hiatus to the midanal opening pb	The greatest depth of the vagina tvl

1.13. Limitation of the POP-Q system

Critics of the POP-Q system claim that it is hard to learn and does not address all pelvic support abnormalities; problems like paravaginal dysfunction and relaxation of the proximal anterior or posterior walls are usually forgotten by this system [53]. The clinical POP-Q evaluation system is not conducive to discerning the full extent prolapse. In the office setting, the patient is afraid of urinating or defecating while straining and

conscious of someone watching, which makes it more likely that the patient will contract the pelvic floor while straining. Additionally, not all patients understand how to Valsalva [54]. There is anecdotal evidence from several members of the ICS and AUGS that the POP-Q system is not being broadly used. The most common causes cited were that it is time consuming and too confusing [55].

1.14. A new simplified POP classification system

A new simplified POP grading system was suggested by IUGA at the end of 2006 [50]. In the new simplified system, just four vaginal segments are specified to be assessed: the anterior vaginal wall, the apex or posterior fornix, the cervix (when present), and the posterior vaginal wall. The classified system for each segment is close to that of POP-Q of 1996, but there are no specific measuring tools suggested for quantitatively grading the prolapse segments.

The simplified POP-Q points for each segment are different from those of the validated POP-Q system as follows: (1) the anterior vaginal segment is graded by using point Ba, (2) the posterior vaginal segment is graded by using point Bp, (3) the cervix is graded by using point C, and (4) the apex/posterior fornix is graded using point C in non-hysterectomy women and point D in hysterectomy women.

1.15. Surgery

Surgical treatment of POP has increased as quality of life has become an increasingly significant factor in patients' lives. Accordingly, the annual incidence of POP surgery is now 1.5 to 1.8 patients per 1000 [56]; by the age of 80 years 11% of women have undergone POP surgery ; up to 30% require a repeat operation; and the total cost of POP surgery is more 1 billion dollars per year in the United States [57].

Repeat surgery implies surgical failure. However, reoperation commonly happens due to successful operation in a single compartment predisposing the patient to worsening prolapse in the other compartment or due to onset of UI [56]. When POP reoccurs after hysterectomy, it often exists as vaginal apical prolapse. There are several surgical reasons for vaginal apical prolapse [58].

1.16. Surgical procedures

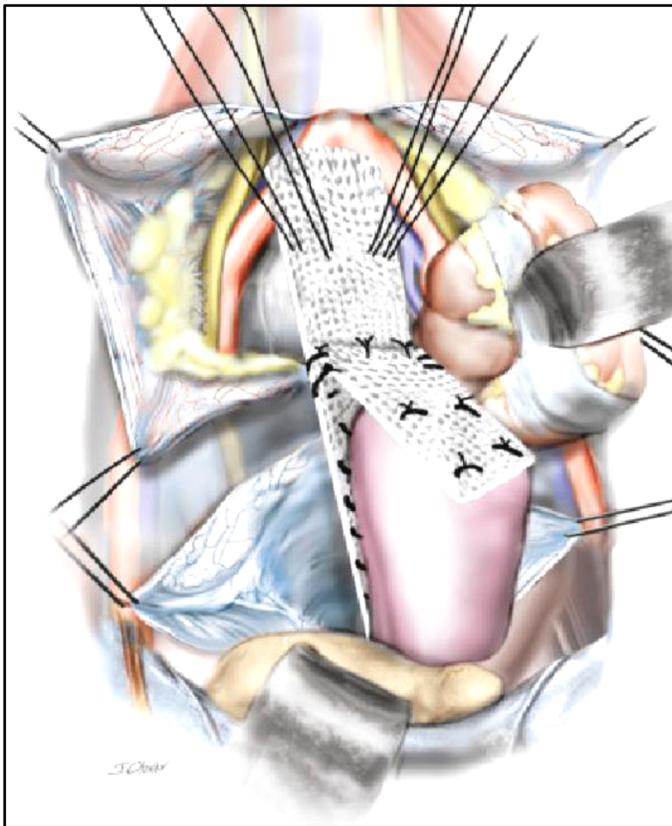
1.16.1. Sacral colpopexy (open, robotic, and laparoscopic)

For a long time, abdominal sacral colpopexy (ASC) has been considered the best intervention for vaginal vault prolapse. In this technique, the displaced vaginal vault is fixed anteriorly to the longitudinal ligament of the sacrum by using polypropylene mesh. After the vaginal vault is dissected and separated from the nearby organs, the bladder and rectum, one end of the mesh is stitched to the vaginal vault while the other end is stitched to the longitudinal ligament (Fig. 1.6) [59]. Because the mesh is helping support the vagina, it has maximal stabilization consequences, with a great success rate and minimum recurrence rate. On the other hand, ASC is a relatively long operation associated with a long hospital stay, abundant blood loss, and elevated risk of significant complications.

There are many vessels next to the sacrum, and a secure region to suture is finite. To make matters more complex, vessel site differs between patients, and their routes are hard to anticipate. Moreover, the ureter is very near to the promontorial midsacral, which is a landmark for sacrocolpopexy, and its position varies between patients [60]. Traditionally, sacrocolpopexy has been performed through an open

transverse abdominal route; however, currently, robotic or laparoscopic sacrocolpopexy is usually performed.

Figure 1.6. The vagina is fixed by two pieces of mesh (one end of the mesh extending farther down in the posterior portion). On the other end the two pieces are jointly attached to the sacrum (adopted from Baggish and Karram [59] open access).

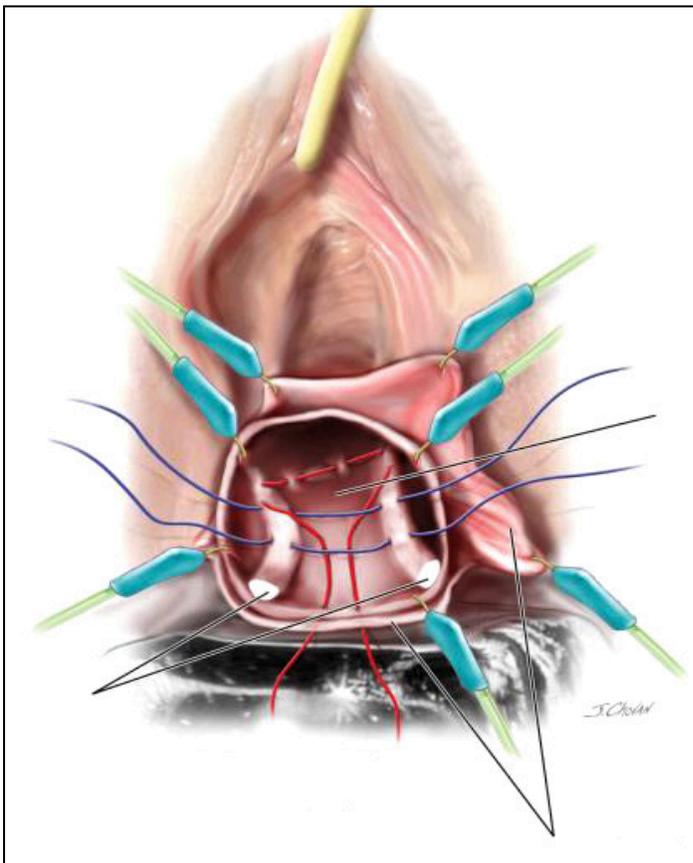


1.16.2. McCall culdoplasty

Among the several techniques of suspending the vaginal apex while performing vaginal hysterectomy, the most popular method is McCall culdoplasty. Although McCall

culdoplasty was not primarily introduced for vaginal vault prolapse, it is recognized to assist in avoiding prolapse recurrence after hysterectomy. McCall is performed by obliterating the posterior cul-de-sac and placing the uterosacral ligaments across the midline (Fig. 1.7) [59, 61].

Figure 1.7. McCall stitches from internal and external (adopted from Baggish and Karram [59] open access).



1.16.3. Sacrospinous ligament fixation

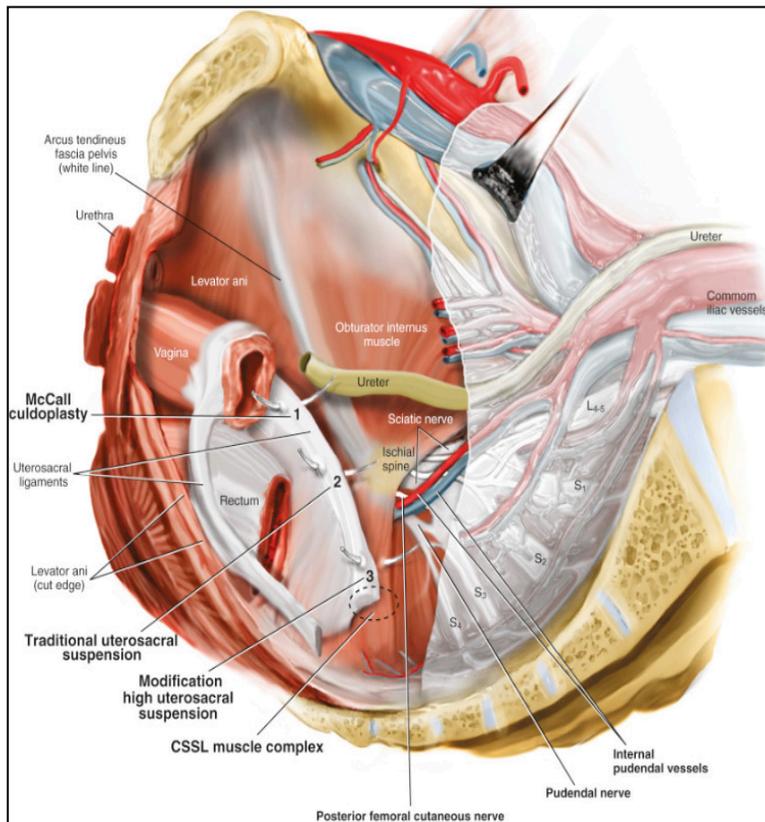
Sacrospinous ligament fixation (SSLF) is a popular technique for fixing apical vault prolapse through a vaginal route. Sederl [62] in 1958 in Germany reported that SSLF includes connecting the vault to the sacrospinous ligament, approaching via the dissected pararectal space [59, 63]. The sacrospinous ligament is situated among the

ischial spine and the lower portion of sacrum and coccyx. It lies within the coccygeus muscle, which is often known as the coccygeus-sacrospinous ligament complex [59]. The vaginal vault can be attached unilaterally or bilaterally to the ligaments. When done unilaterally, the end of the vagina deviates to one side. Despite the minimum recurrence range, prolapse of the anterior compartment appears and can recur more readily than that of the posterior compartment [64]. Many authors have proposed that this is because of deviation of the vagina toward the posterior orientation. This moves the anterior vaginal wall rearward and makes it more likely the anterior compartment must support more weight [65].

1.16.4. Uterosacral ligament suspension

Uterosacral ligament suspension (USLS) is another technique of apical vault fixation through vaginal approach. Miller's USLS has become a popular technique since it was first developed in 1957. When performing McCall culdoplasty, the uterosacral ligament is also utilized to suspend the vaginal vault, followed by internal McCall sutures [66]. In traditional USLS, the uterosacral ligament is plicated at or above the ischial spine level (Figs) [59]. Currently, a changed technique, indicated to be a modified high USLS, has been developed. The suture location is shown in Figure 1.8 [59]. High USLS can involve passage of the suture via the coccygeus-sacrospinous ligament complex, due to a part of the uterosacral ligament inserted into this structure [59]. Additionally, subjective symptoms were felt to be relieved in 82% to 100% of patients, giving evidence that USLS is a strongly efficient technique [67].

Figure 1.8. Intraperitoneal suite of sutures in a cross-section of the pelvic floor for (1) McCall culdoplasty, (2) traditional uterosacral suspension, and (3) adjusted high uterosacral suspension. CSSL, coccygeus-sacrospinous ligament complex (adopted from Baggish and Karram [59] open access).



1.16.5. Iliococcygeus fascia suspension

Iliococcygeus fascia suspension (ICG) was first developed by Inmon in 1963 [68] for patients whose uterosacral ligament was too complicated to be determined or too deficient to support the vaginal vault. It was modulated in 1993 by Shull et al. [69]. ICG uses the fascia of the iliococcygeus muscle below the ischial spine and lateral to the rectum, where there are fewer major blood vessels and nerves [70]. Because of this location of vaginal fixation, the vaginal axis is not disfigured notably and there is no deviation anteriorly or posteriorly, as in SSLF [71].

1.16.6. Vaginal mesh to augment apical suspension

It is important to repair vaginal apical prolapse using the patient's own tissue. There is another method to fix the vaginal apex that utilizes mesh and a transvaginal approach. However, when using mesh, there are several risks possible: erosion, pain, vaginal immobility, and inconvenience. Three of five exposures demand a surgical technique to take out mesh, and three patients had recurrent surgery for prolapse, whereas no patient in the no-mesh group demanded a recurrent surgery ($P = 0.017$) [71].

1.17. Pessary

1.17.1. History of pessary

Over numerous centuries several civilisations, such as the ancient Egyptians, Indians, and Chinese and through to the Christian and modern eras, have developed their own unique treatments and potions for cure of prolapse. 2000 years before the birth of Christ, scripts from the Kahun papyrus from ancient Egypt suggested standing the patient over a variety of burning substances to compel the displaced organs to return into the pelvis [72]. Many ingredients, including mould, fermented beer, and compost, have been suggested either for usage on the displacement organs or for consumption by the patient to cure prolapse. Hippocrates suggested succussion, where the patient was overturned to be head down and was shaken to put back the displaced organs into the pelvis with the assistance of gravity. Polybus, the Greek physician, produced one of the earliest "pessaries", half a pomegranate was inserted into the vagina (Fig. 1.9) [73]. Then Soranus, another Greek physician, suggested other techniques, including putting a linen tampon soaked with vinegar or a piece of beef into

the vagina. In the late sixteenth century the first device to be utilized as a pessary was developed, rather than using naturally occurring objects. Ambroise Paré developed oval-shaped pessaries, followed by Caspar Bauhin (1588) and William Fabry of Hilden in (1592), who devised pessaries of several shapes ranging from oval to globular. The word “pessary” emerges from the Greek word “pessos”, meaning an oval stone used in a checkers-like game. Oval stones were put into the uteruses of saddle camels using a hollow tube to prohibit conception during long desert voyages. This technique was used widely in both Arabia and Turkey and would have translated to insertion of all intrauterine devices [74].

Figure 1.9. Treatment by Polybus of vaginal prolapse by inserting a halved pomegranate soaked in wine into the vagina adopted from (Lamers BH, Broekman BM, Milani AL. [75] open access).



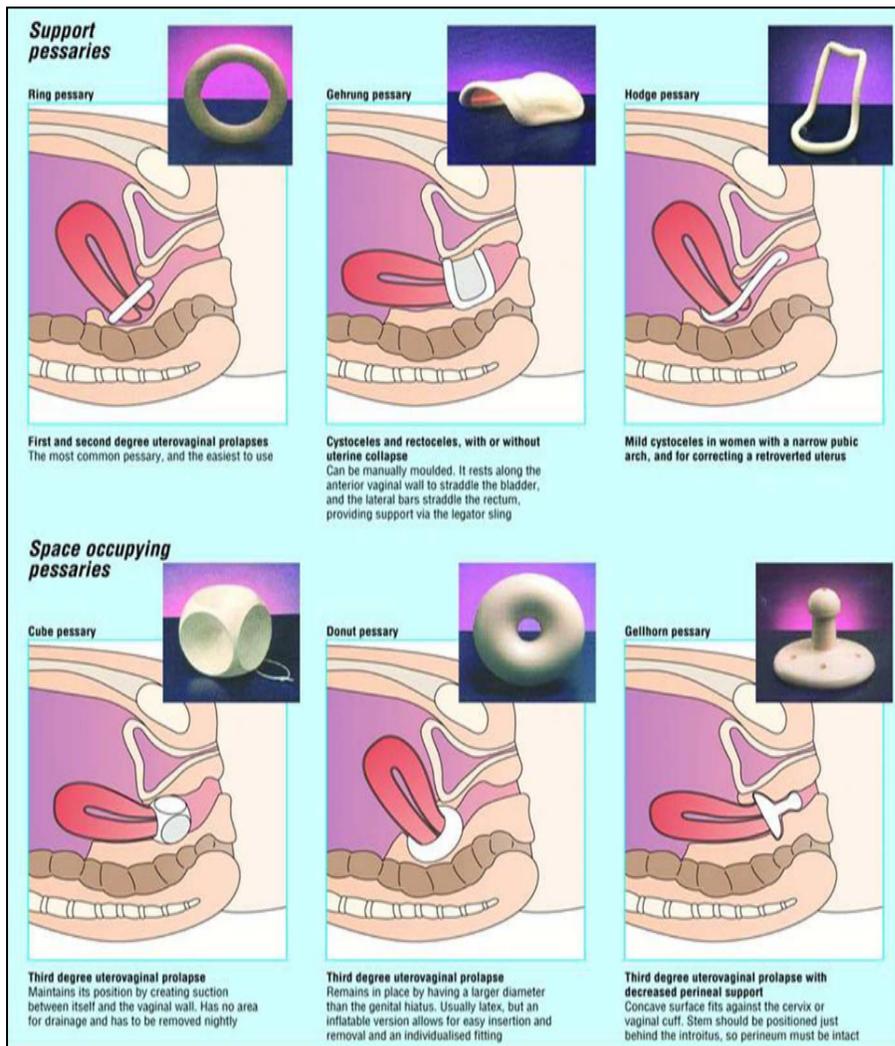
1.17.2. Indication for pessary usage

Today, the main indication for a pessary is the existence of a symptomatic prolapse when surgery is not possible. As a result, pessaries are usually used in older women, or in those with several comorbidities, for whom an operation is not possible [76]. However, full data on the most common age groups utilizing pessaries are scarce. Pessaries may be utilized as a diagnostic tool when there are unclear symptoms of back pain or urinary urgency. The usage of a pessary before surgery permits the gynaecologist to decide if an operation will effectively provide relief of symptoms. It may be also temporarily utilized in cases of denudation of the vaginal walls because of a severe prolapse or to promote the integrity of the vaginal tissues prior surgery. In cases of prolapse during pregnancy, when the prolapse is usually temporary until after childbirth when spontaneous return to a normal location can be predicted, a pessary can be suggested [77]. There is no consensus opinion in regard to whether they should be suggested as a first-line treatment for prolapse and which types are the most suitable [78]. Manufacturers' brochures provide common guidelines for the option of pessary type used but do not give direction as to which one patients should use [79].

1.17.3. Types of pessaries

Of the great number of pessaries developed, only 20 models still generally apply (Fig. 1.10) [80]. Modern pessaries are made of inert silicone-coated rubber and can be utilized in patients allergic to latex. Vaginal pessaries can be widely divided into two types: support pessaries and space-filling pessaries [74].

Figure 1.10. Varieties of vaginal pessary types used adopted from (Thakar R, Stanton S. [80] open access).



1.17.3.1. Support pessaries

Ring: The ring is the most widely used pessary. It is commonly successful in women with first and second stage prolapse. Due to the opening, it has some limitation, with the cervix protruding via the opening. The advantages of ring fitting are the capability to continue penetrative intercourse and the capability to keep the ring in the vagina for a long time; there is no need for daily removal [74].

Gehrung: The Gehrung is a folding pessary that supplies support to the rectoceles, cystoceles, and procidentia. It is useful in that it may be manually molded to suit the patient's type of prolapse.

Incontinence ring/dish: This is similar in shape to the ring pessary but with an anterior protuberance that supplies support to the urethra and bladder neck. Intercourse is possible with the incontinence ring but not the incontinence dish in place.

1.17.3.2. Space-filling pessaries

Gellhorn: This pessary is beneficial in several stages of prolapse. The Gellhorn is not compatible with sexual intercourse. The concave surface should be located against the vaginal cuff or the cervix, and the stem should be located posterior to the introitus. Short-stemmed differences are obtainable for women with shorter vaginal lengths. The Gellhorn will not stay in place if the perineal support is lax.

Donut: The donut pessary is successful for the severe staging of prolapse, particularly if the perineal support is lax.

Cube: The cube pessary must be removed before penetrative sexual intercourse. It is held inside the vagina by suction of its six concave surfaces on the vaginal wall, and it is important to remove and replace it daily, as the suction can cause of erosions and fistulas of the vaginal walls.

1.17.3.3. Inflatable pessary

These are a selection of flexible pessaries that can be self-adjusted and chosen for certain or irregular use according to the patient's conditions. As with the cube pessary, the inflatable pessary, as a result of impaction against the vaginal walls, must

be removed and replaced every 1–2 days. Its main disadvantage is that it cannot be fitted in latex allergic patients because it is made of rubber.

1.17.4. Pessary maintenance and follow-up

There is a lack of uniformity concerning follow-up, as it is commonly based on the patient's capability to insert and self-remove, the integrity of the vaginal epithelium, and potential for complications. Informing the patient about the symptoms and signs of possible complications is necessary so that she is conscious of any alteration in her voiding pattern. Any ulceration or vaginal excoriation observed should result in rapid cessation of pessary use until the vaginal skin recovers and replacement with a smaller-sized pessary or another type of pessary. Mild vaginal irritation is most common and does not require cessation of the pessary. Follow-up every six months is recommended for self-inserting patients, with more frequent follow-up visits for patients who are incapable to self-insertion [74].

Evidence is lacking on who should be responsible for cleaning and changing pessaries and how often this should be performed [81, 82]. Ideally, the physician can teach a patient how to remove and replace the pessary herself. This increases a patient's autonomy, allowing her to use it and clean it when needed [83, 84]. Patients who are not willing or able to handle pessary auspices themselves require more frequent doctor (or nurse practitioner) visits.

1.17.5. Guidelines for pessary fitting

In postmenopausal women, combining fitting with local estrogen therapy for a minimum of 6 weeks enhances effective fitting [85]. However, there is a lack of evidence about a combination of hormone replacement therapy (HRT) with the use of pessary or

training using pelvic floor exercises [78]. Hormone replacement therapy is prescribed to reduce vaginal irritation and ulceration because of pressure of the pessary in an elderly and atrophic vagina [86]. Prior to pessary fitting, there should be post-void inspection for remaining urine, as pessaries can result in obstruction of urinary flow. To fit a pessary, first examine the vaginal vault size with two fingers. Then, choose a covered ring pessary or the design suitable for the diagnosis. Next, lubricate the pessary on the end and then place and tilt it up back to the symphysis pubis. A finger breadth should fit between the pessary and the vaginal mucosa. As soon as the pessary has been fitted, the patient should walk around and exercise in the clinic to confirm that it will not instantly fall out. It is most important to confirm that patients are able to void and are provided with sufficient education prior to leaving the clinic with their fitted pessary. If pessaries are hard to remove, fishing wire or dental floss can be connected to the pessary to assist in removal. Recent Canadian practice recommends that a woman who is able to remove her own pessary should remove, clean, and replace it once per week [87].

1.17.6. Effectiveness of pessary usage

There can be a reduction in the size of the genital hiatus with continuous pessary wearing. The reduced size of the genital hiatus can be observed even after 2 weeks of continued pessary use [88]. There is observed improvement in POP stage after 1 year of pessary use. Such improvements may be due to a transient impact of using a pessary [83].

1.18. Current imaging techniques

Evaluation using imaging modalities is recommended in international guidelines when the appropriate indication(s), such as pelvic floor dysfunction, repeated unsuccessful surgery on posterior vaginal wall, and suspected fixed urethra, are present, and imaging is highly recommended in specific situations [89]. Imaging modalities employed currently include 2D and 3D ultrasound, computed tomography, and magnetic resonance imaging.

1.18.1. Ultrasound

Imaging the pelvic floor in cases of dysfunction dates back to the 1920s [90]. Radiological techniques were used first to show changes in the bladder's location within the pelvis and subsequently to demonstrate central and posterior compartment prolapse. During the 1980s the advent of B-mode real-time ultrasound allowed a clear image to be obtained by the transperineal or the vaginal route [91]. Translabial ultrasound can define uterovaginal prolapse [92]. The inferior border of the symphysis pubis works as a line of reference against which the higher descent of bladder, uterus, cul de sac, and rectal ampulla on the Valsalva maneuver can be measured [92]. Ultrasound imaging for prolapse quantification is especially helpful in outcome evaluation after pelvic reconstructive surgery, both clinically and in a research context, and it has also led to a re-appraisal of what is meant by prolapse.

The structures used for evaluation of the three compartments are (a) the bladder neck or the leading edge of a cystocele for the anterior vaginal wall, (b) the cervix (or, within certain limitations, the pouch of Douglas) for the central compartment, and (c) the rectal ampulla for the posterior compartment. All these structures are imaged in real

time in the mid-sagittal plane. An exception is a high undescended uterus that may be hidden by a rectocele [89]. Because of its non-invasive nature, ready availability, and lack of distortion, perineal or translabial ultrasound is now commonly applied in clinical practice [92], and almost all gynecologists and urologists are trained in its use [91].

Current developments such as the evaluation of levator ani muscle activity and prolapse and the use of color Doppler to define urine leakage are further promoting the clinical utility of ultrasound. Hopefully, improved standardization of parameters will facilitate the ability of clinicians and researchers to compare data [92]. Ultrasound imaging of the pelvic floor is safer, lower in cost, and better at providing visualization of the pelvic floor structures in real time than MRI. This includes evaluation of levator function and dynamic changes during contraction and Valsalva [93]. As yet, there are no comparisons of pre- and postnatal results gained with MRI, possibly because of cost and logistic problems. However, such a comparison is available for many hundreds of women studied by 4D translabial ultrasound [90].

