
Assessment of pelvic organ prolapse extend during the day using PCA – An MRI study

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1 Samenvatting

Dit onderzoek omvat de beoordeling van de vorm van de ondersteunende spieren van de bekkenbodem gedurende de dag. Voor vrouwen nemen over het algemeen de klachten gedurende de dag toe. Er is onderzocht of dit terug te zien is in de levator plate (LP) shape, de vorm van de het mediale aanhechtingspunt van de levator ani, met behulp van de statistische methode principal component analysis (PCA).

Er hebben 60 vrouwen, waarvan 15 met een bekkenbodemverzakking en 45 zonder bekkenbodemverzakking, deelgenomen aan dit onderzoek. Al deze vrouwen werden in de ochtend, middag en namiddag gedurende een dag gescand, wat heeft geleid tot een totaal van 171 bruikbare scans. Vervolgens werd er met behulp van (PCA) een analyse uitgevoerd om de verschillen in LP shape gedurende de dag in beeld te kunnen brengen. Op deze data werd een statistische test, de Two-Way ANOVA, toegepast.

Hieruit blijkt dat er geen significant verschil is in de ligging en vorm van de LP shape gedurende de dag. Wel is er een significant verschil te zien in LP shape tussen vrouwen met en zonder een bekkenbodemverzakking ($p < 0.01$) met een meer dorsaal gelegen LP shape voor de vrouwen met een verzakking.

Concluderend kan er gezegd worden dat er gedurende de dag geen verschil is in LP shape bij vrouwen met een verzakking.

2 Introduction

Pelvic organ prolapse (POP) is a common condition affecting 25 – 41% of middle-aged and elderly women [1]. It is a condition described as a downward displacement of one or more of the pelvic organs, including the bladder, uterus, bowel and rectum. Symptoms associated to POP include vaginal bulging, irritative bladder, voiding difficulty and defecatory difficulty [2]. Besides that, women have reported that they experience an increase in symptoms during the day, especially after a prolonged time on their feet or during or after lifting [3].

Currently, the most used evaluation method of POP is called POP quantification (POP-Q). This is a physical examination which is executed with the patient in supine position. Due to this supine position the results can lead to underestimation of POP, since the effect of gravity is neglected. To stimulate the effect of gravity, the patients are instructed to put strain on their pelvic floor. However, the effect of the strain is dependent on the instructions of the physician and the ability of the patients to relax their pelvic floor muscles [1]. Imaging techniques such as ultrasound and magnetic resonance imaging (MRI) are used to gather more information about both the diagnosis and management of POP. MRI is a valuable technique, since it can visualize several of the pelvic organs and supportive structures at once [4].

In recent studies, the added value of upright MRI has been looked into [1]. Upright imaging enables a realistic image of the placement of the pelvic organs and surrounding structures including the levator plate (LP), since women experience most of their symptoms in standing position. The levator plate is the shelf on which the pelvic organs rest [5]. According to literature, there are significant changes in the anatomy of the pelvis and the extend of the prolapse when a patient is scanned in upright position compared to supine position [6, 7]. Subsequently it has been shown that there is a significant difference between upright and supine MR imaging regarding the LP shape. The LP shape starts near the coccyx and ends near the anal sphincter. A shape with a slightly steeper slope usually corresponds with the LP shape of POP women [8]. Besides that, the LP shape has a steeper slope in upright position than in the supine position [6], which indicates that evaluation of POP in standing position may provide greater insight in the diagnosis and management of POP.

In the research of Schmidt et al. [9] the statistical method principal component analysis (PCA) was used to visualize the LP shape. PCA is a dimensionality reduction method that is used for large data sets [10] and could be of great use in this research to visualize the LP shape.

As there is a correlation between prolapse and LP shape and women have reported to experience more symptoms by the end of the day, it is of interest to study the extend of POP during the day in standing position. Besides that, PCA is the method that can be used to visualize the LP shape and make the shapes quantitatively comparable. We hypothesize that at the end of the day the LP shape will have a slightly steeper slope than at the beginning of the day for women with POP.

3 Background information

3.1 Pathophysiology of pelvic organ prolapse

3.1.1 Pelvic floor support

The pelvic floor is mostly supported by the interactions between the levator ani and pelvic connective tissue [11]. The main contributing muscles to pelvic floor support are the levator ani and the coccygeus muscles and together they form the pelvic diaphragm (Figure 1, 2). The levator ani exist out of the pubococcygeus and the iliococcygeus muscles which together cover a large part of the inferior pelvic outlet from medial to lateral [5]. The median raphe, where the two sides of the levator ani meet, is called the levator plate (LP). As can be seen in Figure 2, it is the midline posterior to the rectum [11]. When the body is in upright position, the LP should be horizontal while supporting the rectum and upper two thirds of the vagina [5]. It acts as a kind of trampoline, receiving and resisting sudden increases in abdominal pressure [12].

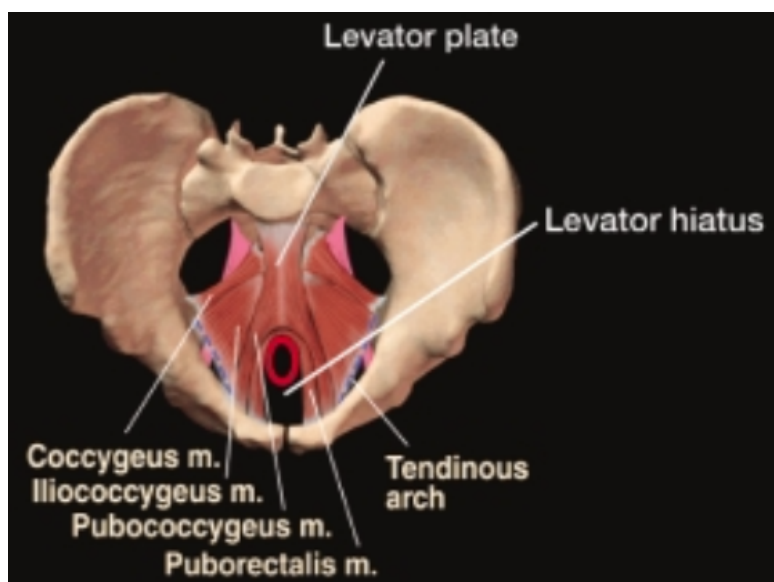


Figure 1: This figure shows a depiction of the pelvic diaphragm from the inferior view. It can be seen that the levator ani and coccygeus muscles cover most of the inferior pelvic outlet [5].