Disadvantages of ultrasound include that a large bowel-filled prolapse, i.e., an enterocele or rectocele, may cause incomplete imaging of the cervix and vault if these structures remain high. In addition, variable transducer pressure can result in an underestimation of severe prolapse. Procidentia or complete vaginal eversion prevents translabial imaging, and sometimes what appears to be anterior vaginal wall prolapse will turn out to be due to a urethral diverticulum [94, 95].

1.18.2. Computerized tomography (CT)

CT scans are not usually recommended for imaging the pelvic floor because of the level of radiation required. However, this modality can offer accurate visualization of

the pelvic soft tissue and bony structures and has been used to increase the diagnostic accuracy of pelvic floor anatomical disorders [96]. Although the soft tissue contrast with CT is inferior to that of MRI, the bladder, uterus, small bowel, peritoneal fat, and rectum are readily identified, and changes in position with the patient straining can be visualized. Additionally, the contour of the levator ani muscles can be evaluated effectively, and images of pelvic anatomy can be produced in multiple planes. Therefore, in patients who cannot tolerate MRI and in whom rapid noninvasive multiplanar assessment of the pelvis is desired, CT has a role [97].

With recent scanners, tube output can be modified depending on the patient's body thickness, and this may help to decrease the radiation dose given. The pelvic floor and viscera can be visualized, and the addition of dynamic imaging can be applied to determine prolapse [97].

1.18.3. Magnetic resonance imaging (MRI)

Techniques associated with urology have developed over the last 30 years. In the 1990s MR techniques were improved with rapid and strong gradients and higher readout bandwidth. The first study depicting the using of MR for imaging pelvic organ prolapse was by Yang et al. [9] The increasing availability of MRI has added the benefit of this form of diagnostic imaging to evaluation in urogynecology and female urology, with more studies being done every year [92]. With the option of cross-sectional imaging methods, MRI has emerged as an alternate method to fluoroscopy for assessing patients with POP [9, 17, 98].

The benefits of MRI include multiplanar imaging and superior soft tissue contrast, which permits evaluation of the pelvic floor levator ani muscle in detail. The anatomy of

the levator ani is now known to be complex; it has been shown not to be a single muscle, being composed of two functional components that differ in thickness and function [93]. In addition, where there is organ prolapse, enhanced visualization of the rectovaginal space improves diagnosis of peritoneoceles and enteroceles and of the cervix clarifies cervical descent [97]. This allows demonstration of enterocele-type defects or peritoneoceles where there is just herniation of peritoneal fat and not bowel, comprehensive evaluation of the levator ani muscle, and visualization of the uterus.

The position and relationship of the pelvic organs are best visualized on MRI in the midsagittal plane. The imaging technique for the pelvic floor involves imaging in various pelvic floor positions. Firstly, the position of the pelvic organs is assessed at rest. Then, the pelvic floor muscle images are recorded during squeezing to view the contractility and the strength of contraction of the pelvic floor. In the third phase, pelvic floor pathologies are assessed during straining and evacuation. In a recent study to view the full extent of pelvic floor pathologies imaging was done during evacuation of a contrast agent; a number of pathologic conditions would have been missed if these defecation phase images had not been acquired [99].

Dynamic MRI techniques have been shown to be more sensitive than pelvic examination in evaluating and grading pelvic floor displacement in supine women and also for diagnosis of rectoceles [100]. In the case of an anorectal problem, MR defecography can identify several components of pelvic floor dysfunction, including rectal descent, enterocele, anterior proctoceles, and internal rectal prolapse [101]. The short acquisition time is relevant because patients do not need to keep on straining for more than 1 to 3 s. Patients are instructed in the Valsalva maneuver before the start of

the examination, and instructions are repeated frequently during the imaging sequence [102, 103]. Dynamic sequences that permit the acquisition of images in 1 to 10 s are helpful to obtain maximal strain [104].

Sometimes, patients cannot tolerate MRI due to claustrophobia, general weakness, or the presence of medical equipment [97]. Positive elements of MRI include the fact that filling the bladder, the vagina, or the rectum does not seem to be a fundamental requirement because of the high resolution of MRI, which prevents distorting the anatomy of the pelvic organs. Also, in a research context, MRI is acceptable to asymptomatic volunteers [105].

The expense of MRI imaging and limited access to scanning facilities has impacted widespread application of this technology. Additionally, because of the dynamic nature of pelvic floor pathology, it is controversial whether even fast MRI imaging can capture reproducible results owing to the dissimilarity of Valsalva maneuvers between studies and possible variations in levator activity [89].

The physical features of MRI systems make it complicated for the operator to ensure efficient conduct of the required maneuvers by patients; over 50% of women do not achieve a proper pelvic floor contraction during examination, and a Valsalva is very often confounded by associated levator ani activation [106]. Without real-time imaging, these confounders cannot be controlled for [90].

1.18.3.1. Upright open MRI (MRO)

This important technological advance provides the ability to replicate normal functional posture and enables the effects of gravity on prolapse to be evaluated for the first time. In POP, posture and gravity impact pelvic organ position, pelvic floor muscle

integrity, degree of prolapse, and symptom severity, and the degree of prolapse may be worse after time in the upright position and better when gravity is not a factor, e.g., when lying in the supine position [96]. In a MRO scanner the magnet is configured with a vertical gap, which enables patients to be scanned in the seated and standing positions as well as when supine, so MRO can replicate normal functional posture and enable the effects of gravity on the body to be evaluated.

Near-real-time sequences allow images to be obtained every 1.5 s. These can be stored and displayed on video, enabling a dynamic assessment of the pelvic floor from the resting position through straining and contraction [105]. The gynecologic literature proposes that straining in the lying position does not give sufficient deformity of the pelvic floor for accurate delineation of prolapse.

MRO allows visualization of all the pelvic organs and the pelvic floor support structures; obviously the technique combines the advance of allowing sitting and standing imaging with the known benefits of conventional MRI. I believe that the importance of this technique is that it enables comprehensive definition of the full extent of organ prolapse due to the effects of posture and gravity [105].

MRO is currently only available as a research entity, but with the imaging protocols developed as part of my research and the superiority of this form of imaging as a means of comprehensively evaluating and staging POP now demonstrated it is likely that as scanners are forthcoming that MRO will be used to improve the diagnosis and staging of POP [107].

1.18.3.2. Reference lines

Image interpretation from conventional and upright open MRI evaluates the three compartments of the pelvic floor [108]. The three compartments are evaluated for morphologic changes such as POP at various pelvic floor positions. To define the existence and descent of POP, the use of a point of reference is beneficial. Several points and lines of reference for measuring POP have been reported (Fig. 1.11) [109]. The more commonly used lines are the pubococcygeal line (PCL) and the mid-pubic line (MPL), both applied on midsagittal images. The PCL introduced by Yang et al. [9] is the line drawn from the inferior part of the symphysis pubis to the last coccygeal joint. Extending the posterior portion of the PCL to the sacrococcygeal joint also has been proposed because there is movability of the coccyx with straining [110].

In the early 2000s the MPL was introduced to define a common reference line for both clinical staging and MRI staging of prolapse [109]. The MPL is a line extending along the long axis of the symphysis pubis. The PCL represents the levator plate, while the MPL correlates with the level of the hymen, which is the landmark applied for clinical staging [111]. To measure pelvic organ prolapse a perpendicular line is drawn from the reference line (PCL or MPL) to the bladder base (anterior compartment), the cervix or vaginal vault (middle compartment), and the anorectal junction (ARJ) (posterior compartment) [112].

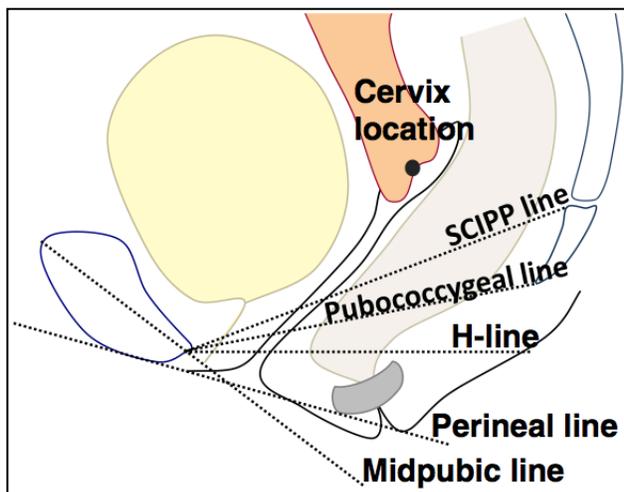
Another classification system, H line, M line, organ prolapse (HMO), has been proposed for measuring prolapse [100]. The H line is drawn from the pubis to the posterior anorectal junction and measures the levator hiatus width. Organ prolapse is measured relative to that line. The M line measures the descent of the levator plate from

the pubococcygeal line. The angle of the levator plate relative to the pubococcygeal line and the width and part of the pelvic hiatus on axial images can be measured as well [113].

The choice of which reference line is used is mostly made by the radiologist and/or the referring clinician, as neither of the two lines has shown distinct superiority [109]. The PCL, however, is the most-used reference line, particularly by surgeons and gastroenterologists. The MPL is better known among urogynecologists, as it is compatible with their clinical staging system. Both reference lines display only moderate to poor agreement with clinical staging of pelvic organ prolapse [103].

Congruity between this clinical standard and MRI imaging analysis should be used to document the utility of MRI and the success of treatment [113]. However, different criteria are currently used for diagnosing prolapse on MRI. Most research that reported using the bony reference lines uses one of the following criteria: (a) descent of the bladder base more than 1 cm inferior to the pubococcygeal line, (b) position of the cervix or vaginal vault less than 1 cm over the PCL or below it, and (c) descent of the posterior compartment more than 2.5 cm below the PCL (International Urogynecological Association and International Continence Society) [96]. There are also other minor differences in the diagnostic criteria applied for prolapse; cystocele has been defined as when the bladder descends to any area below the PCL, and uterocervical prolapse and enterocele are when the cervix or small bowel are below the PCL [17].

Figure 1.11. Shows how the pelvic reference lines will be drawn adopted from (Betschart C, Chen L, Ashton-Miller JA, et al. [250] open access).



1.19. Rationale

Pelvic organ prolapse (POP) exists when there is damage or deformity of the natural supporting structures of the pelvic organs, usually with weakened integrity of the pelvic floor musculature. The resulting loss of effective support of the pelvic floor causes the descent of one or more pelvic structures, including the bladder, rectum, uterus and cervix, or the vaginal vault and the small bowel [114]. POP has become a major health issue, as it can affect approximately 50% of women over age 50 [114]. The lifetime risk of requiring surgery for prolapse or urinary incontinence by 80 years of age is 11.1% in the United States [115] and has been as recorded to be as high as 19% [116]. Even with treatment, up to 30% of patients require repeat surgery [115]. The direct cost of prolapse operations has been calculated as more than \$1 billion per year in the United States [117]. Etiologic factors for pelvic floor prolapse include pregnancy, childbirth trauma, menopause, multiparity menopause, age, obesity, connective tissue problems, smoking, and chronic obstructive pulmonary problems [10]. Current conservative treatment uses a pessary; surgical treatment involves approaches based on the

symptoms and grade of prolapse [118]. Patient position, posture and gravity are known to impact symptom occurrence and severity and affect the stage of POP [119]. However, the current imaging modalities used for assessment can only provide images with patients in the supine position. For this reason, to more accurately stage prolapse and enable optimal treatment to be allocated, an improved imaging methodology is required that enables patients to be evaluated so that the impact of posture and gravity on their pelvic organs is evident.

My research addressed this need; the hypothesis and specific objectives follow.

Hypothesis: That an advanced imaging modality, upright open MRI (MRO), which enables patients with POP to be imaged when supine, sitting and standing, will provide images that enable patients with pelvic organ prolapse influenced by the effect of posture and gravity to be more comprehensively evaluated, by aiding detection of POP and improving the accuracy of disease staging. The following objectives describe my approach in addressing this hypothesis: (1) to develop a protocol for obtaining supine, sitting, and standing images of diagnostic quality using MRO in patients with POP; (2) to use MRO to determine if anatomic changes that are posture- and gravity-dependent in patients with POP are more readily detected in images taken when patients are sitting or standing rather than supine; (3) to evaluate if having MRO images taken when supine, sitting, and standing improves the staging of POP when using validated reference lines; and (4) to develop methodology for creating 3D models of the female pelvic floor from 2D MRO images in patients with POP, in order to improve definition of the anatomy and enhance detection of the impact of posture and gravity.

Chapter 2. An Integrative Review and Severity Classification of Complications Related to Pessary Use in the Treatment of Female Pelvic Organ Prolapse²

2.1. Introduction

Pelvic organ prolapse (POP) is a widespread and troublesome condition related to loss of anatomic support of the pelvic organs [33, 120]. Recognition of the condition can be traced back to Egypt in 1500 BC and treatment with pessary use was demonstrated by Hippocrates in 400 BC [121, 122]. The word “pessary” derives from the Greek word “peso” – an oval stone. The origin for all intrauterine devices is probably the use of oval stones inserted into the uterus in saddle camels to prevent conception during long desert journeys [74, 123-125].

The use of pessaries is common; more than 85% of gynecologists [126] and nearly 98% of urogynecologists prescribe them [78]. They provide anatomic support and can be used as a treatment of choice or in those who decline surgery (e.g., women who plan future childbearing, require temporary relief of prolapse while waiting for surgery or during pregnancy, or do not want surgical repair [127, 128].

Pessaries have few complications, although some authors suggest that they require lifestyle modification [129, 130], and the variety of shapes and sizes available affords choice and individual fitting [131]. However, data on complications relevant to appropriate discussion of consent with patients and planning of long-term follow up strategies are limited. The side effects of pessary use are not obvious; moreover, it is

² A version of Chapter 2 has been published. Abdulaziz M, Stothers L, Lazare D, and Macnab A. *Can Urol Assoc J* 2015;9 E400-6. DOI:10.5489/cuaj.2783

not clear whether the therapeutic impact is high enough to overlook possible risks or which patients benefit the most from pessary treatment [75]. Few studies have tested the relative value of different practice models for pessary use, although pessaries have assumed growing importance in the treatment of POP [79].

A 2004 Cochrane review of pessaries use for POP and updated in 2013 [129, 132] found only one randomized controlled trial examining the efficacy of pessary use [129]. Complications were described as rare and there was no consensus on complication management. Furthermore, there was no reference to complication severity grading.

In this study, we conducted an integrative review of reported complications related to pessary use and classified them according to a standardized severity scale. Since pessaries were used as an alternative to surgical treatment, and are a physical therapy akin to surgical therapy, the Clavien-Dindo [133] complication severity grading system was used. Conceptually this provided a comparison to reported surgical complications and also provided a means to appropriately inform patients about complications in the context of informed consent. A secondary objective was to categorize complications according to pessary shape, size, and material used.

2.2. Methods

2.2.1. Systematic review search strategy

A systematic search via MEDLINE and PubMed using the key terms “complications,” “pessary,” “pelvic organ prolapse,” “side effects” was conducted for the years 1952 to 2014 inclusively. Included articles had to have been published in English,

peer-reviewed journals, with the full-text available. Review articles were excluded because they either did not contain original material or duplicated extant reports.

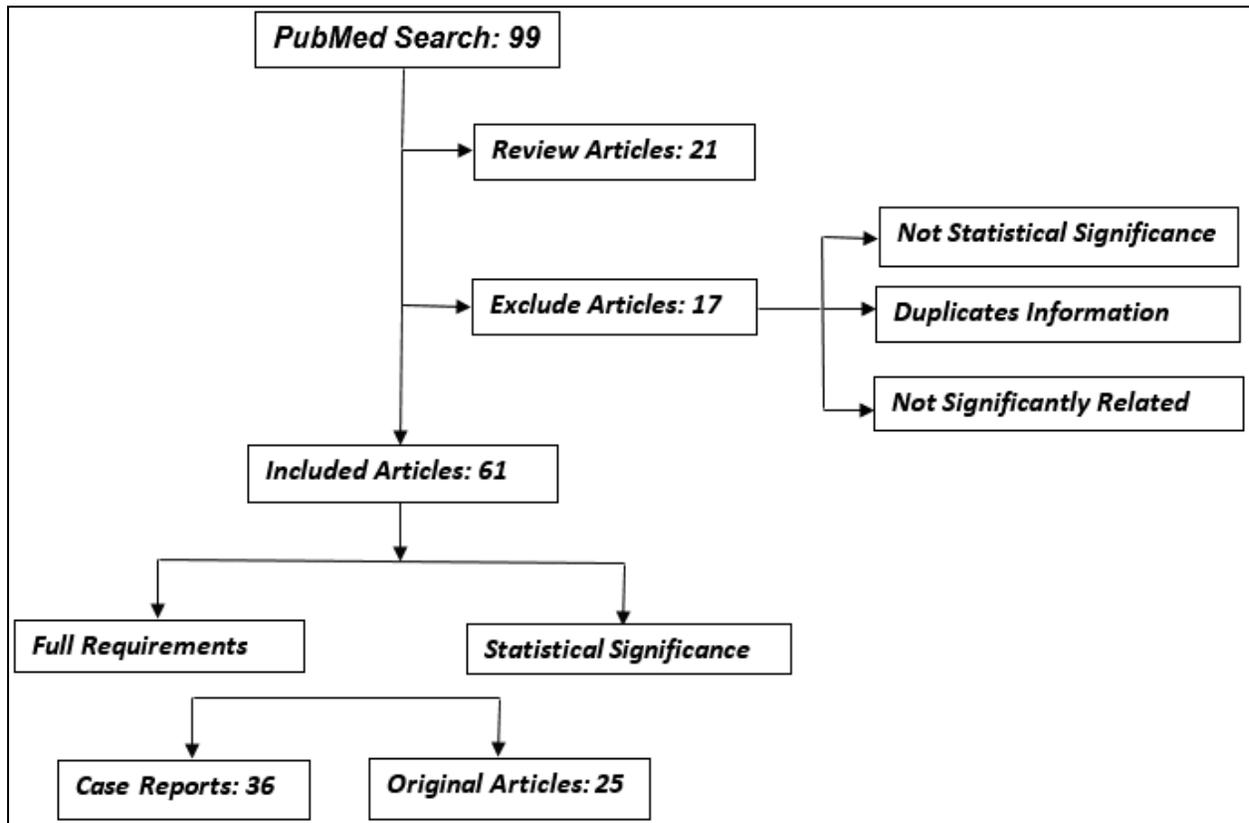
2.2.2. Analytic process

The authors reviewed each article to extract the following: complication(s) of pessary use, number of subjects, age, type of pessary (ring, shelf, Gellhorn, and cube), size, and material composition (silicon, polythene, gold, and metallic). In papers in which the nature or management of the complication was described, I categorized complication severity according to the Clavien-Dindo system [133]. In the instance of multiple reports of a single complication, I reported the severity of the outcome in more than 1 grade based on description of the management. Removal of a pessary as a management strategy, or a change from the treatment plan of self-care to dependent care was classified as a Grade 1 complication. This was felt to be akin to deviation from a standard protocol in the surgical setting.

2.3. Results

In total, I identified 99 full-text articles. Of these, 61 met the inclusion criteria (Fig. 2.1): 25 original case studies and 36 case reports. I excluded 21 review articles and 17 additional articles due to duplication or unrelated content (Fig. 2.1).

Figure 2.1. Flowchart of citation review and inclusion strategy.



In 34 papers, we were able to assess type, shape, size or composition of the pessary with complications (Table 2.1). Thirteen papers discussed complications related to pessary size [134-145]. By combining the data in both case reports and case studies, I found that the most frequent complications were: vaginal discharge, bleeding, vesicovaginal fistula, erosion, ulceration, and foul odor (Table 2.2). We graded the reported complications using the Clavien-Dindo classification (Table 2.3).

Table 2.1. Nature of complications of pessary use and frequency of reporting classified by type of report [83, 85, 146-154]

Type of study	Case report	Case series	Total
No. studies	34	25	61
No. total subjects	52	1138	1190
Erosion	11	44	55
Infection	6	13	18
Vesicovaginal fistula	16	18	34
Bleeding	19	10	29
Ulceration	10	4	14
Death	4	5	9
Pain and discomfort	2	60	62
Vaginitis	3	14	17
Vaginal discharge	21	35	56
Foul odor	9	18	27
Cancer	9	0	9
Fibrosis	2	0	22
Rectovaginal fistula	2	0	2
Bilateral hydronephrosis with urosepsis	1	0	1
Bowel obstruction	1	0	1
Unilateral hydronephrosis	1	0	1
Ureteric obstruction	1	0	1
Hydronephrosis	1	0	1

Table 2.2. Reported complications of individual pessary types [128, 134-145, 155-171]

Type of pessary	Gellhorn	Ring	Shelf	Porcelain	Doughnut	Cube	Metallic ring	Total
No. studies	6	15	8	1	1	1	2	34
No. patients	7	397	9	1	1	1	3	419
Erosion	2	40	2	0	0	0	0	
Vesicovaginal fistula	6	2	4	1	0	0	0	
Infection	3	13	0	0	0	0	0	
Ulceration	0	4	1	0	0	1	0	
Bleeding	1	28	3	1	0	0	1	
Death	0	0	2	0	0	0	0	
Discomfort	1	10	1	0	0	0	0	
Vaginal discharge	1	47	2	0	1	1	2	
Fibrosis	1	1	1	0	0	0	0	
Foul odor	1	23	0	0	0	0	0	
Slipped	0	16	0	0	0	0	0	
Ureteric obstruction	0	2	2	0	1	0	0	
Cancer	1	6	0	0	0	0	0	
Vaginitis	0	18	2	0	0	0	0	
Rectovaginal fistula	0	0	1	0	0	0	1	

Table 2.3. Classification of complications using the Clavien-Dindo system based on management strategies reported in the literature.

Grades (contracted form)	Definition	
Grade I:	Deviation from the standard course of therapy. Allowed therapeutic regimens including drugs: (antiemetics, antipyretics, analgesics, diuretics, electrolytes) and physiotherapy	Vaginal discharge Ulceration Pain Bleeding Constipation Material allergy Inability to self-replace or insert
Grade II:	Requiring pharmacological treatment (drugs other than allowed for grade I complications), blood transfusions, total parenteral nutrition	Vaginal discharge Erosion Vaginitis Ulceration Acute pyelonephritis
Grade III:	Surgical, endoscopic or radiological interventions	Vesicovaginal fistula Rectovaginal fistula Ureteric obstruction Retained pessary requiring surgical removal Decubitus ulceration of the uterus Hydronephrosis – unilateral and bilateral Bowel obstruction Vaginal fibrosis
Grade IV:	Life-threatening complication. Single or multi-organ dysfunction	Vaginal cancer Cervical cancer Small bowel incarceration
Grade V:	Death of a patient	Incarceration Enterovesical fistula Obstructive uropathy urosepsis

*In the case where multiple instances of a single complication were reported, the complication may appear in more than one grade based on how the complication was managed as reported in the literature.

2.4. Discussion

I systematically reviewed the complications of pessary use to treat POP. The frequency of complications varied widely between individual reports and between case series and case reports. Vaginal discharge, bleeding, and odor were frequently reported; however, in rare instances, dangerous complications included death, particularly if the pessary was neglected [134].

I have documented that all five Clavien-Dindo grades of complication occurred as a consequence of pessary use. The Clavien-Dindo approach is based on the type of therapy used to correct a specific complication and is a form of classification used increasingly in surgical research to provide an objective and reproducible ranking for the reporting of complication severity. Hence, extrapolation to pessary use was considered justified, because, like surgery, pessaries offer a physical treatment which makes this type of classification more suitable than those used for pharmacologic treatments.

Despite the frequency of pessary use, complication reports predominantly came from case reports rather than case series [172]. Some authors described pessaries as “outdated” and “risky” [173, 174]; there was even reference to the “dangerous pessary” [74]. I felt it was not appropriate to state the overall frequency of complications related to pessaries from the reviewed literature. As the denominator is either small or unknown in most studies, I was cautious in our data interpretation. Others have reported that complications affect <10% of patients [155, 175]. Overall, very few reports defined pessary complications by type, shape, material, or size and objective classification of severity was lacking. This information is important to ensure patients are properly

informed and to ensure proper patient consent in patients undertaking long-term pessary use and in their follow-up care.

It is important to discuss the following points with patients. A superficial vaginal mucosal erosion is the most frequently reported complication of a pessary [136, 173, 174, 176-178] presenting as foul odor, purulent discharge, irregular blood-stained discharge, and increased vaginal fluid. Localized pressure effects can result in ulceration and abrasions of the vaginal mucosa [154, 179] and in rare cases reduced local blood flow secondary to chronic pressure has caused decubitus ulceration of the uterus [180]. Reported risk factors for erosion include long-term uninterrupted use or placement of a pessary that was too large [145]. Recommendations associated with this literature stress the need for proper sizing and performance of periodic examination [142, 179].

Vaginal flora are affected by pessary use. Many patients have a physiologic watery discharge; this finding is not considered an infectious process unless accompanied by other symptoms (e.g., itching, burning, or foul odor) [179]. Vaginal discharge and infection may affect as many as one-third of users [181]; bleeding, pain, and constipation were also often reported [75, 182]. These issues have led to changes in pessary shape design [122, 183].

Serious complications include fistulae. Unlike minor complications which occur across all design types and materials, fistula frequency and location vary depending on pessary shape and material. Vesicovaginal fistulas (VVF), although uncommon, are among the most serious complications of neglected pessaries [158]. The reports identify Gellhorn and shelf designs most often [128]; rectovaginal fistula and VVFs appear more

common with rubber or PVC pessaries when compared with polythene pessaries [155]. Fistula formation may also be associated with fecal impaction, hydronephrosis, and urosepsis [172]; however, these complications were generally reported in the setting of neglect [136, 137]. Although serious complications caused by neglected pessaries are rare [159], in case reports describing VVFs, bowel fistulae, and incarcerated pessaries, 91% were correlated to neglected pessaries [128], and patients with dementia and nursing home residents could be at higher risk [177].

Several reports implicated pessaries as a causal mechanism for both vaginal and cervical cancer [139]. Chronic inflammation in association with viral infections has been suggested to predispose patients to such cancers as the tumours appeared at the site of pessary placement [184]. It has been proposed that wearing a vaginal ring or cup-and-stem pessary for a long time may cause cancer of the vagina, ulcerative vaginitis, or fistulae. Primary cancer of the vagina was reported in 6 women among a group of 13 with major pelvic complications correlated to long-term pessary use [156], and in a women who developed vaginal and cervical cancer after 18 years of pessary use [184]. Other mechanisms proposed included the generation of metaplastic and subsequent dysplastic change of the squamous mucosa [185], and the potential for personal cleanliness to play a role in carcinogenesis [160]. Although, primary vaginal cancers are uncommon (1%–2% of gynecological malignancies [185]) Jain and colleagues reported that two vaginal cancers occurred in users of shelf pessaries among 9 cases of vaginal carcinoma reported between 2003 and 2005 [160].

Death has resulted from pessary use. An 82-year-old woman with a ring pessary developed vaginal bleeding; biopsies showed extensive surface ulceration, necrosis,

and suppurative inflammation, and she died from acute pyelonephritis with hydronephrosis [134]. A 77-year-old using a shelf pessary for 18 years reported vaginal bleeding and a foul-smelling discharge; examination revealed a vesicovaginal and a rectovaginal fistula, and she also died from acute pyelonephritis and hydronephrosis [156]. Also, an 88-year-old patient died following erosion of a pessary into the upper rectum [161].

The literature reviewed contained sparse information regarding the materials used in pessaries causing complications. This is an omission as pessaries are manufactured from an assortment of materials, including fruit, metal, porcelain, rubber, and acrylic [186], with each material having certain advantages and disadvantages. Most are made of medical grade silicone covering components of surgical steel [76]; some pessaries are radiolucent with elements of silicone, rubber, acrylic, latex, or plastic [185]. Medical-grade silicone pessaries are long-lasting, biologically inactive, do not cause allergy, and are not carcinogenic. Patients find them easy to wash and disinfect, using autoclave, boiling water, or a cold sterilization product [183, 187, 188]. Pessaries rarely cause an allergic reaction. They may change color with use and their material rarely fails or breaks, which would necessitate replacement [189].

No single pessary design was complication free. Historically, a large number of physical shapes exist; the American Medical Association had identified 123 types of pessaries by 1867 [76]. Pessary shapes can be classified as supportive or space-occupying, with or without mechanisms to reduce urinary incontinence. Supportive pessaries consist of ring and lever designs, including the Smith, Hodge, Risser, and Gehrung. Space-occupying pessaries for advanced prolapse include Gellhorn,

doughnut, and cube designs. Ring pessaries are generally easy to displace and Gellhorn/shelf pessaries can be more difficult to remove, resulting in pain and bleeding [187]. Sometimes anesthesia is required [190].

Our review has its limitations. It is limited to English literature. The overall frequency of individual complications of pessary use is unclear as the literature consists principally of case reports rather than prospective randomized studies. Although literature from over 50 years was reviewed, the number of patients studied is not large; hence the frequency of complications from pessary use may be underreported.

2.5. Conclusions

There are few detailed reports of complications of pessary use relative to the estimated frequency of pessary use worldwide. High-grade complications appear related to longevity of pessary use and lack of appropriate maintenance care. The incidence of complications in general also mandates follow-up of all women using pessaries in the long-term. Prospective studies documenting pessary complications by shape, material, and size, and objective classification of severity are required to further the scientific literature related to pessary use. Death, although rare, is a reported complication and should be included in the informed consent of patients undertaking long-term pessary use.

Chapter 3. Relevance of Open Magnetic Resonance Imaging Position (Sitting and Standing) to Quantify Pelvic Organ Prolapse in Women³

3.1. Introduction

The pelvic floor is a complex anatomic and functional structure that is integral to the support of the pelvic organs, maintenance of fecal and urinary continence and for normal coordination of relaxation during defecation and urination. The structural components of the pelvic floor are the endopelvic fascia and ligaments, the pelvic diaphragm, and the urogenital diaphragm [191].

The pelvic diaphragm incorporates four muscles groups: the levator ani muscle comprising the puborectalis, the pubococcygeus muscle, the iliococcygeus muscle, and the ischiococcygeus muscle [191]. The soft tissues of the pelvic floor include the endopelvic fascia, the levator ani muscles, the perineal membrane, the external anal sphincter, and the external genital or perineal muscles [192]. Functionally, the pelvic floor muscles combine sphincteric, supportive, and sexual actions [193]. The PFM have ability to contract voluntarily [194]. Contraction results in elevation and closure of all soft tissues of the pelvic floor and occlusion of the pelvic hiatus to resist descent forces through the pelvis [193].

Loss of integrity of these supportive structures can cause urinary and fecal incontinence, pelvic organ prolapse (POP) with descent of the anterior vaginal wall (cystocele), posterior vaginal wall (rectocele), and vaginal apex (enterocele, vaginal

³A version of Chapter 3 will be published. Abdulaziz, M, Stothers L, Lazare D, and Macnab A. Relevance of open magnetic resonance imaging position (sitting and standing) to quantify pelvic organ prolapse in women, *Can Urol Assoc J*, in press.

vault, or uterus) [47, 195]. Failure in one compartment is most often combined with disorders in other compartments [196-199].

The pathogenesis of POP is complex, with multifactorial causes involved; these include age, menopausal status, pregnancy, vaginal delivery, previous hysterectomy, chronic cough, chronic constipation, congenital factors, and obesity [196, 197]. Vaginal delivery is by far the most robustly associated factor, with over 90% of patients with prolapse being parous [27]. The proper staging of POP is essential for appropriate clinical care and accurate outcome studies [96]. Clinical examination alone is not sufficient to identify POP, particularly in the case of posterior vaginal wall prolapse or a multi-compartment problem [42].

Additional entities used in the diagnosis and staging of POP include dynamic magnetic resonance imaging (MRI) [102], which allows quantification of the degree of POP by relating pelvic organ descent to reliable anatomic landmarks [17, 100]. Other benefits are the lack of ionizing radiation and the clearer anatomical details of the soft tissue, such as muscles and pelvic viscera [109]. However, the lack of a standardized protocol for MRI grading of POP makes it difficult to relate clinical and MRI staging, which complicates clinical care [200].

Also, MRI assessment of POP has been restricted by the closed architecture of conventional MR technology which limits patient positioning to the horizontal plane [53]. With the recent advent of open magnetic resonance imaging (MRO), imaging in different positions including sitting and standing in addition to supine allows multiplane imaging of all three compartments and observation of their reciprocal relationships. Hence, MRO

provides superior visualization of the pelvic organs and musculofascial supportive structures [201].

Previous studies have reported that patient position affects the degree of POP observed on clinical examination. Barber et al. [202] noted that the degree of prolapse manifested in the dorsal lithotomy position corresponds well with a 45° upright quantification in a birthing chair. However, a greater extent of prolapse was observed in the upright position. A comparable finding was reported in a separate study [203]. Also, Visco et al. [204] reported a much greater degree of prolapse in the standing examination as compared with the supine lithotomy position [205]. Swift and Herring [52] made a comparison of POP quantification method assessments in the standing and lithotomy positions, and found that there was no statistical significant difference between the stages or any of the quantification POP measured method points in the dorsal lithotomy and standing orientations [205].

The purpose of this study was to use MRO to determine the anatomic differences in pelvic floor anatomy that occur in POP in relation to the position of the subject, by comparing imaging when sitting and standing to supine images, and relating organ position to validated reference lines. The hypothesis was that imaging in the standing and sitting position would identify POP not apparent in the supine position due to the effect of posture and gravity on the pelvic organs.

3.2. Materials and methods

A prospective study, carried out in the Department of Experimental Medicine and Department of Urological Sciences, University of British Columbia, Vancouver. Ethical approval was obtained from Vancouver Coastal Health (ethical review #V14-03507).

The study cohort was recruited from the urogynecology clinic and included women presenting with symptoms of POP and asymptomatic controls. All subjects signed informed consent and completed a screening sheet for metal devices; patients were included only if they were willing to be available for the time required for imaging. All medical charts were reviewed; clinical data, including symptoms of pelvic floor dysfunction and pelvic organ prolapse staging using the pelvic organ prolapse quantification system (POP-Q) were noted (POP-Q measurements were performed under the supervision of a urogynecologist). The MRO imaging protocol did not require oral or intravenous contrast agents, or bowel preparation; all subjects emptied their bladder prior to entering the scanner.

The scanner was an Open MRI unit made by Paramed Medical Systems (Italy) experimental unit located at the Center for Hip Health at Vancouver Coastal Health Research Institute (VCHRI). The field strength is 0.5 Tesla, and MRO imaging scans of the pelvis were obtained with patients positioned in the scanner when supine, sitting, and standing (Fig. 3.1). The source MR images were obtained in the axial and sagittal plane. Parameters used were: Sagittal Fast Spin-Echo with an echo train length of 9 (FSE9), Field-of-view (FOV) = 30cm x 30cm, Slice thickness = 10mm, Gap = 1mm, Number of slices = 5, Number of excitations (NEX) = 1, Echo Time (TE)=120 ms, Repetition time (TR)=2500 ms and acquisition time = 1m50s. Axial T1 Gradient Field Echo (GFE) pelvis images, which are normally known as Gradient Echo (GRE) (the manufacture of this scanner called the sequence as GFE.), FOV = 24cm x 24cm, Slice thickness = 5mm, Gap = 1mm, Number of slices = 40, Theta = 0 deg, Phi = 0 deg, The slices were prescribed in an oblique way to make the plane parallel/perpendicular to the

orientation of the spine or along the disc. NEX = 1, Flip angle = 80 deg, TE = 10ms, TR=470ms, and Acquisition time = 3m 1 5s (x2). To address the risk of fainting or dizziness during the standing scan we applied a deep venous thrombosis external pneumatic compression device around the legs of all patients scanned (Fig. 3. 2) and used a protocol that limited the time required for image capture in each position to 2 min. After the MR imaging was completed, the images were electronically transmitted to a workstation MRO Storage at UBC) for model generation.

Figure 3.1. Open magnetic resonance imaging. The MRO unit is shown in position to scan the pelvic floor with the patient (A) supine, (B) sitting, and (C) standing. The scanner's safety straps are shown across the abdomen to secure the patient. adopted from (http://www.hiphealth.ca/facilities/our-labs/upright-open-mri/Upright_Open_MRI).



(A)



(C)



(B)

Figure 3.2. A patient in the standing position of open magnetic resonance imaging (MRO) examination with a compression cuff around each leg. (source: original photograph taken for my thesis).

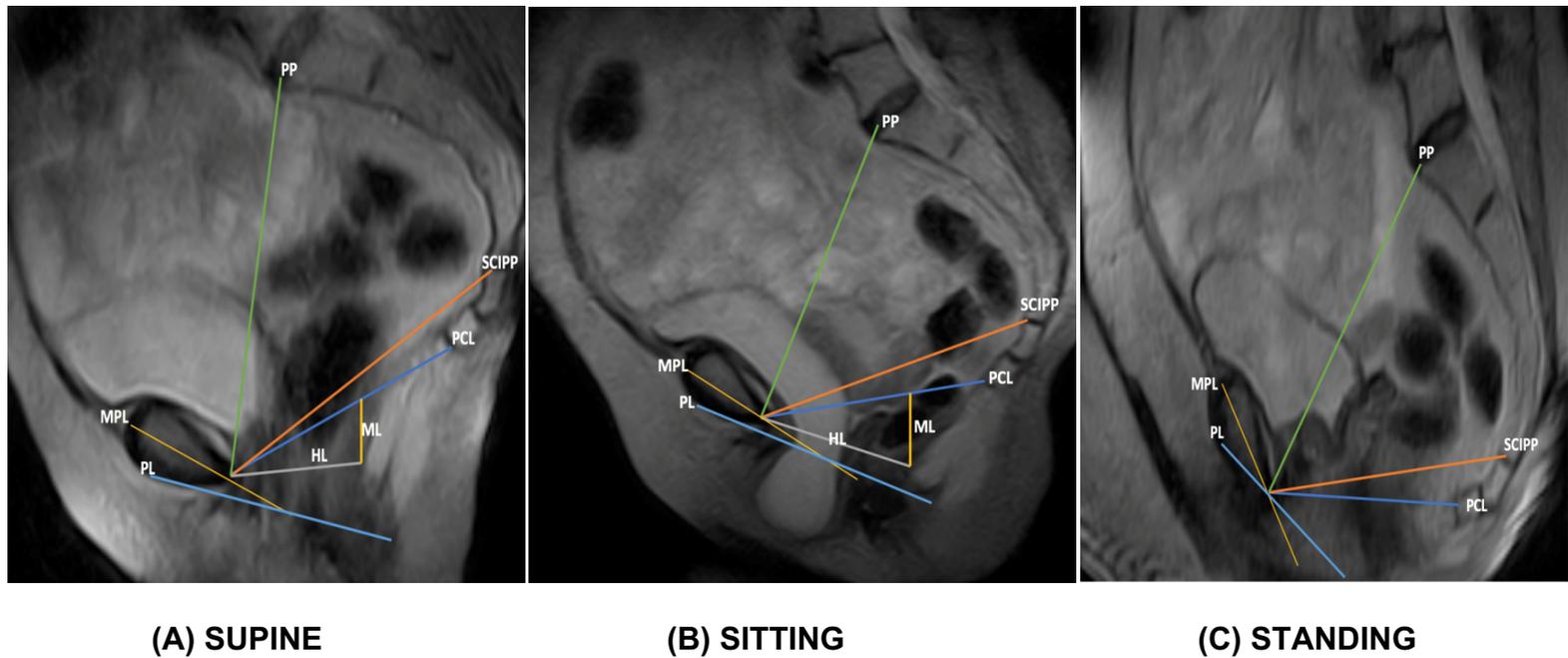


3.2.1. Reference lines

The reference lines used to assess POP are shown in Fig. 3.3. Pubococcygeal line (PCL) measurements for each examination were performed by drawing a midsagittal line from the inferior margin of the symphysis pubis to the last joint of the coccyx [206, 207]. I also used an H line (HL), a straight line between the inferior rim of the pubic and posterior wall of the anal canal on the level of the impression of the puborectal sling [208, 209]; a perineal line (PL), a line from the internal surface of the symphysis pubis down to the caudal end of the external anal sphincter [102]; a mid-pubic line (MPL), a line drawn through the longitudinal axis of the pubic bone and passing through its midequatorial point [102, 210]; and an M line (ML) drawn as a vertical line extending perpendicularly from PCL to the posterior limit of H line [45]. The

sacrococcygeal–inferior pubic point (SCIPP) line extends from the posterior surface of the pubis to the junction between the fifth sacral and first coccygeal bone [211].

Figure 3.3. Sagittal T2-weighted midline views of the female pelvis in a 51-year-old symptomatic subject demonstrating evidence of POP when the patient is imaged standing. The three images (A) supine, (B) sitting, and (C) standing show the pelvic reference lines (PCL, SCIPP, PP, HL, ML, MPL, and ML) used in the diagnosis of POP. (Original images from source subjects).



3.2.2. Anatomical landmarks and clinical measurement points

The MRO images taken in a supine, sitting, and standing position were assessed for POP with reference to anatomical landmarks in three pelvic compartments using the previously mentioned reference lines. The three pelvic compartments are identified based on anatomical landmarks: the most posterocaudal point of the bladder base (anterior compartment), the most antero-caudal point of the cervix or vaginal vault (middle compartment), and the anorectal junction and the most antero-caudal point of the anterior rectal wall (posterior compartment). The perpendicular distances from each reference line to these three different points were assessed using PCL. If the anatomical landmark is located above a reference line, the distance has a negative value; below the reference line it has a positive value [212].

3.2.3. Image analysis

Image analysis was done with Radiant software. RadiAnt DICOM Viewer [213] is an application for processing and showing medical images in format Digital Imaging and Communications in Medicine (DICOM), version 3.4.2, format. (Maciej Frankiewicz Poznan, Poland). An Intel (multicore Intel processor) or AMD 1GHz or faster processor is recommended) with 512MB of RAM (2GB is recommended). All images were analyzed by the same examiner, who was blinded to group status. Image analysis was based on all sagittal source images for the comparison of length of the pelvic reference lines between the patient group and control group (PCL, SCIPP, pubopromontoreal (PP), HL, ML, MPL, and PL) in the supine, sitting, and standing positions.

Perpendicular distances between the PCL and the bladder base, vaginal apex, and anorectal junction were used to grade the degree of downward descent in the anterior, middle, and posterior compartments, respectively. In the supine position with respect to the PCL, the grading system used suggests severity as mild, moderate, and severe. Degree of prolapse below the PCL by 3 cm or less was graded as mild, between 3 and 6 cm as moderate, and more than 6 cm as severe. Also, the distance from each of the anatomical landmarks mentioned above to the PCL was measured in the standing position. A rectocele is graded as follows: absent (displacement inferior to the PCL of less than 1 cm); mild (displacement of 1–2 cm); moderate (displacement of 2–4 cm); and severe (displacement of more than 4 cm) [96].

3.3. Results

Forty women, 20 with organ prolapse and 20 asymptomatic controls, were recruited and underwent MRO. Table 3.1 summarizes their clinical data (age, parity, mode of delivery, prior surgery, symptoms, and body mass index). Comparison data from applying the pelvic reference lines on midsagittal MRO images in women with and without POP when imaged standing, supine, and sitting are summarized in Tables 3.2, 3.3, and 3.4, respectively. (Images from three symptomatic women were excluded due to movement artefact compromising image quality.)

The standing image data (Table 3.2 and Fig. 3.4) show significant differences in the mean lengths of PCL, SCIPP, HL, ML, MPL, and PL between the control group and the POP group. However, the PP line measurement was not significantly different between the two groups. The differences between the women with and without prolapse were predominantly evident in the standing position.

Forty women, 20 with organ prolapse and 20 asymptomatic controls, were recruited and underwent MRO. Table 3.1 summarizes the clinical data (age, parity, mode of delivery, prior surgery, symptoms, and body mass index) for the symptomatic women with POP. Controls by definition through screening had no prior pregnancy, no lower urinary tract or protrusion symptoms and no prior pelvic surgery. These were exclusion criteria. The age range of controls were 26 to 40 (mean 30 years).

Table 3.1. Summary of clinical data on the 20 symptomatic subjects.

Subject	Age (years)	Pregnancy	Delivery	Prior surgery	Symptoms	BMI (kg/m²)
1	53	1	Vaginal delivery	No	Incontinence	22
2	48	3	Vaginal delivery	No	Urinary frequency	26.3
3	65	1	Vaginal delivery	No	Urinary frequency	19.5
4	53	2	Vaginal delivery	No	Protrusion	22.6
5	51	4	Vaginal delivery	Hysterectomy	Incontinence	29.8
6	46	4	Vaginal delivery	No	Frequent UTI	25.1
7	56	3	Vaginal delivery	No	Protrusion	26.8
8	61	2	Vaginal delivery	Mastectomy	Protrusion	26
9	54	3	C-section	No	Urinary frequency	32.5
10	51	3	Vaginal delivery	Mastectomy	Incomplete bladder emptying	30.8
11	52	2	Vaginal delivery	No	Constipation	23.7
12	46	2	Vaginal delivery	Dilation and curettage (D&C)	Frequency-Urgency	19.3

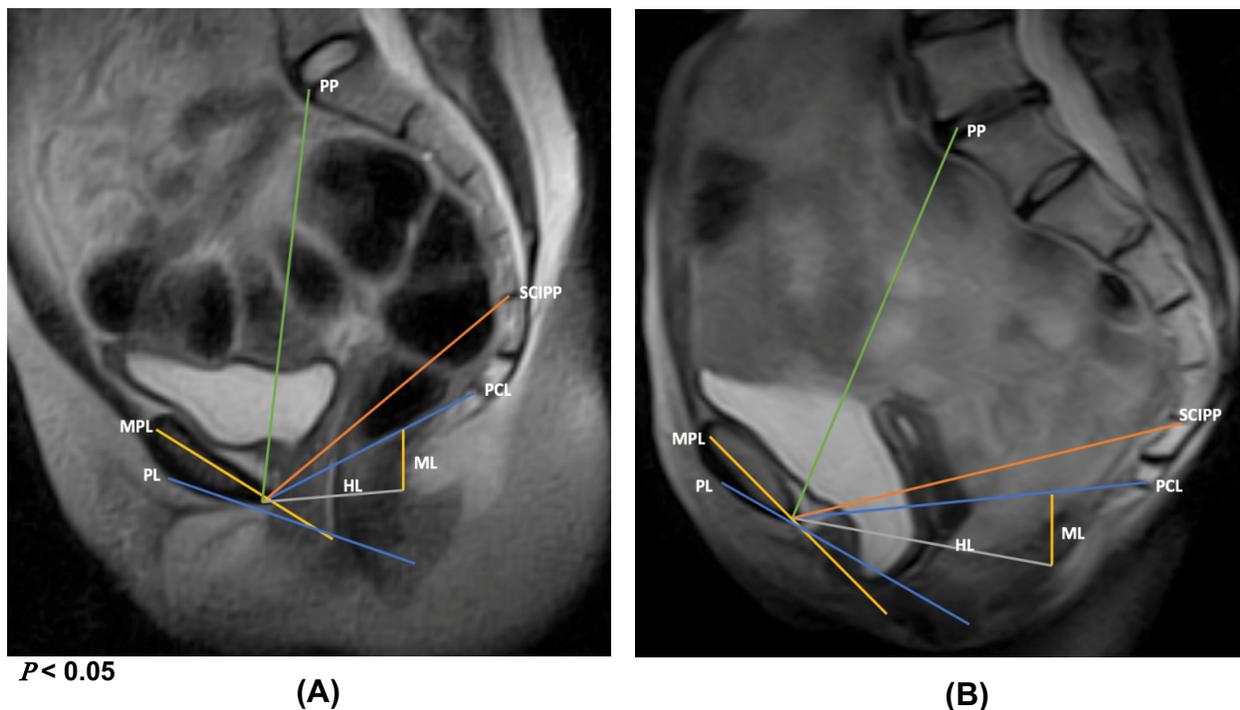
Subject	Age (years)	Pregnancy	Delivery	Prior surgery	Symptoms	BMI (kg/m²)
13	72	5	Vaginal delivery	No	Incontinence	35.5
14	76	3	Vaginal delivery	No	Incontinence	29.8
15	77	1	Vaginal delivery	Hysterectomy	Incontinence	25
16	43	2	Vaginal delivery	No	Urinary leakage	19.1
17	63	2	Vaginal delivery	No	Incontinence	30.5
18	73	2	Vaginal delivery	No	Incontinence	24.1
19	73	2	Vaginal delivery	No	Protrusion	25.6
20	61	3	Vaginal delivery	No	Stress incontinence	27.3

BMI, body mass index

Table 3.2. Comparison of data from pelvic reference line length (cm) between subjects symptomatic for POP and the control group obtained in the standing position.

Lines	Mean difference of control group in cm (N = 20)	Mean difference of POP group in cm (N = 20)	SD	Pvalue
PCL	9.96	10.83	0.61	0.01
SCIPP	11.80	12.58	0.55	0.01
PP	13.92	13.65	0.18	0.41
HL	5.79	7.80	1.42	0.00
ML	1.79	3.54	1.23	0.00
MPL	7.36	9.56	1.55	0.00
PL	8.19	10.89	1.91	0.00

Figure 3.4. Sagittal MRO midline views of the female pelvis obtained in the standing position. A) Midsagittal T2-weighted image of a 27-year-old control subject with measurement of reference line lengths. B) Midsagittal T2-weighted image of a 66-year-old symptomatic subject with measurement of reference line lengths. (Original images from source subjects).



The images taken in the supine position (Table 3.3 and Fig. 3.5) used the HL, ML, MPL, PP, and PL measurements; the increases in mean lengths between the two groups were statically significant. However, the PCL, and SCIPP line of each reference remained stable with no significant change in length between the control group and POP group.

Table 3.4 and Fig. 3.6 show that there were no statistical differences in the sitting position for PCL, SCIPP, MPL, and PL between controls and POP. I did not find it possible to use the HL and ML for the sitting position; the HL extends from the most inferior surface of the pubis to the posterior wall of the anal canal at the level of the anorectal junction, and ML is drawn as a vertical line extending perpendicularly from PCL to the posterior end of the H line. The effect of the sitting position is to cause an upwards movement of anorectal junction location above the PCL, which interferes with measurement using both these reference lines.