3.1.2 Pelvic organ prolapse

Pelvic organ prolapse (POP), as already has been mentioned, is a condition that describes the pelvic floor descent. Symptoms that usually occur are vaginal bulging, irritative bladder, voiding difficulty and defecatory difficulty [2]. Problems with the pelvic support system, which can lead to POP, can occur due to several factors, which are combined most of the time. These factors include age, pregnancy, childbirth, heavy lifting, pelvic surgeries, connective tissue disorders, pelvic neuropathies, congenital factors, stress and others [12]. A weakened or damaged levator ani is a large contributor to problems with the pelvic support system. Once the levator ani weakens, the levator hiatus enlarges, which makes prone to prolapse. Due to intra-abdominal pressure the pelvic organs can

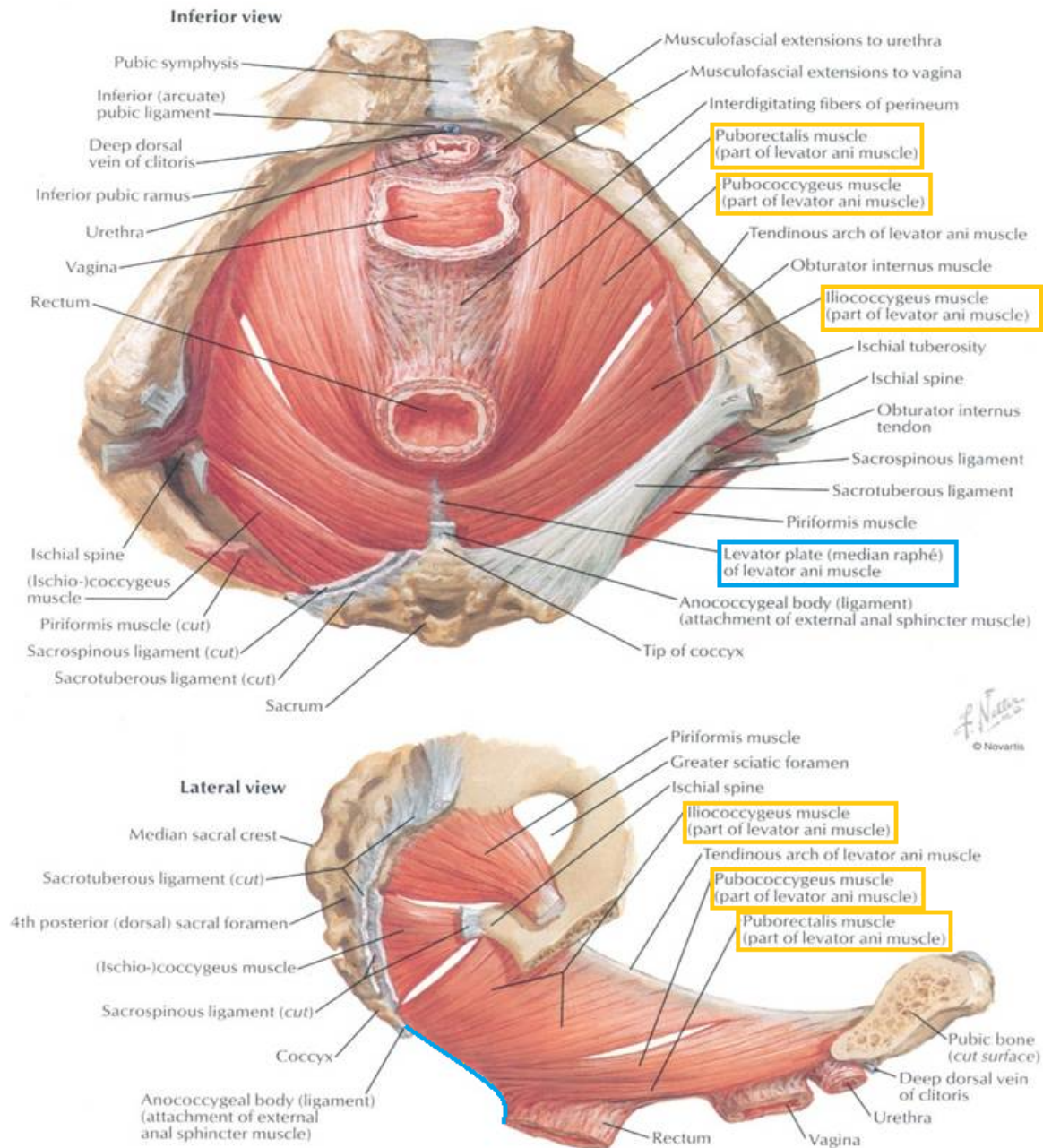


Figure 2: This figure shows a schematic view of the muscles in the pelvic floor. The muscles involved in the levator ani have been marked yellow in the inferior and lateral view. Besides that, the LP has been marked with blue in the inferior view and a blue line has been drawn at the place of the LP in the lateral view [13].

start to push down on the pelvic support system, which causes it to descend and make the pelvic organs prolapse [11, 12].

3.2 Principal component analysis

Principal component analysis (PCA) is a statistical method that is widely used for analysing large data sets. It can be used to identify patterns in data and express this data in a way that it emphasizes their similarities and differences [14]. Large data sets

with large numbers of variables are difficult to interpret. The analysis of these data sets can be simplified by reducing the dimensionality of these data sets, although this causes some loss of statistical information [15]. This loss of information is worthwhile, because due to the dimensionality reduction the data sets have become easier to visualize and analyse. Choosing how much information will be lost, depends on what the PCA is used for. If the PCA is used for visualisation purposes only, usually two or three PCs will be retained. If the PCA is mainly used for dimensionality reduction, one can choose the error to be as small as one desires. So for example an error of 5%. The main goal of PCA is to reduce dimensionality of a data set while preserving as much information as possible [10]. This is done by finding the principle components (PCs). They maximize the variance and reduce to solving an eigenvalue/eigenvector problem [15].

Before the PCA a normalisation or standardisation has to be done. Here this is called the first step. PCA is sensitive to variances of the initial variables, which makes performing standardization prior to the PCA crucial [10]. Standardization can be done by subtracting the mean from each value of each variable and dividing this by the standard deviation:

$$z = \frac{x - \mu}{\sigma}$$

with x being the value, μ being the mean, σ being the standard deviation and z being the standardized value. A normalisation can also be performed by removing any rotation, translation and scaling. This can also be called the alignment and scaling of the data [16].

The second step is the computation of the covariance matrix. This step focuses on finding any correlations between the variables [10]. The covariance matrix is always a square matrix where the number of rows and columns is equal to the number of dimensions. A data set with 3 variables, x, y and z , gives a 3x3 matrix:

$$Cov = \begin{pmatrix} Cov(x, x) & Cov(x, y) & Cov(x, z) \\ Cov(y, x) & Cov(y, y) & Cov(y, z) \\ Cov(z, x) & Cov(z, y) & Cov(z, z) \end{pmatrix}.$$

The covariance values down the diagonal are the covariance of the variable with itself ($Cov(x, x) = Var(x)$), which leads to those values being the variance of each variable. Besides that, the covariance is commutative ($Cov(x, y) = Cov(y, x)$), so the matrix is symmetrical about the diagonal [10, 14].

The sign of the covariance states something about the correlation: when the covariance is positive, then the two variables increase together and they are correlated. When the covariance is negative, then the two variables decrease together and they are inversely correlated [10].