Table 3.3. Comparison of data from pelvic reference line length (cm) between subjects symptomatic for POP and the control group obtained in the supine position.

Lines	Mean difference of control group in cm (N = 20)	Mean difference of POP group in cm (N = 20)	SD	Pvalue
PCL	9.72	10.34	0.44	0.06
SCIPP	11.66	12.07	0.29	0.20
PP	14.34	13.77	0.41	0.04
HL	4.87	6.11	0.88	0.00
ML	1.45	2.12	0.47	0.00
MPL	6.57	7.70	0.80	0.00
PL	7.12	8.97	1.30	0.00

***P* < 0.05**

Figure 3.5. Sagittal MRO midline views of the female pelvis obtained in the supine position A) Midsagittal T2-weighted image of a 27-year-old control subject with measurement of reference line lengths. B) Midsagittal T2-weighted image of a 66-year-old symptomatic subject with measurement of reference line lengths. (Original images from source subjects).

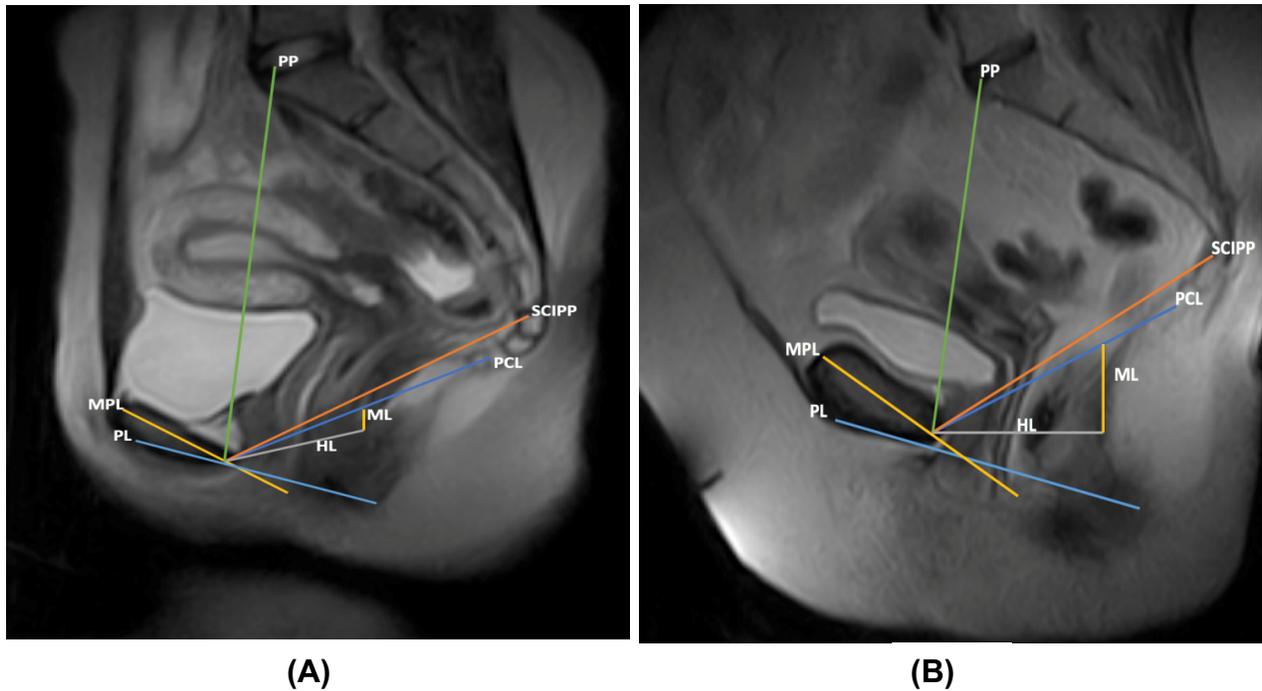
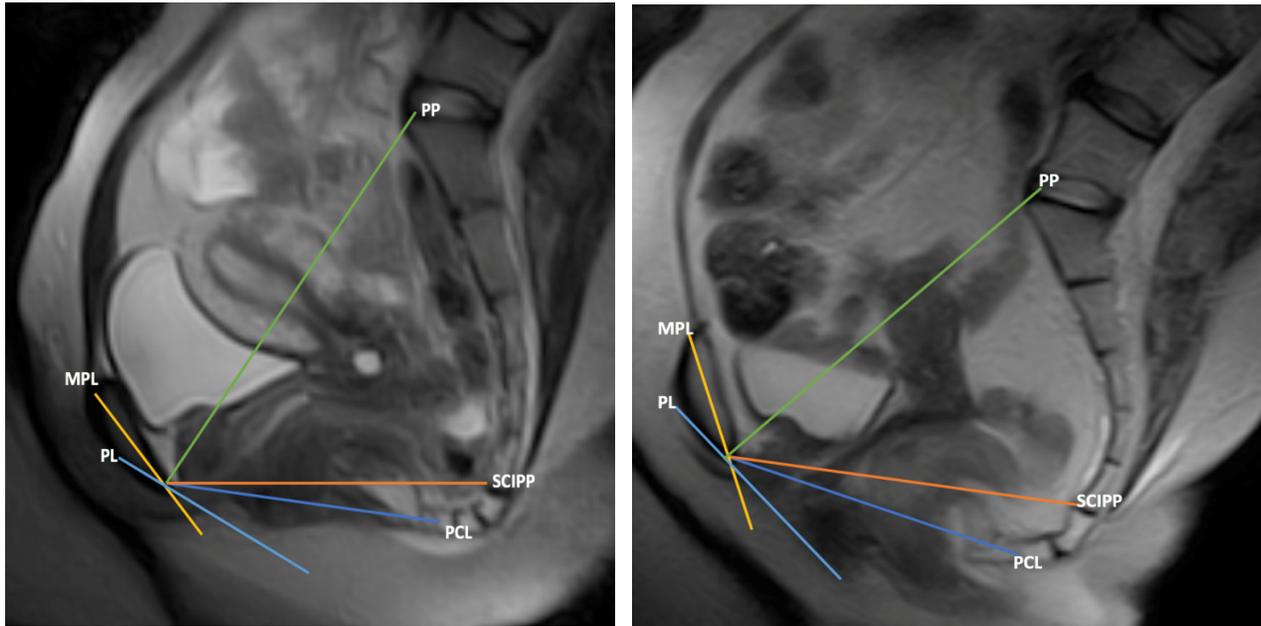


Table 3.4. Comparison of data from pelvic reference line length (cm) between subjects symptomatic for POP and the control group obtained in the sitting position.

Lines	Mean difference of control group in cm (N = 20)	Mean difference of POP group in cm (N = 20)	SD	P value
PCL	10.34	10.69	0.23	0.30
SCIPP	12.34	12.38	0.03	0.90
PP	14.21	13.56	0.46	0.04
MPL	6.61	6.78	0.12	0.44
PL	7.45	7.66	0.15	0.53

$P < 0.05$

Figure 3.6. Sagittal MRO midline views of the female pelvis obtained in the sitting position. (A) 22-year-old control subject midsagittal T2-weighted image showing measurements of reference lines. (B) A 51-year-old symptomatic subject midsagittal T2-weighted image showing measurements of reference lines. (Original images from source subjects).



The grading of symptomatic subjects for POP from images obtained using MRO in the standing and supine positions is summarized in Tables 3.5 and 3.6; the PCL reference line (Fig. 3.7) was used to grade POP (cystocele, vaginal prolapse, and rectal prolapse) as absent, mild, moderate, or severe. The occurrence of prolapse in the anterior and posterior compartments in the standing position was moderately higher than in the anterior and middle compartments in both positions. Our results suggest that the extent of prolapse is best evaluated in the standing position using HL, ML, MPL, and PL as reference lines.

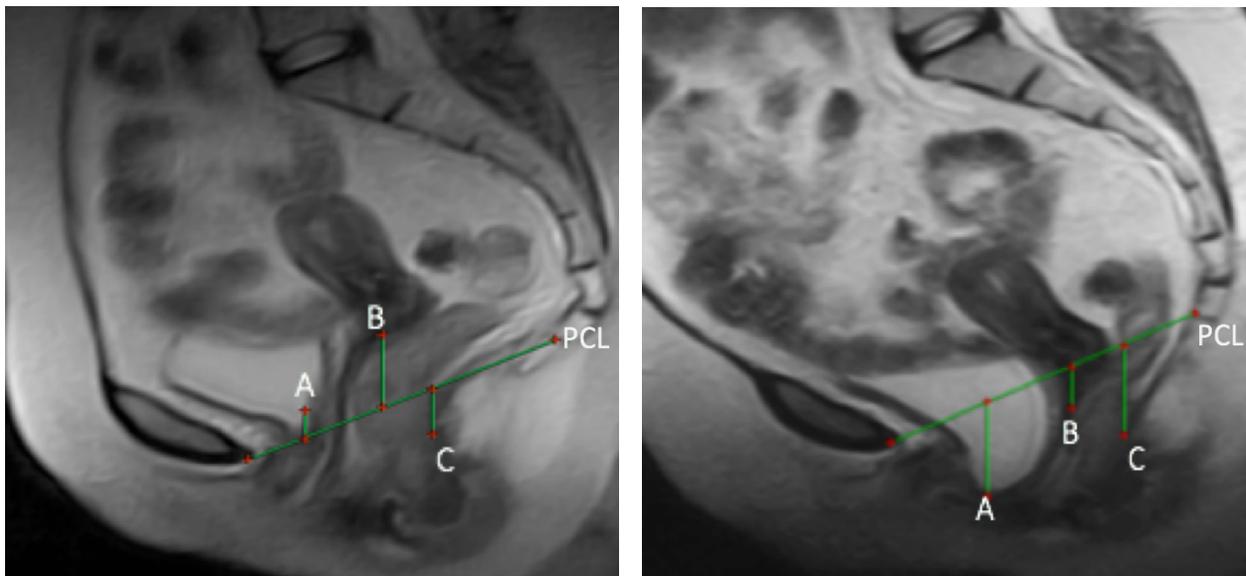
Table 3.5. Detection of POP in MRO standing images from the symptomatic subjects using reference line parameters.

PCL	Absent (%)	Mild (%)	Moderate (%)	Severe (%)
Cyctocele	10	50	30	10
Vaginal prolapse	45	35	20	0
Rectocele	0	10	80	10

Table 3.6. Detection of POP in MRO supine images from the symptomatic subjects using reference line parameters.

PCL	Absent (%)	Mild (%)	Moderate (%)	Severe (%)
Cyctocele	95	5	0	0
Vaginal prolapse	75	25	0	0
Rectocele	0	55	40	5

Figure 3.7. The perpendicular distances from the pubococcygeal reference line (PCL) to the bladder base, vaginal apex, and anorectal junction, which were applied to grade the degree of downward descent in the anterior (A), middle (B), and posterior (C) compartments, respectively; (A) supine, (B) standing. (Original images from source subjects).



(A) Supine

(B) Standing

3.4. Discussion

In this study, I have used MRO images obtained with patients standing, sitting, and supine to quantify the extent of POP using pelvic reference lines. We hypothesized that imaging in the standing and sitting position would identify prolapse not apparent in the supine position in patients reporting symptoms of POP, as the effect of posture and gravity on pelvic organ position would be detected. Currently, POP is assessed on midsagittal images using particular pelvic anatomic landmarks [214] and quantified and graded using reference lines [215]. In the literature, various reference lines have been introduced to assess POP during dynamic MRI. However, validation of these reference lines is lacking [109]. Hence, in this study I made use of multiple lines for comparison (PCL, SCIPP, PP, HL, ML, MPL, and PL).

Our data indicate that in standing MRO images the extent of descent of POP in all three compartments was greater than that seen in supine images, when the PCL, HL, ML, MPL, and PL were used for reference; hence standing position does provide a more comprehensive way of detecting POP and defining the extent of prolapse than any of the existing imaging tools, including conventional supine MRI, as the extent of descent of POP in all three compartments was greater when assessed using the HL, ML, MPL, and PL for reference. This confirms previous findings that the frequency of detection of anterior and posterior compartment downward prolapse can be best assessed when using MRO in the standing position. I have also reported the enhanced diagnostic information generated by creating 3D models of the pelvic architecture from 2D MRO upright imaging [107].

However, imaging in the sitting position did not demonstrate benefit in the context of POP. This was principally due to anatomical landmarks necessary for defining the HL and ML reference lines being obscured by upward movement of the anorectal junction above the PCL. While our hypothesis was only true for standing images, sitting MRO images could benefit POP evaluation in symptomatic patients confined to wheelchairs, such as those with spinal cord injury, even though the information added is less than from standing images.

Prior studies compared dynamic MR imaging and colpocystodefecography (CCD) in the diagnosis of prolapse in each compartment [216]. Their results concluded that dynamic MR imaging in the lying orientation was not precise in the assessment of pelvic floor prolapse [109]. In contrast, a study done by Swift et al. [52] reported no significant difference in prolapse grading between supine and standing positions. Another study reported that a higher extent of prolapse was observed in the standing orientation as compared with the supine examination, although another finding did not show this relationship [52, 202]. However, the effects of bladder fullness and patient posture have not been formerly examined [205].

The optimal choice of reference line is a subject of ongoing debate [109]. The PCL is commonly used because it is readily drawn on sagittal images [9] and was used in initial studies of MRI for POP because it is based on fixed bony points of reference [200]. The PCL also provides an assessment of the pelvic floor, as it is positioned along the plane of the pubococcygeal and puborectalis muscles [9]. Lienemann et al. [28] found the PCL was a beneficial reference line for prolapse in the anterior compartment only; however, Pannu et al. [217] described the PCL to be superior. In this study I found

no significant change in the length for the supine and the sitting positions between the two groups. However, the mean length of the PCL in the standing position was significantly different between the groups.

Lienemann et al. [207] also used the mid-pubic line in their study and reported that the mid-pubic line should only be applied for staging in the posterior compartment. Singh et al. [218] introduced the application of the MPL on MRI grading of POP. They concluded, upon cadaveric dissection, that the MPL passing through the plane of the vaginal hymen should be used in clinical examination. However, two different studies defined poor correlation between clinical assessment and dynamic MRI [102, 210], and some authors have uncertainty about the validity of this line to represent the hymenal level in vivo during maximum strain [102]. An inconvenient aspect of using the MPL for grading POP is that two separate measurements are needed: at rest and during strain [101, 209]. Importantly, in previous studies Woodfield et al. [200] and Singh et al. [218] found that the MPL yielded a much greater frequency of prolapse than the PCL, and our findings indicate that the MPL and PL measurements were significantly different between the control and the patient group for the standing and supine positions.

The SCIPP line has been used to quantify the distance to the perineal body and the angle of the levator plate when comparing women without prolapse and POP patients, grading anterior vaginal wall prolapse, and assessing levator ani recovery following vaginal birth [219]. However, the data I present indicate that for the SCIPP line the increase in length between the control group and POP patients was statically significant in the standing position but not in the supine or sitting positions.

Comiter et al. [100] introduced a new grading system for dynamic MRI scanning. The H line, M line, organ prolapse (HMO) classification system assesses the levator hiatus (LH), the muscular pelvic floor movement downward, and organ descent [53]. MRI and ultrasound studies have demonstrated that a levator ani muscle defect is a significant factor that is clinically related to POP [220]. It is reported that patients with prolapse have enlarged genital hiatuses [13]. This hiatal enlargement might be either the reason for or the outcome of prolapse. Defects and weakening of the levator ani muscle, as observed in prolapse, could lead to inability to keep the hiatus closed [220]. The length of the levator hiatus H line is 5 cm in normal women without pelvic floor laxity [1]. The M line is a line that extends perpendicularly from PCL to the posterior end of H line, and an average length of 2 cm is considered normal [45].

Dietz et al. [221] concluded that there is an association between LH and pelvic organ displacement, even in young nulliparous women. Likewise, a study by DeLancey and Hurd [13] also reported that urogenital hiatus size is related to prolapse size [222]. In this study, MRO images displayed significant elongation in dimensions of H and M lines that was seen in all POP patients in standing and supine positions but not in the control group.

I recognize that movement artefact compromised image quality in three subjects; however, our protocol does limit imaging time, and attention to this and attention to patient comfort in the scanner did improve quality image capture. Also, the ongoing debate over reference lines applied to MRI is a limitation that impacts our study. It remains hard to choose which pelvic reference lines would supply the best reference landmark for the MRO assessments of POP. But further MRO studies are required and

are pending. In this context the fact that few MRO systems are available currently for patient assessment also limits the relevance of our findings. However, the apparent superiority of MRO as an imaging entity for POP predicates that as more units become available clinicians and their patients should benefit from this advance in technology.

3.5. Conclusion

In conclusion, using MRO to image patients with symptoms of POP in an upright position shows that greater levels of downward movement in the anterior and posterior compartments, labeled as cytocele and rectocele, occur under the influence of posture and gravity. The maximal extent of downward movement is best evaluated in the standing position; use of the HL, ML, MPL, and PL reference lines most readily identified downward prolapse, while organ position in the sitting position precluded use of the HL and ML lines. I suggest that as access to MRO becomes available benefits will accrue from the enhanced diagnostic and grading ability of upright imaging in POP.

Chapter 4. Methodology for 3D Image Reconstruction of the Female Pelvis from Upright Open MRI (MRO) 2D Imaging⁴

4.1. Introduction

Magnetic resonance imaging (MRI) of the pelvic organs and pelvic floor muscles is an important element in the evaluation of women with pelvic floor dysfunction. Pelvic organ prolapse (POP) is assessed and staged on the basis of the morphologic features of the levator ani seen on MRI; and the imaging contributes to defining the type of surgery to be offered to a patient with POP and evaluating if and when repeat surgery is required [223].

POP involves the displacement and descent of the female pelvic organs such as bladder, uterus, and intestines [224]. The pelvic floor muscles, ligaments and related connective tissue keep the pelvic organs in place [225], but with childbirth and effects of the menopause the pelvic floor support structures lose their integrity and weakness at different levels results in the evolution of POP [226]. Symptoms include vaginal pain, pressure, urinary incontinence, incomplete bowel evacuation, and sexual disorders [227]. POP is principally classified as a cystocele, rectocele, uterine, or vaginal vault prolapse [227]. More than 55% of women aged 50 to 59 have various grades of prolapse [228].

A problem when evaluating women with POP currently is that images of the pelvic anatomical structures currently obtained using conventional MRI do not always provide the level of detail required to reliably detect and grade the degree of POP

⁴ A version of Chapter 4 has been published: Abdulaziz M, Stothers L, and Macnab A. Methodology for 3D image reconstruction of the female pelvis from upright open MRI (MRO) 2D imaging. *Biomed Spectrosc Imaging* 2018; 7:81-96.

accurately, because many patients with chronic weakness or damage to their supporting pelvic floor muscles only develop organ prolapse in response to changes in posture and the effects of gravity on organ position. Hence patient management based on supine MR imaging is not always optimal [229].

However, the recent evolution of open-configuration magnetic resonance imaging (MRO) now enables patients with POP to be imaged when sitting and standing upright in addition to conventional supine imaging. This is particularly relevant because of the known effect of posture and gravity on the position of the pelvic organs, the degree of prolapse, and the integrity of the pelvic floor musculature [230], and the fact that many women only experience symptoms of urinary incontinence associated with POP when standing [89]. Initial studies using MRO indicate that the standing and sitting images can add important diagnostic detail regarding the effect of posture and offer improved accuracy to the classification of POP severity based on established pelvic reference line methodology [89, 230].

I now suggest that further refinement can be added by reconstructing the original 2D MR images into colored and rotated 3D images [229]. Such 3D models are helpful because they provide a topographical overview that aids in visualizing the complex structure of the levator ani, and displays details of the pelvic floor musculature at its origin and insertion [231]. Furthermore, spatial analysis in 3D models can provide information beyond the level that can be obtained from two-dimensional studies. Therefore, models generated using 3D reconstruction methodology will allow better definition of the morphological features of the bony pelvis, pelvic organs and levator ani in women [231], and provide clinicians with the ability to achieve greater diagnostic

accuracy because of the level of detail in 3D images of the urinary bladder, vaginal canal, uterus, rectum, pelvic floor muscles and connective tissue [225].

Initially, modeling of the pelvic organs focused mainly on the pelvic floor muscles. In 2003, Janda et al. [224] modeled the pelvic floor from dissection of a cadaver to compare the geometric measurements with MRI data [227]. The focus has since moved to the generation of 3D models to investigate pelvic mechanics and prolapse [227]. Rubod et al. [232] created a simple 3D model of the bladder, vaginal canal, and the rectum using an MR image stacking technique to assess the impact of bladder pressure and rectal load on the vaginal canal [227]. In 2004 Lien et al. [233] created a 3D model to evaluate the stretching of levator ani during childbirth. In 2008 Noakes et al. [234, 235] showed normal defecatory mechanisms in the female pelvic floor by developing an anatomically accurate 3D model from MR imaging data. In 2014, Chen et al. [236] generated a 3D model in which a finite down descent load on the uterus was reproduced to study prolapse.

The goal of achieving advanced imaging is relevant in POP as this condition affects millions of women, the resulting symptoms negatively impact their quality of life and approximately 200,000 surgical procedures to correct POP are performed yearly in the USA [109, 172], at a cost of over one billion dollars [117]. The benefits of sitting and standing images over supine imaging in the evaluation of POP have been reported separately [237]. The purpose of this paper is to report our development of methodology for 3D modeling of 2D open MR images of the female pelvic floor in the context of POP, to improve definition of the anatomy and enhance definition of the effects of posture and gravity.

4.2. Methods

4.2.1. Upright open MRI

The study that provided the imaging from which 3D images were generated was conducted at the open MRO unit at the Centre for Hip Health and Mobility in Vancouver. The unit is a 0.5 T scanner (Paramed Medical Systems, Italy); this MRO unit is reserved for researchers and clinicians working to find new ways to image the human body to solve pressing healthcare challenges. In addition to the investigation of the effect of posture and gravity in POP, this unit is also being used to obtain novel views of the hip, knee, spine, and abdomen when patients are upright, weight bearing, and their organs are subject to the influence of gravity.

Images were obtained in the supine, sitting and standing position in two different planes (axial, and sagittal). Transverse T1 pelvis images were obtained at 5-mm slice thickness, with a field of view of 24 cm x 24 cm and matrix of 224 x 192. Sagittal T2 images were obtained at 5 mm slice thickness, with a field of view of 30 cm x 30 cm and matrix of 192 x 160.

4.2.2. Subjects

Women attending a university urogynecology clinic were recruited for a study evaluating the potential for MRO to improve detection of gravity-dependent POP [237]; the cohort included symptomatic women with different levels of prolapse and controls who were healthy premenopausal women without symptoms of POP and who had never undergone pelvic surgery. All signed informed consent as approved by ethical review (#V14-03507). A standardized evaluation of their grade of prolapse was conducted according to the International Continence Society grading system and they

answered questions relating to symptoms of prolapse using a standardized questionnaire [238].

4.2.3. Image acquisition

The source MR images were obtained in the axial and sagittal plane. Obtaining good quality source images is an essential first step in generating a 3D model. Images were obtained using the following MRO parameters: sagittal FSE9, FOV = 30 cm x 30 cm, slice thickness = 10 mm, gap = 1 mm, number of slices = 5, NEX = 1, TE = 120 ms, TR = 2500 ms, and acquisition time = 1 min 50 s; axial T1 GFE pelvis images, FOV = 24 cm x 24 cm, slice thickness = 5 mm, gap = 1 mm, number of slices = 40, Theta = 0 deg, Phi = 0 deg, NEX = 1, flip angle = 80°, TE = 10 ms, TR = 470 ms, and acquisition time = 3 min 15 s (x2). To avoid anatomical distortion, no contrast agent or surface body coil was used. To address the risk of fainting or dizziness during the standing scan we applied a deep venous thrombosis external pneumatic compression device around the legs of all patients. This device was originally developed to prevent deep vein thrombosis by applying oscillating external pneumatic compression to the legs to increase the blood velocity in the deep veins [239]. As some POP patients find standing for a long time uncomfortable we chose a short scan time of 2 min. Also, as undesirable and unpremeditated movement during the standing scan decreases image quality because of motion artefact, patients were secured using the scanner's safety straps and the pressure pump until the scanner returned to the supine position. To reduce any perception of discomfort during the weight-bearing scans, patients were offered the choice of watching TV or listening to music and wearing earplugs to avoid excessive

noise. After the MR imaging was completed, the images were electronically transmitted to a workstation for model generation.