The third step is the computation of the eigenvectors and eigenvalues of the covariance matrix. In this step the PCs are identified. As defined by Zakaria [10], PCs are new variables build as linear combinations of the initial variables in such a way that they are uncorrelated (so orthogonal) to each other. A PC represents the direction of the data with the maximal amount of variance and is expressed as the eigenvector of the covariance matrix. In other words, the direction of the axes with the most variance are the eigenvectors, which are the PCs. A visualisation of the eigenvectors is shown in Figure 3. The amount of variance in each PC is given by the eigenvalues and there are as many

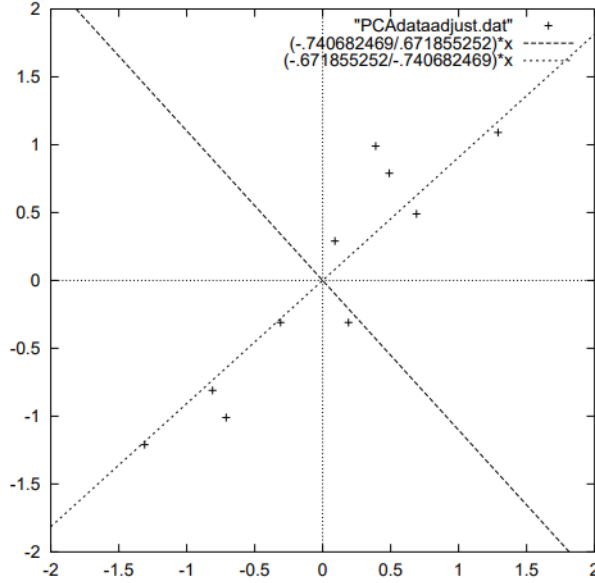


Figure 3: This figure shows a visualisation of de-meaned data with the eigenvectors on top of it. The dots represent the de-meaned data and the diagonal lines represent two eigenvectors [14].

PCs as there are variable. The first PC should contain the largest possible variance, so a data set with 5 dimensions will result in 5 PCs from which the first one contains the largest possible variance, the second the second largest possible variance and so on.

The fourth step is creating a feature vector to decide which PCs should be kept. In this step, one chooses which PCs are to be discarded and which are significant enough to keep. The eigenvectors can be ranked in order of their eigenvalues from highest to lowest, which results in the principal components in order of significance. The PCs of lowest significance, with the lowest eigenvalues, can be ignored. By leaving out these components the dimensionality is reduced while losing the information captured by the these component. As long as the corresponding eigenvalues of these PCs are small, the information loss is very limited. The PCs with the highest eigenvalues will form a matrix together, which is called the feature vector [14]. The feature vector will look like this:

$$F = (eig_1 \ eig_2 \ eig_3 \ \dots \ eig_n)$$

with F being the feature vector and n being the number of dimensions.

The fifth step is to recast the date along the axes of the principle components. This can be done by multiplying the standardized original data set with the feature vector [14]. The corresponding equation is as follows:

$$D = S \times F$$

with D being the final data set, S being the standardized original data set and F being the feature vector.

The final step is getting the original data back [14]. The last equation can be rewritten to the following equation:

$$S = D \times F^T.$$

To get the original data back, the mean of the original data should be added back:

$$O = S + M$$

with O being the original data set and M being the original mean. This concludes all the steps prior to and involved in PCA.

3.3 Two-Way ANOVA

The Two-Way ANOVA is a statistical test that compares the mean differences between two independent variables. With this test it can be shown whether these variables have any interaction with the dependent variable or not [17]. In this research the independent variables would be the different time points during the day and the POP women and the healthy volunteers. If there is interaction, the lines of the two groups will intersect or at least will not be parallel. If there is no interaction, the lines will be parallel [17].

4 Materials and methods

4.1 Population

MRI scans of women who participated in the EPPA study were used. The EPPA study was approved by the local ethics committees (NL74061.091.20), and all women gave written informed consent [18]. 15 patients enrolled from the gynecology department of Ziekenhuis Groep Twente (ZGT) hospital in Hengelo. The 45 control women included in this research did not have any POP symptoms and enrolled via flyers. Out of the 45 volunteers there were 15 nulliparous, 15 parous (minimal of one vaginal delivery) and pre-menopausal and 15 parous and post-menopausal.

All women were 18 years or older. Women were excluded if they were not able to stand for 20 minutes without assistance, were not suitable to undergo an MR scan based on the MRI safety checklist, or had a jeans size larger than 52 (EU) or 22 (US), because of the limited coil circumference [6, 18].

4.2 MRI examination

All women were scanned using a tiltable 0.25T MR scanner (G-Scan; Esaote, Genoa, Italy) in upright position. The table was angled at 81° to enable a natural standing position for all women. A multi-slice 2D T2-weighted fast spin echo (FSE) scan was acquired in midsagittal position (echo time (TE): 2 ms, repetition time (TR): 3480 ms, reconstructed resolution: 1.3×1.3 mm², FOV: 340 x 340 mm², matrix size: 192 x 200, slice thickness: 5 mm, number of slices: 11, total scan time: ± 2 min) [18]. Secondly, a 3D hybrid contrast enhancement (HYCE) MRI scan was obtained in midsagittal position.

All women were scanned three times in one day. The first scan took place between 8AM and 9AM, the second scan between 12AM and 1PM and the third scan between 4PM and 5PM.

4.3 Image analysis

ImageJ software (version 1.53q, LOCI, University of Wisconsin) was used for the levator plate shape analysis on the upright scans. For each scan a total of twelve points were manually assigned in the midsagittal plane (Figure 4). As defined by Schmidt et al. [9], the anatomical landmarks that were marked were the inferior pubic point of the pubic symphysis (1), the perineal body (2), the most superior point of the external anal sphincter (3), the middle of the puborectalis bundle (5) that is approximately the shortest distance from the pubic symphysis to the levator plate, the inferior coccyx (9) and the sacrococcygeal joint (10). The remaining points were equal sampling points (4, 6, 7, 8), which were marked at approximately half the distance between the above-mentioned anatomic landmarks. These were placed in numeric order to allow for more accurate curvature measurements. The LP is defined as a curved line between points (3) to (10). Point (11) was placed at the anterior fornix of the vagina and point (12) at the posterior fornix of the vagina. The points were saved in a .tiff file.

For each scan, the coordinates of each point were analysed and measured. Then, the levator area (LA) in mm², SCIPP length in mm, urogenital hiatus (UGH) in mm, levator hiatus (LH) in mm, and perineal body (PB) location were calculated in mm by a macro

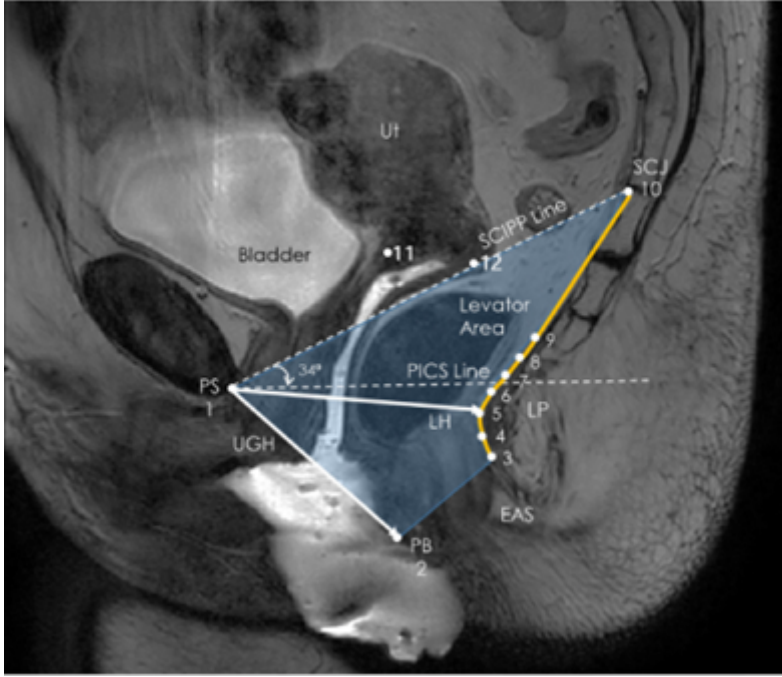


Figure 4: This figure shows a midsagittal view of the MRI with the measurements that have been performed. The abbreviations are as follows, PS: pubic symphysis, UGH: urogenital hiatus, PB: perineal body, EAS: external anal sphincter, LP: levator plate, LH: levator hiatus, SCJ: sacrococcygeal joint, SCIPP line: sacrococcygeal to inferior pubic point line, Ut: uterus, PICS line: horizontal reference line[9].

plugin tool. The coordinates and the information calculated by the macro plugin tool were saved in a .csv file [6].

4.4 Levator plate shape analysis

The levator plate is a curved structure which can be analysed by statistical shape analysis with the use of PCA. The Python software from Schmidt et al. [9] was performed to do this analysis. Besides that, homemade MATLAB code (MATLAB ver. R2022a) was used to replicate their shape analysis. First alignment and scaling was carried out to be confident that all variables (the x,y-coordinates of all points) contributed equally to the analysis. After that, a reshape took place following the principal component analysis.

4.4.1 Alignment and scaling

The first step in the alignment was translating all variables. For the LP shapes of all scans to start at the same origin, a starting point had to be chosen. Point 10, the sacrococcygeal joint, was chosen to be this starting point of the LP shape. For all LP shapes to start at point 10, the x,y-coordinates of point 10 had been subtracted from all variables:

$$T(x, y) = (x, y) - (x_{10}, y_{10})$$

with T being the translated variables. After this had been done for each scan, all variable had been translated to the origin (0,0).

The second step was scaling the data. This step made use of the SCIPP line length, which is the distance between points 1 (pubic symphysis) and 10. All scans were scaled to a reference SCIPP length of 100 mm. For each scan a scaling factor was created by dividing the reference SCIPP length by the actual SCIPP length. The translated variables were multiplied by this scaling factor which led to translated and scaled variables:

$$S(x, y) = T(x, y) * \frac{SCIPP_{ref}}{SCIPP}$$

with S being the translated and scaled variables, $SCIPP_{ref}$ being the reference SCIPP length and $SCIPP$ being the actual SCIPP length.

The third and last step of the alignment and scaling was the rotation. The LP shapes of all scans were rotated to a fixed angle. This was done by creating a rotation matrix with the angle between the SCIPP line and the x-axis. The translated and scaled variables were multiplied by this rotation matrix, which made the SCIPP line equal to the x-axis. Then these rotated variables were again rotated by multiplying with another rotation matrix. In this rotation matrix the angle was made 34° , which matched the PICS angle [19].

$$R = S * M_1 * M_2$$

with R being the translated, scaled and rotated variables, M_1 being the rotation matrix $\begin{pmatrix} \cos(\theta) & -\sin(\theta) \\ \sin(\theta) & \cos(\theta) \end{pmatrix}$ with θ being the angle between the SCIPP line and the x-axis and M_2 being the rotation matrix $\begin{pmatrix} \cos(\phi) & -\sin(\phi) \\ \sin(\phi) & \cos(\phi) \end{pmatrix}$ with ϕ being an angle of 34° . This led to translated, scaled and rotated variables. The implementation of these steps in MATLAB can be viewed in Appendix B section 7.2.1.

4.4.2 Principal Component Analysis (PCA)

After the alignment and scaling and before the PCA a reshape was performed on the data. This reshape converted the matrix containing data from a 12x2 matrix to a 24x1 matrix. Next, the reshaped matrix was transposed, so the rows of the matrix contained the scans and the columns contained the variables. The default MATLAB PCA function was used to calculate the PCs, eigenvalues, percentages of total variance and the estimated mean of each variable [20]. At last, the original data was retrieved by multiplying the score with the transpose of the coeff and adding mu to it. The exact implementation of this section can be found in Appendix B section 7.2.3.

4.5 Statistical analysis

The statistical analysis was performed using SPSS (ver. 28.0.1.0). A Two-Way ANOVA (analysis of variance) was performed on the data. This test was able to show whether there was any interaction between the groups (healthy volunteers and POP) and the time (morning, midday and afternoon) and the times among themselves.

5 Results

The following results were obtained with a total of 43 instead of 45 volunteers and 14 instead of 15 POP women. Out of the 43 volunteers, there were 15 nulliparous, 15 parous and pre-menopausal and 13 parous and post-menopausal women. Two parous and post-menopausal women were excluded, because they appeared to have a prolapse. One POP woman was excluded, because the afternoon scan did not take place.

5.1 Results obtained with Python program

The PC shape analysis performed by the Python program that was developed in the research of Schmidt et al. [9] identified two main PCs with shape variations (PC1 and PC2). PC1 describes the shape in horizontal direction and PC2 describes the shape in vertical direction. PC1 accounted for 61% of shape variation and PC2 accounted for 33% of the shape variation. For PC1 a clear distinction can be made between the healthy volunteers and the POP women with a significance of $p < 0.001$. The PC scores of the group of healthy volunteers at all time points were lower than the group of POP women, as can be seen in Figure 5. The entire LP shape of the POP group seemed to have rotated more dorsally around the sacrococcygeal joint as compared to the healthy volunteers. For PC2 the distinction is less obvious, which corresponds with a marginal significance of $p = 0.049$. as the PC scores show in Figure 5, the group of healthy volunteers scored slightly higher at all time points than the group of POP women.