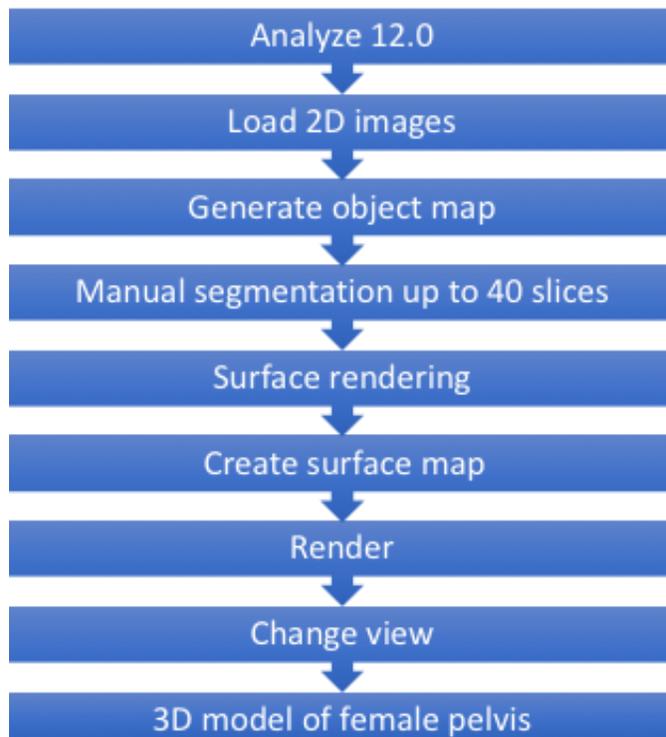
4.2.4. Generation of 3D models

I created three-dimensional surface models from our high-quality 2D MRO images of the pelvis. Axial and sagittal slices of the pelvic organs were manually segmented (i.e., of the bladder, urethra, vagina, uterus, and cervix, and major pelvic floor muscles, including the levator ani, piriformis and obturator internus). Additionally, the pubic bone was segmented for use as a fixed bony reference point. Segmentation was based on an amalgamation of knowledge of the anatomic structures and variation in grey-scale contrast. The software used was Analyze 12.0 (Analyze Direct, Inc. Overland Park, KS, 66005 United States). This is one of a number of sophisticated programs that can generate 3D models from different imaging modalities (X-ray computed tomography, ultrasound tomography, and magnetic resonance imaging) [240]. Others include 3D-Doctor (Able software Corp, Lexington, USA). For image generation, ease of viewing, and image comparison a monitor that provided a large display area was used (Huion Animation Technology Co, China)

Figure 4.1 summarizes the sequence for 2D image analysis and 3D model generation. I began our reconstruction with Analyze 12.0 by loading the image data using the load module Import/Export from the file menu in the main window. The volume tool was used to generate a volume file from the existing manifest of 2D images files. Once the required data is loaded it becomes visible as an icon in the workspace and is ready for manual segmentation. Next, I selected the segment icon and chose “Image Edit”. Then, I selected the file icon to generate an object map that has all the segmented

structures and the colors of all the structures of interest by choosing the image to edit. I segmented the bony pelvis slice by slice through the slice slider for transmission to Slice 40 (Fig. 4.2), outlining the pelvic bones in slices that encompassed the pelvis. The segmented slices were composited to develop a model of the bony pelvis as one unit. This model serves as a framework, which allowed us to build on other structures in the region and display them from any viewpoint in 3D.

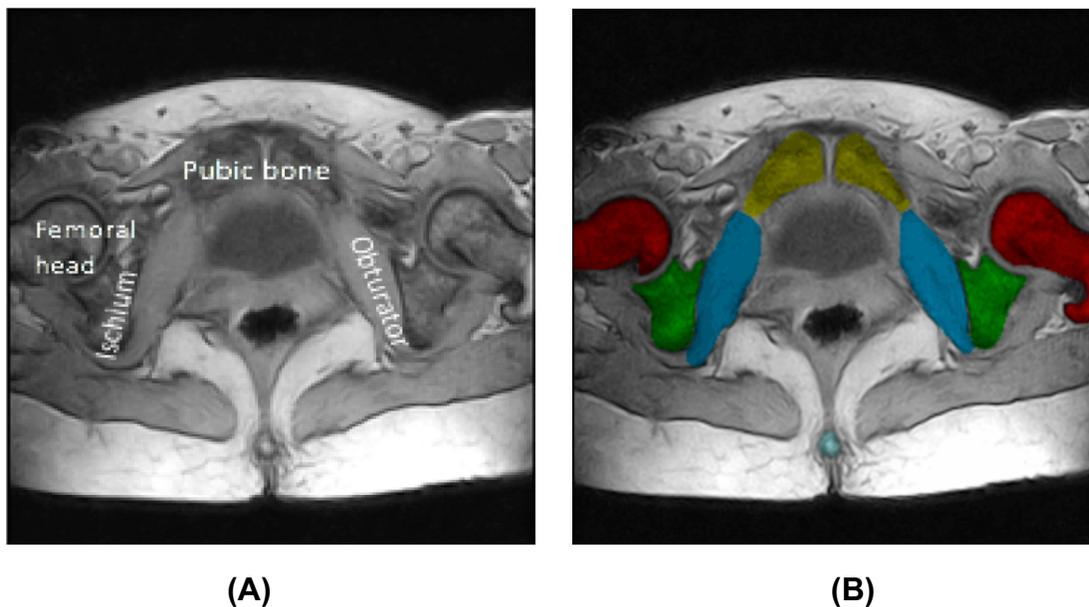
Figure 4.1. A flowchart of the image analysis method to convert 2D MRO images into 3D models of the female pelvis using the software Analyze 12.0. (Original images from source subjects).



Once segmentation of the bony pelvis is completed the pelvic structures of interest are added using the same method. I started by adding the muscles in the pelvic walls. These consist of the muscles that form the lateral walls (obturator internus muscles), the pelvic floor (the levator ani muscles) and the posterior walls (piriformis

muscles) (Fig. 4.3). These muscles are the most substantial; they define the boundaries of the pelvis and give a framework from which the internal relationships of other pelvic organs can be added and visualized. Adding the pelvic muscles to the bony pelvis in sequence allows the individual muscles to be recognized and their relationships to other structures distinguished.

Figure 4.2 (A) Axial T2-weighted MR image of the female pelvis as exported to Analyze 12. (B) Once “segmentation” is complete, colored markings are drawn manually slice by slice around the structures of interest. The segmented structures shown are identified as follows: yellow = pubic bone, blue = obturator internus muscle, red = femoral head, and green = ischium. (Original images from source subjects).

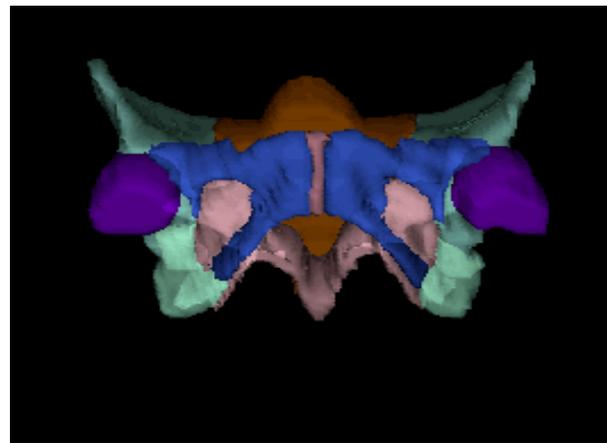
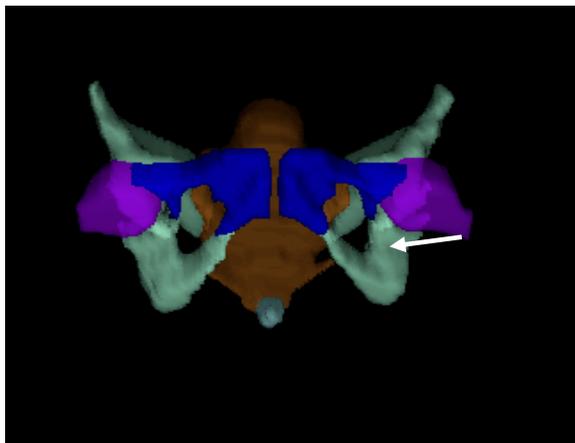


4.2.5. Surface rendering

3D renderings of the pelvic organs, supporting pelvic muscles and bones were reconstructed using the surface-rendering method. To do this open the Surface Render module and load the object map already generated to develop a surface map in the surfaces window. Click “Yes” in the dialog box to create the surface map from all

previous active objects generated. The objects that have their “Display” feature set to “On” in the Objects window will be tiled and a surface map created. Click the “Render” button to display the results. Clicking the “generation” button and “change view” rotates the 3D model, and then clicking the “change view” icon allows simultaneous visualization and measurement of the 3D model created (Fig. 4.4).

Figure 4.3. Examples of three-dimensional models generated of the female pelvis: (A) 3D anterior view of pelvic bone, (B) 3D anterior view of the pelvic floor muscles, (C) 3D inferior view of the pelvis which identifies significant pathology — detachment of the levator ani has occurred (arrows). The segmented structures are identified by color in the legend. (original images sourced from study subjects).



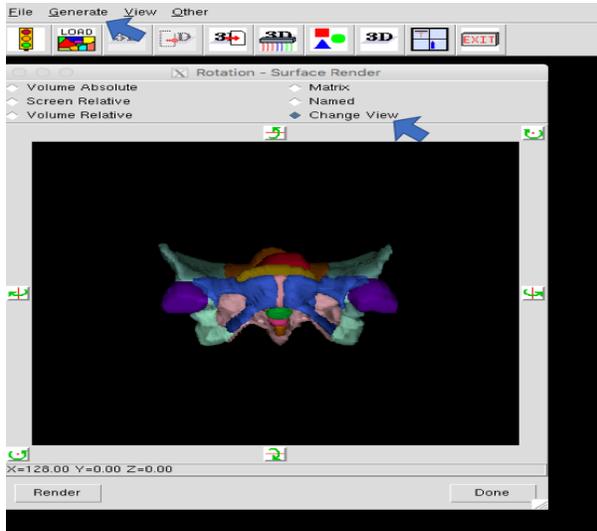
(B)



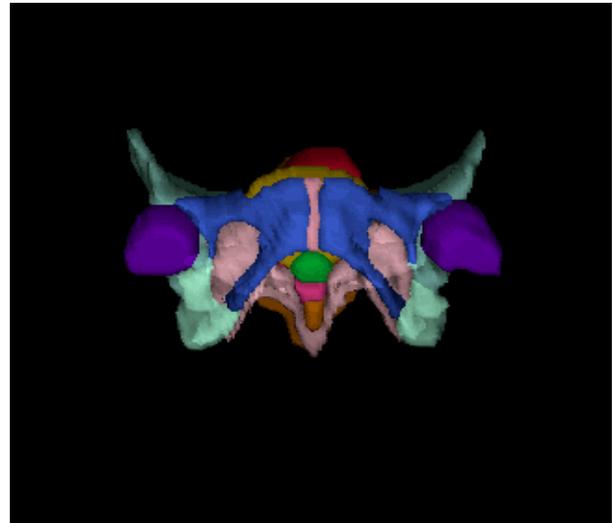
(C)

-  Femoral head
-  Pubic bone
-  Ilium and Ischium
-  Levator ani -obturator and Symphysis
-  Sacrum

Figure 4.4. An example of a 3D model being generated; (A) the model was viewed on a workstation and then through the “generate” < “change view” < “render” command sequence was rotated to create the final image shown in (B), a 3D model of the anterior view of the female pelvis. All 10 structures identified in this segmentation are color coded in the legend (original images sourced from study subjects).



(A)



(B)

- Femoral head
- Pubic bone
- Ilium and Ischium
- Levator ani -obturator and Symphysis
- Sacrum
- Uterus
- Urethra
- Bladder
- Rectum
- Vagina

4.2.6. Image interpretation and grading of POP severity

The presence of POP and grading of severity is determined by overlaying established reference lines on mid-sagittal pelvic images. The pubococcygeal reference

line (PCL) was drawn to define and grade the degree of prolapse in the three separate pelvic compartments. The PCL is a line drawn from the inferoposterior border of the pubic symphysis to the last visible coccygeal joint [230, 241]. Perpendicular distances between the PCL and the bladder base, vaginal apex, and anorectal junction are used to grade the degree of downward descent in the anterior, middle, and posterior compartments, respectively. MRI-detected prolapse is graded as follows: negative (displacement inferior to the PCL of less than 1 cm); mild (displacement of less than 3 cm); moderate (displacement of 3–6 cm); and severe (displacement of more than 6 cm) [237].

4.3. Results

MRO image sets from 31 women (13 with POP and 18 asymptomatic controls) were used to develop the methodology to generate 3D images. Figures 4.5 and 4.6 show the difference in the incidence of POP detected in symptomatic subjects when standing and supine images are compared. When supine, bladder or vaginal prolapse of mild degree was evident in a proportion of cases but no evidence of moderate or severe POP was detected. In contrast, in standing images detection rates for mild POP increased, and multiple subjects with moderate and severe posture-induced POP were clearly identified. All images in control subjects were negative for POP whether standing and supine. Tables 4.1 and 4.2 summarize the difference in staging severity of bladder and vaginal prolapse (distance below pelvic reference lines) in supine and standing images. Figures 4.7 and 4.8 are examples of how MRO can identify POP due to posture and gravity when the patient is imaged standing. Figure 4.7 shows sagittal images taken in the same subject when supine, sitting, and standing. Figure 4.8 shows supine and

standing images in the same patient with bladder prolapse quantified by use of the PCL reference line. Figure 4.9 illustrates 3D models generated using our methodology and shows for comparison the 2D open MR images they were generated from. Examples are shown from two patients; the 3D model/2D image combinations; (A) and (C) are with the patient supine and (B) and (D) when standing.

The 3D pelvic models developed reveal morphology that conforms qualitatively to the real female pelvis, as the qualitative appearance of the 3D models was consistent with the morphological characteristics displayed by typical 2D images. All reconstructed structures can be visualized in groups or united as a whole and rotated as a 3D model, so the end result provides greater structural definition, reveals the extent of downward descent of structures and shows the full effect of posture and gravity in POP.

Figure 4.5. Bar graphs of the percentage of symptomatic subjects with mild POP evident in supine MRO imaging.

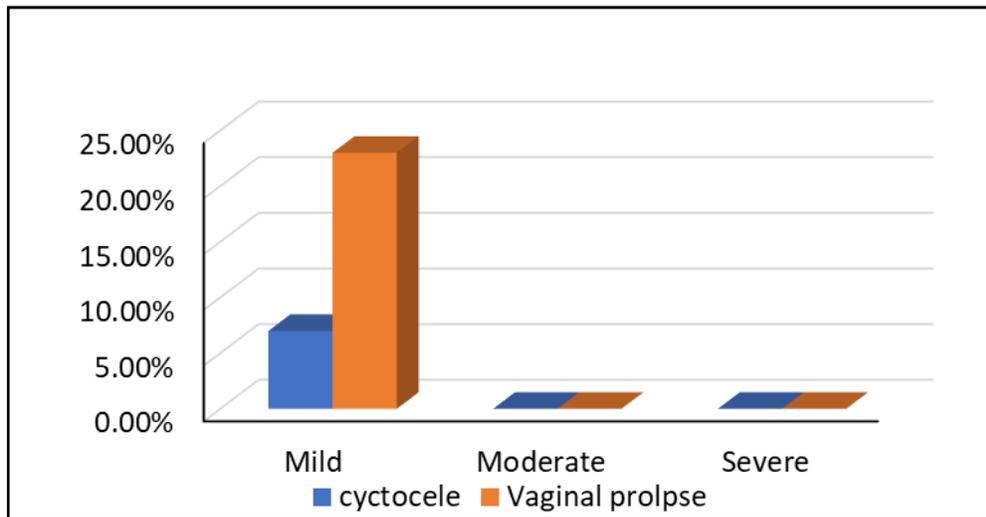


Figure 4.6 Bar graphs of the increased percentage of symptomatic subjects with mild, moderate, and severe POP evident in standing MRO imaging.

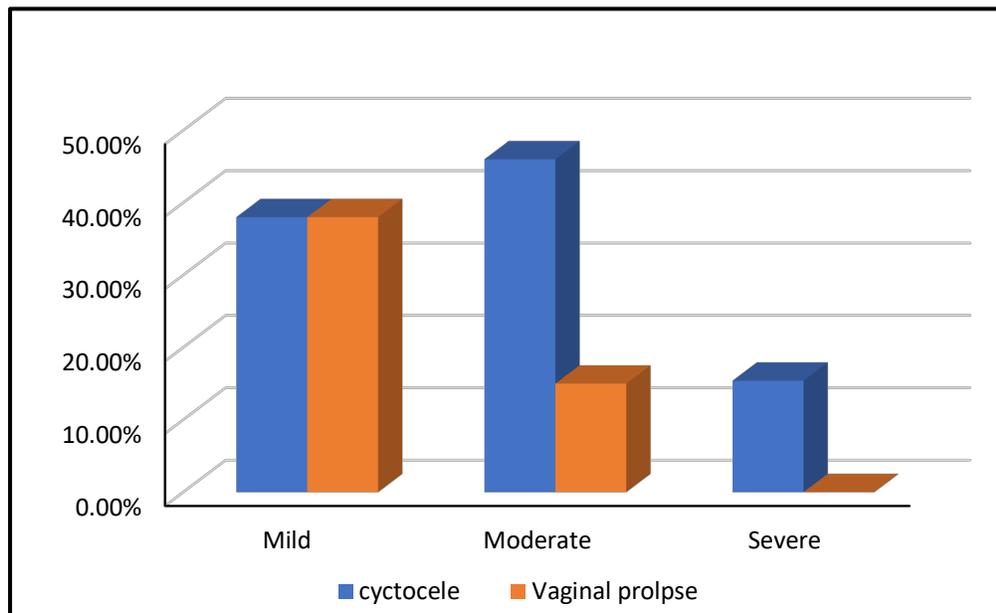


Table 4.1. Presence and extent of pelvic organ prolapse (by distance below the pubococcygeal reference line of the bladder and vagina) in supine MRO imaging in 13 symptomatic subjects.

Bladder	Mild	Moderate	Severe	Vagina	Mild	Moderate	Severe
1-	-----	-----	-----	1-	-----	-----	-----
2-	-----	-----	-----	2-	-----	-----	-----
3-	-----	-----	-----	3-	1.03 cm	-----	-----
4-	-----	-----	-----	4-	-----	-----	-----
5-	-----	-----	-----	5-	1.06 cm	-----	-----
6-	-----	-----	-----	6-	1.03 cm	-----	-----
7-	-----	-----	-----	7-	-----	-----	-----
8-	-----	-----	-----	8-	-----	-----	-----
9-	1.68 cm	-----	-----	9-	-----	-----	-----
10-	-----	-----	-----	10-	-----	-----	-----
11-	-----	-----	-----	11-	-----	-----	-----
12-	-----	-----	-----	12-	-----	-----	-----
13-	-----	-----	-----	13-	-----	-----	-----

Table 4.2. Presence and extent of pelvic organ prolapse (by distance below the pubococcygeal reference line of the bladder and vagina) in standing MRO imaging in 13 symptomatic subjects.

Bladder	Mild	Moderate	Severe	Vagina	Mild	Moderate	Severe
1-	-----	3.18 cm	-----	1-	1.02 cm	-----	-----
2-	-----	-----	8.56 cm	2-	-----	5.0 cm	-----
3-	-----	-----	7.27 cm	3-	-----	-----	-----
4-	2.12 cm	-----	-----	4-	1.41 cm	-----	-----
5-	-----	3.41 cm	-----	5-	2.08 cm	-----	-----
6-	2.42 cm	-----	-----	6-	-----	-----	-----
7-	-----	3.54 cm	-----	7-	-----	-----	-----
8-	2.21 cm	-----	-----	8-	-----	3.27 cm	-----
9-	-----	5.26 cm	-----	9-	2.08 cm	-----	-----
10-	2.89 cm	-----	-----	10-	-----	-----	-----
11-	-----	4.27 cm	-----	11-	-----	-----	-----
12-	1.1 cm	-----	-----	12-	-----	-----	-----
13-	-----	4.42 cm	-----	13-	1.64 cm	-----	-----

4.4. Discussion

The goal of this study was to develop methodology to generate 3D models of the female pelvis from 2D MRO images, to enhance the definition of the effects of posture and gravity in POP. Our protocol for standing and sitting image acquisition described previously allowed the high-quality 2D images that are essential for 3D modeling to be acquired [237], and the way in which the Analyze 12.0 software was used is integral to quality 3D reconstruction. The sequence of steps followed for segmentation of the pelvic structures made it possible to reconstruct a 3D model that included the bony pelvis, pelvic organs, levator ani muscle, and pelvic floor muscles where the anatomical structures were readily defined and their borders could be traced reliably.

Key elements of the MRO protocol relating to image quality include the use of an external pressure pump to provide leg support to avoid blood pooling causing fainting, a

short scan time as POP patients are often uncomfortable when standing and use of the scanner support straps to minimize movement and motion artefact. Movement was reported to compromise another MRO study where patients with back pain were asked to stand for positional MRI for 10 min; this complication meant that the protocol had to be altered to use the sitting position instead, in order to achieve the required image quality [242].

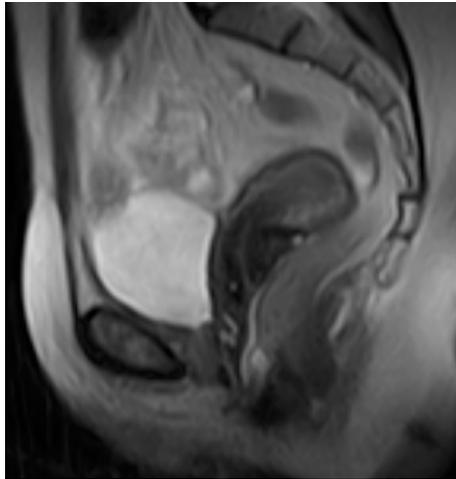
In POP, revealing the extent of organ displacement by clinical examination alone is often hard to achieve. Although MR imaging is advised and MRI delivers multiplane imaging of the pelvic compartments with high resolution [243], because patients are currently only scanned supine, the posture- and gravity-dependent nature of POP is not captured. This is because prolapse may occur, or can become worse, only after time spent in the upright position but is often reduced when gravity is not a factor, e.g., when lying in the supine position [96]. Hence, many patients cannot be evaluated accurately and staged correctly, and consequently are not allocated to appropriate therapy. This diagnostic limitation represents a major health care problem, as POP is such a common condition in older women.

The recent development of MRO scanners, where the magnet is configured with a vertical gap, enables patients to be scanned in the seated and standing positions as well as when supine, so MRO can replicate normal functional posture and enable the effects of gravity on the body to be evaluated [89]. Hence, application of this new technology with the aim of improving evaluation of POP is relevant. The MRO unit I utilized is reserved for researchers and clinicians working to find new ways to image the human body to solve pressing healthcare challenges. In addition to the investigation of

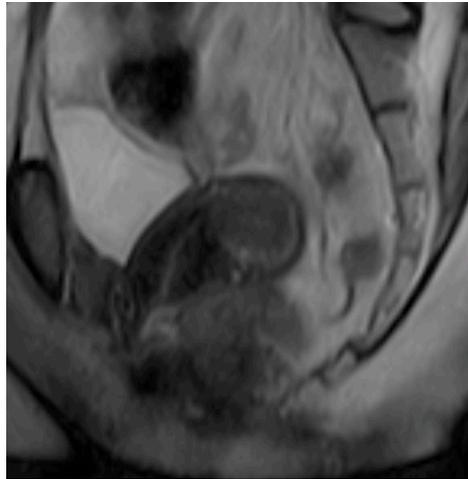
the effect of posture and gravity in POP, this unit is also being used to obtain novel views of the hip, knee, spine, and abdomen when patients are upright, weight bearing, and their organs are subject to the influence of gravity.

Findings from the 2D images I obtained to construct our 3D models reinforce previous observations that MRO imaging improves detection of gravity-induced POP when the standing position is used [89] and research involving defecography and imaging when upright and weight-bearing [244]. Figure 4.7 image (C) is an example; a cystocele is detected, presumably because weakness in the pubocervical fascia caused loss of bladder support when the patient was upright. In 3D images the pubocervical fascia is attached anteriorly to the arcus tendinous pelvic fascia and posteriorly to the cervix [117]. Variations in the tension on pelvic fascia and ligaments, their resting length, and contractile tone also contribute to POP occurring when subjects are upright. In the midsagittal images (Fig. 4.8, image (A)), there is elevation of the base of the bladder neck in the supine position (on average the bladder neck normally rises 5 mm at rest in the supine position compared with standing and descends a further 5 mm during the Valsalva maneuver) [238]. Another variation between the supine and standing position was identified in the same patient (Fig. 4. 9); here there is a rise in the caudal angulation of the levator plate, which causes an increase in the pelvic hiatus. The PCL reference line (Fig. 4. 9) connects defined bony landmarks; is used to identify abnormal organ descent, and as it is reproducible and unaffected by pelvic tilting [244] it is the most widely utilized reference line [245].

Figure 4.7. T2-weighted sagittal MRO images of the same patient: (A) in the supine position; (B) in the sitting position; and (C) in the standing position. This sequence is an example of where gravity-induced prolapse of the bladder (arrow) becomes evident during imaging when standing. (Original images from source subjects).