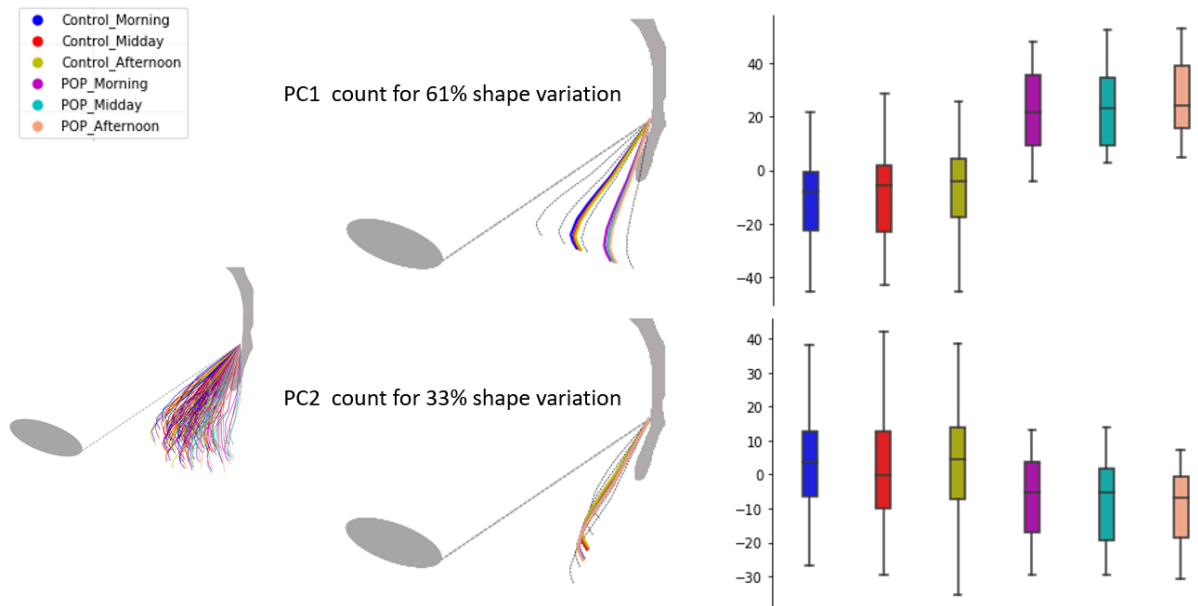


Figure 5: This figure shows the levator plate shape analysis comparing POP women to healthy volunteers in the morning, midday and afternoon. The bottom error bar indicates the minimum value to the 25th percentile, and the top error bar indicates the 75th percentile to the maximum value. This figure has been visualized by Python.

Figure 5 shows that there was no significant difference in LP shape or LP score at the different time points for both the group of healthy volunteers and the group of POP women. There was however a small difference in PC1 between the morning and afternoon

scans in both women with POP and the healthy volunteers with $p < 0.209$, however this was still not significant. In Figure 6 the two lines, which represent the main effect of the different groups are parallel to each other. This shows that there was no interaction between the groups and the different time points. All p-values with regard to the results can be found in Figures 9 and 10 in appendix A.

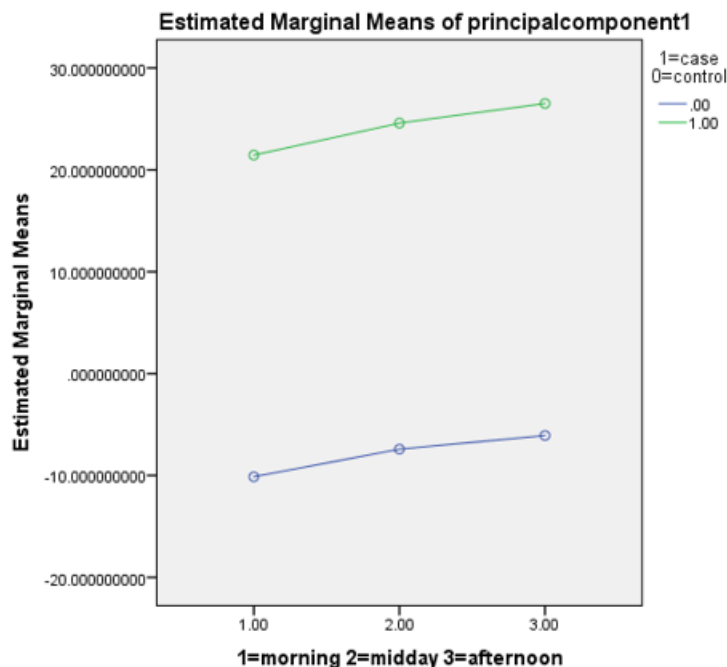


Figure 6: This figure shows the main effect of PC1 for both the POP women and the healthy volunteers at the different time points during the day. There is a large difference in estimated means between the healthy volunteers and the POP women, but the differences during the day are small.

5.2 Comparison MATLAB and Python program

The results from the figures made in MATLAB were similar to those in Python (Figure 5,7). PC1 and PC2 obtained by MATLAB are shown in Figure 8. The mean and standard deviations seem to correspond with the PCs in Figure 5. For MATLAB the total variance of PC1 was 61% and for PC2 was 33%, which corresponded with the total variances for both PCs of the Python program. The plots of PC1 and PC2 are depicted in Figure 8, with (a) and (b) respectively showing PC1 and PC2.

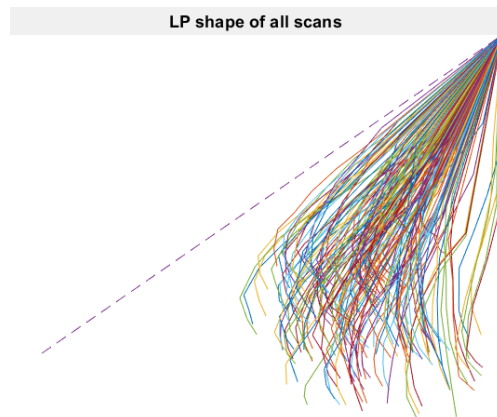


Figure 7: This figure shows the LP shape of all individual scans visualized with MATLAB. The dashed line is the SCIPP line.

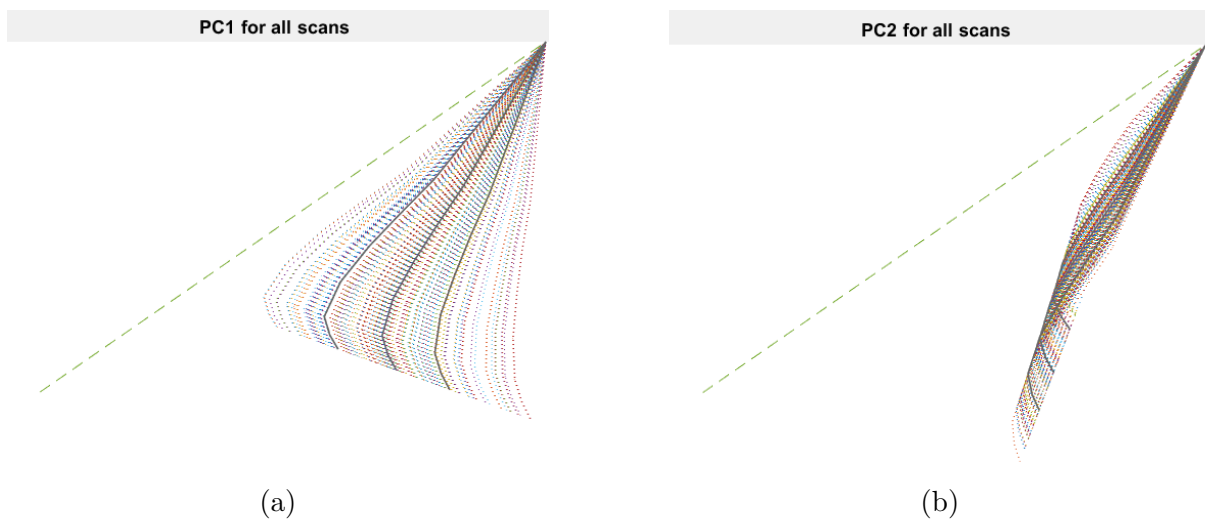


Figure 8: This figure shows for (a) and (b) respectively PC1 and PC2 visualised by MATLAB. The dotted lines represent the PC of all individual scans, the dashed line represents the SCIPP line and the continuous lines represents the mean and standard deviations.