(A)

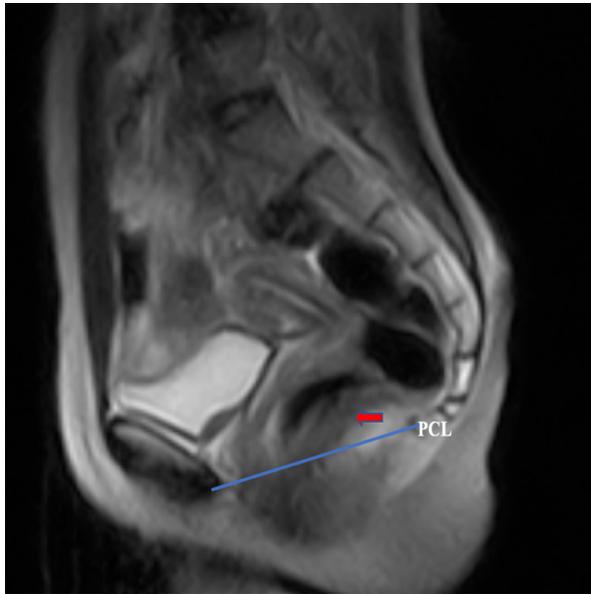


(B)

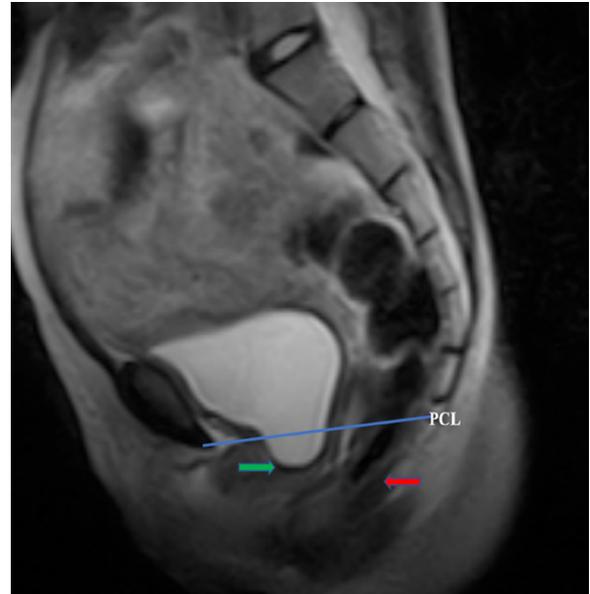


(C)

Figure 4.8. T2-weighted sagittal MRO images of the same 24-year-old patient. (A) The supine image shows no caudal angulation of the levator plate (red arrow), which is above PCL reference line (blue line). (B) In the standing image, caudal angulation of the levator plate is evident, a cystocele is evident with prolapse of the bladder (green arrow) below the PCL (blue line), and caudal angulation of the levator plate muscle (red arrow). (Original images from source subjects).



(A)



(B)

The methodology I describe for the reconstruction of 3D pelvic images from 2D images is novel, being the first time a 3D model of the pelvis has been generated based on thin slices of the adult female pelvis derived from 2D MRO scans. I suggest that the clarity and additional detail evident in the examples illustrated (Figs. 4.2, 4.3, 4.4, and 4.9) indicate that 3D images can be generated that will add to the anatomic evaluation of POP and help to better define the effect of different positional and weight-bearing elements in individual patients. In addition, 3D images have important potential as an interactive tool for teaching purposes. Students find it difficult to visualize the complexities of the pelvic floor from cadaver dissections and anatomical atlas

illustrations [246], and patients often struggle to understand what their POP entails and their options for therapy; three-dimensional models aid visualization and spatial perception [247], aiding better understanding of complex human anatomy [199].

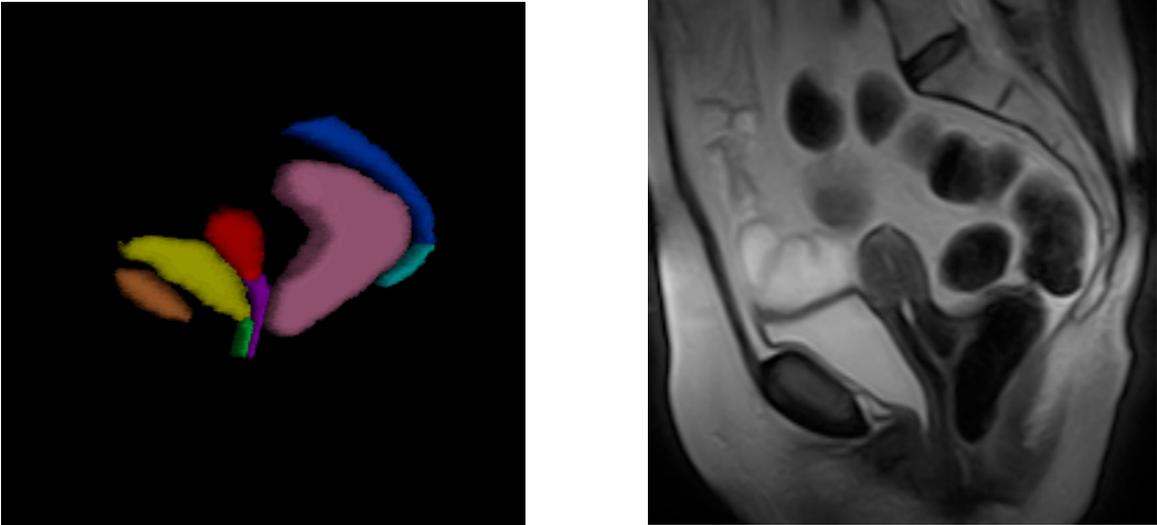
Specific benefits of 3D pelvic models include the ability to assess the shape and extent of each anatomical structure in isolation and in relation to neighboring structures, obtain volumetric analysis, illustrate the spatial relationship of the anatomic structures [223], and to further clarify these relationships, rotate the pelvic structures so they can be seen in a spatial view. The enhanced definition of the bony pelvis and degree of detail in the levator ani provided are particularly important [231], as the configuration of the levator ani can differ in significant ways in women with the same grade of prolapse [223]. Hence, our 3D models add important levels of definition that I suggest will aid clinicians to better identify the nature and extent of POP. Combined with the improvement of open MRO upright imaging, this will add to diagnostic and staging accuracy that will in turn lead to more appropriate allocation of patients to specific treatment modalities.

In the context of planning POP surgery, there are obvious benefits from surgeons having the added anatomic information and assessment of function offered by 3D images as part of their preoperative evaluation of patients. Also, in situations where the pelvic floor is injured, 3D assessment of its structure and internal relationships will likely aid understanding of the nature and extent of the trauma, as incontinence and prolapse frequently occur as a consequence of traumatic injury [246]. As an example, our 3D model clearly showed where detachment of the levator ani had occurred in a 55-year-old patient (Fig. 4.4, panel (C)).

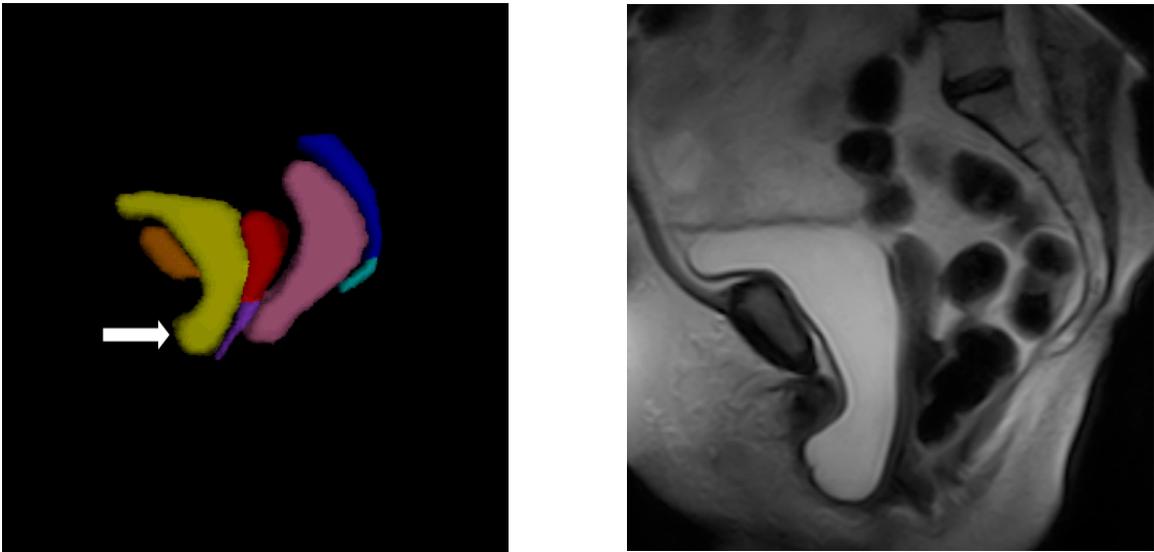
I recognize that the selection of 31 consecutive images to develop our 3D modeling method does not allow the benefit of MRO over conventional supine MRI to be quantified; a prospective study is needed to define the proportion of patients in whom MRO enables a diagnosis of gravity-dependent POP to be made where supine imaging is negative and formally establish the clinical utility of MRO. A limitation of the modeling method reported is that muscle fiber direction and definition of some additional pelvic floor structures such as ligaments, nerves, veins, and arteries were beyond the scope of the current model; but enhanced definition could be incorporated in future modeling. Another limitation was the short time (2 min) used to acquire the standing scans. Patient comfort is a factor that must be balanced with the need to avoid compromising image quality; a good quality 2D image is essential for the generation of accurate models. However, our protocol has proved successful in this regard, and I suggest that 3D modeling warrants further research and development, as the technique allows more comprehensive determination of the extent of organ prolapse due to the impact of posture and gravity.

Figure 4.9. 3D models and the 2D MRO supine and standing images from which they were generated, in two different patients with symptomatic POP. Studies in both patients identified anterior compartment descent cystocele (arrows) when images were captured in the standing position. Color coding of 3D segmentation is in legend. (Original images from source subjects).

Patient 1

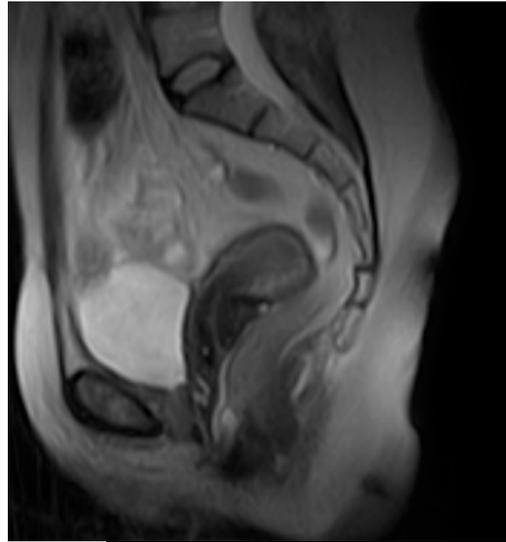
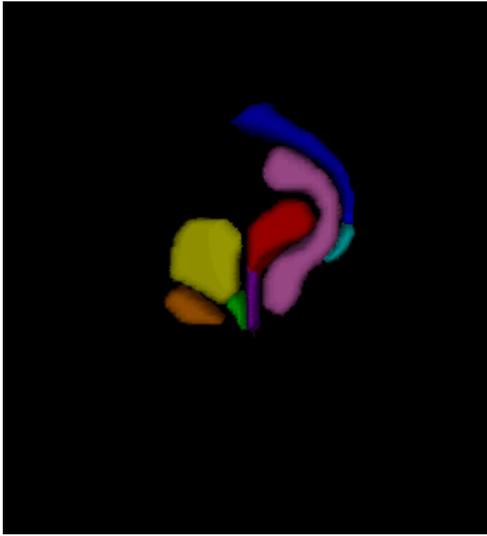


(A) Supine

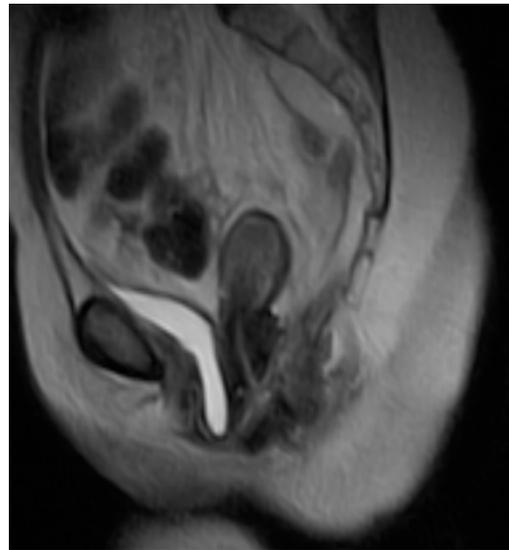
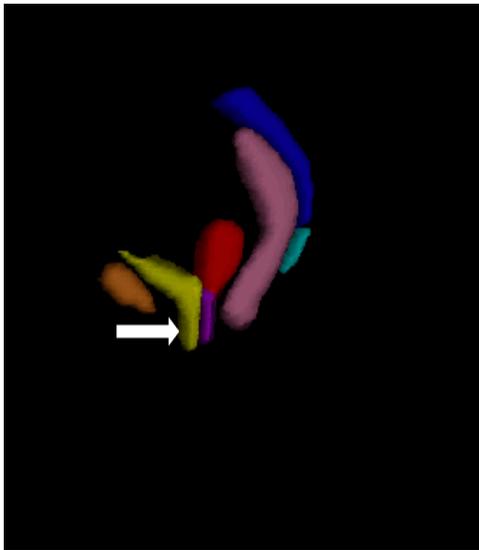


(B) Standing

Patient 2



(C) Supine



(D) Standing

-  Pubic bone
-  Bladder
-  Uterus
-  Vagina
-  Rectum
-  Sacrum
-  Coccyx

4.5. Conclusions

Three-dimensional models of the pelvis can be generated from high quality 2D thin-section MRO images obtained by imaging patients in the supine, sitting, and standing positions using a modeling method employing Analyze 12 software. The ability of MRO to capture images when standing overcomes the limitation of conventional MRI to supine imaging and is an important advance in the evaluation of POP, as the integrity of the pelvic floor and the presence and severity and symptoms are strongly associated with posture and the effect of gravity on the pelvic organs. The 3D models generated provide enhanced definition of the pelvic structures and more comprehensively clarify the extent and anatomical cause of organ prolapse; both are relevant to improved evaluation, staging, and treatment planning for patients with POP.

Chapter 5. Discussion and Conclusion

5.1. Summary and discussion

The anatomy of the pelvic organs, muscles, and supporting structures is complex. The pelvic floor is a musculotendinous termination of the pelvic outlet that permits the anorectal and urogenital viscera to pass through two hiatal openings [247], and the pelvic floor muscles (PFM) support the pelvic organs and maintain their functional integrity. In women, PFM injury or weakness can allow organ descent or prolapse and cause organ dysfunction. The presence and extent of pelvic organ prolapse (POP) is influenced by posture and the effect of gravity, and POP symptoms can appear or be aggravated by a change in posture and resolve when the patient is supine. Symptoms involve urinary, bowel, and sexual function and negatively impact quality of life (QOL). POP is a major health problem; approximately 50% of women over 50 have symptoms related to POP.

Evaluation of POP involves history, inspection, clinical exam, and where indicated, imaging. Classification and staging of the extent of POP determines treatment allocation for patients. Current conservative treatment uses a pessary; surgical treatment involves approaches based on the symptoms and grade of prolapse [74]. Problematically, clinical evaluation and imaging have a limited ability to detect POP that is posture and gravity dependent. Factors influencing clinical exam efficacy include variation in measurement methods (examining a patient when upright is difficult), manner of examination, and patient and examiner variance, and differences in bladder distention, patient position, and the degree of patient straining can all impact the severity of POP [58, 102, 202, 205, 206]. The nature of the prolapse is often difficult to

detect on physical exam, and while anatomic defects are generally well visualized on MRI [217], because imaging is currently limited to the supine position, the ability of MRI to detect POP due to the effects of gravity and posture on organ position is limited. These factors negatively affect the accuracy of diagnosis of POP, the precision of staging, and choices for surgical treatment; hence, the frequency of repeat surgery is high (up to 30%) [9].

The recent evolution of open-configuration magnetic resonance imaging (MRO), where the magnet is configured with a vertical gap, enables patients to be imaged when sitting and standing upright, in addition to conventional supine imaging. So, MRO can replicate normal functional posture and enable the effects of gravity on the body to be evaluated [89, 248]. Hence, MRO has relevance for patients with POP because many women experience symptoms of urinary incontinence associated with POP only when standing [89]. Also, this new technology provides a means to test my hypothesis that upright imaging has the potential to improve detection of POP occurrence because of the known effects of posture and gravity on the position on the pelvic organs, aid assessment of the degree of prolapse, and better evaluate the integrity of the pelvic floor musculature.

Therefore, the goals of this study were to

- 1: Develop a protocol for obtaining supine, sitting, and standing images of diagnostic quality using MRO in patients with POP.
- 2: Use MRO to determine if anatomic changes in POP that are posture and gravity dependent are more readily detected in images taken when patients are sitting or standing rather than supine.

- 3: Evaluate if having MRO images taken when supine, sitting, and standing improves the staging of POP when using validated reference lines.
- 4: Develop a methodology for creating 3D models of the female pelvic floor from 2D MRO images in patients with POP to improve definition of the anatomy and enhance detection of the impact of posture and gravity.

5.1.1. Posture and gravity dependence of POP

The standing posture of humans is commonly considered to be a contributing factor where symptom provocation usually occurs because of the physiological impact of gravity that women with pelvic organ prolapse or urinary incontinence experience when upright. The levator ani muscles are involved to enhance the increased support needed with standing posture.

As seen in Chapter 4, the developed 3D reconstruction model of the female pelvis revealed the abnormality of levator ani in women with POP. The pelvic floor soft tissues (levator ani muscles) are a key factor playing a significant role in keeping the genital hiatus (GH) closed, help to support the pelvic viscera, and have an important role in bladder and bowel continence. The present study showed the relationship between posture and the extent of POP detected in the standing position, which is correlated with levator ani muscle damage seen on MRO scans. Our finding is consistent with the previous study by Barber et al. [202] that demonstrated that the degree of prolapse observed in the dorsal lithotomy position corresponds with a 45° upright evaluation in a birthing chair. However, a maximal degree of prolapse was found in the standing examination. In addition, Visco et al. [204] reported a maximal degree of prolapse in the standing position in contrast with the supine position. Another study by

Swift and Herring [52] compared the pelvic organ prolapse quantification (POP-Q) system in the standing and supine orientations. They reported that there was no significant difference between the stage or the quantified measurement (POP-Q) system points in the lying and standing positions. Also, a previous study by Bo and Finckenhagen [249] demonstrated that there was no statistical difference in measurements of prolapse in the lying and standing positions. In contrast, our study showed statistically significant differences in the detected POP between the supine and the standing positions as seen in Chapters 3 and 4.

I suggest that the potential of the addition of gravity and body weight are considerable contributors to minimizing the ability of the damaged pelvic floor muscle (PFM) contractile function when standing. It can be hard for the PFM to generate additional contraction function upon a pre-loaded base, as the heaviness of pelvic organs and gravity are opposing forces to the pelvic floor. This can partly reveal why differences are seen in the diagnosis of POP with changes in posture. Hypothetically, the function of the entire pelvic floor may be changed due to several influencing factors such as prolapse of pelvic organs when upright, differing tension on fascia and ligaments, and alterations in resting length and tone of the contractile elements. Our data reported that the magnitude of the observed extent of prolapse alters according to the position used for assessment, confirming that an empty bladder and standing position are the optimal conditions used for demonstration of POP.

5.1.2. MRO protocol development

The source MR images were obtained in the axial and sagittal plane. To avoid anatomical distortion, no contrast agent or surface body coil was used. Adequate

patient preparation and fast acquisition time are required to reach extreme patient comfort. A suggested protocol for MRI of pelvic floor dysfunction is summarized in Chapter 4. Key elements of the MRO protocol relating to image quality include the use of an external pressure pump to provide leg support to avoid blood pooling causing fainting, a short scan time as POP patients are often uncomfortable when standing, and use of the scanner support straps to minimize movement and motion artefact. Movement was reported to compromise another MRO study where patients with back pain were asked to stand for positional MRI for 10 min. This complication meant that the protocol had to be altered to use the sitting position instead to achieve the required image quality [242]. To reduce any perception of discomfort during the weight-bearing scans, patients were offered the choice of watching TV or listening to music and wearing earplugs to avoid excessive noise.

5.1.3. MRO and POP staging

There is no standardized method for assessing POP using MRO imaging, so this study sought to compare the mean lengths of the different reference lines of the control women without POP and women with POP on supine, sitting, and standing position images, to provide an assessment of the relationship of the pelvic components in different positions. As shown in Chapter 3, significant differences in the mean lengths of the PCL, SCIPP, HL, ML, MPL, and PL reference lines between the women with and without POP were predominantly evident in the standing position. This advances the original work of Friedman et al. [201] where the bony anatomic reference points used were limited to the pubopromontoreal (PP) and the pubococcygeal (PC) lines.

The first reference line to be applied in MR imaging was a line drawn from the most inferior part of the symphysis pubis to the last visible coccygeal articulation, known as the “pubococcygeal line” (PCL) [9]. Significant component parts of the pelvic floor, such as the pubococcygeal muscle, puborectal muscle, and pubovesical ligament, attach along this line [9]. Hence, the PCL is the line most widely applied in staging POP. The severity of prolapse is graded based on displacement of an organ below the PCL: 3 cm or less is graded as mild, 3–6 cm as moderate, and more than 6 cm as severe. A rectocele is graded as follows: absent (displacement inferior to the PCL of less than 1 cm); mild (displacement of 1–2 cm); moderate (displacement of 2–4 cm); and severe (displacement of more than 4 cm). Using the PCL reference line to grade cystocele, vaginal prolapse, and rectal prolapse in the anterior and posterior compartments on MRO images in the standing position was moderately higher than in the anterior and middle compartments in the supine position. When the most distal part of the rectum (posterior compartment) is measured, the location of the anorectal junction is regarded as simple and reproducible. Through this finding, the sensitivity of supine MRI to define rectoceles has been identified as 76–100% [55, 217]; my observation that the occurrence of mild rectocele in symptomatic POP women in the supine position was 55% using the PCL is in keeping with this figure. A probable explanation is that the causal mechanism is anatomic distortion from pelvic floor damage resulting in widening of the hiatus and laxity or disruption of the musculofascial supporting structures rather than an effect of gravity; or due to the excessive mobility of the posterior compartment.

When a woman is lying supine in the MR scanner her whole-body axis is aligned with the bed and the bore of the machine. This means that the H line (HL) is positioned

perpendicular to this axis, which allows how “high” or “low” an organ is relative to the body axis to be quantified. In contrast, the biological and functional importance of the standing position is that the whole-body axis is parallel to the gravity field — the direction in which prolapse appears; the HL is then “horizontal” and so provides a reference plane for defining how much a structure has displaced [250]. The normal levator hiatus length (H line) is reported to be 5 cm in women without pelvic floor laxity [1]. In this study HL length was identical in controls, as described in Chapter 3, and the mean length of HL in women with POP was statistically different when compared with that of normal women, confirming reports by Ginath et al. [215] that the mean length in women with prolapse was higher than in women without prolapse at rest.

The levator plate is the clinical term used to define the area between the coccyx and the anus composed of the midline fusion (raphe) of the iliococcygeus muscles. Fielding et al. [12] proposed that vertical inclination of the levator plate of more than 10° with respect to the PCL is indicative of loss of pelvic floor support [215]. As reported in Chapter 4, this concept is supported by the observation in this study that in women with POP in the supine position the levator muscle plate is located above the PCL on sagittal images, while in the standing position the levator muscle plate is evident below the PCL with uterine prolapse.

This study’s findings extend current knowledge through this comparison of the mean length of commonly used pelvic reference lines (PCL, SCIPP, PP, HL, ML, MPL, and PL) on midsagittal MRO images in women with and without POP when imaged in supine, sitting, and standing positions.

5.1.4. 3D modeling methodology

With the emergence of computational techniques and advances in computational power, biological systems, organs, tissues, and even cells can be modeled effectively in 3D to simulate the mechanics of both normal and pathological conditions [251]. In the current study MRO provides visualization that allows assessment of the pelvic floor architecture, muscles, and the organs possible in healthy women and detection of the presence of POP.

The last objective of this thesis was to develop a method for generating 3D models of the female pelvic floor from 2D MRO images in patients with POP with the aim of improving definition and visualization further. As described in Chapter 4, the protocol developed for standing and sitting image acquisition allowed the high-quality 2D images that are essential for 3D modeling to be acquired and described the way in which Analyze 12.0 software was used to generate quality 3D reconstruction models.

The sequence of steps followed for segmentation of the pelvic images made it possible to construct a 3D model that included the bony pelvis, pelvic organs, levator ani muscle, and pelvic floor muscles, where the anatomical structures were precisely defined and their borders could be traced reliably. The relevance of such modeling is that the levator ani plays a significant role in maintaining the integrity of the pelvic organs, but cadaveric studies lack detail due the location of the structures within the bony pelvis [115]. The 3D modeling method developed is novel, and the reconstruction of 3D pelvic images from 2D images derived from MRO scans is superior to 3D models generated previously, because of the advanced technology of MRO scanners. As the magnet is configured with a vertical gap, model generation is enhanced as subjects are

imaged in standing and seated positions as well as when supine, providing images where variations in functional posture allow the impact of gravity on the body to be visualized.

Hence, the level of anatomic detail in the 3D constructed models illustrated in Chapter 4 gives a better topographical overview of the complex structure and morphological characteristics of the levator ani and pubovisceral muscle in women with or without POP. Also, spatial analysis in three-dimensional models can yield information that cannot be obtained from two-dimensional studies and is of potential value particularly for surgical planning and to aid education of patients about their condition.

5.2. Limitations

A number of limitations have already been discussed in Chapters 3 and 4. Currently, because access to MRO units is limited to a few research facilities, other researchers and clinicians must wait to make use of the findings from this thesis until units with MRO become generally available.