6 Discussion

In this study, the PC shape analysis showed that there is a significant difference in LP shape between the POP women and healthy volunteers (Figure 5), especially with regards to PC1. For all time points, the LP shape regarding the group of POP women was oriented more dorsally as compared to the group of healthy volunteers. PC2 showed a marginal significance in vertical direction. These results could indicate that the POP women experience less support from the levator plate than the healthy volunteers. The LP shape could be deformed in this manner, due to the pelvic organs being in prolapse and pushing the LP shape more dorsally and caudally. Besides that, the PC shape analysis showed no significant difference in LP shape for the different time points for both the POP women and the healthy volunteers. There was a slight difference in PC1 between the morning and afternoon for both groups, but this was not significant. The results of this research can be implemented in health facilities. Since there is no significant difference of the LP shape during the day, patients don't have to be scheduled at a certain time of the day, which makes it easier for the physician.

Previous research [8, 21] has suggested that the LP angle of POP women is larger than the LP angle of healthy volunteers. This indicates that the orientation of those LP shapes would be more dorsally. This corresponds with the result of Figure 5. The research of Pearce et al. [22] found that there was no difference in POP-Q examination between morning and afternoon exams for women with POP. According to previous research [1, 23] POP-Q and MR examination are two techniques that are not in agreement with one another. Besides that, the POP-Q examination was done at strain in supine position, while the MR measurements were done at rest in upright position. This makes comparing the research of Pearce et al. to this research difficult. Keeping these comparison limitations in mind their results do correspond with our findings.

This study has a few strengths. First, all afternoon scans of the healthy volunteers were compared to the afternoon scans that were used in the research of de Kruif et al. [6]. In that manner there is consistency in the placement of the points for those scans. The placement of the points has been checked by an experienced researcher on all afternoon scans of the POP women. Second, in all 171 scans the placement of the point has been done and checked by the same person, which ensures consistency. Third, the results obtained with the Python and MATLAB programs do correspond with one another. This shows that PCA can be used for different researches regarding the LP shape regardless of which program is used. Besides that, in both programs the means and standard deviations were of the entire group, so these can easily be compared to one another.

Besides that, there are a few limitations in this study. First of all, the small sample size. Although the group of healthy volunteers was sufficiently large, the group of POP women was limited to only 14 women. Therefore, larger studies are needed to verify the results. Second, the interobserver variance could be reduced by having another person landmarking all the scans again. The intrabserver variance could also be reduced, which could be done by having the researcher landmarking all the scans again. A limitation regarding the MATLAB code is that the PCA was not performed with the same groups as the Python version. This is a small step that can be added to the code, which makes comparing the LP shapes of the time groups of both programs easier.

Future research that could be interesting is looking more into the three different groups

among the healthy volunteers. These existed out of nulliparous, parous and pre-menopausal and parous and post-menopausal. There could be differences in LP shape between these groups, because differences in age, parousity and whether or not being pre- or post-menopausal could have an influence on the LP shape of healthy women as well. In this research the women were told to have a normal day on the day they were scanned with only the restriction that they should not lay down. Potentially, the LP shape changes during the day on a high activity day. This could be investigated by having a group of women do a certain amount of activity with for example some lifting and comparing them to a group of women behaving as they would on an everyday basis. There was also data available for the urogenital hiatus, perineal body location, levator hiatus and levator area. Performing calculations on these might provide more insight on the extend of POP during the day. At last, placing the point manually is a time consuming task which has some inter- and intraobserver variations. Placement of some of the landmarks could be automated with the help of machine learning for example.

In conclusion, the difference in LP shape between POP women and healthy volunteers is significant. The LP shape of POP women is oriented more dorsally as compared to the healthy volunteers. However, there is no significant difference of the LP shape for both POP women and healthy volunteers during the day. The LP shape of POP women does not have a steeper slope at the end of the day than at the beginning of the day.

References

- [1] Anique T.M. Grob, Judith olde Heuvel, Jurgen J. Futterer, Diana Massop, Angelique L. Veenstra van Nieuwenhoven, Frank F.J. Simonis, and Carl H. van der Vaart. Underestimation of pelvic organ prolapse in the supine straining position, based on magnetic resonance imaging findings. *International Urogynecology Journal*, 30(11):1939–1944, 2019.
- [2] C. Persu, C. R. Chapple, V. Cauni, S. Gutue, and P. Geavlete. Pelvic Organ Prolapse Quantification System (POP-Q) - a new era in pelvic prolapse staging. *Journal of medicine and life*, 4(1):75–81, 1 2011.
- [3] Cardozo L Wagg A & Wein AJ (eds) Abrams, P. Committee 4 'Pathophysiology of urinary incontinence, faecal incontinence and pelvic organ prolapse'. In *Incontinence, 6th International Consultation on Incontinence*, page 394 – 409. International Continence Society, Bristol, Tokyo, september edition, 2017.
- [4] Vanessa Nicolau-Toulouse, Pari Tiwari, Terry Lee, Geoffrey William Cundiff, and Roxana Geoffrion. Does bilateral sacrospinous fixation with synthetic mesh recreate nulliparous pelvic anatomy? An MRI evaluation. *Female Pelvic Medicine and Reconstructive Surgery*, 20(4):222–227, 2014.
- [5] Sender Herschorn. Female pelvic floor anatomy: the pelvic floor, supporting structures, and pelvic organs. *Reviews in urology*, 6 Suppl 5(Suppl 5):S2–S10, 2004.
- [6] Liselot J De Kruif, Lisan M Morsinkhof, John O L Delancey, L Chen, A Van Der Steen, and F J Frank. Differences in Levator Plate shape in supine and upright position – A magnetic resonance imaging study. 2022.
- [7] Lynn Stothers, Jennifer A. Locke, Marwa Abdulaziz, Darren Lazare, Alex Kavanagh, and Andrew Macnab. Standing open magnetic resonance imaging improves detection and staging of pelvic organ prolapse. *Canadian Urological Association Journal*, 16(1), 8 2021.
- [8] Yvonne Hsu, Aimee Summers, Hero K. Hussain, Kenneth E. Guire, and John O.L. Delancey. Levator plate angle in women with pelvic organ prolapse compared to women with normal support using dynamic MR imaging. *American Journal of Obstetrics and Gynecology*, 194(5):1427–1433, 5 2006.
- [9] Payton Schmidt, Luyun Chen, John O. DeLancey, and Carolyn W. Swenson. Pre-operative level II/III MRI measures predicting long-term prolapse recurrence after native tissue repair. *International Urogynecology Journal*, 33(1):133–141, 1 2022.
- [10] Jaadi Zakaria. A Step-by-step explanation of Principal Component Analysis (PCA), 2021.
- [11] John O.L. De Lancey. What’s new in the functional anatomy of pelvic organ prolapse? *Current Opinion in Obstetrics and Gynecology*, 28(5):420–429, 2016.
- [12] E. J. Gill and W. G. Hurt. PATHOPHYSIOLOGY OF PELVIC ORGAN PROLAPSE. *Obstetrics and Gynecology Clinics of North America*, 25(4):757–769, 12 1998.

- [13] MEDICAL IMAGES: Levator ani muscles.
- [14] Lindsay Smith. A tutorial on Principal Components Analysis. *Communications in Statistics - Theory and Methods*, 17(9):3157–3175, 1988.
- [15] Ian T. Jolliffe and Jorge Cadima. Principal component analysis: A review and recent developments. *Philosophical Transactions of the Royal Society A: Mathematical, Physical and Engineering Sciences*, 374(2065), 4 2016.
- [16] Anna Gebhard, Tobias Geimer, Mathias Unberath, Frank Schebesch, Mena Abdelmalek, and Andreas Maier. A Practical Guide to Statistical Shape Models Featuring Hands-on Examples in CONRAD.
- [17] Two-way ANOVA in SPSS Statistics - Step-by-step procedure including testing of assumptions — Laerd Statistics.
- [18] Lisan M Morsinkhof, Martine K Schulten, John O L Delancey, Frank F J Simonis, and Anique T M Grob. Pelvic Inclination Correction System (PICS) for magnetic resonance imaging analysis of pelvic organ prolapse in upright position. pages 1–16.
- [19] C. Betschart, L. Chen, J. A. Ashton-Miller, and J. O.L. DeLancey. On pelvic reference lines and the MR evaluation of genital prolapse: A proposal for standardization using the Pelvic inclination correction system. *International Urogynecology Journal*, 24(9):1421–1428, 5 2013.
- [20] Principal component analysis of raw data - MATLAB pca - MathWorks Benelux.
- [21] Julia R. Fielding. Practical MR imaging of female pelvic floor weakness. *Radiographics : a review publication of the Radiological Society of North America, Inc*, 22(2):295–304, 2002.
- [22] Melissa Pearce, Steven Swift, and William Goodnight. Pelvic organ prolapse: is there a difference in POPQ exam results based on time of day, morning or afternoon? *American Journal of Obstetrics and Gynecology*, 199(2):1–200, 8 2008.
- [23] Suzan R Broekhuis, Kirsten B Kluivers, Jan C M Hendriks, Jurgen J Fütterer, Jelle O Barentsz, and Mark E Vierhout. POP-Q, dynamic MR imaging, and perineal ultrasonography: do they agree in the quantification of female pelvic organ prolapse? 2009.

7 Appendices

7.1 Appendix A: Results Two-Way ANOVA

Tests of Between-Subjects Effects

Source	Dependent Variable	Type III Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared
Corrected Model	principalcomponent1	33117.929 ^a	5	6623.586	23.951	.000	.421
	principalcomponent2	3633.115 ^b	5	726.623	3.155	.010	.087
Intercept	principalcomponent1	8430.387	1	8430.387	30.485	.000	.156
	principalcomponent2	905.120	1	905.120	3.931	.049	.023
grp	principalcomponent1	32568.761	1	32568.761	117.771	.000	.416
	principalcomponent2	3496.713	1	3496.713	15.185	.000	.084
time_cat	principalcomponent1	450.761	2	225.381	.815	.444	.010
	principalcomponent2	13.059	2	6.530	.028	.972	.000
grp * time_cat	principalcomponent1	5.542	2	2.771	.010	.990	.000
	principalcomponent2	80.345	2	40.173	.174	.840	.002
Error	principalcomponent1	45629.552	165	276.543			
	principalcomponent2	37995.170	165	230.274			
Total	principalcomponent1	78747.481	171				
	principalcomponent2	41628.285	171				
Corrected Total	principalcomponent1	78747.481	170				
	principalcomponent2	41628.285	170				

a. R Squared = .421 (Adjusted R Squared = .403)

b. R Squared = .087 (Adjusted R Squared = .060)

Figure 9: This figure shows the results obtained with the Two-Way Anova. The 'Sig.' column shows the p-values, which are relevant for this study.

Pairwise Comparisons

Dependent Variable	(I) 1=morning 2=midday 3=afternoon	(J) 1=morning 2=midday 3=afternoon	Mean Difference (I-J)	Std. Error	Sig. ^a	95% Confidence interval for Difference ^a	
						Lower Bound	Upper Bound
principalcomponent1	1.00	2.00	-2.926	3.618	.420	-10.070	4.218
		3.00	-4.559	3.618	.209	-11.703	2.585
	2.00	1.00	2.926	3.618	.420	-4.218	10.070
		3.00	-1.633	3.618	.652	-8.777	5.511
	3.00	1.00	4.559	3.618	.209	-2.585	11.703
		2.00	1.633	3.618	.652	-5.511	8.777
principalcomponent2	1.00	2.00	.733	3.302	.825	-5.786	7.252
		3.00	.120	3.302	.971	-6.400	6.639
	2.00	1.00	-.733	3.302	.825	-7.252	5.786
		3.00	-.613	3.302	.853	-7.132	5.906
	3.00	1.00	-.120	3.302	.971	-6.639	6.400
		2.00	.613	3.302	.853	-5.906	7.132

Based on estimated marginal means

a. Adjustment for multiple comparisons: Least Significant Difference (equivalent to no adjustments).

Figure 10: This figure shows the results obtained with the Two-Way Anova. The 'Sig.' column shows the p-values, which are relevant for this study.