Limitations of this current work include the small sample size, which restricts comment on how many patients will benefit from MRO standing image data identifying POP not detected in conventional supine MRI, and how much surgeons and the performance of surgery for POP could be influenced by availability of 2D MRO and 3D models of pelvic floor anatomy. However, a prospective study would define the proportion of patients in whom MRO enables a diagnosis of gravity-dependent POP to be made and formally establish the clinical utility of this application of MRO. The ongoing debate over which pelvic reference lines are the best to apply to MRI is a limitation that impacts the data reported, as it remains difficult to choose which pelvic

reference lines would supply the best reference landmark for MRO assessments of POP. However, as further MRO studies occur there is reason to be confident that which reference lines are optimal to use will emerge. Control subjects were younger than POP subjects overall, however there are no publications in the literature which indicate that the type of anatomic defects I observed with POP can result simply from the aging process.

A limitation of the modeling method reported is that muscle fiber direction and definition of some additional pelvic floor structures such as ligaments, nerves, veins, and arteries were beyond the scope of the current model; nevertheless, enhanced definition could be incorporated in future modeling. Another limitation was the short time (2 min) used to acquire the standing scans. Patient comfort is a factor that must be balanced with the need to avoid compromising image quality; a good quality 2D image is essential for the generation of accurate models. However, the protocol developed has proved successful in this regard, and I suggest that 3D modeling warrants further research and development, as the technique allows more comprehensive determination of the extent of organ prolapse due to the impact of posture and gravity. In addition, adequate defecation is important for a complete assessment of the posterior compartment. Incomplete evacuation of rectal content and persistent rectocele may mask the appearance of the enterocele.

Images of a full bladder were obtained when the patient indicated that they had a volume in their bladder for which they would normally seek the bathroom. No attempt was made to try to equalize the volume in the bladder between subjects given that this was a preliminary study and a fully non-invasive test was sought.

In the standing position the intraabdominal pressure is raised, the vagina displaces and presses against the levator plate, and levator contraction maintains this. This relationship may be distorted in patients with prolapse as the vaginal axis becomes straightened [215]. Additionally, the presence of air in the distal-most section of the rectum may lead to an overestimate of rectal descent.

When women lie in the scanner with different degrees of pelvic flexion, the positions of some reference lines PCL and SCCIP alter, and a similar situation can occur during maneuvers like the Valsalva maneuver

5.3. Significance

In pelvic organ prolapse (POP) posture and gravity impact organ position and symptom severity. The advanced magnet configuration available in open magnetic resonance imaging technology (MRO) allows patients to be imaged when sitting and standing as well in a conventional supine position, as the magnet is configured with a vertical gap.

This study evaluated if sitting and standing MRO images are relevant as a means of improving quantification of POP, because they allow identification of differences in organ position dependent on organ position due to the effects of posture and gravity not seen on supine imaging. This project found that the maximal extent of prolapse is best evaluated in the standing position using PCL, HL, ML, MPL, and PL as reference lines to determine pelvic organ prolapse, and that in 100% of symptomatic patients, gravity-dependent POP not seen in supine imaging was evident in standing images. Conversely, in the context of POP, imaging in the sitting position did not add any demonstrable benefit; in part because anatomical landmarks required for grading were

obscured. Also, the protocol developed for MRO of the pelvic floor can be broadly applied as a means of obtaining quality images, and the method described for construction of 3D models from 2D MRO images can be used and further refined by others.

As MRO becomes available, I suggest that this technology and the protocol and 3D modeling developed will offer clinicians an improved way to evaluate and classify patients with POP. As a result, currently recognized difficulties in diagnosis, classification, and treatment allocation will be overcome, which will allow more patients to benefit from appropriate treatment. Clinicians will be able to more readily visualize the anatomy of the pelvic floor, and surgeons will be enabled to achieve improved operative outcomes. Importantly, I believe that the findings of this research have the potential to benefit the many patients affected by POP by aiding detection and improving the accuracy of disease staging.

5.4. Future studies

Future directions with MRO should include a larger scale study of subjects with POP to determine the full scope of frequency and severity of understaging. Additionally, the relevance of having 3D models generated could be used in an assessment of initial selection of surgical intervention, need for surgical recurrence, as well the educational benefit for explanation to surgically naive patients. Valsalva maneuvers could be added to the imaging protocol to examine for more dynamic components of movement within the pelvis.

References

1. Macura KJ. Magnetic resonance imaging of pelvic floor defects in women. *Top Magn Reson Imag* 2006;17:417-26.
2. Herschorn S. Female pelvic floor anatomy: the pelvic floor, supporting structures, and pelvic organs. *Rev Urol* 2004;6:S2-S10.
3. Oelrich TM. The striated urogenital sphincter muscle in the female. *Anat Rec* 1983;205:223-32.
4. DeLancey JO. Structural anatomy of the posterior pelvic compartment as it relates to rectocele. *Am J Obstet Gynecol* 1999;180:815-23.
5. Woodman PJ, Graney DO. Anatomy and physiology of the female perineal body with relevance to obstetrical injury and repair. *Clin Anat* 2002;15:321-34.
6. Macura KJ, Genadry RR, Bluemke DA. MR imaging of the female urethra and supporting ligaments in assessment of urinary incontinence: spectrum of abnormalities. *Radiographics* 2006;26:1135-49.
7. DeLancey JO. Correlative study of paraurethral anatomy. *Obstet Gynecol* 1986;68:91-7.
8. Cruikshank SH, Kovac SR. The functional anatomy of the urethra: role of the pubourethral ligaments. *Am J Obstet Gynecol* 1997;176:1200-3; discussion 1203-5.
9. Yang A, Mostwin JL, Rosenshein NB, et al. Pelvic floor descent in women: dynamic evaluation with fast MR imaging and cinematic display. *Radiology* 1991;179:25-33.
10. Law YM, Fielding JR. MRI of pelvic floor dysfunction: review. *AJR Am J Roentgenol* 2008;191:S45-53.

11. Kim JK, Kim YJ, Choo MS, et al. The urethra and its supporting structures in women with stress urinary incontinence: MR imaging using an endovaginal coil. *AJR Am J Roentgenol* 2003;180:1037-44.
12. Fielding JR. MR imaging of pelvic floor relaxation. *Radiol Clin North Am* 2003;41:747-56.
13. Delancey JO, Hurd WW. Size of the urogenital hiatus in the levator ani muscles in normal women and women with pelvic organ prolapse. *Obstet Gynecol* 1998;91:364-8.
14. Fielding JR, Griffiths DJ, Versi E, et al. MR imaging of pelvic floor continence mechanisms in the supine and sitting positions. *AJR Am J Roentgenol* 1998;171:1607-10.
15. Unterweger M, Marincek B, Gottstien-Aalame N, et al. Ultrafast MR imaging of the pelvic floor. *AJR Am J Roentgenol* 2001;176:959-63.
16. Kelvin FM, Maglinte DDT, Hale DS, et al. Female pelvic organ prolapse: a comparison of triphasic dynamic MR imaging and triphasic fluoroscopic cystocolpoproctography. *AJR Am J Roentgenol* 2000;174:81-8.
17. Lienemann, A, et al. Dynamic MR colpocystorectography assessing pelvic-floor descent. *Eur Radiol* 1997;7:1309-17.
18. Goh V, Halligan S, Kaplan G, et al. Dynamic MR imaging of the pelvic floor in asymptomatic subjects. *AJR Am J Roentgenol* 2000;174:661-6.
19. DeLancey JO. Anatomy and biomechanics of genital prolapse. *Clin Obstet Gynecol* 1993;36:897-909.
20. Colaiacomo MC, Masselli G, Poletini E, et al. Dynamic MR imaging of the pelvic floor: a pictorial review. *Radiographics* 2009;29:e35. doi: 10.1148/rg.e35

21. Kelvin FM, Hale DS, Maglinte DD, et al. Female pelvic organ prolapse: diagnostic contribution of dynamic cystoproctography and comparison with physical examination. *AJR Am J Roentgenol* 1999;173:31-7.
22. Mellgren A, Johansson C, Dolk A, et al. Enterocele demonstrated by defaecography is associated with other pelvic floor disorders. *Int J Colorectal Dis* 1994;9:121-4.
23. Auwad W, Freeman RM, Swift S. Is the pelvic organ prolapse quantification system (POPQ) being used? A survey of members of the International Continence Society (ICS) and the American Urogynecologic Society (AUGS). *Int Urogynecol J Pelvic Floor Dysfunct* 2004;15:324-7.
24. Persu C, Chapple CR, Cauni V, et al. Pelvic Organ Prolapse Quantification System (POP-Q) - a new era in pelvic prolapse staging. *J Med Life* 2011;4:75-81.
25. Barber MD, Maher C. Epidemiology and outcome assessment of pelvic organ prolapse. *Int Urogynecol J* 2013;24:1783-90.
26. Luber KM, Boero S, Choe JY. The demographics of pelvic floor disorders: current observations and future projections. *Am J Obstet Gynecol* 2001;184:1496-501; discussion 1501-3.
27. Wu JM, Hundley AF, Fulton RG, et al. Forecasting the prevalence of pelvic floor disorders in U.S. women: 2010 to 2050. *Obstet Gynecol* 2009;114:1278-83.
28. Bump RC, Mattiasson A, Bø K, et al. The standardization of terminology of female pelvic organ prolapse and pelvic floor dysfunction. *Am J Obstet Gynecol* 1996;175:10-7.
29. Tan JS, Lukacz ES, Menefee SA, et al. Predictive value of prolapse symptoms: a large database study. *Int Urogynecol J Pelvic Floor Dysfunct* 2005;16:203-9; discussion 209.

30. Ellerkmann RM, Cundiff GW, Melick CF, et al. Correlation of symptoms with location and severity of pelvic organ prolapse. *Am J Obstet Gynecol* 2001;185:1332-7; discussion 1337-8.
31. Yalcin OT, Yildirim A, Hassa H. The effects of severe cystocele on urogynecologic symptoms and findings. *Acta Obstet Gynecol Scand* 2001;80:423-7.
32. Romanzi LJ, Chaikin DC, Blaivas JG. The effect of genital prolapse on voiding. *J Urol* 1999;161:581-6.
33. Mouritsen L. Classification and evaluation of prolapse. *Best Pract Res Clin Obstet Gynaecol* 2005;19:895-911.
34. Tunuguntla HS, Gousse AE. Female sexual dysfunction following vaginal surgery: myth or reality? *Curr Urol Rep* 2004;5:403-11.
35. Weber AM, Walters MD, Piedmonte MR. Sexual function and vaginal anatomy in women before and after surgery for pelvic organ prolapse and urinary incontinence. *Am J Obstet Gynecol* 2000;182:1610-5.
36. Rogers GR, Villarreal A, Kammerer-Doak D, et al. Sexual function in women with and without urinary incontinence and/or pelvic organ prolapse. *Int Urogynecol J Pelvic Floor Dysfunct* 2001;12:361-5.
37. Swift SE, Tate SB, Nicholas J. Correlation of symptoms with degree of pelvic organ support in a general population of women: what is pelvic organ prolapse? *Am J Obstet Gynecol* 2003;189:372-7; discussion 377-9.
38. Bradley CS, Nygaard IE. Vaginal wall descensus and pelvic floor symptoms in older women. *Obstet Gynecol* 2005;106:759-66.

39. Barber MD. Symptoms and outcome measures of pelvic organ prolapse. *Clin Obstet Gynecol* 2005;48:648-61.
40. Barber MD, Brubaker L, Nygaard I, et al. Defining success after surgery for pelvic organ prolapse. *Obstet Gynecol* 2009;114:600-9.
41. Jelovsek JE, Barber MD. Women seeking treatment for advanced pelvic organ prolapse have decreased body image and quality of life. *Am J Obstet Gynecol* 2006;194:1455-61.
42. Altman D, Kierkegaard LA, Zetterström, et al. Assessment of posterior vaginal wall prolapse: comparison of physical findings to cystodefecoperitoneography. *Int Urogynecol J Pelvic Floor Dysfunct* 2005;16:96-103; discussion 103.
43. Rentsch M, Paetzel C, Lenhart M, et al. Dynamic magnetic resonance imaging defecography: a diagnostic alternative in the assessment of pelvic floor disorders in proctology. *Dis Colon Rectum* 2001;44:999-1007.
44. Deval B, Vulierme MP, Poilpot S, et al. [Imaging pelvic floor prolapse]. *J Gynecol Obstet Biol Reprod (Paris)* 2003;32:22-9.
45. Hoyte L, Schierlitz L, Zou K, et al. Two- and 3-dimensional MRI comparison of levator ani structure, volume, and integrity in women with stress incontinence and prolapse. *Am J Obstet Gynecol* 2001;185:11-9.
46. Kester RR, Leboeuf L, Manedola MA, et al. Value of express T2-weighted pelvic MRI in the preoperative evaluation of severe pelvic floor prolapse: a prospective study. *Urology* 2003;61:1135-9.

47. Abrams P, Cardozo L, Fall M, et al. The standardisation of terminology in lower urinary tract function: report from the standardisation sub-committee of the International Continence Society. *Urology* 2003;61:37-49.
48. Borstad E, Rud T. The risk of developing urinary stress-incontinence after vaginal repair in continent women. A clinical and urodynamic follow-up study. *Acta Obstet Gynecol Scand* 1989;68:545-9.
49. Beecham CT. Classification of vaginal relaxation. *Am J Obstet Gynecol* 1980;136:957-8.
50. Swift S, Morris S, McKinnie V, et al. Validation of a simplified technique for using the POPQ pelvic organ prolapse classification system. *Int Urogynecol J Pelvic Floor Dysfunct* 2006;17:615-20.
51. Chen G-D, Ng S-C. Updated definition of female pelvic organ prolapse. *Incont Pelvic Floor Dysfunct* 2007;1:121-4.
52. Swift SE, Herring M. Comparison of pelvic organ prolapse in the dorsal lithotomy compared with the standing position. *Obstet Gynecol* 1998;91:961-4.
53. Koduri S, Sand PK. Recent developments in pelvic organ prolapse. *Curr Opin Obstet Gynecol* 2000;12:399-404.
54. Nosseir S, Schachar J, Naidich J, et al. Midpubic line to stage pelvic organ prolapse by MRI defecography as compared to POP-Q. *Obstet Gynecol Int J* 2014;1:00011. DOI: 10.15406/ogij.2014.01.00011.
55. Hodroff MA, Stolpen AH, Denson MA, et al. Dynamic magnetic resonance imaging of the female pelvis: the relationship with the Pelvic Organ Prolapse quantification staging system. *J Urol* 2002;167:1353-5.

56. Clark AL, Gregory T, Smith VJ, et al. Epidemiologic evaluation of reoperation for surgically treated pelvic organ prolapse and urinary incontinence. *Am J Obstet Gynecol* 2003;189:1261-7.
57. Benson JT, Lucente V, McClellan E. Vaginal versus abdominal reconstructive surgery for the treatment of pelvic support defects: a prospective randomized study with long-term outcome evaluation. *Am J Obstet Gynecol* 1996;175:1418-21; discussion 1421-2.
58. Bertschinger KM, Hetzer FH, Roos JE, et al. Dynamic MR imaging of the pelvic floor performed with patient sitting in an open-magnet unit versus with patient supine in a closed-magnet unit. *Radiology* 2002;223:501-8.
59. Baggish M, Karram M. Vaginal native tissue suture repair of vaginal vault prolapse. *Atlas of Pelvic Anatomy and Gynecologic Surgery*, 4th ed., 2016: p. 647-77.
60. Good MM, Abele TA, Balgobin S, et al. Vascular and ureteral anatomy relative to the midsacral promontory. *Am J Obstet Gynecol* 2013;208:486.e1-486.e7.
61. Barber MD, Maher C. Apical prolapse. *Int Urogynecol J* 2013;24:1815-33.
62. Sederl J. [Surgery in prolapse of a blind-end vagina]. *Geburtshilfe Frauenheilkd* 1958;18:824-8.
63. Bidmead J, Cardozo LD. Pelvic floor changes in the older woman. *Br J Urol* 1998;82(Suppl 1):18-25.
64. Morgan DM, Rogers MA, Huebner M, et al. Heterogeneity in anatomic outcome of sacrospinous ligament fixation for prolapse: a systematic review. *Obstet Gynecol* 2007;109:1424-33.

65. Paraiso MF, Ballard LA, Walters MD, et al. Pelvic support defects and visceral and sexual function in women treated with sacrospinous ligament suspension and pelvic reconstruction. *Am J Obstet Gynecol* 1996;175:1423-30; discussion 1430-1.
66. McCall ML. Posterior culdeplasty; surgical correction of enterocele during vaginal hysterectomy; a preliminary report. *Obstet Gynecol* 1957;10:595-602.
67. Margulies RU, Rogers MA, Morgan DM. Outcomes of transvaginal uterosacral ligament suspension: systematic review and metaanalysis. *Am J Obstet Gynecol* 2010;202:124-34.
68. Inmon WB. Pelvic relaxation and repair including prolapse of vagina following hysterectomy. *South Med J* 1963;56:577-82.
69. Shull BL, Capen CV, Riggs MW, et al. Bilateral attachment of the vaginal cuff to iliococcygeus fascia: an effective method of cuff suspension. *Am J Obstet Gynecol* 1993; 168:1669-74; discussion 1674-7.
70. Walters M, Karram M. *Urogynecology and Reconstructive Pelvic Surgery*. 4th ed., Philadelphia (PA): 2015.
71. Kong MK, Bai SW. Surgical treatments for vaginal apical prolapse. *Obstet Gynecol Sci* 2016;59:253-60.
72. Stevens JM. Gynaecology from ancient Egypt: The papyrus Kahun: A translation of the oldest treatise on gynaecology that has survived from the ancient world. *Med J Aust* 1975;2:949-52.
73. Emge LA, Durfee RB. Pelvic organ prolapse: four thousand years of treatment. *Clin Obstet Gynecol* 1966;9:997-1032.

74. Oliver, R, Thakar R, Sultan AH. The history and usage of the vaginal pessary: a review. *Eur J Obstet Gynecol Reprod Biol* 2011;156:125-30.
75. Lamers BH, Broekman BM, Milani AL. Pessary treatment for pelvic organ prolapse and health-related quality of life: a review. *Int Urogynecol J* 2011;22:637-44.
76. Zeitlin MP, Leberherz TB. Pessaries in the geriatric patient. *J Am Geriatr Soc* 1992;40:635-9.
77. Brown HL. Cervical prolapse complicating pregnancy. *J Natl Med Assoc* 1997;89:346-8.
78. Cundiff GW, Weidner AC, Visco AG, et al. A survey of pessary use by members of the American Urogynecologic Society. *Obstet Gynecol* 2000;95:931-935.
79. Mutone MF, Terry C, Hale DS, et al. Factors which influence the short-term success of pessary management of pelvic organ prolapse. *Am J Obstet Gynecol* 2005;193:89-94.
80. Thakar R, Stanton S. Management of genital prolapse. *BMJ* 2002;324:1258-62.
81. Chaikin DC, Groutz A, Blaivas JG. Predicting the need for anti-incontinence surgery in continent women undergoing repair of severe urogenital prolapse. *J Urol* 2000;163:531-4.
82. Shaikh S, Ong EK, Glavind K, et al. Mechanical devices for urinary incontinence in women. *Cochrane Database Syst Rev* 2006:CD001756.
83. Handa VL, Jones M. Do pessaries prevent the progression of pelvic organ prolapse? *Int Urogynecol J Pelvic Floor Dysfunct* 2002;13:349-51; discussion 352.
84. Jeffery S, Franco A, Fynes M. Vaginal wind-the cube pessary as a solution? *Int Urogynecol J Pelvic Floor Dysfunct* 2008;19:1457.

85. Hanson LA, Schulz JA, Flood GC, et al. Vaginal pessaries in managing women with pelvic organ prolapse and urinary incontinence: patient characteristics and factors contributing to success. *Int Urogynecol J Pelvic Floor Dysfunct* 2006;17:155-9.
86. Vierhout ME. The use of pessaries in vaginal prolapse. *Eur J Obstet Gynecol Reprod Biol* 2004;117:4-9.
87. Kwon JAS. *Pelvic Organ Prolapse — Pessary Treatment*. Springer London, 2008: p. 271-277.
88. Jones K, Yang L, Lowder JL, et al. Effect of pessary use on genital hiatus measurements in women with pelvic organ prolapse. *Obstet Gynecol* 2008;112:630-6.
89. Dietz HP, Haylen BT, Broome J. Ultrasound in the quantification of female pelvic organ prolapse. *Ultrasound Obstet Gynecol* 2001;18:511-4.
90. Dietz HP. Pelvic floor ultrasound in prolapse: what's in it for the surgeon? *Int Urogynecol J* 2011;22:1221-32.
91. Dietz HP. Pelvic floor ultrasound: a review. *Am J Obstet Gynecol* 2010;202:321-34.
92. Dietz HP. Ultrasound imaging of the pelvic floor. Part I: two-dimensional aspects. *Ultrasound Obstet Gynecol* 2004;23:80-92.
93. Athanasiou S, Chaliha C, Tooze-Hobson P, et al. Direct imaging of the pelvic floor muscles using two-dimensional ultrasound: a comparison of women with urogenital prolapse versus controls. *BJOG* 2007;114:882-8.
94. Mouritsen L, Bernstein I. Vaginal ultrasonography: a diagnostic tool for urethral diverticulum. *Acta Obstet Gynecol Scand* 1996;75:188-90.
95. Siegel CL, Middleton WD, Teefey SA, et al. Sonography of the female urethra. *AJR Am J Roentgenol*, 1998;170:1269-74.

96. Haylen BT, Maher CF, Barber MD, et al. An International Urogynecological Association (IUGA) / International Continence Society (ICS) Joint Report on the Terminology for Female Pelvic Organ Prolapse (POP). *Neurourol Urodyn* 2016;35:137-68.
97. Pannu HK, Genadry R, Kaufman HS, et al. Computed tomography evaluation of pelvic organ prolapse. Techniques and applications. *J Comput Assist Tomogr* 2003;27:779-85.
98. Kaufman HS, Butler JL, Thompson JR, et al. Dynamic pelvic magnetic resonance imaging and cystocolpoproctography alter surgical management of pelvic floor disorders. *Dis Colon Rectum* 2001;44:1575-83; discussion 1583-4.
99. Flusberg M, Sahni VA, Erturk SM, et al. Dynamic MR defecography: assessment of the usefulness of the defecation phase. *AJR Am J Roentgenol* 2011;196:W394-9.
100. Comiter CV, Vasavada SP, Barbaric ZL, et al. Grading pelvic prolapse and pelvic floor relaxation using dynamic magnetic resonance imaging. *Urology* 1999;54:454-7.
101. Pizzoferrato AC, Nyangoh Timoh K, Fritel X, et al. Dynamic magnetic resonance imaging and pelvic floor disorders: how and when? *Eur J Obstet Gynecol Reprod Biol* 2014;181:259-66.
102. Fauconnier A, Zareski E, Abichedid J, et al. Dynamic magnetic resonance imaging for grading pelvic organ prolapse according to the International Continence Society classification: which line should be used? *Neurourol Urodyn* 2008;27:191-7.
103. Woodfield CA, Hampton BS, Sung V, et al. Magnetic resonance imaging of pelvic organ prolapse: comparing pubococcygeal and midpubic lines with clinical staging. *Int Urogynecol J Pelvic Floor Dysfunct* 2009;20:695-701.

104. Fritel X, Fauconnier A, Bader G, et al. Diagnosis and management of adult female stress urinary incontinence: guidelines for clinical practice from the French College of Gynaecologists and Obstetricians. *Eur J Obstet Gynecol Reprod Biol* 2010;151:14-9.
105. Law PA, Dean JC, Lamb GM, et al. Dynamic imaging of the pelvic floor using an open-configuration magnetic resonance scanner. *J Magn Reson Imaging* 2001;13:923-9.
106. Orno AK, Dietz HP, Levator co-activation is a significant confounder of pelvic organ descent on Valsalva maneuver. *Ultrasound Obstet Gynecol* 2007;30:346-50.
107. Abdulaziz M, Stothers L, Macnab A. Methodology for 3D image reconstruction of the female pelvis from upright open MRI (MRO) imaging. *Biomed Spectrosc Imaging* 2018;7:81-96.
108. Roos JE, Weishaupt D, Wildermuth S, et al. Experience of 4 years with open MR defecography: pictorial review of anorectal anatomy and disease. *Radiographics* 2002;22:817-32.
109. Broekhuis SR, Fütterer JJ, Barentsz JO, et al. A systematic review of clinical studies on dynamic magnetic resonance imaging of pelvic organ prolapse: the use of reference lines and anatomical landmarks. *Int Urogynecol J Pelvic Floor Dysfunct* 2009;20:721-9.
110. Tunn R, Paris S, Taupitz M, et al. MR imaging in posthysterectomy vaginal prolapse. *Int Urogynecol J Pelvic Floor Dysfunct* 2000;11:87-92.
111. Singh K, Reid WM, Berger LA. Assessment and grading of pelvic organ prolapse by use of dynamic magnetic resonance imaging. *Am J Obstet Gynecol* 2001;185:71-7.