7.2 Appendix B: MATLAB code

7.2.1 Alignment and Scaling

```
1 clear all , close all , clc ;
2
3 % Load all data
4 % Choose all .csv files in the path + total number of files
5 path_data = 'C:\Users\dobbe\Desktop\M12 BSc Prolaps\test\';
6 AllFiles = dir([path_data '*results.csv']);
7 num_files = size(AllFiles,1);
8
9 for scan = 1:num_files
10     file = AllFiles(scan).name;
11     new_name = [file(1:end-12), '_transformed'];      % Assign new
        name to the file
12
13     csvfile = readtable(file , 'PreserveVariableNames' , true);
        % Load data of spicific scan
14     csvfile = renamevars(csvfile , 'SCIPP length' , 'SCIPP_Length')
        ;
15
16     % Alignment and scaling
17     % Extract data from table
18     Landmarks = csvfile{1:12, ["X" , "Y"]};
19     hold on
20
21     % Translate points to (0,0)
22     Translated_LP = Landmarks - Landmarks(10,:);
23
24     % Define SCIPPlength Reference and SCIPPlength
25     SCIPP = csvfile{1,"SCIPP_Length"};
26     SCIPP_ref = 100;      % mm
27
28     % Scaling of the data
29     Scaling_Factor = SCIPP_ref/SCIPP;
30     Scaled_LP = Translated_LP*Scaling_Factor;
31
32     % Check the SCIPP length
33     Check_SCIPP = sqrt((Scaled_LP(1,1)-Scaled_LP(10,1))^2 + (
        Scaled_LP(1,2)-Scaled_LP(10,2))^2);
34
35     % Rotation
36     Angle_SCIPP_Xaxis = -acos((Scaled_LP(10,1)-Scaled_LP(1,1))/
        Check_SCIPP);
37
38     Rotation_Matrix_1 = [cos(Angle_SCIPP_Xaxis) -sin(
        Angle_SCIPP_Xaxis); sin(Angle_SCIPP_Xaxis) cos(
        Angle_SCIPP_Xaxis)];
```

```

39
40 % Rotation of 34 degrees of SCIPP with respect to the x-axis
41 Angle = deg2rad(34);
42 Rotation_Matrix_2 = [cos(Angle) -sin(Angle); sin(Angle) cos(
    Angle)];
43
44 Rotated_LP = Scaled_LP*Rotation_Matrix_1*Rotation_Matrix_2;
45
46 % Plot LP shape en SCIPP line
47 plot(Rotated_LP_2(3:10,1),-Rotated_LP_2(3:10,2));
48 plot(Rotated_LP_2([1 10],1),-Rotated_LP_2([1 10],2));
49
50 % Save the transformed data in new .csvv files
51 writematrix(Rotated_LP_2, [new_name, '.csvv']);
52
53 end

```

7.2.2 Reshape

```
1 clear all , close all , clc ;
2
3 % Load transformed data , reshape , save in new matrix
4 % Choose all .csv files in the path + total number of files
5 path_data = 'C:\Users\dobbe\Desktop\M12 BSc Prolaps\test\';
6 AllFiles = dir([path_data '*transformed.csv']);
7 num_files = size(AllFiles,1);
8
9 % Define 'empty' matrix to add all scans together
10 Empty_Matrix = cell(num_files,1);
11 Empty_Matrix2 = cell(num_files,1);
12
13 for scan = 1:num_files
14     file = AllFiles(scan).name;
15
16     csvfile = readtable(file , 'PreserveVariableNames' , true);
17     csvfile = renamevars(csvfile , ["Var1" ,"Var2"] , ["X" ,"Y"]);
18
19     % Reshape
20     Landmarks = csvfile{:,:};
21     Reshape = reshape(Landmarks , [], 1) ;
22     Reshape_Transpose = Reshape.';
23
24     % Add all data to the 'empty' matrix
25     Empty_Matrix{scan} = Reshape_Transpose;
26 end
27
28 MatrixforPCA = vertcat(Empty_Matrix{:}); % Rows are the scans;
      columns are the x,y values
29 writematrix(MatrixforPCA , 'MatrixforPCA.csv')
```

7.2.3 PCA

```
1 clear all , close all , clc ;
2
3 % Apply PCA
4 % Load data
5 MatrixforPCAcsv = readtable("MatrixforPCA.csv");
6 MatrixforPCAcsv = renamevars(MatrixforPCAcsv, ["Var1", "Var2", "
    Var3", "Var4", "Var5", "Var6", "Var7", "Var8", "Var9", "Var10", "
    Var11", "Var12", "Var13", "Var14", "Var15", "Var16", "Var17", "
    Var18", "Var19", "Var20", "Var21", "Var22", "Var23", "Var24"],
    ["X1"; "X2"; "X3"; "X4"; "X5"; "X6"; "X7"; "X8"; "X9"; "X10"; "X11";
    "X12"; "Y1"; "Y2"; "Y3"; "Y4"; "Y5"; "Y6"; "Y7"; "Y8"; "Y9"; "Y10"; "Y11"
    "; "Y12"]);
7
8 % Extract LP from table
9 MatrixforPCA = MatrixforPCAcsv{:,:};
10
11 PCA_input = MatrixforPCA(:, [3:10 15:22]);
12
13 % Check data
14 figure (1)
15 hold on
16 for i = 1:size(PCA_input,1)
17     plot(PCA_input(i,1:8), -PCA_input(i,9:16))
18     plot(MatrixforPCA(i,[1 10]), -MatrixforPCA(i,[13 22]), '—')
19 end
20 title('LP shape of all scans')
21 axis([-90 1 -70 0])
22 hold off
23
24 % PCA
25 % Performing the PCA
26 [coeff, score, latent, tsquared, explained, mu] = pca(PCA_input);
27
28 % PC1
29 ordata_1 = score(:,1)*coeff(:,1)';
30 ordata_1 = ordata_1+mu;
31
32 standard_deviation_1 = std(score(:,1));
33 std_ortdata_1 = standard_deviation_1*coeff(:,1)'+mu;
34 std1_ortdata_1 = -standard_deviation_1*coeff(:,1)'+mu;
35 mean_ortdata_1 = coeff(:,1)'+mu;
36
37 % Plot PC1 for all scans
38 figure(2)
39 hold on
40 for i = 1:size(PCA_input,1)
```



```

41     plot(ordata_1(i,1:8),-ordata_1(i,9:16),':')
42     plot(MatrixforPCA(i,[1 10]),-MatrixforPCA(i,[13 22]),'—')
43     plot(std_ordata_1(1:8),-std_ordata_1(9:16),'LineWidth',1,'
        color',[0.4 0.4 0.4])
44     plot(std1_ordata_1(1:8),-std1_ordata_1(9:16),'LineWidth',1,'
        color',[0.4 0.4 0.4])
45     plot(mean_ordata_1(1:8),-mean_ordata_1(9:16),'LineWidth',1,'
        color',[0.4 0.4 0.4])
46 end
47 title('PC1 for all scans')
48 axis([-90 1 -70 0])
49 hold off
50
51 % PC2
52 ordata_2 = score(:,2)*coeff(:,2)';
53 ordata_2 = ordata_2 + mu;
54
55 standard_deviation_2 = std(score(:,2));
56 std_ordata_2 = standard_deviation_2*coeff(:,2)'+mu;
57 std1_ordata_2 = -standard_deviation_2*coeff(:,2)'+mu;
58 mean_ordata_2 = coeff(:,2)'+mu;
59
60 % Plot PC2 for all scans
61 figure(3)
62 hold on
63 for i = 1:size(PCA_input,1)
64     plot(ordata_2(i,1:8),-ordata_2(i,9:16),':')
65     plot(MatrixforPCA(i,[1 10]),-MatrixforPCA(i,[13 22]),'—')
66     plot(std_ordata_2(1:8),-std_ordata_2(9:16),'LineWidth',1,'
        color',[0.4 0.4 0.4])
67     plot(std1_ordata_2(1:8),-std1_ordata_2(9:16),'LineWidth',1,'
        color',[0.4 0.4 0.4])
68     plot(mean_ordata_2(1:8),-mean_ordata_2(9:16),'LineWidth',1,'
        color',[0.4 0.4 0.4])
69 end
70 title('PC2 for all scans')
71 axis([-90 1 -70 0])
72 hold off

```