112. Reiner CS, Weishaupt D. Dynamic pelvic floor imaging: MRI techniques and imaging parameters. *Abdom Imaging* 2013;38:903-11.
113. Pannu HK. Magnetic resonance imaging of pelvic organ prolapse. *Abdom Imaging* 2002;27:660-73.
114. Aponte MM, Rosenblum N. Repair of pelvic organ prolapse: what is the goal? *Curr Urol Rep* 2014;15:385.
115. Olsen AL, Smith VJ, Bergstrom JO, et al. Epidemiology of surgically managed pelvic organ prolapse and urinary incontinence. *Obstet Gynecol* 1997;89:501-6.
116. Smith FJ, Holman CD, Moorin RE, et al. Lifetime risk of undergoing surgery for pelvic organ prolapse. *Obstet Gynecol* 2010;116:1096-100.
117. Subak LL, Waetjen LE, van den Eeden S, et al. Cost of pelvic organ prolapse surgery in the United States. *Obstet Gynecol* 2001;98:646-51.
118. Hullfish KL, Trowbridge ER, Stukenborg GJ. Treatment strategies for pelvic organ prolapse: a cost-effectiveness analysis. *Int Urogynecol J* 2011;22:507-15.
119. Daneshgari F, Kefer JC, Moore C, et al. Robotic abdominal sacrocolpopexy/sacrouteropexy repair of advanced female pelvic organ prolapse (POP): utilizing POP-quantification-based staging and outcomes. *BJU Int* 2007;100:875-9.
120. Brubaker L, Bump R, Jacquelin B, et al. Pelvic organ prolapse. In: Abrams P, Cardozo L, Khoury S, Wein A, editors. *Incontinence. 2nd International Consultation on Incontinence*. 2001 Jul 1-3; Paris, France, 2nd ed. Plymouth: Health Publication Ltd; 2002. pp 243-66.

121. Loret de Mola JR, Carpenter SE. Management of genital prolapse in neonates and young women. *Obstet Gynecol Surv* 1996;51:253-60.
122. Bash KL. Review of vaginal pessaries. *Obstet Gynecol Surv* 2000;55:455-60.
- 123 Tegerstedt G, Maehle-Schmidt M. Prevalence of symptomatic pelvic organ prolapse in a Swedish population. *Int Urogynecol J* 2005;16:497-503.
124. Thys SD, Roovers JP, Geomini PM, et al. Do patients prefer a pessary or surgery as primary treatment for pelvic organ prolapse. *Gynecol Obstet Invest* 2012;74:6-12.
125. Raja, AM, Seema SR. Mechanical devices in pelvic organ prolapse. *Int J Med Res Health Sci* 2013;2:643-7.
126. Pott-Grinstein E, Newcomer JR. Gynecologists' patterns of prescribing pessaries. *J Reprod Med* 2001;46:205-8.
127. Pushplata S, Devyani M, Pyari JS, et al. Bizarre foreign objects in the genital tract—our experience and review of literature. *Open J Obstet Gynecol* 2014;4:427-31.
128. Arias BE, Ridgeway B, Barber MD. Complications of neglected vaginal pessaries: case presentation and literature review. *Int Urogynecol J Pelvic Floor Dysfunct* 2008;19:1173-8.
129. Adams E, Thomson A, Maher C, et al. Mechanical devices for pelvic organ prolapse in women. *Cochrane Database Syst Rev* 2004:CD004010.
130. Farrell SA. Selection of a patient for pessary care. In: *Pessaries in clinical practice*. Springer; 2007. Chapter 4; p 25-31.
131. Friedman S, Sandhu KS, Wang C, et al. Factors influencing long-term pessary use. *Int Urogynecol J* 2010;21:673-8.

132. Bugge C, Adams EJ, Gopinath D, et al. Pessaries (mechanical devices) for pelvic organ prolapse in women. *Cochrane Database Syst Rev* 2013;(2):CD004010. DOI: 10.1002/14651858.CD004010.pub3.
133. Dindo D, Demartines N, Clavien P-A. Classification of surgical complications: A new proposal with evaluation in a cohort of 6336 patients and results of a survey. *Ann Surg* 2004;240:205-9.
134. Penrose KJ, Yin JM, Tsokos N. Delayed vesicovaginal fistula after ring pessary usage. *Int Urogynecol J* 2014;25:291-3.
135. Manchana T. Ring pessary for all pelvic organ prolapse. *Arch Gynecol Obstet* 2011;284:391-5.
136. Grody MH, Nyirjesy P, Chatwani A. Intravesical foreign body and vesicovaginal fistula: a rare complication of a neglected pessary. *Int Urogynecol J Pelvic Floor Dysfunct* 1999;10:407-8.
137. Ray A, Esen U, Nwabinehi J. Iatrogenic vesico-vaginal fistula caused by shelf pessary. *J Obstet Gynaecol* 2006;26:275-6.
138. Emmert, C. Neglected porcelain pessary causing postmenopausal bleeding and vesicovaginal fistula. *J Obstet Gynaecol* 2007;27:867-8.
139. Ott R, Richter H, Behr J, et al. Small bowel prolapse and incarceration caused by a vaginal ring pessary. *Br J Surg* 1993;80:1157.
140. Dasgupta P, Booth CM. Uraemia due to ureteric obstruction of a solitary kidney by a vaginal ring pessary. *Scand J Urol Nephrol* 1996;30:493-4.
141. Cumming GP, Narayansingh GV, Parkin DE, et al. Vesicovaginal fistula occurring 48 hours after insertion of a ring pessary. *J Obstet Gynaecol* 2000;20:637.

142. Hay DP, Martin WL, Darné FJ. Potentially dangerous complication of an ineffective shelf pessary. *J Obstet Gynaecol* 1999;19:669.
143. Mohammed M, Sidra L, Haldipur N, et al. Incarcerated appendices epiploicae through the posterior vaginal defect secondary to a ring pessary. *J Obstet Gynaecol* 2008;28:252-4.
144. Popli K, Ranka P, Mustafa FA. Massive vesico-vaginal fistula caused by a shelf pessary. *J Obstet Gynaecol* 2007;27:635-6.
145. Liang SJ, Chow PK, Chou SY, et al. Incarcerated vaginal pessary: a rare complication. *Taiwan J Obstet Gynecol* 2004;43:149-50.
146. Fernando RJ, Thakar R, Sultan AH, et al. Effect of vaginal pessaries on symptoms associated with pelvic organ prolapse. *Obstet Gynecol* 2006;108:93-9.
147. Alperin M, Khan A, Dubina E, et al. Patterns of pessary care and outcomes for medicare beneficiaries with pelvic organ prolapse. *Female Pelvic Med Reconstr Surg* 2013;19:142-7.
148. Potter C. Complications following the use of the gold spring pessary. *Am J Surg* 1930;10:143-8.
149. Bai SW, Yoon BS, Kwon JY, et al. Survey of the characteristics and satisfaction degree of the patients using a pessary. *Int Urogynecol J Pelvic Floor Dysfunct* 2005;16:182-6; discussion 186.
150. Clemons JL, Aquilar VC, Sokol ER, et al. Patient characteristics that are associated with continued pessary use versus surgery after 1 year. *Am J Obstet Gynecol* 2004;191:159-64.

151. Clemons JL, Aquilar VC, Tillinghast TA, et al. Patient satisfaction and changes in prolapse and urinary symptoms in women who were fitted successfully with a pessary for pelvic organ prolapse. *Am J Obstet Gynecol* 2004;190:1025-9.
152. Abdelmagied A, Karoshi M, Yoong W. Egg on my face: an unusual way of reducing prolapse. *J Obstet Gynaecol* 2005;25:222-3.
153. Roberge, RJ, Keller C, Garfinkel M. Vaginal pessary-induced mechanical bowel obstruction. *J Emerg Med* 2001;20:367-70.
154. Clemons JL, Aquilar VC, Tillinghast TA, et al. Risk factors associated with an unsuccessful pessary fitting trial in women with pelvic organ prolapse. *Am J Obstet Gynecol* 2004;190:345-50.
155. Nanda SS, Dash S, Behera A. Prolonged retention of ring pessary resulting in vaginal wall fibrosis: A case report. *Sch J Med Case Rep* 2014;2:50-1.
156. Russell JK. The dangerous vaginal pessary. *Br Med J* 1961;2:1595-7.
157. Roberge RJ, McCandlish MM, Dorfsman ML. Urosepsis associated with vaginal pessary use. *Ann Emerg Med* 1999;33:581-3.
158. Chow SH, LaSalle MD, Rosenberg GS. Urinary incontinence secondary to a vaginal pessary. *Urology* 1997;49:458-9.
159. Hanavadi S, Durham-Hall A, Oke T, et al. Forgotten vaginal pessary eroding into rectum. *Ann R Coll Surg Engl* 2004;86:W18-9.
160. Jain A, Majoko F, Freitas O. How innocent is the vaginal pessary? Two cases of vaginal cancer associated with pessary use. *J Obstet Gynaecol* 2006;26:829-30.
161. Kankam OK, Geraghty R. An erosive pessary. *J R Soc Med* 2002;95:507.

162. Wheeler LD, Lazarus R, Torkington J, et al. Lesson of the week: perils of pessaries. *Age Ageing* 2004;33:510-1.
163. Martin C, Hong L, Siddighi S. What is hiding behind the pessary? *Int Urogynecol J* 2013;24:873-5.
164. Kaaki B, Mahajan ST. Vesicovaginal fistula resulting from a well-cared-for pessary. *Int Urogynecol J Pelvic Floor Dysfunct* 2007;18:971-3.
165. Uprety DK, Regmi MC, Budhathoki B, et al. Metallic vaginal ring pessary: a rare entity. *Kathmandu Univ Med J* 2008;6:508-10.
166. Esin S, Harmanli O. Large vesicovaginal fistula in women with pelvic organ prolapse: the role of colpocleisis revisited. *Int Urogynecol J Pelvic Floor Dysfunct* 2008;19:1711-3.
167. Pankaj S, Choudhary V, Singh RK, et al. Forgotten vaginal pessary retrieved after 35 and 24 years of insertation two case reports. *J Evol Med Dent Sci* 2013;2:7312-6.
168. Meinhardt W, Schuitemaker NW, Smeets MJ, et al. Bilateral hydronephrosis with urosepsis due to neglected pessary. Case report. *Scand J Urol Nephrol* 1993;27:419-20.
169. Duncan LE, Foltzer M, O'Hearn M. Unilateral hydronephrosis, pyelonephritis, and bacteremia caused by a neglected vaginal ring pessary. *J Am Geriatr Soc* 1997;45:1413-4.
170. Fernando RJ, Sultan AH, Thakar R, et al. Management of the neglected vaginal ring pessary. *Int Urogynecol J Pelvic Floor Dysfunct* 2007;18:117-9.
171. Rogo-Gupta L, Le NB, Raz S. Foreign body in the bladder 11 years after intravaginal pessary. *Int Urogynecol J* 2012;23:1311-3.

172. Jelovsek JE, Maher C, Barber, MD. Pelvic organ prolapse. *Lancet* 2007;369:1027-38.
173. Sivasuriya M. Cervical entrapment of a polythene vaginal ring pessary--a clinical curiosity. *Aust N Z J Obstet Gynaecol* 1987;27:168-9.
174. Summers JL, Ford ML. The forgotten pessary: a medical oddity. *Am J Obstet Gynecol* 1971;111:307-8.
175. Wu V, Farrell SA, Baskett TF, et al. A simplified protocol for pessary management. *Obstet Gynecol* 1997;90:990-4.
176. Methfessel HD. Rare foreign body fistulas of the female bladder. *Z Urol Nephrol* 1987;80:545-9.
177. Poma PA. Management of incarcerated vaginal pessaries. *J Am Geriatr Soc* 1981;29:325-7.
178. Goldstein I, Wise GJ, Tancer ML. A vesicovaginal fistula and intravesical foreign body. A rare case of the neglected pessary. *Am J Obstet Gynecol* 1990;163:589-91.
179. Davila GW. Vaginal prolapse: management with nonsurgical techniques. *Postgrad Med* 1996;99:171-6,181,184-5.
180. Levine JM, Shua-Haim J, Gross J. Decubitus on uterus: an unusual complication of procidentia. *Resident Staff Physician* 1995;41:38-48.
181. Alnaif B, Drutz HP. Bacterial vaginosis increases in pessary users. *Int Urogynecol J* 2000;11:219-23.
182. Sarma S, Ying T, Moore KH. Long-term vaginal ring pessary use: discontinuation rates and adverse events. *BJOG* 2009;116:1715-21.

183. Atnip S, O'Dell K. Vaginal support pessaries: indications for use and fitting strategies. *Urol Nurs* 2012;32:114-24.
184. Schraub S, Sun XS, Maingon P, et al. Cervical and vaginal cancer associated with pessary use. *Cancer* 1992;69:2505-9.
185. Merino MJ. Vaginal cancer: the role of infectious and environmental factors. *Am J Obstet Gynecol* 1991;165:1255-62.
186. Shah SM, Sultan AH, Thakar R. The history and evolution of pessaries for pelvic organ prolapse. *Int Urogynecol J Pelvic Floor Dysfunct* 2006;17:170-5.
187. Magali R, Schulz JA, Harvey MA. Technical update on pessary use. *J Obstet Gynaecol Can* 2013;35:664-74.
188. Jones KA, Harmanli O. Pessary use in pelvic organ prolapse and urinary incontinence. *Rev Obstet Gynecol* 2010;3:3-9.
189. Schulz JA, Kwon, E. Pelvic organ prolapse pessary treatment. In: Baessler K, Schüssler B, Burgio KL, Moore K, Stanton SL, editors. *Pelvic Floor Re-education*. London: Springer; 2008; pp 271-7.
190. Khaja A, Freeman RM. How often should shelf/Gellhorn pessaries be changed? A survey of IUGA urogynaecologists. *Int Urogynecol J* 2014;25:941-6.
191. Ren S, Xie B, Wang J, et al. Biomechanics of pelvic organ prolapse. *Sci China Life Sci* 2015;58:218-20.
192. DeLancey JO. Functional anatomy of the female lower urinary tract and pelvic floor. *Ciba Found Symp* 1990;151:57-69; discussion 69-76.
193. Frawley HC, Galea MP, Phillips BA, et al. Reliability of pelvic floor muscle strength assessment using different test positions and tools. *Neurourol Urodyn* 2006;25:236-42.

194. Bo K. Can pelvic floor muscle training prevent and treat pelvic organ prolapse? *Acta Obstet Gynecol Scand* 2006;85:263-8.
195. Bump RC, Norton PA. Epidemiology and natural history of pelvic floor dysfunction. *Obstet Gynecol Clin North Am* 1998;25:723-46.
196. Healy JC, Halligan S, Reznek RH, et al. Patterns of prolapse in women with symptoms of pelvic floor weakness: assessment with MR imaging. *Radiology* 1997;203:77-81.
197. Kelvin FM, Maglinte DD. Dynamic cystoproctography of female pelvic floor defects and their interrelationships. *AJR Am J Roentgenol* 1997;169:769-74.
198. Maglinte DD, Kelvin FM, Fitzgerald K, et al. Association of compartment defects in pelvic floor dysfunction. *AJR Am J Roentgenol* 1999;172:439-44.
199. Stoker J, Halligan S, Bartram CI. Pelvic floor imaging. *Radiology* 2001;218:621-41.
200. Woodfield CA, Hampton BS, Sung V, et al. Magnetic resonance imaging of pelvic organ prolapse: Comparing pubococcygeal and midpubic lines with clinical staging. *Int Urogynecol J Pelvic Floor Dysfunct* 2009;20:695-701.
201. Friedman B, Stothers L, Lazare D, et al. Positional pelvic organ prolapse (POP) evaluation using open, weight-bearing magnetic resonance imaging (MRI). *Can Urol Assoc J* 2015;9:197-200.
202. Barber MD, Lambers A, Visco AG, et al. Effect of patient position on clinical evaluation of pelvic organ prolapse. *Obstet Gynecol* 2000;96:18-22.
203. Hall AF, Theofrastous JP, Cundiff GW, et al. Interobserver and intraobserver reliability of the proposed International Continence Society, Society of Gynecologic

Surgeons, and American Urogynecologic Society pelvic organ prolapse classification system. *Am J Obstet Gynecol* 1996;175:1467-70; discussion 1470-1.

204. Visco AG, Wei JT, McClure LA, et al. Effects of examination technique modifications on pelvic organ prolapse quantification (POP-Q) results. *Int Urogynecol J Pelvic Floor Dysfunct* 2003;14:136-40.

205. Silva WA, Kleeman S, Segal J, et al. Effects of a full bladder and patient positioning on pelvic organ prolapse assessment. *Obstet Gynecol* 2004;104:37-41.

206. Morren GL, Balasingam AG, Wells JE, et al. Triphasic MRI of pelvic organ descent: sources of measurement error. *Eur J Radiol* 2005;54:276-83.

207. Lienemann A, Sprenger D, Janssen U, et al. Assessment of pelvic organ descent by use of functional cine-MRI: which reference line should be used? *Neurourol Urodyn* 2004;23:33-7.

208. Boyadzhyan L, Raman SS, Raz S. Role of static and dynamic MR imaging in surgical pelvic floor dysfunction. *Radiographics* 2008;28:949-67.

209. Broekhuis SR, Kluivers KB, Hendriks, JC, et al, Dynamic magnetic resonance imaging: reliability of anatomical landmarks and reference lines used to assess pelvic organ prolapse. *Int Urogynecol J Pelvic Floor Dysfunct* 2009;20:141-8.

210. Cortes E, Reid WM, Singh K, et al. Clinical examination and dynamic magnetic resonance imaging in vaginal vault prolapse. *Obstet Gynecol* 2004;103:41-6.

211. Nardos R, Thirmond AS, Worstell TR, et al. Reference lines in dynamic magnetic resonance imaging of the pelvic floor. *Female Pelvic Med Reconstr Surg* 2010;16:242-5.

212. Lakeman MM, Zijta FM, Peringa J, et al. Dynamic magnetic resonance imaging to quantify pelvic organ prolapse: reliability of assessment and correlation with clinical findings and pelvic floor symptoms. *Int Urogynecol J* 2012;23:1547-54.
213. Medixant. 2018. RadiAnt DICOM Viewer User Manual. Version 4.6.9. Available at <https://www.radiantviewer.com/dicom-viewer-manual/PDF/radiantmanual469.pdf>.
214. Woodfield CA, Krishnamoorthy S, Hampton BS, et al. Imaging pelvic floor disorders: trend toward comprehensive MRI. *AJR Am J Roentgenol* 2010;194:1640-9.
215. Ginath S, Garely A, Luchs JS, et al. MRI pelvic landmark angles in the assessment of apical pelvic organ prolapse. *Arch Gynecol Obstet* 2011;284:365-70.
216. Gousse AE, Barbaric ZJ, Safir MK, et al. Dynamic half Fourier acquisition, single shot turbo spin-echo magnetic resonance imaging for evaluating the female pelvis. *J Urol* 2000;164:1606-13.
217. Pannu HK, Scatarige JC, Eng J. MRI diagnosis of pelvic organ prolapse compared with clinical examination. *Acad Radiol* 2011;18:1245-51.
218. Singh K, Reid WM, Berger LA. Assessment and grading of pelvic organ prolapse by use of dynamic magnetic resonance imaging. *Am J Obstet Gynecol* 2001;185:71-7.
219. Hsu Y, Summers A, Hussain HK, et al. Levator plate angle in women with pelvic organ prolapse compared to women with normal support using dynamic MR imaging. *Am J Obstet Gynecol* 2006;194:1427-33.
220. DeLancey JO, Morgan DM, Fenner DE, et al. Comparison of levator ani muscle defects and function in women with and without pelvic organ prolapse. *Obstet Gynecol* 2007;109:295-302.

221. Dietz HP, Shek C, Clarke B. Biometry of the pubovisceral muscle and levator hiatus by three-dimensional pelvic floor ultrasound. *Ultrasound Obstet Gynecol* 2005;25:580-5.
222. Clark NA, Brincat CA, Yousuf AA, et al. Levator defects affect perineal position independently of prolapse status. *Am J Obstet Gynecol* 2010;203:595 e17-22.
223. Singh K, Jakab M, Reid WM, et al. Three-dimensional magnetic resonance imaging assessment of levator ani morphologic features in different grades of prolapse. *Am J Obstet Gynecol* 2003;188:910-15.
224. Janda S. *Biomechanics of the Pelvic Floor Musculature*. Delft University of Technology, Delft, The Netherlands: 2006.
225. Boyles SH, Weber AM, Meyn L. Procedures for pelvic organ prolapse in the United States, 1979–1997 *Am J Obstet Gynecol* 2003;188:108-15.
226. Allen RE, Hosker GL, Smith AR, et al. Pelvic floor damage and childbirth: a neurophysiological study. *Br J Obstet Gynaecol* 1990;97: 770-9.
227. Ashton-Miller JA, DeLancey JO. Functional anatomy of the female pelvic floor. *Ann N Y Acad Sci* 2007;1101:266-96. doi: 10.1196/annals.1389.034.
228. Samuelsson EC, Victor FA, Tibblin G, et al. Signs of genital prolapse in a Swedish population of women 20 to 59 years of age and possible related factors. *Am J Obstet Gynecol* 1999;180:299–305.
229. Shin DS, Chung MS, Park HS, et al. Browsing software of the Visible Korean data used for teaching sectional anatomy. *Anat Sci Educ* 2011;4:327–32.

230. Abdulaziz M, Deegan E, Stothers L, et al. Advances in basic science methodologies for clinical diagnosis in female stress urinary incontinence, *Can Urol Assoc J*, 2017;11:S117–S120.
231. Karadimas EJ, Siddiqui M, Smith FW, et al. Positional MRI changes in supine versus sitting postures in patients with degenerative lumbar spine. *J Spinal Disord Tech* 2006;19:495–500.
232. Rubod C, Boukerrou M, Rousseau J, et al. A biomechanical model of the pelvic cavity: first steps. *Conf Proc IEEE Eng Med Biol Soc* 2006;1:968–71.
233. Lien KC, Mooney B, DeLance JO, et al. Levator ani muscle stretch induced by simulated vaginal birth. *Obstet Gynecol* 2004;103:31–40.
234. Noakes KF, Bissett IP, Pullan AJ, et al. Anatomically realistic three-dimensional meshes of the pelvic floor & anal canal for finite element analysis. *Ann Biomed Eng* 2008;36:1060–1071. doi:10.1007/s10439-008-9471-6.
235. Noakes KF, Pullan AJ, Bissett IP, et al. Subject specific finite elasticity simulations of the pelvic floor. *J Biomech* 2008;41:3060–5.
236. Chen ZW, Joli P, Feng ZQ, et al. Female patient-specific finite element modeling of pelvic organ prolapse (POP). *J Biomech* 2014;48:238–45.
237. Abdulaziz M, Stothers L, Lazare D, et al. Relevance of open magnetic resonance imaging position (sitting and standing) to quantify pelvic organ prolapse in women. *Can Urol Assoc J* In press.
238. Dietz HP, Clarke B. The influence of posture on perineal ultrasound imaging parameters. *Int Urogynecol J Pelvic Floor Dysfunct* 2001;12:104–6.

239. Venuti JM, Imielinska C, Molholt P. New views of male pelvic anatomy: role of computer-generated 3D images. *Clin Anat* 2004;17:261–71.
240. Robb RA, Hanson DP, Karwoski RA, et al. Analyze: a comprehensive, operator-interactive software package for multidimensional medical image display and analysis. *Comput Med Imaging Graph* 1989;13:433–454.
241. Hecht EM, Lee VS, Tanpitukpongse TP, et al. MRI of pelvic floor dysfunction: dynamic true fast imaging with steady-state precession versus HASTE. *AJR Am J Roentgenol* 2008;191:352–8. doi: 10.2214/AJR.07.3403.
242. Jones KA, Shepherd JP, Oliphant SS, et al. Trends in inpatient prolapse procedures in the United States, 1979–2006. *Am J Obstet Gynecol* 2010;202:501.e17. doi:10.1016/j.ajog.2010.01.017
243. Cimsit C, Yoldemir T, Akpinar IN. Prevalence of dynamic magnetic resonance imaging-identified pelvic organ prolapse in pre- and postmenopausal women without clinically evident pelvic organ descent. *Acta Radiol* 2016;57:1418–24.
244. Shorvon PJ, McHugh S, Diamant NE, et al. Defecography in normal volunteers: results and implications. *Gut* 1989;30:1737–49.
245. Chanda A, Unnikrishnan V, Roy S, et al. Computational modeling of the female pelvic support structures and organs to understand the mechanism of pelvic organ prolapse: a review *Appl Mech Rev* 2015;67;040801-040801-14. doi:10.1115/1.4030967.
246. Tunn R, Paris, Fischer W, et al. Static magnetic resonance imaging of the pelvic floor muscle morphology in women with stress urinary incontinence and pelvic prolapse. *Neurourol Urodyn* 1998;17:579–89

247. Sora MC, Jilavu R, Matusz P. Computer aided three-dimensional reconstruction and modeling of the pelvis, by using plastinated cross sections, as a powerful tool for morphological investigations. *Surg Radiol Anat* 2012;34:731–6.
248. Strohbehn K. Normal pelvic floor anatomy. *Obstet Gynecol Clin North Am* 1998;25:683-705.
249. Bo K, Finckenhagen HB. Is there any difference in measurement of pelvic floor muscle strength in supine and standing position? *Acta Obstet Gynecol Scand* 2003;82:1120-4.
250. Betschart C, Chen L, Ashton-Miller JA, et al. On pelvic reference lines and the MR evaluation of genital prolapse: a proposal for standardization using the Pelvic Inclination Correction System. *Int Urogynecol J* 2013;24:1421-8.
251. Fuchs TJ, JBuhmann M. Computational pathology: challenges and promises for tissue analysis. *Comput Med Imaging Graph* 2011;35:515-30.